Synthesis and Investigation of Reagents for the Introduction of OCF_3 and Other Fluorinated Groups

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Completion Time and Reviewers

The presented research was carried out under the supervision of Dr. Matthew N. Hopkinson from June 2020 until May 2024 at the Department of Biology, Chemistry, and Pharmacy of the Freie Universität Berlin.

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Authors Declaration

Herewith I certify that I have prepared and written my thesis independently and that I have not used any sources and aids other than those indicated by me. The work was not submitted to any prior doctoral procedure.

Lilian Maria Maas, May 2024

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“Never underestimate the power of a girl with a book.”

-Ruth Bader Ginsburg-

Abstract

This work includes new methods for the introduction of fluorinated groups into organic molecules as well as investigations into photoredox catalysed C-F activation (Figure 1). The evaluation of benzothiazolium (BT) salts as deoxygenative trifluoromethylthiolation and fluorination reagents provided new insights into the Lewis acidity and mechanistic properties of BT-reagents. Both the polymerisation of tetrahydrofuran (THF) to trifluoromethylthioethers and the *α*-deprotonation of THF could be observed and investigated. BT-SCF_3 could also be used for the synthesis of amides via acyl fluoride intermediates, which offers new application possibilities of the BT-reagents for fluorination reactions.

The investigation of sulphur hexafluoride and bis(trifluoromethyl)peroxide (BTMP) as radical sources for pentafluorosulphanylation and trifluoromethoxylation reactions is also presented. BTMP can be used for the synthesis of *α*-OCF_3 ketones and silyl enol ethers, as well as for the synthesis of allyl-OCF_3 products starting from silylated compounds without any activators. In addition, studies on the Wagenknecht reaction with new reaction partners for the direct synthesis of SF_5 compounds were presented and mechanistic properties of the reaction were identified based on the results.

The thesis also discusses the photoredox catalysed reaction of *α*-fluoroacetophenones with silylated coupling partners, with the presented method showing new routes to polyfunctionalised synthetic building blocks.

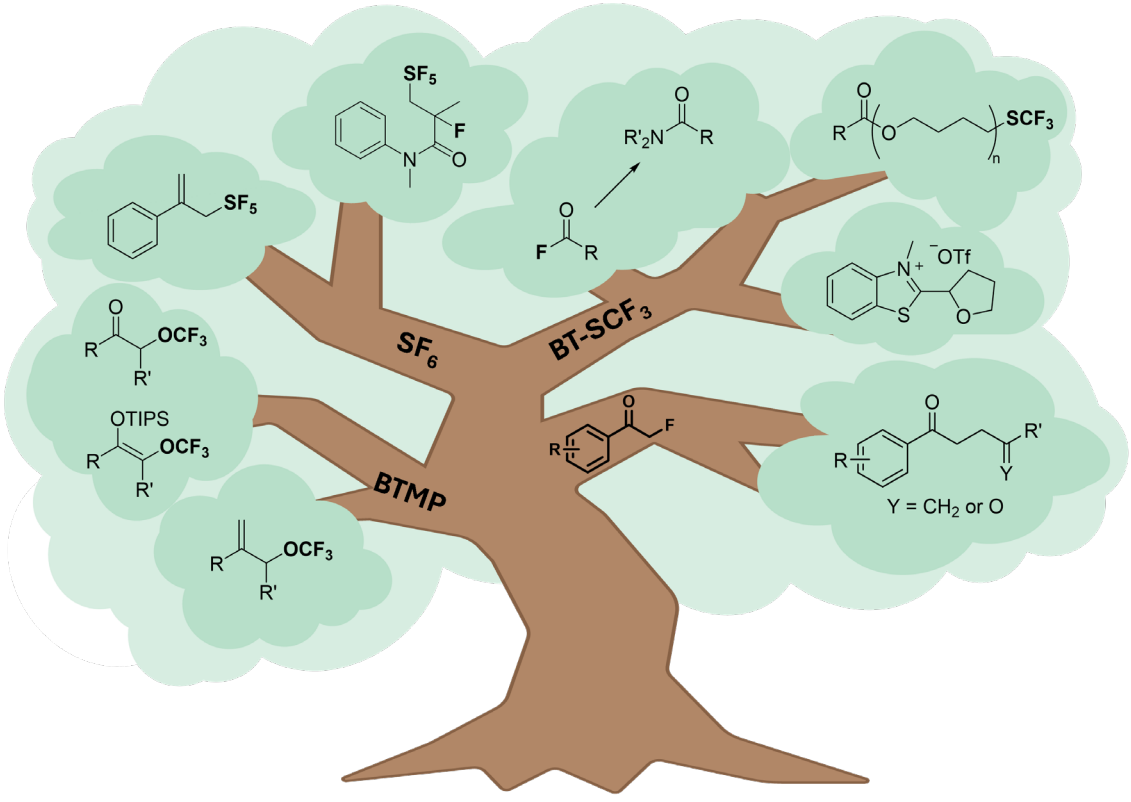


Figure 1: Overview of the projects and main results presented in this thesis.

Zusammenfassung

Diese Arbeit beinhaltet neue Methoden für die Einführung fluorierter Gruppen in organische Moleküle sowie Untersuchungen zur photoredoxkatalytischen C-F-Aktivierung (Abbildung 1). Die Untersuchung von Benzothiazolium (BT) Salzen als deoxygenative Trifluormethylthiolierungs- und Fluorierungsreagenzien lieferte neue Erkenntnisse über die Lewis-Azidität und die mechanistischen Eigenschaften von BT-Reagenzien. Sowohl die Polymerisation von Tetrahydrofuran (THF) zu Trifluormethylthioethern als auch die *α*-Deprotonierung von THF konnten beobachtet und untersucht werden. BT-SCF_3 konnte auch für die Synthese von Amiden über Acylfluorid-Zwischenstufen verwendet werden, was neue Anwendungsmöglichkeiten der BT-Reagenzien für Fluorierungsreaktionen bietet.

Die Untersuchung von Schwefelhexafluorid und Bis(trifluormethyl)peroxid (BTMP) als Radikalquellen für Pentafluorosulphanylierungs- und Trifluormethoxylierungsreaktionen wird ebenfalls vorgestellt. BTMP kann für die Synthese von *α*-OCF_3-Ketonen und Silylenolethern sowie für die Synthese von Allyl-OCF_3-Produkten ausgehend von silylierten Verbindungen ohne jegliche Aktivatoren verwendet werden. Darüber hinaus wurden Untersuchungen zur Wagenknecht-Reaktion mit neuen Reaktionspartnern zur direkten Synthese von SF_5-Verbindungen vorgestellt und anhand der Ergebnisse mechanistische Eigenschaften der Reaktion abgeleitet. In der Arbeit wird auch die photoredoxkatalysierte Reaktion von *α*-Fluoracetophenonen mit silylierten Kupplungspartnern behandelt, wobei die vorgestellte Methode neue Wege zu polyfunktionalisierten Synthesebausteinen aufzeigt.

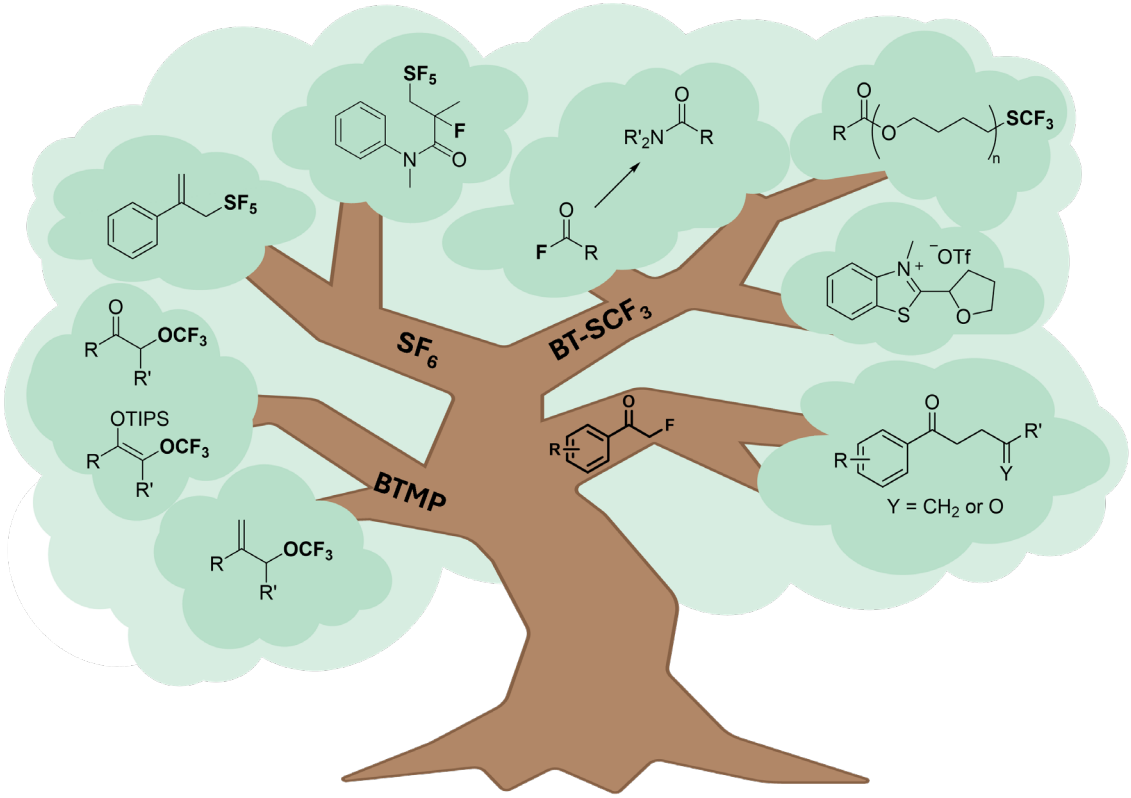


Abbildung 1: Übersicht über die in dieser Arbeit vorgestellten Projekte und wichtigsten Ergebnisse.

Table of Content

Abbreviations and Acronyms

Ac	acetyl
acac	acetylacetonate
ALS	amyotrophic lateral sclerosis
aliph.	aliphatic
Ar	aryl
arom.	aromatic
ATR	attenuated total reflection
BDE	bond dissociation energy
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
bpy	2,2′-bipyridine
BPMED	*N*,*N*-bis(phenylmethylene)-1,2-ethanediamine
BT	benzothiazolium
BTMP	bis(trifluoromethyl)peroxide
Bu	butyl
cat.	catalyst
Cbz	benzyloxycarbonyl
CFC-113	1,1,2-trichloro-1,2,2-trifluoroethane
cis-DCy-18-C-6	*cis*-dicyclohexano-18-crown-6
conc.	concentrated
Cy	cyclohexyl
4-CzIPN	1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene
d	duplet
DAST	diethylaminosulphur trifluoride
DBDMH	1,3-dibromo-5,5-dimethylhydantoin
DCC	*N,N'*-dicyclohexylcarbodiimide
DCE	dichloroethane

DCM	dichloromethane
Deoxofluor	bis(2-methoxyethyl)aminosulfur trifluoride
DFT	density functional theory
$DHQD_2PHAL$	hydroquinidine 1,4-phthalazinediyl diether
DIPEA	di(isopropyl)ethylamine
DMA	*N,N*-dimethylacetamide
DMAP	4-dimethylaminopyridine
DMC	dimethyl carbonate
DME	1,2-dimethoxyethan
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
DNTFB	2,4-dinitro-trifluoromethoxybenzene
EI	electron ionisation
ESI	electrospray ionisation
Et	ethyl
EtOAc	ethyl acetate
equiv.	equivalents
EWG	electron-withdrawing group
fac	facial
FDG	fluorodeoxyglucose
FIA	fluoride ion affinity
FLP	frustrated Lewis pair
hal	halogen
HalEx	halogen exchange
HDF	hydrodefluorination
HFIP	hexafluoroisopropanol
HMDS	bis(trimethylsilyl)amide
HPLC	high performance liquid chromatography

HRMS	high-resolution mass spectrometry
IPr	1,3-bis(2,6-diisopropyl-phenyl)imidazol-2-ylidene
IR	infrared
J	coupling constant
LA	Lewis acid
LED	light-emitting diode
LG	leaving group
m	multiplet
MBT	2-mercaptobenzothiazole
Me	methyl
MeCN	acetonitrile
NCHB	non-classical hydrogen bond
NFSI	*N*-fluorobenzenesulfonimide
Nf	nonaflate
NHC	*N*-heterocyclic carbene
NHPI	*N*-hydroxyphthalimide
NMR	nuclear magnetic resonance
Ns	nosyl
p	pentett
PET	positron emission tomography
PFAS	per- and polyfluoroalkyl substances
Ph	phenyl
pin	pinacol
ppm	parts per million
ppy	2-phenylpyridine
PTFE	polytetrafluoroethylene
PTH	*N*-phenylphenothiazine
$PyOCF_3$	4-(dimethylamino)-1-(2,4-dinitrophenyl)pyridinium trifluoromethanolate

q	quartet
quant.	quantitative
rt	room temperature
s	singlet
sat.	saturated
SET	single electron transfer
SIPr	1,3-bis(2,6-diisopropylphenyl)imidazolin-2-ylidene
t	triplet
TADDOL	*α,α,α',α'*-tetraaryl-1,3-dioxolan-4,5-dimethanol
TAS-OCF_3	tris(dimethylamino)sulfonium trifluoromethoxide
TBAT	tetrabutylammonium difluorotriphenylsilicate
^{t}Butpy	2,6-bis[4-(tert-butyl)pyridin-2-yl)-4-(tert-butyl)pyridine
TCICA	trichloroisocyanuric acid
TDAE	tetrakis(dimethylamino)ethylene
TEDA	triethylenediamine
TEMPO	2,2,6,6-tetramethylpiperidinyloxyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
TFBO	(*E*)-*O*-trifluoromethyl-benzaldoximes
TFBz	trifluoromethyl benzoate
TFMS	trifluoromethyl aryl sulfonate
TFMT	trifluoromethyl triflate
TFNf	trifluoromethyl nonaflate
THF	tetrahydrofuran
THP	tetrahydropyran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMS	trimethylsilyl

TOF	time of flight
Ts	tosyl
TTST	*S*-trifluoromethyl trifluoromethanesulfonothioate
PCM	polarisable continuum model
PFP	pentafluoropyridine
UV	ultraviolet
XRD	X-ray diffraction
XtalFluor-E	(diethylamino)difluorosulfonium tetrafluoroborate
XtalFluor-M	difluoro(morpholino)sulfonium tetrafluoroborate

1 Introduction

1.1 Historical Aspects and Applications of Fluorine Chemistry

Today's fluorine chemistry is a diverse field that covers almost all areas of life and industry. Historically, this development was a long-awaited achievement and proved to be a great success owing to the unique properties of fluorine. As an extremely reactive element, fluorine gas is able to react with almost all other elements to form strong R–F bonds, with the noble gases helium and neon being the only exceptions. The reactivity of fluorine can be ascribed to its high electronegativity (4.0 on the Pauling scale), its highly positive redox potential (2.87 V) and the weakness of the F–F bond (36.9 kcal·mol^{-1}).[1] From this point of view, the great interest in investigating this element from a historical and modern perspective is not surprising.

The first description of a fluorinated compound was made in 1526 by Georgius Agricola, who described the use of the mineral fluorite (CaF_2) in the manufacturing of metals.[2] More detailed information on the composition of fluorite was obtained in 1764 and 1771 by Marggraf and Scheele, who obtained hydrofluoric acid (HF) by reacting fluorite with sulphuric acid.[2-3] These findings laid the foundations for developing methods of isolating an elemental form of fluorine. It was not until 1886 that Henri Moissan succeeded in isolating significant quantities of the extremely corrosive gas, F_2, for the first time by electrolysing a mixture of HF and potassium bifluoride (KHF_2) in a platinum vessel with platinum and iridium electrodes at –50 °C.[2, 4] Moissan's discovery was rewarded with the Nobel Prize in 1906 and his technique is still used for the industrial production of fluorine gas.

In general, fluorine is one of the most abundant halogens below the tropopause. However, it forms very stable binary salts and is in nature almost exclusively bound in insoluble minerals such as fluorite, fluorapatite and cryolite. As a result of its high reactivity, it does not occur in nature in elemental form, apart from traces in antozonite. In this special fluorite variant, the radioactive decay of uranium leads to the formation of elemental fluorine, which is released when the crystals break.[5] The characteristic odour that accompanies the release of the gas is the reason why the mineral is also known as "stink spar".

In contrast to inorganic fluorides, compounds with organically bound fluorine are comparatively rare in nature, and only a small selection of fluorinated biogenic molecules is found in a few tropical and subtropical plants or microorganisms (Figure 2).[6] The most common naturally occurring fluorinated organic compound is fluoroacetic acid, which was discovered in 1943 in *Dichapetalum cymosum*, a South African plant.[1a] The toxicity of most naturally occurring fluorinated compounds and the difficulties in handling F_2 and HF gas initially slowed down the investigation of organic fluorinated compounds and their potential applications.

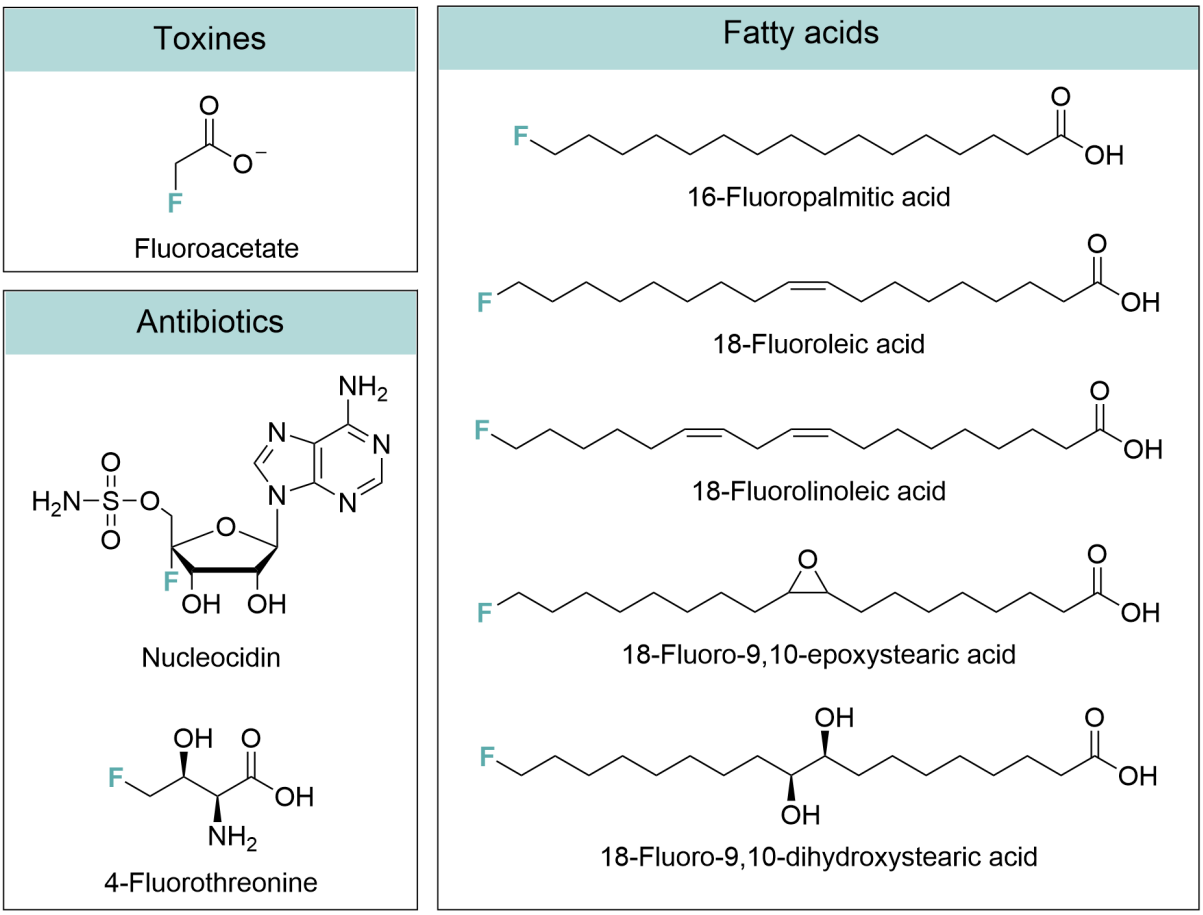


Figure 2: Selection of fluorinated biogenic molecules.

Even before Moissan's breakthrough, first attempts were made to introduce fluorine into organic molecules in order to investigate its influence on existing molecular systems. Stable fluorine containing compounds such as potassium fluoride (KF) or HF were primarily used. In the 1920s, the first experiments were finally carried out with elemental fluorine, which led to the synthesis of tetrafluoromethane. This attracted great interest within the newly emerging field of organofluorine chemistry, as fluorine itself had long been considered too reactive for organic reactions. Organofluorine chemistry grew rapidly and found applications in industry for the synthesis of chlorofluorocarbons as refrigerants, extinguishants and as building blocks for fluoroplastics and -polymers. A prominent example for fluoropolymers is the well-known polytetrafluoroethylene (PTFE), first discovered by Plunkett in 1938. Further studies on fluorinated organic molecules highlighted them as useful compounds for medicinal applications, such as anaesthetics or as tracers for positron emission tomography (PET) imaging, and after World War II as pharmaceuticals and agrochemicals (Figure 3).

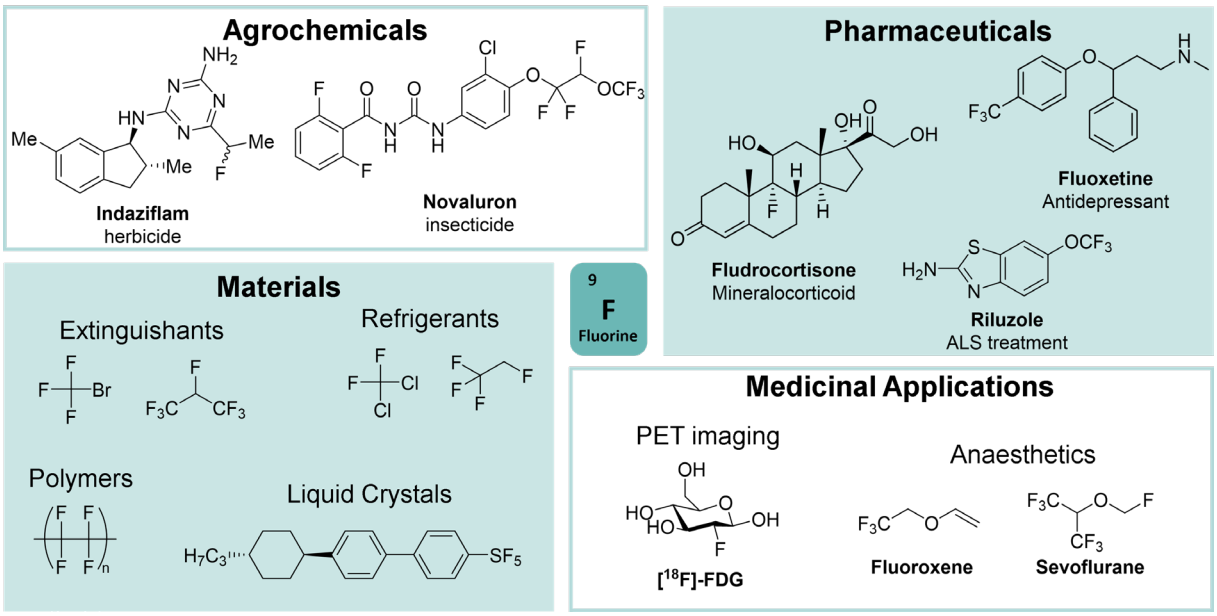


Figure 3: Applications of selected fluorinated molecules.

The influence of fluorine on organic molecules became an important tool and eventually a standard method for modulating chemical properties due to the unique stereoelectronic properties of fluorine, such as its small size, low polarisability and strong inductive effect. As a result, more than 20% of drugs in pharmaceutical development and at least 53% of new agrochemicals in the last three decades contain at least one fluorine atom.[7] One advantage of using fluorine for pharmaceutical applications is its size, which makes it possible to replace hydrogen atoms of a molecule with fluorine without causing a drastic structural change. However, the introduction of fluorine can also create a structural preference, which makes it an important key element for molecular design. One example of these preferences is the *gauche* effect, which was initially observed in 1960 by Klaboe and Nielsen during the spectroscopic investigation of various substituted ethanes.[8] Due to the strong electronegativity of fluorine and the associated high σ* acceptor properties of the C–F bond, the fluorine atoms in 1,2-difluoroethane adopt the *gauche* conformation to benefit from the electron density of the neighbouring $\sigma_{C\text{-}H}$ orbitals (Figure 4). Similar to the *gauche* effect observed in acyclic systems, fluorine can also induce a structural preference in cyclic systems. In 2024, the groups of Cormanich and O'Hagan investigated the conformational properties of (poly)halogenated cyclohexanes. They described the preferred axial arrangement of the F-substituents in 1,1,4-trifluorocyclohexane stabilised by nonclassical CF⋯HC hydrogen bonding (NCHB) interactions.[9]

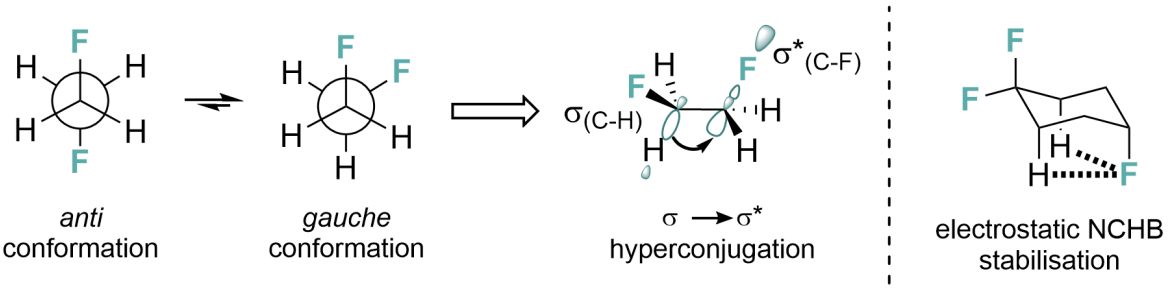


Figure 4: Newman projection of the *anti* and *gauche* conformation and σ→σ* hyperconjugation of 1,2-difluoroethane (left). Electrostatic non-classical hydrogen bond stabilised axial conformation of the 4-fluorine in 1,1,4-trifluorocyclohexane (right).

Another advantage of fluorine incorporation is that fluorine increases the metabolic stability of the compound, due to the strength of the C–F bond. In addition, the high electronegativity of fluorine creates a polarisation of the bonds within the molecule, which can lead to changes in lipophilicity. Fluorine is a bioisostere of the hydroxyl group and is able to act as a weak hydrogen bond acceptor, which can affect the receptor binding of the drug in the body.[10] These effects can be manipulated and customised by applying different fluorinated groups. Hence, interest in trifluoromethyl (CF_3) and later heteroatomic fluorinated groups, has increased in recent years. These groups are characterised by high lipophilicity (Hansch hydrophobicity parameter, π) and electron withdrawing properties (Hammett parameter, σ_p) compared to single fluorine atoms (Table 1).[11]

Table 1: Aromatic substituent constants of selected fluorine-containing groups.[11]

	F	CF_3	OCF_3	SCF_3	SF_5
π^a	0.14	0.88	1.04	1.44	1.23
$\sigma_p{}^b$	0.06	0.54	0.35	0.50	0.68

[a] Hansch hydrophobicity parameter (measured from substituted benzenes).

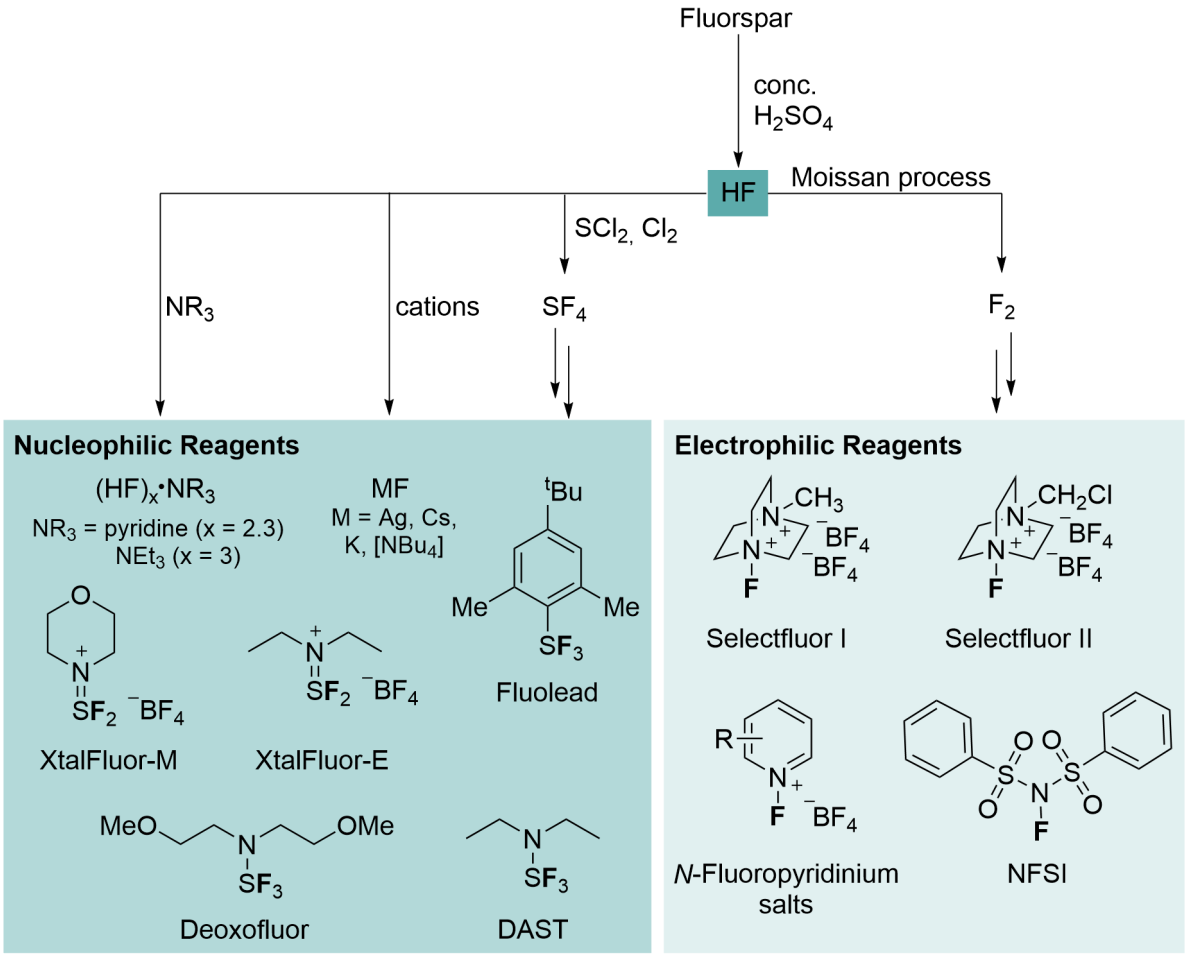
[b] Hammett parameter (measured from 4-substituted benzoic acids).

The investigation of these groups has thus become an important field of organofluorine chemistry, where research is still being carried out into new methods for the efficient introduction of heteroatomic perfluoroalkyl (YR_f), pentafluorosulphanyl (SF_5) or other partially or perfluorinated functional groups into organic molecules.

1.2 C-F Bond Formation and Activation

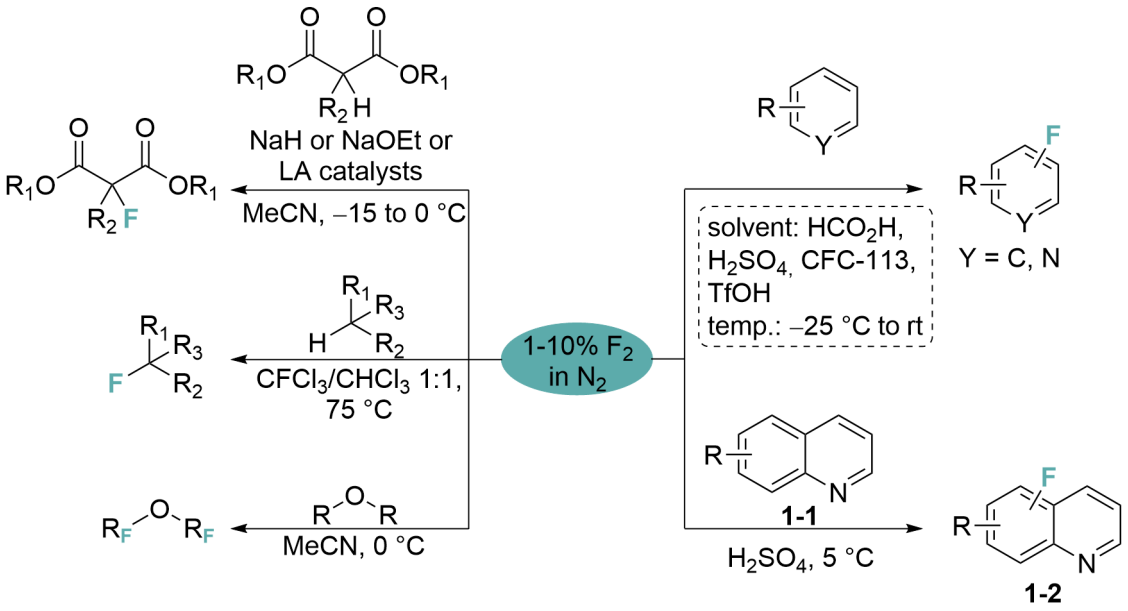
1.2.1 Methods and Reagents for the C-F Bond Formation

Due to the beneficial properties described in *Chapter 1.1*, ongoing effort is put into the investigation of new synthetic methods for the fluorination of organic molecules. All synthetic fluorinated molecules and fluorination reagents are ultimately based on fluorspar (Scheme 1).[12] The mineral can be converted into hydrogen fluoride, a compound that itself can be used as a fluorinating agent, using concentrated sulphuric acid. Starting from HF, both electrophilic and nucleophilic reagents can be produced. The reaction of HF with sulphur dichloride and chlorine enables the synthesis of sulphur tetrafluoride (SF_4). Alternatively, HF can also be converted to convenient nucleophilic fluorinating agents with various cations or amines. Based on SF_4, MF and HF·NR_3 compounds, various nucleophilic easy-to-handle fluorinating reagents have been produced for laboratory scale reactions in recent decades. In terms of electrophilic reagents, F_2 is the most important reagent used both in industry and, with specialised equipment, in smaller laboratories.



Scheme 1: Overview of fluorination reagents and their synthesis starting from fluorspar. Inspired by **Ref. 12** (Fig. 1) with permission from the Royal Society of Chemistry.

Fluorine gas can in turn be used for the synthesis of various electrophilic fluorinating reagents or be used directly itself. The applications are diverse, and the selectivity of fluorination can be modulated by the reaction conditions (Scheme 2). In 1996, Chambers' group investigated the influence of the solvent on the mechanism and selectivity of electrophilic aromatic fluorinations with F_2 and it was shown that there is a correlation between the acidity of the solvent and the selectivity of the reaction.[13] Using formic or sulphuric acid as a solvent, it was possible to perform selective fluorination on 1,4-substituted aromatic compounds, whereby the monofluorination products were observed as the main product in each case. In addition, depending on the degree of activation of the aromatic, small amounts of the difluorination product could be obtained.[14] These conditions can also be used for the direct fluorination of quinoline derivatives **1-1**, whereby the fluorination occurs selectively at the benzenoid ring giving mainly monofluorinated 5- or 8-fluoroquinolines **1-2**.[15] Fluorination of deactivated aromatics under milder conditions can be achieved by flow techniques using acetonitrile-formic acid mixtures as solvents.[16] The range of this reaction can be extended by further adjustments of the solvent, as shown by Langlois or Van Der Puy.[17] The group of Langlois succeeded in synthesising *meta*-fluoroanilines by direct fluorination of aniline derivatives in triflic acid. They were also able to show that the equivalents of fluorine used for the transformation have an influence on the selectivity and the degree of fluorination of the reaction. In contrast, using the polyhalogenated solvent CFC-113, Van Der Puy was able to fluorinate pyridines selectively at the 2-position.

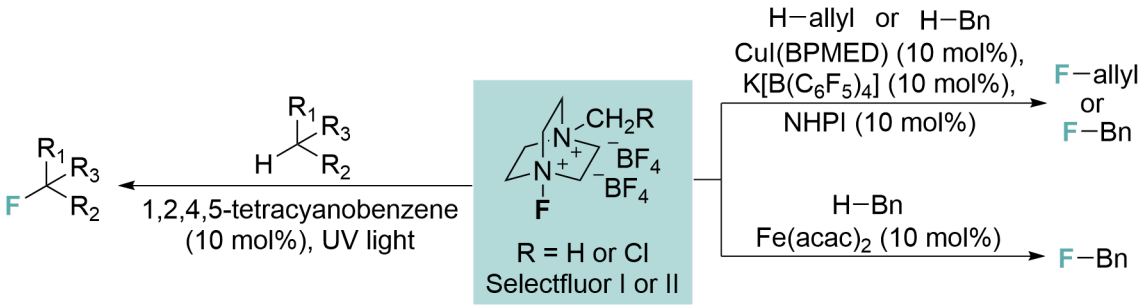


Scheme 2: Selected applications of fluorine gas for the electrophilic fluorination of aromatic and aliphatic compounds.

Fluorination can also take place on enolates as shown by Chambers and co-workers. According to their results, 1,3-dicarbonylated compounds can be selectively fluorinated using

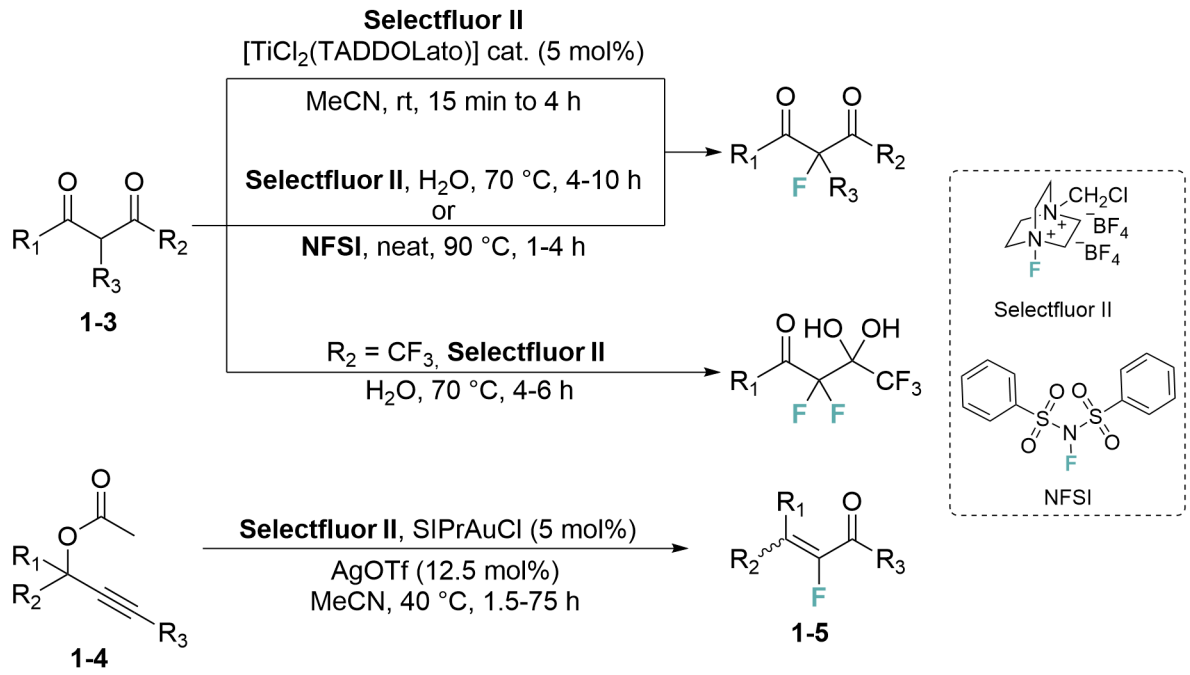
basic additives, like sodium hydride (NaH) or sodium ethanolate (NaOEt), or Lewis acidic (LA) catalysts.[18] Studies on the substitution of tertiary hydrogens in bicyclic compounds with fluorine by the group of Rozen showed that the influence of the *p*-character of the reacting carbon atom plays an important role for an electrophilic reaction pathway.[19] Secondary carbon atoms can also be converted into the corresponding C–F bonds by electrophilic aliphatic fluorination. An example of this is the investigation of the selective fluorination of dialkyl ethers by the group of Sandford.[20] Their work has also shown that comparable results can be achieved with fluorine as a reactive and comparatively harsh reagent under common conditions as with other milder electrophilic reagents such as Selectfluor.

Selectfluor belongs to the class of N–F reagents and has been increasingly used for the electrophilic fluorination of organic compounds since its development by Banks in 1992.[21] Other N–F reagents are for example *N*-fluorobenzenesulfonimide (NFSI) or *N*-fluoropyridinium salts and can also be used in similar transformations.[22] As a versatile electrophilic reagent, Selectfluor can convert a wide variety of substrate classes into their fluorinated derivatives. In 2000, the group of Chambers used Selectfluor for the fluorination of secondary and tertiary saturated C–H bonds under thermal activation.[23] This transformation can also be done at room temperature under organocatalytic conditions, as shown by the group of Bloom (Scheme 3).[24] In 2012, Lectka's group succeeded in broadening the scope to allylic and benzylic fluorides with the help of a polycomponent catalyst system.[25] An easier and milder method based on an iron catalyst was also developed for the synthesis of benzyl fluorides.[26]



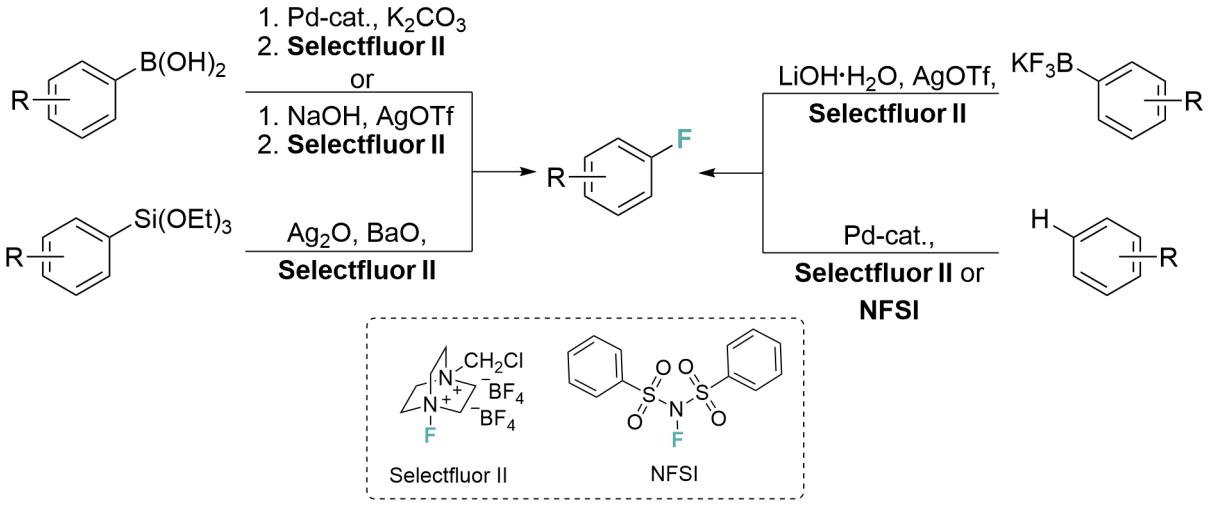
Scheme 3: Examples for catalytic aliphatic, allylic and benzylic fluorination with Selectfluor.

Studies of the reactivity of Selectfluor towards carbonyl compounds by the groups of Togni, Gouverneur or Stavber show that the reaction of enolates with Selectfluor leads to fluorination in the *α*-position to the carbonyl function (Scheme 4).[27] Togni and co-workers succeeded in selectively fluorinating *β*-ketoesters **1-3** using a titanium catalyst at room temperature.[27a] Propargyl acetates **1-4** can also be converted into the corresponding *α*-fluorenones **1-5** under gold catalysis, as shown by Gouverneur and co-workers.[27b] In addition, Stavber's group was able to show that the electrophilic *α*-fluorination of carbonyl compounds is also possible under solvent-free conditions using NFSI or in water using Selectfluor.[27c, 28]



Scheme 4: Electrophilic fluorination of carbonyl compounds using Selectfluor and NFSI.

Another important application of Selectfluor is the electrophilic fluorination of aromatic compounds (Scheme 5). In 2008, the group of Ritter developed a two-step method to fluorinate arylboronic acids.[29] For this purpose, the boronic acid was first converted into a palladium complex by transmetallation and then fluorinated with the help of Selectfluor. This method could be simplified to a one-pot-two-step reaction by replacing the Pd complex with silver triflate in combination with a base.[30] Complete isolation of the transmetallation product was no longer necessary. Further investigations of silver-mediated fluorination of aromatics by the group of Mathew led to a one-pot method starting from potassium aryl trifluoroborates.[31]



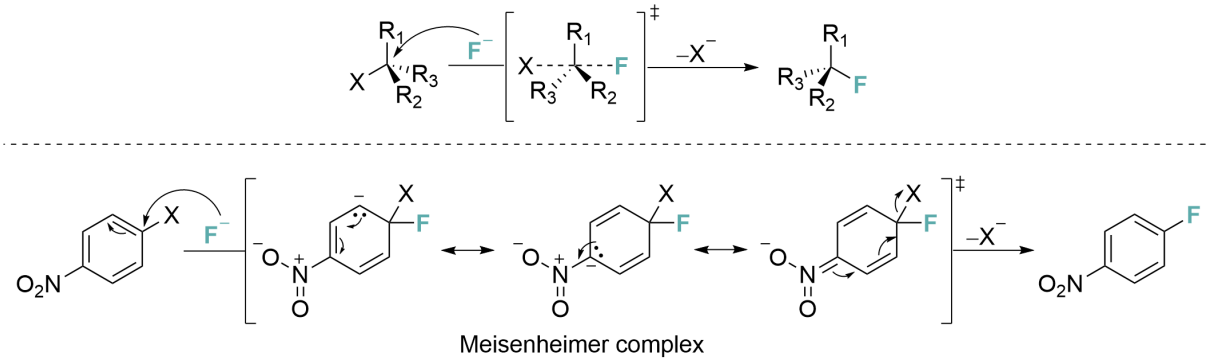
Scheme 5: Synthesis of aryl fluorides via metal catalysed fluorination using Selectfluor and NFSI.

Furthermore, Ritter and co-workers were able to fluorinate arylsilanes using a base-free silver(I) oxide-mediated method with Selectfluor.[32] These methods require prior installation of

the leaving group, which is why direct methods of aromatic C–H activation and fluorination were further investigated. In 2018, the groups of Ritter, Neese and Jacq presented a method for aromatic C–H fluorination using a palladium catalyst and the N–F reagents Selectfluor or NFSI.[33]

The methods for nucleophilic fluorination reactions are mainly based on four sets of reagents: HF amines, fluoride salts, SF_4, and reagents produced from SF_4, such as diethylaminosulphur trifluoride (DAST) or Deoxofluor,[34] or metal fluorides, e.g. Fluolead.[35]

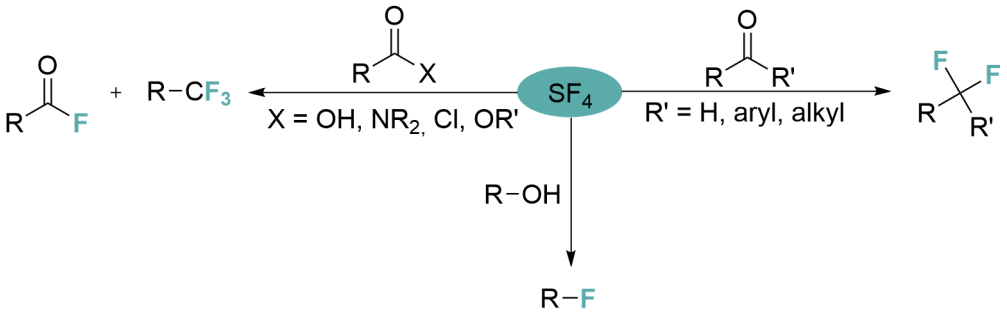
In general, nucleophilic fluorination could be achieved using fluoride sources on aromatic compounds via a nucleophilic aromatic substitution (S_NAr) or on non-aromatic compounds via a concerted nucleophilic substitution (S_N2) (Scheme 6). However, this approach is hampered by various challenges. Usually the common fluoride sources are either expensive (e.g. CsF) or poorly soluble in organic media (e.g. KF),[36] whereby the solubility can be partially improved by the addition of ionic liquids, crown ethers or other additives.[37] Nevertheless, elevated temperatures and long reaction times are often required for these reactions, which can lead to decomposition of the starting materials and a reduced selectivity of the reaction. In addition, the increased basicity of the fluoride ion can lead to unwanted side products, for example through elimination reactions (E2).[38] Furthermore, the metal fluorides used are often hygroscopic and the reactions are sensitive to moisture, as the nucleophilicity of the hydrated fluoride ion is strongly reduced.[1a] In the case of S_NAr fluorinations, electron-withdrawing groups (EWG) are required in order to increase the stability of the Meisenheimer complex.[39] For these reasons, the focus of nucleophilic fluorination is increasingly on deoxyfluorination reagents such as SF_4.



Scheme 6: Concerted nucleophilic fluorination via S_N2 mechanism (top) and fluorinative S_NAr of an aromatic bearing an electron-withdrawing group via a stabilised Meisenheimer complex (bottom).

SF_4 has been used as a fluorinating agent since the middle of the 20th century. It can be used for the deoxygenative fluorination of organic molecules, producing mono-, di- or tri-fluorinated products (Scheme 7). In 1959, Smith *et al.* showed that carboxylic acids and other carbonyl compounds, such as aldehydes and ketones, can be converted to fluorinated compounds under the influence of SF_4.[40] Particularly in the conversion of aldehydes or ketones, selectivity

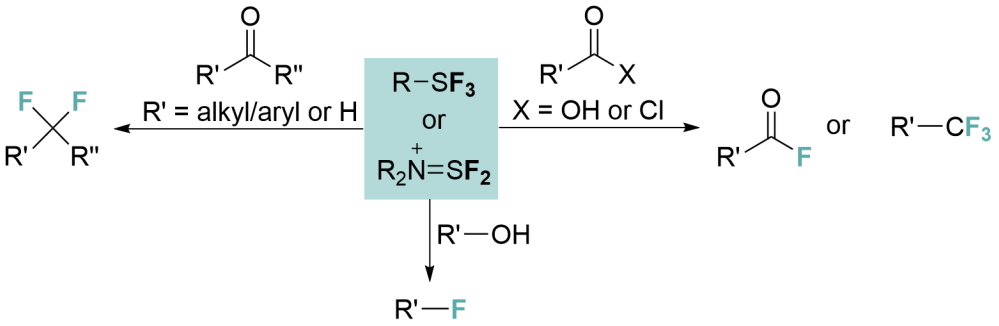
towards the difluorinated compounds can be observed.[40-41] In this context, Haas and co-workers were able to convert *α,β*-unsaturated aldehydes into the desired difluoromethyl (CF_2) compounds under the influence of SF_4 and KF.[41b] The reaction of carboxylic acids with SF_4 usually leads to mixtures of mono-, tri- and in rare cases difluorinated products. These reactions require high temperatures, long reaction times and an excess of the reactive gas but can be used for a wide range of aliphatic, aromatic, and polycarboxylated compounds.[41a, 42]



Scheme 7: Applications of SF_4 as a deoxygenative fluorination reagent.

Extension of the methods to other classes of C=O substrates also allows the fluorination of acid chlorides, esters or anhydrides, and amides to the desired fluorinated molecules.[41a, 43]
In 1960, Hasek *et al.* showed that SF_4 can also be used for the deoxygenative fluorination of alcohols, using the same conditions as for carbonyl compounds.[41a] A rough correlation was found between the acidity of the hydroxyl group and the yield of fluorination products, with more acidic OH groups being converted in higher yields than less acidic OH compounds. The group of Janzen was able to extend the method to benzyl alcohols. To suppress the undesired HF-catalysed polymerisation of benzyl fluorides, pyridine or triethylamine was used as HF scavenger.[44] The method was also used for more sensitive alcohols.[45]
The use of SF_4 is largely limited to industrial applications due to its difficult handling and only a few laboratories have the necessary equipment to work with the reactive gas. For this reason, research into alternative, easy-to-handle reagents has intensified in recent decades, with DAST proving to be a suitable reagent for many nucleophilic fluorination reactions. In addition to DAST, compounds such as Deoxofluor, XtalFluor-E or M, as well as Fluolead can be used as possible alternatives with similar reactivity.[46] The main application of these reagents is the deoxyfluorination of alcohols and carbonyl groups (Scheme 8), however, they are no good substitutes for e.g. metal fluorides or HF·amines in S_N2 reactions. Compared to SF_4, milder conditions can be used, and thus more sensitive substrates can be made accessible for nucleophilic deoxyfluorination. In 1975, Middleton investigated the reactivity of aminosulfuranes towards alcohols and was able to convert primary, secondary, and tertiary alcohols into the corresponding fluorinated compounds.[34a] Studies by Shellhamer and co-workers showed that the fluorination of secondary alcohols by aminosulphur trifluorides primarily proceeds according to an S_N1-like mechanism while primary alcohols undergo an S_N2

process with inversion of the stereoinformation.[47] Also the selective fluorination of carbohydrates was investigated by Somawardhana[48] and Card[49] and the scope of biologically relevant hydroxyl compounds was expanded in the following years. For example, pyranosides or furanosides were fluorinated with DAST under mild conditions.[50]



Scheme 8: Deoxyfluorination of alcohols and carbonyl compounds using organic sulphur trifluorides or aminodifluorosulfinium salts.

Further investigations of the reactivity of DAST by the group of Markovski also showed the possibilities of its application for the deoxyfluorination of carboxylic acids, acid chlorides or inorganic molecules such as phosphorus trichloride and thionyl chloride.[51] Also Deoxofluor and Fluolead can be used for the transformation of carboxylic acids towards acyl fluorides or trifluoromethylated products as shown by the groups of Cheng and Umemoto.[52] In mechanistic investigations, the group of Umemoto suggested a two-step mechanistic pathway for the reaction where the carboxylic acid is transformed into an acyl fluoride and HF in the first step. The second step requires elevated temperatures and, under the influence of another equivalent of the deoxyfluorination agent and HF, the acyl fluoride transforms into the trifluoromethyl compound. The groups of Markovski, Middleton, Sharts and Shellhamer were also able to show that DAST and related reagents can selectively deoxyfluorinate aldehydes and ketones resulting in the corresponding CF_2-compounds.[34a, 47, 51b, 53]

1.2.2 Methods for C-F Activation

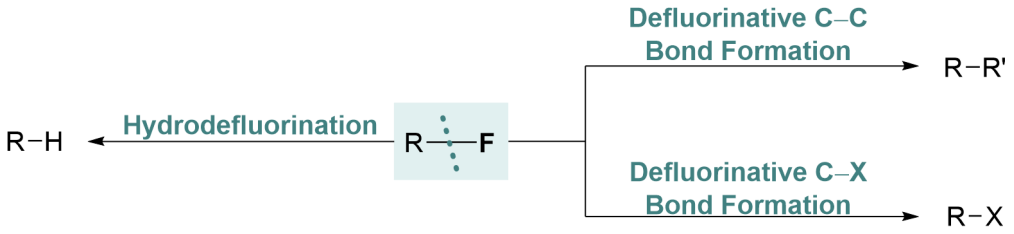
With a bond dissociation energy (BDE) of 110 kcal·mol^{-1} and a bond length of 1.39 Å, the C–F bond is the strongest and shortest of the C–halogen bonds (Table 2). Particularly the high BDE presents a special challenge for the activation and cleavage of the C–F bond. Nevertheless, various methods for C–F activation have been developed in recent decades, allowing the selective cleavage of one or more C–F bonds.

Table 2: Bond dissociation energies (BDE) and bond lengths of carbon-halogen bonds.[1a]

	C–F	C–Cl	C–Br	C–I
BDE [kcal·mol^{-1}]*	110	85	71	57
Bond length [Å]	1.39	1.78	1.93	2.14

*Values for methyl halides with the formular H_3C–X (X = F, Cl, Br, I).

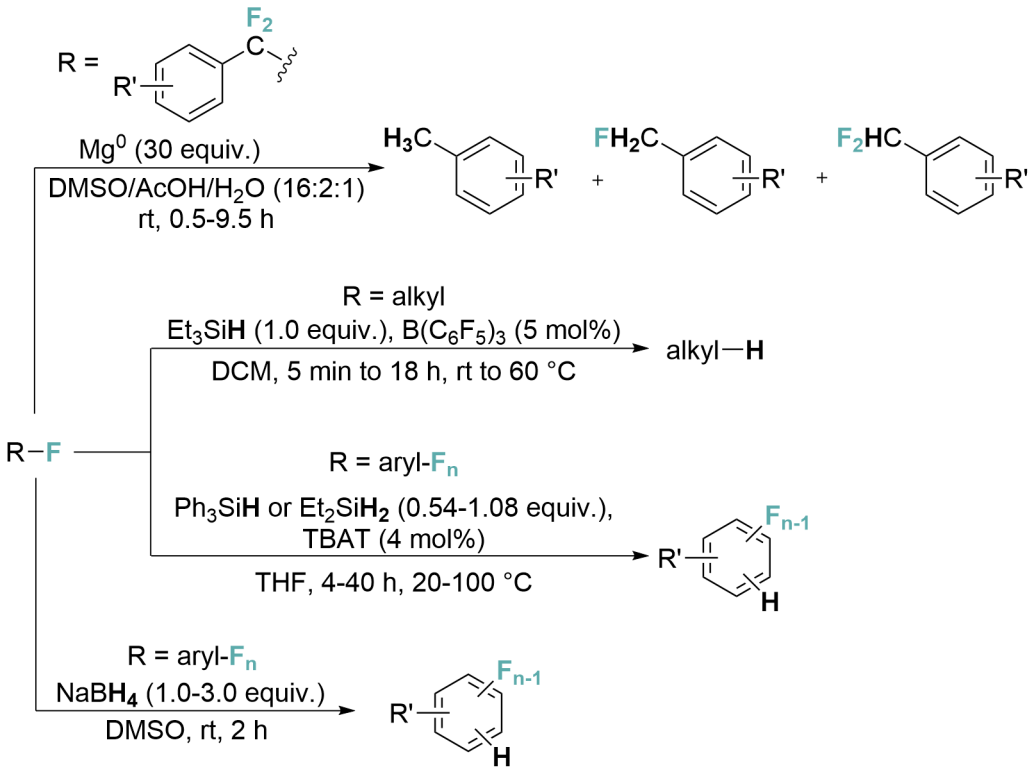
In general, the methods can be categorised into three approaches: hydrodefluorinations, defluorinative C–C bond formation and defluorinative C–X bond formation, where X corresponds to a number of different non-metal and metalloid residues (Scheme 9). This chapter will discuss selected examples of all three approaches.



Scheme 9: Different approaches for C–F bond cleavage.

In the case of hydrodefluorination (HDF), a fluorine atom can be exchanged for a hydrogen atom upon activation of the C–F bond. As shown by Prakash and co-workers, C–F activation can be achieved by reducing the starting material using magnesium (Scheme 10).[54] The work focusses on trifluoromethylated aromatic compounds and leads to the mono-, di- and tridefluorination of a wide range of aromatic compounds using a DMSO-water-acetic acid mixture as solvent and proton source. Other methods use Lewis acids with a high fluoride ion affinity (FIA) to activate the C–F bond. This can be achieved, for example, by using boranes. In 2012, Stephan's group presented a method in which tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) was used to activate aliphatic C–F bonds.[55] The desired HDF can eventually be achieved by the reaction of triethylsilane with the fluorinated compound and catalytic amounts of $B(C_6F_5)_3$. The formation of the stable Si–F bond is the driving force in this reaction. Alternatively, a combination of silicon compounds as hydrogen atom source and tetrabutylammonium difluorotriphenylsilicate (TBAT) as catalyst can be used for the HDF of

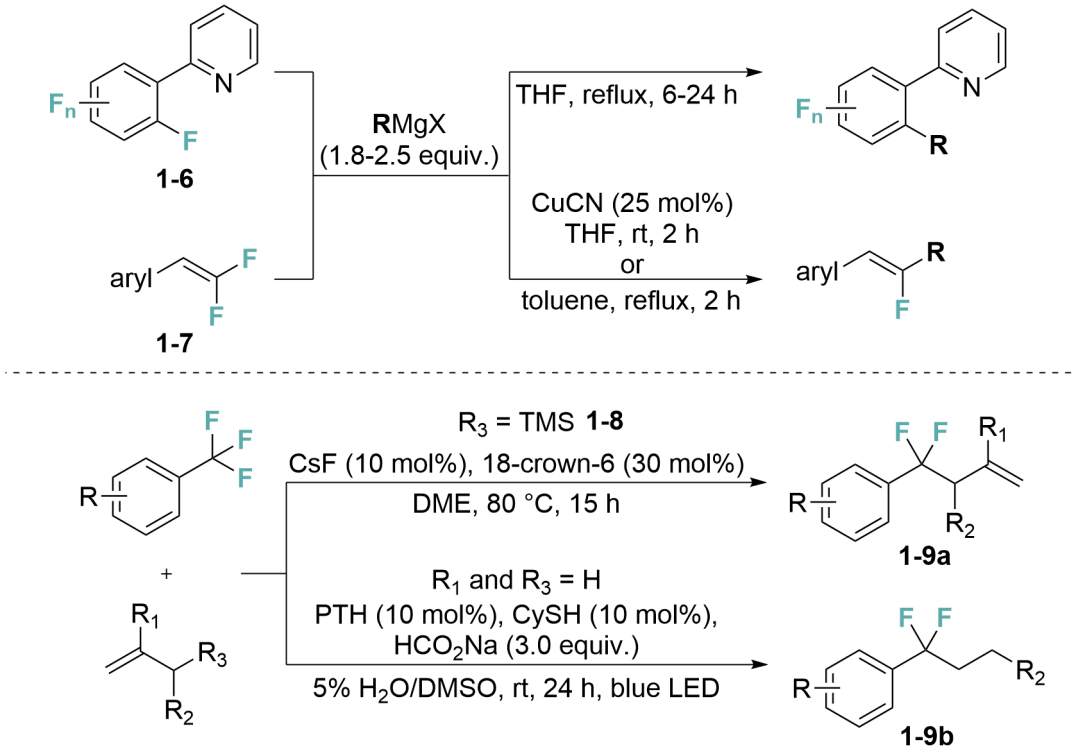
(poly)fluorinated aromatic compounds, as shown by Ogoshi's group.[56] Hydride sources are another activation method for fluorinated compounds. The work of Schoch *et al.*, for example, presents sodium borohydride as a suitable reagent for hydrodefluorination of polyfluorinated aromatic compounds.[57]



Scheme 10: Hydrodefluorination using different reducing agents.

While hydrodefluorination reactions are mainly used for the generation of partially fluorinated functional groups, such as CF_2H or CFH_2 moieties, the defluorinative C–C and C–X bond formation approach offers more diverse application possibilities. A straightforward approach for the formation of C–C bonds from C–F compounds is, for example, cross-coupling using organometal compounds. In 2013 and 2016, Cao's group presented the reaction of (fluorophenyl)pyridines **1-6** or *gem*-difluoroalkenes **1-7** with Grignard reagents (Scheme 11).[58] The approach can be done either using copper(I) cyanide as the catalyst or completely catalyst-free. Other methods use single electron transfer (SET) processes for the alkylation or arylation of C–F bonds. As shown by Luo *et al.*, the reaction of allyl silanes **1-8** with trifluoromethyl compounds and fluoride ions leads to defluoroallylations via a fluoride-induced SET reduction of the starting material and the formation of *gem*-difluoro compounds **1-9a**.[59] A broader scope of *gem*-difluoro compounds can be achieved when photoredox catalysts are used for this kind of transformation. In this context, also frustrated Lewis pairs (FLPs) as reaction partners for C–F activation have gained more and more relevance over the last years.[60] This approach reduces the issue of overreaction towards di- and tridefluorinations and therefore allows for a broad scope of *gem*-difluoro compounds.[61] In 2018, Jui and

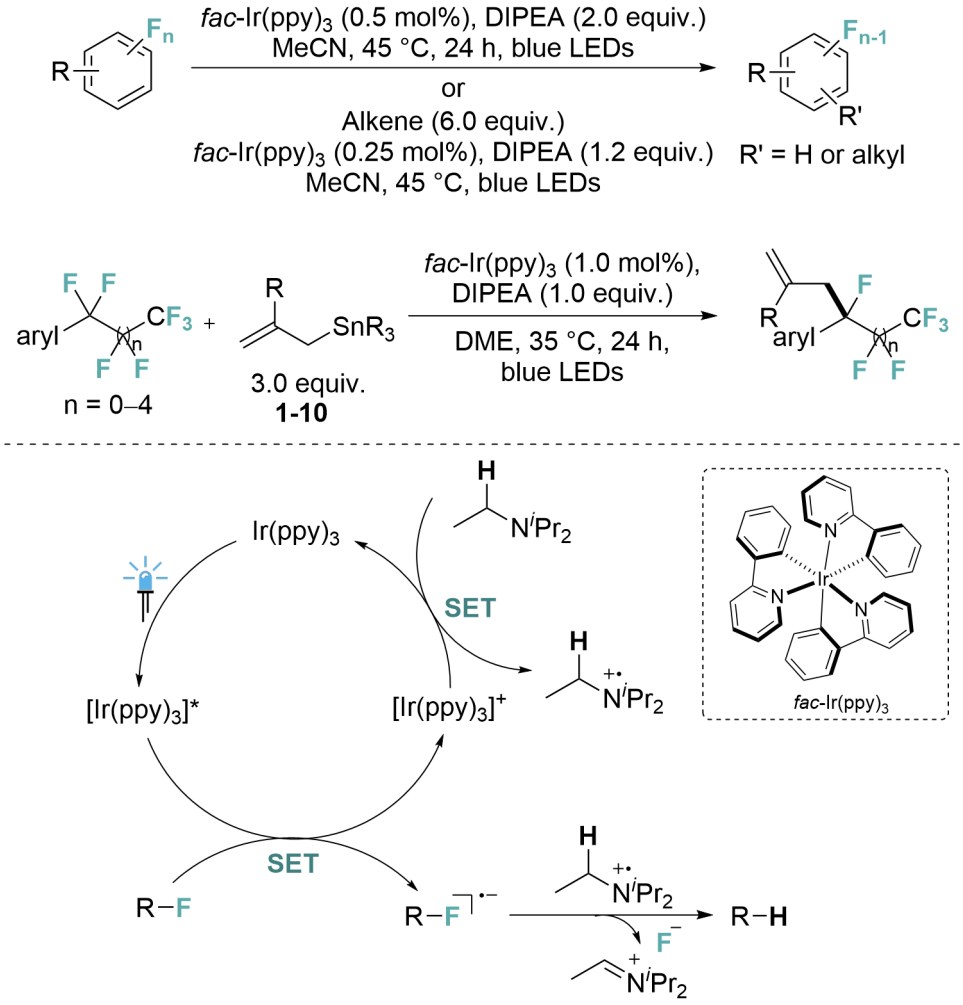
co-workers presented a method for the defluoroalkylation of trifluoromethyl compounds using *N*-phenylphenothiazine (PTH) as the catalyst resulting in products **1-9b**.[62]



Scheme 11: Examples of defluorinative C–C bond formations of aromatic and aliphatic fluorinated compounds.

In recent years, new photocatalytic methods for C–F activation have been continuously investigated, resulting in a wide range of defluorination methods based primarily on photoredox processes and using transition metal catalysts.[63] Both hydrodefluorination and defluorinative alkylation can be achieved via photoredox catalysis using, for example, a combination of tris(2-phenylpyridine)iridium(III) (*fac*-Ir(ppy)$_3$) and *N,N*-diisopropylethylamine (DIPEA) as shown by the groups of Weaver[64] and Nishimoto and Yasuda (Scheme 12, top).[63] In their work, Weaver and co-workers first converted polyfluorinated aromatics with *fac*-Ir(ppy)$_3$ and DIPEA, whereby a C–F bond could be selectively converted into a C–H bond.[64a] If an alkene is added to this system, a defluorinative alkylation of the C–F bond can be achieved.[64b] In 2021, Nishimoto and Yasuda presented a method for C–F bond allylation under iridium catalysis. Allylstannanes **1-10** and perfluoroalkylarenes were reacted using *fac*-Ir(ppy)$_3$ and DIPEA under irradiation with blue light.[63] The mechanism of catalytic photoredox hydrodefluorination is initiated by blue light, which activates the iridium catalyst (Scheme 12, bottom). This can be converted into an Ir(IV) species by a SET with the fluorinated molecule (R–F), whereby the fluorinated molecule becomes a radical anion. The Ir(IV) complex can then accept an electron from DIPEA via a subsequent SET process, whereby both a DIPEA radical cation is formed and the original *fac*-Ir(ppy)$_3$ catalyst is regenerated for a new catalytic cycle. Both the radical anion (R–F$^{\bullet-}$) and

the radical cation (DIPEA$^{\cdot+}$) can finally react to form the corresponding C–H compound and an ammonium fluoride.

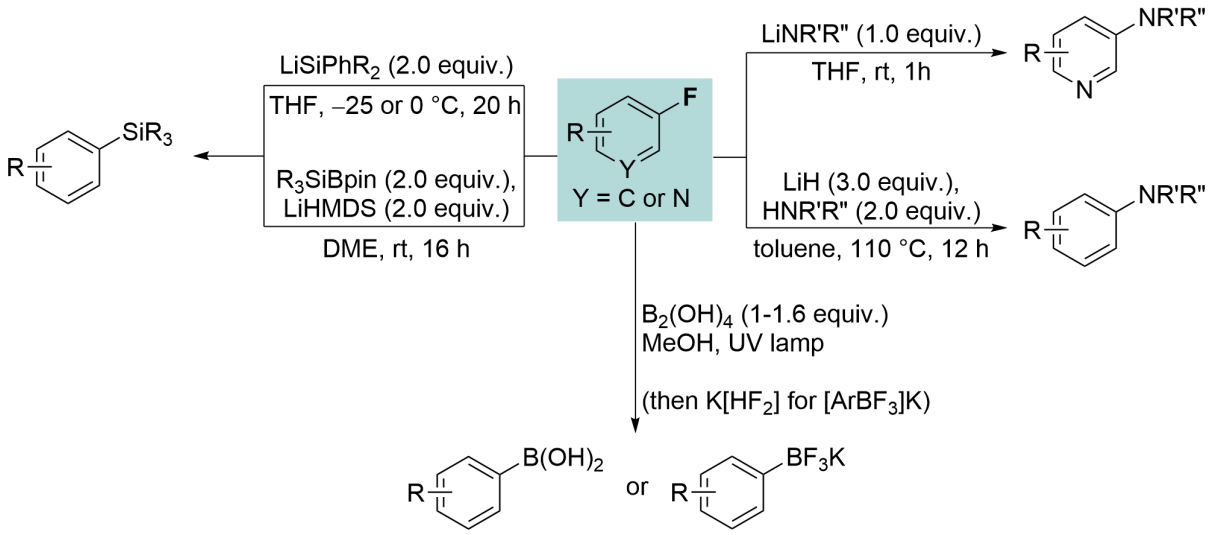


Scheme 12: Photocatalytic hydrodefluorination, defluorinative alkylation (top) and the proposed catalytic cycle of the hydrodefluorination using an iridium catalyst and DIPEA as reductive quencher (bottom).

Defluorinative C–X bond formation is of interest for synthetic chemistry because it can be used to introduce important substituents for follow-up reactions or to access more complex molecules. Of particular interest in this context is the formation of C–Si, C–N and C–B bonds, although there are also methods for the formation of other C–X bonds, such as C–hal or C–P bonds.[65] A common approach for this type of transformation is the activation of the C–F bond by alkali metal bases. In particular, aromatic silicon compounds or amines can be made accessible in this way.

In 2019, Studer's group presented a method for the silyl defluorination of aromatic compounds using silyl lithium compounds (Scheme 13). Here, the Si–F exchange takes place via a concerted aromatic substitution under lithium mediation and the formation of poorly soluble lithium fluoride contributes to the driving force of the reaction.[66] These silyl lithium compounds

can also be generated *in situ* and used for such reactions, whereby aliphatic fluorides can also be reacted, as shown by the Martin group.[67] A similar approach was also used by Ding's and Singaram's groups in the lithium-mediated defluoroamination of aromatic C–F bonds. Ding and co-workers used lithium amides to obtain 2-aminopyridines from 2-fluoropyridines.[68] However, Singaram and co-workers used a combination of amines with lithium hydride for the synthesis of aromatic amines.[69] An alternative approach to defluoroamination by Paquin's group uses 1,1,1-tris(hydroxymethyl)propane instead of alkali metal compounds to activate C–F bonds.[70] The triol acts as a hydrogen bond donor and enables S_N2 substitution of benzylic C–F bonds. Boron compounds also represent a class of compounds that can be accessed via C–F activation. In 2016, Larionov's group presented a method for the photoinduced borylation of haloarenes and aryl ammonium salts.[71] The method also enabled the borylation of fluoroaromatics with tetrahydroxydiboron under ultraviolet light.



Scheme 13: Examples for defluorinative C–X bond formation reactions of aromatics.

1.3 General Approaches towards Fluorinated Groups

1.3.1 Chalcogenic Fluorinated Groups (YR_F)

While the introduction of fluorine atoms or CF_xH_y groups into organic compounds is widely used in different sectors of chemical development, also chalcogen bearing fluorinated groups (YR_F groups) gain growing interest as they can be used for the fine-tuning of the molecule's properties. The introduction of these groups into organic molecules can be achieved in many different ways. The associated methods can be divided into three approaches: *de novo* synthesis, the indirect and the direct approach (Figure 5). The original methods were based on *de novo* synthesis and aimed at either the fluorination of activated R-Y-R_X compounds, such as esters or ethers, or halogen exchange (HalEx) reactions of YR_x compounds. The activation of, for example, phenols with xanthalating reagents achieves an activated ether which can be turned into the trifluoromethoxy (OCF_3) group using different fluorination reagents.[72] In the so-called HalEx reactions, pre-halogenated substrates are converted into the respective fluorinated derivatives by substitution reactions. Appropriate fluorination reagents for this kind of transformation are, for example, HF,[73] $SbF_3/SbCl_5$,[74] KF[75] or Olah's reagent (pyridine-HF 3:7).[76]

The indirect approach uses pre-functionalised compounds in combination with transfer reagents to indirectly construct the desired group. For example, trifluoromethylthio (SCF_3) groups can be obtained by the reaction of thiols or disulphides with the utilisation of various trifluoromethylation reagents.[77] Similar reactions can be observed for seleno- and tellurophenols or related dimers.[78]

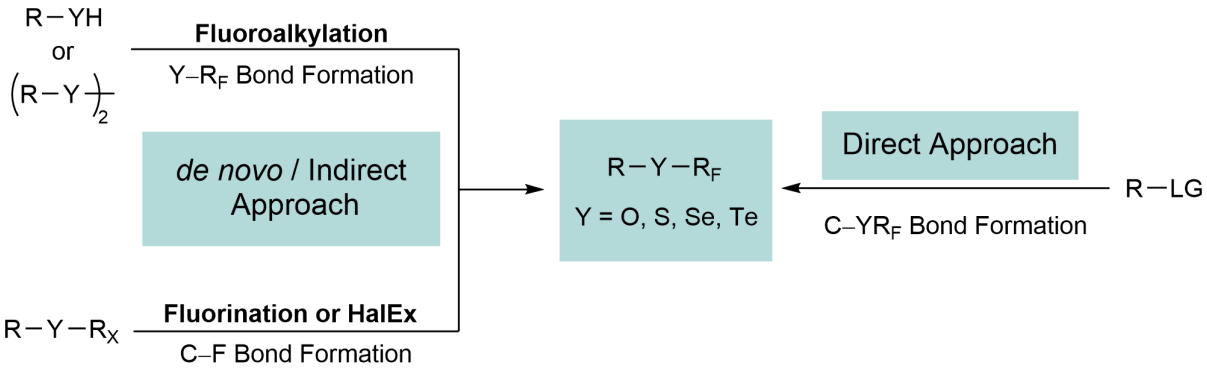


Figure 5: Overview of different approaches for the introduction of YR_F groups.

Both the *de novo* and the indirect approach are widely studied for many YR_F groups and easily accessible due to the abundance of fluorination reagents and methods, as well as the intensive research on (per)fluoroalkylation reagents in recent years. However, they are less suitable for late-stage applications and often require an extra pre-functionalisation step to obtain the desired YR_F-molecule.

The third approach is the direct approach, whereby the desired YR_F moiety is transferred to the molecule in its entirety by group transfer reagents, often by cleavage of a leaving group (LG) or by C–H activation.[79] Therefore, method development tends to be more complex, as the required transfer reagents have to be designed specifically and suitable activation methods have to be found. However, the advantage of this synthetic route is that the design of the methods and reagents makes it possible to avoid pre-functionalisation or multi-step synthesis, which can be particularly interesting for late-stage applications and industry. For this reason, easier to handle reagents for direct synthesis of YR_F compounds are under ongoing development.

1.3.2 Pentafluorochalcogenyl Groups (YF_5)

The methods for the construction of pentafluorochalcogenyl (YF_5) groups and their introduction into organic molecules are compared to other fluorinated groups (e.g. YR_F) very limited. The main methods to achieve their synthesis can be divided into the *de novo* and direct approach. Both approaches are hampered by either unstable intermediates or the limited access to suitable transfer reagents.

The *de novo* synthesis of YF_5 compounds can be achieved by the fluorination of R-YH or the corresponding dimers using different fluorinating reagents such as F_2, AgF_2, XeF_2 or trichloroisocyanuric acid (TCICA)/KF (Figure 6).[80] This synthetic pathway often proceeds via unstable R-YF_3 intermediates. Alternatively, a combination of fluoride and chloride sources can be used to obtain YF_4Cl species in the first step, followed by a HalEx reaction to obtain the desired YF_5 compounds.[81] In general these concepts require several synthetic steps, which is disadvantageous for late-stage applications.

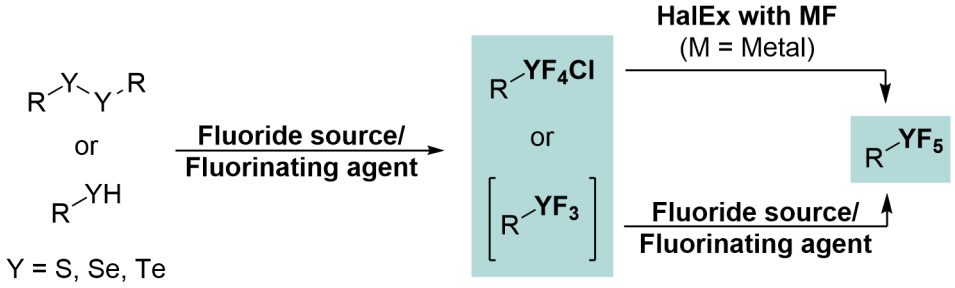


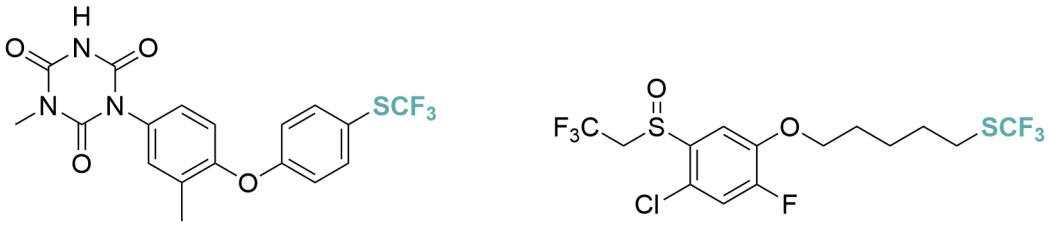
Figure 6: *De novo* approaches for the introduction of YF_5 groups with Y = S, Se or Te.

The direct installation of YF_5 moieties is therefore more advantageous to simplify the synthetic pathways to pentafluorochalcogenyl compounds. In general, only two compound classes, namely YF_5Cl/Br or Y_2F_{10} reagents, offer the direct access towards these products. However, the reagents usually need specialised equipment, are difficult to handle and only offer a limited application scope. Therefore, *de novo* pentafluorochalcogenylation in combination with a YF_5-

building block based total synthesis approach is often used and new direct ways to access more complex YF_5 products are being sought.
The following *Chapters 1.4-1.6* will mainly focus on methods for the direct introduction of the fluorinated groups presented within this work, namely SCF_3, OCF_3 and SF_5.

1.4 The Trifluoromethylthio Group (SCF_3)

The trifluoromethylthio group is one of the more thoroughly researched fluorinated groups and is already widely used in pharmaceutical and agrochemical applications due to its unique properties. In particular, its extremely high lipophilicity, with a Hansch parameter of 1.44 (the highest value among simple fluorinated groups),[11a] and electron-withdrawing properties comparable to those of the trifluoromethyl group make it an excellent candidate for advanced development and fine-tuning of organic molecules. A prominent application example of SCF_3 groups in the pharmaceutical industry is Toltrazuril, which is used as an antiparasitic agent for the treatment of protozoal infections in mammals and birds. Another example of the use of SCF_3 compounds is the acaricide Flupentiofenox, which is used to treat plants against sap-sucking insects such as mites (Figure 7).



Toltrazuril
(coccidiostatic agent)

Flupentiofenox
(acaricide)

Figure 7: Structures of Toltrazuril and Flupentiofenox.

General strategies for the synthesis of trifluoromethylthiolated compounds are, analogous to *Chapter 1.3*, the *de novo*, indirect and direct approach. The *de novo* approach focusses on HalEx reactions and the indirect approach on the trifluoromethylation of thiols and disulphides using common CF_3 reagents such as ICF_3,[82] Umemoto's,[83] Togni's[84] or Langlois' reagent.[85] In recent years, however, the trend has shifted towards direct introduction methods for SCF_3 groups. Here, selected examples of the direct introduction of trifluoromethanesulphenyl groups using radical, electrophilic and nucleophilic reagents are presented (Figure 8).

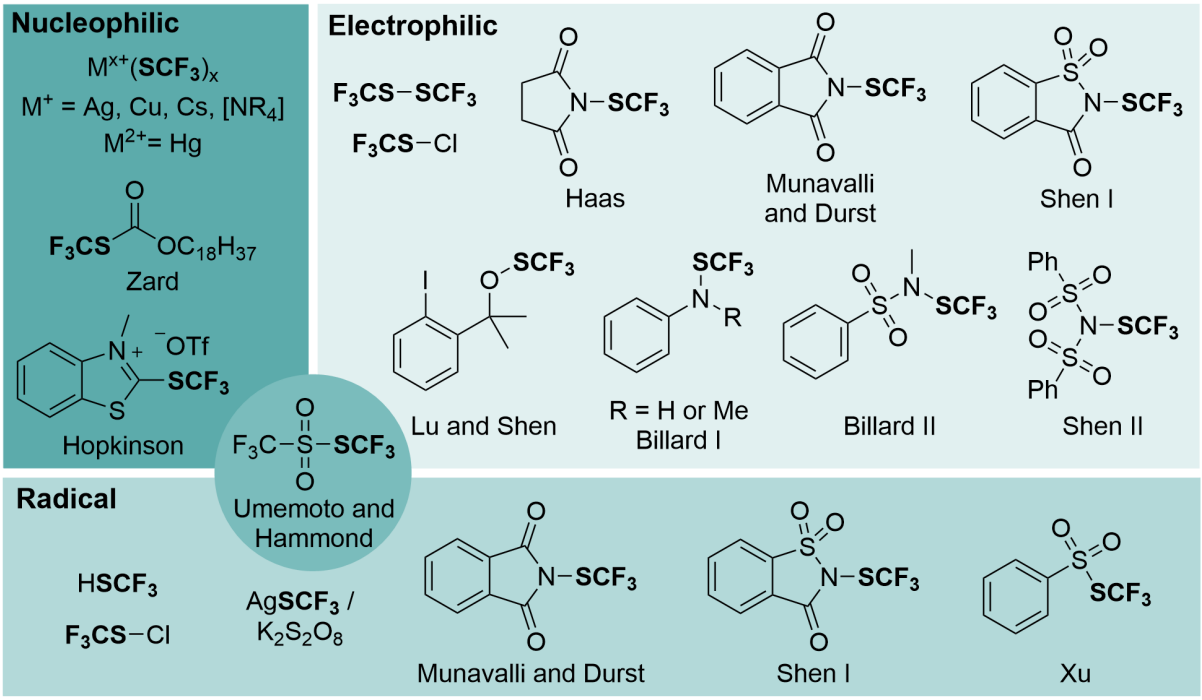
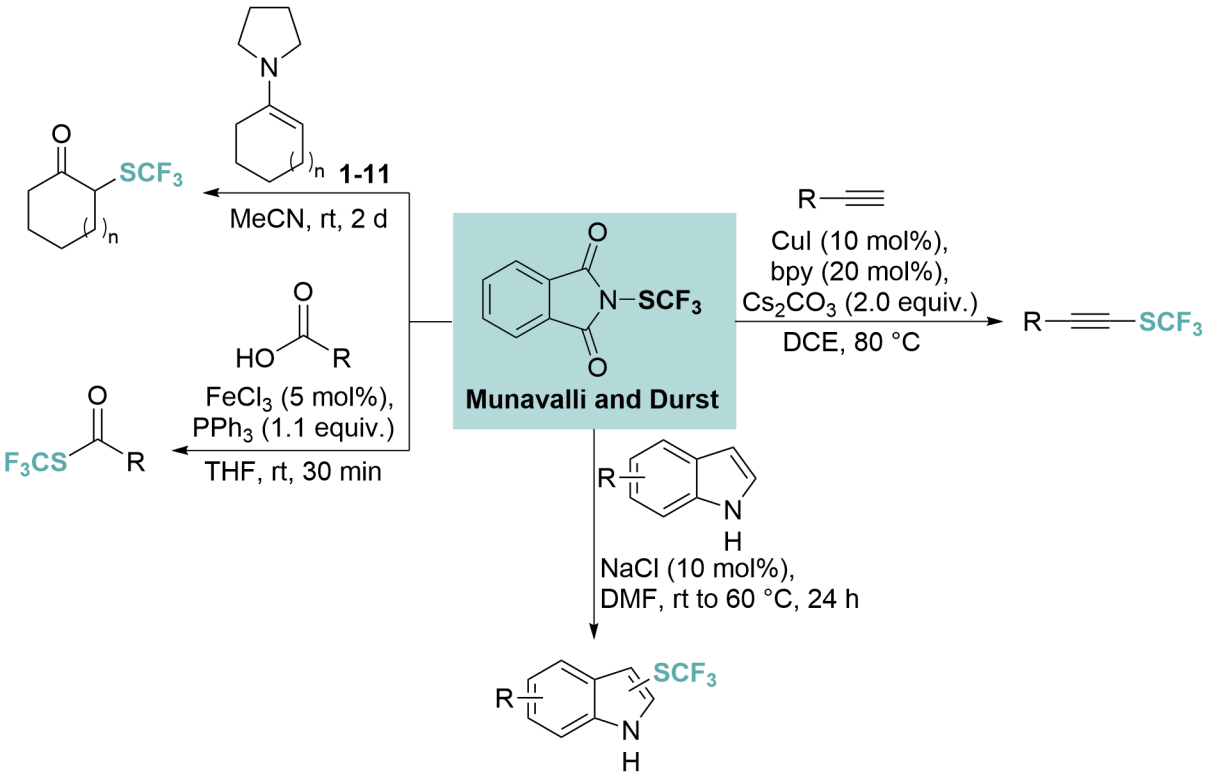


Figure 8: Overview of nucleophilic, electrophilic and radical reagents for direct trifluoromethylthiolation reactions.

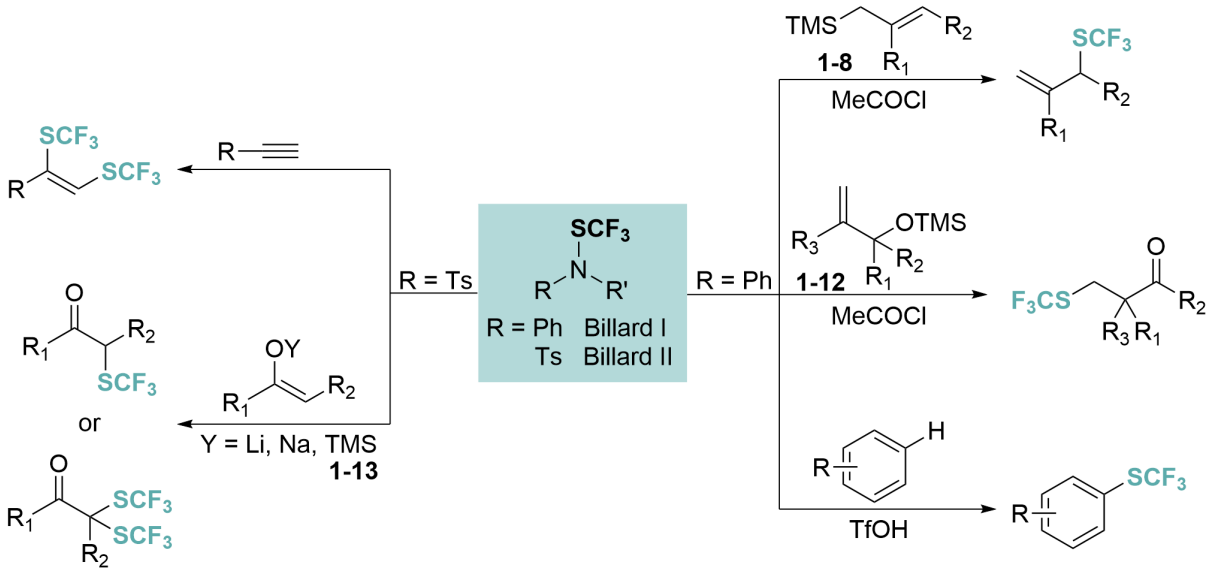
Trifluoromethylthiolation can be carried out using electrophilic reagents. These are frequently described in the literature; therefore, a wide range of reagents is available. Initially, reagents such as trifluoromethanesulfenyl chloride (SCF_3Cl) or bis(trifluoromethyl)disulfide ($(SCF_3)_2$) were used for this type of transformation. They are capable of producing both (hetero)aromatic and aliphatic SCF_3 compounds.[86] However, these reagents are comparatively toxic, leading to the search for alternatives in subsequent years.

In 1996, Haas and Möller presented *N*-trifluoromethylthiosuccinimide, an electrophilic SCF_3 reagent that is able to transfer SCF_3 groups by activating the N–S bond.[87] Using this reagent, Shen and co-workers succeeded in directly trifluoromethylthiolating arenes under palladium catalysis.[88] A structurally similar reagent is *N*-trifluoromethylthiophthalimide (Munavalli reagent). The reagent offers broad utility for electrophilic SCF_3 transfer to various nucleophiles such as enamines **1-11**, carbonyl compounds, alkynes or heteroaromatics (Scheme 14).[89] In 2015, the group of Glorius succeeded in realising a Friedel-Crafts type trifluoromethylthiolation of various heteroaromatic compounds with a combination of the Munavalli reagent and catalytic amounts of sodium chloride.[90]



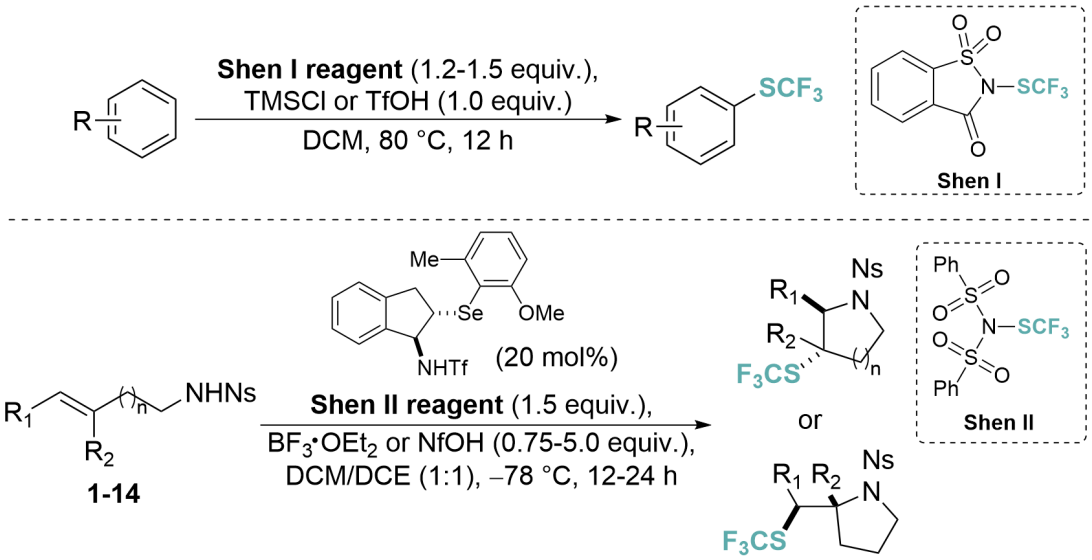
Scheme 14: Applications of the Munavalli reagent for the trifluoromethylthiolation of enamines **1-11**, carboxylic acids and heteroaromatics.

Despite the good reactivity of the Haas and Munavalli reagents, other electrophilic SCF_3 reagents quickly gained importance. In 2008 and 2015 Billard and co-workers developed new nitrogen-based sets of SCF_3 reagents (Billard I and Billard II), which gave good results with a wide range of organic compounds (Scheme 15). The reactivity of the Billard reagents depends strongly on the choice of Lewis or Brønsted acids, which are used as activating reagents for the methods. For example, the trifluoromethylthiolation of allyl silanes **1-8** and allylic silyl ethers **1-12** can be achieved with a combination of Billard I reagent and acetyl chloride, as demonstrated by the groups of Qing and Tu.[91] Furthermore, the Billard I reagent can be used with triflic acid to transfer SCF_3 groups to aromatic compounds.[92] The second generation of Billard reagents (Billard II) show a higher electrophilicity and reactivity, resulting in a broader spectrum of nucleophilic reaction partners, such as silyl enol ethers **1-13** or alkynes, with also ditrifluoromethylthiolations being observed.[93]



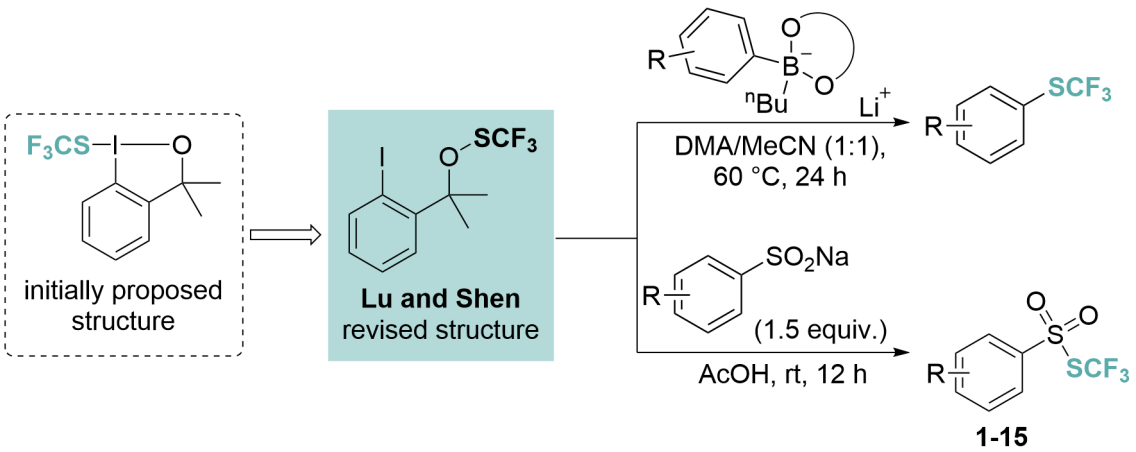
Scheme 15: Trifluoromethylthiolation of enols, alkenes, alkynes and aromatics using the Billard I and II reagents.

With the aim of creating an inexpensive and reactive SCF_3 reagent, Shen's group presented *N*-trifluoromethylthiosaccharin. The reagent proved to be more electrophilic than other common trifluoromethylthiolation reagents and thus enabled a broad variation of nucleophilic reaction partners.[94] In addition, the Shen I reagent is one of the few electrophilic SCF_3 reagents capable of performing Friedel-Crafts type reactions on electron-rich aromatic compounds using only trimethylsilyl chloride (TMSCl) or triflic acid as an additive (Scheme 16).[94] The electrophilicity of the reagent can be further increased by adding another sulfonyl group to the nitrogen centre, resulting in the Shen II reagent. Shen II is able to react with a number of electron-rich aromatic compounds even without the addition of a Lewis or Brønsted acid.[95] Furthermore, Luo *et al*. found that Shen II provides improved enantioselectivities in some asymmetric trifluoromethylthiolation reactions, hence its increased use in this type of conversion.[96]



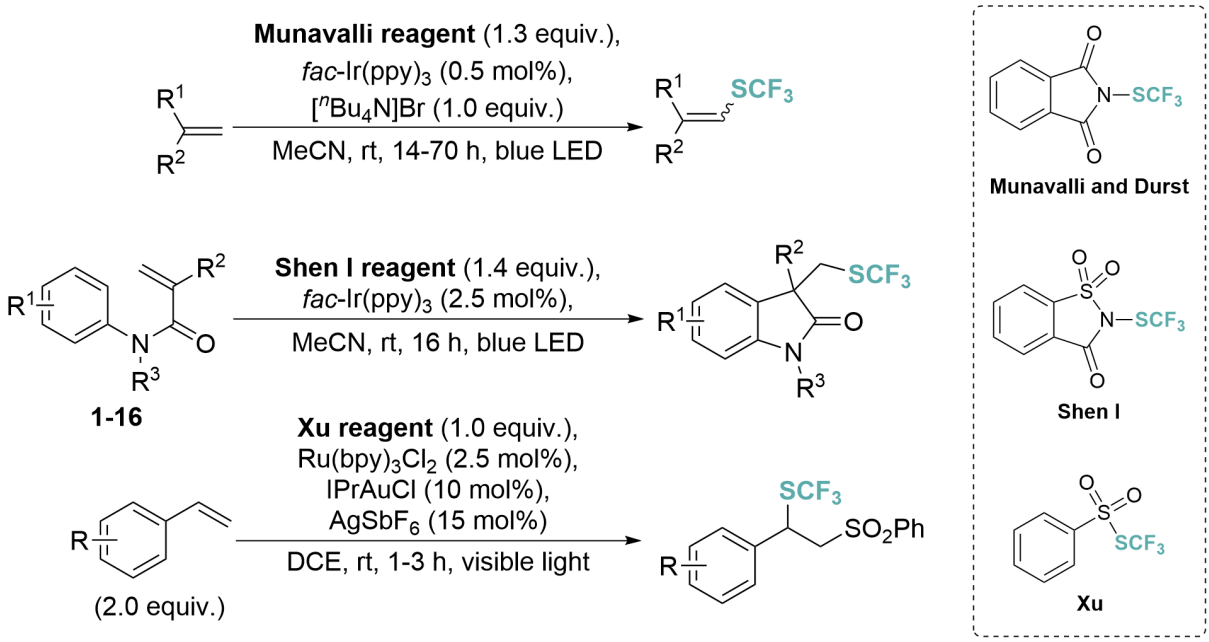
Scheme 16: Trifluoromethylthiolation of aromatics using the Shen I reagent and asymmetric trifluoromethylthiolation and cyclisation of olefinic sulphonamides **1-14** using the Shen II reagent.

In 2013, Shen and Lu discovered a new reagent, similar to Togni's trifluoromethylation reagent, that can efficiently transfer SCF_3 groups.[97] However, the first proposed structure as a hypervalent iodine reagent proved to be incorrect and was eventually revised by Buchwald *et al*.[98] The reagent is less electrophilic than the Shen I and II reagents but has been shown to be a mild transfer reagent for trifluoromethylthiolations of activated aromatics (Scheme 17).[99] It has also proven to be a good reaction partner for the synthesis of trifluorothiosulphonates from sodium aryl sulfinates.[99a] In 2023, the groups of Hammond and Umemoto introduced *S*-trifluoromethyl trifluoromethanesulfonothioate (TTST), a reagent that can be used both as an electrophilic reagent to react with a wide range of O, S, N and C nucleophiles and as a nucleophilic or radical SCF_3 reagent.[100]



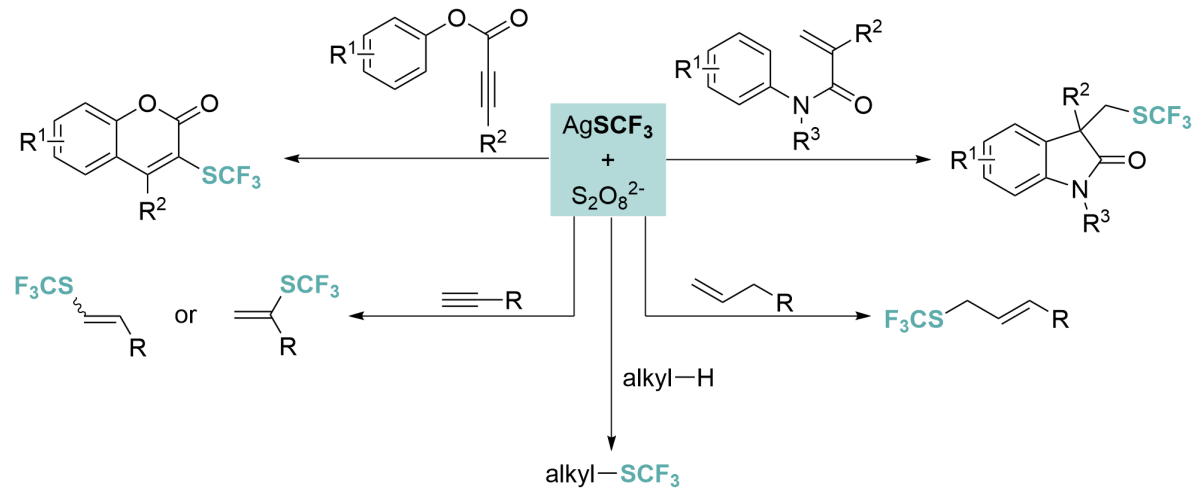
Scheme 17: Initially proposed and revised structure of the Lu-Shen reagent and its applications as a transfer reagent for the synthesis of aryl-SCF_3 compounds and trifluorothiosulphonates **1-15**.

