Universitat Autònoma de Barcelona
Facultat de Ciències
Departament de Química
Estudis de doctorat en química

Proton-Coupled Electron Transfer Activation of Acidic Weak Nucleophiles

Highly Fluorinated Urethanes and Polyurethanes from polyfluorinated alcohols

DOCTORAL THESIS

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Highly Fluorinated Urethanes and Polyurethanes from polyfluorinated alcohols

Memòria presentada per aspirar al Grau de Doctor per:

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Cerdanyola del Vallès, Juliol 2014

Als meus pares

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Part of the results obtained in this thesis have been reported in the following publications:

Soto, M.; Comalrena, H.; Balduzzi, U.; Guirado, G.; Lloveras, V.; Vidal-Gancedo, J.; Sebastián, R. M.; Marquet, J. *Tetrahedron Lett.* **2013**, *54*, 6310-6313. DOI: 10.1016/j.tetlet.2013.09.037 *"Activation of weak nucleophiles: polyfluorocarbamates from polyfluoroalcohols via a fast radical reaction"*

Soto, M.; Sebastián, R. M.; Marquet, J. *J. Org. Chem.* **2014**, *79*, 5019-5027. DOI: 10.1021/jo5005789 "*Photochemical Activation of Extremely Weak Nucleophiles: Highly fluorinated Urethanes and Polyurethanes from Polyfluoroalcohols"*

Other manuscripts concerning the results obtained are currently under preparation.

In addition, part of the results obtained have been also presented in the following congresses and scientific meetings.

Soto, M.; Sebastián, R. M.; Marquet, J.; Vidal, J.; Guirado, G. "*Evidence for a Fast Radical Chain Mechanism in the reaction of Polyfluoroalcohols with Isocyanates"* IV School on Organometallic Chemistry "Marcial Moreno Mañas", Santiago de Compostela, Spain. 27-29th June 2011. Flash presentation and poster

Soto, M.; Sebastián, R. M.; Marquet, J.; Vidal, J.; Guirado, G. "*Evidències d'un nou mecanisme radicalari en la reacció d'alcohols polifluorats amb isocianats"* VII Trobada de Joves Investigadors dels Països Catalans, Palma de Mallorca, Spain. 16 - 17th February 2012. Short presentation.

Soto, M.; Sebastián, R. M.; Marquet, "*Photo-stimulated radical reaction to form Highly fluorinated Carbamates"* V School on Organometallic Chemistry "Marcial Moreno Mañas" Jaca, Spain. 2-4th July 2012. Flash presentation and poster.

Soto, M.; Sebastián, R. M.; Marquet, J. *"Photochemical preparation of highly fluorinated urethanes and oligourethanes"* IV Jornades Doctorals – Dept. Química. Bellaterra, Spain. 13-15th May 2013. Short presentation and poster.

Soto, M.; Sebastián, R. M.; Marquet, J. *"Photochemical preparation of highly fluorinated urethanes and oligourethanes".* VI School on Organometallic Chemistry "Marcial Moreno Mañas" Alicante, Spain. 3-5th June 2013. Flash presentation and poster.

Marquet, J.; Soto, M.; Sebastián, R. M. *"Novel photochemical activation of extremely weak nucleophiles: highly fluorinates urethanes from polyfluoroalcohols"* 18th European Symposium of Organic Chemistry. Marseille, France. 7-12th July 2013. Poster.

ACRONYM INDEX

AOC	Artificial oxygen carrier
ATR	Attenuated total reflectance
CRU	Conformational repeating unit
CTC	Charge transfer complex
CyNCO	Cyclohexyl isocyanate
DABCO	1,4-Diazabicyclo[2.2.2]octane
DBTDL	Dibutyltin dilaurath
DBU	1,8-Diazabicycloundec-7-ene
DMF	*N,N*-Dimethylformamide
DMPO	5,5-Dimethyl-1-pyrroline *N*-oxide
DMSO	Dimethyl sulphoxide
DNB	Dinitrobenzene
DP	Degree of polymerization
DSC	Differential scanning calorimetry
ECI	Electron capture ionization
2EH	2-Ethylhexanol
EPR	Electron paramagnetic resonance
FPU	Fluorinated polyurethane
Galvx.	Galvinoxyl
GC	Gas chromatography
GC-MS	Gas chromatography coupled with a mass spectrometer detector
GPC	Gel permeation chromatography
HBA	Hydrogen-bond acceptor (solvent)
HBD	Hydrogen-bond donor (solvent)
HFIP	1,1,1,3,3,3-Hexafluoro-*iso*-propanol
HMPA	Hexamethylphosphoramida
HNu	General protic nucleophile
HOMO	Highest occupied molecular orbital
IPDI	Isophorone diisocyanate
IR	Infrared spectroscopy
LUMO	Lowest unoccupied molecular orbital
M	Mol $\cdot$ L^{-1}
MDI	4,4'-Methylene diphenyl diisocyanate
MNP	2-methyl-2-nitrosopropane
M.p.	Melting point

MW	Molecular weight
n.d.	No detected
NMR	Nuclear magnetic resonance
PC	Propylene carbonate
PCET	Proton-coupled electron transfer
PFC	Perfluorinated compound
PTFE	Polytetrafluoroethylene (generic name of Teflon® from DuPont Co.)
PTM	poly(2,2,3,3-tetrafluorobutan-1,4-diol-*alt*-4,4'-methylene diphenyl diisocyanate)
PU	Polyurethane
PVDF	Polyvinylidene difluoride
PVF	Polyvinyl fluoride
r.t.	Room temperature
SCE	Saturated calomel electrode
SET	Single electron transfer
S_NAr	Nucleophilic aromatic substitution
TBAF	Tetrabutyl ammonium fluoride
TDI	Toluene 2,4-diisocyanate
TEOS	Tetraethyl orthosilicate
TFE	2,2,2-Trifluoroethanol
TLC	Thin layer chromatography
TMPO	3,3,5,5-Tetramethyl-1-pyrroline *N*-oxide
TMS	Tetramethylsilane
UAB	*Universitat Autònoma de Barcelona*
UV	Ultraviolet light
UV-Vis	Ultraviolet and visible light

Introduction

Carbamates, polyurethanes and polyfluorinated materials

I.1. INTRODUCTION TO CARBAMATES AND ISOCYANATES

The esters derived of carbamic acid or *N*-substituted carbamic acid are called carbamates. This unit is also called urethane, although strictly speaking, the term urethane is correct only when applied to ethyl carbamates. While in chemistry generally *carbamate* is more commonly used, the term *urethane* is predominant in the polymer field (Figure 1).[1]

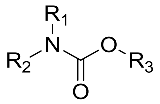
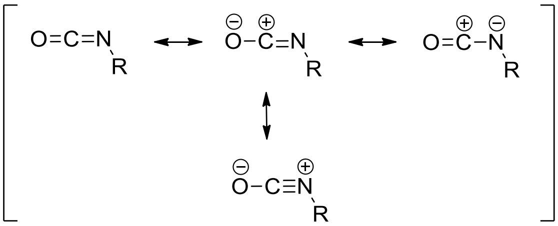


Figure 1. Carbamate functional group.

The most common synthesis of carbamates is through the reactions of an isocyanate with an alcohol. The isocyanate group is a heterocumulene with two consecutive double bonds N=C and O=C. The reactivity of isocyanates is based on the higher electronegativity of nitrogen and oxygen, which makes the central carbon highly electrophilic (Scheme 1).



Scheme 1. Resonance structures of the isocyanate group.

Even though it is a key element at industry level, its structure is not yet well understood. The only point of agreement is the minimum electron density on the central carbon. All the rest, remain in open debate; to date there has been little agreement on what are its charge magnitudes, atomic distances and even angle values.[2]

I.1.1. REACTION OF ISOCYANATES WITH NUCELOPHILES

When isocyanates react with a nucleophilic reagent HNu, the nucleophilic center ends attached to the electrophilic carbon of isocyanate and the proton in the nitrogen. From these reactions, the most important is the addition of an alcohol to the isocyanate to form a carbamate. Thiols, as well as primary and secondary amines also react as nucleophiles with isocyanates to form, respectively, thiocarbamates and ureas. As a rule of thumb, amines are

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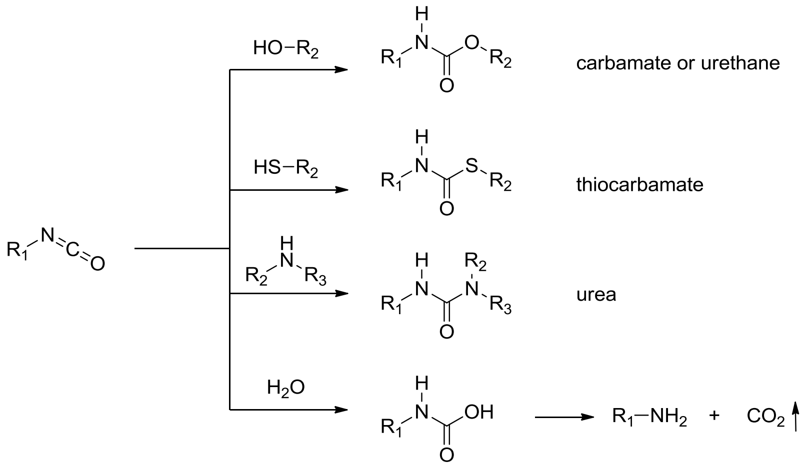
[1] This and other chemical definitions were extracted from: IUPAC. Compendium of Chemical Terminology - Gold book. (Last update: 14th Feb 2014. Version 2.3.3.) <http://goldbook.iupac.org> Nic, M.; Jirat, J.; Kosata, B.; Jenkins, A.

[2] Caraculacu, A. A.; Coseri, S. *Prog. Polym. Sci.* **2001**, *26,* 799-851.

more reactive towards isocyanates than alcohols, and alcohols more reactive than thiols (Scheme 2).[3]



Scheme 2. Common reactions of isocyanates with nucleophiles.

Another important reaction is the one that takes place with a ubiquitous nucleophile, water. In this reaction, unstable carbamic acid is formed, but it quickly decomposes to gaseous carbon dioxide and primary amine. This amine can react with another molecule of isocyanate to form urea.

I.1.2. APPLICATIONS OF CARBAMATES

The carbamate group is present in different applications, pharmaceutical drugs, insecticides, cosmetics and food preservatives. However, by volume of production, carbamates in polymers, polyurethanes PU, deserve a mention apart. Some examples of carbamates commercially produced are presented below.

PHARMACEUTICALS

The introduction of a carbamate unit in place of an acetyl or an ester group in a molecule usually slows its pharmacokinetics. Several carbamate drugs use this principle to act as reversible competing inhibitors.

Rivistagmine is an aromatic carbamate that is used as treatment for neurodegenerative diseases, such as Parkinson and Alzheimer's disease. Physostigmina is an acetylcholinesterase inhibitor used for the treatment of Alzheimer disease and glaucoma. Similar alkylic carbamates like Tybamate and Carisoprodol are used as anxiolytic and muscular

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[3] Delebecq, E.; Pascault, J.-P.; Boutevin, B.; Ganachaud, F. *Chem. Rev.* **2013**, *113,* 80-118.

relaxant, respectively. The more complex Darunavir is a protease inhibitor used in HIV treatment (Figure 2).

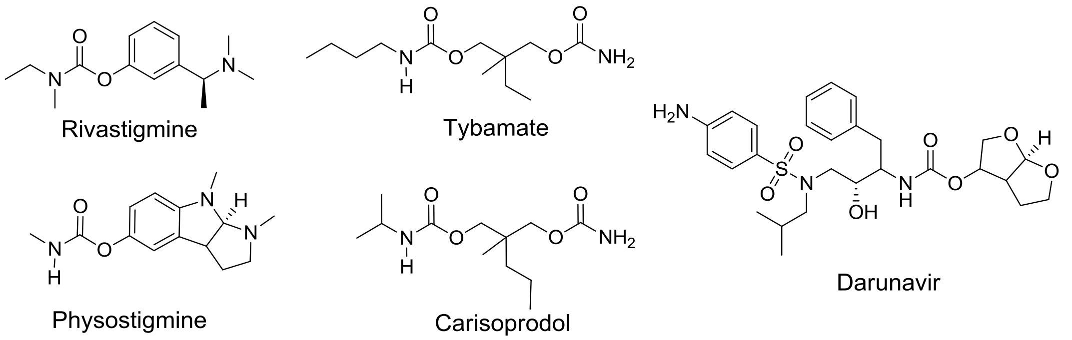

Figure 2. Examples of pharmaceutical drugs with carbamate groups.

CARBAMATE INSECTICIDES

Carbamate insecticides are persistent broad-spectrum insecticides that have sub-lethal effects in beneficial soil fauna, as earthworms. They usually target the nervous system of the insect by competing with acetylcholine. However, as this is a ubiquitous neurotransmitter in animal metabolism, they have a direct impact as well in human health. That is why after decades of use, most of them are gradually being banned in crops destined for human consumption.

Carbaryl is nowadays one of the most used insecticides in the US, even though it is banned in several countries of Europe. Carbofuran is a systemic insecticide, which means that the crop absorbs it and kills the insect when it eat the crop. Both of them share the structure of methylcarbamate linked to an aromatic system, formed by reaction of the corresponding aromatic alcohol with methyl isocyanate (Figure 3).

This simple volatile toxic compound was the cause of Bhopal gas tragedy on the 3rd December 1984. A major leak of methylisocyanate used for production of Sevin (Union Carbide brand name for Carbaryl) caused one of the worst chemical disaster, the immediate death of 3 787 people and over 15 000 more as a consequence of gas-related diseases in the following weeks.

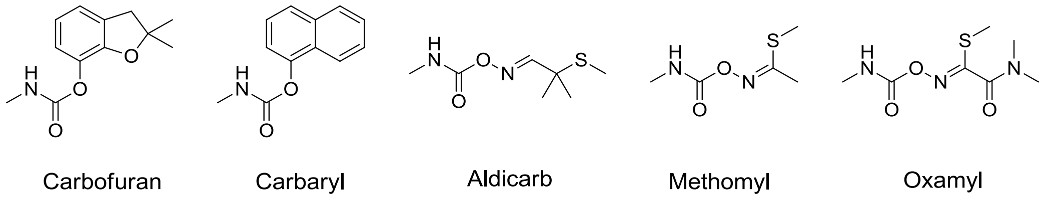

Figure 3. Some examples of carbamate insecticides.

Aldicarb, Methomyl and Oxamyl share a common pattern. They, as well, are highly effective insecticides that are also highly toxic. Although these insecticides are being gradually removed from market, they still can be used if concentration on final product is below limit of detection.

I.2. INTRODUCTION TO POLYURETHANES

More than eighty years ago, in 1929 the chemical company DuPont struck the market with the first synthetic fiber. Carothers developed them based on condensation polymers, first on polyamides and latter on polyesters.[4] After such success, other companies tried to develop their own ones. Otto Bayer, working for Bayer but without any relation with the running family, was attempting to mimic these materials without breaking any licensed patents. His idea was to obtain similar properties with polyureas made by reaction of diisocyanates with diamines. One day, accidentally, some diisocyanate got mixed with glycol forming the first polyurethane, PU.[5]

Nowadays, polyurethanes can be found almost everywhere; a glance around on our surroundings allows us to discover their versatility. It is very likely that flexible foams of chairs you sit in and mattresses you sleep on are made with polyurethanes. Probably PU hard foams are found inside your walls, fridge and freezer as insulation. In addition, PU elastomers are used in sport shoe soles and even in non-allergenic condoms. Hard rigid polyurethanes are used as external elements in automotives, as bumpers and wind spoilers (Figure 4).

Polyurethanes: Versatile Materials and Sustainable Problem Solvers for Today's Challenges

Hans-Wilhelm Engels, Hans-Georg Pirkl, Reinhard Albers, Rolf W. Albach, Jens Krause, Andreas Hoffmann, Holger Casselmann, and Jeff Dormish*

Keywords:
adhesives · coatings · elastomers · flexible foams · rigid foams

Dedicated to the Bayer company on the occasion of its 150th anniversary

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[4] Carothers, W. H. *Trans. Faraday Soc.* **1936**, *32*, 39-49.

[5] (a) Seymour, R. B.; Kauffman G. B. *J. Chem. Ed*. **1992**, *69*, 909-910.
(b) Original: Bayer, O. *Angew. Chem.* **1947**, *59*, 257-272.

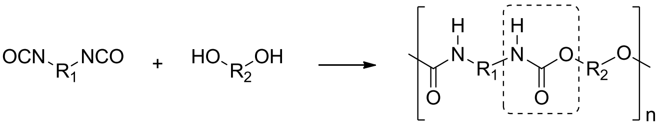
Figure 4. Front cover of a recent review article showing polyurethane versatility.
From Engel, H.-W. *et al. Angew. Chem. Int. Ed.* **2013**, *52*, 9422-9441.6

Polyurethanes are the only polymers that can be thermoplastic, elastomeric or thermoset materials depending on their formulation. By adequately selecting reagents and controlling side reactions, stiffness as well as density can be modulated.[6]

In the ranking of polymers by volume, PU are ranked fifth by world production, right after the family of polyolefins, *i.e.* polyethylene and polypropylene, PVC, polystyrene and diene rubbers.[7]

I.2.1. HOW POLYURETHANES ARE MADE?

Nowadays, the only method used for preparing large-scale polyurethanes is the polyaddition process of diisocyanates with diols or polyols. The carbamate linkage and the presence of hydrogen bonds are responsible for PU good mechanical properties, abrasion resistance, toughness and tensile strength (Scheme 3).



Scheme 3. PU formation by reaction of diol with diisocyanates.

However, as most isocyanates are toxic, nowadays there are several research lines to produce non-isocyanate polyurethanes. One possibility for that are reactions of diamines with dicarbonates (Scheme 4, i), chlorodicarbonates (Scheme 4, ii) or cyclic carbonates (Scheme 4, iii). But for these ways to be worthy, those carbonates should avoid phosgene and better be prepared from CO_2, a currently developing research topic.[8] Other approaches use transcarbamoylation reactions. In general, aliphatic carbamates are more stable than aromatic ones, therefore reaction of aromatic dicarbamates with aliphatic diols lead to aliphatic polyurethanes (Scheme 4, iv). Other interesting approach is to prepare cyclic urethanes that open and polymerise (Scheme 4, v).[9]

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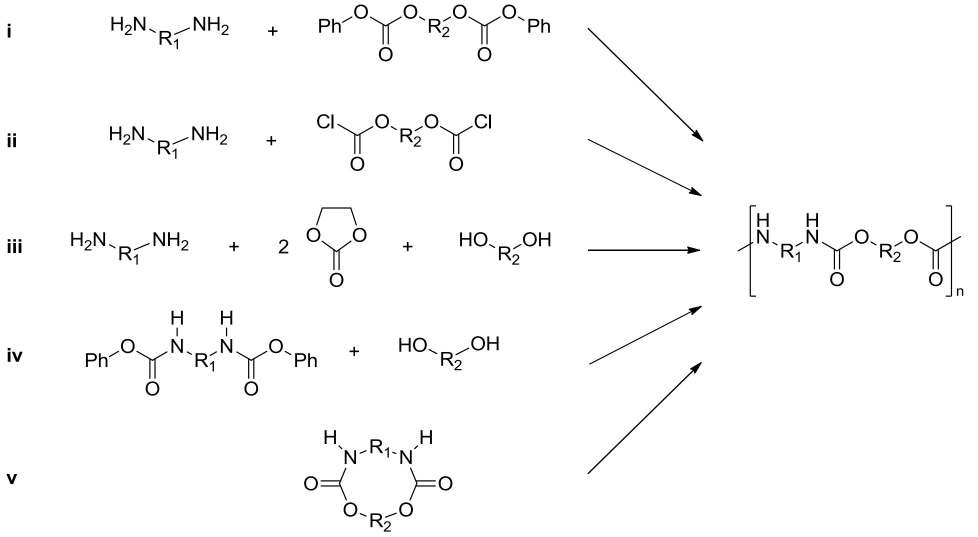
[6] Engels, H.-W.; Pirkl, H.-G.; Albers, R.; Albach, R.W.; Krause, J.; Hoffmann, A.; Casselman, H.; Dormish, J. *Angew. Chem. Int. Ed.* **2013**, *52,* 9422-9441.

[7] Krol, P. *Prog. Mat. Sci.* **2007,** *52*, 915-1015.

[8] Kreye, O.; Mutlu, H.; Meier, M.A.R. *Green Chem.* **2013**, *15*, 1431-1455.

[9] Guan, J.; Song, Y.; Lin, Y.; Yin, X.; Zuo, M.; Zhao, Y.; Tao, X.; Zheng, Q. *Ind. Eng. Chem. Res.* **2011**, *50*, 6517–6527.



Scheme 4. Preparation of non-isocyanate polyurethanes using diamines (i, ii, iii) or preformed carbamates (iv, v).

Although it should change in the future, nowadays polyurethane chemistry is dominated by the reaction of diisocyanates. There are a limited variety of diisocyanate used industrially to produce PU, usually of low molecular weight. The most used are aromatic ones because of its greater reactivity, specially 4,4'-methylene diphenyl diisocyanate, MDI, and toluene 2,4-diisocyanate, TDI, and their isomers. MDI account for 61 % of world isocyanate market, while TDI account for the 34 %. In fact, MDI also includes polymeric methylene diphenyl diisocyanate, PMDI, with an average number of isocyanate functionalities around 2.7, used to obtain branched PU. Aliphatics diisocyanates are represented by isophorone diisocyanate, IPDI, and hexamethylene diisocyanate, HDI. They are less reactive, but they form PU more stable to UV light and sun exposure (Figure 5).[6]

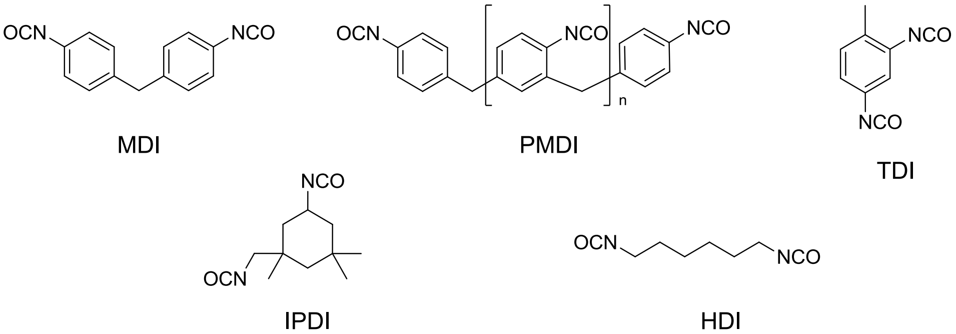


Figure 5. Industrially relevant diisocyanates.

In contrast to the limited variety of diisocyanates, there are wide ranges of diols and polyols avalaible, the other major component used. Final PU properties depend mainly on two factors of the polyol: degree of functionalisation and the length of the chain.

The use of monomers of high degree of functionalization (PMDI instead of MDI or a polyol with a high degree of functionalization) would lead to highly branched polyurethanes, rigid thermoset polymers with good heat and chemical resistance. On the other hand, using diols yield linear PU, usually thermoplastic materials with more flexibility at low temperature and more degradable.

Length of the polyols is another important factor. With small diols *hard* polyurethane phases are obtained, because a high proportion of carbamate units and hydrogen bonds are present, promoting rigidity and not flexibility. On the other hand, the use of macromolecular diols result in *soft* PU phases, flexible materials with low glass transitions. These macromolecular diols usually are polyether or polyester diols.

These two phases, *hard* and *soft*, are not compatible with each other. This fact is exploited in the preparation of thermoplastic polyurethane, elastic linear segmented block copolymers. They are formed by reaction of a diisocyanate, a long diol and a short diol (called chain extender in this context). In these polymer, hard phase islands are surrounded by seas of soft phase. Hydrogen bonded hard phases act as cross-linking points that can be broken by temperature. Thus, thermoplastic urethanes behave like cross-linked polymers, but can be processed as thermoplastics.

An example of this type of polyurethane is elastane, more known as spandex or Lycra®, a polyurethane-polyurea elastomer. To prepare it, prepolymer polyurethane formed by a macrodiol and a diisocyanate is reacted with a short diamine to form elastane. The name of this material reflects its ability to expand its length up to 500 %, for this reason is very used in the clothing industry.

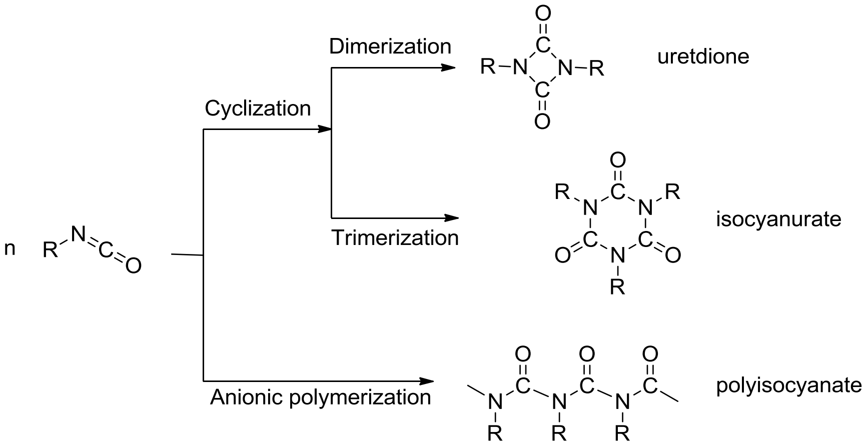
The chemistry of PU is dominated by the reactivity of isocyanate functional group. Apart from the reaction with alcohols to form the carbamates, it reacts with amines to form ureas, in addition to several competing by-reactions that deeply affect the properties of the final PU.

The reaction of isocyanates with water is used in the formation of PU foams. In formulations that have low viscosity, it is possible to use external foaming agents. However, in high viscous formulations the use of external foaming agents is limited. In these cases, carbon dioxide generated *in situ* by reaction of isocyanates with water act as an internal foaming agents. This is the principle used to form rigid foams that cannot be formed otherwise.

ISOCYANATE SELF-REACTIONS

In addition to the reactions of the isocyanate group with nucleophiles, isocyanates can react with themselves. The control of these reactions is very important in the processing of PU. Thus, extensive industrial research is focused on catalysts and conditions that control or promote these reactions.

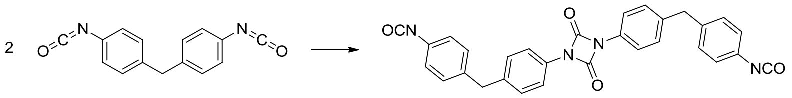
Dimerization is usually a reaction to avoid. However, each trimerization to form isocyanurate of a diisocyanate is potentially a branching point that affects the properties of the final urethane and can be desirable. Formation of polyisocyanate is a reversible reaction that can be used to mask the isocyanate to better handling and releasing them when required (Scheme 5).



Scheme 5. Isocyanate selfaddition reactions.

Aliphatic isocyanates do not tend to form homocouplings or they need specific catalysts. However, aromatic isocyanates can form dimers and trimers just upon heating or in the presence of a nucleophilic catalyst.

In MDI, the most used diisocyanate, the dimerization product generates yellowing and turbidity of the formulation, being a reaction to avoid, especially during storage. For MDI, rate of dimer formation is higher near the melting point (38 ºC) and increases above 50 ºC. Thus, best storage temperatures are below 0 ºC and when processing it as a liquid, keep it between 40 and 45 ºC to minimize dimer formation (Figure 6).[10]



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[10] BASF Corporation. *Polyurethane MDI Handbook*. <http://www.stage.basf.com/urethanechemicals/pdfs/2000mdihandbook.pdf> (Access: 3rd June 2014)

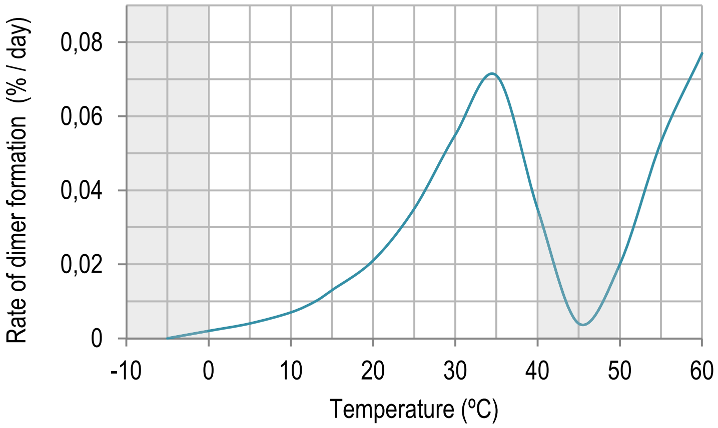

Figure 6. MDI dimer formation rate in function of temperature.

I.2.2. ADDITIVES USED IN POLYURETHANES

Apart from adequately selecting the different comonomers and reaction conditions to tune the properties of the final polyurethane, some additives can be added to modify the properties. This is of special importance on polyurethane foams. When these foams are applied in upholstered furniture or inside-walls insulation, they became an important element in fire propagation.

Thus, several flame retardant components are added to PU foams formulations to improve their resistance to fire. Usually, they are highly halogenated organic compounds. For example, chlorendic acid or decabromo diphenyl ether are excellent in this rolet, but with several concerns about its toxicity and effects on human health (Figure 7).[11] Other flame retardants are polyfluorinated organic compounds and polyfluorinated materials.

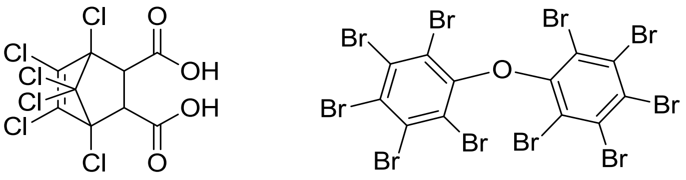

Figure 7. Chlorendic acid and decabromo diphenyl ether, flame retardants.

In general, polyfluorinated materials exhibit unique properties and have special applications that will be further detailed in the next section.

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[11] Shaw, S. D.; Blum, A.; Weber, R. *Rev. Environ. Health* **2010**, *25*, 261-305.

I.3. INTRODUCTION TO POLYFLUORINATED COMPOUNDS AND MATERIALS

Polyfluorinated organic compounds have very interesting properties such as high thermal and chemical stability and low surface energy. Their applications range from oxygen transporters to anesthetics with special significance in the fields of pharmaceutics, catalysis and materials science. Moreover, highly fluorinated materials show at the same time both hydrophobicity and oleophobicity.[12,13]

I.3.1. GENERAL PROPERTIES OF POLYFLUORINATED COMPOUNDS

The special properties of polyfluorinated compounds have their origin in the unique characteristics of fluorine atom. While it is the most electronegative element, it is a relatively small atom, bigger than hydrogen but smaller than carbon. This turns out in a very low polaritzability, in other words, fluorine do not tend to *share* its electrons (Table 1).

Table 1. Radius and electronegativity of H, C and F.

Atom	Covalent radius (Å)	Pauling's χ
H	0.31	2.20
C	0.76	2.55
F	0.57	3.98

These properties strongly affect structure and molecular dynamics of compounds where hydrogen atoms are substituted by fluorine, for example in polyfluorinated chains. While hydrocarbon chains adopt a flexible zigzag conformation, polyfluorinated chains are rigid in helicoidal conformation due to repulsion between 1-3 positions (Figure 8).[14]

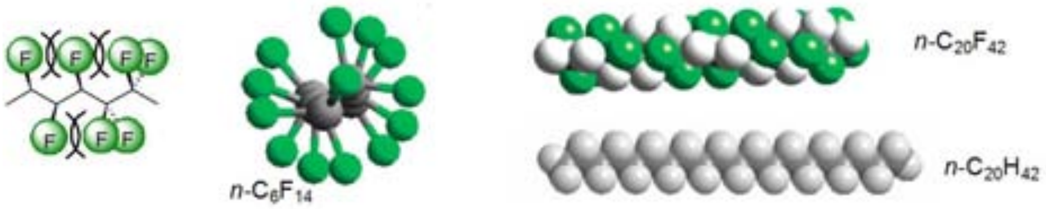

Figure 8. Helicoidal structure of polyfluorinated chains.[14]

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[12] (a) Tuteja, A.; Choi, W.; Ma, M.; Mabry, J. M.; Mazzella, S. A.; Rutledge, G. C.; McKinley, G. H.; Cohen, R. E. *Science*, **2007**, *318*, 1618-1622.
(b) Im, M.; Im, H.; Lee, J-H.; Yoon, J-B.; Choi, Y-K. *Soft Matter* **2010**, *6*, 1401-1404.

[13] Gladysz, J. A.; Curran, D.P. Horváth, I. T. *Handbook of Fluorous Chemistry*. Weinheim: Wiley-VCH, 2004.

[14] Jang, S. S.; Blanco, M.; Goddard III, W. A.; Caldwell, G.; Ross, R. B. *Macromolecules* **2003**, *36*, 5331-5341.

The external surfaces of these chains are partially negatively charged. Due to the high electronegativity of fluorine, it is not polarizable, not forming hydrogen bonds or Van der Waals interactions. In addition, this negative shell protects carbon from nucleophilic attacks.

From a practical point of view, these properties correlate with physical properties of polyfluorinated compounds, which in general can be summarized as low affinity for everything. In liquid, perfluorinated solvents are not miscible at room temperature neither with organic solvents nor water, being possible to obtain stable triphasic systems. In solid state, as perfluorinated materials have low affinity for water they are hydrophobic, but at the same time, they are oleophobic; properties very useful for many applications.

As a consequence of the characteristic of polyfluorinated compounds, special applications have appeared. A brief selection of them is presented below.

I.3.2. POLYFLUORINATED/ORGANIC BIPHASIC CATALISYS

In general, perfluorinated solvents are not miscible with organic solvents at room temperature. However, some mixtures of organic and polyfluorinated solvents present a thermomorphic behavior, being miscible at high temperatures but not at lower ones.

In biphasic catalysis, reagents are solved in the organic phase and a modified catalyst with perfluorinated chain is solved in perfluorinated solvent. When the system is heated up and stirred, both polyfluorinated and organic phase became miscible and the reaction takes place in a homogeneous medium. By cooling down, the system became heterogeneous again, resulting in the separation of catalyst in the fluorinated phase from the product in the organic phase.[15]

For example, palladium nanoparticles stabilized with compounds wearing perfluorinated chains are soluble in perfluorinated solvents, but not in organic solvents, where reactants, phenyl iodide and ethyl acrylate, are solved. By heating up, an homogeneus phase was formed in which the nanoparticles catalyse the Mizoroki-Heck coupling. When the reaction is completed, by cooling down, catalyst and product are separated. That allows an easy recycling of catalyst and an easy separation of the product formed (Scheme 6).[16]

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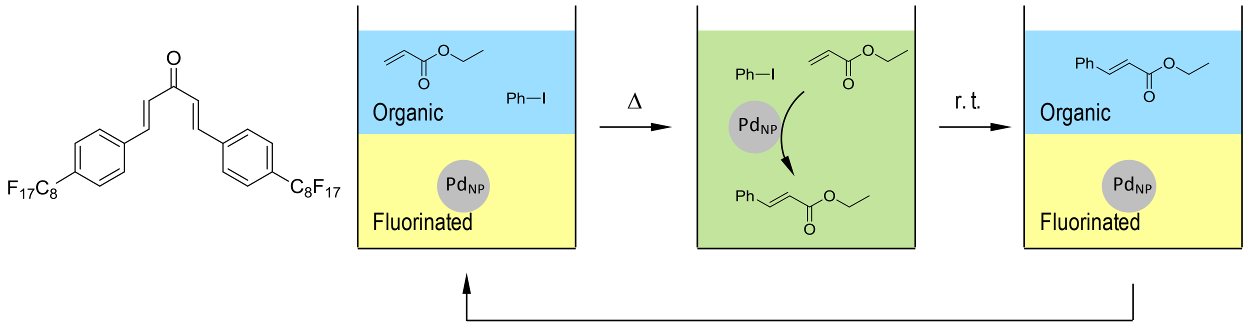
[15] (a) Horwáth, I. T. *Acc. Chem. Res*. **1998**, *31*, 641-650.
(b) Moreno-Mañas, M; Pleixats, R. *Acc. Chem. Res*. **2003**, *36*, 638-643.

[16] Moreno-Mañas, M.; Pleixats, R.; Villaroya, S. *Organometallics* **2001**, *20*, 4524-4528.

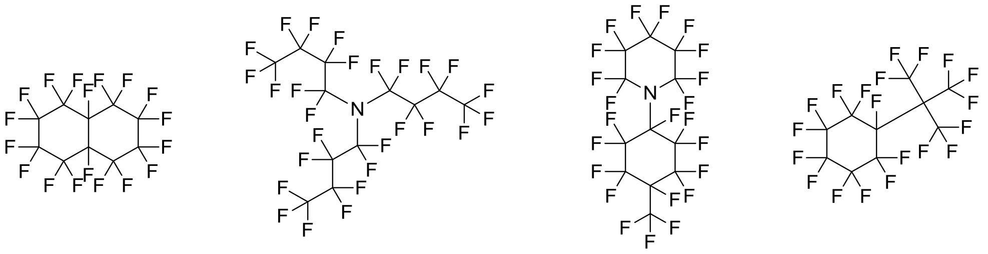


Scheme 6. Example of stabilizer for Pd nanoparticles and scheme of fluorinated/organic biphasic catalysis.[16]

I.3.3. ARTIFICIAL OXIGEN CARRIERS

Artificial oxygen carriers, AOC, are solutions that are able to bind, transport and unload oxygen in the body. Although they do not substitute blood in all the functions, they perform the vital functions of oxygen transport and volume expansion in critical situations. In some circumstances, AOC might be a more desirable solution than blood transfusion, as in countries with shortage of blood donors or high levels of blood-borne diseases or in situations of religious concern on accepting transfused blood. Nowadays there are two viable types of AOC: hemoglobin-based oxygen carriers and based on perfluorocarbon compounds, PFC (Figure 9).

PFC are not miscible in water, thus oxygen carriers are prepared as an emulsion in water. To this emulsion, salts, antibiotics and others are added to complete the formulation. PFC are completely man-made and do not resemble any natural molecule. Thus, metabolism do not recognise them and cannot process it, being slowly eliminated just by breathing. PFC solutions carry more oxygen than blood does, up to five times. In fact, is such the amount of oxygen they carry that mammals, including humans, can breathe liquid PFC.[17]



Fluosol-DA Fluosol-43 Perftoran Oxycite

Figure 9. PFC used as artificial oxygen carriers.

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[17] Henkel-Honke, T. Olek, M. *Am. Ass. Nurse Anest. J.* **2007**, *75,* 205-211.

Nowadays, PFC oxygen carriers are limited to a few specific applications. They are used in cases of severe blood loss, as surgery and trauma, in which is necessary to quickly increase blood volume and oxygen levels. In cases of a severe lack of oxygen, as in acute respiratory distress, they are an appropriate treatment. In addition, they are needed in gaseous related symptoms, as decompression sickness where it is needed to remove nitrogen solved in blood to avoid bubbles formation in tissues.

I.3.4. SURFACE MODIFICATION

Perfluorinated chains have been used to modify surface properties of different materials. Thus, common materials, like glass or cotton, can become highly hydrophobic.

An example of this application of polyfluorinated compounds can be found in our research group. Some years ago, a methodology was developed to prepare azo dyes modified with perfluorinated chains. These dyes were further functionalized with the appropriate group to covalently link to the required material. Thus, dyes modified with isocyanuryl chloride were attached to hydroxyl groups on cotton and dyes modified with triethoxysilyl groups to a glass surface (Figure 10).

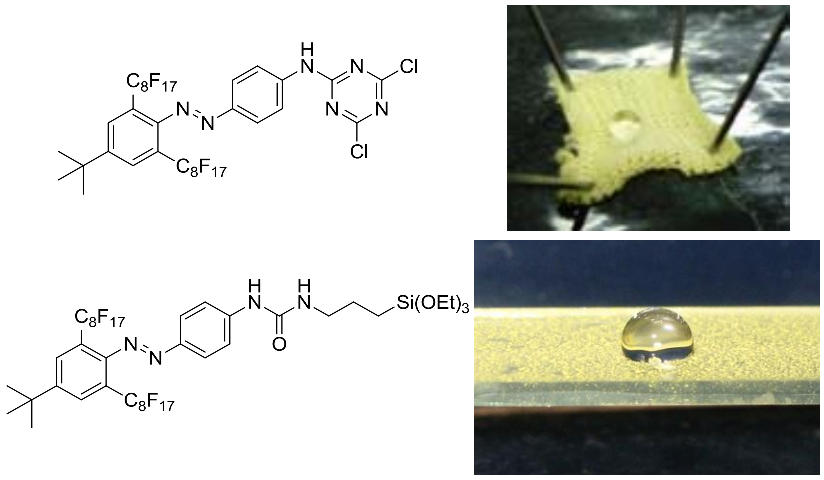

Figure 10. Examples of modified dyes able to attach at cotton or glass.

By this means, these materials were doubly modified: the dye changed the color while the perfluorinated chains improved their surface properties and made them highly hydrophobic, which could be used in several applications.[18]

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[18] Vallribera, A.; Sebastián, R. M.; Soler, R.; Molins, E. *Nuevas sustancias colorantes y el procedimiento para la obtención*. ES-P200802751, 23rd September 2008.

I.3.5. POLYFLUORINATED POLYMERS

The most known application of polyfluorinated compounds is in material science in the form of polymers. In general, polyfluorinated polymers present high thermal and chemical resistance, either to solvents, acids or bases. Below some representative examples are presented (Figure 11).

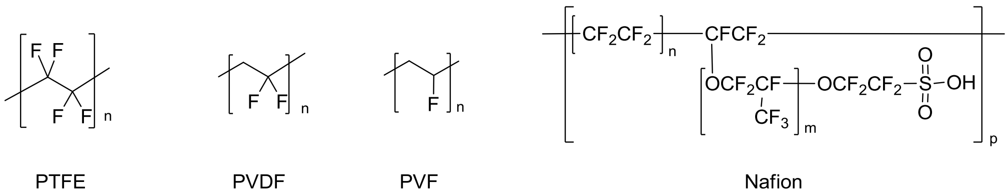

Figure 11. Examples of polyfluorinated polymers.

Polytetrafluoroethylene, PTFE, more known by the commercial name of Teflon®, was accidentally discovered by DuPont in 1938. The properties of this perfluorinated material were very interesting, specially their thermal and chemical stability. That is the reason why its development was linked to The Manhattan Project and nuclear energy, since it was the only material available at that time able to resist the very corrosive uranium hexafluoride.

In the 1960s, it arrived to the general public in the *happy pan*, a frying pan coated with Teflon® that was easily cleaned. Nowaday PTFE is used in multitude of applications, including high-end medical materials, in artificial corneas, bones substitute, heart valves, tendons, tracheas...[19]

While having a great thermal and corrosive resistance, the main limitation of PTFE use is that is not easily processable, thus not being a good engineering material.

Interestingly, polyvinylidene difluoride PVDF has a lower melting point than PTFE, what makes it more processable. Even more interesting is the fact that in the appropriate phase, this material is electronically active, showing piezoelectricity and being ferroelectric. Main applications of this polymer are insulation in electrical wires and high-end paints for metals. For example, one of the highest buildings in the world, the Petronas towers in Malaysia are painted with PVDF.

Polyvinyl fluoride PVF is the product of polymerization of vinyl fluoride using a peroxide catalyst. In comparison to PTFE, it is easily processable using thermoplastic materials techniques. It offers good flame resistance due to thermally induced hydrogen fluoride formation, which in spite of being highly toxic, assists in fire control.

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[19] (a) Becmeur, F.; Geiss, S.; Laustriat, S.; Bientz, J.; Marcellin, L.; Sauvage, P. *Eur Urol.* **1990**, *17,* 299-300.
(b) Laustriat, S.; Geiss, S.; Becmeur, F.; Bientz, J.; Marcellin, L.; Sauvage, P. *Eur Urol.* **1990**, *17*, 301-303.

The alternative bond polarities of PVF gives a tight structure that results in good resistance to cracking and fading, and low permeability. The low coefficient friction allows PVF-coated materials to be essentially self-cleaning as it rains, carrying away dust, bird dropping and graffiti.

As PVF is more expensive than PE and PP, it is not used as generally as them. Thus, PVF is used only in selected high-end coatings and film bulk applications, such as outdoor signs, roofing building panels and solar collectors.

Fluorinated polymers can be modified with functional groups for specific applications. An example of functionalised polyfluorinated polymer would be Nafion®. It is the result of the copolymerization of tetrafluoroethylene with a perfluorinated sulfonic acid. This ionomer, polymer with ionic properties, is used in proton and cation exchange membranes of high resistance to corrosion and temperature.

ENVIRONMENTAL CONCERN OF LONG PERFLUORINATED CHAINS

Recently, there have been a rising concern regarding the use of materials containing long perfluorinated chains and perfluorinated compounds, PFC. As has been explained, the properties of compounds with perfluorinated chains are so interesting that they are incorporated everyday in more applications. However, perfluorinated chains and PFC are exogenous to life metabolism. While this supposes an advantage for biomedical applications, it also supposes an important issue in its degradation.[20]

For seventy years the amount of compounds with perfluorinated chain has only increased in the environment. The major concentrations are detected for medium size perfluorinated chains. Short chains (four or less perfluorocarbons) are short enough to be processed by metabolism. Polymeric perfluorinated chains (more than 20 perfluorocarbons) are not volatile and thus remain unaffected in the soil. However, medium size chains (considered chains with six to twenty perfluorocarbons) are volatile enough to be spread around the world and long enough for not to be degraded by medium or by living organisms.

Since Stockholm Convention in 2009, long chain perfluorinated acids are considered Substances of Very High Concern because they are very persistent and bioaccumulative. The same happen with perfluorooctanoic acid and perfluorooctanesulfonate among others that are moreover toxic (Figure 12, left).

The acids and sulfonic derived from perfluorinated chains are bioaccumulative because they are the termination degradation products, and then accumulate in lipid layer or in liver interacting with proteins. They remain in the lifecycle because anaerobic defluorination does not

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[20] Lindstrom, A. B.; Strynar, M. J.; Libelo, L. *Environ. Sci. Technol.* **2011**, *45*, 7954-7961.

take place,[21] direct photolysis is not possible,[22] and indirect photolysis require high concentrations of Fe(III), light and low pH.[23]

Almost all human blood samples collected worldwide were found to contain measurable amounts of PFC in ng / mL level. The *in vivo* long term effects include organic tumors (liver, pancreas, testicular) and changes in the lipid metabolism. What is surprising is that they can be found in blood samples from wildlife spread around the world, even in relatively isolated arctic mammals.[20] As they are long-lasting, long-range transport is a concern in itself; PFC reach even the furthest place from their origin source (Figure 12, right).[24]

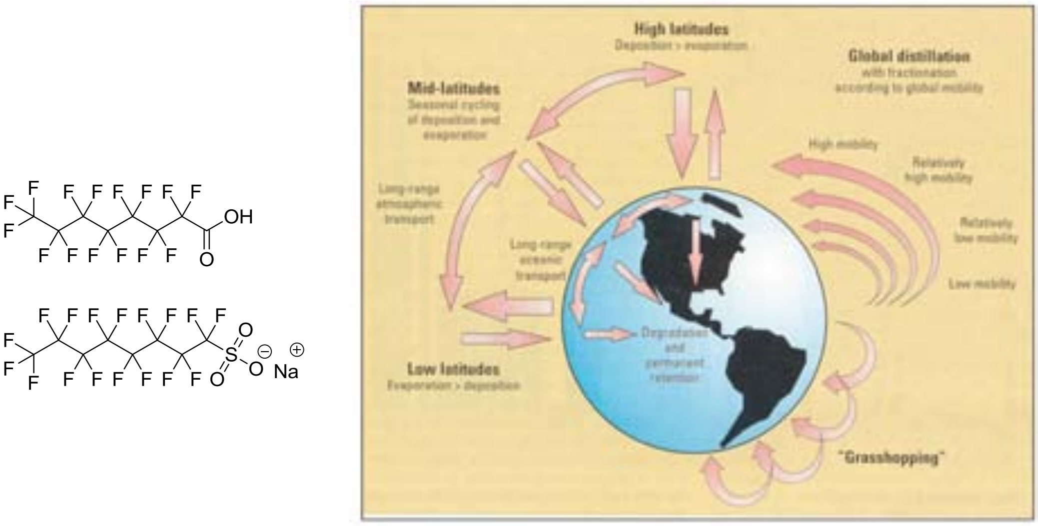

Figure 12. Left: Perfluorooctanoic acid and sodium perfluorooctanesulfonate. Right: Long-range transport mechanism.[24]

Thus, the first political action taken was to limit exposure by reduction of uncontrolled facility emissions. But in the long term, these general observations form the basis for the call to restrict or eliminate the use of long-chain PFC. Big companies as 3M have voluntarily passed PFC with chains of eight or more carbons. Instead, they are using shorter perfluorinated chains linked with mid points, as ester groups, that act as breaking points of the molecule in the degradation process.[25]

Considering this approach, a carbamate group is a feasible possibility to act as breaking points. Thus, the preparation of polyfluorinated PU could provide an interesting alternative to these problems.

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[21] Liou, J. S.; Szostek, B.; DeRito, C.M.; Madsen, E.L. *Chemosphere* **2010**, *80*, 176-183.
[22] Taniyasu, S.; Yamashita, N.; Yamazaki, E.; Petrick, G.; Kannan, K. *Chemosphere* **2013**, *90*, 1686-1692.
[23] Vaalgamaa, S.; Vähätalo, A.; Perkola, N.; Huhtala, S. *Sci. Total Environ.* **2011**, *409*, 3043-3048.
[24] Wania, F.; Mackay, D. *Environ. Sci. Technol,* **1996**, *30*, 390-396.
[25] Ritter, S. K. *Chem. Eng. News* **2010**, *88*, 12-17.

I.4. POLYFLUORINATED CARBAMATES

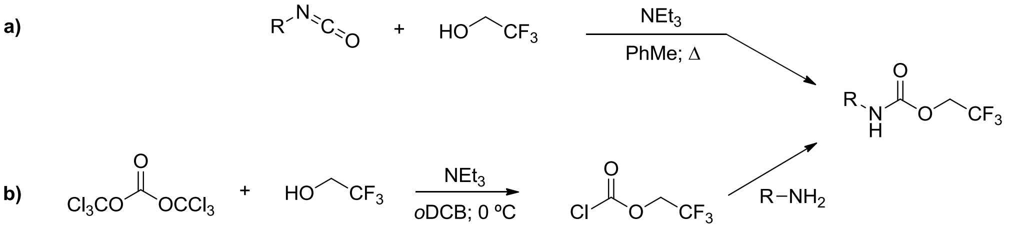
In this section, previously reported literature regarding polyfluorinated carbamates and polyfluorinated PU is presented. The focus will be on the preparation reactions as well as on the main obstacle, that polyfluorinated alcohols are very weak nucleophiles. After that, some relevant precedents from the research group regarding a different reactivity of polyfluorinated alcohols will be presented.

I.4.1. SINGLE CARBAMATES

Polyfluoroalkyl arylcarbamates have found different applications as anti bacterial agents,[26] herbicide antidotes,[27] and have been used to impart water and oil repellecy to materials.[28]

Common building blocks in the construction of polyfluorinated carbamates are polyfluorinated alcohols and isocyanates that react in the presence of a tin catalyst[29] or a tertiary amine.[26] However, polyfluorocarbamates derivatives have not yet developed all their potential, among other reasons, due to the general very low nucleophilicity of polyfluorinated alcohols.

Preparation of trifluoroethyl carbamates through the reaction of isocyanate with a 2,2,2-trifluoroethanol have been reported in reflux of hexane/toluene with triethylamine as catalyst. However, the authors recommended an alternative way, the reaction of amines with trifluoroethyl chloroformate to form the same trifluoroethyl carbamates, in spite of having more synthetic steps and the use of a phosgene derivate (Scheme 7).[30]



Scheme 7. Preparation of trifluoroethyl carbamates by a) reaction of isocyanate with TFE and b) formation of trifluoroethyl chloroformate and posterior reaction with amine.[30]

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[26] Studnev, Y. N.; Frolovskii, V. A.; Krasnov, A. P. *Pharm. Chem. J.* **2002**, *36*, 654-658.

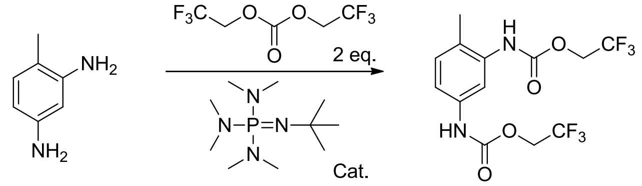
[27] Green, L. L.; Duerksen, C. J.; Rodriquez, B. *Antidotes for pyrrolidinone herbicides and herbicide antidote compositions* European Patent Application. EP 84253 A1, 27th Jul 1983.

[28] Qiu, Z.-M.; Clark, J. C.; Fan, W. W.; Flynn, R. M.; Jariwala, C. P. *Water- and oil-repellency imparting urethane oligomers comprising perfluoroalkyl moieties.* Patent Cooperation Treaty Int. Appl. WO 2002072657 A1, 19th Sep 2002.

[29] Mashlyakovskiy, L.; Khomko, E.; Volynkina, N.; Tonelli, C. *J. Polym. Sci.: Part A: Polym. Chem.* **2002**, *40*, 3771-3795.

[30] Bogolubsky, A. V.; Ryabukhin, S. V.; Pipko S. E.; Lukin, O.; Shivanyuk, A.; Mykytenko, D.; Tolmachev, A. *Tetrahedron* **2011**, *67*, 3619-3623.

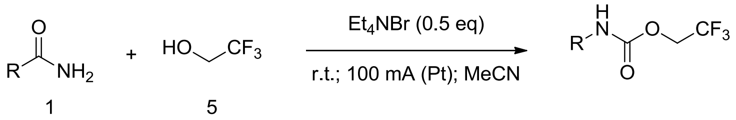
Trifluoroethyl and other carbamates can be prepared by reaction of an amine with the corresponding difluoroalkyl carbonate using a phosphazene organocatalyst (Scheme 8).[31]



Scheme 8. Example of formation of polyfluorinated carbamates from amines and polyfluorinated carbonate.[31]

In the previous examples, instead of the reaction of a polyfluorinated alcohol with an isocyanate, the polyfluorinated alcohol was previously transformed to an electrophilic carbonate, which then reacted with a nucleophilic amine, thus overcoming the weak nucleophilicity of fluorinated alcohols.

Another more exotic example of direct use of polyfluorinated alcohols to form simple polyfluorinated carbamates is the electrochemically induced Hoffman rearrangement of amides in the presence of bromide.[32] In principle, bromide is electrochemically oxidized to bromine cation, that forms the bromamide, then it undergoes rearrangement to form isocyanate, that would react with a polyfluorinated alcohol to form the carbamate. However, it might be possible that other species present, like the own alcohol, were also being oxidized (Scheme 9).



R = $(CH_2)_4CH_3$; Cy, tBu; CH_2Ph; Ph

Scheme 9. Preparation of polyfluorinated carbamates by electroinduced Hoffman rearrangement.[32]

Polyfluorinated carbamates can be additives to synthetic fibers that add soil repellence to textile (Figure 13). In these cases and many others, they are formed by reaction of an aromatic isocyanate with a polyfluorinated alcohol in the presence of a catalyst. However, this polyfluorinated alcohol has two or more non fluorinated carbons between the hydroxyl group and the perfluorinated chain. These spacing carbons limit the influence of polyfluorinated chain in the alcohol.[33,34]

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[31] Padilla, A.; Ruiz, V.; Corma, A.; Garcia, H. Juárez, R. *Process for producing fluorinated isocyanates and carbamates*. European Patent Application 2036884 A1, 18th March 2009.

[32] Matsumura, Y.; Satoh Y.; Maki, T.; Onomura, O. *Electrochimica Acta* **2000**, *45*, 3011-3020.

[33] Anello, L. G.; Ridge, B.; Sweeney, R. F. *Perfluoroalkoxy-alkyl substituted carbamates.* US Patent 3657320, 18th Apr 1972.

[34] Kelly, M. G.; Coventry, R. I. *Multi-ring fluorinated carbamates with textile soil repellence activity.* US Patent 4500438, 19th Feb 1985.

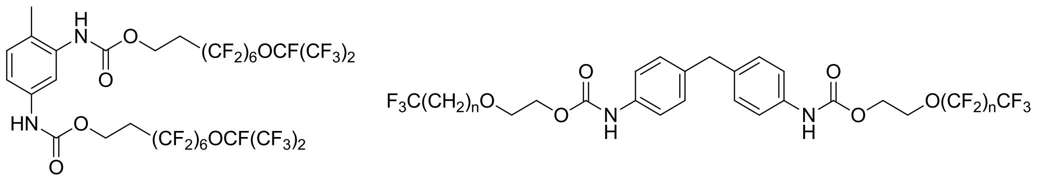

Figure 13. Examples of polyfluorinated carbamates derived from TDI and MDI used as textile additives.[33,34]

I.4.2. POLYFLUORINATED POLYMERS CONTAINING CARBAMATES

Polyurethanes are versatile and have good mechanical properties as previously mentioned. Polyfluorinated polyurethanes, FPU, not only maintain the good mechanical properties, but also combine some virtues of polyurethane and polyfluorinated materials, such as low surface tension, low water absorption, high thermal resistance, high oxygen permeability, excellent flexibility, high weatherability and attractive surface properties. Even though there are some applications of FPU; they have not yet achieved their expected potential.[35]

Fluorinated polyurethanes present an excellent good compatibility with blood and tissues, [36] reason why they have been used in biomedical applications.[37] Also recently, polyfluorinated oligourethanes with special applications as alternatives to polydimethylsiloxane in fouling-releasing coatings,[38] and in microfluidic device fabrication have been described.[39]

NO CARBAMATE LINK FORMED IN THE POLYMERISATION REACTION

One way to obtain the FPU avoiding the reaction between diisocyanates with diols is to prepare a polyfluorinated carbamate with other functional group able to polymerize, for example an acrylate terminated carbamate (Figure 14).

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[35] Xu, W.; Lu, B.; Hu, Y.; Song, L.; Nie, S. *Polym. Adv. Technol.* **2012**, *23*, 877-883.

[36] (a) Yu, X. H.; Okkema, A. Z.; Cooper, S. L. *J. Appl. Polym. Sci* **1990**, *41*, 1777-1795.
(b) Closkey, C. B.; Yip, C. M.; Santerre, J. P. *Macromolecules* **2002**, *35*, 924-933.
(c) Kim, Y. S.; Lee, J. S.; Ji, Q. *Polymer* **2002**, *43*, 7161-7170.
(d) Tan, H.; Li, J.; Guo, M.; Du, R.; Xie, X. *Polymer* **2005**, *46*, 7230-7239.
(e) Massa, T. M.; Yang, M. L.; Ho, J. C.; Brash, J. L.; Santerre, J. P. *Biomaterials* **2005**, *26*, 7367-7376.
(f) Krafft, M. P.; Riess, J. G. *J. Polym. Sci. Part A: Polym. Chem.* **2007**, *45*, 1185-11877.

