Perfluoroalkylation of Olefins by Electrocatalysis

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Magdalena Sommer
Aus Darmstadt

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aus dem Institut für Organische Chemie und Makromolekulare Chemie
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Ich versichere an Eides statt, dass die Dissertation von mir selbständig und ohne unzulässige fremde Hilfe unter Beachtung der „Grundsätze zur Sicherung guter wissenschaftlicher Praxis an der Heinrich-Heine-Universität Düsseldorf“ erstellt worden ist.

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Publikationen

Teile dieser Arbeit wurden bereits publiziert.

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09/2017	International Summerschool on Electrosynthesis, Mainz Poster Präsentation: “Electrocatalytic Perfluoroalkylation of Olefins”

Table of Content

1 Preliminary Notes and Abbreviations

1.1 Preliminary Notes

Compounds, references, figures, schemes and tables are consecutively numbered. New compounds are named according to the chemical nomenclature of IUPAC.[1]

1.2 Abbreviations

b.p.	boiling point
bpy	2,2'-bipyridine
brs	broadened signal
COSY	correlated spectroscopy
CV	cyclic voltammetry
d	doublet
de	diastereomeric excess
d.r.	diastereomeric ratio
ee	enantiomeric excess
e.g.	for example
EI	electron ionisation
eq.	equivalents
ESI	electron spray ionisation
GC	glassy carbon
HFIP	hexafluoroisopropanol
HMBC	heteronuclear multiple bond correlation
HRMS	high resolution mass spectrometry
HSQC	heteronuclear single quantum correlation

IR	infrared spectroscopy
IUPAC	*International Union of Pure and Applied Chemistry*
m	multiplet
m.p.	melting point
MS	mass spectrometry
NMR	*nuclear magnetic resonance*
ntd	not detected
o.n.	over night
ppm	*parts per million*
pybox	(*S*,*S*)-2,6-bis(4-phenyl-2-oxazolin-2-yl)-pyridine
q	quartet
R	residue
R_F	perfluoroalkyl group/substituent
R_f	retention factor
r.t.	room temperature
s	singlet
SET	single electron transfer
t	triplet
TBAF	tetrabutylammonium fluoride
TBAT	tetrabutylammonium difluorotriphenylsilicate
TBATFB	tetrabutylammonium tetrafluoroborate
TFA	trifluoroacetic acid
THF	tetrahydrofuran

TLC	thin layer chromatography
TMS	trimethylsilyl
tpy	2,2’:6’,2’’-terpyridine

2 Abstract

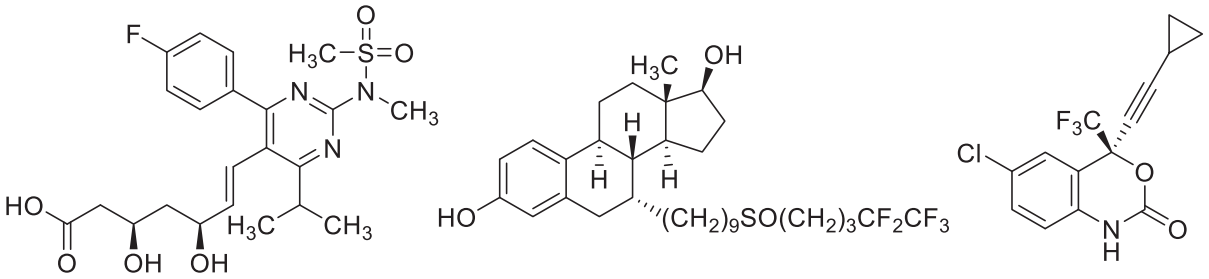
This work describes the development of a novel synthetic protocol for the electrochemical perfluoroalkylation of olefins. A synthetic protocol for the electrocatalytic iodoperfluoroalkylation of olefins was developed. Various factors such as electrode material, solvent, supporting electrolyte and additives were investigated. The electrochemical difunctionalisation can be achieved under constant current condition (10 mA) in a divided cell using hexafluoroisopropanol as solvent and tetrabutylammonium tetrafluoroborate as supporting electrolyte. Various terminal and internal alkenes were converted into the 1,2-addition products in moderate to excellent yield. The reaction proceeds under metal- and catalyst-free conditions using electrons as the sole reagent. The electrochemical hydroperfluoroalkylation of *N*-acyloxazolidinones and acrylamides was investigated. Direct and mediated methods were applied to *N*,*N*-dibutylpropionamide and resulted in the formation of *N*,*N*-dibutyl-4,4,5,5,6,6,7,7,7-nonafluoroheptanamide in 21% yield. Finally, studies were conducted for the perfluoroalkylation of an electrogenerated iminium ion intermediate using either trifluoromethyltrimethylsilane in addition with various initiators or perfluoroiodoalkanes.

3 State of Knowledge

The first part of this chapter gives a short introduction to fluorine and its application in pharmaceuticals, as well as to organic electrosynthesis. In the second part, perfluoroalkylation methods will be discussed, which can be achieved *via* electrophilic, nucleophilic or radical procedures. The focus will be on the electrochemical perfluoroalkylation of alkenes in particular.

3.1 Fluorinated Compounds

Methods for the introduction of fluorinated moieties into organic molecules are of significant synthetic interest, due to the fact that fluorine atoms can exhibit a great impact on the physicochemical properties.[2] The small size, next to the high electronegativity and the low polarizability are only a few attributes that make fluorine so outstanding.[3] Not only is the carbon-fluorine bond (105.4 kcal/mole) one of the strongest bonds known, but it can also increase the strength of neighbouring carbon-carbon single bonds.[4] Because of the high sensitivity of the ^{19}F nucleus and the natural abundance of 100%, ^{19}F NMR spectroscopy is a very powerful method for the analysis of proteins either in *vivo* or in *vitro*.[5] Moreover, the oxidation of a molecule by P450 enzymes is highly affected by the exchange of a proton with a fluorine atom, resulting in a reduced metabolism rate.[6] It is therefore unsurprising, that the installation of fluorine atoms can modify the lipophilicity, solubility, pK_a and hydrogen-bond interactions of bioactive compounds.[2] In 1957, no fluorine containing drug could be found on the market, whereas in 2010, fluorine was already incorporated in 20% of all pharmaceuticals and 30% of all agrochemicals.[4, 7] Over the last couples of years this value has increased even more, so that 30% of the newly introduced drugs now contain at least one fluorine atom.[8] Examples of top-selling fluorinated drugs include Rosuvastatin (Crestor®) (**1**) used for lowering cholesterol levels, the anti-cancer drug Fulvestrant (**2**) and Efavirenz (Sustiva®) (**3**), an HIV−1−reverse transcriptase inhibitor, shown in Figure 1.[7, 9-11]



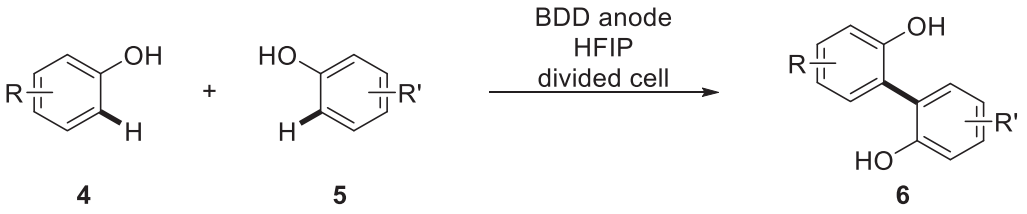
Rosuvastatin (**1**) Fulvestrant (**2**) Efavirenz (**3**)

Figure 1: Rosuvastatin (**1**), Fulvestrant (**2**) and Efavirenz (**3**).

3.2 Organic Electrosynthesis

Electrosynthesis is the anodic oxidation or cathodic reduction of organic compounds employing only electrons as reagents or mediators that are electrochemically regenerated.[12] In the early 19th century, the first example for an organic electrosynthetic process was presented by Faraday converting an acetate solution into gaseous ethane.[13] A few years later, the decarboxylation and dimerization of carboxylic acids was established by Kolbe.[14, 15] After these first demonstrations, a lot of examples followed.[16] However, many organic synthesists still avoid the use of electrosynthetic techniques for the realisation of reactions.[17] This can be rationalized with the fact that the set-up of electrochemical cells is deemed to be very complex. Indeed, many choices must be made between galvanostatic or potentiostatic electrolysis, divided or undivided cells and electrode compositions to name only a few. In addition, an increased number of reaction variables have to be considered. Nevertheless, the development of new methods for electrosynthetic reactions is especially appealing as the use of electric current represents a greener, commercially interesting alternative by avoiding reagent waste.[18] Consequently, a potentially dangerous or toxic terminal oxidizing or reducing agent can be avoided by electroconversion at the electrodes.[19] Moreover, if electricity is provided by renewable sources, electrosynthesis becomes even more sustainable.[12] Fortunately, in the last decades organic electrosynthesis was rediscovered as a powerful tool for the construction of complex structures.[20] Presumably, this development was started by Little *et al*., Schäfer *et al*. and Moeller *et al.* with the invention of electrochemical cyclisation reactions for the synthesis of complex molecules at the end of the 20th century.[21-27] With the cation pool method from Yoshida *et al.* nucleophilic attack can be achieved after anodic oxidation of pyrrolidines and accumulation of cationic reaction intermediates in solution.[28] This reaction is highly versatile and even

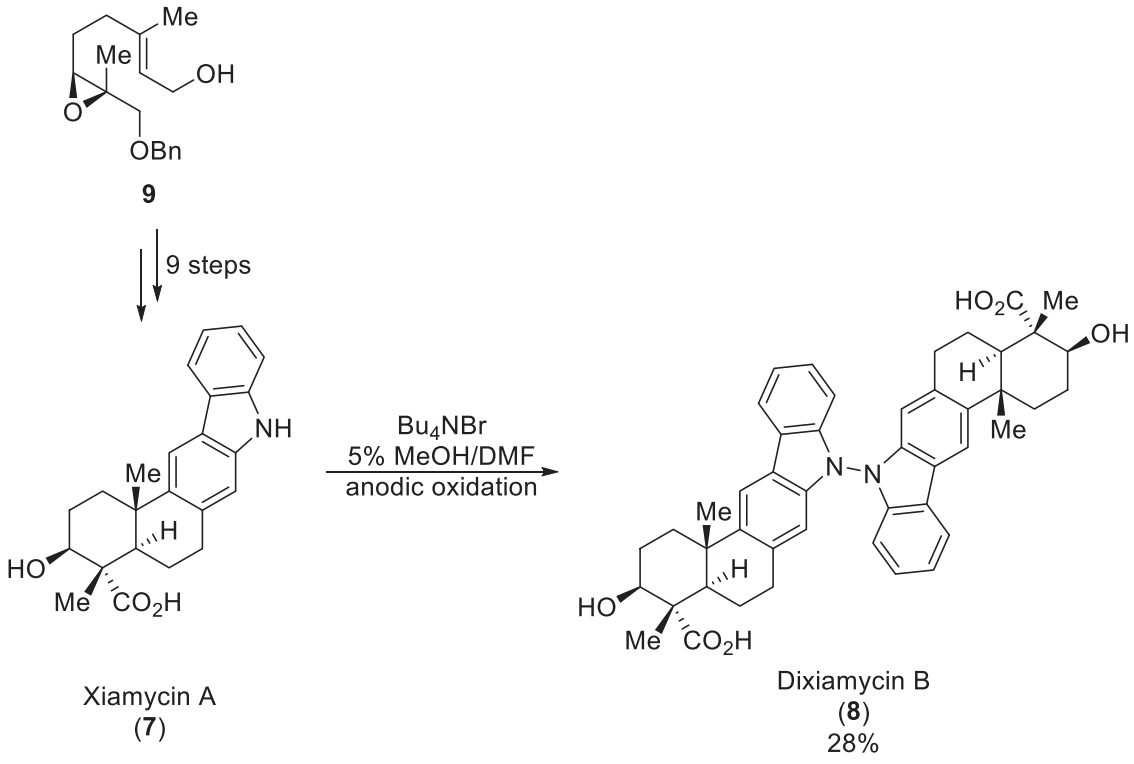
applicable to electrochemical C-H amination if the cationic pool is stabilized by pyridine, which prevents over-oxidation.[29-32] Another notable innovation is the anodic cross-coupling of phenols **4** and **5** towards nonsymmetrical biaryl system **6** demonstrated by Waldvogel *et al.* (Scheme 1).[33-38]



4 **5** **6**

Scheme 1: Biaryl cross coupling.[33]

Furthermore, organic electrochemistry is also successfully applied for the construction of natural products. Some examples are the synthesis of quadrone by Little *et al*., the synthesis of alliacol A by Moeller *et al*., the synthesis of guanacastepene E by Trauner *et al*. and the alkanin and shikonin syntheses by Nicolaou.[39-43] As a last solution, Baran *et al*. turned to electrochemistry when standard synthetic procedures failed for the N-N coupling of xiamycin A (**7**) in the total synthesis of dixiamycin B (**8**) (Scheme 2).[44, 45] Starting from enantioenriched alcohol **9** the natural product can be constructed in only ten steps using the anodic oxidation of xiamycin A.



Xiamycin A (**7**)

Dixiamycin B (**8**) 28%

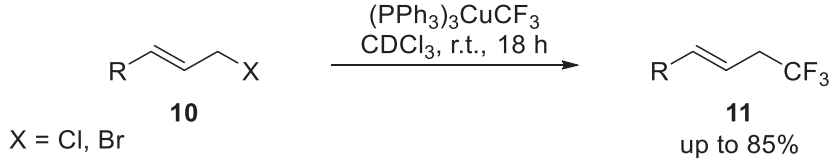
Scheme 2: Synthesis of dixiamycin B.[44, 45]

3.3 Perfluoroalkylation and Trifluoromethylation

The selective incorporation of fluorine atoms in highly functionalized compounds still provides synthetic chemists with a significant challenge. Three general methods are known for the insertion of fluoroalkyl substituents into various substrates.[46] In the nucleophilic version an R_F-anion is formed as reactive species either by deprotonation or exchange of a halogen with a metal. Electrophilic perfluoroalkylation has to handle the strong, destabilizing inductive effect of fluorine atoms, so that only few α- and β-perfluorocarbocation salts, such as perfluoroalkyliodonium salts or fluoroalkylated onium salts of chalcogens, are known.[47, 48] At last, radical perfluoroalkylations involve the generation of perfluoroalkyl radicals by either photochemistry, treatment with radical initiators or electrochemistry.[46] In this chapter, methods for the nucleophilic, electrophilic and radical perfluoroalkylation will be discussed, whereas chapter 3.4 covers the electrochemical procedures for the perfluoroalkylation of alkenes.

3.3.1 Nucleophilic Perfluoroalkylation

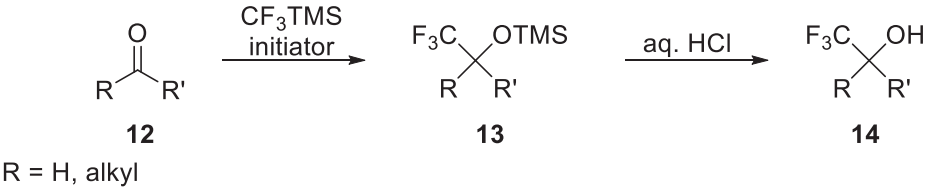
The reactive species involved in a nucleophilic perfluoroalkylation is a R_F-anion, which is stabilised by the negative inductive effect of the fluorine atoms.[46] However, the proximity of the anionic center and the lone pairs of the adjacent fluorine atoms leads to a destabilisation due to p-π-repulsion. The resulting instability of the R_F-anion causes the elimination of fluoride towards a difluorocarbene. A stabilisation can be achieved by using nucleophilic organometallic compounds with one example being organocopper reagents. The regioselective trifluoromethylation of allylic halides **10** by a Cu-CF_3 reagent was demonstrated by Szabó *et al*. (Scheme 3).[49] The reaction towards trifluoromethylated products **11** proceeds presumably through an allyl copper intermediate.



Scheme 3: Allylic trifluoromethylation using a copper reagent.[49]

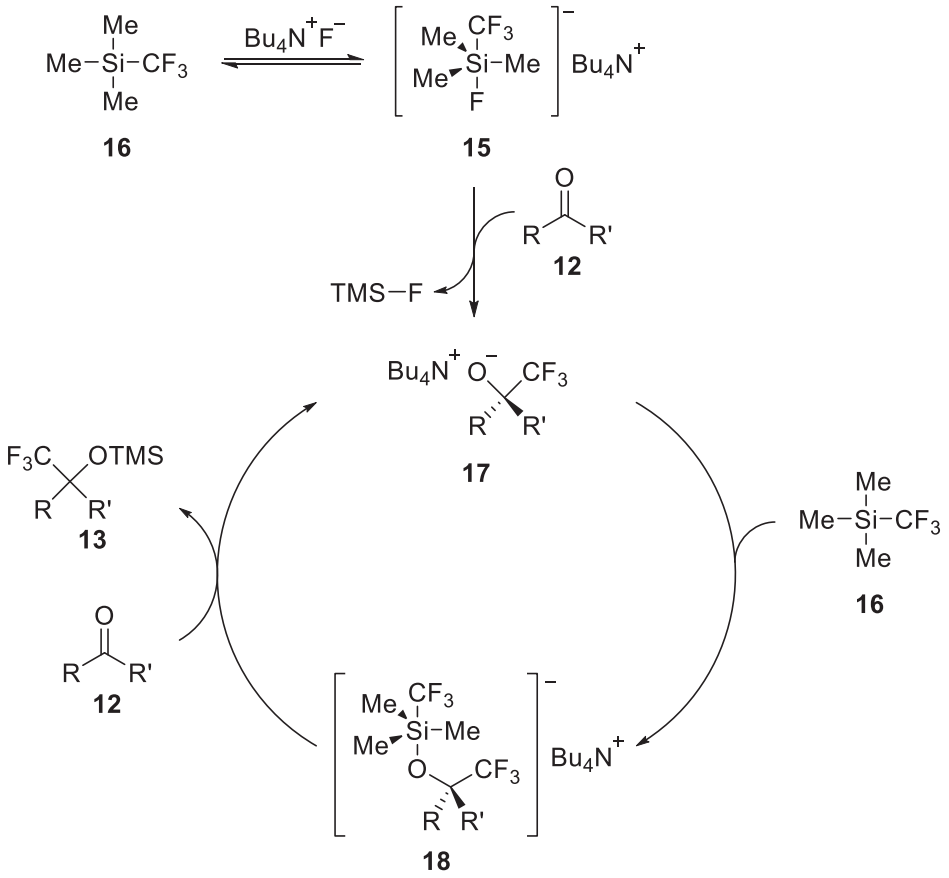
An alternative is represented by organosilicon reagents with the most common being the Ruppert-Prakash reagent.[50] Trifluoromethyltrimethylsilane is successfully applied for the trifluoromethylation of aldehydes and ketones **12** (Scheme 4).[51, 52] The first

step is the addition of the reagent to the carbonyl group using a nucleophilic initiator. Secondly, the formed trimethylsilylated alcohol **13** is desilylated to afford the final product **14**.



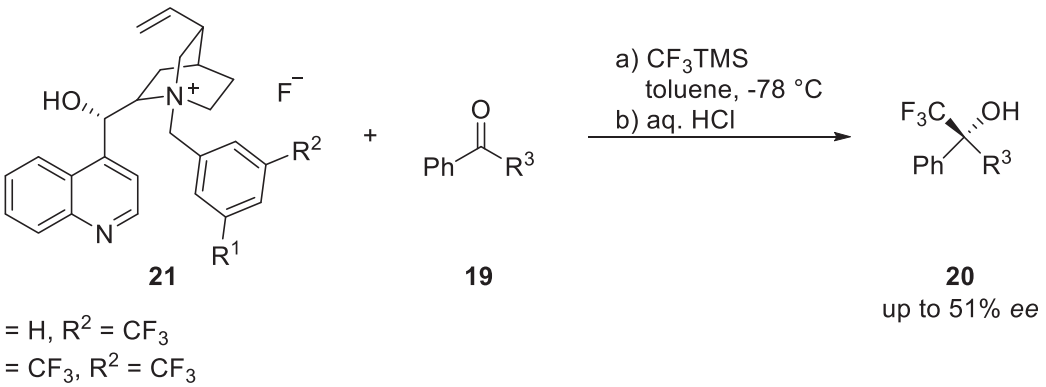
Scheme 4: Trifluoromethylation of aldehydes and ketones with CF_3TMS.[51, 52]

Suitable nucleophilic initiators for the generation of the trifluoromethyl carbanion include tris-(dimethylamino)sulfonium difluorotrimethylsilicate, potassium fluoride or tetrabutylammonium difluorotriphenylstannate.[51] Most commonly, tetrabutylammonium fluoride (TBAF) is used for that purpose. The mechanistic considerations are presented in Scheme 5. Pentaorganosilicate **15** is formed upon addition of TBAF to the Ruppert-Prakasch reagent (**16**). Subsequently, carbonyl compound **12** is added leading to the generation of gaseous trimethylsilyl fluoride and alkoxide **17**, which is stabilised by the tetrabutylammonium cation. The reaction with a second equivalent of CF_3TMS affords the penta-coordinated silicon complex **18**. Finally, the catalytic cycle concludes with the transfer of the trifluoromethyl group to carbonyl compound **12**.



Scheme 5: Mechanistic proposal for the generation of a trifluoromethyl carbanion and trifluoromethylation of carbonyl compounds.[50, 51]

For certain applications such as medicinal purposes a high optical purity of the trifluoromethylated compounds is required.[4] Due to the spatial proximity of the alkoxy intermediate with the tetrabutylammonium cation, an enantiomeric excess could be achieved by application of chiral cations.[51] This theory was proven by Kobayashi *et al*. converting carbonyl compounds **19** into the corresponding trifluoromethylated alcohols **20** with moderate enantiomeric excess using a chiral quaternary ammonium fluoride **21** (Scheme 6).[53]

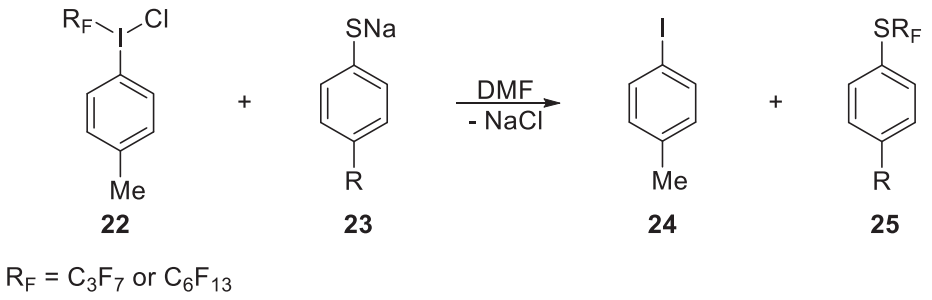


R^1 = H, R^2 = CF_3
R^1 = CF_3, R^2 = CF_3

Scheme 6: Asymmetric trifluoromethylation of carbonyl compounds.[53]

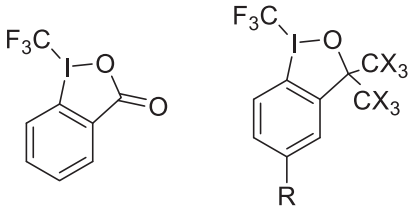
3.3.2 Electrophilic Perfluoroalkylation

Perfluoroalkyl cations involved in electrophilic perfluoroalkylations are stabilised by a mesomeric effect, however, the strong negative inductive effect of the fluorine atoms leads to instability.[46, 54] This problem can be partially solved by the installation of a heteroatom next to the perfluoroalkyl group.[48] Two kinds of α- and β-perfluorocarbocation salts exist. The first are hypervalent iodine derivatives and the second include a chalcogen atom. In 1978, the first example of an electrophilic perfluoroalkylation was reported by Yagupolskii *et al*.[47] The reaction of arylperfluoroalkyliodonium chlorides **22** with sodium thiophenolates **23** affords iodotoluene **24** and perfluoroalkylated sulfides **25** (Scheme 7). Later, Yagupolskii *et al*. changed from chlorides to tetrafluoroborates, which improved the reactivity of the reagents.[55, 56]



Scheme 7: Electrophylic perfluoroalkylation with arylperfluoroalkyliodonium chlorides.[47]

The applicability of iodonium salts for the electrophilic perfluoroalkylation of various nucleophiles was further studied and improved by Umemoto *et al*.[57] The introduction of a triflate group increased the stability and reactivity, so that (perfluoroalkyl)phenyliodonium triflates can even promote the perfluoroalkylation of more challenging nucleophiles such as alkenes or non-activated aromatics.[58] In 2006, a novel, more stable family of hypervalent iodines was synthesized by Togni *et al*.[59, 60] The developed compounds **26** and **27**, also known as Togni reagents, are shown in Figure 2. A multitude of methods for the electrophilic trifluoromethylation of various nucleophiles was reported over the last decade.[61]

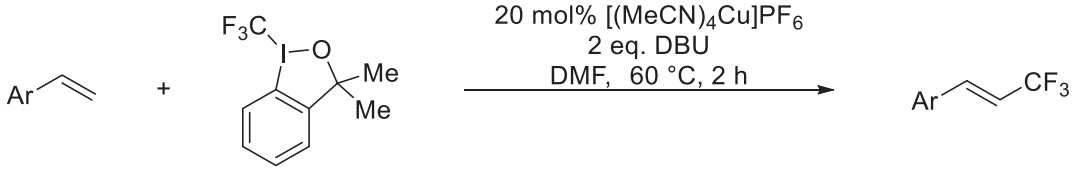


26 **27**

R = H, X = H
R = H, X = F
R = Me, X = F

Figure 2: Togni reagents.[59, 60]

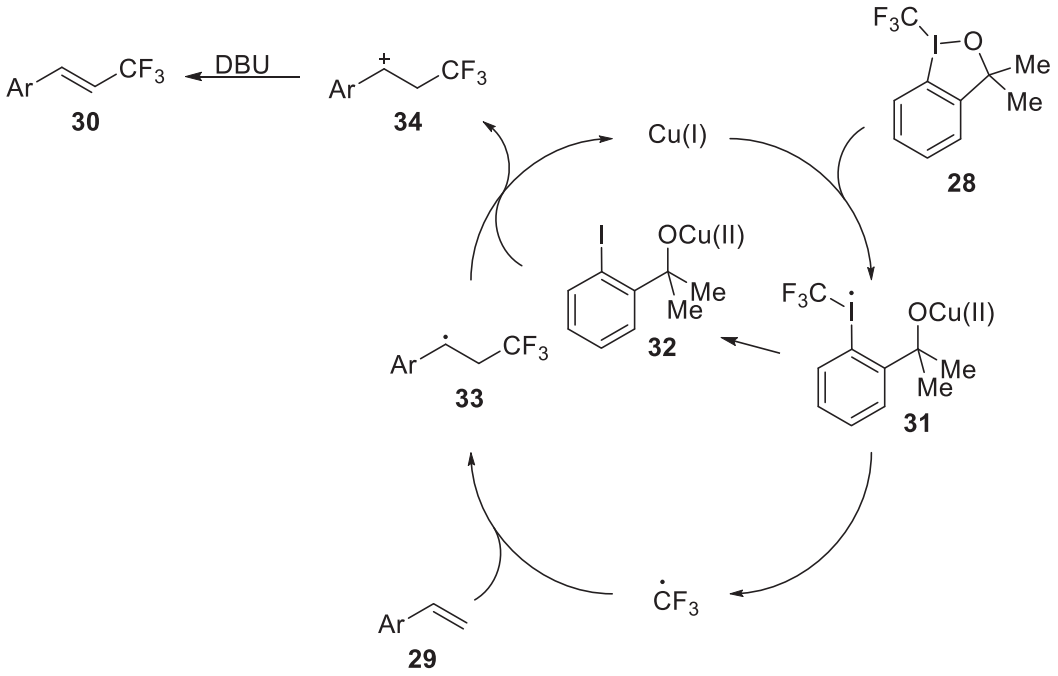
An application of the Togni reagent **28** for the trifluoromethylation of terminal alkenes **29** was demonstrated by Xiao *et al*. (Scheme 8).[62] The combination with a copper-catalyst afforded trifluoromethylated products **30** in good to excellent yields. The reaction proceeded smoothly for a variety of electron-rich and electron-poor styrene derivatives.



29 **28** **30**
63-93%

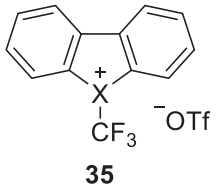
Scheme 8: Copper-catalysed trifluoromethylation of alkenes using Togni's reagent.[62]

The mechanistic considerations are presented in Scheme 9.[62] The initial activation of the electrophilic trifluoromethylating agent **28** by the Cu(I)-catalyst leads to the formation of radical **31**. Subsequently, this intermediate decomposes to afford the trifluoromethyl radical and copper(II)-species **32**. Trapping of the trifluoromethyl radical by alkene **29** forms radical intermediate **33**, which is then oxidized by Cu(II)-compound **32** to release the regenerated Cu(I)-catalyst. Finally, the produced cationic intermediate **34** is deprotonated in the presence of a base to give the final product **30**.



Scheme 9: Proposed mechanism for the copper-catalysed trifluoromethylation of alkenes.[62]

The other important group of electrophilic perfluoroalkylating reagents are fluoroalkylated onium salts of chalcogens. Again, Yagupolskii pioneered in this area synthesizing trifluoromethylated sulfonium salts in 1984.[63] The breakthrough followed some years later with the preparation of a new class of sulfur-, selenium- and tellurium-based reagents **35** by Umemoto *et al*. (Figure 3).[64-66]

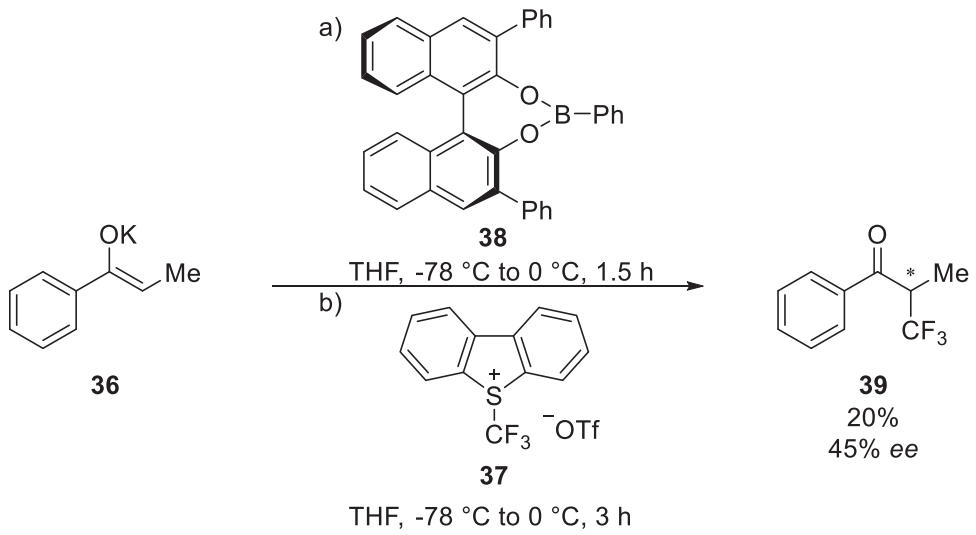


35

X = S, Se, Te

Figure 3: Umemoto reagents.[64-66]

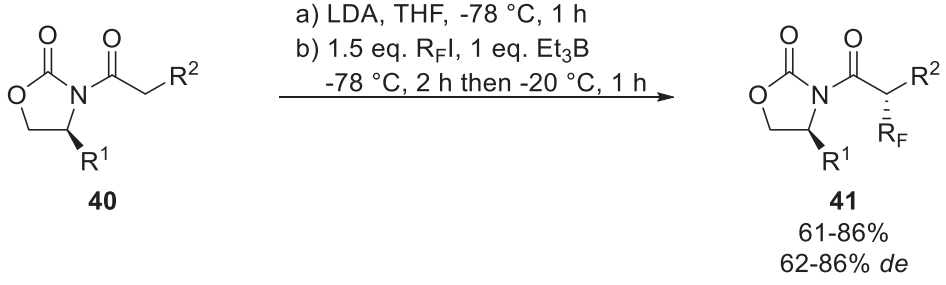
The enantioselective trifluoromethylation of potassium enolate **36** was achieved by combining the sulfur-derived Umemoto reagent **37** with the optically active boron Lewis acid **38** (Scheme 10).[57, 67] Umemoto and Adachi isolated the trifluoromethylated product **39** with a moderate enantiomeric excess of 45% *ee*.



Scheme 10: Enantioselective trifluoromethylation using Umemoto reagent and a chiral boron complex.[67]

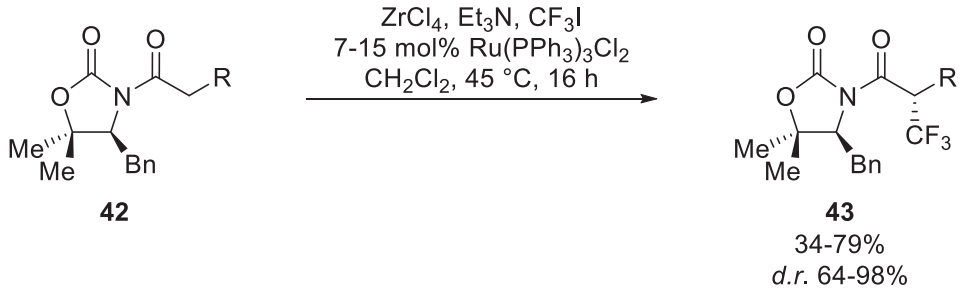
3.3.3 Radical Perfluoroalkylation

The generation of the perfluoroalkyl radicals has to be performed in a fashion that does not influence other functional groups present in the substrates.[46] Methods of choice include the treatment with radical initiators or thermal, photochemical or electrochemical processes. The first three approaches are widely used, however only very few examples for the electrochemical generation are reported. The radicals can be derived from thiolates, selenides, phosphites, alkenes or aromatic compounds. However, the most common source are perfluoroalkyl halides. The asymmetric radical perfluoroalkylation of lithium enolates with triethylborane as a mediator was previously demonstrated by Iseki *et al*. using chiral *N*-acyloxazolidinones **40** (Scheme 11).[68-71] The *α*-perfluoroalkylated carboximides **41** can be treated with $LiBH_4$ to provide the corresponding *β*-perfluoroalkyl alcohols. The attack of the radical on the *Si* face of the lithium-chelated enolate confers a diastereoselectivity of 62-86% *de*.



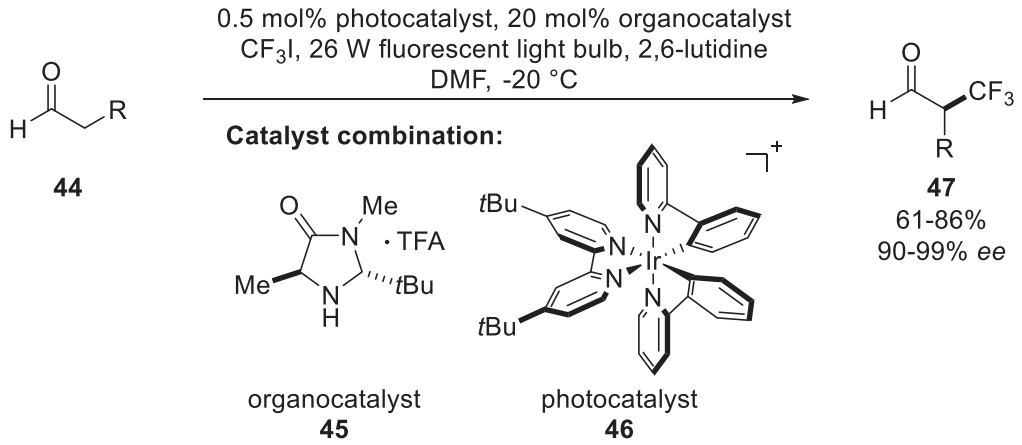
Scheme 11: Stereoselective *α*-perfluoroalkylation of N-acyloxazolidinones.[68-71]

Mikami and co-workers used Et_3B for the enantioselective α-trifluoromethylation of the lithium enolate of 2-phenylcyclohexanone employing (*S*,*S*)-hydrobenzoin and (-)-spartein.[72] However, radicals can also be formed by using transition metal catalysts.[73] For instance, Zakarian *et al*. achieved the ruthenium-catalysed diastereoselective α-trifluoromethylation of chiral *N*-acyloxazolidinones **42** (Scheme 12).[74] The method is compatible with a variety of functional groups and the products **43** were isolated in yields of 34-79% with diastereoselectivities up to 98%.



Scheme 12: Diastereoselective α-trifluoromethylation of *N*-acyloxazolidinones.[74]

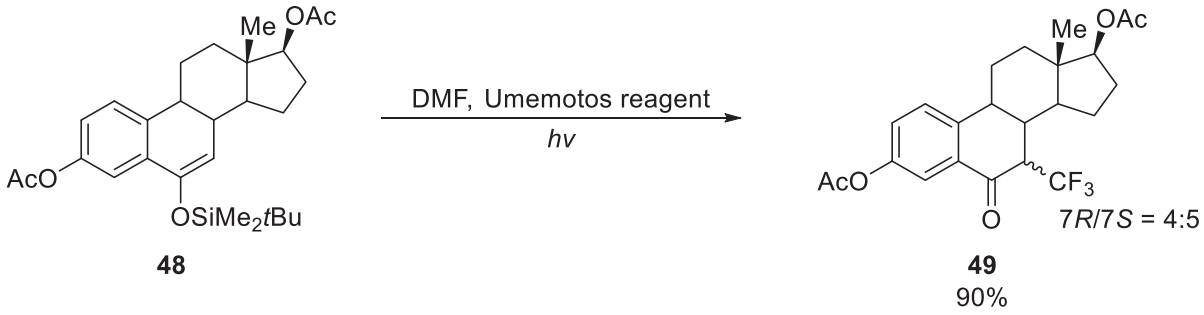
A complimentary method for radical-induced perfluoroalkylation involves photochemistry. MacMillan *et al*. demonstrated the photochemical, highly enantioselective α-trifluoromethylation of aldehydes **44** with chiral organocatalyst **45** and iridium-complex **46** (Scheme 13).[75] The catalyst combination provided products **47** with an enantiomeric excess of 90-99% *ee*.



Scheme 13: Photochemical α-trifluoromethylation of aldehydes.[75]

Photochemically induced trifluoromethylation of a dienyl enol triflate in a steroidal system was also presented by Elliot and co-workers.[76] Noel *et al*. developed the visible light-induced perfluoroalkylation of cysteine residues in batch and continuous flow using $Ru(bpy)_3^{2+}$ as a photocatalyst.[77] Radicals can also be formed by

employing specific reagents. Blazejewski *et al*. were able to introduce a trifluoromethyl group into steroid **48** by reaction of a silyl enol ether with Umemoto's reagent (Scheme 14).[64, 65, 78] UV irradiation increased the yield of product **49** to 90% with the disadvantage of a reduced selectivity (7*R*/7*S* = 4:5).

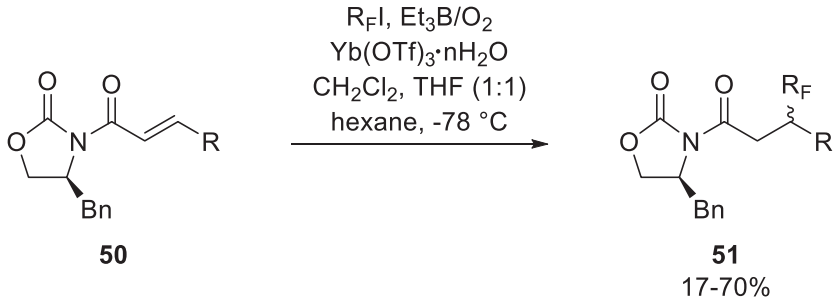


48 **49** 90%

Scheme 14: Trifluoromethylation of a steroidal silyl enol ether.[78]

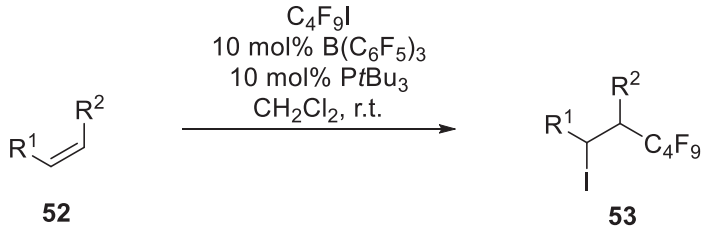
Studer and coworkers presented the radical trifluoromethylation of isonitriles with Togni's reagent as a CF_3 radical precursor.[79] The same approach was utilised by Tan and Liu *et al.* who used Togni's reagent and a chiral Brønsted acid for the C-H bond functionalisation of unactivated alkenes.[80] A tandem radical trifluoromethylation-nucleophilic cyclisation of glucose- and mannose-derived dithioacetals was also developed by Portella *et al*.[81, 82]

The perfluoroalkylation of olefinic substrates is of particular interest within our group. Czekelius *et al*. reported the conjugate *β*-trifluoromethylation of *α*,*β*-unsaturated *N*-acyl-oxazolidinones **50** for the synthesis of chiral fluorinated amino acids and butanolides (Scheme 15).[83-85] In this method perfluoroiodoalkanes are reductively added by employing triethylborane which presumably acts as both a radical initiator and terminator by trapping the enolate radical. The formed boron enolates are then hydrolysed to give the final products. The fluorinated compounds **51** were isolated in yields up to 70%. However, the methodology has limitations, namely, the use of an excess of Et_3B and iodoperfluoroalkanes as well as not providing satisfying diastereoselectivities.



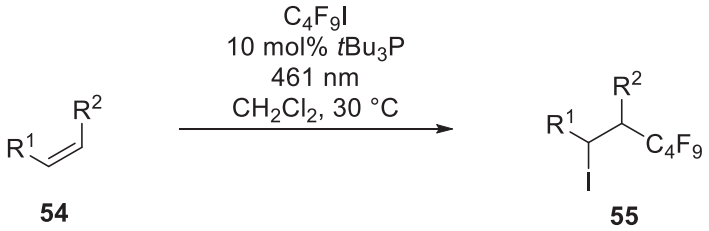
Scheme 15: Conjugate *β*-perfluoroalkylation of acyl-oxazolidinones.[83-85]

The perfluoroalkylation of non-activated olefins was also conducted within our group by a different approach utilizing frustrated Lewis pairs (FLP).[86] It was found that the well-established FLP system $B(C_6F_5)_3/PtBu_3$ catalyses the addition of perfluoroalkyl iodides to alkenes **52** at ambient conditions (Scheme 16). The iodoperfluoroalkylated products **53** were formed with complete regioselectivity.



Scheme 16: Iodoperfluoroalkylation of unsaturated hydrocarbons by FLPs.[86]

During mechanistical studies of the FLP-catalysed reaction, it turned out that the iodoperfluoroalkylation of alkenes **54** can also be achieved under photosynthetic conditions.[87] Visible light in combination with a phosphine catalyst allowed the conversion of the olefin into the 1,2-addition product **55** in moderate to excellent yields for a variety of substrates (Scheme 17).[88]



Scheme 17: Photocatalytic iodoperfluoroalkylation of alkenes.[88]

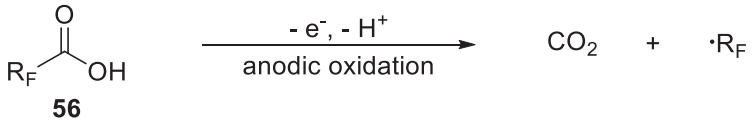
3.4 Electrochemical Perfluoroalkylation of Alkenes

The perfluoroalkylation reagents most commonly used are perfluoroalkanoic acids, sodium trifluoromethanesulfinate (Langlois reagent) and perfluoroiodo alkanes. For

the first two examples the perfluoroalkyl radical is generated at the anode, while the halides are reduced at the cathode. Many examples for an anodic process have been reported, whereas only few examples for a cathodic reaction are known.

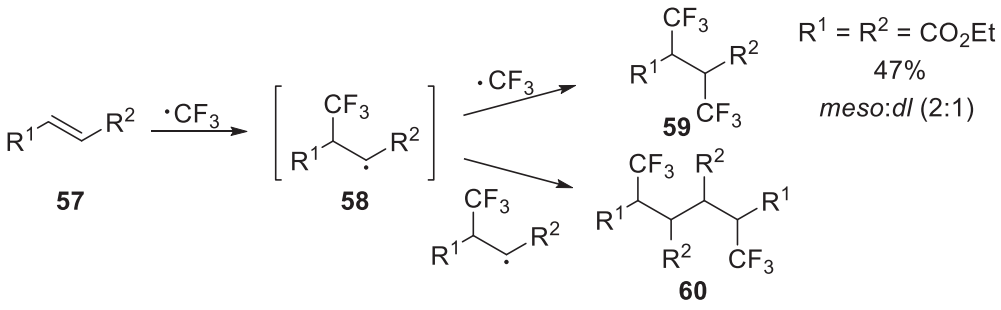
3.4.1 Anodic Reactions

The electrooxidation of perfluoroalkanoic acids **56** is used to generate a perfluoroalkyl radical by decarboxylation (Scheme 18). The formed radical can then be trapped by reaction with an olefin.



Scheme 18: Anodic oxidation of perfluoroalkanoic acid **56**.

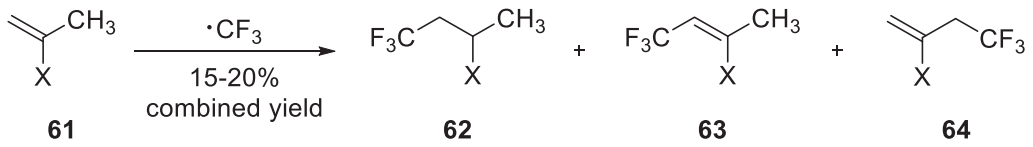
Renaud *et al*. first reported 'crossed' Kolbe electrolysis in the reaction of trifluoroacetic acid (TFA) with acetic acid.[89, 90] Attempted 'crossed' Kolbe electrolysis with unsaturated carboxylic acid esters resulted in the minor addition of trifluoromethyl radicals across the double bond.[91] Therefore, mono- and disubstituted olefins **57** were reacted with trifluoroacetic anions forming intermediate **58** and affording either a dimer **59** or a bis(trifluoromethyl) product **60** (Scheme 19).[92-94] Trifluoromethylation of diethyl fumarate afforded the bis(trifluoromethyl)-succinate derivative in almost pure form in 47% yield with a *meso*:*dl*-isomer ratio of 2:1.



Scheme 19: Electrochemical trifluoromethylation of olefins.[92-94]

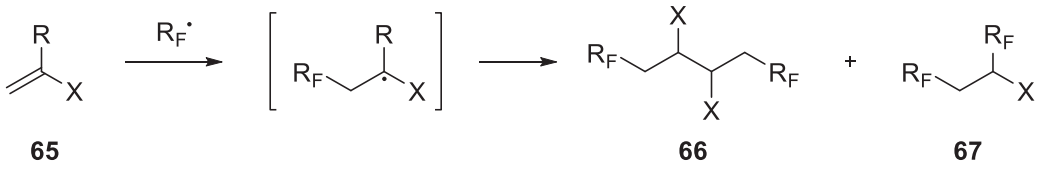
The reactivity of olefinic and acetylenic bonds with electrochemically generated trifluoromethyl radicals was analysed by Brookes *et al.*[95, 96] Muller *et al*. found that the use of a substrate with an isopropenyl group **61** primarily generates monomeric products **62**, **63** and **64** with a single trifluoromethyl group (Scheme 20).[97] After

hydrogenation of the primary product mixture, saturated product **62** was isolated in 15-20% yield.



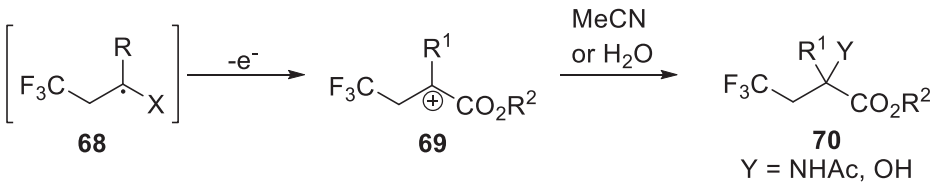
Scheme 20: Trifluoromethylation of isopropenyl derivatives.[97]

The Muller group published several applications of this method, such as the trifluoromethylation of acrylic acids and the synthesis of biologically relevant 5,5,5,-trifluoro-DL-isoleucine as well as 5,5,5,-trifluoro-DL-alloisoleucine.[98-101] In 1992, Uneyama *et al*. presented the perfluoroalkylation of various olefins **65** by electrooxidation of different perfluoroalkanoic acids, affording dimerized mixtures **66** of *dl*- and *meso*-isomers (50:50) (Scheme 21).[102, 103] In contrast to dimerization a geminal bis(trifluoromethylation) was observed by reaction of acrylamides or acrylonitrile with CF_3-radicals affording product **67**.[104]



Scheme 21: Perfluoroalkylation of electron-deficient olefins.

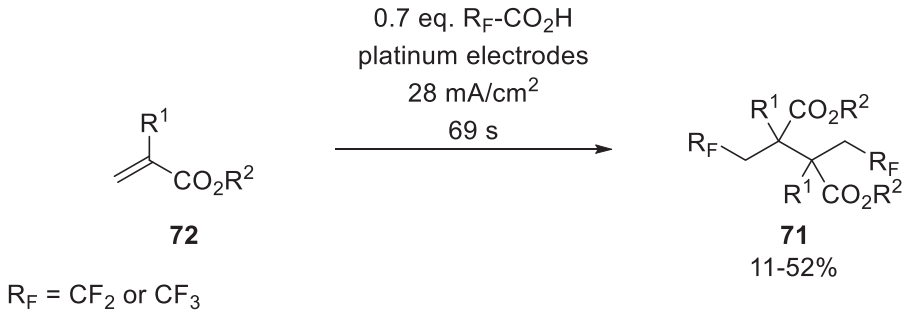
Alternatively, intermediate **68** can be oxidized to form carbocation **69**. Nucleophilic attack by either water or acetonitrile affords side product **70** (Scheme 22).



Scheme 22: Observed side reactions of the perfluoroalkylation.[102]

More recently, Wirth *et al*. presented a similar approach in utilising an electrochemical microreactor that combines electrochemistry with a flow process.[105] Similar to the previously described method, the perfluoroalkylation was performed on platinum electrodes in a mixture of acetonitrile and water. The dimerised products **71** from the reaction of acrylates **72** with di- or trifluoroacetic acid were isolated in yields up to 52% with an isomeric ratio of up to 10:1 (Scheme 23). When the reaction of

methyl methacrylate was carried out in acetonitrile, only di- or trifluoromethyl acetamidation was observed.



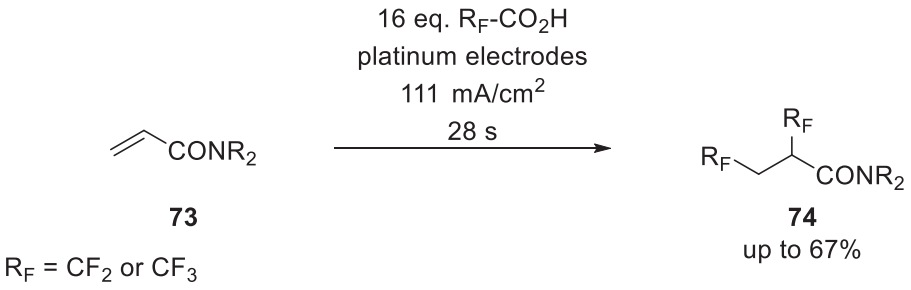
72

R_F = CF_2 or CF_3

71
11-52%

Scheme 23: Electrosynthetic di- and trifluoromethylation of acrylates.[105]

In the case of acrylamide **73**, bis(difluoromethylation) and bis(trifluoromethylation) occurred (Scheme 24). This can be rationalised with the strong absorption of the nitrogen atom to the electrode surface, which leads to the reaction of the radical intermediate with a second perfluoroalkyl radical affording bis(perfluoroalkylated) products **74**. The process is positively affected with the use of a high current.



73

R_F = CF_2 or CF_3

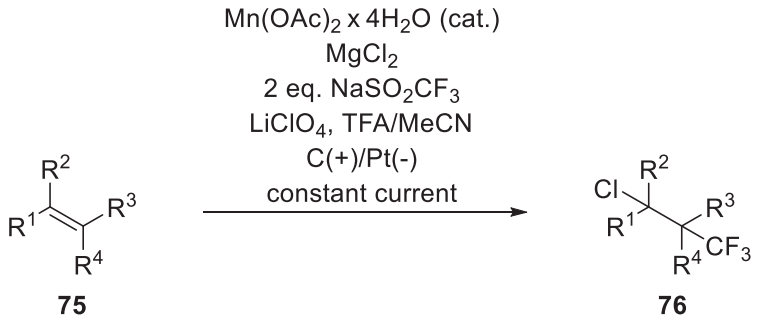
74
up to 67%

Scheme 24: Electrosynthetic di- and trifluoromethylation of acrylamides.[105]

Next to perfluoroalkanoic acids sodium trifluoromethanesulfinate (CF_3SO_2Na) also known as Langlois reagent can be used as source for the trifluoromethyl group.[106] The perfluoroalkyl radical is released by oxidation of the triflinate anion at the anode and formation of sulfur dioxide. The bench-stability, low cost and easy handling are the main advantages of the reagent.

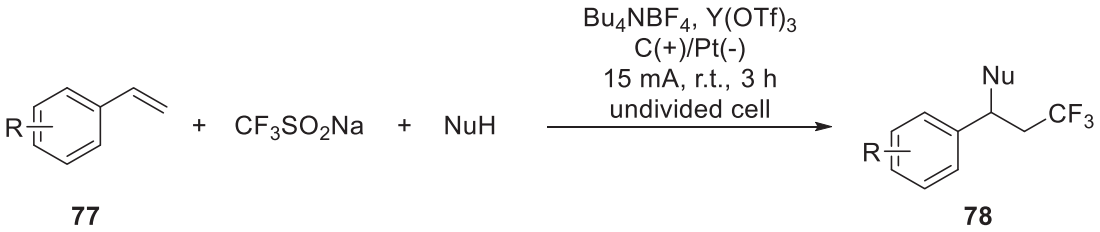
The electrocatalytic chlorotrifluoromethylation of alkenes **75** into difunctionalised products **76** was first demonstrated by Lin *et al*. (Scheme 25).[107, 108] They utilised the Langlois reagent as the source of the trifluoromethyl group. Magnesium chloride provides the chlorine atom, which is activated by a manganese-catalyst in a second anodic reaction resulting in the formation of Mn^{III}-Cl. The low solubility of $MgCl_2$ hinders the formation of dichlorinated side products. Trifluoroacetic acid was used as

sacrificial oxidant. The chlorotrifluoromethylation tolerates a broad range of substrates including oxidatively labile groups such as aldehydes, alcohols or tertiary amines.



Scheme 25: Electrocatalytic chlorotrifluoromethylation of alkenes.[107, 108]

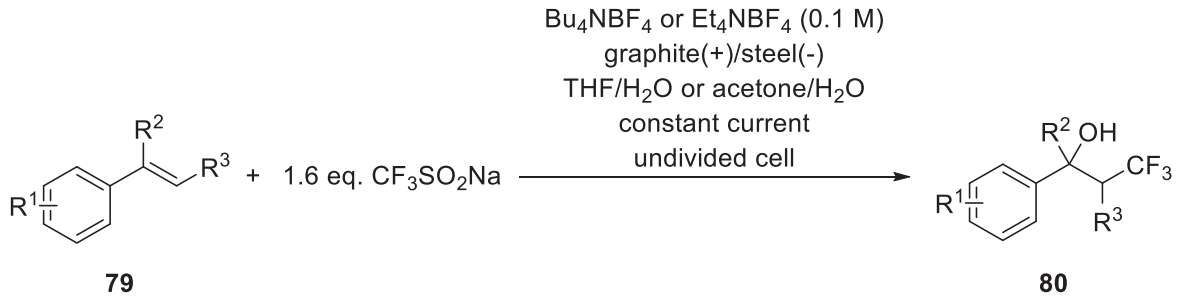
In 2018, Lei *et al.* reported the electrochemical oxytrifluoromethylation and aminotrifluoromethylation of styrene derivatives **77** (Scheme 26).[109] The use of sodium trifluoromethanesulfinate as trifluoromethyl source in combination with yttrium triflate as Lewis acid catalyst leads to 1,2-addition products **78**. Depending on the choice of solvent various nucleophiles were added to the cationic intermediate.



NuH = ROH, RCN, R^1R^2NH

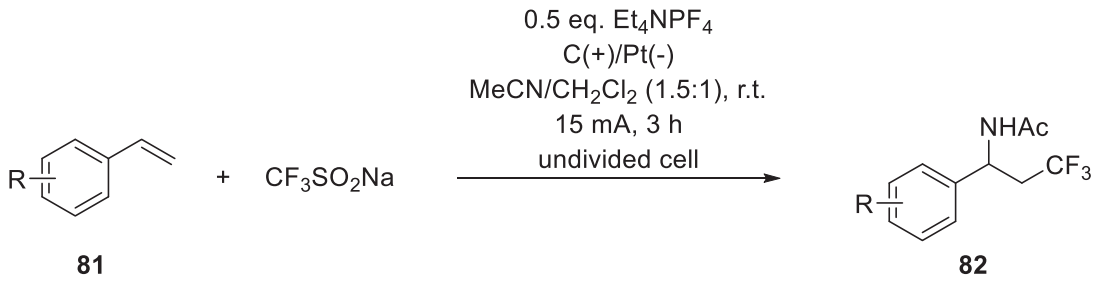
Scheme 26: Electrosynthetic difunctionalization of styrene derivatives.[109]

A catalyst-free method for the oxytrifluoromethylation of styrene derivatives **79** was developed by Kappe and Cantillo *et al*. (Scheme 27).[110] Again, sodium trifluoromethanesulfinate was used as trifluoromethylation reagent and hydroxy-trifluoromethylated products **80** were isolated in moderate to excellent yields. The reaction was performed in an undivided cell utilising water both as oxidant and nucleophile. Only moderate yields were achieved, when water was replaced by alcohols.



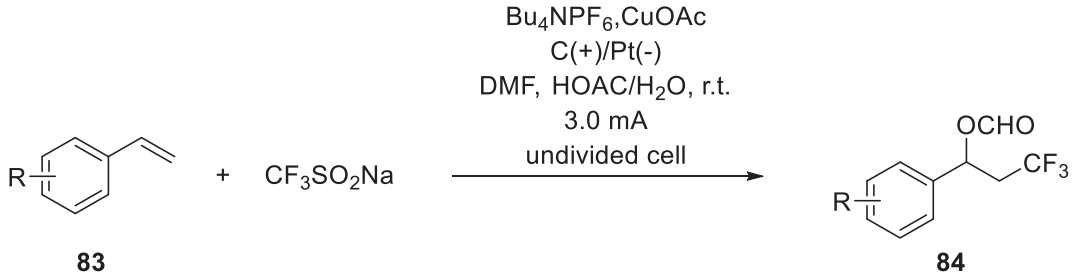
Scheme 27: Electrochemical oxytrifluoromethylation of alkenes.[110]

Furthermore, Chen *et al*. demonstrated the aminotrifluoromethylation of styrene derivatives **81** for the synthesis of β-trifluoroethylamines **82** (Scheme 28).[111] The Langlois reagent was employed as trifluoromethyl precursor, while acetonitrile was used as the *N*-nucleophile. The reaction proceeds without an additional catalyst and the products were isolated in good to excellent yields. Not only electron-rich and electron-deficient substituents in *para*-position were tolerated, but also in *meta*-position. However, when the vicinal aminotrifluoromethylation was performed with a substituent in *ortho*-position only traces of product were formed.



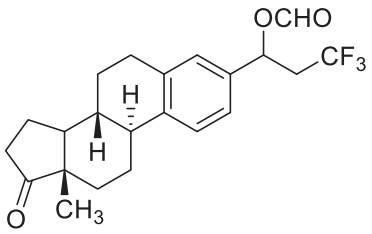
Scheme 28: Electrochemical aminotrifluoromethylation of styrenes.[111]

Moreover, the electrochemical trifluoromethylation and formyloxylation was reported by Fang and Hu *et al*.[112] *N*,*N*-Dimethylformamide was used as formyloxylation reagent and the trifluoromethyl group was again derived from the Langlois reagent. The transformation of a variety of styrene derivatives **83** into the corresponding trifluoromethylformyloxylated products **84** proceeded in good yields for electron-rich substrates (Scheme 29). Moderate yields were achieved in the presence of an electron-withdrawing functional group. Furthermore, the electrochemical formyloxylation and trifluoromethylation of an unsaturated steroid analoga was carried out and product **85** isolated in 83% yield (Figure 4).



83 **84**

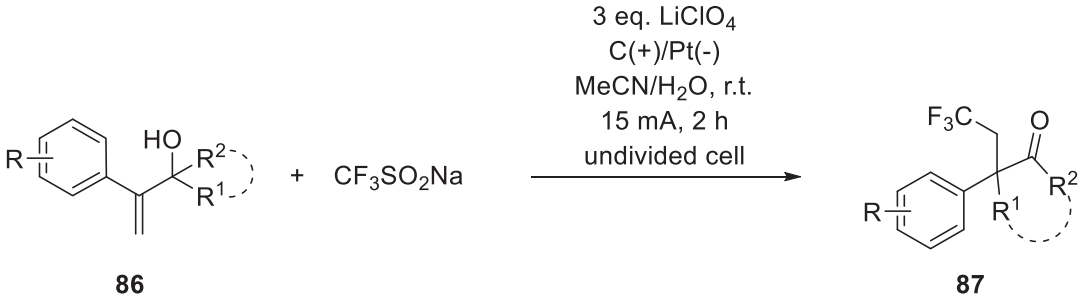
Scheme 29: Electrochemical formyloxylation and trifluoromethylation of styrenes.[112]



85
83%

Figure 4: Formyloxylated and trifluoromethylated product from the reaction of a steroid-derived alkene.[112]

Chen and Zhang *et al*. demonstrated the electrochemical trifluoromethylation/semipinacol rearrangement of various allylic alcohols **86** (Scheme 30).[113] The reaction creates an all-carbon stereocenter, a structural motive that can be found in biologically interesting natural products.[114, 115] Various styrene derivatives were converted into β-trifluoromethylated ketones **87** in moderate to excellent yields. Moreover, no additional catalyst was needed and the transformation proceeded under mild conditions.

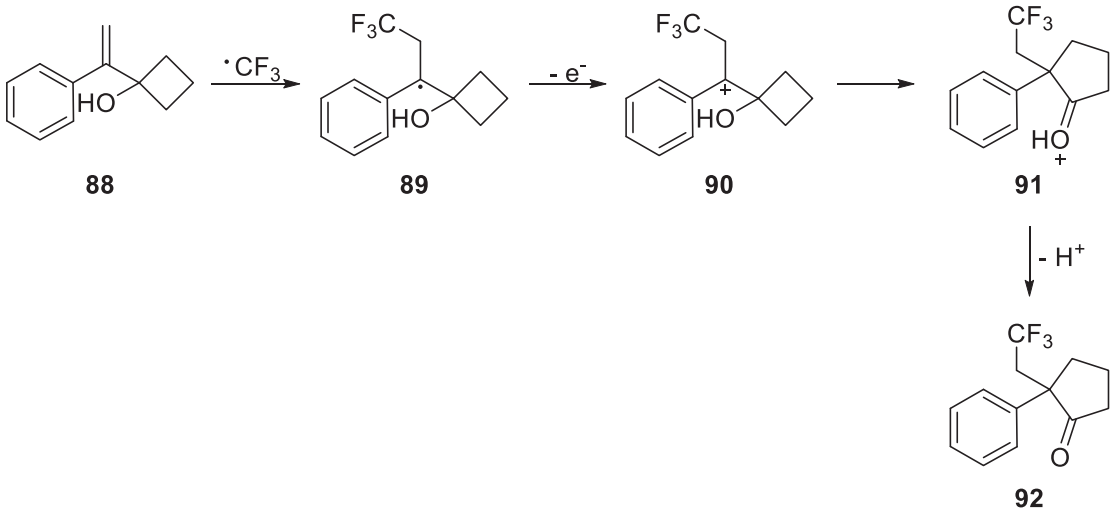


86 **87**

Scheme 30: Electrochemical trifluoromethylation/semipinacol rearrangement of styrenes.[113]

The proposed mechanistical pathway is presented in Scheme 31. After the oxidation of sodium trifluoromethanesulfinate, alkene **88** reacts with the trifluoromethyl radical. The formed benzyl radical **89** is further oxidised to cation **90**. After migration of the adjacent alkyl group and formation of the ketone, deprotonation of intermediate **91**

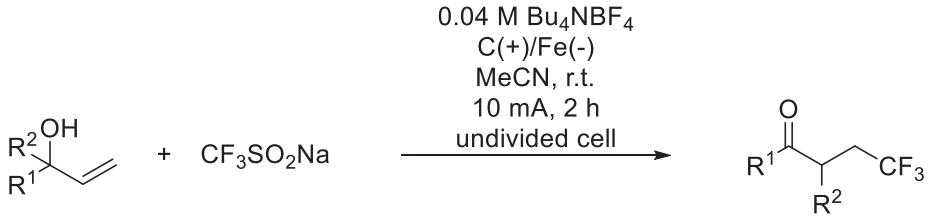
affords final product **92**. The conversion of alkenyl alcohols to β-trifluoromethylated ketones utilising a similar approach was demonstrated by Kim *et al*.[116]



88 **89** **90** **91** **92**

Scheme 31: Mechanistic proposal for the trifluoromethylation followed by semipinacol rearrangement.[113]

In a related fashion, the synthesis of β-trifluoromethylated ketones **93** was realised by Lei *et al*. (Scheme 32).[117] Starting from allylic alcohols **94** the reaction proceeds through a 1,2-migration process. The substrate scope ranges from α,α-diaryl allylic alcohols over α-alkyl-α-aryl allylic alcohols to α,α-dialkyl allylic alcohols. Moreover, cyclic ketones were obtained in an electrochemical ring expansion reaction. A further electrochemical fluoroalkylation of unactivated alkenes followed by distal heteroaryl migration was developed by Wang *et al*.[118]



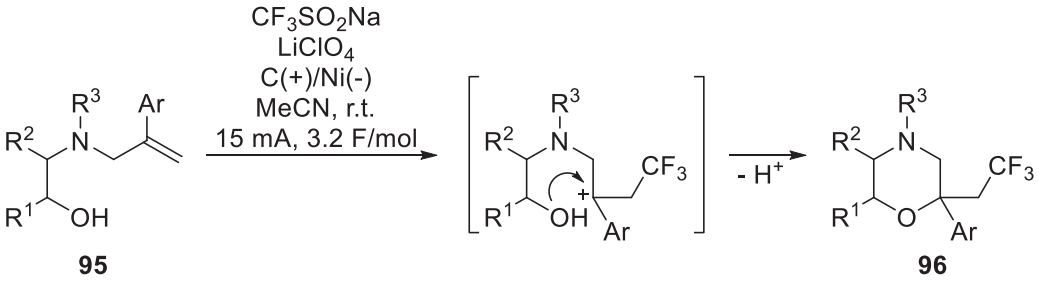
94
R^1 = alkyl, aryl
R^2 = alkyl, aryl

93

Scheme 32: Electrochemical trifluoromethylation followed by 1,2-migration.[117]

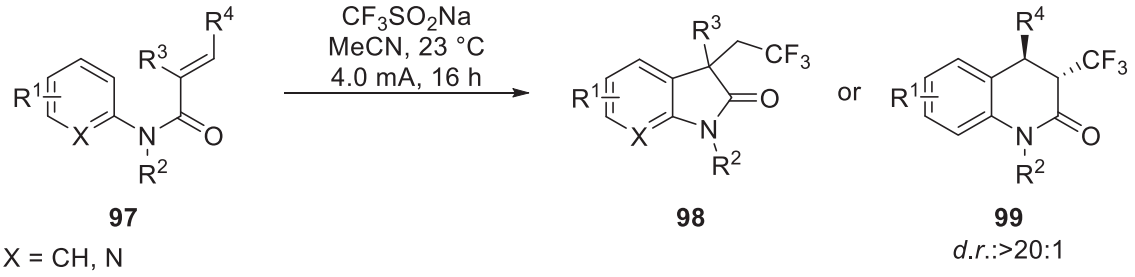
The oxidative trifluoromethylation of alkenes **95** followed by cyclisation was performed by Masson *et al.* for the synthesis of morpholine derivatives **96** (Scheme 33).[119] After the first regioselective addition of the perfluoroalkyl radical to the double bond, a second electron transfer takes place affording a cationic intermediate. Finally, the intramolecular nucleophilic attack of the hydroxy group

leads to cyclisation. The constant current electrolysis was performed in an undivided cell and the products were isolated in yields up to 88%.



Scheme 33: Tandem oxytrifluoromethylation/cyclisation reaction towards morpholine derivatives.[119]

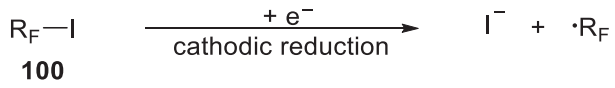
The electrochemical trifluoromethylation of *N*-substituted acrylamides **97** for the synthesis of quinolinones **98** and oxindoles **99** was developed by Ruan and Ackermann *et al*. (Scheme 34).[120] The fluoroalkylation/cyclisation sequence is initiated by the direct electrolysis of the Langlois reagent in an undivided cell. A similar approach for the electrochemical bromide-catalysed transformation of *N*-arylacrylamides was described by Zeng *et al*.[121] Recently, an electrochemical trifluoromethylation/cyclisation sequence in addition with sulfur dioxide insertion for the generation of cyclic *N*-sulfonylimines was presented by Liao *et al*.[122] More examples for an electrochemically induced trifluoromethylation followed by cyclisation using an oxidative approach have been reported.[123, 124]



Scheme 34: Tandem trifluoromethylation/cyclisation reaction towards oxindoles and quinolinones derivatives.[120]

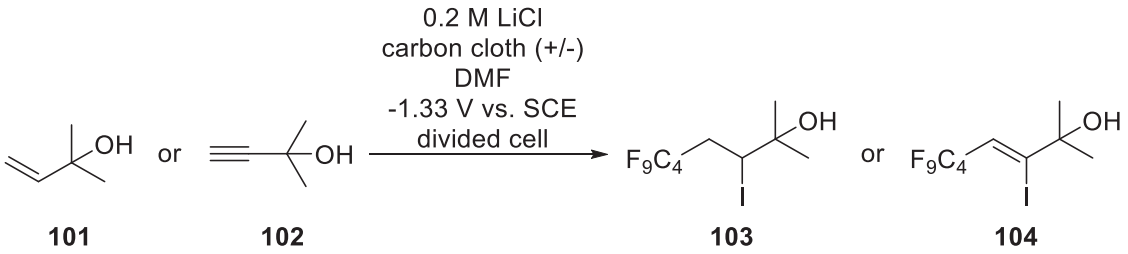
3.4.2 Cathodic Reactions

Alternative perfluoroalkylating reagents are perfluoroiodoalkanes **100**. At the cathode the carbon-iodine bond is reduced affording a perfluoroalkyl radical and iodide (Scheme 35).



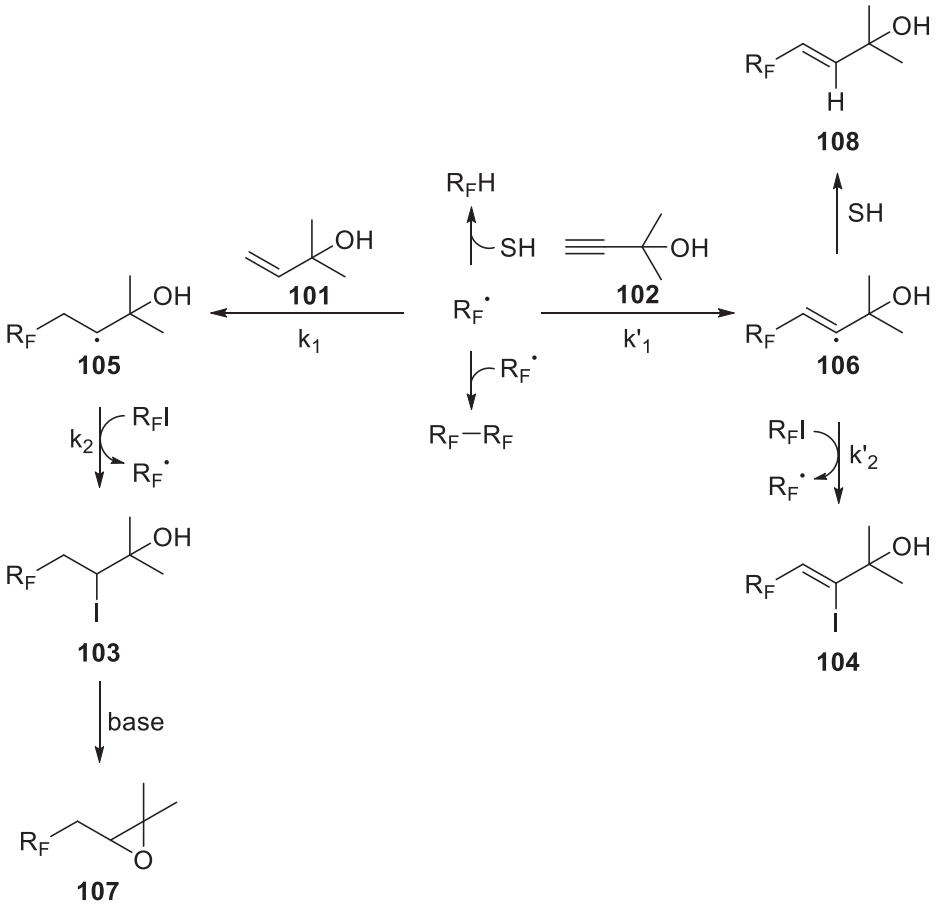
Scheme 35: Cathodic reduction of perfluoroiodoalkanes.

Amatore and Commeyras *et al*. added nonafluoro-1-iodobutane to alkenol **101**, or alkynol **102**, respectively. (Scheme 36).[125-129] The iodo-perfluoroalkylated product **103** resulting from the reaction with the alkene substrate was obtained with fewer side products compared to product **104** obtained from the corresponding alkyne. In their work the rates of iodine transfer were studied using cyclic voltammetry. They found that the addition of the perfluoroalkyl radical to the double bond is considerably slower compared to the transfer of iodine. This results in an increasing concentration of the R_F-radicals throughout the reaction. Therefore, the main termination step is the dimerization of these radicals. Dimerization of other radicals or cross-couplings were not observed.



Scheme 36: Perfluoroalkylation of alkenes or alkynes.[125, 126]

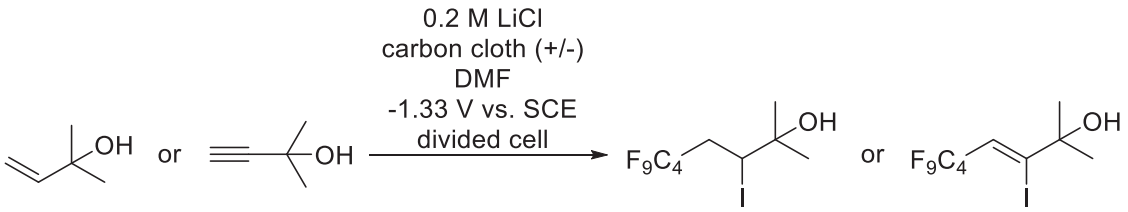
Moreover, cyclic voltammetry was used for an investigation of the mechanism.[126] The proposed mechanism is presented in Scheme 37. The first step is the addition of the perfluoroalkyl radical to the double or triple bond towards radicals **105** and **106**. The abstraction of iodine from a second perfluoroiodoalkanes results in the formation of the iodoperfluoroalkylated products **103** and **104**. Under the basic conditions present in the electrolysis cell, product **103** can further be transformed into epoxide **107**. Abstraction of hydrogen from the starting material by radical intermediate **106** affords olefin **108** as a side product of the alkyne reaction.



Scheme 37: Mechanistical proposal for the iodoperfluoroalkylation of alkenes and alkynes.[125, 126]

Furthermore, the iodoperfluoroalkylation was performed under different conditions. Variation of the concentration of nonafluoro-1-iodobutane, substrates ratio and charge lead to optimized yields of 58% for the iodoperfluoroalkylation of alkene **101** and 54% for alkyne **102**.

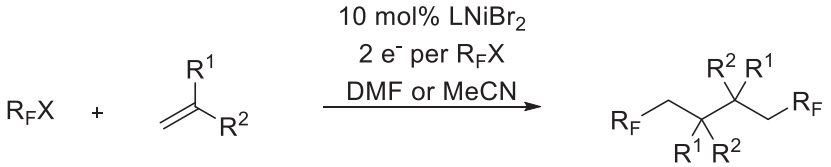
Table 1: Screening for the conditions of the iodoperfluoroalkylation of alkene **101** and alkyne **102**.[125]



101 **102** **103** **104**

Entry	Substrate	C_4F_9I [M]	C_4F_9I:substrate ratio	F/mol C_4F_9I	Product yields [%] 103 or 104	Olefin 108	Epoxide 107
1	**102**	1.00	1:5	0.15	54	16	-
2	**102**	1.00	1:1	0.40	23	43	-
3	**102**	0.27	1:5	0.40	-	70	-
4	**102**	0.27	1:1	0.80	-	53	-
5	**101**	1.00	1:5	0.20	49	-	8
6	**101**	1.00	1:1	0.20	58	-	6
7	**101**	0.27	1:5	0.90	31	-	20
8	**101**	0.27	1:1	0.80	28	-	20

More recently, Budnikova *et al*. reported the indirect electrochemical fluoroalkylation of styrene derivatives induced by nickel-catalysts in DMF in separated compartments.[130, 131] The addition of perfluoroalkyl halides **109** to styrenes **110** leads to the dimerization products **111** in moderate to good yields (Scheme 38).[132] Upon addition of tributyltin hydride as a hydrogen source, dimerization was prevented and the monomeric product was isolated in 52% yield.[131]

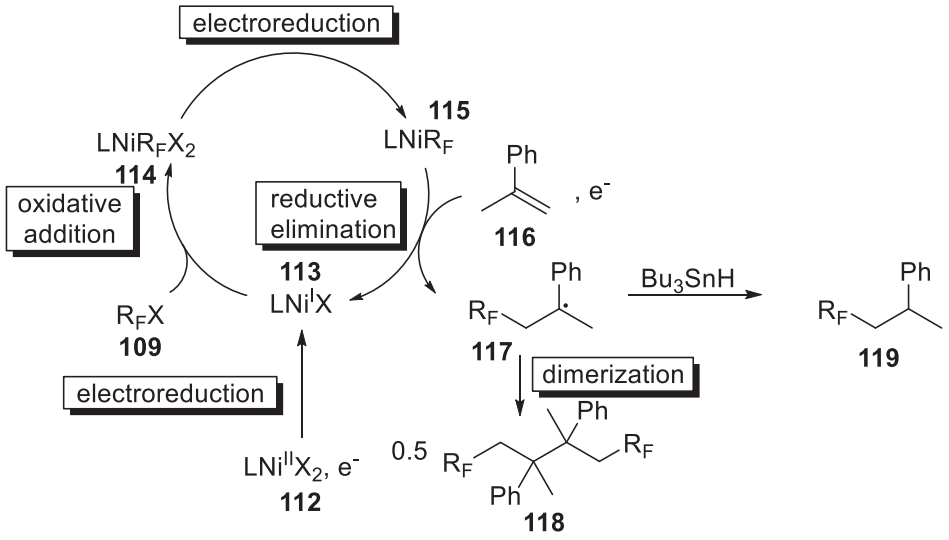


109 **110** **111**
34-72%

Scheme 38: Electrocatalytic fluoroalkylation of olefins: addition-dimerization reaction.[132]

The proposed mechanism of this reaction is illustrated in Scheme 39.[132] The cycle is initiated by reduction of the Ni(II)-complex **112** to catalytically active $Ni^{I}BrL$ **113**. This undergoes oxidative addition with perfluoroalkyl halide **109** to afford σ-complex **114**. After a further electroreduction step, intermediate **115** reacts with olefin **116** in a

reductive elimination step providing radical **117** which can then either form the dimer **118** or be quenched by Bu_3SnH to form the monomeric product **119**.

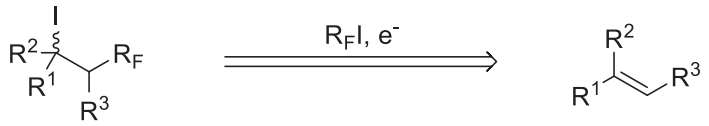


Scheme 39: Proposed catalytic cycle of the nickel-catalysed fluoroalkylation of olefins.[132]

The Budnikova group used several nickel complexes as catalysts.[131] Ligands of choice were bpy (2,2'-bipyridine), tpy (2,2':6',2''-terpyridine) and pybox [(*S*,*S*)-2,6-bis(4-phenyl-2-oxazolin-2-yl)-pyridine]. $NiBr_2$(bpy) proved to be the most effective catalyst for electrocatalytic fluoroalkylation. The application of the chiral ligand pybox resulted in no diastereomeric excess. The group of Budnikova, Dudkina *et al*. extended the homogeneous reaction to a nanoheterogeneous version by immobilization of a (bpy)-$NiBr_2$ complex on silica nanoparticles containing anchoring amino-groups.[133] This design allowed the catalyst to be recycled and reused. In addition, they found that the ratio of monomeric or dimeric product is dependent on the reaction media.

4 Research Question

This work aims to develop a novel electrochemical protocol for the perfluoroalkylation of alkenes. Perfluoroalkylation can be initiated by either reduction of perfluoroiodoalkanes at the cathode or oxidation of the corresponding perfluoroalkylating reagent at the anode. Various examples for an anodic approach can be found in the literature. Therefore, the focus will be on identifying suitable conditions for a cathodic method. Investigations towards a diastereoselective hydroperfluoroalkylation will start with Evans-auxiliary derivatives and acrylamides. The electrochemical difunctionalisation of alkenes represents an elegant strategy to introduce further functional groups next to the perfluoroalkyl group. Accordingly, the electrocatalytic iodoperfluoroalkylation of alkenes will be investigated. The retrosynthetic approach is highlighted in Scheme 40. The 1,2-addition product **120** can be prepared by cathodic reduction of a perfluoroalkyl iodide and its reaction with alkene **121**. Optimisation of this transformation will address conditions such as electrode material, solvent or applied current. Successful establishment of the method shall be followed by exploration of the scope of olefinic substrates and examination of various perfluoroalkylating reagents. Extending the applicability of the developed method further, the introduction of the perfluoroalkyl moiety in electronically neutral alkenes will be attempted. The perfluoroalkylation of unactivated alkenes still poses a significant challenge and the ability to use an electrochemical method for this purpose would be extremely advantageous.



120 **121**

Scheme 40: Retrosynthetic approach for the electrosynthesis of iodoperfluoroalkylated compounds.

A method for the electrosynthetic generation of cationic intermediates and their accumulation in solution was invented by Yoshida *et al*.[29] Investigations towards the perfluoroalkylation of electrogenerated iminium ions will be conducted.

5 Results and Discussion

The following chapter is divided into three parts. The first part will cover steps taken and progress made in the development of an electrochemical hydroperfluoroalkylation of electron-deficient olefins. Investigations for an electrocatalytic iodoperfluoroalkylation of alkenes will be discussed in the second part. Finally, studies concerning the perfluoroalkylation of an electrochemically generated cationic intermediate will be discussed.

The reaction time of the electrosynthetic reactions was calculated using equation (**1**) derived from Faraday's laws of electrolysis.[13, 134-136]

$$t = \frac{Q}{I} = \frac{m \cdot z \cdot F}{M \cdot I} = \frac{n \cdot z \cdot F}{I} \quad (1)$$

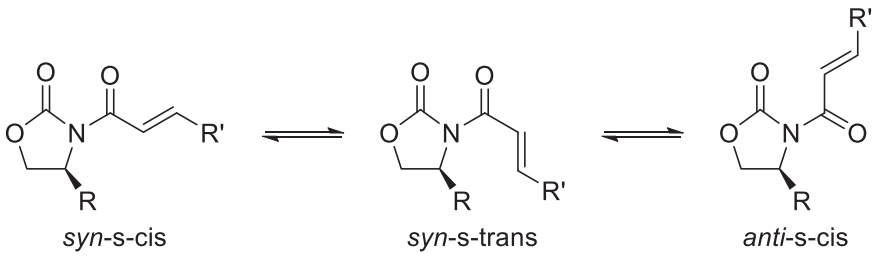
t = electrolysis time [s]
Q = electric charge transferred [C]
I = current employed [A]
n = amount of substance [mol]
z = electrons transferred during reaction
F = Faraday's constant = 96485 C/mol

5.1 Electrochemical Hydroperfluoroalkylation

5.1.1 Preliminary Trials for a Stereoselective Perfluoroalkylation

As discussed above, there is precedent in the literature demonstrating successful, radical and stereoselective perfluoroalkylations of terminal alkenes as well as some examples of electrochemical perfluoroalkylations. However, it would be of significant synthetic interest to develop an electrochemical method for introducing a perfluoroalkyl moiety into internal alkenes in an enantioselective/diastereoselective fashion. Asymmetric radical perfluoroalkylations were previously demonstrated by our group and by Iseki *et al*. using triethylborane in combination with chiral *N*-acyloxazolidinones.[68-71, 83] Therefore, investigations into the diastereoselective, electrochemical method will initially focus on the use of an Evans auxiliary. *N*-Acyloxazolidinones exist as different rotamers unless a chelating Lewis acid is

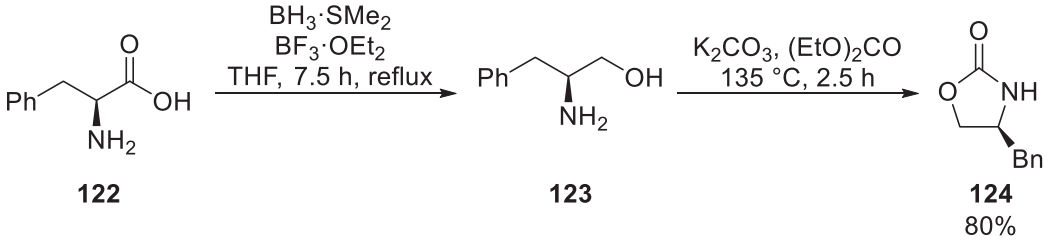
added (Scheme 41).[137, 138] In combination with the appropriate residue on the chiral auxiliary, high diastereoselectivities can be achieved.[139-142]. The chelation of the carbonyl groups by a Lewis acid would lead to a selective reaction with the *syn*-s-cis rotamer due to steric interaction.[143] The addition of the perfluoroalkyl radical would presumably occur from the side opposite to the bulky residue resulting in high stereoselectivity in β-position.



Scheme 41: Possible rotamers of *N*-acyloxazolidinones.

Before the investigations into the electrochemical perfluoroalkylation of internal alkenes were started, the less challenging transformation of terminal olefins was attempted. The acrylic acid derivative is hereby used as a model substrate for preliminary optimisation of the reaction. The perfluoroalkyl moiety of the product can be derived either from a halide or an acid and both options were investigated in detail.

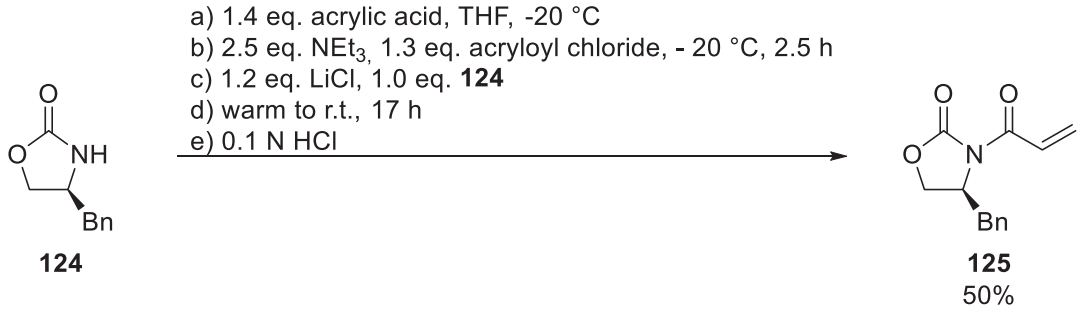
The chiral *N*-acyloxazolidinone derived from (*S*)-phenylalanine was chosen for preliminary tests. Following the procedures of Evans *et al.* (*S*)-phenylalanine (**122**) was first reduced to α-aminoalcohol **123** and then treated with potassium carbonate in boiling diethyl carbonate to yield the benzylated *N*-acyloxazolidinone **124** (Scheme 42).[144, 145] The α-aminoalcohol had previously been prepared on a molar scale within the group so its synthesis was not required. The *N*-acyloxazolidinone **124** was isolated in a yield of 80%.



Scheme 42: Synthesis of benzylated *N*-acyloxazolidinone **124**.

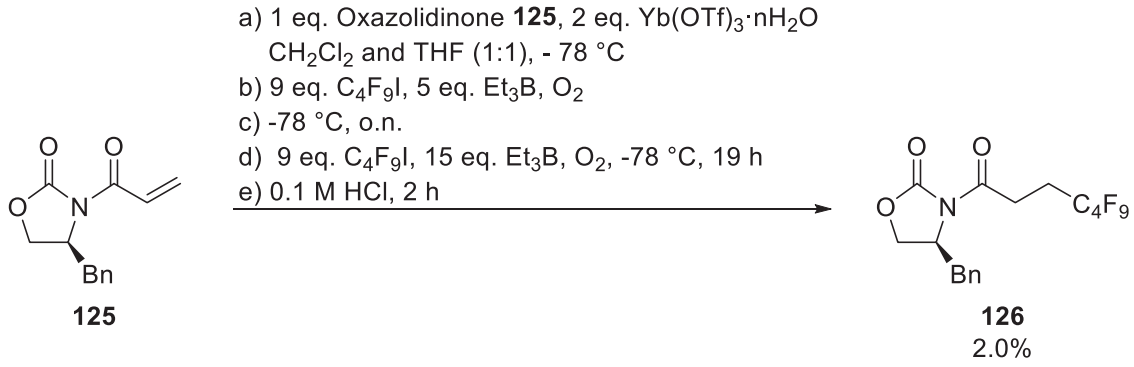
5.1.1.1 Attempted Perfluoroalkylation of Acryloyl-oxazolidinones

N-Acyloxazolidinone **125** was synthesized according to the method of Ho *et al*. (Scheme 43).[146] Reaction of oxazolidinone **124** with acrylic anhydride gave olefin **125** in moderate yield.



