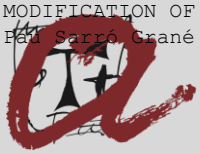
THE DISCOVERY AND DEVELOPMENT OF A RH-CATALYZED CARBYNE TRANSFER PLATFORM FOR THE SKELETAL MODIFICATION OF C(SP2)–C(SP2) BONDS

Pau Sarró Grané



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The Discovery and development of a Rh-catalyzed carbyne transfer platform for the skeletal modification of C(sp^2)–C(sp^2) bonds

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PAU SARRÓ GRANÉ

DOCTORAL THESIS
2022

UNIVERSITAT ROVIRA I VIRGILI
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Doctoral Thesis

Supervised by Prof. Marcos García Suero

URV – Universitat Rovira i Virgili

ICIQ – Institut Català d'Investigació Química

Tarragona

2022

UNIVERSITAT ROVIRA I VIRGILI

ICIQ Institut Català d'Investigació Química

Prof. Dr. Marcos García Suero, Group Leader of the Institut Català d'Investigació Química (ICIQ)

I STATE, that the present Doctoral Thesis entitled: "*The discovery and development of a Rh-catalyzed carbyne transfer platform for the skeletal modification of C(sp2)–C(sp2) bonds*", presented by Pau Sarró Grané to receive the degree of Doctor, has been carried out under my supervision at the Institut Català d'Investigació Química.

Tarragona, March the 3rd, 2022.

PhD Thesis Supervisor

Prof. Marcos García Suero

"S'és intel·ligent en la mesura en què es dubta de tot,
i l'únic real i incontestable són els gustos de cadascú."

Marcel Proust – Pel cantó de Swann
(Trad. Velèria Gaillard)

List of publications

- Zhaofeng Wang‡, Liyin Jiang‡, Pau Sarró‡ and Marcos G. Suero*.
  ‡Authors contributed equally.
  "Catalytic Cleavage of C(sp^2)–C(sp^2) Bonds with Rh-Carbynoids"
  J. Am. Chem. Soc. **2019**, *141*, 15509.
- Liyin Jiang, Pau Sarró, Jordi Llop and Marcos G. Suero*.
  "Catalytic alkene skeletal modification for the construction of fluorinated tertiary stereocenters"
  Chem. Sci.
  Under revision.

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Prologue

For more than half a century, the discovery of new metal–carbon bond-forming strategies has been cornerstone in the development of transition-metal catalysis. The catalytic generation of organometallic species with metal–carbon single/double bonds, such as metal–L (L = alkyl, alkenyl, alkynyl, aryl) or metal–carbene (metal=L) is widely used in reaction discovery and development. However, while metal-carbynes, the organometallic species with a metal–carbon triple bond (metal≡L), have been key catalysts in alkyne metathesis, their catalytic generation and general application in catalytic carbyne transfer has been largely unexplored, mainly due to the lack of suitable monovalent carbon sources (Figure 1). Surprisingly, methodologies circumventing this problem by generating metal-carbynoids as equivalent reactive species of metal-carbynes, have not been reported.

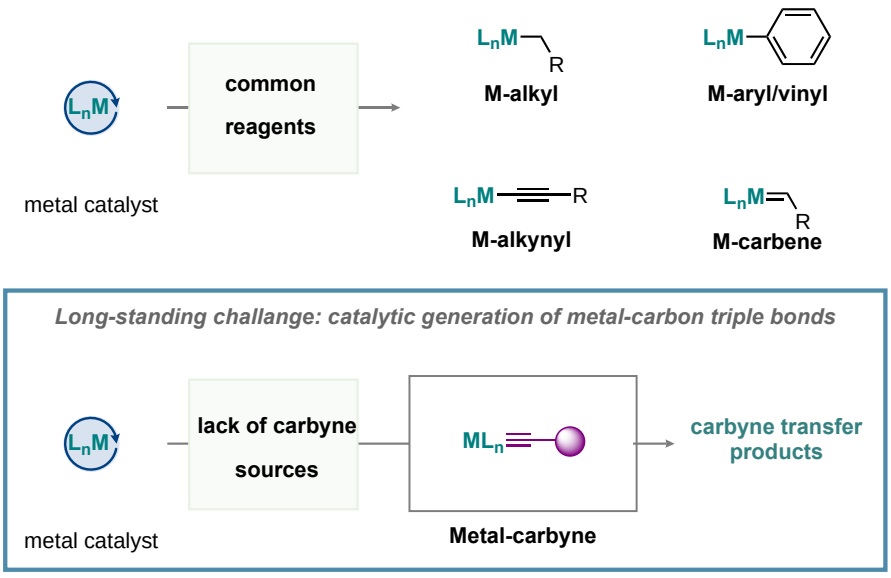


Figure 1 The catalytic generation of metal-carbynes remains unexplored due to the lack of carbyne sources

In this Doctoral Thesis, the reader will find the discovery and development of a new transition-metal-catalyzed carbyne transfer platform for the discovery of new carbon reactivity rules, which was applied in the skeletal editing of unsaturated molecules. We believe that this novel carbyne transfer platform underscores an opportunity as a tool in skeletal editing that will be relevant to reach previously unattainable chemical space in drug discovery and to streamline the synthesis of complex natural products.

General objectives and summary

The main objective of this thesis was the discovery of novel carbon reactive species that could unveil previously unknown transformations. The purpose was to facilitate the synthesis of complex and highly functionalized organic molecules from commercially or readily available substrates such as simple alkenes or massively produced 1,3-butadienes. We thought that such new carbon species could also serve as a platform for the transfer of monovalent carbon units. This would give an alternative for the catalytic carbyne transfer, which has been largely unexplored mainly due to the lack of suitable monovalent carbon sources (Figure 1A).

Recently, our group discovered different stable carbyne sources. Such reagents contain two masking groups that can be separately activated to form a monovalent carbon unit: a hypervalent iodine moiety and a diazo group. Our group found that the hypervalent moiety could be activated by photoredox catalysis, forming a diazomethyl radical able to undergo C–H functionalization of a broad range of arenes.

Considering these previous results, we wondered whether it was possible to selectively activate the diazo moiety of such reagents with metal catalysis without compromising the hypervalent C–$I^{(III)}$ bond. Hence, we would be able to generate metal-carbene species containing a hypervalent iodine moiety. Bearing in mind the outstanding leaving group ability of hypervalent iodine moiety, the $I^{(III)}$-substituted metal-carbene can be regarded as a cationic carbene: a metal carbynoid that serves as a carbyne equivalent (Figure 1B). Such species is previously unknown and its reactivity might open new pathways for the functionalization of different organic molecules.

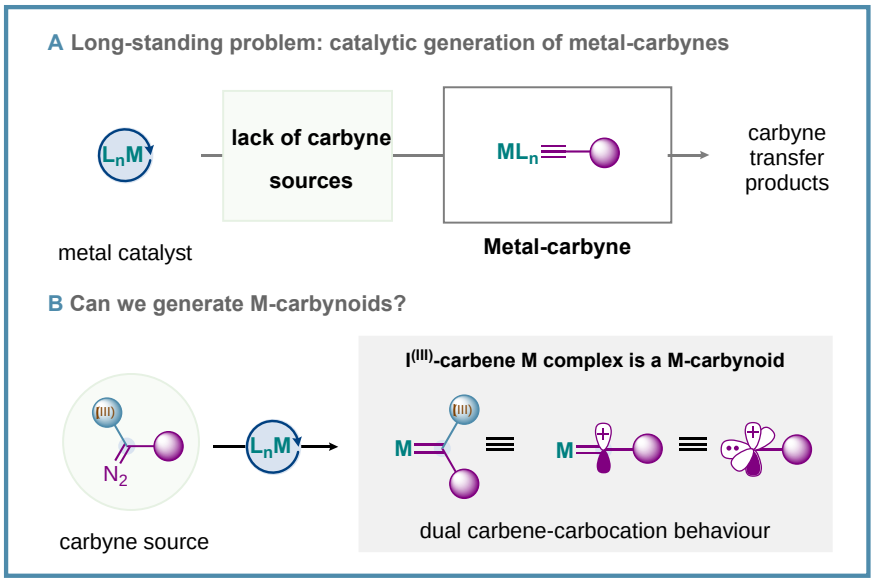


Figure 1

Our hypothesis was that such metal-carbynoids could serve as monovalent carbon units able to cleave C(sp^2)–C(sp^2) bonds from simple alkenes and dienes to form allyl cations. Such intermediates would give rise to allylic building blocks by the use of different nucleophiles (Figure 2). In Chapter II, we show the exploitation of such hypothesis.

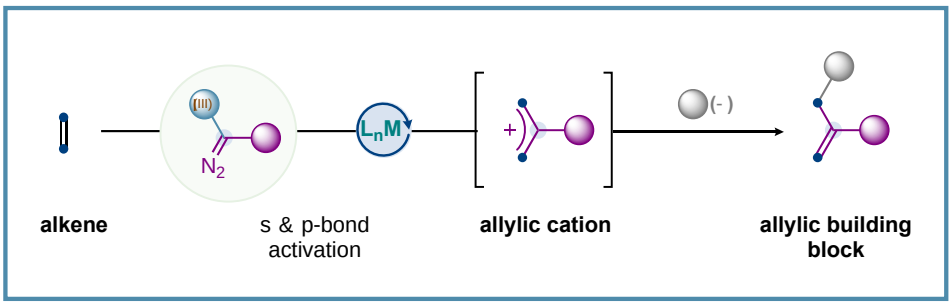


Figure 2

Considering the good results obtained in Chapter II, we next wondered whether we could obtain allylic tertiary fluorides, difficult to reach by other means. In order to prove our hypothesis, we wanted to employ commercially or readily available 1,1-disubstituted alkenes that would form tertiary allyl cations with the positive charge centered on the α-position due to the double substitution on this carbon. This would favor a branched-regioselective fluoride attack, able to form fluorinated allylic tertiary stereocenters.

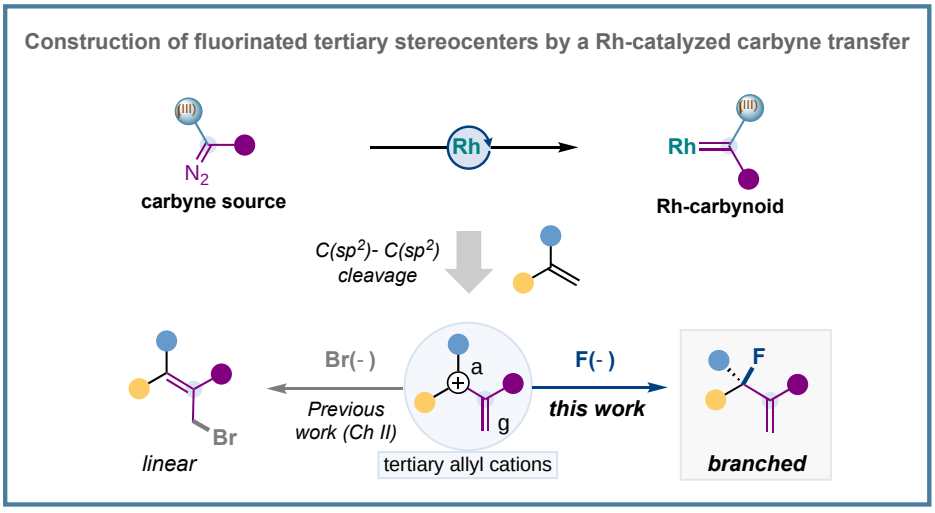


Figure 3

Finally, in Chapter IV we wanted to apply our carbyne transfer platform to the synthesis of 1,3-dienes from commercially or readily available alkenes, which normally require pre-functionalized substrates. We believed that the finding of a suitable base would be key on this project. A base compatible with the intermediates present in the reaction and able to lead to the desired conjugated dienes, avoiding side reactions like polymerization, easy to happen with such highly reactive intermediates. The main point of this strategy was to give an alternative to the underdeveloped desaturation of alkenes for the synthesis of 1,3-dienes from simple olefins.

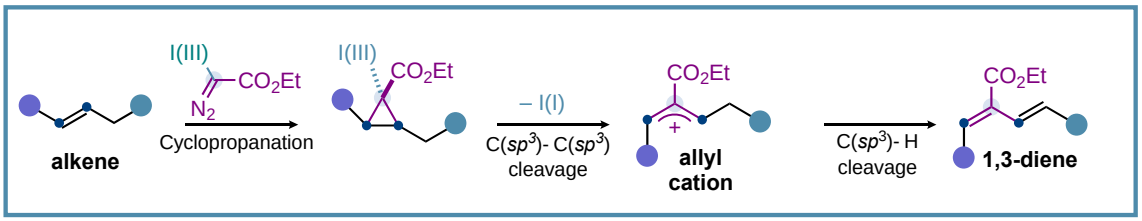


Figure 4

Chapter I

Introduction

1.1. Carbene species

1.1.1. Free carbenes

Carbenes are neutral divalent carbon species with six valence electrons, two of which are non-bonded. Such electrons can be arranged either in a singlet or a triplet spin state. In the first case two electrons are paired in a sp^2-orbital, leaving a *p*-orbital empty; whereas in the triplet carbene one electron is placed in each orbital, the *p*- and the sp^2-orbital (Figure 1). The ground-state spin multiplicity dictates the reactivity of the carbene species. The singlet carbene possesses an ambiphilic character, since it contains a filled and an empty orbital (sp^2- and *p*-orbitals respectively).[1] On the other hand, triplet carbenes bear two singly occupied orbitals, which can be regarded as diradicals.

Figure 1 Schematic representation of singlet and triplet carbene spin-states

The relative orbital energy and in consequence the spin state is influenced by the substituents and their electronic and steric effects. Methylene, for example, has a triplet spin ground-state 9 kcal/mol lower than the singlet state.[2] Substituents can be classified into two groups depending on their mesomeric effect: π-electron-donating groups X (–F, –Cl, –Br, –I, $–NR_2$, $–PR_2$, –OR, –SR,…) and π-electron-withdrawing groups Z (–COR, –CN, $–CF_3$, $–SiR_3$, $–PR_3^+$,…).[3] X substituted carbenes ($:CX_2$) tend to be bent singlet carbenes due to the electron donation from the substituent electron pair to the empty carbene *p*-orbital. Such electron donation gives the C–X bond a multiple bond character, resulting in a four-electron three-center π system with a negative partial charge on the carbon center. On the other hand, Z substituted carbenes (Z–:C–Z) are normally linear singlet carbenes due to the electron donation of the singly-occupied carbene orbitals to

[1] Bourissou, D.; Guerret, O.; Gabbaï, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39.
[2] (a) McKellar, A. R. W.; Bunker, P. R.; Sears, T. J.; Evenson, K. M.; Saykally, R. J.; Langhoff, S. R. *J. Chem. Phys.* **1983**, *79*, 5251; (b) Comeau, D. C.; Shavitt, I.; Jensen, P.; Bunker, P. R. *J. Chem. Phys.* **1989**, *90*, 6491.
[3] (a) Hirai, K.; Itoh, T.; Tomioka, H. *Chem. Rev.* **2009**, *109*, 3275; (b)Gronert, S.; Keeffe, J. R.; More O'Ferrall, R. A. *J. Am. Chem. Soc.* **2011**, *133*, 3381.

the substituents' empty orbitals, perpendicular to the valence plane. This results in a two-electron three-center π system with a positive partial charge on the carbon center. Steric parameters also affect the stability of carbenes (it is well-known that bulky substituents kinetically stabilize all types of carbenes).[4] Steric effects have such a big impact on carbenes that they can also dictate the ground-state spin multiplicity in cases where the electronic effects are negligible. As a general rule, the linear geometry favors the triplet spin state. Hence, the bulkier the substituents are, the broader the carbene bond angle gets, and in consequence the more favored the triplet state will be. As an example, dimethylcarbene has a bent singlet ground state (carbene bond angle of 111º), whereas di(*tert*-butyl)-carbene has a triplet ground state with a wider bond angle of 143º (Figure 2).[1]

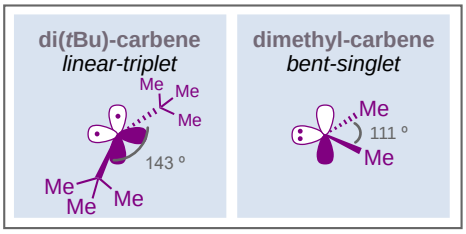


Figure 2 Bond angle difference between di(*t*Bu)- and dimethyl-carbenes

1.1.2. Metal-carbenes

Carbenes can be coordinated to metal species forming organometallic complexes called metal-carbenes ($M{=}CR_2$). It is believed that the first metal carbene was synthesized by the group of Chugaev in 1925,[5] even though at that moment the structure was misreported.[6] It was not until 1964 when Fischer and Maasböl reported and characterized the first metal-carbene complex unambiguously: methoxyphenylmethylene tungsten(0) pentacarbonyl.[7] Since then, many other metal-carbenes have been discovered and have found broad application in synthesis and catalysis.[8]

[4] Kirmse, W. *Angew. Chem. Int. Ed.* **2003**, *42*, 2117.
[5] Chugaev, L.; Skanavy-Grigorieva, M.; Posnjak, A. *Z. Anorg. Allg. Chem.* **1925**, *148*, 37.
[6] Rouschias, G.; Shaw, B. L. *J. Chem. Soc. D* **1970**, 183.
[7] Fischer, E. O.; Maasböl, A. *Angew. Chem. Int. Ed.* **1964**, *3*, 580.
[8] (a) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18; (b) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326; (c) Xia, Y.; Zhang, Y.; Wang, J. *ACS Catal.* **2013**, *3*, 2586; (d) Hu, F.; Xia, Y.; Ma, C.; Zhang, Y.; Wang, J. *Chem. Commun.* **2015**, *51*, 7986.

Metal carbenes can be divided into two main categories: Fischer-type carbenes and Schrock-type carbenes.[9] Fischer carbenes contain highly donating groups, which diminish the back donation from the metal to the carbon center. They normally contain low oxidation state and late transition metals and are electrophilic at the carbon-metal bond, prone to nucleophilic attack at the carbon atom. Fischer carbenes can be regarded as singlet carbenes having a M–C bond which is essentially single: there is a direct donation from the sp^2 orbital of the carbene to the empty metal d_σ-orbital and a weak back donation from the metal d_π-orbital to the empty carbene *p*-orbital (Figure 3).[7,10] On the other hand, Schrock complexes contain poorly stabilized carbenes with substituents like H and alkyl groups which are non-donating groups. In this case, the metals used are early transition metals in high oxidation state and with non-π-acceptor ligands. All this gives the carbene a nucleophilic character, and in fact this type of carbenes can even be considered as metal-ylid compounds. Also, due to the nature of the carbene unit, it can be contemplated as a triplet carbene and the M=C bond is a true double bond, in contrast to the single bond of the Fischer carbenes. This behavior can be explained by the two covalent bonds between the singly occupied orbitals of the metal and the triplet carbene, generating a polarization toward the carbon atom.

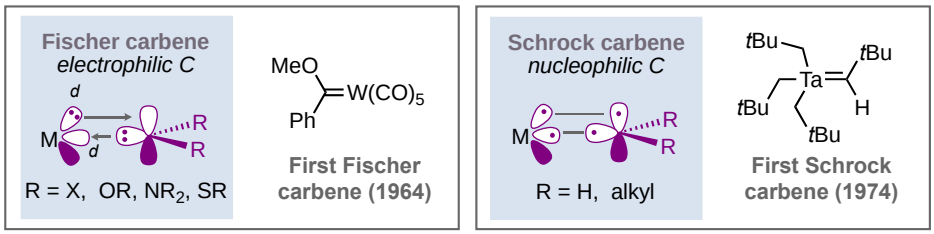
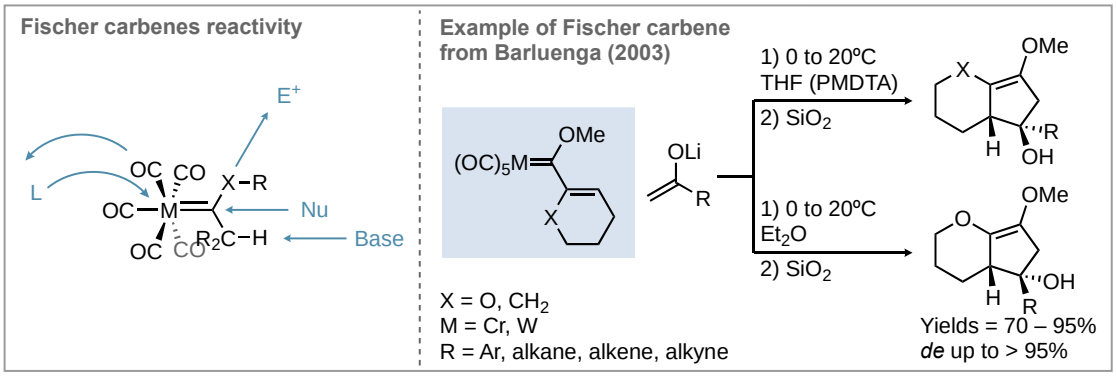


Figure 3 Bonding properties of Fischer and Schrock carbenes

The reactivity of these two classes of carbenes differs greatly. In the case of Fischer carbenes, their high electrophilicity on the carbon-center dictates their reactivity and is summarized in Scheme 1.[11] The carbon center can undergo nucleophilic attack, whereas the carbene substituents can react with electrophiles or proton loss in the presence of a base. In general, the metal center undergoes ligand exchanges, even though both the metal

[9] Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*; John Wiley & Sons, Inc., Hoboken, New Jersey, **2014**.
[10] (a) Schrock, R. R. *J. Am. Chem. Soc.* **1974**, *96*, 6796; (b) Xia, Y.; Qiu, D.; Wang, J. *Chem. Rev.* **2017**, *117*, 13810.
[11] Dötz, K. H.; Stendel, J. Jr. *Chem. Rev.* **2009**, *109*, 3227.

and ligand can participate in ligand- and metal-centered reactivity like cycloadditions.[12] An example from Barluenga is shown in Scheme 1, where wolframium and chromium Fischer carbenes are used for the diastereoselective synthesis of bicyclic cyclopentane derivatives by a [3+2] cyclisation reaction.



Scheme 1 Fischer carbenes reactivity and an application of them

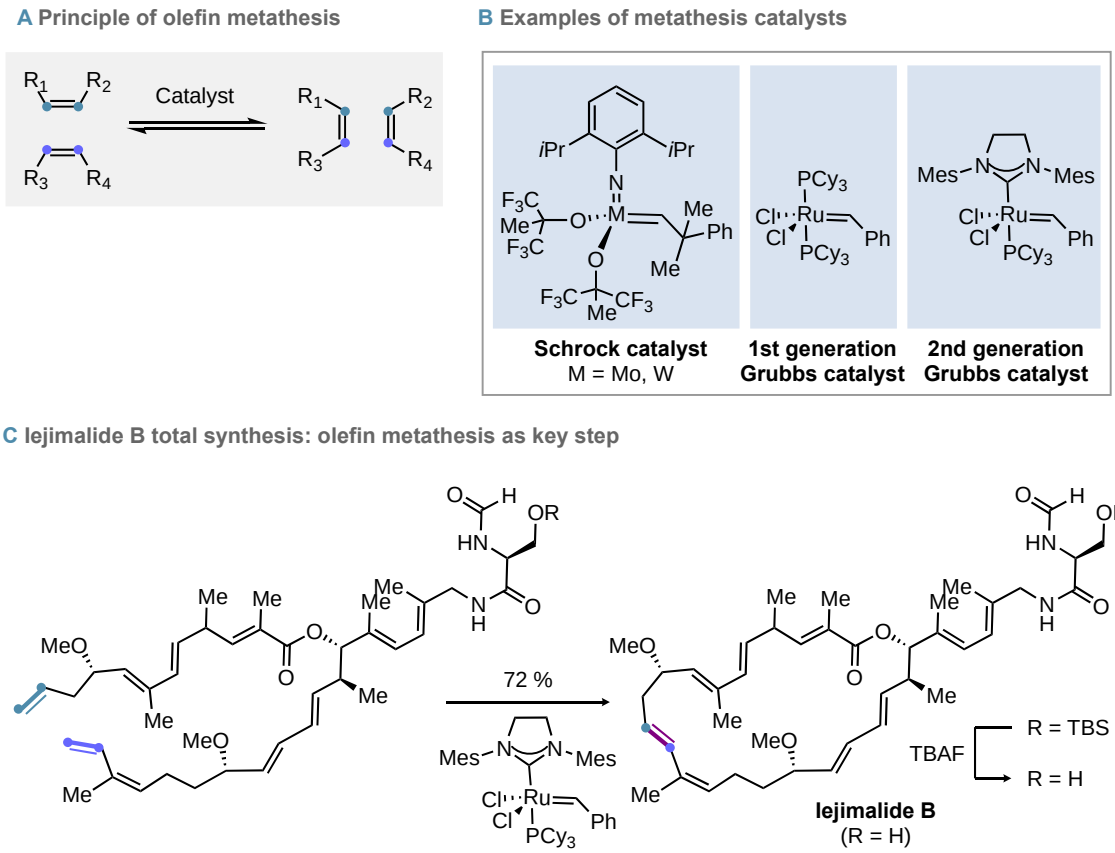
On the other hand, Schrock carbenes show a more nucleophilic character on the carbon center. In terms of reactivity, this type of carbenes show a much broader use in catalysis, especially in the olefin metathesis reaction.

1.1.3. Olefin metathesis

Olefin metathesis reactions consist in the rearrangement of double bonds as showed in Scheme 2A. The discovery of metal alkylidenes in the 1970s as well as the study of the fundamental steps involved in this reaction allowed to develop high-performance, stable and highly tolerant catalysts able to catalyze alkene metathesis.[13] Some of the most used complexes as metathesis catalysts are metal-carbene species like the tungsten or molybdenum alkylidene complexes developed by Schrock[10a] or the first- and second-generation ruthenium carbenes discovered by Grubbs and Hoveyda[14] (Scheme 2B).

[12] Feliciano, A.; Vázquez, J. L.; Benítez-Puebla, L. J.; Velazco-Cabral, I.; Cruz, D. C.; Delgado, F.; Vázquez, M. A. *Chem. Eur. J.* **2021**, *27*, 8233.
[13] (a) Fürstner, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 3012; (b) Deraedt, C.; D'Halluin, M.; Astruc, D. *Eur. J. Inorg. Chem.* **2013**, *28*, 4881.
[14] First generation of ruthenium-based alkene metathesis catalysts: (a) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **1995**, *34*, 2039; (b) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100. Second generation of ruthenium-based alkene metathesis catalysts: (c) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953; (d) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791.

In the last three decades there has been an enormous effort in the development of new metathesis catalysts and their applications in total synthesis [15] and polymer chemistry.[16] An example of the application of alkene metathesis is shown in Scheme 2C. In this case the natural potent tumor growth inhibitor Iejimalide B is synthesized by the group of Fürstner.[17] The key step of the synthesis was the use of ring closing olefin metathesis for the formation of the 24-membered ring. This reaction took place selectively in the terminal alkenes of the molecule, in presence of other double bonds as well as other unprotected functional groups which remained unaltered.



Scheme 2

[15] (a) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4490; (b) Vougioukalakis, G. C.; Grubbs, R. H. *Chem. Rev.* **2010**, *110*, 1746; (b) Ludwig, J. R.; Zimmerman, P. M.; (c) Gianino, J. B.; Schindler, C. S. *Nature* **2016**, *533*, 374.

[16] (a) Truett, W. L.; Johnson, D. R.; Robinson, I. M.; Montague, B. A. *J. Am. Chem. Soc.* **1960**, *82*, 2337; (b) Ivin, K. J.; Mol, J. C. *Olefin Metathesis and Metathesis Polymerization*; Academic Press: San Diego, CA, **1997**.

[17] (a) Fürstner, A.; Nevado, C.; Tremblay, M.; Chevrier, C.; Teplý, F.; Aïssa, C.; Waser, M. *Angew. Chem. Int. Ed.* **2006**, *45*, 5837; (b) Chen, Q.; Schweitzer, D.; Kane, J.; Davisson, V. J.; Helquist, P. *J. Org. Chem.* **2011**, *76*, 5157.

1.1.4. Rhodium-carbenes

The catalytic decomposition of diazo compounds through the formation of metal carbenes has been studied and extensively used in organic chemistry for more than 70 years.[18] Rhodium-carbenes have emerged as stable, highly active complexes since the early 1970s, when it was discovered that dirhodium carboxylates highly efficiently catalyze the decomposition of diazo compounds.[19] They have been developed as catalysts for the transfer of carbenes to a broad range of substrates in C–H[20] and X–H[21] activation, as well as cyclopropanation[22] among other reactions.[23]

Rhodium-carbenes are electrophilic, showing electronic and bonding properties similar to the ones from Fischer carbenes. However, Rh-carbenes tend to be more electrophilic due to the lack of heteroatoms attached to the carbene carbon atom that stabilize it by electron donation from their electron lone pair to the empty carbene *p*-orbital.[24] It has been observed that the metal-carbene electrophilicity dictates the chemo-, regio- and stereoselectivity of the reactions involved. Such electrophilicity does not only arise from the complex ligands but also from the carbene substituents. Carbene precursors, diazo compounds, can be divided into three main categories depending on the electronic features of their substituents, being substituted by (i) one acceptor group, (ii) two acceptor groups and (iii) both an acceptor and a donor group (Figure 4). Acceptor groups will make the rhodium-carbene more electrophilic and in consequence, more reactive; whereas donating groups will decrease such electrophilicity, making the carbene more stable and chemoselective. Hence, the carbene substituents serve as a way to modulate the reactivity.[25]

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[18] (a)Meerwein, H.; Rathsen, H.; Werner, H. *Ber. Dtsch. Chem. Ges.* **1942**, *75*, 1610; (b) Yates, P. *J. Am. Chem. Soc.*, **1952**, *74*, 5376.
[19] Paulisse, R.; Reimling, H.; Hayez, E.; Hubert A. J.; Teyssie, P. *Tetrahedron Lett.*, **1973**, *14*, 2233.
[20] (a) Davies, H. M. L.; Morton, D. *Chem. Soc. Rev.* **2011**, *40*, 1857; (b) Abrams, D. J.; Provencher, P. A.; Sorensen, E. J. *Chem. Soc. Rev.* **2018**, *47*, 8925; (c) Davies, H. M. L.; Liao, K. *Nat. Rev. Chem.* **2019**, *3*, 347.
[21] (a) Miller, D. J.; Moody, C. J. *Tetrahedron* **1995**, *51*, 10811; (b) Gillingham, D.; Fei, N. *Chem. Soc. Rev.* **2013**, *42*, 4918.
[22] (a) Hubert, A. J.; Noels, A. F.; Anciaux, A. J.; Teyssié, P. *Synthesis* **1976**, *9*, 600; (b) Davies, H. M. L.; Antoulinakis, E. G. Intermolecular Metal-Catalyzed Carbenoid Cyclopropanations. In *Organic Reactions*; Overman, L. E., Ed.; John Wiley & Sons, Inc., **2001**.
[23] (a) [3+4] annulations: Davies, H. M. L. *Advances in Cycloaddition*, Vol. 5, p. 119; Harmata, M., Ed.; JAI Press INC., Stamford, Connecticut, 1999; (b) ylide formation: Hodgson, D. M.; Pierard, F. Y. T. M.; Stupple, P. A. *Chem. Soc. Rev.* **2001**, *30*, 50.
[24] Berry, J. F. *Dalt. Trans.* **2012**, *41*, 700.
[25] Davies, H. M. L.; Walji, A. M. *Rhodium(II)-Stabilized Carbenoids Containing Both Donor and Acceptor Substituents*; Evans, P. A., Ed.; Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, **2005**.

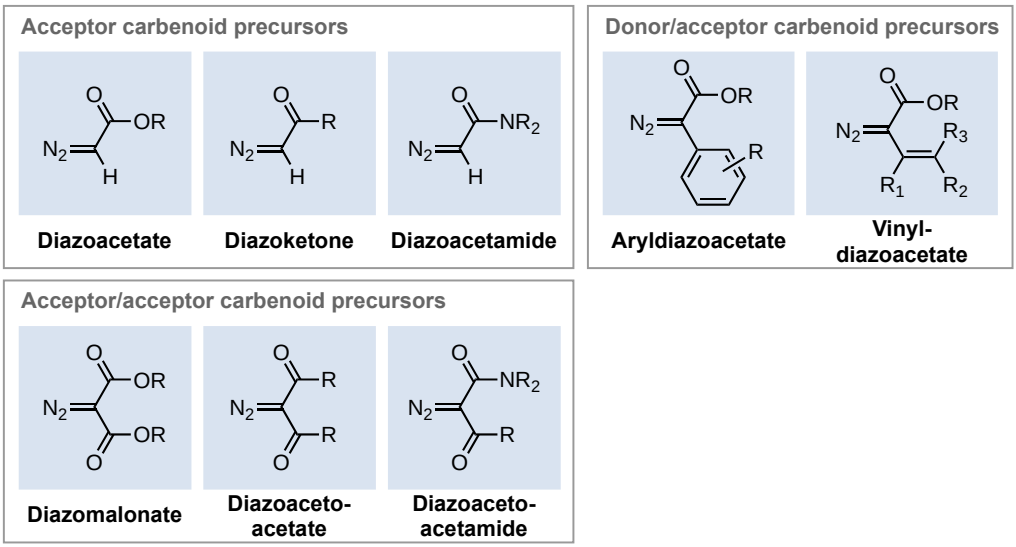
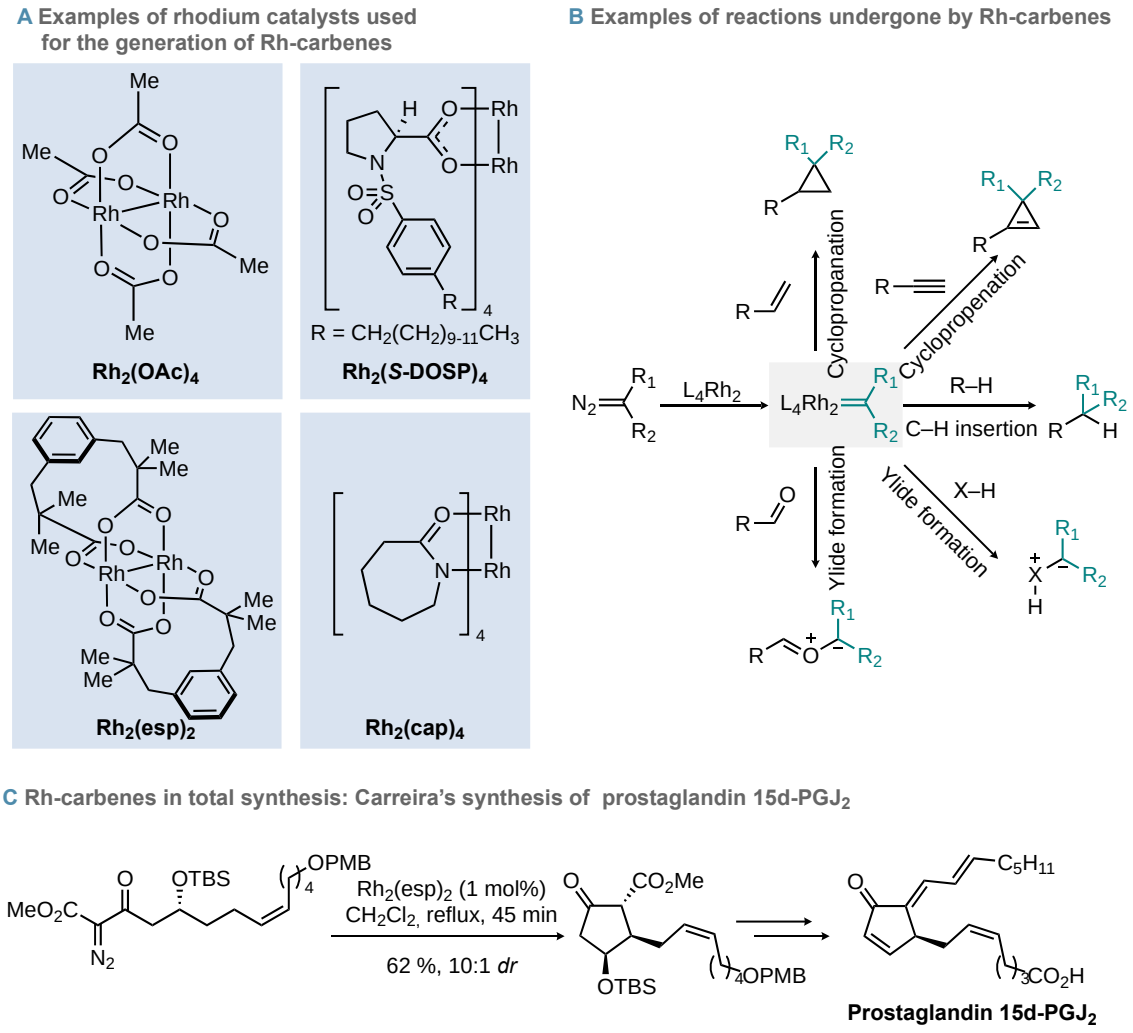


Figure 4 Diazo precursors for the formation of Rh-carbenes

Their use in C–H activation and cyclopropanation is of special importance. It is believed that in dirhodium complexes only one of the two binding sites is active and the other assists in the C–H activation as an electron reservoir, enhancing the electrophilicity of the Rh-carbene and facilitating the Rh–C cleavage to complete the catalytic cycle and recover the catalyst.[26] This assistance does not take place in monometallic complexes. Regarding the ligands of the rhodium complex, carboxylates and amidates are the most common ones, offering a highly symmetric structure which plays a major role specially in asymmetric transformations (Scheme 3A). The symmetry factors on these complexes are easy to control and influence and what is even more important, easy to define and predict the outcome.[27] An example of the application of Rh-carbenes by Carreira is shown in Scheme 3C. [28] In this case the total synthesis of the potent anti-inflammatory 15-deoxy-Δ-12,14-prostaglandin J_2 (15d-PGJ_2) was achieved by using a rhodium(II)-catalyzed cyclization through C–H activation.

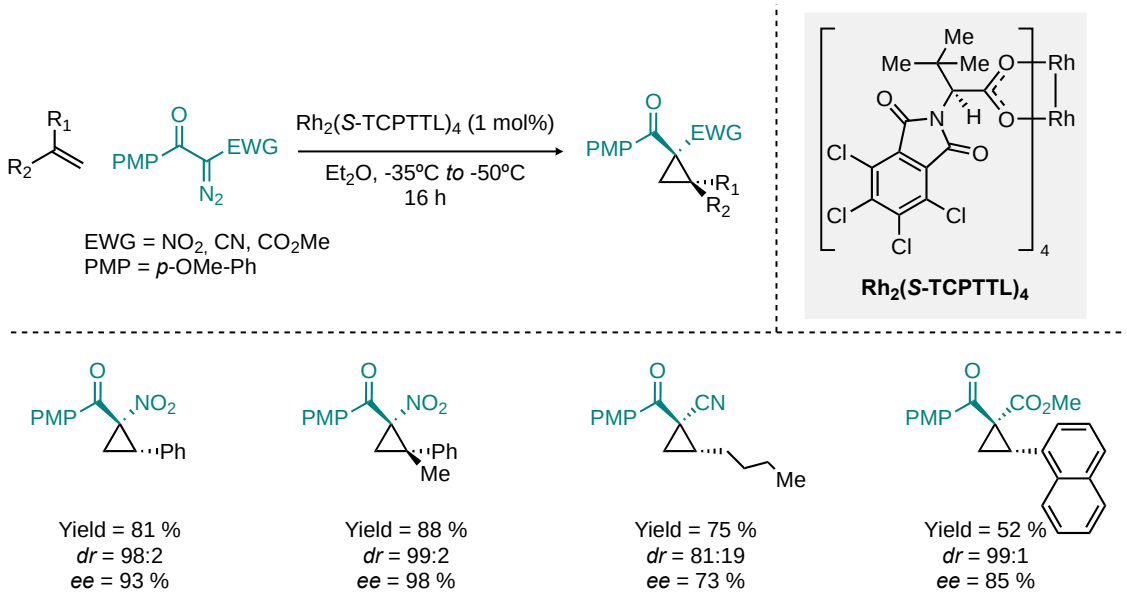
[26] Powers, I. G.; Uyeda, C. *ACS Catal.* **2017**, *7*, 936.
[27] Hansen, J.; Davies, H. M. L. *Coord. Chem. Rev.* **2008**, *252*, 545.
[28] Egger, J.; Fischer, S.; Bretscher, P.; Freigang, S.; Kopf, M.; Carreira, E. M. *Org. Lett.* **2015**, *17*, 4340.



Scheme 3

Another example of the reactivity of Rh-carbenes is shown in Scheme 4.[29] In this case, the group of Charette employed different diazo compounds substituted with two acceptor groups for the cyclopropanation of alkenes catalyzed by rhodium(II). The use of (*para*-methoxy-phenyl)-ketone as an acceptor group was key for the obtention of excellent diastereo- and enantioselectivities (*dr* up to 99:1; *ee* up to 97%).

[29] Lindsay, V. N. G.; Nicolas, C.; Charette, A. B. *J. Am. Chem. Soc.* **2011**, *133*, 8972.

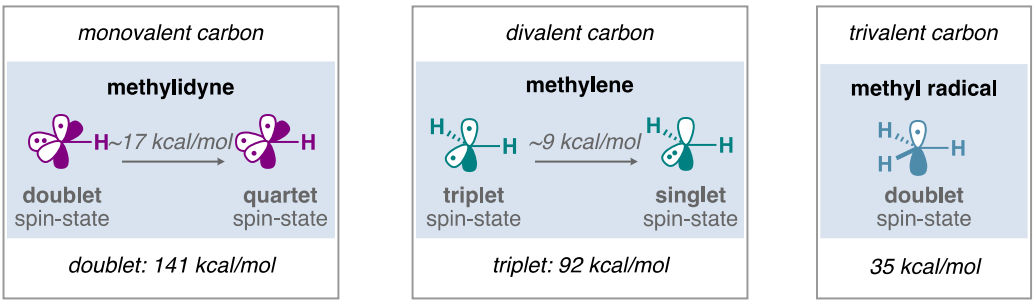


Scheme 4 Example of cyclopropanation using Rh-carbenes by the group of Charette

1.2. Carbyne species

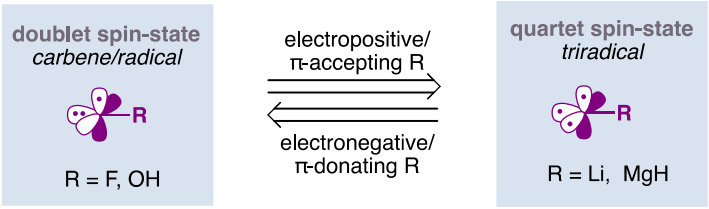
Carbynes are monovalent carbon species with five valence electrons, three of which are non-bonded. Such electrons can be arranged in two different spin-states, a doublet spin-state ($^2\Pi$) and a quartet spin-state ($^4\Sigma^-$). The doublet spin-state ($^2\Pi$) contains four electrons paired in two σ orbitals (one bonding and another non-bonding orbitals) and one electron in a π orbital. On the other hand, the quartet spin-state ($^4\Sigma^-$) has two paired electrons in a bonding orbital, one electron in a σ orbital and two electrons in two degenerated π orbitals. In methylidyne, the simplest carbyne species (:Ċ–H), the ground state is the doublet spin-state ($^2\Pi$), being 17 kcal/mol lower than the quartet spin-state ($^4\Sigma^-$) (Scheme 5).[30] One of the most important features of carbynes is their high reactivity, which can be exemplified by its heat of formation (:Ċ–H, 141 kcal/mol), much higher than the one of divalent methylene (:C–H_2, 92 kcal/mol) or trivalent methyl radical (·CH_3, 35 kcal/mol).[31]

[30] Zeng, T.; Wang, H.; Lu, Y.; Xie, Y.; Wang, H.; Schaefer, H. F.; Ananth, N.; Hoffmann, R. *J. Am. Chem. Soc.* **2014**, *136*, 13388.
[31] Shelvin, P. B. *Reactive Intermediate Chemistry*, Ch. 10, p. 465; Moss, R. A.; Platz, M. S.; Jones Jr M. J., Wiley, New Jersey, **2004**.



Scheme 5 Spin states of methylidyne, methylene and methyl radical

However, the doublet spin-state is not always the lowest in energy. The energy of each spin-state will depend on the substituents in the monovalent carbon and their ability to stabilize the unbonded electrons in the different spin-states (Scheme 6). With electropositive groups like Li, Na or K, the quartet spin-state becomes the ground state. This behavior can be explained qualitatively imaging the limit case in which there is a complete electron transfer, forming the ionic compound [C^-Li^+].[32] In this case, the carbon becomes isoelectronic to N or P atoms, which have a quartet ground state too. On the other hand, substituents that are more electronegative than C, like halogens, induce a doublet spin-state as the ground state. For example, placing a fluorine atom (CF) favors the doublet spin-state over the quartet by 78 kcal/mol. Furthermore, if π-acceptor substituents are placed around the monovalent carbon, they stabilize the two degenerated π orbitals. Hence, their energies would be similar to the non-bonding σ orbital and the quartet spin-state would become more favoured than the doublet.



Scheme 6

Furthermore, experimental and theoretical results indicate that the doublet and quartet spin-state carbynes differ in reactivity. It has been discovered that the doublet ground state carbynes react similar to carbenes, being very reactive toward alkenes and

[32] (a) Mavridis, A.; Harrison, J. F. *J. Am. Chem. Soc.* **1982**, *104*, 3827; (b) Boldyrev, A. I.; Simons, J. *J. Phys. Chem.* **1993**, *97*, 1526.

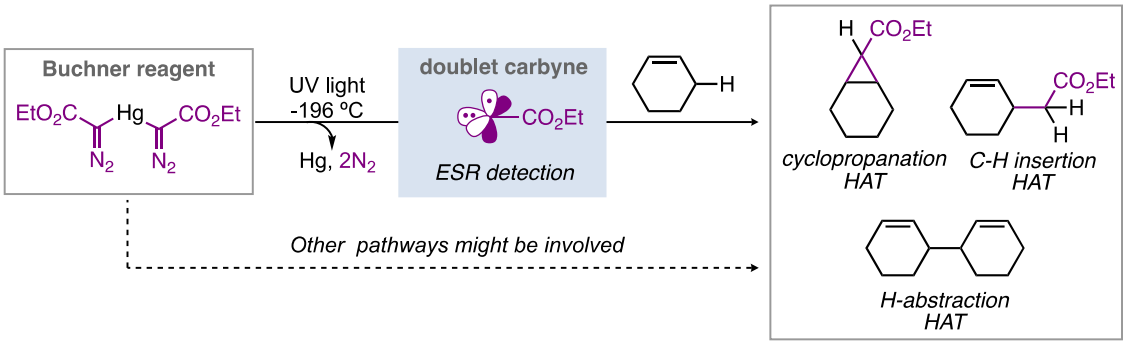
inserting into C–H bonds, but do not participate in H-abstractions.[33] On the other hand, quartet-excited state carbynes prefer to react with radicals or undergo H-abstraction, a behavior similar to the one of radicals. [34]

Free carbynes are found in space and in fact, methylidyne was one of the first molecules detected in interstellar space in 1937, [35] identified by superimposing its absorption spectra with the one of bright stars.[36] Monovalent carbon species can also be generated in the laboratory by high-energy processes. Methylidyne, for example, can be formed by laser photolysis[37] and pulsed radiolysis[38] from methane, as well as from other sources like $CHBr_3$[39] or CH_3NH_2,[40] among other methods.[41]

Some alternatives exist that avoid the use of highly energetic sources for the generation of carbynes. In 1967, Strausz was able to generate monovalent carbon intermediates by photolysis of diethyl mercurybisdiazoacetate (Buchner reagent[42]).[43] Strausz observed that the Buchner reagent, prepared from ethyl diazoacetate and mercuric oxide, could undergo photolysis upon ultraviolet irradiation, generating a doublet carbyne (Scheme 7). This intermediate was detected by electron paramagnetic resonance (ESR) at -196 ºC by observing a single signal which proved the presence of a doublet ground-state radical species with no protons adjacent to it. It was also found that in presence of cyclohexene, multiple reactions took place such as cyclopropanation, C–H insertion and H-abstraction reactions, indicating the dual radical/carbene behavior of the doublet carbyne. Further experimental studies by Strausz to elucidate the mechanism suggested the first cyclopropanation and C–H insertion, either by the Buchner reagent or the *in situ*

[33] (a) Strausz, O. P.; Kennepohl, G. J. A.; Garneau, F. X.; DoMinh, T.; Kim, B.; Valenty, S.; Skell, P. S. *J. Am. Chem. Soc.* **1974**, *96*, 5723; (b) Ruzsicska, B. P.; Jodhan, A.; Choi, H. K. J.; Strausz, O. P.; Bell, T. N. *J. Am. Chem. Soc.* **1983**, *105*, 2489; (c) Loison, J.-C.; Bergeat, A. *Phys. Chem. Chem. Phys.* **2009**, *11*, 655.
[34] Danovich, D.; Bino, A.; Shaik, S. *J. Phys. Chem. Lett.* **2013**, *4*, 58.
[35] Swings, P; Rosenfeld, L. *Astrophys. J.* **1937**, *86*, 483.
[36] Rydbeck, O. E. H.; Elldér, J.; Irvine, W. M. *Nature* **1973**, *246*, 466.
[37] (a) Braun, W.; McNesby, J. R.; Bass, A. M. *J. Chem. Phys.* **1967**, *46*, 2071; (b) Kasdan, A.; Herbst, E. *Chem. Phys. Lett.* **1975**, *31*, 78.
[38] Bosnali, M W.; Perner, D. Z. *Naturforsch.*, **1971**, *26a*, 1768.
[39] (a) Simons, J. P.; Yarwood, A. J. *Trans. Faraday Soc.***1961**, 57, 2167. (b) Dixon, R. N.; Kroto, H. W. *Trans. Faraday Soc.* **1963**, *59*, 1484; (c) Butler, J. E.; Goss, L. P.; Lin, M. C.; Hudgens, J. W. *Chem. Phys. Letters*, **1979**, *63*, 104.
[40] Messing, I.; Sadowski, C. M.; Filseth, S. *Chem. Phys. Lett.* **1979**, *66*, 95.
[41] (a) Merer, A. J.; Travis, D. N. *Can. J. Phys.* **1965**, *43*, 1795; (b) James, F. C.; Choi, J.; Strausz, O. P.; Bell, T. N. *Chem. Phys. Lett.* **1978**, *53*, 206; (c) James, F. C.; Choi, H. K. J.; Strausz, O. P.; Bell, T. N. *Chem. Phys. Lett.* **1979**, *68*, 131; (d) Bayes, K. D. *Chem. Phys. Lett.* **1988**, *152*, 424; (e) Hou, Z.; Bayes, K. D. *J. Phys. Chem.* **1994**, *98*, 6324.
[42] Buchner, E. *Berichte der Dtsch. Chem. Gesellschaft* **1895**, *28*, 215.
[43] (a) DoMinh, T.; Gunning, H. E.; Strausz, O. P. *J. Am. Chem. Soc.* **1967**, *89*, 6785; (b) Strausz, O. P.; DoMinh, T.; Font, J. *J. Am. Chem. Soc.* **1968**, *90*, 1930.

generated free diazoacetate radical, followed by the HAT from another molecule of alkene.[33a] The detection of multiple mercury-substituted cyclopropyl intermediates support the hypothesis of an initial reaction of the diazo group and subsequent radical formation by C–Hg bond cleavage. This path discarded the formation of a carbene upon HAT and additional reaction with cyclohexene, even though different pathways might be involved. Moreover, studies with *trans*- and *cis*-2-butene revealed that a concerted addition takes place, due to the retention of configuration from the starting materials. This fact would also suggest that a $^2\Pi$ ground state is formed by analogy to the singlet carbene.



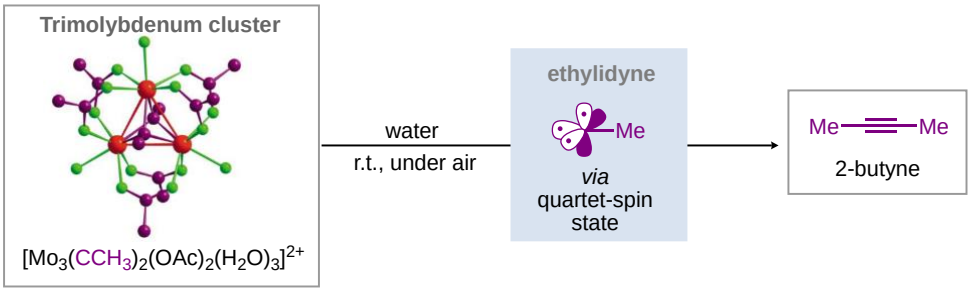
Scheme 7 Strausz generation of doublet carbyne

The group of Patrick also studied the reactivity of carbynes from the photolysis of Buchner reagent. In their case, the photolysis of the organomercuric reagent in the presence of chloroalkanes[44] and heterocycles[45] showed the carbyne insertion into C–Cl, C–H and N–H bonds.

More recently, the group of Bino showed that trimolybdenum clusters with ethyldiyne ligands spontaneously decompose when dissolved in water (Scheme 8).[46] Analysis of the crude reaction mixture showed that 2-butyne was generated, together with other hydrocarbons. In further studies, they proved by isotopically labelling the metal ligands that such transformations occur via the free carbyne species, ruling out the intramolecular mechanism.[47] Even though it was not possible to detect the generated alkyne by EPR due to the presence of paramagnetic molybdenum metal clusters in solution, it was concluded by computational studies and the analyses of the resulting

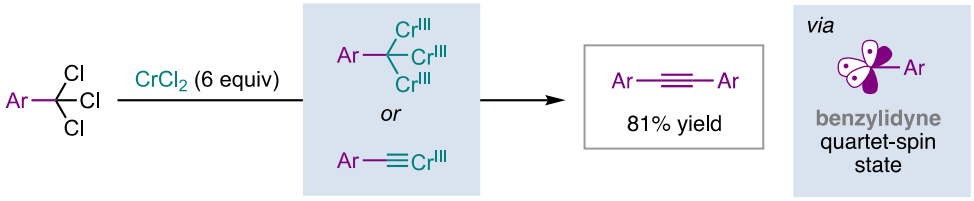
[44] Patrick, T. B.; Kovitch, G. H. *J. Org. Chem.* **1975**, *40*, 1527.
[45] Patrick, T. B.; Wu, T. T. *J. Org. Chem.* **1978**, *43*, 1506.
[46] Bino, A.; Ardon, M.; Shirman, E. *Science* **2005**, *308*, 234.
[47] Bogoslavsky, B.; Levy, O.; Kotlyar, A.; Salem, M.; Gelman, F.; Bino, A. *Angew. Chem. Int. Ed.* **2012**, *51*, 90.

reaction mixture that the carbyne intermediates possessed a quartet spin-state.[48] The metallic system might dissociate in a pseudo-homolytic fashion producing quartet carbynes that dimerize to form alkynes.



Scheme 8 Bino's generation of quartet-spin ethylidyne

The same group of Bino also proved the generation of free carbynes as reaction intermediates in the previously discovered reaction between 1,1,1-trichloroalkyls and low valent Cr^{2+} which leads to the formation of alkynes (Scheme 9).[49,50] Their studies discarded the coupling between organometallic species as the mechanism, showing that it might result from the stepwise reduction of the carbon-halide bonds.



Scheme 9

1.2.1. Carbyne complexes

Metallacarbynes or carbyne complexes (metal complexes containing metal-carbon triple bonds) were first discovered by the groups of E. O. Fischer[51] and R. Schrock,[52] who isolated alkylidyne complexes of chromium and tantalum in 1973 and 1975 respectively.

[48] Danovich, D.; Bino, A.; Shaik, S. *J. Phys. Chem. Lett.* **2013**, *4*, 58.
[49] Bejot, R.; He, A.; Falck, J. R.; Mioskowski, C. *Angew. Chem. Int. Ed.* **2007**, *46*, 1719.
[50] Levy, O.; Bino, A. *Chem. A Eur. J.* **2012**, *18*, 15944.
[51] Fischer, E. O.; Kreis, G.; Kreiter, C. G.; Müller, J.; Huttner, G.; Lorenz, H. *Angew. Chem. Int. Ed.* **1973**, *12*, 564.
[52] Guggenberger, L. J.; Schrock, R. R. *J. Am. Chem. Soc.* **1975**, *97*, 2935.

Metal carbynes can be divided into two main categories (i) Fischer-type carbynes, complexes of group VI to VIII metals in low oxidation states; and (ii) Schrock-type complexes, alkylidyne complexes containing early transition metals and group VI metals in higher oxidation states.[53] Since their discovery, both types have found application in multiple processes and many multi-step protocols have been developed for their synthesis. The M≡C triple bond is based on the interaction of one σ- and two π-orbitals from the carbyne with three different d-orbitals from the metal center (Figure 5).

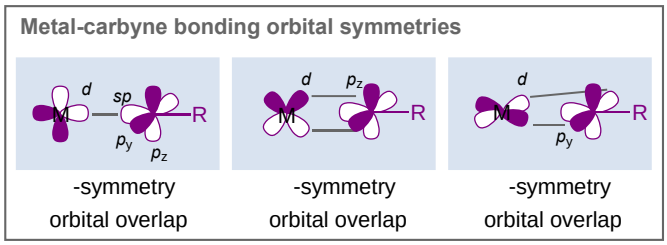


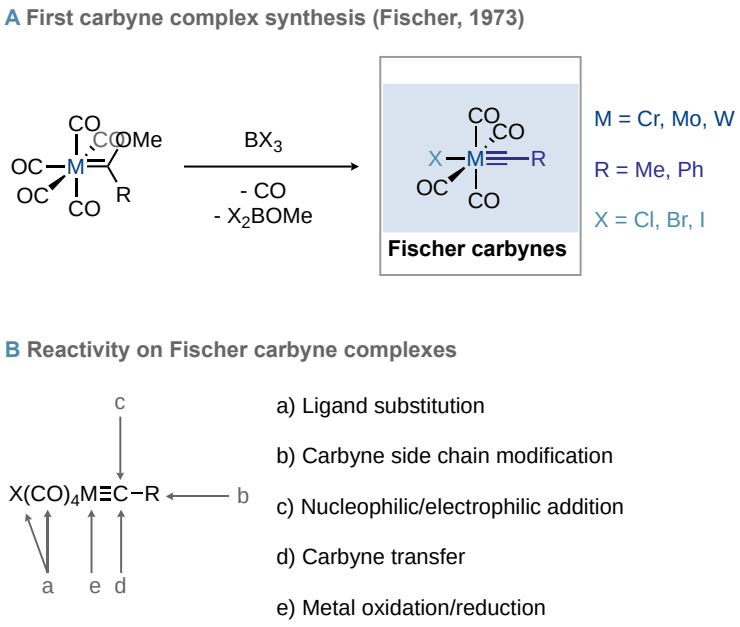
Figure 5

1.2.2. Fischer-type carbyne complexes

The first Fischer-type carbyne complexes were synthesized from the parent alkoxycarbene complex by treatment with boron trihalides as shown in Scheme 10A.[51] This same route is still employed for the synthesis of multiple carbyne complexes, being highly versatile specially for neutral complexes. Other important methods rely on the transformation of transition metal complexes bonded to C(*sp*) atoms like isonitrile, vinylidene or acetylene and transformation of pre-existing carbyne complexes.[53] Fischer alkylidynes contain low valent metals from groups VI to VIII surrounded by π-acceptor ligands such as carbon monoxide. In terms of reactivity, the Fischer-type carbynes show a highly electrophilic character in the carbyne carbon center. Hence, they can undergo ligand substitution, modification of the carbyne side chain, addition of nucleophile/electrophile to the C(*sp*), transfer of the carbyne ligand and oxidation/reduction of the metal center (Scheme 10B). Regarding their catalytic activity, it has been observed that such metal complexes are ineffective in catalyzing the alkyne metathesis and Schrock-type complexes are the only ones that have been employed for

[53] Fischer, H.; Hofmann, P.; Kreissl, F.R.; Schrock, R. R.; Schubert, U.; Weiss, K. Carbyne Complexes, VCH, Weinheim, **1988**.

this purpose for the moment.[54] However, instead of inducing alkyne metathesis, the Fischer carbyne complexes have shown great catalytic activity in alkyne polymerization.[55]



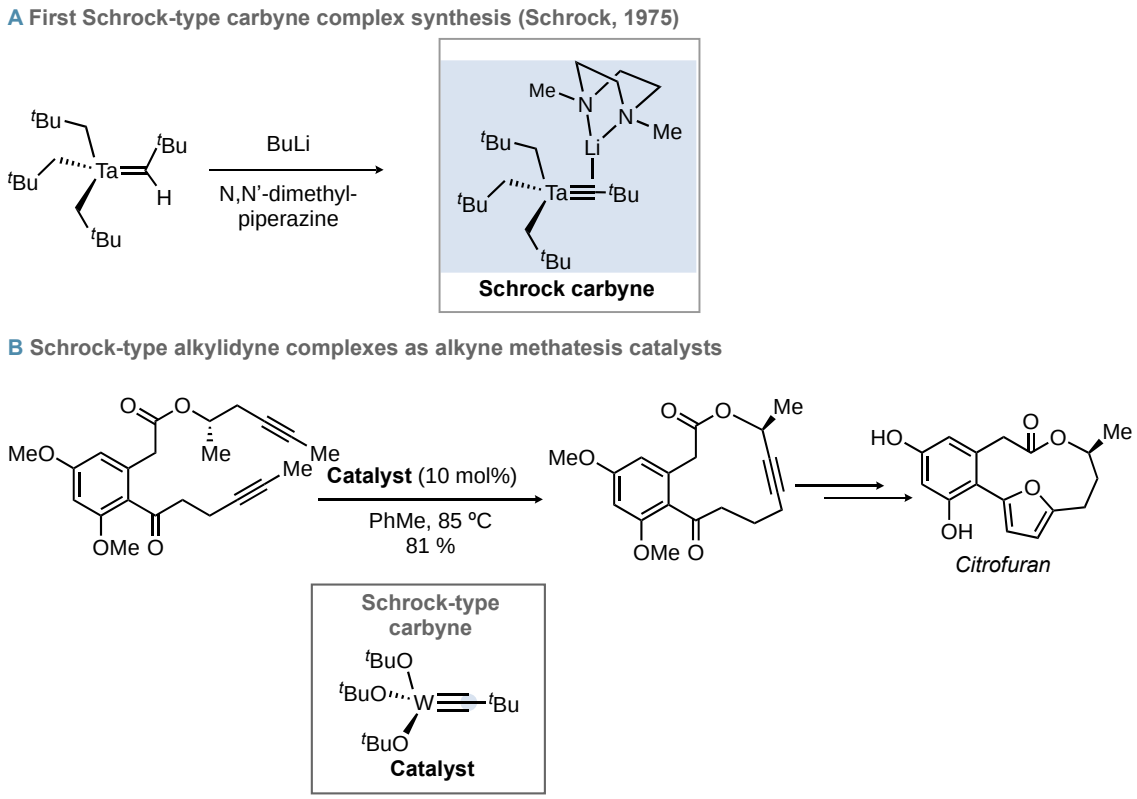
Scheme 10

1.2.3. Schrock-type carbyne complexes

Schrock-type carbyne alkylidyne complexes contain a metal in its highest possible oxidation state, being d^0 metals like Mo, W, Nb, Ta and Re.[56] The high-valent metal centers are stabilized by strong donor ligands like alkoxides and chloride. The first complex of this class was synthesized by the group of Schrock in 1975.[52] It was a tantalum alkylidyne complex which was obtained by deprotonation of the parent tantalum-carbene complex (Scheme 11A). In contrast to the electrophilic character of the monovalent carbon center of the Fischer carbynes, the Schrock carbynes possess a more nucleophilic behavior due to the high electrophilicity of the metal center. Nowadays, Schrock-type alkylidyne complexes are used on a daily basis as catalysts for alkyne metathesis.[54] A beautiful example of such application is shown in Scheme 11B. In this example, the total synthesis of Citrofuran is achieved by employing a ring closing alkyne metathesis as the

[54] Fürstner, A. *Angew. Chem. Int. Ed.* **2013**, *52*, 2794.
[55] Katz, T. J.; Ho, T. H.; Shih, N. Y.; Ying, Y. C.; Van Stuart, I. W. *J. Am. Chem. Soc.* **1984**, *106*, 2659.
[56] Schrock, R. R. *Chem. Rev.* **2002**, *102*, 145.

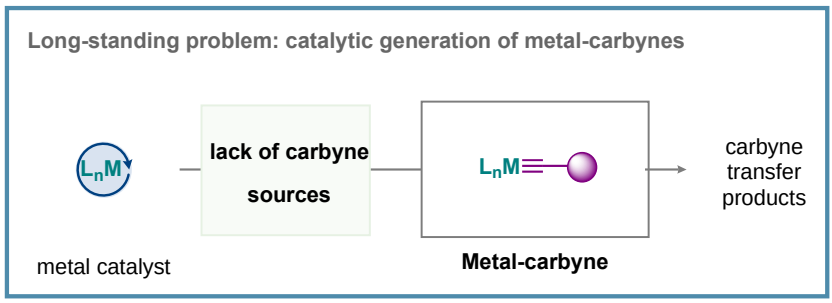
key step by the group of Fürstner.[57] In this case a tungsten (VI) alkylidyne Schrock-type complex is used as catalyst for the 12-membered ring formation.



Scheme 11

Even though the Schrock alkylidyne complexes have found a broader use as catalysts compared to Fischer carbynes, none of them can be used as a general platform for the catalytic carbyne transfer and only have found application for such purpose in alkyne metathesis.[58] There is a lack of carbyne precursors able to transfer monovalent carbon units into organic molecules in a catalytic manner (Scheme 12).

[57] Fürstner, A.; Castanet, A. S.; Radkowski, K.; Lehmann, C. W. *J. Org. Chem.* **2003**, *68*, 1521.
[58] Engel, P. F.; Pfeffer, M. *Chem. Rev.* **1995**, *95*, 2281.



Scheme 12

1.3. Hypervalent iodine

Iodine is one of the heaviest non-metallic atoms of the periodic table. Due to its large size, iodine is able to form hypervalent bonds[59]: linear bonds with two ligands (L–I–L) by the overlap of the 5p orbitals on iodine and the ones from the ligands L, being a three-center-four-electron bond (3c-4e). These features differ from the hybridized orbitals of light *p*-block elements, providing different structural and reactivity properties more similar to the transition metals, able to undergo ligand exchange, oxidative addition, reductive elimination or ligand coupling.[60] Hypervalent iodine compounds can be divided in two classes: trivalent iodine(III) compounds (λ^3-iodanes) and pentavalent iodine(V) compounds (λ^5-iodanes).[61]

λ^3-iodanes are compounds generally with formula RIX_2 or R_2IX depending on the nature of the ligands and contain 10 electrons at the iodine atom. They form a trigonal (pseudo-)bipyramidal geometry with the heteroatom ligands X in the apical positions, showing a T-shaped structure (Figure 6A). The hypervalent bonds between the iodine atom and the ligands are highly polarized, longer and weaker than a usual covalent bond, which explains its highly electrophilic behavior. In consequence, the ligands play a major role on the stabilization of such compounds.

λ^5-iodanes are compounds with formula RIX_4 and have a square bipyramidal geometry, the four electronegative substituents X in the basal positions, containing 12 electrons on the iodine atom (Figure 6B). The X substituents are connected by hypervalent bonds, whereas the R substituent is linked with a normal covalent bond.

[59] Musher, J. *Angew. Chem. Int. Ed.* **1969**, *8*, 54.
[60] Moriarty, R. M. *J. Org. Chem.* **2005**, *70*, 2893.
[61] (a) Zhdankin, V. V.; Stang, P. J. R *Chem. Rev.* **2002**, *102*, 2523; (b) Yoshimura, A.; Zhdankin, V. V. *Chem. Rev*. **2016**, *116*, 3328.

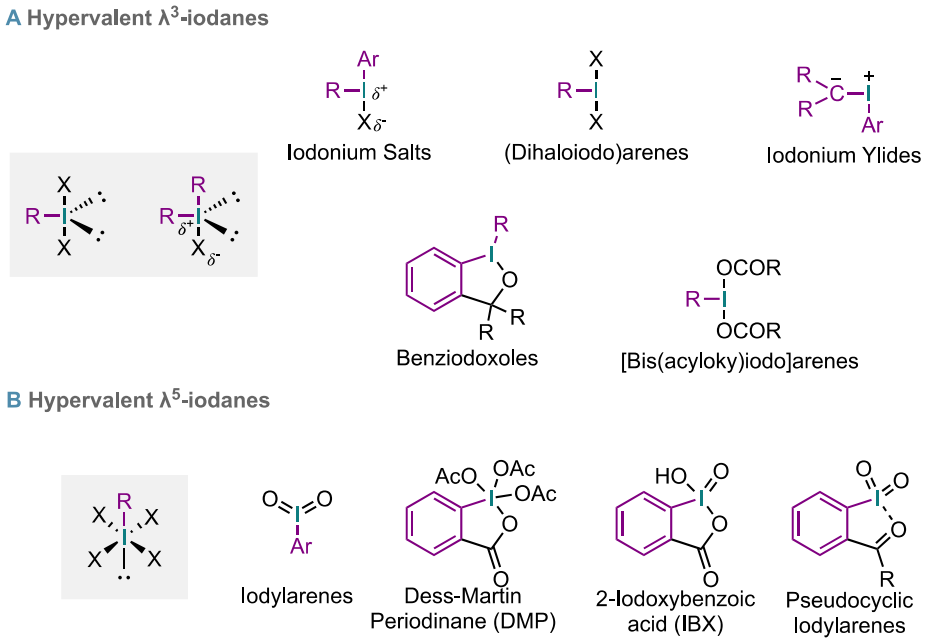


Figure 6

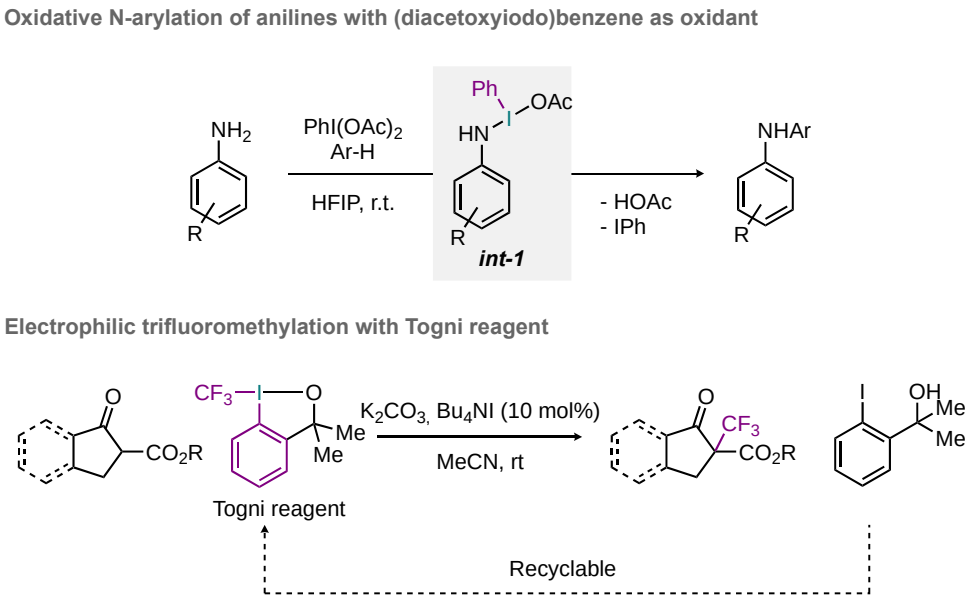
1.3.1. Reactivity of hypervalent iodine reagents

Hypervalent iodine reagents have been extensively studied in the last two decades and nowadays many λ^3- and λ^5-iodane reagents are routinely employed in organic synthesis laboratories. Due to the increasing interest in developing greener synthetic processes, hypervalent iodine reagents have emerged as perfect alternatives to some transition metal reagents thanks to their low toxicity, ready availability, easy handling and recyclability, among other benefits.[62] The main features of such compounds in terms of reactivity are (i) the high electrophilicity of iodine, (ii) the outstanding leaving ability of the phenyliodonio group, based on the entropic factor of splitting one molecule into three and (iii) the tendency of iodine to get reduced to normal valency by reductive elimination.[63] Such properties permit them to be involved in C–C, C–Heteroatom, Heteroatom–Heteroatom bond forming reactions, oxidations and rearrangements. As a

[62] Wirth, T. Hypervalent Iodine Chemistry. *Springer International Publishing*, Topics in Current Chemistry, **2016**, *373*.
[63] Zhdankin, V. V; Stang, P. *J. Chem. Rev.* **2008**, *108*, 5299.

result, there are many hypervalent iodine reagents available for oxidation,[64] C–amination,[65] trifluoromethylation,[66] alkynylation[67] or arylation reactions.[68]

Normally, iodine(III) reagents with structure RIX_2 are used in oxidation reactions, through a first ligand exchange and a subsequent reductive elimination. On the other hand, the reagents with structure R_2IX are not good oxidating agents and normally are used as sources for the transfer of electrophilic R moieties to a variety of nucleophiles. An example of this difference in reactivity can be observed in Scheme 13. In the first case, (diacetoxyiodo)benzene is used for the oxidative N-arylation of anilines via the formation of int-I by ligand exchange between an acetoxy group and the amine.[69] In the second example of Scheme 13, Togni's reagent is used for the electrophilic trifluoromethylation of β-ketoesters.[70] In this case, it is important to remark the recyclability of the hypervalent iodine reagent by reoxidizing the iodine atom.



Scheme 13 Difference in reactivity between iodine(III) reagents RIX_2 and R_2IX

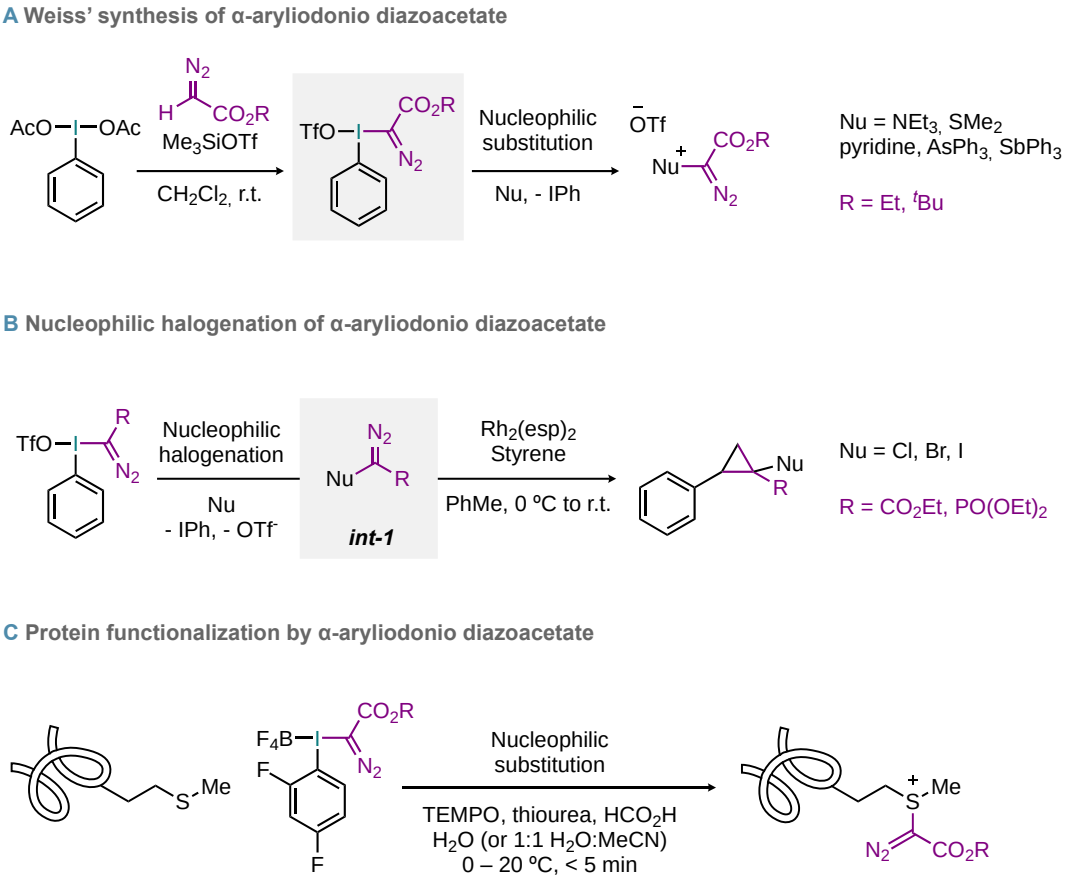
[64] Uyanik, M.; Ishihara, K. *Chem. Commun.* **2009**, 2086.
[65] Muñiz, K. *Acc. Chem. Res*. **2018**, *51*, 1507.
[66] Charpentier, J.; Fru, N.; Togni, A. *Chem. Rev.* **2015**, *115*, 650.
[67] Hari, D. P.; Caramenti, P.; Waser, J. *Acc. Chem. Res.* **2018**, *51*, 3212.
[68] Beringer, F. M.; Daniel, W. J.; Galton, S. A.; Rubin, G. *J. Org. Chem*. **1966**, *31*, 4315.
[69] Manna, S.; Serebrennikova, P. O.; Utepova, I. A.; Antonchick, A. P.; Chupakhin, O. N. *Org. Lett.* **2015**, *17*, 4588.
[70] (a) Kieltsch, I.; Eisenberger, P.; Togni, A. *Angew. Chem. Int. Ed.* **2007**, *46*, 754; (b) Eisenberger, P.; Gischig, S.; Togni, A. *Chem. Eur. J.* **2006**, *12*, 2579.

In a similar way to the CF_3 transfer performed with Togni's reagent, the group of Weiss wanted to transfer a diazoacetate group, keeping the diazo functionality unreactive.[71] This reaction would involve the nucleophilic substitution on the α-C of the diazo moiety, and the aryliodonio group would act as a nucleofuge. The desired alpha-aryliodonio diazoacetate was synthesized from phenyliodoso diacetate with Me_3SiOTf and diazoacetate and it underwent nucleophilic substitution at the α-C with a variety of nucleophiles such as pyridines, sulfides or amines (Scheme 14A).

Albeit the breakthrough finding of Weiss, there are not many examples in which these diazo aryliodonium species are studied or employed. In 2013, the group of Bonge-Hansen used Weiss' reagents for the synthesis of halodiazo compounds through its nucleophilic halogenation (Scheme 14B).[72] The halodiazo species generated were used *in situ* for the catalytic cyclopropanation of styrenes. DFT calculations allowed them to give insight into the mechanism, showing that it changes depending on the nucleophile taking part in the reaction. Nucleophiles like sulfides or amines show a S_N2-type mechanism, whereas bromide exhibits a tetrahedral transition-state more similar to the carbonyl-like addition-elimination reaction mechanism.

The group of Gaunt has recently used a similar strategy for the functionalization of proteins (Scheme 14C).[73] In this case, a slightly modified aryliodonio diazoacetate allowed to functionalize proteins at the methionine residues. Their thioether moieties could undergo a nucleophilic substitution just like in Weiss' work to form diazoacetate-substituted sulfonium conjugates. The tuning of the hypervalent iodine reagent was crucial to obtain high yields and to be selective to the methionine residues.

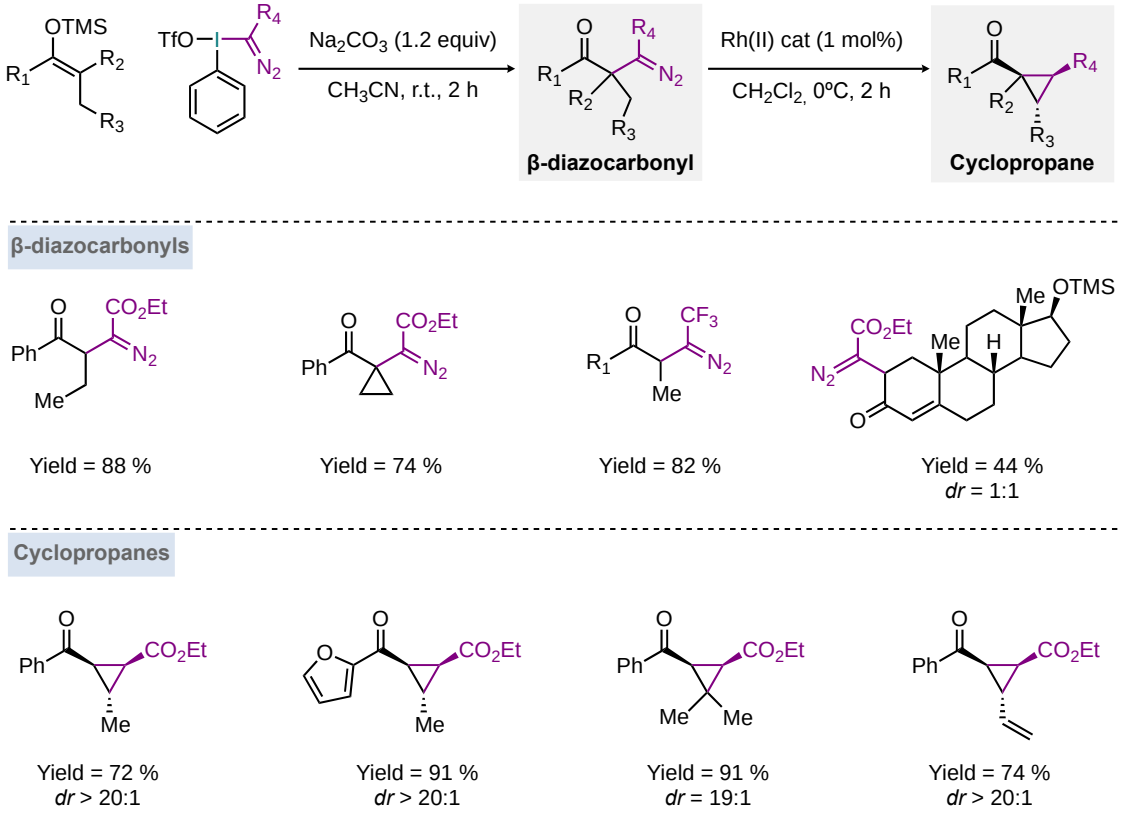
[71] Weiss, R.; Seubert, J.; Hampel, F. *Angew. Chem. Int. Ed.* **1994**, *33*, 1952.
[72] Schnaars, C.; Hennum, M.; Bonge-Hansen, T. *J. Org. Chem.* **2013**, *78*, 7488.
[73] Taylor, M. T.; Nelson, J. E.; Suero, M. G.; Gaunt, M. J. *Nature* **2018**, *562*, 563.



Scheme 14 Different examples of diazomethylation reactions

In 2021, our group published the first diazomethylation of ketone silyl enol ethers for the synthesis of previously underexplored β-diazocarbonyl compounds (Scheme 15).[74] In this work, hypervalent iodine reagents with different electron-withdrawing groups were employed, like multiple acetates, ketone, phosphonate, trifluoromethyl or sulfonate groups. The usefulness of the β-diazocarbonyl products was demonstrated with the discovery of Rh(II)-catalyzed intramolecular 1,3 C–H carbene insertion, able to form complex cyclopropanes in excellent stereocontrol.

[74] Jiang, L.; Wang, Z.; Armstrong, M.; Suero, M. G. *Angew. Chem, Int. Ed.* **2021**, *60*, 6177.



Scheme 15 Diazomethylation of ketone silyl enol ethers

The linear hypervalent iodine reagents like the one discovered by Weiss are relatively unstable and highly reactive. In comparison, the cyclic hypervalent iodine reagents developed by Togni show higher stability, due to the more rigid structure and the addition groups that decrease the electrophilicity of the $I^{(III)}$-atom by electron donation. Inspired by these results and in an attempt to discover novel carbon reactive species, our group synthesized new types of diazoacetate-substituted hypervalent iodine reagents. Our hypothesis was that these compounds could serve as carbyne equivalents, being able to separately activate the hypervalent iodine group and the diazo moiety.[75] The hypervalent I–C bond is redox active whereas the diazo moiety could be cleaved by light and metal catalysis. Hence, if both functional groups were to be activated, a monovalent carbon would be generated (Figure 7).

[75] (a) Zhao, R.; Shi, L. *Angew. Chem. Int. Ed.* **2020**, *59*, 12282; (b) Yang, Y.; Wang, C. *Chinese J. Chem.* **2021**, *39*, 3481.

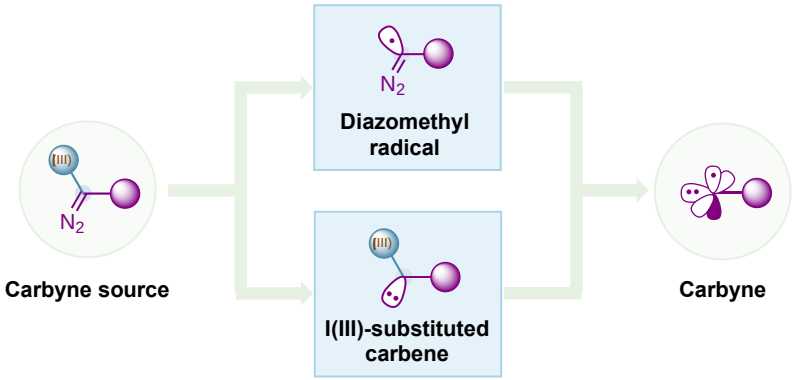
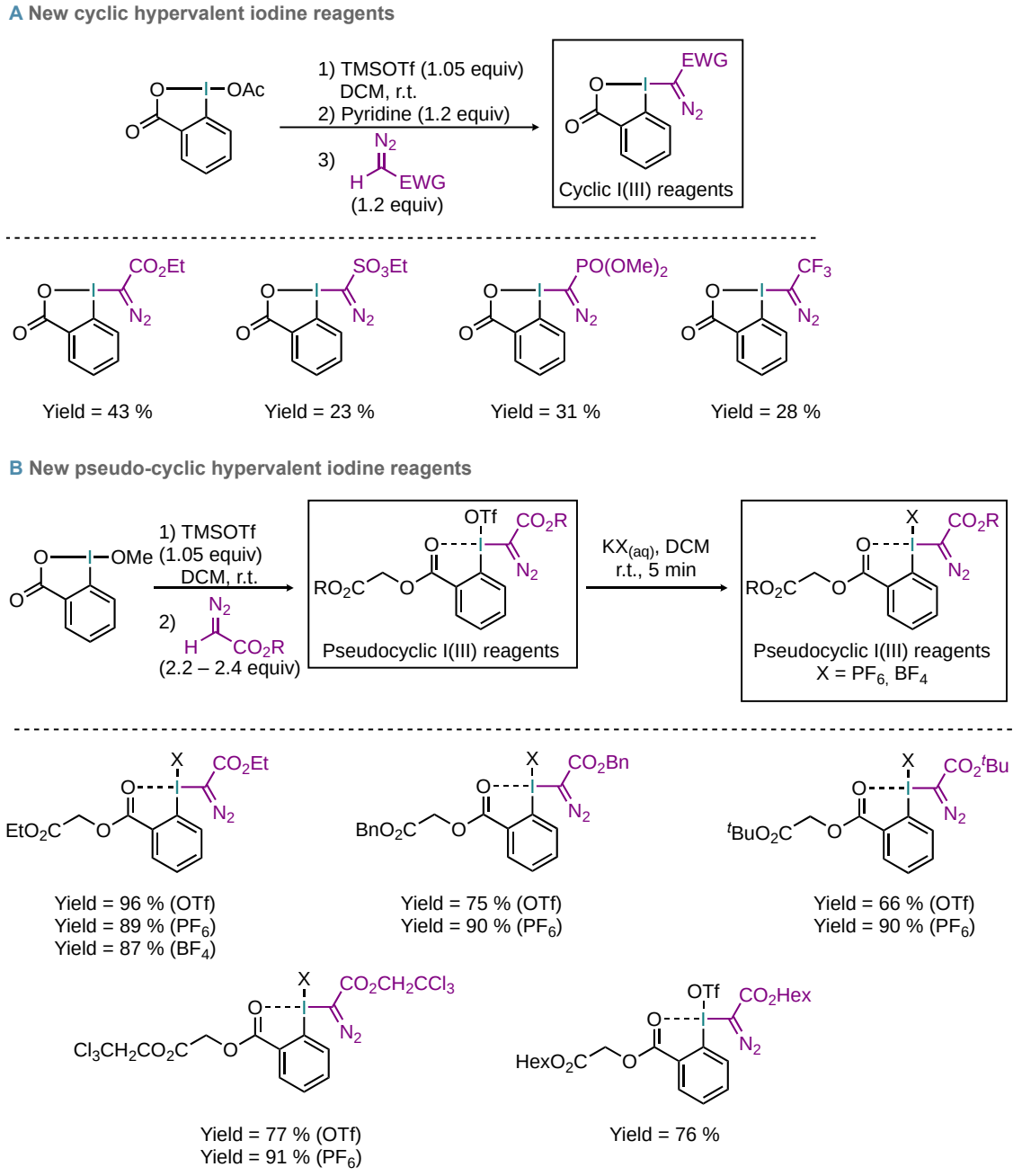


Figure 7 Carbyne sources: monovalent carbon units with two masking groups prone to be activated and with reactivity that resemble the one from free carbynes

For this purpose, we have synthesized different cyclic and pseudo-cyclic hypervalent iodine reagents containing multiple electron-withdrawing groups (EWG) and counter anions which tune their reactivity (Scheme 16). These novel cyclic and pseudo-cyclic hypervalent iodine reagents show a higher stability compared to the linear reagents like the one from Weiss. Such enhancement of stability is provided by the acetate arm, either by a hypervalent bond in the case of the cyclic reagents or by the interaction between the electron lone pair of the oxygen of the side arm acetate with the empty σ^* orbital of the I–C bond, decreasing the electrophilicity of the high valent iodine atom. Both classes of reagents are easy-to-prepare solids stable at room temperature. In this sense, the cyclic reagent is even more stable and less reactive in consequence compared to the pseudo-cyclic, due to the stronger interaction between oxygen and iodine. This higher stability of the cyclic reagents allowed us to attach different electron withdrawing groups other than esters like sulfonate, phosphonate and trifluoromethyl groups.

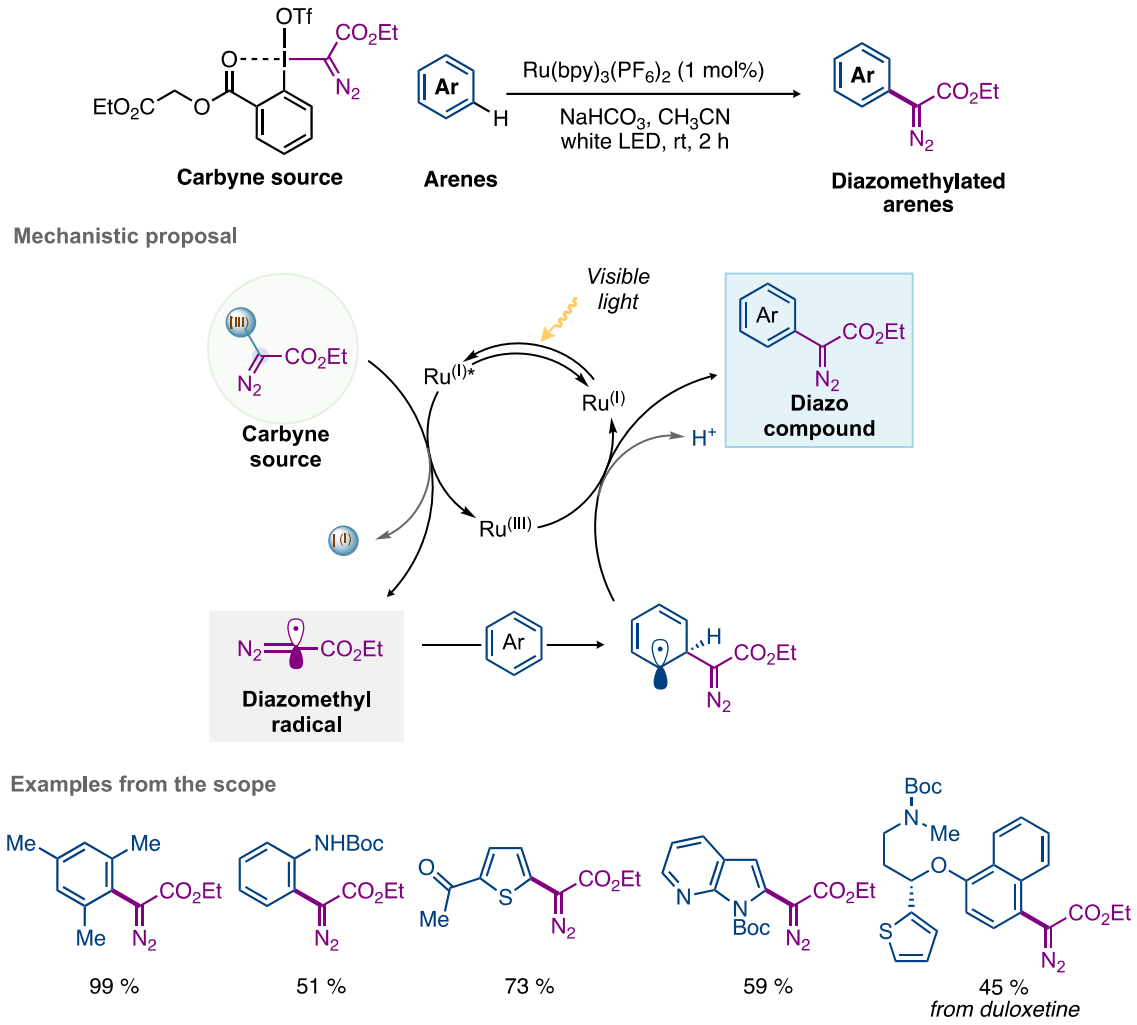


Scheme 16

Our group has recently used such novel hypervalent iodine reagents for the diazomethylation of arenes with photoredox catalysis (Scheme 17).[76] We were able to selectively activate the hypervalent I–C bond using visible-light photoredox catalysis without cleaving the diazo moiety. As a result, diazomethyl radicals were generated and used in situ for the functionalization of aromatic C–H bonds. A broad range of arenes could be employed, including biologically active products, which were further

[76] Wang, Z.; Herraiz, A. G.; Del Hoyo, A. M.; Suero, M. G. *Nature* **2018**, *554*, 86.

derivatized, proving that these carbyne equivalents could be used as a catalytic assembly-point strategy.



Scheme 17

It must also be said that other groups have used the hypervalent iodine reagents discovered in our group for other purposes like the synthesis of 1,3,4-oxadiazoles[77] or 1,2,3-triazoles[78] among others.[79]

[77] Li, J.; Lu, X. C.; Xu, Y.; Wen, J. X.; Hou, G. Q.; Liu, L. *Org. Lett.* **2020**, *22*, 9621.
[78] Dong, J. Y.; Wang, H.; Mao, S.; Wang, X.; Zhou, M. D.; Li, L. *Adv. Synth. Catal.* **2021**, *363*, 2133.
[79] (a) Gao, Z. Z.; Xu, Y. Y.; Wang, Z. K.; Wang, H.; Zhang, D. W.; Li, Z. T. *ACS Appl. Polym. Mater.* **2020**, *2*, 4885; (b) Yip, W. M.; Yu, Q.; Tantipanjaporn, A.; Chan, W. C.; Deng, J. R.; Ko, B. C. B.; Wong, M. K. *Org. Biomol. Chem.* **2021**, *19*, 8507.

Chapter II

Catalytic Cleavage of C(sp^2)–C(sp^2) Bonds with Rh-Carbynoids: Synthesis of Allylic Building Blocks

The work described in this chapter was performed in collaboration with ***Dr. Zhaofeng Wang and Dr. Liyin Jiang****. Part of the work has been published, see:* Zhaofeng Wang, Liyin Jiang, Pau Sarró, Marcos G. Suero *"Catalytic Cleavage of C(sp^2)–C(sp^2) Bonds with Rh-Carbynoids" J. Am. Chem. Soc.* **2019**, *141,* 15509.

2.1 Introduction

For more than half a century, the discovery of new metal−carbon bond-forming strategies has been cornerstone in the development of transition-metal catalysis.[1] The catalytic generation of organometallic species with metal−carbon single/double bonds, such as metal−L (L = alkyl, alkenyl, alkynyl, aryl) or metal−carbene (metal=L) is widely used in reaction discovery and development. However, while metal- carbynes, the organometallic species with a metal−carbon triple bond (metal≡L),[2] have been key catalysts in alkyne metathesis,[3] their catalytic generation and general application in catalytic carbyne transfer has been largely unexplored, mainly due to the lack of suitable monovalent carbon sources (Figure 1).[4] Surprisingly, methodologies circumventing this problem by generating metal-carbynoids as equivalent reactive species of metal-carbynes, have not been reported.

In this chapter we describe development of a novel Rh-catalyzed carbyne transfer platform for the catalytic cleavage of C(sp^2)–C(sp^2) bonds. We have employed carbyne equivalents reagents containing two masking groups: a hypervalent iodine and a diazo moiety. The activation of the diazo group by Rh-catalysis allowed us to form Rh-carbenes containing a hypervalent iodine moiety which can be considered carbyne equivalents or carbynoids thanks to the outstanding lability of the $I^{(III)}$-group. The generation of these novel carbynoid species gave us the opportunity to form allyl cations from a broad range of alkenes, styrenes and butadiene by the catalytic cleavage of C(sp^2)–C(sp^2) bonds.

[1] Hartwig, J. F. Organotransition Metal Chemistry From Bonding to Catalysis; University Science Books, 2010.
[2] (a) Fischer, E. O.; Kreis, G.; Kreiter, C. G.; Müller, J.; Huttner, G.; Lorenz, H. *Angew. Chem., Int. Ed.* **1973**, *12*, 564; (b) Guggenberger, L. J.; Schrock, R. R. *J. Am. Chem. Soc.* **1975**, *97*, 2935.
[3] Fürstner, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 2794.
[4] Engel, P. F.; Pfeffer, M. *Chem. Rev.* **1995**, *95*, 2281.

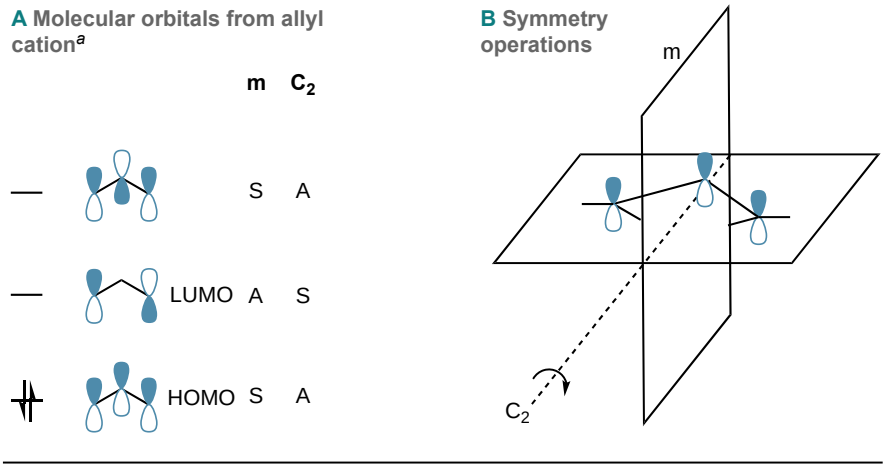
2.2. Allyl cations

Allyl cations are conjugated three-carbon-two-electron systems with a delocalized positive charge. Since they are the smallest and simplest system that can be obtained by electrocyclic ring opening (from cyclopropanols or related substrates), they have served as a model for the study of such transformations. Roberts and Chambers were the first to quantitatively study the solvolysis of cyclopropyl tosylates,[5] proposing the formation of allyl cations in 1951. A decade later, Woodward, Hoffmann and DePuy dictated the laws on which the electrocyclic processes are based. Since then, these intermediates have brought much attention and have been studied and generated in multiple reactions for the synthesis of a broad range of chemicals.

2.2.1. Woodward-Hoffmann rules[6]

If we consider the molecular orbitals from allyl systems, the combination of the atomic orbitals generates three molecular orbitals with 0, 1 and 2 nodes from the lowest to the highest energetic one. In allyl cations, only the lowest molecular orbital will be occupied, being this the Highest Occupied Molecular Orbital (HOMO) and the next one the Lowest Unoccupied Molecular Orbital (LUMO) (Figure 1). The latter, shows a C_2 symmetry operation, with a node in the central carbon and the orbitals in the terminal sites in opposite symmetry. The symmetry of the LUMO dictates the reactivity of the allyl cation, being the terminal sites where most of the reactions take place. It also results in a higher effect on the stability when substituents are placed on these sites compared to the central carbon.

[5] Roberts, J. D.; Chambers, V. C. *J. Am. Chem. Soc.* **1951**, *73*, 5034.
[6] (a) Woodward, R. B.; Hoffmann, R. *J. Am. Chem. Soc.* **1965**, *87*, 395; (b) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed.* **1969**, *8*, 781.



[a] m and C_2 refer to the symmetry operations and S and A to symmetric and antisimmetric with respect to such operations.

Figure 1 Molecular orbitals and symmetry operations from allyl cation

Electrocyclic reactions can be defined as the concerted formation of a single bond between the ends of a linear system containing k π electrons, and the converse process. Such isomerization might take place in a disrotatory or conrotatory mode depending on the symmetry of the molecular orbitals that need to interact in a bonding manner. If the two orbitals that need to overlap are in the same phase, they will need to rotate in a disrotatory mode, to the opposite direction. On the other hand, if they are in opposite phase, they need to rotate in the same direction, being conrotatory (Figure 2). These modes of rotations dictate whether an electrocyclic reaction is allowed or not, in other words, if the overlap between the two orbitals is a bonding or antibonding combination.

Figure 2 Electrocyclic reactions by disrotatory or conrotatory mode

With regard to the symmetry operations, the Woodward-Hoffmann rules state that the symmetry of the orbitals needs to be maintained along the electrocyclic reaction. So, in the disrotatory movement, the plane of symmetry is maintained, whereas in the conrotatory movement the rotation axis of symmetry is the one maintained. As a consequence, in systems with k π electrons, it can be assumed that thermal electrocyclic reactions of k = 4q+2 electrons will be conrotatory (q = 0, 1, 2, …). This is the case in the ring opening of cyclopropyl ring to

form an allyl cation, where 2 π electrons are involved (q = 0). On the other hand, the systems with k = 4q electrons will be disrotatory. In the excited state, since one electron is promoted to the superior energetic level, which has the inverse orbital symmetry properties, these relationships are reversed.

2.3. Stability of allyl cation

Allyl cations have been studied for many decades both experimentally and theoretically, since they were first proved to exist in the solvolysis studies.[7] Of special relevance are the studies undertaken first by Olah[8] and next by Mayr about methyl-substituted allyl cations, in which they present extensive studies on the stability of such intermediates.

