Radical Aromatic Substitutions Mediated by Weak Bases

DISSERTATION

ZUR ERLANGUNG DES DOKTORGRADES DER NATURWISSENSCHAFTEN
(DR. RER. NAT.)
DER FAKULTÄT CHEMIE UND PHARMAZIE
DER UNIVERSITÄT REGENSBURG

vorgelegt von

Denis Koziakov

aus Kazan (Russische Föderation)

Regensburg 2017

Der experimentelle Teil dieser Arbeit wurde in der Zeit zwischen Oktober 2014 und September 2017 am Institut für Organische Chemie der Universität Regensburg unter Anleitung von Prof. Dr. Axel Jacobi von Wangelin angefertigt.

Die Arbeit wurde angeleitet von:		Prof. Dr. Axel Jacobi von Wangelin
Promotionsgesuch eingereicht am:		13.10.2017
Disputationsvortrag am:		10.11.2017
Prüfungsausschuss:	Vorsitz	Prof. Dr. Siavosh Mahboobi
	Erstgutachter	Prof. Dr. Axel Jacobi von Wangelin
	Zweitgutachter	Jun.-Prof. Dr. Ivana Fleischer
	Dritter Prüfer	Prof. Dr. Frank-Michael Matysik

Table of Contents

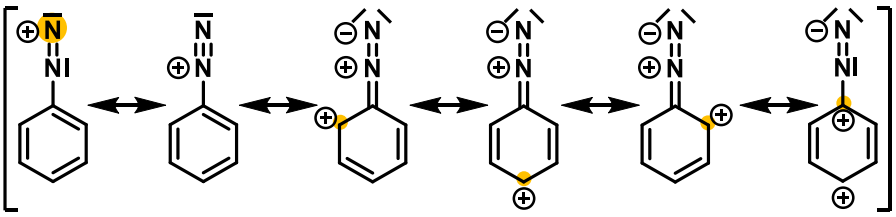
Chapter 1

- Introduction -

1. Introduction

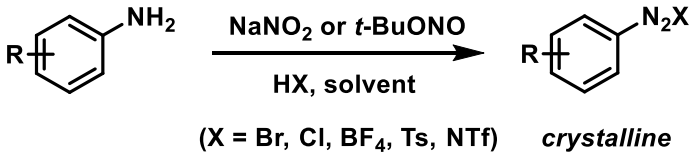
1.1. Properties and Preparation of Arenediazonium Salts

Arenediazonium salts were discovered as a new class of chemicals in 1858 by the German chemist Johann Peter Griess.[1] Over the past 150 years, these organic salts have significantly shaped the art of organic synthesis and today still attract great attention for their special properties and reactivities. Generally, diazonium compounds can be represented by the ionic formula $R-N_2^+ X^-$ (or more accurately in organic solvents by RN_2X), where R is a carbon-based residue (mostly aryl or alkyl) and X is a halide or more often a non-nucleophilic organic or inorganic anion. Alkyldiazonium salts exhibit low stability which poses severe limitations onto their isolation and application to organic synthesis. On the other hand, mesomeric stabilization renders many arenediazonium salts stable which can be easily handled under ambient conditions and therefore entertain a rich chemistry of aromatic *ipso*-substitution and *N*-terminal addition reactions (Scheme 1.1). Nevertheless, the stability of arenediazonium salts is strongly associated with the nature of R and X. For example, arenediazonium chlorides, which have been heavily used in the early years of discoveries of new reactions, are highly unstable and can be explosive above 0 °C. Today, stable crystalline salts with tetrafluoroborate,[2] tosylate (stable up to 600 °C),[3] and triflimide[4] counteranions are mostly being employed.



Scheme 1.1. Resonance structures of arenediazonium ions and sites of electrophilic reactivity.

The process of forming diazonium compounds was termed in the literature 'diazotation', 'diazoniation', or 'diazotization'. The most important method of preparation of arenediazonium salts is the treatment of aromatic amines with nitrous acid. Usually the nitrous acid is generated *in situ* from sodium nitrite or an organic nitrite and a mineral acid HX in aqueous or non-aqueous media (Scheme 1.2).[5]



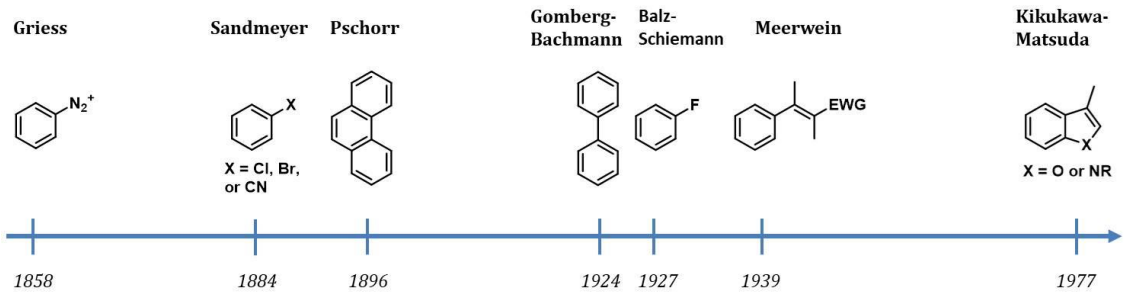
Scheme 1.2. Preparation of arenediazonium salts.

Most synthetically used arenediazonium salts bear a tetrafluoroborate anion due to their high stability and availability. These salts are highly crystalline compounds that can be stored in the dark at -20 °C for several years without major decomposition. Still, arenediazonium tetrafluoroborates are often generated *in situ* or prior to use from the corresponding aniline and *tert*-butyl nitrite (*t*BuONO) in the presence of boron trifluoride etherate, $BF_3 \cdot Et_2O$.[6]

1.2. Reactions of Arenediazonium Salts

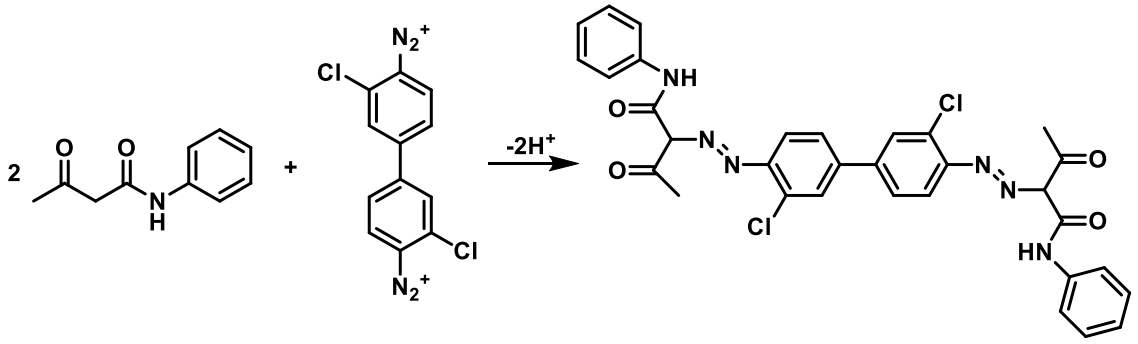
Since the discovery of arenediazonium salts, more than 150 years ago, a number of synthetically useful reactions have been developed. Their significance within the arsenal of organic synthesis methods is illustrated by the fact that many are name reactions and standard textbook knowledge today (Scheme 1.3).

In 1884, the Swiss chemist Traugott Sandmeyer discovered that benzenediazonium salts can be converted to halobenzenes with copper(I) halide. Benzonitrile was obtained when copper(I) cyanide was used.[7] At the end of the 19th century, Pschorr developed a method for the preparation of phenanthrenes from biphenyldiazonium salts under Cu catalysis. The mechanism of this reaction was proposed to involve the generation of an aryl radical by single-electron transfer (SET) from the copper(I) salt and subsequent radical substitution with the pendant aryl substituent.[8] In 1924, the American chemists Gomberg and Bachmann extended Pschorr's original biaryl synthesis to an intermolecular coupling.[9] Another important milestone discovery of new reaction methodologies based on arenediazonium salts was reported by the German scientists Balz and Schiemann in 1927. Aromatic fluorides, which were not accessible from the Sandmeyer reaction, could be obtained by thermal (or photolytic) decomposition of arenediazonium tetrafluoroborates.[10] In 1939, Hans Meerwein and co-workers reported the substitution of an arenediazonium salt with an electron-deficient alkene (i.e. α,β-unsaturated carbonyl compound) in the presence of copper(II) salts.[11] In 1977, the group of Mike P. Doyle discovered a new method of arenediazonium salt formation with organic nitrites in the absence of strong aqueous acids.[12] The field of metal-catalyzed cross-coupling reactions of arenediazonium salts as alternatives to aryl halides has flourished since the first mentioning of palladium-catalyzed C-C- and C-Het couplings by Kikukawa and Matsuda in 1977.[13]



Scheme 1.3. Brief history of the chemistry of diazonium salts.[14]

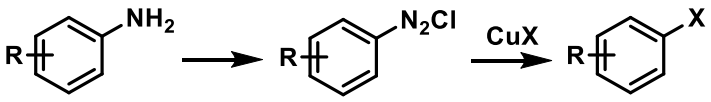
Moreover, the most widely applied synthesis method with arenediazonium salts is the azo-coupling. The resultant azo-benzene is the key functional motif of numerous dyes, pigments, and materials which are produced on large scales.[15] Besides anilines and phenols as nucleophilic coupling partners for such azo-couplings, acetoacetamides are being applied in commercial processes, as exemplified by the manufacture of the diarylide pigment 'Yellow 12'.[16]



Scheme 1.4. Synthesis of the pigment 'Yellow 12'.

Sandmeyer-type reactions of arenediazonium salts

Since the discovery of Sandmeyer (Scheme 1.5) numerous variations and improvements of his reaction have been developed and reported.

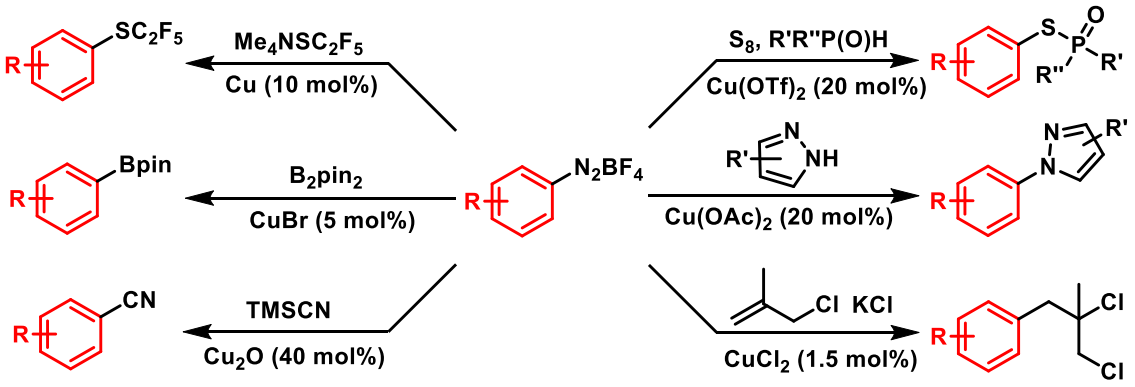


Scheme 1.5. Sandmeyer reaction.

Since its discovery numerous variations and improvements of the Sandmeyer reaction have been developed and reported. For instance, a few other metals ($ZnCl_2$, $FeCl_2$, CoCl) which are able to catalyze this reaction were proposed.[17,18] When just copper metal is used as the initiator, the reaction is called as the Gattermann reaction.[19] There is a hydroxylation method of aromatic diazonium

compounds known as the Sandmeyer hydroxylation reaction, which is initiated by copper salts.[20]

Incorporation of fluoro-containing moieties into molecules is very important task nowadays. In the last years usage of copper-mediated Sandmeyer-type methods for such purposes got high attention. Goossen and co-workers developed a Sandmeyer pentafluoroethylthiolation of aromatic and heteroaromatic diazonium compounds utilizing catalytic amounts of elemental copper (Scheme 1.6).[21] Aryl boronate esters were provided in the cross-coupling reaction of arenediazonium salts with bis(pinacolato)diboron utilizing 5 mol% of CuBr.[22] Copper(I) oxide as an alternative to toxic CuCN in the traditional Sandmeyer reaction was found.[23] Aromatic nitriles were synthesized with trimethylsilyl cyanide. Employment of copper catalyst allowed direct formation P-S and C-S bonds in one reaction from arenediazonium salts.[24] Under mild and ligand-free conditions pyrazole derivatives participated in coupling reactions with arenediazonium compounds in the presence of copper metal.[25] Also Meerwein reaction can be conducted in the presence of a copper salt.[26]

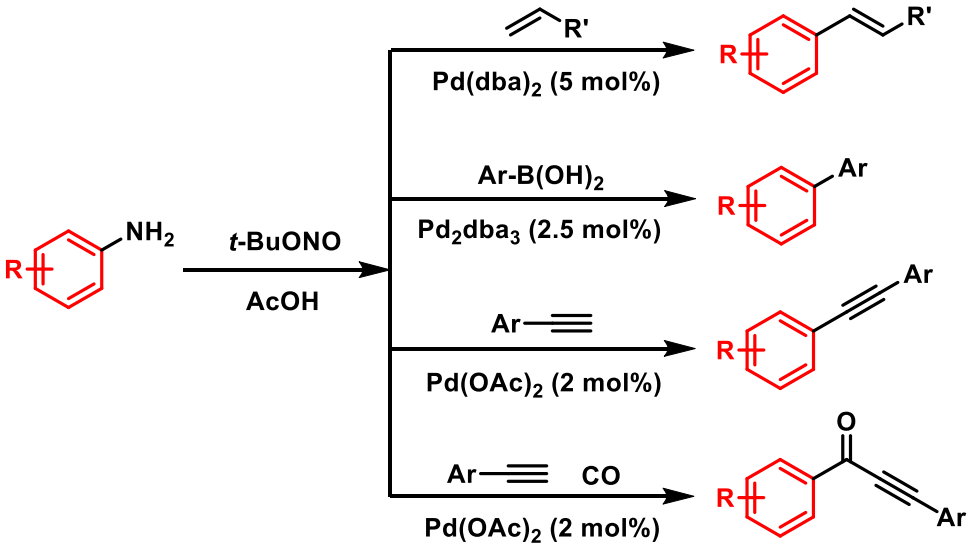


Scheme 1.6. Sandmeyer-type reactions of arenediazonium salts.

Arenediazonium salts in Palladium-catalyzed reactions

Since the first work on Pd-catalyzed cross-coupling reaction of diazonium salts for carbon-carbon and carbon-heteroatom bond formation of Kikukawa and Matsuda in 1977, a lot of research has been done in this field.[14] Generating arenediazonium compounds from anilines and *tert*-butyl nitrite in the presence of acetic and chloroacetic acids, arylation of olefins was performed under palladium catalysis (Scheme 1.7).[27] Other research groups continued using *in situ* diazotization of anilines for palladium-catalyzed coupling reactions. For example, Beller carried out olefination of anilines at room temperature employing ethylene at atmospheric pressure.[28] Wang developed Suzuki cross-coupling of anilines using aryl boronic acids.[29] Notable that one equivalent of acetic acid was enough for diazotization of anilines. Resembling a catalytic

system reported by Beller allowed Sonogashira coupling of anilines with both aliphatic and aromatic alkynes.[30] In this protocol anilines containing electron-donating and electron-withdrawing substituents reacted the same. Beller further expanded his method by adding carbon monoxide (10 bar) and employing similar conditions for the development of the carbonylative Sonogashira reaction.[31] The low stability of arenediazonium acetate salts (for example due to heating) occasionally could lead to the decrease of the product yields. Utilizing tetrafluoroboric acid (HBF_4) as alternative can influence acid-sensitive compounds, especially when excess of the acid is required. Furthermore, water can be also problematic for water-sensitive substrates because of hydrolysis, for instance. Therefore, Doyle and Bryker[32] reported, favored in palladium-catalyzed reactions, the anhydrous preparation of arenediazonium tetrafluoroborates that proceeds through nitrosyl fluoride as a diazotating reactive intermediate. This anhydrous diazotation procedure includes using ethereal solvents (THF, Et_2O) or CH_2Cl_2, alkyl nitrite and boron trifluoride. Several palladium-catalyzed couplings (Heck, Suzuki, Sonogashira) proceeded through anhydrous diazotization of anilines were reported.[33]



Scheme 1.7. Arenediazonium salts in Palladium-catalyzed reactions.

