
# RING-OPENING OF CYCLIC CARBONATES: FROM FINE CHEMICALS TO CO2-BASED POLYMERS

**Jixiang Ni**

UNIVERSITAT ROVIRA i VIRGILI

# Ring-Opening of Cyclic Carbonates: From Fine Chemicals to $CO_2$-based Polymers

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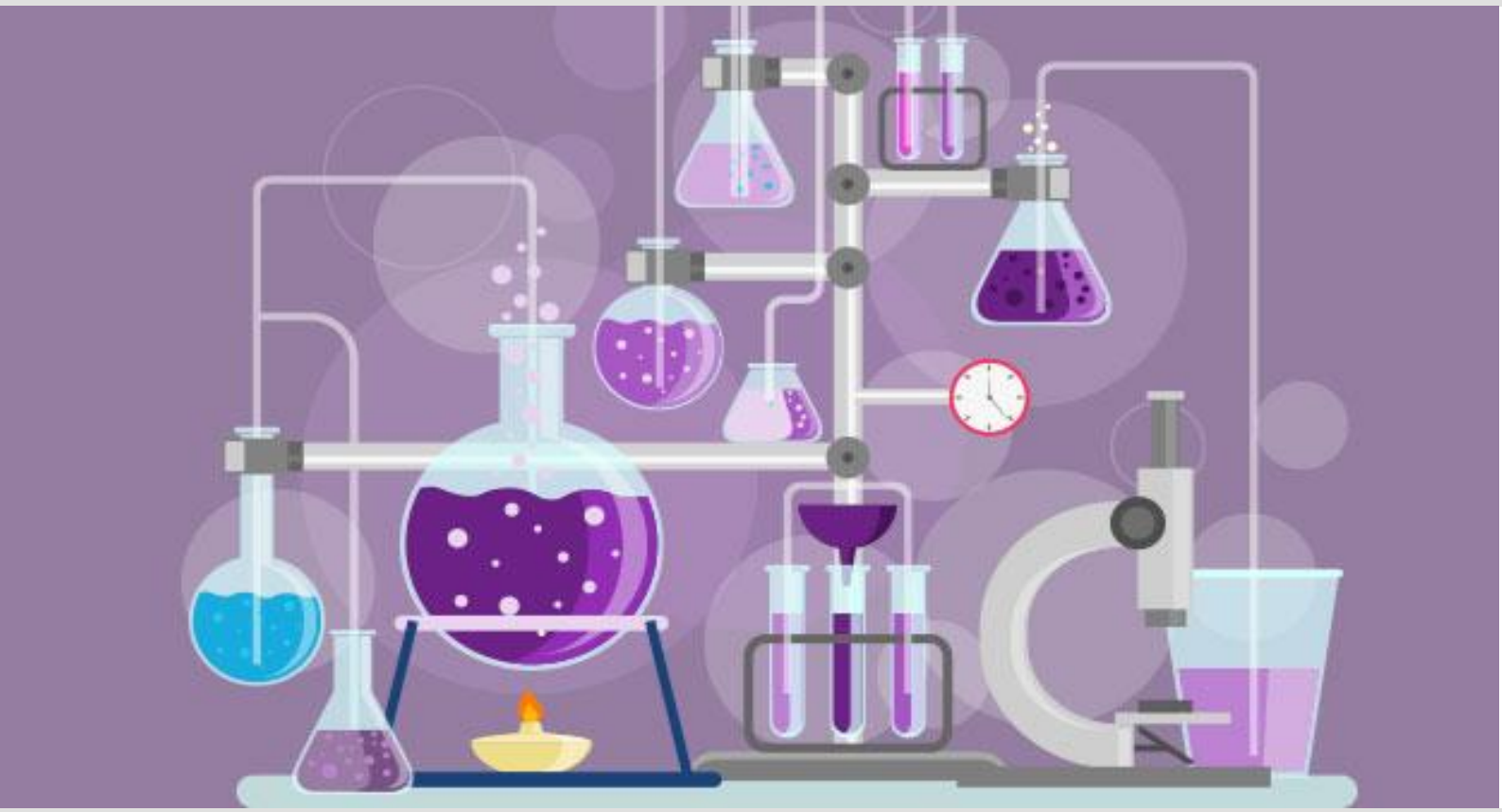

**DOCTORAL THESIS**

**2023**

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PhD Thesis

# "Ring-Opening of Cyclic Carbonates: From Fine Chemicals to $CO_2$-based Polymers"

**Jixiang Ni**

Supervised by Prof. Dr. Arjan W. Kleij

Tarragona

October 2023


UNIVERSITAT ROVIRA I VIRGILI
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Prof. Dr. Arjan W. Kleij, Group Leader at the Institute of Chemical Research of Catalonia (ICIQ) and Research Professor at the Catalan Institution for Research and Advanced Studies (ICREA):

I STATE that the present Doctoral Thesis, entitled "**Ring-Opening of Cyclic Carbonates: From Fine Chemicals to $CO_2$-based Polymers**" presented by Jixiang Ni to receive the degree of Doctor, has been carried out under my supervision at the Institute of Chemical Research of Catalonia (ICIQ).

Tarragona, October 2023

Doctoral Thesis Supervisor

Prof. Dr. Arjan W. Kleij

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# Curriculum Vitae

Jixiang Ni was born on March 21 in 1993 in Zhejiang, China. He obtained his BSc degree in July 2016 at Luoyang Institute of Science and Technology, majoring in Applied chemistry. Then he started his MSc degree in Lanzhou university under the supervision of Prof. Rulong Yan, during which he was working on the synthesis of nitrogen heterocyclic compounds and functionalization of allenes. In July 2019, he obtained his MSc degree and then he joined the Institute of Chemical Research of Catalonia (ICIQ), Tarragona, to pursue his doctoral studies under the supervision of Prof. Arjan W. Kleij. His research was financially supported by Chinese Scholarship Council (CSC). His PhD research focused on novel ring-opening chemistry of cyclic carbonates, and these results are presented in this thesis. Part of this PhD research was communicated as a poster at the XXV Conference on Organometallic Chemistry-EuCOMC in 2023 held in Alcalá de Henares (Spain).

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# Acknowledgments

All the work summarized in the present thesis is the result of a long journey that started 4 years ago. During these years, I was not alone, and now it is time to say thanks to those that have enormously contributed in many different ways.

Obviously, the first person to whom I am immensely grateful is my PhD supervisor Prof. **Arjan W. Kleij**. Arjan is one of the smartest and most patient persons that I ever met. His knowledge and passion for chemistry are a model that he always tries to transmit to the members of his group. He is the source of all what I learned, and I feel lucky that I have been able to absorb a tiny part of his knowledge. Obviously, Arjan also played a crucial role in the development and accomplishment of the results discussed in this thesis. He taught me how to be honest and critical, even with my own work, and how to be an effective and independent researcher. I am proud of all the accomplished work and in addition, I am also in debt to my other initial co-supervisor Kilian Muñiz. As a boss, he could be tough but honest and supportive. In my case, any problem we encountered could be solved with his feedback. Unfortunately, Kilian passed away at the beginning of the COVID-19 pandemic, and I want to thank all people who did their best in order to help the Muñiz group during these difficult times.

Next, I would like to thank all the former and current members of the Kleij research group. I really cherish all the great time we spent together and all the knowledge you have been sharing with me: **Aijie Cai, Jianing Xie, Àlex Cristòfol, Cristina Maquilón, Kun Guo, Chang Qiao, Sijing Xue, Alèria Garcia, Nicola Zanda, Bart Limburg, Francesco Della Monica, Alexander Lücht, Debasish Ghorai, Alba Villar, Xuetong Li, Qian Zeng, Arianna Brandolese, Balázs Tóth, Thirusangumurugan Senthamarai, Wangyu Shi, Fengyun Gao, Chengyang Chang, Alejandro Delgado, Lorenz Dittrich, Dimitrios Skoulas**. In addition, I would like to give my sincere gratitude to those with whom I cooperated in the different projects: **Àlex, Matteo** and **David**. Besides, **Eva Casco, Ingrid,** and **Sorania Jiménez Ávila**: thank you for all the paperwork you prepared for me throughout my PhD. I would also like to thank all the former members of the Muñiz group. I really enjoyed all the time we spent together and all the support you gave to me: **Estefanía del Castillo, Thomas Duhamel, Èric Cots, Eleni Georgiou, Aliénor Jeandin** and **Jiayu Zhang**.

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I would like to thank all the ICIQ research support units. Especially, I express my gratitude to the NMR unit for helping me with the different analyses. **Jordi Benet** from the X-ray unit is thanked for his patience and the small course on X-ray diffraction, and I admired your strict way of doing research. There are also lots of people who helped me during my PhD who I did not mention yet. I would like to give them my sincere gratitude. I could not have done it without their help.

Last but not the least, I would like to give my high appreciation to my family for their support and love. I wish that in the near future I will be able to do something for them in return. Thank you for all your support in whatever way. And I am looking forward to our new life together.

Jixiang, 2023

# List of Publications

The results described in this doctoral thesis are based on the following publications:

- **J. Ni**, À. Cristòfol, A. W. Kleij, *Org. Chem. Front*. **2021**, *8*, 4520-4526.
- **J. Ni**, M. Lanzi, A. W. Kleij, *Org. Chem. Front*. **2022**, *9*, 6780-6785.
- **J. Ni**, M. Lanzi, D. H. Lamparelli, A. W. Kleij, *Polym. Chem.* **2023**, *14*, DOI: 10.1039/d3py00860f

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# List of Abbreviations

In this doctoral thesis, the abbreviations and acronyms most commonly used in organic chemistry are based on the recommendations of the ACS "Guidelines for authors" which can be found and consulted at *https://www.cas.org/support/documentation/references/cas-standard-abbreviations#listinga*.

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# *Chapter 1. Introduction*

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# 1.1 Fine chemicals and $CO_2$-based polymers

## 1.1.1 Fine chemicals from carbonates

En route to sustainability and circularity, the upgrading of $CO_2$ into value-added organic scaffolds has gained importance as a field of research. A variety of products are now accessible from $CO_2$, ranging from commodities (methanol, formic acid, urea)[1] to more sophisticated products (organic carbonates/carbamates, heterocyclic compounds). [2] Amongst the multitude of $CO_2$-sourced molecules, cyclic carbonates represent valuable and modular heterocycles, which have been widely applied as polar aprotic solvents, electrolytes in batteries and as intermediates in the manufacture of fine chemicals, e.g. to construct carbamates.[3]

The alcoholysis of cyclic carbonates (CCs) differs from aminolysis as it is not spontaneous and requires a base to activate the weak (pro)nucleophile and facilitate the ring-opening of the cyclic carbonate. Although there are few reported examples of "methylene attack" in the literature, these processes typically occur at elevated temperatures leading to the release of $CO_2$. Nucleophiles such as amines, thiols, and cyanide have been utilized in these reactions.[4] Cyclic carbonates present an appealing

[1] (a) A. Dibenedetto, F. Nocito, *ChemSusChem* **2020**, *13*, 6219-6228; (b) E. C. Ra, K. Y. Kim, E. H. Kim, H. Lee, K. An, J. S. Lee, *ACS Catal.* **2020**, *10*, 11318-11345; (c) X. Jiang, X. Nie, X. Guo, C. Song, J. G. Chen, *Chem. Rev.* **2020**, *120*, 7984-8034.

[2] (a) M. Alves, B. Grignard, R. Mereau, C. Jérôme, T. Tassaing, C. Detrembleur, *Catal. Sci. Technol.* **2017**, *7*, 2651-2684; (b) L. Guo, K. J. Lamb, M. North, *Green Chem.* **2021**, *23*, 77-118; (c) V. Aomchad, A. Cristofol, F. Della Monica, B. Limburg, V. D'Elia, A. W. Kleij, *Green Chem.* **2021**, *23*, 1077-1113; (d) A. J. Kamphuis, F. Picchioni, P. P. Pescarmona, *Green Chem.* **2019**, *21*, 406-448; (e) B. Grignard, S. Gennen, C. Jérôme, A. W. Kleij, C. Detrembleur, *Chem. Soc. Rev.* **2019**, *48*, 4466-4514; (f) R. R. Shaikh, S. Pornpraprom, V. D'Elia, *ACS Catal.* **2018**, *8*, 419-450; (g) F. D. Bobbink, A. P. van Muyden, P. J. Dyson, *Chem. Commun.* **2019**, *55*, 1360-1373.

[3] P. Rollin, L. K. Soares, A. M. Barcellos, D. R. Araujo, E. J. Lenardao, R. G. Jacob, G. Perin, *Appl. Sci.* **2021**, *11*, 5024.

[4] (a) M. Selva, M. Fabris, V. Lucchini, A. Perosa, M. Noè, *Org. Biomol. Chem.*, 2010, **8**, 5187–5198; (b) F. Monie, B. Grignard, J.-M. Thomassin, R. Mereau, T. Tassaing, C. Jérôme, C. Detrembleur, *Angew. Chem. Int. Ed.* **2020**, *59*, 17033-17041; (c) F. Ouhib, B. Grignard, E. van den Broeck, A. Luxen, K. Robeyns, V. van Speybroeck, C. Jérôme, C. Detrembleur, *Angew. Chem. Int. Ed*. **2019**, *58*, 11768-11773; (d) F. Ouhib, L. Meabe, A. Mahmoud, B. Grignard, J.-M. Thomassin, F. Boschini, H. Zhu, M. Forsyth, D. Mecerreyes, C. Detrembleur, *ACS Appl. Polym. Mater*. **2020**, *2*, 922-931; (e) J. Ni, À. Cristòfol, A. W. Kleij, *Org. Chem. Front*. **2021**, *8*, 4520-4526.

alternative to toxic compounds like phosgene, carbamoyl chlorides, and isocyanates[5] for constructing (cyclic) carbamates, which are important scaffolds in the agrochemical and pharmaceutical industries.[6] Transforming cyclic carbonates in the presence of primary amines yields hydroxy-carbamates, while larger cyclic carbonates, such as six-membered carbonates, can also serve as starting materials (for an overview see Figure 1.1).[7]

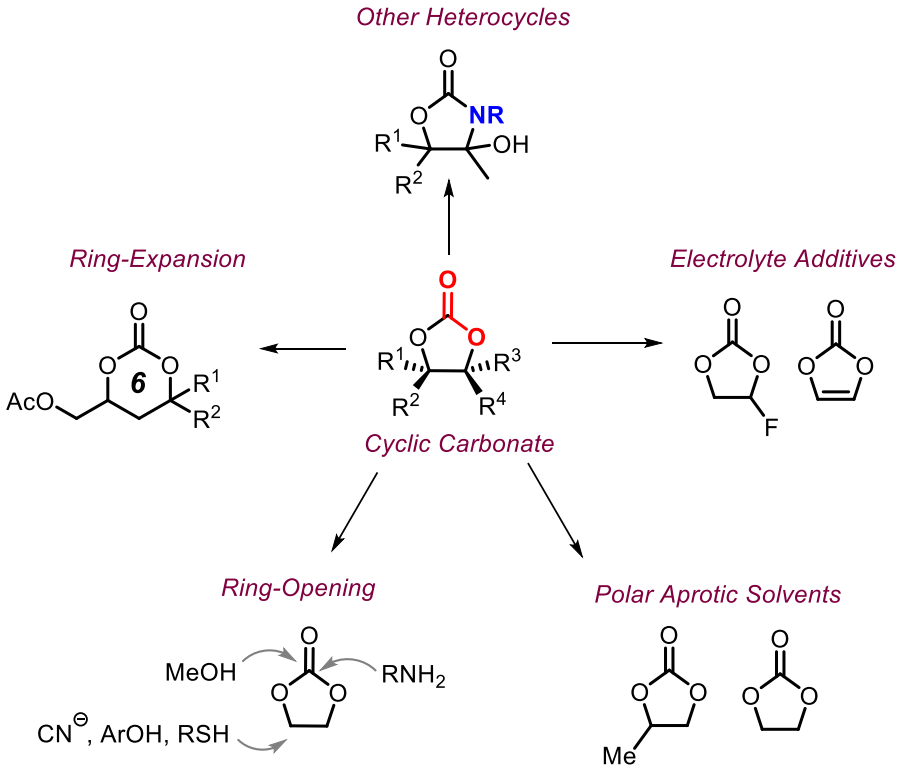



**Figure 1.1** Utilization of Carbonate in a variety of applications.

## 1.1.2 $CO_2$-based polymers

400 million tons of polymers are produced globally each year. This amount has been growing by 3-4 % per year for decades and, as such, polymers have become an integral and important part of the modern world. Despite all their useful and versatile material properties, the synthesis of polymers constitutes a major problem: 90% of them are

[5] (a) H. Babad, A. G. Zeiler, *Chem. Rev.* **1973**, *73*, 75-91; (b) Y. Ren, S. A. L. Rousseaux, *J. Org. Chem.* **2018**, *83*, 913-920; (c) S. Yoganathan, S. J. Miller, *Org. Lett.* **2013**, *15*, 602-605.
[6] A. K. Ghosh, M. Brindisi, *J. Med. Chem.* **2015**, *58*, 2895-2940.
[7] C. Qiao, A. V. Yanez, J. Sprachmann, B. Limburg, C. Bo, A. W. Kleij, *Angew. Chem. Int. Ed.* **2020**, *59*, 18446-18451.

produced from fossil carbon sources and finally end up as $CO_2$ emissions (Figure 1.2) at their end-of-life.[8]

Polymers are versatile materials finding multiple, every day-life applications in the automotive industry, in construction, packaging, medical devices, personal care products, and in electrical and electronic applications among others. To date, most of the polymers have been produced from fossil resources. However, fossil fuel depletion and changing and more restrictive legislative requirements for a circular economy impose that sustainable and renewable plastics become the standard for the chemical industry. Therefore, it is imperative to find realistic alternatives for the production of both chemicals (cf., precursors, intermediates) and polymers.

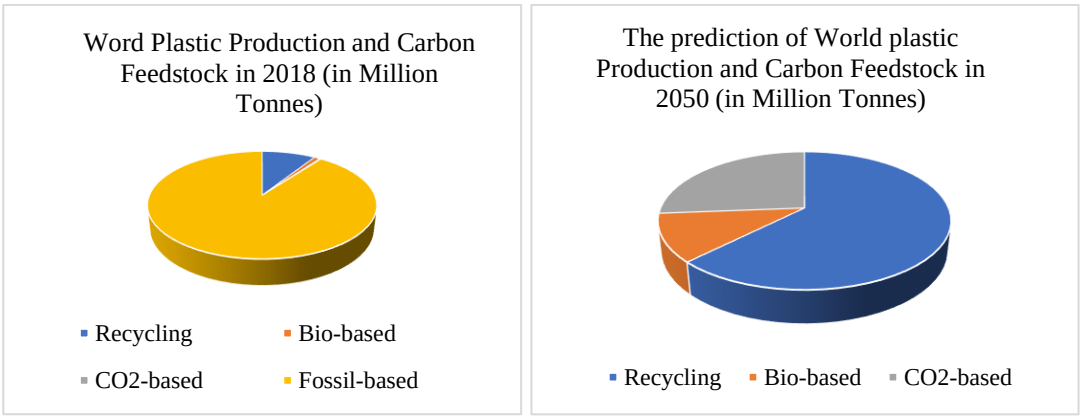



**Figure 1.2** The change in the production of $CO_2$-based polymers.

In recent years, there have been numerous advancements in the development of functional polymers based on $CO_2$. Among these, $CO_2$-based polycarbonates and their copolymers exhibit exceptional thermal properties, making them suitable for various applications including foams, adhesives, engineering plastics, among others. Furthermore, $CO_2$-based amphiphilic polymers have been designed, synthesized, and applied in diverse fields such as bioimaging, therapy and lithium-ion batteries showing their immense potential. Further to this, there are contributions showing that $CO_2$-based polymers with aggregation-induced emission (AIE) characteristics can be designed, finding applications as chemo-sensors, in photo-patterning and as light-emitting diodes (LEDs). Lastly, some $CO_2$-based degradable polymers have shown potential as chemically recyclable materials, nano-catalysts, dynamic gels, and other applications as depicted in Figure 1.3.

[8] The image data has been extracted from: https://renewable-carbon.eu/news/.

*Chapter 1*

The polymerization of $CO_2$ and epoxides is the first reported example within the sub-area of $CO_2$-based polymer development. This seminal discovery opened up a new research field in polymer chemistry, which currently is a rather attractive and competitive field. However, this type of copolymerization process may suffer from several problems, such as product selectivity (polycarbonate versus cyclic carbonate), structural defects (ether versus carbonate connection in the polymer main chain), and regio- and stereoselectivity issues (cf., polymer tacticity). In the past 50 years, various transition metal catalysts have been developed to control the selectivity of the $CO_2$/epoxide copolymerization process. [9] However, metal residues in the polymers might be problematic for their productive use, in particular when medical applications are concerned. Recently, bifunctional organoboron catalysts have emerged as a metal-free catalyst with unprecedented efficiency, which thus represents and interesting alternative these types of polymers.[10]

[9] (a) S. J. Poland, D. J. Darensbourg, *Green Chem.* **2017**, *19*, 4990-5011; (b) J. Huang, J.C. Worch, A.P. Dove, O. Coulembier, *ChemSusChem* **2020**, *13*, 469-487; (c) X. B. Lu, W. M. Ren, G. P. Wu, *Acc. Chem. Res.* **2012**, *45*, 1721-1735; (d) F. D. Bobbink, A. P. van Muyden, P. J. Dyson, P. J. *Chem. Commun*. **2019**, *55*, 1360-1373; (e) M. I. Childers, J. M. Longo, N. J. Van Zee, A. M. LaPointe, G. W. Coates, *Chem. Rev.* **2014**, *114*, 8129-8152.

[10] G. W. Yang, Y. Y. Zhang, R. Xie, G. P. Wu, *J. Am. Chem. Soc.* **2020**, *142*, 12245-12255.

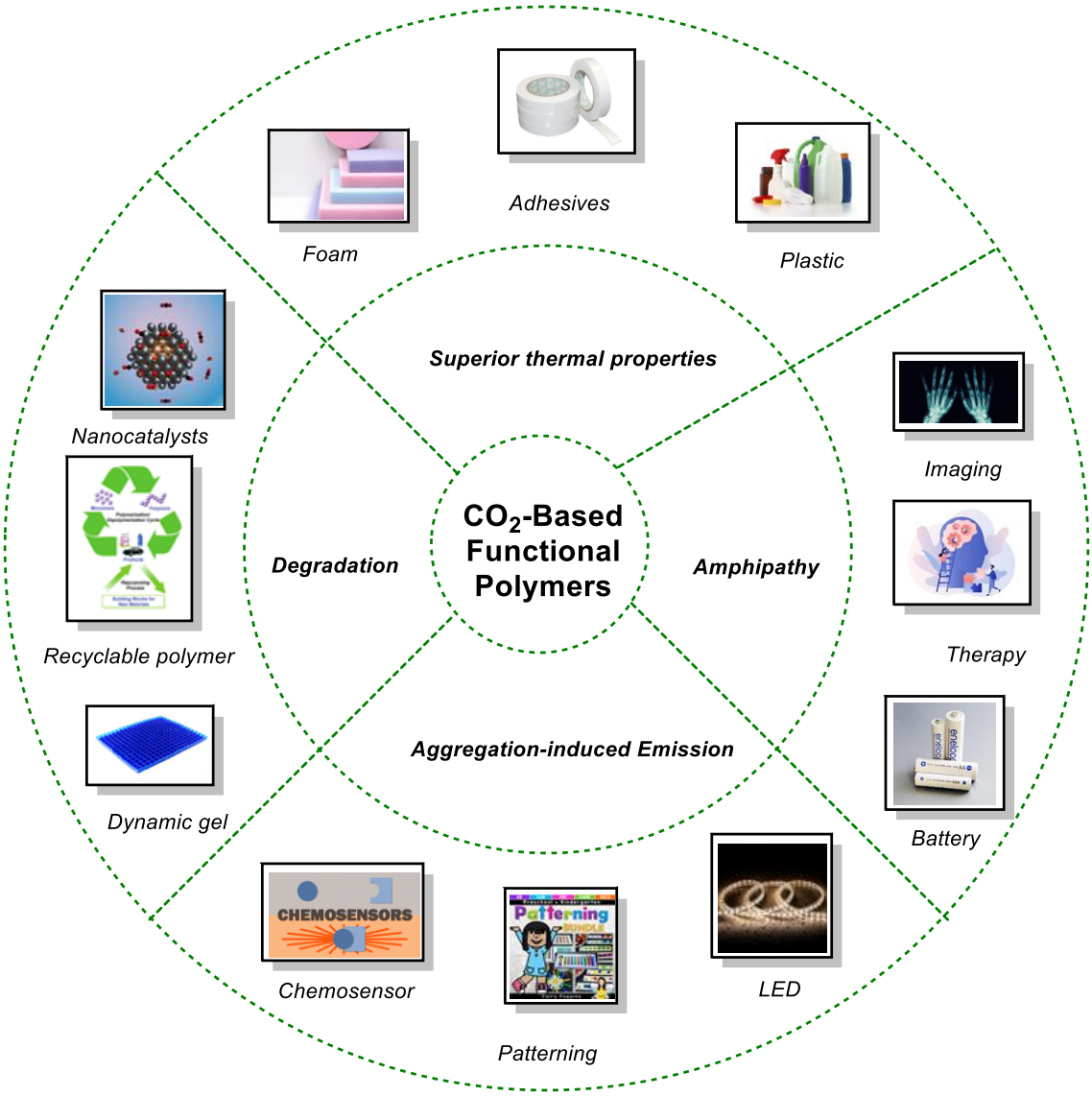



**Figure 1.3** Properties and applications of $CO_2$-based polymers.

## 1.2 Catalytic transformations of functionalized cyclic carbonates

Functionalized cyclic carbonates and related heterocycles have emerged as remarkably modular substrates in catalytic processes involving ring-opening and/or decarboxylation. These transformations, most often promoted by transition metal complexes, have paved the way for the discovery of novel reactions that encompass the stereo- and enantioselective creation of new C–N, C–O, C–C, C–S, and C–B bonds. One of the major advantages of these heterocyclic carbonate scaffolds is their ease of synthesis and

structural diversity making them highly suitable for synthetic applications and explorations. By combining transition metal chemistry concepts and the use of these cyclic substrates, new opportunities have arisen in (*inter alia*) C–H bond functionalization, stereo- and enantioselective Tsuji-Trost allylic alkylations, and within natural product synthesis.

While many of the synthetic conversions still rely on expensive transition-metal catalysts, the potential for the valorization of these cyclic substrates calls for the development of cheaper catalytic strategies based on abundant metals. Additionally, the development of efficient domino processes or cooperative catalytic systems utilizing these substrates would be highly attractive, although the combination of different catalysts and sequential synthetic steps presents a significant challenge. It is crucial to establish a practical operational window for each individual transformation and catalyst without compromising overall catalytic performance. Figure 1.4 represents an overview of various transformation that have been developed over the year using “vinyl” substituted cyclic carbonates (abbreviated as VCCs). These types of carbonates have become popular in modern synthetic chemistry and have shown a wealth of reactivity patterns useful to design stereodefined olefins and chiral allylic and propargylic compounds with elusive quaternary (and similar) stereocenters.

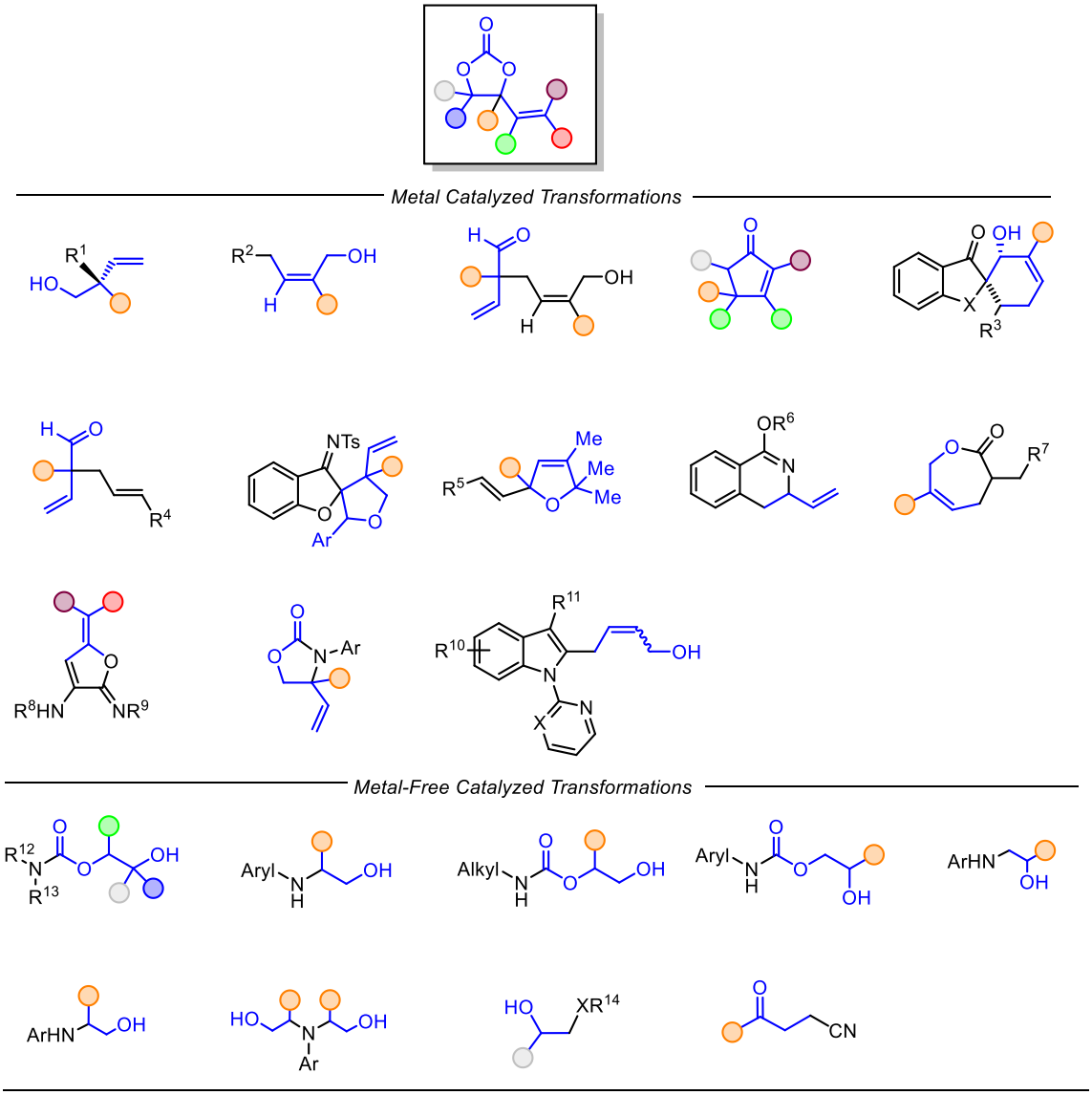
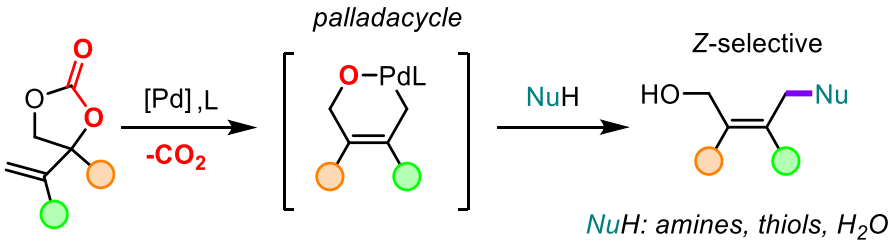



**Figure 1.4** Schematic overview of the use of VCCs as precursors towards fine chemical intermediates/products.

### 1.2.1 Metal catalyzed transformations using VCCs

The conversion of VCCs in the presence of nucleophiles using transition metal catalysts were first reported in the 1990s. It was found that the reactivity of VCCs and their related vinyl epoxides differ significantly. Additionally, substituted VCCs are more easily accessible, and the synthesis of these carbonate precursors is generally straightforward, often starting from simple and accessible β-hydroxy ketones. Kleij et al. investigated the decarboxylative coupling of VCCs with external nucleophiles using palladium (Pd) and copper (Cu) based catalysts. They reported the stereoselective synthesis of various allylic compounds through C–N, C–O, C–S, C–C, and C–B bond formation reactions. In 2016, this group reported a Pd-catalyzed regio- and stereoselective functionalization of VCCs with amines and other weak nucleophiles such as water and thiols towards the synthesis of tri- and tetra-substituted (*Z*)-configured linear allylic amines, (*Z*)-allylic thioethers and (*Z*)-1,4-but-2-ene diols, respectively, in high yields and with excellent levels of stereoselectivity (Scheme 1.1).[11]

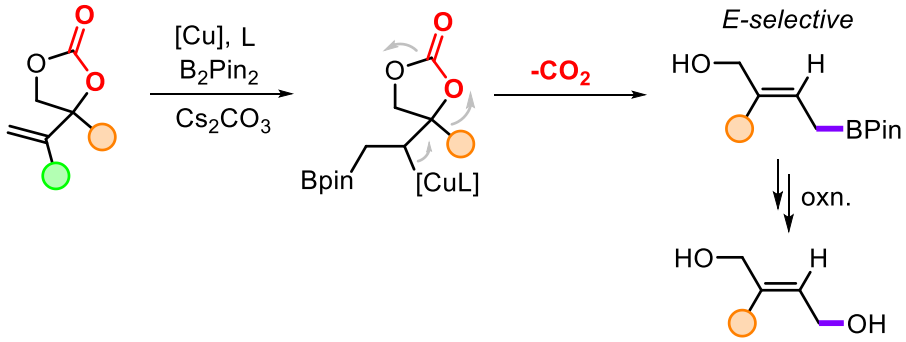



**Scheme 1.1** Pd-catalyzed decarboxylative formation of highly substituted (Z)-configured allylic scaffolds from VCCs.

In 2017, the same authors in collaboration with Fernández extended the use of nucleophilic species to activated boranes under Cu-catalysis and performed selective $S_N2'$ allylic substitutions on VCCs.[12] The developed protocol led to the creation of allylboranes and homoallylboranes with a preferred spatial arrangement. Subsequent oxidative treatment of these products allows for the direct production of important compounds,

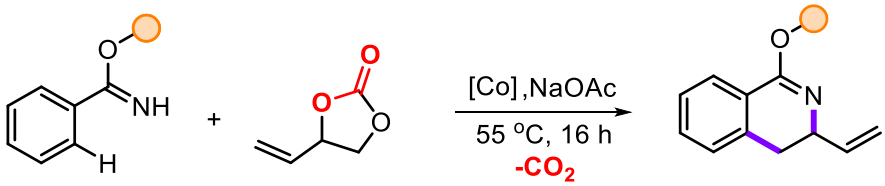
[11] (a) W. Guo, L. Martínez-Rodríguez, E. Martin, E. C. Escudero-Adán, A. W. Kleij, *Angew. Chem. Int. Ed.* **2016**, *55*, 11037-11040; (b) J. E. Gómez, W. Guo, A. W. Kleij, *Org. Lett.* **2016**, *18*, 6042-6045; (c) W. Guo, L. Martínez-Rodríguez, R. Kuniyil, E. Martin, E. C. Escudero-Adán, F. Maseras, A. W. Kleij, *J. Am. Chem. Soc.* **2016**, *138*, 11970-11978.
[12] N. Miralles, J. E. Gómez, A. W. Kleij, E. Fernández, *Org. Lett.* **2017**, *19*, 6096-6099.

namely (*E*)-configured pent-2-ene-1,5-diols and but-2-ene-1,4-diols as illustrated in Scheme 1.2.




**Scheme 1.2** Cu-catalyzed decarboxylative formation of highly substituted (*E*)-configured allylic scaffolds from VCCs.

More recently, the Ackermann group described a sequential reaction involving the allylation of aryl imidates using a flexible cobalt(III) catalyst (Scheme 1.3)[13] This procedure results in the creation of substituted dihydroisoquinolines while producing only $CO_2$ and $H_2O$ as waste products. The directing group from the substrate becomes an integral part of the final product, eliminating the need for its removal post-synthetically. This clearly contributes to the overall atom-efficiency of this cobalt-catalyzed transformation. The developed protocol accommodates a wide range of functional groups in the imidate substrate, including ester and amide groups.

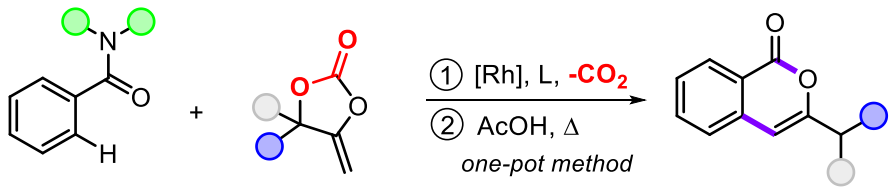



**Scheme 1.3** Co-catalyzed decarboxylative domino allylations of imidates.

Cyclic carbonates, which act as synthetic counterparts to enolates after decarboxylation, were utilized by Kakiuchi in a Rh-catalyzed process for functionalization of aromatic compounds through direct C-H activation. This method was employed to synthesize alpha-aryl ketones. Post-treatment of the reaction mixture with

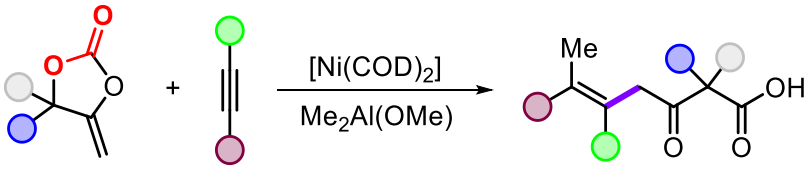
[13] H. Wang, M. M. Lorion, L. Ackermann, *ACS Catal.* **2017**, *7*, 3430.

acetic acid led to the formation of valuable isocoumarins (Scheme 1.4).[14] The formation of the carbon-carbon bond is believed to occur via a migratory insertion mechanism.




**Scheme 1.4** C-H functionalization of arenes to afford isocoumarins.

Recently, Kimura and colleagues published a study on nickel-catalyzed reactions that involve the coupling between cyclic alkenyl carbonates with internal alkynes.[15] A notable distinction from the decarboxylative conversion of vinyl cyclic carbonates (VCCs) is that in this case all the atoms from the carbonate substrate are preserved in the final product (Scheme 1.5). The presence of $Me_2Al(OMe)$ is essential for the formation of β-keto-carboxylic acids, and other organometallic reagents like $Me_3B$ and $Me_2Zn$ demonstrated lower degrees of efficiencies. The proposed key intermediate in this process is an eight-membered nickelacycle.



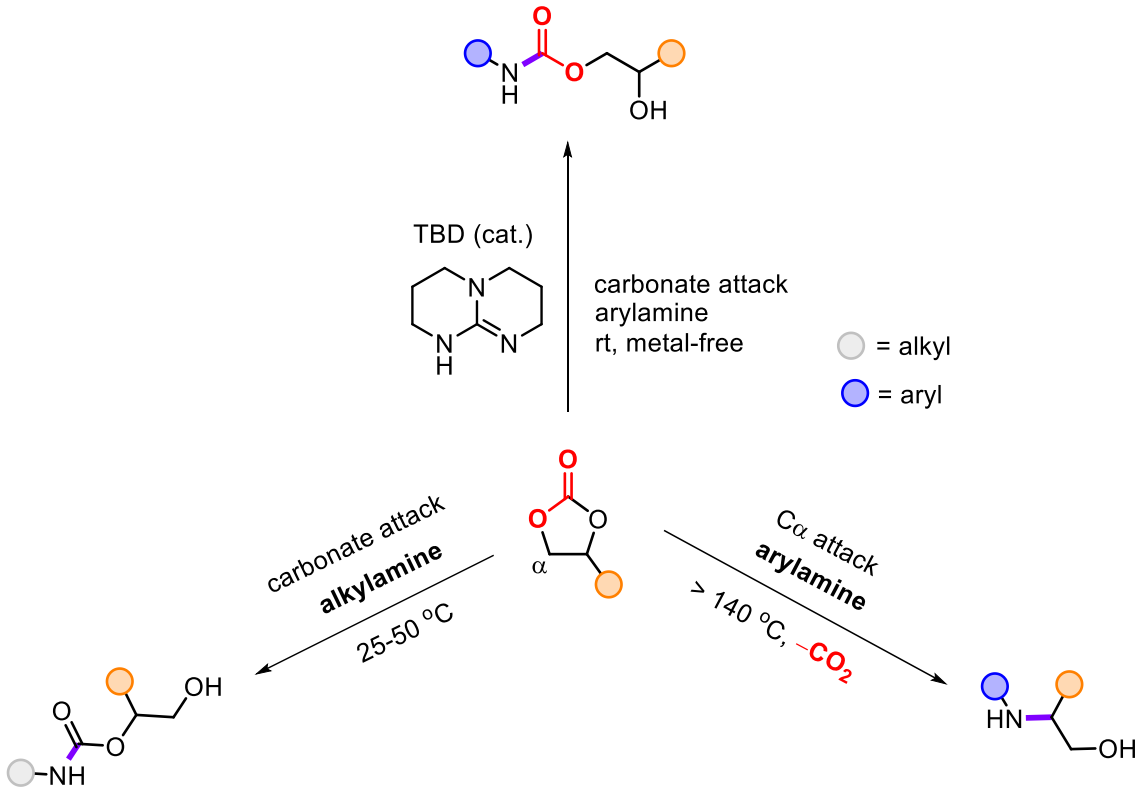

**Scheme 1.5** Ni-catalyzed coupling of cyclic alkenyl carbonates and alkynes with full atom incorporation into the final β-keto-carboxylic acids.

[14] Y. Hara, S. Onodera, T. Kochi, F. Kakiuchi, *Org. Lett.* **2015**, *17*, 4850.
[15] R. Ninokata, T. Yamahira, G. Onodera, M. Kimura, *Angew. Chem. Int. Ed.* **2017**, *56*, 208-211.

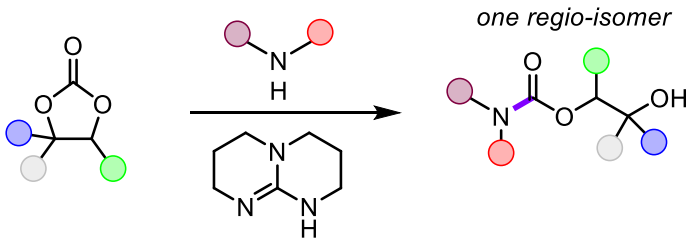
## 1.2.2 Metal-free catalyzed transformations

The Kleij group introduced a novel and highly promising approach for the synthesis of *N*-aryl carbamates, which are typically challenging to obtain. This method utilizes readily accessible cyclic carbonates and aromatic amines under virtually solvent-free and metal-free conditions. They demonstrated that TBD (1,5,7-triazabicyclo[4.4.0]dec-5-ene) serves as an effective organocatalyst for achieving selective and efficient formation of *N*-aryl carbamate products. Through density functional theory (DFT) studies, they also uncovered an intriguing proton-relay mechanism involved in this reaction. This methodology offers several advantages as it is operationally simple, requires minimal amounts of solvent, and can be easily scaled up for larger production. Furthermore, it holds significant potential for various applications in synthetic chemistry (Scheme 1.6).[16] For instance, it was later on demonstrated that this reactivity can be advantageous in the synthesis of regioregular carbamates and related oligourethanes (Scheme 1.7).[17]

[16] W. Guo, J Gónzalez-Fabra, N. A. G. Bandeira, C. Bo, A. W. Kleij, *Angew. Chem. Int. Ed.* **2015**, *54*, 11686-11690.
[17] S. Sopeña, V. Laserna, W. S. Guo, E. Martin, E. C. Escudero-Adan, A. W. Kleij, *Adv. Synth. Catal.* **2016**, *358*, 2172-2178.




**Scheme 1.6** Regioisomer formation in the aminolysis of cyclic carbonates and TBD catalyzed formation of *N*-aryl carbamates.



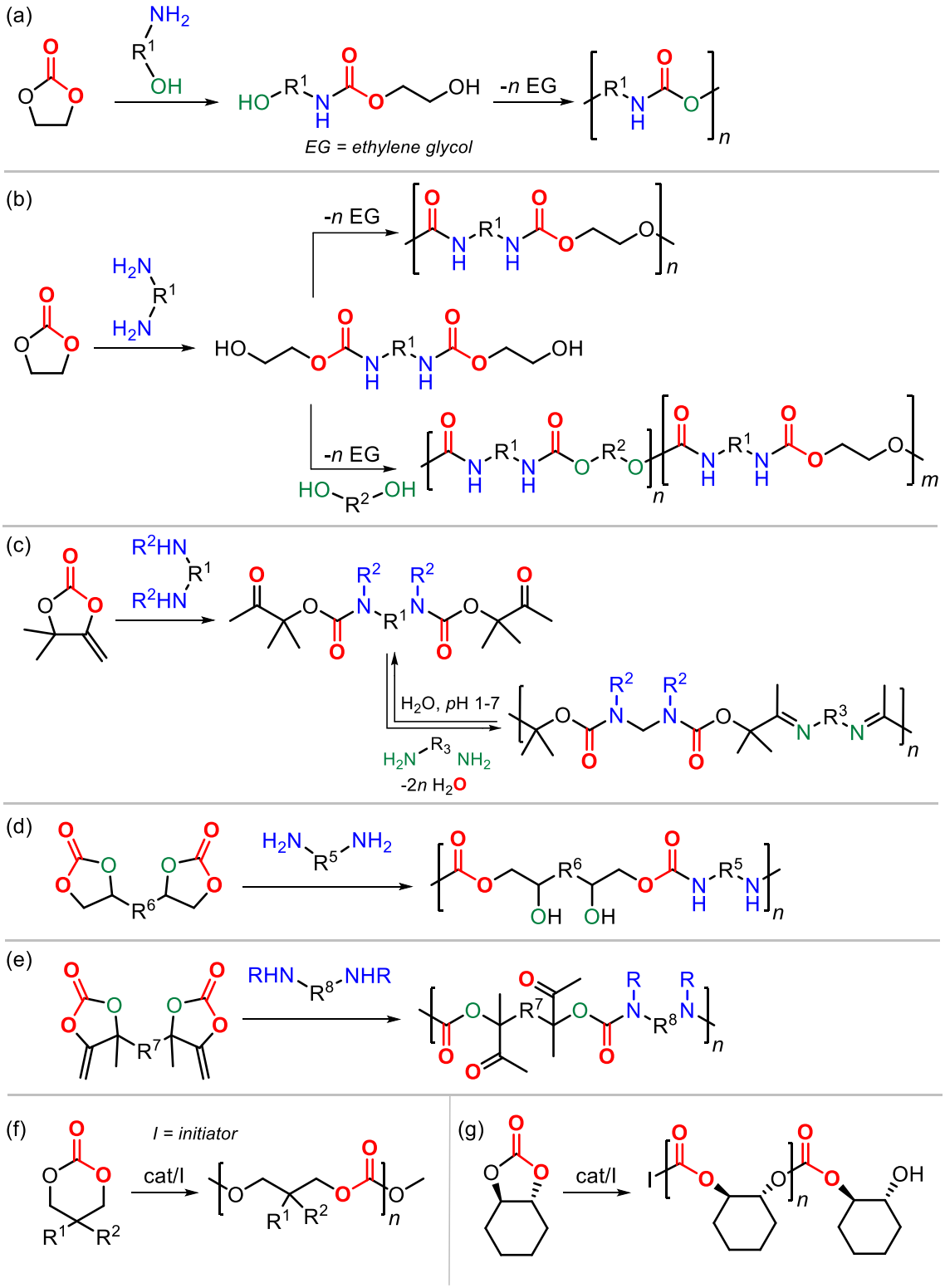

**Scheme 1.7** The organocatalytic, regioselective formation of linear carbamates.

## 1.3 Ring-opening polymerization of cyclic carbonates

Polymers play a crucial role in modern life, offering a wide range of properties and applications that enable diverse consumer products. However, the prevalent use of polymers derived from fossil sources, such as crude oil, presents significant challenges. These conventional polymers are not biodegradable or easily recyclable, leading to their accumulation in the environment and posing risks to ecosystems and human health. Therefore, the development of low-carbon footprint polymers from easily accessible and renewable (bio)carbon resources is of high contemporary interest. Ideally, monomers (the typical precursors of polymers) should empower the production of polymers that are both biodegradable and capable of being reused. Cyclic carbonates (CCs) show promise as suitable monomers in this context, as they have suitable reactivity in processes aimed at polycarbonates (PCs) or non-isocyanate polyurethanes (NIPUs). Scheme 1.8 summarizes some of the previous activities in the area leading to target polymer based on ring-opening chemistry of cyclic carbonates.