Compared to the electrophilic methods, the radical SCF_3 reagents are limited to a few examples, such as CF_3SCl or trifluoromethanethiol (CF_3SH). These reagents can react primarily with alkenes[101] but also occasionally with alkanes[102] to form SCF_3 compounds. However, these reagents are difficult to handle, resulting in ongoing research into more practical radical reagents. One example of radical trifluoromethylthiolation with easy-to-handle reagents is the use of Munavalli's reagent as a radical source upon photoredox activation for SCF_3 transfer to alkenes under preservation of the double bond (Scheme 18).[103] Another example is the trifluoromethylthiolation of acrylamides **1-16** with the Shen I reagent under photoredox catalytic conditions.[104] In 2016, Xu's group presented a new reagent that releases SCF_3 radicals under dual catalysis using a gold and a photoredox catalyst and leads to difunctionalised products upon reaction with double bond systems.[105]

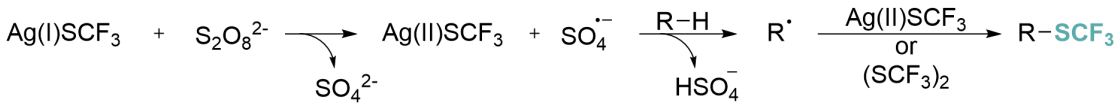


Scheme 18: Examples for visible light promoted radical trifluoromethylthiolations using Munavalli, Shen und Xu reagents.

Another recent approach for the radical introduction of SCF_3 groups is the silver-mediated oxidative trifluoromethylthiolation of activated alkanes, alkenes or alkynes (Scheme 19, top). In this process, silver trifluoromethanethiolate ($AgSCF_3$) is combined with persulphates as oxidising agents, which leads to the formation of SCF_3 radicals that either add to multiple bonds or react with alkanes.[106] The proposed mechanism for the direct trifluoromethylthiolation of unactivated alkanes is initialised by the reaction of $Ag(I)SCF_3$ with the persulphate dianion to form an $[Ag(II)SCF_3]$ species, sulphate dianions and sulphate radical anions (Scheme 19, bottom). The radical anion can abstract a hydrogen resulting in a carbon radical which can further react with either the $[Ag(II)SCF_3]$ species or the SCF_3 dimer potentially formed from the $[Ag(II)SCF_3]$ species.[106f]

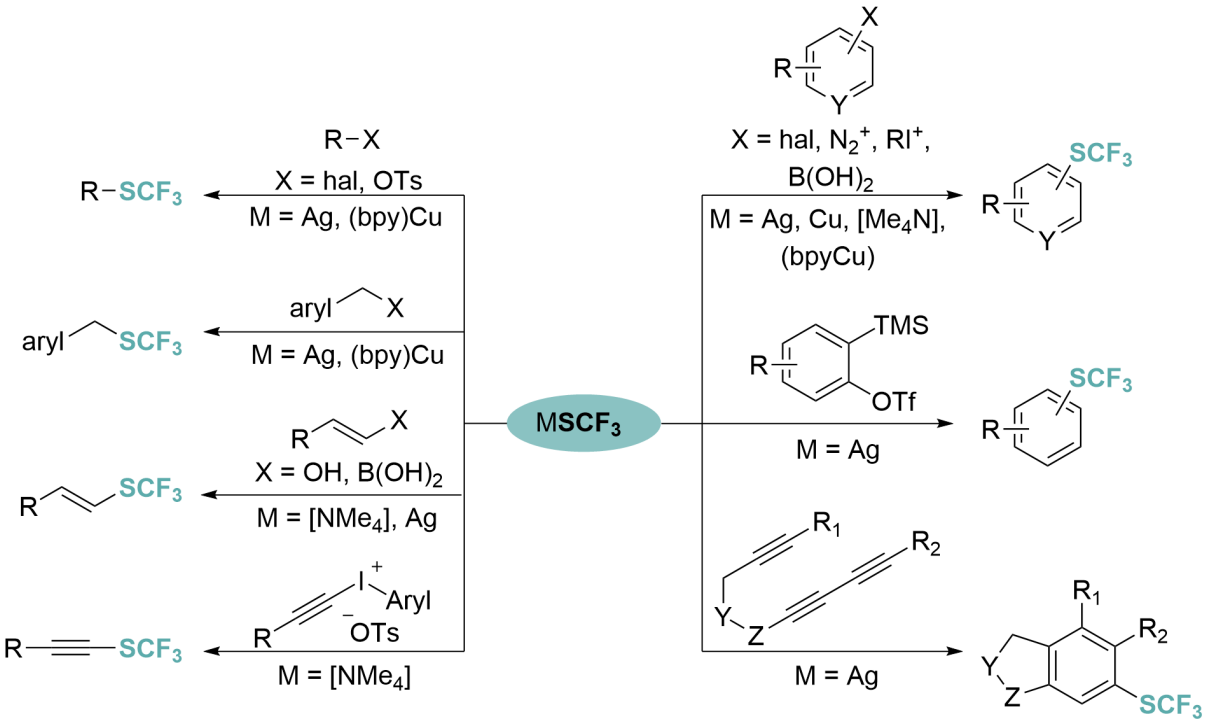


Proposed Mechanism of Trifluoromethylthiolation of Alkanes:



Scheme 19: Examples of radical trifluromethylthiolations using a combination of $AgSCF_3$ and persulfate dianion (top). Proposed mechanism for the trifluoromethylthiolation of alkanes (bottom).

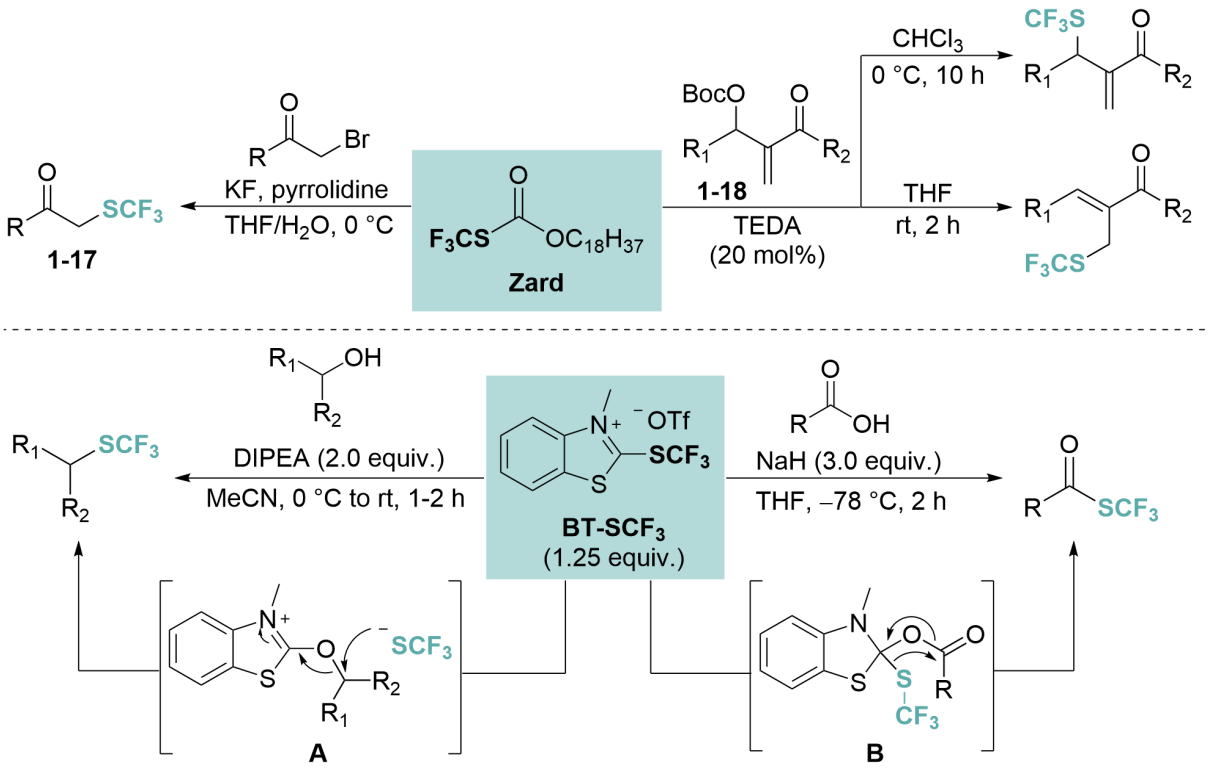
The synthesis of trifluoromethylthiolated compounds can also be achieved using nucleophilic reagents. The variety of reagents is, however, similarly limited as with radical methods, as the easily accessible reagents are to a great extent expensive and toxic. After the development of the first nucleophilic reagent for trifluoromethylthiolation ($Hg(SCF_3)_2$) by Man *et al.*,[107] a number of similar reagents such as $AgSCF_3$, $CuSCF_3$, $CsSCF_3$ or $[Me_4N]SCF_3$ were introduced.[107-108] The reagents described here are extensively used for the synthesis of trifluoromethylthioethers, for example from alkyl or alkenyl halides, alkynyliodonium compounds or activated (hetero)aromatic compounds. A summary of a few selected examples is shown in Scheme 20.[108b, 109]



Scheme 20: Examples for aromatic and aliphatic nucleophilic trifluoromethylthiolation using $MSCF_3$ reagents.

Another nucleophilic method for trifluoromethylthiolation reactions is the *in situ* generation of SCF_3 anions via the activation of a trifluoromethylated precursor. In 2013, Zard *et al*. presented a method to convert *α*-bromoketones directly into *α*-SCF_3 ketones **1-17** using a combination of *O*-octadecyl *S*-(trifluoromethyl) carbonothioate with KF and pyrrolidine (Scheme 21, top).[110] This approach was also used by Shen for the solvent switchable trifluoromethylthiolation of Morita–Baylis–Hillman carbonates **1-18**.[111] In this case, the activation of the precursor was achieved by triethylenediamine (TEDA) and the use of THF as the solvent leads to primary allylic compounds whereas chloroform can be used as the solvent to generate secondary allylic products.

In 2019, our group presented a new set of nucleophilic group transfer reagents based on the benzothiazolium (BT) motif. These reagents can be easily synthesised in two steps from inexpensive 2-mercaptobenzothiazole. They are bench-stable, easy-to-handle and offer a broad spectrum of applications. With BT-SCF_3, the deoxygenative trifluoromethylthiolation of alcohols and carboxylic acid derivatives was accomplished using only base as an additive (Scheme 21, bottom).[112] Mechanistically, the reaction with alcohols starts with the attack of the alcoholate to the carbene-centre of the reagent, releasing the SCF_3 anion in a controlled way. The anion can then attack at the *α*-carbon atom of the intermediate **A** resulting in the trifluoromethylthioether. For the reaction with carboxylic acids, the mechanism goes via an asynchronous concerted pathway after the formation of intermediate **B** producing trifluoromethylthioesters.



Scheme 21: Application of Zard's trifluoromethylthiolating agent for the synthesis of *α*-SCF_3 ketones and allylic SCF_3 compounds (top). Use of BT-SCF_3 and mechanism for the trifluoromethylthiolation of alcohols and carboxylic acids (bottom).

1.5 The Trifluoromethoxy Group (OCF_3)

Like other fluorinated groups, the trifluoromethoxy (OCF_3) group is widely used in the fields of pharmaceutics, agrochemistry and material science.[113] This can be attributed to the special properties of the group including its good metabolic stability, high lipophilicity and the associated influence on membrane permeability.[114] Compared to the OMe residue, the OCF_3 group has special structural characteristics when bound to aromatic systems (Figure 9).[115] The hyperconjugation of the non-bonding orbital (n_o) on the oxygen atom with the antibonding orbital of the C–F bond (σ^*_{C-F}) results in a conformation in which the CF_3 group is oriented outside the plane of the aromatic system. This makes it possible to adapt the structural conditions within molecules and thus also to influence the receptor binding affinity of a compound.[79d] As a result, more and more OCF_3 compounds are finding their way into drug research.[116] In the field of materials research, the group's influence on the temperature range of the liquid state of molecules is utilised to diversify existing standards in polymer technology, liquid crystal research and other areas.[113, 117] The OCF_3 group is also becoming increasingly important due to recent political debates concerning the potential ban of per- and polyfluoroalkyl substances (PFAS). This is because, compared to other perfluorinated and

partially fluorinated functional groups, it has a lower environmental persistence and currently represents an exception to the restriction under discussion.[118]

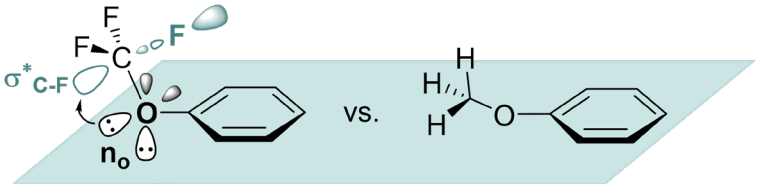


Figure 9: Representation of the orbital interactions for aromatic trifluoromethoxy groups versus aromatic methylethers.

The wide range of applications and the potential political influence creates a demand for easy and broad access to trifluoromethoxylated compounds. In the past decades, many *de novo*, indirect and direct trifluoromethoxylation methods have been presented, with the *de novo* and indirect approaches being limited to three routes: halogen exchange, oxidative fluorination of activated carbonyls or ethers and trifluoromethylation of hydroxylated compounds.[79d, 119]
Due to the advantages of the direct introduction of fluorinated groups, as described in *Chapter 1.3*, efforts to develop direct trifluoromethoxylation methods and reagents have intensified in recent years. The transfer reagents developed, as a result, can be divided into two groups: Nucleophilic reagents, which form OCF_3 anions through activation, and radical reagents, producing OCF_3 radicals within the reaction (Figure 10).

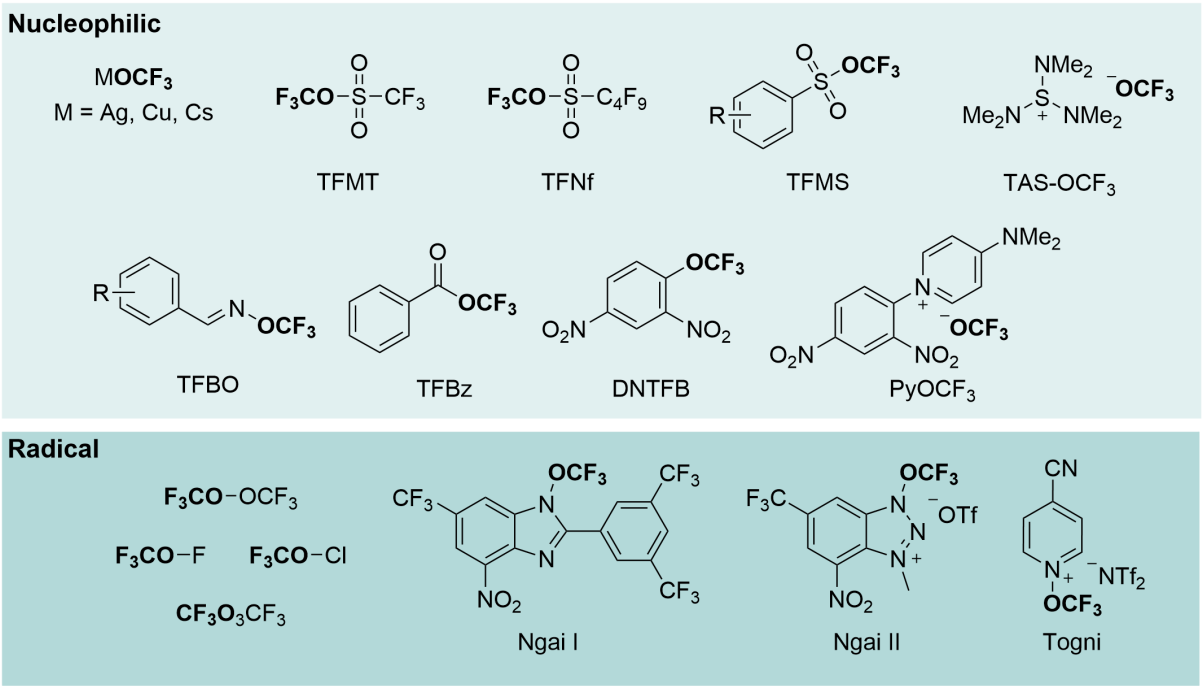
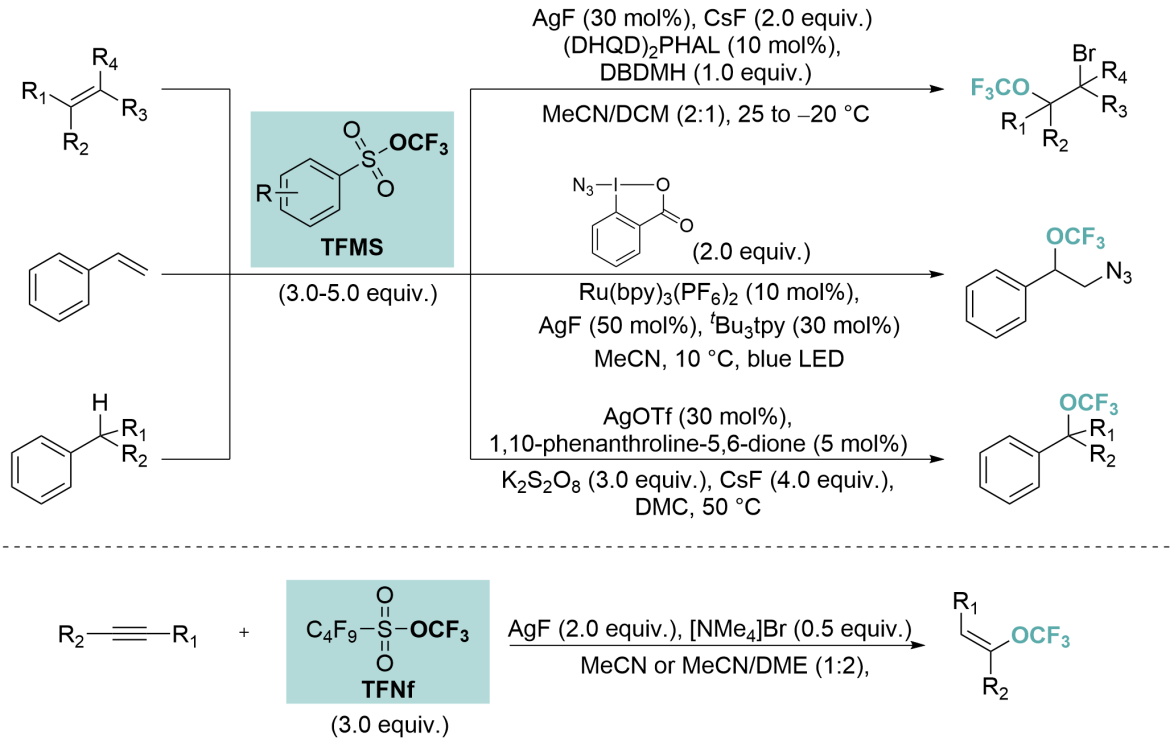


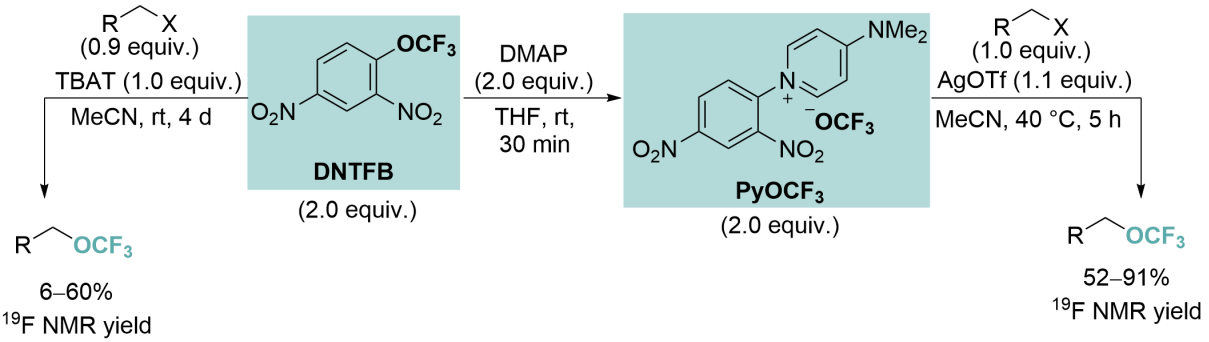
Figure 10: Overview of nucleophilic and radical trifluoromethoxylation reagents.

Nucleophilic methods, in particular, offer a diverse range of reagents. Metal trifluoromethoxylates based, for example, on silver(I), copper(I) and caesium(I), are powerful reagents for the nucleophilic trifluoromethoxylation of double bonds, alkyl halides and aromatic compounds.[120] In 2015, Liu and co-workers presented a palladium-catalysed aminotrifluoromethoxylation with Selectfluor as the oxidant and silver(I) trifluoromethoxide ($AgOCF_3$) as the transfer reagent.[121] By adapting the reaction conditions of this method, a ditrifluoromethoxylation of terminal alkenes could also be performed.[122] Alternatively, caesium(I) trifluoromethoxide ($CsOCF_3$) can be used as a reagent to trifluoromethoxylate allylic double bonds.[123] However, the handling of these trifluoromethoxylates is complicated due to their instability. In 2024, Golz *et al.* presented a possibility to address this issue by using acetonitrile solutions of $AgOCF_3$ and higher homologues.[124] This enabled the trifluoromethoxylation of various alkyl halides. Alternatively, $AgOCF_3$ can also be formed *in situ* by the reaction of, for example, trifluoromethyl triflate (TFMT) and silver(I) fluoride, as shown by the group of Langlois.[125] In the study, trifluoromethoxylated compounds were produced from organic bromides and iodides under mild conditions, however, the method was further improved by Billard's group.[126] In addition to TFMT, trifluoromethyl nonaflate (TFNf) and trifluoromethyl aryl sulfonate (TFMS) can also be used for this type of trifluoromethoxylation (Scheme 22). TFMS was introduced by the Tang group and enables safer access to trifluoromethoxylated alkanes, while TFNf was presented by the Umemoto group and facilitates the nucleophilic OCF_3 transfer onto alkynes.[127]



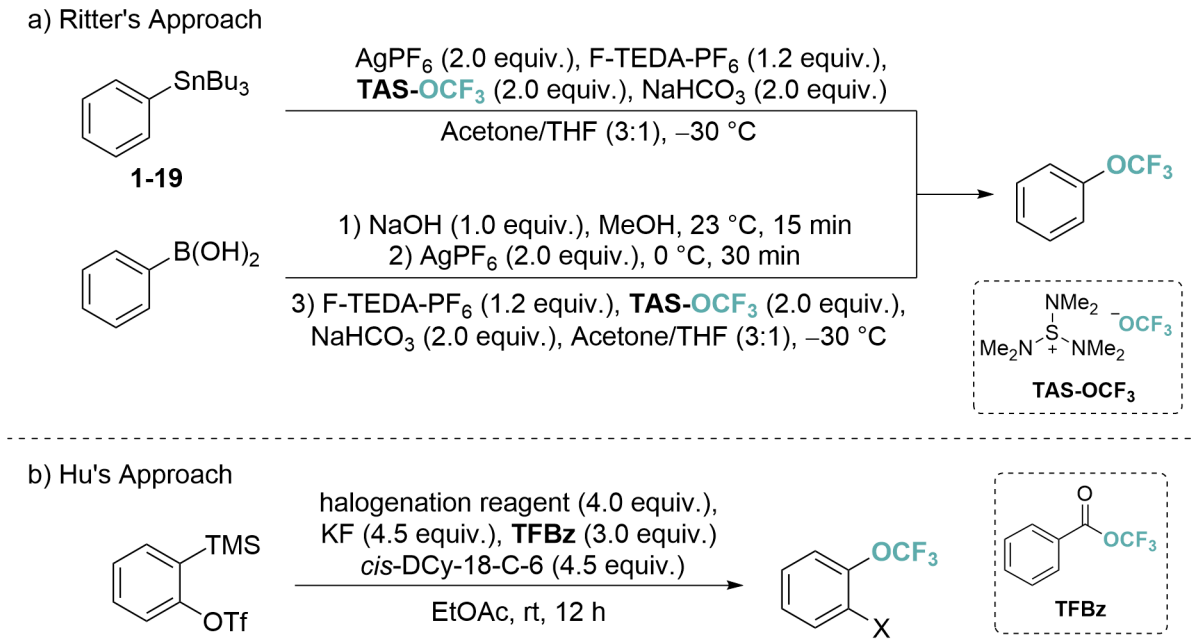
Scheme 22: Applications of TFMS and TFNf as trifluoromethoyxlation reagents via *in situ* formation of $AgOCF_3$.[127]

All of the aforementioned methods require rather expensive silver salts to stabilise the OCF_3 anion generated *in situ*. To circumvent this, in 2020, Li *et al*. presented a silver-free method for the synthesis of alkyl halides using (*E*)-*O*-trifluoromethyl-benzaldoximes (TFBO) as an $^{-}OCF_3$ source.[128] Another reagent capable of generating OCF_3 anions is 2,4-dinitro(trifluoromethoxy)benzene (DNTFB). This commercially available compound can form trifluoromethoxylated products directly from alkyl halides upon tetrabutylammonium difluorotriphenylsilicate (TBAT) activation (Scheme 23, left).[129] However, the yields for this method were comparatively low and hence, in 2021, Sanford's group used DNTFB for the synthesis of the trifluoromethoxide salt, 4-(dimethylamino)-1-(2,4-dinitrophenyl)pyridinium trifluoromethanolate ($PyOCF_3$), to perform nucleophilic OCF_3 transfer reactions (Scheme 23, right).[130] The reagent showed good to very good yields for substitution reactions on alkyl halides.



Scheme 23: Trifluoromethoxylation of alkyl halides using DNTFB (left) and $PyOCF_3$ derived from DNTFB (right).[129-130]

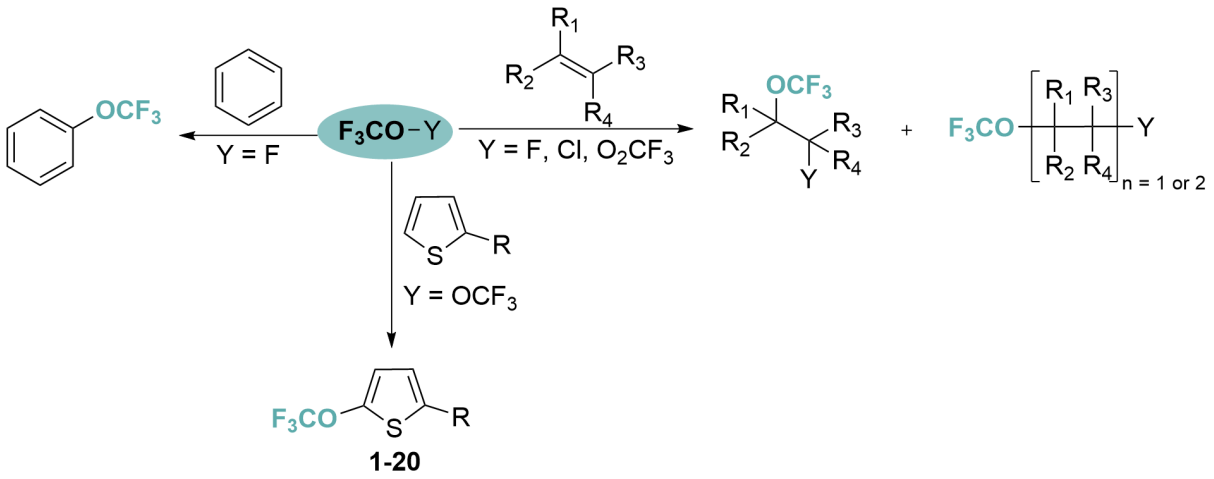
Despite the wide range of nucleophilic OCF_3 reagents, comparatively few methods led to aromatic OCF_3 compounds. In 2011, Ritter's group presented another sulphur-based reagent that is able to trifluoromethoxylate a wide variety of aromatic compounds.[131] This breakthrough was achieved with tris(dimethylamino)sulfonium trifluoromethoxide ($TAS\text{-}OCF_3$) as a transfer reagent (Scheme 24a). $TAS\text{-}OCF_3$ can be easily prepared by reacting TFMS with tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF). The reaction of $TAS\text{-}OCF_3$ with arylstannanes **1-19** or arylboronic acids is one of the few methods that allows direct nucleophilic introduction of the trifluoromethoxy group to aromatic compounds. Another method for the nucleophilic trifluoromethoxylation of aromatics is the trifluoromethoxylation-halogenation of arynes, developed by Hu's group in 2018 (Scheme 24b).[132] As OCF_3 source trifluoromethyl benzoate (TFBz) is used, which can be prepared by sequential conversion of triphosgene with the aid of KF, first to fluorophosgene and finally by reaction with benzoyl bromide to TFBz.



Scheme 24: a) Ritter's Method for the direct synthesis of OCF_3-aryls using TAS-OCF_3. b) Hu's trifluoromethoxylation-halogenation of arynes using TFBz.[131-132]

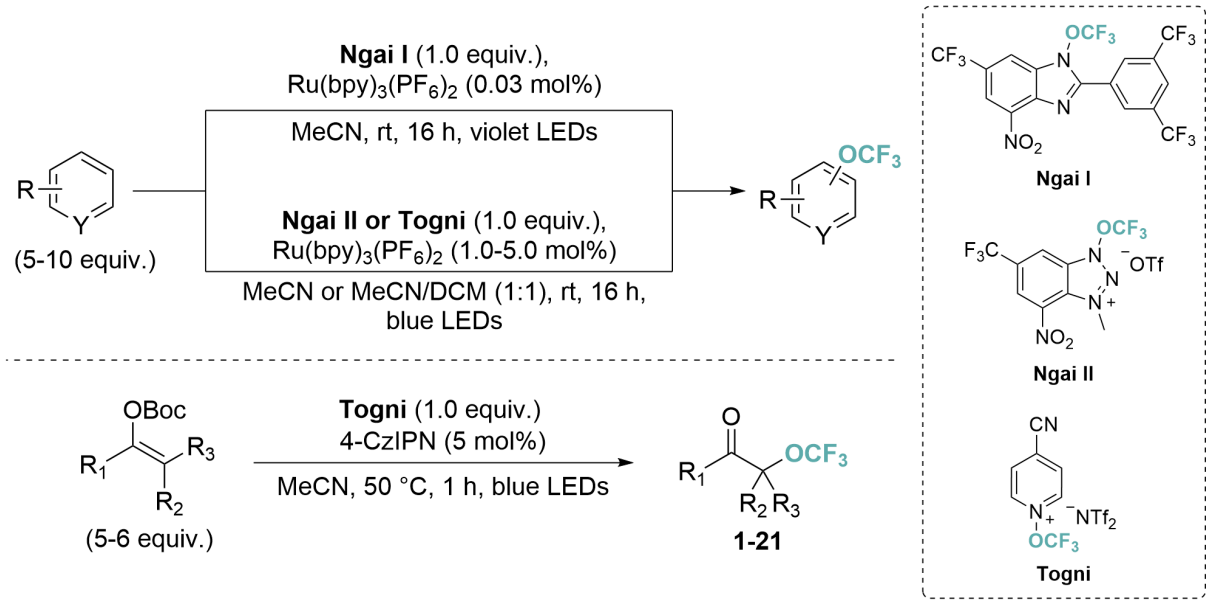
Even though trifluoromethoxylation can be achieved by nucleophilic routes, using numerous reagents, the majority of methods suffer from the inherent instability of $^{-}OCF_3$.[125] The anion is in equilibrium with difluorophosgene and fluoride, requiring either more equivalents of the reagent or an additive for stabilisation. As this increases the general price of the reaction and the amount of unwanted waste, new methods for radical trifluoromethoxylation are constantly being developed.

In the early developmental stages of radical trifluoromethoxylation reagents, mainly reactive gases such as trifluoromethyl hypofluorite or chloride (CF_3OF or CF_3OCl) were used. With these reagents, the direct addition of OCF_3 species to alkenes is realised, usually under thermal activation or through electron-poor double bonds within the starting material (Scheme 25).[133] Bis(trifluoromethyl)trioxide ($CF_3O_3CF_3$) is also suitable for this type of transformation.[134] The main products of these addition reactions are simple trifluoromethoxylated alkanes, although side products that are ditrifluoromethoxylated or dimerised have also been observed. Another interesting reaction, in this context, is the radical trifluoromethoxylation of (hetero)aromatic systems. This was achieved in 2012, by Venturini *et al.*, when CF_3OF was reacted with benzene.[135] Another study describes the synthesis of substituted 5-(trifluoromethoxy)thiophenes **1-20** by reaction with bis(trifluoromethyl)peroxide (BTMP) under thermal conditions.[136] However, the range of reactions is limited by the harsh conditions, and attempts at photochemical activation of CF_3OF, for example, have resulted in explosions.[137] Consequently, efforts have been made to provide new radical reagents that can be activated under mild conditions.



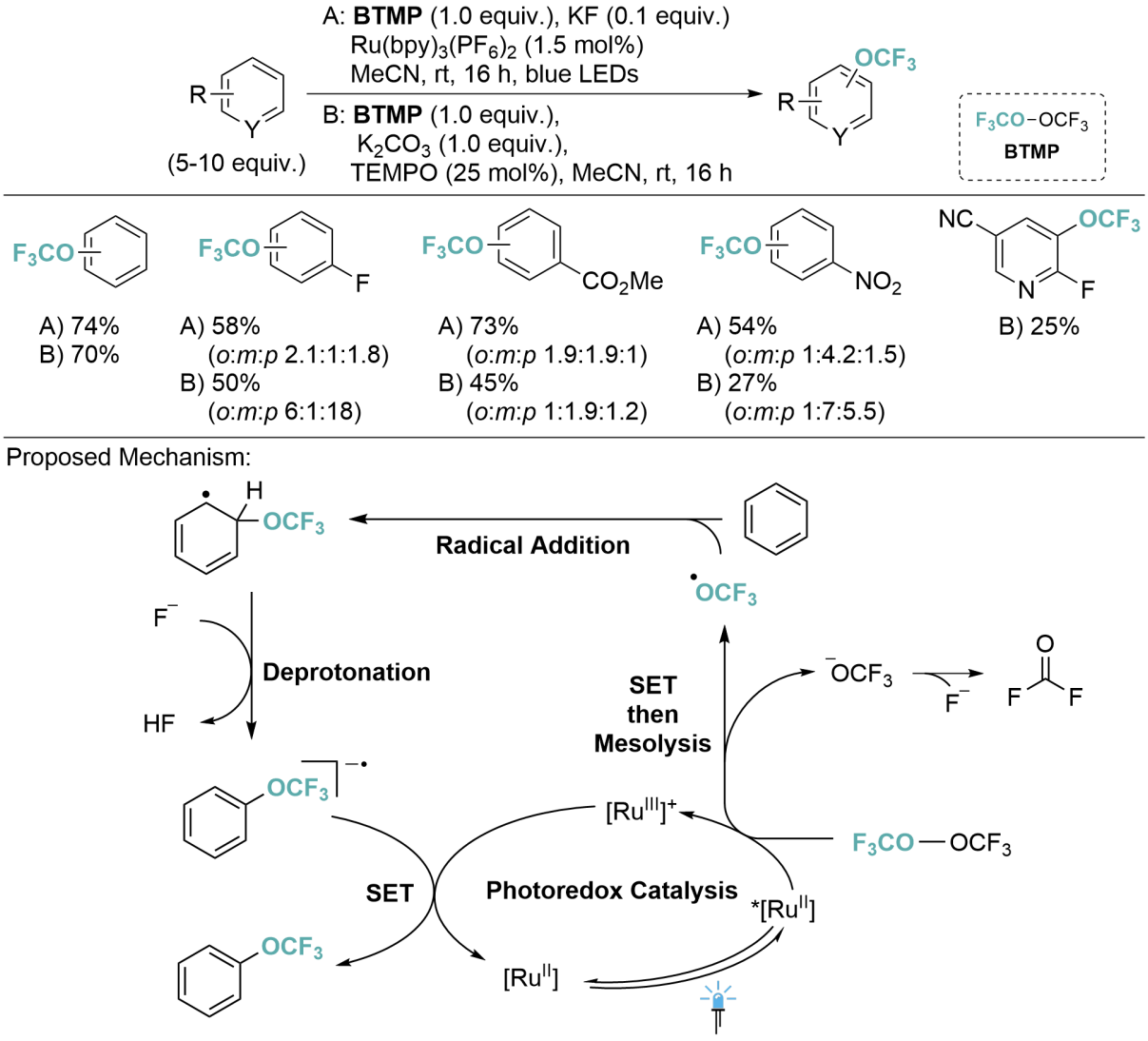
Scheme 25: Applications of Y-OCF_3 reagents for the trifluoromethoxylation of aromatics and alkenes.

In 2018, the Ngai group presented two new reagents that release OCF_3 radicals by N–O bond cleavage under photoredox conditions (Scheme 26).[138] These reagents were used for the direct trifluoromethoxylation of a wide range of (hetero)aromatic compounds. In the same year, Togni's group presented a method for aromatic trifluoromethoxylation using a pyridine-based reagent under photoredox conditions.[139] In a study from 2021, the groups of Dell Amico, Dagousset and Magnier also succeeded in using the Togni-OCF_3 reagent for the radical trifluoromethoxylation of enols to synthesise α-OCF_3 ketones **1-21**.[140] However, all of these methods use reagents with a large backbone that must be removed, creating a significant amount of waste. Additionally, they are made over several steps and from the comparatively expensive Togni-CF_3 reagent.[138-139]



Scheme 26: Applications of Ngai's and Togni's radical OCF_3 reagents.

To circumvent this problem, in 2020, the groups of Hopkinson and Riedel presented a comparatively atom economic method in which BTMP can be activated, either under photoredox conditions or with the help of the stable radical 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO). Within their work the transfer of OCF_3 radicals to (hetero)aromatic systems is presented and the scope of the reaction shows a good reactivity of BTMP with yields similar to other radical trifluoromethoxylation reagents (Scheme 27, top).[141] According to the proposed mechanism of the photoredox catalysed method, the reagent forms OCF_3 radicals through the mesolysis of activated BTMP, resulting in a quickly decomposing OCF_3 anion and the desired OCF_3 radical (Scheme 27, bottom). The $^{\bullet}OCF_3$ can add to the aromatic ring and form an aryl-OCF_3 radical anion upon deprotonation. Finally, the product is formed via a SET of the radical anion with a $[Ru^{III}]^+$ species.

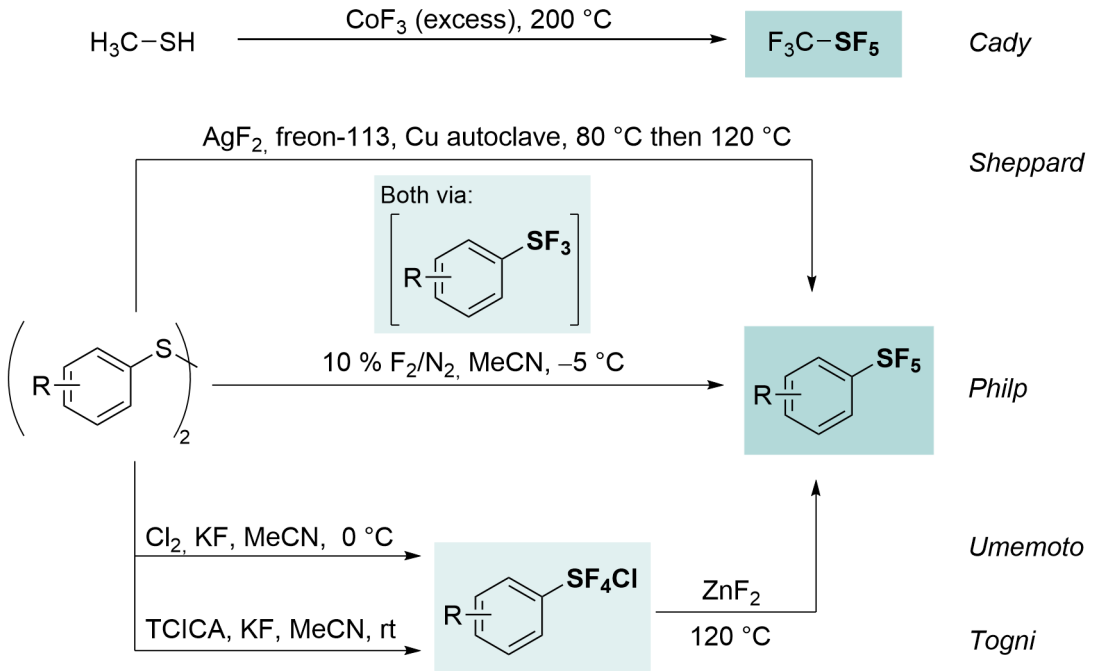


Scheme 27: Photoredox and TEMPO-catalysed trifluoromethoxylation of (hetero)arenes using BTMP as the radical OCF_3 source (top) and the proposed mechanism for the [Ru]-catalysed reaction.

1.6 The Pentafluorosulphanyl Group (SF_5)

Within the broad selection of fluorinated motifs, the pentafluorosulphanyl group is a particularly underrepresented and underexplored one. With a Hammett parameter of 0.68 and a lipophilicity value of 1.23, it ranks higher than the widely used trifluoromethyl group (see *Chapter 1.1*, Table 1).[11] Due to these and other interesting properties such as its thermal, chemical and physiological stability, it has been discussed as a potential bioisostere of CF_3, ^{t}Bu, NO_2 and halogens.[142] For example, by replacing the CF_3 group in Trifluralin with SF_5, the activity of the pesticide against quack grass and crabgrass can be increased fivefold.[143] Aside from agrochemical applications,[144] the SF_5 group can also be found in pharmaceutical research, functional materials and liquid crystals.[142b, 145] Despite their special properties and wide range of applications, there are still only a few methods for installing the SF_5 group onto molecules and a large number of pentafluorosulphanyl compounds are synthesised via SF_5 building blocks.

Considering the *de novo* approaches to SF_5 synthesis, the group can be formed from thiols or disulphides by oxidative fluorination or via the formation of SF_4Cl intermediates. This enables the synthesis of aromatic SF_5 compounds in particular, but can also be used for aliphatic compounds (Scheme 28). The first known synthesis of an organic SF_5 compound was published in 1950 by Cady. Traces of trifluoromethyl sulphur pentafluoride were obtained by the reaction of methanethiol with an excess of cobalt(III) fluoride at 200 °C.[146] With the aim of also generating aromatic SF_5 compounds, Sheppard's group developed a method based on silver(II) fluoride as the fluorinating agent. Thus, in the 1960s, he converted disulphides into aryl SF_5 compounds via SF_3 intermediates for the first time.[142a, 147] However, this method is unprofitable for industrial application due to low yields. A one-step synthesis using fluorine gas, also starting from disulphides, was presented 40 years later by the Philp group and is still used in the chemical industry today.[148] In order to circumvent the use of fluorine gas, Umemoto *et al.* introduced a two-step synthetic route via semi-stable SF_4Cl intermediates.[149] The method is based on the use of chlorine gas and KF to build up the SF_4Cl species, which is then reacted with zinc(II) fluoride to form the SF_5 compound. In 2019, Togni's group replaced the chlorine gas with inexpensive and less reactive TCICA, thus enabling gas-free access to SF_5 (hetero)aromatics.[81] Shibata's group then further developed this method to simplify the access to heteroaromatic systems.[150]



Scheme 28: *De novo* and indirect methods for the synthesis of aliphatic and aromatic pentafluorosulphanyl compounds.

The limitations in available methods and reagents are similar when looking at direct pentafluorosulphanylation. In general, there are four SF_5 group transfer reagents: Disulphur decafluoride (S_2F_{10}), sulphur chloride pentafluoride (SF_5Cl), sulphur bromide pentafluoride (SF_5Br) and sulphur hexafluoride (SF_6). The synthetic routes for preparing these highly reactive to inert reagents are diverse (Figure 11).

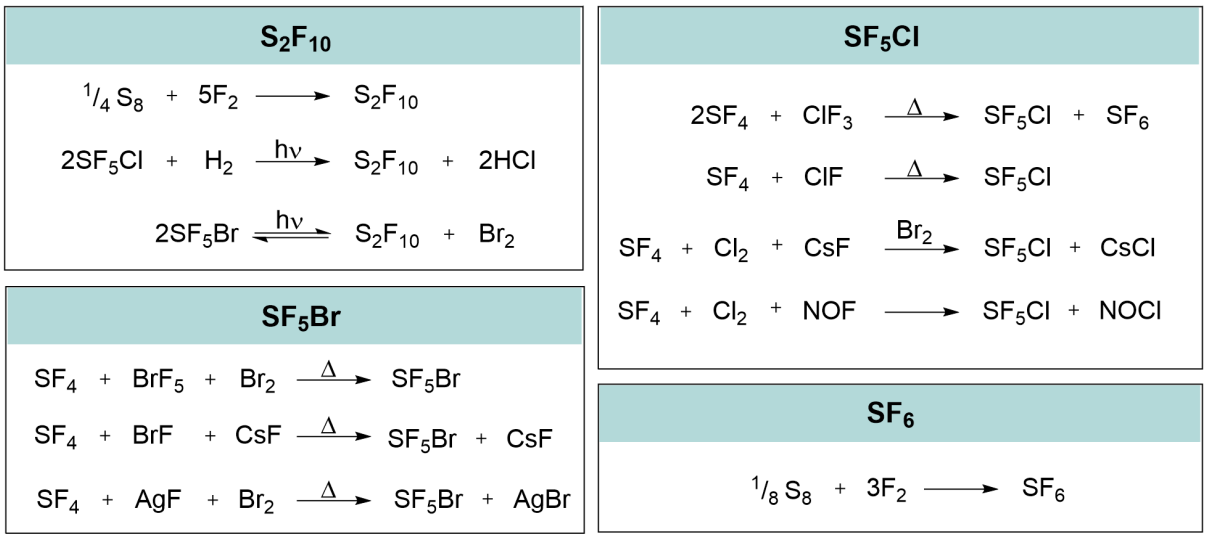
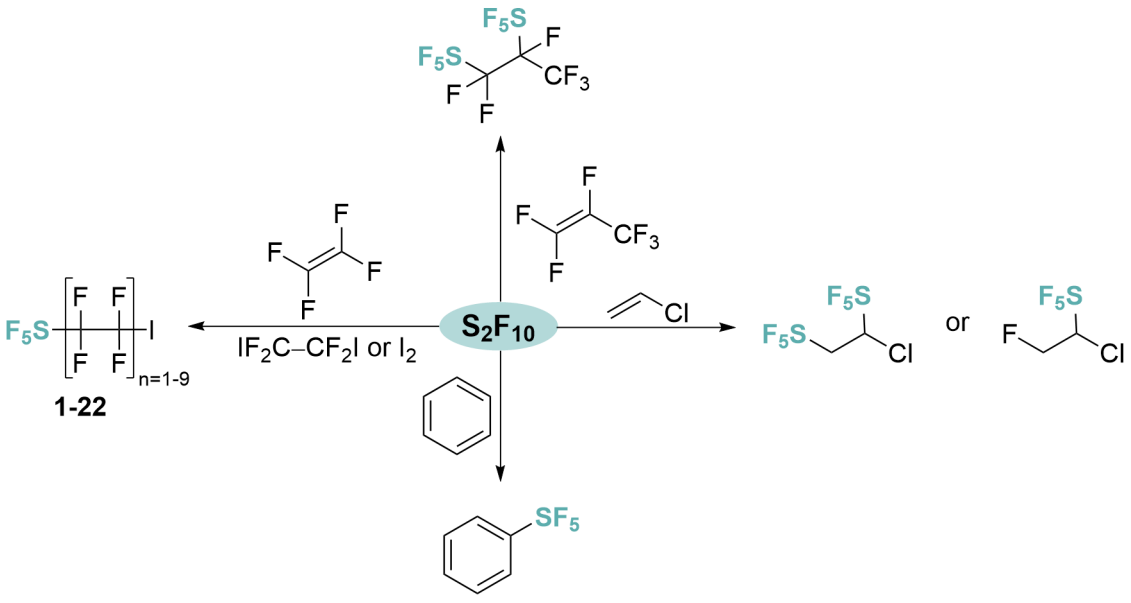


Figure 11: Overview of direct pentafluorosulphanylation reagents and their synthesis.

S_2F_{10} was first synthesised in 1934[151] as a side product during the preparation of SF_6 from elemental sulphur and fluorine gas, a process that was invented in 1930 and is still used for the synthesis of SF_6.[152] Alternatively, S_2F_{10} can be formed by photochemical reduction of

SF_5Cl with hydrogen or by reversible photodecomposition of SF_5Br.[153] Both routes require SF_5X species, which can be synthesised starting from SF_4 in combination with various fluorination and halogenation reagents. For the synthesis of SF_5Br, bromine pentafluoride (BrF_5) or silver(I) fluoride with bromine and SF_4 can be used at elevated temperatures.[80c, 154] Alternatively, the groups of Christe and Seppelt presented a method based on bromine monofluoride (BrF) with caesium fluoride (CsF) and SF_4, which was further developed by Winter *et al*.[155] SF_5Cl can be obtained in a similar way via the reaction of SF_4 with chlorine trifluoride (ClF_3) or chlorine monofluoride (ClF).[156] Alternatively, SF_4 can also be reacted with chlorine gas and caesium(I) fluoride (under bromine catalysis) or nitrosyl fluoride (NOF) to synthesise SF_5Cl.[154, 157]

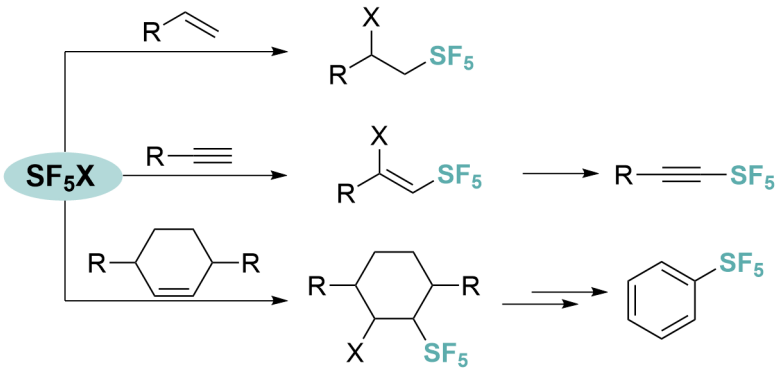
Applications of the aforementioned reagents are mainly limited to the pentafluorosulphanylation of multiple bonds. S_2F_{10}, for example, can mono- and dipentafluorosulphanylate vinyl halides and perfluorinated propene (Scheme 29).[153a, 158] Another study described the synthesis of SF_5-telomers **1-22** starting from perfluoroethene and fluoroalkyl iodides.[159] A very unique reactivity of S_2F_{10}, for example, is the direct pentafluorosulphanylation of benzene.[153a] However, due to its immense toxicity and inertness within chemical reactions, S_2F_{10} has not been further investigated as a pentafluorosulphanylation reagent and, until recently, the focus of SF_5 transfer reagents has been primarily on SF_5X reagents.



Scheme 29: Synthetic applications of S_2F_{10} for the pentafluorosulphanylation of organic molecules.

SF_5Br and SF_5Cl are also suitable reagents for the insertion of SF_5 groups into multiple-bond systems (Scheme 30). The reagents can be activated thermally, photochemically, or chemically, and the reaction mechanism in most cases involves radical processes. However, methods based on thermal activation are limited to simple alkenes and alkynes. This can be

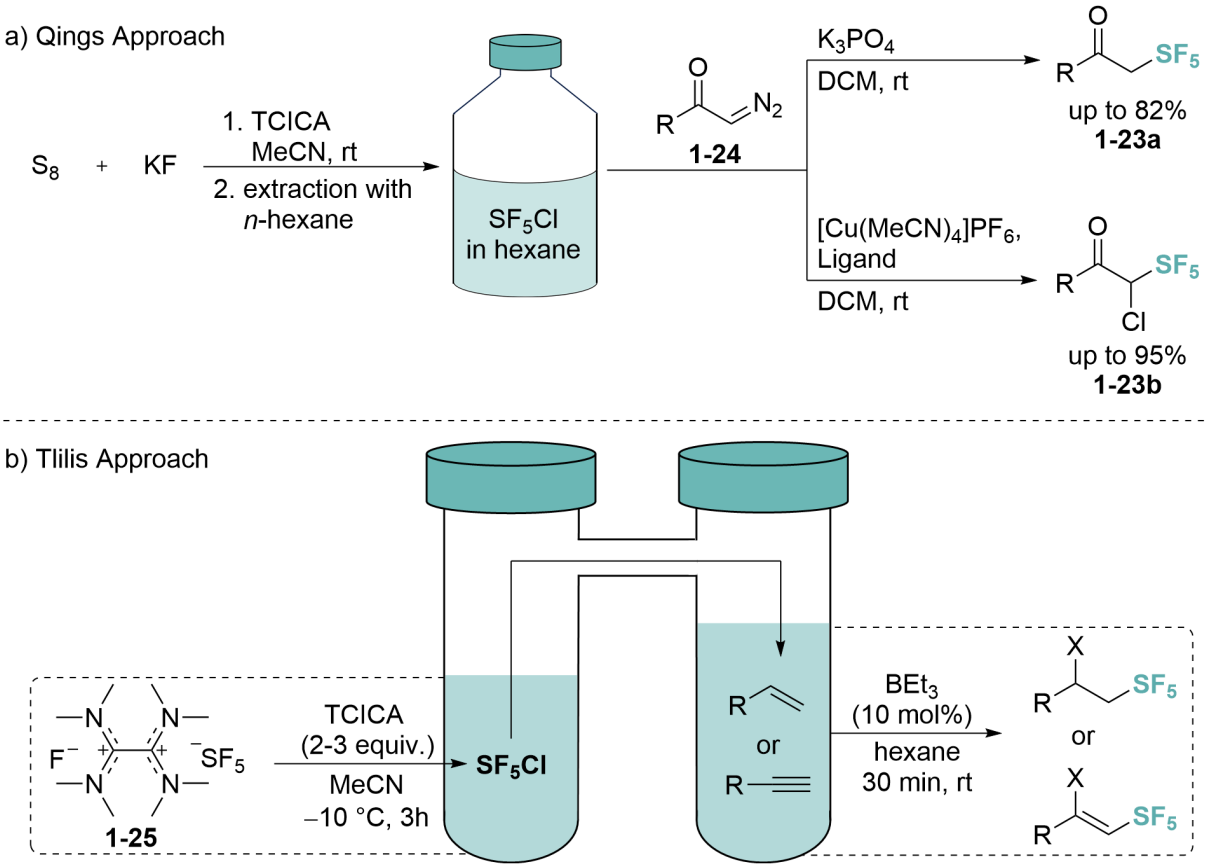
attributed to the harsh reaction conditions, which also influence the selectivity and yields of the methods. For example, cyclohexene can be reacted with SF_5Cl, whereby both the fluoro- and the SF_5-addition product can be observed in a ratio of 73:27, respectively.[160] Such side products are mainly observed for the more reactive SF_5Br and could be explained by the polarised S–X bond. Heterolytic cleavage of the reagents leads to the formation of the SF_5 anion, which decomposes rapidly into SF_4 and fluoride ions.[161] To avoid lower yields for thermal addition reactions, longer reaction times can be used. According to a protocol by Winter *et al.*, electron-deficient acrylates can be converted into the corresponding pentafluorosulphanyl products in good yields with reaction times of 15-22 h using SF_5Br.[162]
The different reactivities of SF_5Cl and SF_5Br can also be observed in the thermal pentafluorosulphanylation of alkynes. The reaction of acetylene with SF_5Cl, according to Hoover, gives the SF_5 alkene in 40% yield, whereas the work by Shreeve describes a yield of 80% for the same reaction but with SF_5Br.[163]



Scheme 30: General addition reactions of SF_5X (X = Cl or Br) reagents to alkenes and alkynes and follow-up chemistry products.

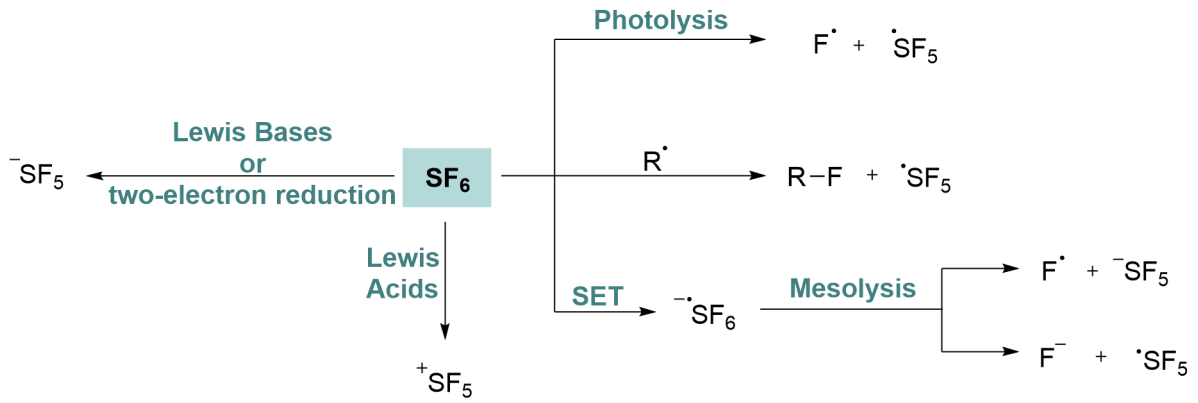
Photochemical and chemical activation generally enables a broader scope, as the reaction conditions are comparatively milder. For example, according to a method developed by Brel, high yields can be obtained for the pentafluorosulphanylation of various activated alkenes with SF_5Cl at ambient temperatures and in a considerably shorter time.[164] However, the Dolbier method, which is based on the chemical activation of SF_5X reagents by triethylborane (BEt_3), represents a major breakthrough in the direct pentafluorosulphanylation of multiple bond systems.[165] After its publication, the method was used and modified in various other works.[166] In general, the addition of SF_5X to multiple bond systems plays a major role in providing building blocks for the synthesis of more complex SF_5 compounds, such as (hetero)aromatics or complex aliphatic products.[161, 167] However, the strong reactivity and toxicity of these SF_5 reagents and their decomposition products led to efforts to improve their handling or to replace them completely. In 2021, Qing's group succeeded in making SF_5Cl accessible as a solution in hexane (Scheme 31a). This was achieved by reacting sulphur with KF and TCICA in acetonitrile. The resulting mixture was extracted with hexane and used for the synthesis of

α-SF_5 ketones **1-23**, starting from diazo compounds **1-24**.[168] Another approach, by Tlili and co-workers, utilises a two-chamber reactor method in which SF_5Cl is generated in chamber one, by reacting the tetrakis(dimethylamino)ethylene (TDAE) salt **1-25** with TCICA and transferred to chamber two to react with various alkenes and alkynes (Scheme 31b).[169]



Scheme 31: Improved access to SF_5Cl via a) a stock solution and b) the two-chamber reactor approach for the pentafluorosulphanylation of organic molecules.[169-170]

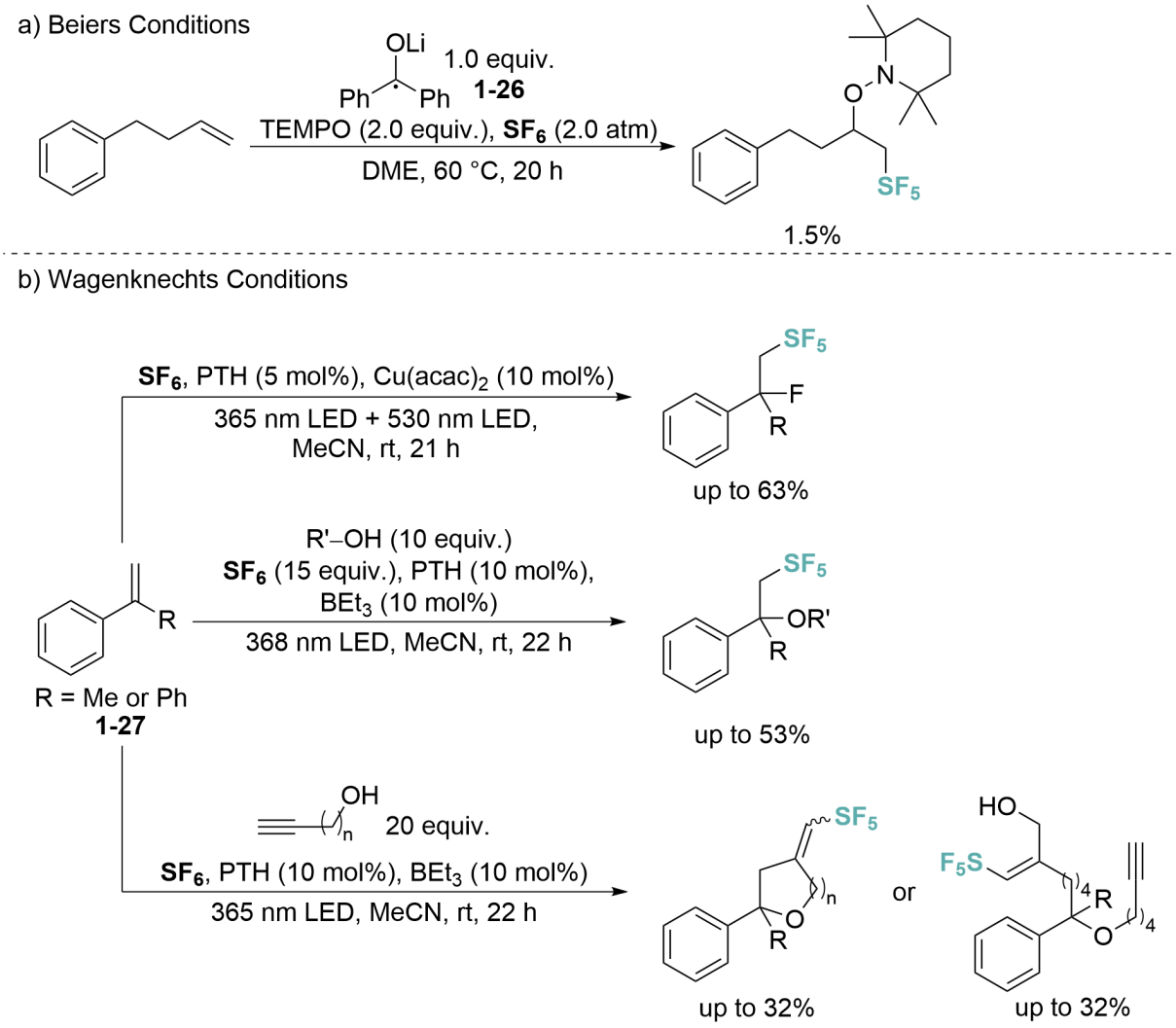
In recent years, sulphur hexafluoride has been investigated as an alternative to the toxic and highly reactive reagents SF_5X and S_2F_{10}. The reagent is non-flammable, non-toxic and inert to almost all chemical reagents, which makes it very easy to handle from a safety perspective.[171] The potent greenhouse gas is used in large quantities in industry as an insulator, therefore it would be desirable to break down the compound into useful organic substances. However, its inertness makes it a challenging candidate for the use as a group transfer reagent. The activation of SF_6 has been intensively studied over the last decades, but the results show a very limited repertoire of activation methods for pentafluorosulphanylations.[172] Activation of SF_6 with Lewis bases or by two-electron reduction has been reported to yield SF_5 anions, but the pentafluorosulfanide salts formed in these conversions are not suitable for pentafluorosulphanylations (Scheme 32).[173]



Scheme 32: Overview of possible methods for SF_6 activation.

Another conceivable approach for SF_6 activation towards SF_5 groups is the abstraction of a fluoride anion via fluorophilic Lewis acids, which leads to a potentially very unstable SF_5 cation and has therefore not yet been realised.[174] The most promising approach for this type of conversion is the formation of SF_5 radicals from SF_6 by photolysis, radical chain processes or single electron reduction. However, various studies have shown that photodissociation is not possible at wavelengths of longer than 160 nm and that activating SF_6 with radicals or radical initiators only leads to the decomposition of the gas.[175]

In 2018, the groups of Beier and Wagenknecht succeeded for the first time in activating and utilising SF_6 for the synthesis of SF_5 compounds by means of one-electron reduction.[174, 176] In Beier's work, SF_6 was activated with 2,2,6,6-tetramethylpiperidinyloxyl lithium (TEMPOLi), which was formed *in situ* via the reaction of lithium benzophenone ketyl **1-26** with TEMPO. However, the reaction of TEMPOLi with an alkene and SF_6 only led to the formation of the SF_5 compound in very low yield (Scheme 33a).[174] In contrast, the Wagenknecht method uses the photoredox catalyst *N*-phenylphenothiazine (PTH) in combination with LEDs, at 365 nm and 525 nm, for the activation and mesolysis of SF_6 to the SF_5 radical and a fluoride ion. With this protocol, the pentafluorosulphanylation and simultaneous fluorination of *α*-methyl and *α*-phenylstyrene (**1-27**) was achieved (Scheme 33b).[176] In later work, the method was developed further and *β*-SF_5-substituted ethers were made accessible by adding alcohols.[177] If increased equivalents of alkynols are used for the transformation, SF_5-substituted cyclic ethers can also be synthesised.[178] The work described opens up a completely new area of investigation for direct pentafluorosulphanylation, but its scope is still very limited, meaning additional efforts are required to develop this area further.

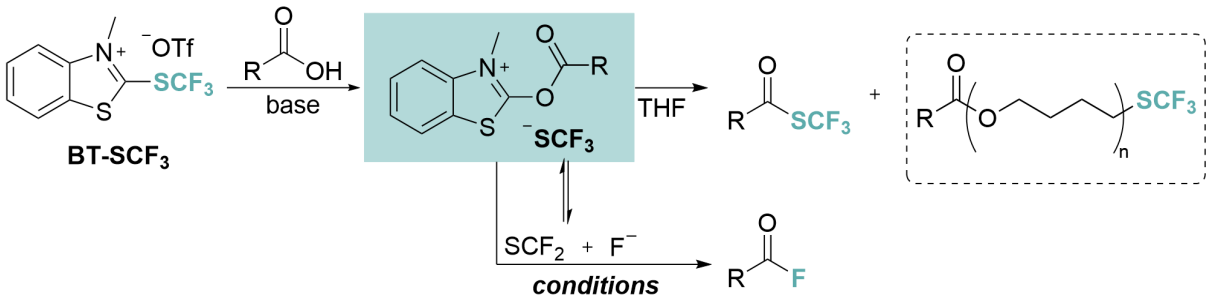


Scheme 33: Synthetic applications of SF_6 for the pentafluorosulphanylation of organic molecules using a) Beier's approach and b) using Wagenknecht's conditions.

2 Objective

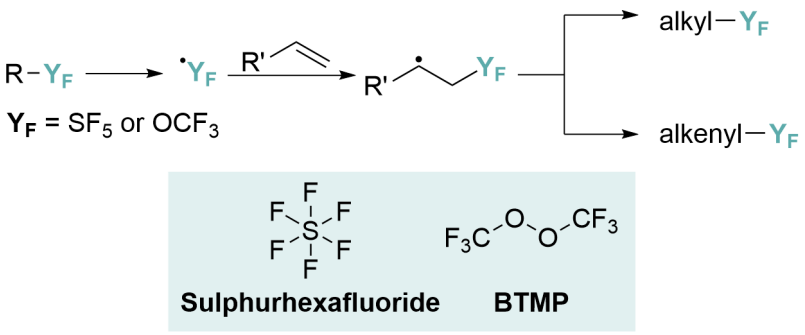
The importance of fluorinated compounds in almost all areas of life is undisputed and in recent years there has been a positive trend towards the extended use of these compounds, particularly in the pharmaceutical, agrochemical and materials science sectors. Nevertheless, heteroatomic fluorinated groups are still underrepresented in these fields, which could be attributed, for example, to their more difficult synthetic access. In addition, the current debate on the PFAS problem results in a high demand for new discoveries and methods for the use of less environmentally persistent fluorinated groups. In this work, new ways of synthesising fluorinated compounds should be investigated, with a general focus on the heteroatomic fluorinated groups SCF_3, OCF_3 and SF_5 due to their exceptional properties. The methods should be based on both nucleophilic and radical reagents and the trends and limits, mechanistic features and possible extensions of the application of existing reagents should be evaluated.

The nucleophilic group transfer reagent BT-SCF_3 and related reagents already show good reactivity with alcohols and carboxylic acids. Within the work, the observed side reactions associated with the trifluoromethylthiolation of carboxylic acids were aimed to be investigated in further detail and tested for potential applications within organofluorine chemistry (Scheme 34). In addition, the properties of the BT-reagents as Lewis acids and potential fluorination reagents were to be analysed.



Scheme 34: The reaction of BT-SCF_3 and carboxylates resulting in an activated intermediate offering multiple reactivities towards fluorinated and trifluoromethylthiolated compounds.

Since nucleophilic reagents often suffer from the inherent instability of the released fluorinated anions, the work should also address the use of radical reagents for the synthesis of novel and underrepresented fluorinated compounds. Here, SF_6 and BTMP were envisioned as atom-economical and industrially attractive group transfer reagents. The work aimed to investigate the use of these reagents for the synthesis of pentafluorosulphanylated and trifluoromethoxylated alkyl and alkenyl compounds starting from alkenes and other multiple bond systems (Scheme 35).



Scheme 35: Sulphurhexafluoride and BTMP as radical reagents for the transfer of SF_5 and OCF_3 groups onto alkenes for the generation of pentafluorosulphanylated and trifluoromethoxylated alkyl and alkenyl compounds.

In addition to their application in the medical and agrochemical fields, fluorinated compounds are increasingly utilised as important building blocks in synthetic chemistry, causing a growing interest in C-F activation methods. The work should investigate the reaction of *α*-fluoroacetophenones with different reaction partners under photocatalytic conditions. Based on preliminary work by Dr. Stefan Dix and Dr. Matthew Hopkinson the reaction of different silylated starting materials with *α*-fluoroacetophenones should be investigated. The silyl-residue might support the F-abstraction and the resulting methods could provide new access to non-fluorinated difunctionalised compounds (Scheme 36).

Scheme 36: Photoredox catalytic and silicon-assisted C-F activation of *α*-fluoroacetophenones towards defluorinative C–X bond formations.

3 Publications

3.1 Activation of Tetrahydrofuran with 2-((Fluoroalkyl)thio)Benzothiazolium Reagents

Lilian Maria Maas, Jonas Rachid Schmid, Carlo Fasting, Patrick Voßnacker, Andreas Mavroskoufis, Matthew N. Hopkinson*

Tetrahedron **2021**, *101*, 132512.

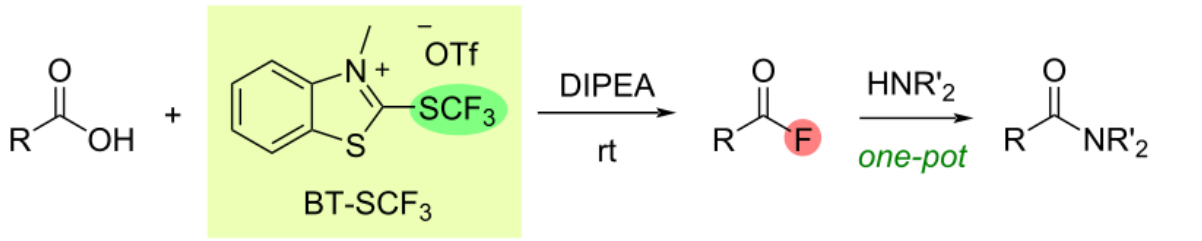
https://doi.org/10.1016/j.tet.2021.132512

(Part of the article collection “Fluorine and Chalcogens”; Guest Editors: E. Magnier & G. Dagousset).

Author Contributions

Lilian Maria Maas designed and managed the project, performed the experiments throughout the optimisation process and the scope and wrote the manuscript. Jonas Rachid Schmid performed all quantum chemical calculations and assisted with the manuscript preparation. Carlo Fasting performed all isolations via preparative HPLC. Patrick Voßnacker performed the XRD measurements. Andreas Mavroskoufis assisted with the interpretation of quantum chemical results. Matthew Hopkinson assisted with the management of the project and revised the manuscript.

3.2 Direct Synthesis of Acyl Fluorides from Carboxylic Acids using Benzothiazolium Reagents



✚ practical conditions ✚ stoichiometric BT-SCF_3 not required ✚ peptide coupling

Lilian M. Maas,‡ Alexander Haswell,‡ Rory Hughes, Matthew N. Hopkinson*

Beilstein J. Org. Chem. **2024**, *20*, 921–930.

https://doi.org/10.3762/bjoc.20.82

(Part of the thematic issue "Organofluorine chemistry VI". Guest Editor: D. O'Hagan)

Author Contributions

Lilian Maria Maas designed and managed the project, performed a major part of the optimisation and experiments for the amide-scope and wrote the manuscript. Alexander Haswell performed the optimisation experiments, a major part of the acyl fluoride scope, some experiments for the amide scope and assisted with the manuscript preparation. Rory Hughes investigated and performed experiments on the amino acid couplings and the side products **6** and **7** (see manuscript). Matthew Hopkinson assisted with the management of the project and revised the manuscript.

BEILSTEIN JOURNAL OF ORGANIC CHEMISTRY

Direct synthesis of acyl fluorides from carboxylic acids using benzothiazolium reagents

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Full Research Paper

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Keywords:
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Abstract

2-(Trifluoromethylthio)benzothiazolium triflate (BT-SCF_3) was used as deoxyfluorinating reagent for the synthesis of versatile acyl fluorides directly from the corresponding carboxylic acids. These acyl fluorides were reacted with amines in a one-pot protocol to form different amides, including dipeptides, under mild and operationally simple conditions in high yields. Mechanistic studies suggest that BT-SCF_3 can generate acyl fluorides from carboxylic acids via two distinct pathways, which allows the deoxyfluorinating reagent to be employed in sub-stoichiometric amounts.

Introduction

Acyl fluorides are attracting much attention as versatile reagents for different applications in organic synthesis. In addition to their use as sources of fluoride ions, they are most commonly employed as acylation reagents [1-3]. The strong C–F bond makes acyl fluorides relatively stable towards hydrolysis and easier to handle than other acyl halides [4-8]. Their reactions with nucleophiles are typically less violent than for the corresponding acyl chlorides with acyl fluorides exhibiting comparable electrophilicity to activated esters; however, with considerably fewer steric restrictions [9,10]. Acylations with acyl fluorides also typically proceed with fewer side-reactions while derivatives bearing an α-stereocentre generally undergo little racemisation [11,12]. The combination of all these properties mean that acyl fluorides can provide significant advantages over acyl chlorides, especially for challenging acylation reactions [13,14].

Nevertheless, acyl chlorides still dominate in the literature; however, the recent development of safer and more practical synthetic routes to acyl fluorides are inspiring greater interest in these compounds. Various synthetic approaches have been investigated with two main strategies being pursued: fluorine-transfer to acyl radicals and nucleophilic fluorination of acyl electrophiles [15]. The latter approach is the most intensively

studied due to the easy accessibility of fluoride ions with many methods directly employing the parent carboxylic acid as substrate. These processes avoid an additional pre-functionalisation step and have been reported using a range of deoxyfluorinating reagents including (diethylamino)sulfur trifluoride (DAST) [16-18], bis(2-methoxyethyl)aminosulfur trifluoride (Deoxo-Fluor®) [10,19,20], (diethylamino)difluorosulfonium tetrafluoroborate (XtalFluor-E®) [21-24], $(Me_4N)SCF_3$ [9,25], pentafluoropyridine (PFP) [26] and cyanuric fluoride [27,28] among others [15].

Since 2019, our group has developed a series of 2-(fluoroalkylthio)benzothiazolium (BT-SR_F) reagents for the deoxygenative transfer of SR_F (R_F = poly- or perfluoroalkyl) groups into organic molecules (Figure 1). In an initial report, the trifluoromethylthio-containing salt, BT-SCF_3, was reacted with unactivated aliphatic alcohols to afford (trifluoromethyl)thioethers, while subsequent work focused on the direct deoxygenative synthesis of fluorinated thioesters from carboxylic acids [29-31]. In each case, the reactions proceeded smoothly under operationally simple conditions while BT-SCF_3 and related BT-SR_F reagents are easy-to-handle solids that can be readily produced on a multigram scale from relatively inexpensive starting materials. During the optimisation studies for the latter process with carboxylic acid substrates, in addition to the desired (trifluoromethyl)thioester products, small amounts of the corresponding acyl fluorides were also observed as by-products. Given the increasing interest in acyl fluorides in organic synthesis and the attractive features of BT-SR_F salts as reagents for organofluorine chemistry, we considered whether optimisation of the reaction conditions could allow for the selective synthesis of acyl fluoride products directly from carboxylic acids. Here, we report the results of this study, which led to the development of a practical and high yielding methodology for the synthesis of acyl fluorides and their subsequent one-pot conversion into amides. Moreover, by virtue of BT-SCF_3's ability to deliver acyl fluorides via two distinct deoxyfluorination pathways, an efficient process could be achieved using only substoichiometric amounts of the fluorinating reagent.

Results and Discussion

In an initial test reaction, 4-methylbenzoic acid (**1a**) was reacted with 1.25 equiv of BT-SCF_3 and 2.0 equiv of NaH in DCM under conditions similar to our previous reports on the deoxygenative trifluoromethylthiolation of carboxylic acids [31]. ^{19}F NMR analysis of the crude reaction mixture after 2 h at rt

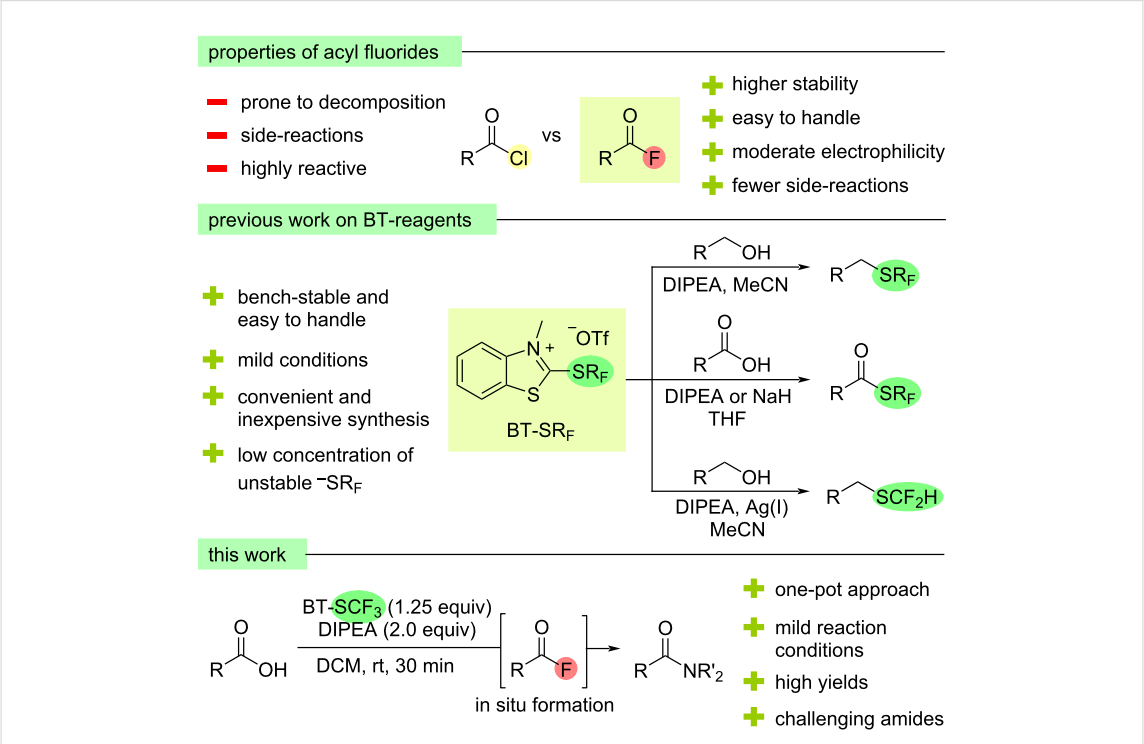
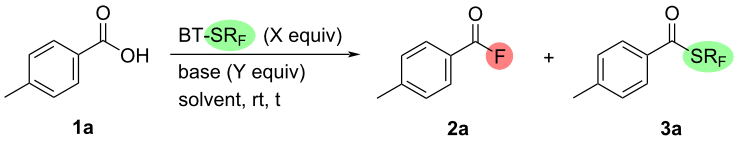


Figure 1: Advantages of acyl fluorides compared to acyl chlorides, previous work on BT-SR_F reagents [29-33] and a summary of this work on the BT-SCF_3-mediated in situ formation of acyl fluorides and their use for the synthesis of amides.

revealed no conversion towards the desired acyl fluoride product **2a**, however, 30% of thioester **3a** was formed (internal standard: $PhCF_3$, Table 1, entry 1). Pleasingly, changing the base to K_2CO_3 led to the formation of **2a** in 7% ^{19}F NMR yield (Table 1, entry 2), while the selectivity of the reaction could be switched significantly upon employing organic amine bases (Table 1, entries 3 and 4). Using 2.0 equiv of diisopropylethylamine (DIPEA), **2a** could be obtained in quantitative ^{19}F NMR yield although a reduction to 1.5 equiv led to a significant drop in efficiency, delivering the acyl fluoride in only 30% ^{19}F NMR yield together with 45% of thioester **3a** (Table 1, entries 4 and 5). At this stage, we were interested in the reactivity of other BT-SR_F reagents developed in our group and tested three longer-chain derivatives under deoxyfluorination conditions. Employing BT-SC_4F_9 and BT-SC_8F_{17}, ^{19}F NMR yields of **2a** of 84% and 81% were achieved (Table 1, entries 6 and 7), however, BT-$SCF(CF_3)_2$, which features a branched perfluoroalkyl chain, gave a comparatively moderate ^{19}F NMR yield of 67% (Table 1, entry 8). BT-SCF_3 still led to the highest ^{19}F NMR yield of **2a** among all the tested reagents and was therefore used throughout the subsequent optimisation and scope studies. An interesting observation was made upon varying the equivalents of BT-SCF_3. Rather than reducing the yield to 50% or lower, conducting the reaction with 0.5 equiv of BT-SCF_3 provided **2a** in 55% ^{19}F NMR yield, suggesting that each equivalent of the benzothiazolium reagent can deliver more than one equivalent of the acyl fluoride product (Table 1, entry 9). Although representing a considerable drop in efficiency compared to using 1.25 equiv of BT-SCF_3, this observation provides an interesting insight into the reaction mechanism (vide infra). Changing the solvent from DCM to THF or MeCN resulted in no significant change in the efficiency of the reaction, whereas a ^{19}F NMR yield of only 11% was achieved in DMF (Table 1, entries 10–12). Increasing the reaction concentration to 0.2 M in DCM led to a reduction in the ^{19}F NMR yield of **2a** to 74% (Table 1, entry 13). Finally, optimisation of the reaction time revealed the starting material was completely converted after only 30 min at rt (Table 1, entry 14).

With the optimised conditions in hand, the scope of the reaction was investigated to assess the practical utility of BT-SCF_3-mediated deoxyfluorination as a method for preparing diverse acyl fluorides. As shown in Scheme 1, the reaction showed excellent functional group tolerance with a range of aromatic carboxylic acids **1**, delivering the corresponding acyl fluorides **2** in very good ^{19}F NMR yields above 75% for all substrates tested. Both electron-withdrawing and electron-donating substituents were tolerated while substituents could be present at

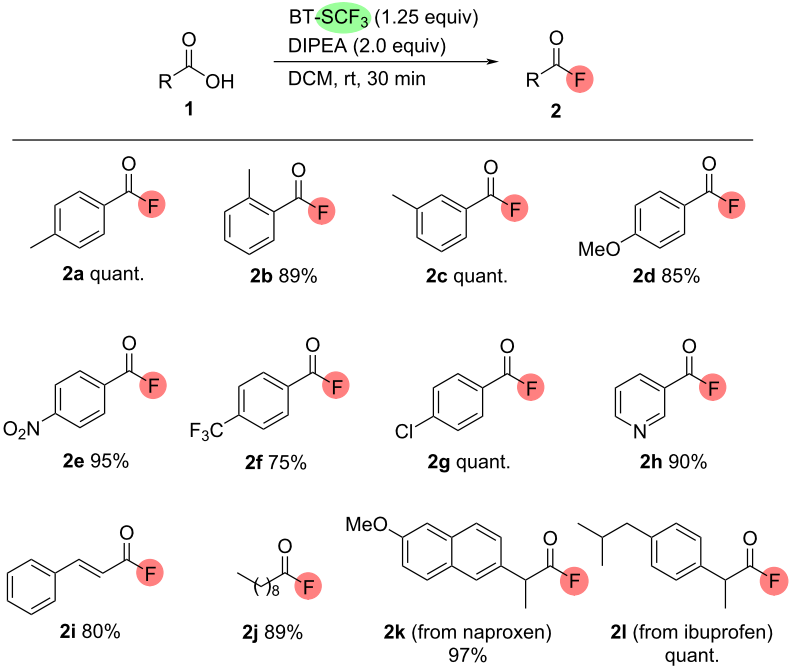
Table 1: Optimisation of the reaction conditions for the deoxygenative fluorination of 4-methylbenzoic acid using benzothiazolium reagents.



1a **2a** **3a**

Entry	R_F (X equiv)	Base (Y equiv)	Solvent (conc.)	*t* (h)	Yield **2a**[a]	Yield **3a**[a]
1	CF_3 (1.25)	NaH (2.0)	DCM (0.1 M)	2	–	30
2	CF_3 (1.25)	K_2CO_3 (2.0)	DCM (0.1 M)	2	7	37
3	CF_3 (1.25)	NEt_3 (2.0)	DCM (0.1 M)	2	96	traces
4	CF_3 (1.25)	DIPEA (2.0)	DCM (0.1 M)	2	quant.	–
5	CF_3 (1.25)	DIPEA (1.5)	DCM (0.1 M)	2	30	45
6	C_4F_9 (1.25)	DIPEA (2.0)	DCM (0.1 M)	2	84	–
7	C_8F_{17} (1.25)	DIPEA (2.0)	DCM (0.1 M)	2	81	–
8	$CF(CF_3)_2$ (1.25)	DIPEA (2.0)	DCM (0.1 M)	2	67	–
9	CF_3 (0.5)	DIPEA (2.0)	DCM (0.1 M)	2	55	–
10	CF_3 (1.25)	DIPEA (2.0)	DMF (0.1 M)	2	11	–
11	CF_3 (1.25)	DIPEA (2.0)	MeCN (0.1 M)	2	88	–
12	CF_3 (1.25)	DIPEA (2.0)	THF (0.1 M)	2	91	–
13	CF_3 (1.25)	DIPEA (2.0)	DCM (0.2 M)	2	74	–
14	CF_3 (1.25)	DIPEA (2.0)	DCM (0.1 M)	0.5	quant.	–

[a]As internal standard for ^{19}F NMR yields α,α,α-trifluorotoluene was used.

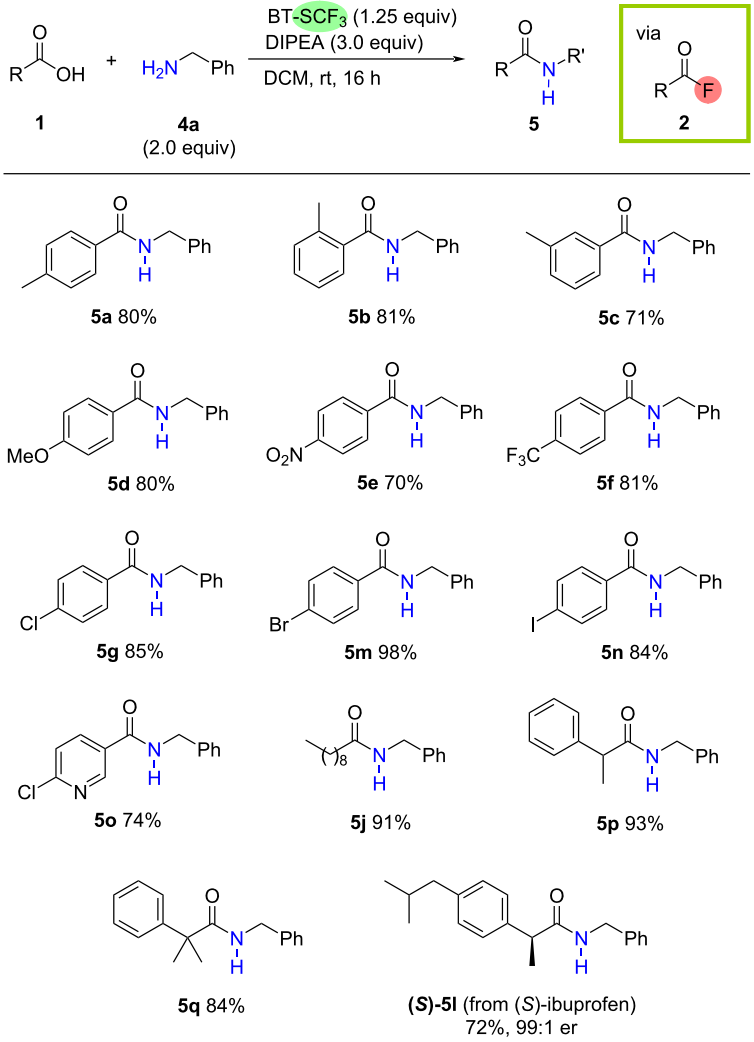


Scheme 1: Scope of the BT-SCF_3-mediated deoxygenative fluorination of carboxylic acids **1**. Reactions were performed on a 0.2 mmol scale. ^{19}F NMR yields using α,α,α-trifluorotoluene as the internal standard.

the *ortho*-, *meta*- or *para*-positions. The heteroaromatic acyl fluoride **2h** could be prepared efficiently while deoxyfluorination of representative olefinic and aliphatic carboxylic acids proceeded smoothly, affording cinnamoyl and decanoyl acyl fluorides **2i** and **2j** in 80% and 89% ^{19}F NMR yields, respectively. Furthermore, the widely available drug molecules naproxen and ibuprofen could be efficiently converted into their acyl fluoride derivatives **2k** and **2l** in 97% and quantitative yields, respectively.

To improve the practicality of the methodology and to avoid the often unreliable isolation of acyl fluoride intermediates, we next considered whether BT-SCF_3-mediated deoxyfluorination of carboxylic acids could be coupled with a subsequent acylation in an overall one-pot process. Selecting amines as nucleophilic coupling partners, a short optimisation study was carried out to identify suitable conditions compatible with the deoxyfluorination process. Pleasingly, adding 2.0 equiv of benzylamine (**4a**) to the standard reaction between 4-methylbenzoic acid (**1a**) and BT-SCF_3 (1.25 equiv) in DCM (0.1 M) and increasing the amount of DIPEA to 3.0 equiv allowed for the efficient formation of the desired amide **5a** after 16 h at rt, which could be isolated in 80% yield after column chromatography. A survey of carboxylic acids **1** revealed that the one-pot approach is efficient for a variety of substitution profiles (Scheme 2). Aromatic acids bearing methyl substituents at the *para*-, *ortho*- or *meta*-positions all reacted smoothly with **4a** to afford the corresponding benzylamides **5a–c** in very good isolated yields up to 81%. Electron-donating and -withdrawing groups at the *para*-position were well tolerated (**5d–f**), including halogen substituents that could serve as handles for follow-up functionalisation chemistry such as coupling reactions (**5g**, **5m**, **5n**). Heteroaromatic (**5o**) and aliphatic carboxylic acids (**5j**, **5p**, **5q**) also reacted smoothly under the optimised conditions. As demonstrated by the efficient formation of amide **5q** in 84% yield, the process is tolerant of significant steric bulk at the carboxyl α-position. Finally, to assess the influence of the reaction on the stereochemical integrity of chiral carboxylic acid substrates, the deoxyfluorination was performed on the enantiopure (*S*)-isomer of ibuprofen (er = 99:1). Pleasingly, efficient conversion to the corresponding amide (*S*)-**5l** was observed (yield = 72%) with analysis by chiral HPLC revealing no erosion of the enantiomeric ratio (er = 99:1).

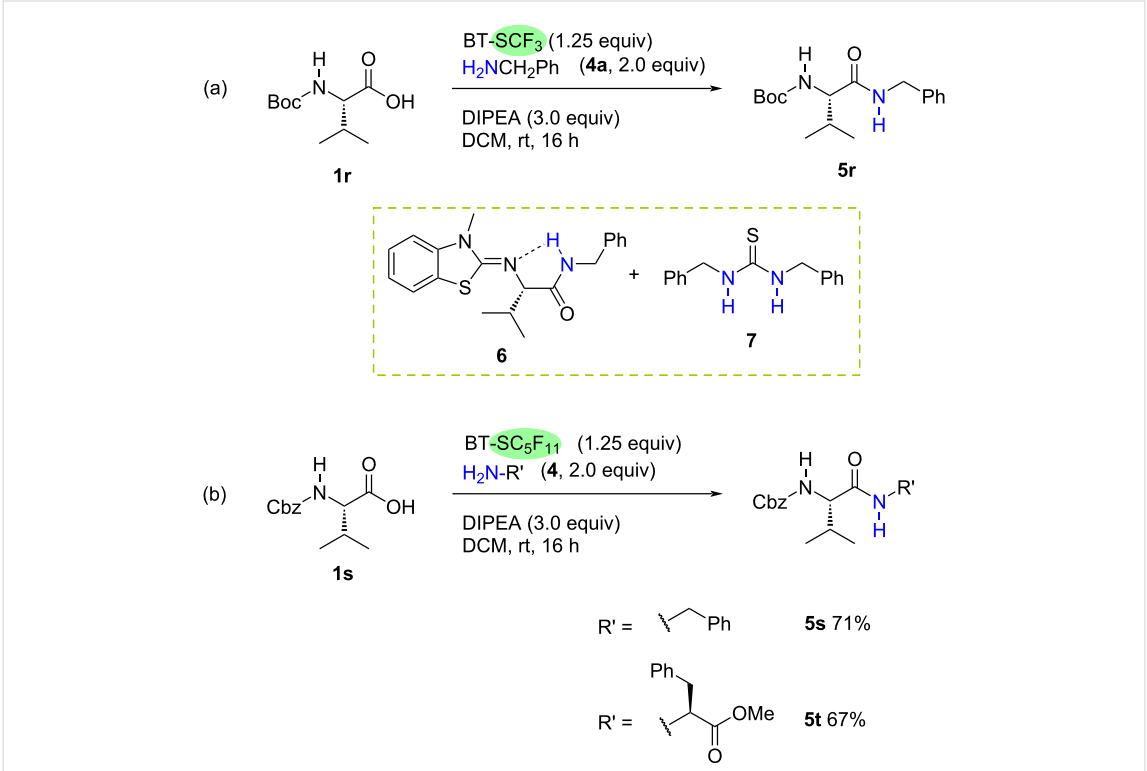
At this stage, the suitability of BT-SCF_3-mediated deoxyfluorination for the one-pot formation of peptide linkages between amino acids was investigated (Scheme 3). Treatment of *N*-Boc-valine under the optimised one-pot conditions with benzylamine (**4a**) resulted in the formation of the desired amide product, however, significant by-products were also observed.



Scheme 2: Scope of the one-pot BT-SCF_3-mediated deoxygenative coupling of carboxylic acids and amines via acyl fluoride derivatives. Reactions conducted on a 0.5 mmol scale, isolated yields after column chromatography.

Careful column chromatography of the crude reaction mixture allowed for the partial isolation and characterisation of the benzothiazolimine species **6** which results from Boc-deprotection and subsequent condensation of the amide product onto the benzothiazolium core. Although the other identified by-product, thiourea **7**, is not derived from the limiting carboxylic acid substrate, it was found to coelute with the amide product, complicating isolation (Scheme 3a). As Boc-deprotection is seemingly feasible under the reaction conditions, to avoid formation of by-product **6**, the process was tested using the *N*-Cbz-valine (**1s**). Moreover, the BT-SCF_3 reagent was substituted for the longer chain BT-reagent BT-SC_5F_{11}. The use of this benzothiazolium species would avoid the formation of thiocarbonyl difluoride, which is most likely responsible for the generation of thiourea **7**. Pleasingly, under these conditions, amide **5s** was formed smoothly with isolation by column chromatography providing the pure product in 71% yield (Scheme 3b). Furthermore, replacing the benzylamine coupling partner with phenylalanine methyl ester provided dipeptide **5t** in 67% yield (Scheme 3b).

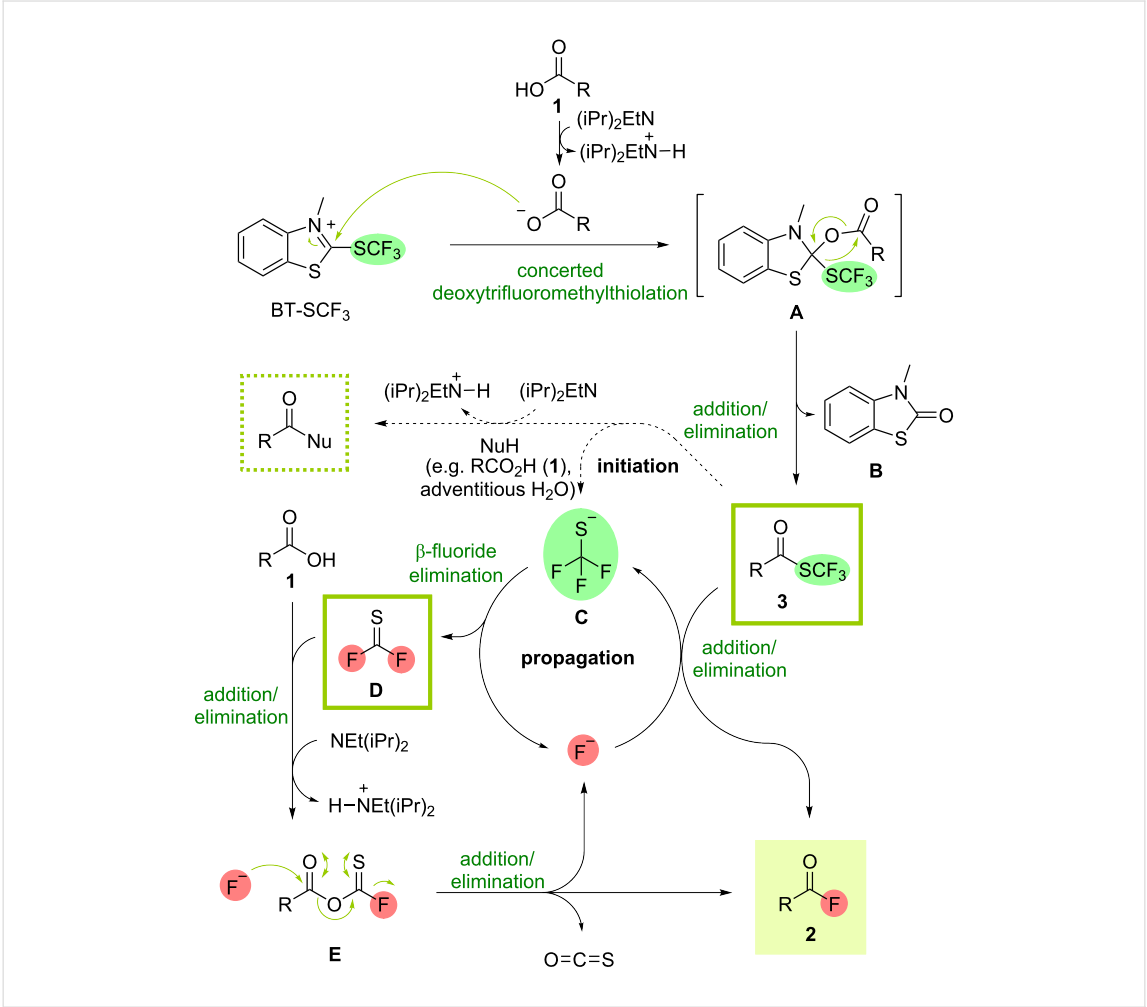
With the scope of the deoxyfluorination process established, our attention turned to an investigation of the reaction mechanism (Scheme 4). As demonstrated in our previous work, reacting



Scheme 3: One-pot BT-SCF_3-mediated deoxygenative coupling of amino acids. Isolated yields after column chromatography.

BT-SCF_3 with carboxylic acids **1** under similar conditions provides (trifluoromethyl)thioesters **3** via a concerted deoxytrifluoromethylthiolation process from tetrahedral intermediate **A** affording thiocarbamate by-product **B** [31]. To test whether thioester species could act as intermediates in the formation of acyl fluorides, **3a** was prepared independently and treated with DIPEA (1.1 equiv) in DCM (Scheme 5a). After 1 h at rt, complete consumption of the thioester was observed with acyl fluoride **2a** being obtained as the only product in quantitative ^{19}F NMR yield. Conversion of **3** into **2** could result from a self-propagating process initiated by addition of an adventitious nucleophile to the electrophilic thioester. This results in elimination of a (trifluoromethyl)thiolate ($^{-}SCF_3$) anion (**C**, Scheme 4), which can subsequently undergo β-fluoride elimination, releasing a fluoride anion. Addition of F^{-} to another molecule of thioester **3** thus sets off a chain process, delivering acyl fluoride **2** and regenerating the fluoride nucleophile. A series of experiments conducted with thioester **3a** suggest a number of nucleophiles feasibly present in the reaction mixture can initiate the chain process [34]. Stirring **3a** in the presence of the sodium carboxylate salt of acid **1a** resulted in the formation of **2a** in 18% ^{19}F NMR yield while only 10 mol % of tetramethylammonium fluoride (TMAF) provided the acyl fluoride in 59% yield (Scheme 5b). Moreover, efficient conversion of **3a** into **2a** could be achieved using only 10 mol % of DIPEA (92% ^{19}F NMR yield, Scheme 5b). This reaction could result from base-assisted nucleophilic attack of adventitious water present in the reaction mixture.