Reactions of arenediazonium salts mediated by other metals

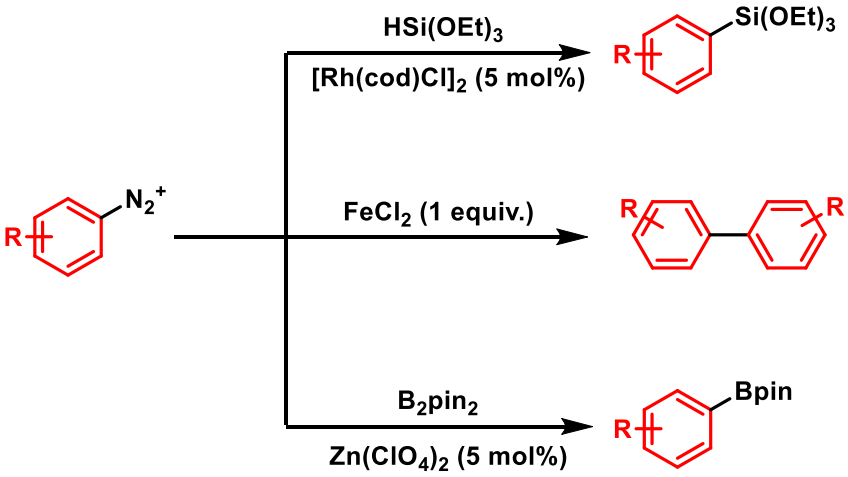
Reactions of arenediazonium salts in the presence of Pd and Cu are more spread than with other metals. There are a few examples where such reactions proceed with transition metals such as Rh, Fe, and Zn (Scheme 1.8).

Aryltriethoxysilanes were prepared from arenediazonium salts in rhodium-catalyzed silylation.[34] Interestingly, arenediazonium tetrafluoroborates gave no reaction products due to the presence of fluorinated groups which can probably interfere with silylation process. Therefore, arenediazonium tosylate salts were

chosen. Tetrafluoroborates, however, were employed for the development of the related hydrodediazoniation.

With stoichiometric amount of iron(II) chloride symmetrical biaryls were accessed from arenediazonium tetrafluoroborates.[35] Homocoupling of arenediazonium salts can be carried out without additives and inert conditions but in carbon tetrachloride as solvent.

Very recently a new zinc-catalyzed borylation method, which does not require any additional ligands, base or any other additives, was developed.[36] Moderate to excellent yields of arylboronates were achieved with B_2pin_2. Notably, the authors also successfully employed aryltriazenes as diazonium salt precursors in the presence of acid to obtain the same products.



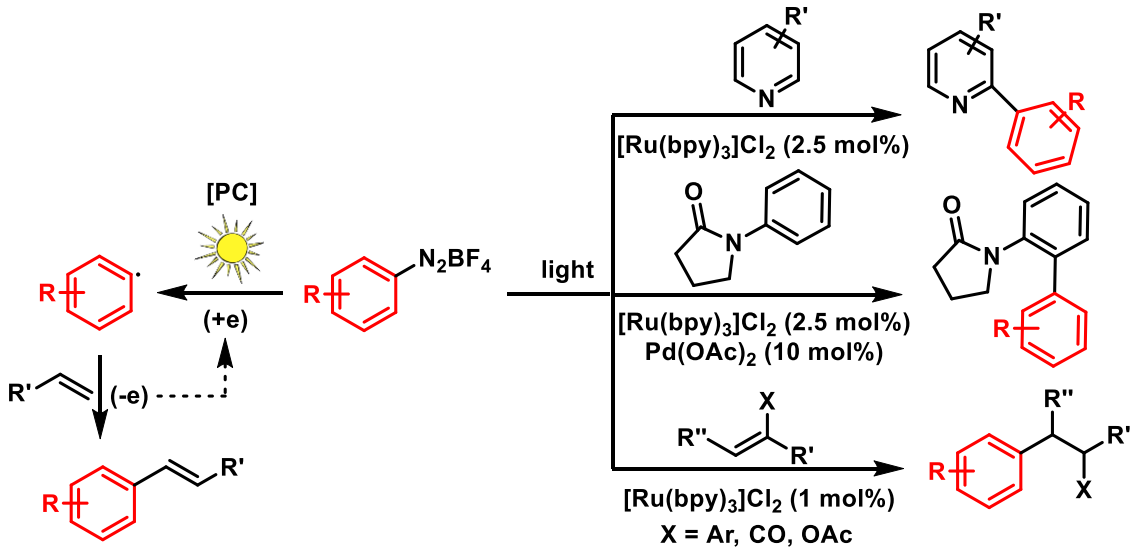
Scheme 1.8. Reactions of arenediazonium salts in the presence of Rh, Fe, and Zn.

Photoredox reactions of arenediazonium salts

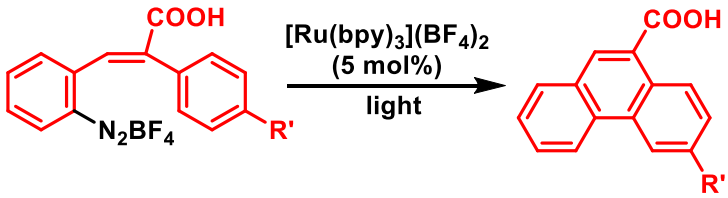
Arenediazonium salts are good electron acceptors as they easily release one of the best leaving groups (dinitrogen, N_2) to generate an aryl radical. In the past, transition-metal salts have been utilized as reductants. Recently, such electron transfer processes have been realized in the presence of photoredox catalysts under irradiation with visible light.[37] Arenediazonium salts usually absorb in the UV range and do not absorb visible light.[38] In order to use visible light several metal complexes and organic dyes were introduced as photoredox catalysts which absorb light in the visible spectral region. All photocatalytic reactions of arenediazonium salts can be divided into two groups according to a photoredox catalyst being used. One of them is $[Ru(bpy)_3]^{2+}$ (bpy = 2,2'-bipyridyl), which contains transition-metal Ru. This catalyst found application in two reaction types. First type is C-H arylation of (hetero)arenes under irradiation of a household light bulb (Scheme 1.9).[39,40,41] These reactions were

performed at room temperature. As additives Sanford used Pd catalyst,[39] Lei used one equivalent of TFA (trufluoroacetic acid).[41] Xiao conducted his coupling reaction in water.[40] Another type is arylation of olefins presented by two articles from the group of König.[42,43] Reactions were carried out already employing visible blue light.

In 1984, a french chemist Deronzier reported the photocatalytic Pschorr reaction utilizing the photoredox catalyst $[Ru(bpy)_3]^{2+}$ (bpy = 2,2'-bipyridyl) under the irradiation of blue light (Scheme 1.10). Tetrafluoroborate salt of the stilbenediazonium ion was successfully converted into the corresponding phenanthrene derivative.[44]



Scheme 1.9. Photoredox reactions of arenediazonium salts with Ru catalyst.

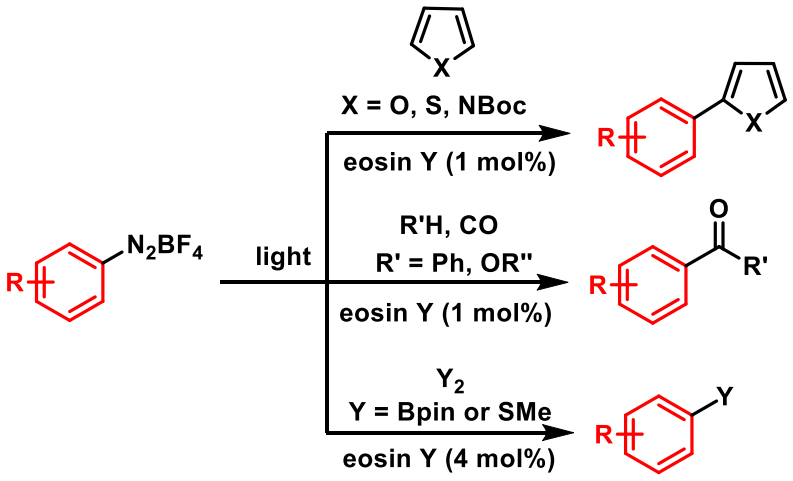


Scheme 1.10. Photocatalytic Pschorr reaction.

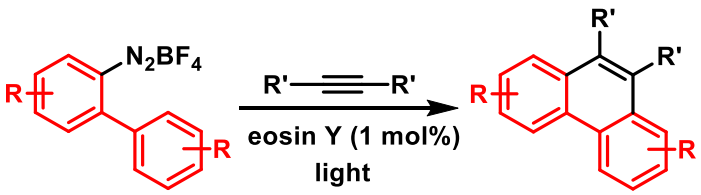
The second most common photocatalyst is Eosin Y. It is a metal-free inexpensive catalyst. Three different types of reactions were achieved by means of Eosin Y (Scheme 1.11). First, it is (hetero)aryl coupling of arenediazonium tetrafluoroborates in DMSO with 5-membered heterocycles compising O, S, or N as a heteroatom.[45,46] In case of the protocol of Ranu arenediazonium salts were generated *in situ* from *tert*-butyl nitrite.[46] Starting from 2015, photocatalytic carbonylations of arenes utilizing arenediazonium salts began to appear. Liu and co-workers discovered an efficient route to aromatic ketones from arenediazonium salts, carbon monoxide, and (hetero)arenes.[47] Our group

reported the synthesis of alkyl benzoates from arenediazonium salts, carbon monoxide, and different alcohols as both reagent and solvent at room temperature under irradiation with visible green light.[48] Eosin Y succeeded also in borylation and thiolation reactions.[49,50]

Chinese chemists under the supervision of Zhou reported visible-light induced benzannulation of biaryldiazonium salts with alkynes (Scheme 1.12).[51] A number of different phenanthrenes were obtained with Eosin Y as photoredox catalyst.



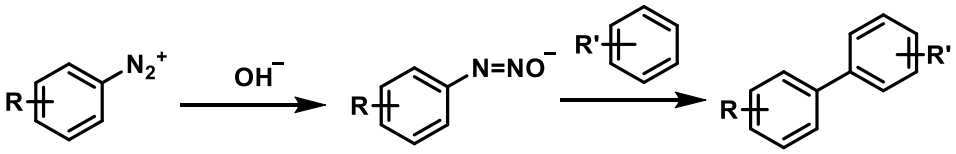
Scheme 1.11. Photoredox reactions of arenediazonium salts with Eosin Y catalyst.



Scheme 1.12. Benzannulation of biaryldiazonium salts with alkynes.

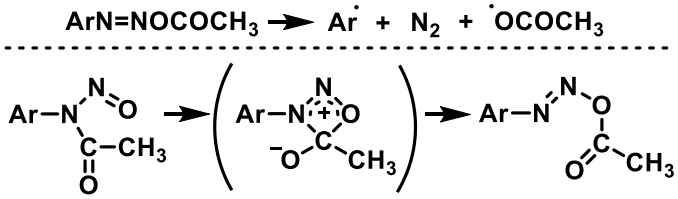
1.3. Reactions of Arenediazonium Salts Mediated by Weak Bases

In 1924, unsymmetrical biaryls were prerared by coupling of arenediazonium salts with arene compounds in alkali mixture.[52] This reaction is known as the Gomberg-Bachmann reaction. The coupling proceeds through formation of aryl diazotate (Scheme 1.13). The main drawback of the reaction was the yields which were often not more than 40%.



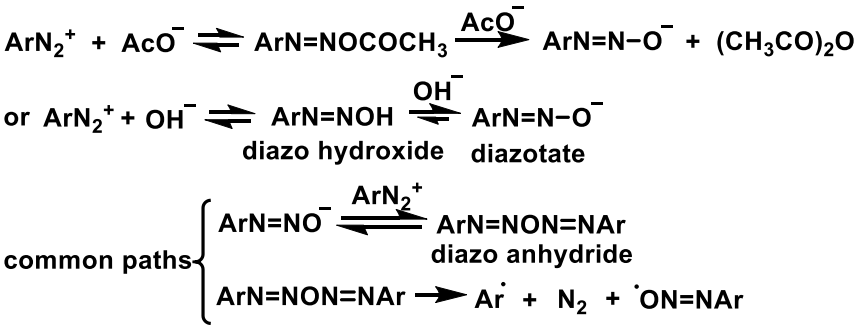
Scheme 1.13. The synthesis of biaryl compounds in alkali solution.

In 1952, Hey and co-workers showed that aryl radical can originate from the decomposition of diazoacetate, which was formed from arenediazonium salt and acetate (Scheme 1.14, top).[53] This diazoacetate is suggested to form *via* a four-center 1,3-rearrangament (Scheme 1.14, bottom).[54]



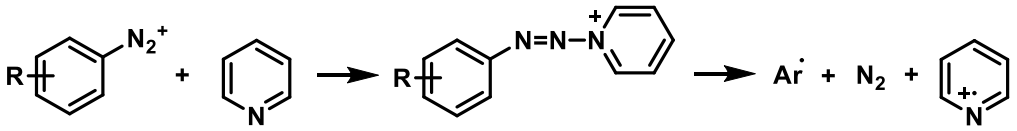
Scheme 1.14. Decomposition and formation of diazoacetate.

In 1965, the group of Rüchardt offered a description of the mechanism of the Gomberg-Bachmann reaction with acetate and hydroxide anions (Scheme 1.15).[55] They, however, excluded the generation of free carboxylate radicals.



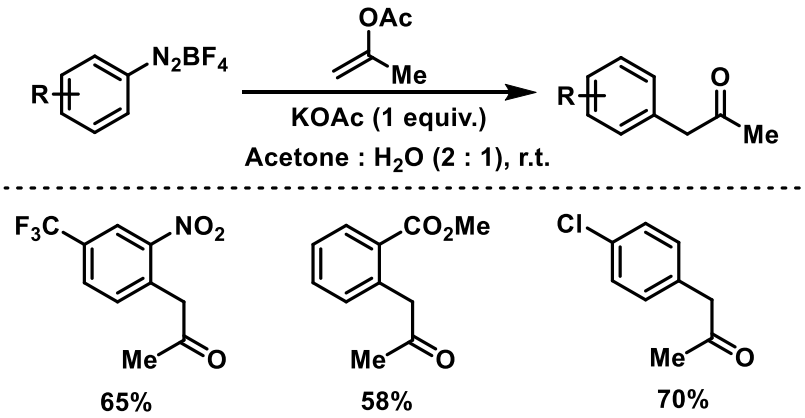
Scheme 1.15. Mechanism of the Gomberg-Bachmann reaction according to Rüchardt.

Later it was shown that also 1 equiv. pyridine can provide a convenient source of phenyl radicals.[56] The mechanism includes homolysis of *N*-phenylazopyridinium tetrafluoroborate (Scheme 1.16).



Scheme 1.16. Mechanism of the interaction between arenediazonium salt and pyridine.

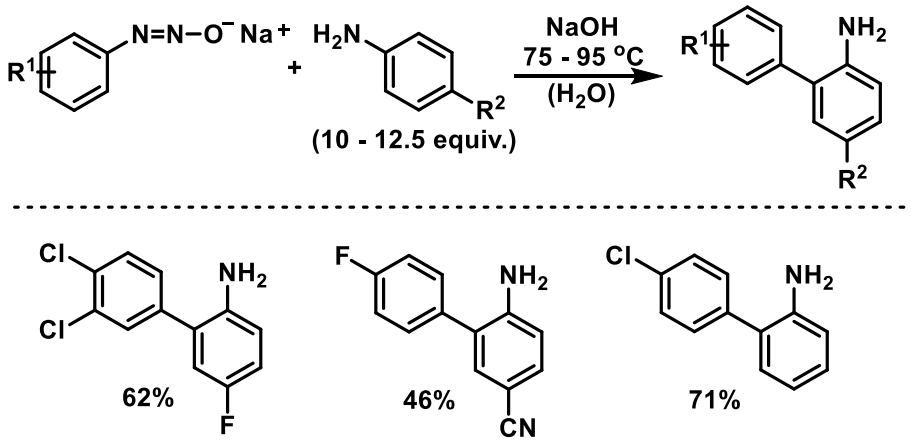
After several decades, initiation of arenediazonium salts by weak bases got again much attention. In 2006, Molinaro and co-workers offered a protocol for the production of α-aryl methyl ketones from arenediazonium salts and isopropenyl acetates under mild conditions.[57] After testing several Cu, Fe, and Pd catalysts, which gave relatively low yields, weak bases NaOAc and KOAc demonstrated the most efficient activity. For better solubility of potassium acetate aqueous acetone solution was used as a solvent mixture. Only 1 equiv. of KOAc was required (Scheme 1.17). Yields were in the range between 13% and 76%. Mechanistic studies were unfortunately not presented. Advantages of this method include employing non-toxic starting materials and applying to the multi-kg scale preparation of one of the products (almost 5 kg).



Scheme 1.17. Synthesis of α-aryl methyl ketones with KOAc as a weak base.