The self-polycondensation of bis-hydroxy-urethanes (Scheme 1.8a) or bis-hydroxy-bis-carbamates (Scheme 1.8b) can be achieved by using $Bu_2SnO$ or $SnCl_2$ catalysts at temperatures ranging from 100 to 150 °C. These monomers are synthesized through the aminolysis of ethylene carbonate with amino alcohols or diamines, such as 1,4-butanediamine, 1,6-hexanediamine, 1,12-dodecanediamine, isophorone diamine or piperazine. Detrembleur et al. recently developed a synthetic route for degradable polyurethanes (PUs) that incorporate reversible imine bonds within their main structure. This is achieved through the polycondensation of $CO_2$-based monomers (Scheme 1.8c).[18] In the field of PUs, there has been a growing focus on the design of isocyanate-free routes for their production, and $CO_2$ plays a crucial role in this transition (see Scheme 1.8d-e). Monomers based on six-membered cyclic carbonates (6MCCs) exhibit higher reactivity for ring-opening polymerization (ROP) compared to five-membered cyclic carbonates (5MCCs).

[18] S. Gennen, B. Grignard, C. Jérôme, C. Detrembleur, *Adv. Synth. Catal.* **2019**, *361*, 355-365.




**Scheme 1.8** Synthetic pathways for polymers derived from $CO_2$-sourced building blocks.

The ring strain in 6MCCs, such as trimethylene carbonate (TMC) or functionalized analogues, enables their ROP under relatively mild temperature conditions (Scheme 1.8f). [19] While the ROP of ethylene carbonate (EC) requires some degree of decarboxylation, other monomers can be polymerized through ROP without decarboxylation such as *trans*-configured cyclohexene carbonate (CHC). The *trans*-fused five-membered carbonate increases the ring strain thereby promoting its ROP (Scheme 1.8g). In contrast, the *cis*-isomer does not undergo polymerization due to a competing and faster ring-closing reaction of a ring-opened carbonate intermediate.[20]

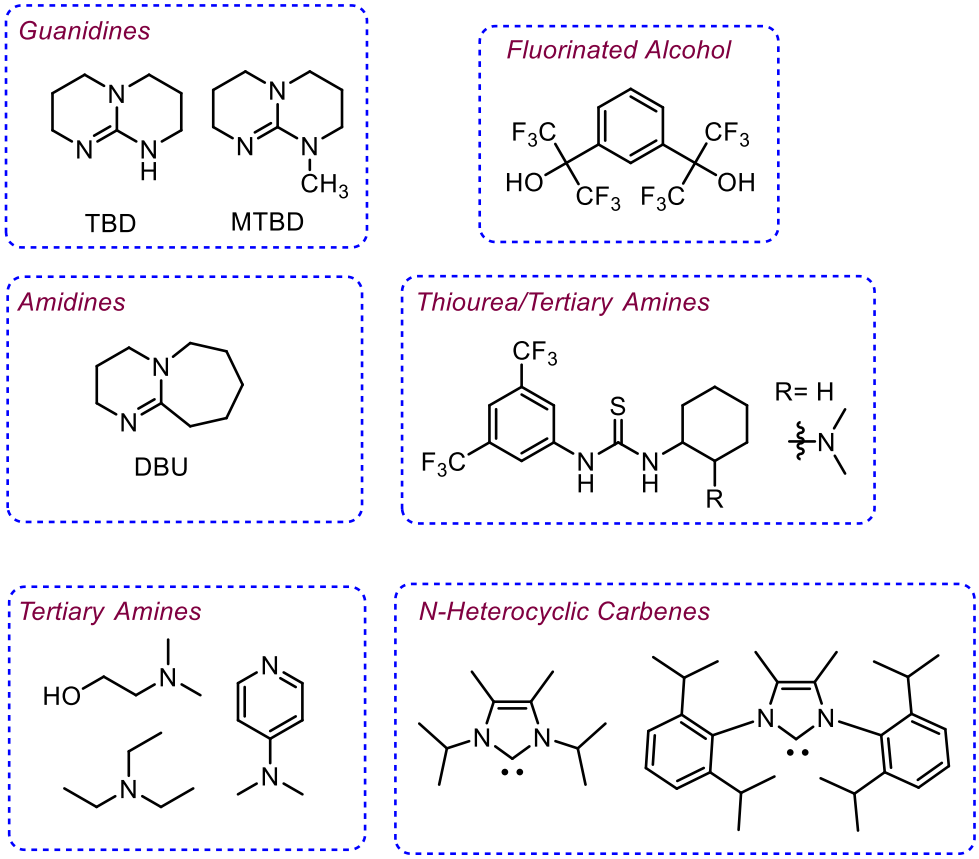



**Figure 1.5** Organic bases used as catalysts in ring-opening polymerization (ROP).

In general, the catalytic activity of base catalysts has been examined in detail towards the ROP of cyclic esters and carbonates. Guanidines, amidines, tertiary amines, *N*-heterocyclic carbenes and thiourea tertiary amines proved to have similar order of

[19] K. Tezuka, K. Komatsu, O. Haba, *Polym. J.* **2013**, *45*, 1183-1187.
[20] W. Guerin, A. K. Diallo, E. Kirilov, M. Helou, M. Slawinski, J.-M. Brusson, J.-F. Carpentier, S. M. Guillaume, *Macromolecules* **2014**, *47*, 4230-4235.

magnitude reactivity in terms of monomer conversion, but the highest degrees of polymerization (DPs) in the ring-opening polymerization of TMC was attained with TBD.[21] This is due to the unique dual hydrogen-bond acceptor-donor functionality of TBD. This dual behavior assures the activation of ROP without TBD being inserted in the growing polymer chain by formation of an amide entity as is the case for other amine-based catalysts.[22] *N*-heterocyclic olefins (NHOs) are an emerging class of organo-polymerization catalysts.[23] The activity of NHOs was investigated for the ROP of both lactones and TMC.

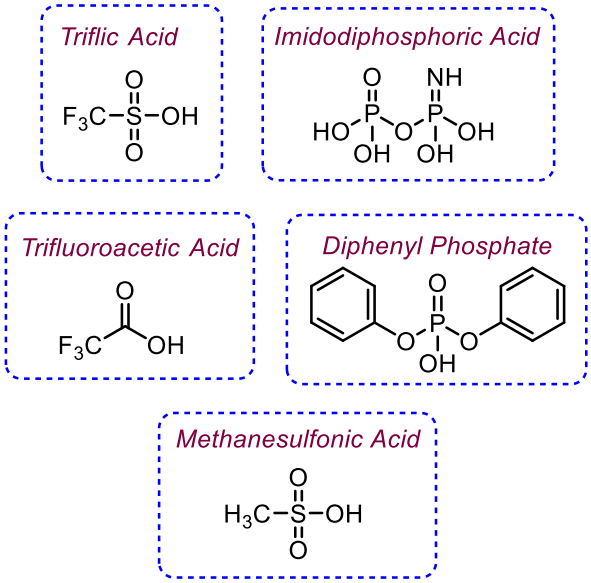


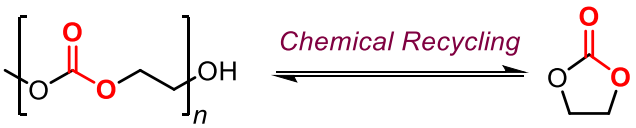

**Figure 1.6** Organic Brønsted acids used as catalysts in ROP.

The organocatalytic initiation of the ROP process can also be based on strong Brønsted acids that allow electrophilic activation of the monomer. Triflic acid (TfOH), methanesulfonic acid (MSA) trifluoroacetic acid (TFA),[24] diphenyl phosphate (DPP)[25]

[21] F. Nederberg, B. G. G. Lohmeijer, F. Leibfarth, R. C. Pratt, J. Choi, A. P. Dove, R. M. Waymouth, J. L. Hedrick, *Biomacromolecules* **2007**, *8*, 153-160.
[22] I. Nifant'ev, A. Shlyakhtin, V. Bagrov, B. Lozhkin, G. Zakirova, P. Ivchenko, O. Legon'kova, *React. Kinet. Mech. Catal.* **2016**, *117*, 447-476.
[23] S. Naumann, A. W. Thomas, A. P. Dove, *ACS Macro Lett.* **2016**, *5*, 134-138.
[24] (a) N. Nemoto, F. Sanda, T. *J.* Endo, *Polym. Sci. Part Polym. Chem*. **2001**, *39*, 1305–1317; (b) Endo, T.; Sanda, F. *Macromol. Symp.* **2000**, *159*, 1-8; (c) W. H. Carothers, F. J. V. Natta, *J. Am. Chem. Soc.* **1930**, *52*, 314-326.
[25] K. Makiguchi, Y. Ogasawara, S. Kikuchi, T. Satoh, T. Kakuchi, *Macromolecules* **2013**, 46, 1772-1782.

and imidodiphosphoric acid (IDPA)[26] have been reported as effective catalysts for the ring-opening polymerization of TMC, where a benzyl alcohol or water was used as the initiator.[27]

## 1.4 Depolymerization




**Scheme 1.9** Depolymerization of a polycarbonate to deliver a cyclic carbonate product.

Worldwide plastics include the use of a wide range of polymers containing additives with innumerable and remarkable physicochemical properties. As a result of the predominant linear economy of plastics, plastic waste continues to accumulate in the environment. Currently, their reprocessing is complex and challenging due to the presence of a wide range of material components that possess different chemical properties which need to be taken into account when recycling is considered.

Chemical recycling, which is the (catalytic) depolymerization of materials into valuable monomers or chemicals, has emerged as a powerful strategy complementary to mechanical recycling.[28] It opens up interesting perspectives for the recovery of carbonaceous matter, the avoidance of the exhaustive use of petroleum resources and limiting the generation of pollution. Suitable pathways for efficient depolymerization under mild conditions are needed to shift from a linear towards a circular and environmentally more friendly plastic economy. Solvolysis processes are well-known and enable the depolymerization of polymers formed from polycondensation reactions (such as in the case of polyesters, polyamides, polycarbonates) by hydrolysis, aminolysis or transesterification reactions. They are catalyzed by a number of bases, acids and ionic

[26] X. He, Y. Ji, Y. Jin, S. Kan, H. Xia, J. Chen, B. Liang, H. Wu, K. Guo, Z. J. Li, *Polym. Sci. Part Polym. Chem.* **2014**, *52*, 1009-1019.
[27] D. Delcroix, B. Martín-Vaca, D. Bourissou, C. Navarro, *Macromolecules* **2010**, 43, 8828-8835.
[28] K. Ragaert, L. Delva, K. van Geem, *Waste Management* **2017**, *69*, 24-58.

liquids.[29] They offer the recovery of pure monomers, useful for the production of new virgin plastics. For polycarbonates, depolymerization has been studied primarily using catalysis, and offers ways to recycle the polymer atoms back into cyclic structures (see Scheme 1.9) or one or more of the original monomers needed for polycarbonate synthesis.

## 1.5 Thesis aims and outline

The **MAIN OBJECTIVE** of this doctoral thesis is to develop innovative ring-opening reactions involving (functionalized) cyclic carbonates as substrates. Cyclic carbonates possess both nucleophilic and electrophilic sites that give impetus for processes that build on this dual type of reactivity. This allows for the expansion of transformations of cyclic carbonates to provide new chemical intermediates and monomers derived from $CO_2$-based heterocycles. Traditionally, the ring-opening chemistry of these heterocycles has focused on approaches via carbonate ring-opening, and these find great utility in the creation of more benign polyurethane polymers. However, less attention has been given to the nucleophilic attack on positions referred to as "methylene" and "*exo*-cyclic" in the cyclic carbonate scaffold. Hence, the discovery of new reactivity principles that enable effective and selective conversion of cyclic carbonates will enhance the versatility and importance of these $CO_2$-derived heterocycles in synthetic and polymer chemistry. This thesis thus explores various novel ring-opening processes, with specific details elaborated below.

In **Chapter 2,** an extraordinary ring-opening process of cyclic carbonates bearing vinyl groups is studied. A unique sequence of decarboxylation, $CH_3CN$ extrusion and Michael addition is noted when vinyl cyclic carbonates are treated with cyanide at elevated temperatures. β-cyano ketones are produced under these conditions in moderate to high yields. The scope of this process is further discussed and a series of mechanistic control experiments (including labeling studies) is

[29] (a) L. Zhao, V. Semetey, *ACS Omega*, **2021**, *6*, 4175–4183. (b) *The New Plastics Economy - Rethinking the future of plastics*, Ellen MacArthur Foundation & McKinsey Company, **2016**. (c) C. Jehanno, M. M. Pérez-Madrigal, J. Demarteau, H. Sardon, A. P. Dove, *Polym. Chem.* **2019**, *10*, 172–186. (d) J. Payne, M. D. Jones, *ChemSusChem* **2021**, *14*, 4041-4070. (e) L. D. Ellis, N. A. Rorrer, K. P. Sullivan, M. Otto, J. E. McGeehan, Y. Román-Leshkov, N. Wierckx, G. T. Beckham, *Nat Catal.* **2021**, *4*, 539-556. (f) E. Feghali, L. Tauk, P. Ortiz, K. van Broekhoven, W. Eevers, *Polymer Degradation and Stability*, **2020**, *179*, 109241. (g) A. C. Fernandes, *Green Chem.* **2021**, *23*, 7330-7360.

presented that allow to propose a viable formation mechanism of the β-cyano ketone products.

In **Chapter 3**, the nucleophilic attack of alkyl- and aryl-thiols onto vinyl cyclic carbonates is examined using DBU as an organocatalyst. This process results in the formation of a series of allylic thioether compounds in moderate to good isolated yields. The process can be seen as a formal allylic substitution reaction that does not require a transition metal, and can be carried out under relatively mild conditions. Several control experiments are presented to validate the mechanistic hypothesis that the base is required to activate the thiol pro-nucleophile towards the attack on the C-terminus of the *exo*-cyclic double bond.

In **Chapter 4**, a diverse series of functional bicyclic monomers is investigated for their propensity for ROP in the presence of TBD as catalyst and benzyl alcohol (BnOH) as initiator. A direct route to densely substituted macromolecular aliphatic carbonates is developed including bifunctional monomers capable of initiating two distinct ring-opening polymerization processes offering versatile options for polymerization and crosslinking strategies. The controlled degradation of a selected polycarbonate is also examined using TBD as catalyst leading to a new type of bicyclic oxetane.

In the final **Chapter 5**, the thesis is summarized and the overarching conclusion of the results described in chapters 2-4 is provided together with a future vision for follow-up research.

# *Chapter 1*

# *Chapter 2. Formation of β-cyano-ketones through cyanide-promoted ring-opening of cyclic organic carbonates*

The results described in this chapter have been published in:

J. Ni, À. Cristòfol, A. W. Kleij, *Org. Chem. Front.* **2021**, *8*, 4520-4526.

UNIVERSITAT ROVIRA I VIRGILI
RING-OPENING OF CYCLIC CARBONATES: FROM FINE CHEMICALS TO CO2-BASED POLYMERS
Jixiang Ni

# 2.1 Introduction

## 2.1.1 Nucleophilic ring-opening reactions

Cyclic organic carbonates are heterocyclic compounds that are most commonly and conveniently prepared from small cyclic ethers and carbon dioxide under catalytic conditions.[30] Their synthesis has now reached a high level of sophistication,[31] and consequently more attention is devoted to the application of these scaffolds in fields ranging from fine chemical synthesis[32] to polymer chemistry.[33] One particularly attractive feature of cyclic carbonates is their potential for ring-opening reactions using suitable nucleophiles such as amines[34] and alcohols.[35] Nucleophilic ring-opening reactions of this type are nowadays extensively used in the fabrication of isocyanate-free based polyurethanes offering a more sustainable approach for these key polymers in

[30] (a) A. J. Kamphuis, F. Picchionia, P. P. Pescarmona, *Green Chem.* **2019**, *21*, 406-448; (b) C. Martín, G. Fiorani, A. W. Kleij, *ACS Catal.* **2015**, *5*, 1353-1370; (c) L. Guo, K. Lamb, M. North, *Green. Chem*. **2021**, *23*, 77-118.; (d) V. Aomchad, À. Cristòfol, F. Della Monica, B. Limburg, V. D'Elia, A. W. Kleij, *Green Chem.* **2021**, *23*, 1077-1113; (e) K. A. Andrea, F. M. Kerton, *Polym. J.* **2021**, *53*, 29-46; (f) R. Rajjak Shaikh, S. Pornpraprom, V. D'Elia, *ACS Catal.* **2018**, *8(1)*, 419-450; (g) B. Limburg, À. Cristòfol, F. Della Monica, A. W. Kleij, *ChemSusChem* **2020**, *13*, 6056-6065; (h) M. Alves, B. Grignard, R. Mereau, C. Jerome, T. Tassaing, C. Detrembleur, *Catal. Sci. Technol.* **2017**, *7*, 2651-2684.

[31] For a selection of highly substituted/functional examples: (a) C. J. Whiteoak, N. Kielland, V. Laserna, E. C. Escudero-Adán, E. Martin, A. W. Kleij, *J. Am. Chem. Soc.* **2013**, *135*, 1228-1231; (b) J. Rintjema, R. Epping, G. Fiorani, E. Martín, E. C. Escudero-Adán, A. W. Kleij, *Angew. Chem. Int. Ed*. **2016**, *55*, 3972-3976; (c) S. Sopeña, M. Cozzolino, C. Maquilón, E. C. Escudero-Adán, M. Martínez Belmonte. A. W. Kleij, *Angew. Chem. Int. Ed.* **2018**, *57*, 11203-11207; (d) C. Qiao, A. Villar-Yanez, J. Sprachmann, B. Limburg, C. Bo, A. W. Kleij, *Angew. Chem. Int. Ed.* **2020**, *59*, 18446-18451; (e) L. Longwitz, J. Steinbauer, A. Spannenberg, T. Werner, *ACS Catal.* **2018**, *8*, 665-672; (f) B. A. Vara, T. J. Struble, W. Wang, M. C. Dobish, J. N. Johnston, *J. Am. Chem. Soc.* **2015**, *137*, 7302-7305; (g) W. Natongchai, J. A. Luque-Urrutia, C. Phungpanya, M. Solà, V. D'Elia, A. Poater H. Zipse, *Org. Chem. Front*. **2021**, *8*, 613-627; (h) Y.-Y. Zhang, G.-W. Yang, R. Xie, L. Yang, B. Li, G.-P. Wu, *Angew. Chem. Int. Ed.* **2020**, *59*, 23291-23298.

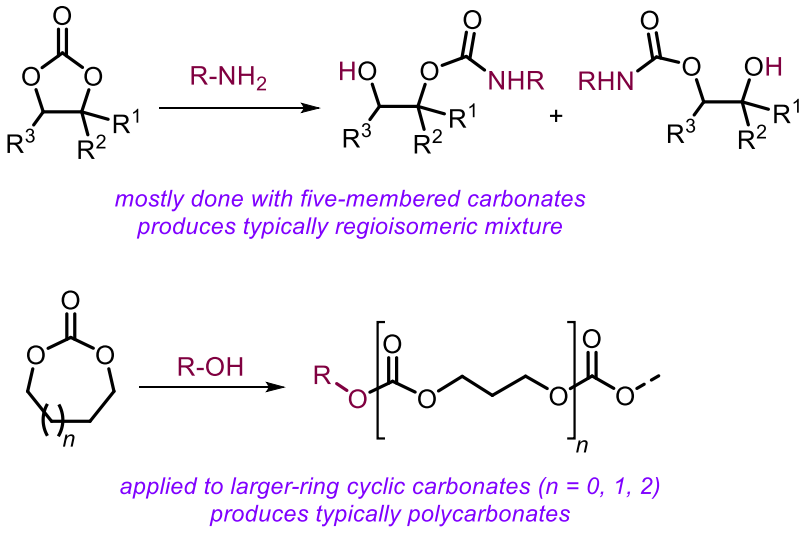
[32] (a) Q. Liu, L. Wu, R. Jackstell, M. Beller, *Nat. Commun.* **2015**, *6*, 5933; (b) W. Guo, J. E. Gómez, À. Cristòfol, J. Xie, A. W. Kleij, *Angew. Chem. Int. Ed.* **2018**, *57*, 13735-13747. (c) L. Zuo, T. Liu, X. Chang, W. Guo, *Molecules* **2019**, *24*, 3930.

[33] (a) F. Suriano, O. Coulembier, J. L. Hedrick, P. Dubois, *Polym. Chem*. **2011**, *2*, 528-533; (b) N. Yadav, F. Seidi, D. Crespy, V. D'Elia, *ChemSusChem* **2019**, *12*, 724-754; (c) B. Grignard, S. Gennen, C. Jérôme, A. W. Kleij, C. Detrembleur, *Chem. Soc. Rev*. **2019**, *48*, 4466-4514.

[34] (a) M. Blain, L. Jean-Gérard, R. Auvergne, D. Benazet, S. B. Caillol, *Green Chem.* **2014**, *16*, 4286-4291; (b) W. Guo, J. Gónzalez-Fabra, N. A. G. Bandeira, C. Bo, A. W. Kleij, *Angew. Chem. Int. Ed*. **2015**, *54*, 11686-11690; (c) P. Olsén, M. Oschmann, E. V. Johnston, B. Åkermark, *Green Chem.* **2018**, *20*, 469-475.

[35](a) J. Matsuo, S. Nakano, F. Sanda, T. Endo, *J. Polym. Sci. A, Polym. Chem.* **1998**, *36*, 2463-2471; (b) K. Tomishige, Y. Gu, Y. Nakagawa, M. Tamura, *Front. Energy Res.* **2020**, *8*, no. 117.

material science.[36] In addition, the formation of discrete linear carbamates/urethanes from cyclic carbonates and amine reagents has also been examined providing a diverse scope of functional synthons.[37]




**Scheme 2.1** Previously reported ring-opening of cyclic carbonates using *N*- or *O*-based nucleophiles.

## 2.1.2 Activated α-alkylidene carbonates

The synthesis of β-cyano ketones has been described by various groups including sophisticated approaches based on decarboxylative oxyalkylation of alkynyl carboxylic acids using alkyl nitriles,[38] the photochemical generation of acyl radicals[39] and metal-

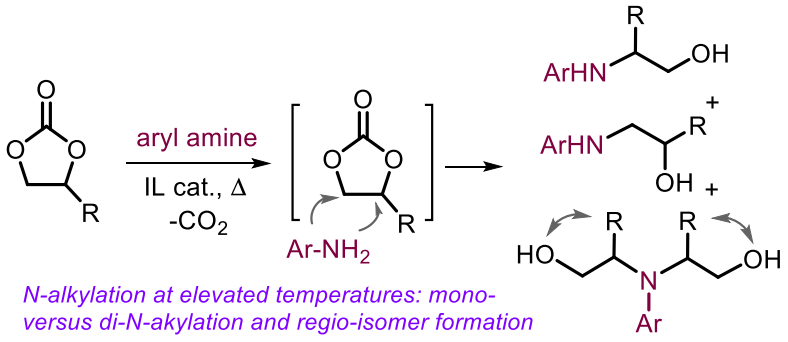
[36] For a selection of recent examples: (a) X. Sheng, G. Ren, Y. Qin, X. Chen, X. Wang, F. Wang, *Green Chem.* **2015**, *17*, 373-379; (b) B. Bizet, E. Grau, H. Cramail, J. M. Asua, *Polym. Chem.* **2020**, *11*, 3786-3799; (c) A. Gomez-Lopez, B. Grignard, I. Calvo, C. Detrembleur, H. Sardon, *ACS Appl. Polym. Mater.* **2020**, *2*, 1839-1847; (d) S. E. Dechent, A. W. Kleij, G. A. Luinstra, *Green Chem.* **2020**, *22*, 969-978; (e) L. Annunziata, A. K. Diallo, S. Fouquay, G. Michaud, F. Simon, J.-M. Brusson, J.-F. Carpentier, S. M. Guillaume, *Green Chem.* **2014**, *16*, 1947-1956; (f) S. Samanta, S. Selvakumar, J. Bahr, D. Suranga Wickramaratne, M. Sibi, B. J. Chisholm, *ACS Sustainable Chem. Eng.* **2016**, *4*, 6551-6561.

[37] (a) W. Guo, V. Laserna, J. Rintjema, A. W. Kleij, *Adv. Synth. Catal.* **2016**, *358*, 1602-1607; (b) S. Sopeña, V. Laserna, W. Guo, E. Martin, E. C. Escudero-Adán, A. W. Kleij, *Adv. Synth. Catal.* **2016**, *358*, 2172-2178.

[38] Y. Li, J.-Q. Shang, X.-X. Wang, W.-J. Xia, T. Yang, Y. Xin, Y.-M. Li, *Org. Lett.* **2019**, *21*, 2227-2230.

[39] E. de Pedro Beato, D. Mazzarella, M. Balletti, P. Melchiorre, *Chem. Sci.* **2020**, *11*, 6312-6324.

mediated conversion of cyanohydrins and aldehydes/ketones to β-cyano ketones.[40] More direct methods rely on the Michael addition of suitable CN-precursors such as TMSCN to α, β-unsaturated ketones.[41]



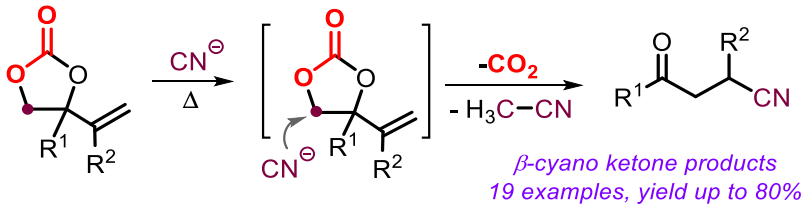

**Scheme 2.2** Aryl amine induced decarboxylative *N*-alkylation reported by Selva et al. IL stands for ionic liquid.

As far as we are aware, there are only scarce examples of nucleophilic species attacking the electrophilic methylene carbon center of the cyclic carbonate. Selva and coworkers reported a decarboxylative amination process providing formally *N*-mono- and *N*-bis-alkylated amines as major products.[42] Detrembleur et al. used alkyl thiol-based nucleophiles providing macromolecular hydroxythioethers as products.[43] More recently, activated α-alkylidene carbonates have also emerged as useful intermediates giving rise to other types of polymer architectures.[44]

[40] Z.-F. Li, Q. Li, L.-Q. Ren, Q.-H. Li, Y.-G. Peng, T.-L. Liu, *Chem. Sci.* **2019**, *10*, 5787-5792.
[41] G. Strappaveccia, T. Angelini, L. Bianchi, S. Santoro, O. Piermatti, D. Lanari, L. Vaccaro, *Adv. Synth. Catal.* **2016**, *358*, 2134-2139.
[42] M. Selva, M. Fabris, V. Lucchini, A. Perosa, M. Noè, *Org. Biomol. Chem.* **2010**, *8*, 5187–5198;
[43] (a) F. Monie, B. Grignard, J.-M. Thomassin, R. Mereau, T. Tassaing, C. Jerome, C. Detrembleur, *Angew. Chem. Int. Ed.* **2020,** *59*, 17033-17041; for related chemistry using α-alkylidene carbonates, see: (b) F. Ouhib, B. Grignard, E. van den Broeck, A. Luxen, K. Robeyns, V. van Speybroeck, C. Jerome, C. Detrembleur, *Angew. Chem. Int. Ed.* **2019**, *58*, 11768-11773; (c) F. Ouhib, L. Meabe, A. Mahmoud, B. Grignard, J.-M. Thomassin, F. Boschini, H. Zhu, M. Forsyth, D. Mecerreyes, C. Detrembleur, *ACS Appl. Polym. Mater.* **2020**, *2*, 922-931.
[44] (a) S. Gennen, B. Grignard, T. Tassaing, C. Jérôme, C. Detrembleur, *Angew. Chem. Int. Ed.* **2017**, *56*, 10394-10398; (b) F. Siragusa, E. van den Broeck, C. Ocando, A. J. Müller, G. de Smet, B. U. W. Maes, J. de Winter, V. van Speybroeck, B. Grignard, C. Detrembleur, *ACS Sustainable Chem. Eng.* **2021**, *9*, 1714-1728.

### 2.1.3 Aims and objectives

Recently, we employed cyclic carbonates as intermediates in a catalytic approach directed towards *cis*-configured *syn*-diols.[45] In this case, water was used as a nucleophile, and the approach is complementary to water-induced epoxide ring-opening that furnishes *trans*-diols.[46] Here we disclose the use of cyanide as a nucleophilic agent, giving access to β-cyano ketones as products after an unusual ring-opening/extrusion/Michael addition cascade process.




**Scheme 2.3** CN-promoted decarboxylative ring-opening/extrusion/Michael process that involves vinyl cyclic carbonates.

Unlike in these latter scenarios, the present methodology (Scheme 2.3) is an unprecedented example of a process that combines decarboxylation and a formal extrusion of $CH_3CN$ with the latter supported by a number of control experiments. Our results help to establish that cyclic organic carbonates can have other reactivity modes than generally noted.

## 2.2 Results and discussion

### 2.2.1 Optimization studies

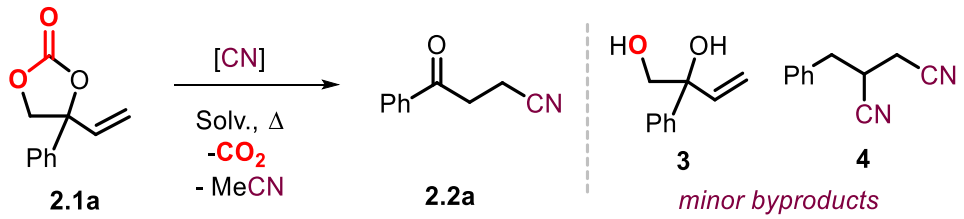
Initially, we decided to examine the ring-opening of cyclic carbonates with nucleophiles other than amines, and for this purpose we selected various cyanide-based salts. The combination of vinyl cyclic carbonate **2.1a** with different cyanide reagents under various reaction conditions was scrutinized (Table 2.1). We started the screening phase using **2.1a**

[45] V. Laserna, G. Fiorani, C. J. Whiteoak, E. Martin, E. Escudero-Adán, A. W. Kleij, *Angew. Chem. Int. Ed.* **2014**, *53*, 10416-10419.
[46] Z. Wang, Y.-T. Cui, Z.-B. Xu, J. Qu, *J. Org. Chem.* **2008**, *73*, 2270-2274.

and KCN (3 equiv) as reagents while varying the reaction temperature (entries 1-6). At lower temperatures (25-60 ºC, entries 1-3), the β-cyano ketone **2.2a** was unexpectedly produced up to 20% NMR yield at 60 ºC, though the chemo-selectivity towards it was moderately low. We found that the major byproducts were the hydrolyzed vinyl cyclic carbonate (1,2-diol **3**)[47] and the bis-cyanated product **4**.[48] At 100 ºC (entry 5) the yield of **2.2a** could be maximized to 72% (isolated product). Changing the solvent from DMF to others (entries 7-11) gave in some cases high conversion of **2.1a** but with poor selectivity towards **2.2a**. The use of cyanating agents other than KCN (entries 12-14) was less efficient (cf., entry 5). The performance under air (entry 15) was comparable to the reaction carried out under an argon atmosphere suggesting that diol formation is mostly related to the moisture introduced by the cyanide reagent itself. We found indeed that the use of an aged sample of KCN produced much more diol byproduct, and therefore fresh KCN kept under argon prior to its use was charged in the reaction media. The use of neat conditions was unproductive (entry 16) likely a result of the heterogeneous nature of the reaction mixture.[49] Changing the volume of the solvent did not have any beneficial effect (entries 17 and 18) giving lower yield of **2.2a**. Finally, we tried to use a solubilizing agent (18-crown-6) to see if the reaction progress could be improved, but there was no observable effect on the process outcome (entry 19).

[47] For reference data of **2.2f**, see: W. Guo, L. Martínez-Rodríguez, E. Martín, E. C. Escudero-Adán, A. W. Kleij, *Angew. Chem. Int. Ed*. **2016**, *55*, 11037-11040.
[48] L. Capaldo, L. Buzzetti, D. Merli, M. Fagnoni, D. Ravelli, *J. Org. Chem*. **2016**, *81*, 7102-7109.
[49] Note that all reaction mixtures in DMF became homogeneous in nature during the reaction time.

**Table 2.1** Screening of the reaction between cyanide-based reagents and vinyl cyclic carbonate **2.1a** providing β-cyano ketone **2.2a** [a]

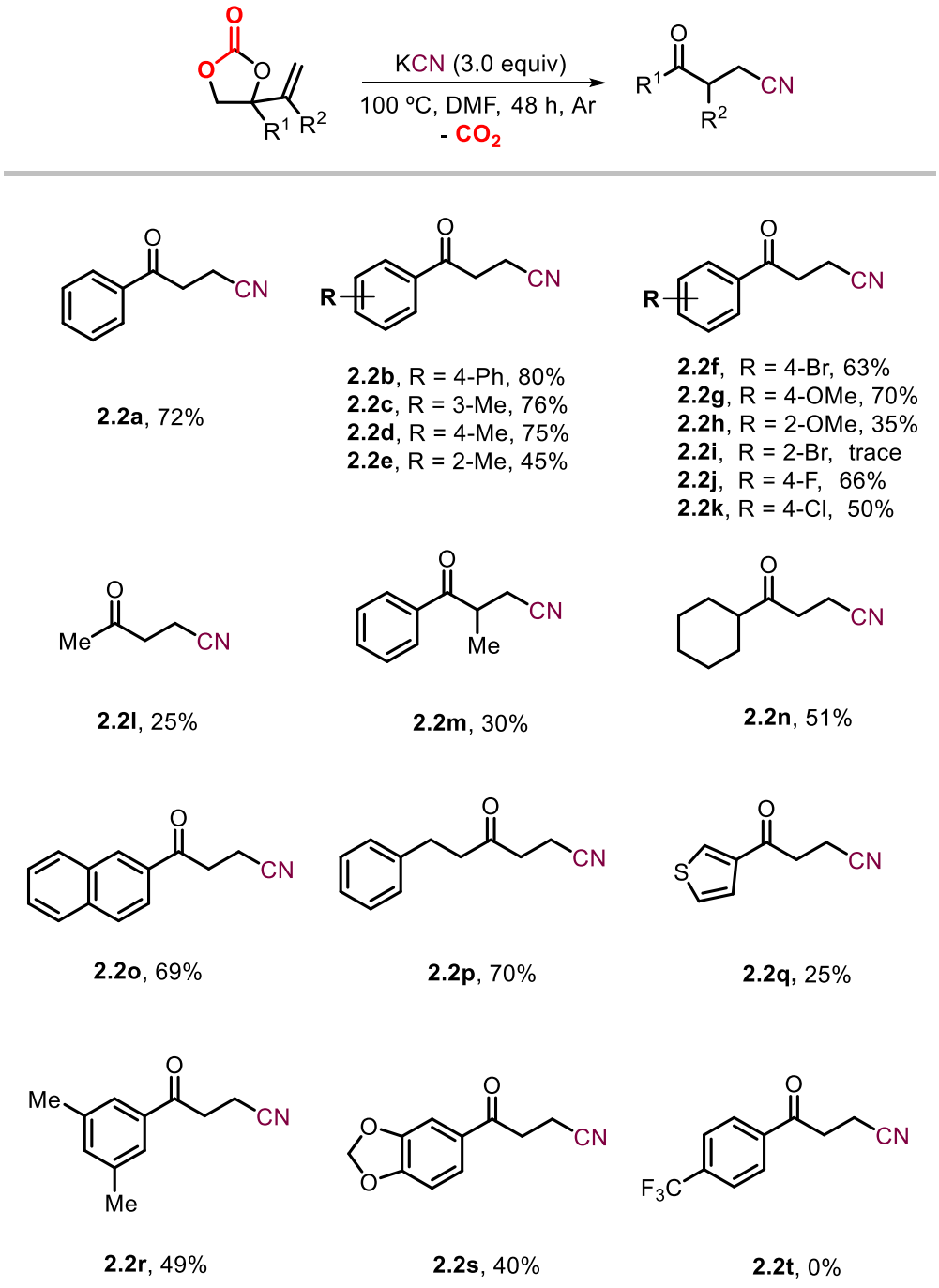



| Entry | [CN] | Solvent | T (º C) | Conv. **2.1a** (%)[b] | **2.2a** (%)[b] |
|---|---|---|---|---|---|
| 1 | KCN | DMF | 25 | 0 | 0 |
| 2 | KCN | DMF | 40 | 0 | 0 |
| 3 | KCN | DMF | 60 | 50 | 20 |
| 4 | KCN | DMF | 80 | 62 | 45 |
| **5** | **KCN** | **DMF** | **100** | **81** | **72**[c] |
| 6 | KCN | DMF | 120 | 90 | 52 |
| 7 | KCN | THF | 60 | 22 | 0 |
| 8 | KCN | MeCN | 80 | 10 | trace |
| 9 | KCN | DMSO | 100 | 100 | 0 |
| 10 | KCN | Toluene | 100 | 43 | 5 |
| 11 | KCN | Dioxane | 100 | 10 | trace |
| 12 | NaCN | DMF | 100 | 65 | 30 |
| 13 | TMSCN | DMF | 100 | 6 | 0 |
| 14 | TBACN | DMF | 100 | 98 | 10 |
| 15[d] | KCN | DMF | 100 | 80 | 70[c] |
| 16[e] | KCN | – | 100 | 100 | 0 |
| 17[f] | KCN | DMF | 100 | 74 | 43 |
| 18[g] | KCN | DMF | 100 | 85 | 60 |
| 19[h] | KCN | DMF | 100 | 80 | 59 |

[a] The reactions were carried out under an argon atmosphere using cyclic vinyl-carbonate **2.1a** (0.2 mmol, 1.0 equiv), cyanide reagent (3 equiv) in 0.50 mL of solvent at the indicated temperature for 48 h. [b]Determined by $^1$H NMR ($CDCl_3$) using mesitylene as internal standard. [c]Yield of the isolated product after column purification. [d]Under air. [e]No solvent. [f]Solvent volume was 0.20 mL. [g]Solvent volume was 1.0 mL. [h]Using 18-crown-6 (5.3 mg, 10 mol%) as additive.

## 2.2.2 Product scope of β-cyano ketones

With the optimized conditions identified (Table 2.1, entry 5), we then examined the scope of this unusual cascade process (Scheme 2.4). In most of the reactions, some 1,2-diol (through the hydrolysis of the cyclic carbonate) was noted as byproduct, and this could be kept to a minimum by performing the reaction as dry as possible. The use of aged KCN typically delivers the β-cyano ketone in lower yield, and therefore in all reactions related to the products shown in Scheme 2.4 as fresh as possible KCN (while kept in a glove box) was used. The highest isolated yield of product was noted for product **2.2b** (80%), while for **2.2a** (72%), **2.2f** (63%), **2.2g** (70%), **2.2c** (76%), **2.2d** (75%), **2.2j** (66%), **2.2o** (69%) and **2.2p** (70%) the yields were also appreciable showing that *meta*- and *para*-substitutions on the aryl group are feasible. For vinyl carbonates with aryl groups ($R^1$) having *ortho*-substituents (**2.2h**, 35%; **2.2i**, trace; and **2.2e**, 45%) lower yields were observed which may be explained by a certain degree of steric modulation in this cascade process. Carbonate precursors with alkyl groups ($R^1$) are also tolerated (**2.2s**, 40%; **2.2n**, 51%; and **2.2p**, 70%), and the presence of heterocyclic substituents such as those present in **2.2q** (25%) and **2.2s** (40%) result into lower product yields. A disubstituted aryl group in the carbonate substrate (**2.2r**, 37%) was endorsed, whereas the presence of a strongly deactivating $CF_3$ group (**2.2t**) was unproductive. Finally, the presence of a further substituent on the olefin bond ($R^2$ = Me; **2.2m**, 30%) provided a moderately low product yield. Whereas the products could be readily identified by comparison of their $^1H$ and $^{13}C$ NMR spectra with literature data,[9-12] for the brominated derivative **2.2f** the atom connectivity could be further supported by X-ray crystallography (Fig. 2.1).




**Scheme 2.4** β-Cyano ketone scope using various vinyl cyclic carbonates and KCN as reagent.

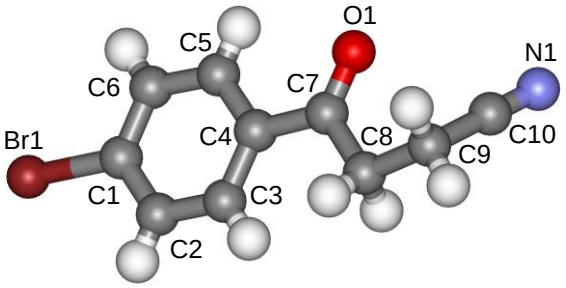
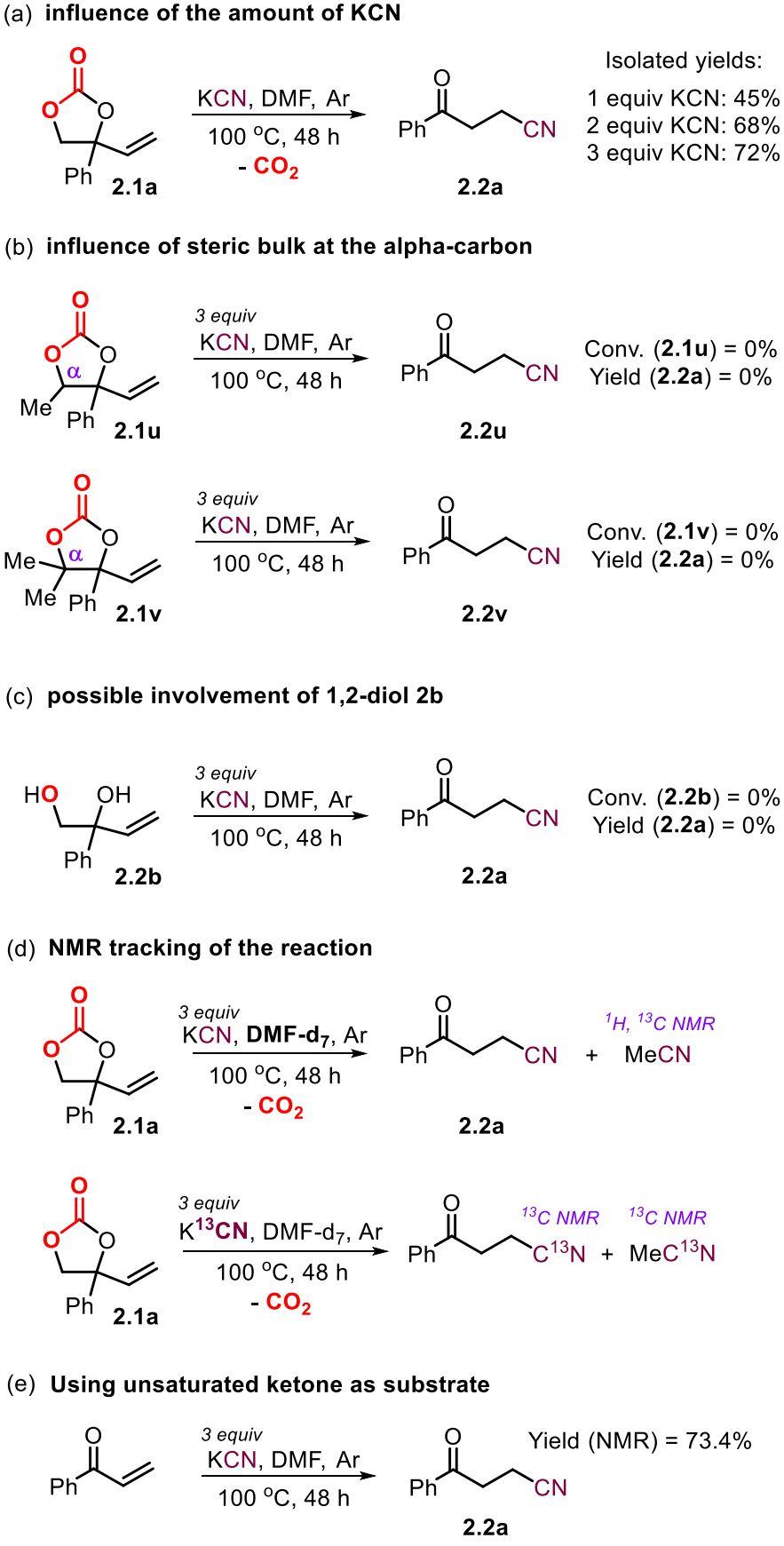



**Figure 2.1** X-ray molecular structure determined for **2.2f**.

## 2.2.3 Mechanistic considerations

In order to collect information about a possible mechanistic scenario of this unusual CN-mediated cascade reaction, several control experiments were conducted (Scheme 2.5). As already shown in Table 2.1, the amount of cyanide reagent (KCN) has a clear influence on the yield of **2.2a** (Scheme 2.5a). Whereas the presence of 2 equiv of KCN results into 68% isolated product yield, a further increase to 3 equiv only marginally improves the isolation of a higher amount of **2.2a** (72%). This suggests that at least two equiv of KCN are needed to achieve the best possible yield of the β-cyano ketone product. Next, the influence of steric bulk at the vinyl cyclic carbonate α-carbon was examined through the use of mono- and di-methyl substituted substrates **2.1u** and **2.1v** (Scheme 2.5b). In both cases, there was neither conversion of the substrate nor formation of the targeted β-cyano ketone products **2.2u** and **2.2v**, respectively. This indicates that the steric crowding at the α-carbon plays a key role in the overall manifold leading to the cyanated ketone **2.2a**. To rule out that the 1,2-diol **3** (Table 1) is involved as an intermediate towards **2.2a**, it was subjected to the optimized reaction conditions, but no conversion into β-cyano ketone was noted (Scheme 2.5c). We then decided to follow the reaction by $^{13}C$ NMR to track possible intermediates (Scheme 2.5d and Figure 2.2).