[37] (a) Chen, K. Y; Kuo, J. F. *Macromol. Chem. Phys.* **2000**, *201*, 2676-2686.
(b) Wang, L. F.; *Polymer* **2007**, *48*, 7414-7418.
(c) Ge, Z.; Zhang, X.; Dai, J.; Li, W.; Luo, Y. *J. Macromol. Sci. Part A: Pure and Appl. Chem.* **2009**, *46*, 215-227.
(d) Jiang, G.; Tuo, X; Wang, D.; Li, Q. *J. Polym. Sci.: Part A: Polym. Chem.* **2009**, *47*, 3248-3256.

[38] (a) Turri, S.; Levi, M.; Trombetta, T. US Patent: US7323435B1, 2008.
(b) Hu, Z.; Finlay, J. A.; Chen, L.; Betts, D. E.; Hillmyer, M. A.; Callow, M. E.; Callow, J. A.; DeSimone, J. M. *Macromolecules*, **2009**, *42*, 6999-7007.

[39] Rolland, J. P.; Van Dam, R. M.; Schorzman, D. A.; Quake, S. R.; DeSimone, J. M. *J. Am. Chem Soc.* **2004**, *126*, 2322-2323.

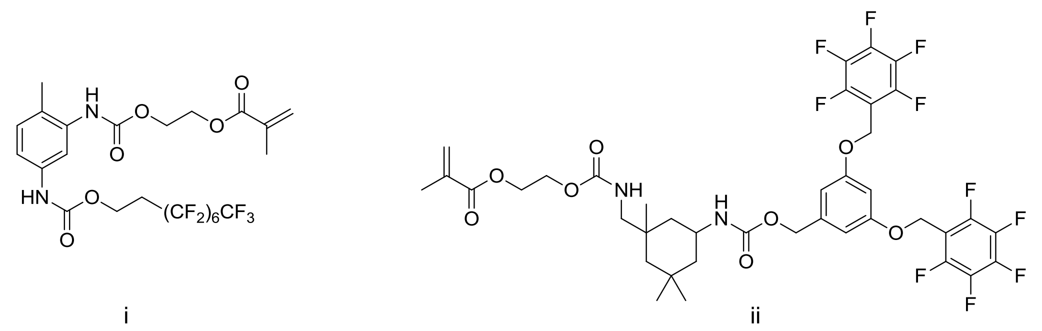
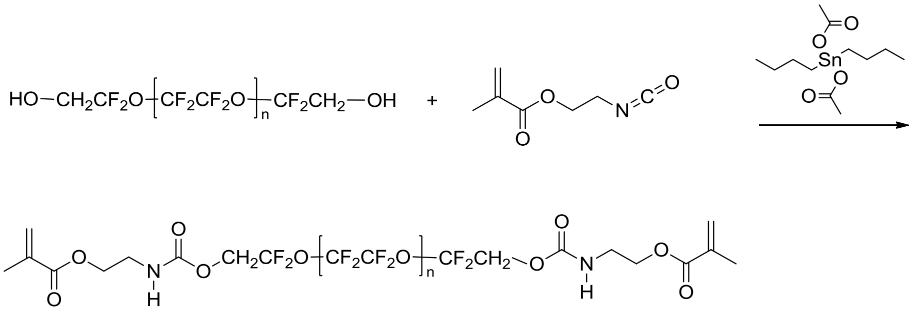


Figure 14. Examples of polyfluorinated carbamates bearing acrylate units.

On the first example (Figure 14, i), TDI is reacted in position 4 with a polyfluorinated alcohol and in position 2 with an alcohol bearing an acrylate unit. Polymerization through the acrylate group led to a polyacrylate polymer with carbamate units and polyfluorinated chains, so *technically* is a polyfluorinated polyurethane.[40] Equivalent is the second example (Figure 14, ii), based on an IPDI derivate containing pentafluorophenyls and an acrylate.[41]

Similarly, DeSimone prepared polyfluorinated polyurethanes with carbamate and polyfluorinated units in the main chain. They were the result of a two step process: first, reaction of a polyfluorinated polyether diol (MW from 1 000 to 4 000 Dal) with 2-isocyanatoethyl metacrylate catalyzed by dibutyltin diacetate, then photopolymerization of this macro diacrylate using a photoinitiator. In this approach the reaction of formation of the carbamate is not the polymerization reaction (Scheme 10).[38,39]



Scheme 10. DeSimone polyfluorinated polyurethane preparation.[38,39]

Although polymers resulting from those processes combine some properties of polyurethanes and fluorine materials, they are not properly polyfluorinated polyurethanes. They would be better described as polyacrylates bearing carbamate and polyfluorinated units in the chain.

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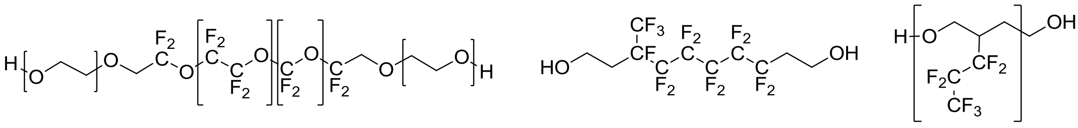
[40] Lina, M.-J.; Lune, T.; Clermont, A. D. *Fluorinated carbamate polymers as hydrophobic and oleophobic agents*. US Patent 4920190, 24th Apr 1990.

[41] Çanak, T. C.; Serhath, I. E. Prog. Org. Coatings. **2013**, *76*, 388-399.

CARBAMATE LINK FORMED IN THE POLYMERISATION REACTION

What would be understood undoubtfully by FPU would be a polymer result of the reaction of diisocyanate and diol, with at least one of those monomers fluorinated. To prepare FPU using polyfluorinated diols, the most common approach is to limit the deactivating effect of the polyfluorinated chain on the alcohol group reactivity by adding spacing groups between them, at least two non fluorinated carbons.

Following this approach, Tonelli prepared a series of FPU using soft phase polyfluorinated polyether macrodiol with MDI and a non-fluorinated small diol as a chain extender.[42] The group of Ho prepared polyfluorinated polyurethane based on a relatively small polyfluorinated diol and HDI using DBTDL as catalyst.[43] And Ge and coworkers used a polyfluorinated chain pending from a hydrocarbonated diol to provide enhanced surface properties (Figure 15).[44]



a) b) c)

Figure 15. Polyfluorinated diols used in PU preparation by the groups of a) Tonelli,[42] b) Ho[43] and c) Ge.[44]

In cases where polyfluorinated diols without spacers were reacted with diisocyanate prepolymers, it was reported that fluorine diols were not being effectively incorporated to the polymer.[45]

I.4.3. LOW NUCLEOPHILICITY OF POLYFLUORINATED ALCOHOLS

In the previous sections, the low nucleophilicity of fluorinated alcohols is exposed as an important drawback in the preparation of polyfluorinated carbamates or FPU. Some alternatives have been used to overcome this problem, as the transformation of the alcohol into a carbonate derivate or adding more space between the hydroxyl group and the perfluorinated chain.

The high electronegativity of fluorine strongly affects the properties of the alcohol group by removing electron density from carbon and oxygen. In the end, this is produce a strongly polarized and weaker OH bond.

A way to visualize the strong effect of fluorine atoms over hydroxyl group is by taking a look at the pK_a in DMSO of simple polyfluorinated alcohols. Difference of acidity from fluorinated to

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[42] a) Tonelli, C.; Trombetta, T.; Scicchitano, M.; Simeone, G.; Ajroldi, G. *J. Appl. Pol. Sci.* **1996**, *59*, 311-327.
b) Ferreri, E.; Giavarini, F.; Tonelli, C.; Trombetta, T.; Zielinski, R. E. *Fluorinated polyurethanes and polyurethanes-ureas and methods for preparing them.* US Patent 5332798, 26th Jul. 1994.

[43] Ho, T.; Wynne, K. J. *Macromolecules* **1992**, *25,* 3521-3527.

[44] Ge, Z.; Zhang, X.; Dai, J.; Li, W.; Luo, Y. *Eur. Pol. J.* **2009**, *45*, 530-536.

[45] Yoon, S.C.; Ratner, B.D. *Macromolecules*, **1986**, *19*, 1068-1079.

hydrocarbonated alcohols depends on substitution and number of fluorine atoms. In the case of primary alcohols, this difference of acidity is around 6 pK_a units, in secondary alcohols is about 12 pK_a units and up to 22 pK_a units in tertiary alcohols (Figure 16).

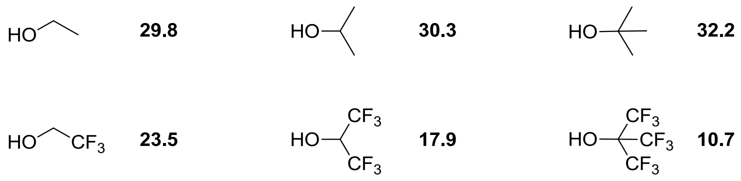

Figure 16. Comparison of pK_a in DMSO of hydrocarbonated and polyfluorinated alcohols.[46]

Polyfluorinated alcohols are more acidic than their hydrocarbonated analogs. Therefore, it is not surprising that polyfluorinated alcohols are far less nucleophilic than hydrocarbonated ones. A fact that supposes a major drawback in the reaction of them with isocyanates, were they should act as nucleophiles. In fact, polyfluorinated alcohols are such weak nucleophiles that TFE and HFIP main uses are as protic non-nucleophilic solvents.

Thus, it is clear that the presence of fluorine atoms decreases the nucleophilicity of the alcohol group. However, some years ago in the research group a not so obvious different reactivity of polyfluorinated alcohols had been observed.

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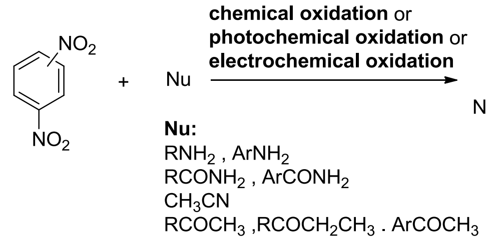
[46] (a) Online table of pK_{DMSO}: Department of Chemistry, University of Wisconsin-Madison. *Brodwell pKa Table (Acidity in DMSO)* **2008** <http://www.chem.wisc.edu/areas/reich/pkatable/> (Updated: 14th Jul 2010).
(b) Original: Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456-463.

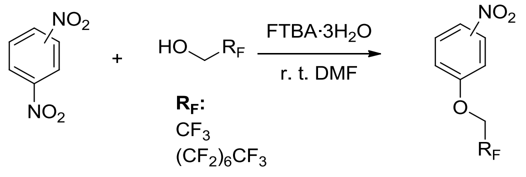
I.5. RELEVANT PRECEDENTS IN THE RESEARCH GROUP

In the early 2000, the research group was working in the nucleophilic aromatic substitution, S_NAr, on dinitrobenzenes DNB of hydrogen atom for carbon or nitrogen centred nucleophiles in oxidative conditions. In this reaction, the nucleophile substituted a hydrogen atom (Scheme 11).[47]



Scheme 11. Reaction of DNB with nitrogen and carbon nucleophiles.

In order to obtain new polyfluoroalkoxyaromatic compounds, this reaction was performed with polyfluorinated alcohols. However, the expected reaction was not observed. In its place a nitro group displacement for the polyfluorinated alcohol was observed. In the proper conditions (presence of tetrabutyl ammonium fluoride, TBAF) the reaction of DNB with polyfluorinated alcohol was practically instantaneous (Scheme 12).[48]



Scheme 12. Reaction of DNB with polyfluorinated alcohols.

The mechanism was studied in detail for the model reaction of *p*-DNB with 2,2,2-trifluoroethanol, TFE, in the presence of TBAF. The mechanistic proposal, supported by experimental results and theoretical calculations, included a radical chain mechanism related to other radical aromatic substitutions (Scheme 13).

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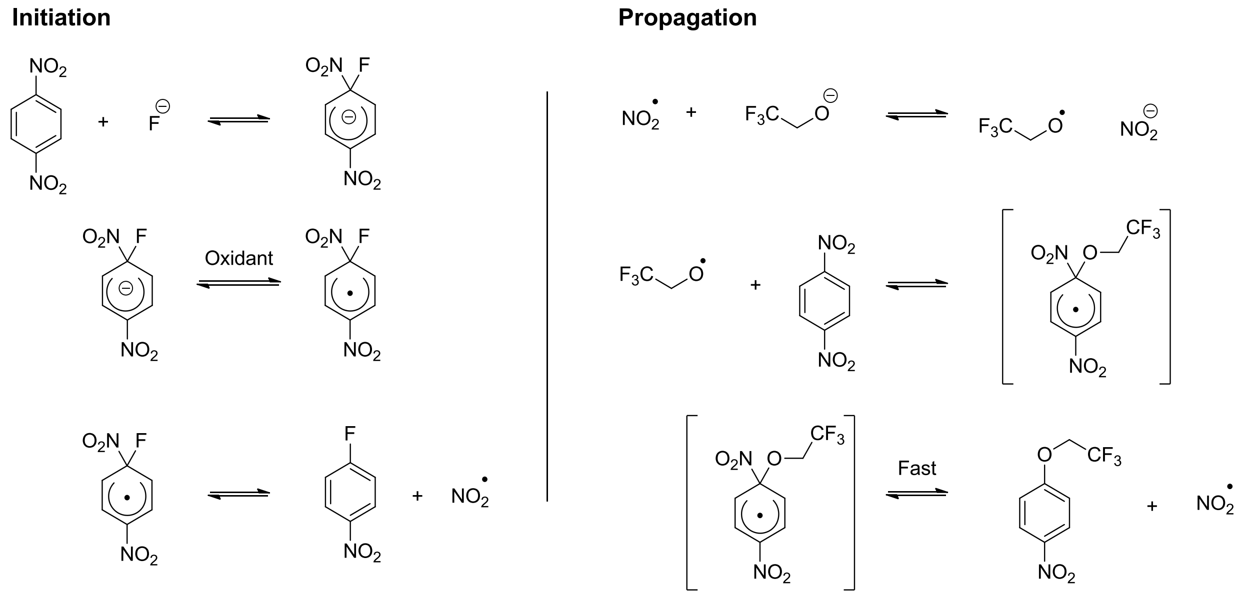
[47] (a) Huertas, I.; Gallardo, I.; Marquet, J. *Tetrahedron Lett.* **2000**, *41*, 279-283.
(b) Gallardo, I. Guirado, G. Marquet, J. *Chem. Eur. J.* **2001**, *7*, 1759-1765.
(c) Gallardo, I.; Guirado, G.; Marquet, J. *Eur. J. Org. Chem.* **2002**, 251-259.
(d) Gallardo, I.; Guirado, G.; Marquet, J. *J. Org. Chem.* **2002**, *67*, 2548-2555.
(e) Gallardo, I.; Guirado, G.; Marquet, J. *J. Org. Chem.* **2003**, *68*, 631-633.

[48] Tejero, I.; Huertas, I.; González-Lafont, A.; Lluch, J. M.; Marquet, J. *J. Org. Chem.* **2005**, *70*, 1718-1727.



Scheme 13. Mechanism of the reaction of *p*-DNB with TFE using TBAF.[48]

The key intermediate of the propagation was the 2,2,2-trifluoroethoxyl radical, derived from TFE. It was proposed based on theoretical calculations but it could not be detected. Indeed, experimental evidences and calculation pointed out to the possibility of triggering a new reactivity for polyfluorinated alcohols. However, the complexity of this mechanism, that includes alcohol, nitro and aromatic radicals and Meisenheimer complexes hided in some way this hypothetical different reactivity, making complex to study it properly.

To achieve this goal, it would be needed a simpler reaction with less disturbing elements.

I.6. WORKING HYPOTHESIS

As a summary of the key points, on one hand, polyurethanes have an enormous industrial importance because they have excellent mechanical properties and they are versatile and also tunable materials. On the other hand, polyfluorinated materials have high chemical and thermal stability while having unique surface properties, as hydrophobicity and oleophobicity at the same time.

So far, however, combinations of both materials in polyfluorinated polyurethanes have not achieved the expected potential, in part due to the difficulties on their preparation. A major drawback is that polyfluorinated alcohols are very weak nucleophiles, a key obstacle to overcome to be able to prepare polyfluorinated carbamates in a practical and efficient way.

Interestingly, in relation with the last point, there are precedents in the research group of a particular reactivity of polyfluorinated alcohols, not acting as a typical nucleophile but as a radical.

At this point, the question is obvious. It is possible to use this distinctive reactivity to prepare polyfluorinated carbamates and polyfluorinated polyurethanes?

GOALS

The final goal is to prepare polyfluorinated carbamates, both small molecules and polymers, by reaction of isocyanates with polyfluorinated alcohols improving the results described in the literature.

The first objective was to find suitable conditions for the reaction of polyfluorinated alcohols with aromatic isocyanates. A simple model reaction would be studied in order to unravel the reactivity of polyfluorinated alcohols. A deeper knowledge of the reaction probably would give some hints on how to promote the reaction.

Then, the reaction would be extended to polyfluorinated diols with fluorinated and non fluorinated aromatic isocyanates and, eventually, to the reaction of polyfluorinated diols with aromatic diisocyanates to prepare polyfluorinated polyurethanes.

Finally, the surface properties, namely hydrophobicity and oleophobicity, of the new compounds and materials prepared would be evaluated.

Chapter 1

Reaction of polyfluorinated alcohols with aromatic isocyanates

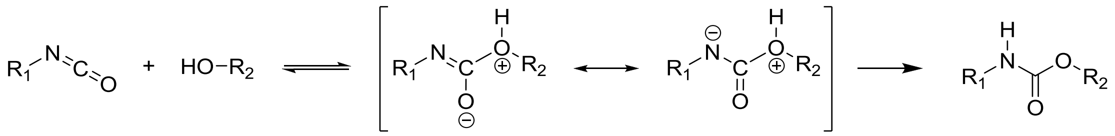
1.1. MECHANISMS OF THE REACTION OF ISOCYANATES WITH ALCOHOLS

Prior to enter in the study of the mechanism of the reaction of polyfluorinated alcohols with aromatic isocyanates, the accepted mechanisms for the reaction of alcohols with isocyanates will be presented.

The first mechanism of carbamate formation by the reaction of alcohol and isocyanate was proposed by Baker back in the in the 40s. However, some deviations from this mechanism were observed lately, which resulted in the proposal of an autocatalytic mechanism. Although not properly a mechanism, other influencing factors, as the aggregation state of the alcohol or effect of catalyst are also considered in the following pages.

1.1.1. THE *CLASSICAL* MECHANISM OF BAKER

The first accepted mechanism for the reaction of isocyanates with a general nucleophile, HNu, was proposed by Baker. If we the focus our attention on alcohols, this proposal involves the nucleophilic attack of the oxygen atom to the electrophilic carbon of the isocyanate group, followed by proton transfer from this oxygen to the nitrogen to form the carbamate product (Scheme 14).[49]



Scheme 14. General mechanism of carbamate formation.

The second step, the proton transfer, is faster than the formation of the covalent bond. Thereby, the rate determining step is the first one, being deduced a second-order kinetics.

$$v = \frac{-d[RNCO]}{dt} = k_1[RNCO][R'OH] \qquad (1)$$

This second order rate law implies a linear dependency of the reaction rate with the concentration of each one of the reactants.

Although this model was fulfilled in low and medium degrees of conversions, some deviations were observed at higher degrees of conversion. Thus, other mechanisms were proposed taking account those deviations were proposed.

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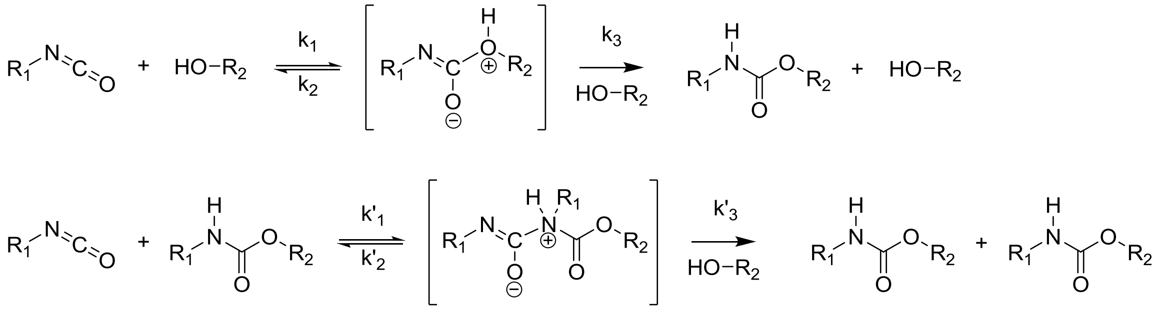
[49] Baker, J. W.; Holdsworth, J. B. *J. Chem. Soc.* **1947,** 713-726.

1.1.2. AUTOCATALITIC MECHANISM

One reason of those deviations was that not only the alcohol but also the carbamate product formed could activate the reaction, but each one in a different extent, distorting the second order rate law (Scheme 15).



Scheme 15. Sato kinetic mechanism for the reaction between an isocyanate and an alcohol.[50]

In this case, the carbamate can be considered as a nucleophilic catalyst. Thereby, Sato developed a kinetic equation taking into account the activation these different steps.[50]

$$v = \frac{k_1k_3[RNCO][ROH]^2}{k_2 + k_3[R'OH]} + \frac{k'_1k'_3[RNCO][R'OH][RNHCOOR]}{k'_2 + k'_3[RNHCOOR]} \qquad (2)$$

$$v = k_a[RNCO][R'OH]^2 + \ k_b\ [RNCO][R'OH][RNHCOOR] \qquad (3)$$

$$v = k_a[RNCO][R'OH]^2 \qquad (4)$$

The denominators on the raw initial equation 2 were simplified considering that $k_2 \gg k_3[R'OH]$ and $k'_2 \gg k'_3[RNHCOOR]$. This approximation meant that the reversion of the activated isocyanate in the first step (k_2 or k'_2) was much faster than the carbamate formation on second reaction step ($k_3[R'OH]$ or $k'_3[RNHCOOR]$) (equation 3).[2]

At initial times with low conversions, carbamate concentration is low and the second term in equation 3, which is related with activation by carbamate, can be neglected. In the end, this simplified rate law is first order on the isocyanate and second order with respect to the alcohol at low conversion. This simplified Sato's rate law is the usual working equation for polyurethanes kinetics (equation 4).3

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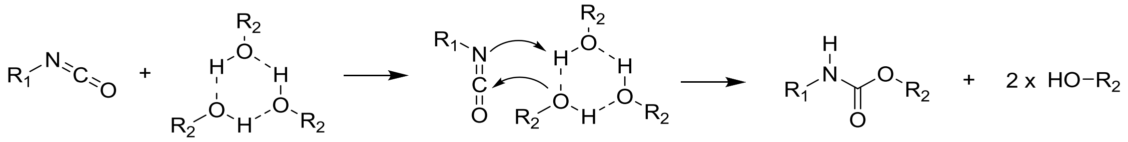
[50] Sato, M. *J. Am. Chem. Soc.* **1960**, *82*, 3893-3897.

1.1.3. IMPORTANCE OF THE AGGREGATION STATES

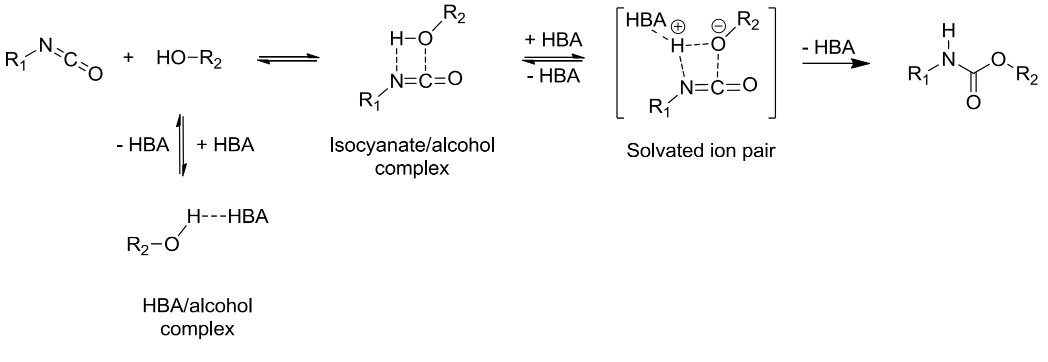
There are also other effects important for the reaction rate, for example, aggregation state of the alcohol. In solution, alcohol molecules can be isolated or forming hydrogen bond complexes, either with solvent or with other alcohol molecules. After studying the influence of the aggregation state, Satchell[51] found that for reaction with isocyanates and ketenes the only relevant states were the isolated alcohol and the trimer; being the trimer between one and three orders of magnitude more reactive (Scheme 16).



Scheme 16. Mechanism of the reaction between isocyanate a alcohol trimer.

Reactivity towards isocyanate highly depends on association state of the alcohol. Solvent and other hydrogen bond acceptor molecules, HBA, strongly affect this association state, as in general, any alcohol/HBA adduct can be formed.

To sum up the previous mechanisms with these possibilities, Chang[52] proposed a general mechanism remarking the importance of HBA molecules. In this proposal, the alcohol and the isocyanate form an isocyanate/alcohol hydrogen bond adduct. Then, a HBA (solvent, alcohol, carbamate, catalyst…) solvates the proton and helps to the formation of a solvated ion pair. At this point, the more negative oxygen atom is able to attack the electrophilic carbon on the isocyanate to form the product (Scheme 17).



Scheme 17. Carbamate formation mechanism via hydrogen bond complex activated by an electron pair donor DN.

However, any HBA also forms hydrogen-bonded adducts with the alcohol, decreasing the amount the key isocyanate/alcohol adduct. Only if stabilization of the solvated ion pair by the

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[51] Donohoe, G.; Satchell, D. P. N.; Satchell, R. S. *J. Chem. Soc. Perkin Trans. 2* **1990**, 1671-1674.
[52] Chang, M. C.; Chen, S. A. *J. Polym. Sci., Part A: Polym. Chem.* **1987**, *25*, 2543-2559.

HBA is high enough, it would counteract the lower isocyanate/alcohol complex concentration to produce an overall catalytic effect.[3]

1.1.4. CATALYSIS OVERVIEW

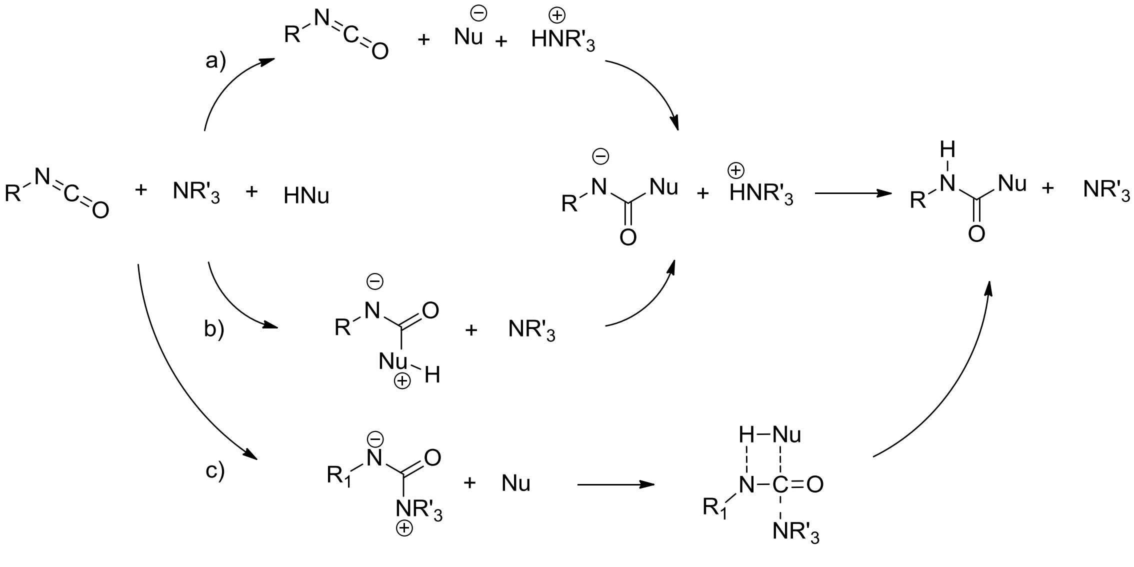
There are hundreds of catalysts for this reaction, but the most used can be broadly divided in two groups, tertiary amines and organometalic compounds, remarkably organotin derivates.

TERTIARY AMINE CATALISIS

For the reaction of isocyanates with a nucleophile HNu catalyzed by tertiary amines (or any electron pair donor in general), two different mechanisms have been proposed: basic catalysis or nucleophilic catalysis.

Basic catalysis can occur in two ways depending on the reagents. Acidic weak nucleophiles, such as phenols, are transformed into the anionic nucleophiles, which are then added to the isocyanate (Scheme 18, a). Less acidic stronger nucleophiles, such as amines, are added directly to the isocyanate followed by a based-catalyzed proton transfer (Scheme 18, b).[53]

Besides, it has been proposed that amines act as nucleophilic catalysts. In this case, they would add to the carbon of the isocyanate forming ionic ureas. Then, the amine is replaced by the nucleophile to form the final product (Scheme 18, c).[54]



Scheme 18. Effect of a tertiary amine as catalyst in the reaction of an isocyanate with a HNu. a) Basic catalysis with acidic weak nucleophiles, b) Basic catalysis with strong nucleophiles and c) Nucleophilic catalysis.

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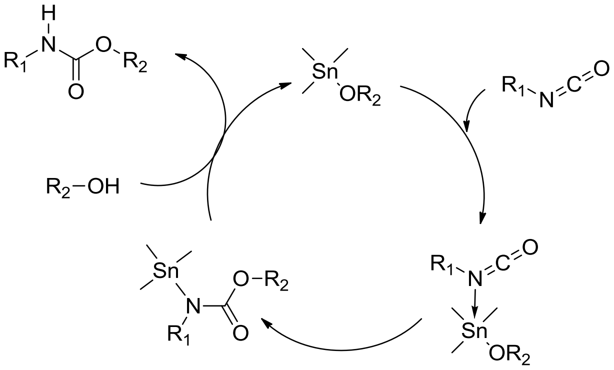
[53] Schwetlick, K.; Noack, R.; Stebner, F. *J. Chem. Soc. Perkin Trans. 2,* **1994**, 599-608.

[54] Bertoldo, M.; Cappelli, C.; Catanorchi, S.; Liuzzo, V.; Bronco, S. *Macromolecules* **2005**, *38,* 1385-1394.

ORGANOTIN CATALISYS

The other main catalysts group is formed by organometallic compounds, dominated by organotin compounds, being preponderant dibutyltin dilaurate, DBTDL. The general accepted mechanism is the isocyanate activation by tin alkoxide. The catalytic cycle involve alkoxide formation, followed by *N*-coordination of the isocyanate to tin and bond transfer of the alkoxide anion to the coordinated isocyanate (or migratory insertion), to yield an urethane coordinated to tin. Alcoholysis generate the product and closes the cycle (Scheme 19).[55]



Scheme 19. Mechanism of the reaction of an isocyanate with an alcohol catalyzed by organotin compounds.

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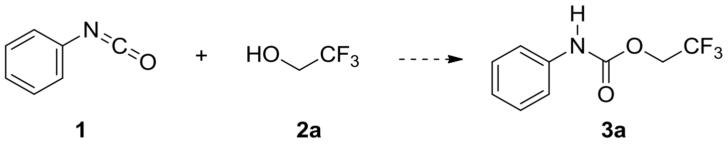
[55] Houghton, R. P.; Mulvaney, A. W. *J. Organomet. Chem.* **1996**, *518*, 21-27.

1.2. STUDY OF PHENYL ISOCYANATE AND 2,2,2-TRIFLUOROETHANOL REACTION

The acidity of polyfluorinated alcohols is higher than *standard* alcohols (henceforth *standard* alcohols should be read as aliphatic non-fluorinated alcohols) and its nucleophilicity much lower. In addition, they have been involved in unexpected reactions. Thus, our aim was to study the reactivity of polyfluorinated alcohols in their reaction with aromatic isocyanate, to find suitable conditions for the reaction and to establish the mechanism.

In order to do so, it was considered a case study approach, which means to study a simple case in deep and then extend the conclusions to other cases. As a model of isocyanate, simplest aromatic isocyanate was chosen, phenyl isocyanate, PhNCO, **1**. For a simple representative polyfluorinated alcohol, primary and small 2,2,2-trifluoroethanol, TFE, **2a** was selected (Scheme 20).



Scheme 20. Reaction of phenyl isocyanate **1** with 2,2,2-trifluoroethanol **2a** to form 2,2,2-trifluoroethyl phenylcarbamate **3a**.

In order to control the evolution of the reaction, gas chromatography GC was chosen since it allowed quick and quantitative measurements of the concentration of PhNCO. Thus, a calibration line for PhNCO was constructed using hexadecane, n-$C_{16}H_{34}$, **4** as internal standard.

To establish a set of conditions to carry out the reaction, first a screening of solvents and proportions was performed. After that, attempts to calculate the kinetic constant were done with some unexpected results.

1.2.1. SOLVENT EFFECT

One key, but often underestimated, factor in the performance of a reaction is the selection of the solvent. Already in 1890 Menschutkin, working in the alkylation of tertiary amines with alkyl halides, concluded that a reaction cannot be separated from the medium in which it is performed. As he wrote to Louis Henry:

> *''Or, l'expérience montre que ces dissolvants exercent sur la vitesse de combinaison une influence considérable. (...), soi-disant indifférents, ne sont pas inertes; ils modifient profondément l'acte de la combinaison chimique''*[56,57]

Until then, solvents were considered just the medium in which the reaction takes place, a simple dilutor, not an input to take in to account. There was a qualitative step forward the change from seeing it just as a continuous medium to thinking of it as molecules interacting with each other and with the reactants.[57]

For these reasons, when studying a reaction, the effect of the solvent should be one of the first factors studied. So in order to identify its influence, the non-catalyzed reaction of phenyl isocyanate **1** with 2,2,2-trifluoroethanol **2a** was performed in eight different solvents, apart from the same alcohol TFE used also as solvent.

Hydrogen bond donor solvents, HBD,[58] as water and alcohols, were excluded from this study because they react with the isocyanate group. The chosen solvents represent a wide range of polarity and variety in functionality (Figure 17). These solvents were carefully dried to avoid the reaction of PhNCO with water to form aniline and *N,N'*-diphenylurea.

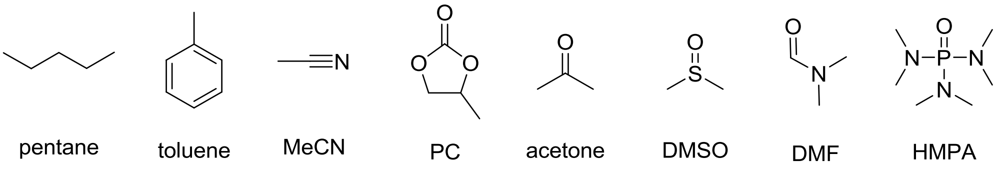


Figure 17. Structure of the studied solvents.

Conversion of the reaction of PhNCO **1** with TFE **2a** at room temperature ($[PhNCO]_0$ = 0.01 M; $[TFE]_0$ = 0.02 M) was measured as the disappearance of PhNCO. The reaction was tested in those eight different solvents and the conversion after 60 minutes compared (Table 2).

The results indicated that the reaction did not take place in apolar solvents, such as pentane or toluene. For polar solvents, there was a group in which the reaction proceeded at slow rates (MeCN<PC<Acetone), then DMSO was in a middle position and finally there were clearly two solvents that favored the reaction (DMF<HMPA). In addition, it is worth noting that the reaction using the alcohol itself as solvent did not evolve at all.

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[56] "*Now experience shows that these solvents have on the speed of combination considerable influence. (...) Supposedly indifferent, they are not inert; they deeply affect the act of chemical combination*" Extract from a letter of Nikolai Menschutkin, Saint-Petersburg, to Louis Henry, Louvain. Original: *Bulletin de l'Académie Royale des Sciences, des Lettres et des Beaux-Arts de Belgique* **1890,** *19*, 513–514.

[57] Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 3rd ed.; Wiley-VCH: Weinheim, Germany, 2003. ISBN: 3-527-30618-8.

[58] Reichardt advices the terms "HBD" and "non-HBD" solvents as replacement for "protic" and "aprotic" because several non-HBD solvents such as DMSO and MeCN reveal protic character where strong bases are used. See previous ref. Reichardt, Chapter 2, p. 18.

Table 2. Conversion of the reaction PhNCO/TFE after 60 min at room temperature and selected physical and chemical parameters characterizing the eight solvents used ordered by polarity, E_T^N.

Solvent	ε_r [a]	μ [b]	E_T^N [c]	DN^N [d]	β [e]	**Conversion 1 h (%)** [f]
Pentane	1.84	0.0	0.009	0	0	0
Toluene	2.38	1.0	0.099	0	0	0
HMPA	29.30	18.5	0.315	1.00	1.05	99
Acetone	20.56	9.0	0.355	0.44	0.48	19
DMF	36.71	12.7	0.386	0.69	0.69	94
DMSO	46.45	13.5	0.444	0.77	0.76	40
MeCN	35.94	13.0	0.460	0.36	0.31	6
PC	64.92	16.5	0.472	0.39	0.40	18
TFE	26.67	2.5	0.898	-	0	0

[a] Relative permittivity ("dielectric constant") of the pure liquid at 25 ºC. [b] Dipole moment 10^{30} C m. [c] Normalized Reichardt solvatochromic parameter, polarity measure based on UV-Vis absorption of a pyridinium *N*-phenolate betaine dye.[59]
[d] Normalized donor number, quantitative measurement of solvent acting as electron pair donor as defined by Gutmann.[60]
[e] Hydrogen bond acceptor index as defined by Kamlet-Taft.[61] [f] Conversion calculated by GC after 60 minutes of reaction using hexadecane as internal standard.

When trying to rationalize these findings, if the conversions were correlated with the physical parameters of the solvent, as relative permittivity or dipole moment, no clear effect was observed. The use of a general measure of polarity, such as the solvatochromic parameter of Reichardt, did not provide an explanation. For example, two solvents with similar polarity, *e.g.* (E_T^N(acetone) = 0.355; E_T^N(DMF) = 0.386), had a very different effect on the reaction (1 h conversion: in acetone 19 %; in DMF 94 %).

Interestingly, some correlation was found between the conversion and *donor number* DN or the *Kamlet-Taft hydrogen bond acceptor index*, β (Figure 18). DN is a quantitative measure of Lewis basicity, *i.e.* the capacity of the solvent to act as an electron pair donor in a Lewis adduct.[1,60] β measures the ability of the solvent to act as an acceptor of hydrogen bonds.

Lewis basicity (quantified by DN) and HBA ability (quantified by β) are two properties derived from the non-bonding electron pairs of solvent molecules. Thus, these effects are related to the shifting of equilibriums by donor molecules proposed by Chang[52] (Section 1.1.3.) and the catalytic effect that tertiary amines have on isocyanate/alcohol reaction (Section 1.1.4.). As tertiary amines, solvent effect can be seen as basic catalysis or nucleophilic catalysis.

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[59] Reichardt, C. *Chem. Rev.* **1994**, *94*, 2319-2358.

[60] (a) Gutmann, V. *Coord. Chem. Rev.* **1976**, *18*, 225-255.
(b) Marcus, Y. *J. Sol. Chem.* **1984**, *13,* 599-624.

[61] Kamlet, M. J.; Abboud, J.-L.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.* **1983**, *48,* 486-489.

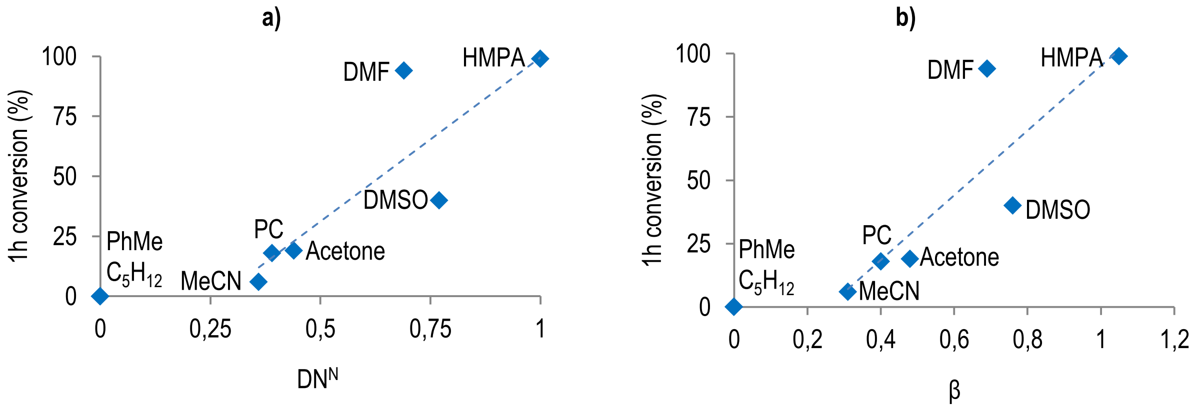
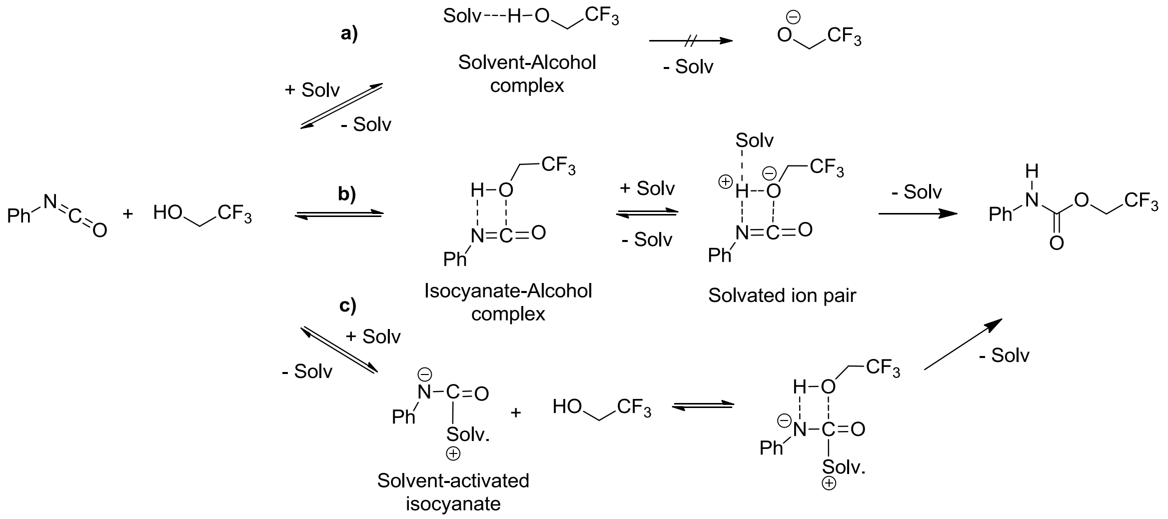


Figure 18. Conversion at 1 h plotted vs. different parameters of the solvent a) Normalized donor number and b) Kamlet-Taft's β, a hydrogen bond accepting scale.

Thus, solvents with lone electron pairs form hydrogen bonds adducts with the alcohol (Scheme 21, a). However, those solvents are not basic enough to completely deprotonate and activate the alcohol, as would amines do. This, in fact, inhibits the reaction as it decrease the isocyanate/alcohol complex. However, if solvent is highly donor, it would stabilize the ion pair derived from the isocyanate/alcohol complex, counteracting the lower complex concentration to produce an overall catalytic effect (Scheme 21, b).[3]

As tertiary amines do, solvent can act as nucleophilic catalyst by its non-bonding electron pair. Solvent would add to the carbon of the isocyanate forming an ionic intermediate. After that, it would be replaced by alcohol to form the product (Scheme 21, c).



Scheme 21. Different routes to explain solvent effect based on Lewis basicity on the reaction of PhNCO/TFE.

In conclusion, the reaction of phenyl isocyanate with 2,2,2-trifluoroethanol **1** is greatly dependent on the solvent. The key of the strong solvent effect relies on the non bonding electron pair, by forming hydrogen bonds that stabilize the ion pair, or by acting as a nuchleophilic catalyst.

These findings suggested that proper solvents for this reaction would be DMF or HMPA. Although the best solvent was HMPA, it is also a 2B group carcinogen according to the International Agency of Research on Cancer IARC,[62] and therefore its use must be avoided when possible. In consequence, DMF was the chosen working solvent for this study.

1.2.2. RELATIVE PROPORTIONS ISOCYANATE:ALCOHOL

The reaction of PhNCO with TFE was performed using different reagents ratios: half, stoichiometric or double amount of TFE initial concentration of PhNCO ($[\mathrm{PhNCO}]_0$ = 0.01 M; DMF). The reaction was monitored by GC and the conversion defined as disappearance of PhNCO.

As expected, using stoichiometric alcohol the initial rate was faster than using half the amount of TFE. It is worth noting that using a half stoichiometric amount of TFE (reagents ratio PhNCO:TFE, 1:0.5), the reaction did not further evolved after a 27 % conversion of PhNCO, (which corresponded with a 54 % of reaction advance considering that there was just 0.5 eq. of TFE). In case of using a stoichiometric ratio, the reaction stopped around a 70 % of conversion.

An excess of alcohol (reagents ratio 1:2) was required to obtain a complete reaction (Figure 19). However, by using a greater excess of TFE (reagents ratio 1:5), the profile was comparable to 1:2 reaction. In the limit of using TFE as solvent, reaction did not evolved at all.

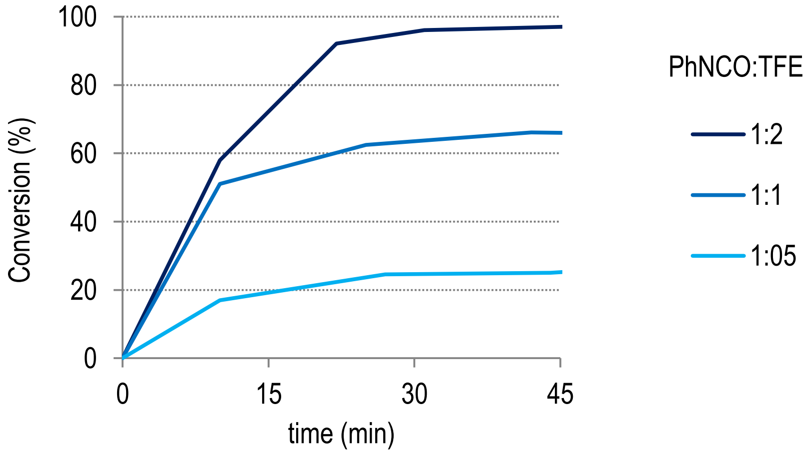


Figure 19. Comparison of PhNCO conversion using different initial proportions of PhNCO:TFE.

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[62] IARC International Agency for Research on Cancer. *Hexamethylphosphoramide*. (Updated: August 2008). <http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-101.pdf> (Access: 15th Oct 2013).

Taking into account these results, the working proportion was set to a ratio PhNCO:TFE 1:2 as default for the rest of the study.

1.2.3. KINETIC CONSTANT BY DESCRIBED RATE LAWS

For the reaction of isocyanates with alcohols, there are mainly two proposed rate laws based on the described mechanisms (Section 1.1.1 and 1.1.2). The first one, global second order, partial first order on the two reagents proposed by Baker,[49] and a more complex described by Sato,[50] that includes autocatalytic effects from the alcohol and the product.

BAKER'S RATE LAW AND PSEUDO-FIRST ORDER APPROXIMATION

A first attempt was to relate the kinetics of this reaction with Baker's rate law (5). As there was an excess of alcohol, it was thought possible to loosely assume a pseudo-first order approximation. In this way, the concentration of alcohol could be enclosed in the constant and the rate would only reflect the concentration of PhNCO (6). Pseudo-first order approximation provides a useful linear relationship between the logarithm of the concentration and time (8).

$$v = \frac{-d[PhNCO]}{dt} = k_{Baker}[PhNCO][TFE] \tag{5}$$

$$v = \frac{-d[PhNCO]}{dt} = k_{obs}[PhNCO] \tag{6}$$

$$\int_{[PhNCO]_0}^{[PhNCO]} \frac{-d[PhNCO]}{[PhNCO]} = \int_{o}^{t} k_{obs} \cdot dt \tag{7}$$

$$ln\frac{[PhNCO]_0}{[PhNCO]} = k_{obs} \cdot t \tag{8}$$

The evolution of the reaction was followed by GC to determine the concentration of PhNCO at different times. According to (8) $\ln([PhNCO]_0/[PhNCO])$ was plotted versus time and a straight line was obtained. In all the cases, the linearity was maintained until more than 90 % of conversion (Figure 20).

a) **b)**

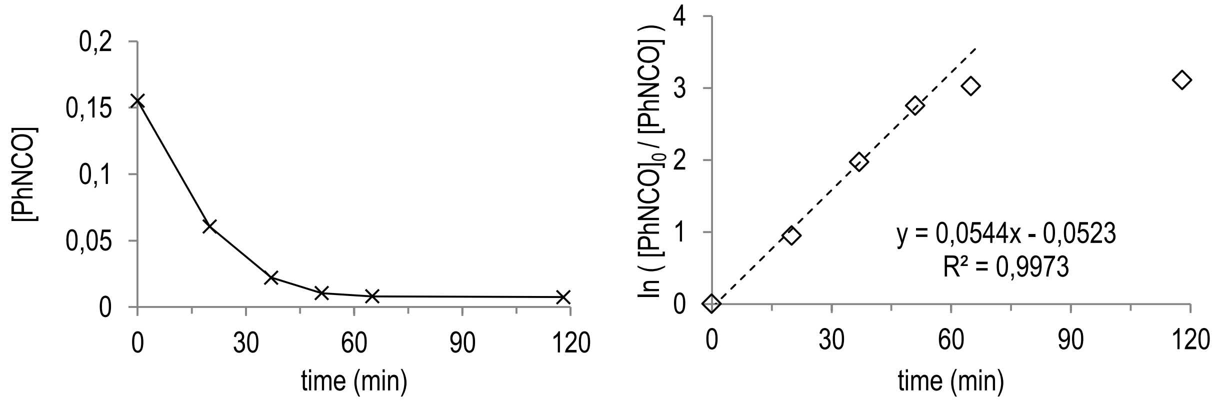

Figure 20. a) Evolution of PhNCO concentration in the reaction with TFE reaction ($[PhNCO]_0$ = 0.15 M; $[TFE]_0$ = 0.3 M; DMF). b) Linearization of the reaction according eq. (8) Slope = k_{obs} (min^{-1}).

The slope of the line was the observed kinetic constant. Dividing it by initial concentration of TFE resulted in the bimolecular kinetic constant. This procedure was done for a range of reagent concentrations keeping the ratio PhNCO:TFE constant. Nevertheless, it was surprising to see that supposedly *kinetic constant* was not so “constant”. It showed a dependency on concentration, obtaining higher values in diluted conditions (Figure 21).

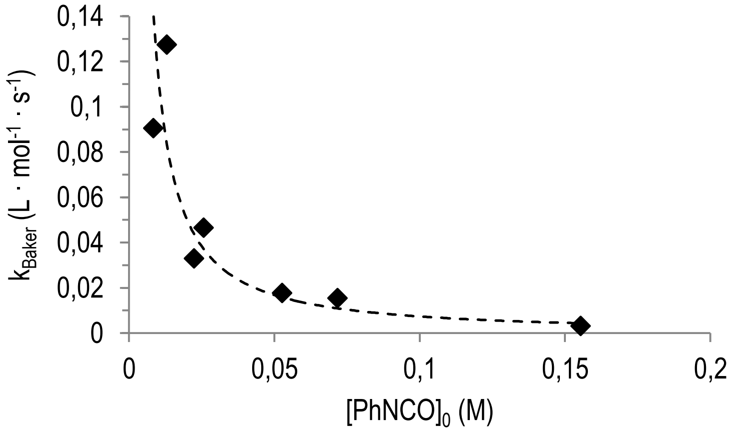

Figure 21. Dependence of the kinetic constant (in L mol^{-1} s^{-1}) calculated according Baker’s rate law with initial PhNCO concentrations (ratio PhNCO:TFE, 1:2) assuming a pseudo-first order approximation.

It could be argued that this anomaly on the kinetic constant was because the excess of alcohol used (1:2) was not enough to establish pseudo-first order conditions. Therefore, to avoid the use of the pseudo-first order approximation the kinetic constant was calculated just using the initial rates method. In principle, this method should yield the same results; however, as it relies just on the first point measured it has more experimental error.

In this approach, just the first control of the reaction is taken into account. The concentrations of reactants could be considered as the initial concentrations. The initial reaction rate could be calculated from the first control by GC of the reaction as difference of PhNCO concentration divided for the control time (Slope from zero to first point on Figure 20; Eq. 9) (Figure 22).

$$v_0 = \frac{[PhNCO]_t - [PhNCO]_0}{\Delta t} = k_{Baker}[PhNCO]_0[TFE]_0 \qquad (9)$$

$$k_{Baker} = \frac{v_0}{[PhNCO]_0[TFE]_0} \qquad (10)$$

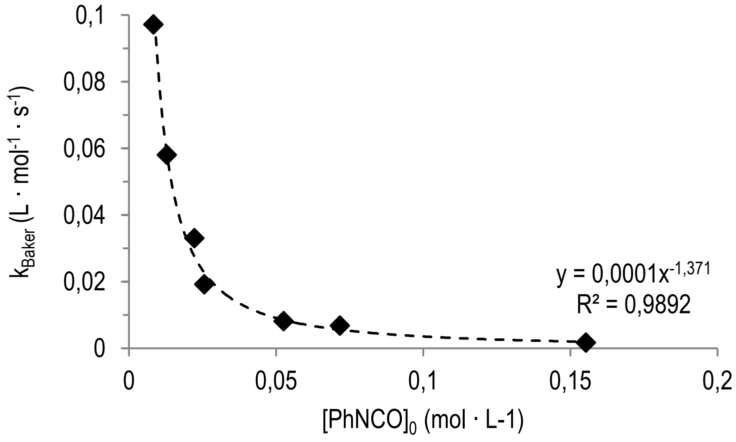

Figure 22. Dependence of the kinetic constant (in L mol^{-1} s^{-1}) calculated according Baker's rate law with PhNCO concentrations (ratio PhNCO:TFE, 1:2) using initial rates method.

With this method to calculate the kinetic constant, the same dependency of kinetic constant on initial concentration was also observed. The obvious interpretation was that pseudo first-order approximation might or might not be valid, but it was not responsible for this effect.

The conclusion was that probably the assumed simple model of Baker might not be an accurate representation for this reaction.

SATO'S RATE LAW

Since Baker's model did not apply to this reaction, it was thought that perhaps a more completed model, as the proposed by Sato, could describe mode adequately the reaction. In Sato's mechanism, the isocyanate is first activated by either alcohol or carbamate product. Then, another molecule of alcohol attacks this complex of activated isocyanate to form the carbamate and releasing the activator molecule.

Sato rate law

$$v = k_a[PhNCO][TFE]^2 \qquad (11)$$

$$k_{Sato} = \frac{v_0}{[PhNCO]_0[TFE]_0^2} \qquad (12)$$

This way the kinetic constant was calculated according Sato's. And again it was possible to see that the rate constant had a inverse dependency on concentration, meaning that the Sato's model was also not able to predict the behavior of this reaction (Figure 23).

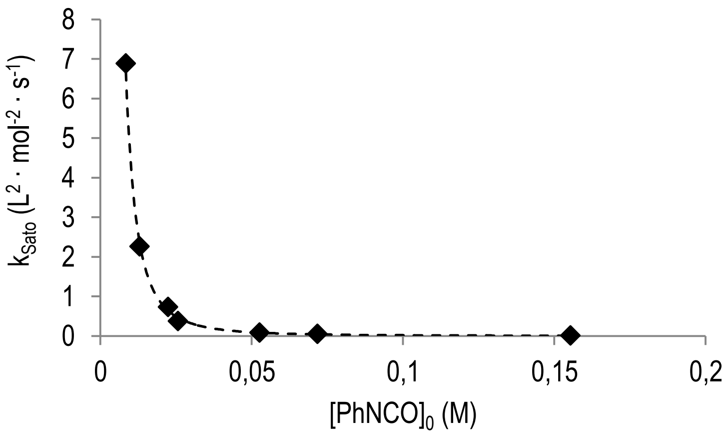

Figure 23. Dependence of the kinetic constant calculated according Sato's rate law with PhNCO concentrations (ratio PhNCO:TFE, 1:2) using initial rates method.

COMPARISON WITH ETHANOL

The rate laws used to calculate the kinetic constant were established for reaction of isocyanates with hydrocarbonated alcohols. So they could be considered valid for the reaction of PhNCO with ethanol. However, it seemed that it was not possible to fit them with the reaction of PhNCO with TFE

A quick comparison between the reaction of PhNCO with EtOH or TFE enlightened the differences. For this purpose, the reaction of phenyl isocyanate with ethanol was compared with the reaction of PhNCO with TFE. In the first case, lowering an order of magnitude of reagents concentration ($[PhNCO]_0$ from 100 mM to 10 mM) led to a decrease in the ten-minutes conversion from 28 % to 15 %; interestingly in the reaction with TFE the same change led to increase from 30 % to 55 %.

While in the reaction with ethanol, the conversion decreased at lower concentrations in accordance with Baker's and Sato's rate laws, in the reaction with TFE it increased. These rate laws, valid for PhNCO with ethanol, clearly did not apply to the reaction of PhNCO with TFE. Would all this mean that we were in the presence of different mechanisms depending on the alcohol?

1.2.4. A SURPRISING RATE LAW

It seemed that the reaction of phenyl isocyanate with TFE should be treated as a new one. In other words, this meant that the previous kinetics studies, rate laws and mechanisms were not valid for the reaction of isocyanates with polyfluorinated alcohols.

GLOBAL ORDER BY INITIAL RATES METHOD

The global order of the reaction was studied by the method of initial rates. This method implies measuring the initial rates in different conditions.

Mathematically, a general equation (13) for the reaction was considered, without previously assuming orders for the reagents. Then, considering the logarithmic version and initial moment, the orders become factors and it was possible to work with the initial concentrations and initial rate (14).[63]

Experimentally, the initial proportion PhNCO:TFE was set to be constant for all the experiments, in this case $[TFE]_0 = 2 \cdot [PhNCO]_0$ (15), and this was applied in equation (16). By operating with logarithms it was possible to obtain equation (18) with two groups of terms, one group constant and another depending on initial concentration. Grouping the constant terms in a generic constant A (19) led to equation (20), in which the natural logarithm of the initial rate is related with the logarithm of the initial concentration. In this equation, the intersection with the x axe would be the constant A, but what was interesting of this equation (20) was that the slope would be the general order of the reaction (m+n).

$$v = k \cdot [PhNCO]^m [TFE]^n \qquad (13)$$

$$ln\, v_0 = ln\, k + m \cdot ln[PhNCO]_0 + n \cdot ln[TFE]_0 \qquad (14)$$

Initialy:

$$[TFE]_0 = 2 \cdot [PhNCO]_0 \qquad (15)$$

$$ln\, v_0 = ln\, k + m \cdot ln[PhNCO]_0 \cdot + n \cdot ln(2 \cdot [PhNCO]_0) \qquad (16)$$

$$ln\, v_0 = ln\, k + m \cdot ln[PhNCO]_0 + n \cdot (ln\, 2 + ln[PhNCO]_0) \qquad (17)$$

$$ln\, v_0 = ln\, k + m \cdot ln[PhNCO]_0 + n \cdot ln\, 2 + n \cdot ln[PhNCO]_0 \qquad (18)$$

Grouping constant terms in A:

$$A = n \cdot ln\, 2 + ln\, k \qquad (19)$$

$$ln\, v_0 = (m + n) \cdot ln[PhNCO]_0 + A \qquad (20)$$

Following this equation and representing the logarithm of the initial rates versus logarithm of initial concentrations a straight line was obtained. From this line, the slope gave the information of the global order of the reaction (Figure 24).

$$\ln v_0 = (m + n) \cdot \ln[PhNCO]_0 + A$$

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[63] Connors, K. A. *Chemical kinetics: The study of reaction rates in solution*, 1st ed.; VCH: New York, USA, 1990. ISBN: 1-56081-053-X.