2.3.1. Substitution effect in allyl cations

In order to analyze the substitution effect on the stability of the allyl cation, the group of Mayr calculated the different bond distances and energies of allyl cations substituted with methyl groups in different positions (Table 1).[9] Mayr found that the addition of a methyl group in a terminal site C3 centers the positive charge in such carbon, decreasing the delocalization of the positive charge (Table 1, allyl cations 1 and 2). It also increases the double bond character on the other end of the allylic system, shortening the C2–C1 distance and increasing the π electron density in C1. The same conclusion was obtained by Olah and Mayr when comparing the C-NMR of C1 and C3.[8] They observed that C3 got more deshielded when substituted, because it adopted a more carbocation behaviour than the non-substituted one; parallelly, C1 appeared to be more shielded, having more π density. In contrast to these findings, when the central carbon C2 is substituted, neither the bond lengths nor C-NMR signals vary significantly (Table 1, allyl cation 3).

What is also interesting is how the C1–C2–C3 angle changes depending on the substitution pattern. It is obvious that when C3 is substituted, this angle will widen due to steric

[7] Deno, N. C. Carbonium Ions. In *Progress in Physical Organic Chemistry Vol. 2*; Cohen, S. G.; Streitwieser, A. Jr.; Taft, R. W., Ed.; Interscience Publishers, **1964**.
[8] (a) Olah, G. A.; Comisarow, M. B. *J. Am. Chem. Soc.* **1964**, *86*, 5682; (b) Olah, G. A.; Bollinger, J. M. *J. Am. Chem. Soc.* **1968**, *90*, 6082; (c) Bollinger, J. M.; Brinich, J. M.; Olah, G. A. *J. Am. Chem. Soc.* **1970**, *92*, 4025; (d) Olah, G. A.; Clifford, P. R.; Halpern, Y.; Johanson, R. G. *J. Am. Chem. Soc.* **1971**, *93*, 4219; (e) Groups, C.; Olah, G. A.; Spear, R. J. *J. Am. Chem. Soc.* **1975**, *97*, 1539; (f) Olah, G. A.; Mayr, H. *J. Am. Chem. Soc.* **1976**, *98*, 7333; (g) Mayr, H.; Olah, G. A. *J. Am. Chem. Soc.* **1977**, *99*, 510.
[9] Mayr, H.; Förner, W.; Schleyer, P. von R. *J. Am. Chem. Soc.* **1979**, *101*, 6032.

effects. If the allyl cation is doubled substituted in C1 and C3, the angle will increase even more (Table 1, allyl cation 4).

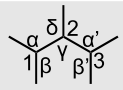
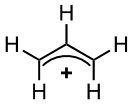
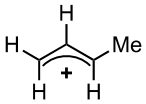
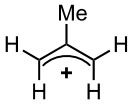
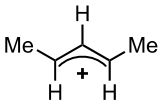
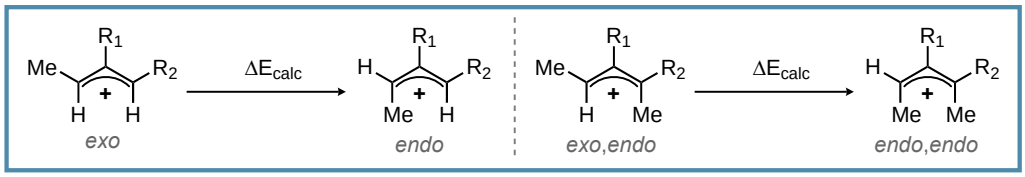
	Allyl cation	bond length C1-C2 / C1-C2	α / β	α' / β'	γ / δ	π density C1 / C3
	**1**	1.385 1.385	120.0 120.0	120.0 120.0	119.0 120.5	0.466 0.466
	**2**	1.370 1.404	120.0 120.0	124.5 118.4	119.2 120.7	0.539 0.435
	**3**	1.391 1.390	120.0 120.0	120.0 120.0	115.2 122.8	0.490 0.498
	**4**	1.386 1.386	124.5 117.8	124.5 117.8	119.5 120.3	0.498 0.498

Table 1 Comparison of bond lengths, angles and π density of substituted allyl cations

Regarding the steric strain, the *exo* conformation is preferred over the *endo*, due to the steric hinderance of the latter (Scheme 1). Such preference amounts to 3 kcal/mol in allyl cations mono-substituted in C1 or C3 and is almost independent of the system. However, smaller energy changes are observed in more crowded systems, due to their inherent steric hinderance of the W-shape conformation. Introduction of a second endo-methyl group increases the strain by 5 kcal/mol. Similar values have been obtained from experimental data.[10] In such experimental work, the rotation activation energy of 1,3-dimethyl-allyl cation was determined to be 17.5 and 24.0 kcal/mol (*cis*/*cis* to *cis*/*trans* and *cis*/*trans* to *trans*/*trans* isomers respectively).

[10] Schleyer, P. von R.; Su, T. M.; Saunders, M.; Rosenfeld, J. C. *J. Am. Chem. Soc.* **1969**, *91*, 5174.

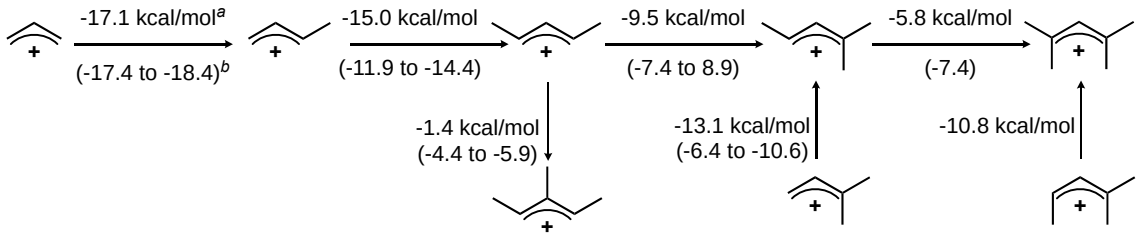


R_1	R_2	ΔE (kcal/mol)
H	H	3.0
Me	H	3.2
H	Me	3.1
Me	Me	2.3

R_1	R_2	ΔE (kcal/mol)
H	H	4.9
Me	H	4.8
H	Me	5.0

Scheme 1 Calculated energy difference between (i) *exo* and *endo* conformations and (ii) *exo,endo* and *endo,endo* conformations

The stabilization of allyl cations by methyl groups is evaluated by isodesmic reactions, considering the successive addition of methyl groups to the allyl cation (Scheme 2). Each methyl group stabilizes the cation. However, the stabilization value decreases with the number of substituents added due to the steric hinderance of the *endo*-methyl groups, which counterbalances the electronic stabilization (from a stabilization of 17.1 kcal/mol when the first methyl is added to 5.8 kcal/mol when the fourth one is added). If only *exo*-methyl groups are considered, the steric effect is much lower and in consequence the stabilization value does not decrease as much (from 17.1 kcal/mol to 10.8). Again, the substitution in C2 has a smaller effect on the stabilization of the cation (only 1.4 kcal/mol when added to 1,3-dimethyl-allyl cation).



[a] The value refers to calculated differences in energy using STO-3G basis set. [b] The values in brackets refer to experimental differences in energy.

Scheme 2 Calculated and experimental energies from the methyl addition to differently substituted allyl cations

This data is comparable to the experimentally obtained in the gas phase (Scheme 2, in parenthesis) and according to Myer, the differences might be associated to inconsistent experimental results.

2.4. Generation of allyl cations

Allyl cations have been generated for a long time in multiple reactions and they can be generated from multiple sources. Even though in the first studies from Olah and Myer they were generated from dienes and alkynes by protonation,[8] the most common methods to form allyl cations are from (*i*) cyclopropyl rings, either cyclopropanol derivatives[11] or dihalo-cyclopropanes,[12] using different Lewis acids for their ring opening and leaving group removal; (*ii*) allylic compounds,[13] such as allylic halides or alcohols,[14] where also different Lewis acids have been used for the leaving group removal; and (*iii*) C–H activation[15].

2.4.1. Cyclopropyl ring opening

Cyclopropanes are the smallest cyclic hydrocarbons, containing three carbon atoms which are highly strained due to the smaller angles in the C–C bonds (60º) compared to the optimum 109.5º of a standard tetrahedral carbon atom. Such inherent ring strain of the cyclopropane (27.5 kcal/mol versus 6.5 kcal/mol for cyclopentane)[16] gives this cycloalkane a reactivity which resembles the one of olefins. The reason of this behaviour comes from their bonding similarity and two models have been proposed to explain it.[17] The first one is the valence bond model,[18] which defines the C–C bond as the overlapping of two sp^5 orbitals from each C atom, describing the higher electron density observed out of the C–C bond. The other theoretical description is the Walsh model of molecular orbitals (MO).[19] Considering the 6 electrons involved in the cyclopropane ring, there should be three occupied MO. The orbital with lowest energy is a linear combination of three sp^2 orbitals pointing inwards the

[11] McDonald, T. R.; Mills, L. R.; West, M. S.; Rousseaux, S. A. L. *Chem. Rev.* **2021**, *121*, 3.
[12] (a) Kostikov, R. R.; Molchanov, A. P.; Hopf, H. *Top. Curr. Chem.* **1990**, *155*, 41; (b) Fedoryński, M. *Chem. Rev.* **2003**, *103*, 1099; (c) Halton, B.; Harvey, J. *Synlett* **2006**, 13, 1975; (d) Thankachan, A. P.; Sindhu, K. S.; Krishnan, K. K.; Anilkumar, G. *Org. Biomol. Chem.* **2015**, *13*, 8780.
[13] (a) Hoffmann, H. M. R.; Matthei, J. *Chem. Ber.* **1980**, *113*, 3837; Smith, C. D.; Rosocha, G.; Mui, L.; Batey, R. A. *J. Org. Chem.* **2010**, *75*, 4716; (b) Troshin, K.; Schindele, C.; (c) Mayr, H. *J. Org. Chem.* **2011**, *76*, 9391.
[14] (a) Rueping, M.; Uria, U.; Lin, M. Y.; Atodiresei, I. *J. Am. Chem. Soc.* **2011**, *133*, 3732; (b) Ding, F.; William, R.; Wang, F.; Liu, X. W. *Chem. Commun.* **2012**, *48*, 8709.
[15] (a) Cheng, D.; Bao, W. *Adv. Synth. Catal.* **2008**, *350*, 1263; (b) Li, Y.; Bao, W. *Adv. Synth. Catal.* **2009**, *351*, 865; (c) Mo, H.; Bao, W. *J. Org. Chem.* **2010**, *75*, 4856; (d) Wang, T.; Xiang, S. K.; Qin, C.; Ma, J. A.; Zhang, L. H.; Jiao, N. *Tetrahedron Lett.* **2011**, *52*, 3208; (e) Wang, Z.; Mo, H.; Cheng, D.; Bao, W. *Org. Biomol. Chem.* **2012**, *10*, 4249; (f) Kong, S.; Zhang, L.; Dai, X.; Tao, L.; Xie, C. *Adv. Synth. Catal.* **2015**, *357*, 2453; (g) Xu, T. T.; Jiang, T. S.; Han, X. L.; Xu, Y. H.; Qiao, J. P. *Org. Biomol. Chem.* **2018**, *16*, 5350; (i) Chen, Q.; Wen, C.; Wang, X.; Yu, G.; Ou, Y.; Huo, Y.; Zhang, K. *Adv. Synth. Catal.* **2018**, *360*, 3590.
[16] (a) de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 809; (b) Wong, H. N. C.; Hon, M. Y.; Tse, C. W.; Yip, Y. C.; Tanko, J.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165.
[17] Flygare, W. H. *Science* **1963**, *140*, 1179.
[18] Coulson, C. A.; Moffitt, W. E. *J. Chem. Phys.* **1947**, *15*, 151.
[19] Walsh, A. D. *Trans. Faraday Soc.* **1949**, *45*, 179.

cyclopropane ring, while the other two orbitals have the same energy and are linear combinations of three p atomic orbitals, directed out of the ring.

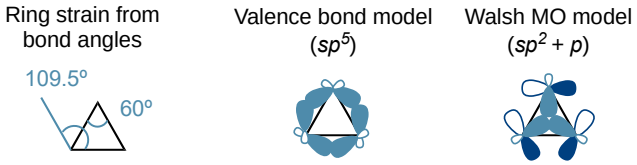


Figure 3 Schematic representations of the C–C bond in cyclopropanes

In fact, the cyclopropane ring opening has been exploited for a long time for the synthesis of different motifs and complex molecules,[20] as well as a model to study the torquo- and stereochemistry of the ring opening processes.

2.4.1.1. DePuy rules

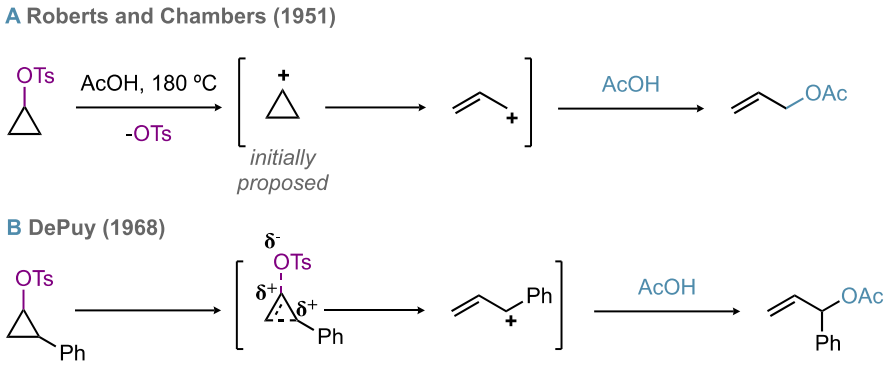
The solvolysis of cyclopropyl (pseudo-)halides was first studied by Roberts and Chambers.[5] They observed that cyclopropyl tosylate releases the tosylate group to form the allyl cation at 180 ºC (Scheme 3A). Due to the high temperature needed, the reaction was initially proposed to take place through a first elimination of the leaving group, forming the cyclopropyl cation, which then opens to form the corresponding allyl cation.

Nearly two decades later, the group of DePuy performed further investigations with aryl-cyclopropyl tosylates and they discovered that 2-aryl-cyclopropyl tosylates ring open much faster than the aryl-substituted at the 1 position.[21] These observations revealed that the ring opening occurs simultaneously with the loss of the leaving group (tosylate in this case), and the initially proposed formation of cyclopropyl cation was refuted. The main argument was that in the transition state a partial positive charge is formed in position 2, leading to an enhancement in the reaction rate when placing an aryl group in it. In this sense, the rearrangement of cyclopropanes to allyl cations is the simplest electrocyclic ring opening, and it follows the Woodward-Hoffmann rules. In fact, the studies of DePuy about the electrocyclic

[20] (a) Halton, B.; Harvey, J. *Synlett* **2006**, *13*, 1975; (b) Reisman, S. E.; Nani, R. R.; Levin, S. *Synlett* **2011**, *17*, 2437; (c) Thankachan, A. P.; Sindhu, K. S.; Krishnan, K. K.; Anilkumar, G. *Org. Biomol. Chem.* **2015**, *13*, 8780; (d) Biletskyi, B.; Colonna, P.; Masson, K.; Parrain, J. L.; Commeiras, L.; Chouraqui, G. *Chem. Soc. Rev.* **2021**, *50*, 7513

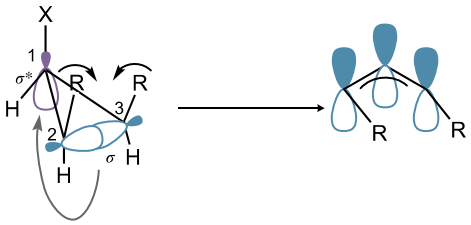
[21] (a) DePuy, C. H.; Schnack, L. G.; Hausser, J. W.; Wiedemann, W. *J. Am. Chem. Soc.* **1965**, *87*, 4006; (b) DePuy, C. H. *Acc. Chem. Res.* **1968**, *1*, 33.

ring opening of cyclopropanes were so important, that were included in such rules, being the Woodward-Hoffmann-DePuy rules.



Scheme 3 First studies on the cyclopropyl tosylate solvolysis

In cyclopropyl (pseudo-)halides, the opening of the cyclopropyl ring and the release of the leaving group happens synergistically.[22] Following the Woodward-Hoffmann rules,[6a,23] the cleavage of the C2–C3 σ bond needs to happen in a disrotatory mode. The disrotatory movement of the substituents in the process assists the C–X bond cleavage by shifting the electron density of the C2–C3 σ bond (in blue) toward the σ^* of the C–X bond (in purple), placed at its back (Figure X). Hence, such electron movement weakens the C–X bond, and facilitates the release of the leaving group.[24]

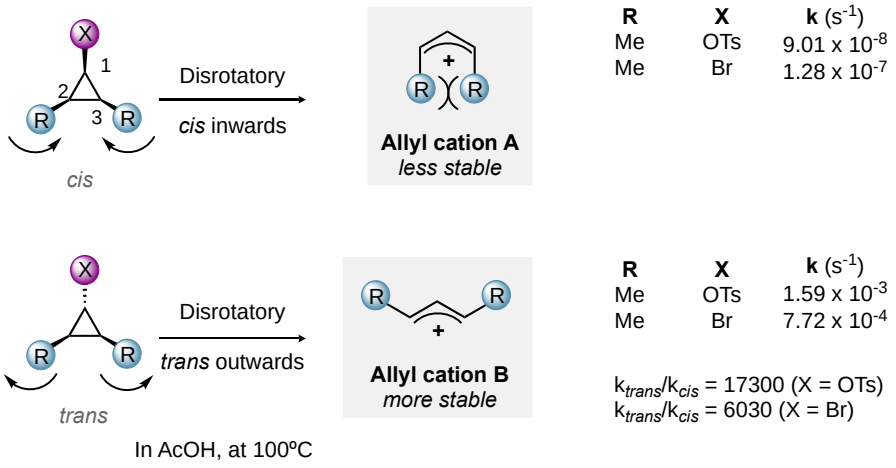


Scheme 4 In cyclopropyl (pseudo-)halides: ring opening and release of leaving group take place synergistically

Having all this in mind, we can then assume that depending on the relative configuration of the substituents in the cyclopropyl ring, there could be two disrotatory modes: moving the substituents inwards or outwards, depending if X and R groups are in *cis* or *trans* respectively. Furthermore, each of these modes would affect the disposition of such groups in the resulting

[22] Faza, O. N.; López, C. S.; Álvarez, R.; De Lera, Á. R. *J. Org. Chem.* **2004**, *69*, 9002.
[23] Hoffmann, R.; Woodward, R. B. *J. Am. Chem. Soc.* **1965**, *87*, 2046.
[24] Faza, O. N.; López, C. S.; Álvarez, R.; De Lera, Á. R. *Org. Lett.* **2004**, *6*, 905.

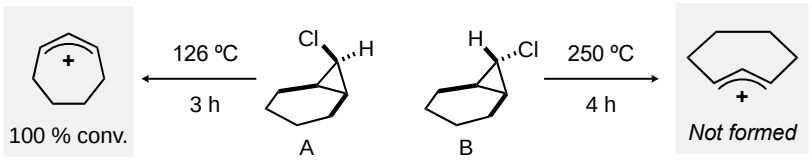
allyl cation. If the R substituents of the cyclopropyl ring are in *cis* disposition with respect to the leaving group X (Scheme 5, allyl cation A), then the disrotatory movement should take place inwards for the overlap of the breaking C2–C3 σ bond with the C–X σ* to happen. In consequence, a *cis*,*cis*-allyl cation would be formed. On the other hand, if X and R groups are in *trans* (Scheme 5, allyl cation B), such substituents need to move outwards forming a *trans*,*trans*-allyl cation, more stable than the *cis*,*cis* one due to the lack of steric hinderance between the R groups (Allyl cation B). The effect of the relative configuration can be observed in Scheme 5, where the rate constants of the opening process for the *cis* and *trans* configuration are compared, when substituted with methyl groups and bromide and tosylate as leaving groups. In both cases (either with bromide or tosylate as X) the ring opening is much faster with the *trans* conformation compared to the cis, basically due to the absence of the steric hinderance in the resulting allyl cation.



Scheme 5 Electrocyclic ring opening of *cis* and *trans* 2,3-disubstituted-cyclopropyl (pseudo-)halide and their relative rate constant

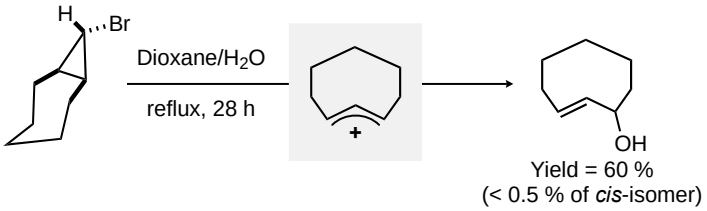
In the case of bicyclic systems, the ring strain of the resulting allyl cation must be considered for the feasibility of a reaction.[21,25] An example of this is the observations of DePuy from 1965, where the solvolysis of A took place at 125 ºC, whereas its epimer B remained unreactive even after 1 month at 210 ºC with acetic acid.[26]

[25] (a) Baird, M. S.; Lindsay, D. G.; Reese, C. B. *J. Chem. Soc. C* **1969**, 1173; (b) P. von R. Schleyer, G. W. Van Dine, U. Schöllkopf, J. Paust, *J. Am. Chem. Soc.* **1966**, *88*, 2868.
[26] S. J. Cristol, R. M. Sequeira, C. H. DePuy, *J. Am. Chem. Soc.* **1965**, *87*, 4007.



Scheme 6 Comparison of reactivities between different epimers of bicyclic chloro-cyclopropanes

These observations proved the stereospecificity of the electrocyclic ring opening of cyclopropanes to form allyl cations. As a general rule, the endo disposition between the leaving group and the cyclic substituent of the cyclopropane is preferred for its ring opening rather than the *exo*. Nonetheless, in bigger systems like the case of bicyclooctane, it has been demonstrated that it can ring open to form the expected W-shaped carbocation.[27]



Scheme 7 Ring opening of 8-bromobicyclo[5.1.0]octane

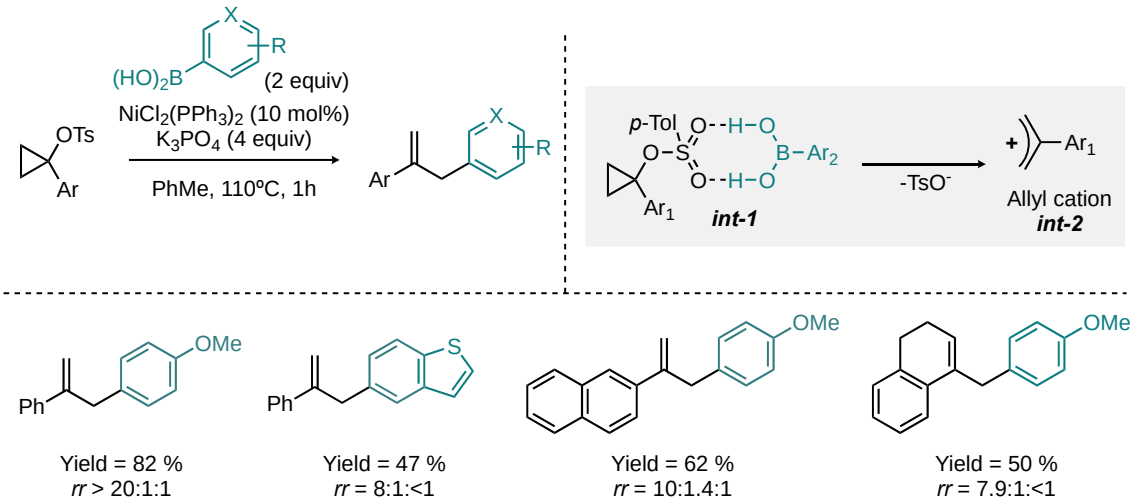
Another aspect to take into consideration is the nature of the leaving group. In Scheme 5, it can be observed how the rate of the reaction changes depending on the leaving group (bromide or tosylate). In this sense, the higher its lability, the faster the reaction will happen. Nonetheless, it is not a general rule, because the reactions conditions (solvent, temperature,…) play a major role in the stabilization of the leaving group, and therefore in its leaving group ability.

2.4.1.2. Recent examples of allyl cation generation from cyclopropanes

Since the findings of Chambers and Roberts in 1951 many studies have been developed around the ring opening of cyclopropanols and their derivatives. What is not so common is their use as synthetic precursors of allyl cations. Normally, instead of cyclopropyl alcohols, the related *gem*-dihalo-cyclopropanes or allylic halides and alcohols are used.

[27] Whitham, G. H.; Wright, M. *Chem. Commun.* **1967**, 294.

There are few examples in which cyclopropanols are used to generate allyl cations.[28] A bit more common are the cases in which their sulfonyl or silyl derivatives are employed as better leaving groups for their removal.[11,29] These cyclopropanol derivatives have been employed for the synthesis of allylic halides[30] and dienes.[31] A recent example is the work of Rousseaux's group,[32] in which 1-arylcyclopropyl tosylates are used for the arylation of allyl cations with aryl-boronic acids. In this example, it is relevant to say that the boronic acid activates the tosylate (***int-1***) in order to form the allyl cation (***int-2***). Finally, it was found that the arylation of such intermediate can happen with or without Ni(0) catalysis.

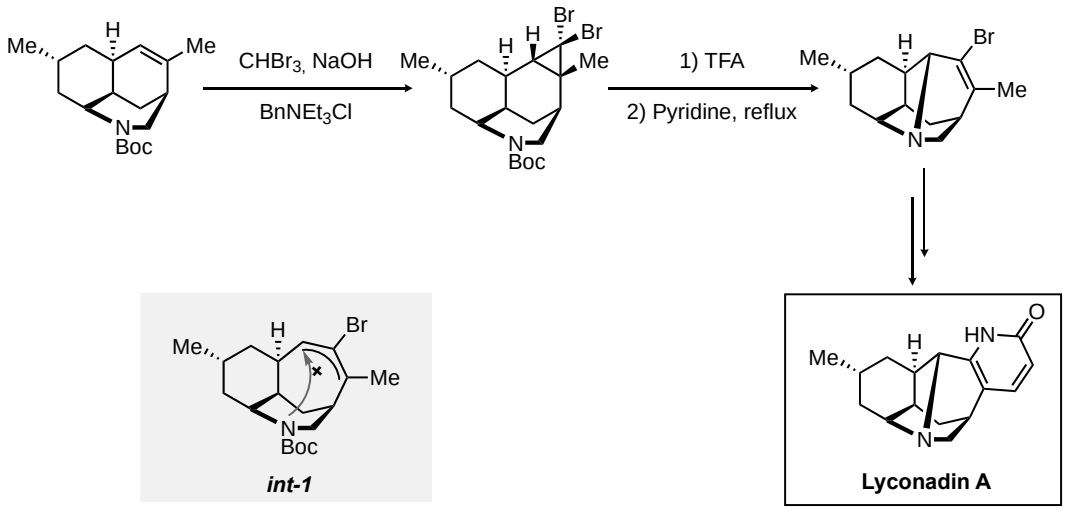


Scheme 8 Example from Rousseaux's group where the ring opening of cyclopropyl tosylates is employed for the generation of allyl cations

As said before, *gem*-dihalo-cyclopropanes are much more used as precursors of allyl cations. Hoffmann and Doering described the first synthesis of dihalocyclopropanes in 1951[33] and since then, these cyclopropyl derivatives have been widely used as synthetic intermediated because of their versatility, being easily transformed into a variety of interesting and useful

[28] (a) Beslin, P.; Vialle, J. *Tetrahedron* **1980**, *36*, 1943; (b) Cho, S. Y.; Lee, H. I.; Cha, J. K. *Org. Lett.* **2001**, *3*, 2891.
[29] Kulinkovich, O. G. *Chem. Rev.* **2003**, *103*, 2597.
[30] (a) Kirihara, M.; Kambayashi, T.; Momose, T. *Chem. Commun.* **1996**, 1103; (b) Kozyrkov, Y. Y.; Kulinkovich, O. G. *Synlett* **2002**, *4*, 443; (c) Kirihara, M.; Kakuda, H.; Tsunooka, M.; Shimajiri, A.; Takuwa, T.; Hatano, A. *Tetrahedron Lett.* **2003**, *44*, 8513; (d) Bekish, A. V.; Prokhorevich, K. N.; Kulinkovich, O. G. *Tetrahedron Lett.* **2004**, *45*, 5253.
[31] (a) Kozyrkov, Y. Y.; Kulinkovich, O. G. *Synlett* **2004**, 2, 344. (b) Quan, L. G.; Lee, H. G.; Cha, J. K. *Org. Lett.* **2007**, *9*, 4439.
[32] Mills, L. R.; Monteith, J. J.; Rousseaux, S. A. L. *Chem. Commun.* **2020**, *56*, 12538.
[33] Doering, W. von E.; Hoffmann, A. K. *J. Am. Chem. Soc.* **1954**, *76*, 6162.

substrates.[12b,25a,34] They are normally prepared through the cyclopropanation of alkenes using dihalocarbenes,[35] although other non-carbene methodologies are also used.[36] There are different methods to ring open dihalocyclopropanes. The most common ones are under thermal conditions or by the use of Lewis acid catalysis, especially with Ag(I) due to its inherent halophilicity, involving much milder reaction conditions. A recent example that shows the usefulness of this procedure is the synthesis of (+)-Lyconadin A by the group of Fukuyama.[37] The key step in the synthesis of this natural product from the Lycopodium alkaloids family was the ring opening of the dibromo-cyclopropane, followed by a ring closing nucleophilic attack of the protected amine to form the fused tricyclic core of the final structure. Even though the cyclopropyl ring opening for the generation of allyl cations is still used for the synthesis of all kinds of products, it still has some drawbacks, like the multiple steps needed, the use of highly hazardous chemicals like bromoform, as well as the use of high temperature or strong Lewis acids for the ring opening, which might not be tolerated with certain functionalities.

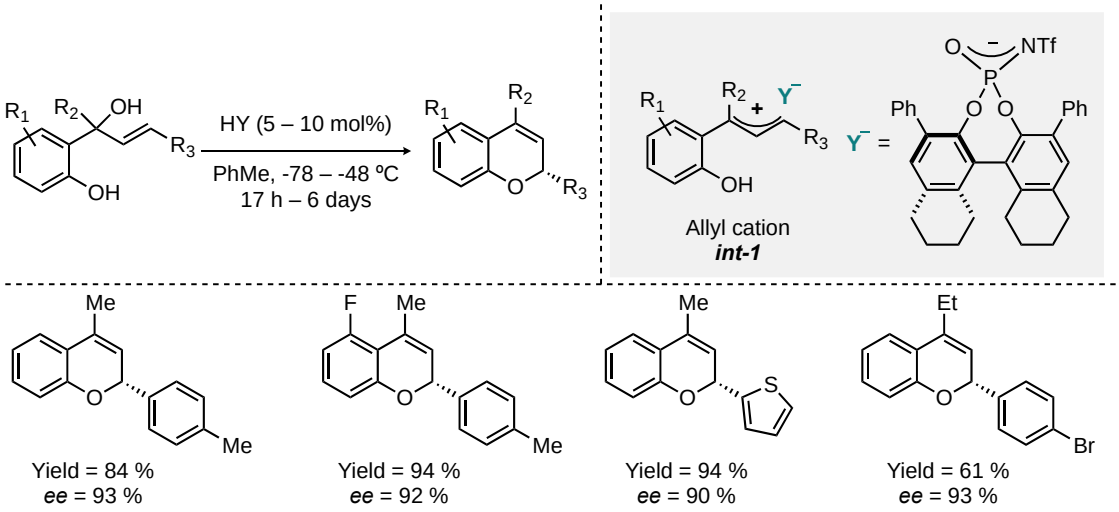


Scheme 9 Example of electrocyclic ring-opening of substituted di-bromo-cyclopropane from Fukuyama for the synthesis of Lyconadin A

[34] (a) Kostikov, R. R.; Molchanov, A. P.; Hopf, H. *Top. Curr. Chem.* **1990**, *155*, 41; (b) Halton, B.; Harvey, J. *Synlett* **2006**, *13*, 1975; (c) Thankachan, A. P.; Sindhu, K. S.; Krishnan, K. K.; Anilkumar, G. *Org. Biomol. Chem.* **2015**, *13*, 8780.
[35] Brahms, D. L. S.; Dailey, W. P. *Chem. Rev.* **1996**, *96*, 1585.
[36] (a) Dolbier, W. R.; Battiste, M. A. *Chem. Rev.* **2003**, *103*, 1071; (b) Adekenova, K. S.; Wyatt, P. B.; Adekenov, S. M. *Beilstein J. Org. Chem.* **2021**, *17*, 245.
[37](a) Nishimura, T.; Unni, A. K.; Yokoshima, S.; Fukuyama, T. *J. Am. Chem. Soc.* **2011**, *133*, 418; (b) Nishimura, T.; Unni, A. K.; Yokoshima, S.; Fukuyama, T. *J. Am. Chem. Soc.* **2013**, *135*, 3243.

2.4.2. Allyl cation generation from allylic compounds

Allyl cations can also be formed from allylic compounds like allylic alcohols,[38] halides[39] or phosphonium salts,[40] by treatment with Lewis acids, heat or light.[41] One of these examples is the work from the group of Rueping.[14a] In their work, a chiral organic Brønsted acid is used to first generate the allyl cation from allylic alcohols which then undergoes an enantioselective allylic alkylation. This work relies on chiral contact ion-pair catalysis, since the counteranion of the allylic carbocation is a chiral phosphoric acid that induces the nucleophilic attack to happen preferentially in one face over the other (Scheme 10).



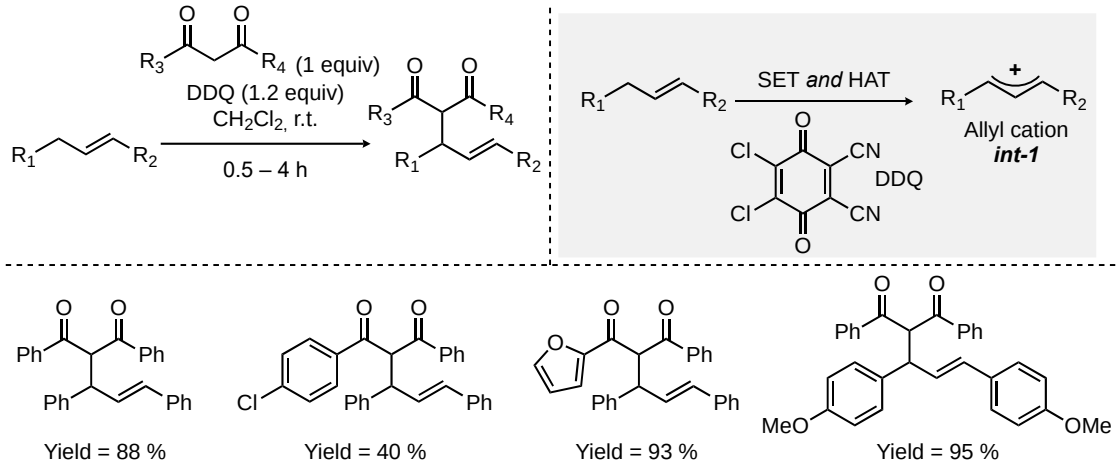
Scheme 10 Example of allyl cation generation from Rueping where allyl cations are generated for the enantioselective synthesis of poly-substituted *2H*-chromenes

It must also be said that in most of the cases, the allylic compounds that serve as allyl cations precursors require multiple steps synthesis. Furthermore, in the generation of such allyl cations, harsh reaction conditions might be needed, such as the use of strong Lewis or Brønsted acids, as well as high temperatures.

2.4.3. Allyl cation generation by C–H bond activation

[38] (a) Hoffmann, H. M. R.; Matthei, J. *Chem. Ber.* **1980**, *113*, 3837; (b) Rosocha, G.; Mui, L.; Batey, R. A. *J. Org. Chem.* **2010**, *75*, 4716; (c) Rohrs, T. M.; Qin, Q.; Floreancig, P. E. *Angew. Chem., Int. Ed.* **2017**, *56*, 10900; (d) Rodriguez Del Rey, F. O.; Floreancig, P. E. *Org. Lett.* **2021**, *23*, 150.
[39] Jüstel, P. M.; Rovó, P.; Mayr, H.; Ofial, A. R. *J. Phys. Org. Chem.* **2021**, 1.
[40] Troshin, K.; Schindele, C.; Mayr, H. *J. Org. Chem.* **2011**, *76*, 9391.
[41] (a) DeWolfe, R. H.; Young, W. G. *Chem. Rev.* **1956**, *56*, 753; (b) Magid, R. M. *Tetrahedron* **1980**, *36*, 1901; Gu, Z.; (c) Zakarian, A. Functional Group Transformation via Allyl Rearrangement; 2014; Vol. 6, 636.

Recently, alkenes with allylic positions prone to be oxidized have been used to generate allyl cations. Even though such substrates have been previously used for the metal-catalyzed generation of π-allyl intermediates,[42] in 2008 the group of Bao discovered that 2,3-dichloro-5,6-dicyanoquinone (DDQ) was able to oxidize the allylic C–H bonds of 1,3-diaryl-propenes to form allyl cations (Scheme 11).[15a] Such oxidation takes place through a first single electron transfer (SET), followed by a hydrogen atom transfer (HAT), both performed by DDQ and with the absence of a metal catalyst. The resulting allyl cations are finally coupled with 1,3-diketones and β-keto-esters, acting as nucelophiles.



Scheme 11 Example of allyl cation generation by Bao through the oxidation of allylic positions with DDQ

Since the publication of Bao's paper in 2008, multiple works have been published using the same strategy to form allylic C–C,[43] C–O,[44] C–P[45] and C–N[46] bonds.

[42] Wang, P. S.; Gong, L. Z. *Acc. Chem. Res.* **2020**, *53*, 2841.
[43] (a) Kong, S.; Zhang, L.; Dai, X.; Tao, L.; Xie, C.; Shi, L.; Wang, M. *Adv. Synth. Catal.* **2015**, *357*, 2453; (b) Cheng, D.; Lijun Wu, L.; Deng, Z.; Xu, X.; Yan J. *Adv. Synth. Catal.* **2017**, *359*, 4317.
[44] Xu, T. T.; Jiang, T. S.; Han, X. L.; Xu, Y. H.; Qiao, J. P. *Org. Biomol. Chem.* **2018**, *16*, 5350
[45] Chen,Q.; Wen, C.; Wang, X.; Yu, G.; Ou, Y.; Huo, Y.; Zhang, K. *Adv. Synth. Catal.* **2018**, *360*, 3590.
[46] Wang, Z.; Mo, H.; Cheng, D.; Bao, W. *Org. Biomol. Chem.* **2012**, *10*, 4249.

2.5. Catalytic cleavage of C(sp^2)–C(sp^2) bonds with Rh-carbynoids

2.5.1. Hypothesis of the project

Even though metal-carbynes have been key catalysts in alkyne metathesis,[3] their catalytic generation and general application in catalytic carbyne transfer has been largely unexplored, mainly due to the lack of suitable monovalent carbon sources (Figure 4A).

Recently, our group demonstrated the first catalytic generation of diazomethyl radicals [N_2=C(·)–R] as carbyne equivalents by means of photoredox catalysis.[47,48] This work highlighted the under-appreciated ability of neutral carbynes to form three new bonds and provided the fundaments of an "assembly-point" coupling for chiral center construction, through a C–H bond diazomethylation reaction in aromatic feedstocks and drug molecules.

Considering our previous results, we believe that such stable carbyne sources decorated with a hypervalent iodine moiety [$I^{(III)}$(Ar)(OTf)] and a diazo functionality (=N_2) might serve as an alternative to the use of metal carbynes for the catalytic transfer of monovalent carbon units. We recently questioned whether well-known dirhodium catalysts in diazo activation[49] might generate Rh-carbynoids as $I^{(III)}$-substituted Rh-carbenes. Considering the outstanding leaving group ability of the $I^{(III)}$-moiety[50] and weakness of the hypervalent bond, we anticipated that the electrophilic carbon center of the Rh-carbynoid would emulate the carbene/carbocation behavior of a monovalent cationic carbyne (:$^+$C–R), and enable a novel route to allylic cations from alkenes, by the insertion of the monovalent carbon unit in the C(sp^2)–C(sp^2) bond (Figure 4B).

Such a process, that involves a σ- and π-bond activation of the alkene double bond and uses both sp^2-hybridized carbons as functional groups, would be a rare example of a catalytic cleavage of strong double C–C bonds (BDE, H_2C=CH_2 = 174.1 kcal/mol), besides processes of metathesis[51] or rearrangements.[52] It would also represent a new way for catalytic skeletal remodeling, complementing "cut and sew" and deconstructive transformations based on single

[47] Wang, Z.; Herraiz, A. G.; Del Hoyo, A. M.; Suero, M. G. *Nature* **2018**, *554*, 86.
[48] For a review in photoredox catalysis, see: Shaw, M. H.; Twilton, J.; MacMillan, D. W. C. *J. Org. Chem.* **2016**, *81*, 6898.
[49] (a) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911; (b) Davies, H. M. L.; Beckwith, R. E. J. *Chem. Rev.* **2003**, *103*, 2861.
[50] Okuyama, T.; Takino, T.; Sueda, T.; Ochiai, M. *J. Am. Chem. Soc.* **1995**, *117*, 3360.
[51] (a) Vougioukalakis, G. C.; Grubbs, R. H. *Chem. Rev.* **2010**, *110*, 1746; (b) Ludwig, J. R.; Zimmerman, P. M.; Gianino, J. B.; Schindler, C. S. *Nature* **2016**, *533*, 374.
[52] Jiménez-Núñez, E. S.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326.

C–C bond functionalization.[53] Notably, accessing allyl intermediates by C(sp^2)–C(sp^2) bond cleavage would represent a complementary, but clearly different strategy, to the well-established transition-metal-catalyzed allylations[54] or allylic C–H bond functionalizations.[55] Herein, we disclose the successful development of a Rh-catalyzed carbyne transfer platform for the catalytic cleavage of C(sp^2)–C(sp^2) bonds that provides a novel route to allylic building blocks.

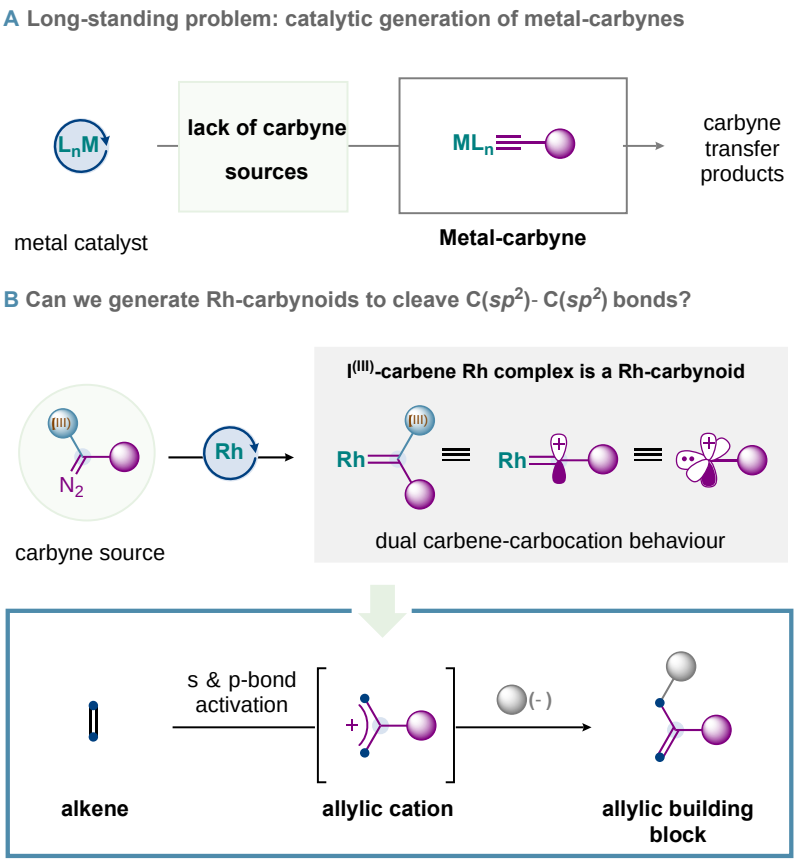
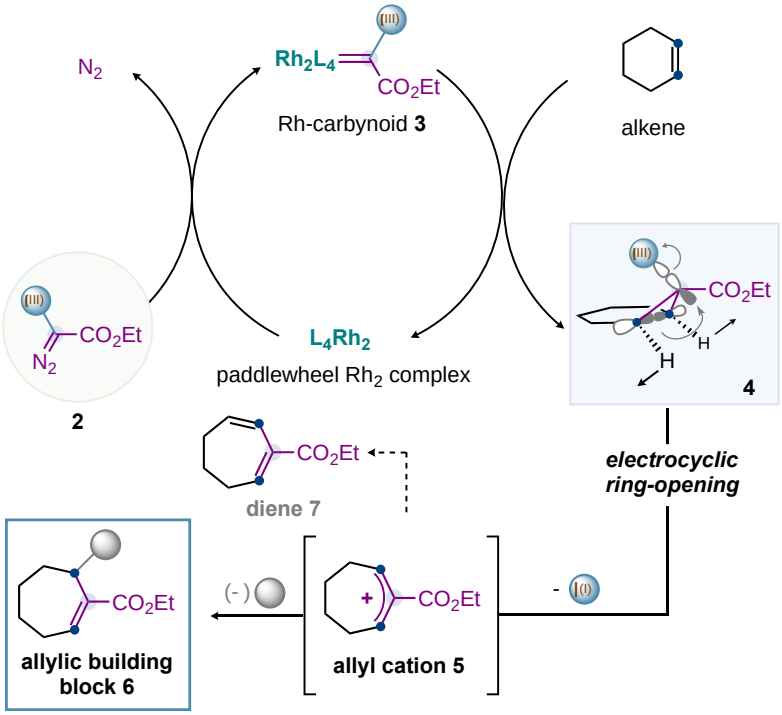


Figure 4

[53] For recent selected examples, see: (a) Xia, Y.; Lu, G.; Liu, P.; Dong, G. *Nature* **2016**, *539*, 546; (b) Roque, J. B.; Kuroda, Y.; Göttemann, L. T.; Sarpong, R. *Science* **2018**, *361*, 171; (c) Xu, Y.; Qi, X.; Zheng, P.; Berti, C. C.; Liu, P.; Dong, G. *Nature* **2019**, *567*, 373; (d) Smaligo, A. J.; Swain, M.; Quintana, J. C.; Tan, M. F.; Kim, D. A.; Kwon, O. *Science* **2019**, *364*, 681; For a review: (e) Souillart, L.; Cramer, N. *Chem. Rev.* **2015**, *115*, 9410.
[54] (a) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921; (b) López, F.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824; (c) Cheng, Q.; Tu, H.-F.; Zheng, C.; Qu, J.-P.; Helmchen, G.; You, S.-L. *Chem. Rev.* **2019**, *119*, 1855.
[55] Newton, C. G.; Wang, S.-G.; Oliveira, C. C.; Cramer, N. *Chem. Rev.* **2017**, *117*, 8908.

2.5.2. Proposed mechanism

We envisioned that the selective diazo activation of reagent **2** with a paddlewheel dirhodium complex L_4Rh_2 would conduct to a highly electrophilic Rh-carbynoid **3**. The latter species would cyclopropanate alkenes to generate a transient cyclopropyl-$I^{(III)}$ intermediate **4**. In analogy to the well-known ring-opening of cyclopropyl tosylates or cyclopropyl bromides with silver salts[12b] and considering the outstanding leaving group ability of hypervalent iodine moiety,[50] we thought **4** would open in concert with the departure of the $I^{(III)}$ leaving group. Such ring opening would happen through a disrotatory mode, following the Woodward−Hoffmann−DePuy rules. This process would lead to a putative allylic cation **5** able to provide the desired allylic product **6** by nucleophile attack, or diene **7** by proton elimination.

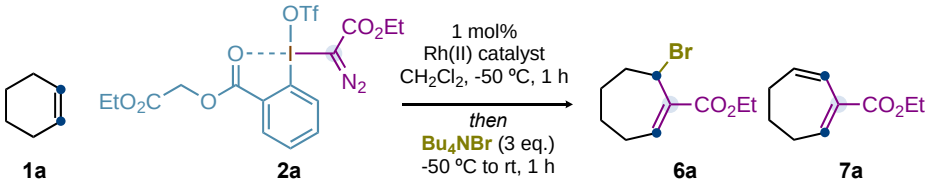


Scheme 12 Proposed mechanism for the catalytic cleavage of C(sp^2)–C(sp^2) bonds with Rh-carbynoids

2.5.3. Reaction optimization

The optimized reaction conditions were obtained by studying the reaction variables as shown in Tables 1–3. We started by evaluating different Rh(II) catalysts. To a mixture of cyclohexene (5 equiv.) and the desired Rh(II) catalyst (1 mol%) in CH_2Cl_2 at -50 ºC, was added

dropwise a solution of **2a** in CH_2Cl_2 during 1 h. After this time, Bu_4NBr (3 equiv.) was added at -50 °C and the resulting mixture was allowed to reach r.t. in 1 h. Initial successful results were found using $Rh_2(Oct)_4$, obtaining allyl bromide **6a** in a promising 17% yield (Table 1, entry 1). Other catalysts such as $Rh_2(OPiv)_4$, $Rh_2(OAc)_4$, $Rh_2(Cap)_4$ or $Rh_2(hfb)_4$ did not give the desired product (Table 1, entries 2–7). Instead, the use of the more sterically demanding catalysts $Rh_2(Adc)_4$ or $Rh_2(esp)_2$ (Du Bois catalyst)[56] provided significantly superior levels of efficiency to obtain **6a** (30 and 48% yield, respectively) and the formation of diene **7a** in less than 10% yield (Entries 8 and 9).[57]

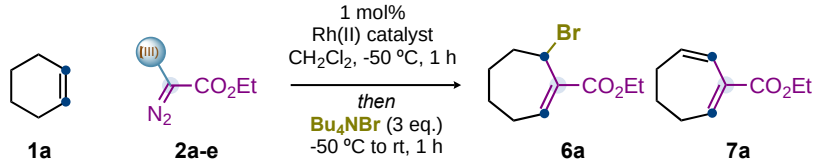


entry	Rh catalyst	yield **6a** (**7a**) [%]
1	$Rh_2(Oct)_4$	17 (0)
2	$Rh_2(OPiv)_4$	0 (0)
3	$Rh_2(TPA)_4$	0 (0)
4	$Rh_2(OAc)_4$	0 (0)
5	$Rh_2(TFA)_4$	0 (0)
6	$Rh_2(Cap)_4$	0 (0)
7	$Rh_2(hfb)_4$	0 (0)
8	$Rh_2(Adc)_4$	30 (8)
9	$Rh_2(esp)_2$	48 (10)

Table 1 Catalyst optimization

After identifying $Rh_2(esp)_2$ as the most promising catalyst, we questioned whether the nature of reagent **2** could have a substantial impact on the efficiency of the process. First, we realized that the pseudocyclic structure of reagent **2a** was crucial for enabling the synthesis of allylic bromide **6a**, since no conversion was observed for cyclic reagent **2b** (Table 2, entry 2) and very poor yields were obtained for the linear analogue **2c** (Table 2, entry 3). Finally, we were pleased to find that pseudocyclic reagents **2d** and **2e** with BF_4 and PF_6 as counterions, dramatically improved the efficiency of the C(sp^2)–C(sp^2) cleaving process, obtaining **6a** in 62 and 76% of yield respectively (Table 2, entries 4 and 5). Next, we reevaluated the catalysts that previously gave the most promising results with **2a**, but we confirmed that $Rh_2(esp)_2$ was the most efficient one.

[56] Espino, C. G.; Fiori, K. W.; Kim, M.; Du Bois, J. *J. Am. Chem. Soc.* **2004**, *126*, 15378.
[57] Other Pd, Cu, Rh(I) and Rh(III) catalysts were tried in the initial attempts but with Pd and Cu no product was detected, and only traces of the desired product were observed by GC-MS with Rh(I) and Rh(III).



entry	Reagent **2**	Rh catalyst	yield **6a** (**7a**) [%]
1	**2a**	$Rh_2(esp)_2$	48 (10)
2	**2b**	$Rh_2(esp)_2$	0 (0)
3	**2c**	$Rh_2(esp)_2$	12 (11)
4	**2d**	$Rh_2(esp)_2$	62 (11)
5	**2e**	$Rh_2(esp)_2$	76 (13)
6	**2e**	$Rh_2(Oct)_4$	60 (0)
7	**2e**	$Rh_2(Adc)_4$	53 (5)

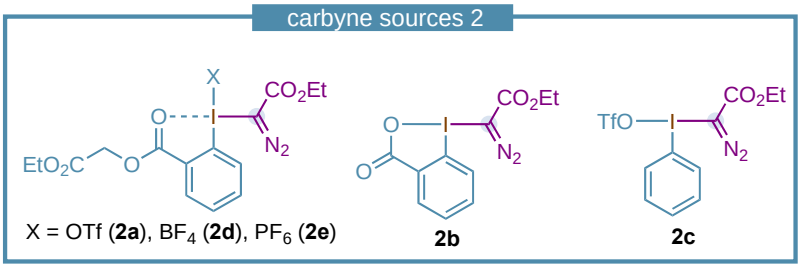
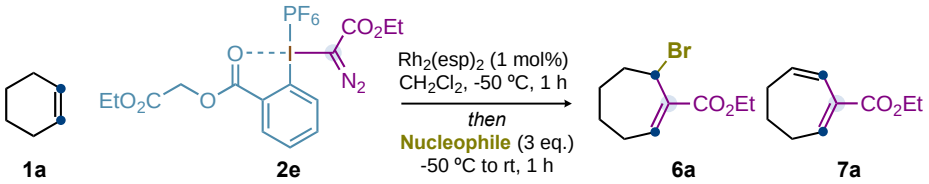


Table 2 Carbyne source optimization

Once we obtained the best combination of reagent **2** and catalyst, we evaluated different bromide sources. Neither the use of other ammonium and phosphonium salts, nor trimethylsilane bromide provided better results (Table 3, entries 1–7). Finally, we also assessed other parameters of the reaction. We appreciated that excess of alkene **1a** was needed to reach good efficiency, even though the use of more than 5 equivalents did not enhance the formation of product **6a** (Table 3, entries 8 and 9). This might suggest that such excess ensures full conversion in the ligand transfer event between the corresponding Rh-carbynoid **3** and cyclohexene, preventing the evolution of **3** through undesired pathways.[58] It is also worth mentioning, that longer addition times as well as lower and higher reaction temperatures were detrimental for the reaction (Table 3, entries 10–12).

[58] At present, the exact mechanisms by which Rh-carbynoid **3** evolves to other pathways instead of cyclopropanation is not fully understood. The dimerization by coupling with **2e** or C–H insertion with CH_2Cl_2, are a priori the potential undesired pathways; however, we did not find reaction products that support such evolutions.



1a **2e** **6a** **7a**

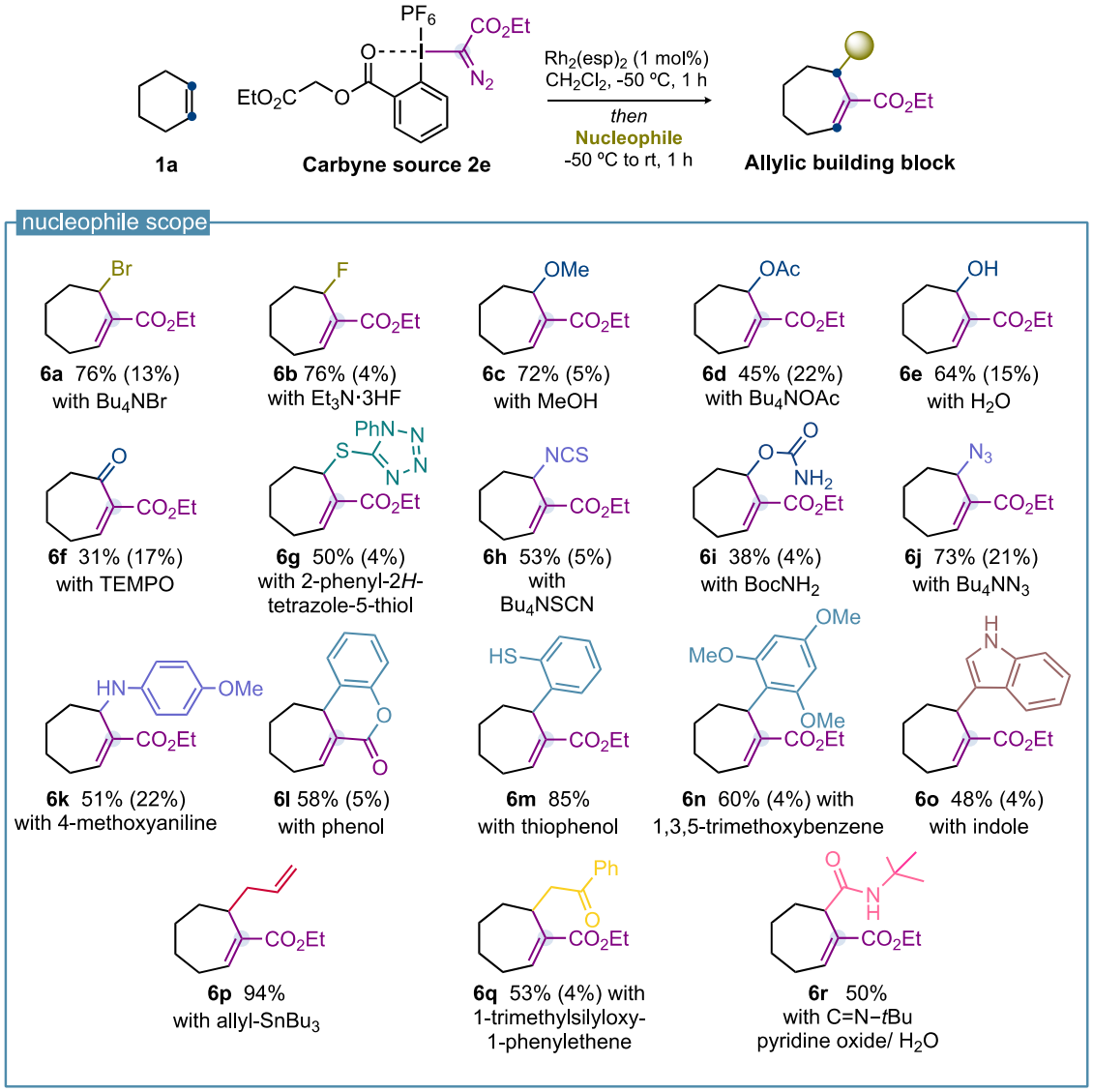
entry	Nucleophile	yield **6a** (**7a**) [%]
1	Bu_4NBr_3	57 (11)
2	$BnMe_3NBr$	70 (14)
3	Me_4NBr	0 (0)
4	$C_{16}H_{31}Me_3NBr$	73 (11)
5	Bu_4PBr	74 (13)
6	Ph_4PBr	65 (12)
7	Me_3SiBr	19 (5)
8	Bu_4NBr	72 (10)[a]
9	Bu_4NBr	45 (7)[b]
10	Bu_4NBr	56 (9)[c]
11	Bu_4NBr	29 (7)[d]
12	Bu_4NBr	46 (9)[e]

[a] Reaction carried out with 10.0 equiv. of cyclohexene; [b] Reaction carried out with 1.0 equiv. of cyclohexene (30% of cyclohexene was detected in the reaction crude); [c] 2 hours addition of **2e**; [d] Reaction carried out at -78 ºC%; [e] Reaction carried out at -30 ºC.

Table 3 Bromide source reaction conditions optimization

2.5.4. Scope of the catalytic cleavage of C(sp^2)–C(sp^2) bonds for allylic building block synthesis

Having the optimized conditions in hand, we evaluated the nucleophile scope by using cyclohexene and reagent **2e**.



[a] Performed with cyclohexene (1.0 mmol, 5 equiv.), reagent **2e** (0.2 mmol, 1 equiv.), CH_2Cl_2 (0.1 M) and nucleophile (3 – 20 equiv.). Yield in parentheses are of diene **7a**.

Table 4 Nucleophile scope

We were delighted to see that our methodology worked well for a broad and diverse range of simple nucleophiles that created: (i) carbon–halogen bonds with Bu_4NBr (**6a**), and $Et_3N{\cdot}3HF$ (**6b**); (ii) carbon–oxygen bonds with methanol (**6c**), tetrabutylammonium acetate (**6d**), water (**6e**), TEMPO (**6f**), and *tert*-butyl carbamate (**6i**); (iii) carbon–sulfur bonds with thiols (**6g**); and (iv) carbon–nitrogen bonds with Bu_4NSCN (**6h**), Bu_4NN_3 (**6j**), and 4-methoxyaniline (**6k**), with yields that ranged from 38 to 76 %. Moreover, our strategy permitted to use a diverse range of carbon nucleophiles, enabling C–H arylation processes with electron-rich arenes (**6l**–**n**) or heterocycles (**6o**), allylation with allyl-$SnBu_3$ (**6p**), alkylation with the trimethylsilyl enol ether derived from acetophenone (**6q**), or amidation with the combination of *tert*-butylisocyanide, pyridine oxide and water (**6r**) (48–94 % of yield). It is noteworthy the

high degree of complexity introduced in the constructive cleaving process: one new single C–C bond and one new double C–C bond are created, in addition to the formation of a chiral center at one of the *sp*^{2}-hybridized carbons of cyclohexene using some of the most simple and abundant nucleophiles. Nevertheless, it is also important to mention that in most of the cases the elimination byproduct **7a** was also formed (yields of **7a** are in parenthesis). It is well known from the ring-opening of *gem*-dihalo-cyclopropanes, that the presence of a base enhances the formation of the elimination product.[59]

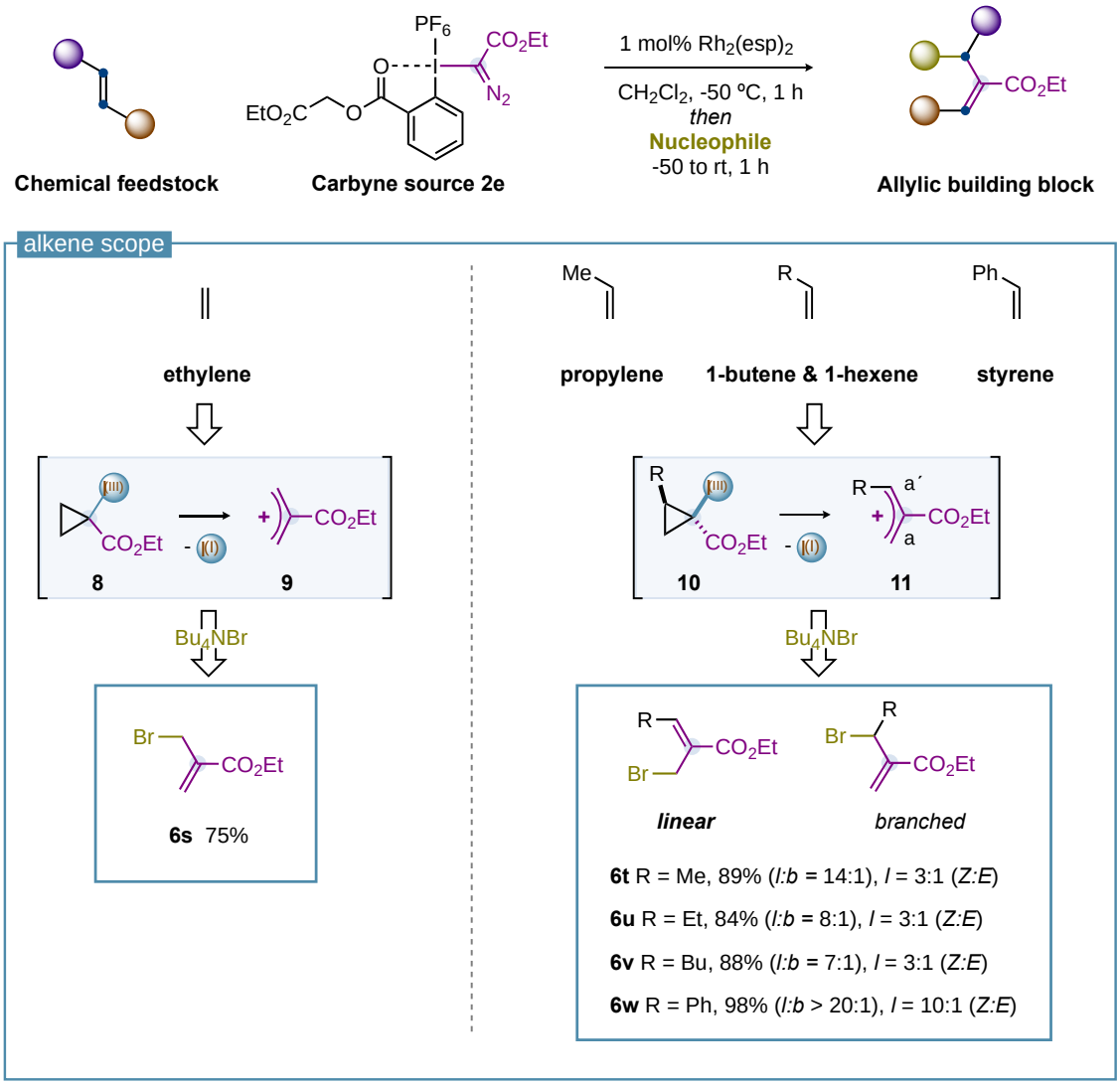


Table 5 Alkene scope: ethylene and mono-substituted alkenes

Next, we wondered whether we could convert olefin petrochemical feedstocks and styrenes into allylic building blocks. We embarked on this journey by first evaluating ethylene,

[59] Sydnes, L. K.; Alnes, K. F. S.; Pettersen, A.; Brinker, U. H. *Monatsh. Chem.* **2009**, *140*, 479.

the most widely produced chemical feedstock by the petrochemical industry. We were glad to find that our methodology was able to convert ethylene into allyl bromide **6s** with high efficiency (75 % of yield). To the best of our knowledge, this is the first example of a catalytic constructive scission in ethylene that provokes its conversion to an allyl bromide. This result can be explained by the initial formation of intermediate **8**, subsequent electrocyclic ring-opening and bromide attack to the resulting allyl cation **9**. Also, our process worked well with propylene, the most important feedstock of the α-olefin family. In this case, allyl bromide **6t** was obtained with a 14:1 *linear*:*branched* selectivity and in 89 % of yield. The 3:1 selectivity observed in favor for the *Z* isomer in the linear isomer is suggesting the preferential formation of **10**, where substituent R and $I^{(III)}$ moiety are in relative *syn* disposition. Subsequently, the electrocyclic ring-opening by disrotatory mode would conduct to **11**, (the R group rotates inwardly), which undergoes bromide attack at the less hindered electrophilic carbon site (α position). Moreover, while similar efficiencies and selectivities were obtained for 1-butene (**6u**; yield = 84 %; *l*:*b* = 8:1; *l* = 3:1 (*Z*:*E*)) and 1-hexene (**6v**; yield = 88 %; *l*:*b* = 7:1; *l* = 3:1 (*Z*:*E*)), the reaction with styrene provided excellent yield and selectivities in favor of the linear isomer **6w** (yield = 98 %; *l*:*b* > 20:1; *l* = 10:1 (*Z*:*E*)).

On the other hand, we anticipated that 1,2-disubstituted alkenes such as (*E*)-2-butene and (*E*)-β-methyl-styrene would potentially challenge our methodology: the formation of **12** and subsequent electrocyclic ring-opening, would provide a trisubstituted allyl cation **13** with two similar electrophilic sites (α and α′ position), and mixtures of allyl bromides could be formed. However, we were delighted to find that the reaction gave allyl bromides **6x** and **6y** with high regio- and stereoselectivity (**6x**: yield = 70 %; *Z*:*E* = 10:1; **6y**: yield = 70 %, *Z*:*E* 16:1). Furthermore, our insertion reaction enabled ring expansion in larger rings, including cycloheptene (**6z**), cyclooctene (**6aa**) and cyclododecene (**6ab**) in moderate yields (yields = 48–54 %).

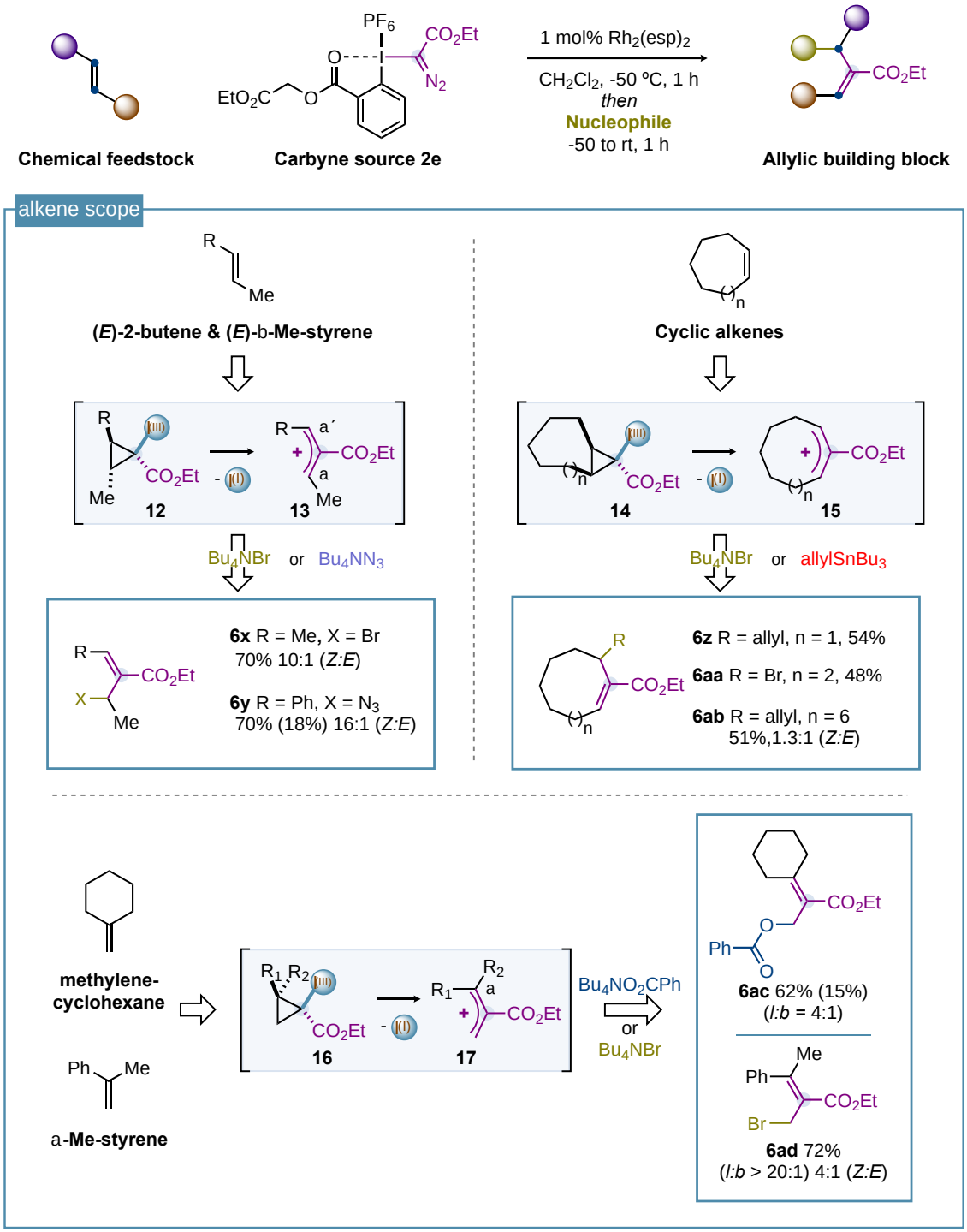


Table 6 Alkene scope: 1,2- and 1,1-di-substituted alkenes

An important feature of our C(sp^2)–C(sp^2) bond cleavage process is the ability to transform simple alkenes into others with higher substitution. We believed that we could provide a new approach for the synthesis of synthetic challenging tetrasubstituted olefins, which lack a general synthesis approach and are present in drug molecules and molecular motors. Based on previous results, we anticipated that 1,1-disubstituted olefins, which are

commercially available or easy to make from ketones by ylide olefination,[60] could be suitable substrates to reach the tetrasubstituted olefin core. We were pleased to find that commercial methylenecyclohexane and α-methylstyrene could be efficiently converted into tetrasubstituted olefins **6ac** and **6ad** by using Bu_4NO_2CPh and Bu_4NBr as nucleophiles, in 62 and 72 % of yields respectively. It is noteworthy the high degree of regioselectivity observed for **6ad** (*l*:*b* > 20:1) compared to **6ac** (*l*:*b* = 4:1). We believe this might derive from the nature of the nucleophile. In the case of bromide, it can either attack selectively the γ position, or first attack the α position, initially forming the branched isomer, and subsequently isomerize to the linear bromide.[61] However, in the case of benzoate, since a C–O bond is forming, the isomerization might be more difficult to take place, due to its higher BDE compared to C–Br bonds (BDE, allylic C–O = 80.1 kcal/mol; allylic C–Br 59 kcal/mol).[62]

The strategic advantage of inserting a monovalent carbon unit into a C(sp^2)–C(sp^2) bond was further exploited to induce cyclization reactions. Simple alkenes with a remote alcohol nucleophile and natural product derivatives were selectively cyclized with moderate to excellent yields (**14**−**18**, 52−91 % yield). On the basis of the previous results, we postulate that the cyclization reactions involve the selective catalytic generation of carbocations **19**−**21** that selectively evolve to the heterocyclic products through exo (**19**, **20**, **22**) and endo cyclizations (21).

[60] Pine, S. H.; Shen, G. S.; Hoang, H. *Synthesis* **1991**, 165.
[61] (a) Young, W. G.; Winstein, S.; Goering, H. L. *J. Am. Chem. Soc.* **1951**, *73*, 1958; (b) Boshkow, J.; Scattolin, T.; Schoenebeck, F.; Carreira, E. M. *Helv. Chim. Acta* **2018**, *101*, 1.
[62] Blanksby, S. J.; Ellison, G. B. *Acc. Chem. Res.* **2003**, *36*, 255.

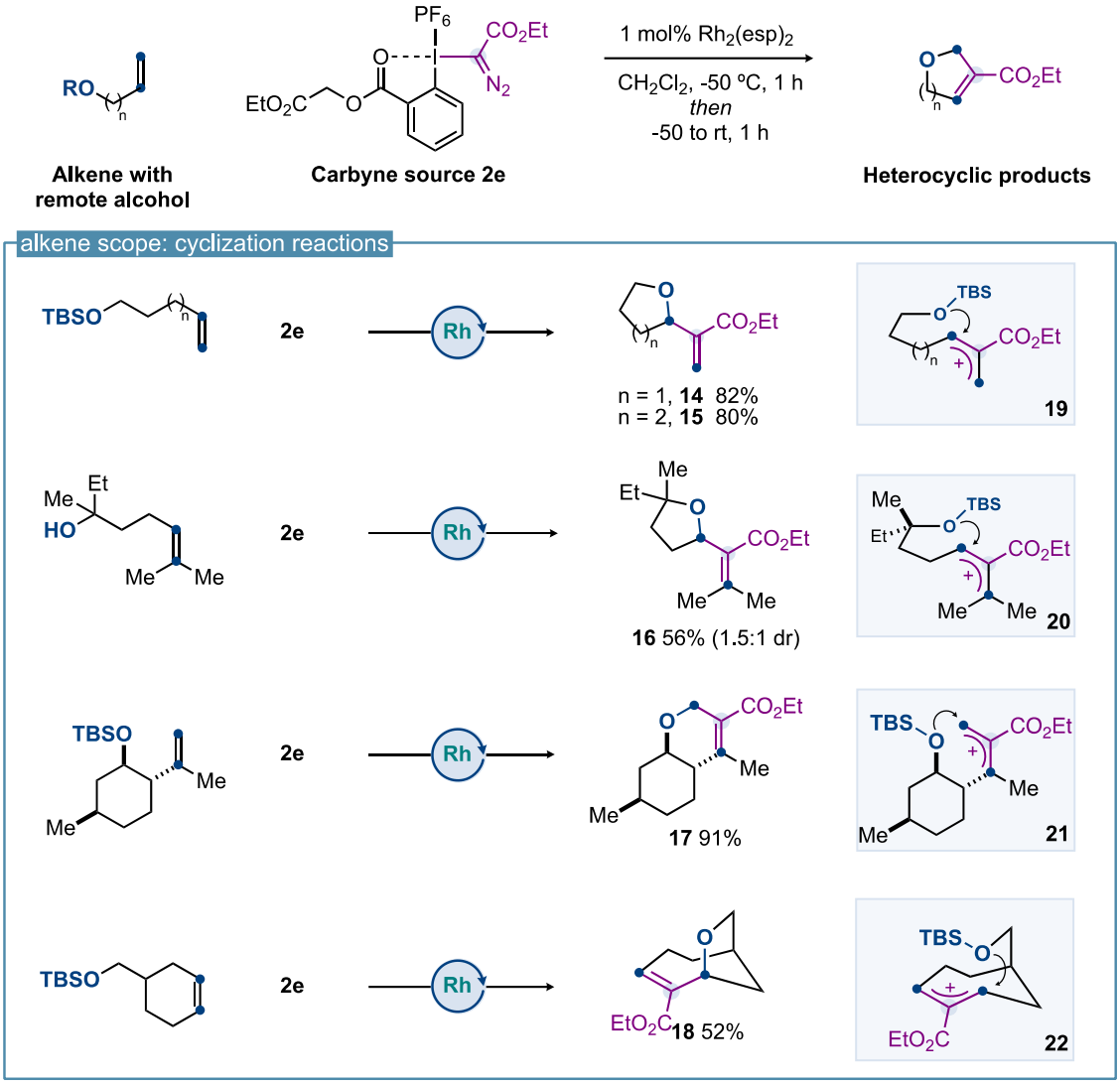
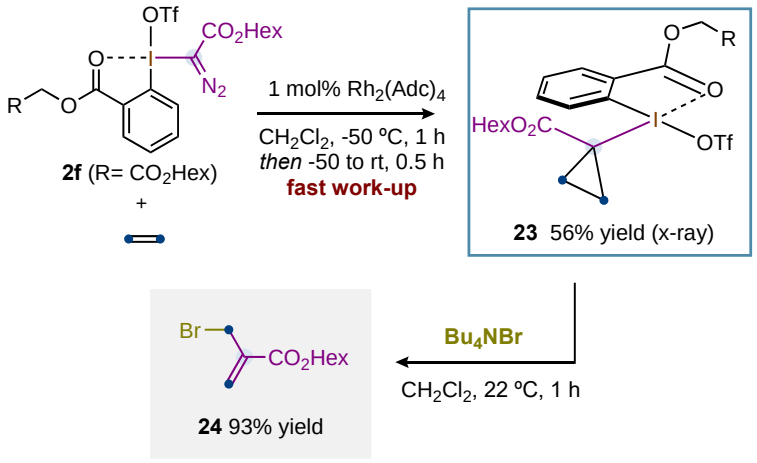


Table 7 Alkene scope:

Finally, we wanted to provide evidence of cyclopropyl hypervalent iodine intermediates **4**, despite the well-known thermodynamic instability of alkyl-I$^{(III)}$ species. Initial efforts toward the isolation of cyclopropyl-I$^{(III)}$ intermediates from mono- and disubstituted olefins (styrene and cyclohexene respectively) at -50 °C were unsuccessful. It is known that the electrocyclic ring-opening in substituted cyclopropyl tosylates is kinetically favored over the non-substituted derivatives.[12b,25a,b] With this information, we hoped that trapping the corresponding cyclopropyl-I$^{(III)}$ intermediate derived from ethylene could be more feasible. By using reagent **2f** and $Rh_2(Adc)_4$ as a catalyst, we were glad to isolate cyclopropyl-I$^{(III)}$ compound **23** at room temperature as a relative stable white solid in 56 % yield, the structure of which was confirmed by single-crystal X-ray diffraction analysis. To the best of our knowledge, this is the first isolable alkyl-I$^{(III)}$ compound of this class, and we hope this result may inspire future endeavors

for the design of novel hypervalent alkyl-$I^{(III)}$ reagents.[63] As a control experiment, we demonstrated that the treatment of **23** with Bu_4NBr gave the expected allyl bromide **24** with high efficiency (93% of yield).



Scheme 13 Isolation of alkyl-$I^{(III)}$ reagent **23**

2.5.5. Expanding the scope: functionalization of 1,3-dienes via catalytic cleavage of C(sp^2)–C(sp^2) bonds with Rh-carbynoids

1,3-butadiene is the smallest conjugated diene and one of the major world commodieties, with an annual production of more than 10 million ton, and an incremental growth of 1–3 % per year. With regards of its production, more than 95 % of butadiene is obtained as a side product of ethylene steam cracking, even though in the recent years more sustainable variants are being developed, like the production of butadiene from biomass.[64] Other simple 1,3-dienes such as isoprene,[65] piperylene or cyclopentadiene are also produced in high amounts, even though they are not comparable to butadiene.

The main use of these simple conjugated dienes is found in the polymer industry, being styrene-butadiene rubber and polybutadiene the polymers with the highest volume in butadiene processing. Nevertheless, due to their high abundance, simple dienes and 1,3-butadiene in particular, have been long used in fine chemistry for the synthesis of more complex, highly functionalized products.

[63] Bosnidou, A. E.; Muñiz, K. *Chem. Eur. J.* **2019**, *25*, 13654.
[64] Makshina, E. V.; Dusselier, M.; Janssens, W.; Degrève, J.; Jacobs, P. A.; Sels, B. F. *Chem. Soc. Rev.* **2014**, *43*, 7917.
[65] Sharkey, T. D. *Endeavour* **1996**, *20*, 74.

Considering the excellent results obtained in the catalytic cleavage of C(sp^2)–C(sp^2) bonds of alkenes with rhodium carbynoids and the ubiquity of dienes in polymer industry[66] and nature,[67] we wondered whether we could expand the scope of our carbyne transfer platform and apply it to the functionalization of dienes. Our aim was to transform simple massively produced dienes such as 1,3-butadiene or isoprene into valuable highly functionalized dienes by inserting a monovalent carbon unit into the double bond and trapping the allyl cation formed along the reaction with a broad range of nucleophiles. This methodology would represent a novel approach for the generation of substituted dienes, which are not trivial to be synthesized, as it will be explained in Chapter IV.

Based on our previous results, our hypothesis was that the cyclopropanation step (***int-1***) could happen stereoselectively, forming ***int-2-cis*** preferentially over ***int-2-trans***, having the hypervalent moiety and the vinylic group in *cis* disposition (Figure 5). Each cyclopropyl intermediate would conduct to a different diastereomer in the allyl cation (***int-3-cis*** and ***-trans*** respectively).

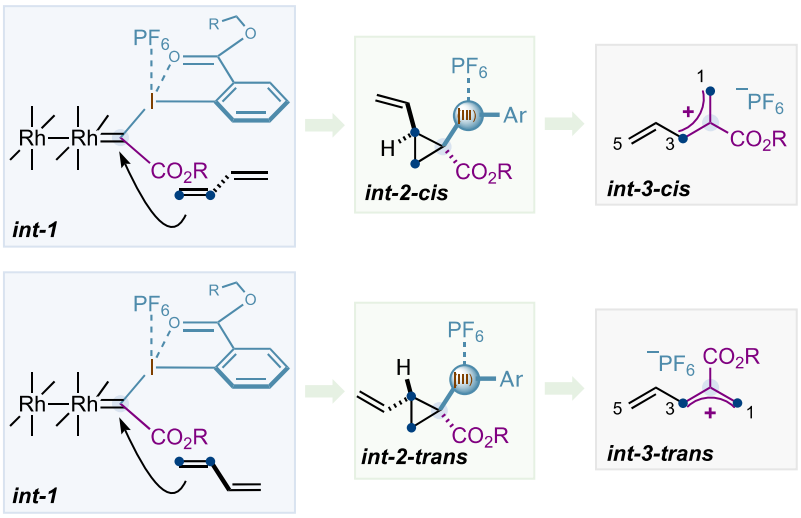


Figure 5 Two different allyl cations could be generated depending on the relative disposition of the Rh-carbynoid and butadiene

Moreover, the nucleophilic attack to the allyl cations generated along the reaction could take place in the 3 different electrophilic positions, placed in C1, C3 and C5 of each allyl cation. In total, 5 different isomers could be obtained from this reaction. From allyl cation ***int-3-cis***,

[66] Ricci, G.; Pampaloni, G.; Sommazzi, A.; Masi, F. *Macromolecules* **2021**, *54*, 5879.
[67] Hubert, P.; Seibel, E.; Beemelmanns, C.; Campagne, J. M.; de Figuereido, R. M. *Adv. Synth. Catal.* **2020**, *362*, 5532.

the nucleophile could attack the position (i) on C1, forming a *cis*-1,2-substituted-pentadiene; (ii) on C3, forming the 2,3-substituted skipped diene and (iii) on C5, forming a 2,5-substituted-pentadiene. On the other hand, in the case of the ***int-3-trans*** allyl cation, the attack on C1 would give the *trans*-isomer of the 1,2-substituted-pentadiene. The nucleophilic attack on the C3 and C5 positions of this isomer, would conduct to the same isomers as obtained from the *cis*-allyl cation.

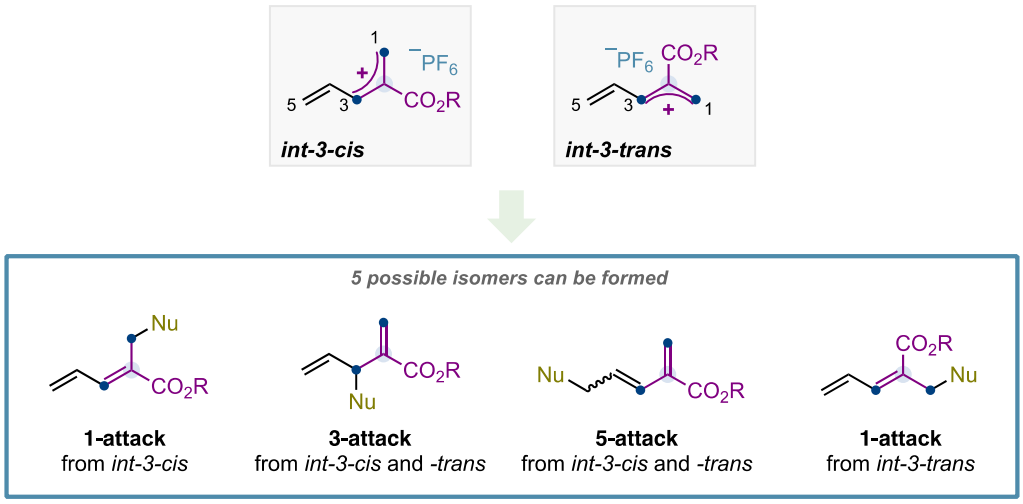
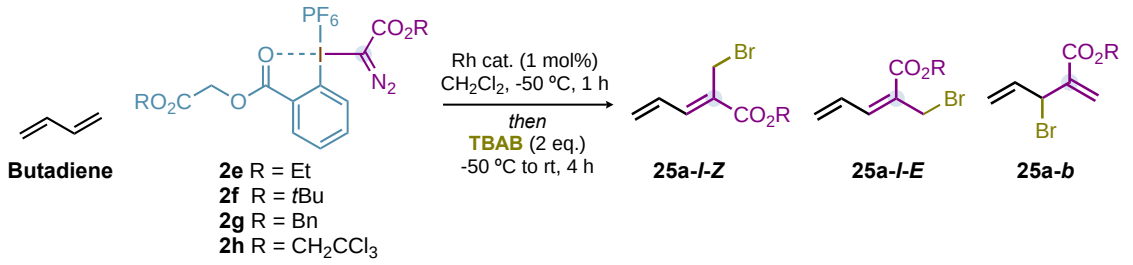


Figure 6 Five possible isomers could be formed depending on the position of the nucleophilic attack

In order to apply our carbyne transfer platform to dienes, we started by employing the same reaction conditions as we used with the alkenes, adding dropwise a solution of salt **2e** on top of a mixture of butadiene (5 equiv.) and $Rh_2(esp)_2$ (1 mol%) in CH_2Cl_2 (0.067 M) during 1 h. Once the carbyne source salt **2e** was fully consumed, tetrabutylammonium bromide (2 equiv.) was added to the solution and the resulting mixture was left to warm up to room temperature in 4 h. With these reaction conditions we were glad to obtain the desired products in 70 % of yield. Even though only the lineal isomer was generated, a 2:1 ratio *Z*:*E* mixture was attained. In order to improve the diastereoselectivity of the nucleophilic attack, bromide in this case, we conducted an optimization study. First of all, we tried different rhodium(II) catalysts. We observed that rhodium(II)-catalysts other than $Rh_2(esp)_2$ diminished the reaction efficiency and did not improve the diastereoselectivity (Table 8, entries 1 – 5). Next, we changed the carbyne source **2**, and we noticed that more sterically demanding substituents like *tert*-butyl- (**2f**), benzyl- (**2g**) or 2,2,2-trichloroethyl- (**2h**) groups had a high impact on the *Z*/*E* selectivity, increasing it up to 10:1, despite slightly decreasing the yield (Table 8, entries 6 – 8).



Butadiene

2e R = Et
2f R = *t*Bu
2g R = Bn
2h R = CH_2CCl_3

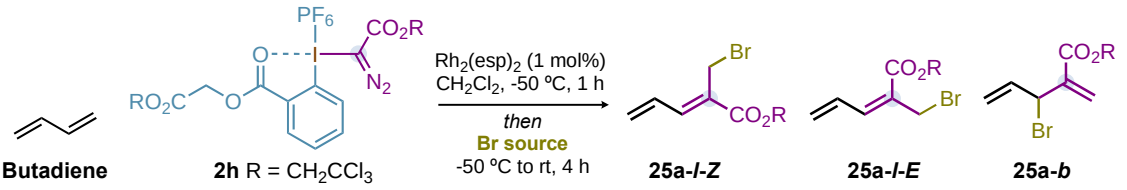
25a-*l*-*Z* **25a-*l*-*E*** **25a-*b***

Entry	Reagent **2**	Catalyst	Yield **25a** (%)[b]	**25a**, ***l*-*Z*:*l*-*E*:*b***
1	**2e**	$Rh_2(esp)_2$	70	2:1:0
2	**2e**	$Rh_2(Adc)_4$	67	2:1:0
3	**2e**	$Rh_2(Oct)_4$	53	2:1:0
4	**2e**	$Rh_2(OAc)_4$	nd[c]	-
5	**2e**	$Rh_2(OPiv)_4$	52	3:1:0
6	**2f**	$Rh_2(esp)_2$	57	4:1:0
7	**2g**	$Rh_2(esp)_2$	55	3:1:0
8	**2h**	$Rh_2(esp)_2$	60	10:1:0

[a] Reaction carried out with 5.0 equiv. of butadiene (15% v/v in hexane) and 1.0 equiv. of reagent **2**; [b] Yield refers to the addition of **25a-*l*-*Z***, **25a-*l*-*E*** and **25a-*b***; [c] nd referes to not detected; [d] esp = α, α, α′ ,α′-tetramethy-1,3-benzenedipropanoate; TBAB = tetrabutylammonium bromide.

Table 8 Catalyst and carbyne source optimization

With the improved selectivity, we moved on to increase the yield of the reaction. In this sense, we changed the equivalents of butadiene, but we realized that neither more nor less equivalents improved the results we obtained with 5 equivalents. (Table 9, entries 1 – 4). We also changed the amount of bromide source and it was seen that higher amounts of tetrabutylammonium bromide (TBAB) diminished the efficiency of the process, even though the selectivity seemed to increase (entry 5). On the other hand, lower amounts of TBAB improved the yield, getting to 82 % of isolated yield by using 1.1 equivalents (entries 5) and keeping excellent regioselectivity (*linear*:*branched* > 20:1) and moderate diastereoselectivity (*Z*:*E* = 5:1). We finally tried some other bromide sources like tetrabutylphosphonium bromide (Bu_4PBr, entry 7) and bromotrimethylsilane (Me_3SiBr, entry 8). Bu_4PBr provided similar the selectivity, even though the yield was lower but Me_3SiBr did not drive to the desired product.



Butadiene **2h** R = CH_2CCl_3 **25a-*l*-*Z*** **25a-*l*-*E*** **25a-*b***

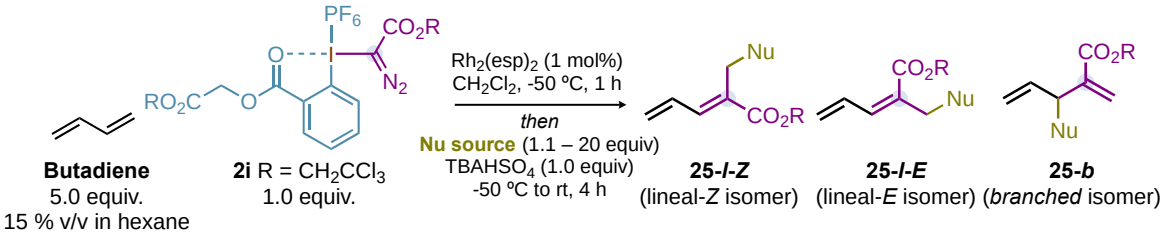
Entry	Butadiene equiv.	Br source (equiv.)	Yield **25a** (%)[b]	**25a**, ***l*-*Z*:*l*-*E*:*b***
1	10 equiv.	TBAB (5)	60	8:1:0
2	2.5 equiv.	TBAB (5)	56	8:1:0
3	1.5 equiv.	TBAB (5)	45	8:1:0
4	Bubbling[c]	TBAB (5)	59	9:1:0
5	5.0 equiv.	TBAB (10)	34	14:1:0
6	5.0 equiv.	TBAB (1.1)	76 (82)	5:1:0
7	5.0 equiv.	Bu_4PBr (1.1)	72	7:1:1
8	5.0 equiv.	Me_3SiBr (1.1)	nd[d]	-

[a] Yield refers to the addition of **25a-*l*-*Z***, **25a-*l*-*E*** and **25a-*b***; [b] The solution of $Rh_2(esp)_2$ in CH_2Cl_2 was bubbled with butadiene at -50 ºC for 1 min.; [c] nd refers to not detected; [d] esp = α, α, α′, α′-tetramethy-1,3-benzenedipropanoate; TBAB = tetrabutylammonium bromide.

Table 9 Reaction conditions optimization

Once we had the optimized reaction conditions, we applied them to various nucleophiles. The use of different halides as nucleophiles like fluoride or chloride allowed us to obtain the desired products in 45 % and 72 % of yield respectively (Table 10, **25b** and **25c**). Regarding the regioselectivity, in both cases the lineal isomer was obtained preferentially, although a trend is observed, decreasing with the nucleophile size (from > 20:1 with Br to 2.5:1 with F). The explanation we found was that with smaller sizes, the nucleophile was able to reach the more sterically demanding branched position. However, the initial formation of the branched and subsequent isomerization to the lineal isomer cannot be discarded. If this was the case, the isomerization of bromide would be easier compared to chloride and this to fluoride.[62] Nonetheless, the diastereoselectivity is kept in all three cases, obtaining the *linear-Z* isomer preferentially, from 4:1 to 5:1. We also tried to use iodide as nucleophile and even that by H-NMR of the crude reaction the desired product seemed to be obtained, it was not stable under the purification conditions, neither with neutral silica nor alumina.

Other nucleophiles such as 1,3,5-trimethoxy-benzene (**25d**), methanol (**25e**) and *tert*-butanol (**25f**) allowed us to obtain the desired aryl and ether-substituted dienes in yields ranging between 35 – 69 %. The decrease in yield might be a consequence of the steric hinderance, being especially low with the biggest nucleophiles. In all cases the linear isomer was formed preferentially (from *l*:*b* ratio of 2.5:1 to >20:1), being the *E* conformation the most favored one (from *l*:*b* ratio of 7:1 to 2.5:1).



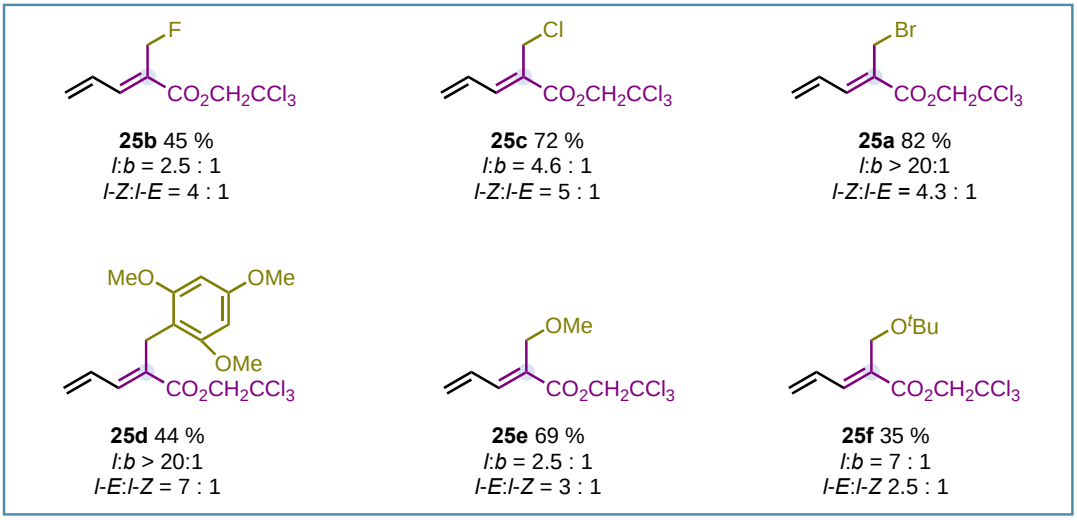
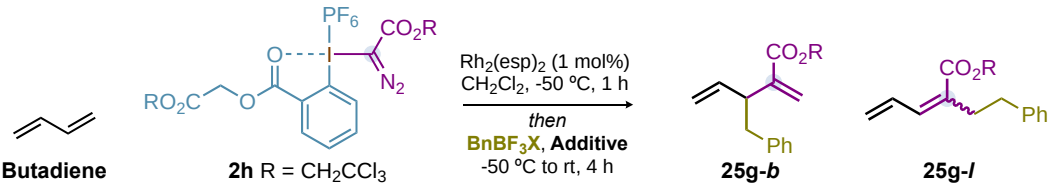


Table 10 Nucleophile scope

In an attempt to expand the nucleophile scope, we wondered whether boronic acids, esters or trifluoroborate salts could be used as sources of C-based nucleophiles given their ubiquity and broad use as nucleophiles. We hypothesized that given the size of the boronic counterpart, the nucleophilic attack could happen with high degree of regio- and diastereoselectivity. We first tried the same reaction conditions as with the previous nucleophiles. To our astonishment, when potassium benzyl-trifluoroborate ($BnBF_3K$) was employed as nucleophile, the branched isomer was obtained in more than 20:1 isomer ratio, even though the yield was moderate (41 %; table 11, entry 1). Analyzing the reaction crude by NMR and GC-MS it was observed that polymerization could be happening as well as side reactions between the product and the remaining butadiene from the reaction mixture. Furthermore, it was observed that the trifluoroborate salt was not completely soluble in the reaction mixture, being the possible cause of undesired reaction pathways. In order to improve the solubility of the salt we tried using tetrabutylammonium (TBA) instead of potassium as the counterion. Even though the solubility of the salt was much better, the efficiency of the reaction dropped (entry 2). Next, seeking a way to solubilize the Molander salts, we found a work by Carreira in which tetrabutylammonium bisulfate ($TBAHSO_4$) was used as a phase transfer

catalyst for the allylic vinylation of allylic alcohols using potassium alkenyltrifluoroborates.[68] Inspired by these results, we added 1 equivalent of $TBAHSO_4$ together with the $BnBF_3K$ salt and we observed that the yield increased up to 51 %, maintaining the high degree of regioselectivity (entry 3). With these encouraging results, we tried to improve the yield by changing the equivalents of $TBAHSO_4$ and $BnBF_3K$ (entries 4 – 8). The best results were found by using 1 equivalent of the bisulfate and 5 equivalents of the Molander salt. Finally, we also tried different phase transfer catalysts like the crown ether 18-crown-6 and other tetraalkylammonium salts (entries 9 – 12). However, none of them improved the yield of the reaction.



Butadiene **2h** R = CH_2CCl_3 **25g-*b*** **25g-*l***

Entry	Additive	Nucleophile	Yield **25a** (%)[a]	**25g, *b*:*l*[b]**
1	-	$BnBF_3K$ (2.5 equiv.)	41	> 20:1
2	-	$BnBF_3TBA$ (2.5 equiv.)	< 10	-
3	$TBAHSO_4$ (1 equiv.)	$BnBF_3K$ (2.5 equiv.)	51	> 20:1
4	$TBAHSO_4$ (10 mol%)	$BnBF_3K$ (2.5 equiv.)	18	> 20:1
5	$TBAHSO_4$ (0.5 equiv.)	$BnBF_3K$ (2.5 equiv.)	36	> 20:1
6	$TBAHSO_4$ (1 equiv.)	$BnBF_3K$ (5 equiv.)	65 (70)	> 20:1
7	$TBAHSO_4$ (2.5 equiv.)	$BnBF_3K$ (5 equiv.)	56	> 20:1
8	$TBAHSO_4$ (1 equiv.)	$BnBF_3K$ (10 equiv.)	53	> 20:1
9	18-Crown-6 (1 equiv.)	$BnBF_3K$ (5 equiv.)	51	> 20:1
10	$TBAH_2PO_4$ (1 equiv.)	$BnBF_3K$ (2.5 equiv.)	47	> 20:1
11	$TBAPF_6$ (1 equiv.)	$BnBF_3K$ (2.5 equiv.)	47	> 20:1
12	$TBABPh_4$ (1 equiv.)	$BnBF_3K$ (2.5 equiv.)	7	-

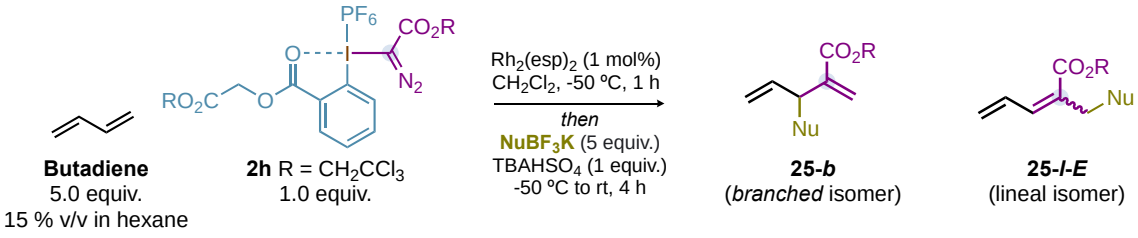
[a] NMR yields calculated by using anisole as internal standard; Yield in brackets referes to isolated yield; [b] *b*:*l* refers to the *branched* to *linear* isomers ratio; [c] esp = α, α, α′, α′-tetramethy-1,3-benzenedipropanoate; TBA = tetrabutylammonium; 18-Crown-6 = 1,4,7,10,13,16-hexaoxacyclooctadecane.

Table 11 Optimization table for the use of $BnBF_3K$ as nucleophile

Once we had the optimized conditions, we explored the scope of the trifluoroborate salts. We hypothesized that different substituents on the trifluoroborate salt could induce different substitution patterns in the nucleophilic attack. First of all, we used benzyl-substituted trifluoroborate salts with different para-substituents on the aromatic ring like methyl (**25h**), *tert*-butyl (**25i**), methyl-ester (**25j**) and trifluoromethoxy (**25k**). All of them worked with moderate to good yields (41 – 69 % of yield, table 12) and good to excellent regioselectivities (from 4:1 to > 20:1 *branched*:*lineal* ratio). Furthermore, more crowded systems like potassium

[68] Hamilton, J. Y.; Sarlah, D.; Carreira, E. M. *J. Am. Chem. Soc.* **2013**, *135*, 994.