**Scheme 2.5** Mechanistic control experiments.

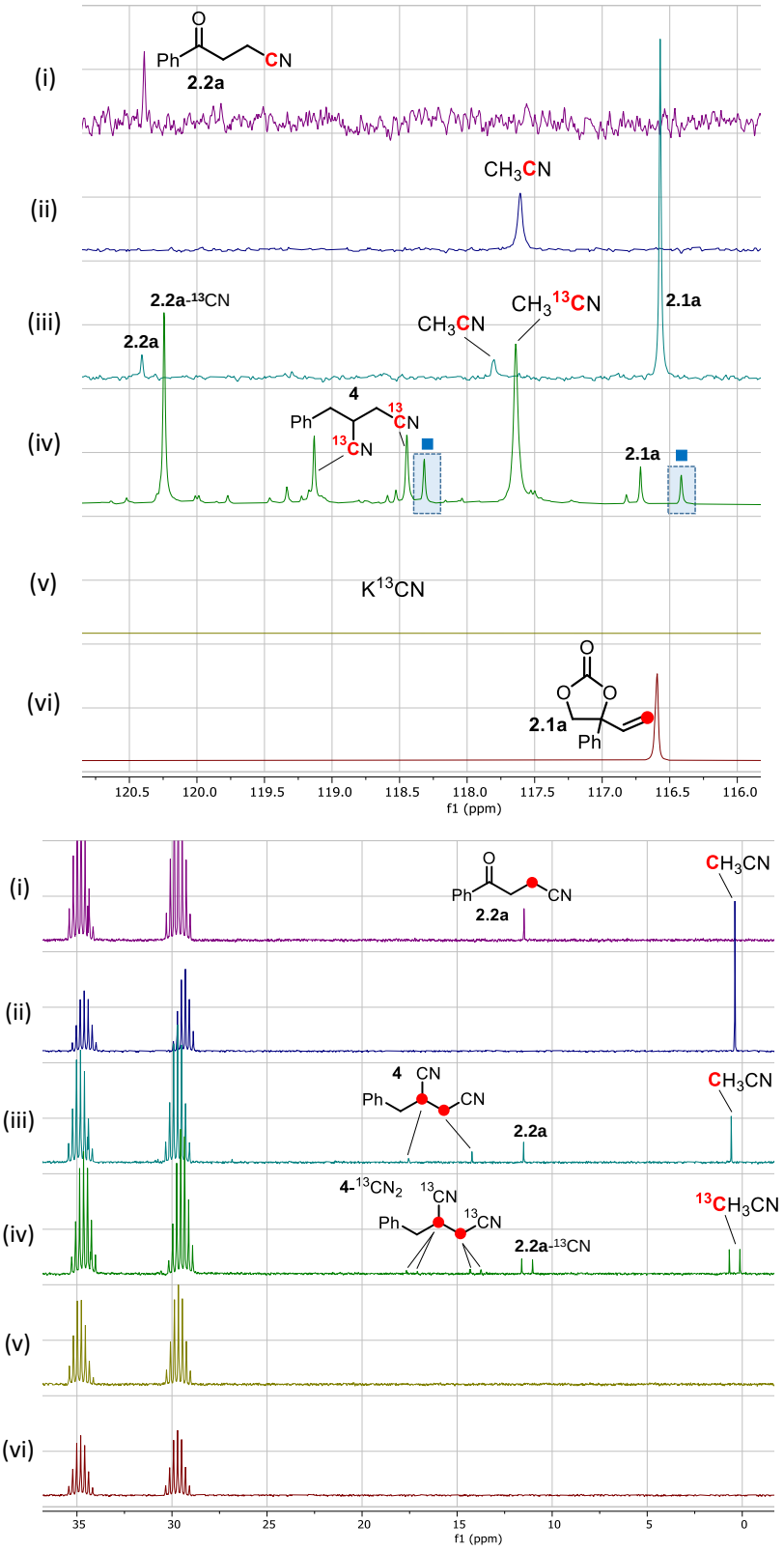
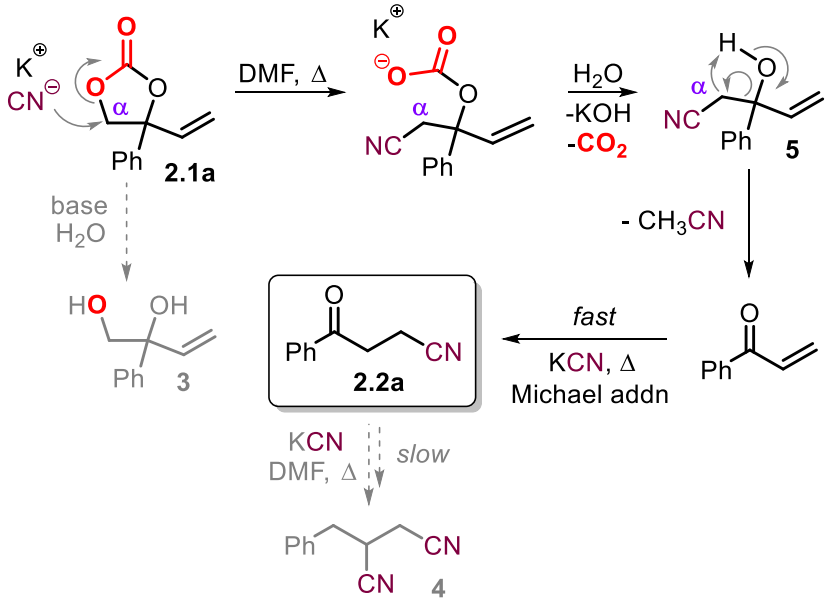



**Figure 2.2** Top: selected region (116-120 ppm) of the $^{13}C$ NMR spectra recorded in DMF-$d_7$ for: (i) β-Cyano ketone product **2.2a**. (ii) An authentic sample of $CH_3CN$. (iii) NMR reaction mixture subjected to the optimized conditions. (iv) As for (iii) but using $K^{13}CN$ as reagent. (v) Reference spectrum for $K^{13}CN$. (vi) Vinyl cyclic carbonate **2.1a**. Below: the same comparative showing the region 0-35 ppm. In red, the carbon centers highlighted for identification.

Interestingly, when using the standard conditions, we observed a steady increase in the amount of acetonitrile ($CH_3CN$) in the reaction mixture (cf., Figure 2.2-ii versus -iii). To further probe the formation of this CN-based byproduct, the same reaction was performed with $^{13}$C-labelled KCN (Scheme 2.5d, and Figure 2.2-iv). This latter experiment provided significant further insight as the formation of labelled product (**2.2a**-$^{13}$CN) and acetonitrile ($CH_3{}^{13}CN$) was clearly noted. Beside the presence of these labelled species, also the presence of the bis-cyanated byproduct **4** (Table 2.1) could be easily substantiated by comparison with literature NMR data.[50] The introduction of $^{13}$C-labelled CN fragments also leaves diagnostic peaks in the aliphatic regions as clear $^1J(^{13}CH_n$-$^{13}CN)$ couplings ($n$ = 2 or 3; $^1J_{C,C}$ = 56-57 Hz) are observed that are very similar to the ones reported before.[51] A last though important indication are the peaks that are highlighted in the blue-colored regions in Figure 2.2-iv. The resonance around 118.4 ppm can be reasonably attributed to a CN fragment whereas the peak near 116.5 seems to suggest the presence of a vinylic carbon (cf., Figure 2.2-vi).




**Scheme 2.6** Proposed formation of **2.2a** from **2.1a** in the presence of KCN.

Combining all observations, control reactions and spectral data, we propose a plausible mechanism for the formation of the β-cyano ketone **2.2a** (Scheme 2.6).

[50] B. Giese, Gebhard Thoma, *Helv. Chim. Acta* **1991**, *74*, 1135-1142.
[51] G. A. Gray, G. E. Maciel, P. D. Ellis, *J. Magn. Res*. **1969**, *1*, 407-417.

In this scenario, the first step is the attack of cyanide on the α-carbon of the vinyl cyclic carbonate **2.1a**. As a result, the carbonate ring is opened enabling first an irreversible decarboxylation (at 100 ºC) and likely producing the intermediate **5** ($\delta_C$ ~ 118.5 and 116.5 ppm). This latter species at elevated temperature provides an α, β-unsaturated ketone by extrusion of acetonitrile (as observed). The unsaturated ketone then undergoes fast Michael addition giving rise to the β-cyano ketone product **2.2a**. Whereas the 1,2-diol **3** can be reasonably explained by carbonate hydrolysis in the reaction mixture, the formation of the bis-cyanated product **4** is believed to be produced slowly from **2.2a**. A control reaction using isolated **2.2a** and 3 equiv of KCN at 100 ºC indeed showed after 23 h the formation of small, though significant amounts of **4** (12%) in line with this hypothesis.

## 2.3 Conclusions

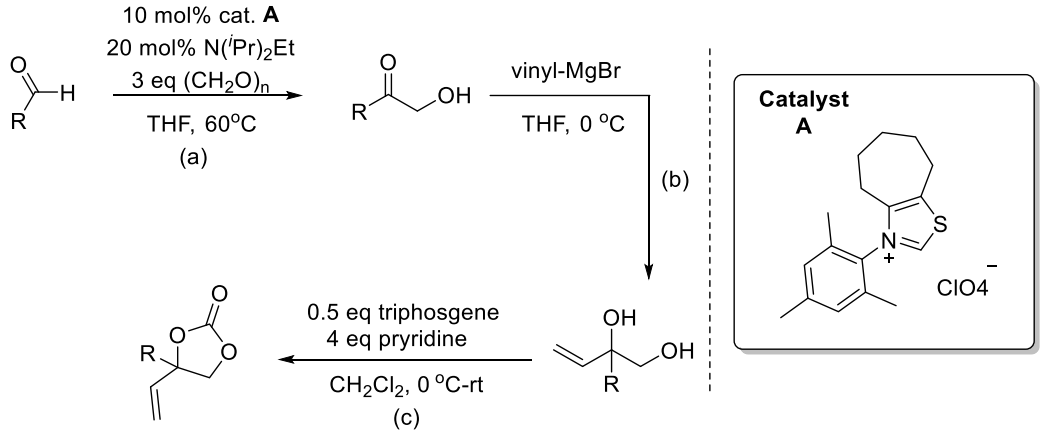
Summarizing, we here present an unprecedented ring-opening reaction of vinyl-substituted cyclic carbonates that involves a rare sequence of decarboxylation/acetonitrile extrusion/Michael addition, affording β-cyano ketones up to moderately high yield. This protocol thus marks a newly discovered reactivity paradigm for cyclic carbonates with nucleophilic attack on the methylenic carbon of the heterocycle of key importance. Studies are underway to further unlock this reactivity potential in the creation of fine chemical intermediates.

# 2.4 Experimental section

## 2.4.1 General information

Potassium cyanide (≥98.0%) was purchased from Sigma Aldrich and was stored in an $N_2$-filled glovebox. The carbonate was prepared according to a reported procedure1 and 2. Solvents were dried using an Innovative Technology PURE SOLV solvent purification system. Air and water-sensitive reactions were carried out in heat-gun-dried glassware under an Ar or $N_2$ atmosphere using standard Schlenk manifold techniques. Reactions were monitored by TLC and $^1$H NMR. TLC was carried out on 0.25 mm Merck aluminum-backed sheets coated with 60 F254 silica gel. Visualization of the silica plates was achieved using a UV lamp (λ = 254 nm) and/or by heating plates that were dipped in a ceric ammonium molybdate stain. Flash chromatography was carried out on Sigma-Aldrich silica gel 60 (70-230 mesh) using the indicated eluent system.$^1$H NMR, $^{13}$C NMR spectra were recorded at room temperature on a Bruker AV-400 spectrometer and referenced to the residual deuterated solvent signals. All reported NMR values are given in parts per million (ppm). FT-IR spectra were collected using a Bruker Optics FTIR Alpha spectrometer. Mass spectrometric analyses (including the HRMS measurements), and X-ray diffraction studies were performed by the Research Support Area (RSA) at ICIQ.

## 2.4.2 General procedure for the preparation of vinyl cyclic carbonates[52]



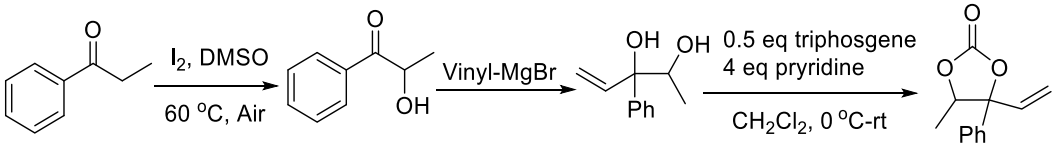

[52] A. Khan, R. Zheng, Y. Kan, J. Ye, J. Xing, Y. J. Zhang, *Angew. Chem. Int. Ed.* **2014**, *53*, 6439.

**Step (a)**: In an oven-dried Schlenk-flask sealed with a rubber septum and equipped with a magnetic stirring bar, thiazolium salt **A** (0.1 mmol, 0.1 equiv), paraformaldehyde (3.0 mmol, 3.0 equiv) and the aldehyde (1.0 mmol, 1.0 equiv) were suspended in dry THF (4 mL). N(*i*-Pr)$_2$Et (0.2 mmol, 0.2 equiv) was added and the resulting mixture was heated to 60 °C. In the case of aliphatic aldehydes, the aldehyde was added after stirring the other reactants for 5 min at room temperature. After a reaction time of 24 h, the solvent was evaporated and the crude product was purified by flash chromatography.

**Step (b)**: To a solution of the respective hydroxy methyl ketone (5 mmol, 1 equiv) in THF (20 mL) was added vinyl magnesium bromide (1.0 M in THF, 2.5 equiv) at 0 °C. The reaction was stirred under an $N_2$ atmosphere at room temperature for 2 h. The reaction mixture was then quenched with saturated aqueous $NH_4Cl$, and extracted with EtOAc. The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered and concentrated affording the crude product which was directly used in step (c).

**Step (c)**: To a solution of diol (5 mmol, 1 equiv) and pyridine (20 mmol, 4 equiv) in $CH_2Cl_2$ (20 mL) was added triphosgene (2.5 mmol, 0.5 equiv, 1.0 M in $CH_2Cl_2$) at 0 °C. The reaction was stirred under an $N_2$ atmosphere at room temperature for 2 h. The reaction mixture was then quenched with saturated aqueous $NH_4Cl$, and extracted with $CH_2Cl_2$. The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered and concentrated. The residue was purified by flash chromatography on silica to afford the corresponding carbonate.

## 2.4.3 Procedure for the preparation of other vinyl cyclic carbonates[53]

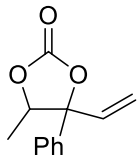



This vinyl carbonate was prepared according to a reported procedure: Propiophenone (1.34 g, 10 mmol), $I_2$ (508 mg, 20 mol%), and DMSO (20 mL) and a stirring bar were added to a round-bottom flask under air. The mixture was stirred at 60 °C for 24 h and monitored by TLC. After cooling down to room temperature, the mixture was diluted with ethyl acetate (10 mL) and washed with 0.1 mol/L $Na_2S_2O_3$ (5 mL) aqueous solution, extracted with ethyl acetate (3 × 100 mL), and evaporated under vacuum. The crude reaction mixture was purified by column chromatography on silica gel (eluent: petroleum

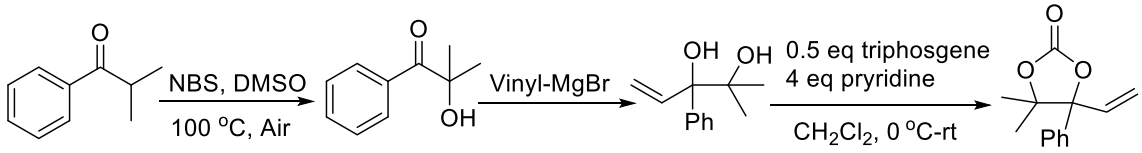
[53] Y. F. Liang, K. Wu, S. Song, X. Y. Li, X. Q. Huang, N. Jiao, *Org. Lett.* **2015**, 17, 876.

ether / ethyl acetate = 20:1 v/v) to get the desired 2-hydroxypropiophenone. The next synthetic step is the same as reported above general procedure for the preparation of vinyl cyclic carbonates.

**4-oxo-4-phenylbutanenitrile (2.1u)**

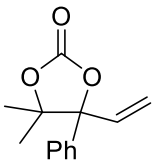


20:1 mixture of diastereoisomers, **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.46-7.37 (m, 3H), 7.35-7.32 (m, 2H), 6.31-6.24 (m, 2H), 5.57-5.43 (m, 2H), 4.98-4.93 (m, 1H), 1.05-1.02 (m, 3H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 153.84, 136.81, 135.86, 128.69, 128.61, 125.45, 116.80, 116.77, 87.75, 80.83, 80.81, 17.23 ppm.




This vinyl carbonate was prepared according to a reported procedure: Isobutyrophenone (1.48 g, 10 mmol), NBS (356 mg, 20 mol%), and DMSO (20 mL) and a stirring bar were added to a round-bottom flask under air. The mixture was stirred at 100 °C for 24 h and monitored by TLC. After cooling down to room temperature, the solution was diluted with ethyl acetate (10 mL) and washed with water (5 mL), extracted with ethyl acetate (3 × 5 mL), and evaporated under vacuum. The crude reaction mixture was purified by column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 20:1 v/v) to get the desired product. The next synthetic step is the same as reported above general procedure for the preparation of vinyl cyclic carbonates**.**

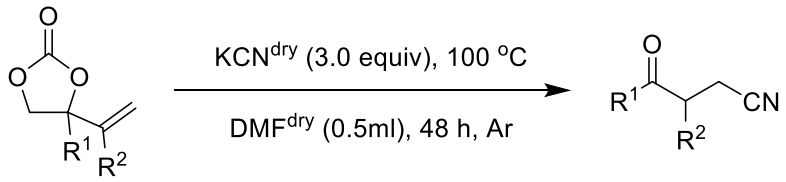
**4-oxo-4-phenylbutanenitrile (2.1v)**[54]



**$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.44-7.33 (m, 5H), 6.33-6.26 (m, 1H), 5.50-5.34 (m, 2H), 1.63 (s, 3H), 1.06 (s, 3H) ppm;**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 153.31, 136.60, 135.09, 128.77, 128.39, 124.51, 116.35, 89.66, 87.75, 24.99, 23.01 ppm.

[54] Y. Mao, X. Zhai, A. Khan, J. Cheng, X. Wu, Y.-J. Zhang, *Tetrahedron Lett.* **2016**, *57*, 3268-3271.

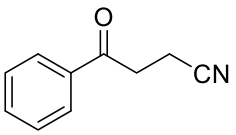
## 2.4.4 Typical procedure for the preparation of the β-cyano ketones




In an $N_2$-filled glovebox, to a Schlenk tube equipped with a magnetic stirring bar, the respective vinyl carbonate (0.2 mmol, 1.0 equiv), KCN (0.6 mmol, 3.0 equiv), and dry DMF (0.5 mL) were added. The resulting mixture was stirred at 100 ºC for 48 h, and then the reaction mixture was cooled to room temperature, the product extracted with EtOAc, and the organic phase washed with $H_2O$ (3 times to remove DMF). The organic phase was dried with $Na_2SO_4$, filtered, and concentrated, after which the product was purified by flash column chromatography on silica gel (eluent hexane/ethyl acetate, Hex/EA) to afford the pure β-cyano ketone product.

## 2.4.5 Characterization data for all compounds

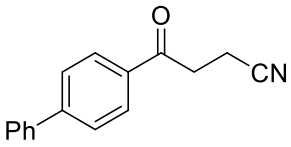
**4-oxo-4-phenylbutanenitrile (2.2a)**




Data comparable to the literature.[55] The product was isolated as a white solid. Yield: 72%; **$^1$H NMR** (400 MHz, CDCl3): δ = 8.00-7.97 (m, 2H), 7.66-7.62 (m, 1H), 7.54-7.50 (m, 2H), 3.41 (t, *J* = 8.0 Hz, 2H), 2.80 (t, *J* = 8.0 Hz, 2H) ppm; **$^{13}$C NMR** (125 MHz, CDCl3): δ 195.33, 135.61, 133.92, 128.89, 128.03, 119.22, 34.28, 11.81 ppm.

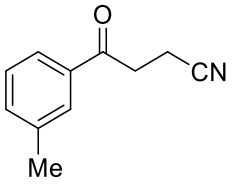
[55] (a) D. Spinnato, B. Schweitzer-Chaput, G. Goti, M. Oseka, P. Melchiorre, *Angew. Chem. Int. Ed*. **2020**, *59*, 9485; (b) S. L. Berrell, J. R. Donald, *Chem. Sci.* **2019**, *10*, 5832. (c) A. Y. Xia, X. Xie, H. Y. Chen, J. D. Zhao, C. L. Zhang, Y. H. Liu, *Org. Lett.* **2018**, *20*, 7735; (d) W. P. Mai, Y. Liu, H. D. Sui, Y. M. Xiao, P. Mao, K. Lu, *Eur. J. Org. Chem.* **2019**, 7814; (e) Y. Li, J. Q. Shang, X. X. Wang, W. J. Xia, T. Yang, Y. C. Xin, Y. M. Li, *Org. Lett.* **2019**, *21*, 2227; (f) P. Cheng, W. Wang, L. Wang, J. G. Zeng, O. Reiser, Y. Liang, *Tetrahedron Lett.* **2019**, *60*, 1408.

**4-([1,1'-biphenyl]-4-yl)-4-oxobutanenitrile (2.2b)**



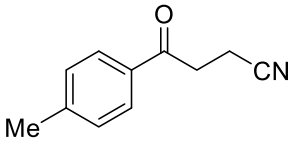
Data comparable to the literature.[55f,56] The product was isolated as a white solid. Yield: 80%. **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.96-7.93 (m, 2H), 7.65-7.62 (m, 2H), 7.57-7.54 (m, 2H), 7.43-7.38 (m, 1H), 7.36-7.32 (m, 1H), 3.33 (t, *J* = 8.0 Hz, 2H), 2.72 (t, *J* = 8.0 Hz, 2H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 194.93, 146.60, 139.56, 134.29, 129.05, 128.65, 128.50, 127.48, 127.29, 119.27, 34.31, 11.86 ppm.

**4-oxo-4-(*m*-tolyl)butanenitrile (2.2c)**



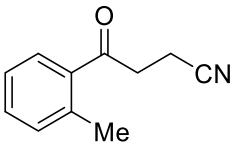
Data comparable to the literature.[55e] The product was isolated as a white solid. Yield: 76%. **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.79-7.75 (m, 2H), 7.46-7.38 (m, 2H), 3.39 (t, *J* = 8.0 Hz, 2H), 2.78 (t, *J* = 8.0 Hz, 2H), 2.44 (s, 3H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 195.56, 138.77, 135.66, 134.68, 128.75, 128.55, 125.25, 119.29, 34.31, 21.35, 11.82 ppm.

**4-oxo-4-(*p*-tolyl)butanenitrile (2.2d)**



Data comparable to the literature.[55e+f,56] The product was isolated as a white solid. Yield: 75%. **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.89-7.86 (m, 2H), 7.32-7.30 (m, 2H), 3.37 (t, *J* = 8.0 Hz, 2H), 2.78 (t, *J* = 8.0 Hz, 2H), 2.45 (s, 3H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 194.93, 144.90, 133.19, 129.56, 128.14, 119.32, 34.14, 21.73, 11.82 ppm.

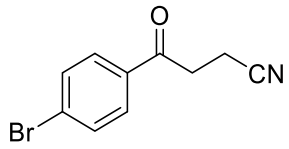
**4-oxo-4-(*o*-tolyl)butanenitrile (2.2e)**



Data comparable to the literature.[55d+e,56] The product was isolated as a yellowish oil. Yield: 45%. **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.72-7.70 (m, 1H), 7.48-7.44 (m, 1H), 7.35-7.28 (m, 2H), 3.34 (t, *J* = 8.0 Hz, 2H), 2.78 (t, *J* = 8.0 Hz, 2H), 2.57 (s, 3H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 198.39, 139.25, 135.73, 132.45, 132.33, 128.79, 125.97, 119.23, 36.48, 21.71, 12.03 ppm.

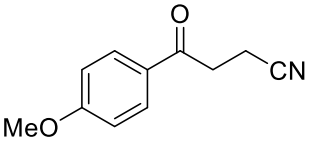
[56] L. J. Qi, R. H. Li, X. R. Yao, Q. Q. Zhen, P. Q. Ye, Y. L. Shao, J. X. Chen, *J. Org. Chem.* **2020**, *85*, 1097.

**4-(4-bromophenyl)-4-oxobutanenitrile (2.2f)**



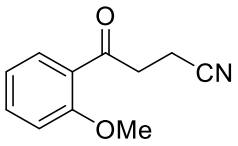

Data comparable to the literature.[55a+e] The product was isolated as a white solid. Yield: 63%; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.86-7.83 (m, 2H), 7.69-7.65 (m, 2H), 3.37 (t, *J* = 8.0 Hz, 2H), 2.80 (t, *J* = 8.0 Hz, 2H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 194.33, 134.31, 132.27, 129.50, 129.26, 118.99, 34.26, 11.77 ppm.

**4-(4-methoxyphenyl)-4-oxobutanenitrile (2.2g)**



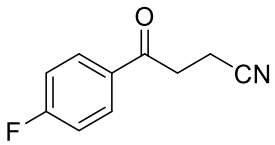

Data comparable to the literature.[55a,d,e,f] The product was isolated as a white solid. Yield: 70%; The product is a mixture of two compounds with ratio of 8:1; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.92-7.89 (m, 2H), 6.95-6.92 (m, 2H), 3.86 (s, 3H), 3.30 (t, *J* = 8.0 Hz, 2H), 2.73 (t, *J* = 8.0 Hz, 2H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 194.17, 164.45, 130.71, 129.10, 119.77, 114.39, 55.92, 34.23, 12.22 ppm.

**4-(2-methoxyphenyl)-4-oxobutanenitrile (2.2h)**



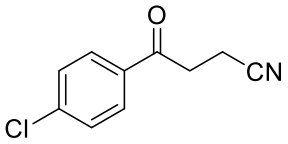

Data comparable to the literature.[55e+f] The product was isolated as a light yellow oil. Yield: 35%. **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.87-7.85 (dd, *J* = 8.0 Hz, 1H), 7.57-7.52 (m, 1H), 7.08-7.01 (m, 2H), 3.97 (s, 3H), 3.43 (t, *J* = 8.0 Hz, 2H), 2.75 (t, *J* = 8.0 Hz, 2H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 196.75, 159.26, 134.68, 130.87, 126.06, 120.91, 119.71, 111.68, 55.57, 39.45, 12.11 ppm.

**4-(4-fluorophenyl)-4-oxobutanenitrile (2.2j)**



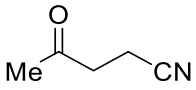

Data comparable to the literature.[55d-f,56] The product was isolated as a white solid. Yield: 66%. **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 8.04-7.99 (m, 2H), 7.22-7.18 (m, 2H), 3.38 (t, *J* = 8.0 Hz, 2H), 2.80 (t, *J* = 8.0 Hz, 2H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 193.70, 166.20 (d, *J* = 256.5 Hz), 130.74 (d, *J* = 9.1 Hz), 119.05, 115.90 (d, *J* = 22.2 Hz), 34.21, 11.81 ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -103.17 ppm.

**4-(4-chlorophenyl)-4-oxobutanenitrile (2.2k)**



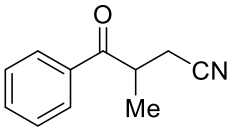
Data comparable to the literature.[55d-f] The product was isolated as a white solid. Yield: 50%; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.94-7.90 (m, 2H), 7.52-7.48 (m, 2H), 3.38 (t, *J* = 8.0 Hz, 2H), 2.80 (t, *J* = 8.0 Hz, 2H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 194.13, 140.51, 133.92, 129.42, 129.26, 119.00, 34.28, 11.78 ppm.

**4-oxopentanenitrile (2.2l)**



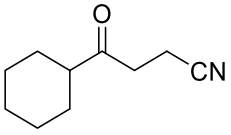
Data comparable to the literature.[55d-f] The product was isolated as a white solid. Yield: 25%; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 2.81 (t, *J* = 8.0 Hz, 2H), 2.54 (t, *J* = 8.0 Hz, 2H), 2.18 (s, 3H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 204.04, 119.10, 38.49, 29.48, 11.32 ppm.

**3-methyl-4-oxo-4-phenylbutanenitrile (2.2m)**



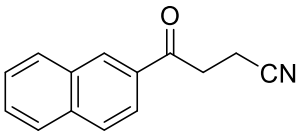
Data comparable to the literature.[55a] The product was isolated as a white solid. Yield: 30%; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.99-7.96 (m, 2H), 7.67-7.62 (m, 1H), 7.56-7.51 (m, 2H), 3.88-3.79 (m, 1H), 2.80-2.62 (m, 2H), 1.44-1.43 (d, *J* = 4.0 Hz, 3H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 199.89, 134.73, 133.80, 128.97, 128.48, 118.58, 38.10, 20.39, 18.09 ppm.

**4-cyclohexyl-4-oxobutanenitrile (2.2n)**



Data comparable to the literature.[57] The product was isolated as a colorless oil. Yield: 51%; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 2.84 (t, *J* = 8.0 Hz, 2H), 2.58 (t, *J* = 8.0 Hz, 2H), 2.42-2.34 (m, 1H), 1.90-1.78 (m, 4H), 1.73-1.66 (m, 1H), 1.42-1.19 (m, 5H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 209.29, 119.21, 50.45, 35.74, 28.36, 25.68, 25.48, 11.46 ppm.

**4-(naphthalen-2-yl)-4-oxobutanenitrile (2.2o)**

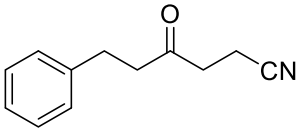


Data comparable to the literature.[55f,58] The product was isolated as a white solid. Yield: 69%; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.50-8.49 (m, 1H), 8.05-7.99 (m, 2H), 7.97-7.91 (m, 2H), 7.68-7.59 (m, 2H), 3.55 (t, *J* = 8.0 Hz, 2H), 2.86 (t, *J* = 8.0 Hz, 2H) ppm; **$^{13}$C NMR** (101 MHz,

[57] E. D. P. Beato, D. Mazzarella, M. Balletti, P. Melchiorre, *Chem. Sci*. **2020**, *11*, 6312.
[58] M. Ociepa, Q. Baka, J. Narodowiec, D. Grykoa, *Adv. Synth. Catal.* **2017**, *359*, 3560.

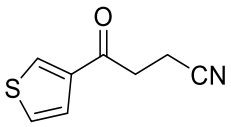
$CDCl_3$) δ 195.24, 135.92, 132.97, 132.44, 129.96, 129.64, 128.97, 128.85, 127.89, 127.12, 123.43, 119.25, 34.36, 11.92 ppm.

**4-oxo-6-phenylhexanenitrile (2.2p)**



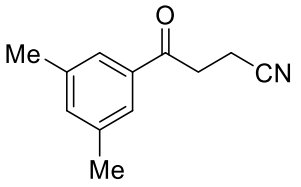
Data comparable to the literature.[59] The product was isolated as a white solid. Yield: 70%; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34-7.28 (m, 3H), 7.21-7.17 (m, 2H), 2.98-2.93 (m, 2H), 2.83-2.79 (m, 2H), 2.78-2.74 (m, 2H), 2.61-2.56 (m, 2H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 205.25, 140.33, 128.65, 128.28, 126.41, 118.92, 43.97, 38.04, 29.67, 11.34 ppm.

**4-oxo-4-(thiophen-3-yl)butanenitrile (2.2q)**



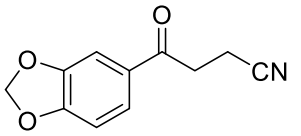
The product was isolated as a white solid. Yield: 25%; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.13-8.12 (m, 1H), 7.59-7.57 (m, 1H), 7.40-7.38 (m, 1H), 3.32 (t, *J* = 8.0 Hz, 2H), 2.78 (t, *J* = 8.0 Hz, 2H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 189.50, 140.83, 132.56, 127.00, 126.62, 119.07, 35.21, 11.64 ppm; **HRMS** (ESI+, MeOH): *m/z* calcd. 188.0140 $(M + Na)^+$, found: 188.0137.

**4-(3,5-dimethylphenyl)-4-oxobutanenitrile (2.2r)**



Data comparable to the literature.[60] The product was isolated as a white solid. Yield: 49%; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.58-7.55 (m, 1H), 7.45-7.44 (d, *J* = 4.0 Hz, 1H), 6.91-6.89 (d, *J* = 8.0 Hz, 1H), 6.09 (s, 2H), 3.32 (t, *J* = 8.0 Hz, 2H), 2.77 (t, *J* = 8.0 Hz, 2H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 193.31, 152.46, 148.46, 130.49, 124.46, 119.27, 108.10, 107.73, 102.08, 34.01, 11.93 ppm.

**4-(benzo[d][1,3]dioxol-5-yl)-4-oxobutanenitrile (2.2s)**



Data comparable to the literature.[61] The product was isolated as a white solid. Yield: 40%; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.58-7.55 (m, 1H), 7.45-7.44 (d, *J* = 4.0 Hz, 1H), 6.91-6.89 (d, *J* = 8.0 Hz, 1H), 6.09 (s, 2H), 3.32 (t, *J* = 8.0 Hz, 2H), 2.77 (t, *J* = 8.0 Hz, 2H) ppm; **$^{13}$C NMR**

[59] J. L. Charlton, H. K. Lai, G. N. Lypka, *Can. J. Chem.* **1980**, *58*, 458.
[60] Q. Zhen, R. Li, L. Qi, K. Hu, X. Yao, Y. Shao, J. Chen, *Org. Chem. Front.* **2020**, *7*, 286.
[61] M. Ociepa, Q. Baka, J. Narodowiec, D. Grykoa, *Adv. Synth. Catal.* **2017**, *359*, 3560.

(101 MHz, $CDCl_3$) δ 193.31, 152.46, 148.46, 130.49, 124.46, 119.27, 108.10, 107.73, 102.08, 34.01, 11.93 ppm.

## 2.4.6 Full $^{13}C$ NMR spectral comparison

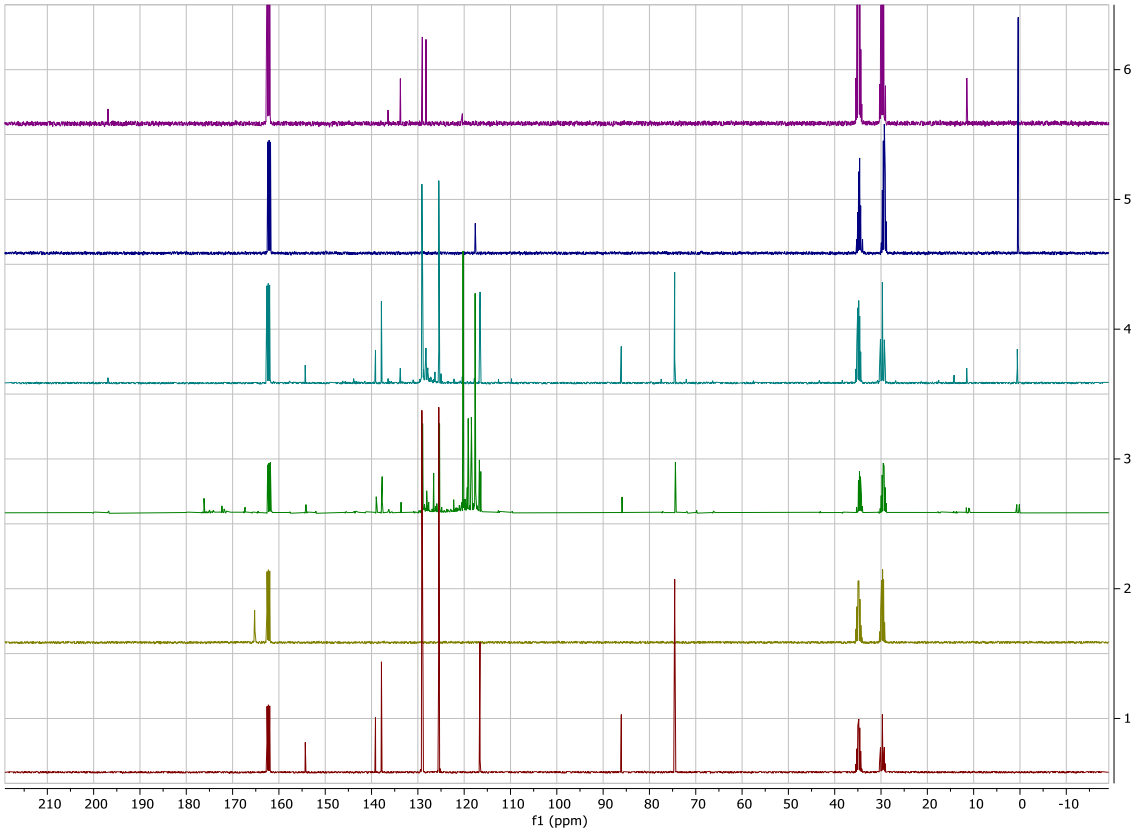



**Figure 2.3** Relates to Figure 2.2 in the main text, all spectra were recorded in DMF-$d_7$ at 100 MHz.

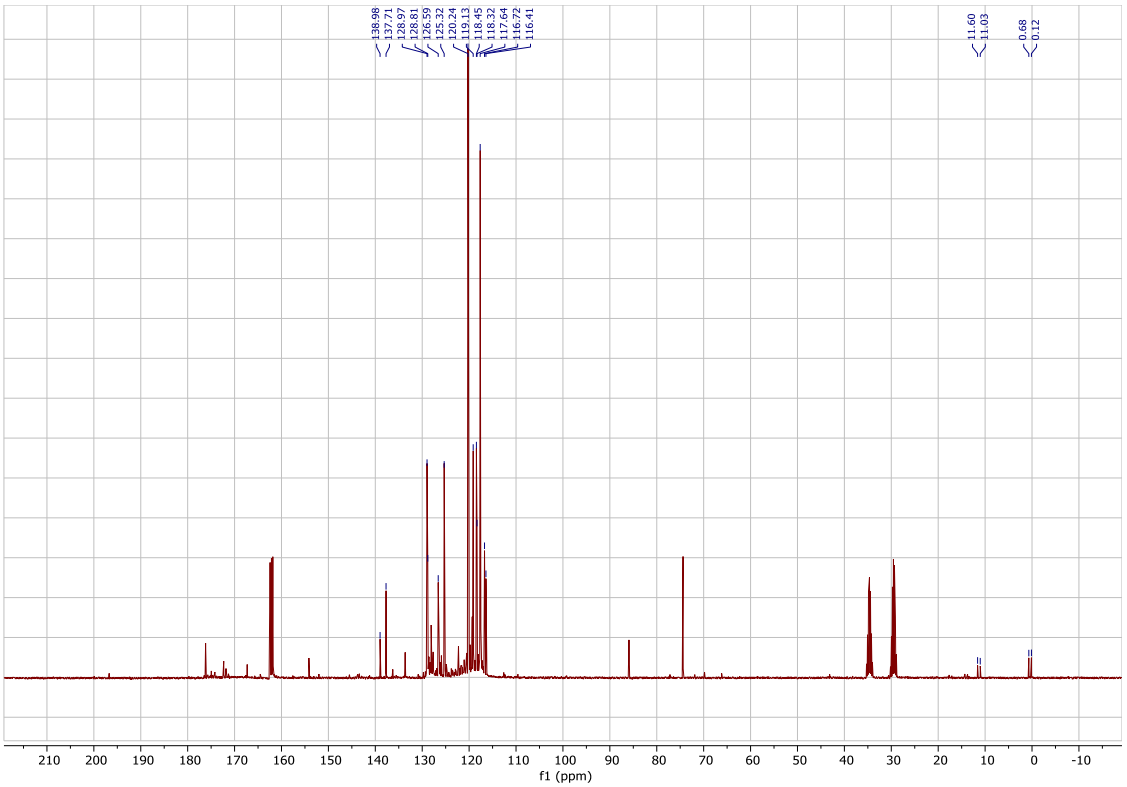
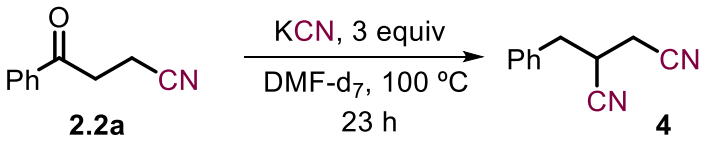



**Figure 2.4** The full spectrum of the reaction mixture after 48 h using $K^{13}CN$ as reagent.

## 2.4.7 Control experiment regarding the formation of byproduct 4




To a solution of 30 mg of **2.2a** (0.19 mmol) in DMF-$d_7$ (0.5 mL) was added KCN (3 molar equiv) and the mixture was kept, while stirring, at 100 ºC under Ar. Then, the mixture was transferred to an NMR tube following $^1$H NMR analysis. The spectrum was compared to the one from isolated and column-purified **2.2a**.

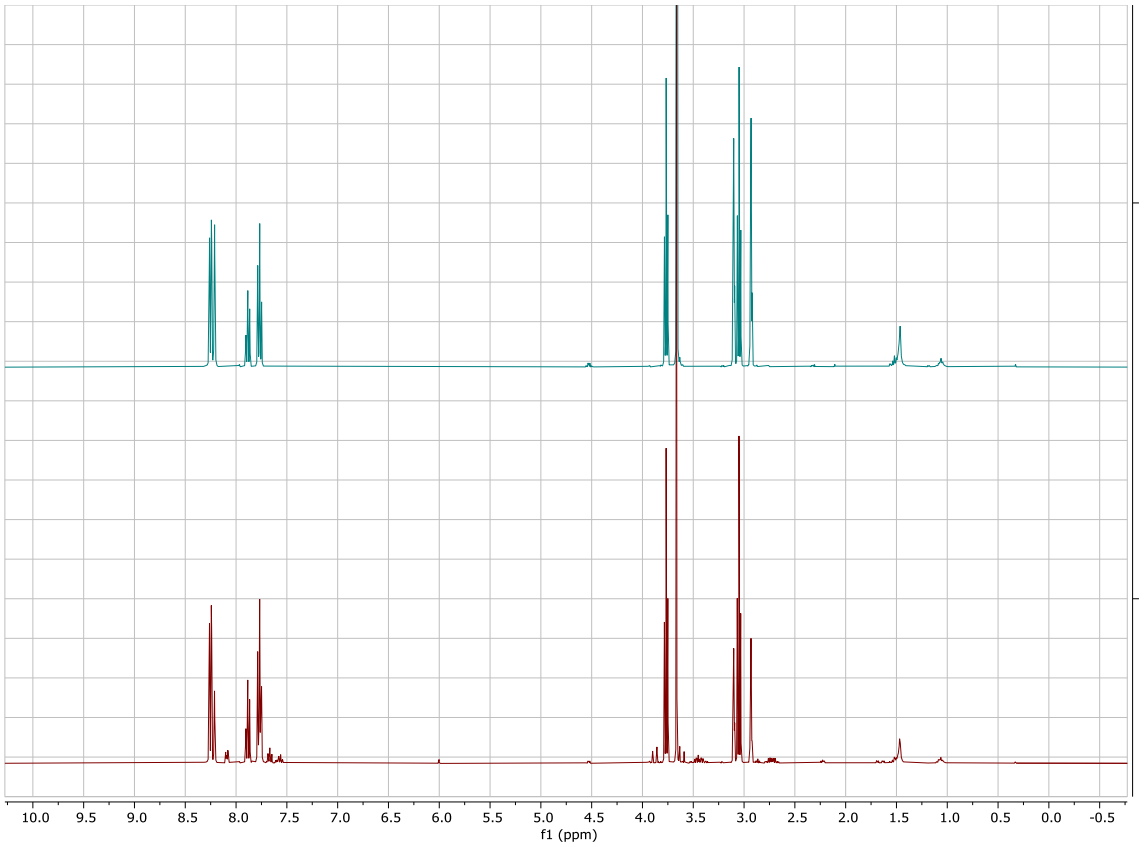
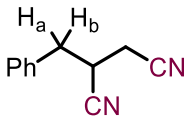


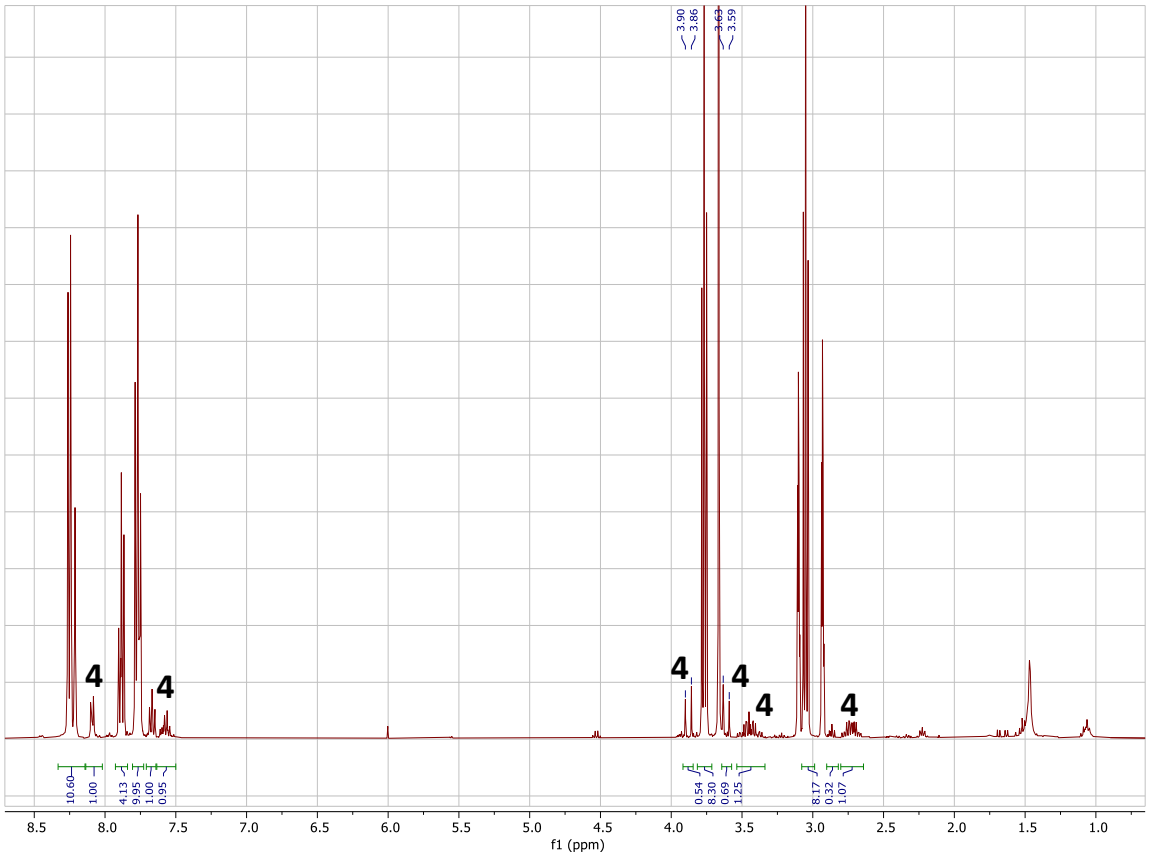

**Figure 2.5** $^{1}$H (DMF-$d_7$) comparison between isolated/pure **2.2a** (top) and post-treated **2.2a** (below) in the presence of KCN.