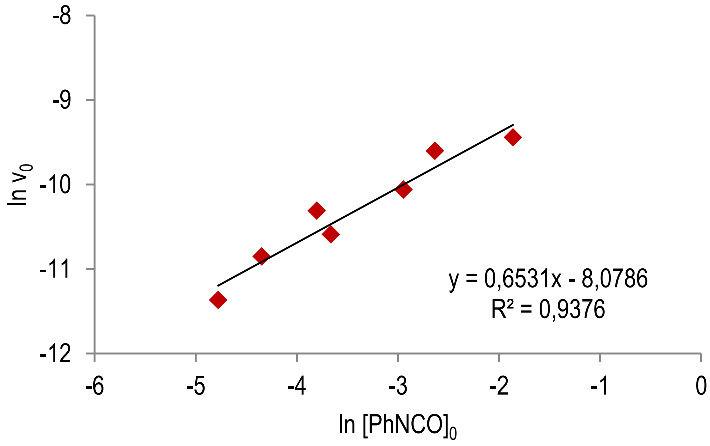


Figure 24. Representation of logarithm of the initial rate in front of logarithm of the initial concentration.

It was quite surprising to find a fractional global order lower than one, closely to 2/3. Although this value by itself cannot easily be explained, it indicates that we are in front of a complex mechanism, suggesting that this reaction includes a chain reaction.

HYPOTHESIS: A NEW RADICAL REACTON

The reaction of TFE with PhNCO have some peculiarities, as the strong solvent effect, that did not match the previously described mechanisms for reaction with non-fluorinated alcohols. In addition, some characteristics of this reaction, as the fractional rate law, could not easily be explained by a polar mechanism.

Taking into account all these results and having in mind the precedents of a radical reactivity with this alcohol,[48] could it be possible that we were facing a new radical chain reaction?

1.3. A RADICAL REACTION REVEALED

From our previous experiments, a chain radical mechanism favored at low concentrations seemed a plausible hypothesis. However, such a claim required additional experiments to be confirmed or rejected.

There are several ways to determine if a reaction follow a polar mechanism or occurs through radical intermediates. A simple one is the use of radical scavengers. More evidence could come from the activation of the reaction by the addition of radical initiators. Complementary confirmation usually comes from the use of spectroscopic techniques for unpaired species, namely, electron paramagnetic resonance, EPR. With this technique it is possible to obtain information about species with unpaired electrons present in the reaction. Once the nature of the radical is envisaged proposed, it is always advisable to collect further evidences by other means, for example performing electrochemical studies by cyclic voltammetry.

1.3.1. EFFECT OF RADICAL SCAVENGER

A radical scavenger is a substance that reacts with free radicals and removes them efficiently from the reaction medium. Therefore, they act as radical reaction inhibitors. Thus, if the presence of radical scavenger does not change the reaction rate, a free radical mechanism has a low probability to operate. The mechanism would be polar, concerted or involve radicals pairs in a cage. Reactions that are significantly slowed or stopped take place normally through free radical intermediates. Furthermore, if a reaction is stopped just with a sub-stoichiometric amount, probably it occurs through a radical chain mechanism.

In this study, the radical scavenger used was galvinoxyl (galvx). It is an air-stable free radical that kills other radicals in the reaction medium by electron transfer or by hydrogen atom transfer. The spin density is delocalized through the entire molecule, between the oxygens and the two aromatic rings. In addition, the *tert*-butyl groups protect the radical by steric hindrance (Figure 25).

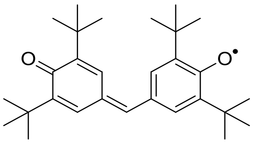


Figure 25. Galvinoxyl, free radical.

As a blank, the effect of galvinoxyl was checked in the reaction of PhNCO with ethanol ($[PhNCO]_0$ = 0.01 M; $[EtOH]_0$ = 0.02 M; $[galvx]_0$ = 1.5 mM; DMF), which is known to be a polar reaction. In this case it was observed that the presence of galvinoxyl did not affect the reaction. This result confirms formation of standard urethanes does not take place through free radical intermediates.

However, the effect of galvinoxyl in the reaction of PhNCO with TFE ($[PhNCO]_0$ = 0.01 M; $[TFE]_0$ = 0.02 M; [Galvx] = 1.5 mM; DMF) was dramatic. The addition of just 0.15 equivalents was enough to stop the reaction for 45 minutes (Figure 26).

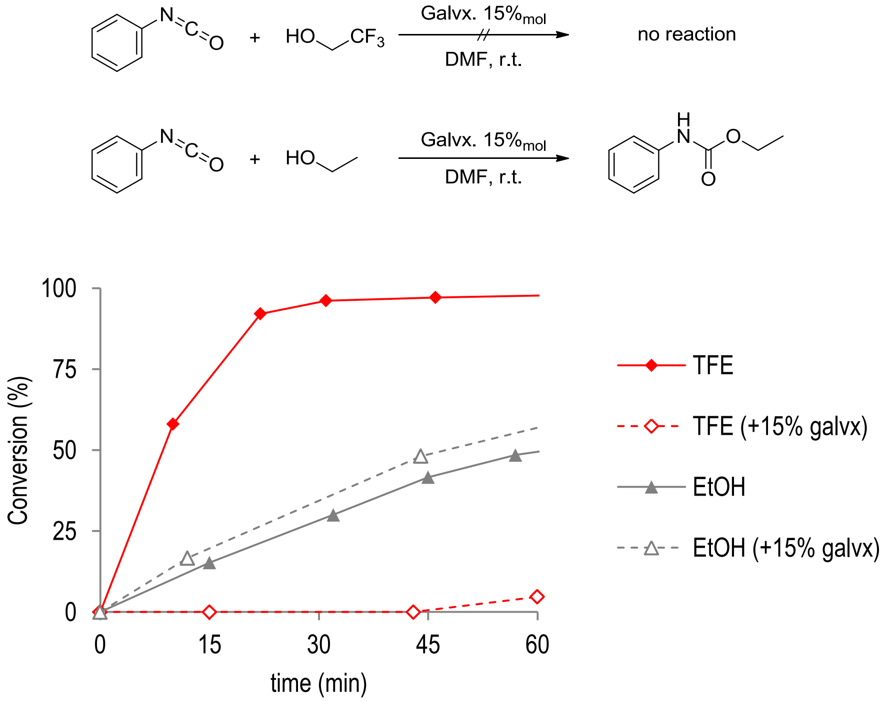
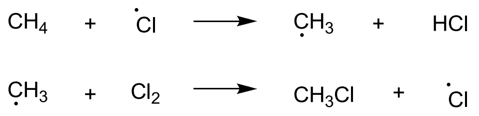


Figure 26. Effect of galvinoxyl on the reaction PhNCO with EtOH or TFE.

The reactivity of PhNCO was compared with the reactivity of cyclohexyl isocyanate, CyNCO. The reaction of TFE with cyclohexyl isocyanate CyNCO was slower than its reaction with PhNCO. After 15 minutes there was a 21 % of conversion, in comparison to 60 % with PhNCO. Nevertheless, addition of 0.15 eq. of galvinoxyl in this case also completely stopped the reaction and no conversion was observed.

The fact that reaction of TFE with isocyanates was affected by galvinoxyl was evidence in favor of a radical mechanism. But not just so, a sub-stoichiometric amount stopped the reaction meaning that probably the reaction involved a radical chain mechanism.

A chain reaction has at least one intermediate, usually radical, continuously regenerated through a repetitive cycle, propagation steps. An illustrative example is presented, the chain propagation step of the chlorination of methane in which the radical Cl· is continuously regenerated (Scheme 22).



$$\mathrm{CH_4} + \overset{\bullet}{\mathrm{Cl}} \longrightarrow \underset{\bullet}{\mathrm{C}}\mathrm{H_3} + \mathrm{HCl}$$

$$\underset{\bullet}{\mathrm{C}}\mathrm{H_3} + \mathrm{Cl_2} \longrightarrow \mathrm{CH_3Cl} + \overset{\bullet}{\mathrm{Cl}}$$

Scheme 22. Propagation steps of radical chlorination of methane.

In the first step, a radical atom of chlorine abstracts a hydrogen atom from methane to form hydrochloric acid and a methyl radical. Then, this methyl radical reacts with dichlorine, to form the product chloromethane and regenerating the radical atom chlorine.

In our reaction, similar steps could be proposed, but more information was required to advance a coherent mechanism.

The effect of galvinoxyl had proved to be a simple way to determine the existence of a radical mechanism. Thus, it was used to check if this radical was only generated in DMF or if it was also observed in other solvents. Moreover, galvinoxyl was also used to test this radical behavior in the reaction of PhNCO with other polyfluorinated alcohols and other acidic nucleophiles.

SOLVENT EFFECT

The important effect that the solvent could exert on the reaction has been described in the section 1.2.1. Solvents with high donor numbers and with the ability to accept hydrogen bonds (DMF, DMSO, and HMPA) provide a better environment for the reaction of TFE with PhNCO.

Reactions performed in solvents that are good electron pair donors (High DN) and hydrogen bond acceptors (High β) were more affected by the presence of galvinoxyl (15 $\%_{mol}$). On the other hand, solvents that are not good electron pair donors were unaffected by galvinoxyl presence (Figure 27).

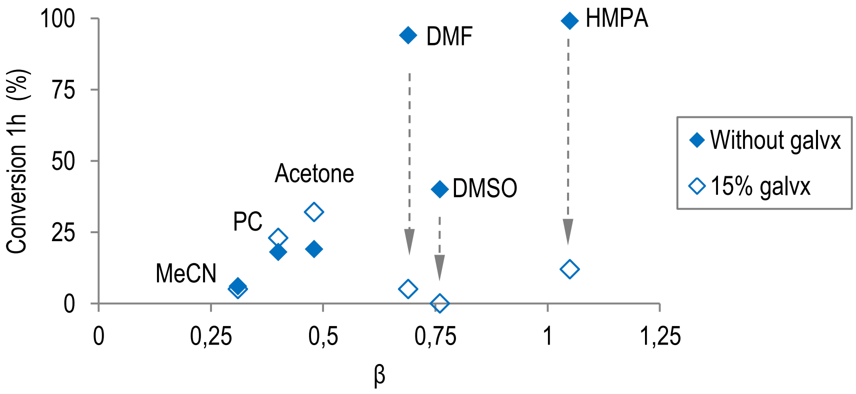
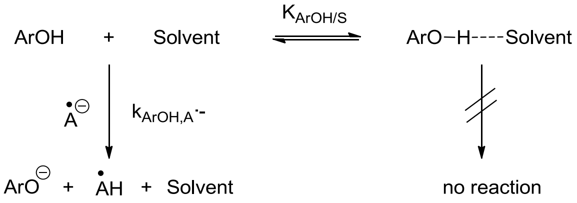


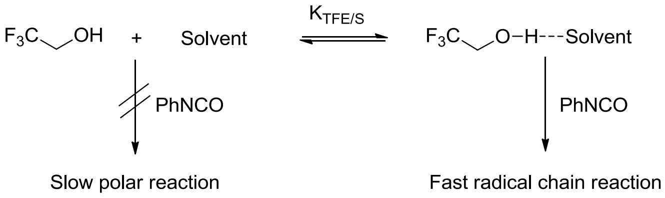
Figure 27. Effect of galvinoxyl in different solvents.

A few years ago, Nielsen and coworkers described a relationship between the kinetic constant of proton transfer and of proton-coupled electron transfer, PCET, from phenols to radical anions and the hydrogen bond accepting ability of the solvent.[64] Interestingly, it was found that reactions were faster in solvents with low hydrogen bond accepting ability. Nielsen interpretation assumed that only free phenol could undergo proton transfer or PCET and that the alcohol/solvent hydrogen bonded complexes were not active (Scheme 23).



Scheme 23. Nielsen explanation for faster reaction between phenols and radical anions in low hydrogen bond accepting solvents.[64]

Six of the eight solvents used in our study were the same than the ones used by Nielsen. However, our reaction showed the opposite trend, being faster with hydrogen bond accepting solvents. Thus, by comparison, if Nielsen proposed an inactive alcohol/solvent complex, in our case the alcohol/solvent complex would be the active specie (Scheme 24).



Scheme 24. Explanation for faster reaction between PhNCO and TFE in high hydrogen bond accepting solvents.

The fast reaction in donor solvents is significantly slowed by the presence of sub-stoichiometric amounts of galvinoxyl, suggesting a radical chain mechanism in our case. Apparently, in our case two different mechanisms co-exist. One polar present in all solvents and one radical just triggered in donor solvents.

EFFECT OF GALVINOXYL AT DIFFERENT REAGENTS CONCENTRATIONS

As the previously found rate law pointed out, the concentration plays a particular effect in this reaction. Thereby, the effect of galvinoxyl for different initial concentrations of the reagents was studied.

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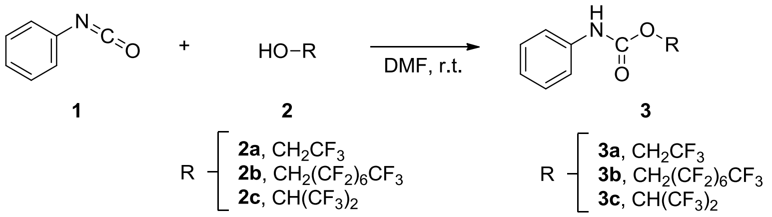
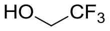
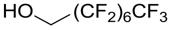
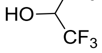
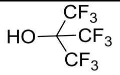
[64] Nielsen, M. F.; Ingold, K. U.; *J. Am. Org. Chem.* **2006**, *128*, 1172-1182.

The reaction of PhNCO with TFE (1:2; DMF) was performed at different initial concentrations. The effect observed by the addition of 15 $\%_{mol}$ respect the PhNCO to the reaction was not constant. The reaction was stopped by galvinoxyl when the initial concentration of PhNCO was 0.01 M or lower. However, the effect of galvinoxyl at higher concentrations, 0.1 M, was not significant (Table 3).

This effect was also observed with other polyfluorinated alcohols. 2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluoro-1-octanol **2b** and 1,1,1,3,3,3-hexafluoro-*iso*-propanol, HFIP, **2c** showed some differences in reactivity with TFE **2a**, but they followed the same general behavior. Reactions of PhNCO with polyfluorinated alcohols were stopped by galvinoxyl when initial concentrations of PhNCO were lower than 0.01 M. Tertiary alcohol, perfluoro-*tert*-butanol, did not react in any of the tried conditions.

Table 3. Conversion at 10 min for the reaction of phenyl isocyanate with polyfluorinated alcohols.[a]



Alcohol	Galvinoxyl ($\%_{mol}$)	Conversion (%) [b]		
		C_0 = 0.1 M	C_0 = 0.01 M	C_0 = 0.001
	0	30	55	85
2a	15	26	0	1.7
	0	12	80	36
2b	15	15	10	7
	0	55	63	47
2c	15	50	10	2
	0	n.d.	n.d.	n.d.
2d				

[a] Initial ratio PhNCO:alcohol 1:2, DMF. [b] Conversion determined by GC as disappearance of PhNCO.

All this data has been represented in graphic bars (Figure 28). For these three alcohols, at 0.1 M, both bars (with and without galvinoxyl) are similar. However, at lower concentrations, 0.01 and 0.001 M, the bar that corresponds to the reaction with galvinoxyl is much lower in all the cases.

2,2,2-trifluoroethanol **2a** 1*H*,1*H*-perfluorooctanol **2b** HFIP **2c**

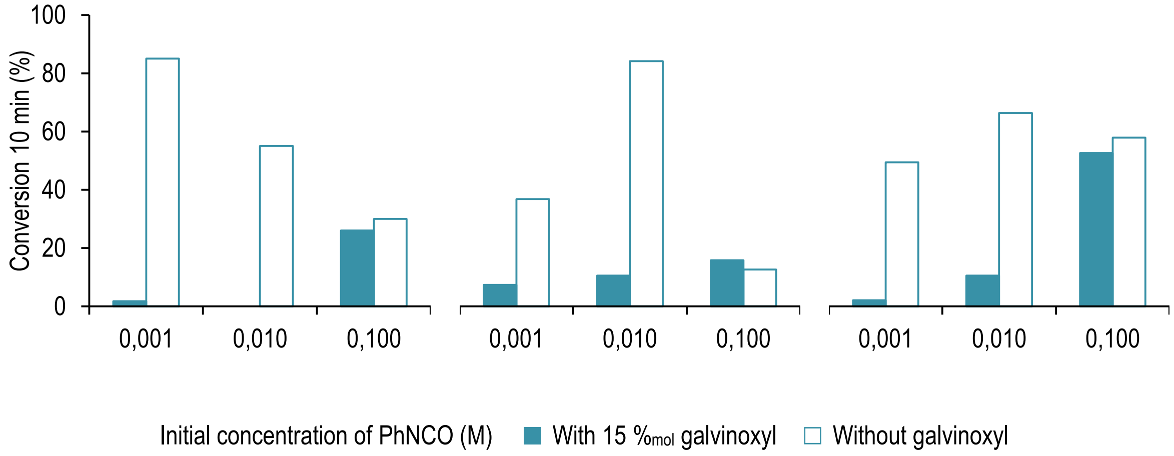


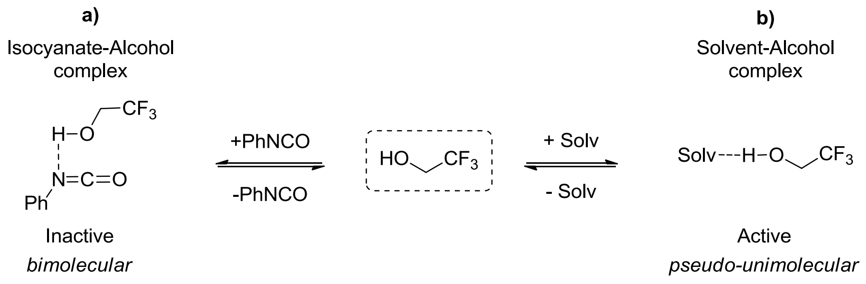
Figure 28. Effect of galvinoxyl in the reaction of PhNCO with polyfluorinated alcohols. 10 min conversion (%) at different initial concentrations of PhNCO with and without galvinoxyl (solid and hollow bars respectively).

A straight-forward interpretation of these results would be that at lower concentrations a radical mechanism is operating and at higher concentrations the null effect of galvinoxyl indicates a non-free radical reaction.

Behavior of the reaction in presence of galvinoxyl, both in different solvents (Figure 27) and at different concentrations (Table 3; Figure 28) seemed to indicate a competence between two different mechanisms. Probably there was the competition between a polar low-productive mechanism with an efficient radical mechanism.

The slow polar mechanism was observed in weak donor solvents and in donor solvents at high reactants concentrations. These conditions favored the formation of a bimolecular isocyanate/alcohol hydrogen bond complex, which probably is inactive or reacts slowly (Scheme 25, a).

The fast radical mechanism just is prompted in high donor solvents at low reactants concentrations. A feasible possibility would be the generation of an alcohol/solvent intermediate able to trigger a fast chain reaction in what would be a pseudo-unimolecular process (Scheme 25, b).



Scheme 25. Equilibriums in the reaction of PhNCO with TFE a) at high concentrations and/or in low donor solvents and b) at low concentrations in high donor solvents.

EXTENSION TO OTHER WEAK NUCLEOPHILES

The most striking difference in the reactivity of polyfluorinated alcohols with respect to standard alcohols seemed to be the fact that those were radical reactions. If those radical reactions were extensible to other acidic weak nucleophiles it could be an important breakthrough.

To check this idea, and also to extend the scope of the reaction, other nucleophilic compounds with a similar acidity to polyfluorinated alcohols were tested (Table 4). The first step was to test their reaction with PhNCO in similar conditions as the ones used with polyfluorinated alcohols, if the reaction took place then effect of radical scavenger would be checked.

Table 4. Acidity of compounds tested.

Compound	$pK_a(H_20)$ [65]	$pK_a(DMSO)$ [46]
TFE	12.5	23.5
HFIP	9.3	18.2
4-nitrophenol	7.1	10.8
4-methoxyphenol	10.2	19.1
ascorbic acid	4.1	-
cyclopentadiene	15	18.0
fluorene	-	22.6

From the different nucleophiles tested only phenols reacted in these conditions with PhNCO. Neither ascorbic acid nor C-H acidic cyclopentadiene nor fluorene yielded any reaction.

Phenols have a comparable acidity to polyfluorinated alcohols. 4-Nitrophenol and 4-methoxyphenol were selected as range limits for phenols. Both of them reacted with phenyl isocyanate, being more reactive 4-nitrophenol (Table 5). Since 4-nitrophenol is more acidic and less nucleophilic than 4-methoxyphenol, this could be interpreted in the way that acidity is an important feature in this reaction.

Table 5. Reaction of phenols with PhNCO.

R	Conversion 1 h (%)	
	-	With galvx. (15 $\%_{mol}$)
NO_2	60	65
OCH_3	28	32

---

[65] Online table of water pK_a: Ripin, D. H.; Evans, D. A. *pKa's of organic compunds* (Updated: 11th Apr 2005) <http://evans.harvard.edu/pdf/evans_pKa_table.pdf> (Accessed: 15th May 2014)

Conditions: $[PhNCO]_0 = 0.01$ M; $[R\text{-}PhOH]_0 = 0.02$ M; $([galvx]_0 = 0.0015$ M; DMF.

Although phenols reacted with isocyanate in DMF, their reaction was unaffected by radical scavenger, which suggested a different reaction path from polyfluorinated alcohols.

So far, it looked like radical reaction with isocyanate was quite specific of polyfluorinated alcohols and not extensible to other acidic weak nucleophilic compounds.

1.3.2. ACTIVATING THE REACTION WITH RADICAL INITIATORS

The strong effect of galvinoxyl points out the operation of a radical mechanism. As the reaction was stopped by a radical scavenger; perhaps it could it be activated by radical initiators.

While the reaction was fast in donor solvents, it failed in other solvents. The reaction of TFE with PhNCO in MeCN barely reached 6 % of conversion after one hour. Therefore, if the presence of a radical initiator triggered the reaction in acetonitrile this would be another support for a radical mechanism.

A radical initiator is a compound that produces free radicals under mild conditions that promote radical reactions. The most used initiators are azo compounds, such as AIBN, and organic peroxides, like benzoyl peroxide (Figure 29).

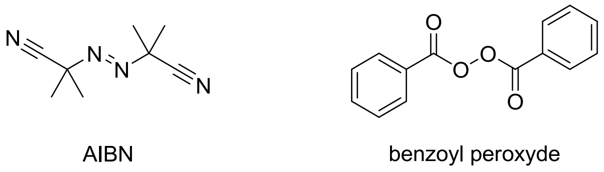


Figure 29. AIBN and benzoyl peroxide structures.

Thus, to a solution of TFE and PhNCO in MeCN was added 10 $\%_{mol}$ of the selected initiator. Nevertheless, the decomposition rate of the initiators depends on the temperature; below certain temperature, the decomposition rate might be too low to observe any effect on the reaction (Table 6).[66]

Table 6. Effect of radical initiators in the reaction of TFE with PhNCO in MeCN.[a]

Initiator	Temperature (ºC)	1 h Conversion (%)

---

[66] For information of decomposition rate of radical initiators: Sigma-Aldrich. Applications: *Free Radical Initiators.* <http://www.sigmaaldrich.com/content/dam/sigma-aldrich/docs/Aldrich/Brochure/al_pp_initiators.pdf> (Accessed: 15th June 2014)

-	R.T.	6
Benzoyl peroxide	R.T.	9
Benzoyl peroxide	60	7
Benzoyl peroxide	90	41[b]
AIBN	R.T.	5
AIBN	60	3
AIBN	90	26[b]

[a] Initial conditions: 0.01 M PhNCO, 0.02 M TFE, 0.002 M initiator. [b] 1,3,5-triphenylisocyanurate as a major product.

The reaction at 60 ºC did not show a higher conversion. Increasing the temperature to 90 ºC did not have a positive effect in the reaction. At that temperature there conversion of PhNCO produced a single product, but it was not carbamate. To identify this compound, it was crucial the information obtained by GC-MS (Figure 30). The molecular ion of this compound was 357 m/z, the triple of PhNCO molecular weight. By comparison with a spectral database (MS Wiley 275) it was identified as 1,3,5-triphenyl-1,3,5-triazine-2,4,6-trione, the cyclic trimer derived from phenyl isocyanate (Scheme 26).

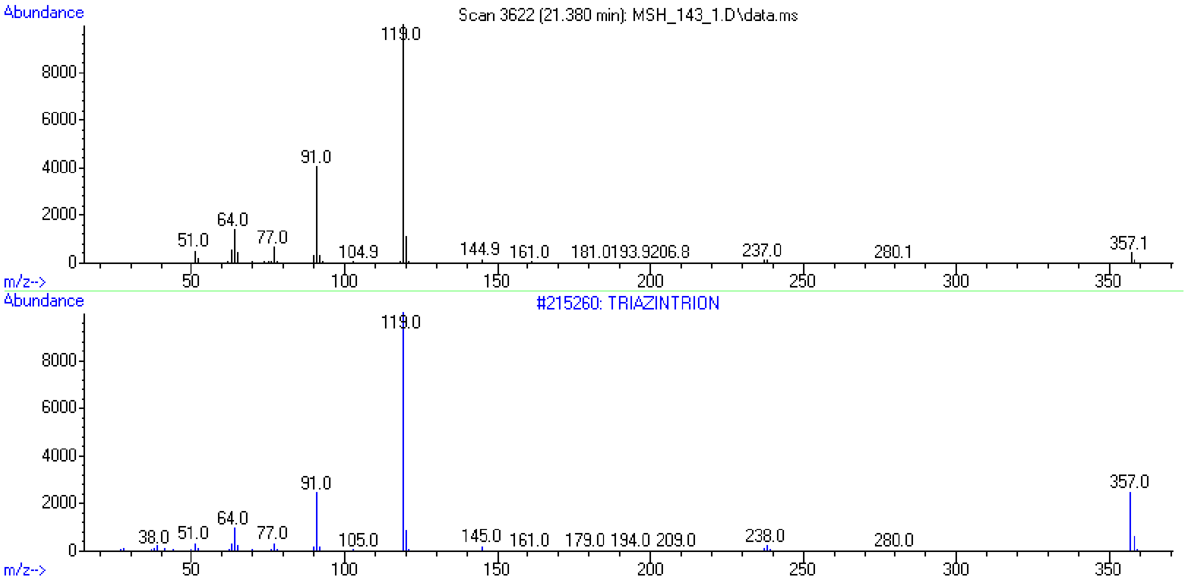
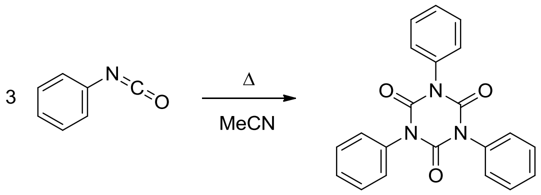


Figure 30. Obtained (Top) and database Wiley 275 (Bottom) m/z spectra of 1,3,5-triphenyl-1,3,5-triazin-2,4,6-trione.



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Scheme 26. Triphenyl isocyanurate derived from heated phenyl isocyanate.

It was mentioned in the introduction that isocyanates can react with themselves. These reactions are enhanced at higher temperatures. Thus, in the absence of a catalyst that promotes the desired reaction over by-reactions, heating would lead to by-products. So this strategy did not provide any light to our reaction mechanism [67]

1.3.3. IS ANY RADICAL IN THERE? ELECTRON PARAMAGNETIC RESSONANCE

Although the scavenger experiments pointed out to a radical mechanism, it would not be fully accepted without including electron paramagnetic resonance, EPR, also known as electron spin resonance, ESR. This spectroscopic technique allows detection and characterization of unpaired electron species, such as organic radicals and transition metal complexes.

An unpaired electron is a spinning charge that generates a magnetic field with two energetically equivalent magnetic spin states, m_s = +1/2 and m_s = -1/2. However, in the presence of an external magnetic field, both states become energetically different. The energy gap depends on the strength of the magnetic field and, as any electronic energy difference, it has associated a frequency of a photon, $\Delta E = h\nu$ (Figure 31 a).

In EPR, an irradiation source is kept constant at a determined frequency, usually in the region of microwaves between 9 ~ 10 GHz. The sample is placed between the irradiation source and a detector. Then a magnetic field is applied with increasing strength, which changes the energy gap between the spin states. Eventually, this gap would be of the same energy (frequency) than the microwave, electrons would be promoted from one state to the other and there will be energy absorption registered in the detector (Figure 31 b).

For historical reasons, EPR spectra usually are presented as the derivate of the absorption. In addition, as the intensity of the signal is based on an arbitrary scale of each machine, y-axis is usually omitted.

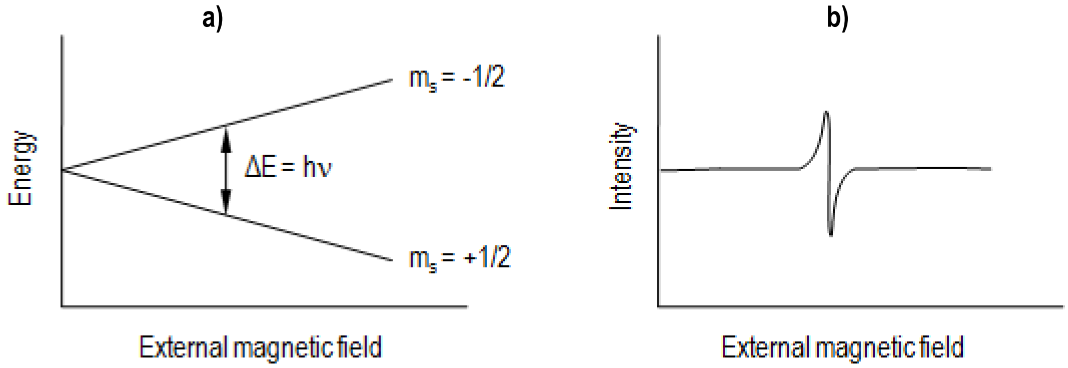

Figure 31. a) Energy diagram of an unpaired electron in a magnetic field. b) EPR spectrum of this electron.

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[67] Schwetlik, K; Noack, R. *J. Chem. Soc. Perkin Trans. 2.* **1995**, 395-402.

This technique can be considered equivalent to NMR but centered on unpaired electron spin instead of atom nuclei spin. An unpaired electron interacts with nuclei in its surroundings that have spin different than zero (*e.g.* $S(^{1}H) = ½$; $S(^{14}N) = 1$; $S(^{19}F) = ½$) which produces an hyperfine coupling, analogous to *J*-coupling in NMR. Following this analogy, the chemical shift δ in NMR would be the dimensionless magnetic moment g_e in EPR. However, differences in g_e are usually small in organic radicals and do not provide useful chemical information.[68]

As this technique allows the detection of just the unpaired species, it is highly specific and other species do not interfere. If a reaction has radical intermediates, usually they have shot lifetimes and are in low concentration, which means that often they are difficult to detect and giving false negatives.

FIRSTS ATTEMPTS

The EPR experiments were carried out in the facilities of ICMAB *Institut de Ciència de Materials de Barcelona* in collaboration with Dr. Jose Vidal and Dr. Vega Lloveras. I prepared samples and reactions *in situ,* while they operate the spectrometer. Samples and reactions were degassed, protected from light and the spectra recorded in a flat cell using a spectrometer Bruker ELEXYS 500 E of 9.5 GHz.

Spectra of the solvent alone (DMF), of a solution of TFE and a solution of PhNCO were recorded individually. In none of these three experiments any radical was detected. These results reject spontaneous radical formation by just the reagents.

Next, the spectrum of the reaction of TFE with PhNCO in DMF was recorded, but no EPR signals were observed. We thought that HFIP would generate more stable radicals, by steric hindrance and by electronic stabilization. Unfortunately, no signal was observed either.

These results could have broadly two different explanations. On one side, perhaps there were no free radicals at all in the reaction and our hypothesis was wrong. On the other, it could be that the transient radicals had too short lifetimes to be detected. If it were the second case, the presence of a spin trap in the reaction medium could help in their detection.

USING SPIN TRAPS IN EPR

A spin trap is a non-radical compound that reacts with transient radical to form a spin adduct, a more persistent radical. The term spin trap should be not confused with radical scavenger. While the former generates a spin adduct still radical in nature; the radical scavenger removes radicals from the medium.

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[68] Hogg, N. *Free Radic Biol Med.* **2010**, *49,* 122-129.

Obviously, the information obtained from the spin adduct is more limited than the obtained of a direct observation of the radical. However, hyperfine couplings of the spin adduct depend on the radical trapped, and by comparing with literature it is possible to obtain indirect information of the nature of the radical.

One of the most used spin trap tried is 2-methyl-2-nitrosopropane, MNP. It is a general spin trap that is particularly suitable for carbon centered radicals; usually it forms relatively stable spin adducts (Figure 32).

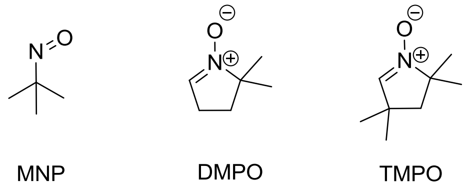
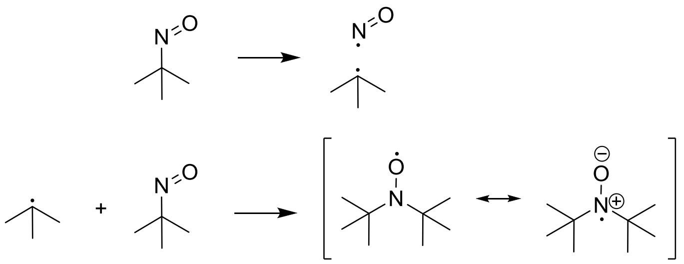


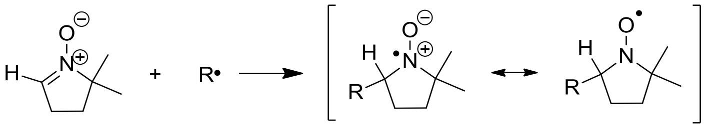
Figure 32. Structure of the used spin traps.

The reaction performed in the presence of MNP (11 µL PhNCO, 0.1 mmol; 15 µL of TFE; 0.2 mmol; 9 mg MNP, 0.1 mmol; 10 mL DMF) did not showed any EPR signal during the firsts 30 minutes. After 30 min, an EPR signal was observed. However, the triplet detected corresponded to *tert*-butyl radical/MNP spin adduct. It seemed that in the conditions of the reaction, the spin trap MNP broke to form NO and *tert*-butyl radical. Then, this radical was trapped by another MNP molecule to give the triplet observed (Scheme 27).[69]



Scheme 27. Decomposition of MNP and formation of ^{t}Bu/MNP radical adduct detected as a triplet in EPR.

Thus, MNP was rejected as spin trap to avoid the problems of self trapping and it was decided to use another one. A family of spin traps without problems of homolytic cleavage are cyclic nitrones, *N*-oxide of an imine, as for example 5,5-dimethyl-1-pyrrolyne *N*-oxide, DMPO (Scheme 28).



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[69] Bowman D. F.; Brokenshire, J.L.; Gillan, T.; Ingold, K.U. *J. Am. Chem. Soc.* **1971**, *93*, 6551-6555.

Scheme 28. Spin trap DMPO forming a spin adduct with a general free radical ·R.

Cyclic nitrones trap free radicals through carbon 2. In this spin adduct, the unpaired electron is placed further from the trapped radical; thus, less information can be gathered. Usually the unpaired electron is just coupled with the nitrogen (nuclear spin I = 1) and hydrogen atom (I = ½). From the spin adduct obtained, the information is deduced from the hyperfine coupling constants and comparing with previously reported values. Roughly, on this type of spin adducts carbon-centered radicals have hyperfine constants approximately of *a*(1N) = 16 G and *a*(1H) = 25 G, in contrast oxygen-centered radical *a*(1N) = 14 G and *a*(1H) = 7 G.[70,71,72] Although a detailed structure cannot be established, at least some valuable information about the nature of the radical can be deduced.

The stability of DMPO was checked by recording EPR spectra of DMPO alone and in combination with each one of the reactants (TFE, HFIP and PhNCO) and in any case no EPR signal was observed.

No radical was detected in the reaction of PhNCO with TFE in DMF in the presence of DMPO. However, in the same conditions but using HFIP something different from background noise was be detected. Although it was just a weak signal above the noise, it could indicate the presence of a radical. However, its concentration was in the EPR detection limits.

The main reasons for such a low concentration of spin-adduct could be two: a short lifetime of the spin adduct and a very low concentration of the transient radical.

It is possible to increase the lifetime of the spin adduct by changing the spin trap to another with more steric hindrance. Therefore, a bulkier analog of DMPO, 3,3,5,5-tetramethyl-1-pyrrolyne *N*-oxide TMPO, was used as spin trap. However, again very weak signals were observed.

This reaction is very sensitive to radical scavengers (Section 1.3.1). In all the EPR experiments tested, spin trap had been present from the beginning. It could be possible that the spin traps were acting also as scavengers; trapping the few radicals generated in the initiation step and stopping the process. However, the concentration of the radical adduct could be not high enough to be detected.

If this were the case, the key would be to wait until the propagation was triggered producing enough radicals before adding the spin trap. At zero time, there were no radicals and the initiation perhaps was stopped by the spin trap. However, after some induction time, the

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[70] Sueishi, Y.; Yoshioka, D.; Yamamoto, S.: Kotake, Y. *Org. Biomol. Chem.* **2006**, *4*, 896-901.
[71] Castellanos, M. M.; Reyman, D.; Sieiro C.; Calle, P. *Ultrason. Sonochem.* **2001**, *8*, 17-22.
[72] Haire, D. L.; Oehlerh, U. M.; Goldman, D.; Dudley, R.;Janzen, E. *Can. J. Chem.* **1988**, *66*, 2396-2402.

reaction would be at maximum speed, with enough radicals to carry on the reaction and perhaps they could be trapped and detected.

Thereby, it was decided to set up the reaction of TFE and PhNCO in DMF and let it react without spin trap for five minutes. After that time TMPO was added to the mixture and the EPR spectrum recorded. This EPR spectra showed a sextuplet signal corresponding to a spin adduct of TMPO, finally confirming the existence of free radical in the reaction mixture (Figure 33).

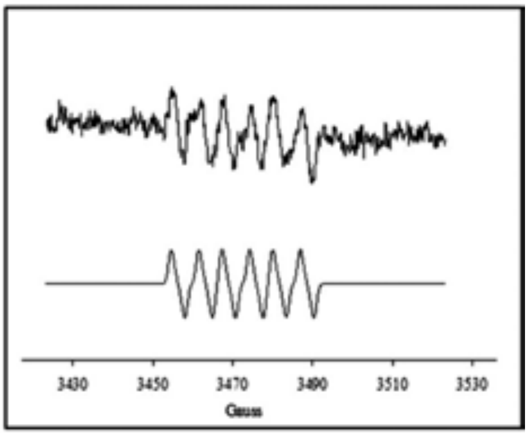

Figure 33. Experimental (up) and simulated (down) EPR spectra of a spin adduct between TMPO and a free radical generated in the reaction of TFE with PhNCO in DMF.

The double triplet observed was centered in g_e = 2.0062 with a hyperfine couplings *a*(1N) = 12.70 G and *a*(1H) = 6.91 G. Once properly simulated and comparing with literature values, it was attributed to the radical adduct of TMPO with the oxygen centered 2,2,2-trifluoroethoxyl radical (Figure 34).

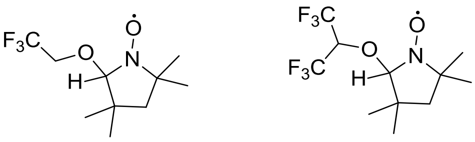

Figure 34. Structure of TFE/TMPO spin adduct (g_e = 2.0062; *a*(1N) = 12.70 G; *a*(1H) = 6.91 G.) and HFIP/TMPO spin adduct ($\mathrm{g_e}$ = 2.0062, *a*(1N) = 13.25 G, *a*(1H) = 7.01) spin adducts.

The detection of an analogous spin adduct in the reaction with HFIP ($\mathrm{g_e}$ = 2.0062, *a*(1N) = 13.25 G, *a*(1H) = 7.01) indicated that the presence of radical seemed to be a general trait in the reaction of polyfluorinated alcohols with phenyl isocyanate. However, it was limited to polyfluorinated alcohols, since no signal was observed in the analogous experiment with ethanol.

The existence of radicals centered in oxygen derived from polyfluorinated alcohols was not something new, as they had been previously proposed.[48,73,74] However, to the best of our knowledge, it was the first time they were trapped and detected as reaction intermediates.

Some more detailed information on the radicals generated in this reaction was obtained by using cyclic voltammetry.

1.3.4. STUDY OF THE RADICALS BY CYCLIC VOLTAMMETRY

The behavior, stability, and electrochemical properties of 2,2,2-trifluoroethoxyl radical were studied using cyclic voltammetry CV. Those experiments were carried out by Helena Comalrrena and Dr. Gonzalo Guirado. Nevertheless, they are presented here because they are directly relevant to the comprehension of this studied mechanism.

A cyclic voltagram of sodium 2,2,2-trifluoroethoxyde in DMF with tetrabutyl ammonium fluoride as supporting electrolyte was performed. A one-electron oxidation wave at 1.05 V versus saturated calomel electrode SCE in the forward scan from 0.0 to 1.6 V was observed. While an irreversible reduction wave at -0.93 V versus SCE was detected in the cathodic back scan from 1.6 to -1.6 V (Figure 35).

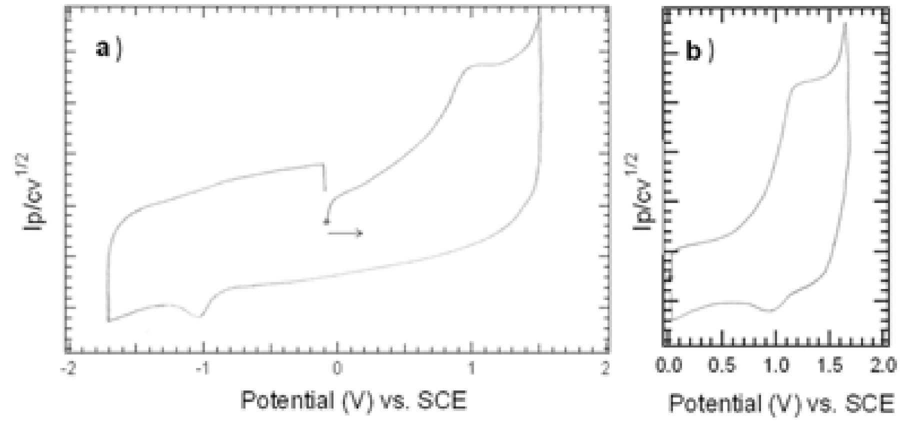

Figure 35. Cyclic voltagram of sodium 2,2,2-trifluoroethoxide at a) 5 and b) 20 V / s.

It is important to remark that when the CV was first scanned in cathodic direction, the irreversible reduction wave at -0.93 V did not exist and the oxidation wave at 1.05 V appeared uncharged.

The voltagram of 2,2,2-trifluoroethoxy anion at higher scan rates, presents a reversible one-electron oxidation wave at 1.1 V versus SCE.

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[73] Wang, Y.; Liu, J.-Y.; Li, Z.-S.; Wang, Li. Sunj, C.-C. *J. Comput. Chem.*, **2007**, *28*, 802-810.
[74] Papadimitriou, V. C.; Prosmitis, A. V.; Lazarou, Y. G.; Papagiannakopoulos, P. *J. Phys. Chem. A,* **2003,** *107*, 3733-3740.

That is, if there were no chemical reactions linked to electron transfer, a reversible one-electron wave was observed at scan rates of 20 V/s or higher. This corresponded to the reversible formation of a first specie A with a half lifetime of 1 ms (22).

$$t_{1/2} = \frac{R \cdot T}{F \cdot v} \tag{21}$$

$$t_{1/2} = \frac{8.31 \frac{J}{K \cdot mol} \cdot 286\, K}{96500\, C \cdot 20 \frac{V}{s}} = 1.2 \cdot 10^{-3} s \tag{22}$$

This specie A evolved to a more stable specie B at longer times or slower scan rates. This second specie, B, underwent one electron reduction giving back the 2,2,2-trifluoroethoxide anion.

Hence, at this point it was fairly to think that specie A corresponded to a radical derived from the oxidation of 2,2,2-trifluoroethoxy anion, whereas specie B should be a more stable isomeric radical. The reduction potential value of B was similar to described for related carbon-centered radicals, so presumably it corresponded to one of these types of species.[75]

The nature of species B was unraveled by combination of electrolysis with EPR. A solution of sodium 2,2,2-trifluoroethoxide with 5 equivalents of spin trap MNP in DMF using tetrabutyl ammonium fluoride as supporting electrolyte, was electrolyzed at controlled potential 1.3 V for 10 min. Immediately after, an EPR spectrum of the electrolyzed solution was recorded to obtain an apparent triple quintuplet (Figure 36).

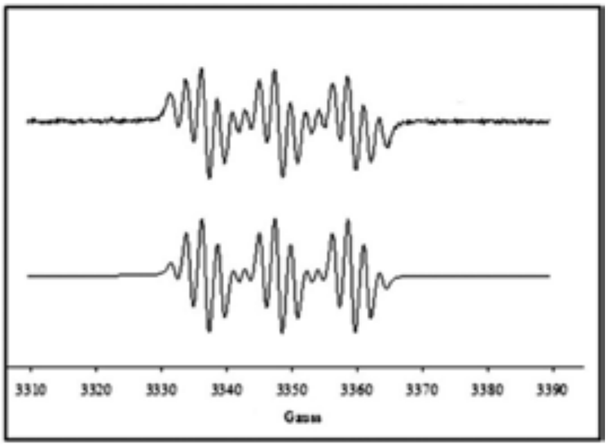

Figure 36. EPR spectrum after electrolysis of sodium 2,2,2-trifluoroethoxide in presence of MNP
g_e = 2.0062; *a*(1N) = 11.21 G; *a*(1H) = 2.33 G; *a*(3F) = 2.39 G.

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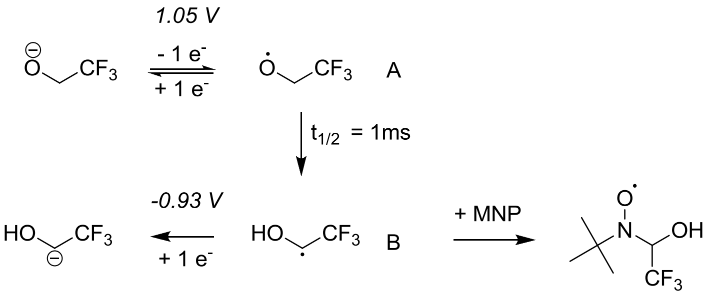
[75] Andrieux, C. P.; Gelis, L.; Medebielle, M.; Pinson, J.; Saveant, J. M. *J. Am. Chem. Soc.* **1990**, *112*, 3509-3520.

This spectrum showed a radical, that after simulation was attributed to adduct of MNP with 2,2,2-trifluoro-1-hydroxy-1-ethyl radical, *i.e.* radical derived from TFE centered on carbon (g_e = 2.0062; *a*(1N) = 11.21 G; *a*(1H) = 2.33 G; *a*(3F) = 2.39 G) (Figure 36).

With all this information, a voltammetric cycle was proposed (Scheme 30). In this cycle, first 2,2,2-trifluoroethoxy anion was oxidized at 1.05 V to the 2,2,2-trifluoroethoxy radical (A), centered in oxygen. This radical A was not very stable and it rearranges in about 1 ms to a more stable 2,2,2-trifluoro-1-hydroxy-1-ethyl radical (B), centered in carbon. This specie B, 2,2,2-trifluoro-1-hydroxy-1-ethyl radical is reduced to the anion at -0.93 V. However, in the presence of MNP, B was trapped and identified as the carbon centered radical B (Figure 36, Scheme 29).



Scheme 29. Proposed voltammetric cycle for sodium 2,2,2-trifluoroethoxide.

This voltammetry cycle proposal is in agreement with previously reported theoretical calculations. Papadimitriou *et al.*[74] have reported that carbon-centered radical B is more stable than oxygen-centered radical A by 69.4 J/mol.

Importantly for our reaction, Wang[73] have reported that for the abstraction of a hydrogen atom from TFE, the hydrogen atom on the hydroxyl group ($CF_3CH_2O\underline{H}$) is preferred over the a hydrogen atom on the methylene ($CF_3C\underline{H}_2OH$).

In conclusion, the oxygen-centered radical A derived from TFE would be formed preferentially, but then if it does not react, it would isomerize to the more stable carbon centered-radical B.

1.3.5. RATIONALIZING THE EFFECT OF SUBSTIUENT: THE HAMMETT EQUATION

Substituents have a profound effect in the reaction of functional groups connected to an aromatic ring because they modify the electronic density. One key point of the *standard* reactivity of isocyanates with nucleophiles is the electron density on the central carbon, generally the more electrophilic, the more reactive.

The effects of aromatic substituent in a reaction can be mathematically treated applying the Hammet equation. It is an equation that describes the influence of *meta* and *para* substituents on the reactivity of a functional group in a substituted benzene ring with two parameters: one depending on the substituent "σ" and another on the reaction "ρ".

$$log\frac{k}{k_H} = \rho \cdot \sigma \qquad\qquad \text{Hammett's equation}$$

The parameter σ of the substituent was defined in function of the influence of substituent in the acid/base equilibrium constants of benzoic acids. Considering the non-substituted benzoic acid as reference (or substituted with hydrogen atoms), a positive σ parameter is related with electron-withdrawing groups while a σ negative with electron-donor group.

Then, these parameters were generalized to describe the influence of substituent over kinetic constants of reactions on other functional groups. Consequently, the slope ρ depends on the reaction, thus positive values correspond to reactions favored by electron withdrawing groups, and negatives ρ values are obtained when electro donating groups favor the reaction.

The Hammett equation has also been applied to the reactions of substituted phenyl isocyanates with hydrocarbonated alcohols with good agreements.[76] It was illustrating to compare one described example with our study reaction. The Hammett equation was plot for the reaction of substituted phenyl isocyanates with two different alcohols: 2,2,2-trifluoroethanol (our reaction) and an hydrocarbonated alcohol, 2-ethylhexanol, 2EH (an example from the literature[76]) (Table 7).

The reactions of *para* substituted phenyl isocyanates X-PhNCO with TFE were performed in the same conditions and concentrations than PhNCO with TFE; the initial rates of each reaction were determined by GC. As the initial concentrations were the same, the quotient of the initial rates is equivalent to the quotients of constant rates (24).

$$\begin{bmatrix} v_0^X = k_0^X[X\text{-}PhNCO]_0[TFE]_0 \\ v_0^H = k_0^H[PhNCO]_0[TFE]_0 \end{bmatrix} \qquad (23)$$

$$\frac{v_0^X}{v_0^H} = \frac{k_x}{k_0} \qquad (24)$$

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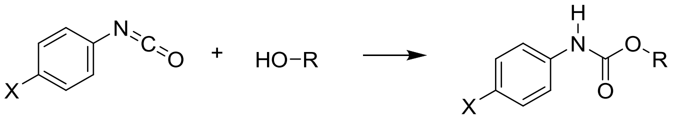
[76] Kaplan, M. *J. Chem. Eng. Data* **1961**, *6*, 272-275.

Table 7. Relative kinetic constants of the reaction of substituted 4-X-PhNCO with TFE and 2-ethylhexanol.[76]



Substituent -X	σ [a]	$\log_{10}(k/k_0)$	
		TFE	2EH[b]
$-OCH_3$	-0.268	-0,268	-0,292
$-CH_3$	-0.170	-0,009	-0,215
-H	0	0,000	0,000
-Cl	+0.227	0,033	0,526
$-NO_2$	+0.778	-0,086	1,621

[a] Hammett substituent constant. [b] Values from literature[76]

The reaction of PhNCO with 2EH has a reaction parameter ρ of approximately +1.9. This large and positive parameter indicates that the reaction is favored with electron withdrawing substituents that enhance the electrophilicity of the isocyanate (Figure 37).

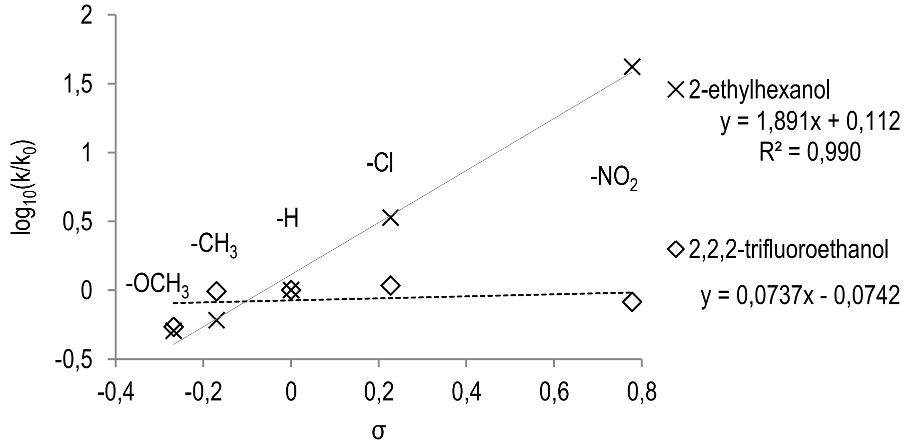


Figure 37. Hammet plot comparing the reaction of substituted PhNCO with 2EH and TFE.

The plot of the reaction of X-PhNCO with TFE had a low linearity and the slope ρ, if calculated, was around +0.07, which indicated a nearly null effect of the substituent. This absence of a trend suggested that either the substituent had no effect over the reactivity of the isocyanate group or that isocyanate was not involved until after the rate determining step. This result, surprising at the first sight, was in accordance with the other traits shown by this reaction. In fact, it was crucial to establish the mechanism proposal detailed in the next section.

1.4. MECHANISTIC PROPOSAL

When available theories or models cannot explain experimental observations a new hypothesis should be proposed. Any new hypothesis should not contradict experimental observations and explain them as much as possible. The following pages describe our mechanistic proposal for this reaction.

First, let us recapitulate peculiarities and experimental observations gathered for the reaction of aromatic isocyanates with polyfluorinated alcohols.

Only with polyfluorinated alcohols
More acid and less nucleophilic than hydrocarbonated alcohols

Solvent effect
Electron pair donor and hydrogen bond acceptor solvents required (DMF, HMPA…)

Concentration effect
Inverse dependence of rate on reactants concentration

Rate law
Experimental rate law with fractional global order lower than one

Effect of radical scavenger
Substoichiometric amounts stopped the reaction

Electron paramagnetic resonance
Detected and identified free oxygen-centered radical derived from the polyfluorinated alcohol

Cyclic Voltammetry
Short lifetime of oxygen-centered radical that isomerizes to carbon-centered radical

Substituent effect
Null dependence of the reaction on the electronic effects of the substituent on PhNCO

The different features suggested a reaction in which hydrogen bond equilibriums, ruled by alcohol acidity, solvent basicity and reactants concentration, are crucial. Effect of radical scavenger complemented with EPR evidences suggested a radical chain mechanism with the oxygen-centered radical derived from alcohol as a free radical intermediated. Kinetic global order lower than one pointed out that this radical was formed in a pseudo-unimolecular rate determining step from the alcohol/solvent complex. Finally, the non-dependence of the reaction rate on electronic effects of substituent on PhNCO suggested PhNCO reaction with a neutral intermediate, most probably a radical.

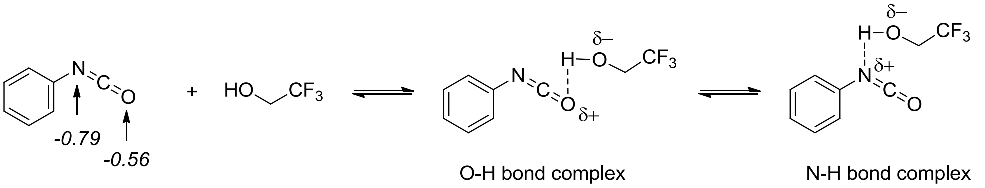
1.4.1. INITIATION

The high electronegativity of fluorine atoms has a strong effect over the alcohol group. It makes this group more acidic than standard alcohols. (Acidity in DMSO: pK_a(TFE) = 23.5; pK_a(EtOH) = 29.8).[46]

In previous reported mechanisms, complexes of the isocyanate with the alcohol are proposed. According to Sato,[50] the oxygen of the alcohol activates the isocyanate, like a nucleophilic catalyst. However, due to the lower nucleophilicity of polyfluorinated alcohols this process is unlikely to happen.

INITIATION BY ISOCYANATE/ALCOHOL ADDUCT

The higher acidity and low nucleophilicity of polyfluorinated alcohols would favor instead the formation a hydrogen bond complex with isocyanate, bringing together the two reagents. In order to find which atom of the isocyanate was forming the hydrogen bond, atomic partial charges were calculated.[77] Both hydrogen bond complexes would be in equilibrium, although the higher charge in nitrogen makes N-H adduct favored. A hydrogen bond complex would generate a partial positive charge on the isocyanate and a negative one over the oxygen of the alcohol (Scheme 30).



Scheme 30. Formation of PhNCO/TFE hydrogen bond complexes. Mulliken charges in italic.[77]

If the transfer of the proton were complete in the nitrogen-hydrogen bond complex, it would lead to an ion pair that could collapse to form the carbamate (Scheme 31). Other possibility was that the proximity of partial charges from the complex would favor the formation of a charge transfer complex, CTC. This complex could undergo a proton coupled electron transfer, PCET. As the proton and the electron are transferred from and to different atoms or orbitals, it cannot be considered a hydrogen atom transfer, but rather an electron-proton transfer.[78] The radical pair generated could directly collapse to form the carbamate product. In this case, there would not be any observable difference from the ion pair path. If instead of collapsing, the radicals diffuse, they could enter in a propagation cycle.