1-pheny-ethyl-trifluoroborate also provided the branched isomer in excellent regioselectivity and moderate yield (**25l**).

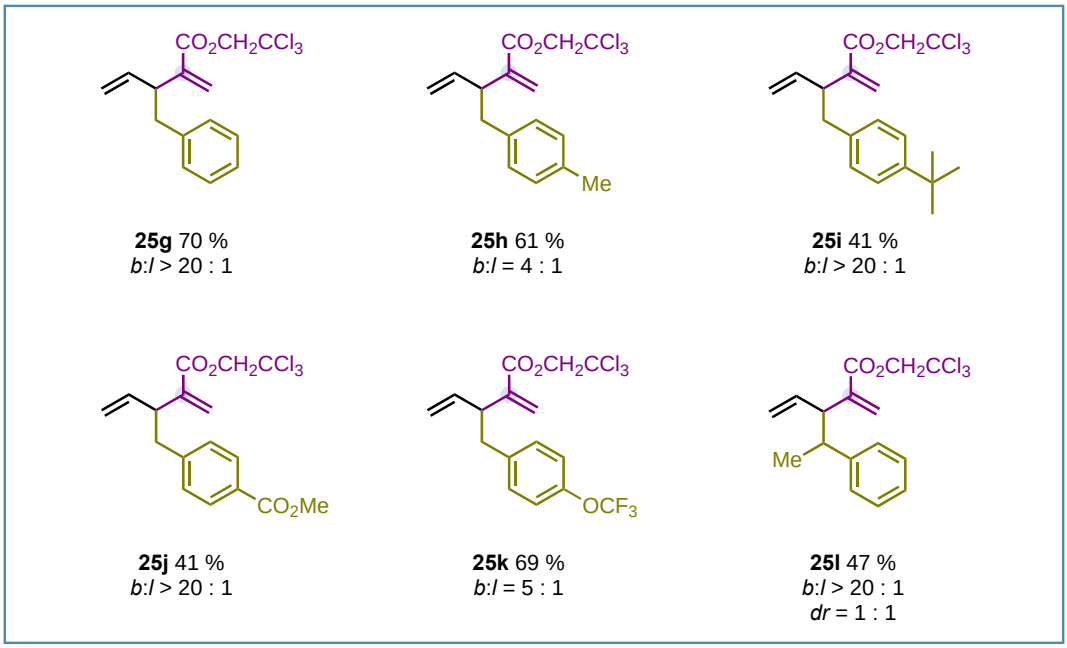


Butadiene
5.0 equiv.
15 % v/v in hexane

2h R = CH_2CCl_3
1.0 equiv.

25-*b*
(*branched* isomer)

25-*l*-*E*
(lineal isomer)



25g 70 %
b:*l* > 20 : 1

25h 61 %
b:*l* = 4 : 1

25i 41 %
b:*l* > 20 : 1

25j 41 %
b:*l* > 20 : 1

25k 69 %
b:*l* = 5 : 1

25l 47 %
b:*l* > 20 : 1
dr = 1 : 1

Table 12 Nucleophile scope: benzylic Molander salts

On the other hand, phenyl-substituted trifluoromethyl salts provided the linear isomers selectively, with regioselectivities of more than 20:1 in all cases (**25n** – **25q**, table 13). Nevertheless, the yields were lower than their benzyl-counterparts, remaining moderate in all cases (39 – 56 % of yield). It must be also said that the stereoselectivity was quite poor, ranging from 1.4:1 to 2.6:1, being the *E* isomer the major one in all cases.

As a summary, we have observed that the nature of the nucleophile dictates the regioselectivity of the reaction. With nucleophiles like halogens, alcohols and arenes (either directly electron-rich ones or from trifluoroborate sources) the lineal isomers are generated preferentially, with selectivity up to > 20:1. On the other hand, benzyl-trifluoroborate salts generate the branched isomers in good to excellent regioselectivity. In this sense we have been able to provide a divergent synthesis from the catalytic generation of allyl-cations, which is able to lead to either conjugated or skipped dienes depending on the nucleophile employed.

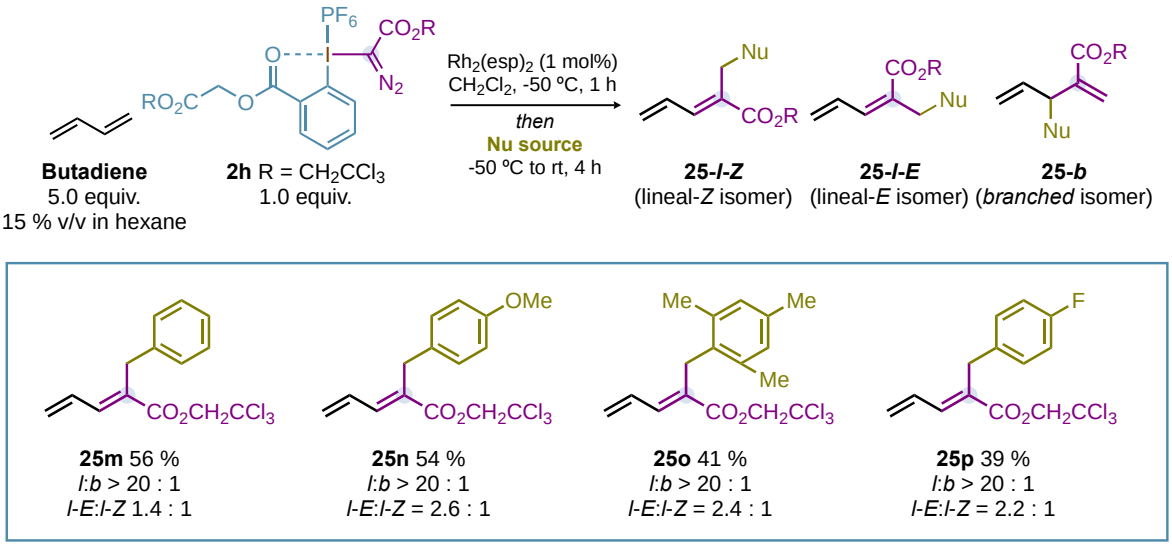


Table 13 Nucleophile scope: $ArBF_3K$

2.6. Conclusions

We have developed a Rh-catalyzed carbyne transfer platform for the catalytic cleavage of C(sp^2)–C(sp^2) bonds. We have demonstrated that this process is able to convert feedstock alkenes, styrenes and a broad diversity of simple nucleophiles into valuable allylic building blocks. Furthermore, we have been able to functionalize butadiene in a divergent manner, obtaining either conjugated or skipped dienes depending on the nucleophile employed. The value of the constructive scission of C–C bonds in alkenes and dienes for the synthesis of more substituted ones is remarkable and is well exemplified with the synthesis of all-carbon tetrasubstituted alkenes from readily available starting materials. The isolation of a cyclopropyl-$I^{(III)}$ compound, which opens following the Woodward–Hoffmann–DePuy rules, clearly proves the involvement of these species as intermediates in the reaction. We anticipate that the insertion of a monovalent carbon unit in C(sp^2)–C(sp^2) bonds underscores an opportunity as a tool in skeletal editing that will be relevant to reach previously unattainable chemical space in drug discovery.

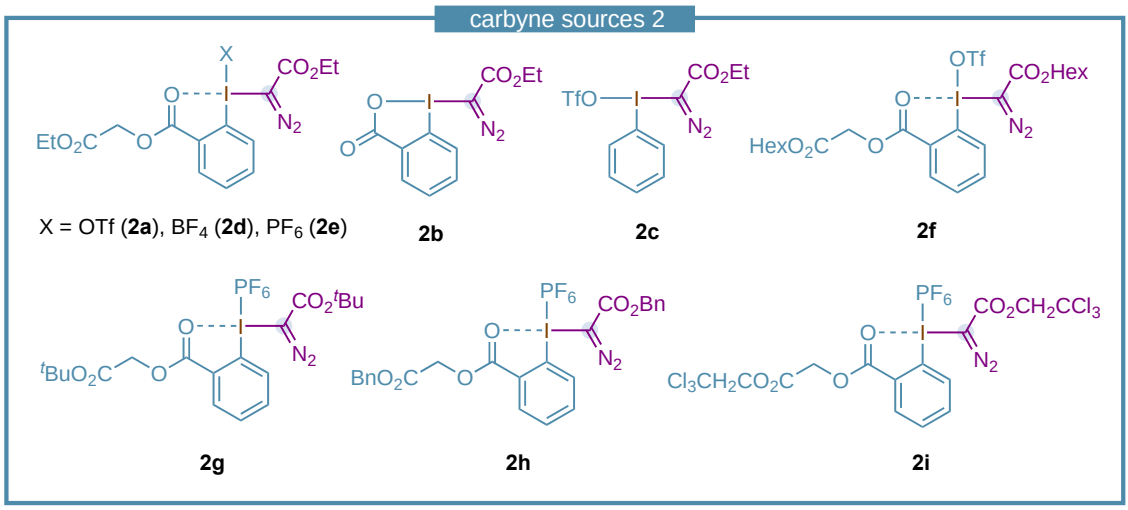
2.7. Experimental section

General Information

All reagents were used as purchased and used with no further purification. Rhodium(II) acetate dimer $Rh_2(OAc)_4$, rhodium(II) trifluoroacetate dimer $Rh_2(TFA)_4$, rhodium(II) heptafluorobutyrate dimer $Rh_2(hfb)_4$, bis[rhodium(α,α,α′,α′-tetramethyl-1,3-benzenedipropionic acid)] $Rh_2(esp)_2$ and dirhodium tetracaprolactamate $Rh_2(cap)_4$ were purchased from Sigma-Aldrich. Rhodium bis(1-adamantate) dimer $Rh_2(Adc)_4$ and rhodium(II) triphenylacetate dimer $Rh_2(TPA)_4$ were prepared according to reported procedures.[69,70] Ethyl diazoacetate (contains ≥13 wt. % dichloromethane, Ref. E22201) and bromoacetic acid-2-^{13}C (isotopic purity = 99 atom % ^{13}C, Ref. 279358) were purchased from Sigma-Aldrich and used without further purification. Anhydrous solvents were dried by passing through an activated alumina column on a PureSolv™ solvent purification system (Innovative Technologies, Inc., MA). Analytical thin layer chromatography (TLC) was carried out using aluminum sheets with 0.2 mm of silica gel (Merck GF234). Visualization of the developed chromatogram was performed by irradiation with UV light or treatment with a solution of potassium permanganate or vanillin stain followed by heating. Flash column chromatography was performed on silica gel (Aldrich, 230-400 mesh) or neutral silica gel (Material Harvest Ltd., 230-400 mesh). Organic solutions were concentrated under reduced pressure on a Büchi rotatory evaporator. Unless otherwise stated, reactions were carried out under argon atmosphere. Yields refer to purified compounds unless otherwise noted. NMR spectra were recorded at 298 K (unless otherwise stated) on Bruker Avance 300, Bruker Avance 400 Ultrashield and Bruker Avance 500 Ultrashield apparatuses. Chemical shifts (δ) are quoted in ppm relative to residual solvent signals, $CDCl_3$ referenced at δ 7.26 and 77.2 ppm, CD_2Cl_2 referenced at δ 5.32 and 53.5 ppm, CD_3CN referenced at δ 1.94 and 1.3, 118.3 ppm respectively. Coupling constants (*J*) are quoted in hertz (Hz). Multiplicity is reported with the following abbreviations: s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, p = quintet, dt = doublet of triplets, td = triplet of doublets, tt = triplet of triplets, sp = septet, m = multiplet, app = apparent. Melting points were measured using open glass capillaries in a Büchi B540 apparatus. Infrared spectra were recorded on a Bruker Tensor 27. Mass spectra were recorded on a Waters LCT Premier spectrometer and Agilent 1260 Infinity - 6130 Quadrupole.

Synthesis of carbyne sources (hypervalent iodine reagents) 2

[69] Song, Z. J.; Thompson, S. A.; Zhao, M.; DeMarco, A.; Reamer, R. A.; Huntington, M. F.; Grabowski, E. J. J.; Reider, P. J.; Nelson, T. D. *Tetrahedron Lett.* **2000**, *41*, 1877.
[70] Guptill, D. M.; Cohen, C. M.; Davies, H. M. L. *Org. Lett.* **2013**, *15*, 6120.



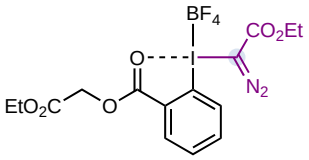
Hypervalent iodine reagents **2a**, **2b**, **2c** are known compounds and were prepared following the reported literature protocols[47,71]. Salts **2d**, **2e**, **2g**, **2h** and **2i** were synthesized by anion exchange from the corresponding triflate salt by following the anion exchange protocol: [72]

Anion exchange protocol

A solution of the corresponding triflate salt (5.0 mmol) in dichloromethane (25 mL, 0.2 M) was added to a 100 mL separation funnel and then washed with a saturated aqueous solution of KPF_6 or KBF_4 (3 x 25 mL). The combined organic layers were dried over Na_2SO_4 and solvent was removed under *vacuum* to give the desired carbyne source **2** as yellow solid.

(*Note: if the product contains impurities, it is recrystallized with dichloromethane/diethyl ether = 1/5*).

(1-diazo-2-ethoxy-2-oxoethyl)(2-(2-ethoxy-2-oxoethoxy)carbonylphenyl)iodonium tetrafluoroborate (2d)



Prepared according to the anion exchange protocol using a solution of **2a** (0.50 g, 0.83 mmol) in dichloromethane (0.2 M). The desired compound **2d** was obtained as a yellow solid (0.39 g, 87% yield).

IR (film, cm^{-1}): 2986, 2121, 1753, 1702, 1661, 1587, 1329, 1272, 1219, 1152, 1029;

^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.45 (dd, *J* = 7.6, 1.6 Hz, 1H), 8.01 (ddd, *J* = 8.4, 7.3, 1.7 Hz, 1H), 7.93 – 7.85 (m, 2H), 5.06 (s, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 6H);

^{13}C NMR (101 MHz, CD_2Cl_2) δ 169.8, 166.2, 161.4, 138.9, 134.1, 132.7, 128.9, 125.5, 65.0, 64.4, 62.7, 31.0, 14.4, 14.2;

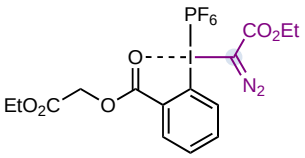
^{19}F NMR (376 MHz, CD_2Cl_2) δ -149.85, -149.90;

^{11}B NMR (128 MHz, CD_2Cl_2) δ -1.16 (p, *J* = 1.4, 1.0 Hz);

HRMS (MALDI) calculated for $C_{15}H_{16}IN_2O_6^+$ $[M\text{-}BF_4]^+$ m/z: 447.0048, found: 447.0050.

[71] Weiss, R.; Seubert, J.; Hampel, F. *Angew. Chem., Int. Ed.* **1994**, *33*, 1952.
[72] Cahard, E.; Male, H. P.; Tissot, M.; Gaunt, M. J. *J. Am. Chem. Soc.* **2015** *137*, 7986.

(1-diazo-2-ethoxy-2-oxoethyl)(2-(2-ethoxy-2-oxoethoxy)carbonylphenyl)iodonium hexafluorophosphate (2e)



Prepared according to the anion exchange protocol using a solution of **2a** (2.98 g, 5.0 mmol) in dichloromethane (0.5 M). The desired compound **2e** was obtained as a yellow solid (2.10 g, 70% yield).

IR (film, cm^{-1}): 2988, 2121, 1752, 1703, 1660, 1589, 1330, 1271, 1220, 1152, 1029, 837;

^{1}H NMR (400 MHz, CD_3CN) δ 8.45 – 8.40 (m, 1H), 8.06 – 8.01 (m, 2H), 7.93 (ddd, *J* = 7.6, 5.7, 2.6 Hz, 1H), 5.07 (s, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 7H);

^{13}C NMR (101 MHz, CD_3CN) δ 170.8, 167.3, 162.1, 139.6, 134.3, 133.6, 130.4, 126.2, 116.8, 65.5, 65.3, 63.0, 14.6, 14.5;

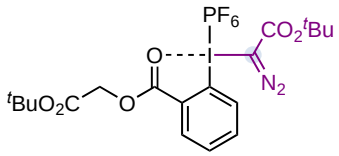
^{13}C NMR (101 MHz, CD_3CN) δ 170.7, 167.2, 162.0, 139.5, 134.3, 133.5, 130.3, 126.1, 116.7, 65.4, 65.2, 62.9, 14.5, 14.4;

^{19}F NMR (376 MHz, CD_2Cl_2) δ -72.77 (d, *J* = 706.9 Hz);

^{31}P NMR (162 MHz, $CDCl_3$) δ -141.43 (sp, *J* = 714.4 Hz);

LRMS (ESI) m/z found for $C_{15}H_{16}IN_2O_6^+$ $[M\text{-}PF_6]^+$: 447.0.

2-(*tert*-butoxy)-2-oxoethyl 2-((2-(*tert*-butoxy)-1-diazo-2-oxoethyl)(hexafluoro-λ^7-phosphaneyl)-λ^3-iodaneyl)benzoate (2g)[47]



Prepared according to the anion exchange protocol using a solution of **2h-OTf** (1.50 g, 2.1 mmol) in dichloromethane (0.2 M). The desired compound **2h** was obtained as a yellow solid (1.35 g, 90% yield).

IR (film, cm^{-1}): 2122, 1705, 1659, 1588, , 1330, 1270, 1215, 1152, 889.

^{1}H NMR (500 MHz, CD_3CN) δ 8.45 – 8.38 (m, 1H), 8.07 – 7.99 (m, 2H), 7.92 (ddd, *J* = 8.2, 6.1, 2.2 Hz, 1H), 4.95 (s, 2H), 1.49 (s, 9H), 1.48 (s, 9H).

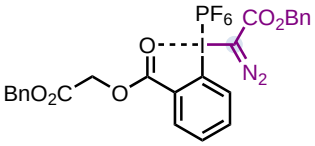
^{13}C NMR (126 MHz, CD_3CN) δ 170.5, 166.2, 160.8, 139.3, 134.2, 133.4, 130.0, 126.2, 116.4, 87.2, 84.2, 65.43, 28.1, 28.1.

^{19}F NMR (471 MHz, CD_3CN) δ -72.81 (d, *J* = 707.3 Hz).

^{31}P NMR (202 MHz, CD_3CN) δ -141.96 (hept, *J* = 706.9 Hz).

LRMS (ESI) calculated for $C_{19}H_{24}IN_2O_6^+$ $[M\text{-}PF_6]^+$ m/z: 503.07, found: 503.07.

2-(benzyloxy)-2-oxoethyl 2-((2-(benzyloxy)-1-diazo-2-oxoethyl)(hexafluoro-λ^7-phosphaneyl)-λ^3-iodaneyl)benzoate (2h)[47]



Prepared according to the anion exchange protocol using a solution of **2h-OTf** (1.50 g, 2.1 mmol) in dichloromethane (0.2 M). The desired compound **2h** was obtained as a yellow solid (1.35 g, 90% yield).

IR (film, cm^{-1}): 2123, 1708, 1658, 1588, 1371, 1330, 1269, 1212, 1152, 889.

^{1}H NMR (400 MHz, Acetone) δ 8.55 – 8.51 (m, 1H), 8.38 – 8.33 (m, 1H), 8.14 – 8.08 (m, 1H), 8.06 – 8.00 (m, 1H), 7.45 – 7.35 (m, 10H), 5.39 (s, 2H), 5.31 (s, 2H), 5.29 (s, 2H).

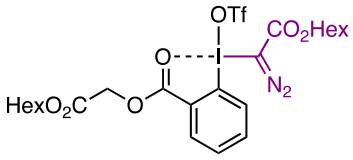
^{13}C NMR (101 MHz, Acetone) δ 170.69, 166.97, 162.11, 139.50, 136.39, 136.10, 134.22, 133.35, 130.56, 129.55, 129.50, 129.45, 129.33, 129.24, 129.16, 126.26, 116.83, 70.08, 67.97, 64.97.

^{19}F NMR (376 MHz, Acetone) δ -72.21 (ddd, *J* = 708.0, 13.6, 7.0 Hz).

^{31}P NMR (162 MHz, Acetone) δ -141.13 (hept, *J* = 707.5 Hz).

HRMS (MALDI) calculated for $C_{25}H_{20}IN_2O_6^+$ $[M\text{-}PF_6]^+$ m/z: 571.0361, found: 571.0387.

(1-diazo-2-hexyloxy-2-oxoethyl)(2-(2-hexyloxy-2-oxoethoxyl)carbonylphenyl)iodonium trifluoromethanesulfonate (2f)



The preparation of **2f** was performed according to an adapted reported protocol:[47] A solution of 1-methoxy-1,2-benziodoxol-3(*1H*)-one (3.0 g, 10.78 mmol, 1.0 equiv) in dichloromethane (20 mL) was treated with trimethylsilyl trifluoromethanesulfonate (1.95 mL, 10.78 mmol, 1.0 equiv) at room temperature. After 30 minutes, a cloudy suspension was observed and hexyl diazoacetate[73] (4.0 g, 23.72 mmol, 2.2 equiv) was added dropwise during 10 minutes. Nitrogen evolution was observed and the resulting reaction mixture was stirred at room temperature until a clear yellow solution was observed (1 hour). Solvent was removed under *vacuum* and the crude was recrystallized from a mixture of diethyl ether/dichloromethane (5/1) during 12 hours at -30 °C (*Note: the recrystallization process may be repeated if impurities are observed*). The desired product was collected by filtration, washed with cold diethyl ether (300 mL), dried under high *vacuum* and stored a -30 °C (5.8 g, 76 %).

IR (film, cm^{-1}): 2930, 2123, 1755, 1705, 1663, 1272, 1027;

[73] Zhang, J.; Li, Y.; Zhang, F.; Hu, C.; Chen, Y. *Angew. Chem., Int. Ed.* **2016**, *55*, 1872.

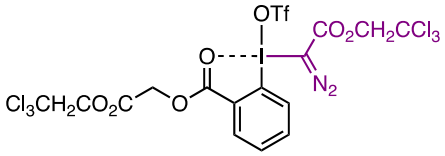
^{1}H NMR (500 MHz, CD_3CN) δ 8.42 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.06 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.04 – 8.00 (m, 1H), 7.92 (td, *J* = 7.4, 1.2 Hz, 1H), 5.07 (s, 2H), 4.28 (t, *J* = 6.5 Hz, 2H), 4.20 (t, *J* = 6.6 Hz, 2H), 1.67 – 1.61 (m, 4H), 1.34 – 1.22 (m, 12H), 0.89 – 0.83 (m, 6H);

^{13}C NMR (126 MHz, CD_3CN) δ 170.7, 167.2, 162.1, 139.4, 134.2, 133.5, 130.5, 126.3, 122.0 (q, *J* = 321.3 Hz), 116.8, 69.1, 66.8, 65.1, 32.0, 32.0, 29.2, 29.1, 26.1, 26.0, 23.2, 23.2, 14.3, 14.2.

^{19}F NMR (471 MHz, CD_3CN): δ -79.28;

HRMS (ESI) calculated for $C_{23}H_{32}IN_2O_6^+$ $[M\text{-}OTf]^+$ m/z: 559.1300, found: 559.1288.

(1-diazo-2,2,2-trichloroethyl)(2-(2,2,2-trifluoroethyl-2-oxoethoxyl)carbonylphenyl)iodonium trifluoromethanesulfonate (2i-OTf)



The preparation of **2i-OTf** was performed according to an adapted reported protocol:[47] A solution of 1-methoxy-1,2-benziodoxol-3(*1H*)-one (3.0 g, 10.78 mmol, 1.0 equiv) in dichloromethane (20 mL) was treated with trimethylsilyl trifluoromethanesulfonate (1.95 mL, 10.78 mmol, 1.0 equiv) at room temperature. After 30 minutes, a cloudy suspension was observed and hexyl diazoacetate (5.60 g, 25.8 mmol, 2.4 equiv) was added dropwise during 10 minutes. Nitrogen evolution was observed and the resulting reaction mixture was stirred at room temperature until a clear yellow solution was observed (1 hour). Solvent was removed under *vacuum* and the crude was recrystallized from a mixture of diethyl ether/dichloromethane (5/1) during 12 hours at -30 °C (*Note: the recrystallization process may be repeated if impurities are observed*). The desired product was collected by filtration, washed with cold diethyl ether (300 mL), dried under high *vacuum* and stored a -30 °C (6.66 g, 77 %).

m.p. 106-107 °C.

IR (film, cm^{-1}): 2961, 2129, 1772, 1716, 1661, 1265, 1148, 1026.

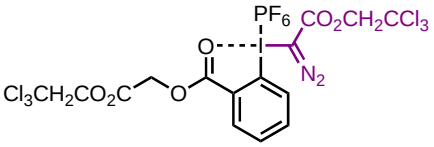
^{1}H NMR (500 MHz, CD_3CN) δ 8.44 (dd, *J* = 7.6, 1.7 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 8.04 (ddd, *J* = 8.5, 7.3, 1.7 Hz, 1H), 7.93 (t, *J* = 7.5 Hz, 1H), 5.25 (s, 2H), 4.97 (s, 2H), 4.94 (s, 2H).

^{13}C NMR (126 MHz, CD_3CN) δ 170.9, 166.0, 161.1, 139.7, 134.4, 133.6, 130.9, 126.1, 122.0 (q, *J* = 321.3 Hz), 117.0, 95.4, 95.2, 76.3, 75.2, 64.9.

^{19}F NMR (471 MHz, CD_3CN) δ -79.18.

HRMS (MALDI) calculated for $C_{15}H_{10}Cl_6IN_2O_6^+$ $[M\text{-}OTf]^+$ m/z: 650.7709, found: 650.7729.

(1-diazo-2,2,2-trichloroethyl)(2-(2,2,2-trifluoroethyl-2-oxoethoxyl)carbonylphenyl)iodonium hexafluorophosphate (2i)



Prepared according to the anion exchange protocol using a solution of **2i-OTf** (2.20 g, 2.8 mmol) in dichloromethane (0.2 M). The desired compound **2i** was obtained as a yellow solid (2.01 g, 91% yield).

IR (film, cm^{-1}): 2962, 2130, 1774, 1719, 1661, 1589, 1428, 1372, 1325, 1265, 1150, 1029, 840.

^{1}H NMR (400 MHz, Acetone) δ 8.55 (dd, *J* = 7.6, 1.7 Hz, 1H), 8.38 (d, *J* = 8.4 Hz, 1H), 8.15 (ddd, *J* = 8.4, 7.4, 1.7 Hz, 1H), 8.04 (td, *J* = 7.5, 0.9 Hz, 1H), 5.45 (s, 2H), 5.07 (s, 2H), 5.01 (s, 2H).

^{13}C NMR (101 MHz, Acetone) δ 170.7, 165.8, 161.0, 139.7, 134.2, 133.3, 130.7, 125.8, 116.7, 95.3, 95.3, 76.1, 74.8, 64.5.

^{19}F NMR (376 MHz, Acetone) δ -71.81 (d, *J* = 708.7 Hz).

^{31}P NMR (162 MHz, Acetone) δ -141.17 (hept, *J* = 708.7 Hz).

HRMS (MALDI) calculated for $C_{15}H_{10}Cl_6IN_2O_6^+$ $[M\text{-}PF_6]^+$ m/z: 650.7709, found: 650.7735.

Notes:

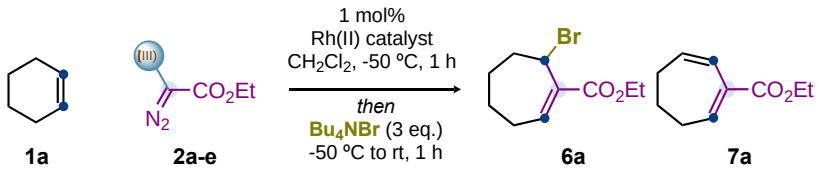
(a) We have never observed any explosion during the preparation or manipulation of reagents **2** at the scales indicated here in our laboratory.

(b) If impurities are observed in the ^{1}H NMR crude, a subsequent recrystallization may be done.

(c) Reagents **2** are kept at ≤ –20 ºC.

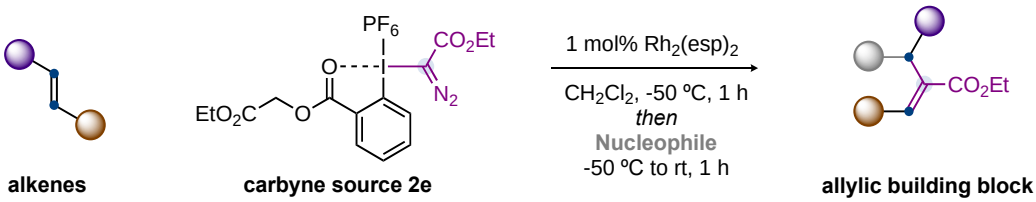
Catalytic cleavage of C(sp^2)–C(sp^2) for the synthesis of allylic building blocks 6: reaction optimization and scope.

General Procedure A for reaction optimization:



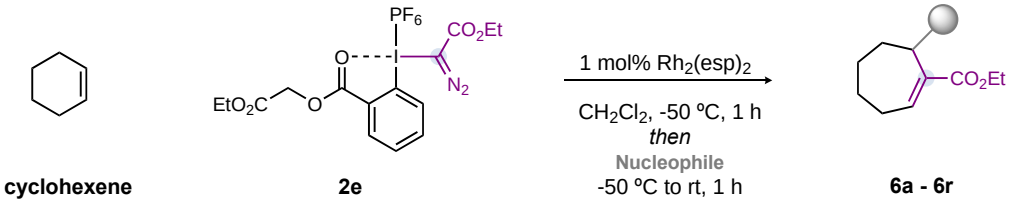
To a 10 mL oven-dried tube equipped with a stirring bar was added the corresponding Rh catalyst (0.001 mmol, 1 mol%). The tube was sealed before being evacuated and backfilled with nitrogen. Cyclohexene (41.0 mg, 50 µL, 0.5 mmol) and degassed dichloromethane (0.5 mL) were added and the resulting mixture was placed into a cooling bath at -50 ºC. Then, a solution of reagent **2** (0.1 mmol, 1.0 equiv.) in degassed dichloromethane (1 mL) was added dropwise during 1 h using a syringe pump and after stirred for 30 min at -50 ºC. After this, nucleophile (0.3 mmol, 3.0 equiv.) was added and the resulting reaction mixture was allowed to warm to room temperature during 1 hour. The resulting reaction mixture was analyzed by ^{1}H NMR using anisole (10.8 mg, 0.1 mmol, 1.0 equiv) as internal standard.

General Procedure B

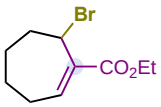


To a 10 mL oven-dried tube equipped with a stirring bar was added $Rh_2(esp)_2$ (2.0 mg, 0.002 mmol, 1 mol%). The tube was sealed before being evacuated and backfilled with nitrogen. The corresponding alkene (1.0 mmol, 5.0 equiv) and degassed dichloromethane (1.0 mL) were added and the resulting mixture was cooled at -50 ºC. Then, a solution of reagent **2e** (120 mg, 0.2 mmol, 1.0 equiv.) in degassed dichloromethane (2.0 mL) was added dropwise during 1 h using a syringe pump and after stirred for 30 min at -50 ºC. After this, the corresponding nucleophile (3-20 equivalents) was added and stirred for 30 min at -50 ºC. Then the resulting reaction mixture was allowed to warm to room temperature during 3 hours, filtered through a short plug of silica gel and washed with dichloromethane. Solvent was removed under *vacuum* and the crude residue was purified by column chromatography to yield the corresponding allylic building blocks **6**.

Nucleophile scope



ethyl-7-bromocyclohept-1-ene-1-carboxylate (6a)



This compound was synthesized following the general procedure B using Bu_4NBr (200 mg, 3.0 equiv, 0.6 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 73 % yield of **6a** and 13 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 40/1) provided the title compound as colorless oil (38.2 mg, 76% yield).

Note: The purification by flash chromatography should be very fast, otherwise decomposition to diene **7a** is observed.

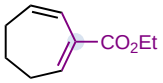
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.28 (m, 1H), 5.67 – 5.56 (m, 1H), 4.22 (qd, *J* = 7.2, 1.0 Hz, 2H), 2.46 – 2.42 (m, 2H), 2.25 – 2.14 (m, 2H), 2.03 – 1.96 (m, 1H), 1.92 – 1.86 (m, 2H), 1.48 – 1.40 (m, 1H), 1.31 (t, *J* = 7.1 Hz, 3H). Peaks at 7.16, 6.37, 5.98 belong to decomposition diene product.

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3, 148.5, 136.2, 61.4, 50.1, 34.8, 28.5, 26.5, 25.9, 14.4;

HRMS: (ESI) calculated for $C_{10}H_{15}BrO_2Na^+$ $[M+Na]^+$m/z: 269.0148, found: 269.0141.

Diene **7a** was also isolated and characterized as follows:

ethyl cyclohepta-1,6-diene-1-carboxylate (7a)



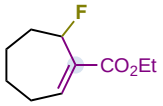
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (t, *J* = 5.9 Hz, 1H), 6.37 (app, 1H), 5.98 (dt, *J* = 11.8, 5.2 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.45 (dt, *J* = 5.8 Hz, 5.8 Hz, 2H), 2.35 (dt, *J* = 5.3 Hz, 5.3 Hz, 2H), 1.91 – 1.85 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ168.0, 143.8, 134.9, 130.0, 123.2, 60.9, 31.6, 30.9, 26.2, 14.5;

HRMS (ESI) calculated for $C_{10}H_{14}NaO_2^+$ $[M+Na]^+$ m/z: 189.0886, found: 189.0891.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl-7-fluorocyclohept-1-ene-1-carboxylate (6b)



This compound was synthesized following the general procedure B using triethylamine trihydrofluoride (161 mg, 5.0 equiv, 1.0 mmol). ^{1}H-NMR and ^{19}F-NMR analysis of crude reaction mixture using fluorobenzene (19.0 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 81 % NMR yield of **6b** and 4 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 50/1) provided the title compound as colorless oil (27.9 mg, 76% yield).

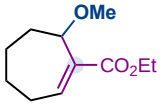
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (dddd, *J* = 7.5, 5.3, 4.2, 1.2 Hz, 1H), 5.76 (ddt, *J* = 45.9, 6.7, 1.3 Hz, 1H), 4.21 (qd, *J* = 7.1, 1.8 Hz, 2H), 2.62 – 2.44 (m, 1H), 2.45 – 2.21 (m, 2H), 2.12 – 1.95 (m, 1H), 1.95 – 1.81 (m, 1H), 1.81 – 1.73 (m, 1H), 1.73 – 1.61 (m, 1H), 1.58 – 1.49 (m, 1H), 1.30 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0 (d, *J* = 3.1 Hz), 150.1 (d, *J* = 5.3 Hz), 133.4 (d, *J* = 17.6 Hz), 87.9 (d, *J* = 40.2 Hz), 61.1, 31.00 (d *J* = 23.2 Hz), 28.3 (d, *J* = 1.8 Hz), 26.2 (d, *J* = 2.2 Hz), 23.6 (d, *J* = 4.7 Hz), 14.4;

^{19}F NMR (376 MHz, $CDCl_3$) δ -177.17;

HRMS: (ESI) calculated for $C_{10}H_{15}FO_2Na^+$ $[M+Na]^+$m/z: 209.0948, found: 209.0950.

ethyl 7-methoxycyclohept-1-ene-1-carboxylate (6c)



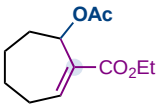
This compound was synthesized following the general procedure B using methanol (40 □L, 5.0 equiv, 1.0 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 67 % yield of **6c** and 5 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 20/1) provided the title compound as colorless oil (30 mg, 72% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (ddd, *J* = 8.2, 5.2, 1.2 Hz, 1H), 4.55 (d, *J* = 6.2 Hz, 1H), 4.18 (qd, *J* = 7.1, 0.9 Hz, 2H), 3.31 (s, 3H), 2.53 (dddd, *J* = 15.7, 11.6, 5.2, 2.5 Hz, 1H), 2.29 – 2.18 (m, 1H), 2.16 – 2.07 (m, 1H), 2.00 (dddt, *J* = 14.2, 12.7, 10.7, 3.6 Hz, 1H), 1.81 (dtt, *J* = 13.1, 6.4, 3.0 Hz, 1H), 1.74 – 1.65 (m, 1H), 1.51 – 1.36 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.0, 148.0, 135.7, 75.4, 60.8, 56.5, 29.8, 27.9, 26.4, 24.4, 14.4;

HRMS: (ESI) calculated for $C_{11}H_{18}NaO_3^+$ $[M+Na]^+$m/z: 221.1148, found: 221.1141.

ethyl 7-acetoxycyclohept-1-ene-1-carboxylate (6d)



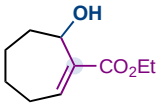
This compound was synthesized following the general procedure B using tetrabutylammonium acetate (180 mg, 3.0 equiv, 0.6 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 42 % yield of **6d** and 22 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 10/1) provided the title compound as colorless oil (20 mg, 45% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (ddd, *J* = 7.5, 5.6, 0.9 Hz, 1H), 5.95 (d, *J* = 5.5 Hz, 1H), 4.19 (qt, *J* = 7.2, 3.6 Hz, 2H), 2.49 (dddd, *J* = 16.3, 10.7, 5.6, 2.4 Hz, 1H), 2.36 – 2.26 (m, 1H), 2.23 – 2.13 (m, 1H), 2.04 (s, 3H), 1.89 – 1.81 (m, 2H), 1.78 – 1.72 (m, 1H), 1.67 – 1.61 (m, 1H), 1.57 – 1.48 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 167.1, 148.5, 134.3, 70.2, 61.0, 29.5, 27.7, 26.1, 24.1, 21.1, 14.3;

HRMS (ESI) calculated for $C_{12}H_{18}NaO_4^+$ $[M+Na]^+$ m/z: 249.1097, found: 249.1100.

ethyl-7-hydroxycyclohept-1-ene-1-carboxylate (6e)



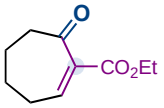
This compound was synthesized following the general procedure B using water (20 □L, 10 equiv, 1.0 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 61 % yield of **6e** and 15 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 10/1) provided the title compound as colorless oil (24.4 mg, 64% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 6.7, 6.2 Hz, 1H), 4.87 – 4.75 (m, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.73 (brs, 1H), 2.51 – 2.38 (m, 1H), 2.33 – 2.20 (m, 1H), 2.03 – 1.90 (m, 2H), 1.86 – 1.75 (m, 1H), 1.75 – 1.64 (m, 2H), 1.66 – 1.54 (m, 1H), 1.31 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 145.3, 136.9, 68.9, 61.0, 32.5, 27.4, 25.8, 23.7, 14.4;

HRMS: (ESI) calculated for $C_{10}H_{16}O_3Na^+$ $[M+Na]^+$m/z: 207.0992, found: 207.0990.

ethyl 7-oxocyclohept-1-ene-1-carboxylate (6f)



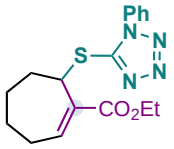
This compound was synthesized following the general procedure B using 2,2,6,6-Tetramethyl-1-piperidinyloxy TEMPO (100 mg, 0.6 mmol, 3.0 equiv). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 29 % yield of **6f** and 17 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 10/1) provided the title compound as colorless oil (13.1 mg, 31 % yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (t, *J* = 5.8 Hz, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 2.71 – 2.68 (t, *J* = 7.0 Hz, 2H), 2.53 – 2.48 (m, 2H), 1.89 – 1.82 (m, 2H), 1.81 – 1.74 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 202.5, 165.3, 148.7, 137.1, 61.4, 43.9, 29.1, 24.6, 22.8, 14.3;

HRMS (ESI) calculated for $C_{10}H_{14}NaO_3^+$ $[M+Na]^+$ m/z: 205.0835, found: 205.0829.

ethyl-7-((2-phenyl-*2H*-tetrazol-5-yl)thio)cyclohept-1-ene-1-carboxylate (6g)



This compound was synthesized following the general procedure B using 1-phenyl-1H-tetrazole-5-thiol (180 mg, 5.0 equiv, 1.0 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 55 % yield of **6g** and 4 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 5/1) provided the title compound as colorless oil (34.0 mg, 50% yield).

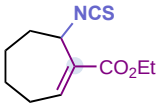
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 – 7.51 (m, 5H), 7.35 – 7.30 (m, 1H), 5.60 (dd, *J* = 5.7, 2.0 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.57 – 2.53 (m, 1H), 2.40 (ddd, *J* = 8.6, 6.1, 4.0 Hz, 2H), 2.04 – 1.96 (m, 1H), 1.96 – 1.92 (m, 1H), 1.89 – 1.80 (m, 2H), 1.552-1.43 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 153.8, 148.4, 134.1, 133.9, 130.2, 129.8, 124.1, 61.4, 47.3, 30.3, 28.3, 26.1, 25.6, 14.3;

HRMS: (ESI) calculated for $C_{17}H_{20}N_4O_2SNa^+$ $[M+Na]^+$m/z: 367.1199, found: 367.1193.

The crystal structure of **6g** has been deposited at the Cambridge Crystallographic Data Centre, CCDC 1875938.

ethyl-7-thiocyanatocyclohept-1-ene-1-carboxylate (6h)



This compound was synthesized following the general procedure B using tetrabutylammonium thiocyanate (300 mg, 5.0 equiv, 1.0 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 47 % yield of **6h** and 5 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 20/1) provided the title compound as colorless oil (24.1 mg, 53% yield).

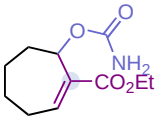
IR (film, cm^{-1}): 2931, 2088, 1705, 1254, 1206, 1065;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (ddd, *J* = 8.0, 5.4, 0.8 Hz, 1H), 5.18 (dd, *J* = 6.0, 1.9 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.51 (dddd, *J* = 16.5, 11.1, 5.3, 2.2 Hz, 1H), 2.45 – 2.34 (m, 1H), 2.20 – 2.10 (m, 1H), 2.08 – 2.00 (m, 1H), 1.94 – 1.87 (m, 2H), 1.69 – 1.61 (m, 1H), 1.54 – 1.43 (m, 1H), 1.31 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3, 148.9, 133.2, 132.0, 61.3, 54.4, 31.7, 27.9, 25.9, 25.3, 14.4;

HRMS: (ESI) calculated for $C_{11}H_{15}NO_2SNa^+$ $[M+Na]^+$m/z: 248.0716, found: 248.0712.

ethyl 7-(carbamoyloxy)cyclohept-1-enecarboxylate (6i)



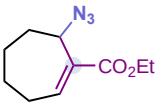
This compound was synthesized following the general procedure B using reagent **2a** (119 mg, 0.2 mmol, 1.0 equiv.) and *tert*-butyl carbamate (117 mg, 5.0 equiv, 1.0 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 40 % yield of **6i** and 4 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 5/1) provided the title compound as colorless oil (17.2 mg, 38% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (ddd, *J* = 7.3, 5.6, 0.8 Hz, 1H), 5.88 – 5.82 (m, 1H), 4.65 (brs, 2H), 4.23 – 4.15 (m, 2H), 2.47 (m, 1H), 2.36 – 2.27 (m, 1H), 2.22 (dddd, *J* = 14.8, 6.7, 4.5, 3.7 Hz, 1H), 1.95 – 1.86 (m, 1H), 1.80 (m, 1H), 1.77 – 1.71 (m, 1H), 1.70 – 1.61 (m, 2H), 1.57 – 1.49 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 156.3, 148.2, 134.3, 70.8, 61.0, 29.8, 27.7, 26.2, 23.9, 14.3;

HRMS: (ESI) calculated for $C_{18}H_{21}NO_2Na^+$ $[M+Na]^+$m/z: 250.1055, found: 250.1051.

Ethyl-7-azidocyclohept-1-ene-1-carboxylate (6j)



This compound was synthesized following the general procedure B using tetrabutylammonium azide (170 mg, 3.0 equiv, 0.3 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 78 % yield of **6j** and 21 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 50/1) provided the title compound as colorless oil (30.5 mg, 73% yield).

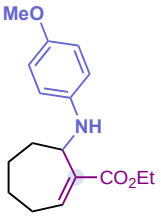
IR (film, cm^{-1}): 2931, 2100, 1704, 1447, 1253;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (ddd, *J* = 7.6, 5.3, 0.9 Hz, 1H), 4.99 – 4.91 (m, 1H), 4.22 (qd, *J* = 7.1, 1.7 Hz, 2H), 2.42 (dddd, *J* = 16.2, 10.9, 5.3, 2.8 Hz, 1H), 2.38 – 2.29 (m, 1H), 2.07 – 1.99 (m, 1H), 1.98 – 1.89 (m, 1H), 1.88 – 1.80 (m, 1H), 1.80 – 1.72 (m, 1H), 1.62 (dddd, *J* = 14.3, 12.3, 3.8, 2.1 Hz, 1H), 1.50 – 1.40 (m, 1H), 1.31 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 148.7, 133.3, 61.3, 58.8, 30.8, 28.2, 26.1, 24.7, 14.3;

HRMS: (ESI) calculated for $C_{10}H_{15}N_3O_2Na^+$ $[M+Na]^+$m/z: 232.1056, found: 231.1060.

ethyl-7-((4-methoxyphenyl)amino)cyclohept-1-ene-1-carboxylate (6k)



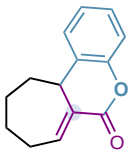
This compound was synthesized following the general procedure B using *p*-anisidine (131 mg, 5.0 equiv, 1.0 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 55 % yield of **6k** and 22 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 10/1) provided the title compound as colorless oil (33.9 mg, 59% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 7.2, 6.1 Hz, 1H), 6.78 – 6.74 (m, 2H), 6.69 – 6.63 (m, 2H), 4.77 (dd, *J* = 6.5, 2.1 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.73 (s, 3H), 2.46 – 2.33 (m, 2H), 2.07 (dtd, *J* = 13.7, 6.0, 3.4 Hz, 1H), 1.94 – 1.83 (m, 1H), 1.79 – 1.71 (m, 2H), 1.70 – 1.63 (m, 1H), 1.61 – 1.51 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.9, 152.4, 144.4, 141.6, 137.9, 115.5, 115.0, 60.9, 55.9, 52.2, 29.8, 27.8, 26.4, 24.8, 14.3;

HRMS: (ESI) calculated for $C_{17}H_{24}NO_3Na^+$ $[M+Na]^+$m/z: 290.1751, found: 290.1744.

9,10,11,11a-tetrahydrocyclohepta[c]chromen-6(*8H*)-one (6l)



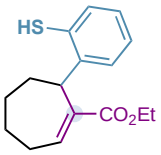
This compound was synthesized following the general procedure B using phenol (92 mg, 5.0 equiv, 1.0 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 62 % yield of **6l** and 5 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 10/1) provided the title compound as colorless oil (25.0 mg, 58% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (ddd, *J* = 9.0, 5.9, 2.3 Hz, 1H), 7.24-7.18 (m, 2H), 7.13-7.19 (m, 1H), 7.02-6.99 (m, 1H), 4.05 (d, *J* = 13.6Hz, 1H), 2.63-2.51 (m, 1H), 2.47-2.28 (m, 1H), 2.25-2.18 (m, 1H), 2.04-1.95 (m, 2H), 1.88-1.81 (m, 1H), 1.73-1.65 (m, 1H), 1.44-1.33 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 162.2, 151.6, 149.8, 131.1, 128.9, 128.2, 124.8, 124.6, 117.1, 39.8, 37.1, 32.7, 28.7, 24.2;

HRMS: (ESI) calculated for $C_{14}H_{14}O_2Na^+$ $[M+Na]^+$m/z: 237.2886, found: 237.2887.

ethyl-7-(2-mercaptophenyl)cyclohept-1-ene-1-carboxylate (6m)



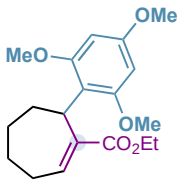
This compound was synthesized following the general procedure B using thiophenol (110 mg, 5.0 equiv, 1.0 mmol). Purification by flash chromatography on silica gel (hexane/ethyl acetate: 10/1) provided the title compound as colorless oil (46.7 mg, 85% yield).

^{1}H NMR (400 MHz, Chloroform-d) δ 7.53 – 7.50 (m, 2H), 7.30 – 7.27 (m, 2H), 7.25 – 7.22 (m, 1H), 4.80 (dd, *J* = 5.5, 2.4 Hz, 1H), 4.14 (qd, *J* = 7.2, 0.6 Hz, 2H), 2.55 (dddd, *J* = 16.4, 11.7, 5.0, 2.6 Hz, 1H), 2.40 – 2.29 (m, 1H), 2.30 – 2.16 (m, 1H), 2.01 – 1.95 (m, 1H), 1.94 – 1.64 (m, 1H), 1.81 – 1.66 (m, 2H), 1.44 – 1.34 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 146.4, 135.8, 135.7, 132.9, 129.2, 128.9, 127.7, 127.4, 61.1, 47.7, 30.5, 28.2, 26.5, 25.4, 14.4.

HRMS: (ESI) calculated for $C_{16}H_{20}O_2SNa^+$ $[M+Na]^+$m/z: 299.1076, found: 299.1073.

ethyl-7-(2,4,6-trimethoxyphenyl)cyclohept-1-ene-1-carboxylate (6n)



This compound was synthesized following the general procedure B using 1,3,5-trimethoxybenzene (168 mg, 5.0 equiv, 1.0 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 62 % yield of **6n** and 4 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 5/1) provided the title compound as white solid (40.3 mg, 60% yield).

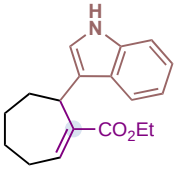
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (ddd, *J* = 8.2, 5.7, 1.9 Hz, 1H), 6.10 (s, 2H), 4.45 – 4.38 (m, 1H), 3.99 – 3.86 (m, 2H), 3.78 (s, 3H), 3.76 (s, 6H), 2.81 – 2.73 (m, 1H), 2.21 – 2.14 (m, 1H), 2.13 – 2.07 (m, 1H), 1.84-1.69 (m, 3H), 1.69 – 1.54 (m, 2H), 1.04 (t, *J* = 7.0 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.4, 159.3, 158.8, 139.0, 137.0, 115.1, 91.2, 60.0, 55.9, 55.3, 37.2, 29.8, 25.9, 25.4, 25.2, 14.1;

HRMS: (ESI) calculated for $C_{19}H_{26}O_5Na^+$ $[M+Na]^+$m/z: 357.1672, found: 357.1674.

The crystal structure of **6n** has been deposited at the Cambridge Crystallographic Data Centre, CCDC 1875907.

ethyl-7-(1H-indol-3-yl) cyclohept-1-ene-1-carboxylate (6o)



This compound was synthesized following the general procedure B using indole (120 mg, 5.0 equiv, 1.0 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard

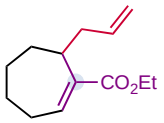
indicated 53 % yield of **6o** and 4 % yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 4/1) provided the title compound as colorless oil (28.1 mg, 48% yield).

^{1}H NMR (500 MHz, $CDCl_3$ δ 7.94 (s, 1H), 7.68 (dt, *J* = 7.9, 0.9 Hz, 1H), 7.39 – 7.30 (m, 2H), 7.18 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 7.11 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 6.81 (dd, *J* = 2.4, 1.1 Hz, 1H), 4.78 (dd, *J* = 5.8, 3.2 Hz, 1H), 4.12 (qq, *J* = 7.3, 3.8 Hz, 2H), 2.50 – 2.33 (m, 3H), 1.93 – 1.85 (m, 1H), 1.83 – 1.74 (m, 1H), 1.66 – 1.59 (m, 1H), 1.50 – 1.39 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.7, 143.6, 138.2, 137.2, 126.9, 122.7, 122.0, 119.7, 119.2, 116.6, 111.2, 60.8, 36.2, 31.5, 28.5, 26.8, 25.3, 14.4;

HRMS: (ESI) calculated for $C_{18}H_{21}NO_2Na^+$ $[M+Na]^+$m/z: 304.1464, found: 304.1463.

ethyl-7-allylcyclohept-1-ene-1-carboxylate (6p)



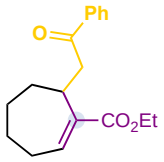
This compound was synthesized following the general procedure B using allyltributylstannane (850 mg, 13 equiv, 2.56 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 87 % yield of **6p** and trace amount of **7a** was observed. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 50/1) provided the title compound as colorless oil (38.8 mg, 94% yield). The unreacted allyltributylstannane was recovered (630 mg, 1.9 mmol, 80% recovery).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 – 7.09 (m, 1H), 5.77 (dddd, *J* = 16.8, 10.1, 7.6, 6.6 Hz, 1H), 5.03 (ddt, *J* = 17.0, 2.2, 1.4 Hz, 1H), 4.97 (ddt, *J* = 10.1, 2.1, 1.0 Hz, 1H), 4.16 (qt, *J* = 7.2, 3.7 Hz, 2H), 3.14 (dtt, *J* = 9.1, 5.8, 3.2 Hz, 1H), 2.37 – 2.27 (m, 3H), 2.26 – 2.20 (m, 1H), 1.85 – 1.71 (m, 4H), 1.52 (dddd, *J* = 13.7, 9.9, 5.3, 3.3 Hz, 1H), 1.43 – 1.34 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.7, 142.9, 139.1, 137.5, 115.8, 60.7, 37.6, 36.0, 29.3, 28.1, 26.8, 24.9, 14.4;

HRMS: (ESI) calculated for $C_{13}H_{20}O_2Na^+$ $[M+Na]^+$m/z: 231.1356, found: 231.1355.

ethyl-7-(2-oxo-2-phenylethyl)cyclohept-1-ene-1-carboxylate (6q)



This compound was synthesized following the general procedure B using 1-phenyl-1-trimethylsilyloxy-ethene (200 mg, 5.0 equiv, 1.0 mmol) as trapping nucleophile. ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 61 % yield of **6q** and 4% yield of **7a**. Purification by flash chromatography on silica gel (hexane/ethyl acetate: 10/1) provided the title compound as colorless oil (29.6 mg, 53% yield).

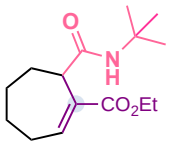
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 – 7.98 (m, 2H), 7.62 – 7.49 (m, 1H), 7.47 (dddd, *J* = 8.1, 6.7, 1.6, 1.0 Hz, 2H), 7.17 (dd, *J* = 7.5, 5.5 Hz, 1H), 4.18 (qd, *J* = 7.1, 0.7 Hz, 2H), 3.68 (dtd, *J* = 10.4, 5.3, 3.0 Hz, 1H), 3.27 (dd,

J = 14.9, 5.2 Hz, 1H), 3.07 (dd, *J* = 14.9, 10.0 Hz, 1H), 2.45 – 2.27 (m, 2H), 1.89 – 1.71 (m, 4H), 1.62 – 1.55 (m, 1H), 1.52 – 1.40 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 199.7, 168.4, 143.8, 138.3, 136.8, 133.1, 128.7, 128.5, 60.9, 41.0, 35.1, 29.2, 28.0, 26.6, 24.8, 14.4.

HRMS: (ESI) calculated for $C_{18}H_{22}O_2Na^+$ $[M+Na]^+$m/z: 309.1461, found: 309.1460.

ethyl-7-(tert-butylcarbamoyl)cyclohept-1-ene-1-carboxylate (6r)



This compound was synthesized following the general procedure B using *tert*-butyl isocyanide (98 mg, 10 equiv, 1.0 mmol) and pyridine 1-oxide (94 mg, 5.0 equiv, 1.0 mmol). The work-up procedure was modified as follows: once the reaction finished and warmed to room temperature, 5.0 mL of water were added and the mixture was stirred for 10 min. The reaction mixture was then extracted with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4 and filtered. The solvent was removed under *vacuum* and the residue was purified by flash column chromatography on silica gel (hexane/ethyl acetate = 5/1) to afford the title compound as colorless oil (28.4 mg, 50% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (t, *J* = 6.5 Hz, 1H), 5.63 (brs, 1H), 4.24 – 4.11 (m, 2H), 3.75 (dd, *J* = 5.7, 3.6 Hz, 1H), 2.36 (ddd, *J* = 8.3, 6.2, 4.1 Hz, 2H), 2.33 – 2.25 (m, 1H), 1.85 – 1.74 (m, 3H), 1.55 (ddt, *J* = 13.9, 11.7, 3.4 Hz, 1H), 1.38 – 1.34 (m, 1H), 1.30 (s, 9H), 1.29 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 168.4, 146.8, 134.4, 61.2, 51.2, 46.2, 29.0, 28.8, 28.4, 26.2, 25.7, 14.4;

HRMS: (ESI) calculated for $C_{15}H_{25}NO_3Na^+$ $[M+Na]^+$m/z: 290.1727, found: 290.1718.

Alkene scope

ethyl 2-(bromomethyl)acrylate (6s)

Prepared according to the general procedure B using $Rh_2(Adc)_4$ (2.0 mg, 0.002 mmol), and Bu_4NBr (193.4 mg, 0.6 mmol) and a saturated solution of ethylene in dichloromethane (1 mL). The reaction was carried with a balloon of ethylene. Purification by flash chromatography on silica gel (hexane/diethyl ether: 100/1) provided the title product as a colorless oil (29.0 mg, 41% yield).

Note: The saturated solution of ethylene in dichloromethane was prepared by bubbling of ethylene gas at -94 ºC during 10 min. After addition of Bu_4NBr, the resulting reaction mixture was stirred at room temperature for 10 hours.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.33 (d, *J* = 0.8 Hz, 1H), 5.94 (dd, *J* = 0.9, 0.9 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.18 (d, *J* = 0.9 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H);

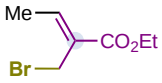
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.0, 137.7, 129.1, 61.5, 29.5, 14.3;

Spectroscopic data consistent with that reported in the literature[6].

ethyl (*Z*)-2-(bromomethyl)but-2-enoate (*Z*-6t), ethyl (*E*)-2-(bromomethyl)but-2-enoate (*E*-6t) and ethyl 3-bromo-2-methylenebutanoate (*branched*-6t)

Prepared according to the general procedure B using propylene and Bu_4NBr (193.4 mg, 0.6 mmol). Ratio of *linear:branched* isomers was determined to be 14:1 (*l* = 3:1, *Z:E*) from the crude reaction mixture using ^{1}H NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/diethyl ether: 100/1) provided the mixture of three isomers as a colorless oil (36.8 mg, 89% yield). The mixture could be separated via preparative TLC using hexane/ dichloromethane: 2/1 as eluent.

ethyl (*Z*)-2-(bromomethyl)but-2-enoate (*Z*-6t)

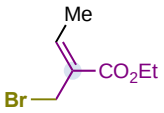


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 (q, *J* = 7.3 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.24 (s, 2H), 1.92 (d, *J* = 7.3 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 143.1, 130.7, 61.2, 24.3, 14.7, 14.4;

HRMS (ESI) calculated for $C_7H_{11}BrNaO_2^+$ $[M+Na]^+$ m/z: 228.9835, found: 228.9832.

ethyl (*E*)-2-(bromomethyl)but-2-enoate (*E*-6t)

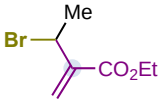


^{1}H NMR (500 MHz, $CDCl_3$) δ 6.45 (q, *J* = 7.3 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.19 (s, 2H), 2.08 (d, *J* = 7.3 Hz, 3H), 1.35 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.6, 143.1, 130.4, 60.9, 33.8, 16.2, 14.4, 0.1;

HRMS (ESI) calculated for $C_7H_{11}BrNaO_2^+$ $[M+Na]^+$ m/z: 228.9835, found:228.9830.

ethyl 3-bromo-2-methylenebutanoate (*branched*-6t)

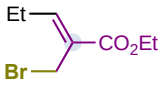


The title compound is quite unstable at preparative TLC plate and all the isolation trials failed to furnish the title pure compound.

ethyl (*Z*)-2-(bromomethyl)pent-2-enoate (linear-*Z*-6u), ethyl (*E*)-2-(bromomethyl)pent-2-enoate (linear-*E*-6u) and ethyl 3-bromo-2-methylenepentanoate (*branched*-6u)

Prepared according to the general procedure B using 1-butene and Bu_4NBr (193.4 mg, 0.6 mmol). Ratio of *linear:branched* isomers was determined to be 8:1 (*l* = 3:1, *Z:E*) from the crude reaction mixture using ^1H NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/diethyl ether: 100/1) provided the mixture of three isomers as a colorless oil (37.1 mg, 84% yield). The mixture could be separated via preparative TLC using hexane/ ethyl acetate: 20/1 as eluent.

ethyl (*Z*)-2-(bromomethyl)pent-2-enoate (linear-*Z*-6u)

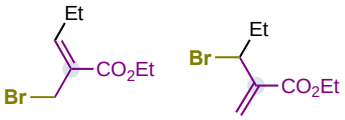


^1H NMR (400 MHz, $CDCl_3$) δ 6.95 (t, *J* = 7.7 Hz, 1H), 4.25 (q, *J* = 7.2, 2H), 4.23 (s, 2H), 2.31 (p, *J* = 7.6 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.5 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 149.5, 129.2, 61.2, 24.4, 22.4, 14.4, 12.7;

HRMS (ESI) calculated for $C_8H_{13}BrNaO_2^+$ $[M+Na]^+$ m/z: 242.9991, found: 242.9993.

Mixture of ethyl (*E*)-2-(bromomethyl)pent-2-enoate (linear-*E*-6u) and ethyl 3-bromo-2-methylenepentanoate (*branched*-6u)



^1H NMR (500 MHz, $CDCl_3$) δ 6.36 (s, 1H), 6.30 (t, *J* = 7.4 Hz, 2.20*1H), 5.94 (s, 1H), 4.86 (dd, *J* = 8.2, 6.0 Hz, 1H), 4.27 (q, *J* = 7.5, 4.51*2H), 4.26 (q, *J* = 7.0, 2H), 4.18 (s, 4.52*2H), 2.54 (p, *J* = 7.5 Hz, 4.48*2H), 2.12 – 2.01 (m, 2H), 1.34 (t, *J* = 7.5, 6.66*3H), 1.33 (t, *J* = 7.0, 3H), 1.06 (t, *J* = 7.4, 3H), 1.05 (t, *J* = 7.4, 6.70*3H); * indicates signals of the other isomer.

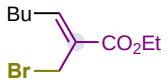
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.6, 165.3, 149.8, 141.9, 129.1, 126.4, 61.4, 60.9, 51.5, 33.9, 30.7, 23.3, 14.3, 14.3, 13.5, 12.7;

HRMS (ESI) calculated for $C_8H_{13}BrNaO_2^+$ $[M+Na]^+$ m/z: 242.9991, found: 242.9993.

ethyl (*Z*)-2-(bromomethyl)hept-2-enoate (linear-*Z*-6v), ethyl 3-bromo-2-methyleneheptanoate (*branched*-6v) and ethyl (*E*)-2-(bromomethyl)hept-2-enoate (linear-*E*-6v)

Prepared according to the general procedure B using 1-hexene (84.2 mg, 124 µL, 1.0 mmol) and Bu_4NBr (193.4 mg, 0.6 mmol). Ratio of *linear:branched* isomers was determined to be 7:1 (*l* = 3:1, *Z:E*) from the crude reaction mixture using ^1H NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/diethyl ether: 100/1) provided the mixture of three isomers as a colorless oil (43.8 mg, 88% yield). The mixture could be separated via preparative TLC using hexane/ ethyl acetate: 20/1 as eluent.

ethyl (*Z*)-2-(bromomethyl)hept-2-enoate (linear-*Z*-6v)

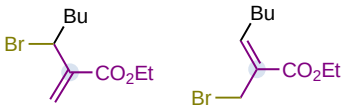


^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (t, *J* = 7.7 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.23 (s, 2H), 2.29 (q, *J* = 7.5 Hz, 2H), 1.55 – 1.46 (m, 2H), 1.43 – 1.35 (m, 2H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 148.4, 129.5, 61.2, 30.4, 28.8, 24.6, 22.6, 14.4, 14.0;

HRMS (ESI) calculated for $C_{10}H_{17}BrNaO_2^+$ $[M+Na]^+$ m/z: 271.0304, found: 271.0298.

Mixture of ethyl 3-bromo-2-methyleneheptanoate (*branched*-6v) and ethyl (*E*)-2-(bromomethyl)hept-2-enoate (linear-*E*-6v)



^{1}H NMR (500 MHz, $CDCl_3$) δ 6.35 (s, 1H), 6.32 (t, *J* = 7.5 Hz, 0.85*1H), 5.94 (s, 1H), 4.91 (ddd, *J* = 8.7, 5.8, 0.9 Hz, 1H), 4.27 (q, *J* = 7.1, 2H), 4.26 (q, *J* = 7.1, 1.70*2H), 4.18 (d, *J* = 0.7 Hz, 1.72*2H), 2.53 (q, *J* = 7.4 Hz, 1.73*2H), 2.12 – 1.95 (m, 2H), 1.55 – 1.49 (m, 0.84*1H), 1.46 – 1.40 (m, 1H, 0.87*1H), 1.40 – 1.31 (m, 3H, 1.67*2H), 1.34 (t, *J* = 7.1, 2.55*3H), 1.33 (t, *J* = 7.1, 3H), 0.92 (t, *J* = 7.1, 2.56*3H), 0.91 (t, *J* = 7.1, 3H); * indicates signals of the other isomer.

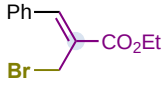
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.6, 165.4, 148.6, 142.1, 129.4, 126.4, 61.4, 60.9, 49.7, 37.2, 34.0, 31.2, 30.2, 29.6, 22.5, 22.2, 14.4, 14.3, 14.0, 14.0;

HRMS (ESI) calculated for $C_{10}H_{17}BrNaO_2^+$ $[M+Na]^+$ m/z: 271.0304, found: 271.0293.

ethyl (*E*)-2-(bromomethyl)-3-phenylacrylate (linear-*Z*-6w) and ethyl (*E*)-2-(bromomethyl)-3-phenylacrylate (linear-*E*-6w)

Prepared according to the general procedure B using styrene (104 mg, 114 µL, 1.0 mmol) and Bu_4NBr (193.4 mg, 0.6 mmol). Ratio of *linear:branched* isomers was determined to be >20:1 (*l* = 10:1, *Z:E*) from the crude reaction mixture using ^{1}H NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ diethyl ether: 50/1) provided the mixture of three isomers as a colorless oil (52.8 mg, 98% yield). The mixture could be separated via preparative TLC using hexane/ ethyl acetate: 20/1 as eluent.

ethyl (*E*)-2-(bromomethyl)-3-phenylacrylate (linear-*Z*-6w)

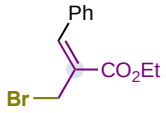


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.61 – 7.54 (m, 2H), 7.48 – 7.44 (m, 2H), 7.45 – 7.36 (m, 1H), 4.40 (s, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 142.8, 134.5, 129.7, 129.7, 129.1, 129.0, 61.6, 27.0, 14.4;

Spectroscopic data consistent with that reported in the literature[74].

ethyl (*E*)-2-(bromomethyl)-3-phenylacrylate (linear-*E*-6w)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.30 (m, 5H), 7.04 (s, 1H), 4.33 (d, *J* = 0.9 Hz, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 1.16 (t, *J* = 7.1 Hz, 3H);

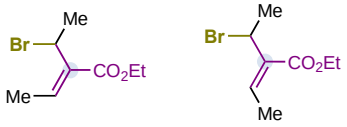
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 138.7, 134.8, 130.7, 129.0, 128.9, 128.3, 61.4, 34.2, 13.9;

HRMS (ESI) calculated for $C_{12}H_{13}BrNaO_2^+$ $[M+Na]^+$ m/z: 290.9991, found: 290.9991.

ethyl (*Z*)-2-(1-bromoethyl)but-2-enoate (*Z*-6x) and ethyl (*E*)-2-(1-bromoethyl)but-2-enoate (*E*-6x)

Prepared according to the general procedure B using *trans*-2-butene and Bu_4NBr (193.4 mg, 0.6 mmol). Ratio of *Z*/*E* isomers was determined to be 10:1 from the crude reaction mixture using ^{1}H NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ diethyl ether: 100/1) provided the mixture of two isomers as a colorless oil (30.9 mg, 70% yield).

Mixture of ethyl (*Z*)-2-(1-bromoethyl)but-2-enoate (*Z*-6x) and ethyl (*E*)-2-(1-bromoethyl)but-2-enoate (*E*-6x)



major isomer **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.91 (q, *J* = 7.4 Hz, 1H), 5.23 (q, *J* = 7.1 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 1.95 (d, *J* = 7.1 Hz, 3H), 1.93 (d, *J* = 7.4 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H);

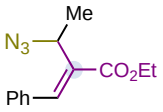
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 140.5, 134.9, 60.9, 41.1, 24.7, 14.6, 14.4;

HRMS (ESI) calculated for $C_8H_{13}BrNaO_2^+$ $[M+Na]^+$ m/z: 242.9991, found: 242,9989.

ethyl (*Z*)-3-azido-2-benzylidenebutanoate (6y)

Prepared according to the general procedure B using *trans*-*β*-methyl styrene (120 mg, 5.0 equiv, 1.0 mmol) and Bu_4NN_3 (170 mg, 0.6 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 66 % yield of **6y** and 18% yield of **7y**. Ratio of *linear:branched* isomers was determined to be >20:1 (*linear* = 16:1, *Z:E*). Purification by flash chromatography on silica gel (hexane/ ethyl acetate: 40/1) provided the title compound as colorless oil (34 mg, 70% yield).

[74] Ying, T.; Bao, W.; Wang, Z.; Zhang, Y. *J. Chem. Res.* **2005**, 96.



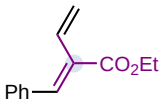
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.43 – 7.39 (m, 2H), 7.39 – 7.36 (m, 1H), 7.32 – 7.29 (m, 2H), 4.61 (q, *J* = 6.9 Hz, 1H), 4.34 (qd, *J* = 7.1, 2.7 Hz, 2H), 1.60 (d, *J* = 6.9 Hz, 3H), 1.39 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 142.2, 134.5, 132.2, 129.1, 129.1, 128.8, 61.3, 53.5, 18.2, 14.4;

HRMS: (ESI) calculated for $C_{13}H_{15}N_3O_2Na^+$ $[M+Na]^+$m/z: 268.1056, found: 268.1046.

^{1}H-^{1}H NOESY spectrum was measured.

Ethyl-(*E*)-2-benzylidenebut-3-enoate (7y)

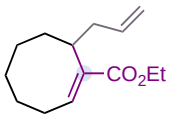


Diene **7y** was also isolated in 25% yield and the spectroscopic data consistent with that reported in the literature.[75,76]

^{1}H NMR (400 MHz, $CDCl_3$), δ 7.54 (s, 1H), 7.45 – 7.31 (m, 5H), 6.64 (ddd, *J* = 17.7, 11.6, 1.1 Hz, 1H), 5.85 (dd, *J* = 17.8, 1.8 Hz, 1H), 5.43 (dt, *J* = 11.6, 1.6 Hz, 1H), 4.32 (q, *J* = 7.2 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (101 MHz, CDCl3) δ 167.6, 139.2, 135.4, 130.6, 130.2, 129.8, 128.8, 128.5, 121.1, 61.1, 14.4.

ethyl (*E*)-8-allylcyclooct-1-ene-1-carboxylate (6z)



Prepared according to the general procedure B using cycloheptene (95.6 mg, 116 µL, 1.0 mmol) and allyltributylstannane (1.32 g, 1.24 mL, 20.0 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether: 200/1) provided the desired compound as a colorless oil (24.1 mg, 54% yield). Traces of the corresponding diene were observed by ^{1}H NMR of the reaction crude mixture.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (t, *J* = 8.5 Hz, 1H), 5.75 (dddd, *J* = 16.8, 10.1, 7.5, 6.6 Hz, 1H), 5.06 – 4.94 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.98 – 2.82 (m, 1H), 2.66 – 2.53 (m, 1H), 2.28 (m, 3H), 1.80 (m, 3H), 1.71 – 1.60 (m, 2H), 1.35 – 1.27 (m, 6H);

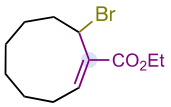
^{13}C NMR (101 MHz, CDCl3) δ 167.9, 142.5, 138.0, 135.9, 115.6, 60.1, 37.3, 36.5, 35.6, 30.0, 28.0, 27.8, 25.8, 14.4;

HRMS (ESI) calculated for $C_{14}H_{22}NaO_2^+$ $[M+Na]^+$ m/z: 245.1512, found: 245.1504.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

[75] Bellina, F.; Carpita, A.; De Santis, M.; Rossi, R. *Tetrahedron* **1994**, *50*, 12029.
[76] Um, J.; Xu.; H, Houk, K.; Tang, W. *J. Am. Chem. Soc.* **2009**, *131*, 6664.

ethyl (*Z*)-9-bromocyclonon-1-ene-1-carboxylate (6aa)



Prepared according to the general procedure B using *cis*-cyclooctene (110.2 mg, 130 µL, 1.0 mmol), and Bu_4NBr (128.9 mg, 0.4 mmol). Purification by flash chromatography on silica gel (hexane/ diethyl ether: 100/1) provided the desired compound as a colorless oil (26.5 mg, 48% yield). Traces of the corresponding diene were observed by ^{1}H NMR of the reaction crude mixture.

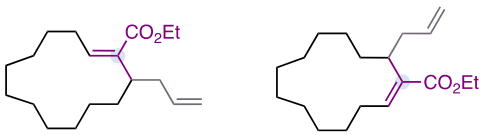
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (dd, *J* = 11.1, 7.8 Hz, 1H), 5.36 (dd, *J* = 12.2, 5.9 Hz, 1H), 4.26 (qd, *J* = 7.1, 2.1 Hz, 2H), 2.80 (m, 2H), 2.40 – 2.16 (m, 2H), 1.65 (m, 4H), 1.56 – 1.43 (m, 4H), 1.35 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 147.5, 133.2, 61.2, 46.4, 36.4, 28.5, 27.1, 27.0, 26.3, 25.9, 14.4;

HRMS (APCI) calculated for $C_{12}H_{20}BrO_2^+$ $[M+H]^+$ m/z: 275.0641, found: 275.0638.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

ethyl (*Z*)-13-allylcyclotridec-1-ene-1-carboxylate and ethyl (*E*)-13-allylcyclotridec-1-ene-1-carboxylate (6ab)



1.7:1 (*Z*:*E*)

Prepared according to the general procedure using cyclododecene (166.3 mg, 191 µL, 1.0 mmol, *E*/*Z* = 2:1) and allyltributylstannane (1.32 g, 1.24 mL, 20.0 mmol). Ratio of isomers was determined to be 1.7:1 (*Z*/*E*) from the crude reaction mixture using ^{1}H NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/diethyl ether: 100/1) provided the mixture of two isomers as a colorless oil (25.8 mg, 51% yield). Traces of the corresponding diene were observed by ^{1}H NMR of the reaction crude mixture.

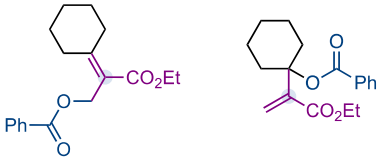
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.71 (dd, *J* = 9.1, 5.6 Hz, 1H), 5.79 – 5.73 (m, 0.31*1H), 5.73 – 5.63 (m, 1H), 5.73 – 5.63 (m, 0.32*1H), 5.01 – 4.93 (m, 0.64*2H), 4.99 – 4.93 (m, 1H), 4.91 (dd, *J* = 10.1, 2.3 Hz, 1H), 4.23 – 4.18 (m, 0.69*2H), 4.17 (qd, *J* = 7.2, 1.7 Hz, 2H), 2.81 (tt, *J* = 10.1, 5.9 Hz, 1H), 2.54 – 2.31 (m, 1.06*3H), 2.45 – 2.31 (m, 2H), 2.31 – 2.23 (m, 1H), 2.31 – 2.22 (m, 0.79*2H), 2.23 – 2.14 (m, 1H), 2.14 – 2.06 (m, 0.38*1H), 1.89 (ddt, *J* = 13.4, 10.6, 5.4 Hz, 1H), 1.43 – 1.17 (m, 18H), 1.43 – 1.17 (m, 7.64*18H), 0.93 – 0.86 (m, 2H), 0.87 – 0.80 (m, 0.74*2H); * *indicates signal of minor isomer*;

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.0, 168.2, 145.0, 141.2, 137.9, 137.5, 135.4, 134.9, 115.8, 115.5, 60.2, 60.1, 43.8, 40.3, 39.5, 37.7, 33.3, 32.2, 32.1, 29.8, 29.2, 28.1, 28.1, 27.8, 27.7, 27.2, 26.9, 26.1, 25.9, 25.7, 25.3, 25.0, 24.9, 24.6, 23.8, 22.8, 14.4, 14.3;

HRMS (ESI) calculated for $C_{19}H_{32}NaO_2^+$ $[M+Na]^+$ m/z: 315.2295, found: 315.2283.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2-cyclohexylidene-3-ethoxy-3-oxopropyl benzoate (*linear*-6ac) and 2-(3-ethoxy-3-oxoprop-1-en-2-yl)cyclohexyl benzoate (*branched*-6ac)



l:b = 4:1

Prepared according to the general procedure using methylene cyclohexane (96.2 mg, 120 µL, 1.0 mmol) and tetrabutylammonium benzoate (145.4 mg, 0.4 mmol). Ratio of *linear:branched* isomers was determined to be 4:1 according to ^{1}H-NMR analysis of crude reaction mixture. Purification by flash chromatography on silica gel (hexane/diethyl ether: 20/1) provided the mixture of two isomers as a colorless oil (37.5 mg, 62% yield).

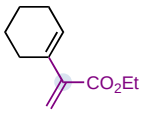
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 8.04 (m, 1.01*2H), 8.04 – 7.98 (m, 2H), 7.58 – 7.51 (m, 1.50*3H), 7.47 – 7.38 (m, 3H), 6.18 (s, 0.49*1 H), 5.72 (s, 0.50*1H), 5.11 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 4.11 (q, *J* = 7.1 Hz, 1.04*2H), 2.69 – 2.61 (m, 1.04*2H), 2.62-2.56 (m, 2H), 2.44 – 2.37 (m, 2H), 1.78 – 1.59 (m, 6H), 1.78 – 1.59 (m, 4.04*8H),1.27 (t, *J* = 7.1 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 1.54*3H); * *indicates signal of minor isomer* ;

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 166.6, 166.1, 165.3, 157.4, 145.2, 133.0, 132.8, 131.4, 130.4, 129.8, 129.7, 128.5, 128.4, 123.2, 120.7, 81.7, 61.7, 60.8, 60.6, 34.9, 32.9, 32.3, 28.6, 28.4, 26.5, 25.4, 22.0, 14.4, 14.2;

HRMS (ESI) calculated for $C_{18}H_{22}NaO_4^+$ $[M+Na]^+$ m/z: 325.1410, found: 325.1410.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

ethyl 2-(cyclohex-1-en-1-yl)acrylate (7ac)



Diene **7ac** was also isolated (5.4 mg, 15% yield) and characterized.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.99 (t, *J* = 4.1 Hz, 1H), 5.69 (s, 1H), 5.46 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.17 – 2.14 (m, 4H), 1.71 – 1.68 (m, 2H), 1.61 – 1.59 (m, 2H), 1.32 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 144.0, 133.5, 128.9, 118.9, 60.9, 26.4, 25.8, 22.7, 22.0, 14.4;

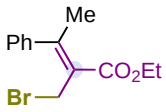
HRMS (ESI) calculated for $C_{11}H_{16}NaO_2^+$ $[M+Na]^+$ m/z: 203.1043, found: 203.1035.

ethyl-*Z*-2-(bromomethyl)-3-phenylbut-2-enoate (*Z*-6ad) and ethyl-*E*-2-(bromomethyl)-3-phenylbut-2-enoate (*E*-6ad)

Prepared according to the general procedure B using *α*-methylstyrene (120 mg, 5.0 equiv, 1.0 mmol) and Bu_4NBr (193.4 mg, 0.6 mmol). ^{1}H-NMR analysis of crude reaction mixture using anisole (21.6 mg, 0.2 mmol, 1.0 equiv.) as internal standard indicated 75 % yield of **6ad** and traces of the corresponding diene. Ratio of *linear:branched*

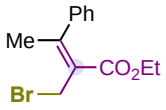
isomers was determined to be >20:1 (linear = 4:1, *Z:E*). Purification by flash chromatography on silica gel (hexane/ ethyl acetate: 40/1) provided a mixture of allyl bromides as colorless oil (40.8 mg, 72% yield).

ethyl-*Z*-2-(bromomethyl)-3-phenylbut-2-enoate (*Z*-6ad)



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.39 (m, 2H), 7.37 – 7.33 (m, 1H), 7.30 – 7.27 (m, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 4.10 (d, *J* = 0.8 Hz, 2H), 2.36 (d, *J* = 0.7 Hz, 3H), 1.38 (t, *J* = 7.1 Hz, 3H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 152.3, 141.9, 128.7, 128.2, 127.0, 126.6, 61.1, 31.6, 24.2, 14.4;
HRMS: (ESI) calculated for $C_{13}H_{15}BrO_2Na^+$ $[M+Na]^+$m/z: 305.0148, found: 305.0139.
NOESY experiments were performed.

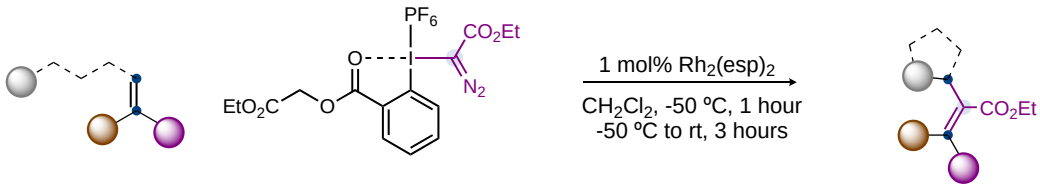
ethyl-*E*-2-(bromomethyl)-3-phenylbut-2-enoate (*E*-6ad)



^{1}H NMR (500 MHz, CDCl3) δ 7.34 – 7.27 (m, 3H), 7.18 – 7.10 (m, 2H), 4.40 (d, *J* = 0.5 Hz, 2H), 3.90 (q, *J* = 7.2 Hz, 2H), 2.24 (d, J = 0.5 Hz, 3H), 0.83 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, CDCl3) δ 167.9, 150.8, 143.2, 128.2, 127.9, 127.7, 126.8, 60.9, 29.2, 22.2, 13.6.
HSQC, HMBC and NOESY experiments were performed.
HRMS (ESI): calculated for $C_{13}H_{15}BrO_2Na^+$ $[M+Na]^+$ m/z: 305.0148, found: 305.0154.

Cyclization reactions induced by C(sp^2)–C(sp^2) bond cleavage: synthesis of heterocycles 14–18.

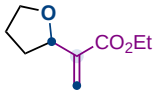
General Procedure C



2e **14 - 18**

To a 10 mL oven-dried tube equipped with a stirring bar was added $Rh_2(esp)_2$ (1.5 mg, 0.002 mmol, 1 mol%). The tube was sealed before being evacuated and backfilled with nitrogen. Alkene substrates (1.0 mmol, 5.0 equiv.) and degassed dichloromethane (1.0 mL) were added and the resulting mixture was cooled at -50 ºC. Then, a solution of reagent **2e** (119.2 mg, 0.2 mmol, 1.0 equiv.) in degassed dichloromethane (2 mL) was added dropwise during 1 h using a syringe pump. The tube was kept in the cooling bath and slowly warmed to room temperature during 3 hours. After that, the reaction mixture was filtered through a short plug of silica gel and washed with dichloromethane. Solvent was removed under *vacuum* and the crude residue was purified by column chromatography to yield product **14** – **18**.

ethyl 2-(tetrahydrofuran-2-yl)acrylate (14)



This compound was synthesized following the general procedure using *tert*-butyldimethyl-(pent-4-enyloxy)silane (200.4 mg, 1.0 mmol, 5.0 equiv.). Purification by flash chromatography on silica gel (hexane/ethyl acetate = 50/1) provided the title compound as a colorless oil (27.9 mg, 82% yield).

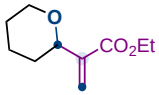
^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.15 (dd, *J* = 1.9, 1.3 Hz, 1H), 5.82 (t, *J* = 1.8 Hz, 1H), 4.66 (ddt, *J* = 7.7, 6.4, 1.5 Hz, 1H), 4.18 (qd, *J* = 7.1, 4.5 Hz, 2H), 4.00 – 3.87 (m, 1H), 3.82 – 3.76 (m, 1H), 2.29 – 2.20 (m, 1H), 1.94 – 1.81 (m, 2H), 1.66 – 1.59 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR δ 166.0, 142.8, 122.4, 77.0, 68.5, 60.5, 32.4, 25.5, 14.0;

HRMS: (ESI) calculated for $C_9H_{14}O_3Na^+$ $[M+Na]^+$m/z: 193.0835, found: 193.0830.

^{1}H-^{13}C HSQC spectrum was measured.

ethyl 2-(tetrahydro-2*H*-pyran-2-yl)acrylate (15)



This compound was synthesized following the general procedure using *tert*-butyldimethyl-(hex-5-enyloxy)silane (214.4 mg, 1.0 mmol, 5.0 equiv.). Purification by flash chromatography on silica gel (hexane/ethyl acetate = 50/1) provided the title compound as a colorless oil (29.4 mg, 80% yield).

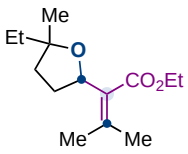
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.23 (dd, *J* = 1.7, 0.9 Hz, 1H), 5.87 (t, *J* = 1.6 Hz, 1H), 4.24 – 4.17 (m, 3H), 4.10 – 4.06 (m, 1H), 3.58 – 3.53 (m, 1H), 1.94 – 1.88 (m, 1H), 1.88 – 1.83 (m, 1H), 1.63 – 1.58 (m, 2H), 1.55 – 1.50 (m, 1H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.28 – 1.23 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2, 142.7, 124.1, 75.7, 69.1, 60.8, 32.6, 26.1, 23.9, 14.3;

HRMS: (ESI) calculated for $C_{10}H_{16}O_3Na^+$ $[M+Na]^+$m/z: 207.0992, found: 207.0995.

^{1}H-^{13}C HSQC spectrum was measured.

ethyl 2-(5-ethyl-5-methyltetrahydrofuran-2-yl)-3-methylbut-2-enoate (16)



This compound was synthesized following the general procedure using 1,2-dihydrolinalool (156.3 mg, 181 µL, 1.0 mmol, 5.0 equiv.). Purification by flash chromatography on silica gel (dichloromethane/hexane = 3:1 200mL, then hexane/ethyl acetate = 20/1) provided the title compound as a colorless oil (26.9 mg, 56% yield). Ratio of *syn*/*anti* was determined to be 1.5:1 from ^{1}H NMR spectroscopy.

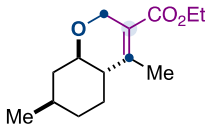
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.82 (dd, *J* = 8.7, 6.7 Hz, 1H), 4.76 (dd, *J* = 9.4, 6.2 Hz, 1.5*1H), 4.27 – 4.16 (m, 2H, 3.34*2H), 2.14 – 1.98 (m, 2H, 3.23*2H), 1.86 – 1.77 (m, 1H, 1.55*1H), 1.76 (s, 4.54*3H), 1.75 (s, 6H, 4.02*3H), 1.74 – 1.68 (m, 1H, 1.64*1H), 1.57 – 1.47 (m, 2H, 3.36*2H), 1.32 (t, *J* = 7.2 Hz, 4.60*3H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.17 (s, 3H), 1.13 (s, 4.69*3H), 0.89 (t, *J* = 7.6 Hz, 4.86*3H), 0.86 (t, *J* = 7.6 Hz, 3H); * *indicates signals of the other isomer*;

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 169.8, 135.9, 135.4, 131.2, 131.1, 83.6, 83.5, 76.4, 75.6, 60.4 (2C), 36.7, 36.6, 34.2, 33.8, 31.3, 31.2, 26.1, 25.3, 22.9, 22.8, 19.8, 19.8, 14.5, 14.4, 9.0, 9.0;

HRMS: (ESI) calculated for $C_{14}H_{24}O_3Na^+$ $[M+Na]^+$m/z: 263.1618, found: 263.1616.

^{1}H-^{13}C HSQC, ^{1}H-^{1}H NOESY spectra was measured.

ethyl (4a*S*,7*R*,8a*R*)-4,7-dimethyl-4a,5,6,7,8,8a-hexahydro-2*H*-chromene-3-carboxylate (17)



This compound was synthesized following the general procedure using *tert*-butyldimethyl(((1*R*,2*S*,5*R*)-5-methyl-2-(prop-1-en-2-yl)cyclohexyl)oxy)silane (268.5 mg, 1.0 mmol, 5.0 equiv.). Purification by flash chromatography on silica gel (hexane/ethyl acetate = 50/1) provided the title compound as a colorless oil (43.3 mg, 91% yield).

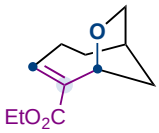
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.52 – 4.45 (m, 1H), 4.32 – 4.25 (m, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.08 (ddd, *J* = 11.4, 9.4, 3.8 Hz, 1H), 2.17 – 2.09 (m, 1H), 2.06 (td, *J* = 2.1, 1.2 Hz, 3H), 1.98 – 1.89 (m, 2H), 1.80 – 1.73 (m, 1H), 1.62 – 1.45 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.03 – 0.98 (m, 2H), 0.96 (d, *J* = 6.6 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 148.8, 123.8, 77.9, 66.7, 60.2, 45.5, 40.8, 35.1, 31.6, 26.7, 22.2, 17.2, 14.4;

HRMS: (ESI) calculated for $C_{14}H_{22}NaO_3^+$ $[M+Na]^+$ m/z: 261.1461, found:261.1457.

^{1}H-^{13}C HSQC spectrum was measured.

ethyl-7-oxabicyclo[4.2.1]non-4-ene-5-carboxylate (18)



This compound was synthesized following the general procedure using *tert*-butyl(cyclohex-3-en-1-ylmethoxy)dimethylsilane (226.4 mg, 1.0 mmol, 5.0 equiv.). Purification by flash chromatography on silica gel (hexane/ethyl acetate = 50/1) provided the title compound as a colorless oil (20.4 mg, 52% yield).

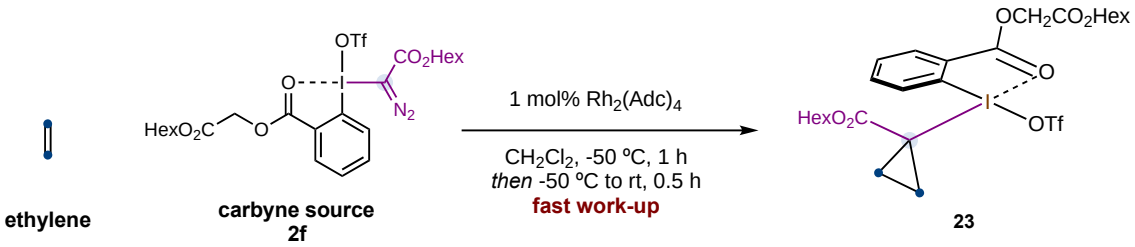
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (ddd, *J* = 8.8, 3.6, 1.5 Hz, 1H), 5.21 – 5.11 (m, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.02 – 3.95 (m, 1H), 3.87 (ddd, *J* = 8.1, 4.9, 1.5 Hz, 1H), 2.65 (dtd, *J* = 16.3, 7.9, 3.9 Hz, 2H), 2.29 (ddd, *J* = 16.6, 8.6, 4.1 Hz, 1H), 2.20 (dddd, *J* = 12.2, 8.7, 6.4, 1.5 Hz, 1H), 1.84 – 1.78 (m, 1H), 1.76 (d, *J* = 12.2 Hz, 1H), 1.63 (ddd, *J* = 12.3, 3.8, 2.0 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 145.0, 140.0, 74.5, 72.8, 60.7, 39.4, 38.3, 30.6, 24.7, 14.4;

HRMS: (ESI) calculated for $C_{11}H_{16}NaO_3^+$ $[M+Na]^+$ m/z: 219.0992, found: 219.0987.

^{1}H-^{13}C HSQC and ^{1}H-^{13}C HMBC spectra were measured.

Synthesis of hypervalent iodine compound 23.



To a 10 mL oven-dried tube equipped with a stirring bar was added $Rh_2(Adc)_2$ (1.0 mg, 0.001 mmol, 1 mol%) and 1.0 mL of dichloromethane. The tube was cooled at -94 ºC (liquid nitrogen/acetone bath) and ethylene gas was bubbled during 1 min. Then, a solution of **2f** (70.8 mg, 0.1 mmol, 1.0 equiv.) in degassed dichloromethane (1 mL) was added dropwise during 1 h using a syringe pump. The reaction mixture was stirred for 30 min while allowing the temperature to reach 22 ºC. After this, the reaction mixture was rapidly concentrated under *vacuum*, covered with 2.0 mL of diethyl ether and left overnight at -30 °C. The supernatant was removed and solids were washed with cold diethyl ether (3 x 2 mL). The title compound was collected and dried under high vacuum as a white-off solid (39.6 mg, 56% yield).

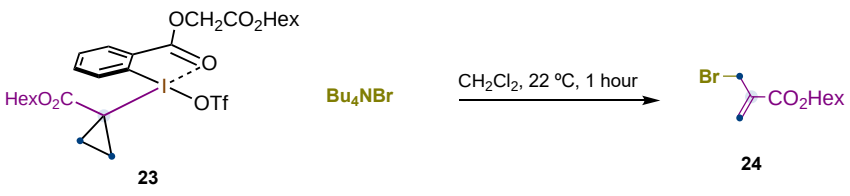
^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.45 (d, *J* = 7.6 Hz, 1H), 7.91 (t, *J* = 7.7 Hz, 1H), 7.84 – 7.79 (m, 2H), 5.02 (s, 2H), 4.23 – 4.19 (m, 4H), 2.51 – 2.46 (m, 2H), 2.19 – 2.15 (m, 2H), 1.69 – 1.64 (m, 2H), 1.62 – 1.57 (m, 2H), 1.38 – 1.29 (m, 6H), 1.24 – 1.20 (m, 6H), 0.89 (t, *J* = 6.6 Hz, 3H), 0.83 (t, *J* = 6.6 Hz, 3H);
^{13}C NMR (126 MHz, CD_2Cl_2) δ 167.5, 166.5, 166.2, 137.6, 133.7, 131.8, 130.3, 126.6, 120.7 (q, *J* =321.3 Hz), 112.0, 68.9, 66.3, 63.4, 31.4, 31.2, 28.4, 28.2, 27.5, 25.4, 25.4, 22.6, 22.5, 21.2, 13.8, 13.7;
^{19}F NMR (471 MHz, CD_2Cl_2) δ -78.81;

LRMS (ESI) *m/z* found for $C_{25}H_{36}IO_6^+$ $[M-OTf]^+$: 559.1.

The crystal structure of **23** has been deposited at the Cambridge Crystallographic Data Centre, CCDC 1896256.

Note: **23** is not stable in solution at room temperature for more than 30 min.

Control experiment to proof participation of 23 as intermediate:



To a 10 mL oven-dried tube equipped with a stirring bar was added compound **23** (35.4 mg, 0.05 mmol), Bu_4NBr (48.3 mg, 0.15 mmol) and 1.0 mL of degassed dichloromethane. The tube was sealed and left at room temperature for 1.0 hour. The solvent was removed under *vacuum* and the residue was purified by flash column

chromatography on silica gel (hexane/diethyl ether = 100/1) to afford the allyl bromide **24** as colorless oil (11.6 mg, 93% yield).

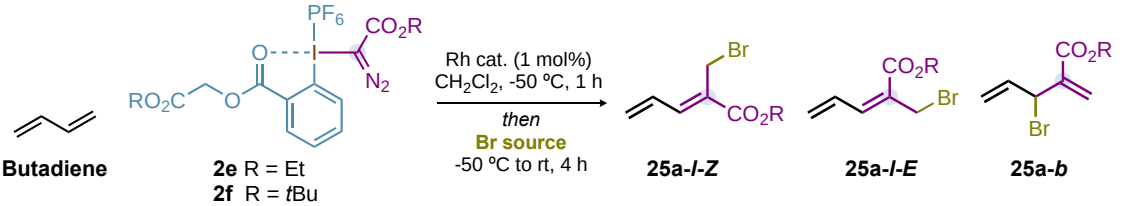
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.33 (d, *J* = 0.8 Hz, 1H), 5.94 (d, *J* = 0.9 Hz, 1H), 4.21 (t, *J* = 6.7 Hz, 2H), 4.18 (d, *J* = 0.9 Hz, 2H), 1.72 – 1.67 (m, 2H), 1.42 – 1.37 (m, 2H), 1.33 – 1.31 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.1, 137.8, 129.1, 65.6, 31.5, 29.5, 28.7, 25.7, 22.7, 14.1.

Optimization study of butadiene functionalization.

General Procedure D

To a 10 mL oven-dried tube equipped with a stirring bar was added $Rh_2(esp)_2$ (0.8 mg, 0.001 mmol, 1 mol%). The tube was sealed before being evacuated and backfilled with nitrogen. 1,3-butadiene (246 µL 15 % v/v in hexane, 0.5 mmol, 5 equiv.) and degassed dichloromethane (0.5 mL) were added and the resulting mixture was cooled at -50 ºC. Then, a solution of reagent **2i** (79.9 mg, 0.1 mmol, 1.0 equiv.) in degassed dichloromethane (1 mL) was added dropwise during 1 h using a syringe pump. Once reagent **2i** was fully consumed by TLC, the desired nucleophile and $TBAHSO_4$ (when necessary) were added to the reaction mixture. The tube was kept in the cooling bath and slowly warmed to room temperature during 4 hours. After that, the reaction mixture was filtered through a short plug of silica gel and washed with dichloromethane. Solvent was removed under *vacuum* and the crude residue was analyzed by GC-MS and ^{1}H-NMR using anisole as internal standard.



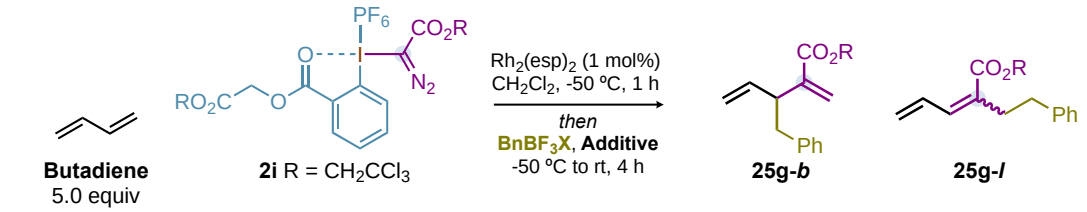
Butadiene

2e R = Et
2f R = *t*Bu
2g R = Bn
2h R = CH_2CCl_3

25a-*l*-*Z* **25a-*l*-*E*** **25a-*b***

Entry	Reagent **2**	Catalyst	Butadiene equiv.	Br source (equiv.)	Yield **25a** (%)[b]	**25a**, ***l*-*Z*:*l*-*E*:*b***
1	**2e**	$Rh_2(esp)_2$	10 equiv.	TBAB (2)	70	2:1:0
2	**2e**	$Rh_2(Adc)_4$	2.5 equiv.	TBAB (2)	67	2:1:0
3	**2e**	$Rh_2(Oct)_4$	1.5 equiv.	TBAB (2)	53	2:1:0
4	**2e**	$Rh_2(OAc)_4$	Bubbling[b]	TBAB (2)	nd[c]	-
5	**2e**	$Rh_2(OPiv)_4$	5.0 equiv.	TBAB (2)	52	2.5:1:0
6	**2g**	$Rh_2(esp)_2$	5.0 equiv.	TBAB (2)	57	10:1:0
7	**2h**	$Rh_2(esp)_2$	5.0 equiv.	TBAB (2)	55	10:1:0
8	**2i**	$Rh_2(esp)_2$	5.0 equiv.	TBAB (2)	60	10:1:0
9	**2i**	$Rh_2(esp)_2$	5.0 equiv.	TBAB (5)	60	10:1:0
10	**2i**	$Rh_2(esp)_2$	5.0 equiv.	TBAB (5)	56	10:1:0
11	**2i**	$Rh_2(esp)_2$	5.0 equiv.	TBAB (5)	45	10:1:0
12	**2i**	$Rh_2(esp)_2$	5.0 equiv.	TBAB (5)	59	10:1:0
13	**2i**	$Rh_2(esp)_2$	5.0 equiv.	TBAB (10)	34	10:1:0
14	**2i**	$Rh_2(esp)_2$	5.0 equiv.	TBAB (1.1)	76 (82)[d]	5:1:0
15	**2i**	$Rh_2(esp)_2$	5.0 equiv.	Bu_4PBr (1.1)	72	7:1:1
16	**2i**	$Rh_2(esp)_2$	5.0 equiv.	Me_3SiBr (1.1)	nd[c]	-

[a] Yield refers to the addition of **25a-*l*-*Z***, **25a-*l*-*E*** and **25a-*b*** and were calculated by using anisole as internal standard; [b] The solution of $Rh_2(esp)_2$ in CH_2Cl_2 was bubbled with butadiene at -50 ºC for 1 min.; [c] nd referes to not detected; [d] Yield in brackets refers to isolated yield; [d] esp = α, α, α′ ,α′-tetramethy-1,3-benzenedipropanoate; TBAB = tetrabutylammonium bromide.



Butadiene
5.0 equiv
15 % v/v in hexane

2i R = CH_2CCl_3

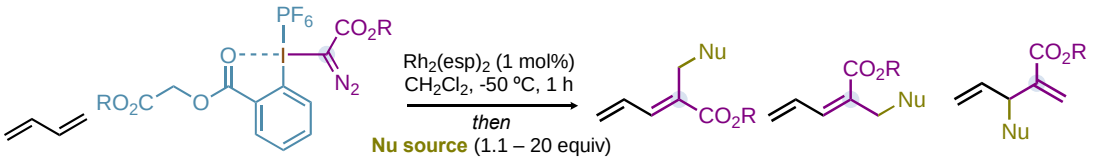
25g-*b* **25g-*l***

Entry	Additive	Nucleophile	Yield **25a** (%)[a]	**25g, *b*:*l*[b]**
1	-	$BnBF_3K$ (2.5 equiv.)	41	> 20:1
2	-	$BnBF_3TBA$ (2.5 equiv.)	< 10	-
3	$TBAHSO_4$ (1 equiv.)	$BnBF_3K$ (2.5 equiv.)	51	> 20:1
4	$TBAHSO_4$ (10 mol%)	$BnBF_3K$ (2.5 equiv.)	18	> 20:1
5	$TBAHSO_4$ (0.5 equiv.)	$BnBF_3K$ (2.5 equiv.)	36	> 20:1
6	$TBAHSO_4$ (1 equiv.)	$BnBF_3K$ (5 equiv.)	65 (70)	> 20:1
7	$TBAHSO_4$ (2.5 equiv.)	$BnBF_3K$ (5 equiv.)	56	> 20:1
8	$TBAHSO_4$ (1 equiv.)	$BnBF_3K$ (10 equiv.)	53	> 20:1
9	18-Crown-6 (1 equiv.)	$BnBF_3K$ (5 equiv.)	51	> 20:1
10	$TBAH_2PO_4$ (1 equiv.)	$BnBF_3K$ (2.5 equiv.)	47	> 20:1
11	$TBAPF_6$ (1 equiv.)	$BnBF_3K$ (2.5 equiv.)	47	> 20:1
12	$TBABPh_4$ (1 equiv.)	$BnBF_3K$ (2.5 equiv.)	7	-

[a] NMR yields calculated by using anisole as internal standard; Yield in brackets referes to isolated yield; [b] *b*:*l* refers to the *branched* to *linear* isomers ratio; [c] esp = α, α, α′, α′-tetramethy-1,3-benzenedipropanoate; TBA = tetrabutylammonium; 18-Crown-6 = 1,4,7,10,13,16-hexaoxacyclooctadecane.