Scheme 43: Synthesis of *N*-acyloxazolidinone **125**.

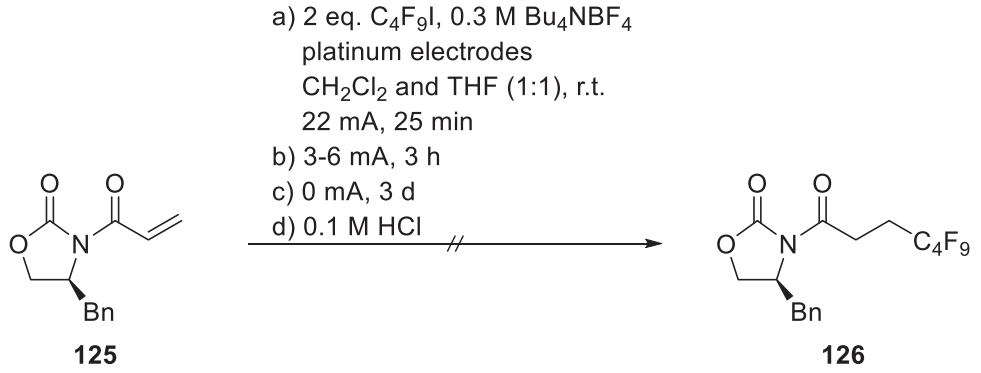
The perfluoroalkylation was first attempted following the procedures of Erdbrink *et al*. using Et_3B/O_2 as radical initiator.[83-85, 147] The perfluoroalkylated product **126** was isolated in a yield of 2.0% (lit. 13-27%). The reaction was not repeated as product **126** was mainly needed as a reference.



Scheme 44: Perfluoroalkylation of *N*-acyloxazolidinone **125** with Et_3B/O_2 as radical initiator.

The electrochemical perfluoroalkylation of *N*-acyloxazolidinone **125** was first attempted using nonafluoro-1-iodobutane as perfluoroalkyl halide under constant current conditions (Scheme 45). The reduction of the carbon-iodine bond on the cathode releases iodide next to the nonafluorobutyl radical, which can then be trapped by the alkene. For the first trial the same solvent system was applied with 0.3 M tetrabutylammonium tetrafluoroborate as supporting electrolyte on platinum electrodes. Applying 22 mA the solution turned first yellow then red, so the current was reduced to 6 mA, then to 3 mA. After 3 hours the current was turned off and the reaction was stirred for 3 days. In total an amount of 0.37 F/mol C_4F_9I was applied.

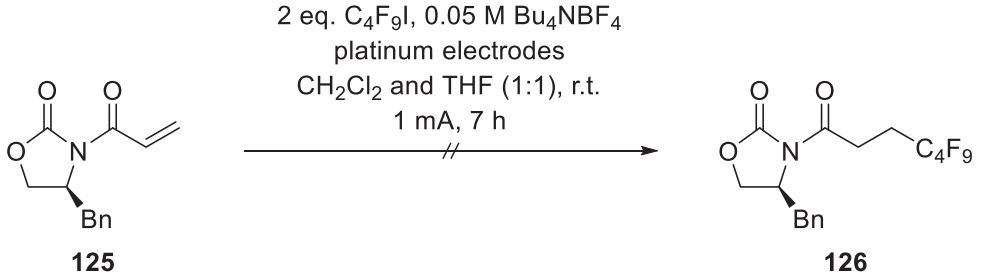
Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no product peaks. One problem could be the dimerization of the nonafluorobutyl radicals, which was also observed by Commeyras *et al*.[125, 126]



125 **126**

Scheme 45: Attempted electrochemical perfluoroalkylation of enon **125** on platinum electrodes using constant current conditions.

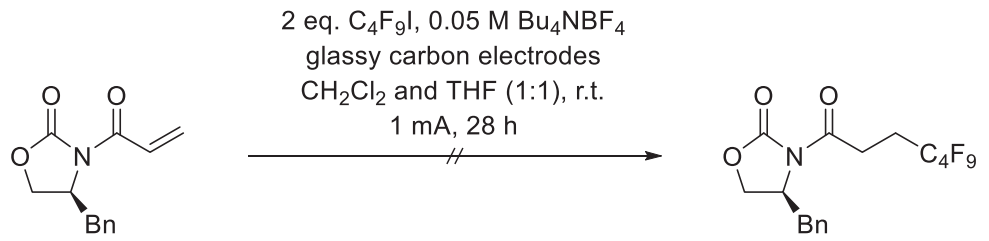
Therefore, the reaction was then attempted with a current of 1 mA and 0.05 M tetrabutylammonium tetrafluoroborate for 2 days (1.0 F/mol C_4F_9I) (Scheme 46). No product was detected and 86% of the substrate were re-isolated following purification by flash column chromatography.



125 **126**

Scheme 46: Attempted electrochemical perfluoroalkylation of enon **125** on platinum electrodes using constant current conditions (1 mA).

The reaction was repeated on glassy carbon electrodes with a current of 1 mA, but purification by flash column chromatography only yielded the substrate in 89% yield (0.60 F/mol C_4F_9I) (Scheme 47). The problem could arise due to the low current which may not be sufficient for the electron transfer from the cathode to perfluorobutyl-iodide. Another challenge might be the low solubility or the electron-deficient nature of the alkene.

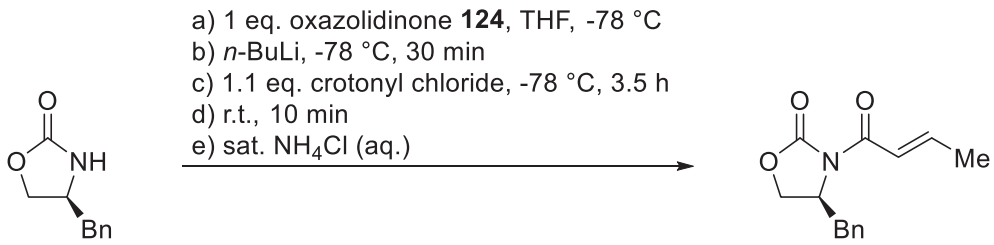


125 **126**

Scheme 47: Attempted electrochemical perfluoroalkylation of enon **125** on glassy carbon electrodes using constant current conditions (1 mA).

5.1.1.2 Attempted Perfluoroalkylation of Crotonyl-oxazolidinones

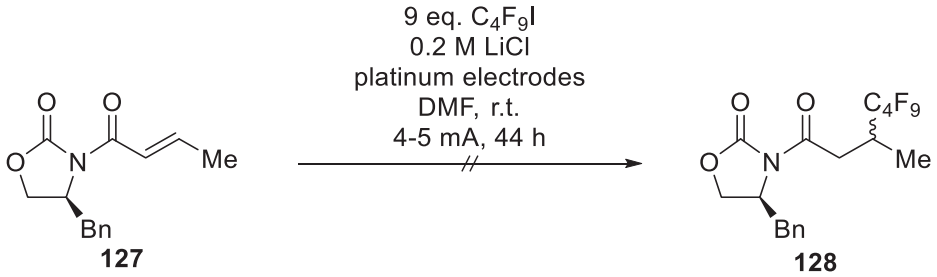
For preliminary trials of an internal perfluoroalkylation the crotonic acid derivative was chosen as the model substrate. *N*-Acyloxazolidinone **127** was synthesized according to the method of Czekelius *et al.* (Scheme 48).[83, 147] It can be accessed from the reaction of oxazolidinone **124** with crotonyl chloride affording olefin **127** in good yield.



124 **127** 90%

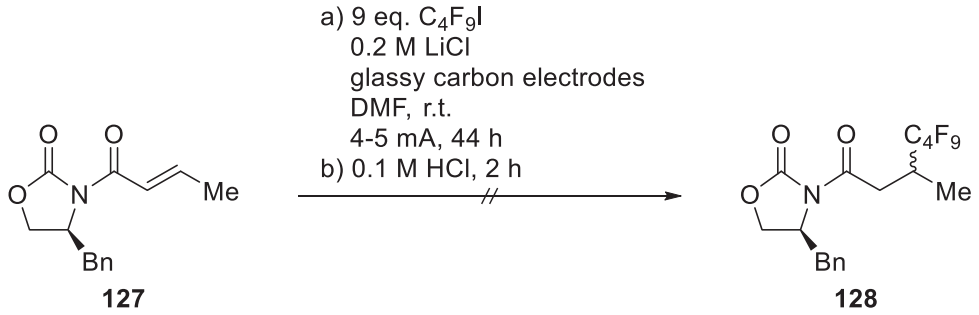
Scheme 48: Preparation of *N*-acyloxazolidinone **127**.

Again, the electrochemical perfluoroalkylation was first attempted using nonafluoro-1-iodobutane as perfluoroalkylating reagent. According to the procedures of Commeyras *et al.*, *N*,*N*-dimethylformamide was chosen as the solvent for the electrochemical perfluoroalkylation.[125, 126] Lithium chloride was used as the supporting electrolyte and Lewis acid. The reduction of the perfluorobutyl iodide on platinum electrodes (1 cm^2) was performed as constant current electrolysis (4-5 mA, 4.4 F/mol C_4F_9I) for 44 hours (Scheme 49). However, no conversion of the substrate to product **128** was observed.



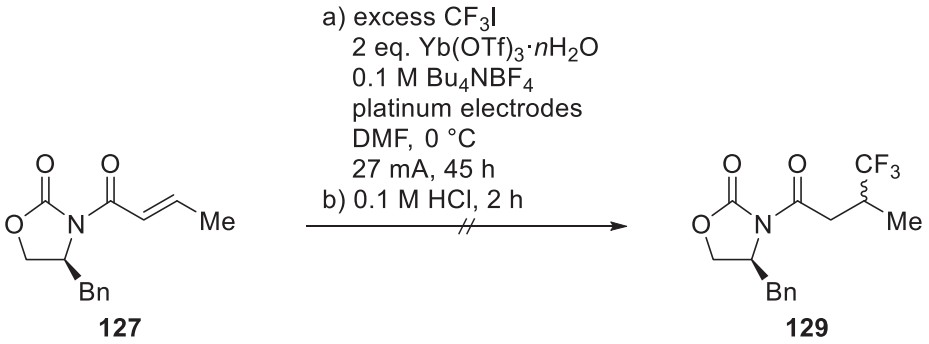
Scheme 49: Attempted electrochemical perfluoroalkylation of oxazolidinone **127** with LiCl as supporting electrolyte and Lewis acid on platinum electrodes.

To rule out that this was due to the electrode material, the reaction was repeated on glassy carbon electrodes (1 cm^2) under galvanostatic conditions (4-5 mA, 3.8 F/mol C_4F_9I) (Scheme 50). Again, the analysis of the crude material by ^{19}F NMR spectroscopy revealed no fluoroalkylation product.



Scheme 50: Attempted electrochemical perfluoroalkylation of oxazolidinone **127** with LiCl as supporting electrolyte and Lewis acid on glassy carbon electrodes.

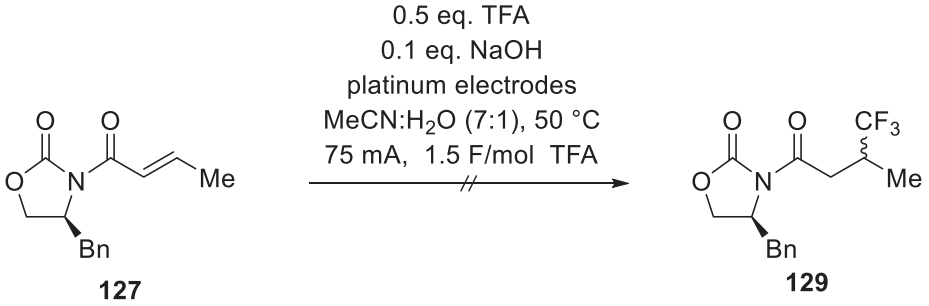
Difficulties in the perfluoroalkylation of *N*-acyloxazolidinone **127** with nonafluoro-1-iodobutane were also observed in the development of the method utilizing triethylborane and oxygen as radical initiators by Erdbrink *et al*.[147] Therefore, the reaction was attempted electrochemically using trifluoromethyl iodide as perfluoroalkylating reagent and ytterbium(III) trifluoromethanesulfonate hydrate as Lewis acid (Scheme 51). The constant current electrolysis (27 mA, 28 F/mol C_4F_9I) was performed on platinum electrodes for 45 hours. Analysis of the crude mixture by ^{19}F NMR spectroscopy and TLC revealed only traces of fluorinated, unidentified compounds and product **129** was not identified.



127 **129**

Scheme 51: Attempted electrochemical perfluoroalkylation of oxazolidinone **125** using trifluoromethyl iodide as perfluoroalkylation reagent.

As a last resort, the perfluoroalkylation of oxazolidinone **127** was also attempted with trifluoroacetic acid following the procedures of Uneyama *et al*. (Scheme 52).[102] However, the reaction on platinum electrodes only afforded a mixture inseparable by flash column chromatography.

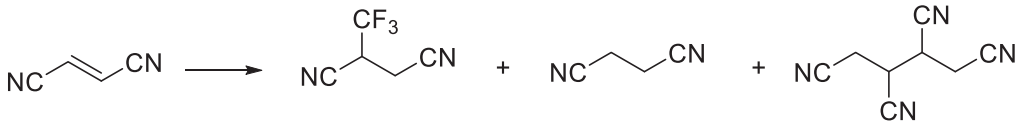


127 **129**

Scheme 52: Attempted electrochemical perfluoroalkylation of oxazolidinone **127** using trifluoroacetic acid as perfluoroalkylation reagent.

5.1.1.3 Attempted Perfluoroalkylation of Oxazolidinonyl-3-cyano-2-propenoates

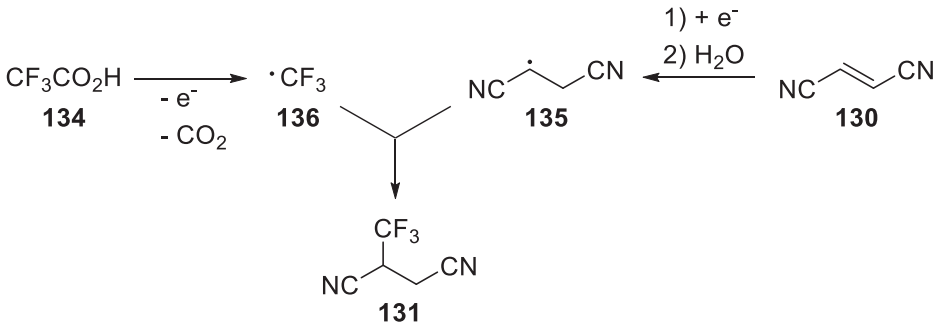
The perfluoroalkylations of the Evans-auxiliary derivatives of acrylic acid and crotonic acid were unsuccessful. Accordingly, finding a more suitable substrate for the perfluoroalkylation was targeted. For that purpose a nitrile derivative might be selected. This was exemplified by Uneyama *et al.* who demonstrated the electrochemical perfluoroalkylation of fumaronitrile (**130**) (Scheme 53).[148] The trifluoromethylated product **131** was isolated in a yield of 65% in combination with the reduced version **132** and dimer **133**.



130 **131** 65% **131** 7% **132** 7%

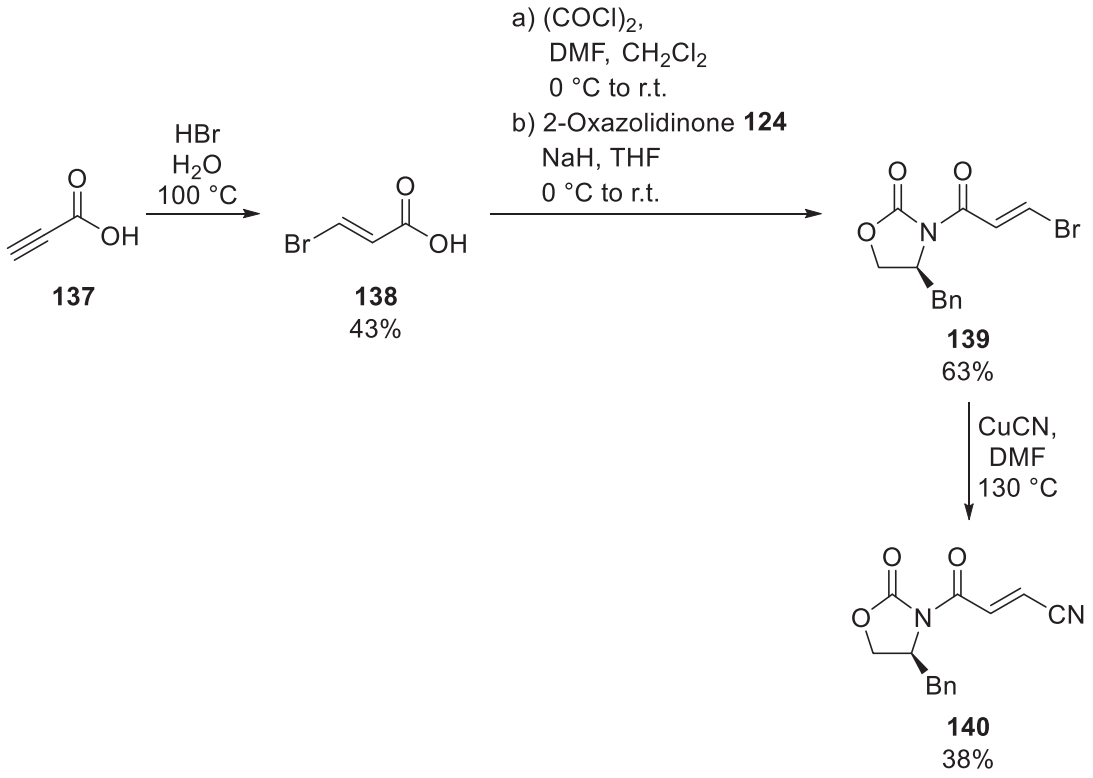
Scheme 53: Electrochemical trifluoromethylation of fumaronitrile (**130**).[148]

After investigation of the mechanism, they concluded that the first steps are two one-electron reductions of trifluoroacetic acid (**134**) and fumaronitrile (**130**). In the second step, radical **135** is coupling with the trifluoromethyl radical **136** to form product **131** (Scheme 53).



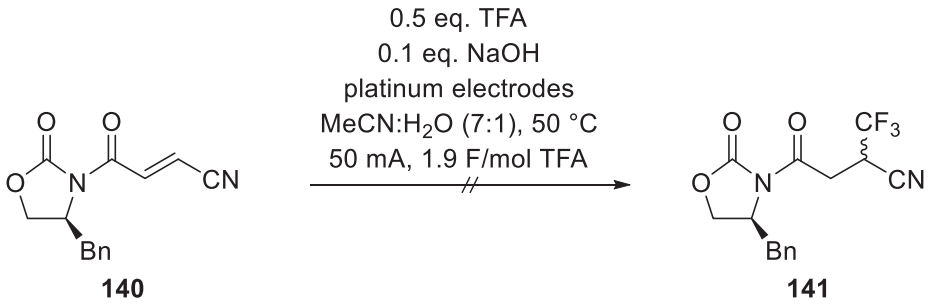
Scheme 54: Proposed mechanism for the electrochemical trifluoromethylation of fumaronitrile (**130**).[148]

With regard to these results, a nitrile compound was chosen to be tested as an alternative substrate. Starting with the bromination of propiolic acid **137** to acrylic bromide **138**, followed by addition of 3-bromoacryloyl chloride to oxazolidinone **124** and the conversion of the formed bromoacryloyl oxazolidinones **139** with CuCN, the nitrile compound **140** was prepared.[149, 150]



Scheme 55: Preparation of oxazolidinone **140**.

Perfluoroalkyation was attempted according to the procedures of Uneyama *et al.* using trifluoroacetic acid in an acetonitrile-water mixture (7:1) with sodium hydroxide as the supporting electrolyte at platinum electrodes. Purification by flash column chromatography did not lead to isolation of product **141**.

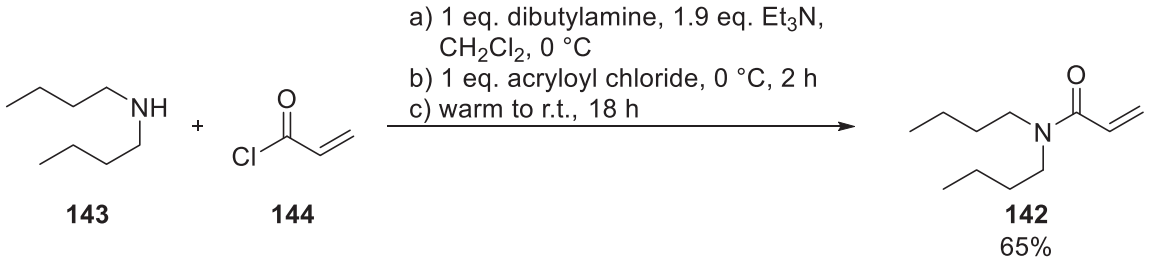


Scheme 56: Attempted electrochemical perfluoroalkylation of enon **140** using trifluoroacetic acid as perfluoroalkylation reagent.

5.1.2 Direct Electrochemical Perfluoroalkylation of Acrylic Acid Derivatives

First attempts for an electrochemical perfluoroalkylation of Evans-auxiliary derivatives of acrylic acid, crotonic acid and 3-cyano-2-propenacid for the development of a stereoselective method were unsuccessful. Therefore, the focus shifted to identifying suitable conditions for a non-stereoselective method. *N*,*N*-Dibutylacrylamide (**142**)

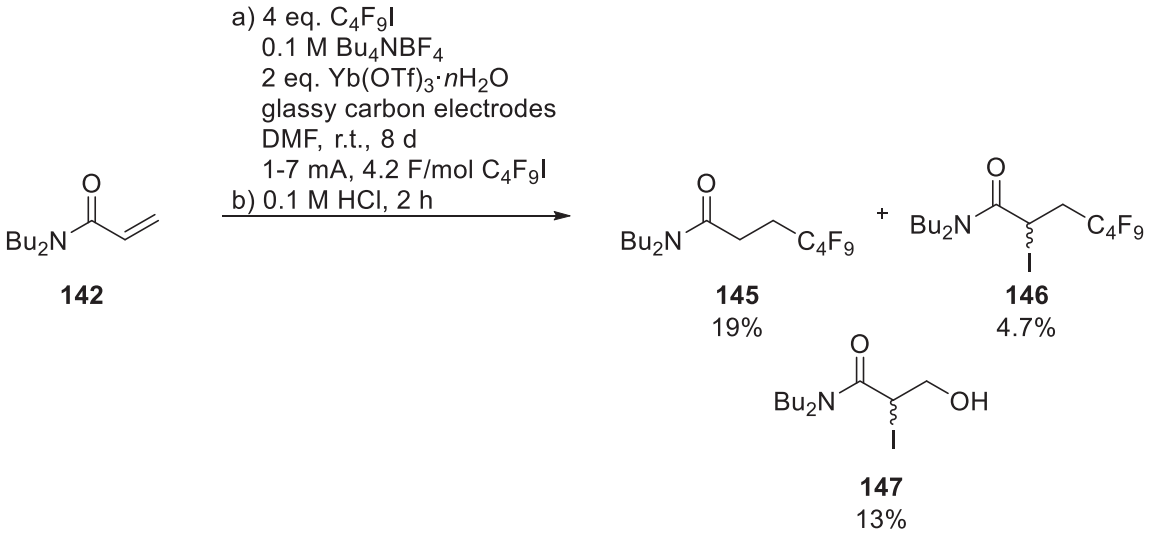
was chosen as a model substrate. It can be accessed from the reaction of dibutylamine (**143**) and acryloyl chloride (**144**) with triethylamine following the procedures of Skrydstrup *et al.* (Scheme 57).[151]



Scheme 57: Synthesis of *N*,*N*-dibutylacrylamide **142**.

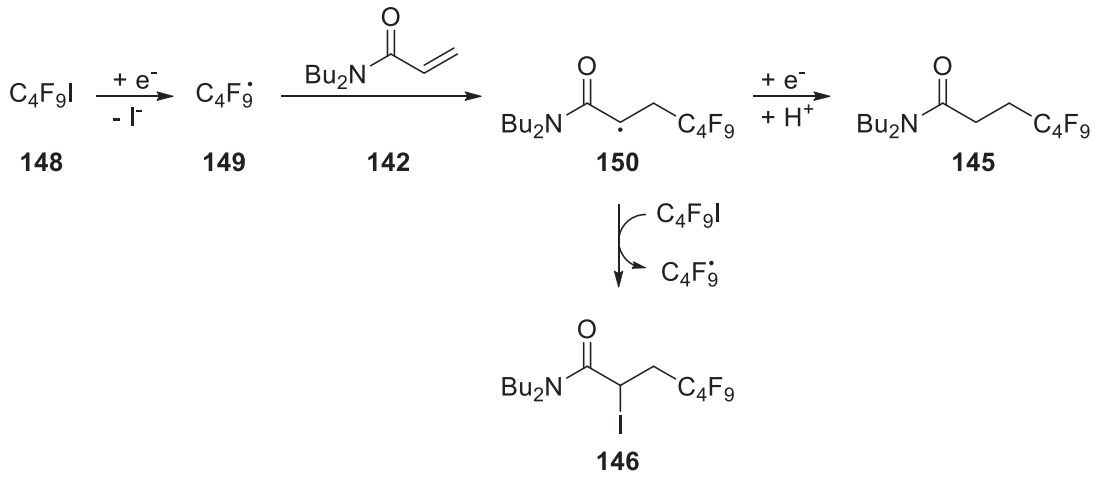
Nonafluoro-1-iodobutane was designated as the model perfluoroalkylating reagent. Following the procedures of Commeyras *et al.*, *N*,*N*-dimethylformamide was chosen as solvent for the perfluoroalkylation.[125, 126] The reaction was performed with 0.1 M tetrabutylammonium tetrafluoroborate as electrolyte and $Yb(OTf)_3$ hydrate as Lewis acid on glassy carbon electrodes (Scheme 58). Initially, a current of 1 mA was applied, which was increased to 7 mA over the course of the reaction. The conversion of the substrate was observed by ^{19}F NMR spectroscopy and TLC. After 8 days (4.2 F/mol C_4F_9I) the reaction was quenched by an aqueous HCl-solution. The reaction did not go to completion and acrylamide **142** was partly re-isolated in a yield of 23%. Hydroperfluoroalkylated product **145** was isolated in a yield of 19% as well as iodoperfluoroalkylated product **146** in a yield of 5%. Hydroxylated iodinated compound **147** was isolated as a side product in 13% yield.

In comparison Erdbrink found yields ranging from 13 to 27% for the corresponding reaction of the *N*-acyloxazolidinone derivative of acrylic acid under Et_3B/O_2 conditions.[147] Even if the yield is still improvable this result confirms that the reaction is generally feasible under electrochemical conditions. A problem might be that acrylic acid derivatives are prone to polymerisation.[152]



Scheme 58: Electrochemical perfluoroalkylation of acrylamide **142**.

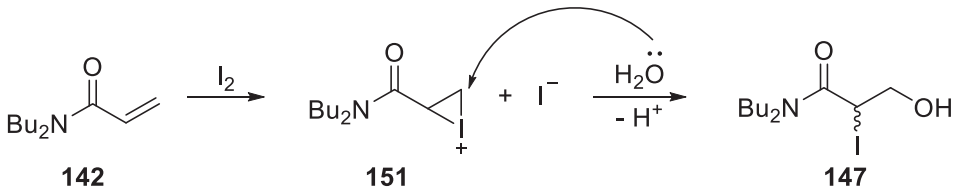
The proposed mechanism for the synthesis of hydroperfluoroalkylated product **145** and iodoperfluoroalkylated product **146** is presented in Scheme 59. The reaction is initiated with the reduction of perfluorobutyl iodide **148** producing perfluoroalkyl radical **149** and iodide, which can be oxidized at the anode to form iodine. Trapping of the perfluoroalkyl radical by olefin **142** is followed by reduction of the intermediate **150** to afford the hydroperfluoroalkylated product **145**. The abstraction of iodine by radical intermediate **150** from a second nonafluoro-1-iodobutane gives the iodoperfluoroalkylated product **146**.



Scheme 59: Proposed mechanism for the perfluoroalkylation using perfluoroalkyl iodides.

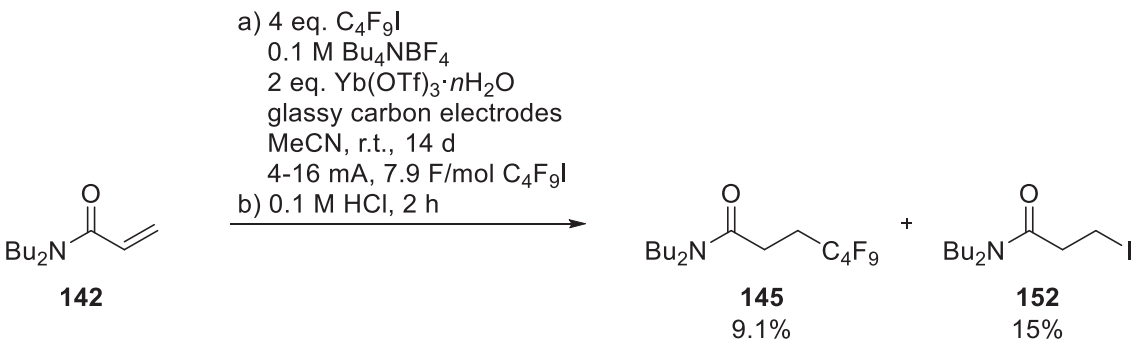
The rationale behind the iodohydroxylation is not intuitive. Contrary to bromohydrins and chlorohydrins, that can be prepared from the simple reaction of the halogen and an alkene in an aqueous solution, the addition of iodide is reversible and therefore not so easily achieved.[153] However, in the presence of iodide scavengers or

oxidizing agents the transformation of alkenes into iodohydrins or epoxides can be performed successfully.[154, 155] In this case, the formed iodide can be oxidized at the anode. A proposal for the mechanism of the formation of iodohydrin **147** is presented in Scheme 60. The cathodic reduction of nonafluoro-1-iodobutane produces iodide, which can be oxidized at the anode to iodine. The reaction of acrylamide **142** with iodine affords the iodonium ion **151**. Subsequently, nucleophilic attack by water leads to the formation of iodohydrin **147**. Another option could be the *in situ* generation of hypoiodous acid (IOH), which could add to the alkene in a similar fashion.[156] The regioselectivity of this process can be rationalized by considering the electron-withdrawing nature of the carbonyl group adjacent to the iodonium ion, which leads to the nucleophilic attack on the β-position.[157]



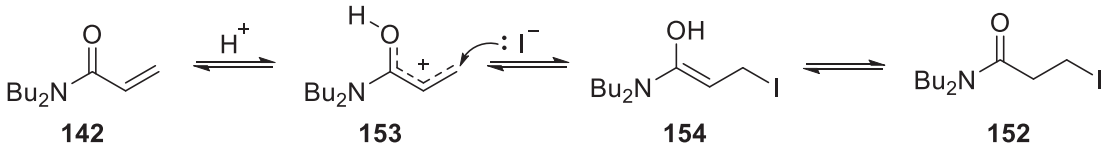
Scheme 60: Mechanistic proposal for the formation of iodohydrin **147**.

In comparison; the reaction was also attempted in acetonitrile following Uneyama *et al*.[103] Initially, a current of 4 mA was applied, which was increased to 16 mA over the course of the reaction. Again, the conversion of the substrate was observed by ^{19}F NMR spectroscopy and TLC. After 14 days (7.9 F/mol C_4F_9I) the reaction was quenched by an aqueous HCl-solution. Hydroperfluoroalkylated product **145** was isolated in a yield of 9.1% and acrylamide **142** was partly re-isolated in a yield of 12%. Moreover, in acetonitrile iodinated compound **152** was identified as a side product (Scheme 61). Interestingly, in DMF more hydroperfluoroalkylated product **145** was formed, whereas in acetonitrile the iodinated product **152** predominates.



Scheme 61: Electrochemical perfluoroalkylation of acrylamide **142** in acetonitrile.

The proposed mechanism for the formation of iodinated product **152** is displayed in Scheme 62. Protonation of acrylamide **142** affords cation **153**.[158, 159] Nucleophilic attack of the iodide to the β-carbon gives intermediate **154** and the following tautomerization leads to iodinated product **152**. The hydrohalogenation occurs anti-Markovnikov, as it was also observed in the reaction of hydrochloric acid with acrolein.[160] Another option could be the direct nucleophilic attack of the iodide to the Michael-system, followed by protonation and tautomerization.



Scheme 62: Proposed mechanism for the formation of iodinated side product **152**.

The conversion of the perfluorobutyl iodide in DMF was observed by ^{19}F NMR (Figure 5). At first the substrate seems to be consumed linearly over time, but the conversion slows down after a certain while. This is a known problem with constant current experiments, wherein the conversion decreases as soon as the concentration of the electroactive compound is dropping low.

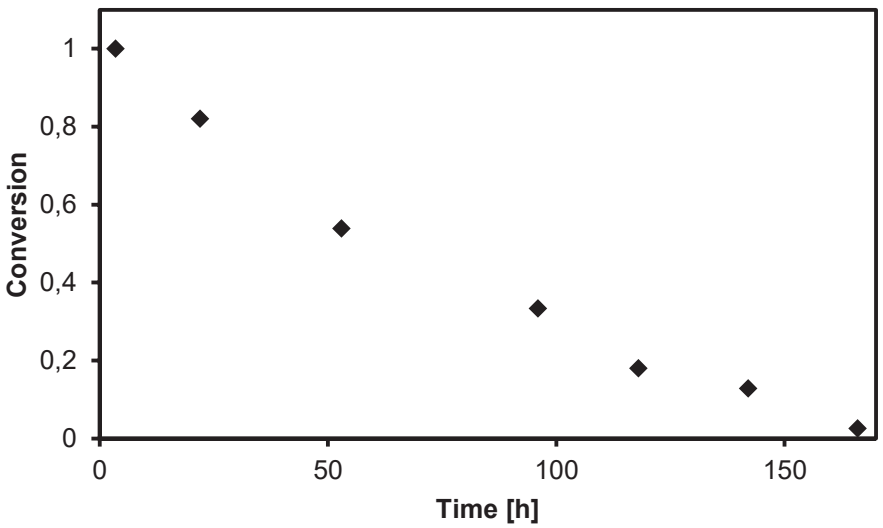


Figure 5: Conversion of the perfluorobutyl iodide with time in DMF observed by ^{19}F NMR spectroscopy.

The cyclic voltammogram of nonafluoro-1-iodobutane in *N*,*N*-dimethylformamide and tetrabutylammonium tetrafluoroborate (0.2 M) as the supporting electrolyte is presented in Figure 6. The reduction potential is -1.52 V vs. Ag/AgCl on a glassy

carbon working-electrode. The decrease of current density in the second cycle shows the consumption of the perfluoroalkylating reagent at the working electrode.

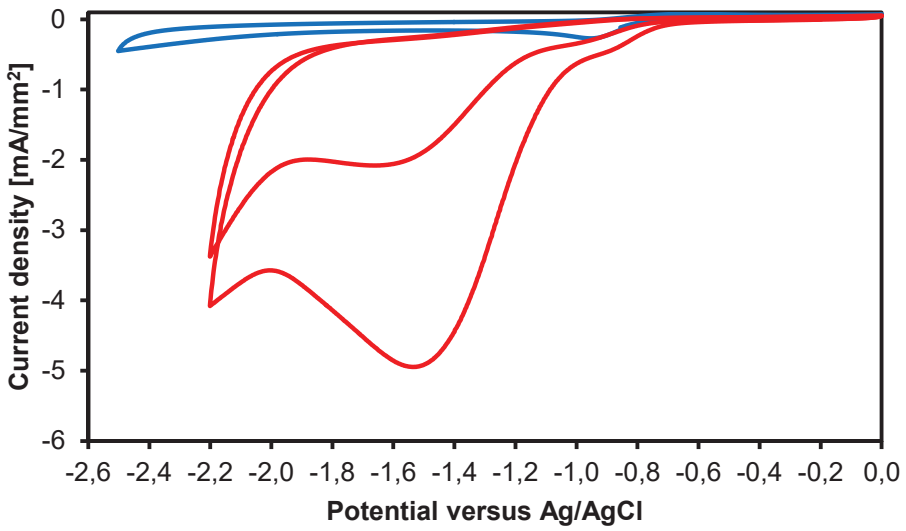


Figure 6: Cyclic voltammogram of nonafluoro-1-iodobutane in DMF/Bu_4NBF_4 with C_4F_9I (red) and electrolyte (blue) at a glassy carbon electrode.

In addition, the reduction potential is highly dependent on the cathode material. Saveant and coworkers reported the reduction potential of trifluoromethyl iodide at different cathodes measured by cyclovoltammetry, shown in Table 2.[161] Thereby, the glassy carbon electrode showed the lowest potential followed by platinum, gold and mercury, respectively. In contrast, Ignat'ev *et al*. reported a greater reduction potential at a glassy carbon electrode compared with platinum.[162]

Table 2: Reduction potentials (Peak Potentials, E_P vs SCE) of CF_3I at various electrodes in 0.1 **M** Bu_4NBF_4/DMF, 0.2 V/s, at 5 °C.

	GC	Pt	Au	Hg
CF_3I	-1.52	-0.95	-0.70	-0.65

Therefore, the reaction in DMF was also performed utilising platinum nets as electrodes. During the first attempt problems arose with corrosion of the clamps which secure the electrodes, leading to a constant instability of the reaction setup. Therefore, the reaction was repeated using a nickel wire to attach the electrodes. The results are displayed in Table 3, in comparison with the corresponding reaction on glassy carbon electrodes. The yields of hydroperfluoroalkylated product **145** and

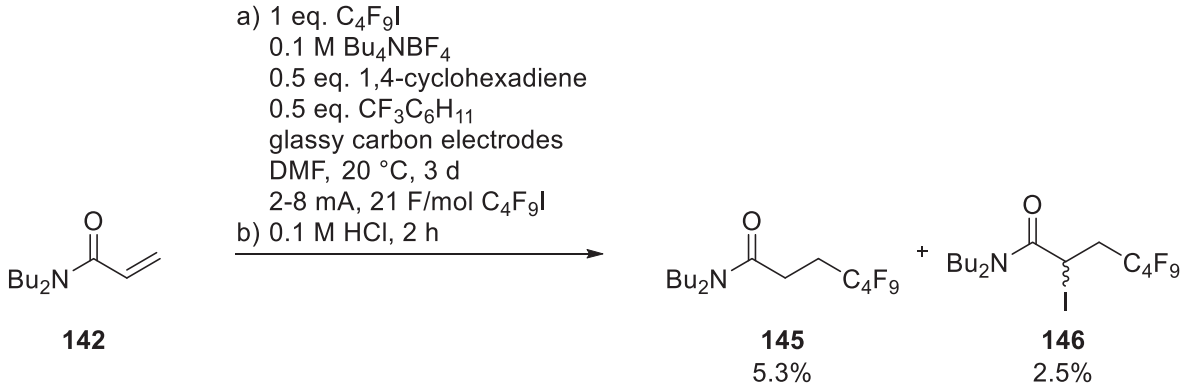
iodoperfluoroalkylated product **146** were both lower for the reaction on platinum electrodes.

Table 3: Yields of re-isolated substrate, hydroperfluoroalkylated product **145** and iodoperfluoroalkylated product **146** in DMF depending of the used electrodes.

Electrodes	Substrate [%]	Yield 145 [%]	146 [%]
GC	23	19	5
Pt[a]	8.8	10	0.8

[a]constant current electrolysis (3-4 mA) was conducted until 40 F/mol C_4F_9I were consumed

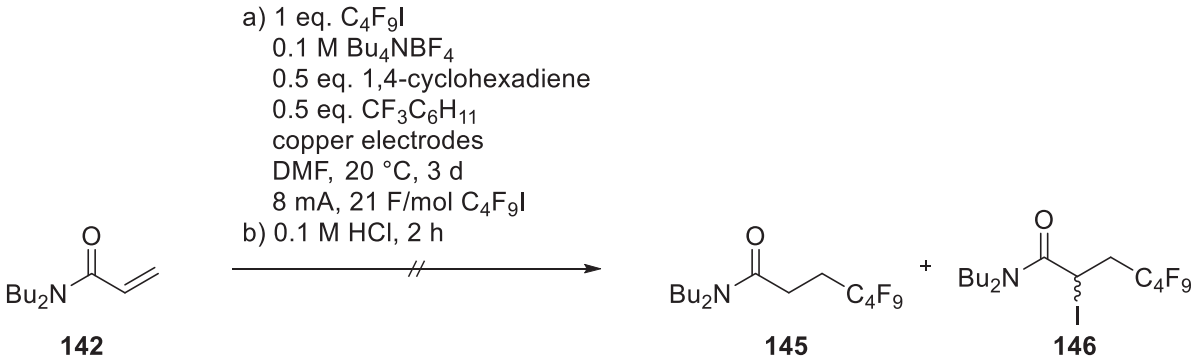
The origin of the hydrogen for the generation of hydroperfluoroalkylated product **145** is not intuitive. One possibility might be a hydrogen atom transfer from the tetrabutylammonium ion.[125, 163] Therefore, 1,4-cyclohexadiene was used as hydrogen donor to study the influence on the course of the reaction. The reaction was performed without $Yb(OTf)_3$ hydrate to prevent water as an hydrogen donor. Trifluorocyclohexane was used as an internal fluorine standard. Iodoperfluoroalkylated product **146** was isolated in 2.5% yield, hydroperfluoroalkylated product **145** in 5.3% yield and the substrate re-isolated in 38% yield (Scheme 58).



142 **145** 5.3% **146** 2.5%

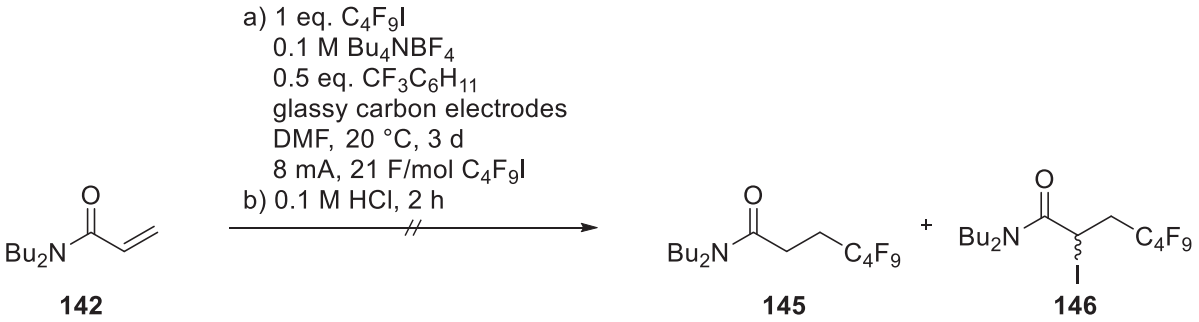
Scheme 63: Electrochemical perfluoroalkylation of acrylamide **142** with 1,4-cyclohexadiene as hydrogenation reagent on glassy carbon electrodes.

A worse result was achieved by repeating the reaction on copper electrodes, affording only a mixture inseparable by flash column chromatography (Scheme 64).



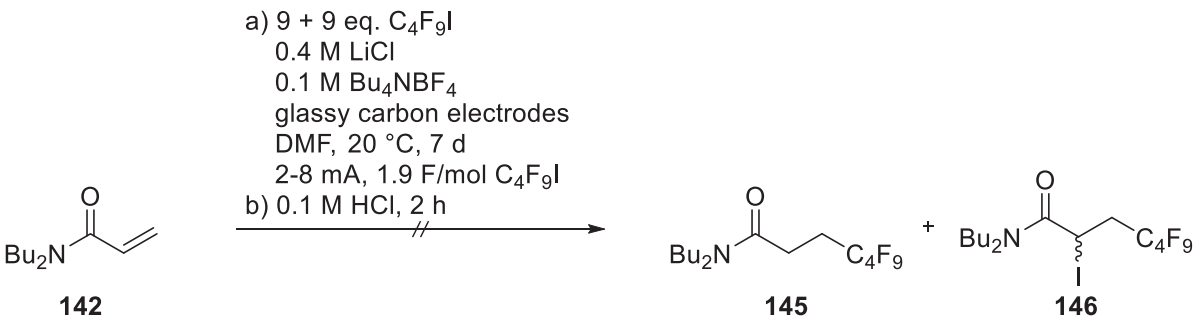
Scheme 64: Attempted electrochemical perfluoroalkylation of acrylamide **142** with 1,4-cyclohexadiene as hydrogenation reagent on copper electrodes.

To rule out that the decrease in yield comes from side reactions by trifluorocyclohexane, used as internal standard, the reaction was repeated under similar conditions on glassy carbon electrodes without the hydrogenation reagent (Scheme 81). Only a complex product mixture was obtained, which implies that trifluorocyclohexane is not the right choice for an internal standard.



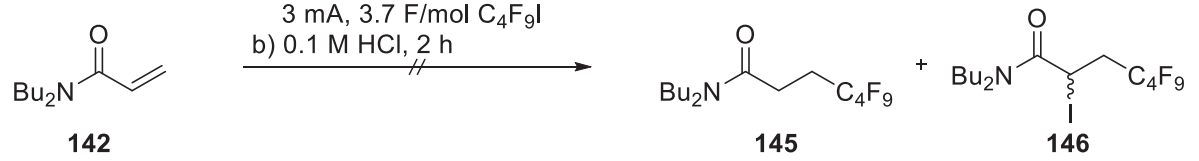
Scheme 65: Attempted electrochemical perfluoroalkylation of acrylamide **142** with trifluorocyclohexane as internal fluorine standard on glassy carbon electrodes.

Another reason for the inferior results might be the lack of a Lewis acid. Therefore, lithium chloride was used as supporting electrolyte, because Li^+ can also perform as Lewis acid to activate the carbonyl group. Moreover, the amount of C_4F_9I was raised to avoid its concentration to be the limiting factor. The reaction conditions are presented in Scheme 67. As the desired level of current was not achieved, tetrabutylammonium tetrafluoroborate was added to the solution, but no difference was observed. Analysis of the reaction mixture by ^{19}F NMR revealed a complicated product mixture.



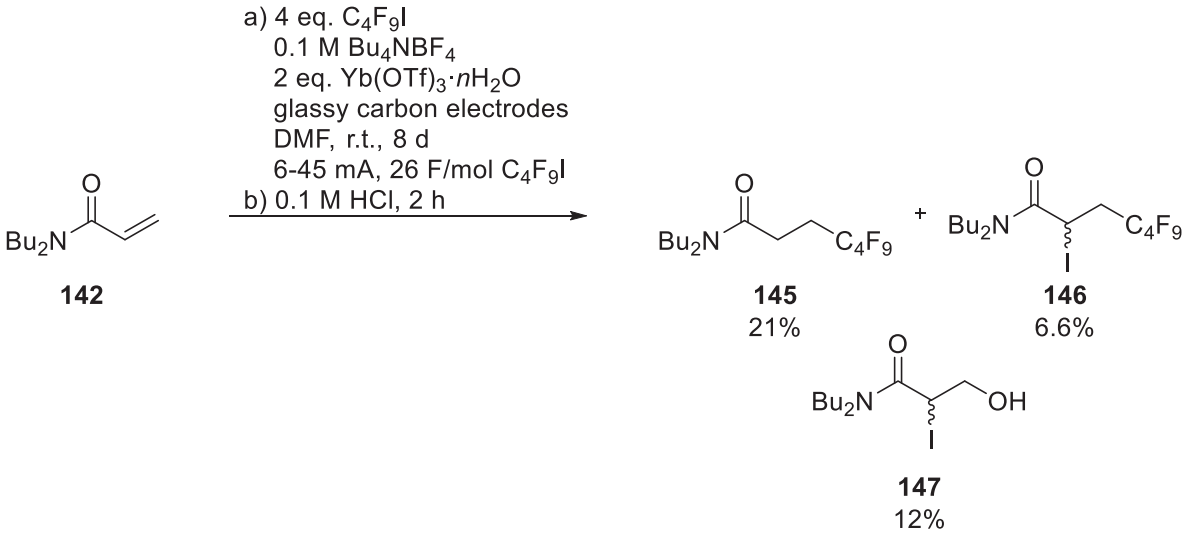
Scheme 66: Attempted electrochemical perfluoroalkylation of acrylamide **142** with LiCl as supporting electrolyte and Lewis acid on glassy carbon electrodes.

As glassy carbon electrodes are reported to have a limited lifetime under certain reaction conditions, perfluoroalkylation was attempted again using the condition that had given the best results up to this point, as presented in Scheme 67. However, analysis of the crude reaction mixture by ^{19}F NMR spectroscopy demonstrated unlike before a mixture with only small amounts of product. This result hints that the glassy carbon electrodes might have been damaged by one of the previous reactions or had just exceeded their life time.



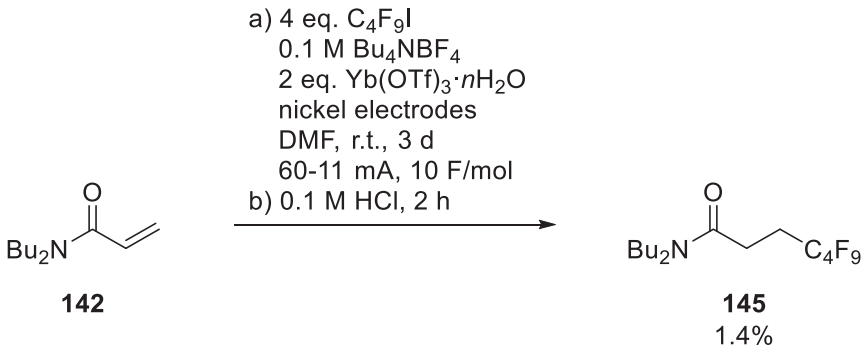
Scheme 67: Attempted electrochemical perfluoroalkylation of acrylamide **142** on glassy carbon electrodes.

To confirm the observation that the constitution of the glassy carbon electrodes shows an influence of the reaction outcome, the reaction was repeated with new electrodes. This time the reaction succeeded with comparable yields as shown in Scheme 68. The substrate **142** was re-isolated in 21% yield. Hydroperfluoroalkylated product **145** was isolated in a yield of 21% whereas iodoperfluoroalkylated product **146** was isolated in a yield of 6.6%. These results represented the best isolated yields for both perfluoroalkylated products to that point. Iodohydrin **147** was isolated in a comparable yield of 12%.



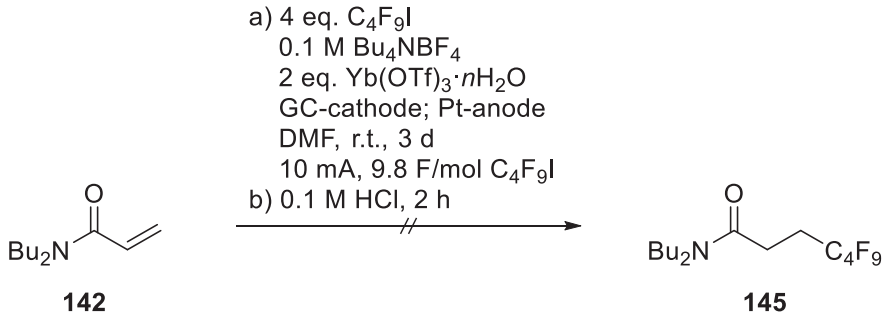
Scheme 68: Electrochemical perfluoroalkylation of acrylamide **142** with new glassy carbon electrodes.

As the lifetime of the glassy carbon electrodes most likely had an influence on the outcome of reaction, it was looked into finding better conditions for the perfluoroalkylation on other electrodes. For that reason perfluoroalkylation was attempted on nickel electrodes (23 mm x 27 mm) (Scheme 69). The reaction was performed using tetrabutylammonium tetrafluoroborate in DMF as supporting electrolyte and ytterbium(III) trifluoromethanesulfonate hydrate as Lewis acid. After 3 days, the reaction was stopped as the anode was completely corroded. Purification by flash column chromatography provided only a yield of 1.4% of product **145**.



Scheme 69: Electrochemical perfluoroalkylation of acrylamide **142** on nickel-electrodes.

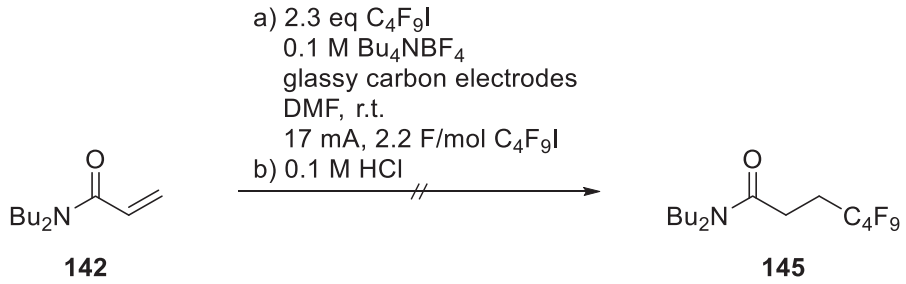
A further option was the use of a glassy carbon cathode and a platinum anode (Scheme 70). However, the analysis of the crude mixture by ^{19}F NMR spectroscopy and TLC only revealed a complicated mixture.



142 **145**

Scheme 70: Attempted electrochemical perfluoroalkylation of acrylamide **142** on a GC-cathode and a Pt-anode.

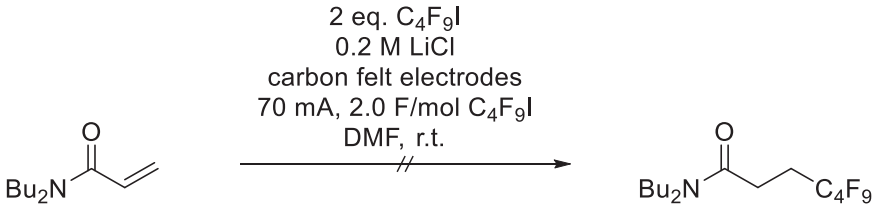
The perfluoroalkylation of acrylamide **142** was also attempted in a divided cell on glassy carbon electrodes (15 mm x 19 mm) (Scheme 71). This might prevent the development of the side product by oxidation at the anode. The constant current electrolysis (17 mA) was carried out until 2.2 F/mol C_4F_9I were consumed. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed only product traces.



142 **145**

Scheme 71: Electrochemical perfluoroalkylation of acrylamide **142** on glassy carbon electrodes in a divided H-type cell.

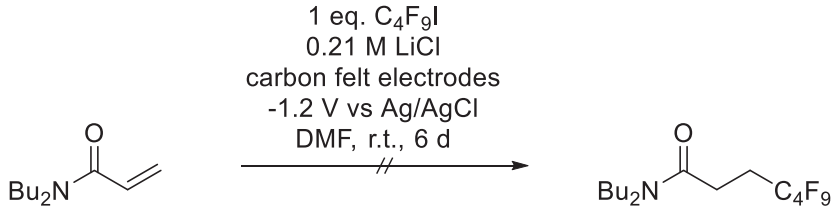
According to the procedures of Commeyras *et al*., the perfluoroalkylation of acrylamide **142** was also attempted using carbon felt electrodes and lithium chloride as supporting electrolyte in a divided H-type cell (Scheme 72).[125, 126] The constant current (70 mA) was applied until 3.5 F/mol C_4F_9I were consumed. Nonafluoro-1-iodobutane was added in portions throughout the course of the reaction. At the beginning a ratio of alkene to C_4F_9I of 1:1 was chosen. Analysis of the crude mixture by ^{19}F NMR spectroscopy revealed only product traces.



142 **145**

Scheme 72: Electrochemical perfluoroalkylation of acrylamide **142** on carbon felt electrodes in a divided H-type cell.

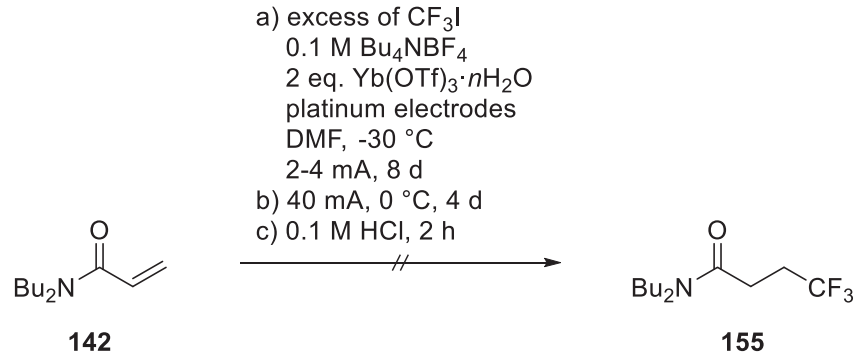
Commeyras *et al*. reported conditions for a successful perfluoroalkylation under galvanostatic and potentiostatic conditions. Therefore, the reaction of acrylamide **142** was also attempted under potentiostatic conditions at -1.2 V vs. an Ag/AgCl reference electrode on carbon felt electrodes in a divided cell (Scheme 73).[125] The initial current was 16 mA, which decreased over time. The reaction was stopped after 6 days as the conversion of the substrate was really slow. Analysis of the crude mixture by ^{19}F NMR spectroscopy showed only product traces.



142 **145**

Scheme 73: Electrochemical perfluoroalkylation of acrylamide **142** on carbon felt electrodes in a divided H-type cell under potentiostatic conditions.

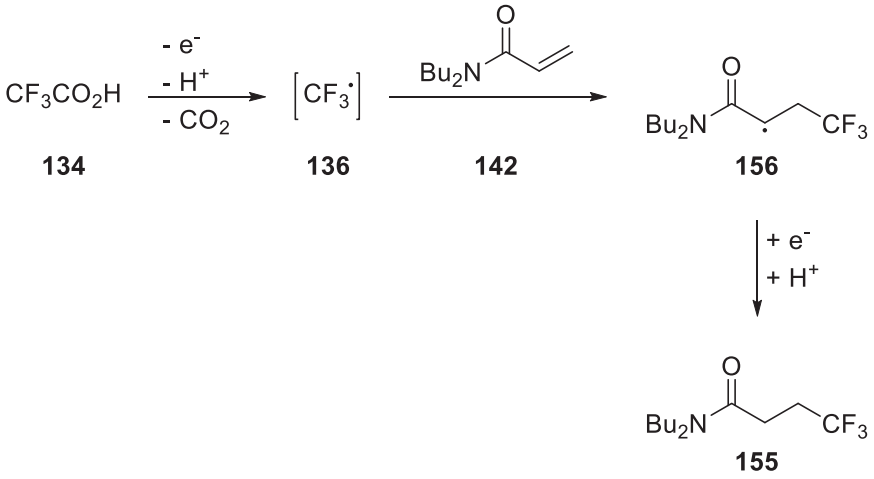
As Erdbrink *et al*. achieved higher yields using trifluoromethyl iodide as perfluoroalkylation agent compared to nonafluoro-1-iodobutane the reaction was further attempted using this compound.[83] An excess of trifluoromethyl iodide was converted on platinum electrodes using tetrabutylammonium tetrafluoroborate as supporting electrolyte and ytterbium(III) trifluoromethanesulfonate hydrate as Lewis acid (Scheme 74). A constant current of 4 mA was applied for 8 days. As the conversion of the substrate seemed really low (TLC and ^{19}F NMR analysis), the current was increased to 40 mA and the reaction warmed to 0 °C for 3 days. Analysis of the crude mixture by ^{19}F NMR spectroscopy and TLC only revealed a complicated product mixture and trifluoromethylated amide **155** was not identified.



142 **155**

Scheme 74: Attempted electrochemical perfluoroalkylation of acrylamide **142** using trifluoromethyl iodide as perfluoroalkylation reagent.

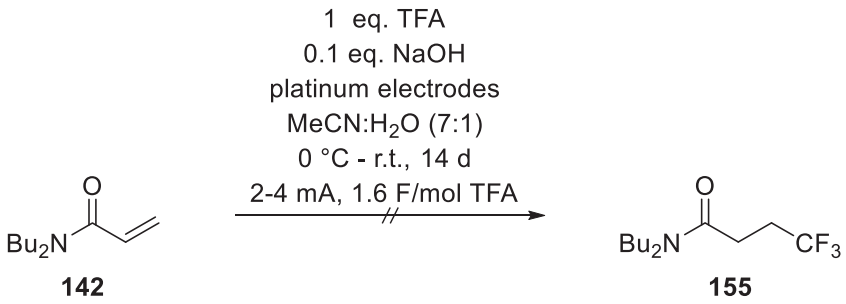
The perfluoroalkylation of *N*,*N*-dibutylacrylamide was also attempted with a perfluoroalkanoic acid following the procedure of Uneyama *et al.*[102] Electrooxidation of trifluoroacetic acid (**134**) involves decarboxylation to afford radical **136**, which can then attack the carbon-carbon double bond of the electron-deficient olefin **142**. Reduction of the formed intermediate **156** will yield the trifluoromethylated product **155**.



134 **136** **142** **156** **155**

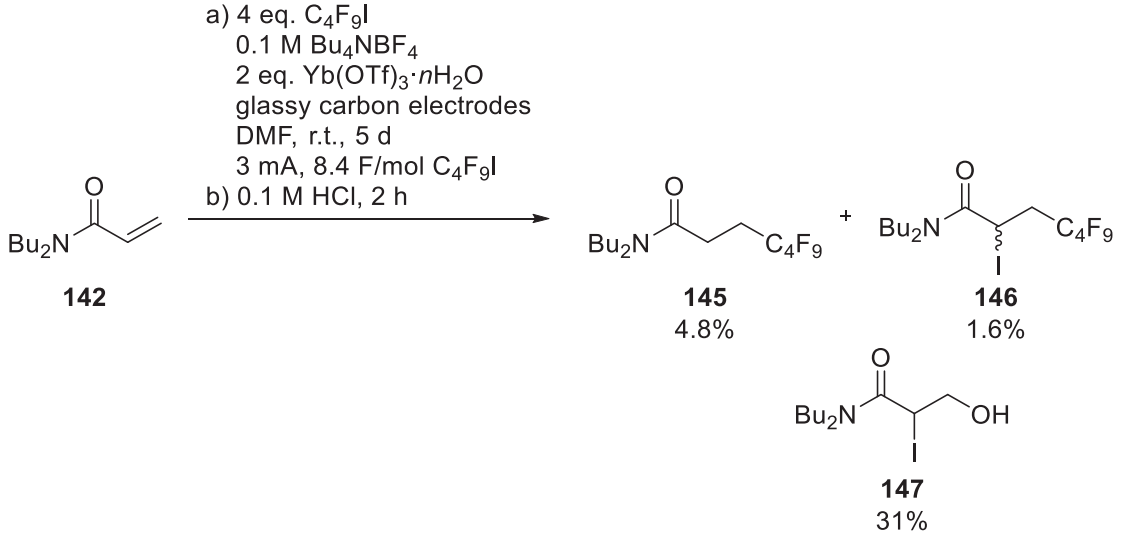
Scheme 75: Trifluoromethylation of acrylamide **142**.

The reaction was conducted in MeCN/H_2O (7:1) using sodium hydroxide as supporting electrolyte on platinum electrodes in an undivided cell (Scheme 76). The constant current electrolysis (2-4 mA) was performed until 1.6 F/mol TFA were consumed. Unfortunately, the reaction afforded a complex product mixture.



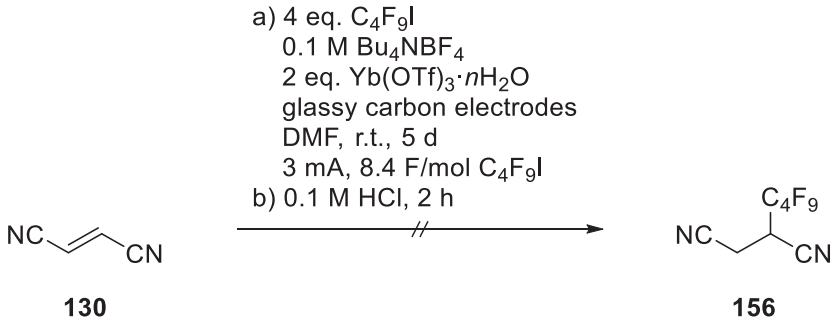
Scheme 76: Conditions of the attempted trifluoromethylation of olefin **142** using TFA.

To rule out that the low yields of the reaction derive from the electron-poor nature of the alkene, three different types of substrates were tried in test reactions in a screening block. For comparison acrylamide was used. The condition that provided the best results so far were chosen. Therefore, tetrabutylammonium tetrafluoroborate in DMF was used as supporting electrolyte and ytterbium(III) trifluoromethanesulfonate hydrate as Lewis acid. The constant current electrolysis (3 mA) was performed on glassy carbon electrodes (10 mm x 10 mm). After purification by flash column chromatography, hydroperfluoroalkylated product **145** was isolated in 4.8% yield, iodoperfluoroalkylated product **146** in 1.6% and iodinated product **147** in 31% yield (Scheme 77). The substrate was re-isolated in 47% yield.



Scheme 77: Electrochemical perfluoroalkylation of acrylamide **142** in a screening block.

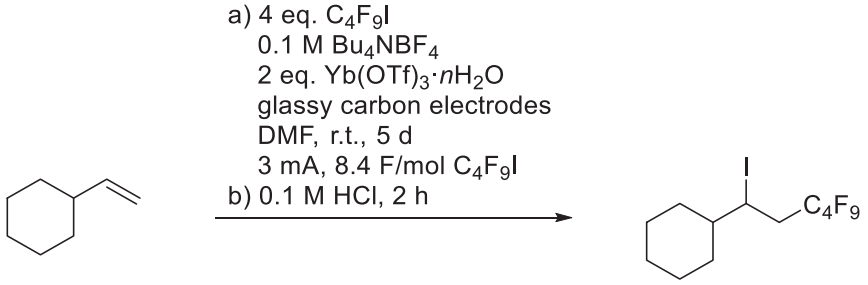
Perfluoroalkylation was also tested with fumaronitrile (**130**) in the screening block under similar conditions (Scheme 78). However, no product **157** was identified in the crude mixture after analysis by ^{19}F NMR spectroscopy.



130 **156**

Scheme 78: Attempted electrochemical perfluoroalkylation of fumaronitrile (**130**) in a screening block.

Furthermore, the reaction was performed with vinylcyclohexane (**158**) under the same conditions (Scheme 79). Following purification by flash column chromatography iodoperfluoroalkylated product **159** was isolated in 11% yield. This was a promising result as that resembled nearly double the amount of perfluoroalkylated product isolated from the reaction with acrylamide **142** (total amount: 6.4%). Consequently, vinylcyclohexane or other electron-rich products might turn out to be more suitable substrates. This phenomenon was also observed for other perfluoroalkylation methods with one example being the FLP-catalysed reaction developed in our group.[87]



158 **159**
11%

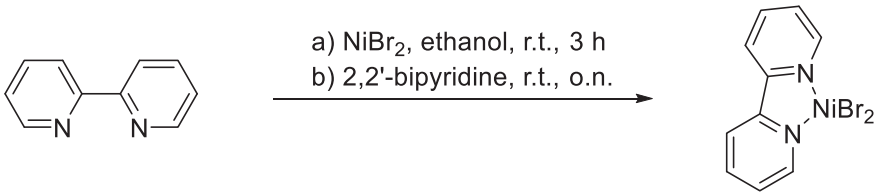
Scheme 79: Electrochemical perfluoroalkylation of vinylcyclohexane (**158**) in a screening block.

5.1.3 Indirect Electrochemical Perfluoroalkylation of Acrylic Acid Derivatives

The attempted direct electrochemical perfluoroalkylation of acrylamides did not provide sufficient results. As the successful transformation of acrylamides would resemble the first step for the development of a stereoselective version due to the similarity of the substrate with Evans-Auxiliary derivatives, indirect methods were examined next.

5.1.3.1 Attempted Perfluoroalkylation of Acrylamide using C_4F_9I and a Nickel Catalyst

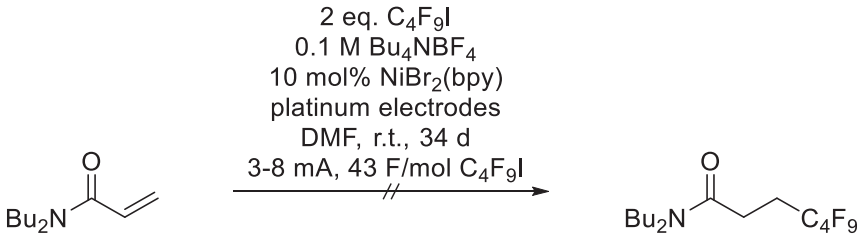
Perfluoroalkylation was attempted with an indirect method using a nickel(II) complex as mediator following the example of Budnikova *et al*., who demonstrated successful transformation of styrene derivatives.[46, 130, 131] The chosen catalyst $NiBr_2$(bpy) **160** was synthesized from nickel bromide and 2,2'-bipyridine **161** in ethanol in 66% yield (Scheme 80).[164]



160 **161** 66%

Scheme 80: Preparation of $NiBr_2$(bpy) **161**.

The conditions for the attempted indirect perfluoroalkylation are displayed in Scheme 81. Platinum nets were used as electrodes in DMF as solvent and tetrabutylammonium tetrafluoroborate as supporting electrolyte with 10 mol% of the nickel catalyst. The reaction was performed at low current (3-8 mA). However, the corrosion of the clamps to secure the platinum nets provided a problem as the anode kept falling in the solution. After 34 days the reaction was stopped as only traces of product **145** were detected by TLC and ^{19}F NMR spectroscopy.



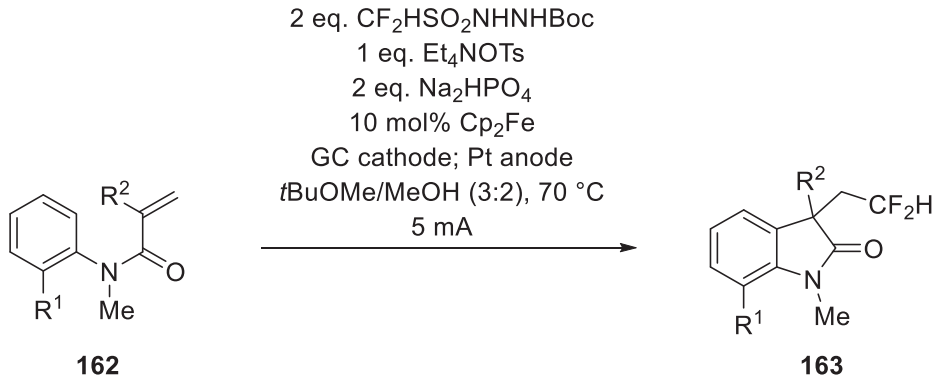
142 **145**

Scheme 81: Conditions for the attempted indirect perfluoroalkylation of acrylamide **145**.

5.1.3.2 Attempted Trifluoromethylation of Acrylamide using TfNHNHBoc and Ferrocene

The electrochemical difluoromethylarylation of alkenes **162** was demonstrated by Xu *et al*. (Scheme 82).[165] The ferrocene-mediated oxidation process utilises

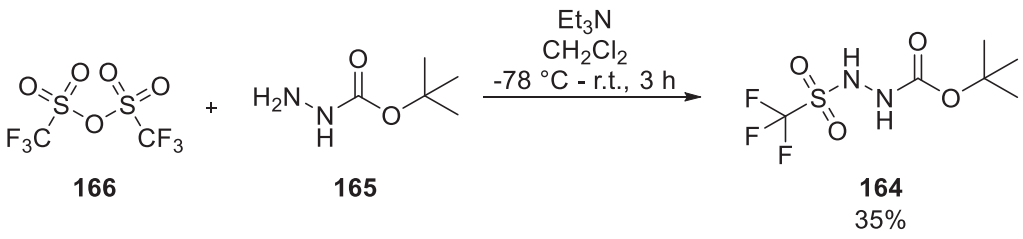
$CF_2HSO_2NHNHBoc$ as difluoromethylation reagent. The addition of the CF_2H radical to the unsaturated bond followed by intramolecular cyclisation provides products **163** in moderate to good yields.



162 **163**

Scheme 82: Ferrocene-mediated electrochemical difluoromethylarylation of alkenes.

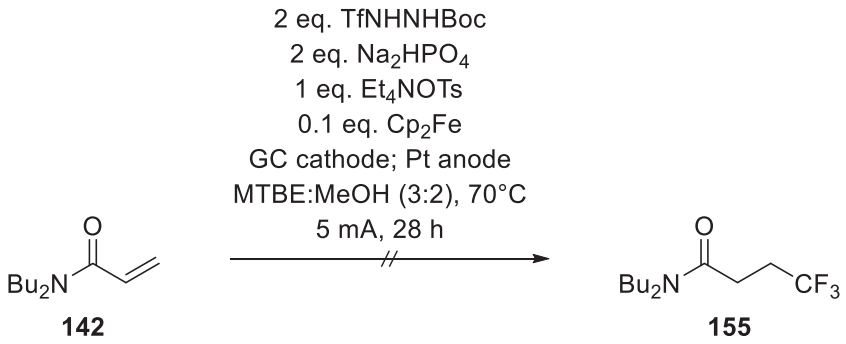
The same approach was attempted for the indirect perfluoroalkylation of acrylamide **142** with the exception that the difluoromethyl group was exchanged with a trifluoromethyl group. The trifluoromethylating reagent **164** was prepared according to the procedure of Tian *et al.* from carbazate **165** and triflic anhydride **166** (Scheme 83).[166]



166 **165** **164**
35%

Scheme 83: Synthesis of hydrazide **164**.

Trifluoromethylation of acrylamide **142** was attempted according to the procedure of Xu *et al*.[165] Thereby, ferrocene was used as a mediator and disodium phosphate as basic additive with tetraethylammonium *p*-toluenesulfonate as supporting electrolyte. The constant current electrolysis (5 mA) was carried out for 28 hours. Purification by flash column chromatography only provided fluorinated, unidentified compounds.



Scheme 84: Attempted trifluoromethylation of acrylamide **142** using TfNHNHBoc.

Because of the difficulties encountered with the perfluoroalkylation of acrylamide **142** the development of the electrochemical perfluoroalkylation was further investigated using a different type of substrate.

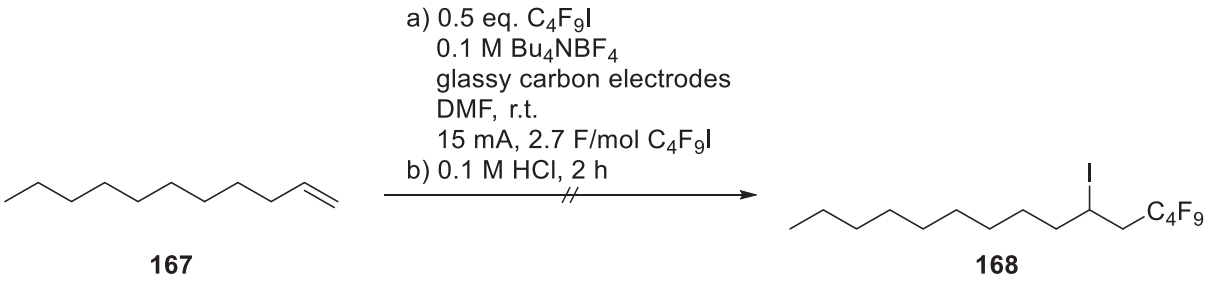
5.2 Electrocatalytic Iodoperfluoroalkylation of Alkenes

The issues encountered with the direct and indirect electrochemical hydroperfluoroalkylation of the Evans-auxiliary derivatives and acrylamide **142** could be attributed to the electron-deficient nature of the substrates. Therefore, investigations were made to identify a more suitable substrate for the development and optimisation of the electrochemical method. Our group has previously utilised more electron-rich molecules as effective model substrates for FLP- or photocatalysed iodoperfluoroalkylations.[87, 88, 167] As mentioned above, mechanistic investigations of the electrochemical addition of iodoperfluoroalkanes to a limited number of alkenes and alkynes were executed by Commeyras *et al*.[125, 126] The following chapter discusses the development of a general synthetic protocol for the iodoperfluoroalkylation of alkenes. The first part will cover preliminary trials, followed by an optimisation of the reaction conditions and the second part will discuss the investigation of the substrate scope and the scalability of the process.

5.2.1 Preliminary Trials

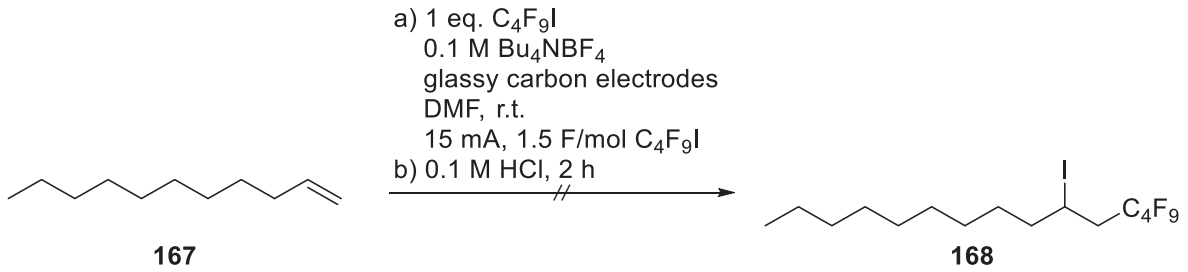
The comparison of the yields following electrochemical perfluoroalkylation of acrylamide **142**, fumaronitrile (**130**) and vinylcyclohexane (**158**) in a screening block shows that the best result was achieved for the most electron-rich substrate. In this case only the formation of the iodoperfluoroalkylated product was observed. Therefore, this setting provided a promising start for the development of the electrochemical methodology. The mechanistic considerations for this transformation

are discussed in chapter 5.1.2 using acrylamide **142** as substrate (Scheme 59, page 41). Because vinylcyclohexane (**158**) exhibits lower bench-stability, iodoperfluoroalkylation was first attempted with other electron-rich substrates. As a consequence the reaction was next attempted with 1-undecene (**167**). Since the best results were achieved with tetrabutylammonium tetrafluoroborate as supporting electrolyte in *N*,*N*-dimethylformamide on glassy carbon electrodes, those were chosen for first trials. The reaction was carried out as constant current electrolysis (15 mA) in an undivided cell until 2.7 F/mol C_4F_9I were consumed. Nonafluoro-1-iodobutane was used as limiting factor to reduce the probability of dimerization. Analysis of the crude mixture by ^{19}F NMR spectroscopy revealed no traces of product **168**.



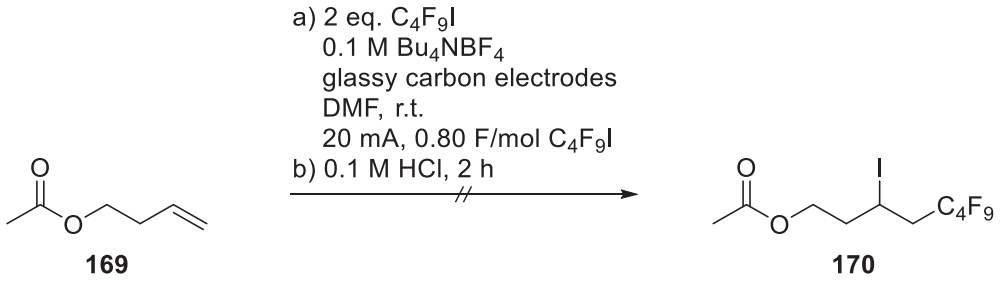
Scheme 85: Attempted electrochemical iodoperfluoroalkylation of 1-undecene (**167**) in an undivided cell.

The iodoperfluoroalkylation of 1-undecene (**167**) was also performed in a divided H-type cell (Scheme 86). Hereby, fluorinated products were formed during the reaction as identified by ^{19}F NMR spectroscopy. Unfortunately, after repeated purification attempts no product was isolated in pure form. Due to the long nonpolar chain, separation of the formed fluorinated products even in pure *n*-pentane turned out very difficult.



Scheme 86: Attempted electrochemical iodoperfluoroalkylation of 1-undecene (**167**) in a divided H-type cell.

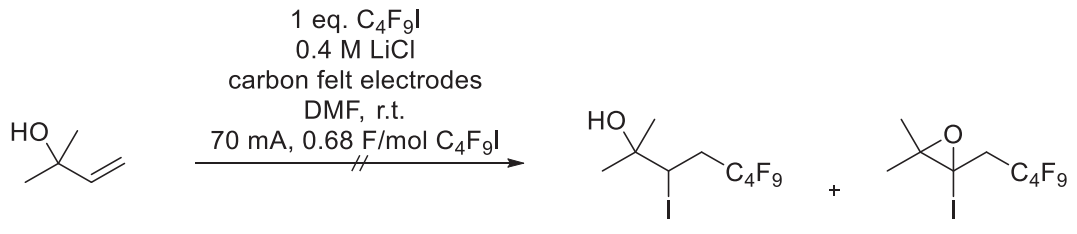
As the separation of the fluorinated products of nonpolar 1-undecene (**167**) provided a challenge, the reaction was next attempted with the transformation of 3-butenyl acetate (**169**) to iodoperfluorobutylated product **170**. The constant current electrolysis (20 mA) was carried out with an increased amount of nonafluoro-1-iodobutane to reduce the possibility for the formation of side products at the cathode (Scheme 87). Unfortunately, also in this case only mixtures of fluorinated, unidentified compounds were isolated after attempted purification by flash column chromatography.



169 **170**

Scheme 87: Attempted electrochemical iodoperfluoroalkylation of 3-butenyl acetate (**169**) in a divided H-type cell.

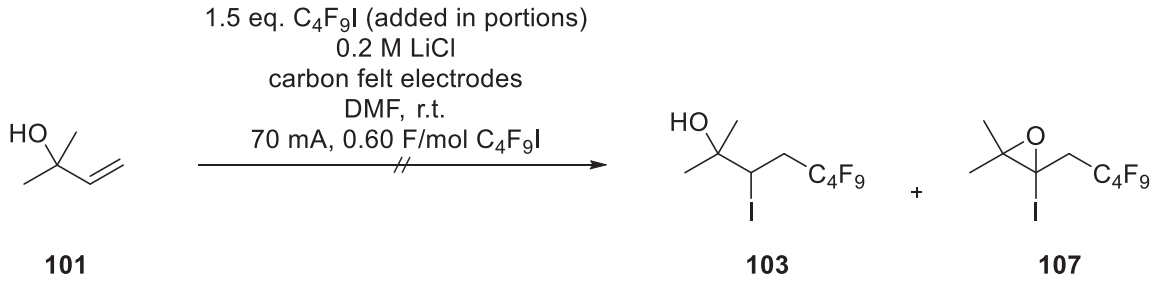
Commeyras *et al.* demonstrated the successful iodoperfluoroalkylation of 2-methyl-3-buten-2-ol (**101**).[125] Therefore, iodoperfluoroalkylation was next attempted with this substrate in a divided H-type cell (Scheme 88). According to their conditions, lithium chloride was used as supporting electrolyte and the reaction carried out with application of a higher current (70 mA) on carbon felt electrodes. Unfortunately, only complicated fluorinated mixtures were isolated by flash column chromatography containing iodoperfluoroalkylated product **103** and epoxide **107**. The formation of the epoxide is related to the basic condition existing in the cell and was also observed by Commeyras *et al*. (see Chapter 3.4.2, p. 25f).[125] The multitude of side products showed the need for an improvement of the protocol.



101 **103** **107**

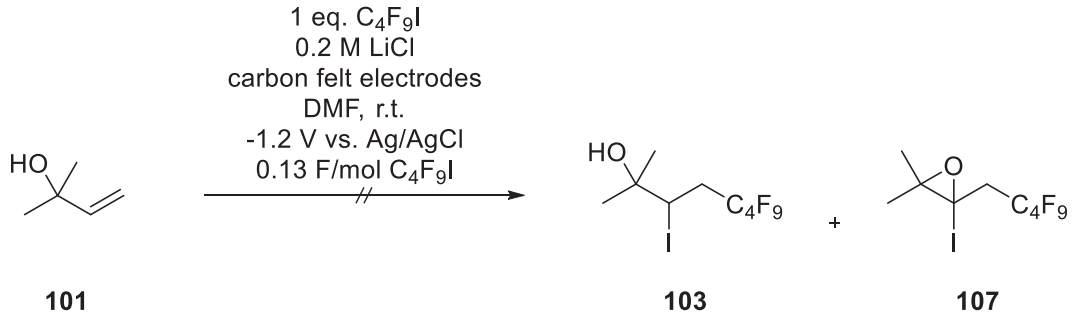
Scheme 88: Attempted electrochemical iodoperfluoroalkylation of hydroxylated alkene **101** in a divided H-type cell.

Accordingly, the electrochemical iodoperfluoroalkylation of 2-Methyl-3-buten-1-ol (**101**) was attempted under changed conditions. The electrolyte concentration was lowered and a second addition of nonafluoro-1-iodobutane was implemented to keep its concentration high during the course of the reaction (Scheme 89). However, analysis of the crude material by ^{19}F NMR spectroscopy only revealed an inseparable mixture of fluorinated compounds.



Scheme 89: Attempted electrochemical iodoperfluoroalkylation of hydroxylated alkene **101** in a divided H-type cell.

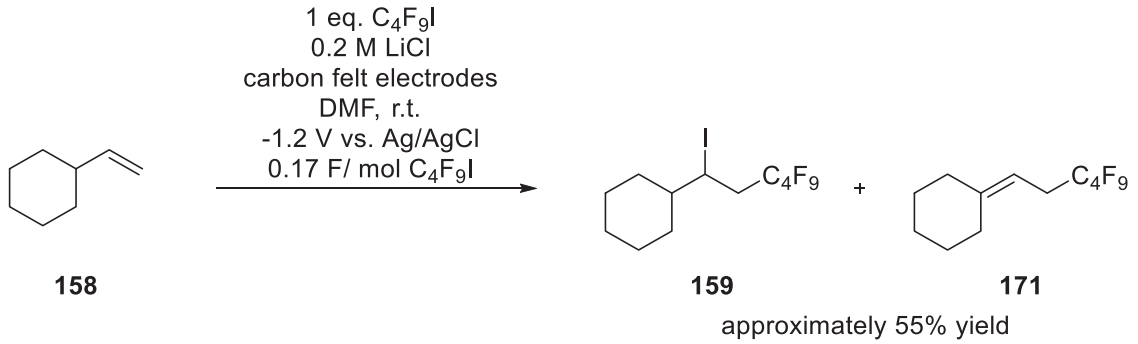
Commeyras et al. reported conditions for successful perfluoroalkylation under galvanostatic and potentiostatic conditions. Therefore, the reaction of 2-methyl-3-buten-1-ol (**101**) was also attempted under potentiostatic conditions at -1.2 V vs. an Ag/AgCl reference electrode on carbon felt electrodes.[125] An increased substrate conversion was observed by analysis of the isolated mixtures by ^{19}F NMR spectroscopy. However, next to product **103** a significant amount of epoxide **107** and further side products was formed.



Scheme 90: Attempted electrochemical iodoperfluoroalkylation of hydroxylated alkene **101** in a divided H-type cell under potentiostatic conditions.

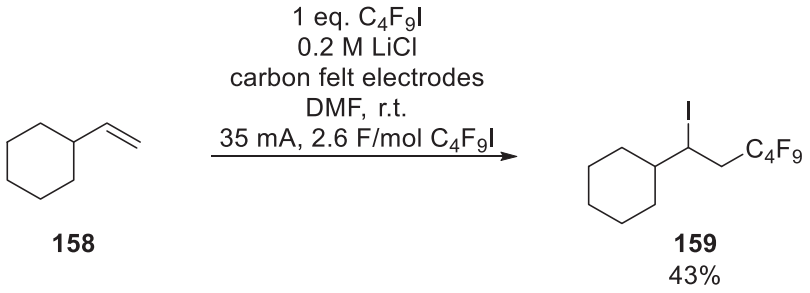
Since vinylcyclohexane (**158**) was identified before as a promising candidate, its iodoperfluoroalkylation was performed under the same potentiostatic conditions (-1.2 V vs. Ag/AgCl). The initial current was 80 mA. Purification by flash column chromatography afforded an inseparable mixture of iodoperfluoroalkylated

product **159** and elimination product **171** in a combined yield of approximately 55% (calculated by ^{19}F NMR analysis). This represented the most promising result; however, the three-electrode set-up in conjunction with the divided cell is very complicated and time-consuming.



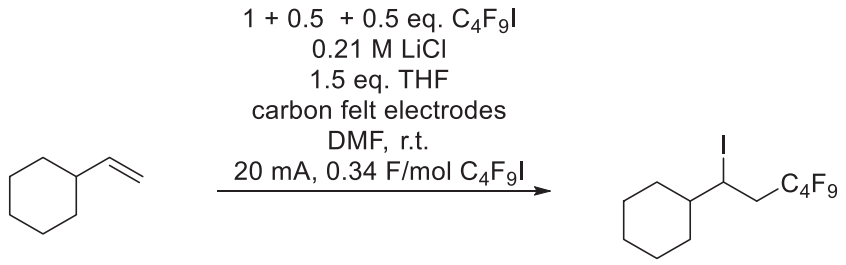
Scheme 91: Attempted electrochemical iodoperfluoroalkylation of vinylcyclohexane (**158**) under potentiostatic conditions in a divided cell.

Therefore, the reaction was also attempted under galvanostatic conditions in an undivided cell (Scheme 92). The constant current electrolysis (35 mA) was carried out until 2.6 F/mol C_4F_9I were consumed. Purification by flash column chromatography afforded the product in moderate yield (43%).



Scheme 92: Electrochemical iodoperfluoroalkylation of vinylcyclohexane (**158**) under galvanostatic conditions in an undivided cell.

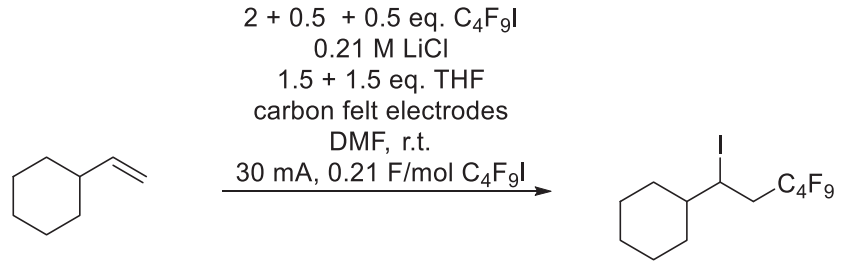
The galvanostatic setting seemed to be a more promising approach compared with the potentiostatic. Therefore, it was next concentrated on evaluating the basic conditions such as cell-type. For that reason, the perfluoroalkylation of vinylcyclohexane (**158**) was performed in a divided cell under galvanostatic conditions applying a current of 20 mA (Scheme 93). Tetrahydrofuran was added to the anodic side as a potential sacrificial substrate. Nonafluoro-1-iodobutane was added in portions throughout the reaction to keep its concentration high and avoid the formation of side products. Purification of the crude material by flash column chromatography afforded the product in a yield of 57%.