In addition to addition/elimination of fluoride ions to thioesters **3**, a second potential mechanistic pathway exists for the formation of acyl fluorides **2**. Alongside a fluoride ion, β-fluoride elimination from a (trifluoromethyl)thiolate ($^{-}SCF_3$) anion (**C**) also generates a thiocarbonyl difluoride species **D**. As previously demonstrated by Schoenebeck and co-workers in a deoxyfluorination of carboxylic acids with NMe_4SCF_3, this highly electrophilic compound can react with the carboxylic acid in the presence of DIPEA via addition/elimination affording a thioic anhydride species **E** and a fluoride ion [9]. Addition of F^{-} to the carboxyl carbon followed by fluoride elimination from the resulting thiocarboxylate would provide acyl fluoride **2**, carbonyl sulfide and another fluoride ion. As a result of this pathway, each molecule of the BT-SCF_3 reagent can in principle lead to the formation of two molecules of acyl fluoride **2**. Indeed, a yield of **2a** above 50% was observed during the optimisation studies using 0.5 equiv of BT-SCF_3 (Table 1, entry 9). To

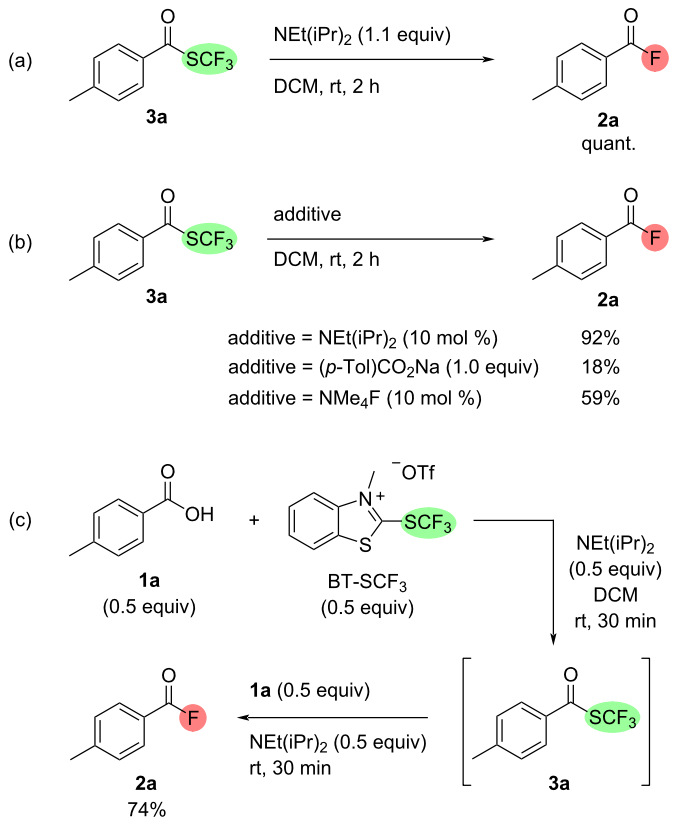


Scheme 4: Plausible mechanism for the deoxyfluorination of carboxylic acids with BT-SCF_3.

further investigate the potential for reducing the loading of the deoxyfluorinating reagent, 0.5 equiv of the carboxylic acid substrate **1a** was reacted with 0.5 equiv of both BT-SCF_3 and DIPEA in DCM for 30 min at rt. ^{19}F NMR analysis of the mixture indicated the clean formation of thioester **3a** and the remaining 0.5 equiv of **1a** and 0.5 equiv of DIPEA were then added (Scheme 5c). According to the mechanism shown in Scheme 4, self-propagating conversion of **3a** into **2a**, presumably initiated by a carboxylate nucleophile, would account for half of the acyl fluoride formed with the remaining product resulting from addition of **1** to thiocarbonyl difluoride. After a further 30 minutes at rt, ^{19}F NMR analysis of the crude mixture indeed indicated the formation of **2a** in an overall yield of 74%, implying both pathways are feasible and that sub-stoichiometric amounts of BT-SCF_3 relative to the carboxylic acid can lead to good overall yields of acyl fluorides.

Conclusion

In conclusion, a practical method for the direct synthesis of acyl fluorides from carboxylic acids using BT-SCF_3 as a deoxyfluorinating reagent has been developed. In a one-pot process, direct access to various amides was achieved under mild and operationally simple conditions while peptide coupling between two amino acids could be efficiently conducted using the longer-chain perfluoroalkyl reagent BT-SC_5F_{11}. Mechanistic studies revealed that each equivalent of the benzothiazolium reagent can feasibly generate two equivalents of the acyl fluoride with addition/elimination of fluoride to a thioester intermediate and independent deoxyfluorination of a second equivalent of the acid substrate by the released $^-SCF_3$ anion both operating under the reaction conditions. This allows for the reduction in the loading of BT-SCF_3 to sub-stoichiometric levels, further increasing the attractiveness of the method.



Scheme 5: Mechanistic experiments. (a) Conversion of thioester **3a** into acyl fluoride **2a** in the presence of DIPEA. (b) Conversion of thioester **3a** into acyl fluoride **2a** in the presence of carboxylate and fluoride nucleophiles. (c) Two-stage deoxyfluorination reaction using 0.5 equiv of BT-SCF_3. ^{19}F NMR yields using α,α,α-trifluorotoluene as internal standard.

Supporting Information

Supporting Information File 1

Experimental procedures, characterisation data of all isolated products as well as copies of NMR spectra for novel compounds.
[https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-20-82-S1.pdf]

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Author Contributions

Lilian M. Maas: conceptualization; investigation; methodology; project administration; resources; supervision; validation; writing – original draft; writing – review & editing. Alex Haswell: conceptualization; investigation; methodology; project administration; resources; supervision; validation; writing – review & editing. Rory Hughes: investigation; methodology;

resources; writing – review & editing. Matthew N. Hopkinson: conceptualization; funding acquisition; methodology; project administration; supervision; writing – original draft; writing – review & editing.

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Data Availability Statement

The data that supports the findings of this study is available from the corresponding author upon reasonable request.

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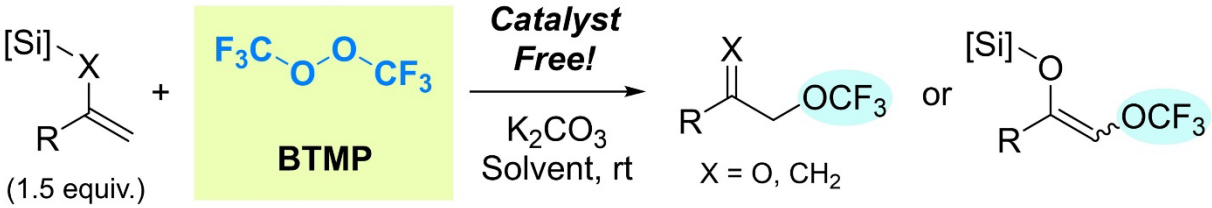
34. Notably, similar reactivity was observed with longer-chain (perfluoroalkyl)thioesters generated upon deoxygenative perfluoroalkylthiolation of carboxylic acids with BT-SR_F reagents. With these very electrophilic compounds, conversion into the corresponding acyl fluorides was often observed as a decomposition pathway during purification or extended storage (see ref. [32]).

3.3 Catalyst-Free Trifluoromethoxylation of Silyl Enol Ethers and Allyl Silanes with Bis(trifluoromethyl)peroxide



Lilian M. Maas, Carlo Fasting, Patrick Voßnacker, Niklas Limberg, Paul Golz, Carsten Müller, Sebastian Riedel,* Matthew N. Hopkinson*

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Author Contributions

Lilian Maria Maas designed and managed the project, performed the experiments throughout the optimisation process and the scope and wrote the manuscript. Carlo Fasting performed all isolations via preparative HPLC. Patrick Voßnacker and Niklas Limberg performed the XRD measurements. Paul Golz assisted with the synthesis and isolation of the gaseous product **8f** (see manuscript) and provided the data for the cyclovoltammetry of BTMP. Carsten Müller performed all quantum chemical calculations and assisted with the manuscript preparation. Sebastian Riedel and Matthew Hopkinson assisted with the management of the project and revised the manuscript.

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Fluorine Chemistry Hot Paper

Catalyst-Free Trifluoromethoxylation of Silyl Enol Ethers and Allyl Silanes with Bis(trifluoromethyl)peroxide

Lilian M. Maas, Carlo Fasting, Patrick Voßnacker, Niklas Limberg, Paul Golz, Carsten Müller, Sebastian Riedel, and Matthew N. Hopkinson**

Abstract: Radical trifluoromethoxylation is an attractive approach to prepare compounds featuring the important OCF_3 group, however most existing methods have focused on aromatic substrates. Here, we report novel methodologies with alkenyl substrates employing bis(trifluoromethyl)peroxide (BTMP) as a practical and comparatively atom economical trifluoromethoxylating reagent. With silyl enol ether substrates, switching reaction solvent allows for the synthesis of either α-(trifluoromethoxy)ketone products or unprecedented alkenyl-OCF_3 species. Furthermore, allyl silanes have been employed as substrates for the first time, affording allyl(trifluoromethyl)ether products in good yields. In each case, the methods operate at room temperature without large excesses of the alkene substrate while, in contrast to previous radical trifluoromethoxylation reactions, no catalyst, light or other activators are required.

Introduction

The trifluoromethoxy (OCF_3) group and its introduction into organic molecules is of growing interest in several different fields, especially agro- and medicinal chemistry, due to its unique properties and good metabolic stability.[1] Often referred to as a "superhalogen", the OCF_3 group exhibits high lipophilicity ($\pi = 1.04$) and comparable electronegativity to an individual fluorine atom ($\chi^{OCF3} = 3.7$, $\chi^{F} = 4.0$), however its electron-withdrawing effect is somewhat lower than many other fluorinated groups.[2] The unique stereoelectronic requirements of OCF_3 moieties can also result in unconventional conformational preferences rarely encountered with alternative groups. Incorporating a trifluoromethoxy group onto a valuable molecule therefore can result in better fine tuning of its properties and an improved overall activity. Furthermore, with perfluoroalkyl substances (PFAS) currently attracting concern as so-called "forever chemicals", the comparatively lower environmental persistence of trifluoromethoxy moieties could make these motifs attractive alternatives to CF_3 and other fluorinated groups in pharmaceuticals, agrochemicals and materials.[3]

Despite this great potential, only a handful of OCF_3-containing molecules are currently employed commercially with only 0.01 % of the fluorinated pharmaceuticals on the market and 0.02 % of fluorinated agrochemicals being trifluoromethoxylated.[1e,g] A major contributing factor for this is the lack of practical methods for introducing OCF_3, especially at a late stage of a synthetic route. Compared to indirect approaches involving fluorination of pre-functionalised ether motifs[4] or trifluoromethylation of alcohols,[5] direct trifluoromethoxylation methods, wherein the whole OCF_3 moiety is attached in one step, are particularly attractive in this regard. The available methods can be categorised into nucleophilic and radical approaches, where nucleophilic methods can be challenging due to the instability of the $^{-}OCF_3$ anion towards β-fluoride elimination.[6] As a result, considerable attention has been devoted to the development of new radical trifluoromethoxylation reactions.[7] In 2018, the groups of Ngai and Togni both introduced bench stable reagents which release $^{\bullet}OCF_3$ radicals upon activation of an N–O bond.[8] These compounds represented a major breakthrough for the field that opened up novel synthetic routes towards OCF_3-substituted molecules directly from unfunctionalised aromatics.[7,9] In 2021, our groups explored bis(trifluoromethyl)peroxide (BTMP) as an alternative source of $^{\bullet}OCF_3$ radicals in related photocatalytic and TEMPO-induced reactions of arenes and heteroarenes.[10] First reported by Swarts in 1933[11] and reinvestigated by Cady in 1957,[12a] BTMP is a remarkably stable (no thermal decomposition below 200 °C) and easy to handle gas which can be synthesised on a large scale from the relatively inexpensive industrial chemicals CO and F_2.[13,14] In comparison to the previous reagents, which are themselves prepared from expensive electrophilic trifluoromethylating reagents and generate significant waste, BTMP offers promise as a practical and atom-economical alternative.

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While there have been a number of reports in recent years on the radical trifluoromethoxylation of arenes and, to a lesser extent, heteroarenes, applications for the synthesis of other important classes of OCF_3-containing molecules are scarce (Figure 1a). In particular, radical methodologies that afford products substituted with OCF_3 groups at sp^3-hybridised carbon atoms have been seldom reported. In 2021, a collaborative study between the Magnier, Dagousset and Dell'Amico groups investigated $^{\bullet}OCF_3$ radical addition to enol carbonate substrates using the Togni trifluoromethoxylating reagent (Figure 1b).[15] Although requiring 5 equivalents of the alkene substrates and employing photoredox catalysis conditions, the success of this process demonstrates the potential of radical trifluoromethoxylation to generate diverse OCF_3-containing products, delivering α-trifluoromethoxylated ketones in generally moderate yields.[16] Inspired by this report and by our previous work on the radical trifluoromethoxylation of aromatics,[10] we considered whether BTMP could be employed as a reagent for preparing a wider range of OCF_3-containing molecules. Here we report the results of this investigation, which not only led to efficient methods for preparing α-trifluoromethoxylated ketones and allyl(trifluoromethoxy)ethers from silyl enol ethers and allyl silanes, respectively, but also gave access to unprecedented alkenyl-OCF_3 products. Moreover, in addition to its practical and atom-economical nature, the use of BTMP also allowed for trifluoromethoxylation to be conducted under catalyst-free conditions without large excesses of the substrate and employing inexpensive potassium carbonate as the only additive (Figure 1c).

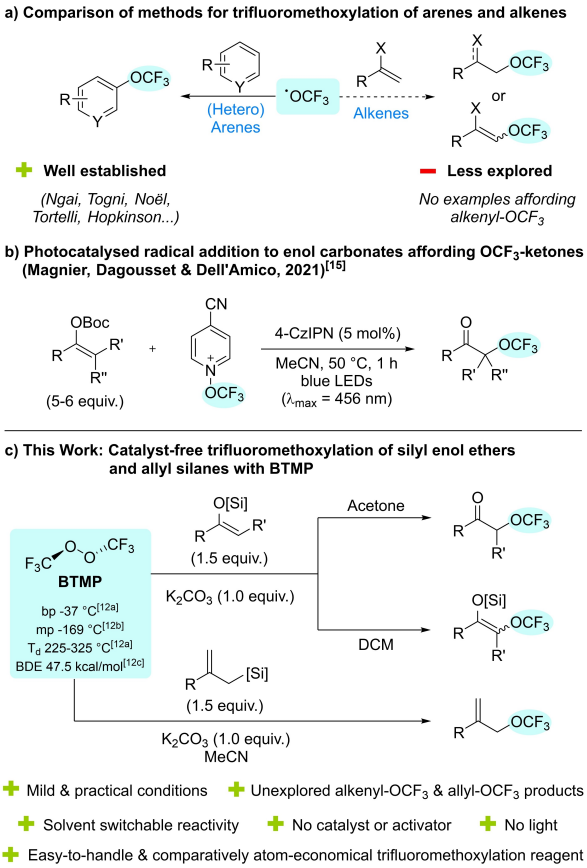
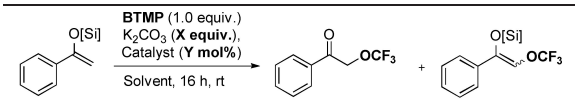


Figure 1. a) Radical trifluoromethoxylation of arenes and alkenes. b) Previous report on the photoredox catalysed trifluoromethoxylation of enol carbonates affording α-(trifluoromethoxy) ketones. c) This work: Catalyst-free trifluoromethoxylation of silyl enol ethers and allyl silanes with BTMP. 4-CzIPN: 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene, T_d: decomposition temperature.

Results and Discussion

At the beginning of the study, we investigated potential alkenyl substrates that could serve as acceptors of $^{\bullet}OCF_3$ radicals, and selected silyl enol ethers as representative substrates. To our delight, an initial test reaction employing the established photocatalytic conditions from our prior work with the trimethylsilyl enol ether of acetophenone (**1a**, 1.5 equiv.) provided the desired α-(trifluoromethoxy)ketone **2a** in a ^{19}F NMR yield of 16 % (internal standard: $PhCF_3$, Table 1, Entry 1).[17] Product **2a** was also generated in 6 % ^{19}F NMR yield when **1a** was reacted in the presence of BTMP, TEMPO ((2,2,6,6-tetramethylpiperidin-1-yl)oxyl, 25 mol %) and K_2CO_3 (1.0 equiv.) under conditions also developed in our previous study with (hetero)arene substrates (Table 1, Entry 2). In both cases, almost complete desilylation of **1a** was observed during the reaction suggesting the relatively low yields could result in part from undesired background hydrolysis of the trimethylsilyl enol ether. We therefore investigated the more hydrolytically stable compound **3a**, which features a sterically more demanding triisopropylsilyl (TIPS) group in place of the trimethylsilyl (TMS) motif. Pleasingly, under the TEMPO-mediated conditions, **3a** reacted smoothly to afford **2a** in an increased ^{19}F NMR yield of 44 %. Furthermore, analysis of the crude NMR spectra revealed the presence of small amounts of trifluoromethoxylated side-products, which could be assigned as the (*Z*) and (*E*) isomers of the silyl enol ether **4a** ((*Z*)-**4a**, 4 %; (*E*)-**4a**, 5 %, Table 1, Entry 3). To the best of our knowledge, products featuring an alkenyl OCF_3 group have not been obtained previously via radical trifluoromethoxylation. Silyl enol ethers of general structure **4** could serve as useful building blocks for the construction of diverse OCF_3-containing compounds. An investigation of the reaction stoichiometry revealed 1.5 equivalents of **3a** to be optimum with 1.0 or 2.0 equivalents leading to lower yields of **2a** (Table 1, Entries 4&5). Such a low loading of the alkene is remarkable and stands in contrast to other radical trifluoromethoxylation methodologies, which typically require 5 equivalents or more of the organic substrate. Reducing the TEMPO catalyst loading to 5 mol % suppressed the formation of silyl enol ethers **4a** and led to an increase in ^{19}F NMR yield of ketone product **2a** to 48 % (Table 1, Entry 6). Moreover, omitting the catalyst entirely did not lead to the expected suppression of reactivity but rather resulted in a further small increase in ^{19}F NMR yield

Table 1: Optimisation of the direct trifluoromethoxylation of silyl enol ethers using BTMP.



1a [Si] = TMS
3a [Si] = TIPS
(1.5 equiv.)

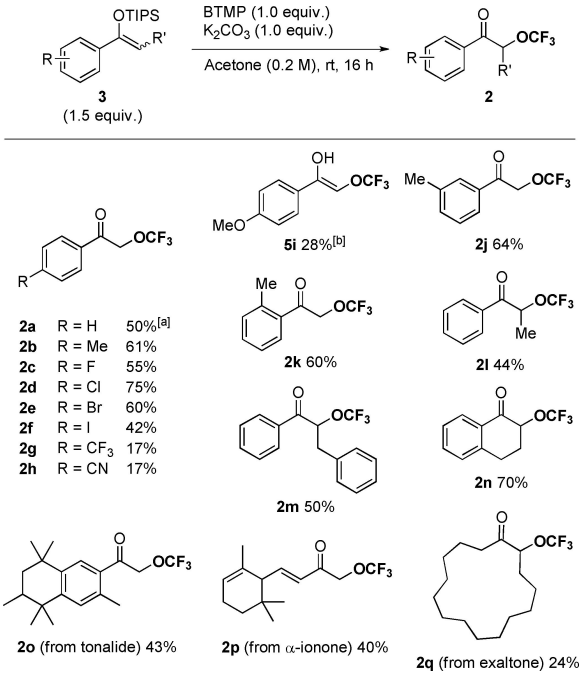
2a **4a**

Entry	[Si]	Catalyst (mol%)	K_2CO_3 (equiv.)	Solvent	Yield **2a**[a]	Yield **4a**[a] (*Z*/*E*)
1[b]	TMS	$[Ru(bpy)_3](PF_6)_2$ (4 mol%)	–	MeCN	16	–
2	TMS	TEMPO (25 mol%)	1.0	MeCN	6	–
3	TIPS	TEMPO (25 mol%)	1.0	MeCN	44	4:5
4[c]	TIPS	TEMPO (25 mol%)	1.0	MeCN	16	–
5[d]	TIPS	TEMPO (25 mol%)	1.0	MeCN	42	5:3
6	TIPS	TEMPO (5 mol%)	1.0	MeCN	48	–
7	TIPS	–	1.0	MeCN	50	–
8	TIPS	–	1.5	MeCN	50	–
9	TIPS	–	0.5	MeCN	31	–
10	TIPS	–	1.0	Acetone	55	–
11	TIPS	–	1.0	$MeNO_2$	12	49:6
12	TIPS	–	1.0	Et_2O	12	34:22
13	TIPS	–	1.0	DCM	5	57:12
14[e]	TIPS	–	1.5	Acetone	49	–
15[e]	TIPS	–	1.5	DCM	2	28:6

[a] ^{19}F NMR yields using α,α,α-trifluorotoluene ($PhCF_3$) as an internal standard. [b] Reaction was performed under irradiation from blue LEDs. [c] With **3a** (1.0 equiv.). [d] With **3a** (2.0 equiv.) [e] inverted stoichiometry: with **3a** (1.0 equiv.) and BTMP (1.5 equiv.). TMS = trimethylsilyl, bpy = 2,2′-bipyridine, TEMPO = 2,2,6,6-tetramethylpiperidin-1-yl)oxyl, TIPS = triisopropylsilyl. DCM = dichloromethane.

of **2a** to 50% (Table 1, Entry 7). This surprising result implies that independent activation of BTMP is not required for a successful reaction and that substrate **3a** may itself directly react with the peroxide. Increasing the amount of the K_2CO_3 additive did not influence the yield of **2a**, however reducing down to 0.5 equiv. resulted in a decreased yield of 31% (Table 1, Entries 8&9). K_2CO_3 likely serves to mop up any HF side-product generated under the reaction conditions. During the solvent screening, a solvent-dependent product distribution was observed. When acetone was used as the solvent, **2a** was selectively formed in a ^{19}F NMR yield of 55% (Table 1, Entry 10). However, when conducted in diethyl ether, nitromethane or dichloromethane (DCM), silyl enol ethers **4a** were generated as the major products of the reaction, with DCM leading to the highest yield (Table 1, Entries 11–13). Finally, both the DCM and acetone methods were tested using inverted stoichiometry using **3a** as the limiting reagent and maintaining a BTMP:K_2CO_3 ratio of 1:1 (Table 1, Entries 14 & 15). In acetone, the reaction proceeded with only a slight decrease in ^{19}F NMR yield of **2a** relative to the standard conditions, however, the reaction in DCM affording **4a** was considerably less efficient. In both reactions, increased formation of aromatic OCF_3 side-products was observed. For these reasons, the conditions from Table 1, entries 10 and 13 were used for further studies. Overall, the optimisation study led to the development of two practical sets of conditions for radical trifluoromethoxylation that employ only a slight excess of the alkenyl substrate, do not require any catalyst and proceed at room temperature with only K_2CO_3 as an additive.

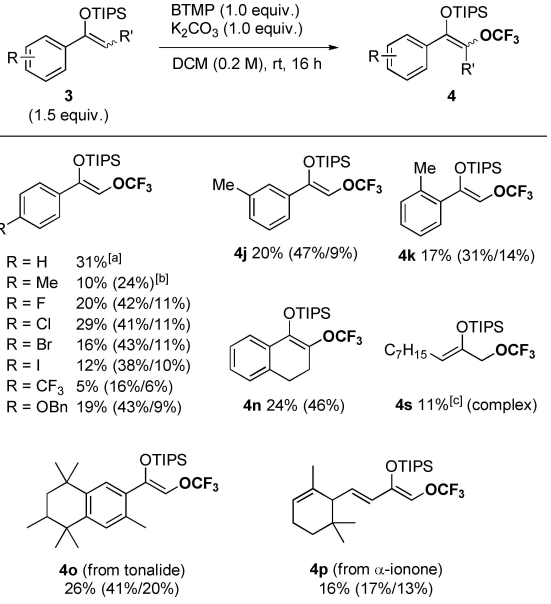
We next set out to evaluate the scope and limitations of the method affording α-(trifluoromethoxy)ketone products **2** (Scheme 1). To our delight, common substituents on the aromatic ring of acetophenone-derived silyl enol ethers such as alkyl moieties and halogens were well tolerated and afforded the corresponding products in moderate to good isolated yields up to 75%.[18] The halogenated products **2d–f** are particularly noteworthy as they offer the potential for further elaboration, for example through cross-coupling methodologies. The reactions with silyl enol ethers bearing strongly electron-withdrawing groups on the aromatic ring, on the other hand, showed reduced reactivity with the α-(trifluoromethoxy)ketones **2g** and **2h** being both obtained in 17% isolated yield. This observation is consistent with our findings in aromatic trifluoromethoxylation reactions with BTMP.[10] Interestingly, NMR analysis of the crude reaction mixture with the methoxy-substituted silyl enol ether **3i** revealed the formation of not only the desired



Scheme 1. Scope of the reaction of silyl enol ethers **3** with BTMP affording α-(trifluoromethoxy)ketones **2**. Isolated yields. [a] Reaction with DCM as the solvent. After reaction time, trifluoroacetic acid (TFA, 3.0 equiv.) was added and reaction mixture was stirred for an additional 4 h at rt. [b] Single diastereomer, configuration not determined.

ketone **2i** but also the corresponding enol **5i**. Two spots were observed by thin layer chromatography (TLC), however, upon purification by column chromatography, both isolated fractions exhibited NMR spectra in $CDCl_3$ consistent with **5i**, implying tautomerisation to the seemingly more stable enol form had occurred (total isolated yield = 28 %).[19,20] Products **2j** and **2k**, which feature substituents at the *ortho*- and *meta*- positions, as well as ketones **2l–n** derived from internal silyl enol ethers could also be obtained in good yields up to 70 %. The *ortho*-methyl-substituted product **2k** was a solid and allowed for confirmation of the structure by single crystal X-ray diffraction (Figure 2).[21] Overall, the yields are largely comparable with those obtained by Magnier, Dagousset and Dell'Amico employing the Togni trifluoromethoxylating reagent and enol carbonate substrates under photoredox catalysis conditions.[15] Moreover, in some ways, the two systems are complementary with the photocatalytic method working somewhat better for relatively electron-deficient substrates and the catalyst-free method with BTMP affording higher yields with more electron-rich derivatives. Finally, to evaluate the applicability of the method for late-stage functionalisation, a selection of silyl enol ethers derived from ketones used in the perfumery industry were tested. Product **2o** derived from the aromatic ketone tonalide was delivered in 43 % isolated yield while silyl enol ethers generated from α-ionone and exaltone also reacted smoothly indicating that alkenyl and aliphatic α-(trifluoromethoxy)ketone products are also readily accessible using BTMP (yield of **2p** = 40 %, yield of **2q** = 24 %).

After evaluating the method affording α-(trifluoromethoxy)ketones **2**, we next turned our attention to the synthesis of OCF_3-substituted silyl enol ethers **4**. Compounds that feature an OCF_3 group at an electron-rich alkene functionality have not been obtained previously as products of radical trifluoromethoxylation and we were therefore eager to investigate the efficiency of this process with a range of different substrates.[22] In each case, the crude yield and Z/E ratio was measured by ^{19}F NMR, and the major isomer was then isolated by preparative HPLC (Scheme 2). As for the reaction in acetone affording α-(trifluoromethoxy)ketones, the process in DCM showed good tolerance of common substituents and substitution patterns on the aryl ring of acetophenone-derived silyl enol ethers **3**. Substrates containing halogens and alkyl groups at the *para*-position reacted



Scheme 2. Scope of the reaction of silyl enol ethers **3** with BTMP affording trifluoromethoxylated silyl enol ethers **4**. Isolated yields of the major isomer. ^{19}F NMR yields of the (*Z*) and (*E*) products using α,α,α-trifluorotoluene ($PhCF_3$) as an internal standard are given in parentheses. [a] Reaction was performed on a 2.4 mmol scale. ^{19}F NMR yield not measured. [b] Minor diastereomer could not be unambiguously observed in the crude ^{19}F NMR. [c] Stereochemistry not determined.

smoothly while both electron-withdrawing groups such as CF_3 and electron-donating substituents such as OBn were tolerated. The isolated major isomer of the benzyloxy-substituted product **4r** was a solid which allowed for the configuration to be confirmed as *Z* by X-ray crystallography (Figure 3).[21] NOE analysis of the major isomer obtained from silyl enol ether **3a** was also consistent with a *Z*-configuration and, by analogy, we tentatively assume that the reaction is moderately selective for this isomer for all the substrates tested with diastereomeric ratios averaging around 4:1.[23] Methyl substitution at the *ortho*- and *meta*-positions of the aryl ring was also well tolerated with the

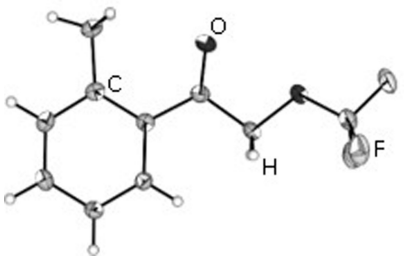


Figure 2. Molecular structure, determined by X-ray diffraction, of ketone **2k**. Thermal ellipsoids set at 50% probability.

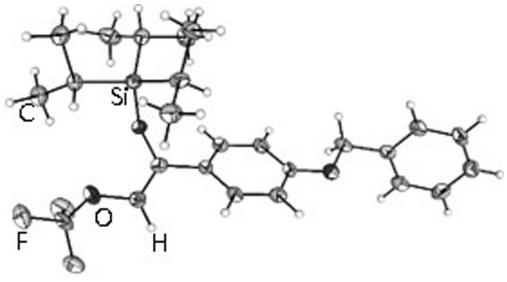


Figure 3. Molecular structure, determined by X-ray diffraction, of trifluoromethoxylated silyl enol ether (*Z*)-**4r**. Thermal ellipsoids set at 50% probability.

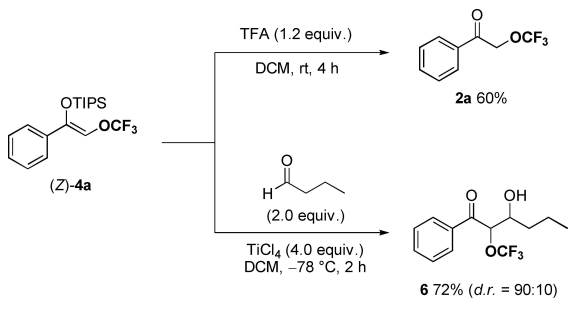
ortho-substituted product reacting with somewhat lower diastereoselectivity (^{19}F NMR yields of (*Z*)-**4k** and (*E*)-**4k** = 31 % and 14 %, respectively). While the silyl enol ether derived from α-tetralone reacted smoothly (^{19}F NMR yield of **4n** = 46 %), the reaction was found to be less successful with other internal alkene substrates with methyl or benzyl substitution at the 2-position suppressing product formation. Subjecting the aliphatic silyl enol ether substrate **3s** led to a complex reaction mixture with the major product isolated by preparative HPLC being the internal alkene product **4s** (isolated yield = 11 %). Finally, (trifluoromethoxy)silyl enol ethers of the compounds derived from tonalide (**4o**) and α-ionone (**4p**) could be obtained in moderate yields.

To probe the potential of trifluoromethoxylated silyl enol ethers **4** as useful OCF_3-containing building blocks, the benchmark compound (*Z*)-**4a** was synthesised on a 2.4 mmol scale and subjected to further transformations. Treatment with trifluoroacetic acid (TFA, 1.2 equiv.) in DCM resulted in smooth desilylation affording the corresponding α-(trifluoromethoxy)ketone **2a** in 60 % yield (Scheme 3).[24] Moreover, following a literature-known protocol,[25] product (*Z*)-**4a** could be successfully converted into the Mukaiyama aldol product **6** in 72 % yield (*d.r.* = 90:10) upon reaction with *n*-butanal and titanium chloride. In both reactions, no cleavage or elimination of the OCF_3 group was observed.

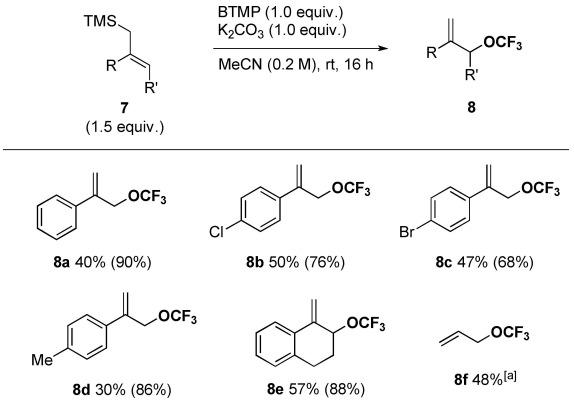
Having established silyl enol ethers as suitable substrates for catalyst-free radical trifluoromethoxylation with BTMP, we next sought to explore alternative potential classes of alkene reaction partner. By virtue of the silicon β-effect, allyl silanes are competent radical acceptors with subsequent desilylation affording functionalised allyl products. To the best of our knowledge, general methods for radical trifluoromethoxylation of alkenyl substrates other than enol ether derivatives have not been reported previously while the potential allyl(trifluoromethyl)ether products could serve as useful OCF_3-containing motifs that feature an alkene handle for further derivatisation. In an initial test reaction, trimethyl(2-phenylallyl)silane **7a** was reacted under the TEMPO-mediated reaction conditions developed in our previous study: TEMPO (25 mol %), K_2CO_3 (1.0 equiv.), MeCN, rt, 1 h. To our delight, smooth conversion to the desired product **8a** was observed with ^{19}F NMR analysis indicating a yield of 53 %. Moreover, switching to catalyst-free conditions without TEMPO led to a significant improvement in efficiency with **8a** being delivered in 90 % ^{19}F NMR yield.

A short scope and limitations study was then conducted with a selection of allyl silane structures **7** (Scheme 4). The *para*-substituted aryl derivatives **7b–d** all reacted efficiently in ^{19}F NMR yields greater than 68 % although product volatility had a detrimental effect on the isolated yields. The reaction with an internal allyl silane was also successful with allyl(trifluoromethyl)ether **8e** being generated in 88 % ^{19}F NMR yield (57 % isolated yield). With this unsymmetrical allyl substrate, selective installation of the OCF_3 group within the carbocyclic ring was observed, indicating that trifluoromethoxylation occurs at the alkenyl β-position and not at the carbon directly bonded to silicon. Finally, to fully probe the extent of suitable allyl silane substrates, the simplest unsubstituted derivative, allyl(trimethyl)silane **7f**, was tested. Radical trifluoromethoxylation proceeded very slowly in this case, however after 14 days at rt, allyl(trifluoromethyl)ether (**8f**) was observed in the crude mixture with distillation providing the gaseous product as an inseparable mixture with the TMS–F side-product (calculated isolated yield = 48 %).

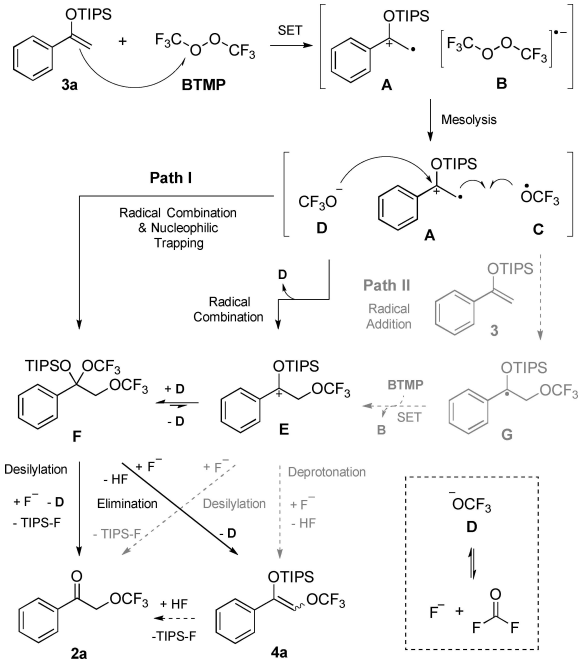
The success of the trifluoromethoxylation reactions under such simple conditions without a catalyst or other activators raises questions regarding the operating mechanism. To provide insight into the potential pathways, preliminary DFT calculations were conducted. A comparison of the computed ionisation energy of silyl enol ether **3a** and electron affinity of BTMP in acetone implies that single electron transfer affording the radical cation **A** and radical anion **B** is thermodynamically feasible ($\Delta G = -7.7$ kJ/mol at 298.15 K, Scheme 5).[26] Subsequent mesolysis of **B** would then provide an $^{\bullet}OCF_3$ radical **C** and an $^{-}OCF_3$ anion **D**. In principle, radical **C** could directly combine with the silyl



Scheme 3. Desilylation and Mukaiyama Aldol Reaction of trifluoromethoxylated silyl enol ether (*Z*)-**4a**. Isolated yields.



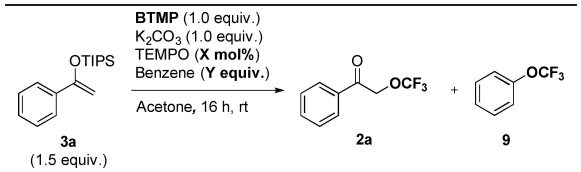
Scheme 4. Scope of the reaction of allyl silanes **7** with BTMP affording allyl(trifluoromethyl)ethers **8**. Isolated yields. ^{19}F NMR yields using α,α,α-trifluorotoluene ($PhCF_3$) as an internal standard are given in parentheses. [a] Reaction was performed on a 20 mmol scale over 14 days. Product **8f** was isolated as a 1:1 mixture with TMS–F. ^{19}F NMR yield not measured.



Scheme 5. Postulated mechanism for the catalyst-free trifluoromethoxylation of silyl enol ethers **3** with BTMP. SET = single electron transfer.

enol ether-derived radical cation **B** affording cation **E** (Path I, Scheme 5) or the 1,2-di(trifluoromethoxy) compound **F** upon additional trapping with $^{-}OCF_3$ (**D**). In an alternative pathway, $^{\bullet}OCF_3$ radical (**C**) could instead add to another molecule of the starting material affording radical species **G**, which could then be oxidised to cation **E** by BTMP as part of a radical chain mechanism (Path II, Scheme 5). To probe the involvement of such a radical chain mechanism, the standard reaction with **3a** in acetone was performed again in the presence of benzene (10 equiv., Table 2). As shown in our previous work,[10] benzene is a competent radical acceptor for free $^{\bullet}OCF_3$ radicals **C**, and it could be expected to provide competition to silyl enol ether **3a** if a radical chain mechanism of the type described above were operating. Analysis of the crude reaction mixture, however, did not indicate the formation of (trifluoromethoxy)benzene (**9**) as a side-product, suggesting that free $^{\bullet}OCF_3$ radicals that then engage with a second molecule of **3a** are not involved (Table 2, Entry 3). Interestingly, conducting the same experiment with additional TEMPO (25 mol%) as a catalyst did result in formation of **9**, implying free radicals **C** are involved in this case (Table 2, Entry 4).[27] In light of these results, we tentatively propose the mechanistic scenario shown as Path I in Scheme 5 where initial single electron reduction of BTMP by the electron-rich alkene substrate is followed by mesolysis and fast radical combination within the solvent cage. Finally, desilylative elimination from 1,2-di(trifluoromethoxy) compound **F** or cation **E** assisted by fluoride generated upon β-elimination from $^{-}OCF_3$ (**D**) would afford α-(trifluoromethoxy)ketones **2**, while α-deprotonation would lead to trifluoromethoxylated silyl enol ethers **4**.[28] Further studies would be required, however, to fully elucidate the reaction mechanism.

Table 2: Mechanistic experiments with benzene as a competing radical acceptor.



Entry	TEMPO (mol%)	Benzene (equiv.)	Yield **2a**[a]	Yield **9**[a]
1	–	–	50	–
2	25	–	44	–
3	–	10	44	–
4	25	10	40	9

[a] ^{19}F NMR yields using α,α,α-trifluorotoluene ($PhCF_3$) as an internal standard.

Conclusion

In conclusion, novel trifluoromethoxylation methodologies of alkene substrates have been developed using bis(trifluoromethyl)peroxide (BTMP). In contrast to previously developed radical trifluoromethoxylation approaches, these methods proceed under catalyst-free conditions without photoredox or any other activation, operate at room temperature with only a slight excess of the organic substrate and employ inexpensive potassium carbonate as the sole additive. With silyl enol ether substrates, judicious selection of the reaction solvent provides access either to α-(trifluoromethoxy)ketones or unprecedented alkenyl-OCF_3-containing silyl enol ether products, which can serve as useful trifluoromethoxylated building blocks. Moreover, allyl silanes have been employed as novel substrates for trifluoromethoxylation, delivering allyl(trifluoromethyl)ethers. Given the increasing importance of the OCF_3 group and the attractive features of BTMP as a practical and comparatively atom-economical reagent, we anticipate these methods will find applications in many areas of chemistry.

Supporting Information

The authors have cited additional references within the Supporting Information.[30–46]

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Conflict of Interest

The results underpinning this work have been protected in a patent application (EP23186390.3, submitted on 19.07.2023). Related use of BTMP for preparing (trifluoromethoxy)-arenes was previously protected in another patent application (EP2021-158495, submitted on 22.02.2021; WO2022-EP54181, submitted on Feb 21, 2022.).

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: Allyl Silanes · Fluorine · Ketones · Silyl Enol Ethers · Trifluoromethoxylation

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[17] For more information on the reaction optimisation, see the Supporting Information.

[18] In some cases, the isolated yields were lowered due to the high volatility of the products (see also ref. [15]).

[19] An NMR spectrum in toluene-d_8 indicated an enol/ketone ratio of 95:5, suggesting the equilibrium position is influenced by the solvent.

[20] The increased stability of the enol form could potentially result from a favourable hyperconjugative interaction between the extended styrenyl π-system and the O–CF_3 σ* antibonding orbital in this electron rich compound. Similar hyperconjugative interactions are thought to lay behind the unconventional conformational preferences observed with (trifluoromethoxy)arenes (see ref. [1]).

[21] Deposition numbers 2306068 (for **2k**), 2306494 (for (*Z*)-**4r**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

[22] To the best of our knowledge, only one example of an OCF_3-substituted silyl enol ether has been reported previously in the literature. This (*tert*-butyl)dimethylsilyl (TBS)-containing species was synthesised from the corresponding α-(trifluoromethoxy)ketone. See: R. Zriba, E. Magnier, J.-C. Blazejewski, *Synlett* **2009**, *2009*, 1131.

[23] DFT calculations on (*Z*)- and (*E*)-**4a** revealed there is little difference in the thermodynamic stability of the isomers with (*Z*)-**4a** being only 0.1 kJ/mol more stable than (*E*)-**4a** in DCM at 298.15 K, which is within the systematic error of the method. This implies the moderate diastereoselectivity observed results from kinetic factors during the deprotonation step.

[24] Surprisingly, treatment of (*Z*)-**4a** with tetra-*n*-butylammonium fluoride (TBAF, 1.2 equiv.) in DCM at rt led to decomposition although desilylation reactivity was somewhat recovered employing potassium fluoride (^{19}F NMR yield of **2a** = 16 % after 16 h at 70 °C).

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[26] Cyclic voltammetry measurements of BTMP and silyl enol ether **3a** revealed reduction and oxidation peaks, respectively. The irreversibility of these redox events and the instability of the decomposition products, however, make it difficult to give a definitive statement about the reduction potentials, especially for BTMP.

[27] Alternative potential reaction pathways include direct nucleophilic attack of the silyl enol ether onto BTMP generating cation **E** directly or a formal [2+2]-cycloaddition generating the 1,2-di(trifluoromethoxy)alkene intermediate **F** (Scheme).

[28] In the presence of TEMPO, direct single electron transfer between the catalyst and BTMP could occur providing an $^{\bullet}OCF_3$ radical without concomitant formation of a reactive radical cation intermediate. In this case, radical addition to the silyl enol ether or, potentially, benzene starting materials as part of a radical chain seemingly occurs.

[29] The origin of the solvent-dependent switch in product distribution is not abundantly clear; however, the different solubility of the KF generated as a reaction side-product could play a role. The generation of a strong Si–F bond is likely a driving force behind the desilylation process and it could be expected that a higher effective fluoride concentration would favor the formation of ketones **2**. A test reaction conducted with $CaCO_3$ in place of K_2CO_3 was accordingly performed to test this hypothesis. In this reaction, the CaF_2 formed as side-product is essentially insoluble and, even in more polar solvents, the degree of desilylation would be expected to be lower. Indeed, under the standard conditions with **3a** in acetone, much less of the ketone **2a** (^{19}F NMR yield = 15 %) was observed with OCF_3-conatining alkene **4a** being obtained as the major product (10:32 %). For a more complete understanding of the likely much more complex influence of the solvent on the reaction outcomes, however, further detailed mechanistic studies would be required.

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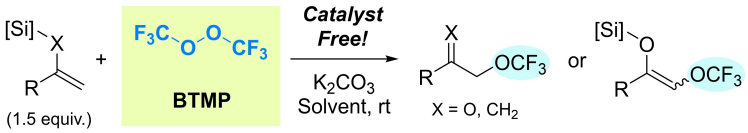
Research Articles

Fluorine Chemistry

L. M. Maas, C. Fasting, P. Voßnacker, N. Limberg, P. Golz, C. Müller, S. Riedel,* M. N. Hopkinson* _____ **e202317770**

Catalyst-Free Trifluoromethoxylation of Silyl Enol Ethers and Allyl Silanes with Bis(trifluoromethyl)peroxide



Catalyst-free trifluoromethoxylation methods of alkenyl substrates under mild conditions have been developed using bis(trifluoromethyl)peroxide (BTMP) as a practical and relatively atom-economical reagent. Silyl enol ether substrates react to form either α-(trifluoromethoxy)ketones or OCF_3-containing silyl enol ethers depending on the solvent used while allyl silanes afford unprecedented allyl(trifluoromethyl)ethers.

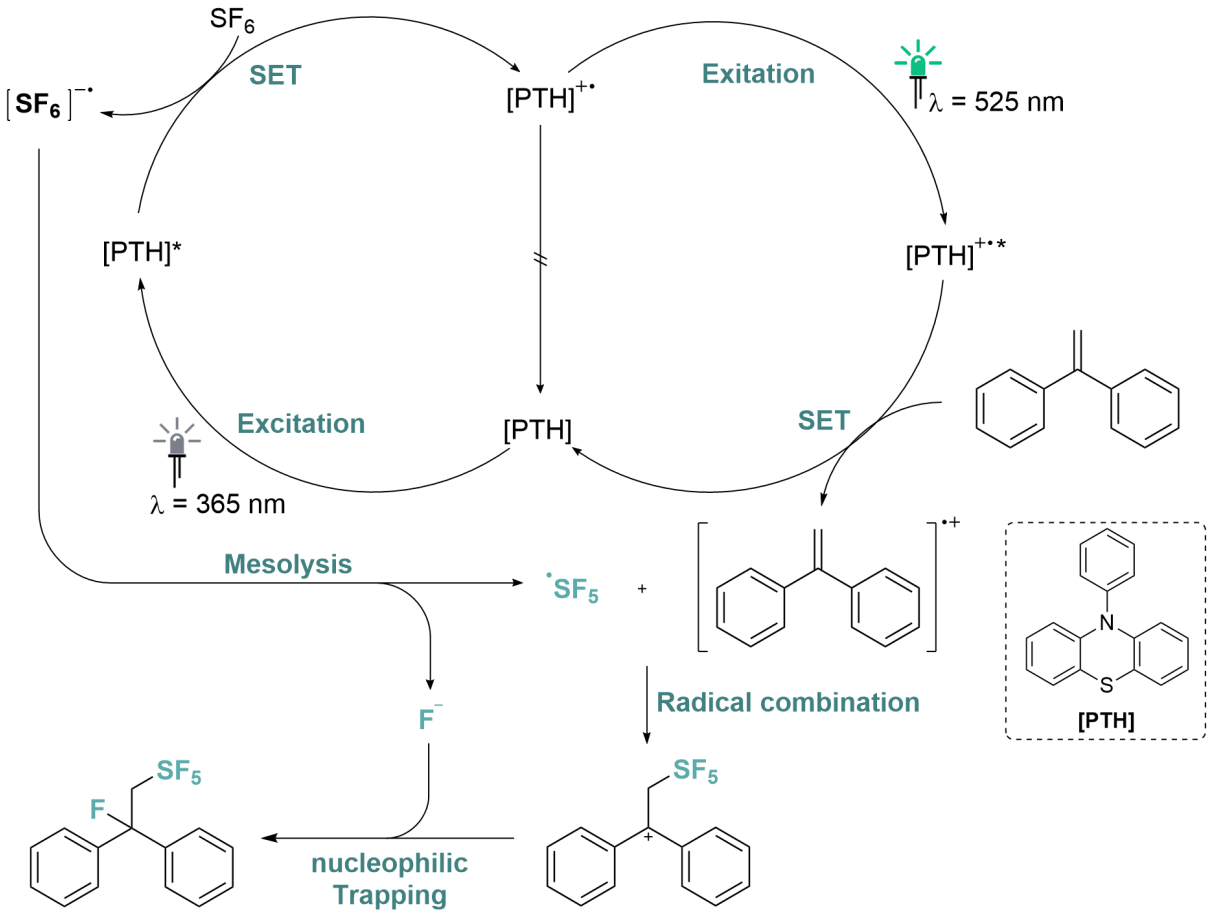
4 Discussion of Unpublished Results

4.1 Investigation of Sulphur Hexafluoride as a Reagent for Photocatalytic Pentafluorosulphanylation Reactions

The overall aim of the project was to investigate the reactivity of sulphur hexafluoride towards different substrate classes to obtain SF_5 compounds. SF_6 is a promising reagent for pentafluorosulphanylation as it is non-toxic, inexpensive and widely available. However, its high stability and inertness is the main challenge to utilise SF_6 as an SF_5 reagent, as described in *Chapter 1.6*. In 2018, Wagenknecht's group presented a photocatalytic method for activating SF_6 and successfully transferred SF_5 groups to *α*-methyl- and *α*-phenylstyrenes.[176]

Theoretical investigations of SF_6 show that the SF_6 radical anion formed by one-electron activation can populate several energetic states.[179] From the first excited state of the radical anion, a decomposition into a fluorine radical and an SF_5 anion can be observed. This pathway can result, for example, in the deoxyfluorination or fluorination of inorganic and organic compounds and has been widely investigated.[180] However, pentafluorosulphanylation is not possible via this pathway due to the instability and poor nucleophilicity of the SF_5 anion. Alternatively, the second excited state of the radical anion can instead be populated. When there is an excess electron energy of at least 2 eV, mesolysis can occur in the other direction, affording a fluoride ion and an SF_5 radical.

With these specifications, the Wagenknecht group investigated *N*-phenylphenothiazines as possible organic photocatalysts for the pentafluorosulphanylation of styrenes. The proposed mechanism of the reaction (Scheme 37) begins with the excitation of the catalyst, PTH, with UVA light. Subsequently, a SET of [PTH]* to SF_6 leads to the formation of the SF_6 radical anion in a sufficiently highly energetic state such that it mesolyses to an SF_5 radical and a fluoride ion. The PTH radical cation also formed during the SET can be converted back to the PTH ground state by further excitation with green light and subsequent SET with the alkene substrate. This produces an alkene radical cation, which can react first with the SF_5 radical and then with the fluoride ion to form the product.



Scheme 37: Proposed mechanism of the photocatalytic pentafluorosulphanylation of *α*-phenylstyrene using SF_6.

The product range of the method can be extended by the addition of alcohols or alkynols, but is generally limited to doubly activated styrenes as alkene starting materials.[177-178] Therefore, this project aimed to investigate the exploration of the PTH-catalysed pentafluorosulphanylation strategy to other substrate classes and thus indirectly gather further mechanistic information. Firstly, the conditions known from the literature were to be recreated with our setup. For the pentafluorosulphanylation reactions, Rombach *et al.* use a cooling block with holes for the reaction vessels, which is equipped with an LED chip at the bottom. In addition, an LED ring is installed on the cooling block as a second light source if required (Figure 12, left). Our setup consists of two LED chips, which are placed to the left and right of the reaction vessel, and a fan, which is placed below or behind the reaction vessel to keep the temperature of the reactions as close as possible to room temperature (Figure 12, right).

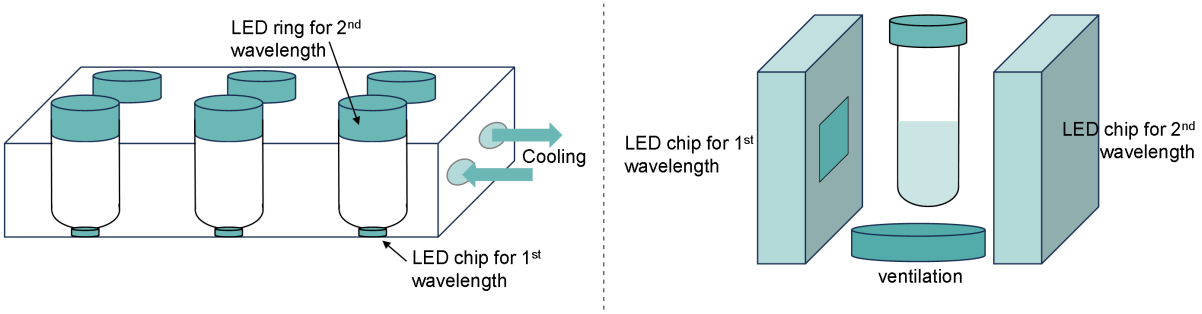
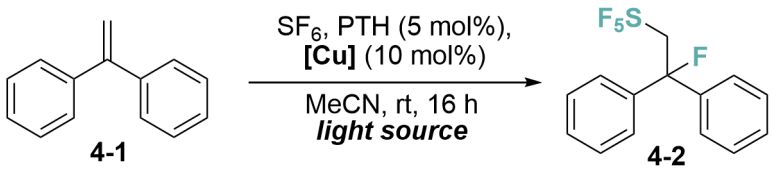


Figure 12: Reaction set-up of the Wagenknecht group (left) and our set-up used for the project (right).

In Wagenknecht's method, a Cu(II) species is used to increase the reaction yield, presenting copper(II) acetylacetonate ($Cu(acac)_2$) as a sufficient additive. For our investigations, however, we initially focussed on the cheaper Cu(II)acetate ($Cu(OAc)_2$). Firstly, we looked for a suitable UVA light source for the reaction between *α*-phenylstyrene **4-1** and SF_6, whereby a Kessil UVA LED proved to be a more suitable light source compared to an LED chip (Table 3, entry 1 & 2). As stated in Wagenknecht's work, the yield is increased by combining the UVA lamp with green light (Table 3, entry 3). To see the influence of $Cu(acac)_2$ in comparison with $Cu(OAc)_2$, a test experiment was also carried out using $Cu(acac)_2$, whereby the ^{19}F NMR yield of pentafluoro(2-fluoro-2,2-diphenylethyl)-λ^6-sulfane **4-2** was increased from 30% (with $Cu(OAc)_2$) to 46% (Table 3, entry 4). The literature yield for the same reaction is 63%, although our setup does not have precise temperature control, suggesting that the temperature fluctuations led to yield losses despite ventilation. Since the ^{19}F NMR yields for both Cu(II) species are in a moderate range, the screening of the different substrate classes was initially carried out with $Cu(OAc)_2$ in order to keep the price of the method lower.

Table 3: Test reactions of *α*-phenylstyrene with SF_6 for the attempted reproduction of Wagenknechts results.



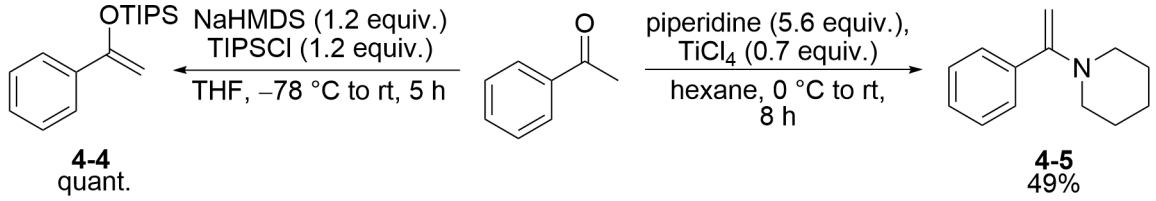
Entry	[Cu]	Light source 1	Light source 2	^{19}F NMR yield[a]
1	$Cu(OAc)_2$	UVA LED chip	--	17%
2	$Cu(OAc)_2$	Kessil UVA LED	--	22%
3	$Cu(OAc)_2$	Kessil UVA LED	green LED chip	30%
4	$Cu(acac)_2$	Kessil UVA LED	green LED chip	46%

[a]using *α,α,α*-trifluorotoluene as the internal standard.

Firstly, substrates with silyl groups were tested for their reactivity with SF_6 under the selected conditions. Here, substrates featuring an activated double bond were explored. An example of such compounds are silyl enol ethers, which could support the abstraction of the fluoride from

the SF_6 radical anion under the established conditions by forming a strong Si–F bond. Additionally, the equilibrium of the mesolysis reaction could be shifted further to the product side (formation of the SF_5 radical) due to the volatility of the formed TMSF.

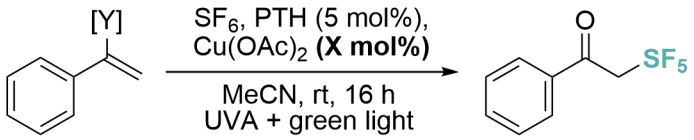
Based on this idea, the commercially available trimethyl((1-phenylvinyl)oxy)silane **4-3a** was chosen as the test substrate. In addition, the triisopropyl((1-phenylvinyl)oxy)silane **4-4** was prepared according to a literature procedure by the Waser group in order to test the influence of the silyl residue on the reactivity of the compound (Scheme 38, left).[181] Enamines could also be of interest for such transformations, as they also exhibit an activated double bond. Therefore, 1-(1-phenylvinyl)piperidine **4-5** was also synthesised using a method known from the literature (Scheme 38, right).[182] In all three cases, the aim was to establish a new method for the synthesis of *α*-SF_5 ketones.

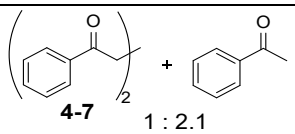
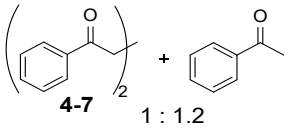
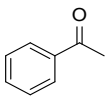


Scheme 38: Synthesis of the TIPS-enol ether according to a procedure of the Waser group and literature conditions for the synthesis of the enamine both starting from acetophenone.

When the general reaction conditions were applied to the TMS enol ether **4-3a**, no SF_5 compounds could be observed in the ^{19}F NMR spectra both with and without copper salt (Table 4, entries 1 & 2). Instead, small amounts of TMSF could be found. In both cases, the ^{1}H NMR spectrum showed the formation of acetophenone and the acetophenone dimer **4-7**, which could have been obtained by the radical combination of two acetophenone radicals. The ratio of the products is 1:2.1 (dimer : monomer), which indicates that the cleavage of the silyl enol ether, due to its instability, could be faster than the activation by light and PTH. Therefore, the reactions were repeated with the more stable TIPS enol ether **4-4** (Table 4, entries 3 & 4). The reaction products in the ^{1}H NMR spectra were identical to the products of the TMS enol ether reactions, although it should be noted that the dimer to monomer ratio changed to 1:1.2. The increased stability of the TIPS enol ether **4-4** indeed seems to have resulted in more acetophenone radicals. However, the ^{19}F NMR spectrum showed no SF_5 groups in either reaction and only small amounts of tri(isopropyl)silylfluoride (TIPSF). The test reactions (with and without Cu(II) species) with the enamine **4-5** led to a complex mixture of products. None of the resulting compounds were fluorinated, as indicated by the ^{19}F NMR spectra, and the main product of the reaction was acetophenone.

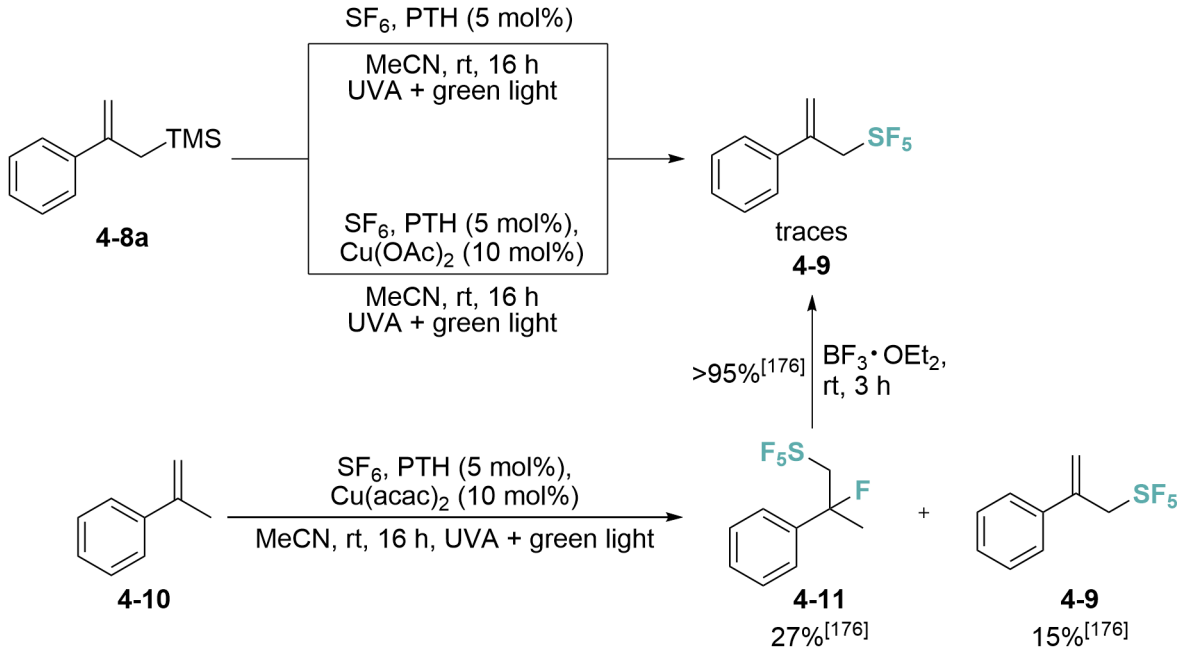
Table 4: Results of the test reactions using silyl enol ethers and enamines as reaction partners for SF_6 to form α-SF_5 ketones.



Entry	[Y]	$Cu(OAc)_2$ [mol%]	^{19}F NMR yield[a]	Observed Products ^1H NMR spectra
1	OTMS	10	--	 **4-7** 1 : 2.1
2	OTMS	--	--	
3	OTIPS	10	--	 **4-7** 1 : 1.2
4	OTIPS	--	--	
5	$N(C_5H_{10})$	10	--	
6	$N(C_5H_{10})$	--	--	

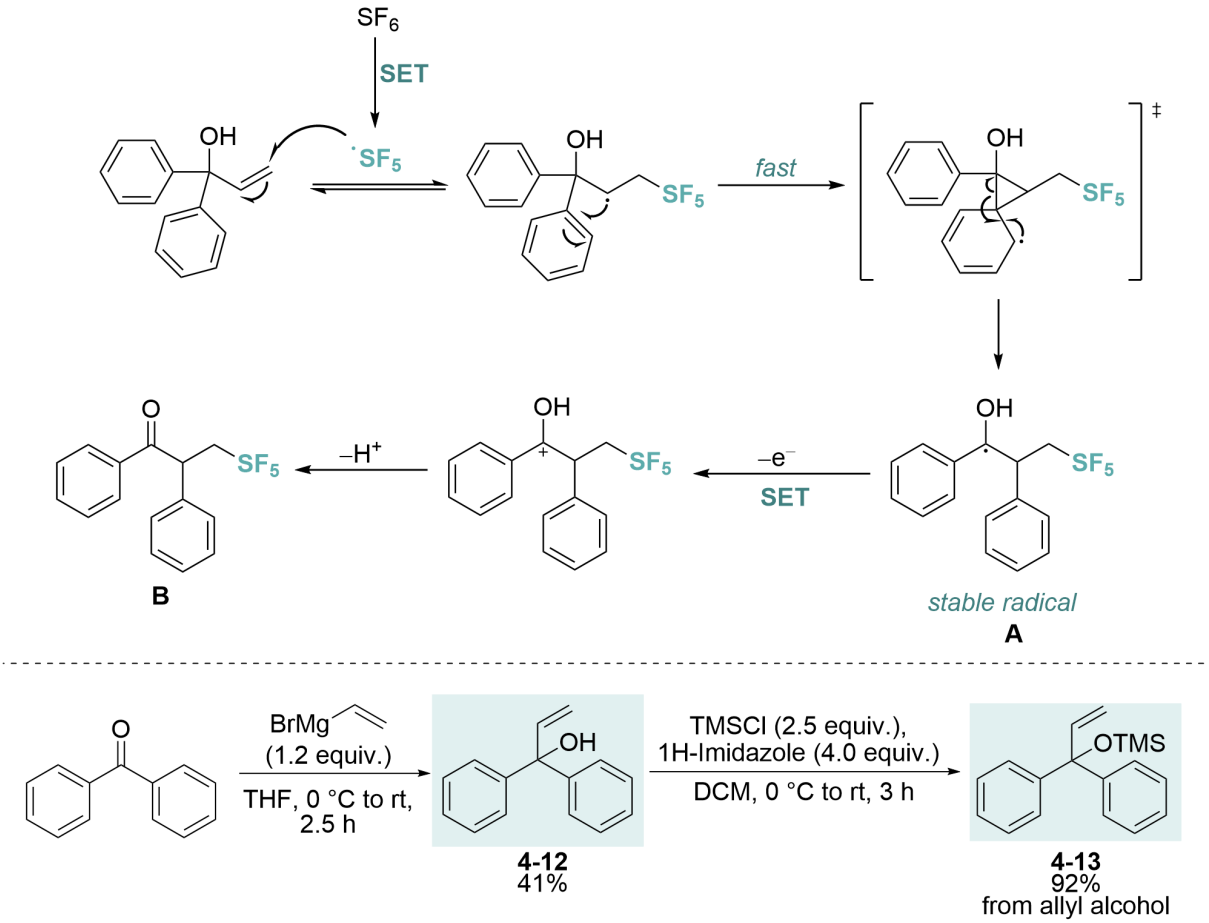
[a]using α,α,α-trifluorotoluene as the internal standard.

To further test the hypothesis of fluoride abstraction using organosilicon compounds, trimethyl(2-phenylallyl)silane **4-8a** was used as a test substrate for the PTH-catalysed pentafluorosulphanylation with SF_6 (Scheme 39, top). The expected product **4-9** of the reaction was known from the literature and could be obtained from α-methylstyrene **4-10** using Wagenknecht's method either directly as a mixture with the SF_5-F addition product **4-11** or starting from the SF_5-F addition **4-11** product by elimination of the vicinal fluoride ion using boron trifluoride diethyl etherate (Scheme 39, bottom).[176] The test experiments with allyl silane **4-8a** led to traces of the desired product **4-9** according to the ^{19}F NMR spectra. However, the proton spectrum for both reactions show that, similar to the silyl enol ethers, the main product of the reaction was the dimer of the allyl radical. The formation of TMSF again indicates the activation of both starting materials.



Scheme 39: Reactions of allyl silane **4-8a** with and without $Cu(OAc)_2$ yielding trace amounts of the desired literature known SF_5 product **4-9** (top). Synthesis of the SF_5 product **4-9** by Rombach *et al.* (bottom).

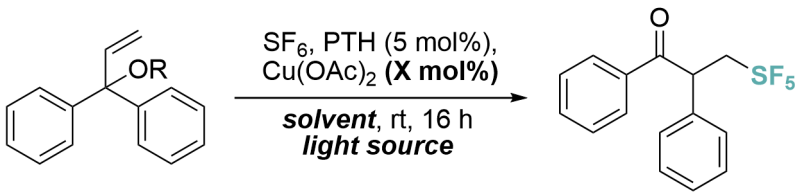
A potential explanation for the low yield of product **4-9** is that addition of the SF_5 radical to the double bond is reversible and that cleavage of the silyl group does not effectively outcompete the reverse process. Therefore, other substrate classes that could suppress *β*-scission of the SF_5 radical by forming stable radical intermediates were tested in further investigations. Allyl aryl alcohols are an interesting substance class for this approach, as they could suppress *β*-cleavage by radical combination of the alkene with the SF_5 radical and subsequent rearrangement to a stable tertiary radical **A** (Scheme 40, top). This could be converted into a *β*-SF_5 ketone **B** by a SET and subsequent deprotonation. A similar reactivity is already literature known for the copper-catalysed trifluoromethylation of allylic alcohols using the Togni-CF_3 reagent.[183] To investigate this theory, 1,1-diphenyl-2-propen-1-ol **4-12** and its TMS-protected version **4-13** were prepared according to procedures known from the literature (Scheme 40, bottom) and tested for their reactivity towards SF_6.[184]



Scheme 40: Concept of the pentafluorosulphanylation of allyl alcohols via stable radical intermediates (top). Synthesis of allyl alcohol **4-12** and TMS-protected allyl alcohol **4-13** (bottom).

Initial test reactions with the allyl alcohol **4-12** were carried out using only a UVA chip to investigate whether activation of the starting material can also be achieved without green light (Table 5, entry 1). Neither activation of SF_6 nor of the starting material could be observed in the ^{19}F and ^{1}H NMR spectra. The next step was to investigate whether the activation and SF_5 radical formation can be supported by fluorine-specific interactions between the SF_6 radical anion and hydrogen bond donors. For this purpose, **4-12** was reacted with SF_6 in a 1:1 mixture of DCM and hexafluoro isopropanol (HFIP) under the influence of PTH and $Cu(OAc)_2$ (Table 5, entry 2). In this case, no signs of activation of SF_6 or **4-12** could be detected in the proton and ^{19}F NMR spectra. To ensure that the lack of green light did not cause the activation to fail, a test reaction was carried out with both light sources and acetonitrile as the solvent, which also did not lead to any reaction (Table 5, entry 3). The test reactions with the TMS-protected allyl alcohol **4-13** were also carried out under the standard conditions with both light sources, with and without $Cu(OAc)_2$ (Table 5, entry 4 & 5). Again, no reaction to the desired SF_5 product **4-14** or related compounds could be observed in both cases, but traces of TMSF and SF_6 decomposition products could be observed in the ^{19}F NMR spectra. However, the proton spectra showed no other signals than those of **4-13**.

Table 5: Approaches and results for the pentafluorosulphanylation of an allyl alcohol and a protected allyl alcohol using different reaction conditions.



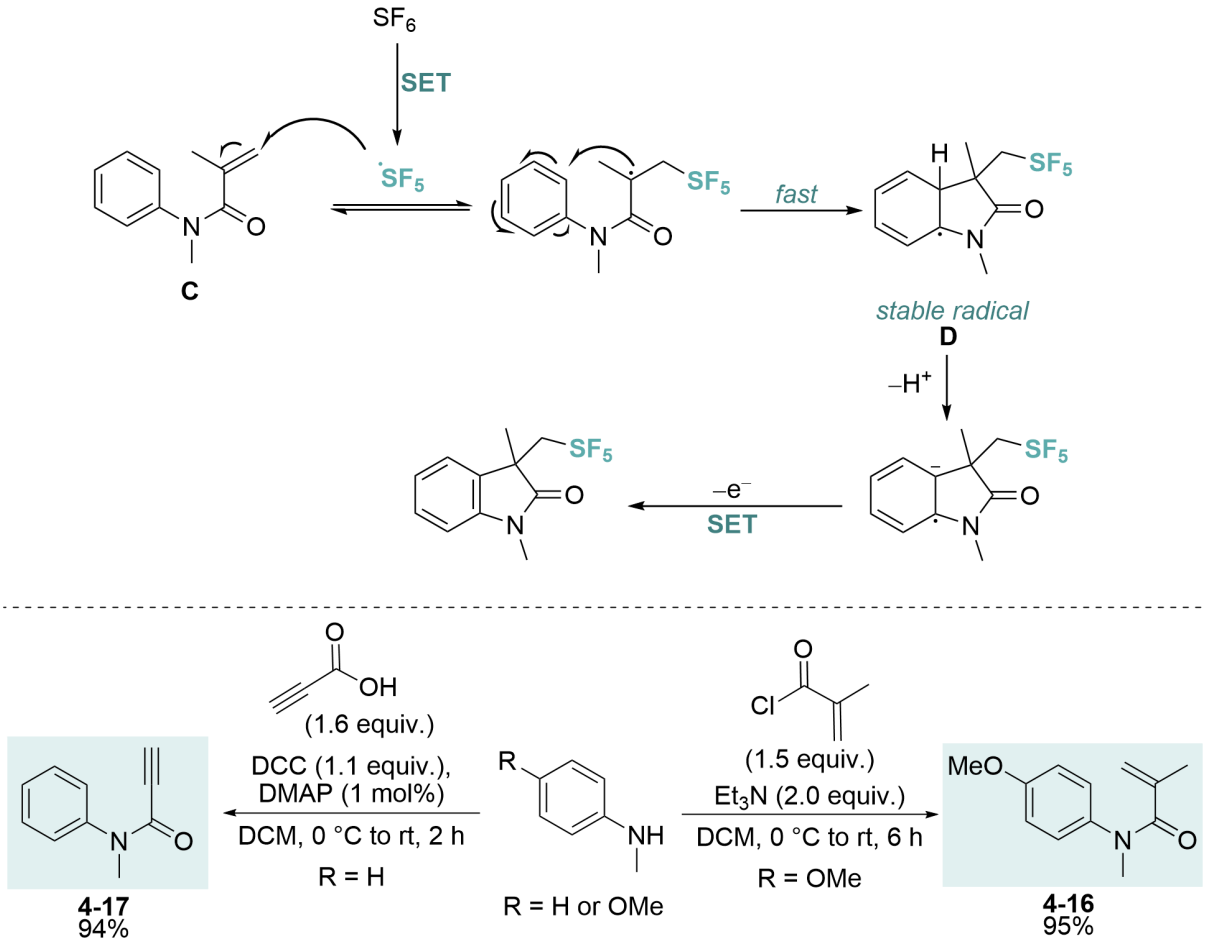
4-12 or **4-13** **4-14**

Entry	R	$Cu(OAc)_2$ [mol%]	Solvent	Light source	^{19}F NMR yield[a]
1	H	10	MeCN	UVA LED chip	--
2	H	10	DCM/HFIP (1:1)	UVA LED chip	--
3	H	10	MeCN	Kessil UVA LED, green LED chip	--
4	TMS	10	MeCN	Kessil UVA LED, green LED chip	--
5	TMS	0	MeCN	Kessil UVA LED, green LED chip	--

[a]using *α,α,α*-trifluorotoluene as the internal standard.

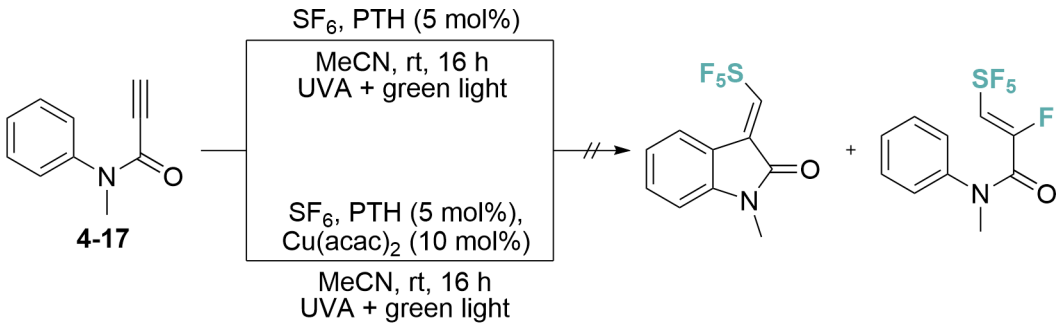
Acrylamides and propiolamides are other substrate classes that may be able to form stable radical intermediates to prevent *β*-cleavage. In the radical pentafluorosulphanylation of acrylamides **C**, for example, the stable radical **D** could be formed by cyclisation and ultimately undergo rearomatisation (Scheme 41, top) similar to the mechanism for the visible light and Lewis acid promoted aryldifluoromethylation of acrylamides presented by Chen *et al*.[185] These substrate classes were also investigated in more detail within the project with regard to their reactivity towards SF_5 radicals. For this purpose, *N*-methyl-*N*-phenylmethacrylamide **4-15** was chosen as the test substrate.

In addition, *N*-(4-methoxyphenyl)-*N*-methylmethacrylamide **4-16**, synthesised by our group's student assistant Armin Ariamajd, and *N*-methyl-*N*-phenylpropiolamide **4-17** were prepared according to procedures known from the literature and also tested (Scheme 41, bottom).[186]



Scheme 41: Concept of the pentafluorosulphanylation of acrylamides via stable radical intermediates (top). Synthesis of *N*-(4-methoxyphenyl)-*N*-methylmethacrylamide and *N*-methyl-*N*-phenylpropiolamide (bottom).

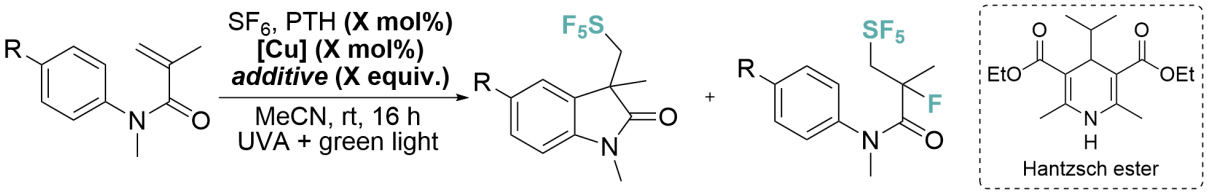
Firstly, the propiolamide **4-17** was reacted with SF_6 under standard conditions, with and without $Cu(acac)_2$ (Scheme 42). No conversion to fluorinated products was observed in the ^{19}F NMR spectra in either case. The proton spectra for both reactions showed only the reactant signals, which is why the focus was then shifted to the acrylamides.



Scheme 42: Reaction conditions of the attempted pentafluorosulphanylation of **4-17**.

The reaction of **4-15** with SF_6 catalysed by PTH resulted in two SF_5-typical doublet-signals for the equatorial fluorine atoms at 67.4 and 70.5 ppm in the ^{19}F NMR spectrum (Table 6, entry 1). The signals could be tentatively assigned to the cyclisation product **4-18a** and the SF_5-F-addition product **4-18b** in the further course of the investigations. This result could also be reproduced for the reaction in the presence of $Cu(OAc)_2$ (Table 6, entry 2).

Table 6: Results of the test reactions and optimisation approaches of the pentafluorosulphanylation of acrylamides using SF_6.



4-15 or **4-16** **4-18a** **4-18b**

Entry	R	PTH [mol%]	[Cu]	Additive [equiv.]	^{19}F NMR yield 4-18a[a]	^{19}F NMR yield 4-18b[a]
1	H	5	--	--	traces	traces
2	H	5	$Cu(OAc)_2$ (10 mol%)	--	traces	traces
3	H	5	$Cu(acac)_2$ (10 mol%)	--	2%	3%
4	H	5	Cu^0 (10 mol%)	--	traces	1%
5	H	20	$Cu(acac)_2$ (10 mol%)	--	--	traces
6	OMe	5	$Cu(acac)_2$ (10 mol%)	--	--	2%
7	H	5	$Cu(acac)_2$ (10 mol%)	BEt_3 (10 mol%)	--	1%
8	H	5	$Cu(acac)_2$ (10 mol%)	$BF_3{\cdot}OEt_2$ (10 mol%)	--	--
9	H	5	--	Hantzsch ester (1.0 equiv.)	--	traces
10	H	5	$Cu(acac)_2$ (10 mol%)	Hantzsch ester (1.0 equiv.)	--	--

[a]using *α,α,α*-trifluorotoluene as the internal standard.

To increase the yield of the reaction and to obtain more information about the products formed, other Cu-sources were tested. Using $Cu(acac)_2$ according to Wagenknecht's protocol, the ^{19}F NMR spectrum of the reaction showed two SF_5 species with signals at 67.4 and 70.5 ppm for the equatorial fluorine atoms and overlapping signals at 84.6 ppm for the axial fluorine atom of the SF_5 group. In addition, a signal was observed at –182.4 ppm which could belong to a fluorine atom vicinal to an SF_5 group. The products were obtained in ^{19}F NMR yields of 2% and 3% under the selected conditions (Table 6, entry 3). Also, Cu^0 was used under the standard conditions leading to small amounts of both products **4-18a** and **b** (Table 6, entry 4). Hence, the following investigations were performed using $Cu(acac)_2$ as the additive. Increasing the amount of PTH during the reaction lead to only trace amounts of the addition product **4-18b**, so the standard conditions remained unchanged during the next optimisation attempts (Table 6, entry 5).

Increasing the electron density of the acrylamide could potentially lead to an increase in its reactivity within the reaction. Therefore, the *para*-methoxy-substituted acrylamide **4-16** was tested for its reactivity towards SF_6 (Table 6, entry 6). One of the two SF_5 products (signal at 67.4 ppm) was observed selectively in the ^{19}F NMR spectrum. The presence of the additional fluoride signal at –182.4 ppm indicates that the addition product **4-18b** was obtained, suggesting that the signal at 70.4 ppm could be indirectly assigned to the cyclisation product **4-18a**. In further investigations to increase the product yields for reactions with the unsubstituted amide **4-15**, the Lewis acids triethylborane (BEt_3) and boron trifluoride diethyl etherate ($BF_3{\cdot}Et_2O$) were used to support the mesolysis step (Table 6, entries 7 & 8). The reaction with BEt_3 did not lead to an increase in yield but to a selective formation of small amounts of product **4-18b**. However, no reaction was observed with $BF_3{\cdot}Et_2O$.

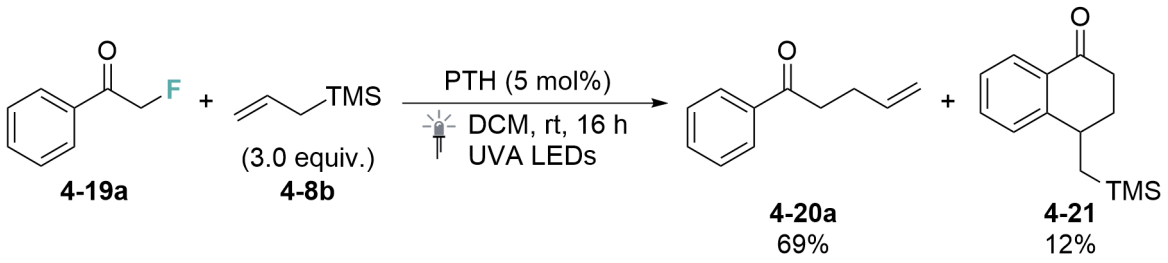
Examining the proton spectra of the reactions, it is noticeable that the starting material appears virtually unaffected and, due to the low yields of SF_5 products, their signals are outweighed by those of the unreacted acrylamide. In order to increase the activation of the amide during the reaction, the Hantzsch ester, diethyl 4-isopropyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate, was added to the reaction as a reductant. Hantzsch esters are generally used for such applications in the literature.[187] However, the use of the Hantzsch ester in the reaction without a Cu(II) source only led to traces of product **4-18b** (Table 6, entry 9). The reaction with $Cu(acac)_2$ did not lead to any reaction to SF_5 products but resulted in a formation of Cu^0 on the glass (Table 6, entry 10).

These results give more insight into the method’s potential applications to other substrates. Especially the tests with silylated reaction partners such as allyl silane **4-8a** indicate that the F-abstraction concept towards SF_5 radicals might prove a valuable approach to pentafluorosulphanylated compounds. The reaction of acrylamides under the selected conditions and the formation of cyclisation product **4-18a** also shows that the use of substrates

that can form stable radical intermediates could be considered. The formation of SF_5-F addition product **4-18b** suggest that the double bond of the acrylamides is reactive enough for the reaction. However, more research must be done to enable the formation of SF_5 products in reasonable yields.

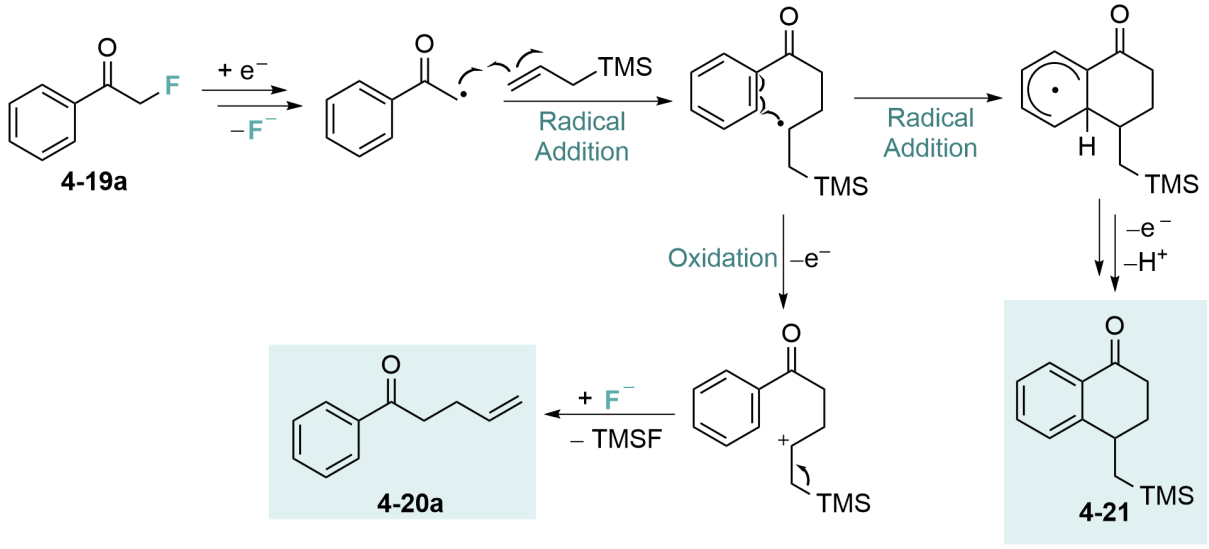
4.2 Photoredox Catalytic C-F Activation of *α*-Fluoroacetophenones

As described in *Chapter 1.2.2*, a growing interest in C–F bond activation can be observed over the past decades. Especially the investigation of fluorine specific interactions and their influence on C-F activation reactions exhibits an academic challenge in this context. Therefore, this project aimed to use fluorine specific interactions to emphasise C–F bond activations and access new pathways towards synthetically interesting building blocks. Despite being gratefully studied these activation processes are conceptually difficult and often require the aid of Lewis acids to overcome the high bond strength of the C–F bond.[188] Within the preliminary work for the project, Dr. Stefan Dix and Dr. Matthew N. Hopkinson investigated the influence of Lewis acids on photocatalytic C–F bond activation reactions of *α*-fluoroacetophenones. However, using PTH as the catalyst, higher yields were observed without the use of a Lewis acid. During further studies of the reaction of *α*-fluoroacetophenone **4-19a** with allyltrimethylsilane **4-8b** under PTH catalysis, an unexpected side-product still bearing the TMS-moiety was observed (Scheme 43). The main product **4-20a** was obtained in 69% crude ^{1}H NMR yield and represents the expected C–C coupling product upon elimination of TMSF. Side product **4-21**, on the other hand, was found to be the product of the cyclisation reaction with preservation of the C–Si bond and was observed in 12% crude ^{1}H NMR yield. These results show an interesting and unexpected chemoselectivity within this reaction. Therefore, the focus of the project was shifted towards the investigation of a potential explanation for the observed chemoselectivity and conditions leading to the different products. Additionally, the preliminary work revealed reproducibility problems for the results with PTH as catalyst, therefore the project was to be further tested with other catalysts and light sources to ensure reproducibility.



Scheme 43: Results by Dr. Stefan Dix and Dr. Matthew N. Hopkinson for the reaction of **4-19a** with **4-8b** under PTH-catalysis yielding the elimination and cyclisation products **4-20a** and **4-21**.

The proposed mechanism for the formation of the different products of the reaction begins with a SET of the light-activated catalyst onto the *α*-fluoroacetophenone, whereby the C–F bond would be cleaved and an acetophenone radical formed (Scheme 44). Subsequently, the radical addition of the acetophenone radical to the allyltrimethylsilane would lead to a *γ*-radical of the addition product. This radical could further react in two pathways to form products **4-20a** or **4-21**. The oxidation of the *γ*-radical to the *γ*-cation and subsequent fluoride-induced cleavage of the TMS residue would lead to product **4-20a**. Alternatively, radical addition with the aromatic backbone of the acetophenone could give the cyclic radical, which would lead to the cyclic product **4-21** through oxidation and deprotonation.



Scheme 44: Proposed mechanism for the reaction of **4-19a** with **4-8b** under PTH-catalysis yielding the elimination and cyclisation products **4-20a** and **4-21**.

Within the thesis, I worked on the investigation towards efficient conditions of the elimination reaction to product **4-20a**. In addition, my colleague M.Sc. Arushi Garg was responsible for the further development of the cyclisation reaction.

Beginning with the reaction conditions of Dr. Stefan Dix, the optimisation of the method towards elimination product **4-20a** was investigated first. The attempts to reproduce the result from Table 7, entry 1 (Dr. Stefan Dix's result) did not lead to comparable ^{1}H NMR yields, even when using UVA lamps of different intensities, with the maximum ^{1}H NMR yield being 35% (Table 7, entries 2 & 3). In the next step, the reactivity of *α*-fluoroacetophenone was compared with other *α*-haloacetophenones. The reaction of *α*-chloroacetophenone with allyltrimethylsilane selectively led to cyclisation product **4-21** (Table 7, entry 4), whereas *α*-bromoacetophenone led to low ^{1}H NMR yields of 14% for **4-20a** and 4% for product **4-21** (Table 7, entry 5). The optimisation experiments with THF and diethyl ether as solvents only led to complex product mixtures (Table 7, entry 6 & 7). The choice of catalyst was then evaluated and $Ru(bpy)_3(PF_6)_2$ and *fac*-$Ir(ppy)_3$ were tested as photocatalysts. Both catalysts can be excited with UV and

visible light.[189] No reaction was observed in the reaction when $Ru(bpy)_3(PF_6)_2$ was used under UVA irradiation (Table 7, entry 8). In contrast, the reaction with *fac*-$Ir(ppy)_3$ under UV light gave 56% ^{1}H NMR yield of product **4-20a** and only small amounts (6%) of product **4-21** (Table 7, entry 9). Changing to blue light in the iridium-catalysed reaction led to a further increase in the crude ^{1}H NMR yield of **4-20a** to 78% (Table 7, entry 10). In direct comparison, only a crude ^{1}H NMR yield of 47% was obtained for product **4-20a** when PTH was used under blue light irradiation (Table 7, entry 11).

Table 7: Optimisation of the reaction of *α*-halogenated acetophenone with allyltrimethylsilane towards the elimination product **4-20a** also yielding the cyclisation side product **4-21**.

4-8b **4-20a** **4-21**

Entry	X	Catalyst	Solvent	Light source	^{1}H NMR yield 4-20a[a]	^{1}H NMR yield 4-21[a]
1	F	PTH	DCM	UVA LED chip	69%	12%
2	F	PTH	DCM	UVA Lamp	32%	4%
3	F	PTH	DCM	Kessil UVA LED	35%	10%
4	Cl	PTH	DCM	UVA Lamp	--	55%
5	Br	PTH	DCM	UVA Lamp	14%	4%
6	F	PTH	Et_2O	UVA Lamp	complex mixture	
7	F	PTH	THF	UVA Lamp	complex mixture	
8	F	$Ru(bpy)_3(PF_6)_2$	DCM	UVA Lamp	--	--
9	F	*fac*-$Ir(ppy)_3$	DCM	UVA Lamp	56%	6%
10	**F**	***fac*-Ir(ppy)$_3$**	**DCM**	**Kessil blue LED**	**78%**	**7%**
11	F	PTH	DCM	Kessil blue LED	47%	3%

[a]with CH_2Br_2 as the internal standard.

Once a suitable catalyst-light combination had been found, the other parameters of the current standard conditions (Table 7, entry 10 or Table 8, entry 1) were further optimised. The reduction of the catalyst amount to 2.5 mol% resulted in a significant loss of ^{1}H NMR yield (Table 8, entry 2). The change to MeCN as the solvent also resulted in a loss of yield (Table 8, entry 3). Reducing the amount of silane from 3 to 2 equivalents showed negligible changes in yield when the reaction was conducted in MeCN, however, it decreased to only 36% with a silane

amount of 1.1 equivalents (Table 8, entry 4 & 5). Based on this observation, solvent optimisation was performed with 2 equivalents of silane **4-8b**. However, only a yield of 60% could be achieved in the standard solvent DCM under these conditions (Table 8, entry 6). Other solvents tested with 2 equivalents of silane were also unable to achieve or exceed the yields of DCM with 2 or 3 equivalents of silane. DMSO showed a complete inversion of the selectivity of the reaction towards the cyclisation product **4-21** (Table 8, entry 7), whereas THF and diethyl ether yielded only small amounts of both products (Table 8, entry 8 & 9). Finally, the method was performed both without a catalyst (Table 8, entry 10) and under exclusion of light (Table 8, entry 11). Neither test reaction resulted in any reaction or activation of the starting materials, indicating that both the blue light and the catalyst are required for the process.

Table 8: Optimisation of the reaction of *α*-fluoroacetophenone with allyltrimethylsilane towards the elimination product **4-20a** also yielding the cyclisation side product **4-21**.

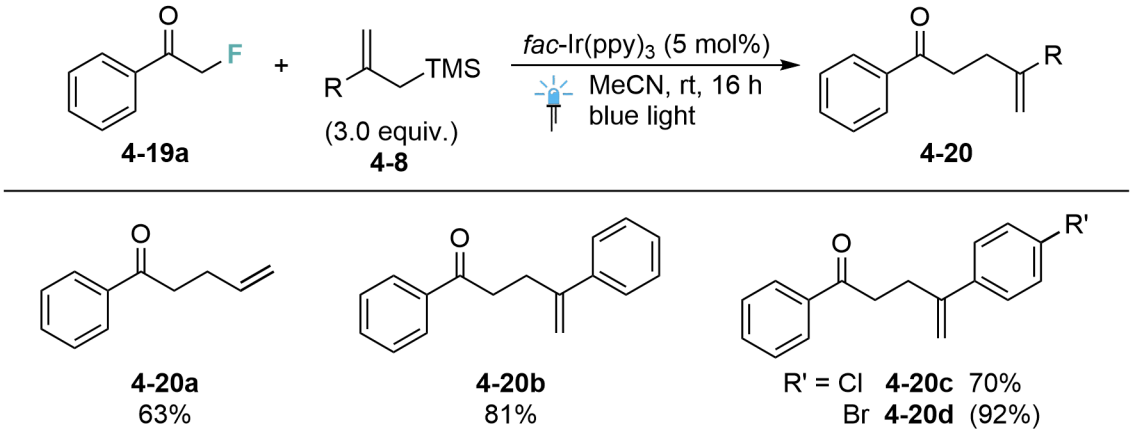
4-19a **4-8b** **4-20a** **4-21**

Entry	Silane [equiv.]	Catalyst amount [mol%]	Solvent	^{1}H NMR yield 4-20a[a]	^{1}H NMR yield 4-21[a]
1	**3**	**5**	**DCM**	**78%**	**7%**
2	3	2.5	DCM	40%	21%
3	3	5	MeCN	43%	16%
4	2	5	MeCN	42%	15%
5	1.1	5	MeCN	36%	9%
6	2	5	DCM	60%	5%
7	2	5	DMSO	20%	60%
8	2	5	THF	10%	12%
9	2	5	Et_2O	traces	4%
10	3	--	DCM	--	--
11[b]	3	5	DCM	--	--

[a]with CH_2Br_2 as the internal standard. [b]no light/ in the dark.

The optimised conditions were then used to perform a proof-of-concept analysis with four different allyl silanes **4-8a-d** (Scheme 45). The reaction with the test substrate allyltrimethylsilane **4-8b** resulted in an isolated yield of 63% for **4-20a**. In addition, the reaction of trimethyl(2-phenylallyl)silane **4-8a** with **4-19a** gave **4-20b** in an isolated yield of 81% under the optimised conditions. The reaction of *para*-halogenated trimethyl(2-phenylallyl)silane **4-8c**

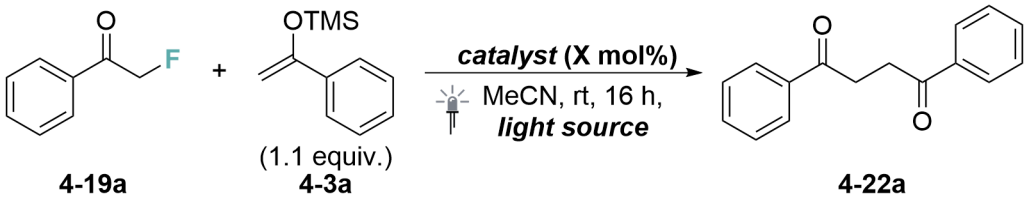
and **4-8d** also gave good to very good crude and isolated yields for the products **4-20c** and **4-20d**.



Scheme 45: Proof-of-concept analysis of the iridium-catalysed coupling of *α*-fluoroacetophenone **4-19a** and allyl silanes **4-8**. Crude ^{1}H NMR yields with CH_2Br_2 as the internal standard are given in parentheses.

The second part of the project focused on the reaction of *α*-fluoroacetophenones **4-19** with silyl enol ethers **4-3**. The starting point for the optimisation of the method was the reaction of *α*-fluoroacetophenone **4-19a** with 1.1 equivalents of trimethyl((1-phenylvinyl)oxy)silane **4-3a** in MeCN under PTH catalysis (5 mol%) and UVA irradiation (Table 9, entry 1). The desired 1,4-diketone **4-22a** was obtained in a ^{1}H NMR yield of 55%, however, changing to blue light drastically reduced the ^{1}H NMR yield to 23% (Table 9, entry 2). Based on the positive results with *fac*-Ir(ppy)$_3$ in the previously investigated elimination reaction, a test experiment was performed using *fac*-Ir(ppy)$_3$ under irradiation with blue light resulting in a ^{1}H NMR yield of 90% (Table 9, entry 3). Reducing the amount of catalyst to 2 mol% only had a slight effect on the efficiency of the reaction (Table 9, entry 4). Nevertheless, all further scope reactions were performed with 5 mol% catalyst to avoid yield fluctuations due to different substitution patterns. As already tested for the elimination reaction, the investigated method was performed both without a catalyst (Table 9, entry 5) and under exclusion of light (Table 9, entry 6). Both test reactions resulted in no reaction or activation of the starting materials, allowing for the full recovery of **4-19a**. This results, again, indicates that both the blue light and the catalyst are required for the process.

Table 9: Optimisation of the reaction of *α*-fluoroacetophenone with trimethyl((1-phenylvinyl)oxy)silane towards the 1,4-diketone **4-22a**.



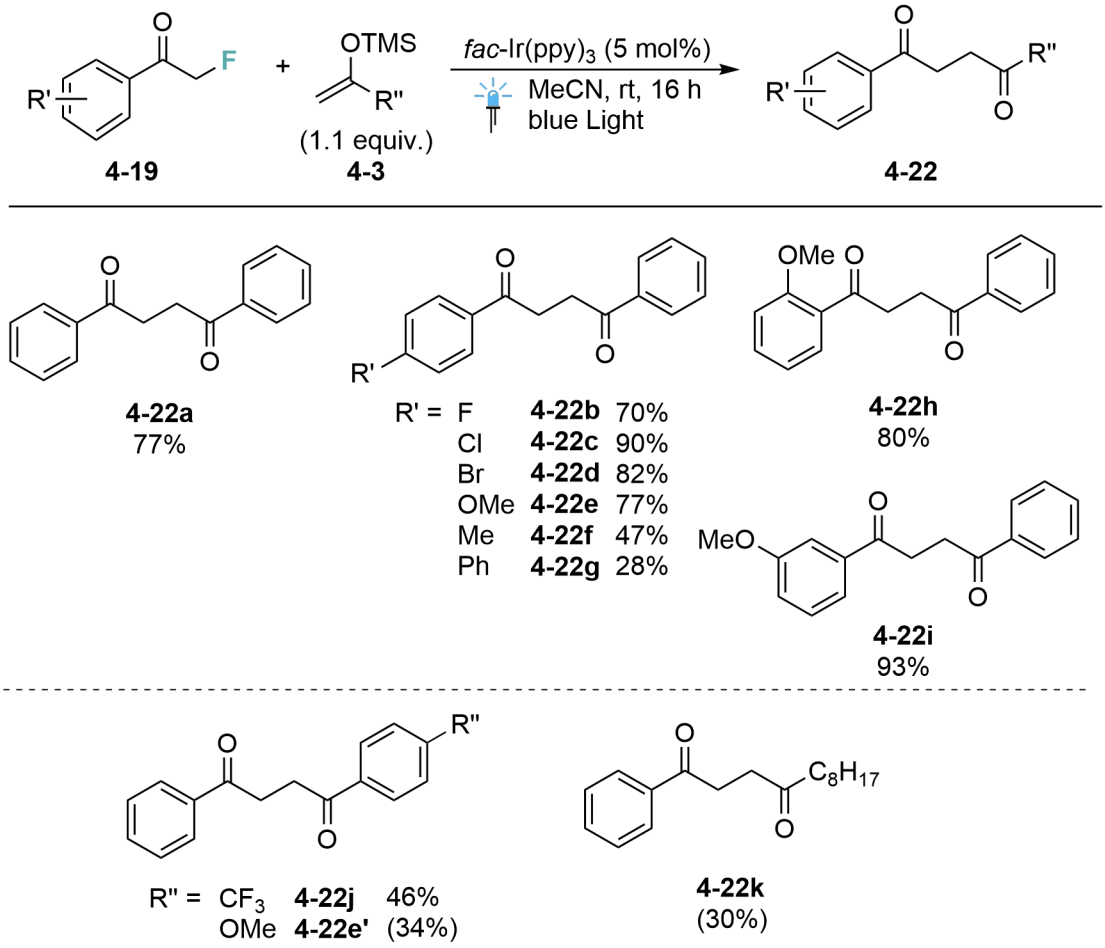
4-19a (1.1 equiv.) **4-3a** **4-22a**

Entry	Catalyst	Catalyst amount	Light source	^{1}H NMR yield 4-22a[a]
1	PTH	5 mol%	Kessil UVA LED	55%
2	PTH	5 mol%	Kessil blue LED	23%
3	***fac*-Ir(ppy)$_3$**	**5 mol%**	**Kessil blue LED**	**90%**
4	*fac*-Ir(ppy)$_3$	2 mol%	Kessil blue LED	85%
5	--	5 mol%	Kessil blue LED	--
6	*fac*-Ir(ppy)$_3$	5 mol%	--	--

[a]with CH_2Br_2 as the internal standard.

After the optimisation was completed, the scope of the method was examined. Different *α*-fluoroacetophenones **4-19** as well as silyl enol ethers **4-3** were reacted to obtain the desired 1,4-diketones **4-22**. The resulting scope of the reaction comprises 11 products with moderate to very good yields (Scheme 46). The product **4-22a** of the optimisation process was obtained in an isolated yield of 77%. In addition, yields of 28% to 90% were obtained for the reaction of **4-3a** with various *para*-substituted *α*-fluoroacetophenones **4-19b-g**. Both electron-withdrawing and electron-donating substituents were tolerated. Reactions with *ortho*- and *meta*-substituted *α*-fluoroacetophenones **4-19h** and **4-19i** also gave good to very good yields.

The method was also tested for its robustness towards the reaction of **4-19a** with different silyl enol ethers **4-3b-d**. An isolated yield of 46% was achieved for 1,4-diketone **4-22j** from the reaction of **4-19a** with the CF_3-substituted silyl enol ether **4-3b**. The reaction of **4-19a** with a MeO-substituted silyl enol ether **4-3c** and an enol ether **4-3d** starting from 1-decanone gave ^{1}H NMR yields of 34% and 30%.