Note that there are several peaks that emerged during this KCN-treatment, which are ascribed to the formation of byproduct **4**.

Comparative integration (**2.2a** versus **4**) reveals that the ratio between the two compounds after heating for 23 h at 100 ºC is 88:12, meaning that about 12% of **4** is formed under these conditions. A characteristic $^{2}J$ ($H_a$,$H_b$) of around 16 Hz is present in the spectrum below for the benzylic H´s located at 3.88 and 3.61 ppm.

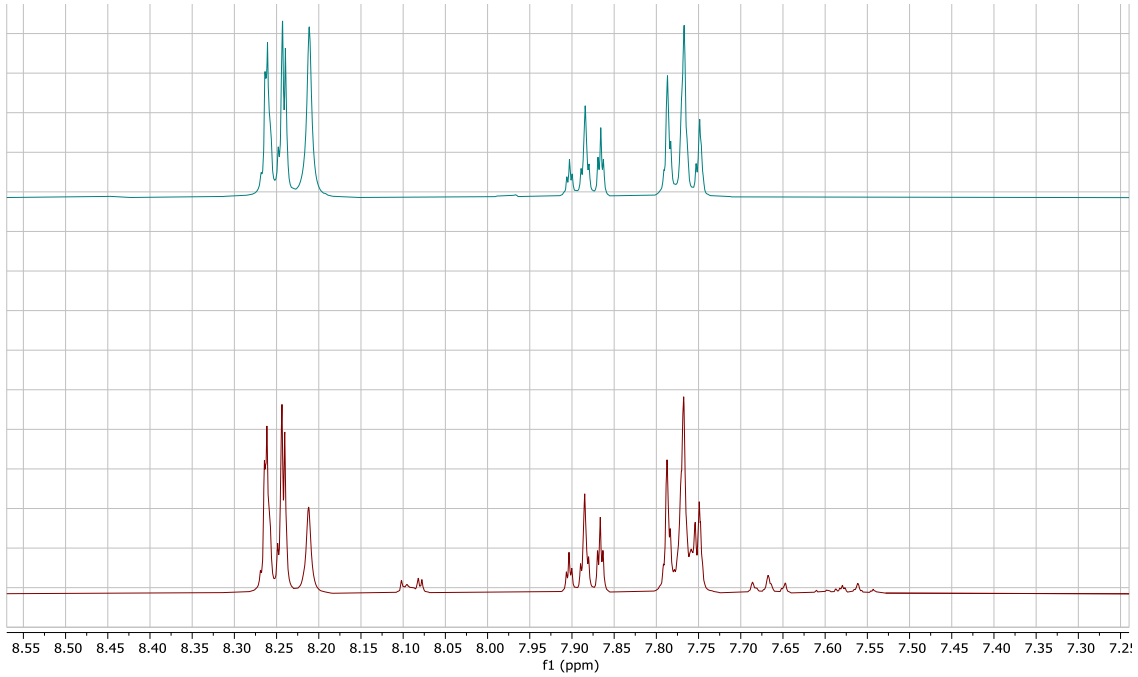


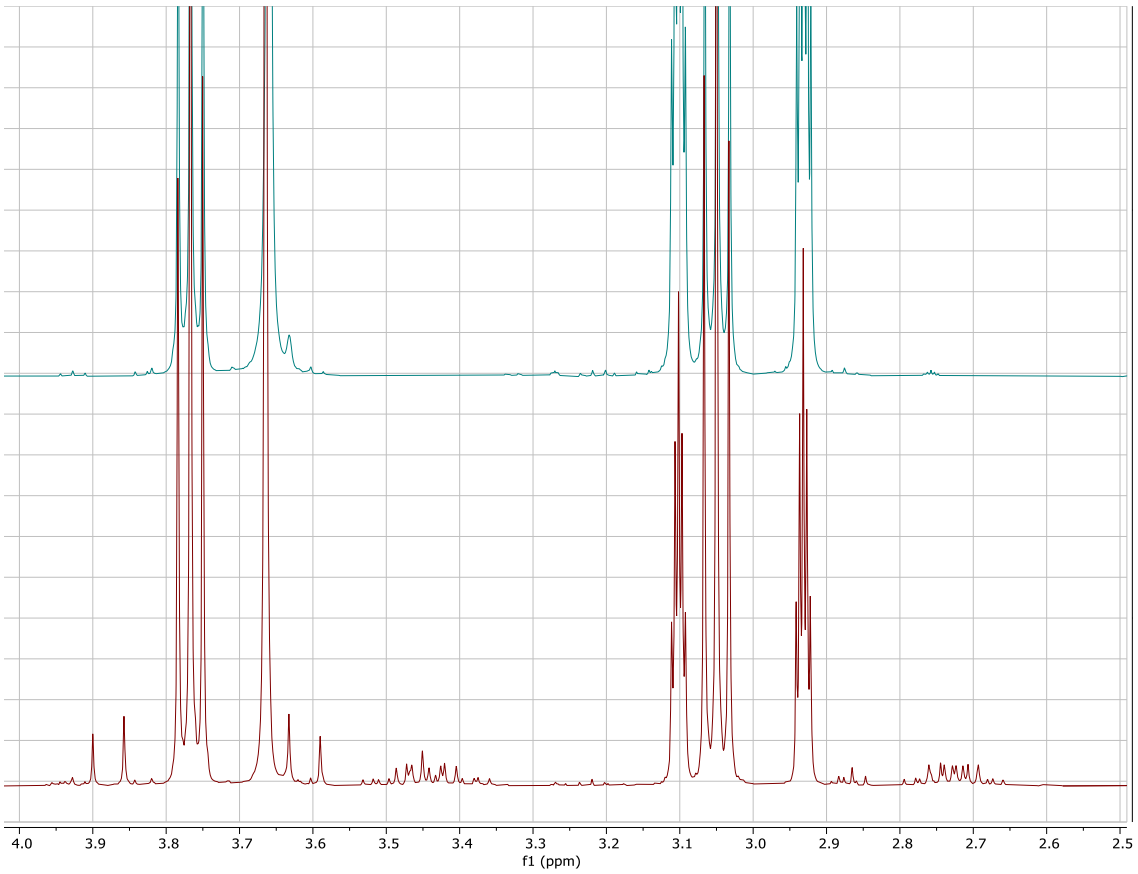

**4**




Note that compound **4** has been reported before, see: B. Giese, G. Thoma, "Dimeric Metal Complexes as Mediators for Radical C-C Bond-Forming Reactions", *Helv. Chim. Acta* **1991**, *74*, 1135-1142.

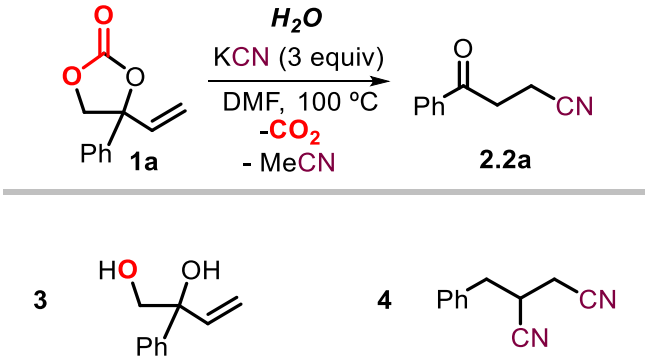
Displayed below are the zoomed areas between 7.2-8.5 ppm and 2.5-4.0 ppm.



## 2.4.8 Influence of amount of water on the yield of 2.2a

The reactions were performed as described in the main text using the optimized protocol while varying the molar amount of water.

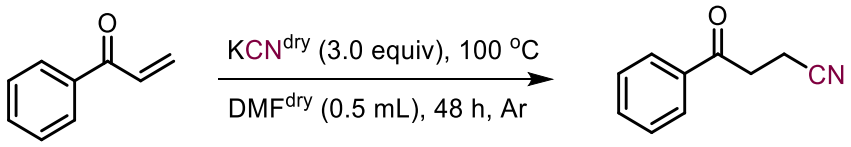



| Entry | [$H_2O$] [mol%] | Conv.[a] [%] | Yield of **2.2a** [%][b] | Yield of **3** [%][b] | Yield of **4** [%][b] |
|---|---|---|---|---|---|
| 1 | 1 | 81% | 64% | 10% | 1% |
| 2 | 10 | 80% | 62% | 11% | 2% |
| 3 | 100 | 80% | 57% | 11% | 1% |
| 4[c] | – | 81% | 64% | 12% | 1% |

[a]Determined by $^1$H NMR ($CDCl_3$) spectroscopy of the crude product. [b]Determined by $^1$H NMR ($CDCl_3$) using mesitylene as internal standard. [c]Dry DMF was used.

## 2.4.9 Control experiment using an α, β-unsaturated ketone as substrate

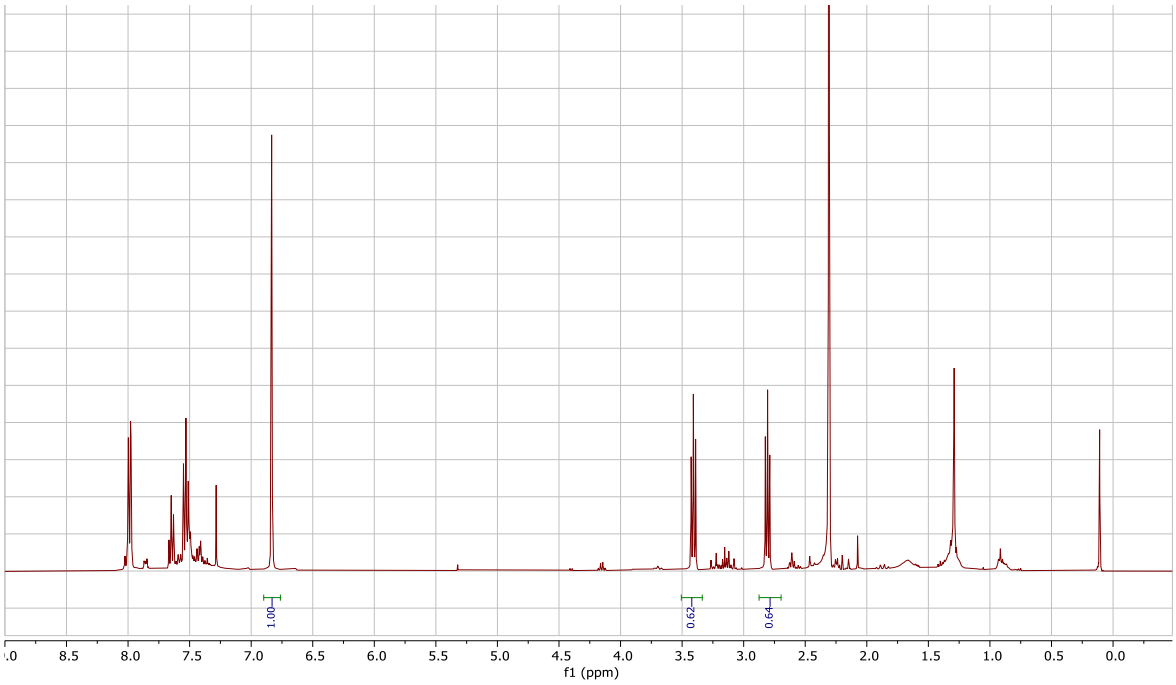
To credit the idea that the formation of product **2.2a** can indeed arise from an α, β-unsaturated ketone intermediate, the following control experiment was carried out (see below).



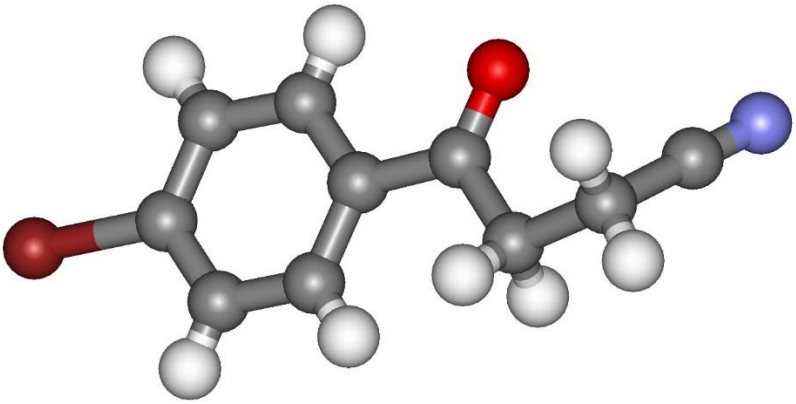

**2.2a**: NMR Yield: 73.4%

In an $N_2$-filled glovebox, to a Schlenk tube equipped with a magnetic stirring bar, the respective α,β-unsaturated ketone (40 mg, 0.30 mmol, 1.0 equiv), KCN (59 mg, 0.90 mmol, 3.0 equiv), and dry DMF (0.5 mL) were added. The resulting mixture was stirred at 100 ºC for 48 h, and then the reaction mixture was cooled to room temperature, the product was extracted with EtOAc, and the organic phase washed with $H_2O$ (3 times to remove DMF). The organic phase was dried with $Na_2SO_4$, filtered, and concentrated, after which to the product was added mesitylene (IS, 28 mg, 0.233 mol) to calculate the NMR yield of the β-cyano ketone product **2.2a**.

The corresponding $^1H$ NMR spectrum ($CDCl_3$) is provided below (IS = 6.8 ppm, 100%, 3H, 0.233 mmol, **2.2a** = 3.48 + 2.82 ppm, 0.63, 2H, 0.220 mmol = 73.4 %).



## 2.4.10 X-ray molecular structure of compound 2.2f



Further details are provided in CCDC-2081268.

**Procedure**: single crystals of **2.2f** suitable for X-ray diffraction were stable under atmospheric conditions; nevertheless, they were treated under inert conditions immersed in perfluoro-polyether as protecting oil for manipulation. Data Collection: measurements were made on a Bruker-Nonius diffractometer equipped with an APPEX II 4K CCD area detector, a FR591 rotating anode with MoKα radiation, Montel mirrors and a Kryoflex low temperature device ($T$ = −173 °C). Full-sphere data collection was used with ω and ϕ scans. Programs used: Data collection Apex2 V2011.3 (Bruker-Nonius 2008), data reduction Saint+Version 7.60A (Bruker AXS 2008) and absorption correction SADABS V. 2008−1 (2008). Structure Solution: SHELXTL Version 6.10 (Sheldrick, 2000) was used (Sheldrick, G. M. SHELXTL Crystallographic System, version 6.10; Bruker AXS, Inc.: Madison, WI, **2000**). Structure Refinement was carried out using SHELXTL-97-UNIX VERSION.

**Crystallographic data for 2.2f**: $C_{10}H_8BrNO$, $Mr$ = 238.08, orthorhombic, $Pca21$, $a$ = 14.6642(17) Å, $b$ = 11.8423(9) Å, $c$ = 5.5080(5) Å, $\alpha$ = 90°, $\beta$ = 90 °, $\gamma$ = 90°, $V$ = 956.52(16) Å$^3$, $Z$ = 4, $\rho$ = 1.653 mg·M$^{-3}$, $\mu$ = 4.254 mm$^{-1}$, $\lambda$ = 0.71073 Å, $T$ = 100(2) K, $F(000)$ = 472, $\theta$(min) = 2.778°, $\theta$(max) = 30.136°, 7851 reflections collected, 2452 reflections unique ($R_{int}$ = 0.0358), GoF = 1.036, $R_1$ = 0.0291, $wR_2$ = 0.0602 [$I$>2σ($I$)], $R_1$ = 0.0413, $wR_2$ = 0.0637 (all indices), min/max residual density = –0.502/0.463 [e·Å$^{-3}$], Completeness to $\theta$(30.136°) = 93.9 %.

*Chapter 2*

# *Chapter 3. Unusual DBU-catalyzed decarboxylative formation of allylic thioethers from vinyl cyclic carbonates and thiols*

The results described in this chapter have been published in:

J. Ni, M. Lanzi, A. W. Kleij, *Org. Chem. Front*. **2022**, *9*, 6780-6785.

UNIVERSITAT ROVIRA I VIRGILI
RING-OPENING OF CYCLIC CARBONATES: FROM FINE CHEMICALS TO CO2-BASED POLYMERS
Jixiang Ni

# 3.1 Introduction

## 3.1.1 Ring-opening of cyclic carbonates through carbonate attack

Organic carbonates represent a major class of compounds that can be derived from carbon dioxide.[62] Typically, five-membered cyclic carbonates are produced from the catalytic (3+2) cycloaddition of $CO_2$ to epoxides and this area of $CO_2$ research has blossomed significantly over the last decade.[63] Their application potential is plural ranging from high-boiling aprotic solvents [64] to polymerizable monomers [65] and fine-chemical intermediates[66]. In the latter two categories of uses, often ring-opening of the cyclic carbonate plays a central role. The well-known and predictable ring-opening of cyclic carbonates at the carbonate carbon (Scheme 3.1) by amine nucleophiles is probably among the most widely studied processes and delivers linear carbamates thereby retaining all the original atoms of the substrate.[67] Nowadays, this kind of transformation has found application in the synthesis of non-isocyanate based polyhydroxy-urethanes (NIPUs)

[62] (a) A.-A. G. Shaikh, S. Sivaram, *Chem. Rev.* **1996**, *96*, 951-976; (b) T. Sakakura, K. Kohno, *Chem. Commun.* **2009**, 1312-1330; (c) B. Schäffner, F. Schäffner, S. P. Verevkin, A. Börner, *Chem. Rev.* **2010**, *110*, 4554-4581; (d) N. Kindermann, T. Jose, A. W. Kleij, *Top. Curr. Chem.* **2017**, *375*, 1-28.

[63] (a) L. Guo, K. Lamb, M. North, *Green. Chem.* **2021**, *23*, 77-118; (b) R. Rajjak Shaikh, S. Pornpraprom, V. D'Elia, *ACS Catal.* **2018**, *8*, 419-450; (c) V. Aomchad, À. Cristòfol, F. Della Monica, B. Limburg, V. D'Elia, A. W. Kleij, *Green Chem.* **2021**, *23*, 1077-1113; (d) A. J. Kamphuis, F. Picchionia, P. P. Pescarmona, *Green Chem.* **2019**, *21*, 406-448.

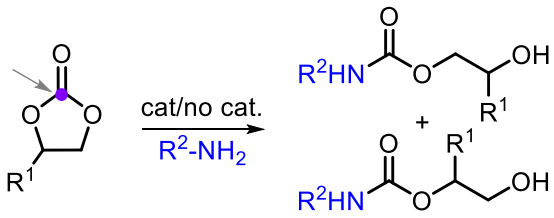
[64] (a) H. L. Parker, J. Sherwood, A. J. Hunt, J. H. Clark, *ACS Sustainable Chem. Eng.*, **2014**, *2*, 1739-1742; (b) M. North, P. Villuendas, *Org. Lett.* **2010**, *12*, 2378-2381. (c) B. Schäffner, F. Schäffner, S. P. Verevkin, A. Börner, *Chem. Rev.* **2010**, *110*, 4554-4581.

[65] (a) C. Qiao, W. Shi, A. Brandolese, J. Benet-Buchholz, E. C. Escudero-Adán, A. W. Kleij, *Angew. Chem. Int. Ed.* **2022**, *61*, e202205053; (b) S. Tempelaar, L. Mespouille, O. Coulembier, P. Dubois, A. P. Dove, *Chem. Soc. Rev.* **2013**, *42*, 1312-1336; (c) J. Matsuo, S. Nakano, F. Sanda, T. Endo, *J. Polym. Sci. A, Polym. Chem.* **1998**, *36*, 2463-2471; (d) W. Zhang, J. Dai, Y.-C. Wu, J.-X. Chen, S.-Y. Shan, Z. Cai, J.-B. Zhu, *ACS Macro Lett.* **2022**, *11*, 173-178; (e) C. Ngassam Tounzoua, B. Grignard, C. Detrembleur, *Angew. Chem. Int. Ed.* **2022**, *61*, e202116066.

[66] (a) W. Guo, J. E. Gómez, À. Cristòfol, J. Xie, A. W. Kleij, *Angew. Chem. Int. Ed*. **2018**, *57*, 13735-13747; (b) L. Zuo, T. Liu, X. Chang, W. Guo *Molecules*, **2019**, *24*, 3930; (c) J. E. Gómez, À. Cristòfol, A. W. Kleij, *Angew. Chem. Int. Ed.* **2019**, *58*, 3903-3907; (d) K. Guo, A. W. Kleij, *Angew. Chem. Int. Ed.* **2021**, *60*, 4901-4906.

[67] (a) W. Guo, V. Laserna, E. Martin, E. C. Escudero-Adán, A. W. Kleij, *Chem. Eur. J.* **2016**, *22*, 1722-1727; (b) M. Blain, L. Jean-Gérard, R. Auvergne, D. Benazet, S. Caillol, B. Andrioletti, *Green Chem.* **2014**, *16*, 4286-4291; (c) W. Guo, J. Gónzalez-Fabra, N. A. G. Bandeira, C. Bo, A. W. Kleij, *Angew. Chem. Int. Ed.* **2015**, *54*, 11686-11690; (d) P. Olsén, M. Oschmann, E. V. Johnston, B. Åkermark, *Green Chem*. **2018**, *20*, 469-475.

providing greener access to these macromolecules.[68] Other nucleophiles, such as alcohols, have also been reported as initiators in the formation of polycarbonates.[69]




**Scheme 3.1** Well-known ring-opening of cyclic carbonates by amines at the carbonate carbon center.

## 3.1.2 Methylene attack in cyclic carbonates

Whereas nucleophilic ring-opening of cyclic carbonates is usually preferred at the electrophilic carbon of the carbonate group, there are fewer examples of "methylene" attack reported in the literature (Scheme 3.2). These processes occur at elevated temperatures with extrusion of $CO_2$, and examples of amine,[70] thiol[71] and cyanide-based nucleophiles (*chapter 2 of this thesis*)[72] have been reported.

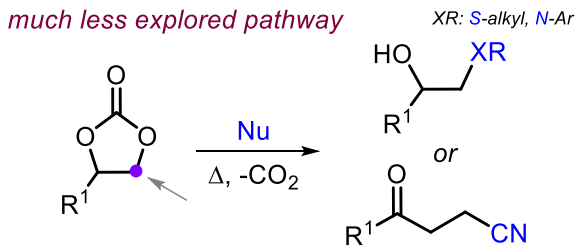
[68] (a) A. Gomez-Lopez, B. Grignard, I. Calvo, C. Detrembleur, H. Sardon, *ACS Appl. Polym. Mater.* **2020**, *2*, 1839-1847; (b) B. Bizet, E. Grau, H. Cramail, J. M. Asua, *Polym. Chem.* **2020**, *11*, 3786-3799; (c) C. Maquilón, A. Brandolese, C. Alter, C. H. Hövelmann, F. Della Monica, A. W. Kleij, *ChemSusChem* **2022**, *15*, e202201123.

[69] (a) J. Matsuo, S. Nakano, F. Sanda, T. Endo, *J. Polym. Sci. A, Polym. Chem.* **1998**, *36*, 2463-2471; (b) S. Gennen, B. Grignard, T. Tassaing, C. Jérôme, C. Detrembleur, *Angew. Chem. Int. Ed.* **2017**, *56*, 10394-10398.

[70] M. Selva, M. Fabris, V. Lucchini, A. Perosa, M. Noè, *Org. Biomol. Chem*, **2010**, *8*, 5187-5198.

[71] (a) F. Monie, B. Grignard, J.-M. Thomassin, R. Mereau, T. Tassaing, C. Jerome, C. Detrembleur, *Angew. Chem. Int. Ed.* **2020**, *59*, 17033-17041; for related chemistry using α-alkylidene carbonates, see: (b) F. Ouhib, B. Grignard, E. van den Broeck, A. Luxen, K. Robeyns, V. van Speybroeck, C. Jerome, C. Detrembleur, *Angew. Chem. Int. Ed*, **2019**, *58*, 11768-11773; (c) F. Ouhib, L. Meabe, A. Mahmoud, B. Grignard, J.-M. Thomassin, F. Boschini, H. Zhu, M. Forsyth, D. Mecerreyes, C. Detrembleur, *ACS Appl. Polym. Mater.* **2020**, *2*, 922-931.

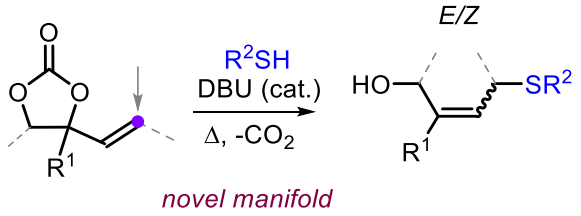
[72] J. Ni, À. Cristòfol, A. W. Kleij, *Org. Chem. Front.* **2021**, *8*, 4520-4526.




**Scheme 3.2** Less explored ring-opening of cyclic carbonates at the "methylene" carbon.

## 3.2 Aims and objectives

Our group has extensively worked on stereoselective transformations of vinyl-functionalized cyclic carbonates (VCCs). These conversions are best described as decarboxylative allylation reactions and a wide scope of nucleophilic partners can be used as reactions partners.[73] Following our interest in the ring-opening of cyclic carbonates and the unique *endo*-cyclic attack of cyanide prior to ring-opening of VCCs, we envisioned that the use of other nucleophiles (i.e., thiols) would offer similar types of reactivity as regioselective, decarboxylative thiolation of the methylene carbon of cyclic carbonates has been reported in the creation of new functional polymers.[10]



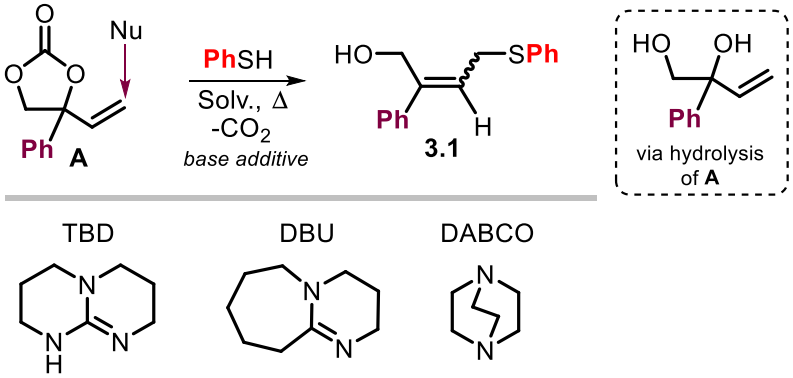

**Scheme 3.3** Unexplored *exo*-cyclic induced ring-opening of VCCs.

However, in the course of our studies we encountered a distinct reactivity behavior of VCCs in the presence of thiols, with the nucleophilic attack occurring at the *exo*-cyclic double bond (Scheme 3.3), affording formally (after loss of $CO_2$) allylic thioethers as products. Here we report on this new transformative process of VCCs into allylic thioethers in the presence of thiols and DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) as organocatalyst together with its mechanistic implications.

[73] For some examples: (a) W. Guo, R. Kuniyil, J. E. Gómez, F. Maseras, A. W. Kleij, *J. Am. Chem. Soc.* **2018**, *140*, 3981-3987; (b) W. Guo, A. Cai, J. Xie, A. W. Kleij, *Angew. Chem. Int. Ed.* **2017**, *56*, 11797-11801.

## 3.3 Results and discussion

**Table 3.1** Screening of the reaction conditions between vinyl cyclic carbonate **A** and thiophenol.[a]




| Entry | Solv. (mL)[b] | T (° C) | PhSH (eq) | Add. (mol%)[b] | Conv. **A** (%)[c] | *E/Z*-**3.1** (%)[c,d] |
|---|---|---|---|---|---|---|
| 1 | $DMF^{0.5}$ | 100 | 3 | – | >99 | 45:55, 60 |
| 2 | $DMF^{0.2}$ | 100 | 1.5 | – | 27 | 34:66, 20 |
| 3 | $DMF^{0.2}$ | 120 | 1.5 | – | 88 | 38:62, 78 |
| 4 | $DMF^{0.2}$ | 120 | 3 | – | >99 | 41:59, 81 |
| 5 | $DMF^{0.2}$ | 50 | 1.5 | $TBD^{40}$ | 90 | 37:63, 63 |
| 6 | $DMF^{0.2}$ | 50 | 1.5 | $TBD^{60}$ | 94 | 39:61, 69 |
| 7 | $DMF^{0.2}$ | 50 | 1.5 | $TBD^{100}$ | >99 | 38:62, 63 |
| 8 | $DMF^{0.2}$ | 25 | 1.5 | $TBD^{100}$ | 64 | 36:64, 33 |
| 9 | $CH_3CN^{0.2}$ | 50 | 1.5 | $TBD^{20}$ | 57 | 38:62, 33 |
| 10 | $CH_3CN^{0.2}$ | 50 | 1.5 | $DBU^{5}$ | 46 | 40:60, 45 |
| 11 | $CH_3CN^{0.2}$ | 50 | 1.5 | $DBU^{10}$ | 82 | 39:61, 69 |
| 12 | $CH_3CN^{0.2}$ | 70 | 1.5 | $DBU^{10}$ | >99 | 38:62, 78 |
| **13** | **$CH_3CN^{0.2}$** | **70** | **1.2** | **$DBU^{10}$** | **97** | **41:59, 81** |
| 14 | $CH_3CN^{0.2}$ | 50 | 1.5 | $DBU^{50}$ | >99 | 46:54, 82 |
| 15 | $CH_3CN^{0.2}$ | 70 | 1.5 | – | 0 | 0 |
| 16 | $CH_3CN^{0.2}$ | 80 | 1.5 | – | 0 | 0 |
| 17 | $CH_3CN^{0.2}$ | 50 | 1.5 | $DABCO^{50}$ | 58 | 38:62, 39 |
| 18 | $CH_3CN^{0.2}$ | 50 | 1.5 | $DMAP^{50}$ | 29 | 44:56, 27 |
| 19 | $CH_3CN^{0.2}$ | 50 | 1.5 | $DIPEA^{50}$ | 40 | 40:60, 30 |
| 20 | $CH_3CN^{0.2}$ | 50 | 1.5 | $TEA^{50}$ | 28 | 40:60, 15 |
| 21 | $CH_3CN^{0.1}$ | 50 | 1.5 | $DBU^{10}$ | 70 | 37:63, 57 |

[a]The reactions were carried out under air using cyclic vinyl-carbonate **A** (0.2 mmol, 1.0 equiv), thiophenol (amount indicated) in 0.20-0.50 mL of solvent at the indicated temperature for 48 h. [b]Amount mentioned in the superscript. [c]Determined by $^1$H NMR ($CDCl_3$) using mesitylene as internal standard. [d]*E/Z* ratio determined by $^1$H NMR. Abbreviations used: DMAP = 4-dimethylamino-pyridine, DIPEA = diisopropylethylamine, TEA = triethyl amine.

As a first approximation, based on the known and preferred regio-attack of thiols on the methylene carbon of cyclic carbonates[10] and our previous experience with aryl amine nucleophiles,[6c] we combined vinyl cyclic carbonate **A** and thiophenol and investigated the influence of the solvent, ratio between both reagents and the reaction temperature on the process outcome (Table 3.1).[74] Under rather demanding conditions (entry 1), full conversion of **A** was accomplished with a major product formed in 60% NMR yield. Detailed inspection of the isolated product by $^1$H NMR spectroscopy revealed the formation of an unexpected product, viz. the allylic thioether **3.1** as a mixture of *E*- and *Z*-isomers.[75] Intrigued by this result, we set out to optimize this process further paying attention to both the yield of **3.1** as well as the reaction conditions and practicality.

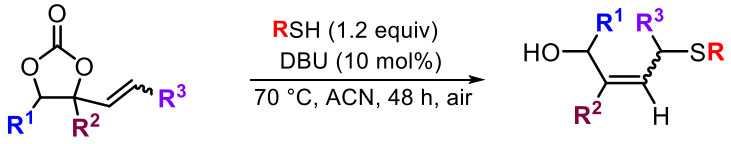
Expectedly, the conversion of **A** into **3.1** depends both on the reaction temperature and relative amount of thiol-to-carbonate (entries 1-4). The best results were first achieved at 120 ºC using 3 equiv of PhSH delivering an 81% NMR yield of **3.1** with the *E/Z* ratio being virtually unaffected (entry 4). Since PhSH itself is a poor, unactivated nucleophile, we envisioned that the presence of a suitable base could help to increase its reactivity (entries 5-8). Indeed, the (sub)stoichiometric addition of TBD (= 1,5,7-triazabicyclo[4.4.0]dec-5-ene) allowed the reaction to be performed adequately at much lower temperatures down to 25 ºC (entry 8) albeit with lower yield of **3.1**. We then chose to replace DMF by greener and more practical $CH_3CN$ (entry 9, at 50 ºC) while using catalytic amounts of TBD (20 mol%). Under these conditions, appreciable conversion of **A** (57%) was noted with a 33% NMR yield of **3.1**. The selectivity for and yield of **3.1** could be further boosted (entries 10-14) by raising the temperature to 70 ºC and changing catalytic TBD for DBU, with entry 13 reporting full conversion of **A** with an 81% NMR yield of **3.1** at 70 ºC and using 10 mol% of base and 1.2 equiv of thiol. Notably, no reaction was noted at 70-80 ºC in the absence of base (entries 15 and 16). Other common bases were also probed (entries 17-20 and table 2) but these proved to be less productive. Finally, a higher concentration of reagents was examined (entries

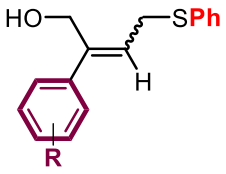
[74] For additional screening results, see the Experimental Section.
[75] NMR Identification of the allylic thioether **3.1** was straightforward by comparison with literature data reported previously, see: J. E. Gómez, W. Guo, A. W. Kleij, *Org. Lett.* **2016**, *18*, 6042-6045.

11 versus 21) but these conditions were less productive with a lower conversion of **A** and yield of **3.1**.

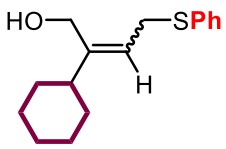
With the optimized conditions reported in entry 12 (Table 3.1), we then set out to investigate the product scope of this transformation (Scheme 3.4, compounds **3.1-3.26**). Apart from the benchmark transformation of **A** delivering the allylic thioether product **3.1** in 78% isolated yield, various other *gem*-vinyl,aryl-substituted cyclic carbonates undergo conversion into their respective allylic thioether products (**3.2-3.11**) with yields varying from 45 to 91%. From the *E/Z* ratios and the differences in yield, there seems to be an apparent substrate and thus thermodynamic control in this manifold driving the stereo-outcome of this conversion. Stereo-electronic modulation seems to control the selectivity towards the target product. Since these reactions are performed under a basic regime, in some of the reactions a significant amount of a 1,2-diol by-product (see insert on the right in Scheme to Table 3.1) was noted. This can be explained by the presence of adventitious $H_2O$ present in the solvent, and under basic conditions this favors hydrolysis of the cyclic carbonate.

In addition, also *gem*-vinyl,alkyl-substituted cyclic carbonates and precursors with larger aromatic or heteroaromatic groups proved to be productive substrates (**3.12-3.16**). Both cycloalkyl (**3.12**) as well as linear alkyl groups (**3.14**) are tolerated in the carbonate reagent. Notably, allylic thioether **3.12** was isolated as a single stereoisomer in 53%, while the chemo-selectivity (and therefore the yield; 90%) for **3.14** was one of the highest among all products. Both thiophenyl-substituted cyclic carbonates showed rather similar behavior in this DBU-promoted process with a similar substrate conversion and yield of product. The scope of allylic thioethers could be further extended by variation of the thiol reagent. Both aryl and alkyl thiols can be utilized as illustrated by the isolation of compounds **3.17-3.23**. *Ortho*-substitution in arylthiols is endorsed (**3.19** versus **3.18**) though with a slightly lower yield of product (72 versus 80%). Synthetically more useful aryl groups (cf., for cross-coupling chemistry) can also be introduced (allylic thioethers **3.22** and **3.23**) with appreciable yields of 82 and 71%, respectively. The introduction of groups in other positions of the carbonate precursors ($R^1$ and $R^3$) was fruitful, giving access to derivatives **3.24** (64%) and **3.25** (63%). Finally, the use of a more complex thiol incorporating a protected α-

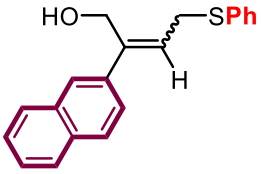


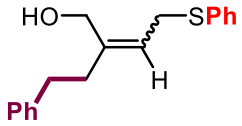
**3.1**: R = H; conv. >99%, *E/Z*: = 4:6, yield 78%
**3.2**: R = *p*-MeO; conv. 86%, *E/Z*: = 4:6; yield 71%
**3.3**: R = *p*-Ph; conv. 79%, *E/Z* = 7:3, yield 47%
**3.4**: R = *m*-Me; conv. >99%, *E/Z* = 1:1, yield 80%
**3.5**: R = *p*-Me; conv. >99%, *E/Z* = 6:4, yield 82%
**3.6**: R = *o*-Me; conv. >99%, *E/Z* = 7:3, yield 91%
**3.7**: R = *p*-F; conv. >99%, *E/Z* = 5:6, yield 67%
**3.8**: R = *p*-Cl; conv. >99%, *E/Z* = 7:3, yield 45%
**3.9**: R = 3,5-di-Me; conv. 94%, *E/Z* = 1:1, yield 55%
**3.10**: R = *p*-*t*Bu; conv. >99%, *E/Z* = 4:6, yield 53%
**3.11**: R = *m*-BnO; conv. >99%, *E/Z* = 7:3, yield 64%



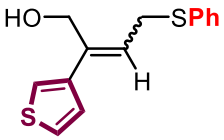
**3.12**: Conv. 65%
*E/Z* = 1:9, yield 53% (*Z*)



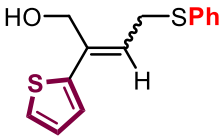
**3.13**: Conv. >99%
*E/Z* = 6:4, yield 51%



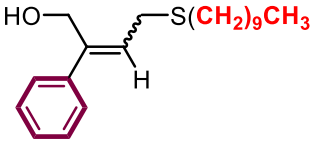
**3.14**: Conv. 99%
*E/Z* = 3:7, yield 90%



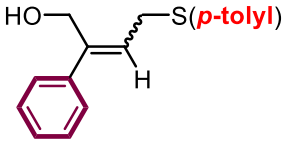
**3.15**:Conv. 97%
*E/Z* = 7:3, yield 56%



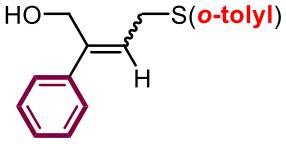
**3.16**: Conv. >99%
*E/Z* = 6:4, yield 60%



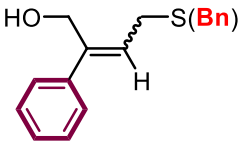
**3.17**: Conv. 31%
*E/Z* = 4:6, yield 16% (*Z*)



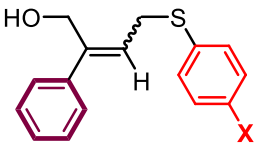
**3.18**: Conv. >99%
*E/Z* = 4:7, yield 80%



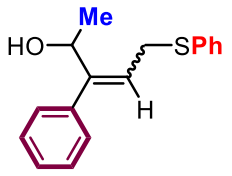
**3.19**: conv. 97%
*E/Z* = 6:4, yield 72%



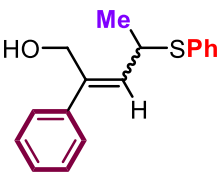
**3.20**: conv. 82%
*E/Z* = 3:7, yield 79%



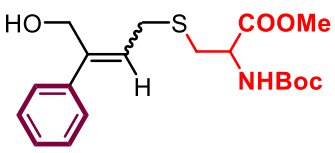
**3.21**: X = OMe, conv. >99%
*E/Z* = 3:7, yield 68%
**3.22**: X = Cl, conv. >99%
*E/Z* = 1:1, yield 82%
**3.23**: X = Br, conv. >97%
*E/Z* = 6:4, yield 71%



**3.24**: conv. 71%
*E/Z* = 9:2, yield 64%



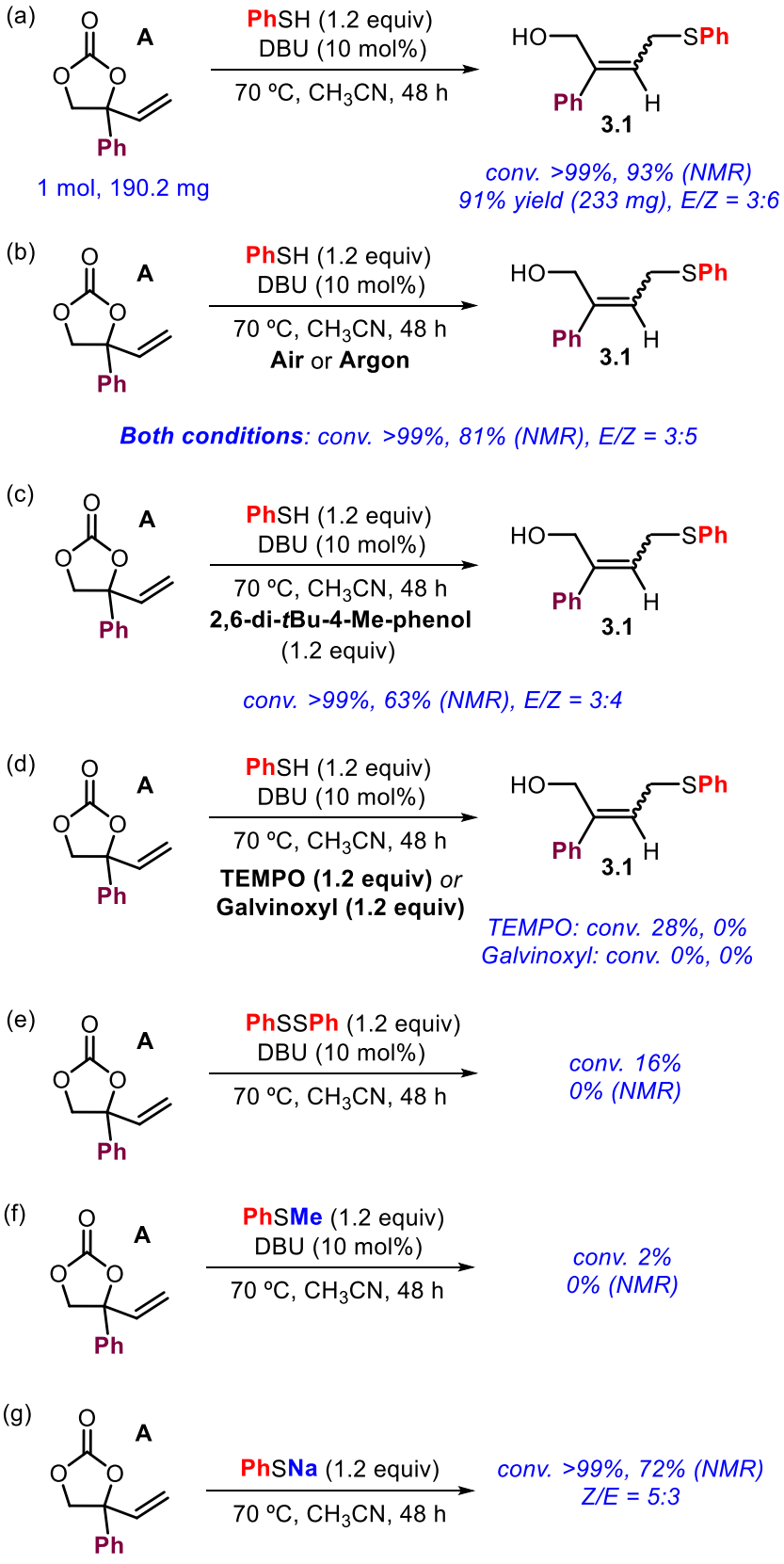
**3.25**: conv. 70%
*E/Z* = 3:7, yield 63%



**3.26**: conv. 37%
*E/Z* = 6:4
yield 26%

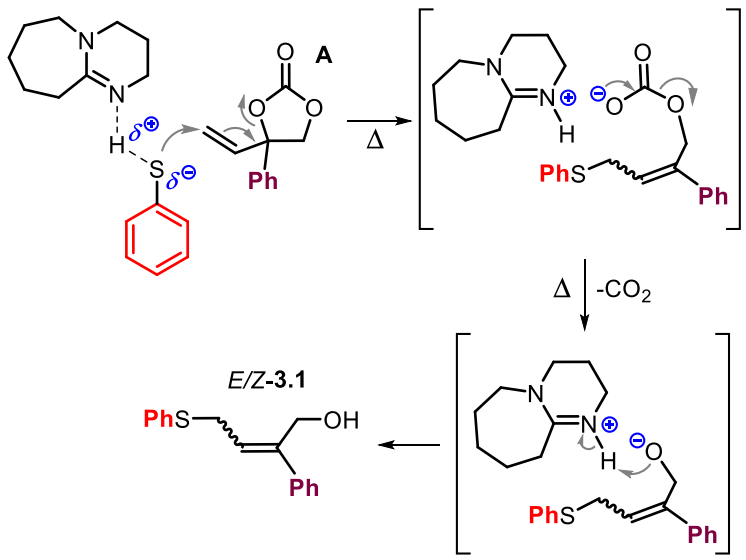
**Scheme 3.4** The scope of allylic thioethers using vinyl cyclic carbonates and alkyl/aryl thiols in the presence of DBU as catalyst.

amino-acid group led to the formation of product **3.26** though with a low substrate conversion and thus yield (26%).