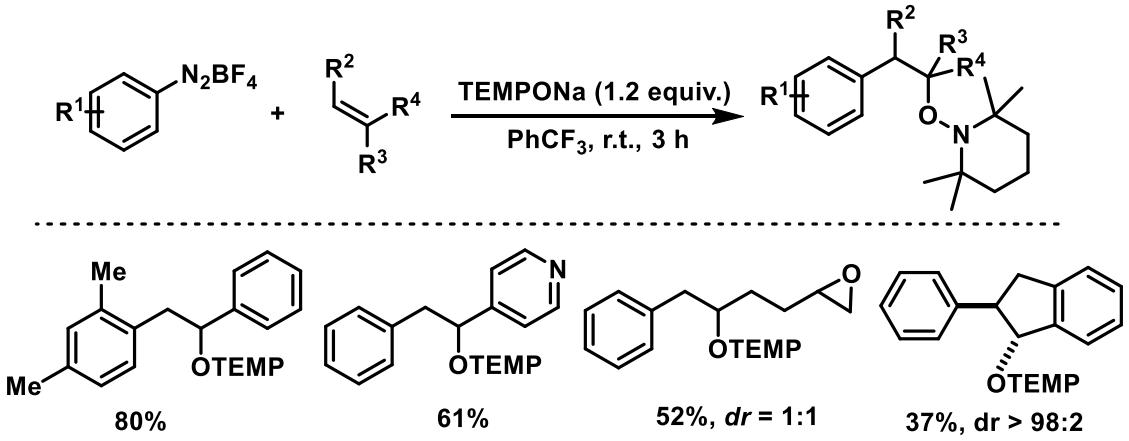
In 2012, a group of Heinrich developed a new version of the Gomberg-Bachmann reaction.[58] In this system were afforded 2-aminobiphenyls from aryl diazotates and anilines under basic conditions of aqueous solution of sodium hydroxide (Scheme 1.18). The metal-free reaction eliminated ionic side reactions (such as formation of triazenes and azo compounds). The authors claimed that for the first time was used the highly radical-stabilizing effect of the free amino substituent. Aryl diazotates as substrates contained mostly fluorine or chlorine in *para*-position of the benzene ring, as polar functional

groups (such as nitro or cyano) produce more triazenes and azo compounds. Therefore, it is difficult to say whether the proposed method can be named as general. Regarding anilines authors tried to change substituents in order to define group tolerance. It was established that electron-donating groups in anilines are able to decrease the product yields as it was shown in case of 4-anisidine (OMe in *p*-position) and 4-phenetidine (OEt in *p*-position) when yields were low. Another disadvantage of the protocol is the possibility of by-product formation when the attack directs not in *ortho*-position of anilines. The authors showed that synthesized 2-aminobiphenyl derivatives are key intermediates for further preparation of compounds used in crop protection, which are in the present time can be achieved only making use of transition metal-catalyzed cross-coupling reactions.



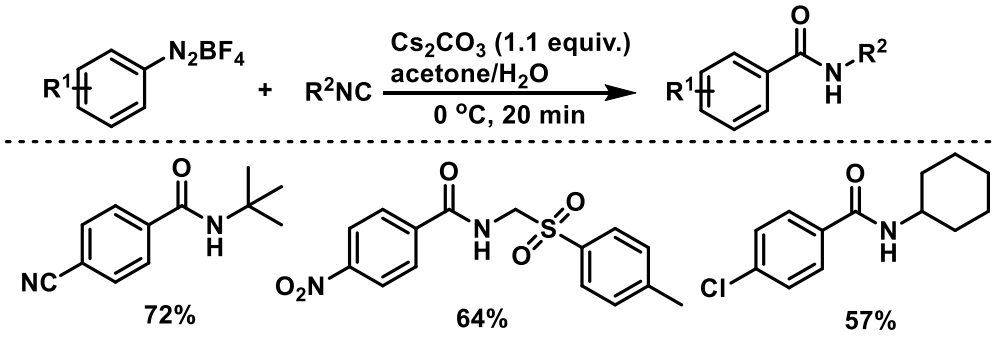
Scheme 1.18. C–H activation of anilines with aryl diazotates.

In the same year, Studer et al. reported the transition-metal-free oxyarylation of alkenes with arenediazonium salts and TEMPO-Na (Scheme 1.19).[59] TEMPO-Na reacted as a reducing agent and was converted through SET (single electron transfer) to the TEMPO (2,2,6,6-tetramethylpiperidin-1-yl)-oxyl radical, which then acted as an oxidant. Interestingly, α,α,α-trifluorotoluene was revealed to be the best solvent during optimization investigations. Different substituents in different positions both in arenediazonium tetrafluoroborates and alkenes were tested and proved to be tolerated with this system. Moreover, steric effects of the *ortho*-substituents were insignificant. Gram-scale experiments were performed. The proposed protocol allowed reactions with styrene derivatives and, with lower yields, also aliphatic alkenes (such as terminal bromide and terminal epoxide alkenes). The oxyarylation products were obtained in good to excellent yields. The proposed radical mechanism was confirmed by two control experiments.



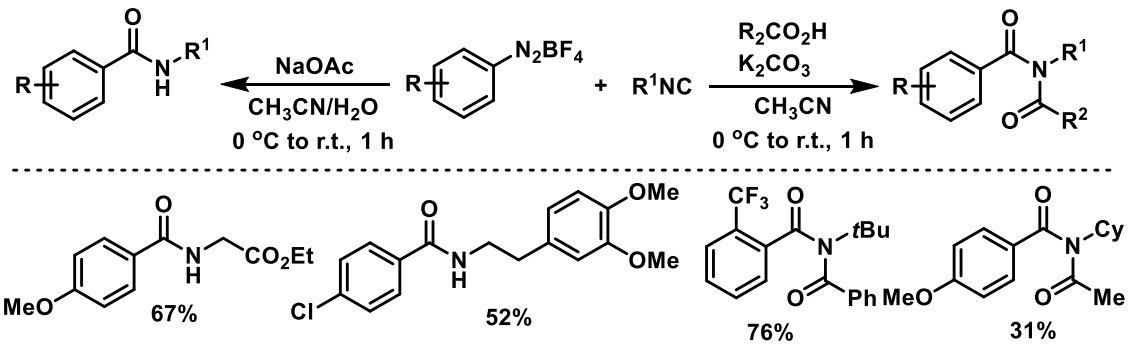
Scheme 1.19. Oxyarylation of alkenes with arenediazonium salts and TEMPO-Na.

In 2013, Zhu and Xia developed a transition-metal-free carboxyamidation process.[60] The process includes arylation of isocyanides which is initiated by the base Cs_2CO_3 (Scheme 1.20). It was demonstrated that palladium catalyst gave very poor yields of arylcarboxyamides. An acetone-water mixture was found to be the best solvent mixture. Better yields were achieved with arenediazonium salts bearing electron-withdrawing functional groups, electron-rich substrates gave lower yields even with increased amount of isocyanide. Even though it is challenging to afford iodine-containing carboxyamides by transition-metal catalysis, substrates with iodine substituents were tolerated in the system. Different isocyanides were tested. Aryl isocyanide (R^2 = Ar) was less consistent with this method. Radical trapping experiments with TEMPO proved the formation of the aryl radical intermediate. Addition to the isocyanide formed the imidoyl radical, and one-electron oxidation occurred followed by hydration and tautomerization of the nitrilium intermediate. However, the authors also assumed the possible coexistence of an ionic pathway.



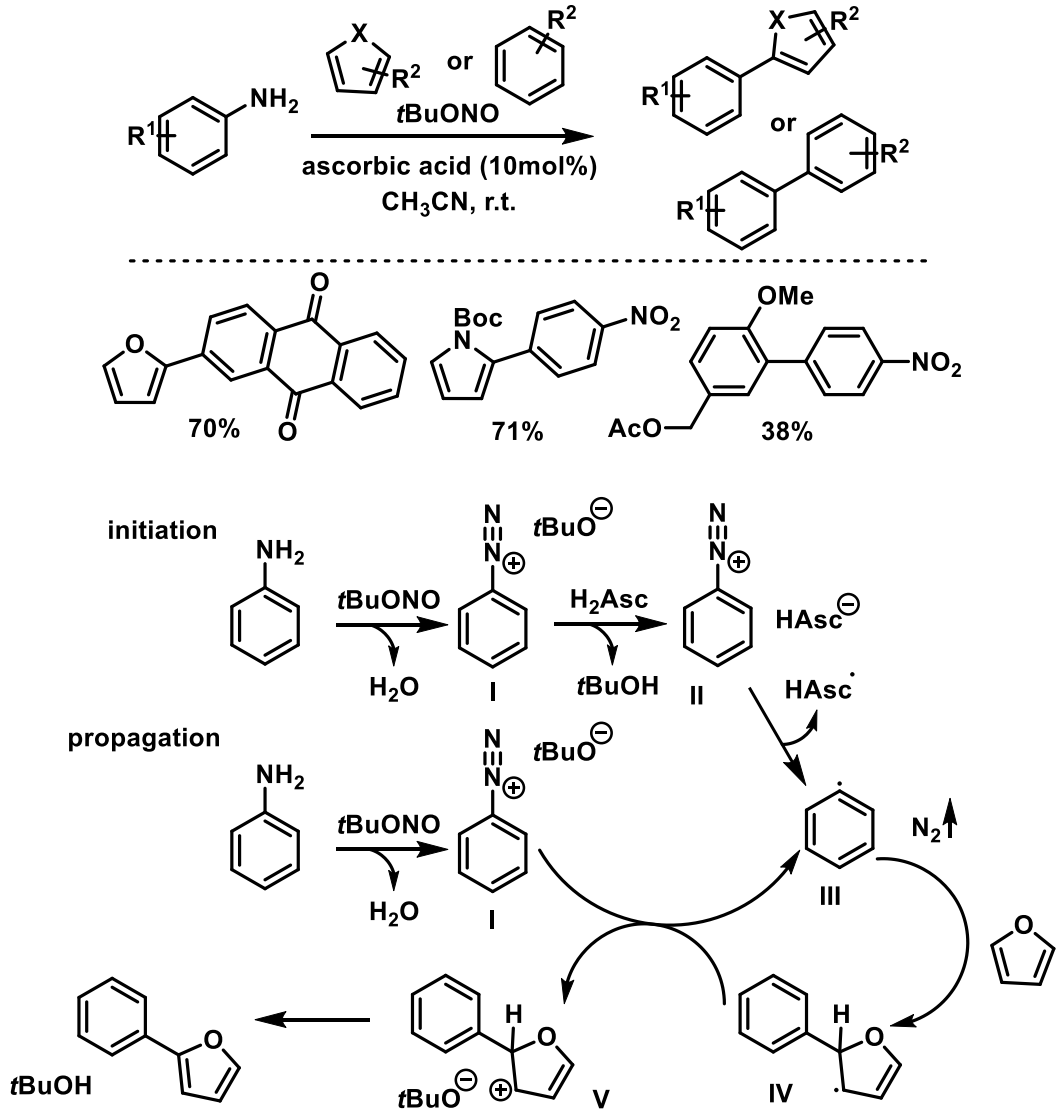
Scheme 1.20. Preparation of arylcarboxyamides from arenediazonium salts and isocyanides mediated by cesium carbonate.

Similar transformations were conducted by another group of chemists. In their work arenediazonium salts reacted with isocyanides in the presence of sodium or potassium carboxylates.[61] Again, nitrilium intermediates are formed, which may further react with water to form amides or with carboxylic acids to form imides after Mumm rearrangement (Scheme 1.21). Different diazonium salts and isocyanides were tested. Yields were moderate, but direct formation of amides from anilines afforded higher yields. Interestingly, in the synthesis of imides two ways can be exploited. One way is using acetic acid and potassium carbonate, another one is the direct use of potassium acetate. The direct method was found to be more satisfying. Authors proposed four different possible mechanisms, both radical and non-radical. Mechanistic experiments unfortunately were not presented.



Scheme 1.21. Base-meadiated three-component arylation of isocyanides.

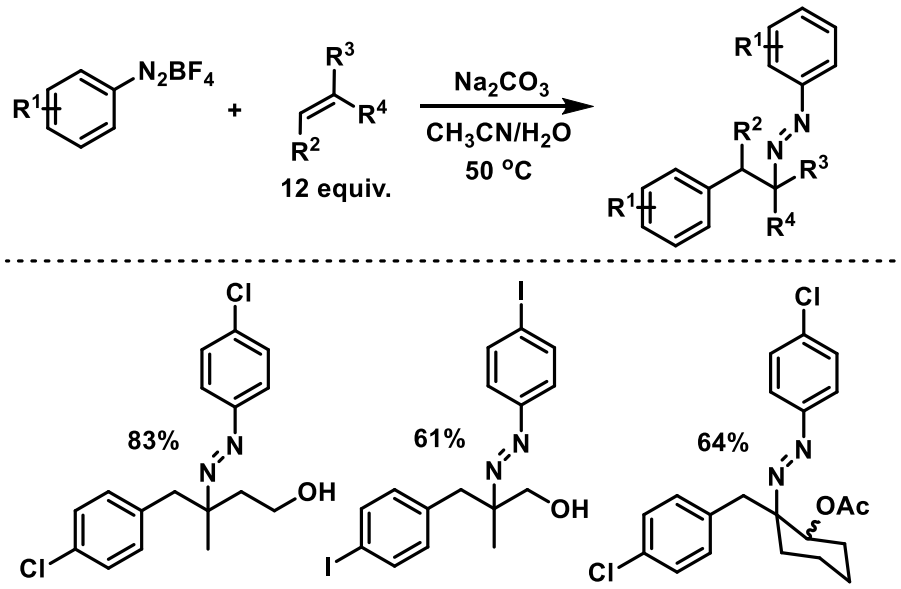
The application of ascorbic acid (vitamin C) as catalytic radical initiator was demonstrated in C–H arylations of (hetero)arenes.[62] Arenediazonium salts were generated *in situ* from anilines and reduced to aryl radicals by ascorbic acid. The aryl radical reacts with a (hetero)arene providing the desired biaryl products (Scheme 1.22). No acid was used for the diazotization, catalytic amounts of ascorbic acid were sufficient. Anilines bearing electron-withdrawing substituents gave better yields. Different heteroarenes were applied, including benzene. Radical mechanism was proposed on the basis of radical trapping experiments with TEMPO. The mechanism was postulated to involve formation of the diazonium salt **I** (Scheme 1.22, bottom) from aniline sequential anion exchange with the ascorbate to give **II**. One-electron reduction affords the aryl radical **III** which undergoes homolytic aromatic substitution to give **IV**. Radical chain propagation occurs by back-electron transfer with another molecule of diazonium salt **I**. The resultant carbocation **V** undergoes rapid deprotonation and rearomatization to give the biaryl product.



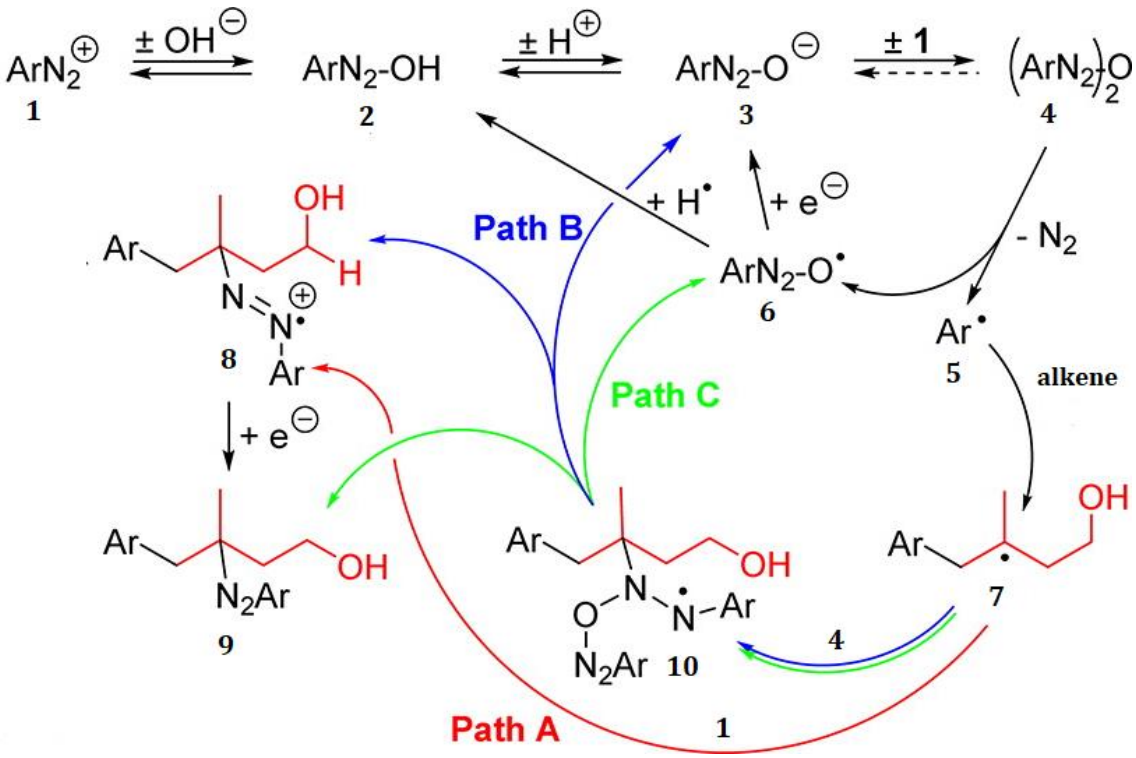
Scheme 1.22. Direct C–H arylation of (hetero)arenes with anilines and ascorbic acid.