Scheme 46: Scope of the iridium-catalysed coupling of substituted *α*-fluoroacetophenones **4-19** and trimethyl((1-phenylvinyl)oxy)silane **4-3a** (top) and of the reaction of *α*-fluoroacetophenone **4-19a** with different silyl enol ethers **4-3** (bottom). Crude ^{1}H NMR yields with CH_2Br_2 as the internal standard are given in parentheses.

Overall, this project opens up new paths to synthetically interesting polyfunctionalised compounds, whereby the methods do not require Lewis acids for the activation of the C–F bond. Both the method of the defluorinative coupling of *α*-fluoroacetophenones with allyl silanes and the reaction of *α*-fluoroacetophenones with silyl enol ethers can be performed using the photocatalyst *fac*-Ir(ppy)$_3$ without further additives. Additionally, a solvent-induced selectivity of the allyl silane reaction was observed. Using DMSO as a solvent, an almost complete inversion of the product ratio to the cyclisation product **4-21** was found. In contrast, other less hydrophilic solvents favoured the formation of the elimination product. With these observations, further discoveries and investigations could be accessed to gain deeper insights into the reaction behaviour of organically bound fluorine atoms, as well as novel pathways towards synthetically relevant non-fluorinated compounds.

5 Summary and Outlook

Fluorinated compounds play an important role in industry and research and have become an essential part of everyday life due to their wide range of applications and distinctive properties. For example, the number of fluorinated pharmaceuticals and agrochemicals has increased rapidly in recent decades. Despite the great application potential of heteroatomic per- and polyfluorinated groups, monofluorinated and trifluoromethylated compounds still dominate (Figure 13). Of the over 400 approved agrochemicals, only 7.0% are OR_F and 5.5% are SR_F compounds.[7b] For pharmaceuticals, this number is even lower with 1.9% (OR_F) and 0.8% (SR_F).[7a] One reason for this trend could be the still limited synthetic access to these groups and their direct introduction into organic molecules, especially for OR_F-substituted compounds. The main focus of this work was to investigate and develop new reagents and methods for the introduction of fluorinated groups. Another goal was to develop both laboratory and industrially attractive methods, whereby environmental aspects, such as the PFAS problem, were not to be disregarded.

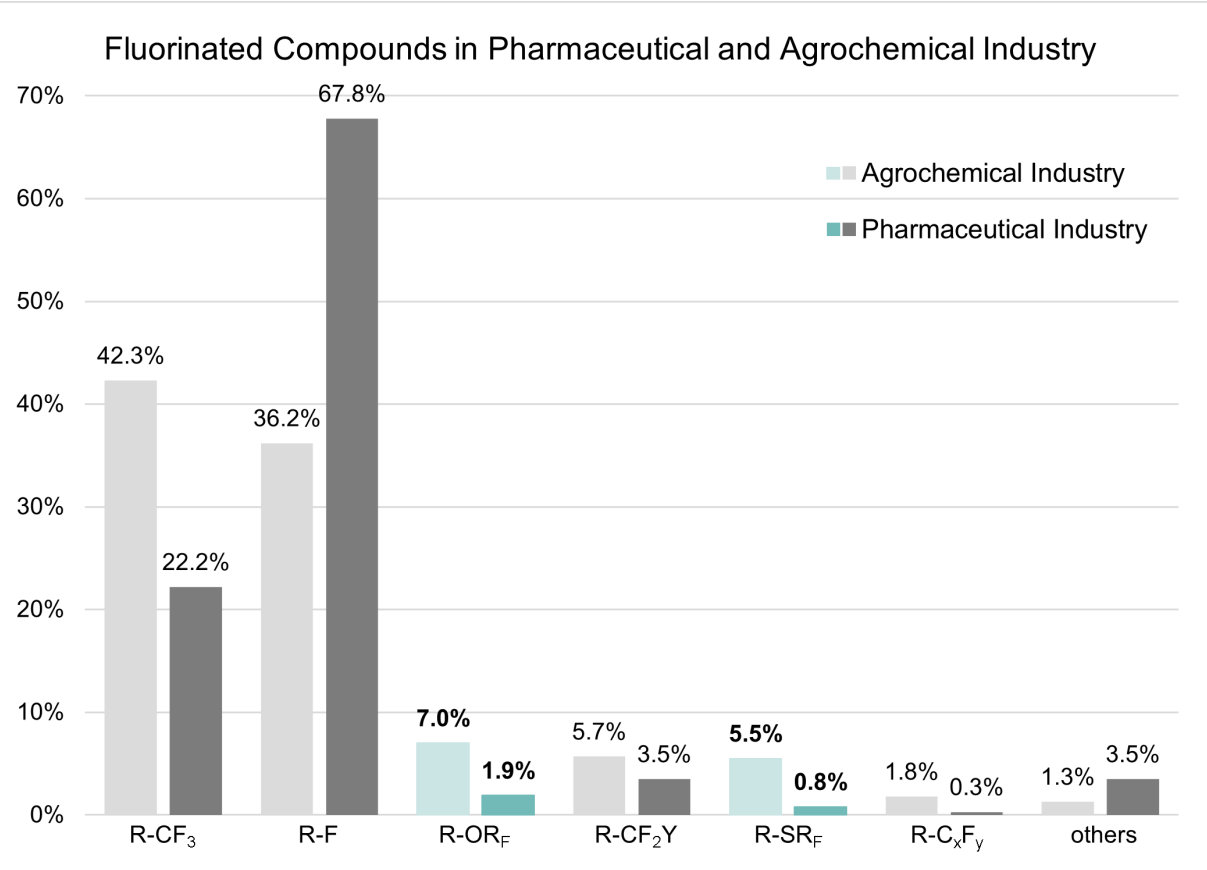
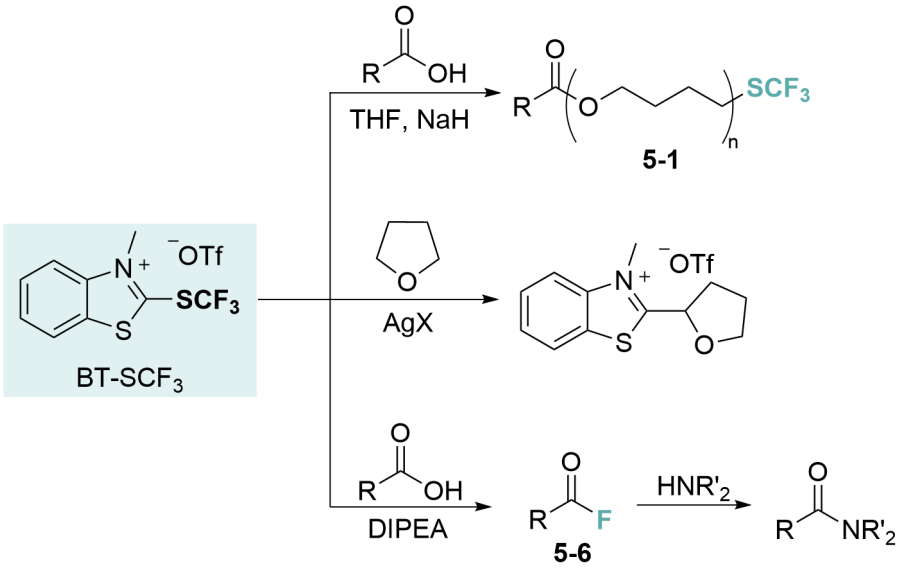


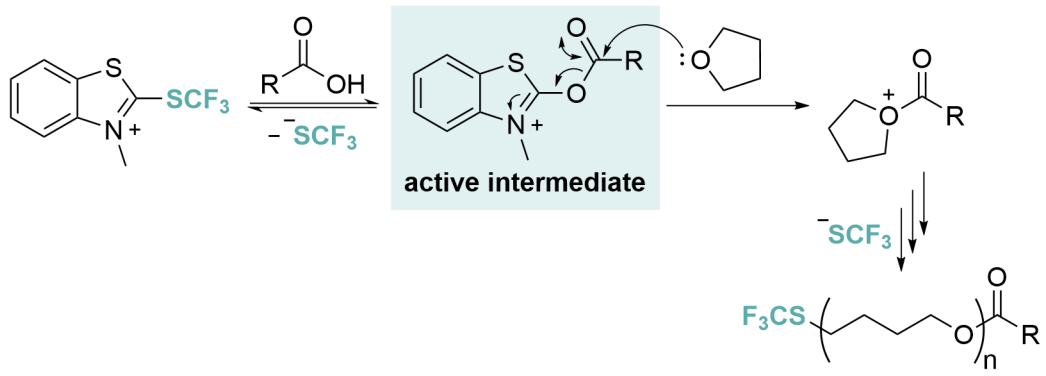
Figure 13: Distribution of fluorination patterns and fluorinated groups in the pharmaceutical and agrochemical industry. The raw data for the diagram originates from **Ref. 7a** (Fig. 4) and **7b** (Fig. 6) and has been summarised in one figure for simplified visualisation.

The first project package covered the benzothiazolium reagents presented by the Hopkinson group. These were to be used as bench-stable and easy-to-handle reagents both for the introduction of SCF_3 and other SR_F groups and as fluorination reagents (Scheme 47).



Scheme 47: Overview of the BT-projects investigated in this thesis. BT-SCF_3 can, in the presence of carboxylates, be used for the ring-opening polymerisation of THF resulting in polymeric trifluoromethylthioethers. THF can also be *α*-deprotonated with BT-reagents and silver(I)species. Changing the solvent and base of the polymerisation reaction allows the *in situ* formation of acyl fluorides.

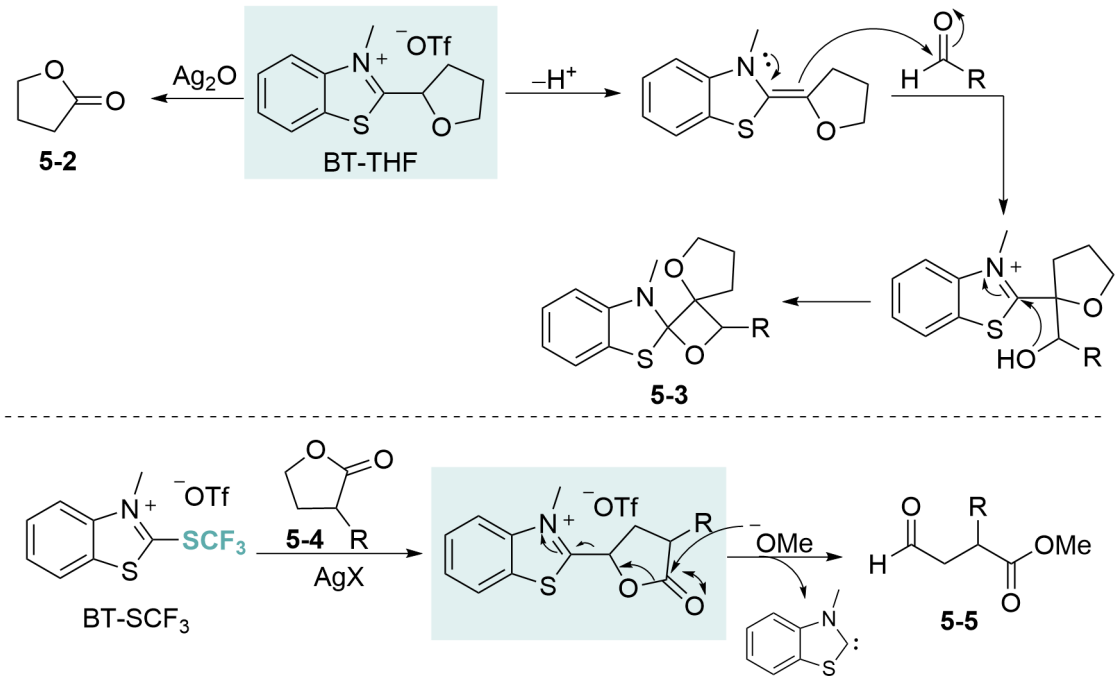
In the presence of carboxylic acids, BT-SCF_3 could be used for the ring-opening polymerisation of THF for the synthesis of trifluoromethylthioethers **5-1** (see *Chapter 3.1*). Mechanistic investigations of the reaction indicate that the activation of THF could take place via a Lewis acidic intermediate of the reaction of BT-SCF_3 with the carboxylate. Therefore, experimental and quantum chemical methods were used to determine the Lewis acidity of the BT-reagents, which both indicated a comparatively low Lewis acidity of BT-SCF_3 and related benzothiazolium salts and further supported the activation process postulated for the reaction (Scheme 48). The ring-opening polymerisation was tested for its tolerance to different substituted benzoic acids as reaction partners and showed good results for the polymerisation reactions. However, electron-withdrawing substituents on the carboxylate suppressed the THF activation.



Scheme 48: Proposed mechanism of the ring-opening polymerisation of THF using BT-SCF_3.

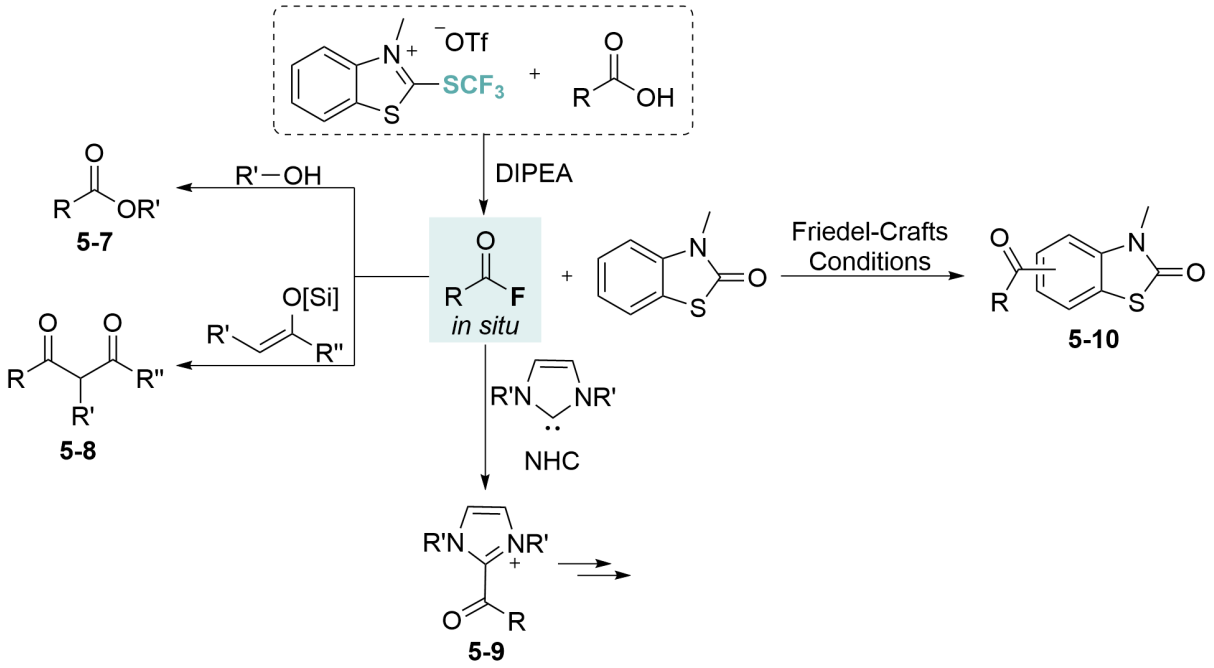
Overall, the method is not selective, with polymers with chain lengths of 2 to 33 monomer units being observed. In further work, deeper insight into the formation of long-chain polymers would be of interest, as these could offer potential for specific applications. Structurally similar compounds are already being investigated for medical applications.[190] Furthermore, studies with other cyclic oxygen compounds could be investigated under the reaction conditions. Initial experiments with epoxides within the work showed no reaction to trifluoromethylthiolated compounds. However, traces of a potential ring-opening species were observed while reinvestigating the reaction with tetrahydropyran (THP). A more in-depth investigation of different ring sizes could also provide information on further mechanistic features of the reaction.

An interesting side product was also discovered within the THF ring-opening project: BT-THF. This benzothiazolium salt is formed in small quantities during the reaction of BT-reagents with THF at elevated temperatures and can also be obtained in yields of up to 80% by using silver(I) oxide as an additive. The molecular structure in the solid state of the compound indicates a comparatively stable C–C bond between the benzothiazolium residue and the *α*-position of THF. However, BT-THF could be oxidised with the aid of Ag_2O in initial test reactions to form γ-butyrolactone **5-2**, which indicates that the compound can be activated (Scheme 49, top). Structurally, BT-THF is almost reminiscent of the precursor of a Breslow intermediate, the key acyl anion equivalent implicated in aldehyde umpolung reactions catalysed by *N*-heterocyclic carbenes (NHCs).[191] Deprotonation of BT-THF could give rise to an active intermediate that could react mechanistically equivalent to Breslow intermediates with aldehydes, for example, to form spiro compounds **5-3**. It would also be interesting to investigate other cyclic oxygen compounds in this context. For example, the *α*-deprotonation of substituted lactones **5-4** could lead to active or easily activated salts (Scheme 49, bottom). These could react with various nucleophiles to generate polyfunctionalised products **5-5** that could be used in total synthesis.



Scheme 49: Oxidation of BT-THF to γ-butyrolactone and potential use of BT-THF as pre-Breslow intermediate for its reaction with aldehydes towards spiro compounds (top). Reaction of BT-SCF_3 with lactones and follow-up chemistry towards polyfunctionalised building blocks (bottom).

Further investigation of the BT-reagents focussed on their potential use as deoxyfluorination reagents. As part of this study, a method for the synthesis and *in situ* application of acyl fluorides **5-6** was developed (see Scheme 47 and *Chapter 3.2*). The reaction of BT-SCF_3 and other BT-SR_F reagents with carboxylic acids under basic conditions gives access to acyl fluorides in high ^{19}F NMR yields. In general, acyl fluorides are versatile and increasingly used for various C–C, C–N and C–O bond formations.[192] In this project, the reaction of acyl fluorides with amines was primarily investigated, whereby fourteen amides of varying complexity, as well as two dipeptides, were synthesised in good to very good yields under one-pot conditions starting from carboxylic acids. Mechanistic investigations also showed that the BT-reagents can be used sub-stoichiometrically, as the reagents are able to provide two equivalents of fluoride ions. This could be utilised in further studies to make the method more sustainable and atom-economical. The *in situ* concept could be applied to other reaction partners, whereby the reduction of reagent amount should also be investigated further (Scheme 50).



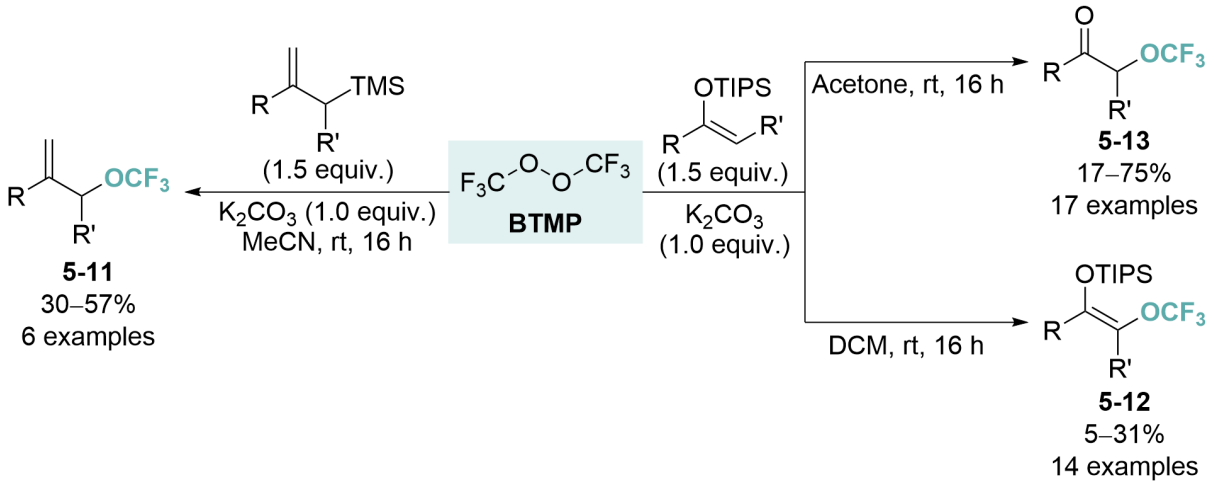
Scheme 50: Potential reaction partners of acyl fluorides formed *in situ* by the reaction of BT-SCF_3 with carboxylic acids under basic conditions. The dual use of BT-reagents within a deoxyfluorination and subsequent Friedel-Crafts type reactions offers sustainable synthesis of acylated benzothiazolones.

For example, the one-pot reaction of BT-SCF_3 with carboxylic acids and alcohols under basic conditions with acyl fluorides as reactive intermediates could yield esters **5-7**. Similar conditions have been used in the literature for other fluorinating agents, but these methods required the reagents in (super-)stoichiometric amounts.[193] Silyl enol ethers could also serve as interesting reaction partners for acyl fluorides, whereby 1,3-diketones **5-8** would be formed. Here again, the reduced reagent quantity could enable sustainable access to these compounds and the *in situ* formation of the acyl fluorides could enable a preparatively simple procedure compared to literature-known methods.[194] *N*-heterocyclic carbenes (NHC) are currently gaining interest due to their wide range of applications in the field of photocatalysis.[195] The combination of acyl fluorides with NHC catalysts enables a large number of interesting and complex transformations. So far, however, isolated acyl fluorides, which can be prone to decomposition, have been used for this purpose. The method developed in this work could be used to achieve acyl azolium intermediates **5-9** directly and in one step.

Even though BT-reagents have many advantages, such as easy handling or the controlled release of SR_F^- and F^-, the BT-backbone leads to significant amounts of waste. On the basis of the acyl fluoride project, a method could be developed to utilise this backbone as a reaction partner to generate acylated benzothiazolones **5-10**. In the first step, the acyl fluoride and the benzothiazolone could be formed as presented in this work and then reacted under Friedel-Crafts conditions. The products of this reaction are important building blocks for synthesis and are investigated in medicinal chemistry, for example, due to their lipid-lowering properties.[196]

With this method, the benzothiazolium salts could fulfil a dual use and the benzothiazolone formed in the reaction could be effectively recycled to generate synthetically important compounds.

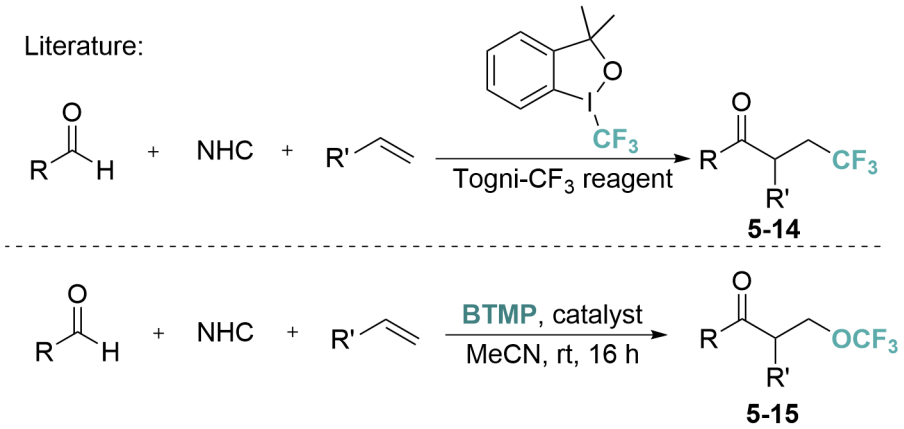
The second part of the thesis focussed on the use of gaseous reagents and investigation of potential industrially interesting methods for the direct introduction of fluorinated groups. In the first part, the introduction of OCF_3 groups using bis(trifluoromethyl)peroxide (BTMP) was investigated based on the work of Dr. Stefan Dix. His work enabled the direct trifluoromethoxylation of (hetero)aromatic compounds with the aid of BTMP and a catalyst.[141] The project presented here was intended to extend this method to non-aromatic multiple bonds. The project resulted in three methods using silylated compounds with BTMP for the synthesis of aliphatic and alkenic OCF_3 compounds (see *Chapter 3.3*). Notably, the reactions do not require an activator or catalyst, as the starting material appears to activate the reagent itself. The reaction of BTMP with allyl silanes led to allyl OCF_3 compounds **5-11** in moderate to good yields, with this method being the first direct and radical one to produce such a structural motif (Scheme 51, left).



Scheme 51: Overview of the activator-free direct trifluoromethoxylations of activated alkenes using BTMP as the OCF_3 radical source presented in this work. The reaction of BTMP with allyl silanes offers access to underrepresented allyl-OCF_3 compounds **5-11** and silyl enol ethers show a solvent switchable reactivity towards trifluoromethoxylated silyl enol ethers **5-12** or *α*-OCF_3 ketones **5-13**.

In contrast, the reaction of BTMP with silyl enol ethers led to either trifluoromethoxylated silyl enol ethers **5-12** in moderate yields or *α*-trifluoromethoxylated ketones **5-13** in moderate to good yields, depending on the choice of solvent (Scheme 51, right). All methods showed a good functional group tolerance and allow the direct synthesis of previously underrepresented compounds. Furthermore, the trifluoromethoxylated ketones **5-13** and silyl enol ethers **5-12** were examined by single crystal X-ray diffraction. For the silyl enol ethers **5-12**, the *Z*-isomer was identified as the main product of the reaction on the basis of crystallographic data and with the aid of nuclear Overhauser effect (NOE) experiments.

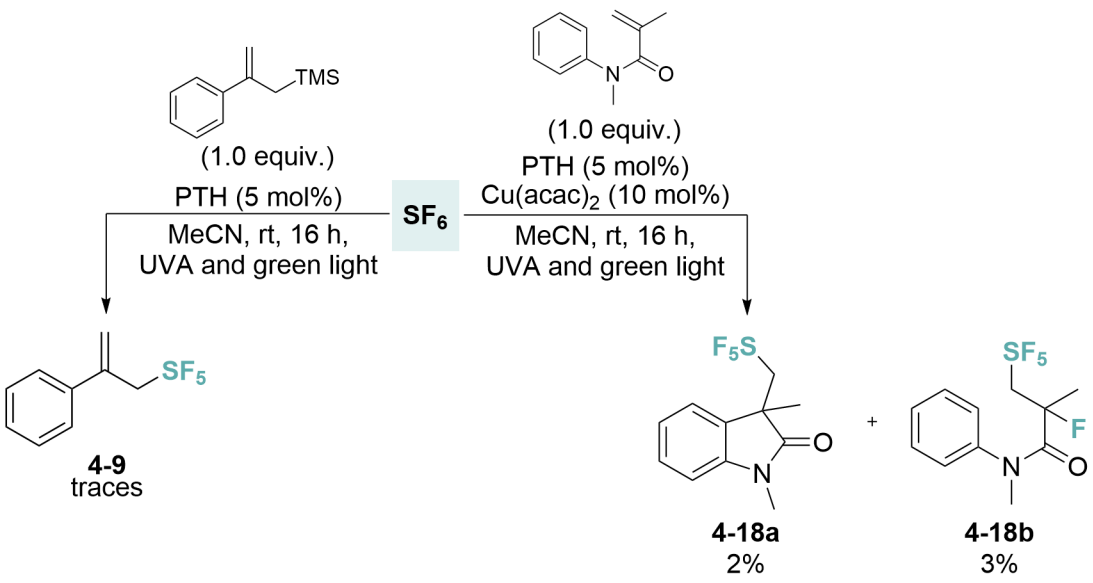
Other reactants bearing activated double bonds were also tested within the project, whereby allyl alcohols showed no reaction with BTMP under the selected TEMPO and photoredox catalysed conditions. Enamines and acrylamides, on the other hand, showed low conversion with BTMP. In general, BTMP holds great potential for further studies with activated multiple bond systems. Inspired by the work of Zhang *et al.* in which *β*-CF_3-*α*-substituted ketones **5-14** were synthesised using Togni's reagent,[197] a combination of BTMP and NHC catalysis would be equally interesting to afford *β*-OCF_3-*α*-substituted ketones **5-15** (Scheme 52). This structural motif has been poorly studied in the literature and could be investigated as a building block for novel herbicides.[198]



Scheme 52: Reaction of aldehydes with alkenes and Togni-CF_3 reagent under NHC catalysis presented by the group of Zhang *et al*. (top).[197] Combination of BTMP and NHC catalysis for the synthesis of underrepresented *β*-OCF_3-*α*-substituted ketones **5-15** (bottom).

Another project, investigating gaseous reagents for the transfer of fluorinated groups, focussed on sulphur hexafluoride. The project was based on the work of the Wagenknecht group, in which SF_6 was reacted with activated styrenes under organocatalysis to form various pentafluorosulphanyl compounds.[176] The aim of the project was to extend the scope of the reaction and thus gather indirect information about the reaction mechanism. For this purpose, 9 different multiple bond systems were tested for their reactivity towards SF_6. Some of the compounds were silylated to enable potential fluoride abstraction by forming a stable Si–F bond and thus facilitate mesolysis towards pentafluorosulphanyl radicals. To some extent, this concept was confirmed, as silicon-fluorine compounds were observed in many test reactions. However, in almost all cases no radical combination, leading to the formation of SF_5 compounds, was observed. Only the allyl silane tested, appeared to show a low reactivity towards SF_5 radicals resulting in traces of an allyl-SF_5 compound **4-9** (Scheme 53, left). Another approach chosen for the synthesis of SF_5 products concerned the inhibition of the reverse *β*-scission process after SF_5 radical addition. For this purpose, compounds were tested that could form stable radicals after SF_5 radical addition through a radical translocation strategy. Thereby acrylamides could be successfully reacted with SF_6. The method led to two

product classes **4-18a** and **b** which, despite first optimisation attempts, could only be observed in low ^{19}F NMR yields of 2% and 3% (Scheme 53, right).

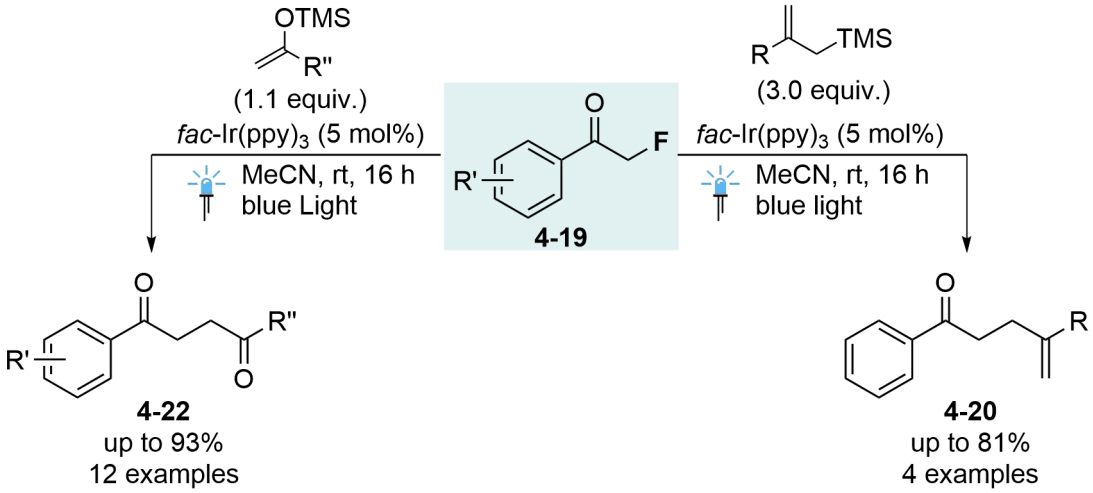


Scheme 53: Results of the test reactions using allyl silanes (left) and acrylamides (right) as reaction partners for SF_6 under Wagenknecht conditions yielding small amounts of synthetically interesting pentafluorosulfanyl compounds.

This project clearly shows the challenges that this transformation involves, however, also offers some new insights into potential solutions. The fluoride abstraction concept should be investigated further in upcoming studies. In addition to silanes and silyl groups, borylated compounds could also be tested, as the B–F bond resulting from fluoride abstraction is also comparatively strong, which could facilitate the mesolysis step effectively.[199] The concept of forming better stabilised radical intermediates to suppress *β*-scission of the SF_5 radical could also provide further information about potential reaction partners. With more extensive optimisation, the acrylamides could become interesting compounds for extending the scope of the Wagenknecht reaction.

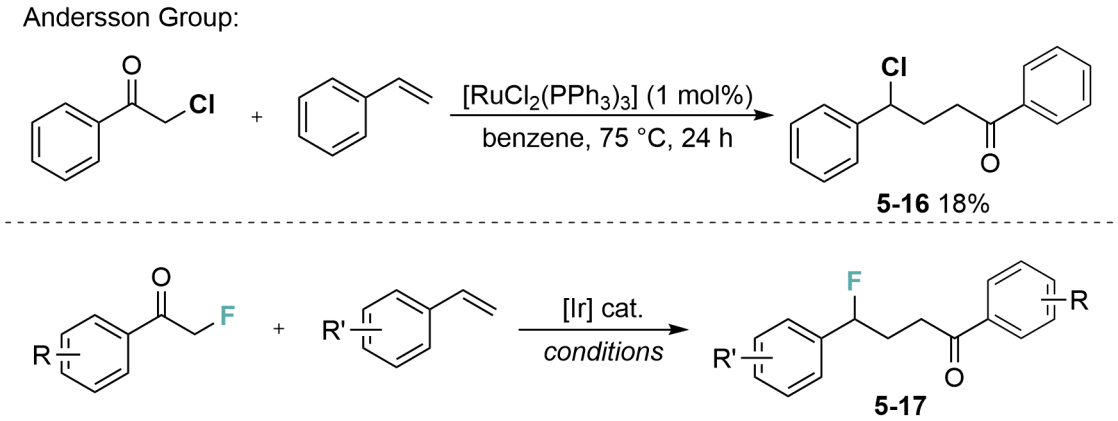
The last part of the thesis investigated the photoredox-catalysed activation of *α*-fluoroacetophenones **4-19** for defluorinative C–C bond formation. The project was based on the investigations within the Hopkinson group, where the reaction of *α*-fluoroacetophenone with allyl silanes and under the influence of PTH and light led to dual functionalised compounds **4-20**. The method was to be optimised and applied to other reaction partners building on the previous work by Dr. Stefan Dix. The optimisation identified *fac*-Ir(ppy)$_3$ as a more suitable catalyst for the reaction, whereby four allyl silanes could be coupled with *α*-fluoroacetophenone using the optimised reaction conditions (Scheme 54, right). Silyl enol ethers were also tested in the course of the project for their reactivity within the C–C bond formation reaction and the conditions were optimised with *fac*-Ir(ppy)$_3$ as a photoredox catalyst. The method enabled the synthesis of twelve 1,4-diketones **4-22** in moderate to very good yields (Scheme 54, left),

whereby both changing substituents on the silyl enol ether and on the fluorinated starting material were tolerated.



Scheme 54: Defluorinative C–C bond formation via the photoredox catalysed reaction of *α*-fluoroacetophenones with silyl enol ethers (left) and allyl silanes (right) to obtain 1,4-difunctionalised products.

This method offers great potential for new applications for C–F activation reactions. In further work, the scope of the allyl silane reaction should first be expanded to explore possible trends and limitations, as well as mechanistic characteristics of the reaction. This information could be used to find other substrate classes for such C–C coupling reactions. One possible extension of the method could be an addition of the *α*-fluoroacetophenone and double bonds within a Kharasch reaction. The Andersson group already presented the photoredox catalysed reaction of *α*-chloroacetophenone with styrene in 2007 (Scheme 55, top).[200]



Scheme 55: Kharasch reaction of *α*-chloroacetophenone with styrene presented by the Andersson group (top). Photoredox catalysed Kharasch-type addition of *α*-fluoroacetophenones to styrene derivatives (bottom).

Their work involves the addition of the chlorinated compound to the double bond of the styrene, resulting in the formation of a bifunctional compound **5-16**. However, the yield of this reaction

with 18% is comparatively low. The utilisation of *α*-fluoroacetophenones under photoredox catalytic conditions could increase the yields through the formation of a stable C–F bond within the reaction and lead to interesting products **5-17** for total synthesis (Scheme 55, bottom). This potential project could benefit from our group's experience with C-F insertion methodology.[201]

Overall, this work made a significant contribution to various areas of organofluorine chemistry. In addition to offering new, attractive approaches to valuable fluorinated derivatives, the focus on YR_F and SF_5 groups has relevance for the current concerns regarding the use of perfluoroalkyl substances (PFAS). Apart from the many beneficial properties of fluorinated organic and inorganic molecules allowing for a broad range of applications, the high C–F bond strength makes many fluorinated compounds highly persistent in the environment. YR_F Groups such as OCF_3 and SCF_3 are expected to be more susceptible to degradation in soil and could therefore help to negate the accumulation of fluorinated compounds. For example, OCF_3 groups are exempted from the current EU draft legislation on a potential PFAS ban. Within the thesis, new methods for the introduction of SCF_3 groups, using BT-reagents, and OCF_3 groups, using BTMP, were presented. The degradation of these groups starts with the cleavage of chalcogen-carbon bonds, which could lead to easily decomposing YR_F anions. Especially the expansion of the application range of BTMP opens up a broad spectrum of new underrepresented OCF_3 compounds. These findings and methods are particularly interesting with regard to the ongoing political debate about a possible PFAS ban, as the trifluoromethoxy group could, according to the current state of discussion, be used in various areas as an alternative to restricted fluorinated groups due to its lower environmental persistence.

On the other hand, the degradation of highly persistent fluorinated compounds bearing a high greenhouse potential, such as SF_6, is of great importance. This challenging topic was investigated within the last two, yet unpublished, projects. New insights and potential reaction partners in the Wagenknecht reaction for the development of new pentafluorosulphanyl compounds were found, which involve the effective consumption of the environmentally harmful SF_6 gas. Additionally, the activation and use of C–F bond containing molecules was investigated to offer new synthetically interesting fluorine-free building blocks.

Overall, this work contributes to the growing field of organofluorine chemistry by providing novel, synthetically useful methods towards fluorinated compounds and offers insights of direct relevance for some of the major current challenges facing the modern chemical industry; namely the environmental concerns associated with the use of PFASs. Advances in organofluorine chemistry are critical to address this challenge and it is hoped that the projects presented in this thesis helped to contribute to this endeavour, inspiring new avenues of research.

6 List of Publications, Patents and Conference Contributions

6.1 Published Manuscripts

M. Tironi,‡ **L. M. Maas**,‡ A. Garg, S. Dix, J. P. Goetze, M. N. Hopkinson, Deoxygenative Tri- and Difluoromethylthiolation of Carboxylic Acids with Benzothiazolium Reagents, *Org. Lett.* **2020**, *22*, 8925-8930. (Master's Thesis)

L. M. Maas, J. R. Schmid, C. Fasting, P. Voßnacker, A. Mavroskoufis, M. N. Hopkinson, Activation of tetrahydrofuran with 2-((Fluoroalkyl)thio) Benzothiazolium reagents, *Tetrahedron* **2021**, *101*, 132512.

L. M. Maas, C. Fasting, P. Voßnacker, N. Limberg, P. Golz, C. Müller, S. Riedel, M. N. Hopkinson, Catalyst-free Trifluoromethoxylation of Silyl Enol Ethers and Allyl Silanes with Bis(trifluoromethyl)peroxide, *Angew. Chem. Int. Ed.* **2024**, *63*, e202317770.

L. M. Maas,‡ A. Haswell,‡ R. Hughes, M. N. Hopkinson, Direct synthesis of acyl fluorides from carboxylic acids using benzothiazolium reagents, *Beilstein J. Org. Chem.* **2024**, *20*, 921–930.

P. Golz, K. Shakeri, **L. Maas**, M. Balizs, A. Pérez-Bitrián, H. D. Kemmler, M. Kleoff, P. Voßnacker, M. Christmann, S. Riedel, Silver(I) Perfluoroalcoholates: Synthesis, Structure, and their Use as Transfer Reagents, *Chem. Eur. J.* **2024**, e202400861.

6.2 Patent Applications

Sebastian Hasenstab-Riedel, Matthew Hopkinson, **Lilian Maas**, Stefan Dix, *A catalyst free synthesis method for introducing a trifluoromethoxy moiety into at least one organic compound*, **2023**, EP23186390.3.

6.3 Conference Contributions

08/2021	GDCh-Wissenschaftsforum Chemie 2021 (online)	Poster
03/2022	20th RSC Fluorine Interest Group Postgraduate Meeting (online)	Poster (Poster award 1st)
06/2022	SNESFest 2022 (Newcastle upon Tyne, United Kingdom)	Poster
08/2022	20th European Symposium on Fluorine Chemistry (Berlin, Germany)	Presentation
11/2022	SNES Organic Symposium 2022 (Newcastle upon Tyne, United Kingdom)	Poster & Presentation
07/2023	23rd International Symposium on Fluorine Chemistry (Québec City, Canada)	Presentation
04/2024	22nd RSC Fluorine Interest Group Postgraduate Meeting (Newcastle upon Tyne, United Kingdom)	Presentation (Presentation award)

7 Curriculum Vitae

The curriculum vitae is not included for reasons of data protection.

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9 Appendix

9.1 Supporting Information of Published Results

9.1.1 Activation of Tetrahydrofuran with 2-((Fluoroalkyl)thio)Benzothiazolium Reagents

The pages 119– 150 contain the Supporting Information of the article of Chapter 3.1 and were removed due to the Copyright.

The article and Supporting Information are available at

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9.1.2 Direct Synthesis of Acyl Fluorides from Carboxylic Acids using Benzothiazolium Reagents

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Supporting Information

for

Direct synthesis of acyl fluorides from carboxylic acids using benzothiazolium reagents

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Experimental procedures, characterisation data of all isolated products as well as copies of NMR spectra for novel compounds

Contents

1 General Information

All compounds and solvents utilised were purchased from commercial suppliers and used without further treatment, unless specified otherwise. Benzothiazolium reagents were synthesised according to literature known procedures.[1]

Thin-layer chromatography was performed on silica gel coated aluminium plates from TLC Silica gel 60 F_{254} and aluminium oxide 60 F_{254} neutral. The product spots were detected by UV light (254 nm) or as permanganate stains. Flash column chromatography was performed with silica gel 60 M (0.040–0.063 mm, 230–400 mesh).

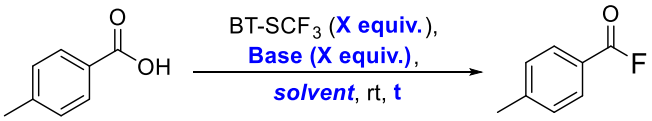
^{1}H, ^{19}F and ^{13}C NMR spectra were acquired on a Bruker Avance III 300 (300 MHz), Bruker Avance II 400 (400 MHz), Bruker Avance Neo 400 (400 MHz), Bruker Avance III HD 500 (500 MHz), or a Bruker Avance III HD 700 (700 MHz) and analysed on MestReNova 14.1.1. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane (TMS) and coupling constants (*J*) are presented in hertz (Hz). CD_3CN or $CDCl_3$ were used as deuterated solvents and the residual solvent signals were used as references in the ^{1}H and ^{13}C NMR spectra. ^{19}F NMR spectra were not calibrated by an internal reference. ^{19}F NMR yields were measured using α,α,α-trifluorotoluene as an internal standard. The multiplicities are described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, and m = multiplet.

High-resolution mass spectra were measured with an Agilent (6210 ESI-TOF; 4 µL/min, 1.0 bar, 4 kV). Infrared spectra were measured with a PerkinElmer UATR Two FT-IR Spectrometer. Characteristic absorption bands are displayed in wavenumbers $\tilde{\nu}$ in cm^{-1}.

Chiral normal phase HPLC was performed on a Dionex Ultimate 3000 HPLC unit equipped with UV–vis diode-array detector, fitted with the appropriate Daicel Chiralpak column (dimensions: 0.46 cm ø × 25 cm) along with the corresponding guard column (0.4 cm ø × 1 cm). Wavelengths (λ) are reported in nm, retention times (τ_R) are reported in minutes and solvent flow rates are reported in mL min^{-1}.

2 Optimisation tables

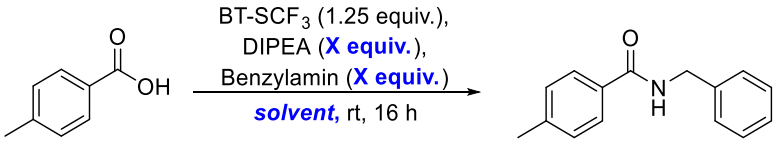
Table S1. Optimisation of the deoxyfluorination of 4-methylbenzoic acid using BT-SCF_3.



Entry[a]	Reagent equiv.	Base (equiv.)	Solvent	t [h]	Yield Acyl fluoride[b]	Yield Thioester[b]
1	1.25	DIPEA (1.1)	DCM	2	12	60
2	1.25	DIPEA (1.5)	DCM	2	30	45
3	1.25	DIPEA (1.75)	DCM	2	68	17
4	**1.25**	**DIPEA (2.0)**	**DCM**	**2**	**Quant.**	**--**
5	1.25	K_2CO_3 (2.0)	DCM	2	7	37
6	1.25	NaH (2.0)	DCM	2	--	30
7	1.25	NEt_3 (2.0)	DCM	2	96	traces
8	1.25	Na_2CO_3 (2.0)	DCM	2	--	26
9	0.5	DIPEA (2.0)	DCM	2	55	--
10	0.75	DIPEA (2.0)	DCM	2	72	--
11	1.0	DIPEA (2.0)	DCM	2	83	--
12	1.5	DIPEA (2.0)	DCM	2	75	--
13	1.25	DIPEA (2.0)	DMF	2	11	--
14	1.25	DIPEA (2.0)	MeCN	2	88	traces
15	1.25	DIPEA (2.0)	EtOAc	2	Quant.	traces
16	1.25	DIPEA (2.0)	THF	2	91	traces
17	**1.25**	**DIPEA (2.0)**	**DCM**	**0.5**	**Quant.**	**--**

[a]Reaction procedure: BT-SCF_3, 4-methylbenzoic acid and base were dissolved in the solvent and the reaction mixture was stirred at rt before being concentrated *in vacuo*. [b]Yields calculated by ^{19}F NMR spectroscopy using *α,α,α*-trifluorotoluene as an internal standard.

Table S2. Optimisation of the amide coupling of 4-methylbenzoic acid with benzylamine using BT-SCF_3.

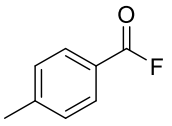


Entry	DIPEA (equiv.)	Benzylamine (equiv.)	Solvent	Yield[c]
1[a]	2.0 then 1.0	1.0	DCM	55
2[a]	2.0 then 2.0	1.0	DCM	50
3[a]	2.0 then 1.0	1.0	MeCN	37
4[a]	2.0 then 1.0	1.0	EtOAc	24
5[a]	2.0 then 1.0	1.5	DCM	83
6[a]	2.0 then 1.0	1.75	DCM	84
7[a]	2.0 then 1.0	2.0	DCM	Quant.
8[b]	3.0	1.0	DCM	43
9[b]	**3.0**	**2.0**	**DCM**	**98**
10[b]	2.0	2.0	DCM	90

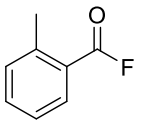
[a]Reaction procedure: BT-SCF_3, 4-methylbenzoic acid and DIPEA (2.0 equiv.) were dissolved in the solvent and the reaction mixture was stirred at rt for 30 min. Then, DIPEA and benzylamine were added and the mixture was stirred at rt for 16 h before being concentrated *in vacuo*. [b]Reaction procedure: BT-SCF_3, 4-methylbenzoic acid and DIPEA were dissolved in the solvent, then, benzylamine was added and the reaction mixture was stirred at rt for 16 h before being concentrated *in vacuo*. [c]Yields calculated by ^1H NMR spectroscopy using CH_2Br_2 as an internal standard.

3 General procedure for the synthesis of acyl fluorides

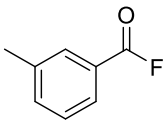
To a solution of BT-SCF_3 (1.25 equiv, 0.63 mmol, 250 mg) in DCM (5 mL) was added benzoic acid derivatives **1** (1.0 equiv, 0.5 mmol) and DIPEA (2.0 equiv, 1.0 mmol, 175 µL). The resulting mixture was stirred for 2 h at rt. The solvent was removed under reduced pressure, $CDCl_3$ (0.65 mL) and α,α,α-trifluorotoluene (0.5 mmol, 63 µL) were added and the crude NMR yields were determined from ^{19}F NMR spectra.



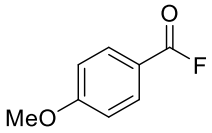
2a (quant.)



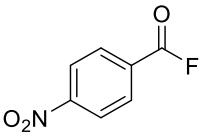
2b (89%)



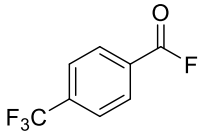
2c (quant.)



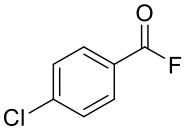
2d (85%)



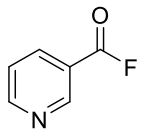
2e (95%)



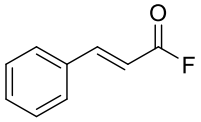
2f (75%)



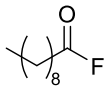
2g (quant.)



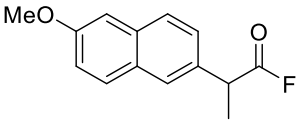
2h (90%)



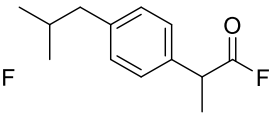
2i (80%)



2j (89%)



2k (97%)



2l (quant.)

Crude **^{19}F NMR (282 MHz, $CDCl_3$)** Signals:

2a	δ [ppm] = 17.3.	**2h**	δ [ppm] = 20.6.
2b	δ [ppm] = 29.1.	**2i**	δ [ppm] = 25.4 (d, *J* = 7.4 Hz).
2c	δ [ppm] = 18.1.	**2j**	δ [ppm] = 45.3.
2d	δ [ppm] = 15.8.	**2k**	δ [ppm] = 39.3.
2e	δ [ppm] = 21.3.	**2l**	δ [ppm] = 39.1.
2f	δ [ppm] = 19.9 (F), –63.5 (CF_3).		
2g	δ [ppm] = 18.3.		

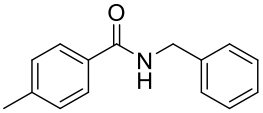
The analytical data are in agreement with the literature data.[2]

4 General procedure for the amide coupling of carboxylic acids with amines

To a solution of BT-SCF_3 (1.25 equiv, 0.63 mmol, 250 mg) in DCM (5 mL) was added benzoic acid derivatives **1** (1.0 equiv, 0.5 mmol) and DIPEA (3.0 equiv, 1.5 mmol, 262 µL). Then, benzylamine **4a** (2.0 equiv, 1.0 mmol, 109 µL) was added and the resulting mixture was stirred overnight at rt. The solvent was removed under reduced pressure and the products **5** were purified by flash chromatography on a silica gel column.

4.1 Analytical data

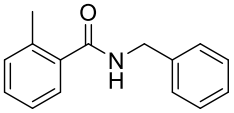
N-Benzyl-4-methylbenzamide (**5a**)



Amide **5a** (90 mg, 0.40 mmol, 80%) was obtained from 4-methylbenzoic acid after flash column chromatography (petroleum ether / EtOAc, 5:1) as a pale-yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 7.65 (d, *J* = 8.2 Hz, 2H), 7.30 – 7.15 (m, 5H), 7.13 (d, *J* = 7.9 Hz, 2H), 6.81 (bs, 1H), 4.53 (d, *J* = 5.8 Hz, 2H), 2.33 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ [ppm] = 167.4, 142.0, 138.5, 131.6, 129.3, 128.8, 128.0, 127.6, 127.1, 44.1, 21.5.
The characterization data agree with the literature values.[3]

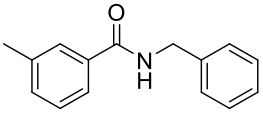
N-Benzyl-2-methylbenzamide (**5b**)



Amide **5b** (91 mg, 0.40 mmol, 81%) was obtained from 2-methylbenzoic acid after flash column chromatography (petroleum ether / EtOAc, 5:1→3:1) as a pale-yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = δ 7.32 – 7.17 (m, 7H), 7.15 – 7.05 (m, 2H), 6.16 (bs, 1H), 4.51 (d, *J* = 5.9 Hz, 2H), 2.36 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ [ppm] = 170.0, 138.3, 136.3, 136.2, 131.1, 130.0, 128.8, 127.9, 127.6, 126.8, 125.8, 43.9, 19.9.
The characterization data agree with the literature values.[4]

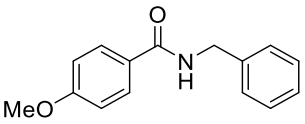
N-Benzyl-3-methylbenzamide (**5c**)



Amide **5c** (80 mg, 0.36 mmol, 71%) was obtained from 3-methylbenzoic acid after flash column chromatography (petroleum ether / EtOAc, 5:1→3:1) as a pale-yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.62 (s, 1H), 7.59 – 7.53 (m, 1H), 7.36 – 7.32 (m, 4H), 7.30 – 7.26 (m, 3H), 6.50 (s, 1H), 4.63 (d, *J* = 5.7 Hz, 2H), 2.38 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ [ppm] = 167.7, 138.6, 138.4, 134.5, 132.4, 128.9, 128.6, 128.0, 127.9, 127.7, 124.0, 44.2, 21.5.
The characterization data agree with the literature values.[4]

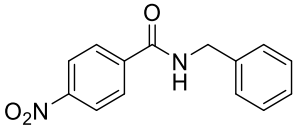
N-Benzyl-4-methoxybenzamide (**5d**)



Amide **5d** (98 mg, 0.4 mmol, 80%) was obtained from 4-methoxybenzoic acid after flash column chromatography (petroleum ether / EtOAc, 2:1→1:1) as a pale-yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 7.71 (d, *J* = 8.8 Hz, 2H), 7.32 – 7.17 (m, 5H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.67 (bs, 1H), 4.53 (d, *J* = 5.7 Hz, 2H), 3.76 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ [ppm] = 167.0, 162.3, 138.6, 128.9, 128.8, 128.0, 127.6, 126.8, 113.9, 55.5, 44.1.
The characterization data agree with the literature values.[3]

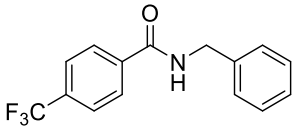
N-benzyl-4-nitrobenzamide (**5e**)



Amide **5e** (89 mg, 0.35 mmol, 70%) was obtained from 4-nitrobenzoic acid after flash column chromatography (petroleum ether / EtOAc, 2:1) as a pale-yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 8.28 (d, *J* = 8.9 Hz, 2H), 7.95 (d, *J* = 8.8 Hz, 2H), 7.43 – 7.29 (m, 5H), 6.49 (bs, 1H), 4.67 (d, *J* = 5.6 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ [ppm] = 165.5, 149.7, 140.0, 137.6, 129.1, 128.3, 128.1, 128.1, 124.0, 44.6. **IR (ATR)**: $\tilde{\nu}$ [cm^{-1}] = 3277, 3035, 2925, 2851, 1944, 1812, 1629, 1596, 1533, 1511, 1484, 1453, 1463, 1362, 1344, 1317, 1281, 1221, 1178, 1147, 1077, 1060, 1031, 1012, 988, 959, 914, 902, 872, 853, 796, 782, 752, 725, 663, 622, 584, 548, 515, 504, 465, 424, 410.
The characterization data agree with the literature values.[5, 3b]

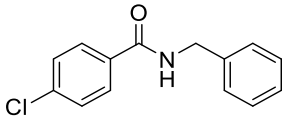
N-Benzyl-4-(trifluoromethyl)benzamide **(5f)**



Amide **5f** (113 mg, 0.4 mmol, 81%) was obtained from 4-(trifluoromethyl)benzoic acid after flash column chromatography (petroleum ether / EtOAc, 5:1→3:1) as a pale-yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.89 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.44 – 7.28 (m, 5H), 6.51 (bs, 1H), 4.65 (d, *J* = 5.6 Hz, 2H). **^{19}F NMR** (282 MHz, $CDCl_3$) δ [ppm] = -62.96. **^{13}C NMR** (75 MHz, $CDCl_3$) δ [ppm] = 166.2, 137.9, 137.8, 133.5 (q, *J* = 33 Hz),129.0, 128.1, 128.0, 127.6, 125.8 (q, *J* = 4 Hz), 123.8 (q, *J* = 273 Hz), 44.5.
The characterization data agree with the literature values.[6]

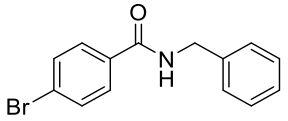
N-Benzyl-4-chlorobenzamide (**5g**)



Amide **5g** (105 mg, 0.43 mmol, 85%) was obtained from 4-chlorobenzoic acid after flash column chromatography (petroleum ether / EtOAc, 5:1) as a pale-yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.77 – 7.68 (m, 2H), 7.44 – 7.27 (m, 7H), 6.47 (bs, 1H), 4.62 (d, *J* = 5.7 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ [ppm] = 166.4, 138.1, 137.9, 132.9, 129.0, 128.5, 128.1, 127.9, 44.4.
The characterization data agree with the literature values.[7]

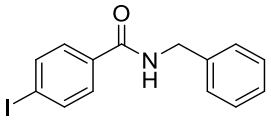
N-Benzyl-4-bromobenzamide (**5m**)



Amide **5m** (145 mg, 0.49 mmol, 98%) was obtained from 4-bromobenzoic acid after flash column chromatography (petroleum ether / EtOAc, 5:1) as a pale-yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.65 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.41 – 7.27 (m, 5H), 6.50 (bs, 1H), 4.61 (d, *J* = 5.7 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ [ppm] = 166.5, 138.0, 133.3, 131.9, 129.0, 128.7, 128.1, 127.9, 126.4, 44.3.
The characterization data agree with the literature values.[8]

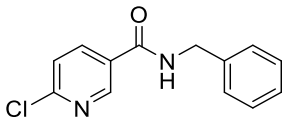
N-Benzyl-4-iodobenzamide (**5n**)



Amide **5n** (142 mg, 0.42 mmol, 84%) was obtained from 4-iodobenzoic acid after flash column chromatography (petroleum ether / EtOAc, 5:1→3:1) as a pale-yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.77 (d, *J* = 8.6 Hz, 2H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.43 – 7.27 (m, 5H), 6.45 (bs, 1H), 4.62 (d, *J* = 5.6 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ [ppm] = 166.7, 138.0, 137.9, 133.9, 129.0, 128.7, 128.1, 127.9, 98.6, 44.4.
The characterization data agree with the literature values.[8]

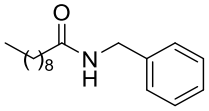
N-Benzyl-6-chloronicotinamide (**5o**)



Amide **5o** (92 mg, 0.37 mmol, 74%) was obtained from 6-chloronicotinic acid after flash column chromatography (petroleum ether / EtOAc, 3:1) as a pale-yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 8.69 (d, *J* = 2.6 Hz, 1H), 8.04 (dd, *J* = 8.3, 2.6 Hz, 1H), 7.38 – 7.13 (m, 6H), 7.13 (dd, *J* = 7.7, 3.1 Hz, 2H), 6.61 (bs, 1H), 4.58 (d, *J* = 5.6 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ [ppm] = 164.6, 154.4, 148.1, 138.1, 137.6, 129.0, 128.4, 128.1, 128.0, 124.5, 44.4.
The characterization data agree with the literature values.[9]

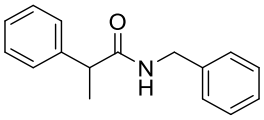
N-Benzyldecanamide (**5j**)



Amide **5j** (119 mg, 0.46 mmol, 91%) was obtained from decanoic acid after flash column chromatography (petroleum ether / EtOAc, 3:1) as a pale-yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 7.35 – 7.21 (m, 5H), 6.26 (bs, 1H), 4.39 (d, *J* = 5.8 Hz, 2H), 2.19 (t, *J* = 7.6 Hz, 2H), 1.67 – 1.58 (m, 2H), 1.33 – 1.24 (s, 12H), 0.89 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ [ppm] = 173.3, 138.6, 128.7, 127.8, 127.4, 43.5, 36.7, 31.9, 29.5, 29.43, 29.39, 29.32, 25.9, 22.7, 14.1.
The characterization data agree with the literature values.[10]

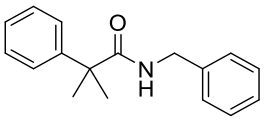
N-Benzyl-2-phenylpropanamide (**5p**)



Amide **5p** (111 mg, 0.46 mmol, 93%) was obtained from 2-phenylpropanoic acid after flash column chromatography (petroleum ether / EtOAc, 3:1) as a pale-yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 7.33 – 7.13 (m, 8H), 7.10 – 7.05 (m, 2H), 5.63 (bs, 1H), 4.41 – 4.26 (m, 2H), 3.55 (q, *J* = 7.2 Hz, 1H), 1.50 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ [ppm] = 174.2, 141.4, 138.4, 129.1, 128.7, 127.8, 127.6, 127.49, 127.45, 47.3, 43.7, 18.7.
The characterization data agree with the literature values.[11]

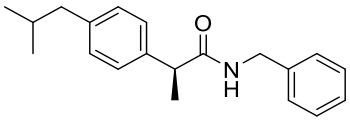
N-Benzyl-2-methyl-2-phenylpropanamide (**5q**)



Amide **5q** (107 mg, 0.42 mmol, 84%) was obtained from 2-methyl-2-phenylpropanoic acid after flash column chromatography (petroleum ether / EtOAc, 3:1) as a pale-yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 7.41 – 7.30 (m, 4H), 7.30 – 7.20 (m, 4H), 7.13 – 7.09 (m, 2H), 5.45 (s, 1H), 4.37 (d, *J* = 5.8 Hz, 2H), 1.61 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ [ppm] = 177.5, 145.2, 138.6, 128.9, 128.7, 127.5, 127.4, 127.2, 126.6, 47.2, 43.8, 27.2.
The characterization data agree with the literature values.[12]

(*S*)-*N*-Benzyl-2-(4-isobutylphenyl)propenamide (**5l**)

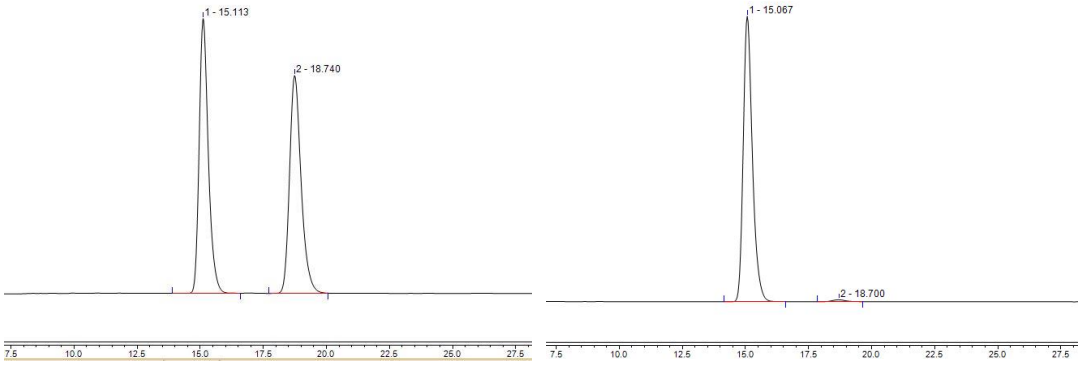


Amide **5l** (107 mg, 0.36 mmol, 72%) was obtained from (2S)-2-(4-Isobutylphenyl)propanoic acid after flash column chromatography (petroleum ether / EtOAc, 3:1) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.27 – 7.12 (m, 5H), 7.12 – 7.03 (m, 4H), 5.67 (bs, 1H), 4.34 (d, *J* = 5.9 Hz, 2H), 3.54 (q, *J* = 7.2 Hz, 1H), 2.41 (d, *J* = 7.1 Hz, 2H), 1.90 – 1.72 (m, 1H), 1.51 (d, *J* = 7.2 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 6H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ [ppm] = 174.5, 140.9, 138.6, 138.5, 129.8, 128.7, 127.5, 127.4, 46.9, 45.1, 43.6, 30.3, 22.5, 18.6.*

*Note: One carbon peak could not be observed, due to overlapping signals.

Chiral HPLC: DAICEL Chiralpak IC column with guard; solvent ratio = 90:10, *n*-hexane:^{i}PrOH. Temperature = 25 °C. Flow rate = 1 mL/min, λ = 210 nm, τ_{ret} = 15.1 min and 18.7 min.



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
15.113	n.a.	49.89	174.2813	415.48
18.740	n.a.	50.11	175.0514	329.64

Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
15.067	n.a.	99.09	147.9451	351.35
18.700	n.a.	0.91	1.3633	2.36

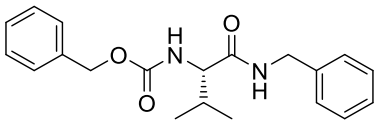
The characterization data agree with the literature values.[13]

5 General procedure and analytical data for the coupling of amino acids

To a solution of BT-SC_5F_{11} (1.25 equiv, 0.63 mmol, 375 mg) in DCM (5 mL) was added Cbz-valine **1s** (1.0 equiv, 0.5 mmol, 126 mg) and DIPEA (3.0–5.0 equiv). Then, amine **4** (2.0 equiv, 1.0 mmol) was added and the resulting mixture was stirred overnight at rt. The solvent was removed under reduced pressure and the products **5s-t** were purified by flash chromatography on a silica gel column.

5.1 Analytical data

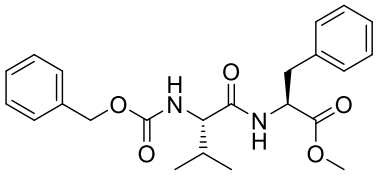
Benzyl (S)-(1-(benzylamino)-3-methyl-1-oxobutan-2-yl)carbamate (**5s**)



Amide **5s** (121 mg, 0.36 mmol, 71%) was obtained using benzylamine (2.0 equiv, 109 µL) and DIPEA (3.0 equiv, 1.5 mmol, 262 µL), after flash column chromatography (petroleum ether / EtOAc, 3:1) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.36 – 7.15 (m, 10H), 6.49 (bs, 1H), 5.42 (d, *J* = 7.7 Hz, 1H), 5.05 – 4.89 (m, 2H), 4.37 (dd, *J* = 14.8, 5.8 Hz, 2H), 4.04 – 3.93 (m, 1H), 2.16 – 2.01 (m, 2H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ [ppm] = 171.3, 156.6, 138.0, 136.3, 128.8, 128.7, 128.3, 128.1, 127.9, 127.7, 67.2, 60.7, 43.7, 31.2, 19.4, 18.0.
The characterization data agree with the literature values.[14]

Methyl ((benzyloxy)carbonyl)-L-valyl-L-phenylalaninate (**5t**)



Amide **5t** (139 mg, 0.34 mmol, 67%) was obtained using methyl L-phenylalaninate hydrochloride (216 mg) and DIPEA (5.0 equiv, 2.5 mmol, 435 µL) after flash column chromatography (petroleum ether / EtOAc, 3:1) as a white solid.

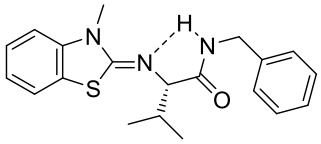
^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.43 – 7.07 (m, 10H), 6.73 (d, *J* = 8.0 Hz, 1H), 5.58 (d, *J* = 9.0 Hz, 1H), 5.20 – 5.01 (m, 2H), 4.93 (m, 1H), 4.19 – 4.08 (m, 1H), 3.72 (s, 3H), 3.19 – 3.05 (m, 2H), 2.10 (h, *J* = 6.9 Hz, 1H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ [ppm] = 171.8, 171.11, 156.4, 136.4, 135.7, 129.3, 128.6, 128.5, 128.2, 128.0, 127.2, 67.0, 60.2, 53.2, 52.3, 38.0, 31.3, 19.1, 17.8.
The characterization data agree with the literature values.[15]

6 Scale-up reaction for the investigation of the side products

To a solution of BT-SCF_3 (1.25 equiv, 6.25 mmol, 2.50 g) in DCM (50 mL) was added Boc-valine **1r** (1.0 equiv, 5.0 mmol, 1.09 g) and DIPEA (3.0 equiv, 15.0 mmol, 1.31 mL). Then, benzylamine (**4a**, 2.0 equiv, 10.0 mmol, 1.09 mL) was added and the resulting mixture was stirred overnight at rt. The solvent was removed under reduced pressure and product **6** and **7** were purified by flash chromatography on a silica gel column.

6.1 Analytical data

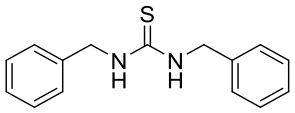
(S,Z)-*N*-Benzyl-3-methyl-2-((3-methylbenzo[d]thiazol-2(3*H*)-ylidene)amino)butanamide (**6**)



Side product **6** was obtained after flash column chromatography (petroleum ether / EtOAc, 3:1) as a pale-yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 7.33 – 7.18 (m, 7H), 7.03 (m, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 4.55 (dd, *J* = 15.0, 6.3 Hz, 1H), 4.38 (dd, *J* = 15.1, 5.7 Hz, 1H), 3.58 (d, *J* = 3.6 Hz, 1H), 3.40 (s, 3H), 2.38 (m, 1H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ [ppm] = 173.1, 157.8, 140.9, 138.8, 128.7, 127.6, 127.4, 126.5, 122.3, 122.2, 121.4, 108.8, 74.1, 43.1, 33.4, 30.4, 20.0, 17.7. **IR (ATR)**: $\tilde{\nu}$ [cm^{-1}]: 3378, 3062, 3030, 2960, 2928, 2871, 1717, 1663, 1629, 1585, 1509, 1480, 1456, 1418, 1383, 1362, 1350, 1305, 1323, 1252, 1160, 1135, 1027, 960, 923, 851, 742, 716, 699, 610, 542, 517, 495, 479. **HRMS (ESI-TOF)** calculated for $[C_{20}H_{23}N_3OS]^+$ ($[M]^+$): 354.1635, measured: 354.1624.

1,3-Dibenzylthiourea (**7**)

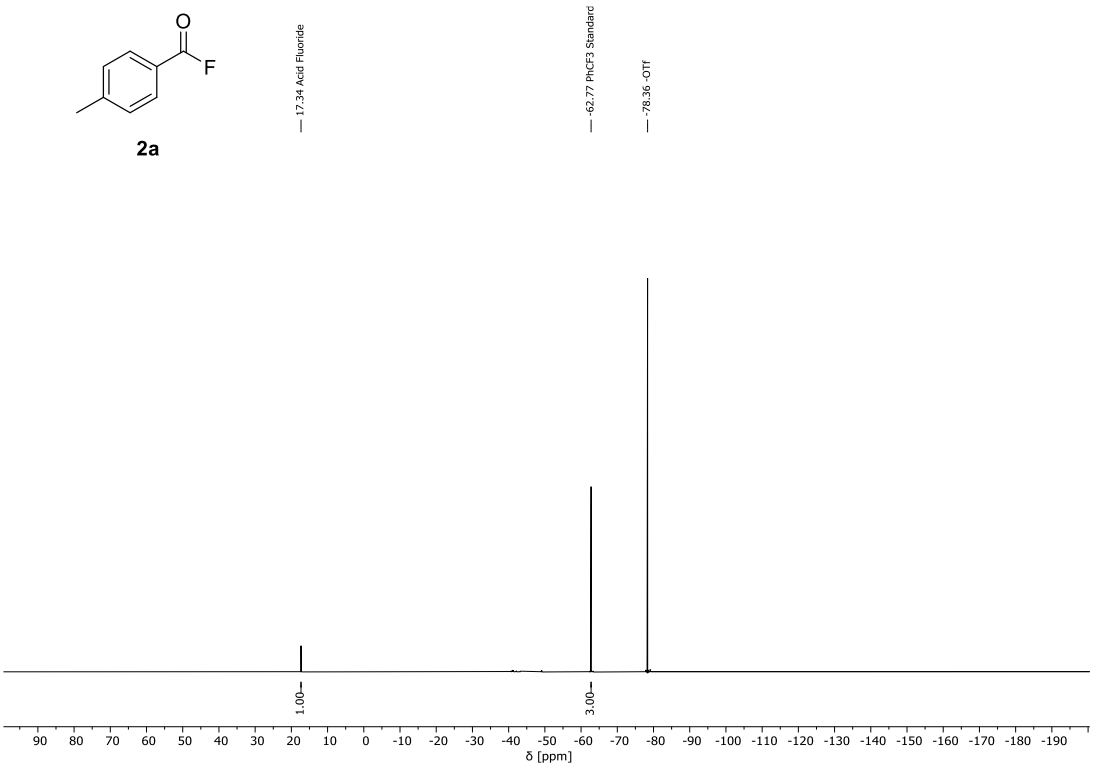


Side product **7** was obtained after flash column chromatography (petroleum ether / EtOAc, 3:1) as a pale-yellow solid.

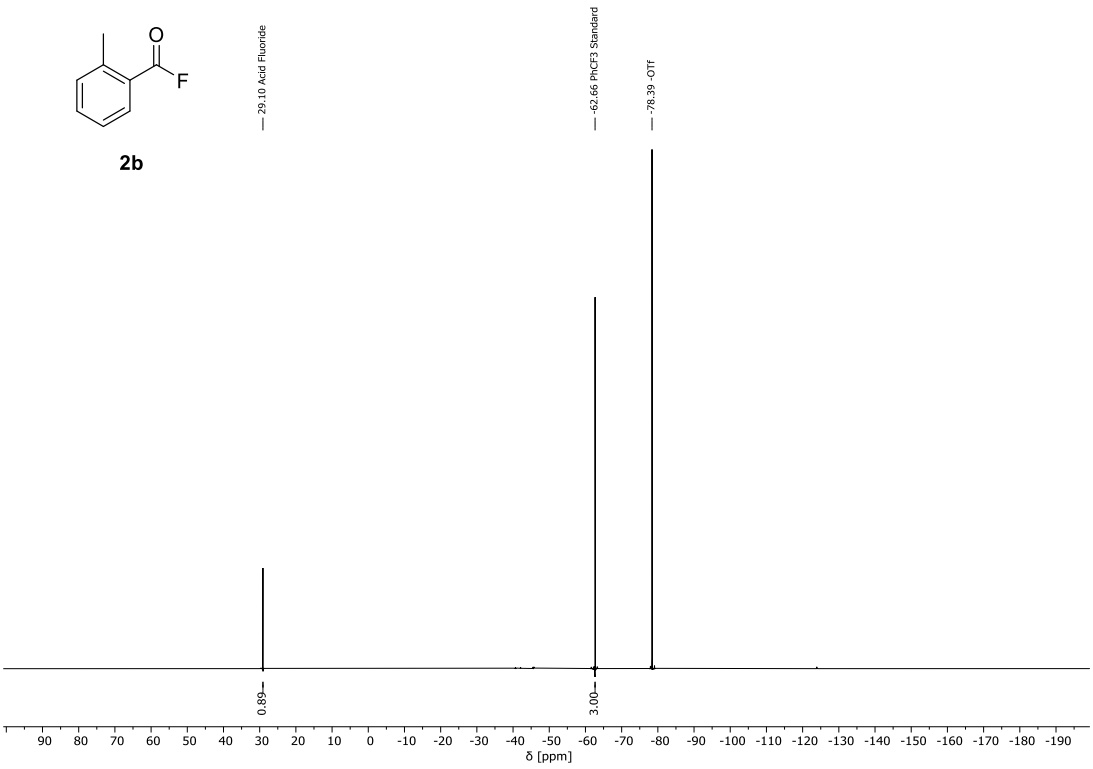
^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 7.35-7.28 (m, 6H), 7.26 – 7.21 (m, 4H), 6.00 (s, 2H), 4.64 (d, J = 5.3 Hz, 4H). The characterization data agree with the literature values.[16]

7 NMR Spectra of crude ^{19}F NMR for acid fluoride synthesis

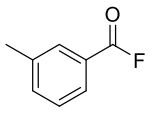
Crude ^{19}F NMR (282 MHz in $CDCl_3$), 298 K



Crude ^{19}F NMR (282 MHz in $CDCl_3$), 298 K

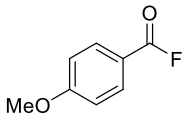


Crude ^{19}F NMR (282 MHz in $CDCl_3$), 298 K



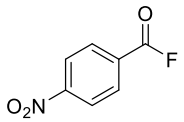
2c

Crude ^{19}F NMR (282 MHz in $CDCl_3$), 298 K



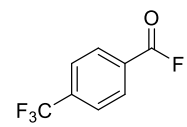
2d

Crude ^{19}F NMR (282 MHz in $CDCl_3$), 298 K



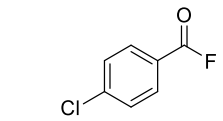
2e

Crude ^{19}F NMR (282 MHz in $CDCl_3$), 298 K



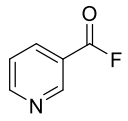
2f

Crude ^{19}F NMR (282 MHz in $CDCl_3$), 298 K



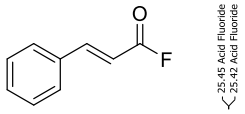
2g

Crude ^{19}F NMR (282 MHz in $CDCl_3$), 298 K



2h

Crude ^{19}F NMR (282 MHz in $CDCl_3$), 298 K

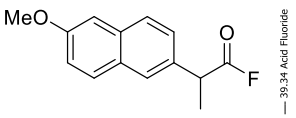


2i

Crude ^{19}F NMR (282 MHz in $CDCl_3$), 298 K

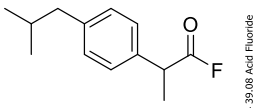
2j

Crude ^{19}F NMR (282 MHz in $CDCl_3$), 298 K



2k

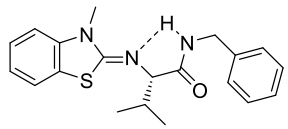
Crude ^{19}F NMR (282 MHz in $CDCl_3$), 298 K

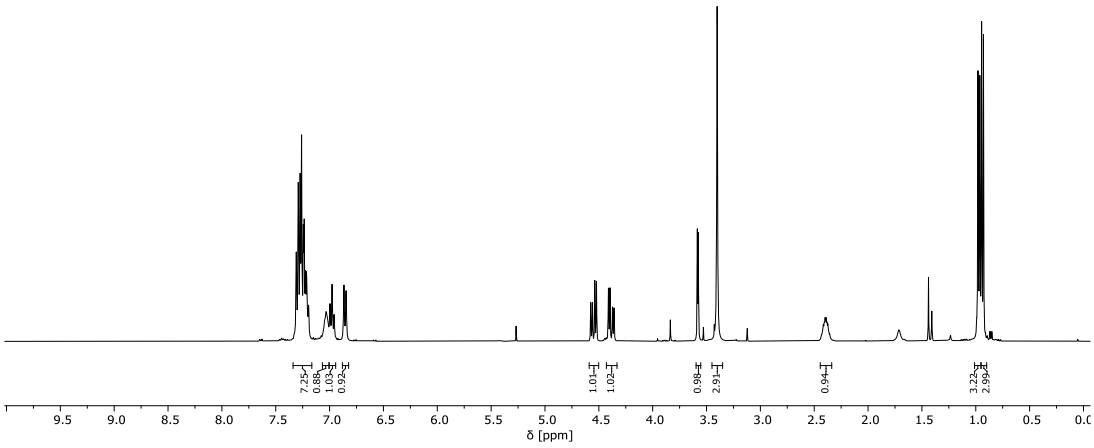


2l

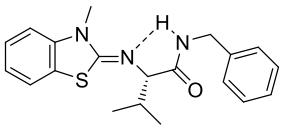
8 NMR Spectra of literature-unknown product 6

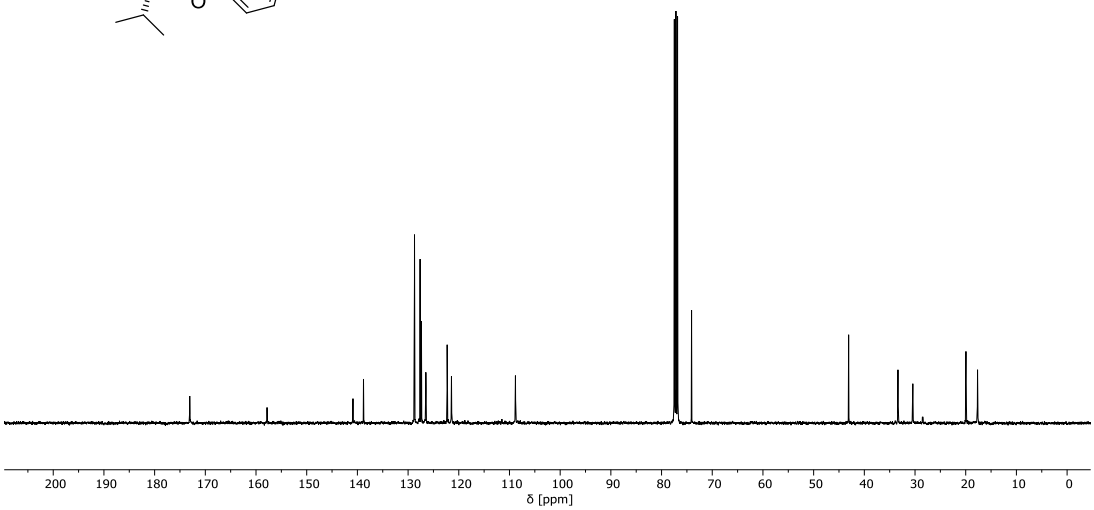
^{1}H NMR (400 MHz in $CDCl_3$), 298 K

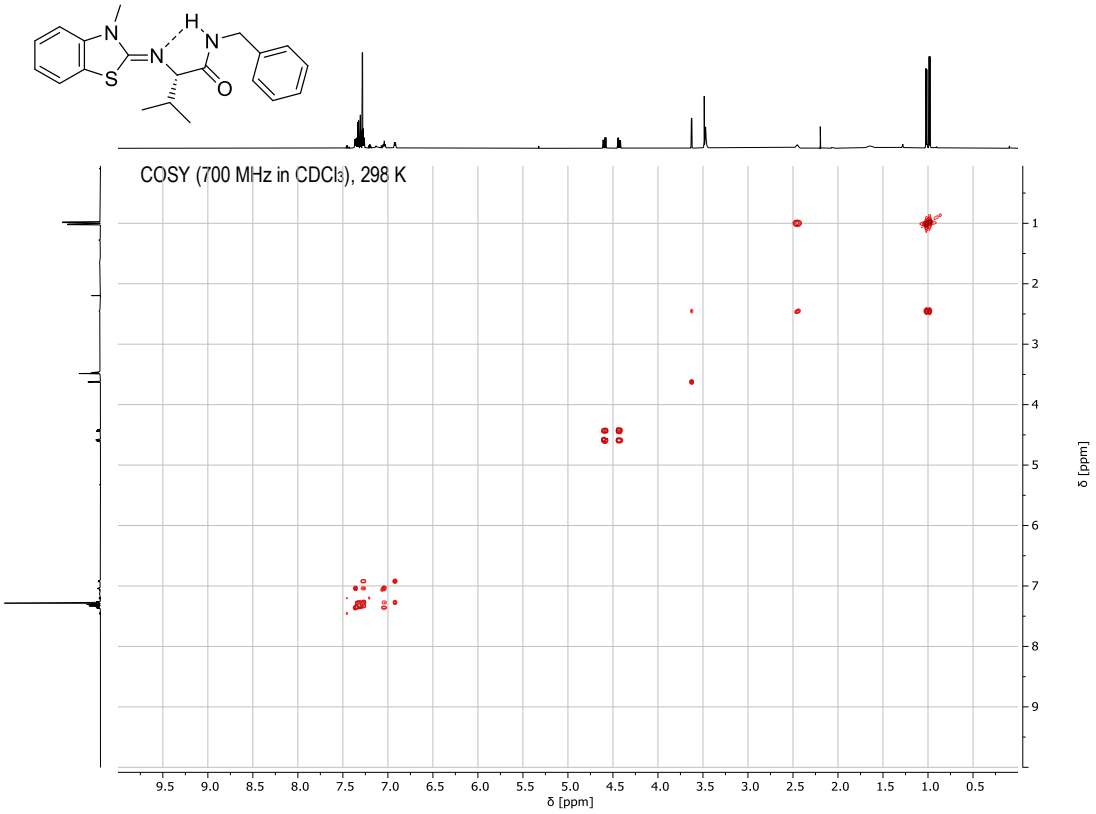


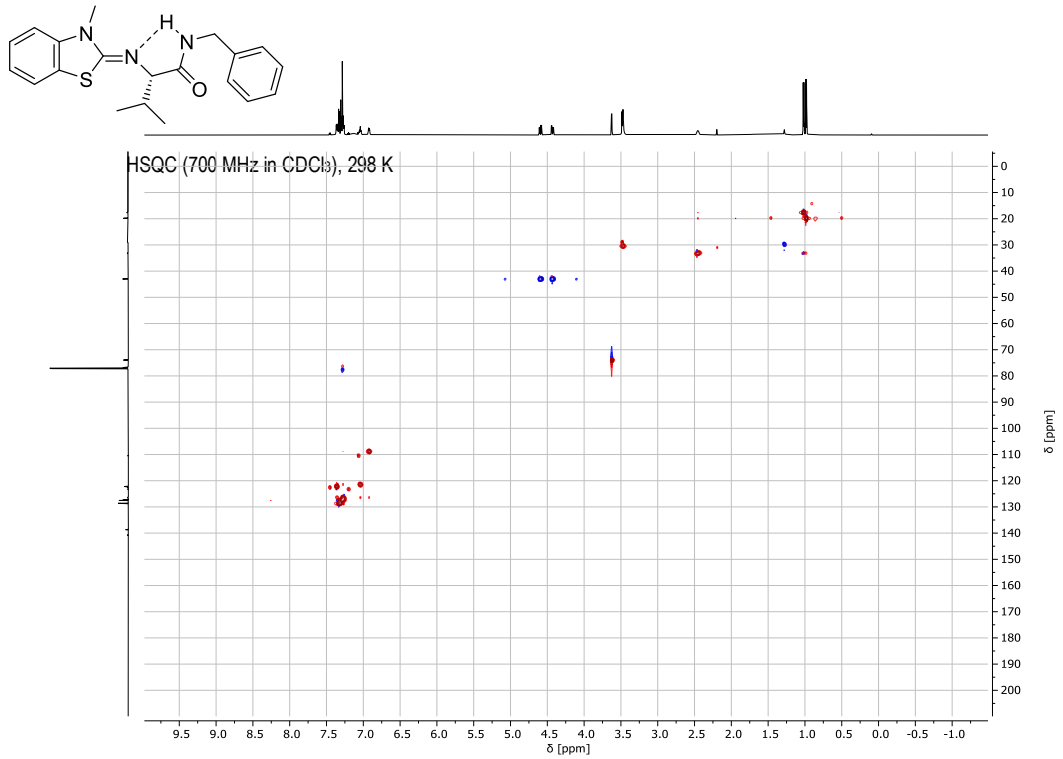


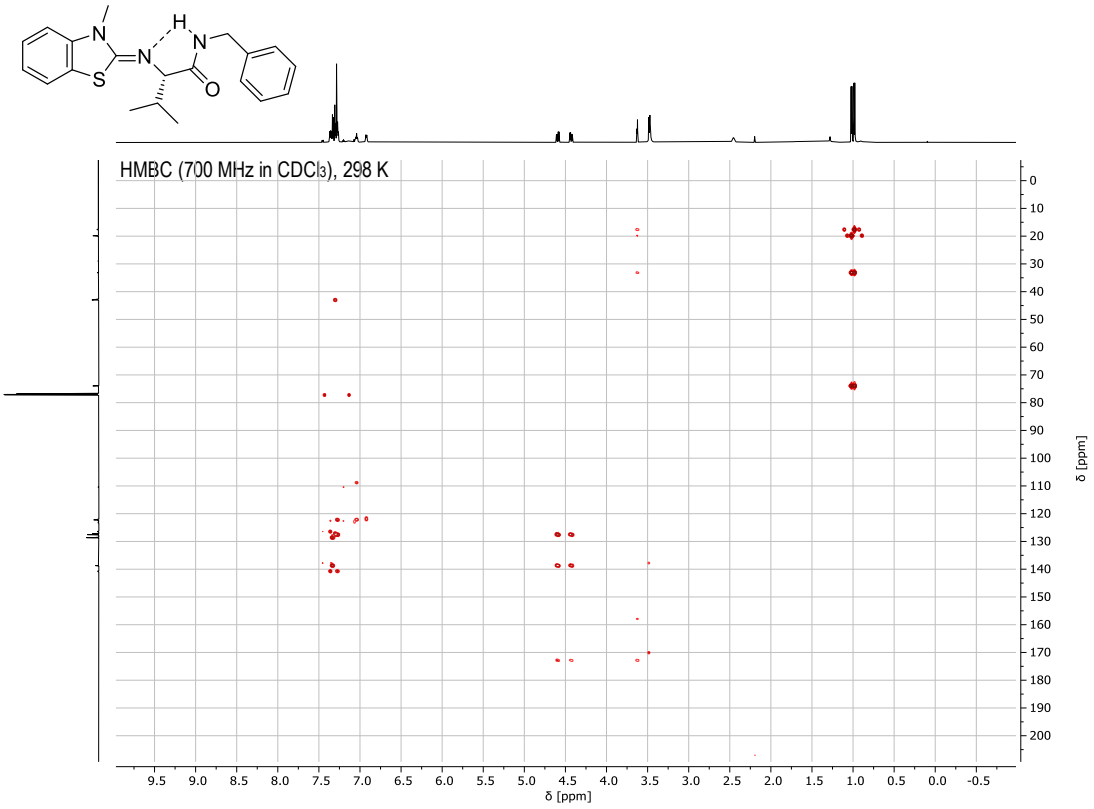
^{13}C NMR (101 MHz in $CDCl_3$), 298 K






COSY (700 MHz in CDCl3), 298 K
δ [ppm]
δ [ppm]


HSQC (700 MHz in CDCl3), 298 K
δ [ppm]
δ [ppm]



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9.1.3 Catalyst-Free Trifluoromethoxylation of Silyl Enol Ethers and Allyl Silanes with Bis(trifluoromethyl)peroxide

Supporting Information

Catalyst-Free Trifluoromethoxylation of Silyl Enol Ethers and Allyl Silanes with Bis(trifluoromethyl)peroxide

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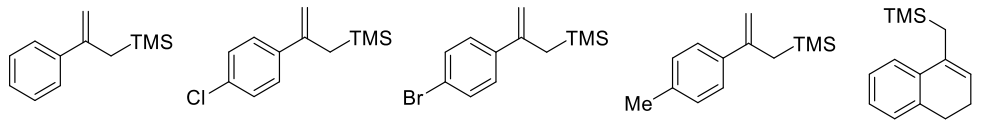
Content

1 General Information

All purchased chemicals were used without further treatment. The allyl silanes **7a-e** and bis(trifluoromethyl)peroxide were synthesized according to literature procedures and the characterisation data agree with literature values.[1,2]



7a **7b** **7c** **7d** **7e**

Thin-layer chromatography was performed on silica gel coated aluminium plates ALUGRAM® Xtra SIL G/UV254 (Macherey-Nagel). The product spots were detected by UV light (254 nm) or as permanganate stains. Flash column chromatography was performed with silica gel 60 M (0.040–0.063 mm, 230–400 mesh, Macherey-Nagel).

^{1}H, ^{19}F and ^{13}C NMR spectra were acquired on a JEOL ECS 400 (400 MHz), JEOL ECZ 400 (400 MHz), JEOL ECX 400 (400 MHz), Bruker Avance 500 (500 MHz), Varian INOVA 600 (600 MHz) or a Bruker Avance 700 (700 MHz) and analysed on MestReNova 14.3.0. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethyl silane (TMS) and coupling constants (J) are presented in hertz (Hz). CD_3CN or $CDCl_3$ are used as deuterated solvent and the residual solvent signals are used as reference in the ^{1}H and ^{13}C NMR spectra. ^{19}F NMR spectra are not calibrated by an internal reference. ^{19}F NMR yields were measured using CF_3-toluene as an internal standard.

High-resolution mass spectra were measured with an Agilent (6210 ESI-TOF; 4 µL/min, 1.0 bar, 4 kV) instrument or a Varian MAT (MAT 711, electron energy 80 *eV*).

Gas Chromatography mass spectra were measured with a Saturn 2100 GC-MS.

Infrared spectra were measured with a NICOLET spectrometer (iS10) equipped with an ATR unit (NICOLET SMART DuraSamplIR).

X-ray diffraction measurements were performed on a Bruker D8 Venture CMOS area detector (Photon 100) diffractometer with $Cu_{K\alpha}$ (λ=0.154178 nm) radiation at 125 K. Single crystals were picked in perfluoroether oil at rt or –20 °C and mounted on a 0.15 mm Mitegen micromount. They were solved using the ShelXT [3] structure solution program with intrinsic phasing and were refined with the refinement package ShelXL [4] using least squares minimizations by using the program OLEX2. [5] Diamond 4 and POV-Ray 3.7 were used for their graphical representation.

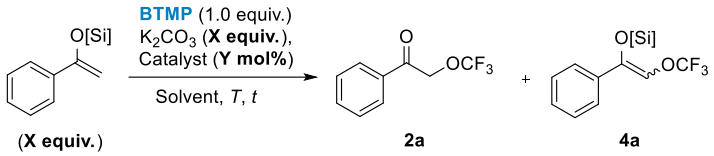
Analytical HPLC was performed in isocratic mode with a Smartline system from Knauer (Berlin, Germany), equipped with pump 1000, degasser, autosampler 3950 and variable wavelength UV detector 2500. The stationary phase usually was a pre-packed RP-18 column (RSC-Gel ec, 5 µm, 125 x 4.6 mm) from Richard Sauerbrey Chromatographie (Reinhardshagen, Germany). Additionally, for two compounds also a PGC column (Hypercarb, 5µm, 125 x 4.6 mm) from Thermo Scientific was employed. UV detection was performed at 210 nm. The flow was 1.5 mL·min^{-1}. Eluents were degassed MeOH-water or MeCN-water mixtures, given as % (v/v) MeOH or MeCN, respectively.

Preparative HPLC was performed on an isocratic system equipped with a Shimadzu LC-8A pump, Shimadzu CBM-20A controller, variable wavelength UV detector from Knauer and a Rheodyne injector with 10 mL sample loop. Stationary phase usually was a RP-18 column (RSC-Gel ec, 5 µm, 250 x 32 mm) from Richard Sauerbrey Chromatographie (Reinhardshagen, Germany). Additionally, for two compounds also a preparative PGC column (Hypercarb, 5µm, 150 x 21 mm) from Thermo Scientific was employed. HPLC runs were performed with a total flow rate of eigther 40mL·min^{-1} (RP-18) or 20mL·min^{-1} (PGC) with UV detection at 210 nm. The purity of collected fractions was determined by analytical HPLC.

Cyclic voltammetry was performed on an Interface 1010 B Potentiostat/Galvanostat/ZRA from Gamry Instruments. The measurements were performed in anhydrous and oxygen free MeCN under argon atmosphere with $TBAPF_6$ as supporting electrolyte and platinum wires as working-, counter-, and quasi-reference electrodes. The voltammograms were internally referenced against $FeCp_2^{0/+}$ for **3a** and against $FeCp_2^{0/+}$ using $CoCp_2PF_6$ as internal reference for BTMP.[6] The software OriginPro 2017G was used to plot the data.[7]

2 Optimization of the Trifluoromethoxylation of Silyl Enol Ethers using BTMP

Table S1. Different optimisation approaches for the trifluoromethoxylation of silyl enol ethers using BTMP affording trifluoromethoxylated ketones and silyl enol ethers.



(**X equiv.**) **2a** **4a**

Entry	[Si] (equiv.)	Catalyst (mol%)	K_2CO_3 (equiv.)	Solvent	T [°C]	t [h]	Yield **2a**[a]	Yield **4a**[a] (*Z*/*E*)
1	TMS (1.5)	$[Ru(bpy)_3](PF_6)_2$ (4 mol%)	-	MeCN (0.2 M)	rt	16	16	-
2	TMS (1.5)	TEMPO (25 mol%)	1.0	MeCN (0.2 M)	rt	16	6	-
3	TIPS (1.5)	TEMPO (25 mol%)	1.0	MeCN (0.2 M)	rt	16	44	4:5
4	TIPS (1.0)	TEMPO (25 mol%)	1.0	MeCN (0.2 M)	rt	16	16	-
5	TIPS (2.0)	TEMPO (25 mol%)	1.0	MeCN (0.2 M)	rt	16	42	5:3
6	TIPS (1.5)	TEMPO (50 mol%)	1.0	MeCN (0.2 M)	rt	16	25	2:6
7	TIPS (1.5)	TEMPO (10 mol%)	1.0	MeCN (0.2 M)	rt	16	44	-
8	TIPS (1.5)	TEMPO (10 mol%)	1.0	MeCN (0.2 M)	rt	6	32	2:3
9	TIPS (1.5)	TEMPO (10 mol%)	1.0	MeCN (0.2 M)	rt	24	42	-
10	TIPS (1.5)	TEMPO (10 mol%)	1.0	MeCN (0.1 M)	rt	16	43	0:11
11	TIPS (1.5)	TEMPO (10 mol%)	1.0	MeCN (0.5 M)	rt	16	26	13:6
12	TIPS (1.5)	TEMPO (10 mol%)	1.0	MeCN (0.2 M)	0	16	20	9:4
13	TIPS (1.5)	TEMPO (5 mol%)	1.0	MeCN (0.2 M)	rt	16	48	-
14	TIPS (1.5)	-	1.0	MeCN (0.2 M)	rt	16	50	-
15	TIPS (1.5)	-	1.5	MeCN (0.2 M)	rt	16	50	-
16	TIPS (1.5)	-	0.5	MeCN (0.2 M)	rt	16	31	-
17	TIPS (1.5)	-	-	MeCN (0.2 M)	rt	16	18	7:6
18	TIPS (1.5)	-	1.0	Et_2O (0.2 M)	rt	16	12	34:22

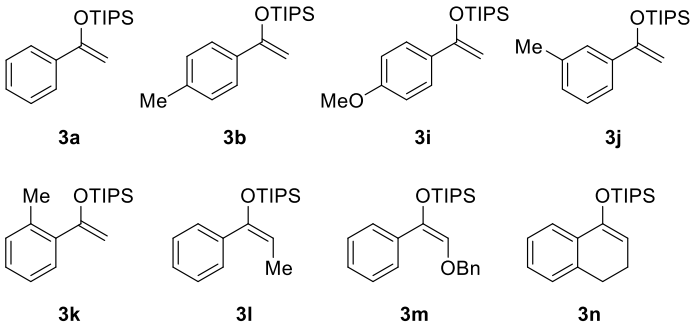
19	TIPS (1.5)	-	1.0	$MeNO_2$ (0.2 M)	rt	16	12	49:6
20	TIPS (1.5)	-	1.0	Acetone (0.2 M)	rt	16	55	-
21	TIPS (1.5)	-	1.0	DCM (0.2 M)	rt	16	5	57:12

[a] ^{19}F NMR yields using *α,α,α*-trifluorotoluene ($PhCF_3$) as an internal standard.

3 General Procedure for the Synthesis of Silyl Enol Ethers

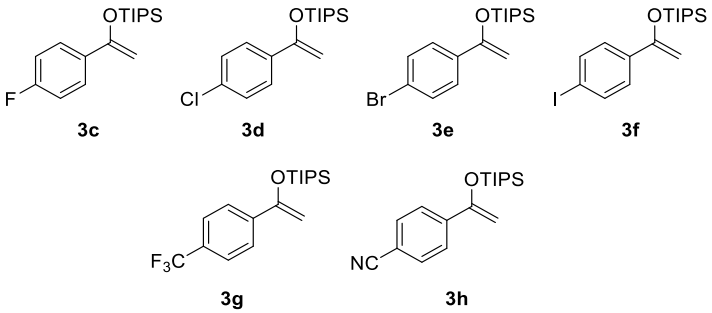
Method A: To a flame dried Schlenk-flask was added dry THF (0.8 M) and the acetophenone (1.0 equiv., 1.0 g) and the mixture was cooled to –78 °C. Sodium bis(trimethylsilyl)amide (1.2 equiv., 1.0–2.0 M in THF) was added dropwise and the rection mixture was stirred for 1 h at rt. The solution was cooled to 0 °C, TIPSCl (1.2 equiv.) was added dropwise, and the mixture was stirred for 2–4.5 h at rt. The suspension was filtered through filter paper, washed with pentane and the solvent removed under reduced pressure. The products were purified by plug or flash column chromatography (SiO_2, petroleum ether or pentane with 1 % NEt_3).

Silyl enol ethers **3a,b, i-n** were synthesised according to **method A** and the characterisation data agree with the values reported in the literature. [8]

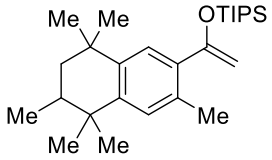


Method B: To a flame dried Schlenk-flask was added dry DCM (0.8 M) and the acetophenone (1.0 equiv., 1.0 g) under inert gas. Triethylamine (1.8 equiv.) and then TIPSOTf (1.2 equiv.) were added, and the reaction mixture was stirred at rt for 2 h. The mixture was diluted with DCM, washed with NH_4Cl-solution (sat. in dist. water) and the aqueous phase was extracted with EtOAc (3x). The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure and the products were purified by plug or flash column chromatography (SiO_2, petroleum ether or pentane with 1 % NEt_3).

Silyl enol ethers **3c-h** were synthesised according to **method B** and the characterisation data agree with the values reported in the literature. [8a-c, 9]



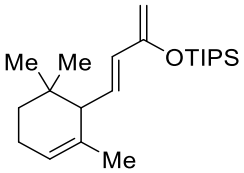
((1-(3,5,5,6,8,8-hexamethyl-5,6,7,8-tetrahydronaphthalen-2-yl)vinyl)oxy)triisopropylsilane **3o**



According to Method A, silyl enol ether **3o** (1.05 g, 2.53 mmol, 65 %) was obtained from tonalide as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33 (s, 1H), 7.12 (s, 1H), 4.54 (d, J = 1.1 Hz, 1H), 4.37 (d, J = 1.0 Hz, 1H), 2.39 (s, 3H), 1.87 (dqd, J = 13.5, 6.8, 2.9 Hz, 1H), 1.67 – 1.50 (m, 2H), 1.32 (s, 3H), 1.28 (s, 3H), 1.30 – 1.18 (m, 3H), 1.24 (s, 3H), 1.09 (d, J = 7.3 Hz, 18H), 1.06 (s, 3H), 0.98 (d, J = 6.8 Hz, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ = 157.9, 145.6, 141.7, 136.5, 132.5, 128.9, 126.8, 94.1, 43.9, 37.6, 36.0, 34.7, 34.1, 31.2, 28.7, 25.1, 20.8, 18.2, 17.0, 12.8. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3154 (w), 2961 (s), 2866 (s), 1620 (m), 1463 (m), 1307 (m), 1265 (m), 1111 (s), 1015 (s), 881 (s), 679 (s), 658 (m). **HRMS (EI):** m/z calculated for $[C_{27}H_{46}OSi]^+$ ([M]$^+$): 414.3318, measured: 414.3309.