Scope of the butadiene functionalization.

General Procedure E



Butadiene
5.0 equiv.
15 % v/v in hexane

2i R = CH_2CCl_3
1.0 equiv.

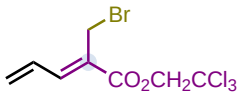
25-*l*-*Z*
(lineal-*Z* isomer)

25-*l*-*E*
(lineal-*E* isomer)

25-*b*
(*branched* isomer)

To a 10 mL oven-dried tube equipped with a stirring bar was added $Rh_2(esp)_2$ (1.5 mg, 0.002 mmol, 1 mol%). The tube was sealed before being evacuated and backfilled with nitrogen. 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol, 5 equiv.) and degassed dichloromethane (1.0 mL) were added and the resulting mixture was cooled at -50 ºC. Then, a solution of reagent **2i** (159.8 mg, 0.2 mmol, 1.0 equiv.) in degassed dichloromethane (2 mL) was added dropwise during 1 h using a syringe pump. Once reagent **2i** was fully consumed by TLC, the desired nucleophile (1.1 – 20.0 equiv.) and $TBAHSO_4$ (67.9 mg, 0.2 mmol, 1.0 equiv.; when necessary) were added to the reaction mixture. The tube was kept in the cooling bath and slowly warmed to room temperature during 4 hours. After that, the reaction mixture was filtered through a short plug of silica gel and washed with dichloromethane. Solvent was removed under *vacuum* and the crude residue was purified by column chromatography to yield products **25**.

2,2,2-trichloroethyl (*Z*)-2-(bromomethyl)penta-2,4-dienoate and 2,2,2-trichloroethyl (*E*)-2-(bromomethyl)penta-2,4-dienoate (25a)



Prepared according to the general procedure E using 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100:1) provided the title compound as a colorless oil (53.9 mg, 82 % yield, *Z*/*E* 4:1, *l*:*b* > 20:1).

2,2,2-trichloroethyl (*Z*)-2-(bromomethyl)penta-2,4-dienoate (25a-*l*-*Z*):

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dt, *J* = 11.6, 0.5 Hz, 1H), 6.79 (ddd, *J* = 16.6, 11.6, 10.0, Hz, 1H), 5.85 (ddd, *J* = 16.7, 1.5, 0.9 Hz, 1H), 5.79 (ddd, *J* = 10.0, 1.5, 0.7 Hz, 1H), 4.88 (s, 2H), 4.37 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 144.3, 131.0, 129.7, 127.3, 95.0, 74.7, 23.5.

HRMS (APCI) calculated for $C_8H_8Cl_3O_2^+$ $[M\text{-}Br]^+$ m/z: 240.9584, found: 240.9585.

2,2,2-trichloroethyl (*E*)-2-(bromomethyl)penta-2,4-dienoate (25a-*l*-*E*):

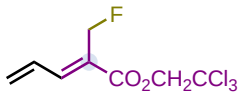
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.47 (ddd, *J* = 16.9, 11.3, 10.0 Hz, 1H), 6.85 (d, *J* = 11.3 Hz, 1H), 5.68 (d, *J* = 16.9 Hz, 1H), 5.64 (dd, *J* = 10.1, 1.6 Hz, 1H), 4.89 (s, 2H), 4.30 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 163.3, 146.5, 133.2, 129.0, 126.3, 94.8, 74.6, 32.8.

HRMS (APCI) calculated for $C_8H_8Cl_3O_2^+$ $[M\text{-}Br]^+$ m/z: 240.9584, found: 240.9580.

^{1}H-^{1}H COSY, ^{1}H-^{1}H NOESY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl (*Z*)-2-(fluoromethyl)penta-2,4-dienoate, 2,2,2-trichloroethyl (*E*)-2-(fluoromethyl)penta-2,4-dienoate and 2,2,2-trichloroethyl 3-fluoro-2-methylenepent-4-enoate (25b)



Prepared according to the general procedure E using 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100 : 1) provided the title compound as a colorless oil (23.5 mg, 45% yield, *Z*/*E* 4:1, *l*:*b* 2.5:1).

2,2,2-trichloroethyl (*Z*)-2-(fluoromethyl)penta-2,4-dienoate (25b-*l*-*Z*):

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 11.6, 3.7 Hz, 1H), 6.87 (dddd, *J* = 16.7, 11.7, 10.0, 1.8 Hz, 1H), 5.84 (dq, *J* = 16.7, 1.1 Hz, 1H), 5.79 – 5.73 (m, 1H), 5.29 (d, *J* = 47.5 Hz, 2H), 4.86 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.8 (d, *J* = 2.4 Hz), 147.1 (d, *J* = 5.5 Hz), 131.1 (d, *J* = 2.1 Hz), 130.2 (d, *J* = 3.4 Hz), 125.2 (d, *J* = 14.8 Hz), 95.0, 76.1 (d, *J* = 165.0 Hz), 74.6.

^{19}F NMR (471 MHz, $CDCl_3$) δ -179.72.

HRMS (APCI) calculated for $C_8H_8Cl_3FO_2^+$ $[M]^+$ m/z: 259.9568, found: 259.9563.

2,2,2-trichloroethyl (*E*)-2-(fluoromethyl)penta-2,4-dienoate (25b-*l*-*E*):

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (dddd, *J* = 16.9, 11.4, 10.0, 1.6 Hz, 1H), 6.90 – 6.84 (m, 1H), 5.74 – 5.64 (m, 2H), 5.15 (d, *J* = 47.2 Hz, 2H), 4.87 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 163.3 (d, *J* = 3.2 Hz), 145.7 (d, *J* = 10.6 Hz), 132.8 (d, *J* = 1.8 Hz), 129.0 (d, *J* = 2.9 Hz), 124.3 (d, *J* = 15.3 Hz), 94.9, 82.7 (d, *J* = 170.1 Hz), 74.4.

^{19}F NMR (471 MHz, $CDCl_3$) δ -178.90.

HRMS (APCI) calculated for $C_8H_8Cl_3FO_2^+$ $[M]^+$ m/z: 259.9568, found: 259.9569.

2,2,2-trichloroethyl 3-fluoro-2-methylenepent-4-enoate (25b-*b*):

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 – 6.56 (m, 1H), 6.15 – 6.12 (m, 1H), 5.99 (dddd, *J* = 17.2, 13.9, 10.6, 6.0 Hz, 1H), 5.83 – 5.71 (m, 1H), 5.49 (ddt, *J* = 17.2, 3.5, 1.2 Hz, 1H), 5.35 (dt, *J* = 10.6, 1.0 Hz, 1H), 4.87 – 4.80 (m, 2H).

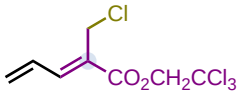
^{13}C NMR (126 MHz, $CDCl_3$) δ 163.2, 147.7, 134.0 (d, *J* = 21.1 Hz), 128.6 (d, *J* = 8.4 Hz), 119.1 (d, *J* = 11.7 Hz), 94.8, 89.5 (d, *J* = 172.6 Hz), 74.4.

^{19}F NMR (471 MHz, $CDCl_3$) δ -178.90.

LRMS (ESI) calculated for $C_8H_8Cl_3FO_2^+$ $[M]^+$ m/z: 260.0, found: 260.0.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl (*Z*)-2-(chloromethyl)penta-2,4-dienoate, 2,2,2-trichloroethyl (*E*)-2-(chloromethyl)penta-2,4-dienoate and 2,2,2-trichloroethyl 3-chloro-2-methylenepent-4-enoate (25c)



Prepared according to the general procedure E using 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100:1) provided the title compound as a colorless oil (40.0 mg, 72% yield, *Z*/*E* 5:1, *l*:*b* 5:1).

2,2,2-trichloroethyl (*Z*)-2-(chloromethyl)penta-2,4-dienoate (25c-*l*-*Z*):

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.45 (dt, *J* = 11.6, 0.5 Hz, 1H), 6.80 (ddd, *J* = 16.6, 11.5, 10.0 Hz, 1H), 5.85 (ddd, *J* = 16.6, 1.4, 0.9 Hz, 1H), 5.77 (dq, *J* = 10.0, 0.7 Hz, 1H), 4.87 (s, 2H), 4.47 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.5, 144.9, 130.9, 129.9, 127.0, 95.0, 74.7, 36.9.

HRMS (APCI) calculated for $C_8H_8Cl_4O_2^+$ $[M]^+$ m/z: 275.9273, found: 275.9273.

Mixture of 2,2,2-trichloroethyl (*E*)-2-(chloromethyl)penta-2,4-dienoate (25c-*l*-*E*) and 2,2,2-trichloroethyl 3-chloro-2-methylenepent-4-enoate (25c-*l*-*Z*):

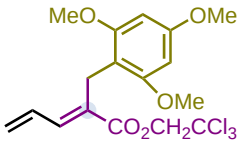
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (ddd, *J* = 16.9, 11.2, 10.0 Hz, 1H), 6.86 (dt, *J* = 11.2, 0.8 Hz, 1H), 6.59 (s, 0.67*1H), 6.16 (d, *J* = 1.1 Hz, 0.66*1H), 6.04 (ddd, *J* = 16.8, 10.1, 7.4 Hz, 0.63*1H), 5.70 – 5.66 (m, 1H), 5.66 – 5.63 (m, 1H), 5.44 (dt, *J* = 16.8, 1.0 Hz, 0.66*1H), 5.41 (dq, *J* = 7.4, 1.1 Hz, 0.60*1H), 5.29 (dt, *J* = 10.0, 0.9 Hz, 0.71*1H), 4.89 (s, 2H), 4.88 – 4.80 (m, 1.46*2H), 4.39 (d, *J* = 0.8 Hz, 2H); * indicates signals of the branched isomer.

^{13}C NMR (126 MHz, $CDCl_3$) δ 163.4, 163.3, 146.4, 139.0, 135.4, 133.0, 129.8, 128.9, 125.8, 118.6, 96.1, 92.0, 74.7, 74.6, 58.0, 45.5.

HRMS (APCI) calculated for $C_8H_8Cl_3O_2^+$ $[M\text{-}Cl]^+$ m/z: 240.9584, found: 240.9578.

^{1}H-^{1}H COSY, ^{1}H-^{1}H NOESY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl (*E*)-2-(2,4,6-trimethoxybenzyl)penta-2,4-dienoate and 2,2,2-trichloroethyl (*Z*)-2-(2,4,6-trimethoxybenzyl)penta-2,4-dienoate (25d)



Prepared according to the general procedure E using 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 50:1) provided the title compound as a colorless oil (36.1 mg, 72 % yield, *E*/*Z* 7:1, *l*:*b* > 20:1).

2,2,2-trichloroethyl (*E*)-2-(2,4,6-trimethoxybenzyl)penta-2,4-dienoate (25d-*l*-*E*):

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (dt, *J* = 11.3, 0.8 Hz, 1H), 6.78 (ddd, *J* = 16.8, 11.3, 10.0 Hz, 1H), 6.09 (s, 2H), 5.49 (ddd, *J* = 16.9, 2.0, 0.9 Hz, 1H), 5.39 (ddd, *J* = 10.0, 1.9, 0.8 Hz, 1H), 4.81 (s, 2H), 3.78 (s, 3H), 7.77 (s, 2H), 3.76 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 159.8, 158.7, 139.7, 132.8, 131.7, 124.6, 109.4, 95.5, 90.8, 74.6, 55.8, 55.4, 20.9.

HRMS (APCI) calculated for $C_{17}H_{20}Cl_3O_5^+$ $[M+H]^+$ m/z: 409.0371, found: 409.0381.

2,2,2-trichloroethyl (*Z*)-2-(2,4,6-trimethoxybenzyl)penta-2,4-dienoate (25d-*l*-*Z*):

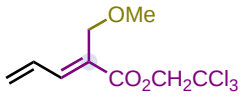
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (ddd, *J* = 16.9, 11.2, 10.1 Hz, 1H), 6.15 (s, 2H), 6.06 (ddt, *J* = 11.3, 1.8, 0.9 Hz, 1H), 5.31 – 5.23 (m, 2H), 4.87 (s, 2H), 3.83 (s, 3H), 3.76 (s, 6H), 3.67 (br s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2, 160.3, 159.2, 139.7, 133.8, 129.4, 123.5, 107.3, 95.3, 90.7, 74.5, 55.9, 55.5, 26.0.

LRMS (ESI) calculated for $C_{17}H_{20}Cl_3O_5^+$ $[M]^+$ m/z: 408.0, found: 408.0.

^{1}H-^{1}H COSY, ^{1}H-^{1}H NOESY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl (*E*)-2-(methoxymethyl)penta-2,4-dienoate, 2,2,2-trichloroethyl (*Z*)-2-(methoxymethyl)penta-2,4-dienoate and 2,2,2-trichloroethyl 3-methoxy-2-methylenepent-4-enoate (25e)



Prepared according to the general procedure E using 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 50:1) provided the title compound as a colorless oil (37.7 mg, 69 % yield, *Z*/*E* 3:1, *l*:*b* 3:1).

2,2,2-trichloroethyl (*E*)-2-(methoxymethyl)penta-2,4-dienoate (25e-*l*-*E*):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 11.5 Hz, 1H), 6.87 (ddd, *J* = 16.7, 11.4, 10.0 Hz, 1H), 5.76 (ddd, *J* = 16.8, 1.6, 0.9 Hz, 1H), 5.66 (ddd, *J* = 10.0, 1.6, 0.7 Hz, 2H), 4.84 (s, 3H), 4.32 (s, 3H), 3.38 (s, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 145.3, 131.7, 128.5, 127.1, 95.2, 74.6, 65.9, 58.5.

HRMS (APCI) calculated for $C_9H_{11}Cl_3O_3^+$ $[M]^+$ m/z: 271.9768, found: 271.9771.

2,2,2-trichloroethyl (*Z*)-2-(methoxymethyl)penta-2,4-dienoate (25e-*l*-*Z*):

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (ddd, *J* = 16.9, 11.3, 10.0 Hz, 1H), 6.80 (d, *J* = 11.3 Hz, 1H), 5.64 – 5.58 (m, 1H), 5.56 (dd, *J* = 10.0, 1.2 Hz, 1H), 4.85 (s, 2H), 4.21 (s, 2H), 3.41 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 143.5, 133.2, 127.0, 126.1, 95.1, 74.3, 72.5, 58.7.

HRMS (APCI) calculated for $C_9H_{11}Cl_3O_3^+$ $[M]^+$ m/z: 271.9768, found: 271.9767.

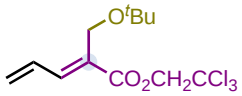
2,2,2-trichloroethyl 3-methoxy-2-methylenepent-4-enoate (25e-*b*):

^{1}H NMR (400 MHz $CDCl_3$) δ 6.49 (dd, *J* = 1.1, 0.6 Hz, 1H), 6.03 (t, *J* = 1.2 Hz, 1H), 5.77 (ddd, *J* = 17.2, 10.3, 6.8 Hz, 1H), 5.37 (dt, *J* = 17.2, 1.3 Hz, 1H), 5.27 (ddd, *J* = 10.3, 1.5, 1.0 Hz, 1H), 4.82 (s, 2H), 4.58 (ddd, *J* = 6.8, 1.2, 0.6 Hz, 1H), 3.37 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 139.3, 136.1, 127.8, 118.3, 95.0, 79.9, 74.4, 57.0.

HRMS (APCI) calculated for $C_9H_{11}Cl_3O_3^+$ $[M]^+$ m/z: 271.9768, found: 271.9768.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl (*E*)-2-(*tert*-butoxymethyl)penta-2,4-dienoate (25f)



Prepared according to the general procedure E using 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 50:1) provided the title compound as a colorless oil (22.1 mg, 35 % yield, *Z*/*E* 3:1, *l*:*b* 7:1).

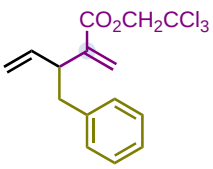
2,2,2-trichloroethyl (*E*)-2-(*tert*-butoxymethyl)penta-2,4-dienoate:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 11.4 Hz, 1H), 6.87 (ddd, *J* = 16.8, 11.4, 10.0 Hz, 1H), 5.71 (ddd, *J* = 16.8, 1.7, 0.9 Hz, 1H), 5.62 (ddd, *J* = 10.0, 1.7, 0.8 Hz, 1H), 4.82 (s, 2H), 4.28 (s, 2H), 1.27 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.85, 144.94, 131.98, 128.16, 127.75, 95.28, 74.60, 73.86, 55.96, 27.67.

HRMS (APCI) calculated for $C_8H_8Cl_3O_2^+$ $[M\text{-}O^tBu]^+$ m/z: 240.9584, found: 240.9584.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl 3-benzyl-2-methylenepent-4-enoate (25g)



Prepared according to the general procedure E using 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100:1) provided the title compound as a colorless oil (46.5 mg, 70 % yield, *b*:*l* > 20:1).

2,2,2-trichloroethyl 3-benzyl-2-methylenepent-4-enoate:

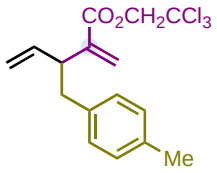
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.24 (m, 2H), 7.20 – 7.14 (m, 3H), 6.40 (d, *J* = 0.7 Hz, 1H), 5.89 (ddd, *J* = 17.1, 10.3, 7.7 Hz, 1H), 5.70 (s, 1H), 5.05 (dt, *J* = 6.9, 1.2 Hz, 1H), 5.04 (dt, *J* = 13.8, 1.2 Hz, 1H), 4.79 (d, *J* = 0.6 Hz, 2H), 3.64 (tdd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 3.04 – 2.83 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.1, 141.5, 139.6, 139.0, 129.4, 128.3, 127.6, 126.3, 116.3, 95.1, 74.5, 46.9, 40.3.

HRMS (APCI) calculated for $C_{15}H_{16}Cl_3O_2^+$ $[M+H]^+$ m/z: 333.0210, found: 333.0210.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl 3-(4-methylbenzyl)-2-methylenepent-4-enoate (25h)



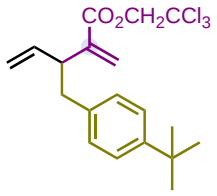
Prepared according to the general procedure E 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100:1) provided the title compound as a colorless oil (42.1 mg, 61 % yield, *b*:*l* 4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 – 7.03 (m, 4H), 6.40 (d, *J* = 0.7 Hz, 1H), 5.88 (ddd, *J* = 17.1, 10.4, 7.6 Hz, 1H), 5.69 (m, 1H), 5.06 – 5.04 (m, 1H), 5.03 – 5.00 (m, 1H), 4.79 (d, *J* = 0.6 Hz, 2H), 3.62 (tdd, *J* = 7.9, 6.8, 1.1 Hz, 1H), 2.95 (dd, *J* = 13.7, 6.8 Hz, 1H), 2.83 (dd, *J* = 13.7, 8.1 Hz, 1H), 2.30 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.2, 141.5, 139.1, 136.4, 135.7, 129.2, 129.0, 127.6, 116.2, 95.1, 74.5, 46.8, 39.8, 21.2.

HRMS (APCI) calculated for $C_{16}H_{18}Cl_3O_2^+$ $[M+H]^+$ m/z: 347.0366, found: 347.0367.

2,2,2-trichloroethyl 3-(4-(*tert*-butyl)benzyl)-2-methylenepent-4-enoate (25i)



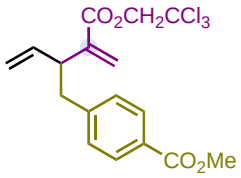
Prepared according to the general procedure E 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100:1) provided the title compound as a colorless oil (31.9 mg, 41 % yield, *b*:*l* > 20:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 2H), 7.11 – 7.08 (m, 2H), 6.41 (d, *J* = 0.7 Hz, 1H), 5.90 (ddd, *J* = 16.7, 10.7, 7.5 Hz, 1H), 5.71 (t, *J* = 0.9 Hz, 1H), 5.07 – 5.06 (m, 1H), 5.05–5.02 (m, 1H), 4.78 (d, *J* = 1.2 Hz, 2H), 3.69–3.62 (m, 1H), 2.98 – 2.82 (m, 2H), 1.30 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.2, 149.0, 141.6, 139.2, 136.4, 129.0, 127.6, 125.2, 116.1, 95.1, 74.4, 46.5, 39.8, 34.5, 31.5.

HRMS (APCI) calculated for $C_{19}H_{24}Cl_3O_2^+$ $[M+H]^+$ m/z: 389.0836, found: 389.0834.

Methyl 4-(3-((2,2,2-trichloroethoxy)carbonyl)-2-vinylbut-3-en-1-yl)benzoate (25j)



Prepared according to the general procedure E 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100:1) provided the title compound as a colorless oil (31.9 mg, 41 % yield, *b*:*l* > 20:1).

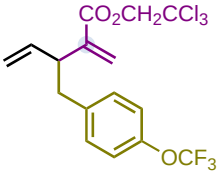
2,2,2-trichloroethyl 3-(4-methylbenzyl)-2-methylenepent-4-enoate:

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 – 7.90 (m, 2H), 7.24 – 7.21 (m, 2H), 6.40 (d, *J* = 0.6 Hz, 1H), 5.85 (ddd, *J* = 17.1, 10.2, 7.7 Hz, 1H), 5.69 (br s, 1H), 5.04 (m, 1H), 5.03 – 4.98 (m, 1H), 4.80 (d, *J* = 2.6 Hz, 2H), 3.89 (s, 3H), 3.67 – 3.58 (m, 1H), 3.11 – 2.85 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 164.9, 145.0, 141.1, 138.4, 129.7, 129.4, 128.3, 127.8, 116.7, 95.0, 74.4, 52.1, 46.8, 40.2.

HRMS (APCI) calculated for $C_{17}H_{18}Cl_3O_4^+$ $[M+H]^+$ m/z: 391.0265, found: 391.0261.

2,2,2-trichloroethyl 2-methylene-3-(4-(trifluoromethoxy)benzyl)pent-4-enoate (25k)



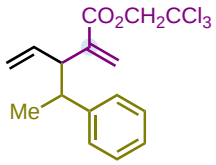
Prepared according to the general procedure E 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 50:1) provided the title compound as a colorless oil (57.7 mg, 69 % yield, *b*:*l* 4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 – 7.15 (m, 2H), 7.13 – 7.08 (m, 2H), 6.42 (d, *J* = 0.6 Hz, 1H), 5.86 (ddd, *J* = 17.1, 10.2, 7.7 Hz, 1H), 5.70 (m, 1H), 5.0 – 5.05 (m, 1H), 5.05 – 5.00 (m, 1H), 4.79 (d, *J* = 1.4 Hz, 2H), 3.64 – 3.56 (m, 1H), 2.99 (dd, *J* = 13.7, 6.8 Hz, 1H), 2.86 (dd, *J* = 13.7, 8.2 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.0, 147.8 (q, *J* = 1.86 Hz), 141.2, 138.5, 138.3, 130.6, 127.8, 120.9, 120.6 (q, *J* = 256.67 Hz), 116.70, 95.08, 74.47, 46.83, 39.61.

HRMS (APCI) calculated for $C_{16}H_{15}Cl_3F_3O_3^+$ $[M+H]^+$ m/z: 417.0033, found: 417.0031.

2,2,2-trichloroethyl 2-methylene-3-(1-phenylethyl)pent-4-enoate (25l)



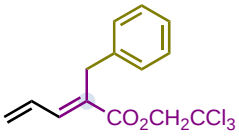
Prepared according to the general procedure E 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100:1) provided the title compound as a colorless oil (32.7 mg, 47 % yield, *b*:*l* > 20:1, *dr* = 1:1).

2,2,2-trichloroethyl 2-methylene-3-(1-phenylethyl)pent-4-enoate (mixture of diastereoisomers):

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 7.17 – 7.12 (m, 5H), 6.47 (d, *J* = 0.8 Hz, 1H), 6.20 (d, *J* = 0.8 Hz, 1H), 5.97 (ddd, *J* = 17.0, 10.1, 9.0 Hz, 1H), 5.71 (ddd, *J* = 17.0, 10.3, 8.4 Hz, 1H), 5.67 – 5.65 (m, 1H), 5.53 – 5.51 (m, 1H), 5.17 – 5.10 (m, 2H), 4.90 (ddd, *J* = 10.3, 1.6, 0.8 Hz, 1H), 4.88 (ddd, *J* = 17.0, 1.6, 1.0 Hz, 1H), 4.85 (s, 2H), 4.77 – 4.66 (m, 2H), 3.50 – 3.43 (m, 2H), 3.17 – 3.07 (m, 2H), 1.28 (d, *J* = 7.0 Hz, 3H), 1.24 (d, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.3, 165.0, 145.3, 144.6, 141.2, 141.0, 138.7, 138.2, 128.4, 128.4, 128.3, 128.2, 128.1, 127.8, 126.4, 126.3, 117.2, 116.6, 95.2, 95.1, 74.5, 74.3, 53.6, 52.9, 43.0, 42.8, 20.5, 20.5.

HRMS (APCI) calculated for $C_{16}H_{18}Cl_3O_2^+$ $[M+H]^+$ m/z: 347.0367, found: 347.0369.

2,2,2-trichloroethyl (*E*)-2-benzylpenta-2,4-dienoate and 2,2,2-trichloroethyl (*Z*)-2-benzylpenta-2,4-dienoate (25m)



Prepared according to the general procedure E 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100:1) provided the title compound as a colorless oil (35.8 mg, 56 % yield, *E*/*Z* 1.4:1, *l*:*b* > 20:1).

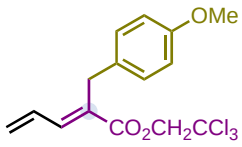
2,2,2-trichloroethyl (*E*)-2-benzylpenta-2,4-dienoate:

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.49 (d, *J* = 11.4 Hz, 1H), 7.29 – 7.16 (m, 5H), 6.82 (ddd, *J* = 16.7, 11.4, 10.1 Hz, 1H), 5.75 (ddd, *J* = 16.7, 0.8, 0.7 Hz, 1H), 5.64 – 5.60 (m, 1H), 4.77 (s, 2H), 3.85 (s, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.25, 141.99, 139.04, 131.97, 129.74, 128.59, 128.46, 127.24, 126.46, 95.20, 74.55, 32.66.

HRMS (APCI) calculated for $C_{14}H_{14}Cl_3O_2^+$ $[M+H]^+$ m/z: 319.0054, found: 319.0047.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl (*E*)-2-(4-methoxybenzyl)penta-2,4-dienoate and 2,2,2-trichloroethyl (*Z*)-2-(4-methoxybenzyl)penta-2,4-dienoate (25n)



Prepared according to the general procedure E using 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100:1) provided the title compound as a colorless oil (37.8 mg, 54 % yield, *E*/*Z* 2.6:1, *l*:*b* 20:1).

2,2,2-trichloroethyl (*E*)-2-benzylpenta-2,4-dienoate:

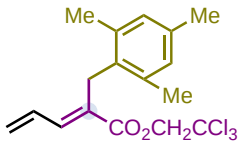
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 11.4 Hz, 1H), 7.14 – 7.09 (m, 2H), 6.90 – 6.81 (m, 1H), 6.82 – 6.78 (m, 2H), 5.74 (ddd, *J* = 16.7, 1.7, 0.9 Hz, 1H), 5.61 (ddd, *J* = 10.0, 1.7, 0.8 Hz, 1H), 4.77 (d, *J* = 2.3 Hz, 2H), 3.79 – 3.77 (m, 2H), 3.77 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 158.3, 141.6, 132.0, 131.1, 130.2, 129.4, 127.1, 114.0, 95.2, 74.5, 55.4, 31.8.

HRMS (APCI) calculated for $C_{15}H_{16}Cl_3O_3^+$ $[M+H]^+$ m/z: 349.0160, found: 349.0159.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl (*E*)-2-(2,4,6-trimethylbenzyl)penta-2,4-dienoate and 2,2,2-trichloroethyl (*Z*)-2-(2,4,6-trimethylbenzyl)penta-2,4-dienoate (25o)



Prepared according to the general procedure E 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel hexane/diethyl ether 100:1) provided the title compound as a colorless oil (29.7 mg, 41% yield, *E*/*Z* 2.4:1, *l*:*b* > 20:1).

Mixture of 2,2,2-trichloroethyl (*E*)-2-(2,4,6-trimethylbenzyl)penta-2,4-dienoate (25o-*l*-*E*) and 2,2,2-trichloroethyl (*Z*)-2-(2,4,6-trimethylbenzyl)penta-2,4-dienoate (25o-*l*-*Z*):

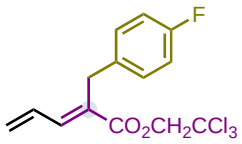
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.32 (m, 0.34*1H), 7.35 – 7.26 (m, 1H), 6.88 (s, 0.76*2H), 6.82 (s, 2H), 6.41 (ddd, *J* = 16.7, 11.4, 10.0 Hz, 1H), 5.89 – 5.84 (m, 0.44*1H), 5.56 (ddd, *J* = 16.7, 1.8, 0.9 Hz, 1H), 5.42 (ddd, *J* = 10.0, 1.8, 0.8 Hz, 1H), 5.35 – 5.31 (m, 0.48*1H), 5.27 – 5.20 (m, 0.48*1H), 4.91 (s, 0.75*2H), 4.78 (s, 2H), 3.82 (s, 2H), 3.72 (s, 0.77*2H), 2.29 (s, 1.34*3H), 2.28 (s, 6H), 2.25 (s, 3H), 2.20 (s, 2.33*6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 165.8, 140.9, 140.1, 137.3, 137.1, 136.3, 135.9, 133.4, 132.8, 131.4, 131.3, 129.3, 129.2, 129.1, 127.8, 126.6, 124.7, 95.4, 95.2, 74.4, 74.4, 32.3, 28.6, 21.1, 21.0, 20.7, 19.9.

HRMS (APCI) calculated for $C_{17}H_{20}Cl_3O_2^+$ $[M+H]^+$ m/z: 361.0523, found: 361.0522.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOESY spectra were measured.

2,2,2-trichloroethyl (*E*)-2-(4-fluorobenzyl)penta-2,4-dienoate and 2,2,2-trichloroethyl (*Z*)-2-(4-fluorobenzyl)penta-2,4-dienoate (25p)



Prepared according to the general procedure E 1,3-butadiene (492 µL 15 % v/v in hexane, 1.0 mmol) and reagent **2i** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel hexane/diethyl ether 100:1) provided the title compound as a colorless oil (26.3 mg, 39% yield, *E*/*Z* 2.2:1, *l*:*b* > 20:1).

Mixture of 2,2,2-trichloroethyl (*E*)-2-(2,4,6-trimethylbenzyl)penta-2,4-dienoate (25o-*l*-*E*) and 2,2,2-trichloroethyl (*Z*)-2-(2,4,6-trimethylbenzyl)penta-2,4-dienoate (25o-*l*-*Z*):

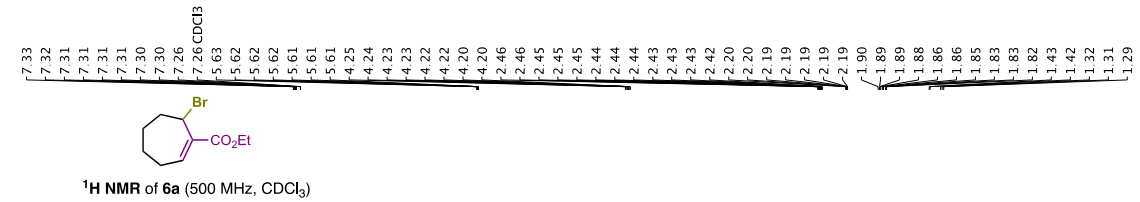
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 – 7.50 (m, 0.42*1H), 7.50 – 7.46 (m, 1H), 7.22 (td, *J* = 7.9, 6.0 Hz, 0.46*1H), 7.18 – 7.13 (m, 2H), 7.00 – 6.97 (m, 0.50*1H), 6.98 – 6.92 (m, 1H+0.85*2H), 6.92 – 6.85 (m, 1H), 6.85 – 6.74 (m, 1H+0.49*1H), 5.80 – 5.76 (m, 0.49*1H), 5.79 – 5.74 (m, 1H), 5.66 – 5.63 (m, 0.47*1H), 5.65 – 5.61 (m, 1H), 4.78 (s, 0.89*2H), 4.77 (s, 2H), 3.83 (s, 0.92*2H), 3.80 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 166.1, 163.1 (d, *J* = 245.5 Hz), 161.7 (d, *J* = 244.4 Hz), 142.4, 142.0, 141.6 (d, *J* = 7.3 Hz), 134.6 (d, *J* = 3.3 Hz), 131.7, 131.7, 130.0 (d, *J* = 8.3 Hz), 129.9 (d, *J* = 7.9 Hz), 129.6, 127.8, 127.6, 124.1 (d, *J* = 2.8 Hz), 115.4 (d, *J* = 21.5 Hz), 113.4 (d, *J* = 21.1 Hz), 95.1, 95.1, 74.6, 74.5, 32.4 (d, *J* = 1.9 Hz), 31.9.

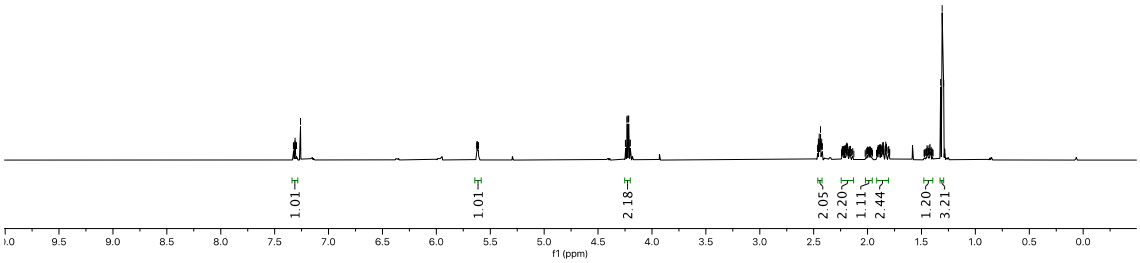
LRMS (ESI) calculated for $C_{14}H_{12}Cl_3FO_2^+$ $[M]^+$ m/z: 335.99, found: 335.99.

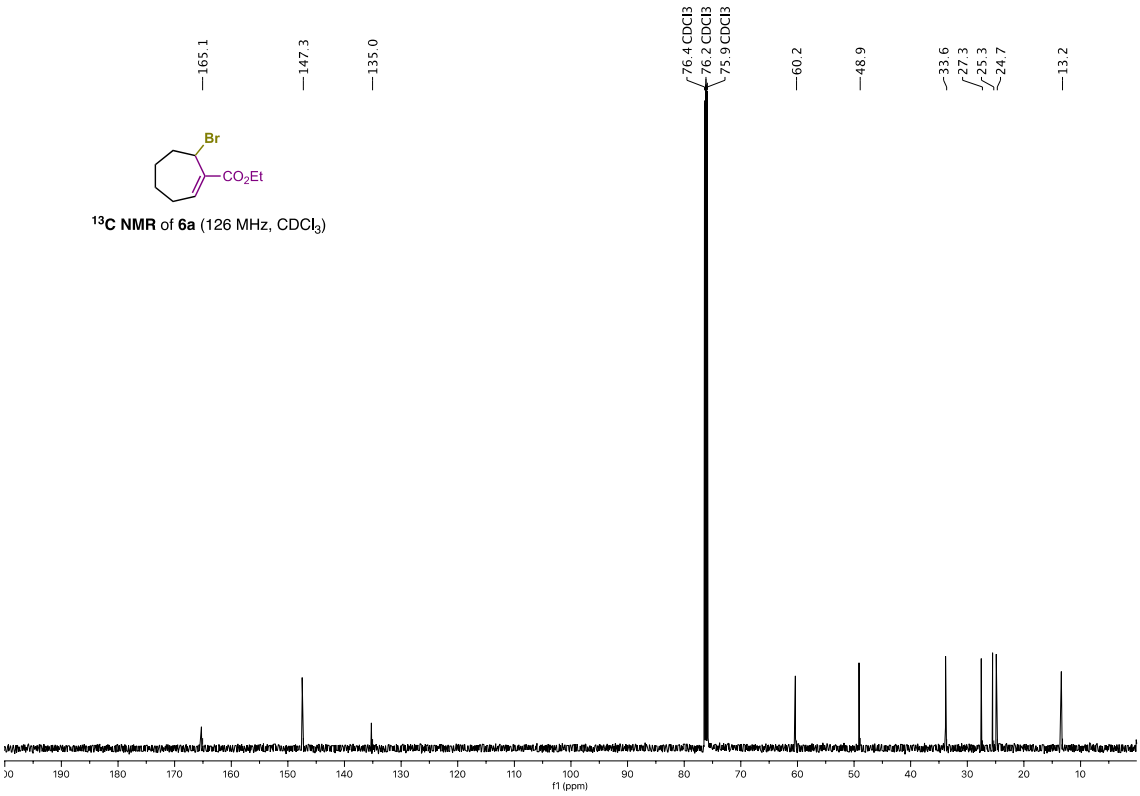
^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOESY spectra were measured.

Selected NMR spectra

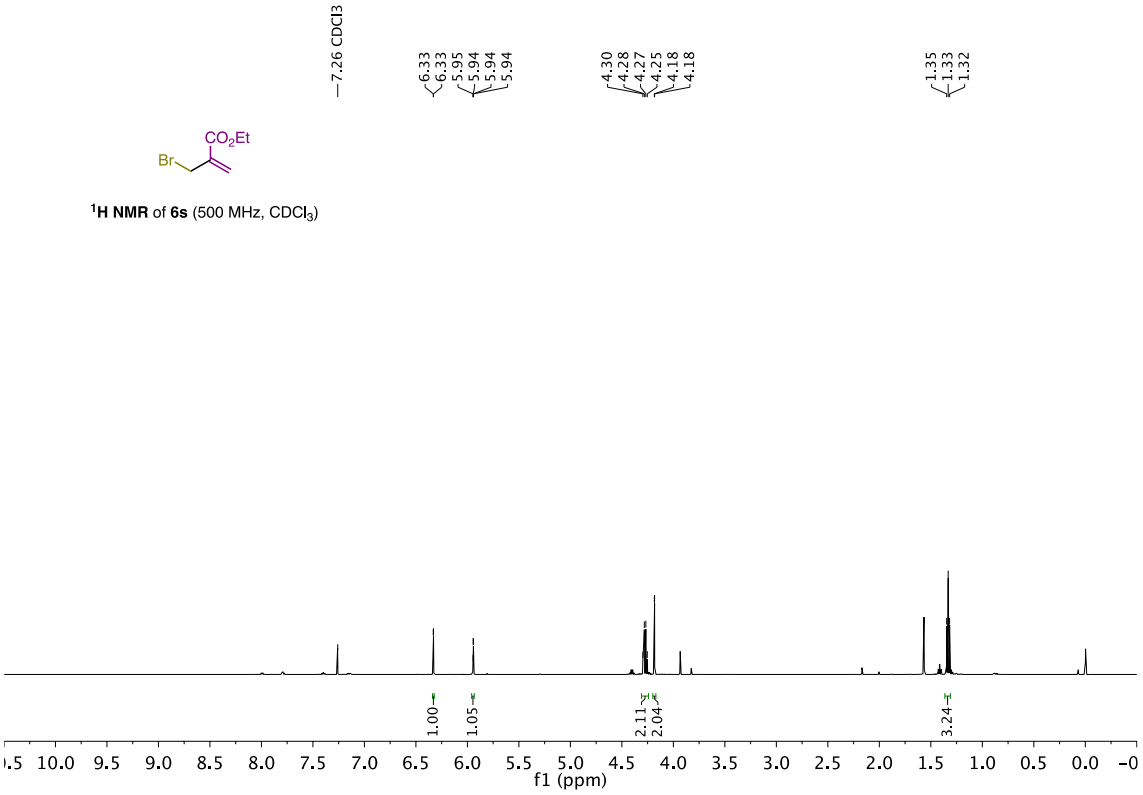


^{1}H NMR of **6a** (500 MHz, $CDCl_3$)

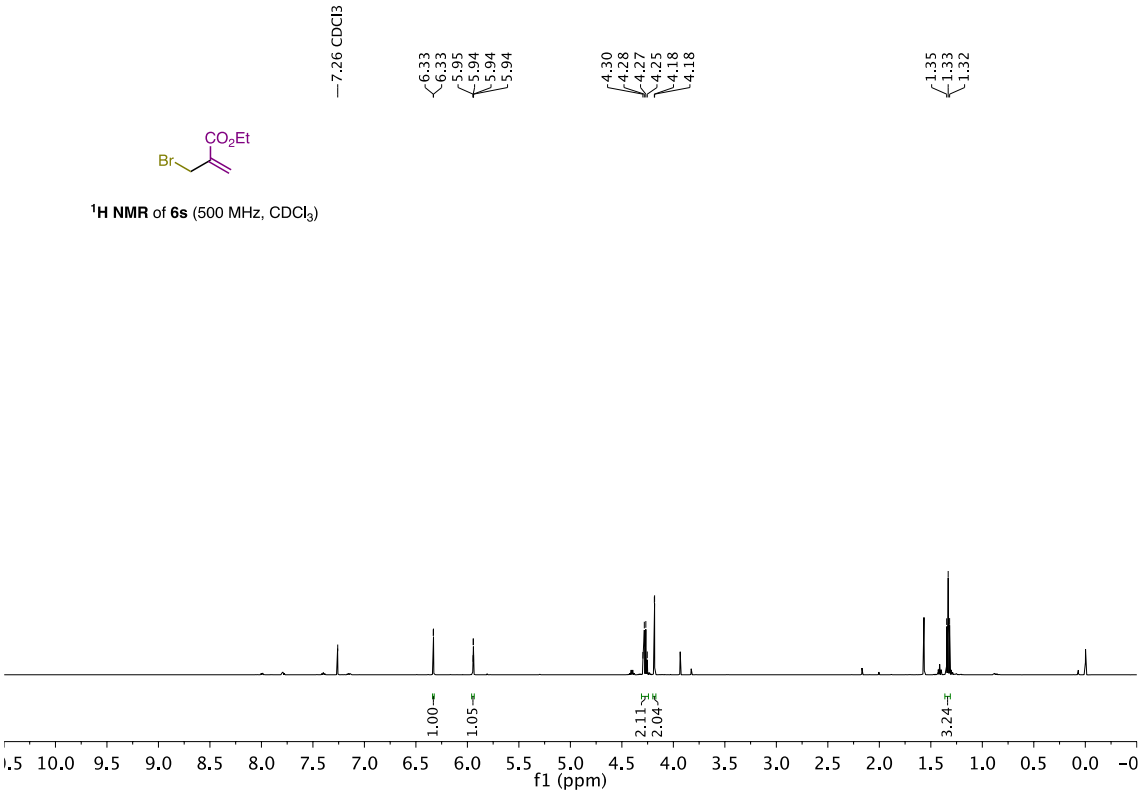




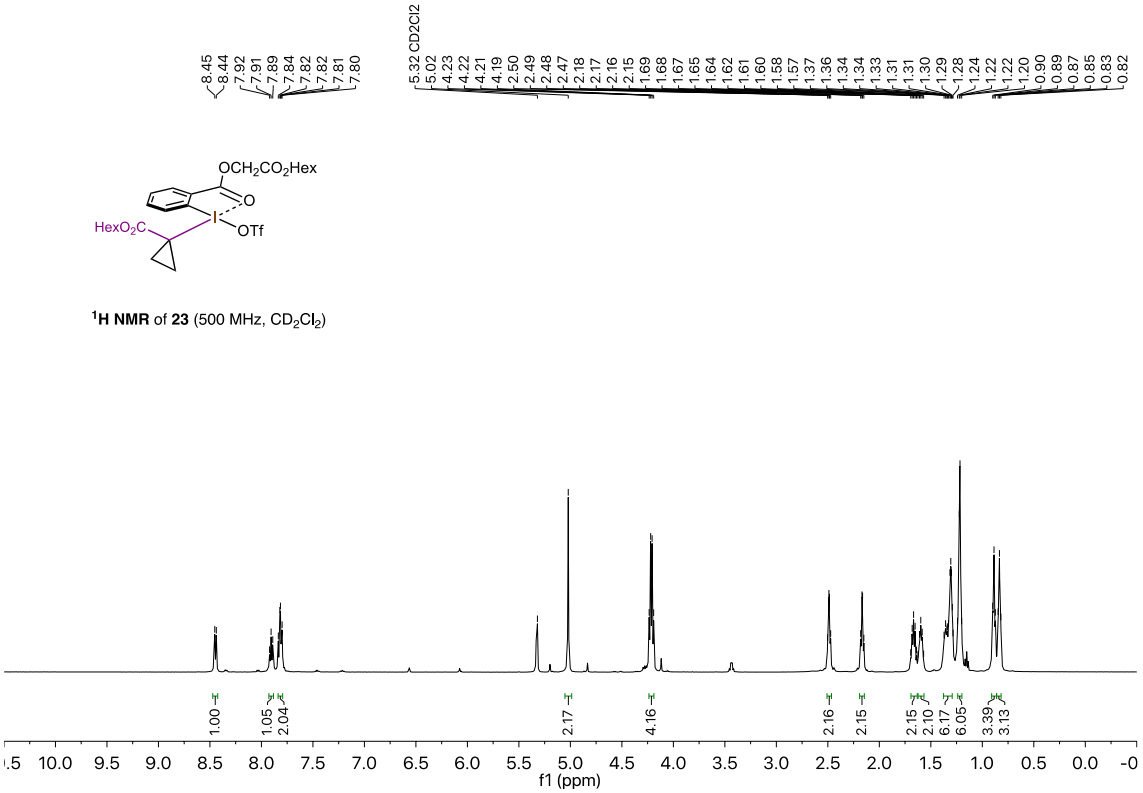
^{13}C NMR of **6a** (126 MHz, $CDCl_3$)



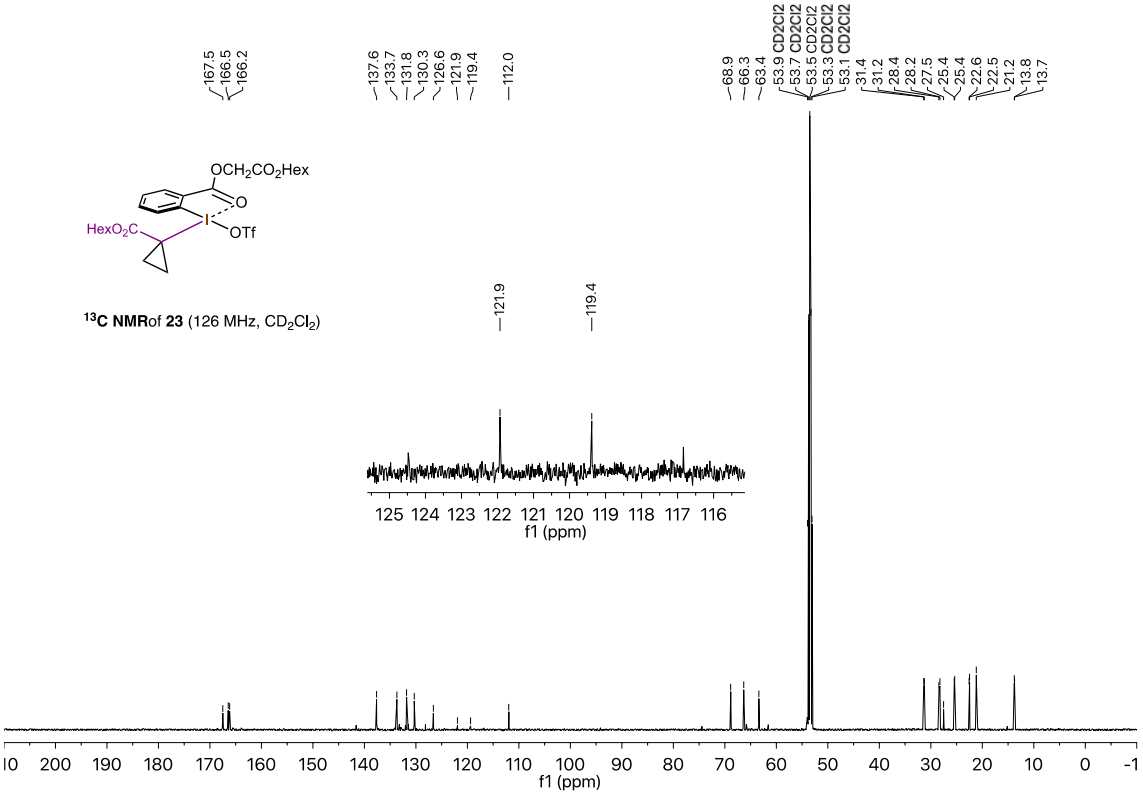
^{1}H NMR of **6s** (500 MHz, $CDCl_3$)



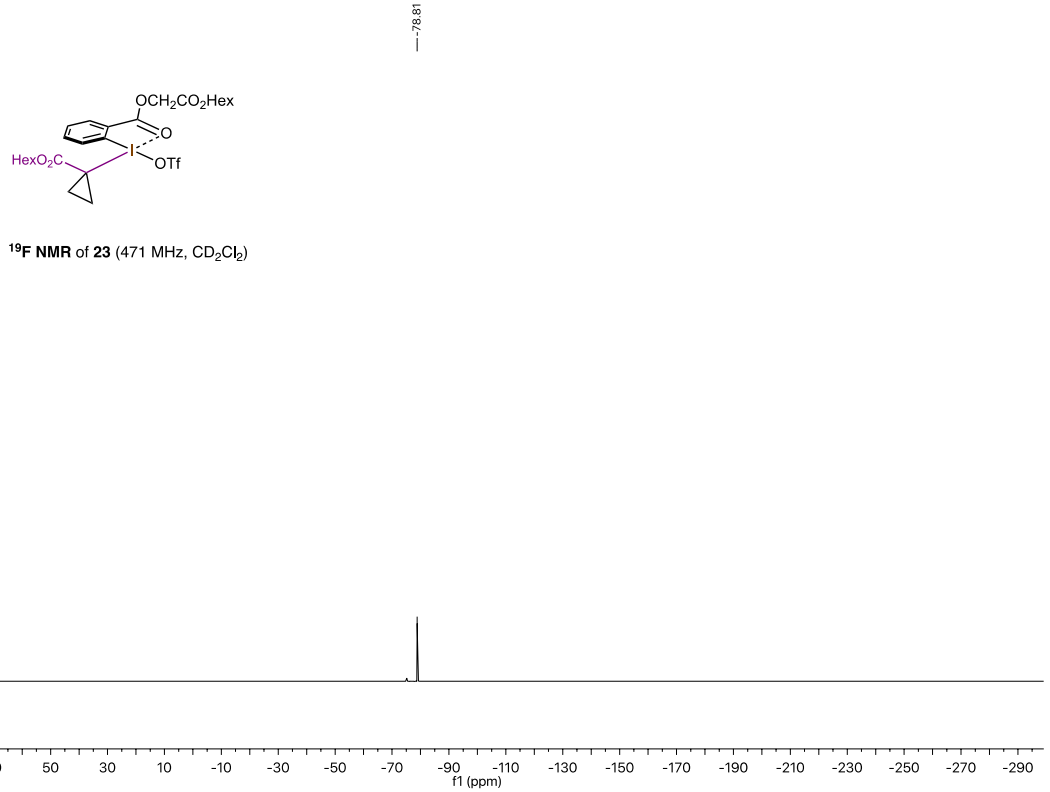
^{1}H NMR of **6s** (500 MHz, $CDCl_3$)



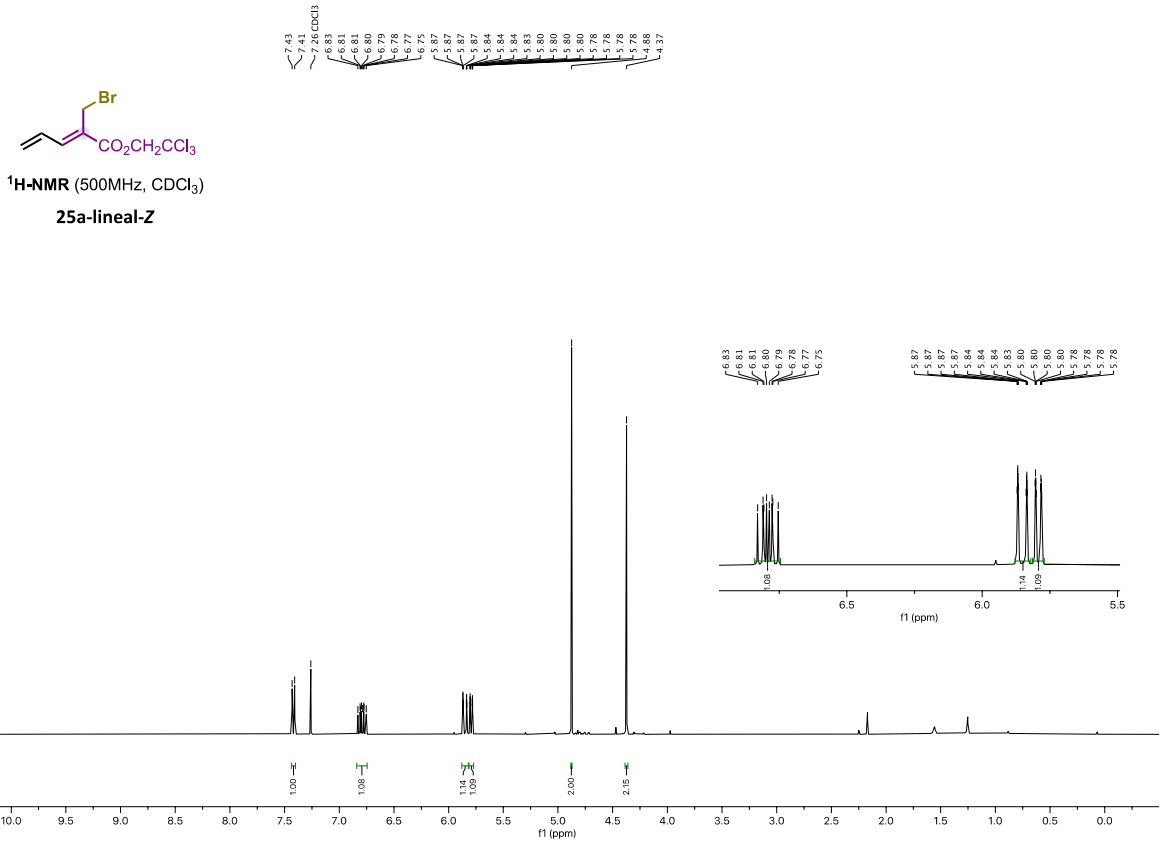
^{1}H NMR of **23** (500 MHz, CD_2Cl_2)



^{13}C NMRof **23** (126 MHz, CD_2Cl_2)

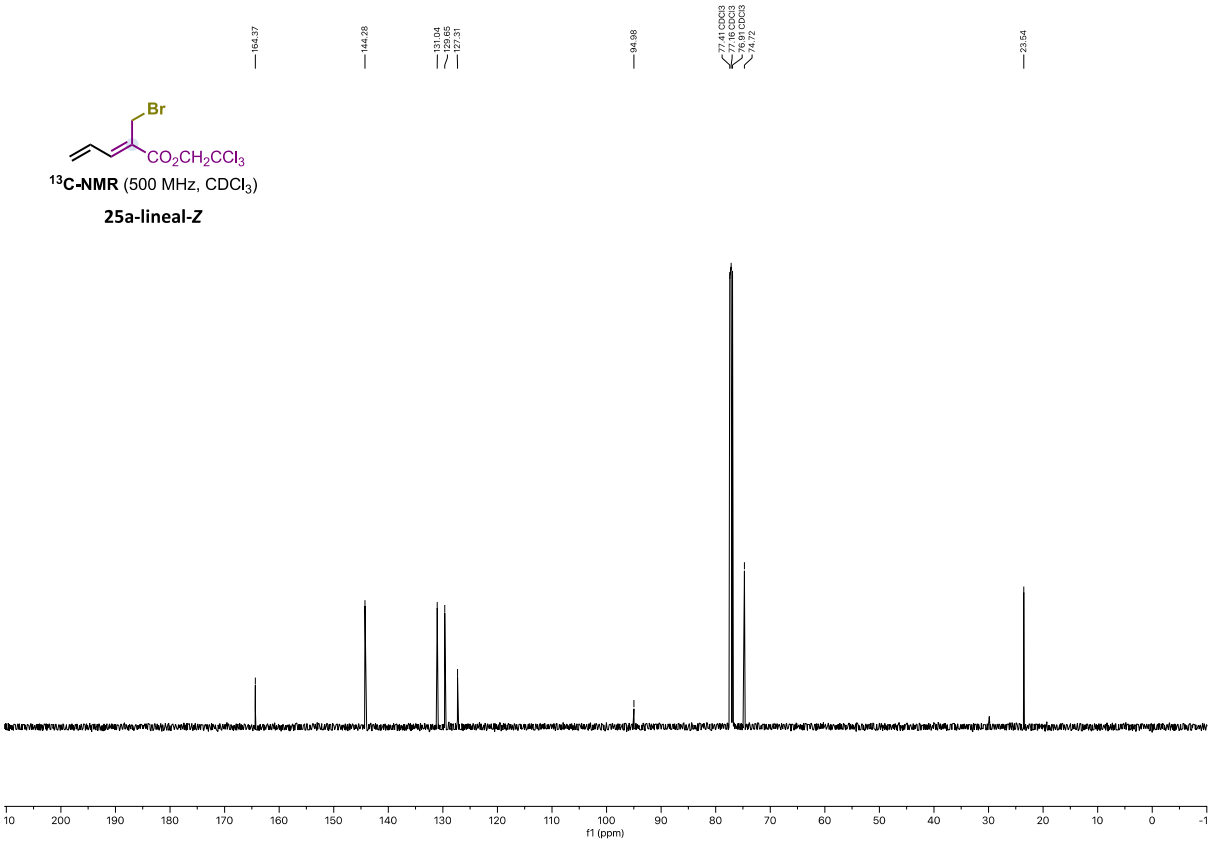


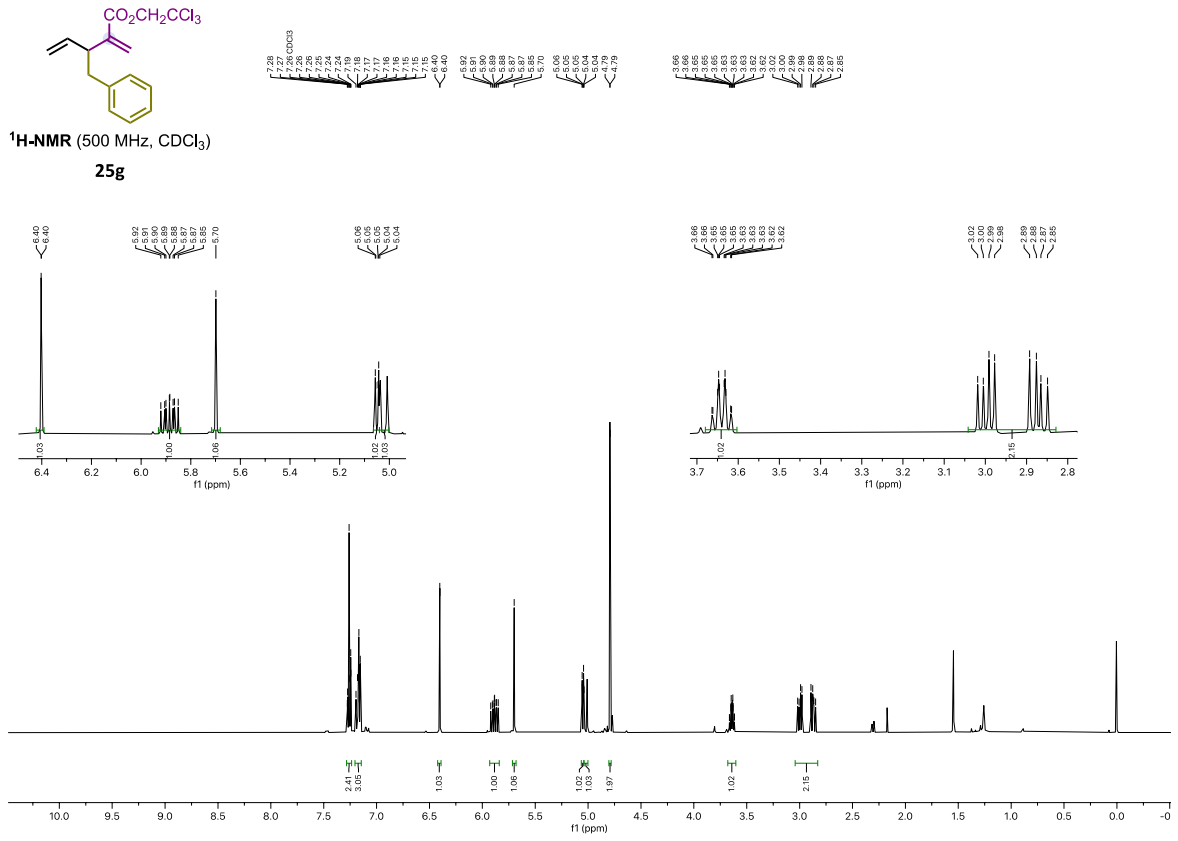
^{19}F NMR of **23** (471 MHz, CD_2Cl_2)

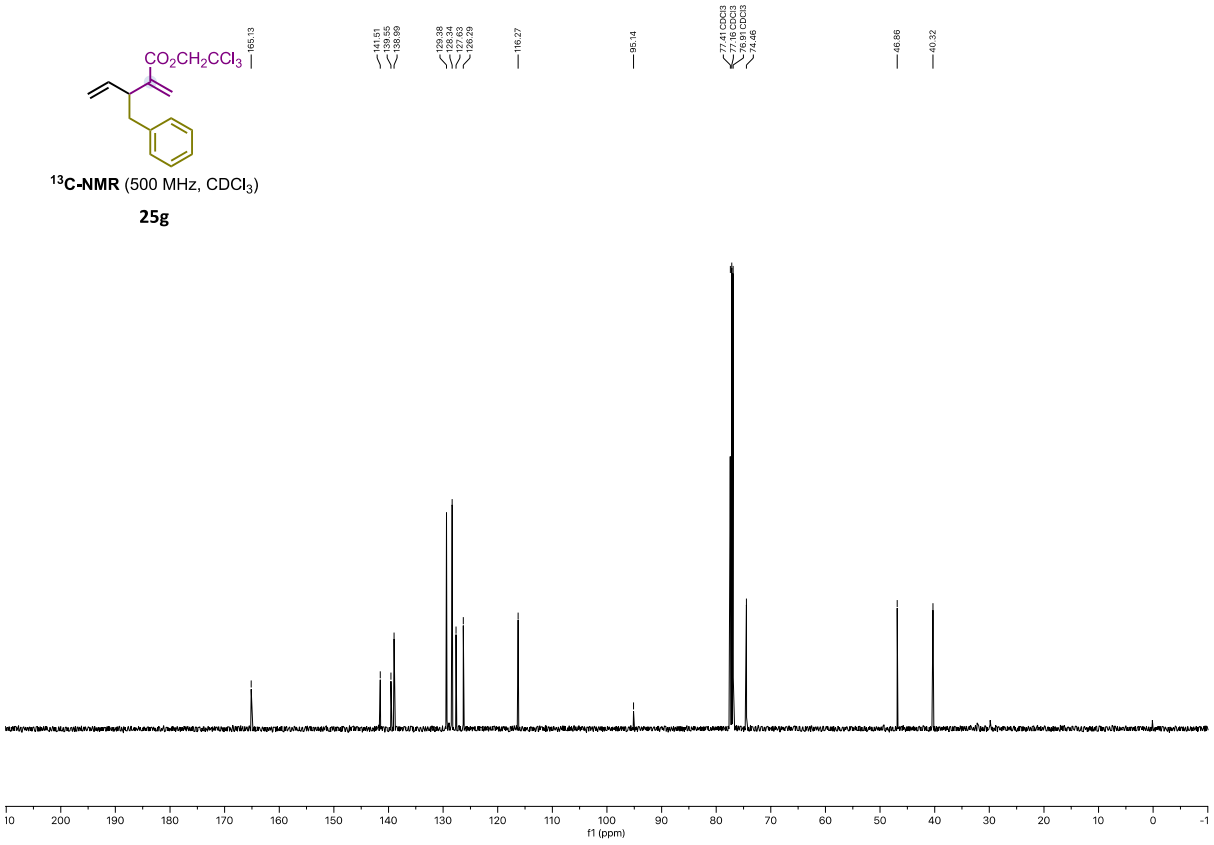


^{1}H-NMR (500MHz, $CDCl_3$)

25a-lineal-*Z*


Br
CO2CH2CCl3
13C-NMR (500 MHz, CDCl3)
25a-lineal-Z
164.37
144.28
131.04
129.65
127.31
94.98
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
74.72
23.54
f1 (ppm)


CO2CH2CCl3
1H-NMR (500 MHz, CDCl3)
25g
f1 (ppm)



^{13}C-NMR (500 MHz, $CDCl_3$)

25g

Chapter III

Catalytic Alkene Skeletal Modification for the Construction of Fluorinated Tertiary Stereocenters

*The work described in this chapter was performed in collaboration with **Dr. Liyin Jiang**.*

3.1. Introduction

The growing number of approved fluorinated small-molecule pharmaceuticals is a testimony of the tremendous research efforts in synthetic organofluorine chemistry[1] and their application in fluorine-based drug design.[2] The most prevalent chemotypes found in fluoro-pharmaceuticals are featured with monofluorinated moieties (Ar–F, Het–F, alkyl–CH_2F) and trifluoromethyl groups (Ar–CF_3, Het–CF_3, alkyl–CF_3).[1d] However, the appearance of fluorinated tertiary stereocenters is very rare (Figure 1A). This is surprising, considering that this fluorinated motif is an ideal bioisoster of tertiary stereocenters – a prevalent motif in drug molecules –, and is found in fludrocortisone – the first approved fluorine-containing drug. The main reason of the lack of fluorinated tertiary stereocenters in drug molecules can be attributed to a less developed area of research and in difficulties of adopting the known synthetic methods into drug molecule design.[2d]

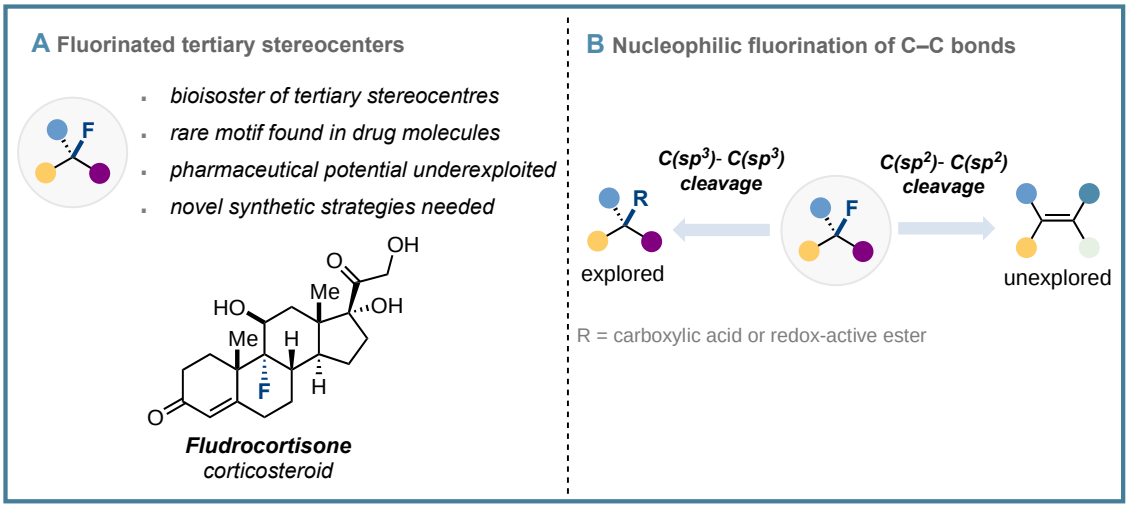


Figure 1

[1] (a) Pacheco, M. C.; Purser, S.; Gouverneur, V. *Chem. Rev.* **2008**, *108*, 1943; (b) O'hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308; (c) Liang, T.; Neumann, C. N.; Ritter, T. *Angew. Chem. Int. Ed.* **2013**, *52*, 8214; (d) Zhu, Y.; Han, J.; Wang, J.; Shibata, N.; Sodeoka, M.; Soloshonok, V. A.; J. Coelho, A. S.; Toste, F. D. *Chem. Rev.* **2018**, *118*, 3887; (e) Szpera, R.; Moseley, D. F. J.; Smith, L. B.; Sterling, A. J.; Gouverneur, V. *Angew. Chem. Int. Ed.* **2019**, *58*, 14824; (f) Sorlin, A. M.; Usman, F. O.; English, C. K.; Nguyen, H. M. *ACS Catal.* **2020**, *10*, 11980.

[2] (a) Hagmann, W. K. *J. Med. Chem.* **2008**, *51*, 4359; (b) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320; (c) Gillis, E. P.; Eastman, K. J.; Hill, M. D.; Donnelly, D. J.; Meanwell, N. A.; *J. Med. Chem.* **2015**, *58*, 8315; (d) Zhou, Y.; Wang, J.; Gu, Z.; Wang, S.; Zhu, W.; Aceña, J. L.; Soloshonok, V. A.; Izawa, K.; Liu, H. *Chem. Rev.* **2016**, *116*, 422; (e) Inoue, M.; Sumii, Y.; Shibata, N. *ACS. Omega* **2020**, *5*, 10633.

Catalytic methodologies that access such motif rely on (*i*) the fluorination of alkenes, enol(ates), phenols and C–H bonds with electrophilic fluorinating reagents[3] (*ii*) transformations of fluorine-containing starting materials[4] and (*iii*) fluorination of alkenes, allylic electrophiles, and C–H bonds with nucleophilic fluoride sources.[5,6] An alternative and underexplored catalytic approach to construct fluorinated tertiary stereocenters rely on the use of C–C bonds as functional groups. Some precedents exist based on catalytic C(sp^3)–C(sp^3) bond cleavages of redox-active esters,[7] carboxylic acids,[8] cyclopropanes,[9] or ketone acetals.[10] However, synthesis of tertiary fluorinated stereocenters through

[3] For recent selected examples: (a) Greedy, B.; Paris, J. M.; Vidal, T.; Gouverneur, V. *Angew. Chem. Int. Ed.* **2003**, *42*, 3291; (b) Phipps, R. J.; Hiramatsu, K.; Toste, F. D. *J. Am. Chem. Soc.* **2012**, *134*, 8376; (c) Wu, J.; Wang, Y. M.; Drljevic, A.; Rauniyar, V.; Phipps, R. J.; Toste, F. D. *Proc. Natl. Acad. Sci.* **2013**, *110*, 13729; (d) Yang, X.; Phipps, R. J.; Toste, F. D. *J. Am. Chem. Soc.* **2014**, *136*, 5225; (e) Yuan, W.; Szabõ, K. J. *Angew. Chem Int. Ed.* **2015**, *54*, 8533; (f) Guo, R.; J. Huang, Zhao, X. *ACS Catal.* **2018**, *8*, 926; (g) Wang, Q.; Lübcke, M.; Biosca, M.; Hedberg, M.; Eriksson, L.; Himo, F.; Szabó, K. J. *J. Am. Chem. Soc.* **2020**, *142*, 20048; (h) Liu, Z.; Oxtoby, L. J.; Liu, M.; Li, Z. Q.; Tran, V. T.; Gao, Y.; Engle, K. M. *J. Am. Chem. Soc.* **2021**, *143*, 8962; (i) Cao, J.; Wu, H.; Wang, Q.; Zhu, J. *Nat. Chem.* **2021**, *13*, 671.

[4] For recent selected examples: (a) Liang, Y.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 5520; (b) Jiao, Z.; Beiger, J. J.; Jin, Y.; Ge, S.; Zhou, J. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2016**, *138*, 15980; (d) Balaraman, K.; Wolf, C. *Angew. Chem Int. Ed.* **2017**, *56*, 1390; (e) Butcher, T. W.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2018**, *57*, 13125; (f) He, Z. T.; Jiang, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **2019**, *141*, 13066; (g) Liu, J.; Yuan, Q.; Toste, F. D.; Sigman, M. S. *Nat. Chem.* **2019**, *11*, 710; (h) Butcher, T. W.; Yang, J. L.; Amberg, W. M.; Watkins, N. B.; Wilkinson, N. D.; Hartwig, J. F. *Nature* **2020**, *583*, 548; (i) Kalkman, E. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2021**, *143*, 11741.

[5] For recent selected examples: (a) Katcher, M. H.; Sha, A.; Doyle, A. G. *J. Am. Chem. Soc.* **2011**, *133*, 15902; (b) Topczewski, J. J.; Tewson, T. J.; Nguyen, H. M. *J. Am. Chem. Soc.* **2011**, *133*, 19318; (c) Liu, W.; Huang, X.; Cheng, M.; Nielsen, R. J.; Iii, W. a G.; Groves, J. T. *Science* **2012**, *337*, 1322; (d) Braun, M.; Doyle, A. G. *J. Am. Chem. Soc.* **2013**, *4*, 1; (e) Lu, Z.; Zeng, X.; Hammond, G. B.; B. Xu, *J. Am. Chem. Soc.* **2017**, *139*, 18202; (f) Bertrand, X.; Paquin, J. F. *Org. Lett.* **2019**, *21*, 9759; (g) Bafaluy, D.; Georgieva, Z.; Muñiz, K. *Angew. Chem Int. Ed.* **2020**, *59*, 14241; (h) Sharma, H. A.; Mennie, K. M.; Kwan, E. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2020**, *142*, 16090; (i) Tang, H. J.; Zhang, X.; Zhang, Y. F.; Feng, C. *Angew. Chem Int. Ed.* **2020**, *59*, 5242; (j) Tang, H. J.; Zhang, B.; Xue, F.; Feng, C. *Org. Lett.* **2021**, *23*, 4040; (k) Qian, H.; Chen, J.; Zhang, B.; Cheng, Y.; Xiao, W. -J.; Chen, J. -R. *Org. Lett.* **2021**, *23*, 6987; (l) Leibler, I. N. M.; Tekle-Smith, M. A.; Doyle, A. G. *Nat. Commun.* **2021**, *12*, 1; (m) Zhang, Y.; Fitzpatrick, N. A.; Das, M.; Bedre, I. P.; Yayla, H. G.; Lall, M. S.; Musacchio, P. Z. A. *Chem Catal.* **2022**, *2*, 1. For non-catalytic methods: (n) Olah, G. A.; Nojima, M.; Kerekes. I. *Synthesis.* **1973**, 779; (o) Olah, G. A.; Welch, J. T.; Vankar, Y. D.; Nojima, M.; Kerekes, I.; Olah, J. A. *J. Org. Chem.* **1979**, *44*, 3872; (p) Barluenga, J.; Campos, P. J.; Gonzalez, J. M.; Suarez, J. L.; Asensio, G.; Asensio, G. *J. Org. Chem.* **1991**, *56*, 2234.

[6] For alternative catalytic methods: (a) Sandford, C.; Rasappan, R.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2015**, *137*, 10100; (b) Dauncey, E. M.; Morcillo, S. P.; Douglas, J. J.; Sheikh, N. S.; Leonori, D. *Angew. Chem Int. Ed.* **2018**, *57*, 744; (c) Lovett, G. H.; Chen, S.; Xue, X. S.; Houk, K. N.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2019**, *141*, 20031; (d) Vincent, É.; Brioche, J. *Eur. J. Org. Chem.* **2021**, *2021*, 2421.

[7] Webb, E. W.; Park, J. B.; Cole, E. L.; Donnelly, D. J.; Bonacorsi, S. J.; Ewing, W. R.; Doyle, A. G. *J. Am. Chem. Soc.* **2020**, *142*, 9493.

[8] Xiang, J.; Shang, M.; Kawamata, Y.; Lundberg, H.; Reisberg, S. H.; Chen, M.; Mykhailiuk, P.; Beutner, G.; Collins, M. R.; Davies, A.; Del Bel, M.; Gallego, G. M.; Spangler, J. E.; Starr, J.; Yang, S.; Blackmond, D. G.; Baran, P. S. *Nature* **2019**, *573*, 398.

[9] (a) Zhao, H.; Fan, X.; Yu, J.; Zhu, C. *J. Am. Chem. Soc.* **2015**, *137*, 3490; (b) Pitts, C. R.; Ling, B.; Snyder, J. A.; Bragg, A. E.; Lectka, T. *J. Am. Chem. Soc.* **2016**, *138*, 6598; (c) Banik, S. M.; Mennie, K. M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2017**, *139*, 9152; (d) Ilchenko, N. O.; Hedberg, M.; Szabó, K. J. *Chem. Sci.* **2017**, *8*, 1056; (e) Roque, J. B.; Kuroda, Y.; Göttemann, L. T.; Sarpong, R. *Science.* **2018**, *361*, 171; (f) Wang, M. M.; Waser, J. *Angew. Chem Int. Ed.* **2020**, *59*, 16420; (g) Lanke, V.; Marek, I. *J. Am. Chem. Soc.* **2020**, *142*, 5543; (h) Ren, J.; Du, F. -H.; Jia, M. -C.; Hu, Z. -N.; Chen, Z.; Zhang, C. *Angew. Chem Int. Ed.* **2021**, *60*, 24171.

[10] Pitts, C. R.; Bloom, M. S.; Bume, D. D.; Zhang, Q. A.; Lectka, T. *Chem. Sci.* **2015**, *6*, 5225.

catalytic alkene C(sp^2)–C(sp^2) bond cleavage is previously unknown, despite that this strategy would provide a unique disconnection approach, while complementing current strategies (Figure 1B)

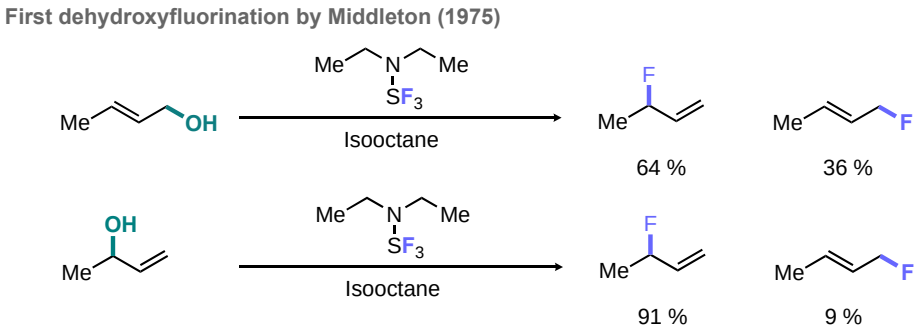
In this chapter we present a new synthetic methodology for the synthesis of tertiary allylic fluorides from 1,1-disubstituted alkenes. The protocol is based on the generation of a tertiary allyl cations, mediated by a catalytically-generated Rh-carbynoid, that undergoes nucleophilic fluorination with excellent branched/selectivity ratio.

3.2. Synthesis of allylic fluorides by nucleophilic fluorination

Allylic fluorides are popular motifs in many biologically active species, PET radiotracers and synthetic intermediate structures.[1a] For this reason, in the recent years there has been a tremendous effort in the development of new methodologies that allow the synthesis of such motifs, even in a stereoselective manner. Nonetheless, there are few methodologies able to reach tertiary allylic fluorides, specially via nucleophilic fluorination, which this chapter will be focused on.

3.2.1. Dehydroxyfluorination of allylic alcohols: DAST and other fluorinating agents

The most common methodology for the nucleophilic synthesis of allylic fluorides is the dehydroxy-fluorination of allylic alcohols, firstly reported by Middleton in 1975 (Scheme 1).[11] Since then, many other protocols have been developed for the nucleophilic synthesis of allylic fluorides, like the nucleophilic substitution of allylic products or by C–H activation of allylic positions, among others.

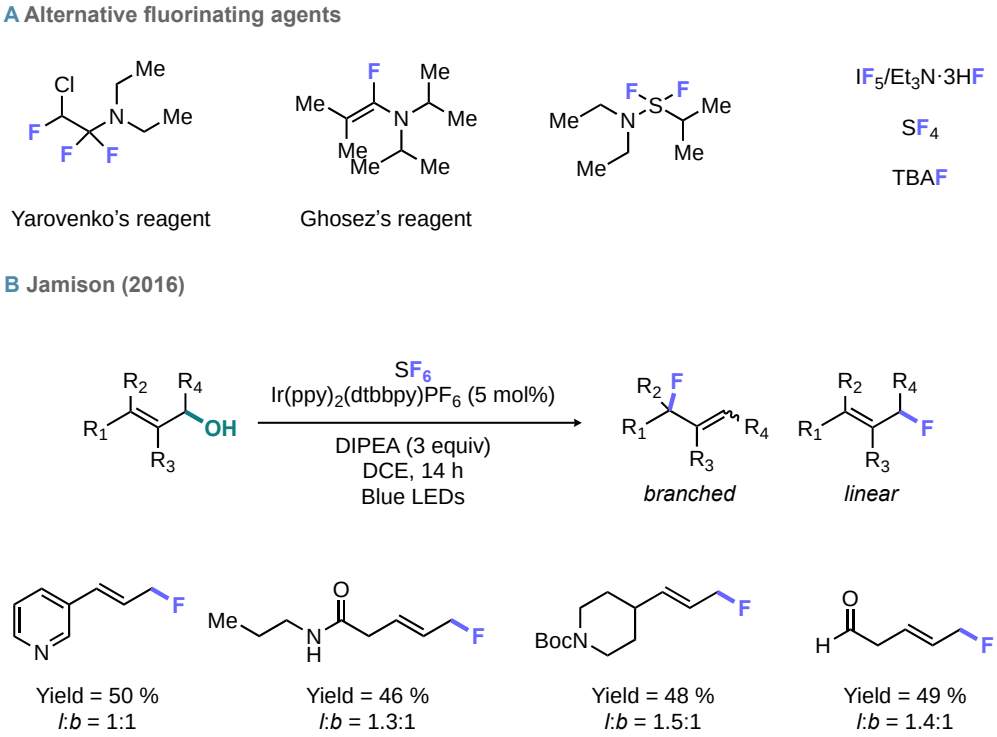


Scheme 1

[11] Middleton, W. J. *J. Org. Chem.* **1975**, *40*, 574.

Even though (diethylamino)sulfur trifluoride (DAST) is probably the most extended reagent for the dihydroxy-fluorination of allylic alcohols, the difficulties to control the regio- and stereoselectivity of the process have urged to develop new methodologies. Apart from these problems, it must be also said that it is an expensive and potentially explosive chemical that lacks functional group tolerance. In order to overcome such limitations, multiple new reagents have been developed for the dehydroxyfluorination of allylic alcohols like Yarovenko's and Ghosez's[12] reagents or bis(dialkylamino)sulfur difluorides among others (Figure 3A).[13] An example of this is the paper that the Jamison group published in 2016, in which SF_6 is employed as a fluorinationg agent in the dehydroxyfluorination of allylic alcohols by photoredox catalysis (Figure 3B).[14] In this protocol, SF_6 can fluorinate a wide variety of allylic alcohols after being converted into an active fluorinating agent by the action of an iridium photocatalyst under visible light. Under this reaction conditions, even though the yields are moderate (around 50% in most of the cases), carbonyl groups can be tolerated, which would undergo a *gem*-difluorination or form acyl fluorides in the presence of DAST. Also, this fluorinating agent is safer and cheaper compared to DAST. Nevertheless, tertiary allylic fluorides are still difficult to obtain through this strategy and new deoxyfluorinating agents do not solve the regioselectivity problems already present with DAST.[15]

[12] Munyemana, F.; Frisque-Hesbain, A.; Devos, A.; Ghosez, L. *Tetrahedron Lett.* **1989**, *30*, 3077.
[13] Norihiko, Y.; Tsuyoshi, F. *Chem. Lett.* **2001**, 222.
[14] McTeague, T. A.; Jamison, T. F. *Angew. Chem. Int. Ed.* **2016**, *55*, 1.
[15] Aggarwal, T.; Sushmita; Verma, A. K. *Org. Chem. Front.* **2021**, *8*, 6452.



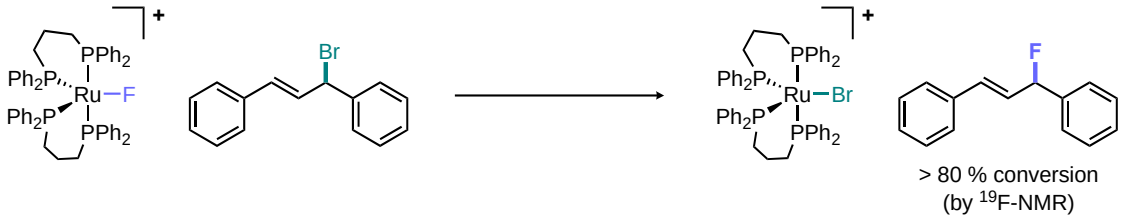
Scheme 2 Dehydroxyfluorination of allylic alcohols

3.2.2. Nucleophilic displacement and C–H functionalization

Another strategy is the nucleophilic substitution of allylic leaving groups (halogens, tosylates,…) by fluoride. Even though the traditional S_N2 fluorination have been used in the synthesis of many allylic fluorinated products, it possesses many limitations, like selectivity problems, competitive side reactions promoted by the basicity of fluoride and substrate scope restrictions.[1f] A solution to such problems was found in the use of transition metals that catalyze the allylic substitution, as it had been previously used for the formation of allylic carbon-carbon and carbon-heteroatom bonds. The first allylic fluorination mediated by a transition metal was reported by Togni in 1999 (Scheme 3).[16] In this work, a Ru(II) complex was used as a fluoride source. Even though at that moment it was not possible to find a catalytic variant, many metal-catalyzed protocols have been published since then, even in the synthesis of natural/biologically active products.[17] Of

[16] Barthazy, P.; Hintermann, L.; Stoop, R. M.; Wörle, M.; Mezzetti, A.; Togni, A. *Helv. Chim. Acta* **1999**, *82*, 2448.
[17] M. J.; Howell, L.; Goodman, M. M. *J. Med. Chem.* **2010**, *53*, 5549.

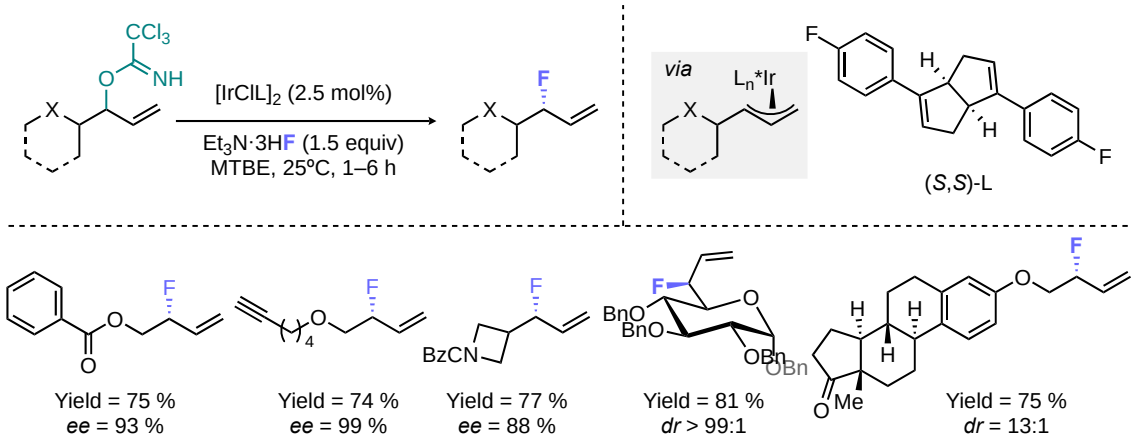
extremely importance in this field have been the contributions of Togni, [18] Gouverneur,[1a,19] Doyle[5a,20] and Nguyen[1f,5b,21].



Scheme 3 First allylic fluorination employing transition metals by Togni

In 2018, the group of Nguyen reported a methodology for the synthesis of allylic fluorides with high degree of enantioselectivity (Scheme 4).[21b] Key on this work was the use of a chiral Iridium catalyst able to form the π-allyliridium complex by release of the trichloroacetamide group and which guides the enantioselective attack of the nucleophilic fluoride. The utility of this protocol was shown by a broad scope and the synthesis of different fluorinated drugs. Nevertheless, the prefunctionalization of the starting materials diminishes the applicability of this methodology, since most of them require multiple steps for their synthesis.

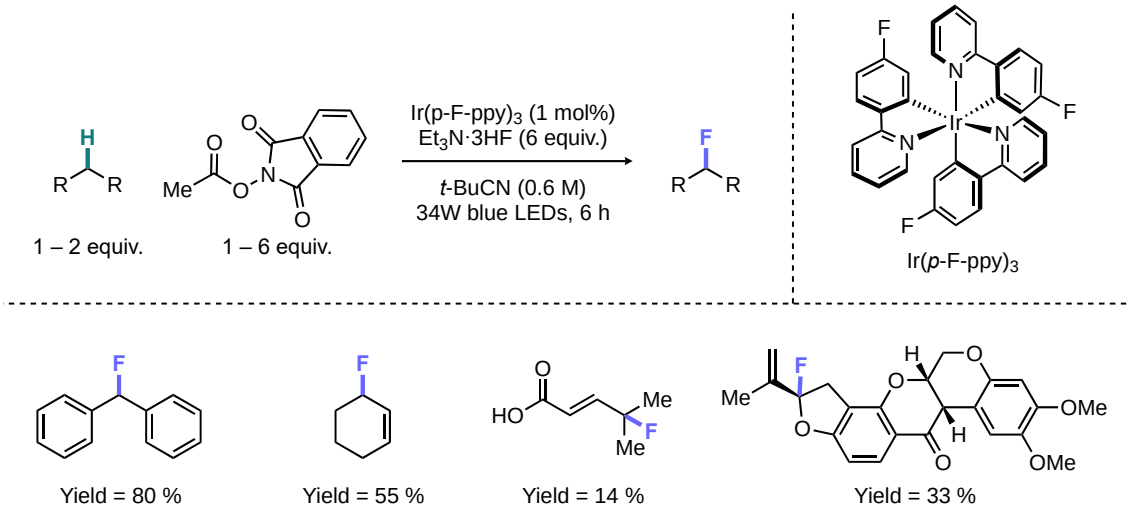
[18] (a) Hintermann, L.; Läng, F.; Maire, P.; Togni, A. *Eur. J. Inorg. Chem.* **2006**, *7*, 1397; (b) Barthazy, P.; Stoop, R. M.; Worle, M.; Togni, A.; Mezzetti, A. *Organometallics* **2000**, *19*, 2844.
[19] (a) Thibaudeau, S.; Gouverneur, V. *Org. Lett.* **2003**, *5*, 4891; (b) Tredwell, M.; Tenza, K.; Pacheco, M. C.; Gouverneur, V. *Org. Lett.* **2005**, *7*, 4495; (c) Sawicki, M.; Kwok, A.; Tredwell, M.; Gouverneur, V. *Beilstein J. Org. Chem.* **2007**, *3*, 1; (d) Boldon, S.; Moore, J. E.; Gouverneur, V. *Chem. Commun.* **2008**, *7345*, 3622; (e) Hazari, A.; Gouverneur, V.; Brown, J. M. *Angew. Chem. Int. Ed.* **2009**, *48*, 1296; (f) Hollingworth, C.; Hazari, A.; Hopkinson, M. N.; Tredwell, M.; Benedetto, E.; Huiban, M.; Gee, A. D.; Brown, J. M.; Gouverneur, V. *Angew. Chem. Int. Ed.* **2011**, *50*, 2613; (g) Hollingworth, C.; Gouverneur, V. *Chem. Commun.* **2012**, *48*, 2929; (h) Benedetto, E.; Keita, M.; Tredwell, M.; Hollingworth, C.; Brown, J. M.; Gouverneur, V. *Organometallics* **2012**, *31*, 1408; (i) Benedetto, E.; Tredwell, M.; Hollingworth, C.; Khotavivattana, T.; Brown, J. M.; Gouverneur, V. *Chem. Sci.* **2013**, *4*, 89.
[20] (a) Katcher, M. H.; Doyle, A. G. *J. Am. Chem. Soc.* **2010**, *132*, 17402; (b) Braun, M. G.; Doyle, A. G. *J. Am. Chem. Soc.* **2013**, *135*, 12990; (c) Katcher, M. H.; Norrby, P. O.; Doyle, A. G. *Organometallics* **2014**, *33*, 2121.
[21] (a) Arnold, J. S.; Zhang, Q.; Nguyen, H. M. *European J. Org. Chem.* **2014**, *2014*, 4925; (b) Mixdorf, J. C.; Sorlin, A. M.; Zhang, Q.; Nguyen, H. M. *ACS Catal.* **2018**, *8*, 790; (c) Mixdorf, J. C.; Sorlin, A. M.; Dick, D. W.; Nguyen, H. M. *Org. Lett.* **2019**, *21*, 60; (d) Sorlin, A. M.; Mixdorf, J. C.; Rotella, M. E.; Martin, R. T.; Gutierrez, O.; Nguyen, H. M. *J. Am. Chem. Soc.* **2019**, *141*, 14843.



Scheme 4 Example of allylic fluorination from allylic trichloroacetamides by Nguyen

The group of Doyle developed a methodology to form allylic fluorides through the allylic C–H functionalization.[22] This strategy avoids the need of prefunctionalized olefins, which improves the atom economy of the previous S_N2 protocols for such purpose. Since the work from Doyle some more groups have studied the feasibility of allylic fluorination by C–H functionalization.[3f,23] A more recent example from the group of Doyle published in 2021 is shown in Scheme 5.[5l] In this case, the C–H functionalization is achieved by the use of a methyl radical as hydrogen atom abstractor. This strategy was suitable for a broad range of substrates (mainly benzylic, but also allylic and aliphatic positions were fluorinated) and nucleophiles other than fluoride could be used too, like water, alcohols, thiols or electron-rich arenes. However, even though tertiary allylic fluorides could be obtained, only three examples of allylic substrates were given, with yields ranging between 14 – 55 %.

[22] Braun, M.; Doyle, A. *J. Am. Chem. Soc.* **2013**, *135*, 12990.
[23] Bower, J. K.; Cypcar, A. D.; Henriquez, B.; Stieber, S. C. E.; Zhang, S. *J. Am. Chem. Soc.* **2020**, *142*, 8514.

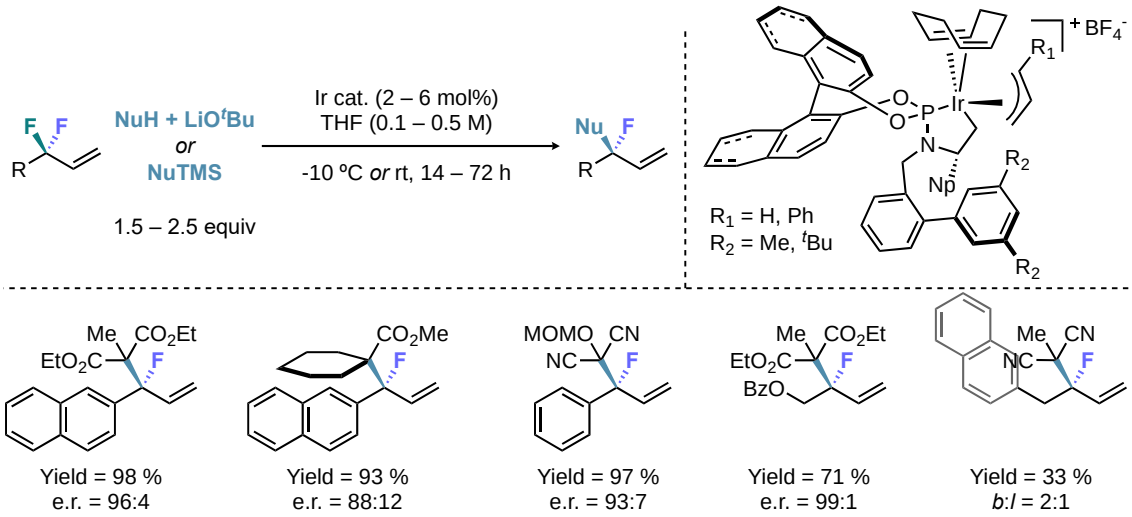


Scheme 5 Example from Doyle for the allylic fluorination via C–H functionalization

3.2.3. Synthesis of allylic fluorides by the use of fluorinated substrates

A way to obtain allylic tertiary C–F bonds which is gaining importance in the last decade is the use of fluorinated substrates. This strategy avoids the fluoride addition to allylic electrophiles, difficult to happen specially in an enantioselective manner. However, it requires the use of already fluorinated substrates which might not always be trivial to synthesize. Multiple protocols have been reported employing this strategy, like allylic substitution[3e] and S_N2' reaction of fluoroalkenes,[24] C–F bond activation of allylic difluoromethyl groups[4h] or sigmatropic rearrangement of fluoroalkenes.[25] One of the last works reported by Hartwig shows an elegant strategy for the enantioselective synthesis of allylic tertiary C–F bonds by the desymmetrization of allylic difluoromethylene units (Scheme 6).[3h] This work provides a broad scope with high yields and enantioselectivities, together with mechanistic studies. However, the synthesis of the fluorinated starting materials, requiring multiple steps in some cases, diminishes the usability, generality and atom economy of this protocol. The same problems are found in all the works reported using this strategy.

[24] Konno, T.; Ikemoto, A.; Ishihara, T. *Org. Biomol. Chem.* **2012**, *10*, 8154.
[25] Kasten, K.; Slawin, A. M. Z.; Smith, A. D. *Org. Lett.* **2017**, *19*, 5182.



Scheme 6 Example of the synthesis of allylic fluorides from fluorinated substrates by Nguyen

3.2.4. Other methodologies

Many other methodologies have been developed in the last few years for the synthesis of allylic fluorides using nucleophilic fluorinating agents. Some of these strategies are the amino-[26] and carbofluorination,[27] (radio)fluorination of vinyl diazoacetates[28] or the ring opening of either epoxides[29] or cyclopropyl silyl ethers.[30]

3.3. ^{18}Fluorine in positron emission tomography

^{18}Fluorine [^{18}F] is emerging as one of the most prominent radionuclides in the application of positron emission tomography (PET), a fundamental technology in precision medicine for (pre)clinical imaging. Its broad use as a radiotracer in PET is caused by its half-life (109.8 min, being long enough to allow long sample preparation protocols and still be detectable), the low β+-energy (0.64 MeV, which involves a short

[26] Zhang, Z.; Chen, P.; Liu, G. *Chem. Commun.* **2018**, *54*, 8709.
[27] (a) Braun, M. G.; Katcher, M. H.; Doyle, A. G. *Chem. Sci.* **2013**, *4*, 1216; (b) Liu, S.; Zhao, J.; Zhang, G. *Tetrahedron Lett.* **2015**, *56*, 2214.
[28] (a) Qin, C.; Davies, H. M. L. *Org. Lett.* **2013**, *15*, 6152; (b) Thompson, S.; Lee, S. J.; Jackson, I. M.; Ichiishi, N.; Brooks, A. F.; Sanford, M. S.; Scott, P. J. H. *Synthesis* **2019**, *51*, 4401.
[29] (a) Sutherland, J. K.; Watkins, W. J.; Bailey, J. P.; Chapman, A. K.; Davies, G. M. *J. Chem. Soc. Chem. Commun.* **1989**, 1386; (b) Hedhli, A.; Baklouti, A. *J. Fluor. Chem.* **1995**, *70*, 141; (c) Hunter, L.; O'Hagan, D.; Slawin, A. M. Z. *J. Am. Chem. Soc.* **2006**, *128*, 16422; (d) Kasai, Y.; Matsumori, N.; Ueno, H.; Nonomura, K.; Yano, S.; Michio, M.; Oishi, T. *Org. Biomol. Chem.* **2011**, *9*, 1437; (e) Zhu, J.; Tsui, G. C.; Lautens, M. *Angew. Chem. Int. Ed.* **2012**, *51*, 12353; (f) Zhang, Q.; Nguyen, H. M. *Chem. Sci.* **2014**, *5*, 291.
[30] (a) Kirihara, M.; Kambayashi, T.; Momose, T. *Chem. Commun.* **1996**, 1103; (b) Kirihara, M.; Kakuda, H.; Tsunooka, M.; Shimajiri, A.; Takuwa, T.; Hatano, A. *Tetrahedron Lett.* **2003**, *44*, 8513; (c) McDonald, T. R.; Mills, L. R.; West, M. S.; Rousseaux, S. A. L. *Chem. Rev.* **2021**, *121*, 3.

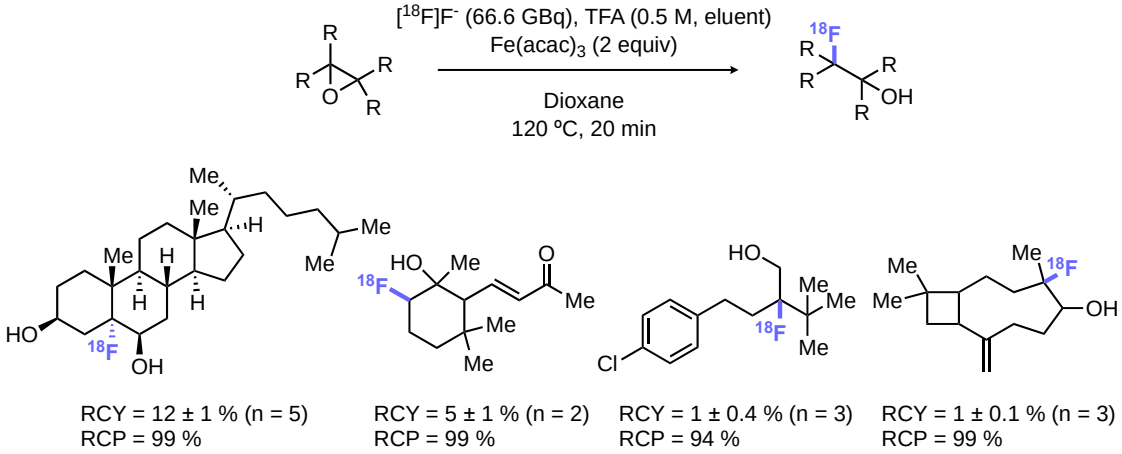
positron linear range, in other words, it offers a high resolution in PET imaging) and the ease of production. Furthermore, due to its high resolution in PET imaging, it is feasible to work with small radiation doses. [^{18}F] can be obtained either as gaseous [^{18}F]F_2, used for electrophilic and radical fluorination reactions, or as an aqueous solution of [^{18}F]F^-, employed for the nucleophilic reactions. Normally, the latter is more convenient, because it is easier to handle and avoids the difficulties to work with gaseous F_2 (highly oxidizing and toxic gas). Also, in order to avoid the use of fluorine gas, other electrophilic [^{18}F]-fluorinating agents have been developed, even though they require extra steps for their synthesis. On the other hand, the manipulation of the aqueous [^{18}F]F^- solution only needs to be trapped in a separation cartridge previously to be used, making it a really fast and useful source.