158 **159**
57%

Scheme 93: Electrochemical iodoperfluoroalkylation of vinylcyclohexane (**158**) under galvanostatic conditions in a divided cell.

As the amount of nonafluoro-1-iodobutane could have a high impact on the outcome of the reaction, the perfluoroalkylation was performed with two equivalents of nonafluoro-1-iodobutane from the start (Scheme 94). The iodoperfluoroalkylated product was isolated in an improved yield of 65%. Due to these first promising attempts, vinylcyclohexane was chosen as a model substrate. The next objective was to carry out a thorough investigation of various reaction parameters.



158 **159**
65%

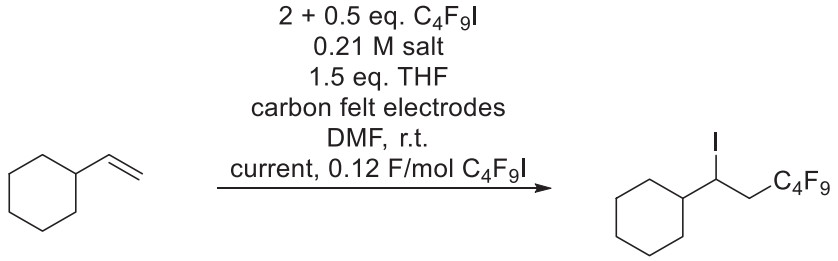
Scheme 94: Electrochemical iodoperfluoroalkylation of vinylcyclohexane (**158**) under galvanostatic conditions in a divided cell.

5.2.2 Optimisation of the Reaction Conditions for the Electrocatalytic Iodoperfluoroalkylation of Vinylcyclohexane

The first attempts for the electrocatalytic iodoperfluoroalkylation of vinylcyclohexane with nonafluoro-1-iodobutane provided a promising start for a systematic study. In the following, the influence of a variety of reaction conditions such as supporting electrolyte, solvent or electrode material is investigated. To avoid a more complicated three-electrode set-up it was concentrated on finding conditions for a galvanostatic experiment. If not indicated otherwise, the reactions were performed in a divided H-type cell. The optimisation process was started by looking closer into the nature of the salt and the applied current. Lithium chloride and tetrabutylammonium

tetrafluoroborate were both tested as supporting electrolytes applying either a current of 20 or 30 mA (Table 4). After performing the reaction with either LiCl or Bu_4NBF_4 and application of a specific current, the differences in isolated product yield were marginal. However, at both applied currents the use of Bu_4NBF_4 provided slightly better yields. The best results were achieved using tetrabutylammonium tetrafluoroborate with a current of 20 mA (Entry 3).

Table 4: Yield of product **159** after performing the perfluoroalkylation of vinylcyclohexane (**158**) with lithium chloride or tetrabutylammonium tetrafluoroborate as salts applying a current of 20 or 30 mA.

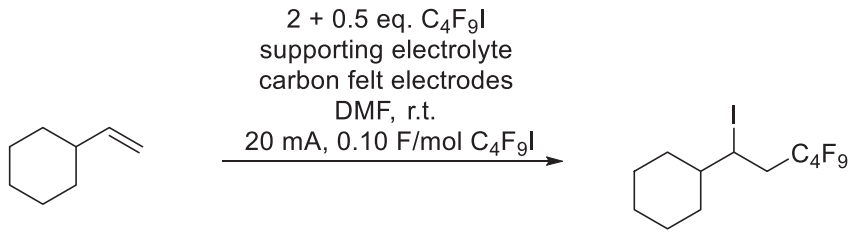


158 **159**

Entry	Salt	Current [mA]	Yield [%]
1	LiCl	20	77-79
2	LiCl	30	77
3	Bu_4NBF_4	20	81-85
4	Bu_4NBF_4	30	79

Secondly, it was examined whether tetrahydrofuran is essential as sacrificial substrate. The iodoperfluoroalkylation of vinylcyclohexane with either lithium chloride or tetrabutylammonium tetrafluoroborate as supporting electrolyte showed no decrease in isolated yield without the addition of THF to the anodic side (Table 5, Entries 1 and 2; Table 4, Entries 2 and 3). This indicates that a different process must be taking place at the anode. The deep red colouring of the solution in the anodic part of the cell can be decoloured by sodium thiosulfate. Hence, it can be concluded that the formed iodide must be passing through the glass frit and gets then oxidized to iodine at the anode. Before that either the electrolyte or residual water must be oxidized. Furthermore, a decrease of the salt concentration from 0.2 M to 0.1 M Bu_4NBF_4 achieved the same yield (Entries 2 and 3).

Table 5: Yield of product **159** after performing the perfluoroalkylation of vinylcyclohexane (**158**) with lithium chloride or tetrabutylammonium tetrafluoroborate as salts without addition of THF.

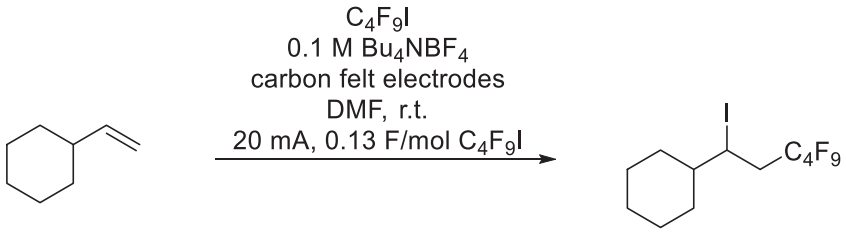


158 **159**

Entry	Salt	Concentration [M]	Yield [%]
1	LiCl	0.21	81
2	Bu_4NBF_4	0.21	82
3	Bu_4NBF_4	0.10	82

It was shown before, that the amount of nonafluoro-1-iodobutane has a great impact on the course of the reaction. Accordingly, the equivalents added were varied next (Table 6). If the reaction was started with only one equivalent of C_4F_9I the achieved product yield (52%, Entry 5) was considerably lower compared to straight addition of two equivalents (84%, Entry 4). To keep the concentration of the perfluoroalkylating reagent at a high level, the reagent was added several times throughout the course of the reaction. However, this only had a small influence on the reaction outcome (Entries 1, 3 and 4). Starting with two equivalents nonafluoro-1-iodobutane was sufficient and resulted in an isolated yield of 84% of the iodoperfluoroalkylated product **159**.

Table 6: Yield of product **159** after performing the perfluoroalkylation of vinylcyclohexane (**158**) adding different amounts of nonafluoro-1-iodobutane.



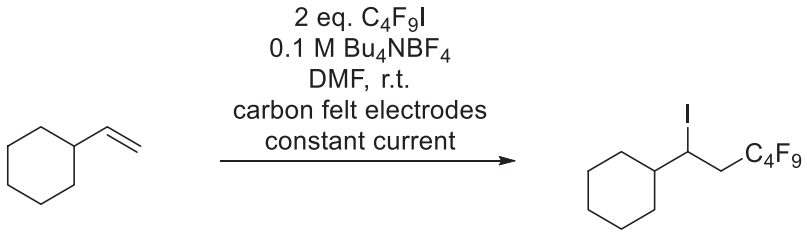
158 **159**

Entry	C_4F_9I [eq.]	Yield [%]
1	2 + 0.5 + 0.5[a]	82
2	1 + 0.5 + 0.5[a]	75
3	2 + 0.5[a]	81-85
4	2	84
5	1	52

[a] with 1.5 eq. THF

Next, the applied current as well as the applied charge were analysed (Table 7). Only a small influence on the yield was detected by varying the applied current between 10 mA and 20 mA (Entries 2 and 3). On the contrary, the applied charge proved to have a great impact on the reaction outcome. The amount could be lowered from 0.13 to 0.075 F/mol C_4F_9I without loss of yield (Entries 1 and 2). However, a further decrease to 0.038 F/mol C_4F_9I provided only a yield of 69% (Entry 4). The best yield of 86% was achieved using 10 mA and 0.075 F/mol C_4F_9I (Entry 3). The catalytic amounts of applied charge that are needed for a successful addition of nonafluoro-1-iodobutane to vinylcyclohexane show, that the reaction is following a chain reaction mechanism.

Table 7: Yield of product **159** after performing the perfluoroalkylation of vinylcyclohexane (**158**) varying the applied current and the electrons transferred per atom.



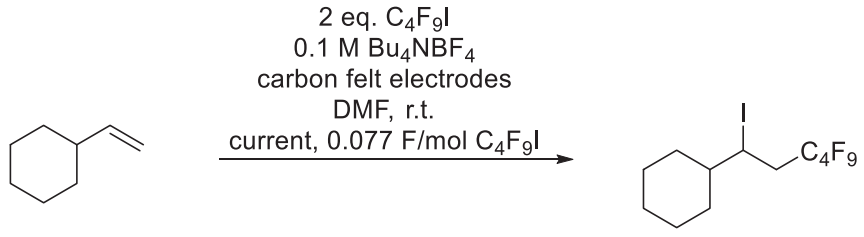
158 **159**

Entry	Current [mA]	Q (F/mol C_4F_9I)	Yield [%]
1	20	0.13	84
2	20[a]	0.075	84
3	10	0.075	86
4	10	0.038	69

[a]0.2 M Bu_4NBF_4

Additionally, the current was further lowered to examine, whether the yield could be even more improved (Table 8). Initially, this seemed to be the case, as a current of 5.0 mA afforded a yield of 91% (Entry 3). However, this result was not reproduced. A further lowering to 2.5 mA only led to a decrease in yield. Since the reaction time also increases, when a lower current is applied, the choice of current remained at 10 mA (reaction time: 4 hours). Furthermore, a control experiment was performed, in which no electricity was applied to the cell. After stirring the reaction mixture for 24 hours, no product formation was observed by ^{19}F NMR spectroscopy (Entry 5). Purification of the crude material by flash column chromatography afforded the substrate vinylcyclohexane (**158**) in 95% yield. This verifies the assumption that a current is indeed needed for successful iodoperfluoroalkylation.

Table 8: Yield of product **159** after performing the perfluoroalkylation of vinylcyclohexane (**158**) varying the applied current.

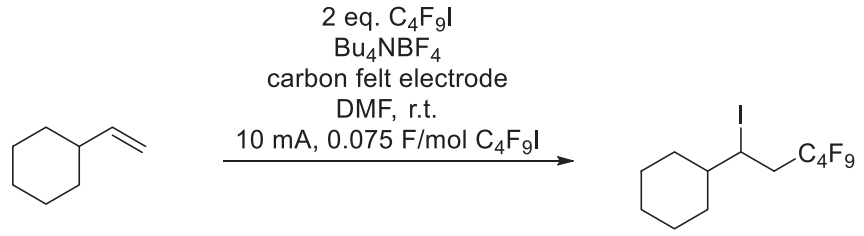


158 **159**

Entry	Current [mA]	Reaction time [h]	Yield [%]
1	20	2	84
2	10	4	86
3	5.0	8	77, 84 and 91
4	2.5	16	80
5	None	24	Ntd

Additionally, the substrate and salt concentration were varied (Table 9). Lowering the concentration of the supporting electrolyte only afforded a product yield of 83% (Entry 2). Moreover, the substrate concentrations needed to be high as a reduction led to a decrease in yield achieving only 60-65% (Entry 3). This is a known phenomenon for chain reactions.

Table 9: Yield of product **159** after performing the perfluoroalkylation of vinylcyclohexane (**158**) varying the concentration of the supporting electrolyte and alkene concentration.



158 **159**

Entry	Conc. 158 [M]	Conc. Salt [M]	Yield [%]
1	1	0.1	86
2	1	0.05	83
3	0.5	0.1	60-65

With these conditions at hand a further investigation regarding the nature of the electrode material was performed. The iodoperfluoroalkylation of vinylcyclohexane was very successful by using carbon felt as electrode material. Therefore, various carbon materials were tested as alternatives. The reaction was performed on glassy carbon, boron-doped diamond (BDD) and graphite. The achieved product yields of **159** are shown in Table 10. Compared to carbon felt, all other materials accomplished considerably lower yields. A reason for that might be the available surface area, which was restricted to 2 cm^2 for electrode plates due to the cell-design, while carbon felt (160 mg) was utilised in form of a bundle. Moreover, since carbon felt is in comparison one of the more inexpensive materials, it was the electrode of choice for further optimisation.

Table 10: Yield of product **159** after performing the perfluoroalkylation of vinylcyclohexane (**158**) varying the carbon material of the electrodes.

158 **159**

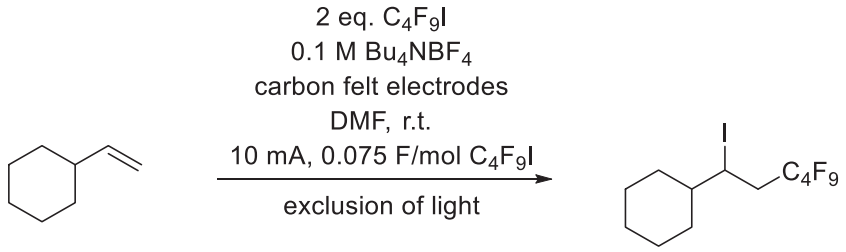
Entry	Electrode-material	Yield [%]
1[a]	Carbon felt	86
2[b]	Glassy carbon	53
3[b]	BDD	41
4[b]	Graphite	36

[a]160 mg were used

[b]surface area: 2 cm^2

For a better understanding of the transformation some control reactions were performed. Many examples for photo-catalysed iodoperfluoroalkylations can be found in literature.[88, 168-171] For that reason, the conversion of vinylcyclohexane (**158**) into the 1,2-addition product **159** was also performed under the exclusion of light (Scheme 95). Fortunately, this had no impact on the reaction outcome and the iodoperfluoroalkylated product **159** was isolated in a yield of 83%, confirming the

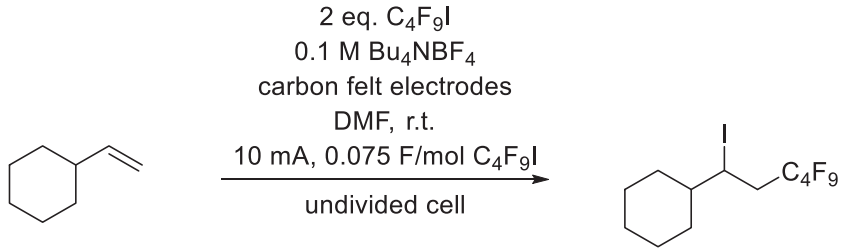
assumption that the reaction is indeed catalysed by electron transfer at the electrodes.



158 **159** 83%

Scheme 95: Electrocatalytic iodoperfluoroalkylation of vinylcyclohexane (**158**) under the exclusion of light.

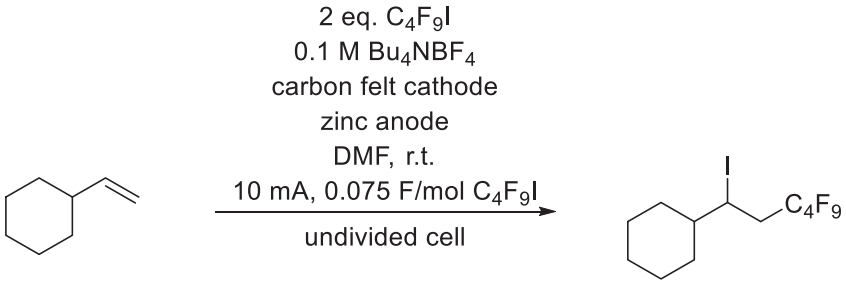
As a divided set-up is more complicated, the reaction was again performed in an undivided cell using the optimised conditions (Scheme 96). However, the isolated yield of 44% was significantly lower in comparison.



158 **159** 44%

Scheme 96: Electrocatalytic iodoperfluoroalkylation of vinylcyclohexane (**158**) in an undivided cell.

A further option for inhibiting the formation of potential side products might be a sacrificial anode.[172] In this case, the material of the anode, for example zinc, is oxidized preferentially, preventing the oxidation of organic material. Accordingly, the iodoperfluoroalkylation of vinylcyclohexane was performed using a zinc sheet as a sacrificial anode and carbon felt as the cathode in an undivided set-up (Scheme 97). This improved the yield up to 53%. Nonetheless, the divided set-up still provided better results.

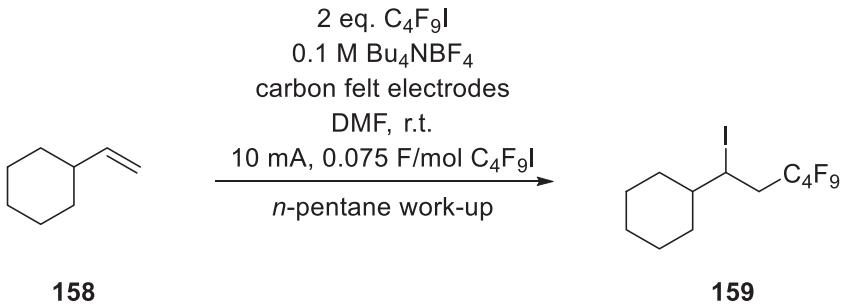


158 **159**
53%

Scheme 97: Electrocatalytic iodoperfluoroalkylation of vinylcyclohexane (**158**) in an undivided cell using zinc as sacrificial anode material.

Nonafluoro-1-iodobutane was extensively filtered over basic aluminium oxide and molecular sieves (4 Å) to remove any impurities such as iodide, before it was used in the reactions. However, in this process a large amount was lost due to its volatility. Therefore, the iodoperfluoroalkylation of vinylcyclohexane was also attempted with unfiltered nonafuoro-1-iodobutane. The isolated yield of 83% demonstrated that purification of the substrate prior to use is not essential for a successful transformation.

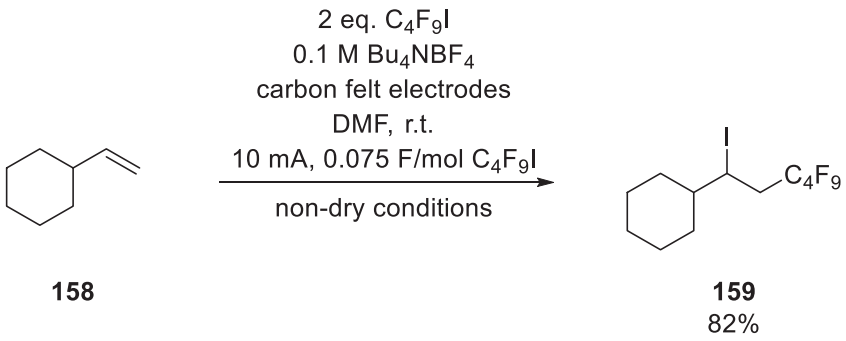
Until this point the work-up of the reaction was performed using dichloromethane for extraction of the product. However, the removal of *N*,*N*-dimethylformamide made an extensive washing process necessary. To circumvent this problem, the work-up procedure was switched to *n*-pentane for product extraction, as it is not miscible with *N*,*N*-dimethylformamide. The product was afterwards isolated in a yield of 86% (Scheme 98).



158 **159**
86%

Scheme 98: Electrocatalytic iodoperfluoroalkylation of vinylcyclohexane (**158**) using *n*-pentane as solvent for work-up.

Another aspect, which was looked into is the performance of the reaction at ambient conditions (Scheme 99). In this case a yield of 82% was achieved; the discrepancy can be explained with the reaction of remaining water to hydrogen gas at the cathode, which leads to an increased amount of electrons needed for a complete conversion. However, this result still demonstrates that the reaction is working fine under non-dry conditions.

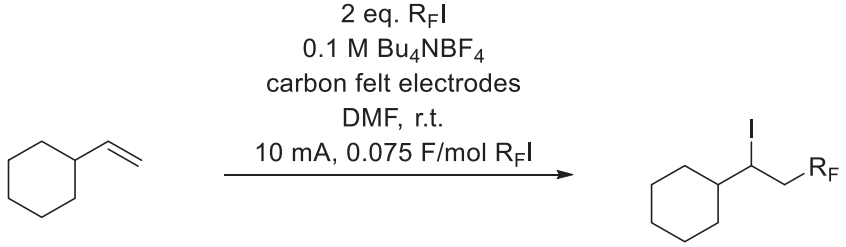


158 **159**
82%

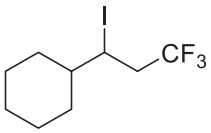
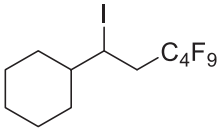
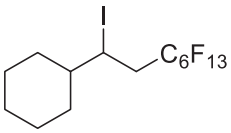
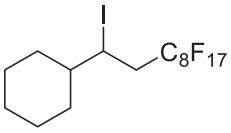
Scheme 99: Electrocatalytic iodoperfluoroalkylation of vinylcyclohexane (**158**) under non-dry condition.

After successfully identifying suitable conditions for the iodoperfluoroalkylation of vinylcyclohexane (**158**) with nonafluoro-1-iodobutane, the perfluoroiodoalkanes were varied next (Table 11). Satisfyingly, comparable yields were achieved for perfluorobutyl product **159**, perfluorohexyl product **172** and perfluorooctyl product **173** (Entry 2-4). Only the yield of trifluoromethylated product **174** was considerable lower with 64%, which is explainable by its gaseous nature and lower concentration in solution.

Table 11: Yield of product after performing the perfluoroalkylation of vinylcyclohexane (**158**) varying the perfluoroalkyl iodide.



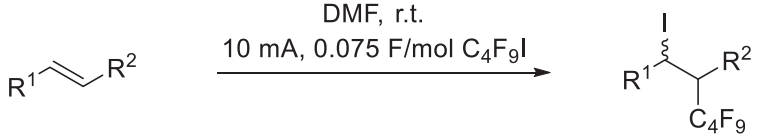
158

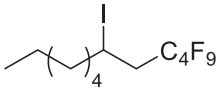
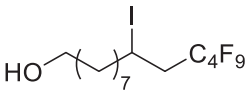
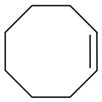
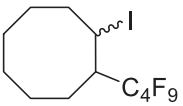
Entry	R_FI	Product	Compound No.	Yield [%]
1	CF_3I[a]		**174**	64
2	C_4F_9I		**159**	86
3	$C_6F_{13}I$		**172**	87
4	$C_8F_{17}I$		**173**	86

[a]excess CF_3I; 0.15 F/mol alkene, 4 hours

The next objective was the exploration of the substrate scope. To rule out that the reaction is only feasible for highly electron-rich substrates such as vinylcyclohexane, the existing protocol was first applied to a selected number of substrates (Table 12). The reaction of 1-octene with nonafluoro-1-iodobutane afforded iodoperfluoroalkylated product **175** in a good yield (Entry 1). Gratifyingly, the reaction tolerated also a hydroxy group and iodoperfluoroalkylated product **176** was isolated in a yield of 74% (Entry 2). However, the conversion of cyclooctene was minimal and iodoperfluoroalkylated product **177** was isolated in poor yield as a mixture of diastereomers (*d.r.*:78:22, Entry 3).

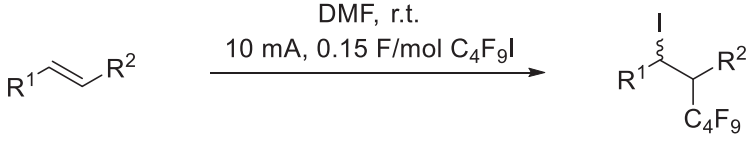
Table 12: Yield of product after performing the perfluoroalkylation of various alkenes.

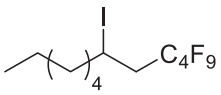
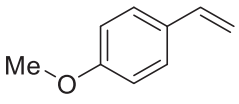
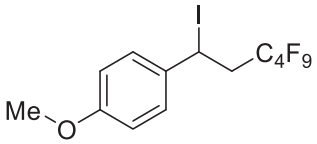
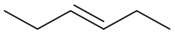
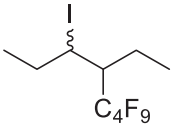
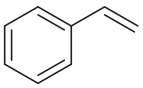
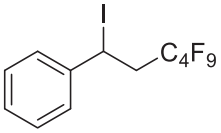


Entry	Substrate	Product	Compound No.	Yield [%]
1			**175**	70
2			**176**	74
3			**177**	18 (*d.r.*:78:22)

Compared to the iodoperfluoroalkylation of vinylcyclohexane, all isolated yields were considerably lower. As the substrates are not as electron-rich, the chain propagation could be slower. Therefore, the reaction was carried out until 0.15 F/mol C_4F_9I were consumed (Table 13). This lead to an increase in yield to 83% for product **175** resulting from the reaction of 1-octene (Entry 1). Furthermore, 4-allylanisole was successfully converted into product **178** (Entry 2). However, the yield of product **179** from the transformation of *trans*-hex-3-en as an internal alkene was still very low (Entry 3). Moreover, following the reaction of styrene with nonafluoro-1-iodobutane no product **180** was detected by ^{19}F NMR spectroscopy. These first attempts for the iodoperfluoroalkylation of alkenes demonstrated that the reaction is in general feasible for a variety of substrates. However, the reaction conditions needed to be improved further to achieve higher yields.

Table 13: Yield of product after performing the iodoperfluoroalkylation of various alkenes.

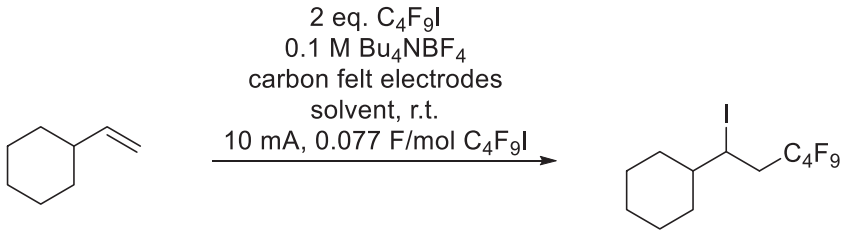


Entry	Substrate	Product	Compound No.	Yield [%]
1			**175**	83
2			**178**	69
3			**179**	16 (*d.r.*:55:45)
4[a]			**180**	Ntd

[a]0.30 F/mol C_4F_9I

As a consequence, the reaction was performed in several polar and nonpolar solvents (Table 14). All tested solvents provided good isolated yields with one exception being benzene. The best result was achieved with dichloromethane, but the product showed an unusual yellow colour, which could not be removed (Entry 4). The beneficial effects of using hexafluoroisopropanol as a solvent for electrosynthetic reactions have been previously reported.[34, 35, 173, 174] Hexafluoroisopropanol is praised for its ability to stabilise radical cations and promoting the formation of radicals.[175-178] Furthermore, fluorinated alcohols are very stable towards oxidation.[179] Therefore, the reaction was also attempted using HFIP as solvent (Entry 5).

Table 14: Yield of product **159** after performing the iodoperfluoroalkylation of vinylcyclohexane (**158**) in different solvents.



158 **159**

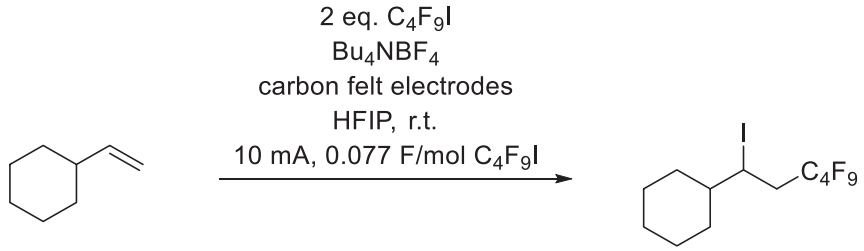
Entry	Solvent	Yield [%]
1	DMF	86
2[a]	THF	83
3	CH_2Cl_2	87
4	HFIP	83
5[a]	MeCn	84
6[b]	Benzene	-

[a]0.21 M Bu_4NBF_4

[b]substrate and supporting electrolyte not miscible; no current

The iodoperfluoroalkylation of vinylcyclohexane in hexafluoroisopropanol showed a very high conversion and selectivity. With a supporting electrolyte concentration of 0.1 M the yield was slightly lower compared to the performance in *N*,*N*-dimethylformamide. However, an increase of supporting electrolyte to 0.21 M achieved a yield of 89% (Table 15). Furthermore, the flash column chromatography of the crude product seemed to be unnecessary. Indeed, a short filtration through a plug of silica for the removal of remaining salts provided the product in 97% yield.

Table 15: Yield of product **159** after performing the perfluoroalkylation of vinylcyclohexane (**158**) in hexafluoroisopropanol varying the supporting electrolyte concentration and the purification process.



158 **159**

Entry	Bu_4NBF_4 [M]	Purification process	Yield [%]
1	0.10	Filtration & Flash column chromatography	83
2	0.21	Filtration & Flash column chromatography	89
3	0.21	Filtration	97

The cyclic voltammogram of nonafluoro-1-iodobutane in hexafluoroisopropanol and tetrabutylammonium tetrafluoroborate (0.2 M) as supporting electrolyte is presented in Figure 7. The reduction potential is -1.65 V vs. Ag/AgCl.

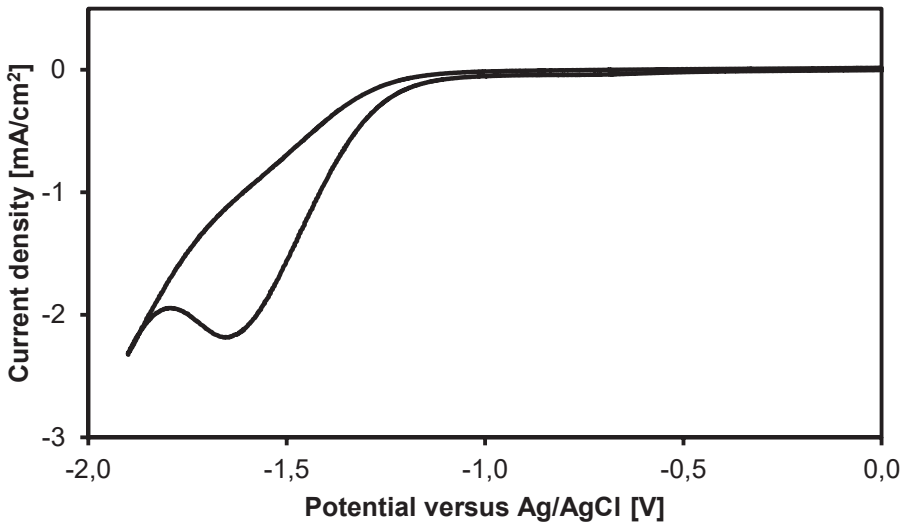


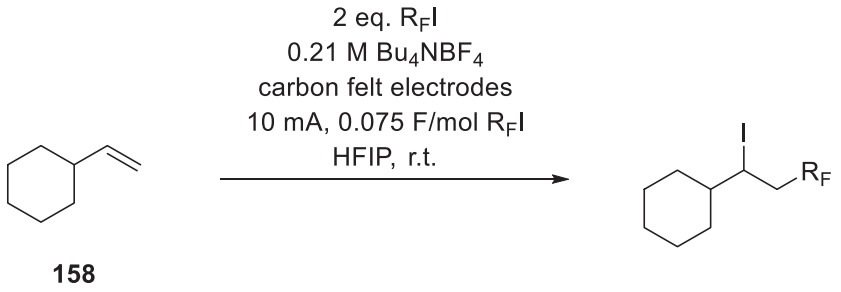
Figure 7: Cyclic voltammogram of nonafluoro-1-iodobutane in HFIP/Bu_4NBF_4 at a glassy carbon electrode.

After successfully identifying the ideal reaction conditions for the conversion of vinylcyclohexane into the iodoperfluoroalkylated product, the next objective was a thorough investigation of the substrate scope.

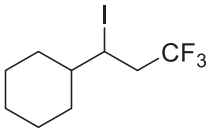
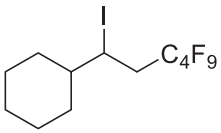
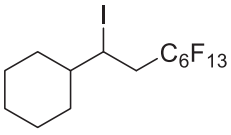
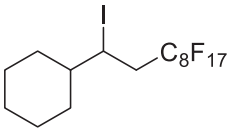
5.2.3 Investigation of the Substrate Scope

The electrocatalytic addition of nonafluoro-1-iodobutane to vinylcyclohexane was successfully optimised. With the optimal conditions for the iodoperfluoroalkylation at hand, a thorough investigation of both reaction partners will be performed next. Accordingly, the addition of perfluoroiodoalkanes with various chain lengths to vinylcyclohexane was carried out (Table 16). Excellent yields were achieved using perfluorobutyl-, perfluorohexyl- and perfluorooctyl iodide (Entries 2-4). An exception was the addition of trifluoromethyl iodide, which was reacted longer (8 hours) and still gave a significantly lower yield (Entry 1). This could be attributed to its volatility.

Table 16: Yield of products after performing the perfluoroalkylation of vinylcyclohexane (**158**) in HFIP varying the perfluoroiodoalkane.



158

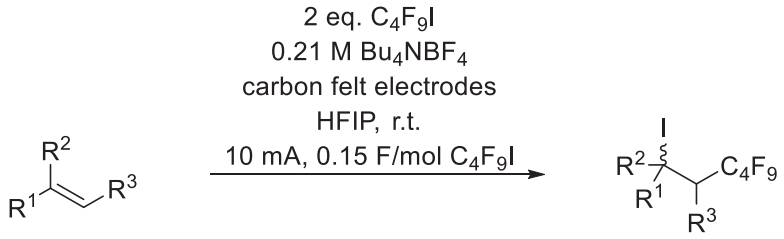
Entry	R_FI	Product	Compound No.	Yield [%]
1	CF_3I[a]		**174**	59
2	C_4F_9I		**159**	97
3	$C_6F_{13}I$		**172**	95
4	$C_8F_{17}I$		**173**	92

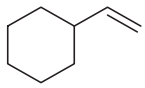
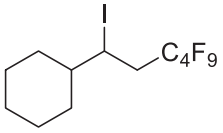
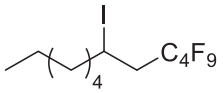
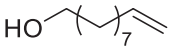
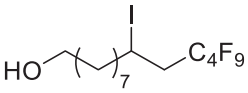
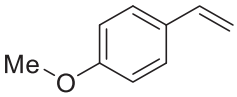
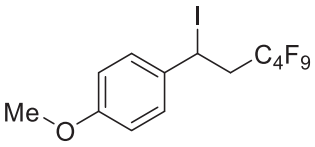
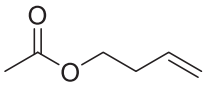
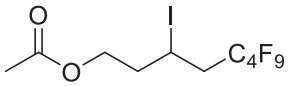
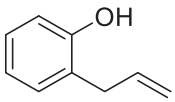
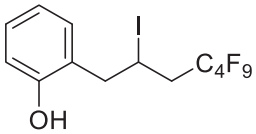
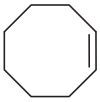
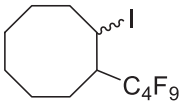
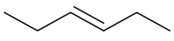
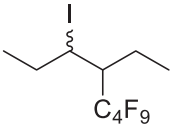
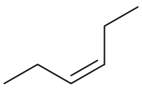
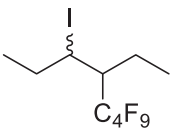
[a]excess CF_3I; 0.30 F/mol alkene

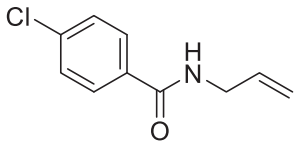
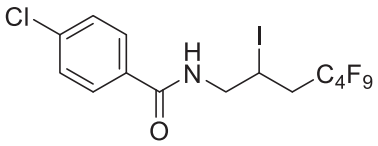
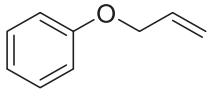
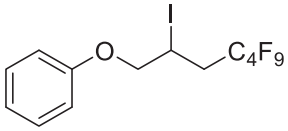
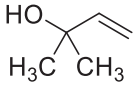
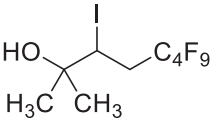
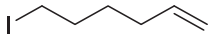
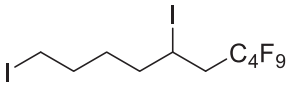
The next objective was the examination of the substrate scope and the functional group tolerance of the reaction. Accordingly, the addition of nonafluoro-1-iodobutane

to a diverse set of alkenes was executed (Table 17). Since the conversion of less electron-rich substrates into the iodoperfluoroalkylated products were incomplete applying only 0.075 F/mol C_4F_9I, the reaction time was doubled (8 hours). The electrocatalytic iodoperfluoroalkylations were performed in a 10 mmol scale. The protocol is suitable for both terminal and internal alkenes. The 1,2-addition products from the reaction of terminal olefins are formed in complete regioselectivity. Various functional groups such as alcohols, esters and ethers are tolerated and the addition products formed in good to excellent yields (Entries 3-5). In the case of internal alkenes four equivalents of nonafluoro-1-iodobutane were used. Independent of the *cis*- or *trans*-configuration of hex-3-ene, iodoperfluoroalkylated product **179** was synthesized in moderate yield and poor diastereoselectivity (Entries 8 and 9). The successful transformation of the (*E*)-3-hexene is especially noteworthy as it is an unsuitable substrate for the FLP-catalysed iodoperfluoroalkylation.[167] Furthermore, the electrocatalytic reaction even achieved the conversion of 2-allylphenol into product **181**, which is likewise impossible with both the FLP-catalysed and also the photosynthetic method developed in our group (Entry 6). The conversion of a cyclic substrate afforded the corresponding product **177** in a diastereoselectivity of 3:1 (Entry 7). Good yields were achieved for product **182** from the transformation of an aromatic amide, which also does not work with FLP catalysis (Entry 10). The reaction of allyl phenyl ether afforded iodoperfluoroalkylated product **183** in excellent yield (Entry 11). The reaction of 2-methyl-3-buten-2-ol (**101**) was also successful, as only iodoperfluoroalkylated product **103** was isolated in a yield of 71% (lit. 58%) (Entry 12).[125] Even halides are tolerated and 1,2-addition product **184** from the reaction of 6-iodo-1-hexene was isolated in good yield (Entry 13).

Table 17: Yield of products after performing the iodoperfluoroalkylation with nonafluoro-1-iodobutane of a variety of alkenes in 10 mmol scale.



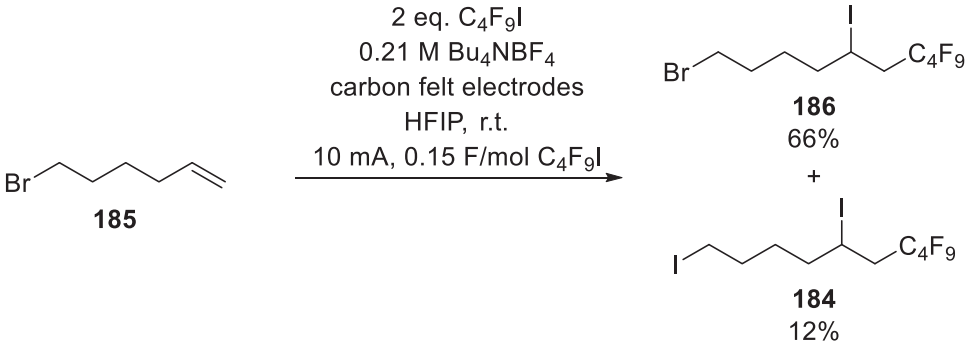
Entry	Substrate	Product	Compound No.	Yield [%]
1[a]			**159**	97
2			**175**	92
3			**176**	93
4			**178**	83
5			**170**	76
6			**181**	61
7[b]			**177**	79 (*d.r.*:55:45)
8[b]	 *trans*		**179**	60 (*d.r.*:62:38)
9[b]	 *cis*		**179**	64 (*d.r.*:58:42)

10			**182**	76
11			**183**	90
12			**103**	71
13			**184**	77

[a]0.075 F/mol C_4F_9I

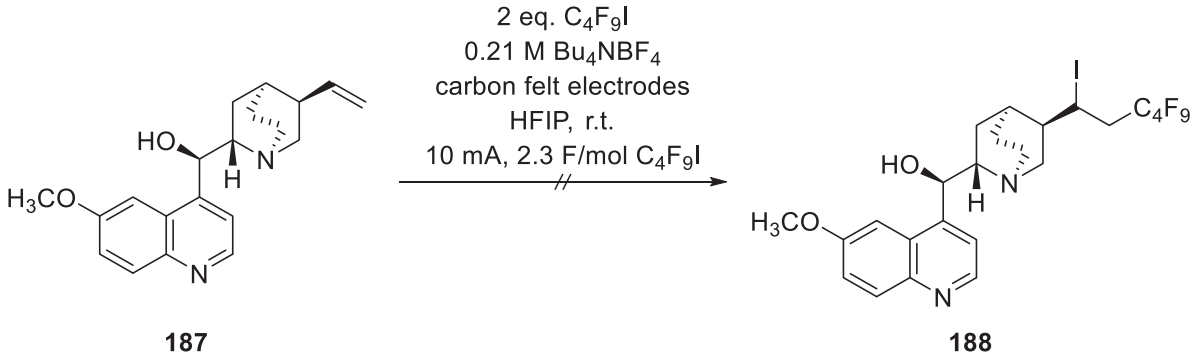
[b]4 eq. of C_4F_9I

The developed electrocatalytic iodoperfluoroalkylation has however some limitations. Purification of the crude material from the reaction of 6-bromo-1-hexene (**185**) afforded brominated iodoperfluoro product **186** in conjunction with the iodinated product **184** (Scheme 100). The iodide formed at the cathode promotes the halogen exchange in a Finkelstein-type fashion.[180]



Scheme 100: Electrocatalytic iodoperfluoroalkylation of 6-bromo-1-hexene (**185**).

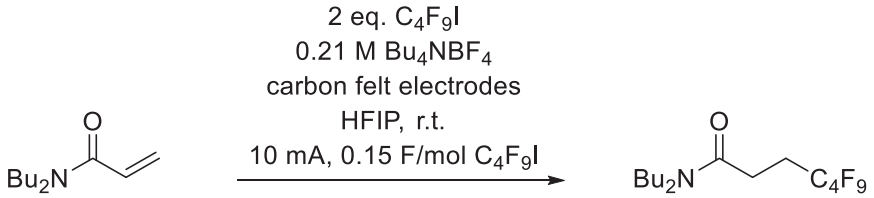
The conversion of quinine **187** as a sterically more demanding alkene into the corresponding product **188** was unsuccessful (Scheme 101). A reason for that might be the low solubility of the substrate in the solvent/supporting electrolyte system.



187 **188**

Scheme 101: Attempted electrocatalytic iodoperfluoroalkylation of quinine **187**.

The attempted electrocatalytic iodoperfluoroalkylation of acrylamide **142** only resulted in the formation of hydroperfluoroalkylated product **145** in a poor yield of 13% (Scheme 102). The hydrogen atom might thereby derive from the tetrabutylammonium ion.[125, 163] Compared to the reaction time of 8 days (<4.0 F/mol C_4F_9I), which was needed to afford 21% of product **145** under previously described conditions (see chapter 5.1.2), catalytic amounts of electrons achieved more than half as much yield in only 8 hours.



142 **145** 13%

Scheme 102: Attempted electrocatalytic iodoperfluoroalkylation of acrylamide **142**.

To gain a better understanding of the different outcomes of the acrylamide reaction in comparison to vinylcyclohexane, cyclic voltammograms were recorded for the corresponding iodoperfluoroalkylated products (Figure 8). Indeed, iodoperfluoroalkylated amide **146** has reduction potentials at -1.29 V and -1.76 V vs. Ag/AgCl whereas the reduction potential of iodoperfluoroalkylated cyclohexane **159** is at -2.11 V vs. Ag/AgCl. This shows that the iodoperfluoroalkylated product from the reaction of acrylamide is more easily reduced and explains why the hydroperfluoroalkylated amide is formed as the main product.

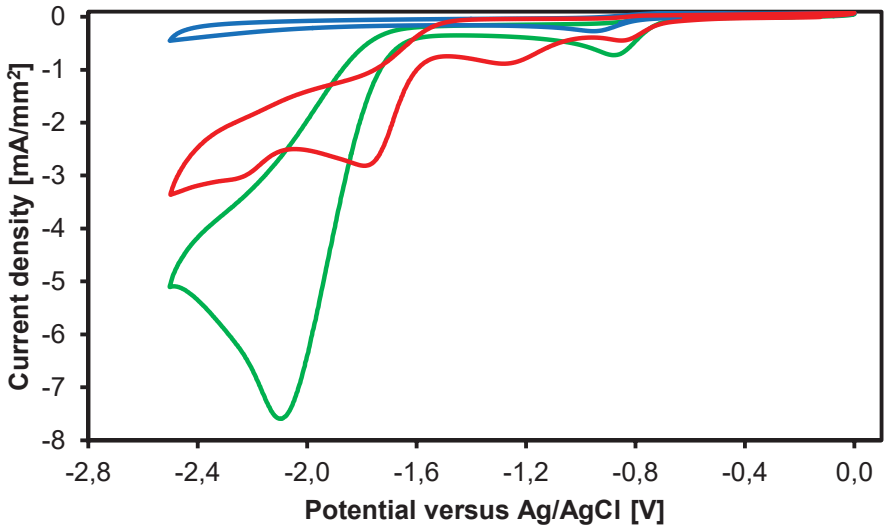
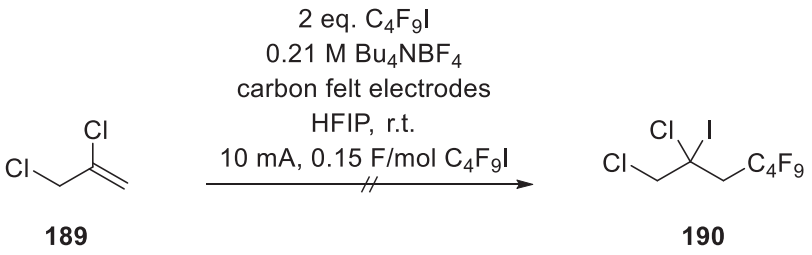


Figure 8: Cyclic voltammogram of (3,3,4,4,5,5,6,6,6-nonafluoro-1-iodohexyl)cyclohexane (**159**) (green), *N*,*N*-dibutyl-4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptanamide (**146**) (red) and electrolyte (blue) in DMF/Bu_4NBF_4 at a glassy carbon electrode.

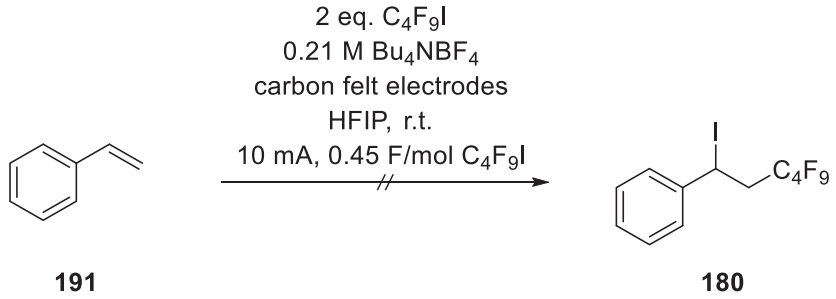
To verify that electron-deficient alkenes are in general not suitable as substrates for the developed conditions, the reaction was also attempted with 2,3-dichloropropene (**189**) (Scheme 103). Analysis of the crude material by ^{19}F NMR spectroscopy revealed no traces of product **190**.



189 **190**

Scheme 103: Attempted electrocatalytic iodoperfluoroalkylation of 2,3-dichloropropene (**189**).

Finally, the conversion of styrene (**191)** into 1,2-addition product **180** was attempted again under the optimised conditions (Scheme 104). Unfortunately, no product formation was observed by ^{19}F NMR analysis of the crude material. The rubbery consistence of the obtained material might suggest that a polymerisation has taken place instead. Another problem might be the high stability of the produced benzylic radical.[181]



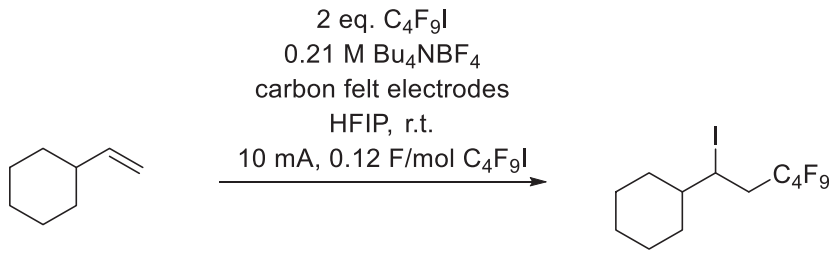
191 **180**

Scheme 104: Attempted electrocatalytic iodoperfluoroalkylation of styrene (**191**).

The developed protocol successfully achieved the electrocatalytic iodoperfluoroalkylation of a diverse set of alkenes in moderate to excellent yields. Limitations of the method are the conversion of electron-deficient substrates and styrene. The reaction was performed with a high alkene concentration on a 10 mmol scale. Next was the exploration of the scalability of the reaction.

5.2.4 Large Scale Transformation

After successful application of the developed protocol to a variety of substrates, the next objective was an examination of the scalability of the process. Therefore, vinylcyclohexane (**158**) was converted into iodoperfluoroalkylated product **159** on a 30 mmol scale in an H-type cell with a larger volume (Scheme 105). Purification of the crude material by filtration through a pad of silica afforded 13.0 g of the product in a yield of 95%. This result was very pleasing as it proves that the process is scalable and still produces excellent yields.

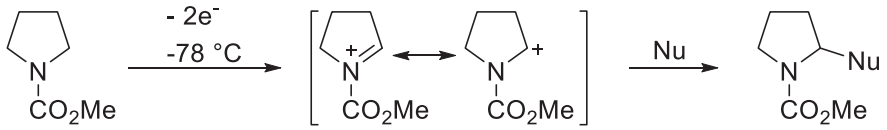


158 **159**
95%
13.0 g

Scheme 105: Electrocatalytic iodoperfluoroalkylation of vinylcyclohexane (**158**) on a 30.0 mmol scale.

5.3 Perfluoroalkylation of *N*-acyliminium Ion Pool

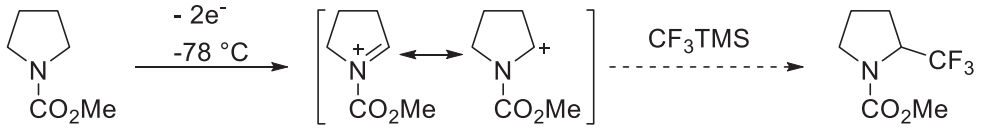
An alternative route to achieve perfluoroalkylation could be provided by the cation pool method which was invented by Yoshida *et al*.[28] Thereby, pyrrolidine **192** is electrochemically oxidized to *N*-acyliminium ion **193** (Scheme 106).[182] The cationic reaction intermediate accumulates in solution and is afterwards trapped by a nucleophile to provide a variety of products **194**. Successful application of the iminium cation pool method was proven by Yoshida and Suga *et al*., who trapped the iminium intermediate successfully with various nucleophiles such as allylsilanes, enol silyl ethers and enol acetates.[28]



192 **193** **194**

Scheme 106: Nucleophilic trapping following accumulation of a cation pool.[182]

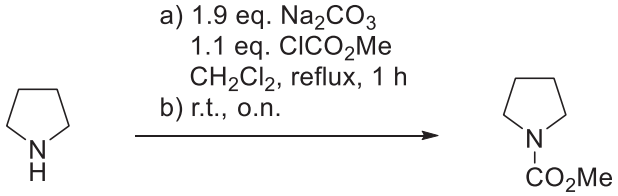
The right choice of nucleophile could provide a new method for the trifluoromethylation or perfluoroalkylation of the N-acyliminium ion pool. Nucleophilic trapping by trifluoromethyltrimethylsilane could afford the trifluoromethylated product **195** (Scheme 107).



192 **193** **195**

Scheme 107: Perfluoroalkylation following cation pool method.

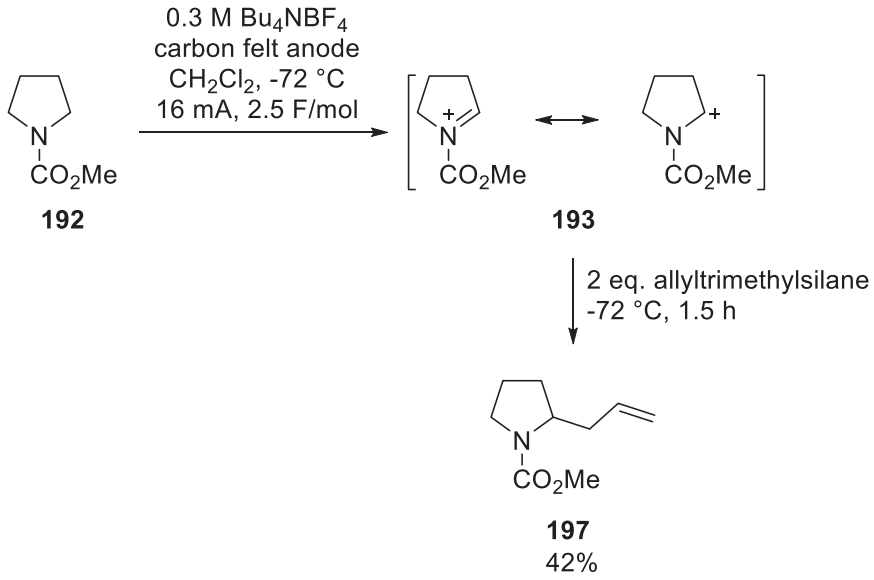
N-Carbomethoxypyrrolidine (**192**) was prepared according to the procedure of Tsubata *et al*. from pyrrolidine (**196**) (Scheme 108).[183] Following distillation, the product was isolated in a yield of 89% (lit. 90-92%).



196 **192** 89%

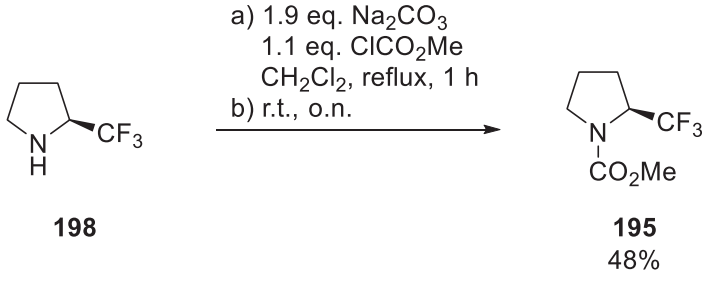
Scheme 108: Synthesis of *N*-carbomethoxypyrrolidine (**192**).

Unfortunately, the exact carbon felt material utilised by Yoshida *et al.* was unavailable to purchase. Therefore, the reaction was first attempted with allyltrimethylsilane following the conditions of Yoshida *et al*. to assure that the reaction is generally feasible with the alternatively purchased carbon felt material (Scheme 109).[28] The oxidation was performed in a divided cell using tetrabutylammonium tetrafluoroborate as supporting electrolyte in dichloromethane. Trifluoromethanesulfonic acid was used as sacrificial substrate and was reduced on the platinum anode. The constant current electrolysis (16 mA) was performed at -72 °C until 2.5 F/mol were consumed. The reaction was successful and the product **197** isolated in 42% yield (lit. 82%).



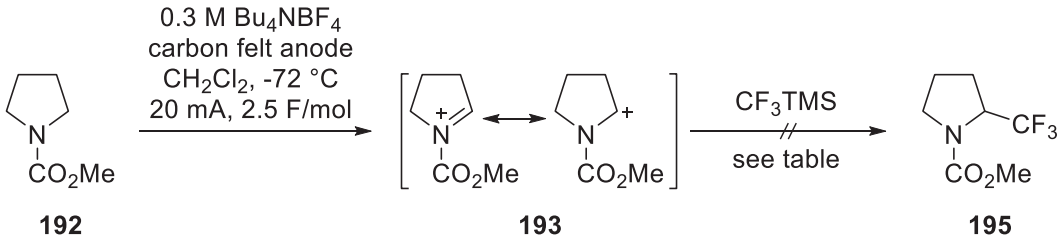
Scheme 109: Oxidative carbon bond formation following the cation pool method with allyltrimethylsilane.

The trifluoromethylated carbamate **195** was prepared according to the procedure of Tsubata *et al*. from 2(*S*)-trifluoromethylpyrrolidine (**198**) as a reference for the electrochemical attempts (Scheme 107).[183] The product was isolated by flash column chromatography in moderate yield (48%).



Scheme 110: Synthesis of trifluoromethyl carbamate **195**.

Trifluoromethylation was first attempted by substitution of allyltrimethylsilane with trifluoromethyltrimethylsilane (Scheme 111). The oxidative step was performed in a divided cell using a carbon felt anode under constant current conditions. After 2.5 F/mol were consumed, the nucleophile was added to the mixture. The addition of trifluoromethyltrimethylsilane was attempted with different initiators (Table 18). Unfortunately, no conversion of trifluoromethyltrimethylsilane into product **195** was observed.



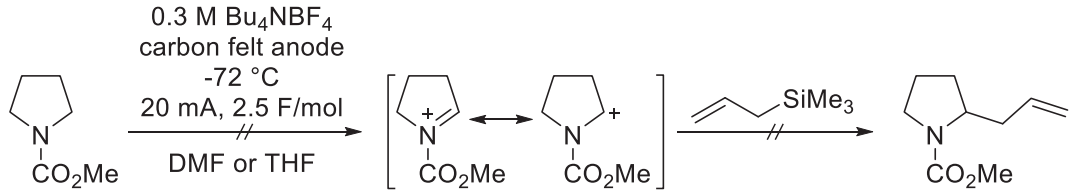
192 **193** **195**

Scheme 111: Attempted perfluoroalkylation following the cation pool method using trifluoromethyl TMS.

Table 18: Attempted one-pot synthesis by adding CF_3TMS (2.1 eq.) and initiator to the reaction at different temperatures.

Initiator	Temperature [°C]	Yield 195 [%]
None	-72	-
TBAF	-72	-
TBAF	-20	-
CsF / HF-pyridine	-72	-

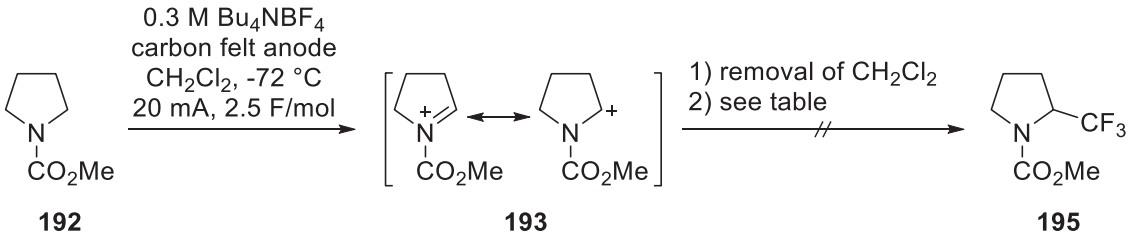
The one-pot strategy did not provide any conversion into the trifluoromethylated product. The reason for that could be that dichloromethane is an unsuitable solvent for the desilylation of trifluoromethyl TMS. Potentially, the cationic pool formation is also feasible with a different solvent. To prove that hypothesis, the reaction was also attempted using *N*,*N*-dimethylformamide and tetrahydrofuran as solvents (Scheme 112). After the cationic pool was formed, allyltrimethylsilane was added. However, no product was isolated in either case.



Scheme 112: Oxidative carbon bond formation following the cation pool method with allyltrimethylsilane in *N*,*N*-dimethylformamide or tetrahydrofuran.

Therefore, the reaction mixture was transferred into a second flask after accumulation of the cationic pool (2.5 F/mol were applied) and dichloromethane was removed under reduced pressure. Afterwards, various solvents and initiators were added in conjunction with trifluoromethyltrimethylsilane. The applied conditions are presented in Table 19. The use of anhydrous sodium acetate as initiators resulted in a conversion of CF_3TMS. However, upon attempted purification by flash column chromatography no product was isolated. Therefore, the reaction was repeated with anhydrous sodium acetate, which was additionally dried in the vacuum oven. No product was isolated in this case either.

Table 19: Conditions for the attempted trifluoromethylation using CF_3TMS with appropriate equivalents, initiators, temperatures and solvents.



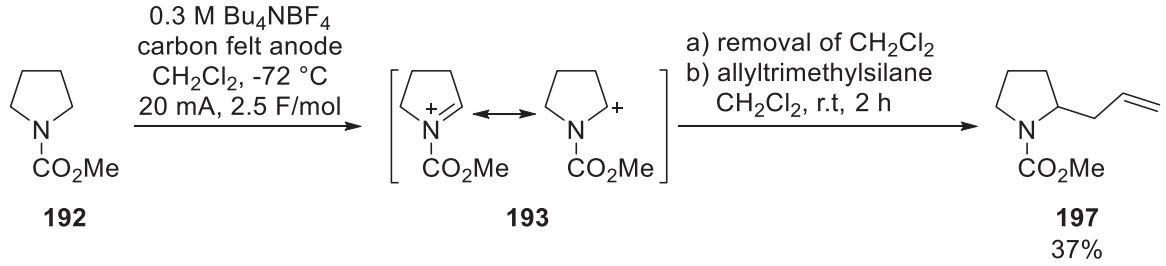
CF_3TMS [eq.]	Initiator	Initiator [eq.]	Temperature [°C]	Solvent	Yield 195 [%]
1.3	TBAT	1.2	-55	THF	-
1.5	NaOAc	2	r.t.	DMF	-
3	NaOAc[a]	4	r.t.	DMF	-
3	KF[a]	4	r.t.	DMF	-
3	NaOAc[b]	4	r.t.	DMF	-
3[c]	NaOAc[b]	4	r.t.	DMF	-

[a]dried in vacuum oven 150 °C

[b]dried in vacuum oven 200 °C

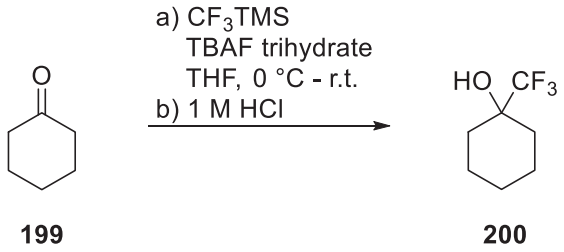
[c]addition of trifluoromethylated cyclohexane as internal fluorine standard

To prove that the cationic pool withstands the removal of the solvent, the reaction was repeated with the known addition of allyltrimethylsilane.[28] Again, the reaction mixture was transferred into a second flask after 2.5 F/mol were applied and dichloromethane was removed under reduced pressure. Afterwards allyltrimethylsilane and dichloromethane were added (Scheme 113). The product **197** was isolated in 37% yield. Compared to the yield of 42% achieved following literature procedure, only a small decrease is noticeable. Therefore, it can be assumed, that this proves that the cationic pool is still intact before addition of further reagents.



Scheme 113: Oxidative carbon bond formation following the cation pool method with allyltrimethylsilane after removal of dichloromethane.

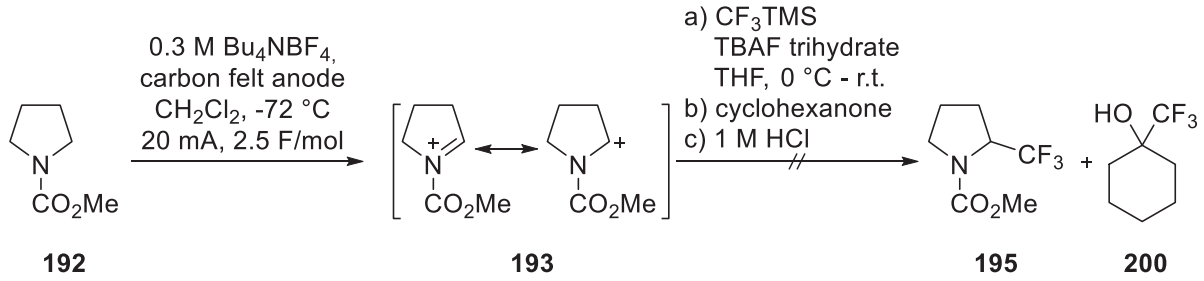
To verify that there is no problem with the trifluoromethyltrimethylsilane as trifluoromethylating reagent, cyclohexanone **199** was transformed into product **200** according to the procedure by Prakash *et al*.[52] This reaction was performed successfully, which demonstrates that the used chemicals are in working order.



Scheme 114: Trifluoromethylation of cyclohexanone.

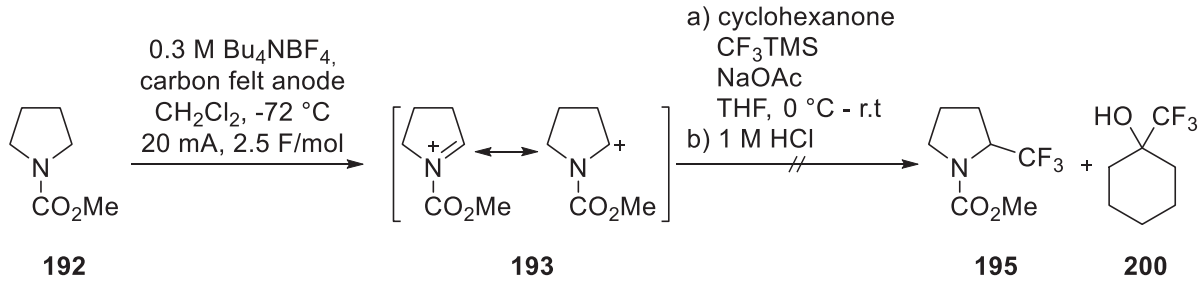
However, when the trifluoromethylation of cyclohexanone was performed using a mixture of dichloromethane and tetrahydrofuran (1:1) the formation of a side product was observed by ^{19}F NMR spectroscopy. This leads to the conclusion, that the recess of dichloromethane might change the course of the trifluoromethylation of the cationic pool. For that reason, tetrahydrofuran, trifluoromethyltrimethylsilane and tetrabutylammonium fluoride trihydrate were added, after the evaporation of dichloromethane (Scheme 115). The reaction was stirred overnight and cyclohexanone was added. The analysis of the crude mixture revealed no

trifluoromethylated products of either substrate. Since not even trifluoromethylated cyclohexanone was found indicates, that something is interfering with the aspired reaction.



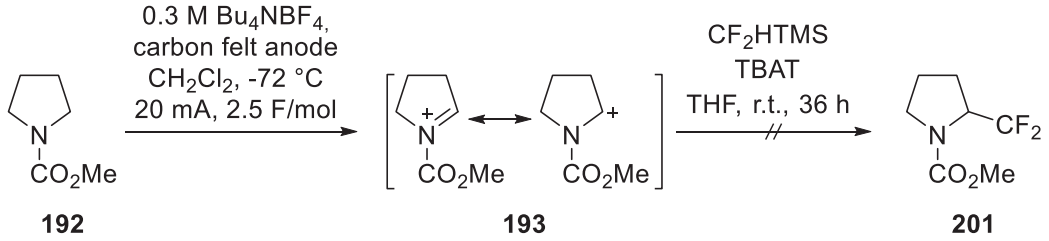
Scheme 115: Attempted perfluoroalkylation following the cation pool method using trifluoromethyltrimethylsilane.

This approach was attempted again using anhydrous sodium acetate as initiator and immediate addition of cyclohexanone after removal of dichloromethane (Scheme 116). However, also in this case no fluorinated product was identified.



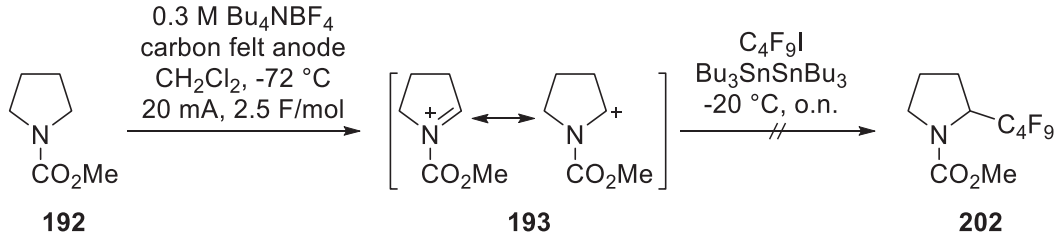
Scheme 116: Attempted perfluoroalkylation following the cation pool method using trifluoromethyltrimethylsilane.

As the trifluoromethylation was not feasible, difluoromethylation was attempted due to the different sterics. Accordingly, tetrahydrofuran, TBAT and difluoromethyltrimethylsilane were added to the cationic pool after removal of dichloromethane (Scheme 117). However, no product **201** was isolated after purification with flash column chromatography.



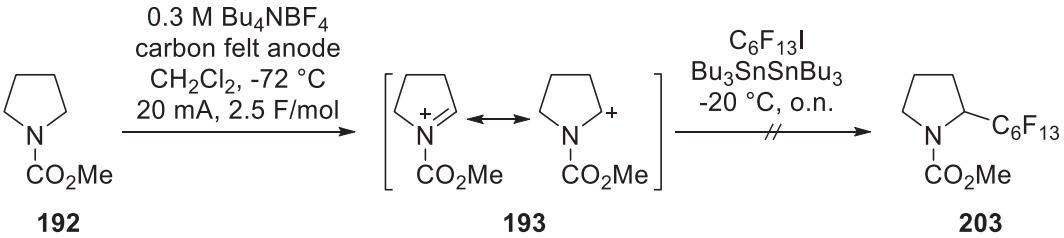
Scheme 117: Attempted perfluoroalkylation following the cation pool method using difluoromethyl TMS.

As the attempts of perfluoroalkylation with trifluoromethyltrimethylsilane were unsuccessful, a different approach was chosen. Yoshida *et al.* demonstrated the coupling of the cation pool intermediate with alkyl iodides using distannane.[184] Therefore, the perfluoroalkylation of the *N*-acyliminium ion pool was attempted using nonafluoro-1-iodobutane and hexabutylditin (Scheme 118). However, no product **202** was isolated upon reaction.



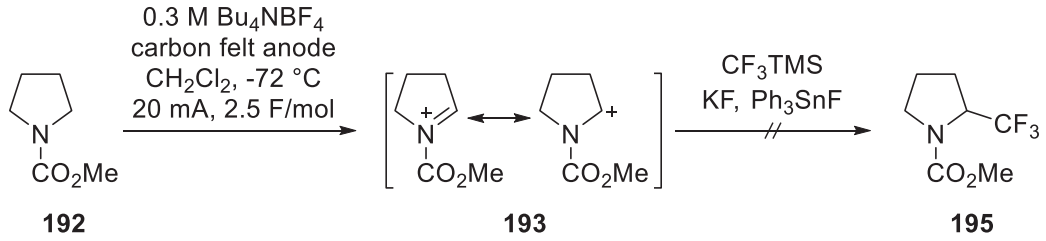
Scheme 118: Attempted perfluoroalkylation following the cation pool method using nonfluoro-1-iodobutane and hexabutylditin.

Perfluoroalkylation was also attempted using a longer perfluoroalkylated chain as also mainly longer alkyl chains (*e.g.* $C_7H_{15}I$) were utilised in the literature.[184] However, upon reaction with perfluorohexyl iodide and hexabutylditin only a complicated mixture was observed by analysis of the crude mixture with ^{19}F NMR spectroscopy and no product **203** was identified.



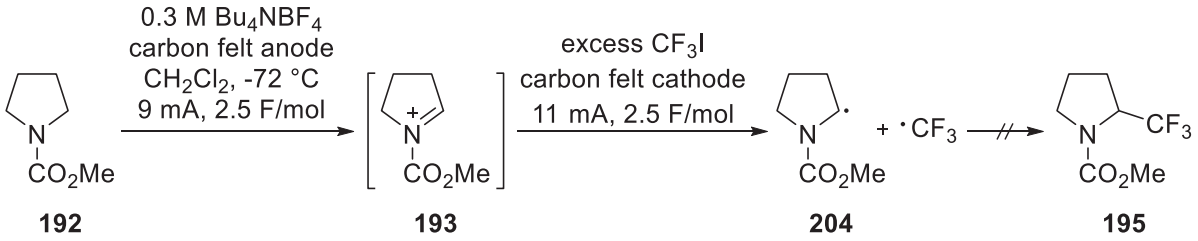
Scheme 119: Attempted perfluoroalkylation following the cation pool method using perfluorohexyl iodide and hexabutylditin.

Makosza *et al.* demonstrated the trifluoromethylation of quinolinium salts by phase transfer reactions using trifluoromethyltrimethylsilane, potassium fluoride (solid) and triphenyltin fluoride as catalyst.[185] After the cationic pool was formed following the procedure of Yoshida *et al.*, trifluoromethylation was attempted as a phase transfer reaction according to Makosza. However, no product was identified upon analysis of the crude mixture by ^{19}F NMR spectroscopy.



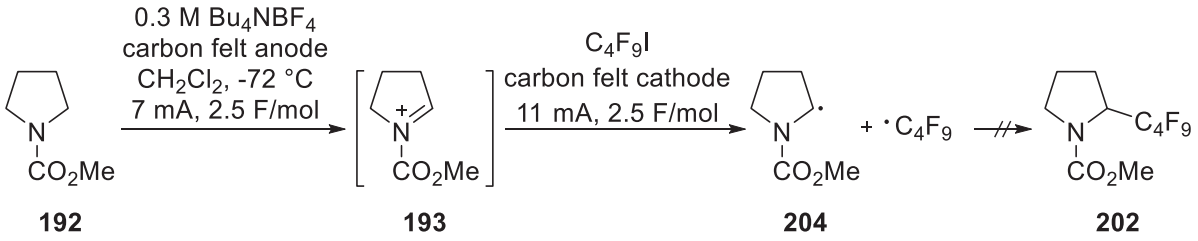
Scheme 120: Attempted trifluoromethylation following the cation pool method and phase transfer reaction with triphenyltin fluoride.

Yoshida *et al.* demonstrated the reduction of the cationic pool and reaction of the formed radical intermediate **204** with alkene bonds.[186] The same approach was attempted to achieve perfluoroalkylation. After the cationic pool was formed, trifluoromethyl iodide gas was let into the reaction and the reduction was performed according to literature (Scheme 121). The platinum cathode was switched to a graphite anode and tetrahydrofuran was added as sacrificial substrate. The constant current electrolysis (11 mA) was performed until 2.5 F/mol were applied. However, no product formation was observed.



Scheme 121: Attempted trifluoromethylation following reduction of the cation pool method using CF_3I.

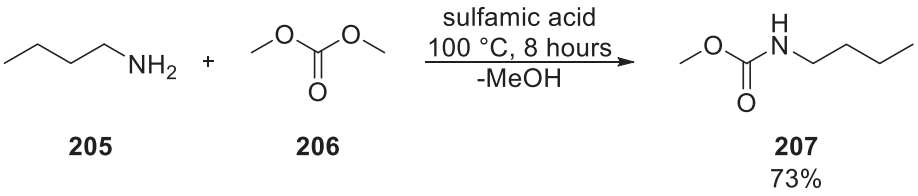
As the addition of a gas can provide some problems, the reaction was also attempted using nonafluoro-1-iodobutane (Scheme 122). Nevertheless, no product was identified by analysis of the crude mixture by ^{19}F NMR spectroscopy.



Scheme 122: Attempted perfluoroalkylation following reduction of the cation pool method using C_4F_9I.

To rule out that steric reasons prevent the attack of the perfluoroalkyl radical or anion, a sterically less hindered substrate was needed. The first step towards that purpose was the reaction of butylamine **205** and dimethyl carbonate **206** with

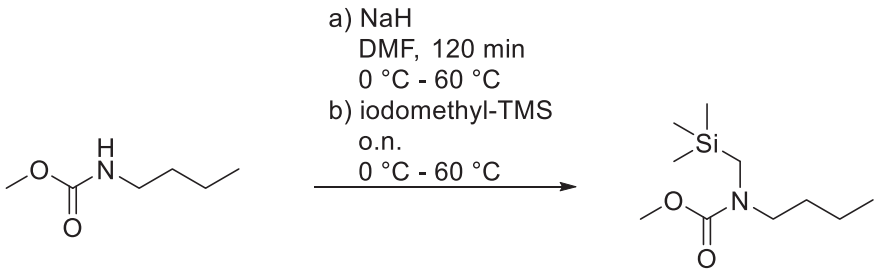
sulfamic acid towards carbamate **207** (Scheme 123). After two filtrations the product **207** was isolated in a yield of 73%.[187]



205 **206** **207**
73%

Scheme 123: Synthesis of carbamate **207**.

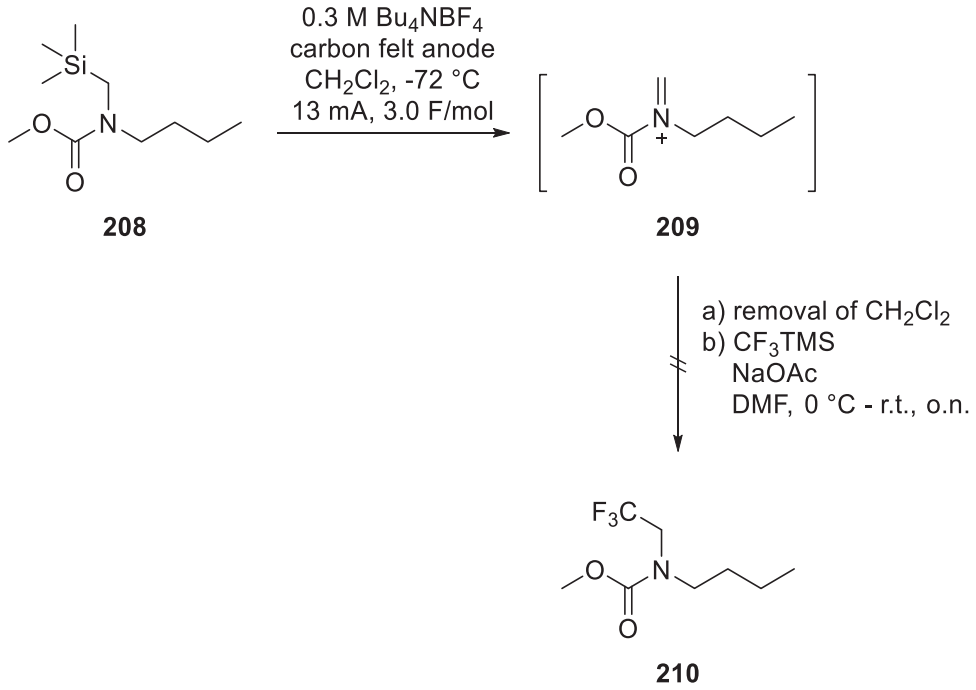
The next step was the reaction of carbamate **207** with iodomethyl TMS and sodium hydride towards trimethylsilyl carbamate **208** providing a new, sterically less hindered substrate for trifluoromethylation (Scheme 124).[188]



207 **208**
6%

Scheme 124: Synthesis of carbamate **208**.

The iminium ion pool **209** was generated following the procedure of Yoshida *et al*. (Scheme 125).[188] The constant current electrolysis (13 mA) was carried out until 3.0 F/mol were applied. The trifluoromethylation was attempted with trifluoromethyltrimethylsilane and sodium acetate in DMF. Analysis of the reaction mixture by ^{19}F NMR spectroscopy revealed no traces of product **210**. This gives rise to the assumption, that the problems of the trifluoromethylation are not related to steric hindrance of the iminium ion.

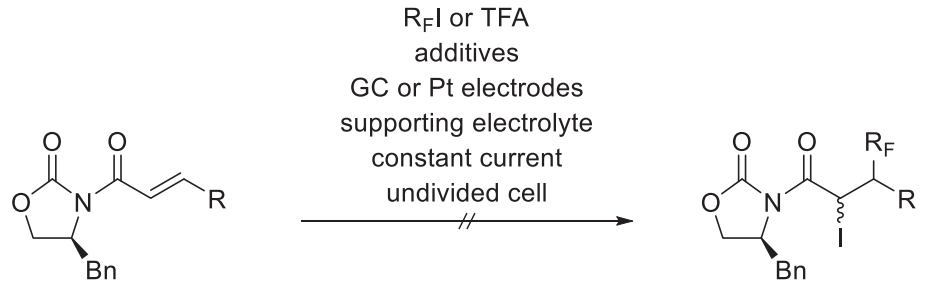


Scheme 125: Attempted trifluoromethylation following the cation pool method using trifluoromethyltrimethylsilane with sodium acetate as initiator.

The failures of the trifluoromethylation and perfluoroalkylation of the iminium ion pools were unfortunate. None of the attempts resulted in the formation of the desired products. A combination of trifluoromethyltrimethylsilane and an initiator proved ineffective. Problems might thereby arise from the residual dichloromethane or other molecules contained in the solution, which might prevent the reaction. A reductive approach utilising perfluoroalkyl iodides or the combination of those with distannane proved to be unsuccessful. Switching from pyrrolidine to a sterically less demanding substrate resulted in no different reaction outcome.

6 Conclusion and Outlook

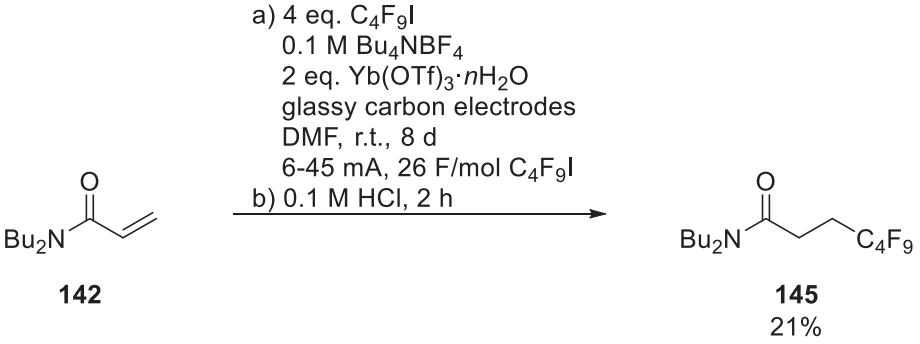
This work aimed to develop a novel method for the electrochemically perfluoroalkylation of olefins. This report has highlighted both progress and setbacks encountered in the efforts towards a more economically appealing introduction of fluoroalkyl moieties based on perfluoroalkyl iodides. Preliminary trials for a diastereoselective version were conducted with Evans-auxiliary derivatives. The perfluoroalkylation of these compounds was previously demonstrated by Czekelius and Erdbrink *et al*. using Et_3B/O_2 as radical initiator.[83-85, 147] This procedure has some drawbacks, namely, the use of 27 equivalents of perfluoroalkylation reagent and 15 equivalents of triethylborane. The literature-known hydroperfluoroalkylation of acrylic acid derivative **125** afforded product **126** in 2.0% yield (lit. 13-27%). Attempts for the electrochemical perfluoroalkylation of oxazolidinone **125** with nonafluoro-1-iodobutane were unsuccessful (Scheme 126). No different outcome was achieved for the attempted perfluoroalkylation of crotonic acid derivative **127** employing perfluoroiodoalkanes or trifluoroacetic acid. Finally, the electrochemical trifluoromethylation of nitrile **140** was conducted following a literature known protocol that utilises trifluoroacetic acid as trifluoromethylating reagent, but no product formation was observed.[189] Problems could thereby arise from the electron deficient nature of the *N*-acyloxazolidinones.



Scheme 126: Attempted electrochemical perfluoroalkylation of *N*-acyloxazolidinones.

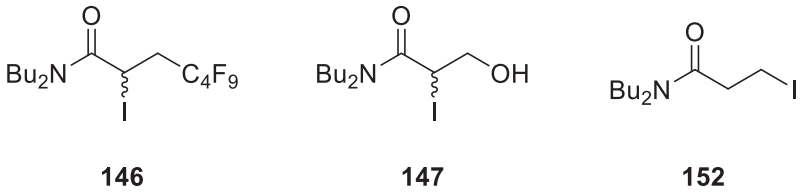
Next, *N*,*N*-dibutylacrylamide (**142**) was chosen as substrate. The electrochemical perfluoroalkylation was first conducted in *N*,*N*-dimethylformamide as suggested by Commeyras *et al.* and acetonitrile following Uneyama *et al.*[103, 125, 126] The better result was achieved with the former solvent. Platinum or glassy carbon electrodes were both tested. The reaction was performed with 0.1 M tetrabutylammonium

tetrafluoroborate as electrolyte and $Yb(OTf)_3$ hydrate as Lewis acid. The conditions for the highest achieved yield of 21% for hydroperfluoroalkylated product **145** are depicted in Scheme 127. Nonafluoro-1-iodobutane was used as perfluoroalkylating reagent on glassy carbon electrodes. Due to the slow conversion of the substrate the current was increased during the course of the reaction.



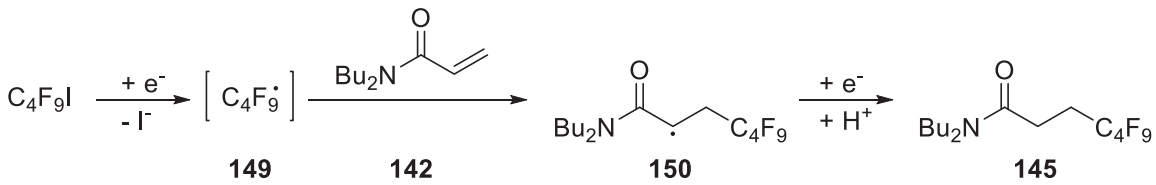
Scheme 127: Electrochemical hydroperfluoroalkylation of acrylamide **142**.

Next to the hydroperfluoroalkylated product, three side products were identified, iodoperfluoroalkylated compound **146**, iodohydroxylated compound **147** and iodinated compound **152** (Scheme 128).



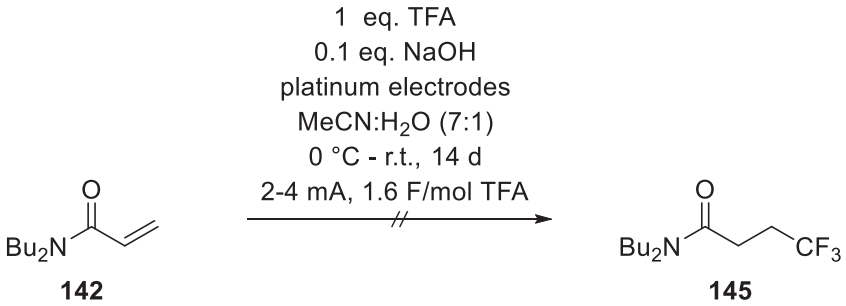
Scheme 128: Identified iodinated side products.

The proposed mechanism for the electrosynthetic hydroperfluoroalkylation is initiated by the reduction of the perfluorobutyl iodide to perfluorobutyl radical **149** and iodide, which can be oxidized at the anode to from iodine (Scheme 129). The perfluorobutyl radical **149** is trapped by acrylamide **142** followed by a reduction of the formed radical intermediate **150** to afford hydroperfluoroalkylated product **145**. Another option could be the reduction of iodoperfluoroalkylated side product **146**.



Scheme 129: Proposed mechanism for the hydroperfluoroalkylation of acrylamide **142**.

The origin of the hydrogen for the formation of hydroperfluoroalkylated product **145** is not intuitive. One option could be a hydrogen transfer from the tetrabutylammonium ion.[125, 163] Therefore, 1,4-cyclohexadiene was tested as hydrogen donor using trifluorocyclohexane as internal fluorine standard. Perfluoroalkylation was performed without $Yb(OTf)_3$ hydrate to prevent hydrogen donation from water. However, for both glassy carbon and copper electrodes lower yields were achieved. Further attempts for optimising the reaction with lithium chloride as both Lewis acid and supporting electrode, varying the electrode material and the perfluoroiodoalkane or conduction as potentiostatic experiment were unsuccessful. The trifluoromethylation of *N*,*N*-dibutylacrylamide (**142**) was further attempted as an anodic process using trifluoroacetic acid following the procedures of Uneyama *et al.*[102] The reaction was conducted in MeCN:H_2O (7:1) using sodium hydroxide as supporting electrolyte on platinum electrodes (Scheme 130). Unfortunately, the reaction afforded only an inseparable mixture.

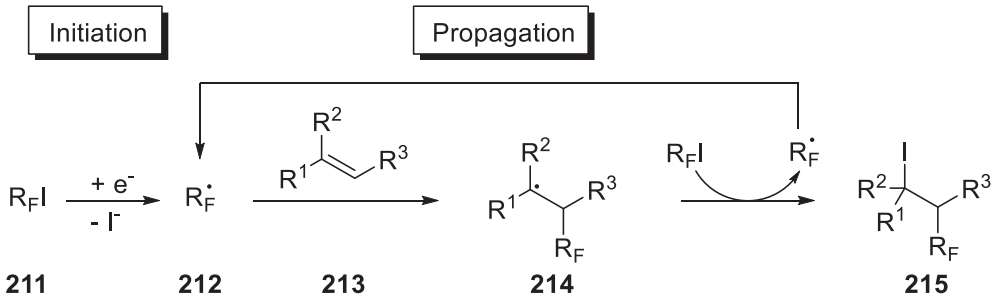


Scheme 130: Attempted electrosynthetic trifluoromethylation of acrylamide **142** using TFA.

Perfluoroalkylation was also attempted indirectly using a nickel(II)-catalyst as mediator following the procedures of Budnikova *et al*.[46, 164] Reaction with 10 mol% of the $NiBr_2$bpy in DMF on platinum nets resulted only in traces of product **145**, detected by TLC and ^{19}F NMR spectroscopy. Furthermore, indirect trifluoromethylation of acrylamide **142** was investigated with TfNHNHBoc as trifluoromethylation reagent using ferrocene as mediator, which resulted in no product formation.[165] A reason for the low conversion of acrylamide **142** into hydroperfluoroalkylated product could be the electron-deficient double-bond.

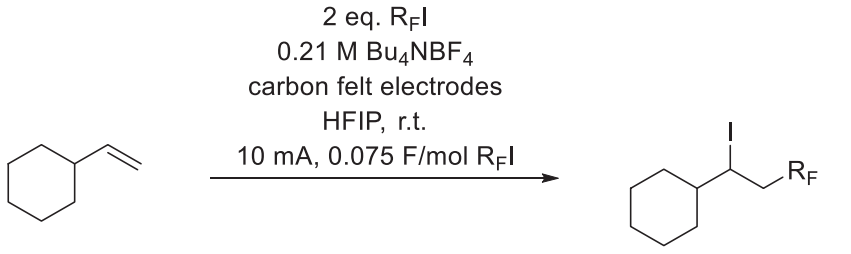
Preliminary trials for the electrocatalytic iodoperfluoroalkylation led to the identification of vinylcyclohexane as a suitable substrate. The reaction was optimised by using nonafluoro-1-iodobutane as perfluoroalkylating reagent. An extensive screening of various reaction conditions such as applied current, electrode material,

supporting electrolytes, equivalents of nonafluoro-1-iodobutane and solvent was conducted. Performance of the reaction in hexafluoroisopropanol with a constant current of 10 mA on carbon felt electrodes afforded iodoperfluoroalkylated product in 97% yield (Scheme 132). The developed protocol has many advantages, the reagent proceeds under metal- and catalyst-free conditions with catalytic amounts of electrons as sole reagent. A proposal for the mechanism is presented in Scheme 131. Reduction of the carbon-iodine bond of iodoperfluoroalkane **211** initiates the reaction by producing perfluoroalkyl radical **212**, which is then trapped by alkene **213**. The abstraction of iodine from another iodoperfluoroalkane by radical intermediate **214** affords the iodoperfluoroalkylated product **215** and perfluoroalkyl radical **212**, which is needed for successful chain propagation.