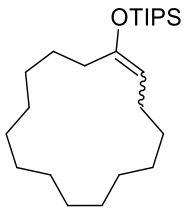
(E)-triisopropyl((4-(2,6,6-trimethylcyclohex-2-en-1-yl)buta-1,3-dien-2-yl)oxy)silane **3p**



According to Method A, silyl enol ether **3p** (0.76 g, 2.17 mmol, 42 %) was obtained from *α*-ionone as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.91 (dd, J = 15.1, 9.1 Hz, 1H), 5.82 (d, J = 15.1 Hz, 1H), 5.42 – 5.38 (m, 1H), 4.21 (d, J = 15.4 Hz, 2H), 2.17 (d, J = 9.2 Hz, 1H), 2.04 – 1.96 (m, 2H), 1.58 (q, J = 1.9 Hz, 3H), 1.41 (dt, J = 13.2, 7.9 Hz, 1H), 1.28 – 1.17 (m, 4H), 1.10 (d, J = 7.2 Hz, 18H), 0.89 (s, 3H), 0.82 (s, 3H). **^{13}C NMR** (101 MHz, CD_3CN) δ = 156.3, 133.4, 130.1, 121.9, 118.3, 94.2, 54.5, 33.0, 32.3, 27.8, 27.2, 23.8, 23.1, 18.5, 13.6. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 2944 (s), 2866 (s), 1587 (m), 1463 (m), 1324 (m), 1288 (m), 1022 (s), 882 (s), 814 (m), 741 (s), 676 (s), 660 (s). **HRMS (EI):** m/z calculated for $[C_{22}H_{40}OSi]^+$ ([M]$^+$): 348.2848, measured: 348.2869.

(Cyclopentadec-1-en-1-yloxy)triisopropylsilane **3q**

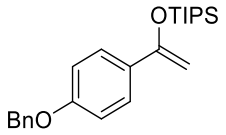


According to Method A, silyl enol ether **3q** (176 mg, 0.46 mmol, 10 %) was obtained as a mixture of two diastereomers (d.r. 1:2.4) from cyclopentadecanone as a colourless oil.

^{1}H NMR* (400 MHz, $CDCl_3$) δ = 4.54 (t_1, J = 7.5 Hz, 1H), 4.32 (t_2, J = 6.7 Hz, 1H), 2.08 ($m_{1,2}$, 3 x 2H), 1.92 (q_1 , J = 7.4 Hz, 2H), 1.55 (dt_1, J = 14.1, 6.8 Hz, 2H), 1.48 – 1.42 (m_2, 2H), 1.40 – 1.24 ($m_{1,2}$, 2 x 18H and 2 x 2H), 1.21 – 1.11 ($m_{1,2}$, 2 x 3H), 1.11 – 1.05 ($m_{1,2}$, 2 x 18H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 152.1, 150.5, 107.9, 106.2, 36.2, 31.0, 29.5, 29.3, 27.7, 27.7, 27.5, 27.4, 27.4, 27.3, 27.3, 27.2, 27.2, 27.1, 27.1, 27.0, 27.0, 26.9, 26.9, 26.6, 26.6, 26.5, 26.4, 26.2, 25.8, 24.7, 18.3, 18.2, 13.6, 12.9. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 2924 (s), 2857 (s), 1666 (w), 1461 (m),

1367 (m), 1249 (w), 1133 (w), 1061 (m), 1014 (w), 997 (w), 882 (s), 839 (w), 674 (s). **HRMS (EI):** m/z calculated for $[C_{24}H_{48}OSi]^+$ ($[M]^+$): 380.3474, measured: 380.3480.
*Note: Proton multiplets of minor product marked as 1 and protons of the proton multiplets of major product marked as 2.

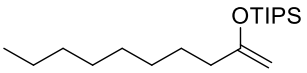
((1-(4-(benzyloxy)phenyl)vinyl)oxy)triisopropylsilane **3r**



According to Method A, silyl enol ether **3r** (0.95 g, 2.5 mmol, 57 %) was obtained from 4'-benzyloxyacetophenone as a colourless oil.

^{1}H NMR (400 MHz, CD_3CN) δ = 7.64 – 7.54 (m, 2H), 7.45 – 7.40 (m, 2H), 7.40 – 7.35 (m, 2H), 7.37 – 7.27 (m, 1H), 6.98 – 6.90 (m, 2H), 5.06 (s, 2H), 4.79 (d, J = 1.8 Hz, 1H), 4.34 (d, J = 1.8 Hz, 1H), 1.38 – 1.20 (m, 3H), 1.12 (d, J = 7.2 Hz, 18H). **^{13}C NMR** (151 MHz, CD_3CN) δ = 160.0, 156.9, 138.3, 131.5, 129.6, 129.5, 129.1, 128.9, 128.7, 128.7, 127.6, 115.6, 115.4, 89.4, 70.9, 18.6, 13.7. **HRMS (EI):** m/z calculated for $[C_{24}H_{34}O_2Si]^+$ ($[M]^+$): 382.2328, measured: 382.2303.
*Note: Due to the rapid decomposition of the molecule, the ^{13}C NMR shows slight formation of the corresponding acetophenone and no clean IR spectrum could be measured.

(dec-1-en-2-yloxy)triisopropylsilane **3s**



According to Method A, silyl enol ether **3s** (1.4 g) was obtained as a mixture of three products (ratio 1:2.9:1.9) from 2-decanone, with **3s** being the second major product. The mixture was used without further purification.

4 Trifluoromethoxylation of Silyl Enol Ethers

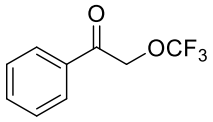
4.1 Synthesis of α-Trifluoromethoxylated Ketones

Method A: Silyl enol ether **3a** (1.5 equiv., 0.75 mmol) and K_2CO_3 (1.0 equiv., 0.5 mmol, 69 mg) were added to a 15 mL Schlenk-pressure tube with DCM (2.5 mL). The mixture was frozen with liquid N_2 and degassed using freeze-pump-thaw technique. BTMP (1.0 equiv., 0.5 mmol, 85 mg) was condensed in, the reaction mixture was allowed to warm to rt and stirred vigorously at rt for 16 h. The pressure tube was opened carefully in the back of the fume hood to release possible excess gas. Trifluoroacetic acid (3.0 equiv., 1.5 mmol, 244 µL) was added and the resulting mixture was stirred 4 h at rt. The solvent was evaporated under reduced pressure and the products were obtained after column chromatography (SiO_2, pentane/DCM).

Method B: Silyl enol ethers **3b-q** (1.5 equiv., 0.75 mmol) and K_2CO_3 (1.0 equiv., 0.5 mmol, 69 mg) were added to a 15 mL Schlenk-pressure tube with acetone (2.5 mL). The mixture was frozen with liquid N_2 and degassed using freeze-pump-thaw technique. BTMP (1.0 equiv., 0.5 mmol, 85 mg) was condensed in, the reaction mixture was allowed to warm to rt and stirred vigorously at rt for 16 h. The pressure tube was opened carefully in the back of the fume hood to release possible excess gas. The solids were filtered off and the solvent was evaporated under reduced pressure. The products were obtained after column chromatography (SiO_2, pentane/DCM).

4.2 Analytical Data for α-Trifluoromethoxylated Ketones

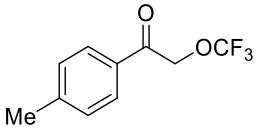
1-phenyl-2-(trifluoromethoxy)ethan-1-one **2a**



According to the general method A ketone **2a** (51 mg, 0.25 mmol, 50 %) was obtained from silyl enol ether **3a** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93 – 7.87 (m, 2H), 7.67 – 7.61 (m, 1H), 7.55 – 7.47 (m, 2H), 5.18 (s, 2H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –60.95. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 190.3, 134.5, 133.8, 129.2, 128.0, 121.8 (q, *J* = 257 Hz), 68.4 (q, *J* = 3 Hz).
The characterisation data agree with literature values. [10]

1-(*p*-tolyl)-2-(trifluoromethoxy)ethan-1-one **2b**

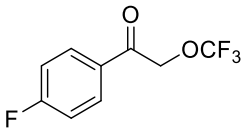


According to the general method B ketone **2b** (67 mg, 0.3 mmol, 61 %) was obtained from silyl enol ether **3b** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.80 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.15 (s, 2H), 2.43 (s, 3H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –60.9. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 189.8, 145.5, 131.3, 129.8, 128.0, 121.7 (q, *J* = 256 Hz), 68.3 (q, *J* = 3 Hz), 21.8.

The characterisation data agree with literature values. [10]

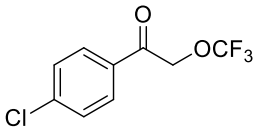
1-(4-fluorophenyl)-2-(trifluoromethoxy)ethan-1-one **2c**



According to the general method B ketone **2c** (61 mg, 0.275 mmol, 55 %) was obtained from silyl enol ether **3c** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.99 – 7.92 (m, 2H), 7.24 – 7.15 (m, 2H), 5.13 (s, 2H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –61.0 (OC**F$_3$**), –102.3 (tt, *J* = 8, 5 Hz, 1F). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 188.9, 166.5 (d, *J* = 257 Hz), 130.9 (d, *J* = 10 Hz), 130.4 (d, *J* = 257 Hz), 121.8 (q, *J* = 257 Hz), 116.5 (d, *J* = 22 Hz), 68.3 (q, *J* = 3 Hz).
The characterisation data agree with literature values. [11]

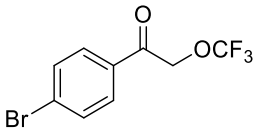
1-(4-chlorophenyl)-2-(trifluoromethoxy)ethan-1-one **2d**



According to the general method B ketone **2d** (90 mg, 0.375 mmol, 75 %) was obtained from silyl enol ether **3d** as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84 (d, *J* = 8.7 Hz, 2H), 7.47 (d, *J* = 8.6 Hz, 2H), 5.14 (s, 2H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –61.04. **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 189.3, 141.0, 132.1, 129.5, 129.5, 121.7 (q, *J* = 257 Hz), 68.3 (q, *J* = 3 Hz). **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3097 (w), 2950 (w), 2870 (w), 1708 (m), 1592 (m), 1404 (m), 1264 (s), 1220 (s), 1142 (s), 1091 (s), 982 (s), 816 (s), 802 (s), 616 (m), 563 (s). **HRMS (EI):** m/z calculated for $[C_9H_6ClF_3O_2]^+$ ($[M]^+$): 238.0008, measured: 237.9977.

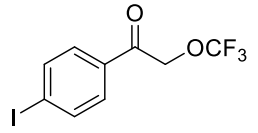
1-(4-bromophenyl)-2-(trifluoromethoxy)ethan-1-one **2e**



According to the general method B ketone **2e** (85 mg, 0.3 mmol, 60 %) was obtained from silyl enol ether **3e** as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.82 – 7.74 (m, 2H), 7.69 – 7.64 (m, 2H), 5.13 (s, 2H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –61.0. **^{13}C NMR** (176 MHz, $CDCl_3$) δ = 189.4, 132.4, 132.4, 129.7, 129.4, 121.6 (q, *J* = 257 Hz), 68.2 (q, *J* = 3 Hz).
The characterisation data agree with literature values. [11]

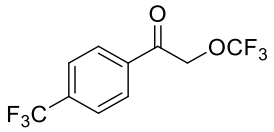
1-(4-iodophenyl)-2-(trifluoromethoxy)ethan-1-one **2f**



According to the general method B ketone **2f** (69 mg, 0.21 mmol, 42 %) was obtained from silyl enol ether **3f** as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.91 – 7.86 (m, 2H), 7.64 – 7.59 (m, 2H), 5.11 (s, 1H).**^{19}F NMR** (377 MHz, $CDCl_3$) δ = –61.0. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 189.9, 138.5, 133.1, 129.3, 125.6, 121.7 (q, *J* = 257 Hz), 102.7, 68.2 (q, *J* = 3 Hz). **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3095 (w), 3057 (w), 2952 (w), 2879 (w), 1696 (s), 1580 (s), 1391 (m), 1374 (m), 1268 (s), 1197 (s), 1148 (s), 1096 (s), 1057 (s), 981 (s), 813 (s), 601 (m), 561 (s). **HRMS (EI):** m/z calculated for $[C_9H_6F_3IO_2]^+$ ($[M]^+$): 329.9365, measured: 329.9343.

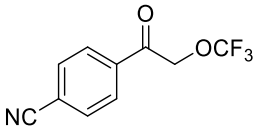
2-(trifluoromethoxy)-1-(4-(trifluoromethyl)phenyl)ethan-1-one **2g**



According to the general method B ketone **2g** (23 mg, 0.09 mmol, 17 %) was obtained from silyl enol ether **3g** as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.1 – 8.0 (m, 2H), 7.8 – 7.8 (m, 2H), 5.2 (s, 2H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –61.1 (OCF_3), –63.3 (CF_3). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 189.8, 136.5, 135.7 (q, J = 33 Hz), 128.6, 126.3 (q, J = 4 Hz), 123.4 (q, J = 273 Hz), 121.7 (q, J = 257 Hz), 68.5 (q, J = 3 Hz). **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3120 (w), 3075 (w), 2948 (w), 2872 (w), 1709 (m), 1516 (w), 1415 (m), 1326 (m), 1280 (m), 1218 (s), 1133 (s), 1111 (s), 1065 (s), 1016 (m), 993 (m), 846 (m), 831 (m), 614 (m), 601 (m). **HRMS (EI):** m/z calculated for $[C_{10}H_6F_6O_2]^+$ ($[M]^+$): 272.0272, measured: 272.0255.

4-(2-(trifluoromethoxy)acetyl)benzonitrile **2h**

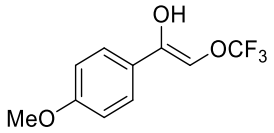


According to the general method B ketone **2h** (20 mg, 0.09 mmol, 17 %) was obtained from silyl enol ether **3h** as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.01 (d, J = 8.6 Hz, 2H), 7.83 (d, J = 8.5 Hz, 2H), 5.15 (s, 2H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –61.1. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 189.5, 136.7, 132.9, 128.6, 121.6 (d, J = 257 Hz), 117.7, 117.5, 68.4 (q, J = 3 Hz).

The characterisation data agree with literature values.[11]

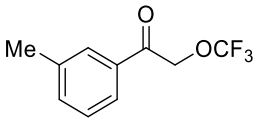
(Z)-1-(4-methoxyphenyl)-2-(trifluoromethoxy)ethen-1-ol **5i**



According to the general method B enol **5i** (33 mg, 0.14 mmol, 28 %) was obtained from silyl enol ether **3i** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.10 – 7.99 (m, 2H), 7.19 (bs, 1H), 7.05 – 6.96 (m, 2H), 6.25 (s, 1H), 3.91 (s, 3H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –58.7. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 184.1, 165.2, 132.6, 123.9, 120.7 (q, *J* = 261 Hz), 114.5, 93.8 (p, *J* = 3 Hz), 55.8. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3085 (w), 3026 (w), 2929 (w), 2850 (w), 1688 (m), 1600 (s), 1515 (m), 1235 (s), 1166 (s), 1063 (m), 1027 (s), 983 (w), 875 (s), 839 (m), 700 (m), 588 (s). **HRMS (EI):** m/z calculated for $[C_{10}H_9F_3O_3]^+$ ($[M]^+$): 234.0504, measured: 234.0483.

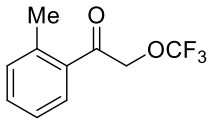
1-(*m*-tolyl)-2-(trifluoromethoxy)ethan-1-one **2j**



According to the general method B ketone **2j** (70 mg, 0.32 mmol, 64 %) was obtained from silyl enol ether **3j** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.75 – 7.65 (m, 2H), 7.49 – 7.42 (m, 1H), 7.39 (t, J = 7.6 Hz, 1H), 5.17 (s, 2H), 2.43 (s, 3H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –41.1. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 190.4, 139.2, 135.3, 133.9, 129.0, 128.5, 125.2, 121.8 (q, *J* = 257 Hz), 68.4 (q, *J* = 3 Hz), 21.5.
The characterisation data agree with literature values. [11]

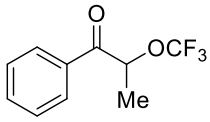
1-(*o*-tolyl)-2-(trifluoromethoxy)ethan-1-one **2k**



According to the general method B ketone **2k** (66 mg, 0.3 mmol, 60 %) was obtained from silyl enol ether **3k** as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.45 (td, *J* = 7.5, 1.4 Hz, 1H), 7.33 – 7.27 (m, 2H), 5.04 (s, 2H), 2.54 (s, 3H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –60.9. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 193.5, 139.7, 133.7, 132.8, 132.6, 128.3, 126.0, 121.8 (q, *J* = 257 Hz), 69.3 (q, *J* = 3 Hz), 21.3.
The characterisation data agree with literature values. [11]

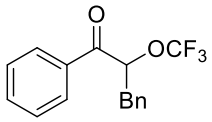
1-phenyl-2-(trifluoromethoxy)propan-1-one **2l**



According to the general method B ketone **2l** (48 mg, 0.22 mmol, 44 %) was obtained from silyl enol ether **3l** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00 – 7.93 (m, 2H), 7.68 – 7.58 (m, 1H), 7.56 – 7.46 (m, 2H), 5.49 (q, J = 7.0 Hz, 1H), 1.65 (d, J = 6.9 Hz, 3H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –58.8. **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 195.1, 134.2, 133.7, 129.1, 128.9, 121.6 (d, *J* = 257 Hz), 75.4 (q, *J* = 3 Hz), 18.8.
The characterisation data agree with literature values. [11]

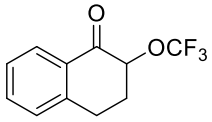
1,3-diphenyl-2-(trifluoromethoxy)propan-1-one **2m**



According to the general method B ketone **2m** (79 mg, 0.27 mmol, 54 %) was obtained from silyl enol ether **3m** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.94 – 7.89 (m, 2H), 7.66 – 7.58 (m, 1H), 7.52 – 7.46 (m, 2H), 7.33 – 7.25 (m, 3H), 7.25 – 7.20 (m, 2H), 5.51 (dd, *J* = 7.8, 5.3 Hz, 1H), 3.25 – 3.20 (m, 2H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –58.9. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 194.7, 135.0, 134.2, 129.5, 129.1, 128.9, 128.8, 127.6, 121.4 (q, *J* = 257 Hz), 79.5 (q, *J* = 2 Hz), 53.6, 39.0.
The characterisation data agree with literature values. [11]

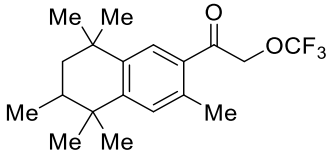
2-(trifluoromethoxy)-3,4-dihydronaphthalen-1(2H)-one **2n**



According to the general method B ketone **2n** (85 mg, 0.37 mmol, 74 %) was obtained from silyl enol ether **3n** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.54 (td, *J* = 7.5, 1.5 Hz, 1H), 7.36 (ddt, *J* = 8.0, 7.4, 1.4 Hz, 1H), 7.32 – 7.23 (m, 1H), 4.84 (dd, *J* = 12.1, 4.8 Hz, 1H), 3.16 (dd, *J* = 8.1, 4.4 Hz, 2H), 2.54 (dq, *J* = 13.3, 4.5 Hz, 1H), 2.39 (tt, *J* = 12.6, 8.1 Hz, 1H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –58.5. **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 191.0, 142.8, 134.4, 131.3, 128.8, 128.3, 127.4, 121.9 (q, *J* = 256 Hz), 78.0 (q, *J* = 2 Hz), 30.2, 27.3.
The characterisation data agree with literature values. [12]

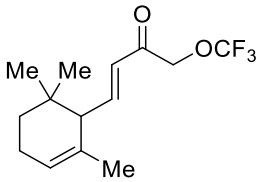
1-(3,5,5,6,8,8-hexamethyl-5,6,7,8-tetrahydronaphthalen-2-yl)-2-(trifluoromethoxy)ethan-1-one **2o**



According to the general method B ketone **2o** (52 mg, 0.15 mmol, 43 %) was obtained from silyl enol ether **3o** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54 (s, 1H), 7.32 (s, 1H), 5.09 (s, 2H), 2.56 (s, 3H), 1.94 (dqd, J = 13.4, 6.8, 2.6 Hz, 1H), 1.70 (t, J = 13.2 Hz, 1H), 1.47 (dd, J = 13.6, 2.7 Hz, 1H), 1.39 (s, 3H), 1.38 (s, 3H), 1.33 (s, 3H), 1.13 (s, 3H), 1.06 (d, J = 6.8 Hz, 3H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –60.8. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 192.9, 151.6, 142.6, 136.4, 131.2, 127.1, 121.7 (d, J = 256 Hz), 69.2 (q, J = 3 Hz), 43.3, 38.1, 34.4, 34.1, 32.5, 31.9, 28.3, 24.7, 21.2, 16.8.
The characterisation data agree with literature values. [11]

(E)-1-(trifluoromethoxy)-4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one **2p**

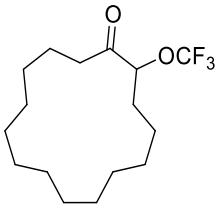


According to the general method B ketone **2p** (55 mg, 0.2 mmol, 40 %) was obtained from silyl enol ether **3p** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.86 (dd, *J* = 15.7, 9.8 Hz, 1H), 6.27 (d, *J* = 15.7 Hz, 1H), 5.52 (pd, *J* = 2.4, 1.4 Hz, 1H), 4.61 (s, 2H), 2.31 (d, *J* = 9.8 Hz, 1H), 2.09 – 1.98 (m, 2H), 1.55 (q, *J* = 1.9 Hz, 3H), 1.51 – 1.39 (m, 1H), 1.26 – 1.18 (m, 1H), 0.92 (s, 3H), 0.84 (s, 3H).**^{19}F NMR** (377 MHz, $CDCl_3$) δ = –61.1. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 191.0, 151.8, 131.3, 125.8, 123.4, 121.7 (q, *J* = 256 Hz), 69.5 (q, *J* = 3 Hz), 54.7, 32.8, 31.1, 28.0, 26.8, 23.1, 22.8.

The characterisation data agree with literature values. [11]

2-(trifluoromethoxy)cyclopentadecan-1-one **2q**



According to the general method B ketone **2q** (23 mg, 0.07 mmol, 24 %) was obtained from silyl enol ether **3q** as a colourless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ = 4.50 (dd, J = 6.5, 5.2 Hz, 1H), 2.74 (ddd, J = 17.9, 8.1, 6.0 Hz, 1H), 2.43 (dt, J = 17.8, 6.3 Hz, 1H), 1.93 – 1.70 (m, 3H), 1.69 – 1.50 (m, 1H), 1.42 – 1.27 (m, 18H), 1.14 – 1.00 (m, 2H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –58.9. **^{13}C NMR** (176 MHz, $CDCl_3$) δ = 208.0, 121.6 (q, J = 256 Hz), 82.2 (q, J = 2.5 Hz), 37.4, 31.7, 27.5, 27.2, 26.8, 26.8, 26.7, 26.6, 26.3, 26.3, 26.1, 22.6, 21.9. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 2927 (m), 2858 (m), 1724 (m), 1460 (m), 1362 (w), 1271 (s), 1222 (s), 1141 (s), 1061 (w), 881 (w), 626 (w). **HRMS (EI):** m/z calculated for $[C_{16}H_{27}F_3O_2]^+$ ([M]$^+$): 308.1963, measured: 308.1947.

4.3 Synthesis of Trifluoromethoxylated Silyl Enol Ethers

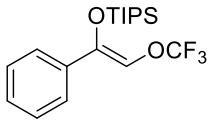
Silyl enol ethers **3a-g,j,k,n-p,r,s** (1.5 equiv., 0.75 mmol) and K_2CO_3 (1.0 equiv., 0.5 mmol, 69 mg) were added to a 15 mL Schlenk-pressure tube with DCM (2.5 mL). The mixture was frozen with liquid N_2 and degassed using freeze-pump-thaw technique. BTMP (1.0 equiv., 0.5 mmol, 85 mg) was condensed in, the reaction mixture was allowed to warm to rt and stirred vigorously at rt for 16 h. The pressure tube was opened carefully in the back of the fume hood to release possible excess gas.

Crude NMR yields: Trifluorotoluene (1.0 equiv., 0.5 mmol, 61 µL) and $CDCl_3$ (1 mL) was added to the reaction mixture. Up to 0.8 mL of the crude mixture was filtered through cotton into an NMR tube for ^{19}F NMR analysis.

Isolation: The products were isolated using preparative HPLC (solvent system see individual product).

4.4 Analytical Data for Trifluoromethoxylated Silyl Enol Ethers

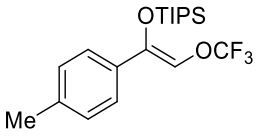
(Z)-Triisopropyl((1-phenyl-2-(trifluoromethoxy)vinyl)oxy)silane **(*Z*)-4a**



According to the general method enol ether **(*Z*)-4a** (270 mg, 0.75 mmol, 31 %) was purified by repeated preparative HPLC using two different solvent systems (first 80% MeCN, second 90% MeOH) and obtained as a colourless oil on a 2.4 mmol (BTMP) scale. The reaction was also conducted on a 0.5 mmol scale under the same conditions with ^{19}F NMR of the crude mixture indicating both **(*Z*)-4a** and **(*E*)-4a** were formed in 56% and 12% yield, respectively. The (*Z*)-configuration was assigned using NOE experiments (see section 7).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.56 – 7.47 (m, 2H), 7.44 – 7.35 (m, 3H), 6.46 (s, 1H), 1.24 (dq, *J* = 13.1, 7.1 Hz, 3H), 1.12 (d, *J* = 7.2 Hz, 18H).**^{19}F NMR** (377 MHz, $CDCl_3$) δ = –60.4. **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 142.7, 135.6, 128.8, 128.5, 125.7, 121.0 (d, *J* = 257 Hz), 118.8 (q, *J* = 4 Hz), 17.9, 13.4. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3108 (w), 3065 (w), 2947 (m), 2869 (m), 1668 (m), 1465 (m), 1364 (m), 1259 (s), 1214 (s), 1160 (s), 1137 (s), 1081 (m), 1067 (m), 882 (m), 850 (m), 684 (s), 599 (s). **HRMS (EI):** m/z calculated for $[C_{18}H_{27}F_3O_2Si]^+$ ([M]$^+$): 360.1732, measured: 360.1705.

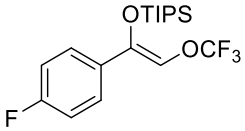
(Z)-triisopropyl((1-(*p*-tolyl)-2-(trifluoromethoxy)vinyl)oxy)silane **(*Z*)-4b**



Applying the general method to the silyl enol ether **3b** the ^{19}F NMR of the crude mixture indicated that both **(*Z*)-4b** and **(*E*)-4b** were formed in 24% and 2% yield, respectively. Purification by repeated preparative HPLC using two different solvent systems (first 88% MeCN, second 90% MeOH) allowed for isolation of the major isomer **(*Z*)-4b** (18 mg, 0.05 mmol, 10 %) as a colourless oil. The (*Z*)-configuration is tentatively assigned by analogy to the related reactions affording **(*Z*)-4a** and **(*Z*)-4r**.

^{1}H NMR (600 MHz, CD_3CN) δ = 7.44 – 7.37 (m, 2H), 7.24 – 7.16 (m, 2H), 6.58 (s, 1H), 2.34 (s, 3H), 1.25 – 1.11 (m, 3H), 1.06 (d, *J* = 7.0 Hz, 18H). **^{19}F NMR** (565 MHz, CD_3CN) δ = –60.9. **^{13}C NMR** (151 MHz, CD_3CN) δ = 143.9, 140.0, 133.2, 130.0, 126.6, 121.9 (q, *J* = 255 Hz), 119.7 (q, *J* = 3 Hz), 21.2, 18.1, 14.0. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3118 (w), 3030 (w), 2946 (m), 2869 (m), 1670 (m), 1464 (m), 1363 (m), 1259 (s), 1214 (s), 1158 (s), 1136 (s), 1078 (s), 1067 (s), 1018 (m), 882 (m), 854 (m), 821 (s), 725 (m), 683 (s), 568 (m). **HRMS (EI):** m/z calculated for $[C_{19}H_{29}F_3O_2Si]^+$ ([M]$^+$): 374.1889, measured: 374.1898.

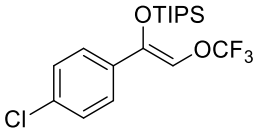
(Z)-((1-(4-fluorophenyl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **(*Z*)-4c**



Applying the general method to the silyl enol ether **3c** the ^{19}F NMR of the crude mixture indicated that both **(*Z*)-4c** and **(*E*)-4c** were formed in 42% and 11% yield, respectively. Purification by preparative HPLC (85% MeOH) allowed for isolation of the major isomer **(*Z*)-4c** (38 mg, 0.1 mmol, 20 %) as a colourless oil. The (*Z*)-configuration is tentatively assigned by analogy to the related reactions affording **(*Z*)-4a** and **(*Z*)-4r**.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.49 – 7.40 (m, 2H), 7.09 – 6.98 (m, 2H), 6.34 (s, 1H), 1.25 – 1.11 (m, 3H), 1.06 (d, J = 7.0 Hz, 18H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –60.4 (OCF_3), –112.7 (tt, *J* = 9, 5 Hz, F). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 163.1 (d, *J* = 249 Hz), 141.9, 131.8 (d, *J* = 3 Hz), 127.6 (d, *J* = 8. Hz), 121.0 (q, *J* = 257 Hz), 118.6 (qd, *J* = 4 Hz), 115.5 (d, *J* = 22 Hz), 17.9, 13.4. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3112 (w), 3054 (w), 2947 (m), 2869 (m), 1671 (m), 1605 (m), 1509 (m), 1365 (m), 1262 (s), 1213 (s), 1156 (s), 1139 (s), 1079 (m), 1067 (m), 882 (m), 839 (s), 684 (s), 567 (s). **HRMS (EI):** m/z calculated for $[C_{18}H_{26}F_4O_2Si]^+$ ($[M]^+$):378.1638, measured: 378.1668.

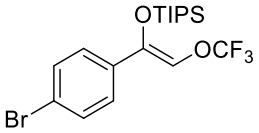
(Z)-((1-(4-chlorophenyl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **(*Z*)-4d**



Applying the general method to the silyl enol ether **3d** the ^{19}F NMR of the crude mixture indicated that both **(*Z*)-4d** and **(*E*)-4d** were formed in 41% and 11% yield, respectively. Purification by preparative HPLC (90% MeOH) allowed for isolation of the major isomer **(*Z*)-4d** (57 mg, 0.15 mmol, 29 %) as a colourless oil. The (*Z*)-configuration is tentatively assigned by analogy to the related reactions affording **(*Z*)-4a** and **(*Z*)-4r**.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.44 – 7.36 (m, 2H), 7.36 – 7.28 (m, 2H), 6.39 (s, 1H), 1.25 – 1.12 (m, 3H), 1.06 (d, J = 7.1 Hz, 18H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –60.4. **^{13}C NMR** (176 MHz, $CDCl_3$) δ = 141.7, 134.6, 134.2, 128.8, 126.9, 121.0 (q, *J* = 258 Hz), 119.0 (q, *J* = 4 Hz), 17.9, 13.4. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3116 (w), 2947 (m), 2869 (m), 1669 (m), 1598 (w), 1367 (m), 1259 (s), 1212 (s), 1161 (s), 1140 (s), 1092 (m), 1079 (m), 1013 (m), 882 (m), 851 (m), 833 (s), 684 (m). **HRMS (EI):** m/z calculated for $[C_{18}H_{26}ClF_3O_2Si]^+$ ($[M]^+$): 394.1343, measured: 394.1315.

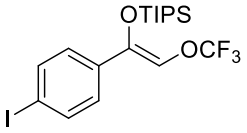
(Z)-((1-(4-bromophenyl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **(*Z*)-4e**



Applying the general method to the silyl enol ether **3e** the ^{19}F NMR of the crude mixture indicated that both **(*Z*)-4e** and **(*E*)-4e** were formed in 43% and 11% yield, respectively. Purification by repeated preparative HPLC using two different solvent systems (first 92% MeOH, second 85% MeCN) allowed for isolation of the major isomer **(*Z*)-4e** (36 mg, 0.08 mmol, 16 %) as a colourless oil. The (*Z*)-configuration is tentatively assigned by analogy to the related reactions affording **(*Z*)-4a** and **(*Z*)-4r**.

^{1}H NMR (400 MHz, CD_3CN) δ = 7.58 – 7.50 (m, 2H), 7.48 – 7.39 (m, 2H), 6.68 (s, 1H), 1.24 – 1.13 (m, 3H), 1.06 (d, J = 7.1 Hz, 18H). **^{19}F NMR** (377 MHz, CD_3CN) δ = –60.9. **^{13}C NMR** (101 MHz, CD_3CN) δ = 142.6, 135.3, 132.5, 128.4, 123.2, 121.8 (q, *J* = 256 Hz), 120.5 (q, *J* = 3.5 Hz), 18.1, 14.0. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3116 (w), 2946 (m), 2869 (m), 1668 (m), 1591 (w), 1365 (m), 1258 (s), 1212 (s), 1161 (s), 1140 (s), 1092 (m), 1080 (m), 1009 (m), 882 (m), 850 (m), 830 (s), 684 (m), 611 (s). **HRMS (EI):** m/z calculated for $[C_{18}H_{26}BrF_3O_2Si]^+$ ($[M]^+$): 438.0838, measured: 438.0817.

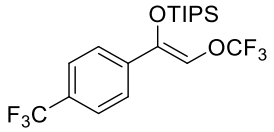
(Z)-((1-(4-iodophenyl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **(*Z*)-4f**



Applying the general method to the silyl enol ether **3f** the ^{19}F NMR of the crude mixture indicated that both **(*Z*)-4f** and **(*E*)-4f** were formed in 38% and 10% yield, respectively. Purification by repeated preparative HPLC using two different solvent systems (first 93% MeOH, second 85% MeCN) allowed for isolation of the major isomer **(*Z*)-4f** (29 mg, 0.06 mmol, 12 %) as a colourless oil. The (*Z*)-configuration is tentatively assigned by analogy to the related reactions affording **(*Z*)-4a** and **(*Z*)-4r**.

^{1}H NMR (400 MHz, CD_3CN) δ = 7.72 – 7.63 (m, 2H), 7.25 – 7.15 (m, 2H), 6.41 (s, 1H), 1.23 – 1.12 (m, 3H), 1.06 (d, J = 7.1 Hz, 18H). **^{19}F NMR** (377 MHz, CD_3CN) δ = –60.4. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 141.7, 137.7, 135.2, 127.3, 120.9 (q, *J* = 256 Hz), 119.1 (q, *J* = 3.5 Hz), 94.4, 17.9, 13.3. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3114 (w), 2946 (m), 2868 (m), 1668 (m), 1464 (m), 1365 (m), 1258 (s), 1212 (s), 1161 (s), 1139 (s), 1080 (s), 1004 (s), 882 (m), 849 (m), 826 (s), 724 (m), 683 (s), 608 (m). **HRMS (EI):** m/z calculated for $[C_{18}H_{26}IF_3O_2Si]^+$ ([M]$^+$): 486.0699, measured: 486.0670.

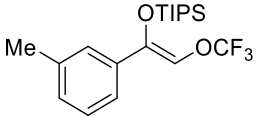
(Z)-triisopropyl((2-(trifluoromethoxy)-1-(4-(trifluoromethyl)phenyl)vinyl)oxy)silane **(*Z*)-4g**



Applying the general method to the silyl enol ether **3g** the ^{19}F NMR of the crude mixture indicated that both **(*Z*)-4g** and **(*E*)-4g** were formed in 16% and 6% yield, respectively. Purification by repeated preparative HPLC using two different solvent systems (first 90% MeOH, second 85% MeCN) allowed for isolation of the major isomer **(*Z*)-4g** (11 mg, 0.03 mmol, 5 %) as a colourless oil. The (*Z*)-configuration is tentatively assigned by analogy to the related reactions affording **(*Z*)-4a** and **(*Z*)-4r**.

^{1}H NMR (400 MHz, CD_3CN) δ = 7.72 – 7.68 (m, 4H), 6.80 (s, 1H), 1.24 – 1.16 (m, 3H), 1.07 (d, *J* = 7.3 Hz, 18H). **^{19}F NMR** (377 MHz, CD_3CN) δ = –60.9 (OCF_3), –63.1 (CF_3). **^{13}C NMR** (151 MHz, CD_3CN) δ = 141.2, 139.2, 129.9 (q, J = 32 Hz), 126.1, 125.5 (q, J = 4 Hz), 124.3 (d, J = 272.0 Hz), 122.6 (q, J = 258 Hz), 120.7 (q, J = 3 Hz), 17.2, 13.1. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3116 (w), 2948 (m), 2870 (m), 1669 (m), 1465 (w), 1324 (s), 1261 (s), 1214 (s), 1165 (s), 1128 (s), 1110 (s), 1082 (s), 1067 (s), 1015 (m), 882 (m), 846 (s), 721 (m), 685 (m), 613 (m). **HRMS (EI):** m/z calculated for $[C_{19}H_{26}F_6O_2Si]^+$ ([M]$^+$): 428.1606, measured: 428.1594.

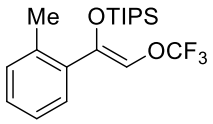
(Z)-triisopropyl((1-(*m*-tolyl)-2-(trifluoromethoxy)vinyl)oxy)silane **(*Z*)-4j**



Applying the general method to the silyl enol ether **3j** the ^{19}F NMR of the crude mixture indicated that both **(*Z*)-4j** and **(*E*)-4j** were formed in 47% and 9% yield, respectively. Purification by repeated preparative HPLC using two different solvent systems (first 88% MeCN, second 90% MeOH) allowed for isolation of the major isomer **(*Z*)-4j** (38 mg, 0.1 mmol, 20 %) as a colourless oil. The (*Z*)-configuration is tentatively assigned by analogy to the related reactions affording **(*Z*)-4a** and **(*Z*)-4r**.

^{1}H NMR (400 MHz, CD_3CN) δ = 7.38 – 7.29 (m, 2H), 7.26 (t, *J* = 7.5 Hz, 1H), 7.21 – 7.17 (m, 1H), 6.61 (s, 1H), 2.33 (s, 3H), 1.26 – 1.11 (m, 3H), 1.07 (d, *J* = 6.9 Hz, 18H). **^{19}F NMR** (377 MHz, CD_3CN) δ = –60.9. **^{13}C NMR** (101 MHz, CD_3CN) δ = 143.9, 139.2, 136.0, 130.5, 129.4, 127.2, 123.7, 121.9 (d, *J* = 256 Hz), 120.1 (q, *J* = 4 Hz), 21.4, 18.1, 14.0. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3106 (w), 3030 (w), 2946 (m), 2869 (m), 1669 (m), 1464 (w), 1360 (m), 1260 (s), 1219 (s), 1192 (s), 1158 (s), 1133 (s), 1080 (m), 881 (s), 851 (m), 788 (m), 721 (m), 684 (s), 603 (m). **HRMS (EI):** m/z calculated for $[C_{19}H_{29}F_3O_2Si]^+$ ($[M]^+$): 374.1889, measured: 374.1884.

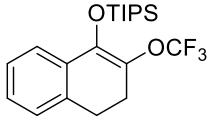
(Z)-triisopropyl((1-(*o*-tolyl)-2-(trifluoromethoxy)vinyl)oxy)silane **(*Z*)-4k**



Applying the general method to the silyl enol ether **3k** the ^{19}F NMR of the crude mixture indicated that both **(*Z*)-4k** and **(*E*)-4k** were formed in 31% and 14% yield, respectively. Purification by repeated preparative HPLC using two different solvent systems (first 88% MeCN, second 90% MeOH) allowed for isolation of the major isomer **(*Z*)-4k** (33 mg, 0.09 mmol, 18 %) as a colourless oil. The (*Z*)-configuration is tentatively assigned by analogy to the related reactions affording **(*Z*)-4a** and **(*Z*)-4r**.

^{1}H NMR (400 MHz, CD_3CN) δ = 7.32 – 7.26 (m, 2H), 7.24 (ddt, J = 7.4, 1.4, 0.7 Hz, 1H), 7.18 (tdd, J = 7.0, 1.5, 0.7 Hz, 1H), 6.18 (q, J = 0.9 Hz, 1H), 2.38 (s, 3H), 1.15 – 1.04 (m, 3H), 0.99 (d, J = 6.7 Hz, 18H).**^{19}F NMR** (377 MHz, CD_3CN) δ = –60.9. **^{13}C NMR** (101 MHz, CD_3CN) δ = 144.4, 138.4, 135.6, 131.3, 130.3, 130.2, 126.5, 121.9 (d, *J* = 255 Hz), 121.2 (q, *J* = 3 Hz), 20.0, 17.9, 13.7. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3106 (w), 3067 (w), 3026 (w), 2946 (m), 2869 (m), 1673 (m), 1464 (m), 1356 (s), 1257 (s), 1216 (s), 1158 (s), 1133 (s), 1064 (s), 1045 (m), 882 (s), 856 (s), 768 (s), 683 (s), 605 (s). **HRMS (EI):** m/z calculated for $[C_{19}H_{29}F_3O_2Si]^+$ ($[M]^+$): 374.1889, measured: 374.1870.

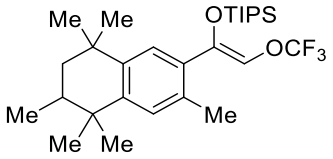
triisopropyl((2-(trifluoromethoxy)-3,4-dihydronaphthalen-1-yl)oxy)silane **4n**



Applying the general method to the silyl enol ether **3n** the ^{19}F NMR of the crude mixture indicated that **4n** was formed in 46% yield, respectively. Purification by repeated preparative HPLC using two different solvent systems (first 91% MeOH, second 85% MeCN) allowed for isolation of the major isomer **4n** (46 mg, 0.12 mmol, 24 %) as a colourless oil.

^{1}H NMR (400 MHz, CD_3CN) δ = 7.48 (dd, *J* = 7.1, 1.8 Hz, 1H), 7.23 (dtd, *J* = 14.2, 7.3, 1.7 Hz, 2H), 7.19 – 7.15 (m, 1H), 2.90 (t, *J* = 7.1 Hz, 2H), 2.60 (dt, *J* = 7.2, 1.2 Hz, 2H), 1.32 – 1.21 (m, 3H), 1.10 (d, *J* = 7.4 Hz, 18H). **^{19}F NMR** (377 MHz, CD_3CN) δ = –56.8. **^{13}C NMR** (101 MHz, CD_3CN) δ = 140.2, 135.8, 133.8, 131.8, 128.9, 128.0, 127.4, 123.4, 122.0 (d, *J* = 256 Hz), 28.9, 26.0 (q, *J* = 1 Hz), 23.0, 18.2, 14.2. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3071 (w), 3024 (w), 2946 (m), 2869 (m), 1670 (m), 1465 (m), 1327 (s), 1236 (s), 1200 (s), 1150 (s), 1093 (m), 1001 (m), 909 (m), 883 (m), 795 (m), 764 (s), 684 (s). **HRMS (EI):** m/z calculated for $[C_{20}H_{29}F_3O_2Si]^+$ ($[M]^+$): 386.1889, measured: 386.1859.

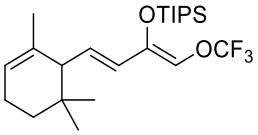
(Z)-((1-(3,5,5,6,8,8-hexamethyl-5,6,7,8-tetrahydronaphthalen-2-yl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **(*Z*)-4o**



Applying the general method to the silyl enol ether **3o** the ^{19}F NMR of the crude mixture indicated that both **(*Z*)-4o** and **(*E*)-4o** were formed in 41% and 20% yield, respectively. Purification by repeated preparative HPLC using two different solvent systems (first 95% MeOH, second 95% MeCN) allowed for isolation of the major isomer **(*Z*)-4o** (66 mg, 0.13 mmol, 26 %) as a colourless oil. The (*Z*)-configuration is tentatively assigned by analogy to the related reactions affording **(*Z*)-4a** and **(*Z*)-4r**.

^{1}H NMR (400 MHz, CD_3CN) δ = 7.27 (s, 1H), 7.17 (s, 1H), 6.54 (q, *J* = 1.0 Hz, 1H), 2.27 (s, 3H), 1.87 (ddd, *J* = 13.0, 6.7, 2.6 Hz, 1H), 1.62 (t, *J* = 13.2 Hz, 1H), 1.39 (dd, *J* = 13.5, 2.6 Hz, 1H), 1.31 (s, 3H), 1.23 (s, 3H), 1.20 (s, 3H), 1.18 – 1.08 (m, 3H), 1.05 (s, 3H), 1.03 – 1.00 (m, 18H), 1.00 (s, 3H). **^{19}F NMR** (377 MHz, CD_3CN) δ = –61.3. **^{13}C NMR** (101 MHz, CD_3CN) δ = 149.7, 147.9, 142.6, 134.3, 132.1, 129.7, 128.3, 123.3 (q, *J* = 3 Hz), 121.8 (q, *J* = 254 Hz), 44.1, 38.3, 35.4, 34.6, 32.3, 32.0, 28.8, 25.0, 19.3, 18.0, 17.0, 13.3. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3028 (w), 2963 (m), 2869 (m), 1463 (m), 1364 (w), 1271 (m), 1232 (s), 1214 (s), 1157 (s), 1140 (s), 997 (w), 909 (m), 882 (m), 823 (m), 686 (m), 660 (m). **HRMS (EI):** m/z calculated for $[C_{28}H_{45}F_3O_2Si]^+$ ([M+]$^+$): 498.3141, measured:498.3123.

triisopropyl(((1E,3E)-1-(trifluoromethoxy)-4-(2,6,6-trimethylcyclohex-2-en-1-yl)buta-1,3-dien-2-yl)oxy)silane **(*Z*)-4p**



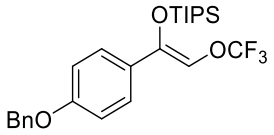
According to the general method enol ether **(*Z*)-4p** (34 mg, 0.08 mmol, 16 %) was purified by preparative HPLC (95% MeOH) and obtained as a colourless oil.

Applying the general method to the silyl enol ether **3p** the ^{19}F NMR of the crude mixture indicated that both **(*Z*)-4p** and **(*E*)-4p** were formed in 17% and 13% yield, respectively. Purification by preparative HPLC (95% MeOH) allowed for isolation of the major isomer **(*Z*)-4p** (34 mg, 0.08 mmol, 16 %) as a colourless oil. The (*Z*)-configuration is tentatively assigned by analogy to the related reactions affording **(*Z*)-4a** and **(*Z*)-4r**.

^{1}H NMR (400 MHz, CD_3CN) δ = 6.27 (s, 1H), 5.91 (dd, J = 15.2, 9.4 Hz, 1H), 5.79 (d, J = 15.3 Hz, 1H), 5.45 – 5.40 (m, 1H), 2.27 – 2.20 (m, 1H), 2.05 – 1.96 (m, 2H), 1.55 (q, J = 1.9 Hz, 3H), 1.42 (dt, J = 13.2, 8.1 Hz, 1H), 1.29 – 1.16 (m, 4H), 1.10 (d, J = 7.2 Hz, 18H), 0.89 (s, 3H), 0.82 (s, 3H). **^{19}F NMR** (377 MHz, CD_3CN) δ = –61.1. **^{13}C NMR** (101 MHz, CD_3CN) δ = 142.2, 134.5, 133.7, 125.4, 122.1, 121.1 (q, *J* = 4 Hz), 121.7 (q, *J* = 255 Hz)*, 54.7, 33.0, 32.1, 27.9, 27.0, 23.7, 23.0, 18.2, 14.1. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3106 (w), 3030 (w), 2946 (m), 2869 (m), 1669 (m), 1464 (w), 1360 (m), 1260 (s), 1219 (s), 1192 (s), 1158 (s), 1133 (s), 1080 (m), 881 (s), 851 (m), 788 (m), 721 (m), 684 (s), 603 (m). **HRMS (EI):** m/z calculated for $[C_{23}H_{39}F_3O_2Si]^+$ ([M]$^+$): 432.2671, measured: 432.2644.

*Note: in the ^{13}C NMR only two signals of the quartet of the OCF_3 group are visible due to overlap with other ^{13}C signals.

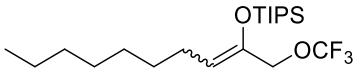
(Z)-((1-(4-(benzyloxy)phenyl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **(*Z*)-4r**



Applying the general method to the silyl enol ether **3r** the ^{19}F NMR of the crude mixture indicated that both **(*Z*)-4r** and **(*E*)-4r** were formed in 43% and 9% yield, respectively. Purification by repeated preparative HPLC using two different columns (first RP-18 with 91% MeOH, second PGC with 100% THF) allowed for isolation of the major isomer **(*Z*)-4r** (44 mg, 0.09 mmol, 19 %) as a colourless solid. The (*Z*)-configuration assigned by x-ray analysis (see section 8).

^{1}H NMR (400 MHz, CD_3CN) δ = 7.5 – 7.4 (m, 4H), 7.4 – 7.4 (m, 2H), 7.4 – 7.3 (m, 1H), 7.0 – 7.0 (m, 2H), 6.5 (s, 1H), 5.1 (s, 2H), 1.2 – 1.1 (m, 3H), 1.1 (d, J = 6.8 Hz, 18H). **^{19}F NMR** (377 MHz, CD_3CN) δ = –60.9. **^{13}C NMR** (101 MHz, CD_3CN) δ = 160.4, 143.8, 138.2, 129.5, 129.0, 128.7, 128.2, 121.9 (q, J = 255 Hz), 119.2 (q, J = 4 Hz), 115.7, 70.8, 18.2, 14.1. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3112 (w), 2946 (m), 2868 (m), 1668 (w), 1607 (m), 1511 (m), 1363 (m), 1243 (s), 1215 (s), 1158 (s), 1136 (s), 1080 (s), 1012 (m), 882 (m), 833 (m), 733 (s), 684 (s), 609 (m). **HRMS (EI):** m/z calculated for $[C_{25}H_{33}F_3O_3Si]^+$ ($[M]^+$): 466.2151, measured: 466.2122.

Triisopropyl((1-(trifluoromethoxy)dec-1-en-2-yl)oxy)silane **4s**



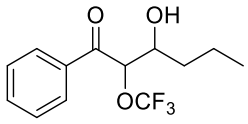
According to the general method enol ether **4s** (22 mg, 0.06 mmol, 11 %) was purified by preparative HPLC (95% MeCN) and obtained as a mixture of two diastereomers (d.r. 1:1) as a colourless oil.*

^{1}H NMR (600 MHz, CD_3CN) δ = 4.95 (t, J = 7.9 Hz, 1H,), 4.87 (t, J = 7.2 Hz, 1H), 4.48 (s, 2H), 4.37 (s, 2H), 2.06 (q, J = 7.2 Hz, 2H), 2.03 – 1.96 (m, 2H), 1.34 – 1.21 (m, 20H), 1.21 – 1.12 (m, 6H), 1.07 (d, J = 7.2 Hz, 18H), 1.05 (d, J = 7.4 Hz, 18H), 0.85 (t, J = 7.1 Hz, 6H). **^{19}F NMR** (377 MHz, CD_3CN) δ = –60.4, –60.6. **^{13}C NMR** (151 MHz, CD_3CN) δ = 145.1, 144.5, 122.8 (d, J = 253 Hz), 122.6 (d, J = 253 Hz), 116.0, 114.4, 71.3 (q, J = 3.5 Hz), 66.2 (q, J = 3 Hz), 32.5, 32.5, 30.9, 30.0, 29.8, 29.7, 29.7, 29.5, 27.1, 26.0, 23.3, 23.2, 18.2, 18.2, 14.3, 13.9, 13.3. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 2927 (m), 2868 (m), 2262 (w), 1669 (w), 1464 (m), 1379 (w), 1256 (s), 1213 (s), 1197 (s), 1140 (s), 1015 (m), 1000 (m), 882 (m), 681 (s). **HRMS (EI):** m/z calculated for $[C_{20}H_{39}F_3O_2Si]^+$ ($[M]^+$): 396.2671, measured: 396.2679.

*Note: As the starting material was a mixture of **3s** and two other products, the amount of starting material was upscaled accordingly to reach 1.5 equiv. of **3s**.

4.5 Mukaiyama Aldol Reaction to afford Product **6**

3-hydroxy-1-phenyl-2-(trifluoromethoxy)hexan-1-one **6**



Butyraldehyde (14.4 mg, 0.20 mmol) and enol ether **4a** (36 mg, 0.10 mmol) were added to DCM (1.5 mL). The solution was cooled to -78 °C and $TiCl_4$ (0.04 mL, 0.37 mmol) was added. The mixture was stirred at -78 °C for 2 h, was warmed to 0 °C for 30 min and then quenched with NH_4Cl (sat. in H_2O, 4 mL). The aqueous phase was extracted with Et_2O (3 × 20 mL), and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The Aldol product **6** (20 mg, 0.07 mmol, 72 %) was obtained as a mixture of two diastereomers (d.r. 90:10) after column chromatography (SiO_2, pentane/EtOAc 5:1) as a colourless oil.

^{1}H NMR* (400 MHz, $CDCl_3$) δ = 7.97 – 7.94 (m, 2H), 7.64 (ddt, J = 8.0, 6.9, 1.3 Hz, 1H), 7.54 – 7.48 (m, 2H), 5.26 (d, J = 4.1 Hz, 1H), 4.18 – 4.04 (m, 1H), 2.14 (d, J = 6.6 Hz, 1H), 1.66 – 1.47 (m, 4H), 0.92 (t, J = 7.1 Hz, 3H). **^{19}F NMR*** (377 MHz, $CDCl_3$) δ = –58.8. **^{13}C NMR*** (101 MHz, $CDCl_3$) δ = 194.5, 134.9, 134.2, 129.1, 128.9, 121.8 (q, J = 257 Hz), 81.4, 71.6, 35.2, 18.8, 13.8. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3453 (bw), 3067 (w), 2963 (w), 2876 (w), 1691 (m), 1598 (w), 1449 (w), 1259 (s), 1215 (s), 1144 (s), 1075 (m), 909 (w), 733 (m), 689 (m). **HRMS (ESI):** m/z calculated for $[C_{13}H_{15}F_3O_3Na]^+$ ($[M+Na]^+$): 299.0866, measured: 299.0859.

*Note: Characterisation data are listed for the major isomer.

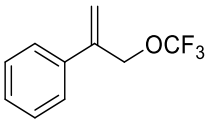
5 Procedure and Analytical Data for the Trifluoromethoxylation of Allyl Silanes

Allyl silanes **7a-f** (1.5 equiv., 0.75 mmol) and K_2CO_3 (1.0 equiv., 0.5 mmol, 69 mg) were added to a 15 mL Schlenk-pressure tube with MeCN (1 mL). The mixture was frozen with liquid N_2 and degassed using the freeze-pump-thaw technique. BTMP (1.0 equiv., 0.5 mmol, 85 mg) was condensed in, the reaction mixture was allowed to warm to rt and stirred vigorously at rt for 16 h. The pressure tube was opened carefully in the back of the fume hood to release possible excess gas.

Crude NMR yields: Trifluorotoluene (1.0 equiv., 0.5 mmol, 61 µL) and $CDCl_3$ (1 mL) was added to the reaction mixture. Up to 0.8 mL of the crude mixture was filtered through cotton into an NMR tube for ^{19}F NMR analysis.

Isolation: The solids were filtered off and the solvent was evaporated under reduced pressure. The products were obtained after column chromatography (SiO_2, pentane/DCM).

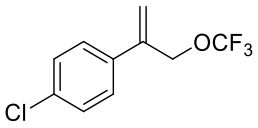
(3-(trifluoromethoxy)prop-1-en-2-yl)benzene **8a**



According to the general method allyl product **8a** (40 mg, 0.2 mmol, 40 % (90 % crude ^{19}F NMR yield)) was obtained from allyl silane **7a** as a colourless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 – 7.42 (m, 2H), 7.42 – 7.32 (m, 3H), 5.64 (s, 1H), 5.47 (q, J = 1.1 Hz, 1H), 4.86 (d, J = 1.2 Hz, 2H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –60.4. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 141.1, 137.4, 128.7, 128.5, 126.1, 121.8 (q, *J* = 255 Hz), 116.7, 68.8 (q, *J* = 3.5 Hz). **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3089 (w), 3061 (w), 3030 (w), 2962 (w), 2915 (w), 1254 (s), 1212 (s), 1134 (s), 1027 (m), 912 (m), 873 (m), 776 (s), 707 (s), 693 (s), 568 (m). **HRMS (EI):** m/z calculated for $[C_{10}H_9F_3O]^+$ ($[M]^+$): 202.0605, measured: 202.0619.

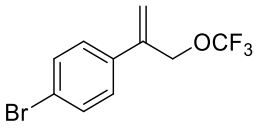
1-chloro-4-(3-(trifluoromethoxy)prop-1-en-2-yl)benzene **8b**



According to the general method allyl product **8b** (59 mg, 0.25 mmol, 50 % (76 % crude ^{19}F NMR yield)) was obtained from allyl silane **7b** as a colourless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40 – 7.30 (m, 4H), 5.61 (s, 1H), 5.48 – 5.46 (m, 1H), 4.81 (d, J = 1.1 Hz, 2H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –60.5. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 140.1, 135.8, 134.5, 129.0, 127.4, 121.8 (q, *J* = 256 Hz), 117.5, 68.7 (q, *J* = 4 Hz). **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3100 (w), 3048 (w), 2964 (w), 2907 (w), 1495 (m), 1252 (s), 1212 (s), 1137 (s), 1093 (m), 1013 (m), 921 (m), 875 (m), 832 (s), 770 (m), 737 (m), 558 (m). **HRMS (EI):** m/z calculated for $[C_{10}H_8ClF_3O]^+$ ($[M]^+$): 236.0191, measured: 236.0216.

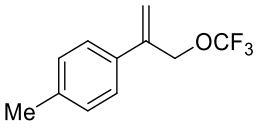
1-bromo-4-(3-(trifluoromethoxy)prop-1-en-2-yl)benzene **8c**



According to the general method allyl product **8c** (66 mg, 0.235 mmol, 47 % (68 % crude ^{19}F NMR yield)) was obtained from allyl silane **7c** as a colourless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54 – 7.46 (m, 1H), 7.32 – 7.27 (m, 1H), 5.62 (s, 1H), 5.47 (s, 1H), 4.80 (s, 1H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –60.5. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 140.2, 136.3, 131.9, 127.7, 122.6, 121.8 (q, J = 256 Hz), 117.6, 68.6 (q, *J* = 3 Hz). **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3098 (w), 3038 (w), 2966 (w), 2911 (w), 2858 (w), 1491 (m), 1254 (s), 1212 (s), 1136 (s), 1073 (m), 1008 (s), 919 (m), 875 (m), 828 (s), 760 (m), 734 (m), 581 (m). **HRMS (EI):** m/z calculated for $[C_{10}H_8BrF_3O]^+$ ($[M]^+$): 279.9718, measured: 279.9711.

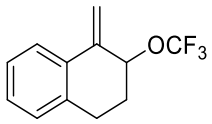
1-methyl-4-(3-(trifluoromethoxy)prop-1-en-2-yl)benzene **8d**



According to the general method allyl product **8d** (32 mg, 0.15 mmol, 30 % (86 % crude ^{19}F NMR yield)) was obtained from allyl silane **7d** as a colourless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37 – 7.28 (m, 2H), 7.18 (d, *J* = 8.1 Hz, 2H), 5.59 (s, 1H), 5.40 (q, *J* = 1.1 Hz, 1H), 4.82 (d, *J* = 1.2 Hz, 2H), 2.36 (s, 3H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –60.4. **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 140.9, 138.4, 134.5, 129.4, 125.9, 121.8 (q, *J* = 255 Hz), 115.9, 68.9 (q, *J* = 3 Hz), 21.3. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3093 (w), 3059 (w), 3030 (w), 2956 (w), 2926 (w), 2895 (w), 1515 (m), 1251 (s), 1213 (s), 1138 (s), 1019 (m), 912 (m), 854 (s), 839 (s), 821 (s), 734 (m), 563 (m). **HRMS (EI):** m/z calculated for $[C_{11}H_{11}F_3O]^+$ ($[M]^+$): 216.0760, measured: 216.0762.

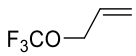
1-methylene-2-(trifluoromethoxy)-1,2,3,4-tetrahydronaphthalene **8e**



According to the general method allyl product **8e** (65 mg, 0.285 mmol, 57 % (88 % crude ^{19}F NMR yield)) was obtained from allyl silane **7e** as a colourless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.62 (dd, J = 7.6, 1.7 Hz, 1H), 7.22 (td, J = 6.7, 1.8 Hz, 2H), 7.17 – 7.11 (m, 1H), 5.70 (s, 1H), 5.33 (s, 1H), 5.04 (dd, J = 6.6, 2.8 Hz, 1H), 3.13 (ddd, J = 17.5, 9.6, 5.5 Hz, 1H), 2.87 (dt, J = 17.1, 5.5 Hz, 1H), 2.28 (ddt, J = 13.6, 6.6, 5.4 Hz, 1H), 2.16 – 2.06 (m, 1H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –57.3. **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 140.7, 135.5, 132.1, 129.0, 128.5, 126.6, 125.1, 122.0 (d, *J* = 255 Hz), 112.4, 77.8 (q, *J* = 2 Hz), 29.3, 25.4. **IR (ATR):** $\tilde{\nu}$ [cm^{-1}] = 3098 (w), 3071 (w), 3020 (w), 2962 (w), 2935 (w), 2852 (w), 1487 (m), 1272 (s), 1219 (s), 1204 (s), 1183 (m), 1127 (s), 1028 (m), 908 (m), 846 (m), 773 (s), 743 (m), 735 (m), 576 (m). **HRMS (EI):** m/z calculated for $[C_{12}H_{11}F_3O]^+$ ($[M]^+$): 228.0762, measured: 228.0745.

3-(trifluoromethoxy)prop-1-ene **8f**



According to the general method allyl product **8f** (1.2 g, 9.5 mmol, 48 %)* was obtained from allyltrimethylsilane **7f** on a 20 mmol scale as a liquid and colourless 1:1 mixture of TMSF and **8f**. The product was directly distilled out of the crude mixture via trap-to-trap and successive common distillation (bp = 26-32 °C).

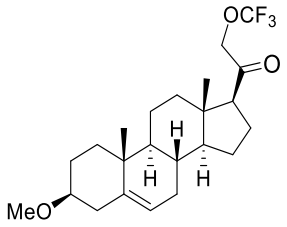
^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.0 – 5.8 (m, 1H), 5.4 (dq, J = 17.2, 1.4 Hz, 1H), 5.3 (dq, J = 10.4, 1.2 Hz, 1H), 4.5 (dt, J = 5.7, 1.4 Hz, 2H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = –60.4. **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 130.8, 121.7 (d, J = 255 Hz), 119.6, 68.1 (q, J = 3 Hz). **GC-MS:** m/z calculated for $[C_4H_5F_3O]^+$ ($[M]^+$): 126.09, measured: 126.1.**
The NMR data agree with the literature values. [13]

* Note: ^{19}F NMR yield not measured. The yield was calculated from the ^{1}H NMR of the product mixture.
**Note: Due to the volatility of the product mixture no high-resolution mass spectrometry measurement was possible.

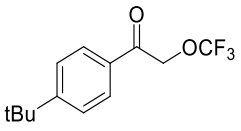
6 Limits of the Methods

Using the general methods described in Chapters 4.1 and 4.3, the following OCF_3-products were either not observed or observed in poor ^{19}F NMR yields ($CDCl_3$, CF_3-toluene as internal standard):

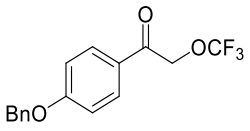
Chapter 4.1 Method A[a] and B[b]:



(11 %)[a]

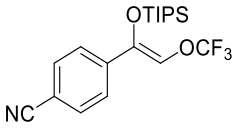


(10 %)[a]
(10 %)[b]

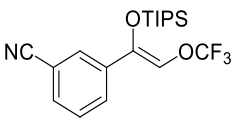


(6 %)[a]
(11 %)[b]

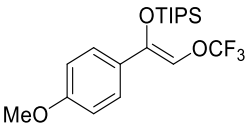
Chapter 4.3:



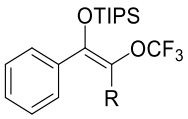
(9 %)



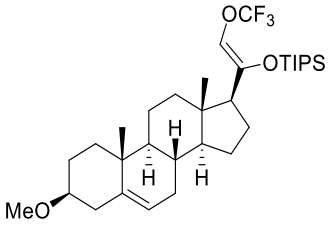
(11 %)



(0 %)



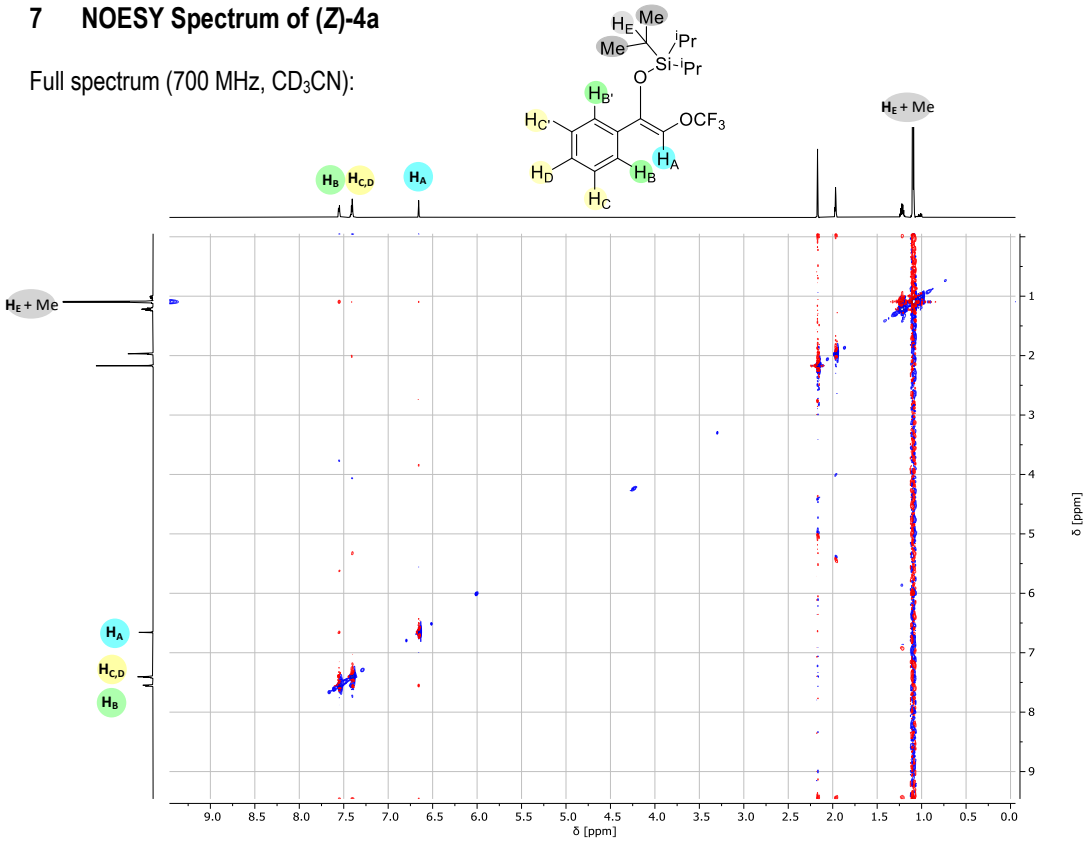
R = Me, Bn
(0 %)



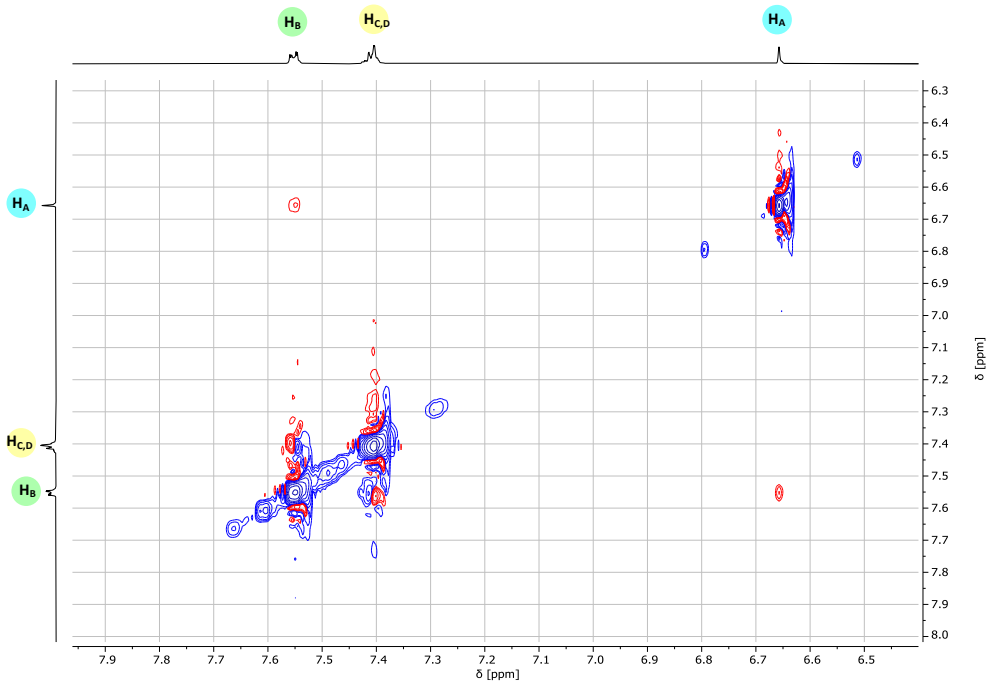
complex mixture

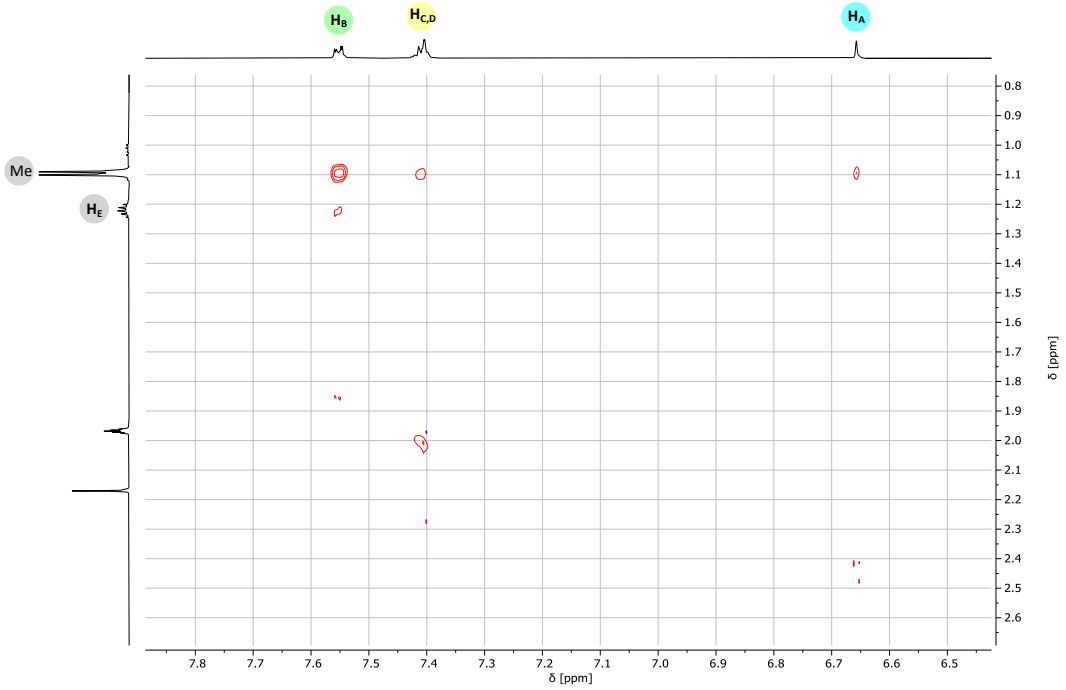
7 NOESY Spectrum of (*Z*)-4a

Full spectrum (700 MHz, CD_3CN):

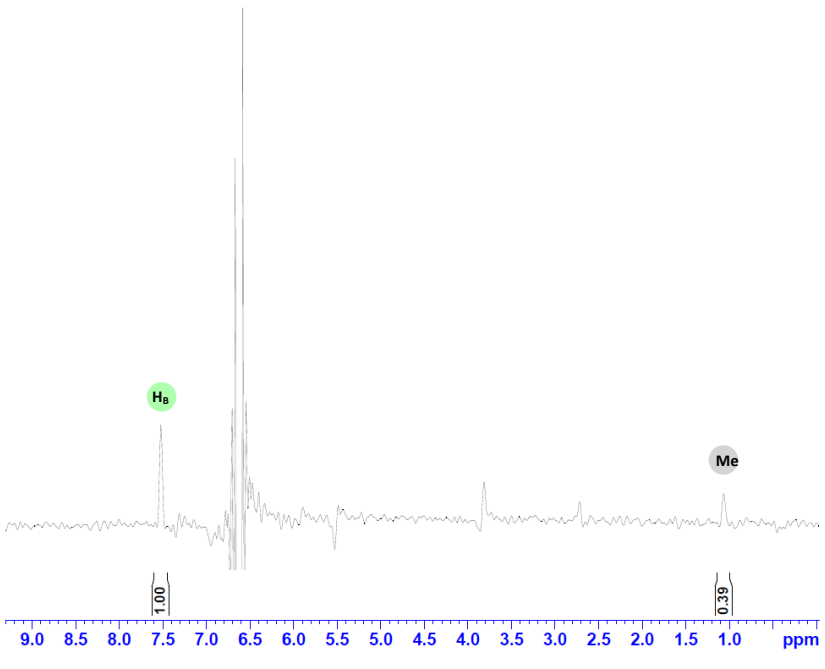


Zoom on $\mathbf{H_A}$ (1. aromatic area, 2. aliphatic area):





Spectrum slice of H_A:

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PROCNO             604

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PULPROG        noesy.eth
TD                 2048
SOLVENT            CD3CN
NS                    8
DS                    8
SWH             6666.667 Hz
FIDRES          3.255208 Hz
AQ              0.1536000 sec
RG                   10
DW                75.000 usec
DE                 6.00 usec
TE               298.0 K
D0              0.00006653 sec
D1              2.00000000 sec
D7              0.39875999 sec
D8              0.40000001 sec
IN0             0.00015000 sec

======== CHANNEL f1 ========
SFO1         700.2332911 MHz
NUC1               1H
P1                6.65 usec
PLW1          6.30959988 W
PLW9          0.00000001 W

====== GRADIENT CHANNEL =====
GPNAM[0]      SMSQ10.100
GPNAM[1]      SMSQ10.100
GPZ0              50.00 %
GPZ1              27.00 %
P20             1000.00 usec
P21             1000.00 usec

F1 - Acquisition parameters
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FIDRES        26.041666 Hz
SW                9.521 ppm
FnMODE      States-TPPI