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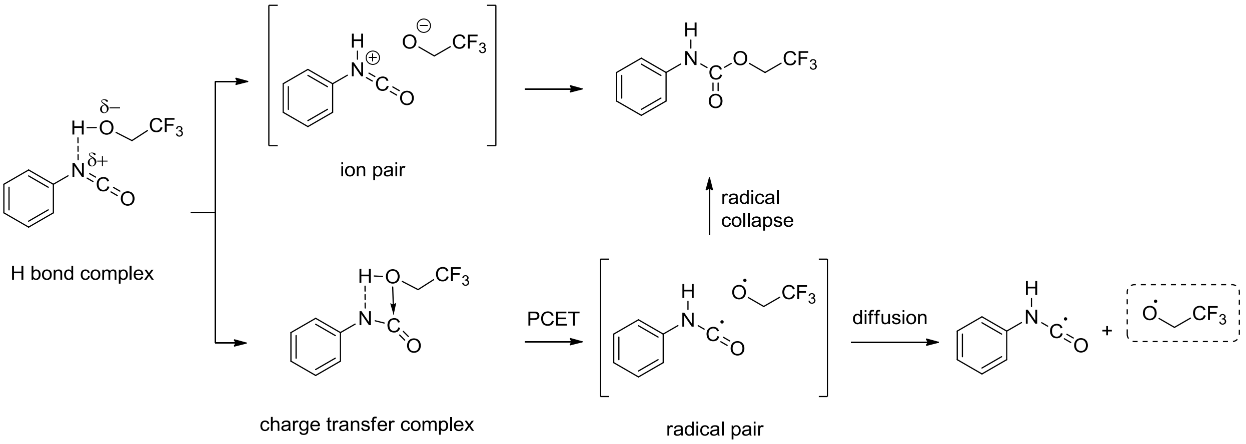
[77] Mulliken charges were calculated after AM1 energy minimization of structure using RHF/3-21G calculation of charges implemented in Chem3D Pro 12.0 in suit ChemBioOffice 2010.

[78] For an explanation on the subtle differences: Weinberg, D. R.; Gagliardi, C. J.; Hull, J. F. Murphy, C. F.: Kent, C. A.; Westlake, B. C.; Paul, A.; Ess, D. H.; McCafferty, D. G.; Meyer, T. J. *Chem. Rev.* **2012**, *112*, 4016-4093.



Scheme 31. Possible initiation and direct formation of product via ion pair and radical pair collapse.

However, several evidences claim against this interpretation. First, the strong effect of the solvent that makes the reaction only viable in strong electron pair donors and hydrogen bond acceptor solvents. In the reaction mixture, solvent are much more abundant and more Lewis basic than phenyl isocyanate, thus favoring an isocyanate/alcohol hydrogen bond complex (Solvent effect: Section 1.2.1.).

Second, the global kinetic order lower than one suggested a pseudofirst order initiation by interaction of one of the reagents with the solvent, rather than a bimolecular interaction between both reagents (Rate law: Section 1.2.4.)

Third, the fact that the reaction rate did not depend on the electronic effect of the substituent on phenyl isocyanate. Formation of an isocyanate/alcohol hydrogen bond adduct would be influenced by substituent on phenyl isocyanate. Instead, this result suggested the interaction of phenyl isocyanate with a neutral specie, probably a radical, not involved in the rate determining step (Effect of substituent: Section 1.3.5.).

INITIATION BY SOLVENT/ALCOHOL ADDUCT

An explanation for solvent effect and global order lower than one could lie in an alternative formation of free alkoxyl radical. Alcohol and solvent could form hydrogen bond complexes in what would be a pseudo-unimolecular process. The solvent/alcohol adduct could undergo the same process than isocyanate/alcohol to generate the reactive radical by a PCET (Scheme 32). In fact, there are several examples of DMF and DMSO generating radicals in simple conditions, with base or sonication.[79,80]

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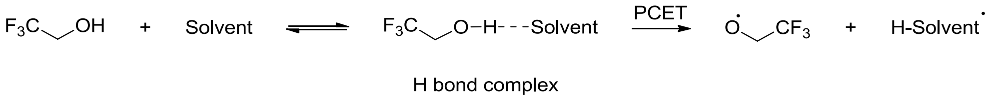
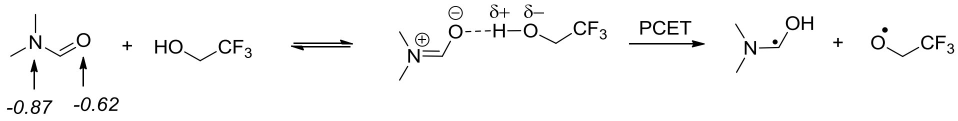
[79] Øpstad, C. L.; Melø, T.-B.; Sliwka H.R.; Partali, V. *Tetrahedron* **2009**, *65,* 7616–7619.

[80] Misik, V.; Kirschenbaum, L.J.; Riesz, P. *J. Phys. Chem.* **1995***, 99,* 5970-5976.



Scheme 32. Initiation by alcohol-solvent complex.

Using DMF as a solvent, this molecule was the most abundant compound in the reaction medium. Additionally, its amide group presents more negative charge than the isocyanate group. Thus, by both reasons, TFE would form a hydrogen bond complex with DMF rather than with PhNCO. This DMF/TFE hydrogen bond complex could undergo a PCET to form 2,2,2-trifluoroethoxyl radical (Scheme 33).



Scheme 33. Radical formation in DMF. Mulliken charges in italics.

The unproductive radical from DMF would rapidly be delocalized trough all the solvent and quickly collapse with other radical or abstract a hydrogen atom from another molecule.

The effect of concentration can be explained by the coexistence of these two competitive equilibriums. The bimolecular isocyanate/alcohol complex should be highly dependent on reactant concentration, favored in concentrated conditions. However, bimolecular solvent/alcohol complex formation could be considered a pseudo-unimolecular process, and thus, not so affected by concentration. These equilibriums also account for the effect of solvent, as highly donor solvents clearly would favor the active solvent/alcohol complex.

This initiation proposal would fulfill the requirements of the results obtained for solvent, concentration and null effect of substituent.

1.4.2. PROPOSED MECHANISM

In the propagation steps, the active intermediates are continuously regenerated while the products of the reactions are formed.

The chain reaction was suggested by the fact that this reaction was stopped by a sub-stoichiometric amount of radical scavenger. By EPR, a clear clue for the key radical intermediate was obtained. The oxygen-centered 2,2,2-trifluoroethoxy radical was the radical detected, probably because it was the resident radical specie before the rate determining step.

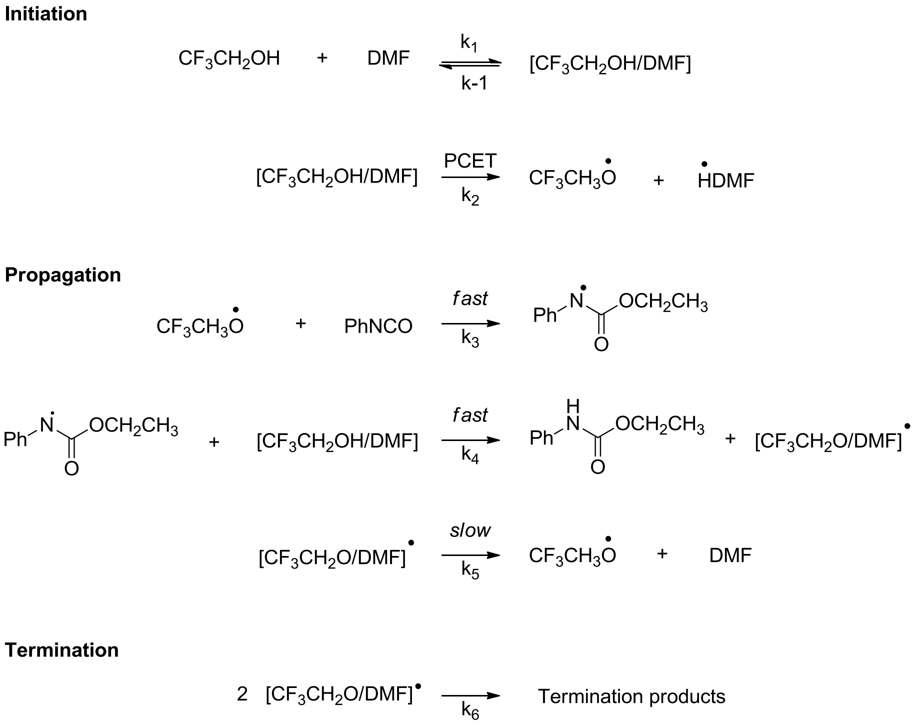
A mechanistic proposal that has into account all the experimental evidences is explained in the following pages.

In reaction conditions, TFE forms a complex with DMF (Scheme 34, k_1). This complex could undergo a PCET to form 2,2,2-trifluoroethoxyl radical (Scheme 34, k_2).

This 2,2,2-trifluoroethoxyl radical would add to phenyl isocyanate to form a carbamate radical (Scheme 34, k_3). Then, this carbamate radical could abstract a hydrogen atom (or one proton and one electron) from the DMF/TFE complex to form the product while generating the complex radical (Scheme 34, k_4).

Then, in order to close the cycle, the radical complex should fell apart to liberate the 2,2,2-trifluoroethoxyl free radical (Scheme 34, k_5).

The termination are the steps in which the reactive intermediates are destroyed or inactivated to carry on the chain propagation. In accordance with the mechanistically proposal for the propagation steps, termination processes will be mainly due to the evolution of the complex radical $[CF_3CH_2O/DMF)\cdot$, the intermediate before the slow step. In most cases, bimolecular reactions are probably involved as disproportion of two radicals, isomerizations or couplings. Thus, in this proposal a general bimolecular termination step was considered (Scheme 34, k_6).



Scheme 34. Proposed mechanism for the reaction of TFE with PhNCO in DMF.

This mechanistic proposal takes into account the strong solvent effect, the effect of radical scavengers, the no-effect of standard radical initiators, the spectroscopic studies and the no-dependence on electronic effects on substituted PhNCO. To check if this mechanism was also in agreement with a fractional order lower than one the kinetic equations were developed.

FRACTIONAL KINETIC ORDER LOWER THAN ONE

A fractional global order lower than one would fit with the proposed mechanism considering a pseudo-unimolecular process in the initiation, a pseudo-unimolecular process in the rate determining step of propagation cycle and a general bimolecular termination step.

In a chain reaction, the product is formed mainly in the propagation cycle. Thus, the rate of product formation can be considered the same as the rate of the determining step in the propagation (25) (Scheme 34, 5).

Considering the steady state approximation, rate of initiation is the same than rate of termination (26), (27). Isolating the concentration of the complex radical (28) and substituting in the rate law (25) resulted in a rate law in function of alcohol concentration (29).

$$\begin{gathered}\textit{Rate determining step}\\ v = k_5[(CF_3CH_2O/DMF)^{\cdot}]\end{gathered} \tag{25}$$

$$\begin{gathered}\textit{Steady state approximation}\\ v_I = v_T\end{gathered} \tag{26}$$

$$\frac{k_1}{k_{-1}} k_2[CF_3CH_2OH] = k_6[(CF_3CH_2O/DMF)^{\cdot}]^2 \tag{27}$$

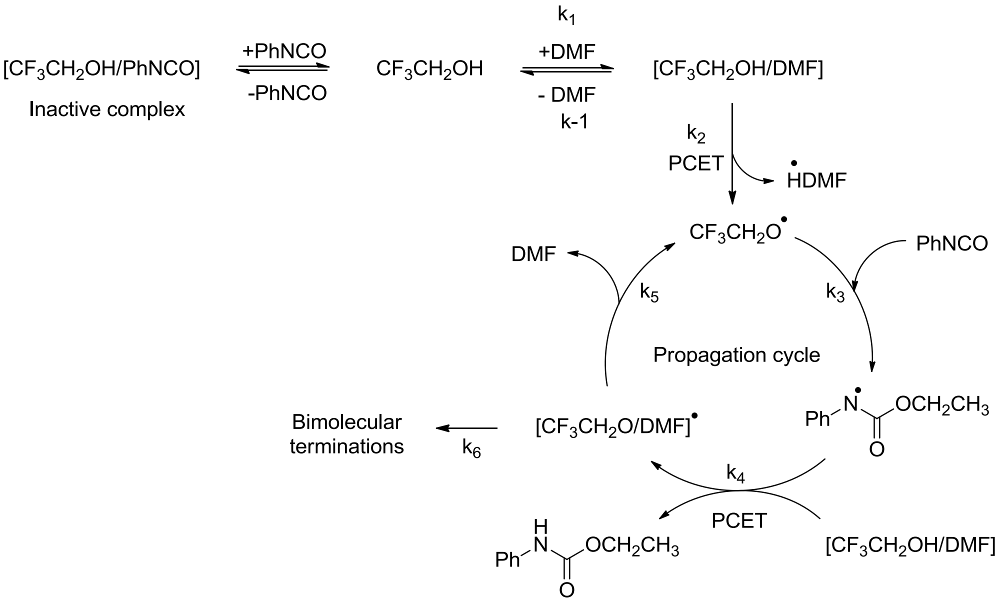
$$\left(\frac{k_1k_2}{k_{-1}k_6}\right)^{1/2} [CF_3CH_2OH]^{1/2} = [(CF_3CH_2O/DMF)^{\cdot}] \tag{28}$$

$$v = k_5\left(\frac{k_1k_2}{k_{-1}k_6}\right)^{1/2} [CF_3CH_2OH]^{1/2} \tag{29}$$

The resulting kinetic equation (29) had a fractional global order lower than one. Although this rate law had a global order of 1/2 and the experimentally found was 2/3, they were in agreement with the fact that both have fractional orders lower than one. The discrepancy might be explained by more complex termination processes than the generalization that has been conisdered.

1.4.3. OVERVIEW OF THE MECHANISM

To sum up all, this is the first mechanistic proposal for carbamate formation via radical intermediates. This mechanism can account for all the experimental observations (Scheme 35).



Scheme 35. Proposed radical chain mechanism for reaction of PhNCO with TFE.

A preliminary partial study of the reaction of polyfluorinated alcohols with phenyl isocyanate and this new radical mechanism proposal has been recently published as a short communication.[81]

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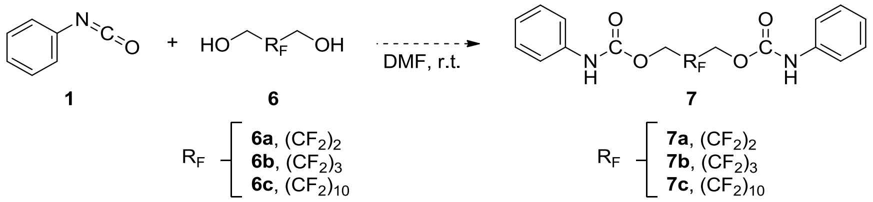
[81] Soto, M.; Comalrena, H.; Balduzzi, U.; Guirado, G.; Lloveras, V.; Vidal-Gancedo, J.; Sebastián, R. M.; Marquet, J. *Tetrahedron Lett.* **2013**, *54*, 6310-6313.

1.5. EXTENSION TO POLYFLUORINATED DIOLS: A SURPRISING RESULT

In previous sections, the reaction of simple polyfluorinated alcohols with aromatic isocyanates was studied and a mechanistic proposal was advanced. Towards our goal to obtain polyfluorinated polyurethanes from reaction of aromatic diisocyanates with polyfluorinated diols, the next step was to study the reaction of polyfluorinated diols with aromatic isocyanates.

1.5.1. REACTION OF POLYFLUORINATED DIOLS WITH PHNCO

The objective was to find conditions in which the reactions of a polyfluorinated diol with phenyl isocyanate produced polyfluorinated bis(phenylcarbamate). Suitable conditions for the reaction of alcohols with aromatic isocyanates had been found and a mechanism had been proposed. In principle; it was thought that by using similar conditions as the reaction of monoalcohols with PhNCO the biscarbamate compounds would be obtained without any further issue (Scheme 36).



Scheme 36. Expected reaction of polyfluorinated diols with PhNCO.

The reaction of fluorinated diols **6** with PhNCO was tested. In a first attempt, diol **6b** was reacted with PhNCO in DMF at stoichiometric ratio ($[PhNCO]_0$ = 20 mM; $[\mathbf{6b}]_0$ = 10 mM). In this reaction, diol just reacted by one end, forming hydroxyalkyl phenylcarbamate **8b** (Table 8, entry 3). Contrary to expectations, even no traces of the biscarbamate **7b** were observed.

The amount of PhNCO was monitored by GC and the final distribution of the fluorine segments was determined by integration of ^{19}F NMR. In acetone-d_6, **6b** presented one signal for the central CF_2 (δ -127.0; 2F) and one for the other two CF_2 (δ -122.9; 4F). The completely reacted biscarbamate **7b** have two different fluorine signals (δ -127.3, central CF_2; -121.1, 2 external CF_2). When it has reacted by one hydroxyl group, thus forming 2,2,3,3,4,4-Hexafluoro-5-hydroxypentyl phenylcarbamate **8b**, has three different signals. (δ -127.3, CF_2 position 3; -123,14, CF_2 position 4; -121.3 position 2 CF_2).

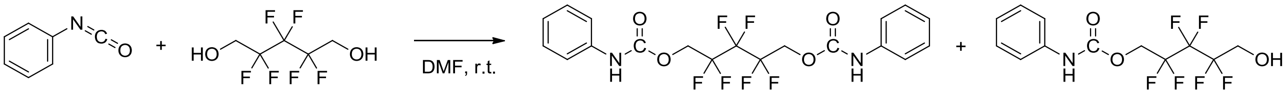
Controls by GC after 60 minutes showed that there was still unreacted PhNCO and **8b**. Interestingly, those concentrations did not change in posterior GC controls; the reaction was stopped.

The first thought was that there might be a problem with proportion PhNCO:diol. In reaction of single alcohols with PhNCO, an excess of alcohol had been found to be optimum (PhNCO:TFE 1:2). However, in the reaction of PhNCO with diols, an excess of alcohol would be against stoichiometry to form biscarbamate.

A brief screening of the proportions PhNCO:diol was performed maintaining constant the concentration of diol ([**6b**]$_0$ = 0.01 M). In all cases, GC showed that there was not more evolution of the reaction after 120 minutes, even though there were unreacted PhNCO.

Using a molar ratio PhNCO:diol 1:2, the reaction barely proceeded (Table 8, entry 1). In case of using a 1:1 molar ratio (Table 8, entry 2) and in stoichiometric conditions, molar ratio 2:1 (Table 8, entry 3), similar proportions of **8b** was formed: around 60 % and no biscarbamate observed. A large excess of PhNCO, molar ratio 5:1, was required to consume diol **6b**. With this excess some **7b** was formed, but in very low proportions (**7b**:**8b** 1:19) (Table 8, entry 4).

Table 8. Reaction of diol **6b** with PhNCO to form **8b**.[a]



1 **6b** **7b** **8b**

none or minor product

Major product

Entry	[**1**]$_0$ (M)	[**6b**]$_0$ (M)	Molar ratio **1**:**6b**	Fluorine distribution (%)[b] **6b**	**7b**	**8b**
1	0.005	0.01	1:2	95	0	5
2	0.01	0.01	1:1	31	0	59
3	0.02	0.01	2:1	35	0	65
4	0.05	0.01	5:1	0	5	95

[a] Reaction performed in DMF. [b] Percentages determined by ^{19}F NMR.

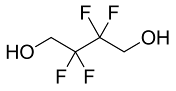
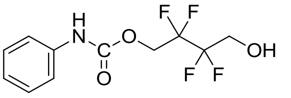
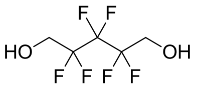
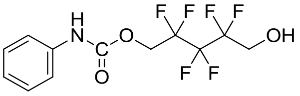
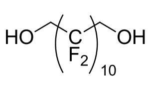
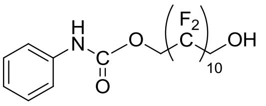
The reaction of PhNCO with other polyfluorinated diols (**6a**, **6c**) also behaved in the same way, eliminating the possibility of this being a special case just for diol **6b**. Although this was not the expected outcome, it turned out to be a valid methodology to obtain new polyfluorinated hydroxyalkyl phenylcarbamates from polyfluorinated diols with moderate yields (Table 9).

Table 9. Preparation of hydroxyalkyl phenylcarbamates from polyfluorinated diols.[a]

1 **6** **8**

R_F – **6a**, $(CF_2)_2$; **6b**, $(CF_2)_3$; **6c**, $(CF_2)_{10}$

R_F – **8a**, $(CF_2)_2$; **8b**, $(CF_2)_3$; **8c**, $(CF_2)_{10}$

Entry	Diol	Product	Isolated yield (%)
1	 **6a**	 **8a**	74
2	 **6b**	 **8b**	57
3	 **6c**	 **8c**	61

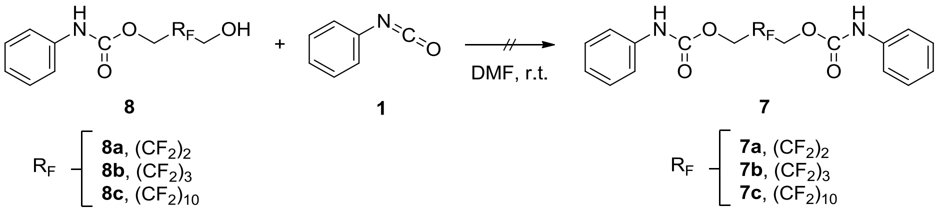
[a] Conditions: $[PhNCO]_0$ = 0.02 M; $[diol]_0$ = 0.01 M; dry DMF, 60 min.

1.5.2. ATTEMPTS TO OBTAIN BISCARBAMATES

In spite of having an interesting methodology for the preparation of new polyfluorinated hydroxyalkyl phenylcarbamates, the desired outcome was a complete reaction of polyfluorinated diols with phenyl isocyanate to obtain biscarbamates.

REACTION OF HYDROXYALKYL PHENYLCARBAMATES COMPOUNDS WITH PHNCO

The reaction of isolated hydroxyalkyl phenylcarbamates with PhNCO using a molar ratio PhNCO:**8b** 1:1 was attempted. However, the starting materials were recovered unaltered. The optimal conditions for the reactions PhNCO:TFE were with an excess of alcohol 1:2. When using an excess of **8b** 1:2 no reaction was observed either. The same behavior was observed with hydroxyalkyl carbamates **8a** and **8c** (Scheme 37).



Scheme 37. Polyfluorinated hydroxyalkyl phenylcarbamates **8** do not react with PhNCO in DMF, r.t.

USE OF CATALYSTS

After the precedent failures, it was decided to test some sort of activation. The use of one of the catalysts described for the reaction of isocyanate with alcohols to form urethanes and polyurethanes could be a solution. The most used catalysts are tertiary amines, like DABCO or DBU and organotin compounds, as dibutyltin dilaurate DBTDL $Bu_2Sn(n\text{-}C_{11}H_{23}COO)$ (Figure 38).[6,3]

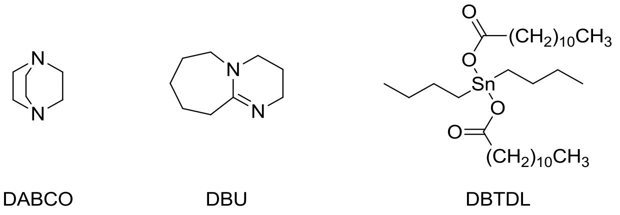
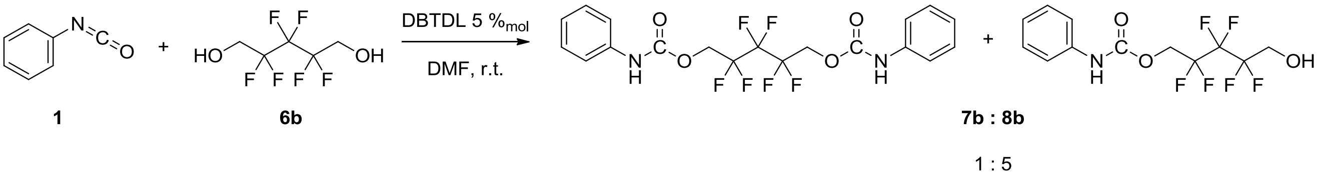


Figure 38. Catalyst typically used in the polymerization of diisocyanates with diols.

In addition, another interesting catalysts used for the formation of carbamates are copper (I) salts. This caught our attention because copper(I) catalytic cycles involve the redox pair Cu(I)/Cu(II), that required the transfer of one electron, not the typical two electron cycles.[82] This could, in principle, help the PCET process proposed in the mechanism.

The model reaction of PhNCO with diol **6b** was performed in a molar ratio 2:1 in the presence of catalyst. DABCO (10 $\%_{mol}$) and DBU (10 $\%_{mol}$) did not improve the reaction and no product biscarbamate **7b** was formed. The use of copper(I) iodide as intended catalyst for this reaction led to the same bad result.

Finally, the reaction was performed using DBTDL (5 $\%_{mol}$) as catalyst. Although the major product formed was **8b**, in this case, **7b** was also obtained in a proportion **7b**:**8b** 1:5.(Scheme 38).



Scheme 38. Reaction of PhNCO with **6b** catalyzed by DBTDL.
$[PhNCO]_0 = 0.02$ M; $[\mathbf{6b}]_0 = 0.01$ M; $[DBTDL]_0 = 0.5$ mM.

So, in conclusion, from the catalyst tested, DABCO, DBU and CuI did not yield **7b**. DBTDL was the only catalyst that was successful in forming **7b**, even though it was obtained in smaller

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[82] For example Cu(I) catalyzed Ullman-type reactions: Jones, G. O.; Liu, P.; Houk, K. N.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 6205-6213.

proportions than **8b**. In spite of being a relative success, it was clear that this reaction was far away from the efficiency of PhNCO/TFE reaction. Additionally, the low extent of the reaction was a major drawback in its used on polymer preparation, were high degrees of conversion would be required.

At this point, the question was why this process only produced reaction in just one hydroxyl group and, more importantly, what could be done to activate the second hydroxyl group reaction.

INTERPRETATION ACCORDING THE PROPOSED MECHANISM

A crucial event in the proposed mechanism seemed to be the PCET process in the DMF/TFE hydrogen bonded adduct between the acidic alcohol and the donor solvent that could generate the free radicals that initiate the propagation cycle. An increase in reactants concentration leads to the quenching of the reaction, probably due to the competitive formation of an inactive complex PhNCO/TFE.

Simple theoretical calculations indicate that the electronic density in the amide group of DMF is higher than in the isocyanate group (Figure 39). This together with the fact that DMF is present in excess as a solvent makes DMF/TFE complex preferred, especially at low concentrations.

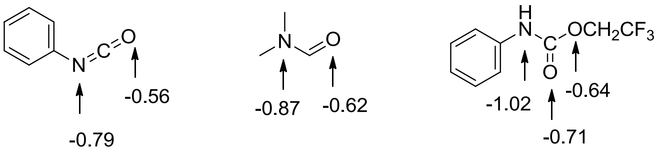

Figure 39. Mulliken charges and preferred protonation position in carbamate, isocyanate and DMF.[83]

However, once enough carbamate was present in the solution, it will compete with DMF and the isocyanate for complexation with the polyfluoroalcohol. The presence of carbamates in the solution would produce carbamate/alcohol complexes that would displace the solvent/alcohol complex, and hence quenching of the reaction at some point in its advance. However, in reaction at low concentrations, the effect of carbamate is partially hidden. The mechanism probably had short chains and, therefore, needs multiple initiations.

This phenomenon probably can also explain the unreactivity of the second hydroxyl group in diols. Indeed, in this case the carbamate group and the hydroxyl are in the same molecule and can easily form intramolecular hydrogen bond complexes that would completely quench the

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[83] AM1 energy minimization of structure and RHF/3-21G calculation of charges. Chem3D, ChemBio Office, 2010.

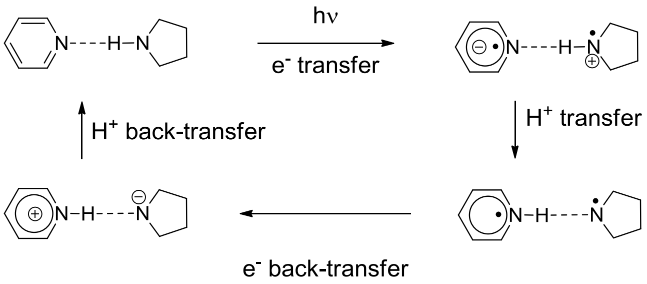
reaction of the second hydroxyl group. Simple semiempirical calculations carried out for **8b** as a model indicate that the intramolecular complex is the deepest minimum in the potential surface.

ACTIVATION OF CHARGE TRANSFER COMPLEXES

Taking into account what have been described up to here, it seems clear that the reaction mixture included different hydrogen bond and charge transfer complexes. From these different complexes, only the one formed between the polyfluorinated alcohol and DMF was able to initiate the reaction. Even more, the own final carbamate product quenched the reaction.

In principle, the inactive complexes, especially the isocyanate/alcohol complex could undergo a PCET if properly activated by the use of light.

There is an extensive literature on PCET and exited-states hydrogen-bond dynamics in organic molecules.[78] An example of the photochemistry of hydrogen bonds is pyridine-pyrrole hydrogen-bonded adduct, a system studied for its biological implications. Upon irradiation an electron-transfer process from pyrrole to pyridine takes place, followed by proton transfer in the exited state. Then, it decays to ground state by backward electron transfer and adiabatic proton back-transfer, restoring the system in its initial structure (Scheme 39). [84]



Scheme 39. Pyridine-pyrrole hydrogen-bonded adduct photoinduced PCET.

This is an example how upon irradiation a hydrogen bonded system can undergo a PCET, generating a radical pair.

Could light promote PCET activating inactive complexes? Could light be used to achieve the reaction of both alcohol groups? The answers to these questions are detailed in the next chapter. .

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[84] Frutos, L. M.; Markmann, A.; Sobolewski, A. L.; Domcke, W. *J. Phys. Chem. B* **2007**, *111*, 6110-6112.

Chapter 2

Photochemical reaction of aromatic isocyanates with polyfluorinated alcohols

2.1. INTRODUCTION TO PHOTOCHEMISTRY

As the name suggest, photochemistry is the branch of chemistry concern with chemical effects caused by light absorption. In this context, light is considered to be ultraviolet, UV, (wavelength λ from 100 to 400 nm), visible (λ from 400 to 700 nm) and infrared, IR, (λ from 700 nm to 1 mm) electromagnetic irradiation. When light is absorbed by a molecule, it produces physical changes in it that can lead to chemical change.

Many ground-state reactions have their photochemical counterpart. Photochemical paths offer the advantage over thermal methods of forming thermodynamically disfavored products, overcome large activation barriers in a short period of time, and allow reactivity otherwise inaccessible by thermal processes.

2.1.1. BASICS OF PHOTOCHEMISTRY

Most organic molecules have, in their ground state, all the electrons occupying orbitals by pairs with opposite spin, as required by *Pauling Exclusion Principle*. In this situation, the spin multiplicity (2S + 1) is one, singlet state, and is noted S_0 for the ground state singlet.

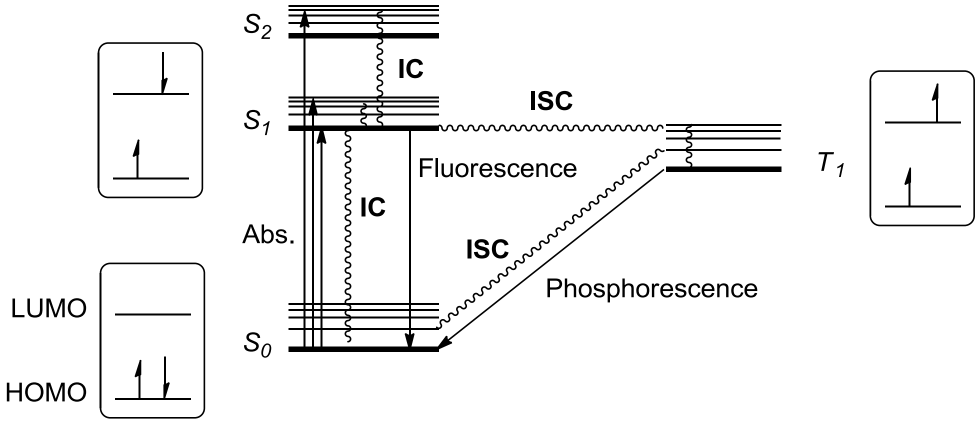
When a molecule absorbs light, one electron is excited to a higher orbital level. This electron maintains its spin according to *spin selection rule; o*nly $\Delta S = 0$ transitions are allowed, as other transitions violate the law of conservation of angular momentum. This excitation to a higher singlet state can be from HOMO to LUMO or to a higher orbital, thus being possible different singlet excitation states S_1, S_2, S_3… depending on its energy.

Kasha's rule stipulates that higher singlet states would quickly relax by radiationless decay or *internal conversion,* IC, to S_1. Thus, S_1 is usually, but not always, the only relevant singlet exited state. This excited state S_1 can further relax to S_0 by IC, but also by an allowed radiative transition from S_1 to S_0 that emits a photon, called *fluorescence*.

Alternatively, it is possible for the excited state S_1 to undergo spin inversion and to generate a different excited state with the two unpaired electrons with the same spin, thus having a triplet multiplicity, T_1. This violation of the spin selection rule is possible by *intersystem crossing,* ISC, of vibration and electronic levels of S_1 and T_1. According to *Hund's rule* of maximum multiplicity, this T_1 state would be somewhat more stable than S_1.

This triplet state can relax to ground state S_0 by radiationless IC or by a radiation pathway that is called *phosphorescence*. This process implies a change on electronic spin, it is forbidden by spin selection rule, being phosphorescence ($T_1 \rightarrow S_0$) much slower than fluorescence ($S_1 \rightarrow S_0$). Thus, triplet states generally have longer lifetimes than singlet states.

These transitions are usually summarized in a state energy diagram or *Jablonsky diagram*, which can be considered the paradigm of molecular photochemistry (Scheme 40).



Scheme 40. Simple Jablonski diagram and molecular orbitals.
Straight lines: photon emission or absorption. Wavy lines: non-radiative pathsways.

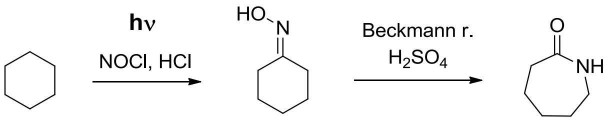
These exited species, either in S_1 or T_1, have a hole in a low energy orbital, consequently are more oxidizing. But at the same time, they have an electron in a high energy orbital, thus they are more reducing. In general, exited species are prone to participate in electron transfer processes.

2.1.2. INDUSTRIAL PHOTOCHEMICAL EXAMPLES

Photochemistry is not just a lab curiosity. Nowadays, it is used, for example, in the production of ε-caprolactame (monomer for the preparation of nylon-6) and it plays a key role in the industrial production of artemisinin, the most used treatment for malaria.

TORAY PHOTOCHEMICAL PRODUCTION OF ε-CAPROLACTAME

One relevant example of photochemical industrial process is the synthesis of cyclohexanone oxime, precursor of ε-caprolactame. This process consists on the photonitrosation of cyclohexane. Nowadays, it is carried out at large scale by Toray in Japan using mercury UV-lamps (Scheme 41).[85]



Scheme 41. Toray process: photonitrosation of cyclohexane to form cyclohexanone oxime hydrochloride, precursor of ε-caprolactame.

The reaction is carried out by bubbling NOCl into cyclohexane under UV irradiation. The photocleavage of a molecule of NOCl produce a reactive chlorine atom radical and a persistent

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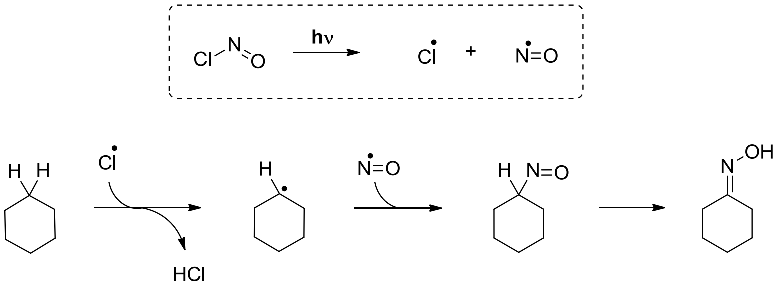
[85] Protti, S.; Fagnoni, M. *Photochem. Photobiol. Sci.* **2009**, *8*, 1499-1516.

radical NO that acts as radical trap. The chlorine atom abstracts a hydrogen atom from cyclohexane. Combination between the cyclohexyl and NO radical produces nitrosocyclohexane, than evolves to cyclohexanone oxime (Scheme 42).



Scheme 42. Mechanism of photonitrosation of cyclohexane.

PHOTOCHEMICAL PRODUCTION OF ARTEMISININ

Every year there are more than 200 million cases of malaria, a disease that annually kills more than 655 000 people. Until now, the only source of *artemisinin*, the most effective treatment, was the sweet wormwood plant, with variable harvest and production cycles of minimum 14 months.

Recently, in April of 2013 Sanofi launched a new photochemical production facility in Garessio, Itally, to produce up to 60 tonnes per year of artemisinin, equivalent to one-third of global need (Figure 40). The semi-synthetic approach combines genetically engineered yeast to produce artemisinic acid with late-stage photochemical modifications.[86]

Figure 40. Sanofi photochemical facilities with three photochemical reactors.

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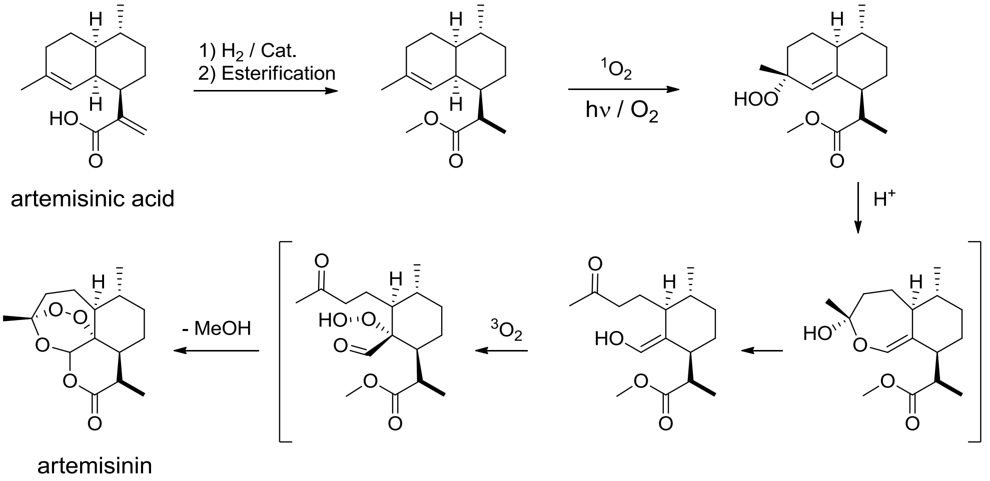
[86] Lemonde-San F.; Pantjushenko, E. *Sanofi oficial press release* (Updated: 11th Apr 2013): <http://en.sanofi.com/Images/32474_20130411_ARTEMISININE_en.pdf>

Artemisinic acid *exo* double bond is reduced and acid is protected as methyl ester, to avoid undesired by-reactions. Then, key step is the photochemical generation of highly reactive singlet oxygen that forms peroxide to produce an atom oxygen insertion that generates a hemiacetal. Once it is open, it is oxidized by *normal* triplet oxygen to generate peroxide, which triggers a cascade of reactions that finally generates artemisinin (Scheme 43).[87]



Scheme 43. Synthesis route from artemisinic acid to artemisinin.

2.1.3. EXPERIMENTAL CONSIDERATIONS

As it seen in the synthesis of artemisinin, oxygen in ground state $^3O_2$, which is a relatively reactive triplet, becomes singlet oxygen $^1O_2$ under irradiation, which is highly reactive. In photochemical reactions, unless a specific reaction with oxygen is desired, it is important to remove all oxygen present.

There are three common ways to remove oxygen at lab-scale without adding chemicals: displacement of solved oxygen by bubbling an inert gas as nitrogen or argon; sonication under reduced pressure and the method called *freeze-pump-thaw*, the more effective. This method consists on, first freezing the solvent with liquid nitrogen, then applying vacuum and finally, without refilling with inert gas, solvent is allowed to melt. By repeating this process three times, the majority of gasses in solution, including oxygen, are removed from the solution.

Another important aspect to keep in mind is the effect of UV light in living cells. This type of irradiation can provoke the cycloaddition between two adjacent thymines in DNA, leading to

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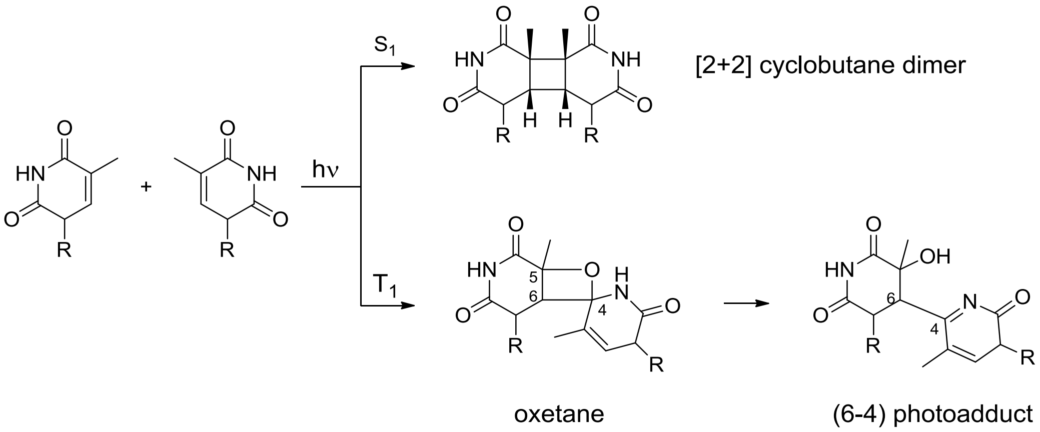
[87] (a) Peplow, M. *Chemistry World* (17th Apr 2013) < http://www.rsc.org/chemistryworld/2013/04/sanofi-launches-malaria-drug-production>
(b) Paddon, C. J.; Westfall, P. J.; Pitera, D. J.; Benjamin, K.; Fisher, K.; McPhee, D.; Leavell, M. D.; Tai, A.; Main, A.; Eng, D.; Polichuk, D. R.; Teoh, K. H.; Reed, D. W.; Treynor, T.; Lenihan, J.; Jiang, H.; Fleck, M.; Bajad, S.; Dang, G.; Dengrove, D.; Diola, D.; Dorin, G.; Ellens, K. W.; Fickes, S.; Galazzo, J. *Nature,* **2013**, *496*, 528-532.

cyclobutane dimers by a [2+2] cycloaddition or to (6-4) adducts via an oxetane intermediate (Scheme 44).[88] The repair of this DNA damage by nucleotide excision (removing the affected bases and filling the gaps with new nucleotides) is very efficient. Even so, it breaks down when the damage is extensive. If so, it could leads to mutations and precancerous cells or cellular death if the damage is massive.[89]

This principle is use in short-wavelength UV germicidal lamps that are used for disinfection of laboratory surfaces, food industry and water treatment. However, it also means that the appropriate cautions should be taken when working with UV light.



Scheme 44. Thymine dimer formation under UV light.

2.1.4. IMMERSION WELL PHOTOCHEMICAL REACTORS

Photochemical reactions are usually performed using immersion well reactors (Figure 41). In this kind of reactors a lamp irradiate the reaction from the center, and thus, most of irradiation reach the solution. These reactors consist in two part glassware: the reaction vessel and the cooling jacket were the lamp is placed. The cooling jacket has a double wall where there is a cooling flow between lamp and reaction to avoid heating the solution. As this cooling jacket is in the way of the photons, the material it is made has a determining importance. While Pyrex filters out wavelengths shorter than 275 nm, quartz transmits all the wavelengths longer than 200 nm.

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[88] Banyasz, A.; Douki, T.; Improta, R.; Gustavsson, T.; Onidas, D.; Vayá, I.; Perron, M.; Markovitsi, D. *J. Am. Chem. Soc.* **2012**, *134*, 14834−14845.

[89] Nakajima, S.; Lan, L.; Kanno, S.; Takao, M.; Yamamoto, K.; Eker, A. P.; Yasui, A. *J. Bio. Chem.* **2004**, *279*, 46674-46677.

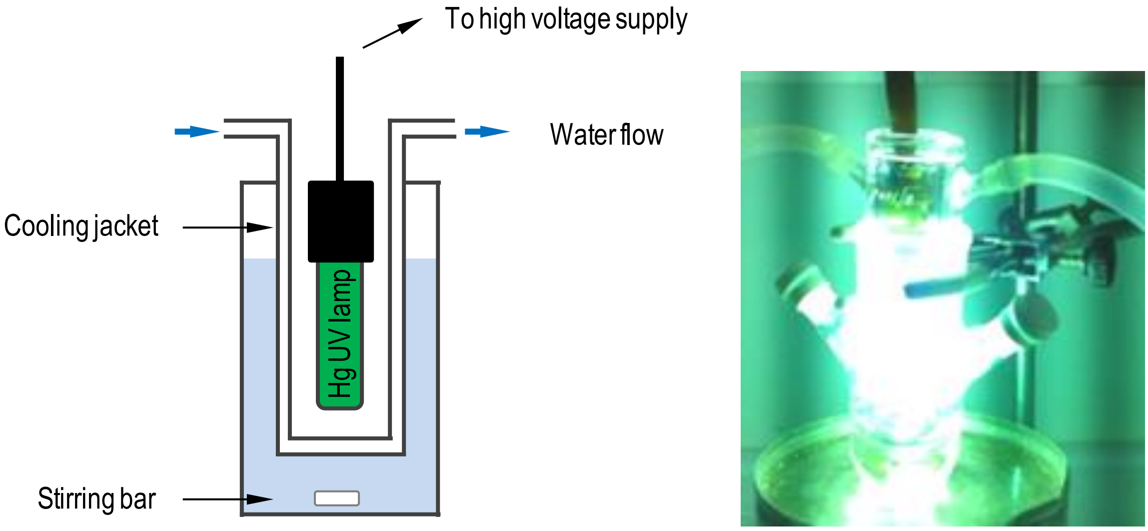

Figure 41. Photochemical reactor scheme and picture.

2.2. PHOTOCHEMICAL REACTION OF POLYFLUORINATED ALCOHOLS AND PhNCO

2.2.1. FIRST LAW OF PHOTOCHEMISTRY

The first law of photochemistry, formulated in the works of Grotthus (1817) and Draper (1843) near two centuries ago, states that:

> *"Only the light which is absorbed by a molecule can be effective*
> *in producing photochemical change in the molecule"* [90] [91]

This law implies that for a photochemical reaction to occur the appropriate light should be absorbed by the system. Thus, some overlap between the absorption spectrum of the compound (or sensitizer) and the emission spectrum of the lamp source must exist. However, photons generated in the lamp have to pass through the immersion well, the cooling liquid and solvent before reaching the molecule. The effects of these determining factors for a photochemical reaction are commented below.

LAMP EMISION SPECTRUM AND ABSORPTION SPECTRUM OF PHNCO

The UV-Vis spectrum of TFE did not have any absorption band, even at high concentrations or pure TFE. On the other hand, PhNCO spectrum shows an absorption band at 226 nm corresponding to the allowed π→π* transition of the substituted benzene ring (ε = 8 900 cm^{-1} L mol^{-1}). At longer wavelengths, it has three absorption bands of lower intensity that are better observed at higher concentration (ε_{261} = 407 cm^{-1} L mol^{-1}; ε_{269} = 398 cm^{-1} L mol^{-1}; ε_{276} = 285 cm^{-1} L mol^{-1}). One of those peaks correspond to the forbidden π→π* aromatic transition and the others to transitions corresponding to the isocyanate group (Figure 42).[92] Additionally, the UV absorption spectrum of the mixture PhNCO/TFE in MeCN was recorded, but it was virtually identical to the spectrum of PhNCO alone.

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[90] Calvert, J. G.; Pitts, J. N. *Photochemistry*. Wiley & Sons: New York, US, 1966. Congress Catalog number: 65-24288.

[91] Wayne, C. E.; Wayne, R. P. *Photochemistry*, 1st ed.; Oxford University Press: Oxford, United Kingdom, reprinted 2005. ISBN: 0-19-855886-4.

[92] Pretsch, E.; Bühlmann, P.; Affolter, C.; Herrera, A.; Martínez, R. *Structure Determination of Organic Compounds.* Ed. Masson: Barcelona, 2005. ISBN: 84-458-1215-7.

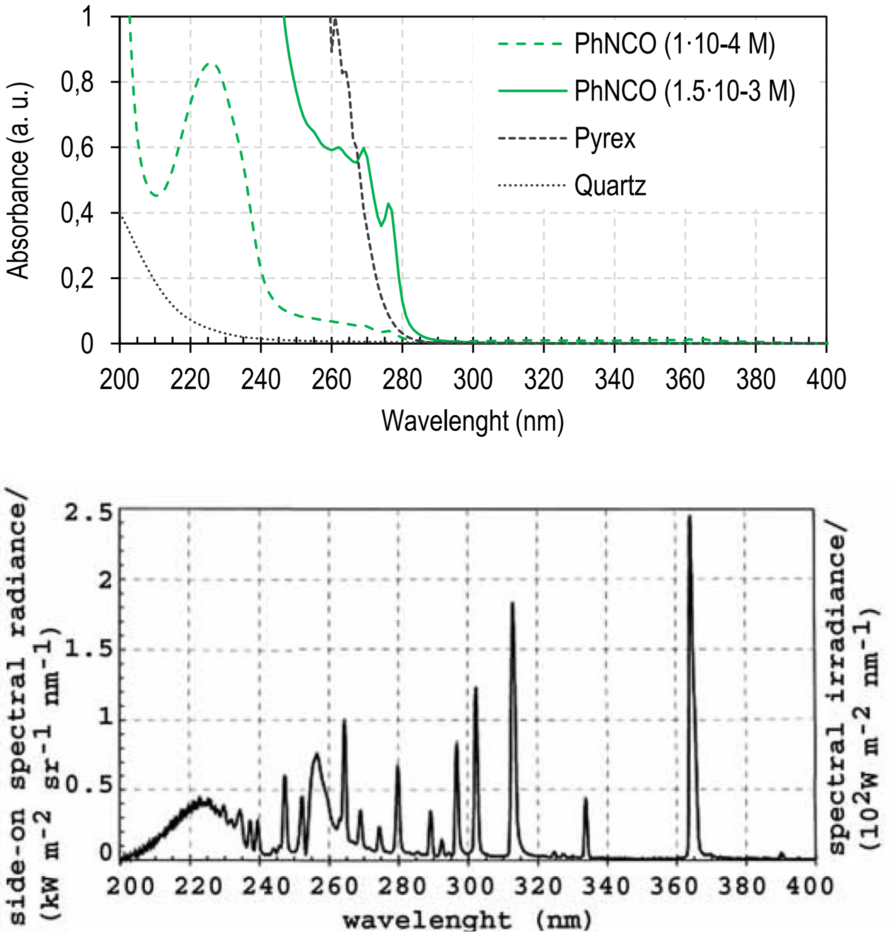


Figure 42. Top: Absorption spectra of PhNCO in MeCN, Pyrex and quartz. Bottom: Emission spectra of a high pressure Hg lamp.

A Philips HPK 125 W lamp has two emission bands at 275 and 280 nm that approximately match the absorption bands of isocyanate group. These emission/absorption peaks are the near cut-off wavelength of Pyrex glass.

SOLVENT CUT-OFF

One important element in photochemical reactions is the solvent cut-off point (Figure 43). It is the wavelength limit in which it ceases to be transparent. Formally, it is defined as the wavelength at which the absorbance approaches one unit using a 1 cm cell.

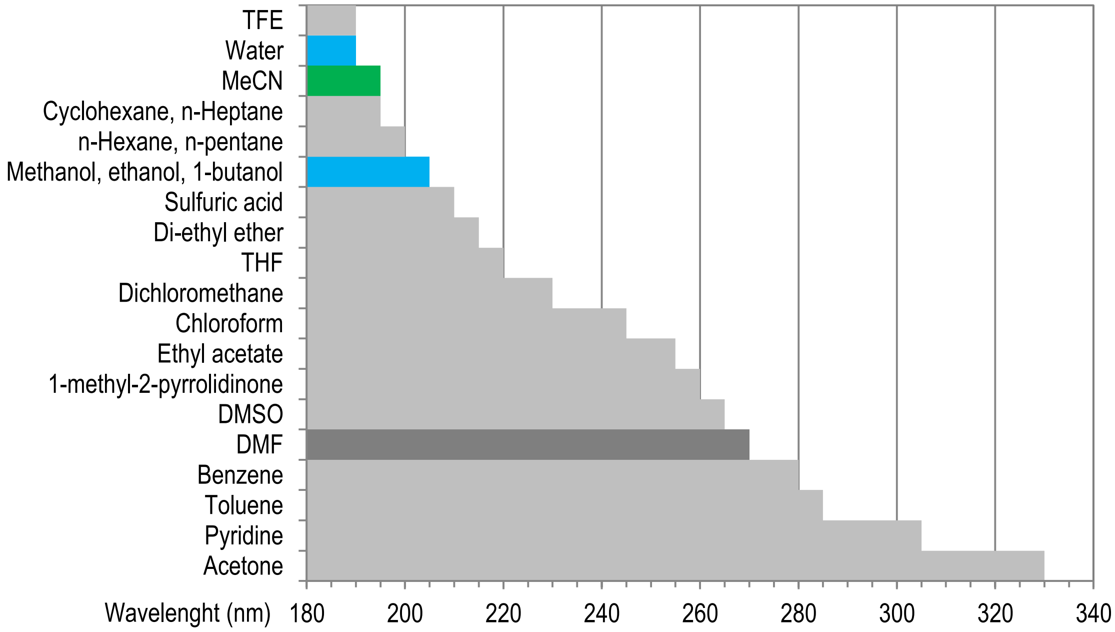


Figure 43. Solvents wavelength cut-off.[57]

The cooling flows used in the immersion well reactors are usually of water or methanol because these solvents have a low cut-off pint (190 and 205 nm, respectively). Thus, in principle they are not supposed to interfere in the photoreaction.

For our ground state reaction, donor solvents were required, being one of the best DMF. Its cut-off point is 270 nm and while Pyrex cut-off point is 275 nm. Thus, it was thought that Pyrex would filter out irradiation that could cleavage DMF.

Ground state reactions of polyfluorinated diols **6** with PhNCO yielded only hydroxyalkyl phenylcarbamates **8** (Section 1.5.). It was thought that the complete reaction of diols could perhaps be achieved in photochemical conditions. The reaction of diol **6b** with PhNCO was performed in the same concentration conditions but under irradiation with UV light (DMF; Philips HPK 125 W; Pyrex filter). After 60 minutes of irradiation, all PhNCO was completely consumed and almost just a single compound was formed. Although it seemed a promising result, GCMS analysis revealed that the entire product formed was *N,N*-dimethyl-*N'*-phenyl urea (Figure 44).

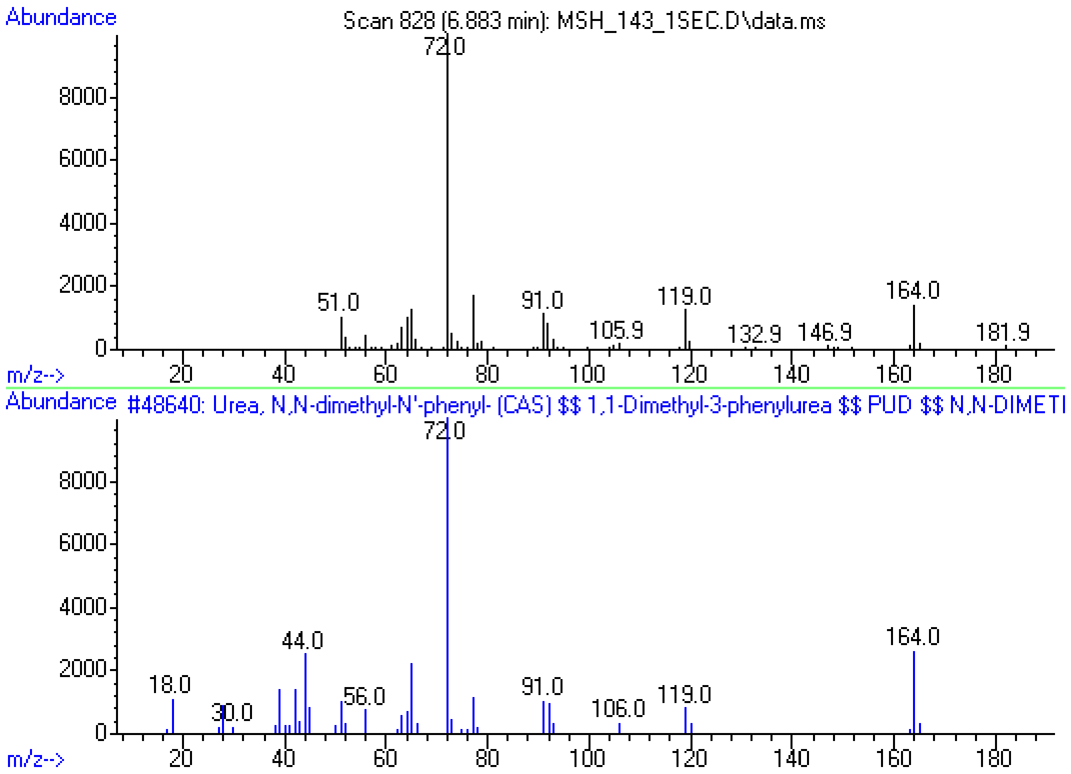
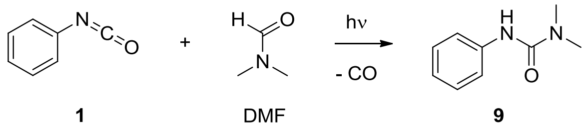


Figure 44. Obtained and database Wiley 275 m/z spectra from GC-MS of *N,N*-dimethyl-*N'*-phenyl urea.

This result proved that DMF was not a suitable solvent for photochemical reactions. Upon light absorption DMF can broke to produce dimethylamine, which would react with PhNCO to form *N,N*-dimethyl-*N'*-phenyl urea (Scheme 45).



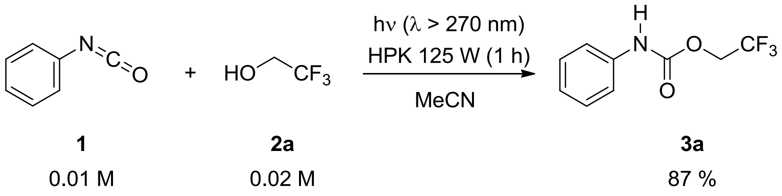
Scheme 45. Formation of N,N-dimethyl-N'-phenylurea **9** by irradiation of PhNCO in DMF.

Thus, after this failure and before trying more long shots for the complete reaction of polyfluorinated diols with PhNCO, a previous study using a simpler model photoreaction was carried out. Thereby, reaction of PhNCO with 2,2,2-trifluoroethanol **2a** was studied to check if photoactivation was possible and to find suitable conditions.

As acetonitrile is a transparent solvent it would not interfere or produce undesired reactions. However, it is worth to remember that ground state reactions of polyfluorinated alcohols with PhNCO failed in acetonitrile. If they resulted activated by UV light in this solvent, this would be a support for a PCET mechanism.

2.2.2. PHOTOCHEMICAL PREPARATION OF FLUORINATED CARBAMATES

The photochemical reaction of PhNCO with TFE was tested in acetonitrile MeCN using a 125 W mercury lamp with Pyrex filter (Scheme 46).



Scheme 46. Photochemical reaction of PhNCO with TFE in MeCN.
([**1**]$_0$ = 10 mM; [**2a**]$_0$ = 20 mM; dry and degassed MeCN; Philips HPK 125 W; Pyrex filter).

In MeCN, the ground state version of this reaction barely took place; after 60 min this slow reaction had a conversion of just a 6 %. However, in the same conditions under irradiation with UV light the conversion was higher than 90 % (Isolated yield 87 %) (Figure 45).