Scheme 131: Proposed mechanism for the electrocatalytic iodoperfluoroalkylation.

With the optimised conditions at hand a thorough investigation of the substrate scope was performed. Excellent yields were achieved for iodoperfluorohexyl and iodoperfluorooctyl products **172** and **173**. The reaction with trifluoromethyl iodide afforded the corresponding product **174** in 59% yield, which can be reasoned by its volatility. The yield of the electrocatalytic trifluoromethylation could be increased by performing the reaction as a flow reaction. Thereby, the amount of trifluoromethyl iodide gas could be more easily controlled and consequently also the applied charge per atom. The combination of electrochemistry with a flow process to achieve perfluoroalkylation was exemplified by Wirth *et al*.[105]

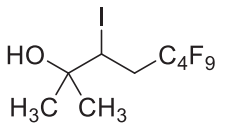


158

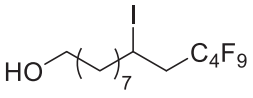
$R_F = CF_3$ **174**, 59%[a]
$R_F = C_4F_9$ **159**, 97%
$R_F = C_6F_{13}$ **172**, 95%
$R_F = C_8F_{17}$ **173**, 92%

Scheme 132: Electrocatalytic iodoperfluoroalkylation of vinylcyclohexane (**158**) with 1-iodoperfluoroalkanes in various chain length. [a]0.30 F/mol alkene

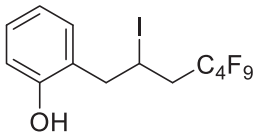
The developed protocol accepts a broad range of substrates. Alcohols, amides, esters, halides and ethers were successfully converted into the 1,2-addition products in complete regioselectivity (Scheme 133). Furthermore, the electrocatalytic transformation was also achieved for 2-allylphenol and *N*-allyl-4-chlorobenzamide, which are unsuitable substrates for the FLP-catalysed reaction developed in our group.[167]



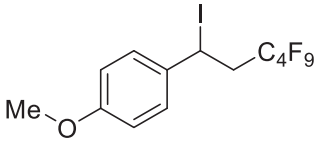
103
71%



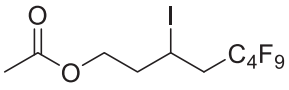
176
89%



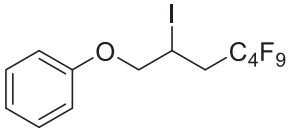
181
61%



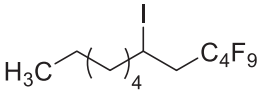
178
83%



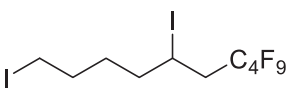
170
76%



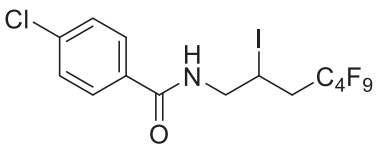
183
90%



175
92%



179
77%



182
76%

Scheme 133: Iodoperfluoroalkylated products from the reaction of heteroatom functionalised alkenes and 1-octene.

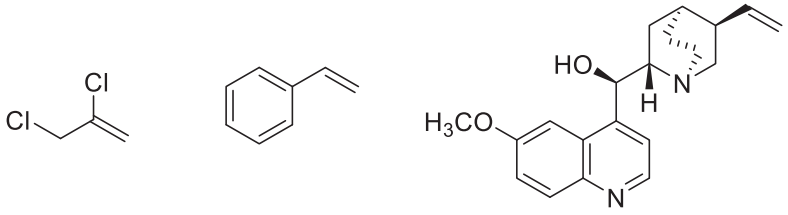
Electrocatalytic iodoperfluoroalkylation was also conducted with internal alkenes. In this case four equivalents of nonafluoro-1-iodobutane were used to increase its availability. The reaction was successful for hex-3-ene independent of its *cis*- or *trans*-configuration. Iodoperfluoroalkylated product **177** from the reaction of cyclooctene was isolated in good yield and a diastereoselectivity of 3:1.

179
from *cis*-3-hexene: 64%, d.r. 59:41
from *trans*-3-hexene: 60%, d.r. 62:38

177
79%, d.r. 75:25

Scheme 134: Iodoperfluoroalkylated products from the conversion of internal alkenes.

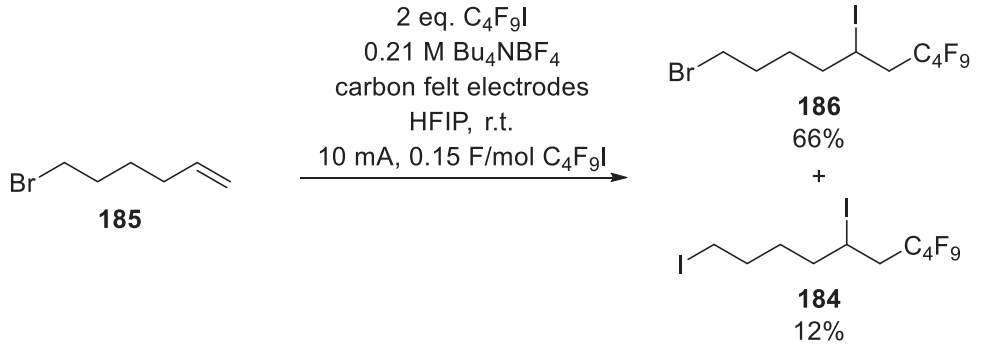
However, the developed protocol also has some limitations (Scheme 135). The conversion of 2,3-dichloropropen **189** as an electron-deficient alkene was unsuccessful. No conversion was observed for quinine **187**, which might be attributed to its low solubility in the reaction mixture. Furthermore, the reaction of styrene **191** failed, problems might thereby derive from the high stability of the benzylic radical.[181]



189 **191** **187**

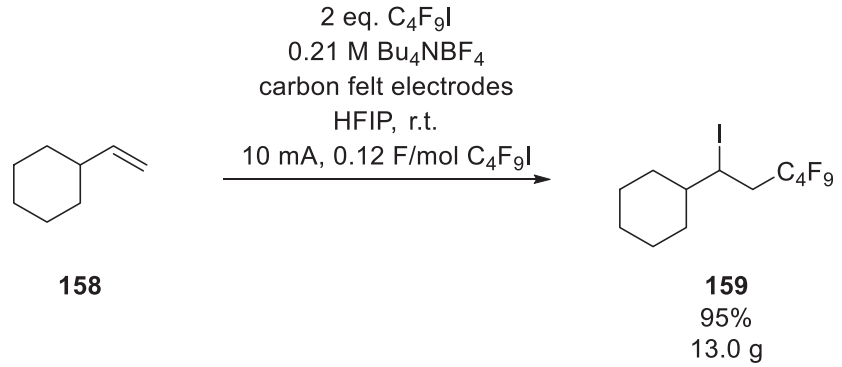
Scheme 135: Unsuccessful substrates in the electrocatalytic iodoperfluoroalkylation.

The conversion of 6-bromo-1-hexene (**185**) afforded the desired iodoperfluoroalkylated product **186** in conjunction with iodinated compound **184** (Scheme 136). Iodide, which is formed at the cathode, can thereby exchange with bromide in a S_N2-reaction.



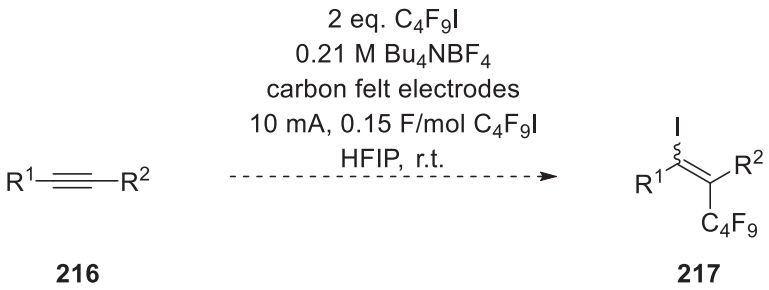
Scheme 136: Electrocatalytic iodoperfluoroalkylation of 6-bromo-1-hexene (**185**).

After examination of the substrate scope and functional group tolerance, the scalability of the process was investigated next. Vinylcyclohexane (30.0 mmol) was successfully converted into 13.0 g of iodoperfluoroalkylated product **159** in a yield of 95%.



Scheme 137: Electrocatalytic iodoperfluoroalkylation of vinylcyclohexane (**158**) in a 30.0 mmol scale.

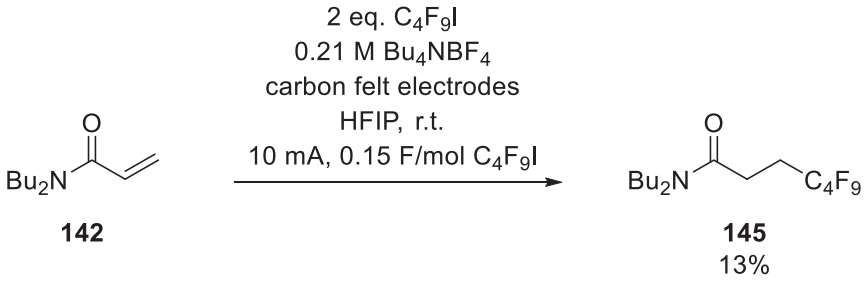
Czekelius et al demonstrated the FLP-catalysed iodoperfluoroalkylation of an internal alkyne.[86] The electrocatalytic conversion of alkynes **216** into iodoperfluoroalkylated alkenes **217** could provide an interesting new substrate class (Scheme 138).



Scheme 138: Electrocatalytic iodoperfluoroalkylation of alkynes.

The conditions for the electrocatalytic iodoperfluoroalkylation were also applied to acrylamide **142**. Catalytic amounts of electrons lead to the isolation of hydroperfluoroalkylated product **145** in 13% yield. This result provides a promising

start for a systematic study of the reaction condition for the electrochemical hydroperfluoroalkylation. If the desired product is formed by reduction of iodoperfluoroalkylated product **146**, more applied charge is needed. Therefore, the reaction time would have to be increased, which might already result in satisfying yields.

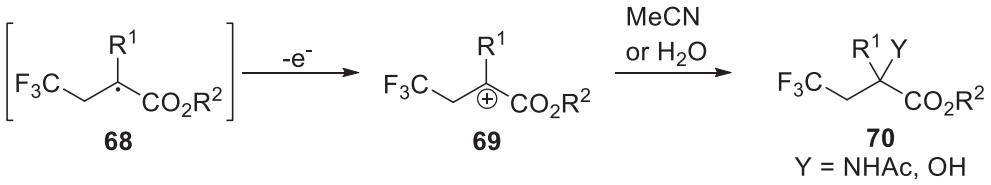


142 **145** 13%

Scheme 139: Attempted electrocatalytic iodoperfluoroalkylation of acrylamide **142**.

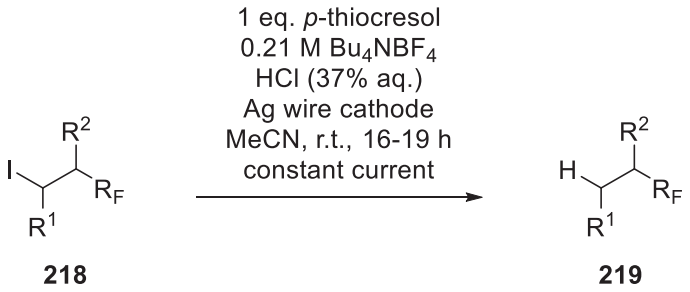
Additionally, the choice of supporting electrolyte could be further investigated. Various lithium salts such as lithium perchlorate could both provide the required conductivity as well as the Lewis acidity for the activation of the substrate. Moreover, Uneyama *et al.* showed that the generation of C_F-radicals is highly temperature-dependent.[189, 190] A temperature gradient could be run from -30 °C up to 50 °C. If this results in the identification of suitable reaction conditions for the electrosynthetic hydroperfluoroalkylation of acrylamide **142**, the development of a diastereoselective version could be approached. For that purpose Evans-auxiliary derivatives could again be examined as potential substrates. The diastereoselectivity of the reaction could be optimised testing various Lewis acids in an attempt to utilise the chelating effect by their interaction with the two carbonyl groups of the *N*-acyloxazolidinones. Additionally, the residues on the chiral auxiliary could be varied as they are known to highly influence the degree of diastereoselectivity.[71]

Further functionalisation of the products in one-pot could be exemplified by utilising nucleophiles attacking the intermediate in α-position. This was previously observed as a side reaction by Uneyama *et al.* as intermediate **68** was oxidized forming carbocation **69** which was then attacked by either water or acetonitrile to afford product **70**.[102]



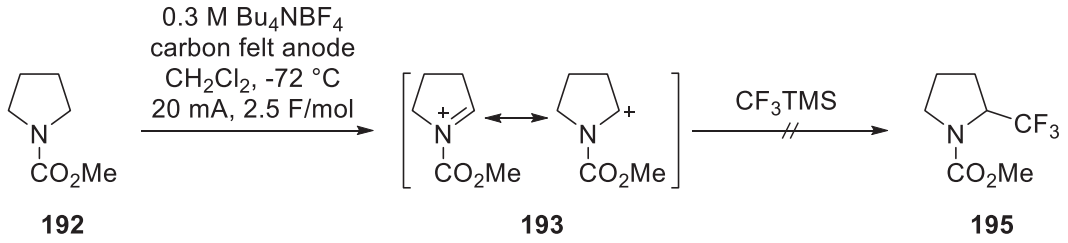
Scheme 140: Observed side reactions of the perfluoroalkylation.[102]

The hydroperfluoroalkylated products could further be obtained by electrosynthetic deiodination of the iodoperfluoroalkylated products. This approach was studied by Moritz Klischan as objective of his master thesis.[191] The developed method is depicted in Scheme 141. The conversion of iodoperfluoroalkylated compounds **218** into hydroperfluoroalkylated products **219** is accomplished by combining a thiol as hydrogen source with hydrochloric acid. The constant current experiment was conducted in a divided cell (Nafion^{TM}) using a silver wire cathode. First promising results were achieved for the development of a one-pot-synthesis starting from alkenes.



Scheme 141: Electrosynthetic deiodination of iodoperfluoroalkylated products.

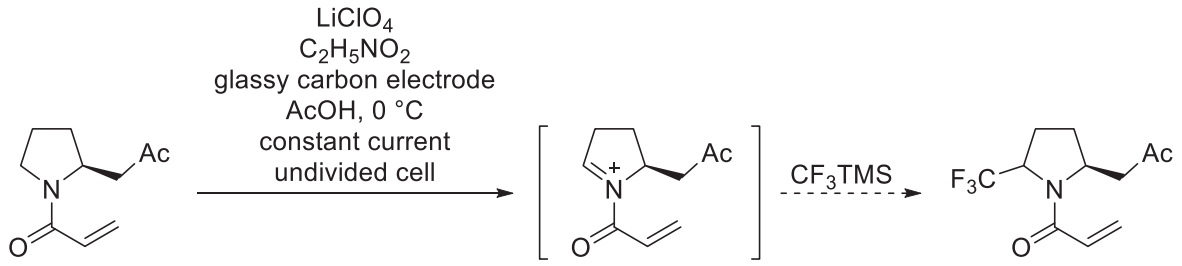
Next, the cation pool method invented by Yoshida *et al.* was used to perform a perfluoroalkylation of the iminium ion intermediate.[28, 182] The oxidation of carbamate **192** results in the accumulation of cationic intermediate **193**. However, all trifluoromethylation attempts using trifluoromethyltrimethylsilane in addition with various initiators and different solvents in either an one-pot or two step synthesis were unsuccessful (Scheme 142). The problem with the solubility of the initiators might be overcome by using a phase transfer catalyst. Therefore, the perfluoroalkylation was conducted with trifluoromethyltrimethylsilane, potassium fluoride (solid) and Ph_3SnF as a phase transfer catalyst.[192] Unfortunately, no product was formed. Further attempts using perfluoroalkyl iodides or a sterically-less demanding substrate were unsuccessful.[184, 186, 188]



192 **193** **195**

Scheme 142: Attempted perfluoroalkylation following cation pool method.

A new approach could be the indirect cation pool method; hereby, an active reagent is accumulated electrochemically.[193] The reaction with a cation precursor leads to the generation of a cation pool, which can then react with a nucleophile. Perfluoroalkylation could be attempted with this more stabilised cation pool. Furthermore, proline derivative **220** could provide a new substrate for further studies. Its anodic oxidation can be carried out at 0 °C in an undivided cell (Scheme 143).[194] The supporting electrolyte/ solvent system or the substrate properties lead to higher stability of the cationic intermediate.[29] The trifluoromethylation of *N*-acyliminium ion **221** to product **222** could be attempted with a combination of the Prakash-reagent and an appropriate initiator.



210 **211** **212**

Scheme 143: Trifluoromethylation of *N*-acyliminium ion **221**.[194]

7 Experimental

7.1 Materials and Equipment

7.1.1 Glassware and Chemicals

The glassware and the magnetic stir bars for reactions under inert conditions were stored at 115 °C overnight before use. Chemicals were ordered from *Sigma-Aldrich*, *Apollo Scientific*, *Tokyo Chemical Industries* (*TCI*), *Alfa Aesar GmbH & Co KG, Carbolution Chemicals GmbH* or *Fluorochem*. Unless stated otherwise, chemicals were used without further purification. *N*,*N*-Dimethylformamide and hexafluoroisopropanol were dried using activated molecular sieve (4 Å). THF and CH_2Cl_2 were dried using the Solvent Purification System MB-SPS-800 manufactured by *M. BRAUN INERTGAS-SYSTEME GmbH*. All other solvents were bought in pure form or freed from water and contamination according to established procedures.[195]

7.1.2 Software

NMR-analysis was performed with *MestReNova* software. The tables and graphs were made with *Microsoft Excel 2010*. The structures were drawn with *ChemBioDraw Ultra 14.0*. The software used for recording cyclic voltammograms was *NOVA 2.1*.

7.1.3 Laboratory Devices

TRIVAC D4B by *Leybold GmbH* was used as rotary vane pump. Reactants and products were weighed with the analytic balance AE 163 by *Mettler Toledo*. Sonication was performed with the ultrasonic cleaning unit T310 by *Elma Schmidbauer GmbH*. The evaporation of solvents was conducted with rotavapor R-210 by *Büchi Labortechnik GmbH*. The used vacuum drying oven *Kelvitron*® was manufactured by *Thermo Electron LED GmbH*.

Galvanostatic electrolysis was conducted using either a CPX400D & DP by *Aim Thurlby Thandar Instruments* (*Aim-TTi*) (Voltage range: 0-60 V, current range: 0.01-20.00 A) or a RIGOL DP832A (Voltage range: 0-30 V, current range: 0.001-3.000 A) power supply. Potentiostatic electrolysis was conducted using a potentiostat PGSTAT204 in conjunction with Autolab Booster10A by *Metrohm AG*.

7.1.4 Electrodes

Glassy carbon, silver, copper, platinum and nickel plates and the silver wires required for attaching the electrodes were stored at 115 °C overnight before use. The electrodes were attached with crocodile clips at a silver wire in a septum, which was then further connected to the power supply. The carbon felt *Carbolon*® Graphite fabric GF-20-P21E by *Nippon Carbon Co., Ltd* was first disentangled into single fibres and then dried 2-16 hours at 200 °C at 1 mbar. The bundle was connected to the silver wire either by cable ties or using a long fibre of carbon felt. The carbon felt was disposed after use.

7.1.5 Electrochemical Cells

7.1.5.1 Undivided Cells

Next to standard three- and four- neck flasks in various sizes, specially manufactured tubes were used as undivided cell (Figure 9). The screening block with undivided Teflon cells (volume: 5 mL) was manufactured according to the procedures by Waldvogel *et al*.[196]

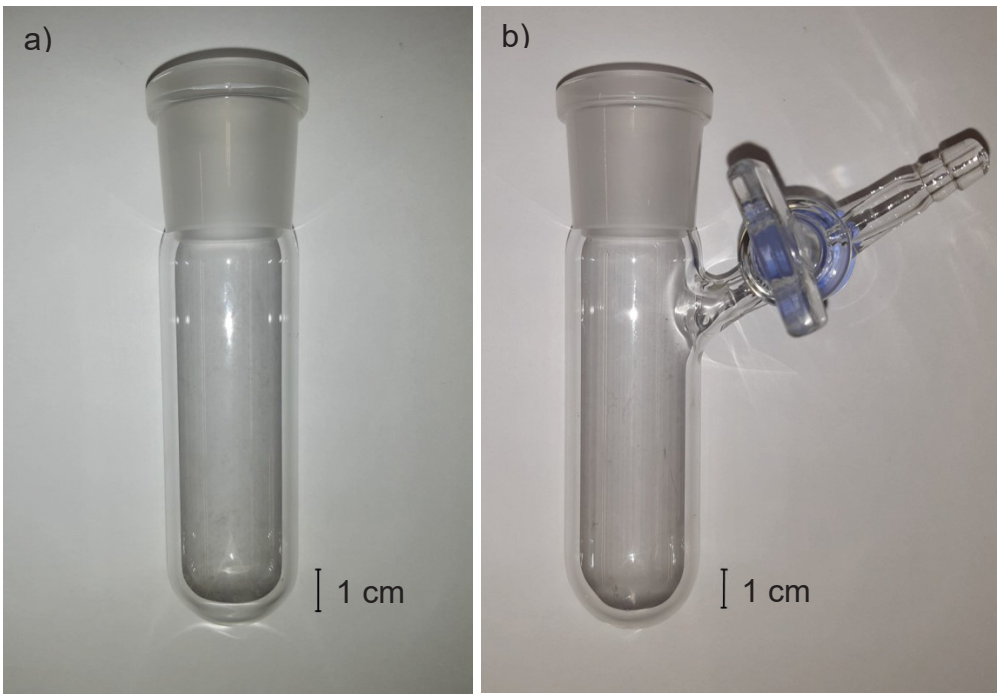


Figure 9: Picture of the undivided cell **A** as tube (a) and Schlenk tube (b).

7.1.5.2 Divided cells

The divided cells were manufactured in two sizes. Divided cell **A** was used for volumes over 15 mL and was manufactured either normally or as Schlenk vessel with a connection tube between the two compartments for pressure equalization (Figure 10). The H-type cells consist of a 4G-glass filter. Divided cell **B** was used for volumes lower than 15 mL. Similarly, it consists of a 4G-glass filter a connection tube and a side arm for evacuation or as gas inlet (Figure 11).

Figure 10: Picture of divided cell **A**, standard (a) and with Schlenk connections (b).

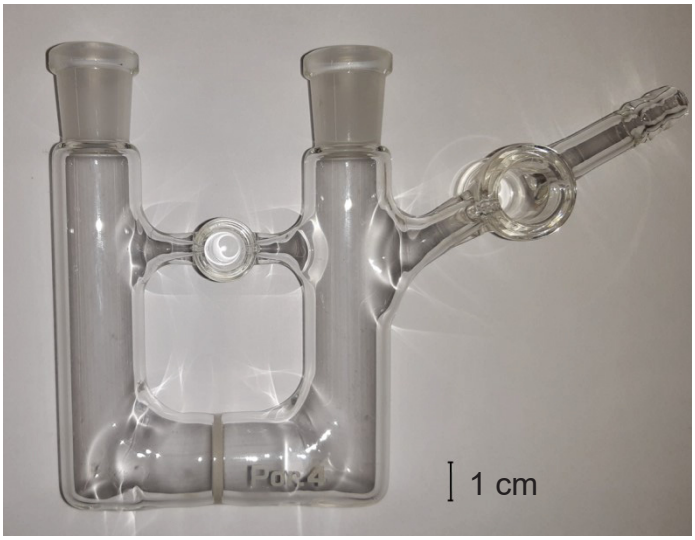


Figure 11: Picture of divided cell **B**.

7.2 Analytic Methods

7.2.1 Thin Layer and Column Chromatography

Thin layer chromatography was performed on pre-coated aluminium-backed silica gel plates (ALUGRAM® Xtra SIL G/UV254, Silica gel 60 F_{254}, thickness 0.2 mm, *Macherey-Nagel*). The detection was achieved with potassium permanganate dip (3 g potassium permanganate, 20 g potassium carbonate dissolved in 5 mL 5% aq. sodium hydroxide and 300 mL water) followed by visualisation of the spots with a hot air gun, or by UV detection at 254 nm.
Column chromatography was performed manually or with a Büchi Sepacore system with the Fraction collector C-660 using silica gel 60 (40-63 µm, *Macherey-Nagel*). Hexane, ethyl acetate and pentane were distilled before chromatography.

7.2.2 IR Spectroscopy

IR spectra were recorded on a JASCO FT/IR-6200 IR spectrometer. The assignment of the absorption bands is shown in wave numbers $\tilde{\nu}$ (cm^{-1}). The classification was reduced to the characteristic bands which could be identified.[197]

7.2.3 Mass Spectrometry

Electron Ionisation (EI) mass spectra were recorded on a Thermo. Electron Corp. FINNIGAN Trace DSQ with Finnigan Trace GC Ultra. Electron Spray Ionisation (ESI) mass spectra were recorded on a Bruker Daltonics UHR-QTOF MaXis 4G. Acetone was used as solvent.

7.2.4 NMR Spectroscopy

NMR spectra were recorded on Bruker Avance-III-300 and Bruker Avance-III-600 spectrometers. The ^{1}H, ^{13}C and ^{19}F NMR spectra were received using the deuterated solvent ($CDCl_3$ and D_2O) as lock and the residual solvent as the internal reference. The calibration was performed with the characteristic chemical shifts of 7.26 ppm for $CHCl_3$ and 4.79 ppm for H_2O for the ^{1}H NMR spectra and of 77.16 ppm for $CHCl_3$ in the ^{13}C NMR spectra. If needed for solving the structure HSQC, COSY, DEPT-135 and HMBC spectra were recorded.

The chemical shifts were indicated in ppm and the size of the coupling constant *J* in Hz. The multiplets were labelled with the conventional abbreviations shown in chapter 1.2. The assignment of the signals was performed by using the coupling constant or by appropriate 2D homo- or hetero nuclear experiments.

7.2.5 Cyclic Voltammetry (CV)

Cyclic voltammetry was performed with a potentiostat PGSTAT204 manufactured by *Metrohm AG*. All cells and electrodes were purchased from *Metrohm AG*. The electrochemical measurements were performed on a glassy carbon working electrode with a surface of 2 mm^2 and a glassy carbon or platinum counter electrode. The Ag/AgCl reference electrode was filled with a KCl-solution (3 M) for the inner filling. A solution of the salt (0.5-1 M) and solvent in which the measurement was conducted, was used for the outer filling. The measurements were performed under nitrogen atmosphere and in a volume of 10 mL. The scan rate was 100 mV/s.

7.3 Working under Inert Conditions

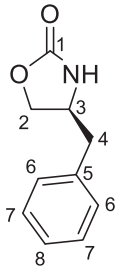
Reactions under inert conditions were realised by using Schlenk technique. A high vacuum from a rotary vane pump was applied to the reaction vessels, which were heated with a hot air gun. After cooling down, the flasks were flushed with nitrogen, which was dried over molecular sieve. This process was repeated three times using a nitrogen/vacuum Schlenk line. Electrodes were attached and solids added beforehand or under nitrogen counterflow. Liquids were added through the septum by a syringe flushed with nitrogen.

7.4 Procedures for Synthesis

7.4.1 Preparation of Substrates and Reagents

7.4.1.1 Preparation of the Evans Auxiliary

(*S*)-4-Benzyloxazolidin-2-one (**124**)



124

Prepared according to the procedure of Evans *et al*.[198]

(*S*)-Phenylalanol (2.77 g, 18.3 mmol, 1.0 eq.); anhydrous potassium carbonate (2.53 g, 18.3 mmol, 1.0 eq.) and diethyl carbonate (8.4 mL, 69.4 mmol, 3.8 eq.) were added to a dry flask fitted with a Vigreux column. The solution was heated to 125 °C and ethanol was distilled from the mixture for 4 hours. The reaction was cooled to room temperature and dichloromethane (60 mL) was added. The organic phase was washed with distilled water (2 x 25 mL), brine (25 mL), dried (Na_2SO_4) and concentrated. The crude mixture (3.34 g as yellow crystals) was purified by recrystallization with cyclohexane and toluene (1:1, 4 mL) at 140 °C. (*S*)-4-Benzyloxazolidin-2-one (2.60 g, 14.7 mmol, 80%) was isolated as white crystals.

m.p. = 85-87 °C (lit. 84.5-86.5 °C)[198]

R_f = 0.22 (50% ethyl acetate in hexane)

^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 2.81 – 2.93 (m, 2 H, 4-H), 4.05 – 4.17 (m, 2 H, 2-H), 4.39 – 4.45 (m, 1 H, 3-H), 5.96 (br. s, 1 H, N*H*), 7.15 – 7.20 (m, 2 H, 6-H), 7.24 – 7.29 (m, 1 H, 8-H), 7.30 – 7.36 (m, 2 H, 7-H).

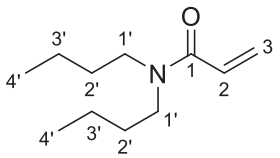
^{13}C NMR (151 MHz, chloroform-*d*):
δ [ppm] = 41.5 (C-4), 53.9 (C-3), 69.7 (C-2), 127.3 (C-8), 129.1 (C-6), 129.1 (C-7), 136.0 (C-5),

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 3283; 2919; 1750; 1604; 1406; 1362; 1244; 1064; 1027; 937; 749; 703.

The observed data is consistent with the literature.[198]

7.4.1.2 Preparation of Alkenes

***N*,*N*-Dibutylacrylamide (142)**



142

Prepared according to the procedure of Skrydstrup *et al*.[151]

Dibutylamine (1.32 mL, 7.40 mmol, 1.0 eq.) and triethylamine (1.95 mL, 14.0 mmol, 1.9 eq.) were dissolved in dichloromethane (20 mL) and the mixture was cooled to 0 °C. Acryloyl chloride (0.63 mL, 7.40 mmol, 1.0 eq.) was added dropwise and the mixture stirred at 0 °C for 2 hours and at room temperature for 18 hours. The reaction mixture was poured in water (50 mL) and extracted with dichloromethane (3 x 20 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated. The crude reaction mixture (1.39 g as an orange oil) was purified by flash column chromatography (50 g silica, 25% ethyl acetate in hexane) to afford *N*,*N*-dibutylacrylamide (**142**) as a colourless oil (925 mg, 5.05 mmol, 65%).

R_f = 0.30 (25% ethyl acetate in hexane)

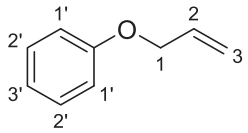
^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 0.92 (t, $^3J_{4',3'}$ = 7.3 Hz, 6 H, 4'-H), 1.31 (m_c, 4 H, 3'-H), 1.41 – 1.57 (m, 4 H, 2'-H), 3.31 (m_c, 4 H, 1'-H), 5.63 (dd, $^2J_{3a,2}$ = 10.3 Hz, $^3J_{3a,3b}$ = 2.2 Hz, 1 H, 3-H_a), 6.32 (dd, $^3J_{3b,2}$ = 16.7 Hz, $^3J_{3b,3a}$ = 2.2 Hz, 1 H, 3-H_b), 6.53 (dd, $^3J_{2,3b}$ = 16.7 Hz, $^2J_{2,3a}$ = 10.3 Hz, 1 H, 2-H).

^{13}C NMR (75 MHz, chloroform-*d*):
δ [ppm] = 13.9 and 13.9 (C-4'), 20.1 and 20.4 (C-3'), 30.0 and 31.8 (C-2'), 46.5 and 48.0 (C-1'), 127.5 (C-3), 128.0 (C-2), 166.0 (C-1).

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 3684; 3546; 2958; 2932; 2873; 1650;1612; 1455; 1428; 1374; 978; 795.

The observed data is consistent with the literature.[151]

Allyl phenyl ether



Prepared according to the procedure of Zhang *et al*.[199]

Phenol (9.41 g, 10.0 mmol, 1.0 eq.) and potassium carbonate (13.8 g, 10.0 mmol, 1.0 eq.) were added to acetone (40 mL). After heating to reflux, allyl chloride (10.0 mL, 12.0 mmol, 1.2 eq.) was slowly added and the mixture stirred for 6 hours. After filtration, the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography (150 g silica, 10% ethyl acetate in hexane). Allyl phenyl ether was isolated as a colourless oil (4.58 g, 34.1 mmol, 34%).

R_f = 0.66 (20% ethyl acetate in hexane)

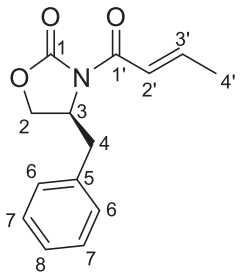
^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 4.55 – 4.60 (m, 2 H, 1-H), 5.30 – 5.36 (m, 1 H, 3-H$_a$), 5.42 – 5.52 (m, 1 H, 3-H$_b$), 6.03 – 6.19 (m, 1 H, 2-H), 6.94 – 7.03 (m, 3 H, 1'-H and 3'-H), 7.29 – 7.39 (m, 2 H, 2'-H).

The observed data is consistent with the literature.[199]

7.4.1.3 Preparation of Chiral *N*-Acyloxazolidinones

n-Butyllithium (1.6 M solution in hexanes) was titrated according to the method of Duhamel and Plaquevent.[200]

(4*S*,2'*E*)-4-Benzyl-3-(but-2'-enoyl)oxazolidin-2-one (127)



127

Prepared according to the procedure of Czekelius *et al.*[83, 147]

n-Butyllithium (3.50 mL of a 1.6 M solution in hexanes, 5.60 mmol, 1.0 eq.) was added dropwise to a solution of (*S*)-4-benzyloxazolidin-2-one (1.00 g, 5.60 mmol, 1.0 eq.) in tetrahydrofuran (16.8 mL) at -78 °C and the reaction mixture was stirred at this temperature for 30 minutes. (*E*)-Crotonyl chloride (0.59 mL, 6.16 mmol, 1.1 eq.) in tetrahydrofuran (6.20 mL) was added slowly. The yellow mixture was stirred at -78 °C for 3.5 hours and the reaction was monitored by TLC. After full conversion, the reaction was allowed to warm to room temperature and stirred at this temperature for 10 minutes. The reaction mixture was quenched with ammonium chloride (15 mL of a saturated aqueous solution). The phases were separated and the mixture was extracted with diethyl ether (4 x 20 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated. The crude product (1.47 g as a yellow solid) was purified by flash column chromatography (60 g silica, 20% ethyl acetate in hexane) to afford (*S*,*E*)-4-benzyl-3-(but-2-enoyl)oxazolidin-2-one (**127**) as a white solid (1.24 g, 5.03 mmol, 90%).

m.p. = 84-85 °C (lit. 85-86 °C)[201]

R_f = 0.37 (25% ethyl acetate in hexane)

^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 1.99 (dd, $^3J_{4',3'}$ = 6.5 Hz, $^4J_{4',2'}$ = 1.3 Hz, 3 H, 4'-H), 2.80 (dd, $^3J_{4a,4b}$ = 13.4 Hz, $^4J_{4a,3}$ = 9.5 Hz, 1 H, 4-H_a), 3.33 (dd, $^3J_{4b,4a}$ = 13.4 Hz, $^4J_{4b,3}$ = 3.3 Hz,

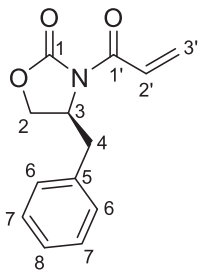
1 H, 4-H_b), 4.14 – 4.22 (m, 2 H, 2-H), 4.72 (m_c, 1 H, 3-H), 7.17 – 7.39 (m, 7 H, 2'-H, 3'-H, 6-H, 7-H and 8-H).

^{13}C NMR (151 MHz, chloroform-*d*):
δ [ppm] = 18.7 (C-4'), 38.0 (C-4), 55.4 (C-3), 66.2 (C-2), 122.0 (C-2'), 127.4 (C-8), 129.0 (C-6), 129.6 (C-7), 135.5 (C-5), 147.1 (C-3'), 153.6 (C-1), 165.1 (C-1').

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 3028; 2917; 1776; 1684; 1636; 1496; 1443; 1388; 1352; 1210; 1032; 968; 913; 747; 701.

The observed data is consistent with the literature.[83, 201]

(*S*)-3-Acryloyl-4-benzyloxazolidin-2-one (125)



125

Prepared according to the literature.[83, 146, 147, 202]

Triethylamine (2.56 mL, 18.5 mmol, 2.5 eq.) and acryloyl chloride (770 µL, 9.50 mmol, 1.3 eq.) were added to a solution of acrylic acid (700 µL, 10.2 mmol, 1.4 eq.) in tetrahydrofuran (30 mL) at -20 °C. The reaction mixture was stirred at this temperature for 2.5 hours. Lithium chloride (372 mg, 8.80 mmol, 1.2 eq.) and (*S*)-4-benzyloxazolidin-2-one (1.30 g, 7.30 mmol, 1.0 eq.) were added. The yellow mixture was allowed to warm to room temperature and stirred for 17 hours. The reaction was quenched by addition of HCl (10 mL, 0.1 N) and the solvent was removed *in vacuo*. The residue was partitioned between ethyl acetate (20 mL) and HCl (20 mL, 0.1 N) and the organic layer was washed with $NaHCO_3$ (20 mL of a half saturated aqueous solution) and brine (20 mL), dried (Na_2SO_4) and concentrated to afford the crude reaction mixture as a yellow oil. The crude product (1.00 g) was purified by flash column chromatography (50 g silica, 25% ethyl acetate in hexane) to

afford (*S*)-3-acryloyl-4-benzyloxazolidin-2-one (**125**) as a white, slightly pink solid (840 mg, 3.63 mmol, 50%).

m.p. = 73-75 °C (lit. 73-74 °C)[202]

R_f = 0.31 (25% ethyl acetate in hexane)

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 2.81 (dd, $^2J_{4a,4b}$ = 13.4 Hz, $^3J_{4a,3}$ = 9.6 Hz,1 H, 4-H_a), 3.35 (dd, $^2J_{4b,4a}$ = 13.4 Hz, $^3J_{4b,3}$ = 3.3 Hz,1 H, 4-H_b), 4.13 – 4.29 (m, 2 H, 2-H), 4.74 (ddt, $^3J_{3,4a}$ = 9.6 Hz, $^3J_{3,2}$ = 7.0 Hz, $^3J_{3,4b}$ = 3.3 Hz, 1 H, 3-H), 5.94 (dd, $^3J_{3'a,2}$ = 10.5 Hz, $^2J_{3'a,3'b}$ = 1.8 Hz,1 H, 3'-H_a), 6.61 (dd, $^3J_{3'b,2}$ = 17.0 Hz, $^2J_{3'b,3'a}$ = 1.8 Hz,1 H, 3'-H_b), 7.16 – 7.42 (m, 5 H, 6-H, 7-H and 8-H), 7.52 (dd, $^3J_{2',3'b}$ = 17.0 Hz, $^3J_{2',3'a}$ = 10.5 Hz, 1 H, 2'-H).

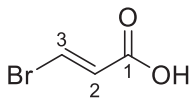
^{13}C NMR (75 MHz, chloroform-*d*):
δ [ppm] = 37.9 (C-4), 55.4 (C-3), 66.4 (C-2), 127.5 (C-8), 127.5 (C-3'), 129.1 (C-6), 129.6 (C-7), 132.0 (C-2'), 135.3 (C-5), 153.4 (C-1), 165.0 (C-1').

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 3029; 2920; 1779; 1686; 1496; 1454; 1409; 1389; 1352; 1212; 1114; 984; 914; 744; 703.

The observed data is consistent with the literature.[202]

For the synthesis of **(*S*,*E*)-4-(4-benzyl-2-oxooxazolidin-3-yl)-4-oxobut-2-enenitrile** (**140**):

(*E*)-Methyl-3-bromopropenoate (138)



138

Prepared following the procedure of Heck *et al*.[203]

Propiolic acid (9.30 g, 130 mmol, 1.0 eq.) was added dropwise to hydrobromic acid (50.0 mL of a 48% solution in water, 440 mmol, 3.3 eq.) and the solution was boiled

under a reflux condenser for 90 minutes. The solution was then cooled to 0 °C. The thereby crystallised acid was collected by filtration and air-dried to afford (*E*)-methyl-3-bromopropenoate (**138**) (8.50 g, 56.3 mmol, 42%) as a white solid mixed with a black impurity.

m.p. = 116-118 °C (lit. 117.5-118.5 °C)[203]

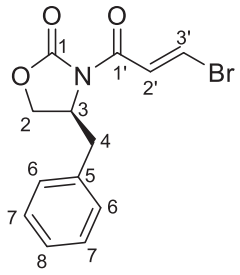
^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 6.54 (d, $^{3}J_{2,3}$ = 13.9 Hz, 1 H, 2-H), 7.76 (d, $^{3}J_{3,2}$ = 13.9 Hz, 1 H, 3-H).

^{13}C NMR (151 MHz, chloroform-*d*):
δ [ppm] = 128.2 (C-2), 130.1 (C-3), 169.7 (C-1).

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 3074; 2544; 1699; 1666; 1602, 1417; 1295; 1264; 1173; 957; 908; 734; 651.

The observed data is consistent with the literature.[203]

(4*S*,2'*E*)-4-Benzyl-3-(3'-bromoacryloyl)oxazolidin-2-one (139)



139

Prepared according to the procedure of Nishida *et al*.[150]

(*E*)-3-Bromoacrylic acid **138** (1.00 g, 6.60 mmol, 1.0 eq.) was dissolved in dichloromethane (7 mL) and oxalyl chloride (0.63 mL, 7.30 mmol, 1.1 eq.) was added dropwise at 0 °C. Afterwards, *N*,*N*-dimethylformamide (5 drops) was added and the reaction was stirred under reflux for 3 hours. In a second flask, (*S*)-4-Benzyloxazolidin-2-one (1.26 g, 7.10 mmol, 1.1 eq.) was dissolved in tetrahydrofuran (29 mL) and sodium hydride (60% in oil, 242 mg, 8.60 mmol, 1.3 eq.) was added in portions at 0 °C. The mixture was stirred for 30 minutes at 0 °C and 1 hour at room temperature. The solution of 3-bromoacryloyl chloride was added to

the second flask at 0 °C and the mixture was stirred for 3 hours at room temperature. The reaction was quenched with water (5 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organic phases were dried (Na_2SO_4) and concentrated to afford the crude reaction mixture as black oil. The crude product (2.20 g) was purified by flash column chromatography (100 g silica, 20% ethyl acetate in hexane), followed by recrystallization from hexane and ethyl acetate and a further flash column chromatography (95 g silica, 16% ethyl acetate in hexane) to afford (4*S*,2'*E*)-4-benzyl-3-(3'-bromoacryloyl)oxazolidin-2-one (**139**) as a partially solidified oil (1.29 g, 4.10 mmol, 63%).

m.p. = 116-118 °C

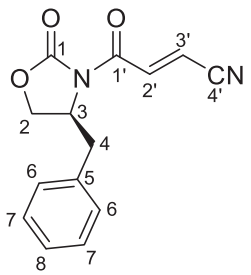
R_f = 0.52 (20% ethyl acetate in hexane)

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 2.81 (dd, $^2J_{4a,4b}$ = 13.4 Hz, $^3J_{4a,3}$ = 9.5 Hz,1 H, 4-H_a), 3.31 (dd, $^2J_{4b,4a}$ = 13.4 Hz, $^3J_{4b,3}$ = 3.4 Hz,1 H, 4-H_b), 4.16 – 4.30 (m, 2 H, 2-H), 4.71 (ddt, $^3J_{3,4a}$ = 9.5 Hz, $^3J_{3,2}$ = 7.0 Hz, $^3J_{3,4b}$ = 3.4 Hz, 1 H, 3-H), 7.14 – 7.40 (m, 5 H, 6-H, 7-H and 8-H), 7.83 (d, $^3J_{3',2'}$ = 13.6 Hz, 1 H, 3'-H), 7.98 (d, $^3J_{2',3'}$ = 13.6 Hz, 1 H, 2'-H).

^{13}C NMR (75 MHz, chloroform-*d*):
δ [ppm] = 37.8 (C-4), 55.3 (C-3), 66.4 (C-2), 127.6 (C-8), 127.8 (C-3'), 129.1 (C-6), 129.1 (C-2'), 129.5 (C-7), 135.1 (C-5), 153.2 (C-1), 162.7 (C-1').

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 3090; 2925; 1780; 1682; 1589; 1388; 1355; 1213; 1189; 1109; 1000; 913; 743; 660.

(*S*,*E*)-4-(4-Benzyl-2-oxooxazolidin-3-yl)-4-oxobut-2-enenitrile (140)



140

Prepared according to the procedure of Nishida *et al*.[150]

N,*N*-Dimethylformamide (10.2 mL) and copper(I) cyanide (952 mg, 10.6 mmol, 2.7 eq.) were added to a flask containing oxazolidinone **139** (1.24 g, 3.98 mmol, 1.0 eq.) at room temperature. The reaction was heated to 130 °C and stirred for 4 hours. The mixture was allowed to warm to room temperature. Ethyl acetate (12 mL) was added and the mixture was concentrated under reduced pressure. Water (15 mL) was added and the mixture was extracted with ethyl acetate (3 x 15 mL). The combined organic extracts were washed with brine, dried ($NaSO_4$) and concentrated *in vacuo* to afford the crude product (926 mg) as a black oil. Purification by flash column chromatography (80 g silica, 33% ethyl acetate in hexane) afforded (*S*,*E*)-4-(4-benzyl-2-oxooxazolidin-3-yl)-4-oxobut-2-enenitrile (**140**) as a white solid (391 mg, 1.50 mmol, 38%).

m.p. = 115-117 °C

R_f = 0.44 (30% ethyl acetate in hexane)

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 2.83 (dd, $^2J_{4a,4b}$ = 13.5 Hz, $^3J_{4a,3}$ = 9.4 Hz,1 H, 4-H_a), 3.33 (dd, $^2J_{4b,4a}$ = 13.5 Hz, $^3J_{4b,3}$ = 3.4 Hz,1 H, 4-H_b), 4.21 – 4.35 (m, 2 H, 2-H), 4.75 (ddt, $^3J_{3,4a}$ = 9.4 Hz, $^3J_{3,2}$ = 7.1 Hz, $^3J_{3,4b}$ = 3.4 Hz, 1 H, 3-H), 6.63 (d, $^3J_{3',2'}$ = 16.1 Hz, 1 H, 3'-H), 7.15 – 7.40 (m, 5 H, 6-H, 7-H and 8-H), 8.12 (d, $^3J_{2',3'}$ = 16.1 Hz, 1 H, 2'-H).

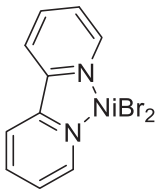
^{13}C NMR (75 MHz, chloroform-*d*):
δ [ppm] = 37.6 (C-4), 55.4 (C-3), 66.8 (C-2), 113.5 (C-3'), 115.8 (C-4'), 127.7 (C-8), 129.2 (C-6), 129.5 (C-7), 134.6 (C-5), 138.2 (C-2'), 153.0 (C-1), 161.9 (C-1').

IR (Film):
$\tilde{\nu}$ [cm^{-1}] =3097; 2923; 1781; 1684; 1620; 1455; 1390; 1362; 1269; 1212; 1116; 1002; 960; 759; 702.

HRMS (ESI):
Calculated for $C_{14}H_{12}N_2O_3H$: 257.0921 [$(M+H)^+$], found: 257.0920; calculated for $C_{14}H_{12}N_2NaO_3$: 279.0740 [$(M+Na)^+$], found: 279.0738.

7.4.1.4 Preparation of the Nickel Catalyst

$NiBr_2$(bpy) (161)



161

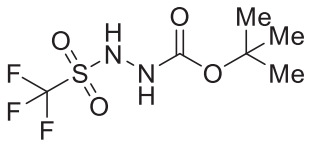
$NiBr_2$(bpy) (**161**) was prepared following the procedure of Budnikova *et al.*[164]

$NiBr_2$ (2.73 g, 12.5 mmol, 1.0 eq.) was dissolved in ethanol (25 mL) and stirred for 3 hours. Afterwards, 2,2'-bipyridine (1.95 g, 12.5 mmol, 1.0 eq.) was added to the solution under continuous stirring. After 16 hours the precipitated product was filtered off, washed with ethanol and dried in vacuum at 30 °C for 24 hours. $NiBr_2$(bpy) (**161**) (3.07 g, 8.20 mmol, 66%) was isolated as a green solid.

R_f = 0.74 (20% ethyl acetate in hexane)

7.4.1.5 Preparation of the Trifluoromethylation Reagent

***tert*-Butyl 2-[(trifluoromethyl)sulfonyl]hydrazine carboxylate (164)**



164

Prepared according to the procedures of Tian *et al.*[166]

tert-Butyl carbazate (2.64 g, 20.0 mmol, 1.0 eq.) and triethylamine (3.05 mL, 22.0 mol, 1.1 eq.) were added to dichloromethane (100 mL) at -78 °C. A solution of trifluoromethanesulfonic anhydride (3.36 mL, 20.0 mmol, 1.0 eq.) in dichloromethane (20 mL) was added dropwise over 25 minutes. The mixture was allowed to warm to room temperature and stirred for 3 hours. Afterwards, it was washed with water (2 x 100 mL), aqueous HCl-solution (100 mL, 1 M) and water (1 x 100 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude reaction mixture (3.35 g as a white solid) was purified by three flash column chromatographies (60 g silica, 10% methanol in ethyl acetate; 60 g silica, 33% hexane in ethyl acetate; 90 g

silica, 20% ethyl acetate in hexane) to afford hydrazine **164** (1.85 g, 6.98 mmol, 35%) as a white solid.

^{19}F NMR (282 MHz, dimethyl sulfoxide-d_6):
δ [ppm] = -76.4 (s, 3 H, CF_3).

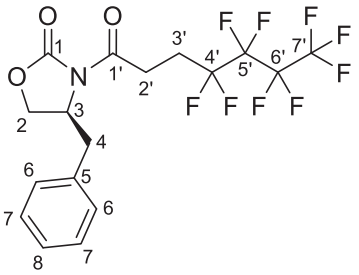
^{1}H NMR (300 MHz, dimethyl sulfoxide-d_6):
δ [ppm] = 1.41 (s, 9 H, CH_3), 9.66 (s, 1 H, CO_2NH), 11.39 (s, 1 H, SO_2NH).

The observed data is consistent with the literature.[166]

7.4.2 Hydroperfluoroalkylation

7.4.2.1 Perfluoroalkylation of α,β-Unsaturated Chiral *N*-Acyloxazolidinones Initiated by Et_3B/O_2

(4*S*)-4-Benzyl-3-(4,4,5,5,6,6,7,7,7-nonafluoro-3-methylheptanoyl)oxazolidin-2-one (126)



126

Prepared according to the procedure of Czekelius *et al.*[83, 147]

(*S*)-3-Acryloyl-4-benzyloxazolidin-2-one (**125**) (200 mg, 0.865 mmol, 1.0 eq) was added to ytterbium(III) trifluoromethanesulfonate hydrate (1.10 g, 1.72 mmol, 2.0 eq.) in CH_2Cl_2/THF (1:1, 9 mL). The reaction mixture was stirred at room temperature and -78 °C for each 30 minutes. After the addition of nonafluoro-1-iodobutane (1.24 mL, 7.79 mmol, 9.0 eq.) and triethylborane (4.32 mL of a 1 M solution in hexanes, 4.32 mmol, 5.0 eq.), oxygen (10 mL O_2 per mmol Et_3B) was added in intervals of 15 minutes over 90 minutes. The reaction was stirred for 72 hours at -78 °C. The addition of nonafluoro-1-iodobutane (1.24 mL, 7.79 mmol, 9.0 eq.), triethylborane (4.32 mL of a 1 M solution in hexanes, 4.32 mmol, 5.0 eq.) and oxygen (10 mL O_2 per mmol Et_3B) was repeated. The yellow reaction mixture was stirred

overnight at -78 °C and was then quenched by addition of an aqueous HCl-solution (20 mL, 0.1 M). The white mixture was stirred at room temperature for 2 hours, the phases were separated and the mixture was extracted with dichloromethane (4 x 40 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated to afford the crude reaction mixture. The crude product (779 mg as a black oil) was purified by flash column chromatography (50 g silica, 33-50% toluene in dichloromethane). Product **48** was isolated as a colourless oil (7.9 mg, 0.018 mmol, 2.0%).

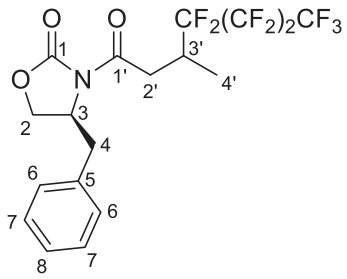
^{19}F NMR (282 MHz, chloroform-*d*):
δ [ppm] = -81.0 (tt, $^3J_{7',6'}$ = 9.7 Hz, $^4J_{7',5'}$ = 3.2 Hz, 3 F, 7'-F), -114.5 (m_c, 2 F, 4'-F), -124.4 (m_c, 2 F, 5'-F), -126.0 (m_c, 2 F, 6'-F).

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 2.57 (m_c, 2 H, 3'-H), 2,79 (dd, $^2J_{4a,4b}$ = 13.4 Hz, $^3J_{4a,3}$ = 9.6 Hz, 1 H, 4-H_a), 3.17 – 3.42 (m, 3 H, 4-H_b and 2'-H), 4.16 – 4.30 (m, 2 H, 2-H), 4.69 (m_c, 1 H, 3-H), 7.07 – 7.46 (m, 5 H, 6-H, 7-H and 8-H).

^{13}C NMR (75 MHz, chloroform-*d*):
δ [ppm] = 25.7 (t, $^3J_{C,F}$ = 22.1 Hz, C-3'), 27.4 (C-2'), 38.0 (C-4), 55.4 (C-3), 66.7 (C-2), 127.7 (C-8), 129.2 (C-7), 129.5 (C-6), 135.1 (C-5), 153.5 (C-1), 170.6 (C-1'). Signals for C-4', C-5', C-6' and C-7' were not found.

The observed data is consistent with the literature.[83, 147]

Attempted Preparation of (4*S*)-4-Benzyl-3-(4,4,5,5,6,6,7,7,7-nonafluoro-3-methylheptanoyl)oxazolidin-2-one (128)



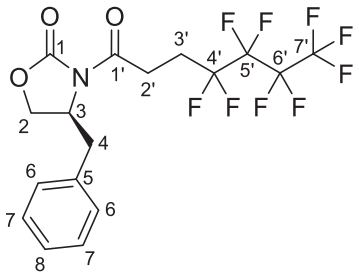
128

Perfluoroalkylation was attempted following the procedure of Czekelius *et al.*[83, 147]

(4*S*,2'*E*)-4-Benzyl-3-(but-2'-enoyl)oxazolidin-2-one (245 mg, 1.00 mmol, 1.0 eq.) was added to ytterbium(III) trifluoromethanesulfonate hydrate (1.24 g, 2.00 mmol, 2.0 eq.) in CH_2Cl_2/THF (1:1, 10 mL). The reaction mixture was stirred at room temperature and -78 °C for each 30 minutes. After the addition of nonafluoro-1-iodobutane (1.55 mL, 9.00 mmol, 9.9 eq.) and Et_3B (5.00 mL of a 1 M solution in hexanes, 5.00 mmol, 5.0 eq.), oxygen (10 mL O_2 per mmol Et_3B) was added in intervals of 15 minutes over 90 minutes. These additions were performed three times. The yellow reaction mixture was stirred for 18 hours at -78 °C and was then quenched by addition of an aqueous HCl-solution (0.1 M). The white mixture was stirred at room temperature for 2 hours, the phases were separated and the mixture was extracted with dichloromethane (4 x 50 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated to afford the crude reaction mixture. The crude product (982 mg as a black oil) was purified by flash column chromatography (50 g silica, 33% toluene in dichloromethane). No product was identified and (*S*,*E*)-4-benzyl-3-(but-2-enoyl)oxazolidin-2-one was re-isolated as a white solid (177 mg, 0.72 mmol, 72%).

7.4.2.2 Attempted Direct Electrochemical Perfluoroalkylation of Chiral *N*-Acyloxazolidinones

Attempted Preparation of (4*S*)-4-Benzyl-3-(4,4,5,5,6,6,7,7,7-nonafluoro-3-methylheptanoyl)oxazolidin-2-one (126)



126

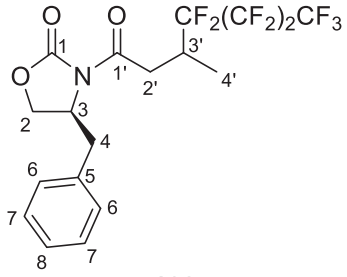
(*S*)-3-Acryloyl-4-benzyloxazolidin-2-one (**125**) (231 mg, 1.00 mmol, 1.0 eq.), nonafluoro-1-iodobutane (0.34 mL, 2.00 mmol, 2.0 eq.) and tetrabutylammonium tetrafluoroborate (2.61 g, 7.90 mmol, 0.3 M) were added to dichloromethane (15 mL per mmol substrate) and THF (15 mL per mmol substrate) in a 100 mL four-neck round-bottom flask. Platinated razor blades (*Braun*, Germany) were used as electrodes. A current of 22 mA was applied for 25 minutes and the mixture turned from colourless to yellow to red. The current was reduced to 6 mA for 50 minutes and

then to 3 mA for 2 hours and then turned off. In total 0.37 F/mol C_4F_9I were applied. The mixture was stirred for 66 hours and was then quenched by addition of an aqueous HCl-solution (0.1 M). The yellow mixture was stirred at room temperature for 2 hours, the phases were separated and the mixture was extracted with dichloromethane (4 x 20 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated to afford the crude reaction mixture. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no fluoroalkylation product.

The reaction was repeated using (*S*)-3-acryloyl-4-benzyloxazolidin-2-one (**125**) (200 mg, 0.870 mmol, 1.0 eq.), nonafluoro-1-iodobutane (0.30 mL, 1.73 mmol, 2.0 eq.) and tetrabutylammonium tetrafluoroborate (493 mg, 1.50 mmol, 0.05 M). A current of 1 mA was applied for 47 hours (1.0 F/mol C_4F_9I). The crude material (651 mg as a yellow solid) was purified by flash column chromatography (30 g silica, 50% toluene in dichloromethane). (*S*)-3-Acryloyl-4-benzyloxazolidin-2-one (**125**) (172 mg, 0.740 mmol, 86%) was re-isolated as a white solid.

The reaction was repeated using (*S*)-3-acryloyl-4-benzyloxazolidin-2-one (**125**) (200 mg, 0.870 mmol, 1.0 eq.), nonafluoro-1-iodobutane (0.30 mL, 1.73 mmol, 2.0 eq.) and tetrabutylammonium tetrafluoroborate (493 mg, 1.50 mmol, 0.05 M) with glassy carbon electrodes. A current of 1 mA was applied for 28 hours (0.60 F/mol C_4F_9I). The crude material (665 mg as a yellow solid) was purified by flash column chromatography (30 g silica, 50% toluene in dichloromethane). (*S*)-3-Acryloyl-4-benzyloxazolidin-2-one (**125**) (181 mg, 0.780 mmol, 90%) was re-isolated as a white solid.

Attempted Preparation of (4*S*)-4-Benzyl-3-(4,4,5,5,6,6,7,7,7-nonafluoro-3-methylheptanoyl)oxazolidin-2-one (128)

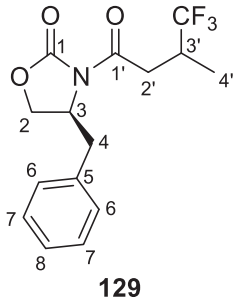


128

(4*S*,2'*E*)-4-Benzyl-3-(but-2'-enoyl)oxazolidin-2-one (**127**) (245 mg, 1.00 mmol, 1.0 eq.), lithium chloride (127 mg, 4.00 mmol, 0.2 M) and nonafluoro-1-iodobutane (1.55 mL, 9.00 mmol, 9.0 eq.) were added to *N*,*N*-dimethylformamide (20 mL), which was degassed for 1 hour in undivided cell **A**. Glassy carbon plates (surface: ~1 cm^2) were used as electrodes. A current of 4-5 mA was applied for 44 hours (4.4 F/mol C_4F_9I). The mixture was then quenched by addition of an aqueous HCl-solution (20 mL, 0.1 M,). The yellow mixture was stirred at room temperature for 2 hours, the phases were separated and the mixture was extracted with dichloromethane (100 mL). The combined organic extracts were washed with water (5 x 150 mL) to remove *N*,*N*-dimethylformamide, dried ($MgSO_4$) and concentrated to afford the crude reaction mixture. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no fluoroalkylation product.

The reaction was repeated using (4*S*,2'*E*)-4-Benzyl-3-(but-2'-enoyl)oxazolidin-2-one (**127**) (245 mg, 1.00 mmol, 1.0 eq.), lithium chloride (127 mg, 4.00 mmol, 0.2 M), nonafluoro-1-iodobutane (1.55 mL, 9.00 mmol, 9.0 eq.) and *N*,*N*-dimethylformamide (20 mL), which was degassed for 1 hour. Platinum nets (surface: ~1 cm^2) were used as electrodes. A current of 4 mA was applied for 44 hours (3.8 F/mol C_4F_9I). Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no fluoroalkylation product.

Attempted Preparation of (4*S*)-4-Benzyl-3-(3'-trifluoromethyl-heptanoyl)oxazolidin-2-one (129)



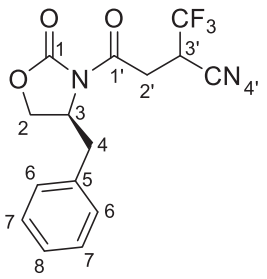
129

(4*S*,2'*E*)-4-Benzyl-3-(but-2'-enoyl)oxazolidin-2-one (**127**) (392 mg, 1.60 mmol, 1.0 eq.), ytterbium(III) trifluoromethanesulfonate hydrate (1.98 g, 3.20 mmol, 2.0 eq.) and tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol, 0.1 M) were added to *N*,*N*-dimethylformamide (20 mL), which was degassed for 1 hour in undivided cell **A**. The mixture was cooled to 0 °C. A balloon of trifluoromethyl iodide was connected *via* a syringe. Glassy carbon plates (surface: ~1 cm^2) were used as electrodes. A current of 27 mA was applied. After 22 hours, trifluoromethyl iodide (100 mL) was added again. After 45 hours (28 F/mol alkene), the mixture was quenched by addition of an aqueous HCl-solution (20 mL, 0.1 M), which lead to gas development. The yellow mixture was stirred at room temperature for 2.5 hours, the phases were separated and the mixture was extracted with dichloromethane (100 mL). The combined organic extracts were washed with sodium sulphite (100 mL of a saturated aqueous solution) and water (4 x 150 mL) to remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford the crude reaction mixture as brown oil. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed only product traces.

The reaction was further attempted following the procedure of Uneyama *et al*.[102]
(4*S*,2'*E*)-4-Benzyl-3-(but-2'-enoyl)oxazolidin-2-one (**127**) (491 mg, 2.00 mmol, 1.0 eq.), trifluoroacetic acid (0.62 mL, 8.0 mmol, 4.0 eq.) and sodium hydroxide (32 mg, 0.80 mmol, 0.40 eq.) were added to a mixture of acetonitrile (6 mL) and water (1 mL). The mixture was heated to 50 °C. Platinum nets were used as anode (1.5 cm^2) and cathode (2 cm^2). A constant current of 75 mA was applied until 1.5 F/mol TFA were consumed. The solvent was removed and the mixture was quenched by addition of an aqueous HCl-solution (10 mL, 0.05 M). The mixture was extracted with dichloromethane (4 x 20 mL), washed with brine (50 mL), dried

(Na_2SO_4) and concentrated under reduced pressure to afford the crude reaction mixture (529 mg) as a brown solid. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed an inseparable mixture.

Attempted Preparation of (4*S*)-4-Benzyl-3-(3'-trifluoromethyl-heptanoyl)oxazolidin-2-one (141)



141

The reaction was attempted following the procedure of Uneyama *et al*.[102]

(*S*,*E*)-4-(4-Benzyl-2-oxooxazolidin-3-yl)-4-oxobut-2-enenitrile (**140**) (180 mg, 0.700 mmol, 1.0 eq.), trifluoroacetic acid (0.21 mL, 2.80 mmol, 4.0 eq.) and sodium hydroxide (11.2 mg, 0.280 mmol, 0.40 eq.) were added to a mixture of acetonitrile (2.10 mL) and water (0.35 mL). The mixture was heated to 50 °C. Platinum nets were used as anode (0.5 cm^2) and cathode (1 cm^2). A constant current of 50 mA was applied until 1.9 F/mol TFA were consumed. The solvent was removed and water (10 mL) was added. The mixture was extracted with ethyl acetate (5 x 10 mL), washed with brine (20 mL), dried (Na_2SO_4) and concentrated to afford the crude reaction mixture (337 mg) as a brown oil. Purification by flash column chromatography (50 g silica, 1 - 5% methanol in dichloromethane) afforded only substrate **140** as a colourless oil (925 mg, 5.05 mmol, 65%).

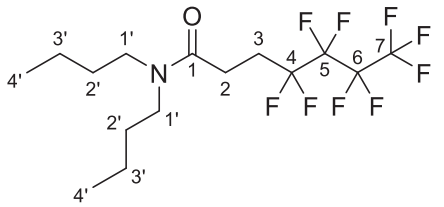
7.4.2.3 Direct Electrochemical Perfluoroalkylation of Acrylamides

General procedure A

N,*N*-Dibutylacrylamide (**142**) (293 mg, 1.60 mmol, 1.0 eq.), ytterbium(III) trifluoromethanesulfonate hydrate (1.98 g, 3.20 mmol, 2.0 eq.), nonafluoro-1-iodobutane (1.10 mL, 6.40 mmol, 4.0 eq.) and tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol, 0.1 M) were added to *N*,*N*-dimethylformamide (20 mL), which was degassed for 1 hour. Platinum nets or glassy carbon (~2.8 cm^2) were used as electrodes. A constant current was applied for a certain amount of time. The mixture was then quenched by addition of an aqueous HCl-solution (0.1 M). The

yellow mixture was stirred at room temperature for 2 hours, the phases were separated and the mixture was extracted with dichloromethane (100 mL). The combined organic extracts were washed with water (4 x 150 mL) to remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (3 x 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a black oil. The crude product was purified by flash column chromatography (100 g silica, 15% ethyl acetate in hexane). *N*,*N*-Dibutyl-4,4,5,5,6,6,7,7,7-nonafluoroheptanamide (**145**) and *N*,*N*-dibutyl-4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptanamide (**146**) were isolated as colourless oils.

_N_,_N_-Dibutyl-4,4,5,5,6,6,7,7,7-nonafluoroheptanamide (145)



145

R_f = 0.74 (20% ethyl acetate in hexane)

^{19}F NMR (282 MHz, chloroform-*d*):
δ [ppm] = -81.0 (tt, $^3J_{7,6}$ = 9.7 Hz, $^4J_{7,5}$ = 3.3 Hz, 3 F, 7-F), -114.7 (tt, $^3J_{4,5}$ = 12.9 Hz, $^4J_{4,6}$ = 3.7 Hz, 2 F, 4-F), -124.5 (m_c, 2 F, 5-F), -126.0 (m_c, 2 F, 6-F).

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 0.85 – 1.02 (m, 6 H, 4‘-H), 1.32 (m_c, 4 H, 3‘-H), 1.43 – 1.66 (m, 4 H, 2‘-H), 2.41 – 2.67 (m, 4 H, 2-H and 3-H), 3.18 – 3.38 (m, 4 H, 1’-H).

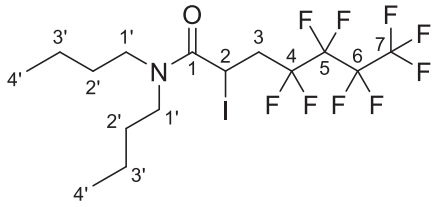
^{13}C NMR (75 MHz, chloroform-*d*):
δ [ppm] = 13.8 and 13.9 (C-4’), 20.2 and 20.4 (C-3’), 24.2 (t, $^3J_{C,F}$ = 3.5 Hz, C-2), 27.0 (t, $^2J_{C,F}$ = 21.3 Hz, C-3), 30.0 and 31.9 (C-2’), 46.2 and 47.8 (C-1’), 169.3 (C-1). Signals for C-4, C-5, C-6 and C-7 were found in the area of 105.0 – 127.0 ppm.

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 2963; 2936; 2877; 1651; 1460; 1431; 1357; 1298; 1231; 1134; 1099; 978; 880; 749; 717.

HRMS (ESI):

Calculated for $C_{15}H_{22}F_9NOH$: 404.1630 [$(M+H)^+$], found: 404.1638.

***N*,*N*-Dibutyl-4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptanamide (146)**



146

R_f = 0.87 (20% ethyl acetate in hexane)

^{19}F NMR (282 MHz, chloroform-*d*):

δ [ppm] = -81.0 (tt, $^3J_{7,6}$ = 9.7 Hz, $^4J_{7,5}$ = 3.1 Hz, 3 F, 7-F), -112.1 – 116.2 (m, 2 F, 4-F) -124.5 (m_c, 2 F, 5-F), -125.9 (m_c, 2 F, 6-F).

^{1}H NMR (300 MHz, chloroform-*d*):

δ [ppm] = 0.84 – 1.04 (m, 6 H, 4‘-H), 1.21 – 1.43 (m, 4 H, 3‘-H), 1.43 – 1.81 (m, 4 H, 2‘-H), 2.55 – 2.84 (m, 1 H, 3-H_a), 2.97 – 3.75 (m, 5 H, 1’-H and 3-H_b), 4.70 (dd, $^3J_{2,3}$ = 9.9 Hz = 3.2 Hz, 2-H).

^{13}C NMR (75 MHz, chloroform-*d*):

δ [ppm] = 6.0 (C-2), 13.8 and 14.0 (C-4’), 20.2 and 20.2 (C-3’), 29.0 and 31.4 (C-2’), 38.5 (t, $^2J_{C,F}$ = 21.4 Hz, C-3), 47.1 and 48.7 (C-1’), 168.6 (C-1). Signals for C-4, C-5, C-6 and C-7 were not identified.

IR (Film):

$\tilde{\nu}$ [cm^{-1}] = 2962; 2935; 2876; 1652; 1457; 1354; 1235; 1134; 1102; 1021; 878; 844; 750; 727 517.

HRMS (ESI):

Calculated for $C_{15}H_{21}F_9INOH$: 530.0597 [$(M+H)^+$], found: 530.0597; calculated for $C_{15}H_{21}F_9NO$: 402.1474 [$(M-I)^+$], found: 402.1479.

The results of the perfluoroalkylation attempts following general procedure **A** are displayed in Table 20.

Table 20: Yields of re-isolated substrate **142**, hydroperfluoroalkylated product **145** and iodoperfluoroalkylated product **146** of the reactions performed following general procedure **A** with corresponding time, solvent and used electrodes.

Entry	Electrodes	Current [mA]	Solvent	F/mol C_4F_9I	Time [d]	Yield 142 [%]	145 [%]	146 [%]
1[a]	GC	1-7	DMF	4.2	8	23	19	4.7
2[b]	GC	4-16	MeCN	7.9	14	12	9.1	ntd
3[c]	Pt	5-21	DMF	41	27	-	-	-
4	Pt	3	DMF	2.9	7	8.8	10	0.8
5[d]	Ni	11-60	DMF	10	3		1.4	-
6	Old GC	3	DMF	3.7	9	complicated mixture		
7[a]	New GC	6-45	DMF	26	7	21	21	6.6
8	GC cathode/ Pt anode	10	DMF	9.8	7	complicated mixture		

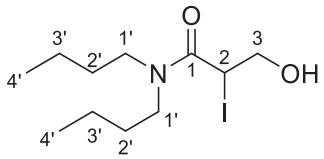
[a] *N*,*N*-Dibutyl-3-hydroxy-2-iodopropanamide (**147**) was identified as side product

[b] *N*,*N*-Dibutyl-3-iodopropanamide (**152**) (73 mg, 0.23 mmol, 15%) was identified as side product

[c] No $Yb(OTf)_3$, platinum net loss due to corrosion of clamp

[d] Ni anode as sacrificial electrode, corroded after reaction; starting current 5 mA/cm^2 degreased during reaction to 1 mA/cm^2

N,*N*-Dibutyl-3-hydroxy-2-iodopropanamide (147)



147

Hydroxylated side product **147** was isolated as a white solid (70.1 mg, 0.210 mmol, 13%) upon the reaction following general procedure **A** with glassy carbon electrodes (Table 20, Entry 1).

Hydroxylated side product **147** was isolated as a yellow solid (65.2 mg, 0.20 mmol, 12%) upon the reaction following general procedure **A** with new glassy carbon electrodes (Table 20, Entry 7).

R_f = 0.42 (30% ethyl acetate in hexane)

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 0.85 – 0.97 (m, 6 H, 4‘-H), 1.22 – 1.43 (m, 4 H, 3‘-H), 1.45 – 1.83 (m, 4 H, 2’-H), 2.94 – 3.21 (m, 2 H, 1’-H_a), 3.31 – 3.68 (m, 3 H, 1’-H_b and -O*H*), 3.78 (ddd, $^{2}J_{3a,3b}$ = 11.6 Hz, $^{3}J_{3a,OH}$ = 7.3 Hz, $^{3}J_{3a,2}$ = 4.0 Hz, 1 H, 3-H_a), 4.05 (ddd, $^{2}J_{3b,3a}$ = 11.6 Hz, $^{3}J_{3b,2}$ = 7.8 Hz, $^{3}J_{3b,\,OH}$ = 6.9 Hz, 1 H, 3-H_b), 4.45 (dd, $^{3}J_{2,3b}$ = 7.8 Hz, $^{3}J_{2,3b}$ = 4.0 Hz, 1 H, 2-H).

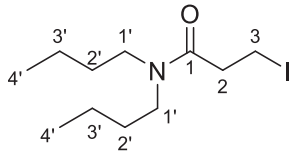
^{13}C NMR (75 MHz, chloroform-*d*):
δ [ppm] = 13.9 and 14.0 (C-4’), 20.2 and 20.2 (C-3’), 20.3 (C-2), 29.1 and 31.3 (C-2’), 46.1 and 48.6 (C-1’), 65.6 (C-3), 169.8 (C-1).

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 3393; 2958; 2931; 2872; 1635; 1542; 1457; 1436; 1374; 1197; 1146; 1101; 1039; 1005; 592.

MS (EI)
m/z (%) = 128 (25) [($C_8H_{18}N)^+$], 284 (10) [(M-$C_3H_7)^+$], 328 (2) [(M+H)$^+$].

HRMS (ESI):
Calculated for $C_{11}H_{23}INO_2$: 328.0768 [(M+H)$^+$], found: 328.0770.

_N_,_N_-Dibutyl-3-iodopropanamide (152)



152

N,*N*-Dibutyl-3-iodopropanamide (73.0 mg, 0.235 mmol, 15%) was isolated as a brown oil upon the reaction following general procedure **A** in acetonitrile instead of *N*,*N*-dimethylformamide (Table 20, Entry 2).

R_f = 0.32 (10% ethyl acetate in hexane)

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 0.85 – 0.97 (m, 6 H, 4‘-H), 1.29 (m_c, 4 H, 3‘-H), 1.42 – 1.60 (m, 4 H, 2‘-H), 2.91 (t, $^{3}J_{2,3}$ = 7.2 Hz, 2 H, 2-H), 3.18 (m_c, 2 H, 1‘-H), 3.30 (m_c, 2 H, 1‘-H), 3.38 (t, $^{3}J_{3,2}$ = 7.2 Hz, 2 H, 3-H).

^{13}C NMR (75 MHz, chloroform-*d*):
δ [ppm] = -1.0 (C-3), 13.9 and 13.9 (C-4’), 20.2 and 20.3 (C-3’), 29.9 and 31.3 (C-2’), 37.4 (C-2), 46.1 and 47.7 (C-1’), 170.2 (C-1).

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 2958; 2930; 2871; 1644; 1457; 1374; 1217; 1144; 1114; 978; 795; 745; 532.

MS (ESI)
m/z (%) = 312 (100) [$(M+H)^+$], 184 (8) [$(M-I)^+$].

HRMS (ESI):
Calculated for $C_{11}H_{22}INOH$: 312.0819 [$(M+H)^+$], found: 312.0821; calculated for $C_{11}H_{22}NO$: 184.1696 [$(M-I)^+$], found: 184.197.

Lithium chloride as Conducting Salt

The perfluoroalkylation was performed following general procedure **A** with lithium chloride as the conducting salt, using *N*,*N*-dibutylacrylamide (**142**) (183 mg, 1.00 mmol, 1.0 eq.), LiCl (127 mg, 4.00 mmol, 0.2 M), two times nonafluoro-1-iodobutane (1.55 mL, 9.00 mmol, 9.0 eq.) and *N*,*N*-dimethylformamide (20 mL), which was degassed for 1 hour. Glassy carbon was used as electrodes. The constant current electrolysis was carried out until 1.9 F/mol C_4F_9I were consumed. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no fluoroalkylation product.

General procedure B

The perfluoroalkylation was performed following general procedure **A** using *N*,*N*-dibutylacrylamide (**142**) (183 mg, 1.00 mmol, 1.0 eq.), nonafluoro-1-iodobutane (0.28 mL, 1.0 mmol, 1.0 eq.), 1,4-cyclohexadiene (0.05 mL, 0.5 mmol, 0.5 eq.), (trifluoromethyl)cyclohexane (97%, 75 mg, 0.50 mmol, 0.5 eq.) and

tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol, 0.1 M). The reaction was performed at 20 °C with an applied current of 8 mA and quenched after 3 days (21 F/mol C_4F_9I).

The results of the experiments following general procedure **B** are shown in Table 21.

Table 21: Yields of re-isolated substrate **142**, hydroperfluoroalkylated product **145** and iodoperfluoroalkylated product **146** of the reactions performed following general procedure **B** with used electrodes.

Entry	Electrodes	142 [%]	Yield 145 [%]	146 [%]
1	GC	38	5.3	2.5
2[a]	Cu	complicated mixture[c]		
3[b]	GC	complicated mixture[c]		

[a]Cu anode as sacrificial electrode, corroded after reaction

[b]No 1,4-cyclohexadiene was used

[c]by ^{19}F NMR spectroscopy

Galvanostatic Electrolysis in a Divided Cell Using Glassy Carbon Electrodes

Perfluoroalkylation of acrylamide **142** was also attempted in a divided H-type cell (4G glass filter) using glassy carbon electrodes (15 mm x 19 mm). Acrylamide **142** (825 mg, 4.50 mmol, 1.0 eq.) was added to tetrabutylammonium tetrafluoroborate (1.25 g, 3.8 mmol for both sides) in *N*,*N*-dimethylformamide to the cathodic compartment (19 mL in anode, 17 mL in cathode, 0.1 M), which was degassed for 20 minutes. Nonafluoro-1-iodobutane (1.82 mL, 10.5 mmol, 2.3 eq.) was added in portions (0.26 mL, 1.50 mmol, 0.33 eq.) during the course of the reaction. The constant current electrolysis (17 mA) was carried out with magnetic stirring at room temperature until 2.2 F/mol C_4F_9I were consumed. The mixture was then quenched by addition of an aqueous HCl-solution (20 mL, 0.1 M). The mixture was extracted with dichloromethane (100 mL). The organic extract was washed with water (4 x 150 mL) to remove *N*,*N*-dimethylformamide, dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a black oil. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed only product traces.

Galvanostatic Electrolysis in a Divided Cell Using Carbon Felt as Electrodes and LiCl as Conducting Salt

The cathodic reduction was performed in a divided H-type cell (4G glass filter) with a carbon felt anode and cathode (340 mg, dried at 140 °C/1 mbar for 16 hours). Lithium chloride (136 mg, 3.20 mmol, 0.2 M, dried o.n. 140 °C/1 mbar) and *N*,*N*-dimethylformamide (10 mL) were added to both chambers and degassed (N_2) for 30 minutes. Nonafluoro-1-iodobutane (0.14 mL, 0.80 mmol, 1.0 eq.) and acrylamide **142** (147 mg, 0.80 mmol, 1.0 eq.) were added to the cathodic chamber. The constant current electrolysis (37 mA) was carried out with magnetic stirring at room temperature until 1.5 F/mol were consumed. Analysis of the reaction mixture by ^{19}F NMR spectroscopy revealed no fluoroalkylation product. Nonafluoro-1-iodobutane (0.07 mL, 0.40 mmol, 0.5 eq.) was added and the reduction continued until 3.5 F/mol alkene were consumed. Nonafluoro-1-iodobutane (0.07 mL, 0.40 mmol, 0.5 eq.) was added and the reduction continued until 4.0 F/mol alkene were consumed. Aqueous HCl-solution (5 mL, 1 M) and water (75 mL) were added and the mixture extracted with dichloromethane (150 mL). The organic extracts were washed (4 x 75 mL), dried (Na_2SO_4) and concentrated. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed only product traces.

Potentiostatic Electrolysis in a Divided Cell Using Carbon Felt as Electrodes and LiCl as Conducting Salt

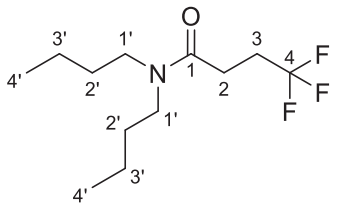
According to the procedure of Commeyras *et al*. perfluoroalkylation was attempted in a divided H-type cell (4G glass filter) with a carbon felt anode (720 mg, dried at 140 °C/1 mbar for 16 hours).[125] Acrylamide **142** (6.42 g, 35.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (6.02 mL, 35.0 mmol, 1.0 eq.) were added to the cathodic side and *N*,*N*-dimethylformamide (13 mL) was added to the anodic side. A solution of lithium chloride (623 mg, dried at 140 °C/1 mbar for 16 hours) in *N*,*N*-dimethylformamide (22 mL), which was degassed for 20 minutes was divided between both sides. The volume was 35 mL per side with a concentration of lithium chloride of 0.21 M. The constant potential electrolysis was carried out at -1.2 V vs. Ag/AgCl (initial current of 16 mA) with magnetic stirring at room temperature for 6 days. The mixture was added to a solution of sodium thiosulfate (150 mL of a saturated aqueous solution). Dichloromethane (150 mL) and water (250 mL) were added and the phases separated. The organic extract was washed with water (4 x 250 mL) to remove *N*,*N*-dimethylformamide and back-extracted with

dichloromethane (2 x 75 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed only product traces.

Galvanostatic Electrolysis in a Screeningblock (Teflon Vial)

The perfluoroalkylation was performed following general procedure **A** in a Teflon vial. *N*,*N*-Dibutylacrylamide (**142**) (73.0 mg, 0.40 mmol, 1.0 eq.), nonafluoro-1-iodobutane (0.28 mL, 1.6 mmol, 4.0 eq.) and ytterbium(III) trifluoromethanesulfonate hydrate (496 mg, 0.80 mmol, 2.0 eq.) were added to a solution of tetrabutylammonium tetrafluoroborate (165 mg, 0.5 mmol, 0.1 M) in *N*,*N*-dimethylformamide (5 mL), which was degassed for 20 minutes. Glassy carbon plates (10 mm x 30 mm) were used as electrodes. A current of 3 mA (1 mA per cm^2) was applied for 5 days (8.4 F/mol C_4F_9I). The crude product was purified by flash column chromatography (25 g silica, 10% ethyl acetate in hexane). Hydroperfluoroalkylated product **145** (7.8 mg, 0.019 mmol, 4.8%) and iodoperfluoroalkylated product **146** (3.4 mg, 0.0064 mmol, 1.6%), acrylamide **142** (34.4 mg, 0.188 mmol, 47%) and iodinated amide **147** (40.2 mg, 0.123 mmol, 31%) were isolated as colourless oils.

Attempted Preparation of *N*,*N*-Dibutyl-4-trifluoroheptanamide (155)



155

N,*N*-Dibutylacrylamide (**142**) (293 mg, 1.60 mmol, 1.0 eq.), ytterbium(III) trifluoromethanesulfonate hydrate (1.98 g, 3.20 mmol, 2.0 eq.) and tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol, 0.1 M) were added to *N*,*N*-dimethylformamide (20 mL), which was degassed for 1 hour. The mixture was cooled to -30 °C. A balloon of trifluoromethyl iodide (excess) was connected *via* a syringe. Platinum nets were used as electrodes. A current of 2-4 mA was applied. After 17.5 hours another balloon of trifluoromethyl iodide was added. After 7 days the solution was warmed to 0 °C and the current increased to 35-40 mA. The mixture was quenched after 4 days (57.7 F/mol alkene) by addition of an aqueous HCl-solution (20 mL, 0.1 M), which lead to gas development. The yellow mixture was stirred at room temperature for 2 hours, the phases were separated and the mixture

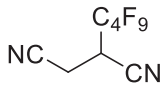
was extracted with dichloromethane (100 mL). The combined organic extracts were washed with water (4 x 150 mL) to remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford the crude reaction mixture (1.42 g) as a black oil. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed an inseparable mixture.

Attempted Perfluoroalkylation Using Trifluoroacetic Acid

The preparation was further attempted following the procedure of Uneyama *et al*.[102] *N*,*N*-Dibutylacrylamide (**142**) (183 mg, 1.00 mmol, 1.0 eq.), trifluoroacetic acid (0.38 mL, 0.50 mmol, 0.50 eq.) and sodium hydroxide (4.0 mg, 0.10 mmol, 0.10 eq.) were added to a mixture of acetonitrile (3.5 mL) and water (0.5 mL). The mixture was cooled to 0 °C. Platinum nets were used as electrodes. A current of 2-4 mA was applied. After 7 hours the mixture was warmed to room temperature. After 24 hours the reaction was cooled again to 0 °C and trifluoroacetic acid (0.38 mL, 0.50 mmol, 0.5 eq.) was added again. After 14 days (1.6 F/mol TFA), water was added and the mixture was extracted with ethyl acetate (3 x 15 mL). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$) and concentrated under reduced pressure to afford the crude reaction mixture (67 mg) as a brown oil. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed an inseparable mixture.

7.4.2.4 Direct Electrochemical Perfluoroalkylation of Alkenes

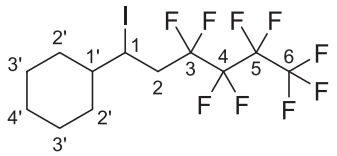
Attempted Preparation of 2-(Perfluorobutyl)succionitrile (157)



157

The perfluoroalkylation of the alkene was performed following general procedure **A** in a Teflon vial. Fumaronitrile (**130**) (31.0 mg, 0.40 mmol, 1.0 eq.), nonafluoro-1-iodobutane (0.28 mL, 1.6 mmol, 4.0 eq.) and ytterbium(III) trifluoromethanesulfonate hydrate (496 mg, 0.800 mmol, 2.0 eq.) were added to a solution of tetrabutylammonium tetrafluoroborate (165 mg, 0.5 mmol, 0.1 M) in *N*,*N*-dimethylformamide (5 mL), which was degassed for 20 minutes. Glassy carbon plates (10 mm x 30 mm) were used as electrodes. A current of 3 mA (1 mA per cm^2) was applied for 5 days (8.4 F/mol C_4F_9I). Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no fluoroalkylation product.

(3,3,4,4,5,5,6,6,6-Nonafluoro-1-iodohexyl)cyclohexane (159)

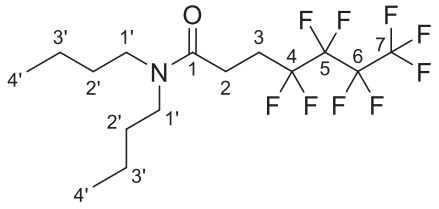


159

The perfluoroalkylation of the alkene was performed following general procedure **A** in a Teflon vial using vinylcyclohexane (**158**) (0.06 mL, 0.4 mmol, 1.0 eq.), nonafluoro-1-iodobutane (0.28 mL, 1.6 mmol, 4.0 eq.) and ytterbium(III) trifluoromethanesulfonate hydrate (496 mg, 0.800 mmol, 2.0 eq.) were added to a solution of tetrabutylammonium tetrafluoroborate (164.6 mg, 0.5 mmol, 0.1 M) in *N*,*N*-dimethylformamide (5 mL), which was degassed for 20 minutes. Glassy carbon plates (10 mm x 30 mm) were used as electrodes. A current of 3 mA (1 mA per cm^2) was applied for a 5 days (8.4 F/mol C_4F_9I). The crude product was purified by flash column chromatography (25 g silica, 100% pentane). Iodoperfluoroalkylated product **159** (19.8 mg, 0.0434 mmol, 11%) was isolated as a colourless oil. The analytical data can be found in chapter 7.4.3.5.

7.4.2.5 Attempted Indirect Electrochemical Perfluoroalkylation of Acrylamide

Attempted Preparation of *N*,*N*-Dibutyl-4,4,5,5,6,6-nonafluoroheptanamide (145)



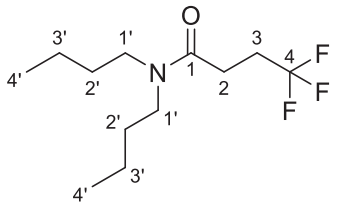
145

The preparation of hydroperfluoroalkylated amide **145** was attempted following the procedures of Budnikova *et al*.[46, 130]

N,*N*-Dibutylacrylamide (**142**) (293 mg, 1.60 mmol, 1.0 eq.), nonafluoro-1-iodobutane (0.55 mL, 3.2 mmol, 2.0 eq.), $NiBr_2$(bpy) (60.0 mg, 0.160 mmol, 10 mol%) and tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol, 0.1 M) were added to *N*,*N*-dimethylformamide (20 mL), which was degassed for 1 hour. Platinum nets were used as electrodes. A current of 3-7 mA was applied for 34 days (43 F/mol C_4F_9I). The corrosion of the clamps led to the repeating loss of the platinum nets. The mixture was quenched by addition of an aqueous HCl-solution (0.1 M). The yellow mixture was stirred at room temperature for 2 hours, the phases were separated and

the mixture was extracted with dichloromethane (100 mL). The combined organic extracts were washed with water (4 x 150 mL) to remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (3 x 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed only product traces.