**Scheme 3.5** Scaling up of allylic thioether **3.1** and various control experiments.

In order to investigate the formation of these allylic thioethers, various control experiments were conducted (Scheme 3.5). The synthesis of **3.1** could be scaled up 5 times offering access to sub-gram quantities of product and an improved isolated yield of 91% (Scheme 3.5a). Then, the benchmark synthesis of **3.1** was carried out under argon to examine the influence of oxygen on the reaction progress. The presence of an inert atmosphere (Scheme 3.5b) did not alter the outcome of the transformation, which may hint that no radical species are involved. Addition of a phenolic radical scavenger (Scheme 3.5c) still provided a 63% NMR yield of **3.1** in line with this notion, though the presence of two other known radical scavenging species (TEMPO or galvinoxyl, Scheme 3.5d) fully shut down the formation of **3.1**.[76]




**Scheme 3.6** The proposed activation mode of DBU and envisioned pathway towards product **3.1** from vinyl cyclic carbonate **A** and thiophenol.

We interpret these results such that these latter radical species may abstract a hydrogen from the thiol reagent leading to an unreactive disulfide and thus prevent product formation. This hypothesis was tested by replacing the thiol for a disulfide reagent and examine potential product formation (Scheme 3.5e), and indeed formation of **3.1** was not observed. The crucial role of a thiol reagent was further substantiated as the presence of a thioether (PhSMe, Scheme 3.5f) was not

[76] (a) L. Yang, S. Li, Y. Dou, S. Zhen, H. Li, P. Zhang, B. Yuan, G. Yang, *Asian J. Org. Chem.* **2017**, *6*, 265-268; (b) X. Zhang, S. Huang, M. Podgórski, X. Han, M. Claudino, C. N. Bowman. *Polym. Chem*. **2018**, *9*, 4294-4302.

productive. Finally, by replacing the thiol by a thiolate (Scheme 3.5g), there was no need for a thiol-activator, as the more nucleophilic thiolate is potent itself (in the absence of DBU) to facilitate the formation of allylic thioether **3.1**.

With all this information gathered, the catalytic role of DBU can be rationalized by a base-activated mechanism (Scheme 3.6). First, DBU interacts with the thiol reagent increasing its nucleophilic character and allowing for much lower reaction temperatures to be applied (Table 3.1). Attack of a "thiolate" nucleophile onto the least hindered carbon center of the *exo*-cyclic C=C bond of the carbonate causes ring-opening giving access to an intermediate hemi-carbonate that undergoes decarboxylation and finally protonation occurs by DBU-$H^+$. Apparently, methylene attack (Scheme 3.2) by the thiol reagent is not competitive under the reaction conditions and demonstrates the unique reactivity of these vinyl-substituted cyclic carbonates compared to other functionalized congeners.

## 3.4 Conclusions

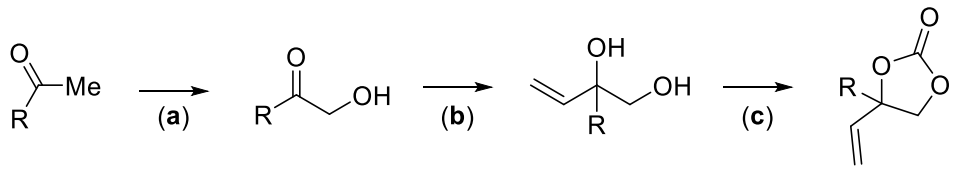
We here present an unprecedented nucleophilic attack of thiols onto vinyl-substituted cyclic carbonates that delivers allylic thioether products in moderate to good isolated yields. The process can be carried out under relatively mild reaction conditions using an organocatalyst (DBU). Control experiments have helped to rationalize that the base catalyst (DBU) activates the thiol *pro*-nucleophile for attack onto the C-terminus of the double bond, after which decarboxylation takes place and protonation subsequently delivers the final product. This new manifold adds new perspectives for the use of functionalized cyclic carbonates as precursors in organic synthesis and currently we are examining others types of nucleophiles and their reactivity towards cyclic organic carbonates.

# 3.5 Experimental section

## 3.5.1 General information

Thiophenols and catalysts were purchased from Aldrich or TCI, and used without further purification. Solvents were dried using an Innovative Technology PURE SOLV solvent purification system. Reactions were monitored by TLC and $^{1}$H NMR. TLC was carried out on 0.25 mm Merck aluminum-backed sheets coated with 60 F254 silica gel. Visualization of the silica plates was achieved using a UV lamp ($\lambda$ = 254 nm) and/or by heating plates that were dipped in a ceric ammonium molybdate stain. Flash chromatography was carried out on Sigma-Aldrich silica gel 60 (70-230 mesh) using the indicated eluent system. $^{1}$H NMR, $^{13}$C NMR, $^{19}$F NMR and related 2D NMR spectra were recorded at room temperature on a Bruker AV-400 or AV-500 spectrometer and referenced to the residual deuterated solvent signals. All reported NMR values are given in parts per million (ppm).

## 3.5.2 General procedure for the preparation of vinyl cyclic carbonates[77]



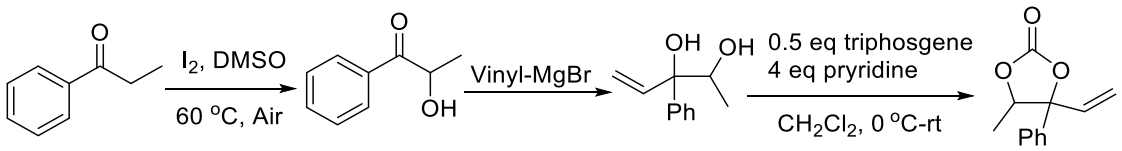

**Step (a)**: In a round bottom flask, powdered KOH (5.5 equiv.) was added portion-wise to a cold solution of ketone (10 mmol, 1 equiv.) in MeOH (0.6 M). (Diacetoxyiodo)benzene (1.1 equiv.) was subsequently added portion-wise. The resulting mixture was allowed to return to room temperature and stirred at this temperature for 3h. Then, the mixture was concentrated under reduced pressure, the residue was partitioned in $H_2O$ (15 mL) and $Et_2O$ (15 mL). The organic phase was separated, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The residue was dissolved in MeOH (20 mL) and 2M HCl (20 mL) was added. The mixture was stirred for 16 hours at room temperature. A saturated aqueous solution of $NaHCO_3$ was added to the mixture until pH 7, the resulting biphasic mixture was diluted with DCM and separated. The organic phase was collected, dried over $Na_2SO_4$, filtered and concentrated. The pure diol was obtained through flash chromatography on silica.

[77] A. Khan, R. Zheng, Y. Kan, J. Ye, J. Xing, Y. J. Zhang, *Angew. Chem. Int. Ed.* **2014**, *53*, 6439.

**Step (b)**: To a solution of the respective hydroxy methyl ketone (5 mmol, 1 equiv) in THF (20 mL) was added vinyl magnesium bromide (1.0 M in THF, 2.5 equiv) at 0 °C. The reaction was stirred under an $N_2$ atmosphere at room temperature for 2 h. The reaction mixture was then quenched with saturated aqueous $NH_4Cl$, and extracted with EtOAc. The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered and concentrated affording the crude product which was directly used in step (c).

**Step (c)**: To a solution of diol (5 mmol, 1 equiv) and pyridine (20 mmol, 4 equiv) in $CH_2Cl_2$ (20 mL) was added triphosgene (2.5 mmol, 0.5 equiv, 1.0 M in $CH_2Cl_2$) at 0 °C. The reaction was stirred under an $N_2$ atmosphere at room temperature for 2 h. The reaction mixture was then quenched with saturated aqueous $NH_4Cl$, and extracted with $CH_2Cl_2$. The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered and concentrated. The residue was purified by flash chromatography on silica to afford the corresponding carbonate.

## 3.5.3 Procedure for the preparation of other vinyl cyclic carbonates[78]

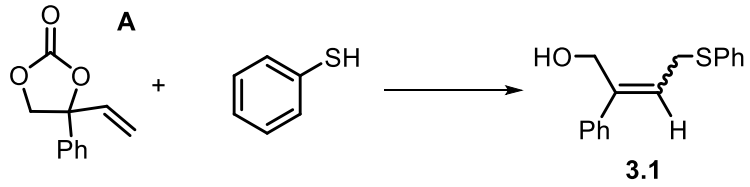



The more substituted vinyl carbonates were prepared according to a reported procedure (see below). Propiophenone (1.34 g, 10 mmol), $I_2$ (508 mg, 20 mol%), and DMSO (20 mL) and a stirring bar were added to a round-bottom flask under air. The mixture was stirred at 60 °C for 24 h and monitored by TLC. After cooling down to room temperature, the mixture was diluted with ethyl acetate (10 mL) and washed with 0.1 mol/L $Na_2S_2O_3$ (5 mL) aqueous solution, extracted with ethyl acetate (3 × 100 mL), and evaporated under vacuum. The crude reaction mixture was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1 v/v) to get the desired 2-hydroxypropiophenone. The next synthetic steps are the same as reported in section 3.5.2.

[78] Y. F. Liang, K. Wu, S. Song, X. Y. Li, X. Q. Huang, N. Jiao, *Org. Lett.*, **2015**, *17*, 876.

### 3.5.4 Further screening data for the reaction between vinyl cyclic carbonate A and thiophenol.

**Table 3.2.** Additional screening data for the formation of allylic thioether **3.1**.




**3.1**

| Entry | Base (mol%) | Solv. | T (º C) | Conv. **A** (%) | *E/Z*-**3.1** | NMR yield **3.1** (%) |
|---|---|---|---|---|---|---|
| 1 | DABCO (5) | ACN(0.2 ml) | rt | 3 | 0/0 | 0 |
| 2 | DABCO (10) | ACN(0.2 ml) | rt | 3 | 0/3 | 3 |
| 3 | DABCO (20) | ACN(0.2 ml) | rt | 3 | 0/3 | 3 |
| 4 | DABCO (30) | ACN(0.2 ml) | rt | 6 | 3/3 | 6 |
| 5 | DABCO (50) | ACN(0.2 ml) | rt | 9 | 3/6 | 9 |
| 6 | DABCO (50) | ACN(0.2 ml) | 50 | 58 | 15/24 | 39 |
| 7 | TBD (50) | ACN(0.2 ml) | 50 | 79 | 24/33 | 57 |
| 8 | DBU (50) | ACN(0.2 ml) | 50 | 94 | 30/48 | 78 |
| 9 | DMAP (50) | ACN(0.2 ml) | 50 | 29 | 12/15 | 27 |
| 10 | i-$Pr_2Et$ (50) | ACN(0.2 ml) | 50 | 40 | 12/18 | 30 |
| 11 | $NEt_3$ (50) | ACN(0.2 ml) | 50 | 28 | 6/9 | 15 |
| 12 | NMM (50) | ACN(0.2 ml) | 50 | 0 | 0/0 | 0 |
| 13 | NMP (50) | ACN(0.2 ml) | 50 | 0 | 0/0 | 0 |
| 14 | DBU (5) | ACN(0.2 ml) | 50 | 46 | 18/27 | 45 |
| 15 | DBU (10) | ACN(0.2 ml) | 50 | 82 | 27/42 | 69 |
| 16 | DBU (50) | ACN(0.2 ml) | 80 | 100 | 33/33 | 66 |
| 17[a] | DBU (50) | ACN(0.2 ml) | 50 | 100 | 27/45 | 72 |
| 18 | – | ACN(0.2 ml) | 80 | ~0 | 0/0 | 0 |
| **19** | **DBU (10)** | **ACN(0.2 ml)** | **70** | **100** | **30/48** | **78** |
| 20 | DBU (10) | ACN(0.1 ml) | 70 | 100 | 30/48 | 78 |
| 21[a] | DBU (10) | ACN(0.1 ml) | 70 | 100 | 30/45 | 75 |

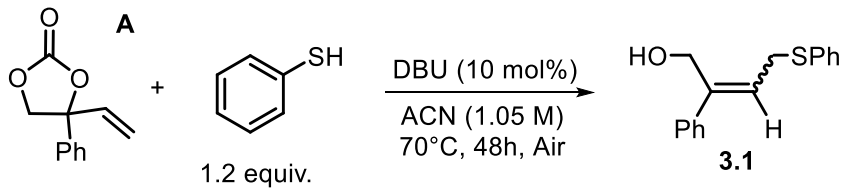
*Continuation of Table 3.2*

| | | | | | | |
|---|---|---|---|---|---|---|
| 22 | DBU (5) | ACN(0.1 ml) | 70 | 85 | 30/45 | 75 |
| 23 | DBU (10) | ACN(0.1 ml) | 50 | 70 | 21/36 | 57 |
| 24[a] | DBU (10) | ACN(0.1 ml) | 50 | 73 | 21/39 | 60 |
| **25**[a] | **DBU (10)** | **ACN(0.2 ml)** | **70** | **97** | **33/48** | **81(81)**[b] |
| 26[a] | DBU (10) | ACN(0.1 ml) | 70 | 97 | 27/39 | 66 |

[a]Thiophenol (1.2 equiv). [b]In brackets, the isolated yield of **3.1**.

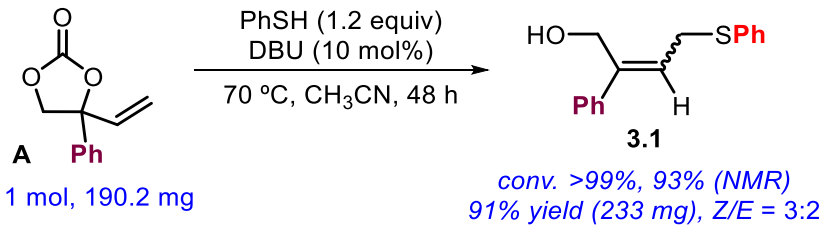
**Procedure**: A screw-capped vial was charged with the vinyl cyclic carbonate **A** (0.1 mmol, 1 equiv), the base catalyst (amount indicated) and thiophenol (0.15 mmol, 1.5 equiv) followed by dry ACN. The reaction mixture was stirred at the corresponding temperature as reported in Table 3.2. The resulting crude mixture was concentrated under reduced pressure and a $^1$H NMR ($CDCl_3$) spectrum was recorded. The NMR yield of **3.1** was calculated using mesitylene as internal standard.

### 3.5.5 General procedure for the preparation of the allylic thioethers

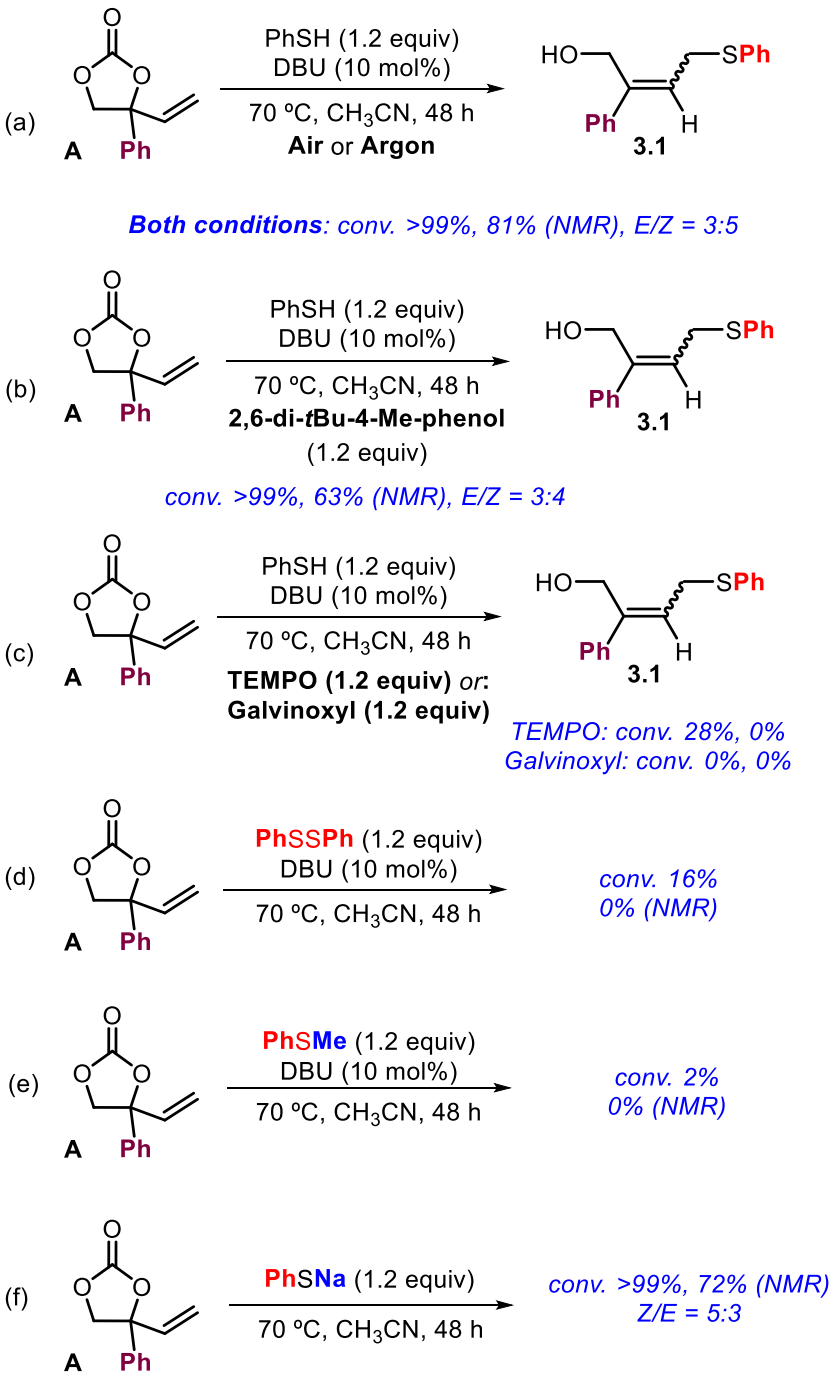



A screw-capped vial was charged with the vinyl cyclic carbonate **A** (0.21 mmol, 1 equiv), DBU (3.2 mg, 0.021 mmol, 10 mol%), thiophenol (26 µL, 0.252 mmol, 1.2 equiv) and dry ACN (0.2 mL). The reaction mixture was stirred at 70 ºC for 48 h. The reaction mixture was purified by flash column chromatography on silica gel to afford the corresponding allylic thioether product **3.1** (hexane:ethyl acetate, 5:1 v/v) These separation conditions were used for **all** the allylic thioether compounds.

**Scale-up of 3.1**: A screw-capped vial was charged with **A** (190.2 mg, 1 mmol, 1 equiv), DBU (15 mg, 0.1 mmol, 10 mol%), thiophenol (132 mg, 1.2 mmol, 1.2 equiv) and dry ACN (5 mL). The reaction mixture was stirred at 70 ºC for 48 h. The reaction mixture was purified by flash column chromatography on silica gel to afford **3.1** as colorless oil in 91% yield (282 mg, 0.91 mmol). The *Z/E* ratio was determined by $^{1}$H NMR to be 3:2.



### 3.5.6 Control experiments




**Scheme 3.7** Various control experiments.

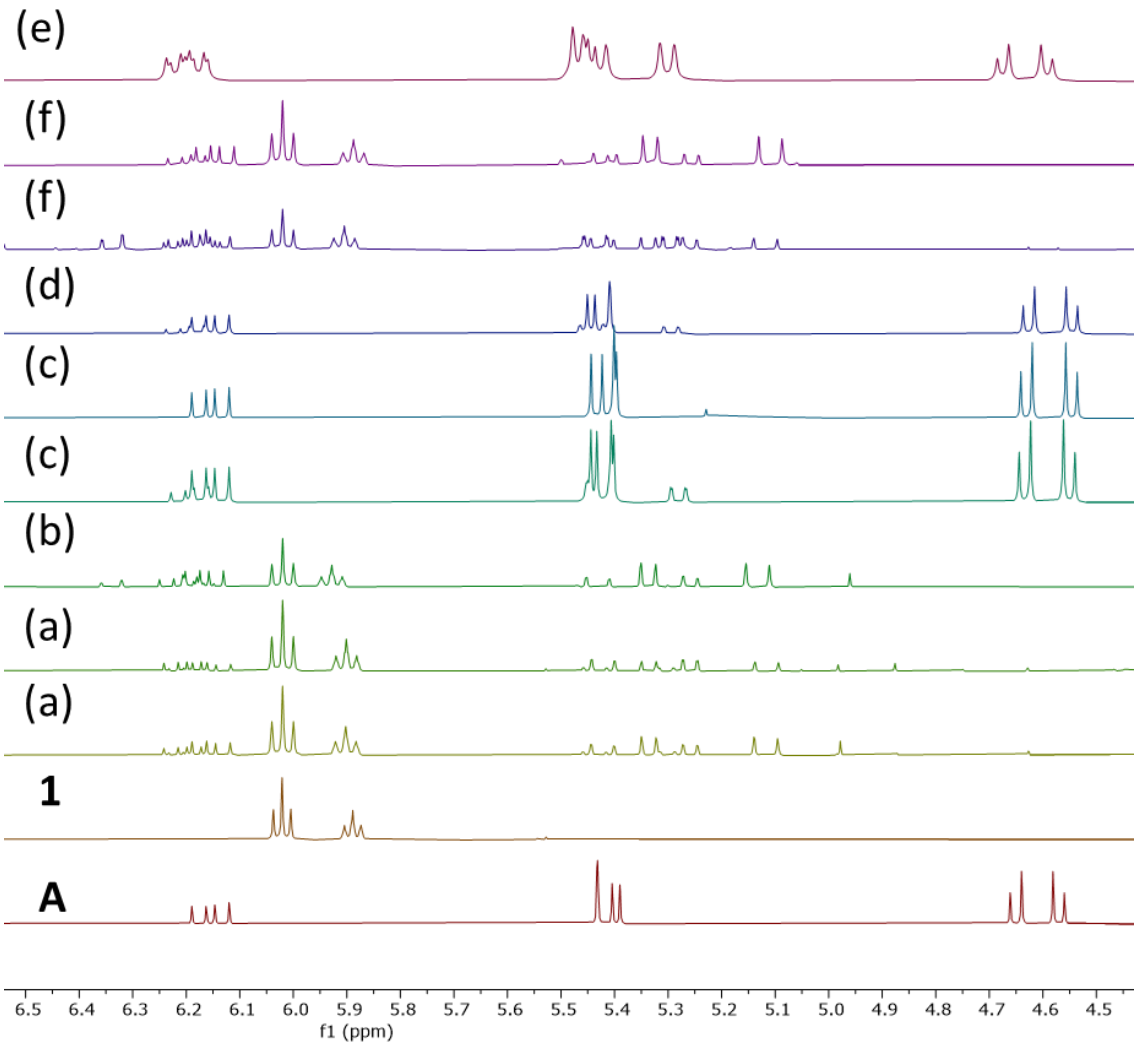
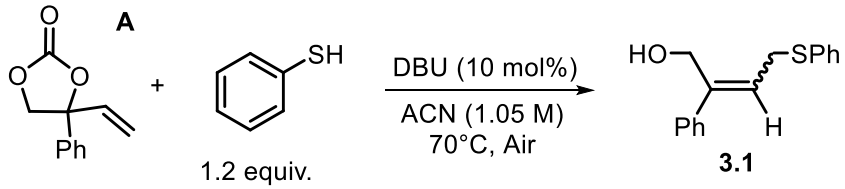



**Figure 3.1** Selected NMR region (4.5-6.5 ppm) for identification of the products of the control experiments of Scheme 3.7.

### 3.5.7 Kinetic studies




Six screw-capped vials were charged with a solution of the vinyl cyclic carbonate **A** (0.21 mmol, 1 equiv), DBU (3.2 mg, 0.021 mmol, 10 mol%), thiophenol (26 µL, 0.252 mmol, 1.2 equiv) and dry ACN (0.2 mL). The reaction mixtures were stirred at 70 ºC and examined by NMR at respectively 0, 2, 4, 6, 8 and 10 h of reaction time. The crude products were concentrated under vacuum and conversions and yields were determined by $^{1}H$ NMR ($CDCl_3$) using $CH_2Br_2$ as an internal standard.

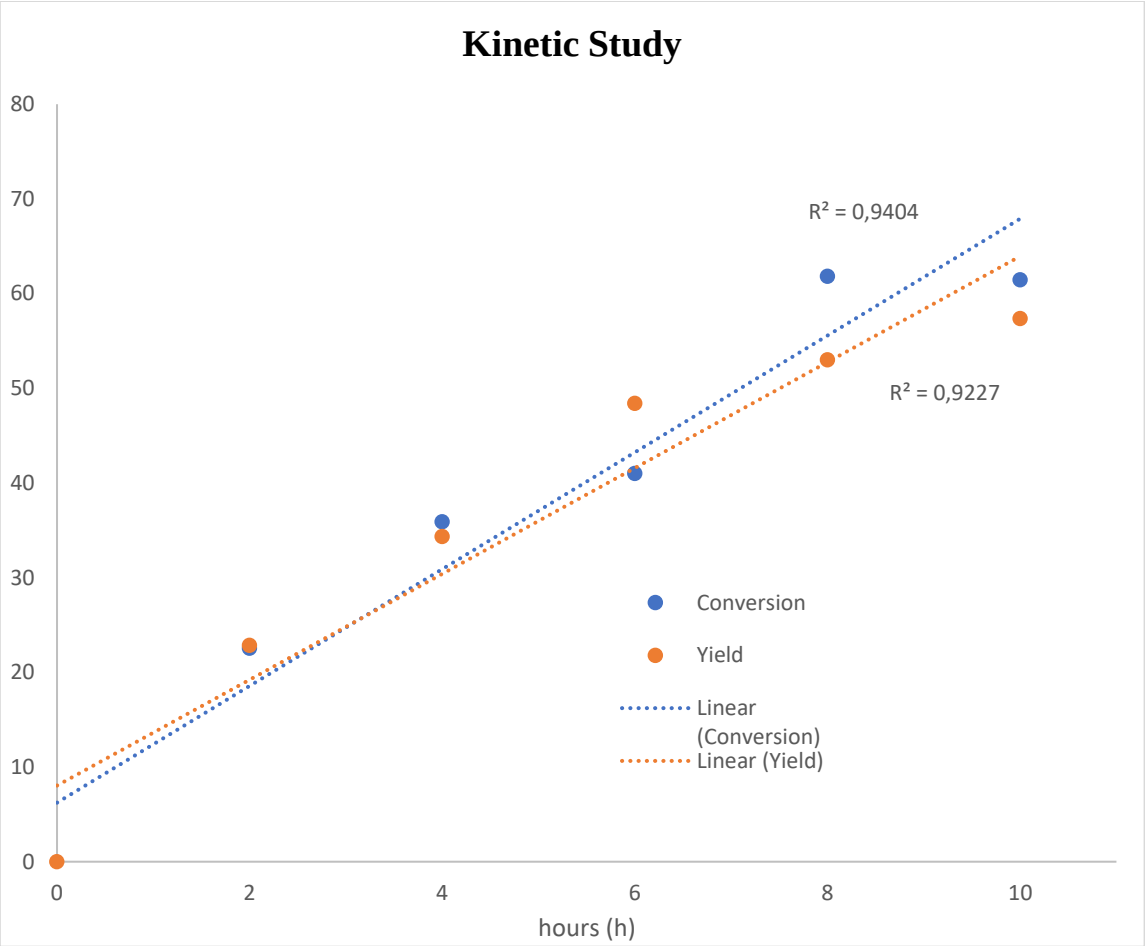
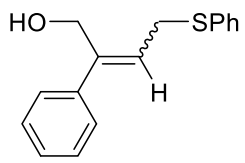



**Figure 3.2** Kinetic study for the formation of allylic thioether **3.1** from substrate **A**.

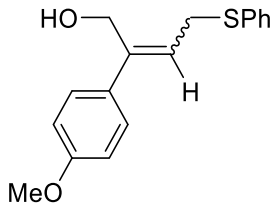
## 3.5.8 Characterization data for all compounds

**2-Phenyl-4-(phenylthio)but-2-en-1-ol (3.1)**[75]



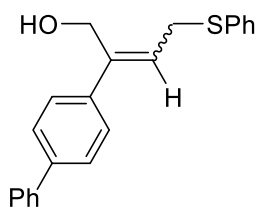

Following the general procedure, product **3.1** was isolated as an orange oil in 81% yield (43.5 mg, 0.17 mmol). Z/E ratio was determined by $^1$H NMR to be 6/4; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.49-7.47 (m, 2H, 2H M), 7.43-7.41 (m, 2H, 2H M), 7.38-7.34 (m, 5H, 5H M), 7.33-7.27 (m, 9H, 1H M + 8H m), 7.16-7.14 (m, 2H, 2H m), 6.02 (t, *J* = 8.1 Hz, 1H, 1H M *Z* isomer), 5.89 (tt, *J* = 7.7, 1.4 Hz, 1H, 1H m *E* isomer), 4.37 (s, 2H, 2H M), 4.32 (s, 2H. 2H m), 3.78 (d, *J* = 8.1 Hz, 2H, 2H M), 3.55 (d, *J* = 7.9 Hz, 2H, 2H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.6, 142.1, 140.2, 137.2, 135.8, 135.0, 132.0 (2C), 129.9, 129.1 (2C), 128.8 (2C), 128.6, 128.5, 128.5 (2C), 127.7, 127.7, 127.4, 126.4, 126.3, 126.2, 122.9, 67.3, 59.4, 33.1, 32.5 ppm.

**2-(4-Methoxyphenyl)-4-(phenylthio)but-2-en-1-ol (3.2)**



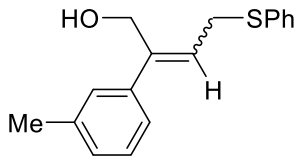

Following the general procedure, product **3.2** was isolated as a brown oil in 71% yield (37.0 mg, 0.13 mmol). Z/E ratio was determined by $^1$H NMR to be 6/4; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.48-7.45 (m, 2H, 2H M), 7.37-7.32 (m, 4H, 4H M), 7.29-7.26 (m, 5H, 1H M + 4H m), 7.11-7.10 (m, 2H, 2H m), 6.92-6.88 (m, 5H, 3 H m + 2H M), 5.95 (t, *J* = 8.1 Hz, 1H, 1H M *Z* isomer), 5.84 (tt, *J* = 7.7, 1.4 Hz, 1H, 1H *E* isomer), 4.35 (s, 2H M), 4.30 (s, 2H m), 3.84 (s, 3H m), 3.83 (s, 3H M), 3.77 (d, *J* = 8.1 Hz, 2H M), 3.57 (d, *J* = 7.6 Hz, 2H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 159.3, 159.1, 143.2, 141.5, 136.0, 135.1, 132.5, 131.9 (2C), 129.7 (3C), 129.0 (2C), 128.8 (2C), 127.6 (2C), 127.3 (2C), 126.1, 124.6, 122.5, 113.9 (3C), 113.9 (2C), 67.4, 59.3, 55.3, 55.3, 33.1, 32.5 ppm; **HRMS** (ESI+, MeOH): *m*/*z* calcd for $C_{17}H_{18}NaO_2S$, $[M + Na]^+$: 309.0920, found: 309.0921.

**2-([1,1'-Biphenyl]-4-yl)-4-(phenylthio)but-2-en-1-ol (3.3)**[75]



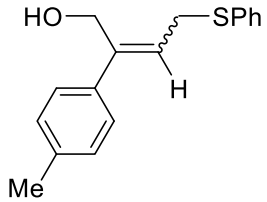

Following the general procedure, product **3.3** was isolated as a white solid in 47% yield (23.4 mg, 0.07 mmol). *Z/E* ratio was determined by $^1$H NMR to be 3:7; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.65-7.59 (m, 8H), 7.52-7.45 (m, 6H), 7.42-7.34 (m, 4H), 7.29-7.23 (m, 10H), 6.10 (t, *J* = 8.0 Hz, 1H, 1H m *Z* isomer), 5.93 (tt, *J* = 7.8, 1.5 Hz, 1H, 1H m *E* isomer), 4.41 (s, 2H, 2H m), 4.38 (s, 2H, 2H M), 3.81 (d, *J* = 8.1 Hz, 2H, 2H m), 3.62 (d, *J* = 7.8 Hz, 2H, 2H M) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.2, 141.6, 140.6, 140.6, 140.6, 140.5, 139.0, 136.1, 135.8, 135.0, 132.2, 130.0, 129.1, 129.0, 128.9, 128.8, 128.8, 127.5, 127.5, 127.4, 127.3, 127.2, 127.1, 127.0, 126.8, 126.3, 126.3, 123.2, 67.4, 59.3, 33.2, 32.6 ppm.

**4-(phenylthio)-2-(*m*-tolyl)but-2-en-1-ol (3.4)**




Following the general procedure, product **3.4** was isolated as an orange oil in 80% yield (42.3 mg, 0.16 mmol). *Z/E* ratio was determined by $^1$H NMR to be 1:1; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.49-7.46 (m, 2H), 7.37-7.33 (m, 2H), 7.30-7.20 (m, 10H), 7.16-7.12 (m, 2H), 6.96-6.93 (m, 2H), 6.00 (t, *J* = 8.1 Hz, 1H, 1H M *Z* isomer), 5.86 (tt, *J* = 7.7, 1.4 Hz, 1H, 1H m *E* isomer), 4.37 (s, 2H, 2H M), 4.31 (s, 2H, 2H m), 3.78 (d, *J* = 8.1 Hz, 1H, 1H M), 3.55 (dt, *J* = 7.7, 1.0 Hz, 1H, 1H m), 2.38 (s, 3H, 3H M), 2.37 (s, 3H, 3H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.6, 142.2, 140.2, 138.1, 138.1, 137.1, 135.8, 135.1, 131.9, 130.1, 129.1, 129.0, 128.8, 128.5, 128.3, 127.3, 127.2, 126.2, 126.1, 125.6, 123.5, 122.8, 67.4, 59.4, 33.1, 32.6, 21.5, 21.5 ppm; **HRMS** (ESI+, MeOH): *m*/*z* calcd for $C_{17}H_{18}NaOS$, $[M + Na]^+$: 293.0971, found: 293.0973.

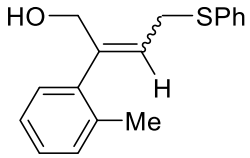
**4-(phenylthio)-2-(*p*-tolyl)but-2-en-1-ol (3.5)**[75]




Following the general procedure, product **3.5** was isolated as an orange oil in 82% yield (43.4 mg, 0.16 mmol). *Z/E* ratio was determined by $^1$H NMR to be 4:6; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.49-7.47 (m, 2H), 7.37-7.32 (m, 4H), 7.31-7.25 (m, 4H), 7.23-7.17 (m, 6H), 7.09-7.07 (m, 2H), 6.00 (t, *J* = 8.1 Hz, 1H, 1H m *Z* isomer), 5.87 (tt, *J* =

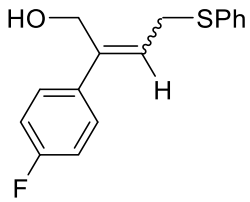
7.7, 1.5 Hz, 1H. 1H *E* isomer), 4.36 (s, 2H, 2H m), 4.31 (d, *J* = 1.3 Hz, 2H, 2H M), 3.78 (d, *J* = 8.1 Hz, 2H, 2H m), 3.58 (d, *J* = 7.7 Hz, 2H, 2H M), 2.40 (s, 3H, 3H M), 2.38 (s, 3H, 3H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.6, 141.9, 137.5, 137.4, 137.3, 136.0, 135.1, 134.2, 131.9 (2C), 129.7 (2C), 129.3 (2C), 129.2 (2C), 129.0 (2C), 128.8 (2C), 128.4 (2C), 127.3, 126.3 (2C), 126.1, 125.5, 122.5, 67.3, 59.4, 33.1, 32.5, 21.3, 21.1 ppm.

**4-(phenylthio)-2-(*o*-tolyl)but-2-en-1-ol (3.6)**



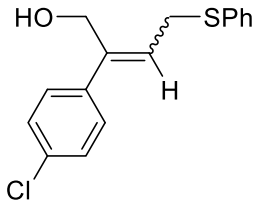

Following the general procedure, product **3.6** was isolated as a yellow oil in 91% yield (48.2 mg, 0.18 mmol). *Z/E* ratio was determined by $^1$H NMR to be 4:7; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2H), 7.38-7.34 (m, 2H), 7.30-7.15 (m, 10H), 7.06-7.04 (m, 2H), 6.89-6.87 (m, 2H), 5.93 (tt, *J* = 7.5, 1.6 Hz, 1H, 1H M, *E* isomer,), 5.62 (t, *J* = 8.0 Hz, 1H, 1H M *Z* isomer), 4.29 (s, 2H, 2H m), 4.23 (s, 2H, 2H M), 3.79 (d, *J* = 8.0 Hz, 2H, 2H m), 3.35 (d, *J* = 7.6 Hz, 2H, 2H M), 2.22 (s, 3H, 3H M), 2.20 (s, 3H, 3H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.2, 142.9, 140.6, 136.4, 136.0, 135.9, 135.6, 135.3, 131.5, 130.3, 130.2 (2C), 129.9 (2C), 129.2, 129.1, 129.0 (2C), 128.8 (2C), 127.8, 127.5, 127.4, 127.1, 126.2, 125.8, 125.6, 122.6, 66.8, 61.0, 32.4, 32.4, 19.9, 19.4 ppm; **HRMS** (ESI+, MeOH): *m*/*z* calcd for $C_{17}H_{18}NaOS$, $[M + Na]^+$: 293.0971, found: 293.0981.

**2-(4-fluorophenyl)-4-(phenylthio)but-2-en-1-ol (3.7)**[75]



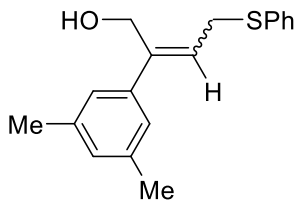

Following the general procedure, product **3.7** was isolated as a white solid in 67% yield (35.2 mg, 0.13 mmol). *Z/E* ratio was determined by $^1$H NMR to be 6:4. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.51-7.45 (m, 2H), 7.40-7.33 (m, 6H), 7.31-7.25 (m, 4H), 7.11-7.01 (m, 6H), 5.96 (t, *J* = 8.1 Hz, 1H, 1H *Z* isomer), 5.89 (tt, *J* = 7.8, 1.5 Hz, 1H, 1H *E* isomer), 4.33 (s, 2H, 2H M), 4.27 (s, 2H, 2H m), 3.76 (d, *J* = 8.1 Hz, 2H, 2H M), 3.51 (d, *J* = 7.8 Hz, 2H, 2H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 162.4 (d, *J* = 247.0 Hz), 162.2 (d, *J* = 246.7 Hz), 142.6, 141.1, 136.3 (d, *J* = 3.3 Hz), 135.6, 135.0, 133.1 (d, *J* = 3.3 Hz), 132.0 (2C), 130.2 (2C), 130.2 (d, *J* = 8.0 Hz, 2C), 129.1 (2C), 128.9 (2C), 128.1 (d, *J* = 7.9 Hz, 2C), 127.4, 126.4, 126.2, 124.4, 115.3 (d, *J* = 21.4 Hz, 2C), 115.4 (d, *J* = 21.2 Hz, 2C), 67.3, 59.4, 33.0, 32.6 ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.0, -114.5.

**2-(4-chlorophenyl)-4-(phenylthio)but-2-en-1-ol (3.8)**



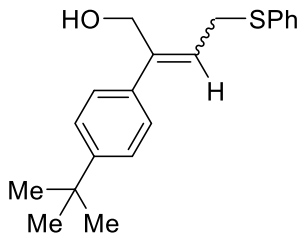

Following the general procedure, product **3.8** was isolated as a yellow oil in 45% yield (23.2 mg, 0.08 mmol). *Z/E* ratio was determined by $^1$H NMR to be 3:7; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.48-7.46 (m, 2H), 7.36-7.32 (m, 6H), 7.29-7.23 (m, 6H), 7.06-7.04 (m, 4H), 6.00 (t, *J* = 8.2 Hz, 1H, 1H m *Z* isomer), 5.90 (tt, *J* = 7.8, 1.4 Hz, 1H, 1H M *E* isomer), 4.32 (s, 2H, 2H m), 4.29 (s, 2H, 2H M), 3.76 (d, *J* = 8.1 Hz, 2H, 2H m), 3.50 (d, *J* = 7.8 Hz, 2H, 2H M) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 142.4, 140.9, 138.7, 135.6, 135.5, 134.8, 133.6, 132.3, 130.4 (2C), 129.9 (2C), 129.1 (2C), 128.9 (2C), 128.7 (2C), 128.6 (2C), 127.7, 127.6, 126.5 (2C), 123.8 (2C), 67.2, 59.2, 33.1, 32.7 ppm; **HRMS** (APCI+, MeOH): *m/z* calcd for $C_{16}H_{14}ClOS$, $[M-H]^+$: 289.0448, found: 289.0444.

**2-(3,5-dimethylphenyl)-4-(phenylthio)but-2-en-1-ol (3.9)**




Following the general procedure, product **3.9** was isolated as an orange oil in 55% yield (28.7 mg, 0.10 mmol). *Z/E* ratio was determined by $^1$H NMR to be 1:1; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.49-7.47 (m, 2H), 7.37-7.33 (m, 2H), 7.31-7.21 (m, 6H), 7.05 (s, 2H), 6.97 (s, 2H), 6.74-6.74 (m, 2H), 6.00 (t, *J* = 8.1 Hz, 1H, 1H *Z* isomer), 5.85 (tt, *J* = 7.7, 1.5 Hz, 1H, 1H *E* isomer), 4.37 (s, 2H), 4.30 (s, 2H), 3.78 (d, *J* = 8.1 Hz, 2H), 3.56 (d, *J* = 7.7 Hz, 2H), 2.35 (s, 6H), 2.34 (s, 6H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.8, 142.4, 140.2, 138.0 (2C), 137.9 (2C), 137.1, 135.8, 135.2, 131.8 (2C), 130.2 (2C), 129.4, 129.3, 129.0 (2C), 128.8 (2C), 127.2, 126.3 (2C), 126.2, 125.9, 124.3 (2C), 122.6, 67.4, 59.5, 33.0, 32.7, 21.4, 21.3 ppm; **HRMS** (ESI+, MeOH): *m/z* calcd for $C_{18}H_{20}NaOS$, $[M + Na]^+$: 307.1127, found: 307.1141.

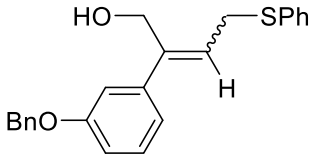
**2-(4-(*tert*-butyl)phenyl)-4-(phenylthio)but-2-en-1-ol (3.10)**




Following the general procedure, product **3.10** was isolated as an orange oil in 53% yield (26.9 mg, 0.09 mmol). *Z/E* ratio was determined by $^1$H NMR to be 6:4; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2H), 7.43-7.33 (m, 8H), 7.30-7.19 (m, 6H), 7.15-7.13 (m, 2H), 6.03 (t, *J* = 8.1 Hz, 1H, 1H M *Z* isomer),

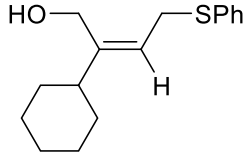
5.88 (tt, *J* = 7.8, 1.6 Hz, 1H, 1H m *E* isomer), 4.38 (s, 2H M), 4.32 (s, 2H m), 3.80 (d, *J* = 8.1 Hz, 2H, 2H M), 3.61 (d, *J* = 7.7 Hz, 2H, 2H m), 1.39 (s, 9H, 9 H m), 1.37(s, 9H, 9H M) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 150.7, 150.6, 143.5, 141.8, 137.2, 136.2, 135.2, 134.1, 131.9 (2C), 129.6 (2C), 129.0 (2C), 128.8 (2C), 128.2 (2C), 127.3, 126.1 (2C), 126.1, 125.6, 125.5 (2C), 125.4 (2C), 122.5, 67.3, 59.3, 34.6, 34.5, 33.1, 32.4, 31.4 (*t*Bu), 31.3 (*t*Bu) ppm; **HRMS** (ESI+, MeOH): *m*/*z* calcd for $C_{20}H_{24}NaOS$, $[M + Na]^+$: 335.1440, found: 335.1443.