The synthesis of C–^{18}F is not straightforward. Due to the decay of radioactivity of ^{18}F, the synthesis and purification must be performed quickly to obtain as much activity as possible. Furthermore, when [^{18}F]-fluorinated tertiary stereocenters need to be synthesized, the preparation becomes even more challenging. In fact, only a few methodologies are available to prepare such motifs,[7,31] none of which can synthesize allylic tertiary radiofluorides.[5b,32] One of the few protocols in which a nucleophilic ^{18}F-fluorinating source is used for the synthesis of tertiary stereocenters is the one from Sanford and Scott shown in Scheme 7.[33] In their work, an iron-radiofluride is generated in situ as the fluorinating agent for the radiofluorination of secondary and tertiary stereocenters through the ring opening of epoxides. The main drawbacks of this protocol are the low radiochemical yields (RCY, up to 12 %) and the small scope (only 4 examples are presented), even though pre-clinical evaluation with one of the radiofluorinated products is performed as radio-tracer.

[31] (a) Cortés González, M. A.; Nordeman, P.; Bermejo Gómez, A.; Meyer, D. N.; Antoni, G.; Schou, M.; Szabó, K. J. *Chem. Commun.* **2018**, *54*, 4286; (b) Liu, W.; Huang, X.; Placzek, M. S.; Krska, S. W.; McQuade, P.; Hooker, J. M.; Groves, J. T. *Chem. Sci.* **2018**, *9*, 1168; (c). Brooks, A. F.; Topczewski, J. J.; Ichiishi, N.; Sanford, M. S.; Scott, P. J. H. *Chem. Sci.* **2014**, *5*, 4545

[32] (a) Benedetto, E.; Tredwell, M.; Hollingworth, C.; Khotavivattana, T.; Brown, J. M.; Gouverneur, V. *Chem. Sci.* **2013**, *4*, 89; (b) Mixdorf, J. C.; Sorlin, A. M.; Dick, D. W.; Nguyen, H. M. *Org. Lett.* **2019**, *21*, 60.

[33]. Verhoog, S.; Brooks, A. F.; Winton, W. P.; Viglianti, B. L.; Sanford, M. S.; Scott, P. J. H. *Chem. Commun.* **2019**, *55*, 6361



Scheme 7 Example of nucleophilic radiofluorination by Scott and Sanford

3.4. Catalytic alkene skeletal modification for the construction of fluorinated tertiary stereocenters

3.4.1. Hypothesis of the project

Considering the previous results shown in Chapter II, we wondered whether we could exploit our alkene skeletal modification platform for the catalytic conversion of 1,1-disubsituted alkenes into fluorinated tertiary stereocenters. Such process would involve the catalytic cleavage of the C(sp^2)–C(sp^2) bond for the formation of tertiary allyl cations (Figure 2). We hypothesized that the fluoride nucleophilic attack to the allyl cation would proceed with high site-selectivity towards the α position considering that both the charge and the highest LUMO coefficient of the allyl cation, may be centered at the α position, due to the double substitution with two stabilizing groups (alkyl and aromatic groups).[34] Previous reports in fluorination of allyl cations showed a preference of fluoride for the most substituted electrophilic carbon site.[5l, 35] However, we recognized that constructing a sterically demanding tertiary allylic fluoride could bring some problems associated with (i) parasitic proton eliminations promoted by fluoride and (ii) generation of undesirable branched/linear mixtures due to lack of regiocontrol in the nucleophilic fluoride attack.

[34] (a) Fleming, I. *Molecular Orbitals and Organic Chemical Reactions*; John Wiley & Sons, 2009, page. 142; (b) Mayr, H.; Forner, W.; Schleyer P. v. R. *J. Am. Chem. Soc.* **1979**, *101*, 6032.
[35] (a) Kirihara, M.; Kambayashi, T.; Momose, T. *Chem. Commun.* **1996**, 1103; (b) Mixdorf, J. C.; Sorlin, A. M.; Zhang, Q.; Nguyen, H. M. *ACS Catal.* **2018**, *8*, 790.

The successful development of such nucleophilic branched-selective fluorination of tertiary allyl cations would unlock a novel access to fluorinated tertiary stereocenters using readily or commercially available 1,1-disubstituted alkenes, and nucleophilic fluoride sources. In addition, our strategy would also represent a novel approach to a class of allylic fluorides difficult to obtain with traditional bimolecular nucleophilic substitutions or transition metal-catalyzed platforms.[36]

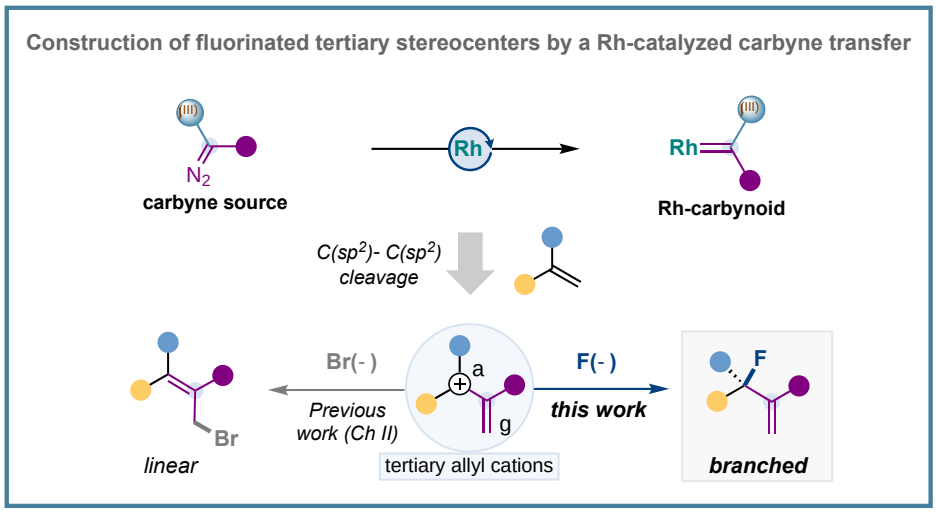


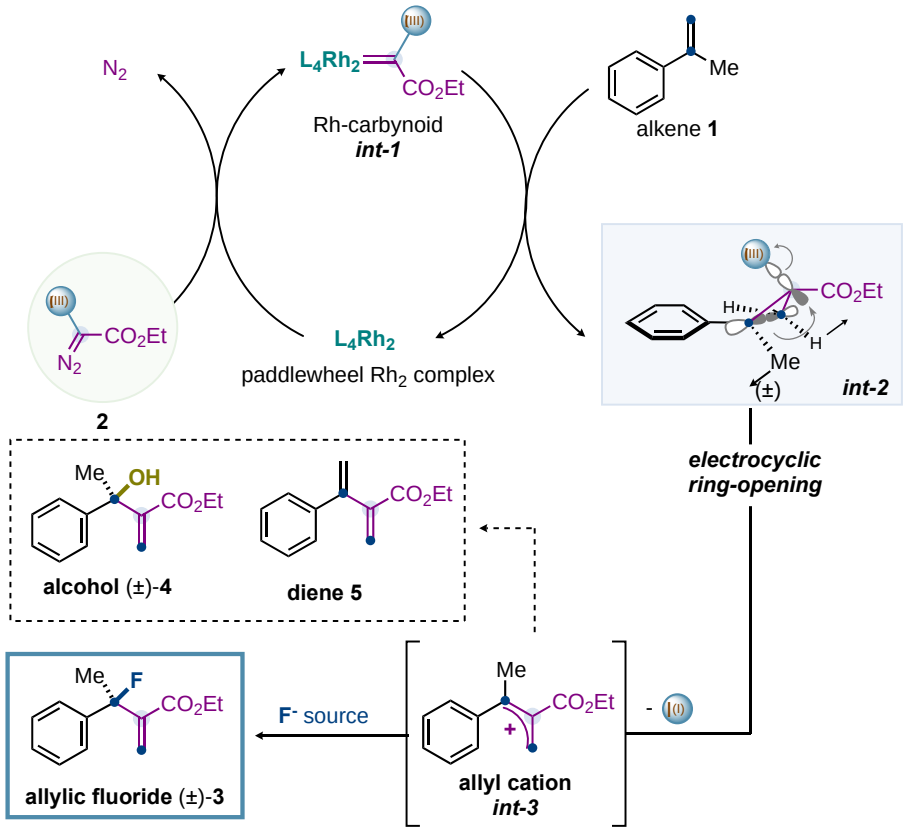
Figure 2

3.4.2. Proposed mechanism

In our previous studies shown in Chapter II, we observed that when the allyl cations generated from 1,1-disubstituted alkenes were treated with bromide, the linear product was obtained. In this case, there are two possibilities: either bromide attacks selectively the γ-position or it first attacks the α-position and subsequently isomerizes to the linear isomer. However, we thought that due to the higher BDE of C–F bond compared to the C–Br,[37] this isomerization might be more difficult to take place in the case of fluoride. The formation of the branched allylic fluoride was proposed to proceed via (*i*) catalytic generation of Rh-carbynoid by diazo activation of the carbyne source, (*ii*) steroselective cyclopropanation (***int-1***) to deliver a transient cyclopropyl–$I^{(III)}$ intermediate ***int-2***; (*iii*) disrotatory ring-opening (Ph ring rotates inwardly and Me rotates outwardly) to give allyl

[36] Takizawa, S.; Arteaga, F. A.; Kishi, K.; Hirata, S.; Sasai, H. *Org. Lett.* **2014**, *16*, 4162.
[37] Blanksby, S. J.;Ellison, G. B. *Acc. Chem. Res.* **2003**, *36*, 255.

cation ***int-3***; and (*iv*) regioselective fluoride attack. The positive charge would be centered at the α position due to the double substitution with two stabilizing groups (alkyl and aromatic groups) (Scheme 8).



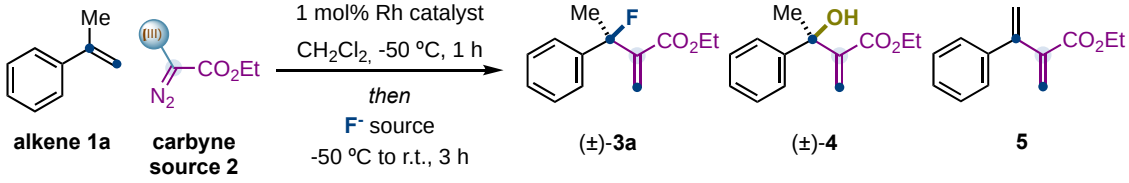
Scheme 8 Proposed mechanism

3.4.3. Reaction optimization

Initial experiments were performed using α-methylstyrene (**1a**, 2 equiv), hypervalent iodine reagent **2a** (1 equiv), tetrabutylammonium fluoride trihydrate $Bu_4NF \cdot 3H_2O$ (3 equiv) and Du Bois catalyst $Rh_2(esp)_2$ (1 mol %) in dichloromethane. We were pleased to find that branched allylic fluoride (±)-**3a** was formed in a promising 36% isolated yield with excellent branched/linear selectivity (*b:l* = >20:1). In addition to (±)-**3a**, alcohol (±)-**4** and diene **5** were also formed as subproducts of the reaction in low yields formed by water attack and proton elimination respectively (Table 1, entry 1).

With these promising results, we were encouraged to optimize this novel fluorination reaction by evaluating a diverse variety of fluoride sources, hoping to improve the efficiency of the C–F bond-forming process while minimizing the parasitic

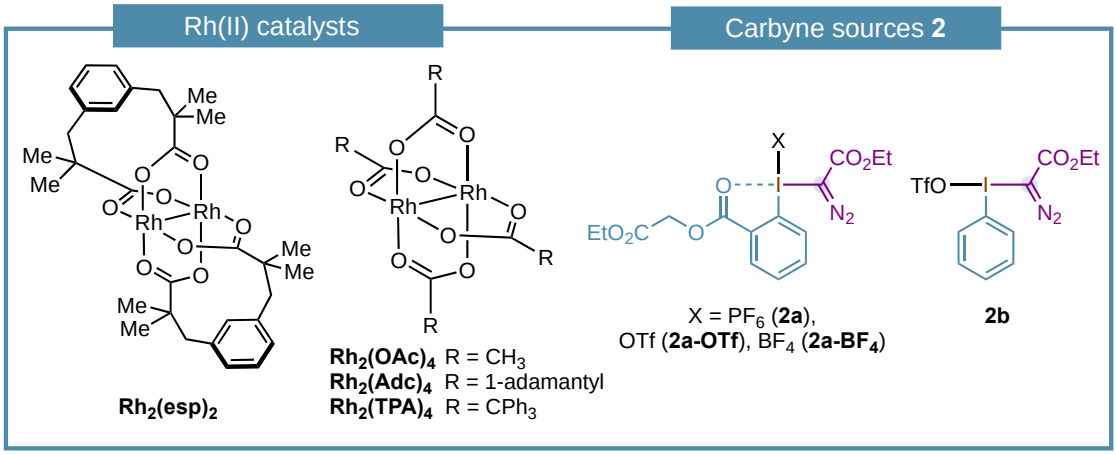
proton elimination or water attack. We were pleased to find that $Et_3N{\cdot}3HF$ led to (±)-**3a** in 71% isolated yield and the formation of (±)-**4** and **5** was certainly suppressed (<5% yield). In contrast, metallic fluorides MF (M = Na, K, Cs) or Olah´s reagent [$Py(HF)_x$] did not provide (±)-**3a** and certain amounts of elimination byproduct **5** were observed, probably due to low solubility and high basicity of the reagents, respectively. In addition, the use of more soluble and less basic fluoride sources such as tetrabutylammonium difluorotriphenylsilicate (TBAT) or tetrabutylammonium fluoride bispinacol complex ($TBAF(pin)_2$) provided (±)-**3a** in poor yields (entries 2 – 8). Other Rh(II)-catalysts like $Rh_2(OAc)_4$, $Rh_2(Adc)_4$ or $Rh_2(TPA)_4$ did not improve the efficiency of the reaction (entries 9 – 11). Furthermore, different pseudo-cyclic and lineal carbyne sources were tried, but they did not provide higher yields (entries 12 – 14). Finally, we proved that 3 equivalents of $Et_3N{\cdot}3HF$ were necessary to obtain good yields (entry 15) and the presence of water in the reaction mixture quenched the desired reaction, while forming alcohol (±)-**4a** in 66% of yield (entry 16).



alkene 1a **carbyne source 2** (±)-**3a** (±)-**4** **5**

Entry	Catalyst	Carbyne source	F^- source (equiv.)	(±)-**3a**[a]	*b*:*l*[b]	(±)-**4a**:**5**[a]
1	$Rh_2(esp)_2$	**2a**	TBA**F**·$3H_2O$ (3)	36%	> 20:1	17%:14%
2	$Rh_2(esp)_2$	**2a**	TBA**F**·$(pin)_2$ (3)	< 5%	-	nd:12%
3	$Rh_2(esp)_2$	**2a**	TBAT (3)	20%	> 20:1	nd:20%
4	$Rh_2(esp)_2$	**2a**	Py(H**F**)x (3)	nd	-	nd:15%
5	$Rh_2(esp)_2$	**2a**	Na**F** (3)	nd	-	1%:5%
6	$Rh_2(esp)_2$	**2a**	K**F** (3)	nd	-	1%:6%
7	$Rh_2(esp)_2$	**2a**	Cs**F** (3)	nd	-	1%:26%
8	$Rh_2(esp)_2$	**2a**	Et_3N·3H**F** (3)	73%	> 20:1	<3%:<2%
9	$Rh_2(OAc)_4$	**2a**	Et_3N·3H**F** (3)	47%	> 20:1	3%:nd
10	$Rh_2(Adc)_4$	**2a**	Et_3N·3H**F** (3)	65%	> 20:1	2%:3%
11	$Rh_2(TPA)_4$	**2a**	Et_3N·3H**F** (3)	29%	> 20:1	2%:2%
12	$Rh_2(esp)_2$	**2a-OTf**	Et_3N·3H**F** (3)	65%	> 20:1	3%:7%
13	$Rh_2(esp)_2$	**2a-BF_4**	Et_3N·3H**F** (3)	68%	> 20:1	4%:3%
14	$Rh_2(esp)_2$	**2b**	Et_3N·3H**F** (3)	45%	> 20:1	2%:8%
15	$Rh_2(esp)_2$	**2a**	Et_3N·3H**F** (1)	10%	> 20:1	45%:8%
16	$Rh_2(esp)_2$	**2a**	Et_3N·3H**F** (3)[c]	nd	-	66%:4%

[a]Yields are reported on the basis of ^{1}H-NMR analysis using anisole as internal standard. [b]Branched/linear ratio was determined by ^{19}F-NMR analysis of crude reaction mixture. [c]Water (10 equiv.) was added together with the fluoride source. nd refers to not detected. TBAF refers to tetrabutylammonium fluoride. TBAT refers to tetrabutylammonium difluorotriphenylsilicate. Py(HF)x refers to Olah's reagent.



$Rh_2(esp)_2$

$Rh_2(OAc)_4$ R = CH_3
$Rh_2(Adc)_4$ R = 1-adamantyl
$Rh_2(TPA)_4$ R = CPh_3

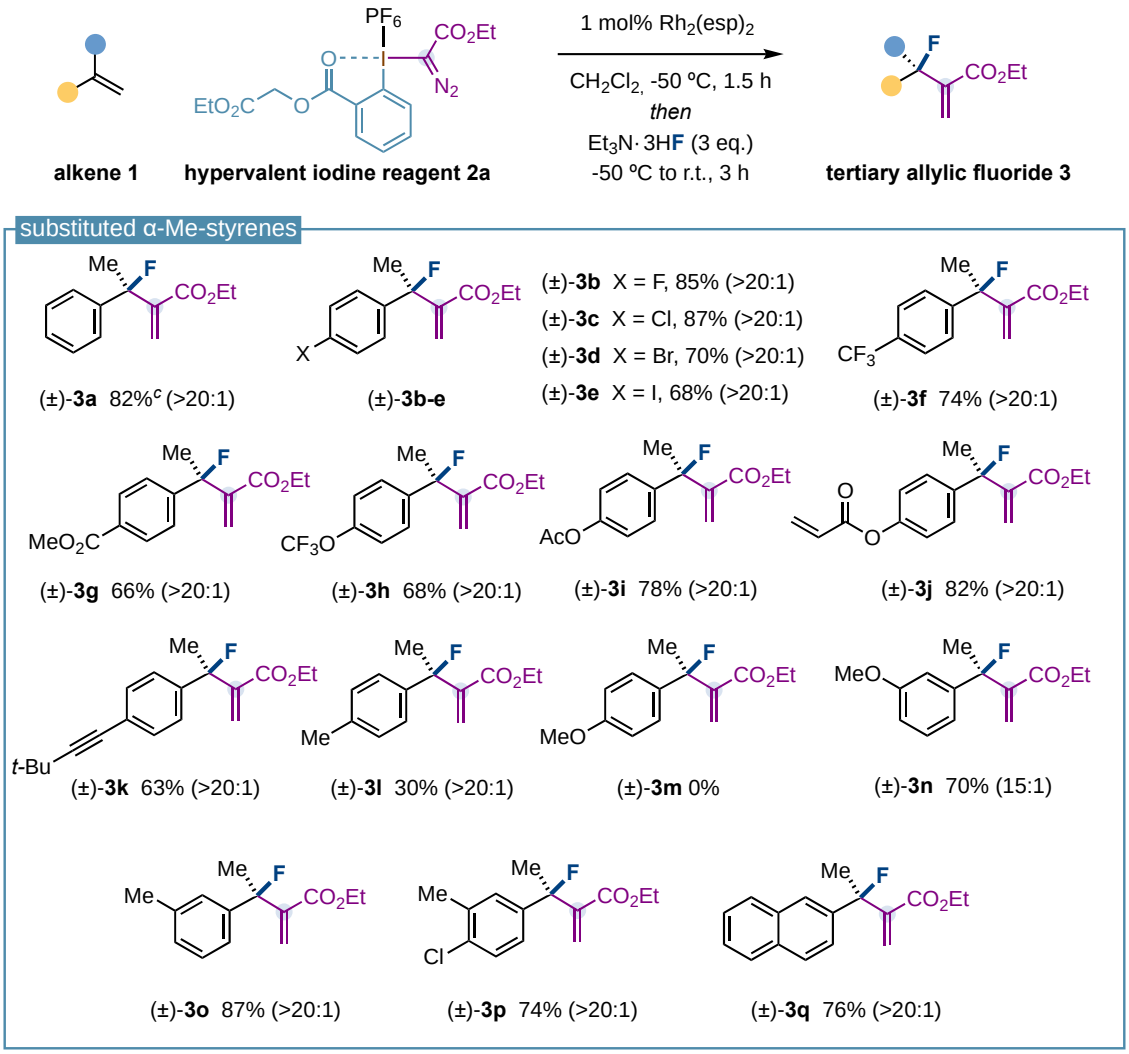
X = PF_6 (**2a**), OTf (**2a-OTf**), BF_4 (**2a-BF_4**)

2b

Table 1 Reaction conditions optimization

3.4.4. Scope of the catalytic alkene skeletal modification for the construction of fluorinated tertiary stereocenters

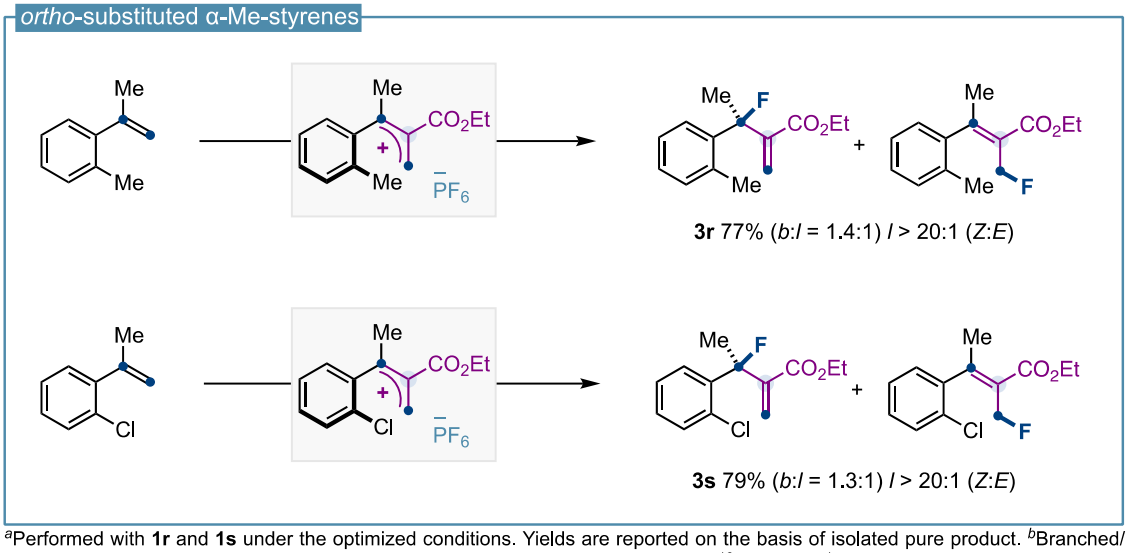
With the optimized reaction conditions in hand, we next investigated the scope of this fluorination reaction by examining a broad range of α-substituted styrenes (Table 2). We were delighted to observe that substrates substituted in *para* position of the aromatic ring with halogens [(±)-**3b-e**], trifluoromethyl [(±)-**3f**], ester [(±)-**3g**], trifluoromethoxy [(±)-**3h**], acyloxy [(±)-**3i-j**] and alkyne [(±)-**3k**] were well tolerated (63–87% of yields). However, methyl or methoxy substituents provided low levels of efficiency [(±)-**3l**, 30% of yield] or no product [(±)-**3m**] respectively, as notable polymerizations were noticed with full starting material consumption. This observation might be suggesting that the corresponding allyl carbocation species are generated, before $Et_3N{\cdot}3HF$ is added to the reaction, due to a significant acceleration in the ring-opening of cyclopropyl–$I^{(III)}$ intermediates (***int-2***) caused by the electron-rich aromatic rings. We later hypothesized that those electron-donating groups may not provoke such significant acceleration in the ring-opening step when placed in *meta* position. As predicted, the reactions carried out with *meta*-MeO- and *meta*-Me-substituted α-methylstyrenes provided the desired products (±)-**3n,o** with satisfactory yields and excellent branched/linear ratios (70 and 87% of yield respectively). Moreover, *para*- and *meta*-disubstituted aromatic rings or naphthalene provided the desired products with high level of efficiencies [(±)-**3p,q**, 74 and 76% of yield each].



[a]Performed with **1a**–**1q** (0.4 mmol, 2 equiv), **2a** (0.2 mmol, 1 equiv), $Rh_2(esp)_2$ (0.002 mmol, 1 mol%), $Et_3N{\cdot}3HF$ (3 equiv) in CH_2Cl_2 (0.1 M). Yields are reported on the basis of isolated pure product. [b]Branched/linear ratio, indicated in parentheses, and diastereoselectivity ratio, indicated in brackets, were determined by ^{19}F NMR or ^{1}H NMR analysis of crude reaction mixture. [c]Yield of isolated product using 1.7 grams of **1a** and 4.2 grams of **2a**.

Table 2 Substrate scope: substituted α-Me-styrenes

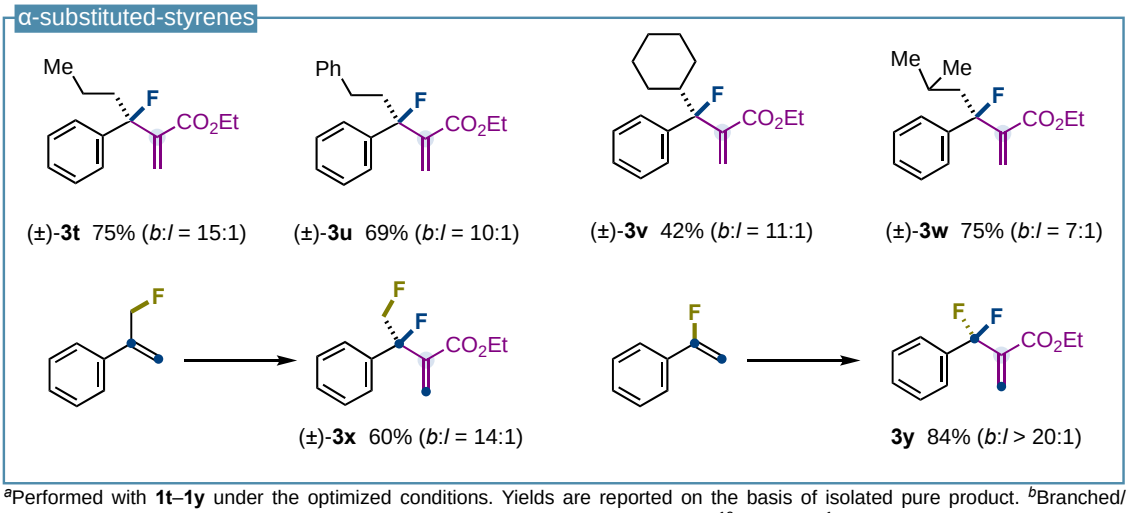
In contrast to the exquisite branched selectivity obtained for *para*- and *meta*-substituted α-methylstyrenes, a different situation was observed for *ortho*-substituted derivatives (Table 3). Equimolecular mixtures of branched/linear fluorides were obtained (**3r,s**) when using substrates substituted with a methyl or a chlorine group. Although this is a clear limitation of our method, it underlines a potential subtle effect of the *ortho* substituent in preventing the aromatic ring to stabilize the charge at the α position of the tertiary allyl cation and distorting the conjugation of the whole π system. Thus, the positive charge might not be that centered in the α position. Moreover, the change in the regioselectivity might be also caused by the steric effect from the *ortho* substituent, blocking the branched position.



[a]Performed with **1r** and **1s** under the optimized conditions. Yields are reported on the basis of isolated pure product. [b]Branched/linear and diastereoseletivity ratios, indicated in parentheses, were determined by ^{19}F NMR or ^{1}H NMR analysis of crude reaction mixture.

Table 3

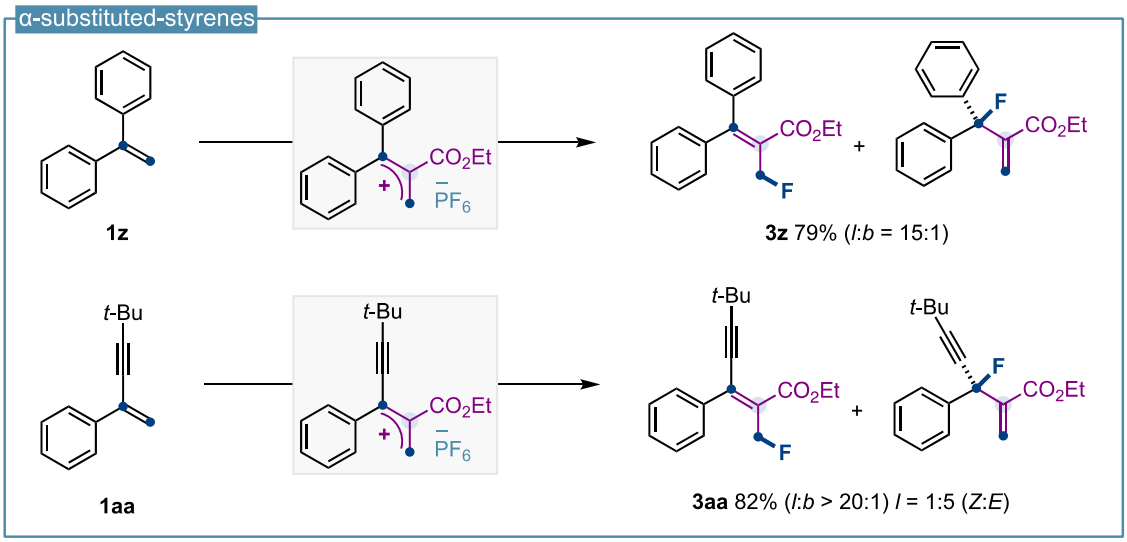
After this, we decided to extend the scope by varying the substituent in α position of the styrene. We observed that styrenes substituted with alkyl groups such as propyl, phenethyl, cyclohexyl, or *iso*-butyl [(±)-**3t**–**w**] worked well, however, a general decrease in the branched/linear ratio was observed (42–75 % of yield; 7:1 to 15:1 *b*/*l* ratio, Table 4). Fluoromethyl and fluor substituents were well tolerated and provided access to difluoromethyl and 1,2-difluoroethyl compounds (±)-**3x,y** with high efficiency. The latter results highlight an added-value of our methodology in accessing an interesting and useful subset of organofluorine compounds.



[a]Performed with **1t–1y** under the optimized conditions. Yields are reported on the basis of isolated pure product. [b]Branched/linear and diastereoseletivity ratios, indicated in parentheses, were determined by ^{19}F NMR or ^{1}H NMR analysis of crude reaction mixture.

Table 4

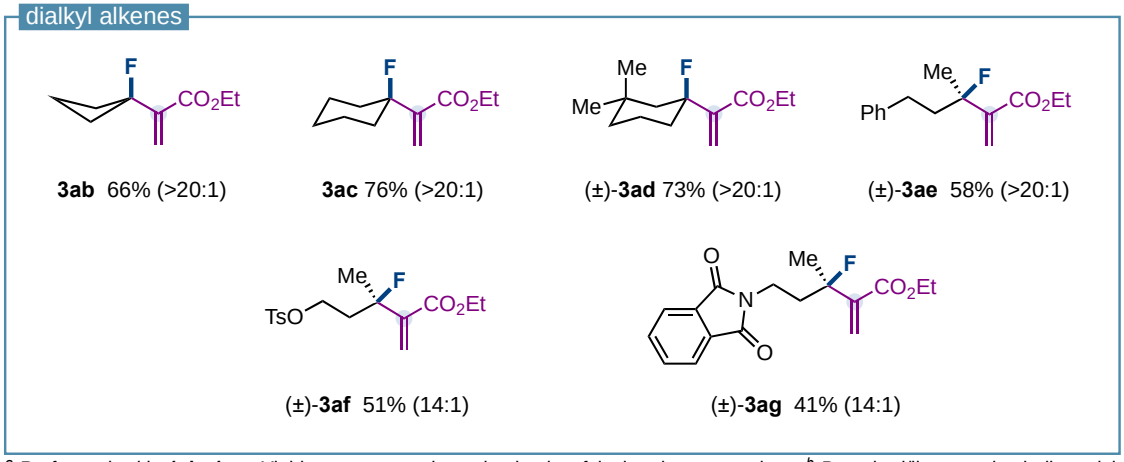
Phenyl or alkyne groups did not provide the expected branched fluorides and instead, the corresponding linear derivatives were obtained (Table 5, **3z**,**aa**), even though the yields did not diminish (**3z**: 79 % of yield; **3aa**: 82 % of yield). These results indicate that those substituents may provoke a delocalization of the charge in the allylic π system, however, we do not have a clear explanation for the excellent linear selectivity observed.



[a]Performed with **1z–1aa** under the optimized conditions. Yields are reported on the basis of isolated pure product. [b]Branched/linear and diastereoseletivity ratios, indicated in parentheses, were determined by ^{19}F NMR or ^{1}H NMR analysis of crude reaction mixture.

Table 5

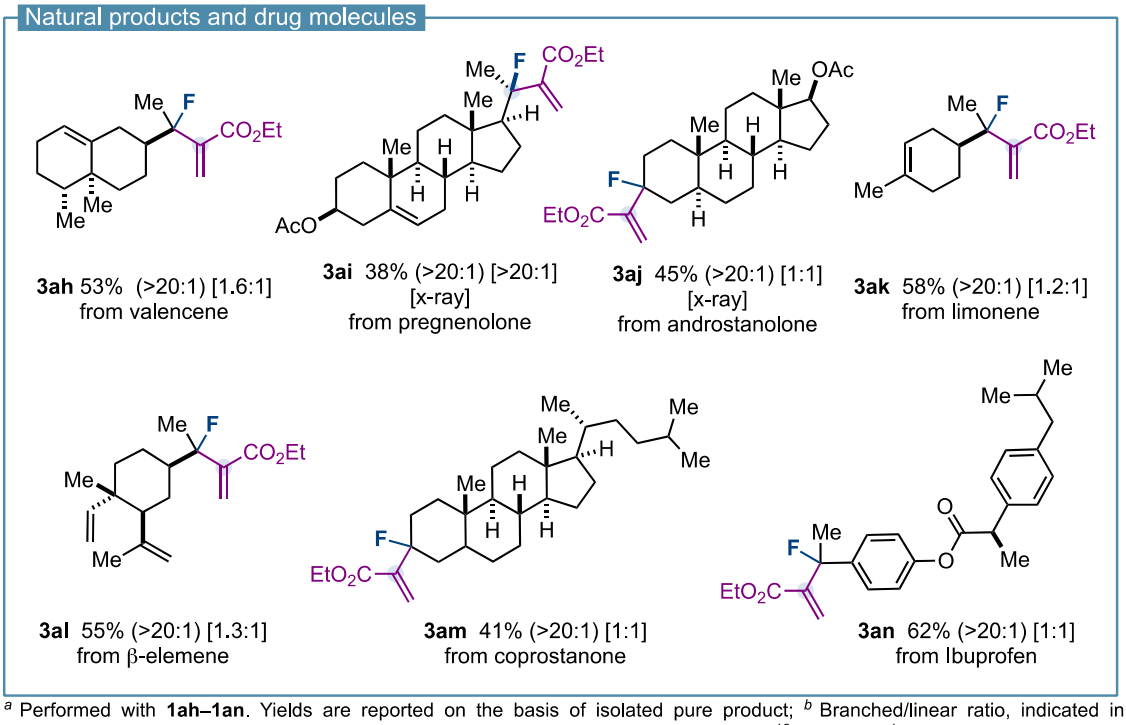
The latter examples led us to question the behavior of allyl carbocations doubly-substituted in α position with alkyl groups, which are generated from 1,1-dialkylsubstituted alkenes. We were delighted to find that exocyclic and acyclic aliphatic olefins were well tolerated and provide tertiary allylic fluorides (Table 6, **3ab**–**ag**) with good to excellent branched/linear ratio (41–76 % of yield; from 14:1 to >20:1 *b*/*l* ratio).



[a] Performed with **1ab**–**1ag**. Yields are reported on the basis of isolated pure product. [b] Branched/linear ratio, indicated in parentheses, and diastereoselectivity ratio, indicated in brackets, were determined by ^{19}F NMR or ^{1}H NMR analysis of crude reaction mixture.

Table 6

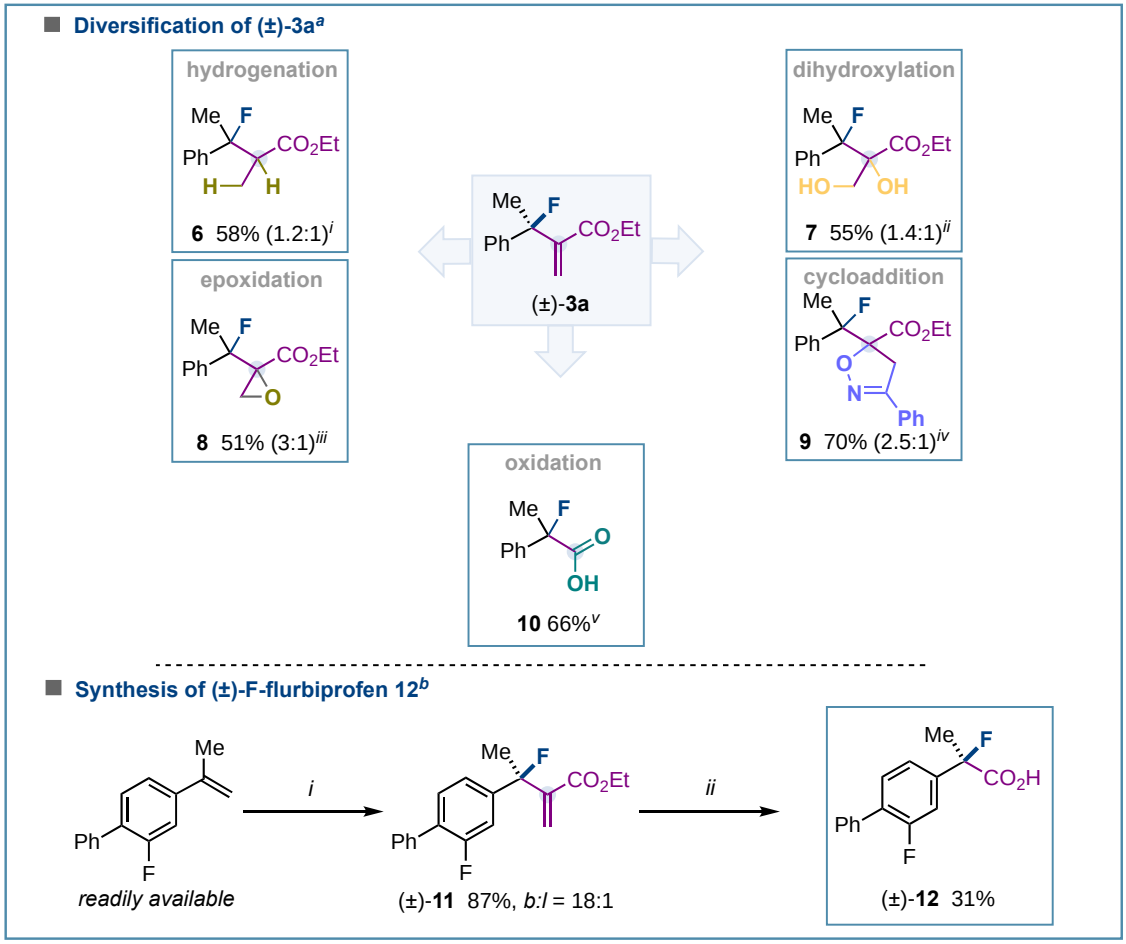
Further demonstration of the potential of our methodology was demonstrated in the late-stage fluorination of a selection of natural products and drug molecule derivatives (Table 7, **3ah**–**an**). It is worth highlighting the excellent degree of regioselectivity observed in substrates containing more than one alkene. The results indicate that highly-substituted alkenes are less reactive, however, the excellent selectivity observed for β-elemene (**3al**) highlights that the initial alkene cyclopropanation to form a cyclopropyl–$I^{(III)}$ intermediate can be affected by steric effects.



[a] Performed with **1ah–1an**. Yields are reported on the basis of isolated pure product; [b] Branched/linear ratio, indicated in parentheses, and diastereoselectivity ratio, indicated in brackets, were determined by ^{19}F NMR or ^{1}H NMR analysis of crude reaction mixture.

Table 7

We next aimed to transform the alkenyl-carboxylate moiety of (±)-**3a** into useful functionalities without compromising the integrity of the fluorinated tertiary stereocenter (Table 8). Hydrogenation (**6**), dihydroxylation (**7**), epoxidation (**8**) 1,3-cycloaddition reactions (**9**) and oxidation (**10**) provided a suit of fluorinated derivatives that would be otherwise difficult to obtain by other means. To demonstrate the synthetic utility of our methodology in providing access to fluorinated analogues of medically relevant agents containing a tertiary stereocenter, we sought to synthesize (±)-F-flurbiprofen **11**. Although this fluorinated analogue is known, it was synthesized using electrophilic fluoronium reagents, which generally suffer from safety, cost and functional group compatibility. Initially, we performed our fluorination reaction using a readily available styrene and obtained branched tertiary fluoride (±)-**11** with high efficiency (87 % of yield, Table 8). Finally, oxidation with OsO_4 transformed (±)-**11** into the desired (±)-F-flurbiprofen **12**.



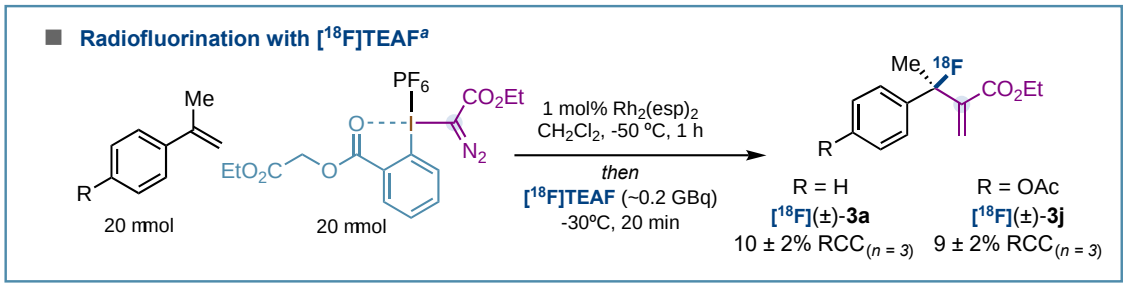
[a] Reaction conditions: (i) $TsNHNH_2$, NaOEt, EtOH, 1 hour, 80 °C; (ii) OsO_4 (1 mol %), Oxone, DMF/H_2O, 1 hour, rt; (iii) *m*-CPBA, CH_2Cl_2, 14 hours, reflux; (iv) chlorobenzaldoxime, Et_3N, 5 hours, 0 °C; (v) OsO_4 (1 mol %), Oxone, DMF, 14 hours, rt, *then* H_2O_2, NaOH 2M, THF. [b](i) 2-fluoro-4-(prop-1-en-2-yl)-1,1'-biphenyl, $Rh_2(esp)_2$ (1 mol%), $Et_3N{\cdot}3HF$; (ii) OsO_4 (1 mol %), Oxone, DMF, 14 hours, rt, *then* H_2O_2, NaOH 2M, THF.

Table 8

^{18}Fluorine [^{18}F] is emerging as one of the most prominent radionuclides in the application of positron emission tomography (PET), a fundamental technology in precision medicine for (pre)clinical imaging. The preparation of radioactive molecules containing a [^{18}F] fluorinated tertiary stereocenter remains a critical challenge. Those motifs cannot be synthesized by nucleophilic substitution of alkylsulfonates with [^{18}F]KF-K_{222} and current synthetic methodologies are limited in scope. Initial experiments were performed with α-methylstyrene, reagent **2a**, $Rh_2(esp)_2$, and [^{18}F]KF-K_{222} (~ 0.2 GBq). The latter [^{18}F]-fluoride source was added at –50 °C and the reaction mixture was warmed until –30 °C during 20 min.[38] Unfortunately, the radiolabelled

[38] The radiofluorination experiments shown in this chapter were performed in the Radiochemistry and Nuclear Imaging Lab of CICbiomaGUNE (Donostia, Spain) under the supervision of Prof. Jordi Llop. Such collaboration was possible thanks to the funding provided by the Spanish Ministry of Economy, Industry and Competitivity by the FPI fellowship BES-2017-080163.

product [^{18}F](±)-**3a** was not detected, probably due to the low solubility of [^{18}F]KF-K$_{222}$. However, when using [^{18}F]tetraethylammonium fluoride [^{18}F]TEAF (~ 0.2 GBq), we were glad to find formation of the labelled difluoromethylated product [^{18}F](±)-**3a** in 10% ± 2% (n = 3) of radiochemical conversion (RCC) (Scheme 9). In addition, we observed that the radiolabelling could also work with other substrates ([^{18}F](±)-**3j,** 9% ± 2% (n = 3) RCC. Even though the RCC obtained are low and further reaction design might be needed, these preliminary results underline a new entry to [^{18}F] fluorinated tertiary stereocenters.



[a] **1a** or **1j** (20 µmol), **2a** (20 µmol), $Rh_2(esp)_2$ (1 mol%), CH_2Cl_2, 1 hour, –50 °C, *then* [^{18}F]TEAF (0.2 GBq) in CH_2Cl_2 (100 µL), 20 min, –50 °C → –30 °C. RCC were calculated with radio-HPLC.

Scheme 9 Application of the carbyne transfer platform to the synthesis of radiofluorinated allylic tertiary stereocenters

3.5. Conclusions

In summary, we have developed a new synthetic methodology for the construction of fluorinated tertiary stereocenters from 1,1-disubstitued alkenes. The process relies on the generation of a tertiary allyl cations, mediated by a catalytically-generated Rh-carbynoid, that undergoes nucleophilic fluorination with excellent branched/selectivity ratio. Notable features of this process are the broad alkene scope, including natural products and drug molecule derivatives, applications in the synthesis of a fluorinated drug molecule – (±)-F-flurbiprofen– and its translation to radiofluorination with [^{18}F]TEAF. The generality of our methodology and synthetic applications, based on a Rh-catalyzed carbyne transfer with alkenes, stands as a testament of its potential utility to expand the chemical space in fluorine-based drug design.

3.6. Experimental section

General Information

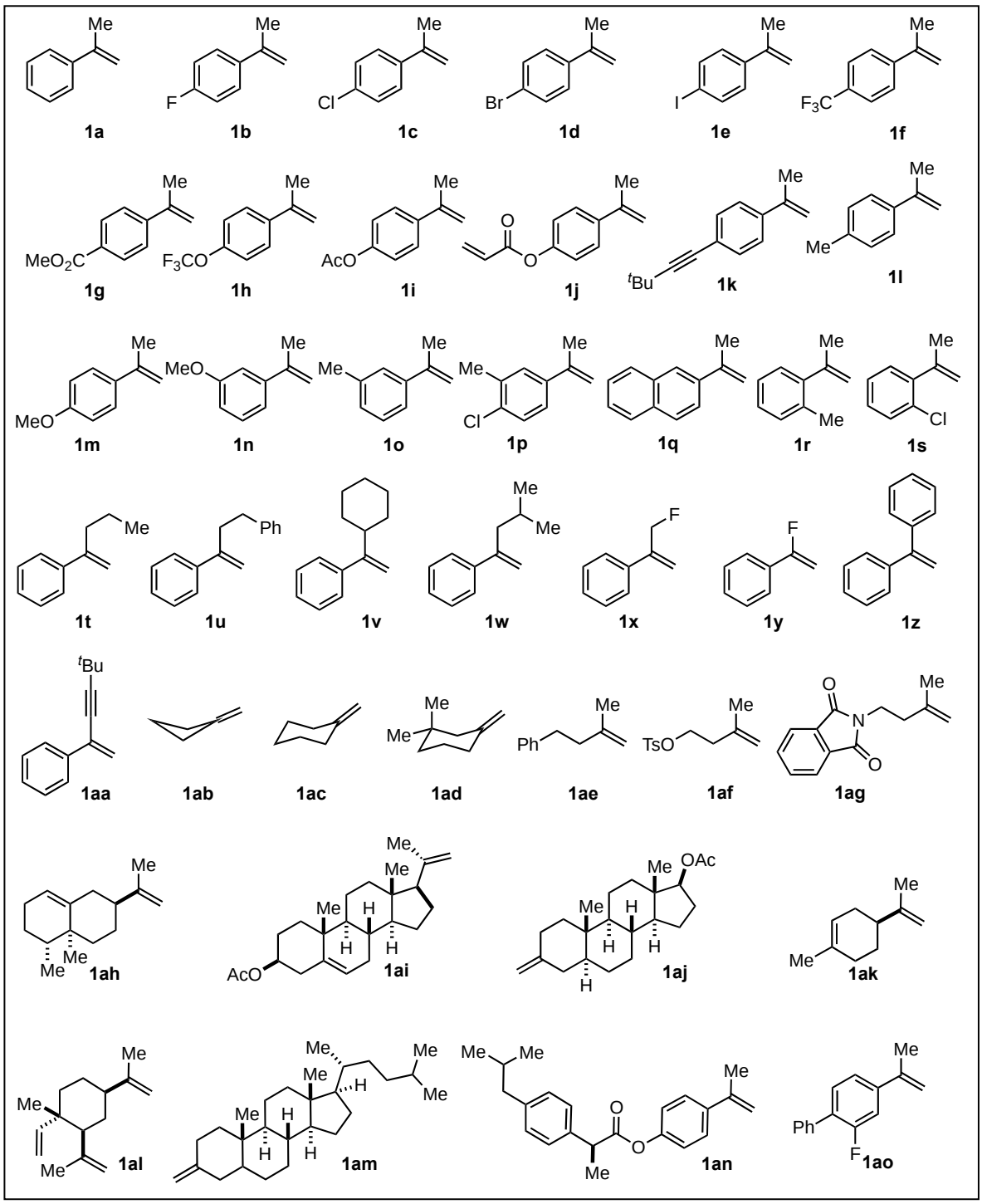
All reagents were directly used as purchased without any further purification. Ethyl diazoacetate, (contains ≥13 wt. % dichloromethane) was purchased from Sigma-Aldrich (Ref. E22201). Anhydrous solvents were dried by passing them through an activated alumina column on a PureSolvTM solvent purification system (Innovative Technologies, Inc., MA). Analytical thin layer chromatography (TLC) was carried out using aluminum sheets with 0.2 mm of silica gel (Merck GF234). Visualization of the developed chromatogram was performed by irradiation with UV light. Flash column chromatography was performed on silica gel (Aldrich, 230-400 mesh) or neutral silica gel (Material Harvest Ltd., 230-400 mesh). Preparative thin layer chromatography (PLC) was carried out using glass plate with 0.5 mm of silica gel 60. Organic solutions were concentrated under *vacuum* on a Büchi rotatory evaporator. Unless otherwise stated, reactions were carried out under argon atmosphere. NMR spectra were recorded at 298 K on Bruker Avance 300, Bruker Avance 400 Ultrashield and Bruker Avance 500 Ultrashield apparatuses. Chemical shifts (δ) are quoted in ppm relative to residual solvent signals, $CDCl_3$ referenced at δ 7.26 and 77.16 ppm, CD_3CN referenced at δ 1.94 and 1.39, 118.69 ppm respectively, Acetone-D_6 referenced at 2.05 and 29.8 ppm, CD_2Cl_2 referenced at δ 5.32 and 53.84 ppm. Coupling constants (*J*) are quoted in hertz (Hz). Multiplicity is reported with the following abbreviations: s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, dt = doublet of triplets, td = triplet of doublets, tt = triplet of triplets, tq = triplet of quartets, qd = quartet of doublets, qt = quartet of triplets, ddd = doublet of doublets of doublets, sp = septet, m = multiplet, app = apparent. Melting points were measured using open glass capillaries in a Büchi B540 apparatus. Infrared spectra were recorded on a Bruker Tensor 27. Mass spectra were recorded on a Waters LCT Premier spectrometer. Specific optical rotation measurements were carried out on a Jasco P-1030 model polarimeter equipped with a PMT detector using the Sodium line at 589 nm using a 100 mm pathlength cell and are reported as: $[\alpha]_D^T$ (concentration in 10 mg/1 mL, solvent).

2. Synthesis of alkenes 1.

1a, 1b, 1f, 1l, 1ab,1ac, 1ad, 1ae, 1ah, 1am, 1al were commercially available and used directly as received. **1c**[39], **1d**[39], **1e**[40], **1g**[41], **1h**[42], **1i**[40], **1n**[41], **1o**[41], **1p**[43], **1q**[40], **1r**[41], **1s**[39], **1t**[44], **1u**[44], **1v**[45], **1w**[46], **1z**[39] were prepared

[39] Huang, J.; Hu, G.; An, S.; Chen, D.; Li, M.; Li, P. *J. Org. Chem.* **2019**, *84*, 9758.
[40] Zhang, L.; Zuo, Z.; Wan, X.; Huang, Z. *J. Am. Chem. Soc.* **2014**, *136*, 15501.
[41] Wen, Z. K.; Ge, X. M.; Zhao, Z. K.; Chao, J. Bin. *Adv. Synth. Catal.* **2019**, *361*, 983.
[42] Xing, Y.; Yu, R.; Fang, X. *Org. Lett.* **2020**, *22*, 1008.
[43] Liu, W.; Lau, F.; Liu, K.; Wood, H. B.; Zhou, G.; Chen, Y.; Li, Y.; Akiyama, T. E.; Castriota, G.; Einstein, M.; Wang, C.; McCann, M. E.; Doebber, T. W.; Wu, M.; Chang, C. H.; McNamara, L.; McKeever, B.; Mosley, R. T.; Berger, J. P.; Meinke, P. T. *J. Med. Chem.* **2011**, *54*, 8541.
[44] Zhang, S.; Bedi, D.; Cheng, L.; Unruh, D. K.; Li, G.; Findlater, M. *J. Am. Chem. Soc.* **2020**, *142*, 8910.
[45] Chatalova-Sazepin, C.; Wang, Q.; Sammis, G. M.; Zhu, J. *Angew. Chemie* **2015**, *127*, 5533.
[46] Huang, C. Y.; Doyle, A. G. *J. Am. Chem. Soc.* **2015**, *137*, 5638.

according to the general procedure A[5] from the corresponding commercial ketone compounds. **1x**[47], **1y**[48], **1af**[49], **1ag**[49] were synthesized by following reported protocols.

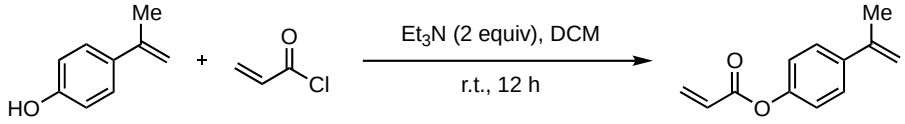


General procedure A:[39,40] To an oven-dried flask was charged methyltriphenylphosphonium bromide (5.3 g, 15 mmol), potassium *tert*-butoxide (1.9 g, 16 mmol) and THF (15 mL). The reaction mixture was stirred

[47] Baudoux, J.; Cahard, D. *Org. React.* **2008**, *69*, 1.
[48] Kozikowski, A. P. *Eur. J. Med. Chem.* **2019**, *182*.
[49] Siu, J. C.; Parry, J. B.; Lin, S. *J. Am. Chem. Soc.* **2019**, *141*, 2825.

at room temperature for 1 hour. After this, the mixture was cooled to 0 °C and the corresponding ketone (12 mmol, 1.0 equiv.) was added dropwise. The reaction mixture was allowed to reach room temperature and stirred overnight. Then, the reaction was quenched with a saturated aqueous solution of NH_4Cl (40 mL) and extracted with diethyl ether (3 x 20 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of solvent under *vacuum* and purification by flash column chromatography with hexane/ethyl acetate mixtures afforded the desired alkenes **1**.

4-(Prop-1-en-2-yl)phenyl acrylate (1j)



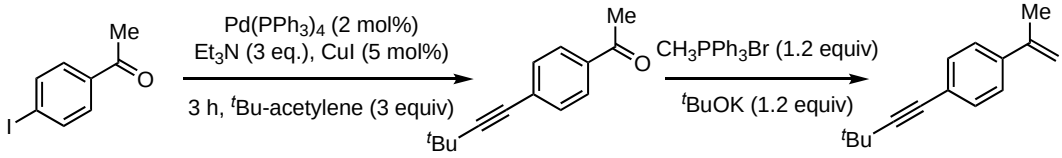
1j

To an oven-dried flask was charged 4-(prop-1-en-2-yl)phenol (550 mg, 4.1 mmol), Et_3N (0.6 mL, 8.2 mmol) and dichloromethane (10 mL). The mixture was cooled at 0 °C and acryloyl chloride (0.65 mL, 8.2 mmol) was added dropwise. After this, the reaction mixture was warmed to room temperature and stirred for 12 hours. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (25 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of solvent under *vacuum* and purification by flash column chromatography (hexane/ethyl acetate = 10/1) provided product **1j** as colorless oil (520 mg, 68% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.7 Hz, 2H), 7.16 – 7.06 (m, 2H), 6.62 (dd, *J* = 17.3, 1.4 Hz, 1H), 6.33 (dd, *J* = 17.3, 10.4 Hz, 1H), 6.02 (dd, *J* = 10.4, 1.3 Hz, 1H), 5.37 – 5.34 (m, 1H), 5.13 – 5.05 (m, 1H), 2.15 (dd, *J* = 1.5, 0.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 164.7, 150.0, 142.6, 139.2, 132.7, 128.1, 126.7, 121.3, 112.8, 22.0.

HRMS (ESI): calculated for $C_{12}H_{12}O_2Na^+$ $[M+Na]^+$ m/z: 211.0730, found: 211.0728.

1-(3,3-Dimethylbut-1-yn-1-yl)-4-(prop-1-en-2-yl)benzene (1k)



A **1k**

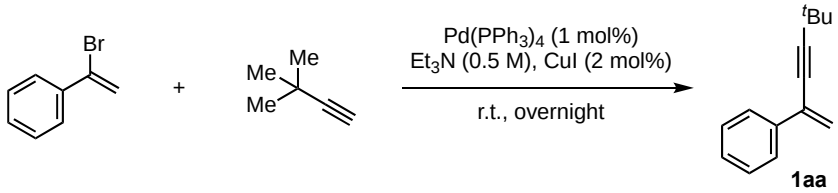
Compound **1k** was prepared according to the general procedure A using ketone **A** (1.5 g, 7.5 mmol, *prepared following a reported protocol*)[50] and obtained as a colorless oil (1.4 g, 93% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.31 (m, 4H), 5.41 – 5.38 (m, 1H), 5.12 – 5.09 (m, 1H), 2.14 (dd, *J* = 1.5, 0.8 Hz, 3H), 1.34 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 142.8, 140.2, 131.5, 125.3, 123.2, 112.8, 99.2, 79.1, 31.2, 28.1, 21.8.

HRMS (APCI): calculated for $C_{15}H_{19}$ $[M]^+$ m/z: 199.1841, found: 199.1843.

[50] Ruiz, J.; Cutillas, N.; López, F.; López, G.; Bautista, D. *Organometallics* **2006**, *25*, 5768.

(5,5-Dimethylhex-1-en-3-yn-2-yl)benzene (1aa)

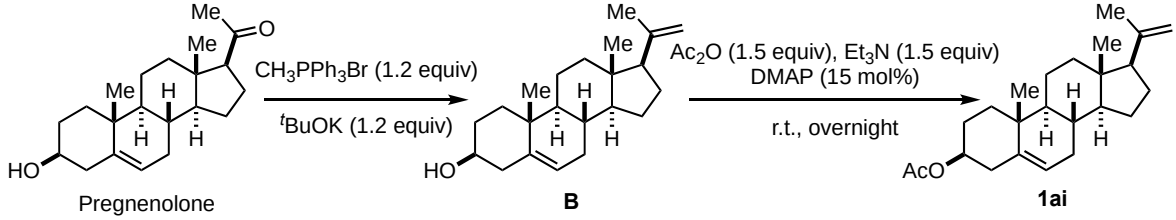


To a solution of (1-bromovinyl)benzene (1.8 g, 10 mmol) in triethylamine (20 mL, 0.5M) were added $Pd(PPh_3)_4$ (108 mg, 0.1 mmol, 1 mol%) and CuI (38 mg, 0.2 mmol). After this, 3,3-dimethylbut-1-yne (0.52 g, 25 mmol, 2.5 equiv.) was added and the reaction mixture was stirred overnight. The reaction was quenched with a saturated aqueous solution of NH_4Cl (40 mL) and extracted with diethyl ether (3 x 20 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of solvent under *vacuum* and purification by flash column chromatography (hexane) provided product **1aa** as colorless oil (1.5 g, 83% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 – 7.57 (m, 2H), 7.39 – 7.32 (m, 2H), 7.32 – 7.27 (m, 1H), 5.83 (d, *J* = 1.2 Hz, 1H), 5.57 (d, *J* = 1.2 Hz, 1H), 1.33 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 138.1, 131.0, 128.4, 128.2, 126.2, 119.2, 100.3, 78.4, 31.2, 28.2.

HRMS (APCI): calculated for $C_{14}H_{17}^+$ $[M+H]^+$ m/z: 185.1325, found: 185.1321.

(3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-Dimethyl-17-(prop-1-en-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl acetate (1ai)



To an oven-dried flask was charged compound **B** (2.7 g, 8.7 mmol, *prepared following the general procedure A*),[51] *N*,*N*-dimethyl-4-aminopyridine (160 mg, 1.3 mmol), Et_3N (1.8 mL, 13 mmol) and dichloromethane (25 mL). The reaction was cooled to 0 °C and acetic anhydride (1.3 mL, 13 mmol) was added dropwise. The reaction mixture was allowed to reach room temperature and stirred overnight. After this, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (20 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of solvent under *vacuum* and purification by flash column chromatography (hexane/ethyl acetate = 10/1) provided product **1ai** as colorless oil (1.8 g, 58% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.39 – 5.36 (m, 1H), 4.94 – 4.82 (m, 1H), 4.73 – 4.67 (m, 1H), 4.66 – 4.52 (m, 1H), 2.43 – 2.24 (m, 2H), 2.09 – 1.93 (m, 5H), 1.91 – 1.81 (m, 3H), 1.80 – 1.72 (m, 4H), 1.72 – 1.62 (m, 2H), 1.62 – 1.51 (m, 3H), 1.50 – 1.38 (m, 2H), 1.29 – 1.05 (m, 4H), 1.02 (s, 3H), 1.01 – 0.92 (m, 1H),

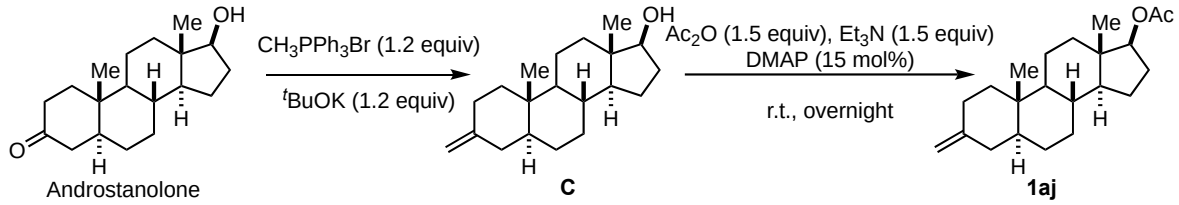
[51] La, D. S.; Salituro, F. G.; Martinez Botella, G.; Griffin, A. M.; Bai, Z.; Ackley, M. A.; Dai, J.; Doherty, J. J.; Harrison, B. L.; Hoffmann, E. C.; Kazdoba, T. M.; Lewis, M. C.; Quirk, M. C.; Robichaud, A. J. *J. Med. Chem.* **2019**, *62*, 7526.

0.58 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.6, 145.7, 139.8, 122.6, 110.8, 74.1, 57.4, 56.6, 50.3, 43.2, 38.8, 38.2, 37.2, 36.8, 32.3, 31.9, 27.9, 25.5, 24.8, 24.4, 21.6, 21.2, 19.5, 12.8.

HRMS (ESI): calculated for $C_{24}H_{36}O_2Na^+$ $[M+Na]^+$ m/z: 379.2608, found: 379.2603.

Spectra were consistent with the previously reported.[52]

(5*S*,8*R*,10*S*,13*S*,14*S*,17*S*)-10,13-Dimethyl-3-methylenehexadecahydro-1H-cyclopenta[a]phenanthren-17-yl acetate (1aj)

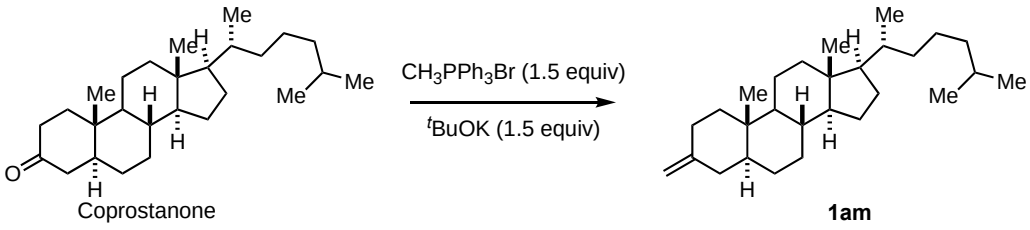


To a 50 mL oven dried flask was charged **C** (0.92 g, 3.1 mmol, *prepared following the general procedure A*),[53] *N*,*N*-dimethylpyridin-4-amine (38 mg, 0.31mmol), Et_3N (0.6 mL, 4.3 mmol) and dichloromethane (25 mL). The reaction was cooled to 0 °C and acetic anhydride (0.45 mL, 4.3 mmol) was added dropwise. The reaction mixture was allowed to reach room temperature and stirred overnight. Then, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (20 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of solvent under *vacuum* and purification by flash column chromatography (hexane/ethyl acetate = 10/1) provided **1aj** as white solid (780 mg, 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.62 – 4.50 (m, 3H), 2.24 – 2.06 (m, 3H), 2.03 (s, 3H), 2.02 – 1.86 (m, 2H), 1.81 – 1.74 (m, 2H), 1.68 – 1.35 (m, 5H), 1.35 – 1.20 (m, 4H), 1.09 – 0.99 (m, 2H), 0.99 – 0.92 (m, 2H), 0.92 – 0.80 (m, 4H), 0.78 (d, *J* = 0.6 Hz, 3H), 0.66 (ddd, *J* = 12.2, 10.5, 4.2 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 150.0, 106.3, 83.0, 54.5, 50.9, 48.2, 42.7, 40.0, 38.0, 37.1, 36.2, 35.4, 31.6, 31.1, 28.8, 27.7, 23.7, 21.3, 20.7, 12.3, 11.9.

HRMS (ESI): calculated for $C_{22}H_{34}O_2Na^+$ $[M+Na]^+$ m/z: 353.2451, found: 353.2461.

(8*R*,10*S*,13*R*,17*R*)-10,13-Dimethyl-3-methylene-17-((*R*)-6-methylheptan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthrene (1am)



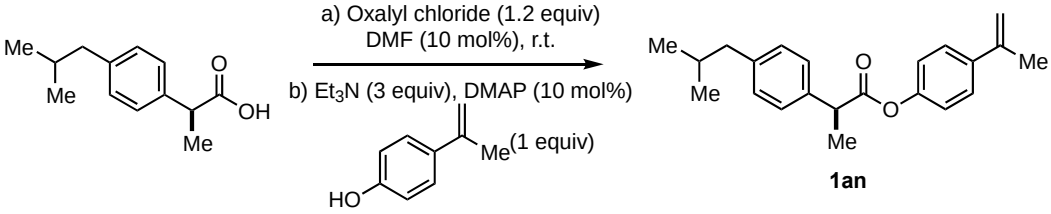
Compound **1am** was prepared according to the general procedure A using Coprostanone (600 mg, 1.6 mmol) and obtained as white solid (560 mg, 93% yield).

[52] Maity, S.; Manna, S.; Rana, S.; Naveen, T.; Mallick, A.; Maiti, D. *J. Am. Chem. Soc.* **2013**, *135*, 3355.
[53] Cook, C. E.; Corley, R. C.; Wall, M. E. *Steroids.* **1968**, *83*, 5.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.60 – 4.51 (m, 2H), 2.19 – 2.14 (m, 2H), 2.07 – 1.93 (m, 2H), 1.91 – 1.86 (m, 1H), 1.86 – 1.74 (m, 2H), 1.65 – 1.45 (m, 3H), 1.60 – 1.55 (m, 1H), 1.53 – 1.45 (m, 2H), 1.45 – 1.20 (m, 8H), 1.19 – 1.06 (m, 6H), 1.06 – 0.93 (m, 4H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 1.8 Hz, 3H), 0.86 (d, *J* = 1.8 Hz, 6H), 0.66 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.4, 106.1, 56.7, 56.5, 54.6, 48.3, 42.7, 40.2, 40.0, 39.7, 38.1, 36.3, 36.2, 36.0, 35.7, 32.2, 31.2, 29.1, 28.4, 28.2, 24.4, 24.0, 23.0, 22.7, 21.3, 18.8, 12.2, 11.9.

HRMS (APCI): calculated for $C_{28}H_{49}^+$ $[M+H]^+$ m/z: 385.3829, found: 385.3832.

4-(Prop-1-en-2-yl)phenyl (*S*)-2-(4-isobutylphenyl)propanoate (1an)

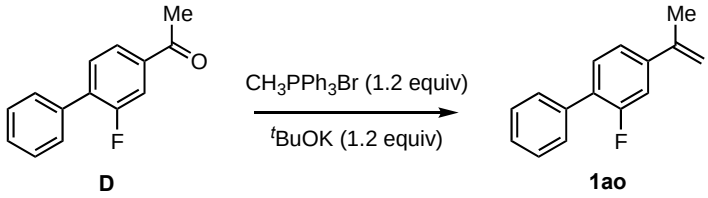


To an oven-dried flask was charged ibuprofen (1.5 g, 7.3 mmol), DMF (55 µl, 10 mol%) and dichloromethane (15 mL). Then, the reaction mixture was cooled to 0 °C and oxalyl chloride (0.7 mL, 8.0 mmol) was added dropwise. The reaction mixture was allowed to reach room temperature and stirred overnight. After this, the solvent was removed under *vacuum* and the crude was re-dissolved in dichloromethane (5 mL). Then, this solution was added dropwise to a second oven-dried flask charged with 4-(prop-1-en-2-yl)phenol (800 mg, 6.0 mmol), *N*,*N*-dimethylpyridin-4-amine (73 mg, 10 mol%), Et_3N (2.5 mL, 18.0 mmol) and dichloromethane (15 mL). The resulting reaction mixture was stirred overnight at room temperature and then quenched with a saturated aqueous solution of $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of solvent and purification by flash column chromatography (hexane/ethyl acetate = 10/1) provided **1an** as colorless oil (1.2 g, 54% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.37 (m, 2H), 7.35 – 7.27 (m, 2H), 7.17 – 7.11 (m, 2H), 7.01 – 6.90 (m, 2H), 5.34 – 5.28 (m, 1H), 5.09 – 5.02 (m, 1H), 3.93 (q, *J* = 7.1 Hz, 1H) 2.47 (d, *J* = 7.3 Hz, 2H), 2.12 (s, 3H), 1.87 (sp, *J* = 6.8 Hz, 1H), 1.61 (d, *J* = 7.2 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.4, 150.4, 142.6, 141.0, 139.0, 137.4, 129.7, 127.4, 126.6, 121.2, 112.7, 77.5, 77.2, 76.8, 45.4, 45.2, 30.3, 22.6, 22.0, 18.7.

HRMS (ESI): calculated for $C_{22}H_{27}O_2^+$ $[M+H]^+$ m/z: 323.2006, found: 323.1997.

2-Fluoro-4-(prop-1-en-2-yl)-1,1'-biphenyl (1ao)

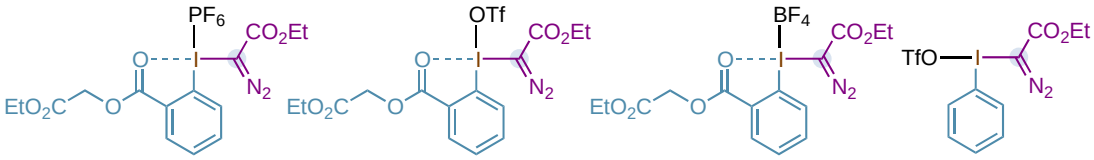


Compound **1ao** was prepared according to the general procedure A using ketone **D** (2.1 g, 9.7 mmols, *prepared following a reported protocol*)[54] and obtained as a white solid (1.8 g, 87% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.54 (m, 2H), 7.50 – 7.42 (m, 2H), 7.42 – 7.38 (m, 1H), 7.38 – 7.31 (m, 2H), 7.30 – 7.22 (m, 1H), 5.46 (q, *J* = 1.0 Hz, 1H), 5.19 – 5.14 (m, 1H), 2.18 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.8 (d, 248.1 Hz), 142.6 (d, *J* = 7.7 Hz), 141.9 (d, *J* = 2.1 Hz), 135.8 (d, *J* = 1.4 Hz), 130.5 (d, *J* = 4.1 Hz), 129.1 (d, *J* = 6.0 Hz), 128.6, 128.0 (d, *J* = 13.8 Hz), 127.8, 121.5 (d, *J* = 3.2 Hz), 113.6, 113.3 (d, *J* = 23.8 Hz), 21.8; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -118.56 (dd, *J* = 12.5, 8.2 Hz).

HRMS (APCI): calculated for $C_{15}H_{14}F$ $[M+H]^+$ m/z: 213.1074, found: 213.1081.

3. Synthesis of hypervalent iodine reagents 2.



2a **2a-OTf** **2a-BF$_4$** **2b**

The hypervalent iodine reagents **2** indicated above are known compounds and were prepared following reported protocols.[55, 56] **2a** was prepared by the following modification of a reported protocol:[55] a solution of **2a-OTf** (3.0 g, 5.1 mmol) in dichloromethane (25 mL, 0.2 M) was added to a 100 mL separation funnel and then washed with a saturated aqueous solution of KPF_6 (3 x 25 mL). The combined organic layers were dried over Na_2SO_4 and solvent was removed under *vacuum* to give **2a** as yellow solid (2.7 g, 89 % yield). Spectra were consistent with the previously reported.[55]

(*Note: if the product contains impurities, it is recrystallized with dichloromethane/diethyl ether = 1/5*).

4. Optimization studies.

General procedure B: To a 10 mL oven-dried tube was added the corresponding Rh catalyst (0.001 mmol, 1 mol%). The tube was sealed before being evacuated and backfilled with argon three times. α-methylstyrene **1a** (24 mg, 27 μL, 0.2 mmol) and degassed dichloromethane (0.5 mL) were added and the resulting mixture was cooled at -50 ºC. Then, a solution of reagent **2** (0.1 mmol, 1.0 equiv.) in degassed dichloromethane (1 mL) was added dropwise during 1 h using a syringe pump. After this, the reaction mixture was stirred at -50 ºC for 30 minutes. Next, fluoride nucleophile was added and the resulting reaction mixture was allowed to warm to room temperature during 3 hours. The resulting reaction mixture was analyzed by ^{1}H-NMR and ^{19}F-NMR using anisole (10.8 mg, 0.1 mmol, 1.0 equiv.) as internal standard.

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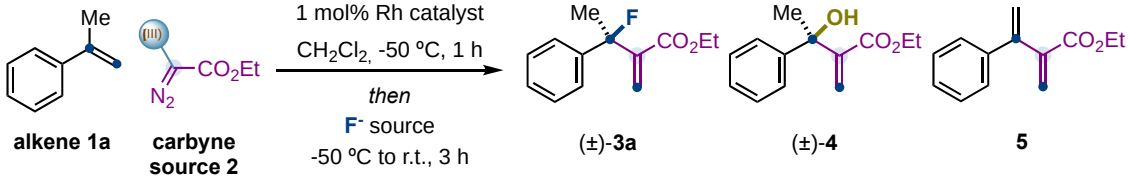
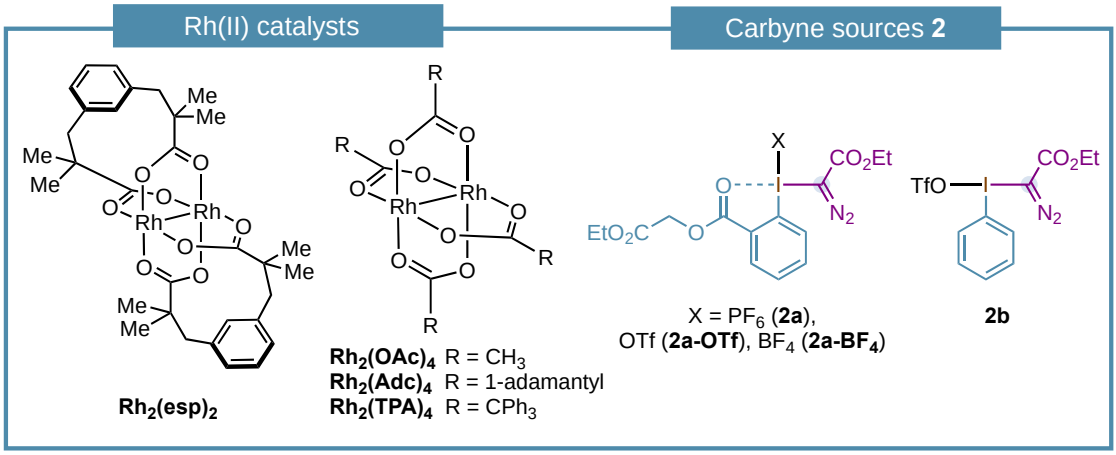
[54] Byrd, J. C.; Bennett, C. E.; Vibhute, S. M.; Hertlein, E.; Elgamal, O. A.; Wilson, T. A. U.S. Patent WO 2021134042, July 01, 2021.
[55] Wang, Z.; Jiang, L.; Sarró, P.; Suero, M. G. *J. Am. Chem. Soc.* **2019**, *141*, 15509.
[56] Weiss, R.; Seubert, J.; Hampel, F. *Angew. Chem. Int. Ed.* **1994**, *33*, 1952.



alkene 1a **carbyne source 2** (±)-**3a** (±)-**4** **5**

Entry	Catalyst	Carbyne source	F^- source (equiv.)	(±)-**3a**[a]	*b*:*l*[b]	(±)-**4a**:**5**[a]
1	$Rh_2(esp)_2$	**2a**	TBA**F**·$3H_2O$ (3)	36%	> 20:1	17%:14%
2	$Rh_2(esp)_2$	**2a**	TBA**F**·$(pin)_2$ (3)	< 5%	-	nd:12%
3	$Rh_2(esp)_2$	**2a**	TBAT (3)	20%	> 20:1	nd:20%
4	$Rh_2(esp)_2$	**2a**	Py(H**F**)x (3)	nd	-	nd:15%
5	$Rh_2(esp)_2$	**2a**	Na**F** (3)	nd	-	1%:5%
6	$Rh_2(esp)_2$	**2a**	K**F** (3)	nd	-	1%:6%
7	$Rh_2(esp)_2$	**2a**	Cs**F** (3)	nd	-	1%:26%
8	$Rh_2(esp)_2$	**2a**	Et_3N·3H**F** (3)	73%	> 20:1	<3%:<2%
9	$Rh_2(OAc)_4$	**2a**	Et_3N·3H**F** (3)	47%	> 20:1	3%:nd
10	$Rh_2(Adc)_4$	**2a**	Et_3N·3H**F** (3)	65%	> 20:1	2%:3%
11	$Rh_2(TPA)_4$	**2a**	Et_3N·3H**F** (3)	29%	> 20:1	2%:2%
12	$Rh_2(esp)_2$	**2a-OTf**	Et_3N·3H**F** (3)	65%	> 20:1	3%:7%
13	$Rh_2(esp)_2$	**2a-BF_4**	Et_3N·3H**F** (3)	68%	> 20:1	4%:3%
14	$Rh_2(esp)_2$	**2b**	Et_3N·3H**F** (3)	45%	> 20:1	2%:8%
15	$Rh_2(esp)_2$	**2a**	Et_3N·3H**F** (1)	10%	> 20:1	45%:8%
16	$Rh_2(esp)_2$	**2a**	Et_3N·3H**F** (3)[c]	nd	-	66%:4%

[a]Yields are reported on the basis of ^{1}H-NMR analysis using anisole as internal standard. [b]Branched/linear ratio was determined by ^{19}F-NMR analysis of crude reaction mixture. [c]Water (10 equiv.) was added together with the fluoride source. nd refers to not detected. TBAF refers to tetrabutylammonium fluoride. TBAT refers to tetrabutylammonium difluorotriphenylsilicate. Py(HF)x refers to Olah's reagent.



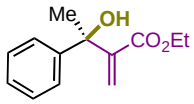
$Rh_2(esp)_2$

$Rh_2(OAc)_4$ R = CH_3
$Rh_2(Adc)_4$ R = 1-adamantyl
$Rh_2(TPA)_4$ R = CPh_3

X = PF_6 (**2a**), OTf (**2a-OTf**), BF_4 (**2a-BF_4**)

2b

Ethyl 3-hydroxy-2-methylene-3-phenylbutanoate ((±)-4)

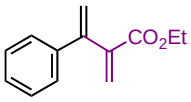


This product was obtained with the reaction byproduct 2-ethoxy-2-oxoethyl 2-iodobenzoate.[57]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 2H), 7.26 – 7.21 (m, 1H), 7.22 – 7.09 (m, 2H), 6.40 (s, 1H), 5.96 (s, 1H), 4.20 – 4.03 (m, 2H), 1.67 (s, 3H), 1.19 (td, *J* = 7.1, 0.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) 167.5, 147.0, 144.7, 128.3, 127.0, 124.9, 124.7, 94.6, 61.2, 29.4, 14.1.

Spectra are consistent with previously reported.[58]

Ethyl 2-methylene-3-phenylbut-3-enoate (5)

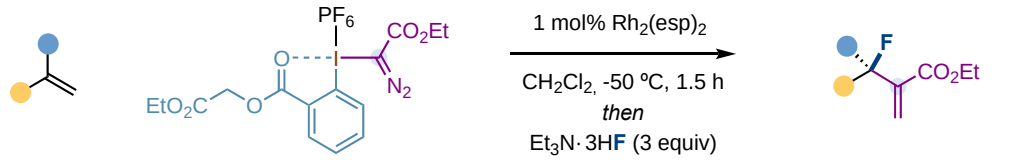


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 5H), 6.31 (d, *J* = 1.7 Hz, 1H), 5.81 (d, *J* = 1.7 Hz, 1H), 5.50 (d, *J* = 1.4 Hz, 1H), 5.40 (d, *J* = 1.4 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 1.09 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.7, 146.4, 142.5, 140.0, 128.4, 127.9, 127.6, 126.7, 116.4, 61.0, 14.0.

HRMS (ESI) calculated for $C_{13}H_{14}NaO_2^+$ $[M+Na]^+$ m/z: 225.0886, found: 225.0884.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

5. Synthesis of tertiary allylic fluorides 3.

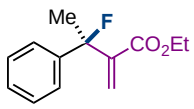


alkene 1 **hypervalent iodine reagent 2a** **tertiary allylic fluoride 3**

General procedure C: To a 10 mL oven-dried tube was added $Rh_2(esp)_2$ (2.0 mg, 0.002 mmol, 1 mol%). The tube was sealed before being evacuated and backfilled with argon three times. The corresponding alkene **1** (0.4 mmol, 2.0 equiv.) and degassed dichloromethane (1.0 mL) were added and the resulting mixture was cooled at -50 ºC. Then, a solution of reagent **2a** (0.2 mmol, 1.0 equiv.) in degassed dichloromethane (2.0 mL) was added dropwise during 1 h using a syringe pump. After addition, the reaction mixture was stirred for 30 min at -50 ºC. Next, Et_3N•3HF (3.0 equiv., 0.1 mL, 96 mg) was added, and the resulting reaction mixture was allowed to warm to room temperature during 3 hours. The resulting reaction mixture was filtered through a short plug of silica gel and washed with dichloromethane. Solvent was removed under *vacuum* and the resulting crude residue was analyzed by ^{19}F-NMR spectroscopy for the determination of the *branched:linear* ratio. Purification by flash chromatography on silica gel (hexane & ethyl acetate mixtures) provided the corresponding tertiary allylic fluoride compounds **3**.

Ethyl 3-fluoro-2-methylene-3-phenylbutanoate ((±)-3a)

[57] Dong, J. Y.; Wang, H.; Mao, S.; Wang, X.; Zhou, M. D.; Li, L. *Adv. Synth. Catal.* **2021**, *363*, 2133.
[58] Ramachandran, P. V.; Rudd, M. T.; Burghardt, T. E.; Ram Reddy, M. V. *J. Org. Chem.* **2003**, *68*, 9310.



Prepared according to general procedure C using α-methylstyrene **1a** (52 µL, 0.4 mmol, 0.2 equiv.), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (32 mg, 73% yield).

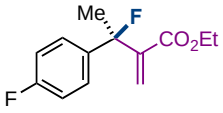
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.42 (m, 2H), 7.38 – 7.32 (m, 2H), 7.32 – 7.27 (m, 1H), 6.38 (dd, *J* = 4.3, 1.0 Hz, 1H), 6.12 (d, *J* = 1.0 Hz, 1H), 4.14 – 4.00 (m, 2H), 2.02 (d, *J* = 23.5 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 164.9 (d, *J* = 6.3 Hz), 144.0 (d, *J* = 25.2 Hz), 142.0 (d, *J* = 22.8 Hz), 128.2, 128.1 (d, *J* = 2.5Hz), 125.7 (d, *J* = 6.3 Hz), 124.8 (d, = 11.3 Hz), 95.9 (d, *J* = 173.9 Hz), 60.8, 25.8, (d, *J* = 23.9 Hz), 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -132.0 (qd, *J* = 23.5, 4.3 Hz).

HRMS (ESI): calculated for $C_{13}H_{15}O_2FNa^+$ $[M+Na]^+$ m/z: 245.0948, found: 245.0948.

Note: we have observed that this particular product is unstable in solution.

Gram-scale reaction: To a 100 mL oven-dried round bottom flask was added $Rh_2(esp)_2$ (50.0 mg, 0.07 mmol, 1.0 mol%). The tube was sealed before being evacuated and backfilled with argon three times. α-methyl styrene **1a** (14.2 mmol, 1.67 g, 2.0 equiv.) and degassed dichloromethane (10 mL) were added and the resulting mixture was cooled at -50 ºC. Then, a solution of reagent **2a** (4.2 g, 7.1 mmol, 1.0 equiv.) in degassed dichloromethane (50 mL) was added dropwise during 1 h using a syringe pump. After addition, the reaction mixture was stirred for 30 min at -50 ºC. Next, Et_3N•3HF (3.4 g, 3.0 equiv.) was added and the resulting reaction mixture was allowed to warm to room temperature during 3 hours. The resulting reaction mixture was quenched with aqueous solution of NH_3 (10%, 50 mL) and extracted with dichloromethane (3 x 30 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of solvent under *vacuum* and purification by flash column chromatography provided (±)-**3a** as colorless oil (1.3 g, 82% yield, *b*:*l* > 20:1).

Ethyl 3-fluoro-3-(4-fluorophenyl)-2-methylenebutanoate ((±)-3b)

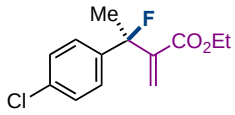


Prepared according to general procedure C using alkene **1b** (52 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (41 mg, 85% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.40 (m, 2H), 7.03 – 7.01 (m, 2H), 6.38 (dd, *J* = 4.5, 1.0 Hz, 1H), 6.13 (d, *J* = 1.0 Hz, 1H), 4.11 – 4.01 (m, 2H), 2.01 (d, *J* = 23.6 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 164.8 (d, *J* = 6.6 Hz), 162.6 (dd, *J* = 247.4, 2.7 Hz), 143.8 (d, *J* = 24.4 Hz), 137.9 (dd, *J* = 22.2, 3.2 Hz), 127.7 (dd, *J* = 8.3, 6.2 Hz), 124.8 (d, *J* = 12.0 Hz), 115.1 (d, *J* = 21.6 Hz), 95.5 (d, *J* = 174.2 Hz), 60.9, 25.8 (d, *J* = 24.8 Hz), 14.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.5 (m, 1H), -130.4 (m, 1H).

HRMS (ESI): calculated for $C_{13}H_{14}O_2F_2Na^+$ $[M+Na]^+$ m/z: 263.0854, found: 263.0849.

Ethyl 3-(4-chlorophenyl)-3-fluoro-2-methylenebutanoate ((±)-3c)

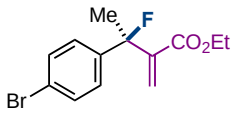


Prepared according to general procedure C using alkene **1c** (60 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 20/1) provided the title compound as colorless oil (45 mg, 87% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 2H), 7.35 – 7.28 (m, 2H), 6.39 (dd, *J* = 4.5, 0.9 Hz, 1H), 6.14 (d, *J* = 0.9 Hz, 1H), 4.07 (qd, *J* = 7.1, 3.2 Hz, 2H), 1.99 (d, *J* = 23.5 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.6 (d, *J* = 6.4 Hz), 143.5 (d, *J* = 24.2 Hz), 140.6 (d, *J* = 22.3 Hz), 134.0 (d, *J* = 2.8 Hz), 128.3, 127.2 (d, *J* = 6.6 Hz), 125.0 (d, *J* = 12.0 Hz), 95.4 (d, *J* = 174.8 Hz), 60.9, 25.7 (d, *J* = 24.7 Hz), 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -132.3 (qd, *J* = 23.5, 4.5 Hz).

HRMS (ESI): calculated for $C_{13}H_{14}ClFO_2Na^+$ $[M+Na]^+$ m/z: 279.0559, found: 279.0558.

Ethyl 3-(4-bromophenyl)-3-fluoro-2-methylenebutanoate ((±)-3d)

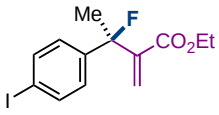


Prepared according to general procedure C using alkene **1d** (80 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 50/1) provided the title compound as colorless oil (43 mg, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.40 (m, 2H), 7.38 – 7.28 (m, 2H), 6.39 (dd, *J* = 4.4, 0.9 Hz, 1H), 6.13 (d, *J* = 0.9 Hz, 1H), 4.07 (qd, *J* = 7.1, 3.1 Hz, 2H), 1.98 (d, *J* = 23.5 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.7 (d, *J* = 6.8 Hz), 143.4 (d, *J* = 21.1 Hz), 141.2 (d, *J* = 22.1 Hz), 131.3, 127.5 (d, *J* = 6.6 Hz), 125.1 (d, *J* = 11.8 Hz), 122.3 (d, *J* = 2.9 Hz), 95.5 (d, *J* = 174.8 Hz), 61.0, 25.7 (d, *J* = 24.6 Hz), 14.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -132.7 (qd, *J* = 23.5, 4.4 Hz).

HRMS (ESI): calculated for $C_{13}H_{14}BrO_2FNa^+$ $[M+Na]^+$ m/z: 323.0053, found: 323.0050.

Ethyl 3-fluoro-3-(4-iodophenyl)-2-methylenebutanoate ((±)-3e)

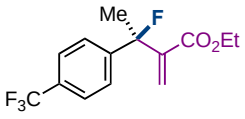


Prepared according to general procedure C using alkene **1e** (96 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (49 mg, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$ δ 7.70 – 7.63 (m, 2H), 7.21 – 7.14 (m, 2H), 6.39 (dd, *J* = 4.4, 0.9 Hz, 1H), 6.13 (d, *J* = 0.9 Hz, 1H), 4.07 (qd, *J* = 7.1, 3.0 Hz, 2H), 1.97 (d, J = 23.6 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.6 (d, *J* = 6.4 Hz), 143.4 (d, *J* = 24.2 Hz), 141.9 (d, *J* = 22.1 Hz), 137.3, 127.7 (d, *J* = 6.6 Hz), 125.1 (d, *J* = 11.8 Hz), 95.6 (d, *J* = 174.9 Hz), 94.0 (d, *J* = 3.2 Hz), 61.0, 25.7 (d, *J* = 24.7 Hz), 14.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -133.2 (qd, *J* = 23.6, 4.5 Hz).

HRMS (ESI): calculated for $C_{13}H_{14}O_2FINa^+$ $[M+Na]^+$ m/z: 370.9915, found: 370.9918.

Ethyl 3-fluoro-2-methylene-3-(4-(trifluoromethyl)phenyl)butanoate ((±)-3f)

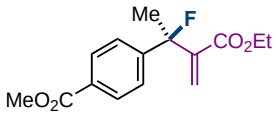


Prepared according to general procedure C using alkene **1f** (76 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless oil (43 mg, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.59 (m, 2H), 7.56 – 7.54 (m, 2H), 6.43 (d, *J* = 4.2 Hz, 1H), 6.17 (s, 1H), 4.13 – 4.01 (m, 2H), 2.01 (d, *J* = 23.6 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 164.6 (d, *J* = 6.1 Hz), 146.2 (d, *J* = 20.4 Hz), 143.2 (d, *J* = 23.8 Hz), 130.3 (qd *J* = 32.6, 2.2 Hz), 126.0 (d, *J* = 7.0 Hz), 125.5 (d, *J* = 11.6 Hz), 125.2 (q, *J* = 3.8 Hz), 124.2 (q, *J* = 271.9 Hz), 95.5 (d, 175.5 Hz), 61.0, 26.0 (d, *J* = 24.8 Hz), 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.7 (s, 3F), -134.7 (qd, *J* = 23.5, 4.2 Hz, 1F).

HRMS (ESI): calculated for $C_{14}H_{14}F_4O_2Na^+$ $[M+Na]^+$ m/z: 313.0822, found: 313.0825.

Methyl 4-(3-(ethoxycarbonyl)-2-fluorobut-3-en-2-yl)benzoate ((±)-3g)

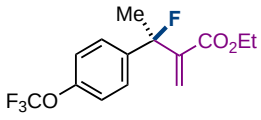


Prepared according to general procedure C using alkene **1g** (70 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 10/1) provided the title compound as colorless oil (40 mg, 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 8.00 (m, 2H), 7.51 – 7.49 (m, 2H), 6.42 (dd, *J* = 4.1, 0.8 Hz, 1H), 6.16 – 6.14 (m, 1H), 4.09 – 4.03 (m, 2H), 3.91 (s, 3H), 2.00 (d, *J* = 23.5 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.9, 164.6 (d, *J* = 5.8 Hz), 147.1 (d, *J* = 21.8 Hz), 143.3 (d, *J* = 23.9 Hz), 129.8 (d, *J* = 2.2 Hz), 129.5, 125.6 (d, *J* = 6.8 Hz), 125.5 (d, *J* = 11.4 Hz), 95.6 (d, *J* = 175.2 Hz), 61.0, 52.3, 26.0 (d, *J* = 24.8 Hz), 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -134.7 (qd, *J* = 23.5, 4.1 Hz).

HRMS (ESI): calculated for $C_{15}H_{17}O_4FNa^+$ $[M+Na]^+$ m/z: 303.1003, found: 303.1015.

Ethyl 3-fluoro-2-methylene-3-(4-(trifluoromethoxy)phenyl)butanoate ((±)-3h)

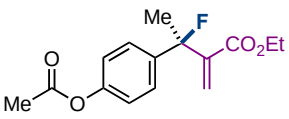


Prepared according to general procedure C using alkene **1h** (80 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 20/1) provided the title compound as colorless oil (41 mg, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.43 (m, 2H), 7.21 – 7.16 (m, 2H), 6.45 – 6.38 (m, 1H), 6.21 – 6.10 (m, 1H), 4.15 – 4.01 (m, 2H), 2.01 (d, *J* = 23.6 Hz, 3H), 1.15 (td, *J* = 7.1, 0.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.7 (d, *J* = 6.5 Hz), 149.0 (m), 143.5 (d *J* = 24.2 Hz), 140.8 (d, *J* = 22.4 Hz), 127.4 (d, *J* = 6.7 Hz), 125.1 (d, *J* = 11.9 Hz), 120.6 (q, *J* = 258.3 Hz), 120.5, 95.4 (d, *J* = 174.9 Hz), 61.0, 25.9 (d, *J* = 24.6 Hz), 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -58.9 (s, 3F), -132.2 (qd, *J* = 23.6, 4.5 Hz, 1F).

HRMS (ESI): calculated for $C_{14}H_{14}O_2F_4Na^+$ $[M+Na]^+$ m/z: 329.0770, found: 329.0771.

Ethyl 3-(4-acetoxyphenyl)-3-fluoro-2-methylenebutanoate ((±)-3i)

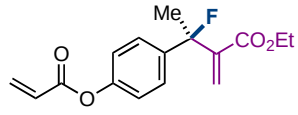


Prepared according to general procedure C using alkene **1i** (74 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 10/1) provided the title compound as colorless oil (44 mg, 78% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.37 (m, 2H), 7.10 – 7.03 (m, 2H), 6.38 (dd, *J* = 4.4, 1.0 Hz, 1H), 6.12 (d, *J* = 1.0 Hz, 1H), 4.07 (qd, *J* = 7.1, 3.6 Hz, 2H), 2.29 (s, 3H), 2.01 (d, *J* = 23.6 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.4, 164.8 (d, *J* = 6.5 Hz), 150.4 (d, *J* = 2.6 Hz), 143.7 (d, *J* = 24.4 Hz), 139.6 (d, *J* = 22.2 Hz), 127.0 (d, *J* = 6.7 Hz), 124.9 (d, *J* = 12.0 Hz), 121.2, 95.6 (d, *J* = 174.7), 60.1, 25.9 (d, *J* = 24.8 Hz), 21.3, 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -131.8 (qd, *J* = 23.6, 4.5 Hz).

HRMS (ESI): calculated for $C_{15}H_{17}OF_4Na^+$ $[M+Na]^+$ m/z: 303.1003, found: 303.0998.

Ethyl 3-(4-(acryloyloxy)phenyl)-3-fluoro-2-methylenebutanoate ((±)-3j)

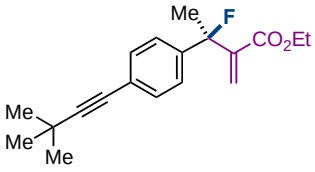


Prepared according to general procedure C using alkene **1j** (76 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 20/1) provided the title compound as colorless oil (48 mg, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 8.8, 1.1 Hz, 2H), 7.15 – 7.08 (m, 2H), 6.60 (dd, *J* = 17.3, 1.3 Hz, 1H), 6.38 (dd, *J* = 4.4, 1.0 Hz, 1H), 6.31 (dd, *J* = 17.3, 10.4 Hz, 1H), 6.13 (d, *J* = 1.0 Hz, 1H), 6.01 (dd, *J* = 10.4, 1.3 Hz, 1H), 4.14 – 4.00 (m, 2H), 2.01 (d, *J* = 23.6 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.8 (d, *J* = 6.6 Hz), 164.5, 150.3 (d, *J* = 2.6 Hz), 143.7 (d, *J* = 24.3 Hz), 139.7 (d, *J* = 22.3 Hz), 132.8, 128.0, 127.0 (d, *J* = 6.6 Hz), 125.0 (d, *J* = 11.9 Hz), 121.2, 95.6 (d, *J* = 169.1 Hz), 60.9, 25.9 (d, *J* = 24.7 Hz), 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -131.4 (qd, *J* = 23.6, 4.4 Hz).

HRMS (ESI): calculated for $C_{16}H_{17}O_4FNa^+$ $[M+Na]^+$ m/z: 315.1003, found: 315.0998.

Ethyl 3-(4-(3,3-dimethylbut-1-yn-1-yl)phenyl)-3-fluoro-2-methylenebutanoate ((±)-3k)

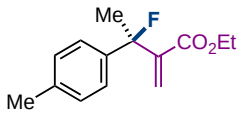


Prepared according to general procedure C using alkene **1k** (80 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (90 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless oil (38 mg, 63% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 4H), 6.37 (dd, *J* = 4.3, 1.0 Hz, 1H), 6.10 (d, *J* = 1.0 Hz, 1H), 4.11 – 3.99 (m, 2H), 1.99 (d, *J* = 23.5 Hz, 3H), 1.31 (s, 9H), 1.15 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.8 (d, *J* = 6.3 Hz), 143.7 (d, *J* = 24.3 Hz), 141.1 (d, *J* = 21.7 Hz), 131.4, 125.5 (d, *J* = 6.6 Hz), 124.9 (d, *J* = 11.7 Hz), 124.0 (d, *J* = 2.4 Hz), 99.1, 95.7 (d, *J* = 174.5 Hz), 78.8 (d, *J* = 1.4 Hz), 60.9, 31.1, 28.1, 25.7 (d, *J* = 24.8 Hz), 14.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -132.6 (qd, *J* = 23.5, 4.3 Hz).

HRMS (ESI): calculated for $C_{19}H_{23}O_2FNa^+$ $[M+Na]^+$ m/z: 325.1574, found: 325.1564.

Ethyl -3-fluoro-2-methylene-3-(p-tolyl)butanoate ((±)-3l)

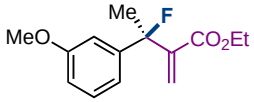


Prepared according to general procedure C using alkene **1l** (53 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless oil (15 mg, 30% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.18 – 7.12 (m, 2H), 6.36 (dd, *J* = 4.4, 1.1 Hz, 1H), 6.11 (d, *J* = 1.1 Hz, 1H), 4.12 – 4.03 (m, 2H), 2.33 (s, 3H), 2.00 (d, *J* = 23.5 Hz, 3H), 1.36 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.8 (d, *J* = 7.0 Hz), 144.0 (d, *J* = 24.8 Hz), 143.9 (d, *J* = 24.8 Hz), 137.8 (d, *J* = 2.4 Hz), 128.7, 125.5 (d, *J* = 6.2 Hz), 124.4 (d, *J* = 11.8 Hz), 95.8 (d, *J* = 173.8 Hz), 60.7, 25.6 (d, *J* = 24.7 Hz), 21.1, 13.9 (*peaks at 46.8, 29.7 and 8.6 are from inseparable impurities*); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -130.2 (q, *J* = 23.5 Hz).

HRMS (ESI): calculated for $C_{14}H_{17}O_2FNa^+$ $[M+Na]^+$ m/z: 259.1105, found: 259.1106.