Attempted Preparation of *N*,*N*-Dibutyl-4-trifluoroheptanamide (155)



155

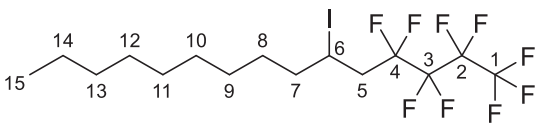
Perfluoroalkylation was attempted following the procedures of Tian *et al.*[166]

N,*N*-Dibutylacrylamide (**142**) (36.7 mg, 0.200 mmol, 1.0 eq.), ferrocene (3.7 mg, 0.020 mmol, 0.10 eq.), TfNHNHBoc (106 mg, 0.400 mmol, 2.0 eq.), Na_2HPO_4 (56.8 mg, 0.400 mmol, 2.0 eq.) and tetraethylammonium *p*-toluenesulfonate (60.3 mg, 0.200 mmol, 1.0 eq.), anhydrous MTBE (3 mL) and anhydrous methanol (2 ml) were added to a 10 mL three-neck flask equipped with an reflux condenser. The reaction was performed using a glassy carbon cathode (10 mm x 10 mm) and a platinum plate anode (10 mm x 8 mm) at 70 °C. The constant current electrolysis (5 mA) was carried out with magnetic stirring until 26.0 F/mol acrylamide were consumed. The solvent was removed. Attempted purification by flash column chromatography was unsuccessful.

7.4.3 Electrocatalytic Iodoperfluoroalkylation

7.4.3.1 Preliminary Trials for the Electrosynthetic Iodoperfluoroalkylation

Attempted Preparation of 1,1,1,2,2,3,3,4,4-Nonafluoro-6-iodo-pentadecane (168)



168

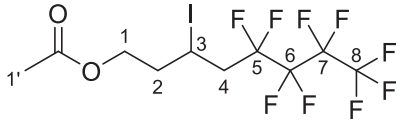
1-Undecene (0.24 mL, 1.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (0.10 mL, 0.60 mmol, 0.50 eq.) were added to tetrabutylammonium tetrafluoroborate (494 mg,

1.50 mmol, 0.1 M) in *N*,*N*-dimethylformamide (15 mL), which was degassed for 20 minutes in an undivided cell. Glassy carbon plates (15 mm x 20 mm) were used as electrodes. The constant current electrolysis (15 mA) was carried out with magnetic stirring at room temperature until 2.7 F/mol C_4F_9I were consumed. The mixture was quenched by addition of an aqueous HCl-solution (20 mL, 0.1 M) and extracted with dichloromethane (100 mL). The organic extract was washed with water (4 x 150 mL) to remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (5 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a black oil. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no fluoroalkylation product.

Attempted Preparation in a Divided H-Type Cell

The reaction was also performed in a divided H-type cell (4G glass filter) and glassy carbon plates (15 mm x 17 mm) were used as electrodes. Tetrabutylammonium tetrafluoroborate (626 mg, 1.90 mmol, 0.1 M) and *N*,*N*-dimethylformamide (19 mL in anode, 17 mL in cathode), which was degassed for 20 minutes, were added to both sides. 1-Undecene (1.09 mL, 5.29 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (0.9 mL, 5.29 mmol, 1.0 eq.) were added to the cathodic compartment. The constant current electrolysis (15 mA) was carried out with magnetic stirring at room temperature until 1.5 F/mol C_4F_9I were consumed. The mixture was extracted with dichloromethane (100 mL). The organic extract was washed with water (5 x 300 mL) to remove *N*,*N*-dimethylformamide. The organic extract was dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as black oil. Attempted purification by flash column chromatography (35 g silica, 100% pentane, then 30 g silica 100% pentane and 15 g silica, 100% pentane) afforded only mixtures of fluorinated, unidentified compounds.

Attempted Preparation of 5,5,6,6,7,7,8,8,8-Nonafluoro-3-iodooctyl Acetate (170)

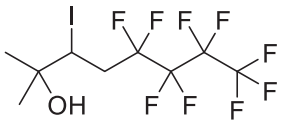


52

The reaction was performed in a divided H-type cell (4G glass filter) and glassy carbon plates (20 mm x 17 mm) were used as electrodes. Tetrabutylammonium tetrafluoroborate (626 mg, 1.90 mmol, 0.1 M) and *N*,*N*-dimethylformamide (19 mL in anode, 17 mL in cathode), which was degassed for 20 minutes, were added to both

sides. 3-Butenyl acetate (0.50 mL, 4.0 mmol, 1.0 eq.) was added to the cathodic compartment. Nonafluoro-1-iodobutane (1.36 mL, 8.00 mmol, 2.0 eq.) was added in portions (0.17 mL, 1.0 mmol, 0.25 eq.) during the course of the reaction. The constant current electrolysis (20 mA) was carried out with magnetic stirring at room temperature until 0.80 F/mol C_4F_9I were consumed. The mixture was quenched by addition of an aqueous HCl-solution (20 mL per side, 0.1 M) and extracted with dichloromethane (100 mL). The organic extract was washed with water (5 x 150 mL) to remove *N*,*N*-dimethylformamide and washed with sodium thiosulfate (80 mL of a saturated aqueous solution). The organic extract was dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as black oil. Purification by flash column chromatography (90 g silica, 50% cyclohexane in dichloromethane) afforded only inseparable fluorinated mixtures.

Attempted Preparation of 5,5,6,6,7,7,8,8,8-Nonafluoro-3-iodo-2-methyloctan-2-ol (103)



52

Prepared according to the procedure of Commeyras *et al*.[125]

The cathodic reduction was performed in a divided H-type cell (4G glass filter) with a carbon felt anode and cathode (720 mg, dried at 140 °C/1 mbar for 16 hours). Lithium chloride (0.420 g, 9.90 mmol, 0.4 M, dried o.n. 140 °C/1 mbar) and *N*,*N*-dimethylformamide (25 mL) were added to both chambers and degassed (N_2) for 15 minutes. 2-Methyl-3-buten-2-ol (**101**) (3.63 mL, 34.7 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (6.00 mL, 34.7 mmol, 1.0 eq.) were added to the cathodic chamber and *N*,*N*-dimethylformamide (10 mL) was added to the anodic chamber. The constant current electrolysis (70 mA) was carried out with magnetic stirring at room temperature until 0.68 F/mol were consumed. The mixture was stirred for an additional 15 hours. Water (50 mL) was added and the mixture extracted with diethyl ether (1 x 50 mL, 3 x 100 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. Purification by flash column chromatography (90 g silica, 10% ethyl acetate in hexane) afforded only fluorinated mixtures.

Galvanostatic Electrolysis in a Divided Cell Adding Nonafluoro-1-iodobutane (1.5 eq.) in Portions

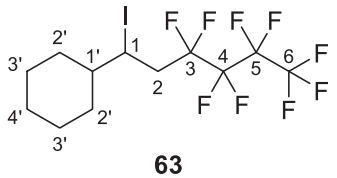
The cathodic reduction was performed in a divided H-type cell (4G glass filter) with a carbon felt anode and cathode (340 mg, dried at 140 °C/1 mbar for 16 hours). Lithium chloride (136 mg, 3.20 mmol, 0.2 M, dried o.n. 140 °C/1 mbar) and *N*,*N*-dimethylformamide (11.6 mL) were added to both chambers and degassed (N_2) for 30 minutes. 2-Methyl-3-buten-2-ol (**101**) (1.67 mL, 16.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (2.75 mL, 16.0 mmol, 1.0 eq.) were added in the cathodic chamber and *N*,*N*-dimethylformamide (4.4 mL) was added to the anodic chamber. The constant current electrolysis (70 mA) was carried out with magnetic stirring at room temperature until 0.50 F/mol were consumed. Nonafluoro-1-iodobutane (1.38 mL, 8.00 mmol, 0.50 eq.) was added and the reduction continued until 0.90 F/mol alkene were consumed. Water (100 mL) was added and the mixture extracted with diethyl ether (150 mL). The organic extracts were washed (4 x 150 mL), dried (Na_2SO_4) and concentrated. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed only inseparable mixtures.

Potentiostatic Electrolysis in a Divided Cell Using LiCl as Conducting Salt

Attempted preparation according to the procedure of Commeyras *et al*.[125]

The perfluoroalkylation of 2-methyl-3-buten-2-ol (**101**) was performed in a divided H-type cell (4G glass filter) with a carbon felt anode and cathode (720 mg, dried at 140 °C/1 mbar for 16 hours). 2-Methyl-3-buten-2-ol (**101**) (2.61 mL, 25.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (4.30 mL, 25.0 mmol, 1.0 eq.) were added to the cathodic side and DMF (7 mL) was added to the anodic side. A solution of lithium chloride (424 mg, 9.00 mmol, dried at 140 °C/1 mbar for 16 hours) in *N*,*N*-dimethylformamide (36 mL), which was degassed for 20 minutes, was divided between both sides. The volume was 25 mL per side with a concentration of lithium chloride of 0.20 M. The constant potential electrolysis was carried out at -1.2 V vs. Ag/AgCl (initial current of 50 mA) with magnetic stirring at room temperature until 0.13 F/mol were consumed. The mixture was added to water (100 mL) and extracted with diethylether (3 x 50 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated to afford the crude reaction mixture as a yellow oil. Purification by flash column chromatography (280 g silica, 100% *n*-pentane) afforded only fluorinated mixtures.

(3,3,4,4,5,5,6,6,6-Nonafluoro-1-iodohexyl)cyclohexane (159)



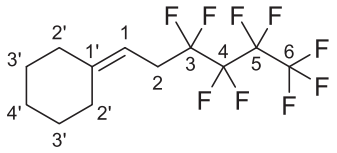
63

Potentiostatic Electrolysis in a Divided Cell using LiCl as Conducting Salt

Prepared according to the procedure of Commeyras *et al*.[125]

The iodoperfluoroalkylation of vinylcylcohexane (**158**) was performed in a divided H-type cell (4G glass filter) with a carbon felt anode (720 mg, dried at 140 °C/1 mbar for 16 hours). Vinylcyclohexane (**158**) (5.88 mL, 43.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (7.40 mL, 43.0 mmol, 1.0 eq.) were added to the cathodic side and DMF (13.3 mL) was added to the anodic side. A solution of lithium chloride (766 mg, dried at 140 °C/1 mbar for 16 hours) in *N*,*N*-dimethylformamide (60 mL), which was degassed for 20 minutes, was divided between both sides. The volume was 43 mL per side with a concentration of lithium chloride of 0.21 M. The constant potential electrolysis was carried out at -1.2 V vs. Ag/AgCl (initial current of 80 mA) with magnetic stirring at room temperature until 0.17 F/mol were consumed. The mixture was added to sodium thiosulfate (150 mL of a saturated aqueous solution). Dichloromethane (150 mL) and water (250 mL) were added and the phases separated. The organic extract was washed with water (4 x 250 mL) to remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (2 x 75 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **159** and the elimination product **171** were isolated as a mixture (3.25 g, approximately 55% by NMR analysis) as a colourless oil. The analytical data of product **159** can be found in chapter 7.4.3.5.

(3,3,4,4,5,5,6,6,6-Nonafluorohexylidene)cyclohexane (171)



171

R_f = 0.79 (100% *n*-pentane)

The following signals were attributed to (3,3,4,4,5,5,6,6,6-nonafluorohexylidene)cyclohexane (**171**):

^{19}F NMR (282 MHz, chloroform-*d*):
δ [ppm] = -80.9 – -81.1 (m, 3 F, 6-F), -113.5 – -113.7 (m, 2 F, 3-F), -124.1 (m_c, 2 F, 4-F), -126.1 (m_c, 2 F, 5-F).

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 1.49 – 1.63 (m, 6 H, 3‘-H and 4‘-H), 2.05 – 2.21 (m, 4 H, 2’-H), 5.11 (t, $^3J_{1,2}$ = 7.5 Hz, 1 H, 1-H).

Galvanostatic Electrolysis in an Undivided Cell Using LiCl as Conducting Salt

The iodoperfluoroalkylation was performed in an undivided cell with a carbon felt anode and cathode (340 mg, dried at 140 °C/1 mbar for 16 hours). Lithium chloride (178 mg, 4.20 mmol, 0.21 M), vinylcyclohexane (2.74 mL, 20.0 mmol, 1.0 eq.) and nonfluoro-1-iodobutane (3.44 mL, 20.0 mmol, 1.0 eq.) were added to *N*,*N*-dimethylformamide (13.8 mL), which was degassed (N_2) for 20 minutes. The constant current electrolysis (35 mA) was carried out with magnetic stirring at room temperature until 2.6 F/mol C_4F_9I were consumed. The mixture was added to sodium thiosulfate (100 mL of a saturated aqueous solution). Dichloromethane (150 mL) and water (100 mL) were added and the phases separated. The organic phase was washed with water (4 x 200 mL) to remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (1 x 25 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil. The crude product was purified by flash column chromatography (25 g silica and 250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **159** (3.91 g, 8.5 mmol, 43%) was isolated as a colourless oil.

Galvanostatic Electrolysis (20 mA) in a Divided Cell with Tetrahydrofuran in the Anodic Compartment

The iodoperfluoroalkylation was performed in a divided H-type cell (4G glass filter) with a carbon felt anode and cathode (170 mg, dried at 140 °C/1 mbar for at least 16 hours). A solution of lithium chloride (178 mg, 4.20 mmol, 0.21 M) in *N*,*N*-dimethylformamide (14 mL), which was degassed (N_2) for 20 minutes, was added to both sides (7 mL per side). The volume was 10 mL per side with a concentration of lithium chloride of 0.21 M. Vinylcyclohexane (1.37 mL, 10.0 mmol, 1.0 eq.) was added to the cathodic side and *N*,*N*-dimethylformamide (2 mL) and tetrahydrofuran (0.96 mL, 15 mmol, 1.5 eq.) were added to the anodic side. Nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.) was added in three portions during the reaction to the cathodic compartment. At the beginning, 1.0 equivalent (1.72 mL, 10.0 mmol) was used and during the reaction two further portions (0.86 mL, 5.0 mmol, 0.50 eq.) were added. The constant current electrolysis (20 mA) was carried out with magnetic stirring at room temperature until 0.34 F/mol C_4F_9I were consumed. Dichloromethane (150 mL) and water (200 mL) were added and the phases separated. The organic phase was washed with sodium thiosulfate (100 mL of a saturated aqueous solution) and water (3 x 200 mL) to remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (2 x 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil. The crude product was purified by flash column chromatography (25 g silica and 250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **159** (2.59 g, 5.67 mmol, 57%) was isolated as a colourless oil.

Galvanostatic Electrolysis (20 mA) in a Divided Cell with Tetrahydrofuran in the Anodic Compartment Starting with 2.0 Equivalents of C_4F_9I

The iodoperfluoroalkylation was performed in a divided H-type cell (4G glass filter) with a carbon felt anode and cathode (170 mg, dried at 140 °C/1 mbar for at least 16 hours). A solution of lithium chloride (178 mg, 4.20 mmol) in *N*,*N*-dimethylformamide (14 mL), which was degassed (N_2) for 20 minutes, was added to both sides (7 mL per side). The volume was 11.8 mL per side with a concentration of lithium chloride of 0.18 M. Vinylcyclohexane (1.37 mL, 10.0 mmol, 1.0 eq.) was added to the cathodic side and *N*,*N*-dimethylformamide (3.9 mL) was added to the anodic side. Tetrahydrofuran (1.92 mL, 30.0 mmol, 3.0 eq.) was added

to the anodic side in two portions (0.96 mL, 15 mmol, 1.5 eq.) at the beginning of the reaction and after 4 hours. Nonafluoro-1-iodobutane (5.16 mL, 30.0 mmol, 3.0 eq.) was added in three portions to the cathodic compartment. At the beginning, 2.0 equivalents (3.44 mL, 20.0 mmol, 2.0 eq.) were used and during the reaction two further portions (0.86 mL, 5.0 mmol, 0.50 eq.) were added. The constant current electrolysis (20 mA) was carried out with magnetic stirring at room temperature until 0.21 F/mol C_4F_9I were consumed. Dichloromethane (150 mL), sodium thiosulfate (50 mL of a saturated aqueous solution) and water (150 mL) were added and the phases separated. The organic phase was washed with water (4 x 200 mL) to remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (2 x 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil. The crude product was purified by flash column chromatography (25 g silica and 250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **159** (2.59 g, 5.67 mmol, 57%) was isolated as a colourless oil.

Galvanostatic Electrolysis (30 mA) in a Divided Cell with Tetrahydrofuran in the Anodic Compartment Starting with 2.0 Equivalents of C_4F_9I

The iodoperfluoroalkylation was performed in a divided H-type cell (4G glass filter) with a carbon felt anode and cathode (170 mg, dried at 140 °C/1 mbar for at least 16 hours). A solution of lithium chloride (178 mg, 4.20 mmol) in *N*,*N*-dimethylformamide (10 mL), which was degassed (N_2) for 20 minutes, was added to both sides (5 mL per side). The volume was 10 mL per side with a concentration of lithium chloride of 0.21 M. Vinylcyclohexane (1.37 mL, 10.0 mmol, 1.0 eq.) was added to the cathodic side and *N*,*N*-dimethylformamide (3.9 mL) was added to the anodic side. Tetrahydrofuran (1.92 mL, 30.0 mmol, 3.0 eq.) was added to the anodic side in two portions (0.96 mL, 15 mmol, 1.5 eq.) at the beginning of the reaction and after 2 hours. Nonafluoro-1-iodobutane (5.16 mL, 30.0 mmol, 3.0 eq.) was added in three portions to the cathodic compartment. At the beginning, 2.0 equivalents (3.44 mL, 20.0 mmol, 2.0 eq.) were used and during the reaction two further portions (0.86 mL, 5.0 mmol, 0.50 eq.) were added. The constant current electrolysis (30 mA) was carried out with magnetic stirring at room temperature until 0.21 F/mol C_4F_9I were consumed. Dichloromethane (150 mL), sodium thiosulfate (50 mL of a saturated aqueous solution) and water (150 mL) were added and the phases separated. The organic phase was washed with water (4 x 200 mL) to

remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (2 x 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil. The crude product was purified by flash column chromatography (25 g silica and 250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **159** (2.95 g, 6.48 mmol, 65%) was isolated as a colourless oil.

7.4.3.2 Screening for Optimal Conditions of the Iodoperfluoroalkylation of Vinylcyclohexane (**158**)

General Conditions for all Screenings:

The iodoperfluoroalkylation of vinylcyclohexane (**158**) was performed in a divided H-type cell (4G glass filter) with a carbon felt anode and cathode (170 mg, dried at 140 °C - 200 °C/1 mbar for 16 hours). The volume was 10 mL per side. After the reaction, the mixture was added to a solution of sodium thiosulfate (50 mL of a saturated aqueous solution). Dichloromethane (150 mL) and water (150 mL) were added and the phases separated. The organic extract was washed with water (4 x 200 mL) to remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (2 x 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil. The residue was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (25 g) and washed with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane).

7.4.3.2.1 Screening of the Conducting Salt in Conjunction with the Applied Current

General procedure C

A solution of lithium chloride (178 mg, 4.20 mmol) or tetrabutylammonium tetrafluoroborate (1.38 g, 4.20 mmol) in *N*,*N*-dimethylformamide (10 mL), which was degassed (N_2) for 20 minutes, was added to both sides (5 mL per side). The volume was 10 mL per side with a concentration of the salt of 0.21 M. Vinylcyclohexane (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.) were added to the cathodic side. *N*,*N*-Dimethylformamide (4 mL) and tetrahydrofuran (0.96 mL, 15.0 mmol, 1.5 eq.) were added to the anodic side. The constant current electrolysis (20 mA or 30 mA) was carried out with magnetic stirring

at room temperature until 0.11-0.13 F/mol C_4F_9I were consumed. During the reaction nonafluoro-1-iodobutane (0.86 mL, 5.00 mmol, 0.50 eq.) was added a second time to the cathodic compartment.

TBATFB and an Applied Current of 20 mA

The iodoperfluoroalkylation was performed following general procedure **C** using tetrabutylammonium tetrafluoroborate as conducting salt. After the constant current electrolysis (20 mA), iodoperfluoroalkylated product **159** (3.88 g, 8.51 mmol, 83%) was isolated as a colourless oil.

The reaction was performed again under similar conditions. Iodoperfluoroalkylated product **159** (3.96 g, 8.68 mmol, 85%) was isolated as a colourless oil.

The reaction was performed again under similar conditions. Iodoperfluoroalkylated product **159** (3.77 g, 8.29 mmol, 81%) was isolated as a colourless oil.

TBATFB and an Applied Current of 28 mA

The iodoperfluoroalkylation was performed following general procedure **C** using tetrabutylammonium tetrafluoroborate as conducting salt. After the constant current electrolysis (28 mA), iodoperfluoroalkylated product **159** (3.69 g, 8.10 mmol, 79%) was isolated as a colourless oil.

Lithium Chloride and an Applied Current of 20 mA

The iodoperfluoroalkylation was performed following general procedure **C** using lithium chloride as conducting salt. After the constant current electrolysis (20 mA), iodoperfluoroalkylated product **159** (3.59 g, 7.88 mmol, 77%) was isolated as a colourless oil.

Lithium Chloride and an Applied Current of 30 mA

The iodoperfluoroalkylation was performed following general procedure **C** using lithium chloride as conducting salt. After the constant current electrolysis (30 mA), iodoperfluoroalkylated product **159** (3.57 g, 7.83 mmol, 77%) was isolated as a colourless oil.

TBATFB and an Applied Current of 20 mA without THF

The iodoperfluoroalkylation was performed following general procedure **C** using tetrabutylammonium tetrafluoroborate as conducting salt, without the addition of tetrahydrofuran in the anodic chamber. After the constant current electrolysis (20 mA), iodoperfluoroalkylated product **159** (3.83 g, 8.39 mmol, 82%) was isolated as a colourless oil.

Lithium Chloride and an Applied Current of 20 mA without THF

The iodoperfluoroalkylation was performed following general procedure **C** using lithium chloride as conducting salt, without the addition of tetrahydrofuran in the anodic chamber. After the constant current electrolysis (20 mA), iodoperfluoroalkylated product **159** (3.77 g, 8.28 mmol, 81%) was isolated as a colourless oil.

TBATFB (0.1 M) and an Applied Current of 20 mA without THF

The iodoperfluoroalkylation was performed following general procedure **C** using tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol, 0.1 M) as conducting salt, without the addition of tetrahydrofuran in the anodic chamber. After the constant current electrolysis (20 mA), iodoperfluoroalkylated product **159** (3.84 g, 8.41 mmol, 82%) was isolated as a colourless oil.

7.4.3.2.2 Optimisation of the Used Equivalents of Nonafluoro-1-iodobutane

General procedure D

A solution of tetrabutylammonium tetrafluoroborate (1.38 g, 4.20 mmol) in *N*,*N*-dimethylformamide, which was degassed (N_2) for 20 minutes, was divided between both sides. The concentration of tetrabutylammonium tetrafluoroborate was 0.21 M. Vinylcyclohexane (1.37 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane were added to the cathodic side and *N*,*N*-dimethylformamide was added to the anodic side. The constant current electrolysis (20 mA) was carried out with magnetic stirring at room temperature until 0.13 F/mol C_4F_9I were consumed.

Two Equivalents of Nonafluoro-1-iodobutane (Added in Portions)

The iodoperfluoroalkylation was performed following general procedure **D** using nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.), which was added in three portions. At the beginning, one equivalent (1.72 mL, 10.0 mmol, 1.0 eq.) was used

and during the reaction two further portions (0.86 mL, 5.0 mmol, 0.50 eq.) were added. Tetrahydrofuran (0.96 mL, 15.0 mmol, 1.5 eq.) was added to the anodic side. Iodoperfluoroalkylated product **159** (3.40 g, 7.48 mmol, 75%) was isolated after distillation (60 °C/10^{-3} mbar) as a colourless oil.

Two Equivalents of Nonafluoro-1-iodobutane

The iodoperfluoroalkylation was performed following general procedure **D** using vinylcyclohexane (1.40 mmol, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.)**.** Iodoperfluoroalkylated product **159** (3.90 g, 8.54 mmol, 84%) was isolated as a colourless oil.

One Equivalent of Nonafluoro-1-iodobutane

The iodoperfluoroalkylation was performed following general procedure **D** using vinylcyclohexane (1.40 mmol, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (1.76 mL, 10.2 mmol, 1.0 eq.). The constant current electrolysis (20 mA) was carried out with magnetic stirring at room temperature until 0.15 F/mol C_4F_9I were consumed. Iodoperfluoroalkylated product **159** (2.44 g, 5.36 mmol, 52%) was isolated as a colourless oil.

7.4.3.2.3 Optimisation of the Applied Current and Charge (F/mol C_4F_9I)

General procedure E

A solution of tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol, 0.1 M) in *N*,*N*-dimethylformamide (10 mL), which was degassed (N_2) for 20 minutes, was added to both sides (5 mL per side). Vinylcyclohexane (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.) were added to the cathodic side and *N*,*N*-dimethylformamide (5 mL) was added to the anodic side.

Applied Current of 20 mA and 0.075 F/mol C_4F_9I

The iodoperfluoroalkylation was performed following general procedure **E** using tetrabutylammonium tetrafluoroborate (1.38 mg, 4.20 mmol, 0.21 M) The constant current electrolysis (20 mA) was carried out with magnetic stirring at room temperature until 0.075 F/mol C_4F_9I were consumed. Iodoperfluoroalkylated product **159** (3.94 g, 8.63 mmol, 84%) was isolated as a colourless oil.

Applied Current of 10 mA and 0.075 F/mol C_4F_9I

The iodoperfluoroalkylation was performed following general procedure **E**. The constant current electrolysis (10 mA) was carried out with magnetic stirring at room temperature until 0.075 F/mol C_4F_9I were consumed. Iodoperfluoroalkylated product **159** (4.02 g, 8.81 mmol, 86%) was isolated as a colourless oil.

Applied Current of 10 mA and 0.038 F/mol C_4F_9I

The iodoperfluoroalkylation was performed following general procedure **E**. The constant current electrolysis (10 mA) was carried out with magnetic stirring at room temperature until 0.038 F/mol C_4F_9I were consumed. Iodoperfluoroalkylated product **159** (3.19 g, 6.99 mmol, 69%) was isolated as a colourless oil.

Applied Current of 5.0 mA and 0.077 F/mol C_4F_9I

The iodoperfluoroalkylation was performed following general procedure **E**. The constant current electrolysis (5.0 mA) was carried out with magnetic stirring at room temperature until 0.077 F/mol C_4F_9I were consumed. Iodoperfluoroalkylated product **159** (4.23 g, 9.28 mmol, 91%) was isolated as a colourless oil.

The reaction was performed again under similar conditions. Iodoperfluoroalkylated product **159** (3.57 g, 7.83 mmol, 77%) was isolated as a colourless oil.

The reaction was performed again under similar conditions. Iodoperfluoroalkylated product **159** (3.93 g, 8.61 mmol, 84%) was isolated as a colourless oil.

Applied Current of 2.5 mA and 0.077 F/mol C_4F_9I

The iodoperfluoroalkylation was performed following general procedure **E**. The constant current electrolysis (2.5 mA) was carried out with magnetic stirring at room temperature until 0.077 F/mol C_4F_9I were consumed. Iodoperfluoroalkylated product **159** (3.07 g, 8.51 mmol, 80%) was isolated as a colourless oil.

7.4.3.2.4 Optimisation of the Concentrations for Conducting Salt and Substrate

General procedure F

A solution of tetrabutylammonium tetrafluoroborate in *N*,*N*-dimethylformamide (10 mL), which was degassed (N_2) for 20 minutes, was added to both sides (5 mL per side). Vinylcyclohexane (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane

(3.44 mL, 20.0 mmol, 2.0 eq.) were added to the cathodic side and *N*,*N*-dimethylformamide (5 mL) was added to the anodic side. The constant current electrolysis (10 mA) was carried out with magnetic stirring at room temperature until 0.075 F/mol C_4F_9I were consumed.

Concentration of 0.05 M TBATFB

The iodoperfluoroalkylation was performed following general procedure **F** using tetrabutylammonium tetrafluoroborate (329 mg, 1.00 mmol, 0.05 M). Iodoperfluoroalkylated product **159** (3.88 g, 8.50 mmol, 83%) was isolated as a colourless oil.

Concentration of 0.05 M Vinylcyclohexane

The iodoperfluoroalkylation was performed following general procedure **F** using vinylcyclohexane (0.69 mL, 5.00 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (1.72 mL, 10.0 mmol, 2.0 eq.). The concentration of tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol) was 0.1 M. Iodoperfluoroalkylated product **159** (1.35 g, 3.01 mmol, 60%) was isolated as a colourless oil.

7.4.3.2.5 Screening of the Electrode Material

General procedure G

The iodoperfluoroalkylation was performed on the according electrodes. A solution of tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol) in *N*,*N*-dimethylformamide (10 mL), which was degassed (N_2) for 20 minutes, was added to both sides (5 mL per side). The concentration of tetrabutylammonium tetrafluoroborate was 0.1 M. Vinylcyclohexane (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.) were added to the cathodic side and *N*,*N*-dimethylformamide (5 mL) was added to the anodic side. The constant current electrolysis (10 mA) was carried out with magnetic stirring at room temperature until 0.077 F/mol C_4F_9I were consumed.

Boron-Doped Diamond Electrodes

The iodoperfluoroalkylation was performed following general procedure **G** using boron-doped diamond plates (10 mm x 20 mm) as electrodes. Iodoperfluoroalkylated product **159** (1.89 g, 4.15 mmol, 41%) was isolated as a colourless oil.

Glassy Carbon Electrodes

The iodoperfluoroalkylation was performed following general procedure **G** using glassy carbon plates (10 mm x 20 mm) as electrodes. Iodoperfluoroalkylated product **159** (2.47 g, 5.41 mmol, 53%) was isolated as a colourless oil.

Graphite Electrodes

The iodoperfluoroalkylation was performed following general procedure **G** using graphite plates (10 mm x 20 mm) as electrodes. Iodoperfluoroalkylated product **159** (1.67 g, 3.67 mmol, 36%) was isolated as a colourless oil.

Carbon Felt Cathode and a Zinc Anode in an Undivided Cell

The iodoperfluoroalkylation was performed following general procedure **G** on a carbon felt cathode (170 mg, dried at 200 °C/1 mbar for 16 hours) and a zinc anode (5 mm x 30 mm) in an undivided cell **A** using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The concentration of tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol) in *N*,*N*-dimethylformamide (15 mL) was 0.1 M in a volume of 20 mL. Iodoperfluoroalkylated product **159** (2.49 g, 5.44 mmol, 53%) was isolated as a colourless oil.

Iron Electrodes

The iodoperfluoroalkylation was performed following general procedure **G** using iron plates (10 mm x 20 mm) as electrodes. Vinylcyclohexane (**158**) (1.37 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (1.72 mL, 10.0 mmol, 1.0 eq.) were added to the cathodic compartment. *N*,*N*-Dimethylformamide (2 mL) and tetrahydrofuran (0.96 mL, 15.0 mmol, 1.5 eq.) were added to the anodic side. The concentration of lithium chloride (178 mg, 4.20 mmol) in *N*,*N*-dimethylformamide (14 mL) was 0.21 M. Analysis of the purified material (2.83 g) by ^{19}F NMR spectroscopy revealed an inseparable mixture of fluorinated compounds.

7.4.3.2.6 Solvent-Screening

General procedure H

A solution of tetrabutylammonium tetrafluoroborate (1.38 g, 4.20 mmol) in the according solvent (10 mL), which was degassed (N_2) for 20 minutes, was added to both sides (5 mL per side). The volume was 10 mL per side with a concentration of

the salt of 0.21 M. Vinylcyclohexane (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.) were added to the cathodic side. The according solvent (5 mL) was added to the anodic side. The constant current electrolysis (10 mA) was carried out with magnetic stirring at room temperature until 0.077 F/mol C_4F_9I were consumed.

Tetrahydrofuran

The iodoperfluoroalkylation was performed following general procedure **H** using tetrahydrofuran as solvent. Iodoperfluoroalkylated product **159** (3.85 g, 8.84 mmol, 83%) was isolated as a colourless oil.

Dichloromethane

The iodoperfluoroalkylation was performed following general procedure **H** using dichloromethane as solvent. The concentration of tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol) was 0.1 M. After the reaction, the mixture was added to a solution of sodium thiosulfate (50 mL of a saturated aqueous solution). Dichloromethane (50 mL) and water (50 mL) were added and the phases separated. The organic extract was washed with water (1 x 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil. Iodoperfluoroalkylated product **159** (4.06 g, 8.90 mmol, 87%) was isolated as a colourless oil.

Acetonitrile

The iodoperfluoroalkylation was performed following general procedure **H** using acetonitrile as solvent. Iodoperfluoroalkylated product **159** (3.92 g, 8.60 mmol, 84%) was isolated as a colourless oil.

Benzene

The iodoperfluoroalkylation was performed following general procedure **H** using benzene as solvent. The concentration of tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol) was 0.1 M. The substrate was not miscible with the solvent and no current was observed.

Hexafluoroisopropanol

The iodoperfluoroalkylation was performed following general procedure **H** using hexafluoroisopropanol as solvent. The concentration of tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol) was 0.1 M. After the reaction, the mixture was added to sodium thiosulfate (50 mL of a saturated aqueous solution). Dichloromethane (100 mL) and water (150 mL) were added and the phases separated. The mixture was extracted with dichloromethane (3 x 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil. Iodoperfluoroalkylated product **159** (3.87 g, 8.48 mmol, 83%) was isolated as a colourless oil.

Hexafluoroisopropanol and Unfiltered Nonafluoro-1-iodobutane

The iodoperfluoroalkylation was performed following general procedure **H** using hexafluoroisopropanol as solvent with tetrabutylammonium tetrafluoroborate (1.38 g, 4.20 mmol, 0.21 M), vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). After the reaction, the mixture was added to sodium thiosulfate (50 mL of a saturated aqueous solution). Dichloromethane (100 mL) and water (150 mL) were added and the phases separated. The mixture was extracted with dichloromethane (3 x 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil. Iodoperfluoroalkylated product **159** (4.14 g, 9.07 mmol, 89%) was isolated as a colourless oil.

7.4.3.3 Control Reactions

General procedure I

The iodoperfluoroalkylation of vinylcyclohexane (**158**) was performed in a divided H-type cell (4G glass filter) with a carbon felt anode and cathode (170 mg, dried at 200 °C/1 mbar for 16 hours). The volume was 10 mL per side. A solution of tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol, 0.1 M) in *N*,*N*-dimethylformamide (10 mL), which was degassed (N_2) for 20 minutes, was added to both sides (5 mL per side). Vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.) were added to the cathodic side and *N*,*N*-dimethylformamide (5 mL) was added to the anodic side. The constant current electrolysis (10 mA) was carried out with magnetic stirring at room temperature until 0.075 F/mol C_4F_9I were consumed. The mixture was added to

a solution of sodium thiosulfate (50 mL of a saturated aqueous solution). Dichloromethane (150 mL) and water (150 mL) were added and the phases separated. The organic extract was washed with water (4 x 200 mL) to remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (2 x 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil. The residue was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (25 g) and washed with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane).

Exclusion of Light

The iodoperfluoroalkylation was performed following general procedure **I** under exclusion of light using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). Iodoperfluoroalkylated product **159** (3.85 g, 8.45 mmol, 83%) was isolated as a colourless oil.

No Applied Current (0 mA)

The iodoperfluoroalkylation was performed following general procedure **I** without applying current using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The reaction was stirred for 24 hours. The crude mixture was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washed with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. Vinylcyclohexane (**158**) (1.07 g, 9.72 mmol, 95%) was re-isolated as a colourless oil. No iodoperfluoroalkylated product was found by ^{19}F NMR spectroscopy.

Ambient Condition

The iodoperfluoroalkylation was performed following general procedure **I** open to air without degassing of the electrolyte using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). Iodoperfluoroalkylated product **159** (3.82 g, 8.38 mmol, 82%) was isolated as a colourless oil.

n-Pentane as Solvent for Work_up

The iodoperfluoroalkylation was performed following general procedure **I** using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The mixture was added to a solution of sodium thiosulfate (50 mL of a saturated aqueous solution). Pentane (150 mL) and water (150 mL) were added and the phases separated. The product was extracted with pentane (2 x 100 mL). Iodoperfluoroalkylated product **159** (4.01 g, 8.78 mmol, 86%) was isolated as a colourless oil after filtration and flash column chromatography.

Unfiltered Nonafluoro-1-iodobutane

The iodoperfluoroalkylation was performed following general procedure **I** using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.), which was not filtered over basic aluminium oxide. Iodoperfluoroalkylated product **159** (3.85 g, 8.43 mmol, 83%) was isolated as a colourless oil.

Galvanostatic Electrolysis in an Undivided Cell

The perfluoroalkylation was performed following general procedure **I** in an undivided cell. Vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.) were added to a solution of tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol, 0.1 M) in *N*,*N*-dimethylformamide (15 mL). Iodoperfluoroalkylated product **159** (2.03 g, 4.46 mmol, 44%) was isolated as a colourless oil.

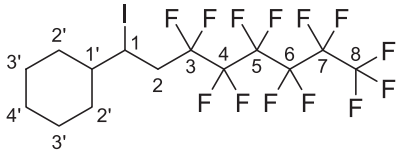
7.4.3.4 Investigation of the Substrate Scope for the Iodoperfluoroalkylation of Alkenes with *N*,*N*-Dimethylformamide as Solvent

General procedure J

The iodoperfluoroalkylation was performed in a divided H-type cell (4G glass filter) with a carbon felt anode and cathode (170 mg, dried at 200 °C/1 mbar for 16 hours). A solution of tetrabutylammonium tetrafluoroborate (658 mg, 2.00 mmol) in *N*,*N*-dimethylformamide (10 mL), which was degassed (N_2) for 20 minutes, was added to both sides (5 mL per side). The volume was 10 mL per side with a concentration of tetrabutylammonium tetrafluoroborate of 0.1 M. Alkene (10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.) were added to the cathodic side and *N*,*N*-dimethylformamide (5 mL) was added to the anodic side.

The constant current electrolysis (10 mA) was carried out with magnetic stirring at room temperature until 0.075 F/mol R_FI were consumed. The mixture was added to a solution of sodium thiosulfate (50 mL of a saturated aqueous solution). Dichloromethane (150 mL) and water (150 mL) were added and the phases separated. The organic extract was washed with water (4 x 200 mL) to remove *N*,*N*-dimethylformamide and back-extracted with dichloromethane (2 x 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil.

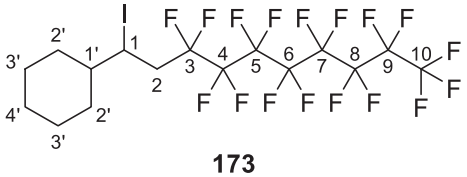
(3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-iodooctyl)cyclohexane (172)



172

The iodoperfluoroalkylation was performed following general procedure **J** using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and perfluorohexyl iodide (4.32 mL, 20.0 mmol, 2.0 eq.). The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washing with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **172** (4.92 g, 8.85 mmol, 87%) was isolated as a colourless oil. The analytical data can be found in chapter 7.4.3.5.

(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododecyl)cyclohexane (173)

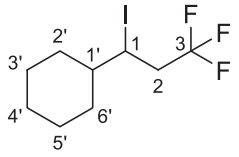


173

The iodoperfluoroalkylation was performed following general procedure **J** using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and perfluorooctyl iodide (10.9 g, 20.0 mmol, 2.0 eq.). The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washing with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane).

Iodoperfluoroalkylated product **173** (5.76 g, 8.78 mmol, 86%) was isolated as a white solid. The analytical data can be found in chapter 7.4.3.5.

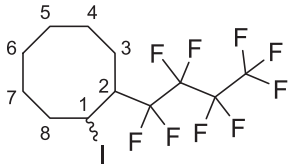
(3,3,3-Trifluoro-1-iodopropyl)cyclohexane (174)



174

The iodoperfluoroalkylation was performed following general procedure **J** using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and an excess of trifluoromethyl iodide which was supplied using a balloon. The constant current electrolysis (10 mA) was carried out until 0.15 F/mol alkene were consumed. The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (25 g) and washing with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane). Trifluoromethylated product **174** (2.00 g, 6.53 mmol, 64%) was isolated as a colourless oil. The analytical data can be found in chapter 7.4.3.5.

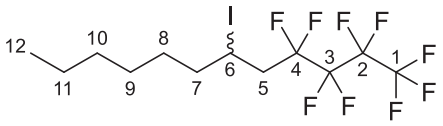
1-Iodo-2-(perfluorobutyl)cyclooctane (177)



177

The iodoperfluoroalkylation was performed following general procedure **J** using cyclooctene (1.30 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washed with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-hexane). Iodoperfluoroalkylated product **177** (822 mg, 1.80 mmol, 18%) was isolated as a colourless oil as a mixture of diastereomers (*d.r.*:78:22). The analytical data can be found in chapter 7.4.3.5.

1,1,1,2,2,3,3,3-Nonafluoro-6-iodododecane (175)

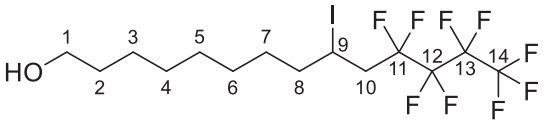


175

The iodoperfluoroalkylation was performed following general procedure **J** using 1-octene (1.58 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washed with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-hexane). Iodoperfluoroalkylated product **175** (3.23 g, 7.04 mmol, 70%) was isolated as a colourless oil. The analytical data can be found in chapter 7.4.3.5.

The reaction was repeated until 0.15 F/mol C_4F_9I were consumed. Iodoperfluoroalkylated product **175** (3.80 g, 8.30 mmol, 83%) was isolated as a colourless oil.

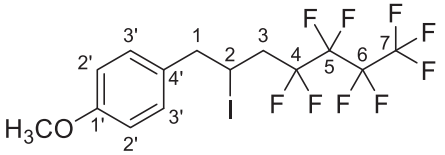
11,11,12,12,13,13,14,14,14-Nonafluoro-9-iodotetradecan-1-ol (176)



176

The iodoperfluoroalkylation was performed following general procedure **J** using 9-decen-1-ol (1.85 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washed with diethyl ether (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 5% diethyl ether in *n*-hexane). Iodoperfluoroalkylated product **176** (3.69 g, 7.35 mmol, 74%) was isolated as a colourless oil. The analytical data can be found in chapter 7.4.3.5.

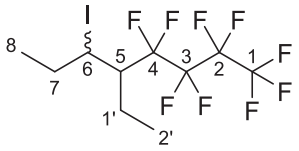
1-Methoxy-4-(4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptyl)benzene (178)



178

The iodoperfluoroalkylation was performed following general procedure **J** using 4-allylanisole (1.54 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washed with diethyl ether (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, first, 2% ethyl acetate in *n*-hexane and then, 1% ethyl acetate in hexane). Iodoperfluoroalkylated product **178** (3.43 g, 6.94 mmol, 69%) was isolated as a colourless oil. The analytical data can be found in chapter 7.4.3.5.

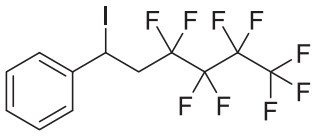
5-Ethyl-1,1,1,2,2,3,3,4,4-nonafluoro-6-iodooctane from *trans*-3-hexene (179)



179

The iodoperfluoroalkylation was performed following general procedure **J** using *trans*-3-hexene (1.24 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washed with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **179** (707 mg, 1.64 mmol, 16%) was isolated as a colourless oil as a mixture of diastereomers (*d.r.*:55:45). The analytical data can be found in chapter 7.4.3.5.

Attempted Preparation of (3,3,4,4,5,5,6,6,6-Nonafluoro-1-iodohexyl)benzene (180)



180

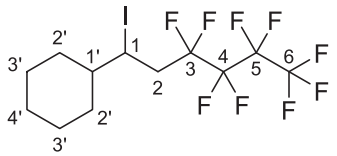
The iodoperfluoroalkylation was performed following general procedure **J** using styrene (**191**) (1.15 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out with magnetic stirring at room temperature until 0.30 F/mol C_4F_9I were consumed. The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (25 g) and washed with *n*-pentane (250 mL). The residue (1.27 g as a yellow oil) was concentrated under reduced pressure. Analysis of the crude material by ^{19}F NMR spectroscopy revealed only product traces and an inseparable mixture of fluorinated, unidentified compounds.

7.4.3.5 Investigation of the Substrate Scope for the Iodoperfluoroalkylation of Alkenes with Hexafluoroisopropanol as Solvent

General Procedure K

The iodoperfluoroalkylation was performed in a divided H-type cell (4G glass filter) with a carbon felt anode and cathode (170 mg, dried at 200 °C/1 mbar for at least 16 hours). A solution of tetrabutylammonium tetrafluoroborate (1.38 g, 4.20 mmol) in hexafluoroisopropanol (10 mL), which was degassed (N_2) for 20 minutes, was added to both sides (5 mL per side). The volume was 10 mL per side with a concentration of tetrabutylammonium tetrafluoroborate of 0.21 M. Alkene (10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.) were added to the cathodic side and hexafluoroisopropanol (5 mL) was added to the anodic side. The constant current electrolysis (10 mA) was carried out with magnetic stirring at room temperature until 0.075 F/mol C_4F_9I were consumed. The mixture was added to sodium thiosulfate (50 mL of a saturated aqueous solution). Dichloromethane (100 mL) and water (150 mL) were added and the phases separated. The mixture was extracted with dichloromethane (3 x 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil.

(3,3,4,4,5,5,6,6,6-Nonafluoro-1-iodohexyl)cyclohexane (159)



159

The iodoperfluoroalkylation was performed following general procedure **K** using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The crude product was purified by filtration through a glass sinter funnel (1 cm diameter) containing a pad of silica (25 g) and washing with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. Iodoperfluoroalkylated product **159** (4.54 g, 9.96 mmol, 97%) was isolated as a colourless oil.

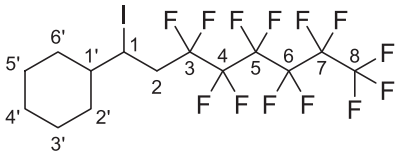
R_f = 0.79 (100% *n*-pentane)

^{19}F NMR (565 MHz, chloroform-*d*):
δ [ppm] = -80.9 – -81.1 (m, 3 F, 6-F), -113.9 (m_c, 2 F, 3-F), -124.5 (m_c, 2 F, 4-F), -125.9 (m_c, 2 F, 5-F).

^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 0.83 (m_c, 1 H, 1‘-H), 1.08 – 1.27 (m, 3 H, 2‘-H – 4‘-H), 1.35 (m_c, 2 H, 2’-H - 4’-H), 1.63 – 1.75 (m, 3 H, 2‘-H – 4‘-H), 1.76 – 1.84 (m, 2 H, 2‘-H – 4‘-H), 2.76 - 2.92 (m, 2 H, 2-H), 4.35 (td, $^{3}J_{1,2}$ = 6.7, $^{3}J_{1,1'}$ = 3.0 Hz, 1 H, 1-H).

The observed data is consistent with the literature.[86]

(3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-iodooctyl)cyclohexane (172)



172

The iodoperfluoroalkylation was performed following general procedure **K** using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and perfluorohexyl iodide (4.32 mL, 20.0 mmol, 2.0 eq.). The crude product was purified by filtration through a glass sinter funnel (1 cm diameter) containing a pad of silica (25 g) and washing with *n*-pentane (200 mL). The residue was concentrated under reduced pressure.

Iodoperfluoroalkylated product **172** (5.38 g, 9.68 mmol, 95%) was isolated as a colourless oil.

R_f = 0.71 (100% *n*-pentane)

^{19}F NMR (282 MHz, chloroform-*d*):
δ [ppm] = -80.9 – -81.4 (m, 3 F, 8-F), -113.8 (m_c, 2 F, 3-F), -122.0 (m_c, 2 F, 4-F), -123.0 (m_c, 2 F, 5-F), -123.8 (m_c, 2 F, 6-F), -126.4 (m_c, 2 F, 7-F).

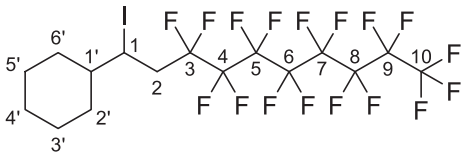
^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 0.83 (m_c, 1 H, 1‘-H), 1.06 – 1.45 (m, 5 H, 2‘-H – 6‘-H), 1.62 – 1.90 (m, 5 H, 2‘-H – 6‘-H), 2.74 – 2.97 (m, 2 H, 2-H), 4.35 (td, $^{3}J_{1,2}$ = 6.7, $^{3}J_{1,1‘}$ = 3.0 Hz, 1 H, 1-H).

^{13}C NMR (75 MHz, chloroform-*d*):
δ [ppm] = 25.7, 25.9 and 26.2 (C-3’ – C-5’), 29.9 (C2’/C-6’) 30.4 (C-1), 33.9 (C-2‘/C-6‘), 39.3 (t, $^{3}J_{C,F}$ = 20.7 Hz, C-2), 44.4 (C-1‘), 104.0 – 124.6 (m, C-3 – C-6).

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 2931; 2857; 1452; 1434; 1365; 1353; 1239; 1205; 1145; 1070; 813; 734; 700; 661; 529.

The observed data is consistent with the literature.[167]

(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododecyl)cyclohexane (173)



173

The iodoperfluoroalkylation was performed following general procedure **K** using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and perfluorooctyl iodide (10.9 g, 20.0 mmol, 2.0 eq.). The crude product was purified by filtration through a glass sinter funnel (1 cm diameter) containing a pad of silica (25 g) and washing with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by distillation (60 °C/10^{-3} mbar). Iodoperfluoroalkylated

product **173** (6.15 g, 9.44 mmol, 92%) was isolated as a colourless oil, which solidified upon standing.

m.p. = 32-34 °C

R_f = 0.78 (100% *n*-pentane)

^{19}F NMR (565 MHz, chloroform-*d*):
δ [ppm] = -80.7 (m_c, 3 F, 10-F), -113.6 (m_c, 2 F, 3-F), -121.4 – -121.6 (m, 2 F, 4-F), -121.8 – -122.0 (m, 4 F, 5-F and 6-F), -122.6 – -122.8 (m, 2 F, 7-F), -123.5 – -123.6 (m, 2 F, 8-F), -126.0 – -126.2 (m_c, 2 F, 9-F).

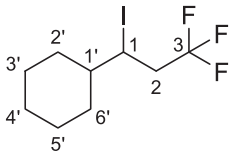
^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 0.83 (m_c, 1 H, 1‘-H), 1.08 – 1.48 (m, 5 H, 2‘-H – 6‘-H), 1.62 – 1.91 (m, 5 H, 2‘-H – 6‘-H), 2.75 – 2.95 (m, 2 H, 2-H), 4.36 (td, $^{3}J_{1,2}$ = 6.7, $^{3}J_{1,1‘}$ = 3.0 Hz, 1 H, 1-H).

^{13}C NMR (75 MHz, chloroform-*d*):
δ [ppm] = 25.7, 25.9 and 26.2 (C-3’ – C-5’), 29.9 (C2’/C-6’) 30.5 (C-1), 33.9 (C-2‘/C-6‘), 39.3 (t, $^{3}J_{C,F}$ = 20.7 Hz, C-2), 44.4 (C-1‘), 103.4 – 124.3 (m, C-3 – C-8).

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 2931; 2857; 1452; 1368; 1327; 1240; 1203; 1148; 977; 913; 872; 744; 705; 657; 557.

elemental analysis:
calculated (%) for $C_{16}H_{14}F_{17}I$: C, 29.29; H, 2.15; found: C, 29.26; H, 2.33.

(3,3,3-Trifluoro-1-iodopropyl)cyclohexane (174)



174

The iodoperfluoroalkylation was performed following general procedure **K** using vinylcyclohexane (**158**) (1.40 mL, 10.2 mmol, 1.0 eq.) and an excess of trifluoromethyl iodide which was supplied using a balloon. The constant current electrolysis (10 mA) was carried out until 0.30 F/mol alkene were consumed. The

crude product was purified by filtration through a glass sinter funnel (1 cm diameter) containing a pad of silica (25 g) and washing with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane). Trifluoromethylated product **152** (1.86 g, 6.06 mmol, 59%) was isolated as a colourless oil.

R_f = 0.72 (100% *n*-pentane)

^{19}F NMR (565 MHz, chloroform-*d*):
δ [ppm] = -64.2 (m_c, 3 F, 3-F).

^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 0.86 (m_c, 1 H, 1‘-H), 1.08 – 1.46 (m, 5 H, 2‘-H – 4‘-H), 1.63 – 1.91 (m, 5 H, 2‘-H – 4‘-H), 2.87 (m_c, 2 H, 2-H), 4.35 (td, $^{3}J_{1,2}$ = 6.9, $^{3}J_{1,1‘}$ = 3.1 Hz, 1 H 1-H).

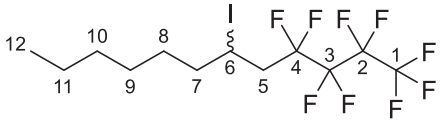
^{13}C NMR (75 MHz, chloroform-*d*):
δ [ppm] = 25.8, 26.0 and 26.2 (C-3’ – C5’), 30.1 (C-2‘/C-6‘), 31.6 (q, $^{4}J_{C,F}$ = 2.6 Hz, C-1), 33.6 (C-2‘/C-6‘), 42.8 (q, $^{3}J_{C,F}$ = 22.3 Hz, C-2), 44.1 (C-1‘), 126.1 (q, $^{2}J_{C,F}$ = 278.4 Hz, C-3).

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 2929; 2855; 1450; 1388; 1371; 1346; 1253; 1194; 1164; 1149; 1072; 958; 841; 686; 602.

elemental analysis:
calculated (%) for $C_9H_{14}F_3I$: C, 35.31; H, 4.61; found: C, 34.69; H, 4.52.

The found value for carbon exceeds the range of 0.4%, probably due to incomplete burning of the CF_3-group or the high volatility.

1,1,1,2,2,3,3,3-Nonafluoro-6-iodododecane (175)



175

The iodoperfluoroalkylation was performed following general procedure **K** using 1-octene (1.60 mL, 10.2 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washed with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **175** (4.32 g, 9.43 mmol, 92%) was isolated as a colourless oil.

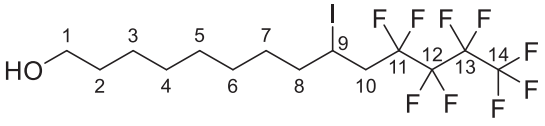
R_f = 0.81 (100% *n*-pentane)

^{19}F NMR (565 MHz, chloroform-*d*):
δ [ppm] = -80.9 – -81.3 (m, 3 F, 1-F), -113.5 (m_c, 2 F, 4-F), -124.4 – -124.8 (m, 2 F, 3-F), -126.0 (m_c, 2 F, 2-F).

^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 0.86 – 0.93 (m, 1 H, 12-H), 1.24 – 1.47 (m, 7 H, 8-H – 11-H), 1.50 – 1.58 (m, 1 H, 8-H – 11-H), 1.73 – 1.89 (m, 2 H, 7-H), 2.70 – 3.00 (m, 2 H, 5-H), 4.33 (m_c, 1 H, 6-H).

The observed data is consistent with the literature.[204]

11,11,12,12,13,13,14,14,14-Nonafluoro-9-iodotetradecan-1-ol (176)



176

The iodoperfluoroalkylation was performed following general procedure **K** using 9-decen-1-ol (1.85 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (25 g) and washed with diethyl ether in

n-pentane (95:5 – 50:50). The residue was concentrated under reduced pressure. Iodoperfluoroalkylated product **176** (4.64 g, 9.25 mmol, 93%) was isolated as a colourless oil.

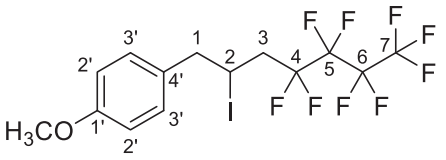
R_f = 0.34 (50% diethyl ether in *n*-pentane)

^{19}F NMR (565 MHz, chloroform-*d*):
δ [ppm] = -80.0 (m_c, 3 F, 14-F), -113.6 (m_c, 2 F, 11-F), -124.6 (m_c, 2 F, 12-F), -125.9 (m_c, 2 F, 13-F).

^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 1.20 – 1.45 (m, 10 H, 2-H – 7-H and -O*H*), 1.50 – 1.61 (m, 3 H, 2-H – 7-H and -O*H*), 1.80 (m_c, 2 H, 8-H), 2.70 – 2.98 (m, 2 H, 10-H), 3.65 (m_c, 2 H, 1-H), 4.33 (m_c, 1 H, 9-H).

The observed data is consistent with the literature.[205]

1-Methoxy-4-(4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptyl)benzene (**178**)



178

The iodoperfluoroalkylation was performed following general procedure **K** using 4-allylanisole (1.54 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. The crude product was purified by flash column chromatography (25 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **178** (4.11 g, 8.31 mmol, 83%) was isolated as a colourless oil.

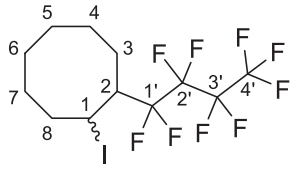
R_f = 0.18 (100% *n*-pentane)

^{19}F NMR (565 MHz, chloroform-*d*):
δ [ppm] = -80.9 – -81.0 (m, 3 F, 7-F), -113.2 (m_c, 2 F, 4-F), -124.4 – -124.6 (m, 2 F, 5-F), -125.8 – -126.0 (m, 2 F, 6-F).

^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 2.86 (m_c, 2 H, 3-H), 3.11 – 3.25 (m, 2 H, 1-H), 3.81 (s, 3 H, OCH_3), 4.42 (m_c, 2 H, 2-H), 6.87 (m_c, 2 H, 2'-H), 7.12 (m_c, 2 H, 3'-H).

The observed data is consistent with the literature.[168]

1-Iodo-2-(perfluorobutyl)cyclooctane (177)



177

The iodoperfluoroalkylation was performed following general procedure **K** using cyclooctene (1.30 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. After 0.075 F/mmol were consumed, nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.) was added a second time. The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washed with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **177** (3.60 g, 7.90 mmol, 79%) was isolated as a colourless oil as a mixture of diastereomers (*d.r.*:75:25).

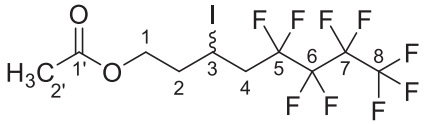
R_f = 0.46 (100% *n*-pentane)

^{19}F NMR (565 MHz, chloroform-*d*):
δ [ppm] = -80.7 – -81.1 (m, 6 F, 4'-F), -115.4 – -118.0 (m, 4 F, 1'-F), -124.0 – -121.7 (m, 4 F, 2'-F), -125.4 – -126.9 (m, 4 F, 3'-F).

^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 1.34 – 1.78 (m), 1.78 – 1.96 (m), 1.96 – 2.18 (m), 2.21 – 2.53 (m), 4.52 (m_c, 1 H, 2-H of diastereomer 1), 4.61 (m_c, 1 H, 2-H of diastereomer 2).

The observed data is consistent with the literature.[86]

5,5,6,6,7,7,8,8,8-Nonafluoro-3-iodooctyl acetate (170)



170

The iodoperfluoroalkylation was performed following general procedure **K** using 3-butenyl acetate (**169**) (1.14 g, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. The crude product was purified by flash column chromatography (25 g silica, 1% ethyl acetate in hexane). Iodoperfluoroalkylated product **170** (3.47 g, 7.55 mmol, 76%) was isolated as a colourless oil.

R_f = 0.38 (10% diethyl ether in *n*-pentane)

^{19}F NMR (282 MHz, chloroform-*d*):
δ [ppm] = -81.0 (tt, $^3J_{8,7}$ = 9.7 Hz, $^4J_{8,6}$ = 3.3 Hz, 3 F, 8-F), -113.2 (m_c, 2 F, 5-F), -124.5 (m, 2 F, 6-F), -125.9 (m, 2 F, 7-F).

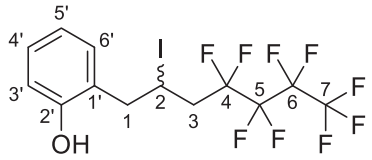
^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 2.06 – 2.17 (m, 4 H, 2-H_a and 2'-H), 2.18 – 2.25 (m, 1 H, 2-H_b), 2.79 – 3.06 (m, 2 H, 4-H), 4.15 – 4.23 (m, 1 H, 1-H_a), 4.31 – 4.37 (m, 1 H, 3-H), 4.40 – 4.47 (m, 1 H, 1-H_b).

^{13}C NMR (151 MHz, chloroform-*d*):
δ [ppm] = 15.3 (C-3), 20.9 (C-2'), 39.0 (C-2), 41.9 (t, $^3J_{C,F}$ = 19.5 Hz, C-4), 64.2 (C-1), 106.0 – 120.4 (m, C-5 – C-8), 170.8 (C-1').

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 2962; 1746; 1541; 1433; 1368; 1352; 1226; 1168; 1135; 1039; 879; 851; 771; 729; 605.

HRMS (ESI):
Calculated for $C_{10}H_{11}F_9IO_2$: 460.9655 [$(M+H)^+$], found: 460.9655; calculated for $C_{10}H_{14}F_9INO_2$: 477.9921 [$(M+NH_4)^+$], found: 477.9920; calculated for $C_{10}H_{10}F_9INaO_2$: 482.9478 [$(M+Na)^+$], found: 482.9474.

2-(4,4,5,5,6,6,7,7,7-Nonafluoro-2-iodoheptyl)phenol (181)



181

The iodoperfluoroalkylation was performed following general procedure **K** using 2-allylphenol (1.31 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washed with ethyl acetate in hexane (95:5). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 2% ethyl acetate in hexane). Iodoperfluoroalkylated product **181** (2.91 g, 6.06 mmol, 61%) was isolated as a white solid.

m.p. = 38-40 °C

R_f = 0.49 (20% ethyl acetate in hexane)

^{19}F NMR (282 MHz, chloroform-*d*):
δ [ppm] = -81.0 (tt, $^3J_{7,6}$ = 9.3 Hz, $^4J_{7,5}$ = 3.2 Hz, 3 F, 7-F), -113.5 (m_c, 2 F, 4-F), -124.6 (m_c, 2 F, 5-F), -125.9 (m_c, 2 F, 6-F).

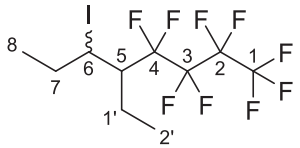
^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 2.81 – 2.98 (m, 2 H, 3-H), 3.23 (dd, $^2J_{1a,1b}$ = 14.3 Hz, $^3J_{1a,2}$ = 8.7 Hz, 1-H_a), 3.36 (dd, $^2J_{1b,1a}$ = 14.3 Hz, $^3J_{1b,2}$ = 6.3 Hz, 1-H_b), 4.69 (m_c, 1 H, 2-H), 6.75 (m_c, 1 H, 3‘-H – 6‘-H), 6.92 (m_c, 1 H, 3‘-H – 6‘-H), 7.13 (m_c, 1 H, 3‘-H – 6‘-H), 7.18 (m_c, 1 H, 3‘-H – 6‘-H).

^{13}C NMR (75 MHz, chloroform-*d*):
δ [ppm] = 18.3 (C-2), 41.0 (t, $^3J_{C,F}$ = 21.1 Hz, C-3), 42.7 (C-1), 115.7 (C-3’), 121.2 (C-5’), 125.7 (C-1’), 128.9 (C-4’), 131.7 (C-6’), 153.6 (C-2’).

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 3535; 3037; 2930; 1610; 1594; 1504; 1457; 1351; 1223; 1134; 1019; 883; 754; 729; 600.

elemental analysis:
calculated (%) for C13H10F9IO: C, 32.52; H, 2.10; found: C, 32.65; H, 2.05.

5-Ethyl-1,1,1,2,2,3,3,4,4-nonafluoro-6-iodooctane from *cis*-3-hexene (179)



179

The iodoperfluoroalkylation was performed following general procedure **K** using *cis*-3-hexene (1.24 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. After 0.075 F/mmol were consumed, nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.) was added a second time. The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washed with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **179** (over all: 2.73 g, 6.35 mmol, 64%) was isolated as two diastereomers (*d.r.*:58:42). Diastereomer 1 (1.60 g, 3.71 mmol, 37%) and diastereomer 2 (1.14 g, 2.64 mmol, 26%) were isolated as colourless oils.

Diastereomer 1:

R_f = 0.83 (100% *n*-pentane)

^{19}F NMR (565 MHz, chloroform-*d*):
δ [ppm] = -80.8 – -81.0 (m, 3 F, 1-F), -109.8 – -114.5 (m, 2 F, 4-F), -121.2 – -123.3 (m, 2 F, 3-F), -125.0 – -126.8 (m, 2 F, 2-F).

^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 1.02 (t, $^{3}J_{8,7}$ = 7.1 Hz, 3 H, 8-H), 1.13 (t, $^{3}J_{2',1'}$ = 7.5 Hz, 3 H, 2'-H), 1.51 - 1.59 (m, 1 H, 1'-H_a), 1.74 – 1.83 (m, 1 H, 1'-H_b), 1.85 – 1.92 (m, 2 H, 7-H), 2.58 – 2.69 (m, 1 H, 5-H), 4.38 (dt, $^{3}J_{6,5}$ = 11.4 Hz, $^{3}J_{6,7}$ = 2.7 Hz, 1 H, 6-H).

Diastereomer 2:

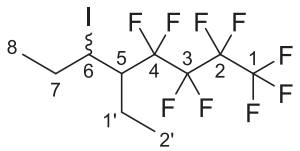
R_f = 0.78 (100% *n*-pentane)

^{19}F NMR (565 MHz, chloroform-*d*):
δ [ppm] = -80.8 – -81.0 (m, 3 F, 1-F), -113.0 – -115.3 (m, 2 F, 4-F), -120.8 – -123.2 (m, 2 F, 3-F), -125.3 – -126.6 (m, 2 F, 2-F).

^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 1.03 – 1.08 (m, 3 H, 8-H), 1.09 – 1.14 (m, 3 H, 2‘-H), 1.64 – 1.80 (m, 2 H, 1‘-H_a and 7-H_a), 1.84 – 1.93 (m, 1 H, 1‘-H_b), 1.99 – 2.16 (m, 2 H, 5-H and 7-H_b), 4.27 – 4.32 (m, 1 H, 6-H).

The observed data is consistent with the literature.[86]

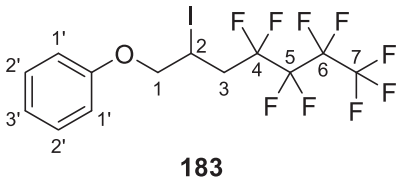
5-Ethyl-1,1,1,2,2,3,3,4,4-nonafluoro-6-iodooctane from *trans*-3-hexene (179)



179

The iodoperfluoroalkylation was performed following general procedure **K** using *trans*-3-hexene (1.24 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. After 0.075 F/mmol were consumed, nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.) was added a second time. The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (15 g) and washed with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **179** (2.60 g, 6.04 mmol, 60%) was isolated as two diastereomers (*d.r.*:62:38). Diastereomer 1 (1.60 g, 3.72 mmol, 37%) and diastereomer 2 (1.00 g, 2.32 mmol, 23%) were isolated as colourless oils.

[(4,4,5,5,6,6,7,7,7-Nonafluoro-2-iodoheptyl)oxy]benzene (183)



183

The iodoperfluoroalkylation was performed following general procedure **K** using allyl phenyl ether (1.34 g, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The crude product was purified by filtration through a glass sinter funnel (1 cm diameter) containing a pad of silica (25 g) and washing with *n*-pentane (200 mL). The residue was concentrated under reduced pressure. Iodoperfluoroalkylated product **183** (4.30 g, 8.96 mmol, 90%) was isolated as a colourless oil.

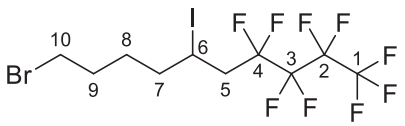
R_f = 0.34 (100% *n*-pentane)

^{19}F NMR (282 MHz, chloroform-*d*):
δ [ppm] = -81.0 (m_c, 3 F, 7-F), -113.8 (m_c, 2 F, 4-F), -124.5 (m_c, 2 F, 5-F), -125.9 (m_c, 2 F, 6-F).

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 2.68 – 2.93 (m, 1 H, 3-H_a), 3.07 – 3.31 (m, 1 H, 3-H_b), 4.18 (dd, $^{2}J_{1a,1b}$ = 10.4 Hz, $^{3}J_{1a,2}$ = 6.8 Hz, 1 H, 1-H_a), 4.30 (dd, $^{2}J_{1b,1a}$ = 10.4 Hz, $^{3}J_{1a,2}$ = 4.9 Hz, 1 H, 1-H_b), 4.52 (tdd, $^{3}J_{2,1b}$ = 6.8 Hz, $^{3}J_{2,3}$ = 6.0 Hz, $^{3}J_{2,1a}$ = 4.9 Hz, 1 H, 2-H), 6.88 – 6.96 (m, 2 H, 1‘-H), 7.01 (m_c, 1 H, 3‘-H), 7.31 (m_c, 2 H, 2‘-H).

The observed data is consistent with the literature.[206]

10-Bromo-1,1,1,2,2,3,3,4,4-nonafluoro-6-iododecane (186)



186

The iodoperfluoroalkylation was performed following general procedure **K** using 6-bromo-1-hexene (**185**) (1.34 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. The crude product was filtered through a

glass sinter funnel (1 cm diameter) containing a pad of silica (25 g) and washed with *n*-pentane. The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **186** (3.38 g, 6.63 mmol, 66%) was isolated as a colourless oil. In addition, 1,1,1,2,2,3,3,4,4-nonafluoro-6,10-diiododecane (**184**) (0.67 g, 1.20 mmol, 12%) was isolated as side product as a colourless oil.

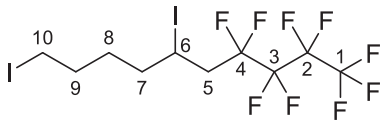
R_f = 0.41 (100% *n*-pentane)

^{19}F NMR (282 MHz, chloroform-*d*):
δ [ppm] = -81.0 (tt, $^3J_{1,2}$ = 9.8 Hz, $^4J_{1,3}$ = 3.5 Hz, 3 F, 1-F), -113.3 (m_c, 2 F, 4-F), -124.5 (m_c, 2 F, 3-F), -125.9 (m_c, 2 F, 2-F).

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 1.49 – 2.02 (m, 6 H, 7-H, 8-H and 9-H), 2.65 – 3.05 (m, 2 H, 5-H), 3.20 (t, $^3J_{10,9}$ = 6.7 Hz, 2 H, 10-H), 4.32 (m_c, 1 H, 6-H).

The observed data is consistent with the literature.[86]

1,1,1,2,2,3,3,4,4-Nonafluoro-6,10-diiododecane (184)



184

The iodoperfluoroalkylation was performed following general procedure **K** using 6-iodo-1-hexene (2.10 g, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. The crude product was filtered through a glass sinter funnel (1 cm diameter) containing a pad of silica (25 g) and washed with *n*-pentane. The residue was concentrated under reduced pressure. The crude product was purified by flash column chromatography (250 g silica, 100% *n*-pentane). Iodoperfluoroalkylated product **184** (4.27 g, 7.68 mmol, 77%) was isolated as a colourless oil.

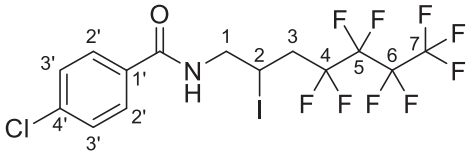
R_f = 0.44 (100% *n*-pentane)

^{19}F NMR (282 MHz, chloroform-*d*):
δ [ppm] = -81.0 (tt, $^{3}J_{1,2}$ = 9.8 Hz, $^{4}J_{1,3}$ = 3.4 Hz, 3 F, 1-F), -113.3 (m_c, 2 F, 4-F), -124.5 (m_c, 2 F, 3-F), -125.9 (m_c, 2 F, 2-F).

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 1.49 – 1.77 (m, 2 H, 8-H), 1.77 – 2.00 (m, 4 H, 7-H and 9-H), 2.65 – 3.05 (m, 2 H, 5-H), 3.20 (m_c, 2 H, 10-H), 4.32 (m_c, 1 H, 6-H).

The observed data is consistent with the literature.[86]

4-Chloro-*N*-(4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptyl)benzamide (182)



182

The iodoperfluoroalkylation was performed following general procedure **K** using *N*-allyl-4-chlorobenzamide (**158**) (1.96 g, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. The crude product was purified by flash column chromatography (150 g silica, 20% ethyl acetate in hexane). Iodoperfluoroalkylated product **182** (4.09 g, 7.56 mmol, 76%) was isolated as a colourless oil.

m.p. = 85 – 87 °C (lit. 87.0 – 87.9)[88]

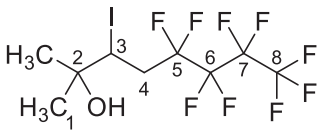
R_f = 0.35 (20% ethyl acetate in hexane)

^{19}F NMR (282 MHz, chloroform-*d*):
δ [ppm] = -81.0 (tt, $^{3}J_{7,6}$ = 9.7 Hz, $^{4}J_{7,5}$ = 3.2 Hz, 3 F, 7-F), -113.2 (m_c, 2 F, 4-F), -124.4 (m_c, 2 F, 5-F), -125.8 (m_c, 2 F, 6-F).

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 2.78 – 3.00 (m, 2 H, 3-H), 3.63 – 3.75 (m, 1 H, 1-H_a), 3.91 – 4.02 (m, 1 H, 1-H_b), 4.55 (m_c, 1 H, 2-H), 6.40 – 6.58 (m, 1 H, N*H*), 7.42 – 7.48 (m, 2 H, 3‘-H), 7.71 – 7.78 (m, 2 H, 2‘-H).

The observed data is consistent with the literature.[88]

5,5,6,6,7,7,8,8,8-Nonafluoro-3-iodo-2-methyloctan-2-ol (103)



103

The iodoperfluoroalkylation was performed following general procedure **K** using 2-methyl-3-buten-2-ol (**158**) (1.05 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. The crude product was purified by flash column chromatography (150 g silica, 10% diethyl ether in *n*-pentane). Iodoperfluoroalkylated product **103** (3.04 g, 7.05 mmol, 71%) was isolated as a colourless oil.

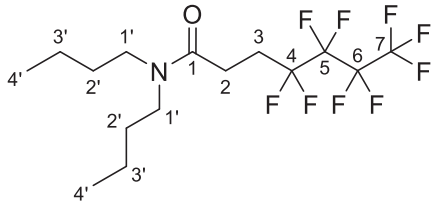
R_f = 0.21 (10% diethyl ether in *n*-pentane)

^{19}F NMR (282 MHz, chloroform-*d*):
δ [ppm] = -81.0 (tt, $^3J_{8,7}$ = 9.7 Hz, $^4J_{8,6}$ = 3.3 Hz, 3 F, 8-F), -113.5 – -116.4 (m, 2 F, 5-F), -124.6 (m_c, 2 F, 6-F), -125.9 (m_c, 2 F, 7-F).

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 1.44 (s, 3 H, CH_3), 1.47 (s, 3 H, CH_3), 1.75 (s, 1 H, O*H*), 2.63 – 2.87 (m, 1 H, 4-H_a), 3.03 – 3.26 (m, 1 H, 4-H_b), 4.25 (dd, $^3J_{3,4a}$ = 9.2 Hz, $^3J_{3,4b}$ = 1.9 Hz, 1 H, 3-H).

The observed data is consistent with the literature.[125]

***N*,*N*-Dibutyl-4,4,5,5,6,6,7,7,7-nonafluoroheptanamide (145)**

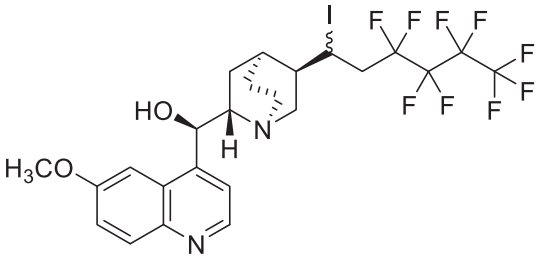


52

The iodoperfluoroalkylation was performed following general procedure **K** using *N*,*N*-dibutylacrylamide (**142**) (1.83 g, 10.0 mmol, 1.0 eq.) and nonafluoro-1-

iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. The crude product was purified by flash column chromatography (150 g silica, 20% ethyl acetate in hexane). No iodoperfluoroalkylated product **146** was isolated. Hydroperfluoroalkylated product **145** (708 mg, 1.33 mmol, 13%) was isolated as a colourless oil.

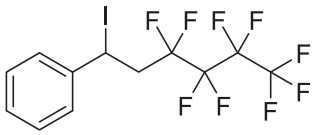
Attempted Preparation of (*R*)-(6-Methoxyquinolin-4-yl)(1*S*,2*S*,4*S*,5*R*)-5-(3,3,4,4,5,5,6,6,6-nonafluoro-1-iodohexyl)quinuclidin-2-yl)methanol (**188**)



188

The iodoperfluoroalkylation was performed following general procedure **K** using quinine (**187**) (3.244 g, 10.0 mmol, 1 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 1.96 eq.). The solubility of quinine was very poor; therefore additional HFIP (5 mL) was added. The constant current electrolysis (10 mA) was carried out until 2.33 F/mol C_4F_9I were consumed. The solution turned black. Analysis of the crude product by ^{19}F-NMR showed only product traces.

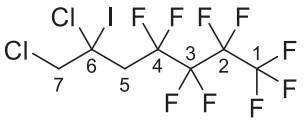
Attempted Preparation of (3,3,4,4,5,5,6,6,6-Nonafluoro-1-iodohexyl)benzene (**180**)



180

The iodoperfluoroalkylation was performed following general procedure **K** using styrene (**191**) (1.15 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.45 F/mol C_4F_9I were consumed. A white rubbery precipitate was formed during the reaction. Analysis of the crude material by ^{19}F NMR spectroscopy revealed only traces of fluorinated, unidentified compounds.

Attempted Preparation of 6,7-Dichloro-1,1,1,2,2,3,3,4,4-nonafluoro-6-iodoheptane (190)

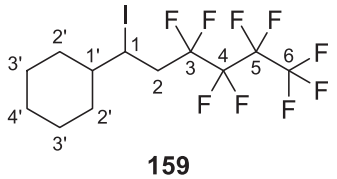


190

The iodoperfluoroalkylation was performed following general procedure **K** using 2,3-dichloropropene (**189**) (0.92 mL, 10.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (3.44 mL, 20.0 mmol, 2.0 eq.). The constant current electrolysis (10 mA) was carried out until 0.15 F/mol C_4F_9I were consumed. Analysis of the crude material by ^{19}F NMR spectroscopy revealed no fluoroalkylation product.

7.4.3.6 Large Scale Transformation

(3,3,4,4,5,5,6,6,6-Nonafluoro-1-iodohexyl)cyclohexane (159)



159

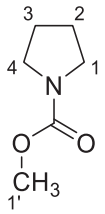
The perfluoroalkylation was performed in a divided H-type cell (4G glass filter) with a carbon felt anode and cathode (170 mg, dried at 200 °C/1 mbar for at least 16 hours). A solution of tetrabutylammonium tetrafluoroborate (4.15 g, 12.6 mmol) in hexafluoroisopropanol (30 mL), which was degassed (N_2) for 20 minutes, was added to both sides (15 mL per side). The volume was 30 mL per side with a concentration of tetrabutylammonium tetrafluoroborate of 0.21 M. Vinylcyclohexane (**158**) (4.10 mL, 30.0 mmol, 1.0 eq.) and nonafluoro-1-iodobutane (10.32 mL, 60.0 mmol, 2.0 eq.) were added to the cathodic side and hexafluoroisopropanol (15 mL) was added to the anodic side. The constant current electrolysis (10 mA) was carried out with magnetic stirring at room temperature until 0.12 F/mol C_4F_9I were consumed. The mixture was added to a solution of sodium thiosulfate (150 mL of a saturated aqueous solution). Dichloromethane (200 mL) and water (200 mL) were added and the phases separated. The product was extracted with dichloromethane (3 x 200 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford the crude reaction mixture as a yellow oil. The crude product was purified by filtration through a glass sinter funnel (1 cm diameter) containing a pad of silica (25 g)

and washing with *n*-pentane (400 mL). The residue was concentrated under reduced pressure. Iodoperfluoroalkylated product **159** (13.0 g, 28.6 mmol, 95%) was isolated as a colourless oil.

7.4.4 Perfluoroalkylation Using the *N*-Acyliminium Ion Pool Method

7.4.4.1 Preparation of Carbamates

_N_-Carbomethoxypyrrolidine (192)



192

Prepared according to the procedure of Tsubata *et al*.[183]

Anhydrous sodium carbonate (100 g, 0.945 mol, 1.9 eq.), pyrrolidine (41.0 mL, 0.500 mol, 1.0 eq.) and dichloromethane (200 mL) were added to a 500 mL three-necked round-bottomed flask equipped with a 100 mL pressure-equalizing dropping funnel and a reflux condenser protected by a calcium chloride tube. Methyl chlorocarbonate (42.1 mL, 0.550 mol, 1.1 eq.) was added dropwise over an hour, sustaining a gentle reflux. The reaction mixture was stirred overnight at room temperature. After 17.5 hours the reaction mixture was filtered through a Büchner funnel and the white precipitate washed with dichloromethane (4 x 100 mL). The filtrate was concentrated on a vacuum rotary evaporator. The crude mixture (yellow oil) was purified by distillation under reduced pressure to afford *N*-carbomethoxy pyrrolidine (**192**) (57.4 g, 0.445 mol, 89%) as a colourless oil.

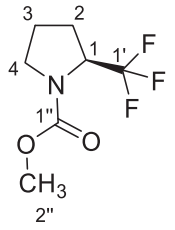
b.p. = 30 °C/0.1 Torr

R_f = 0.23 (20% ethyl acetate in hexane)

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 1.85 (m_c, 4 H, 2-H and 3-H), 3.35 (m_c, 4 H, 1-H and 4-H), 3.69 (s, 3 H, 1'-H).

The observed data is consistent with the literature.[183]

Methyl (*S*)-2-(trifluoromethyl)pyrrolidine-1-carboxylate (195)



195

Prepared according to the procedure of Tsubata *et al*.[183]

Anhydrous sodium carbonate (401 mg, 3.78 mmol, 1.9 eq.), (*S*)-2-trifluoromethylpyrrolidine (278 mg, 2.00 mmol, 1.0 eq.) and dichloromethane (1 mL) were added to a 10 mL Schlenk flask equipped with a reflux condenser protected by a calcium chloride tube. Methyl chlorocarbonate (0.17 mL, 2.2 mmol, 1.1 eq.) was added dropwise, sustaining a gentle reflux. The reaction mixture was stirred overnight at room temperature. After 24 hours the reaction mixture was filtered through a Büchner funnel and the white precipitate washed with dichloromethane (4 x 100 mL). The filtrate was concentrated with a rotary evaporator. The crude mixture (colourless oil) was purified by flash column chromatography (25 g silica, 10% diethyl ether in pentane) to afford methyl (*S*)-2-(trifluoromethyl)pyrrolidine-1-carboxylate (**195**) (190 mg, 0.960 mmol, 48%) as a colourless oil.

R_f = 0.22 (10% diethyl ether in pentane)

^{19}F NMR (565 MHz, chloroform-*d*):
δ [ppm] = -75.2 (s, 3 F, CF_3).

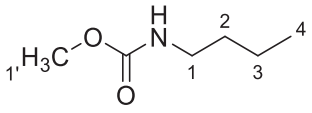
^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 1.87 – 2.15 (m, 4 H, 2-H and 3-H), 3.39 – 3.64 (m, 2 H, 4-H), 3.72 (s, 3 H, 2''-H), 4.25 – 4.65 (s, 1 H, 1-H).

^{13}C NMR (151 MHz, chloroform-*d*):
δ [ppm] = 23.4 (app. d, $^{3}J_{C,F}$ = 150.6 Hz, C-2), 26.1 (app. d, $^{4}J_{C,F}$ = 122.0 Hz, C-3), 47.1 (C-4), 53.0 (C-2''), 58.1 (m, C-1), 125.9 (q, $^{2}J_{C,F}$ = 285.9 Hz, C-1'), 156.4 (C-1'').

IR (Film):
$\tilde{\nu}$ [cm^{-1}] = 2961; 2898; 1715; 1448; 1371; 1272; 1203; 1167; 1139; 1117; 1070; 989; 898; 775; 680.

HRMS (ESI):
Calculated for $C_7H_{10}F_3NO_2H$: 198.0736 [$(M+H)^+$], found: 198.0739.

Methyl butylcarbamate (207)



207

Prepared according to the procedure of Wang *et al*.[187]

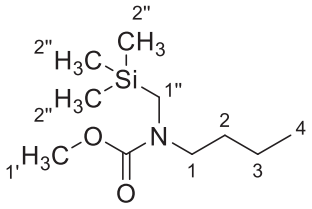
Butylamine (0.95 mL, 9.60 mmol, 1.0 eq.), dimethyl carbonate (4.04 mL, 48.0 mmol, 5.0 eq.) and sulfamic acid (186 mg, 1.92 mmol, 0.19 eq.) were added to a 25 mL two-neck flask equipped with a reflux condenser protected by a calcium chloride tube. The reaction mixture was heated to 100 °C and stirred for 8 hours. The mixture was cooled to room temperature and transferred to a flask containing dichloromethane (30 mL). After filtration the solvent was evaporated under reduced pressure. The residue was filtered through a Büchner funnel, washed with dichloromethane and concentrated under reduced pressure. Methyl butylcarbamate (**207**) (461 mg, 3.52 mmol, 73%) was isolated as a light-yellow oil.

R_f = 0.75 (20% ethyl acetate in hexane)

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 0.91 (t, $^3J_{4,3}$ = 7.2 Hz, 3 H, 4-H), 1.21 – 1.55 (m, 4 H, 2-H and 3-H), 3.05 – 3.27 (m, 2 H, 1-H), 3.65 (s, 3 H,1'-H), 4.64 (s, 1 H, N*H*).

The observed data is consistent with the literature.[187]

Methyl butyl[(trimethylsilyl)methyl]carbamate (208)



208

Prepared according to the procedure of Yoshida *et al*.[188]

Sodium hydride (60% dispersion in mineral oil, 158 mg, 3.94 mmol, 1.2 eq.) was added to a Schlenk flask containing *N*,*N*-dimethylformamide (3 mL). Methyl butylcarbamate (432 mg, 3.30 mmol, 1.0 eq.) in *N*,*N*-dimethylformamide (1 mL) was added at 0 °C. The reaction mixture was heated to 60 °C and stirred for 120 minutes. Iodomethyl trimethylsilane (0.59 mL, 3.98 mmol, 1.2 eq.) was added at 0 °C. The reaction was heated to 60 °C and stirred for 19.5 hours. Afterwards the mixture was poured into water (10 mL) and extracted with diethyl ether (4 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated to afford the crude reaction mixture. The crude product (447 mg) was purified by flash column chromatography (70 g silica, 10 – 20% ethyl acetate in hexane) to afford carbamate **208** (46.1 mg, 0.212 mmol, 6.4%) as a colourless oil.

R_f = 0.49 (20% ethyl acetate in hexane)

^{1}H NMR (600 MHz, chloroform-*d*):
δ [ppm] = 0.04 (s, 9 H, 2''-H), 0.90 (t, $^3J_{4,3}$ = 7.3 Hz, 3 H, 4-H), 1.27 (m_c, 2 H, 3-H), 1.40 – 1.57 (m, 2 H, 2-H), 2.70 (brs, 2 H, 1''-H), 3.04 – 3.19 (m, 2 H, 1-H), 3.64 (s, 3 H, 1'-H).

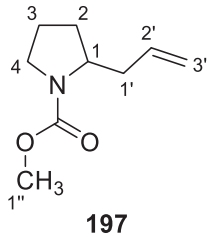
The observed data is consistent with the literature.[188]

7.4.4.2 Attempted Perfluoroalkylation of *N*-Acyliminium Ion Pool

General procedure L

According to the procedures of Suga and Yoshida *et al*. the anodic oxidation was performed in a divided H-type cell (4G glass filter) with a carbon felt anode (320 mg, dried at 200 °C/1 mbar for 2-12 hours) and a platinum plate cathode (40 mm x 20 mm).[28] *N*-carbomethoxy pyrrolidine (**192**) (1.0 eq.) and Bu_4NBF_4/dichloromethane (0.3 M, 20 mL/mmol) were added in the anodic chamber. To the cationic chamber were added Bu_4NBF_4/dichloromethane (0.3 M, 20 mL/mmol) and trifluoromethanesulfonic acid (1.0 eq.). The constant current electrolysis (16-20 mA) was carried out with magnetic stirring at -72 °C until 2.5 F/mol were consumed.

Methyl 2-(2'-propenyl)pyrrolidinecarboxylate (197)



197

Prepared according to the procedure of Yoshida *et al*.[28]

The electrolysis (16 mA) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (112 mg, 0.86 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (120 mg, 0.80 mmol, 0.93 eq.). Allyltrimethylsilane (0.28 mL, 1.77 mmol, 2.05 eq.) was added to the cationic pool in the anodic chamber at -72 °C and the mixture was stirred for 90 minutes. The solvent was removed under reduced pressure. The crude reaction mixture (2.00 g as brown oil) was purified by flash column chromatography (90 g silica, 10% ethyl acetate in hexane) to afford methyl 2-(2-propenyl)pyrrolidinecarboxylate (**197**) as a colourless oil (61.4 mg, 0.363 mmol, 42%).

R_f = 0.20 (10% ethyl acetate in hexane)

^{1}H NMR (300 MHz, chloroform-*d*):
δ [ppm] = 1.61 – 2.01 (m, 4 H, 2-H and 3-H), 2.02 – 2.24 (m, 1 H, 1'-H_a), 2.34 – 2.64 (m, 1 H, 1'-H_b), 3.29 – 3.51 (m, 2 H, 4-H), 3.69 (s, 3 H, 1''-H), 4.91 – 5.14 (m, 2 H, 3'-H), 5.62 – 5.85 (m, 1 H, 2'-H).