**2-(3-(benzyloxy)phenyl)-4-(phenylthio)but-2-en-1-ol (3.11)**



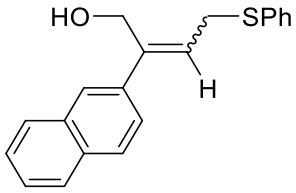

Following the general procedure, product **3.11** was isolated as a yellow oil in 64% yield (31.3 mg, 0.09 mmol). *Z*/*E* ratio was determined by $^1$H NMR to be 3:7; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.48-7.40 (m, 10H), 7.38-7.31 (m, 4H), 7.30-7.25 (m, 6H), 7.22-6.74 (m, 8H), 6.01 (t, *J* = 8.1 Hz, 1H, 1H m *Z* isomer), 5.87 (tt, *J* = 7.8, 1.4 Hz, 1H. 1H M *E* isomer), 5.09 (s, 2H, 2H m), 5.08 (s, 2H, 2H M) 4.33 (s, 2H, 2H m), 4.31 (s, 2H, 2H M), 3.77 (d, *J* = 8.2 Hz, 2H, 2H m), 3.54 (d, *J* = 7.9 Hz, 2H, 2H M) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 159.0, 158.8, 143.3, 141.9, 141.7, 138.5, 137.0, 136.9, 135.9, 132.1, 129.8 (2C), 129.6, 129.5, 129.1, 129.0, 128.8 (2C), 128.6 (3C), 128.0, 128.0, 127.5 (2C), 127.4, 126.5, 126.2, 123.1, 121.1, 119.1, 115.1, 114.2, 113.9, 113.3, 77.2, 70.0, 67.3, 59.4, 33.1, 32.4 ppm; **HRMS** (ESI+, MeOH): *m*/*z* calcd for $C_{23}H_{22}NaO_2S$, $[M + Na]^+$: 385.1233, found: 385.1233.

**(*Z*)-2-cyclohexyl-4-(phenylthio)but-2-en-1-ol (3.12)**[75]



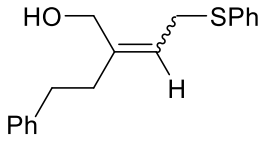

Following the general procedure, product **3.12** was isolated as a colorless oil in 53% yield (28.3 mg, 0.11 mmol). *Z*/*E* ratio was determined by $^1$H NMR of the crude to be 9:1. Note that only the *Z* isomer has been isolated; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.44-7.41 (m, 2H), 7.35-7.31 (m, 2H), 7.28-7.24 (m, 1H), 5.49 (td, *J* = 8.0, 1.0 Hz, 1 H), 3.96 (s, 2H), 3.62 (d, *J* = 8.0 Hz, 2 H), 2.07-2.00 (m, 1 H), 1.80-1.69 (m, 6H), 1.25-1.10 (m, 5H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 148.3, 135.4, 131.9 (2C), 128.9 (2C), 127.1, 121.8, 59.4, 43.3, 32.6 (2C), 32.5 (2C), 26.7 (2C), 26.2 (2C) ppm.

**2-(naphthalen-2-yl)-4-(phenylthio)but-2-en-1-ol (3.13)**[75]



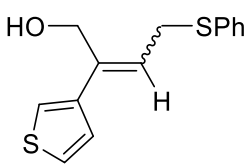

Following the general procedure, product **3.13** was isolated as a yellow oil in 51% yield (26.0 mg, 0.085 mmol). *Z/E* ratio was determined by $^{1}$H NMR to be 4:6; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.89-7.81 (m, 8H), 7.58-7.47 (m, 8H), 7.38-7.26 (m, 6H), 7.24-7.22 (m, 2H), 6.17 (t, *J* = 8.1 Hz, 1H, 1 H m *Z* isomer), 5.97 (tt, *J* = 7.7, 1.4 Hz, 1H, 1H M *E* isomer), 4.48 (s, 2H., 2H m), 4.42 (s, 2H, 2H M), 3.84 (d, *J* = 8.1 Hz, 2H, 2H m), 3.59 (d, *J* = 7.7 Hz, 2H, 2H M) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.5, 142.0, 137.4, 135.6, 135.0, 134.6, 133.4, 133.2, 132.9, 132.7, 132.2 (2C), 130.3 (2C), 129.1 (2C), 128.8 (2C), 128.2, 128.2, 128.1, 128.0, 127.7, 127.6, 127.6, 127.5, 126.8, 126.5, 126.4, 126.3, 126.3, 126.2, 126.0, 125.3, 124.5, 123.6, 67.5, 59.4, 33.3, 32.8 ppm.

**2-phenethyl-4-(phenylthio)but-2-en-1-ol (3.14)**



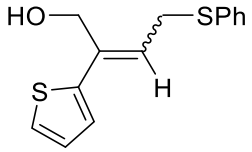

Following the general procedure, product **3.14** was isolated as a yellow oil in 90% yield (46.8 mg, 0.16 mmol). *Z/E* ratio was determined by $^{1}$H NMR to be 3:7; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.41-7.27 (m, 10H), 7.24-7.17 (m, 10H), 5.64 (t, *J* = 7.7 Hz, 1H, 1H *E* M isomer), 5.52 (t, *J* = 8.0 Hz, 1H, 1H m *Z* isomer), 4.06 (s, 2H, 2H M), 4.00 (s, 2H, 2H m), 3.59 (d, *J* = 8.0 Hz, 2H, 2H m), 3.46 (d, *J* = 7.7 Hz, 2H, 2H M), 2.76-2.72 (m, 2H, 2H m), 2.71-2.67 (m, 2H, 2H M), 2.47-2.43 (m, 2H, 2H m), 2.41-2.37 (m, 2H, 2H M) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 142.0, 141.6, 131.6, 130.0, 128.9, 128.9, 128.4, 126.3, 126.1, 122.1, 66.6, 34.8, 31.4, 30.1 ppm (Only the *E* isomer identified); **HRMS** (ESI+, MeOH): *m*/*z* calcd for $C_{18}H_{20}NaOS$, $[M+Na]^+$: 307.1127, found: 307.1134.

**4-(phenylthio)-2-(thiophen-3-yl)but-2-en-1-ol (3.15)**



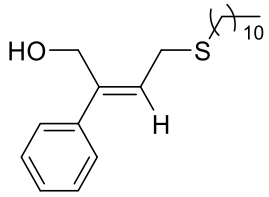

Following the general procedure, product **3.15** was isolated as an orange oil in 56% yield (30.0 mg, 0.11 mmol). *Z/E* ratio was determined by $^{1}$H NMR to be 3:7; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.47-7.45 (m, 2H), 7.37-7.19 (m, 12H), 7.05-7.04 (m, 2H), 6.12 (t, *J* = 8.2 Hz, 1H, 1H m *Z* isomer), 5.90 (t, *J* = 7.9, 1.4 Hz, 1H, 1H M *E* isomer), 4.33 (s, 2H), 4.32 (s, 2H), 3.77 (d, *J* = 8.2 Hz, 2H), 3.67 (d, *J* = 7.8 Hz, 2H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.2, 138.4, 137.3, 136.8, 135.8, 135.0, 132.0, 129.8 (2C), 129.1 (2C), 128.8 (2C), 127.7, 127.4, 126.3 (2C), 125.8, 125.7, 125.6, 124.8, 123.6, 123.5, 121.2, 67.4, 59.5, 33.0, 32.7 ppm; **HRMS** (ESI+, MeOH): *m*/*z* calcd for $C_{14}H_{14}NaOS_2$, $[M + Na]^+$: 285.0378, found: 285.0380.

**4-(phenylthio)-2-(thiophen-2-yl)but-2-en-1-ol (3.16)**



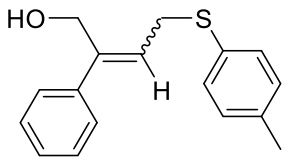

Following the general procedure, product **3.16** was isolated as a yellow oil in 60% yield (32.1 mg, 0.12 mmol). *Z/E* ratio was determined by $^{1}$H NMR to be 4:6; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.49-7.46 (m, 2H), 7.37-7.26 (m, 8H), 7.22-7.19 (m, 2H), 7.14-7.00 (m, 4H), 6.16 (t, *J* = 8.2 Hz, 1H, 1H m, *Z* isomer), 5.95 (tt, *J* = 7.7, 1.3 Hz, 1H, 1H m, *E* isomer), 4.35 (s, 2H, 2H M), 4.31 (s, 2H, 2H m), 3.81 (d, *J* = 7.8 Hz, 2H, 2H M), 3.75 (d, *J* = 8.2 Hz, 2H, 2H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.1 (2C), 135.9 (2C), 135.8 (2C), 132.5, 129.6, 129.1, 128.9, 127.6, 127.6, 127.1, 127.0, 126.3, 125.9, 125.2, 124.8, 124.5, 124.1, 67.9, 59.4, 33.3, 32.5 ppm; **HRMS** (APCI+, MeOH): *m*/*z* calcd for $C_{14}H_{15}OS_2$, $[M+H]^+$: 263.0559, found: 263.0555.

**(*Z*)-4-(decylthio)-2-phenylbut-2-en-1-ol (3.17)**



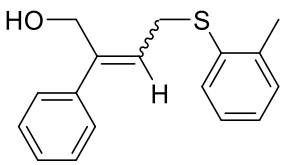

Following the general procedure, product **3.17** was isolated as a yellow oil in 16% yield (7.0 mg, 0.034 mmol). *Z/E* ratio was determined by $^{1}$H NMR to be 6:4. Note that only the *Z* isomer was isolated; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.51-7.48 (m, 2H), 7.40-7.36 (m, 2H), 7.33-7.28 (m, 1H), 6.04 (t, *J* = 8.0 Hz, 1H, *Z* isomer), 4.60 (s, 2H), 3.43 (d, *J* = 8.0 Hz, 2H), 2.58 (t, *J* = 8.0 Hz, 2H), 1.67-1.60 (m, 2H), 1.28 (m, 16H), 0.91 (t, *J* = 6.7 Hz, 3H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.8, 140.4, 128.6 (2C), 127.6, 127.5, 126.3 (2C), 59.7, 31.9, 31.7, 29.6, 29.6, 29.5, 29.3, 29.3, 29.2, 28.9, 22.7, 14.1 ppm; **HRMS** (ESI+, MeOH): *m*/*z* calcd for $C_{21}H_{34}NaOS$, $[M+Na]^+$: 357.2223, found: 357.2230.

**2-phenyl-4-(*p*-tolylthio)but-2-en-1-ol (3.18)**[75]




Following the general procedure, product **3.18** was isolated as a yellow oil in 80% yield (45.4 mg, 0.17 mmol). *Z/E* ratio was determined by $^{1}$H NMR to be 7:4; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.44-7.28 (m, 12H), 7.19-7.07 (m, 6H), 6.01 (t, *J* = 8.2 Hz, 1H, 1H M, *Z* isomer), 5.87 (tt, *J* = 7.8, 1.4 Hz, 1H, 1H m, *E* isomer), 4.32 (s, 4H, 2H M + 2H m), 3.72 (d, *J* = 8.2 Hz, 2H, 2H M), 3.50 (d, *J* = 7.6 Hz, 2H, 2H m), 2.35 (s, 6H, 3H M + 3H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.3, 141.8, 140.3, 137.8, 137.2, 136.5, 133.0 (2C), 132.0, 131.1, 130.8 (2C), 129.8 (2C), 129.6 (2C), 128.5 (2C), 128.5 (2C), 128.4 (2C), 127.6, 127.6, 126.6, 126.4 (2C), 123.3, 67.4, 59.4, 33.8, 33.2, 21.1, 21.0 ppm.

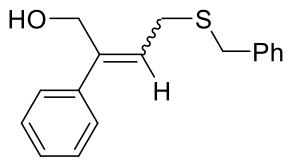
**2-phenyl-4-(*o*-tolylthio)but-2-en-1-ol (3.19)**[75]




Following the general procedure, product **3.19** was isolated as a yellow oil in 72% yield (40.8 mg, 0.15 mmol). *Z/E* ratio was determined by $^{1}$H NMR to be 4:6; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.46-7.30 (m, 8H), 7.27-7.11 (m, 10H), 6.03 (t, *J* = 8.2 Hz, 1 H, 1H m, *Z* isomer), 5.90 (tt, *J* = 7.8, 1.4 Hz, 1 H, 1H M, *E* isomer), 4.36 (s, 2H, 2H m), 4.33 (q, *J* = 1.1 Hz, 2H, 2H M), 3.74 (d, *J* = 8.2 Hz, 2H, 2H m), 3.51 (dt, *J* = 7.8, 1.0 Hz, 2H, 2H M), 2.48 (s, 3H, 3H m), 2.34 (s, 3H, 3H M) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.7, 142.1, 140.2, 139.8, 138.2, 137.2, 135.0, 134.3, 132.0, 130.4, 130.1, 129.5, 128.5

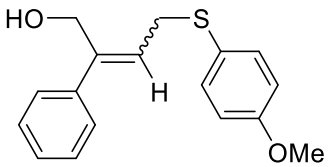
(4C), 128.5 (2C), 127.7, 127.6, 127.4, 126.5, 126.4 (2C), 126.3, 126.2, 126.1, 122.8, 67.4, 59.4, 32.2, 31.7, 20.7, 20.3 ppm.

**4-(benzylthio)-2-phenylbut-2-en-1-ol (3.20)**[75]



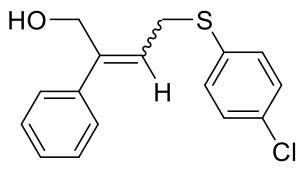

Following the general procedure, product 3.20 was isolated as a yellow oil in 79% yield (44.8 mg, 0.17 mmol). *Z/E* ratio was determined by $^{1}$H NMR to be 7:3; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.48-7.45 (m, 4H), 7.40-7.29 (m, 12H), 7.25-7.14 (m, 4H), 5.99 (t, *J* = 8.0 Hz, 1 H, 1H M, *Z* isomer ), 5.82 (tt, *J* = 7.8, 1.5 Hz, 1H, 1H m, *E* isomer), 4.48 (s, 2H, 2H M), 4.37 (s, 2H, 2H m), 3.80 (s, 2H, 2H M), 3.63 (s, 2H, 2H m), 3.33 (d, *J* = 8.0 Hz, 2H, 2H M), 3.11 (d, *J* = 7.8 Hz, 2H, 2H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 142.7, 142.1, 140.3, 138.5, 138.0, 137.3, 128.9 (2C), 128.8 (2C), 128.7 (2C), 128.6 (2C), 128.6 (2C), 128.5 (2C), 128.4, 127.7 (2C), 127.6, 127.2, 127.1, 126.9, 126.3 (2C), 124.1, 67.4, 59.6, 36.0, 35.9, 29.6, 28.7 ppm.

**4-((4-methoxyphenyl)thio)-2-phenylbut-2-en-1-ol (3.21)**[75]



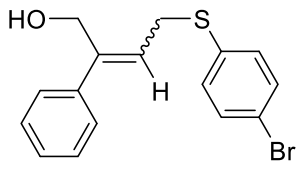

Following the general procedure, product **3.21** was isolated as a yellow oil in 68% yield (40.8 mg, 0.14 mmol). *Z/E* ratio was determined by $^{1}$H NMR to be 7:3; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.47-7.41 (m, 6H), 7.38-7.26 (m, 6H), 7.06-7.04 (m, 2H), 6.90-6.81 (m, 4H), 5.99 (t, *J* = 8.2 Hz, 1H, 1H M, *Z* isomer), 5.85 (tt, *J* = 7.8, 1.4 Hz, 1H, 1H m, *E* isomer), 4.29 (s, 2H, 2H m), 4.25 (s, 2H, 2H M), 3.82 (s, 3H, 3H m), 3.81 (s, 3H, 3H M), 3.66 (d, *J* = 8.2 Hz, 2H, 2H M), 3.43 (d, *J* = 7.7 Hz, 2H, 2H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 159.8, 159.2, 143.2, 141.7, 140.4, 137.3, 135.7 (2C), 134.0 (2C), 128.5 (2C), 128.5 (2C), 128.3 (2C), 127.6 (2C), 127.5, 126.7 (2C), 126.4 (2C), 125.8, 124.9, 123.3, 114.6, 114.5, 67.4, 59.3, 55.4 (2C), 34.7, 34.5 ppm.

**4-((4-chlorophenyl)thio)-2-phenylbut-2-en-1-ol (3.22)**



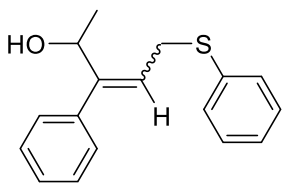

Following the general procedure, product **3.22** was isolated as a yellow oil in 82% yield (49.9 mg, 0.17 mmol). *Z/E* ratio was determined by $^{1}$H NMR to be 1:1; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.43-7.28 (m, 12H), 7.22-7.20 (m, 2H), 7.16-7.12 (m, 4H), 5.98 (t, *J* = 8.0 Hz, 1 H, 1H M, *Z* isomer), 5.85 (tt, *J* = 7.7, 1.5 Hz, 1H, 1H m, *E* isomer), 4.41 (s, 2H, 2H M), 4.31 (s, 2H, 2H m), 3.77 (d, *J* = 8.1 Hz, 2H, 2H M), 3.52 (d, *J* = 7.7 Hz, 2H, 2H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.9, 142.4, 140.0, 137.0, 134.3, 133.7, 133.3, 132.8 (2C), 132.3, 131.3 (2C), 129.1, (2C) 128.9 (2C), 128.6 (2C), 128.5 (4C), 127.8, 127.8, 126.4 (2C), 126.0, 122.4, 67.2, 59.5, 33.0, 32.7 ppm; **HRMS** (APCI+, MeOH): *m*/*z* calcd for $C_{16}H_{14}ClS$, $[M–CH_3OH]^+$: 273.0499, found: 273.0495.

**4-((4-bromophenyl)thio)-2-phenylbut-2-en-1-ol (3.23)**[75]




Following the general procedure, product **3.23** was isolated as a yellow oil in 71% yield (49.8 mg, 0.15 mmol). *Z/E* ratio was determined by $^{1}$H NMR to be 6:4; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.47-7.28 (m, 14H), 7.15-7.12 (m, 2H), 7.09-7.05 (m, 2H), 5.98 (t, *J* = 8.0 Hz, 1H, 1H M, *Z* isomer), 5.85 (tt, *J* = 7.7, 1.5 Hz, 1H, 1H m, *E* isomer), 4.43 (s, 2H, 2H M), 4.32 (m, 2H, 2H m), 3.78 (d, *J* = 8.1 Hz, 2H, 2H M), 3.52 (dt, *J* = 7.7, 1.0 Hz, 2H, 2H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.9, 142.5, 140.0, 137.0, 135.1, 134.4, 132.8 (2C), 132.1 (2C), 131.8 (2C), 131.4 (2C), 128.6 (2C), 128.5 (2C), 128.5 (2C), 127.8, 127.8, 126.4 (2C), 125.9, 122.3, 121.2, 120.1, 67.2, 59.5, 32.8, 32.5 ppm.

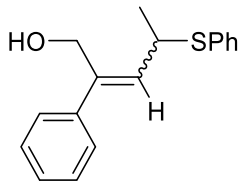
**3-phenyl-5-(phenylthio)pent-3-en-2-ol (3.24)**




Following the general procedure, product **3.24** was isolated as a gray oil in 64% yield (33.9 mg, 0.13 mmol). *Z/E* ratio was determined by $^{1}$H NMR to be 2:9; **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.52-7.48 (m, 2H), 7.37-7.20 (m, 14H), 7.05-7.03 (m, 4H), 5.88 (t, *J* = 7.6 Hz, 1H, 1H M, *E* isomer), 5.70 (t, *J* = 8.2 Hz, 1H, 1H m, *Z* isomer), 4.84 (q, *J* = 6.6 Hz, 1H, 1H m), 4.51 (q, *J* = 6.4 Hz, 1H, 1H M), 3.81 (dd, *J* = 8.1, 4.3 Hz, 2H, 2H m), 3.43 (d, *J* = 7.7 Hz, 2H, 2H M), 1.20 (d, *J* = 6.4 Hz, 3H, 3H M), 1.16 (d, *J* = 6.5

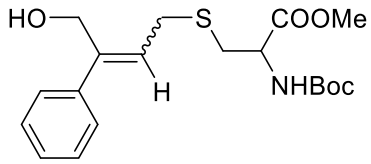
Hz, 3H, 3H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 148.1, 146.8, 140.3, 137.1, 135.7, 135.2, 132.3, 132.0 (2C), 130.4 (2C), 129.0 (2C), 128.8 (2C), 128.3 (2C), 128.2 (2C), 128.0 (2C), 127.4, 127.3 (2C), 127.2, 126.4, 126.0, 122.0, 71.8, 66.2, 32.7, 32.5, 22.2, 21.9 ppm; **HRMS** (ESI+, MeOH): *m*/*z* calcd for $C_{17}H_{18}NaOS$, $[M + Na]^+$: 293.0971, found: 293.0973.

**2-phenyl-4-(phenylthio)pent-2-en-1-ol (3.25)**




Following the general procedure, product **3.25** was isolated as a yellow oil in 63% yield (33.3 mg, 0.12 mmol). *Z/E* ratio was determined by $^1$H NMR to be 7:3; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.56-7.54 (m, 4H), 7.41-7.25 (m, 14H), 6.98-6.96 (m, 2H), 5.76 (d, *J* = 10.4 Hz, 1H, 1H M, *Z* isomer), 5.67 (dt, *J* = 10.6, 1.5 Hz, 1H, 1H m, *E* isomer), 4.30 – 4.22 (m, 2H, 2H M), 4.18 (m, 3H, 1H M + 2H m), 3.88 (dq, *J* = 10.5, 6.8 Hz, 1H, 1H m), 1.49 (d, *J* = 6.6 Hz, 3H, 3H M), 1.40 (d, *J* = 6.8 Hz, 3H, 3H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.1, 140.2, 139.5, 137.5, 135.2 (2C), 134.4, 134.0, 133.4 (2C), 133.4 (2C), 130.1, 129.0 (2C), 128.6, 128.5 (2C), 128.4 (2C), 128.4, 128.3, 127.5 (2C), 127.5, 127.3, 126.4 (2C), 67.4, 59.7, 43.1, 42.1, 21.2, 21.1 ppm; **HRMS** (ESI+, MeOH): *m*/*z* calcd for $C_{17}H_{18}NaOS$, $[M + Na]^+$: 293.0971, found: 293.0970.

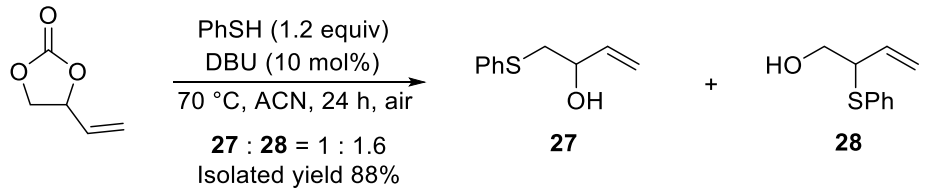
**Methyl-*N*-(*tert*-butoxycarbonyl)-*S*-(4-hydroxy-3-phenylbut-2-en-1-yl)cysteinate (3.26)**



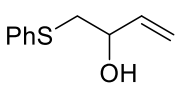

Following the general procedure, product **3.26** was isolated as a yellow oil in 26% yield (20.8 mg, 0.05 mmol). *Z/E* ratio was determined by $^1$H NMR to be 4:6; **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.51-7.49 (m, 2H), 7.42-7.30 (m, 6H), 7.25-7.23 (m, 2H), 5.93 (t, *J* = 8.0 Hz, 1H, 1H M, *Z* isomer), 5.85 (t, *J* = 7.8 Hz, 1H, 1H m, *E* isomer), 5.41 (d, *J* = 7.0 Hz, 1H, 1H m), 5.21 (d, *J* = 8.6 Hz, 1H, 1H M), 4.60 (d, *J* = 3.7 Hz, 2H, 2H m), 4.36 (s, 2H, 2H M), 3.79 (s, 3H, 3H m), 3.72 (s, 3H, 3H M), 3.48 (qd, *J* = 13.6, 8.0 Hz, 2H, 2H m), 3.18 – 3.16 (m, 2H, 2H M), 2.97 (dd, *J* = 5.8, 2.8 Hz, 2H, 2H M), 2.77 (dd, *J* = 13.8, 6.4 Hz, 2H, 2H m), 1.47 (s, 9H, 9H M), 1.46 (s, 9H, 9H m) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.7 (2C=O), 155.2, 143.8, 142.5 (2Cq), 140.3, 137.4, 128.6 (2C), 128.5 (2C),

128.5 (2C), 127.7, 127.6, 126.6, 126.4 (2C), 123.3, 80.6, 80.4, 67.2, 59.3, 53.6, 53.5, 52.7, 52.5, 34.3, 33.5, 31.0, 29.7, 28.3 (2 × *t*Bu) ppm; **HRMS** (ESI+, MeOH): *m*/*z* calcd for $C_{19}H_{27}NNaO_5S$, $[M + Na]^+$: 404.1502, found: 404.1514.

## 3.5.9 Reaction with an unsubstituted vinyl carbonate

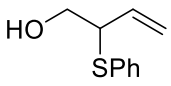



A screw-capped vial was charged with the unsubstituted vinyl cyclic carbonate (19 µL, 0.21 mmol, 1 equiv), DBU (3.2 mg, 0.021 mmol, 10 mol%), thiophenol (26 µL, 0.252 mmol, 1.2 equiv) and dry ACN (0.2 mL). The reaction mixture was stirred at 70 ºC for 24 h, and then purified by flash column chromatography on silica gel (hexane:ethyl acetate, 5:1 v/v) to afford **27** and **28** in a 88% combined yield as a separable mixture of products in a 1:1.6 ratio (note: this ratio was determined from the crude mixture by $^{1}$H NMR).



**27**

**$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.41 (m, 2H), 7.35 – 7.23 (m, 3H), 5.91 (ddd, *J* = 17.3, 10.5, 5.8 Hz, 1H), 5.35 (dt, *J* = 17.2, 1.4 Hz, 1H), 5.21 (dt, *J* = 10.5, 1.3 Hz, 1H), 4.23 (dddt, *J* = 8.5, 5.5, 4.1, 1.3 Hz, 1H), 3.19 (dd, *J* = 13.7, 4.1 Hz, 1H), 2.98 (dd, *J* = 13.7, 8.5 Hz, 1H); **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.4, 130.3, 129.1, 126.7, 116.3, 70.4, 41.9; **HRMS** (ESI+, MeOH, mixture of **27** and **28**): *m/z* calcd for $C_{10}H_{12}NaOS$, $[M + Na]^+$: 209.0501, found: 209.0499.



**28**

**$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.48 – 7.45 (m, 2H), 7.35 – 7.29 (m, 3H), 5.82 (ddd, *J* = 17.6, 10.0, 7.9 Hz, 1H), 5.20 (ddt, *J* = 14.1, 4.1, 1.1 Hz, 2H), 3.82 – 3.67 (m, 3H); **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 135.2, 133.2, 128.9, 127.7, 118.2, 63.6, 54.6; **HRMS** (ESI+, MeOH, mixture of **27** and **28**): *m/z* calcd for $C_{10}H_{12}NaOS$, $[M + Na]^+$: 209.0501, found: 209.0499.

*Chapter 3*

# *Chapter 4. Ring-opening polymerization of functionalized aliphatic bicyclic carbonates*

The results described in this chapter have been submitted as:

J. Ni, M. Lanzi, D. H. Lamparelli, A. W. Kleij, *Polym. Chem.* **2023**, *14*, DOI: 10.1039/d3py00860f

UNIVERSITAT ROVIRA I VIRGILI
RING-OPENING OF CYCLIC CARBONATES: FROM FINE CHEMICALS TO CO2-BASED POLYMERS
Jixiang Ni

# 4.1. Introduction

## 4.1.1 Background of aliphatic polycarbonates

Environmentally friendly and modular approaches to functional polymers are key to the development of sustainable materials.[79] Among the functional polymers developed to date, aliphatic polycarbonates (APCs) have received considerable consideration as a result of their low toxicity, high biocompatibility, and degradability.[80] These features are especially attractive in the context of applications that focus on medical devices and drug delivery systems.[81] Whereas the conventional way of polycarbonate synthesis relies on the use of phosgene derivatives, alternative strategies based on the use of carbon dioxide ($CO_2$) have recently emerged. The utilization of $CO_2$ as an abundant, cheap and safe reagent is considered to be a key factor for innovative process design towards APCs with biodegradation potential. APCs are typically prepared via two main approaches, either via ring-opening copolymerization (ROCOP) of epoxides and carbon dioxide,[82] or through anionic ring-opening polymerization (AROP) of suitable cyclic carbonate monomers. Although the use of $CO_2$ as a monomer is attractive, the ROCOP approach using (acyclic) epoxides typically suffers from limitations in functional group diversity or compatibility, is frequently accompanied by the formation of "ether" linkages (i.e., structural defects) and the concomitant formation of five-membered cyclic carbonates as by-products affecting the overall chemo-selectivity.

[79] (a) K. Wang, K. Amin, Z. An, Z. Cai, H. Chen, H. Chen, Y. Dong, X. Feng, W. Fu, J. Gu, Y. Han, D. Hu, R. Hu, D. Huang, F. Huang, F. Huang, Y. Huang, J. Jin, X. Jin, Q. Li, T. Li, Z. Li, Z. Li, J. Liu, J. Liu, S. Liu, H. Peng, A. Qin, X. Qing, Y. Shen, J. Shi, X. Sun, B. Tong, B. Wang, H. Wang, L. Wang, S. Wang, Z. Wei, T. Xie, C. Xu, H. Xu, Z.-K. Xu, B. Yang, Y. Yu, X. Zeng, X. Zhan, G. Zhang, J. Zhang, M. Q. Zhang, X.-Z. Zhang, X. Zhang, Y. Zhang, Y. Zhang, C. Zhao, W. Zhao, Y. Zhou, Z. Zhou, J. Zhu, X. Zhu, B. Z. Tang, Mater. *Chem. Front.* **2020**, *4*, 1803-1915; (b) G. Chyr, J. M. DeSimone, *Green Chem.* **2023**, *25*, 453-466.

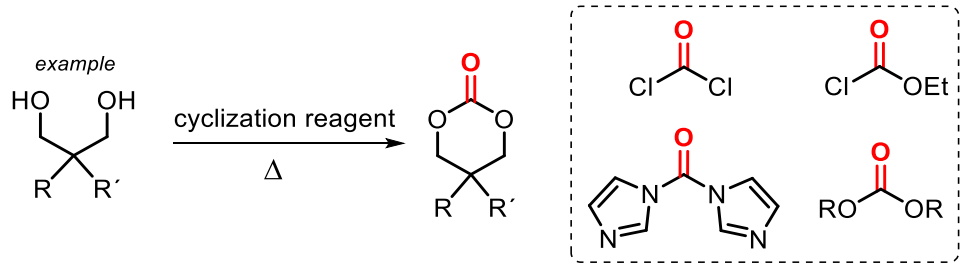
[80] (a) B. Grignard, S. Gennen, C. Jérôme, A. W. Kleij and C. Detrembleur, *Chem. Soc. Rev*, **2019**, 48, 4466-4514; (b) W. Yu, E. Maynard, V. Chiaradia, M. C. Arno and A. P. Dove, *Chem. Rev.* 2021, **121**, 10865-10907; (c) J. Xu, E. Feng, J. Song, *J. Appl. Polym. Sci.* **2014**, *131*, no. 39822; (d) K. J. Zhu, R. W. Hendren, K. Jensen, C. G. Pitt, *Macromolecules* **1991**, *24*, 1736-1740; (e) G. A. Bhat, M. Luo, D. J. Darensbourg, *Green Chem.* **2020**, *22*, 7707-7724.

[81] H. Tian, Z. Tang, X. Zhuang, X. Chen, X. Jing, *Progress in Polym. Sci.* **2012**, *37*, 237-280.

[82] (a) S. Paul, Y. Zhu, C. Romain, R. Brooks, P. K. Saini, C. K. Williams, *Chem. Commun.* **2015**, *51*, 6459-6479; (b) C. A. L. Lidston, S. M. Severson, B. A. Abel, G. W. Coates, *ACS Catal.* **2022**, *12*, 11037-11070; (c) X. Liang, F. Tan, Y. Zhu, *Front. Chem.* **2021**, *9*, no. 647245.

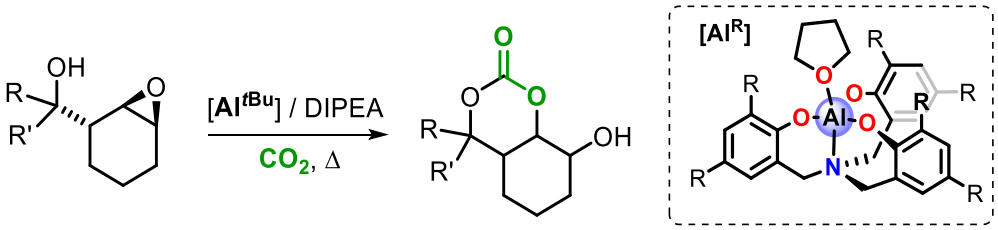
### 4.1.2 Synthesis of larger ring cyclic carbonates

The AROP reaction of 6- and 7- membered cyclic carbonates (abbreviated as 6MCCs and 7MCCs) has emerged as a more robust and versatile approach for the preparation of functional polycarbonates.[83] Larger ring cyclic carbonates such as 6MCCs have over time become popular monomers but are often prepared using harmful and low-atom economy reagents such as phosgene and its derivatives (Scheme 4.1).[84]




**Scheme 4.1** Common approach towards polymerizable six-membered cyclic carbonates

## 4.2 Objectives

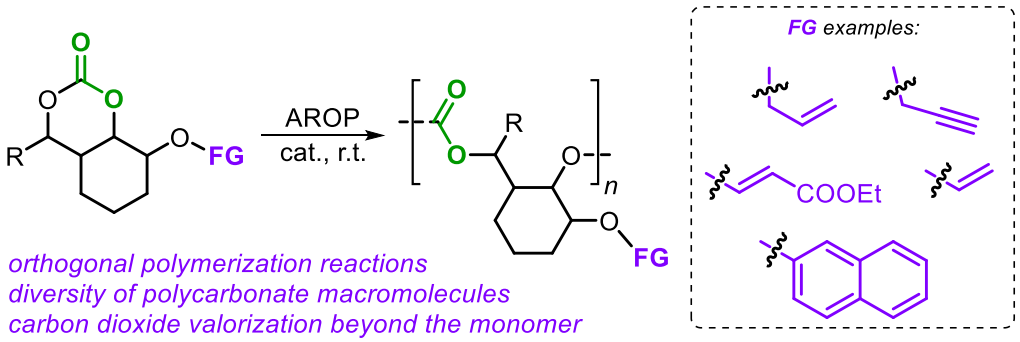



**Scheme 4.2** Previously reported bicyclic monomer comprising of a secondary free alcohol.

[83] (a) S. Tempelaar, L. Mespouille, O. Coulembier, P. Dubois, A. P. Dove, *Chem. Soc. Rev.* **2013**, *42*, 1312-1336; (b) T. M. McGuire, C. Pérale, R. Castaing, G. Kociok-Köhn, A. Buchard, *J. Am. Chem. Soc.* **2019**, *141*, 13301-13305; (c) W. Guerin, A. Khadri Diallo, E. Kirilov, M. Helou, M. Slawinski, J.-M. Brusson, J.-F. Carpentier, S. M. Guillaume, *Macromolecules* **2014**, *47*, 4230-4235; (d) J. L. Hedrick, V. Piunova, N. H. Park, T. Erdmann, P. L. Arrechea, *ACS Macro Lett.* **2022**, 11, 368-375; (e) P. Brignou, M. Priebe Gil, O. Casagrande, J.-F. Carpentier, S. M. Guillaume, *Macromolecules* **2010**, *43*, 8007-8017; (f) W. Zhang, J. Dai, Y.-C. Wu, J.-X. Chen, S.-Y. Shan, Z Cai, J.-B. Zhu, *ACS Macro Lett.* **2022**, *11*, 173-178.

[84] Y. Watanabe, S. Takaoka, Y. Haga, K. Kishi, S. Hakozaki, A. Narumi, T. Kato, M. Tanaka, K. Fukushima, *Polym. Chem.* **2022**, *13*, 5193-5199.

Our group recently reported a simple catalytic $CO_2$-based approach towards bicyclic 6MCCs (Scheme 4.2).[85] This approach benefits from a double and cooperative activation strategy with a pendent alcohol group activating $CO_2$ while an Al-complex promotes intramolecular ring-opening of the oxirane in the substrate through coordination. This approach allowed to devise a structurally diverse range of novel bicyclic 6MCCs under mild conditions, and importantly enabled the isolation of compounds featuring a synthetically useful hydroxyl group. We envisioned that these –OH groups could be exploited such that different functionalities could be introduced in these 6MCC monomers. This would then offer a simple protocol to functional carbonates for AROP leading ultimately to functionalized APCs (Scheme 4.3), and herein we describe the advances we have made in the area.




**Scheme 4.3** Current approach towards functional polycarbonates through AROP of 6MCCs.

## 4.3 Results and discussion

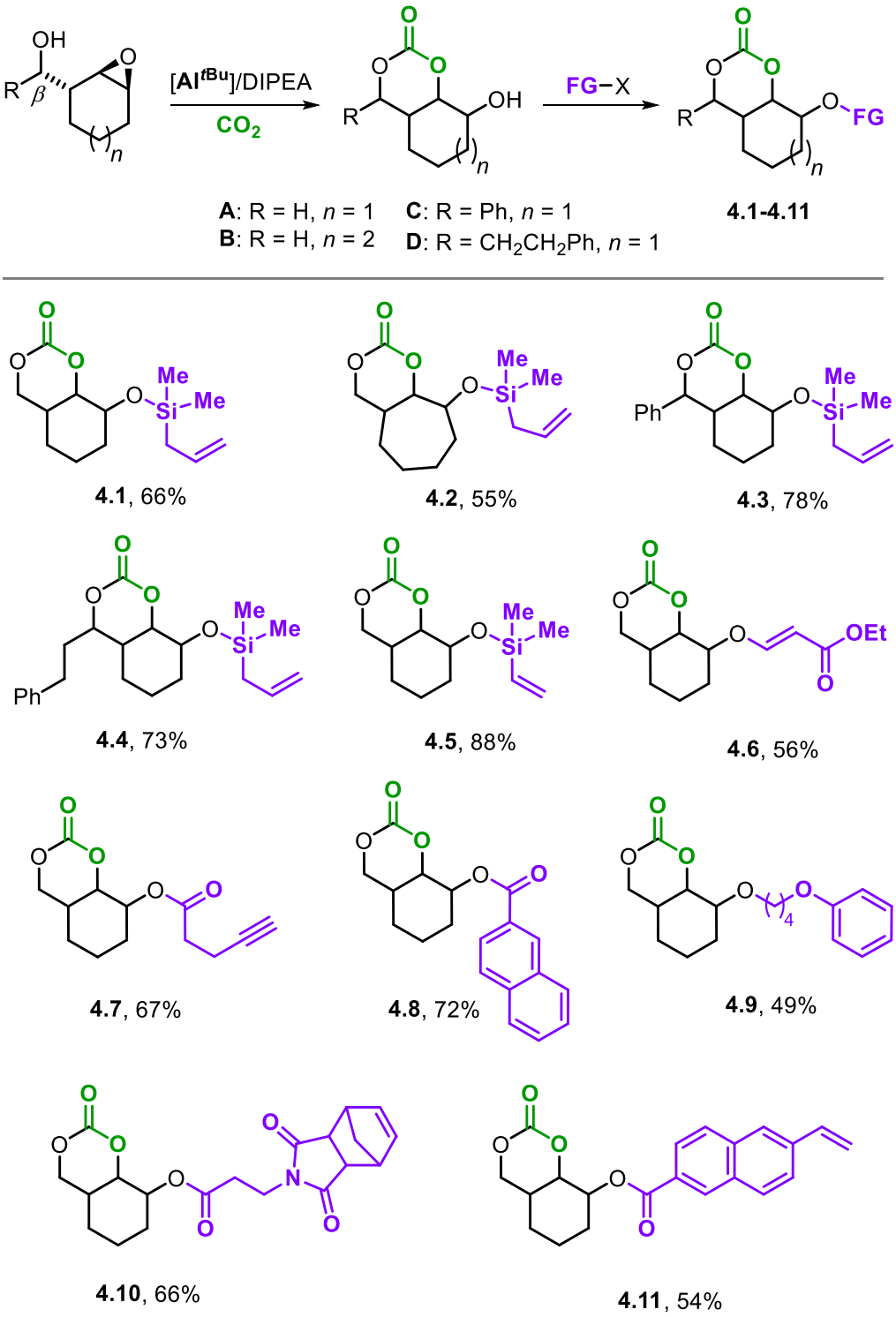
Taking advantage of the residual hydroxy group in precursors **A**-**D**, we began our investigation with the synthesis of a small library of 6MCCs decorated with various synthetically useful moieties (Scheme 4.4). The silyl-ether derivatives **4.1**-**4.5** were all prepared using the respective silyl-chloride reagent and performing the coupling reaction in the presence of an excess of triethylamine in dry $CH_2Cl_2$ at r.t. This approach allowed to introduce in the different parent scaffolds (**A**-**D**) either allyl (products **4.1**-**4.4**) or vinyl groups (compound **4.5**) with appreciable yields obtained for the isolated bicyclic 6MCCs.

[85] (a) C. Qiao, W. Shi, A. Brandolese, J. Benet-Buchholz, E. C. Escudero-Adán, A. W. Kleij, *Angew. Chem. Int. Ed* **2022**, *61*, e202205053; (b) C. Qiao, A. Villar-Yanez, J. Sprachmann, B. Limburg, C. Bo, A. W. Kleij, *Angew. Chem. Int. Ed*. **2020**, *59*, 18446-18451.

Monomers **4.3** and **4.4** are additionally equipped with an aryl/alkyl substituent at the other side of the bicycle allowing to scrutinize their influence on the polymerizability of these 6MCCs. An oxo-Michael addition of precursor **A** to ethyl propiolate in the presence of *N*-methyl morpholine (NMM, 20 mol%) in $CH_3CN$ at r.t. afforded monomer **4.6** in 56% yield, and shows that also acrylic esters can be readily introduced as functional groups.

Steglich esterification (using DCC, dicyclohexylcarbodiimide) enables the coupling of various functional carboxylic acids with the secondary alcohol group of **A**. Homopropargylic carboxylic acid is smoothly coupled with **A** providing **4.7** in 67% yield, expanding the functionality pool to terminal alkynes. At this stage, we believed that the introduction of a rigid naphthyl moiety in the bicyclic 6MCC scaffold could be a way to produce, after AROP, APCs with larger aromatic groups favorable towards a higher thermal resistance. Product **4.8** that comprises a naphthyl ester group could be isolated in 72% yield. To further modulate the thermal properties of the target APCs, a more flexible aliphatic chain could also be introduced (**4.9**, 49%) by performing a coupling between **A** and Kobayashi aryne precursors in THF.[86] Finally, we aimed at designing bifunctional monomers that contain two distinct and polymerizable units (**4.10** and **4.11**) so that orthogonal polymerization strategies could be enabled. Monomer **4.10** was attained in 66% yield by esterification of **A** with 3-(1,3-dioxo-1,3,3a,4,7,7a-hexahydro-2*H*-4,7-methanoisoindol-2-yl)-propanoic acid, whereas **4.11** could be prepared in 54% yield by treatment of **A** with 6-vinyl-2-naphthoic acid in the presence of DCC. All new monomers **4.1**-**4.11** were fully characterized by $^{1}H$ NMR, $^{13}C$ NMR, high-resolution ESI(+)-MS and IR analysis.

[86] (a) S. S. Bhojgude, A. Bhunia, A. T. Biju, *Acc. Chem. Res*. **2016**, *49*, 1658-1670; (b) M. Thangaraj, S. S. Bhojgude, M. V. Mane, A. T. Biju, *Chem. Commun.* **2016**, *52*, 1665-1668.




**Scheme 4.4** General synthetic scheme for the functionalized bicyclic six-membered cyclic carbonate monomers **4.1-4.11** derived from precursor 6MCCs **A-D**. **FG**-X stands for the coupling agent used to produce the functionalized bicyclic 6MCC.

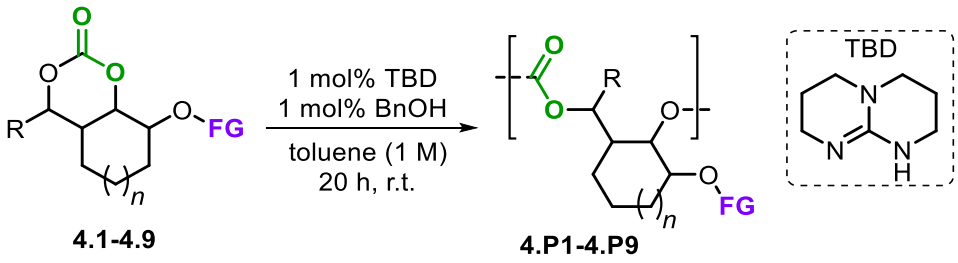
To study the reactivity of the monomers **4.1**-**4.9**, we then directed our attention towards AROP using 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) as a benchmark organocatalyst in the presence of an equimolar quantity of benzyl alcohol as initiator at r.t.[87] These preferable mild temperature conditions were chosen as to avoid possible depolymerization of the formed polycarbonates, which is feasible with TBD at elevated temperatures.[88] In nearly all cases, reasonable control of the polymerization process was achieved (*Đ* values in the range 1.29–1.64) delivering the functionalized APCs with low to moderately high molecular weights ($M_n$´s 3.2–11.7 Kg/mol). Allyl-functionalized monomers **4.1** and **4.2** were both "ring-open polymerized" to their APCs **4.P1** and **4.P2** with around 90% conversion (Table 4.1, entries 1-2). Contrary to these promising results, monomers **4.3** and **4.4** proved to be completely unreactive towards formation of **4.P3** and **4.P4** even when raising the reaction temperature to 60 °C and extending the reaction time to 48 h (entries 3 and 4). This can be explained by the additional substitution on the carbonate ring, which apparently creates a too large steric impediment for the incoming hydrogen-bond activator (TBD) and BnOH initiator.

The AROP of the vinyl derivative **4.5** (entry 5) gave **4.P5** with the highest molecular weight ($M_n$ = 11.7 Kg/mol, *Đ* = 1.44) among the series. Other functional groups such as an acrylic ester (**4.6**) and a terminal alkyne (**4.7**) were compatible with the reaction conditions delivering **4.P6** and **4.P7** with modest $M_n$ values and somewhat lower dispersities (entries 6 and 10). We used monomer **4.6** to examine the effect of the catalyst and initiator loading (cf., entries 6-9), but found that the best conditions (1 mol% of both TBD and BnOH) is most beneficial for these kind of bicyclic carbonate monomers. Macromolecule **4.P8** showed a substantial decrease in molecular weight ($M_n$ = 3.2 Kg/mol, entry 11), which we ascribe to the more hindered carbonate ring upon activation by TBD following ring-opening by the initiator.