Ethyl 3-fluoro-3-(3-methoxyphenyl)-2-methylenebutanoate ((±)-3n)

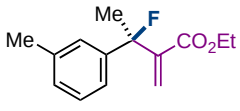


Prepared according to modified general procedure C using alkene **1n** (60 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). The addition of **2a** was carried out at -70 ºC instead of -50 ºC. Ratio of *branched*:*linear* isomers was determined to be 15:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 20/1) provided the title compound as colorless oil (35 mg, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 1H), 7.04 – 6.97 (m, 2H), 6.85 – 6.82 (m, 1H), 6.38 (dd, *J* = 4.1, 1.0 Hz, 1H), 6.10 (dd, *J* = 1.0, 0.5 Hz, 1H), 4.12 – 4.04 (m, 2H), 3.80 (s, 3H), 2.00 (d, *J* = 23.5 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.9 (d, *J* = 6.0 Hz), 159.5, 143.8 (d, *J* = 24.2 Hz), 143.7 (d, *J* = 21.8 Hz), 129.2, 124.9 (d, *J* = 11.6 Hz), 118.0 (d, *J* = 6.5 Hz), 113.4 (d, *J* = 2.1 Hz), 111.7 (d, *J* = 7.1 Hz), 95.8 (d, *J* = 174.7 Hz), 60.8, 55.4, 26.0 (d, *J* = 24.9 Hz), 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -132.4 (qd, *J* = 23.6, 4.1 Hz).

HRMS (ESI): calculated for $C_{14}H_{17}O_3FNa^+$ $[M+Na]^+$ m/z: 275.1054, found: 275.1050.

Ethyl 3-fluoro-2-methylene-3-(m-tolyl)butanoate ((±)-3o)



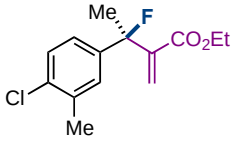
Prepared according to general procedure C using alkene **1o** (54 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless oil (47 mg, 87% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.22 (m, 3H), 7.12 – 7.09 (m, 1H), 6.37 (dd, *J* = 4.4, 1.1 Hz, 1H), 6.11 (d, *J* = 1.1 Hz, 1H), 4.13 – 4.01 (m, 2H), 2.35 (s, 3H), 2.00 (d, *J* = 23.6 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.9 (d, *J* = 6.3 Hz), 144.0 (d, *J* = 24.3 Hz), 141.9 (d *J* = 21.6 Hz), 137.8, 128.9 (d, *J* = 2.4 Hz), 128.1, 126.3 (d, *J* = 6.5 Hz), 124.8 (d, *J* = 11.8 Hz), 122.8 (d, *J* = 6.5 Hz),

95.9 (d, *J* = 173.9 Hz), 60.8, 25.9 (d, *J* = 24.9 Hz), 21.7, 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -131.6 (qd, *J* = 23.6, 4.4 Hz).

HRMS (ESI): calculated for $C_{14}H_{17}O_2FNa^+$ $[M+Na]^+$ m/z: 259.1105, found: 295.1104.

Ethyl 3-(4-acetoxyphenyl)-3-fluoro-2-methylenebutanoate ((±)-3p)

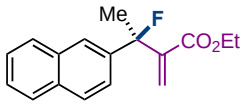


Prepared according to general procedure C using alkene **1p** (66 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless oil (40 mg, 74% yield).

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.32 – 7.30 (m, 2H), 7.21 – 7.18 (m, 1H), 6.38 (dd, *J* = 4.3, 0.9 Hz, 1H), 6.10 (d, *J* = 0.9 Hz, 1H), 4.10 – 4.01 (m, 2H), 2.37 (s, 3H), 1.96 (d, *J* = 23.6 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 164.9 (d, *J* = 6.3 Hz), 143.9 (d, *J* = 24.0 Hz), 141.1 (d, *J* = 21.9 Hz), 136.1, 134.3 (d, *J* = 2.8 Hz), 128.9, 128.6 (d, *J* = 6.5 Hz), 125.1 (d, *J* = 11.7 Hz), 124.9 (d, *J* = 6.3 Hz), 95.8 (d, *J* = 174.0 Hz), 61.2, 25.9 (d, *J* = 24.7 Hz), 20.3, 14.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -131.9 (qd, *J* = 23.6, 4.4 Hz).

HRMS (ESI): calculated for $C_{14}H_{16}O_2FClNa^+$ $[M+Na]^+$ m/z: 293.0715, found: 293.0704.

Ethyl 3-fluoro-2-methylene-3-(naphthalen-2-yl)butanoate ((±)-3q)



Prepared according to general procedure C using alkene **1q** (68 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless oil (41 mg, 76% yield).

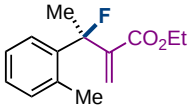
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 2.0 Hz, 1H), 7.89 – 7.78 (m, 3H), 7.54 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.52 – 7.44 (m, 2H), 6.43 (dd, *J* = 4.3, 1.1 Hz, 1H), 6.19 (d, *J* = 1.1 Hz, 1H), 4.04 (qd, *J* = 7.1, 4.0 Hz, 2H), 2.13 (d, *J* = 23.5 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.9 (d, *J* = 6.3 Hz), 143.9 (d, *J* = 24.2 Hz), 139.4 (d, *J* = 21.6 Hz), 133.1 (d, *J* = 1.7 Hz), 133.0, 128.5, 127.9, 127.7, 126.4 126.3, 125.0 (d, *J* = 11.8 Hz), 124.9 (d, *J* = 7.3 Hz), 123.7 (d, *J* = 6.1 Hz), 96.1 (d, *J* = 174.1 Hz), 60.9, 26.0 (d, *J* = 24.8 Hz), 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -132.0 (qd, *J* = 23.5, 4.3 Hz).

HRMS (ESI): calculated for $C_{17}H_{17}O_2FNa^+$ $[M+Na]^+$ m/z: 295.1105, found: 295.1113.

Ethyl 3-fluoro-2-methylene-3-(o-tolyl)butanoate ((±)3r) and Ethyl (*Z*)-2-(fluoromethyl)-3-(o-tolyl)but-2-enoate (3r')

Prepared according to general procedure C using alkene **1r** (54 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be 1:1.4 and ratio of *Z*:*E* isomers from the *linear* isomer was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided a mixture of the title compounds as colorless oil (38 mg, 77% yield). Separation of **(±)-3r** and **3r'** was achieved using a PLC plate.

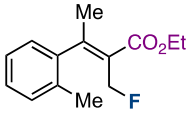
(±)-3r



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.42 (m, 1H), 7.24 – 7.16 (m, 2H), 7.15 – 7.09 (m, 1H), 6.34 (dd, *J* = 3.2, 1.0 Hz, 1H), 5.99 – 5.97 (m, 1H), 4.13 – 3.97 (m, 2H), 2.39 – 2.33 (m, 3H), 2.06 (d, *J* = 23.9 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.2 (d, *J* = 5.6 Hz), 143.8 (d, *J* = 23.2 Hz), 138.9 (d, *J* = 20.4 Hz), 136.8 (d, *J* = 1.5 Hz), 132.2 (d, *J* = 1.6 Hz), 128.4 (d, *J* = 1.8 Hz), 127.4 (d, *J* = 7.4 Hz), 125.4, 125.0 (d, *J* = 9.5 Hz), 97.0 (d, *J* = 174.2 Hz), 60.8, 27.5 (d, *J* = 25.6 Hz), 21.2 (d, *J* = 6.1 Hz), 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -136.5 (q, *J* = 23.9 Hz).

HRMS (ESI): calculated for $C_{14}H_{17}O_2FNa^+$ $[M+Na]^+$ m/z: 259.1105, found: 259.1096.

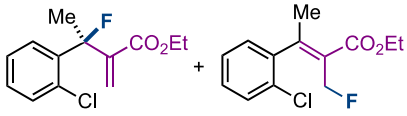
3r'



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.16 (m, 3H), 7.00 – 6.98 (m, 1H), 4.88 – 4.77 (m, 1H), 4.77 – 4.67 (m, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 2.38 – 2.32 (m, 3H), 2.21 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.2, 156.2 (d, *J* = 8.2 Hz), 141.4 (d, *J* = 2.7 Hz), 133.7 (d, *J* = 2.1 Hz), 130.5, 128.0, 126.7 (d, *J* = 2.5 Hz), 126.2, 126.1, 80.6 (d, *J* = 162.6 Hz), 60.9, 23.3 (d, *J* = 2.3 Hz), 19.3, 14.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -208.2 (tq, *J* = 47.1, 6.2 Hz); ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC, ^{1}H-^{1}H NOESY and ^{1}H-^{19}F HOESY spectra were measured.

HRMS (ESI): calculated for $C_{14}H_{17}O_2FNa^+$ $[M+Na]^+$ m/z: 259.1105, found: 259.1098.

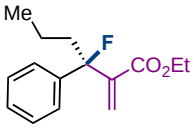
Ethyl 3-(2-chlorophenyl)-3-fluoro-2-methylenebutanoate ((±)-3s) and ethyl (*Z*)-3-(2-chlorophenyl)-2-(fluoromethyl)but-2-enoate (3s')



Prepared according to general procedure C using alkene **1s** (60 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be 1:1.3 and ratio of *Z*:*E* isomers from the *linear* isomer was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (40 mg, 79% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.9, 1.6 Hz, 1H*), 7.44 – 7.39 (m, 1H), 7.32 – 7.27 (m, 2H+1H*), 7.26 – 7.23 (m, 2H*), 7.18 – 7.13 (m, 1H), 6.53 (s, 1H*), 6.12 (dd, *J* = 3.0, 0.6 Hz, 1H*), 4.99 (dd, *J* = 10.2, 0.8 Hz, 1H), 4.93 (dd, *J* = 10.1, 0.8 Hz, 1H), 4.40 – 4.28 (m, 2H), 4.06 (q, *J* = 7.1 Hz, 2H*), 2.38 (d, *J* = 6.3 Hz, 3H), 2.04 (d, *J* = 23.7 Hz, 3H*), 1.37 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.9, 165.0* (d, *J* = 3.2 Hz), 153.3 (d, *J* = 8.4 Hz), 141.4 (d, *J* = 21.6 Hz), 140.4, 140.3*, 139.7* (d, *J* = 22.1 Hz), 131.3, 131.3*, 131.1*, 129.9, 129.2* (d, *J* = 1.5 Hz), 128.8 (d, J = 2.3 Hz), 128.2* (d, *J* = 2.3 Hz), 128.1 (d, *J* = 2.2 Hz), 127.1, 127.1* (d, *J* = 16.6 Hz), 126.7* (d, *J* = 1.8 Hz), 95.1* (d, *J* = 175.2 Hz), 80.4 (d, *J* = 163.7 Hz), 61.1, 60.8*, 25.9* (d, *J* = 25.4 Hz), 22.7 (d, *J* = 2.4 Hz), 14.4, 14.0*; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -208.0 (tq, *J* = 47.1, 6.2 Hz), -135.0* (qd, *J* = 23.7, 3.2 Hz); * *indicates the signals of the branched isomer*; ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC, ^{1}H-^{1}H NOE and ^{1}H-^{19}F HOESY spectra were measured.

HRMS (ESI): calculated for $C_{13}H_{14}ClFO_2Na^+$ $[M+Na]^+$ m/z: 279.0559, found: 279.0554.

Ethyl 3-fluoro-2-methylene-3-phenylhexanoate ((±)-3t)

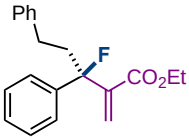


Prepared according to general procedure C using alkene **1t** (60 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be 15:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (38 mg, 75% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.42 (m, 2H), 7.38 – 7.20 (m, 2H), 7.30 – 7.24 (m, 1H), 6.36 (dd, *J* = 4.9, 1.1 Hz, 1H), 6.10 (d, *J* = 1.1 Hz, 1H), 4.14 – 4.02 (m, 2H), 2.62 – 2.41 (m, 1H), 2.35 – 2.17 (m, 1H), 1.51 – 1.28 (m, 2H), 1.16 (t, *J* = 7.1 Hz, 3H), 1.02 – 0.92 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.0 (d, *J* = 7.7 Hz), 143.0 (d, *J* = 25.2 Hz), 142.0 (d, *J* = 22.2 Hz), 128.1, 127.9 (d, *J* = 2.1 Hz), 125.9 (d, *J* = 7.4 Hz), 125.0 (d, *J* = 12.9 Hz), 98.6 (d, *J* = 179.3 Hz), 60.8, 39.2 (d, *J* = 22.6 Hz), 17.0 (d, *J* = 3.7 Hz), 14.4, 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -142.7 (ddd, *J* = 34.9, 22.5, 5.0 Hz).

HRMS (ESI): calculated for $C_{15}H_{19}O_2FNa^+$ $[M+Na]^+$ m/z: 273.1261, found: 273.1270.

Ethyl 3-fluoro-2-methylene-3,5-diphenylpentanoate ((±)-3u)

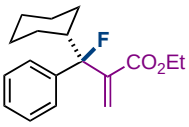


Prepared according to general procedure C using alkene **1u** (83 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be 10:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (43 mg, 69% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.48 (m, 2H), 7.38 – 7.33 (m, 2H), 7.32 – 7.27 (m, 3H), 7.21 – 7.18 (m, 3H), 6.42 (dd, *J* = 1H), 6.18 (d, *J* = 1H), 4.16 – 4.03 (m, 2H), 2.99 – 2.83 (m, 1H), 2.75 – 2.52 (m, 3H), 1.19 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.9 (d, *J* = 7.6 Hz), 142.4 (d, *J* = 24.8 Hz), 141.9, 141.2 (d, *J* = 22.1 Hz), 128.6, 128.6, 128.2, 128.1 (d, *J* = 2.0 Hz), 126.1, 125.9 (d, *J* = 7.5 Hz), 125.4 (d, *J* = 13.1 Hz), 97.7 (d, *J* = 178.7 Hz), 60.9, 39.2 (d, *J* = 22.3 Hz), 30.1 (d, *J* = 4.0 Hz), 14.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -144.9 (ddd, *J* = 30.1, 19.4, 5.1 Hz).

HRMS (ESI): calculated for $C_{20}H_{21}O_2FNa^+$ $[M+Na]^+$ m/z: 335.1418, found: 335.1414.

Ethyl 2-(cyclohexylfluoro(phenyl)methyl)acrylate ((±)-3v)

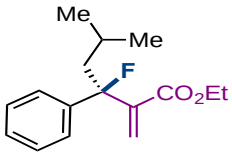


Prepared according to general procedure C using alkene **1v** (75 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be 11:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (24 mg, 42% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 – 7.43 (m, 2H), 7.38 – 7.28 (m, 2H), 7.26 – 7.21 (m, 1H), 6.21 (dd, *J* = 6.4, 1.2 Hz, 1H), 6.10 – 6.05 (m, 1H), 4.16 – 4.05 (m, 2H), 2.82 – 2.70 (m, 1H), 1.86 – 1.77 (m, 1H), 1.76 – 1.61 (m, 3H), 1.55 – 1.48 (m, 1H), 1.38 – 1.24 (m, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.19 – 1.05 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.2 (d, *J* = 8.8 Hz), 143.0 (d, *J* = 25.9 Hz), 141.0 (d, *J* = 23.2 Hz), 128.0 (d, *J* = 1.2 Hz), 127.4 (d, *J* = 1.3 Hz), 125.9 (d, *J* = 9.9 Hz), 124.1 (d, *J* = 15.4 Hz), 100.3 (d, *J* = 183.6 Hz), 60.8, 42.1 (d, *J* = 20.6 Hz), 27.3 (d, *J* = 2.0 Hz), 26.7, 26.7, 26.6, 26.5, 14.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -162.7 (dd, *J* = 32.8, 6.6 Hz).

HRMS (ESI): calculated for $C_{18}H_{23}O_2FNa^+$ $[M+Na]^+$ m/z: 313.1574, found: 313.1586.

Ethyl 3-fluoro-6-methyl-2-methylene-3-phenylheptanoate ((±)-3w)



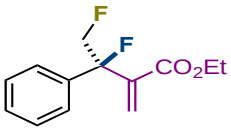
Prepared according to general procedure C using alkene **1w** (68 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be 7:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (34 mg, 67% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.41 (m, 2H), 7.38 – 7.22 (m, 3H), 6.37 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.13 (d, *J* = 1.2 Hz, 1H), 4.13 – 4.02 (m, 2H), 2.54 (ddd, *J* = 34.7, 14.7, 5.3 Hz, 1H), 2.22 – 2.08 (m, 1H), 1.83 – 1.70 (m, 1H), 1.18 (t, *J* = 7.1 Hz, 3H), 0.99 – 0.90 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.1 (d, *J* = 7.7 Hz), 143.0 (d, *J* = 25.2 Hz), 142.0 (d, *J* = 22.2 Hz), 128.1, 127.9 (d, *J* = 2.1 Hz), 125.9 (d, *J* = 7.4 Hz), 125.0 (d, *J* = 12.9 Hz), 98.6 (d, *J* = 179.2 Hz), 60.8, 45.2 (d, *J* = 21.1 Hz), 24.6, 24.4 (d, *J* = 1.6 Hz), 24.0 (d, *J* = 2.5 Hz), 14.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -142.4 (ddd, *J* = 31.0, 21.1, 4.9 Hz).

HRMS (ESI): calculated for $C_{16}H_{21}O_2FNa^+$ $[M+Na]^+$ m/z: 287.1418, found: 287.1408.

Ethyl 3,4-difluoro-2-methylene-3-phenylbutanoate ((±)-3x)

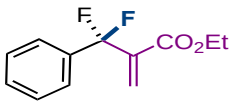
Prepared according to general procedure C using alkene **1x** (54 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be 14:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (29 mg, 60% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.40 (m, 2H), 7.40 – 7.32 (m, 3H), 6.55 (dd, *J* = 4.5, 0.7 Hz, 1H), 6.25 (d, *J* = 0.8 Hz, 1H), 5.35 – 5.13 (m, 1H), 5.12 – 4.94 (m, 1H), 4.19 – 4.07 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.7 (d, *J* = 6.7 Hz), 138.9 (dd, *J* = 24.4, 3.2 Hz), 137.3 (dd, *J* = 11.0, 4.0 Hz), 129.0 (d, *J* = 2.2 Hz), 128.5, 128.3 (d, *J* = 12.9 Hz), 125.9 (d, *J* = 7.1 Hz), 96.5 (dd, *J* = 181.4, 18.7 Hz), 84.7 (dd, *J* = 181.9, 23.7 Hz), 61.2, 14.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -150.2 (m, 1F), -226.3 (td, *J* = 47.1, 15.6 Hz, 1F).

HRMS (ESI): calculated for $C_{13}H_{14}O_2F_2Na^+$ $[M+Na]^+$ m/z: 263.0854, found: 263.0855.

Ethyl 2-(difluoro(phenyl)methyl)acrylate (3y)

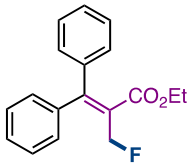


Prepared according to general procedure C using alkene **1y** (48 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless oil (37 mg, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.48 (m, 2H), 7.41 (dd, *J* = 5.3, 1.9 Hz, 3H), 6.63 (q, *J* = 0.8 Hz, 1H), 6.36 (q, *J* = 0.8 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 1.17 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.1 (t, *J* = 2.6 Hz), 137.7 (t, *J* = 28.1 Hz), 136.2 (t, *J* = 27.0 Hz), 130.1 (t, *J* = 0.4 Hz), 129.9 (t, *J* = 7.6 Hz), 128.3, 125.7 (t, *J* = 5.8 Hz), 118.4 (t, *J* = 243.7 Hz), 61.3, 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -93.0 (s, 2F).

HRMS (ESI): calculated for $C_{12}H_{12}O_2F_2Na^+$ [M+Na]$^+$ m/z: 249.0698, found: 249.0689.

Ethyl 2-(fluoromethyl)-3,3-diphenylacrylate (3z)

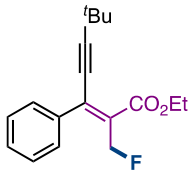


Prepared according to general procedure C using alkene **1z** (74 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et$_3$N•3HF (96 mg, 0.6 mmol). The addition of **2a** was carried out at -70 ºC instead of -50 ºC. Ratio of *branched*:*linear* isomers was determined to be 1:15 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as yellowish oil (46 mg, 79% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 5.1, 1.8 Hz, 3H), 7.35 – 7.30 (m, 4H), 7.29 – 7.26 (m, 1H), 7.17 – 7.11 (m, 2H), 5.11 (d, *J* = 47.7 Hz, 2H), 3.99 (q, *J* = 7.1 Hz, 2H), 0.89 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.1, 155.5 (d, *J* = 8.7 Hz), 141.6 (d, *J* = 2.2 Hz), 139.6 (d, *J* = 2.8 Hz), 129.9 (d, J = 2.8 Hz) 129.2, 128.9 (d, *J* = 2.7 Hz), 128.6, 128.4, 128.2, 127.3, 82.0 (d, *J* = 163.0 Hz), 61.1, 13.6; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -203.8 (t, *J* = 47.7 Hz).

HRMS (ESI): calculated for $C_{18}H_{17}O_2F_2Na^+$ [M+Na]$^+$ m/z: 307.1105, found: 307.1106.

(*E*)-Ethyl-2-(fluoromethyl)-6,6-dimethyl-3-phenylhept-2-en-4-ynoate (3aa)

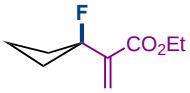


Prepared according to general procedure C using Enynes **1aa** (74 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et$_3$N•3HF (96 mg, 0.6 mmol). Ratio of *linear*:*branched* isomers was determined to be > 20:1 and ratio of *Z*:*E* isomers in the *linear* isomer was determined to be 1:5 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as yellowish oil (46 mg, 82%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.38 (m, 5H), 5.03 (d, *J* = 47.3 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.28 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.8 (d, *J* = 1.0 Hz), 138.0 (d, *J* = 2.9 Hz), 137.8 (d, *J* = 8.9 Hz), 129.1, 128.9, 128.9, 128.3, 112.3 (d, *J* = 4.1 Hz), 79.7 (d, *J* = 163.4 Hz), 79.2 (d, *J* = 4.7 Hz), 61.2, 30.6, 30.5, 14.3; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -203.0 (t, *J* = 47.3 Hz).

HRMS (ESI): calculated for $C_{18}H_{21}O_2FNa^+$ [M+Na]$^+$ m/z: 311.1423, found: 311.1421.

Ethyl 2-(1-fluorocyclobutyl)acrylate (3ab)

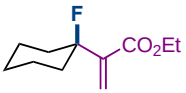


Prepared according to general procedure C using alkene **1ab** (30 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et$_3$N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 50/1) provided the title compound as colorless oil (26 mg, 66% yield).

^{1}H NMR (400 MHz, CDCl3) δ 6.32 (d, *J* = 0.9 Hz, 1H), 5.86 (dd, *J* = 3.4, 0.9 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 2.61 – 2.41 (m, 4H), 2.06 – 1.95 (m, 1H), 1.73 – 1.61 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.4 (d, *J* = 2.3 Hz), 140.5 (d, *J* = 22.7 Hz), 125.4 (d, *J* = 8.7 Hz), 96.7 (d, *J* = 204.1 Hz), 60.9, 33.6 (d, *J* = 23.2 Hz), 14.3, 13.0 (d, *J* = 7.4 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -131.6 (m).

HRMS (ESI): calculated for $C_9H_{13}O_2FNa^+$ [M+Na]$^+$ m/z: 195.0792, found: 195.0788.

Ethyl-2-(1-fluorocyclohexyl) acrylate (3ac)

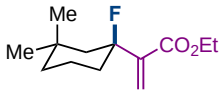


Prepared according to general procedure C using alkene **1ac** (39 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (35 mg, 88% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.18 (dd, *J* = 6.0, 1.3 Hz, 1H), 5.93 (d, *J* = 1.3 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 2.08 (dddd, *J* = 44.8, 14.0, 12.6, 5.8 Hz, 2H), 1.79 – 1.61 (m, 7H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.27 – 1.24 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.7 (d, *J* = 8.4 Hz), 144.8 (d, *J* = 21.8 Hz), 123.9 (d, *J* = 14.9 Hz), 95.8 (d, *J* = 175.6 Hz), 60.8, 34.3 (d, *J* = 22.6 Hz), 24.7, 21.7 (d, *J* = 1.7 Hz), 14.3; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -155.6 (m).

HRMS (ESI): calculated for $C_{11}H_{17}O_2FNa^+$ $[M+Na]^+$ m/z: 223.1092, found: 223.1100.

Ethyl 2-(1-fluoro-3,3-dimethylcyclohexyl)acrylate ((±)-3ad)

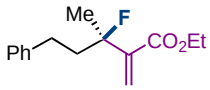


Prepared according to general procedure C using alkene **1ad** (39 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (35 mg, 73% yield).

^{1}H NMR (400 MHz, CDCl3) δ 6.20 (dd, *J* = 6.4, 1.3 Hz, 1H), 5.96 (dd, *J* = 1.3, 0.6 Hz, 1H), 4.28 – 4.17 (m, 2H), 2.17 – 1.89 (m, 2H), 1.87 – 1.71 (m, 2H), 1.68 – 1.51 (m, 3H), 1.51 – 1.43 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.08 (d, *J* = 2.2 Hz, 3H), 0.95 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.8 (d, *J* = 6.8 Hz), 144.8 (d, *J* = 18.0 Hz), 124.1 (d, *J* = 12.5 Hz), 97.1 (d, *J* = 143.2 Hz), 60.8, 45.7 (d, *J* = 16.9 Hz), 38.0, 34.2, 34.0 (d, *J* = 18.6), 30.7 (d, *J* = 1.3 Hz), 26.7 (d, *J* = 5.1 Hz), 18.3, 14.2; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -155.6 (m).

HRMS (ESI): calculated for $C_{13}H_{21}O_2FNa^+$ $[M+Na]^+$ m/z: 251.1418, found: 251.1420.

Ethyl 3-fluoro-3-methyl 2-methylene-5-phenylpentanoate ((±)-3ae)

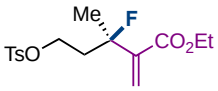


Prepared according to general procedure C using alkene **1ae** (59 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless oil (29 mg, 58% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 2H), 7.20 – 7.16 (m, 3H), 6.33 (dd, *J* = 6.4, 1.4 Hz, 1H), 6.04 – 6.02 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.79 – 2.63 (m, 1H), 2.57 – 2.47 (m, 1H), 2.47 – 2.31 (m, 1H), 2.26 – 2.08 (m, 1H), 1.64 (d, *J* = 23.2 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.3 (d, *J* = 9.8 Hz), 142.8 (d, *J* = 22.3 Hz), 142.0, 128.5, 128.5, 125.9, 125.0 (d, *J* = 15.1 Hz), 96.9 (d, *J* = 176.5 Hz), 60.9, 40.8 (d, *J* = 22.4 Hz), 30.2 (d, *J* = 3.3 Hz), 26.3 (d, *J* = 24.3 Hz), 14.3; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -144.9 (m).

HRMS (ESI): calculated for $C_{15}H_{19}O_2FNa^+$ $[M+Na]^+$ m/z: 273.1261, found: 273.1265.

Ethyl 3-fluoro-3-mEthyl 2-methylene-5-(tosyloxy)pentanoate ((±)-3af)

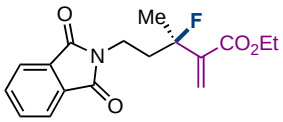


Prepared according to general procedure C using alkene **1af** (96 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be 14:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 15/1) provided the title compound as colorless oil (35 mg, 51% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.74 (m, 2H), 7.35 – 7.26 (m, 2H), 6.22 (dd, *J* = 6.6, 1.2 Hz, 1H), 5.86 – 5.84 (m, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 4.13 – 3.96 (m, 2H), 2.71 – 2.46 (m, 1H), 2.45 (s, 3H), 2.17 – 2.12 (m, 1H), 1.58 (d, *J* = 23.4 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.8 (d, *J* = 9.6 Hz), 144.8, 141.7 (d, *J* = 21.8), 133.1, 129.8, 128.1, 125.2, (d, *J* = 15.1Hz), 95.2 (d, *J* = 177.0 Hz), 66.0 (d, *J* = 3.8 Hz), 61.2, 37.7 (d = 21.9 Hz), 26.6 (d, *J* = 23.9 Hz), 21.8, 14.2; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -144.7 (m).

HRMS (ESI): calculated for $C_{16}H_{21}O_5SFNa^+$ $[M+Na]^+$ m/z: 367.0986, found: 367.0987.

Ethyl 5-(1,3-dioxoisoindolin-2-yl)-3-fluoro-3-methyl-2-methylenepentanoate ((±)-3ag)

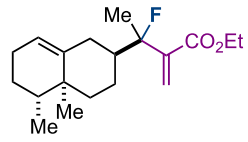


Prepared according to general procedure C using alkene **1ag** (86 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be 14:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 5/1) provided the title compound as colorless oil (27 mg, 41% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.73 – 7.65 (m, 2H), 6.32 (dd, *J* = 6.5, 1.2 Hz, 1H), 6.04 – 6.02 (m, 1H), 4.22 – 4.09 (m, 2H), 3.81 – 3.63 (m, 2H), 2.63 – 2.47 (m, 1H), 2.33 – 2.22 (m, 1H), 1.64 (d, *J* = 23.3 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.2, 165.0 (d, *J* = 9.7 Hz), 141.7 (d, *J* = 23.1 Hz), 134.0, 132.3, 125.8 (d, *J* = 15.2 Hz), 123.3, 96.0 (d, *J* = 176.8 Hz), 61.0, 36.9 (d, *J* = 21.7 Hz), 33.5 (d, *J* = 4.3 Hz), 26.4 (d, *J* = 23.9 Hz), 14.2; **^{19}F NMR** (376 MHz, CDCl3) δ -146.3 (m) .

HRMS (ESI): calculated for $C_{17}H_{18}FNO_4Na^+$ $[M+Na]^+$ m/z: 342.1112, found: 342.1125.

Ethyl 3-((2*R*,8*R*,8a*S*)-8,8a-dimethyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-2-yl)-3-fluoro-2-methylenebutanoate (3ah)

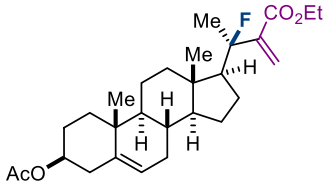


Prepared according to the modified general procedure C using valencene **1ah** (82 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). The addition of **2a** was carried out at -70 ºC instead of -50 ºC. Ratio of *branched*:*linear* isomers was determined to be > 20:1 and the ratio of *diastereoisomers* was determined to be 1.6:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless oil (35 mg, 53% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.25 – 6.21 (m, 1H), 5.94 – 5.86 (m, 1H), 5.32 – 5.29 (m, 1H), 4.29 – 4.14 (m, 2H), 2.36 – 2.16 (m, 2H), 2.15 – 1.88 (m, 4H), 1.64 – 1.51 (m, 5H), 1.45 – 1.36 (m, 3H), 1.35 – 1.18 (m, 4H), 1.13 – 0.95 (m, 1H), 0.95 – 0.82 (m, 5H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.6* (d, *J* = 9.7 Hz) 165.6 (d, *J* = 9.6 Hz), 147.8* (d, *J* = 22.6 Hz), 143.5 (d, *J* = 22.8 Hz), 142.9, 142.9*, 124.5 (d, *J* = 15.3 Hz), 124.2* (d, *J* = 15.3 Hz), 120.2*, 120.2, 98.7 (d, *J* = 179.6 Hz), 98.6* (d, *J* = 180.0 Hz), 60.9*, 60.8, 41.2, 41.0*, 40.2, 40.2*, 39.1* (d, *J* = 24.8 Hz), 38.9 (d, *J* = 21.3 Hz), 39.0*, 37.7, 37.6*, 32.5, 28.7 (d, *J* = 2.7 Hz), 27.4* (d, *J* = 3.8 Hz), 27.4, 27.3*, 26.0, 26.0*, 23.9* (d, *J* = 25.0 Hz), 23.6 (d, *J* = 24.6 Hz), 18.6, 18.3*, 15.9, 15.8*, 14.3*, 14.3; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -156.6 (m), -157.6 (m)*; * *indicates the signals of the minor diastereoisomer*.

HRMS (ESI): calculated for $C_{19}H_{29}FO_2Na^+$ $[M+Na]^+$ m/z: 331.2044, found: 331.2032.

Ethyl 3-((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-acetoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl)-3-fluoro-2-methylenebutanoate (3ai)



Prepared according to general procedure C using alkene **1ai** (142 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless solid (35 mg, 38% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.14 (dd, *J* = 7.4, 1.5 Hz, 1H), 5.85 (t, *J* = 1.4 Hz, 1H), 5.36 (dt, *J* = 3.9, 1.6 Hz, 1H), 4.65 – 4.56 (m, 1H), 4.22 – 4.14 (m, 2H), 2.34 – 2.29 (m, 2H), 2.18 – 2.06 (m, 2H), 2.02 (s, 3H), 1.98 – 1.92 (m, 1H), 1.86 (dt, *J* = 12.7, 3.1 Hz, 2H), 1.72 (s, 3H), 1.66 – 1.58 (m, 2H), 1.58 – 1.47 (m, 5H), 1.41 – 1.33 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.17 – 1.05 (m, 3H), 1.02 (s, 3H), 0.99 – 0.93 (m, 1H), 0.87 (d, *J* = 4.2 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.6, 165.6 (d, *J* = 9.7 Hz), 144.7 (d, *J* = 22.3 Hz), 139.8, 123.3 (d, *J* = 16.7 Hz), 122.6, 98.2 (d, *J* = 182.9 Hz), 74.1, 60.8, 57.1, 54.1 (d, *J* = 20.1 Hz), 50.1, 42.7, 39.9, 38.2, 37.1, 36.7, 31.8, 31.5, 27.9, 25.4 (d, *J* = 25.0 Hz), 23.6, 23.0 (d, *J* = 4.2 Hz), 21.6, 21.0, 19.4, 14.2, 13.2 (d, *J* = 6.0 Hz); **^{19}F NMR** (471 MHz, $CDCl_3$) δ -153.4 (m).

HRMS (ESI): calculated for $C_{28}H_{41}O_4FNa^+$ $[M+Na]^+$ m/z: 483.2881, found: 483.2877.

$[\alpha]^{25}_D$ = -64.0 (*c* = 0.11, $CHCl_3$).

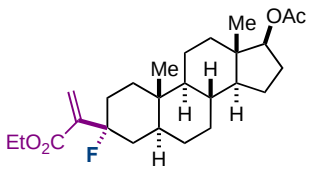
m.p. 111-113 ºC.

The crystal structure of the title compound has been deposited at the Cambridge Crystallographic Data Centre, CCDC No. 2092729.

Ethyl 2-((3*R,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*,17*S*)-17-acetoxy-3-fluoro-10,13-imethylhexadecahydro-1H-cyclopenta[a]phenanthren-3-yl)acrylate (3aj)**

Prepared according to general procedure C using alkene **1aj** (132 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (90 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 and the ratio of *diastereoisomers* was determined to be 1:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless oil (39 mg, 45% yield).

(3*R*)-3aj



^{1}H NMR (500 MHz, $CDCl_3$) δ 6.30 – 6.20 (m, 1H), 5.98 (s, 1H), 4.59 (t, *J* = 8.5 Hz, 1H), 4.21 (q, *J* = 6.9 Hz, 2H), 2.40 – 2.20 (m, 1H), 2.20 – 2.07 (m, 2H), 2.03 (s, 3H), 1.78 – 1.61 (m, 4H), 1.58 – 1.53 (m, 2H), 1.52 – 1.38 (m, 3H), 1.38 – 1.11 (m, 10H), 1.10 – 1.01 (m, 1H), 0.90 (d, *J* = 6.2 Hz, 4H), 0.79 (d, *J* = 5.8 Hz, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$), 171.2, 165.7 (d, *J* = 8.9 Hz), 144.2 (d, *J* = 21.8 Hz), 124.4 (d, *J* = 15.4 Hz), 96.3 (d, *J* = 176.7 Hz), 83.0, 60.9, 53.9, 50.9, 42.8, 41.0, 37.5 (d, *J* = 22.4 Hz), 37.1, 35.5, 33.9, 31.6, 30.6 (d, *J* = 23.2 Hz), 28.2, 27.7, 23.6, 21.3, 20.6, 14.3, 12.3, 11.4, 11.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -150.7 (m). ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC, ^{1}H-^{19}F HOESY were measured.

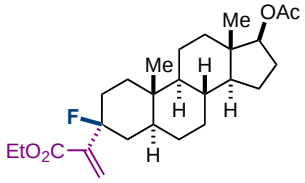
HRMS (ESI): calculated for $C_{26}H_{39}O_4FNa^+$ $[M+Na]^+$ m/z: 457.2725, found: 457.2730.

$[\alpha]^{25}_D$ = +3.65 (*c* = 0.10, $CHCl_3$).

m.p. 118 – 120 ºC.

The crystal structure of title compound has been deposited at the Cambridge Crystallographic Data Centre, CCDC No. 2092730.

(3*S*)-3aj

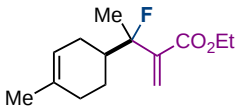


^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (d, *J* = 1.1 Hz, 1H), 5.88 (d, *J* = 4.5 Hz, 1H), 4.57 (dd, *J* = 9.2, 7.8 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.40 – 2.29 (m, 1H), 2.25 – 2.18 (m, 1H), 2.17 – 2.09 (m, 1H), 2.03 (s, 3H), 1.98 – 1.89 (m, 1H), 1.84 – 1.58 (m, 6H), 1.51 – 1.44 (m, 2H), 1.44 – 1.37 (m, 1H), 1.31 (t, *J* = 7.1 Hz, 5H), 1.27 – 1.22 (m, 2H), 1.16 – 0.92 (m, 5H), 0.90 (s, 3H), 0.78 – 0.76 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 166.4, 141.3 (d, *J* = 22.0 Hz), 127.1 (d, *J* = 7.2 Hz), 95.2 (d, *J* = 170.1 Hz), 82.9, 61.0, 54.5 (d, *J* = 2.4 Hz), 50.9, 43.8 (d, *J* = 8.7 Hz), 42.8, 37.2 (d, *J* = 20.6 Hz), 37.0, 36.9, 36.1 (d, *J* = 1.6 Hz), 35.3, 31.6, 31.1 (d, *J* = 21.4 Hz), 28.4, 27.7, 23.6, 21.3, 20.9, 14.3, 12.4, 12.3; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -122.8 (m); .

HRMS (ESI): calculated for $C_{26}H_{39}O_4FNa^+$ $[M+Na]^+$ m/z: 457.2725, found: 457.2730.

$[\alpha]^{25}_D$ = +13.44 (c = 0.185, $CHCl_3$).

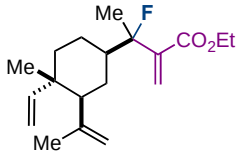
Ethyl 3-fluoro-3-(4-methylcyclohex-3-en-1-yl)-2-methylenebutanoate (3ak)



Prepared according to general procedure C using alkene **1ak** (55 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (90 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 and the ratio of *diastereoisomers* was determined to be 1.1:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless oil (31 mg, 58% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.28 – 6.23 (m, 1H), 5.91 (dt, *J* = 2.7, 1.1 Hz, 1H), 5.44 – 5.27 (m, 1H), 4.23 – 4.16 (m, 2H), 2.26 – 1.80 (m, 5H), 1.64 – 1.61 (m, 3H), 1.60 – 1.54 (m, 3H), 1.48 – 1.32 (m, 1H), 1.32 – 1.28 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.6 (d, *J* = 9.4 Hz), 165.4 (d, *J* = 9.6 Hz), 143.5 (d, *J* = 22.4 Hz), 143.3 (d, *J* = 22.5 Hz), 134.0, 133.8, 124.7 (d, *J* = 15.5 Hz), 124.4 (d, 15.7 Hz), 120.6, 120.4, 98.5 (d, *J* = 179.6Hz), 98.1 (d, *J* = 180.3 Hz), 60.9, 39.4 (d, *J* = 21.7 Hz), 39.3 (d, *J* = 21.5 Hz), 30.9, 30.8, 26.7 (d, *J* = 2.7 Hz), 25.5 (d, *J* = 3.8 Hz), 23.9, 23.6, 23.6, 23.4, 23.4, 23.4, 22.7, 22.6, 14.3, 14.3; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -156.9 (m), -158.2 (m).

HRMS (ESI): calculated for $C_{14}H_{21}O_2FNa^+$ $[M+Na]^+$ m/z: 263.1418, found: 263.1414.

Ethyl 3-fluoro-3-((1*R*,3*S*,4*S*)-4-methyl-3-(prop-1-en-2-yl)-4-vinylcyclohexyl)-2-methylenebutanoate (3al)



Prepared according to the modified general procedure C using β-elemene **1al** (82 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 and the ratio of *diastereoisomers* was determined to be 1.3:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (37 mg, 57% yield).

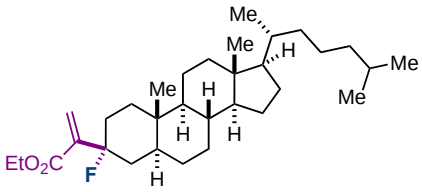
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.27 – 6.25 (m, 1H), 5.93 – 5.91 (m, 1H), 5.83 – 5.72 (m, 1H), 4.91 – 4.89 (m, 1H), 4.87 – 4.86 (m, 1H), 4.84 – 4.78 (m, 1H), 4.53 – 4.55 (m, 1H), 4.26 – 4.17 (m, 2H), 2.12 – 2.02 (m, 1H), 2.00 – 1.89 (m, 1H), 1.74 – 1.72 (m, 2H), 1.68 – 1.64 (m, 2H), 1.61 (d, *J* = 1.4 Hz, 2H), 1.57 – 1.51 (m, 2H), 1.49 – 1.36 (m, 3H), 1.34 – 1.28 (m, 4H), 0.97 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.5 (d, *J* = 9.8 Hz), 165.4 (d, *J* = 9.8 Hz), 150.3, 150.2, 148.0, 147.9, 124.7 (d, *J* = 15.7 Hz), 124.5 (d, *J* = 15.6 Hz), 112.3, 112.2, 110.1 (2C), 98.5 (2C) (d, *J* = 180.0 Hz), 60.9 (2C), 52.7, 52.5, 43.2 (d, *J* = 21.3 Hz), 43.9 (d, *J* = 21.3 Hz), 39.7, 39.7, 39.7, 39.7, 28.1, 28.1, 27.1, 27.0, 24.9, 24.9, 23.8, 23.6, 22.4 (d, *J* = 3.1 Hz), 21.2 (d, *J* = 3.6 Hz), 16.5, 16.5, 14.3, 14.3; **^{19}F[^{1}H] NMR** (376 MHz, $CDCl_3$) δ -156.4, -157.5; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -156.5 (m, 2F); ^{1}H-^{13}C HSQC and ^{1}H-^{13}C HMBC were performed.

HRMS (ESI): calculated for $C_{19}H_{29}O_2FNa^+$ $[M+Na]^+$ m/z: 331.2044, found: 331.2043.

Ethyl 2-((3*R,8*R*,10*S*,13*R*,17*R*)-3-fluoro-10,13-dimethyl-17-((*R*)-5-methylhexan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthren-3-yl)acrylate (3am)**

Prepared according to general procedure C using alkene **1am** (153 mg, 0.4 mmol), reagent **2b** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Due to the poor solubility of starting alkene, 10 mL of CH_2Cl_2 was employed to dissolve rhodium catalyst and alkene. Ratio of *branched*:*linear* isomers was determined to be > 20:1 and the ratio of *diastereoisomers* was determined to be 1:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compounds as white solid (37 mg, 41% yield).

(3*R*)-3am

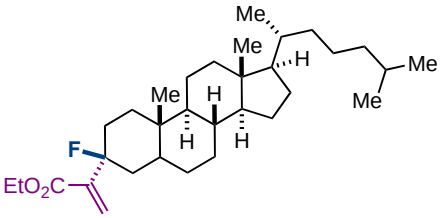


^{1}H NMR (400 MHz, $CDCl_3$) δ 6.21 (dd, *J* = 6.5, 1.5 Hz, 1H), 5.97 (d, *J* = 1.4 Hz, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 2.37 – 2.21 (m, 1H), 2.19 – 2.04 (m, 1H), 1.97 (dt, *J* = 12.7, 3.5 Hz, 1H), 1.84 – 1.77 (m, 1H), 1.68 – 1.58 (m, 3H), 1.54 – 1.48 (m, 3H), 1.39 – 1.30 (m, 10H), 1.26 – 1.20 (m, 4H), 1.15 – 1.09 (m, 6H), 1.04 – 0.97 (m, 3H), 0.92 – 0.85 (m, 13H), 0.66 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.8 (d, *J* = 8.9 Hz), 144.3 (d, *J* = 22.0 Hz), 124.3 (d, *J* = 15.4 Hz), 96.4 (d, *J* = 176.4 Hz), 60.9, 56.7, 56.4, 53.9, 42.8, 41.0, 40.2, 39.7, 37.6 (d, *J* = 22.5 Hz), 36.3, 36.0, 35.7, 35.7, 33.9, 32.1, 30.7 (d, *J* = 23.6 Hz), 28.5, 28.4, 28.2, 24.4, 24.0, 23.0, 22.7, 21.1, 18.8, 14.3, 12.2, 11.4; **^{19}F NMR** (376MHz, $CDCl_3$) δ -150.6 (ttd, *J* = 44.4, 12.3, 6.3 Hz).

HRMS (ESI): calculated for $C_{32}H_{53}O_2FNa^+$ $[M+Na]^+$ m/z: 511.3922, found: 511.3916.

$[\alpha]^{25}_D$ = +23.5 (*c* = 0.175, $CHCl_3$).

(3*S*)-3am

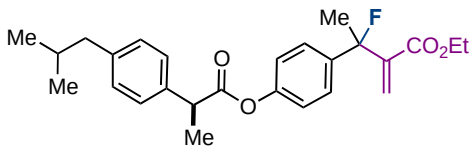


^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (d, *J* = 1.1 Hz, 1H), 5.89 (d, *J* = 4.5 Hz, 1H), 4.28 – 4.21 (m, 2H), 2.33 (d, *J* = 13.7 Hz, 1H), 2.21 – 2.16 (m, 2H), 1.96 (d, *J* = 9.4 Hz, 1H), 1.90 – 1.62 (m, 5H), 1.58 – 1.52 (m, 2H), 1.51 – 1.23 (m, 15H), 1.15 – 0.96 (m, 10H), 0.91 – 0.82 (m, 13H); **^{13}C NMR** (101 MHz, $CDCl_3$), δ 166.4, 141.4 (d, *J* = 21.8 Hz), 127.1 (d, *J* = 7.6 Hz), 95.4 (d, *J* = 169.8 Hz), 61.0, 56.6, 56.4, 54.5 (d, *J* = 2.3 Hz), 43.8 (d, *J* = 8.6 Hz), 42.8, 40.1, 39.7, 37.2 (d, *J* = 20.5 Hz), 36.9 (d, *J* = 10.0 Hz), 36.3, 36.0 (d, *J* = 1.6 Hz), 35.9, 35.5, 32.1, 31.2 (d, *J* = 21.6 Hz), 28.6, 28.4, 28.2, 24.3, 24.0, 23.0, 22.7, 21.4, 18.8, 14.3, 12.4, 12.2; **^{19}F NMR** (471MHz, $CDCl_3$) δ -122.6 (m).

HRMS (ESI): calculated for $C_{32}H_{53}O_2FNa^+$ $[M+Na]^+$ m/z: 511.3922, found: 511.3916.

$[\alpha]^{25}_D$ = +12.5 (*c* = 0.15, $CHCl_3$).

Ethyl 3-fluoro-3-(4-(((*S*)-2-(4-isobutylphenyl)propanoyl)oxy)phenyl)-2-methylenebutanoate (3an)



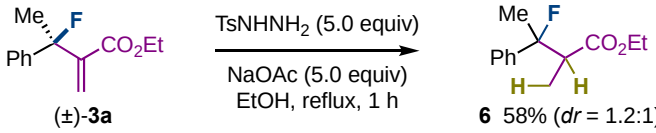
Prepared according to general procedure C using alkene **1an** (129 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be > 20:1 and the ratio of *diastereoisomers* was determined to be 1:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided the title compound as colorless oil (53 mg, 62% yield).

^{1}H NMR (400 MHz, $CDCl_3$), δ 7.43 – 7.37 (m, 2H), 7.33 – 7.27 (m, 2H), 7.15 – 7.12 (m, 2H), 7.01 – 6.95 (m, 2H), 6.36 (dd, *J* = 4.4, 1.0 Hz, 1H), 6.10 (d, *J* = 1.0 Hz, 1H), 4.10 – 4.01 (m, 2H), 3.92 (q, *J* = 7.1 Hz, 1H), 2.47 (d, *J* = 7.2 Hz, 2H), 2.02 (s, 3H), 1.86 (dt, *J* = 13.5, 6.8 Hz, 1H), 1.60 (d, *J* = 7.1 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H), 0.92 (s, 3H), 0.90 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.2, 164.8 (d, *J* = 6.4 Hz), 150.7 (d, *J* = 2.6 Hz), 143.7 (d, *J* = 24.3 Hz), 141.0, 139.5 (d, *J* = 22.1 Hz), 137.3, 129.6, 127.3, 126.9 (d, *J* = 6.6 Hz), 124.9 (d, *J* = 11.8 Hz), 121.0, 95.6 (d, *J* = 174.6 Hz), 60.9, 45.4, 45.2, 30.3, 25.9 (d, *J* = 24.8 Hz), 22.5, 18.6, 14.3; **^{19}F[^{1}H] NMR** (376 MHz, CD_2Cl_2) δ -131.4, -131.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -131.8 (m, 2F).

HRMS (ESI): calculated for $C_{26}H_{31}O_4FNa^+$ $[M+Na]^+$ m/z: 449.2099, found: 449.2089.

6. Derivatizations of (±)-3a.

Ethyl 3-fluoro-2-methyl-3-phenylbutanoate (6)[59]

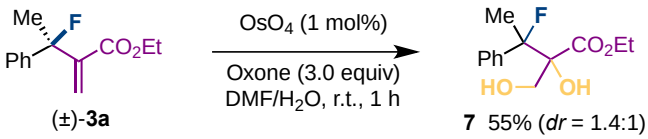


To an oven-dried reaction tube was added **3a** (88 mg, 0.4 mmol), $TsNHNH_2$ (360 mg, 2.0 mmol), NaOAc (160 mg, 2.0 mmol) and anhydrous EtOH (5 mL). The resulting reaction mixture was heated to reflux during 1 hour. After this, the reaction was quenched with water and (30 mL) extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and the solvent was removed under *vacuum*. Ratio of *diastereoisomers* was determined to be 1.2:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided the title compound as colorless oil (50 mg, 58% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.26 (m, 5H), 4.15 – 3.97 (m, 2H), 3.04 – 2.90 (m, 1H), 1.80 – 1.73 (m, 3H), 1.18 – 1.10 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$), 173.05 (d, *J* = 6.1 Hz), 173.0* (d, *J* = 3.5 Hz), 143.4 (d, *J* = 21.9 Hz), 142.9* (d, *J* = 22.1 Hz), 128.3 (d, *J* = 1.7 Hz), 128.2* (d, *J* = 0.9 Hz), 127.8 (d, *J* = 1.5 Hz), 127.7* (d, *J* = 1.1 Hz), 125.0* (d, *J* = 9.2 Hz), 124.5 (d, *J* = 9.7 Hz), 97.4* (d, *J* = 179.0 Hz), 96.9 (d, *J* = 181.5), 60.6, 60.6*, 50.6*, 50.3, 24.4 (d, *J* = 24.5 Hz), 23.5* (d, *J* = 24.5 Hz), 14.2, 14.1*, 12.5* (d, *J* = 6.5 Hz), 12.3 (d, *J* = 4.3 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -146.9* (qd, *J* = 23.2, 15.6 Hz), -153.6 (m); ** indicates the signals of the minor diastereoisomer*

HRMS (ESI): calculated for $C_{13}H_{17}O_2FNa^+$ $[M+Na]^+$ m/z: 247.1105, found: 247.1116.

Ethyl 3-fluoro-2-hydroxy-2-(hydroxymethyl)-3-phenylbutanoate (7)[60]



To an oven-dried reaction tube was added **3a** (80 mg, 0.4 mmol), DMF (2.0 mL), H_2O (2.0 mL) and OsO_4 (1 mg, 1.0 mol%). After 5 minutes, Oxone (180 mg, 1.2 mmol) was added in one portion and the reaction was stirred during 1 hour at room temperature. The reaction mixture was quenched with a saturated aqueous solution of $Na_2S_2O_3$ (10 mL) and stirred for 1 hour. After this, the reaction mixture was extracted with ethyl acetate (3 x 15 mL), washed with brine, dried over Na_2SO_4 and the solvent was removed under *vacuum*. Ratio of *diastereoisomers* was determined to be 1.4:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 2/1) provided the title compound as colorless oil (56 mg, 70% yield).

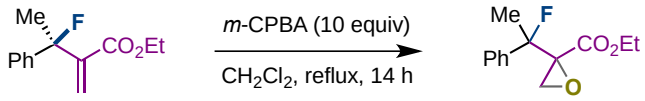
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 5H), δ 7.39 – 7.29 (m, 5H*), 4.29 (q, *J* = 7.1 Hz, 2H*), 4.18 (dd, *J* = 11.4, 2.8 Hz, 1H), 4.13 – 4.03 (m, 1H*), 4.11 – 4.05 (m, 2H), 3.93 (dd, *J* = 11.4, 0.9 Hz, 1H), 3.55 (dd, *J* = 11.4, 0.8 Hz, 1H*), 1.79 (d, *J* = 23.7 Hz, 3H), 1.74 (d, *J* = 23.8 Hz, 3H*), 1.29 (t, *J* = 7.1 Hz, 3H*), 1.20 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.0 (2C), 140.8 (d, *J* = 22.2 Hz), 140.3*

[59] Tu, H. F.; Yang, P.; Lin, Z. H.; Zheng, C.; You, S. L. *Nat. Chem.* **2020**, *12*, 838.
[60] Travis, B. R.; Narayan, R. S.; Borhan, B. *J. Am. Chem. Soc.* **2002**, *124*, 3824.

(d, *J* = 22.0 Hz), 128.2 (d, *J* = 0.9 Hz), 128.2* (d, *J* = 0.9 Hz), 128.1 (d, *J* = 1.8 Hz), 128.0* (d, *J* = 1.8 Hz), 125.6* (d, *J* = 10.7 Hz), 125.0 (d, *J* = 10.5 Hz), 97.4 (d, *J* = 184.4 Hz), 97.3* (d, *J* = 183.7 Hz), 81.9* (d, *J* = 26.0 Hz), 81.6 (d, *J* = 27.4 Hz), 63.8* (d, *J* = 3.3 Hz), 63.6 (d, *J* = 5.4 Hz), 63.1*, 62.9 23.2* (d, *J* = 23.4 Hz), 22.9 (d, *J* = 23.0 Hz), 14.1*, 14.1; **^{19}F NMR** (101 MHz, $CDCl_3$) δ -155.2* (qd, *J* = 24.0, 3.7 Hz), -156.7 (qd, *J* = 23.7, 3.1 Hz); * *indicates the signals of the minor diastereoisomer.*

HRMS (ESI): calculated for $C_{13}H_{17}O_4FNa^+$ $[M+Na]^+$ m/z: 279.1003, found: 279.0996.

Ethyl 2-(1-fluoro-1-phenylethyl)oxirane-2-carboxylate (8)[61]



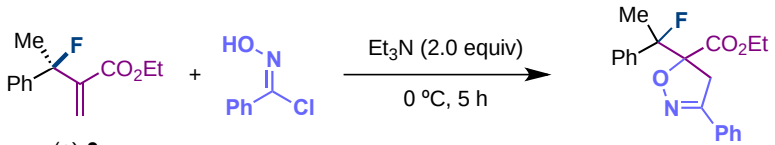
(±)-**3a** — **8** 51% (*dr* = 3:1)

To an oven-dried reaction tube was added **3a** (44 mg, 0.2 mmol), CH_2Cl_2 (4.0 mL) and *meta*-chloroperoxybenzoic acid (*m*-CPBA) (254 mg, 2.0 mmol, 10.0 equiv.). The reaction mixture was heated to reflux during 14 hours. After this, the reaction was quenched with a saturated aqueous solution of $Na_2S_2O_3$ (10 mL) and stirred for 1 hour. The organic layer was separated, and the aqueous solution was extracted with CH_2Cl_2 (3 x 10 mL) washed with brine, dried over Na_2SO_4 and the solvent was removed under *vacuum*. Ratio of *diastereoisomers* was determined to be 3:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 20/1) provided the title compound as colorless oil (71 mg, 51% yield).

^{1}H NMR (400 MHz, $CDCl_3$,) δ 7.48 – 7.45 (m, 2H), 7.40-7.30 (m, 3H), 4.13 – 3.98 (m, 2H), 3.28 – 3.06 (m, 2H), 1.93 – 1.82 (m, 3H), 1.15 – 1.03 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.5 (d, *J* = 3.8 Hz, 2C), 140.8 (d, *J* = 22.1 Hz), 140.4* (d, *J* = 22.5 Hz), 128.8*, 128.5 (d, *J* = 1.7 Hz), 128.4* (d, *J* = 1.4 Hz), 128.3, 128.3* (d, *J* = 4.7 Hz), 125.5 (d, *J* = 7.6 Hz), 94.6 (d, *J* = 180.4 Hz), 94.3* (d, *J* = 179.5 Hz), 61.9*, 61.8, 60.8* (d, *J* = 28.0 Hz), 60.7 (d, *J* = 29.2 Hz), 49.7* (d, *J* = 5.7 Hz), 49.2 (d, *J* = 6.6 Hz), 24.0* (d, *J* = 24.5 Hz), 22.5 (d, *J* = 24.5 Hz), 13.9*, 13.8; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -147.8 (q, *J* = 23.2 Hz), -150.8* (q, *J* = 23.7 Hz); * *indicates the signals of the minor diastereoisomer*.

HRMS (ESI): calculated for $C_{13}H_{15}O_3FNa^+$ $[M+Na]^+$ m/z: 261.0897, found: 261.0891.

Ethyl 5-(1-fluoro-1-phenylethyl)-3-phenyl-4,5-dihydroisoxazole-5-carboxylate (9)[62]



(±)-**3a** — **9** 70% (*dr* = 2.5:1)

To a 10 mL oven-dried reaction tube equipped with a stirring bar was added chlorobenzaldoxime (96 mg, 0.6 mmol) and CH_2Cl_2 (6.0 mL). The reaction mixture was cooled at 0°C and triethylamine (90 μL, 0.6

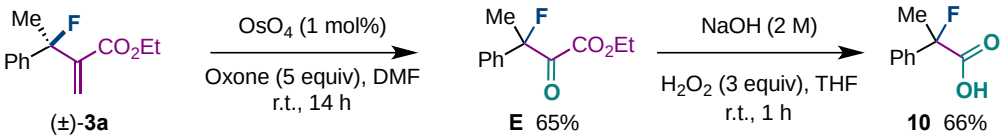
[61] Orrling, K. M.; Marzahn, M. R.; Gutiérrez-de-Terán, H.; Åqvist, J.; Dunn, B. M.; Larhed, M. *Bioorganic Med. Chem.* **2009**, *17*, 5933.
[62] Nishimine, T.; Taira, H.; Tokunaga, E.; Shiro, M.; Shibata, N. *Angew. Chemie - Int. Ed.* **2016**, *55*, 359.

mmol) was added. After stirring for 10 min, tertiary allylic fluoride **3a** (66 mg, 0.3 mmol) was added dropwise. The mixture was stirred at 0 °C for 5 h. Then the reaction was quenched with water (5 mL) and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL), the combined organic layers were dried over Na_2SO_4 and the solvent was removed under *vacuum*. Ratio of *diastereoisomers* was determined to be 2.5:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 10/1) provided the title compound as colorless oil (71 mg, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.67 (m, 2H), 7.50 – 7.26 (m, 8H), 7.50 – 7.26 (m, 10H*). 4.37 – 4.22 (m, 2H*), 4.09 – 3.96 (m, 2H), 3.87 – 3.81 (m, 2H), 3.78 – 3.77 (m, 1H), 3.81 (d, *J* = 1.5 Hz, 1H), 3.77 (dd, *J* = 4.6, 1.2 Hz, 1H*), 3.49 (d, *J* = 17.6 Hz, 1H*),1.95 (d, *J* = 23.8 Hz, 3H*), 1.91 (d, *J* = 23.7 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H*), 1.06 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.4* (d, *J* = 1.1 Hz), 169.7 (d, *J* = 3.0 Hz), 156.8*, 156.7, 140.0 (d, *J* = 20.0 Hz), 139.3* (d, *J* = 21.7 Hz), 130.7, 130.5*, 128.9, 128.8*, 128.7, 128.6* 128.5, 128.3 (d, *J* = 1.9 Hz), 128.2* (d, *J* = 2.0 Hz), 127.0, 126.8*, 125.8* (d, *J* = 10.4 Hz), 125.1 (d, *J* = 10.1 Hz), 97.5 (d, *J* = 186.9 Hz), 96.8* (d, *J* = 184.8 Hz), 93.0 (d, *J* = 26.4 Hz), 92.3* (d, *J* = 28.7 Hz), 62.6*, 62.3, 41.2*, 40.5 (d, *J* = 4.7 Hz), 23.7* (d, *J* = 22.5 Hz), 22.6 (d, *J* = 23.3 Hz), 14.2*, 13.8 (one aromatic *C is missing); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -153.8* (q, *J* = 23.8 Hz), -154.9 (q, *J* = 23.7 Hz); ** indicates the signals of the minor diastereoisomer*.

HRMS (ESI): calculated for $C_{20}H_{20}NO_3FNa^+$ $[M+Na]^+$ m/z: 364.1319, found: 364.1303.

2-Fluoro-2-phenylpropanoic acid (10)[60]



Synthesis of **E**: To an oven-dried reaction tube was added **3a** (80 mg, 0.4 mmol), DMF (2.0 mL) and OsO_4 (1 mg, 1.0 mol%). After 5 minutes, Oxone (300 mg, 2.0 mmol) was added in one portion and stirred for 14 hours, the reaction was quenched with saturated $Na_2S_2O_3$ aqueous solution (10 mL) and it was stirred for an additional hour. The reaction mixture was extracted with ethyl acetate (3 x 15 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4 and the solvent was removed under *vacuum*. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided **E** as colorless oil (52 mg, 65% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.34 (m, 5H), 4.33 – 4.25 (m, 2H), 1.95 (d, *J* = 22.9 Hz, 3H), 1.29 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.6 (d, *J* = 37.5 Hz), 162.2, 137.4 (d, *J* = 22.5 Hz), 129.0 (d, *J* = 1.2 Hz), 128.0 (d, *J* = 1.2 Hz), 124.8 (d, *J* = 8.6 Hz), 99.2 (d, *J* = 183.0 Hz), 62.6, 24.5 (d, *J* = 23.3 Hz), 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -156.9 (q, *J* = 22.9 Hz).

HRMS (ESI): calculated for $C_{12}H_{13}O_3FNa^+$ $[M+Na]^+$ m/z: 247.0741, found: 247.0731.

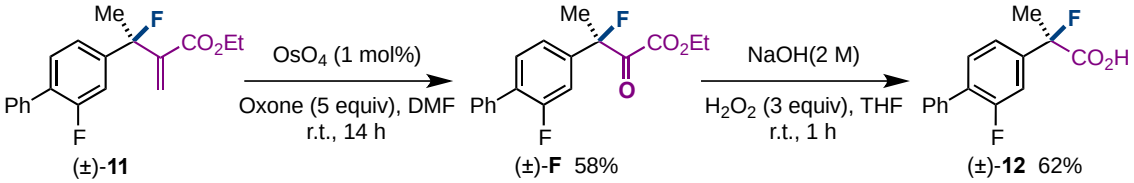
Synthesis of **10**: To an oven-dried reaction tube equipped with stirring bar was added **E** (67 mg, 0.3 mmol), THF (2.0 mL) and NaOH (0.75 mL, 2M in water, 5.0 equiv.). The reaction mixture was cooled at 0 ºC and H_2O_2 (91 µL, 30% w/w, 3.0 equiv.) was added. Then, it was stirred for 1 hour at room temperature. After this time, the reaction was quenched with $Na_2S_2O_3$ saturated aqueous solution (1 mL), and it was stirred for

an additional hour. The reaction mixture was then extracted with ethyl acetate (3 x 15 mL), the combined organic layers were washed with brine, dried over Na_2SO_4 and the solvent was removed under *vacuum*. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 5/1 to 2/1) provided **10** as colorless oil (33 mg, 66% yield).

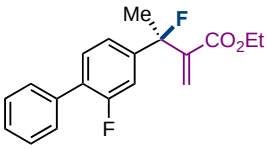
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (brs, 1H), 7.59 – 7.50 (m, 2H), 7.44 – 7.34 (m, 3H), 1.97 (d, *J* = 22.3 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.6 (d, *J* = 28.1 Hz), 138.4 (d, *J* = 22.7 Hz), 129.1 (d, *J* = 1.5 Hz), 128.7 (d, *J* = 1.2 Hz), 124.8 (d, *J* = 8.5 Hz), 94.3 (d, *J* = 187.1 Hz), 24.6 (d, *J* = 23.7 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$,) δ -151.3.

Spectra are consistent with previously reported.[63]

7. Synthesis of F-flurbiprofen 12.



Ethyl 3-fluoro-3-(2-fluoro-[1,1'-biphenyl]-4-yl)-2-methylenebutanoate ((±)-11)

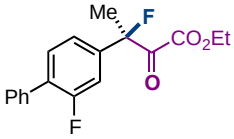


Prepared according to general procedure C using alkene **1ao** (85 mg, 0.4 mmol), reagent **2a** (120 mg, 0.2 mmol) and Et_3N•3HF (96 mg, 0.6 mmol). Ratio of *branched*:*linear* isomers was determined to be 18:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 20/1) provided the title compound as colorless oil (55 mg, 87% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.54 (m, 2H), 7.47 – 7.36 (m, 4H), 7.31 – 7.24 (m, 2H), 6.45 (dd, *J* = 4.4, 0.9 Hz, 1H), 6.19 (d, *J* = 0.9 Hz, 1H), 4.17 – 4.09 (m, 2H), 2.04 (d, *J* = 23.5 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.7 (d, *J* = 6.3 Hz), 159.5 (d, *J* = 248.9), 143.6 (dd, *J* = 16.5, 7.4 Hz), 143.3 (d, *J* = 24.3 Hz), 135.5, 130.5 (d, *J* = 3.8 Hz), 129.1 (d, *J* = 2.9 Hz), 128.7 (dd, *J* = 13.6, 2.2 Hz), 128.6, 127.9, 125.3 (d, *J* = 11.9 Hz), 121.6 (dd, *J* = 6.5, 3.5 Hz), 113.8 (dd, *J* = 24.9, 7.1 Hz), 95.3 (dd, *J* = 175.2, 1.7 Hz), 61.0, 25.8 (d, *J* = 24.6 Hz), 14.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.9 (dd, *J* = 11.7, 8.1 Hz), -132.4 (qd, *J* = 23.5, 4.4 Hz).

HRMS (ESI): calculated for $C_{19}H_{18}O_2F_2Na^+$ $[M+Na]^+$ m/z: 339.1167, found: 339.1162.

Ethyl 3-fluoro-3-(2-fluoro-[1,1'-biphenyl]-4-yl)-2-oxobutanoate (±)-F



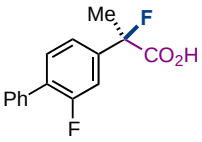
Synthesis of **(±)-F** was done following the previous protocol described for the synthesis of **E** using **(±)-11** (90 mg, 0.28 mmol), DMF (2.0 mL), OsO_4 (0.7 mg, 1.0 mol%) and Oxone (300 mg, 2.0 mmol). Purification by flash chromatography on silica gel (hexane/ethyl acetate = 20/1) provided the **(±)-F** as colorless oil (52 mg, 58% yield).

[63] Tengeiji, A.; Shiina, I. *Molecules* **2012**, *17*, 7356.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.53 (m, 2H), 7.50 – 7.43 (m, 3H), 7.41 – 7.37 (m, 1H), 7.33 – 7.26 (m, 2H), 4.38 – 4.30 (m, 2H), 1.97 (d, *J* = 22.8 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.2 (d, *J* = 37.8 Hz), 162.1, 159.8 (dd, J =250.2, 1.8 Hz), 138.7 (dd, *J* = 23.2, 7.7 Hz), 135.1 (d, *J* = 1.4 Hz), 131.2 (d, *J* = 3.7 Hz), 129.8 (d, *J* = 14.2 Hz), 129.1 (d, *J* = 2.9 Hz), 128.7, 128.2, 120.7 (dd, *J* = 8.4, 3.7 Hz), 113.0 (d, *J* = 25.9, 9.6 Hz), 98.7 (dd, *J* = 184.1, 1.7 Hz), 62.8, 24.6 (d, *J* = 23.2 Hz), 14.1; **^{19}F NMR** (376 MHz, CDCl3) δ -116.5 (m), -157.1 (q, J = 22.8 Hz).

HRMS (ESI): calculated for $C_{18}H_{16}O_3F_2Na^+$ $[M+Na]^+$ m/z: 341.1222, found: 341.1225.

2-Fluoro-2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanoic acid (±)-12



Synthesis of **(±)-12** was done following the previous protocol described for the synthesis of **10** using **(±)-F** (64 mg, 0.2 mmol), THF (2.0 mL), NaOH (0.8 mL, 2M in water, 4.0 equiv.) and H_2O_2 (102 μL, 30% w/w, 5.0 equiv.). Purification by flash chromatography on silica gel (dichloromethane/methanol = 20/1) provided the title compound as white solid (32 mg, 62 % yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 – 7.52 (m, 2H), 7.51 – 7.42 (m, 3H), 7.43 – 7.32 (m, 3H), 2.00 (d, *J* = 22.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.1 (d, *J* = 27.7 Hz), 159.7 (d, *J* = 249.6 Hz), 139.6 (dd, *J* = 23.2, 7.6 Hz), 135.1, 131.1 (d, *J* = 4.0 Hz), 129.9 (d, *J* = 13.4 Hz), 129.1 (d, *J* = 3.1 Hz), 128.7, 128.2, 120.8 (dd, *J* = 5.2 Hz, 3.8 Hz), 113.2 (dd, *J* = 25.7, 9.5 Hz), 93.9 (dd, *J* = 188.0, 1.7 Hz), 24.7 (d, *J* = 23.6 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -116.6 (m), -151.6 (q, *J* = 22.2 Hz).

Spectra are consistent with previously reported.[64]

8. Radiofluorination of styrenes 1a and 1i.

Procedure for preparation of a [^{18}F]TEAF solution in CH_2Cl_2:

[^{18}F]Fluoride was generated in an IBA Cyclone 18/9 cyclotron by irradiation of ^{18}O-enriched-water with high energy protons (18 MeV) via ^{18}O(p,n) ^{18}F reaction.

[^{18}F]Fluoride (0.5 – 1.0 GBq) was separated from ^{18}O-enriched-water using a Waters Plus QMA Plus Light ^{18}F separation cartridge (130 mg) and subsequently released with a solution of tetraethylammonium bicarbonate (9 mg/mL) in MeCN/H2O, 4:1 (3 x 300 μL) into a 5 mL V-vial. The solution was dried with three cycles of azeotropic drying with MeCN (3 x 500 μL) under a flow of N_2 at 105 °C. The dried [^{18}F]TEAF residue was re-dissolved in anhydrous CH_2Cl_2 (250 – 500 μL) to obtain a concentration of radioactivity of 0.2 GBq/100 μL approximately.

Procedure for the ^{18}F-Fluorination of substrates:

To a 10 mL reaction tube was weighed the desired substrate (0.02 mmol). A freshly prepared solution of $Rh_2(esp)_2$ in dry degassed CH_2Cl_2 was added to it (200 μL, 1.0 M). The tube was sealed and evacuated and backfilled with nitrogen 3 times. The resulting mixture was cooled down to -50 ºC. Then, a solution of reagent **2a** (12.0 mg, 0.02 mmol, 1.0 equiv.) in degassed CH_2Cl_2 (1.0 mL) was added dropwise during 1 h

[64] Schiefer, I. T.; Abdul-Hay, S.; Wang, H.; Vanni, M.; Qin, Z.; Thatcher, G. R. J. *J. Med. Chem.* **2011**, *54*, 2293.

using a syringe pump. After the addition, a solution of [^{18}F]TEAF in dry CH_2Cl_2 (0.2 GBq in 100 μL) was added and the reaction mixture was heated up to -30 ºC and stirred at this temperature for 20 min. After this time, an aliquot (300 μL) was taken for analysis by radio HPLC, CH_2Cl_2 was removed under a flow of N_2 and the residue was redissolved in dry MeCN (300 μL). Analysis was performed using an Agilent 1120 Compact LC system equipped with a variable wavelength UV detector and a radioactivity detector (Gabi, Raytest) interfaced using an analog-to-digital converter. Occasionally, an Agilent 1200 series HPLC system equipped with a variable wavelength UV detector and a radioactivity detector (Gabi, Raytest) controlle

HPLC conditions for small scale ^{18}F-Fluorination of substrates [^{18}F]3a and [^{18}F]3i:

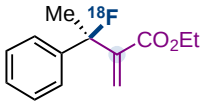
Agilent 1120 Compact LC with a Teknokroma Mediterranea Sea C18 Column, 5 μm, 4.6 x 150 mm; flow rate: 1 mL/min; solvent A: Water with 0.1 % TFA, solvent B: MeCN with 0.1 % TFA., gradient: 0 – 1 min (A : B 80/20) isocratic, 1 – 10 min (A : B 80/20 to 20/80) linear increase, 10 – 15 min (A : B 20/80) isocratic, 15 – 18 min (A : B 20/80 to 80/20) linear decrease and 18 – 20 min (A : B = 80:20) isocratic.

Radio-HPLC of substrates [^{18}F]3a and [^{18}F]3i:

Crude Radio-HPLC traces of the crude mixture following the general procedure. The top chromatogram shows the UV trace for cold reference material (wavelength = 220 nm) and the bottom one the crude radio-HPLC trace. Radiochemical conversions (RCC) were calculated dividing the area of the peak from the desired product by the sum of areas of the rest of the peaks that appear in the radio-HPLC chromatogram.

[^{18}F] Ethyl 3-fluoro-2-methylene-3-phenylbutanoate ([^{18}F]3a)

Prepared according to the described procedure using prop-1-en-2-ylbenzene **1a** (2.4 mg 0.02 mmol) and



[^{18}F]3a
10 ±2 % RCY$_{(n = 3)}$

reagent **2** (12.0 mg, 0.02 mmol, 1.0 equiv.). The radiochemical conversions (RCC) and the Radio-HPLC chromatograms are shown below:

Reaction	RCC
1	12
2	8
3	10
RCC mean ± Standard deviation	10 ± 2

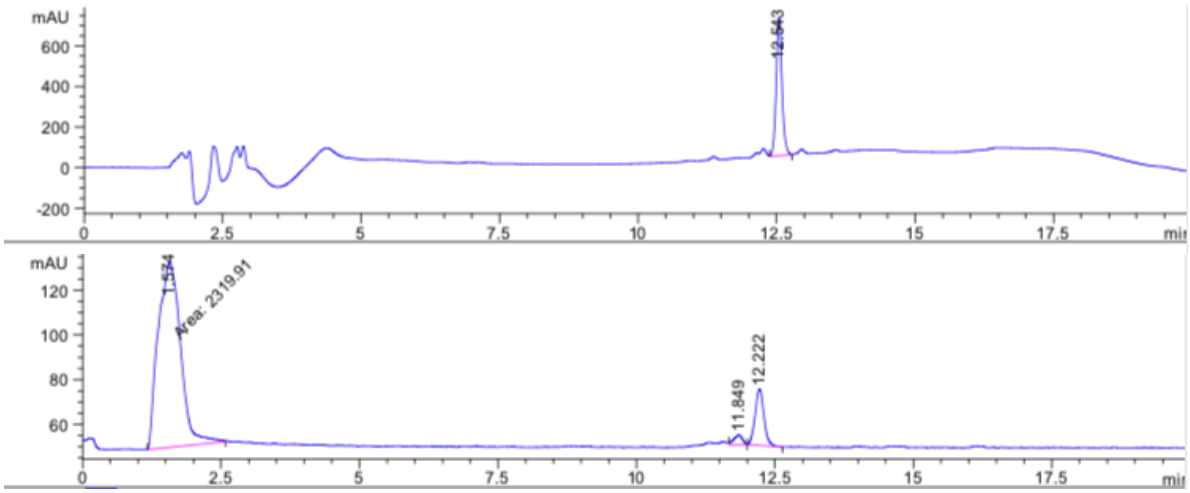
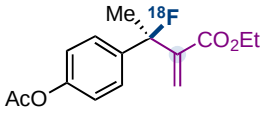


*Figure 1: The top chromatogram shows the UV trace for cold reference material (wavelength = 220 nm) and the bottom one the crude radio-HPLC trace for **[^{18}F]3a**.*

[^{18}F] Ethyl 3-(4-acetoxyphenyl)-3-fluoro-2-methylenebutanoate ([^{18}F]3i)



[^{18}F]3i
9 ±2 % RCY$_{(n = 3)}$

Prepared according to the general procedure using 4-(prop-1-en-2-yl)phenyl acetate **1i** (3.5 mg, 0.02 mmol) and reagent **2** (12.0 mg, 0.02 mmol, 1.0 equiv.). The radiochemical conversions (RCC) and the Radio-HPLC chromatograms are shown below:

Reaction	RCC
1	10
2	7
3	9
RCC mean ± Standard deviation	9 ± 2

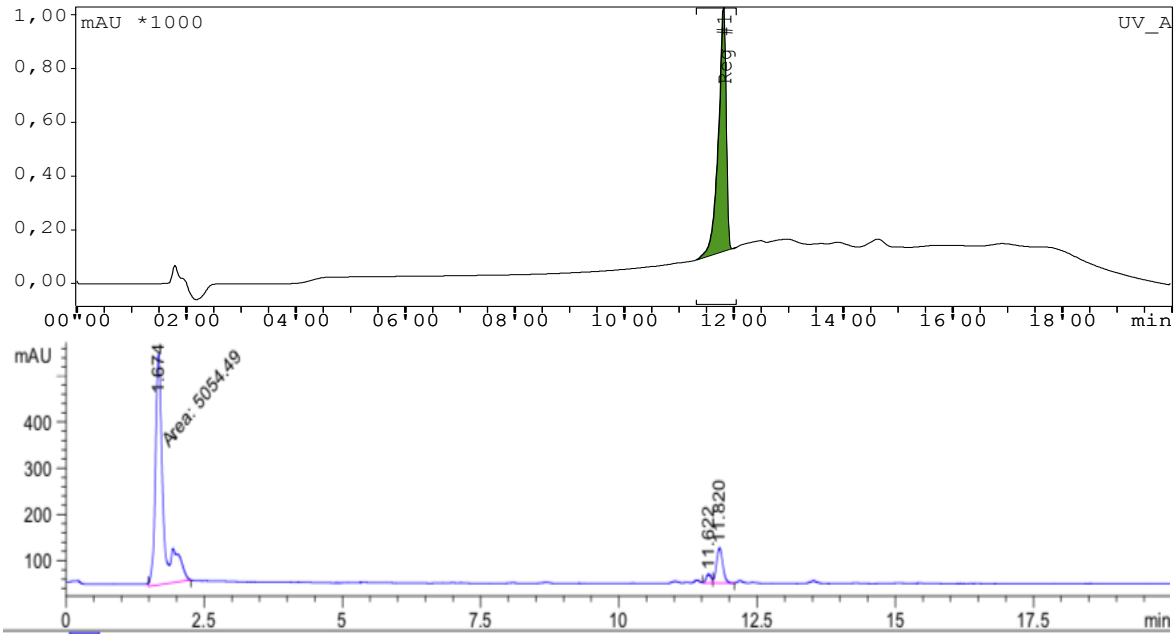


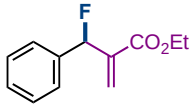
Figure 2: The top chromatogram shows the UV trace for cold reference material (wavelength = 220 nm) and the bottom one the crude radio-HPLC trace for ***[^{18}F]3i****.*

9. Fluorination of styrene and β-methylstyrene.

Ethyl 2-(fluoro(phenyl)methyl)acrylate (13) and Ethyl (*Z*)-2-(fluoromethyl)-3-phenylacrylate (13')

Prepared according to general procedure C using styrene (42 mg, 0.4 mmol, 2.0 equiv.). Ratio of *branched*:*linear* isomers was determined to be 3:1 and the *Z*:*E* ratio from the *linear* isomer was determined to be 6:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 30/1) provided a mixture of the title compounds as colorless oil (41 mg, 65% yield). Further separation of two isomers was achieved with a PLC plate (hexane/ethyl acetate = 50/1).

Ethyl 2-(fluoro(phenyl)methyl)acrylate (13)

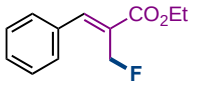


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.28 (m, 5H), 6.45 (dt, *J* = 2.7, 1.0 Hz, 1H), 6.28 (dt, *J* = 46.0, 1.3 Hz, 1H), 6.01 (t, *J* = 1.3 Hz, 1H), 4.27 – 4.08 (m, 2H), 1.22 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.9 (d, *J* = 6.3 Hz), 139.8 (d, *J* =

22.8 Hz), 137.6 (d, *J* = 20.4 Hz), 129.1 (d, *J* = 2.6 Hz), 128.6, 127.3 (d, *J* = 5.6 Hz), 125.8 (d, *J* = 8.9 Hz), 91.0 (d, *J* = 174.5 Hz), 61.1, 14.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -171.0 (dd, *J* = 46.0, 2.7 Hz).

Spectra are consistent with previously reported.[65]

Ethyl (*Z*)-2-(fluoromethyl)-3-phenylacrylate (13')



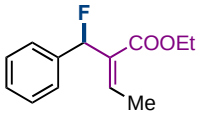
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 2.0 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.47 – 7.40 (m, 3H), 5.23 (d, *J* = 47.6 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.9 (d, *J* = 1.3 Hz), 147.3 (d, *J* = 7.1 Hz), 139.2 (d, *J* = 10.7 Hz), 130.1, 129.9 (d, *J* = 3.8 Hz), 129.8, 128.2, 77.2 (d, *J* = 162.9 Hz), 61.5, 14.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -205.1 (td, *J* = 47.6, 4.0 Hz); ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOE spectra were measured.

HRMS (ESI): calculated for $C_{12}H_{13}O_2FNa^+$ $[M+Na]^+$ m/z: 231.0792, found: 231.0795.

Ethyl (*Z*)-2-benzylidene-3-fluorobutanoate (14-branched) and Ethyl (*E*)-2-(fluoro(phenyl)methyl)but-2-enoate (14-branched')

Prepared according to the general procedure C using a-methyl styrene (47 mg, 0.4 mmol, 2.0 equiv.). Ratio of *branched:branched´* isomers was determined to be 1.4:1; the *E*:*Z* ratio from the *branched* isomer was determined to be 8:1 and the *Z*:*E* ratio from the *branched* isomer was determined to be 10:1 from the crude reaction mixture using ^{19}F-NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 40/1) provided a mixture of the title compounds as colorless oil (41 mg, 77% yield).

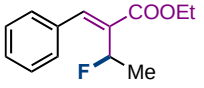
-14-branched



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 5H), 6.37 (m, 1H), 6.35 – 6.20 (m, 1H), 4.17 (qd, *J* = 7.1, 0.2 Hz, 2H), 2.10 (dq, *J* = 1.8, 0.3 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.7 (d, *J* = 3.6 Hz), 139.8 (d, *J* = 9.6 Hz), 138.2 (d, *J* = 21.2 Hz), 132.1 (d, *J* = 20.4), 128.6 (d, *J* = 2.3 Hz), 128.4, 126.8 (d, *J* = 6.1 Hz), 92.1 (d, *J* = 174.1 Hz), 60.5, 15.6, 14.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -169.0 (m); ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOE spectra were measured.

HRMS (ESI): calculated for $C_{13}H_{15}O_2FNa^+$ $[M+Na]^+$ m/z: 245.0948, found: 245.0939.

-14-branched´

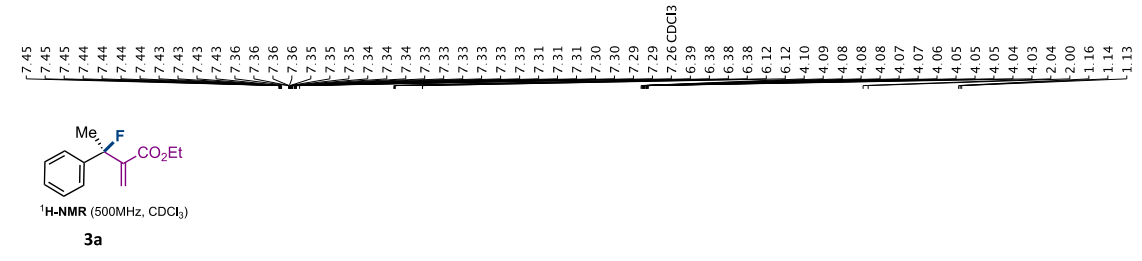


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.44 – 7.30 (m, 5H), 5.67 (dq, *J* = 46.3, 6.6 Hz, 1H), 4.39 – 4.25 (m, 2H), 1.72 (dd, *J* = 22.6, 6.6 Hz, 3H), 1.38 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$), δ 166.3 (d, *J* = 1.8 Hz), 142.9 (d, *J* = 6.2 Hz), 134.4 (d, *J* = 2.0 Hz), 131.9 (d, *J* = 18.8 Hz), 129.5 (d, *J* = 2.8 Hz), 129.2, 128.7, 85.6 (d, *J* = 167.3 Hz), 61.0, 20.2 (d, *J* = 25.4 Hz), 14.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -168.5 (m); ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOE spectra were measured.

HRMS (ESI): calculated for $C_{13}H_{15}O_2FNa^+$ $[M+Na]^+$ m/z: 245.0948, found: 245.0938.

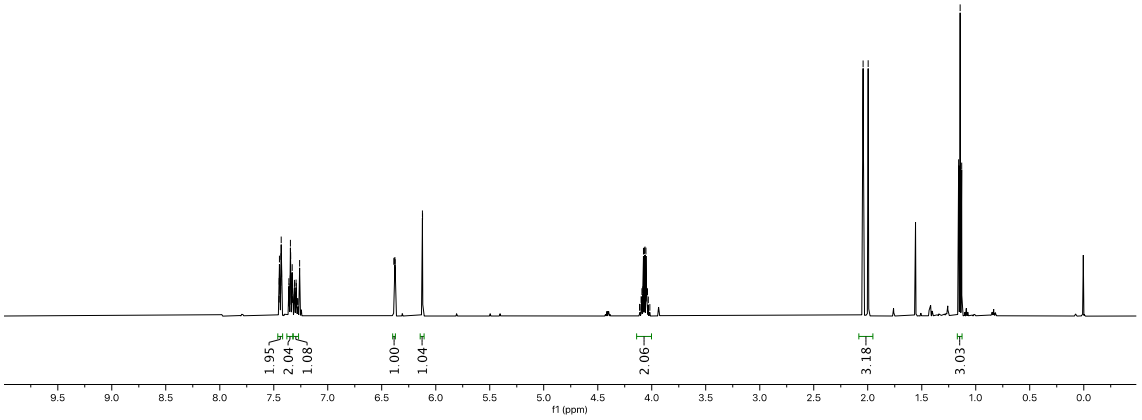
[65] Zi, Y.; Lange, M.; Vilotijevic, I. *Chem. Commun.* **2020**, *56*, 5689.

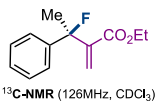
Selected NMR spectra



^{1}H-NMR (500MHz, $CDCl_3$)

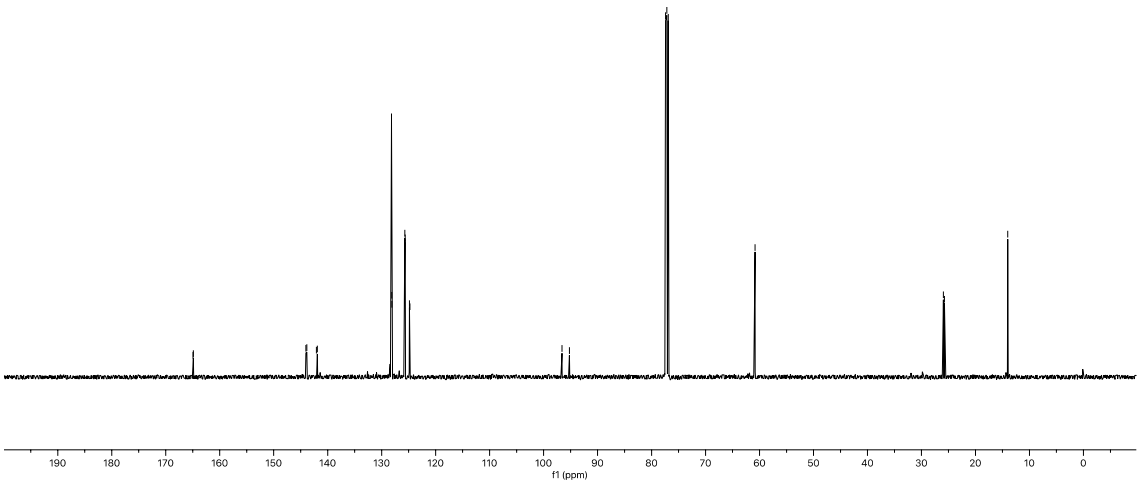
3a

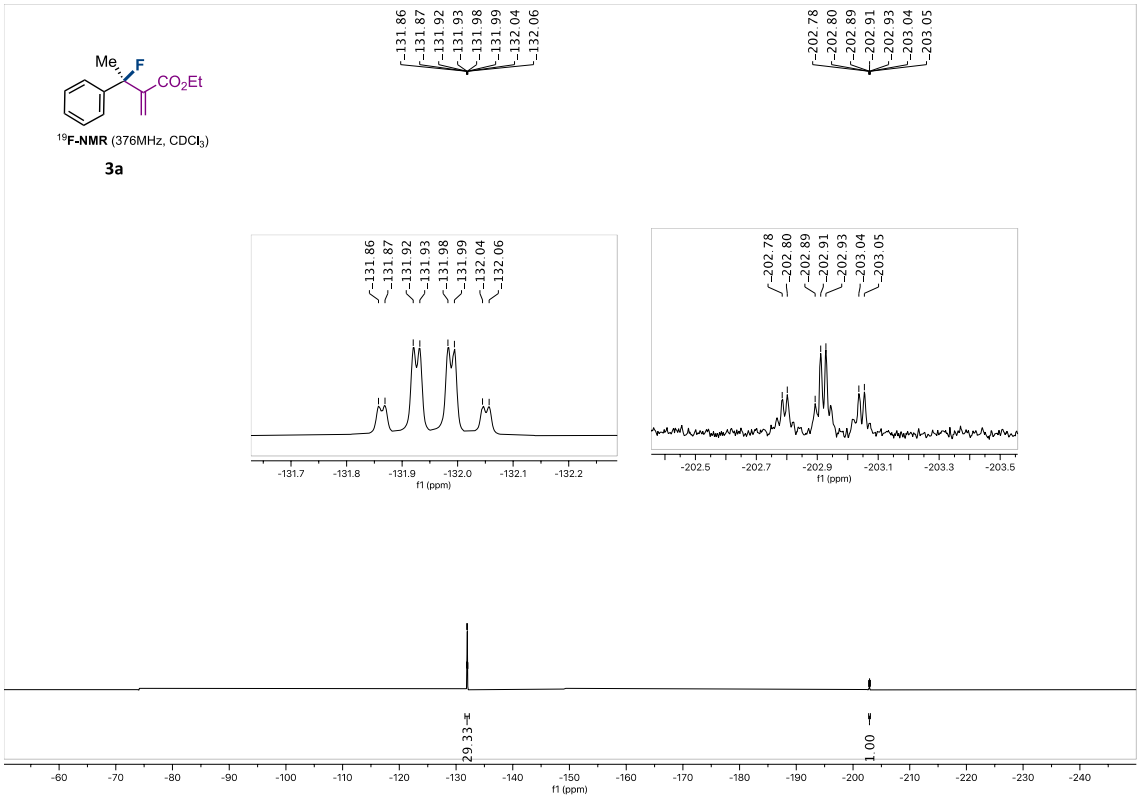


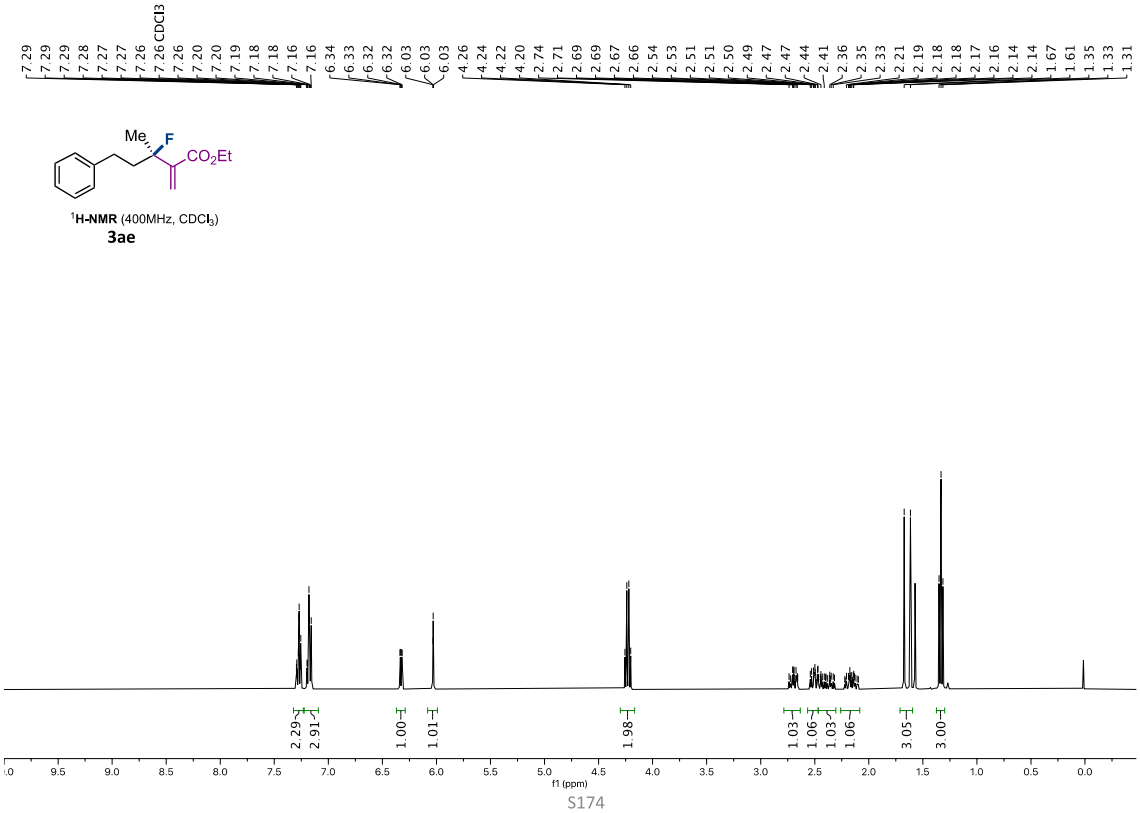


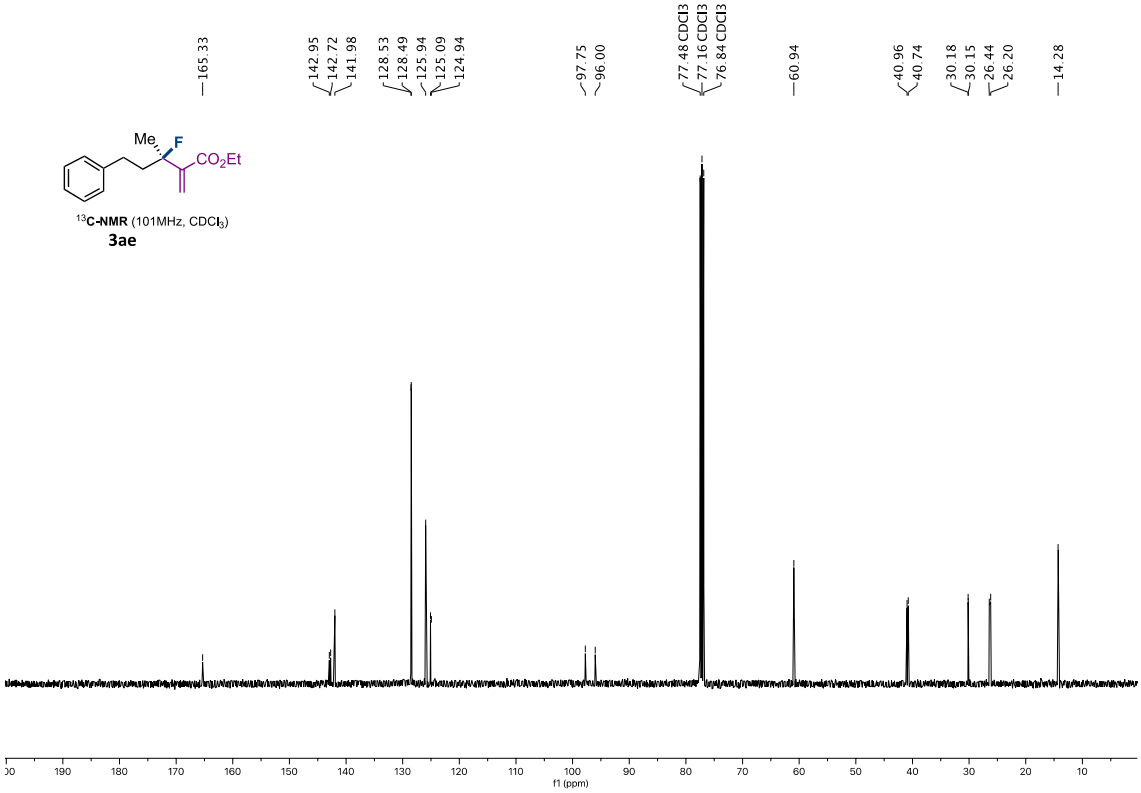
^{13}C-NMR (126MHz, $CDCl_3$)

3a



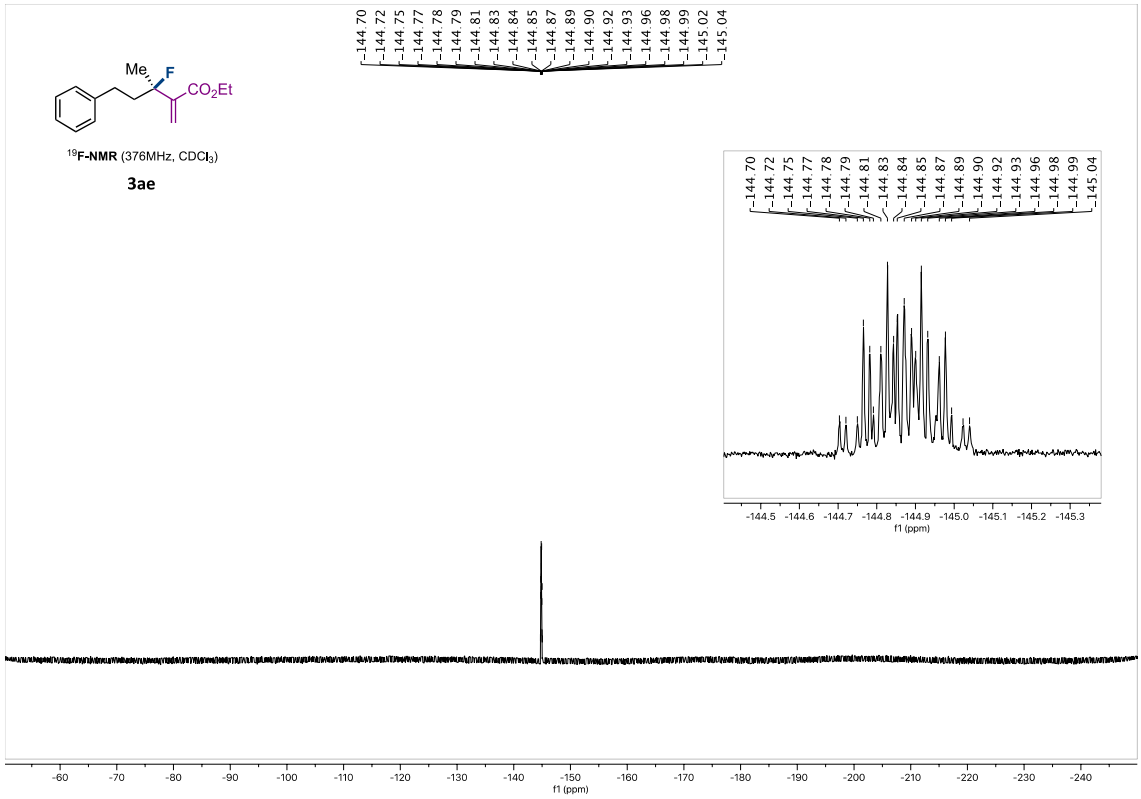

Me
F
CO2Et
19F-NMR (376MHz, CDCl3)
3a
-131.86
-131.87
-131.92
-131.93
-131.98
-131.99
-132.04
-132.06
-202.78
-202.80
-202.89
-202.91
-202.93
-203.04
-203.05
29.33
1.00
f1 (ppm)


7.29
7.28
7.27
7.26
7.26 CDCl3
7.20
7.19
7.18
7.16
6.34
6.33
6.32
6.03
4.26
4.24
4.22
4.20
2.74
2.71
2.69
2.67
2.66
2.54
2.53
2.51
2.50
2.49
2.47
2.44
2.41
2.36
2.35
2.33
2.21
2.19
2.18
2.17
2.16
2.14
1.67
1.61
1.35
1.33
1.31
Me
F
CO2Et
1H-NMR (400MHz, CDCl3)
3ae
2.29
2.91
1.00
1.01
1.98
1.03
1.06
1.03
1.06
3.05
3.00
f1 (ppm)



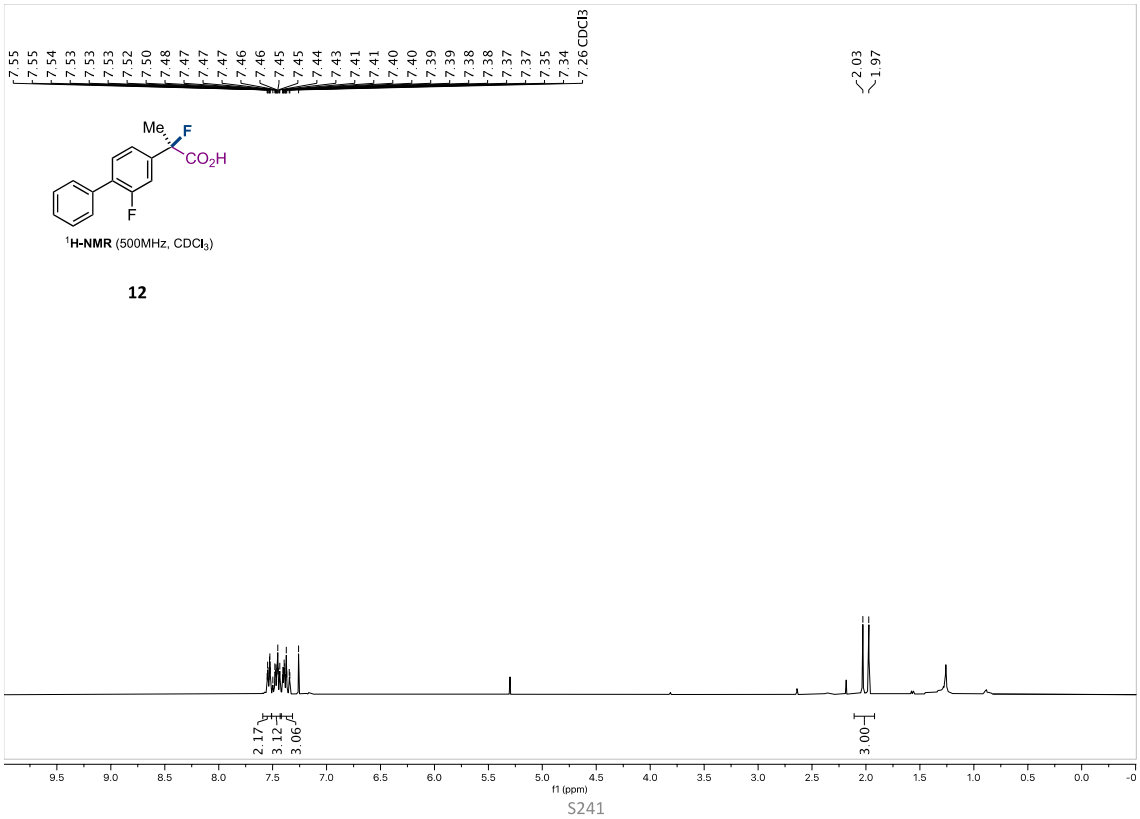
^{13}**C-NMR** (101MHz, $CDCl_3$)

3ae

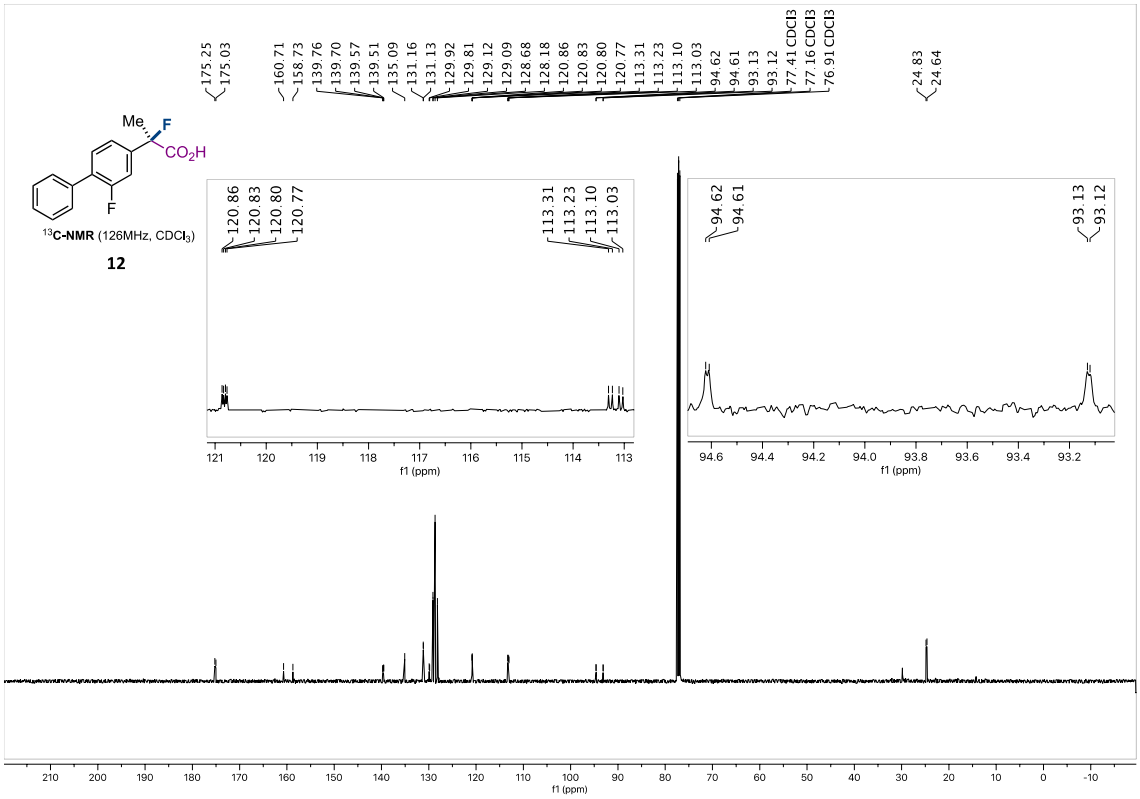


^{19}**F-NMR** (376MHz, $CDCl_3$)

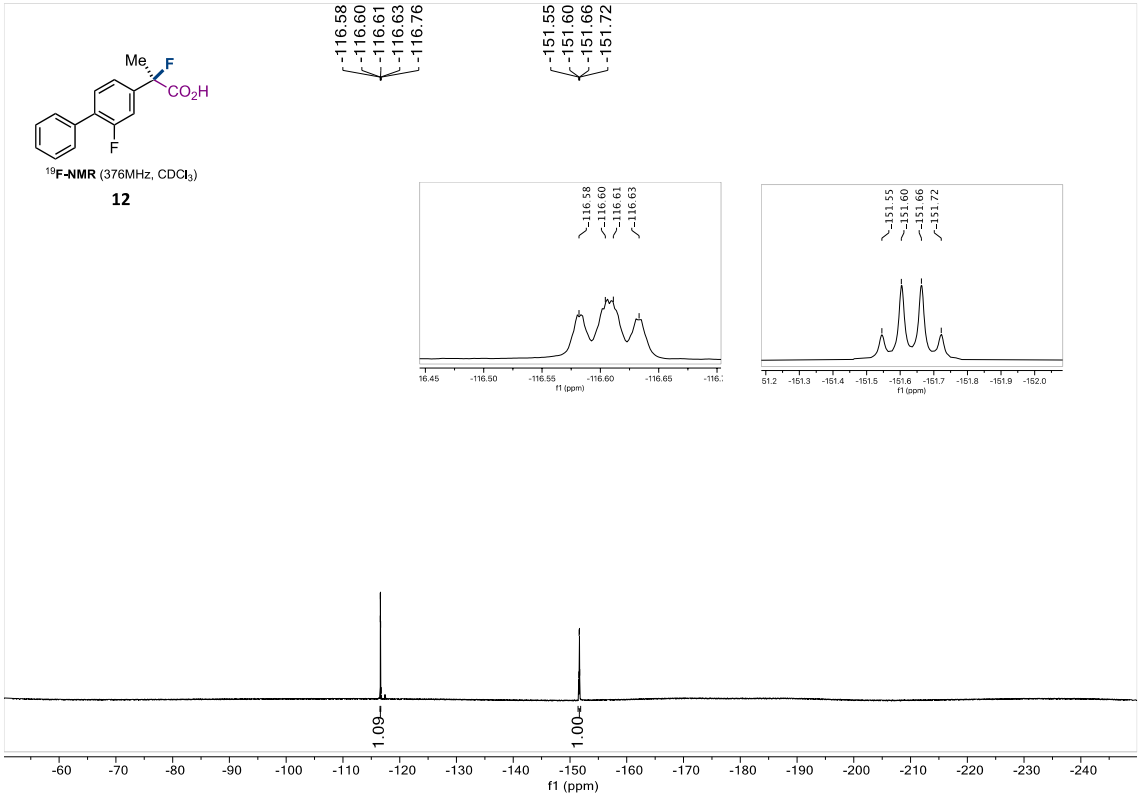
3ae


Me
F
CO2H
F
1H-NMR (500MHz, CDCl3)
12

S241


Me
F
CO2H
F
13C-NMR (126MHz, CDCl3)
12

S242


-116.58
-116.60
-116.61
-116.63
-116.76
-151.55
-151.60
-151.66
-151.72
Me
F
CO2H
F
19F-NMR (376MHz, CDCl3)
12
1.09
1.00
f1 (ppm)

Chapter IV

Catalytic Desaturative C(sp^2)–C(sp^2) Insertion with Rh-Carbynoids

The work described in this chapter was performed in collaboration with ***Dr. Zhaofeng Wang****.*

4.1. Introduction

1,3-Dienes represent one of the most versatile and valuable class of organic compounds in the synthesis of natural products,[1,2] therapeutic agents, and polymers.[3] A large number of processes exist in which 1,3-dienes are employed as building blocks, like Diels-Alder reaction,[4] as well as many other cycloaddition reactions[5] and other diene functionalizations.[6] This increasing interest in conjugated dienes has been accompanied by the development of stereo- and regioselective catalytic processes that enable their synthesis.