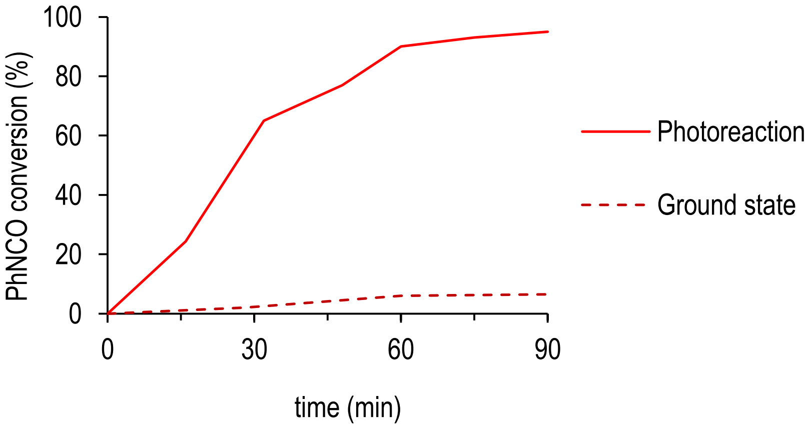
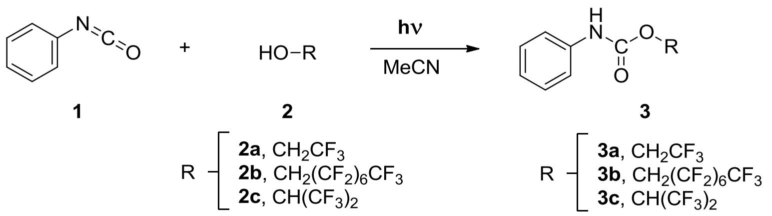


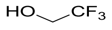
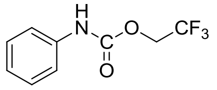
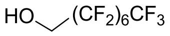
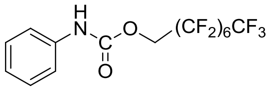
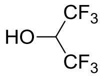
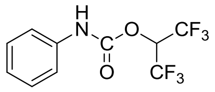
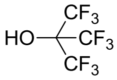
Figure 45. Evolution of TFE/PhNCO reaction in MeCN.
Ground state (dashed line) or under irradiation (Philips HPK 125 W; Pyrex filter) (Solid line).

To check the applicability of this methodology, these conditions were used with other polyfluorinated alcohols and the corresponding carbamates were obtained in fair to good yields. When using 1*H*,1*H*-perfluorooctanol **2b** instead of TFE, the yields obtained were lower. In the same way, reaction of 1,1,1,3,3,3-hexafluoro-2-propanol **2c** with PhCNO yielded carbamate **3c** in a moderate 66 % yield (Table 10).

It was not possible to achieve the reaction of perfluorinated *tert*-butanol, a reaction that also did not take place in ground state with DMF and a carbamate that has not been described in the literature.

Table 10. Photochemical reactions of phenyl isocyanate with polyfluorinated alcohols.[a]



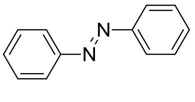
entry	alcohol	product	Yield (%)
1	 **2a**	 **3a**	87
2	 **2b**	 **3b**	36
3	 **2c**	 **3c**	66
4	 **2d**	--	n. d.

[a] Reaction conditions: 0.5 mmol of PhNCO, 1.0 mmol of polyfluorinated alcohol, 50 mL dry degassed CH_3CN, under nitrogen, 60 min irradiation with mercury high pressure lamp Philips HPK 125W

QUARTZ FILTER

The UV light able to promote the reaction had a wavelengths around 270-280 nm, close to the cut-off point of Pyrex. That means that part of this light was absorbed by Pyrex and not arriving to the reaction. If the filter was substituted for one made of a more transparent material, a higher percentage of this productive light would pass through, which would accelerate the reaction.

Thus, the reaction was performed in the same conditions but using a quartz filter. In these conditions, the reaction turned strong yellow color and instead of obtaining the carbamate as a single product, a complex mixture was obtained. The only product that could be identified by GCMS was azobenzene, responsible, at least partially, of the yellow coloration (Figure 46). This result indicated that the light of short wavelengths was too energetic for our purposes, giving place to several by-reactions.



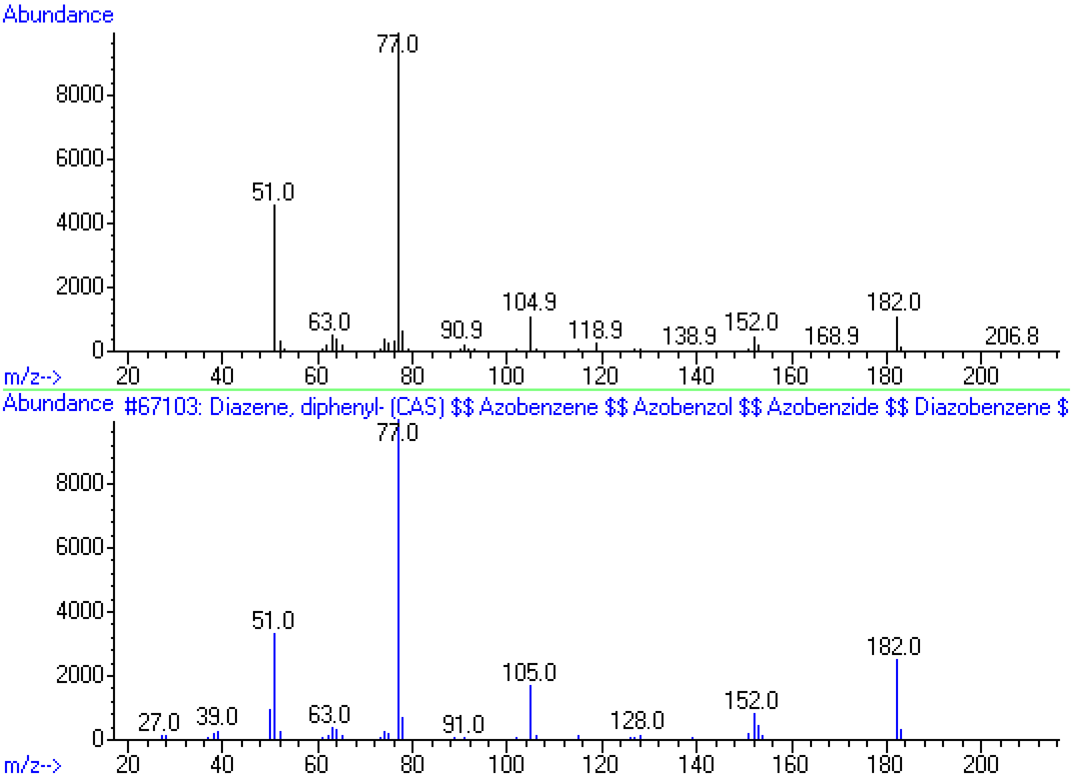
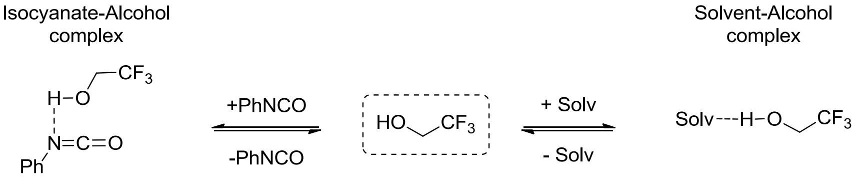


Figure 46. Obtained and database Wiley 275 m/z spectra from GC-MS of azobenzene.

2.2.3. MECHANISM OF THE PHOTOCHEMICAL REACTION

In chapter one there has been proposed a radical chain mechanism that explained the peculiarities of the ground state reaction between PhNCO and TFE. Several peculiarities were explained by the equilibriums established between free TFE and the complexes with PhNCO or with solvent (Scheme 47). In ground state conditions, it was proposed that solvent/TFE adduct undergoes a PCET to generate the key radical intermediate.



Scheme 47. Hydrogen bond equilibriums of PhNCO and TFE in HBA solvents.

In principle several possibilities exist when applying irradiation to the system described in the previous scheme.

a) Acceleration of the *ground state reaction* by photoactivation of the PCET process on the solvent/TFE complex.
b) Triggering of an alternative mechanism by photoactivation of the *inactive* PhNCO/TFE complex.
c) Coexistence of both pathways.

A first hint came from stopping irradiation when reaction was still uncompleted. With continuous irradiation, the reaction had a conversion of around 20 % after 15 min and about 93 % after 60 min. By contrast, if irradiation was turned off after 15 minutes, and the reaction leaved in dark for 45 min more (total reaction time 60 min), the conversion then was just 34 %. Thus, the reaction did not significantly evolve in the absence of irradiation.

This suggested that, in case there was a photoinduced initiation of the chain mechanism described for the ground state reaction (pathway a), this initiation was not efficient enough to overcome the termination processes, in other words, in this conditions propagations chains would be too short to carry on the process without continuous initiation.

Another alternative is that irradiation activated the PhNCO/TFE hydrogen bond complex, inactive in ground state conditions (pathway b). In this case, a photoinduced PCET would generate the radical pair of PhNCO/TFE, which could collapse directly, not entering in a chain cycle. Thus, the reaction would not proceed without irradiation.

RADICAL SCAVENGING

One important characteristic of ground state chain reaction was its observable radical nature. An important difference between both pathways would be the presence of free radicals in the first case. In order to investigate presence or absence of free radicals in photochemical conditions, the photoreaction between PhNCO and TFE in MeCN was carried out in the presence of different radical-interacting species.

The previously used radical scavenger galvinoxyl has intense UV absorption bands, thus not being suitable to use in photochemical reactions. As an alternative, 20 $\%_{mo}$ of (2,2,6,6-tetramethyl-piperidin-1-yl)oxyl, TEMPO, free radical was used being photoreaction rate not affected (Figure 47).

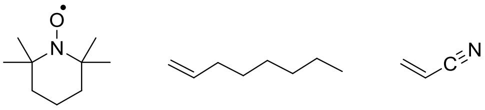


Figure 47. TEMPO, 1-octene and acrylonitrile.

Another way to check the presence of free radicals is by performing the reaction in the presence of monomers that could undergo radical polymerization. If there was monomer disappearance and polymer formation, this would be an evidence for the presence of free radicals in the medium. Suitable monomers, apart from reacting by radical polymerization, should be transparent to irradiation at wavelengths longer than 270 nm; thus, carbonyl containing monomers were avoided.

Reactions were performed in the presence of 1-octene or acrylonitrile. In any cases, no effect on the reaction was observed, nor was polymer formation detected by ^1H NMR or GPC. These results ruled out the existence of free radicals out of a radical pair in a solvent cage, thus rejecting pathway a.

COMPETITIVE EXPERIMENT

In order to obtain complementary kinetic data of this new photoreaction, the reactivity of TFE was compared with that of ethanol. Performing the reaction of PhNCO with ethanol in the same conditions under irradiation did not produce any noticeable acceleration of the reaction (Figure 48).

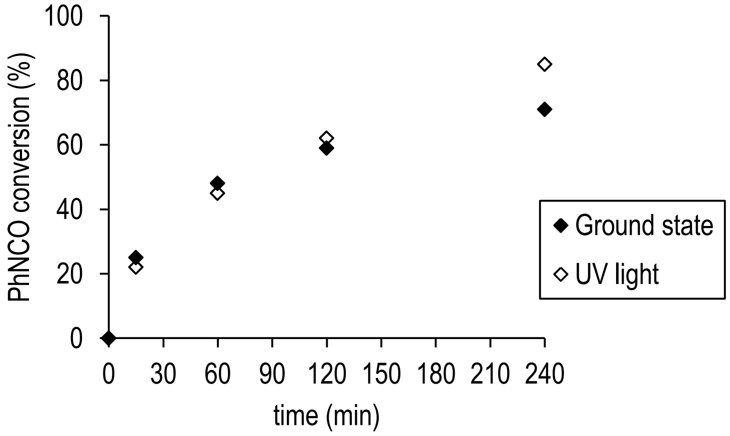
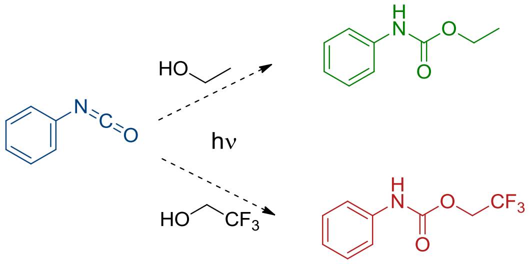


Figure 48. Comparison of ground state and irradiated reaction of PhNCO with ethanol in MeCN. $[PhNCO]_0$ = 10 mM; $[EtOH]_0$ = 20 mM; Philips HPK 125 W; Pyrex filter.

It is interesting to explore the differences between the behaviors of both alcohols. The reaction of TFE with PhNCO in MeCN that failed in the absence of irradiation was activated by UV irradiation. In contrast, the reaction of ethanol with PhNCO in MeCN does not show significant differences in absence or presence of UV light. This comparison suggests the existence of important differences between the preferred reactivity channels of the two alcohols.

This was confirmed by a competition experiment. The objective was to compare both reaction rates. Thus, the photochemical reaction was set with PhNCO and both alcohols using a proportion 1:1:1 monitored by GC ($[PhNCO]_0 = [TFE]_0 = [EtOH]_0$ = 0.02 M; MeCN; Philips HPK 125W Pyrex filter). In these conditions, no reaction of ethanol was observed at 15 minutes, while 2,2,2-trifluoroethyl phenylcarbamate was produced as a single product with a 75 % yield. Remarkably, upon irradiation the reaction of TFE with PhNCO was fast enough to make reaction with ethanol negligible (Figure 49).



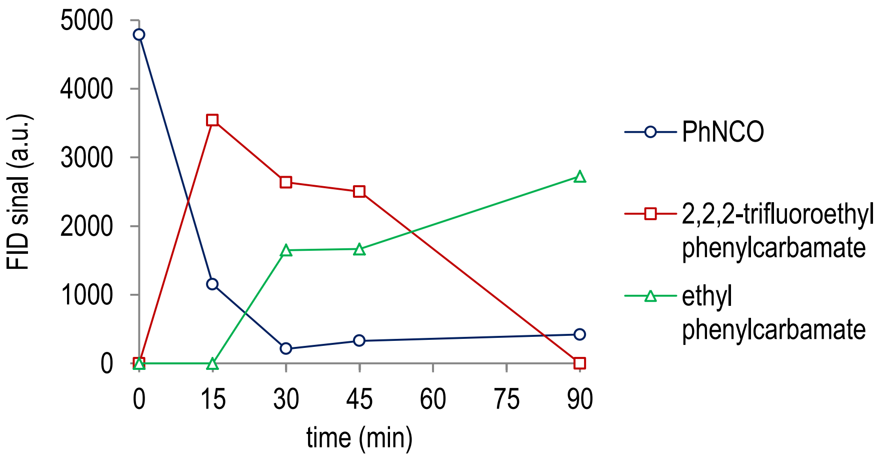
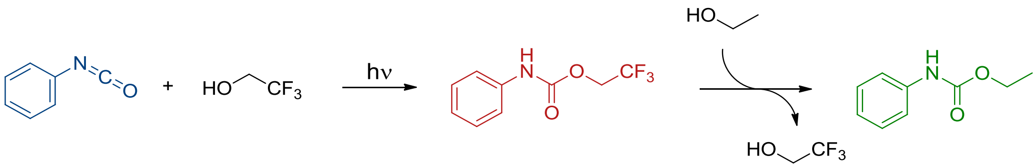


Figure 49. Competition experiment between TFE and ethanol in front PhNCO in photochemical conditions.

However, after 15 min the concentration of polyfluorinated carbamate decreased linked to the appearance of an increasing amount of ethyl phenylcarbamate. The reaction taking place was a transcarbamoylation, conceptually the equivalent of transesterification with carbamate groups. In this reaction, 2,2,2-trifluoroethoxy group was substituted by the more nucleophilic ethanol. Thus, there were two different reactions, a quick photochemical formation of 2,2,2-trifluoroethyl phenylcarbamate, and the posterior reaction of it with ethanol to form ethyl phenylcarbamates (Scheme 48).



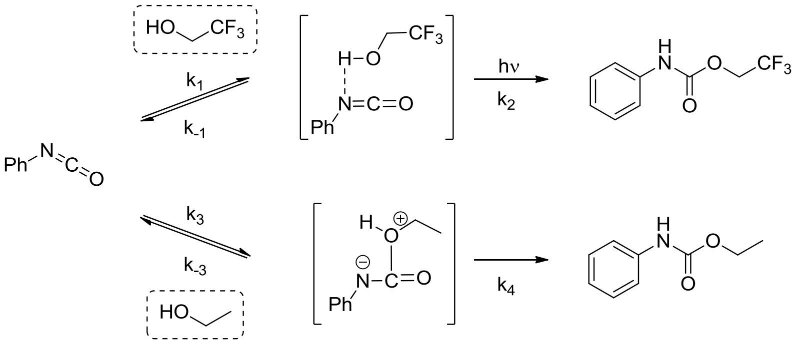
Scheme 48. Polyfluorinated carbamate formation and posterior transcarbamoylation.

The most relevant observation for our interpretation was the fact that in a competition in photochemical conditions, TFE reacted much faster than ethanol.

An interpretation for these competition experiments was proposed (Scheme 49). It is well accepted that in the reactions of non-fluorinated alcohols with isocyanates, the nucleophilic center of the alcohol is first added to the electrophilic carbon of the isocyanate group; then proton is transferred to the nitrogen.[3] This would correspond to the reactivity of ethanol with phenyl isocyanate, which is not affected by light (Scheme 49, steps 3 and 4).

However, 2,2,2-trifluoroethanol is much less nucleophile (but much more acidic) than ethanol, and therefore, the standard order of events seem not to be followed in this case. Thus, the opposite order of events is proposed for TFE. This alcohol would produce a strong hydrogen bond complex with the isocyanate. Upon irradiation this complex could undergo a PCET to generate a radical pair, quickly collapsing without leaving the solvent cage. Nevertheless, there were not evidences for free radicals in the photochemical reaction. Thus, a formally equivalent view of this process would be that the complex undergoes a proton transfer followed by nucleophilic addition (Scheme 49, steps 1 and 2).

The results from the competition experiment indicated that the photochemical step was fast ($k_2 >> k_{-1}$) and that the step 1 was not an equilibrium in the presence of irradiation. These results also indicate that $k_1 >> k_3$, as expected since step 1 is a fast hydrogen bond formation process while step 3 is a slower covalent bond formation.



Scheme 49. Competitive experiments of 2,2,2-trifluoroethanol and ethanol towards phenyl isocyanate.

MECHANISTIC INTERPRETATION

In the ground state mechanism in DMF it was hypothesized that the radical was generated from a DMF/TFE hydrogen bond adduct. This was partially based on the higher partial charge of oxygen atom in DMF *versus* nitrogen and oxygen atoms in PhNCO (Figure 50).

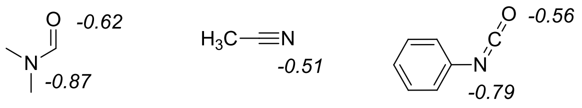


Figure 50. Mulliken charges of hydrogen bond accepting atoms in DMF, MeCN and PhNCO.[93]

However, the structure of MeCN is quite different from DMF. Partial charge on nitrogen atom in acetonitrile is slightly lower than partial charge in oxygen in PhNCO. Thus, the equilibrium of hydrogen bond complexes would not be shifted completely to solvent/TFE complex. In addition, as the hydrogen bond solvent/TFE is weaker, a proton-coupled electron transfer PCET to the solvent would be less probable.

In contrast, a higher proportion of PhNCO/TFE complex would be probably present. Upon absorption of light, phenyl isocyanate (as all molecules) becomes more eager to both accept

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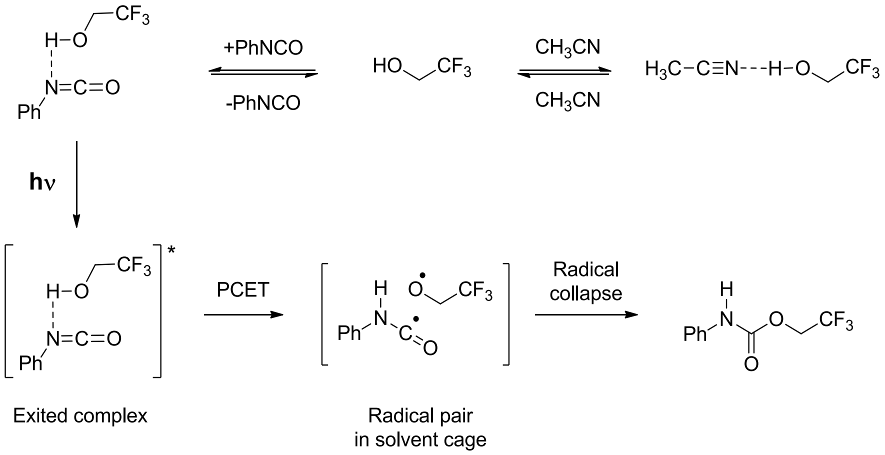
[93] Mulliken charges were calculated after AM1 energy minimization of structure using RHF/3-21G calculation of charges implemented in Chem3D Pro 12.0 in suit ChemBioOffice 2010.

and donate electrons, facilitating PCET that generates a radical pair. As there have not been evidences of free radicals in photochemical conditions, it was assumed that this radical pair would quickly collapse after formation without leaving the solvent cage (Scheme 50).



Scheme 50. Proposed photochemical mechanism for the reaction of TFE with PhNCO in MeCN.

Even though no extended mechanistic studies have been carried out for the photochemical reaction, this proposed mechanism is in agreement with the results and with the theoretical calculations described. In addition, and perhaps more important, the mechanistic proposal keeps the coherence with the proposed mechanism of the ground state reaction.

2.3. PHOTOCHEMICAL REACTION OF POLYFLUORINATED DIOLS AND AROMATIC ISOCYANATES

The ground state reaction of polyfluorinated diols with phenyl isocyanate was not complete, the diols just reacted by one end and the hydroxyl carbamate formed did not further react. On another hand, reaction of polyfluorinated alcohols with phenyl isocyanate was activated by UV light.

Those results suggested the possibility of activating the reaction of polyfluorinated diols with phenyl isocyanate under irradiation in order to obtain polyfluorinated biscarbamates.

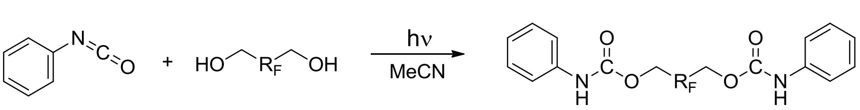
PHOTOREACTION TO FORM PARTIALLY FLUORINATED BIS(PHENYLCARBAMATES) **7**

To test that, the reaction of PhNCO with 2,2,3,3,4,4-hexafluoropentane-1,5-diol **6b** in acetonitrile was set. After 4 h of irradiation, PhNCO was totally consumed. The crude of the reaction revealed by ^{19}F NMR a proportion of **7b**:**8b** 14:1 and the biscarbamate **7b** was isolated in a 63 % yield (Table 11).

The viability of this new photoreaction was explored with other polyfluorinated diols with remarkable results. While in ground state only one hydroxyl group reacted to form products **8**, under irradiation biscarbamates could be obtained in good yields, thus overcoming the previous limitations.

Thus, biscarbamate **7a** and **7c** could be obtained in an average 70 % yield by photoreaction of PhNCO with polyfluorinated diols **6a** and **6c** respectively. In a similar way, **7d** was obtained in a 77 % yield from polyfluorinated ether diol **6d**.

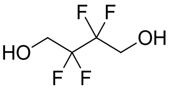
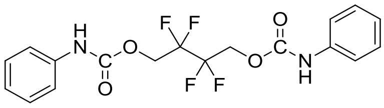
Table 11. Photochemical reaction of phenyl isocyanate with polyfluorinated diols.[a]

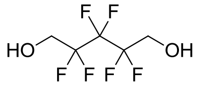
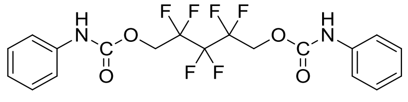
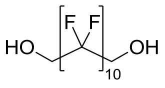
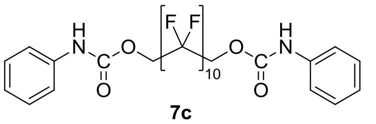
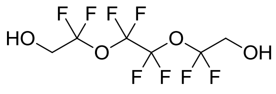
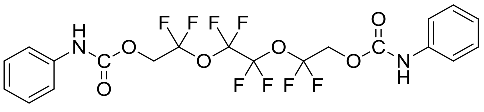


1 **6** **7**

R_F
- **6a**, $(CF_2)_2$
- **6b**, $(CF_2)_3$
- **6c**, $(CF_2)_{10}$
- **6d**, $CF_2O(CF_2)_2OCF_2$

R_F
- **7a**, $(CF_2)_2$
- **7b**, $(CF_2)_3$
- **7c**, $(CF_2)_{10}$
- **7d**, $CF_2O(CF_2)_2OCF_2$

Diol	Product	Isolated yield (%)[a]
 **6a**	 **7a**	71

 **6b**	 **7b**	63
 **6c**	 **7c**	68
 **6d**	 **7d**	77

[a] Reaction conditions: 1 mmol of PhNCO **1**; 0.5 mmol of polyfluorinated diol **6**; 50 mL dry CH_3CN; nitrogen atmosphere; Pyrex filter; Philips HPK 125 W lamp; 4 h.

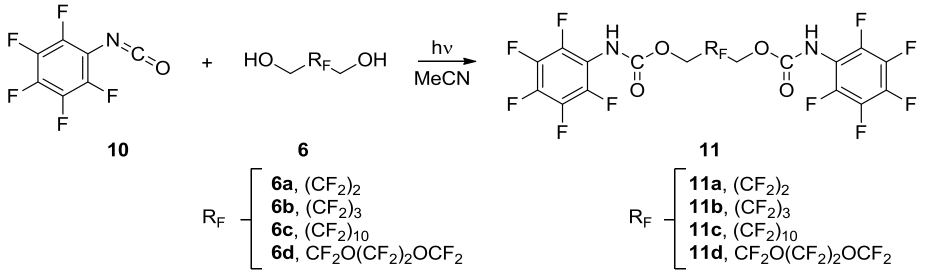
PHOTOREACTION TO FORM QUASI-PERFLUORINATED BISCARBAMATES **11**

One of our aims was to build molecules with a high content of fluorine; therefore, the corresponding photochemical reactions between polyfluorinated diols and pentafluorophenyl isocyanate **10** were also tested.

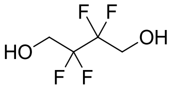
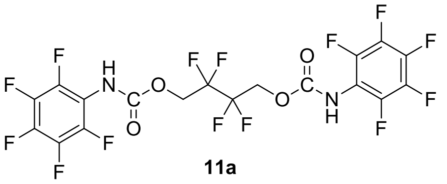
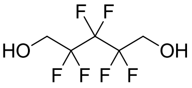
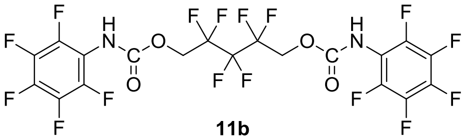
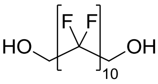
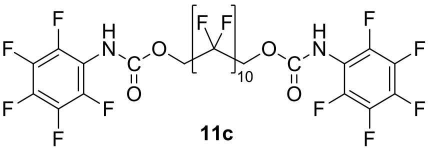
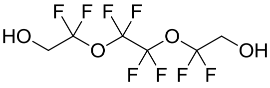
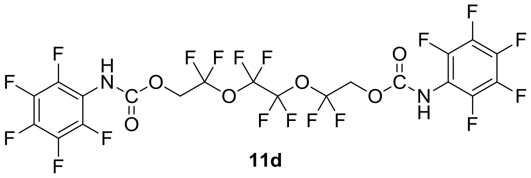
It is worth to notice that the blank reactions, in the absence of irradiation, failed completely in all the cases. However, upon irradiation, the biscarbamates products were obtained in good yields (Up to 85 %, Table 12).

Thus, the photochemical reaction of **6a** with **10** yield the almost completely perfluorinated biscarbamate 2,2,3,3-tetrafluorobutan-1,4-diyl bis(pentafluorophenylcarbamate) **11a** in a 79 % isolated yield. In a similar way, pentafluorophenyl isocyanate **10** reacted with diols **6b** and **6c** to yield quasi-perfluorinated biscarbamates **7b** and **7c** in moderate yields (50 % average). In the same conditions, polyfluorinated ether diol **6d** yield the corresponding carbamate **7d** in a 85 % yield (Table 12).

Table 12. Photochemical reaction to prepare quasi-perfluorinated bis(phenylcarbamates). [a]



Diol	Product	Isolated yield (%)

 **6a**	 **11a**	79
 **6b**	 **11b**	45
 **6c**	 **11c**	54
 **6d**	 **11d**	85

[a] Reaction conditions: 1 mmol of **10**; 0.5 mmol of polyfluorinated diol **6**; 50 mL dry CH_3CN; nitrogen atmosphere; Pyrex filter; Philips HPK 125 W lamp; 4 h.

2.4. SURFACE PROPERTIES OF POLYFLUORINATED BISCARBAMATES

Our hypothesis was that this new family of biscarbamates could show interesting wettability properties. Highly fluorinated compounds normally show hydrophobic and oleophobic properties that give rise to many potential applications.[12]

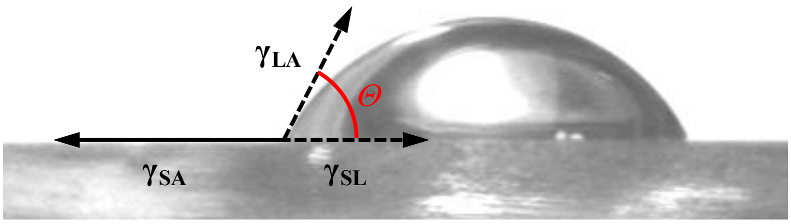
WETTABILITY

Wetting is the process in which a liquid spreads on a solid surface. The degree of wetting or wettability is determined by the balance of the adhesive force liquid-surface and the cohesive force between liquid molecules. The chemical composition and the topographic structure affect this balance.[94] The standard measurement of wettability is the *sessile drop contact angle measurement* of a droplet of a standard liquid probe on a surface.

The equilibrium contact angle is the angle the solid surface makes with the tangent of the liquid. It is determined by three factors: liquid, surface and medium. At the equilibrium, all forces are balanced, as are the three inter-phase surface tensions (surface-air γ_{SA}; surface-liquid γ_{SL} and liquid-air γ_{LA}) in the horizontal axe. Young's equation relates this balance of forces with the contact angle. In this equation it is seen that the tension surface-air is equivalent to the tension surface liquid plus the horizontal term of the liquid-air tension, thus depending on the contact angle (Figure 51).[95]

If there is a high interaction between surface and liquid, drop would be flat and contact angle narrow. However, in a surface with low affinity with the liquid, the drop would be rounder and contact angle are larger

Young's equation



γ_{SA}	Surface tension solid-air
γ_{SL}	Surface tension solid-liquid
γ_{LA}	Surface tension liquid-air
Θ	Equilibrium contact angle

Figure 51. Graphical interpretation of Young's equation for a drop resting over a smooth surface.

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[94] Aulin, C.; Yun, S. H.; Wagberg, L.; Lindström, T. *Appl. Mater. Interfaces.* **2009**, *1*, 2443-2452.

[95] Krol, P. *Linear polyurethanes: Synthesis Methods, Chemical Structures, Properties and Applications.* CRC Press, 2008. ISBN: 9789004188167.

The contribution of the chemical composition to the contact angle is measured in a completely flat surface, with no substructure. This angle is referred normally as the *intrinsic contact angle* of the surface. When the intrinsic contact angle is large enough, a roughening of the surface will result in an increase of the value. With a good base from the chemical composition and the appropriate substructure in the ideal situation can give rise to superhydrophobic (Θ > 150 º)and superoleophobic surfaces.[96]

SPIN COATING

A simple way to modify a surface is by spin coating. A drop of a solution of the compound in a volatile solvent is placed on a surface, and then it is spun (typically at 6 000 rpm) to form a thin homogeneous layer of the solution over the surface. After evaporation of solvent, a thin coating over the initial surface is obtained (Figure 52).

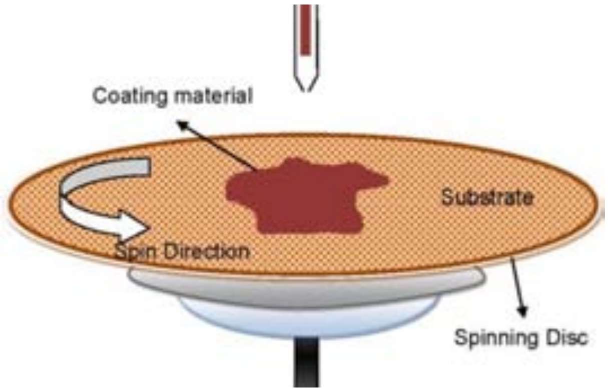

Figure 52. Schematic representation of spin coating technique.

The experiments of spin coating and contact angle measurements were carried in the clean room facilities of *Nanostructuration platform* on *Institut de Ciència dels Materials de Barcelona* ICMAB under the surveillance of Neus Roma.

CONTACT ANGLE MEASUREMENTS

Surface properties of polyfluorinated biscarbamates **7** and quasi-perfluorinated biscarbamates **11** were studied. First, they were deposited over a glass surface by spin coating and then water and hexadecane contact angle were measured to obtain an experimental value related with their hydrophobicity and oleophobicity.

Thus, over a smooth clean glass surface of 1 x 1 cm was placed a drop of 80 µL of a solution of 10 mg of the corresponding biscarbamate in 0.5 mL of acetone. Then, the glass was spun at

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[96] (a) Wenzel, R. N. *Ind. Eng. Chem.* **1936**, *28*, 988-994. (b) Cassie, A. B. D.; Baxter, S. *Trans Faraday Soc*. **1944**, *40*, 546-551. (c) Pease, D. C. *J. Phys. Chem.* **1945**, *49*, 107-110. (d) Gao, L.; McCarthy, T. J. *Langmuir* **2007**, *23*, 3762-3765.

6000 rpm for 120 s after 6 seconds of acceleration at 1000 rpm s^{-1}. Then, the acetone was evaporated on a moisture controlled atmosphere.

Cohesive forces of water are stronger than in hexadecane (liquid probe for oleophobicity), thus generally water contact angles values are higher than with hexadecane.

Using a KRÜSS Contact Angle Measuring System DSA 100, a small drop of 4 µL of the liquid probe was deposited over the modified glass surface, then a picture was taken and the intrinsic contact angle was measured. This was done at least two times for each measurement. The values of the sessile drop contact angle with water and hexadecane deposited on the glasses modified with the biscarbamates are summarized in Table 13 and compared of those of the experimentally found for PTFE (Teflon®), which matched those previously reported on literature.[97]

Water contact angles obtained for partially polyfluorinated biscarbamates **7** were approximately constant around 83º. These values indicated that length of polyfluorinated chain seems not to have an effect in the hydrophobicity of **7**. (Table 13 and Figure 53)

In the case of quasi-perfluorinated biscarbamates **11** there was a clearer tendency. The smaller a biscarbamate, the higher water contact angle value. As the chain length seemed to have no effect for compounds **7**, then pentafluorophenyl rings would be responsible of the hydrophobicity. If this assumption were true, it would justify also this tendency of smaller biscarbamates having better properties. Small quasi-perfluorinated biscarbamates have proportionally more pentafluorophenyl moieties, thus showing higher hydrophobicity, expressed in greater contact angles. In any case, PTFE with a higher content of fluorine 76 $\%_{wt}$ showed the highest water contact angle value (117 º). However, in our case, the compound with a higher content of fluorine **11c** gave the smallest contact angle (Table 13 and Figure 53).

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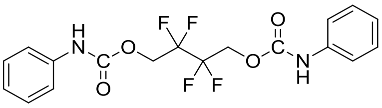
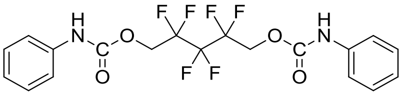
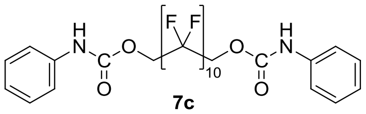
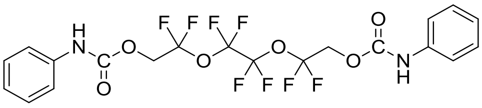
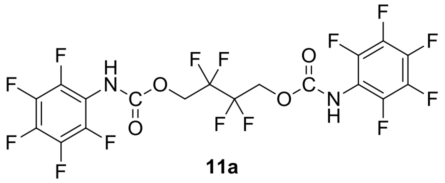
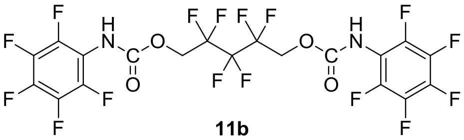
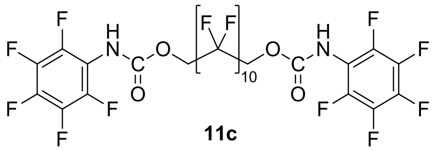
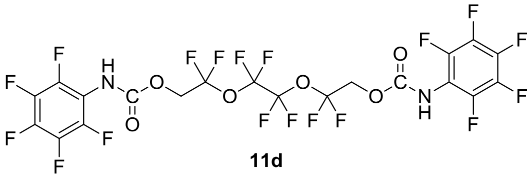
[97] Law, K.Y.; Zhao, H. *Soc. Imag. Sci. Techn.* **2009**, 53-57.

Table 13. Contact angle measurements of polyfluorinated **7** and quasi-perfluorinated **11** biscarbamates.[a]

Compound	Fluorine content ($\%_{wt}$)	Contact angle (°)[b]	
		H_2O	n-$C_{16}H_{34}$
 **7a**	19.0	86	24
 **7b**	25.3	81	19
 **7c**	47.5	84	11
 **7d**	28.6	82	41
 **11a**	45.8	96	58
 **11b**	48.2	85	47
 **11c**	58.1	44	53
 **11d**	48.0	72	40
PTFE[c]	76.0	117	48

[a] 80 µL of biscarbamate solution (10 mg in 0.5 mL acetone) deposited by spin coating (6 000 rpm; 120 s) over a 1 x 1 cm surface of cleaned glass. [b] Sessile drop contact angle measurement. [c] Commercial sealing tape of Teflon®

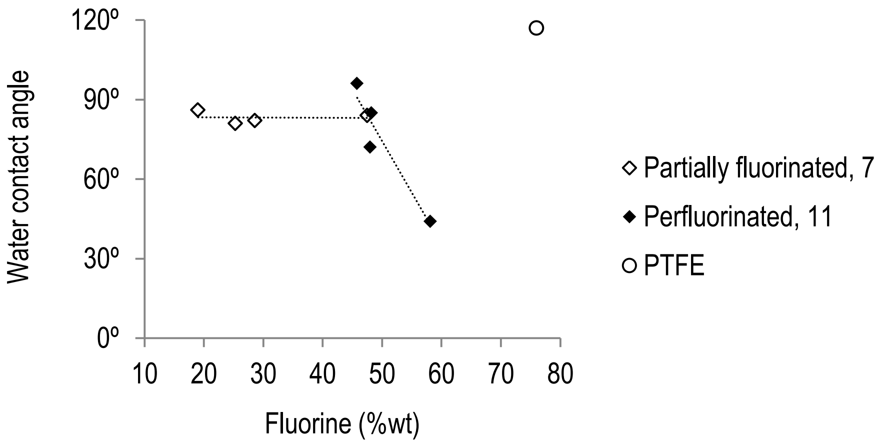
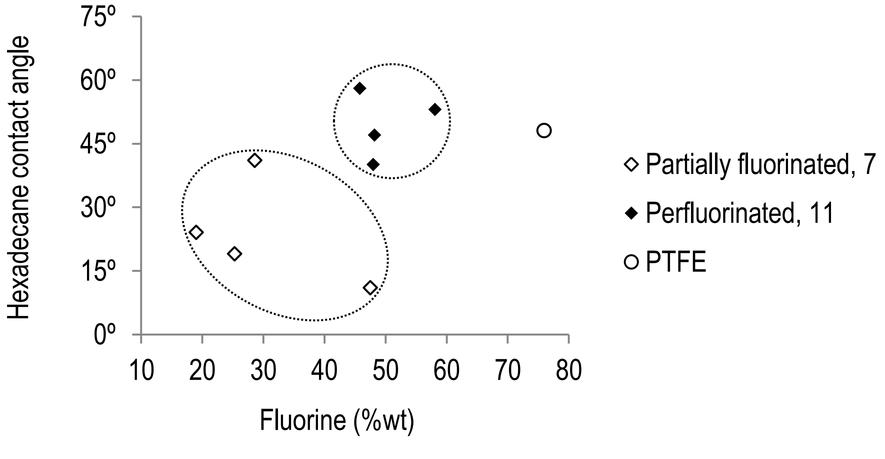


Figure 53. Relationship between the fluorine content and water contact angle for partially fluorinated **7** and quasi-perfluorinated **11** biscarbamates and PTFE.

In the case of oleophobicity the liquid probe was hexadecane. It was observed a general but loose relationship between hexadecane contact angle and fluorine content in the compounds. In spite of the high dispersion, these results confirmed the already known effect of the fluorine content on the oleophobicity of a particular molecule: the higher fluorine content, the higher oleophobicity. Bis(pentafluorophenylcarbamates) **11** showed lower dispersion and a significantly higher average contact angle value (50±8 º) than the bis(phenylcarbamates) **7** (in a range from 11º to 41º). In the case of polyfluorinated ether chain (Compounds **7d** and **11d**), both have similar hexadecanes contact angle values (40º), indicating that the effect of this polyfluorinated ether chain dominates over the effect of the (perfluorinated or not) aromatic ring. Interestingly, PTFE, a polymer with a 76 $\%_{wt}$ of fluorine content, showed lower value for hexadecane contact angle than quasi-perfluorinated bis(phenylcarbamates) **11**. This constitutes a significant result for a small molecule (Figure 54).[98]



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[98] Mueller, A.; Kowalewsky, T.; Wooley, K. L. *Macromolecules*, **1998**, *31*, 776-786.

Figure 54. Relationship between the fluorine content and hexadecane contact angle for partially fluorinated **7** and quasi-perfluorinated **11** biscarbamates and PTFE.

Let us focus on one noteworthy case, the compound **11a**, obtained by the photoreaction of a short polyfluorinated diol with pentafluorophenyl isocyanate. Although it was not the biscarbamate with the higher weight percentage of fluorine, it was the one with more interesting results. In this case, the water contact angle was 96º, an important value but lower than the 117º of PTFE. However, the hexadecane contact angle with this compound was 58º, a value greater than 48º angle of Teflon®, a material known for its oleophobic properties (Figure 55).

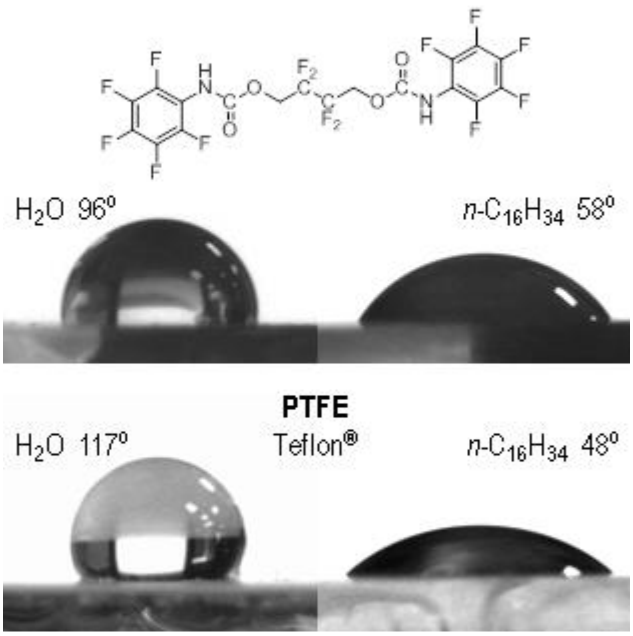

Figure 55. Drops of water (left) and hexadecane (right) in a Teflon® surface (bottom) and spin-coated with **6a** (top).

Here, it is worth to mention the prominence that small molecules with a high content of fluorine are gaining recently attention due to the strong environmental concern over persistent long-chain perfluoroalkyl compounds.[20,99]

Remarkably, a thin layer of compound **11a**, a small molecule, made glass even more oleophobic than Teflon®, pointing out an interesting avenue for potential applications.

These positive results encouraged us to go a step further. Instead of just depositing a polyfluorinated carbamate over the surface, which is something non-permanent, it was tried a covalent binding between glass and the polyfluorinated carbamate.

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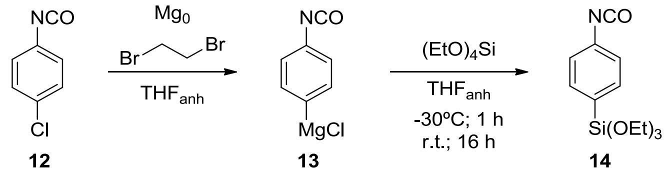
[99] Ritter, S. K. *Chem. Eng. News* **2010**, *88*, 12-17.

2.5. PERMANENT SURFACE MODIFICATION

The possibility to apply this methodology (ground state or photochemical) to obtain a modified glass surface was explored. The reaction could offer in principle an easy and direct approach to surface modified with hydrophobic and oleophobic fluorinated carbamates pendants that can significantly alter its properties.

Thus, an isocyanate would be anchored to a glass surface; then, a fluorinated alcohol would be reacted generating a polyfluorinated carbamate covalently attached to the glass surface.

The simplest option could have been the use of 4-(triethoxysilyl)propyl isocyanate. A commercially available molecule used to modify silica or glass surfaces through the triethoxysilyl group. However, as the reaction explored in this thesis was the reaction of aromatic isocyanates with polyfluorinated alcohols, but there were not commercially available aromatic isocyanates containing trimethoxysilyl or triethoxysilyl groups. Thus, the triethoxysilyl derivate had to be prepared adapting a described synthesis (Scheme 51).[100]



Scheme 51. Synthesis of 4-(triethoxysilyl)phenyl isocyanate **14**.

Commercially available 4-chlorophenyl isocyanate **12** was transformed into the arylmagnesium chloride, which was then reacted with tetraethyl orthosilicate TEOS to form 4-(triethoxysilyl)phenyl isocyanate. Then, once this isocyanate were attached to glass surface, it could be reacted with a polyfluorinated alcohol to obtain a polyfluorinated carbamate covalently linked to the surface.

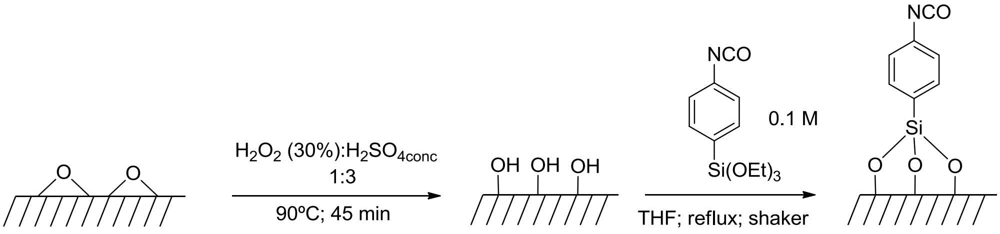
The glasses to be modified were ordinary microscope slides of 2 x 7 cm (*Glass-0*). They were cleaned and activated with an *acid piranha solution* to generate hydroxyl terminations on the surface. This method generates smoother surfaces than using concentrated base or fluorhydric acid.[101] An *acid piranha solution* is a mixture 1:3 of hydrogen peroxide (30 %) and concentrated sulfuric acid.

---

[100] (a) Sherry, B. D.; Fürstner, A. *Chem. Commun.* **2009**, 7116-7118.
(b) Manoso, A. S.; Ahn, C.; Soheili, A.; Handy, C. J.; Correia, R.; Seganish, W. M.; DeShong, P. *J. Org. Chem.* **2004**, *69*, 8305-8314.

[101] (a) Park, J.; Henn-Lecordier, L. Univeristy of Maryland. *Standard Operating Procedures for Piranha Solutions, Laboratory for advanced Material Processing.* (Last update: August 2003) <http://www.lamp.umd.edu/Sop/Piranha_SOP.htm>
(b) Vogel, A. I. *Vogel's textbook of practical organic chemistry 5th ed*. Furniss, B. S. Essex, England, 1989.

In this case, acid is added slowly to hydrogen peroxide under ice bath, and then the glasses to be activated were carefully introduced in the solution. Then, the temperature was set to 90 ºC for 45 min. After that, glass was rinsed with abundant deionized water and dried in vacuum (Scheme 52).



Scheme 52. Activation and modification of glass surface.

Then, this activated glass was placed in a solution of 4-(triethoxysilyl)phenyl isocyanate **14** (0.1 M in THF; 20 mL) in a closed reaction tube. Then, it was sealed and heated up to 50 ºC and agitated with an oscillatory shaker at 120 oscillations per minute for 18 h. Then, the glass was cleaned with acetone and dried in vacuum (*Glass-1*).

This modified *Glass-1* should be essentially phenyl isocyanate anchored to a glass surface. Not surprisingly, the presence of organic molecule on the surface made it more hydrophobic and less oleophobic than the initial *Glass-0* (Table 14).

Two different procedures to react PhNCO with polyfluorinated alcohols have been described in previous sections: Ground state reaction in DMF and photoreaction in MeCN. Thus, both methods were tested using a long polyfluorinated alcohol in order to have both a carbamate group and a polyfluorinated chain in the surface, then unreacted isocyanate groups remaining would be blocked by reaction with the more active TFE.

Thereby, the modified *Glass-1* was placed in a reaction tube with a solution of 2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluoro-1-octanol **2b** (0.02 M; 20 mL dry DMF) and stirred at room temperature with the shaker for 18 h. Then, it was placed in a solution of TFE **2a** (0.01 M; 20 mL dry DMF) for 4 h to block the possible unreacted isocyanate groups (*Glass-2*). The results of water and hexadecane contact angles (94º and 20º respectively) were comparable to those obtained for partially fluorinated bisphenylcarbamates **7** (average of 83º and 24º respectively). This was attributed to the relative similarity of structures, because all consist on polyfluorinated chains and phenylcarbamates moieties.

Table 14. Contact angle for modified glasses.

Glass	Observation	Contact angle	
		H_2O	n-$C_{16}H_{34}$
Glass-0	Commercial glass	45 °	23 °
Glass-1	Modified with **14**	63 °	14 °
Glass-2	DMF-ground state procedure	94 °	20 °
Glass-3	MeCN-photochemical procedure	65 ~ 86 °	-

Glass-1 was also modified using the photochemical procedure. In this case, the glass sample had to be cut at 2 x 6 cm in order to fit inside the immersion well reactor. As inside the photoreactor glass was in a vertical position, the upper part received a direct irradiation from the lamp, while the lower part did not (Figure 56).

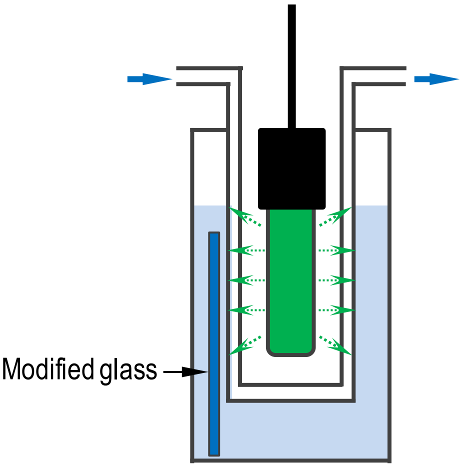


Figure 56. Simple scheme of a glass inside an immersion well photoreactor.

This glass was reacted in MeCN with 1*H*,1*H*-perfluoro-1-octanol **2b** under irradiation of UV light ([**2b**]$_0$ = 0.02 M; Philips HPK 125 W; Pyrex filter). After four hours, TFE (72 µL, 1 mmol) was added in order to block the free remaining isocyanate groups and 60 min latter irradiation was turned off. The glass was washed with acetone and dried in vacuum (*Glass-3*).

The water contact angle values obtained for *Glass-3* showed a dependency on the position of the drop in the glass. Drops deposited on the higher part had values up to 86º; these contact angles gradually decrease with height until reaching the lower part, with values around 65º, similar to *Glass-1*, probably indicating that photoreaction had not taken place in the lower part of the glass (Figure 57).

Figure 57. Water contact angle in photo-chemically modified glass surface dependence on height.

These results showed a correlation between the intensity of the irradiation and the observed water contact angle, being the extent of the reaction greater where more light was available. This gave a clear relationship between irradiation and final properties, thus demonstrating that modification of the surface with this method was possible.

In this section, the intention was just to explore the possibility of translate the reactivity developed in solution to a glass anchored system. Once it was demonstrated that glass modification with polyfluorinated carbamates was possible, the optimization and development was left for further research, since at the same time we were involved in the development of polyfluorinated polyurethanes, the subject of the next chapter.

Chapter 3

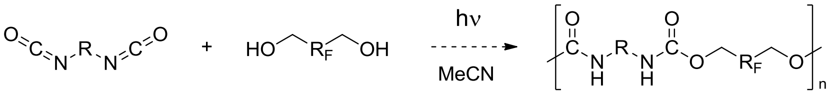
Photochemical formation of polyfluorinated polyurethanes

3. PHOTOCHEMICAL FORMATION OF POLYFLUORINATED POLYURETHANES

This chapter is divided in four sections. The first one describes the photopolymerization of an aromatic diisocyanate with three different polyfluorinated diols, then the second section focuses on one of these reactions to study the main influencing factors. After that, it is explained the application of this photopolymerization methodology in two preliminary studies, one to prepare quasi-perfluorinated polyurethanes and another that uses a non-fluorinated acidic dihydroxyl monomers.

3.1. POLYFLUORINATED POLYURETHANES FROM POLYFLUORINATED DIOLS

As it was explained in the first chapter, polyfluorinated diols react with aromatic isocyanates just by one end in ground state conditions. This reaction required activation by UV irradiation to be complete and form bis(phenylcarbamates). As polymer formation required complete reaction of the diol, the photochemical conditions seemed a good starting point for reaction of polyfluorinated diols with aromatic diisocyanates to form polyfluorinated polyurethanes (Scheme 53).



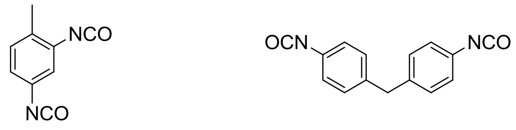
Scheme 53. General photoreaction of polyfluorinated diol with diisocyanate.

Although these reactions probably take place through a radical mechanism, they are not radical chain polymerizations. In a *chain-growth polymerization,* an active site in the polymer reacts with monomer, producing then a new active site. However, in this photoreaction polymer grows because monomers are bifunctional, reacting one alcohol with one isocyanate each time, no because they regenerate a radical active site. Thus, this reaction should be classified as a *step-growth polymerization.*

Thus, to study these photoactivated *step-growth polymerizations* that probably occurs via a radical reaction, a case-study approach was used. Thereby, after selecting a diisocyanate and a polyfluorinated diol for model photoreaction the parameters affecting the reactions were studied in deep detail.

3.1.1. DIISOCYANATE

The most used diisocyanates for PU production are aromatic diisocyanates, especially 2,4-toluene diisocyanate, TDI, and 4,4'-methyle diphenyl 4,4'-diisocyanate, MDI. In the case of TDI, the isocyanate groups are in different positions respect the methyl group, thus having different reactivity. In addition, as both isocyanate groups are in the same aromatic system, they affect the other, giving complicated kinetics.[102] In MDI, both isocyanates are equivalents by symmetry and as both aromatic systems are not connected they have a more limited influence in each other.



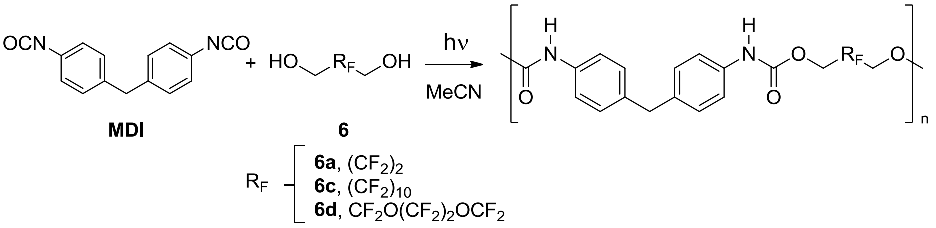
TDI **MDI**

Figure 58. Structures of TDI and MDI.

Conveniently, the reactivity of each isocyanate group of MDI is similar to the studied PhNCO. Therefore, for this and to avoid unnecessary complications that could emerge from the use of TDI, MDI was the selected diisocyanate.

3.1.2. PRELIMINARY REACTIONS: SELECTING THE DIOL

Three different polyfluorinated diols were tested in their photoreaction with MDI: an example of short diol 2,2,3,3-tetrafluorobutan-1,4-diol **6a**, a long diol 2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11-icosafluoro-dodecan-1,12 **6c** and a polyether diol 2,2,4,4,5,5,7,7-octafluoro-3,6-dioxa-octane-1,8-diol **6d**. These reactions were carried out using similar conditions to the ones for the photoreaction of polyfluorinated diols with PhNCO. The aim was to get familiar with the peculiarities of the photopolymerization process before selecting a diol as a model (Scheme 54).



Scheme 54. Reactions of MDI with polyfluorinated diols.

Solving MDI in acetonitrile was a slow process. It somehow improved by previously crushing the pellets in a mortar, but what really accelerated the process was applying ultrasounds. When it was completely solved, the corresponding diol was added and the irradiation (Philips HPK 125 W) was turned on for four hours. After that time, solvent was evaporated and the final extent of photopolymerization was checked by gel permeation chromatography GPC.

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[102] Bertoldo, M.; Cappelli, C.; Catanorchi, S. Liuzzo, V.; Bronco, S. *Macromolecules* **2005**, *38*, 1385-1394.

SIZE EXCLUSION CHROMATOGRAPHY / GEL PERMEATION CHROMATOGRAPHY

One of the most used techniques to determine the molecular weight of polymers is gel permeation chromatography GPC, a type of liquid chromatography based on size exclusion SEC. The chromatographic column is packed with small, round porous particles. Although polymers are often described as long chains, they do not exist like that in solution. When solved, molecules coil up on themselves, like a ball of string. Although they are chains, they behave like spheres which size (technically, the hydrodynamic or Stokes radius) is related to the length or molecular weight of the polymer.