In 2015, Heinrich and co-workers developed a new variant of the Meerwein arylation, the radical carboamination of alkenes with arenediazonium salts which form aryl radicals in the presence of the weak bases Na_2CO_3, K_2CO_3, or KOAc.[63] The interesting feature of this system is that two nitrogen atoms of the arenediazonium salts remain in the final products (Scheme 1.23). Sodium carbonate gave the highest selectivity and minimal amounts of the pyrazolidone by-product. Water as a co-solvent was employed. Good yields were observed only with halogenated substrates. Different functional groups of alkenes were tolerated (such as alkohols, esters, ketones, phenyl ethers, cyclic acetales, and azides). Mono-substituted alkenes gave azo compounds with low yields. The authors assumed that the reaction proceeds through the same intermediates of the Gomberg-Bachmann reaction. Three different mechanistic pathways were discussed (Scheme 1.24).

The arenediazonium salt **1** was stepwise converted through diazohydroxide **2**, diazotate **3**, and diazoanhydride **4** to aryl radical **5**, nitrogen, and diazenyloxyl radical **6**. Then aryl radical addition to 3-methyl-3-buten-1-ol occurs to give alkyl radical **7**. Further three mechanistic pathways are possible. Alkyl radical **7** may interact with the starting arenediazonium ion forming radical cation **8** and then azo compound **9** (path A). Paths B and C include formation of a radical **10**, fragmentation of which can proceed through **8** (path B) or can give directly the final product **9** (path C).

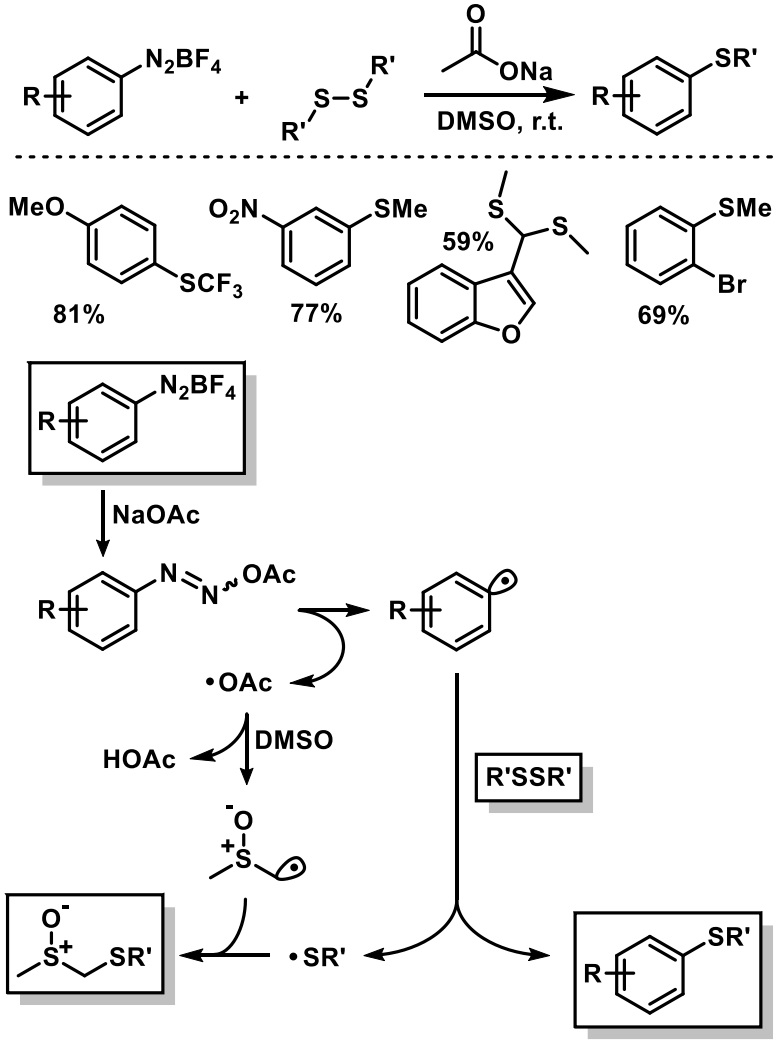


Scheme 1.23. Base-induced radical carboamination of alkenes.



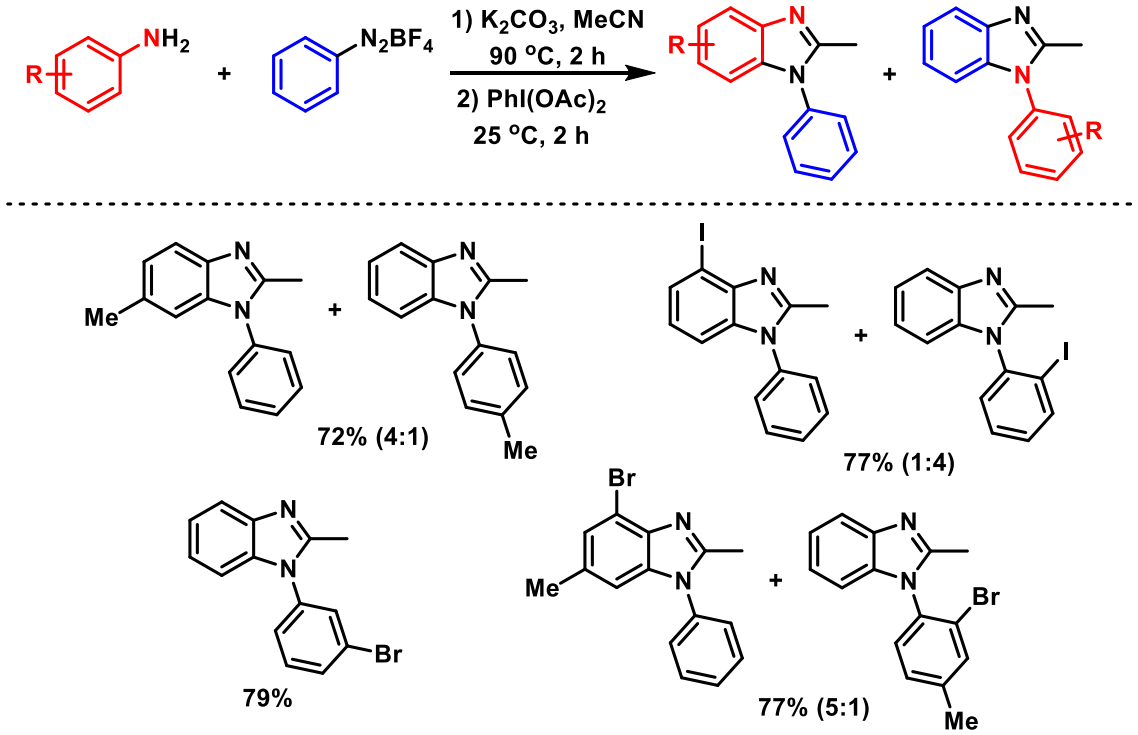
Scheme 1.24. Reaction mechanisms of carboamination.

In 2016, our group developed metal-free radical thiolations mediated by weak bases.[64] We tested different both strong and weak bases and found that NaOAc showed the best reactivity. Reactions were performed between arenediazonium salts and disulfides at room temperature (Scheme 1.25, top). Good reactivity was shown regardless the nature of a substituent or a disulfide. By using this system we managed to carry out selenations, tellurations, and radical cyclization-thiolation under similar conditions. Elemental sulfur was also compatible with the conditions but with lower yields. We performed some mechanistic experiments and got reliable evidence that proves high probability of the postulated mechanism (Scheme 1.25, bottom). The mechanism involves homolysis of the diazoacetate. It was proved that during the reaction are also thiyl, acetyloxyl, and dimsyl radicals formed. DFT calculations supported the presented mechanistic pathway.



Scheme 1.25. Thiolations mediated by very weak bases and postulated mechanism.

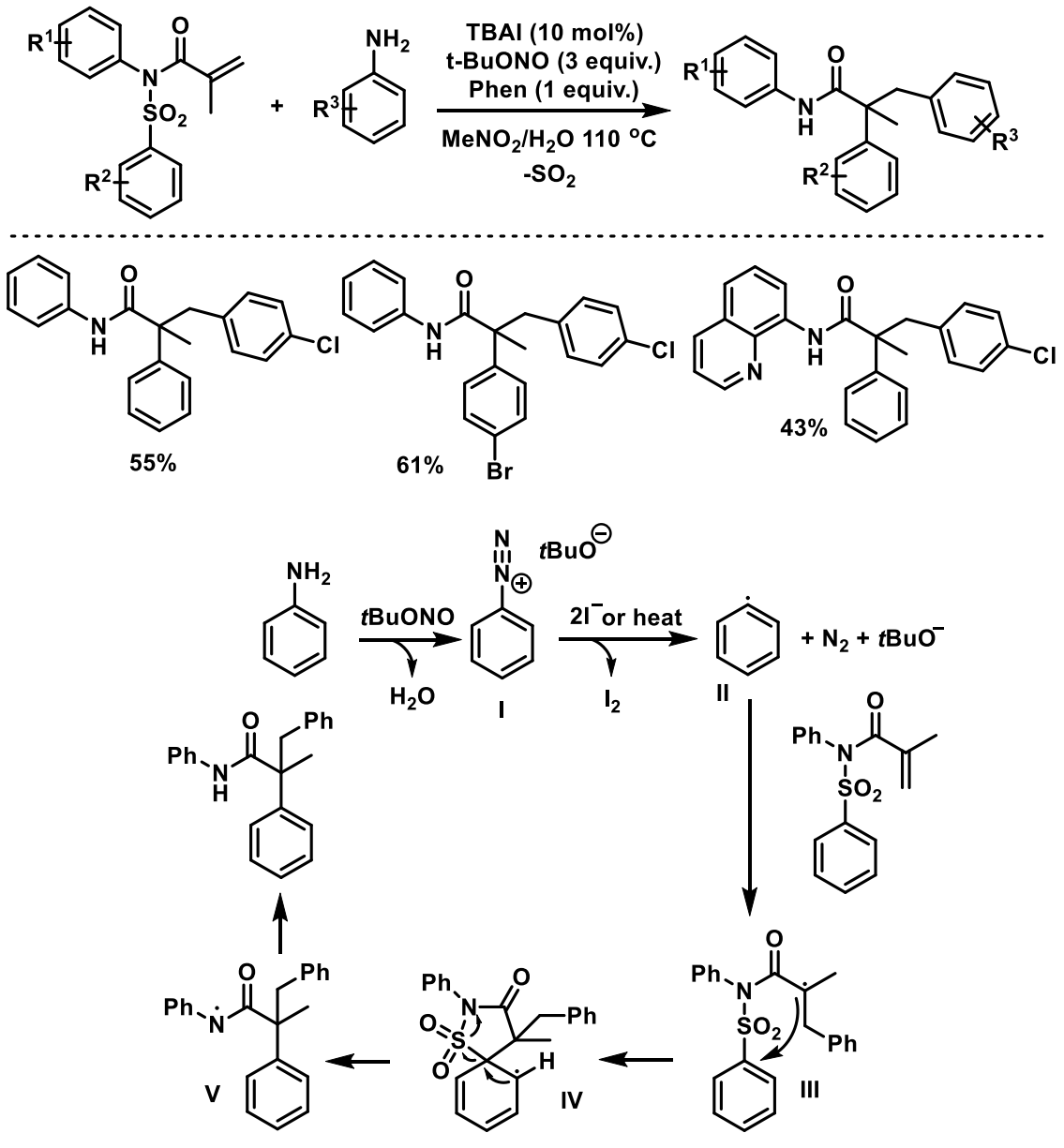
In the same year, Youn and Lee reported the one-pot synthesis of *N,N'*-diarylamidines and *N*-arylbenzamidazoles from arenediazonium salts, nitriles, and free anilines.[65] Potassium carbonate and acetonitrile were found as the most effective base and solvent, respectively, to give the amidine products. Other bases and solvents did not produce amidines at all. Addition of $PhI(OAc)_2$ triggered the oxidative cyclization to give *N*-arylbenzamidazoles (Scheme 1.26). The authors investigated very carefully influence of substituents of the starting reactants. For instance, different substituents of the anilines were well tolerated, except for anisidine derivatives where decomposition occurred. Strongly electron-donating substituents, such as OMe, at the *ortho*- and *para*-positions of the diazonium salts did not work well. Among nitriles bulky *tert*-alkyl nitriles failed to give products. The authors presented the method of *in situ* preparation of the arenediazonium salts. Although some experiments with TEMPO radical were performed, authors were not sure whether radical or ionic pathways in the reaction mechanism take place.



Scheme 1.26. Synthesis of *N*-arylbenzamidazoles from arenediazonium salts in the presence of a base.

A radical cascade arylation, aryl migration, and desulfonylation of conjugated alkenes was reported by Pan.[66] Catalytic amounts of tetrabutylammonium iodide (TBAI) triggered the formation of aryl radicals from diazonium salts (Scheme 1.27, top). Different bases were tested, among them phenanthroline (phen) was the most efficient. Nitromethane was found to be the best solvent. Aniline bearing strong electron-withdrawing substituent NO_2 gave decreased

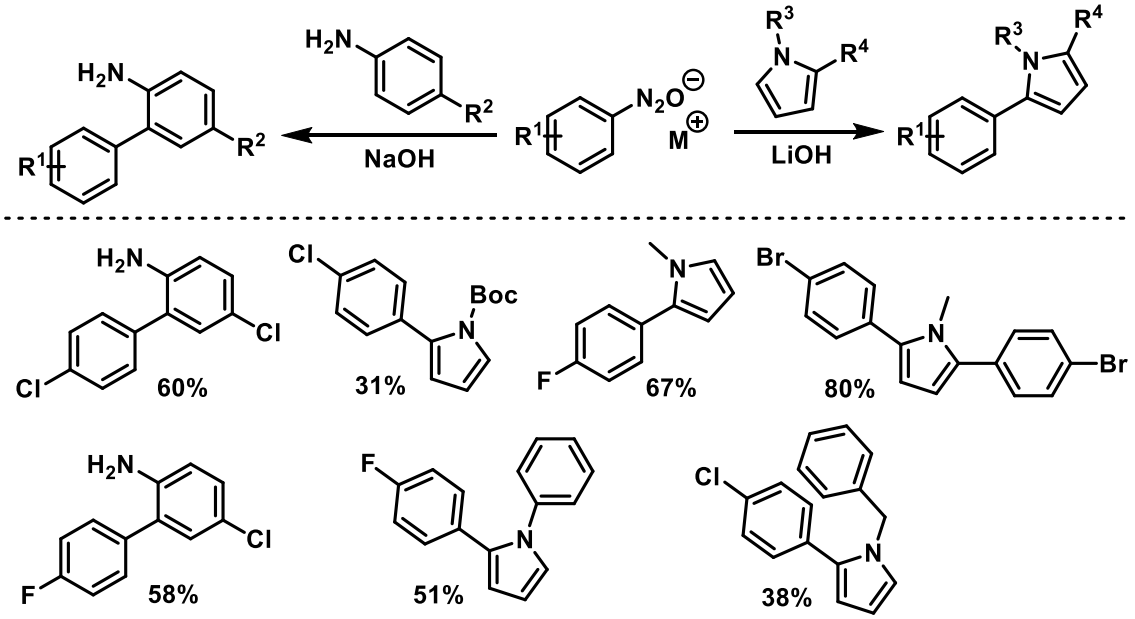
yield of the product in comparison to other anilines. Steric hindrance slowed down the reaction, especially at the methacrylamide starting materials. The authors carried out one experiment with TEMPO (2,2,6,6-tetramethylpiperidin-1-yl)-oxyl and proposed radical mechanism of their reaction. Generated from the diazonium salt **I** (Scheme 1.27, bottom) aryl radical **II** adds to double carbon bond to form radical intermediate **III**. This step is followed by generation of intermediate **IV** through 5-*ipso*-cyclization and amidyl radical **V** *via* desulfonylation. The last radical intermediate abstracts a hydrogen atom to obtain the final product.



Scheme 1.27. Radical cascade reaction of conjugated alkenes.

Very recently a group of Heinrich presented radical arylation reactions *via* aryldiazotates.[67] In this work in comparison to the publication in 2012[58] were

included pyrroles along with anilines as reactants (Scheme 1.28). Different conditions for diazotization and diazotate formation were screened. Interestingly, argon atmosphere was the most efficient. One of the drawbacks is possible formation of triazenes. Gram-scale reactions were presented. Computational studies were performed by authors in order to support the mechanistic insights and to explain narrow substrate scope and low yields.



Scheme 1.28. Radical arylation *via* aryldiazotates.

1.4. References

[1] P. Griess, *Liebigs Ann. Chem*. **1858**, *106*, 123–125.

[2] D. T. Flood, *Org. Synth*. **1943**, *2*, 295–298.

[3] V. D. Filimonov, M. Trusova, P. Postnikov, E. A. Krasnokutskaya, Y. M. Lee, H. Y. Hwang, H. Kim, K.-W. Chi, *Org. Lett*. **2008**, *10*, 3961–3964.

[4] M. Barbero, M. Crisma, I. Degani, R. Fochi, P. Perracino, *Synthesis* **1998**, 1171–1175.