F2 - Processing parameters
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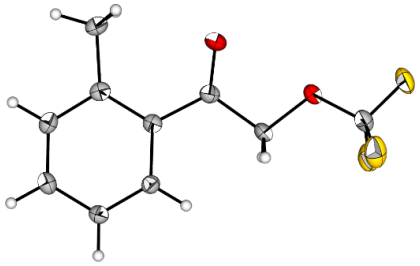
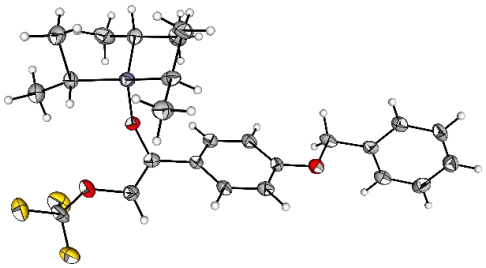
SF          700.2300183 MHz
WDW                QSINE
SSB                   2
LB                    0 Hz
GB                    0
PC                 4.00
```

8 Crystallographic Data of 2k and (*Z*)-4r



Compound	1-(*o*-tolyl)-2-(trifluoromethoxy)ethan-1-one **2k**
Identification code	full_p1_a
Empirical formula	$C_{10}H_9F_3O_2$
Formula weight	218.17
Temperature/K	125
Crystal system	triclinic
Space group	P-1
a/Å	6.9785(6)
b/Å	11.1739(9)
c/Å	12.5948(10)
α/°	81.760(3)
β/°	89.952(3)
γ/°	79.239(3)
Volume/Å^3	954.53(14)
Z	4
ρ_{calc}/g/cm^{-3}	1.518
μ/mm^{-1}	1.260
F(000)	448.0
Crystal size/mm^3	0.578 × 0.343 × 0.136
Radiation	$Cu_{K\alpha}$ (λ = 1.54178)
2Θ range for data collection/°	7.094 to 145.016
Index ranges	-8 ≤ h ≤ 8, -13 ≤ k ≤ 13, -15 ≤ l ≤ 15
Reflections collected	12764
Independent reflections	3744 [R_{int} = 0.0322, R_{sigma} = 0.0337]
Data/restraints/parameters	3744/0/273
Goodness-of-fit on F^2	1.088
Final R indexes [I>=2σ (I)]	R_1 = 0.0358, wR_2 = 0.0912
Final R indexes [all data]	R_1 = 0.0389, wR_2 = 0.0944
Largest diff. peak/hole / e Å^{-3}	0.23/-0.24
CCDC deposition number	2306068



Compound	(Z)-((1-(4-(benzyloxy)phenyl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **(*Z*)-4r**
Identification code	full18_P21c_a
Empirical formula	$C_{25}H_{33}F_3O_3Si$
Formula weight	466.60
Temperature/K	125
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	9.0582(6)
b/Å	31.786(2)
c/Å	9.2148(6)
α/°	90
β/°	110.780(4)
γ/°	90
Volume/Å^3	2480.6(3)
Z	4
ρ_{calc}/g/cm^{-3}	1.249
μ/mm^{-1}	1.233
F(000)	992.0
Crystal size/mm^3	0.093 × 0.075 × 0.05
Radiation	$Cu_{K\alpha}$ (λ = 1.54178)
2Θ range for data collection/°	5.56 to 137.124
Index ranges	-10 ≤ h ≤ 10, -36 ≤ k ≤ 38, -11 ≤ l ≤ 9
Reflections collected	25887
Independent reflections	4500 [R_{int} = 0.1283, R_{sigma} = 0.0786]
Data/restraints/parameters	4500/0/295
Goodness-of-fit on F^2	1.076
Final R indexes [I>=2σ (I)]	R_1 = 0.0882, wR_2 = 0.2190
Final R indexes [all data]	R_1 = 0.1385, wR_2 = 0.2521
Largest diff. peak/hole / e Å^{-3}	0.50/-0.51
CCDC deposition number	2306494

9 DFT Calculation Data

Molecular structure optimizations were performed at the density functional theory (DFT) level with the B3LYP functional as implemented in the GAUSSIAN16 program[14]. Grimme's empiric dispersion correction with Becke-Johnson damping[15] was included, as well as implicit solvent effects for acetone (ε = 20.493) through a polarizable continuum model (PCM) in the integrated equation formalism variant (IEFPCM) as used by default in the GAUSSIAN16 program. For all atoms Ahlrichs' def2-TZVP basis set[16] was used. For the Gibbs free energy values zero-point energy vibration and thermal corrections for 298.15 K were considered.

Molecule	Total Energy [H]	T = 298.15 K
3a	-1029.85288874	-1029.493381
BTMP	-826.010543548	-826.009246
A	-1029.63728459	-1029.279077
B	-826.221978850	-826.226475
C	-412.971334584	
D	-413.224255655	
E	-1442.72912280	
F	-1855.98646401	
3a + BTMP → A + B	+11.0 kJ/mol	-7.7 kJ/mol
B → C + D	+69.3 kJ/mol	
A + B → F	-334.0 kJ/mol	
F → E + D	+86.9 kJ/mol	
A + C → E	-316.4 kJ/mol	

Table S2. Total energy of the E ($\mathbf{E_E}$) and Z ($\mathbf{E_Z}$) isomer of **4a** in Hartree and energy difference of the two isomers ($\mathbf{\Delta_{E-Z} = E_E - E_Z}$) in kJ/mol evaluated for T = 0 K and including zero point energy and thermal corrections at T = 298.15 K. Solvent effects for acetone or DCM were included through a polarizable continuum model (PCM) in the integrated equation formalism variant (IEFPCM) as used by default in the GAUSSIAN16 program.

environment	**E_E [H]**		**E_Z [H]**		**Δ_{E-Z} [kJ/mol]**	
	T = 0 K	*T = 298.15 K*	*T = 0 K*	*T = 298.15 K*	*T = 0 K*	*T = 298.15 K*
vacuum	−1442.29695725	−1441.936485	−1442.29879947	−1441.935234	4.84	−3.28
acetone	−1442.30163227	−1441.940690	−1442.30292520	−1441.940799	3.39	0.29
DCM	−1442.30104522	−1441.940196	−1442.30240975	−1441.940217	3.58	0.06

10 Cyclic Voltammetry

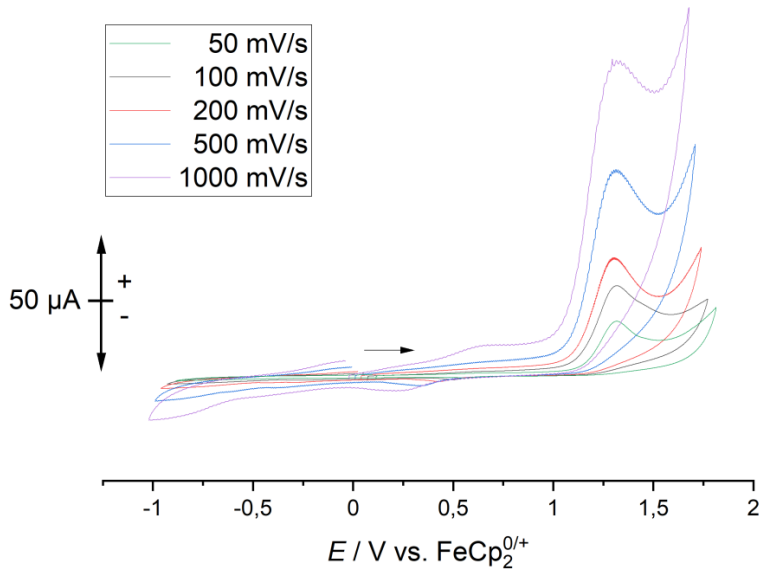


Figure S1. Cyclic voltammogram of **3a** in MeCN at room temperature with $TBAPF_6$ as supporting electrolyte and at different scan rates.

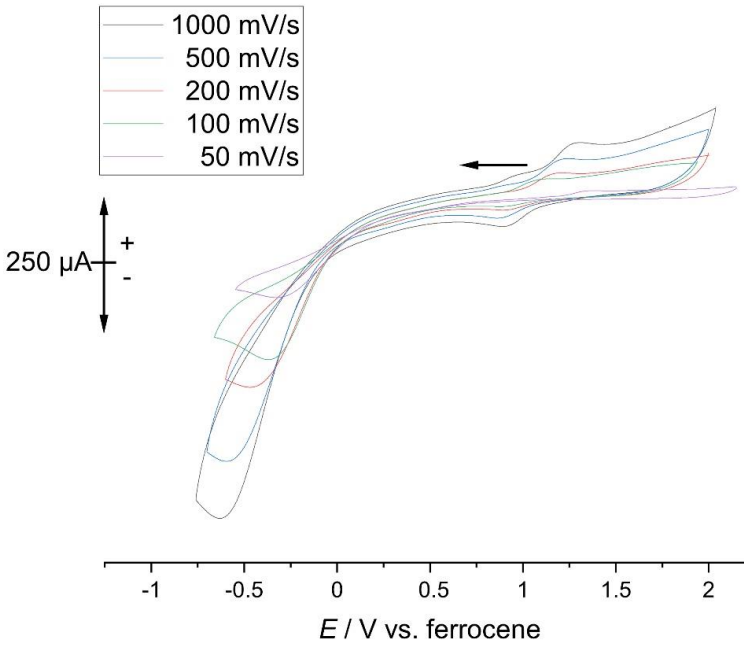


Figure S2. Cyclic voltammogram of BTMP in MeCN at room temperature with $TBAPF_6$ as supporting electrolyte and using $CoCp_2PF_6$ as internal reference at different scan rates.

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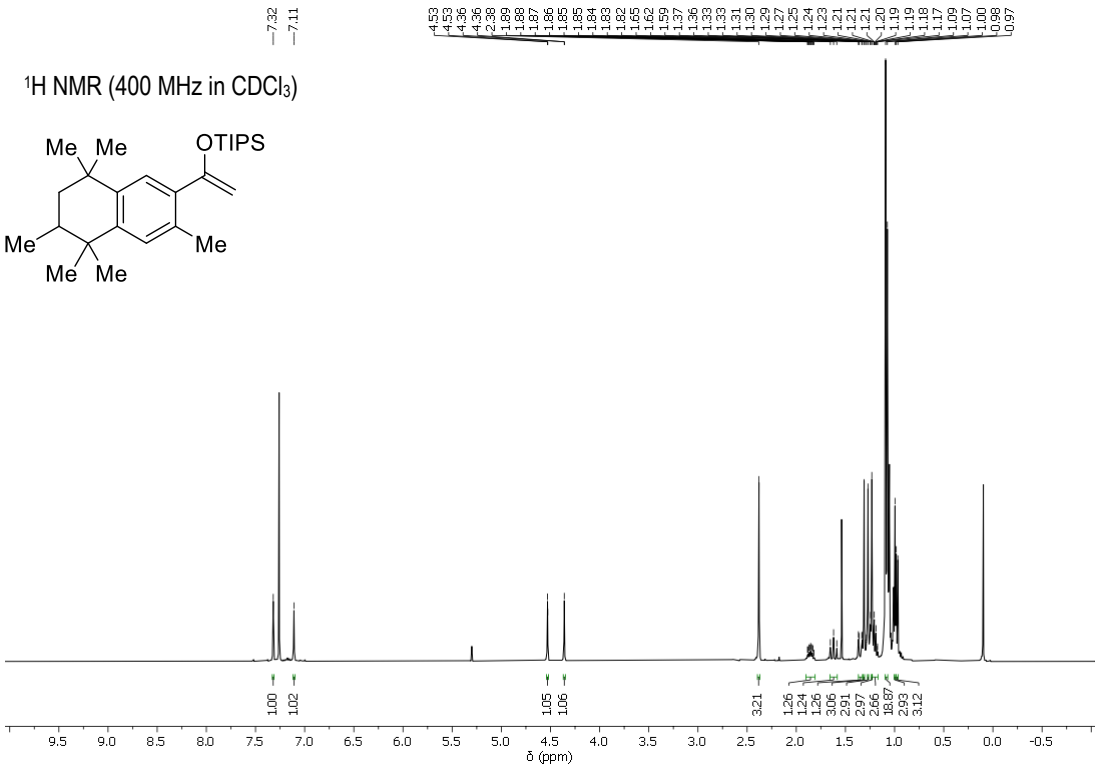
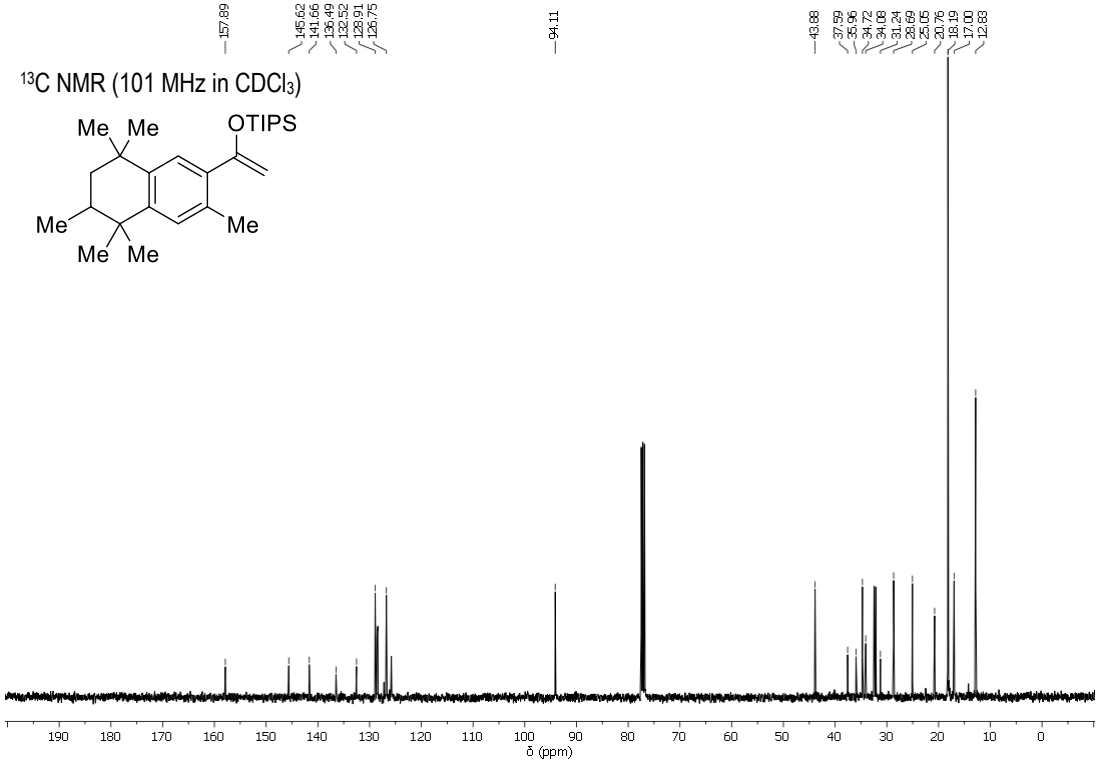
12 NMR Spectra of Literature-Unknown Substances

((1-(3,5,5,6,8,8-hexamethyl-5,6,7,8-tetrahydronaphthalen-2-yl)vinyl)oxy)triisopropylsilane **3o**

^{1}H NMR (400 MHz in $CDCl_3$)

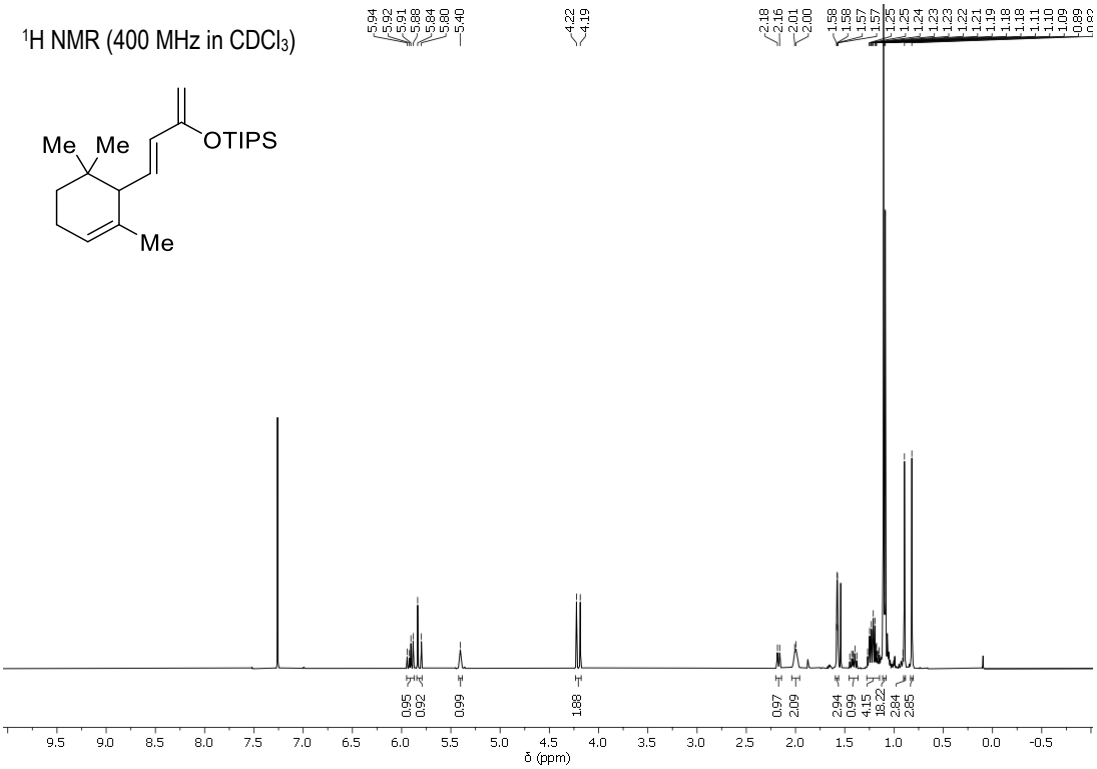


^{13}C NMR (101 MHz in $CDCl_3$)

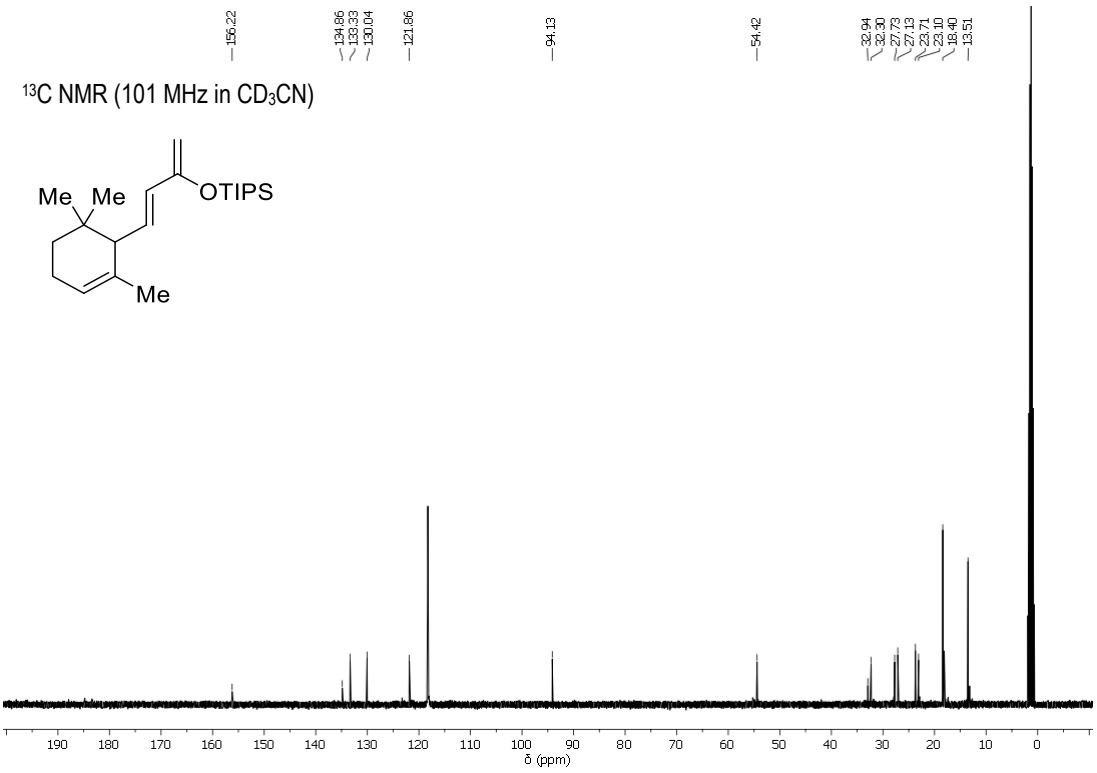


(E)-triisopropyl((4-(2,6,6-trimethylcyclohex-2-en-1-yl)buta-1,3-dien-2-yl)oxy)silane **3p**

^{1}H NMR (400 MHz in $CDCl_3$)



^{13}C NMR (101 MHz in CD_3CN)



(Cyclopentadec-1-en-1-yloxy)triisopropylsilane **3q**

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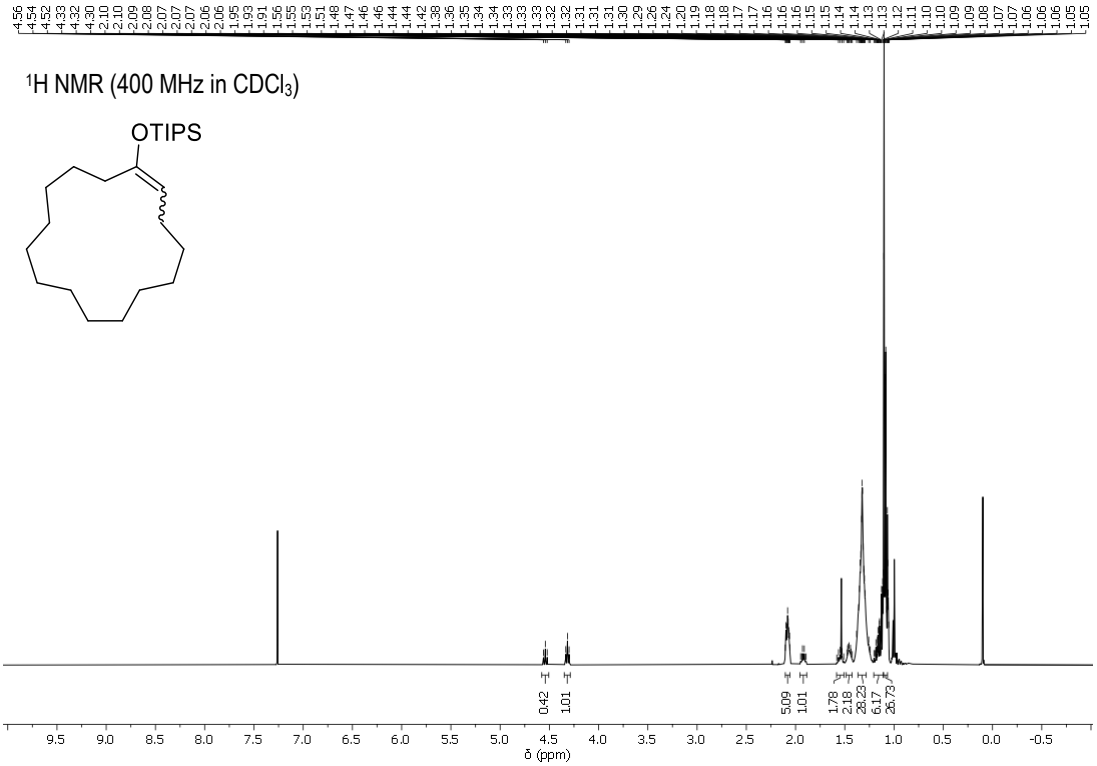
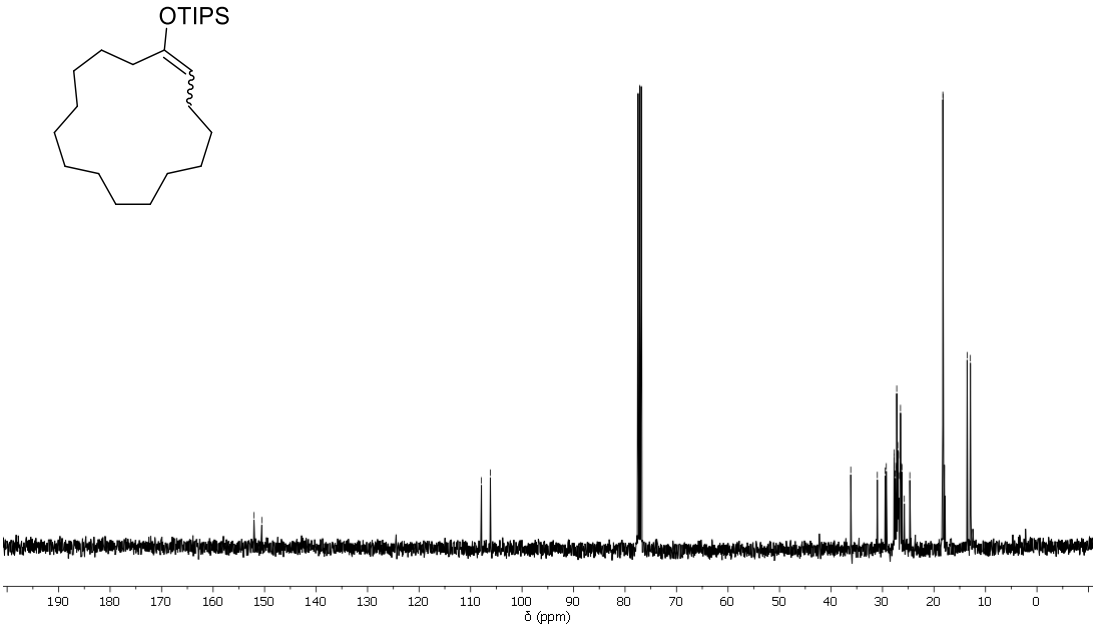
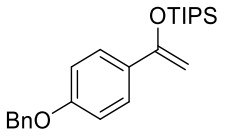


^{13}C NMR (101 MHz in $CDCl_3$)

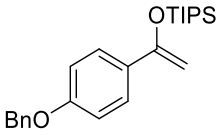


((1-(4-(benzyloxy)phenyl)vinyl)oxy)triisopropylsilane **3r**

^{1}H NMR (400 MHz in CD_3CN)

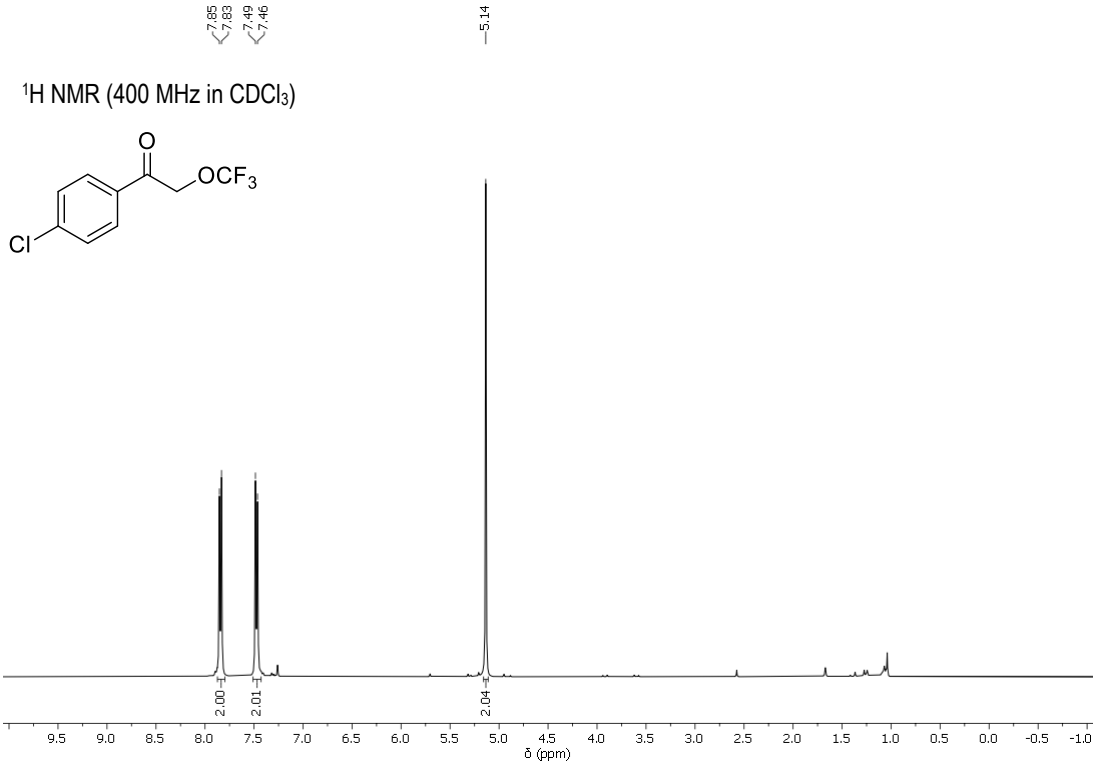


^{13}C NMR (101 MHz in CD_3CN)

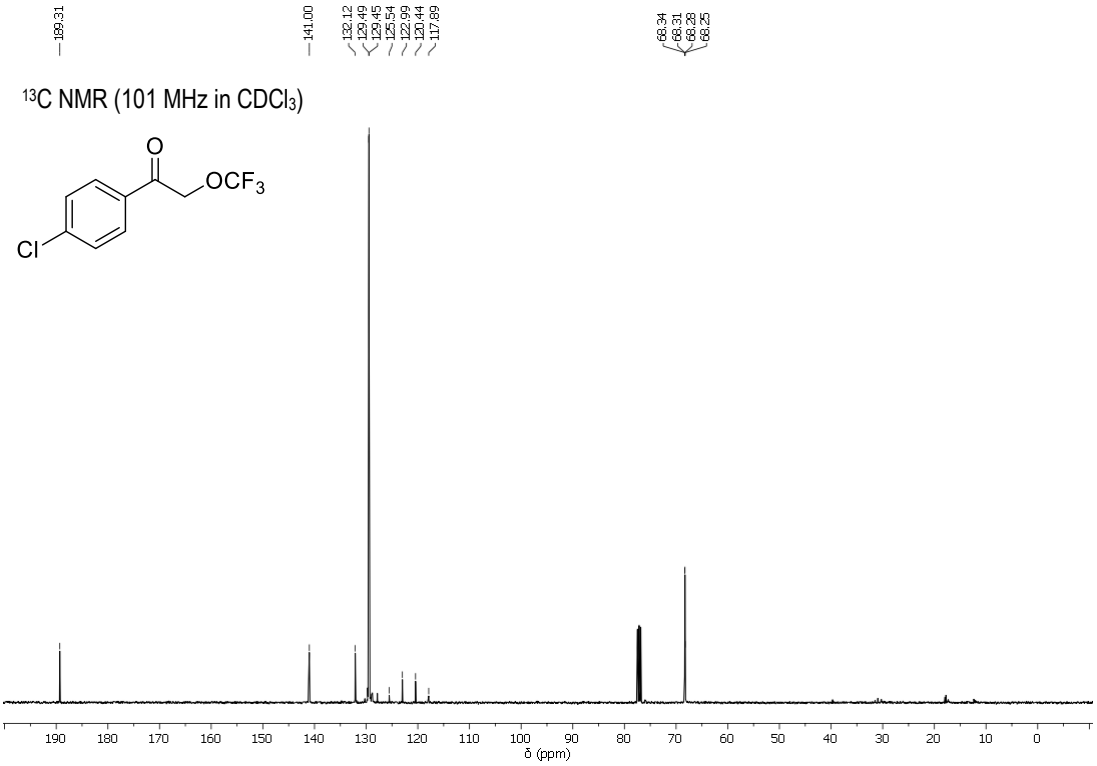


1-(4-chlorophenyl)-2-(trifluoromethoxy)ethan-1-one **2d**

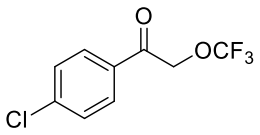
^{1}H NMR (400 MHz in $CDCl_3$)



^{13}C NMR (101 MHz in $CDCl_3$)



^{19}F NMR (377 MHz in $CDCl_3$)



1-(4-iodophenyl)-2-(trifluoromethoxy)ethan-1-one **2f**

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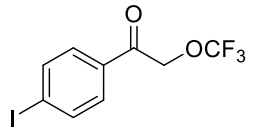

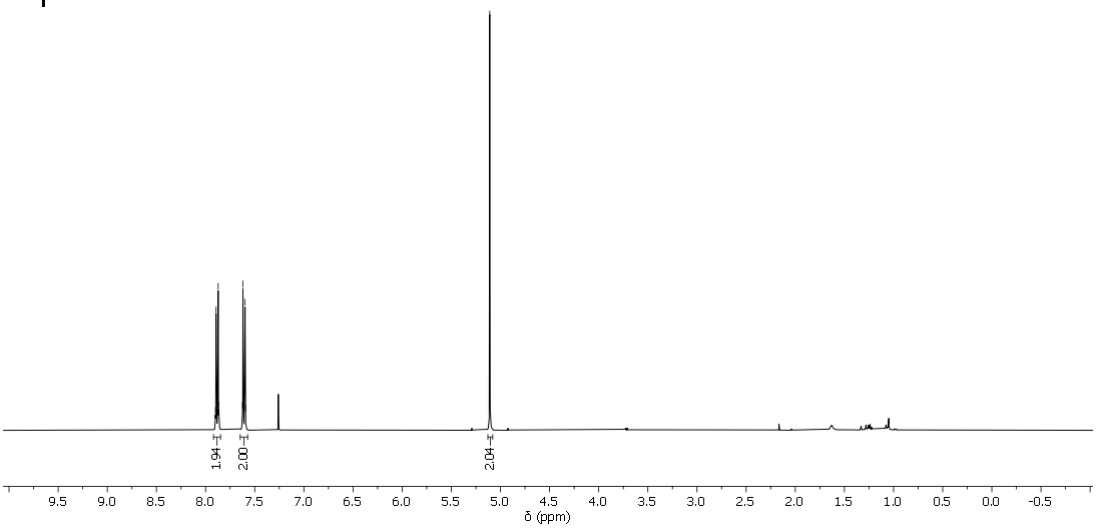

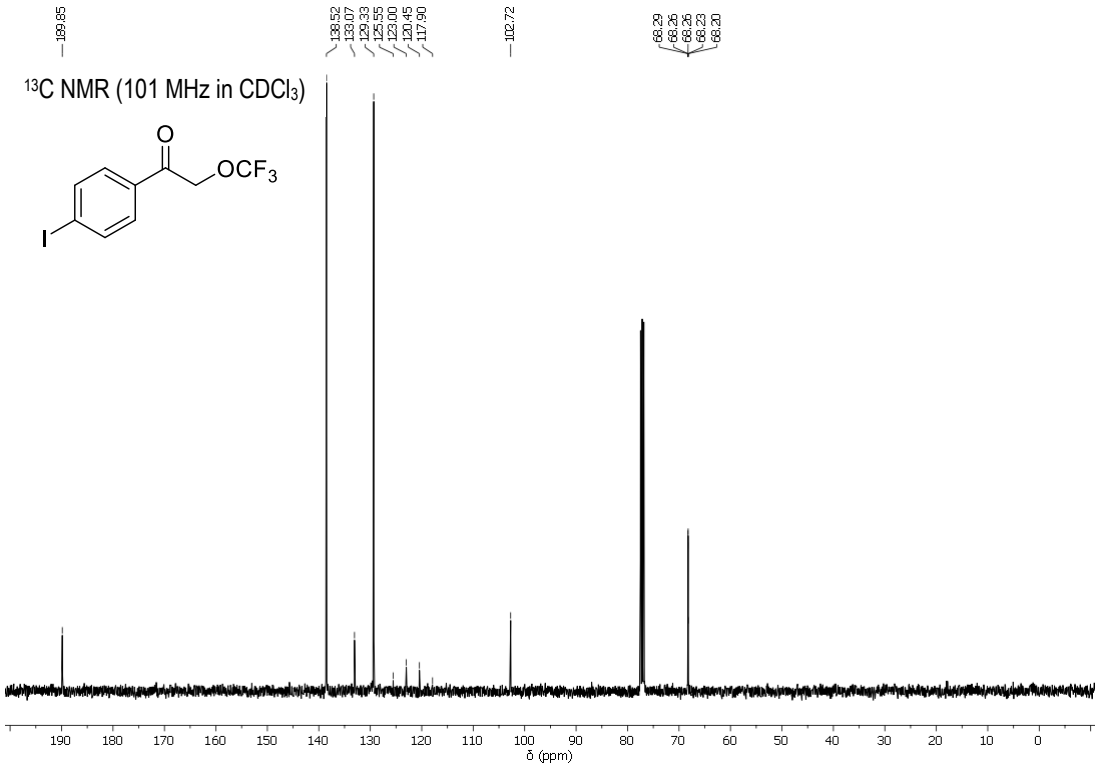
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138.52
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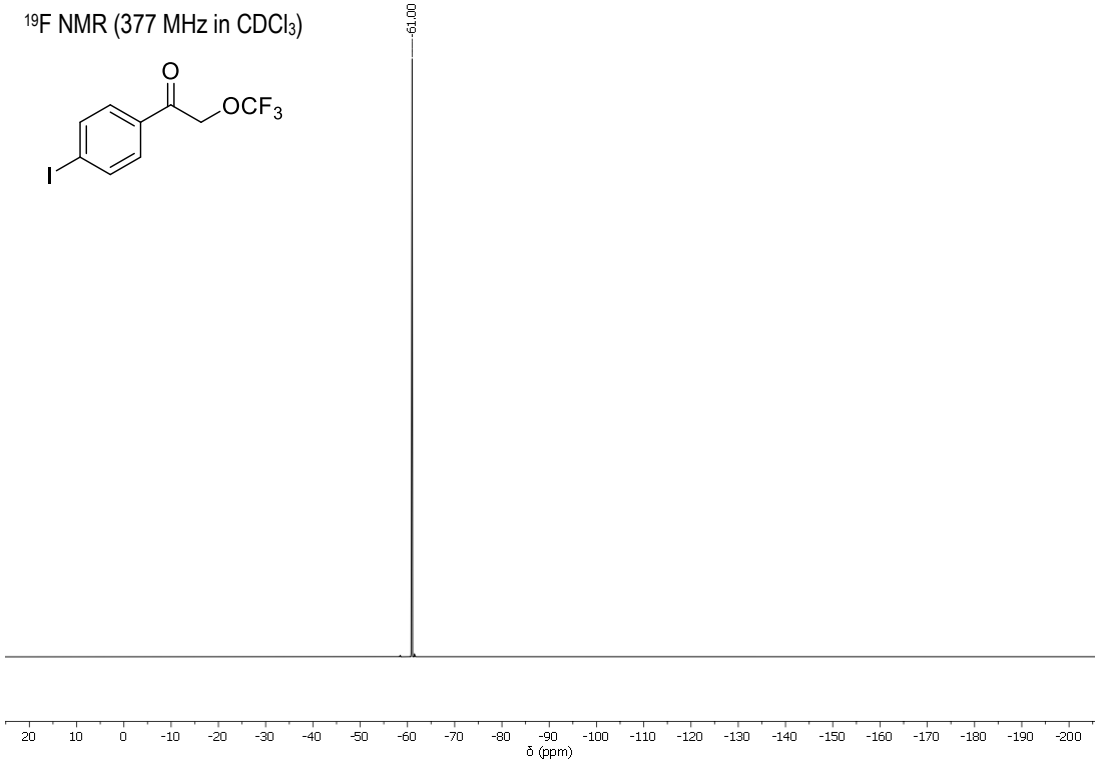
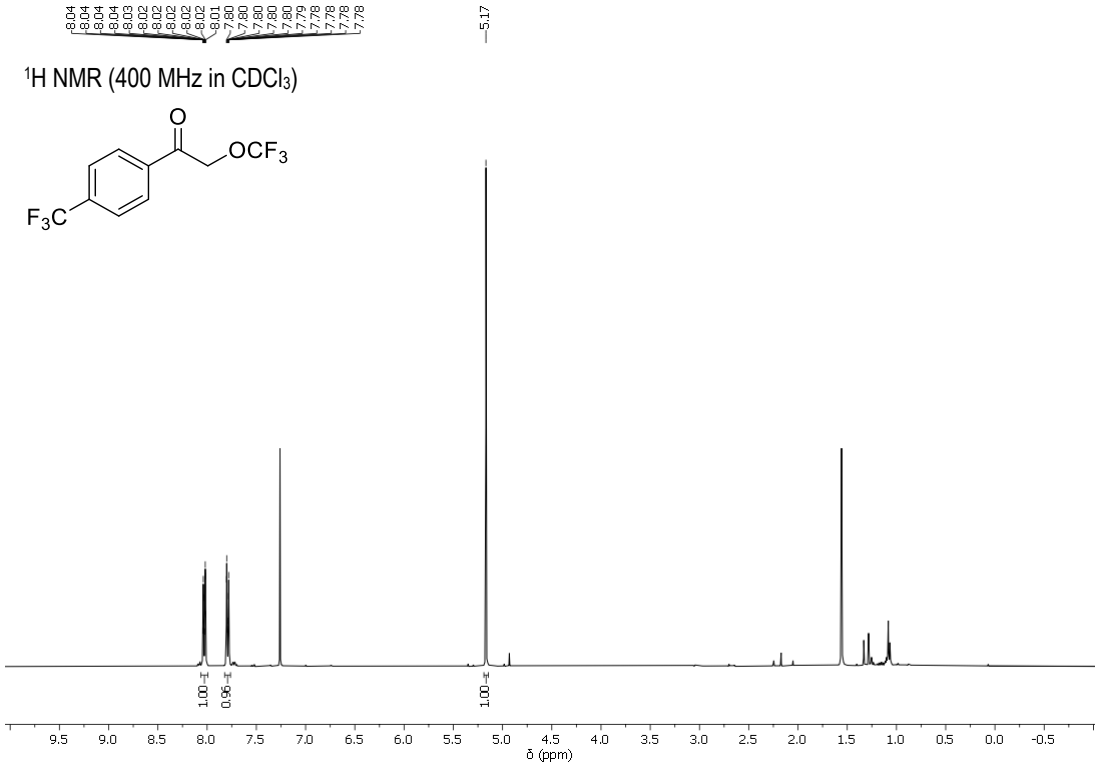
129.33
125.55
123.00
120.45
117.90
102.72
68.29
68.26
68.25
68.23
68.20
13C NMR (101 MHz in CDCl3)
O
OCF3
I
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)

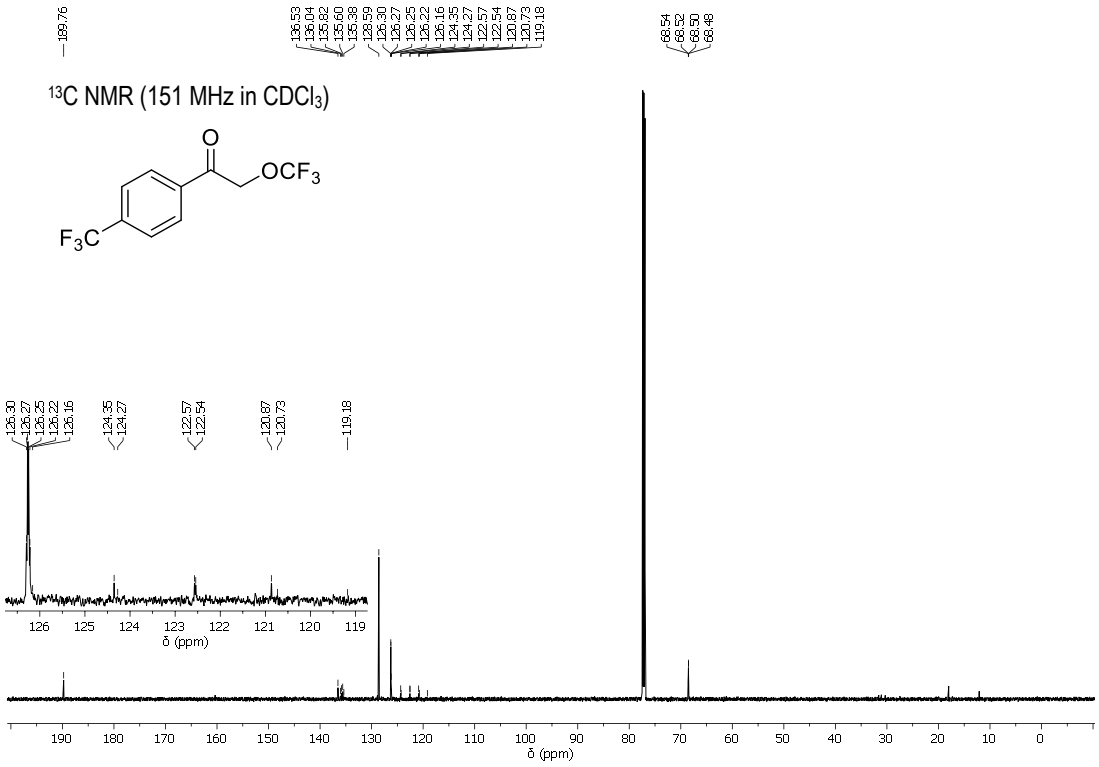

19F NMR (377 MHz in CDCl3)
-61.00
O
OCF3
I
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
δ (ppm)

2-(trifluoromethoxy)-1-(4-(trifluoromethyl)phenyl)ethan-1-one **2g**

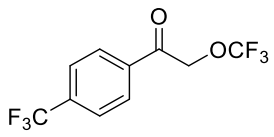
^{1}H NMR (400 MHz in $CDCl_3$)



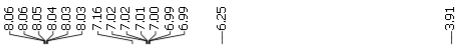
^{13}C NMR (151 MHz in $CDCl_3$)



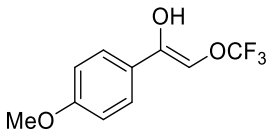
^{19}F NMR (377 MHz in $CDCl_3$)

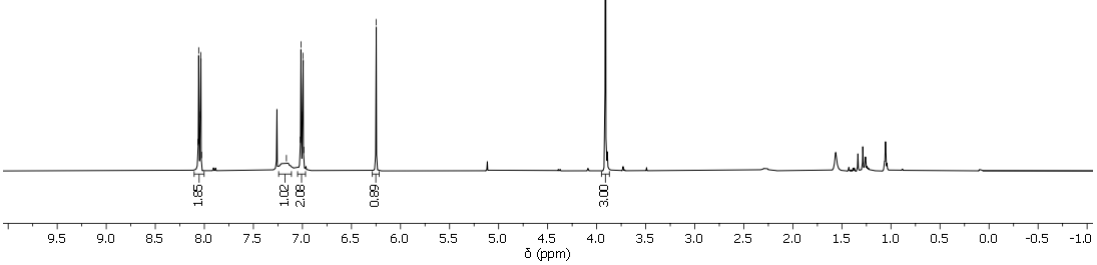


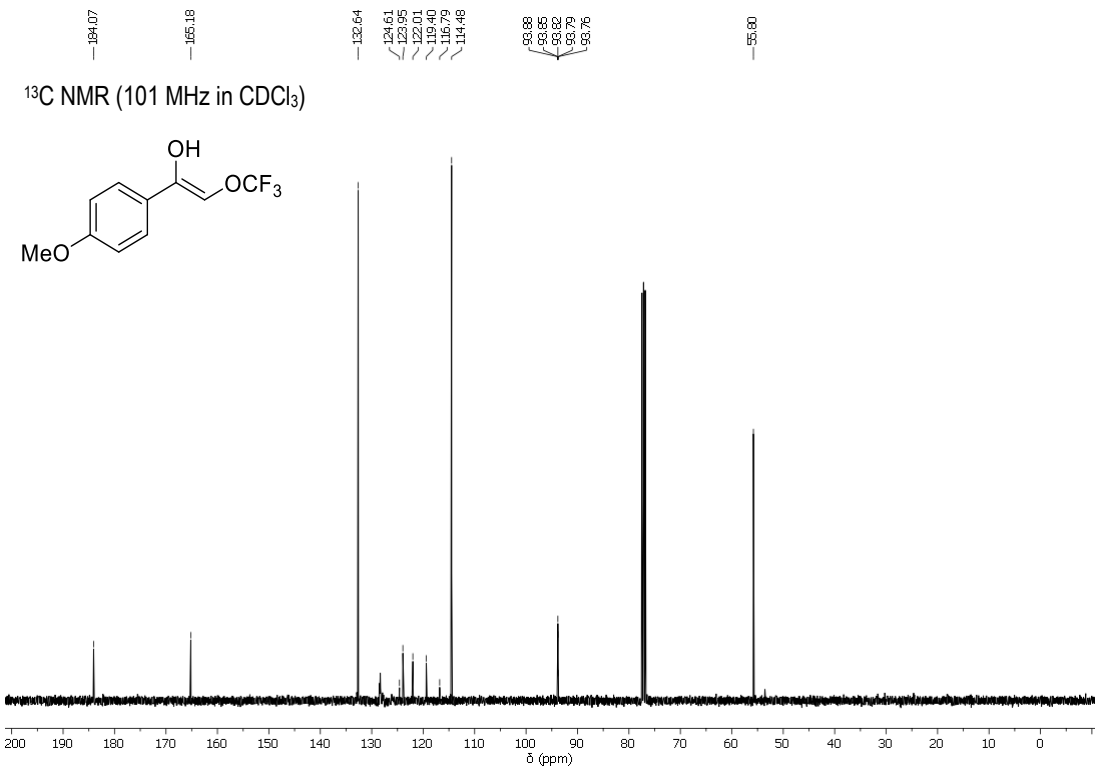
(Z)-1-(4-methoxyphenyl)-2-(trifluoromethoxy)ethen-1-ol **5i**

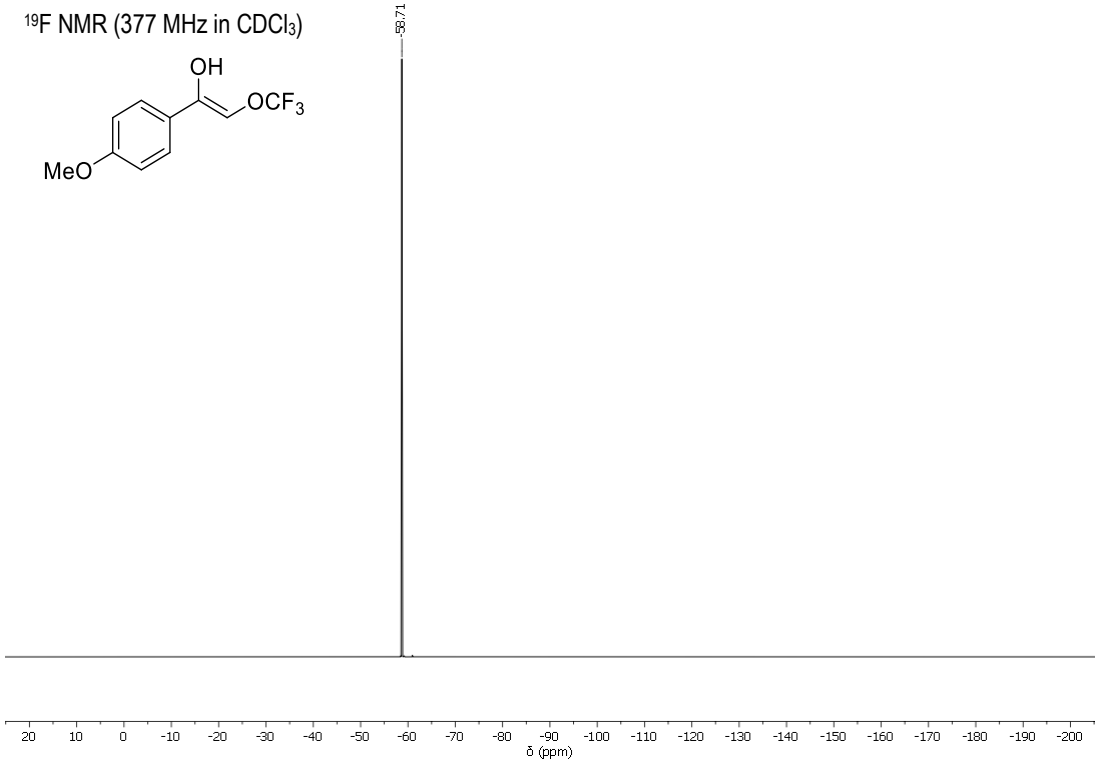


^{1}H NMR (400 MHz in $CDCl_3$)

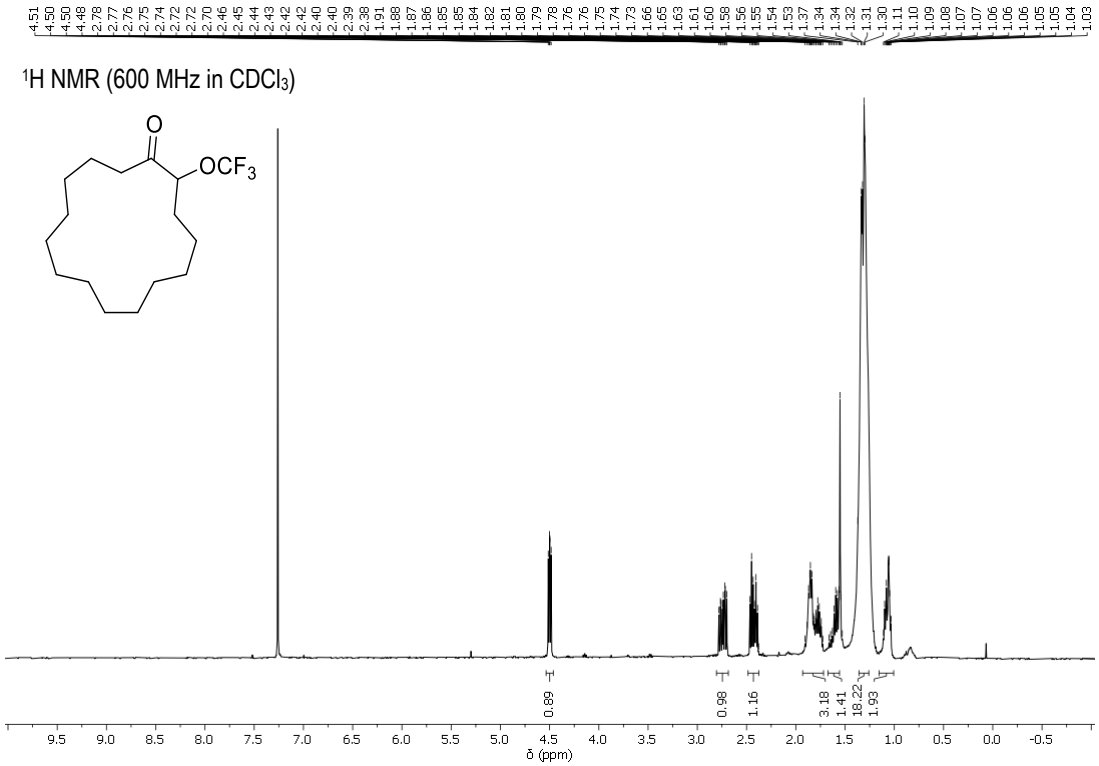




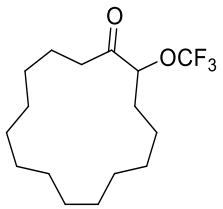

194.07
165.18
132.64
124.61
123.95
122.01
119.40
116.79
114.48
93.88
93.85
93.82
93.79
93.76
55.60
13C NMR (101 MHz in CDCl3)
OH
OCF3
MeO
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)


19F NMR (377 MHz in CDCl3)
-58.71
OH
OCF3
MeO
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
δ (ppm)

2-(trifluoromethoxy)cyclopentadecan-1-one **2q**

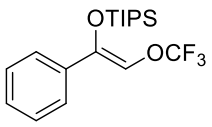


^{19}F NMR (377 MHz in $CDCl_3$)

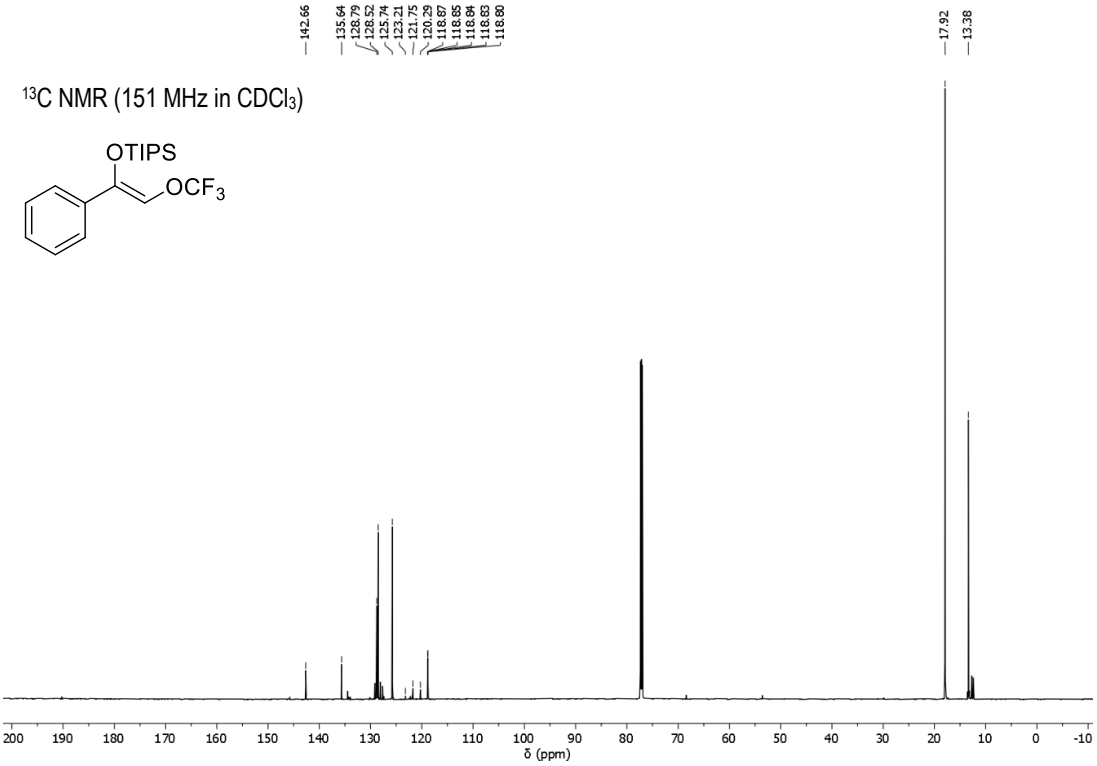


(Z)-Triisopropyl((1-phenyl-2-(trifluoromethoxy)vinyl)oxy)silane **4a**

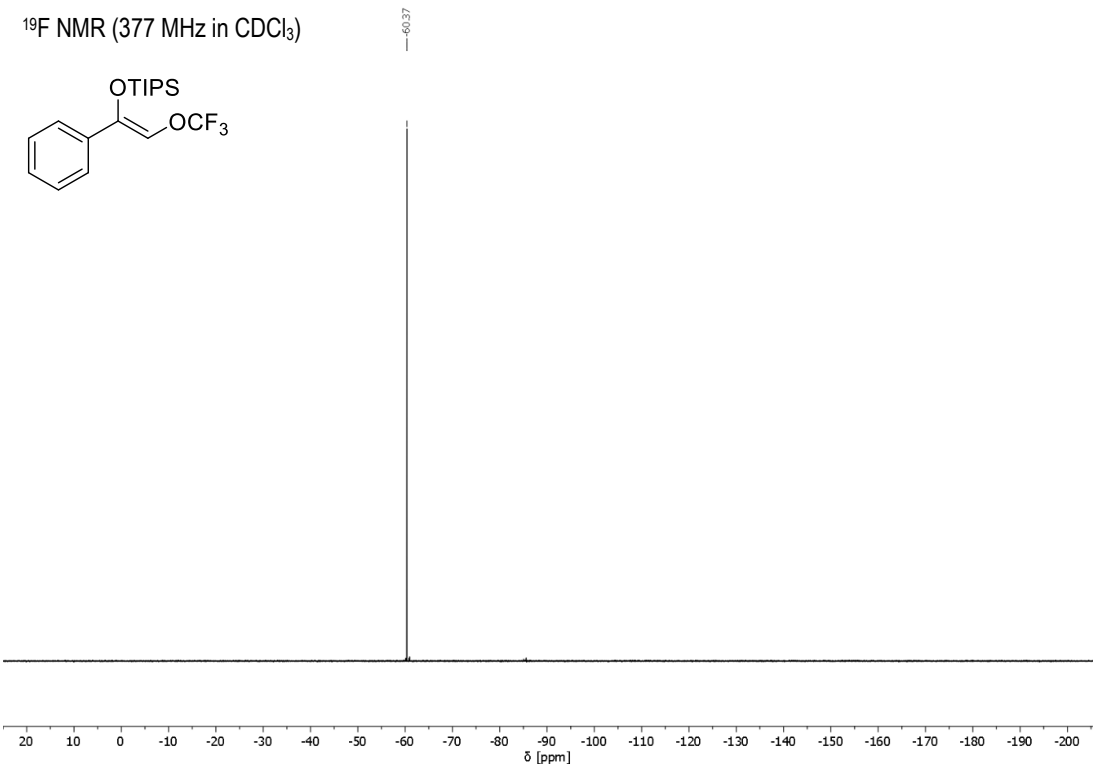
^{1}H NMR (400 MHz in $CDCl_3$)



^{13}C NMR (151 MHz in $CDCl_3$)

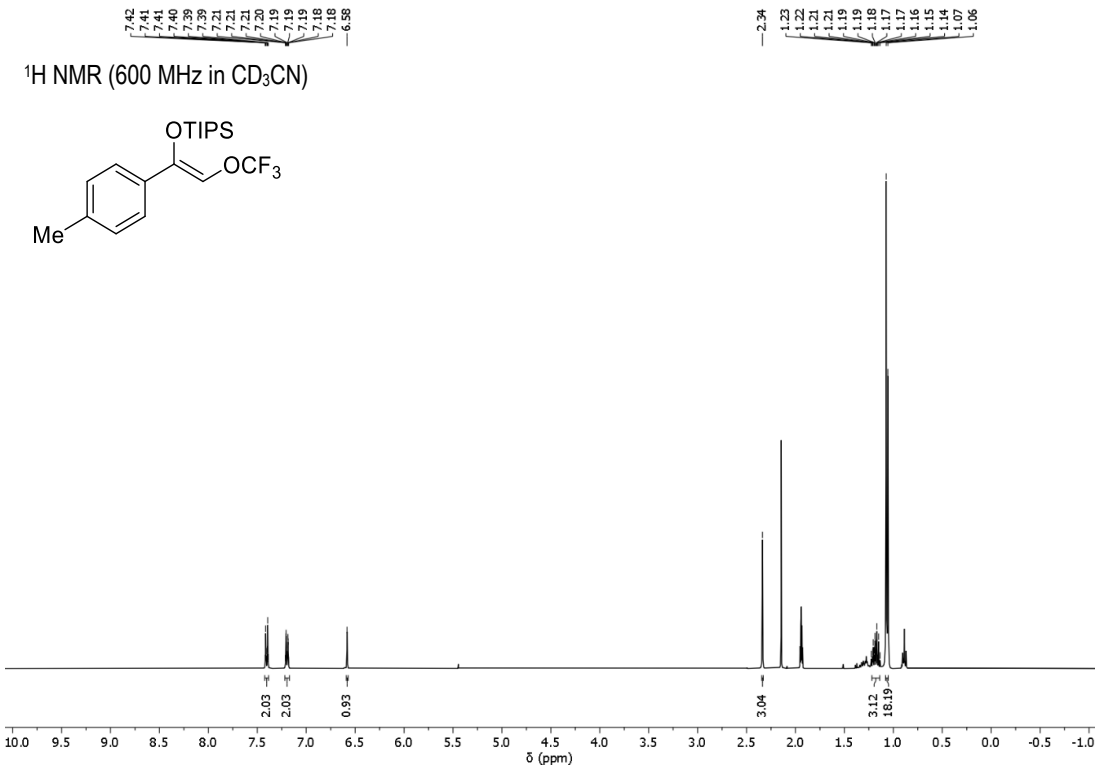


^{19}F NMR (377 MHz in $CDCl_3$)

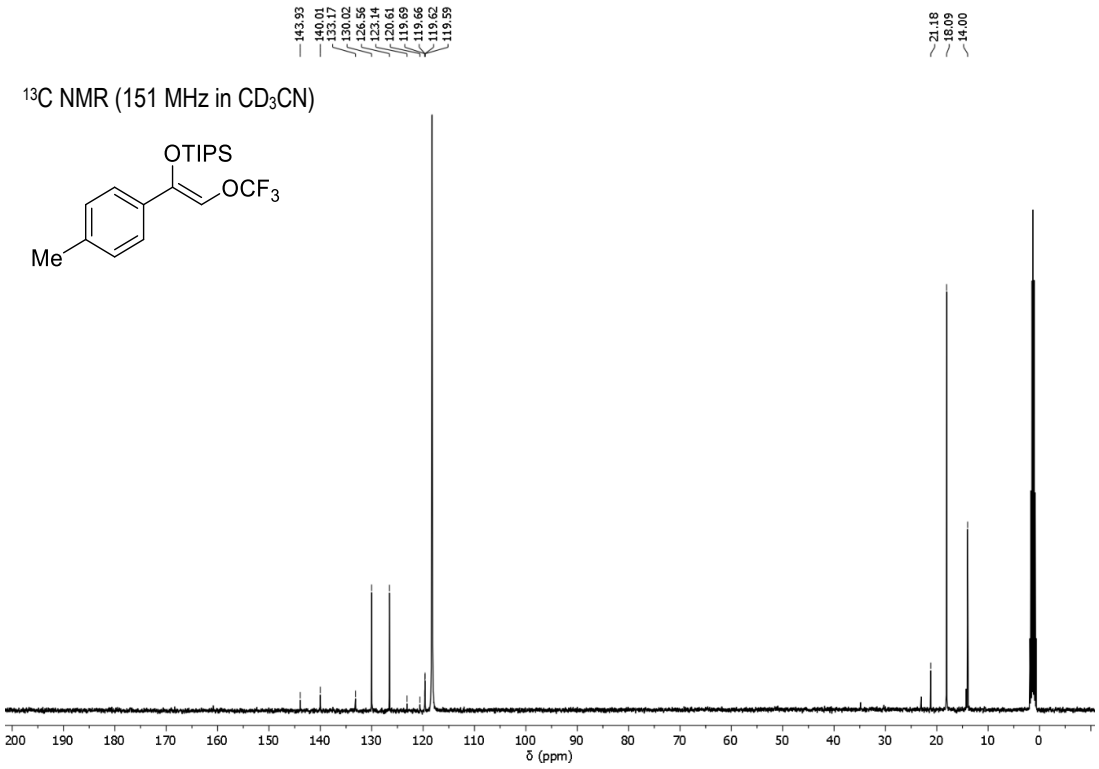


(Z)-triisopropyl((1-(*p*-tolyl)-2-(trifluoromethoxy)vinyl)oxy)silane **4b**

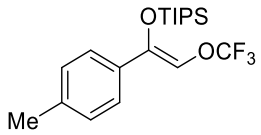
^{1}H NMR (600 MHz in CD_3CN)



^{13}C NMR (151 MHz in CD_3CN)

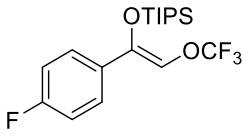


^{19}F NMR (565 MHz in CD_3CN)

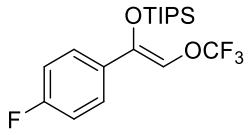


(Z)-((1-(4-fluorophenyl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **4c**

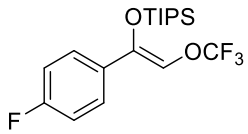
^{1}H NMR (400 MHz in $CDCl_3$)



^{13}C NMR (126 MHz in $CDCl_3$)

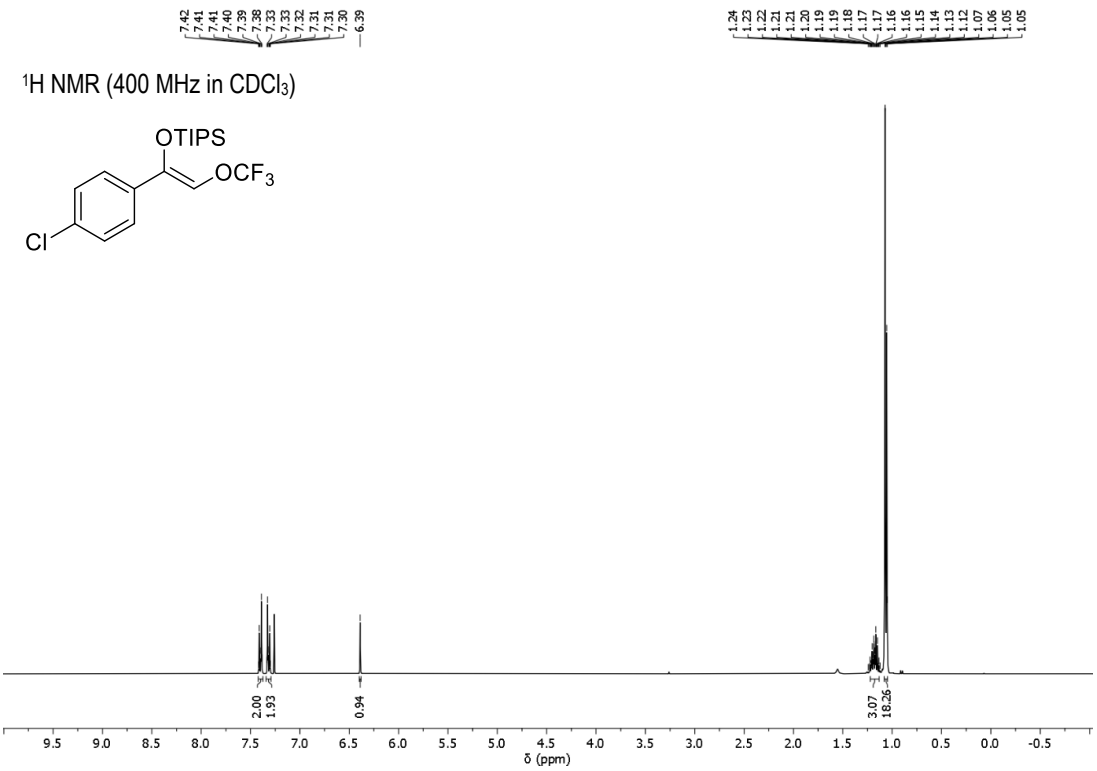


^{19}F NMR (377 MHz in $CDCl_3$)

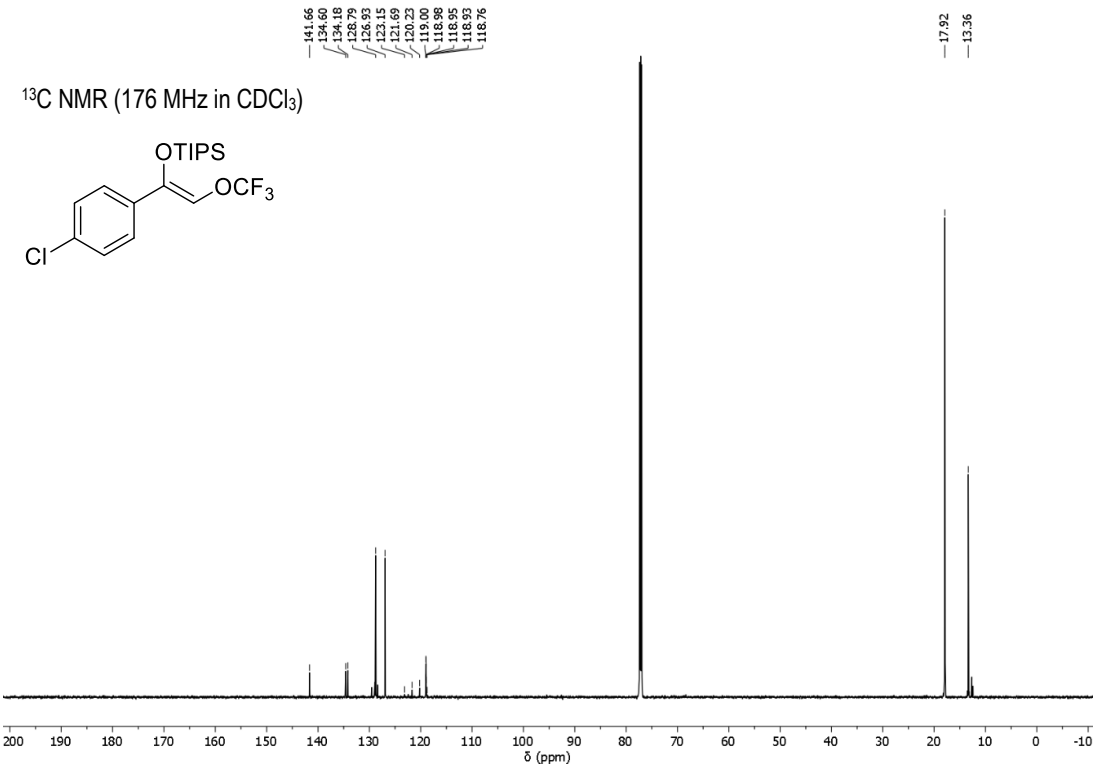


(Z)-((1-(4-chlorophenyl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **4d**

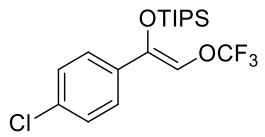
^{1}H NMR (400 MHz in $CDCl_3$)



^{13}C NMR (176 MHz in $CDCl_3$)

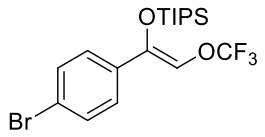


^{19}F NMR (377 MHz in $CDCl_3$)

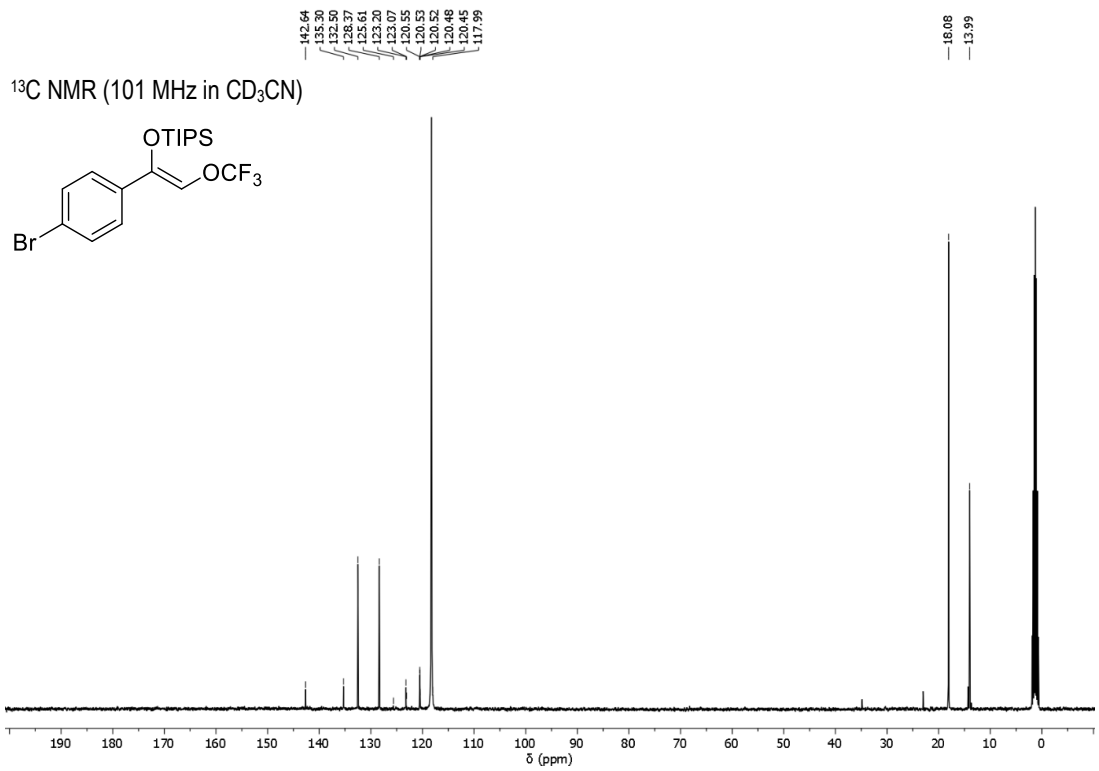


(Z)-((1-(4-bromophenyl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **4e**

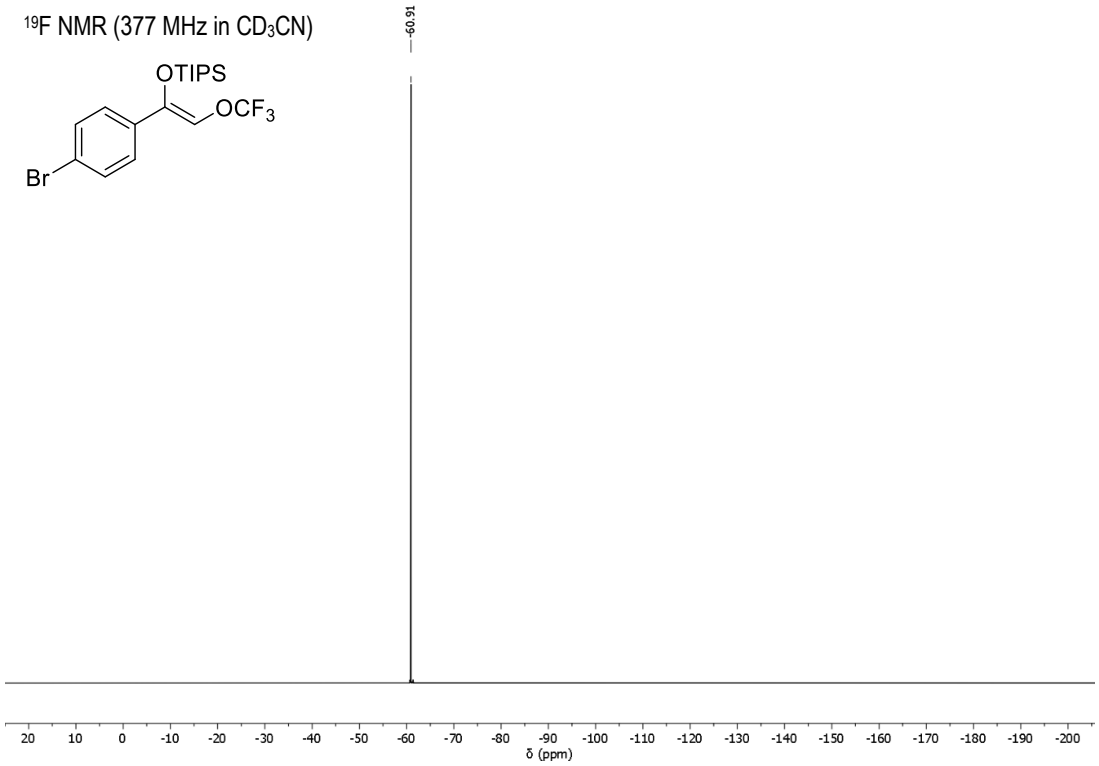
^{1}H NMR (400 MHz in CD_3CN)



^{13}C NMR (101 MHz in CD_3CN)

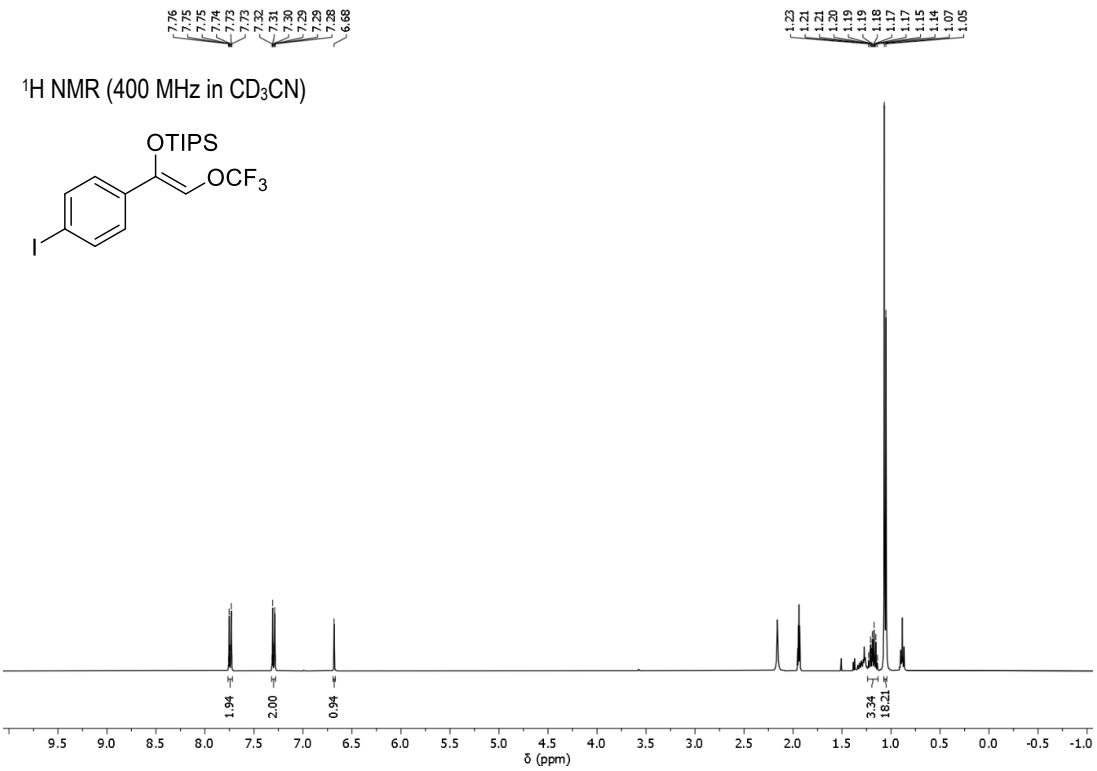


^{19}F NMR (377 MHz in CD_3CN)

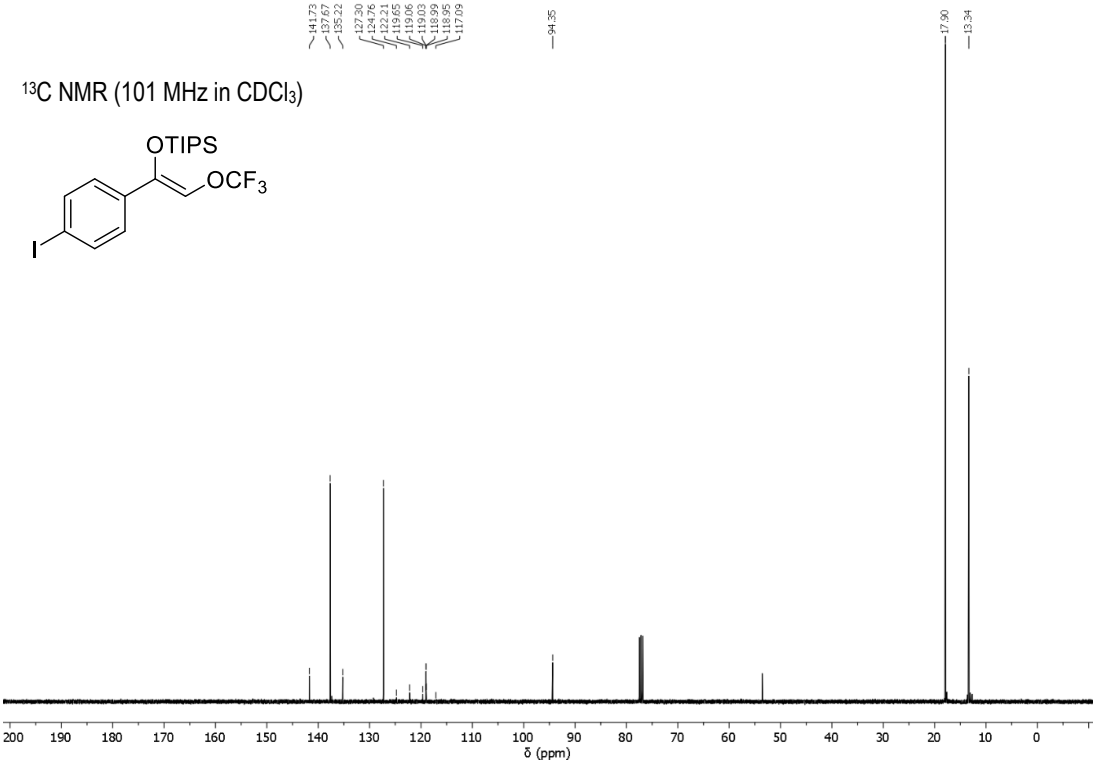


(Z)-((1-(4-iodophenyl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **4f**

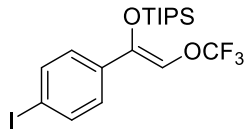
^{1}H NMR (400 MHz in CD_3CN)



^{13}C NMR (101 MHz in $CDCl_3$)

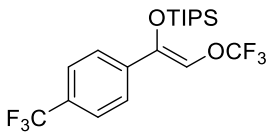


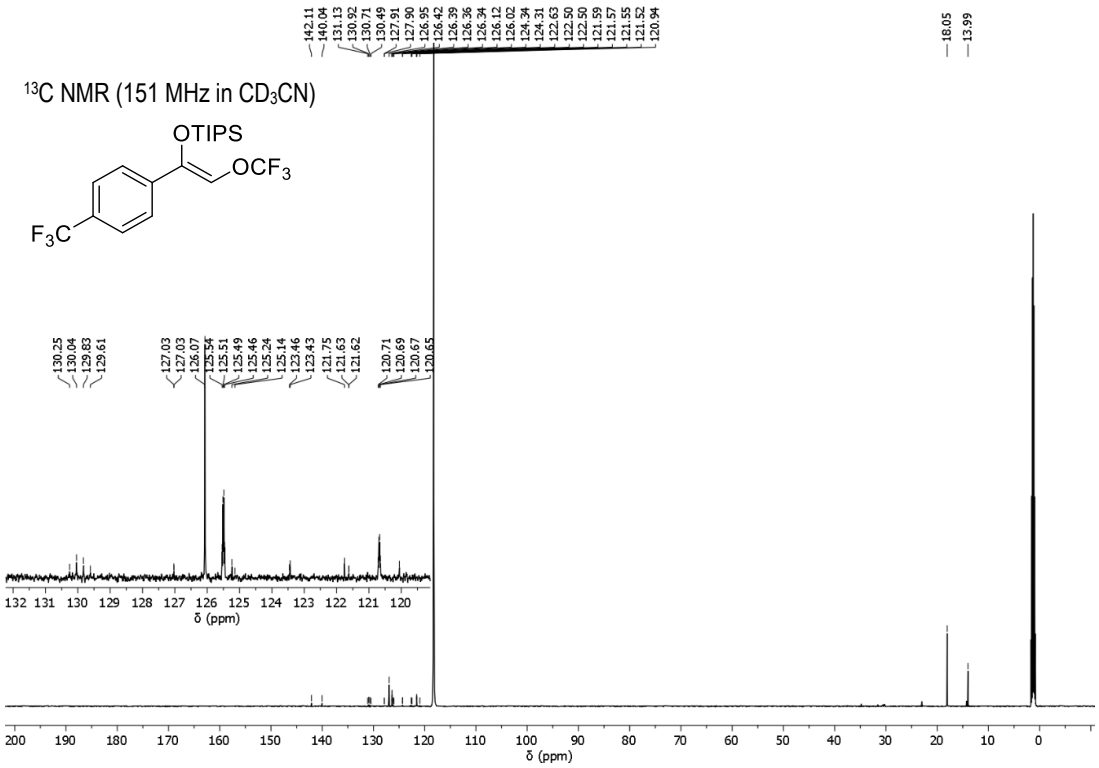
^{19}F NMR (377 MHz in CD_3CN)



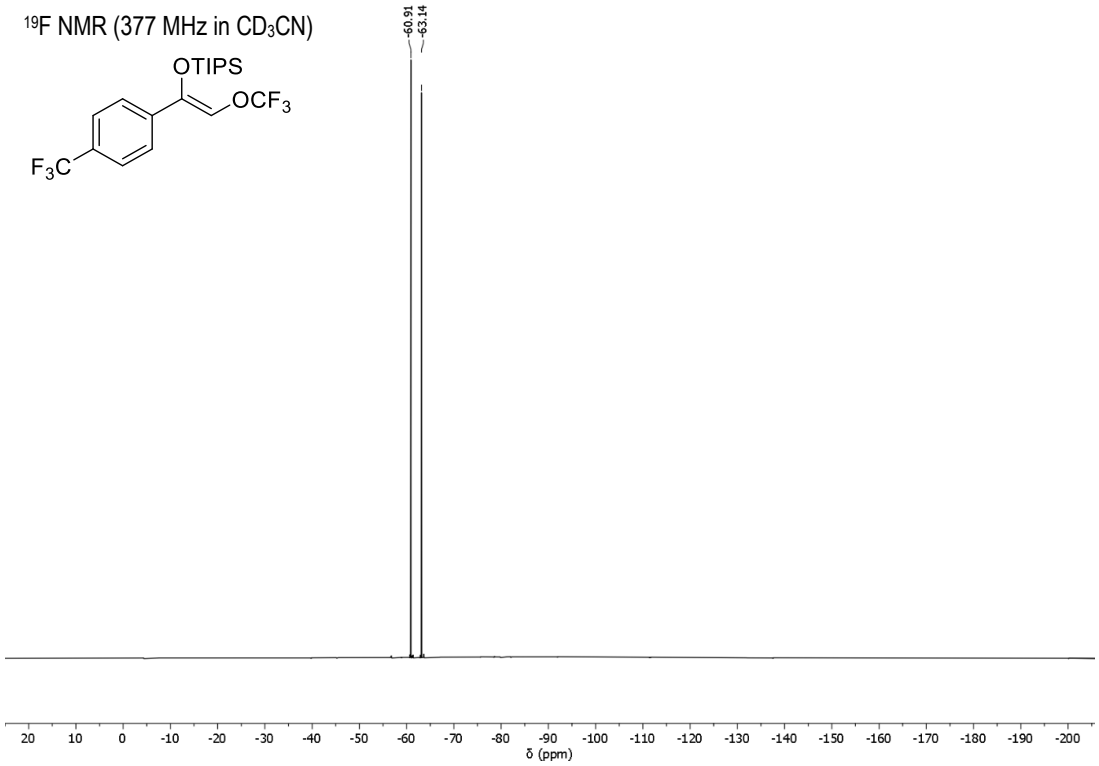
(Z)-triisopropyl((2-(trifluoromethoxy)-1-(4-(trifluoromethyl)phenyl)vinyl)oxy)silane **4g**

^{1}H NMR (400 MHz in CD_3CN)





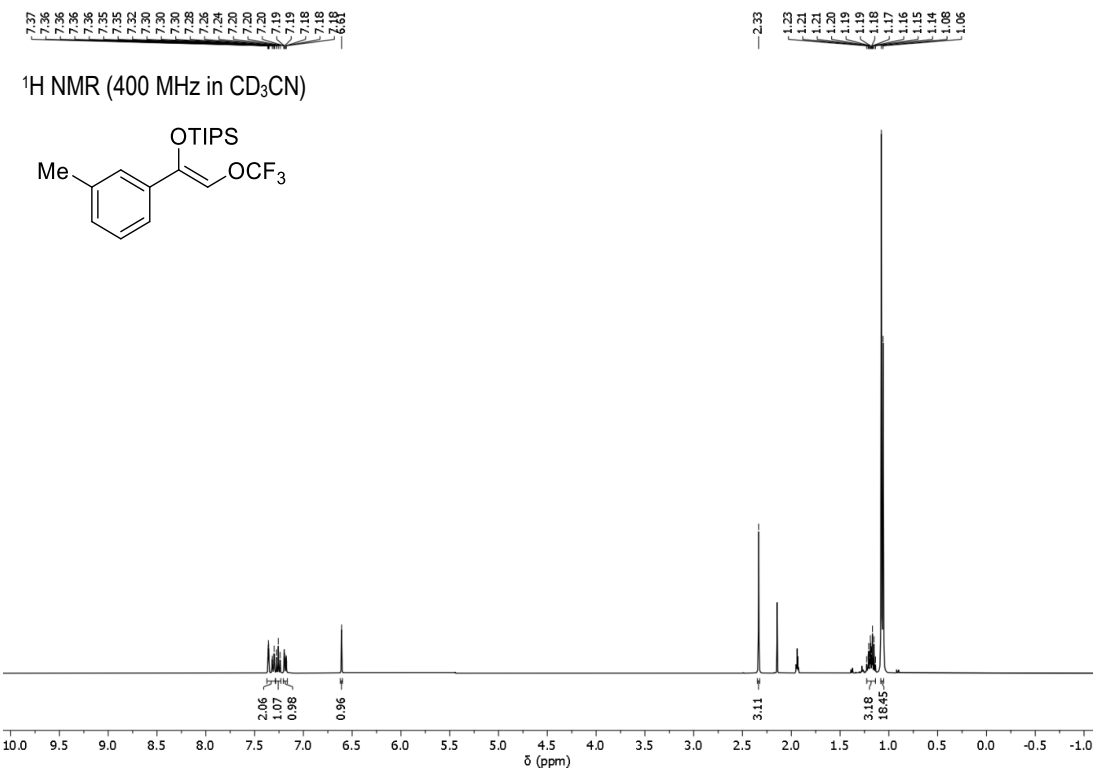
^{13}C NMR (151 MHz in CD_3CN)



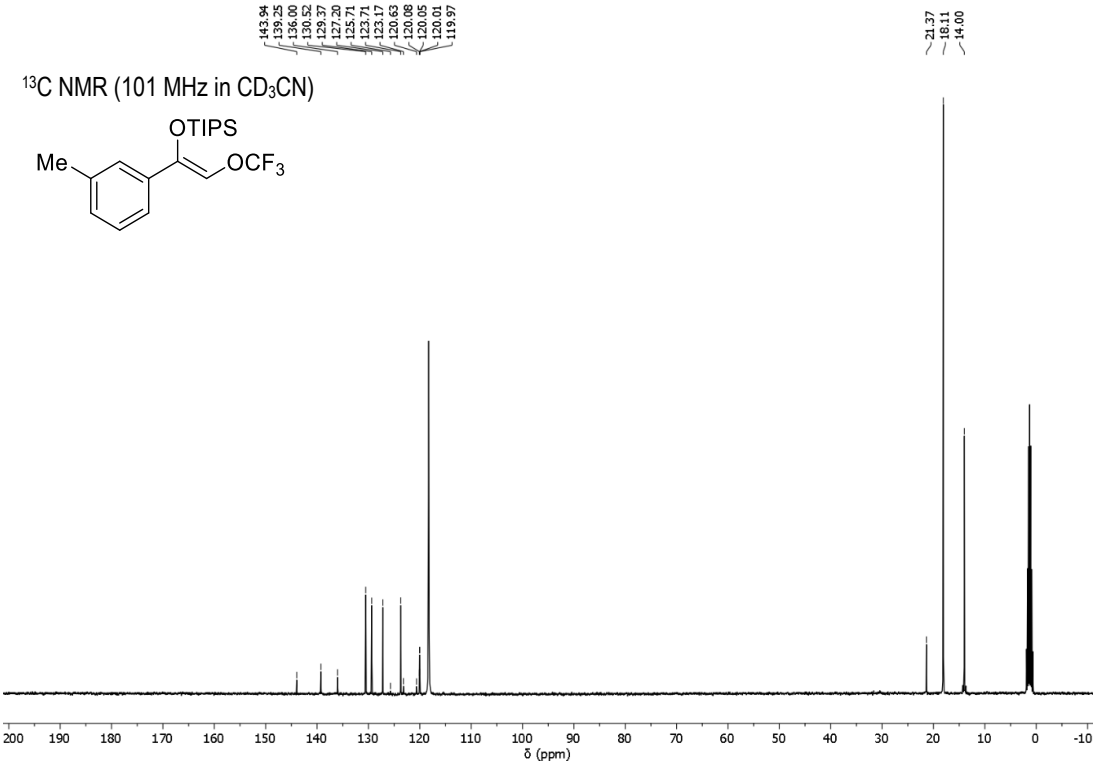
^{19}F NMR (377 MHz in CD_3CN)

(Z)-triisopropyl((1-(*m*-tolyl)-2-(trifluoromethoxy)vinyl)oxy)silane **4j**

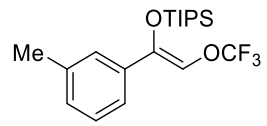
^{1}H NMR (400 MHz in CD_3CN)



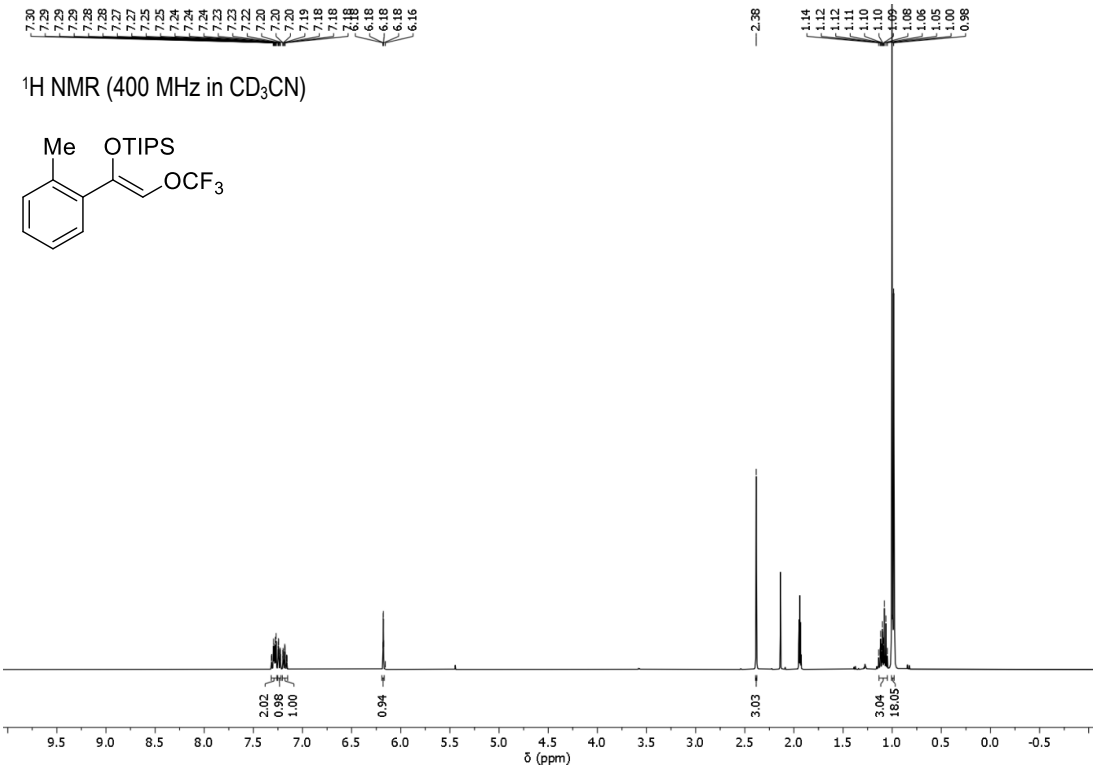
^{13}C NMR (101 MHz in CD_3CN)



^{19}F NMR (377 MHz in CD_3CN)

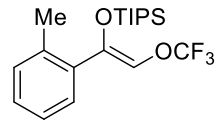


(Z)-triisopropyl((1-(*o*-tolyl)-2-(trifluoromethoxy)vinyl)oxy)silane **4k**

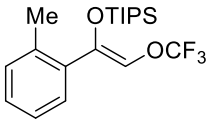


^1H NMR (400 MHz in CD_3CN)

^{13}C NMR (101 MHz in CD_3CN)

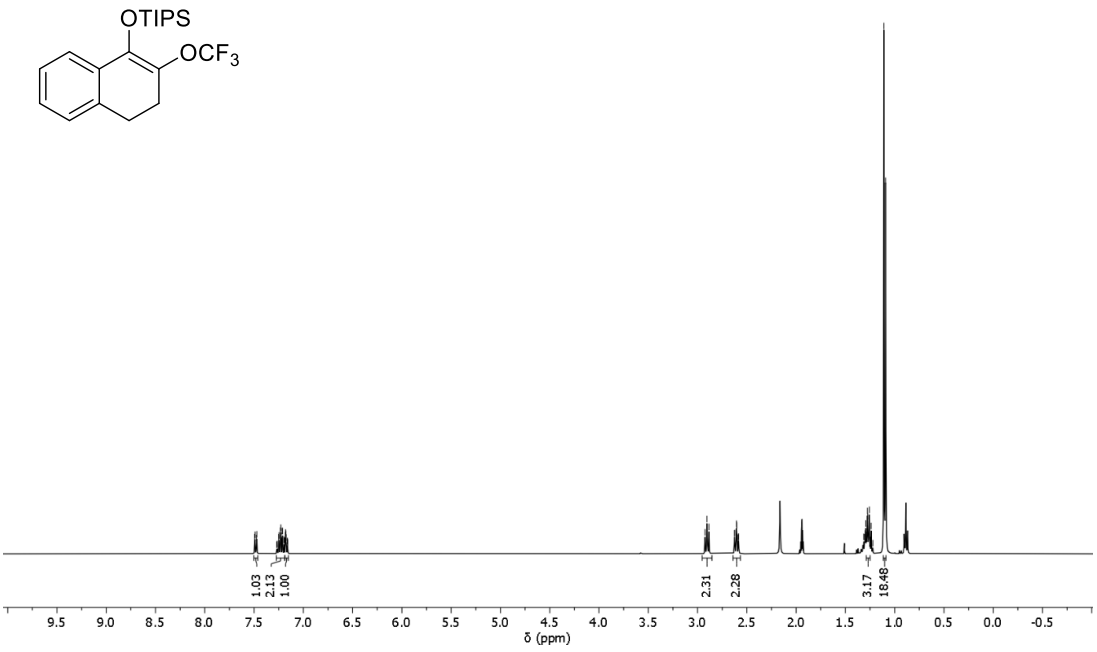


^{19}F NMR (377 MHz in CD_3CN)

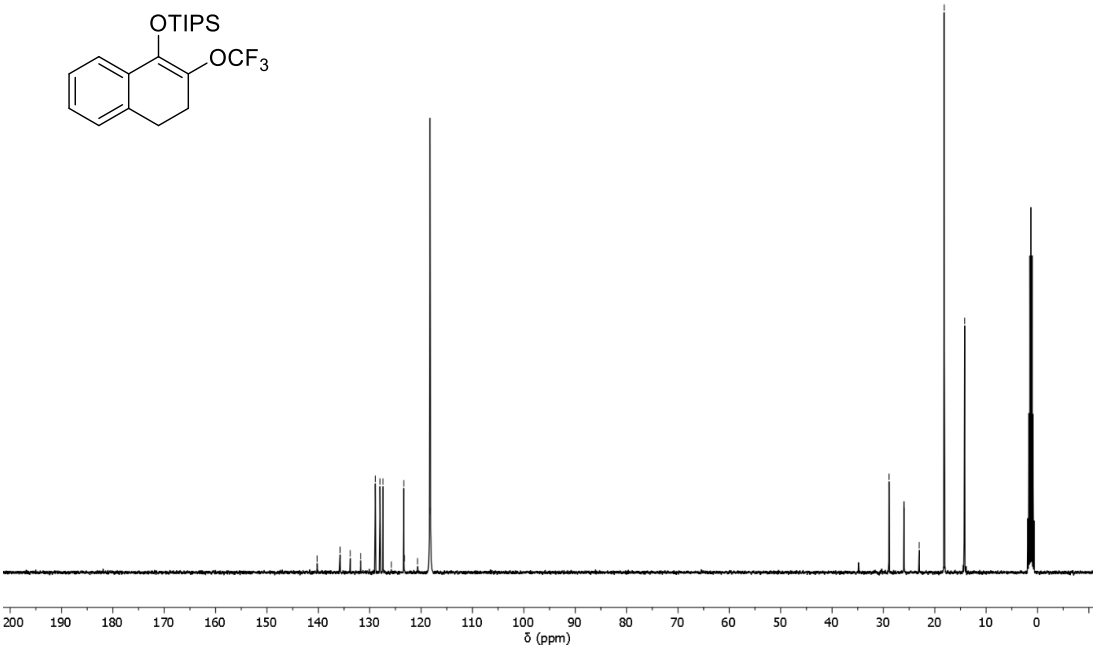


triisopropyl((2-(trifluoromethoxy)-3,4-dihydronaphthalen-1-yl)oxy)silane **4n**

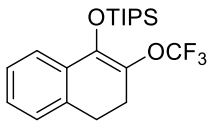
^{1}H NMR (400 MHz in CD_3CN)



^{13}C NMR (101 MHz in CD_3CN)

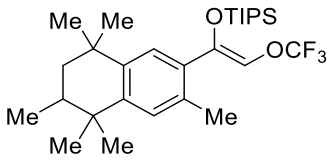


^{19}F NMR (377 MHz in CD_3CN)

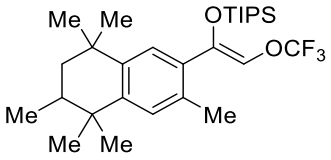


(Z)-((1-(3,5,5,6,8,8-hexamethyl-5,6,7,8-tetrahydronaphthalen-2-yl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **4o**

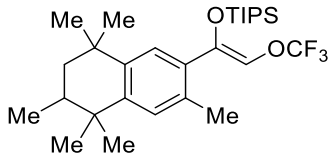
^{1}H NMR (400 MHz in CD_3CN)



^{13}C NMR (101 MHz in CD_3CN)

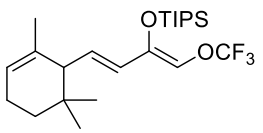


^{19}F NMR (377 MHz in CD_3CN)

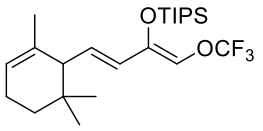


triisopropyl(((1E,3E)-1-(trifluoromethoxy)-4-(2,6,6-trimethylcyclohex-2-en-1-yl)buta-1,3-dien-2-yl)oxy)silane **4p**

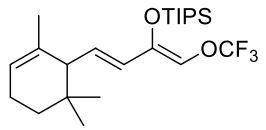
^{1}H NMR (400 MHz in CD_3CN)



^{13}C NMR (101 MHz in CD_3CN)

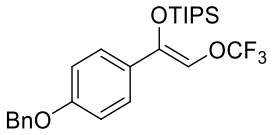


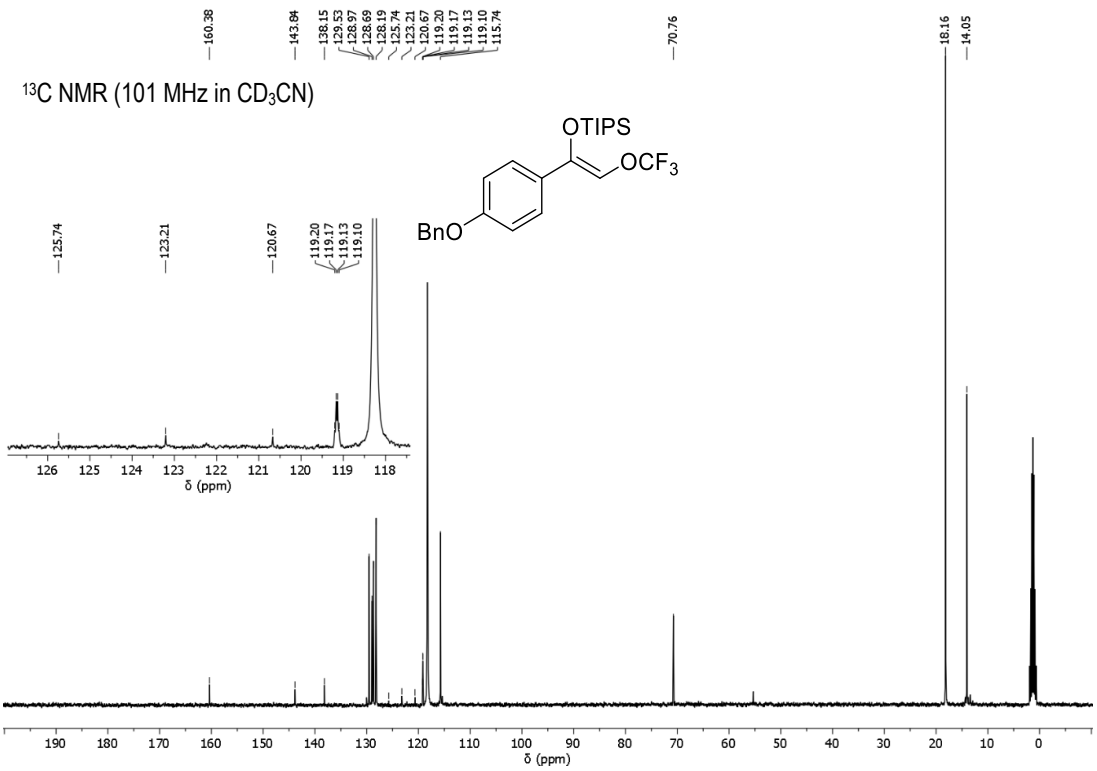
^{19}F NMR (377 MHz in CD_3CN)

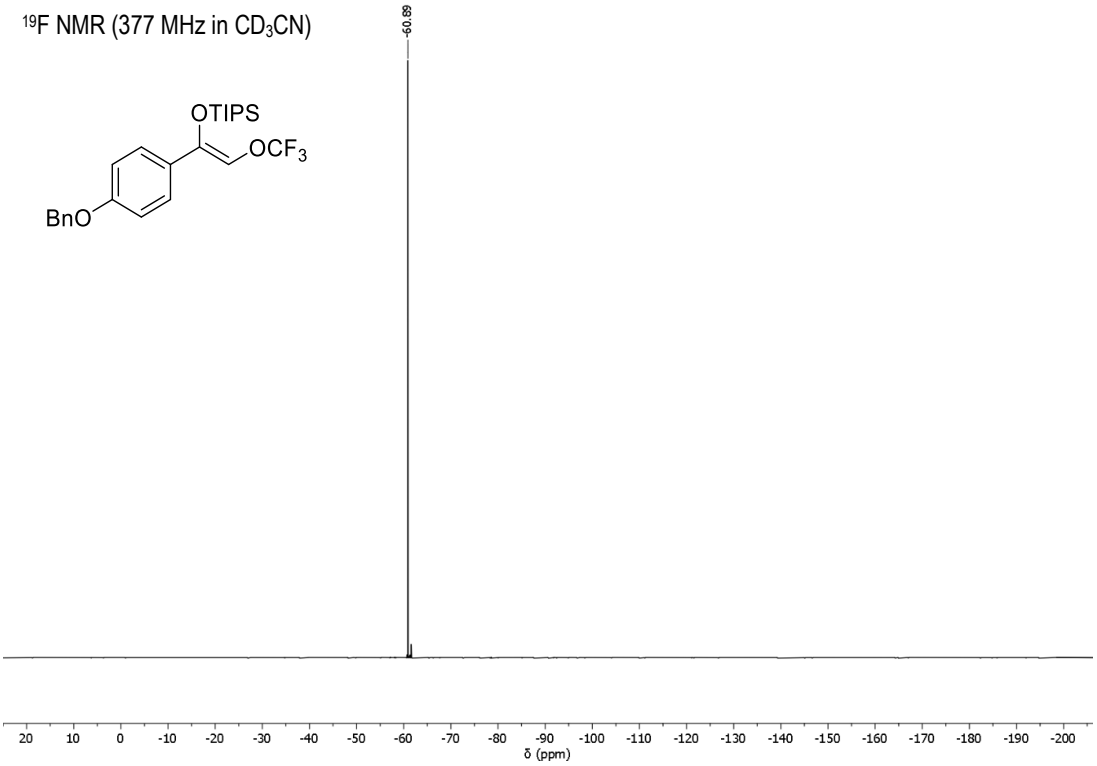


(Z)-((1-(4-(benzyloxy)phenyl)-2-(trifluoromethoxy)vinyl)oxy)triisopropylsilane **4r**

^{1}H NMR (400 MHz in CD_3CN)

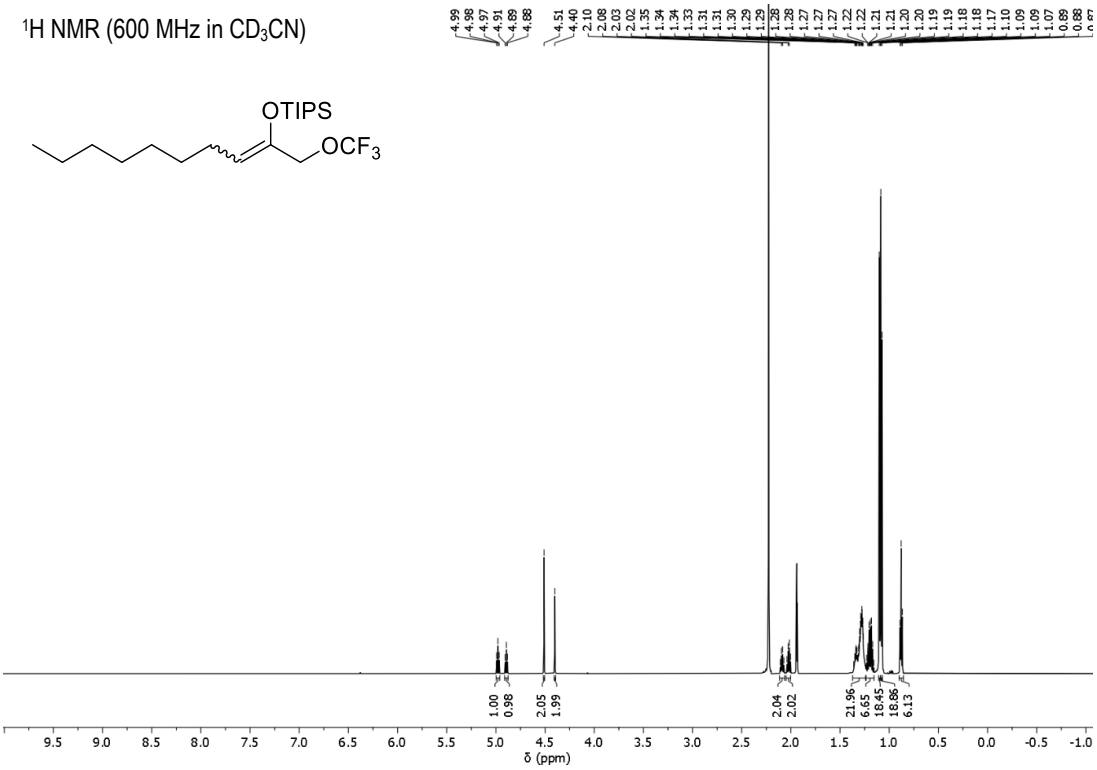



160.38
143.84
138.15
129.53
128.97
128.69
128.19
125.74
123.21
120.67
119.20
119.17
119.13
119.10
115.74
70.76
18.16
14.05
13C NMR (101 MHz in CD3CN)
OTIPS
OCF3
BnO
δ (ppm)

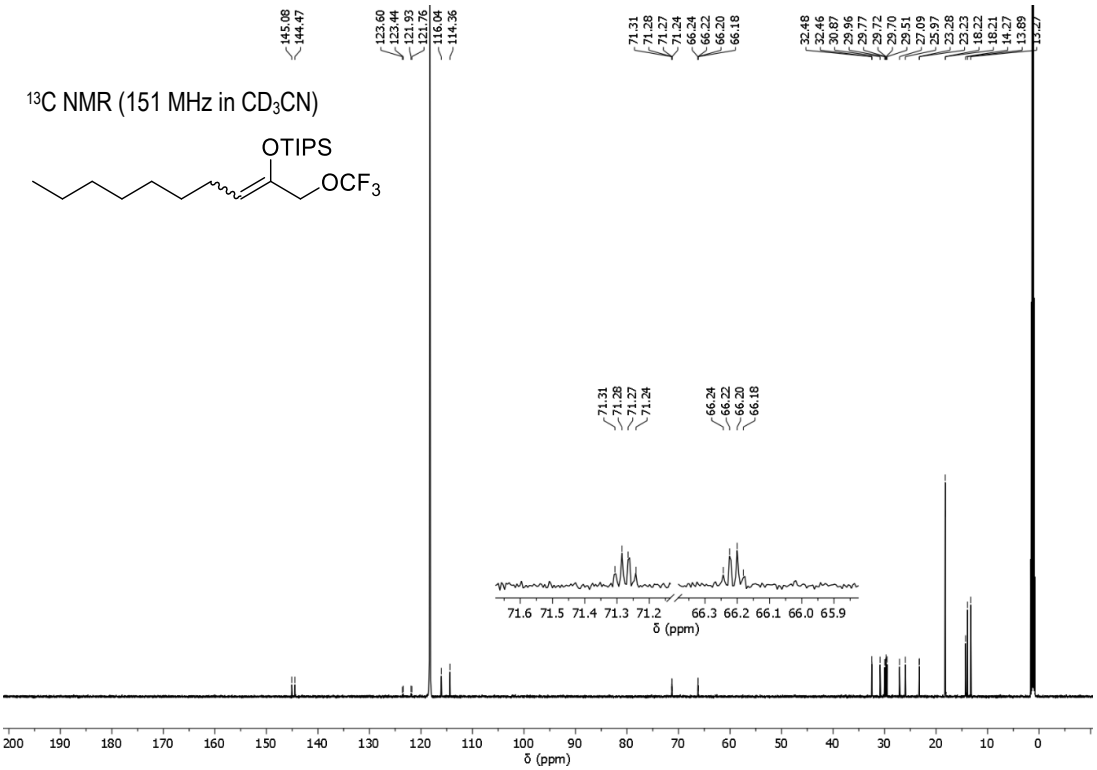

-60.89
19F NMR (377 MHz in CD3CN)
OTIPS
OCF3
BnO
δ (ppm)

Triisopropyl((1-(trifluoromethoxy)dec-1-en-2-yl)oxy)silane **4s**

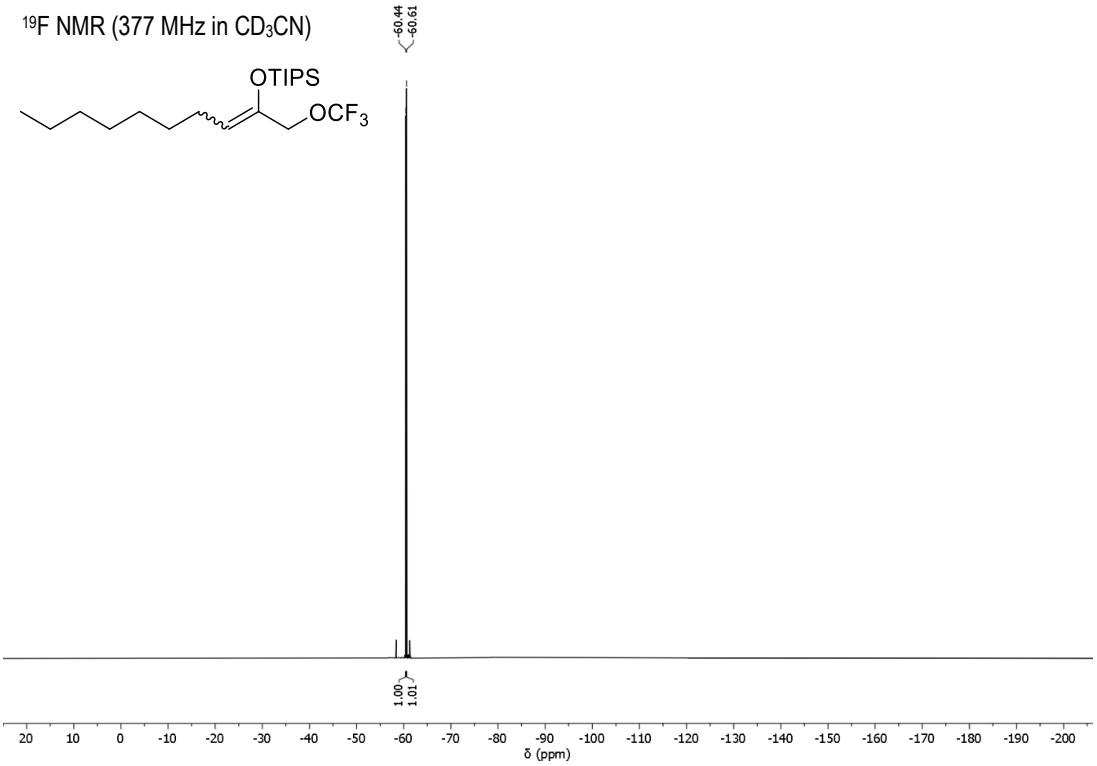
^{1}H NMR (600 MHz in CD_3CN)



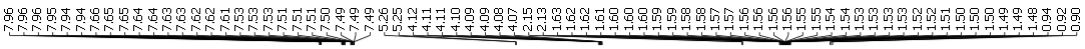
^{13}C NMR (151 MHz in CD_3CN)



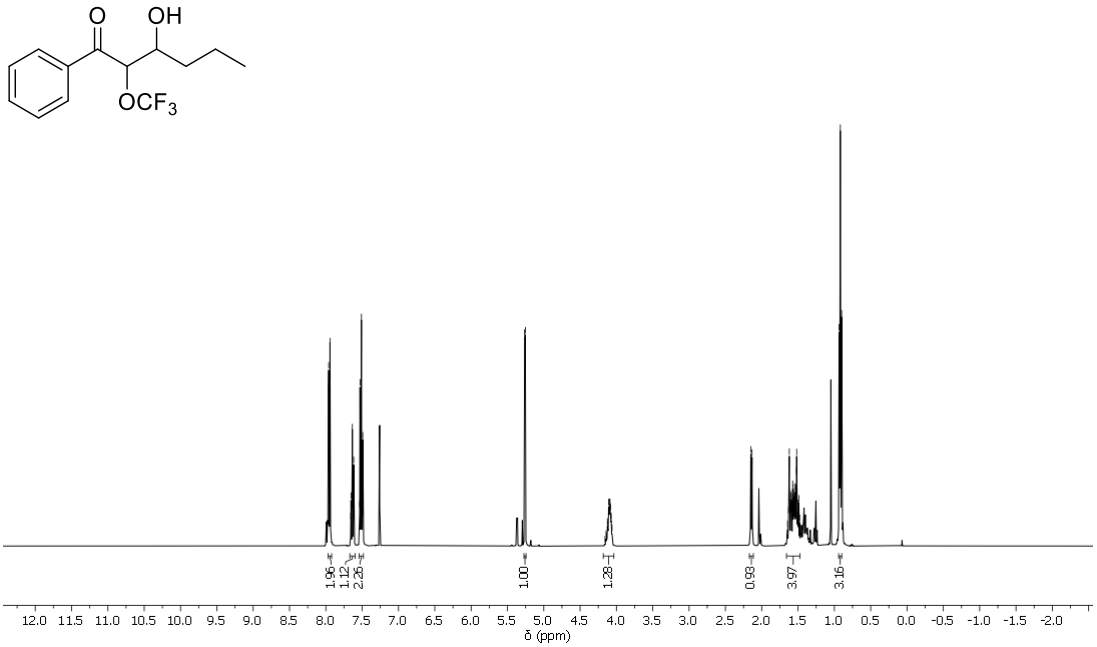
^{19}F NMR (377 MHz in CD_3CN)

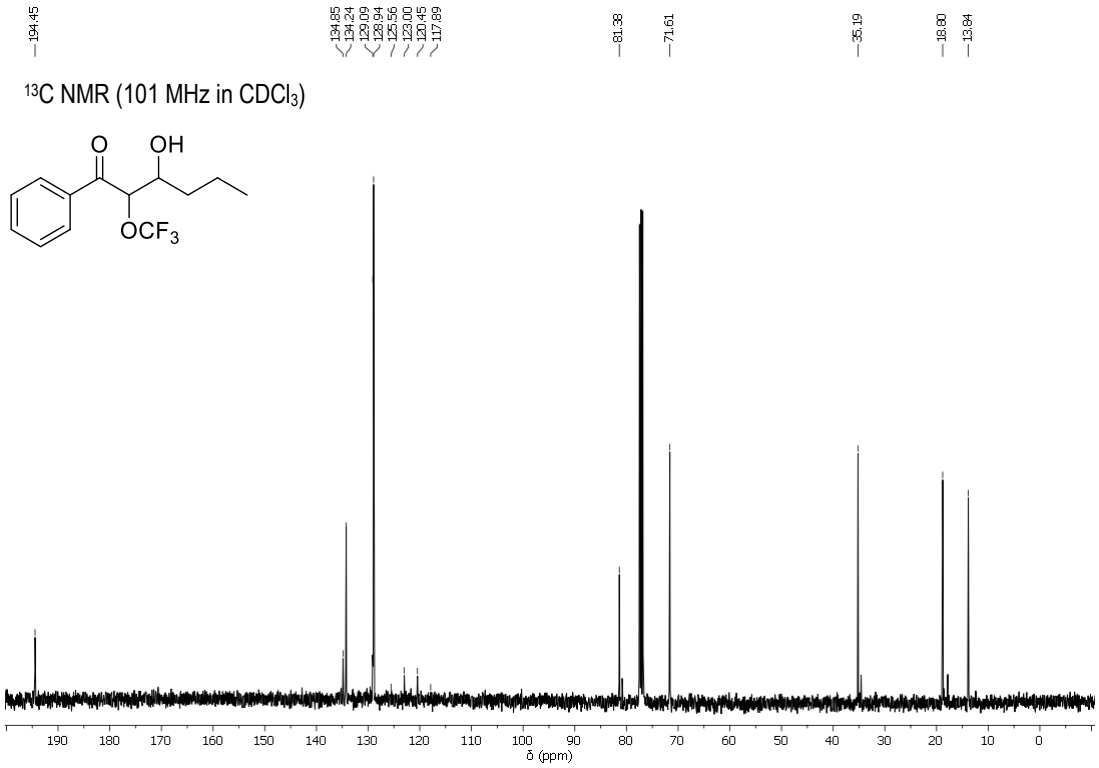


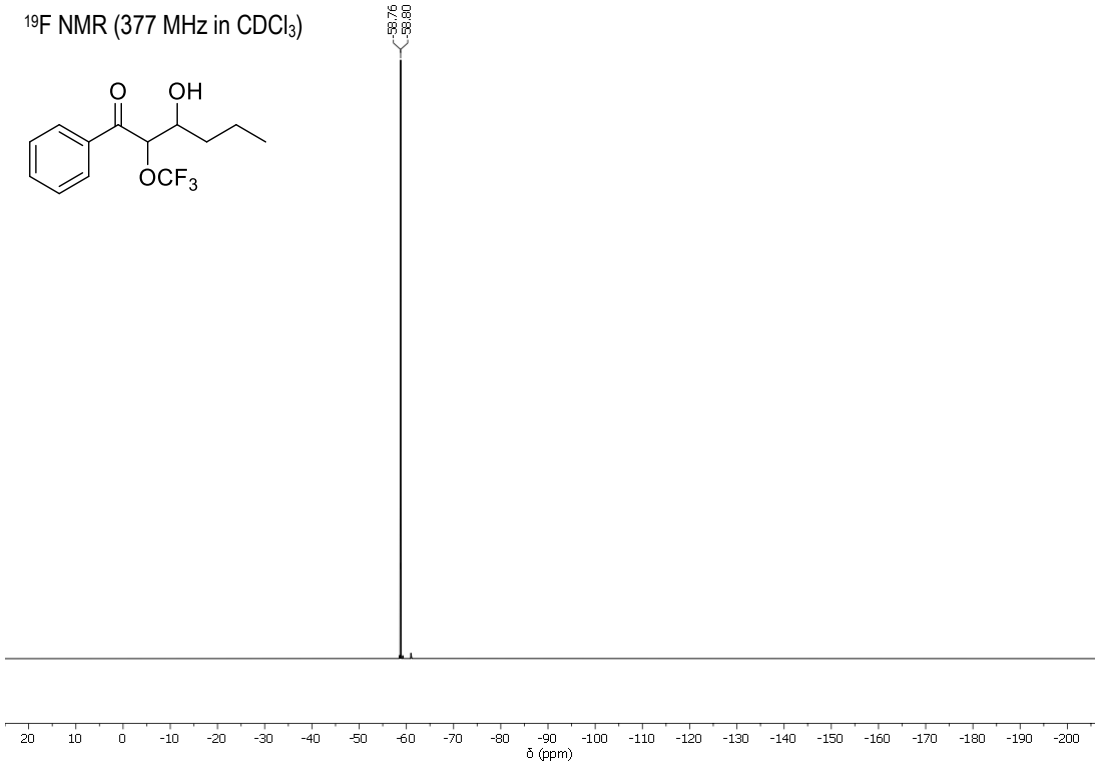
3-hydroxy-1-phenyl-2-(trifluoromethoxy)hexan-1-one **6**



^{1}H NMR (400 MHz in $CDCl_3$)

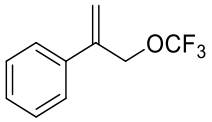


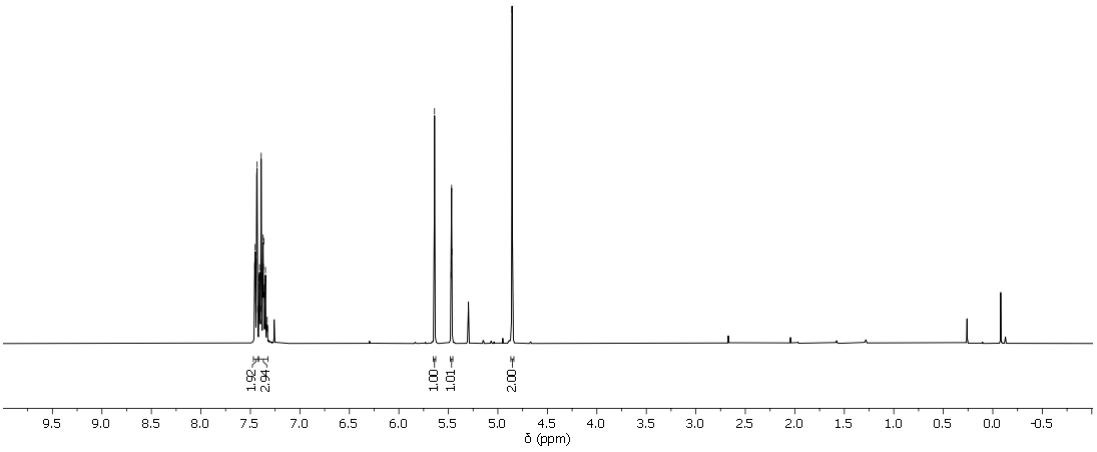

194.45
134.85
134.24
129.09
128.94
125.56
123.00
120.45
117.89
81.38
71.61
35.19
18.80
13.84
13C NMR (101 MHz in CDCl3)
O
OH
OCF3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)


-58.76
-58.80
19F NMR (377 MHz in CDCl3)
O
OH
OCF3
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
δ (ppm)

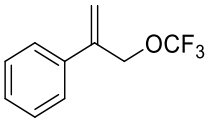
(3-(trifluoromethoxy)prop-1-en-2-yl)benzene **8a**

^{1}H NMR (400 MHz in $CDCl_3$)

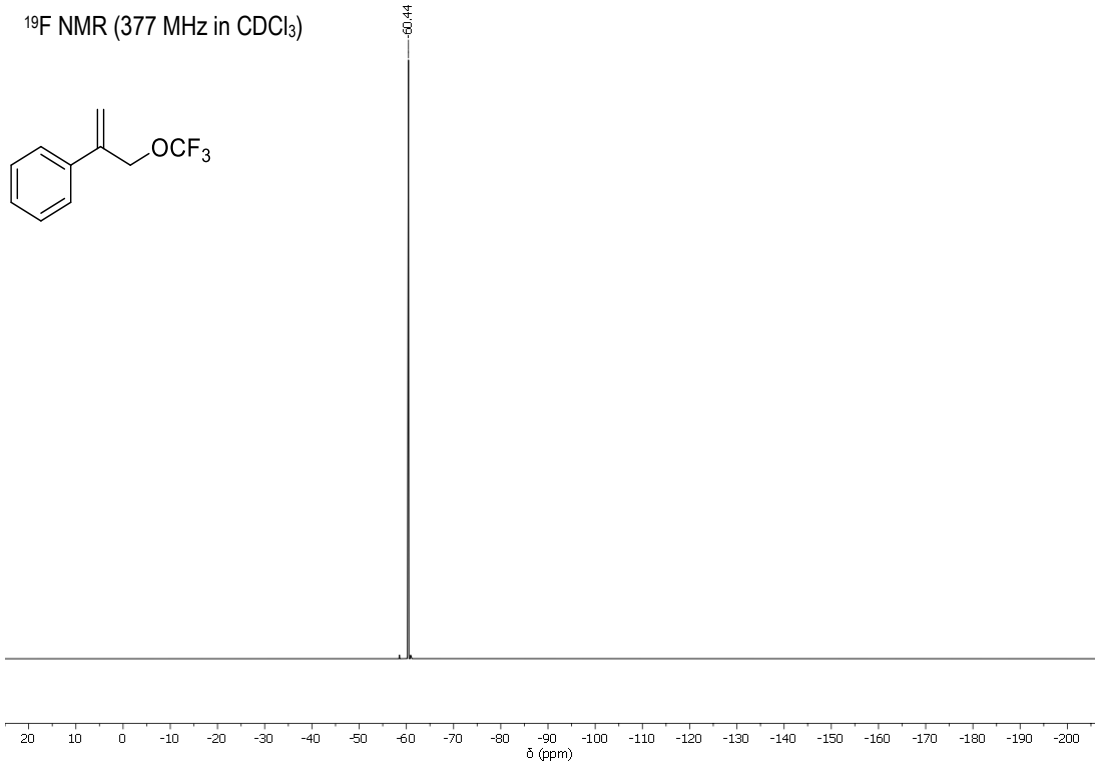




^{13}C NMR (101 MHz in $CDCl_3$)

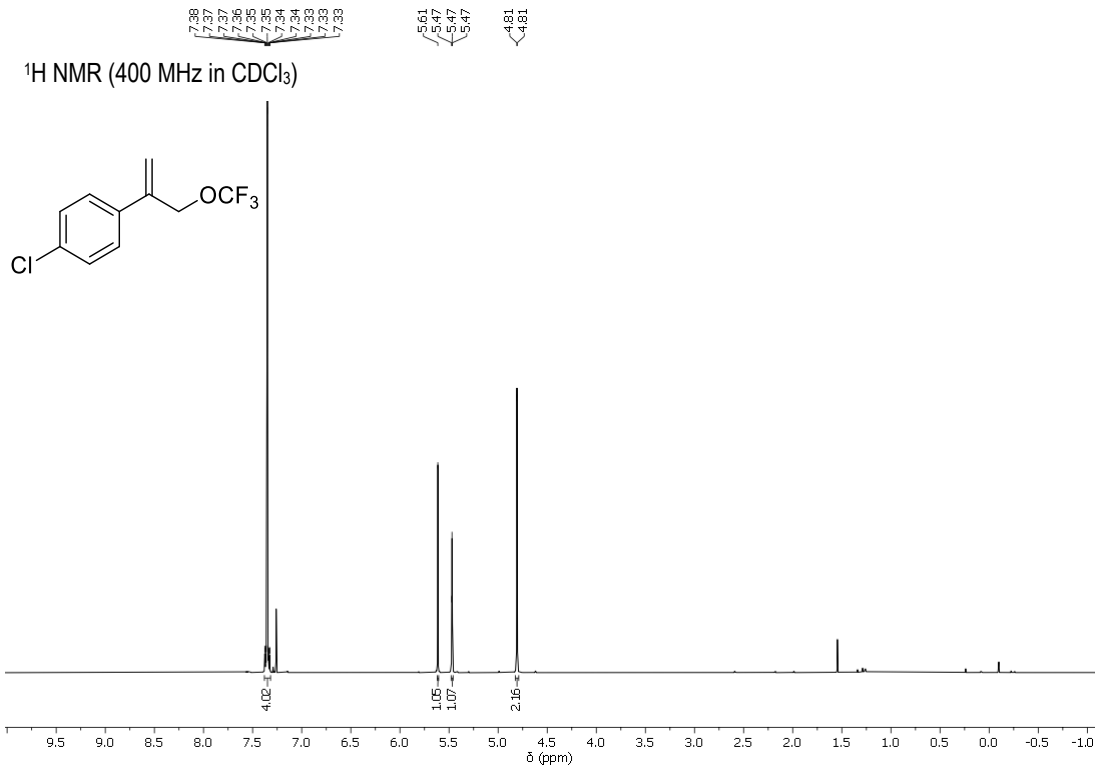


^{19}F NMR (377 MHz in $CDCl_3$)

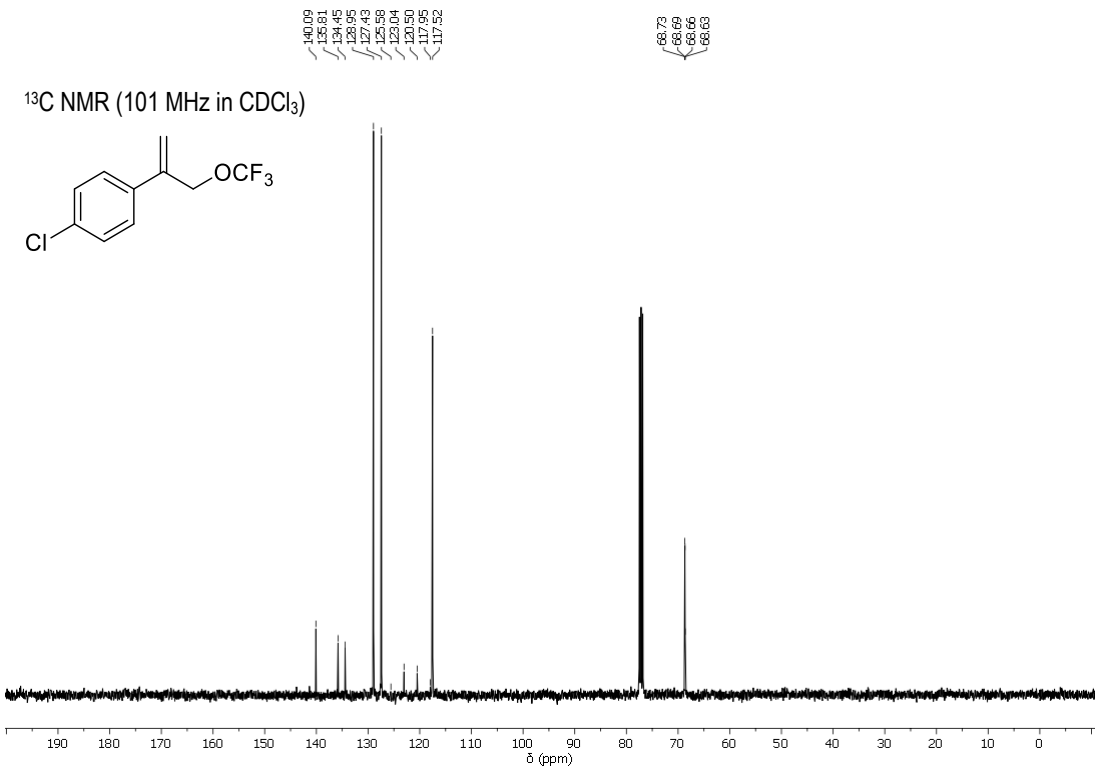


1-chloro-4-(3-(trifluoromethoxy)prop-1-en-2-yl)benzene **8b**

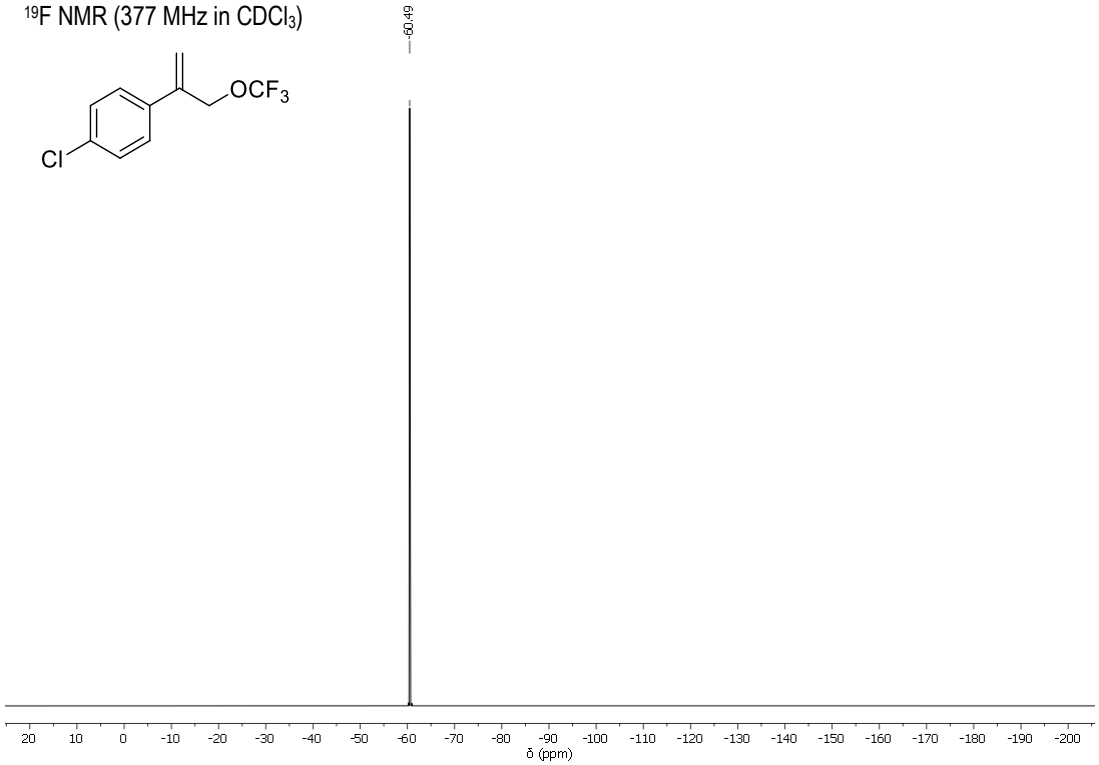
^{1}H NMR (400 MHz in $CDCl_3$)



^{13}C NMR (101 MHz in $CDCl_3$)

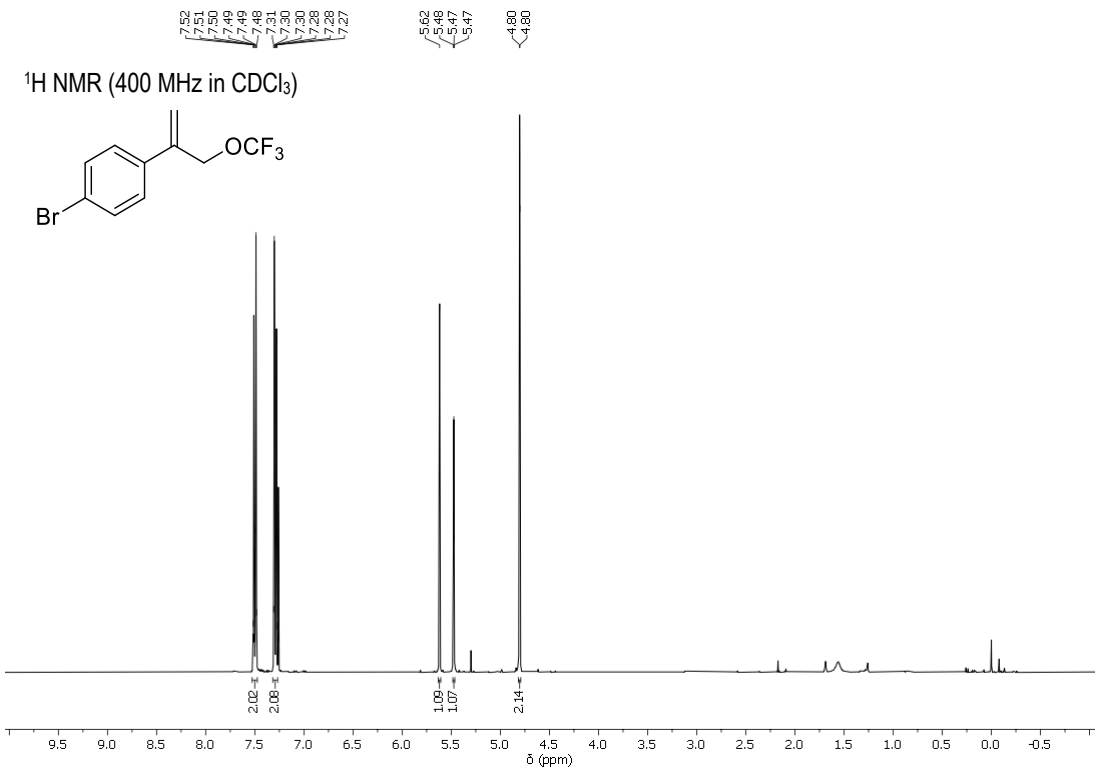


^{19}F NMR (377 MHz in $CDCl_3$)

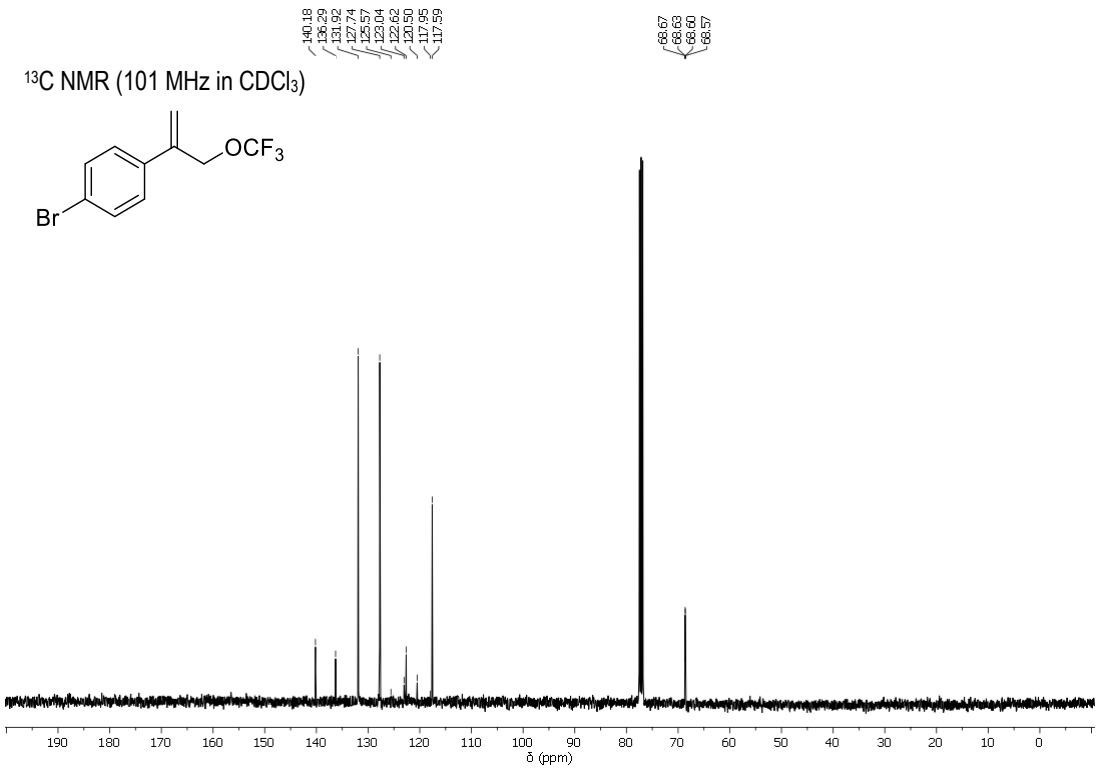


1-bromo-4-(3-(trifluoromethoxy)prop-1-en-2-yl)benzene **8c**

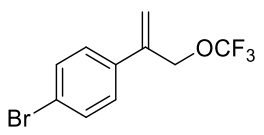
^{1}H NMR (400 MHz in $CDCl_3$)



^{13}C NMR (101 MHz in $CDCl_3$)

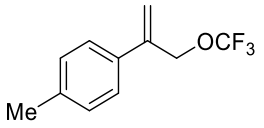


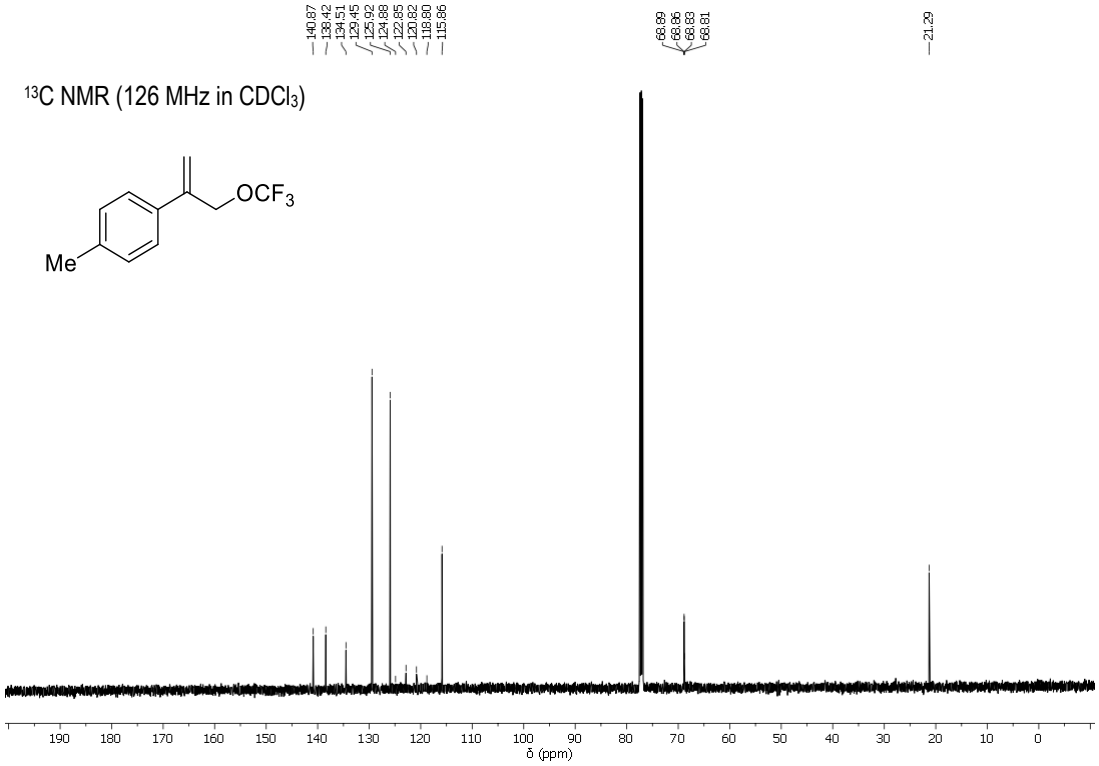
^{19}F NMR (377 MHz in $CDCl_3$)

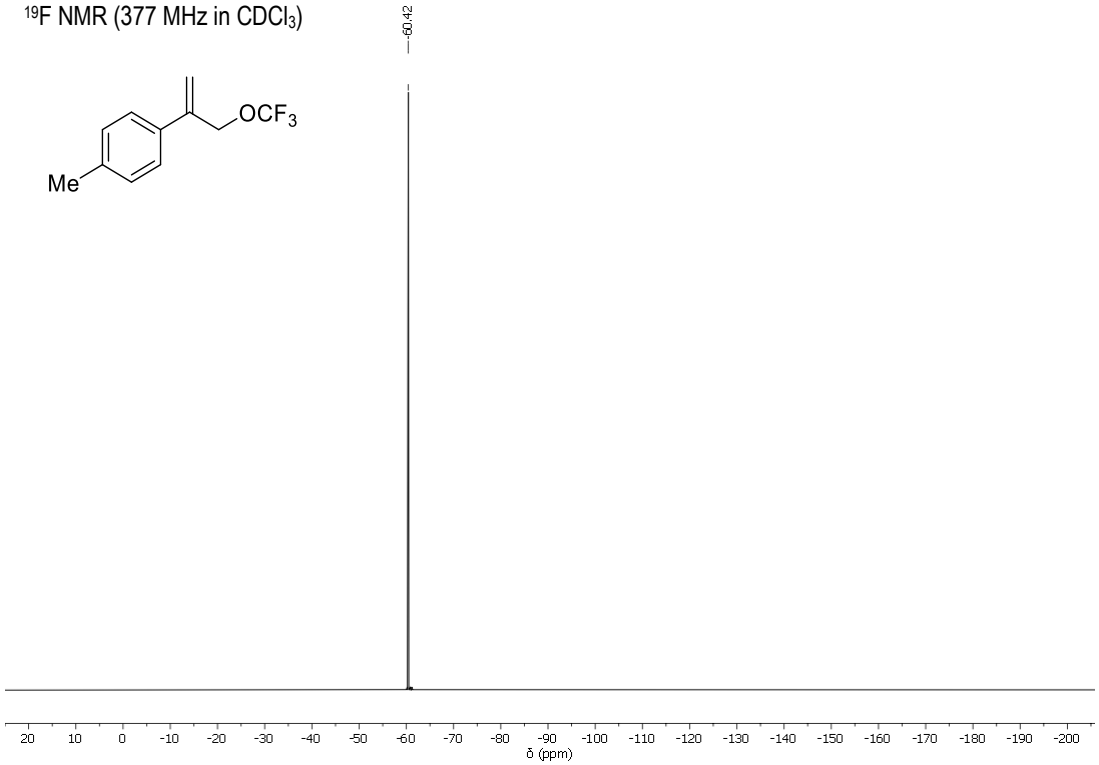


1-methyl-4-(3-(trifluoromethoxy)prop-1-en-2-yl)benzene **8d**

^{1}H NMR (400 MHz in $CDCl_3$)

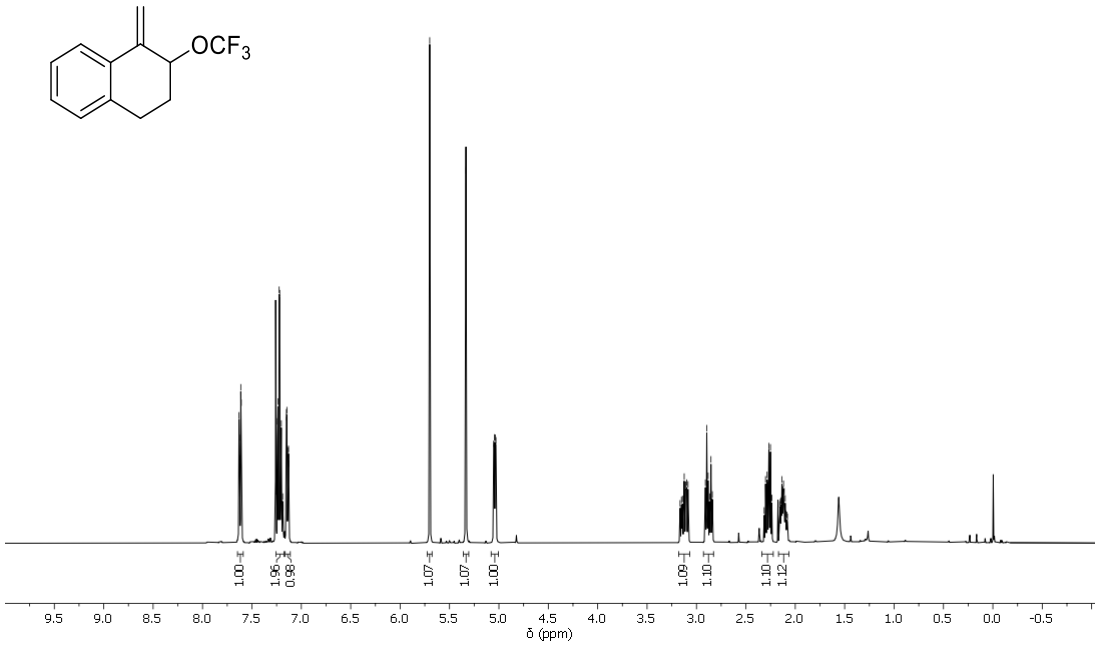



140.87
138.42
134.51
129.45
125.92
124.88
122.85
120.82
118.80
115.86
68.89
68.86
68.83
68.81
21.29
13C NMR (126 MHz in CDCl3)
OCF3
Me
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)

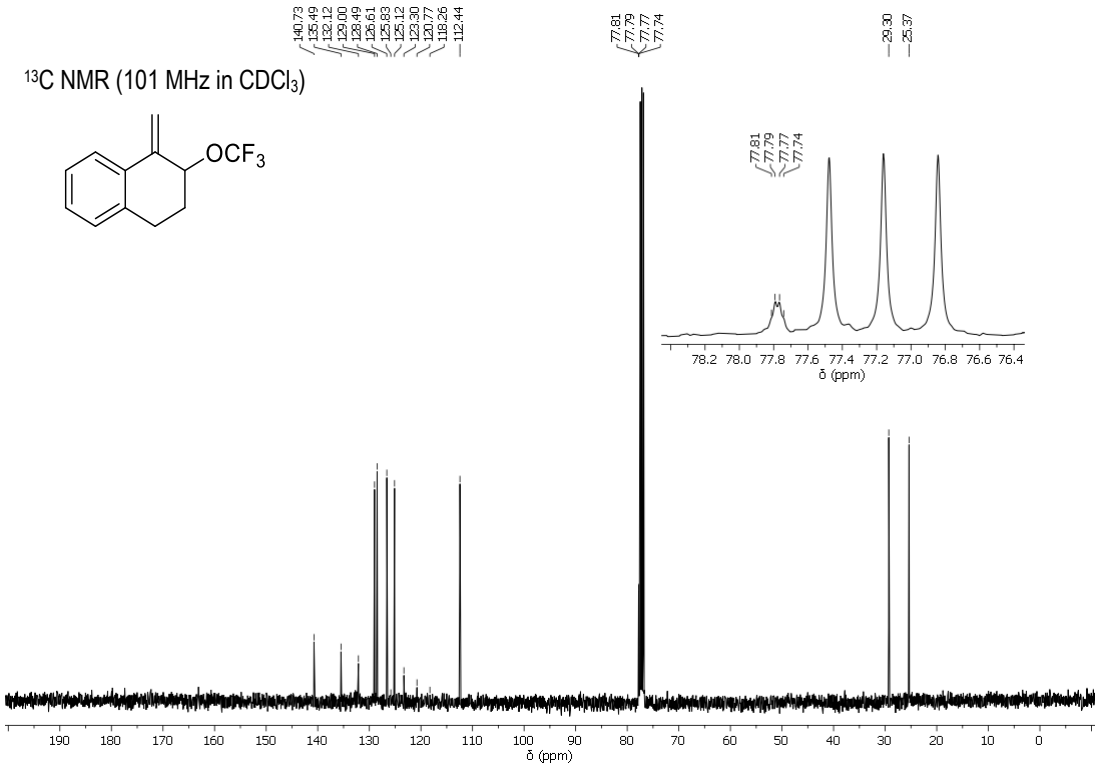

-60.42
19F NMR (377 MHz in CDCl3)
OCF3
Me
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
δ (ppm)

1-methylene-2-(trifluoromethoxy)-1,2,3,4-tetrahydronaphthalene **8e**

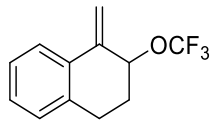
^{1}H NMR (400 MHz in $CDCl_3$)



^{13}C NMR (101 MHz in $CDCl_3$)

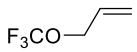


^{19}F NMR (377 MHz in $CDCl_3$)

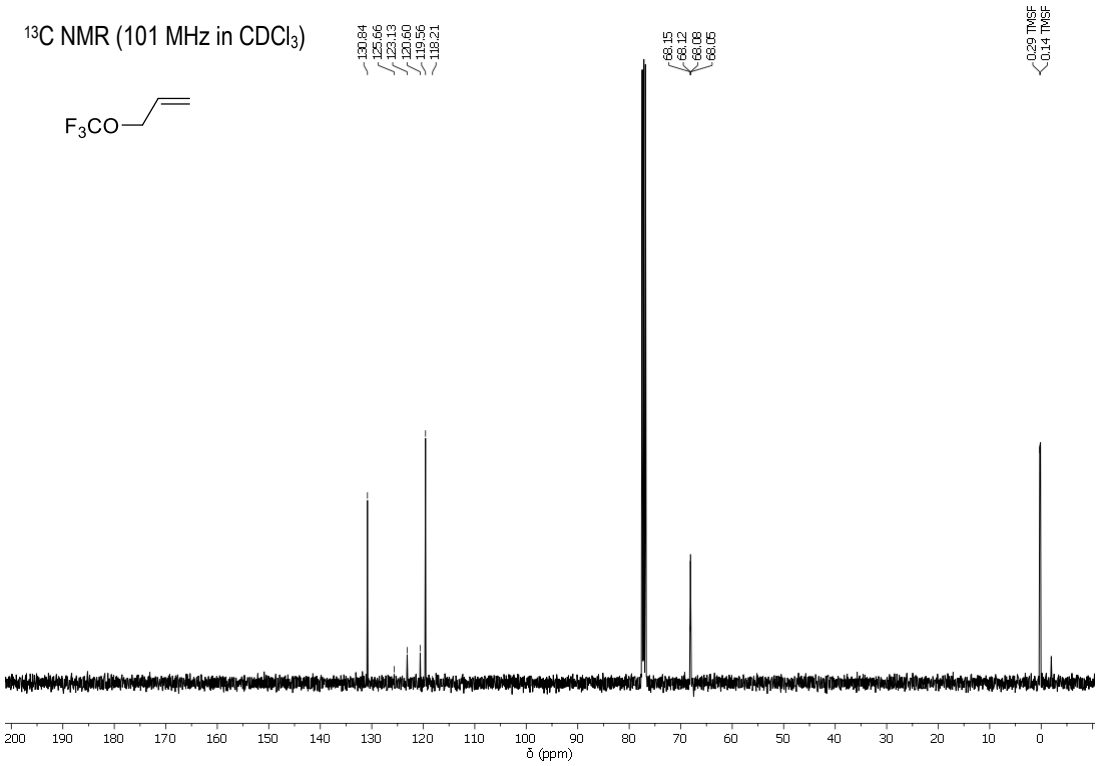


3-(trifluoromethoxy)prop-1-ene **8f**

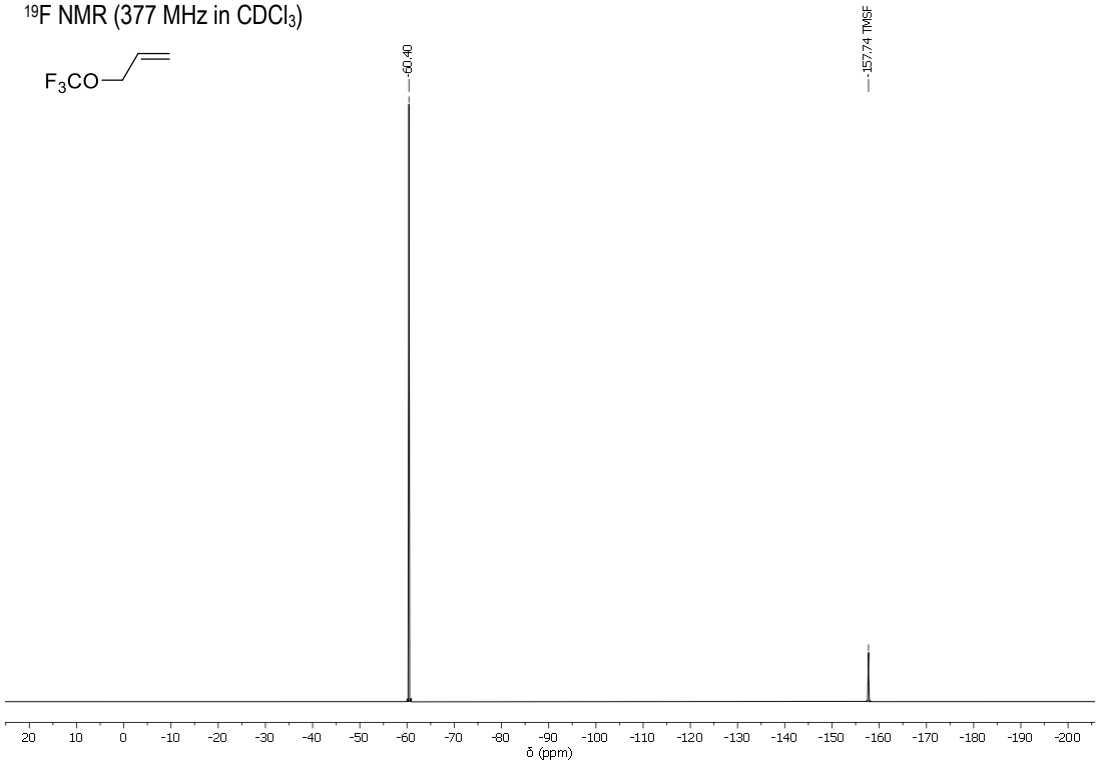
^{1}H NMR (400 MHz in $CDCl_3$)



^{13}C NMR (101 MHz in $CDCl_3$)



^{19}F NMR (377 MHz in $CDCl_3$)



9.2 Supporting Information of Unpublished Results

9.2.1 Investigation of Sulphur Hexafluoride as a Reagent for Photocatalytic Pentafluorosulphanylation Reactions

General Information

All purchased **chemicals** were used without further treatment. *N*-(4-methoxyphenyl)-*N*-methylmethacrylamide **4-16** was synthesised by Armin Ariamajd according to a literature procedure.[186a]

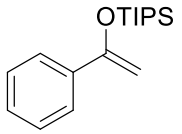
Light reactions were performed using a UVA LED chip (4 × 4 cm^2, 2 × 10 diodes, 20 W total, λ_{max} ≈ 370 nm), Kessil UVA LED (Model: PR160L, 43 W, λ_{max} ≈ 370 nm) and a green LED chip (4 × 4 cm^2, 2 × 10 diodes, 23 W total, λ_{max} ≈ 520 nm). If not stated otherwise the used lamp combination consisted of the Kessil UVA LED and the green LED chip.

Thin-layer chromatography was performed on silica gel coated aluminium plates from TLC Silica gel 60 F_{254}. The product spots were detected by UV light (254 nm) or as permanganate stains. Flash column chromatography was performed with silica gel 60 M (0.040–0.063 mm, 230–400 mesh).