When they pass though the porous particles in the column, big coils would not enter any pore, medium coils would enter in bigger pores, being held back; the even smaller coils that could enter in big and small pores would be more held back, having a longer retention times (Figure 59).[103]

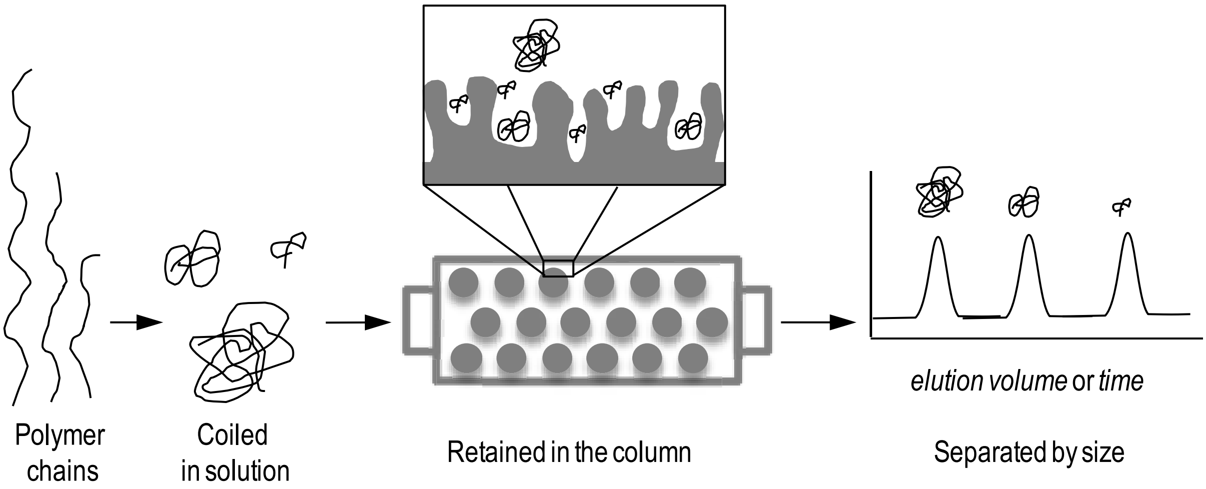

Figure 59. Schematic representation of how GPC separates polymers by size.

The elugram obtained (detector signal *vs* elution volume or time), can be used directly to compare between samples. Conveniently, they can be transformed to molecular weight distribution using a calibration with molecular weight standards.

A refractive index detector that gives a dimensionless relative signal between refractive index of solvent (THF in this case) and effluent from the column was used. It was calibrated using narrow band polystyrene standards of a molecular weight range from 500 to 200 000 Da.

Usually, from a polymerization process instead of a uniform polymer a distribution of molecular weights is obtained. Thus, several parameters are used to describe this distribution.

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[103] Agilent Technologies. *An Introduction to Gel Permeation Chromatography and Size Exclusión Chromatography.* (Uploaded: February 2014) <http://www.chem.agilent.com/Library/primers/Public/5990-6969EN%20GPC%20SEC%20Chrom%20Guide.pdf>

The average weight of this distribution depends on the property of the polymer used to calculate the mean.

The *number-average molecular weight* $\bar{M}_n$ is the statistical average of polymer molecular weight of all polymer chains. The number of chains with $M_i > \bar{M}_n$ is the same than $M_i < \bar{M}_n$. Thus, it is conceptually and mathematically related with the molar fraction x_i. Experimentally, it can be directly determined by end-group analysis by NMR or calculated from a molecular weight distribution obtained from a GPC elugram.[104]

$$\bar{M}_n = \frac{\sum_i N_i M_i}{\sum_i N_i} = \sum_i x_i M_i$$

M_i Molecular weight of a chain
N_i Number of chains of M_i molecular weight
x_i Molar fraction

The *weight-average molecular weight* $\bar{M}_w$ takes into account the molecular weight of each chain. The higher molecular weight of a chain, the more it contributes to $\bar{M}_w$. It means that there is the same weight of chains on either side of $\bar{M}_w$ in the distribution. It is related with the weight fraction. It can be obtained by scattering techniques or calculated from a molecular weight distribution from GPC.

$$\bar{M}_w = \frac{\sum_i W_i M_i}{\sum_i W_i} = \frac{\sum_i N_i M_i^2}{\sum_i N_i M_i} = \sum_i w_i M_i$$

W_i Weight of chains with molecular weight M_i
w_i Weight fraction

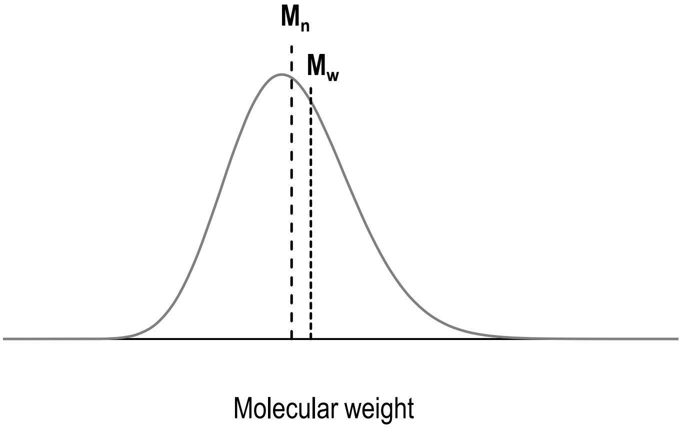

Figure 60. Molecular weight distribution with M$_n$ and M$_w$ indicated.

By definition $\bar{M}_w$ is always bigger or equal to $\bar{M}_n$. The ratio between the two averages should be called dispersity $Đ = \frac{\bar{M}_w}{\bar{M}_n}$, although often it is named polydispersity index.[105] It is a measure of the broadness of a polymer distribution. A uniform polymer would have a $Đ = 1$ and polymer distributions would have higher values.

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[104] Agilent Technologies. *Polymer Molecular Weight Distribution and Definition of MW Averages.* 10th June 2011 <https://www.chem.agilent.com/Library/technicaloverviews/Public/5990-7890EN.pdf> (Accessed: 1st July 2014)

[105] Stepto, R. F. T.; Gilbert, R. G.; Hess, M.; Jenkins, A. D.; Jones, R. G.; Kratochvíl P. *Pure Appl. Chem.* **2009**, *81*, 351-353.

First of all the reaction of the three diols with MDI was performed and the result of the reaction analyzed by GPC. In the elugram of the photoreaction of MDI with diol **6a** solvent appeared after 19.5 mL elution volume as two intense peaks (Figure 58, a). Those should not be considered in the transformation to molecular weight distribution because they would distort the average molecular weight. In the distribution obtained (M_n = 973 Da; M_w = 1.82·10^3 Da; Đ = 1.87; n_{GPC} = 1.0), it is possible to distinguish different low molecular weight oligomers (Figure 58, b). As in this representation the scale is logarithmic, low molecular weight oligomers can appear separated as discreet peaks, but as molecular weight increases, they tend to overlap to produce a continuous distribution. Qualitatively, it was observed that small oligomers were more abundant, decreasing the amount with molecular weight.

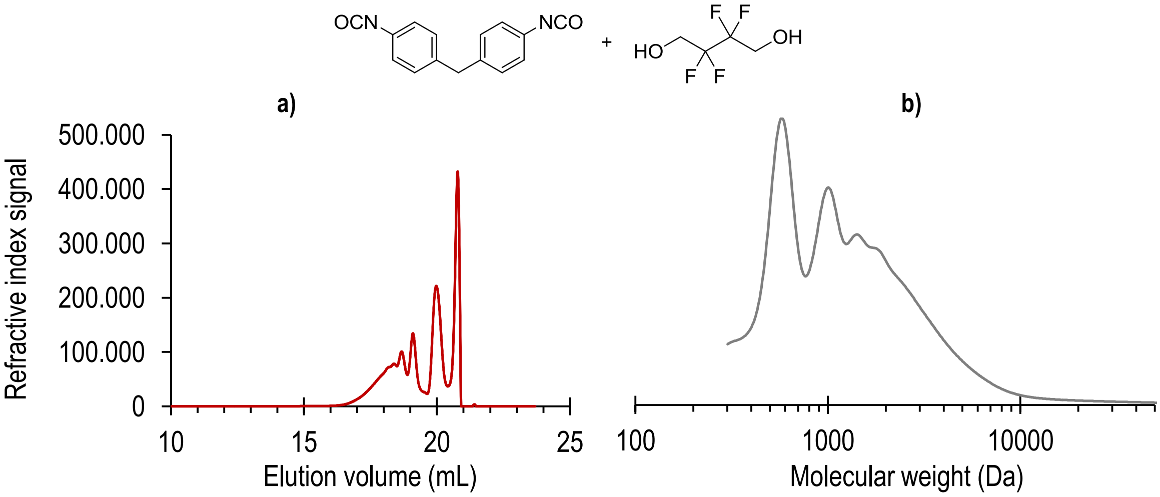


Figure 61. Photoreaction MDI with diol **6a**. a) Elugram. b) Molar mass distribution (M_n = 973 Da; M_w = 1.82·10^3 Da; Đ = 1.87).

The result of the photopolymerization of MDI with **6c** (Figure 59, a) showed an irregular distribution (M_n = 2.35·10^3 Da; M_w = 6.65·10^3 Da; Đ = 1.65; n_{GPC} = 1.2). In the reaction of polymerization of MDI with **6d** (Figure 59, b), it was not possible to see different peaks, just a distribution was observed (M_n = 1.34·10^3 Da; M_w = 1.81·10^3 Da; Đ = 1.34; n_{GPC} = 0.9).

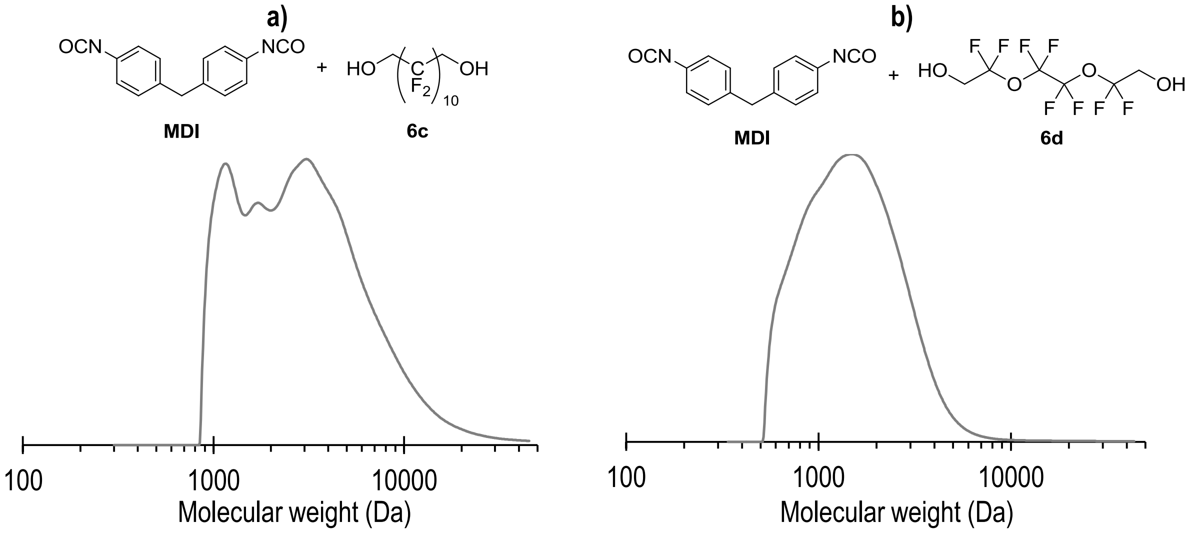
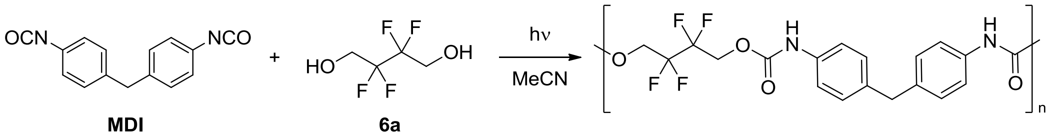


Figure 62. GPC results of MDI polymerizations with **6c** and **6d**.

In the three cases the products obtained have a relatively low molecular weight. Thus, this reaction required a deeper study to produced higher polymers. As in the GPC results of the photoreaction between MDI and diol **6a** was possible to distinguish different oligomers, which provided more useful information, this one was used as a model.

3.2. PHOTOPOLYMERIZATION OF MDI WITH 2,2,3,3-TETRAFLUOROBUTAN-1,4-DIOL

The selected model was the photoreaction between MDI and 2,2,3,3-tetrafluorobutan-1,4-diol diol **6a** (Scheme 55). This system presented two practical advantages, one was the observation of discreet oligomers by GPC and the other was a simple monitoring by ^{19}F NMR. Before entering in too much detail, some concepts as degree of polymerization and nomenclature would be discussed.



Scheme 55. Photopolymerization of MDI and diol **6a**.

DEGREE OF POLYMERIZATION

One concept used to express the extent of a polymerization reaction is the degree of polymerization, DP. It is a number that quantifies the units of monomers present in the oligomer or polymer.

However, it is necessary here to clarify what DP exactly means because in the field of polymers, various definitions are found. IUPAC defines DP as directly the number of monomer units. This is useful in the case of homopolymers, because DP_{IUPAC} corresponds to the ratio between the weight of polymer and the weight of monomer.

However, in the literature another DP definition is more extended. In this second definition, the term DP_2 refers to number of conformational repeating units, CRU. For homopolymers, both definitions turn out to be identical, but not for copolymers, especially in polyaddition and polycondensation polymers.

To compare both definitions, visualize a hypothetic copolymer $(AB)_{1000}$. This polymer would have a DP_{IUPAC} of 2 000 (1 000 A monomers + 1 000 B monomers). However, with the second definition it would have DP_2 of 1 000 (1 000 repeating units AB). As you can see, the final value of DP is clearly different, which can be misleading.

Throughout this text to avoid any confusion, the extent of polymerization was described using a clear parameter "n" related with the structure of the polymer. In order to define it, information about the end-groups of the polymer was obtained by IR, which is very sensitive to isocyanate and carbonyl groups. No signal of isocyanate groups was detected, which indicated that terminations were hydroxyl ended (Figure 63).

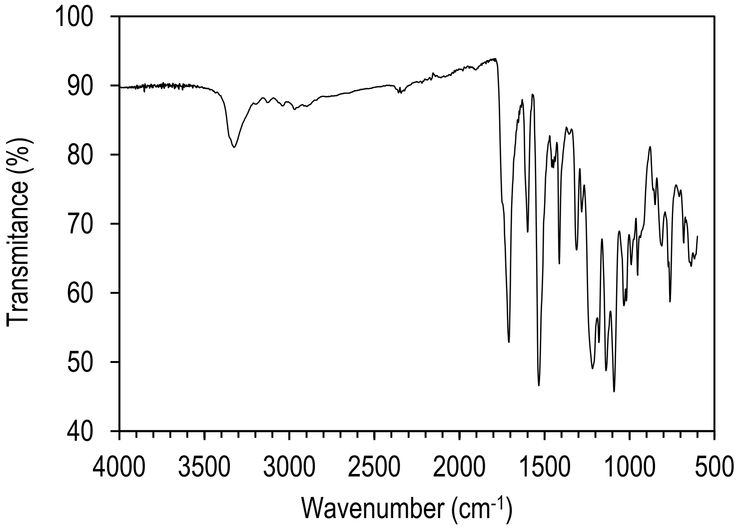
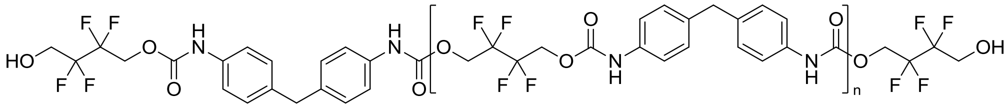


Figure 63. IR spectrum after photopolymerization of polyfluorinated diol **6a** with MDI.

Additionally, the MW of oligomers peaks in GPC matched those corresponding to structures starting and ending with diol monomer. Consequently, it was assumed that both end-groups were hydroxyl terminated.

With this information, the parameter "n" was defined as the number of CRU without considering the terminations (Figure 64). Knowing the polymer structure allowed end-group analysis by ^{19}F NMR. Polyfluorinated sections can be found in terminal positions (outside brackets) or in inner positions forming part of CRU, in a ratio between them that would be [Terminal / Inner] = 2 / n.



PTM$_n$

Figure 64. Representation of polymer PTM$_n$.

Considering this structure, MW for different polymer lengths was calculated in function of "n" and correlated to the different definitions of degree of polymerizations. According to IUPAC definition then, counting the monomers in the endings, three, and in the CRU, two times "n", results in a DP$_{IUPAC}$ = 3 + 2n. According to the second extended definition, the leftmost part in the Figure 64 is also a repeating unit, therefore, DP$_2$ = n+1 (Table 15).

Table 15. "n", degrees of polymerization and their relation with molecular weight.

n	DP$_{IUPAC}$	DP$_2$	MW (Da)
0	3	1	574

1	5	2	987
2	7	3	1 399
3	9	4	1 811
4	11	5	2 224
5	13	6	2 636
6	15	7	3 048
7	17	8	3 461
8	19	9	3 873
9	21	10	4 285
10	23	11	4 698
15	33	16	6 759
25	53	26	10 883
35	73	36	15 006
50	103	51	21 191
100	203	101	41 808

NOMENCLATURE CONSIDERATIONS

According to IUPAC Purple book[106], which concerns the polymer field, there are two proper ways to name a polymer, one based on its structure and another based on its origin. The explicit structure-based name does not allow any chance for mistake, but it's a complex nomenclature not easy to use.

Structure based name:

poly(2,2,3,3-tetrafluorooxybutane-1,4-diyl-oxycarbonylimino(methylenebis-4,1-phenylene-4,4'-diyl)iminocarbonyl)

On the other hand, source-based name describe polymers in a simpler way, based on origin monomers. However, it can be ambiguous in some cases, for example with monomers that can polymerize in more than one way (*e.g.* vinyloxiranes). Infix "*alt*" means that both monomers are alternating and are not randomly, "*ran*", distributed in the chain. As in our case there are no chances for confusion, this nomenclature was selected and the polymer was named by simply picking the initials: PTM.

Generic source-based name:

poly(2,2,3,3-tetrafluorobutan-1,4-diol-*alt*-4,4'-methylene diphenyl diisocyanate)

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[106] Hiorns, R.C.; Boucher, R. J.; Duhlev, R.; Hellwich, K. H.; Hodge, P.; Jenkins, A. D.; Jones, R. G.; Kahovec, J.; Moad, G.; Ober, C. K.; Smith, D. W.; Stepto, R. F. T.; Vairon, J. P.; Vohlídal, J. *IUPAC. Pure Appl. Chem*. **2012**. *84*, 2167-2169.

In addition it is advisable to state further structure information in the polymer name, if it is known, by using the appropriate prefixes. For example, in this case the Greek letter ω can be used to indicate that the polymer is terminated with a diol monomer.

Complete generic source-based name:

ω-(2,2,3,3-tetrafluoro-4-hydroxy-1-butoxy)-poly(2,2,3,3-tetrafluorobutan-1,4-diol-*alt*-4,4'-methylene diphenyl diisocyanate)

In order to identify a specific polymer chain length "n" as subscript was added when required. For example, PTM_3 would correspond to a polymer with an "n" of 3. When describing a polymer distribution, the "n" used would be the one calculated by ^{19}F NMR or equivalently the one that more closely matched with M_n obtained by GPC.

Although there is not a clear limit between oligomer and polymer, in this text the limit would be set arbitrary at 1 000 Da. Thus, PTM_0 and PTM_1, which GPC peaks are relatively separated, are considered oligomers while higher chains polymers.

3.2.1. MONITORING THE EVOLUTION OF THE PHOTOREACTION BY ^{19}F NMR

One advantage of using diol **6a** was the fact that allowed an easy monitoring of the evolution of the photoreaction by ^{19}F NMR. By comparison with previously prepared compounds 2,2,3,3-tetrafluoro-1-hydroxybutan-4-yl phenylcarbamate **8a** and 2,2,3,3-tetrafluorobutan-1,4-diyl bis(phenylcarbamate) **7a**, signals of fluorine atoms in the end-group and in CRU segments of polymer were identified. This provided a methodology to quantify the distribution of polyfluorinated fragments (Figure 65).

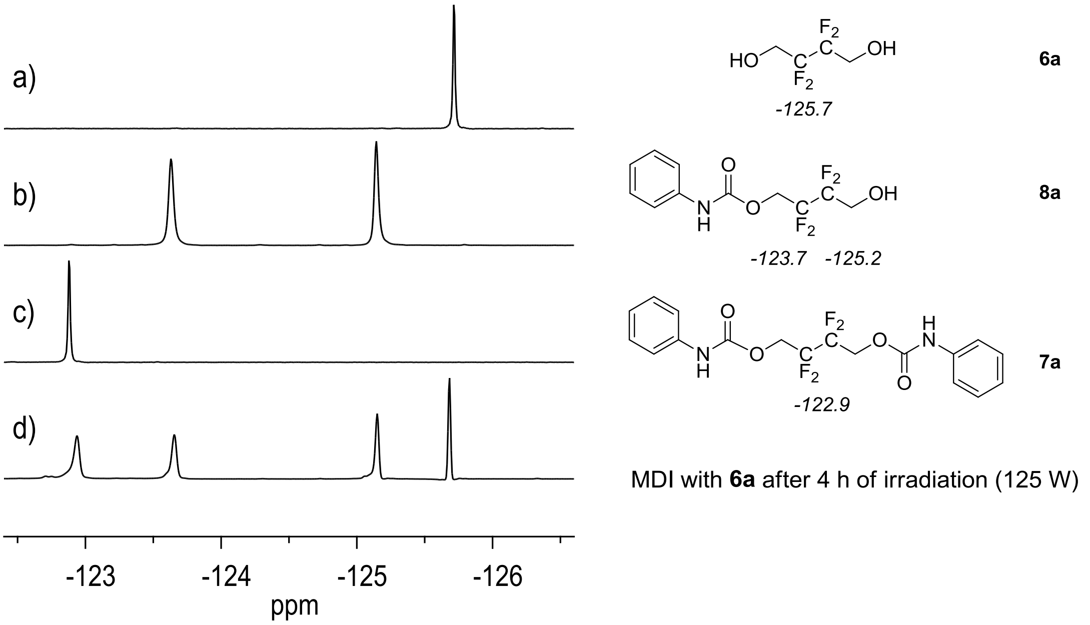
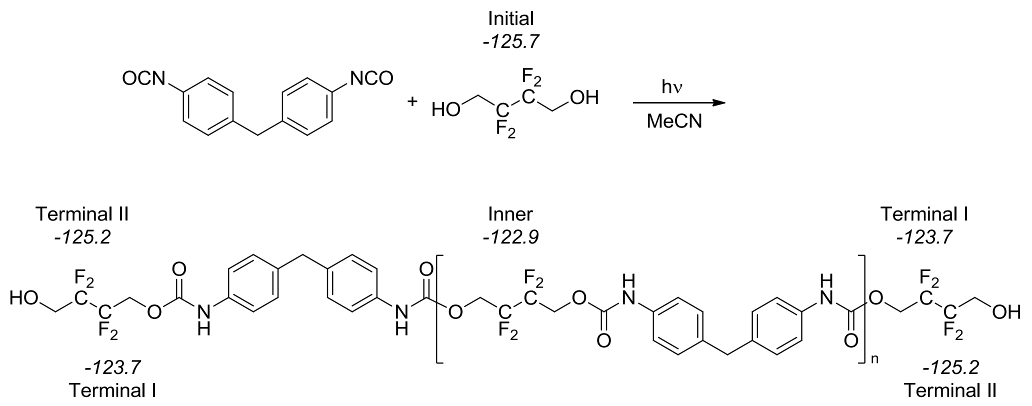


Figure 65. ^{19}F NMR spectra in acetone-d_6 of a) unreacted diol **6a**, b) hydroxyl carbamate **8a**, c) biscarbamate **7a**, d) photoreaction of MDI with diol **6a** after 4h irradiation with HPK Philips 125 W.

Initially, the symmetrical starting diol **6a** just presents one signal for the two centrals CF_2 (-125.7 ppm). During polymerization, when it has only reacted by one end, it has a structure similar to **8a** (CF_2CH_2OH, -125.2 ppm; $CF_2CH_2OC(O)$, -123.7 ppm). When diol has reacted by both ends, and form part of a CRU, this fragment could be considered symmetric as in **7a**, showing just one signal for both CF_2 (-122.9 ppm) (Scheme 56).



Scheme 56. Photopolymerization of MDI with **6a** to form PTM. ^{19}F NMR chemical shifts in acetone-d$_6$ in italics.

Once signals were identified and assigned, ^{19}F NMR could be used for quantification of the monomer consumption and also to calculate the relative proportions of [Terminal/Inner] polyfluorinated fragments. When the mixture of MDI and diol **6a** ([MDI]$_0$ = [**6a**]$_0$ = 5 mM) was irradiated in MeCN for 4 h with a HPK Philips 125 W lamp, a ratio of 22 % of unreacted **6a**, 47 % of terminal and 31 % of CRU (inner fragments) was established by ^{19}F NMR. From this information, the value n_{NMR} = 1.3 was calculated in this particular case.

$$[Terminal\ /\ Inner] = \frac{2}{n} \qquad (30)$$

On the other hand, it was also possible to calculate “n” by GPC (M_n = 973 Da; M_w = $1.82 \cdot 10^3$ Da; Đ = 1.87). Number-average molecular weight can be visualized as the addition of external part (equivalent to PTM$_0$) and the inner part inside brackets (“n” times the conformational repeating unit CRU). Thereby, calculating its value from GPC results was n_{GPC} = 1.0.

$$M_n = MW(PTM_0) + n \cdot MW(CRU) \qquad (31)$$

In comparison, values of “calculated by both methods (n_{GPC} = 1.0; n_{NMR} = 1.3) indicate a similar oligomer size, not being discordant one with the other.

From the previous results, it was significant that during the polymerization monomer diol **6a** was not completely consumed after 4 h of irradiation with a 125 W lamp. This conditions wwere enough for the photoreaction of polyfluorinated diols with PhNCO to be completed. By using a longer irradiation times, 8 h, finally diol was nearly consumed. (Figure 66, a). Thus, from 4 to 8 h of irradiation time, diol was consumed to form more terminations, however, the amount of inner fragments (CRU) did not increased, which meant that the already formed chains were not growing (Figure 66, b).

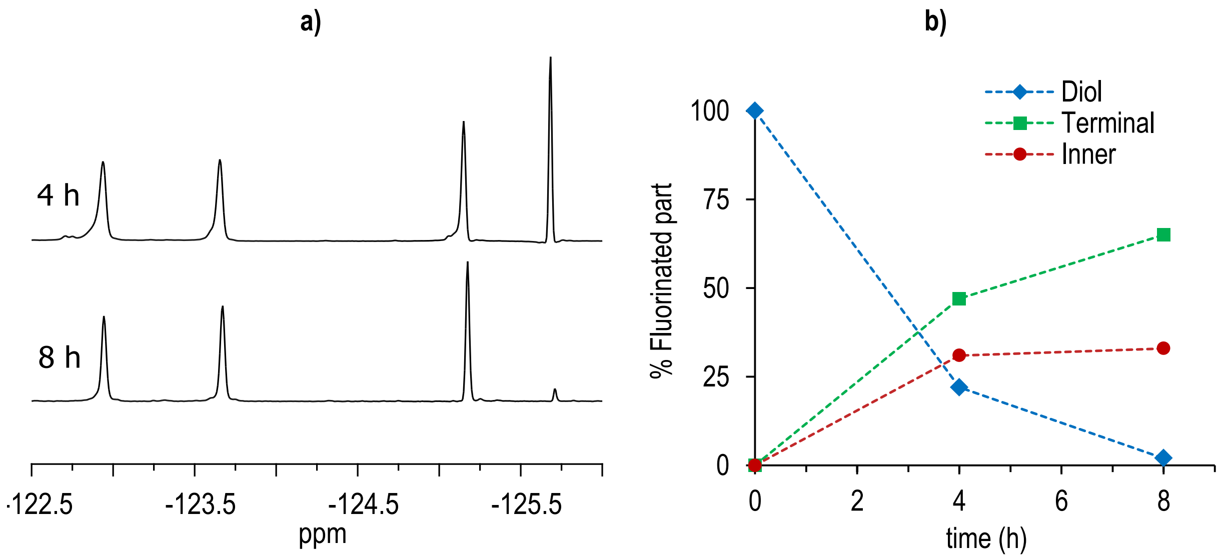


Figure 66. Evolution of photopolymerization of MDI and **6a** using a 125 W lamp.
a) ^{19}F NMR at 4 h or 8 h irradiation time with a 125 W lamp.
b) Polyfluorinated part distribution in function of irradiation time.

3.2.2. THE USE OF A MORE POWERFUL IRRADIATION SOURCE

The optimized conditions for the photoreaction of polyfluorinated diols with PhNCO were not enough to accomplish total conversion in the photopolymerization of diol **6a** with MDI. The first option explored was to increase the irradiation time (as commented on the previous section) but another option was to use a more powerful irradiation source.

Thus, mercury vapor lamp used (Philips HPK 125 W) was changed to a more powerful lamp (RQ3040 400 W; from Photochemical reactors ltd.) as irradiation source (Figure 67).

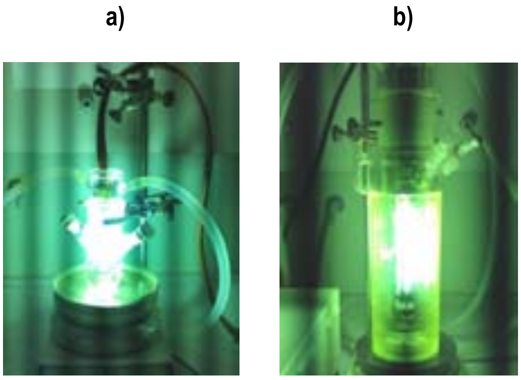


Figure 67. Picture of photoreactors. a) 50 mL reactor with a 125 W lamp. b) 750 mL reactor with a 400 W lamp.

Just for comparison purpose, a domestic light bulb has approximately a light output 1300 lm. However, a chemist would feel more comfortable knowing that this corresponds to $4.9 \cdot 10^{18}$ photons/s. According to specifications, a brand new Philips HPK 125 W lamp have a luminous flux of 4750 lm or light output of $1.81 \cdot 10^{19}$ photons/s, a little bit more than three domestic light bulbs. The RQ3040 400 W lamp has a light output of 5.00·10^{19} photons/s, approximately ten light bulbs and about three times the output of a 125 W lamp.

After irradiating 1 h the reaction of **6a** with MDI in MeCN with the 400 W lamp there was a 71 % of unreacted diol. One hour latter (2 h of irradiation) there was just a 5 %, and it got completely consumed at 4 h (Figure 68). However, when using this lamp, an insoluble *yellow solid* appeared. In different reaction runs the amount of this solid was between 15 to 20 % of total dry mass (More details about this *yellow solid* Section 3.2.4.).

At short reaction times just PTM_0 is formed as there are terminations but no inner fragments formed (1 h, n_{NMR} = 0.1). After one hour, the proportion [Terminal/Inner] revealed n_{NMR} = 1.0, PTM_1 was the most abundant chain. When diol was almost consumed, with this lamp the terminations did react to produce longer polymers, PTM_5.

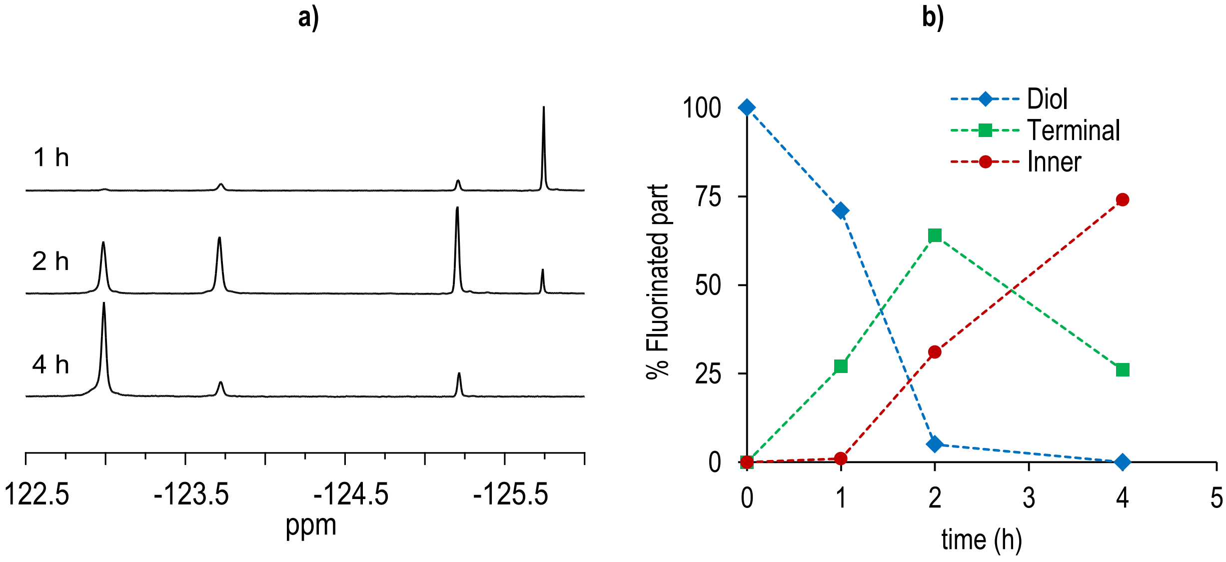


Figure 68. Evolution of photopolymerization of MDI and **6a** (C_0 = 5 mM) using a 400 W lamp.
a) ^{19}F NMR in acetone-d_6 at 1, 2 and 4 h of irradiation with a 400 W lamp
b) Polyfluorinated part distribution in function of irradiation time.

Monitoring with ^{19}F NMR and GPC interpretation were coherent with each other and provided complementary information. Initially a fast formation of PTM_0 (574 Da) was observed, its GPC peak was the main peak after 1 h of irradiation. Then, its evolution leaded to the formation of higher molecular chains and this peak decreased with time.

Most probably PTM_0 reacted to form PTM_1 (987 Da), as it was the most abundant chain after 2 h. However, after 4 h it was still the major peak, which might be indicating that this oligomer photoreacted very slowly (Figure 69, a).

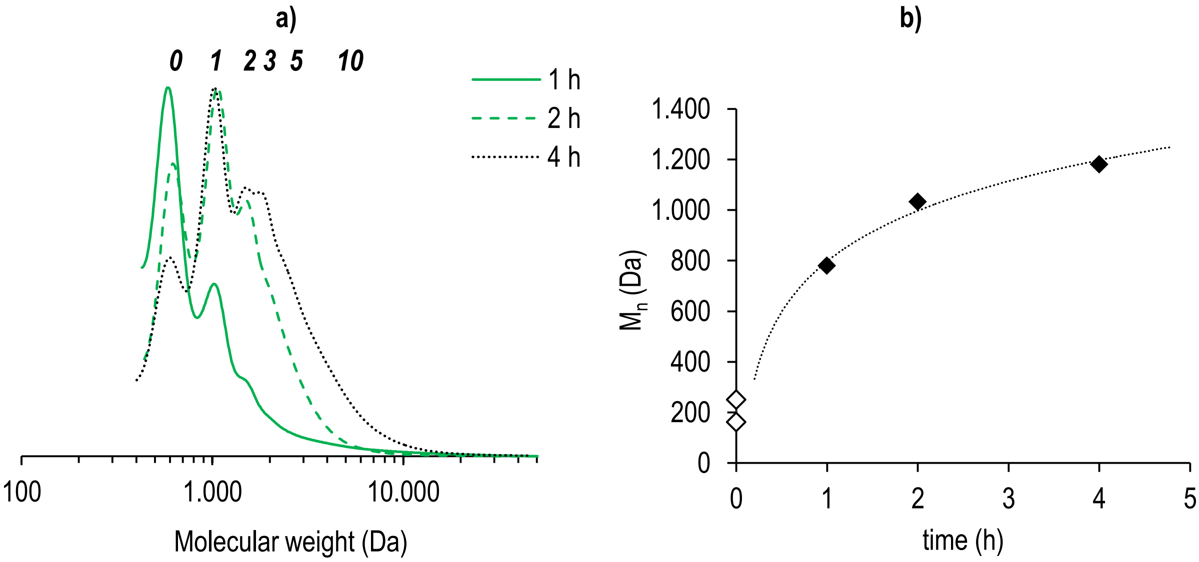


Figure 69. Evolution of photopolymerization of MDI and **6a** (C_0 = 5 mM) using a 400 W lamp.
a) GPC molecular weight distribution at different irradiation times.
b) Evolution of M_n with the irradiation time (At zero time, monomers. Dot line as eye guide).

Higher chains appeared after 2h of reaction and increased at 4 h. However, instead of continuous growing of the polymer, there seemed to be a limit and no higher polymers than approximately PTM_6 were produced (Figure 69, b).

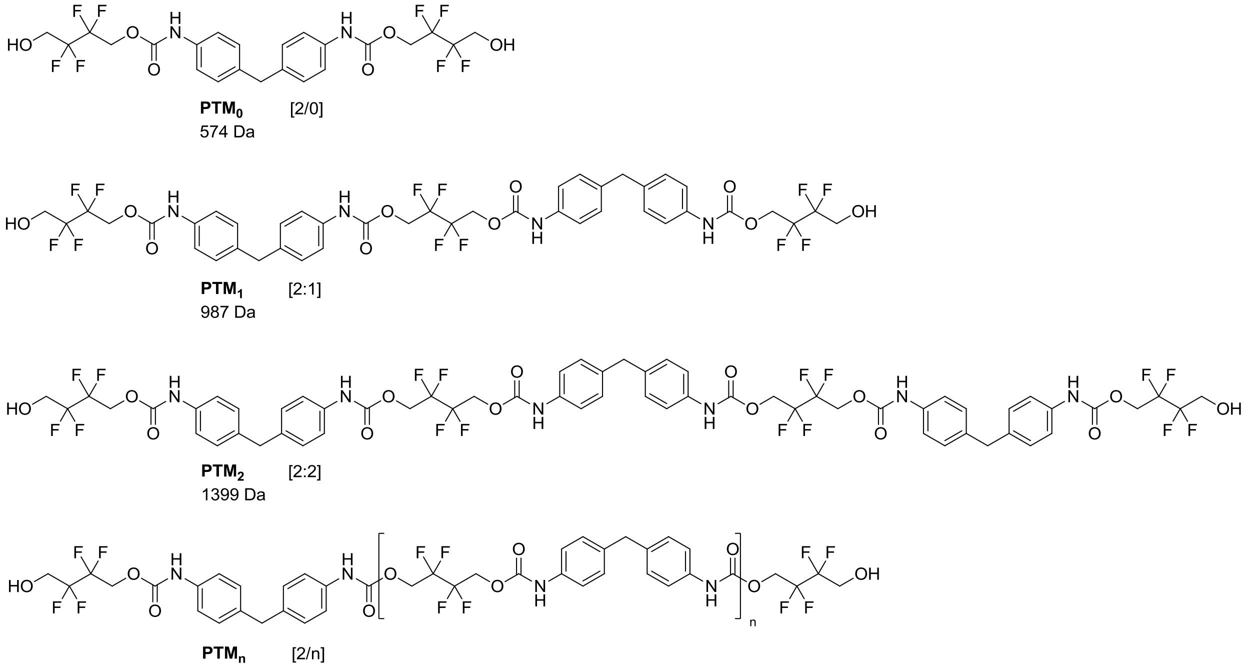


Figure 70. Structures of PTM oligomers and general polymer structure. MW and [Terminal/inner] ratio indicated.

EVOLUTION OF POLYMER STRUCTURE

By using both techniques (^{19}F NMR and by GPC) the evolution of the photopolymerization of MDI with **6a** was monitored. In order to establish relationships between the structure ([Terminal/Inner] ratio from ^{19}F NMR) and the polymer size (M_n from GPC), both data were correlated in a single graphic.

As the horizontal axis corresponds to M_n, this means that for a given M_n half the chains have lower MW and the other half higher MW. Thus, at 1 h when M_n is 780, it means that half the chains are PTM_0 and the other half correspond to all the others.

It can be seen that diol **6a** reacted to form hydroxyl terminations. It seems that only when diol is near to be consumed (After 2 h), these terminations reacted. This indicated that the terminations are less reactive than the diol (Figure 71).

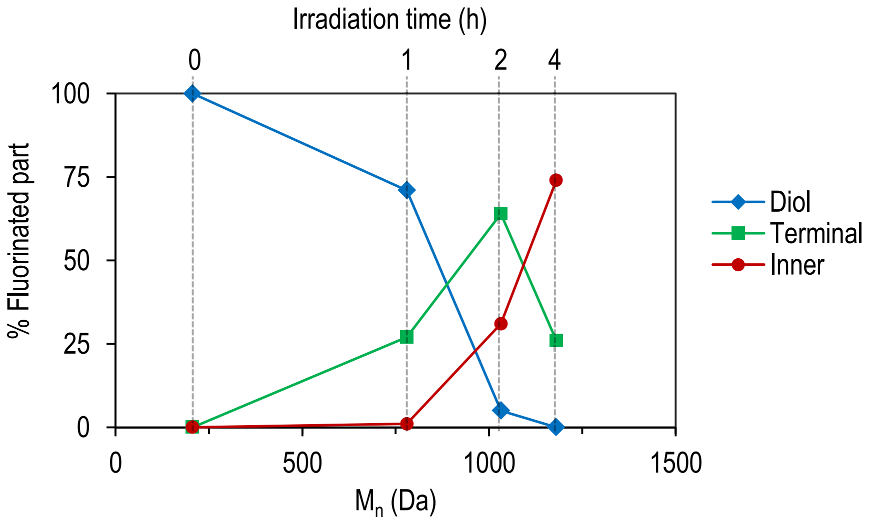


Figure 71. Correlation between distribution of polyfluorinated segments with number-average molecular mass M_n.

Thereby, first hydroxyl-ended oligomers (PTM_0 and PTM_1) accumulated and their concentration reached a maximum just before diol is completely consumed. At this point, the ratio was [Terminal/Inner] ≈ 2/1 and the M_n was around 1 000. Both are in accordance with PTM_1.

After that, hydroxyl-ended oligomers reacted to generate inner fragments. The relationship between molecular weight and amount of inner fragments is clear and logical, as polymers with higher molecular weight have more CRU units, and thus more inner fragments.

In short, diol decreases, as a reagent does. Terminal fragments accumulate and then decreased, as an intermediate would do. And finally, there was an increasing amount of inner fragments, as correspond to the final product.

LAMP COMPARISON BY GPC

The molecular weight distributions obtained by GPC from the photopolymerization of **6a** with MDI using both lamps (125 W and 400 W) in the same conditions (C_0 = 5 mM; $MeCN_{anh}$; 4 h) were compared. In both cases the polymers obtained ranged from PTM_0 to approximately PTM_5. Although distributions were different, both cases seemed to have a limit of maximum molecular weight around 3 000 (Figure 72).

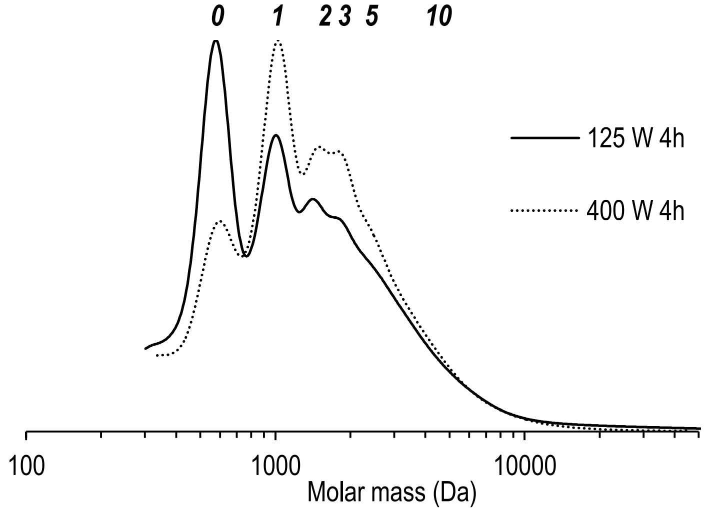


Figure 72. Comparison of lamps in the polymerization of MDI with **6a**.
Molecular weight distribution by GPC. Solid line: 125 W lamp. Dot line: 400 W lamp.

In the case of the 125 W lamps, the amount of oligomers observed were ranged in decreasing order (PTM_0 > PTM_1 >PTM_2 > PTM_3…). However, PTM_1 was the most abundant peak in the photoreaction with the 400 W lamp, followed by PTM_2 and PTM_3.

In conclusion, a distribution with higher molecular weight was obtained with the 400 W lamp ($M_n = 1.18 \cdot 10^3$ Da; $M_w = 2.06 \cdot 10^3$; Đ = 1.74) than with the 125 W lamp (M_n = 973 Da; $M_w = 1.82 \cdot 10^3$ Da; Đ = 1.87).

3.2.3. EXTRA ADDITION OF MDI

From results described in the previous section, it was apparent that hydroxyl-terminated oligomers photoreacted slower than diol (And PTM_1 slower than PTM_0). Thus, it was thought that addition of more MDI when concentration of terminations was higher could force the reaction of these dormant hydroxyls.

Thus, in the photopolymerization of **6a** with MDI after 2 h of irradiation with a 400 W lamp (% diol < 5 %), an extra equivalent of MDI was added. Then, the reaction mixture was irradiated for 2 h more, to a total irradiation time of 4 h.

As observed from the molecular weight distribution, higher molecular weights were obtained with this addition of MDI ($M_n = 1.54 \cdot 10^3$ Da; $M_w = 2.64 \cdot 10^3$; Đ = 1.71; n = 2.3) than without the addition ($M_n = 1.18 \cdot 10^3$ Da; $M_w = 2.06 \cdot 10^3$; Đ = 1.74; n = 1.5) (Figure 73).

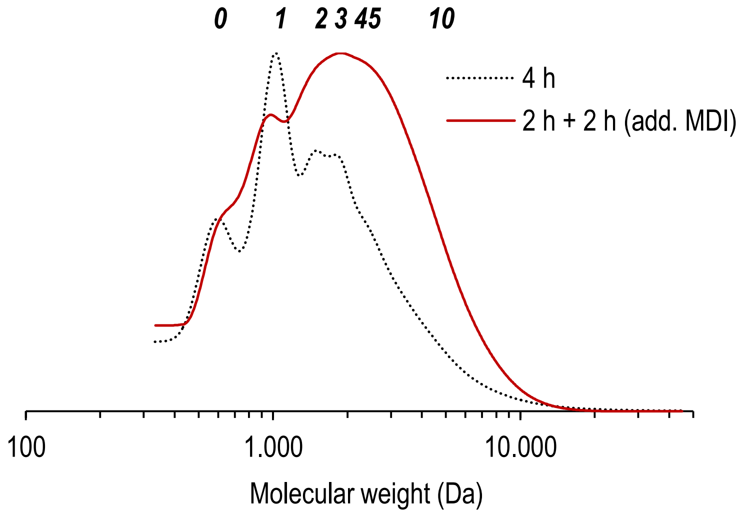


Figure 73. Effect of addition of extra MDI in the photopolymerization of MDI and **6a** (400 W lamp). Molecular weight distribution obtained by GPC. Black dot line: 4 h of continuous irradiation. Red: 2 h irradiation, extra addition of MDI, 2 h of irradiation.

The main polymer obtained with the extra addition was no longer PTM_1. Instead it was between it was between PTM_2 and PTM_3. In spite of this increase, there still seemed to be a molecular weight limit approximately 6 000 (PTM_{14}) were obtained.

In addition, in the photoreaction with the extra addition of MDI a larger amount of the above-mentioned insoluble *yellow solid* was isolated.

There were several possibilities that explained the formation of this *yellow solid*. It could be insoluble high MW polymers, which would explain the observed limit in molecular weight. However, other possibilities existed; therefore more information about this insoluble material would provide interesting insight into the reaction.

3.2.4. IR STUDY OF THE UNSOLUBLE SOLID

The amount of insoluble *yellow solid* generated in different runs of the photoreaction between MDI and **6a** using the 400 W lamp was about 15~20 % of total dry mass. This *yellow solid* was insoluble in HBD solvents (EtOH, TFE), polar (MeCN, DMF, THF, acetone, DMSO) or apolar (Hexanes, toluene) solvents, being that a major drawback for its analysis with the previously used techniques.

However, information about its nature was obtained by attenuated total reflectance infrared spectroscopy ATR-IR. This technique is especially suitable for the analysis of carbonyl group in all its different variations.

From higher wavenumbers to lower, the first peak appeared at 3300 cm^{-1}. This band correspond to the presence of an unassociated NH or OH stretching, although by itself this did not report any key information, indicated the presence of certain functional groups (Figure 71, a).

More revealing was the signal at 2294 cm^{-1}, characteristic of the isocyanate functional group. Although it was weak, compared with the one in pure MDI, it indicated the existence of unreacted terminal isocyanate in the *yellow solid* (Figure 74, a).

Observing the carbonyl stretching region (loosely between 1800 and 1600 cm^{-1}) more meaningful information was extracted. In this region, the polymer PTM presented its carbamate signal at 1710 cm^{-1}. However, this peak was absent in the *yellow solid;* hence carbamate links were not part of the solid. Then, the possibility of the solid being an insoluble PTM long chain was dismissed (Figure 74, b).

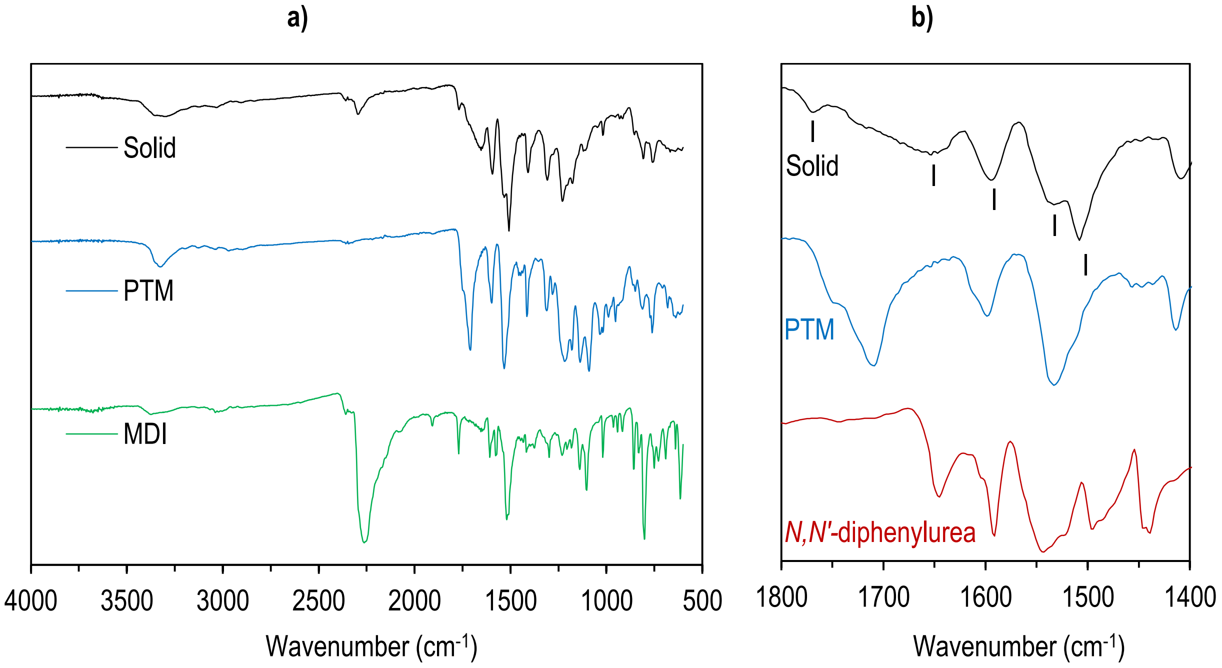


Figure 74. Infrared spectra comparison. a) *Yellow solid*, PTM and MDI. b) *Yellow solid*, PTM and N,N'-diphenylurea.

The signal that that the *yellow solid* presented at 1770 cm^{-1} could correspond to the carbonyl stretching of a four-member ring of 2,4-diazetidine-1,3-dione, present in MDI dimer (Explained in Section I.2.1.; more details below).

Other revealing signals were the ones at 1647 and 1537 cm^{-1}. Taken together, this pair of signals could correspond to a urea (CO st and N-H δ, respectively). In order to confirm that, *N,N'*-diphenylurea was prepared by reacting phenyl isocyanate with aniline. This example of diaromatic urea had comparable bands at 1643 and 1544 cm^{-1}, suggesting the presence of aromatic urea groups in the insoluble *yellow solid* (Figure 74, b).

The peak observed in all cases around 1593-1598 cm^{-1} due to aromatic carbon-carbon stretching confirmed the presence of aromatic rings, and thus, that this by-product involved MDI, but did not further clarify the structure.

From this IR study, it is important to highlight that the *yellow solid* was not derived from a PTM polymer (no carbamate was present). Only evidences of MDI and derivates, like dimer or urea, were found, being the urea linkage predominant.

Formation of MDI dimer is a temperature dependent reaction. In solid state, reaction rate is higher before melting, between 35 to 40 ºC (More details in the next section).

The formation of a diaromatic urea might be explained by reaction of MDI with an arylamine. They could be formed in the reaction mixture by two different ways: by the presence of water or by a photo-degradation process.

The presence of water could come from air moisture or a not properly dried solvent. Water could react with isocyanate to form unstable carbamic acid and after carbon dioxide elimination it would produce an arylamine. Although presence of water was a real possibility, this reaction was carried on under nitrogen atmosphere and special care had been taken to remove water from solvent. However, if water in solvent was the cause of urea formation, this by-reaction would also have taken place in the photoreaction using 125 W lamp, but in those reactions formation of this *yellow solid* was not observed.

The other possible way to the formation of free arylamine would be a photodegradation process, in a process mechanistically related with photo-Fries rearrangement. This rearrangement, in the case of alkyl *N*-arylcarbamates would produce aromatic aminoesters that could react with isocyanates and even with carbamates groups (Scheme 57).[107]

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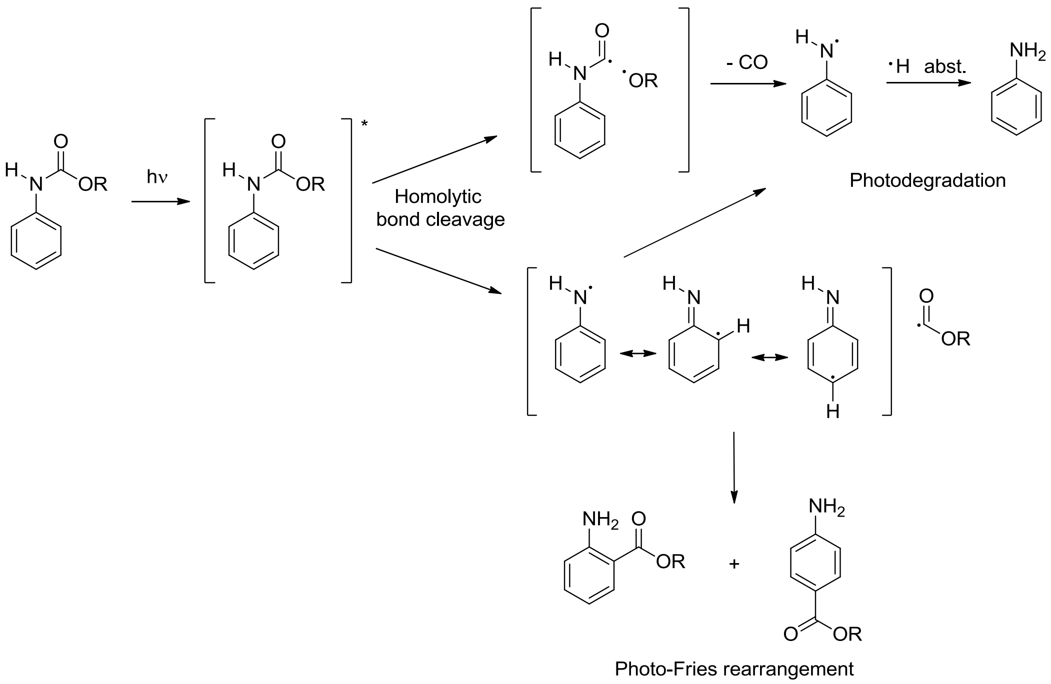
[107] Herweh, J. E.; Hoyle, C. E. *J. Org. Chem*. **1980**, *45*, 2195-2201.



Scheme 57. Photo-Fries rearrangement mechanism and amine formation.[107]

In apolar solvents that favor solvent cage, photo-Fries rearrangement products are favored. However, polar solvents tend more to solvate, favoring by-reaction to produce arylamine.[107]

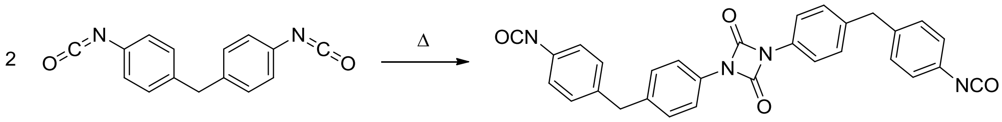
In conditions of photopolymerization (*i.e.* strong irradiation in MeCN), the formation of an arylamines derived from a carbamate moiety should not be surprising. Using a less powerful lamp, the irradiation might not be enough for this photodegradation to be observed, and thus, the solid would not be formed.

Thereby, the insoluble *yellow solid* seemed to be formed mainly by urea derivates generated by the presence of arylamine. Probably, they came from a photodegradation of carbamate links under powerful irradiation.

3.2.5. EFFECT OF THE TEMPERATURE

Isocyanates can undergo dimerization reaction by a thermal [2+2] cycloaddition of two CN double bonds. Although it is a pericyclic reaction of 4 π electrons, which in principle is thermally forbidden, in isocyanates there are orthogonal π orbitals that allow a crossed transition state (Scheme 58).[108]

Formation of four-membered ring 2,4-diazetidine-1,3-dione MDI dimer is a temperature dependent reaction, that should be avoided during MDI storage. As its maxim rate is just before melting point, *i.e.* from 35 to 40 ºC, industrial large volumes of MDI are storage refrigerated below 0 ºC temperature at which dimerization is negligible.[109]



Scheme 58. [2+2] MDI dimerization process.

In principle, reducing the temperature of the photoreaction would slow down this by-reaction and lead to less MDI dimer formation.

During previously described reactions with 400 W lamp, the immersion well was cooled using with a water flow room temperature achieving a stable temperature within a range from 28 to 30 ºC. In order to reduce the reaction temperature a circulatory flow of methanol at -10 ºC was used instead. In these conditions, the photoreaction temperature was monitored to be in the range -5 ºC to 0 ºC during the irradiation time.

Performing the photoreaction of diol **6a** with MDI using 400 W lamp at that low temperature reduced the amount of insoluble solid, but no to a great extend. The *yellow solid* (15~20 % of dry mass in the photoreaction at 30 ºC) was reduced to a bit less than 10 % in the photoreaction at 0 ºC. Although it was a significant decrease, insoluble solid still was an important part.

In the photopolymerization at 0 ºC, at least two different facts deserved attention. One was the formation of higher molecular weight polymers than in the photoreaction at 30 ºC, reaching up to 30 000 Da. The other fact was the persistence of a single peak around 1 000 Da in the molecular weight distribution (Figure 75).

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[108] Ulrich, H. *Cumulenes in Click Reactions*, 1st ed.; Wiley: West Sussex, United Kingdom, 2009. ISBN: 978-0-470-77932-3.
[109] Szycher, M. *Szycher's Handbook of Polyurethanes,* 2nd ed.; CRC Press: Florida, USA, 2012. ISBN: 978-1439839584.