[5] a) M. P. Doyle, W. J. Bryker, *J. Org. Chem.* **1979**, *44*, 1572–1574; b) G. Schiemann, W. Winkelmüller, *Org. Synth.* **1943**, *2*, 299–302.

[6] M. B. Andrus, C. Song, *Org. Lett*. **2001**, *3*, 3761–3764.

[7] a) T. Sandmeyer, *Ber. Dtsch. Chem. Ges*. **1884**, *17*, 1633–1635; b) T. Sandmeyer, *Ber. Dtsch. Chem. Ges*. **1884**, *17*, 2650–2653.

[8] R. Pschorr, *Ber. Dtsch. Chem. Ges*. **1896**, *29*, 496–501.

[9] a) M. Gomberg, W. E. Bachmann, *J. Am. Chem. Soc*. **1924**, *46*, 2339–2343; b) O. C. Dermer, M. T. Edmison, *Chem. Rev*. **1957**, *57*, 77–122; c) A. Wetzel, G. Pratsch, R. Kolb, M. R. Heinrich, *Chem. Eur. J*. **2010**, *16*, 2547–2556.

[10] G. Balz, G. Schiemann, *Ber. Dtsch. Chem. Ges*. **1927**, *60*, 1186–1190.

[11] H. Meerwein, E. Buchner, K. van Emsterk, *J. Prakt. Chem*. **1939**, *152*, 237–266.

[12] a) M. P. Doyle, B. Siegfried, J. F. Dellaria Jr., *J. Org. Chem*. **1977**, *42*, 2426–2431; b) M. P. Doyle, J. F. Dellaria Jr., B. Siegfried, S. W. Bishop, *J. Org. Chem*. **1977**, *42*, 3494–3498.

[13] a) K. Kikukawa, T. Matsuda, *Chem. Lett*. **1977**, 159–162; b) K. Kikukawa, K. Nagira, T. Matsuda, *Bull. Chem. Soc. Jpn*. **1977**, *50*, 2207; c) K. Kikukawa, K. Nagira, N. Terao, F. Wada, T. Matsuda, *Bull. Chem. Soc. Jpn*. **1979**, *52*, 2609–2610.

[14] F. Mo, G. Dong, Y. Zhang, J. Wang, *Org. Biomol. Chem*. **2013**, *11*, 1582–1593.

[15] H. Zollinger in *Color Chemistry. Syntheses, Properties, and Applications of Organic Dyes and Pigments*, Wiley-VCH Verlag, Zürich, 3rd revised ed., **2003**.

[16] K. Hunger, W. Herbst in *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, **2012**.

[17] H. H. Hodgson, S. Birtwell, J. Walker, *J. Chem. Soc*. **1944**, 18–19.

[18] H. H. Hodgson, C. K. Foster, *J. Chem. Soc*. **1942**, 581–583.

[19] L. Gattermann, *Ber*. **1890**, *25*, 1218.

[20] T. Cohen, A. G. Jr. Dietz, J. R. Miser, *J. Org. Chem*. **1977**, *42*, 2053–2058.

[21] C. Matheis, B. Bayarmagnai, K. Jouvin, L. J. Goossen, *Org. Chem. Front*. **2016**, *3*, 949–952.

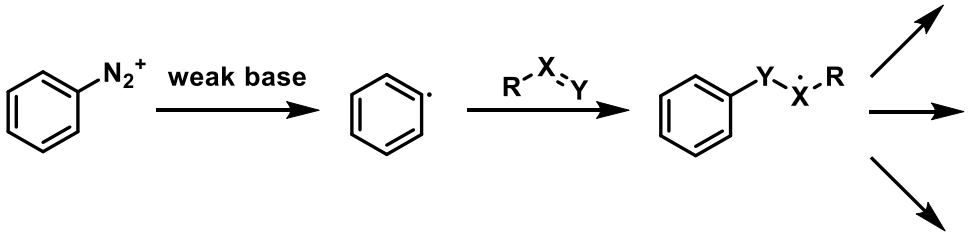
[22] J. Zhang, X. Wang, H. Yu, J. Ye, *Synlett* **2012**, *23*, 1394–1396.

[23] W.-B. Xu, Q.-H. Xu, Z.-F. Zhang, J.-Z. Li, *Asian J. Org. Chem.* **2014**, *3*, 1062–1065.
[24] L. Zhang, P. Zhang, X. Li, J. Xu, G. Tang, Y. Zhao, *J. Org. Chem.* **2016**, *81*, 5588–5594.
[25] D. Toummini, A. Tlili, J. Bergès, F. Ouazzani, M. Taillefer, *Chem. Eur. J.* **2014**, *20*, 14619–14623.
[26] P. M. Gorbovoi, G. N. Tulaidan, B. D. Grishchuk, *Russ. J. Gen. Chem.* **2008**, *78*, 133–135.
[27] a) K. Kikukawa, K. Maemura, K. Nagira, F. Wada, T. Matsuda, *Chem. Lett*. **1980**, 551–552; b) K. Kikukawa, K. Maemura, Y. Kiseki, F. Wada, T. Matsuda, C. S .Giam, *J. Org. Chem*. **1981**, *46*, 4885–4888.
[28] M. Beller, H. Fischer, K. Kühlein, *Tetrahedron Lett*. **1994**, *35*, 8773–8776.
[29] F. Mo, D. Qiu, Y. Jiang, Y. Zhang, J. Wang, *Tetrahedron Lett*. **2011**, *52*, 518–522.
[30] X.-F. Wu, H. Neumann, M. Beller, *Chem. Commun*. **2011**, *47*, 7959–7961.
[31] X.-F. Wu, H. Neumann, M. Beller, *Angew. Chem. Int. Ed*. **2011**, *50*, 11142–11146.
[32] M. P. Doyle, W. J. Bryker, *J. Org. Chem*. **1979**, *44*, 1572–1574.
[33] a) M. B. Andrus, C. Song, J. Zhang, *Org. Lett*. **2002**, *4*, 2079–2082; b) M. B. Andrus, C. Song, *Org. Lett*. **2001**, *3*, 3761–3764; c) B. Panda, T. K. Sarkar, *Chem. Commun*. **2010**, *46*, 3131–3133; d) Y. Zong, J. Hu, P. Sun, X. Jiang, *Synlett* **2012**, *23*, 2393–2396.
[34] Z. Y. Tang, Y. Zhang, T. Wang, W. Wang, *Synlett* **2010**, *5*, 804–808.
[35] Y. Ding, K. Cheng, C. Qi, Q. Song, *Tetrahedron Letters* **2012**, *53*, 6269–6272.
[36] X. Qi, L.-B. Jiang, C. Zhou, J.-B. Peng, X.-F. Wu, *ChemistryOpen* **2017**, *6*, 345–349.
[37] C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev*. **2013**, *113*, 5322–5363.
[38] E. S. Lewis, R. E. Holliday, L. D. Hartung, *J. Am. Chem. Soc*. **1969**, *91*, 430–433.
[39] D. Kalyani, K. B. McMurtrey, S. R. Neufeldt, M. S. Sanford, *J. Am. Chem. Soc*. **2011**, *133*, 18566–18569.
[40] D. Xue, Z.-H. Jia, C.-J. Zhao Y.-Y. Zhang, C. Wang, J. Xiao, *Chem. Eur. J*. **2014**, *20*, 2960–2965.
[41] J. Zhang, J. Chen, X. Zhang, X. Lei, *J. Org. Chem*. **2014**, 79, 10682–10688.
[42] P. Schroll, D. P. Hari, B. König, *ChemistryOpen* **2012**, *1*, 130–133.
[43] T. Hering, D. P. Hari, B. König, *J. Org. Chem*. **2012**, *77*, 10347–10352.
[44] H. Cano-Yelo, A. Deronzier, *J. Chem. Soc. Perkin Trans. 2* **1984**, 1093–1098.
[45] D. P. Hari, P. Schroll, B. König, *J. Am. Chem. Soc*. **2012**, *134*, 2958–2961.
[46] P. Maity, D. Kundu, B. C. Ranu, *Eur. J. Org. Chem*. **2015**, *2015*, 1727–1734.
[47] L. Gu, C. Jin, J. Liu, *Green Chem*. **2015**, *17*, 3733–3736.

[48] M. Majek, A. Jacobi von Wangelin, *Angew. Chem. Int. Ed*. **2015**, *54*, 2270–2274.
[49] J. Yu, L. Zhang, G. Yan, *Adv. Synth. Catal*. **2012**, *354*, 2625–2628.
[50] M. Majek, A. Jacobi von Wangelin, *Chem. Commun*. **2013**, *49*, 5507–5509.
[51] T. Xiao, X. Dong, Y. Tang, L. Zhou, *Adv. Synth. Catal*. **2012**, *354*, 3195–3199.
[52] M. Gomberg, W. E. Bachmann, *J. Am. Chem. Soc*. **1924**, *46*, 2339–2343.
[53] D. H. Hey, W. A. Waters, *J. Chem. Soc*. **1948**, 882–885.
[54] R. Huisgen, L. Krause, *Ann. Chem*. **1951**, *574*, 157–171.
[55] Ch. Rüchardt, B. Freudenberg, E. Merz, *Spec. Publ. Chem. Soc*. **1965**, *19*, 154.
[56] a) R. A. Abramovitch, J. G. Saha, *Tetrahedron*, **1965**, *21*, 3297–3303; b) H. Loewenschuss, G. H.Wahl, H. Zollinger, *Helv. Chim. Acta* **1976**, *59*, 1438–1448.
[57] C. Molinaro, J. Mowat, F. Gosselin, P. D. O'Shea, J.-F. Marcoux, R. Angelaud, I. W. Davies, *J. Org. Chem*. **2007**, *72*, 1856–1858.
[58] G. Pratsch, T. Wallaschowski, M. R. Heinrich, *Chem. Eur. J*. **2012**, *18*, 11555–11559.
[59] M. Hartmann, Y. Li, A. Studer, *J. Am. Chem. Soc*. **2012**, *134*, 16516–16519.
[60] Z. Xia, Q. Zhu, *Org. Lett*. **2013**, *15*, 4110–4113.
[61] U. M. V. Basavanag, A. Dos Santos, L. El Kaim, R. Gamez-Montano, L. Grimaud, *Angew. Chem. Int. Ed*. **2013**, *52*, 7194–7197.
[62] F. P. Crisostomo, T. Martin, R. Carrillo, *Angew. Chem. Int. Ed*. **2014**, *53*, 2181–2185.
[63] S. Kindt, K. Wicht, M. R. Heinrich, *Org. Lett*. **2015**, *17*, 6122–6125.
[64] D. Koziakov, M. Majek, A. Jacobi von Wangelin, *Org. Biomol. Chem.* **2016**, *14*, 11347–11352.
[65] S. W. Youn, E. M. Lee, *Org. Lett*. **2016**, *18*, 5728–5731.
[66] Z. Ni, X. Huang, Y. Pan, *Org. Lett*. **2016**, *18*, 2612–2615.
[67] J. Hofmann, E. Gans, T. Clark, M. R. Heinrich, *Chem. Eur. J*. **2017**, *23*, 9647–9656.

Chapter 2

- Aim of the Work -



2. Aim of the Work

Many of the current synthetic approaches to the fusion of C-C and C-X bonds rely on the use of highly energetic reagents, harsh reaction conditions, or toxic or noble metal catalysts. While catalytic methods exhibit at the present time enhanced sustainability, they mostly involve heavy metals in combination with complex ligands. Therefore, new methods based on more abundant, less toxic, and cheaper reagents are necessary. However, these milder conditions still have to assure the generation of reactive species that undergo the desired chemical transformations. Organic radicals fulfill the requirements of easy accessibility from simple reagents and high reactivity which is exemplified by the numerous applications of radical intermediates in industrial and biological processes.

The alternative procedure exploits bases as single-electron transfer reagents which trigger a radical reaction pathway. Bases can be divided into two groups: strong bases and weak bases. Strong bases as powerful electron donors play important roles in various organic transformations. However, they can be incompatible with starting compounds or used solvents. For instance, some functional groups are too sensitive to strong bases or nucleophiles. Protic solvents are able to interact with strong bases. Hence, employment of strong bases as single-electron donors has also certain limitations.

Fortunately, weak bases do not possess the described above disadvantages and can trigger radical processes. Weak bases have features, which are significant for a green chemistry concept. They are inexpensive, environmentally benign, and easy to handle. Especially inorganic bases caught our attention. They are easily removed from organic products while organic bases are mostly more expensive, hazardous, and miscible with organic phases. We want to use weak inorganic bases for radical aromatic substitution reactions.

As starting materials arenediazonium salts seem to be attractive due to the ease of preparation from anilines and high electrophilic ability, which comes from the high stability of dinitrogen. Such high stability promotes the release of dinitrogen from arenediazonium compound.

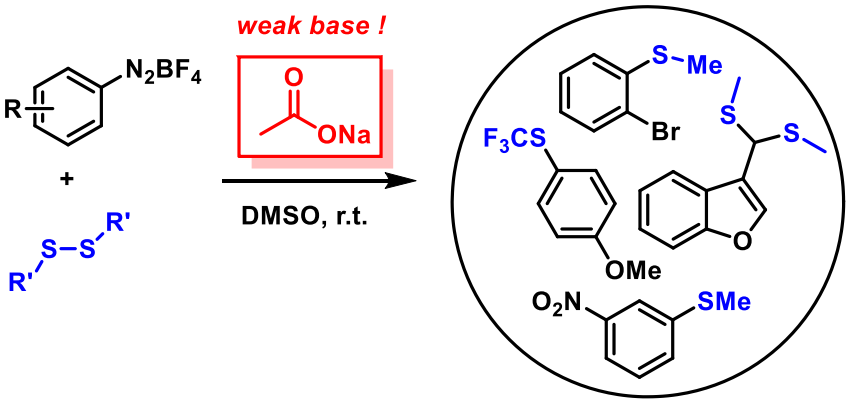
The main aim of this work is to develop transition metal-free radical aromatic substitutions mediated by weak, cheap, and non-toxic inorganic bases. Our goal is to replace poisonous aryl halides with more reactive arenediazonium salts, which are known to be beneficial aryl donors. They are easily accessible from anilines and also can be employed under mild conditions with benign solvents.

We want to perform metal-free thiolations (with disulfides) and alkoxycarbonylations (with carbon monoxide and alcohols) in order to synthesize aromatic thioethers and benzoates. These products find many

applications in the synthetic organic chemistry and as structural motif in different biologically active compounds. We aim to find the most effective weak base and best reaction conditions to make synthesis cheaper and greener.

Chapter 3

- Metal-free Radical Thiolations Mediated by Very Weak Bases -



Abstract: Aromatic thioethers and analogous heavier chalcogenides were prepared by reaction of arenediazonium salts with disulfides in the presence of cheap and weak base NaOAc. The mild and practical reaction conditions (equimolar reagents, DMSO, r.t., 8 h) tolerate various functional groups (*e.g.* Br, Cl, NO_2, CO_2R, OH, SCF_3, furans). Mechanistic studies indicate the operation of a radical aromatic substitution mechanism *via* aryl, acetyloxyl, thiyl, and dimsyl radicals.

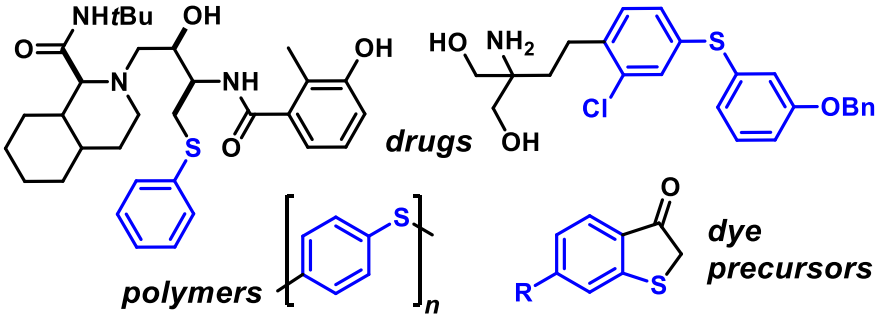
This chapter has been published:
D. Koziakov, M. Majek, A. Jacobi von Wangelin, *Org. Biomol. Chem*. **2016**, *14*, 11347–11352.

Author contributions:
Denis Koziakov synthesized starting materials, did reactions, and wrote the manuscript. Michal Majek performed calculations.

3. Metal-free Radical Thiolations Mediated by Very Weak Bases

3.1. Introduction

Sulfur-substituted aromatics constitute a versatile class of building blocks which find numerous applications in the synthesis of bioactive compounds, materials, and fine chemicals (Scheme 3.1).[1]

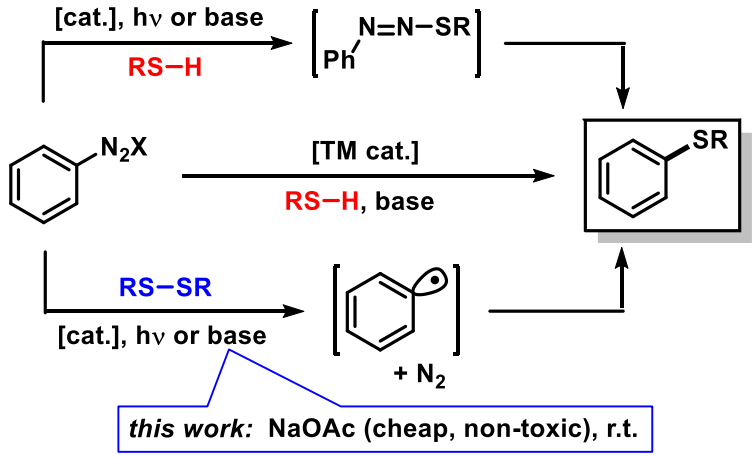


Scheme 3.1. Selected compounds containing aryl-S entities.