The observed data is consistent with the literature.[188]

Removal of Dichloromethane

The electrolysis (20 mA) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (129 mg, 1.00 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.10 mL, 1.14 mmol, 1.14 eq.). After 2.5 F/mol were consumed the solution was transferred to a Schlenk tube and dichloromethane removed under reduced pressure. Allyltrimethylsilane (0.28 mL, 1.77 mmol, 1.77 eq.) and dichloromethane (20 mL) were added to the cationic pool at room temperature and the mixture was stirred for 2 hours. The solvent was removed under reduced pressure. The crude reaction mixture (2.00 g as a brown oil) was purified by flash column chromatography (90 g silica, 10% ethyl acetate in hexane) to afford methyl 2-(2-propenyl)pyrrolidinecarboxylate (**197**) as a colourless oil (62.0 mg, 0.366 mmol, 37%).

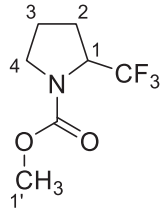
Tetrahydrofuran as Solvent

The electrolysis (20 mA) was performed following general procedure **L** in tetrahydrofuran as solvent at 0 °C using *N*-carbomethoxy pyrrolidine (**192**) (106 mg, 0.800 mmol, 1.0 eq.), trifluoromethanesulfonic acid (0.07 mL, 0.8 mmol, 1.0 eq.) and allyltrimethylsilane (0.28 mL, 1.8 mmol, 2.1 eq.). Analysis of the crude material by ^{1}H NMR spectroscopy and TLC revealed only product traces.

N,*N*-Dimethylformamide as Solvent

The electrolysis (20 mA) was performed following general procedure **L** in *N*,*N*-dimethylformamide as solvent using *N*-carbomethoxy pyrrolidine (**192**) (106 mg, 0.800 mmol, 1.0 eq.), trifluoromethanesulfonic acid (0.07 mL, 0.8 mmol, 1.0 eq.) and allyltrimethylsilane (0.28 mL, 1.8 mmol, 2.1 eq.) at -55° C. No product was isolated upon purification of the crude material by flash column chromatography (90 g silica, 10% ethyl acetate in hexane).

Attempted Preparation of Methyl 2-(Trifluoromethyl)pyrrolidine-1-carboxylate (195)



195

Attempted Trifluoromethylation Using Trifluoromethyltrimethylsilane

The electrolysis (15 mA, 640 mg carbon felt, dried 2 hours) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (108 mg, 0.840 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (120 mg, 0.800 mmol, 0.95 eq.). Trifluoromethyltrimethylsilane (0.25 mL, 1.7 mmol, 2.0 eq.) was added to the cationic pool in the anodic chamber at -72 °C and the reaction mixture was stirred for 17 hours. The solvent was removed under reduced pressure and the residue filtered through a glass sinter funnel (3 cm diameter) containing a pad of silica (7 g) and washed with diethyl ether (200 mL). The residue was concentrated under reduced pressure. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no trifluoromethylated product.

Attempted Trifluoromethylation using Trifluoromethyltrimethylsilane and TBAF

The electrolysis (15 mA, 640 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (108 mg, 0.840 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (120 mg, 0.800 mmol, 0.95 eq.). Trifluoromethyltrimethylsilane (0.25 mL, 1.68 mmol, 2.0 eq.) and tetrabutylammonium fluoride (1.68 mL of a 1 M solution in tetrahydrofuran, 1.68 mmol, 2.0 eq.) were added to the cationic pool in the anodic chamber at -72 °C and the reaction mixture was stirred overnight. The solvent was removed under reduced pressure and the residue filtered through a glass sinter funnel (3 cm diameter) containing a pad of silica (7 g) and washed with diethyl ether (200 mL). The residue was concentrated under reduced pressure. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no trifluoromethylated product.

Attempted Trifluoromethylation using Trifluoromethyltrimethylsilane and TBAF at -72 °C to Room Temperature

The electrolysis (20 mA, 320 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (155 mg, 1.20 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.11 mL, 1.2 mmol, 1.0 eq.). Trifluoromethyltrimethylsilane (0.37 mL, 2.5 mmol, 2.1 eq.) and tetrabutylammonium fluoride (2.52 mL of a 1 M solution in tetrahydrofuran, 2.52 mmol, 2.1 eq.) were added to the cationic pool in the anodic chamber at -72 °C and the reaction mixture was allowed to warm to 0 °C and stirred overnight. Afterwards, the reaction was allowed to warm to room temperature and stirred for another 3 hours. The solvent was removed under reduced pressure and the residue filtered through a glass sinter funnel (3 cm diameter) containing a pad of silica (7 g) and washed with diethyl ether (200 mL). The residue was concentrated under reduced pressure. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no trifluoromethylated product.

Attempted Trifluoromethylation Using Trifluoromethyltrimethylsilane and CsF

The electrolysis (11-20 mA, 320 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (155 mg, 1.20 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.11 mL, 1.2 mmol, 1.0 eq.). Trifluoromethyltrimethylsilane (0.37 mL, 2.5 mmol, 2.1 eq.), cesium fluoride (382 mg, 2.52 mmol, 2.1 eq., dried with heat gun in high vacuum for 2 hours), dissolved in tetrahydrofuran (4.5 mL) and *N*,*N*-dimethylformamide (0.5 mL) were added to the cationic pool in the anodic chamber at -72 °C and the reaction mixture was stirred for 24 hours. Analysis of the reaction mixture by ^{19}F NMR spectroscopy and TLC showed no conversion. Therefore, HF/pyridine (0.07 mL, 3.6 mmol, 3.0 eq.) was added and the reaction stirred for an additional 20 hours. The solvent was removed under reduced pressure and the residue filtered through a glass sinter funnel (3 cm diameter) containing a pad of silica (7 g) and washed with diethyl ether (200 mL). The residue was concentrated under reduced pressure. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no trifluoromethylated product.

Attempted Trifluoromethylation using Trifluoromethyltrimethylsilane and TBAT, after Changing the Solvent to Tetrahydrofuran

The electrolysis (14 mA, 320 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (106 mg, 0.800 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.07 mL, 0.8 mmol, 1.0 eq.). After 2.5 F/mol were consumed, the solution was transferred to a two-necked flask and dichloromethane removed under reduced pressure. Trifluoromethyltrimethylsilane (0.17 mL, 1.0 mmol, 1.3 eq.), tetrahydrofuran (15 mL) and tetrabutylammonium difluorotriphenylsilicate (556 mg, 1.03 mmol, 1.3 eq.) were added at -55 °C and the reaction mixture was stirred for 18.5 hours. The solvent was removed under reduced pressure and the residue filtered through a glass sinter funnel (3 cm diameter) containing a pad of silica (7 g) and washed with diethyl ether (200 mL). The residue was concentrated under reduced pressure. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no trifluoromethylated product.

Attempted Trifluoromethylation Using Trifluoromethyltrimethylsilane (1.5 eq.) and Sodium Acetate (2.0 eq.)

Attempted preparation following the procedure of Tartakovsky *et al*.[192]

The electrolysis (13 mA, 320 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (106 mg, 0.800 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.07 mL, 0.8 mmol, 1.0 eq.). After 2.5 F/mol were consumed, the solution was transferred in a two-necked flask and dichloromethane removed under reduced pressure. Trifluoromethyltrimethylsilane (0.19 mL, 1.3 mmol, 1.5 eq.), *N*,*N*-dimethylformamide (15 mL) and anhydrous sodium acetate (141 mg, 1.72 mmol, 2.0 eq., dried at 200 °C/1 mbar for 2 hours) were added at room temperature and the reaction mixture was stirred for 18.5 hours. Sodium carbonate (1 mL of a saturated aqueous solution) was added, followed by dichloromethane (15 mL). The solution was washed with water (4 x 50 mL), dried (Na_2SO_4) and concentrated. The crude reaction mixture (138 mg as brown oil) was purified by flash column chromatography (32 g silica, 10% ethyl acetate in hexane). No product was isolated.

Attempted Trifluoromethylation Using Trifluoromethyltrimethylsilane (3.0 eq.) and Sodium Acetate (4.0 eq.) in a Smaller Volume (3 mL)

Attempted preparation following the procedure of Tartakovsky *et al*.[192]

The electrolysis (10-20 mA, 320 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (129 mg, 1.00 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.22 mL, 2.5 mmol, 2.5 eq.). After 2.5 F/mol were consumed, the solution was transferred in a two-necked flask and dichloromethane removed under reduced pressure. Trifluoromethyltrimethylsilane (0.44 mL, 3.0 mmol, 3.0 eq.), *N*,*N*-dimethylformamide (3 mL) and anhydrous sodium acetate (328 mg, 4.00 mmol, 4.0 eq., dried at 150 °C/1 mbar for 3.5 hours) were added at room temperature and the reaction mixture was stirred for 18 hours. Sodium carbonate (3 mL of a saturated aqueous solution) was added and the mixture stirred for 2 minutes. Subsequently, water was added (15 mL) and the mixture extracted with diethyl ether and hexane (1:1, 3 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. The crude reaction mixture (93 mg as brown oil) was purified by flash column chromatography (30 g silica, 10% ethyl acetate in hexane). No product was isolated.

Attempted Trifluoromethylation Using Trifluoromethyltrimethylsilane (3.0 eq.) and Potassium Fluoride (2.0 eq.)

Attempted preparation following the procedure of Tartakovsky *et al*.[192]

The electrolysis (19 mA, 320 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (129 mg, 1.00 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.22 mL, 2.5 mmol, 2.5 eq.). After 2.5 F/mol were consumed, the solution was transferred in a two-necked flask and dichloromethane removed under reduced pressure. Trifluoromethyltrimethylsilane (0.44 mL, 3.0 mmol, 3.0 eq.), *N*,*N*-dimethylformamide (3 mL) and anhydrous potassium fluoride (232 mg, 2.00 mmol, 2.0 eq., dried at 150 °C/1 mbar for 2 hours) were added at room temperature and the reaction mixture was stirred for 18 hours. Sodium carbonate (3 mL of a saturated aqueous solution) was added and the mixture stirred for 2 minutes. Subsequently, water was added (15 mL) and the mixture extracted with diethyl ether and hexane (1:1, 3 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. The crude reaction mixture (82 mg as brown oil) was purified by flash column chromatography (30 g silica, 10% ethyl acetate in hexane). No product was isolated.

Attempted Trifluoromethylation Using Trifluoromethyltrimethylsilane (3.0 eq.) and Sodium Acetate (4.0 eq.) with (Trifluoromethyl)cyclohexane as Internal Standard

Attempted preparation following the procedure of Tartakovsky *et al*.[192]

The electrolysis (20 mA, 320 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (129 mg, 1.00 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.22 mL, 2.5 mmol, 2.5 eq.). After 2.5 F/mol were consumed, the solution was transferred in a two-necked flask and dichloromethane removed under reduced pressure. Trifluoromethyltrimethylsilane (0.44 mL, 3.0 mmol, 3.0 eq.), *N*,*N*-dimethylformamide (3 mL), anhydrous sodium acetate (328 mg, 4.00 mmol, 4.0 eq., dried at 200 °C/1 mbar for 5.5 hours) and (trifluoromethyl)cyclohexane (0.03 mL, 0.2 mmol, 0.22 eq.) as internal standard were added at room temperature and the reaction mixture was stirred for 23 hours. Sodium hydrogen carbonate (1 mL of a saturated aqueous solution) was added and the mixture stirred for 2 minutes. Subsequently, water was added (20 mL) and the mixture extracted with diethyl ether and hexane (1:1, 3 x 10 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. The crude reaction mixture (95 mg as a yellow oil) was purified by flash column chromatography (30 g silica, deactivated with 1% triethylamine, 20% diethyl ether in pentane). No product was isolated.

Attempted Trifluoromethylation Using Trifluoromethyltrimethylsilane (3.0 eq.) and Sodium Acetate (4.0 eq.) and Attempted Purification over Aluminium Oxide

Attempted preparation following the procedure of Tartakovsky *et al*.[192]

The electrolysis (17-19 mA, 320 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (129 mg, 1.00 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.22 mL, 2.5 mmol, 2.5 eq.). After 2.5 F/mol were consumed, the solution was transferred in a two-necked flask and dichloromethane removed under reduced pressure. Trifluoromethyltrimethylsilane (0.44 mL, 3.0 mmol, 3.0 eq.), *N*,*N*-dimethylformamide (3 mL) and anhydrous sodium acetate (328 mg, 4.00 mmol, 4.0 eq., dried at 200 °C/1 mbar for 5.5 hours) were added at room temperature and the reaction mixture was stirred for 23 hours. Sodium hydrogen carbonate (1 mL of a saturated aqueous solution) was added and the mixture stirred for 2 minutes. Subsequently water was added (20 mL) and the mixture extracted with a mixture of diethyl ether and hexane (1:1, 3 x 10 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. The crude reaction mixture

(175 mg as a yellow oil) was purified by flash column chromatography (aluminium oxide, activity III, 10% diethyl ether in pentane). No product was isolated.

Attempted Trifluoromethylation Using Trifluoromethyltrimethylsilane (2.0 eq.) and TBAF (2.1 eq.) Followed by Addition of Cyclohexanone (1.0 eq.)

The electrolysis (22 mA, 340 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (129 mg, 1.00 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.10 mL, 1.1 mmol, 1.1 eq.). After 2.5 F/mol were consumed, the solution was transferred to a Schlenk tube and dichloromethane removed under reduced pressure. Trifluoromethyltrimethylsilane (0.30 mL, 2.0 mmol, 2.0 eq.), tetrahydrofuran (5 mL) and tetrabutylammonium fluoride trihydrate (665 mg, 2.10 mmol, 2.1 eq.) were added at room temperature and the reaction mixture was stirred for 18 hours. Cyclohexanone (0.10 mL, 1.0 mmol, 1.0 eq.) was added and the reaction stirred for 5 hours. Aqueous HCl-solution (20 mL, 0.1 M) was added, followed by water (20 mL) and the mixture extracted with ethyl acetate (3 x 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no trifluoromethylated product.

Attempted Trifluoromethylation Using Trifluoromethyltrimethylsilane (4.0 eq.) and Sodium Acetate (7.0 eq.) and Addition of Cyclohexanone (1.0 eq.)

The electrolysis (20 mA, 320 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (129 mg, 1.00 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.10 mL, 1.1 mmol, 1.14 eq.). After 2.5 F/mol were consumed the solution was transferred in a Schlenk tube and dichloromethane removed under reduced pressure. Trifluoromethyltrimethylsilane (0.59 mL, 4.0 mmol, 4.0 eq.), tetrahydrofuran (5. mL), cyclohexanone (0.10 mL, 1.0 mmol, 1.0 eq.) and anhydrous sodium acetate (574 mg, 7.00 mmol, 7.0 eq., dried at 200 °C/1 mbar for 2 hours) were added at room temperature and the reaction mixture was stirred for 23 hours. Aqueous HCl-Solution (5 mL, 1 M) was added and the mixture stirred for 130 minutes. Subsequently, water was added (15 mL) and the mixture extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. The crude reaction mixture was filtered through a glass sinter funnel (3 cm diameter) containing a pad of silica (7 g) and washed with diethyl ether (200 mL). The residue was concentrated under reduced pressure.

Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no trifluoromethylated product.

Attempted Trifluoromethylation Using Trifluoromethyltrimethylsilane (2.4 eq.), Potassium Fluoride (3.5 eq.) and Triphenyltin Fluoride (0.60 eq.) as Phase Transfer Catalyst

Attempted preparation according to the procedures of Makosza *et al*.[185]

The electrolysis (16 mA, 320 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (129 mg, 1.00 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.22 mL, 2.5 mmol, 2.5 eq.). Trifluoromethyltrimethylsilane (0.35 mL, 2.4 mmol, 2.4 eq.) and potassium fluoride (203 mg, 3.50 mmol, 3.5 eq., dried at 150 °C/1 mbar for 3 hours) and triphenyltin fluoride (221 mg, 0.600 mmol, 0.60 eq.) were added to the cationic pool in the anodic chamber at room temperature and the reaction mixture was stirred for 5 days. The solvent was removed under reduced pressure and the residue filtered through a glass sinter funnel (3 cm diameter) containing a pad of silica (7 g) and washed with diethyl ether (200 mL). The residue was concentrated under reduced pressure. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no trifluoromethylated product.

Repetition of the experiment with a further washing step after the reaction (before filtering) showed no different outcome.

Attempted Trifluoromethylation Using the Cathodic Reduction of Trifluoromethyl Iodide

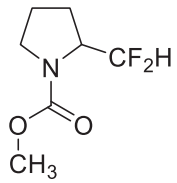
Attempted preparation following the procedure of Yoshida *et al*.[186]

The electrolysis (9 mA, 340 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (56 mg, 0.43 mmol, 1.0 eq.), trifluoromethanesulfonic acid (0.10 mL, 1.1 mmol, 2.7 eq.) and tetrabutylammonium tetrafluoroborate in dichloromethane (0.06 M, 40 mL). After 2.5 F/mol were consumed, tetrahydrofuran (0.3 mL) was added to the anodic chamber and the platinum electrode exchanged with a graphite electrode. A balloon filled with an excess of trifluoromethyl iodide gas (~200 mL) was added to the cationic chamber. The cathode and anode connection were switched and the electrolysis (11 mA) was performed until 2.5 F/mol were consumed. The reaction was

stirred for an additional 72 minutes. The solvent was removed under reduced pressure and the residue filtered through a glass sinter funnel (3 cm diameter) containing a pad of silica (7 g) and washed with diethyl ether (200 mL). The residue was concentrated under reduced pressure. The crude reaction mixture was purified by flash column chromatography (25 g silica, 10% diethyl ether in pentane). No product was isolated.

This attempt for a trifluoromethylation was performed two times.

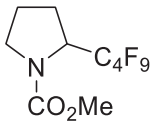
Attempted Preparation of Methyl 2-Difluoromethyl Pyrrolidinecarboxylate (201)



201

The electrolysis (18 mA, 340 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (129 mg, 1.00 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.10 mL, 1.1 mmol, 1.1 eq.). After 2.5 F/mol were consumed the solution was transferred to a Schlenk tube and dichloromethane removed under reduced pressure. Difluoromethyltrimethylsilane (186 mg, 1.50 mmol, 1.5 eq.), tetrahydrofuran (5 mL) and tetrabutylammonium difluorotriphenylsilicate (556 mg, 1.03 mmol, 1.0 eq.) were added at room temperature and the reaction mixture was stirred for 36 hours. The solvent was removed under reduced pressure and the residue filtered through a glass sinter funnel (3 cm diameter) containing a pad of silica (7 g) and washed with diethyl ether (200 mL). The residue was concentrated under reduced pressure. The crude reaction mixture was purified by flash column chromatography (70 g silica, 30% ethyl acetate in hexane). No product was isolated.

Attempted Preparation of Methyl-2-(perfluorobutyl)pyrrolidine-1-carboxylate (202)



202

Attempted Perfluoroalkylation Using Nonafluoro-1-iodobutane and Hexabutyldistannane

Attempted preparation following the procedure of Yoshida *et al*.[182, 184]

The electrolysis (20 mA, 320 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (155 mg, 1.20 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (450 mg, 3.00 mmol, 2.5 eq.). Nonafluoro-1-iodobutane (1.03 mL, 6.00 mmol, 5.0 eq.) and hexabutyldistannane (0.91 mL, 1.8 mmol, 1.5 eq.) were added to the cationic pool in the anodic chamber at -20 °C and the reaction mixture was stirred for 16.5 hours. Triethylamine (0.80 mL, 5.8 mmol, 4.8 eq.) was added and the solvent was removed under reduced pressure. The residue was filtered through a glass sinter funnel (3 cm diameter) containing a pad of silica (7 g) and washed with diethyl ether (200 mL). The filtrate was concentrated under reduced pressure. The crude reaction mixture (321 mg as a yellow oil) was purified by flash column chromatography (75 g silica, 22% ethyl acetate in hexane). No product was isolated.

Attempted Perfluoroalkylation Using the Cathodic Reduction of Nonafluoro-1-iodobutane

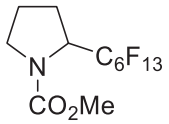
Attempted preparation following the procedure of Yoshida *et al*.[186]

The electrolysis (7 mA, 340 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (56 mg, 0.43 mmol, 1.0 eq.), trifluoromethanesulfonic acid (0.1 mL, 1.1 mmol, 2.7 eq.) and tetrabutylammonium tetrafluoroborate in dichloromethane (0.06 M, 40 mL). After 2.5 F/mol were consumed tetrahydrofuran (0.3 mL) was added to the anodic chamber and the platinum electrode exchanged with a graphite electrode. Nonafluoro-1-iodobutane (2.00 mL, 11.6 mmol, 11.6 eq.) was added to the cationic chamber. The cathode and anode connection were switched and the electrolysis (10 mA) was performed until 2.5 F/mol were consumed. The reaction was stirred for an additional 165 minutes. The solvent was removed under reduced pressure and

the residue filtered through a glass sinter funnel (3 cm diameter) containing a pad of silica (7 g) and washed with diethyl ether (200 mL). The residue was concentrated under reduced pressure. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no trifluoromethylated product.

The reaction was repeated with a smaller amount of nonafluoro-1-iodobutane (0.60 mL, 3.5 mmol, 3.5 eq.) to avoid dimerization. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no trifluoromethylated product.

Attempted Preparation of Methyl-2-(perfluorohexyl)pyrrolidine-1-carboxylate (203)

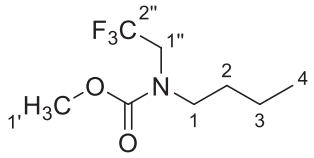


203

Preparation attempted according to the procedure of Yoshida *et al*.[184]

The electrolysis (18 mA, 320 mg carbon felt, dried o.n.) was performed following general procedure **L** using *N*-carbomethoxy pyrrolidine (**192**) (129 mg, 1.00 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.22 mL, 2.5 mmol, 2.5 eq.). Perfluorohexyl iodide (1.51 mL, 4.50 mmol, 4.5 eq.) and hexabutyldistannane (0.71 mL, 1.4 mmol, 1.4 eq.) were added to the cationic pool in the anodic chamber at -20 °C and the reaction mixture was stirred for 16.5 hours. Triethylamine (0.80 mL, 5.8 mmol, 5.8 eq.) was added and the solvent was removed under reduced pressure. The residue was filtered through a glass sinter funnel (3 cm diameter) containing a pad of silica (7 g) and washed with diethyl ether (200 mL). The filtrate was concentrated under reduced pressure. Analysis of the crude material by ^{19}F NMR spectroscopy and TLC revealed no trifluoromethylated product.

Methyl butyl(2,2,2-trifluoroethyl)carbamate (210)



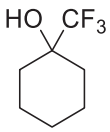
210

Preparation attempted according to the procedure of Yoshida *et al.*[188]

The electrolysis (13 mA, 120 mg carbon felt, dried o.n.) was performed following general procedure **L** using methyl butyl[(trimethylsilyl)methyl]carbamate (**208**) (46.1 mg, 0.212 mmol, 1.0 eq.) and trifluoromethanesulfonic acid (0.05 mL, 0.53 mmol, 2.5 eq.). After 3.0 F/mol were consumed the solution was transferred in a Schlenk tube and dichloromethane removed under reduced pressure. Trifluoromethyltrimethylsilane (0.09 mL, 0.6 mmol, 3.0 eq.), *N*,*N*-dimethylformamide (3 mL) and anhydrous sodium acetate (68.9 mg, 0.840 mmol, 4.0 eq., dried at 200 °C/1 mbar for 2 hours) were added at 0 °C and the reaction mixture was stirred overnight at room temperature. Analysis of the reaction mixture by ^{19}F NMR spectroscopy and TLC revealed no trifluoromethylated product.

7.4.4.3 Perfluoroalkylation of Cyclohexanone

1-(Trifluoromethyl)cyclohexan-1-ol (200)



200

Prepared according to the procedures of Prakash *et al.*[52]

Cyclohexanone (0.52 mL, 5.00 mmol, 1.0 eq.) and trifluoromethyltrimethylsilane (0.89 mL, 6.00 mmol, 1.2 eq.) were added to tetrahydrofuran (12.5 mL) at 0 °C. Tetrabutylammonium fluoride trihydrate (10 mg, 0.030 mmol, 0.60 mol%) was added and the mixture warmed to room temperature. After 4 hours, aqueous HCl-solution (13 mL, 1 M) was added. After an additional 75 minutes, water (15 mL) was added and the reaction mixture extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. Analysis of the crude material by ^{19}F NMR spectroscopy revealed the expected product peak.

^{19}F NMR (282 MHz, chloroform-*d*):
δ [ppm] = -85.1 (s, 3 H, C*F*$_3$).

The reaction was repeated following the reported procedure. Instead of tetrahydrofuran a mixture of tetrahydrofuran and dichloromethane (1:1) was used as solvent. Analysis of the crude material by ^{19}F NMR spectroscopy revealed the expected product peak as well as an additional peak at -82.6 ppm.

8 References

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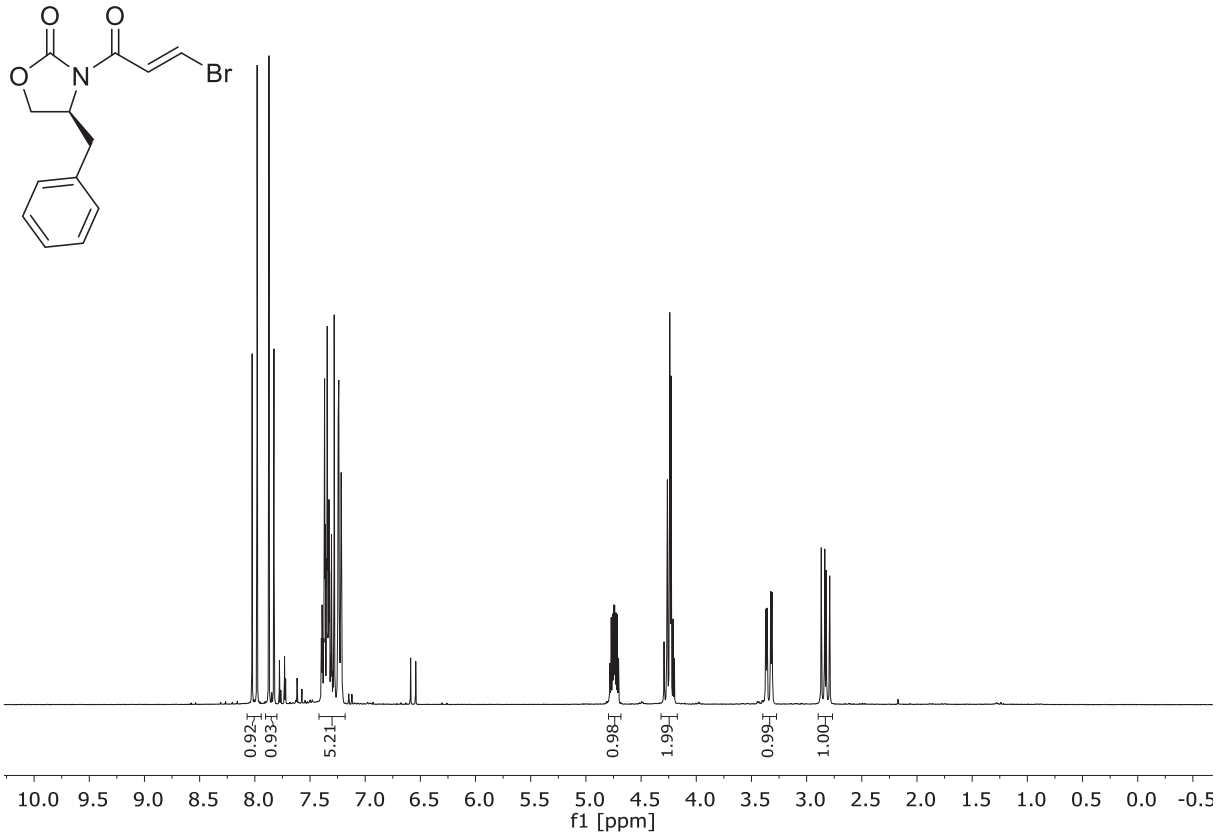
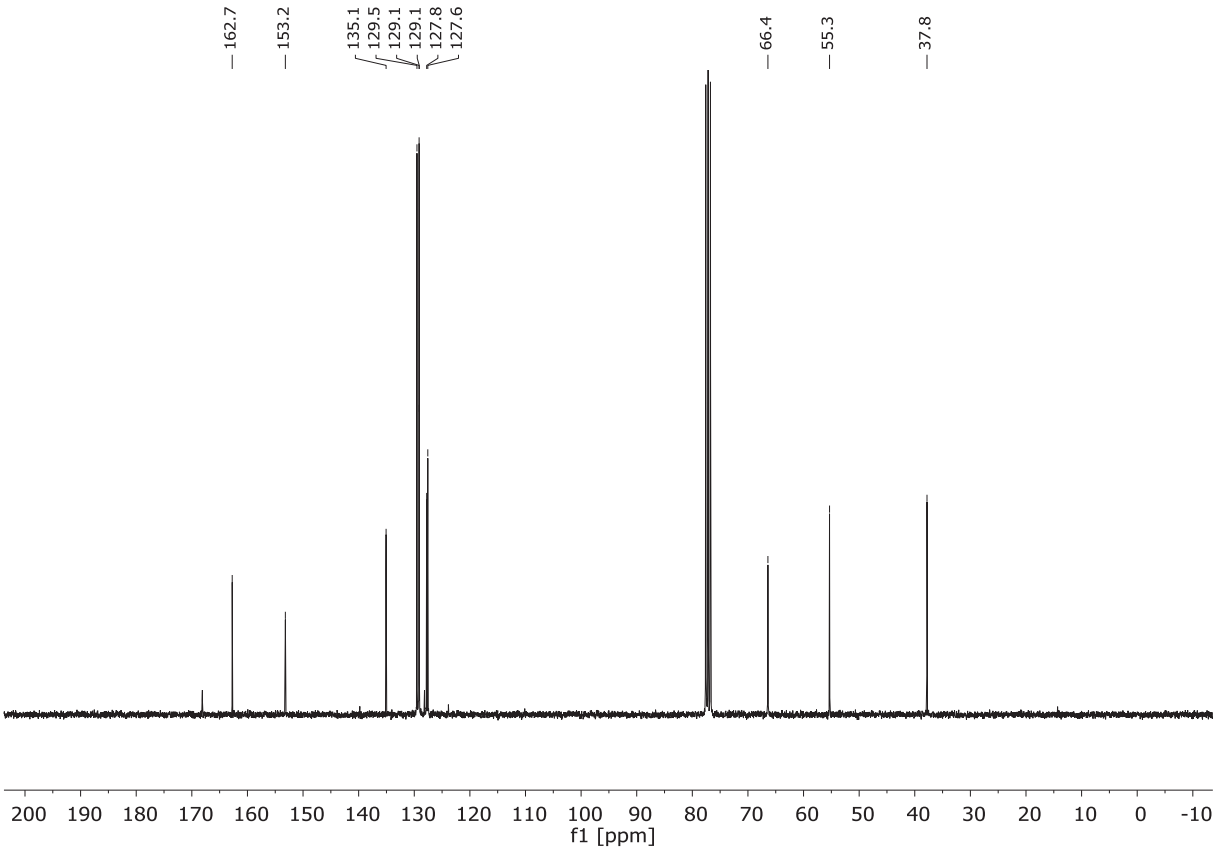
9 Spectra

Copies of ^{1}H-NMR-, ^{13}C-NMR- and ^{19}F-NMR-chromatograms and IR-chromatograms from the synthesized new compounds, as well as ^{1}H-NMR- and ^{19}F-NMR-chromatograms of the hydro- and iodoperfluoroalkylated products.

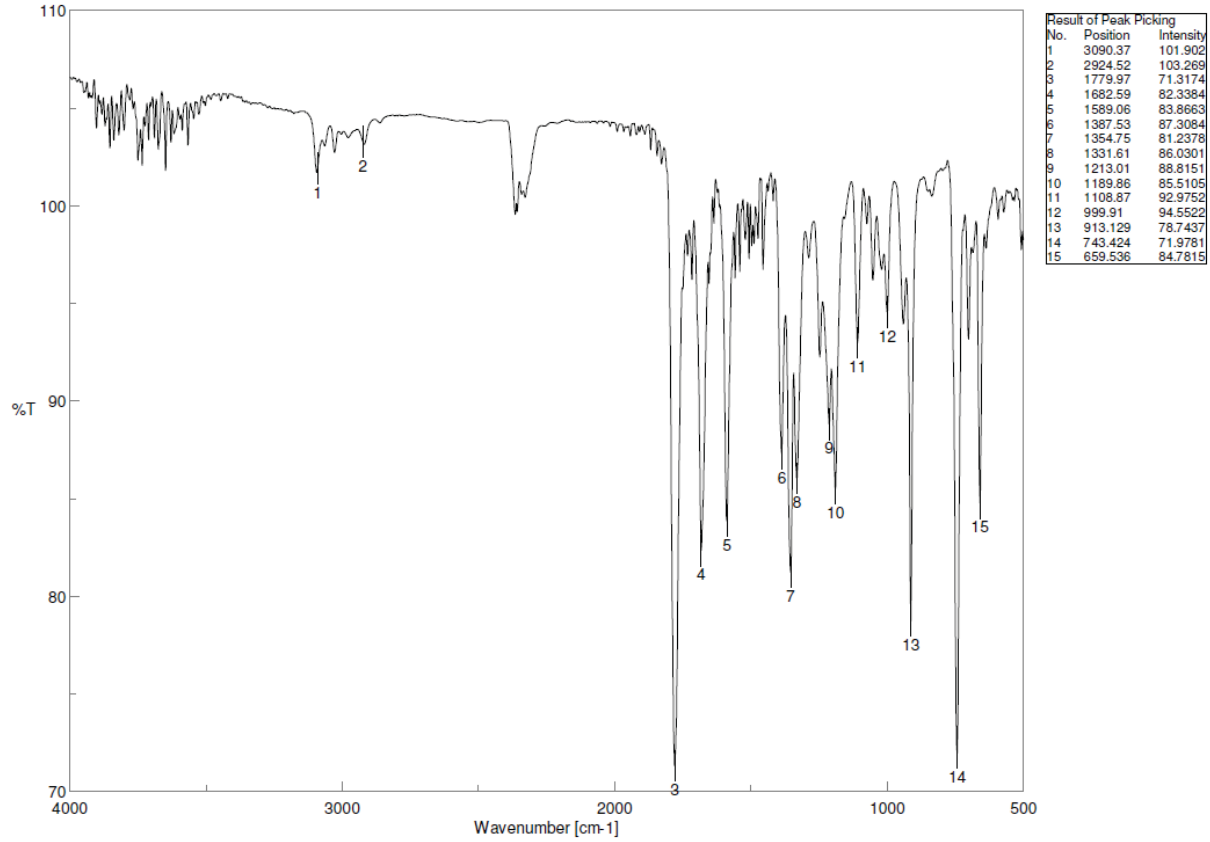
(4*S*,2'*E*)-4-Benzyl-3-(3'-bromoacryloyl)oxazolidin-2-one (139)



^{1}H NMR (300 MHz, chloroform-*d*)

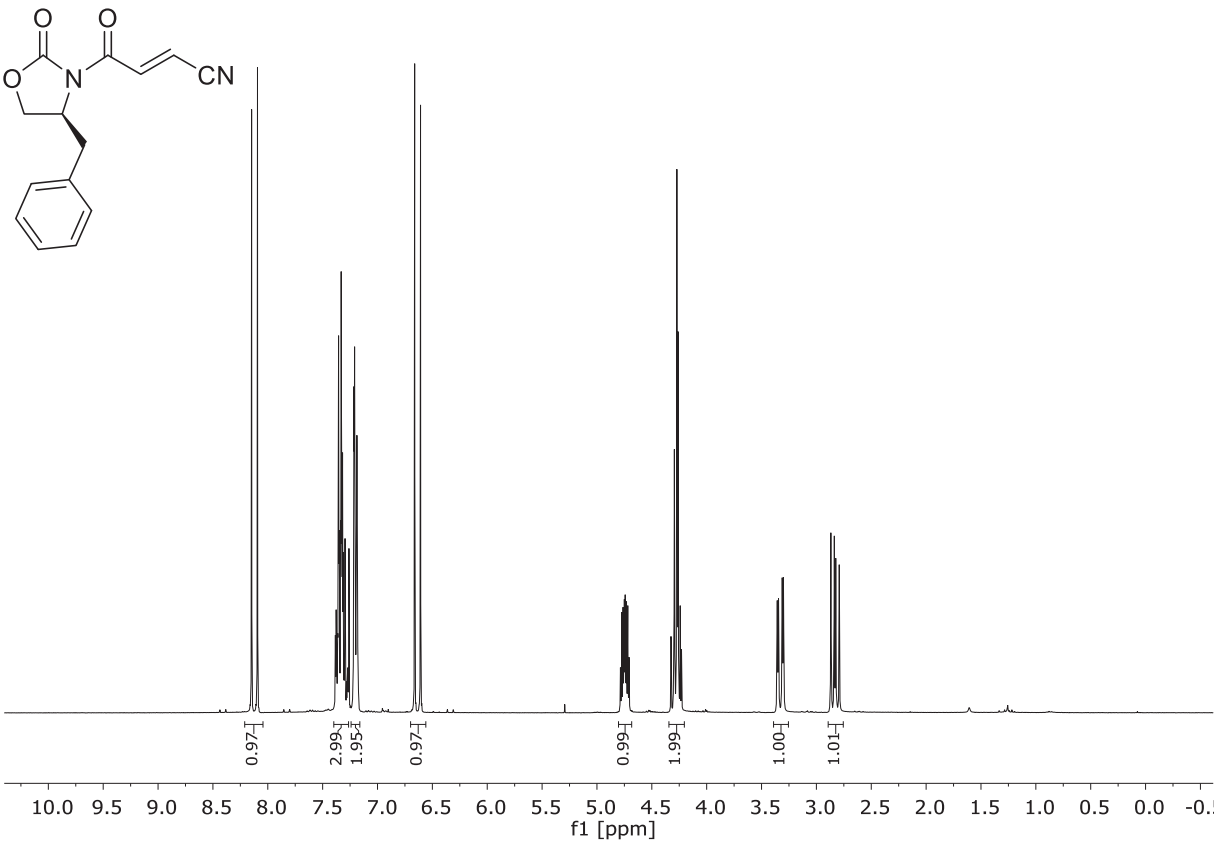


^{13}C NMR (75 MHz, chloroform-*d*)

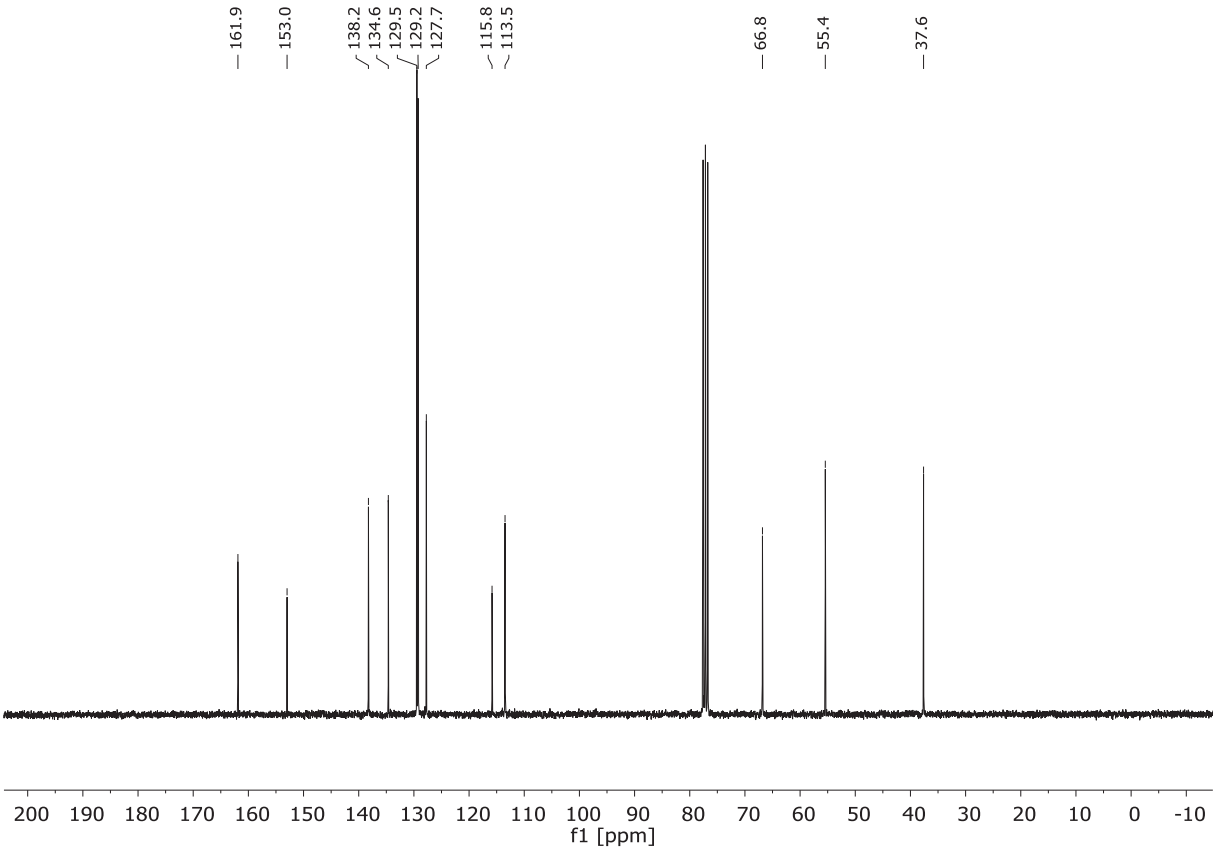


IR (Film)

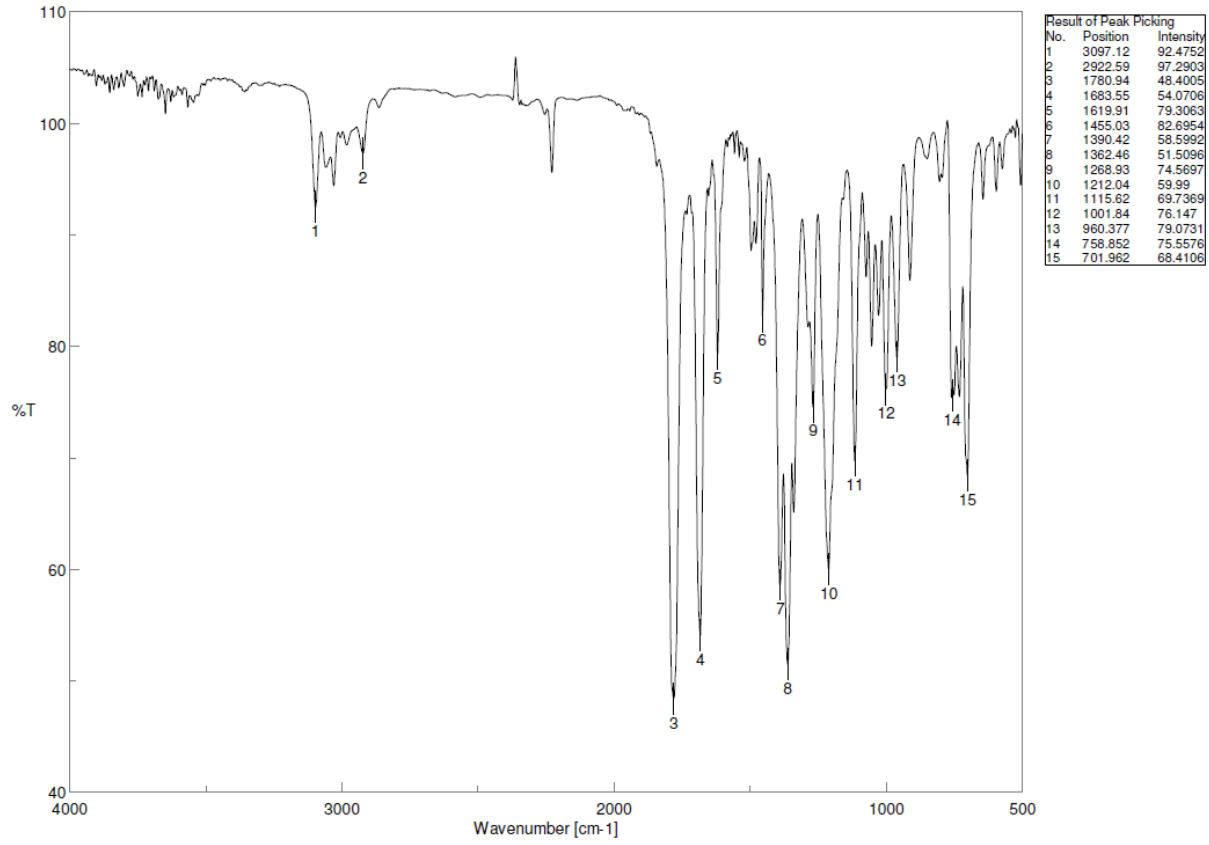
(*S*,*E*)-4-(4-Benzyl-2-oxooxazolidin-3-yl)-4-oxobut-2-enenitrile (140)



^{1}H NMR (300 MHz, chloroform-*d*)

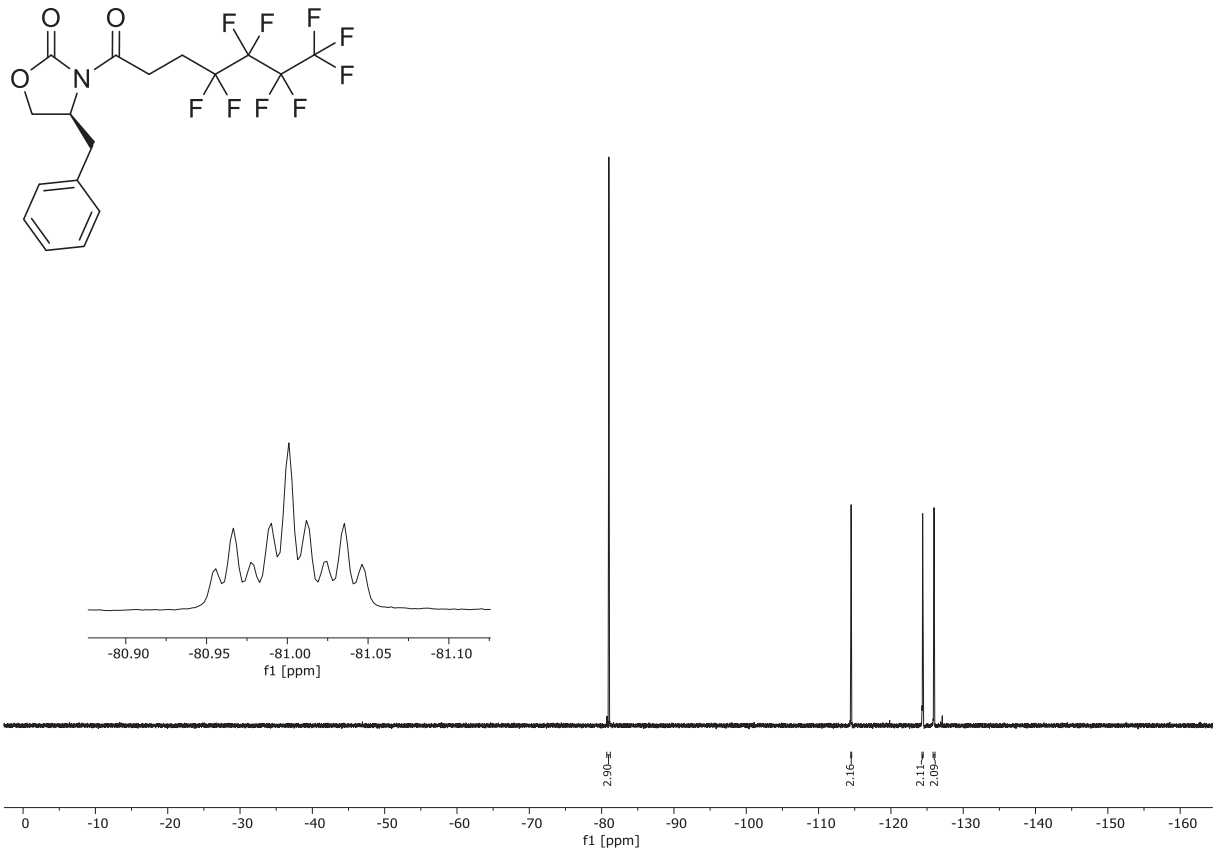


^{13}C NMR (75 MHz, chloroform-*d*)

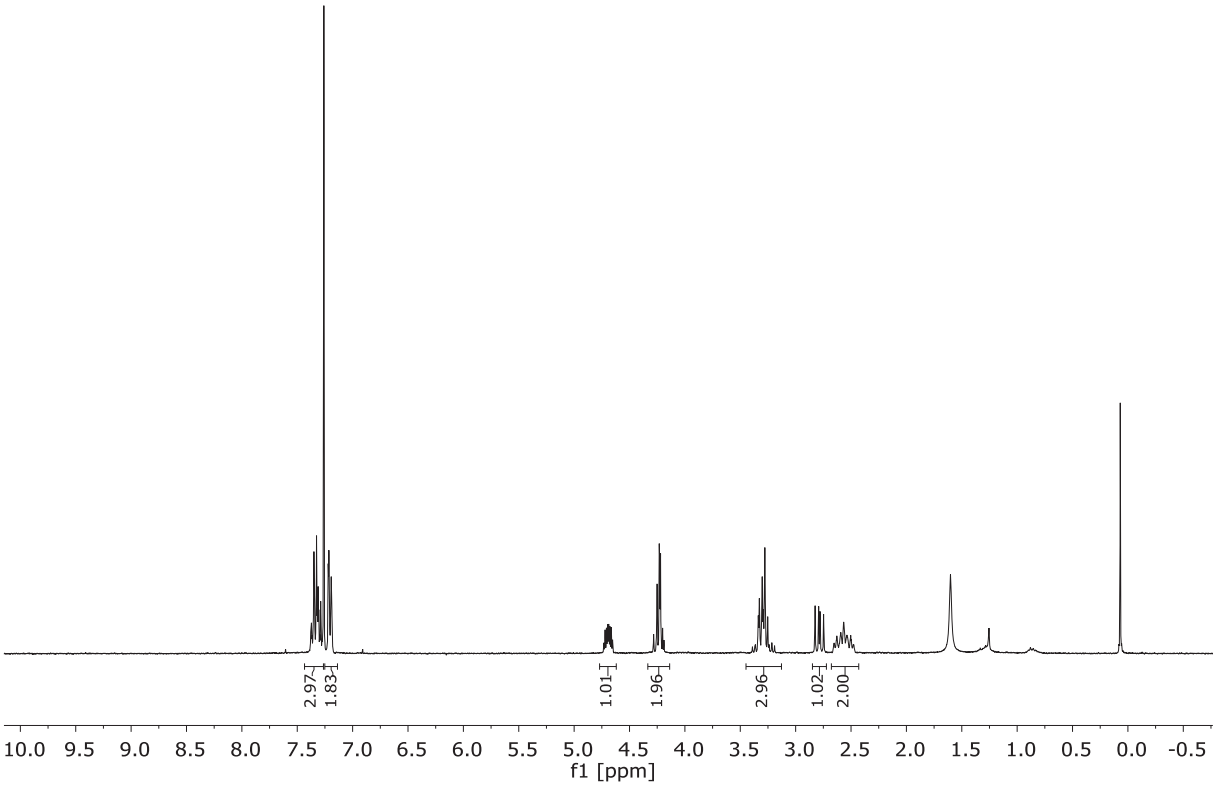


IR (Film)

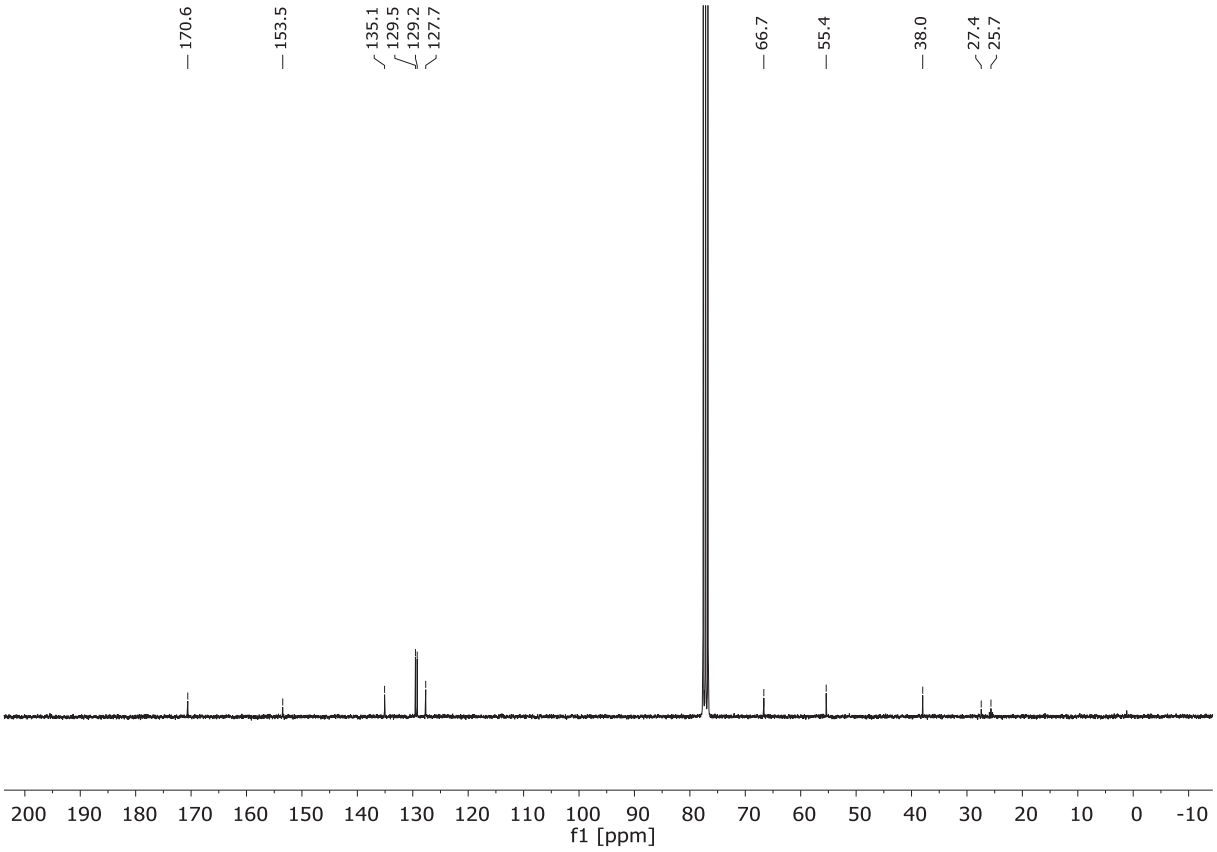
(4*S*)-4-Benzyl-3-(4,4,5,5,6,6,7,7,7-nonafluoro-3-methylheptanoyl)oxazolidin-2-one (126)



^{19}F NMR (282 MHz, chloroform-*d*)

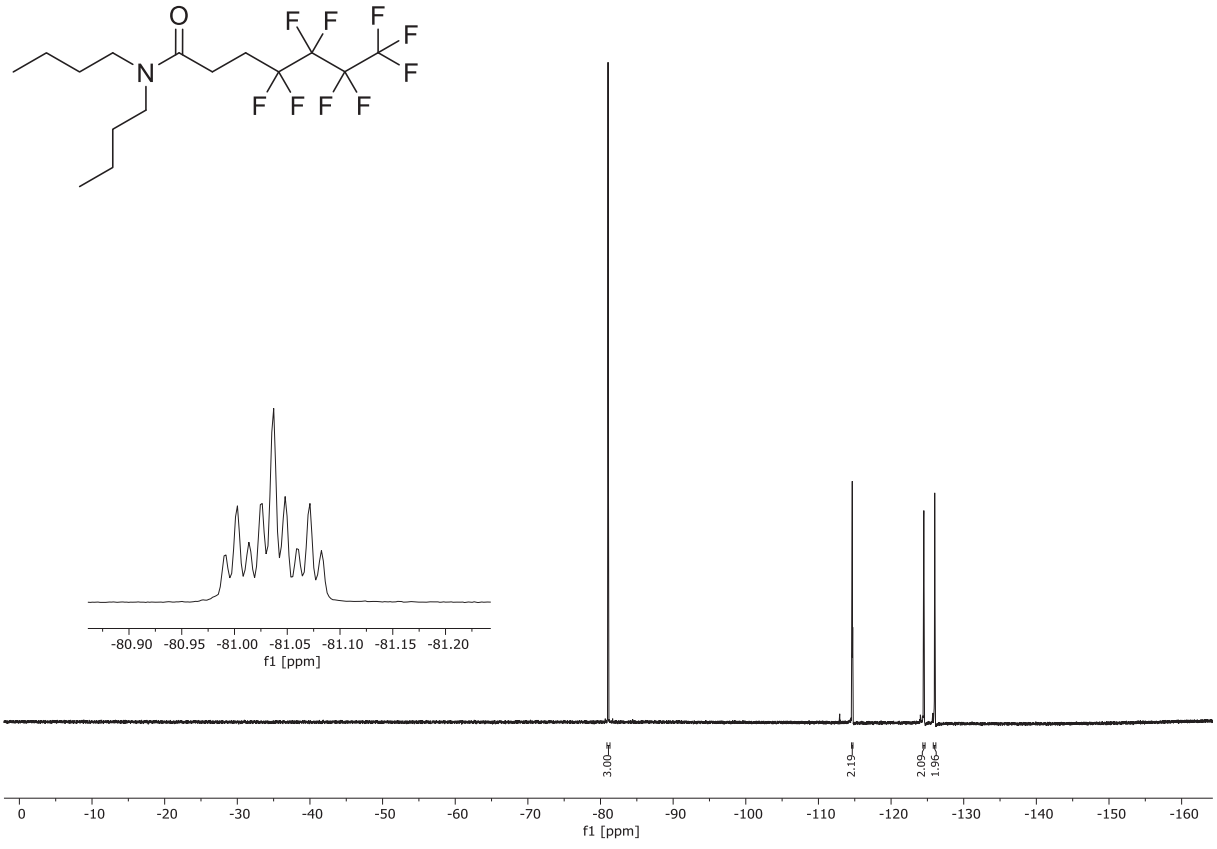


^{1}H NMR (300 MHz, chloroform-*d*)

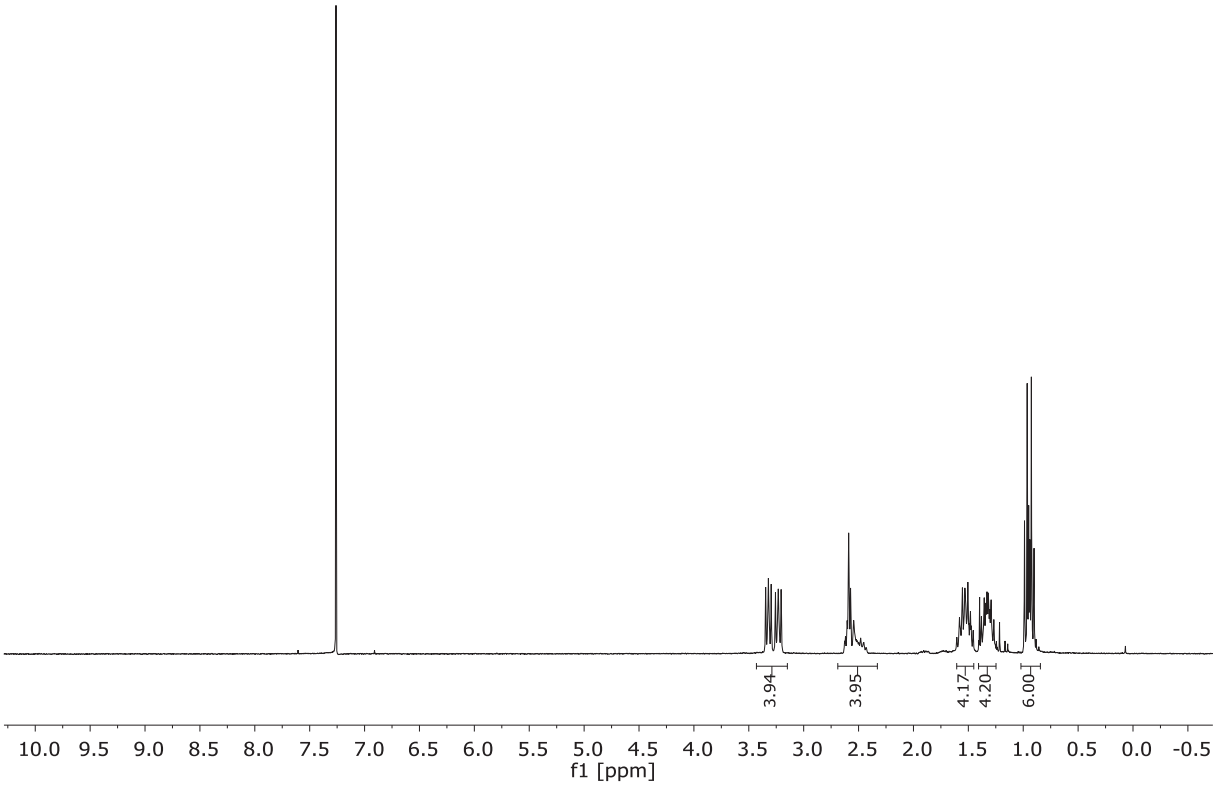


^{13}C NMR (75 MHz, chloroform-*d*)

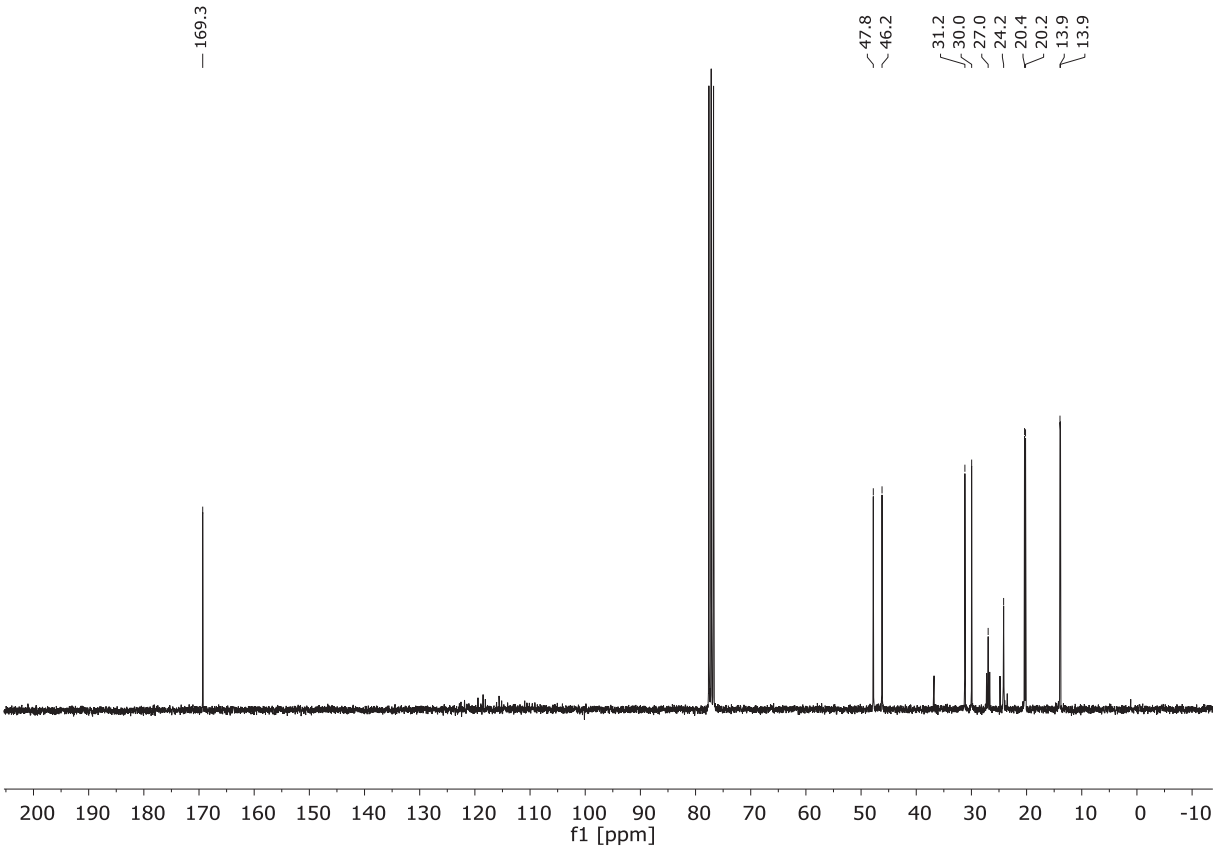
N,*N*-Dibutyl-4,4,5,5,6,6,7,7,7-nonafluoroheptanamide (145)



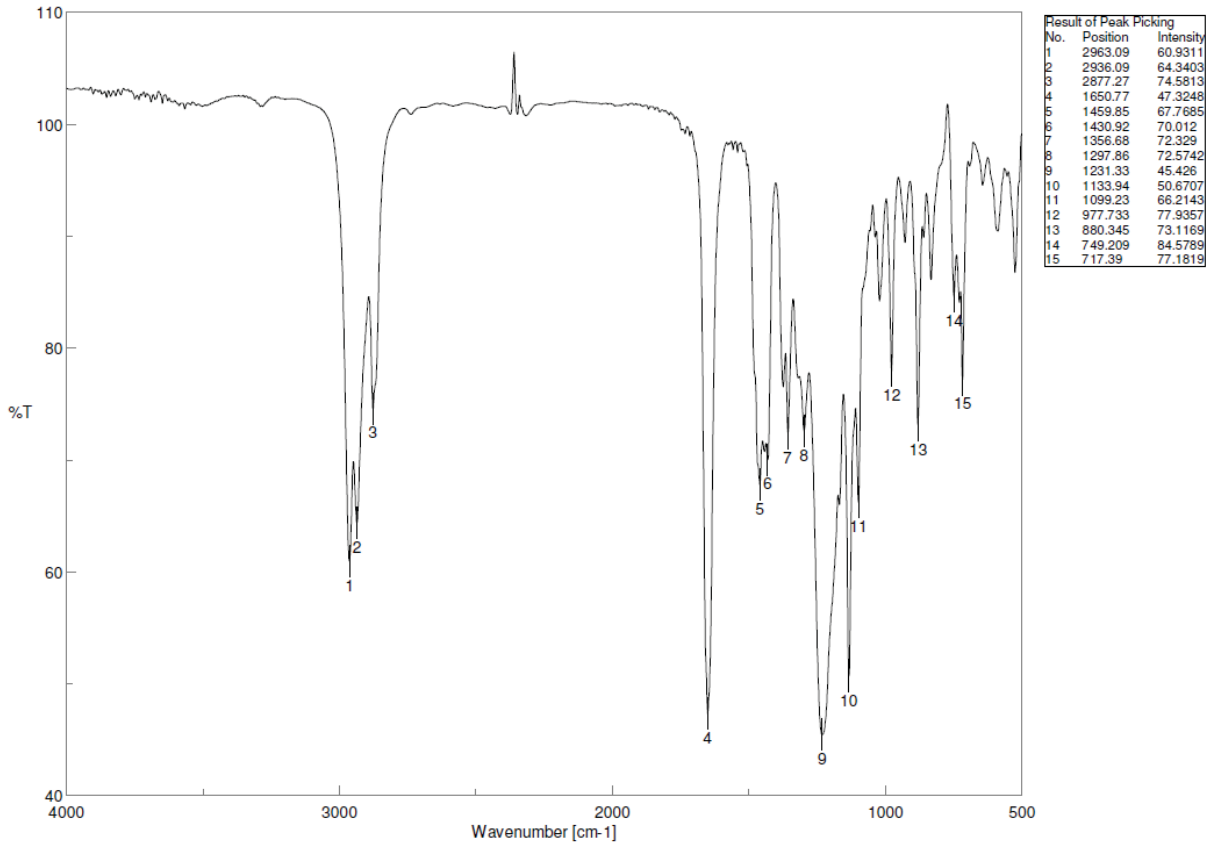
^{19}F NMR (282 MHz, chloroform-*d*)



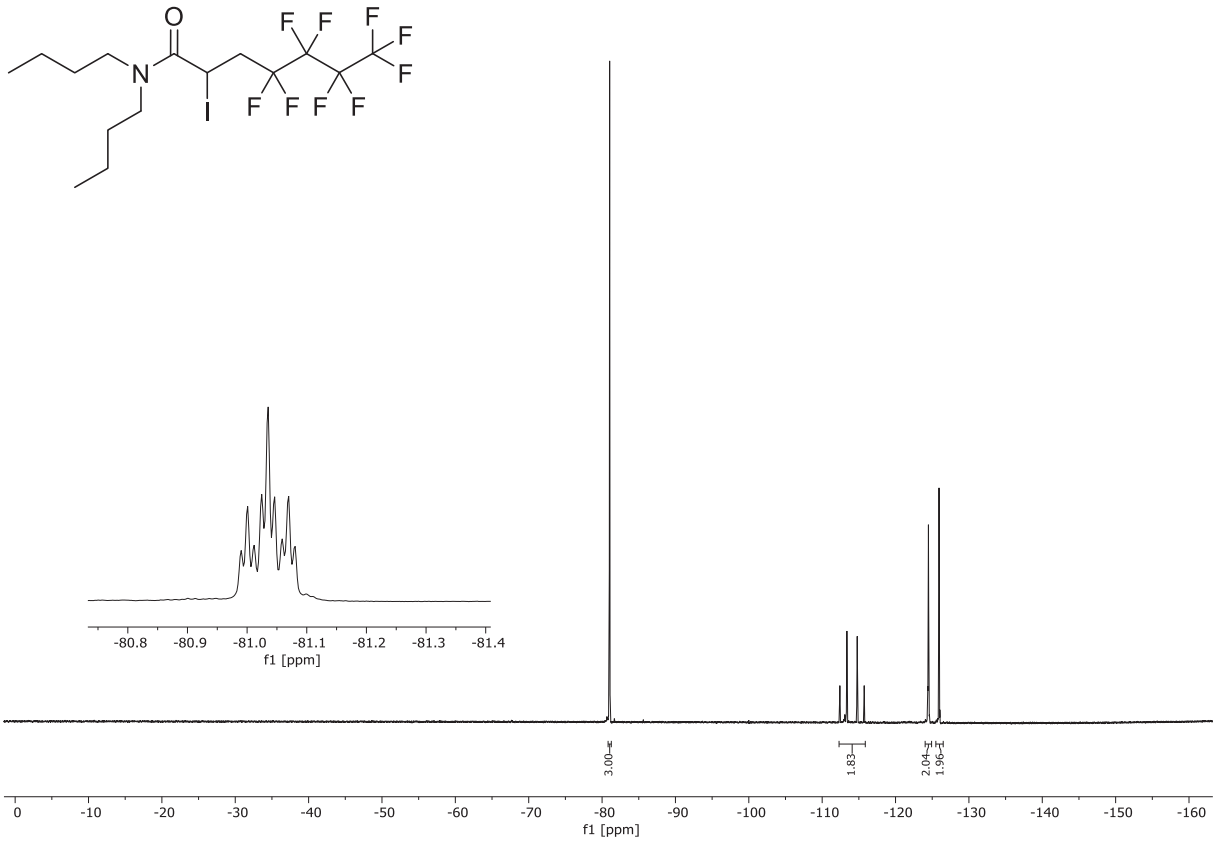
^{1}H NMR (300 MHz, chloroform-*d*)



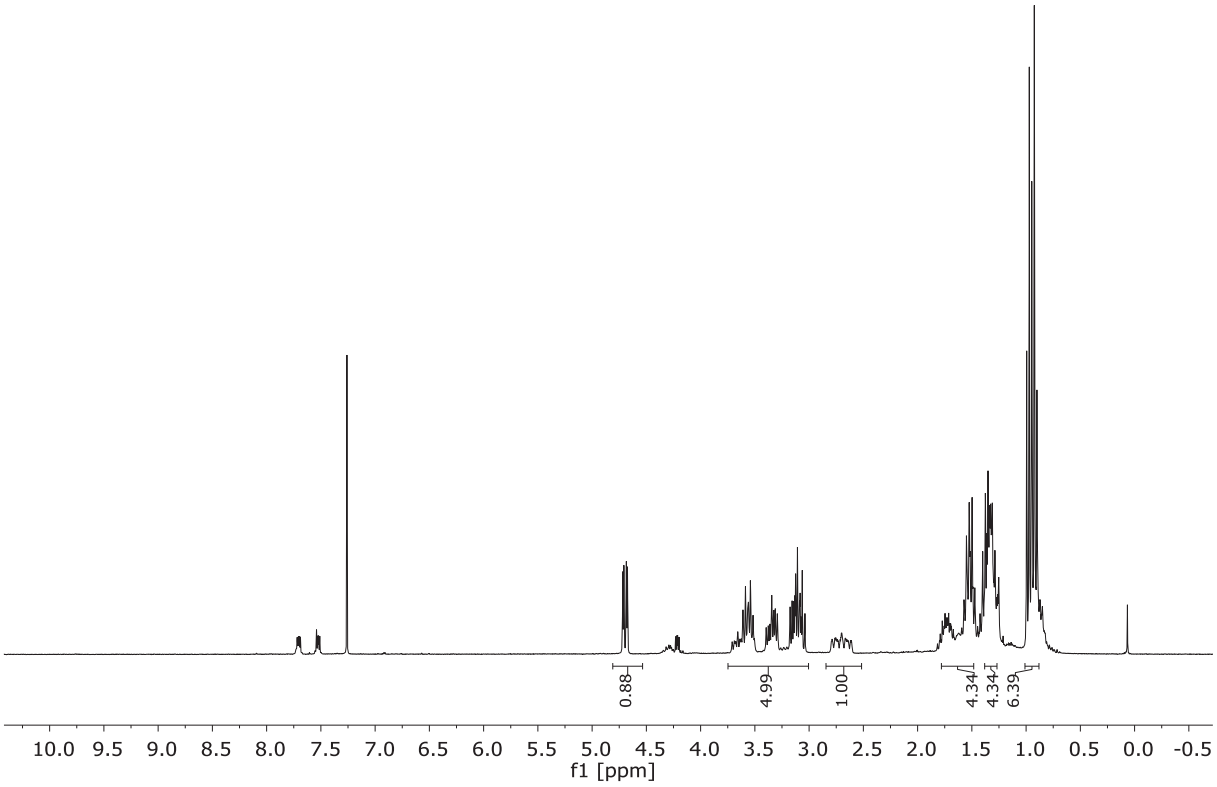
^{13}C NMR (75 MHz, chloroform-*d*)



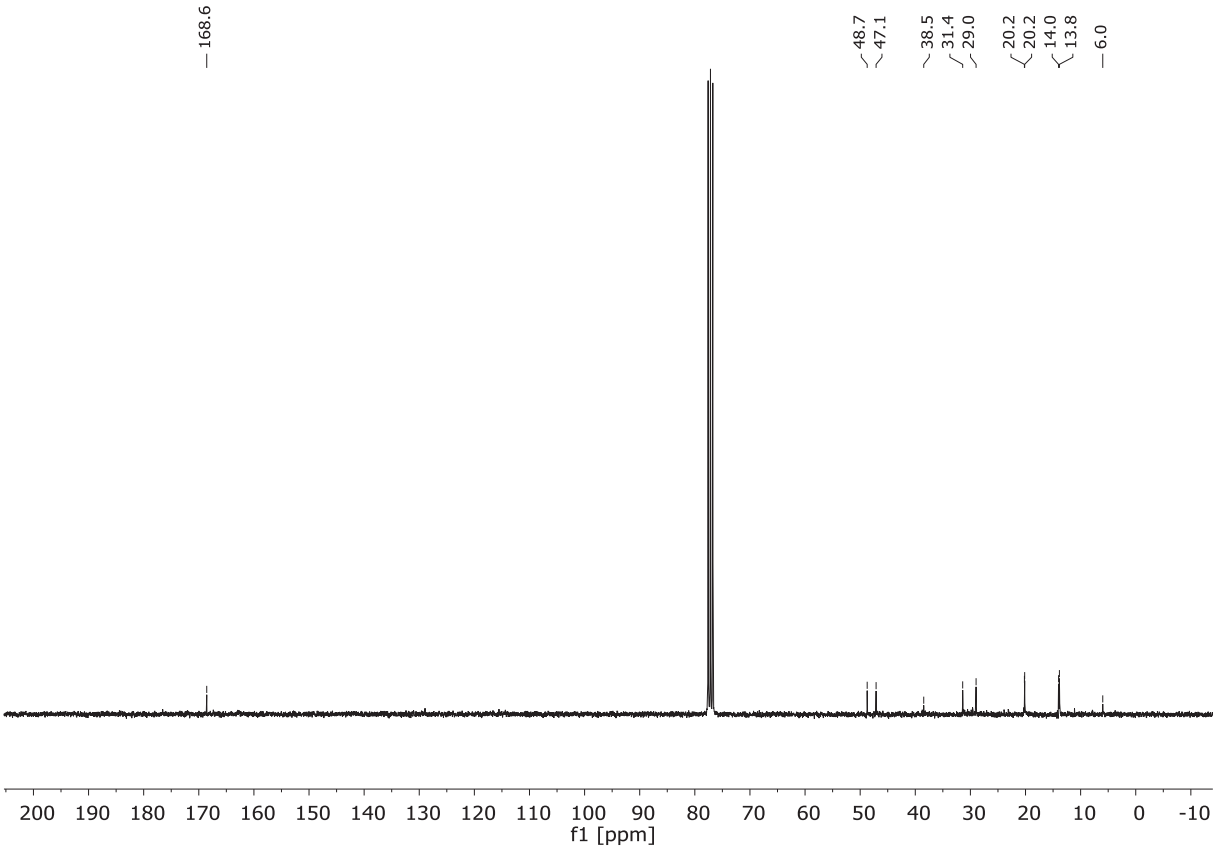
N,*N*-Dibutyl-4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptanamide (146)



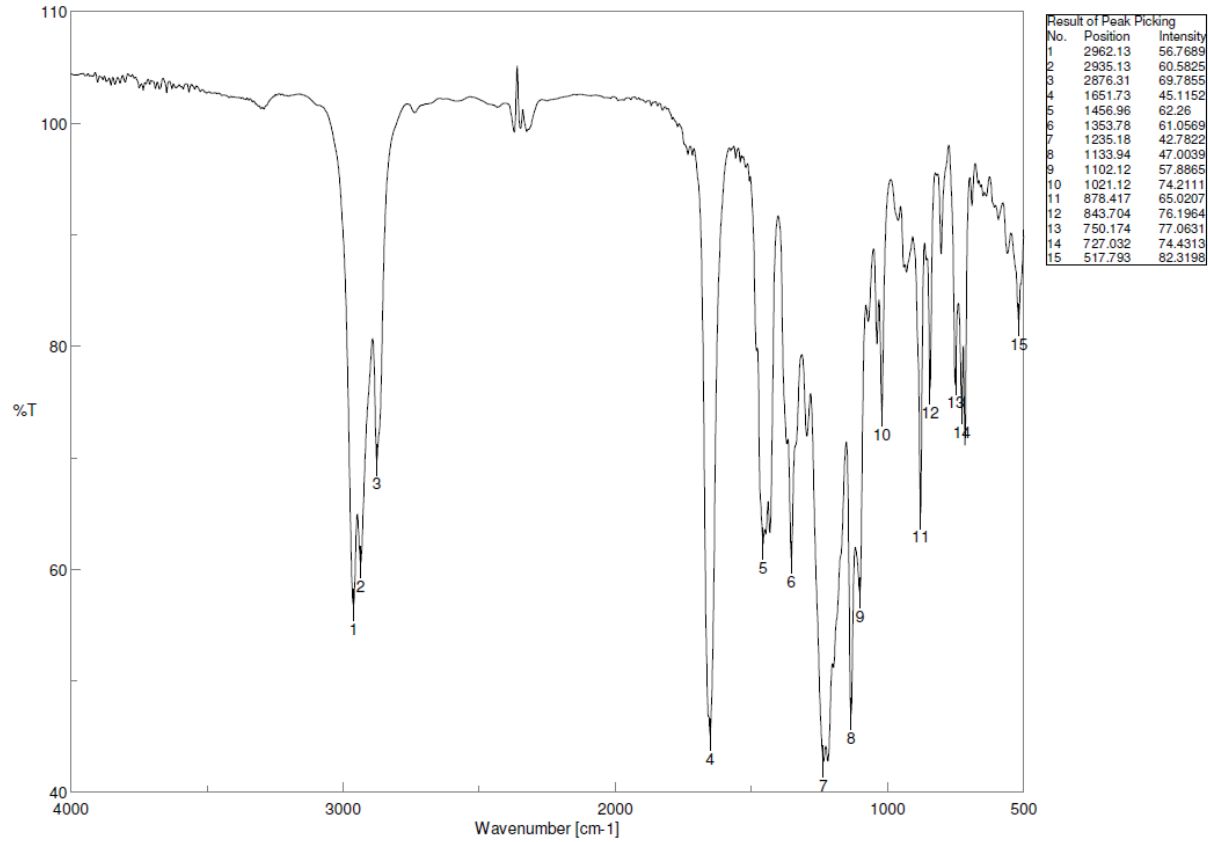
^{19}F NMR (282 MHz, chloroform-*d*)



^{1}H NMR (300 MHz, chloroform-*d*)

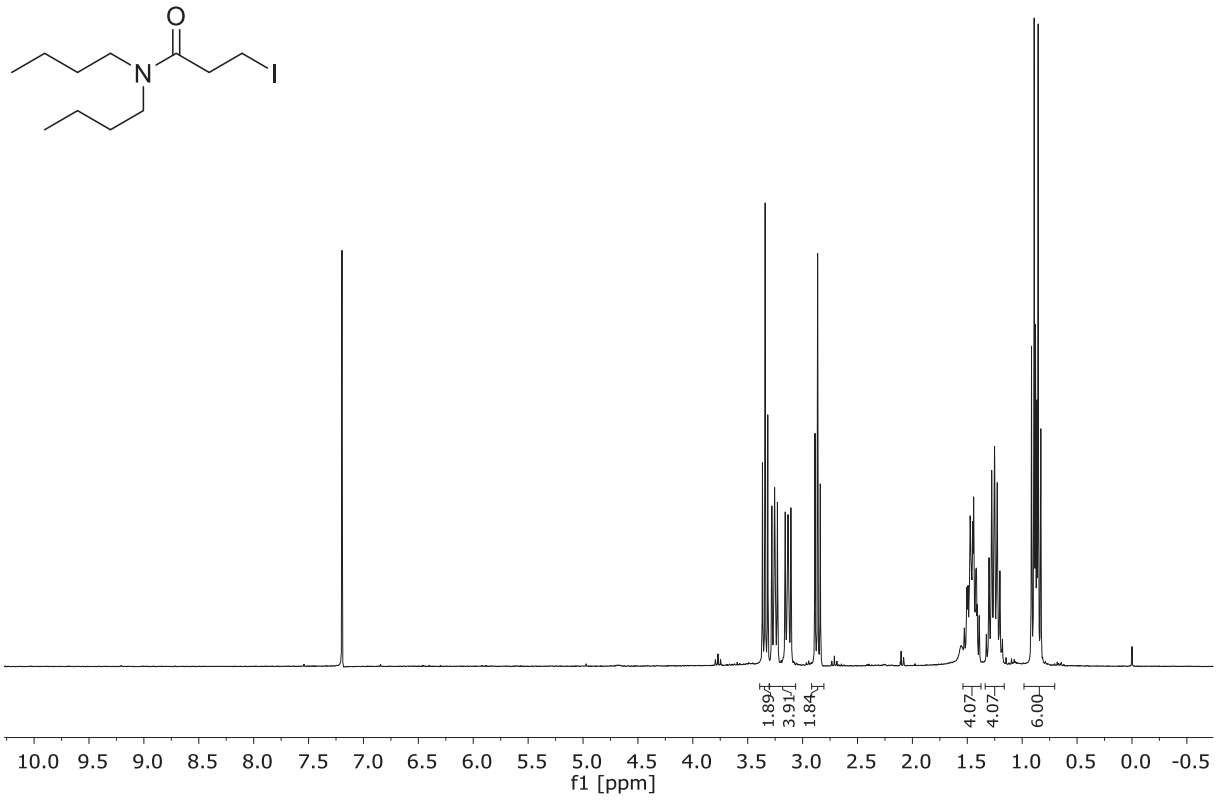


^{13}C NMR (75 MHz, chloroform-*d*)

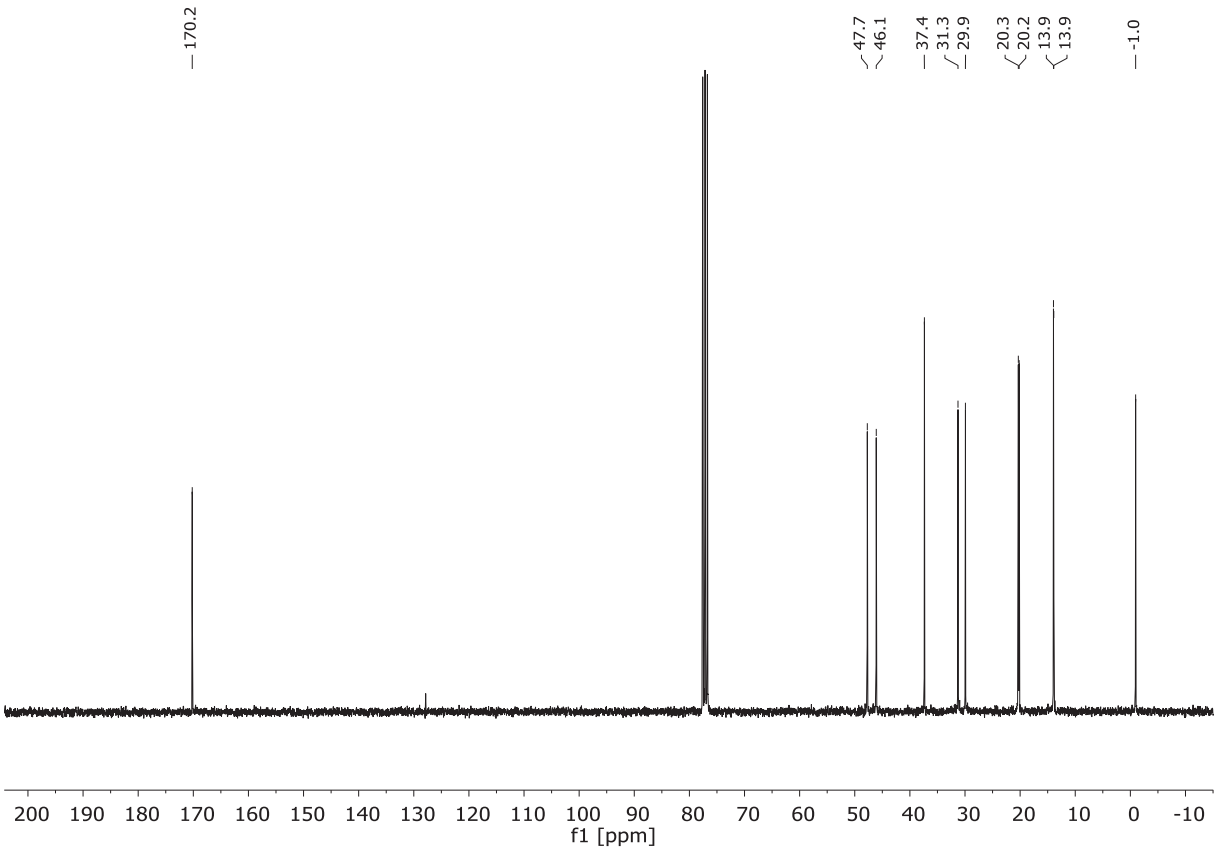


IR (Film)

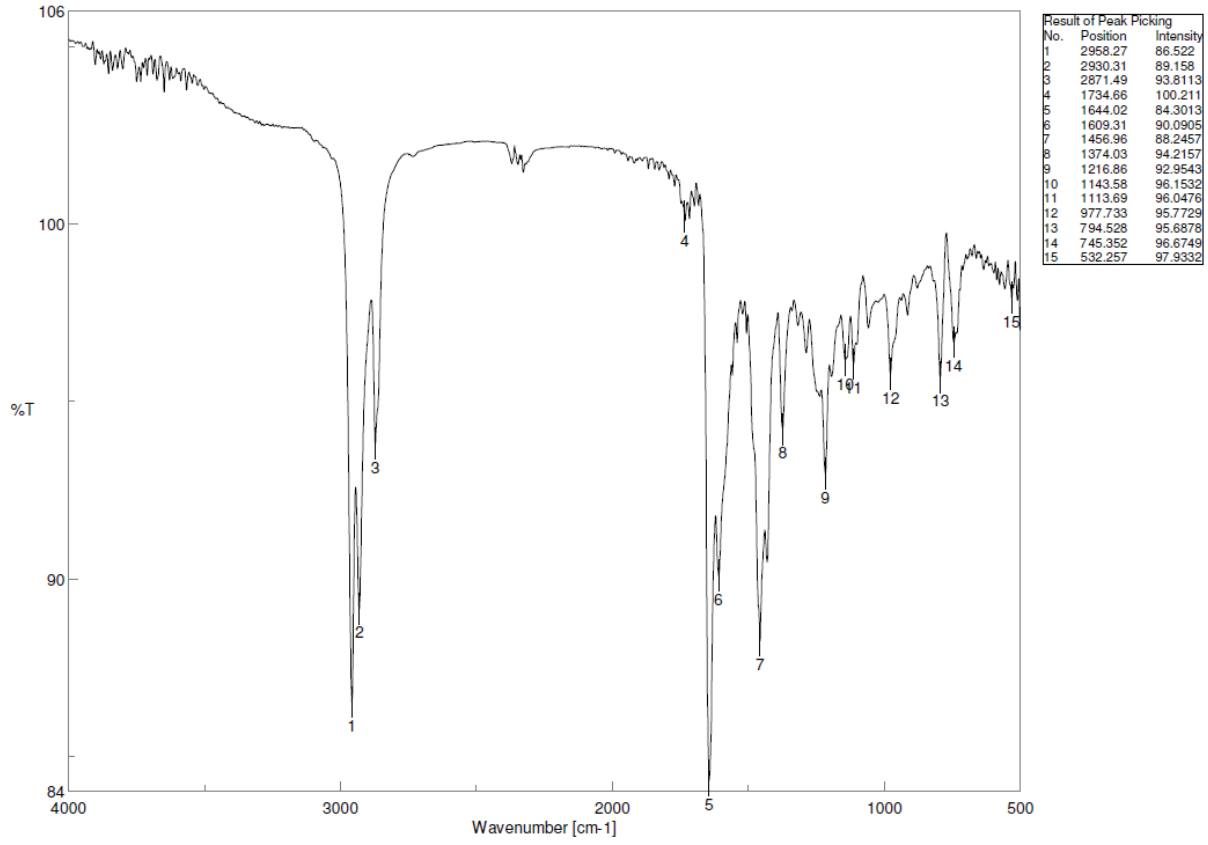
N,*N*-Dibutyl-3-iodopropanamide (152)