[87] C. Maquilón, F. Della Monica, B. Limburg, A. W. Kleij, *Adv. Synth. Catal.* **2021**, *363*, 4033-4040.

[88] (a) C. Li, R. J. Sablong, R. A. T. M. van Benthem, C. E. Koning, *ACS Macro Lett.*, **2017**, *6*, 684-688; See also: (b) F. N. Singer, A. C. Deacy, T. M. McGuire, C. K. Williams, A. Buchard, *Angew. Chem. Int. Ed.* **2022**, *61*, e202201785.

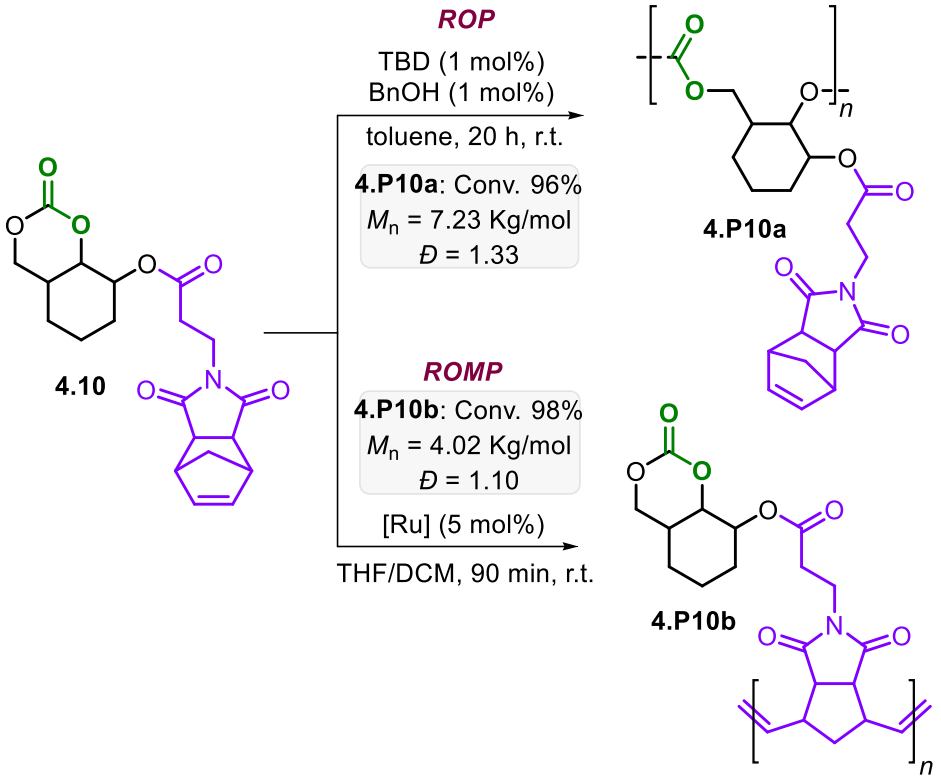
**Table 4.1** AROP of the monomers **4.1-4.9** using TBD/BnOH in toluene.[a]




| Entry | M | Conv. (%)[b] | $M_n$ (Kg/mol)[c] | $Đ$[c] | $T_g$ (°C)[d] |
|---|---|---|---|---|---|
| 1[e] | **4.1** | 91 | 5.6 | 1.54 | 19 |
| 2 | **4.2** | 86 | 6.8 | 1.64 | 11 |
| 3[f] | **4.3** | – | – | – | – |
| 4[f] | **4.4** | – | – | – | – |
| 5[e] | **4.5** | 95 | 11.7 | 1.44 | 57 |
| 6 | **4.6** | 87 | 6.8 | 1.50 | 70 |
| 7[g] | **4.6** | 90 | 3.5 | 1.59 | – |
| 8[h] | **4.6** | 89 | 5.0 | 1.36 | – |
| 9[i] | **4.6** | 88 | 4.3 | 1.71 | – |
| 10 | **4.7** | 98 | 6.9 | 1.29 | 41 |
| 11 | **4.8** | 90 | 3.2 | 1.61 | 106 |
| 12 | **4.9** | 84 | 7.0 | 1.44 | 15 |

[a]Unless otherwise specified, the polymerization reactions were performed using 0.30 mmol of monomer, 1 mol% of TBD, 1 mol% of BnOH in toluene (1 M) for 20 h at r.t. (20 ºC). [b]Conversion of the monomer was determined by $^1$H NMR ($CDCl_3$) spectroscopy. [c]Determined by GPC in THF calibrated with PPO standards. [d]Obtained from DSC analysis, the data refer to the second heating. [e]Reaction was performed at a 0.60 mmol scale. [f]Polymerization was performed both at 45 °C and 60 °C for 48 h with the same results. [g]TBD/BnOH loading was 0.5/0.5 mol%. [h]TBD/BnOH loading was 2.0/2.0 mol%. [i]TBD/BnOH loading was 2.0/1.0 mol%. Note that M stands for monomer.

Though a low(er) molecular weight was attained for **4.P8**, the measured glass transition temperature ($T_g$ = 106 ºC) was significantly higher compared to the other APCs, which is likely due to an increase in pi-pi stacking in the solid state. The polymerization of monomer **4.9** provided a molecular weight, polymer dispersity and $T_g$ (entry 12) similar to polymers **4.P1** and **4.P2**. Purified samples of all the APCs (white powders) reported in Table 4.1 were obtained through simple precipitation of the crude reaction mixtures from methanol, and the analytical data and spectra are provided in the experimental section.

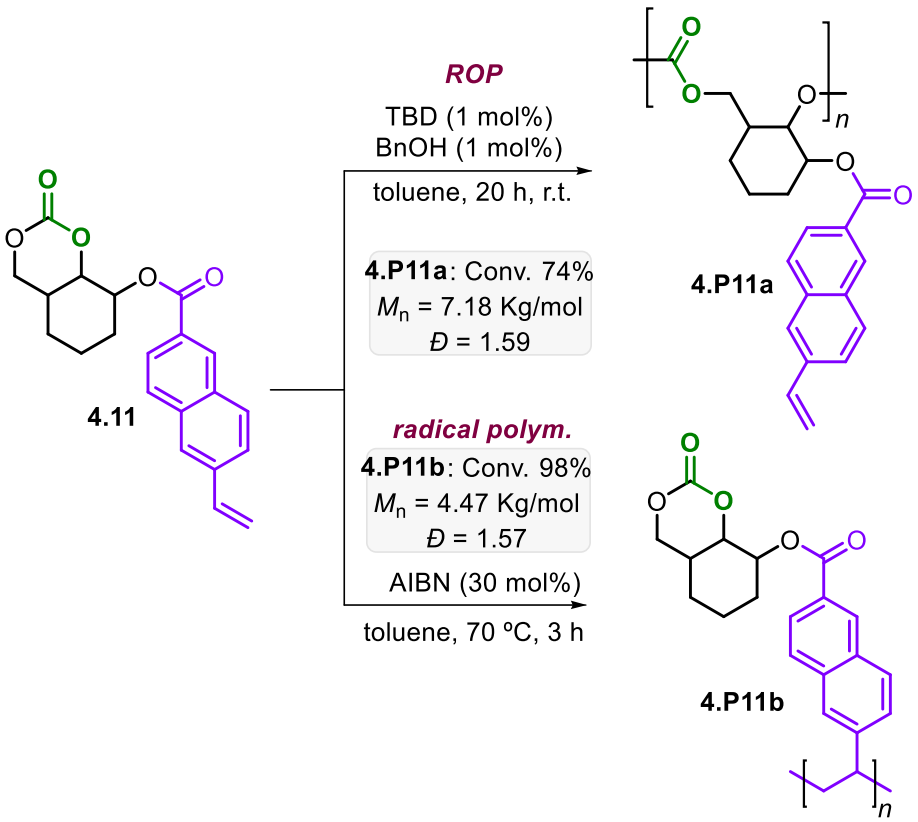



**Scheme 4.5** Synthesis of polymers **4.P10a** and **4.P10b**.

Additionally, bifunctional monomers **4.10** and **4.11** bearing orthogonal polymerizable groups were tested (Schemes 4.5 and 4.6). Under the AROP reaction conditions reported in Table 4.1, the monomers **4.10** and **4.11** are smoothly transformed delivering **4.P10a** and **4.P11a** with appreciable molecular weight ($M_n$ = 7.23 and 7.18 Kg/mol, respectively) and reasonable polydispersities ($Đ$ = 1.33 and 1.59, respectively). Monomer **4.10** has apart from the 6MCC fragment an additional strained cyclohexene moiety, which is suitable for ring-opening metathesis polymerization (ROMP). ROMP is nowadays a robust and selective approach for the controlled preparation of polyolefins, especially starting from strained structures.[89] Treatment of **4.10** with Grubbs 3rd generation catalyst, a complete conversion was obtained within 90 min at r.t. yielding the desired polyolefin **4.P10b** (Scheme 4.5) with a low polydispersity ($Đ$ = 1.10) and a modest molecular weight ($M_n$ = 4.02 Kg/mol). It should be noted that lower amounts of Ru-catalyst also worked well leading to gel-like products. However, in these cases,

[89] (a) S. Sutthasupa, M. Shiotsuki, F. Sanda, *Polym. J.* **2010**, *42*, 905–915; (b) M. Yasir, P. Liu, I. K. Tennie, A. F. M. Kilbinger, *Nat. Chem.* **2019**, *11*, 488–494; (c) Y.-C. Wu, H.-Z. Fan, W. Zhang, M.-Y. Wang, Z. Cai, J.-B. Zhu, *Macromolecules* **2022**, *55*, 9232–9241. See also ref. 5b.

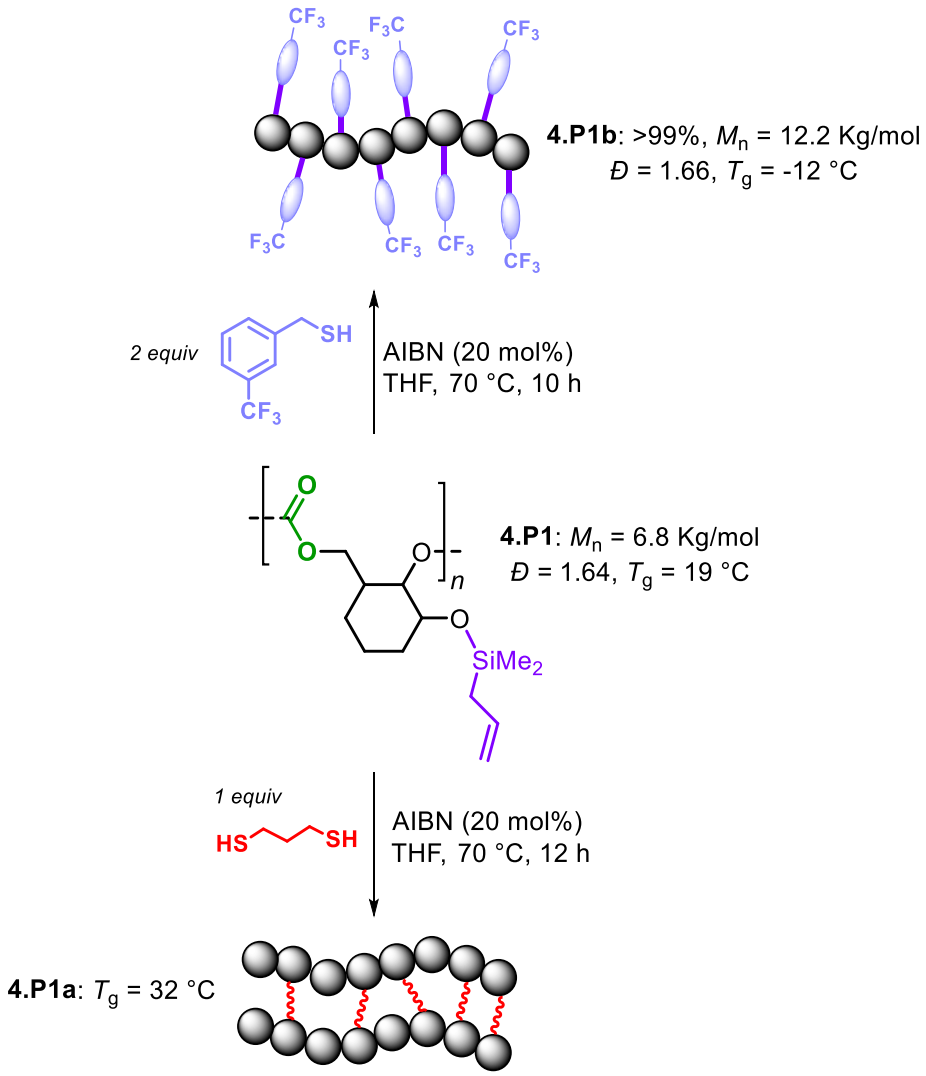
solubility issues did not allow for further characterization. Azobisisobutyronitrile (AIBN) initiated radical polymerization of the vinyl moiety present in monomer **4.11** led to full conversion in 3 h at 70 °C yielding poly-naphthalene product **4.P11b** ($M_n$ = 4.47 Kg/mol, $Đ$ = 1.57). Noteworthy, complete chemoselectivity is observed in all transformations of **4.P10** and **4.P11** preserving the other functional groups (i.e., the 6MCC, norbornene or vinyl moieties, respectively) reprsenting additional handles for further transformations.




**Scheme 4.6** Synthesis of polymers **4.P11a** and **4.P11b**.

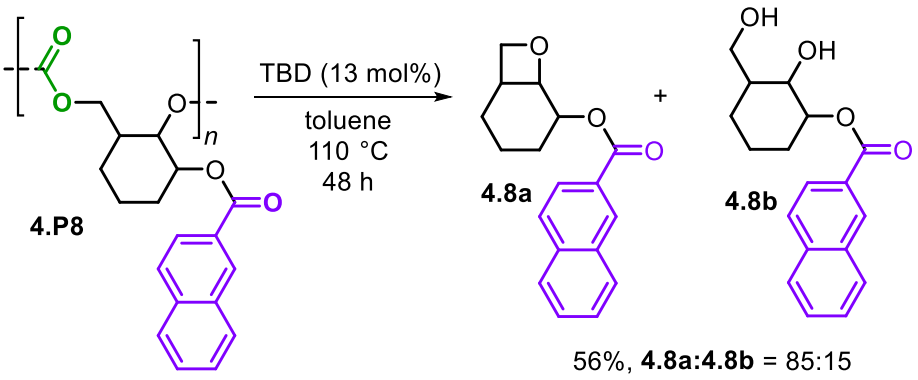
Post-polymerization modification of **4.P1** was also conducted to show the robustness of the polycarbonate macromolecules (Scheme 4.7). Two approaches were considered, a "click" reaction using a mono-thiol and a cross-linking reaction using a di-thiol reagent. First, **4.P1** was subjected to cross-linking in the presence of 1,3-propanedithiol and AIBN as radical initiator at 70 °C. Under these conditions, full conversion of the alkenes moieties was observed after 12 h. Due to the high level of crosslinking, **4.P1a** was insoluble in the typical organic solvents preventing thus further characterization by NMR and GPC. IR analysis of **4.P1a** showed a disappearance of the initial C=C–H absorption (in **4.P1**) at 3077 $cm^{-1}$,

suggesting that most of the double bonds had reacted. Differential scanning calorimetry (DSC) analysis showed that **4.P1a** has a $T_g$ of 32 ºC, which is 12 º higher than the parent polymer **4.P1** thus implying that at least part of the silyl-allyl fragments took part in the crosslinking event. The same silyl-allyl groups were also allowed to react with trifluorobenzyl thiol under similar reaction conditions to quantitatively afford (soluble) **4.P1b**. Gel-permeation chromatography analysis (GPC) of **4.P1b** displayed a significant increase in the polymer weight (the $M_n$ rose to 12.2 Kg/mol) while the polydispersity remained virtually the same. This seems to corroborate with a high functionalization degree of **4.P1** and a substantial mass increase of the repeat units (270→462 g/mol, ΔM = 42%), and thus the polymer as a whole.




**Scheme 4.7** Thiol-ene based functionalization and cross-linking of **4.P1**.

Finally, chemical degradation studies were conducted to examine whether these new polycarbonates could be (selectively) depolymerized. Depolymerization of **4.P8** was assessed using TBD as catalyst in toluene at 110 °C, as previously a biobased polycarbonate was reported to fully decompose towards its original monomers under such conditions.[90] In the present case, a similar catalytic degradation was performed and the reaction delivered two new products: a fused bicyclic oxetane **4.8a** and the diol **4.8b** as an inseparable 85:15 mixture in a combined 56% yield. Whilst basic conditions for the degradation of polycarbonates often release the corresponding diol as a byproduct,[91] to the best of our knowledge, the formation of a fused bicyclic oxetane **4.8a** from the decomposition of polycarbonate is a new observation. Recently, both Buchard and Wooley showed that similar types of bicyclic oxetanes can be used to prepare different kinds of polymers including polycarbonates and polyethers,[92] thus providing a potential recycling or repurposing route for **4.8a**.




**Scheme 4.8** Depolymerization of **4.P8** using TBD as catalyst.

[90] (a) C. Li, R. J. Sablong, R. A. T. M. van Benthem, C. E. Koning, *ACS Macro Lett.* **2017**, *6*, 684-688; See also: (b) F. N. Singer, A. C. Deacy, T. M. McGuire, C. K. Williams, A. Buchard, *Angew. Chem. Int. Ed.* **2022**, *61*, e202201785.
[91] C. Maquilón, F. Della Monica, B. Limburg, A. W. Kleij, *Adv. Synth. Catal.* **2021**, *363*, 4033-4040.
[92] (a) D. K. Tran, A. Z. Rashad, D. J. Darensbourg, K. L. Wooley, *Polym. Chem.* **2021**, *12*, 5271-5278; (b) T. M. McGuire, J. Bowles, E. Deane, E. H. E. Farrar, M. N. Grayson, A. Buchard, *Angew. Chem. Int. Ed.* **2021**, *60*, 4524-4528; (c) T. M. McGuire, A. Buchard, *Polym. Chem.* **2021**, *12*, 4253-4261.

## 4.4 Conclusions

In summary, we have prepared a family of functional, bicyclic 6MCC monomers bearing synthetically useful groups. The catalytic AROP provides straightforward access to densely substituted macromolecular aliphatic carbonates. Bifunctional monomers were also designed allowing to trigger two different types of polymerizations and offering orthogonal polymerization/crosslinking strategies. Post-synthetic functionalization of these APCs was also demonstrated, which permits to change and modulate the (thermal) properties. A TBD-catalyzed degradation of one selected oligocarbonate led to a new fused bicyclic oxetane, which should have potential to be recycled or repurposed to different kinds of polymeric materials. This work exemplifies that properly equipped carbonate monomers can be designed to extend the pool of functionality eventually present in APCs. We expect that this gives new impetus to different curing opportunities and post-polymerization adjustment of relevant physical properties such as hydrophobicity/philicity, polymer processability and miscibility.

# 4.5 Experimental section

## 4.5.1 General information

Solvents were dried using an Innovative Technology PURE SOLV solvent purification system. Reactions were monitored by TLC and $^{1}$H NMR. TLC was carried out on 0.25 mm Merck aluminum-backed sheets coated with 60 F254 silica gel. Visualization of the silica plates was achieved using a UV lamp ($\lambda$ = 254 nm) and/or by heating plates that were dipped in a ceric ammonium molybdate stain. Flash chromatography was carried out on Sigma Aldrich silica gel 60 (70-230 mesh) using the indicated eluent system. Benzyl alcohol (BnOH) was dried over calcium hydride and distilled under reduced pressure. TBD (1,5,7-triazabicyclo[4.4.0]dec-5-ene) was dissolved in DCM, stirred over calcium hydride, filtered and dried in vacuum prior to use.

**NMR spectroscopy**: NMR spectra were obtained on a Bruker 400 MHz, a 500 MHz or a 500 MHz with cryoprobe spectrometers equipped with probe-heads capable of producing gradients in the z direction with a maximum strength of 53.5 G/cm. $^{1}$H, $^{13}$C and $^{19}$F NMR chemical shifts are reported in parts per million (ppm), relative to tetramethylsilane (TMS) for $^{1}$H and $^{13}$C with the residual solvent peak used as an internal reference. Multiplicities are reported as follows: singlet (s), broad band (br), d (doublet), dd (doublet of doublets), triplet (t) and multiplet (m).

**Mass analysis**: High resolution mass spectrometry (HRMS) data was recorded using two different methodologies depending on the complex to be analyzed. ESI-MS analyses were performed in a MicroTOF Focus mass spectrometer (Bruker Daltonics) by direct injection. Cold-spray ionization-MS (CSIMS) analyses were performed in a MicroTOF Focus mass spectrometer (Bruker Daltonics) equipped with a cold-spray ionization source by direct injection and using nitrogen as sprayer and dry gas.

**Thermal analysis**: Differential scanning calorimetry (DSC) analyses for glass transition temperatures ($T_g$) determination were measured under an $N_2$ atmosphere using Mettler Toledo equipment (model DSC822e). Samples were weighed into 40 μL aluminum crucibles and subjected to three heating cycles at a heating rate of 10 °C/min. Thermogravimetric analyses (TGA) were recorded under an $N_2$ atmosphere using Mettler Toledo equipment (model TGA/SDTA851). Samples were weighed into 40 μL aluminum crucibles and heated to 600 ºC at a heating rate of 10 °C/min.

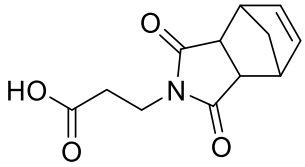
**Gel permeation chromatography** (GPC) measurements were performed using an Agilent 1200 series HPLC system, equipped with PSS SDV Analytical linear M GPC column (8 x 300 mm; 5 μm particle size) in tetrahydrofuran at 30 °C at a flow rate of 1 $mL \cdot min^{-1}$. Samples were analyzed at a concentration of 1 $mg \cdot mL^{-1}$ after filtration through a 0.45 μm pore-size membrane. $M_n$, $M_w$, and $Đ$ data were derived from the RI signal by a calibration curve based on polystyrene standards (PS from Polymer Standards Service) for the analysis of the polymers. The GPC samples were prepared by dissolving the polymer (3−5 mg) in THF (2 mL) and filtering the solution through a 0.45 μm pore-size membrane.

Ligand **L1**, and catalysts **C1** and **C2** were prepared according to previously reported procedures.[93] All the monomers were dissolved in dichloromethane (1 to 5 mL) and allowed to stir for 16 h with $CaH_2$ before the AROP experiments. The solid was removed through filtration, the residue solvent was evaporated under vacuum yielding the corresponding dry monomer, which was used without further purification.

[93] (a) A. Chandrasekaran, R. O. Day, R. R. Holmes, *J. Am. Chem. Soc.* **2000**, *122*, 1066-1072; (b) C. J. Whiteoak, N. Kielland, V. Laserna, F. Castro-Gómez, E. Martin, E. C. Escudero-Adán, C. Bo, A. W. Kleij, *Chem. Eur. J.* **2014**, *20*, 2264-2275; (c) J. A. Love, J. P. Morgan, T. M. Trnka, R. H. Grubbs, *Angew. Chem. Int. Ed.* **2002**, *41*, 4035-4037.

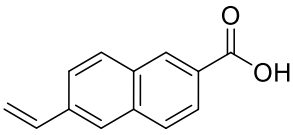
## 4.5.2 General procedure for the synthesis of precursor Z1-Z2

**3-(1,3-dioxo-1,3,3a,4,7,7a-hexahydro-2*H*-4,7-methanoisoindol-2-yl)propanoic acid Z1**



An oven-dried flask was charged with 3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1,3-dione (2.5 g, 15.2 mmol, 1 equiv) and 3-aminopropanoic acid (1.7 g, 19 mmol, 1.25 equiv). The flask was evacuated and back-filled with nitrogen three times. Then, triethyl amine (270 μL, 0.125 mmol, 13 mol%) and toluene (10 mL, 1.52 M) were added. The resulting mixture was allowed to stir at reflux temperature for 16 h under a nitrogen atmosphere. The crude mixture was allowed to cool to room temperature, and concentrated under vacuum. The residue was dissolved in $CH_2Cl_2$, the organic phase was washed with 1 N HCl and NaCl, dried over $Na_2SO_4$ and concentrated to afford **Z1** in 50% yield as white solid (1.8 g, 7.65 mmol). The spectral data of **Z1** correspond to the literature.[94] **$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.08 (t, *J* = 1.9 Hz, 2H), 3.65 (t, *J* = 7.4 Hz, 2H), 3.39 (dh, *J* = 3.4, 1.7 Hz, 2H), 3.26 (dd, *J* = 3.0, 1.5 Hz, 2H), 2.54 (dd, *J* = 7.8, 7.0 Hz, 2H), 1.73 (dt, *J* = 8.8, 1.7 Hz, 1H), 1.53 (dt, *J* = 8.8, 1.5 Hz)

**6-vinyl-2-naphthoic acid Z2**



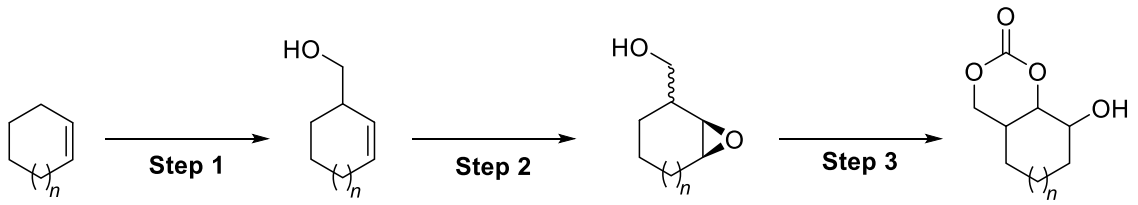
A Schlenk tube equipped with a magnetic stirrer was charged with potassium vinyl trifluoroborate (500 mg, 3.73 mmol, 1 equiv), $PdCl_2$ (13 mg, 0.075 mmol, 2 mol%), $PPh_3$ (60 mg, 0.23 mmol, 6 mol%), $Cs_2CO_3$ (3.68 g, 11.3 mmol, 3 equiv) and methyl 6-bromo-2-naphthoate (1 g, 3.77 mmol, 1 equiv). The tube was evacuated and backfilled with argon three times, and then 7 mL of THF and 0.75 mL of $H_2O$ were added. The reaction mixture was stirred at 85 °C for 16 h. The reaction mixture was allowed to cool to room temperature, then diluted with $H_2O$ followed by extraction with DCM, dried with anhydrous $Na_2SO_4$ and concentrated in vacuo. The product was obtained in quantitative yield and it was used without further purification for the next step. To a solution of the crude product in THF (13 mL) was added $H_2O$ (13 mL) followed by LiOH monohydrate (525 mg, 19 mmol, 5

[94] K. Zhang, Y. Zha, B. Peng, Y. Chen, G. N. Tew, *J. Am. Chem. Soc.* **2013**, *135*, 15994-15997.

equiv). The resulting mixture was stirred for 5 h at room temperature. The reaction mixture was concentrated under a vacuum, and then 1 M HCl was added till pH 5. The white precipitate that formed was collected, washed with $Et_2O$ and dried under a high vacuum to give **Z2** in 57% overall yield (430 mg, 2.16 mmol).

**$^1$H NMR** (400 MHz, DMSO) δ 8.54 (s, 1H), 8.06 (d, *J* = 8.6 Hz, 1H), 7.99 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.96 – 7.93 (m, 2H), 7.81 (dd, *J* = 8.6, 1.7 Hz, 1H), 6.94 (dd, *J* = 17.6, 11.0 Hz, 1H), 6.05 (dd, *J* = 17.6, 0.9 Hz, 1H), 5.43 (dd, *J* = 10.8, 0.8 Hz, 1H). **$^{13}$C NMR** (101 MHz, DMSO) δ 167.7, 136.5 (2C), 134.9, 131.9, 129.8, 129.5, 127.9 (2C), 126.0, 125.8, 123.8, 115.9. **HRMS** (ESI): m/z $[M-H]^-$ calcd for $C_{13}H_9O_2$: 197.0608; found: 196.0612. **IR** (neat) $\nu_{max}$ = 3389, 1679 (C=O), 1624 $cm^{-1}$.

## 4.5.3 General procedure for the preparation of bicyclic precursors A-D



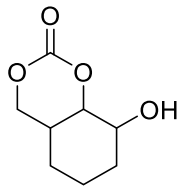

**Step 1** (example): A 500 mL round bottom flash was charged with cyclohexene (54 mL, 0.53 mol) and KO*t*Bu (6.8 g, 60.4 mmol), and the resulting suspension was degassed for 30 min with argon. The resulting mixture was cooled to 0°C and *n*BuLi (1.6 M in hexanes, 40 mL, 64 mmol) was added dropwise, and the mixture then stirred at the same temperature for 2 h. Then it was allowed to warm to room temperature and stirred for a further 16 h. The resultant pale-yellow suspension was cooled to 0 °C and $(HCHO)_n$ (2 g, 66.4 mmol) was added. The reaction mixture was allowed to warm to room temperature and heated to 60 ºC for 3 h. Subsequently, the mixture was cooled to 0 °C and quenched with a saturated aqueous $NaHCO_3$ solution (40 mL). The mixture was extracted with $CH_2Cl_2$ (3 × 40 mL). The combined organic phases were washed sequentially with a saturated aqueous $NaHCO_3$ solution (40 mL) and brine (40 mL), dried over $MgSO_2$, concentrated in vacuo to give the desired product in 76% (5.1 g, 44.6 mmol) as colorless oil.

**Step 2**: To a solution of the product of step 1 (2.5 g, 22.3 mmol, 1 equiv.) in dry MeOH (112 mL, 0.2 M) at 0 °C, *m*CPBA (7.5 g, 33.5 mmol, 1.5 equiv, 77%) was added portion-wise. The reaction was allowed to warm to room temperature and stirred for 16 h. The solvent was removed, the residue was dissolved in DCM and then washed with $Na_2CO_3$. The organic phase was dried over $MgSO_4$, concentrated and purified through column chromatography (hexane:ethyl acetate, 6:4 v/v) to obtain the target homoallylic alcohol product as a colorless oil in 84% as a 1:1 mixture of *syn* and *anti*-isomers (2.39 g, 18.6 mmol).

**Step 3**: A 25 mL stainless-steel reactor was charged the product of step 2 (1.2 g, 9.3 mmol, 1 equiv), MEK (5 mL, 1.86 M), **C1** (100 mg, 0.19 mmol, 2 mol%) and DIPEA (175 µL, 0.94 mmol, 10 mol%). The reactor was purged three times and then then charged with $CO_2$ (10 bar). The mixture was stirred at 100 °C for 22 h, then cooled with an ice/water bath and carefully depressurized. The solvent was removed in vacuo and the resulting

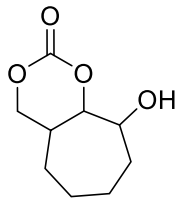
product was purified by flash chromatography (hexane:ethyl acetate, 1:1 v/va) affording the desired product in 85% as a pale-yellow solid (735 mg, 4.27 mmol).

**8-hydroxyhexahydro-4*H*-benzo[d][1,3]dioxin-2-one A**



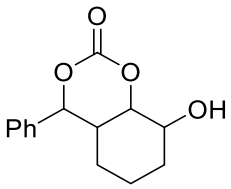
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 4.46 – 4.40 (m, 2H), 4.26 (dd, *J* = 11.1, 3.9 Hz, 1H), 4.07 – 4.03 (m, 1H), 2.44 – 2.31 (m, 2H), 1.85 – 1.70 (m, 2H), 1.67 – 1.52 (m, 4H). The spectral data correspond to the literature.[83]

**9-hydroxyoctahydrocyclohepta[*d*][1,3]dioxin-2-one B**



Following the overall procedure (steps 1-3) using cycloheptene (7 mL, 60 mmol, 1 equiv, in 50 mL cyclohexane) **B** was obtained in 13% yield (248 mg, 1.13 mmol) as a colorless oil. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.61 – 4.58 (m, 1H), 4.44 (dd, *J* = 11.0, 3.6 Hz, 1H), 4.16 (dd, *J* = 11.0, 3.6 Hz, 1H), 3.93 – 3.88 (m, 1H), 2.65 (brs, 1H), 2.31 – 2.24 (m, 1H), 2.01 – 1.89 (m, 3H), 1.72 – 1.61 (m, 3H), 1.65 – 1.45 (m, 1H), 1.43 – 1.35 (m, 1H). The spectral data correspond to the literature.[95]

**8-hydroxy-4-phenylhexahydro-4*H*-benzo[*d*][1,3]dioxin-2-one C**

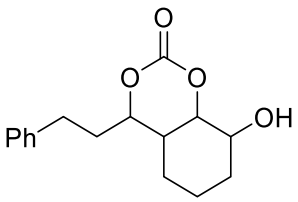


A modified procedure (regarding step 1) was followed: To a 10 mL Schlenk flask was sequentially added iron powder (1.7 g, 30 mmol, 1.9 equiv) and DMSO (20 mL). Then the iron was activated by the addition of 1,2-dibromoethane (280 μL, 3.2 mmol, 0.2 equiv) and TMSCl (406 μL, 3.2 mmol, 0.2 equiv). After stirring for 30 min, $BiCl_3$ (1 g, 3.2 mmol, 0.2 equiv), 3-bromocyclohexene (2.8 mL, 24 mmol, 1.5 equiv) and freshly distilled benzaldehyde (1.6 mL, 16 mmol, 1 equiv) were sequentially added to the reaction mixture. The suspension was vigorously stirred at r.t. for 24 h before quenching it with a saturated aqueous $NaHCO_3$ solution (60 mL) following extraction by ethyl acetate (3 × 20 mL). The combined extracts were washed with brine (30 mL), dried over anhydrous $Na_2SO_4$

[95] C. Qiao, W. Shi, A. Brandolese, J. Benet-Buchholz, E. C. Escudero-Adán, A. W. Kleij, *Angew. Chem. Int. Ed*. **2022**, *61*, e202205053.

and concentrated in vacuo. The residue obtained was purified by silica gel column chromatography to give the pure product. Subsequently the product was used in steps 2+3. Following this procedure, the target product was obtained in 32% yield as a colorless oil (434 mg, 1.75 mmol). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.37 (m, 2H), 7.35 – 7.29 (m, 3H), 5.63 (d, *J* = 3.1 Hz, 1H), 4.71 (t, *J* = 3.1 Hz, 1H), 4.18 (q, *J* = 3.0 Hz, 1H), 2.47 (ddt, *J* = 12.8, 5.5, 2.9 Hz, 1H), 1.81 – 1.68 (m, 2H), 1.62 – 1.48 (m, 2H), 1.26 – 1.10 (m, 2H). The spectral data correspond to the literature.[83]

**8-hydroxy-4-phenethylhexahydro-4*H*-benzo[*d*][1,3]dioxin-2-one D**

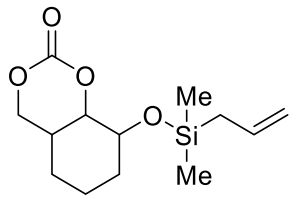



A modified procedure (regarding step 1) was used: To a 10 mL Schlenk flask was sequentially added iron powder (1.7 g, 30 mmol, 1.9 equiv.) and DMSO (20 mL). Then the iron was activated by the addition of 1,2-dibromoethane (280 μL, 3.2 mmol, 0.2 equiv) and TMSCl (406 μL, 3.2 mmol, 0.2 equiv). After stirring for 30 min, $BiCl_3$ (1 g, 3.2 mmol, 0.2 equiv), 3-bromocyclohexene (2.8 mL, 24 mmol, 1.5 equiv) and freshly distilled 3-phenylpropionaldehyde (2 mL, 16 mmol, 1 equiv) were sequentially added to the reaction mixture. The suspension was vigorously stirred at r.t. for 24 h before quenching it with a saturated aqueous $NaHCO_3$ solution (60 mL) following extraction with ethyl acetate (3 × 20 mL). The combined extracts were washed with brine (30 mL), dried over anhydrous $Na_2SO_4$ and concentrated in vacuo. The residue obtained was purified by silica gel column chromatography to give the pure product. Subsequently the product was used for steps 2+3. Following this sequence of events, the target product was obtained in 60% yield as a colorless oil (441 mg, 1.60 mmol). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.31 (m, 2H), 7.26 – 7.21 (m, 3H), 4.44 – 4.41 (m, 2H), 4.12 – 4.10 (m, 1H), 2.88 (ddd, *J* = 14.3, 9.2, 5.3 Hz, 1H), 2.73 (ddd, *J* = 13.9, 8.9, 7.3 Hz, 1H), 2.21 – 2.15 (m, 1H), 2.14 – 2.07 (m, 1H), 1.88 – 1.80 (m, 1H), 1.76 – 1.64 (m, 4H), 1.41 – 1.29 (m, 2H). The spectral data correspond to the literature. [95]

## 4.5.4 General procedure for the preparation of silyl ethers derivatives

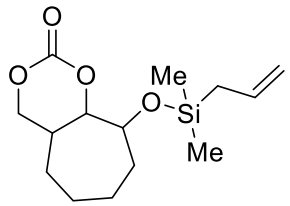
To a solution of one of the precursors **A-D** (1 equiv) and triethyl amine (5 equiv) in dry DCM (0.1 M), the respective chlorosilane (3 equiv) was added dropwise. The resulting mixture was stirred at room temperature for 3 h. The solvent was removed and the crude was purified by column chromatography (hexane/ethyl acetate) to give the desired product.

**8-((allyldimethylsilyl)oxy)hexahydro-4*H*-benzo[*d*][1,3]dioxin-2-one (4.1)**



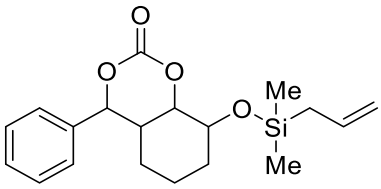
Following the general procedure using **A** (390 mg, 2.26 mmol) and allyl(chloro)dimethylsilane, monomer **4.1** was obtained in 66% yield (405 mg, 1.50 mmol) as a colorless oil. **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 5.81 – 5.70 (m, 1H), 4.92 – 4.86 (m, 2H), 4.45 (ddd, *J* = 11.0, 3.7, 1.2 Hz, 1H), 4.33 (t, *J* = 3.5 Hz, 1H), 4.17 (dt, *J* = 11.0, 1.7 Hz, 1H), 4.01 (d, *J* = 3.1 Hz, 1H), 2.24 (dt, *J* = 13.6, 4.8 Hz, 1H), 1.76 – 1.50 (m, 8H), 0.13 (s, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 148.1, 133.5, 114.1, 78.9, 72.9, 67.1, 27.6, 27.3, 24.6, 22.6, 17.7, -2.1, -2.1. **HRMS** (ESI): m/z $[M+Na]^+$ calcd for $C_{13}H_{22}NaO_4Si$: 293.1180; found: 293.1183. **IR** (neat) $\nu_{max}$ = 2940, 2869, 1751 (C=O) $cm^{-1}$.

**9-((allyldimethylsilyl)oxy)octahydrocyclohepta[*d*][1,3]dioxin-2-one (4.2)**



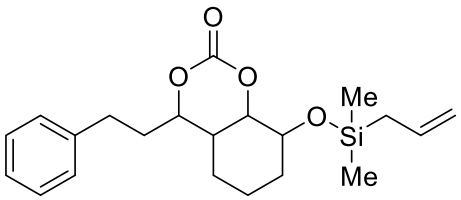
Following the general procedure using **B** (390 mg, 2.09 mmol) and allyl(chloro)dimethylsilane, **4.2** was obtained in 55% yield (326 mg, 1.15 mmol) as a colorless oil. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 5.82 (ddt, *J* = 17.0, 10.1, 8.1 Hz, 1H), 4.95 – 4.88 (m, 2H), 4.55 (ddd, *J* = 5.5, 4.2, 1.2 Hz, 1H), 4.45 (dd, *J* = 10.9, 3.2 Hz, 1H), 4.18 (dd, *J* = 10.8, 2.2 Hz, 1H), 3.92 (ddd, *J* = 9.3, 5.7, 1.9 Hz, 1H), 2.18 – 2.13 (m, 1H), 1.94 – 1.85 (m, 2H), 1.81 – 1.61 (m, 6H), 1.51 – 1.43 (m, 2H), 0.19 (s, 3H), 0.19 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 148.7, 133.8, 113.9, 87.0, 75.5, 73.8, 34.3, 31.7, 27.9, 26.3, 24.8, 24.5, -1.9, -2.0. **HRMS** (ESI): m/z $[M-C_5H_{11}Si+Na]^+$ calcd for $C_9H_{14}NaO_4$: 209.0784; found: 209.0780. **IR** (neat) $\nu_{max}$ = 3411, 2928, 2860, 1720 (C=O), 1109 $cm^{-1}$.

**8-((allyldimethylsilyl)oxy)-4-phenylhexahydro-4*H*-benzo[*d*][1,3]dioxin-2-one (4.3)**



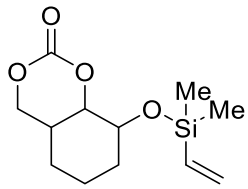
Following the general procedure using **C** (433 mg, 1.74 mmol) and allyl(chloro)dimethylsilane, **4.3** was obtained in 78% yield (468 mg, 1.35 mmol) as a colorless oil. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.37 (m, 2H), 7.35 – 7.31 (m, 3H), 5.79 (ddt, *J* = 16.9, 10.1, 8.0 Hz, 1H), 5.61 (d, *J* = 3.1 Hz, 1H), 4.96 – 4.89 (m, 2H), 4.52 (t, *J* = 3.1 Hz, 1H), 4.10 (q, *J* = 2.9 Hz, 1H), 2.41 (ddt, *J* = 12.8, 5.3, 2.9 Hz, 1H), 1.68 – 1.53 (m, 5H), 1.45 – 1.40 (m, 1H), 1.23 – 1.10 (m, 2H), 0.16 (s, 3H), 0.16 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 148.4, 136.0, 133.5, 128.5, 128.2, 125.1, 114.1, 82.9, 79.6, 67.2, 33.2, 27.3, 24.7, 18.1, 17.4, -2.0, -2.1. **HRMS** (ESI): m/z $[M+Na]^+$ calcd for $C_{19}H_{26}NaO_4Si$: 369.1493; found: 369.1495. **IR** (neat) $\nu_{max}$ = 2944, 2869, 1748 (C=O) $cm^{-1}$.

**8-((allyldimethylsilyl)oxy)-4-phenethylhexahydro-4*H*-benzo[*d*][1,3]dioxin-2-one (4.4)**



Following the general procedure using **D** (441 mg, 1.59 mmol) and allyl(chloro)dimethylsilane, **4.4** was obtained in 73% yield (433 mg, 1.15 mmol) as a colorless oil. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 2H), 7.24 – 7.19 (m, 3H), 5.75 (ddt, *J* = 17.0, 10.1, 8.1 Hz, 1H),4.91 – 4.85 (m, 2H), 4.37 (ddd, *J* = 9.3, 4.3, 2.8 Hz, 1H), 4.24 (t, *J* = 3.1 Hz, 1H), 4.02 (brs, 1H), 2.88 (ddd, *J* = 14.2, 9.2, 5.3 Hz, 1H), 2.72 (ddd, *J* = 13.9, 8.9, 7.4 Hz, 1H), 2.13 – 2.04 (m, 2H), 1.84 – 1.76 (m, 1H), 1.69 – 1.65 (m, 2H), 1.63 – 1.52 (m, 5H), 1.33 – 1.25 (m, 1H), 0.12 (s, 3H), 0.12 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 148.7, 140.5, 133.5, 128.6, 128.5, 126.3, 114.1, 81.6, 79.6, 67.0, 33.2, 31.1, 30.8, 27.3, 24.7, 18.0, 17.3, -2.0, -2.1. **HRMS** (ESI): m/z $[M+Na]^+$ calcd for $C_{21}H_{30}NaO_4Si$: 397.1806; found: 397.1810. **IR** (neat) $\nu_{max}$ = 2944, 1749 (C=O) $cm^{-1}$.

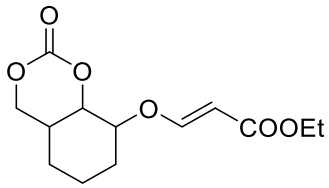
**8-((dimethyl(vinyl)silyl)oxy)hexahydro-4*H*-benzo[*d*][1,3]dioxin-2-one (4.5)**



Following the general procedure using **A** (386 mg, 2.24 mmol) and chloro(dimethyl)vinylsilanes, **4.5** was obtained in 88% yield (503 mg, 1.96 mmol) as a white solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 6.14 – 6.01 (m, 2H), 5.79 (dd, *J* = 19.7, 4.4 Hz, 1H), 4.45 (dd, *J* = 11.0, 3.7 Hz, 1H), 4.18 (dd, *J* = 11.0, 1.8 Hz, 1H), 4.01 (q, *J* = 3.2 Hz, 1H), 2.28 – 2.23 (m, 1H), 1.79 – 1.70 (m, 1H), 1.68 – 1.49 (m, 6H), 0.19 (d, *J* = 0.8 Hz, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 148.1, 136.9, 133.8, 78.9, 72.8, 67.1, 27.6, 27.2, 22.6, 17.8, -1.8, -1.9. **HRMS** (ESI): m/z $[M+Na]^+$ calcd for $C_{12}H_{20}NaO_4Si$: 279.1023; found: 279.1033. **IR** (neat) $\nu_{max}$ = 2939, 2884, 1749 $cm^{-1}$.