Besides electrophilic aromatic substitutions with concentrated sulfuric acid, various synthetic procedures have been reported for the construction of aryl-S bonds from aryl electrophiles and sulfur nucleophiles. The most prominent methods are transition metal-catalyzed thiolations of aryl halides[2] and Sandmeyer-type[3] radical substitutions of arenediazonium salts[4] (Scheme 3.2, top). The latter procedure can be performed under metal-free basic conditions but affords only moderate yields and bears significant hazard potential due to the intermediacy of explosive azosulfides.[5] An elegant alternative is the use of disulfides in radical aromatic substitutions which are initiated by single-electron transfer (SET) and operate under mild conditions.[6] Base-free aromatic thiolations with disulfides were recently realized by organic photoredox-catalysis.[7] However, light-mediated processes require the presence of a suitable photo-sensitizer and irradiation with a powerful light source, operate at low concentrations over long reaction times, and generally suffer from the attenuation of light intensity in solution (Lambert-Beer law).

Powerful metal-free electron donors are mostly strong bases[8] and nucleophiles which are incompatible with sensitive functional groups and protic solvents. However, even weak bases and nucleophiles can trigger radical aromatic substitutions (S_RAr) at electrophilic aryl-X if the elimination of X was irreversible or a facile bond homolysis can occur.[9,10] Following observations on mechanistically related photo-redox substitutions,[7] we directed our attention at SET-mediated reactions of disulfides with arenediazonium salts.[11] Here, we present an operationally facile protocol which utilizes the cheap, environmentally benign, and weak base sodium acetate (NaOAc) in radical aromatic substitutions of arenediazonium salts with disulfides under mild

reaction conditions (Scheme 3.2, bottom).



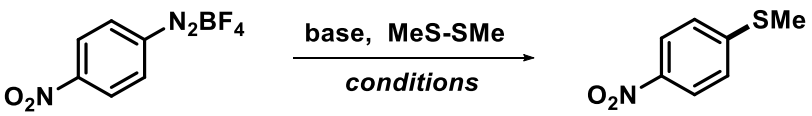
Scheme 3.2. Thiolation methods of arenediazonium salts.

3.2. Results and Discussion

Simple inorganic bases are attractive due to their low price, low toxicity, and facile removal from organic products while organic bases are mostly more expensive, environmentally problematic, and less facile to remove from organic phases. We studied the model reaction of 4-nitrobenzenediazonium tetrafluoroborate, containing two π-electrophilic sites, with dimethyldisulfide (Table 3.1).

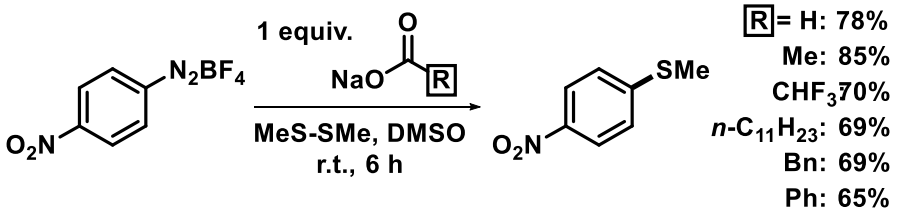
Various simple bases were competent in this thiolation protocol. *N*,*N*-Dimethylhydrazine was most active;[12] however, we refrained from further studies due to the toxicity and hazard potential as carcinogen, explosive, and groundwater pollutant.[13] Strong bases (*e.g.* KO*t*Bu, KHMDS, *n*-BuLi) gave lower selectivities and many by-products. Polar solvents (acetonitrile, methanol, dimethylsulfoxide (DMSO)) exhibited high reagents solubility and good yields. Identical reactions in *N*,*N*-dimethylformamide (DMF) underwent competing hydrodediazotation (25%); in benzene 4-nitrobiphenyl was formed (15%). Significantly higher selectivities were observed in the absence of air and moisture. Gratifyingly, no excess of reagents was required. The optimized conditions (equimolar ArN_2BF_4, NaOAc, Me_2S_2, 0.2 M in DMSO, 18 °C, 8 h) enabled clean conversion to the arylthioether with minimal formation of nitrobenzen as reduction by-product (<3%). Similar yields were obtained when using other simple carboxylates (Scheme 3.3).

Table 3.1. Selected optimization experiments.[a]



Entry	Equiv. Me_2S_2	Base (equiv.)	Conditions	Yield [%] [b]
1	5	-		0
2	1	*n*-Bu_4NI (1.5)		66
3	5	KO^tBu (5)		65
4	5	NaOAc (5)		85
5	1.5	NaOAc (5)		85
6	1.5	NaOAc (1)		83
7	1.5	NaOAc (0.5)	16 h	56
8	1.5	NaOAc (0.2)	16 h	29
9	1	KOAc (1)	DMSO, r.t., 8 h	80
10	0.5	NaOAc (1)	DMSO, r.t., 8 h	42
11	1	NaOAc (1)	H_2O/THF/AcMe	66/31/73
12	1	NaOAc (1)	MeOH/DMF/MeCN	77/62/75
13	1	NaOAc (1)	DMSO, r.t., 8 h	85[c] (90)[d] (83)[e]

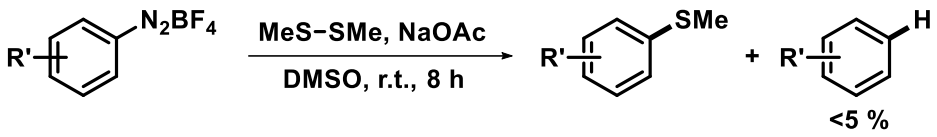
[a] Optimized conditions: 4-Nitrobenzenediazonium tetrafluoroborate (0.6 mmol), NaOAc (0.6 mmol) under N_2, DMSO (3 mL), r.t., 8 h. [b] GC yields *vs.* internal 1-dodecanenitrile [c] 80% isolated yield. [d] after 60 h. [e] 60°C, 1 h.



Scheme 3.3. Similar activity of various sodium carboxylates.

We then applied the optimized conditions to a series of diversely substituted arenediazonium salts (Table 3.2).

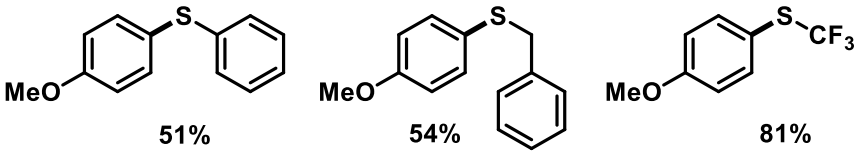
Table 3.2 NaOAc-mediated methylthiolation of arenediazonium salts.[a]



R'	Yield [%]	R'	Yield [%]
4-OMe	89	3-NO_2	77
4-Cl	70	2-NO_2	80
4-NO_2	85	2-Br	69
4-OH	87	2-SMe	73
4-Ph	58	2-CO_2Me	71
2,4,6-Cl_3	56	1-naphthyl	53

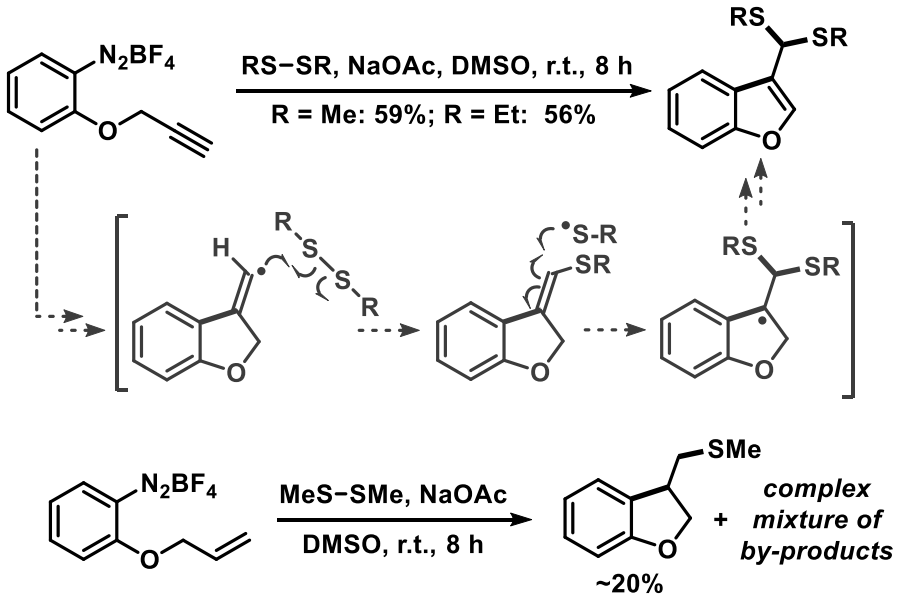
[a] Conditions: Arenediazonium tetrafluoroborate (0.6 mmol), dimethyl disulfide (0.6 mmol), NaOAc (0.6 mmol), DMSO (2 mL), 20 °C, 8 h.

The protocol proved to be rather general with regard to substituents at the arene and the disulfide, respectively. Chloro, bromo, ester, nitro, hydroxy, and naphthyl moieties within the diazonium salts were tolerated. Alkyl disulfides afforded slightly higher yields than aryl disulfides (Scheme 3.4).



Scheme 3.4. Preparation of other unsymmetrical aryl thioethers.

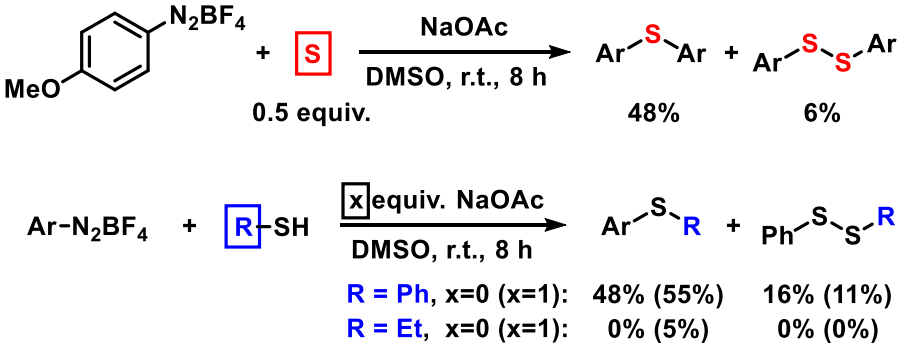
The trifluoromethylsulfanyl moiety, which attracts great interest from pharmaceutical programs due to their lipophilic properties, could also be introduced by reaction with commercial bis(trifluoromethyl) disulfide in the same (Scheme 3.4).[14] Sequential radical 5-*exo*-dig cyclization and thiolation was observed with 2-(propynyloxy)benzenediazonium tetrafluoroborate to give 3-thioketal benzofurans (Scheme 3.5).[15]



Scheme 3.5 Base-mediated radical cyclization-thiolation.

The attack of the *S*-centered radical on the newly formed double bond is facilitated by the stabilization of the resulting benzyl radical. On the other hand, the corresponding 2-allyloxybenzenediazonium salt failed to undergo a similarly effective domino reaction but afforded a different thioether skeleton and many by-products (Scheme 3.5, bottom).

We employed elemental sulfur as alternative thiolation reagents which indeed led to the formation of symmetrical diaryl sulfides in moderate to good yields (Scheme 3.6, top). While thiols are easy available, they result in the formation of explosive azosulfide intermediates and under our conditions gave only moderate to low yields of the desired thioethers. The direct thiolation with benzenethiol proceeded with moderate yields in the absence of base. With ethanethiol, mostly hydrodediazotation was observed (Scheme 3.6, bottom).

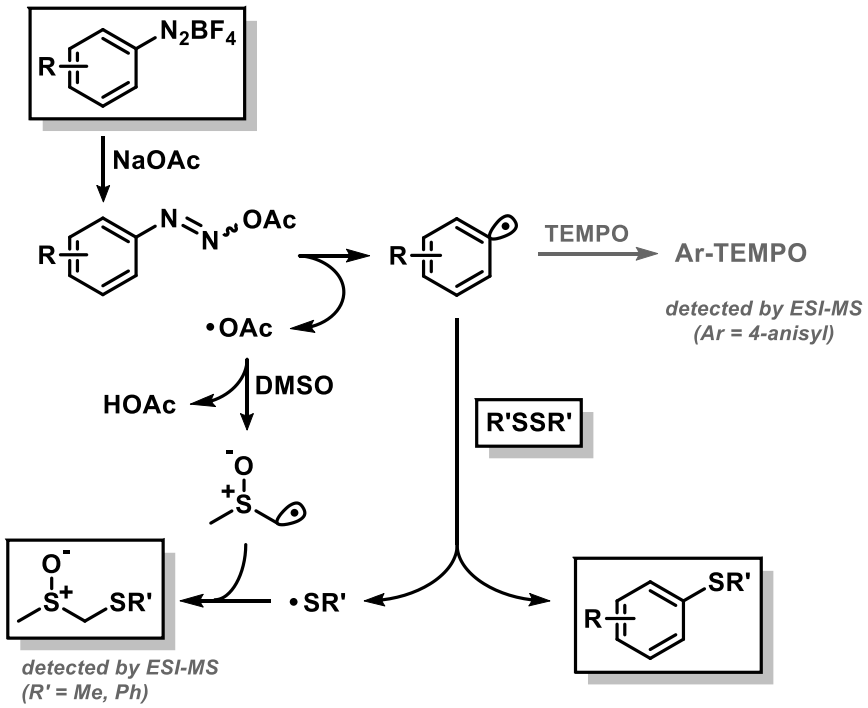


Scheme 3.6 Procedures with alternative sulfur sources (Ar = 4-$MeOC_6H_4$).

Reaction progress analysis documented an immediate onset of reactivity within less than 10 s, more than 50% conversion within 1 h, and a significantly slower

turnover after 1-2 h. This behaviour could be a consequence of two competing reaction mechanisms: a rapid base-induced thiolation and a slow radical chain propagation.[16] The operation of the latter is also supported by experiments with catalytic amounts of NaOAc (20 mol% and 50 mol%) which afforded 29% and 56% yield, respectively, after 16 h. Further mechanistic insight has already been gained by the initial optimization experiments (see Table 3.1). The stoichiometry of the reaction (equimolar ArN_2BF_4, R_2S_2, and NaOAc) indicates a loss channel of one half of the disulfide molecule which is *not electron transfer in nature* ($RS^{\bullet} \rightarrow RS^{+} + e^{-}$)[16] as such a scenario could operate with catalytic amounts of base.

We postulate a mechanism that involves homolysis of the initially formed diazoacetate (Scheme 3.7).

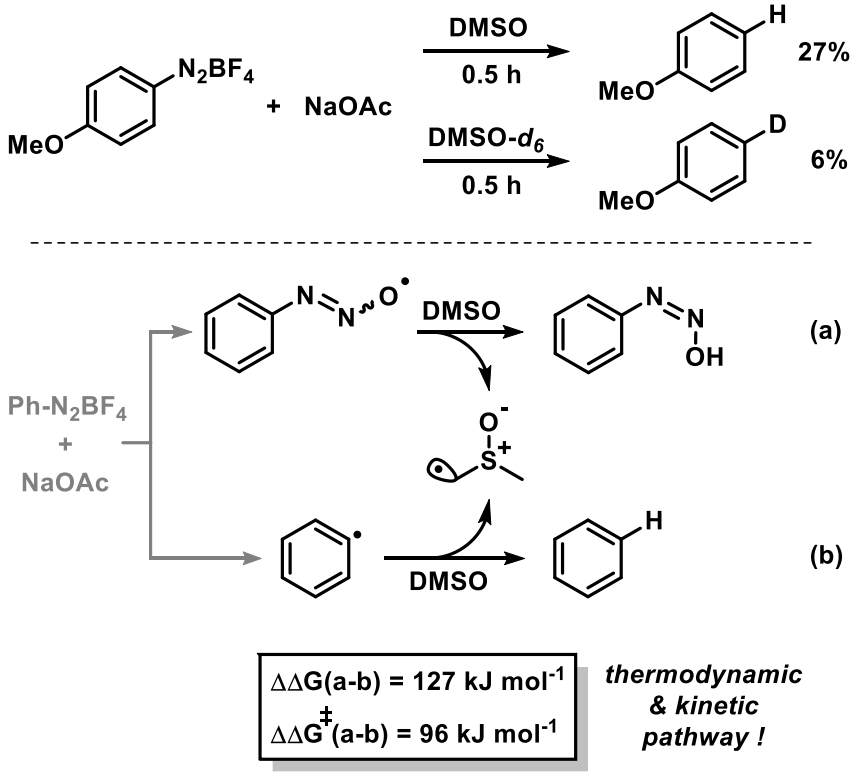


Scheme 3.7. Postulated weak base-mediated S_RAr mechanism.