^{1}H and ^{19}F NMR spectra were acquired on a JEOL ECS 400 (400 MHz), JEOL ECZ 400 (400 MHz) or JEOL ECX 400 (400 MHz) and analysed on MestReNova 14.3.0. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethyl silane and coupling constants (J) are presented in hertz (Hz). CD_3CN or $CDCl_3$ are used as deuterated solvent and the residual solvent signals are used as reference in the ^{1}H NMR spectra. ^{19}F NMR spectra are not calibrated by an internal reference but with $CFCl_3$ as reference substance. ^{19}F NMR yields were measured using *α,α,α*-trifluorotoluene as an internal standard.

Synthesis of Starting Materials

Triisopropyl((1-phenylvinyl)oxy)silane **4-4**

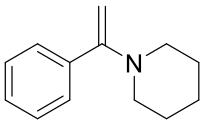


To a flame dried Schlenk-flask was added dry THF (10 mL) and acetophenone (1.0 equiv., 8.6 mmol, 1.0 g) and the mixture was cooled to –78 °C. Sodium bis(trimethylsilyl)amide (1.2 equiv., 10 mL, 1.0 M in THF) was added dropwise at –78 °C and the reaction mixture was stirred for 1 h at rt. The solution was cooled to 0 °C, TIPSCl (1.2 equiv., 10 mmol, 2.1 mL) was added dropwise, and the mixture was stirred for 4.5 h at rt. The suspension was filtered through filter paper, washed with pentane and the solvent removed under reduced pressure. Product **4-4** (2.4 g, 8.7 mmol, quant.) was purified by flash column chromatography (pentane with 1% NEt_3).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.69 – 7.62 (m, 2H), 7.37 – 7.28 (m, 3H), 4.85 (d, J = 1.9 Hz, 1H), 4.42 (d, J = 1.8 Hz, 1H), 1.40 – 1.22 (m, 3H), 1.14 (d, J = 7.4 Hz, 18H).

The characterisation data agree with the literature values.[181]

1-(1-Phenylvinyl)piperidine **4-5**

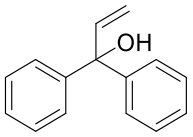


To a flame dried Schlenk-flask was added dry hexane (6 mL) and piperidine (5.6 equiv., 70 mmol, 7.0 mL) and the solution was cooled to 0 °C. In a separate flame dried Schlenk-flask was added $TiCl_4$ (0.7 equiv., 8.8 mmol, 1.0 mL) to dry hexane (6 mL) and the solution was added dropwise to the piperidine-solution at 0 °C. Additional hexane (dry, 23 mL) and acetophenone (1.0 equiv., 12.5 mmol, 1.5 g) were added and the reaction mixture was stirred for 7.5 h at rt. The suspension was filtered, washed with pentane and the solvent was removed under reduced pressure. Product **4-5** (1.1 g, 6.1 mmol, 49%) was obtained as a yellow liquid after Kugelrohr-distillation (215 °C at 15 mbar).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.52 – 7.44 (m, 2H), 7.38 – 7.27 (m, 3H), 4.25 (s, 1H), 4.15 (s, 1H), 2.92 – 2.73 (m, 4H), 1.74 – 1.48 (m, 6H).

The characterisation data agree with the literature values.[182]

1,1-Diphenyl-2-propen-1-ol **4-12**

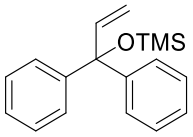


Benzophenone (1.0 equiv., 27 mmol, 5 g) and THF (dry, 27 mL) were added to a flame dried Schlenk-flask equipped with a dripping funnel. The solution was cooled to 0 °C and vinylmagnesium bromide (1.2 equiv., 33 mmol, 47 mL, 0.7 M in THF) was added over 25 min. The mixture was allowed to warm to rt and stirred for additional 2.5 h. The reaction was quenched with NH_4Cl (sat. in H_2O) and extracted with Et_2O (3x). The combined organic layers were dried over $MgSO_4$, filtrated and the solvent was removed under reduced pressure. Allyl alcohol **4-12** (2.4 g, 11 mmol, 41%) was obtained after flash column chromatography (pentane / DCM, 2:1) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41 – 7.36 (m, 4H), 7.36 – 7.30 (m, 4H), 7.30 – 7.24 (m, 2H), 6.51 (dd, J = 16.9, 10.4 Hz, 1H), 5.38 – 5.29 (m, 2H), 2.37 (t, J = 1.0 Hz, 1H).

The characterisation data agree with the literature values.[202]

((1,1-Diphenylallyl)oxy)trimethylsilane **4-13**

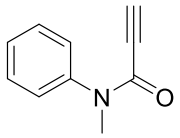


To a flame dried Schlenk-flask with DCM (dry, 24 mL) was added 1,1-diphenyl-2-propen-1-ol (1.0 equiv., 2.4 mmol, 0.5 g). The solution was cooled to 0 °C and imidazole (4.0 equiv., 9.6 mmol, 0.65 g) and TMSCl (2.5 equiv., 6.0 mmol, 0.76 mL) were added slowly. The mixture was allowed to warm to rt and stirred for 4 h. The reaction was quenched with distilled water and the aqueous layer was extracted with DCM (3x). The combined organic layers were washed with brine solution, dried over Na_2SO_4, filtrated and the solvent was removed under reduced pressure. Allyl silyl ether **4-13** (2.2 mmol, 0.6 g, 92%) was obtained after flash column chromatography (pentane / EtOAc, 15:1) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41 – 7.36 (m, 4H), 7.35 – 7.29 (m, 4H), 7.29 – 7.23 (m, 2H), 6.55 – 6.46 (m, 1H), 5.30 (dt, J = 10.4, 1.5 Hz, 1H), 5.25 – 5.19 (m, 1H), –0.01 (s, 9H).

The characterisation data agree with the literature values.[184b]

N-Methyl-*N*-phenylpropiolamide **4-17**



N-methylaniline (1.0 equiv., 9.3 mmol, 1.0 g), propiolic acid (1.6 equiv., 14.6 mmol, 0.9 mL) and DMAP (1 mol%, 11 mg) were added to dry DCM (11 mL) at 0 °C. A solution of DCC (1.1 equiv., 10.2 mmol, 2.1 g) in dry DCM (11 mL) was added slowly to the aniline solution at 0 °C. The reaction mixture was allowed to warm to rt and stirred for 2 h. The solution was filtered through Celite® and the solvent was removed under reduced pressure. Product **4-17** (1.4 g, 8.8 mmol, 94%) was obtained after flash column chromatography (pentane / EtOAc, 7:3) as a beige solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 – 7.34 (m, 3H), 7.31 – 7.27 (m, 2H), 3.34 (s, 3H), 2.82 (s, 1H).

The characterisation data agree with the literature values.[203]

General Procedure of Wagenknechts Conditions

Method A: In a flame dried 15 mL Schlenk tube the substrate (0.1 mmol), the Cu species (10 mol%) and PTH (5 or 20 mol%) were added to MeCN (1.0 mL). The reaction mixture was frozen using liquid nitrogen and degassed (3x) using the freeze-pump-thaw technique. SF_6 (4.75 mmol) as condensed into the reaction tube and the mixture was allowed to warm to rt. The reaction was stirred for 18 h under irradiation with the light sources of choice. Then the reaction vessel was carefully opened and released gas was passed through a KOH solution (10% in MeOH) to quench potentially formed S_2F_{10}. *α,α,α*-Trifluorotoluene (0.1 mmol) was added as standard and the mixture was diluted with CD_3CN (1 mL). The crude reaction mixture was investigated by ^{19}F and ^{1}H NMR spectroscopy.

Method B: In a flame dried 15 mL Schlenk tube the substrate (0.1 mmol) and PTH (5 mol%) were added to MeCN (1.0 mL). The reaction mixture was frozen using liquid nitrogen and degassed (3x) using the freeze-pump-thaw technique. SF_6 (4.75 mmol) as condensed into the reaction tube and the mixture was allowed to warm to rt. The reaction was stirred for 18 h under irradiation with the light sources of choice. Then the reaction vessel was carefully opened and released gas was passed through a KOH solution (10% in MeOH) to quench potentially formed S_2F_{10}. *α,α,α*-Trifluorotoluene (0.1 mmol) was added as standard and the mixture was diluted with CD_3CN (1 mL). The crude reaction mixture was investigated by ^{19}F and ^{1}H NMR spectroscopy.

Method C: In a flame dried 15 mL Schlenk tube the substrate (0.1 mmol), $Cu(acac)_2$ (10 mol%), the Lewis acid (10 mol%) and PTH (5 mol%) were added to MeCN (1.0 mL). The reaction mixture was frozen using liquid nitrogen and degassed (3x) using the freeze-pump-thaw technique. SF_6 (4.75 mmol) as condensed into the reaction tube and the mixture was allowed to warm to rt. The reaction was stirred for 18 h under irradiation with the light sources of choice. Then the reaction vessel was carefully opened and released gas was passed through a KOH solution (10% in MeOH) to quench potentially formed S_2F_{10}. *α,α,α*-Trifluorotoluene (0.1 mmol) was added as standard and the mixture was diluted with CD_3CN (1 mL). The crude reaction mixture was investigated by ^{19}F and ^{1}H NMR spectroscopy.

Method D: In a flame dried 15 mL Schlenk tube the substrate (0.1 mmol), $Cu(acac)_2$ (10 or 0 mol%), the Hantzsch ester (1.0 equiv.) and PTH (5 mol%) were added to MeCN (1.0 mL). The reaction mixture was frozen using liquid nitrogen and degassed (3x) using the freeze-pump-thaw technique. SF_6 (4.75 mmol) as condensed into the reaction tube and the mixture was allowed to warm to rt. The reaction was stirred for 18 h under irradiation with the light sources of choice. Then the reaction vessel was carefully opened and released gas was passed through a KOH solution (10% in MeOH) to quench potentially formed S_2F_{10}. *α,α,α*-Trifluorotoluene (0.1 mmol) was added as standard and the mixture was diluted with CD_3CN (1 mL). The crude reaction mixture was investigated by ^{19}F and ^{1}H NMR spectroscopy.

^{19}F NMR Spectra of Test Reactions

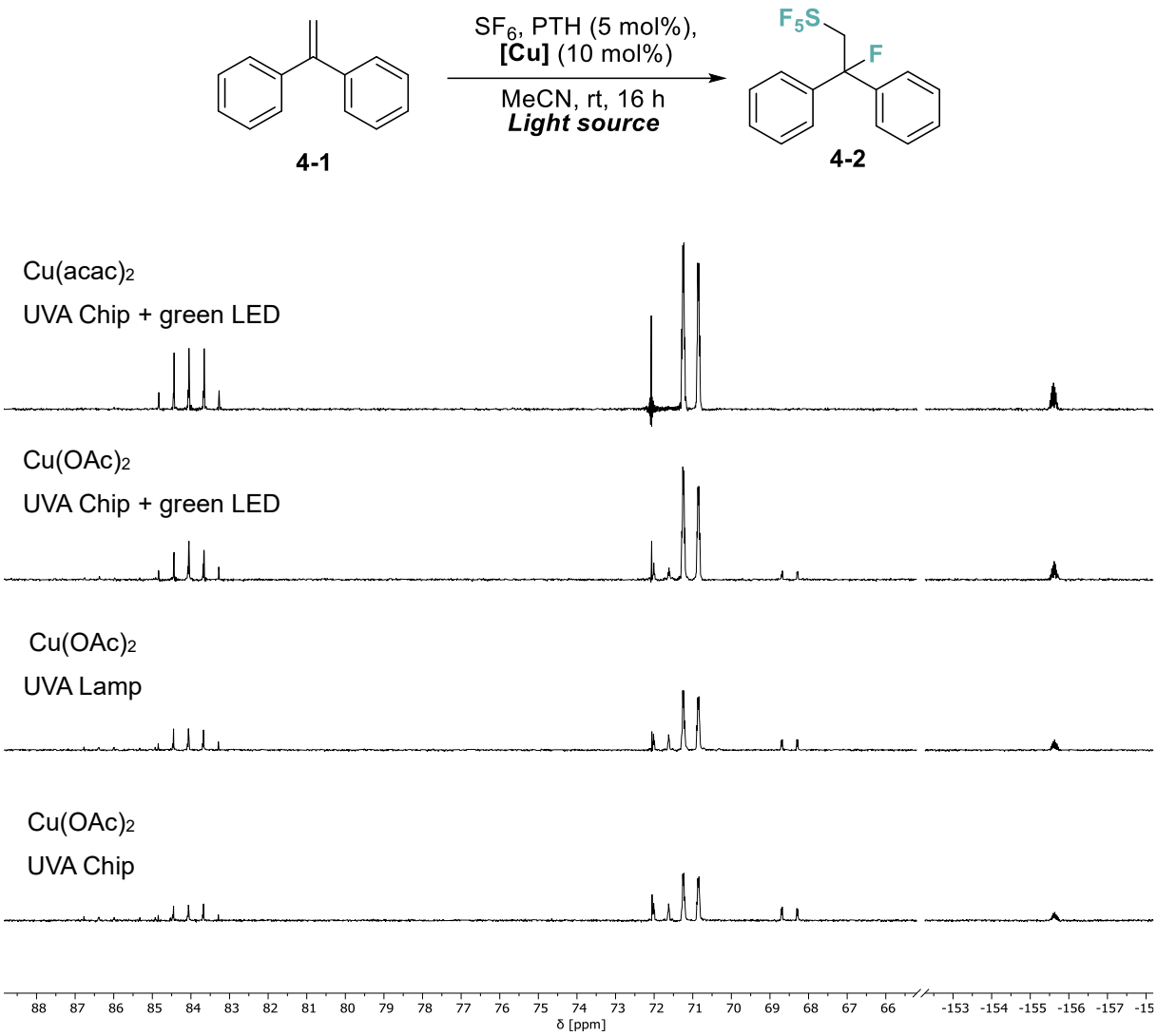
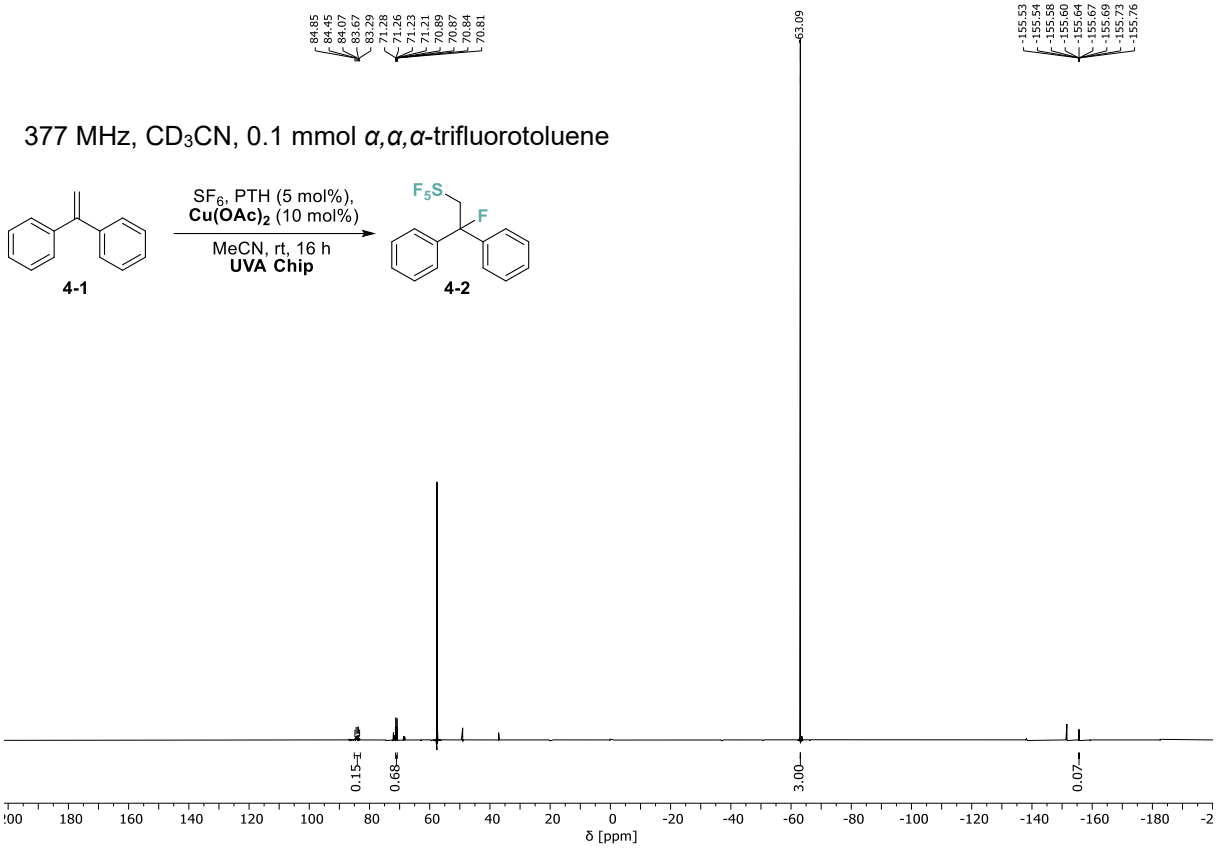
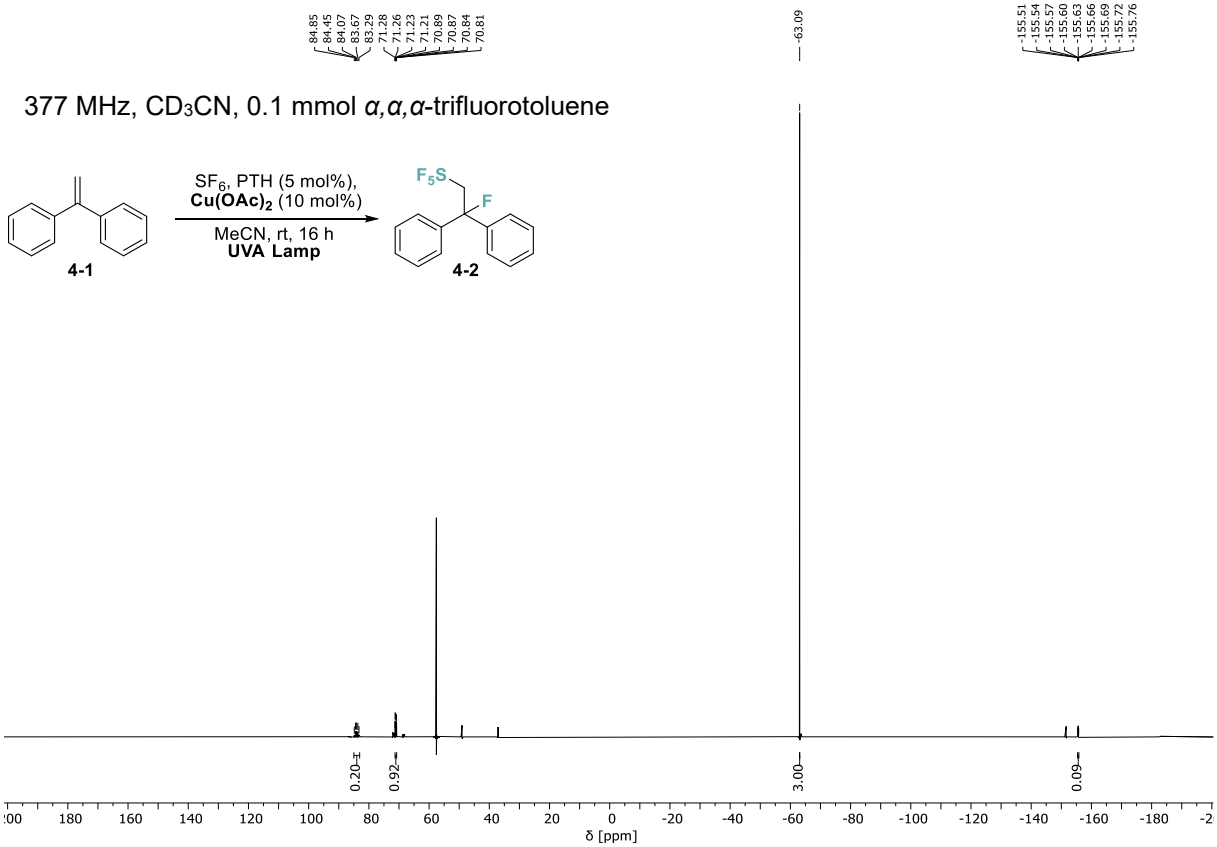
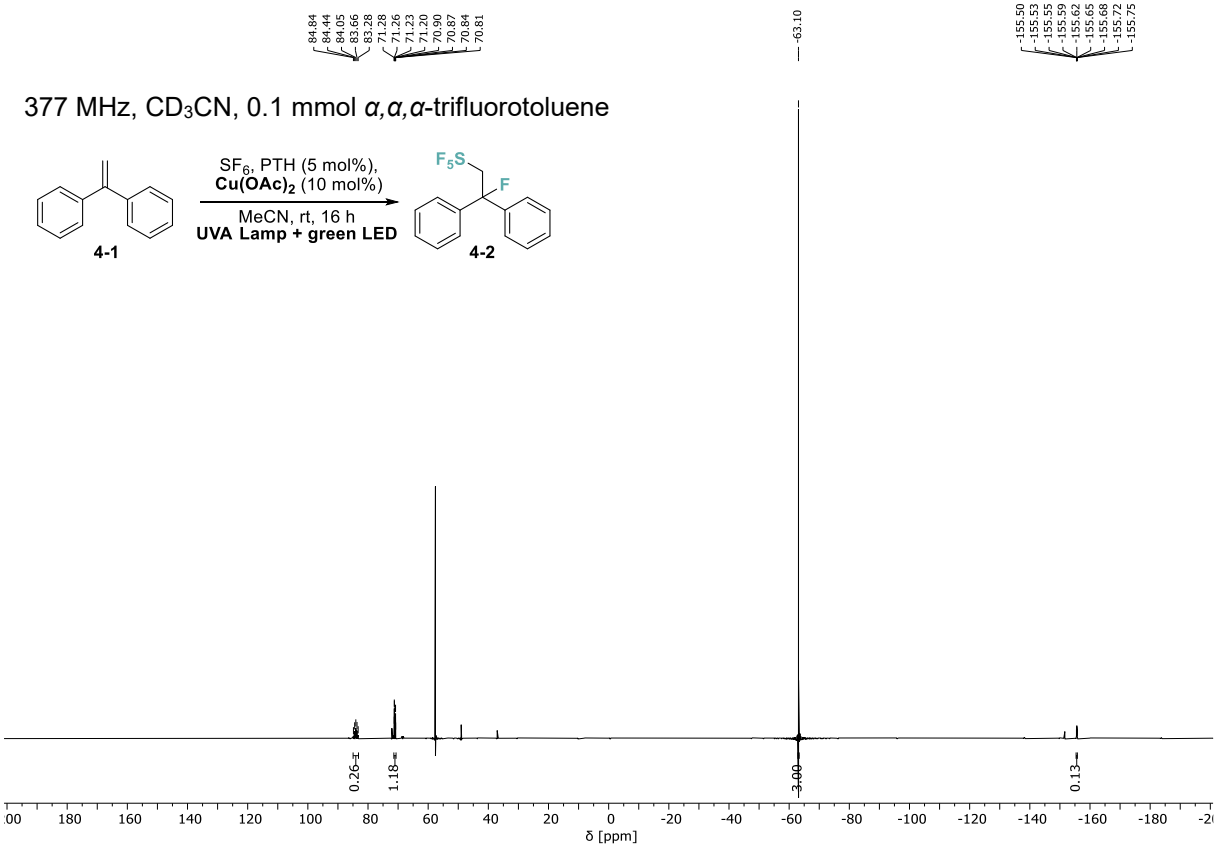
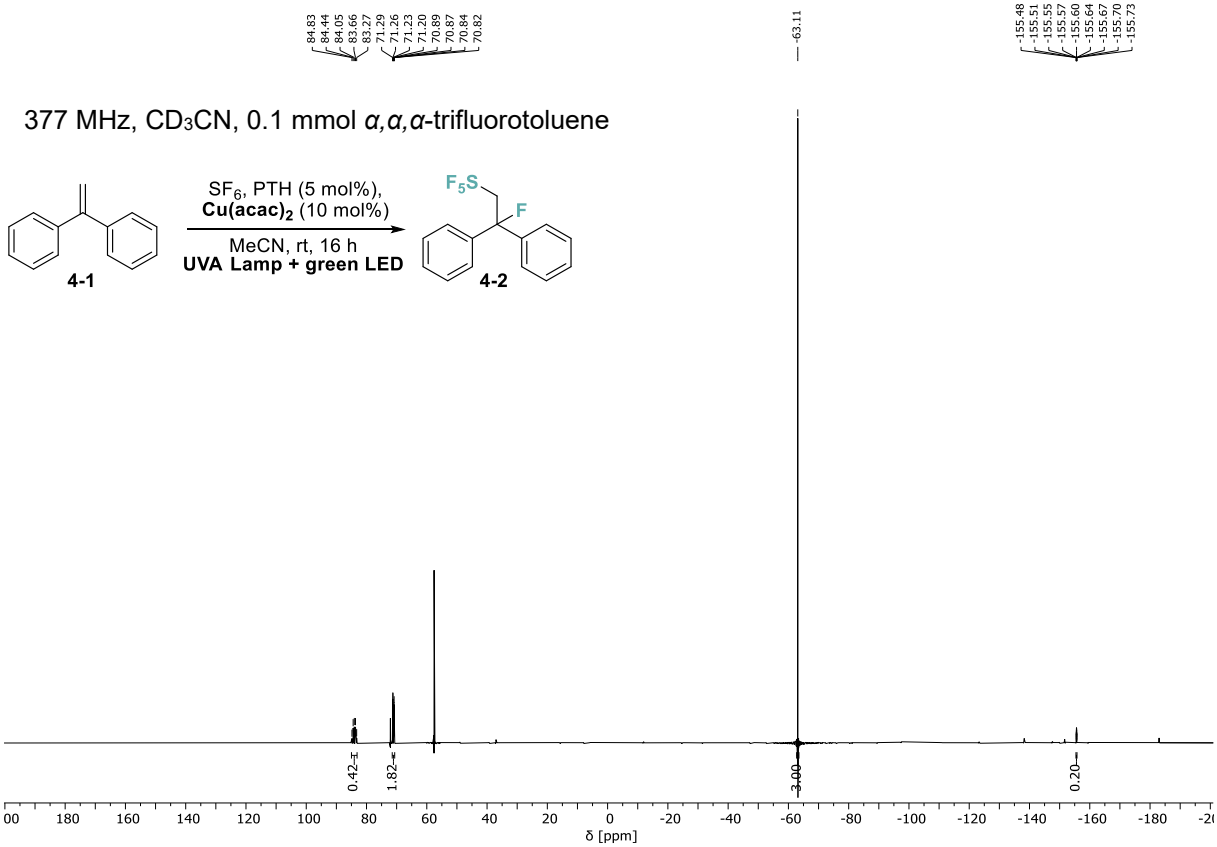


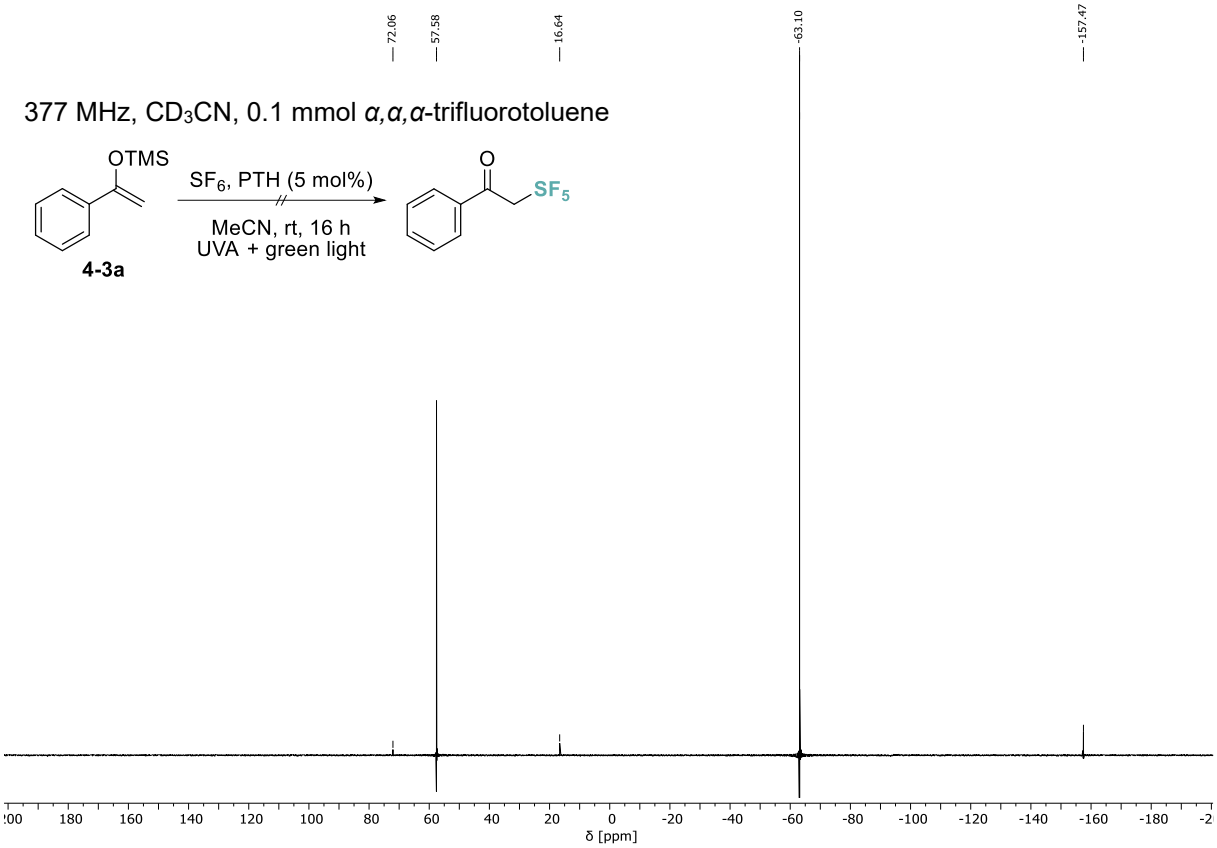
Figure 14: Product specific areas of ^{19}F NMR spectra (377 MHz, CD_3CN) of the reaction between ethene-1,1-diyldibenzene and SF_6.

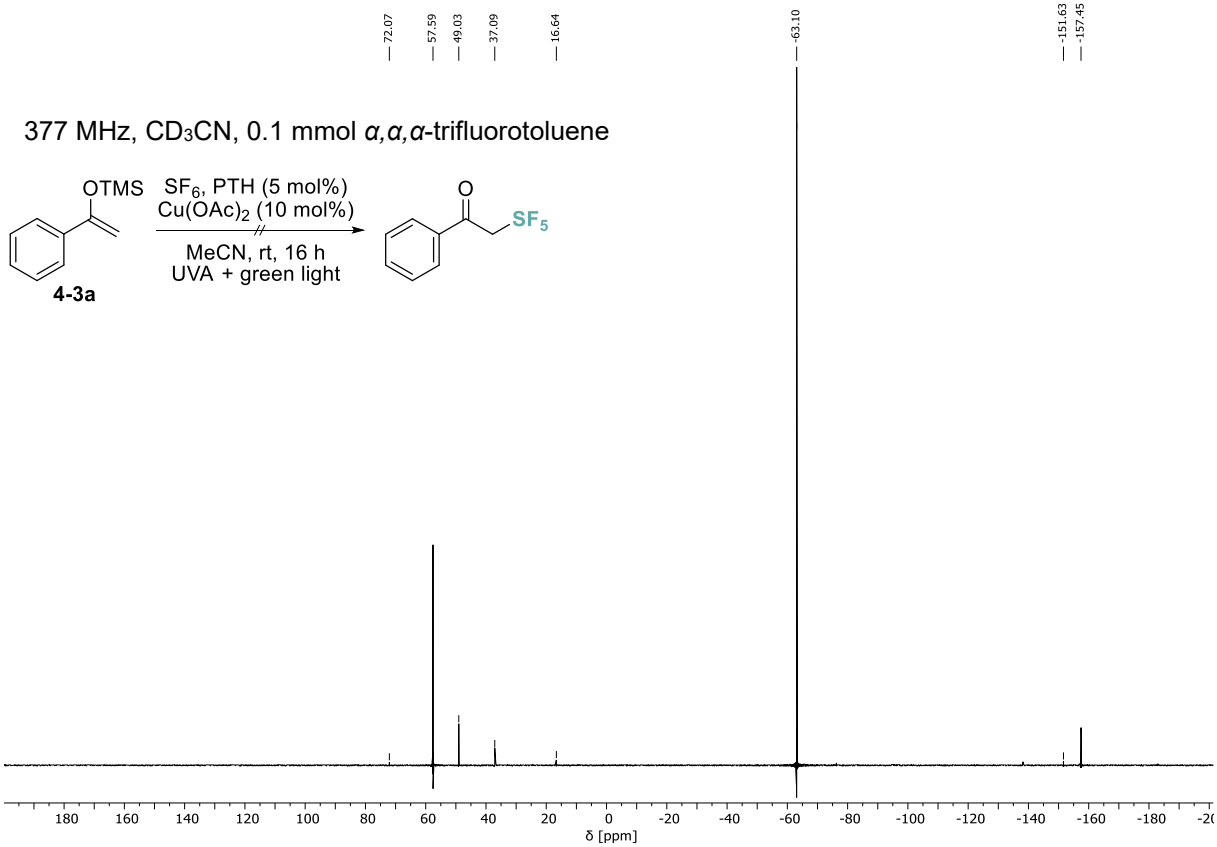

84.85
84.45
84.07
83.67
83.29
71.28
71.26
71.23
71.21
70.89
70.87
70.84
70.81
-63.09
-155.53
-155.54
-155.58
-155.60
-155.64
-155.67
-155.69
-155.73
-155.76
377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
SF6, PTH (5 mol%),
Cu(OAc)2 (10 mol%)
MeCN, rt, 16 h
UVA Chip
F5S
F
4-1
4-2
0.15
0.68
3.00
0.07
δ [ppm]

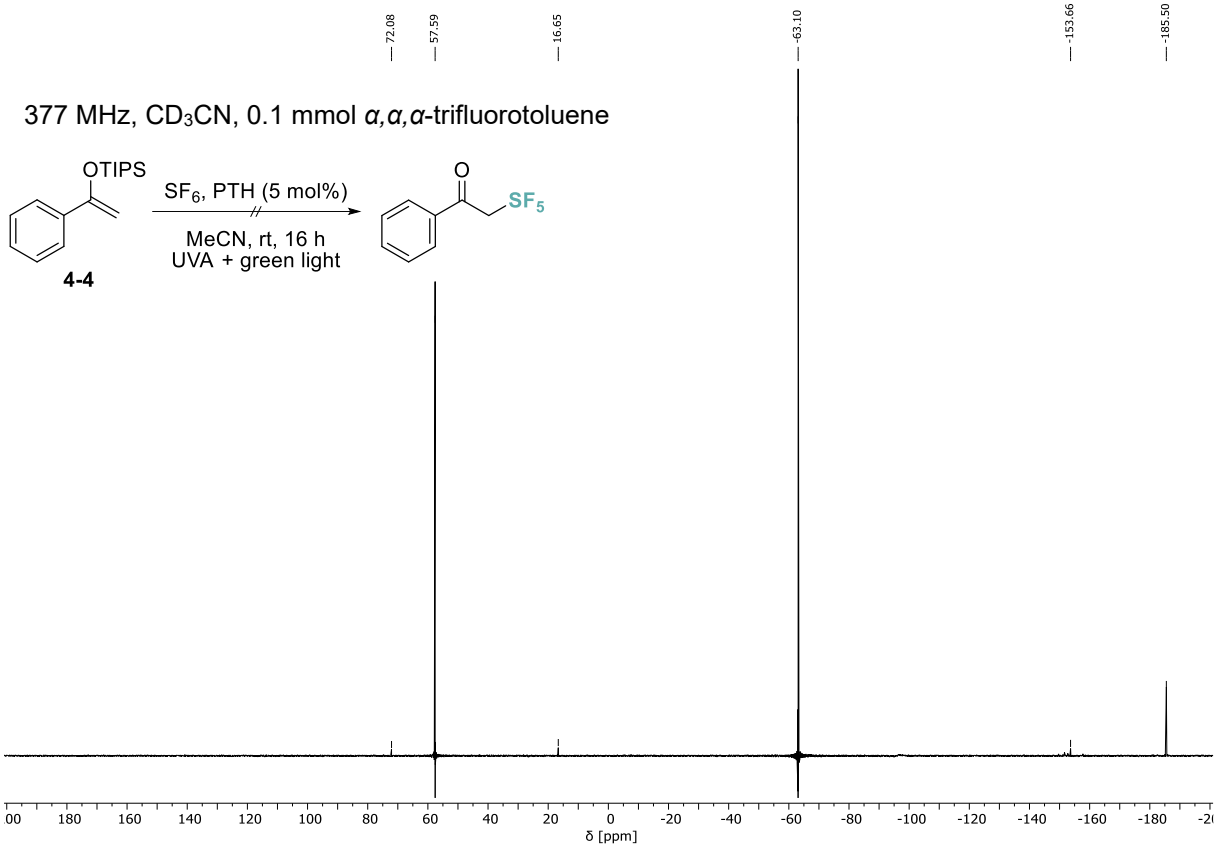

84.85
84.45
84.07
83.67
83.29
71.28
71.26
71.23
71.21
70.89
70.87
70.84
70.81
-63.09
-155.51
-155.54
-155.57
-155.60
-155.63
-155.66
-155.69
-155.72
-155.76
377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
SF6, PTH (5 mol%),
Cu(OAc)2 (10 mol%)
MeCN, rt, 16 h
UVA Lamp
F5S
F
4-1
4-2
0.20
0.92
3.00
0.09
δ [ppm]

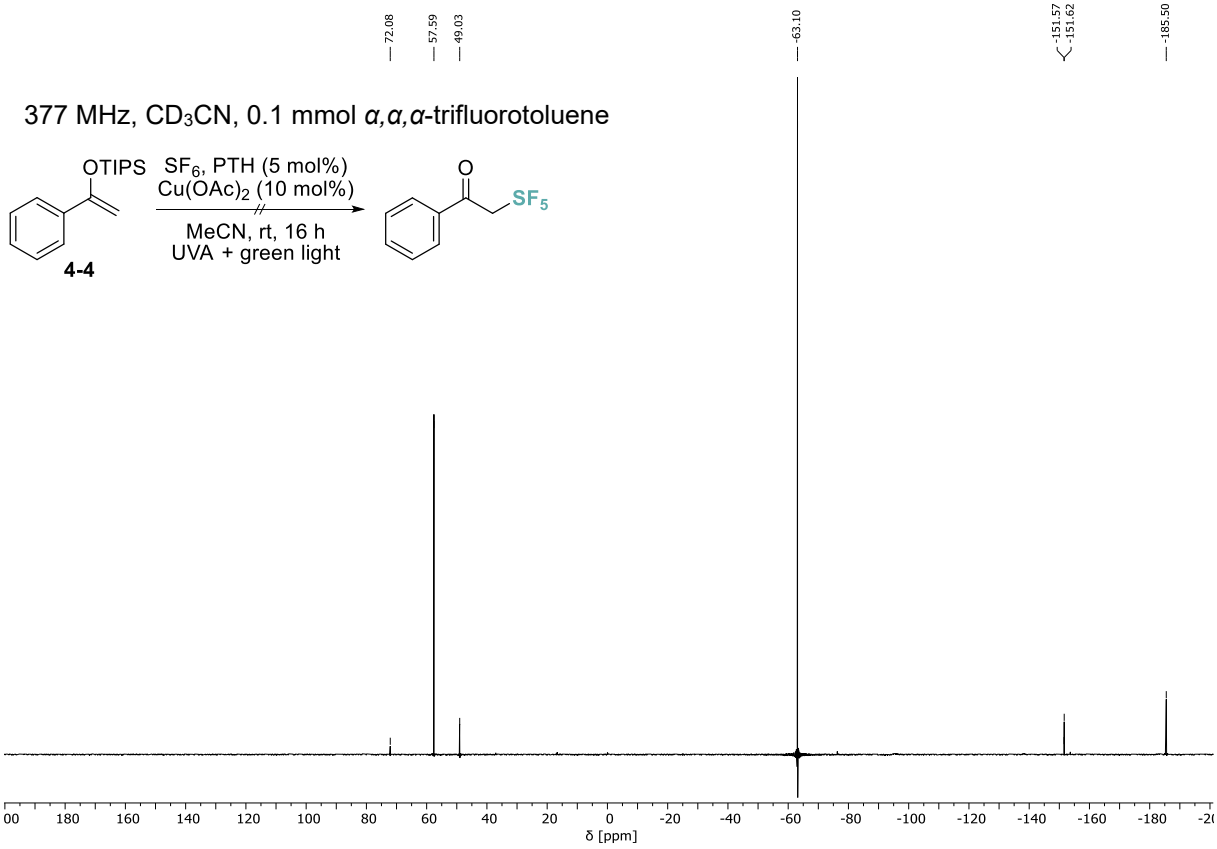

84.84
84.44
84.05
83.66
83.28
71.28
71.26
71.23
71.20
70.90
70.87
70.84
70.81
-63.10
-155.50
-155.53
-155.55
-155.59
-155.62
-155.65
-155.68
-155.72
-155.75
377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
SF6, PTH (5 mol%),
Cu(OAc)2 (10 mol%)
MeCN, rt, 16 h
UVA Lamp + green LED
F5S
F
4-1
4-2
0.26
1.18
3.00
0.13
δ [ppm]

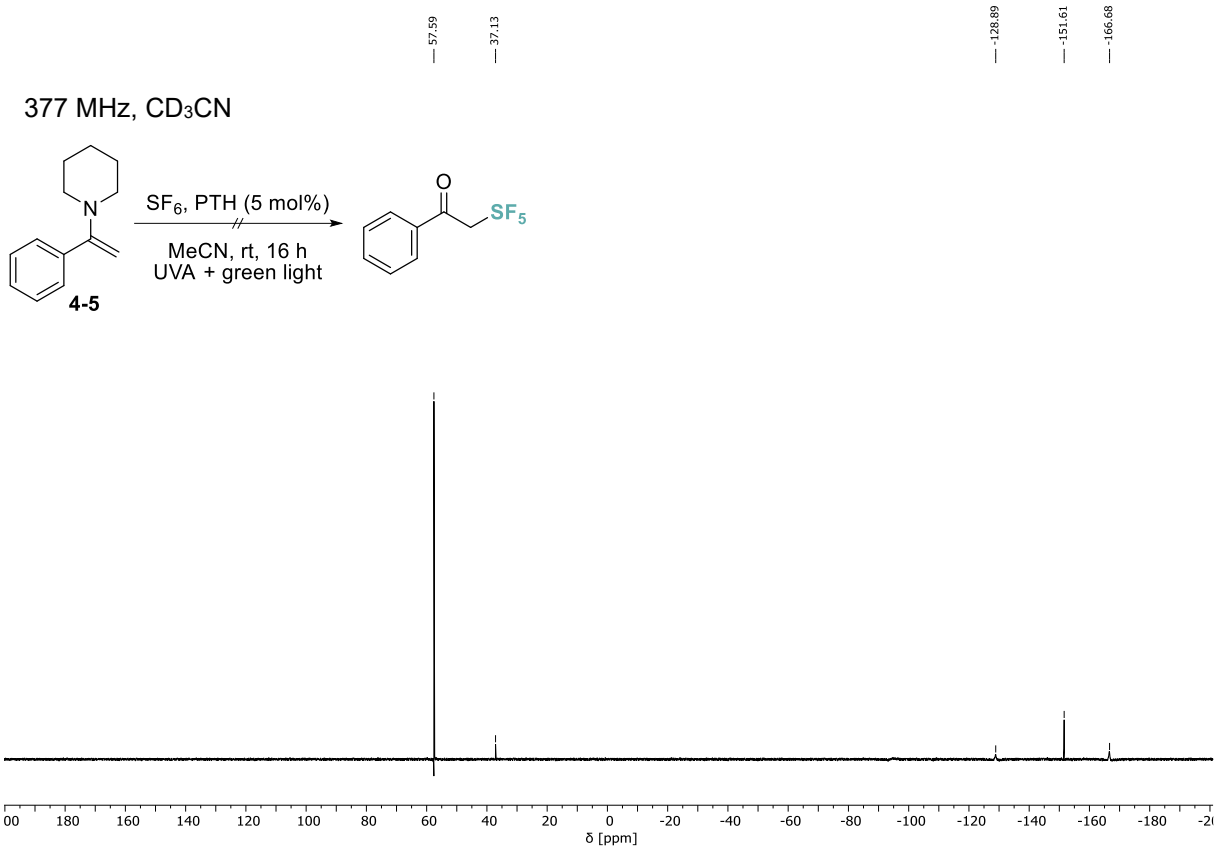

84.83
84.44
84.05
83.66
83.27
71.29
71.26
71.23
71.20
70.89
70.87
70.84
70.82
-63.11
-155.48
-155.51
-155.55
-155.57
-155.60
-155.64
-155.67
-155.70
-155.73
377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
SF6, PTH (5 mol%),
Cu(acac)2 (10 mol%)
MeCN, rt, 16 h
UVA Lamp + green LED
F5S
F
4-1
4-2
0.42
1.82
3.00
0.20
δ [ppm]

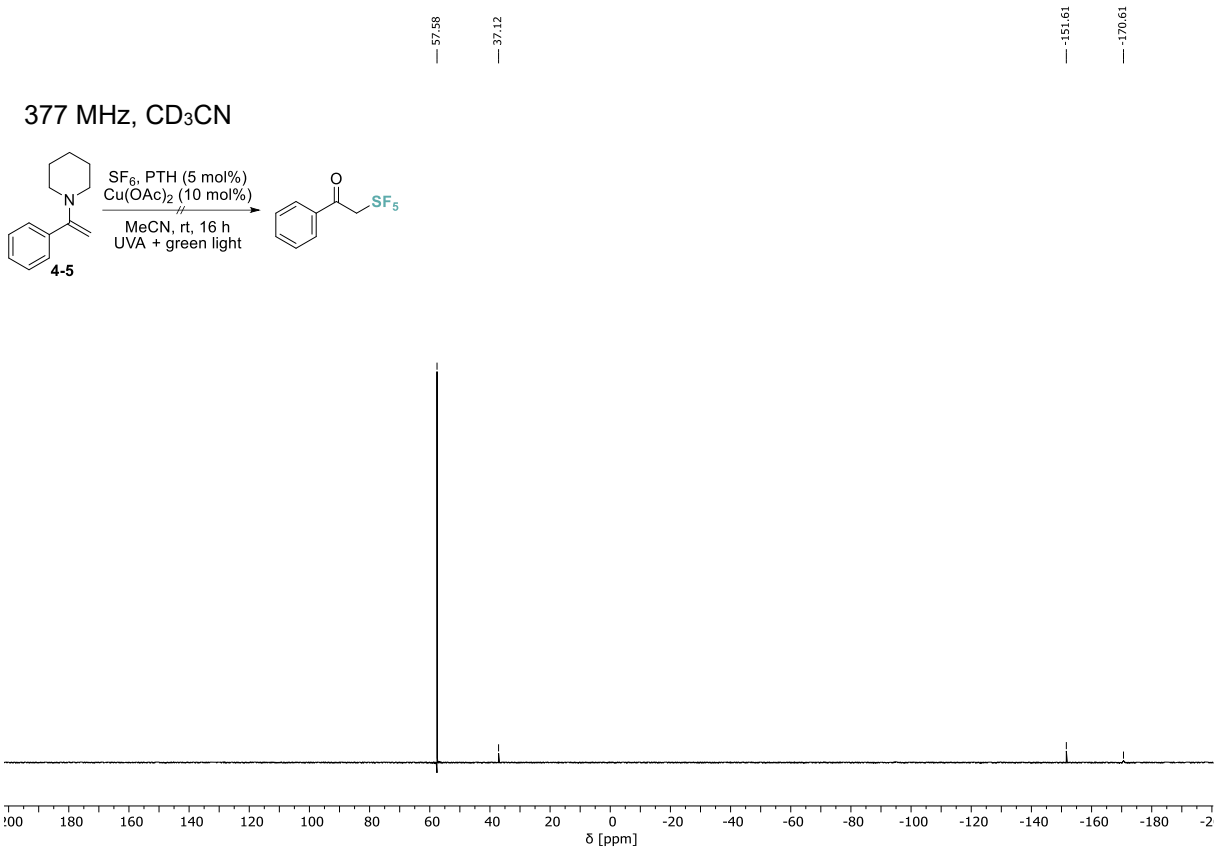

377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
OTMS
SF6, PTH (5 mol%)
MeCN, rt, 16 h
UVA + green light
O
SF5
4-3a
72.06
57.58
16.64
-63.10
-157.47
δ [ppm]

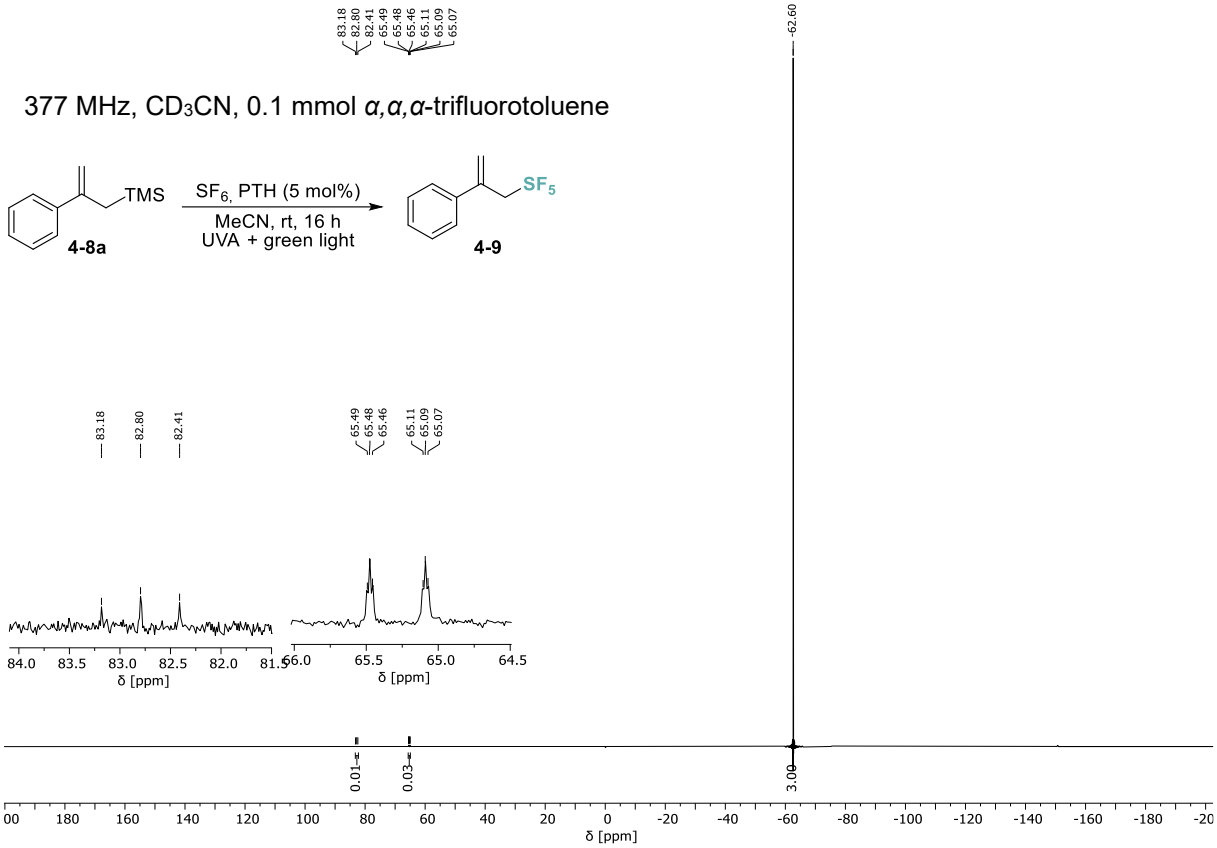

377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
OTMS
SF6, PTH (5 mol%)
Cu(OAc)2 (10 mol%)
MeCN, rt, 16 h
UVA + green light
O
SF5
4-3a
72.07
57.59
49.03
37.09
16.64
-63.10
-151.63
-157.45
δ [ppm]

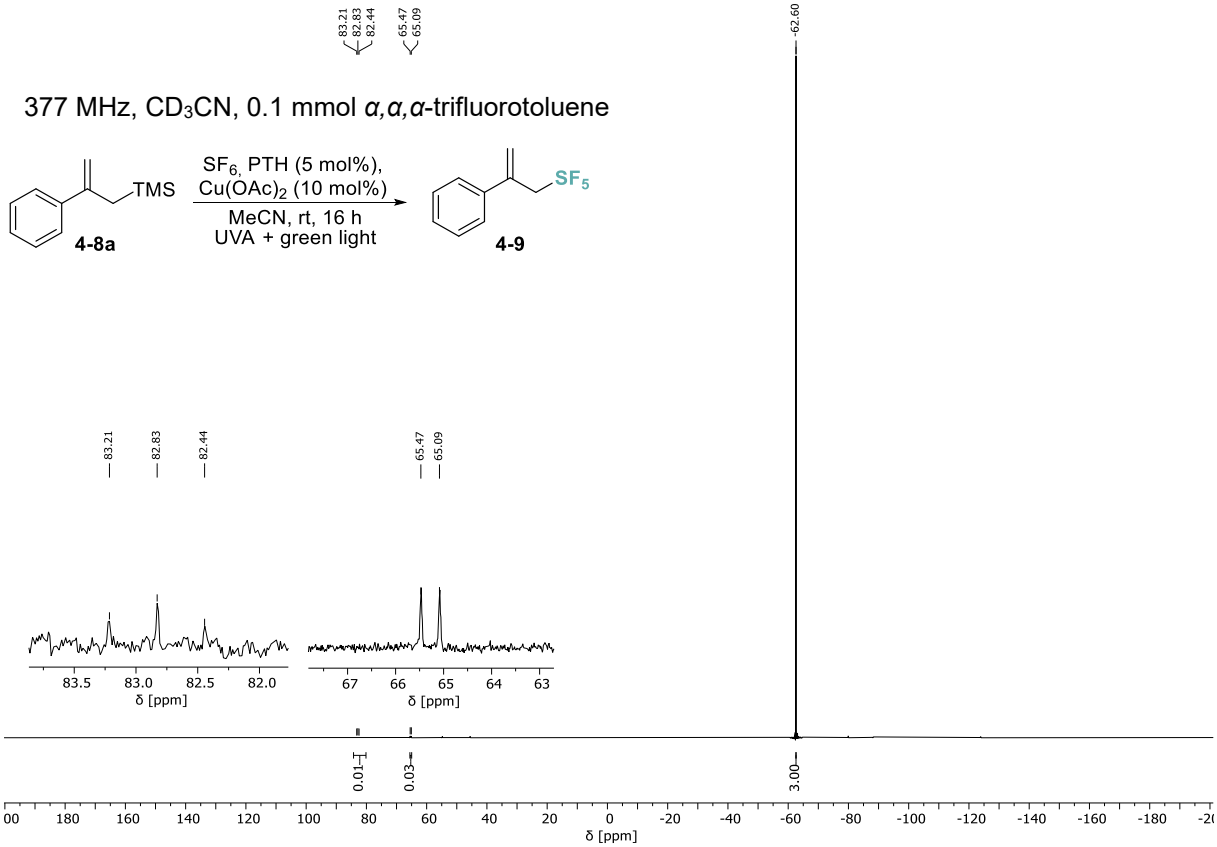

377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
OTIPS
SF6, PTH (5 mol%)
MeCN, rt, 16 h
UVA + green light
4-4
O
SF5
72.08
57.59
16.65
-63.10
-153.66
-185.50
δ [ppm]

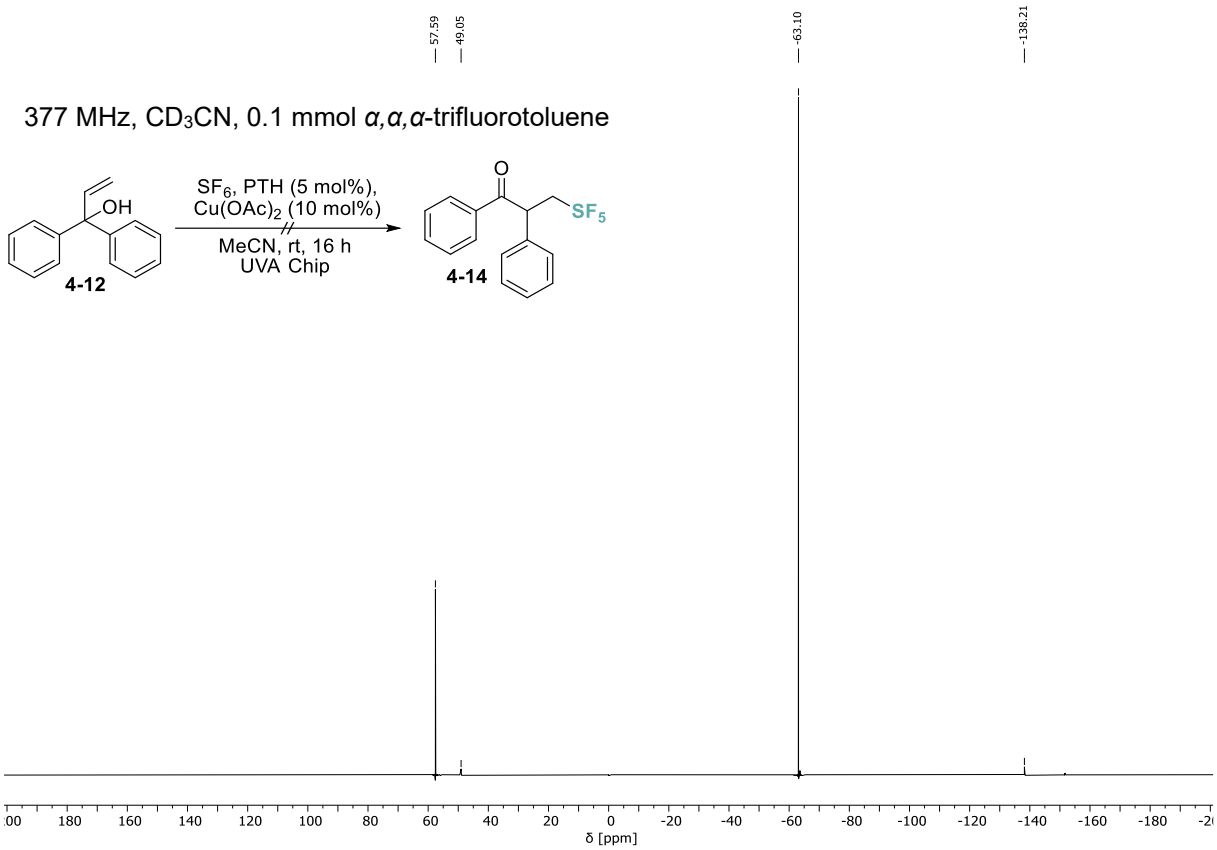

377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
OTIPS
SF6, PTH (5 mol%)
Cu(OAc)2 (10 mol%)
MeCN, rt, 16 h
UVA + green light
4-4
O
SF5
72.08
57.59
49.03
-63.10
-151.57
-151.62
-185.50
δ [ppm]

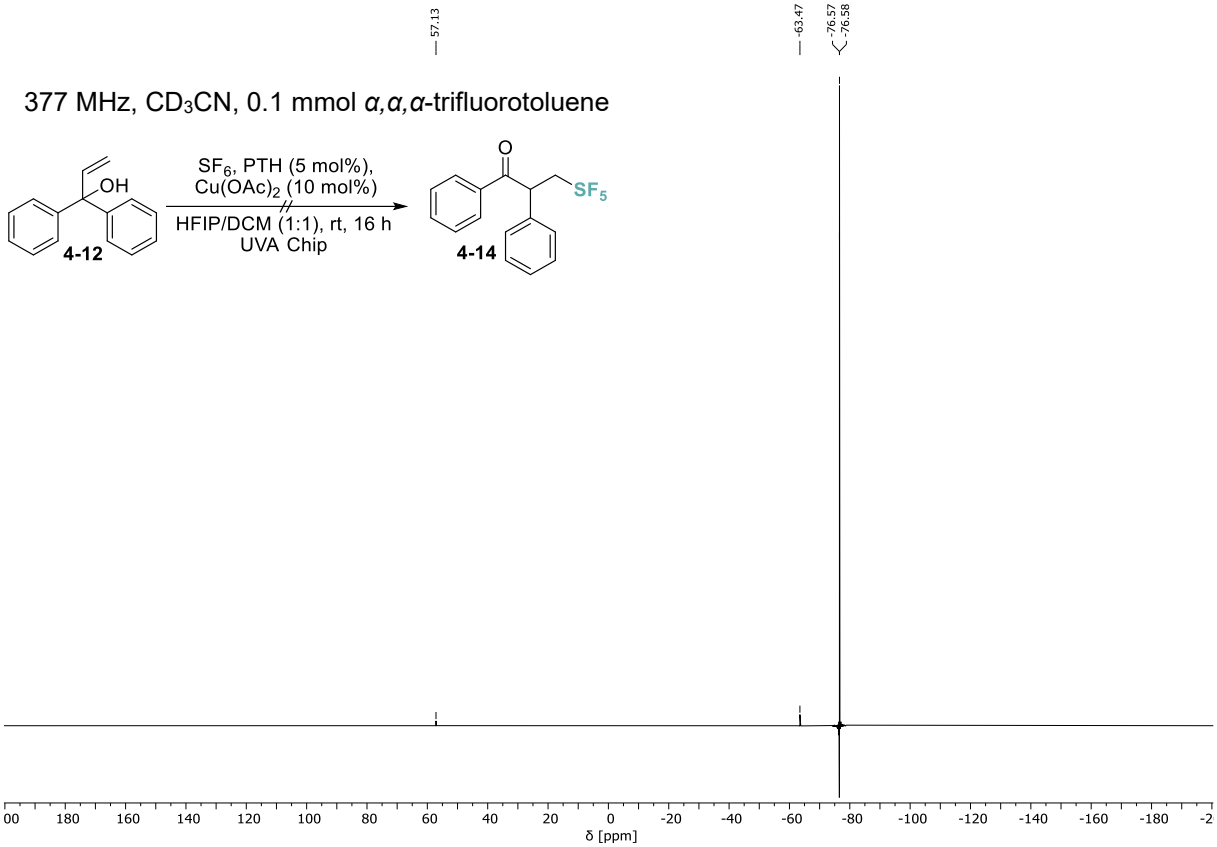

57.59
37.13
-128.89
-151.61
-166.68
377 MHz, CD3CN
SF6, PTH (5 mol%)
MeCN, rt, 16 h
UVA + green light
4-5
SF5
δ [ppm]

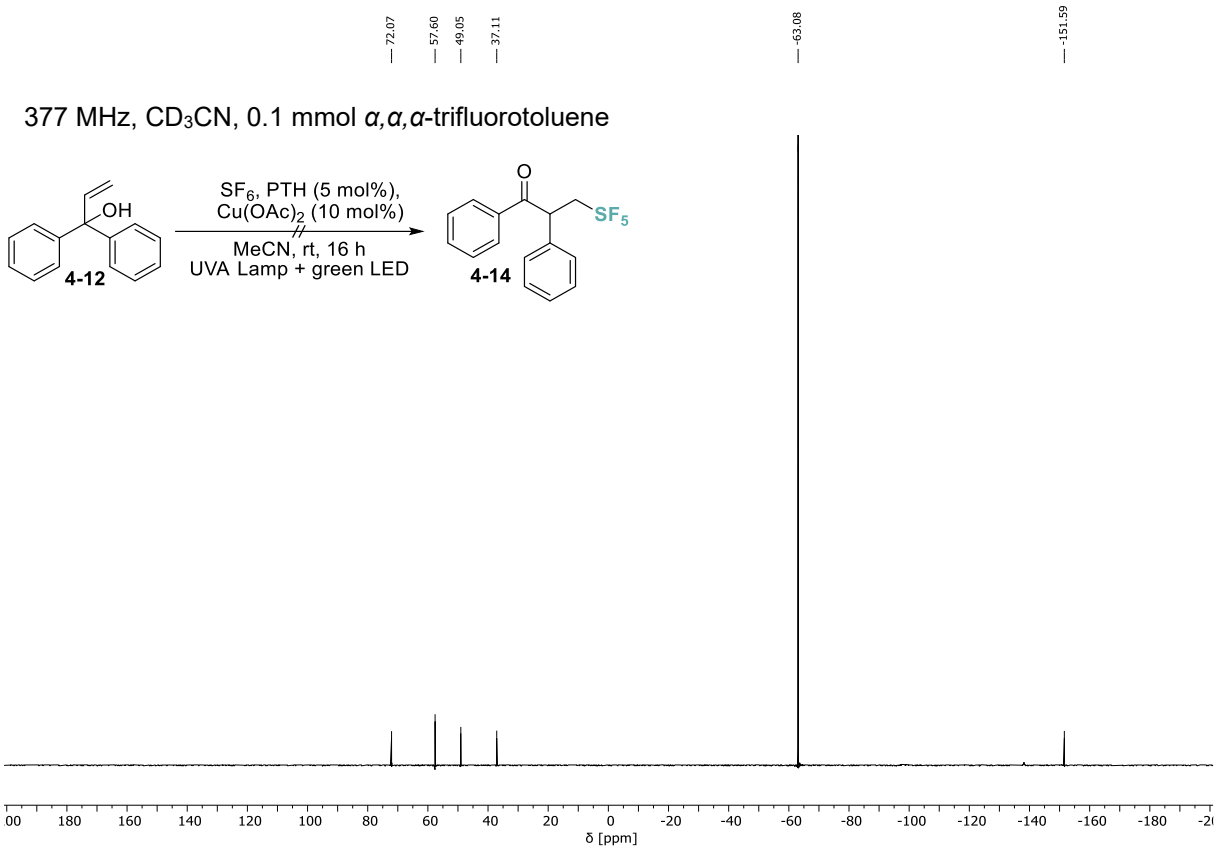

57.58
37.12
-151.61
-170.61
377 MHz, CD3CN
SF6, PTH (5 mol%)
Cu(OAc)2 (10 mol%)
MeCN, rt, 16 h
UVA + green light
4-5
SF5
δ [ppm]

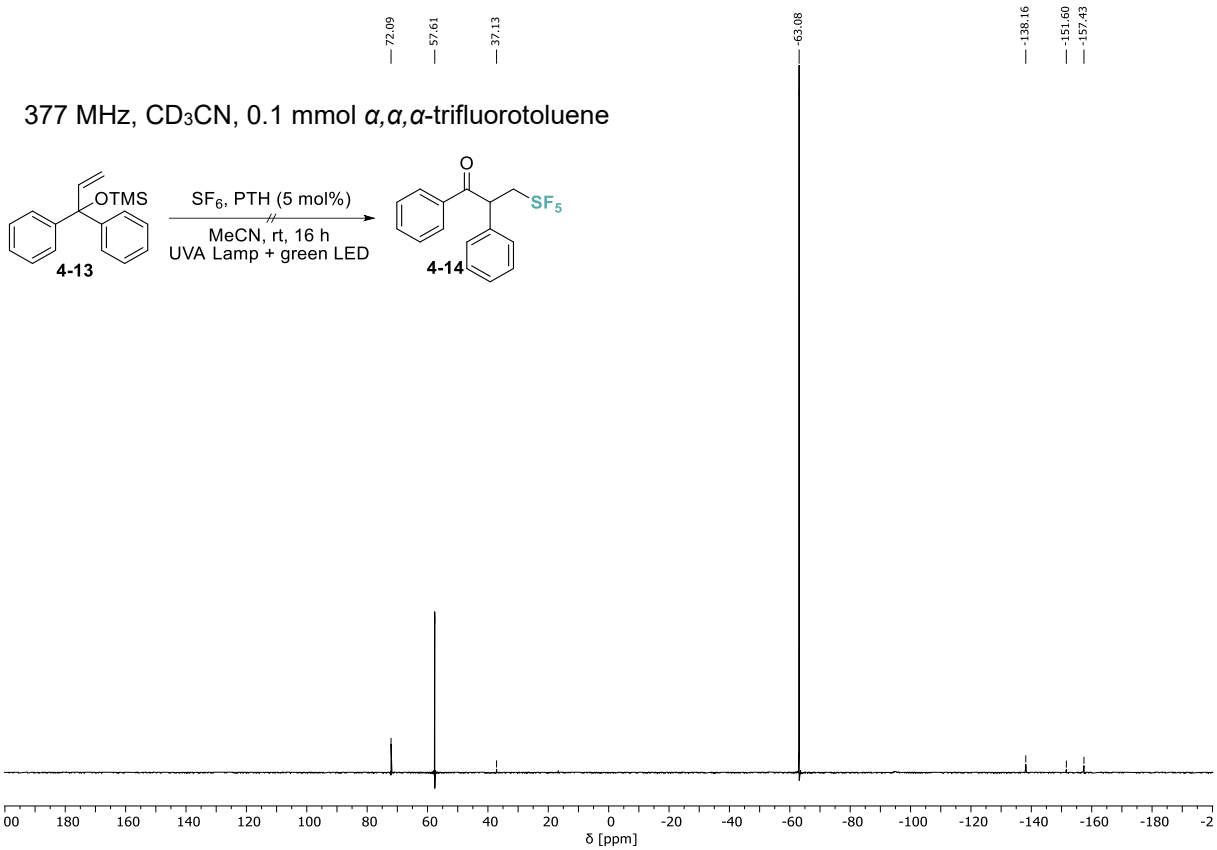

377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
TMS
4-8a
SF6, PTH (5 mol%)
MeCN, rt, 16 h
UVA + green light
SF5
4-9
δ [ppm]

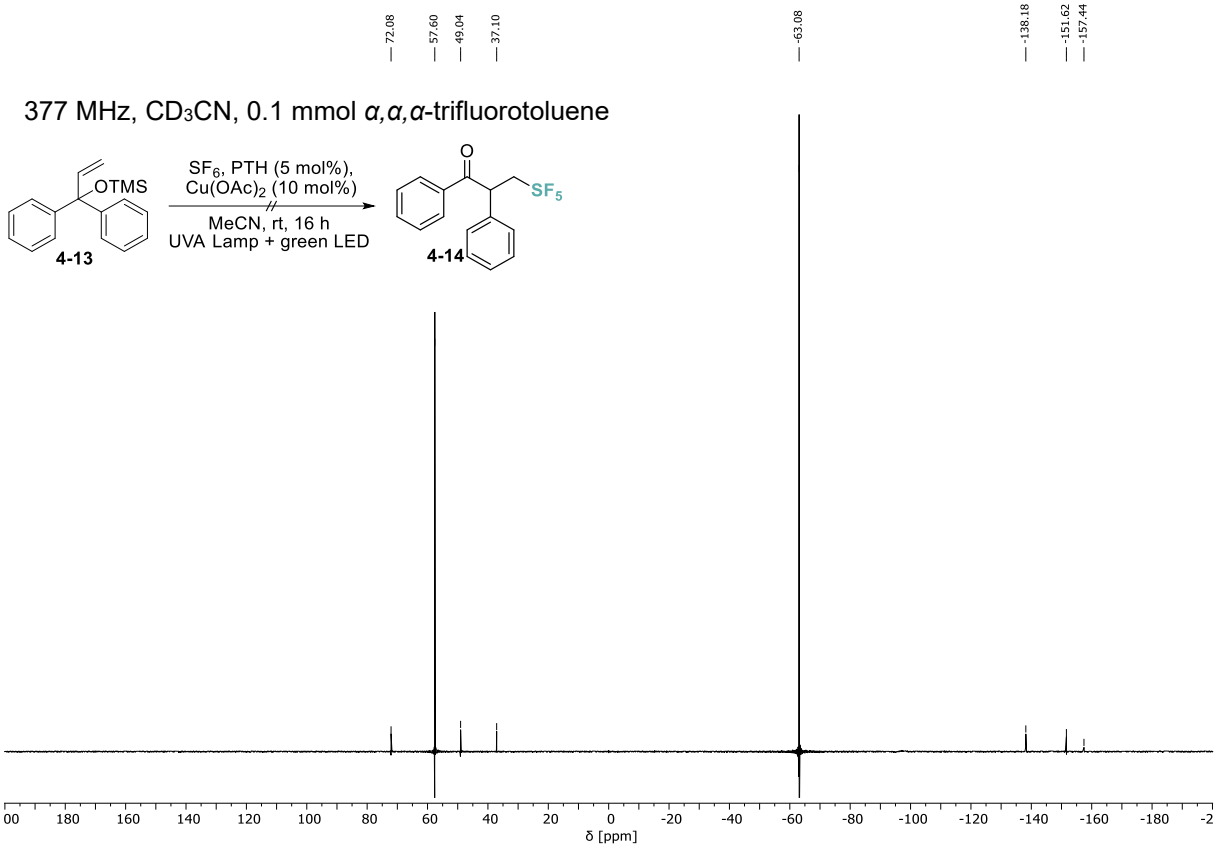

377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
TMS
4-8a
SF6, PTH (5 mol%),
Cu(OAc)2 (10 mol%)
MeCN, rt, 16 h
UVA + green light
SF5
4-9
δ [ppm]

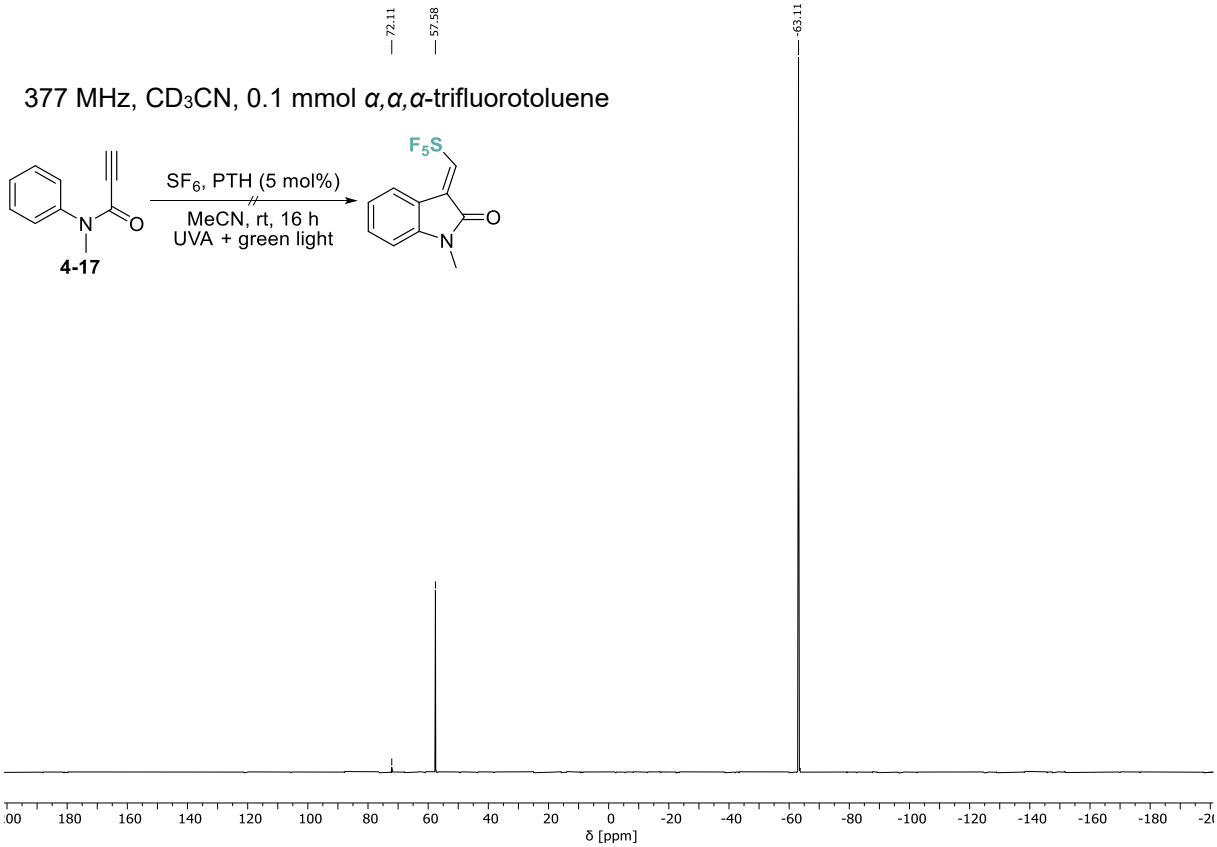

57.59
49.05
-63.10
-138.21
377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
OH
4-12
SF6, PTH (5 mol%),
Cu(OAc)2 (10 mol%)
MeCN, rt, 16 h
UVA Chip
O
SF5
4-14
δ [ppm]


57.13
-63.47
-76.57
-76.58
377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
OH
4-12
SF6, PTH (5 mol%),
Cu(OAc)2 (10 mol%)
HFIP/DCM (1:1), rt, 16 h
UVA Chip
O
SF5
4-14
δ [ppm]

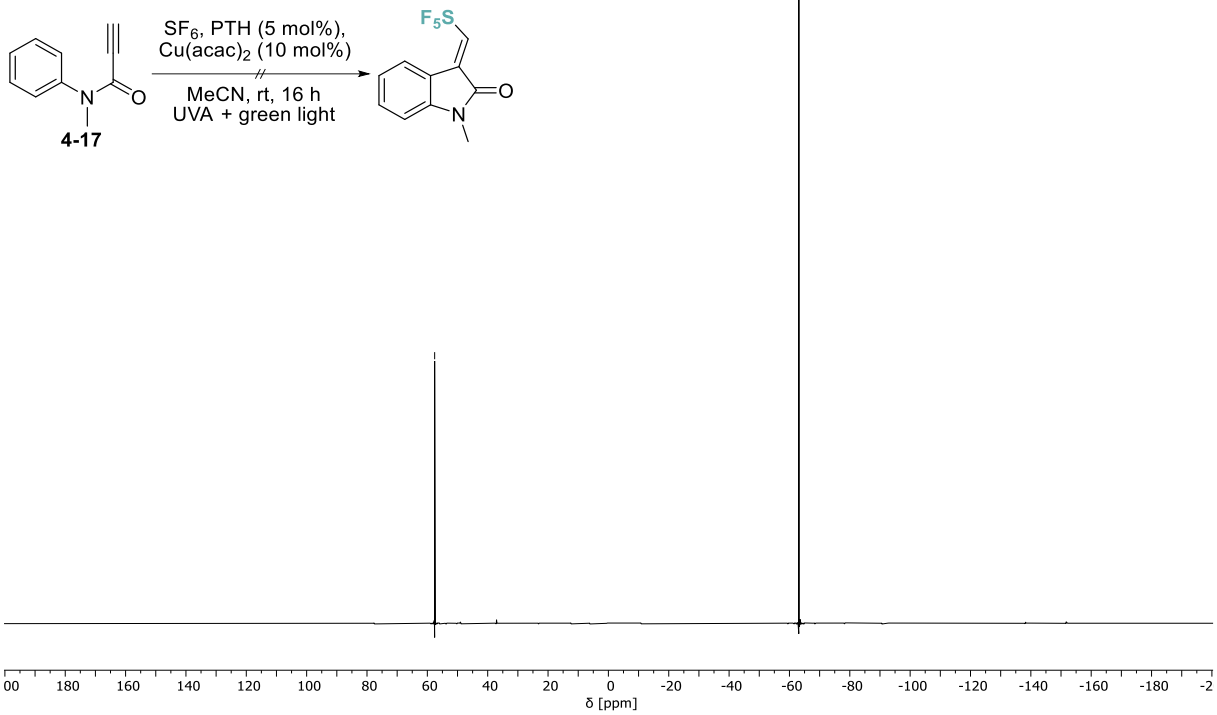

72.07
57.60
49.05
37.11
-63.08
-151.59
377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
OH
4-12
SF6, PTH (5 mol%),
Cu(OAc)2 (10 mol%)
MeCN, rt, 16 h
UVA Lamp + green LED
O
SF5
4-14
δ [ppm]


72.09
57.61
37.13
-63.08
-138.16
-151.60
-157.43
377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
OTMS
4-13
SF6, PTH (5 mol%)
MeCN, rt, 16 h
UVA Lamp + green LED
O
SF5
4-14
δ [ppm]

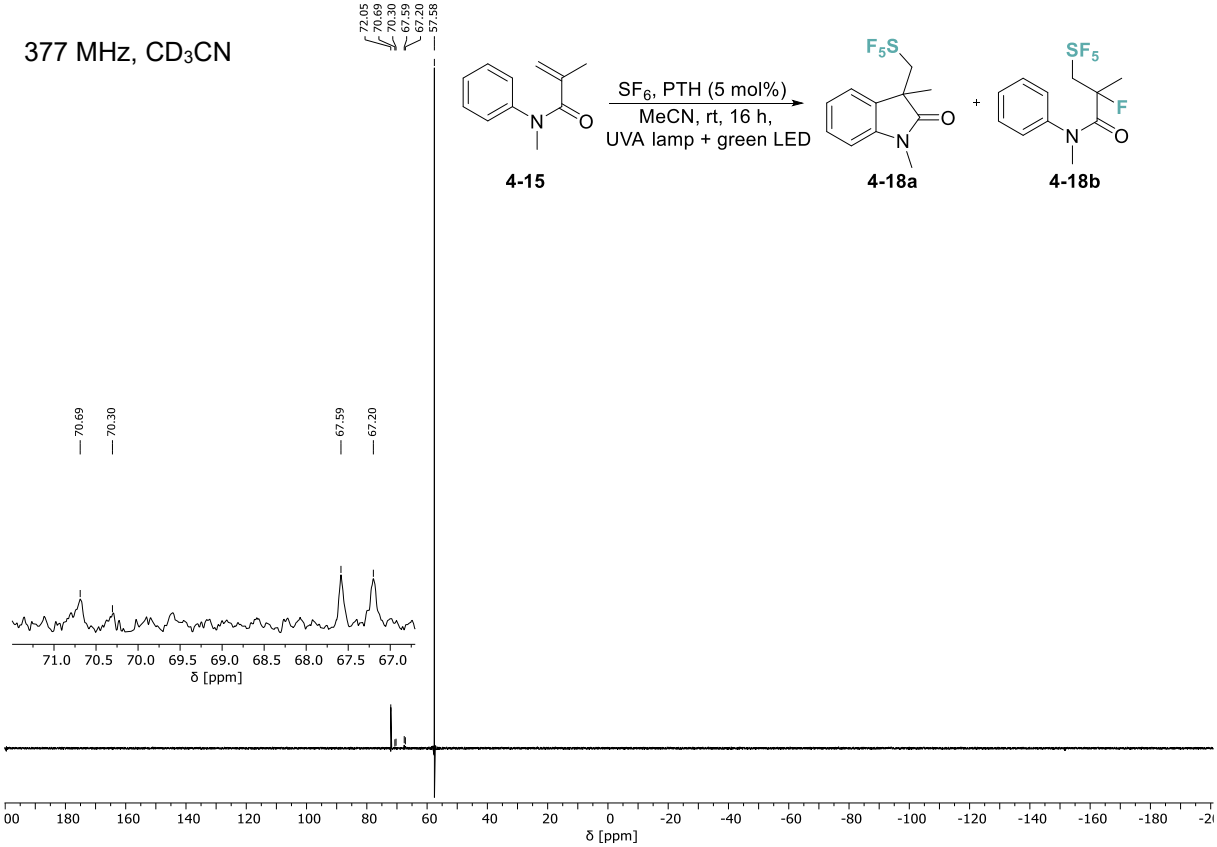

72.08
57.60
49.04
37.10
-63.08
-138.18
-151.62
-157.44
377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
OTMS
4-13
SF6, PTH (5 mol%),
Cu(OAc)2 (10 mol%)
MeCN, rt, 16 h
UVA Lamp + green LED
O
SF5
4-14
δ [ppm]


72.11
57.58
-63.11
377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
4-17
SF6, PTH (5 mol%)
MeCN, rt, 16 h
UVA + green light
F5S
O
N
δ [ppm]

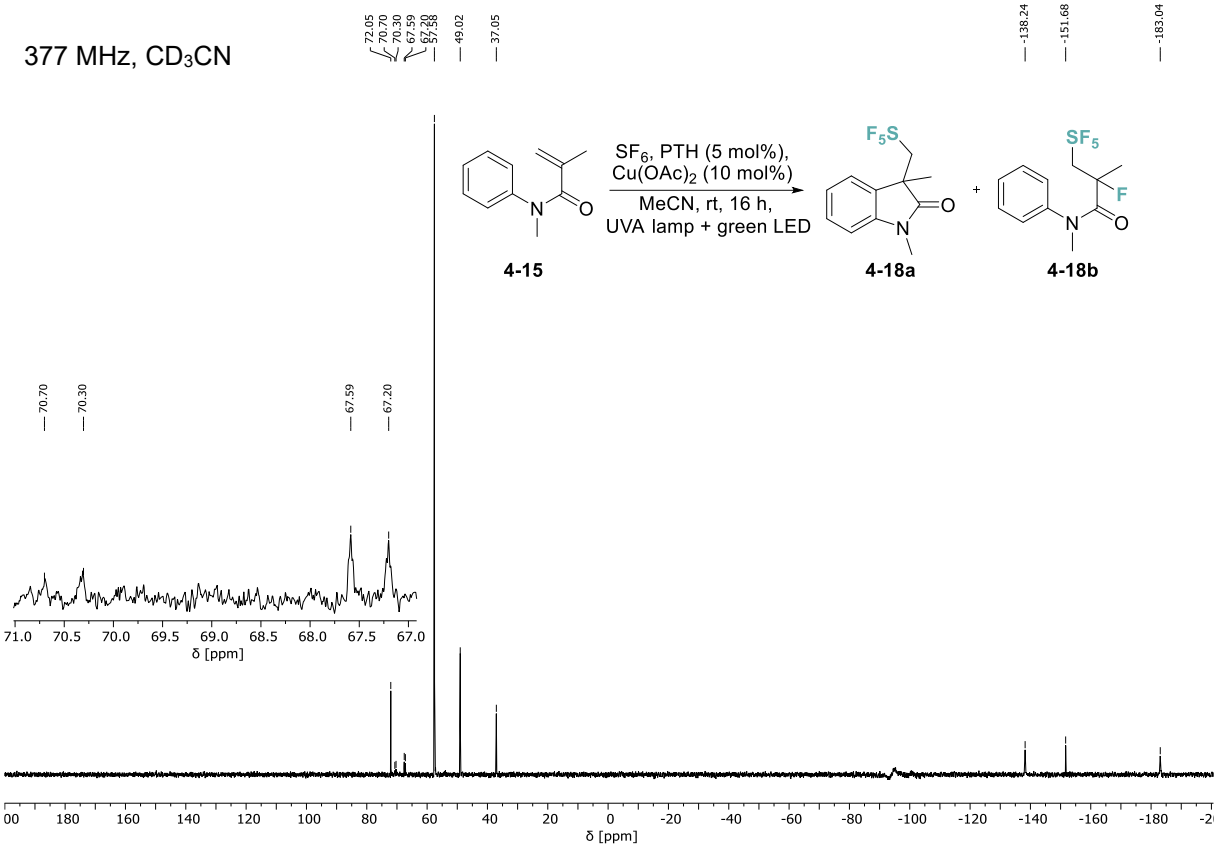
377 MHz, CD_3CN, 0.1 mmol *α,α,α*-trifluorotoluene

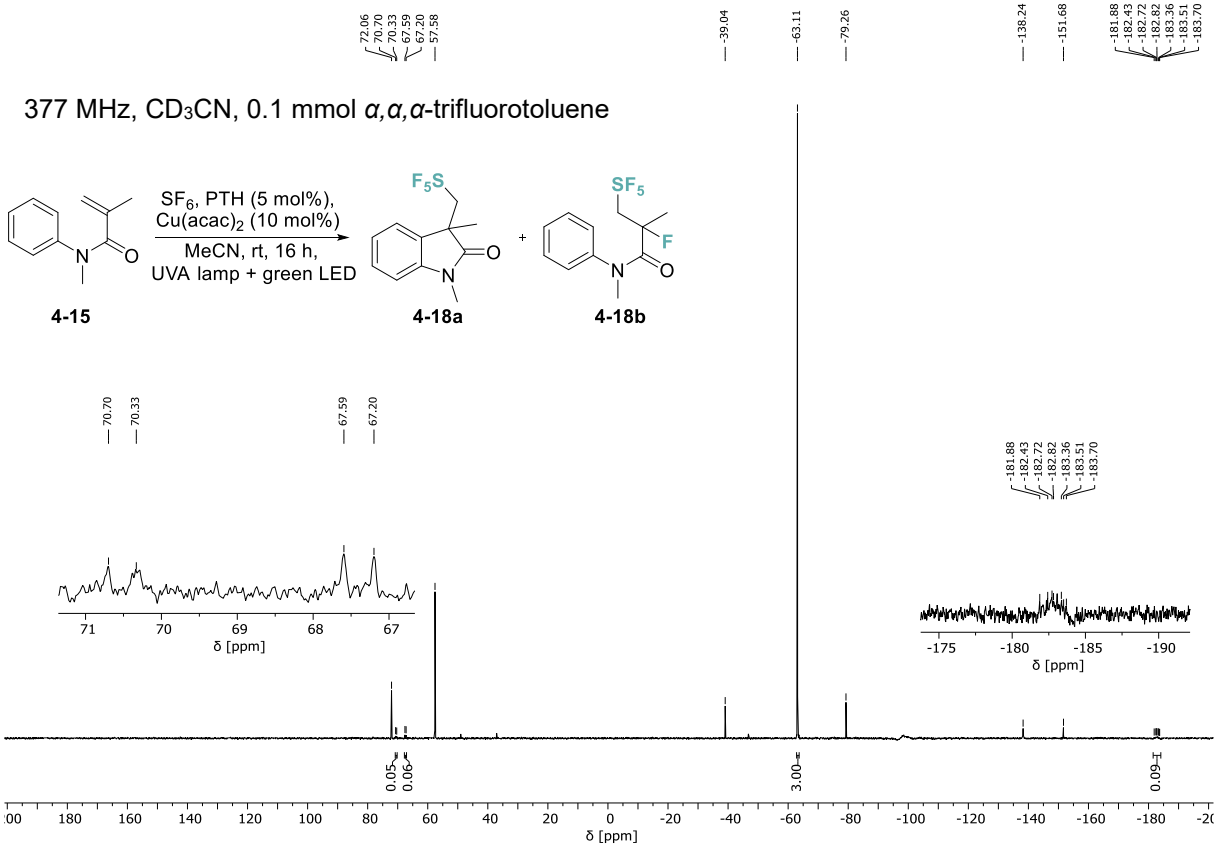


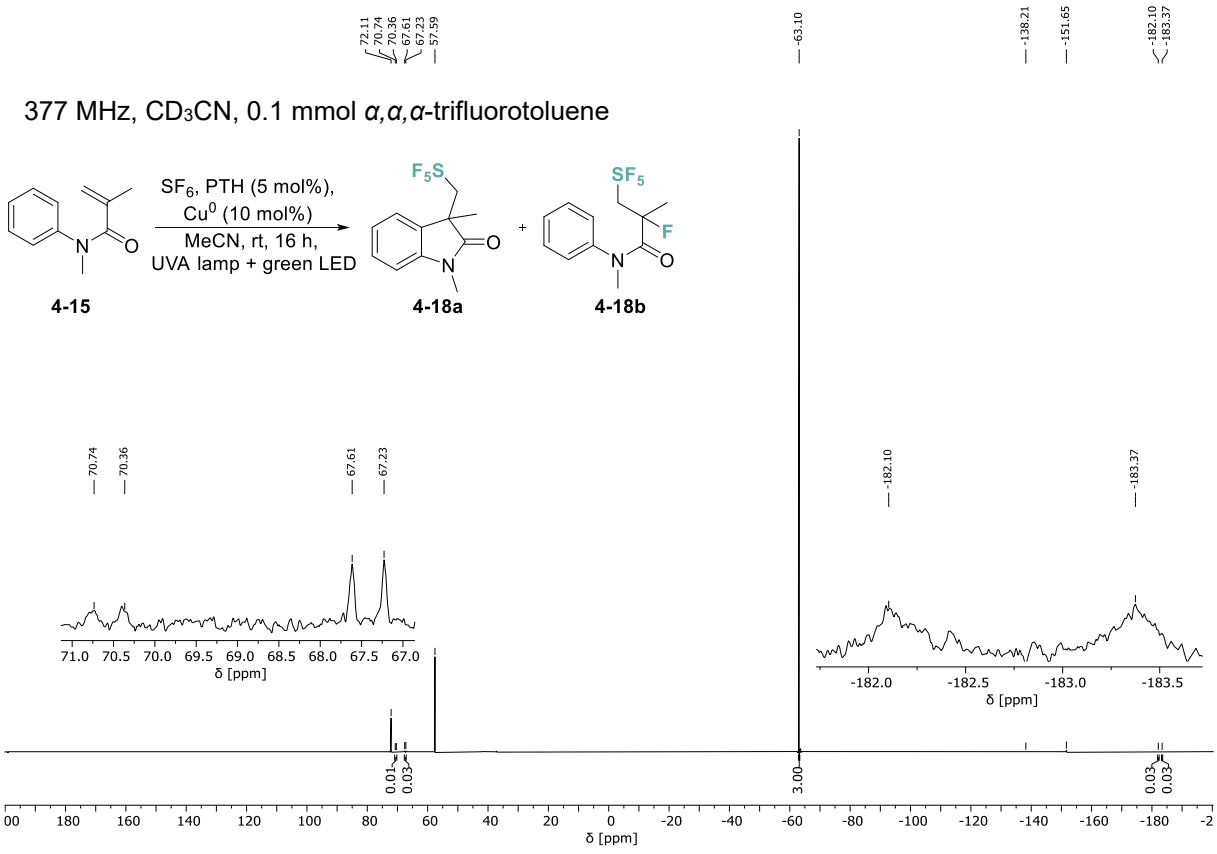
377 MHz, CD_3CN

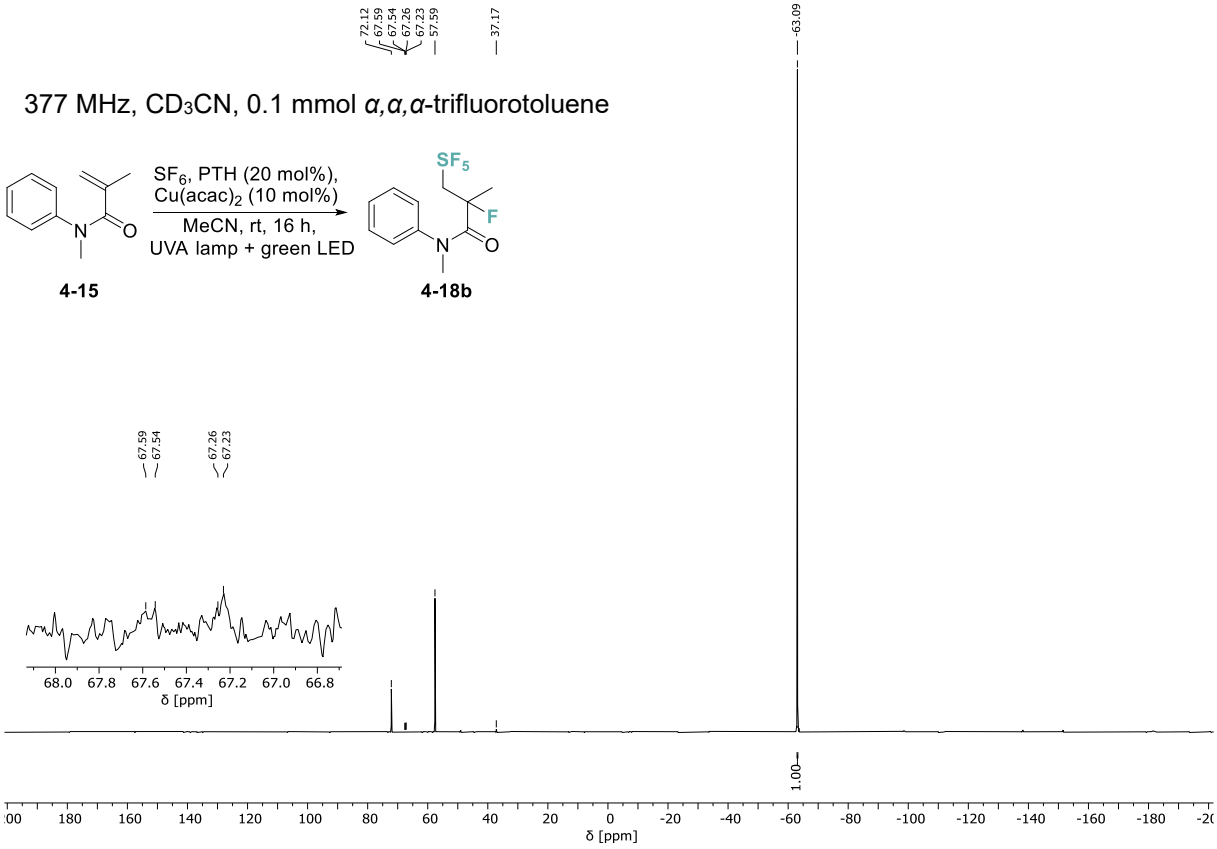


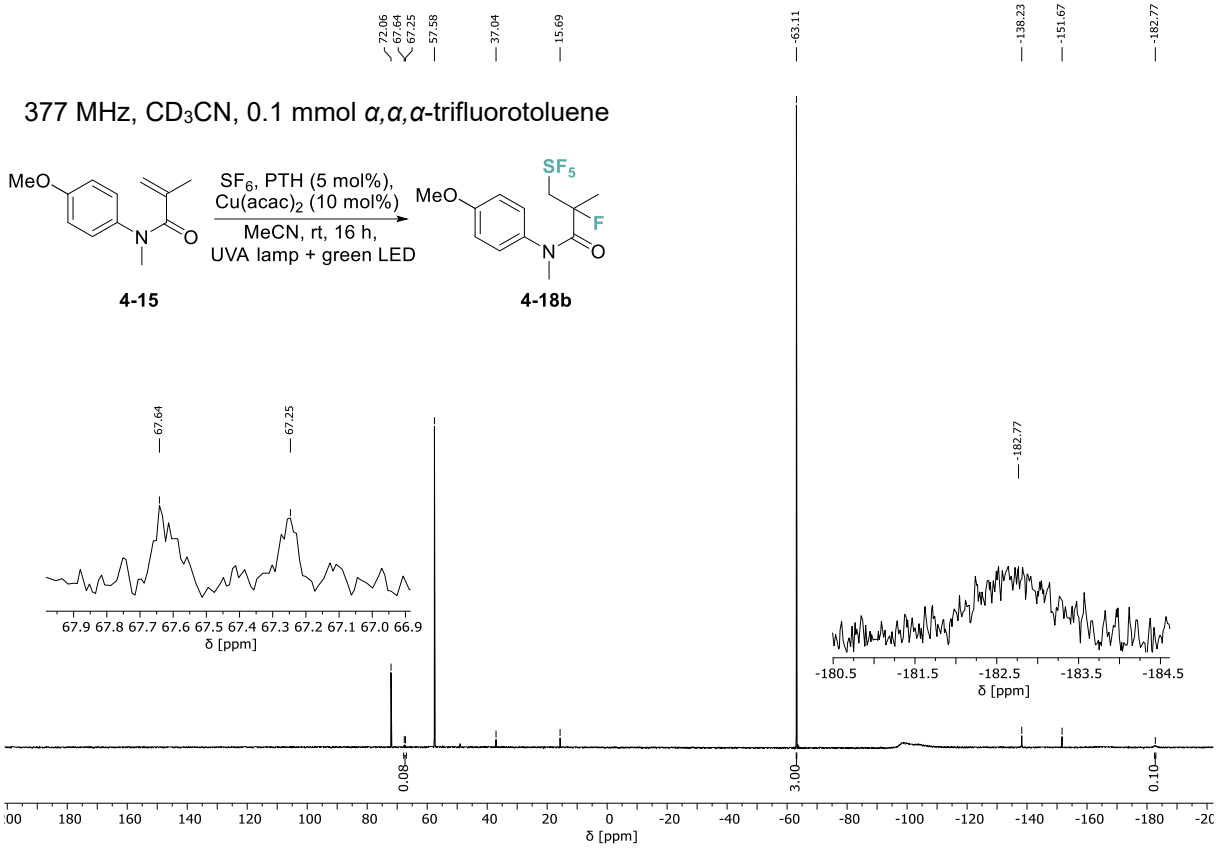
377 MHz, CD_3CN

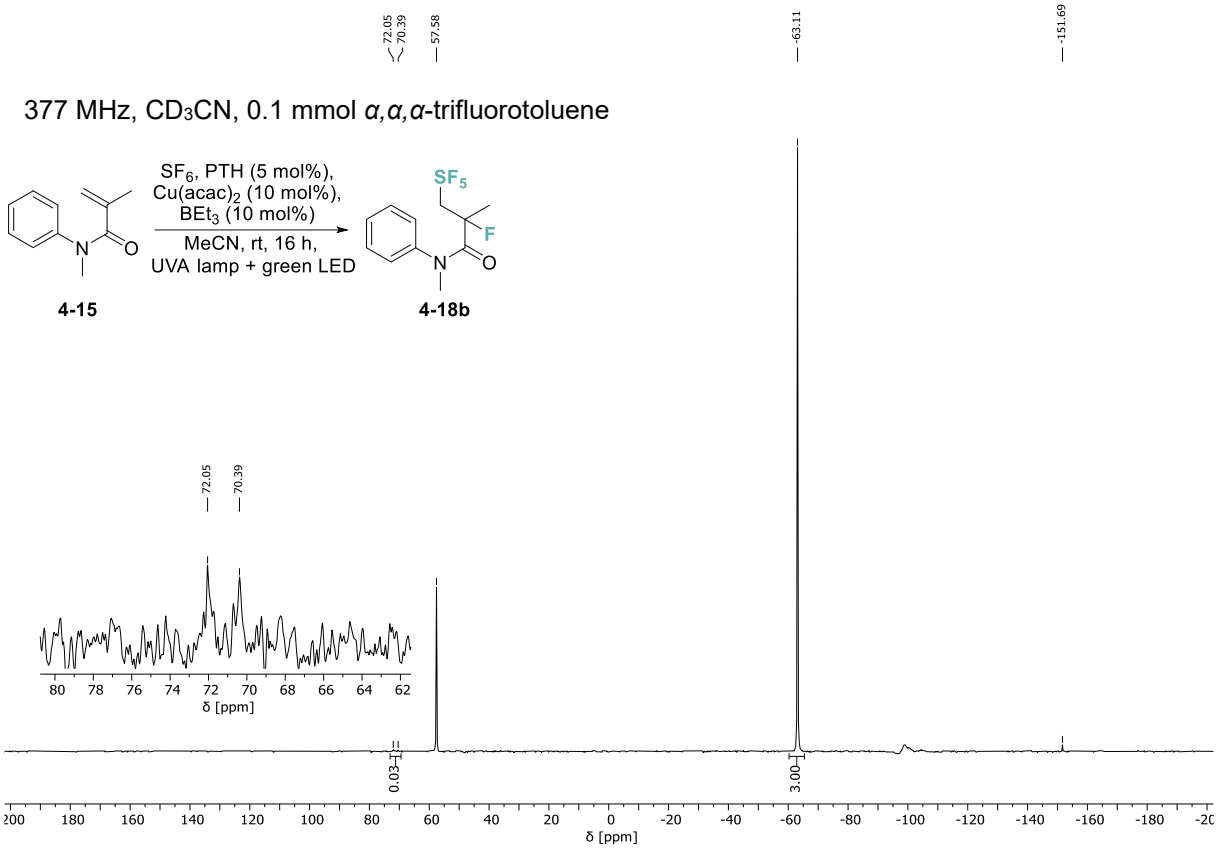


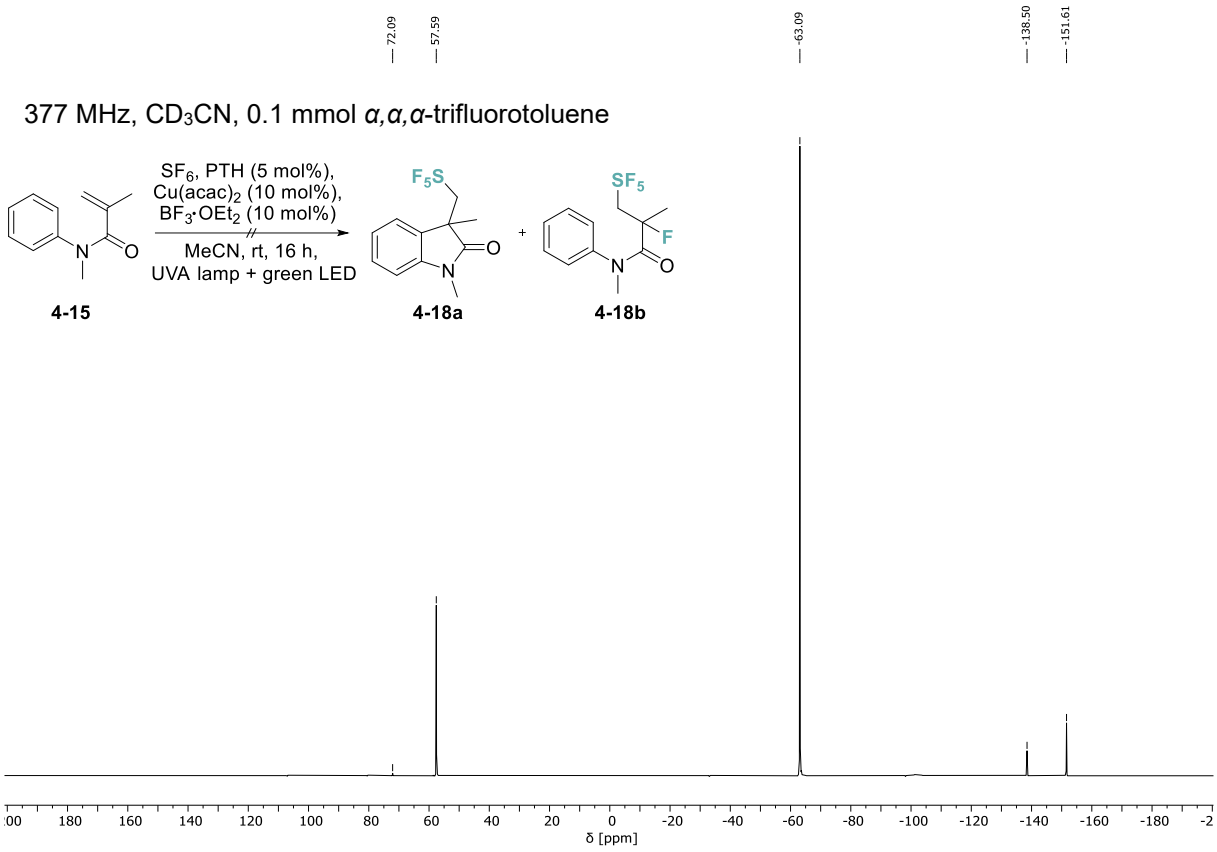


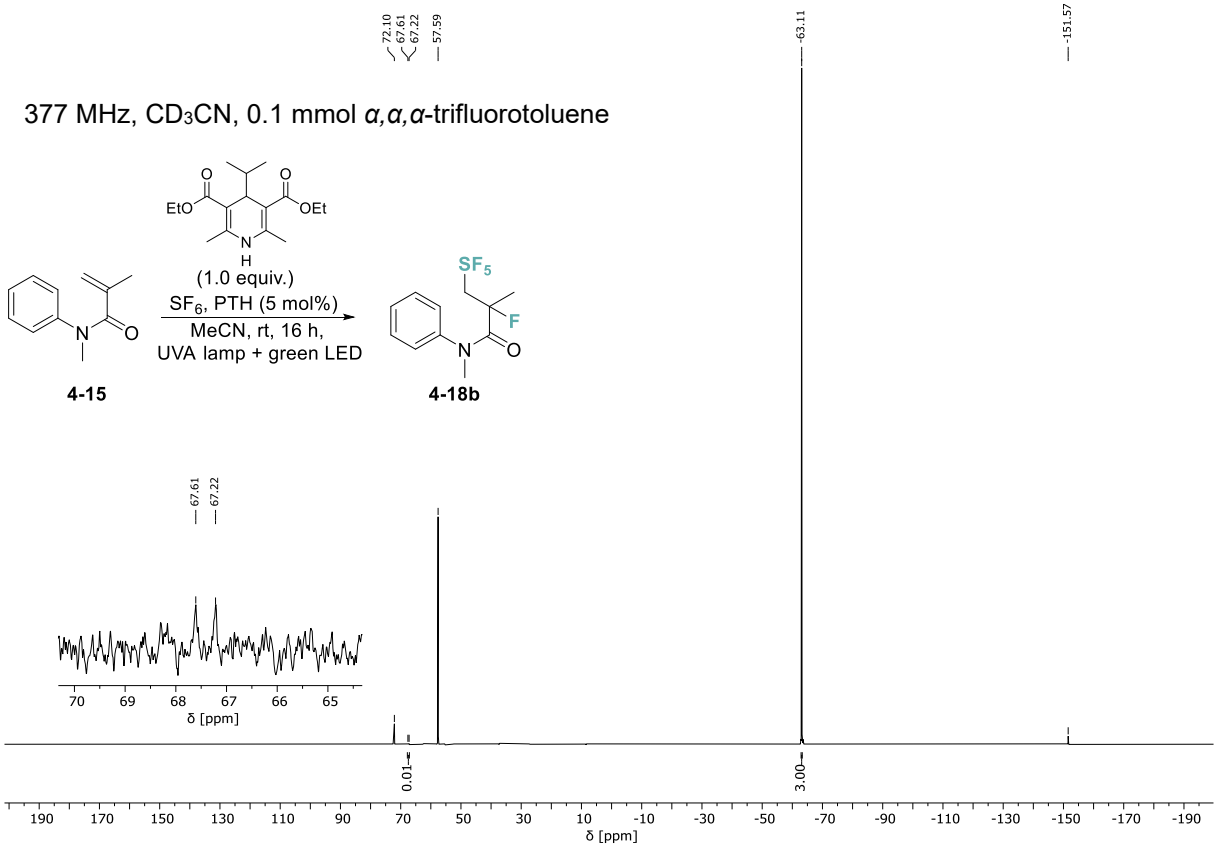

72.11
70.74
70.36
67.61
67.23
57.59
-63.10
-138.21
-151.65
-182.10
-183.37
377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
SF6, PTH (5 mol%),
Cu0 (10 mol%)
MeCN, rt, 16 h,
UVA lamp + green LED
F5S
SF5
F
N
O
4-15
4-18a
4-18b
70.74
70.36
67.61
67.23
-182.10
-183.37
71.0 70.5 70.0 69.5 69.0 68.5 68.0 67.5 67.0
δ [ppm]
-182.0 -182.5 -183.0 -183.5
δ [ppm]
0.01
0.03
3.00
0.03
0.03
δ [ppm]

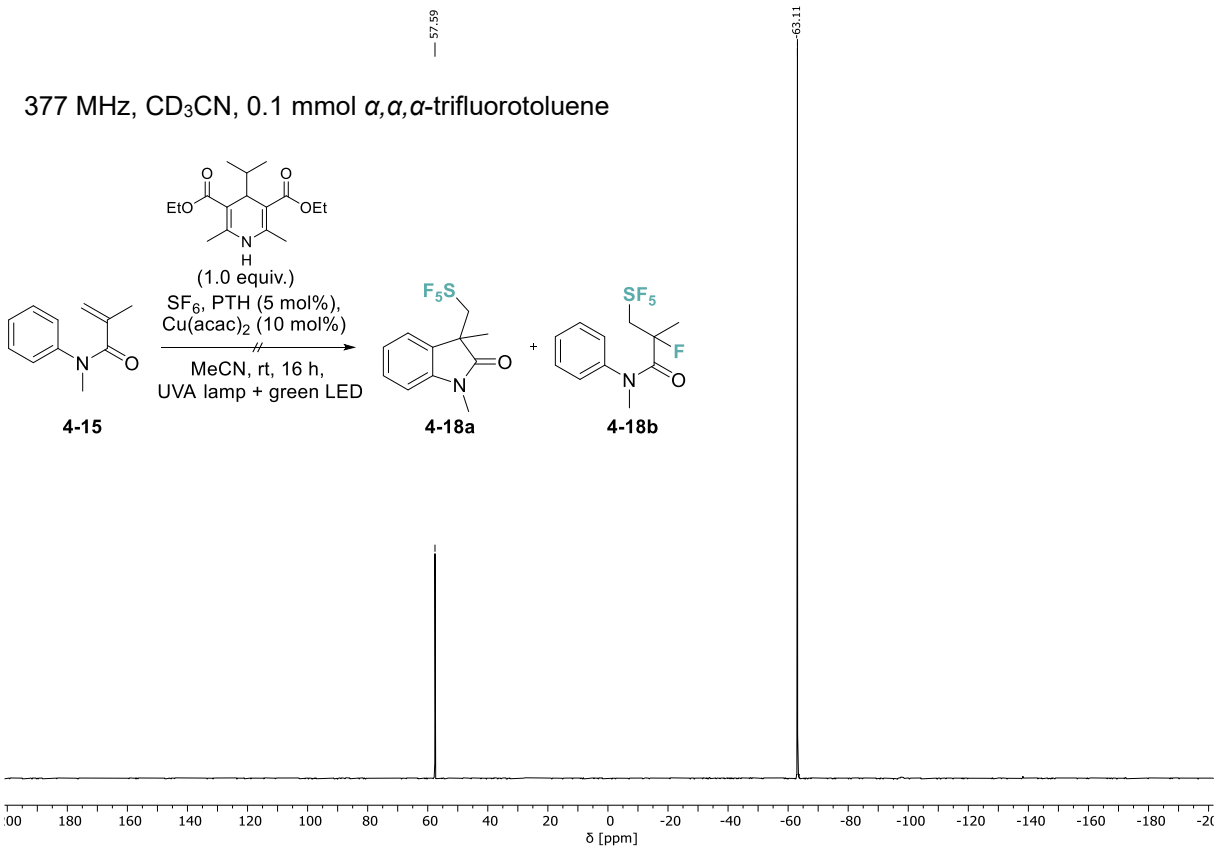

72.12
67.59
67.54
67.26
67.23
57.59
37.17
-63.09
377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
SF6, PTH (20 mol%),
Cu(acac)2 (10 mol%)
MeCN, rt, 16 h,
UVA lamp + green LED
SF5
F
N
O
4-15
4-18b
67.59
67.54
67.26
67.23
68.0 67.8 67.6 67.4 67.2 67.0 66.8
δ [ppm]
1.00
δ [ppm]


377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
MeO
N
O
SF6, PTH (5 mol%),
Cu(acac)2 (10 mol%)
MeCN, rt, 16 h,
UVA lamp + green LED
SF5
F
4-15
4-18b
72.06
67.64
67.25
57.58
37.04
15.69
-63.11
-138.23
-151.67
-182.77
δ [ppm]
0.08
3.00
0.10

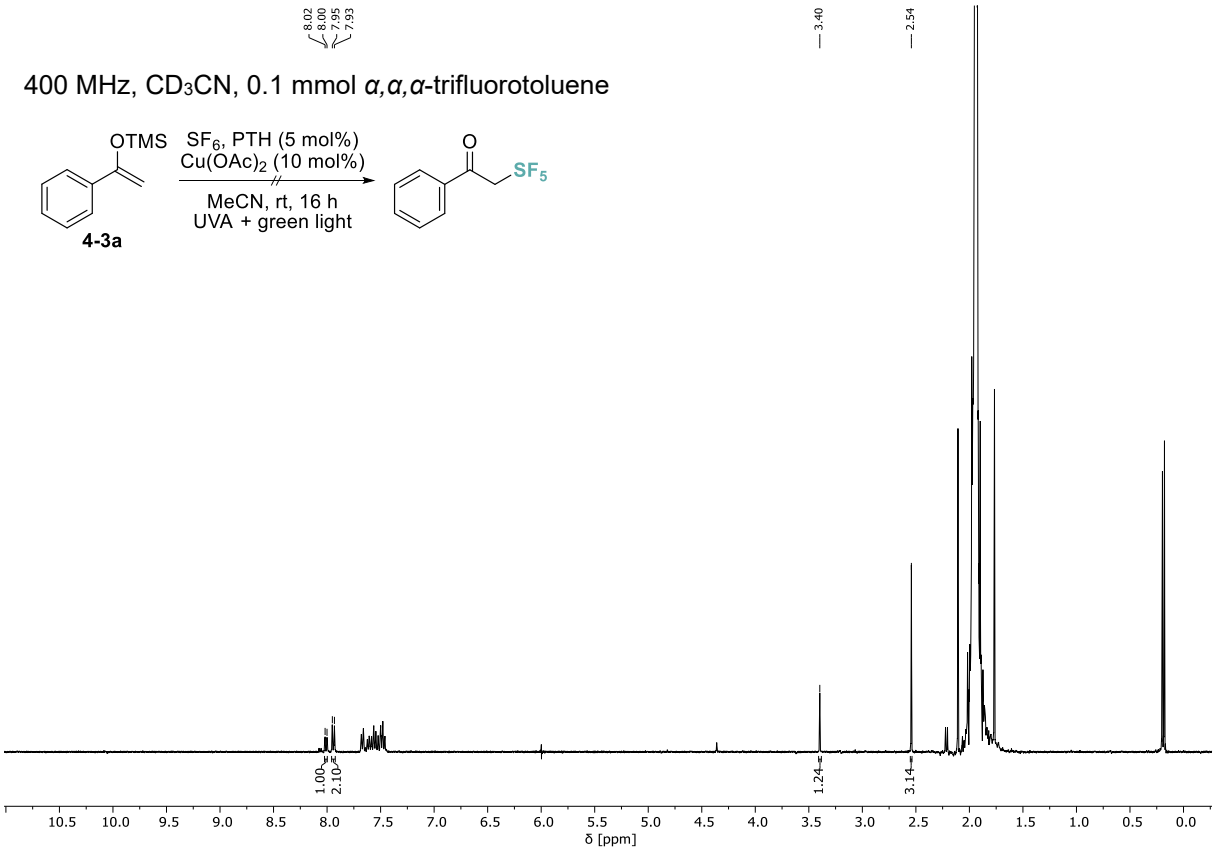

377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
SF6, PTH (5 mol%),
Cu(acac)2 (10 mol%),
BEt3 (10 mol%)
MeCN, rt, 16 h,
UVA lamp + green LED
SF5
F
4-15
4-18b
72.05
70.39
57.58
-63.11
-151.69
δ [ppm]
0.03
3.00

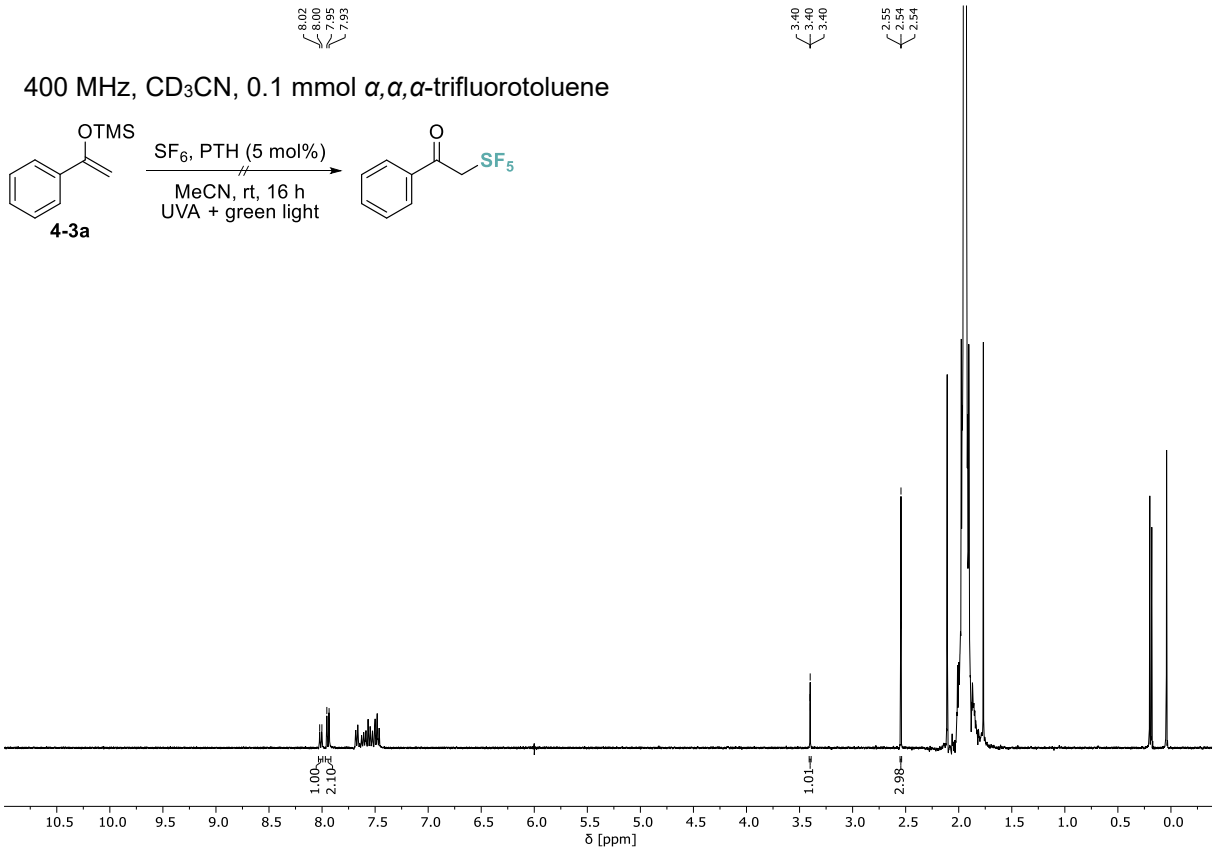

377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
SF6, PTH (5 mol%),
Cu(acac)2 (10 mol%),
BF3·OEt2 (10 mol%)
MeCN, rt, 16 h,
UVA lamp + green LED
F5S
SF5
F
4-15
4-18a
4-18b
72.09
57.59
63.09
-138.50
-151.61
δ [ppm]

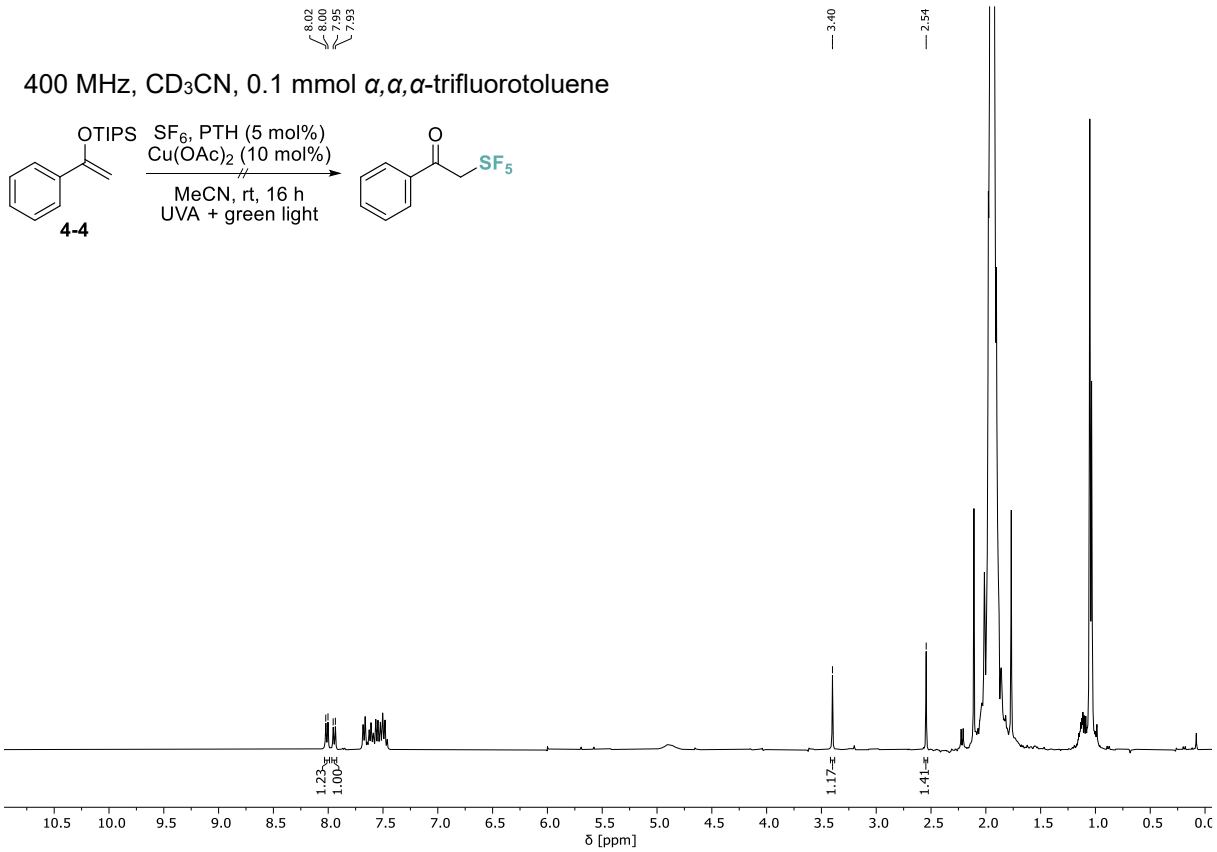

377 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
EtO
OEt
(1.0 equiv.)
SF6, PTH (5 mol%)
MeCN, rt, 16 h,
UVA lamp + green LED
SF5
F
4-15
4-18b
72.10
67.61
67.22
57.59
63.11
-151.57
0.01
3.00
δ [ppm]



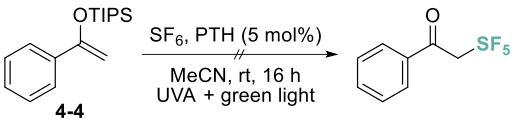
^{1}H NMR Spectra of Test Reactions from Table 4




400 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
OTMS
SF6, PTH (5 mol%)
MeCN, rt, 16 h
UVA + green light
O
SF5
4-3a
δ [ppm]

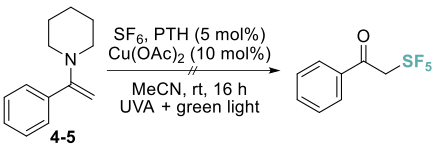

400 MHz, CD3CN, 0.1 mmol α,α,α-trifluorotoluene