^{1}H NMR (300 MHz, chloroform-*d*)

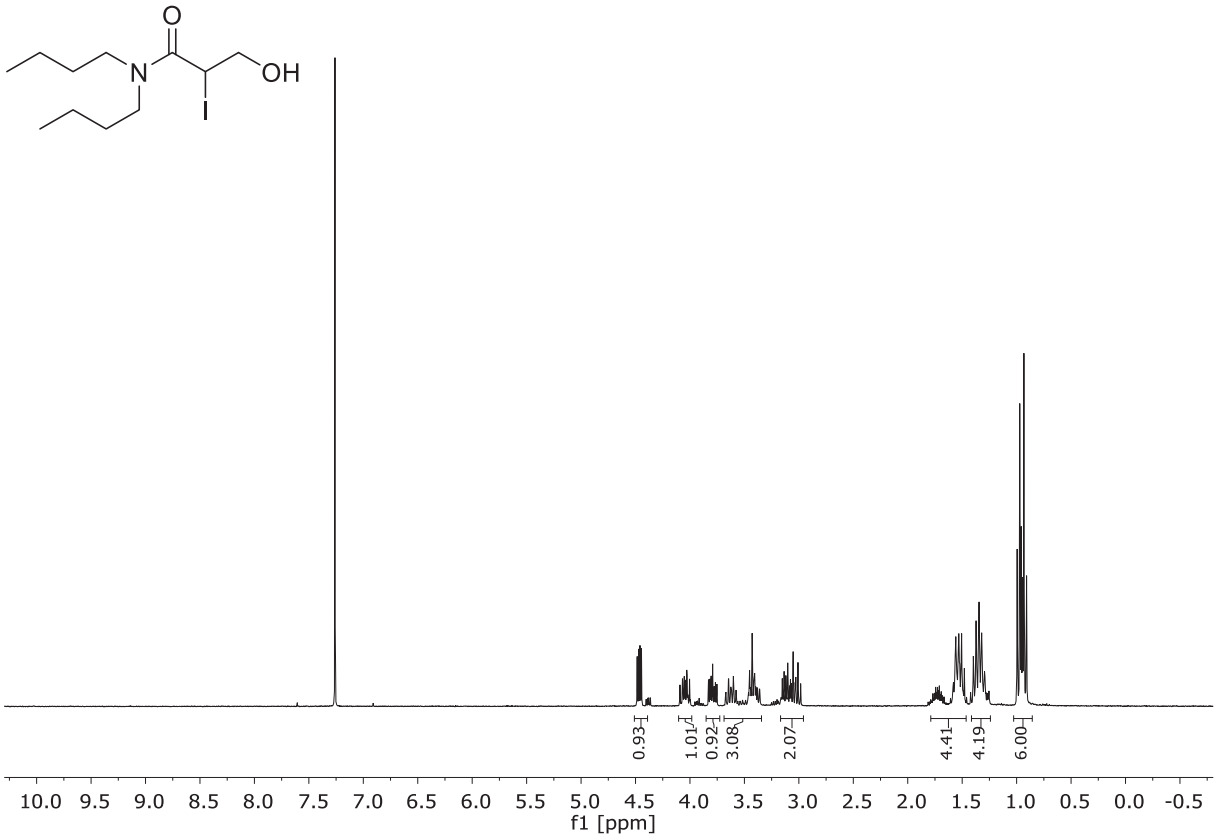


^{13}C NMR (75 MHz, chloroform-*d*)

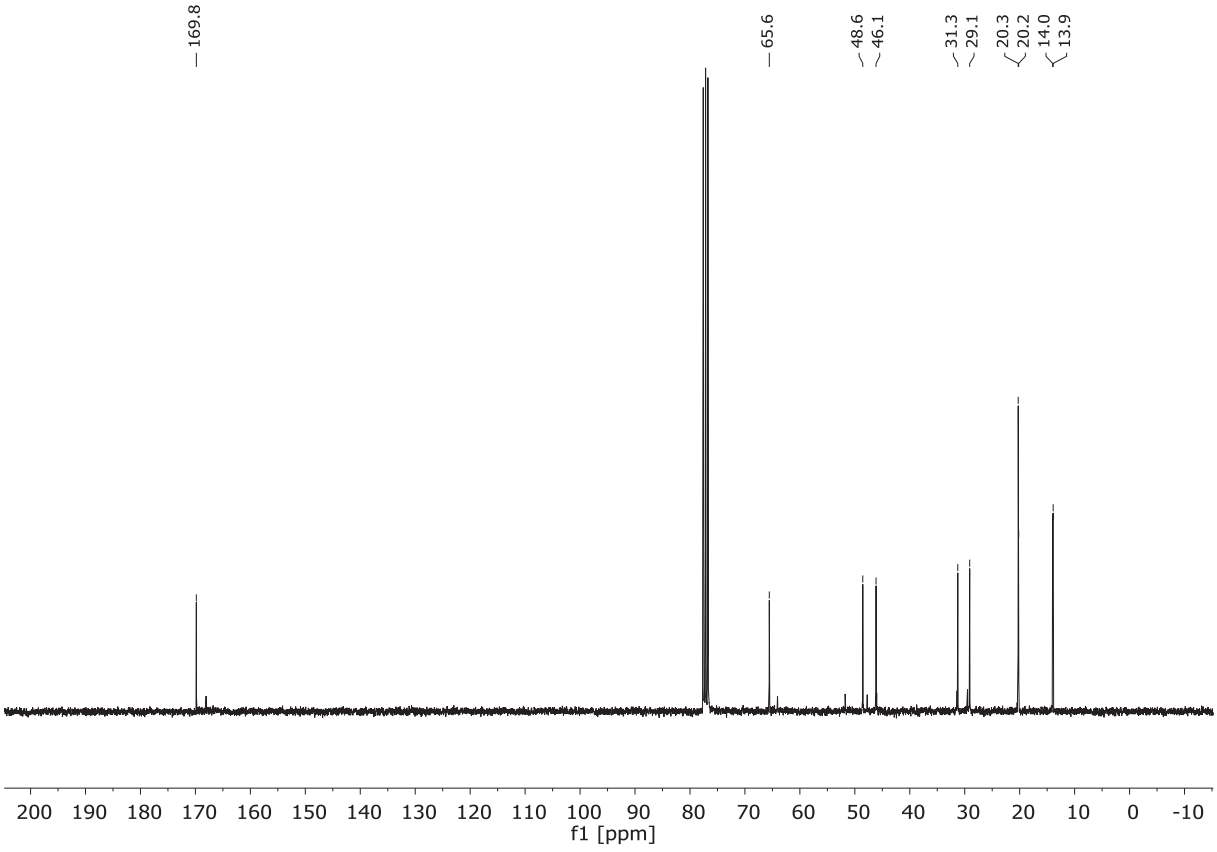


IR (Film)

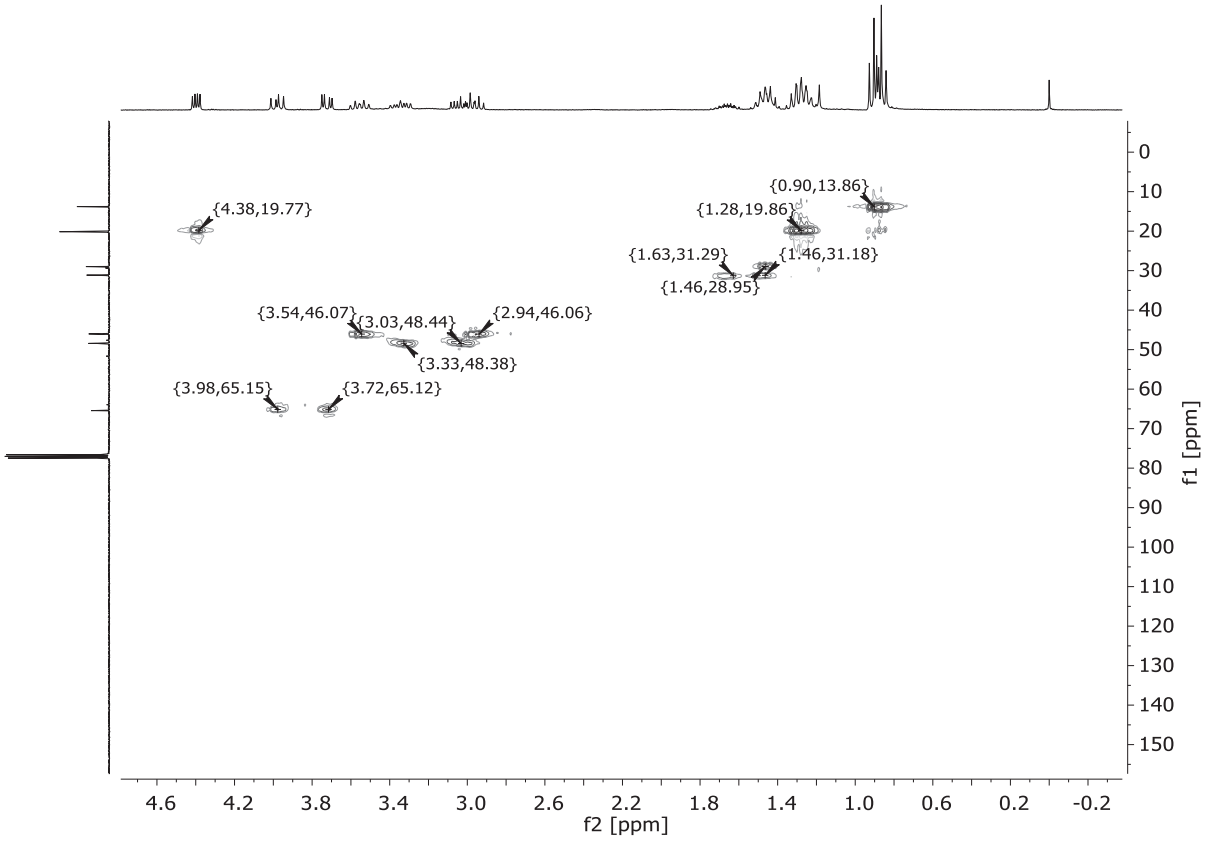
N,*N*-Dibutyl-3-iodopropanamide (147)



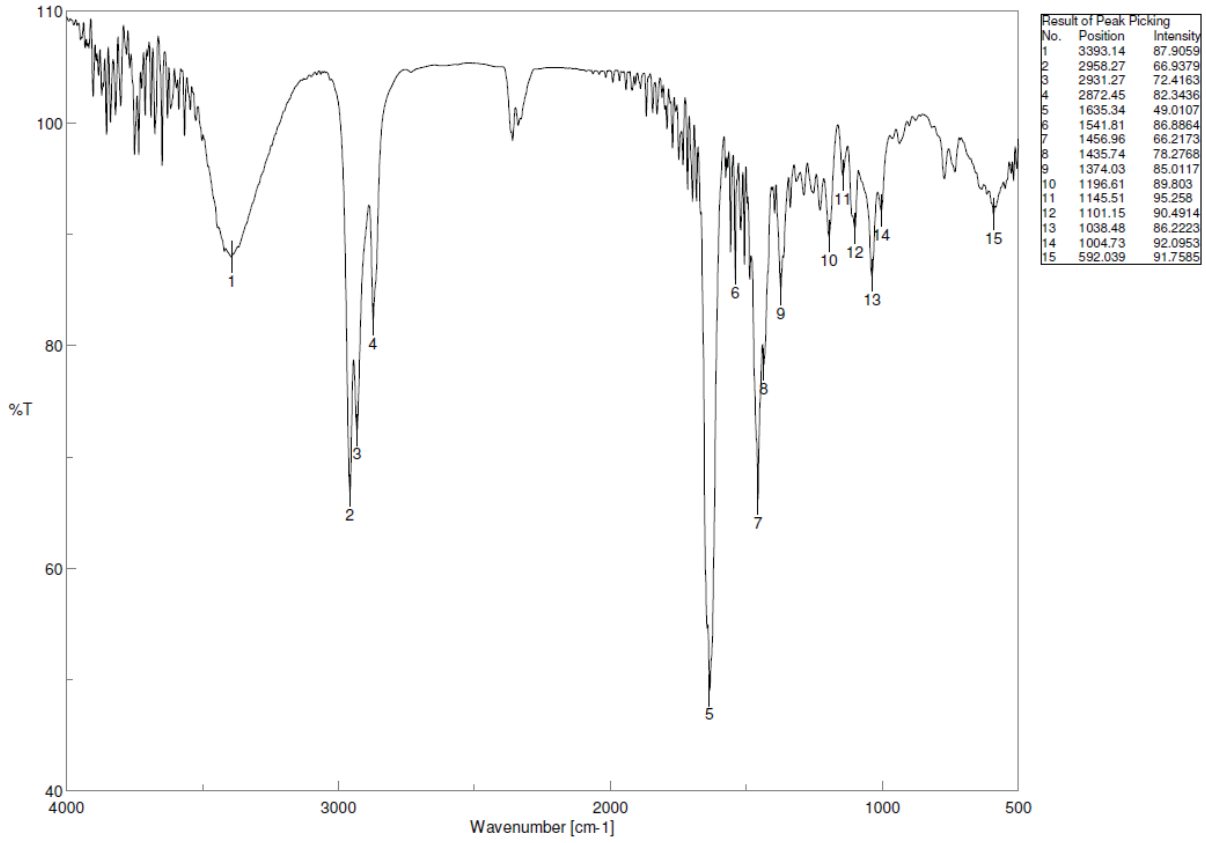
^{1}H NMR (300 MHz, chloroform-*d*)



^{13}C NMR (75 MHz, chloroform-*d*)

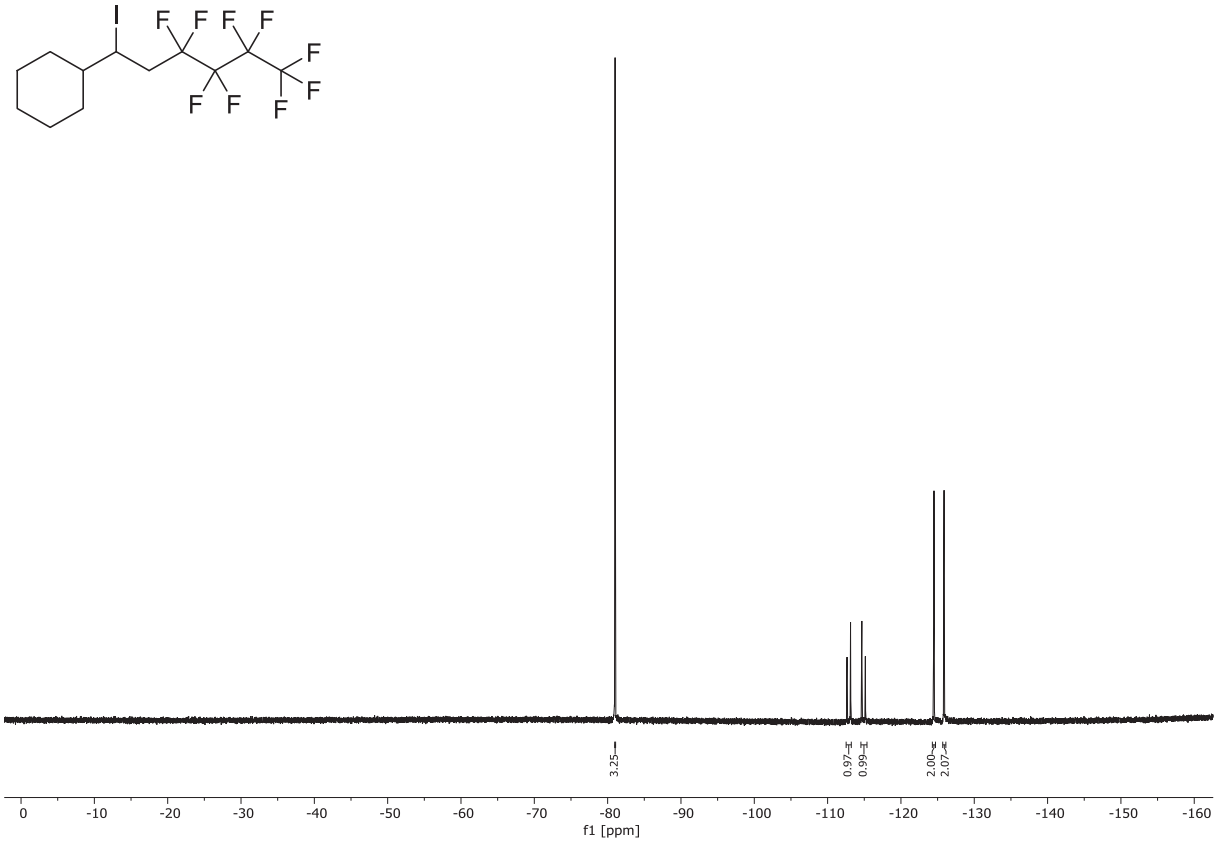

{4.38,19.77}
{0.90,13.86}
{1.28,19.86}
{1.63,31.29}
{1.46,31.18}
{1.46,28.95}
{3.54,46.07}
{3.03,48.44}
{2.94,46.06}
{3.33,48.38}
{3.98,65.15}
{3.72,65.12}
f2 [ppm]
f1 [ppm]

HSQC

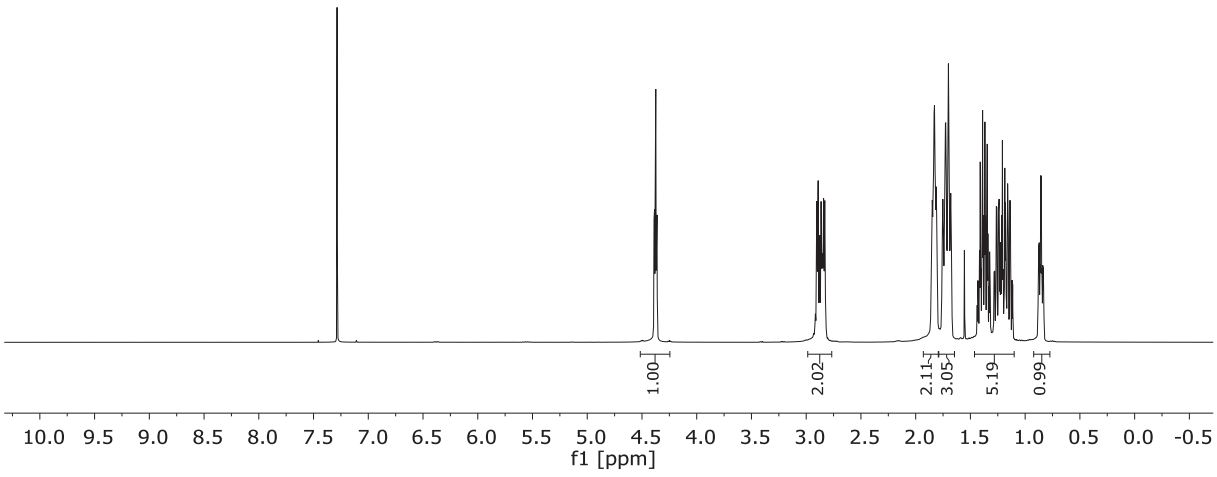

%T
Wavenumber [cm-1]
Result of Peak Picking
No. Position Intensity
1 3393.14 87.9059
2 2958.27 66.9379
3 2931.27 72.4163
4 2872.45 82.3436
5 1635.34 49.0107
6 1541.81 86.8864
7 1456.96 66.2173
8 1435.74 78.2768
9 1374.03 85.0117
10 1196.61 89.803
11 1145.51 95.258
12 1101.15 90.4914
13 1038.48 86.2223
14 1004.73 92.0953
15 592.039 91.7585

IR (Film)

(3,3,4,4,5,5,6,6,6-Nonafluoro-1-iodohexyl)cyclohexane (159)

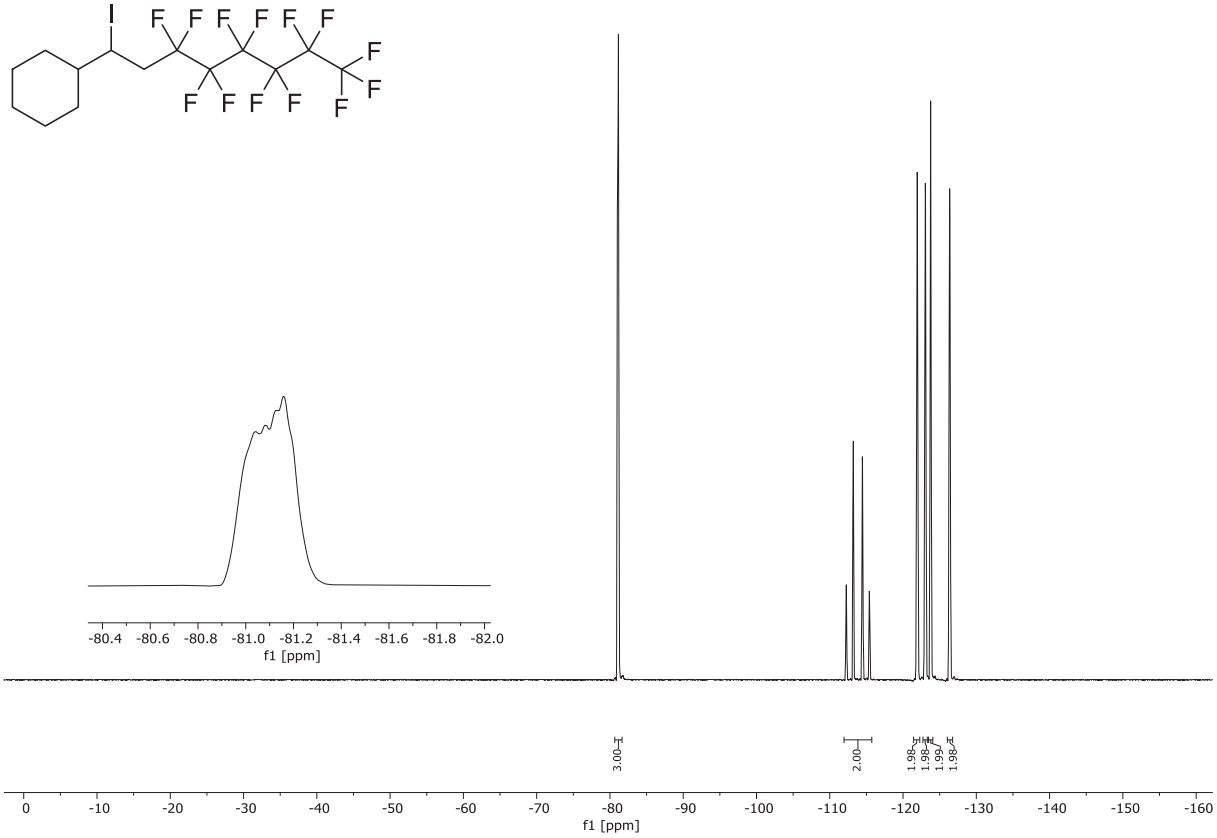


^{19}F NMR (565 MHz, chloroform-*d*)

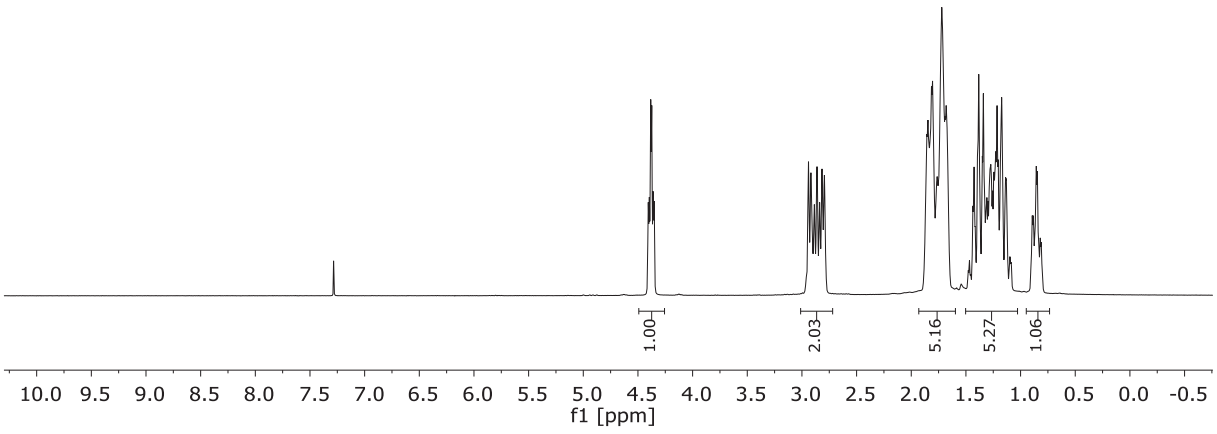


^{1}H NMR (600 MHz, chloroform-*d*)

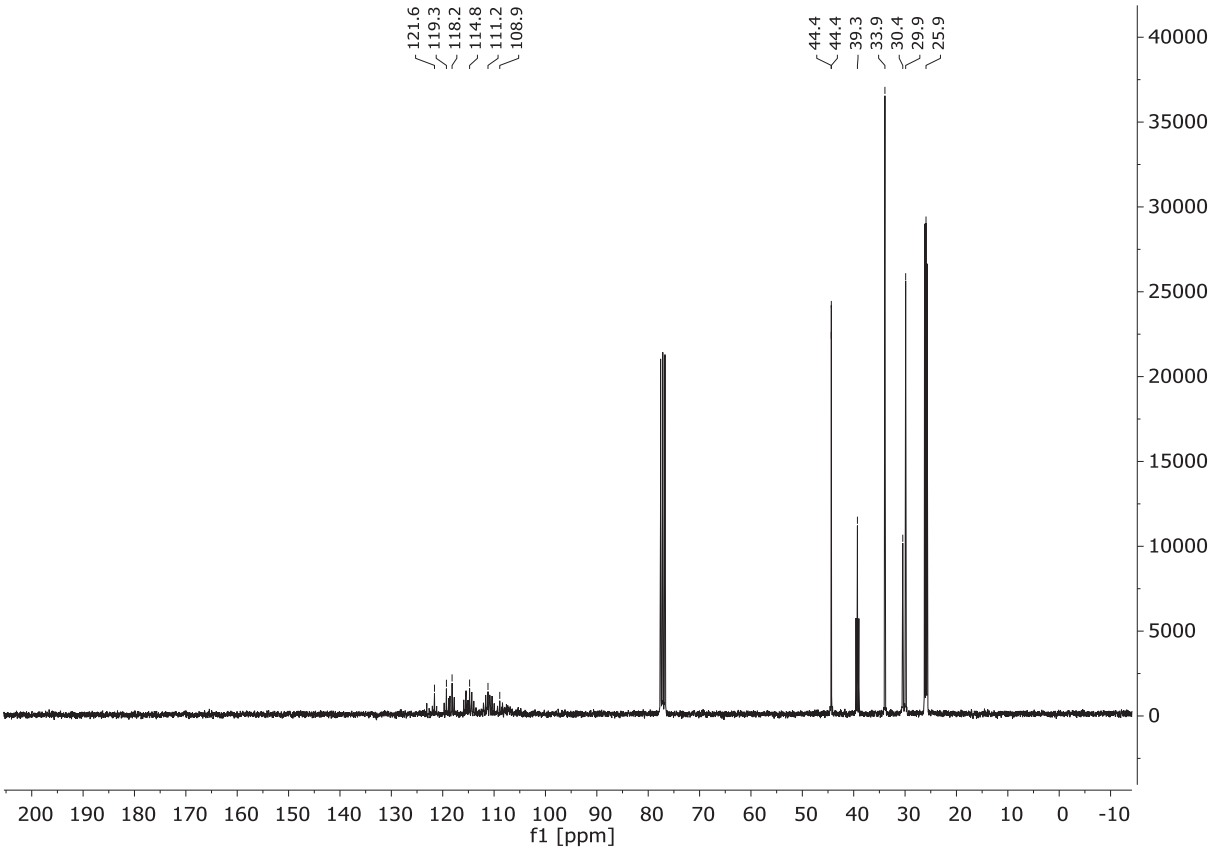
(3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-iodooctyl)cyclohexane (172)



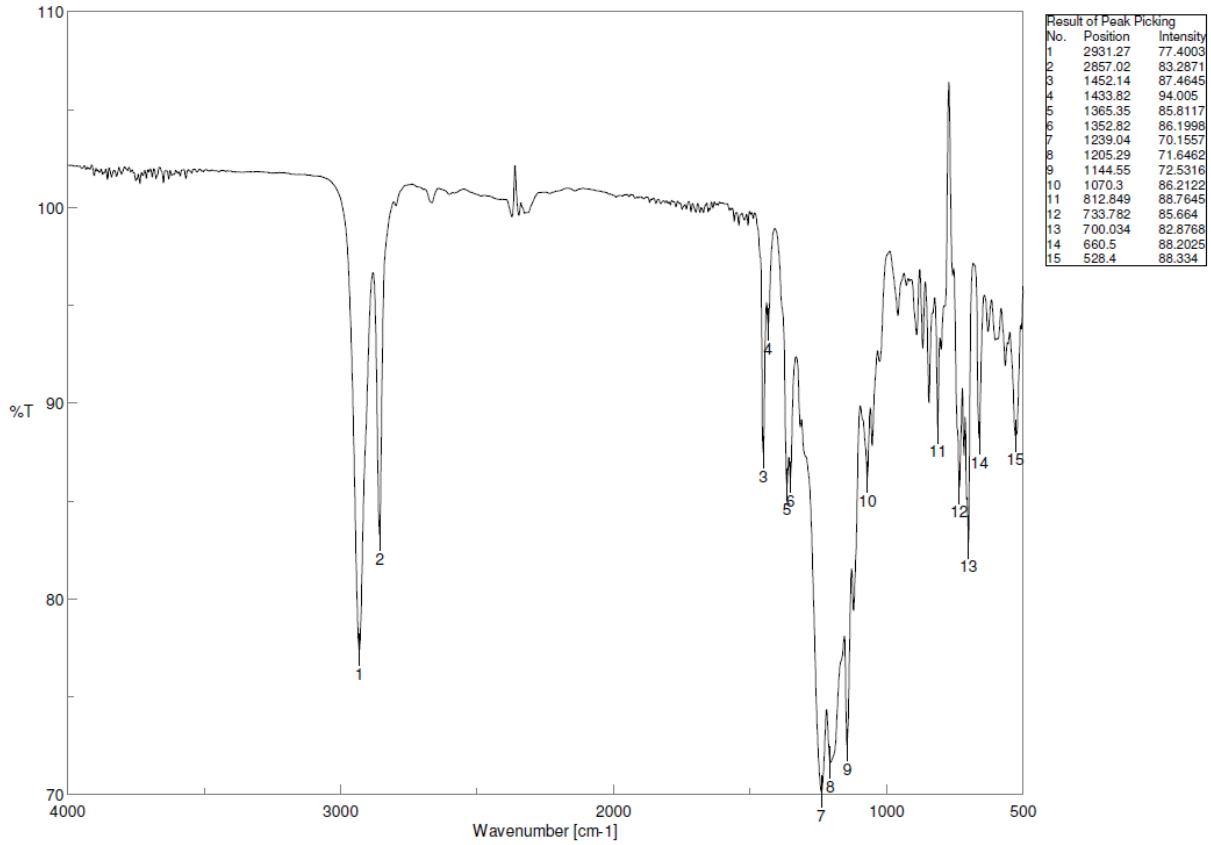
^{19}F NMR (282 MHz, chloroform-*d*)



^{1}H NMR (300 MHz, chloroform-*d*)



^{13}C NMR (75 MHz, chloroform-*d*)

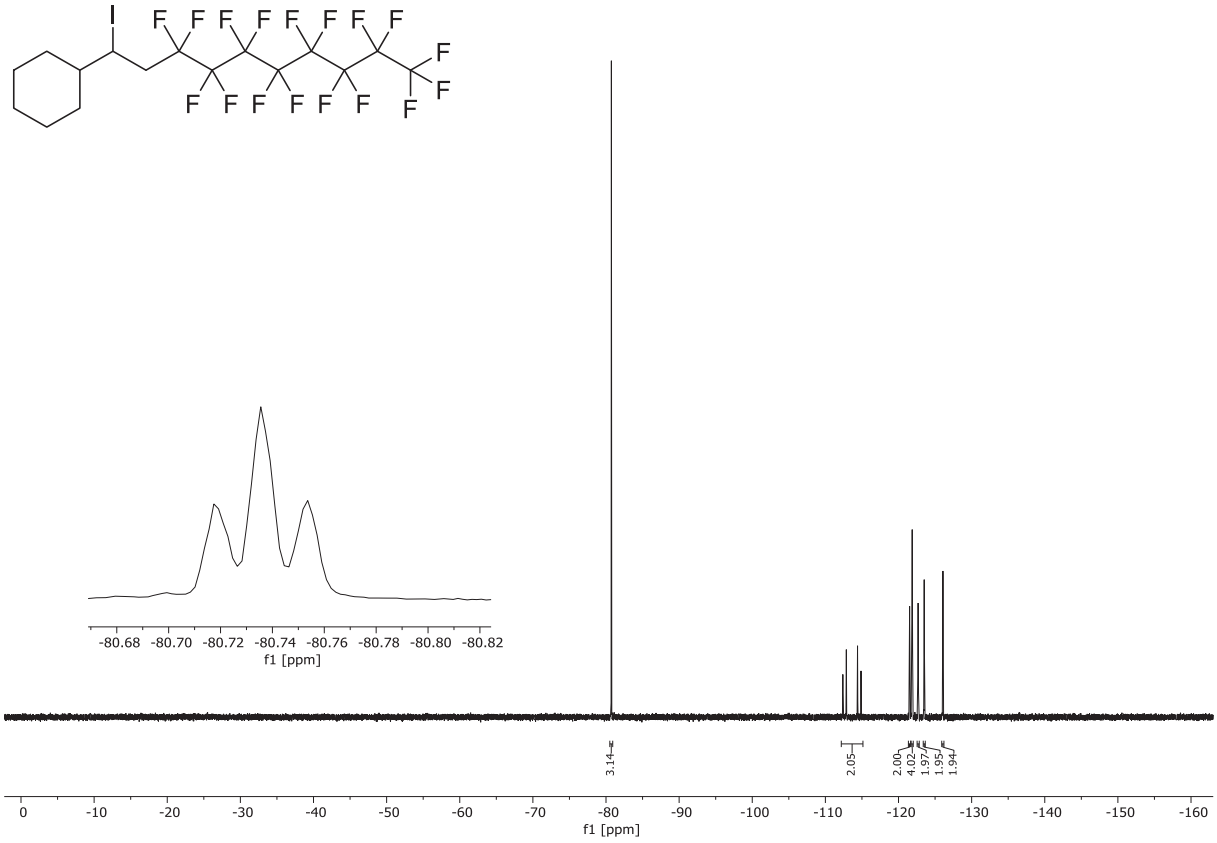


Result of Peak Picking

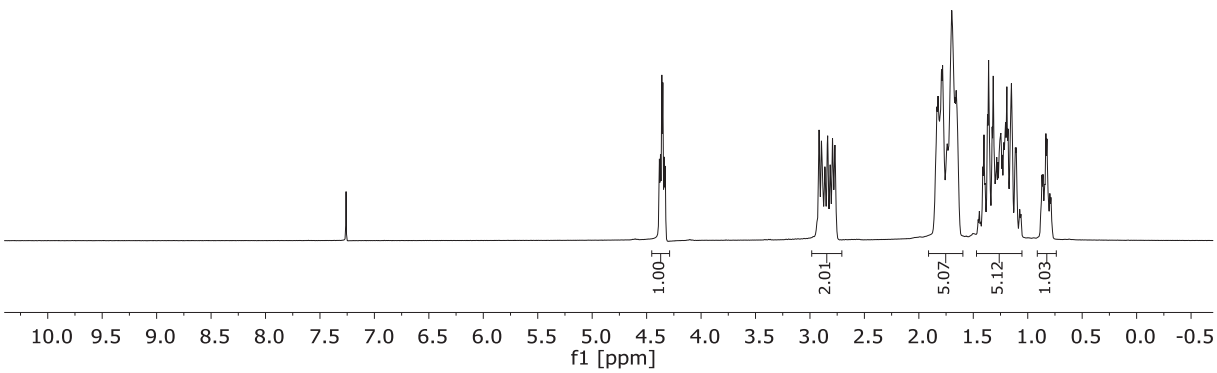
No.	Position	Intensity
1	2931.27	77.4003
2	2857.02	83.2871
3	1452.14	87.4645
4	1433.82	94.005
5	1365.35	85.8117
6	1352.82	86.1998
7	1239.04	70.1557
8	1205.29	71.6462
9	1144.55	72.5316
10	1070.3	86.2122
11	812.849	88.7645
12	733.782	85.664
13	700.034	82.8768
14	660.5	88.2025
15	528.4	88.334

IR (Film)

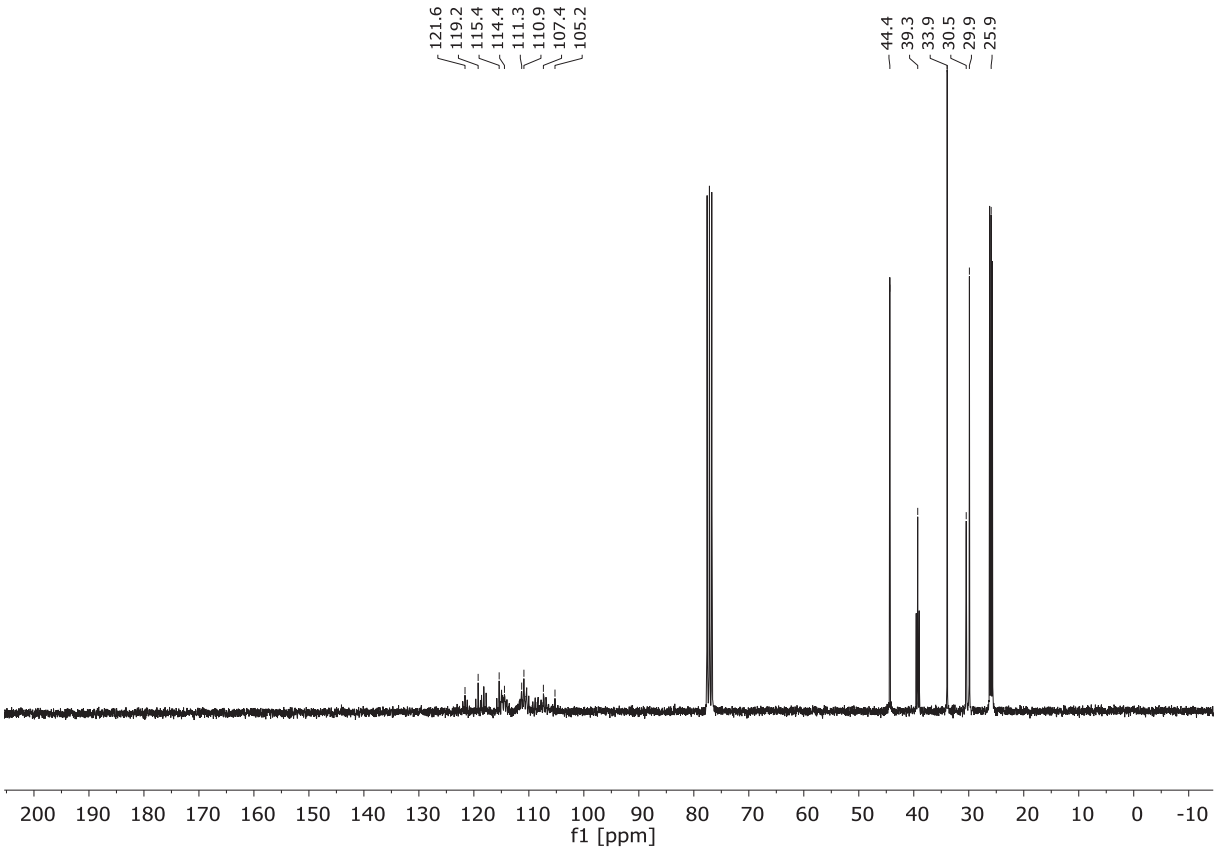
(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododecyl)cyclohexane (173)



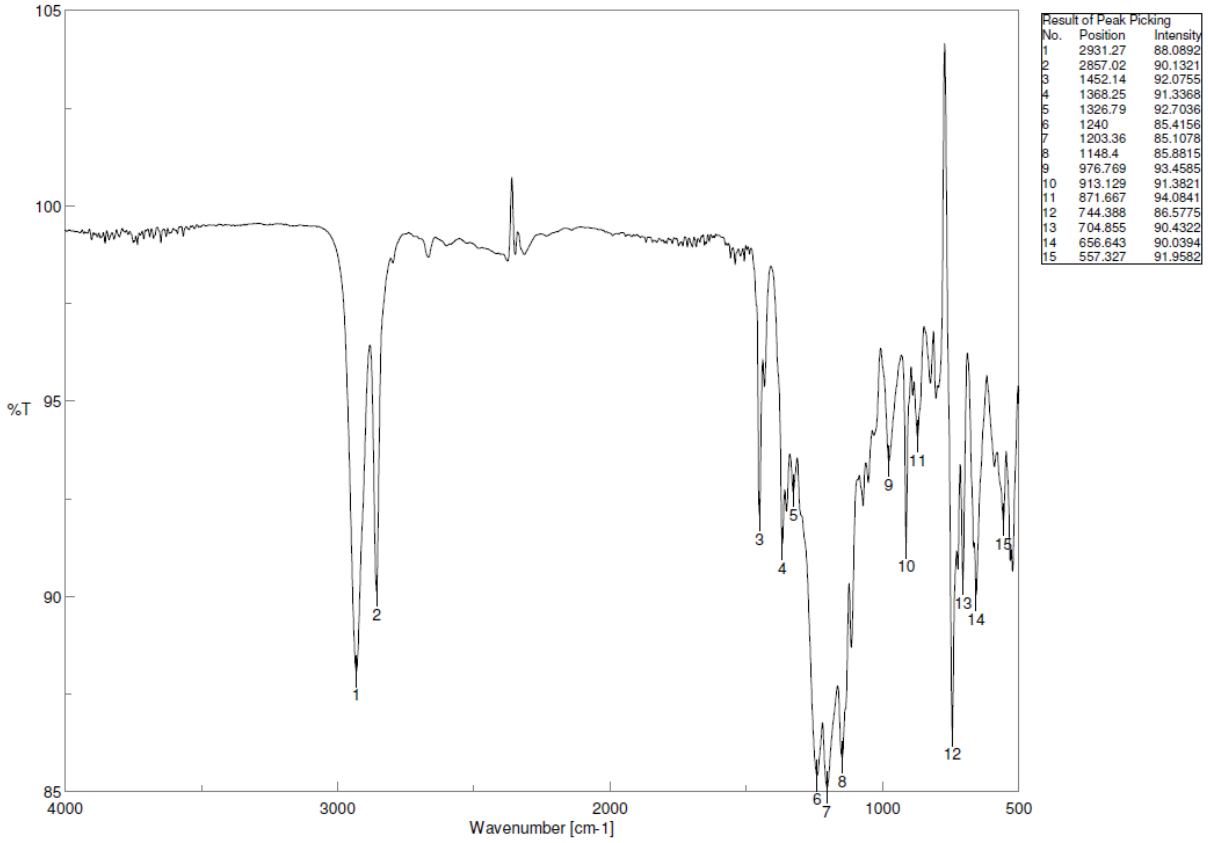
^{19}F NMR (565 MHz, chloroform-*d*)



^{1}H NMR (300 MHz, chloroform-*d*)



^{13}C NMR (75 MHz, chloroform-*d*)

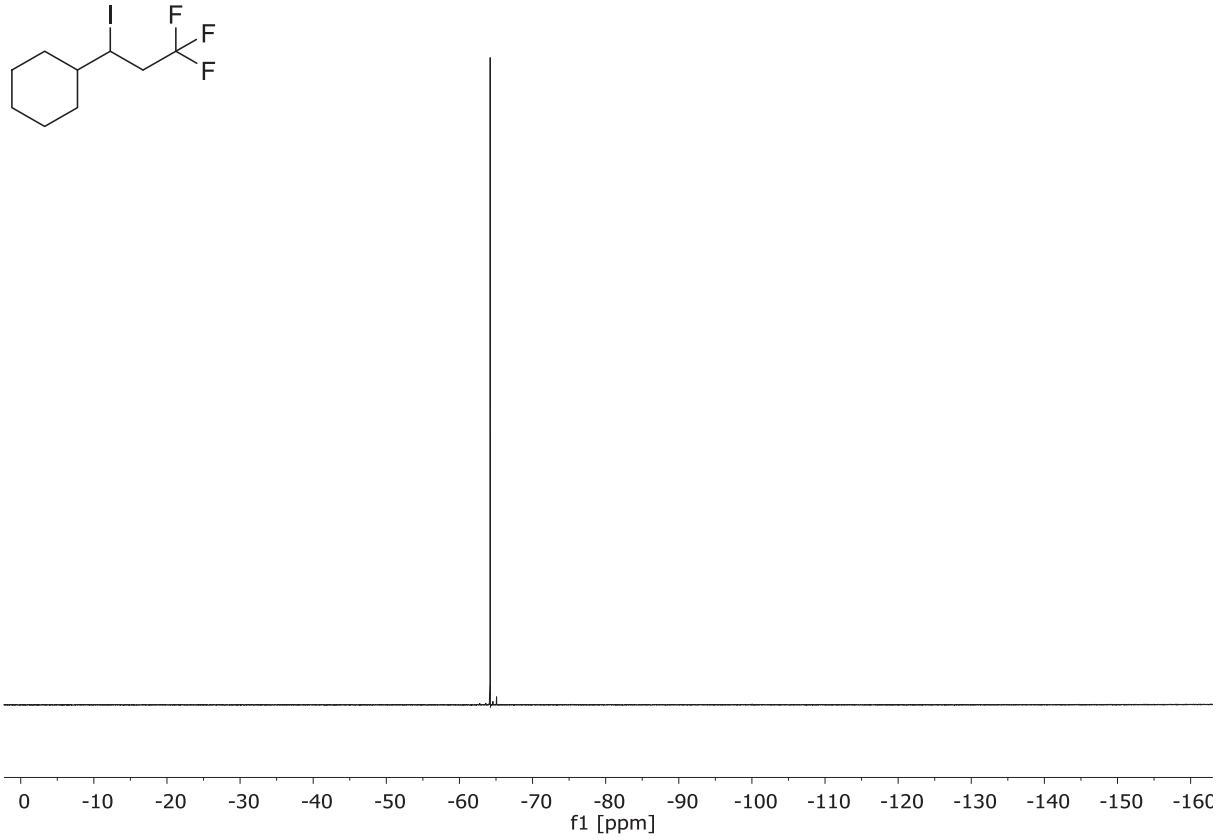


Result of Peak Picking

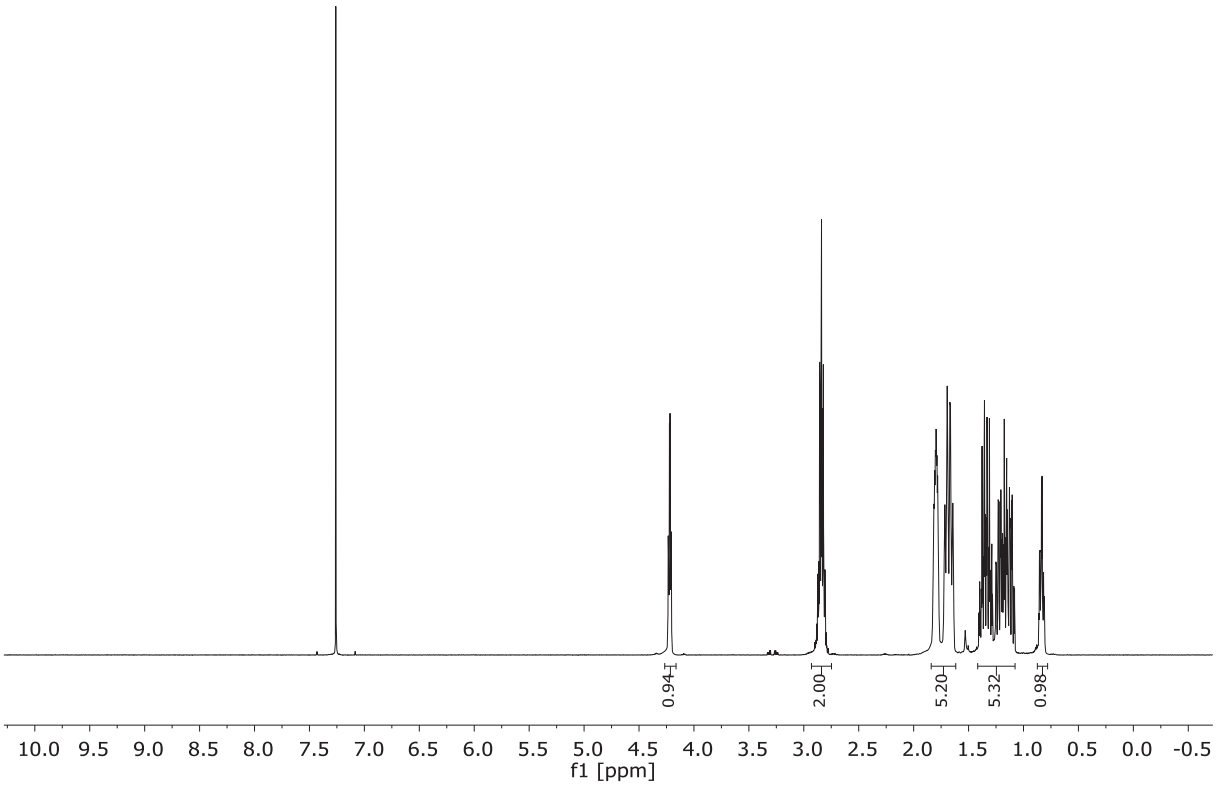
No.	Position	Intensity
1	2931.27	88.0892
2	2857.02	90.1321
3	1452.14	92.0755
4	1368.25	91.3368
5	1326.79	92.7036
6	1240	85.4156
7	1203.36	85.1078
8	1148.4	85.8815
9	976.769	93.4585
10	913.129	91.3821
11	871.667	94.0841
12	744.388	86.5775
13	704.855	90.4322
14	656.643	90.0394
15	557.327	91.9582

IR (Film)

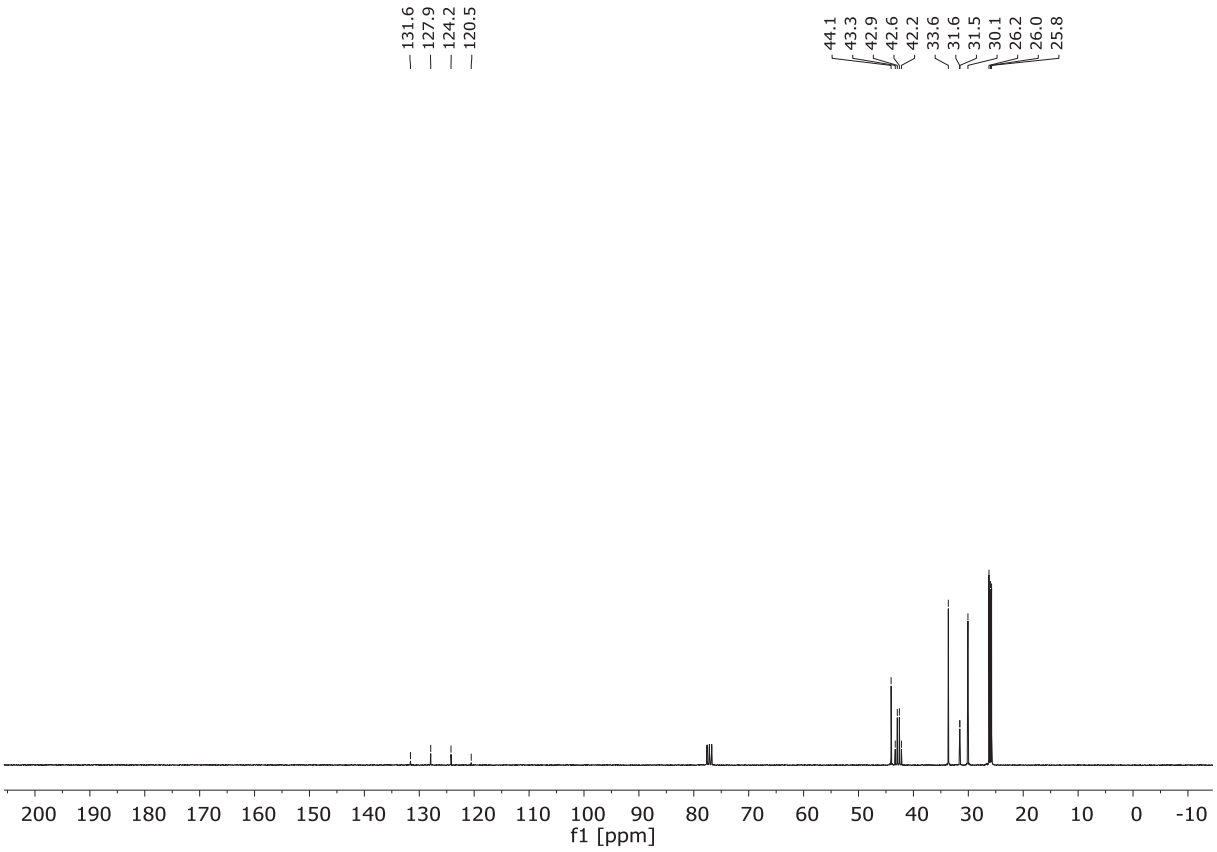
(3,3,3-Trifluoro-1-iodopropyl)cyclohexane (159)



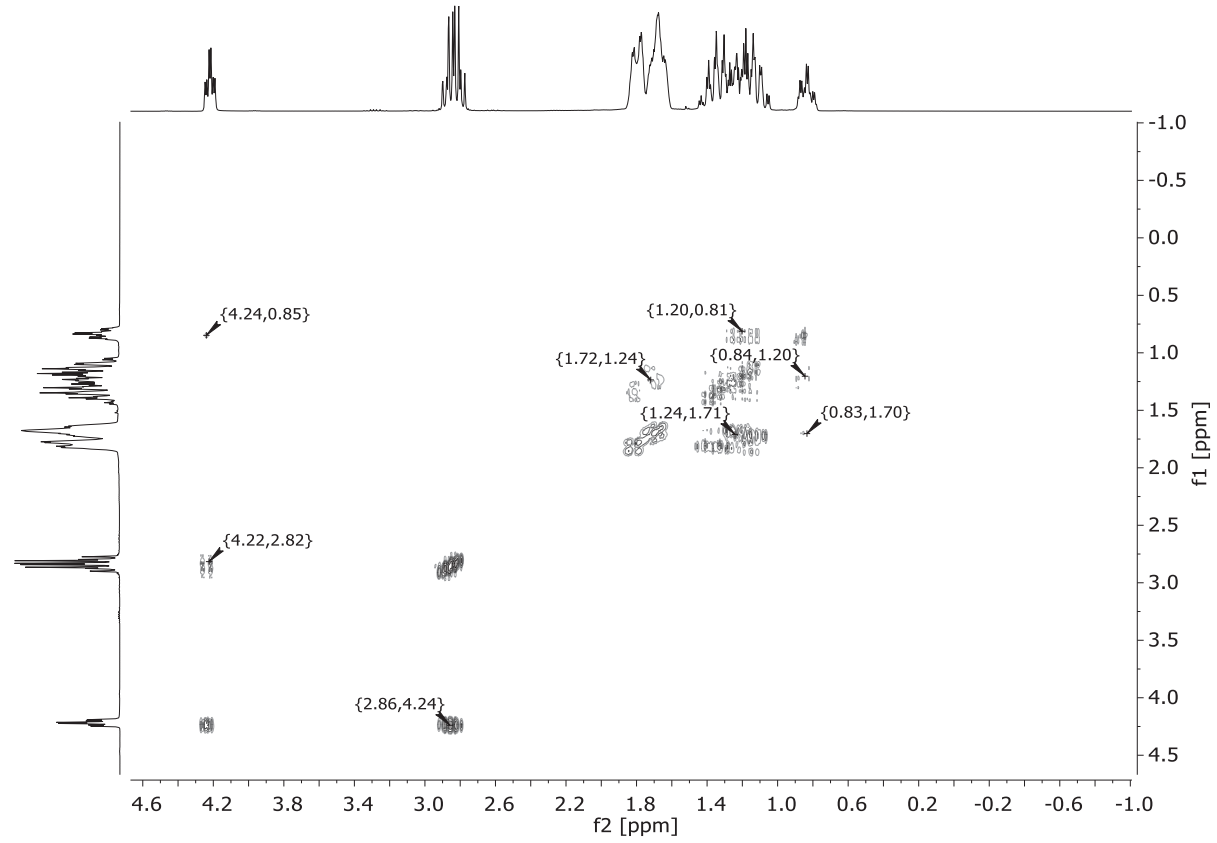
^{19}F NMR (565 MHz, chloroform-*d*)



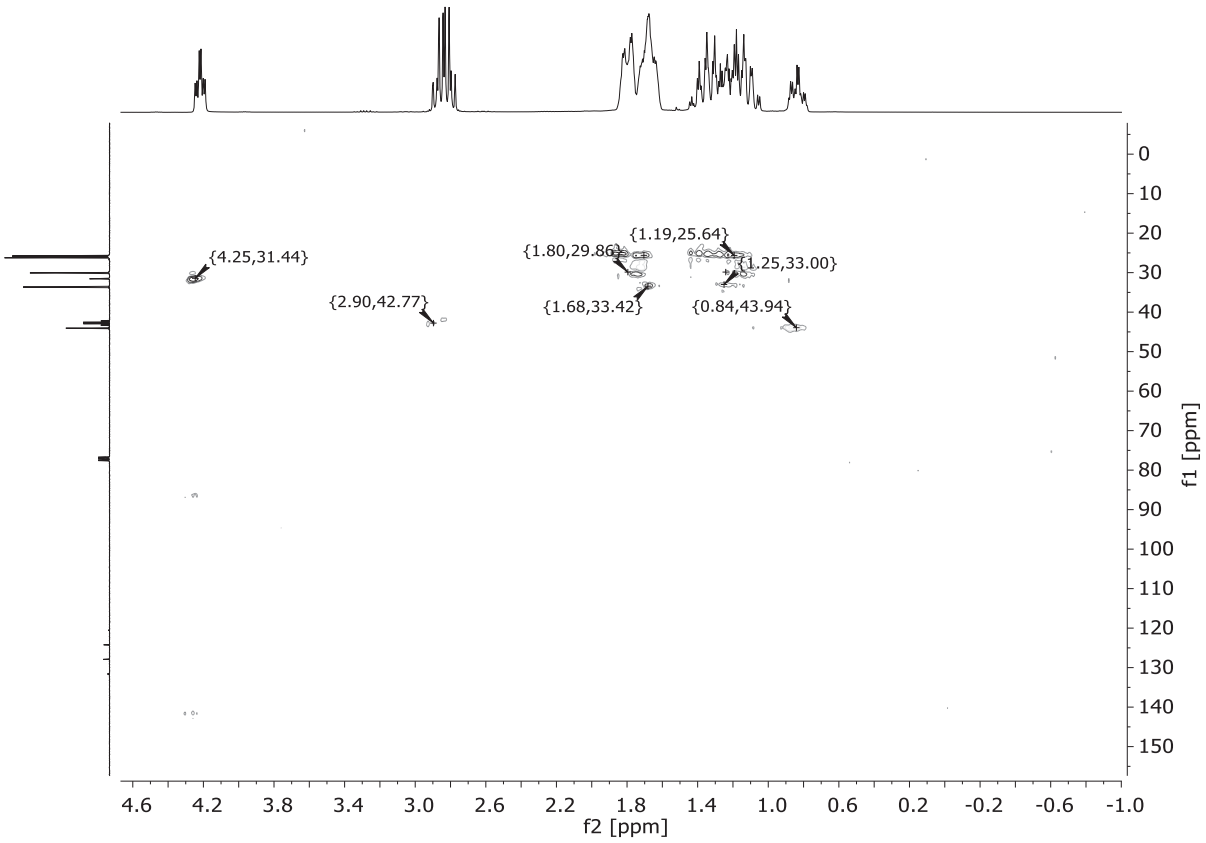
^{1}H NMR (600 MHz, chloroform-*d*)



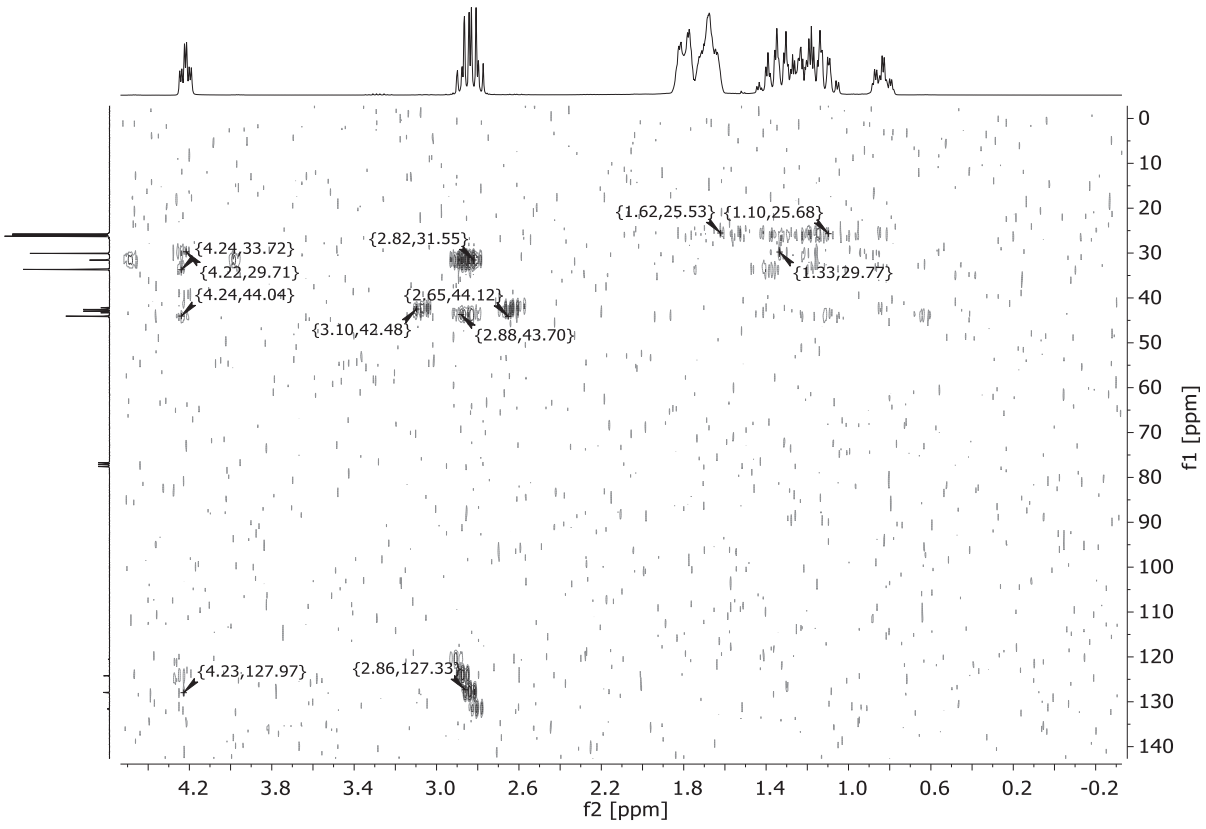
^{13}C NMR (75 MHz, chloroform-*d*)



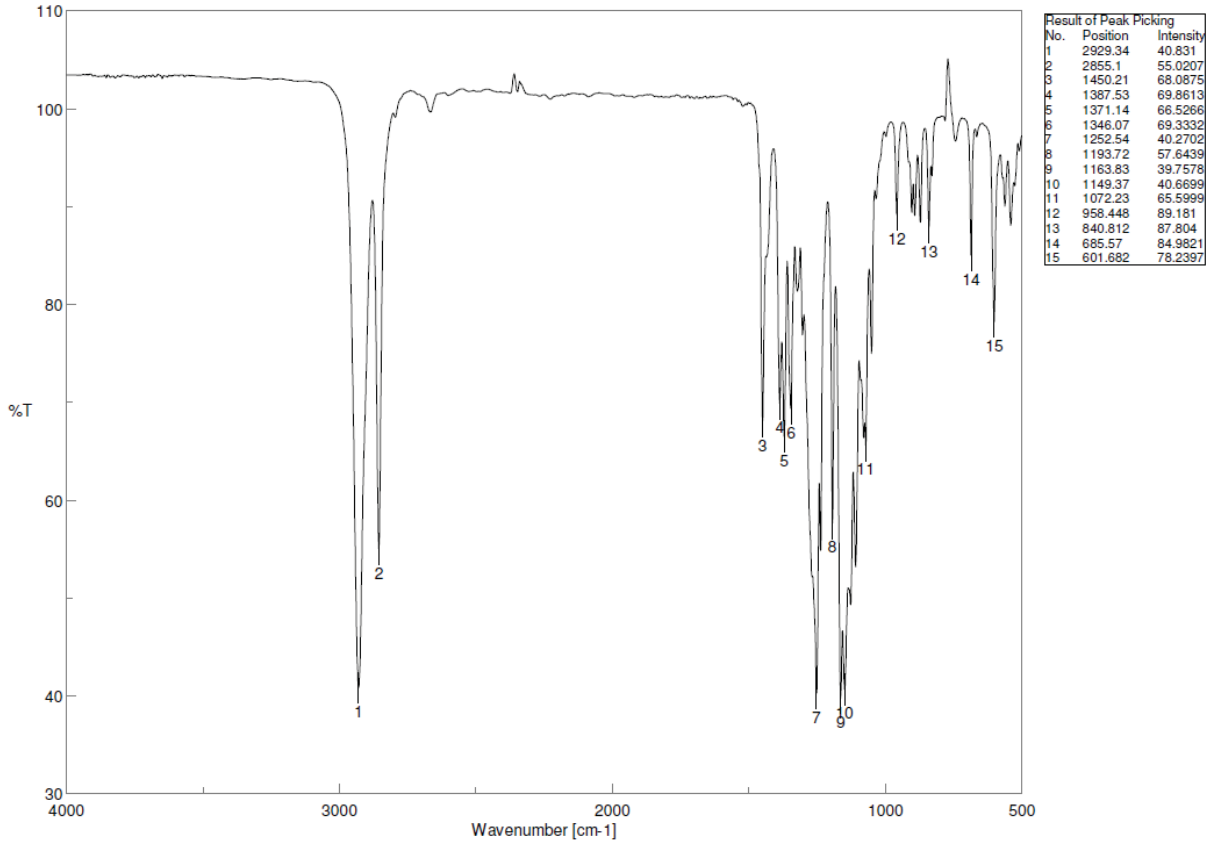
COSY


{4.25,31.44}
{2.90,42.77}
{1.80,29.86}
{1.19,25.64}
{1.25,33.00}
{1.68,33.42}
{0.84,43.94}
f2 [ppm]
f1 [ppm]

HSQC

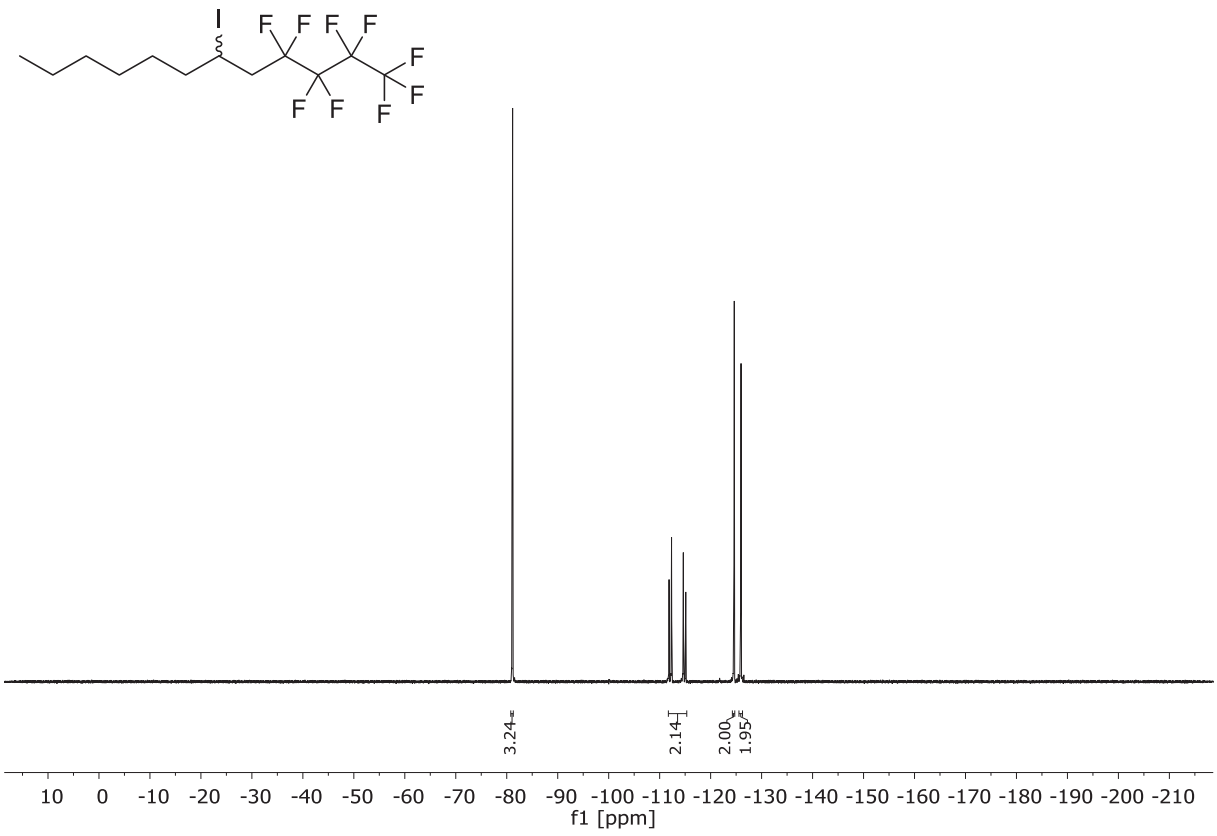

{4.24,33.72}
{4.22,29.71}
{4.24,44.04}
{2.82,31.55}
{2.65,44.12}
{3.10,42.48}
{2.88,43.70}
{1.62,25.53}
{1.10,25.68}
{1.33,29.77}
{4.23,127.97}
{2.86,127.33}
f2 [ppm]
f1 [ppm]

HMBC

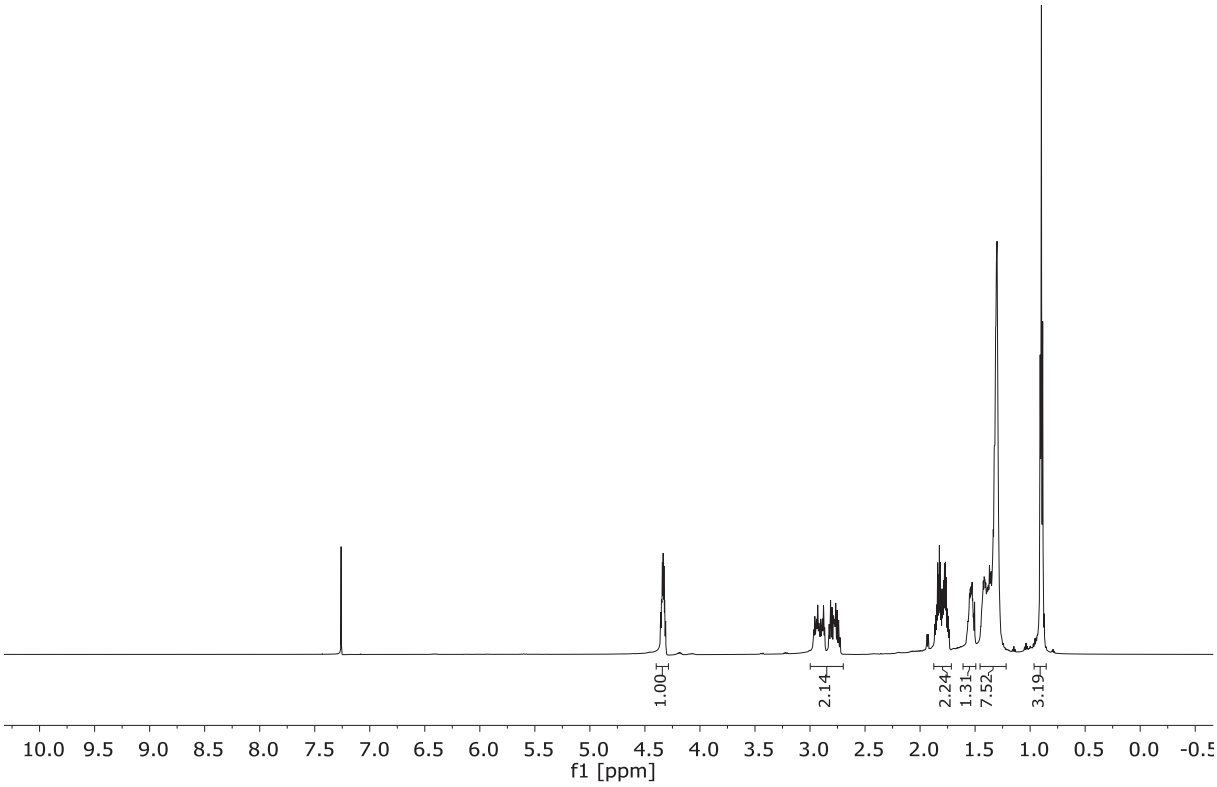


IR (Film)

1,1,1,2,2,3,3,3-Nonafluoro-6-iododododecane (175)

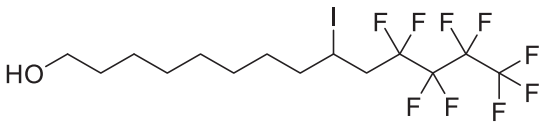


^{19}F NMR (565 MHz, chloroform-*d*)

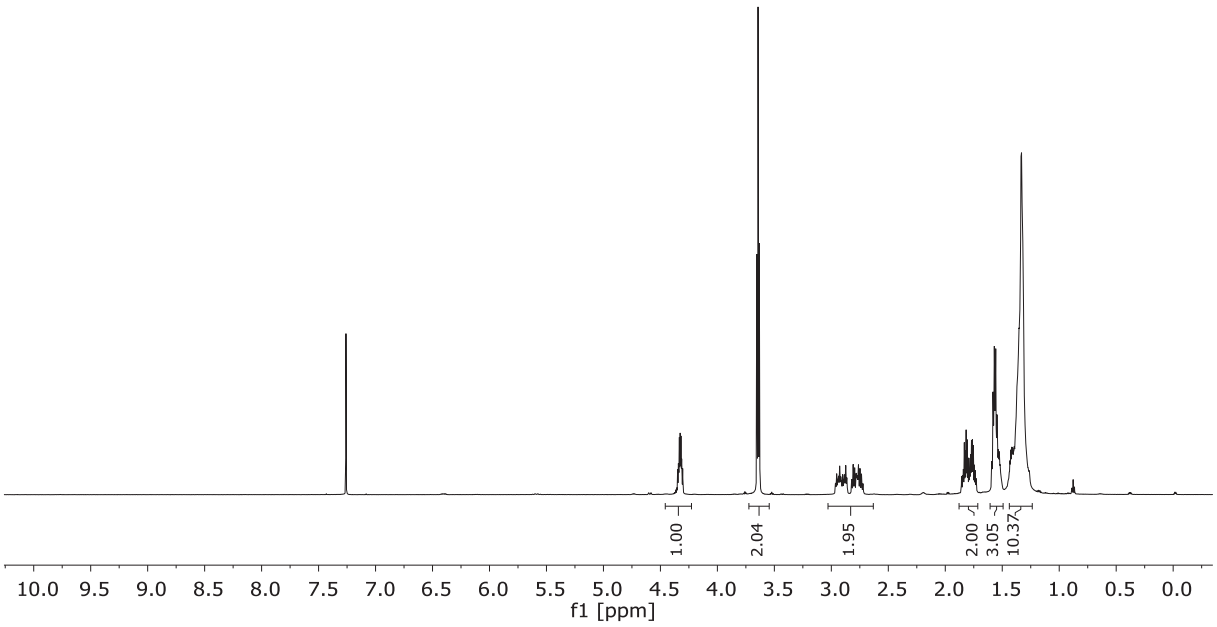


^{1}H NMR (600 MHz, chloroform-*d*)

11,11,12,12,13,13,14,14,14-Nonafluoro-9-iodotetradecan-1-ol (176)

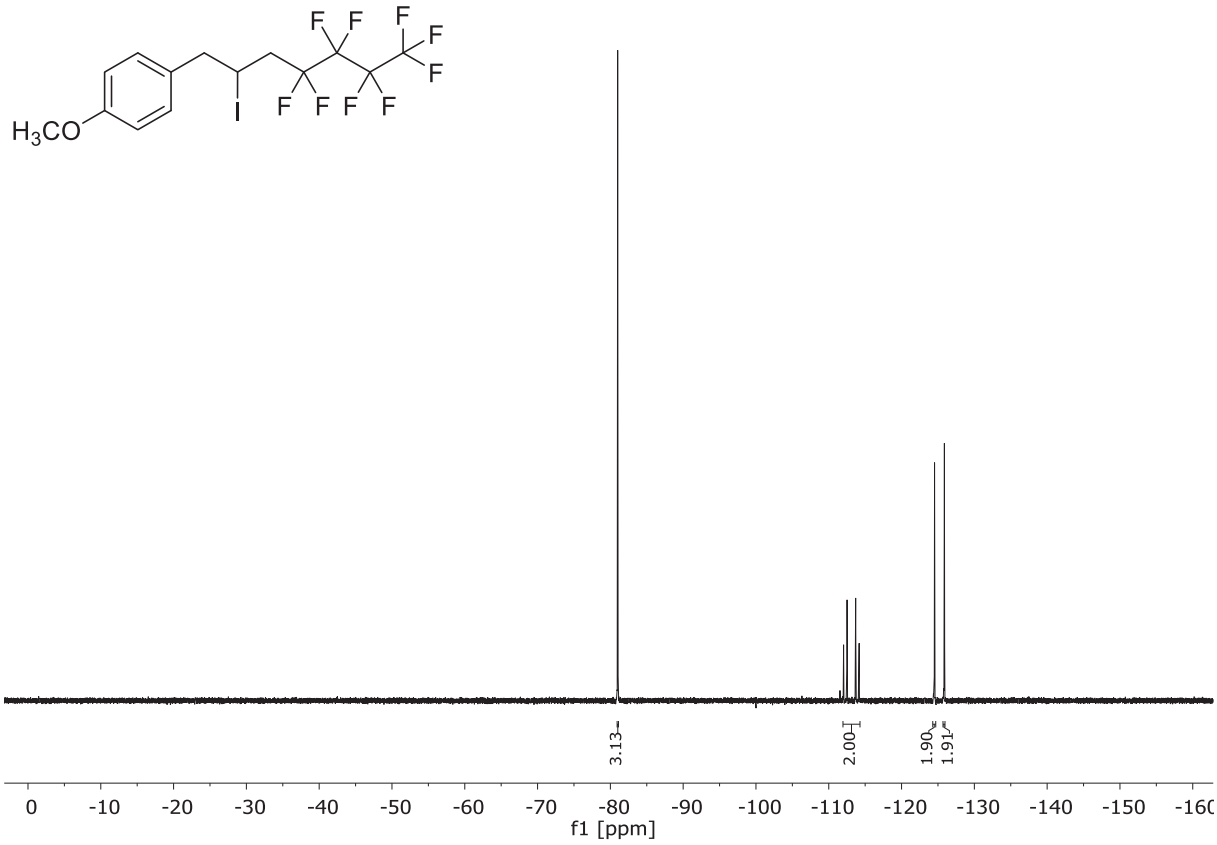


^{19}F NMR (565 MHz, chloroform-*d*)

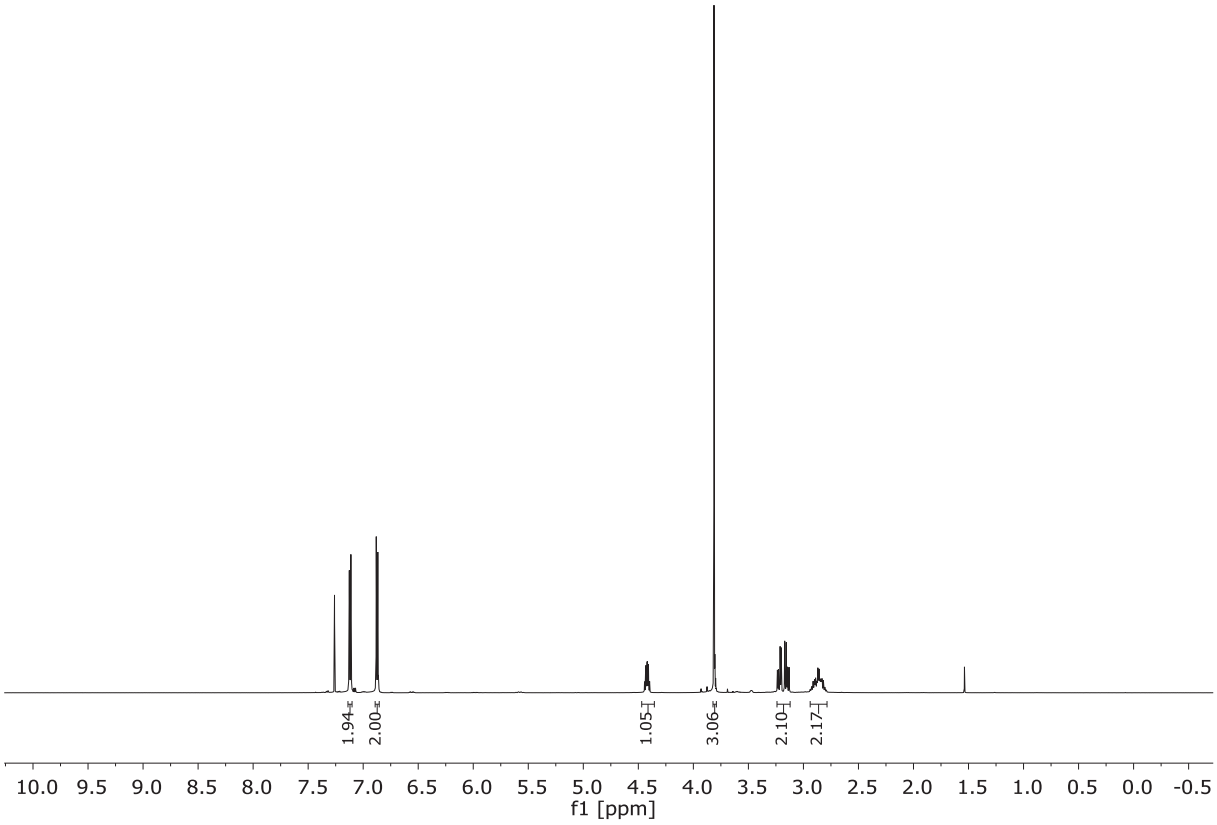


^{1}H NMR (300 MHz, chloroform-*d*)

1-Methoxy-4-(4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptyl)benzene (178)

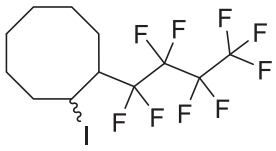


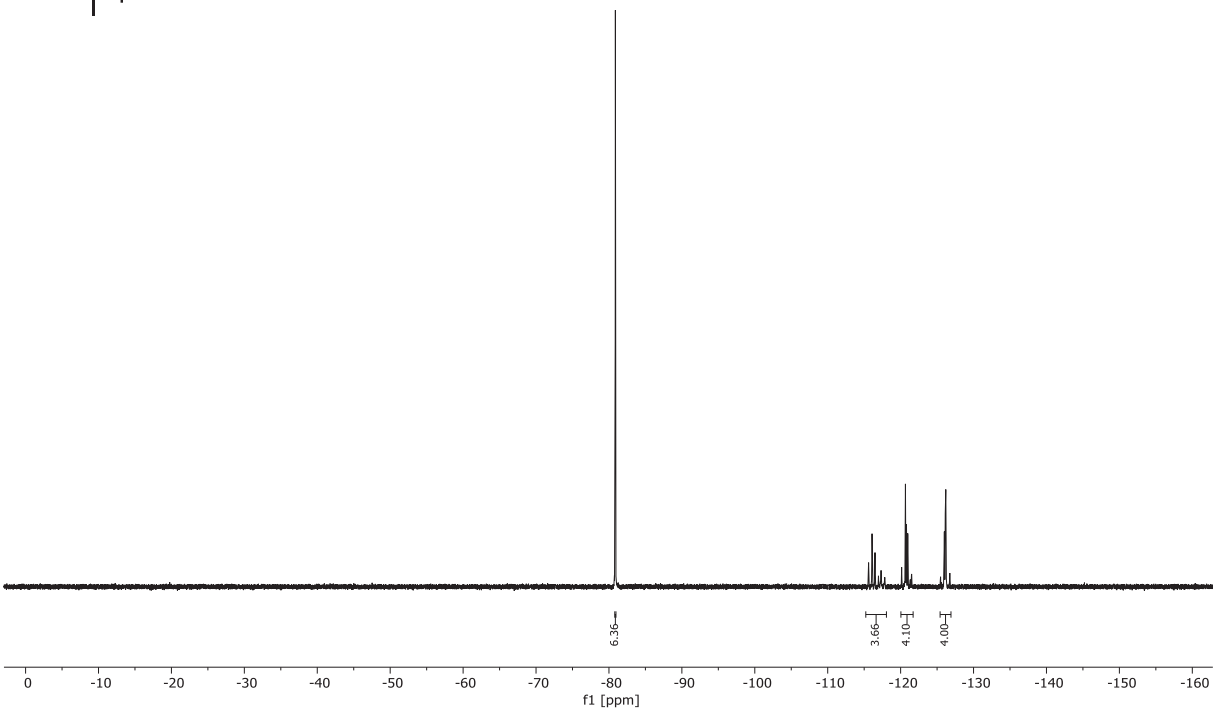
^{19}F NMR (565 MHz, chloroform-*d*)



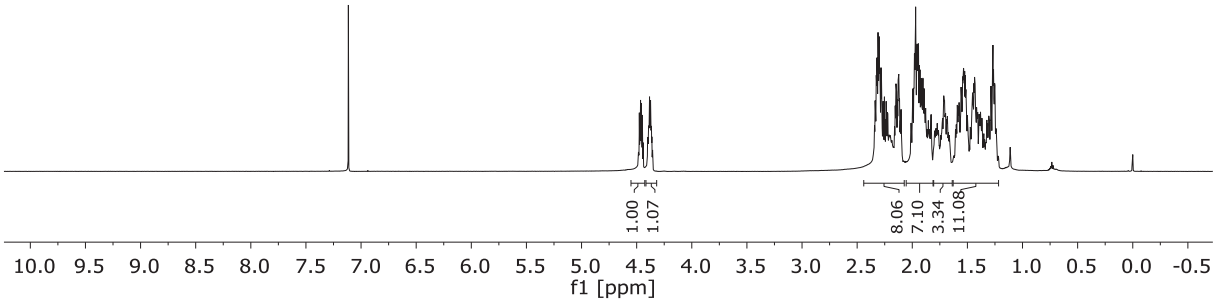
^{1}H NMR (600 MHz, chloroform-*d*)

1-Iodo-2-(perfluorobutyl)cyclooctane (177)



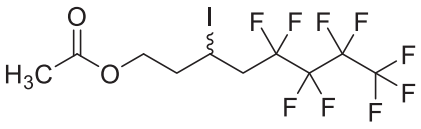


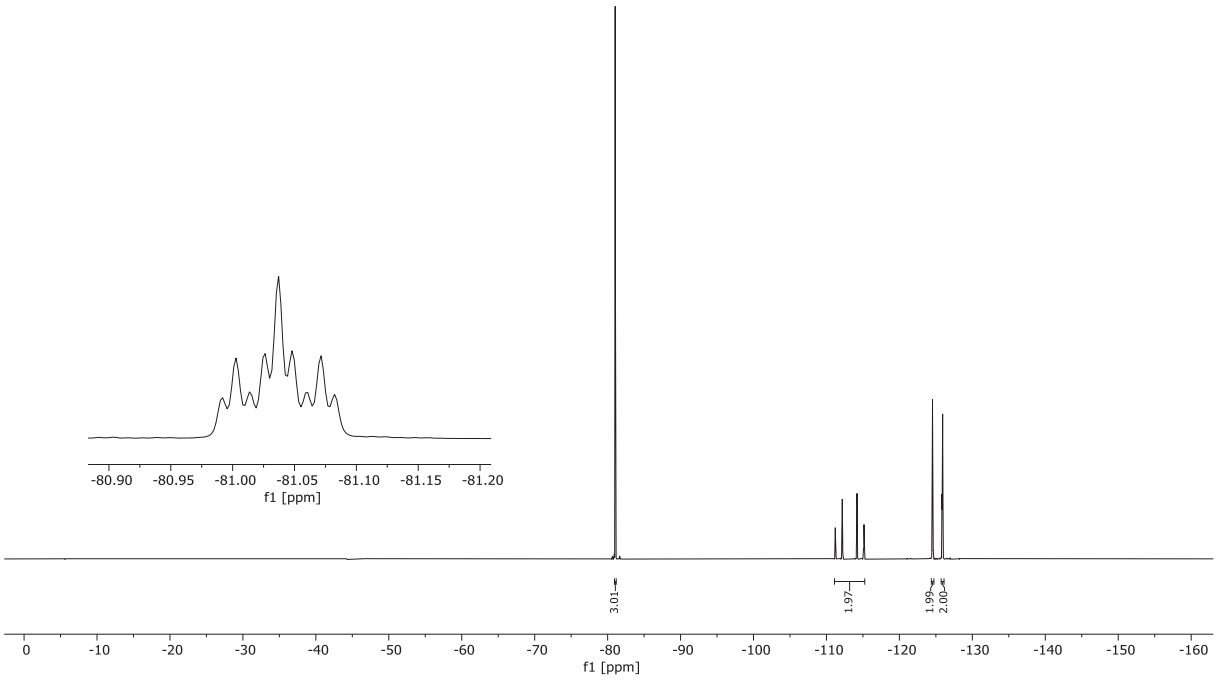
^{19}F NMR (565 MHz, chloroform-*d*)