The resultant aryl and acetyloxyl radicals engage in orthogonal onward reactions. The former reacts with the disulfide upon release of a thiyl radical which is trapped by a dimsyl radical derived from H atom transfer (HAT) with acetyloxyl. The presence of the aryl radical intermediate $Ar^{\bullet}$ was confirmed by radical trapping with TEMPO (2,2,6,6-tetramethylpiperidin-1-yl)-oxyl in a standard reaction. The aryl radical intermediate attacks the disulfide in an S_H2 fashion by homolysis of the S-S bond in a single step.[17] The resulting DMSO-SR adducts (R = Me, Ph) were detected by ESI-MS (Scheme 3.7, bottom left).[7a,18] The generation of acetic acid as major byproduct was monitored indirectly by the continuous decrease of the pH value over the course of the reaction (pH 8 →

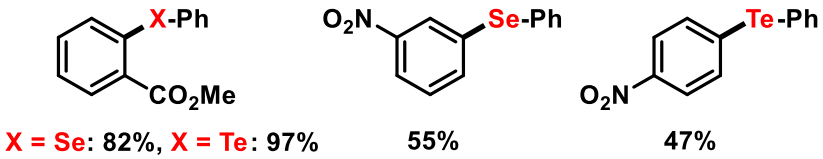
4, after aqueous quench) despite the buffering effect of the weak acid/base pair and the solvent. Crossover-experiments with dimethyldisulfide and diphenyldisulfide resulted in the formation of the mixed methylphenyl disulfide (MeS-SPh) as byproduct by recombination of free thiyl radicals.

Other mechanistic scenarios could be excluded based on the following instructive experiments and considerations: *i)* The operation of the acetate anion as single-electron transfer reagent[19] is discouraged by the lack of any detectable CO_2 formation by head-space MS analyses and gas phase absorptions into aqueous $Ba(OH)_2$. *ii)* A direct disulfide-mediated electron transfer was already disproven in entry 1 of Table 3.1. Consistently, a solution of arenediazonium salt and NaOAc in DMSO underwent significant hydrodediazotation after 30 min in the absence of disulfides; deuterium incorporation from DMSO-d_6 was also observed (Scheme 3.8, top). *iii)* Base-mediated aryl radical formation from arenediazonium salts could in principle proceed by SET from the diazotate anion;[20] on thermodynamic grounds, the diazotate anion/radical appears to be a reasonable 1e-redox couple under weakly basic conditions.[21] However, this mechanism requires the operation of a highly selective H atom transfer (HAT) from a suitable H-donor (DMSO) to the azotate radical[19] but not to the aryl radical intermediate. A DFT-based analysis excludes such mechanism because the HAT to the aryl radical is thermodynamically and kinetically highly favoured (Scheme 3.8, bottom).[20,22] *iv)* The operation of a dimsyl anion-mediated $S_{RN}1$ mechanism can be excluded by the large pK_a difference of acetic acid (~12) and DMSO (~35) in DMSO.[23]



Scheme 3.8. Experimental and calculated H atom transfer (HAT).

Under identical conditions, the general protocol was applied to the synthesis of arylselenoethers and aryltelluroethers (Scheme 3.9).[24] Employment of the diphenyl dichalcogenides afforded very good yields of the methyl 2-phenylcarboxylate derivatives and moderate yields of nitrobenzene derivatives. Mechanistic studies on related systems were performed by Pandey and coworkers which reported the facile SET oxidation of diselenides in the presence of suitable acceptors and subsequent mesolysis to a phenylselenyl radical and phenylselenyl cation.[6b,25]



Scheme 3.9. Selenations and tellurations under similar conditions.

3.3. Conclusion

We have developed a new metal-free thiolation method for synthesis of arylsulfides which employs the cheap, weak, and environmentally benign base sodium acetate. Experimental and theoretical studies indicated the operation of an initial homolysis of diazoacetates and exclude alternative base-, dimsyl-, and diazotate-mediated electron transfer mechanisms. Applications to the synthesis of various functionalized thioethers, selenides, and tellurides demonstrate the scope of this mild base-mediated protocol. Further applications of similar activation mechanisms in radical substitution reactions are currently being investigated.

3.4. Experimental Section

General

Chemicals and Solvents. Commercial chemicals were used as obtained from Sigma-Aldrich or Fisher. Solvents were used without further purification. DMSO was dried over molecular sieves (certified <0.005% water content, Sigma-Aldrich).

Analytical thin-layer chromatography. TLC was performed using aluminium plates with silica gel and fluorescent indicator (Merck, 60F254). Thin layer chromatography plates were visualized by exposure to UV light.

Column chromatography. Flash column chromatography with silica gel 60 Å (220-240 mesh) from *Acros*. Pentane or mixtures thereof with ethyl acetate were used as eluents. Product yields were determined as isolated by column chromatography.

Gas chromatography with mass-selective detector. *Agilent* 6890N Network GC-System, mass detector 5975 MS. Column: BPX5 (30m x 0.25 mm x 0.25, from *SGE*, carrier gas: H_2. Standard heating procedure: 50°C (2 min), 25°C/min -> 300°C (5 min).

Gas chromatography with FID. *Agilent* 7820A GC-Systems. Column: HP 5 19091J 413 (30 m x 0.32 mm x 0.25 µm) from *Agilent*, carrier gas: N_2. GC-FID was used for reaction optimization screening (Calibration with internal standard 1-dodecanenitrile and analytically pure samples).

NMR. ^{1}H and ^{13}C nuclear magnetic resonance spectra were recorded on a *Bruker* Avance 300 (300 MHz ^{1}H; 75 MHz ^{13}C, 282 MHz ^{19}F) and *Bruker* Avance 400 (400 MHz ^{1}H, 101 MHz ^{13}C) spectrometers. Chemicals shifts are reported in ppm (δ) relative to solvent residual peak as internal reference. Coupling constants (*J*) are reported in Hertz (Hz). Following abbreviations are used for spin multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, dt = doublet of triplet, dq = doublet of quartet, ddt = doublet of doublet of triplet.

IR spectroscopy. Infrared spectra were recorded on a Cary 630 FTIR Spectrometer equipped with an ATR unit. Wavenumbers are indicated in cm^{-1}. Intensive absorption bands are indicated with „s“ (strong), medium bands with „m“ (medium), and weak bands with „w“ (weak).

High resolution mass spectrometry (HRMS). The spectra were recorded by the Central Analytics Lab at the Department of Chemistry, University of Regensburg, on a MAT SSQ 710 A from *Finnigan*.

General procedure for the synthesis of arenediazonium salts

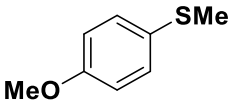
The parent aniline (10 mmol) was dissolved in glacial acetic acid (6 mL) and 32% aqueous tetrafluoroboric acid (1.6 mL) at room temperature. Then, a solution of *tert*-butyl nitrite (1.2 mL) in glacial acetic acid (2 mL) was slowly added at room temperature over 5 min. Diethylether (15 mL) was added, and the reaction mixture was cooled to -30 °C in order to induce crystallization of the ionic product. The crystals were filtered off, washed with cold diethylether (2 x 10 mL) and dried on air to give analytically pure arenediazonium tetrafluoroborates.

General procedure for base-induced thiolation, selenylation and telluration

A vial (5 mL) was charged with a magnetic stir bar, the arenediazonium salt (0.5 mmol), disulfide (0.5 mmol) and sodium acetate (0.5 mmol) and capped with a rubber septum. The vial was purged with N_2 (5 min). Dry DMSO (2.5 mL) was

added. After 8 h of stirring water (5 mL) was added to give an emulsion, which was extracted with diethylether (3 x 5 mL). The organic phases were washed with brine (5 mL) and dried over MgSO4. The solvent was evaporated *in vacuo*, and the residue was purified by flash column chromatography (silica gel) using pentane/ethyl acetate mixtures (from 100/0 to 100/20) as eluent to obtain pure product.

4-Methoxyphenylmethylsulfane



$C_8H_{10}OS$, 154.23 g/mol

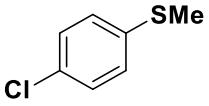
Yield 68.5 mg, 0.44 mmol, 89% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.27 (d, *J* = 8.9 Hz, 2H), 6.85 (d, *J* = 8.9 Hz, 2H), 3.79 (s, 3H), 2.44 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 158.1, 130.1, 128.7, 114.5, 55.3, 18.0.

LR MS (EI, 70 eV, m/z): 154 [M^+]

4-Chlorophenylmethylsulfane



C_7H_7ClS, 158.64 g/mol

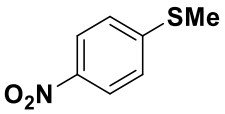
Yield 55.3 mg, 0.35 mmol, 70% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.25 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 2H), 2.47 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 136.9, 130.8, 128.9, 127.8, 16.0.

LR MS (EI, 70 eV, m/z): 158 [M^+]

4-Nitrophenylmethylsulfane



$C_7H_7NO_2S$, 169.20 g/mol

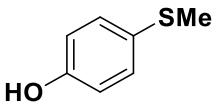
Yield 67.7 mg, 0.40 mmol, 85% (isolated)

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 8.15 (d, *J* = 9.0 Hz, 2H), 7.29 (d, *J* = 9.0 Hz, 2H), 2.55 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 148.8, 144.8, 125.0, 123.9, 14.8.

LR MS (EI, 70 eV, m/z): 169 [M^+]

4-Methylthiophenol



C_7H_8OS, 140.20 g/mol

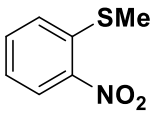
Yield 61.0 mg, 0.44 mmol, 87% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.19 (d, *J* = 8.7 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 2.42 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 154.8, 130.5, 128.0, 116.1, 18.2.

LR MS (EI, 70 eV, m/z): 140 [M^+]

2-Nitrophenylmethylsulfane



$C_7H_7NO_2S$, 169.20 g/mol

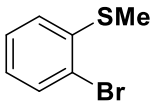
Yield 40.8 mg, 0.24 mmol, 80% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.26 (dd, *J* = 8.3 Hz, *J* = 1.2 Hz, 1H), 7.59 (ddd, *J* = 8.6 Hz, *J* = 7.3 Hz, *J* = 1.3 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.26 (ddd, *J* = 8.2 Hz, *J* = 7.2 Hz, *J* = 1.2 Hz, 1H), 2.50 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 145.4, 139.3, 133.7, 126.2, 125.6, 124.1, 15.9.

LR MS (EI, 70 eV, m/z): 169 [M^+]

2-Bromophenylmethylsulfane



C_7H_7BrS, 203.10 g/mol

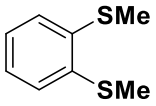
Yield 40.1 mg, 0.20 mmol, 66% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.52 (dd, *J* = 7.9 Hz, *J* = 1.4 Hz, 1H), 7.30 (ddd, *J* = 7.9 Hz, *J* = 7.4 Hz, *J* = 1.3 Hz, 1H), 7.13 (dd, *J* = 8.0 Hz, *J* = 1.5 Hz, 1H), 7.0 (ddd, *J* = 7.8 Hz, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H), 2.47 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 139.6, 132.6, 127.8, 125.6, 125.3, 121.6, 15.7.

LR MS (EI, 70 eV, m/z): 203 [M^+]

1,2-Bis(methylthio)benzene



$C_8H_{10}S_2$, 170.29 g/mol

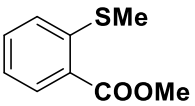
Yield 37.2 mg, 0.22 mmol, 73% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.24-7.13 (m, 4H), 2.48 (s, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 137.3 (s), 126.6 (s), 125.8 (s), 16.2 (s).

LR MS (EI, 70 eV, m/z): 170 [M^+]

Methyl-2-(methylthio)benzoate



$C_9H_{10}O_2S$, 182.24 g/mol

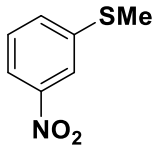
Yield 64.7 mg, 0.36 mmol, 71% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.98 (dd, *J* = 7.9 Hz, *J* = 1.5 Hz, 1H), 7.30 (ddd, *J* = 8.2 Hz, *J* = 7.3 Hz, *J* = 1.5 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.14 (ddd, *J* = 8.0 Hz, *J* = 7.8 Hz, *J* = 1.1 Hz, 1H), 3.90 (s, 3H), 2.44 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 166.7, 143.2, 132.4, 131.2, 126.6, 124.2, 123.3, 52.0, 15.5.

LR MS (EI, 70 eV, m/z): 182 [M^+]

3-nitrophenylmethylsulfane



$C_7H_7NO_2S$, 169.20 g/mol

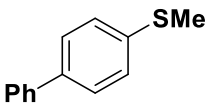
Yield 36.2 mg, 0.36 mmol, 77% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.04 (t, *J* = 2.0 Hz, 1H), 7.95 (ddd, *J* = 8.1 Hz, *J* = 2.2 Hz, *J* = 1.1 Hz, 1H), 7.52 (ddd, *J* = 7.9 Hz, *J* = 1.8 Hz, *J* = 1.1 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 1H), 2.55 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 141.6, 131.9, 129.4, 120.2, 119.7, 119.0, 15.4.

LR MS (EI, 70 eV, m/z): 169 [M^+]

[1,1'-Biphenyl]-4-yl(methyl)sulfane



$C_{13}H_{12}S$, 200.30 g/mol

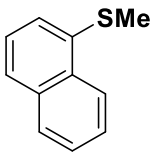
Yield 35.6 mg, 0.18 mmol, 58% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.60-7.50 (m, 4H), 7.47-7.40 (m, 2H), 7.37-7.30 (m, 3H), 2.53 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 140.5, 138.0, 137.5, 128.8, 127.5, 127.2, 126.9, 126.8, 15.9.

LR MS (EI, 70 eV, m/z): 200 [M⁺]

Naphthalen-1-ylmethylsulfane



$C_{11}H_{10}S$, 174.26 g/mol

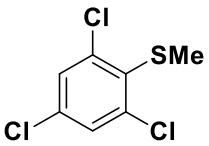
Yield 46.2 mg, 0.27 mmol, 53% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.30 (d, *J* = 7.2 Hz, 1H), 7.85 (d, *J* = 7.4 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.57-7.51 (m, 2H), 7.57-7.37 (m, 2H), 2.59 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 135.7, 133.5, 131.5, 128.5, 126.2, 126.1, 125.7, 125.6, 124.2, 123.5, 16.1.

LR MS (EI, 70 eV, m/z): 174 [M⁺]

2,4,6-Trichlorophenylmethylsulfane



$C_7H_5Cl_3S$, 227.53 g/mol

Yield 78.3 mg, 0.34 mmol, 55% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.40 (s, 2H), 2.42 (s, 3H).

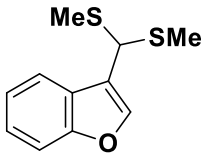
^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 141.4 (s), 134.9 (s), 133.3 (s), 128.5 (s), 18.3 (s).

LR MS (EI, 70 eV, m/z): 226 [M⁺]

HR MS (m/z): found: 225.91721 [M⁺] (calculated: 225.91721)

FT-IR: 794(s), 828(s), 857(s), 1118(m), 1178(m), 1364(s), 1532(s), 1562(m), 2922(w), 3068(w).

3-(Bis(methylthio)methyl)benzofuran



$C_{11}H_{12}OS_2$, 224.34 g/mol

Yield 62.6 mg, 0.28 mmol, 58% (isolated)

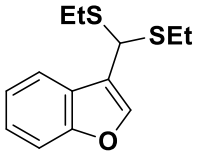
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.79 (d, *J* = 7.4 Hz, 1H), 7.67 (d, *J* = 0.6 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.35-7.24 (m, 2H), 5.05 (d, *J* = 0.9 Hz, 1H), 2.14 (s, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 155.6, 142.8, 125.9, 124.8, 122.6, 120.7, 119.0, 111.6, 47.2, 14.2.

LR MS (EI, 70 eV, m/z): 224 [M^+]

HR MS (m/z): found: 224.03292 [M^+] (calculated: 224.03241)

3-(Bis(ethylthio)methyl)benzofuran



$C_{13}H_{16}OS_2$, 252,39 g/mol

Yield 54.3 mg, 0.22 mmol, 56% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.85-7.81 (m, 1H), 7.69 (d, *J* = 0.5 Hz, 1H), 7.50-7.45 (m, 1H), 7.35-7.23 (m, 2H), 5.18 (d, *J* = 0.7 Hz, 1H), 2.85-2.45 (m, 4H), 1.26 (t, *J* = 7.4 Hz, 6H).

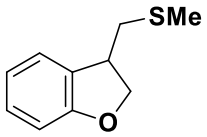
^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 155.7 (s), 142.7 (s), 125.9 (s), 124.7 (s), 122.6 (s), 121.0 (s), 119.8 (s), 111.6 (s), 43.4 (s), 25.7 (s), 14.2 (s).