OTIPS
SF6, PTH (5 mol%)
Cu(OAc)2 (10 mol%)
MeCN, rt, 16 h
UVA + green light
O
SF5
4-4
δ [ppm]

400 MHz, CD_3CN, 0.1 mmol *α,α,α*-trifluorotoluene

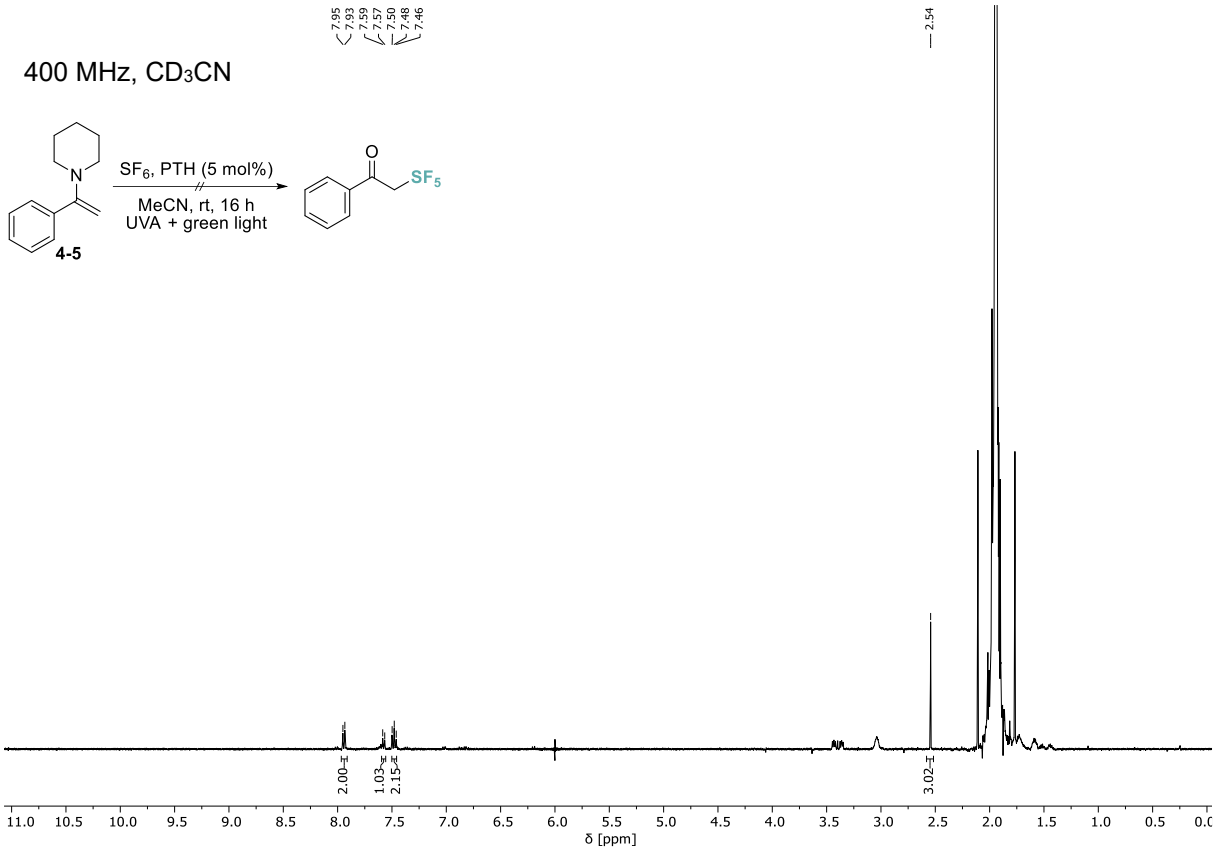


4-4

400 MHz, CD_3CN



4-5


400 MHz, CD3CN
SF6, PTH (5 mol%)
MeCN, rt, 16 h
UVA + green light
4-5
SF5
7.95
7.93
7.59
7.57
7.50
7.48
7.46
2.54
2.00
1.03
2.15
3.02
δ [ppm]

9.2.2 Photoredox Catalytic C-F Activation of *α*-Fluoroacetophenones

General Information

All purchased **chemicals** were used without further treatment. All substituted *α*-fluoroacetophenones **4-19b-i** were synthesised by M.Sc. Arushi Garg according to a literature procedure.[204] The allyl silanes **4-8b-d** were synthesised according to literature procedures and the characterisation data agree with literature values.[205]

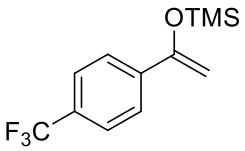
Light reactions were performed using a UVA lamp (Prolinx GmbH, λ = 365–400 nm), Kessil UVA LED (Model: PR160L, 43 W, $\lambda_{max} \approx 370$ nm) and the Kessil blue LED (Model: H150-BLUE, 34 W, $\lambda_{max} \approx 495$ nm).

Thin-layer chromatography was performed on silica gel coated aluminium plates from TLC Silica gel 60 F_{254}. The product spots were detected by UV light (254 nm) or as permanganate stains. Flash column chromatography was performed with silica gel 60 M (0.040–0.063 mm, 230–400 mesh).

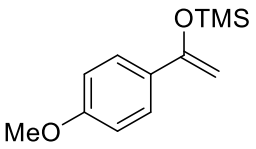
^{1}H, ^{19}F and ^{13}C NMR spectra were acquired on a Bruker Avance III 300 (300 MHz) and analysed on MestReNova 14.1.1. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethyl silane and coupling constants (J) are presented in hertz (Hz). $CDCl_3$ is used as deuterated solvent and the residual solvent signals are used as reference in the ^{1}H and ^{13}C NMR spectra. ^{19}F NMR spectra are not calibrated by an internal reference but with $CFCl_3$ as reference substance. ^{1}H NMR yields were measured using CH_2Br_2 as an internal standard.

Infrared spectra were measured with a PerkinElmer UATR Two FT-IR Spectrometer. Characteristic absorption bands are displayed in wavenumbers $\tilde{\nu}$ in cm^{-1}.

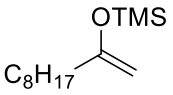
General Procedure for the Synthesis of Silyl enol ethers 4-3b-d



4-3b



4-3c



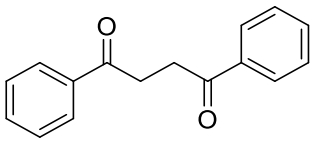
4-3d

In a Schlenk-flask sodium iodide (1.4 equiv.) was dried under vacuum. Under inert gas dry MeCN (5.5–7 mL), the acetophenones (1.0 equiv., 1.0 g) and NEt_3 (1.5 equiv.) were added, and the mixture was cooled to 0 °C. TMSCl (1.3 equiv.) was added and the mixture was stirred for 12 h at rt. The solvent was removed under reduced pressure and the solid residue washed with petroleum ether (3x). The combined organic layers were concentrated under reduced pressure. The crude silyl enol ethers **4-3b-d** were used without further purification.

General Procedure and Analytical Data for the Coupling of Silyl enol ethers with 2-Fluoroacetophenones

The 2-fluoroacetophenones **4-19** (1.0 equiv., 0.3 mmol), silyl enol ethers **4-3** (1.1 equiv., 0.33 mmol) and *fac*-Ir(ppy)$_3$ (5 mol%, 10 mg) were added to dry MeCN (3 mL) and the resulting mixture was frozen using liquid nitrogen. The reaction mixture was degassed (3x) using freeze-pump-thaw technique and was stirred over night at rt under irradiation with blue light. The solvent was removed under reduced pressure and the products were purified by flash chromatography on a silica gel column.

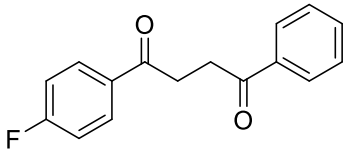
1,4-Diphenylbutane-1,4-dione **4-22a**



1,4-Dione **4-22a** (55 mg, 0.23 mmol, 77%) was obtained from phenacyl fluoride **4-19a** and trimethyl((1-phenylvinyl)oxy)silane **4-3a** after flash column chromatography (petroleum ether / EtOAc, 5:1) as a colourless solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.10 – 8.00 (m, 4H), 7.62 – 7.55 (m, 2H), 7.54 – 7.42 (m, 4H), 3.47 (s, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 198.8, 136.9, 133.3, 128.7, 128.3, 32.7.
The characterisation data agree with the literature values.[206]

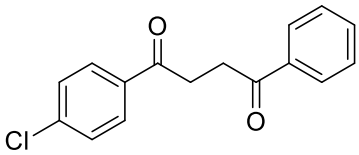
1-(4-fluorophenyl)-4-phenylbutane-1,4-dione **4-22b**



1,4-Dione **4-22b** (54 mg, 0.21 mmol, 70%) was obtained from 2-fluoro-1-(4-fluorophenyl)ethan-1-one **4-19b** and trimethyl((1-phenylvinyl)oxy)silane **4-3a** after flash column chromatography (petroleum ether / EtOAc, 5:1) as a colourless solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.14 – 7.99 (m, 4H), 7.65 – 7.53 (m, 1H), 7.49 (ddt, J = 8.3, 6.7, 1.3 Hz, 2H), 7.22 – 7.09 (m, 2H), 3.53 – 3.37 (m, 4H). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = –105.24. **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 198.6, 197.1, 165.8 (d, J = 254 Hz), 136.7, 133.2, 130.8, 130.7, 128.6, 128.1, 115.71 (d, J = 22 Hz), 32.6, 32.5.
The characterisation data agree with the literature values.[207]

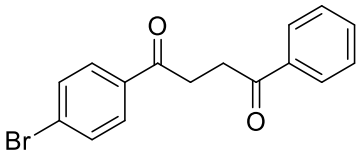
1-(4-chlorophenyl)-4-phenylbutane-1,4-dione **4-22c**



1,4-Dione **4-22c** (75 mg, 0.27 mmol, 90%) was obtained from 2-fluoro-1-(4-chlorophenyl)ethan-1-one **4-19c** and trimethyl((1-phenylvinyl)oxy)silane **4-3a** after flash column chromatography (petroleum ether / EtOAc, 5:1) as a colourless solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.10 – 7.93 (m, 4H), 7.59 (ddt, J = 8.2, 6.5, 1.4 Hz, 1H), 7.53 – 7.42 (m, 4H), 3.53 – 3.36 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 198.6, 197.6, 139.7, 136.8, 135.3, 133.4, 129.7, 129.1, 128.8, 128.3, 32.7, 32.6.
The characterisation data agree with the literature values.[208]

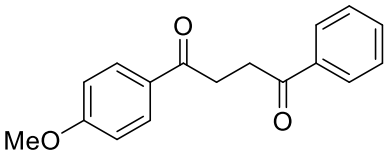
1-(4-bromophenyl)-4-phenylbutane-1,4-dione **4-22d**



1,4-Dione **4-22d** (78 mg, 0.25 mmol, 82%) was obtained from 2-fluoro-1-(4-bromophenyl)ethan-1-one **4-19d** and trimethyl((1-phenylvinyl)oxy)silane **4-3a** after flash column chromatography (petroleum ether / EtOAc, 5:1) as a colourless solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.09 – 7.99 (m, 2H), 7.96 – 7.85 (m, 2H), 7.68 – 7.58 (m, 2H), 7.63 – 7.53 (m, 1H), 7.55 – 7.42 (m, 2H), 3.53 – 3.36 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 198.6, 197.8, 136.8, 135.7, 133.4, 132.1, 129.8, 128.8, 128.5, 128.3, 32.7, 32.6.
The characterisation data agree with the literature values.[207]

1-(4-methoxyphenyl)-4-phenylbutane-1,4-dione **4-22e**

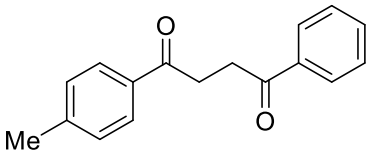


1,4-Dione **4-22e** (62 mg, 0.23 mmol, 77%) was obtained from 2-fluoro-1-(4-methoxyphenyl)ethan-1-one **4-19e** and trimethyl((1-phenylvinyl)oxy)silane **4-3a** after flash column chromatography (petroleum ether / EtOAc, 5:1) as a colourless solid.

The reaction of phenacyl fluoride **4-19a** and silyl enol ether **4-3c** resulted in 34% crude ^{1}H NMR yield of **4-22e'**.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.07 – 7.97 (m, 4H), 7.60 – 7.52 (m, 1H), 7.51 – 7.40 (m, 2H), 6.94 (d, J = 8.9 Hz, 2H), 3.86 (s, 3H), 3.49 – 3.34 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 199.0, 197.2, 163.6, 136.9, 133.2, 130.5, 130.0, 128.7, 128.2, 113.8, 55.5, 32.7, 32.3.
The characterisation data agree with the literature values.[206]

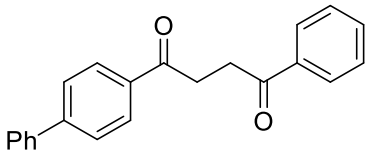
1-phenyl-4-(p-tolyl)butane-1,4-dione **4-22f**



1,4-Dione **4-22f** (36 mg, 0.14 mmol, 47%) was obtained from 2-fluoro-1-(p-tolyl)ethan-1-one **4-19f** and trimethyl((1-phenylvinyl)oxy)silane **4-3a** after flash column chromatography (petroleum ether / EtOAc, 5:1) as a colourless solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.10 – 8.00 (m, 2H), 7.99 – 7.89 (m, 2H), 7.64 – 7.52 (m, 1H), 7.48 (ddt, J = 8.3, 6.8, 1.3 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 3.45 (s, 4H), 2.42 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 198.9, 198.5, 144.1, 137.0, 134.5, 133.3, 129.4, 128.7, 128.4, 128.3, 32.8, 32.6, 21.8.
The characterisation data agree with the literature values.[208]

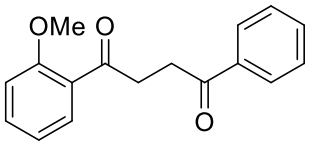
1-([1,1'-biphenyl]-4-yl)-4-phenylbutane-1,4-dione **4-22g**



1,4-Dione **4-22g** (26 mg, 0.08 mmol, 28%) was obtained from 1-([1,1'-biphenyl]-4-yl)-2-fluoroethan-1-one **4-19g** and trimethyl((1-phenylvinyl)oxy)silane **4-3a** after flash column chromatography (petroleum ether / EtOAc, 5:1) as a colourless solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.16 – 8.09 (m, 2H), 8.11 – 8.01 (m, 2H), 7.76 – 7.66 (m, 2H), 7.69 – 7.60 (m, 2H), 7.65 – 7.53 (m, 1H), 7.54 – 7.45 (m, 4H), 7.45 – 7.37 (m, 1H), 3.50 (s, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 198.9, 198.5, 146.0, 140.1, 136.9, 135.6, 133.3, 129.1, 128.9, 128.8, 128.4, 128.3, 127.4, 127.4, 32.8, 32.8. **IR (ATR)**: $\tilde{\nu}$ [cm^{-1}] = 3053 (C-$H_{arom.}$), 2922 (C-$H_{aliph.}$), 1676 (C=O).
The characterisation data agree with the literature values.[209]

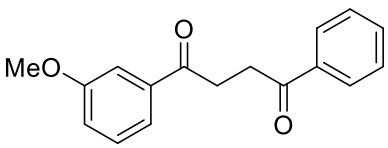
1-(2-methoxyphenyl)-4-phenylbutane-1,4-dione **4-22h**



1,4-Dione **4-22h** (44 mg, 0.16 mmol, 80%) was obtained on a 0.2 mmol scale from 2-fluoro-1-(2-methoxyphenyl)ethan-1-one **4-19h** and trimethyl((1-phenylvinyl)oxy)silane **4-3a** after flash column chromatography (petroleum ether / EtOAc, 5:1) as a colourless solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.09 – 7.99 (m, 2H), 7.77 (dd, J = 7.7, 1.9 Hz, 1H), 7.63 – 7.52 (m, 1H), 7.52 – 7.43 (m, 3H), 7.08 – 6.94 (m, 2H), 3.93 (s, 3H), 3.53 – 3.36 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 200.8, 199.2, 159.0, 137.1, 133.7, 133.1, 130.7, 128.7, 128.3, 128.0, 120.8, 111.7, 55.7, 38.1, 33.1. **IR (ATR)**: $\tilde{\nu}$ [cm^{-1}] = 3070 (C-$H_{arom.}$), 2921 (C-$H_{aliph.}$), 1681 (C=O), 1663 (C=O), 1178 (C-O-C).

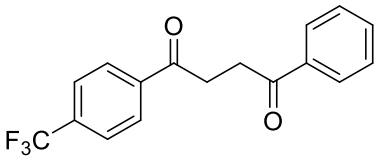
1-(3-methoxyphenyl)-4-phenylbutane-1,4-dione **4-22i**



1,4-Dione **4-22i** (77 mg, 0.28 mmol, 94%) was obtained from 2-fluoro-1-(3-methoxyphenyl)ethan-1-one **4-19i** and trimethyl((1-phenylvinyl)oxy)silane **4-3a** after flash column chromatography (petroleum ether / EtOAc, 5:1) as a colourless solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.10 – 8.00 (m, 2H), 7.64 (dd, J = 7.6, 1.6 Hz, 1H), 7.62 – 7.53 (m, 2H), 7.53 – 7.44 (m, 2H), 7.39 (dd, J = 8.1, 7.6 Hz, 1H), 7.13 (dd, J = 8.2, 2.7, Hz, 1H), 3.86 (s, 3H), 3.46 (s, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 198.8, 198.6, 160.0, 138.3, 136.9, 133.3, 129.7, 128.7, 128.3, 121.0, 119.9, 112.4, 55.6, 32.9, 32.7. **IR (ATR)**: $\tilde{\nu}$ [cm^{-1}] = 3016 (C-$H_{arom.}$), 2920 (C-$H_{aliph.}$), 1673 (C=O), 1174 (C-O-C).
The characterisation data agree with the literature values.[210]

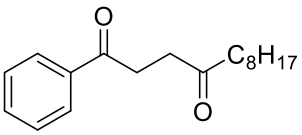
1-phenyl-4-(4-(trifluoromethyl)phenyl)butane-1,4-dione **4-22j**



1,4-Dione **4-22b** (43 mg, 0.14 mmol, 46%) was obtained from phenacyl fluoride **4-19a** and silyl enol ether **4-3b** after flash column chromatography (petroleum ether / acetone, 5:1) as a colourless solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.15 (d, J = 8.0 Hz, 2H), 8.07 – 8.00 (m, 2H), 7.76 (d, J = 8.0 Hz, 2H), 7.63 – 7.55 (m, 1H), 7.49 (tt, J = 6.2, 1.5 Hz, 2H), 3.56 – 3.41 (m, 4H). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = –63.10. **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 198.5, 198.0, 139.6, 136.7, 134.8, 134.4, 133.5, 128.8, 128.6, 128.3, 125.9 (q, J = 4 Hz), 32.9, 32.7. **IR (ATR)**: $\tilde{\nu}$ [cm^{-1}] = 3057 (C-$H_{arom.}$), 2920 (C-$H_{aliph.}$), 1675 (C=O).

1-phenyldodecane-1,4-dione **4-22k**



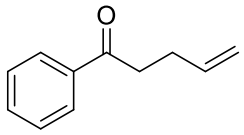
1,4-Dione **4-22k** was obtained from phenacyl fluoride **4-19a** and silyl enol ether **4-3d** in a crude ^{1}H NMR yield of 35%.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.89 – 7.84 (m, 2H), 7.39 – 7.30 (m, 3H), 3.16 (t, J = 6.4 Hz, 2H), 2.74 (t, J = 6.3 Hz, 2H), 2.41 (t, J = 7.5 Hz, 2H), 1.50 (p, J = 7.2 Hz, 2H), 1.24 – 1.11 (m, 10H), 0.76 (t, J = 6.2 Hz, 3H).

General Procedure and Analytical Data for the Coupling of Allyl silanes with 2-Fluoroacetophenones

The 2-fluoroacetopenones (1.0 equiv., 0.3 mmol), allyl silanes (3.0 equiv., 0.9 mmol) and *fac*-Ir(ppy)$_3$ (5 mol%, 10 mg) were added to dry MeCN (3 mL) and the resulting mixture was frozen using liquid nitrogen. The reaction mixture was degassed (3x) using freeze-pump-thaw technique and was stirred over night at rt under irradiation with blue light. The solvent was removed under reduced pressure and the products were purified by flash chromatography on a silica gel column.

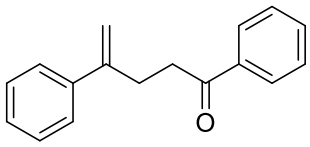
1-phenylpent-4-en-1-one **4-20a**



1,4-Enone **4-20a** (44 mg, 0.19 mmol, 63%) was obtained from phenacyl fluoride **4-19a** and allyl silane **4-8a** after flash column chromatography (petroleum ether / EtOAc, 15:1) as a colourless solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.00 – 7.93 (m, 2H), 7.60 – 7.52 (m, 1H), 7.50 – 7.43 (m, 2H), 5.91 (ddt, *J* = 16.8, 10.2, 6.5 Hz, 1H), 5.09 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.02 (dq, *J* = 10.2, 1.4 Hz, 1H), 3.08 (t, *J* = 6.9 Hz, 2H), 2.56 – 2.45 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 199.6, 137.5, 137.1, 133.1, 128.7, 128.2, 115.4, 37.9, 28.3.
The characterisation data agree with the literature values.[211]

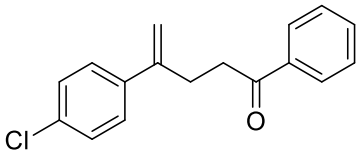
1,4-diphenylpent-4-en-1-one **4-20b**



1,4-Enone **4-20b** (39 mg, 0.24 mmol, 81%) was obtained from phenacyl fluoride **4-19a** and allyl silane **4-8b** after flash column chromatography (petroleum ether / EtOAc, 10:1) as a colourless solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.96 – 7.89 (m, 2H), 7.54 (ddt, *J* = 8.3, 6.6, 1.3 Hz, 1H), 7.49 – 7.39 (m, 4H), 7.38 – 7.24 (m, 2H), 5.34 (d, *J* = 1.2 Hz, 1H), 5.14 (q, *J* = 1.3 Hz, 1H), 3.18 – 3.09 (m, 2H), 3.02 – 2.92 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 199.6, 147.5, 140.7, 137.0, 133.1, 128.7, 128.6, 128.2, 127.7, 126.3, 113.0, 37.6, 29.8.
The characterisation data agree with the literature values.[212]

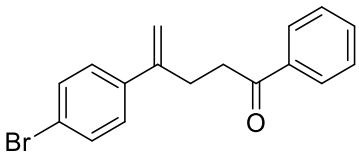
4-(4-chlorophenyl)-1-phenylpent-4-en-1-one **4-20c**



1,4-Enone **4-20c** (57 mg, 0.21 mmol, 70%) was obtained from phenacyl fluoride **4-19a** and allyl silane **4-8c** after flash column chromatography (petroleum ether / EtOAc, 5:1) as a colourless solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.97 – 7.89 (m, 2H), 7.55 (ddt, J = 8.3, 6.6, 1.4 Hz, 1H), 7.49 – 7.40 (m, 2H), 7.40 – 7.27 (m, 4H), 5.32 (d, J = 1.0 Hz, 1H), 5.15 (q, J = 1.3 Hz, 1H), 3.17 – 3.07 (m, 2H), 2.99 – 2.89 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 199.3, 146.3, 139.2, 136.9, 133.5, 133.2, 128.7, 128.7, 128.1, 127.6, 113.5, 37.4, 29.6.
The characterisation data agree with the literature values.[212]

4-(4-bromophenyl)-1-phenylpent-4-en-1-one **4-20d**



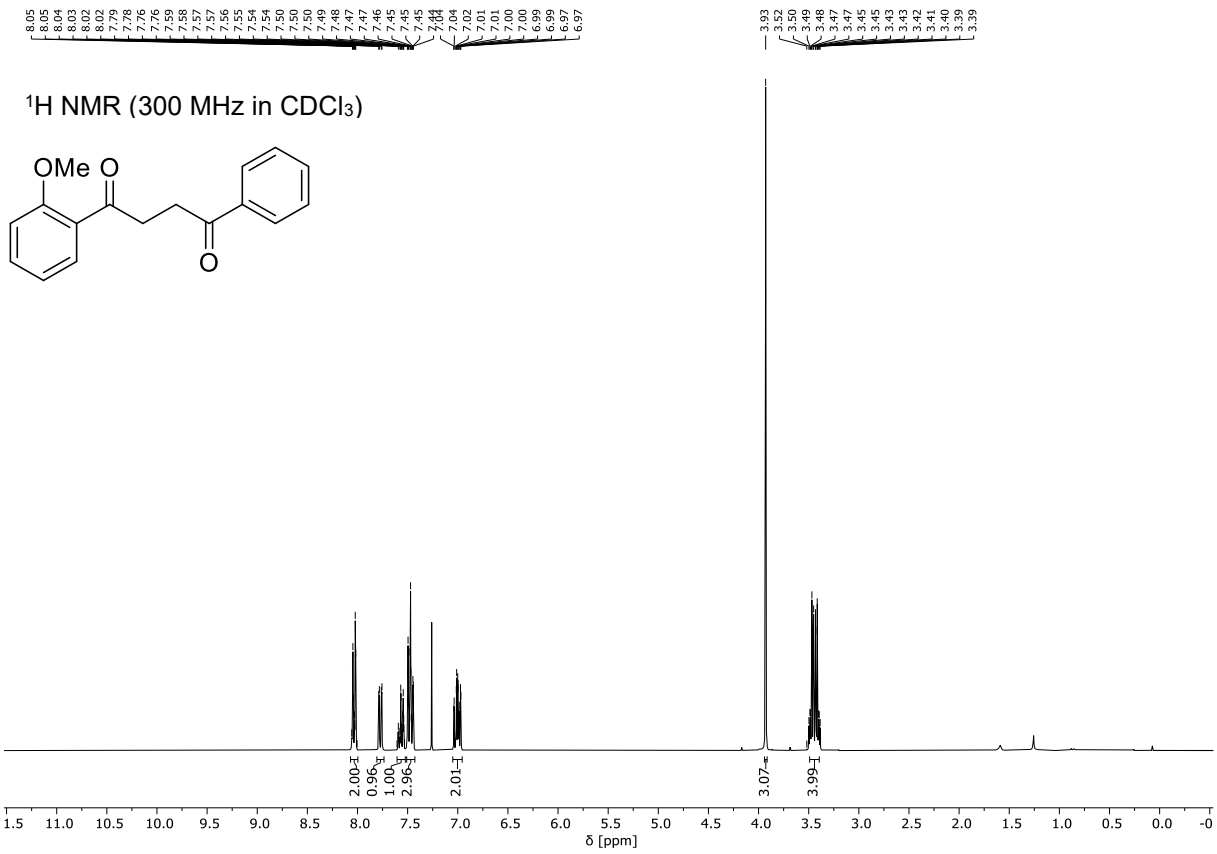
1,4-Enone **4-20d** was obtained from phenacyl fluoride **4-19a** and allyl silane **4-8d** in a crude ^{1}H NMR yield of 92%.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.96 – 7.88 (m, 2H), 7.60 – 7.51 (m, 1H), 7.50 – 7.40 (m, 4H), 7.34 – 7.27 (m, 2H), 5.32 (d, J = 1.0 Hz, 1H), 5.16 (q, J = 1.3 Hz, 1H), 3.16 – 3.06 (m, 2H), 2.98 – 2.89 (m, 2H).

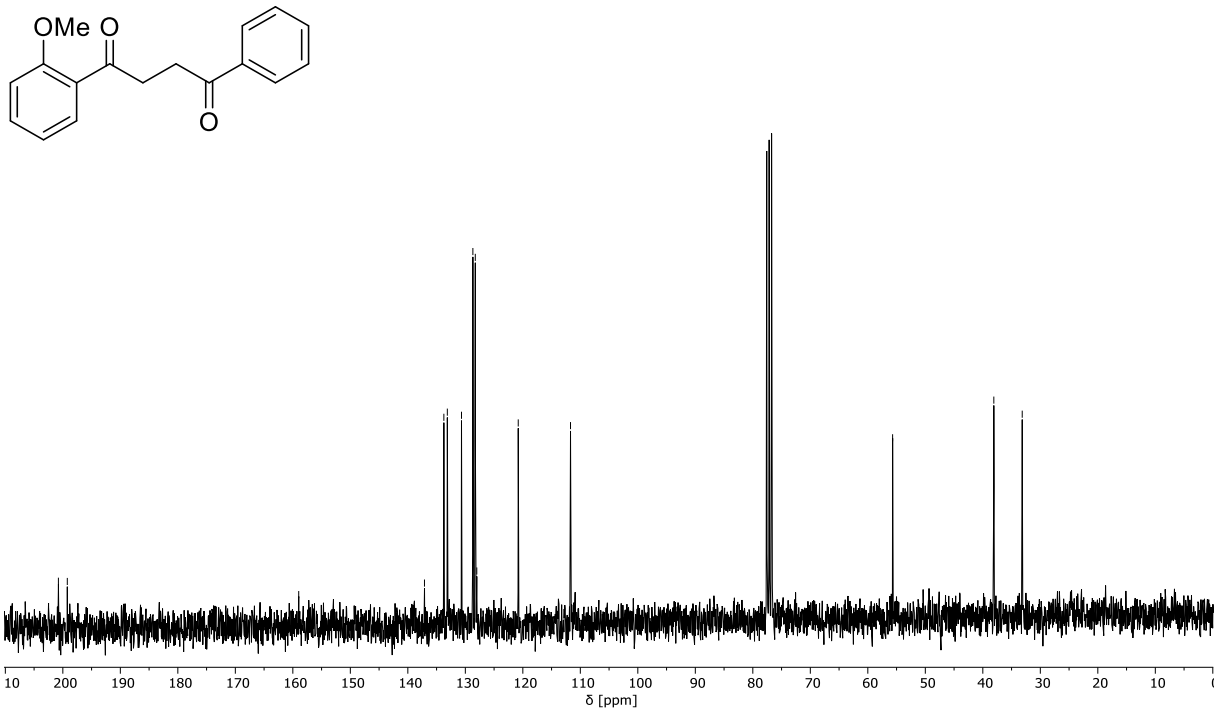
NMR Spectra of Literature-Unknown Substances

1-(2-methoxyphenyl)-4-phenylbutane-1,4-dione **4-22h**

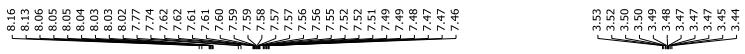
^{1}H NMR (300 MHz in $CDCl_3$)



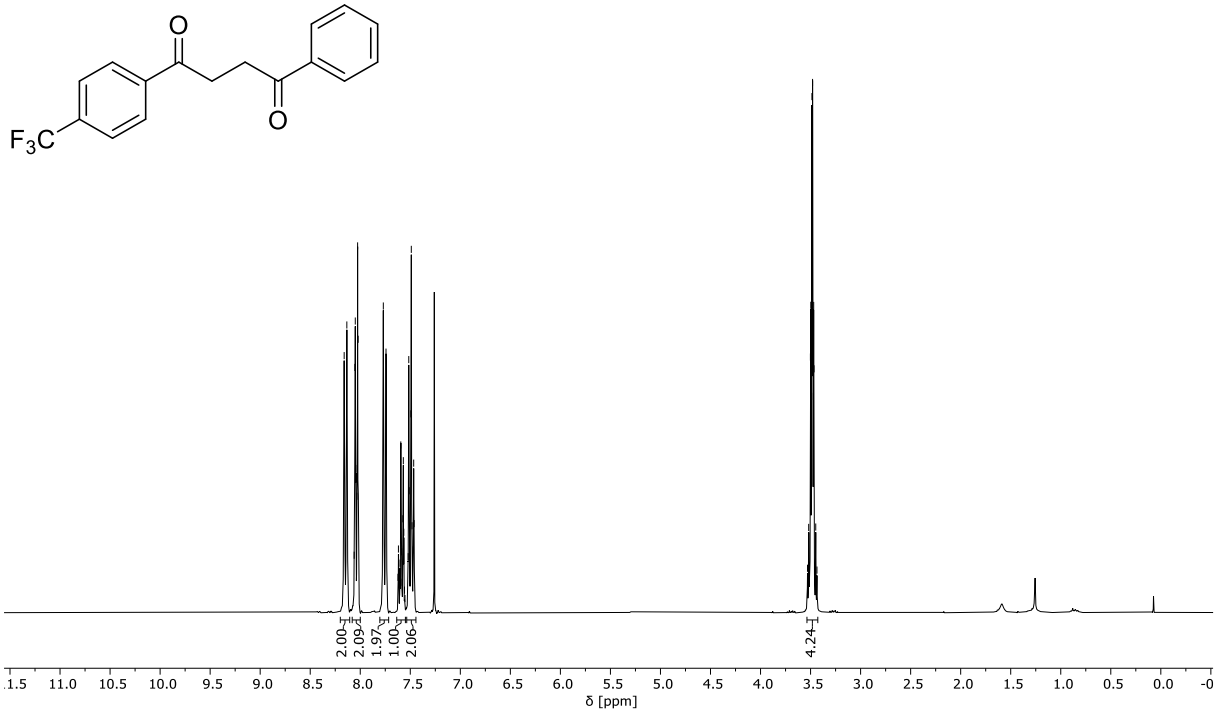
^{13}C NMR (75 MHz in $CDCl_3$)



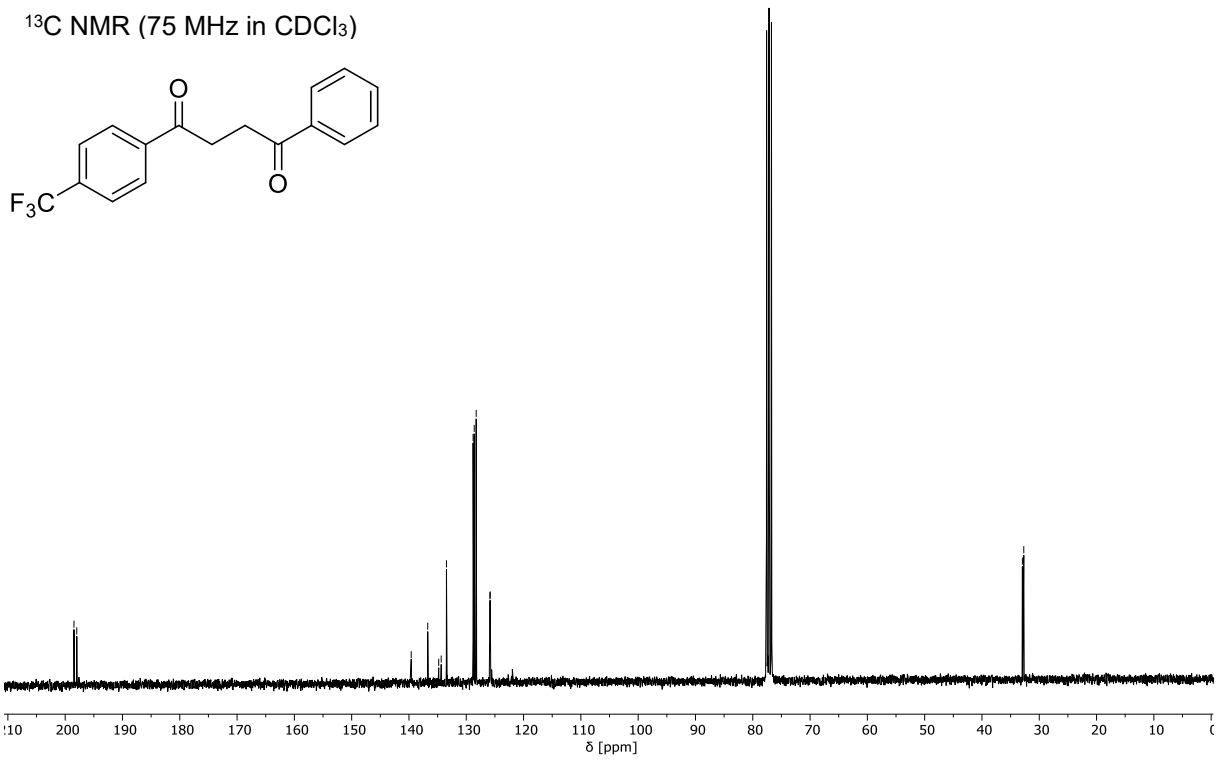
1-phenyl-4-(4-(trifluoromethyl)phenyl)butane-1,4-dione **4-22j**



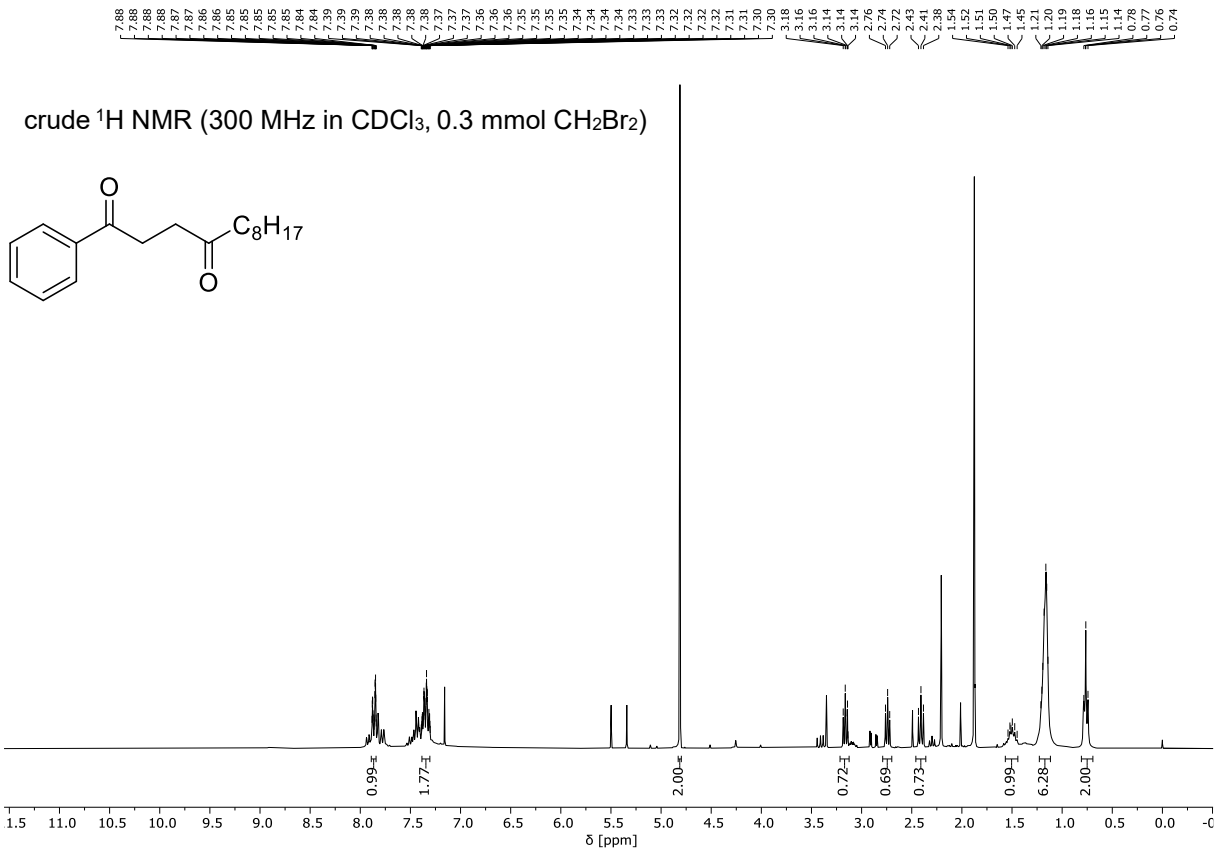
^{1}H NMR (300 MHz in $CDCl_3$)



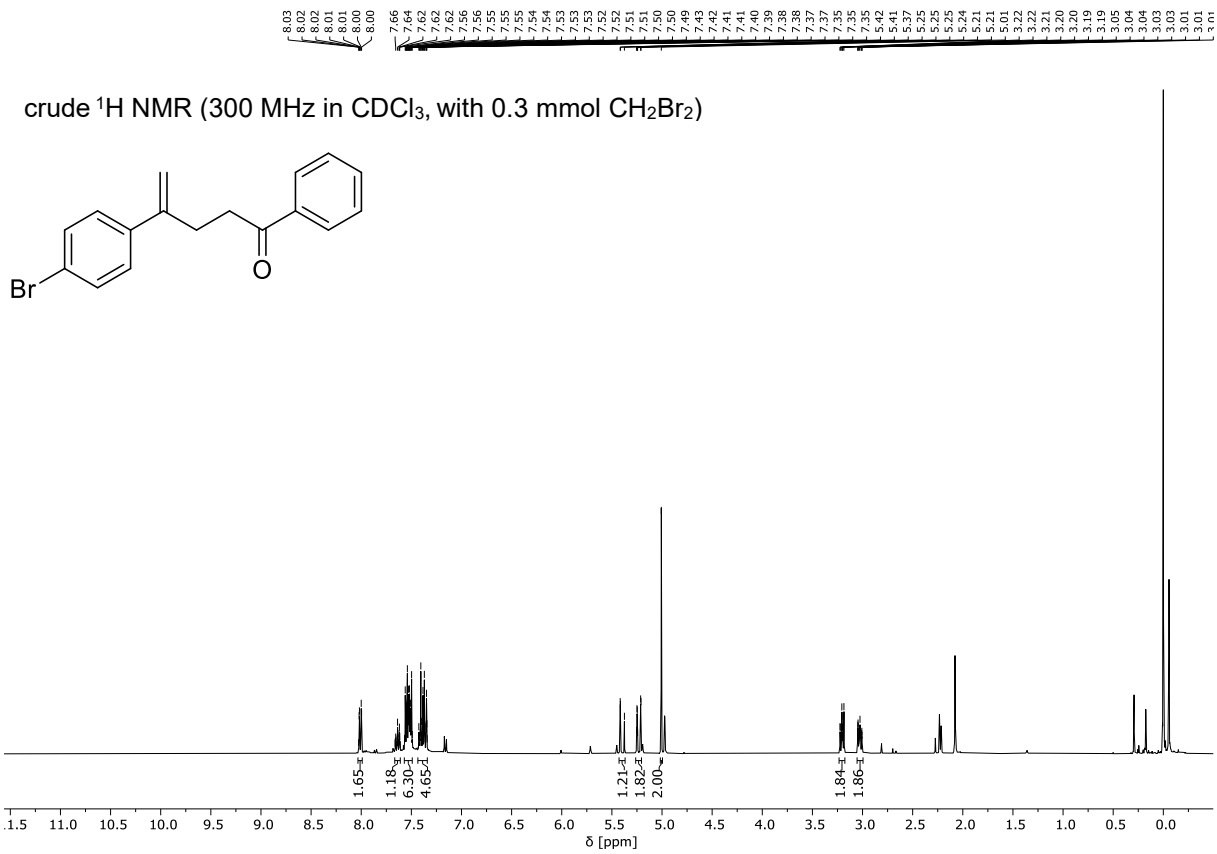
^{13}C NMR (75 MHz in $CDCl_3$)

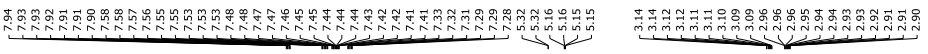


1-phenyldodecane-1,4-dione **4-22k**



4-(4-bromophenyl)-1-phenylpent-4-en-1-one **4-20d**





pre-purified ^{1}H NMR (300 MHz in $CDCl_3$)