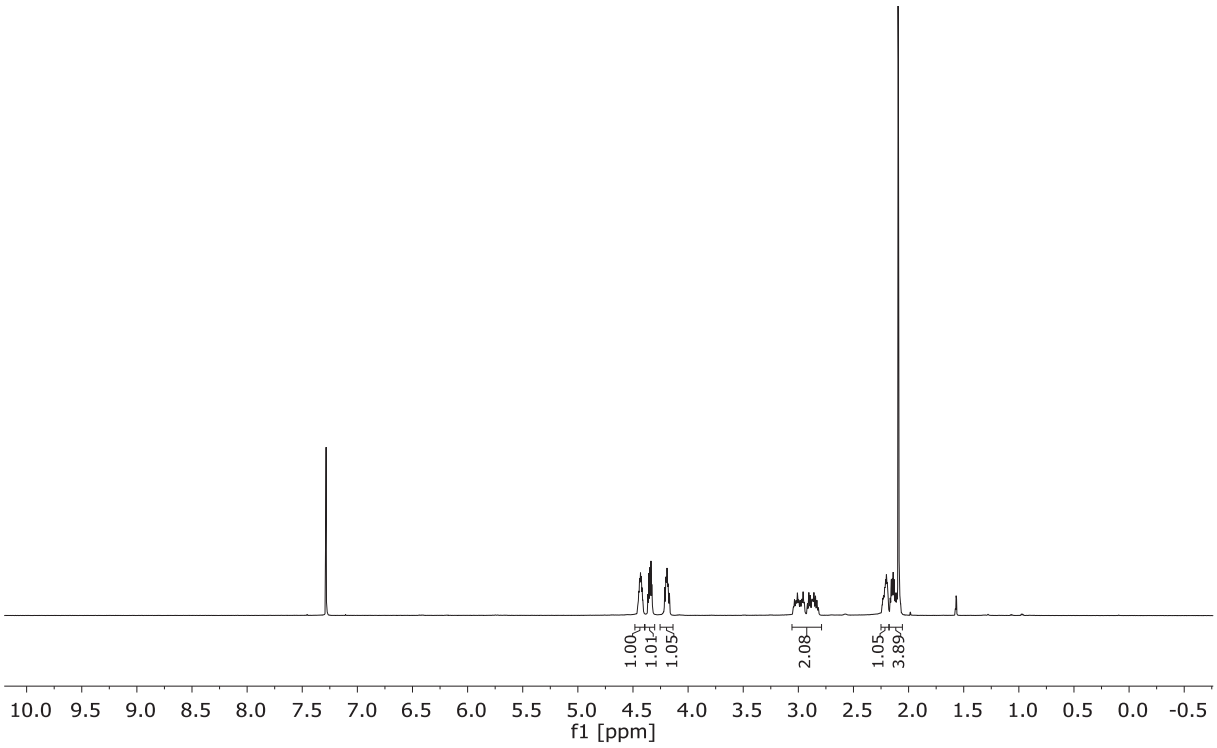
^{1}H NMR (600 MHz, chloroform-*d*)

5,5,6,6,7,7,8,8,8-Nonafluoro-3-iodooctyl acetate (170)

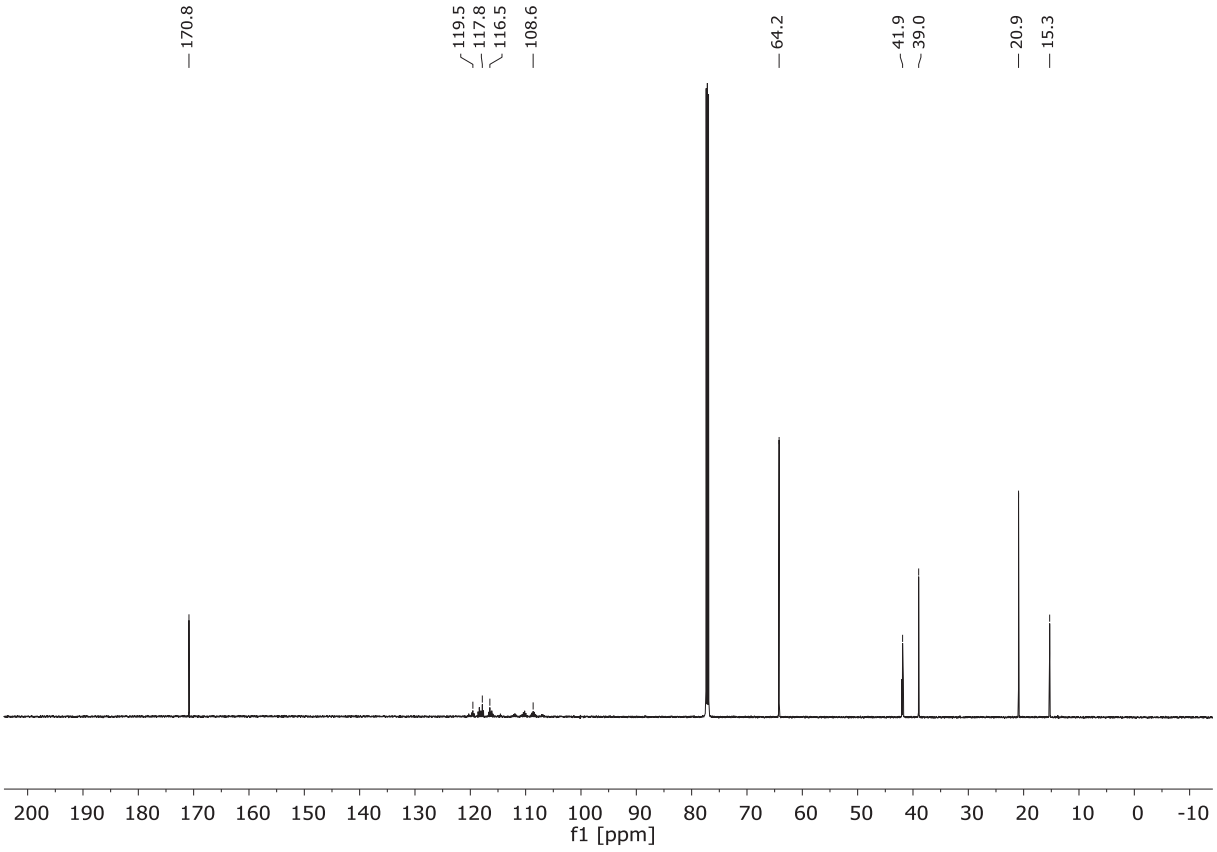




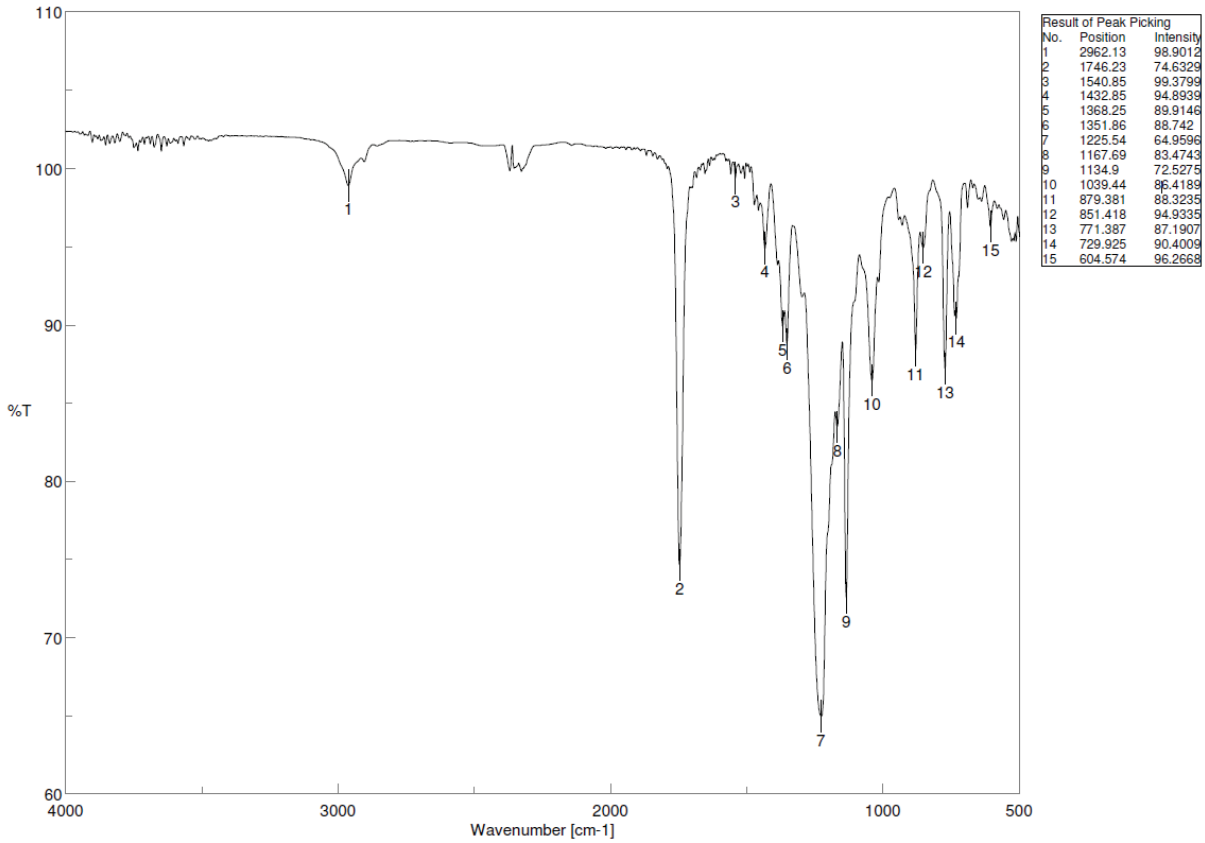
^{19}F NMR (282 MHz, chloroform-*d*)



^{1}H NMR (600 MHz, chloroform-*d*)

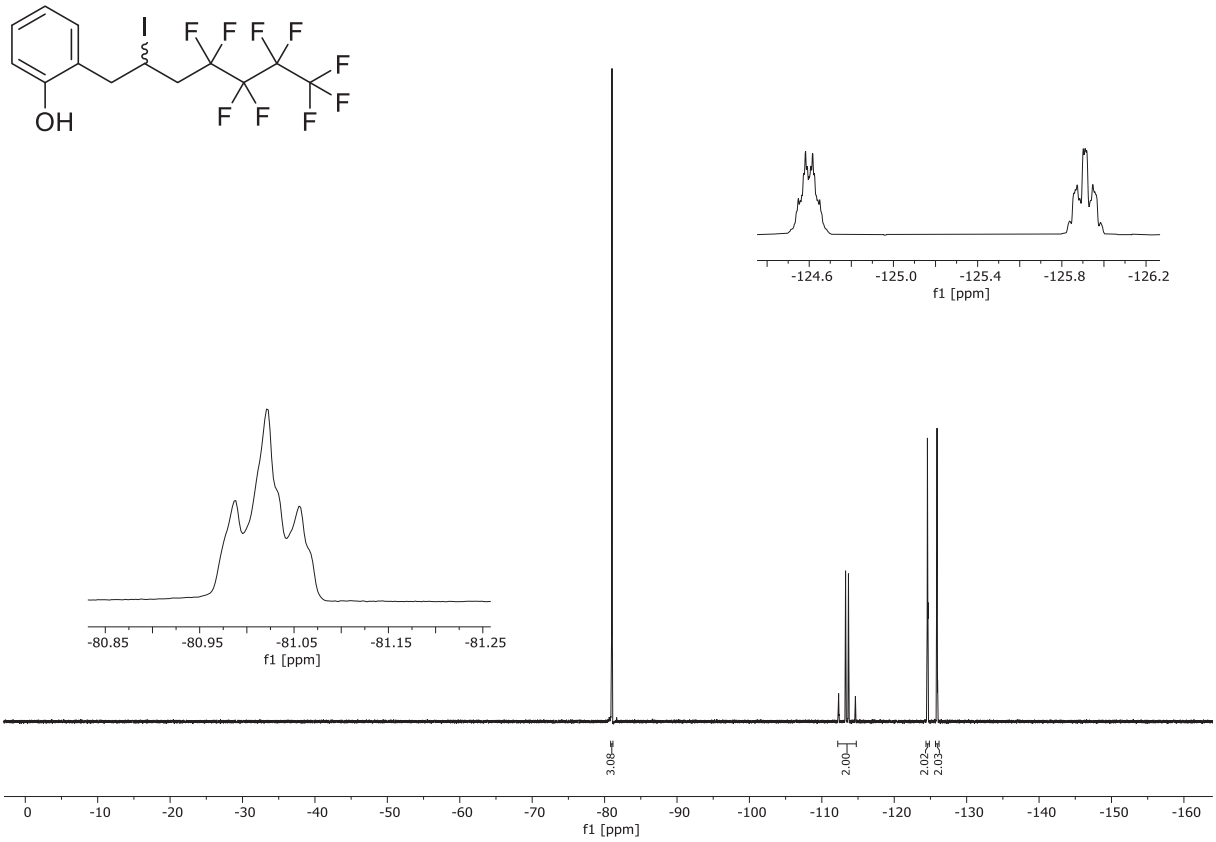


^{13}C NMR (151 MHz, chloroform-*d*)

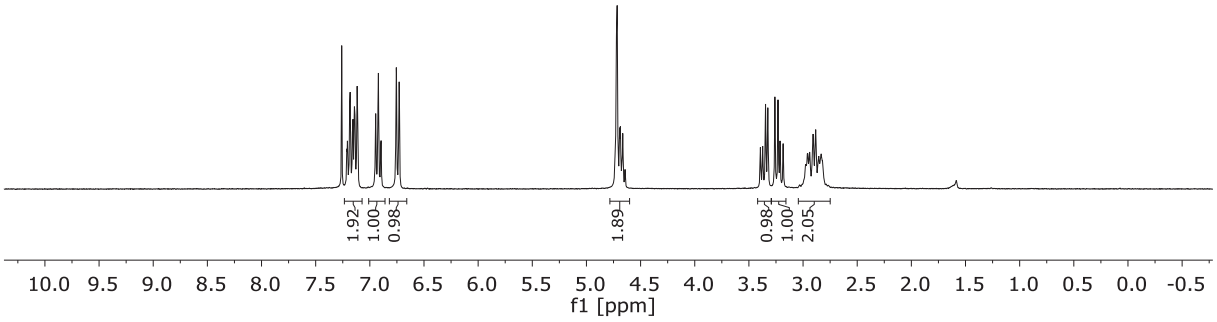


IR (Film)

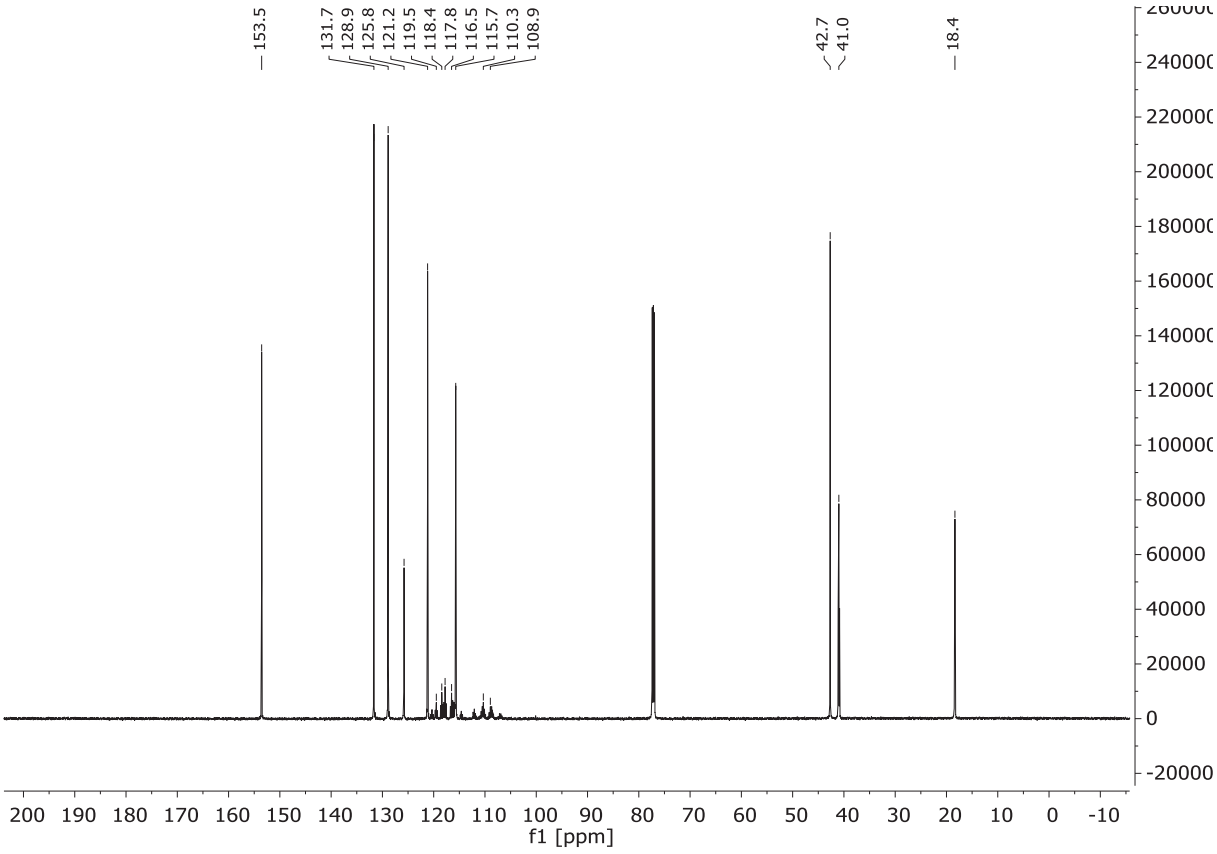
2-(4,4,5,5,6,6,7,7,7-Nonafluoro-2-iodoheptyl)phenol (181)



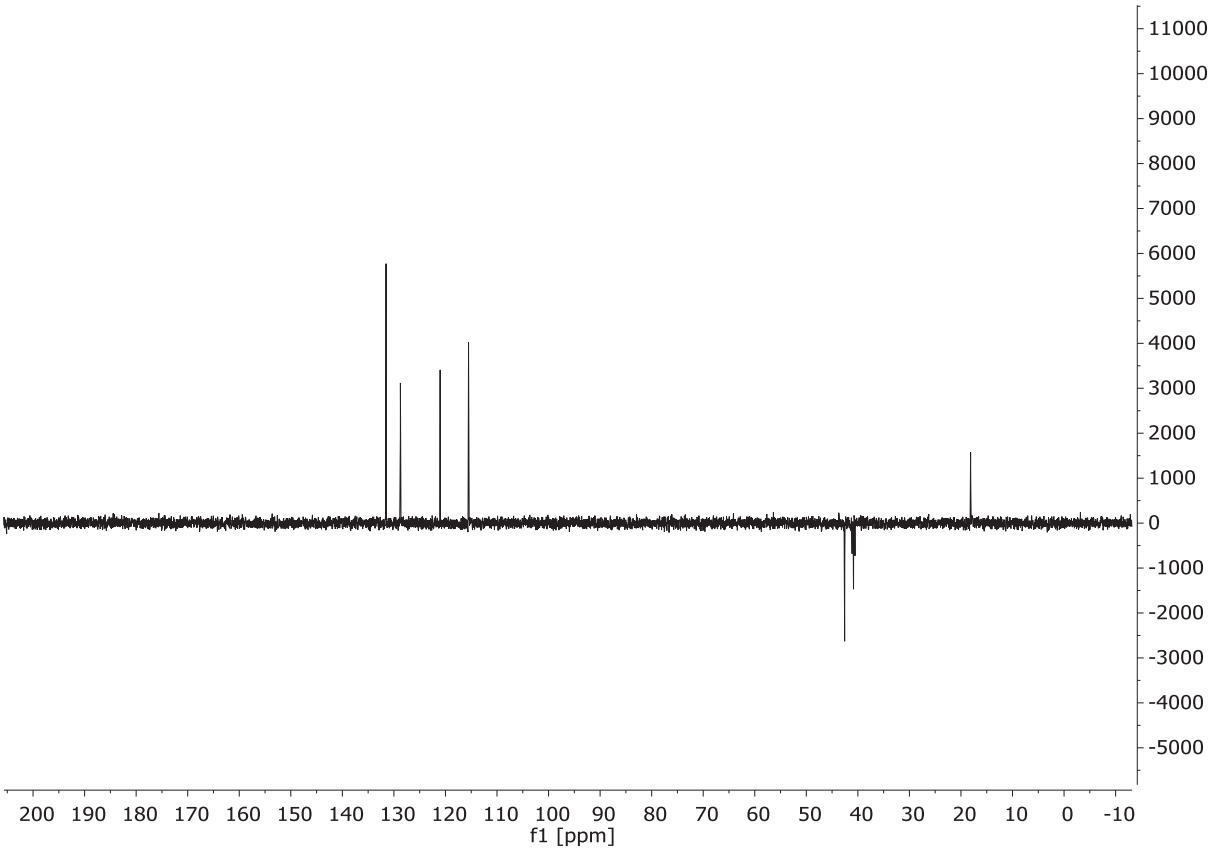
^{19}F NMR (282 MHz, chloroform-*d*)



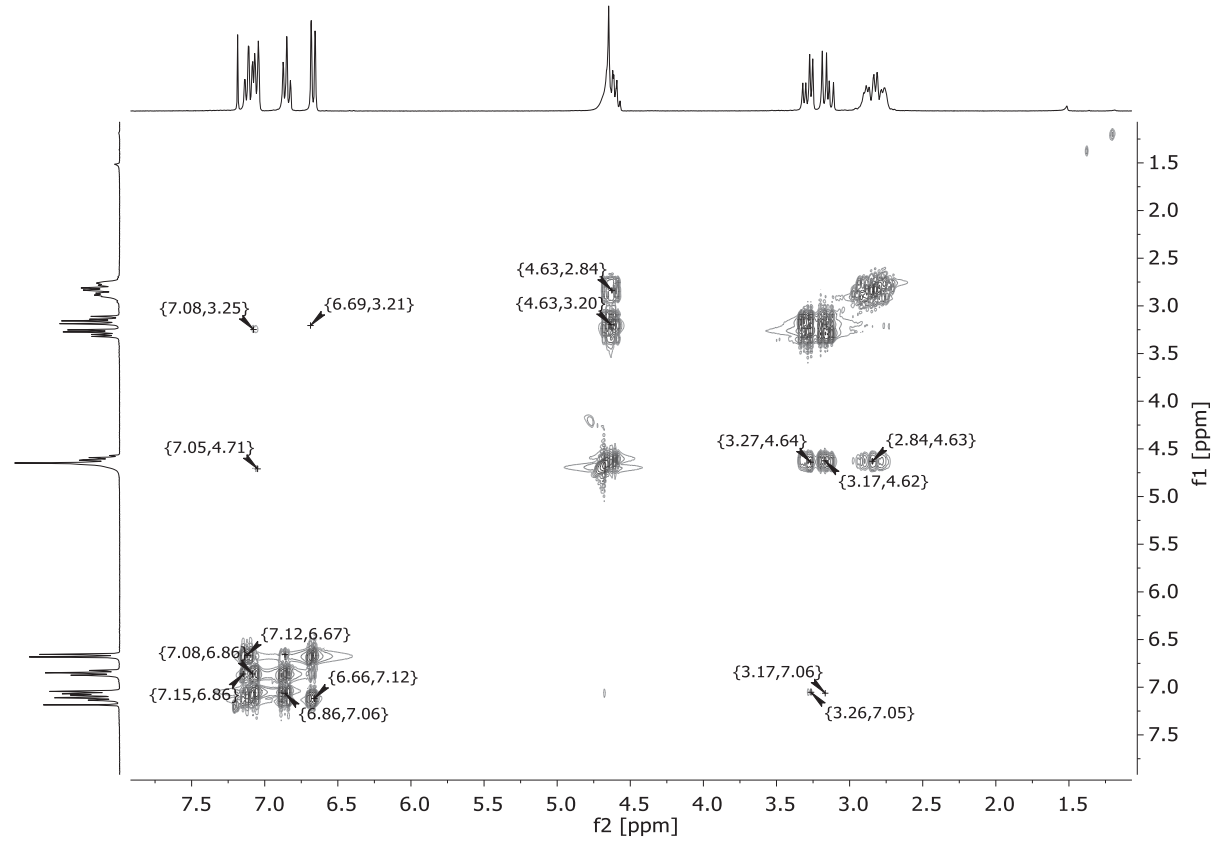
^{1}H NMR (300 MHz, chloroform-*d*)



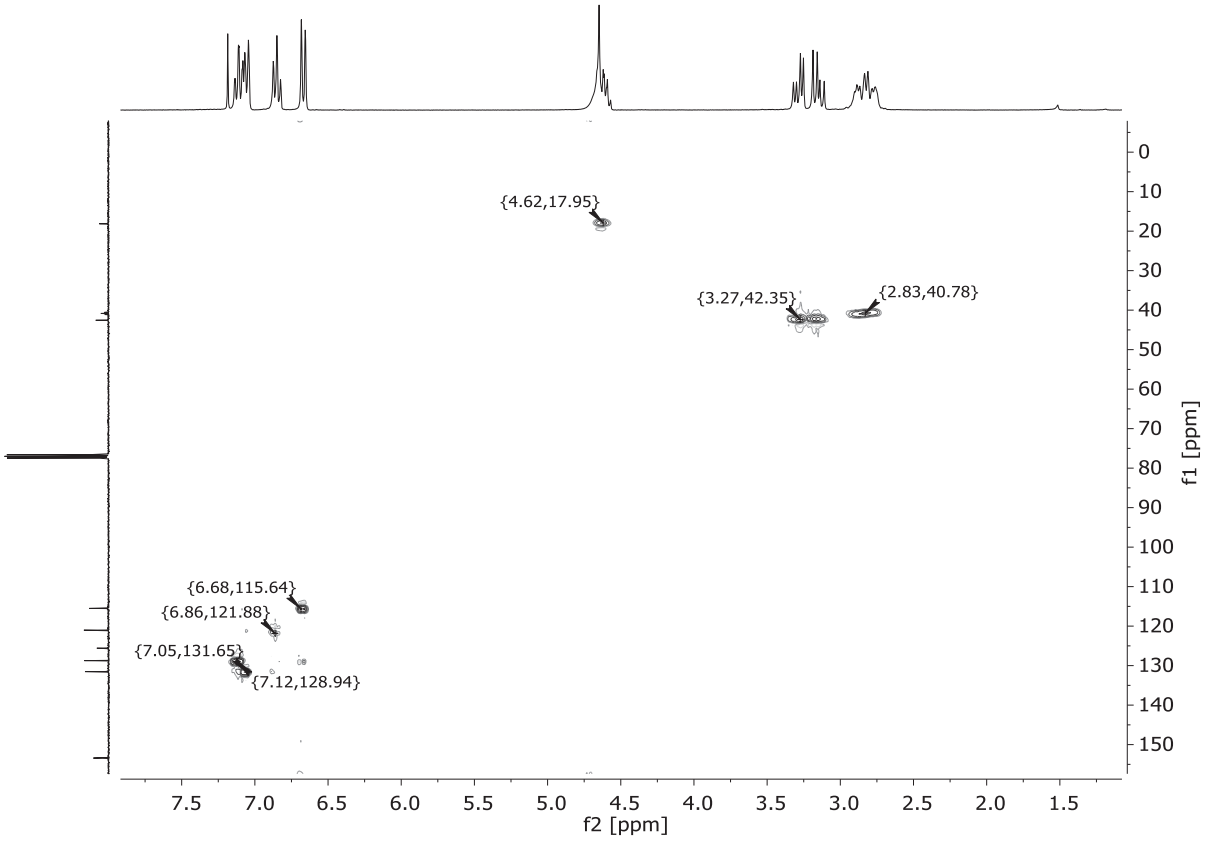
^{13}C NMR (75 MHz, chloroform-*d*)



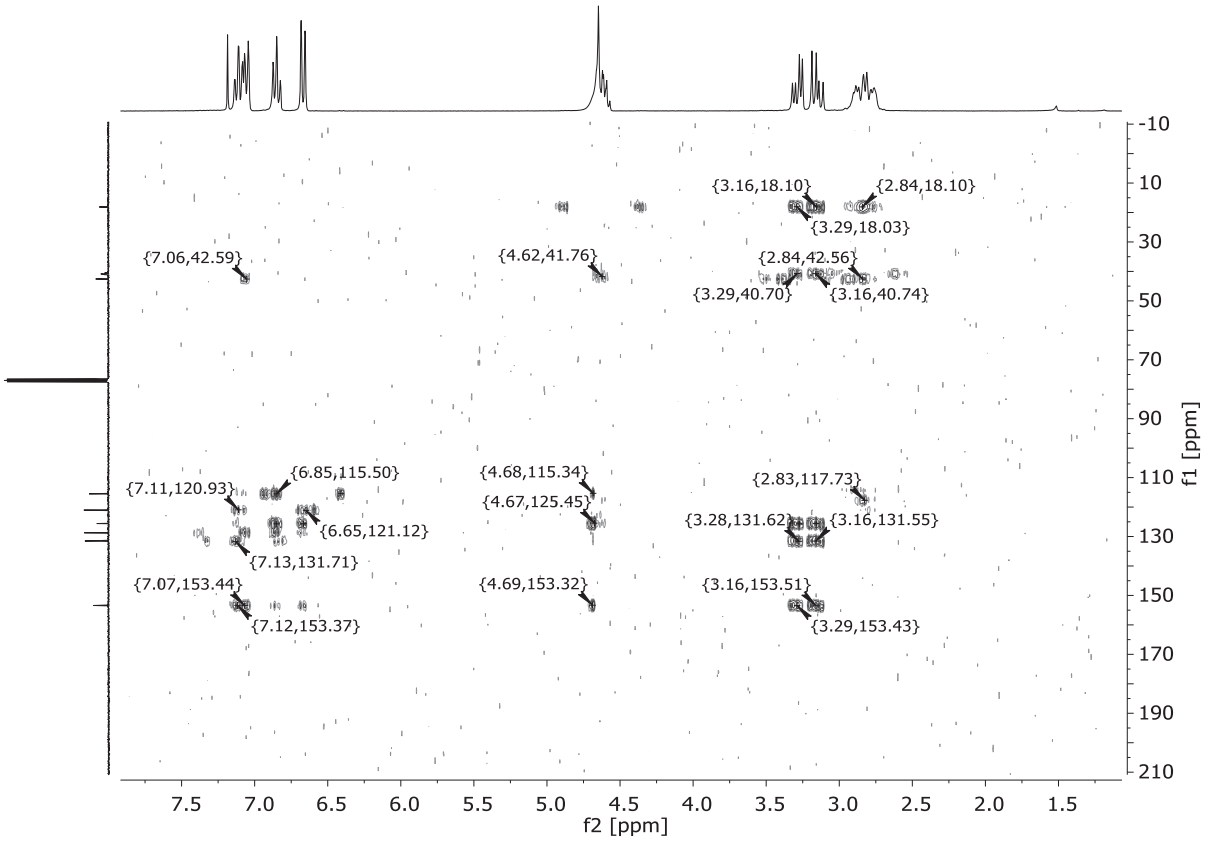
DEPT 135



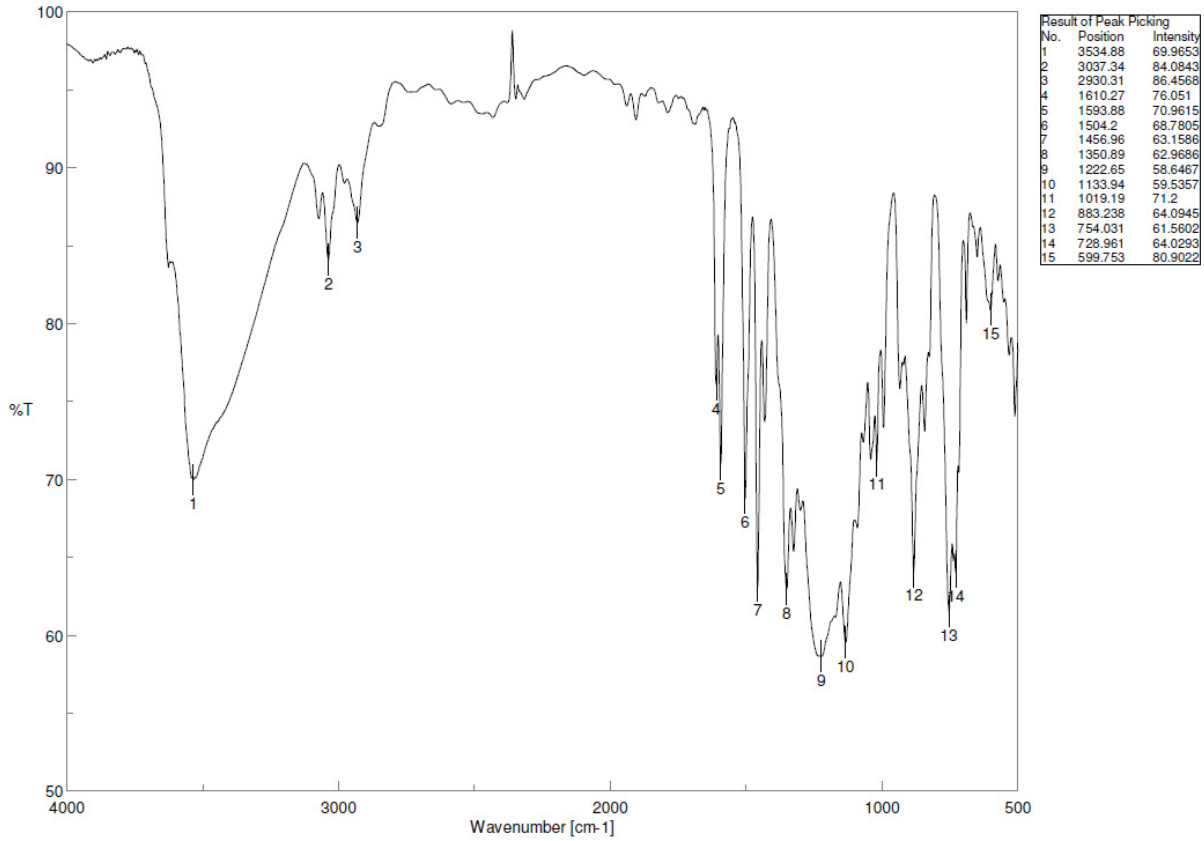
COSY


{4.62,17.95}
{3.27,42.35}
{2.83,40.78}
{6.68,115.64}
{6.86,121.88}
{7.05,131.65}
{7.12,128.94}
f2 [ppm]
f1 [ppm]

HSQC

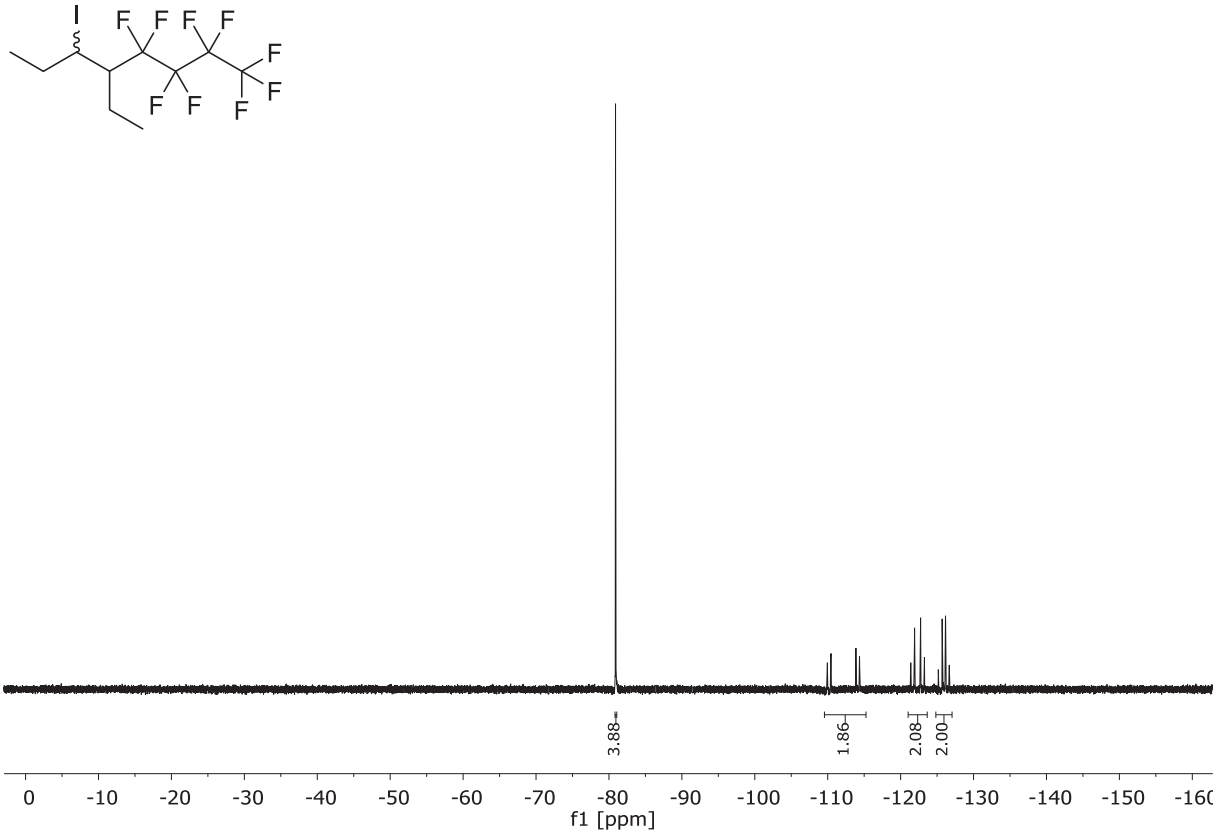

{3.16,18.10}
{2.84,18.10}
{3.29,18.03}
{7.06,42.59}
{4.62,41.76}
{2.84,42.56}
{3.29,40.70}
{3.16,40.74}
{6.85,115.50}
{7.11,120.93}
{6.65,121.12}
{7.13,131.71}
{4.68,115.34}
{4.67,125.45}
{2.83,117.73}
{3.28,131.62}
{3.16,131.55}
{7.07,153.44}
{7.12,153.37}
{4.69,153.32}
{3.16,153.51}
{3.29,153.43}
f2 [ppm]
f1 [ppm]

HMBC

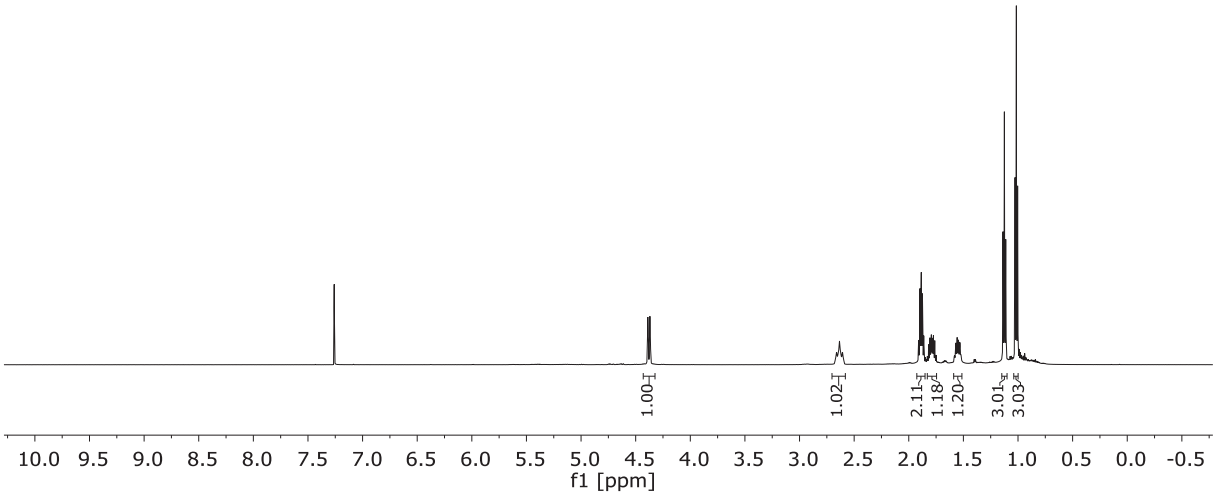


IR (Film)

5-Ethyl-1,1,1,2,2,3,3,4,4-nonafluoro-6-iodooctane (179) – Diastereomer 1

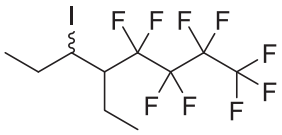


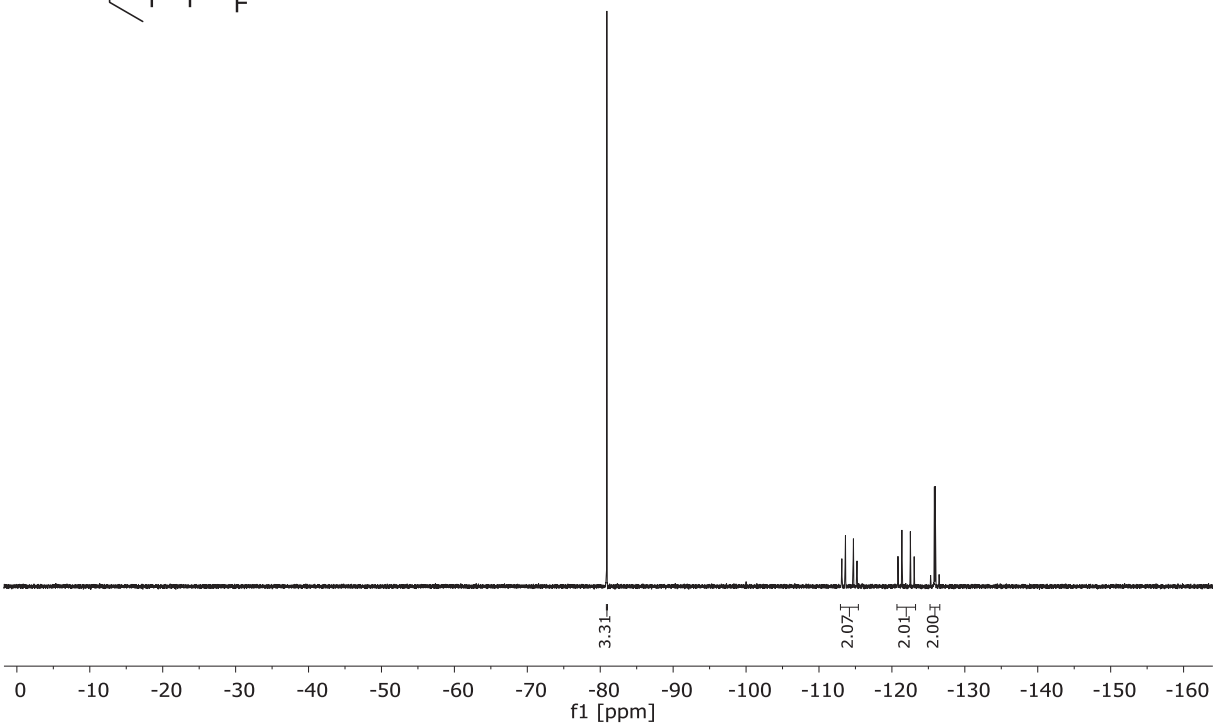
^{19}F NMR (565 MHz, chloroform-*d*)



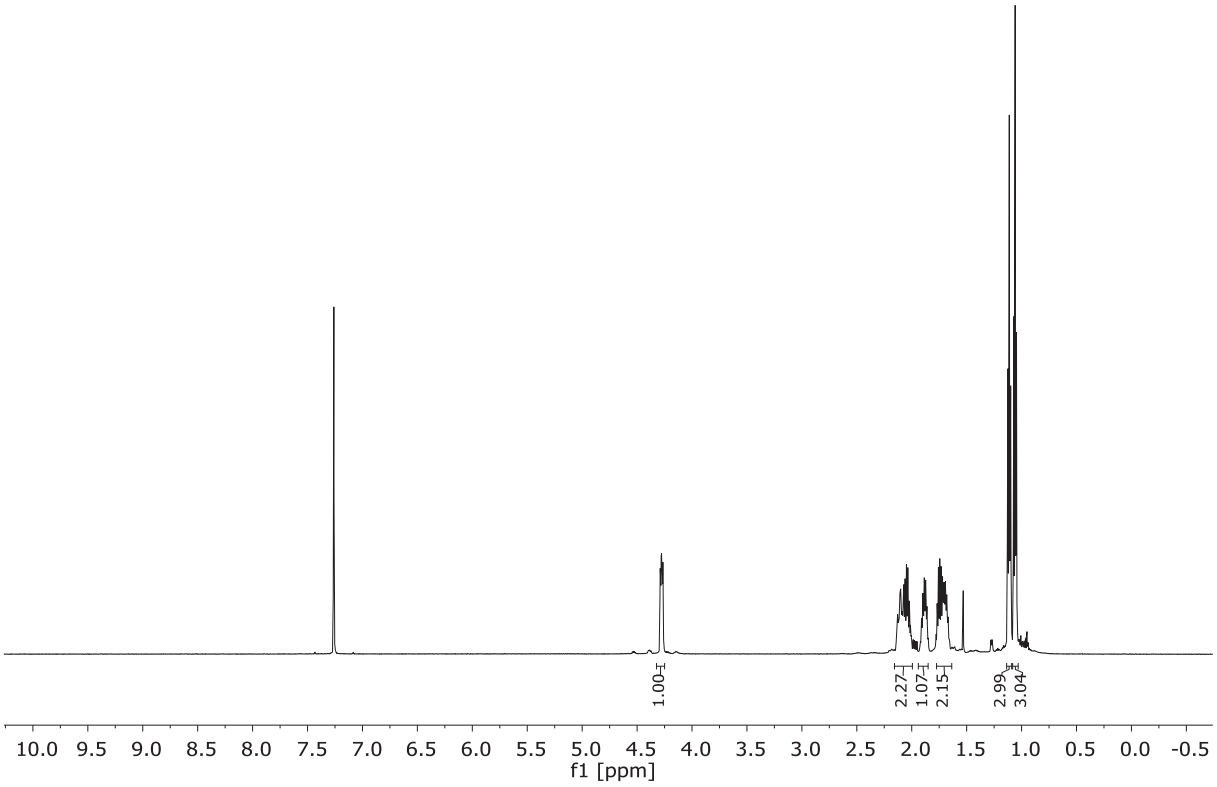
^{1}H NMR (600 MHz, chloroform-*d*)

5-Ethyl-1,1,1,2,2,3,3,4,4-nonafluoro-6-iodooctane (179) – Diastereomer 2



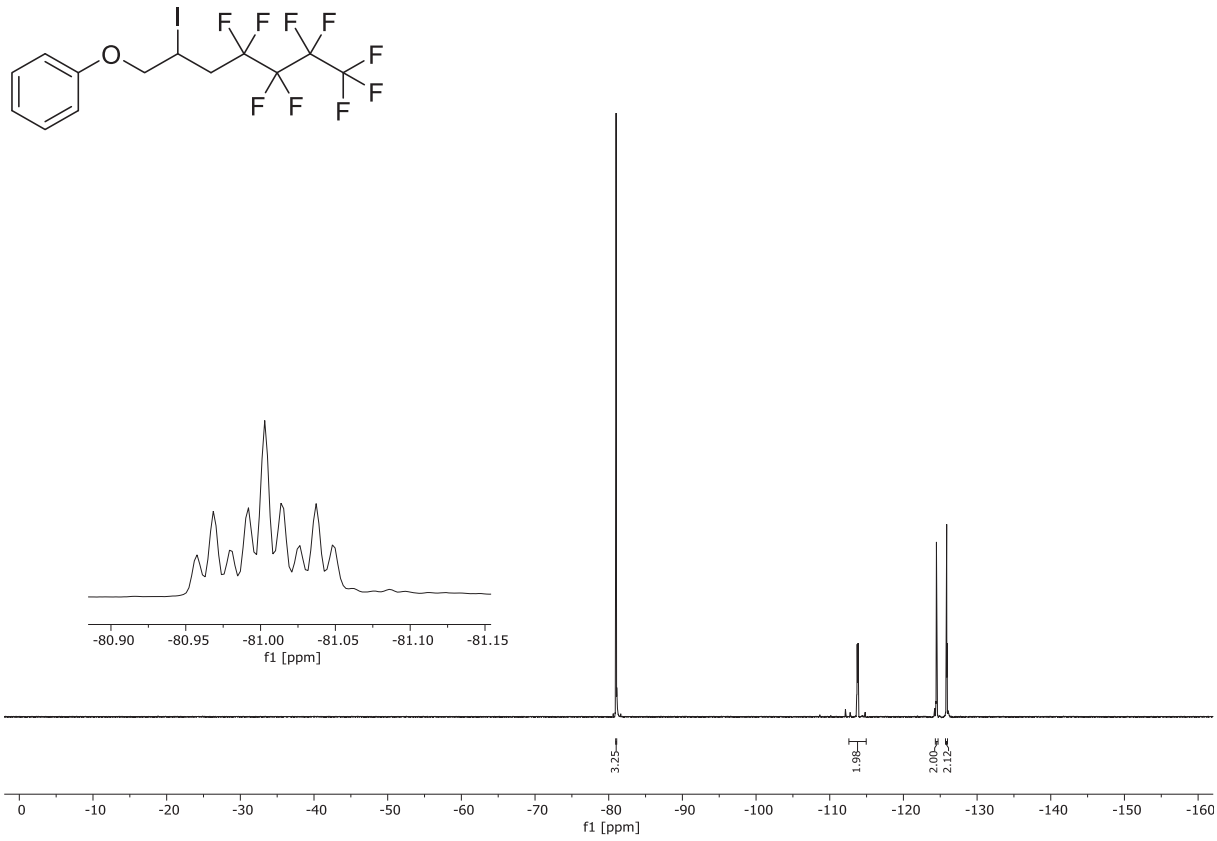


^{19}F NMR (565 MHz, chloroform-*d*)

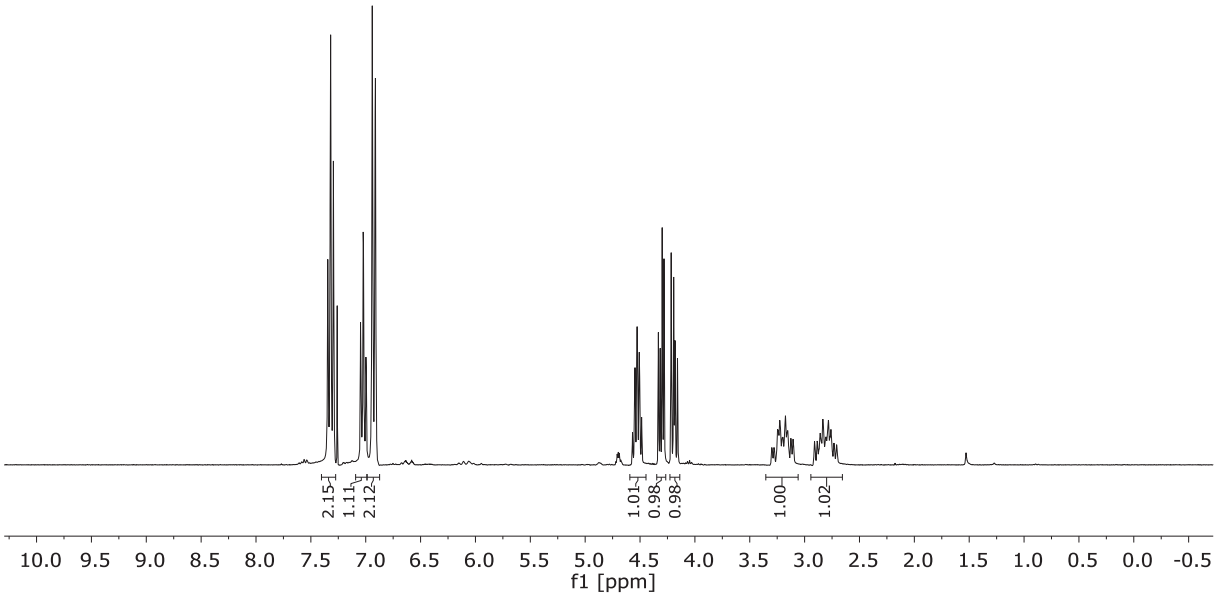


^{1}H NMR (600 MHz, chloroform-*d*)

[(4,4,5,5,6,6,7,7,7-Nonafluoro-2-iodoheptyl)oxy]benzene (183)

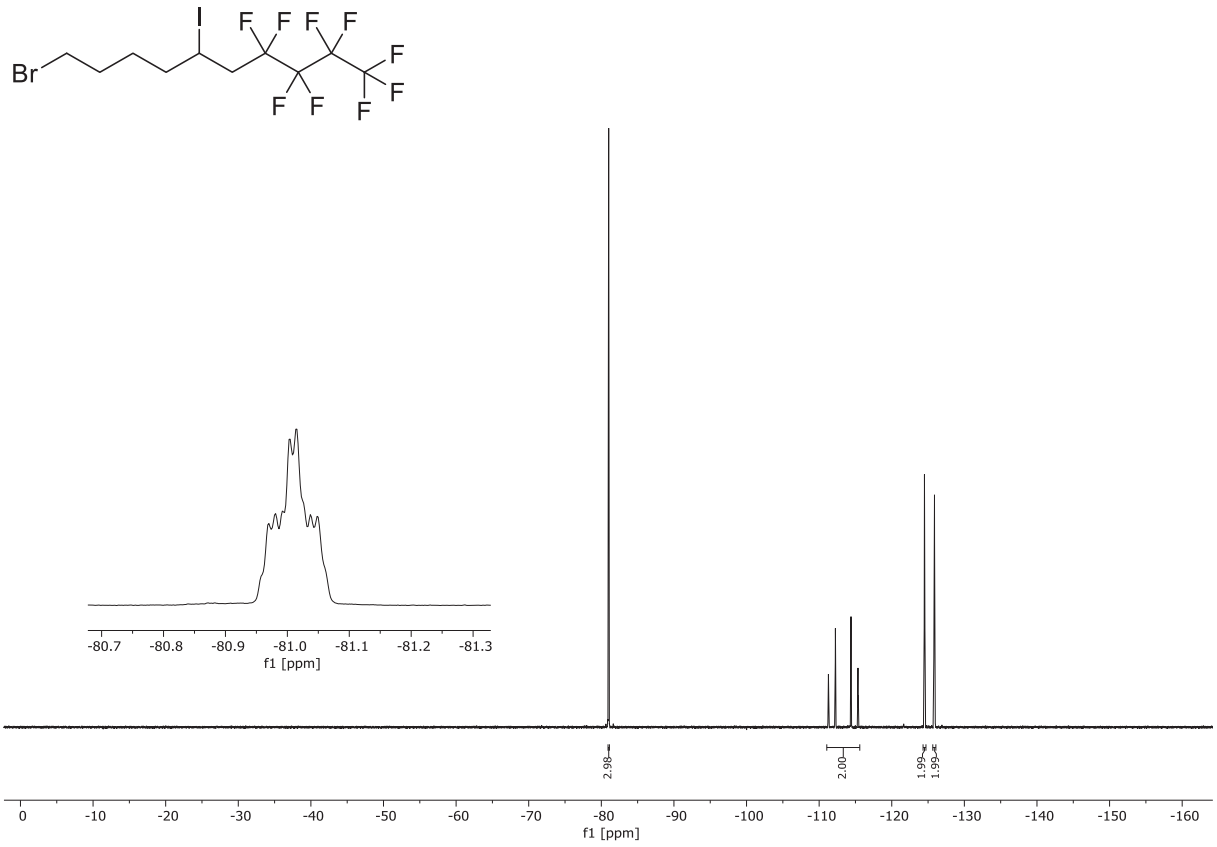


^{19}F NMR (282 MHz, chloroform-*d*)

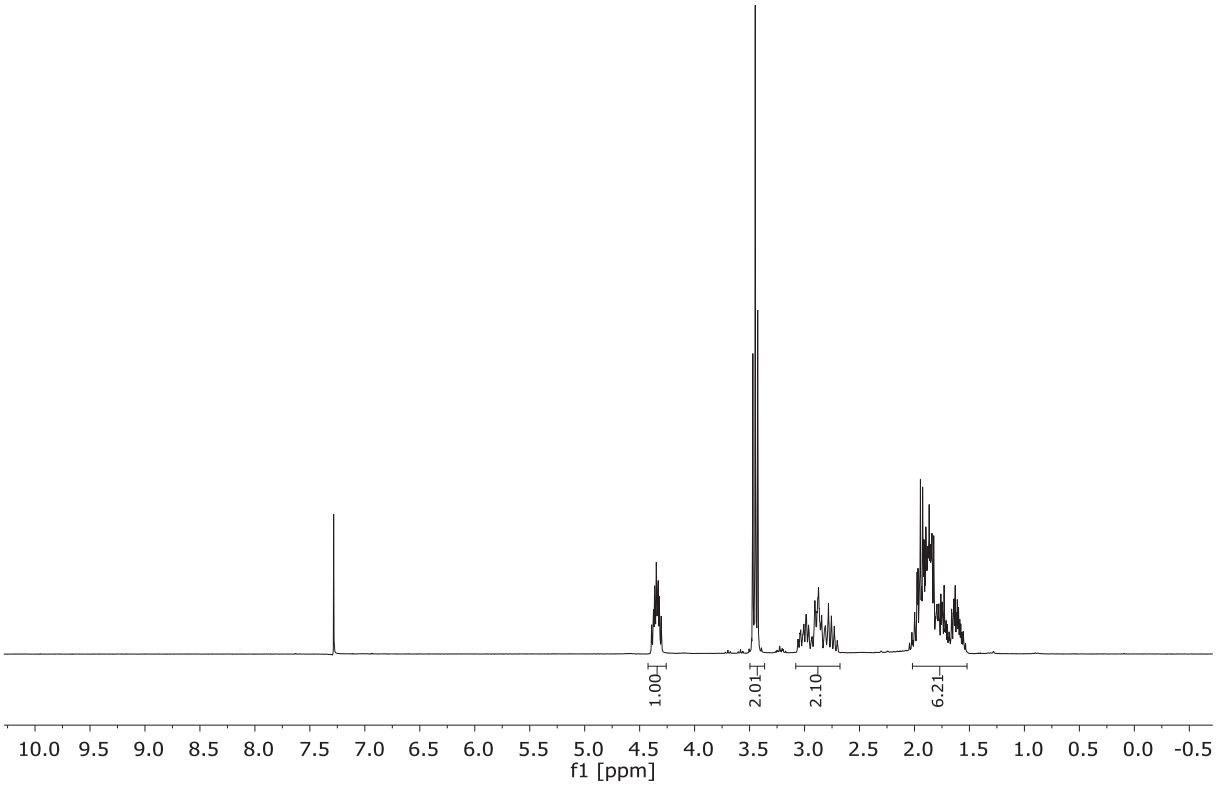


^{1}H NMR (300 MHz, chloroform-*d*)

10-Bromo-1,1,1,2,2,3,3,4,4-nonafluoro-6-iododecane (186)

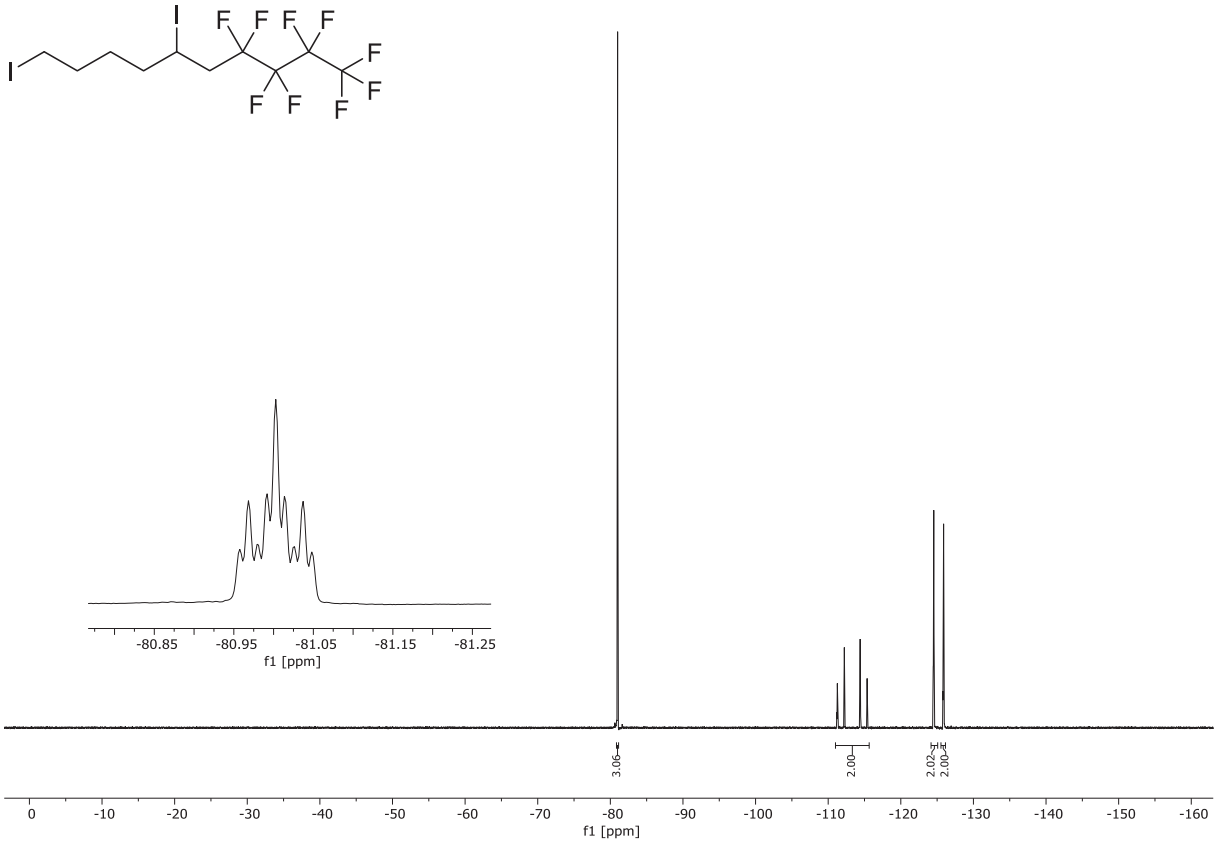


^{19}F NMR (282 MHz, chloroform-*d*)

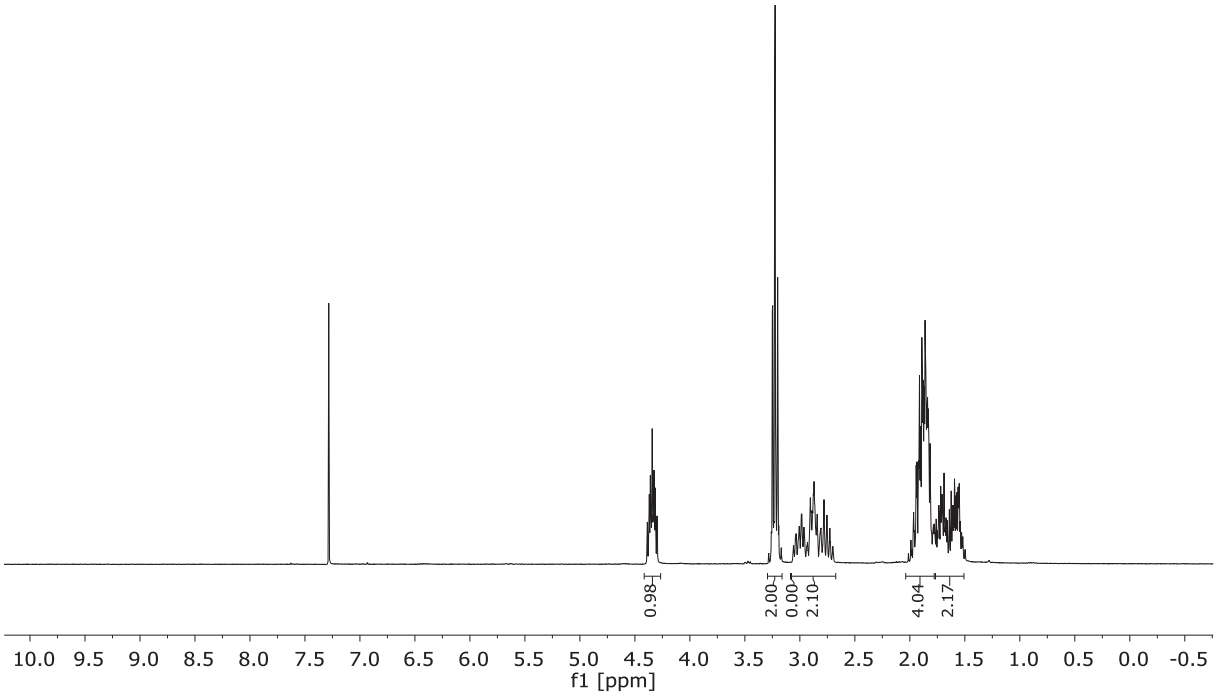


^{1}H NMR (300 MHz, chloroform-*d*)

1,1,1,2,2,3,3,4,4-Nonafluoro-6,10-diiododecane (184)

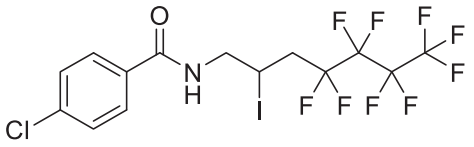


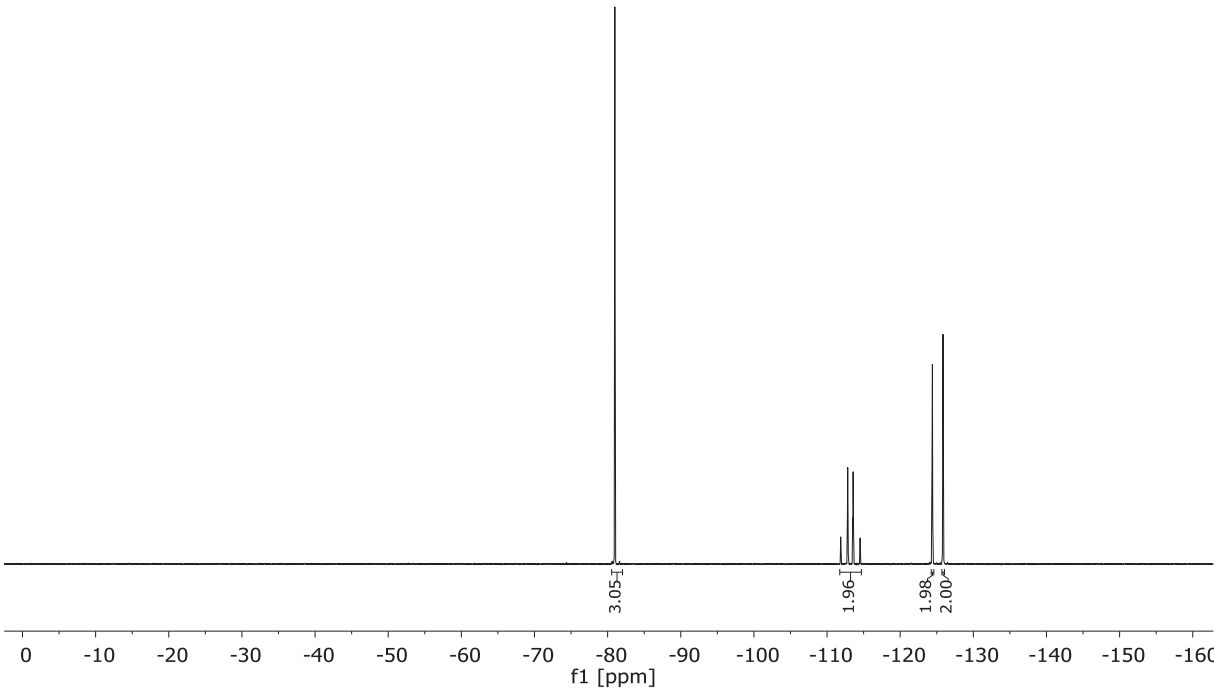
^{19}F NMR (282 MHz, chloroform-*d*)



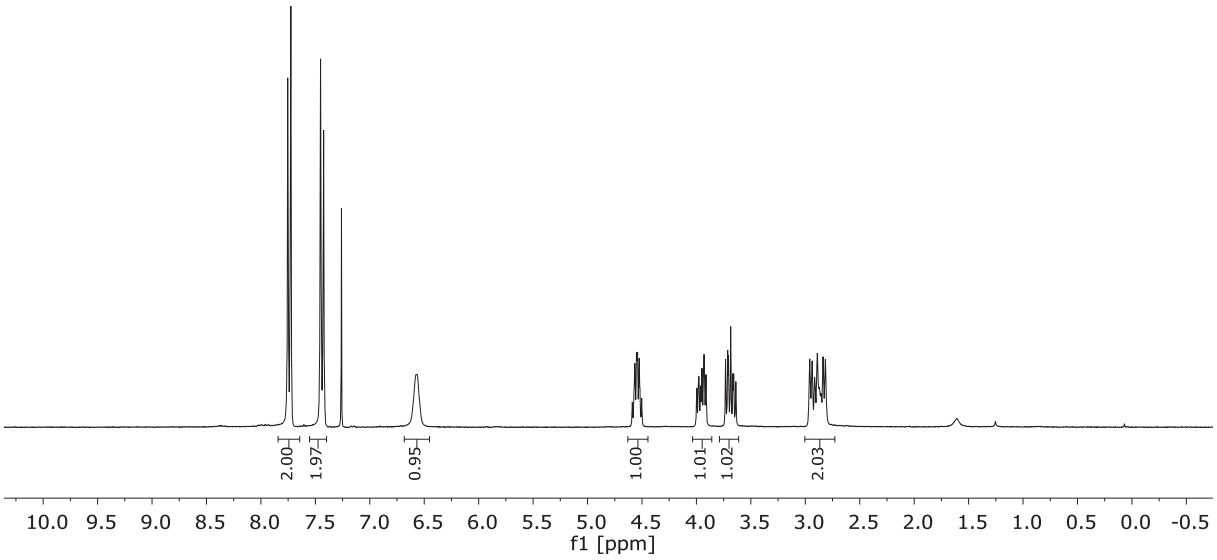
^{1}H NMR (300 MHz, chloroform-*d*)

4-Chloro-*N*-(4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptyl)benzamide (182)



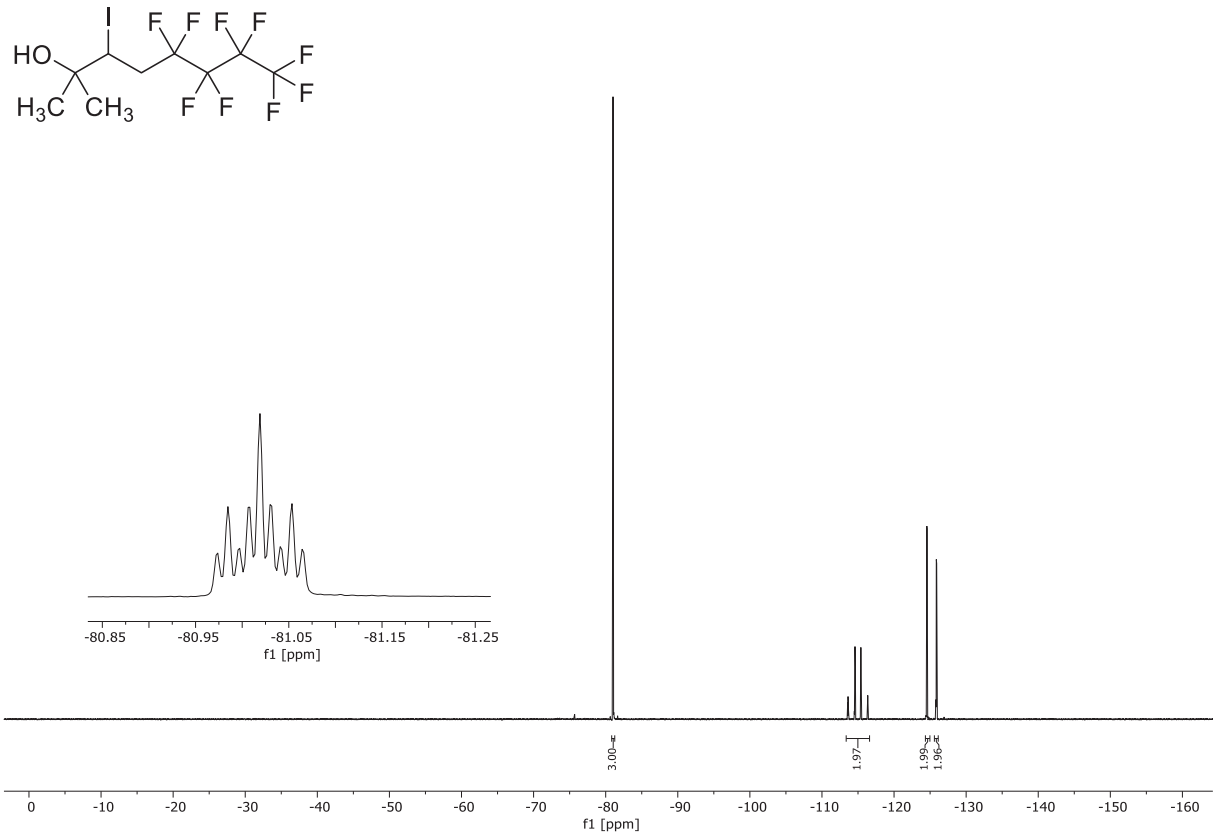


^{19}F NMR (282 MHz, chloroform-*d*)

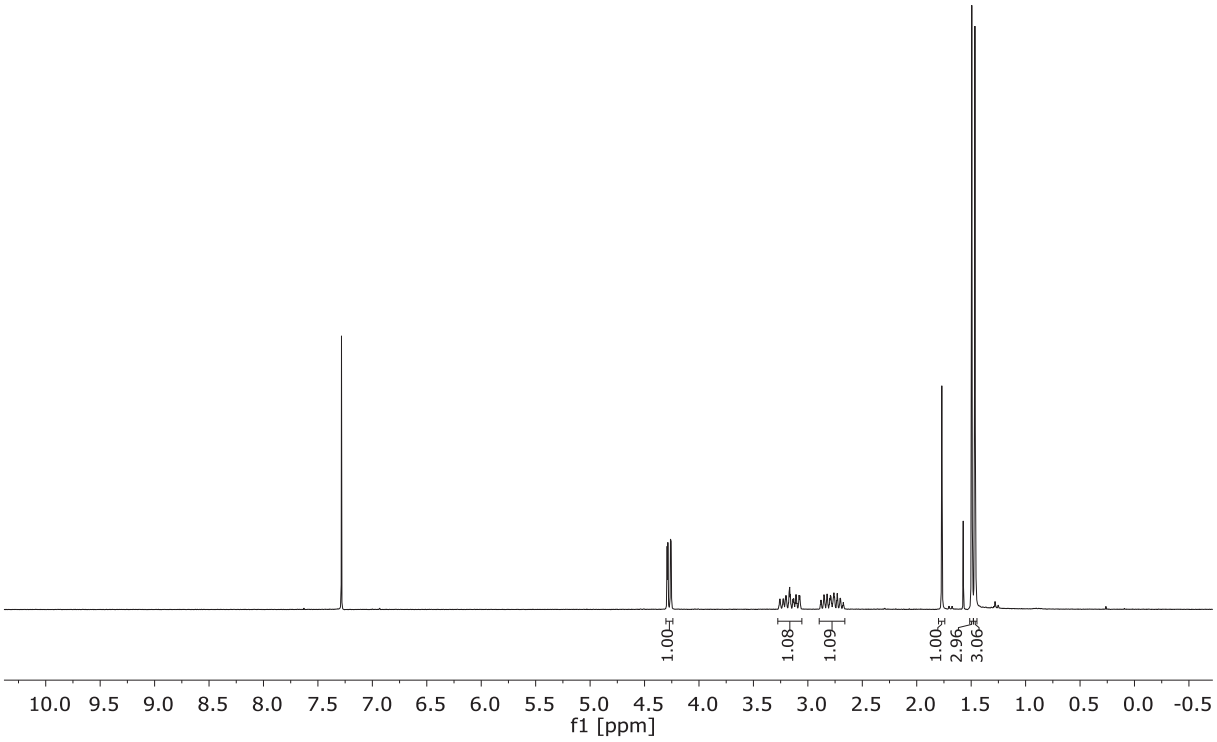


^{1}H NMR (300 MHz, chloroform-*d*)

5,5,6,6,7,7,8,8,8-Nonafluoro-3-iodo-2-methyloctan-2-ol (103)

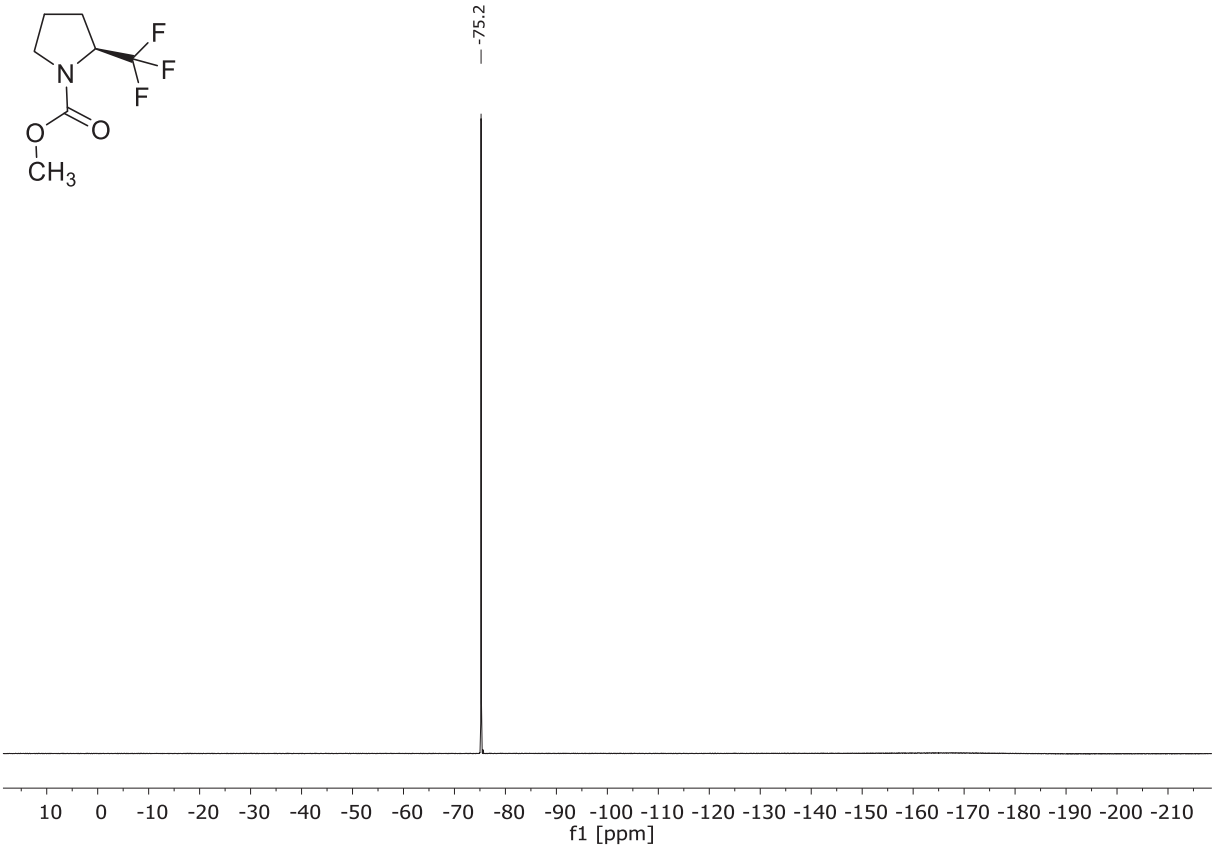


^{19}F NMR (282 MHz, chloroform-*d*)

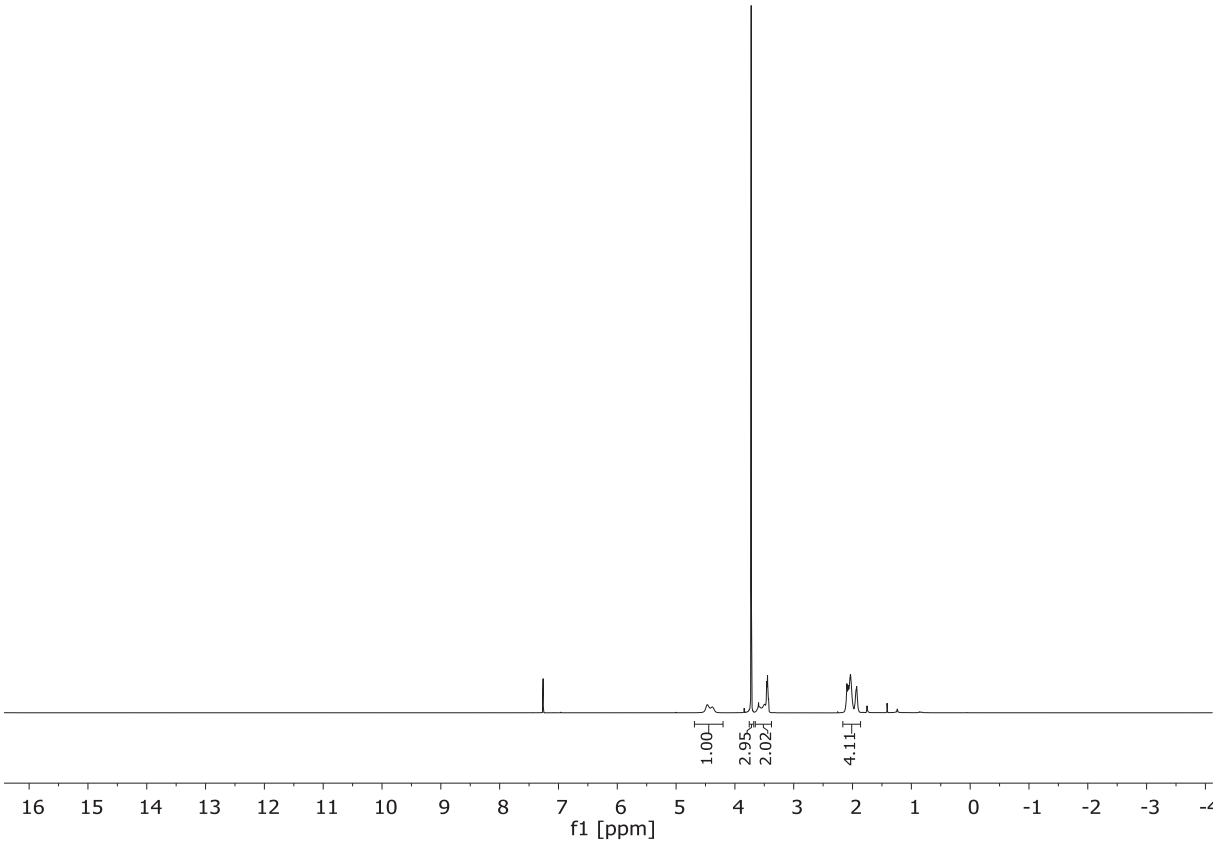


^{1}H NMR (300 MHz, chloroform-*d*)

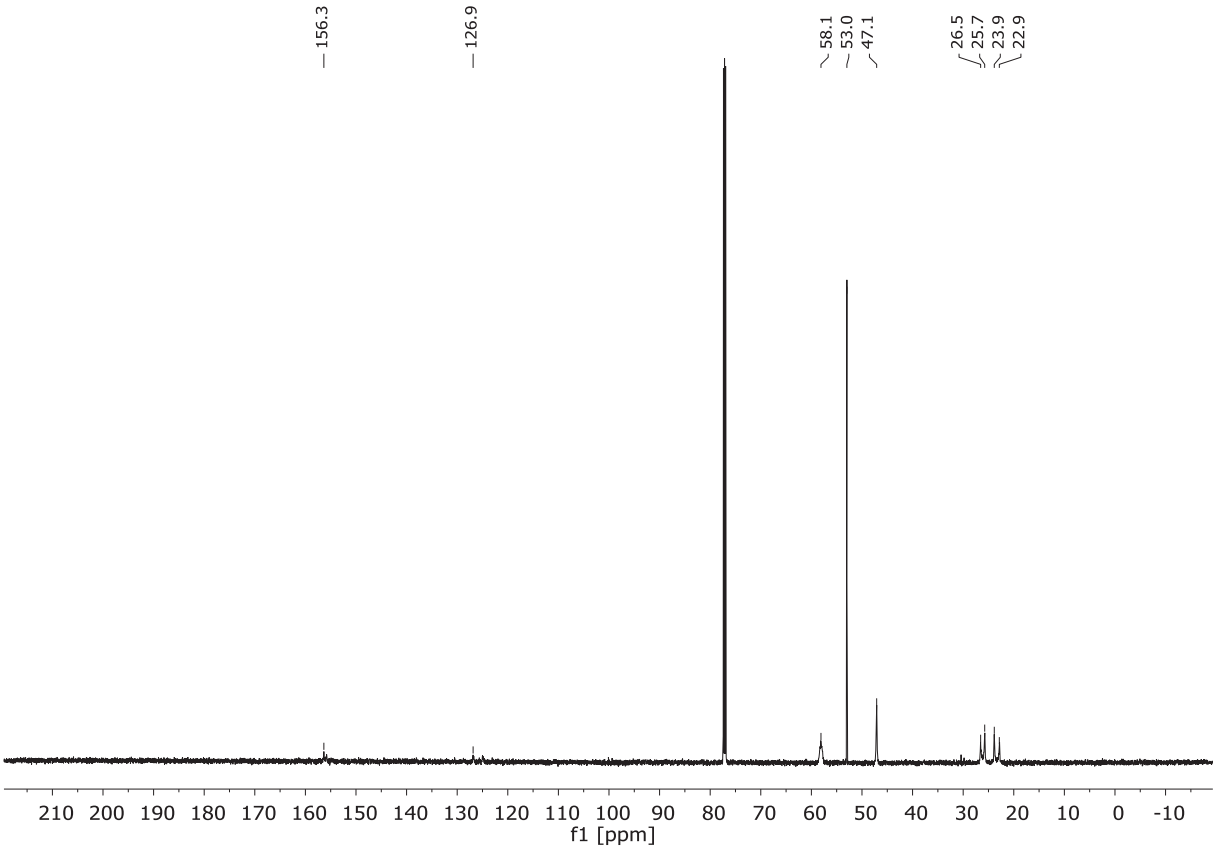
Methyl (*S*)-2-(trifluoromethyl)pyrrolidine-1-carboxylate (103)



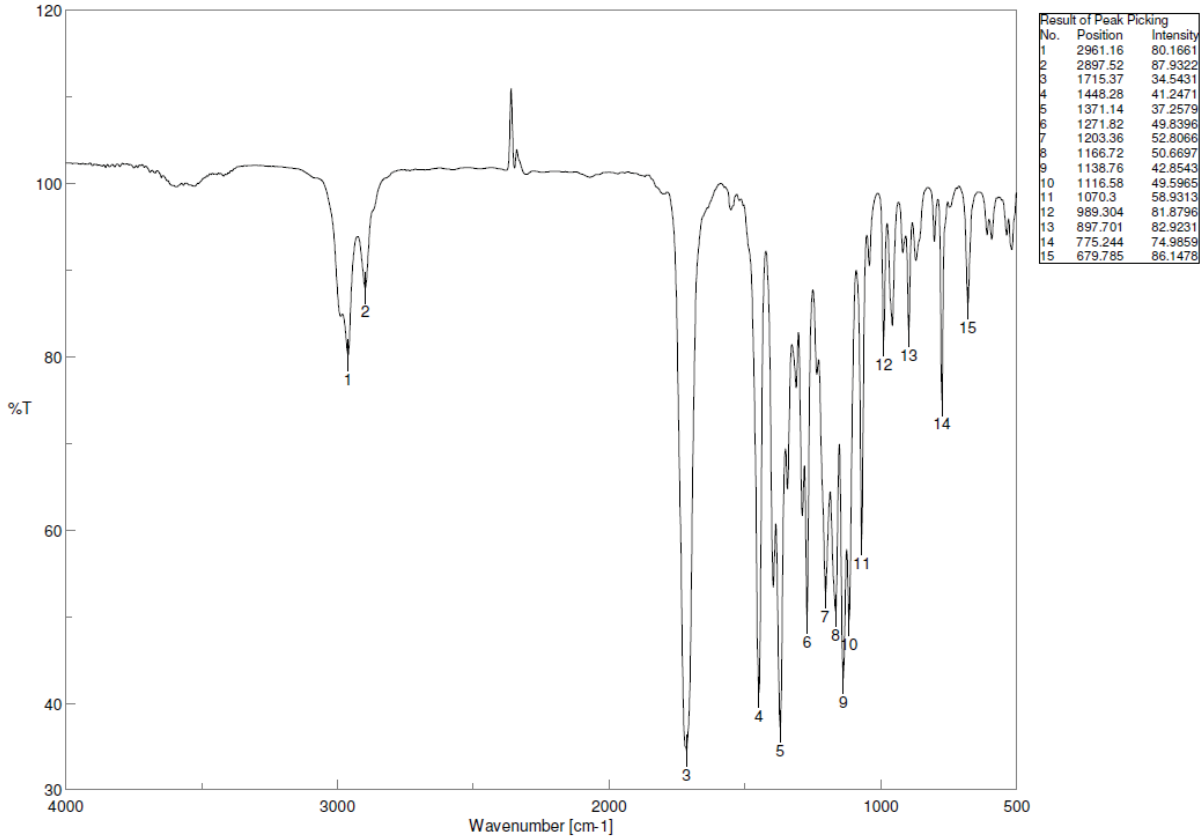
^{19}F NMR (565 MHz, chloroform-*d*)



^{1}H NMR (600 MHz, chloroform-*d*)



^{13}C NMR (151 MHz, chloroform-*d*)



Result of Peak Picking

No.	Position	Intensity
1	2961.16	80.1661
2	2897.52	87.9322
3	1715.37	34.5431
4	1448.28	41.2471
5	1371.14	37.2579
6	1271.82	49.8396
7	1203.36	52.8066
8	1166.72	50.6697
9	1138.76	42.8543
10	1116.58	49.5965
11	1070.3	58.9313
12	989.304	81.8796
13	897.701	82.9231
14	775.244	74.9859
15	679.785	86.1478

IR (Film)