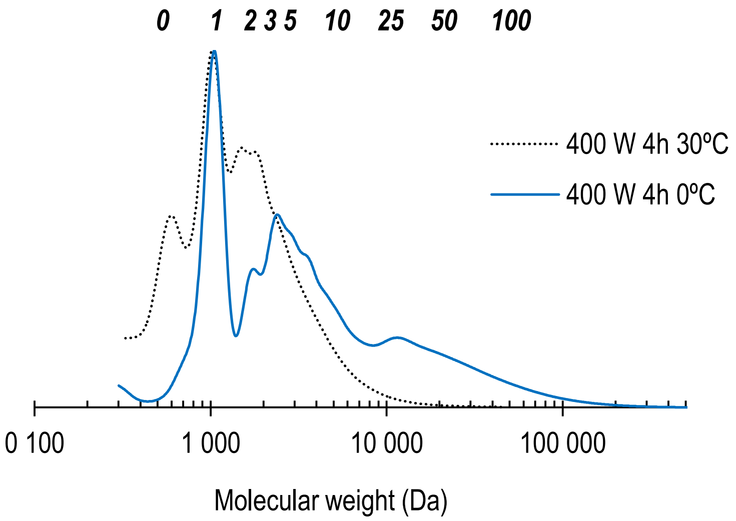

Figure 75. Effect of temperature in the photopolymerization of MDI and **6a** (4 h; 400 W lamp). Molecular weight distribution obtained by GPC. Black dot line: 30 ºC. Blue line: 0 ºC.

In order to identify this persistent peak, high molecular weight fractions (centered in PTM_{35} (M_n = $1.51 \cdot 10^4$ Da; M_w = $2.86 \cdot 10^4$ Da; Đ = 1.90) were gradually removed by successive precipitations of the mixture using THF/pentane until the peak around 1 000 was obtained as a major product (Figure 76).

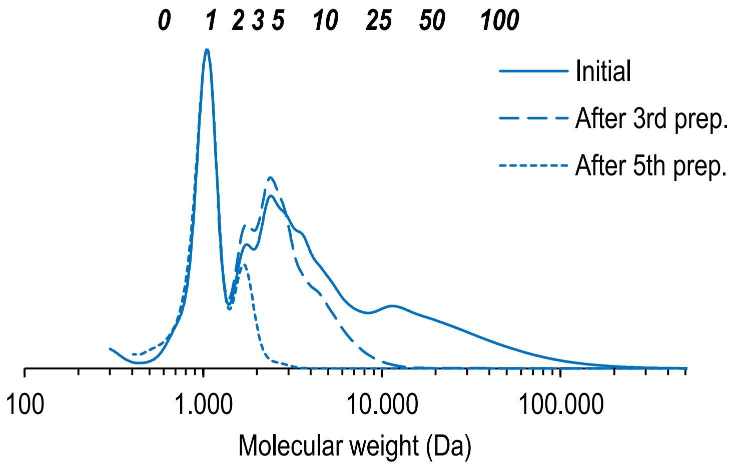

Figure 76. Consecutive precipitations of high molecular weight polymers. MW distribution obtained by GPC. Solid line: Photopolymerization of MDI and **6a** at 0ºC. Dash line: After 3 precipitations. Dot line: After 5 precipitation.

Then, this GPC peak around 1 000 Da could be undoubtfully assigned by HRMS as PTM_1 (m/z calc. for $C_{42}H_{39}F_{12}N_4O_{10}$ $[M+H]^+$ 987.2500; found 987.2469). Curiously, neither the smaller PTM_0, nor the longer ones PTM_2, PTM_3, etc. seemed especially favored. It was not easy to propose even a speculative hypothesis for the selective formation of PTM_1.

In order to find extra information, this oligomer was modeled.[110] After molecular dynamics simulation and energy minimization, it was found that preferred conformations were folded; a fact that perhaps could affect its reactivity (Figure 77).

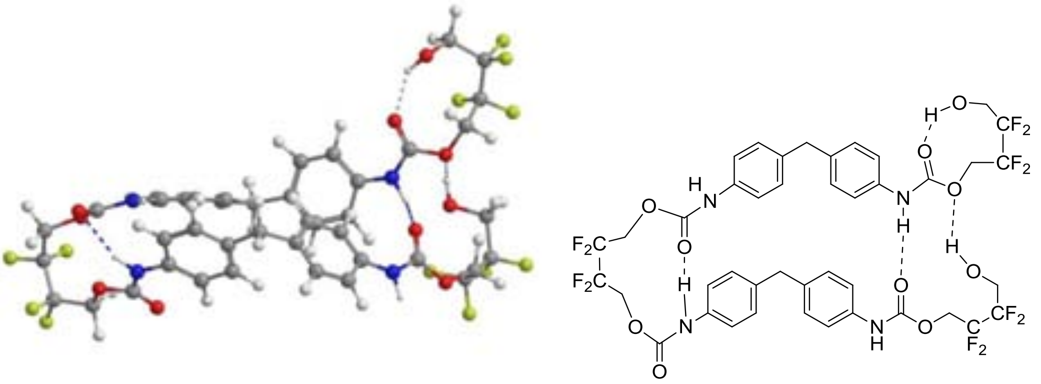

Figure 77. PTM_1 minimum energy conformation.[110]

This structure simulation showed several non-covalent interactions that contribute to higher conformation stability. The internal hydrogen bonds formed between terminal hydroxyl (or NH from a carbamate link) as hydrogen bond donors and a carbonyl of a carbamates as acceptor would sustain a folded conformation.

What is important to remark is that in a structure like that, the terminal hydroxyl groups (the ones that should react) are not available to react because they are forming hydrogen bonds. This fact was related with the proposed mechanism, in which a hydrogen bond complex alcohol/isocyanate should be formed before photoreacting. If this complex cannot be formed because the end-group hydroxyl is involved in intramolecular hydrogen bonds, reaction would not take place. This is, at least, a plausible explanation for the lack of reactivity of this molecule that was coherent with mechanistic proposal.

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[110] Energy minimization after molecular dynamics simulation. MM2 method embedded in Chem3D Pro 12.0, suite ChemBioOffice 2010.

3.2.6. CONCLUSIONS IN THE STUDY OF PHOTOPOLYMERIZATION OF DIOL 6A WITH MDI

In this chapter, photopolymerization between diol **6a** (2,2,3,3-tetrafluorobutan-1,4-diol) and MDI (4,4'-methyle diphenyl diisocyanate) has been assayed following process by ^{19}F NMR and polymer formation by GPC.

The effect of lamp power was a key factor in this step-growth photopolymerization. With the use of a more powerful lamp, higher molecular weights were achieved but there seemed to be the same MW limit as polymers higher than PTM_6 were not produced. This problem was partially overcome by extra addition of MDI at mid reaction, as polymers reached up to PTM_{14}, but this also increased the amount of an insoluble *yellow solid* generated with the more powerful lamp.

Trying to solve the MW limitation and to reduce the amount of insoluble solid (probably ureas), the importance of temperature was found. At lower temperatures, higher polymers PTM_{35} were accessible. However, the photoreaction seemed stacked by the lower relative reactivity of PTM_1 due to the existence of internal hydrogen bonding.

3.3. PRELIMINARY STUDY: QUASI-PERFLUORINATED POLYURETHANES FORMATION

Up to this point, the study involved the photoreaction of a polyfluorinated diol with an aromatic diisocyanate. However, we were also interested in the preparation of complete (or almost complete) perfluorinated polyurethanes. In this case, the reaction should involve a perfluorinated diisocyanate instead of a hydrocarbonated one.

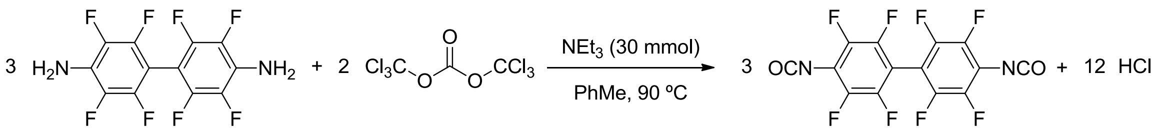
Although polyfluorinated diols are available commercially, it was not possible to find any perfluorinated aromatic diisocyanate. Thus, the first step was to prepare it.

3.3.1. PREPARATION OF A PERFLUORINATED DIISOCYANATE

The standard procedure of synthesis of isocyanates starts from an amine. However, there was not a wide range of aromatic perfluorinated diamines available. The one that seemed to suit the most our purpose was perfluoro-(1,1'-biphenyl)-4,4'-diamine. The diisocyanates derived from this amine will differ from MDI in the fluorine atoms, but also in the fact that both aromatic rings are directly attached without any methylene spacing group as in MDI, which might affect the reactivity.

Traditional method for preparing isocyanates from amines implies the use of phosgene Cl_2CO, a gas so toxic that was used as a chemical weapon in the World War I. An alternative to phosgene is the use of bis(trichloromethyl)carbonate or triphosgene, a suitable substitute for laboratory procedures. As a solid, it has a low vapor pressure, being easier and safer to handle. Nevertheless, it generates three molecules of phosgene, so it must always be handled in the fumehood, avoiding moisture and using with extreme caution.

In this case, the reaction of the perfluorinated diamine **15** with triphosgene **16** produced perfluorinated diisocyanate **17** in a 92 % of isolated yield (Scheme 59).



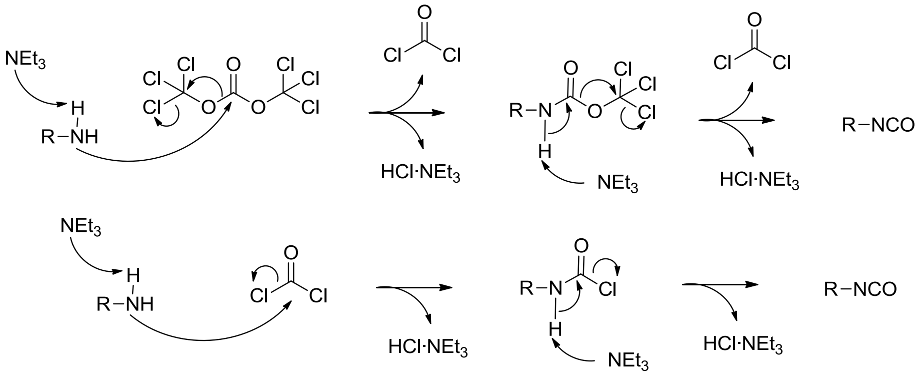
15
5.0 mmol

16
4.5 mmol

17
92 %

Scheme 59. Preparation of a perfluorinated aromatic diisocyanate.

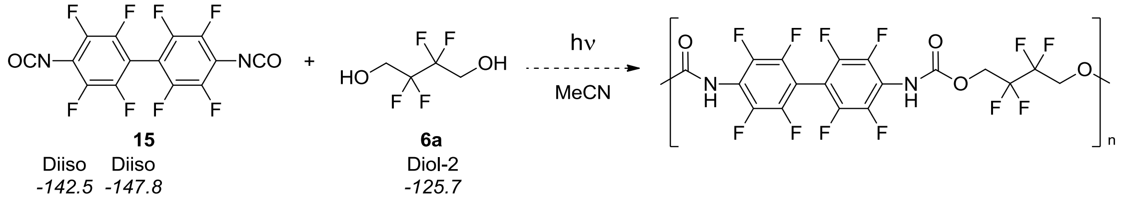
The described reaction mechanism starts by the attack of the amine to triphosgene assisted by a base. This produces a trichloromethylcarbamate derived from the amine and liberates a phosgene molecule. This carbamate further evolves to produce the final isocyanate by eliminating hydrochloric acid and another phosgene molecule. The molecules of phosgene generated also react with more amine to produce the desired isocyanate (Scheme 60).



Scheme 60. Reaction mechanism of isocyanate formation with triphosgene and phosgene.

3.3.2. PHOTOREACTION OF PERFLUORINATED DIISOCYANATE AND POLYFLUORINATED DIOL

Using perfluorinated diisocyanate **17**, the photopolymerization with diol **6a** was tested. The conditions used ($[\text{diiso}]_0 = [\text{diol}]_0 = 5$ mM; 400 W lamp, acetonitrile, 0 °C) were the ones optimized for the photoreaction of MDI with **6a** (Scheme 61).



Scheme 61. Photopolymerization of perfluorinated diisocyanate **17** with diol **6a**.
^{19}F NMR chemical shifts (ppm) in acetone-d$_6$ in italics.

However, after 4 h of irradiation with a 400 W lamp the monomers were not completely consumed. In fact, by ^{19}F NMR it was measured that the amount of initial diol **6a** (^{19}F NMR: -125.7 ppm) was still 67 % of the initial amount, just a 33 % being consumed.

From the consumed diol, 85 % had reacted by just one hydroxyl group and were occupying terminal positions (^{19}F NMR: -125.1; -123.8 ppm). The rest, the other 15 %, reacted by both ends forming inner parts of the chain (^{19}F NMR: -123.6 ppm) (Figure 78).

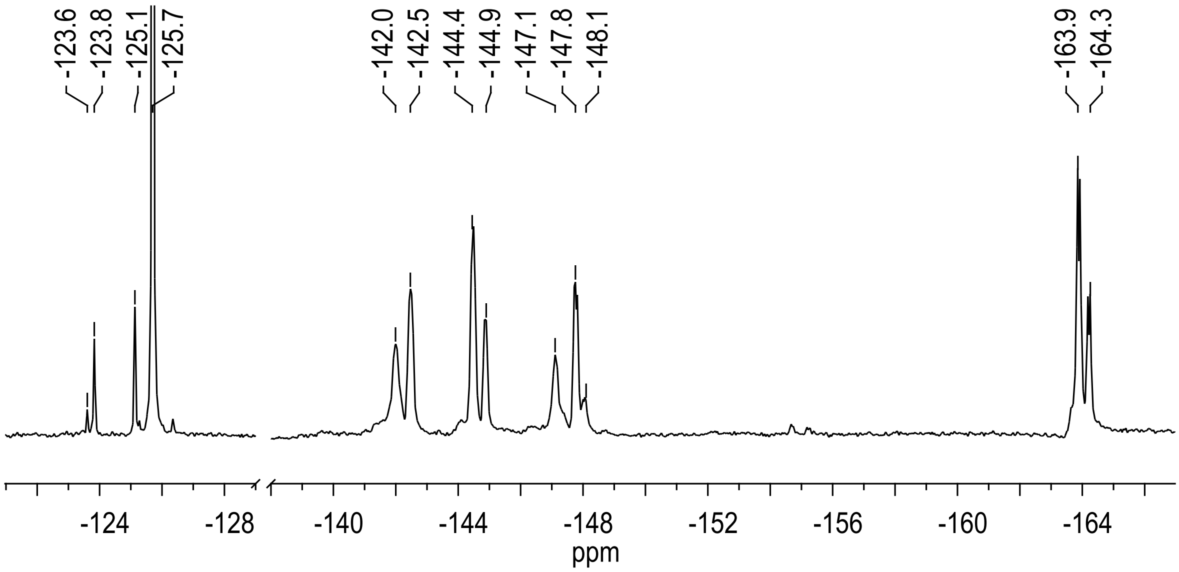


Figure 78. ^{19}F NMR in acetone-d_6 of the photopolymerization of diol **6a** with diisocyanate **17** after 4h of irradiation.

The ^{19}F NMR section of fluoroaromatic region showed an overlap of different peaks, being difficult to identify the different species present. It was possible to quantify that the remaining diisocyanate **17** (^{19}F NMR: -147.8; -142.5 ppm) was just 24 % of initial amount. Presence of polyfluorinated aromatic amine compounds was also observed (^{19}F NMR: -163.9; -164.3 ppm). The other peaks in the region from -140 to -150 ppm possibly correspond to diisocyanate reacted by one or both sides (Figure 78).

The discrepancy between remnant amount of diol **6a** (67 %) and the remnant of diisocyanate **17** (just 24 %) and the mixture observed in the perfluoroaromatic region indicated that the diisocyanate intervened in several by-reactions, not just carbamate formation.

Analysis by GPC indicated the presence of diisocyanate monomer **17** (380 Da). The peaks around 900, 1500 and 2000 Da seemed to coincide with oligomers double-ended with isocyanate groups (922, 1467 and 2007 Da respectively) (Figure 79 and Figure 80).

Despite the reactivity of PhNCO and pentafluorophenyl isocyanate **10** in front of fluorinated diols was similar (Section 2.3), perfluorinated diisocyanate **17** seemed to be less reactive towards fluorinated diols than MDI. As fluorine atoms seemed not responsible of the lower reactivity, perhaps it was because both aromatic rings were directly attached without a methylene spacing group.

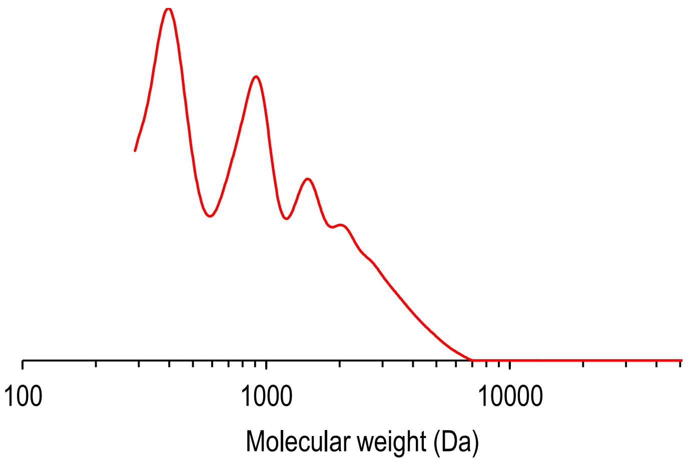


Figure 79. Molecular weight distribution after photoreaction of perfluorinated diisocyanate **17** with diol **6a**.

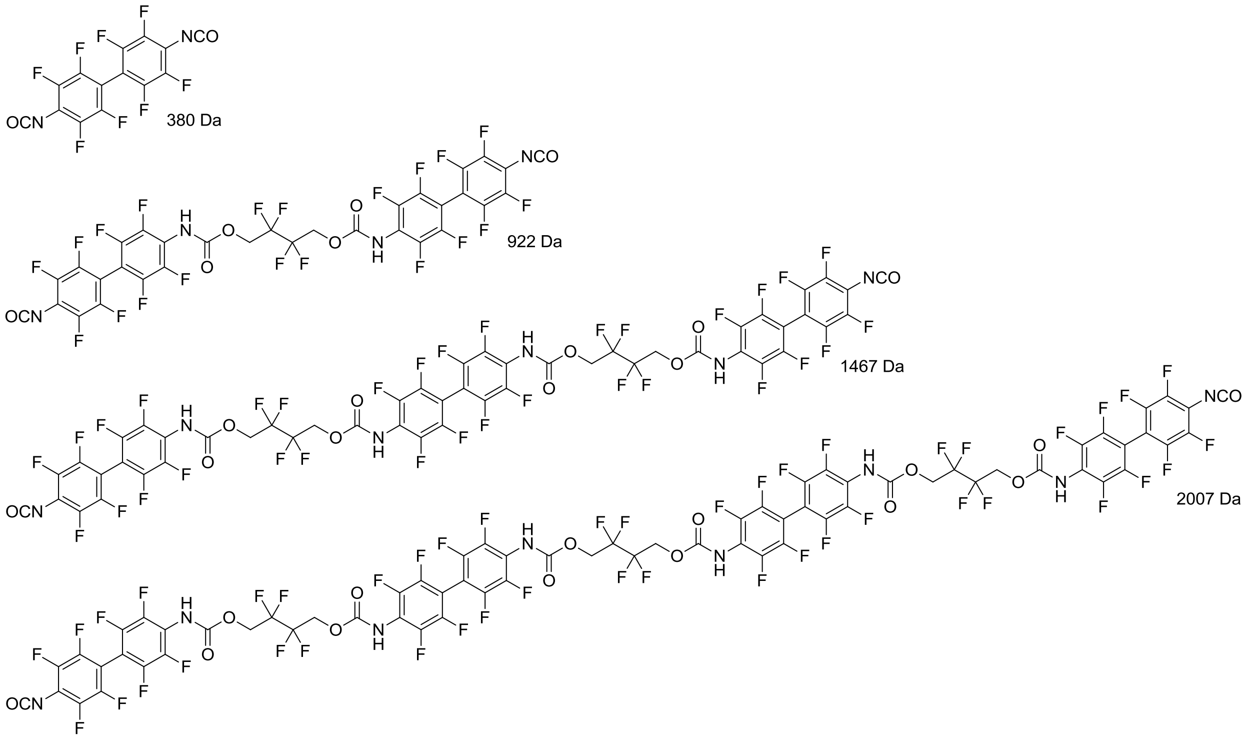


Figure 80. Monomer and oligomers that match with the peaks in the molecular weight distribution.

In spite of being far from a complete polymerization success, the photoreaction took place to some extent. The development of this process will be a future line of research directed to the preparation of quasi-perfluorinated polyurethanes.

3.4. PRELIMINARY STUDY: POLYURETHANE FORMATION FROM BISPHENOL

In order check if the photochemical methodology was limited to the reaction of MDI with polyfluorinated diols, the photopolymerization of other acidic non-fluorinated hydroxyl compounds was studied. One of the most used hydroxyl compounds with a similar acidity to polyfluorinated alcohols are phenols. The reactions of PhNCO with phenols did not take place trough free-radical intermediates (Section 1.3.1.). However, perhaps it was possible to activate the alternative photoreaction and take advantage of the knowledge acquired. Thus, the corresponding photopolymerization between MDI and a bisphenol was explored.

3.4.1. BISPHENOL-A

The most used aromatic diols in polymerizations are the family of bisphenols. This family of compounds consists in two hydroxyphenyls linked by an spacing groups. From them, the most used is 4,4'-(propane-2,2-diyl)diphenol, known by the commercial name of bisphenol A, BPA (Figure 81).

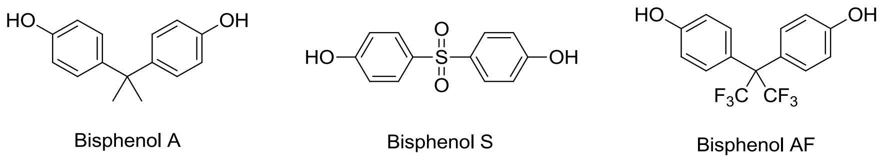


Figure 81. Structure of different bisphenols.

Nowadays BPA is not used in the production of polyurethanes. The main applications of BPA are mainly in the preparation of polycarbonates and epoxy resins.

3.4.2. PRECEDENTS OF THE REACTION OF BPA WITH MDI

As these two monomers, BPA and MDI, are some of the most used in polymer industry, it might be expected to find a significant amount of literature covering their reaction. However, in spite of their individual importance, searches on SciFinder just retrieved 13 reaction results in English. Among them, none of those publications deals with the direct reaction of MDI with BPA.

In some of these cases, reaction involves other functionalities as phosphoryl choline,[111] or *in situ* prepared bezoxazines.[112] In others, MDI is used as a modifier of epoxy resins[113] or as a resin hardener.[114]

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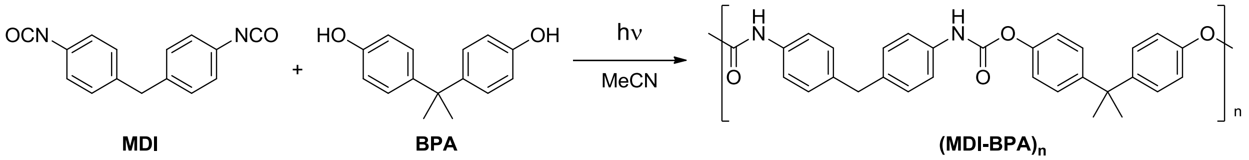
[111] Zhang, Q.; Zhu, D.; Su, F.; Xie, Y.; Ma, Z.; Shen, J. *J. Biomed. Mat. Res. Part A*, **2012**, *100A*, 1868-1876.
[112] Erden, N.; Jana, S. C. *Macromol. Chem. Phys.,* **2013**, *214*, 1225-1237.
[113] Kim, J. H.; Shin, K. M.; Rhee, H. C.; Chang, Y. J.; Jin, S. C. PCT Int. Appl., WO2013100494, 04 Jul 2013.

When MDI and BPA were both introduced in the same step, there were also other reagents involved and in all cases, presence of catalyst was required. For example, to obtain a hard/soft phase system, MDI was reacted with BPA and polyether diol using DBTDL as catalyst.[115] Other reactions involved the use of benzene-1,3,5-triol as cross-linker but catalysts as pyridine[116] or copper(I)[117] were required.

Thus, to the best of our knowledge the direct reaction of BPA and MDI has not been previously reported.

3.4.3. PHOTOCHEMICAL REACTION OF MDI WITH BPA

With the absence of precedents for this polymerization, it was tried the photochemical reaction between MDI and BPA (Scheme 62).



Scheme 62. Photopolymerization of MDI with BPA to form aromatic polyurethane

Reference compounds were prepared using photochemical conditions described in the previous chapters. MDI photoreacted with phenol to form dicarbamate **18**. ^{1}H NMR of central methylene in deuterated acetone shifted from 3.98 in MDI to 3.93 ppm in **18**. Likewise, BPA was also photoreacted with PhNCO to form **19**. In this case, the shift of the two methyl group of BPA changed from 1.60 to 1.73 ppm in **19**. The central methylene of MDI and the two methyl groups of BPA were used to follow the photoreaction. Aromatic signals were not suitable because they appeared overlapped (Figure 82).

This information allowed a monitoring of the extent of the photoreaction by ^{1}H NMR. As an example, the ^{1}H NMR spectrum of the photopolymerization of MDI and BPA under irradiation from 125 W lamp for 4 h is shown (Figure 82, e).

Analyzing this spectrum, from down field to high field, signal at 9.06 ppm corresponds to carbamate links. At 8.10 and 8.04 ppm are observed the hydroxyl proton from phenols. The first correspond to one-side reacted BPA and the second to monomer BPA (Table 16; Figure 82).

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[114] Chang, Y. J.; Shin, K. M.; Rhee, H. C.; Kim, J. H.; Jin, S. C. PCT Int. Appl., WO2013066000, 10 May 2013.

[115] Kumar, T. P.; Sivasankar, B. *J. Appl. Pol. Sci.*, **2008**, *107*, 193-202.

[116] Schirhagl, R.; Latif, U.; Podlipna, D.; Blumenstock, H.; Dickert, F.L. *Anal. Chem.*, **2012**, *84*, 3908-3913.

[117] Gonzalez-Gago, C.; Bordel, N.; Pereiro, R.; Sanz-Medel, A. *J. Mass Spectr.*, **2011**, *46*, 757-763.

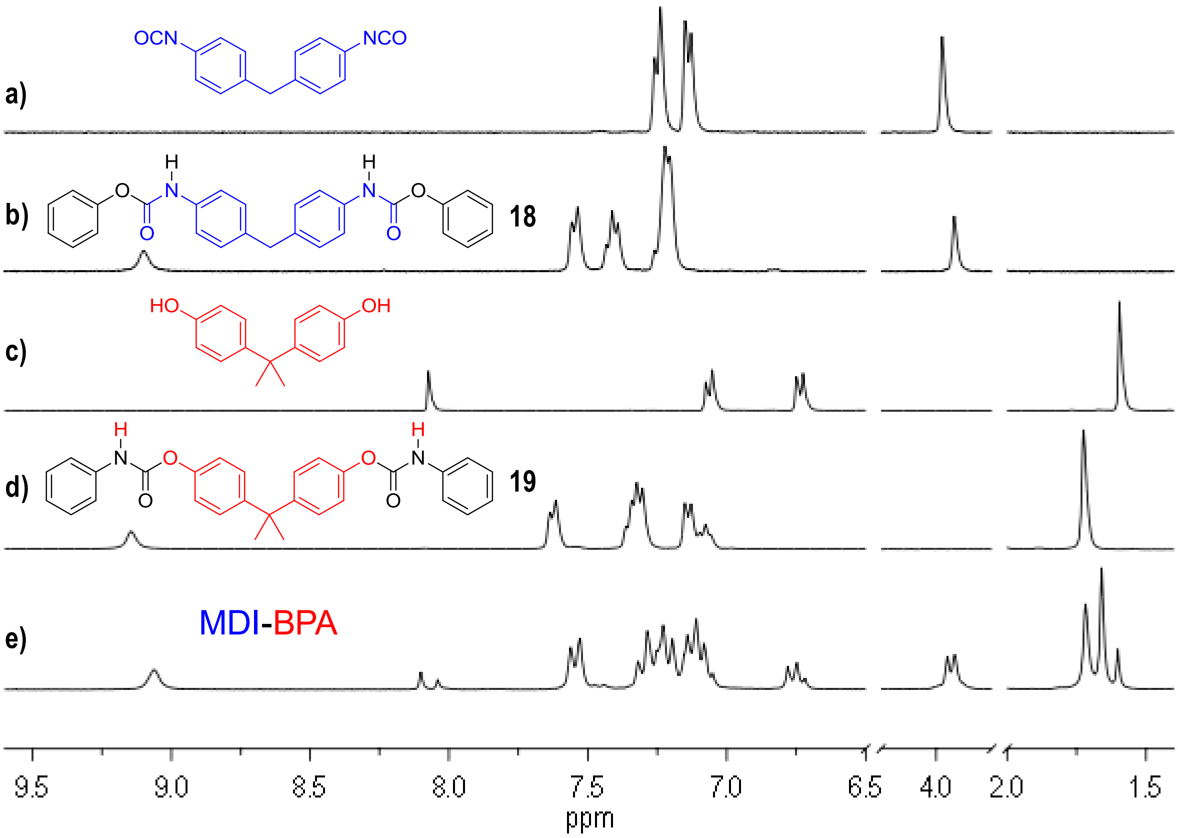


Figure 82. ^{1}H NMR in acetone-d_6 of a) MDI, b) **18**, c) BPA, d) **19** and e) MDI photoreacted with BPA ($[MDI]_0 = [BPA]_0 = 5$ mM; 50 mL $MeCN_{anh}$; HPK 125 W; 4 h).

No useful information could easily be extracted from the complex overlap of signals in the aromatic region. However, changes in the shift of MDI methylene group provided information if MDI had reacted one by one isocyanate end (2H at 3.96 ppm) or by both groups (2H 3.93 ppm).

Finally, the region that corresponded to the two methyl groups from BPA was also significant. In this region of the spectrum three signals were observed, the one at 1.72 ppm (6H) was assigned to BPA reacted by both ends; at 1.66 ppm (6H) probably correspond to BPA just reacted by one end; and the third signal at 1.60 ppm (2H) was unreacted BPA.

This information obtained from ^{1}H NMR was used to make a proposal of the most representative structures from the polymer. Approximately, considering the integrations in Table 16, the average of polymer chains would have one terminal unit MDI and one inner unit (CH_2 integrations: 2 H each); also it would have a terminal BPA and an inner BPA ($C(CH_3)_2$ integration: 6 H each) (Figure 83).

Table 16. ^{1}H NMR in acetone-d_6 of photochemical reaction of BPA and MDI ($[MDI]_0 = [BPA]_0 = 5$ mM; 50 mL MeCN; Philips HPK 125 W; 4 h).

Chemical shift (ppm)	Group	Integration (H)	Assignation
9.06	Carbamate group	3	NH
8.10	One-side reacted BPA (*Terminal*)	1	ArOH
8.04	BPA	0.3	
7.6-6.5	Aromatic overlap	*34*	aromatic
3.98	MDI	0	CH_2
3.96	One-side reacted MDI (*Terminal*)	2	
3.93	Two-sides reacted MDI (*Inner*, type **18**)	2	
1.72	Two-sides reacted BPA (*Inner*, type **19**)	6	$C(CH_3)_2$
1.66	One-side reacted BPA (*Terminal*)	6	
1.60	BPA	1.5	

$BPA_{Terminal}$-MDI_{Inner}-BPA_{Inner}-$MDI_{Terminal}$

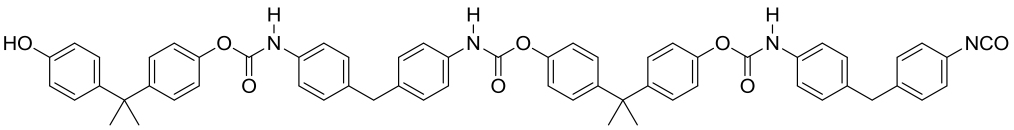


Figure 83. Most representative structure found by ^{1}H NMR.

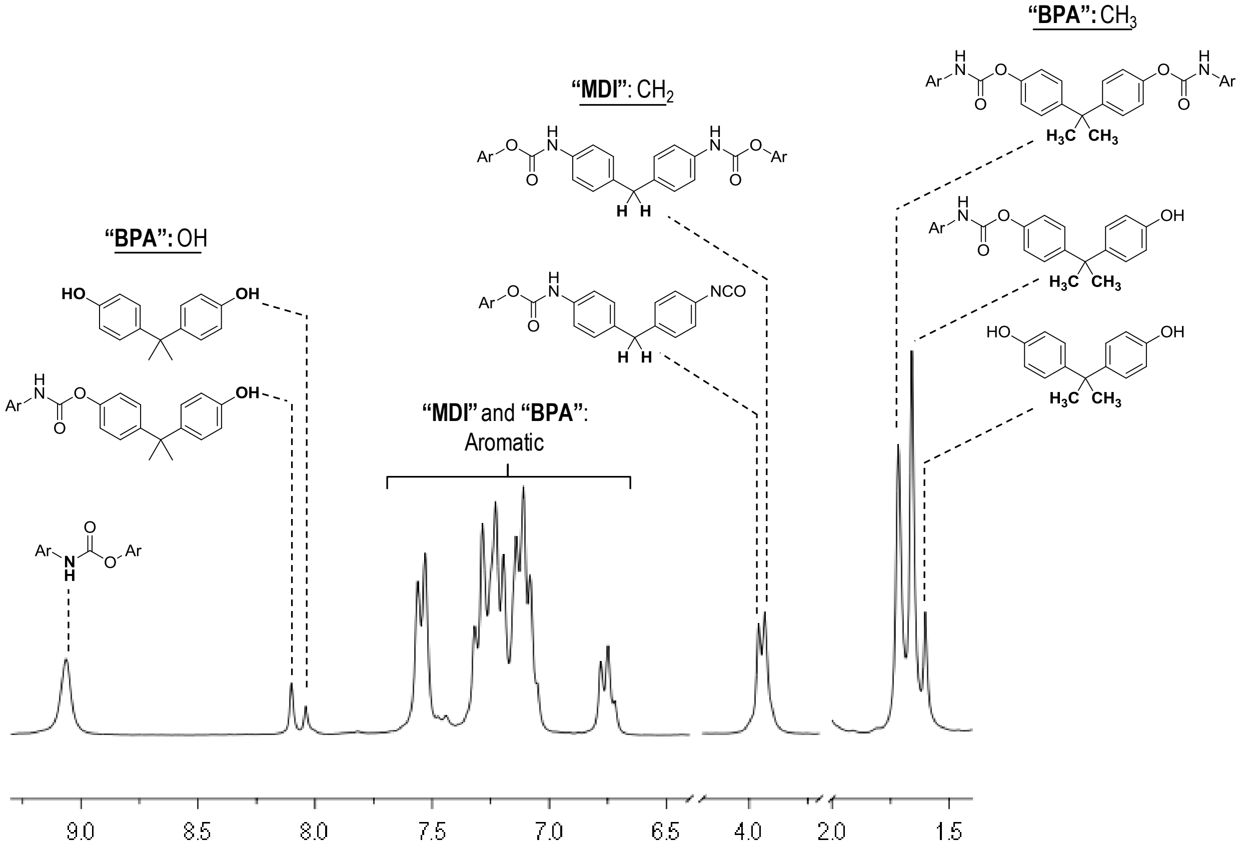


Figure 84. ^{1}H NMR in acetone-d_6 of photoreaction of MDI with BPA after 4 h.

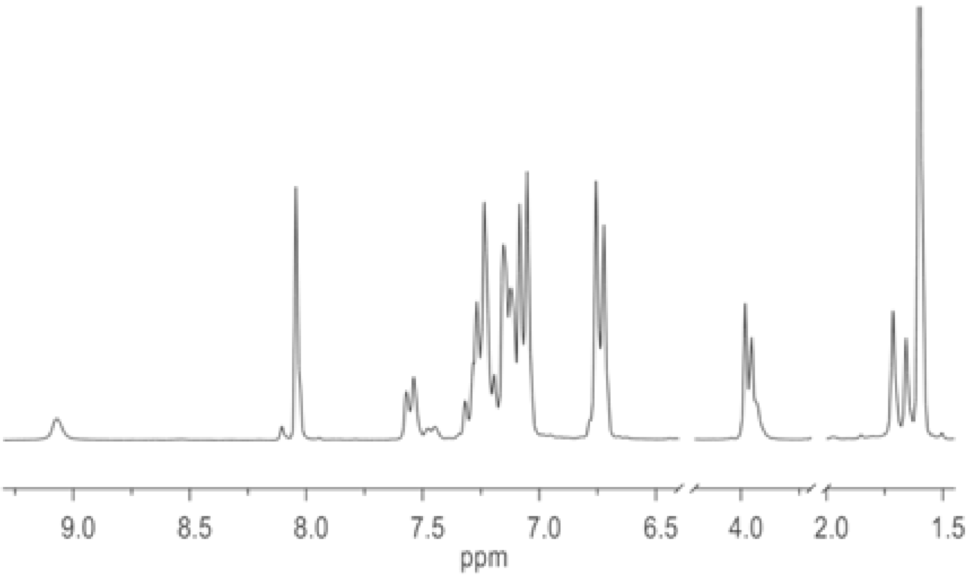


Figure 85. ^{1}H NMR acetone-d_6 of ground state reaction of MDI with BPA after 8 h.

Remarkably, the ground state reaction in the same conditions of solvent and concentration did not evolve so much. After 8 h of reaction protected from light, there was still a 75 % of unreacted BPA and a 57 % of unreacted MDI (Figure 85).

The evolution of the photoreaction was also monitored by GPC. After 1 h of irradiation with a 125 W lamp, BPA and MDI had just reacted once, forming BPA-MDI repeating unit (main peak observed in MW distribution, 478 Da). After 4h, this unit reacted to give a disperse polymer distribution up to 7 000 Da ($M_n = 1.41 \cdot 10^3$; $M_w = 4.16 \cdot 10^3$; Đ = 2.96) (Figure 86).

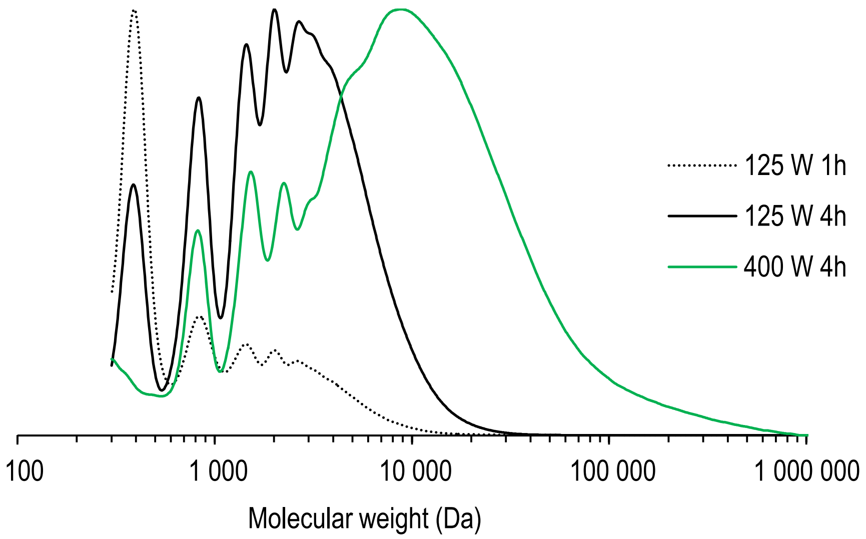


Figure 86. Molecular weight distribution by GPC of photoreaction between BPA and MDI. Black dot line: 125 W lamp 1 h. Black solid line: 125 W lamp 4 h. Green solid line: 400 W lamp 4 h.

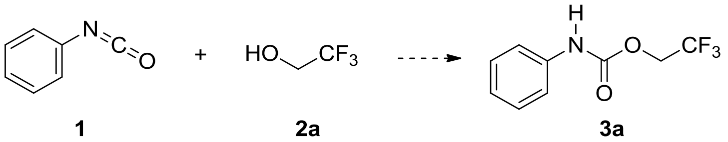
The effect of a more powerful irradiation is also evident in this case. In the same conditions but irradiating with a 400 W lamp, the polymer distribution obtained corresponded to much higher molecular weight polymers, up to 35 000 ($M_n = 3.96 \cdot 10^3$; $M_w = 3.55 \cdot 10^4$; $Đ = 8.96$) (Figure 86).

This study has discovered that the reaction between BPA and MDI in acetonitrile is activated by UV-Vis irradiation. Despite its exploratory nature, these results suggest that the methodology used for these and previous polymerizations might be applied to other acidic weak nucleophiles, not being limited to polyfluorinated diols.

SUMMARY AND CONCLUSIONS

This thesis is focused on the reaction of aromatic isocyanates with polyfluorinated alcohols. This reaction could be an avenue to polyfluorinated polyurethanes, a family of materials that combine the versatility of polyurethanes with the unique properties of polyfluorinated materials. However, the low nucleophilicity of polyfluorinated alcohols is a major drawback for this reaction. Thus, in this research, the main aim was to find suitable conditions for this type of reactions in order to prepare polyfluorinated carbamates and polyfluorinated polyurethanes.

First of all, the focus was centered on the study of a simple model; for this purpose the reaction between phenyl isocyanate with 2,2,2-trifluoroethanol was monitored under different conditions of solvent, concentration, etc (Scheme 63).



Scheme 63. Reaction of phenyl isocyanate **1** with 2,2,2-trifluoroethanol **2a** to form 2,2,2-trifluorethyl phenylcarbamate **3a**.

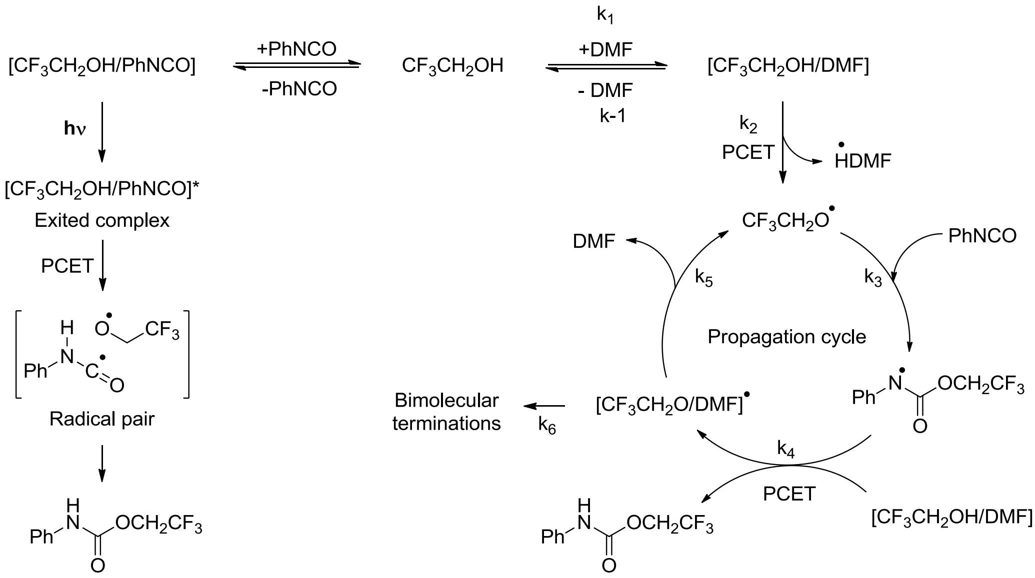
This reaction showed interesting peculiarities not present in the equivalent reaction with non-fluorinated alcohols. Remarkably, this reaction required hydrogen bond acceptor solvents and low concentrations to proceed at useful rates. In addition and more surprisingly, a fractional global reaction order was calculated and there was a null effect of substituent on phenyl isocyanate according to the Hammett equation.

Those findings suggested a more complex pathway than the previously reported polar mechanism, probably involving free radicals. This hypothesis was supported by radical scavenging experiments with galvinoxyl, sub-stoichiometric amounts stopped the reactions. Spin-trapping electron paramagnetic resonance revealed the presence of oxygen-centered radicals derived from the polyfluorinated alcohol, probably reaction intermediates with a lifetime in the order of milliseconds determined by cyclic voltammetry.

According to all these experimental results, a pseudo-unimolecular radical chain mechanism was proposed for the reaction of aromatic isocyanates with polyfluorinated alcohols.

Depending on the reaction conditions, polyfluorinated alcohol would be forming a hydrogen bond adduct with solvent (low concentrations in donor solvents) or with the isocyanate (high concentrations or low donor solvents).

In a highly donor solvent, polyfluorinated alcohol molecules would be preferentially forming a solvent/alcohol hydrogen bond adduct. Then, the key step of the initiation would be a proton-coupled electron transfer, PCET, on this complex from the alcohol to the solvent. This would generate an oxygen-centered radical, which could quickly collapse with an isocyanate molecule to form a carbamate-radical. Then, there would be a PCET from the solvent/alcohol complex to the carbamate-radical. This step would form the product carbamate and generate a solvent/alcohol radical that could diffuse and close the propagation cycle (Scheme 64).



Scheme 64. Proposed mechanisms for the reaction of phenyl isocyanate with 2,2,2-trifluoroethanol.

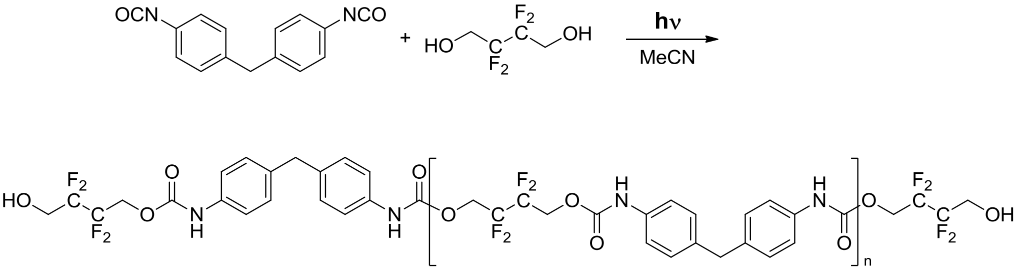
In these conditions, polyfluorinated diols just react by one hydroxyl end with phenyl isocyanate. Additionally, in low donor solvents, the solvent/alcohol adduct is not formed, thus the radical chain is not triggered and the ground state reaction does not proceed.

To overcome these limitations, in low donor solvents the proton-coupled electron transfer could be promoted on the isocyanate/alcohol complex by irradiation with UV light. In this case no evidences of free radicals were found; presumably under irradiation the radical pair generated does not diffuse because it quickly collapses to form the product carbamate.

This photochemical activation was required to obtain complete reaction of polyfluorinated diols with phenyl isocyanates and with pentafluorophenyl isocyanate to obtain polyfluorinated and quasi-perfluorinated bisphenylcarbamates respectively.

Surface properties of those new highly fluorinated compounds have been tested using spin coating deposition and contact angle measurements. Remarkably, length of the polyfluorinated chain seemed not as important as the presence of pentafluorophenyl rings to obtain hydrophobic and oleophobic compounds. Small quasi-perfluorinated bis(phenylcarbamates) turned glass even more oleophobic than Teflon.

This photochemical methodology was also applied to the reaction of polyfluorinated diols with aromatic diisocyanates to obtain polyfluorinated polyurethanes. The photopolymerization between 2,2,3,3-tetrafluorobutan-1,4-diol and methylene diphenyl 4,4'-diisocyanate was studied as a model.



Scheme 65. Model photopolymerization studied between a polyfluorinated diol and an aromatic diisocyanate.

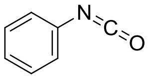
By IR, no signal of isocyanate was observed in the final polymer, which indicated that the polymer was hydroxyl-ended in both sides. This knowledge allowed the use of end-group analysis by ^{19}F NMR to calculate M_n, in agreement with the results obtained by GPC. An important factor in the photopolymerization was the lamp power; a stronger irradiation lamp reduced the time required for monomer consumption.

In the photoreaction, first, hydroxyl-terminated small oligomers were generated but they did not further react until diol monomer was consumed. These hydroxyl-terminated polymers seemed to grow just up to a certain limit (around 3 000 Da), probably due to intramolecular hydrogen bond interactions that blocked the hydroxyl group. Addition of more diisocyanate monomer forced in part the reaction. However, by lowering reaction temperature to 0 ºC larger molecular weights (up to 15 000 Da) were obtained.

Preliminary studies were carried with this methodology to prepare other polyurethanes. Quasi-perfluorinated polyurethane formation by reaction of a polyfluorinated diol with a perfluorinated diisocyanate just took place in a limited extend, requiring further research and optimization in the future. Extending the photopolymerization methodology to other acidic weak nucleophiles, as bisphenols, was more successful, indicating the possibility to use this photochemical method to other polymerizations processes.

To sum up all, a new photochemical reaction of polyfluorinated alcohols with isocyanates has been deeply studied. It has been successfully applied to the preparation of polyfluorinated polyurethanes, opening an avenue for further studies and improvements.

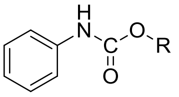
MOLECULE INDEX



1

$HO-R$

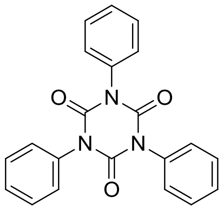
2



3

n-$C_{16}H_{34}$

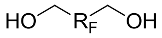
4



5

R
2a, CH_2CF_3
2b, $CH_2(CF_2)_6CF_3$
2c, $CH(CF_3)_2$
2d, $C(CF_3)_3$

R
3a, CH_2CF_3
3b, $CH_2(CF_2)_6CF_3$
3c, $CH(CF_3)_2$



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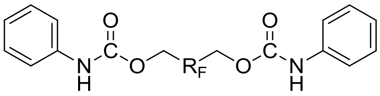

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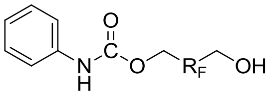
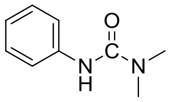


8

R_F
6a, $(CF_2)_2$
6b, $(CF_2)_3$
6c, $(CF_2)_{10}$
6d, $CF_2O(CF_2)_2OCF_2$

R_F
7a, $(CF_2)_2$
7b, $(CF_2)_3$
7c, $(CF_2)_{10}$
7d, $CF_2O(CF_2)_2OCF_2$

R_F
8a, $(CF_2)_2$
8b, $(CF_2)_3$
8c, $(CF_2)_{10}$



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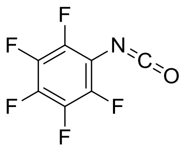

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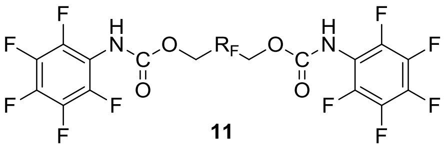
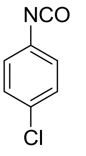


11

R_F
11a, $(CF_2)_2$
11b, $(CF_2)_3$
11c, $(CF_2)_{10}$
11d, $CF_2O(CF_2)_2OCF_2$



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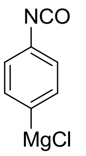

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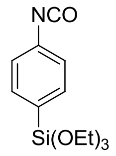

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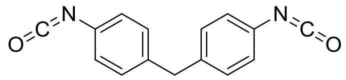
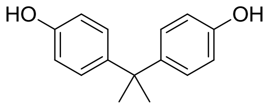
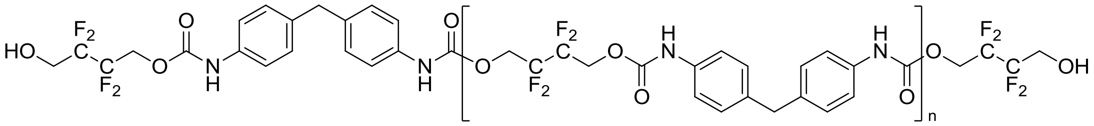


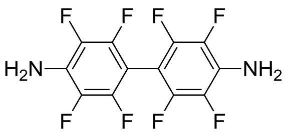
MDI



BPA



PTM$_n$



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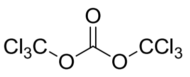
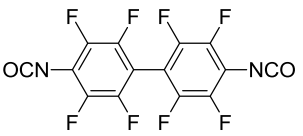


$Cl_3C-O-C(=O)-O-CCl_3$

16



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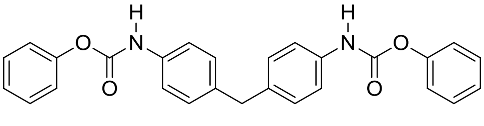

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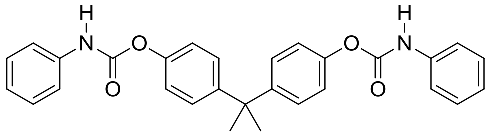

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Experimental section

E.1. GENERAL REMARKS

Nuclear magnetic resonance NMR spectra were recorded in the facilities of *Servei de Ressonància Magnètica Nuclear* from *Universitat Autónoma de Barcelona UAB.* ^{1}H NMR and ^{19}F NMR were recorded at room temperature using a Bruker DPX250 spectrometer (250 MHz ^{1}H NMR; 235.2 MHz ^{19}F NMR), chemical shift are in ppm relative to δ(TMS) = 0 and δ($CFCl_3$) = 0 respectively. ^{13}C{^{1}H} NMR spectra were recorded by broadband proton spin decoupling at ambient temperature on Bruker DPX360 (360 MHz ^{1}H NMR; 90.5 MHz ^{13}C NMR), chemical shift in ppm relative to δ(TMS) = 0.

Infrared spectra IR were recorded with a spectrometer Bruker Tensor 27 fitted with a universal Attenuated Total Reflectance ATR Golden Gate module with a diamond window from the *Servei d'Anàlisi Quimic* of the UAB.

Gas chromatography GC was done in an Agilent Technologies A7890 chromatograph equipped with Agilent HP-5 column (30 m × 0,320 mm × 0,25 µm) and a FID detector. The standard methods used were called NORMAL75 (finishes after ramp 1) or a longer version called LONG75 (finishes after ramp 2).

	Heating rate (ºC/min)	Final Tº (ºC)	Final time (min)	Accumulated time (min)
Initial	-	75	0.5	0.5
Ramp 1	25	240	4	11.1
Ramp 2	10	280	4	19.1

Gas chromatography coupled with mass spectrometry GC-MS was performed with an Agilent A6850 equiped with a mass detector MSD Triple Axis 5975C VL in positive mode.

Melting points have been recorded in a Reichert-Koffler block without further correction. Alternatively, for melting point measurements it was used **Differential Scanning Calorimetry DSC** in a TA Instrument Q20 using Tzero^{TM} pans and lids calibrated with indium (T_m = 429.75 K, ΔH_m = 3267 kJ/mol).

Gel permeation chromatography GPC was performed in an instrument equipped with a guard column before two analytical columns: one PL Mixed gel C 5 µm column and another PL gel, 5 µm, 10.000 A column, using THF as solvent and a refractive index detector. The method used injects 40 µL of sample, elutes at a flow of 1 mL/min at an isothermal temperature of 30 ºC and was calibrated using polystyrene standards.

Electronic paramagnetic resonance EPR experiments were recorded in the *Institut de Ciència de Materials de Barcelona* using a spectrometer Bruker ELEXYS 500 E (× band 9.5 GHz) in collaboration with Dr. Jose Vidal and Dr. Vega Lloveras.

High resolution mass spectra HRMS were analyzed in *Universidad de Zaragoza* using equipment Bruker MicroTOF-Q with electrospray ionisation ESI.

Spin coating were performed in an equipment from Laurell Technologies model WS-650SZ-6NPP/LITE. An 80 µL drop of the compound (solution of 10 mg in 0.5 mL of acetone) was spun at 6000 rpm for 120 s (1000 rpm s^{-1}) over a 12 x 12 mm clean glass surface and then dried in a controlled humidity atmosphere.

Sessile drop contact angle was measured using a Contact Angle Measuring System DSA 100 from KRÜSS. Both, spin coating and contact angle measurements, were performed in clean room facilities Nanostructuration platform in *Institut de Ciència de Materials de Barcelona* assisted by Neus Roma.

Experiments were carried out using standard high vacuum and **Schlenk techniques** under nitrogen atmosphere using dry solvents. When required, *e.g.* photochemical reactions, solvents were degassed by three cycles of freeze-pump-thaw. Each cycle consists on three steps. First, freezing solvent in a Schlenk tube with liquid nitrogen; second, applying vacuum to the solid solvent; and third, closing the vacuum and, without refilling with nitrogen, solvent was thawed (melted) in a warm water bath.

Dry solvents were obtained according standard procedures from Vogel.[118] DMF was kept during 24 h with activated molecular sieves before distillation at reduced pressure (10 mmHg). Use of CaH_2 in DMF drying process was avoided to prevent dimethylamine formation. Dry MeCN was obtained by distillation after reflux in the presence of phosphorus pentoxide. Toluene was dried by reflux with sodium and benzophenone prior to distillation. Dry pentane and dry THF were obtained from a commercial anhydrizer PureSolv-MD-2 from Innovative Technology.

Purifications by **flash chromatography** were performed using Scharlau silica gel 60, 0.04 mm - 0.06 mm, 230-400 mesh, usually eluted with a mixture of hexane with ethyl acetate with the appropriate polarity.

Thin layer chromatography TLC was performed in plates from Alugram Sil G/UV_{254} of 0.25 mm revealed by UV light or permanganate solution.

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[118] Vogel, A. I. *Vogel's textbook of practical organic chemistry 5th ed*. Furniss, B. S. Essex, England, 1989.

E.2. KINETICS STUDIES OF THE REACTION OF PHENYL ISOCYANATE WITH TFE

E.2.1. GAS CHROMATOGRAPHY

These reactions were followed by GC chromatography using NORMAL75 method. In order to quantify the concentration of PhNCO **1** (t_R = 1.79 min) a calibration line was constructed using hexadecane **4** (t_R = 4.92 min) as internal standard. Thus, solutions with different known concentration of **1** and **4** were prepared and measured in the GC using the method NORMAL75. Fraction of signal integrations (S_1/S_4) *vs.* fraction of concentrations ([**1**] / [**4**]) resulted in a line used for quantification of **1**.

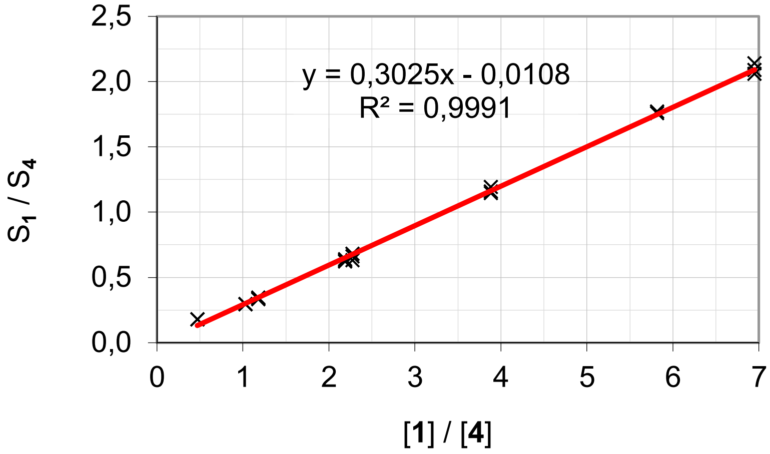
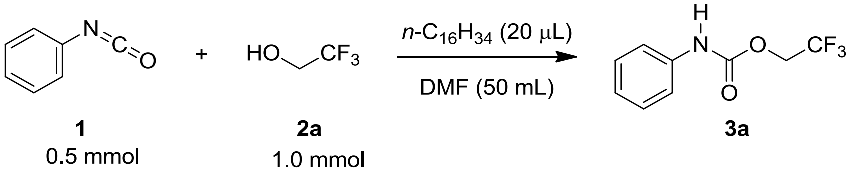


Figure 87. Calibration line of PhNCO **1** by GC using hexadecane **4** as internal standard in DMF.