Metal-catalyzed cross-coupling processes of pre-functionalized alkenyl substrates[7] and alkyne-alkene metathesis[8] remain as the most general strategies. On the other hand, approaches aiming to reach 1,3-dienes directly from alkenes would be ideal given the high availability of olefins both commercially and easily prepared from readily available materials, avoiding the need of pre-functionalized substrates. However, such strategies have not been fully exploited and only few limited examples exist for the moment due to many difficulties involved such as side reactions like polymerization and low efficiencies and selectivities inherent to the process. An alternative to the direct abstraction of hydrogen would be the first generation of the ally cation and consequent generation of the diene by proton elimination. However, examples exploring this path have not been able to isolate the generated dienes along the reaction mainly due to the high temperatures, presence of the oxidant in the reaction mixture as well as the coexistence

[1] (a) Thirsk, C.; Whiting, A. *J. Chem. Soc., Perkin Trans.* **2002**, *1*, 999; (b) Madden, K. S.; Mosa, F. A.; Whiting, A. *Org. Biomol. Chem.* **2014**, *12*, 7877.
[2] (a) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668; (b) Eschenbrenner-Lux, V.; Kumar, K.; Waldmann, H. *Angew. Chem., Int. Ed.* **2014**, *53*, 11146; (c) Xiong, Y.; Sun, Y.; Zhang, G. *Tetrahedron Lett.* **2018**, *59*, 347.
[3] Thiele, S. K. H.; Wilson, D. R.. *Macromol. Sci. - Polym. Rev.* **2003**, *43*, 581.
[4] (a) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668; (b) Corey, E. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 1650.
[5] (a) Robinson, J. E. in *Modern Rhodium-Catalyzed Organic Reactions* (Ed.: P.A. Evans), Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, **2005**, pp. 241; (b) Croatt, M. P.; Wender, P. A. *European J. Org. Chem.* **2010**, 19; (c) Harmata, M. *Chem. Commun.* **2010**, *46*, 8886; (d) Chen, J. R.; Hu, X. Q.; Lu, L. Q.; Xiao, W. J. *Chem. Rev.* **2015**, *115*, 5301.
[6] (a) McNeill, E.; Ritter, T. *Acc. Chem. Res.* **2015**, *48*, 2330.
[7] (a) Paolis, M. D.; Chataigner, I.; Maddaluno, J. *Top. Curr. Chem.*, **2012**, *327*, 87; (b) Soengas, R. G.; Rodríguez-Solla, H. *Molecules* **2021**, *26*, 249.
[8] (a) Kinoshita, A.; Sakakibara, N.; Mori, M. *J. Am. Chem. Soc.* **1997**, *119*, 12388; (b) Diver, S. T.; Giessert, A. J. *Chem. Rev.* **2004**, *104*, 1317; (c) Mori, M.; Kitamura, T. *Compr. Organomet. Chem. III* **2007**, *11*, 271; (d) Mori, M. *Adv. Synth. Catal.* **2007**, *349*, 121; (e) Diver, S. T. *Sci. Synth.* **2013**, *46*, 97; (f) *Handbook of Metathesis*, Vol. 2, (Ed.: R. H. Grubbs, D. J. O'Leary), Wiley, Weinheim, **2015**.

of initial alkene, allyl cation and diene which can cause their polymerization and other undesired side reactions(Figure 1).[9]

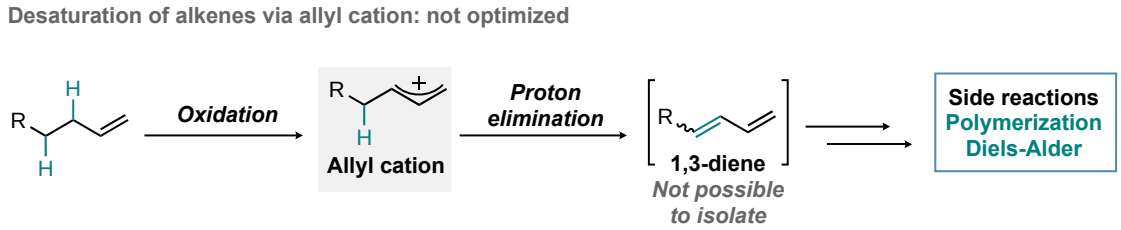


Figure 1 The desaturation of alkenes through the formation of allyl cation has not been fully optimized yet

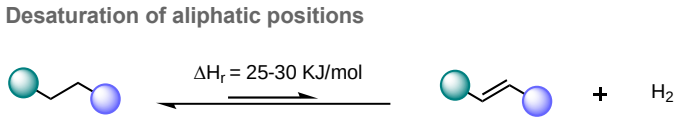
In this sense, the use of novel strategies for the generation of allyl cations by alternative ways might represent a good alternative to synthesize 1,3-dienes from simple alkenes avoiding the difficulties implicated in the direct desaturation of olefins and without using pre-functionalized substrates like in the current methodologies. Furthermore, even though the dehydrogenation of unactivated aliphatics has gained much interest in the last decade and new protocols have been developed, [14b,10] the desaturation of alkenes to form 1,3-dienes remains unattainable.

In this chapter we present a new synthetic methodology for the synthesis of 1,3-dienes from alkenes by the desaturative insertion of Rh-carbynoids into C(sp^2)–C(sp^2) bonds. This process is based on the formation of allyl cations by catalytic cleavage of C=C bonds and subsequent proton elimination to deliver the desired conjugated dienes.

4.2. Synthesis of 1,3-dienes from alkenes

The dehydrogenation of saturated substrates is an impressive tool to produce alkenes (and other unsaturated compounds like dienes) in a simple and atom-economical manner, since it only involves the removal of hydrogen and does not require prefunctionalized starting materials. Such transformation is thermodynamically unfavored, showing an enthalpy of 25–30 KJ/mol (Scheme 1).[11]

[9] (a) Qi, C.; Cong, H.; Cahill, K. J.; Müller, P.; Johnson, R. P.; Porco, J. A. *Angew. Chem., Int. Ed.* **2013**, *52*, 8345; (b) Xu, W. L.; Zhang, H.; Hu, Y. L.; Yang, H.; Chen, J.; Zhou, L. *Org. Lett.* **2018**, *20*, 5774; (c) Xu, W. L.; Hu, W.; Zhao, W. M.; Wang, M.; Chen, J.; Zhou, L. *Org. Lett.* **2020**, *22*, 7169.
[10] Desaturation of aliphatics
[11] Kirsch, S. F.; Wegener, M. Oxidation by Dehydrogenation. *Comprehensive Organic Synthesis*, Second Edition; Elsevier Ltd., 2014; Vol. 7, 1.



Scheme 1

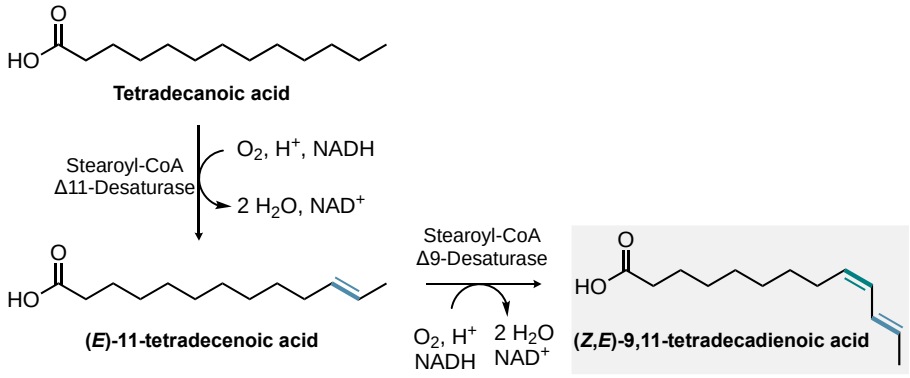
In industry, this issue is addressed using high temperatures and low pressures, removing the hydrogen formed in the system to move the equilibrium toward the formation of the unsaturated product.[12] Furthermore, once the reaction proceeds, it might encounter selectivity problems. In this sense, once a molecule is dehydrogenated, it contains allylic positions which are more reactive towards C–H activation, and in consequence to dehydrogenation, than the aliphatic moiety in the starting material, which could lead to overoxidation (BDE = 95–109 kcal/mol (cycloalkane C–H) and 82–100 kcal/mol (cycloalkene allyl C–H)).[13] In the case of complex molecules with different functional groups and aliphatic positions, multiple reactive sites might be prone to dehydrogenation and it might be quite challenging to perform such transformation in a chemo- and regioselective manner. For these reasons, even though multiple protocols have been developed for the desaturation of alkanes, the generation of dienes from olefins have not had the same fate and only a few examples exist that perform a formal desaturation of alkenes.

Some methodologies have been developed to try to overcome such difficulties. These methodologies are based on (*i*) radical or bio-inspired desaturations,[14] which lack generality and either need the prefunctionalization of the substrates or an external oxidant; (*ii*) desaturations via hydrogen transfer,[15] which show low generality and selectivity; and (*iii*) desaturations via π-allyl complexes[16] and allylic olefinations,[17] which show limited scopes, low yields and the presence of side reactions like polymerization.

[12] Buyanov, R. A.; Pakhomov, N. A. *Kinet. Catal.* **2001**, *42*, 64.
[13] Tian, Z.; Fattahi, A.; Lis, L.; Kass, S. R. *J. Am. Chem. Soc.* **2006**, *128*, 17087.
[14] (a) Ramirez, T. A.; Zhao, B.; Shi, Y. *Tetrahedron Lett.* **2010**, *51*, 1822; (b) Voica, A. F.; Mendoza, A.; Gutekunst, W. R.; Fraga, J. O.; Baran, P. S. *Nat. Chem.* **2012**, *4*, 629.
[15] (a) Lyons, T. W.; D. Guironnet, M. Findlater, M.; Brookhart, M. *J. Am. Chem. Soc.* **2012**, *134*, 15708; (b) Kundu, S.; Lyons, T. W.; Brookhart, M. *ACS Catal.* **2013**, *3*, 1768.
[16] Stang, E. M.; White, M. C. *J. Am. Chem. Soc.* **2011**, *133*, 14892.
[17] (a) Wang, P. S.; Lin, H. C.; Le Zhou, X.; Gong, L. Z. *Org. Lett.* **2014**, *16*, 3332; (b) Li, C.; Li, M.; Zhong, W.; Jin, Y.; Li, J.; Wu, W.; Jiang, H. *Org. Lett.* **2019**, *21*, 872; (c) Shigeno, M.; Kajima, A.; Nakaji, K.; Nozawa-Kumada, K.; Kondo, Y. *Org. Biomol. Chem.* **2021**, *19*, 983.

4.2.1. Alkene desaturation in Nature

The formation of dienes by dehydrogenation of alkenes is broadly found in Nature catalyzed by a family of enzymes called desaturases. These natural enzymes are present in nearly all the organisms discovered and are essential for the structural integrity of the biological membranes.[18] In membrane glycerolipids, some unsaturations provide fluidity, necessary for the activation of certain membrane-bound enzymes. In order to maintain such fluidity in the cell membrane when temperature changes, membrane lipids are able to get saturated and unsaturated selectively. Apart from membrane fatty acids, desaturases are fundamental for the synthesis of a broad range of unsaturated fatty acids with important biological properties in all sorts of living systems (like the synthesis of *Z*,*E*-9,11-tetradecadienoate, which is the main component of the sex pheromone of *Spodoptera litoralis* moths,[19] shown in Scheme 2), from plants and bacteria to animals, fungal and yeast cells.



Scheme 2 Desaturation of (*E*)-tetradecenoic acid by Δ9-desaturase

Desaturases are part of the oxygenases biocatalysts family and are formed by a high-valent di-iron core surrounded by non-heme carboxylate ligands (structure of the Δ9 desaturase from castor bound to the acyl carrier protein is shown in Figure 2[20]).[21] It is known that small changes in their ligand structure change their activity, allowing it to perform different reactions (apart from desaturations, they are able to perform different

[18] Los, D. A.; Murata, N. *Biochim. Biophys. Acta* **1998**, *1394*, 3.
[19] Abad, J. L.; Camps, F.; Fabriàs, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 3279.
[20] Guy, J. E.; Whittle, E.; Moche, M.; Lengqvist, J.; Lindqvist, Y.; Shanklin, J. *Proc. Natl. Acad. Sci.*, **2011**, *108*, 16594.
[21] Lee, D.; Lippard, S. J. Nonheme Di-Iron Enzymes. In *Comprehensive Coordination Chemistry II*; Elsevier Ltd, 2003; pp 309–342.

oxidative reactions like hydroxylation, epoxidation or dihydroxylation), perform it to different substrates or changing the site selectivity of the reaction.

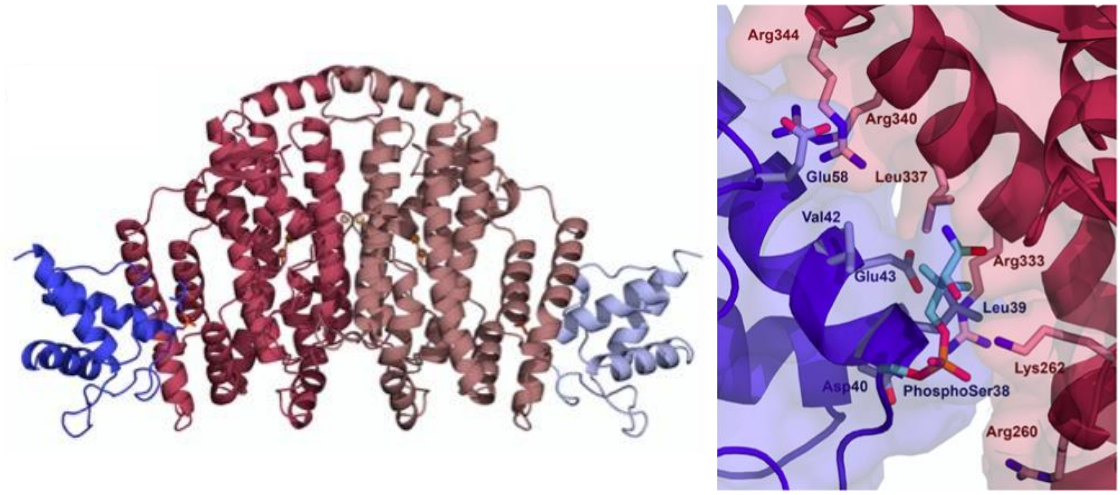
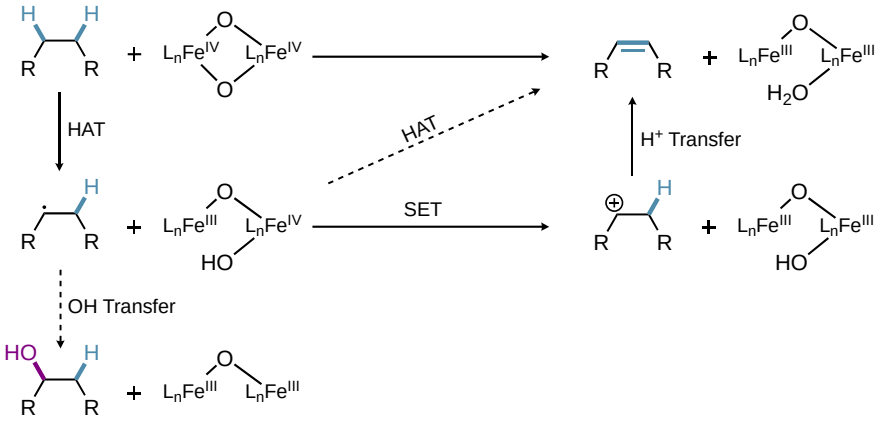


Figure 2 Structure of the Δ9 acyl carrier protein desaturase, responsible of desaturating the position 9 of multiple fatty acids

The proposed mechanism for the desaturation catalyzed by desaturases proceeds through a first Hydrogen Atom Transfer (HAT) from the substrate to the oxo iron complex. The carbon-radical formed generates the desired unsaturated product either by a second HAT or by a first Single Electron Transfer (SET), followed by a proton transfer to the catalyst (Scheme 3).[22] It has also been observed that depending on the substrate, hydroxylation of the first radical formed could take place by the same catalyst as a by-product. Two main parameters have been proven to favor the desaturation in front of the hydroxylation: the *syn*-periplanar alignment of the C–H bond to be cleaved and the half-filled orbital together with the positioning of the iron hydroxyl catalyst closer to the hydrogen to be removed rather than the radical carbon atom.

[22] Buist, P. H. *Nat. Prod. Rep.* **2004**, *21*, 249.



Scheme 3 Proposed mechanism for the desaturation of fatty acids by desaturases

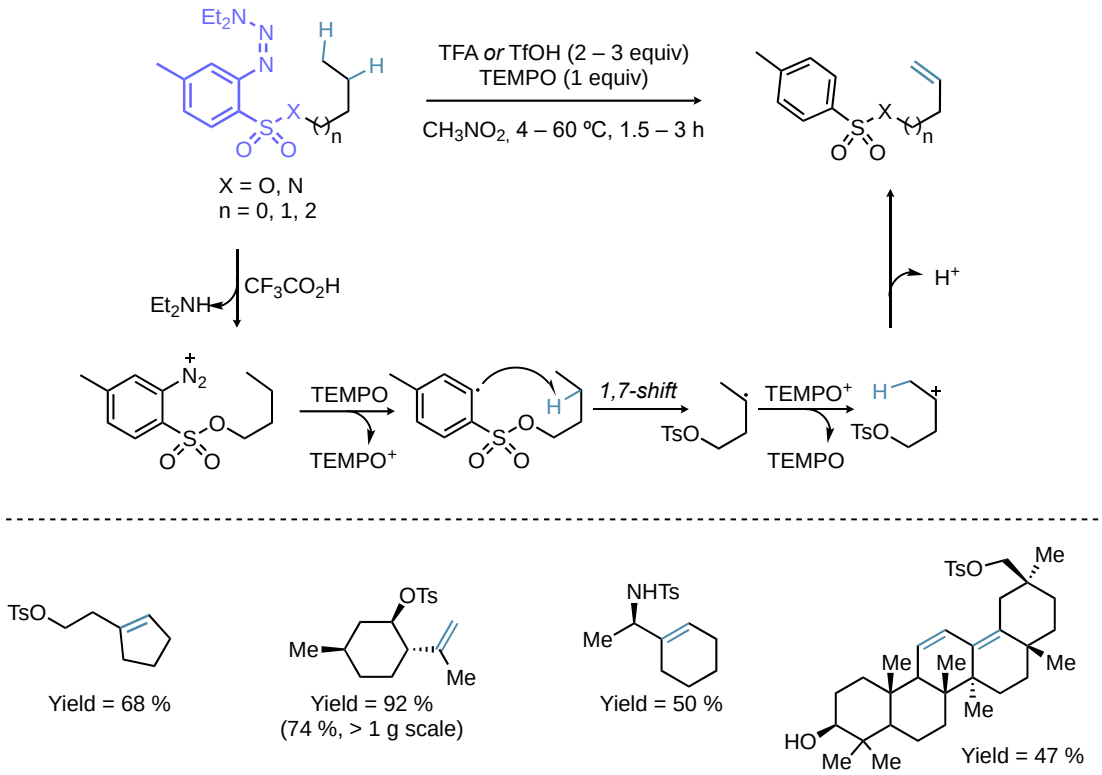
4.2.2. Bio-inspired alkene desaturations

Most of the unnatural dehydrogenation models are inspired by the enzymatic desaturations, following very similar mechanisms. Nevertheless, in these cases it is more difficult to find desaturations of alkenes compared to the desaturation of alkanes.

One of the first methodologies developed for the desaturation of aliphatics of this kind was the internal hydrogen abstraction. This strategy is based on the use of labile, internal functional groups able to cleave the desired C–H bond and due to their proximity, perform it with high regioselectivity.[14b,23,24] One prominent example in this category is shown in scheme X. The group of Baran, inspired by the seminal work from Breslow[25], developed a methodology in which a triazenyl *p*-toluolsulfonyl group was attached to the substrate and used for the desaturation of aliphatic moieties.[14b] When in presence of triflic or trifluoroacetic acid, the triazenyl group cleaves forming the aryl diazonium species and releasing the amine. Then, a SET by TEMPO takes place, forming the aryl radical which undergoes a 1,7-hydrogen shift to give the corresponding tosylate group and alkyl radical. Next, the oxopiperidinium cation ($TEMPO^+$) formed by the oxidation of TEMPO gets reduced back to TEMPO generating the alkyl cation, which finally forms the olefin by proton elimination (Scheme 4). Baran showed a much higher functional group tolerance and broader substrate scope compared to the previous approaches, using both alcohol and amine substituted substrates and being able to desaturate simple molecules, like the cyclopentanyl example showed above, as well as complex ones such as natural products,

[23] (a) Parasram, M.; Chuentragool, P.; Sarkar, D.; Gevorgyan, V. *J. Am. Chem. Soc.* **2016**, *138*, 6340; (b) Chuentragool, P.; Parasram, M.; Shi, Y.; Gevorgyan, V. *J. Am. Chem. Soc.* **2018**, *140*, 2465.
[24] Parasram, M.; Chuentragool, P.; Wang, Y.; Shi, Y.; Gevorgyan, V. *J. Am. Chem. Soc.* **2017**, *139*, 14857.
[25] Breslow, R.; Baldwin, S.; Flechtner, T.; Kalicky, P.; Liu, S.; Washburn, W. *J. Am. Chem. Soc.* **1973**, *95*, 3251.

peptides or an olefinic steroid to form the diene, even though it is the only example of alkene desaturation. On the other hand, the average yields are moderate and in some cases the product is obtained together with a non-oxidized side product.

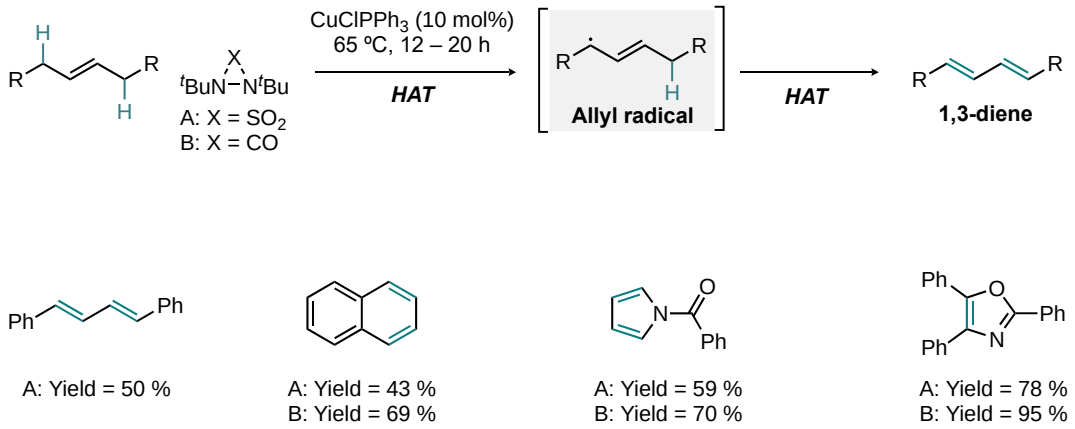


Scheme 4 Example from the group of Baran of desaturation by internal hydrogen abstraction

Similar approaches were used for the desaturation of other substrates with labile groups like hydroperoxides[26], bromo- and iodoarenes[23,27] (and other iodine-containing moieties)[24] or even directing groups that serve as ligands for the metal-catalyzed hydrogen abstraction.[28] The main drawback of the internal dehydrogenation strategy is the need of pre-functionalized substrates and the unfeasibility to desaturate simple chemical feedstocks. Furthermore, this strategy has been applied mostly to the formation of alkenes from alkanes. To the best of our knowledge, the example from Baran is the only one that has been reported showing the desaturation of alkenes to synthesize dienes.

[26] (a) Caramella, P.; Huisgen, R.; Schmolke, B. *J. Am. Chem. Soc.* **1974**, *96*, 3000; (b) Acott, B.; Beckwith, A. L. J. *Aust. J. Chem.* **1964**, *17*, 1342.
[27] (a) Baudoin, O.; Herrbach, A.; Guéritte, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 5736; (b) Motti, E.; Catellani, M. *Adv. Synth. Catal.* **2008**, *350*, 565.
[28] (a) Johnson, J. A.; Sames, D. *J. Am. Chem. Soc.* **2000**, *122*, 6321; (b). *J. Am. Chem. Soc.* **2002**, *124*, 6900.

Some authors like Que,[29] Morandi,[30] Sorensen[31] or Pérez[32] have developed different non-enzymatic approaches for the dehydrogenation of aliphatics using external oxidants. However, again few examples exist that apply it to the desaturation of alkenes. One of the only examples is shown in scheme X.[33] In this work from Shi, a thiadiaziridine (previously used in the same group for the dehydrogenative deamination of alkenes)[34] serves as oxidant for the Cu(I)-catalyzed desaturation of alkenes. The reaction proceeds through the first radical formation in the thiadiaziridine molecule which is able to abstract an allylic hydrogen from the alkene forming the corresponding allyl radical. Such radical undergoes the same process again to finally form the diene, together with the sulfamide as a side product. However, this strategy offers moderate yields and limited scope –10 examples and not being possible to use terminal alkenes–.



Scheme 5 Example of desaturation from the group of Shi by external oxidation of alkene's allylic positions

4.2.3. Alkene desaturation via transfer-dehydrogenation

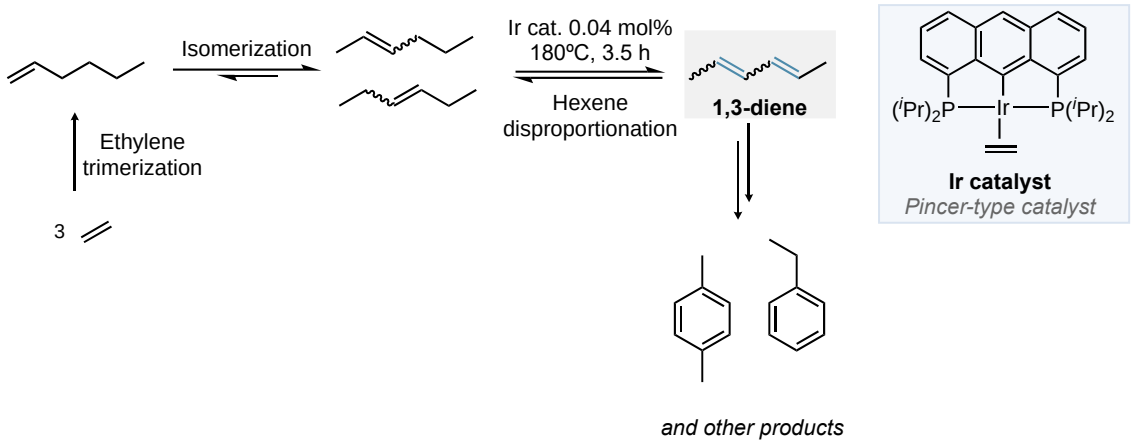
Even though heterogeneous catalysts are commonly used in industrial lower hydrocarbon dehydrogenation, their harsh reaction conditions and low selectivity limit

[29] (a) Dong, Y.; Fujii, H.; Hendrich, M. P.; Leising, R. A.; Pan, G.; Randall, C. R.; Wilkinson, E. C.; Zang, Y.; Que, L.; Fox, B. G.; Kauffmann, K.; Münck, E. *J. Am. Chem. Soc.* **1995**, *117*, 2778; (b) Kim, C.; Dong, Y.; Que L., J. *J. Am. Chem. Soc.* **1997**, *119*, 3635.
[30] Huang, L.; Bismuto, A.; Rath, S. A.; Trapp, N.; Morandi, B. *Angew. Chem., Int. Ed.* **2021**, *60*, 7290.
[31] West, J. G.; Huang, D.; Sorensen, E. J. *Nat. Commun.* **2015**, *6*, 1.
[32] Conde, A.; Vilella, L.; Balcells, D.; Díaz-Requejo, M. M.; Lledós, A.; Pérez, P. J. *J. Am. Chem. Soc.* **2013**, *135*, 3887.
[33] Ramirez, T. A.; Zhao, B.; Shi, Y. *Tetrahedron Lett.* **2010**, *51*, 1822.
[34] Wang, B.; Du, H.; Shi, Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 8224.

their application in alkane and alkene desaturation.[35] Instead, the C–H bond activation by homogeneous transition metal catalysts offers a good alternative for the selective dehydrogenation of higher hydrocarbons. The first stoichiometric hydrocarbon dehydrogenation by homogeneous complexes was reported by the group of Crabtree in 1979, where cyclooctene was transformed into 1,4-cyclooctadiene[36]. Since then, many catalytic variants have been developed for the desaturation of hydrocarbons, specially using pincer-ligated catalysts. These catalysts have been broadly used in the desaturation of aliphatic compounds.[37] In the case of alkenes however, their dehydrogenation can be more problematic. In all the examples reported, the reaction produces a mixture of products which can be quite complex, mainly due to (*i*) the use of sacrificial alkenes (which are not fully converted), (*ii*) low yields (with respect to diene obtained) and (*iii*) side reactions (Diels-Alder reactions between the final diene and alkenes present or between two diene molecules). These issues, together with the use of harsh reaction conditions, make it difficult to use such procedures for the synthesis of 1,3-dienes by alkene dehydrogenation.

The group of Brookhart is one of the only that persued to desaturate alkenes for the synthesis of 1,3-dienes.[38] One of their most representative examples might be a work from 2012 where hexadiene is synthesized from ethylene through the dehydrogenation of hexene (Scheme 6).[39] The reaction proceeds through the first trimerization of ethylene to form a mixture of hexenes (1-hexene is initially formed but it rapidly isomerizes to form internal hexenes). Once the alkenes are formed, they disproportionate (one equivalent of alkene acts as hydrogen acceptor of a second equivalent) to form hexadiene, in a reaction catalyzed by Ir pincer catalysts at 180 ºC. After 3.5 h the equilibrium is reached and a mixture of products is obtained, containing a mixture of *n*-hexane, hexenes (internal alkenes mainly) and hexadienes (also with internal 2,4-hexadienes as the main isomers) in a nearly equimolar proportion.

[35] (a) Buyanov, R. A.; Pakhomov, N. A. *Kinet. Catal.* **2001**, *42*, 64; (b) Nawaz, Z. *Rev. Chem. Eng.* **2015**, *31*, 413.
[36] Crabtree, R. H.; Mihelcic, J. M.; Quirk, J. M. *J. Am. Chem. Soc.* **1979**, *101*, 7738.
[37]
[38] Kundu, S.; Lyons, T. W.; Brookhart, M. *ACS Catal.* **2013**, *3*, 1768.
[39] Lyons, T. W.; Guironnet, D.; Findlater, M.; Brookhart, M. *J. Am. Chem. Soc.* **2012**, *134*, 15708.

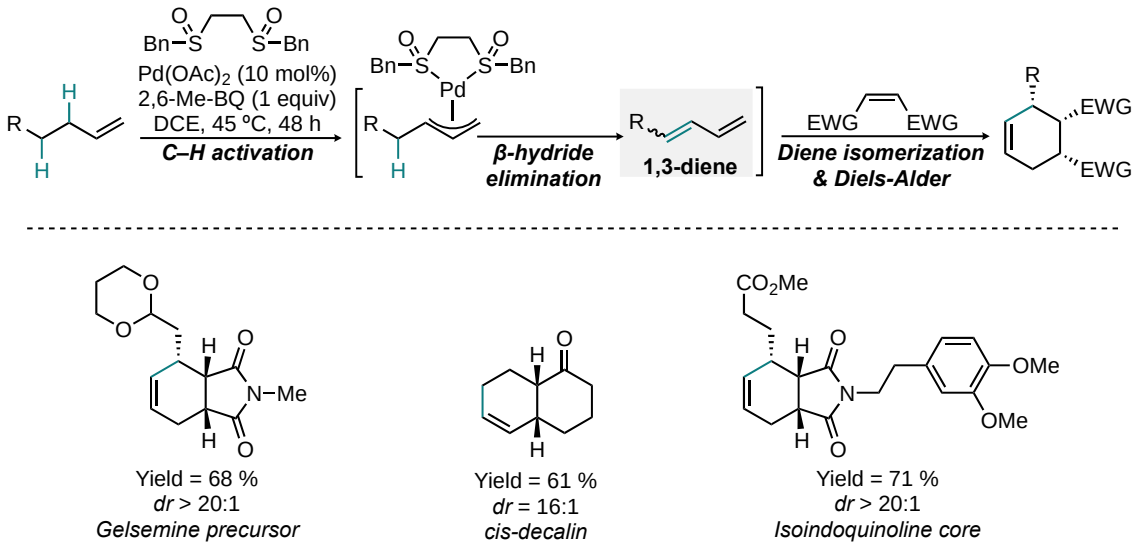


Scheme 6 Example from Brookhart of desaturation of alkenes by hydrogen transfer

Even though the group of Brookhart found application of these results in the synthesis of xylenes by Diels-Alder reaction of the hexadienes formed and subsequent dehydrogenation, they might not be very useful for the selective alkene dehydrogenation.

4.2.4. Alkene desaturation via π-allyl complexes

A similar but more selective approach was employed by the group of White, in which a Pd catalyst was used for the generation of π-allyl species by C–H activation from alkenes (Scheme 7).[16] The reaction proceeds through the first allylic hydrogen atom abstraction with an external oxidant (2,6-dimethyl-1,4-benzoquinone in this case) to form the Pd π-allyl complex. Finally, the 1,3-diene is formed by a β-hydride elimination. Nevertheless, the dienes could not be isolated in acceptable yields, due to side reactions like polymerization –as the authors claimed–, and instead they were engaged in [4+2] cycloaddition reactions to form complex bicyclic structures in moderate to excellent yields and diastereoselctivity.



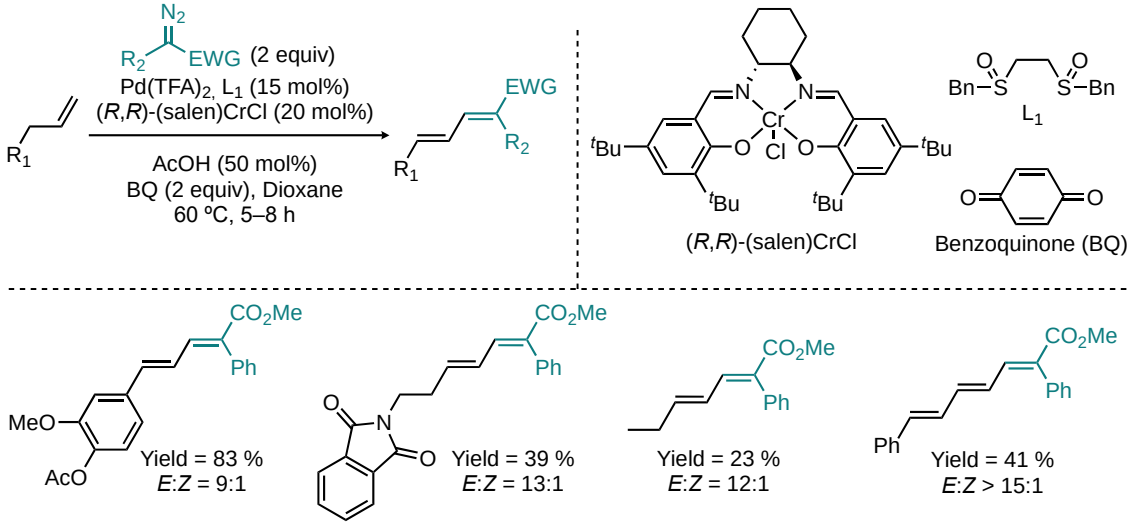
Scheme 7 Example from the group of White of desaturation of alkenes via π-allyl complexes

A similar strategy has also been employed for the generation of allyl cations.[40] However, this route has not been fully exploited for the synthesis of conjugated dienes, and normally the dienes generated along the reaction undergo [4+2] cycloadditions for the synthesis of cyclohexenes in a dehydrogenative Diels-Alder reaction,[41] like in White's work, and other reactions.[42] However, following this approach, the group of Gong found a way to form 1,3-dienes from Pd-π-allyl complexes via allylic olefination with diazo compounds.[17a] In this case, they used the same catalytic system developed by White to generate the π-allyl complexes from terminal olefins and then, they performed a Cr(III)-catalyzed diazo transfer for the synthesis of 1,3-dienes. Similar allylic olefinations have been developed lately following the idea of Gong.[17b,c] Even though it is a good alternative to the direct desaturation, this methodology is restricted to terminal alkenes, the yields are moderate to low in most of the cases and it requires the use of an external oxidant as well as Cr(III) as co-catalyst.

[40] (a) Cheng, D.; Bao, W. *Adv. Synth. Catal.* **2008**, *350*, 1263; 4) Li, Y.; Bao, W. *Adv. Synth. Catal.* **2009**, *351*, 865; (b) Mo, H.; Bao, W. *J. Org. Chem.* **2010**, *75*, 4856; (c) Wang, T.; Xiang, S. K.; Qin, C.; Ma, J. A.; Zhang, L. H.; Jiao, N. *Tetrahedron Lett.* **2011**, *52*, 3208; (c) Wang, Z.; Mo, H.; Cheng, D.; Bao, W. *Org. Biomol. Chem.* **2012**, *10*, 4249; (d) Kong, S.; Zhang, L.; Dai, X.; Tao, L.; Xie, C. *Adv. Synth. Catal.* **2015**, *357*, 2453; (e) Chen, Q.; Wen, C.; Wang, X.; Yu, G.; Ou, Y.; Huo, Y.; Zhang, K. *Adv. Synth. Catal.* **2018**, *360*, 3590; (f) Xu, T. T.; Jiang, T. S.; Han, X. L.; Xu, Y. H.; Qiao, J. P. *Org. Biomol. Chem.* **2018**, *16*, 5350.

[41] (a) Stang, E. M.; White, M. C. *J. Am. Chem. Soc.* **2011**, *133*, 14892; (b) Qi, C.; Cong, H.; Cahill, K. J.; Müller, P.; Johnson, R. P.; Porco, J. A. *Angew. Chem., Int. Ed.* **2013**, *52*, 8345; (c) Li, W.; Zhou, L.; Zhang, J. *Chem. - A Eur. J.* **2016**, *22*, 1558; (d) Jiang, B.; Liang, Q. J.; Han, Y.; Zhao, M.; Xu, Y. H.; Loh, T. P. *Org. Lett.* **2018**, *20*, 3215; (e) Xu, W. L.; Zhang, H.; Hu, Y. L.; Yang, H.; Chen, J.; Zhou, L. *Org. Lett.* **2018**, *20*, 5774; (f) Xu, W. L.; Tang, L.; Ge, C. Y.; Chen, J.; Zhou, L. *Adv. Synth. Catal.* **2019**, *361*, 2268.

[42] Du, H.; Yuan, W.; Zhao, B.; Shi, Y. A *J. Am. Chem. Soc.* **2007**, *129*, 7496.



Scheme 8 Example from the group of Gong for the allylic olefination via π-allyl complexes

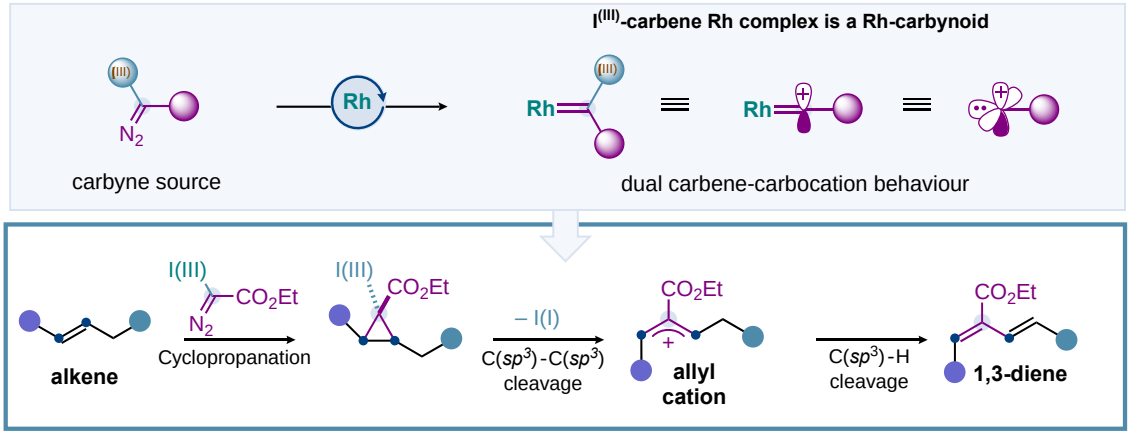
In summary, the desaturation of alkenes *via* either allyl cations or π-allyl complexes has not been achieved yet. Even though there are some methods that reach the desired conjugated dienes, they cannot be obtained selectively and normally side reactions like Diels-Alder and polymerization take place.

4.3. Catalytic desaturative C(sp^2)–C(sp^2) insertion with Rh-carbynoids

4.3.1. Hypothesis of the project

As it has been presented in the introduction, few examples exist in the literature able to form conjugated dienes starting from alkenes, either through direct desaturation or other protocols, and the few that exist show small scopes, low yields and the need of external oxidants/reductants. In few words: there is not a general catalytic methodology to transform olefins into conjugated dienes.

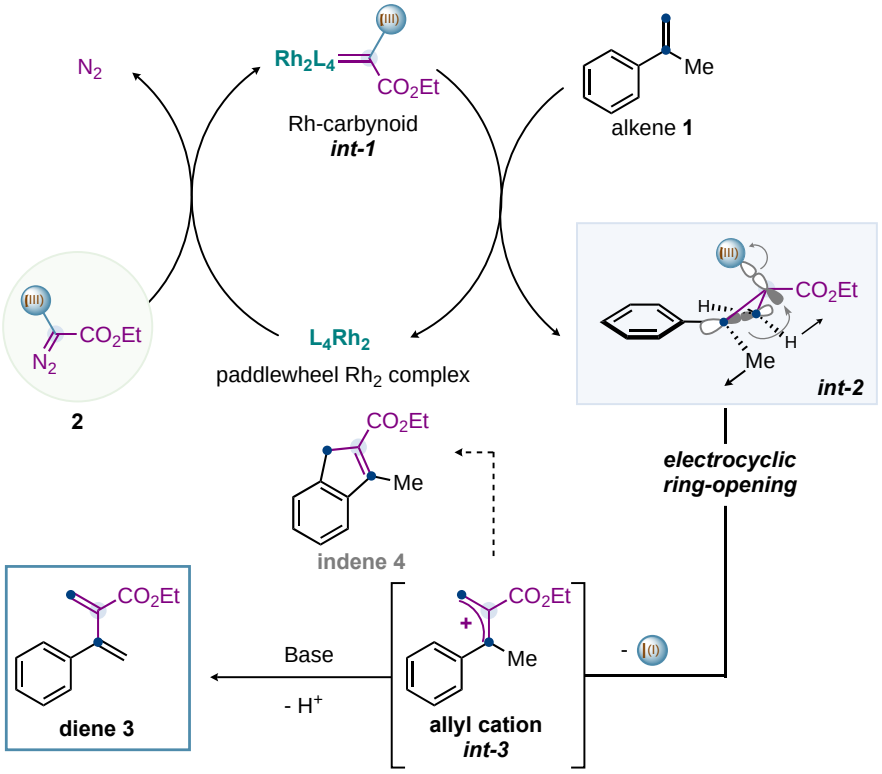
While developing the projects from Chapter II and III, we observed by crude NMR the formation of traces of dienes as byproducts of the reactions. For these reasons, we believed it was possible to obtain 1,3-dienes from alkenes by applying our carbyne transfer platform, previously used for the synthesis of allylic building blocks and allylic fluorides (Scheme 9).



Scheme 9

4.3.2. Proposed mechanism

The mechanism we envisaged was similar to the one from the previous chapters (Scheme 10): first of all, the selective diazo activation of reagent **2** with a paddlewheel dirhodium complex L_4Rh_2 would conduct to a highly electrophilic Rh-carbynoid ***int-1***. In presence of an alkene, ***int-1*** would cyclopropanate it to generate a transient cyclopropyl-$I^{(III)}$ intermediate ***int-2***. Considering the outstanding leaving group ability of hypervalent iodine moiety, we thought ***int-2*** would open in concert with the departure of the $I^{(III)}$ leaving group. Such ring opening would happen through a disrotatory mode, following the Woodward–Hoffmann–DePuy rules. This process would lead to a putative allylic cation ***int-3*** able to provide a 1,3-diene **3** by proton elimination. In order to get high rection efficiency and avoid side reactions like polymerization or the cyclisation of the allyl cation to form the corresponding indene **4**, it would be key to find a base able to selectively abstract the proton in ***int-3*** and lead to the desired product. The nucleophilicity of such base needs to be as low as possible not to attack the allyl cation generated.



Scheme 10 Proposed mechanism

4.3.3. Reaction optimization

We embarked on this journey by reproducing the optimized protocol from Chapter II but without adding any nucleophile: a solution of **2a** was added on top of a solution of $Rh_2(esp)_2$ with 2 equivalents of α-methyl-styrene during 1 hour at -50 ºC without the presence of a nucleophile. After the salt addition, once it was fully consumed by TLC, the temperature was increased to room temperature. Using these reaction conditions, the corresponding 1,3-diene **3a** was obtained in 14 % of yield, together with indene **4a** as a side product (Table 1, Entry 1). With these encouraging results, we recognized that the key to achieve high conversion would rely on the use of an appropriate proton acceptor, compatible with ***int-2*** and ***int-3*** (Figure X), not nucleophilic, favouring the formation of diene **3a** in front of the side product **4a**. First, we tried different inorganic and organic bases but no improvement in the yield was observed, probably due to low solubility and too high nucleophilicity respectively (Table 1, Entries 2 – 9). Seeing that the yields could not be improved, we thought about using a proton acceptor that even if it acted as a nucleophile, the corresponding product would not be stable and would eliminate forming the desired elimination product.

In this sense, when TBAOMs and TBAOTs were used, the yield rose to 39 % and 52 % respectively (Table 1, Entries 10–11). We were impressed to find that if TBAOTf was used, excellent selectivity was achieved (99 % yield; Table 1, Entry 12). Furthermore, in the three cases the formation of indene **4a** was completely suppressed. Regarding the function of triflate in the reaction, even though it can act as a mild proton acceptor,[43] we cannot discard that its high performance relies on its ability to attack the carbocation, forming an allylic triflate which might be highly prone to eliminate to form the diene (Figure 2, ***int-4*** and ***int-5***).[44] Finally, we showed that $Rh_2(esp)_2$ and ethanoate hypervalent salt **2a** were the best catalyst and substrate for the reaction (Table 1, Entries 14–18).

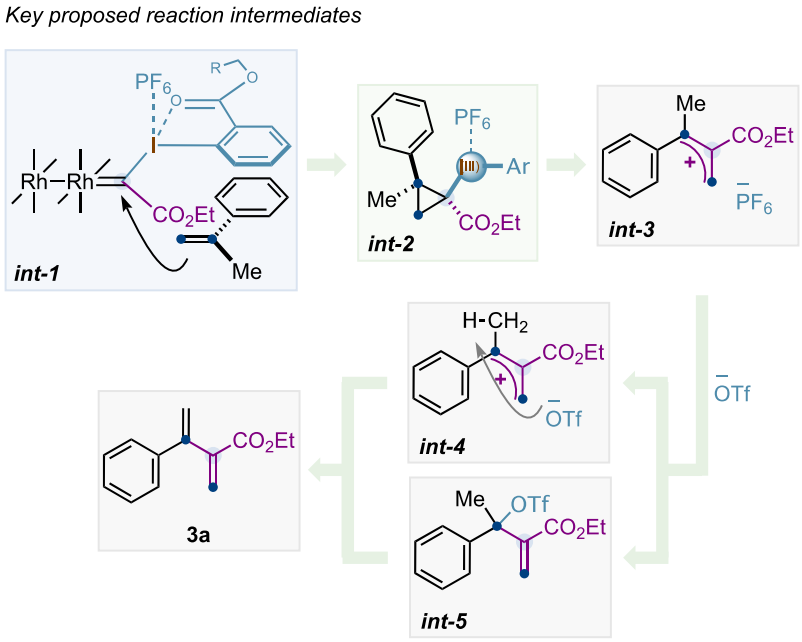
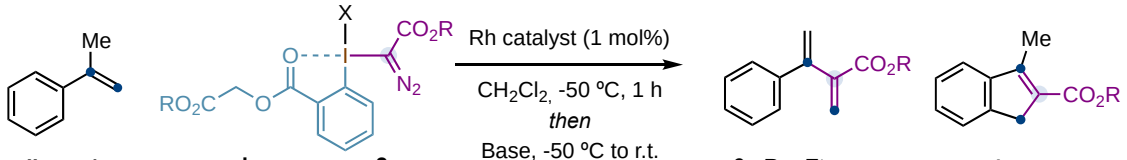


Figure 3 Proposed mechanisms for the action of triflate

[43] Reddy, G. S.; Corey, E. J. *Org. Lett.* **2021**, *23*, 3399.
[44] Dhakal, B.; Bohé, L.; Crich, D. *J. Org. Chem.* **2017**, *82*, 9263.



alkene 1a

carbyne source 2
2a R = Et; X = PF_6
2b R = CH_2Ph; X = PF_6
2c R = CH_2CCl_3; X = PF_6
2a-OTf R = Et; X = PF_6

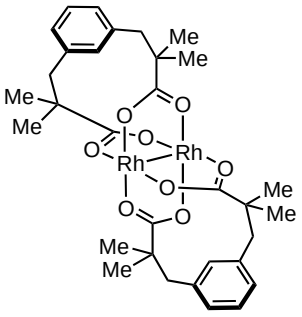
3a R = Et
3b R = CH_2Ph
3c R = CH_2CCl_3

4

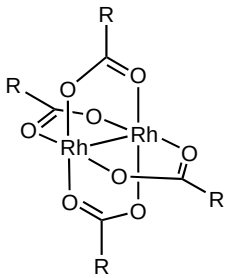
Entry	Catalyst	Carbyne source	Base	**3a-c**	**4**
1	$Rh_2(esp)_2$	2a	-	14 %	7 %
2	$Rh_2(esp)_2$	2a	$NaHCO_3$	9 %	< 5 %
3	$Rh_2(esp)_2$	2a	Na_2CO_3	5 %	24 %
4	$Rh_2(esp)_2$	2a	K_2HPO_4	14 %	< 5 %
5	$Rh_2(esp)_2$	2a	NaOAc	8 %	5 %
6	$Rh_2(esp)_2$	2a	NaOBz	18 %	6 %
7	$Rh_2(esp)_2$	2a	DBU	10 %	nd[b]
8	$Rh_2(esp)_2$	2a	DABCO	9 %	nd
9	$Rh_2(esp)_2$	2a	DTBPy	10 %	5 %
10	$Rh_2(esp)_2$	2a	TBAOMs	39 %	nd
11	$Rh_2(esp)_2$	2a	TBAOTs	52%	nd
12	$Rh_2(esp)_2$	2a	TBAOTf	99 %	nd
13	$Rh_2(esp)_2$	2a	TBAOTf	20 %[c]	9 %
14	$Rh_2(OAc)_4$	2a	TBAOTf	23 %	nd
15	$Rh_2(hfb)_2$	2a	TBAOTf	0 %	nd
16	$Rh_2(Adc)_4$	2a	TBAOTf	54 %	4 %
17	$Rh_2(esp)_2$	2b	TBAOTf	72 %	nd
18	$Rh_2(esp)_2$	2c	TBAOTf	48 %	nd
19	$Rh_2(esp)_2$	2a-OTf	-	< 5 %	5 %

[a]Yields are reported on the basis of ^1H NMR analysis using anisole as internal standard. [b]nd = not detected [c]1 equiv of TBAOTf was added. DBU = 1,8-diazabicyclo(5.4.0)undec-7-ene; DABCO = 1,4-diazabicyclo[2.2.2]ocatane; DTBPy = 2,6-di-^{t}Bu-pyridine; hfb = heptafluorobutyrate; Adc = 1-adamantylcarboxylate; esp = α,α,α′,α′-tetramethy-1,3-benzenedipropanoate.

Rh(II) catalysts

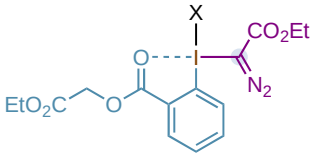


$Rh_2(esp)_2$

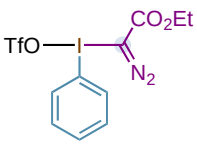


$Rh_2(OAc)_4$ R = CH_3
$Rh_2(Adc)_4$ R = 1-adamantyl
$Rh_2(TPA)_4$ R = CPh_3

Carbyne sources 2



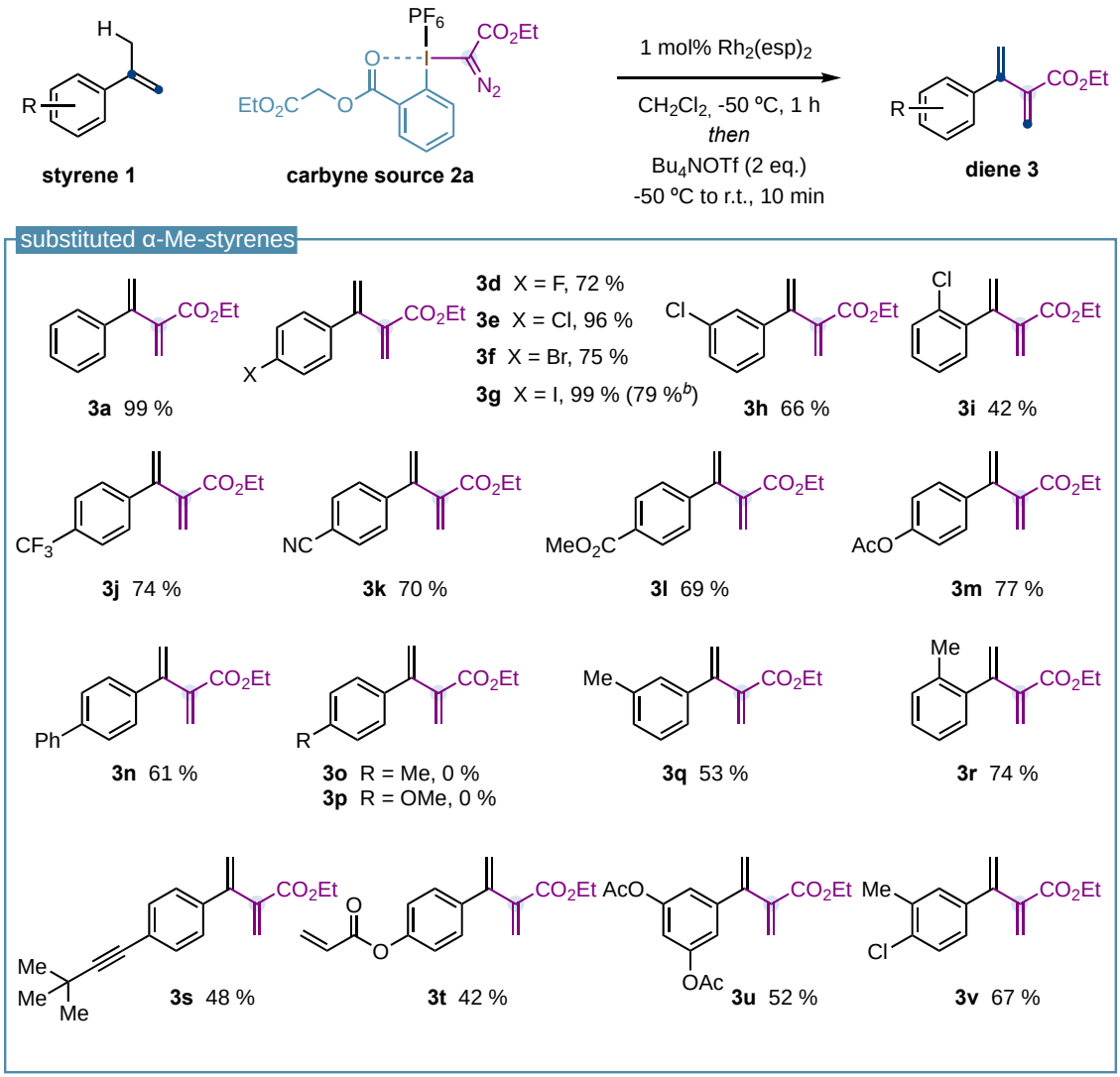
X = PF_6 (**2a**),
OTf (**2a-OTf**), BF_4 (**2a-BF_4**)



2b

4.3.4. Scope of the catalytic desaturative C(sp^2)–C(sp^2) insertion with Rh-carbynoids

Once we had the optimized reaction conditions, we evaluated the scope of the reaction. We first investigated the role of the substituents in the aromatic ring. Our protocol was suitable for a broad range of styrenes, substituted with halides in *para*-, *meta*- and *ortho*- positions (**3d**–**3i**; 42 – 99 % of yield) as well as strong electron withdrawing groups such as trifluoromethyl (**3j**), cyano (**3k**) and methyl ester (**3l**) in moderate to excellent yields (69 – 74 % of yield). Our methodology was able to tolerate electron-richer substituents such as acetate and phenyl moieties (**3m** and **3n** respectively). Even though the reaction did not work with highly electron-rich substituents like methyl and methoxy (**3o** and **3p**) in the *para*- position, we were able to obtain the desired products in moderate to good yields when methyl was placed in both *meta*- and *ortho*- positions (**3q** and **3r**). The presence of strong electron-donating groups in the *para*- position might increase the rate in the cyclopropyl ring opening and in consequence, enhance the polymerization, since full consumption of the olefin but no product was detected in the reaction. Apart from this, we were also glad to see that our reaction was chemoselective over triple bonds (**3s**) and electron-deficient olefins (**3t**). Disubstituted styrenes (**3u** and **3v**) proved to work in moderate to good yields too (52 % and 67 % of yield respectively).

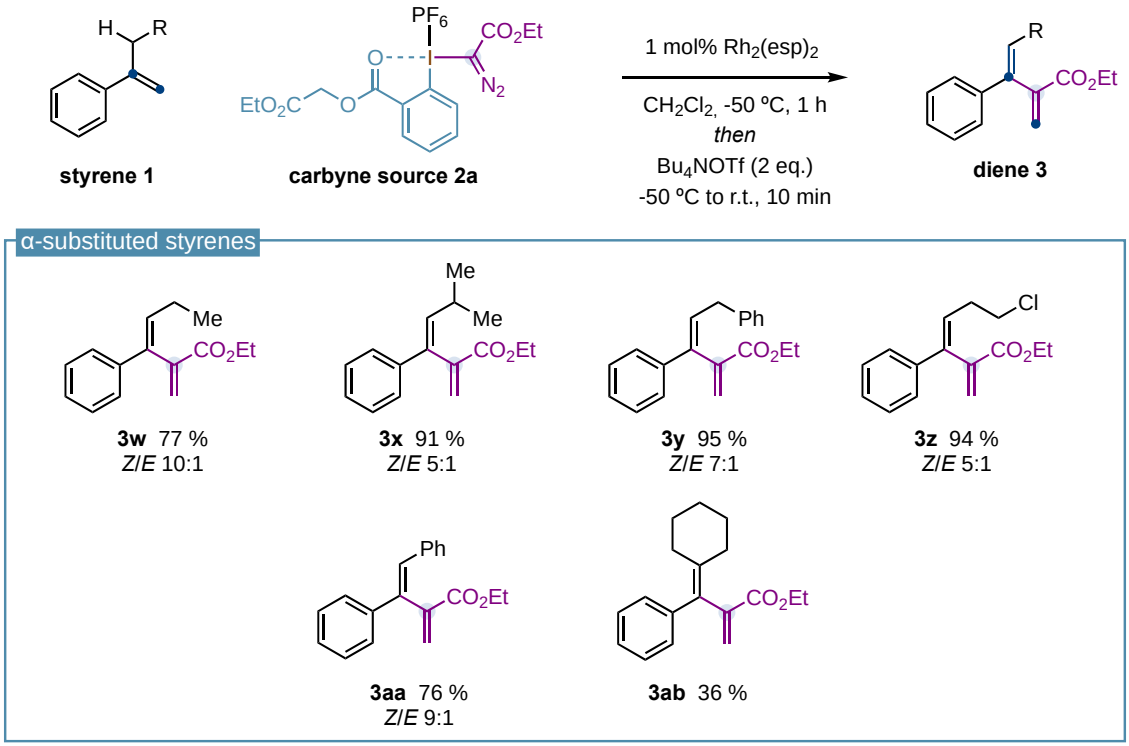


[a] Performed with **1** (0.4 mmol, 2 equiv), **2a** (0.2 mmol, 1 equiv), $Rh_2(esp)_2$ (0.002 mmol, 1 mol%), Bu_4NOTf (0.4 mmol, 2 equiv) in CH_2Cl_2 (0.067 M); Yields are reported on the basis of isolated pure product; [b] Yield of isolated product using 1.7 grams of **1g** (5.2 mmols, 1.0 equiv) and 4.2 grams of **2a** (7.1 mmols, 1.4 equiv); esp = α, α, α′, α′-tetramethy-1,3-benzenedipropanoate.

Table 2 Substrate scope: substituted α-Me-styrenes

We next wondered whether we could form 1,3-dienes containing tri- and tetra-substituted dienes. Substituents other than methyl in the α-position of styrenes would allow us to form 1,3-dienes containing two double bonds with different substitution patterns, one of which might be tri- or even tetra-substituted. Our hypothesis proved to be right and we were able to apply this methodology to a range of α-substituted styrenes bearing different moieties like Et, *i*Pr, CH_2Ph, CH_2CH_2Cl and Ph in good to excellent yields (**3w**–**3aa**; 76 – 95 % of yield). It is important to mention that in all cases the *Z* isomer was obtained preferentially, with *Z*/*E* ratios from 5:1 to 10:1 depending on the steric hinderance played by the substituent. We could also form the tetra-substituted alkene using the cyclohexyl α-substituted styrene, even though in moderate yield (**3ab**). The decrease in yield might be due to the steric hinderance played by the cyclohexyl

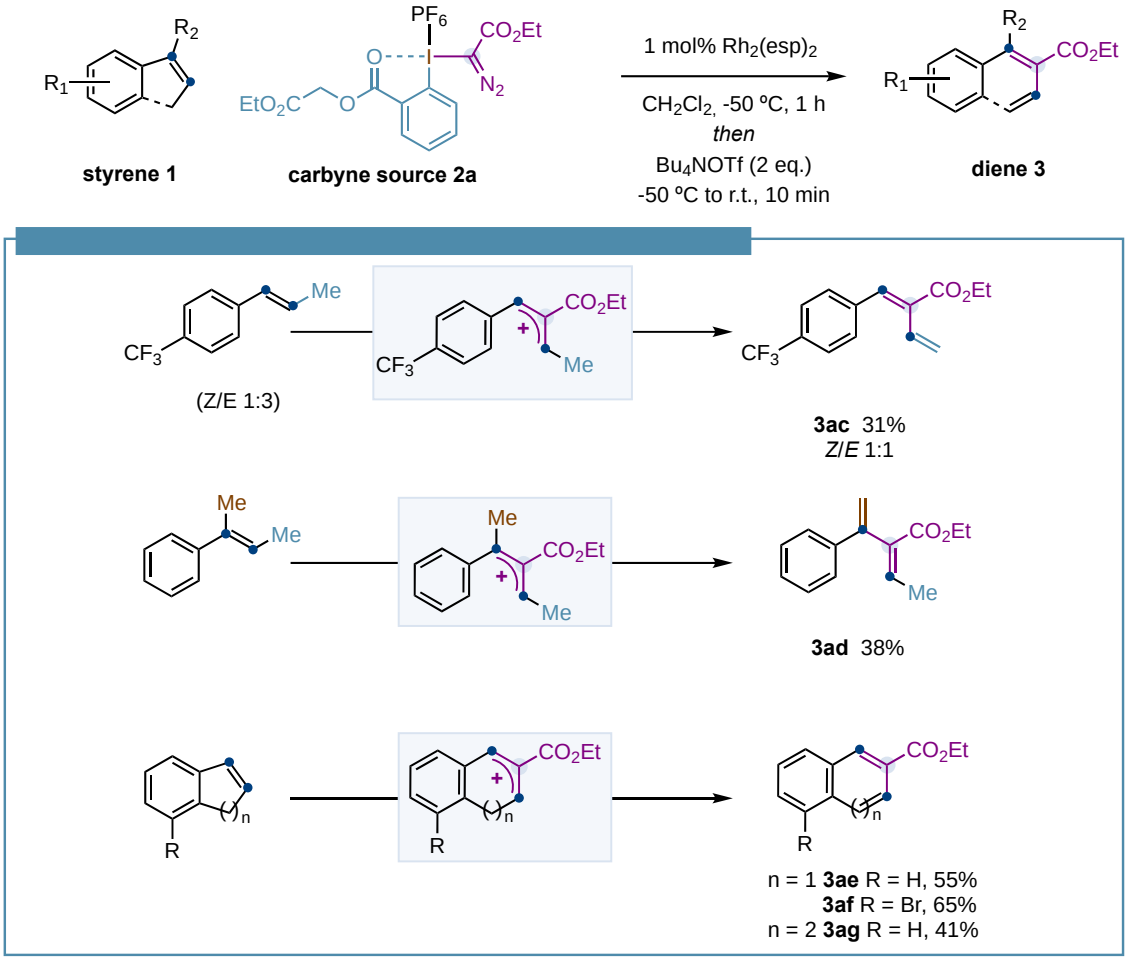
group, that did not favor neither the cyclopropanation nor the correct placement of the proton for its elimination.



[a] Performed with **1** (0.4 mmol, 2 equiv), **2a** (0.2 mmol, 1 equiv), $Rh_2(esp)_2$ (0.002 mmol, 1 mol%), Bu_4NOTf (0.4 mmol, 2 equiv) in CH_2Cl_2 (0.067 M); Yields are reported on the basis of isolated pure product.esp = α, α, α′, α′-tetramethy-1,3-benzenedipropanoate.

Table 3 Substrate scope: α-substituted styrenes

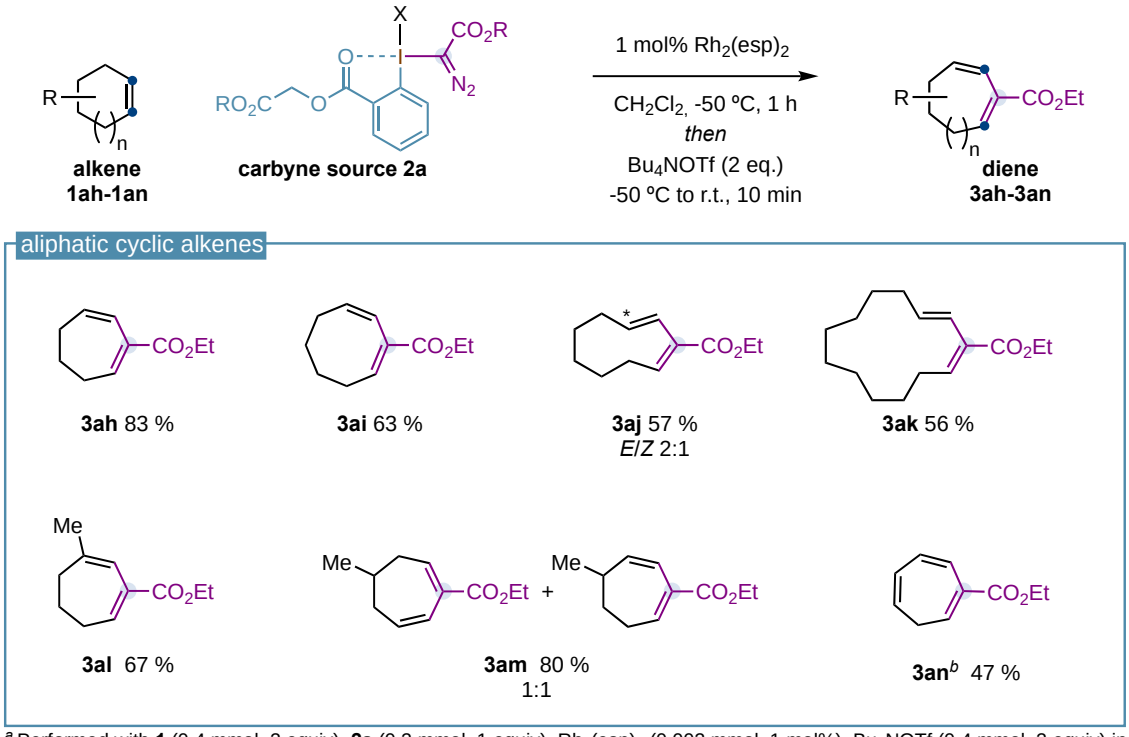
Next, we extended the scope to β- and α,b-substituted styrenes. We were able to obtain the desired products but in moderate yields (**3ac** and **3ad**). In the case of β-Me-styrene, we obtained a 1:1 mixture of *E*/*Z* isomers, which did not agree with our hypothesis of selectively forming a trans,cis-allyl cation which would lead to the *E* isomer. In order to get more information, we run a control experiment which consisted in trapping the cation formed with bromide as nucleophile. The reaction supported our predictions and we only obtained products with *E* geometry in the double bond (experimental details in the Supporting Information). Thus, we believe the problem might come from an isomerization of the double bond catalyzed by the acid generated in the reaction. With respect to α,β-di-Me-styrene, we only observed one isomer, even though 4 possible isomers could be generated.



[a]Performed with **1** (0.4 mmol, 2 equiv), **2a** (0.2 mmol, 1 equiv), $Rh_2(esp)_2$ (0.002 mmol, 1 mol%), Bu_4NOTf (0.4 mmol, 2 equiv) in CH_2Cl_2 (0.067 M); Yields are reported on the basis of isolated pure product; esp = α, α, α′, α′-tetramethy-1,3-benzenedipropanoate.

Table 4 Substrate scope: β-, α,β-substituted and cyclic styrenes

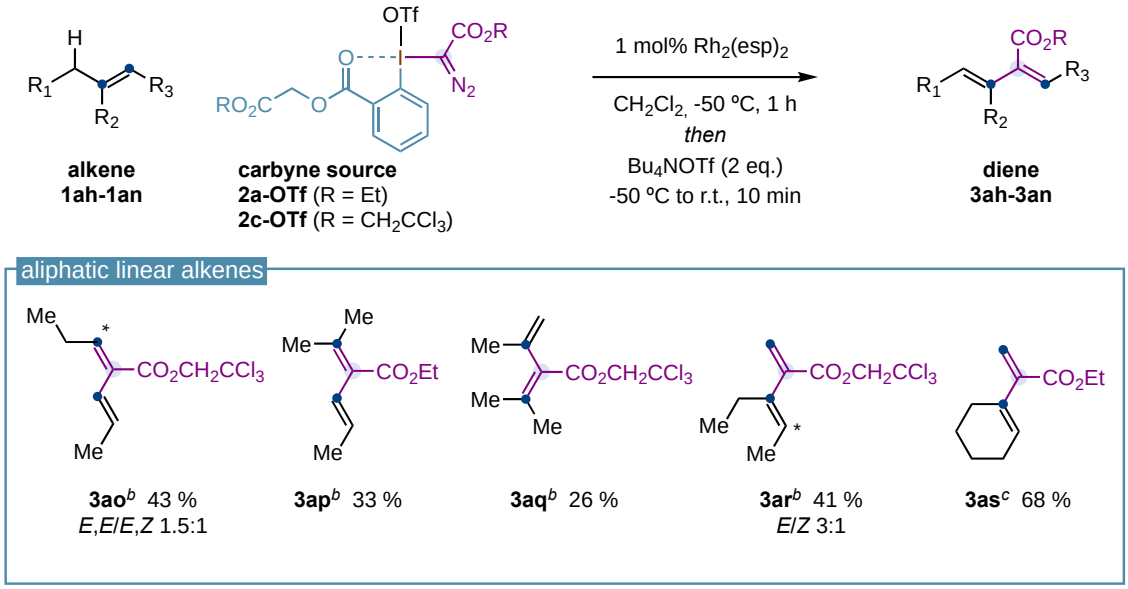
Next, we moved to the aliphatic alkenes. In the cases of cycloalkenes, we were able to perform a ring expansion via carbynoid insertion to the double bond. We could apply our methodology to simple cycloalkenes like cyclohexene (**3ah**), cycloheptene (**3ai**), cyclooctene (**3aj**) and cyclododecene (**3ak**) in yields ranging between 56 – 83 %. With substituted cyclohexenes in which the proton could eliminate from different positions, the most substituted diene was obtained exclusively (**3al**). However, when the substitution pattern did not affect the substitution in the resulting diene, no selectivity was observed (**3am**). Moreover, we were glad to see that our reaction could form the corresponding triene from the cyclic skipped diene 1,4-cyclohexadiene in moderate yield (**3an**).



[a] Performed with **1** (0.4 mmol, 2 equiv), **2a** (0.2 mmol, 1 equiv), $Rh_2(esp)_2$ (0.002 mmol, 1 mol%), Bu_4NOTf (0.4 mmol, 2 equiv) in CH_2Cl_2 (0.067 M); Yields are reported on the basis of isolated pure product; [b] Performed using 1,4-cyclohexadiene.

Table 5 Substrate scope: aliphatic cyclic alkenes

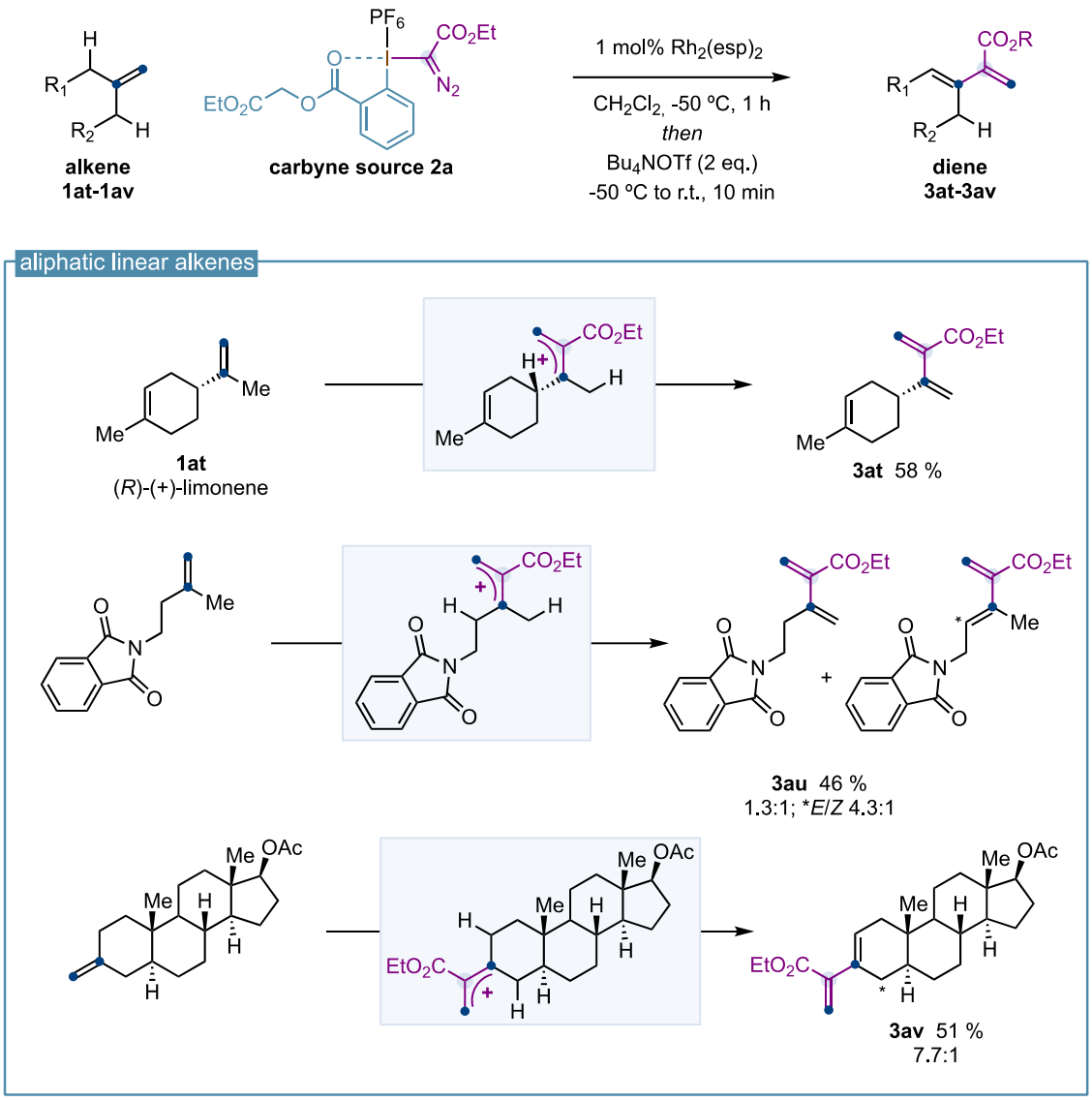
We then tested the linear aliphatic alkenes. We were able to obtain the desired product using α,β-disubstituted alkenes such as 3-hexene (**3ao**), tri-substituted 2-methyl-2-pentene (**3ap**) and even tetra-substituted 2,3-di-methyl-2-butene (**3aq**), even though the yields were low (from 43 – 26 % of yield). We observed that *gem*-disubstituted alkenes worked more efficiently, obtaining moderate yields in the case of 2-ethyl-1-butene (**3ar**) and methylenecyclohexene (**3as**). It is worth mentioning that in reactions **3ao**-**3as** the use of triflate as counteranion in the salt was crucial for the reaction.



[a] Performed with **1** (0.4 mmol, 2 equiv), **2a** (0.2 mmol, 1 equiv), $Rh_2(esp)_2$ (0.002 mmol, 1 mol%), Bu_4NOTf (0.4 mmol, 2 equiv) in CH_2Cl_2 (0.067 M); Yields are reported on the basis of isolated pure product; [b] Performed using carbyne source **2c-OTf**; [c] Performed carbyne source **2a-OTf**; esp = α, α, α′ ,α′-tetramethy-1,3-benzenedipropanoate

Table 6 Substrate scope: aliphatic linear alkenes

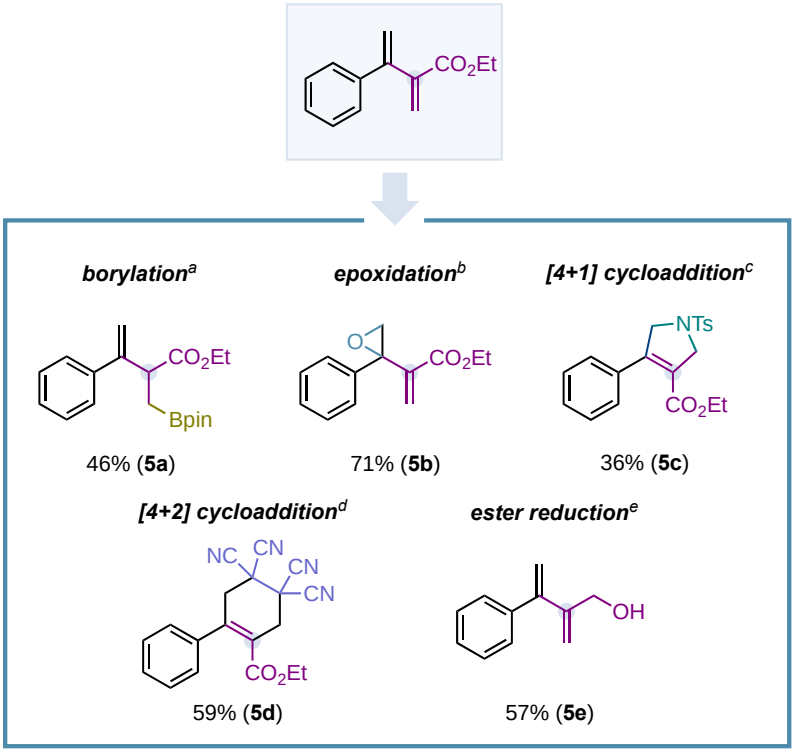
With the aliphatic alkenes, we also studied the selectivity of the elimination step depending on the substitution in the α position. In the case of (*R*)-(+)-limonene, we were surprised to see that only the least substituted diene was formed in 58 % of yield (**3at**). This behavior might be explained due to the steric hinderance of the cyclohexyl group that did not allow a correct conformation for the elimination of the proton. With respect to the phthalimide substituted 2-methyl-butene **2au** we also observed a slight preference in the elimination of the methyl proton, even though in this case the selectivity was lower (1.3:1). The desired product was obtained in 46 % of yield (**3au**). In the same sense, we were glad to see that with the androstanolone derivative **2av**, even though the two protons prone to eliminate do not seem to differ much neither electronically nor sterically, we preferentially formed isomer **3av** in a 7.7:1 ratio and 51 % of yield.



[a] Performed with **1** (0.4 mmol, 2 equiv), **2a** (0.2 mmol, 1 equiv), $Rh_2(esp)_2$ (0.002 mmol, 1 mol%), Bu_4NOTf (0.4 mmol, 2 equiv) in CH_2Cl_2 (0.067 M); Yields are reported on the basis of isolated pure product; esp = α, α, α′, α′-tetramethy-1,3-benzenedipropanoate

Table 7 Substrate scope: aliphatic linear alkenes

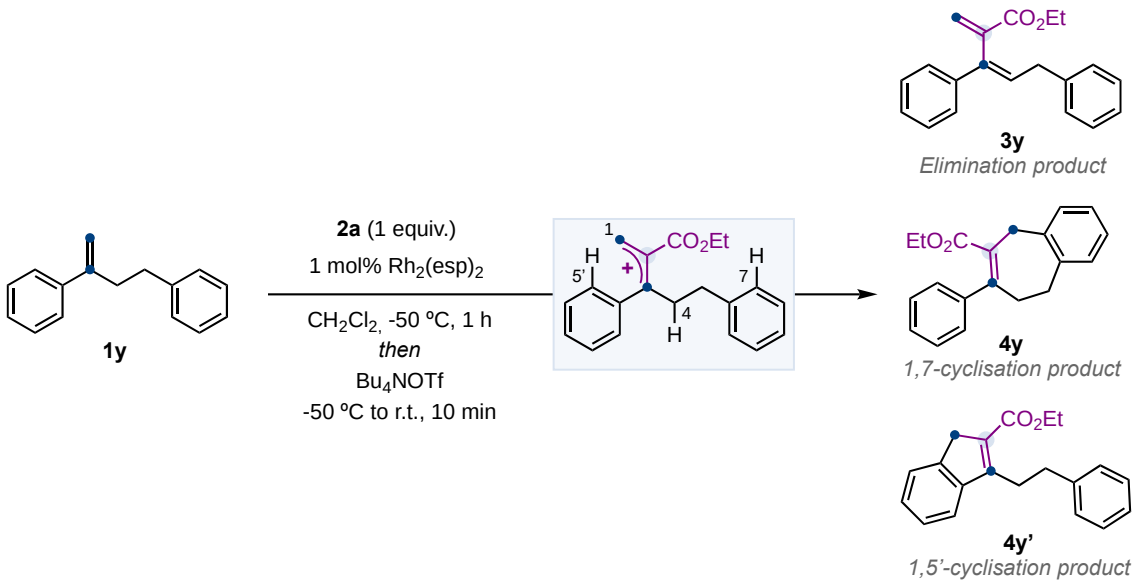
In order to show the utility of the products we conducted multiple transformations with them. To exhibit the different electronic behavior of each double bond in the diene, we performed a hydroborylation in the most electrophilic double bond (**5a**) and an electrophilic epoxidation in the most nucleophilic one (**5b**). In each case we observed complete selectivity toward the desired double bond. After that, different electrocyclization reactions involving the 4π electrons system of the 1,3-diene were carried out, such as a [4+1] cycloaddition with a nitrene precursor (**5c**) and a [4+2] cycloaddition with tetracyanoethylene (**5d**), both working in moderate yields. Finally, we were also able to reduce the ester using DIBAL-H in 57 % of yield (**5e**).



Reaction conditions: (*a*) CuCl (15 mol%), DPEphos (15 mol%), NaO^{t}Bu, B_2pin_2, MeOH, THF, 24 hours, rt; (*b*) *m*-CPBA, CH_2Cl_2, 90 min, rt; (*c*) $Cu(hfacac)_2$ (5 mol%), TsN=IPh, PhCl, 24 hours, 100 ºC; (*d*) tetracyanoethylene, AcOEt, 2 days, rt; (*e*) DIBAL-H, Toluene, 7 hours, -78 ºC rt.

Table 8 Derivatization reactions of diene **3a**

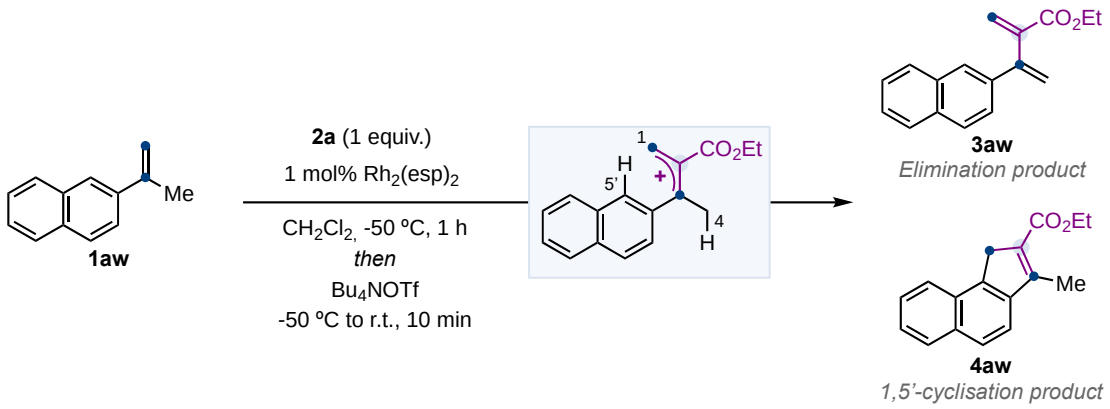
Even though in the optimization of the reaction we were able to suppress the formation of cyclisation side-products, we were surprised to encounter them along the substrate scope. An example of it is the 2,4-diphenyl-1-butene (**1y**). Using the optimized reaction conditions for the synthesis of 1,3-dienes, a 2.4:1 mixture of the desired diene **3y** and the cyclisation product **4y** was obtained in 81 % of yield. We wondered that the cyclisation reaction could be suppressed by increasing the equivalents of TBAOTf and in fact, when we used 5 equivalents, the yield and selectivity of the reaction improved, obtaining selectively the 1,3-diene product **3y** in 95 % of yield. Next, we observed that if triflate was removed from the reaction mixture, the cyclisation product was obtained as the only product, even though the yield was lower than the obtained in the case of 1,3-diene. It must also be said that the expected 1,5'-cyclisation product **4y'** was not observed in any case, meaning that the 7-member ring formation of **4y** might be more favoured.



entry	TBAOTf (equiv.)	yield (**3y**: *Z*/*E* ratio)	**3y**:**4y**:**4y'** ratio
1	2 equiv.	81 % (5:1)	2.4:1:nd
2	5 equiv.	95 % (9:1)	> 20:1:nd
3	-	63 % (-)	< 1:20:nd

Scheme 11 Small optimization study with alkene **1y**

Similar results were found with the naphthalene substituted **1aw**. In this case, when 2 equivalents of TBAOTf were used, a 1.6:1 mixture of the 1,5-cyclisation product **4aw** and 1,3-diene **3aw** was obtained in excellent yield. However, increasing the TBAOTf equivalents did not improve the results in this case and when it was removed from the reaction mixture the yield dropped to 34 %, even though the cyclisation **4aw** product was obtained selectively.



entry	TBAOTf (equiv.)	yield	**3aw**:**4aw** ratio
1	2 equiv.	99 %	1:1.6
2	5 equiv.	99 %	1:2
3	-	34 %	< 1:20

Scheme 12 Small optimization study with alkene **1aw**

Considering the results obtained, we aimed to optimize the cyclization reaction. We selected the methoxy-substituted α-methyl-styrene as the substrate, thinking that the more electron-donating group would enhance the cyclisation instead of the elimination reaction. Using the previously optimized reaction conditions for the elimination reaction, with 2 equivalents of styrene, salt **2a** (1 equiv), $Rh_2(esp)_2$ and TBAOTf (2 equiv), a 1.2:1 **4aw**:**3aw** mixture was obtained in 37 % of yield. It was thought that the main side reaction could be the polymerization. In order to avoid it, the reaction temperature was lowered to -70 ºC and the amount of styrene was decreased to 1 equivalent without changing the yield. By removing the triflate salt, the yield was maintained too and the selectivity improved to more than 20:1. Next, multiple rhodium(II) catalysts were tried and it was observed that $Rh_2(Oct)_4$ and $Rh_2(Adc)_4$ improved the yield up to 52 and 57 % respectively. Further changes in the carbyne source, temperature or concentration did not improve the yield.

In summary, despite our efforts to improve the efficiency of the reaction it was not possible to reach acceptable yields and we believe that further study of the reaction in the group will obtain better results.

4.4. Conclusions

In summary, we have been able to transform simple alkenes to 1,3-dienes *via* Rh-carbynoid insertion to double bonds through the formation of allyl cations. The utility of

this protocol was demonstrated by the use of a broad range of non-pre-functionalized olefins as well as the further derivatization of the obtained 1,3-dienes into highly functionalized products.

4.5. Experimental section

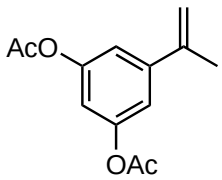
General Information.

All reagents were used as purchased and used with no further purification. Rhodium(II) acetate dimer $Rh_2(OAc)_4$, rhodium(II) trifluoroacetate dimer $Rh_2(TFA)_4$, rhodium(II) heptafluorobutyrate dimer $Rh_2(hfb)_4$, bis[rhodium(α,α,α′,α′-tetramethyl-1,3-benzenedipropionic acid)] $Rh_2(esp)_2$ and dirhodium tetracaprolactamate $Rh_2(cap)_4$ were purchased from Sigma-Aldrich and used directly. Rhodium bis(1-adamantate) dimer $Rh_2(Adc)_4$[1] and rhodium(II) triphenylacetate dimer $Rh_2(TPA)_4$[2] were prepared according to reported procedures. Ethyl diazoacetate (contains ≥13 wt. % dichloromethane, Ref. E22201) and bromoacetic acid-2-^{13}C (isotopic purity = 99 atom % ^{13}C, Ref. 279358) were purchased from Sigma-Aldrich and used without further purification. Anhydrous solvents were dried by passing through an activated alumina column on a PureSolv^{TM} solvent purification system (Innovative Technologies, Inc., MA). Analytical thin layer chromatography (TLC) was carried out using aluminum sheets with 0.2 mm of silica gel (Merck GF234). Visualization of the developed chromatogram was performed by irradiation with UV light or treatment with a solution of potassium permanganate or vainillin stain followed by heating. Flash column chromatography was performed on silica gel (Aldrich, 230-400 mesh) or neutral silica gel (Material Harvest Ltd., 230-400 mesh). Organic solutions were concentrated under reduced pressure on a Büchi rotatory evaporator. Unless otherwise stated, reactions were carried out under argon atmosphere. Yields refer to purified compounds unless otherwise noted. NMR spectra were recorded at 298 K (unless otherwise stated) on Bruker Avance 300, Bruker Avance 400 Ultrashield and Bruker Avance 500 Ultrashield apparatuses. Chemical shifts (δ) are quoted in ppm relative to residual solvent signals, $CDCl_3$ referenced at δ 7.26 and 77.16 ppm, CD_2Cl_2 referenced at δ 5.32 and 53.5 ppm, CD_3CN referenced at δ 1.94 and 1.39, 118.69 ppm respectively. Coupling constants (*J*) are quoted in hertz (Hz). Multiplicity is reported with the following abbreviations: s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, p = quintet, dt = doublet of triplets, td = triplet of doublets, tt = triplet of triplets, sp = septet, m = multiplet, app = apparent. Melting points were measured using open glass capillaries in a Büchi B540 apparatus. Infrared spectra were recorded on a Bruker Tensor 27. Mass spectra were recorded on a Waters LCT Premier spectrometer and Agilent 1260 Infinity - 6130 Quadrupole.

Synthesis of alkenes 1

1a, **1d**, **1j**, **1o**, **1s**, **1t**, **1ad**, **1ae**, **1af**, **1ag**, **1ah**, **1ai**, **1aj**, **1ak**, **1al**, **1am**, **1an**, **1ao**, **1ap**, **1aq**, **1ar**, **1as**, **1at** and **1av** were commercially available and used directly as received. **1e**[45], **1f**[45], **1g**[46], **1h**[45], **1i**[46], **1k**[47], **1l**[48], **1m**[49], **1n**[48], **1p**[48], **1q**[45], **1r**[45], **1v**[50], **1w**[45], **1x**[51], **1y**[52], **1z**[51,] **1aa**[52], **1ab**[53], **1ac**[54], **1ad**[55] and **1au**[56] were prepared according to the reported protocols.

5-(prop-1-en-2-yl)-1,3-phenylene diacetate (1u)



Prepared according to an adapted reported protocol[45] using 5-acetyl-1,3-phenylene diacetate (1.42 g, 6.0 mmol), methyl triphenylphosphonium bromide (4.29 g, 12.0 mmol) and KO^{t}Bu (1.35 g, 12.0 mmol). Purification by flash chromatography on silica gel (hexane) provided **2s** as a colorless oil (0.25 g, 25% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (d, *J* = 2.1 Hz, 2H), 6.84 (t, *J* = 2.1 Hz, 1H), 5.40 – 5.35 (m, 1H), 5.16 – 5.10 (m, 1H), 2.28 (s, 6H), 2.13 – 2.08 (m, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.1, 151.0, 143.6, 141.6, 116.3, 114.4, 114.2, 21.6, 21.1.

HRMS (ESI) calculated for $C_{13}H_{14}NaO_4^+$ $[M+Na]^+$ m/z: 257.0784, found: 257.0789.