## 4.5.5 Procedure for Synthesis of monomer 4.6

**Ethyl (*E*)-3-((2-oxohexahydro-4*H*-benzo[*d*][1,3]dioxin-8-yl)oxy)acrylate (4.6)**

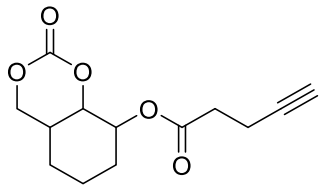



To a stirred solution of **A** (386 mg, 2.24 mmol, 1 equiv) in $CH_3CN$ (11 mL, 0.2 M), N-methyl-morpholine (NMM, 50 μL, 0.45 mmol, 0.2 equiv) was added followed by ethyl propiolate (275 μL, 2.65 mmol, 1.2 equiv). The resulting mixture was allowed to stir at room temperature for 16 h. The solvent was removed and the crude was purified by column chromatography to give the etherified product **6** in 56% yield (344 mg) as a colorless oil. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 12.5 Hz, 1H), 5.31 (d, *J* = 12.5 Hz, 1H), 4.60 (t, *J* = 3.3 Hz, 1H), 4.49 (dd, *J* = 11.1, 3.6 Hz, 1H), 4.27 (q, *J* = 3.2 Hz, 1H), 4.21 (dd, *J* = 11.2, 1.7 Hz, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 2.23 – 2.20 (m, 1H), 1.91 – 1.87 (m, 1H), 1.79 – 1.72 (m, 1H), 1.68 – 1.56 (m, 4H), 1.26 (t, *J* = 7.1 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 167.2, 159.9, 147.3, 99.2, 76.1, 75.6, 72.4, 60.0, 28.0, 24.1, 22.1, 17.8, 14.3. **HRMS** (ESI): m/z $[M+Na]^+$ calcd for $C_{13}H_{18}NaO_6$: 293.0996; found: 293.1006. **IR** (neat) $\nu_{max}$ = 2940, 2870, 1749, 1701, 1639, 1621 $cm^{-1}$.

## 4.5.6 General procedure for the preparation of ester-derivatives

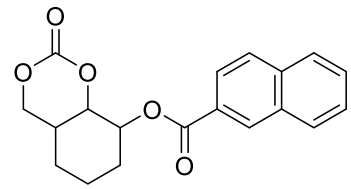
To a solution of **A** (1 equiv) and DMAP (0.1 equiv) in dry DCM (0.2 M) the desired carboxylic acid was added (1.05 equiv) followed by the *N,N'*-dicyclohexylcarbodiimide (DCC, 1.1 equiv; 1 M in DCM). The resulting mixture was stirred at room temperature for 2 h. The white precipitate was filtered off, the resulting organic phase was washed twice with sutured solution of $Na_2CO_3$, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude was purified by column chromatography (hexane/ethyl acetate) to give the desired product.

**2-oxohexahydro-4*H*-benzo[*d*][1,3]dioxin-8-yl pent-4-ynoate (4.7)**



Following the general procedure using **A** (730 mg, 4.24 mmol) and 4-pentynoic acid, **4.7** was obtained in 67% yield (712 mg, 2.86 mmol) as a pale-yellow oil. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 5.15 (q, *J* = 3.9 Hz, 1H), 4.55 (t, *J* = 3.7 Hz, 1H), 4.46 (dd, *J* = 11.1, 3.8 Hz, 1H), 4.24 (dd, *J* = 11.1, 2.5 Hz, 1H), 2.60 – 2.57 (m, 2H), 2.54 – 2.51 (m, 2H), 2.26 – 2.23 (m, 1H), 1.98 (t, *J* = 2.6 Hz, 1H), 1.84 – 1.75 (m, 2H), 1.70 – 1.62 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 170.3, 147.5, 82.1, 76.0, 72.0, 69.3, 68.9, 33.4, 28.6, 24.6, 22.4, 18.5, 14.5. **HRMS** (ESI): m/z $[M+Na]^+$ calcd for: $C_{13}H_{16}NaO_5$: 275.0890; found: 275.0898. **IR** (neat) $\nu_{max}$ = 3279, 2938, 1736 (C=O) $cm^{-1}$.

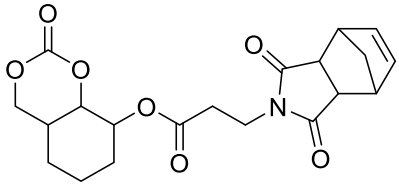
**2-oxohexahydro-4*H*-benzo[*d*][1,3]dioxin-8-yl 2-naphthoate (4.8)**



Following the general procedure using **A** (390 mg, 2.26 mmol) and 2-naphthoic acid, **4.8** was obtained in 72% yield (531 mg, 1.63 mmol) as a white solid. Column chromatography conditions: hexane/ethyl acetate 8:2 v/v). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.05 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.99 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.92 (d, *J* = 8.3 Hz, 2H), 7.64 (ddd, *J* = 8.2, 6.8, 1.4 Hz, 1H), 7.59 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 1H), 5.44 (q, *J* = 3.5 Hz, 1H), 4.78 (t, *J* = 3.6 Hz, 1H), 4.54 (dd, *J* = 11.1, 3.7 Hz, 1H), 4.30 (dd, *J* = 11.1, 2.3 Hz, 1H), 2.41 – 2.37 (m, 1H), 2.00 – 1.97 (m, 2H), 1.92 – 1.84 (m, 1H), 1.83 – 1.72 (m, 2H), 0.92 – 0.86 (m, 1H). **$^{13}$C NMR** (126 MHz,

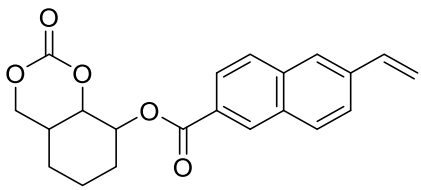
$CDCl_3$) δ 165.2, 147.5, 135.7, 132.4, 131.2, 129.3, 128.6, 128.4, 127.8, 126.9, 126.8, 125.0, 76.0, 72.1, 69.1, 28.8, 24.6, 22.5, 18.8. **HRMS** (ESI): m/z $[M+Na]^+$ calcd for $C_{19}H_{18}NaO_5$: 349.1046; found: 349.1045. **IR** (neat) $\nu_{max}$ = 2938, 2868, 1750 (*C*=*O*OR), 1711 (C=O) $cm^{-1}$.

**2-oxohexahydro-4*H*-benzo[*d*][1,3]dioxin-8-yl 3-(1,3-dioxo-1,3,3a,4,7,7a-hexahydro-2*H*-4,7-methanoisoindol-2-yl)propanoate (4.10)**



Following the general procedure using **A** (420 mg, 2.43 mmol) and **Z1** (603 mg, 2.56 mmol, 1.05 equiv), **4.10** was obtained in 66% yield (620 mg, 1.59 mmol) as a white solid. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.08 (s, 1H), 5.07 (q, *J* = 3.6 Hz, 1H), 4.54 (t, *J* = 3.6 Hz, 1H), 4.51 (dd, *J* = 11.1, 3.7 Hz, 1H), 4.23 (dd, *J* = 11.1, 2.4 Hz, 1H), 3.70 – 3.59 (m, 2H), 3.39 – 3.37 (m, 2H), 3.26 – 3.26 (m, 2H), 2.50 (t, *J* = 7.1 Hz, 2H), 2.26 – 2.23 (m, 1H), 1.18 – 1.53 (m, 9H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 177.3, 177.3, 169.2, 147.6, 134.5, 134.4, 75.7, 72.1, 68.9, 52.2, 45.8, 45.7, 44.9, 44.9, 34.0, 32.6, 28.5, 24.4, 22.3, 18.5. **HRMS** (ESI): m/z $[M+Na]^+$ calcd for $C_{20}H_{23}NNaO_7$: 412.1367; found: 412.1383. **IR** (neat) $\nu_{max}$ = 2945, 2870, 1741 (C=O), 1692 (C=O) $cm^{-1}$.

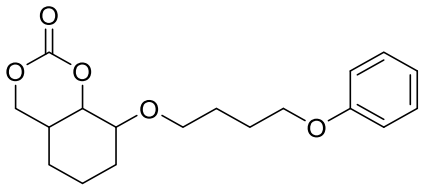
**2-oxohexahydro-4*H*-benzo[*d*][1,3]dioxin-8-yl 6-vinyl-2-naphthoate (4.11)**



Following the general procedure using **A** (340 mg, 1.97 mmol) and **Z2** (430 mg, 2.17 mmol, 1.1 equiv) **4.11** was obtained in 54% yield (376 mg, 1.07 mmol) as white solid. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.01 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.91 (d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 8.6 Hz, 1H), 7.79 (s, 1H), 7.71 (dd, *J* = 8.6, 1.7 Hz, 1H), 6.89 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.94 (d, *J* = 17.6 Hz, 1H), 5.44 – 5.40 (m, 2H), 4.75 (t, *J* = 3.6 Hz, 1H), 4.51 (dd, *J* = 11.1, 3.7 Hz, 1H), 4.28 (dd, *J* = 11.1, 2.3 Hz, 1H), 2.38 – 2.35 (m, 1H), 1.97 – 1.95 (m, 2H), 1.87 – 1.73 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 165.2, 147.5, 137.7, 136.4, 135.9, 132.0, 130.9, 129.5, 128.4, 126.7, 126.0, 125.5, 124.3, 115.9, 76.0, 72.1, 69.1, 28.7, 24.6, 22.4, 18.8. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{21}H_{21}O_5$: 353.1384; found: 353.1381. **IR** (neat) $\nu_{max}$ = 2936, 1765 (C=O), 1712 (C=O) $cm^{-1}$.

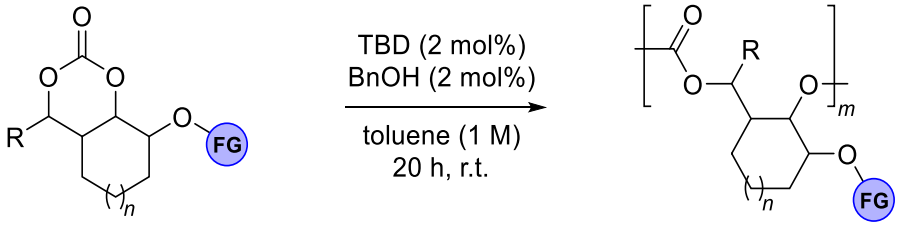
## 4.5.7 Procedure for the synthesis of monomer 4.9

**8-(4-phenoxybutoxy)hexahydro-4*H*-benzo[*d*][1,3]dioxin-2-one (4.9)**

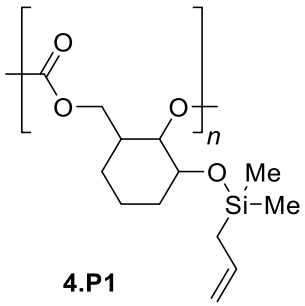


To a stirred solution of **A** (277 mg, 1.61 mmol, 1 equiv.) in dry THF (9.5 mL, 0.17 M), was added 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (470 μL, 1.93 mmol, 1.2 equiv) followed by 18-crown-6 (510 mg, 1.93 mmol, 1.2 equiv) and dry KF (112 mg, 1.93 mmol, 1.2 equiv). The resulting mixture was allowed to stir at room temperature for 120 h. The solvent was removed and the crude was purified by column chromatography giving **9** in 49% yield (255 mg, 0.79 mmol) as a colorless oil. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 2H), 6.94 (tt, *J* = 7.4, 1.1 Hz, 1H), 6.90 – 6.88 (m, 2H), 4.50 (t, *J* = 3.3 Hz, 1H), 4.43 (dd, *J* = 11.0, 3.7 Hz, 1H), 4.16 (dd, *J* = 11.0, 1.7 Hz, 1H), 3.99 (t, *J* = 6.3 Hz, 2H), 3.65 – 3.59 (m, 2H), 3.49 (dt, *J* = 9.2, 6.1 Hz, 1H), 2.18 – 2.15 (m, 1H), 1.89 – 1.72 (m, 5H), 1.6 7 -1.53 (m, 5H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.9, 148.2, 129.4, 120.6, 114.4, 77.2, 73.8, 72.7, 68.9, 67.4, 28.2, 26.6, 26.2, 23.6, 22.5, 18.1. **HRMS** (ESI): m/z $[M+Na]^+$ calcd for $C_{18}H_{24}NaO_5$: 343.1516; found: 343.1515. **IR** (neat) $\nu_{max}$ = 2937, 2867, 1748 (C=O) $cm^{-1}$.

## 4.5.8 General procedure for the ring-opening polymerization

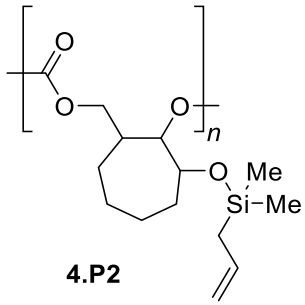



In a nitrogen-filled glovebox, a vial equipped with a stirring bar was charged with the desired monomer (1 equiv) followed by benzyl alcohol (59.2 mM stock solution in toluene, 2.0 mol%) and TBD (29.5 mM stock solution in toluene, 2 mol%). The resulting homogeneous solution was stirred for 20 h at room temperature. Then, the reaction mixture was quenched with benzoic acid (stock solution in toluene, 12 μmol, 83 mM) and a sample was analyzed by $^{1}$H NMR ($CDCl_3$) to determine the conversion. Precipitation from DCM/MeOH provided the purified polymer product as a white solid, which was collected by filtration and dried in a vacuum drying oven at 40 °C for three days.



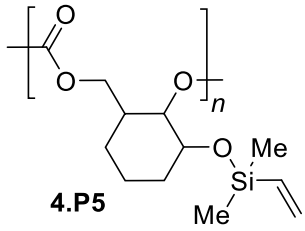

**4.P1**

**4.P1** was obtained following the general procedure using monomer **4.1** (159 mg, 0.59 mmol). The conversion of **4.1** was determined by $^{1}$H NMR to be 91%. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 5.78 – 5.74 (1H), 4.91 – 4.85 (2H), 4.62 (1H), 4.11 – 3.97 (3H), 2.37 (1H), 1.65 (1H), 1.62 – 1.40 (7H), 0.13 – 0.13 (6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 155.2, 154.7, 154.1, 133.9, 133.7, 114.0, 113.8, 75.9, 75.5, 68.6, 66.7, 36.6, 34.6, 28.7, 24.9, 24.9, 24.7, 24.7, 24.7, 23.2, 22.5, 22.1, 19.2, 19.0, 18.8, 18.5, -1.7, -1.8, -1.9, -2.0, -2.1, -2.1, -2.1, -2.2, -2.2. **IR** (neat) $\nu_{max}$ = 2939, 2867, 1742, 1238 cm$^{-1}$. **DSC**: $T_g$ (° C) = 19. **TGA**: $T_d^5$ (°C) = 282. **GPC**: $M_n$ = 5.56 kg/mol, $M_w$ = 8.59 kg/mol, $Đ$ = 1.55.



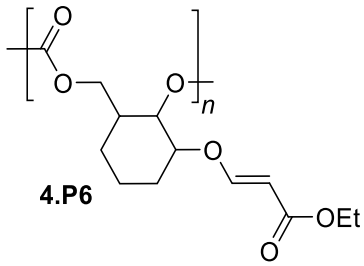

**4.P2**

**4.P2** was obtained following the general procedure using monomer **4.2** (82 mg, 0.29 mmol). Conversion of **4.2** was determined by $^1$H NMR at 86%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 5.82 – 5.71 (1H), 4.90 – 4.86 (2H), 4.84 – 4.656 (1H), 4.03 – 3.96 (3H), 2.37 – 2.04 (1H), 1.83 – 1.25 (10), 0.15 – 0.11 (6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 155.2, 154.8, 154.4, 133.9, 133.9, 113.8, 113.7, 83.2, 79.8, 79.3, 73.6, 73.2, 70.0, 69.5, 40.6, 40.0, 36.0, 32.6, 32.0, 31.8, 29.7, 29.2, 28.9, 27.5, 25.9, 24.9, 24.7, 24.7, 23.6, 23.2, 22.5, 19.8, -1.9, -1.9, -2.0, -2.0, -2.0, -2.1, -2.1, -2.2, -2.2, -2.2. **IR** (neat) $\nu_{max}$ = 2931, 2865, 1742, 1243 cm$^{-1}$. **DSC**: $T_g$ (º C) = 11. **TGA**: $T_d^5$ (º C) = 307. **GPC**: $M_n$ = 6.82 kg/mol, $M_w$ = 1.12 kg/mol, $Đ$ = 1.64.



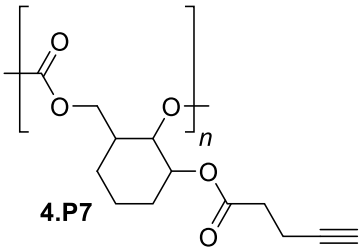

**4.P5**

**4.P5** was obtained following the general procedure using monomer **4.5** (148 mg, 0.58 mmol). Conversion of **4.5** was determined by $^1$H NMR at 95%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.16 – 6.09 (1H), 6.02 – 5.98 (1H), 5.80 – 5.76 (1H), 4.64 – 6.62 (1H), 4.09 – 3.91 (3H), 2.38 - 2.07 (1H), 1.69 – 1.40 (6H), 0.19 (6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 155.2, 154.7, 154.6, 154.1, 137.5, 137.5, 137.4, 137.1, 133.5, 133.5, 133.5, 133.2, 133.2, 133.2, 75.6, 75.4, 75.3, 75.2, 68.9, 68.6, 68.4, 66.8, 36.6, 34.6, 34.5, 28.6, 25.0, 23.2, 22.1, 19.3, 19.2, 19.1, 18.5, 1.0, -1.5, -1.5, -1.6, -1.7, -1.8, -1.8, -1.9. **IR** (neat) $\nu_{max}$ = 2944, 1745, 1252 cm$^{-1}$. **DSC**: $T_g$ (º C) = 57; **TGA**: $T_d^5$ (º C) = 277. **GPC**: $M_n$ = 1.17 kg/mol, $M_w$ = 1.69 kg/mol, $Đ$ = 1.44.

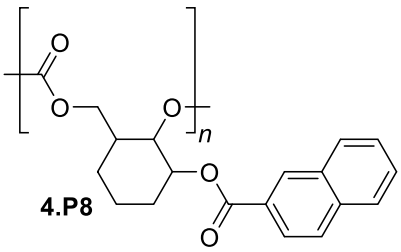



**4.P6**

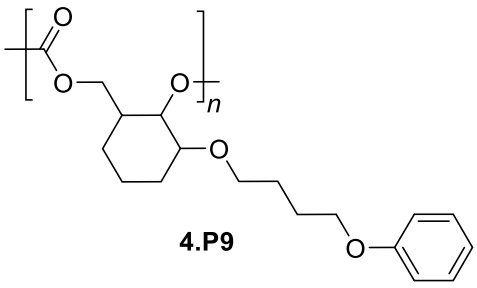
**4.P6** was obtained following the general procedure using monomer **4.6** (78 mg, 0.29 mmol). Conversion of **4.6** was determined by $^1$H NMR at 89%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.51 – 7.47 (1H), 5.41 – 5.33 (1H), 4.85 (1H), 4.30 – 3.93 (5H), 2.30 (1H), 1.83 – 1.44 (6H), 1.27 – 1.25 (3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 167.6, 160.6, 155.1, 155.0, 154.4, 154.3, 153.8, 98.6, 75.6, 67.8, 59.9, 59.8, 40.8, 35.2, 28.7, 25.6, 25.2, 22.6, 22.3, 18.6, 14.4, 14.3, 14.2. **IR** (neat) $\nu_{max}$ = 2940, 1745, 1710, 1251, 1130 cm$^{-1}$. **DSC**: $T_g$ (º C) = 70; **TGA**: $T_d^5$ (º C) = 268. **GPC**: $M_n$ = 5.00 kg/mol, $M_w$ = 6.84 kg/mol, $Đ$ = 1.36.



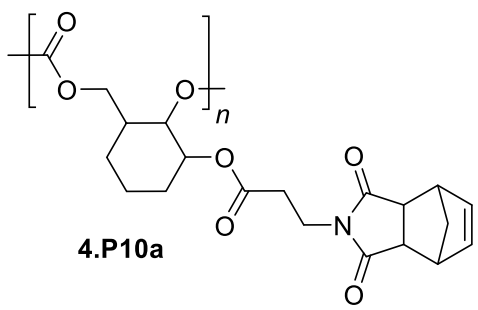

**4.P7** was obtained following the general procedure using monomer **4.7** (75 mg, 0.30 mmol). Conversion of **7** was determined by $^1$H NMR at 98%. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.10 – 5.06 (1H), 4.85 – 4.79 (1H), 4.15 – 3.95 (2H), 2.58 – 2.51 (4H), 2.36 – 2.30 (1H), 2.04 – 2.01 (1H), 1.81 – 1.76 (2H), 1.60 – 1.55 (4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 170.4, 154.2, 128.6, 128.3, 82.3, 72.4, 69.4, 68.8, 68.6, 67.8, 35.7, 33.6, 33.5, 31.6, 29.0, 25.6, 22.6, 21.0, 18.9, 14.5, 14.4, 14.2, 14.1, 11.4. **IR** (neat) $\nu_{max}$ = 3296, 2943, 1736, 1233 cm$^{-1}$. **DSC**: $T_g$ (º C) = 41; **TGA**: $T_d^5$ (º C) = 246. **GPC**: $M_n$ = 6.86 kg/mol, $M_w$ = 8.88 kg/mol, $Đ$ = 1.29.




**4.P8** was obtained following the general procedure using monomer **4.8** (94 mg, 0.29 mmol), the reaction was also performed at 1.5 mmol scale (500 mg, 1.53 mmol). The conversions of **4.8** were determined by $^1$H NMR at 90% and 93%, respectively. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.52 (1H), 7.95 – 7.82 (4H), 7.51 (2H), 5.39 – 4.91 (2H), 4.27 – 3.95 (2H), 2.47 (1H), 1.87 – 1.57 (6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 165.2, 155.0, 154.3, 135.5, 132.4, 131.1, 129.4, 128.2, 127.7, 127.2, 126.6, 125.2, 72.6, 70.1, 69.0, 68.0, 35.9, 29.7, 25.6, 23.4, 22.9, 19.7, 19.1. **IR** (neat) $\nu_{max}$ = 2939, 1746, 1715, 1224, 1193 cm$^{-1}$. **DSC**: $T_g$ (º C) = 106; **TGA**: $T_d^5$ (º C) = 224. **GPC**: $M_n$ = 3.24 kg/mol, $M_w$ = 5.22 kg/mol, $Đ$ = 1.60.

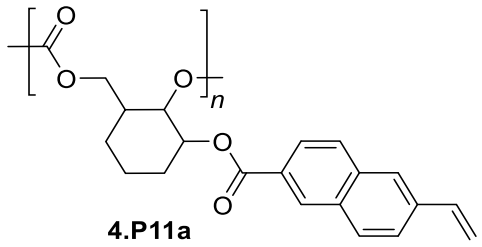



**4.P9** was obtained following the general procedure using monomer **4.9** (96 mg, 0.3 mmol). Conversion of **4.9** was determined by $^1$H NMR at 84%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.29 – 7.26 (2H), 6.95 – 6.89 (3H), 4.84 (1H), 4.17 – 3.98 (4H), 3.61 - 3.54 (3H), 2.33 (1H), 1.86 (2H), 1.73 (3H), 1.58 – 1.51 (5H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.0, 129.4, 120.5, 114.5, 73.5, 68.8, 68.5, 67.5, 35.1, 26.7, 26.2, 26.2, 25.3, 23.1, 18.9. **IR** (neat) $\nu_{max}$ = 2939, 2867, 1742 (C=O), 1238 cm$^{-1}$. **DSC**: $T_g$ (º C) = 15; **TGA**: $T_d^5$ (º C) = 301. **GPC**: $M_n$ = 7.06 kg/mol, $M_w$ = 10.20 kg/mol, $Đ$ = 1.44.




**4.P10a**

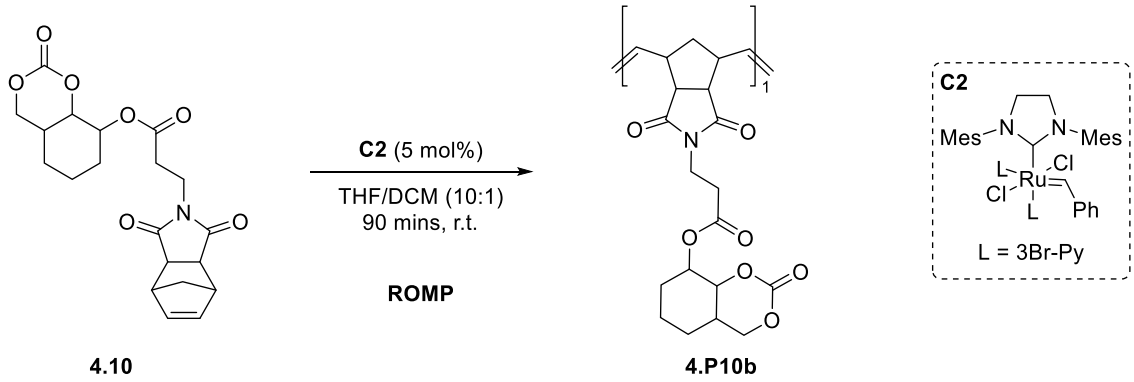
**4.P10a** was obtained following the general procedure using monomer **4.10** (112 mg, 0.29 mmol). Conversion of **4.10** was determined by $^1$H NMR at 96%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.09 (2H), 5.04 – 4.99 (1H), 4.76 – 4.74 (1H), 4.15 – 3.94 (2H), 3.61 (2H), 3.36 (2H), 3.25 (2H), 2.49 – 2.48 (2H), 2.29 (1H), 1.77 – 1.52 (8H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 177.2, 177.2, 169.3, 169.1, 155.0, 154.2, 154.0, 134.4, 72.7, 72.3, 69.6, 68.7, 67.9, 52.1, 45.7, 44.9, 35.5, 34.0, 33.8, 33.7, 32.2, 32.0, 25.4, 23.1, 22.8, 18.9. **IR** (neat) $\nu_{max}$ = 2943, 1740, 1694, 1235 cm$^{-1}$. **DSC**: $T_g$ (º C) = 120; **TGA**: $T_d^5$ (º C) = 315. **GPC**: $M_n$ = 7.23 kg/mol, $M_w$ = 9.63 kg/mol, $Đ$ = 1.33.




**4.P11a**

**4.P11a** was obtained following the general procedure using monomer **4.11** (106 mg, 0.3 mmol). Conversion of **4.11** was determined by $^1$H NMR at 91%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.46 (1H), 7.95 – 7.47 (5H), 6.82 (1H), 5.87 (1H), 5.36 – 5.04 (3H), 4.27 – 4.00 (2H), 2.77 – 2.48 (1H), 1.88 – 1.43 (6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 165.1, 155.0, 154.4, 137.4, 136.6, 135.8, 132.1, 130.8, 129.6, 128.3, 127.1, 126.0, 125.6, 124.0, 115.6, 72.7, 68.9, 36.0, 25.6, 23.0, 19.2. **IR** (neat) $\nu_{max}$ = 2931, 2866, 1746 (C=O), 1714 (C=O), 1235 cm$^{-1}$. **DSC**: $T_g$ (º C) = 156; **TGA**: $T_d^5$ (º C) = 221. **GPC**: $M_n$ = 7.18 kg/mol, $M_w$ = 11.5 kg/mol, $Đ$ = 1.59.

## 4.5.9 Procedure for ring opening metathesis polymerization

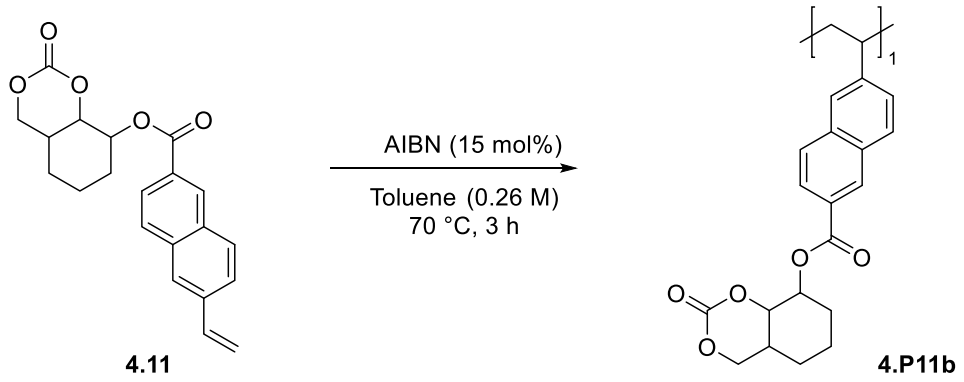



**4.10** **4.P10b**

In a nitrogen-filled glovebox, to a solution of **4.10** (78 mg, 0.2 mmol, 1 equiv.) in THF (2 mL, 0.1 M) was added a freshly prepared solution of **C2** (9 mg, 0.01 mmol, 5 mol%) in DCM (0.2 mL, 50 μM). The reaction mixture was stirred at room temperature for 1 h and 30 minutes. Hereafter, the mixture was quenched with ethyl vinyl ether (1 mL). A sample was taken to determine the conversion of **4.10** by $^{1}$H NMR ($CDCl_3$) which was determined at 96%. Precipitation from MeOH provided the polymer as a white powder. The supernatant was removed, the residue was dissolved in $CHCl_3$ and reprecipitated with MeOH. The white powder produced was collected and dried in high vacuum.

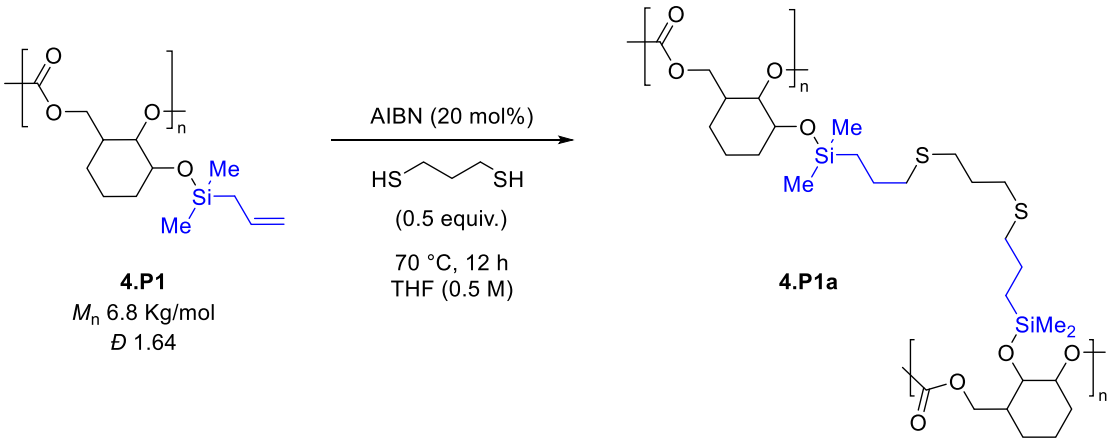
**$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 5.69 – 5.45 (2H), 5.03 (1H), 4.67 (2H), 4.19 (1H), 3.74 (2H), 3.21 (2H), 2.91 (1H), 2.59 (2H), 2.31 (1H), 1.83 – 1.35 (9H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 176.4, 175.9, 169.6, 148.2, 148.0, 129.5, 128.5, 128.4, 75.3, 72.5, 68.8, 48.9, 45.3, 40.2, 34.8, 33.2, 28.2, 24.3, 22.2, 18.6. **IR** (neat) $\nu_{max}$ = 2936, 1744 (C=O), 1695 (C=O) cm$^{-1}$. **DSC**: $T_g$ (º C) = 156; **TGA**: $T_d^5$ (º C) = 242. **GPC**: $M_n$ = 4.12 kg/mol, $M_w$ = 4.56 kg/mol, $Đ$ = 1.10.

## 4.5.10 Procedure for the radical polymerization of 4.11




In a nitrogen-filled glovebox, a vial equipped with a stirring bar was charged with **4.11** (70 mg, 0.26 mmol, 1 equiv) followed by dry and degassed toluene (0.8 mL, 0.25 M). Then 200 μL of a freshly prepared solution of AIBN (10 mg, 0.06 mmol, 15 mol%) in toluene (300 μL, 0.2 M) was added. The reaction mixture was stirred at room temperature for 3 h at 70 °C. The reaction mixture was then quenched by the addition of MeOH. The conversion of **4.11** was determined by $^{1}$H NMR ($CDCl_3$) to be >98%. The resulting white precipitate was collected as pure polymer **4.P11b**, and dried in vacuo. **$^{1}$H NMR** (300 MHz, $CDCl_3$) δ 8.55 (1H), 7.98 – 7.85 (4H), 7.54 (2H), 5.34 (1H), 5.03 (1H), 4.20 (2H), 2.53 (1H), 1.86 – 1.53 (8H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 165.3, 154.3, 135.6, 132.4, 131.2, 129.4, 128.2, 127.7, 127.2, 126.7, 125.2, 92.3, 72.6, 69.1, 68.0, 35.9, 26.0, 25.6, 23.5, 22.9, 19.1. **IR** (neat) $\nu_{max}$ = 2937, 1743 (C=O), 1714 (C=O), 1249, 1224 cm$^{-1}$. **DSC**: $T_g$ (º C) = 95; **TGA**: $T_d^5$ (º C) = 257. **GPC**: $M_n$ = 4.47 kg/mol, $M_w$ = 7.04 kg/mol, $Đ$ = 1.57.

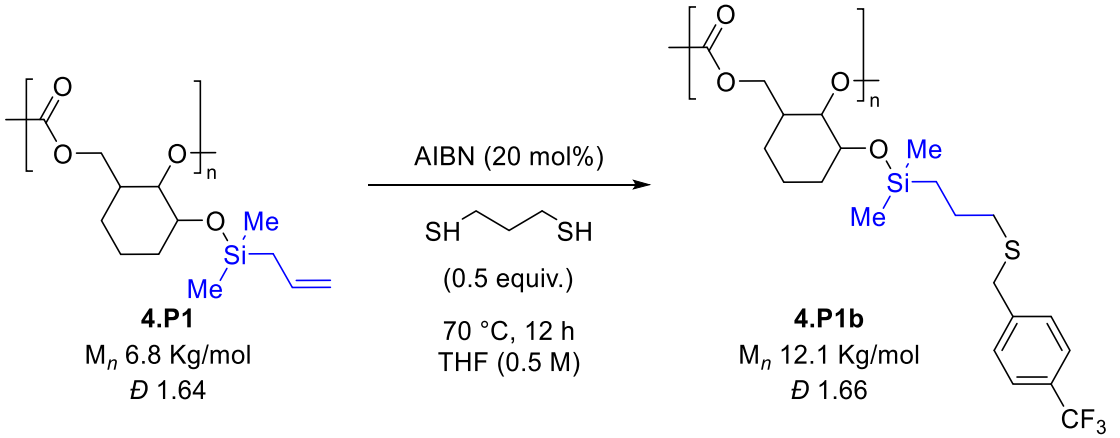
## 4.5.11 Procedure for post-polymerization modifications




**4.P1**
$M_n$ 6.8 Kg/mol
*Đ* 1.64

**4.P1a**

To a solution of **4.P1** (45 mg, 0.16 mmol, 1 equiv) in dry THF (0.3 mL, 0.5 M) under nitrogen was added 1,3-propanedithiol (8 μL, 0.08 mmol, 0.50 equiv) followed by AIBN (5.3 mg, 0.032 mmol, 20 mol%). The resulting mixture was then stirred at 70 °C for 12 h. The volatiles were removed in vacuo, and the crude reaction product was washed three times with methanol. The resulting purified polymer **4.P1a** was insoluble either in THF and $CDCl_3$, it was therefore characterized only through DSC, TGA and IR. **IR** (neat) $\nu_{max}$ = 2936, 2665, 1741 (C=O), 1237 $cm^{-1}$. **DSC**: $T_g$ (º C) = 32; **TGA**: $T_d^5$ (º C) = 326.



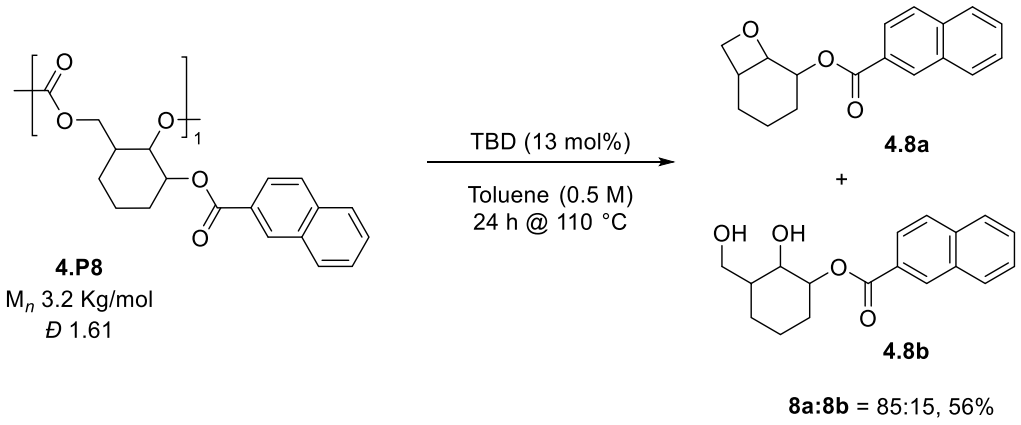

**4.P1**
$M_n$ 6.8 Kg/mol
*Đ* 1.64

**4.P1b**
$M_n$ 12.1 Kg/mol
*Đ* 1.66

To a solution of **4.P1** (45 mg, 0.16 mmol, 1 equiv) in dry THF (0.3 mL, 0.5 M) under nitrogen was added 3-(trifluoromethyl)benzyl mercaptan (61.5 mg, 0.32 mmol, 2 equiv) followed by AIBN (5.3 mg, 0.032 mmol, 20 mol%). The resulting mixture was then stirred at 75 °C for 10 h. The volatiles were removed in vacuo, and the crude product was washed three times with methanol. The purified polymer **4.P1b** was then collected and

dried in high vacuum. **$^{1}$H NMR** (300 MHz, CDCl3) δ 7.59 – 7.41 (4H), 4.61 (1H), 4.09 – 3.91 (3H), 3.75 (2H), 2.45 (t, *J* = 7.4 Hz, 2H), 2.35 – 2.09 (1H), 1.84 (1H), 1.67 – 1.47 (9H), 0.68 – 0.63 (1H), 0.15 – 0.10 (6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 155.2, 154.7, 139.9, 138.3, 132.7, 132.2, 131.0, 130.6, 129.1, 128.9, 126.1, 125.9, 125.5, 123.8, 122.3, 68.2, 66.6, 42.5, 36.7, 35.9, 35.0, 34.8, 29.2, 25.1, 23.2, 19.1, 18.5, 16.2, -1.6, -1.9. **$^{19}$F NMR** (282 MHz, $CDCl_3$) δ 62.7. **IR** (neat) $\nu_{max}$ = 2941, 1742 (C=O), 1449, 1329, 1250 $cm^{-1}$. **DSC**: *T*g (º C) = -12; **TGA**: $T_d^5$ (º C) = 251. **GPC**: $M_n$ = 1.21 kg/mol, $M_w$ = 2.02 kg/mol, $Đ$ = 1.66.

## 4.5.12 Procedure of TBD-catalyzed polymer degradation of 4.P8




In a nitrogen-filled glovebox, a vial equipped with a stirring bar was charged with **4.P8** (50 mg, 0.15 mmol carbonate repeat units) followed by a freshly prepared solution of TBD (3.5 mg, 0.02 mmol, 13 mol%) in toluene (0.3 mL, [M] = 0.50), transferred into a closed vial (10 mL), and placed in an oil bath heated to 110 °C for 24 h. The reaction mixture was allowed to cool to room temperature and the crude product purified through column chromatography to afford **4.8a** and **4.8b** as an inseparable 85:15 mixture in 56% yield (17 mg). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 1.6 Hz, 1H), 8.07 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.98 – 7.96 (m, 1H), 7.90 – 7.87 (m, 2H), 7.60 – 7.54 (m, 2H), 4.45 (dd, *J* = 11.0, 5.6 Hz, 1H), 4.37 (dd, *J* = 11.0, 7.8 Hz, 1H), 3.24 (dt, *J* = 4.1, 2.1 Hz, 1H), 3.19 (d, *J* = 3.9 Hz, 1H), 2.43 (ddt, *J* = 11.3, 7.8, 5.9 Hz, 1H), 2.16 – 2.12 (m, 1H), 1.79 – 1.70 (m, 2H), 1.49 – 1.44 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 166.7, 135.6, 132.5, 131.1, 129.3, 128.3, 128.2, 127.8, 127.2, 126.7, 125.1, 66.7, 53.6, 52.5, 34.4, 24.7, 24.0, 16.9. (**4.8a**) **HRMS** (ESI): m/z $[M+Na]^+$ calcd for $C_{18}H_{18}NaO_3$: 305.1148; found: 305.1159. (**4.8b**) **HRMS** (ESI): m/z $[M+Na]^+$ calcd for $C_{18}H_{20}NaO_4$: 323.1254; found: 323.1252. **IR** (neat) $\nu_{max}$ = 3507, 2936, 1714 (C=O), 1279, 1196 $cm^{-1}$.

# *Chapter 4*

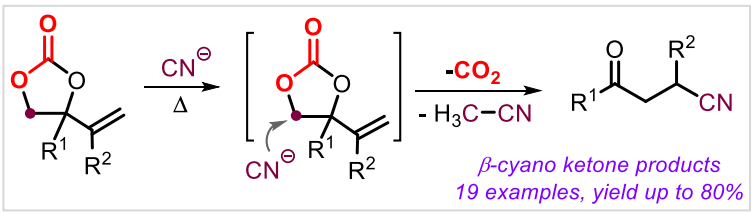
# *Chapter 5. Summary and General Conclusions*

UNIVERSITAT ROVIRA I VIRGILI
RING-OPENING OF CYCLIC CARBONATES: FROM FINE CHEMICALS TO CO2-BASED POLYMERS
Jixiang Ni

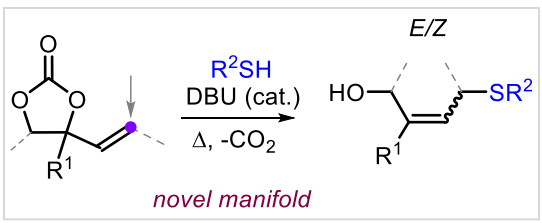
*Chapter 5*

The main objective of this doctoral thesis was the development of the novel ring-opening reactions of cyclic carbonates acting as substrates. Cyclic carbonates have unique reactivity comprising both nucleophilic and electrophilic sites. This dual behavior allows expanding the portfolio of functional intermediates and monomers derived from a $CO_2$-derived heterocycle. So far, the ring-opening chemistry of these heterocycles has been mostly limited to carbonate-attack approaches, which are useful in the context of fine-chemical (linear carbamates) and polymer chemistry (polyurethanes) applications. Much less explored are nucleophilic attacks on positions that are referred to as "methylene" and "*exo*-cyclic" in the cyclic carbonate precursor, and new approaches that can unleash effective and selective protocols for such pathways will help to increase the applicability of these $CO_2$ based heterocycles in synthetic chemistry. Several new types of ring-opening processes have been studied in this thesis and details of these advancements are described below.

In **Chapter 2**, we present an unprecedented ring-opening reaction of vinyl-substituted cyclic carbonates by cyanide that involves a rare sequence of decarboxylation/acetonitrile extrusion/Michael addition. This newly developed process affords β-cyano ketones up to moderately high yield. This protocol marks a newly discovered reactivity paradigm for cyclic carbonates with nucleophilic attack on the methylene carbon of the heterocycle being key. The hard nature of the cyanide anion is a factor likely determining the site-selectivity that is observed, and nucleophiles that can mimic this reactivity could further help to expand this type of manifold.

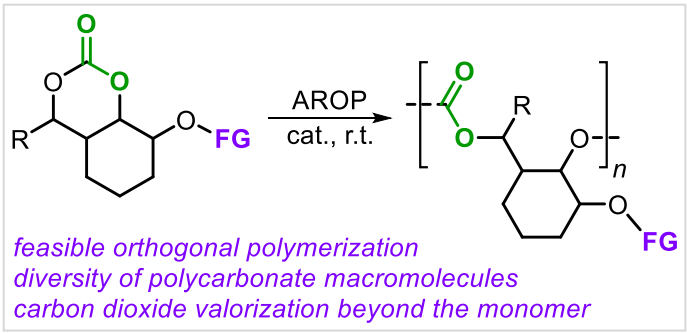



In **Chapter 3**, we report an unprecedented nucleophilic *exo*-cyclic attack of thiols onto vinyl-substituted cyclic carbonates that delivers allylic thioether products in moderate to good isolated yields. The process can be carried out under relatively mild reaction conditions using an organocatalyst (DBU). Control experiments support the view that the base



activates the thiol pro-nucleophile prior to attack onto the C-terminus of the double bond, after which decarboxylation takes place and finally protonation delivering the product. This new manifold adds new perspectives for the use of functionalized cyclic carbonates as precursors in organic synthesis. Other types of relatively soft nucleophiles might be of interest to expand the observed reactivity, while producing further variations of this formal allylic substitution process.

In **Chapter 4**, we present a family of functional, bicyclic six-membered cyclic carbonate (6MCC) monomers bearing synthetically useful groups. The catalytic anionic ring-opening polymerization (AROP) provides straightforward access to densely substituted macromolecular aliphatic carbonates (APCs). Bifunctional monomers were also designed allowing to trigger two different types of polymerizations and offering orthogonal polymerization/crosslinking strategies. Post-synthetic functionalization of these APCs was also demonstrated, which permits to change and modulate the (thermal) properties. A TBD-catalyzed degradation of one selected oligocarbonate led to a new fused bicyclic oxetane, which should have the potential to be recycled or repurposed to different kinds of polymeric materials. This work further exemplifies that properly equipped carbonate monomers can be ring-opened selectively to afford new types of APCs with controllable thermal and physical properties.




**Generally concluding**, the results presented in this thesis show that (functionalized) cyclic carbonates are versatile synthons for the preparation of a wide variety of new and functional heterocyclic products, and aliphatic polycarbonates. These approaches significantly expand the repertoire of the applications that have been developed so far in the field of non-reductive conversions of $CO_2$ and their use as intermediates in new synthetic transformations as exemplified by the results shown in Chapters 2-4. The combined efforts of this thesis provide important incentives for catalytic carbon recycling into designer

heterocycles with functionalities that help to mediate their controlled ring-opening using different nucleophiles. Future directions may include the use of other types of nucleophiles such as sulfinates and thiocyanates, and using other cyclic carbonates including those having (terminal) alkyne or allene groups. It is fair to say that this part of chemical space remains relatively unexplored providing inspiration for follow-up research.

# *Chapter 5*

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RING-OPENING OF CYCLIC CARBONATES: FROM FINE CHEMICALS TO CO2-BASED POLYMERS
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