E.2.2. STANDARD PROCEDURE TO FOLLOW THE EVOLUTION OF THE REACTION

Next, it is described an example of the procedure used to follow the evolution of the reaction. This methodology has been used as well for other reactions changing the required parameter: initial concentration, reagents proportion, polyfluorinated alcohol…

EVOLUTION OF THE REACTION BETWEEN PHNCO AND TFE IN DMF



Scheme 66. Reaction of phenyl isocyanate **1** with 2,2,2-trifluoroethanol **2a** to form 2,2,2-trifluorethyl phenylcarbamate **3a**.

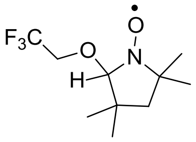
In a 100 mL Schlenk flask provided with magnetic stirring under inert atmosphere of nitrogen, phenyl isocyanate **1** (55 µL; 0.50 mmol) and hexadecane **4** (20 µL; 0.07 mmol) were solved in dried DMF (50 mL). Special caution should be employed when handling PhNCO to avoid its tearing vapors. After 5 minutes for homogenization, an aliquot was taken to check the concentration by GC.

After addition of TFE **2a** (73 µL; 1.0 mmol) (and other additives if required, *e.g.* galvinoxyl) mixture was allowed to react and samples were extracted periodically for GC analysis until concentration of PhNCO remained constant.

E.3. ELECTRON PARAMAGNETIC RESONANCE

E.3.1. 2,2,2-TRIFLUOROETHOXY RADICAL TRAPPED WITH TMPO

A solution of phenyl isocyanate (11 µL; 0.1 mmol) in dry DMF (10 mL) is bubbled with argon. After the addition of TFE (15 µL; 0.2 mmol), it was allowed to react for 5 minutes before adding the spin trap TMPO (15 mg; 0.1 mmol). The mixture was then transferred to a flat cell, degassed with argon and EPR spectrum recorded.



a(1N) = 12.70, *a*(1H) = 6.91, g_e = 2.0062

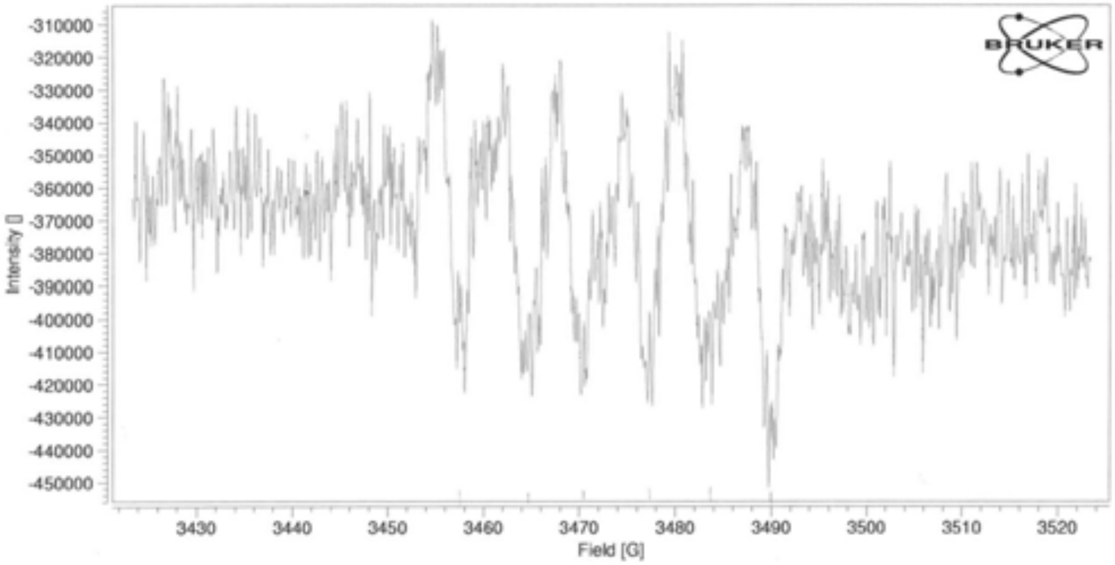
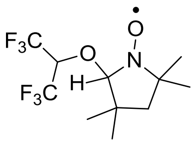


Figure 88. EPR spectrum obtained in the reaction of PhNCO with TFE in DMF, adding TMPO after 5 minutes.

E.3.2. 1,1,1,3,3,3-HEXAFLUORO-2-PROPOXY RADICAL TRAPPED WITH TMPO

A solution of phenyl isocyanate (11 µL; 0.1 mmol) in dry DMF (10 mL) is bubbled with argon. After the addition of HFIP (21 µL; 0.2 mmol), it was allowed to react for 5 minutes before adding the spin trap TMPO (15 mg; 0.1 mmol. The mixture was then transferred to a flat cell, degassed with argon and EPR spectrum recorded.



$a(1N) = 13.25$, $a(1H) = 7.0$, $g_e = 2.0062$

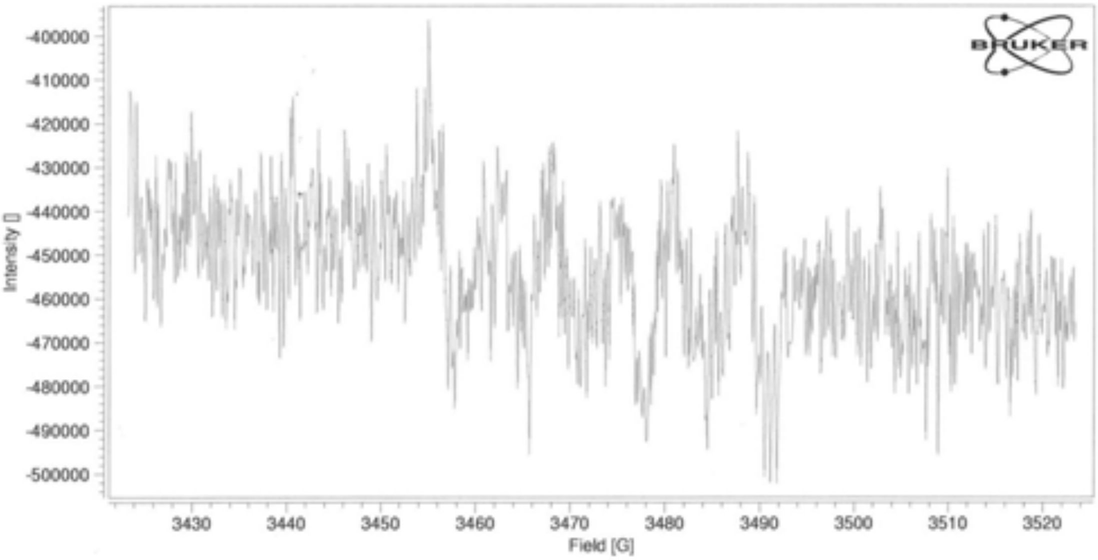
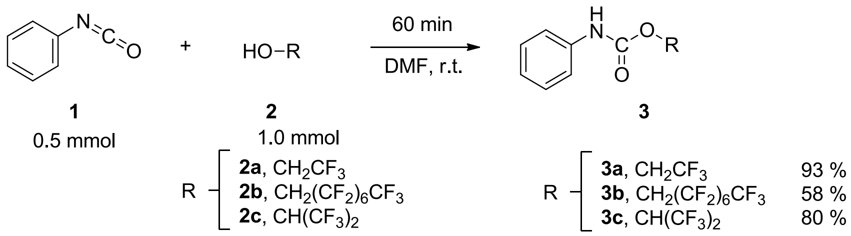


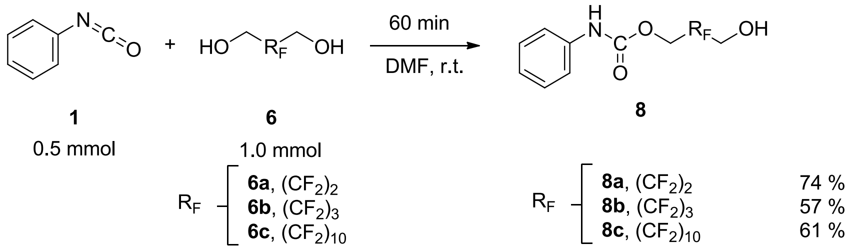
Figure 89. EPR spectrum obtained in the reaction of PhNCO with HFIP in DMF, adding TMPO after 5 minutes.

E.4. PREPARATIVE REACTIONS OF POLYFLUORINATED CARBAMATES

E.4.1. POLYFLUORINATED MONO(PHENYLCARBAMATES)

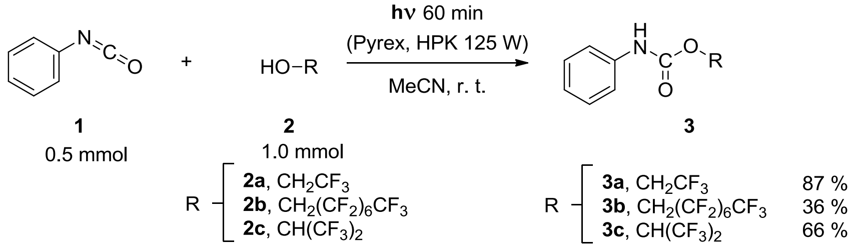
GENERAL PROCEDURE A





In a 100 mL Schlenk flask provided with magnetic stirring under inert atmosphere, phenyl isocyanate (55 µL; 0.50 mmol) is solved in dried DMF (50 mL). Special caution should be employed when handling PhNCO to avoid its tearing vapours. After addition of polyfluorinated alcohol (1.0 mmol for polyfluorinated alcohol; 0.5 mmol for polyfluorinated diol), the mixture was allowed to react for 60 minutes. After that reaction time, water (20 mL) was added to hydrolyze the remaining isocyanate. The mixture DMF/water was extracted with ethyl acetate (3 × 20 mL), the organic phase washed with diluted hydrochloric acid (1 M; 3 × 20 mL) and water (20 mL). Then it was dried up with anhydrous magnesium sulphate and evaporated in the rotary evaporator. The product was obtained after purification by a flash chromatography initially eluted with hexanes:ethyl acetate 5:1 with increasing polarity. Yields are reported in the description of each compound as Yield procedure A.

GENERAL PROCEDURE B



Dry acetonitrile (50 mL) was degassed by three cycles of freeze-pump-thaw and placed in a photochemical reactor equipped with a magnetic stirring, a glass stopper, a stopcock and a water-flow cooled pyrex immersion well under nitrogen atmosphere. Phenyl isocyanate (54 μL, 0.5 mmol) was added and stirred for five minutes. polyfluorinated alcohol (1.0 mmol) was added and stirred for five further minutes to homogenize the solution. Then, the UV-vis irradiation source, a mercury high pressure lamp Philips HPK 125W, was turned on. After 60 minutes of reaction the lamp was switched off and the solvent and the alcohol were evaporated in vacuo. The yellowish residue was purified by flash column chromatography using initially as eluent hexanes/ethyl acetate 5:1 and then with increasing polarity. Yields are reported in the description of each compound as Yield procedure B.

2,2,2-Trifluoroethyl phenylcarbamate, **3a** [32]

Crystalline white solid. Yield procedure A: 104 mg, 93 %. Yield procedure B: 95 mg, 87 %. M.p. (ºC): 57-58. ^{1}H NMR (250 MHz, acetone-d$_6$): δ 4.74 (q, $^3J_{HF}$ = 9.3 Hz, 2H, CH_2), 7.09 (t, $^3J_{HH}$ = 7.5 Hz, 1H, para), 7.35 (t, $^3J_{HH}$ = 7.5 Hz, 2H, meta), 7.59 (d, $^3J_{HH}$ = 7.9 Hz, 2H, ortho), 9.07 (s, 1H, NH). ^{13}C{^{1}H} NMR (90.5 MHz, acetone-d$_6$): δ 60.1 (q, $^2J_{CF}$ = 35.9 Hz, CH_2), 118.6 (s, ortho), 123.3 (s, para), 123.7 (q, $^1J_{CF}$ = 276.9 Hz, CF_3), 128.9 (s, meta), 138.5 (s, ipso), 151.7 (s, C=O). ^{19}F NMR (235.2 MHz, acetone-d$_6$): δ -75.36 (t, $^3J_{FH}$ = 9.3 Hz, 3F, CF_3). IR (ATR): 3327 (N-H st), 2969 (C-H st), 1716 (C=O st), 1538 (N-H δ), 1226 (N-CO-O st as), 1160 (C-F st), 1079 cm^{-1}. HRMS-ESI$^+$: m/z calcd for $C_9H_9F_3NO_2$ $[M+H]^+$ 220.0580, found: 220.0579. Calcd for $C_9H_8F_3NNaO_2$ $[M+Na]^+$ 242.0399, found: 242.0395.

2,2,2-Trifluoroethyl (4-chlorophenyl)carbamate, **3a-Cl** [30]

Crystalline white solid. Yield procedure A: 126 mg, 99 %. M.p. (ºC): 73.1-73.6. ^{1}H NMR (250 MHz, $CDCl_3$): δ 4.58 (q, $^3J_{HF}$ = 8.3 Hz, 2H, CH_2), 6.81 (bs, 1H, NH) 7.28-7.40 (m, 4H, ar.). ^{19}F{^{1}H} NMR (235.2 MHz, $CDCl_3$): δ -74.61 (s, CF_3).

2,2,2-Trifluoroethyl (4-nitrophenyl)carbamate, **3a-NO$_2$**[26]

Yellow solid. Yield procedure A: 128 mg, 97 %. M.p. (ºC): 129.9-130.5. ^{1}H NMR (250 MHz, acetone-d$_6$): δ 4.79 (q, $^3J_{HF}$ = 8.3 Hz, 2H, CH$_2$), 7.82 (d, $^3J_{HF}$ = 10 Hz, 2H,ortho), 8.25 (d, $^3J_{HF}$ = 10 Hz, 2H, meta), 9.85 (bs, 1H, NH). ^{19}F{^{1}H} NMR (235.2 MHz, acetone-d$_6$): δ -75.29 (s, CF$_3$).

2,2,2-Trifluoroethyl (4-methoxyphenyl)carbamate, **3a-OMe**[32]

White solid. Yield procedure A: 94 mg, 76 %. M.p. (ºC): 69.7-70.0. ^{1}H NMR (250 MHz, CDCl$_3$): δ 3.83 (s, 3H, OCH$_3$), 4.57 (q, $^3J_{HF}$ = 8.3 Hz, 2H, CH$_2$), 6.68 (bs, 1H, NH), 6.90 (d, $^3J_{HF}$ = 7.5 Hz, 2H, meta), 7.31(d, $^3J_{HF}$ = 7.5 Hz, 2H, ortho). ^{19}F{^{1}H} NMR (235.2 MHz, CDCl$_3$): δ -70.86 (s, CF$_3$).

2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-Pentadecafluorooctyl phenylcarbamate, **3b***:*

White solid. Yield procedure A: 151 mg, 58 %. Yield procedure B: 93 mg, 36 %. ^{1}H NMR (250 MHz, acetone-d$_6$): δ 4.90 (t, $^3J_{\mathrm{HF}}$ = 15 Hz, 1H, CH$_2$), 7.10 (t, $^3J_{\mathrm{HH}}$ = 7.5 Hz, 1H, para), 7.35 (t, $^3J_{\mathrm{HH}}$ = 7.5 Hz, 2H, meta), 7.60 (d, $^3J_{\mathrm{HH}}$ = 7.5 Hz, 2H, ortho), 9.13 (bs, 1H, NH). ^{13}C{^{1}H} NMR (90.5 MHz, acetone-d$_6$): δ 59.3 (t, $^2J_{\mathrm{CF}}$ = 26.7 Hz, CH$_2$), 106-120 (undefined, CF$_n$) 118.6 (s, ortho), 123.4 (s, para), 128.8 (s, meta), 138.4 (s, ipso), 151.7 (s, CO). ^{19}F{^{1}H} NMR (235 MHz, acetone-d$_6$): δ -127.18 (bs, 2F, CF$_2$), -124.27 (bs, 2F, CF$_2$), -123.71 (bs, 2F, CF$_2$), -122.98 (bs, 4F, CF$_2$), -120.70 (bs, 2F, CF$_2$), -82.14 (t, $^3J_{\mathrm{FF}}$ = 9.4 Hz, 3F, CF$_3$). IR (ATR): 3354 (N-H st), 2958, 2935 (C-H st), 1728 (C=O st), 1539, 1201 (N-CO-O st as), 1147, 1101 (C-F). HRMS-ESI$^+$: m/z calcd for $C_{15}H_9F_{15}NO_2$ [M+H]$^+$ 520.0388, found: 520.0393. Calcd for $C_{15}H_8F_{15}NNaO_2$ [M+Na]$^+$ 542.0208, found: 542.0220.

1,1,1,3,3,3-Hexafluoropropan-2-yl phenylcarbamate, **3c**[119]

White solid. Yield procedure A: 115 mg, 80 %. Yield procedure B: 95 mg, 66 %. M.p. (ºC): 104-105. ^{1}H NMR (250 MHz, acetone-d$_6$): δ 6.30 (septet, $^3J_{\mathrm{HF}}$ = 6.7 Hz, 1H, CH), 7.16 (t, $^3J_{\mathrm{HH}}$ = 7.5 Hz, 1H, para), 7.39 (t, $^3J_{\mathrm{HH}}$ = 7.5 Hz, 2H, meta), 7.61 (d, $^3J_{\mathrm{HH}}$ = 10.0 Hz, 2H, ortho), 9.54 (bs, 1H, NH). ^{13}C{^{1}H} NMR (90.5 MHz, acetone-d$_6$): δ 67.0 (septet, $^2J_{\mathrm{CF}}$ = 34.0 Hz, CH), 118.9 (s, ortho), 121.2 (q, $^1J_{\mathrm{CF}}$ = 285.0 Hz, CF$_3$), 124.1 (s, para), 129.0 (s, meta), 137.6 (s, ipso), 149.8 (s, CO). ^{19}F NMR (235 MHz, acetone-d$_6$): δ -74.76 (d, $^3J_{\mathrm{HF}}$ = 6.7 Hz, CF$_3$). IR (ATR): 3296 (N-H st), 2978 (C-H st), 1731 (C=O st), 1537, 1224 (N-CO-O st as), 1193 (C-F st), 1104 cm^{-1}. HRMS-ESI$^+$: m/z calcd for $C_{10}H_8F_6NO_2$ [M+H]$^+$ 288.0454, found: 288.0462.

2,2,3,3-Tetrafluoro-4-hydroxybutyl phenylcarbamate, **8a**

White solid. Yield procedure A: 104 mg, 74 %. M.p. (ºC): 79.3-79.9. ^{1}H NMR (250 MHz, acetone-d$_6$): δ 4.05 (dt, $^3J_{\mathrm{HF}}$ = 14.3 Hz, $^3J_{\mathrm{HH}}$ = 6.3 Hz, 2H, CH$_2$OH), 4.74 (t, $^3J_{\mathrm{HF}}$ = 15.2 Hz, 2H,

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[119] Koetzsch, H. J. *Chem. Berichte* **1966**, *99*, 4, 1143-1148.

CH_2OCO, 2H), 5.01 (t, $^3J_{HH}$ = 6.3 Hz, 1H, OH), 7.08 (t, $^3J_{HH}$ = 7.5 Hz, 1H, *para*), 7.34 (t, $^3J_{HH}$ = 7.5 Hz, 2H, *meta*), 7.59 (d, $^3J_{HH}$ = 7.5 Hz, 2H, *ortho*), 9.01 (s, 1H, NH). $^{13}C\{^1H\}$ NMR (90.5 MHz, CD_3OD): 59.9 (t, $^2J_{CF}$ = 27 Hz, CH_2), 60.6 (t, $^2J_{CF}$ = 25 Hz, CH_2), 112-123 (Complex absorption, 2 CF_2), 118.9 (s, *ortho*), 123.6 (s, *para*), 129.2 (s, *meta*), 139.1 (s, *ipso*), 152.6 (s, CO). $^{19}F\{^1H\}$ NMR (235.2 MHz, acetone-d_6): δ -125.14 (CF_2CH_2OH), -123.63 (s, 2F, CF_2CH_2OCO). IR (ATR): 3323 (N-H, OH st), 2955 (C-H st), 1721 (C=O st), 1602 (arC-C), 1541 (N-H δ), 1449, 1264 (N-CO-O st as), 1116 (C-F st), 1101, 930. HRMS-ESI$^+$: m/z calcd. for $C_{11}H_{12}F_4NO_3$ $[M+H]^+$ 282.0748, found 282.0786. calcd. for $C_{11}H_{12}F_4NNaO_3$ $[M+Na]^+$ 304.0567, found 304.0577.

2,2,3,3,4,4-Hexafluoro-5-hydroxypentyl phenylcarbamate, **8b**

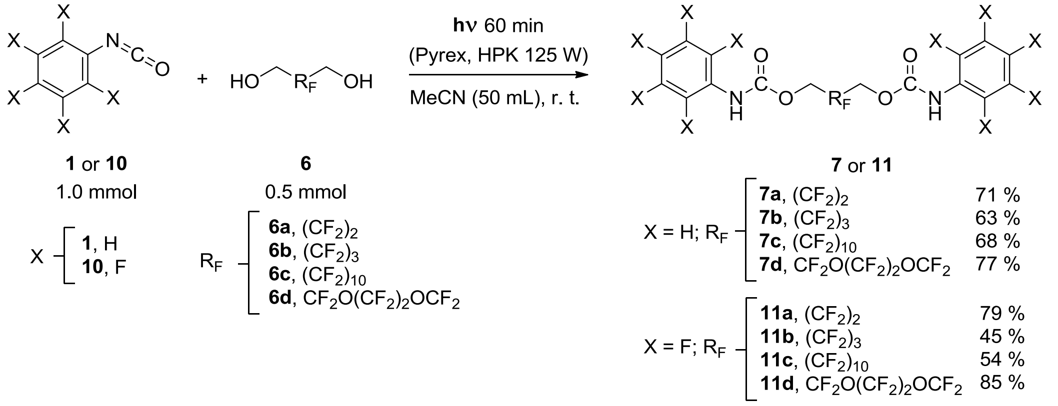
White solid. Yield procedure A: 94 mg, 57 %. ^1H NMR (360 MHz, acetone-d_6): δ 4.11 (dt, $^3J_{HF}$ = 15.1 Hz, $^3J_{HH}$ = 6.7 Hz, 2H, CH_2OH), 4.79 (t, $^3J_{HF}$ = 14.9 Hz, 2H, CH_2OCO, 2H), 5.08 (t, $^3J_{HH}$ = 6.9 Hz, 1H, OH), 7.09 (t, $^3J_{HH}$ = 7.5 Hz, 1H, *para*), 7.34 (t, $^3J_{HH}$ = 7.5 Hz, 2H, *meta*), 7.60 (d, $^3J_{HH}$ = 7.5 Hz, 2H, *ortho*), 9.11 (s, 1H, NH). $^{13}C\{^1H\}$ NMR (90.5 MHz, acetone-d_6): 59.5 (m, CH_2), 59.7 (m, CH_2), 111-119 (complex absorption, 3 CF_2), 118.5 (s, *ortho*), 123.2 (s, *para*), 128.8 (s, *meta*), 138.6 (s, *ipso*), 152.0 (s, CO). ^{19}F NMR (235.2 MHz, acetone-d_6): δ -127.25 (s, 2F, central CF_2), -123,14 (t, $^3J_{HF}$ = 15.1 Hz, 2F, CF_2CH_2OH), -121.31 (t, $^3J_{HF}$ = 14.9 Hz, 2F, CF_2CH_2OCO). IR (ATR): 3331 (N-H, OH st), 1719 (C=O st), 1536 (N-H δ), 1501, 1445, 1226 (N-CO-O st as), 1185, 1153 (C-F st), 1091, 750, 689. HRMS-ESI$^+$: m/z calcd. for $C_{12}H_{11}F_6NNaO_3$ $[M+Na]^+$ 354.0535, found 354.0575.

2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11-Icosafluoro-12-hydroxydodecyl phenylcarbamate, **8c**

White-yellowish solid. Yield procedure A: 208 mg, 61 %. ^1H NMR (360 MHz, acetone-d_6): δ 3.91 (dt, $^3J_{HF}$ = 14.3 Hz, $^3J_{HH}$ = 6.1 Hz, 2H, CH_2OH), 4.59 (t, $^3J_{HF}$ = 15.4 Hz, 2H, CH_2OCO), 4.87 (t, $^3J_{HH}$ 6.7 Hz, 1H, OH), 6.93 (t, $^3J_{HH}$ = 7.3 Hz, 1H, *para*), 7.19 (t, $^3J_{HH}$ = 7.3 Hz, 2H, *meta*), 7.45 (d, $^3J_{HH}$ = 7.3 Hz, 2H, *ortho*), 8.87 (s, 1H, NH). $^{13}C\{^1H\}$ NMR (90.5 MHz, acetone-d_6): 60.0 (m, CH_2), 60.6 (m, CH_2), 111-119 (complex weak absorption, 10 CF_2), 119.6 (s, *ortho*), 124.3 (s, *para*), 129.8 (s, *meta*), 139.4 (s, *ipso*), 152.7 (s, CO). $^{19}F\{^1H\}$ NMR (235.2 MHz, acetone-d_6): δ -124.44 (bs, 4F), -123,00 (bs, 4F), -122.81 (bs, 6F), -122.76 (bs, 4F), -122.71 (bs, 2F). HRMS-ESI$^+$: m/z calcd. for $C_{19}H_{12}F_{20}NO_3$ $[M+H]^+$ 682.0531, found 682.0492.

E.4.2. POLYFLUORINATED BIS(PHENYLCARBAMATES)

GENERAL PROCEDURE C



Dry acetonitrile (45 mL) was degassed by three cycles of freeze-pump-thaw and placed under inert atmosphere in a photochemical reactor equipped with a magnetic stirring, a glass stopper, a stopcock and a water-flow cooled pyrex immersion well. Aromatic isocyanate (1.0 mmol) was added and stirred for five minutes.

Afterwards a solution of polyfluorinated diol (0.5 mmol) in dried and degassed acetonitrile (5 mL) was added and stirred for five further minutes to homogenize the solution. Then, the irradiation source (Philips HPK 125W) was turned on. After 4 h of reaction the lamp was switched off and the solvent and the alcohol were evaporated *in vacuo*. After a flash column chromatography using initially hexanes/ethyl acetate 5:1 and then increasing polarity, the product was obtained in the yield described in the following description as Yield procedure C.

2,2,3,3-Tetrafluorobutane-1,4-diyl bis(phenylcarbamate), **7a**

White solid. Yield procedure C: 141 mg, 71 %. M.p. (ºC): 178.1 (DSC). ^{1}H NMR (250 MHz, acetone-d$_6$): δ 4.77 (t, $^3J_{HF}$ = 15.0 Hz, 4H, CH$_2$), 7.09 (t, $^3J_{HH}$ = 7.5, 2H, *para*), 7.34 (t, $^3J_{HH}$ = 7.5 Hz, 4H, *meta*), 7.58 (d, $^3J_{HH}$ = 7.5 Hz, 4H, *ortho*), 9.06 (bs, 2H, NH). ^{13}C{^{1}H} NMR (90.5 MHz, acetone-d$_6$): δ 59.6 (t, $^2J_{CF}$ = 26.0 Hz, CH$_2$), 115.4 (tt, $^1J_{CF}$ = 252.0 Hz, $^2J_{CF}$ = 31.0 Hz, CF$_2$), 118.6 (s, *ortho*), 123.2 (s, 4C, *para*), 128.8 (s, *meta*), 138.6 (s, *ipso*), 152.0 (s, CO). ^{19}F NMR (235.2 MHz, acetone-d$_6$): δ -122.88 (t, $^3J_{HF}$ = 15 Hz). IR (ATR): 3350 (N-H st), 3052 (arom. C-H st), 2968 (C-H st), 1721 (C=O st), 1598 (arom. C-C), 1532 (N-H δ), 1228 (N-CO-O st as), 1179, 1143 (C-F st), 1091, 952, 934, 749 (C-F δ) cm^{-1}. HRMS-ESI$^+$: m/z calcd for $C_{18}H_{17}F_4N_2O_4$ [M+H]$^+$ 401.1119, found 401.1126. Calcd for $C_{18}H_{16}F_4N_2NaO_4$ [M+Na]$^+$ 423.0938, found 423.0958, found. Calcd for $C_{18}H_{16}F_4KN_2O_4$ [M+K]$^+$ 439.0678, found 439.0680, found.

2,2,3,3,4,4-Hexafluoropentane-1,5-diyl bis(phenylcarbamate), **7b**

White solid. Yield procedure C: 0.139 g, 63 %. M.p.(ºC): 134.5-135.1. ^{1}H NMR (250 MHz, acetone-d$_6$): δ 4.83 (t, $^3J_{HF}$ = 7.5 Hz, 4H, CH$_2$), 7.07 (t, $^3J_{HH}$ = 7.5 Hz, 2H, *para*), 7.35 (t, $^3J_{HH}$ = 7.5 Hz, 4H, *meta*), 7.60 (d, $^3J_{HH}$ = 7.5 Hz, 4H, *ortho*), 9.12 (s, 2H, NH). ^{13}C{^{1}H} NMR (90.5 MHz, CD$_3$OD): δ 59.5 (t, $^2J_{CF}$ = 28.0 Hz, CH$_2$), 111.3 (m, central CF$_2$), 115.0 (tt, $^1J_{CF}$ = 257.0 Hz, $^2J_{CF}$ = 30.0 Hz, CH$_2$*C*F$_2$), 118.6 (s, *ortho*), 123.1 (s, *para*), 128.5 (s, *meta*), 138.2 (s, *ipso*), 152.5 (s, CO). ^{19}F{^{1}H} NMR (235.2 MHz, acetone-d$_6$): δ -127.31 (s, 2F, central CF$_2$), -121.15 (s, 4F, CH$_2$C*F*$_2$). IR (ATR): 3336 (N-H st), 1705 (C=O st), 1600 (arom. C-C), 1540 (N-H δ), 1448, 1315, 1240 (N-CO-O st as), 1201, 1150 (C-F st), 1088, 963, 937, 885, 763 (C-F δ), 686, 637 cm^{-1}. HRMS-ESI$^+$: m/z calcd for $C_{19}H_{17}F_6N_2O_4$ [M+H]$^+$ 451.1087, found 451.1102. Calcd for $C_{19}H_{16}F_6N_2NaO_4$ [M+Na]$^+$ 473.0906, found 473.0912. Calcd for $C_{19}H_{16}F_6KN_2O_4$ [M+K]$^+$ 489.0646, found 489.0621.

2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11-Icosafluorododecan-1,12-diyl bis(phenylcarbamate), **7c**

White solid. Yield procedure C: 0.272 g, 68 %. M.p. (ºC): 146.4 (DSC). ^{1}H NMR (360 MHz, acetone-d$_6$): δ 4.90 (t, $^3J_{HF}$ = 10.8 Hz, 4H, CH$_2$), 7.09 (t, $^3J_{HH}$ = 7.2 Hz, 2H, *para*), 7.34 (t, $^3J_{HH}$ = 7.2 Hz, 4H, *meta*), 7.59 (d, $^3J_{HH}$ = 7.2 Hz, 4H, *ortho*), 9.15 (s, 2H, NH). ^{13}C{^{1}H} NMR (90.5 MHz, acetone-d$_6$): δ 59.4 (t, $^2J_{CF}$ = 27.2 Hz, CH$_2$), 107-123 (undefined, CF$_2$), 118.6 (s, *ortho*), 123.4 (s, *para*), 128.9 (s, *meta*), 138.4 (s, *ipso*), 151.7 (s, CO). ^{19}F{^{1}H} NMR (235.2 MHz, acetone-d$_6$): δ -124.28 (m, 4F), -122.73 (m, 12F), -120.69 (m, 4F). IR (ATR): 3351 (N-H st), 1722 (C=O st), 1599 (arom. C-C), 1536 (N-H δ), 1447, 1274 (N-CO-O st as), 1143 (C-F st), 988, 953, 806, 759 (C-F δ), 689, 622 cm^{-1}. HRMS-ESI$^+$: m/z calcd for $C_{26}H_{17}F_{20}N_2O_4$ [M+H]$^+$ 801.0863, found 801.0889. Calcd for $C_{26}H_{16}F_{20}N_2NaO_4$ [M+Na]$^+$ 823.0683, found 823.0705. Calcd for $C_{26}H_{16}F_{20}KN_2O_4$ [M+K]$^+$ 839.0422, found 839.0439.

2,2,4,4,5,5,7,7-Octafluoro-3,6-dioxaoctane-1,8-diyl bis(phenylcarbamate), **7d**

White solid. Yield procedure C: 0.205 g, 77 %. ^{1}H NMR (250 MHz, acetone-d$_6$): δ 4.73 (t, $^3J_{HF}$ = 10.0 Hz, 4H, CH$_2$), 7.09 (t, $^3J_{HH}$ = 7.5 Hz, 2H, *para*), 7.34 (t, $^3J_{HH}$ = 7.5 Hz, 4H, *meta*), 7.59 (d, $^3J_{HH}$ = 7.5 Hz, 4H, *ortho*), 9.11 (s, 2H, NH). ^{13}C{^{1}H} NMR (62.5 MHz, acetone-d$_6$): δ 61.8 (t, $^2J_{CF}$ = 32.7 Hz, CH$_2$), 119.1 (s, *ortho*), 112-127 (undefined, CF$_2$), 123.7 (s, *para*), 129.2 (s, *meta*), 138.8 (s, *ipso*), 152.1 (s, CO). ^{19}F{^{1}H} NMR (235.2 MHz, acetone-d$_6$): -89.81 (t, $^3J_{FF}$ = 13.4 Hz, CH$_2$C*F*$_2$O), -78.66 (t, $^3J_{FF}$ = 13.4 Hz, OC*F*$_2$CF$_2$). IR (ATR): 3349 (N-H st), 1721 (C=O st), 1603 (arom. C-C), 1538 (N-H δ), 1449, 1401, 1276 (N-CO-O st as), 1151 (C-F st), 1080, 986, 940, 760, 736 (C-F δ), 691 cm^{-1}. HRMS-ESI$^+$: m/z calcd for $C_{20}H_{17}F_8N_2O_6$ [M+H]$^+$ 533.0953, found 533.0967. Calcd for $C_{20}H_{20}F_8N_3O_6$ [M+NH$_4$]$^+$ 550.1219, found 550.1222. Calcd for

$C_{20}H_{16}F_8N_2NaO_6$ [M+Na]$^+$ 555.0773, found 555.0798. Calcd for $C_{20}H_{16}F_8KN_2O_6$ [M+Na]$^+$ 571.0512, found 571.0529.

2,2,3,3-Tetrafluorobutane-1,4-diyl bis(pentafluorophenylcarbamate), **11a**

White solid. Yield procedure C: 0.229 g, 79 %. ^{1}H NMR (250 MHz, acetone-d$_6$): δ 4.81 (t, $^3J_{HF}$ = 13.9 Hz, 2H, CH$_2$), 9.03 (bs, 2H, NH). ^{13}C{^{1}H} NMR (90.5 MHz, acetone-d$_6$): 60.6 (t, $^2J_{CF}$ = 26.7 Hz, CH$_2$), 112.7 (t, $^2J_{CF}$ = 16 Hz, *ipso*), 116.3 (tt, $^1J_{CF}$ = 253.0 Hz, $^2J_{CF}$ = 32 Hz, CF$_2$), 137.7 (dm, $^1J_{CF}$ = 249.0 Hz, *meta/para*), 139.3 (dm, $^1J_{CF}$ = 251 Hz, *para/meta*), 143.6 (dm, $^1J_{CF}$ = 249.0 Hz, *orto)*, 152.4 (s, CO). ^{19}F NMR (235.2 MHz, acetone-d$_6$): δ -165.78 (t, $^3J_{FF}$ = 18.8 Hz, 4F, *meta*), -159.83 (t, $^3J_{FF}$ = 19.7 Hz, 2F, *para*), -148.37 (d, $^3J_{FF}$ = 17.1 Hz, 4F, *orto*), -123.01 (t, $^3J_{HF}$ = 13.9 Hz, 4F, CF$_2$). IR (ATR): 3350 (N-H st), 1723 (C=O st), 1599 (arom. C-C), 1535 (N-H δ), 1500, 1448, 1274 (N-CO-O st as), 1144 (C-F st), 980, 824, 759 (C-F δ), 689, 624 cm^{-1}. HRMS-ESI$^+$: m/z calcd for $C_{18}H_7F_{14}N_2O_4$ [M+H]$^+$ 581.0177, found 581.0212. Calcd for $C_{18}H_{10}F_{14}N_3O_4$ [M+NH$_4$]$^+$ 598.0442, found 598.0462. Calcd for $C_{18}H_6F_{14}N_2NaO_4$ [M+Na]$^+$ 602.9996, found 603.0031. Calcd for $C_{18}H_6F_{14}KN_2O_4$ [M+K]$^+$ 618.9736, found 618.9751.

2,2,3,3,4,4-Hexafluoropentane-1,5-diyl bis(pentafluorophenylcarbamate), **11b**

White solid. Yield procedure C: 0.144 g, 45 %. ^{1}H NMR (250 MHz, acetone-d$_6$): δ 4.88 (t, $^3J_{HF}$ = 15.0 Hz, 4H, CH$_2$), 9.11 (bs, 2H, NH). ^{13}C{^{1}H} NMR (90.5 MHz, acetone-d$_6$): 60.7 (t, $^2J_{CF}$ = 26.8 Hz, CH$_2$), 108-112 (undefined, central CF$_2$), 112.6 (t, $^2J_{CF}$ = 16 Hz, *ipso*), 115.0 (tt, $^1J_{CF}$ = 256 Hz, $^2J_{CF}$ = 32 Hz, CH$_2$CF$_2$), 137.8 (dm, $^1J_{CF}$ = 250 Hz, *meta/para*), 140.1 (dm, $^1J_{CF}$ = 251 Hz, *para/meta*), 143.6 (dm, $^1J_{CF}$ = 248 Hz, *orto)*, 152.4 (s, CO). ^{19}F{^{1}H} NMR (235.2 MHz, acetone-d$_6$): δ -165.71 (aparent t, $^3J_{FF}$ = 18.8 Hz, 4F, *meta*), -159.70 (t, $^3J_{FF}$ = 19.0 Hz, 2F, *para*), -148.38 (d, $^3J_{FF}$ = 16.9 Hz, 4F, *orto*), -127.08 (s, 2F, central CF$_2$), -121.22 (s, 4F, CH$_2$CF$_2$). IR (ATR): 3349 (N-H st), 1722 (C=O st), 1601 (arom. C-C), 1536 (N-H δ), 1448, 1400, 1274 (N-CO-O st as), 1145 (C-F st), 1118, 987, 940, 759 (C-F δ), 735, 690, 625 cm^{-1}. HRMS-ESI$^+$: m/z calcd for $C_{19}H_6F_{16}N_2NaO_4$ [M+Na]$^+$ 652.9964, found 652.9969.

2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11-Icosafluorododecan-1,12-diyl bis(pentafluorophenylcarbamate), **11c**

Yield procedure C: 0.265 g, 54 %. ^{1}H NMR (250 MHz, acetone-d$_6$): δ 4.95 (t, $^3J_{HF}$ = 13.8 Hz, 4H, CH$_2$), 9.09 (bs, 2H, NH). ^{13}C{^{1}H} NMR (90.5 MHz, acetone-d$_6$): 60.5 (t, $^2J_{CF}$ = 26.7 Hz, CH$_2$), 105-120 (complex absorption, CF$_2$), 112.6 (t, $^2J_{CF}$ = 14.0 Hz, *ipso*), 138.0 (dm, $^1J_{CF}$ = 250 Hz, *meta/para*), 139.7 (dm, $^1J_{CF}$ = 251 Hz, *para/meta*), 143.6 (dm, $^1J_{CF}$ = 249 Hz, *orto)*, 152.2 (s, CO). ^{19}F{^{1}H} NMR (235.2 MHz, acetone-d$_6$): δ -165.77 (aparent t, $^3J_{FF}$ = 21.1 Hz, 4F, *meta*), -159.67 (t, $^3J_{FF}$ = 16.0 Hz, 2F, *para*), -148.44 (d, $^3J_{FF}$ = 16.5 Hz, 4F, *orto*), -124.38 (bs, 4F, CF$_2$), -

122.35 (bs, 12F, CF_2), -120.38 (bs, 4F, CF_2). IR (ATR): 3349 (N-H st), 1722 (C=O st), 1602 (arom. C-C), 1536 (N-H δ), 1448, 1273 (N-CO-O st as), 1146 (C-F st), 940, 759 (C-F δ), 735, 690 cm^{-1}. HRMS-ESI$^+$: m/z calcd for $C_{26}H_7F_{30}N_2O_4$ $[M+H]^+$ 980.9921, found 980.9909. Calcd for $C_{26}H_{10}F_{30}N_3O_4$ $[M+NH_4]^+$ 998.0187, found 998.0184. Calcd for $C_{26}H_6F_{30}N_2NaO_4$ $[M+Na]^+$ 1002.9741, found 1002.9739. Calcd for $C_{26}H_6F_{30}KN_2O_4$ $[M+K]^+$ 1018.9480, found 1018.9477.

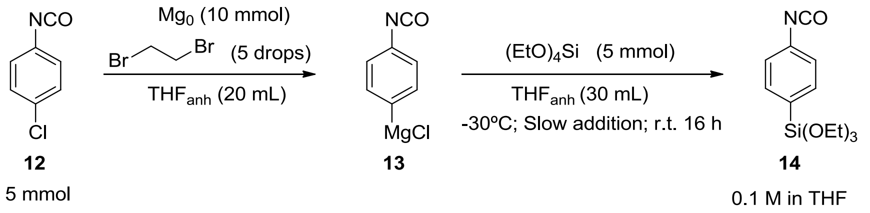
2,2,4,4,5,5,7,7-Octafluoro-3,6-dioxaoctane-1,8-diyl bis(pentafluorocarbamate), **11d**

White solid. Yield procedure C: 0.303 g, 85 %. ^{1}H NMR (360 MHz, acetone-d_6): δ 4.79 (t, $^3J_{HF}$ = 10.8 Hz, 4H, CH_2), 9.12 (bs, 2H, NH). ^{13}C{^{1}H} NMR (90.5 MHz, acetone-d_6): 62.4 (t, $^2J_{CF}$ = 33.5 Hz, CH_2), 112-122 (undefined, OCF_2CF_2), 112.5 (t, $^2J_{CF}$ = 22.0 Hz, *ipso*), 121.7 (t, $^1J_{CF}$ = 278 Hz, CH_2CF_2O), 137.2 (dm, $^1J_{CF}$ = 251 Hz, *meta/para*), 139.8 (dm, $^1J_{CF}$ = 251 Hz, *para/meta*), 143.6 (dm, $^1J_{CF}$ = 249 Hz, *orto)*, 152.1 (s, CO). ^{19}F{^{1}H} NMR (235.2 MHz, acetone-d_6): δ -165.74 (t, $^3J_{FF}$ = 18.7 Hz, 4F, *meta*), -159.74 (t, $^3J_{FF}$ = 19.6 Hz, 2F, *para*), -148.42 (d, $^3J_{FF}$ = 19.3 Hz, 4F, *orto*), -89.92 (t, $^3J_{FF}$ = 11.7 Hz, 4F, CH_2CF_2O), -78.88 (t, $^3J_{FF}$ = 12.9 Hz, 4F, OCF_2CF_2). IR (ATR): 3290 (N-H st), 1725(C=O st), 1601 (arom. C-C), 1536 (N-H δ), 1500, 1449, 1402, 1271 (N-CO-O st as), 1147 (C-F st), 1001, 941, 792, 759 (C-F δ), 689, 624 cm^{-1}. HRMS-ESI$^+$: m/z calcd for $C_{20}H_7F_{18}N_2O_6$ $[M+H]^+$ 713.0011, found 713.0042. Calcd for $C_{20}H_{10}F_{18}N_3O_6$ $[M+NH_4]^+$ 730.0277, found 730.0304. Calcd for $C_{20}H_6F_{18}N_2NaO_6$ $[M+Na]^+$ 734.9831, found 734.9869. Calcd for $C_{20}H_6F_{18}KN_2O_6$ $[M+K]^+$ 750.9570, found 750.9589.

E.5. PERMANENT MODIFICATION OF GLASS SURFACE

E.5.1. PREPARATION OF 4-(TRIETHOXYSILYL)PROPYL ISOCYANATE

This product was prepared from the corresponding chloride precursor following a described protocol.[100]



Magnesium turnings were activated to remove superficial oxide by stirring them in hydrochloric acid 10 % for two minutes, and then washed with acetone and dried in vacuum.

A 50 mL three-neck round-bottom flask containing a magnetic stirring bar was fitted with an addition funnel, a reflux condenser and a silicone septum. It was dried with the heating gun under vacuum and filled with nitrogen; then charged with activated magnesium turnings (244 mg, 10 mmol) and 10 mL of dry THF.

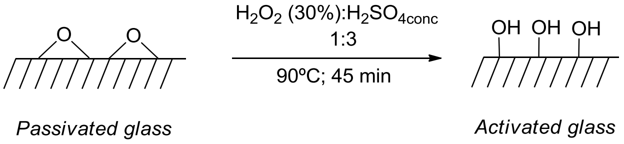
The addition funnel was charged with a solution of 4-chlorophenyl isocyanate **12** (640 µL;5.0 mmol) in 10 mL THF. After 1 mL of dropwise addition, 5 drops of 1,2-dibromoethane were added, followed by gentle heating, to initiate the reaction. The rest of the solution was added at a rate of one drop per second. After four hours, a quenched aliquot of the reaction indicated complete consumption of **13**.

A 100 mL three-neck round-bottom flask was fitted with an addition funnel and a Schlenk adaptor. Under nitrogen atmosphere, it was charged with a solution of tetraethyl orthosilicate TEOS (5 mmol) in THF (30 mL) and cooled to -30 ºC. Then, THF solution of **13** (20 mL) was transferred via filtering cannula to the second addition funnel and added dropwise at low temperature over TEOS solution. The solution was allowed to react for 1 h at -30 ºC and 16 h at room temperature.

The solution was filtered and transferred via canula to a Schlenk to obtain 50 mL of a solution 0.1 M of **14**.

E.5.2. GLASS ACTIVATION

Glass activation consists on produce surface hydroxyls on a typical laboratory glass or silicon.



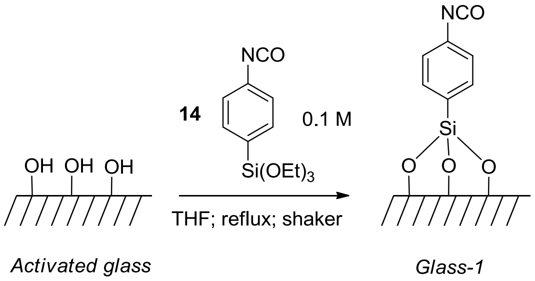
The glasses to be modified were ordinary microscope slides of 2 x 7 cm from Labbox (*Glass-0*). This *Glass-0* were clean and activated with an *acid piranha solution* to generate hydroxyl terminations on the surface, this method generate smoother surfaces than using concentrated base or fluorhydric acid.[120]

On a beaker cooled with ice were poured 10 mL of hydrogen peroxide 30 %. Carefully, 30 mL of concentrated sulfuric acid was poured down, always ice-cooled. It is important to highlight that extreme caution should be used in this operation, as it is an exothermic reaction to form a high corrosive solution.

Then, glasses to be activated were introduced in the solution, still under ice. When bubbling is stopped, beaker was covered with a watch glass and heated up to 90 ºC for 45 min. After that, glass was rinsed with abundant deionized water and dried in vacuum.

E.5.3. GLASS MODIFICATION WITH AROMATIC ISOCYANATE

Activated glass reacted with **14** in order to obtain a glass surface modified with an aromatic isocyanate.



Dry activated glass was placed in the solution of 4-(triethoxysilyl)phenyl isocyanate **14** (0.1 M in THF; 20 mL) in a closed reaction tube. It was sealed and heated up to 50 ºC and agitated with an oscillatory shaker at 120 oscillations per minute. The use of shacker allows the stirring the reaction but without a stirring magnetic bar that could break the glass.

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[120] Park, J.; Henn-Lecordier, L. *Standard Operating Procedures for Piranha Solutions,* Laboratory for advanced Material Processing, Univeristy of Maryland, **2003.** http://www.lamp.umd.edu/Sop/Piranha_SOP.htm (Access date: 27th March 2014)

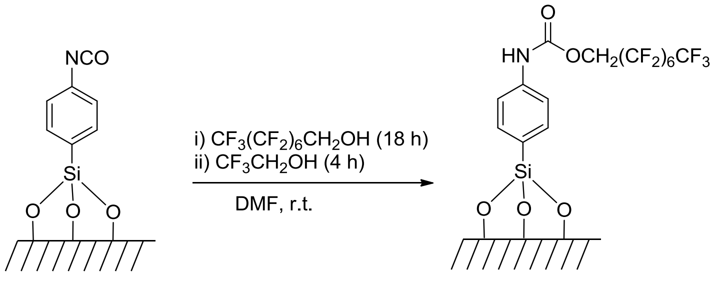
After 18 h glass was cleaned with acetone and dried in vacuum to obtain a glass modified with the aromatic isocyanate *Glass-1*.

E.5.4. CARBAMATE FORMATION OVER GLASS SURFACE

In order to react the aromatic isocyanates linked in the surface of *Glass-1* two procedures were assayed. The first one is ground state reaction in DMF (*Glass-2*) and the second, photochemical reaction in MeCN (*Glass-3*).

The reactions were carried out first with long polyfluorinated alcohol **2b** and then, in case there was some unreacted isocyanate group, a second reaction was performed with the more reactive 2,2,2-trifluoroethanol **2a**.

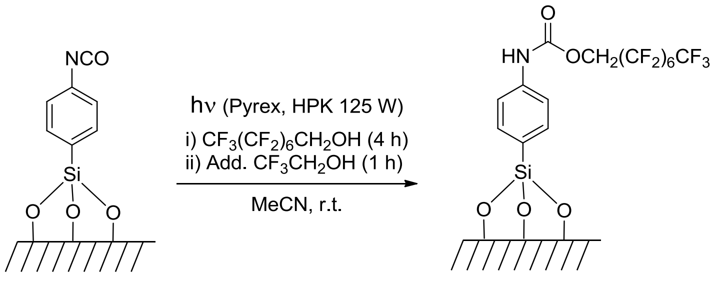
GROUND STATE REACTION



Glass-1 *Glass-2*

A sample of *Glass-1* was placed in a reaction tube in a solution of 2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluoro-1-octanol **2b** (0.02 M; 20 mL dry DMF). This tube was stirred at room temperature with shaker for 18 h at 120 oscillations per minute. After that, it was placed in a solution of TFE **2a** (0.01 M; 20 mL dry DMF) for 4 h to complete reaction of possible unreacted isocyanate groups. Finally, this glass was washed with acetone and dried in vacuum to obtain a modified glass named *Glass-2*.

PHOTOCHEMICAL REACTION

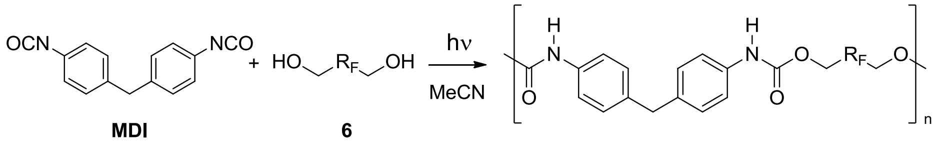


Glass-1 *Glass-3*

A sample of *Glass-1* was cut down using a diamond pen to 2 x 6 cm in order to be placed inside a 50 mL photochemical reactor. This photochemical reactor was fitted with a Schlenk adaptor, a glass stopper and a small stirring bar. It was charged with 50 mL of a previously degassed solution of **2b** (0.02 M in MeCN). Then, cooling water flow and UV irradiation were turned on (Philips HPK 125 W; Pyrex filter). After 4 h of irradiation TFE **2a** was added to the solution (72 µL, 1 mmol) and 1 h later, irradiation was turned off. The glass was washed with acetone and dried in vacuum (*Glass*-*3*).

E.6. PHOTOPOLYMERIZATION REACTIONS

E.6.1. PHOTOREACTION OF MDI WITH POLYFLUORINATED DIOLS USING 125 W LAMP



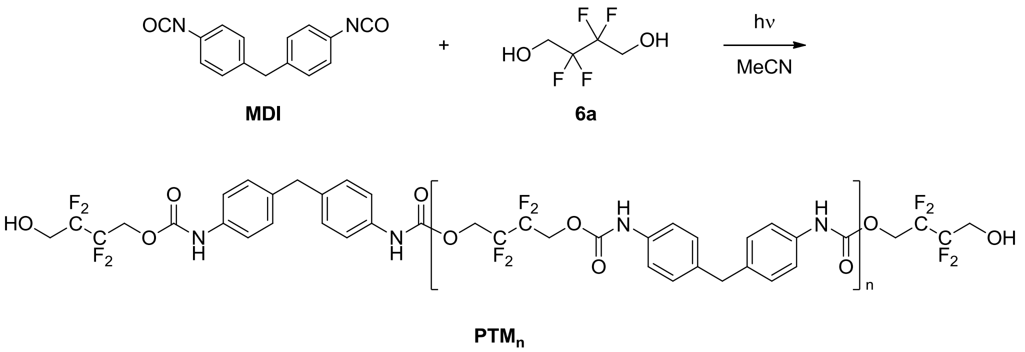
MDI **6**

R_F:
- **6a**, $(CF_2)_2$
- **6c**, $(CF_2)_{10}$
- **6d**, $CF_2O(CF_2)_2OCF_2$

Dry acetonitrile (45 mL) was degassed by three cycles of freeze-pump-thaw and placed under inert atmosphere in a 50 mL photochemical reactor equipped with a magnetic stirring, a glass stopper, a stopcock and a water-flow cooled pyrex immersion well. Crunched 4,4’-methylene diphenyl diisocyanate MDI (63 mg, 0.25 mmol) was added and solved using vigorous stirring and ultrasounds until clear solution.

Afterwards a solution of the corresponding polyfluorinated diol **6** in dried and degassed acetonitrile (5 mL) was added to the reactor. Cooling flow was turned on and mixture was stirred for five minutes to homogenize before the irradiation source (HPK Philips 125 W) was turned on. After four hours, lamp was switched off and solvent evaporated *in vacuo* to obtain a white-yellowish solid. To perform GPC analysis, 10 mg were solved in 1 mL THF and filtered with nylon syringe filter.

E.6.2. PHOTOREACTION OF MDI WITH 6A USING 400 W LAMP



PTM$_n$

Dry acetonitrile (730 mL) was placed in a photochemical reactor under inert atmosphere equipped with magnetic stirring, a glass stopper, a stopcock and a water-flow cooled pyrex immersion well. Oxygen was removed by bubbling nitrogen while vigorous stirring for 45 min.

4,4’-methylene diphenyl diisocyanate MDI (938 mg; 3.75 mmol) was crunched in a morter until a fine powder was obtained. Then, MDI was added to the photochemical reaction and solved with the aid of ultrasounds (This could take up to one hour). Afterwards, a solution of diol **6a** (608 mg; 3.75 mmol) in dried and degassed acetonitrile (20 mL) was added to the reactor.

Cooling flow was turned on and mixture was stirred for ten minutes to homogenize it before irradiation source (RQ3040 400 W) was turned on. If the cooling flow was a water flow at room temperature, then reaction temperature was not higher than 30 ºC. If cooling flow used was a methanol flow at -10 ºC, then reaction temperature was lower than 0 ºC.

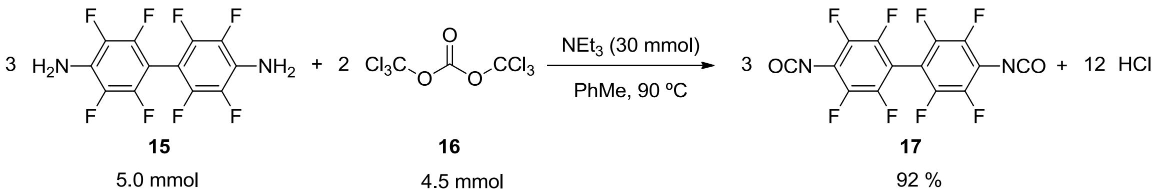
Samples were taken under nitrogen flow to avoid oxygen entering in the reaction. From a sample of 10 mL, approximately 20 mg of dried solid were obtained after evaporation; they were used for GPC and NMR analysis.

After the corresponding reaction time, lamp was switched off. When the lamp was cool enough, cooling flow was turned off. Then, solution was evaporated in the rotary evaporator at a temperature of no more than 30 ºC to obtain a yellow solid.

If required, this solid could be successfully solved in THF and re-precipitated by adding hexane to obtain different molecular weight fractions of the polymer obtained.

E.6.3. PREPARATION OF A PERFLUORINATED AROMATIC DIISOCYANATE

perfluoro-(1,1'-biphenyl)-4,4'-diisocyanate, **17** [121]



This reaction involves the use of solid triphosgene ***16*** *which can generate toxic phosgene gas. Extreme precaution must be employed in its handling. Bottle, flasks and solutions containing or having contained triphosgene should never be opened outside the fumehood.*

In a three-necked round bottom flask fitted with a reflux condenser, a compensated pressure addition funnel and a Schlenk adaptor, a suspension of triphosgene **16** (1.34 g; 4.5 mmol) and dry triethylamine (4.15 mL; 30.0 mmol) in dry toluene was prepared under nitrogen atmosphere.

Using the addition funnel a solution of perfluoro-(1,1'-biphenyl)-4,4'-diamine **15** (1.62 g; 5.0 mmol) in toluene was added drop-wise. The mixture was stirred at 60 ºC for 60 min and then at 90 ºC for 60 min more, until analysis by GC-MS showed that diamine **15** was consumed and that there was just diisocyanate **17**, with no signal of aminoisocyanate intermediate. When mixture was cooled at room temperature, solid containing salts and unreacted triphosgene were filtered out and washed with toluene. First, this waste solid was treated with ethanol 96 %, later with basic aqueous solution, to degrade the possible unreacted triphosgene.

The solution filtered containing diisocyanate, was evaporated *in vacuo* and recrystallized with THF/pentane to obtain perfluoro-(1,1'-biphenyl)-4,4'-diisocyanate **17** as an orange solid (1.74 g; 92 %).

^{19}F NMR (235.2 MHz, $CDCl_3$): δ -147.8 (s, 4F, F_{orto}) -142.5 (s, 4F, F_{meta}).

GCMS-ECI: m/z calcd. for $C_{14}F_8N_2O_2$ [M^-] 380.0; found 380.0 m/z.

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[121] Gosnell, R.; Hollander, J. J. *Macromol. Sci. Phys.* **1967**, *1*, 831-850.