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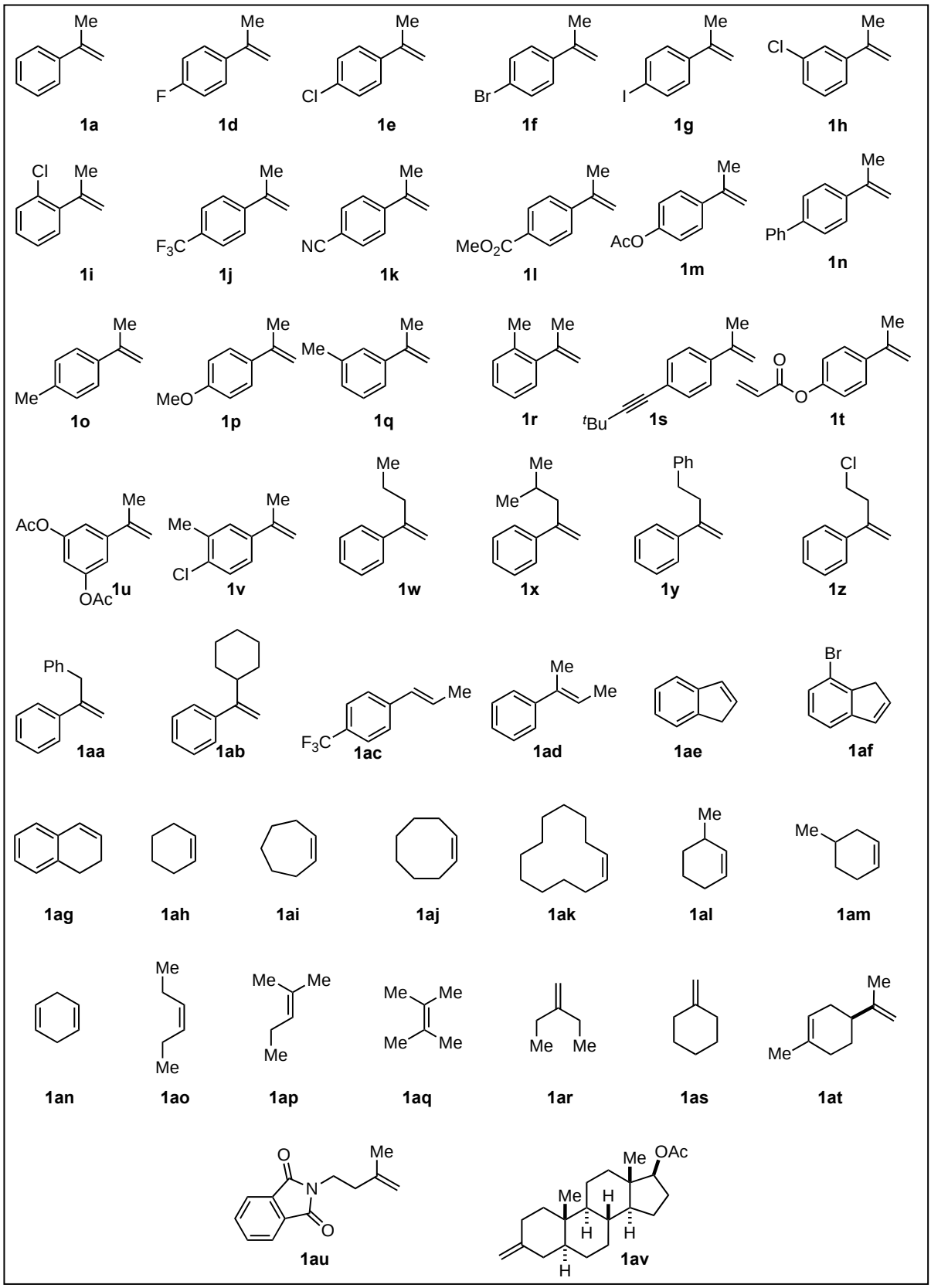
1a
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1e
1f
1g
1h
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1k
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1m
1n
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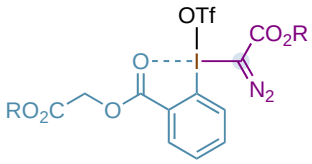
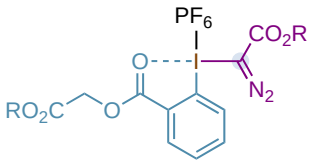
Synthesis of carbyne sources (hypervalent iodine Reagents) 2.



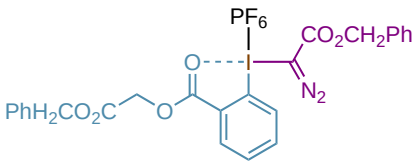
R = Et (**2a-OTf**),
CH_2Ph (**2b-OTf**), CH_2CCl_3 (**2c-OTf**)



R = Et (**2a**),
CH_2Ph (**2b**), CH_2CCl_3 (**2c**)

Hypervalent iodine reagents **2a-OTf**, **2b-OTf** and **2a** are known compounds and were prepared following the reported literature protocols.[57] **2a**, **2b** and **2c** were prepared by the following modification of a reported protocol: **General procedure A:** a solution of **2-OTf** in dichloromethane (0.2 M) was added to a separation funnel and then washed with a saturated aqueous solution of KPF_6 (3 x 25 mL). The combined organic layers were dried over Na_2SO_4 and solvent was removed under *vacuum* to give **2** as yellow solid.
(*Note: if the product contains impurities, it is recrystallized with dichloromethane/diethyl ether = 1/5*).

2-(benzyloxy)-2-oxoethyl 2-((2-(benzyloxy)-1-diazo-2-oxoethyl)(hexafluoro-λ^7-phosphaneyl)-λ^3-iodaneyl)benzoate (2b)

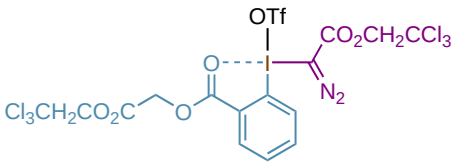


Prepared according to the general procedure A using **2b-OTf** (1.50 g, 2.1 mmol). The title compound was isolated by recrystallization from diethyl ether/dichloromethane as a yellow solid (1.35 g, 90 %).

IR (film, cm^{-1}): 2123, 1708, 1658, 1588, 1371, 1330, 1269, 1212, 1152, 889.

^{1}H NMR (400 MHz, Acetone) δ 8.55 – 8.51 (m, 1H), 8.38 – 8.33 (m, 1H), 8.14 – 8.08 (m, 1H), 8.06 – 8.00 (m, 1H), 7.45 – 7.35 (m, 10H), 5.39 (s, 2H), 5.31 (s, 2H), 5.29 (s, 2H); **^{13}C NMR** (101 MHz, Acetone) δ 170.7, 167.0, 162.1, 139.5, 136.4, 136.1, 134.2, 133.4, 130.6, 129.6, 129.5, 129.5, 129.3, 129.2, 129.2, 126.3, 116.8, 70.1, 68.0, 65.0; **^{19}F NMR** (376 MHz, Acetone) δ -72.21 (ddd, *J* = 708.0, 13.6, 7.0 Hz); **^{31}P NMR** (162 MHz, Acetone) δ -141.13 (hept, *J* = 707.5 Hz).
HRMS (MALDI) calculated for $C_{25}H_{20}IN_2O_6^+$ $[M\text{-}PF_6]^+$ m/z: 571.0361, found: 571.0387.

(1-diazo-2,2,2-trichloroethyl)(2-(2,2,2-trifluoroethyl-2-oxoethoxyl)carbonylphenyl)iodonium trifluoromethanesulfonate (2c-OTf)



[57] Wang, Z.; Herraiz, A. G.; Del Hoyo, A. M.; Suero, M. G. *Nature* **2018**, *554*, 86.

Prepared according to an adapted reported protocol[57] using 2,2,2-trichloroethyl 2-diazoacetate[54] (5.60 g, 25.8 mmol, 2.4 equiv.). The title compound was isolated by recrystallization from diethyl ether/dichloromethane as a yellow solid (6.66 g, 77 %).

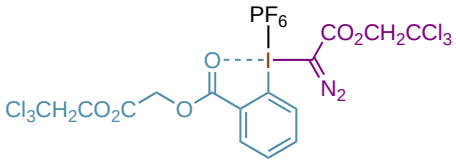
m.p. 106-107 °C.

IR (film, cm^{-1}): 2961, 2129, 1772, 1716, 1661, 1265, 1148, 1026.

^{1}H NMR (500 MHz, CD_3CN) δ 8.44 (dd, *J* = 7.6, 1.7 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 8.04 (ddd, *J* = 8.5, 7.3, 1.7 Hz, 1H), 7.93 (t, *J* = 7.5 Hz, 1H), 5.25 (s, 2H), 4.97 (s, 2H), 4.94 (s, 2H); **^{13}C NMR** (126 MHz, CD_3CN) δ 170.9, 166.0, 161.1, 139.7, 134.4, 133.6, 130.9, 126.1, 122.0 (q, *J* = 321.3 Hz), 117.0, 95.4, 95.2, 76.3, 75.2, 64.9; **^{19}F NMR** (471 MHz, CD_3CN) δ -79.2.

HRMS (MALDI) calculated for $C_{15}H_{10}Cl_6IN_2O_6^+$ $[M\text{-}OTf]^+$ m/z: 650.7709, found: 650.7729.

(1-diazo-2,2,2-trichloroethyl)(2-(2,2,2-trifluoroethyl-2-oxoethoxyl)carbonylphenyl)iodonium hexafluorophosphate (2c)



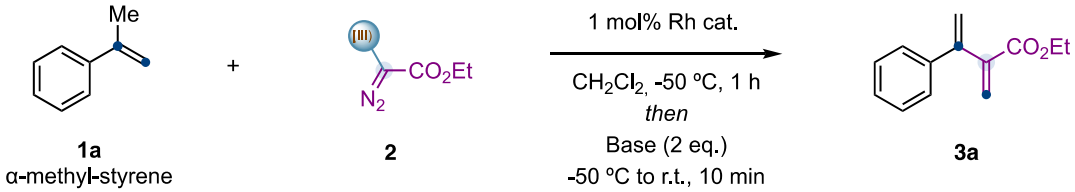
Prepared according to the general procedure A using **2c-OTf** (2.20 g, 2.8 mmol). The title compound was isolated by recrystallization from diethyl ether/dichloromethane as a yellow solid (2.01 g, 91 %).

IR (film, cm^{-1}): 2962, 2130, 1774, 1719, 1661, 1589, 1428, 1372, 1325, 1265, 1150, 1029, 840.

^{1}H NMR (400 MHz, Acetone) δ 8.55 (dd, *J* = 7.6, 1.7 Hz, 1H), 8.38 (d, *J* = 8.4 Hz, 1H), 8.15 (ddd, *J* = 8.4, 7.4, 1.7 Hz, 1H), 8.04 (td, *J* = 7.5, 0.9 Hz, 1H), 5.45 (s, 2H), 5.07 (s, 2H), 5.01 (s, 2H); **^{13}C NMR** (101 MHz, Acetone) δ 170.7, 165.8, 161.0, 139.7, 134.2, 133.3, 130.7, 125.8, 116.7, 95.3, 95.3, 76.1, 74.8, 64.5; **^{19}F NMR** (376 MHz, Acetone) δ -71.8 (d, *J* = 708.7 Hz); **^{31}P NMR** (162 MHz, Acetone) δ -141.2 (hept, *J* = 708.7 Hz).

HRMS (MALDI) calculated for $C_{15}H_{10}Cl_6IN_2O_6^+$ $[M\text{-}PF_6]^+$ m/z: 650.7709, found: 650.7735.

Optimization studies



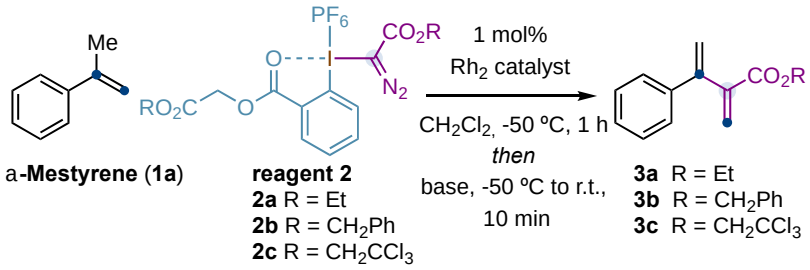
1a
α-methyl-styrene

2

3a

General procedure B: To a 10 mL oven-dried tube was added the corresponding Rh catalyst (0.001 mmol, 1 mol%). The tube was sealed before being evacuated and backfilled with nitrogen. **1a** (0.1–1.0 mmol) and degassed dichloromethane (0.5 mL) were added and the resulting mixture was cooled at -50 ºC. Then, a solution of reagent **2** (0.1 mmol, 1.0 equiv.) in degassed dichloromethane (1 mL) was added dropwise during 1 h using a syringe pump. Once the iodine salt was fully consumed by TLC (ethyl acetate 100%),

base (0.2 mmol, 2.0 equiv.) was added to the reaction mixture and it was allowed to warm up to room temperature during 10 min. Next, the reaction mixture was washed with a saturated aqueous solution of $NaHCO_3$ (3 mL) and extracted with DCM (3 x 3 mL). The combined organic phases were dried over anhydrous $NaSO_4$ and the solvent was removed under *vacuum*. The crude residue was analyzed by ^{1}H-NMR using anisole (10 □L, 0.092 mmol).



a-**Mestyrene** (**1a**)

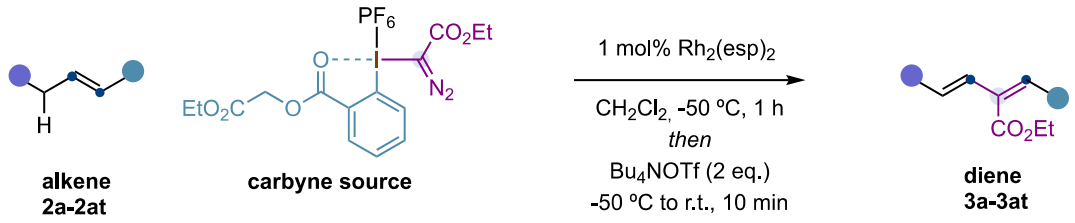
reagent 2
2a R = Et
2b R = CH_2Ph
2c R = CH_2CCl_3

3a R = Et
3b R = CH_2Ph
3c R = CH_2CCl_3

Entry	Rh_2 catalyst	reagent **2a-c,** R	Base	Yield **3a-c** [%][a]
1	$Rh_2(esp)_2$	Et	no base	14
2	$Rh_2(esp)_2$	Et	$NaHCO_3$	9
3	$Rh_2(esp)_2$	Et	Na_2CO_3	5
4	$Rh_2(esp)_2$	Et	K_2HPO_4	14
5	$Rh_2(esp)_2$	Et	NaOAc	8
6	$Rh_2(esp)_2$	Et	NaOBz	18
7	$Rh_2(esp)_2$	Et	DBU	10
8	$Rh_2(esp)_2$	Et	DABCO	9
9	$Rh_2(esp)_2$	Et	DTBPy	10
10	$Rh_2(esp)_2$	Et	TBAOMs	39
11	$Rh_2(esp)_2$	Et	TBAOTs	52
12	$Rh_2(esp)_2$	Et	TBAOTf	99
13	$Rh_2(esp)_2$	Et	TBAOTf	20[b]
14	$Rh_2(OAc)_4$	Et	TBAOTf	23
15	$Rh_2(hfb)_2$	Et	TBAOTf	0
16	$Rh_2(Adc)_4$	Et	TBAOTf	54
17	$Rh_2(esp)_2$	CH_2Ph	TBAOTf	72
18	$Rh_2(esp)_2$	CH_2CCl_3	TBAOTf	48

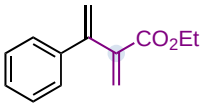
[a]Yields are reported on the basis of ^{1}H NMR analysis using anisole as internal standard. [b]1 equiv of TBAOTf was added. DBU = 1,8-diazabicyclo(5.4.0)undec-7-ene; DABCO = 1,4-diazabicyclo[2.2.2]ocatane; DTBPy = 2,6-di-^{t}Bu-pyridine; hfb = heptafluorobutyrate; Adc = 1-adamantylcarboxylate; esp = α,α,α′,α′-tetramethy-1,3-benzenedipropanoate.

Synthesis of dienes 3



General procedure C: To a 10 mL oven-dried tube was added $Rh_2(esp)_2$ (1.5 mg, 0.002 mmol, 1 mol%). The tube was sealed before being evacuated and backfilled with nitrogen. The corresponding alkene (0.4 mmol, 2.0 equiv.) and degassed dichloromethane (1.0 mL) were added and the resulting mixture was cooled at -50 ºC. Then, a solution of reagent **2** (0.2 mmol, 1.0 equiv.) in degassed dichloromethane (2 mL) was added dropwise during 1 h using a syringe pump. Once the iodine salt was fully consumed by TLC (ethyl acetate 100%), TBAOTf (156.6 mg, 2.0 equiv.) was added to the reaction mixture and it was allowed to warm up to room temperature during 10 min. Then, the reaction mixture was washed with a saturated aqueous solution of $NaHCO_3$ (3 mL) and extracted with DCM (3 x 3 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and the solvent was removed under *vacuum*. The crude residue was purified by column chromatography to yield the corresponding diene **6**.

Ethyl 2-methylene-3-phenylbut-3-enoate (3a)



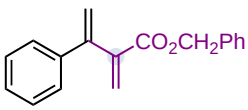
Prepared according to the general procedure C using **1a** (47.3 mg, 52 µL, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided the title compound as a colorless oil (40.0 mg, 99% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 5H), 6.31 (d, *J* = 1.7 Hz, 1H), 5.81 (d, *J* = 1.7 Hz, 1H), 5.50 (d, *J* = 1.4 Hz, 1H), 5.40 (d, *J* = 1.4 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 1.09 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.7, 146.4, 142.5, 140.0, 128.4, 127.9, 127.6, 126.7, 116.4, 61.0, 14.0.

HRMS (ESI) calculated for $C_{13}H_{14}NaO_2^+$ $[M+Na]^+$ m/z: 225.0886, found: 225.0884.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Benzyl 2-methylene-3-phenylbut-3-enoate (3b)



Prepared according to the general procedure C using **1a** (47.3 mg, 52 µL, 0.4 mmol) and reagent **2b** (143.3 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3b** compound as a colorless oil (38.1 mg, 72% yield).

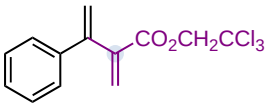
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.20 (m, 5H), 7.19 – 7.14 (m, 3H), 7.00 – 6.93 (m, 2H), 6.30 (d, *J* = 1.7 Hz, 1H), 5.77 (d, *J* = 1.7 Hz, 1H), 5.43 (d, *J* = 1.3 Hz, 1H), 5.32 (d, *J* = 1.3 Hz, 1H), 5.00 (s, 2H); **^{13}C**

NMR (101 MHz, $CDCl_3$) δ 166.5, 146.2, 142.1, 139.8, 135.8, 128.5, 128.5 (2C), 128.1, 127.9, 127.9, 126.7, 116.6, 66.7.

HRMS (ESI) calculated for $C_{18}H_{16}NaO_2^+$ $[M+Na]^+$ m/z: 287.1043, found: 287.1033.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl 2-methylene-3-phenylbut-3-enoate (3c)



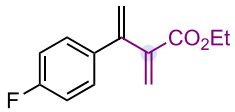
Prepared according to the general procedure D using **1a** (47.3 mg, 52 μL, 0.4 mmol) and reagent **2c** (159.8 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3c** as a colorless oil (27.1 mg, 44% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.34 (m, 2H), 7.34 – 7.30 (m, 2H), 7.30 – 7.27 (m, 1H), 6.51 (d, *J* = 1.5 Hz, 1H), 5.97 (d, *J* = 1.5 Hz, 1H), 5.56 (d, *J* = 1.2 Hz, 1H), 5.46 (d, *J* = 1.2 Hz, 1H), 4.72 (s, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 164.8, 145.7, 141.0, 139.6, 130.1, 128.6, 128.1, 126.8, 117.1, 94.8, 74.5.

HRMS (ESI) calculated for $C_{13}H_{11}Cl_3NaO_2^+$ $[M+Na]^+$ m/z: 326.9717, found: 326.9721.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 3-(4-fluorophenyl)-2-methylenebut-3-enoate (3d)



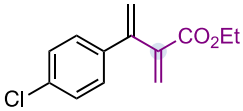
Prepared according to the general procedure C using **1d** (54.5 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3d** as a colorless oil (31.5 mg, 72% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.25 (m, 2H), 7.04 – 6.96 (m, 2H), 6.31 (d, *J* = 1.7 Hz, 1H), 5.80 (d, *J* = 1.7 Hz, 1H), 5.44 (d, *J* = 1.2 Hz, 1H), 5.38 (d, *J* = 1.1 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 1.11 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.6, 162.6 (d, *J* = 246.8 Hz), 145.4, 142.3, 136.2 (d, *J* = 3.3 Hz), 128.4 (d, *J* = 8.1 Hz), 127.8, 116.4, 115.3 (d, *J* = 21.5 Hz), 61.0, 14.1; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -114.8.

HRMS (ESI) calculated for $C_{13}H_{13}FNaO_2^+$ $[M+Na]^+$ m/z: 243.0792, found: 243.0792.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 3-(4-chlorophenyl)-2-methylenebut-3-enoate (3e)



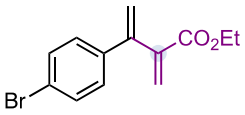
Prepared according to the general procedure C using **1e** (61.1 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3e** as a colorless oil (45.6 mg, 96% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.23 (m, 4H), 6.32 (d, *J* = 1.7 Hz, 1H), 5.81 (d, *J* = 1.7 Hz, 1H), 5.47 (d, *J* = 1.2 Hz, 1H), 5.40 (d, *J* = 1.2 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 1.11 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.4, 145.4, 142.0, 138.5, 133.7, 128.6, 128.1, 128.0, 116.9, 61.1, 14.1.

HRMS (ESI) calculated for $C_{13}H_{13}ClNaO_2^+$ $[M+Na]^+$ m/z: 259.0496, found: 259.0507.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 3-(4-bromophenyl)-2-methylenebut-3-enoate (3f)



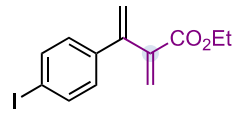
Prepared according to the general procedure C using **1f** (78.8 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3f** as a colorless oil (42.3 mg, 75% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.42 (m, 2H), 7.21 – 7.17 (m, 2H), 6.32 (d, *J* = 1.7 Hz, 1H), 5.81 (d, *J* = 1.7 Hz, 1H), 5.48 (d, *J* = 1.2 Hz, 1H), 5.41 (d, *J* = 1.2 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.4, 145.4, 142.0, 139.0, 131.6, 128.4, 128.1, 121.9, 117.0, 61.1, 14.1.

HRMS (ESI) calculated for $C_{13}H_{13}BrNaO_2^+$ $[M+Na]^+$ m/z: 302.9991, found: 302.9988.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 3-(4-iodophenyl)-2-methylenebut-3-enoate (3g)



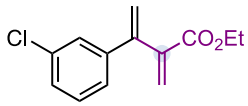
Prepared according to the general procedure C using **1g** (97.6 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3g** as a colorless oil (65.3 mg, 99% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.60 (m, 2H), 7.10 – 7.03 (m, 2H), 6.32 (d, *J* = 1.7 Hz, 1H), 5.81 (d, *J* = 1.7 Hz, 1H), 5.48 (d, *J* = 1.2 Hz, 1H), 5.40 (d, *J* = 1.2 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.4, 145.5, 141.9, 139.6, 137.5, 128.6, 128.1, 117.0, 93.5, 61.1, 14.1.

HRMS (ESI) calculated for $C_{13}H_{13}INaO_2^+$ $[M+Na]^+$ m/z: 350.9852, found: 350.9846.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 3-(2-chlorophenyl)-2-methylenebut-3-enoate (3h)



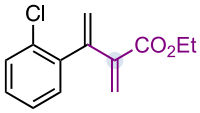
Prepared according to the general procedure C using **1h** (130.2 mg, 130 µL, 1.0 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3h** as a colorless oil (19.8 mg, 42% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.34 (m, 1H), 7.27 – 7.22 (m, 3H), 6.14 (s, 1H), 5.85 (d, *J* = 1.2 Hz, 1H), 5.49 (d, *J* = 1.1 Hz, 1H), 5.36 (s, 1H), 4.19 (q, *J* = 7.1 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.5, 143.3, 141.0, 139.8, 133.0, 131.2, 129.8, 128.9, 126.7, 126.4, 120.9, 61.0, 14.2.

HRMS (ESI) calculated for $C_{13}H_{13}ClNaO_2^+$ $[M+Na]^+$ m/z: 259.0496, found: 259.0498.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 3-(3-chlorophenyl)-2-methylenebut-3-enoate (3i)



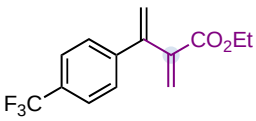
Prepared according to the general procedure C using **1i** (61.1 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3i** as a colorless oil (31.3 mg, 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (dt, *J* = 1.7, 1.1 Hz, 1H), 7.27 – 7.23 (m, 2H), 7.23 – 7.17 (m, 1H), 6.34 (d, *J* = 1.6 Hz, 1H), 5.82 (d, *J* = 1.6 Hz, 1H), 5.50 (d, *J* = 1.1 Hz, 1H), 5.44 (d, *J* = 1.1 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 1H), 1.12 (t, *J* = 7.1 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.4, 145.4, 142.0, 141.9, 134.5, 129.8, 128.4, 128.0, 127.0, 125.0, 117.6, 61.2, 14.2.

HRMS (ESI) calculated for $C_{13}H_{13}ClNaO_2^+$ $[M+Na]^+$ m/z: 259.0496, found: 259.0494.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 2-methylene-3-(4-(trifluoromethyl)phenyl)but-3-enoate (3j)



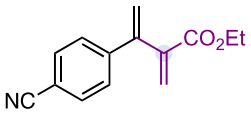
Prepared according to the general procedure C using **1j** (74.5 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3j** as a colorless oil (40.2 mg, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, 2H), 7.46 – 7.40 (m, 2H), 6.37 (d, *J* = 1.6 Hz, 1H), 5.85 (d, *J* = 1.6 Hz, 1H), 5.55 (d, *J* = 1.1 Hz, 1H), 5.50 (d, *J* = 1.1 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 1.10 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.2, 145.4, 143.6, 141.7, 129.9 (q, *J* = 32.4 Hz), 128.5, 127.0, 125.4 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 273.0 Hz), 118.3, 61.1, 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.25.

HRMS (ESI) calculated for $C_{14}H_{13}F_3NaO_2^+$ $[M+Na]^+$ m/z: 293.0760, found: 293.0764.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 2-methylene-3-(4-cyanophenyl)but-3-enoate (3k)



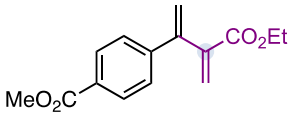
Prepared according to the general procedure C using **1k** (57.3 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3k** as a colorless oil (31.8 mg, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.59 (m, 2H), 7.45 – 7.39 (m, 2H), 6.40 (d, *J* = 1.6 Hz, 1H), 5.87 (d, *J* = 1.6 Hz, 1H), 5.57 (d, *J* = 1.0 Hz, 1H), 5.53 (d, *J* = 1.0 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 1.10 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.0, 145.2, 144.7, 141.3, 132.4, 129.0, 127.3, 119.1, 119.0, 111.5, 61.2, 14.0.

HRMS (ESI) calculated for $C_{14}H_{13}NNaO_2^+$ $[M+Na]^+$ m/z: 250.0838, found: 250.0838.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Methyl 4-(3-(ethoxycarbonyl)buta-1,3-dien-2-yl)benzoate (3l)



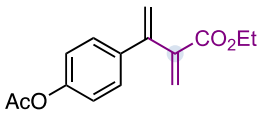
Prepared according to the general procedure C using **1l** (70.5 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 50/1) provided **3l** as a colorless oil (35.9 mg, 69% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.97 (m, 2H), 7.42 – 7.35 (m, 2H), 6.36 (d, *J* = 1.7 Hz, 1H), 5.84 (d, *J* = 1.6 Hz, 1H), 5.57 (d, *J* = 1.2 Hz, 1H), 5.49 (d, *J* = 1.2 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.91 (s, 3H), 1.07 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.0, 166.3, 145.7, 144.6, 141.9, 129.8, 129.5, 128.4, 126.6, 118.1, 61.1, 52.2, 14.0.

HRMS (APCI) calculated for $C_{15}H_{17}O_4^+$ $[M+H]^+$ m/z: 261.1121, found: 261.1119.

^{1}H-^{13}C HSQC spectra was measured.

Ethyl 3-(4-acetoxyphenyl)-2-methylenebut-3-enoate (3m)



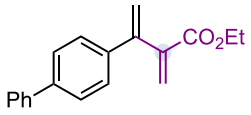
Prepared according to the general procedure C using **1m** (70.5 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 20/1 – 10/1) provided **3m** as a colorless oil (40.1 mg, 77% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 2H), 7.06 – 7.01 (m, 2H), 6.31 (d, *J* = 1.7 Hz, 1H), 5.80 (d, *J* = 1.7 Hz, 1H), 5.47 (d, *J* = 1.3 Hz, 1H), 5.39 (d, *J* = 1.3 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 2.29 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.5, 166.6, 150.4, 145.5, 142.23, 137.8, 127.9, 127.8, 121.5, 116.7, 61.0, 21.3, 14.0.

HRMS (ESI) calculated for $C_{15}H_{16}NaO_4^+$ $[M+Na]^+$ m/z: 283.0941, found: 283.0940.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 3-([1,1'-biphenyl]-4-yl)-2-methylenebut-3-enoate (3n)



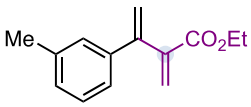
Prepared according to the general procedure C using **1n** (130.2 mg, 130 μL, 1.0 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Styrene and catalyst were dissolved in 10 mL of DCM, due to low solubility of the substrate. Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3n** as a colorless oil (34.1 mg, 61% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.59 (m, 2H), 7.59 – 7.54 (m, 2H), 7.46 – 7.40 (m, 4H), 7.37 – 7.32 (m, 1H), 6.35 (d, *J* = 1.8 Hz, 1H), 5.86 (d, *J* = 1.7 Hz, 1H), 5.57 (d, *J* = 1.3 Hz, 1H), 5.43 (d, *J* = 1.3 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 1.13 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.7, 145.9, 142.4, 140.8, 140.7, 138.9, 128.9, 127.8, 127.5, 127.1, 127.1, 116.4, 61.0, 14.1.

HRMS (ESI) calculated for $C_{19}H_{19}O_2^+$ $[M+H]^+$ m/z: 279.1380, found: 279.1379.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 2-methylene-3-(*m*-tolyl)but-3-enoate (3q)

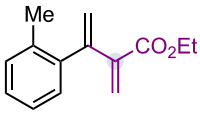


Prepared according to the general procedure C using **1q** (52.9 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 50/1) provided **3q** as a colorless oil (22.9 mg, 53% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.18 (m, 1H), 7.15 – 7.11 (m, 2H), 7.11 – 7.07 (m, 1H), 6.29 (d, *J* = 1.8 Hz, 1H), 5.80 (d, *J* = 1.8 Hz, 1H), 5.48 (d, *J* = 1.4 Hz, 1H), 5.38 (d, *J* = 1.4 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 2.34 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.8, 146.4, 142.5, 139.9, 138.0, 128.6, 128.3, 127.5, 127.4, 123.9, 116.2, 60.9, 21.6, 14.0.

HRMS (ESI) calculated for $C_{14}H_{16}NaO_2^+$ $[M+Na]^+$ m/z: 239.1043, found: 239.1046.

Ethyl 2-methylene-3-(*o*-tolyl)but-3-enoate (3r)

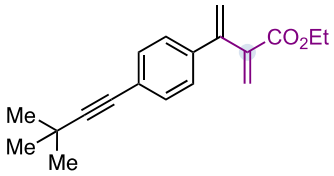


Prepared according to the general procedure C using **1r** (52.9 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3r** as a colorless oil (31.9 mg, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.09 (m, 4H), 6.01 (m, 1H), 5.78 (d, *J* = 1.5 Hz, 1H), 5.34 (d, *J* = 1.3 Hz, 1H), 5.24 (m, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.25 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.1, 145.0, 141.9, 140.6, 135.9, 130.2, 129.6, 127.6, 125.7, 125.4, 119.4, 61.0, 19.9, 14.2.

HRMS (ESI) calculated for $C_{14}H_{16}NaO_2^+$ $[M+Na]^+$ m/z: 239.1043, found: 239.1050.

Ethyl 3-(4-acetoxyphenyl)-2-methylenebut-3-enoate (3s)



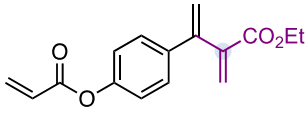
Prepared according to the general procedure C using **1s** (79.3 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3s** as a colorless oil (27.2 mg, 48% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 2H), 7.25 – 7.21 (m, 2H), 6.31 (d, *J* = 1.7 Hz, 1H), 5.79 (d, *J* = 1.7 Hz, 1H), 5.49 (d, *J* = 1.3 Hz, 1H), 5.38 (d, *J* = 1.3 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 1.31 (s, 9H), 1.10 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.6, 145.9, 142.3, 139.0, 131.6, 127.8, 126.5, 123.6, 116.5, 99.3, 79.1, 61.0, 31.2, 28.1, 14.1.

HRMS (ESI) calculated for $C_{19}H_{23}O_2^+$ $[M+H]^+$ m/z: 283.1693, found: 283.1689.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 3-(4-(acryloyloxy)phenyl)-2-methylenebut-3-enoate (3t)



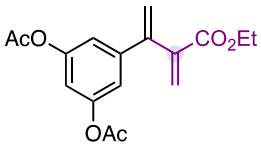
Prepared according to the general procedure C using **1t** (75.3 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/ethyl acetate 20/1) provided **3t** as a colorless oil (22.8 mg, 42% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 2H), 7.11 – 7.06 (m, 2H), 6.59 (dd, *J* = 17.3, 1.3 Hz, 1H), 6.31 (dd, *J* = 17.3, 10.5 Hz, 1H), 6.31 (d, *J* = 1.7 Hz, 1H), 6.00 (dd, *J* = 10.4, 1.3 Hz, 1H), 5.80 (d, *J* = 1.7 Hz, 1H), 5.48 (d, *J* = 1.3 Hz, 1H), 5.40 (d, *J* = 1.3 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 1.10 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.5, 164.5, 150.3, 145.4, 142.2, 137.8, 132.7, 128.0, 127.9, 127.8, 121.4, 116.6, 61.0, 14.0.

HRMS (ESI) calculated for $C_{16}H_{16}NaO_4^+$ $[M+Na]^+$ m/z: 295.0941, found: 295.0933.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

5-(3-(ethoxycarbonyl)buta-1,3-dien-2-yl)-1,3-phenylene diacetate (3u)

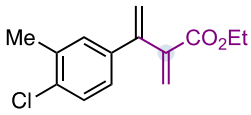


Prepared according to the general procedure C using **1u** (130.2 mg, 130 μL, 1.0 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 20/1 – 10/1) provided **3u** as a colorless oil (32.9 mg, 52% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (d, *J* = 2.1 Hz, 2H), 6.86 (t, *J* = 2.1 Hz, 1H), 6.34 (d, *J* = 1.6 Hz, 1H), 5.81 (d, *J* = 1.6 Hz, 1H), 5.51 (d, *J* = 1.1 Hz, 1H), 5.44 (d, *J* = 1.1 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 2.27 (s, 6H), 1.09 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.0, 166.3, 151.1, 144.8, 142.3, 141.6, 128.5, 117.8, 117.4, 114.8, 61.2, 21.2, 13.9.

HRMS (ESI) calculated for $C_{17}H_{18}NaO_6^+$ $[M+Na]^+$ m/z: 341.0996, found: 341.0995.

Ethyl 3-(4-chloro-3-methylphenyl)-2-methylenebut-3-enoate (3v)



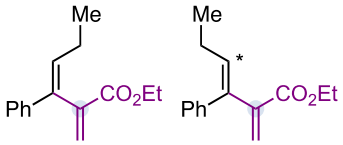
Prepared according to the general procedure C using **1v** (66.7 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 50/1) provided **3v** as a colorless oil (33.7 mg, 67% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.1 Hz, 1H), 7.18 (dd, *J* = 2.3, 0.9 Hz, 1H), 7.08 (ddd, *J* = 8.2, 2.3, 0.6 Hz, 1H), 6.31 (d, *J* = 1.7 Hz, 1H), 5.80 (d, *J* = 1.7 Hz, 1H), 5.46 (d, *J* = 1.3 Hz, 1H), 5.38 (d, *J* = 1.3 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.36 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.5, 145.5, 142.2, 138.6, 136.0, 133.9, 129.2, 129.0, 127.9, 125.5, 116.7, 61.0, 20.2, 14.1.

LRMS (APCI) calculated for $C_{14}H_{16}ClO_2^+$ $[M+H]^+$ m/z: 251.0833, found: 251.0832.

^{1}H-^{13}C HSQC spectra was measured.

Ethyl (*Z*)-2-methylene-3-phenylhex-3-enoate and ethyl (*E*)-2-methylene-3-phenylhex-3-enoate (3w)



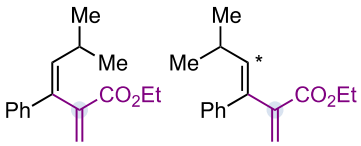
Prepared according to the general procedure C using **1w** (58.5 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3w** as a colorless oil (35.4 mg, 77% yield; *Z*:*E* ratio 9.5 : 1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.25 (m, 4H), 7.33 – 7.25 (m, 0.34*3H), 7.23 – 7.19 (m, 1H), 7.18 – 7.15 (m, 0.21*2H), 6.56 (d, *J* = 1.9 Hz, 1H), 6.03 (t, *J* = 7.5 Hz, 1H), 5.98 – 5.93 (m, 0.2*2H), 5.67 (d, *J* = 1.9 Hz, 1H), 5.42 (d, *J* = 1.6 Hz, 0.1*1H), 4.11 (q, *J* = 7.1 Hz, 2H), 4.15 – 4.07 (m, 0.16*2H, overlapped), 2.18 (app p, *J* = 7.5 Hz, 2H), 2.07 (app p, *J* = 7.5 Hz, 0.21*2H), 1.16 (t, *J* = 7.2 Hz, 0.33*3H), 1.12 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.5 Hz, 3H), 0.98 (t, *J* = 7.5 Hz, 0.33*3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.7*, 166.8, 144.1*, 141.5*, 141.1, 139.3, 138.7*, 137.7*, 137.0, 134.8*, 133.5, 129.4*, 129.1, 128.4, 128.2*, 127.1, 126.3, 124.2*, 60.9, 60.8*, 23.4, 22.9*, 14.3, 14.3*, 14.1 (2C); * *indicates signals of the minor isomer*.

HRMS (ESI) calculated for $C_{20}H_{21}NaO_2^+$ $[M+Na]^+$ m/z: 253.1199, found: 253.1195.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOESY spectra were measured.

Ethyl (*Z*)-5-methyl-2-methylene-3-phenylhex-3-enoate and ethyl (*E*)-5-methyl-2-methylene-3-phenylhex-3-enoate (3x)



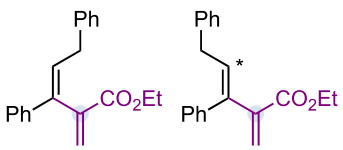
Prepared according to the general procedure C using **1x** (64.1 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3x** as a colorless oil (44.4 mg, 91% yield; *Z*:*E* ratio 7 : 1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.25 (m, 4H), 7.33 – 7.25 (m, 0.51*3H), 7.23 – 7.19 (m, 1H), 7.18 – 7.15 (m, 0.30*2H), 6.54 (d, *J* = 2.0 Hz, 1H), 5.93 (d, *J* = 1.5 Hz, 0.14*1H), 5.83 (d, *J* = 10.1 Hz, 1H), 5.77 (d, *J* = 10.2 Hz, 0.14*1H), 5.66 (d, *J* = 2.0 Hz, 1H), 5.37 (d, *J* = 1.6 Hz, 0.14*1H), 4.13 (q, *J* = 7.1 Hz, 0.29*2H), 4.11 (q, *J* = 7.1 Hz, 2H), 2.57 (dhept, *J* = 10.1, 6.6 Hz, 1H), 2.39 (dhept, *J* = 10.3, 6.6 Hz, 0.14*1H), 1.17 (t, *J* = 7.1 Hz, 0.45*3H), 1.13 (t, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 6H), 0.97 (d, *J* = 6.6 Hz, 0.87*6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.6*, 166.8, 144.2*, 140.9, 140.3*, 139.6, 139.0*, 138.8, 135.9*, 135.1, 129.3*, 128.8, 128.3, 128.2*, 127.1, 127.0*, 126.3, 124.1*, 60.9, 60.8*, 29.3, 28.5*, 23.1 (2C), 14.1 (2C); * *indicates signals of the minor isomer*.

HRMS (ESI) calculated for $C_{16}H_{21}O_2^+$ $[M+H]^+$ m/z: 245.1536, found: 245.1531.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOESY spectra were measured.

Ethyl (*Z*)-2-methylene-3,5-diphenylpent-3-enoate and ethyl (*E*)-2-methylene-3,5-diphenylpent-3-enoate (3y)



Prepared according to the general procedure C using **1y** (83.3 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). 5 equiv. of TBAOTf were necessary for the reaction (391.5 mg, 1.0 mmol). Purification by

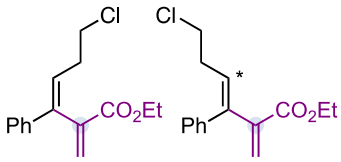
flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3y** as a colorless oil (55.3 mg, 95% yield, *Z*:*E* ratio 7 : 1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.14 (m, 10H), 7.37 – 7.14 (m, 1.40*10H), 6.62 (d, *J* = 1.8 Hz, 1H), 6.21 (t, *J* = 7.6 Hz, 1H), 6.15 (t, *J* = 7.6 Hz, 0.14*1H), 6.02 (d, *J* = 1.5 Hz, 0.12*1H), 5.75 (d, *J* = 1.8 Hz, 1H), 5.48 (d, *J* = 1.5 Hz, 0.12*1H), 4.12 (q, *J* = 7.1 Hz, 0.28*2H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.55 (d, *J* = 7.6 Hz, 2H), 3.42 (d, *J* = 7.6 Hz, 0.25*2H), 1.15 (t, *J* = 7.1 Hz, 0.45*3H), 1.12 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.4*, 166.6, 143.9*, 140.6 (2C), 140.6, 139.1*, 139.0, 138.5, 138.3*, 131.0*, 129.7, 129.6, 129.4*, 128.7, 128.6*, 128.6, 128.5*, 128.4, 128.3*, 127.4, 127.4*, 126.4, 126.3, 126.2*, 125.1*, 61.1, 60.9*, 36.1, 35.6*, 14.1 (2C); * *indicates signals of the minor isomer*.

HRMS (ESI) calculated for $C_{20}H_{21}O_2^+$ $[M+H]^+$ m/z: 293.1536, found: 293.1539.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOESY spectra were measured.

Ethyl (*Z*)-6-chloro-2-methylene-3-phenylhex-3-enoate and ethyl (*E*)-6-chloro-2-methylene-3-phenylhex-3-enoate (3z)



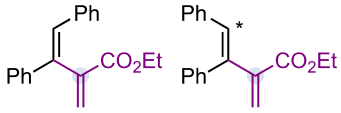
Prepared according to the general procedure C using **1z** (72.3 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 50/1) provided **3z** as a colorless oil (49.6 mg, 94% yield; *Z*/*E* ratio 5.3 : 1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.22 (m, 5H), 7.40 – 7.22 (m, 0.48*4H), 7.19 – 7.15 (m, 0.24*2H), 6.61 (d, *J* = 1.8 Hz, 1H), 6.06 (t, *J* = 7.4 Hz, 1H), 6.03 (t, *J* = 7.3 Hz, 0.12*1H), 5.73 (d, *J* = 1.8 Hz, 1H), 5.48 (d, *J* = 1.5 Hz, 0.12*1H), 4.17 – 4.11 (m, 0.24*2H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.60 (t, *J* = 6.9 Hz, 2H), 3.53 (t, *J* = 6.8 Hz, 0.24*2H), 2.67 (q, *J* = 7.0 Hz, 2H), 2.54 (q, *J* = 6.9 Hz, 0.24*2H), 1.17 (t, *J* = 7.2 Hz, 0.36*3H), 1.14 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.2*, 166.3, 143.5*, 140.9*, 140.4, 140.3, 138.9, 138.1*, 129.7, 129.2*, 128.5, 128.4*, 128.2*, 127.6, 127.5*, 126.7, 126.4, 125.5*, 61.1, 61.0*, 44.1*, 44.1, 33.2, 32.6*, 14.1 (2C); * *indicates signals of the minor isomer*.

HRMS (ESI) calculated for $C_{15}H_{17}ClNaO_2^+$ $[M+Na]^+$ m/z: 287.0809, found: 287.0815.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOESY spectra were measured.

Ethyl (*Z*)-2-methylene-3,4-diphenylbut-3-enoate and ethyl (*E*)-2-methylene-3,4-diphenylbut-3-enoate (3aa)



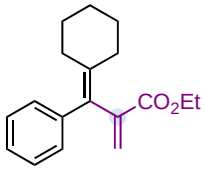
Prepared according to the general procedure C using **1aa** (77.7 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 50/1) provided **3aa** as a colorless oil (42.2 mg, 76% yield; *Z*/*E* ratio 9 : 1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.42 (m, 2H), 7.39 – 7.33 (m, 4H), 7.33 – 7.27 (m, 3H), 7.33 – 7.27 (m, 0.26*2H), 7.25 – 7.17 (m, 1H), 7.25 – 7.17 (m, 0.52*3H), 7.14 – 7.10 (m, 0.46*3H), 7.00 (m, 0.28*2H), 6.94 (s, 1H), 6.88 (s, 0.14*1H), 6.51 (d, *J* = 1.6 Hz, 1H), 6.11 (d, *J* = 1.4 Hz, 0.13*1H), 5.70 (d, *J* = 1.6 Hz, 1H), 5.62 (d, *J* = 1.4 Hz, 0.13*1H), 4.15 (q, *J* = 7.1 Hz, 0.27*2H), 4.04 (q, *J* = 7.1 Hz, 2H), 1.15 (t, *J* = 7.1 Hz, 0.44*3H), 1.02 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.4*, 166.8, 144.8*, 142.1, 140.7, 139.0*, 138.7*, 138.4, 137.5, 136.7*, 130.7, 130.5*, 130.4, 129.9*, 129.8*, 129.2, 128.6, 128.5*, 128.4, 128.0*, 127.8, 127.6*, 127.3, 127.3*, 127.0, 125.5*, 61.1, 61.0*, 14.1*, 14.0; * *indicates signals of the minor isomer*.

HRMS (ESI) calculated for $C_{19}H_{18}NaO_2^+$ $[M+Na]^+$ m/z: 301.1199, found: 301.1189.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOESY spectra were measured.

Ethyl 2-(cyclohexylidene(phenyl)methyl)acrylate (3ab)



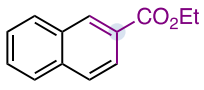
Prepared according to the general procedure C using **1ab** (74.5 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3ab** as a colorless oil (19.5 mg, 36% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 2H), 7.22 – 7.16 (m, 3H), 6.32 (d, *J* = 2.0 Hz, 1H), 5.57 (d, *J* = 2.0 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 2.29 – 2.21 (m, 2H), 2.19 – 2.12 (m, 2H), 1.59 (m, 4H), 1.54 (m, 2H), 1.18 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.2, 142.2, 141.2, 141.1, 130.0, 129.6, 127.9, 127.3, 126.4, 60.8, 32.8, 31.8, 28.6, 28.5, 26.8, 14.2.

HRMS (ESI) calculated for $C_{19}H_{19}O_2^+$ $[M+H]^+$ m/z: 271.1693, found: 271.1685.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 2-naphthoate (3ac)



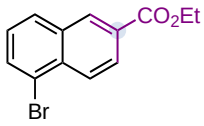
Prepared according to the general procedure C using **1ac** (116.2 mg, 116 μL, 1.0 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3ac** as a colorless oil (21.9 mg, 55% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 0.8 Hz, 1H), 8.08 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.96 (dd, *J* = 8.1, 0.7 Hz, 1H), 7.88 (d, *J* = 8.5 Hz, 2H), 7.59 (ddd, *J* = 8.2, 6.8, 1.4 Hz, 1H), 7.54 (ddd, *J* = 8.2, 6.9, 1.4 Hz,

1H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.46 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.9, 135.6, 132.7, 131.1, 129.5, 128.3, 128.2, 127.9, 127.9, 126.7, 125.4, 61.2, 14.5.

Spectra are consistent with those reported in the literature[14].

Ethyl 5-bromo-2-naphthoate (3ad)



Prepared according to the general procedure C using **1ad** (195.1 mg, 134 μL, 1.0 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3ad** as a colorless oil (36.4mg, 65% yield).

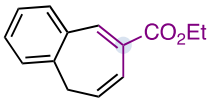
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 1.5 Hz, 1H), 8.27 (d, *J* = 8.9 Hz, 1H), 8.16 (dd, *J* = 8.9, 1.7 Hz, 1H), 7.92 (d, *J* = 8.3 Hz, 1H), 7.88 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.38 (dd, *J* = 8.2, 7.4 Hz, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 1.46 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.4, 134.2, 133.9, 132.2, 131.3, 129.4, 128.8, 127.6, 127.1, 126.8, 122.9, 61.5, 14.5.

HRMS (ESI) calculated for $C_{13}H_{11}BrNaO_2^+$ $[M+Na]^+$ m/z: 300.9835, found: 300.9841.

^{1}H-^{13}C HSQC spectra was measured.

The crystal structure of **3ad** has been deposited at the Cambridge Crystallographic Data Centre, CCDC 1875941.

Ethyl 5*H*-benzo[7]annulene-8-carboxylate (3ae)

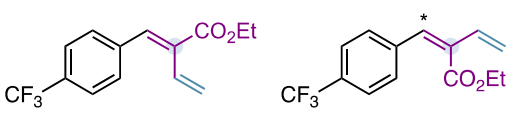


Prepared according to the general procedure C using **1ae** (130.2 mg, 130 μL, 1.0 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3ae** as a colorless oil (17.7 mg, 41% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.44 (td, *J* = 7.5, 1.4 Hz, 1H), 7.28 (td, *J* = 7.5, 1.3 Hz, 1H), 7.21 (d, *J* = 7.5 Hz, 1H), 6.58 (d, *J* = 10.0 Hz, 1H), 5.89 (dt, *J* = 10.0, 6.9 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.05 (d, *J* = 6.9 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.7, 140.6, 137.6, 134.5, 130.9, 130.5, 129.8, 127.8, 127.6, 126.0, 124.2, 61.3, 34.3, 14.5.

HRMS (ESI) calculated for $C_{14}H_{14}NaO_2^+$ $[M+Na]^+$ m/z: 237.0886, found: 238.0891.

Ethyl (*Z*)-2-(4-(trifluoromethyl)benzylidene)but-3-enoate and ethyl (*E*)-2-(4-(trifluoromethyl)benzylidene)but-3-enoate (3af)

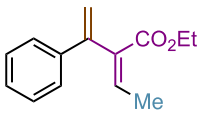


Prepared according to the general procedure C using 1-(prop-1-en-1-yl)-4-(trifluoromethyl)benzene **1af** (*E*/*Z* ratio 3 : 1, 74.5 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 50/1 – 20/1) provided **3af** as a colorless oil (16.6 mg, 31% yield; *Z*/*E* ratio 1 : 1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.1 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 0.70*2H), 7.54 – 7.49 (m, 3H), 7.41 (d, *J* = 7.8 Hz, 0.70*2H), 6.65 (s, 0.35*1H), 6.56 (ddd, *J* = 17.7, 11.6, 1.0 Hz, 1H), 6.47 (ddd, *J* = 17.5, 10.8, 0.8 Hz, 0.35*1H), 5.86 (dd, *J* = 17.7, 1.4 Hz, 1H), 5.50 – 5.44 (m, 1H), 5.40 (d, *J* = 17.5 Hz, 0.35*1H), 5.35 (d, *J* = 10.7 Hz, 0.35*1H), 4.33 (q, *J* = 7.1 Hz, 2H), 4.27 (q, *J* = 7.1 Hz, 0.70*2H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 1.05*3H); * *indicates signals of the minor isomer*; **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.1, 167.1, 139.0, 139.0, 137.1, 136.7, 135.0, 132.6, 131.3, 131.1, 130.4 (q, *J* = 32.5 Hz) 130.2, 129.2, 128.6, 125.5 (q, *J* = 3.7 Hz), 125.4 (q, *J* = 3.8 Hz), 125.1 (q, *J* = 272.2 Hz), 124.1 (q, *J* = 272.0 Hz), 122.3, 118.1, 61.6, 61.4, 14.4, 14.0; C–CF_3 from the minor isomer missing; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.71 (s, 1.05*3F), -62.76 (s, 3F).

HRMS (ESI) calculated for $C_{14}H_{13}F_3NaO_2^+$ $[M+Na]^+$ m/z: 293.0760, found: 293.0771.

Ethyl (*Z*)-2-(1-phenylvinyl)but-2-enoate (3ag)

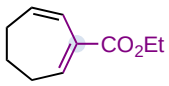


Prepared according to the general procedure C using but-2-en-2-ylbenzene **1ag** (*E*/*Z* ratio 9 : 1, 52.9 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1 – 50/1) provided **3ag** as a colorless oil (16.6 mg, 38% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 2H), 7.33 – 7.25 (m, 3H), 7.18 (q, *J* = 7.1 Hz, 1H), 5.79 (d, *J* = 1.4 Hz, 1H), 5.12 (d, *J* = 1.4 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 1.86 (d, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.0, 142.7, 140.7, 139.7, 135.1, 128.5, 127.8, 126.0, 116.6, 60.7, 15.6, 14.1.

HRMS (ESI) calculated for $C_{14}H_{16}NaO_2^+$ $[M+Na]^+$ m/z: 239.1043, found: 239.1053.

Ethyl cyclohepta-1,6-diene-1-carboxylate (3ah)



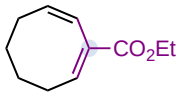
Prepared according to the general procedure C using **1ah** (82.1 mg, 101 μL, 1.0 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3ah** as a colorless oil (26.8 mg, 64% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (t, *J* = 5.9 Hz, 1H), 6.37 (app, 1H), 5.98 (dt, *J* = 11.8, 5.2 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.45 (dt, *J* = 5.8 Hz, 5.8 Hz, 2H), 2.35 (dt, *J* = 5.3 Hz, 5.3 Hz, 2H), 1.91 – 1.85 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.9, 143.8, 134.9, 130.0, 123.1, 60.9, 31.6, 30.8, 26.1, 14.4.

HRMS (ESI) calculated for $C_{10}H_{14}NaO_2^+$ $[M+Na]^+$ m/z: 189.0886, found: 189.0891.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOESY spectra were measured.

Ethyl (1*E*,7*Z*)-cycloocta-1,7-diene-1-carboxylate (3ai)



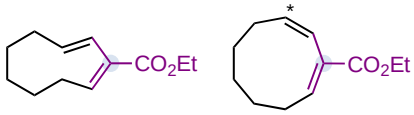
Prepared according to the general procedure C using **1ai** (96.2 mg, 117 µL, 1.0 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3ai** as a colorless oil (22.7 mg, 63% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (t, *J* = 8.1 Hz, 1H), 6.13 (d, *J* = 11.3 Hz, 1H), 5.84 (dt, *J* = 11.3, 7.2 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 2.34 – 2.23 (m, 2H), 2.15 – 2.08 (m, 2H), 1.57 – 1.50 (m, 2H), 1.47 – 1.43 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.6, 142.6, 133.5, 130.5, 123.3, 60.7, 28.5, 28.4, 22.9, 22.4, 14.4.

HRMS (ESI) calculated for $C_{11}H_{17}O_2^+$ $[M+H]^+$ m/z: 181.1223, found: 181.1221.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOESY spectra were measured.

Ethyl (1*E*,8*E*)-cyclonona-1,8-diene-1-carboxylate and ethyl (1*E*,8*Z*)-cyclonona-1,8-diene-1-carboxylate (3aj)



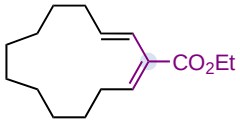
Prepared according to the general procedure C using **1aj** (110.2 mg, 130 µL, 1.0 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Ratio of isomers was determined to be 2:1 from the crude reaction mixture using ^{1}H NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3aj** as a mixture of two isomers as a colorless oil (22.0 mg, 57% yield, *E*,*E*/*E*,*Z* 2 : 1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (t, *J* = 8.5 Hz, 0.50*1H), 6.87 (t, *J* = 8.6 Hz, 1H), 5.76 (dt, *J* = 10.7, 7.9 Hz, 0.52*1H), 5.63 – 5.52 (m, 2H), 5.48 (dt, *J* = 10.6, 8.5 Hz, 0.52*1H), 4.19 (q, *J* = 6.8 Hz, 1.08*2H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.00 (dd, *J* = 8.6, 7.2 Hz, 2H), 2.54 (t, *J* = 6.3 Hz, 2H), 2.33 – 2.23 (m, 2H, 1.08*2H), 2.11 – 2.06 (m, 1.10*2H), 1.89 – 1.83 (m, 1.00*2H), 1.69 – 1.61 (m, 2H, 1.13*2H), 1.57 – 1.51 (m, 2H, 1.23*2H), 1.30 (t, *J* = 7.2 Hz, 1.93*3H), 1.28 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.2 (2C), 142.7*, 139.5, 134.5, 132.5*, 132.1, 131.0*, 130.2*, 126.4, 60.5, 60.4*, 28.5*, 28.0, 27.6, 27.5*, 26.6, 25.0*, 24.5*, 23.9*, 22.7, 21.6, 14.4*, 14.4; * *indicates signals of the minor isomer*.

HRMS (ESI) calculated for $C_{12}H_{18}NaO_2^+$ $[M+Na]^+$ m/z: 217.1199, found: 217.1205.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOESY spectra were measured.

Ethyl (1*E*,12*E*)-cyclotrideca-1,12-diene-1-carboxylate (3ak)

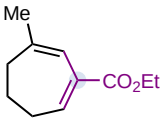


Prepared according to the general procedure C using **1ak** (166.3 mg, 191 μL, 1.0 mmol, *E*/*Z* = 2:1) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/ diethyl ether 50/1) provided **3ak** as a colorless oil (28.2 mg, 56 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.71 (t, *J* = 8.6 Hz, 1H), 6.10 (d, *J* = 16.9 Hz, 1H), 5.85 (dt, *J* = 16, 7.2, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.26 (dt, *J* = 8.6, 7.1 Hz, 2H), 2.20 (ddd, *J* = 11.6, 7.2, 1.3 Hz, 2H), 1.46 (d, *J* = 32.7 Hz, 4H), 1.39 – 1.23 (m, 13H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.7, 142.6, 137.1, 131.8, 123.4, 60.65, 33.6, 27.0, 26.9, 26.8, 26.8, 26.3, 26.2, 26.2, 25.5, 14.4.

HRMS (ESI) calculated for $C_{16}H_{26}NaO_2^+$ $[M+Na]^+$ m/z: 273.1825, found:273.1813.

Ethyl 6-methylcyclohepta-1,6-diene-1-carboxylate (3al)



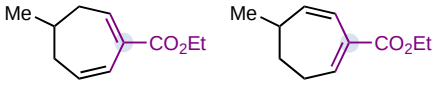
Prepared according to the general procedure C using **1al** (96.2 mg, 120 μL, 1.0 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3al** as a colorless oil (24.3 mg, 67% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (t, *J* = 5.9 Hz, 1H), 6.16 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 2.39 (dt, *J* = 6.0 Hz, 6.0 Hz, 2H), 2.26 (t, *J* = 6.0 Hz, 2H), 1.91 – 1.87 (m, 5H), 1.30 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.2, 144.1, 141.9, 129.9, 118.9, 60.8, 36.0, 30.3, 27.3, 26.5, 14.4.

HRMS (ESI) calculated for $C_{11}H_{16}NaO_2^+$ $[M+Na]^+$ m/z: 203.1043, found: 203.1035.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 4-methylcyclohepta-1,6-diene-1-carboxylate (3am)



major *minor*

Prepared according to the general procedure C using **1am** (96.2 mg, 120 μL, 1.0 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Ratio of isomers was determined to be 1.5:1 from the crude reaction mixture using ^{1}H NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided the the mixture of two isomers as a colorless oil (29.0 mg, 80% yield, isomer ratio 1 : 1).

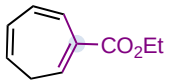
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (t, *J* = 5.9 Hz, 0.81*1H), 7.12 (t, *J* = 5.9 Hz, 1H), 6.36 (d, *J* = 11.9 Hz, 1H), 6.29 (d, *J* = 12.2 Hz, 0.79*1H), 5.95 (dt, *J* = 11.9, 5.5 Hz, 1H), 5.82 (dd, *J* = 12.2, 4.4 Hz, 0.80*1H), 4.20 (q, *J* = 7.1 Hz, 2H, 1.63*2H), 2.57 – 2.50 (m, 0.85*1H), 2.44 – 2.37 (m, 2H, 0.80*1H), 2.36 – 2.31 (m, 0.85*1H), 2.22 – 2.12 (m, 2H), 2.11 – 2.03 (m, 1H), 1.88 – 1.84 (m, 0.84*1H), 1.70 – 1.67 (m, 0.82*1H), 1.30 (t, *J* = 7.1 Hz, 3H, 2.44*3H), 1.07 (d, *J* = 7.2 Hz, 2.49*3H), 1.00 (d, *J* = 6.3 Hz, 3H; **^{13}C**

NMR (126 MHz, $CDCl_3$) δ 167.9*, 167.7, 144.3*, 142.5, 140.6*, 133.5, 130.3, 129.7*, 123.5, 121.2*, 60.9*, 60.8, 38.9, 38.1, 36.1*, 33.7, 33.7*, 28.2*, 22.4, 21.9*, 14.4 (2C); * *indicates signals of the minor isomer*.

HRMS (ESI) calculated for $C_{11}H_{16}NaO_2^+$ $[M+Na]^+$ m/z: 203.1043, found: 203.1039.

^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl cyclohepta-1,4,6-triene-1-carboxylate (3an)

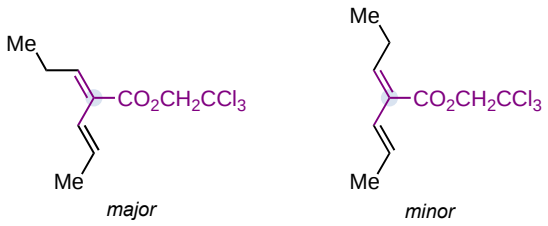


Prepared according to the general procedure C using **1an** (80.5 mg, 95 µL, 1.0 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3an** as a colorless oil (15.3 mg, 47% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 – 7.12 (m, 1H), 6.75 – 6.67 (m, 1H), 6.52 – 6.45 (m, 1H), 6.22 – 6.18 (m, 1H), 5.48 – 5.37 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.38 – 2.32 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.9, 131.9, 130.6, 129.8, 128.4, 127.7, 120.9, 60.9, 27.7, 14.4.

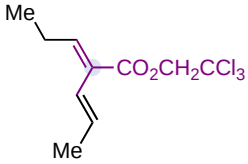
HRMS (ESI) calculated for $C_{10}H_{12}NaO_2^+$ $[M+H]^+$ m/z: 187.0730, found: 187.0731.

2,2,2-trichloroethyl (*E*)-2-((*E*)-prop-1-en-1-yl)pent-2-enoate and 2,2,2-trichloroethyl (*Z*)-2-((*E*)-prop-1-en-1-yl)pent-2-enoate (3ao)



Prepared according to the general procedure C using **1ao** (84.2 mg, 124 µL, 1.0 mmol) and reagent **2a-OTf** (160.6 mg, 0.2 mmol). Ratio of isomers was determined to be 1.5:1 from the crude reaction mixture using ^{1}H NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ dichloromethane 50/1) provided a mixture of isomers as a colorless oil (23.6 mg, 43% yield, *E*/*Z* 1 : 1). The two isomers could be separated on preparative TLC plate.

2,2,2-trichloroethyl (*E*)-2-((*E*)-prop-1-en-1-yl)pent-2-enoate

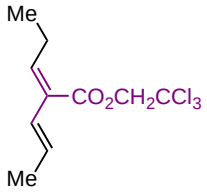


^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.76 (t, *J* = 7.5 Hz, 1H), 6.22 – 6.09 (m, 2H), 4.82 (s, 2H), 2.38 – 2.31 (m, 2H), 1.84 (dt, *J* = 5.4, 0.5 Hz, 3H), 1.08 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 166.0, 146.1, 132.2, 129.0, 123.1, 95.9, 74.6, 22.8, 19.4, 13.7.

HRMS (ESI) calculated for $C_{10}H_{13}Cl_3NaO_2^+$ $[M+Na]^+$ m/z: 292.9873, found: 292.9877.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl (*Z*)-2-((*E*)-prop-1-en-1-yl)pent-2-enoate

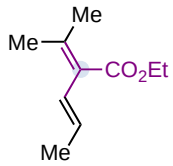


^{1}H NMR (400 MHz, $CDCl_3$) δ 6.08 (d, *J* = 16.6 Hz, 1H), 5.98 (t, *J* = 7.8 Hz, 1H), 5.82 (dq, *J* = 15.6, 6.6 Hz, 1H), 4.86 (s, 2H), 2.37 (p, *J* = 7.6 Hz, 2H), 1.78 (dd, *J* = 6.6, 1.2 Hz, 3H), 1.06 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.2, 141.4, 130.8, 128.5, 127.3, 95.0, 74.4, 23.5, 18.5, 14.0.

HRMS (ESI) calculated for $C_{10}H_{13}Cl_3NaO_2^+$ $[M+Na]^+$ m/z: 292.9873, found: 292.9878.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl (*E*)-2-(propan-2-ylidene)pent-3-enoate (3ap)



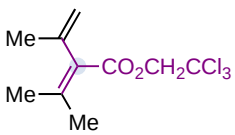
Prepared according to the general procedure C using **1ap** (84.2 mg, 122 µL, 1.0 mmol) and reagent **2a-OTf** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) **3ap** as a colorless oil (11.1 mg, 33% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (dq, *J* = 16.0, 1.7 Hz, 1H), 5.61 – 5.49 (m, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 1.81 (s, 3H), 1.80 – 1.76 (m, 6H), 1.33 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.3, 133.7, 129.8, 126.9, 125.4, 60.7, 22.8, 19.8, 18.8, 14.4.

HRMS (ESI) calculated for $C_{10}H_{16}NaO_2^+$ $[M+Na]^+$ m/z: 191.1043, found: 191.1035.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl 3-methyl-2-(prop-1-en-2-yl)but-2-enoate (3aq)



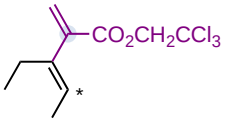
Prepared according to the general procedure C using **1aq** (84.2 mg, 119 µL, 1.0 mmol), reagent **2a-OTf** (160.6 mg, 0.2 mmol) and $Rh_2(Adc)_4$ (2.0 mg, 0.002 mmol). Purification by flash chromatography on silica gel (hexane/ dichloromethane 50/1) provided **3aq** as a colorless oil (14.1 mg, 26% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.13 (p, *J* = 1.5 Hz, 1H), 4.79 – 4.78 (m, 3H), 2.13 (s, 3H), 1.91 (dd, *J* = 1.6, 1.0 Hz, 3H), 1.89 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.7, 149.3, 142.1, 129.8, 116.5, 95.4, 74.1, 24.0, 23.4, 22.6.

HRMS (ESI) calculated for $C_{10}H_{13}Cl_3NaO_2^+$ $[M+Na]^+$ m/z: 292.9873, found: 292.9874.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

2,2,2-trichloroethyl (*E*)-3-ethyl-2-methylenepent-3-enoate and 2,2,2-trichloroethyl (*Z*)-3-ethyl-2-methylenepent-3-enoate (3ar)



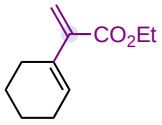
Prepared according to the general procedure C using **1ar** (84.2 mg, 122 µL, 1.0 mmol), reagent **2a-OTf** (160.6 mg, 0.2 mmol) and $Rh_2(Adc)_4$ (2.0 mg, 0.002 mmol). Ratio of isomers was determined to be 3:1 from the crude reaction mixture using ^{1}H NMR spectroscopy. Purification by flash chromatography on silica gel (hexane/ dichloromethane 50/1) provided a mixture of isomers as a colorless oil (22.2 mg, 41% yield, *E*/*Z* 3 : 1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.53 (d, *J* = 1.7 Hz, 0.3*1H), 6.13 (d, *J* = 1.4 Hz, 1H), 5.69 (d, *J* = 1.4 Hz, 1H), 5.64 (q, *J* = 7.2 Hz, 1H), 5.63 (d, *J* = 1.7 Hz, 0.27*1H), 5.54 (qt, *J* = 6.8, 1.5 Hz, 0.32*1H), 4.82 (s, 2H), 4.81 (s, 0.59*2H), 2.33 (q, *J* = 7.6 Hz, 2H), 2.22 (qt, *J* = 7.5, 1.4 Hz, 0.64*2H), 1.72 (d, *J* = 6.9 Hz, 3H), 1.57 (dt, *J* = 6.8, 1.6 Hz, 1.09*3H), 0.98 (t, *J* = 7.5 Hz, 1.05*3H), 0.95 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.8, 164.9*, 142.4, 139.1, 138.8*, 138.8*, 129.8*, 125.7, 125.4, 123.0*, 95.2 (2C), 74.5*, 74.4, 30.3*, 21.8, 14.7*, 13.7, 12.8*, 12.8; * *indicates signals of the minor isomer*.

HRMS (ESI) calculated for $C_{11}H_{14}Cl_{13}NaO_2^+$ $[M+Na]^+$ m/z: 271.0054, found: 271.0052.

^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC spectra were measured.

Ethyl 2-(cyclohex-1-en-1-yl)acrylate (3as)

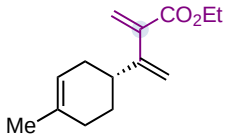


Prepared according to the general procedure C using **1as** (96.2 mg, 120 µL, 1.0 mmol) and reagent **2a-OTf** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3as** as a colorless oil (24.5 mg, 68% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.99 (t, *J* = 4.1 Hz, 1H), 5.69 (s, 1H), 5.46 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.17 – 2.14 (m, 4H), 1.71 – 1.68 (m, 2H), 1.61 – 1.59 (m, 2H), 1.32 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.3, 144.0, 133.5, 128.9, 118.9, 60.9, 26.4, 25.8, 22.7, 22.0, 14.4.

HRMS (ESI) calculated for $C_{11}H_{16}NaO_2^+$ $[M+Na]^+$ m/z: 203.1043, found: 203.1035.

Ethyl (*R*)-3-(4-methylcyclohex-3-en-1-yl)-2-methylenebut-3-enoate (3at)

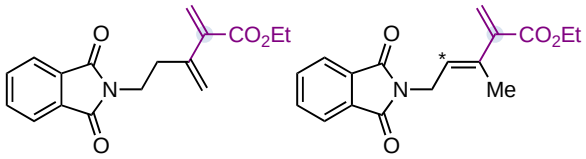


Prepared according to the general procedure C using **1at** (54.5 mg, 65µL, 0.4 mmol) and reagent **2a** (141.6 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 100/1) provided **3at** as a colorless oil (25.6 mg, 58 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.05 (d, *J* = 1.8 Hz, 1H), 5.59 (d, *J* = 1.8 Hz, 1H), 5.41 – 5.36 (m, 1H), 5.08 (dd, *J* = 1.4, 0.6 Hz, 1H), 5.02 (t, *J* = 1.4 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.47 – 2.37 (m, 1H), 2.19 – 2.04 (m, 2H), 2.04 – 1.94 (m, 2H), 1.92 – 1.85 (m, 2H), 1.67 – 1.64 (m, 3H), 1.30 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.2, 151.3, 143.6, 133.9, 124.9, 120.6, 113.1, 61.0, 37.4, 31.5, 30.7, 28.3, 23.5, 14.3.

HRMS (ESI) calculated for $C_{14}H_{20}NaO_2^+$ $[M+Na]^+$ m/z: 243.1356, found: 243.1345

Ethyl 5-(1,3-dioxoisoindolin-2-yl)-2,3-dimethylenepentanoate and ethyl (*E*)-5-(1,3-dioxoisoindolin-2-yl)-3-methyl-2-methylenepent-3-enoate (3au)



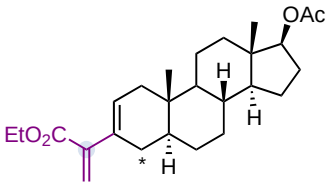
Prepared according to the general procedure C using **1au** (86.1 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 20/1) provided **3au** as a colorless oil (27.6 mg, 46% yield; Terminal/internal ratio 1.3 : 1; internal *E*/*Z* ratio 4.3 : 1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.78 (m, 2H), 7.86 – 7.78 (m, 1.73*2H), 7.73 – 7.66 (m, 2H), 7.73 – 7.66 (m, 1.86*2H), 6.08 (d, *J* = 1.2 Hz, 1H), 5.93 (d, *J* = 1.3 Hz, 0.71*1H), 5.77 (d, *J* = 1.2 Hz, 1H), 5.70 (tq, *J* = 7.0, 1.4 Hz, 0.72*1H), 5.58 (d, *J* = 1.3 Hz, 0.72*1H), 5.25 (d, *J* = 1.4 Hz, 1H), 5.12 (d, *J* = 1.3 Hz, 1H), 4.38 (dd, *J* = 7.0, 0.9 Hz, 1.52*2H), 4.22 (q, *J* = 7.1 Hz, 2H), 4.19 (q, *J* = 7.1 Hz, 1.73*2H), 3.82 – 3.74 (m, 2H), 2.69 (m, 2H), 2.03 – 1.98 (m, 2.19*3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 2.50*3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.3, 168.1*, 166.9*, 166.7, 144.1*, 141.9, 141.5, 136.5*, 134.0*, 134.0, 132.3*, 132.2, 125.4, 124.2*, 123.6*, 123.4*, 123.3, 118.3, 61.1, 61.0*, 37.1, 36.0*, 33.6, 15.7*, 14.3 (2C); * *indicates signals of the minor isomer*.

HRMS (ESI) calculated for $C_{17}H_{17}NNaO_4^+$ $[M+Na]^+$ m/z: 322.1050, found: 322.1043.

Ethyl 2-((5*S*,8*R*,10*S*,13*S*,14*S*,17*S*)-17-acetoxy-10,13-dimethyl-4,5,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)acrylate and ethyl 2-((5*S*,8*R*,10*R*,13*S*,14*S*,17*S*)-

17-acetoxy-10,13-dimethyl-2,5,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)acrylate (3av)



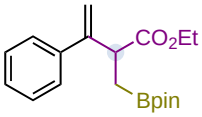
Prepared according to the general procedure C using **1av** (132.2 mg, 0.4 mmol) and reagent **2a** (119.2 mg, 0.2 mmol). Purification by flash chromatography on silica gel (hexane/diethyl ether 50/1 – 20/1) provided **3av** as a colorless oil (42.3 mg, 51% yield; isomer ratio 7.7 : 1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 – 5.87 (m, 1H), 5.69 (d, *J* = 1.2 Hz, 1H), 5.44 (d, *J* = 1.3 Hz, 1H), 4.57 (dd, *J* = 9.2, 7.8 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.21 – 2.08 (m, 2H), 2.02 (s, 3H), 1.91 – 1.80 (m, 2H), 1.75 – 1.68 (m, 2H), 1.67 – 1.56 (m, 2H), 1.52 – 1.44 (m, 3H), 1.42 – 1.33 (m, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.18 – 1.07 (m, 2H), 1.07 – 0.97 (m, 1H), 0.88 – 0.81 (m, 3H), 0.77 (s, 3H), 0.74 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.3, 168.1, 143.3, 132.2, 127.5, 119.2, 83.0, 60.8, 53.9, 50.8, 42.6, 41.5, 40.5, 37.0, 35.5, 34.5, 31.4, 31.4, 28.7, 27.6, 23.6, 21.3, 20.6, 14.3, 12.2, 12.0.

HRMS (ESI) calculated for $C_{26}H_{38}NaO_4^+$ $[M+Na]^+$ m/z: 437.2662, found: 437.2653.

Derivatization of 3a

Ethyl 3-phenyl-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)but-3-enoate (5a)



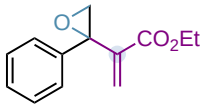
Prepared according to the reported protocol.[58] CuCl (1.5 mg, 0.015 mmol), NaO^{t}Bu (4.3 mg, 0.045 mmol) and DPEphos ligand (8.1 mg, 0.015 mmol) were placed in an oven-dried tube and THF (0.40 mL) was added under nitrogen. The reaction mixture was stirred for 30 min at room temperature and then, bis(pinacolato)diboron (28.0 mg, 0.11 mmol) and THF (0.3 mL) were added. The reaction mixture was stirred for 10 min and then **3a** (20.0 mg, 0.1 mmol) was added, followed by MeOH (16 µL, 0.2 mmol). The reaction tube was washed with THF (0.3 mL), sealed, and stirred until no starting material was detected by TLC (24 h). The reaction mixture was filtered through a pad of Celite and concentrated under *vacuum*. Purification by flash chromatography on silica gel (hexane/diethyl ether 50/1) provided **4a** as a colorless oil (15.1 mg, 46% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.37 (m, 2H), 7.34 – 7.23 (m, 3H), 5.33 (d, *J* = 0.6 Hz, 1H), 5.22 (m, 1H), 4.09 (qd, *J* = 7.1, 3.0 Hz, 2H), 3.79 (ddd, *J* = 9.2, 7.0, 0.9 Hz, 1H), 1.43 – 1.36 (m, 1H), 1.23 – 1.21 (m, 1H), 1.20 (d, *J* = 2.5 Hz, 12H), 1.16 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.7, 149.1, 141.5, 128.3, 127.6, 126.9, 114.3, 83.4, 60.8, 46.5, 25.0, 24.8, 14.2; **^{11}B NMR** (128 MHz, $CDCl_3$) δ 35.93 – 30.98 (m).

[58] Knott, K.; Fishovitz, J.; Thorpe, S. B.; Lee, I.; Santos, W. L. *Org. Biomol. Chem.* **2010**, *8*, 3451.

HRMS (ESI) calculated for $C_{19}H_{27}NaO_4B^+$ $[M+Na]^+$ m/z: 352.1931, found: 352.1922.

Ethyl 2-(2-phenyloxiran-2-yl)acrylate (5b)

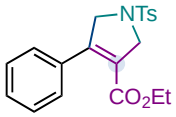


Prepared according to the reported protocol.[59] Diene **3a** (20.0 mg, 0.1 mmol) was dissolved in DCM (3.5 mL) and mCPBA (77%, 230.0 mg, 1.0 mmol) was added to the reaction mixture. The resulting solution was stirred at r.t. for 90 min, when the starting material was fully consumed. The reaction mixture was washed with 10% aqueous solution of $Na_2S_2O_3$, saturated aqueous solution of $NaHCO_3$ (4 x 5 mL) and the solvent was removed under *vacuum*. Purification by flash chromatography on silica gel (hexane/diethyl ether 5/1) provided **4b** as a colorless oil (15.4 mg, 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 5H), 6.49 (d, *J* = 1.3 Hz, 1H), 6.07 (d, *J* = 1.3 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.18 (d, *J* = 5.4 Hz, 1H), 3.15 (d, *J* = 5.4 Hz, 1H), 1.18 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.4, 140.1, 138.5, 128.4, 128.2, 128.1, 126.5, 61.1, 60.0, 55.9, 14.1.

HRMS (ESI) calculated for $C_{13}H_{14}NaO_3^+$ $[M+Na]^+$ m/z: 241.0835, found: 241.0826.

Ethyl 4-phenyl-1-tosyl-2,5-dihydro-1*H*-pyrrole-3-carboxylate (5c)



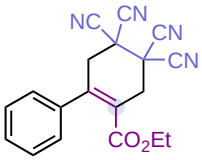
Prepared according to the reported protocol.[60] A 10 mL reaction tube was charged with $[Cu(hfacac)_2]$ (2.4 mg, 0.005 mmol), diene **3a** (30.0 mg, 0.15 mmol), TsN=IPh (37.4 mg, 0.10 mmol) and dry chlorobenzene (0.5 mL). The reaction mixture was stirred at r.t. for 1 h and then it was heated with vigorous stirring at 100 ºC for 24 h until no more product was formed (monitored by GC). The reaction mixture was cooled to r.t. and Purification by flash chromatography on neutral silica gel (hexane/ethyl acetate 100/0 – 5/1) provided **4c** as colorless oil (13.5 mg, 36 %).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 2H), 7.38 – 7.32 (m, 5H), 7.30 – 7.26 (m, 2H), 4.54 – 4.48 (m, 4H), 4.09 (q, *J* = 7.1 Hz, 2H), 2.44 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.7, 147.5, 144.1, 133.8, 132.1, 130.1, 129.6, 128.2, 128.2, 127.7, 123.6, 60.9, 59.6, 56.4, 21.7, 14.0.

HRMS (ESI) calculated for $C_{20}H_{21}NNaO_4S^+$ $[M+Na]^+$ m/z: 394.1083, found: 394.1078.

Ethyl 4,4,5,5-tetracyano-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-carboxylate (5d)

[59] Orrling, K. M.; Marzahn, M. R.; Gutiérrez-de-Terán, H.; Åqvist, J.; Dunn, B. M.; Larhed, M. *Bioorganic Med. Chem.* **2009**, *17*, 5933.
[60] Wu, Q.; Hu, J.; Ren, X.; Zhou, J. *Chem. - A Eur. J.* **2011**, *17*, 11553.



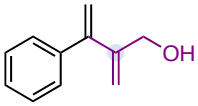
Prepared according to the reported protocol.[61] Diene **3a** (20.0 mg, 0.1 mmol) was dissolved with dry ethyl acetate (0.3 mL) in a 10 mL reaction tube. Then, a solution of tetracyanoethylene (12.8 mg, 0.1 mmol) in dry ethyl acetate (0.2 mL) was slowly added to the reaction mixture and it was stirred at r.t. for 2 days (monitored by GC). Next, the solvent was removed under reduced pressure. Recrystallization (ethanol 100%) provided **4d** as white solid (19.5 mg, 59 %).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 3H), 7.16 – 7.11 (m, 2H), 3.96 (q, *J* = 7.1 Hz, 2H), 3.57 (t, *J* = 2.0 Hz, 2H), 3.44 (t, *J* = 2.0 Hz, 2H), 0.88 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 141.1, 137.6, 129.4, 129.0, 126.9, 121.7, 110.2, 62.0, 39.1, 37.9, 37.8, 33.3, 13.5.

LRMS (EI) calculated for $C_{19}H_{14}N_4O_2^+$ $[M]^+$ m/z: 330.1, found: 330.1.

2-methylene-3-phenylbut-3-en-1-ol (5e)



Prepared according to the reported protocol.[62] To a flame-dried tube was added diene **3a** (20.0 mg, 0.1 mmol) and it was dissolved in toluene (1 mL). After the tube was stirred at -78 ^{o}C for 10 min, DIBAL-H (0.2 mL, 1.0 M in hexane, 0.2 mmol) was added dropwise within 5 min. The resulting mixture was stirred at -78 ºC for 3 hours and at r.t. for 4 hours. Next, the reaction mixture was quenched with a saturated aqueous solution of NH_4Cl (2 mL), extracted with Et_2O (3 x 5 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under *vacuum*. Purification by flash chromatography on silica gel (hexane/diethyl ether 5/1) provided **4e** as a colorless oil (9.1 mg, 57% yield).

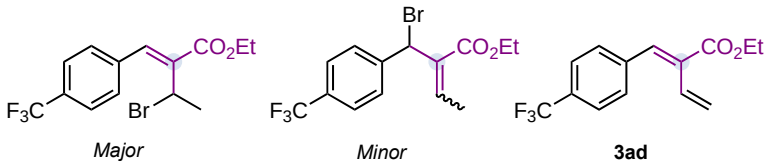
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 5H), 5.41 – 5.38 (m, 1H), 5.35 (d, *J* = 1.2 Hz, 1H), 5.28 – 5.25 (m, 1H), 5.14 – 5.11 (m, 1H), 4.38 – 4.33 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.2, 147.8, 140.8, 128.3, 128.2, 127.7, 115.9, 114.5, 64.6.

HRMS (APCI) calculated for $C_{11}H_{13}O^+$ $[M+H]^+$ m/z: 161.0961, found: 161.0962.

Other products

Ethyl (*Z*)-3-bromo-2-(4-(trifluoromethyl)benzylidene)butanoate ()

[61] Ide, J.; Kishida, Y. *Chem. Pharm. Bull.* **1968**, *16*, 793.
[62] Yuan, Y.; Jia, M.; Zhang, W.; Ma, S. *Chem. Commun.* **2019**, *55*, 7938.

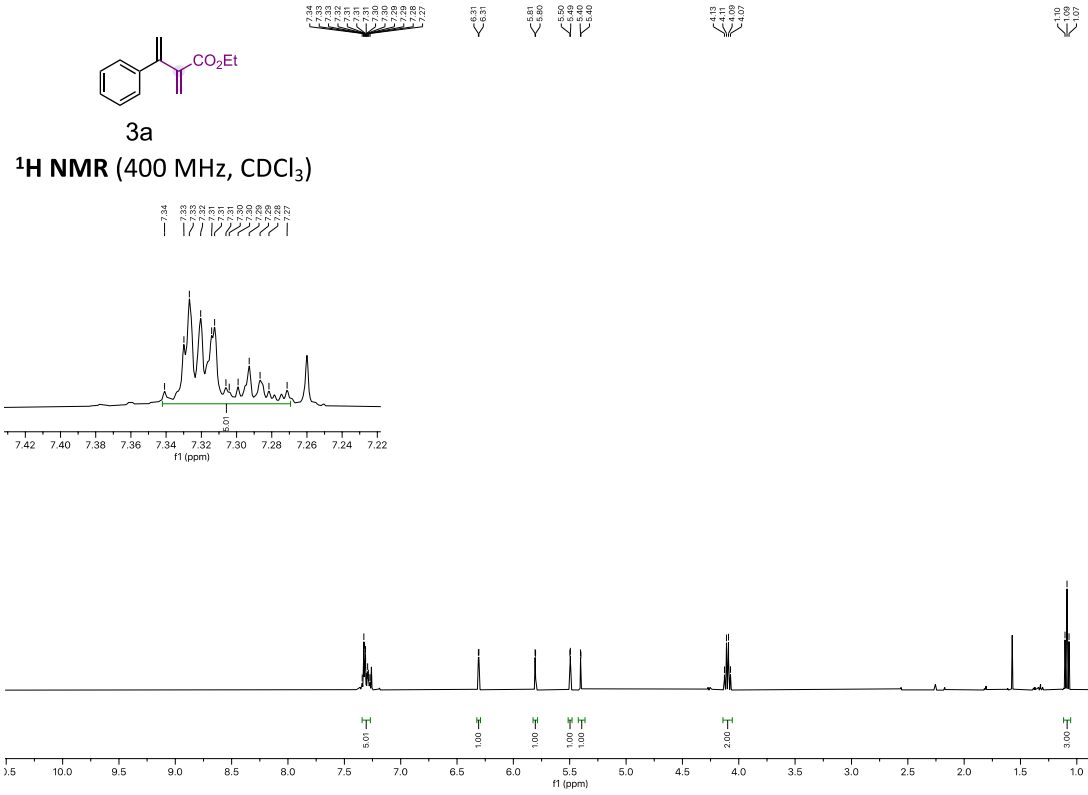


Prepared according to the general procedure D using 1-(prop-1-en-1-yl)-4-(trifluoromethyl)benzene (*E*/*Z* ratio 3 : 1, 74.5 mg, 0.4 mmol) and reagent **2b** (119.2 mg, 0.2 mmol). After the slow addition of the solution of **2a**, TBAB (128.9 mg, 0.4 mmol) was added to the reaction mixture, and it was slowly heated up to room temperature (4 h). Removal of the solvent and purification by flash chromatography on silica gel (hexane/diethyl ether 50/1) provided the title compound as a colorless oil (42.6 mg, 61% yield, isomer ratio 28 :1; 14 % of **3ad** was also obtained).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.1 Hz, 2H), 7.67 (s, 1H), 7.53 (d, *J* = 8.2 Hz, 2H), 5.16 (q, *J* = 7.0 Hz, 1H), 4.36 (q, *J* = 7.2 Hz, 2H), 1.96 (d, *J* = 7.0 Hz, 3H), 1.40 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.4, 138.4, 136.1, 130.9 (q, *J* = 32.7 Hz), 130.2, 129.1, 125.9 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 272.5 Hz), 61.5, 41.8, 24.7, 14.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.6.

HRMS (ESI) calculated for $C_{14}H_{14}BrF_3NaO_2^+$ $[M+Na]^+$ m/z: 373.0021, found: 373.0017.

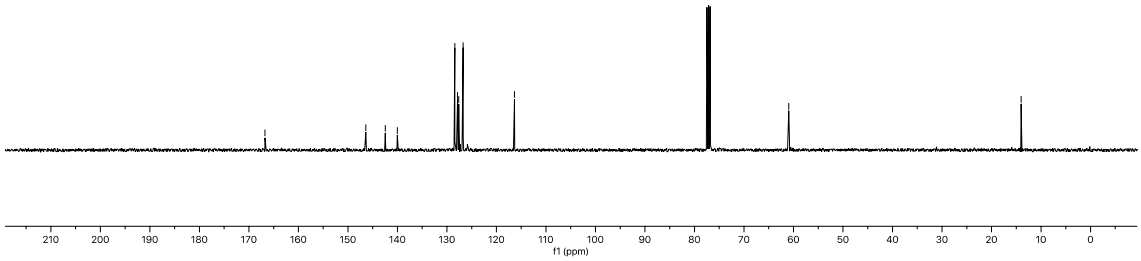
Selected NMR Spectra

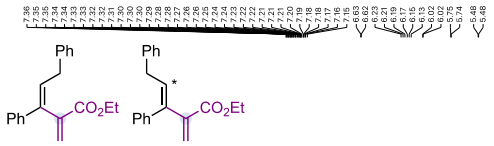


^{1}H NMR (400 MHz, $CDCl_3$)

3a

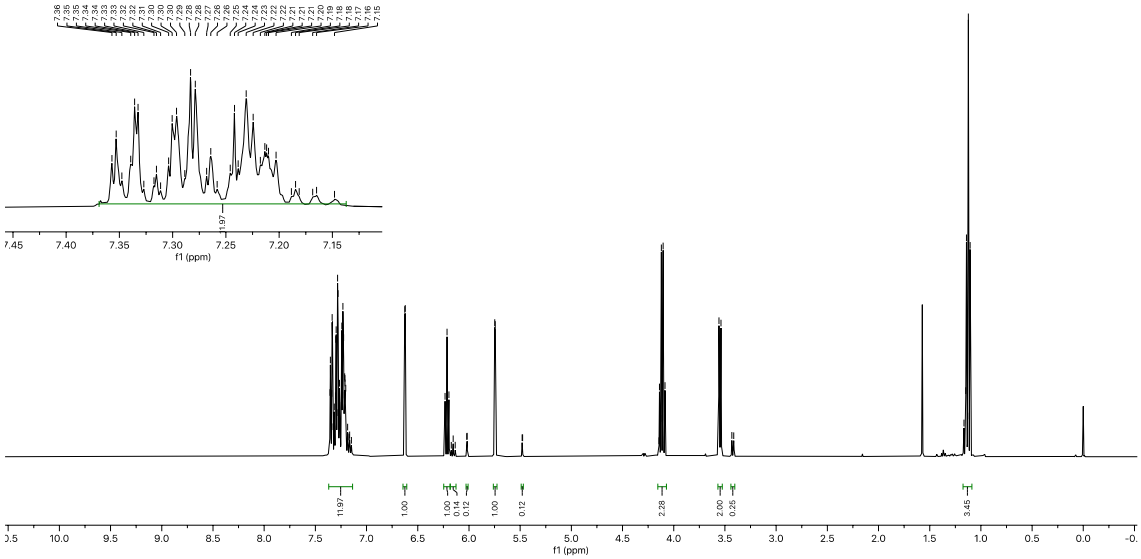
^{13}C NMR (101 MHz, $CDCl_3$)

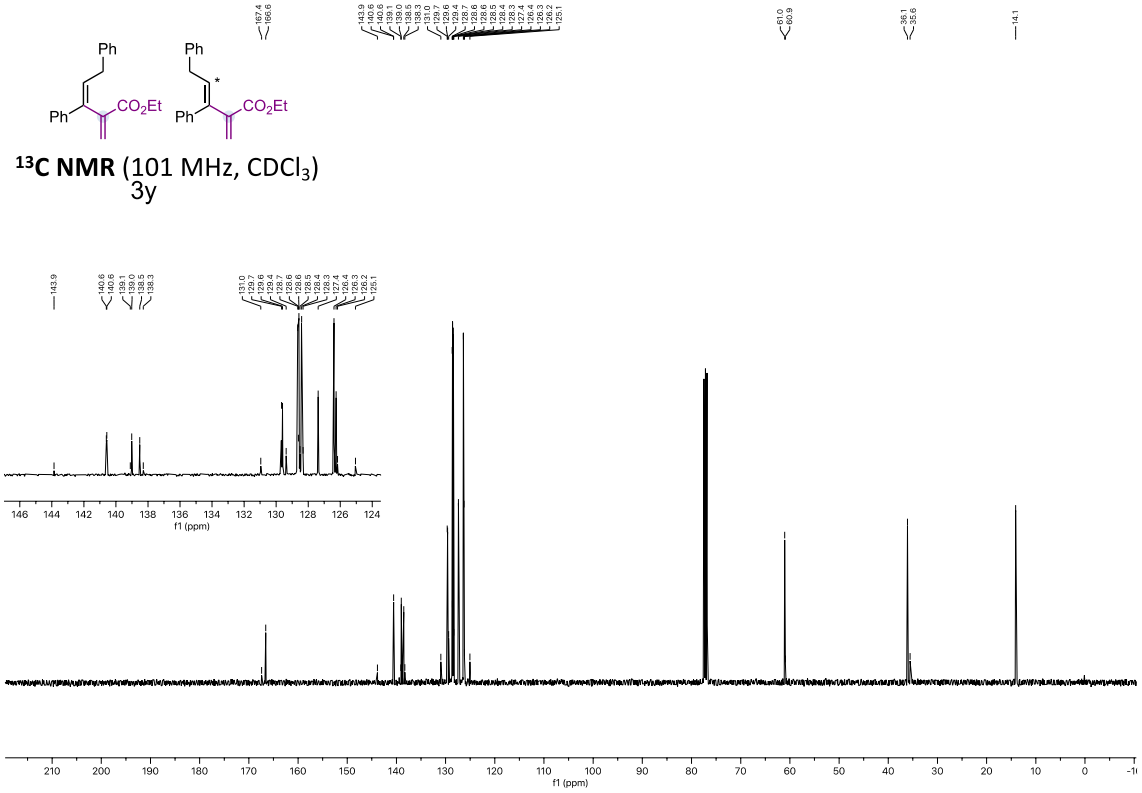


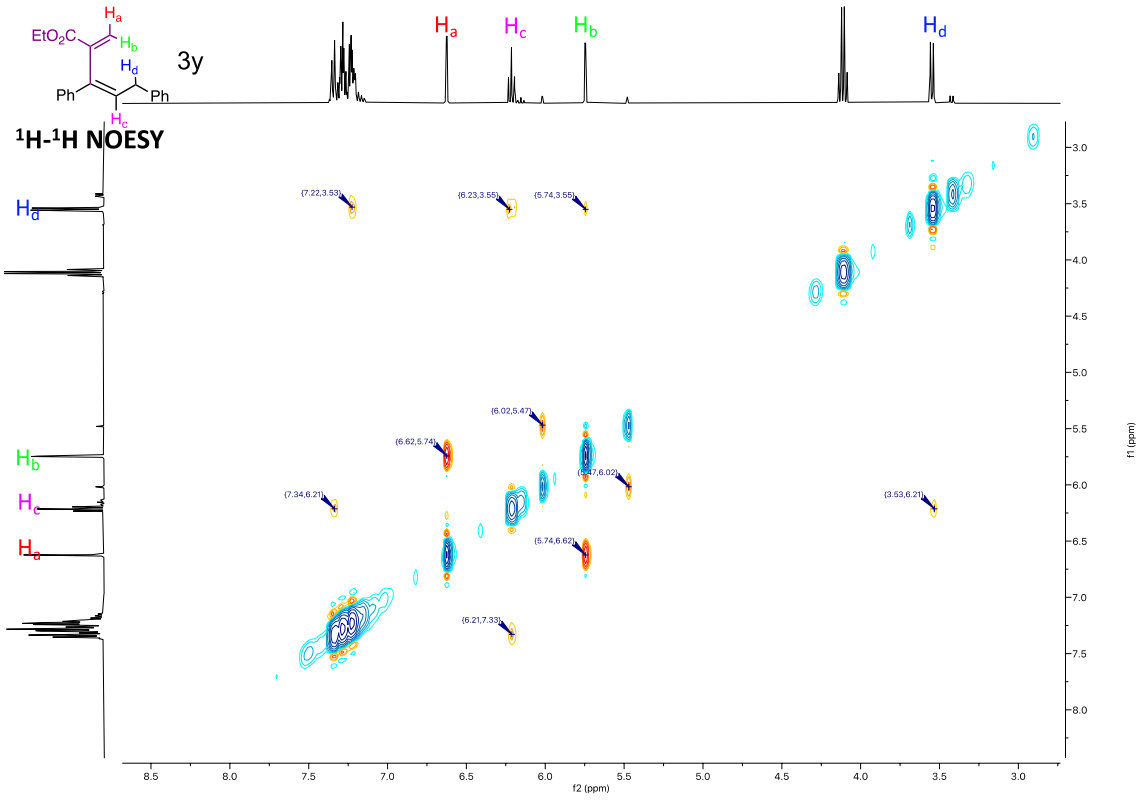


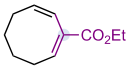
^{1}H NMR (400 MHz, $CDCl_3$)

3y



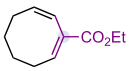

Ph
Ph
CO2Et
Ph
Ph
CO2Et
13C NMR (101 MHz, CDCl3)
3y
f1 (ppm)


Ha
EtO2C
Hb
Hd
Ph
Ph
Hc
3y
1H-1H NOESY
f2 (ppm)
f1 (ppm)



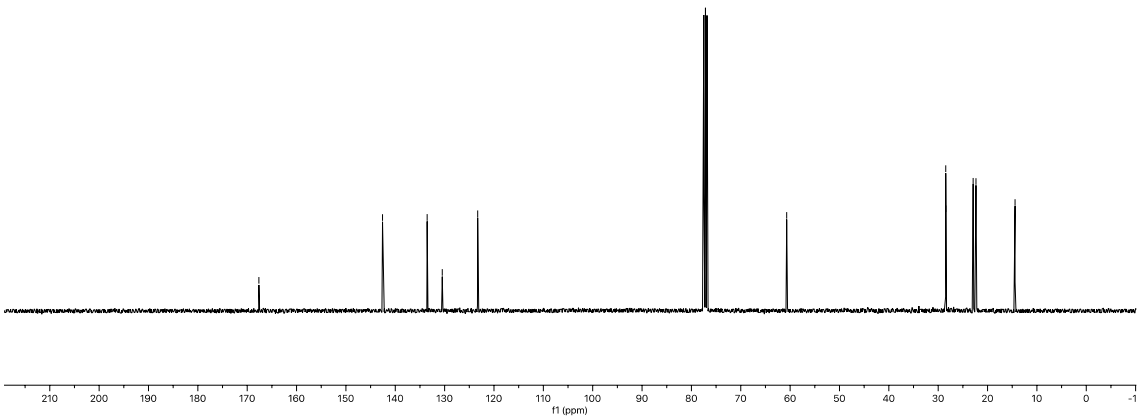
3ai

^{1}H NMR (400 MHz, $CDCl_3$)



3ai

^{13}C NMR (101 MHz, $CDCl_3$)



General conclusions

We have been able to develop a new metal-catalyzed carbyne transfer platform. We employed our previously discovered hypervalent iodine reagents containing a diazo moiety and we discovered that rhodium paddle-wheel catalysts were able to activate the diazo moiety of our reagents, generating rhodium-carbenes containing a hypervalent iodine group. Given the outstanding leaving group ability of the $I^{(III)}$-group, these reactive intermediates can be considered as cationic rhodium-carbenes and carbyne equivalents in consequence.

In Chapter II, we have developed a Rh-catalyzed carbyne transfer platform for the catalytic cleavage of C(sp^2)–C(sp^2) bonds. We have demonstrated that this process is able to convert feedstock alkenes, styrenes and butadiene together with a broad diversity of simple nucleophiles into valuable allylic building blocks. The value of the constructive scission of C–C bonds in alkenes for the synthesis of more substituted ones is remarkable and is well exemplified with the synthesis of all-carbon tetrasubstituted alkenes from readily available starting materials.

In Chapter III, we have expanded the application of our Rh-catalyzed monovalent carbon transfer to the synthesis of fluorinated tertiary stereocenters. In order to fulfill this goal, we employed 1,1-disubstituted alkenes to form tertiary allyl cations that underwent nucleophilic fluorination with excellent branched/selectivity ratio. Notable features of this process are the broad alkene scope, including natural products and drug molecule derivatives, applications in the synthesis of a fluorinated drug molecule – (±)-F-flurbiprofen– and its translation to radiofluorination with [^{18}F]TEAF.

Finally, in Chapter IV we have been able to transform simple alkenes to 1,3-dienes *via* Rh-carbynoid insertion to double bonds through the formation of allyl cations, providing a synthetic alternative to the direct desaturation of alkenes. The utility of this protocol was demonstrated by the use of a broad range of non-pre-functionalized olefins as well as the further derivatization of the obtained 1,3-dienes into highly functionalized products.

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Primero de todo quiero dar las gracias a mi director de tesis, **Prof. Marcos García Suero**. Ha sido un placer realizar la tesis en tu grupo. Siempre te estaré agradecido por todo lo que me has enseñado y aportado. La constante dedicación que le transmites al grupo y la motivación que inculcas, así como la exigencia para llegar a la excelencia son ejemplares. Me has hecho crecer tanto como químico como persona.

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One of the best things I take home from my PhD is the people I met during these last four years. I will always remember my lab-mates, the former members which were already in the group when I arrived and have already left, **Dr. García**, **Dr. Jiang** and **Dr. Wang**. You have been the best colleagues possible, helping me with everything I needed, always in a good mood and joking. I will always keep you in my heart. **Liyin** needs a special mention, since we have shared the same lab for nearly 4 years. I have learnt so much from you during these past years, from your chemistry, your exquisite chinese cuisine and specially on how to deal with the failures, dealing with them always joking and laughing in the lab. Thank you for everything. También **Ani**. Pasamos muchos buenos momentos tanto dentro como fuera del lab y siempre me diste los mejores consejos. Gracias por todo.

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A part de la gent del nostre grup, també vull agrair el suport rebut per part d'amics que he anat fent a l'ICIQ. Per suposat a l'**Alèria**, que després de fer la carrera junts ens hem retrobat i ha sigut un plaer tenir-te com a conillet d'índies per les meves cerveses i com a professora de pàdel. També a l'**Èric**, amb qui hem format el comando Manresa a Tarragona i sempre hi has sigut quan necessitàvem esbargir-nos amb alguna cerveseta que altra. Moltes gràcies a tots dos per ser-hi sempre que us he necessitat!

Sara, muchas gracias por todo y espero que vaya muy bien tu experiencia americana, ¡nos vemos a la vuelta para seguir con el pádel! **Pablo** y **Patri**, habéis sido unos compañeros de piso estupendos. Muchísimas gracias por cuidar del pisito durante mis ausencias. **Ángel**, **David**, **Jesús** y **Ana**, agradeceros las noches míticas por Tarragona.

Abans d'acabar voldria mostrar l'immens agraïment que tinc per la meva familia i a qui mai podré retornar tot el que m'han donat. Gràcies **Rosa Mari**, **Joan** i **Marc**. Sense vosaltres segur que hauria sigut imposible fer aquesta tesi i ser la persona qui sóc. Us estimo.

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