LR MS (EI, 70 eV, m/z): 252 [M^+]

HR MS (m/z): found: 252.06298 [M^+] (calculated: 252.06371)

FT-IR: 742(s), 857(m), 1178(m), 1264(m), 1450(s), 1573(w), 2870(w), 2926(w), 2967(w).

3-((methylthio)methyl)-2,3-dihydrobenzofuran



$C_{10}H_{12}OS$, 180,06 g/mol

Yield 70.2 mg, 0.39 mmol, 20% (isolated)

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.26 (d, *J* = 7.4 Hz, 1H), 7.16 (t, *J* = 7.5 Hz, 1H), 6.88 (t, *J* = 7.1 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 4.66 (t, *J* = 9.0 Hz, 1H), 4.42 (dd, *J* = 9.1 Hz, *J* = 5.7 Hz, 1H), 3.66 (tt, *J* = 9.0 Hz, *J* = 4.8 Hz, 1H), 2.78 (q, *J* = 7.3 Hz, 1H), 2.77 (q, *J* = 7.3 Hz, 1H), 2.15 (s, 3H).

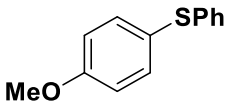
^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 160.0 (s), 129.3 (s), 128.7 (s), 124.4 (s), 120.4 (s), 109.7 (s), 76.1 (s), 41.4 (s), 39.2 (s), 15.8 (s).

LR MS (EI, 70 eV, m/z): 180 [M^+]

HR MS (m/z): found: 180.06031 [M^+] (calculated: 180.06034)

FT-IR: 746(s), 958(m), 1230(s), 1480(s), 1595(m), 2915(w).

(4-Methoxyphenyl)(phenyl)sulfane



$C_{13}H_{12}OS$, 216.30 g/mol

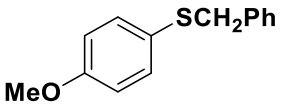
Yield 32.8 mg, 0.15 mmol, 51% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.43 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 7.30-7.10 (m, 5H), 3.83 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 159.8 (s), 138.6 (s), 135.4 (s), 128.9 (s), 128.1 (s), 125.7 (s), 124.2 (s), 114.9 (s), 55.3 (s).

LR MS (EI, 70 eV, m/z): 216 [M^+]

Benzyl(4-methoxyphenyl)sulfane



$C_{14}H_{14}OS$, 230.33 g/mol

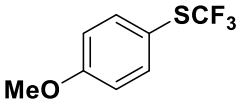
Yield 37.4 mg, 0.16 mmol, 54% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.28-7.16 (m, 2H), 6.83-6.76 (m, 2H), 3.99 (s, 2H), 3.78 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 159.2, 138.1, 134.0, 128.8, 128.3, 126.9, 126.0, 114.4, 55.3, 41.2.

LR MS (EI, 70 eV, m/z): 230 [M^+]

(4-Methoxyphenyl)(trifluoromethyl)sulfane



$C_8H_7F_3OS$, 208.20 g/mol

Yield 84.2 mg, 0.40 mmol, 81% (isolated)

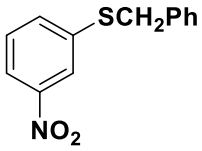
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.57 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.9 Hz, 2H), 3.84 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 161.9, 138.3, 134.8, 129.6 (q, J = 308.1 Hz), 115.0, 55.4.

^{19}F-NMR (282 MHz, $CDCl_3$): δ_F [ppm] = -44.43.

LR MS (EI, 70 eV, m/z): 208 [M^+]

Benzyl(3-nitrophenyl)sulfane



$C_{13}H_{11}NO_2S$, 245.30 g/mol

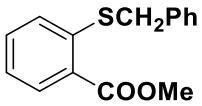
Yield 19.2 mg, 0.08 mmol, 39% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.13 (t, *J* = 2.0 Hz, 1H), 7.99 (ddd, *J* = 8.2 Hz, *J* = 2.2 Hz, *J* = 1.1 Hz, 1H), 7.55 (ddd, *J* = 7.9 Hz, *J* = 1.7 Hz, *J* = 1.0 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.36-7.26 (m, 5H), 4.21 (s, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 148.4, 139.4, 136.0, 134.6, 129.4, 128.8, 128.7, 127.6, 123.2, 120.8, 38.3.

LR MS (EI, 70 eV, m/z): 245 [M^+]

Methyl 2-(benzylthio)benzoate



$C_{15}H_{14}O_2S$, 258.34 g/mol

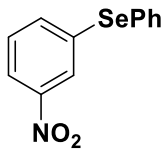
Yield 11.5 mg, 0.04 mmol, 22% (isolated)

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.96 (dd, *J* = 7.8 Hz, *J* = 1.4 Hz, 1H), 7.44-7.26 (m, 7H), 7.16 (td, *J* = 7.5 Hz, *J* = 1.1 Hz, 1H), 4.17 (s, 2H), 3.90 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 166.9, 141.9, 136.1, 132.4, 131.2, 129.1, 128.6, 127.5, 127.3, 126.0, 124.1, 52.1, 37.3.

LR MS (EI, 70 eV, m/z): 258 [M^+]

(3-Nitrophenyl)(phenyl)selane



$C_{12}H_9NO_2Se$, 278.17 g/mol

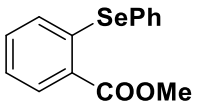
Yield 51.6 mg, 0.19 mmol, 55% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.20 (t, *J* = 1.9 Hz, 1H), 8.05 (ddd, *J* = 8.2 Hz, *J* = 2.2 Hz, *J* = 1.0 Hz, 1H), 7.64 (ddd, *J* = 7.7 Hz, *J* = 1.6 Hz, *J* = 1.1 Hz, 1H), 7.61-7.56 (m, 2H), 7.42-7.35 (m, 4H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 148.5, 136.9, 134.7, 129.9, 129.8, 128.8, 128.3, 125.7, 121.5.

LR MS (EI, 70 eV, m/z): 278 [M^+]

Methyl 2-(phenylselanyl)benzoate



$C_{14}H_{12}O_2Se$, 291.21 g/mol

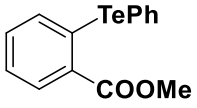
Yield 71.7 mg, 0.25 mmol, 82% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.05 (dd, *J* = 7.0 Hz, *J* = 2.2 Hz, 1H), 7.74-7.68 (m, 2H), 7.50-7.38 (m, 3H), 7.23-7.12 (m, 2H), 6.93-6.89 (m, 1H), 3.97 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 167.2, 140.4, 137.5, 132.6, 131.2, 129.7, 129.1, 128.9, 128.8, 126.9, 124.7, 52.3.

LR MS (EI, 70 eV, m/z): 292 [M^+]

Methyl 2-(phenyltellanyl)benzoate



$C_{14}H_{12}O_2Te$, 339.85 g/mol

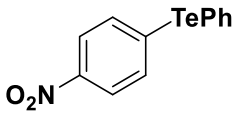
Yield 99.3 mg, 0.29 mmol, 97% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.13-8.08 (m, 1H), 7.98 (dd, *J* = 8.0 Hz, *J* = 1.3 Hz, 2H), 7.47 (tt, *J* = 7.4 Hz, *J* = 2.0 Hz, 1H), 7.40-7.33 (m, 2H), 7.24-7.10 (m, 3H), 3.99 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 168.4, 141.7, 133.3, 132.7, 131.4, 129.7, 129.2, 128.9, 127.1, 125.6, 117.7, 52.7.

LR MS (EI, 70 eV, m/z): 342 [M^+]

(4-Nitrophenyl)(phenyl)tellane



$C_{12}H_9NO_2Te$, 326.81 g/mol

Yield 40.5 mg, 0.12 mmol, 41% (isolated)

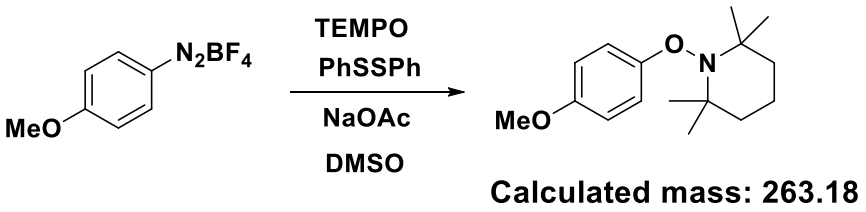
^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.99-7.94 (m, 2H), 7.89-7.84 (m, 2H), 7.58 (dt, *J* = 8.9 Hz, *J* = 2.1 Hz, 2H), 7.45 (tt, *J* = 7.4 Hz, *J* = 1.6 Hz, 1H), 7.37-7.30 (m, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 147.1, 140.3, 135.2, 130.1, 129.3, 127.9, 123.7, 112.6.

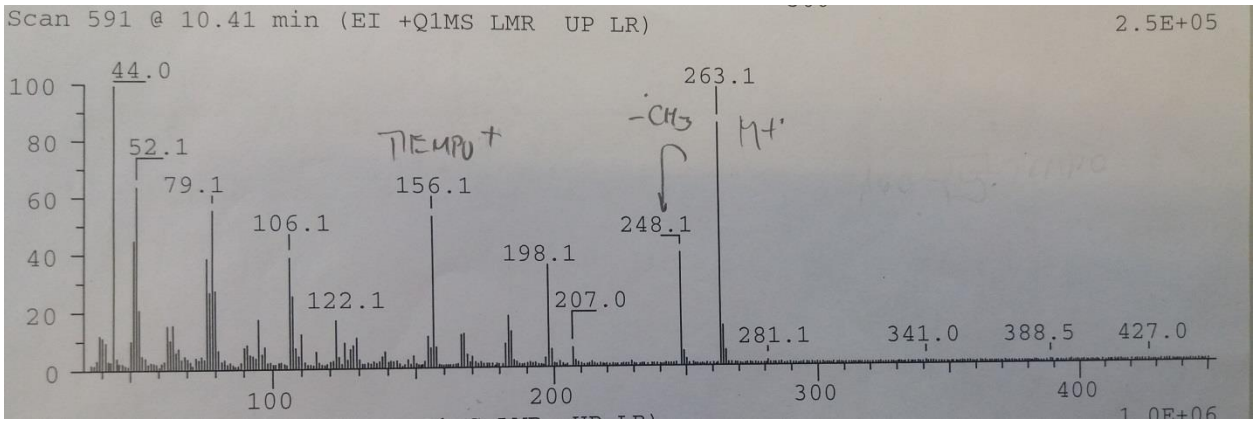
LR MS (EI, 70 eV, m/z): 329 [M^+]

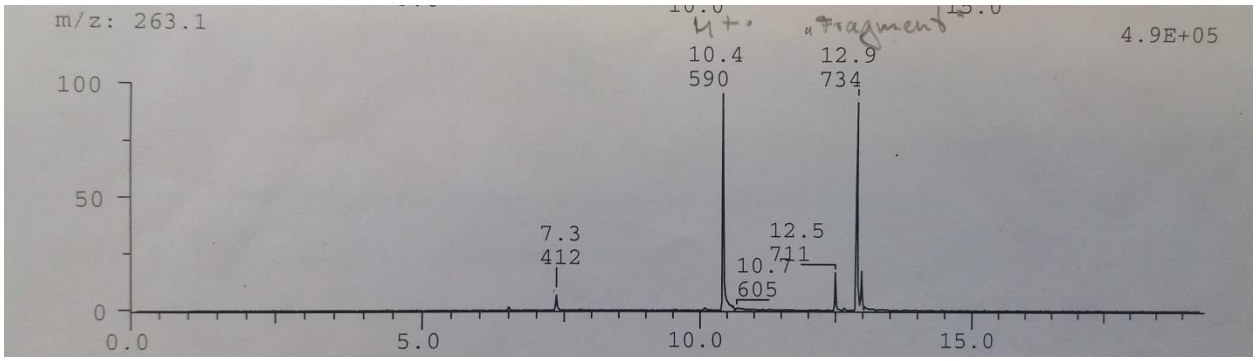
Radical trapping experiment

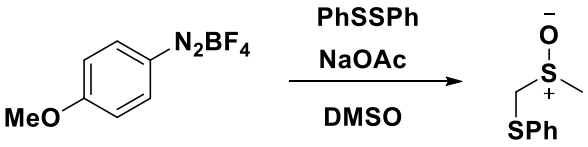
See standard procedure above but with addition of TEMPO (1 equiv., 0.5 mmol) after 30 min.

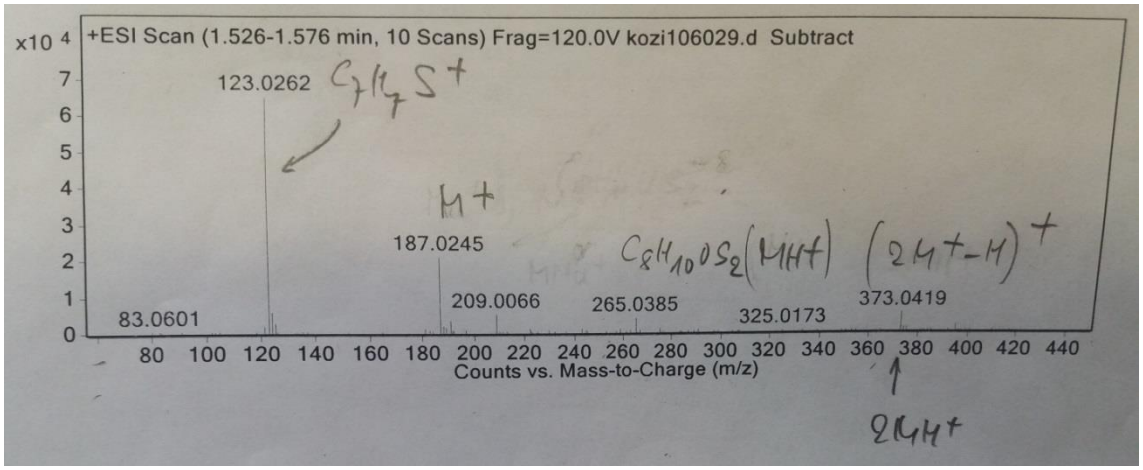


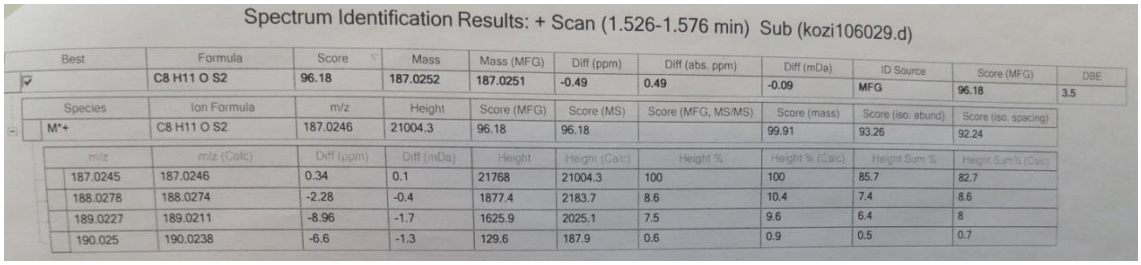
Calculated mass: 263.18









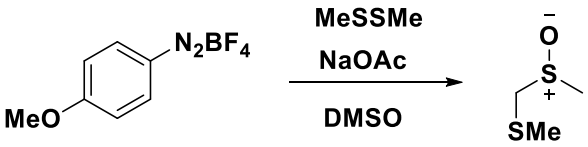


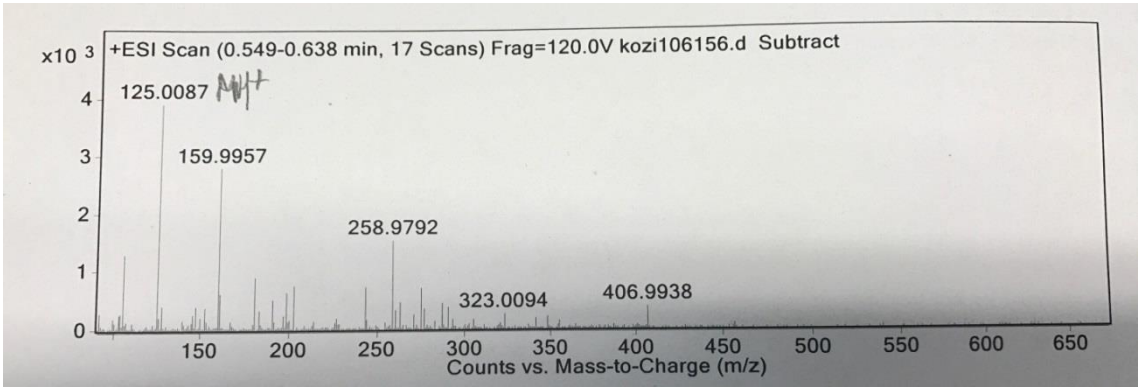
Spectrum Identification Results: + Scan (1.526-1.576 min) Sub (kozi106029.d)

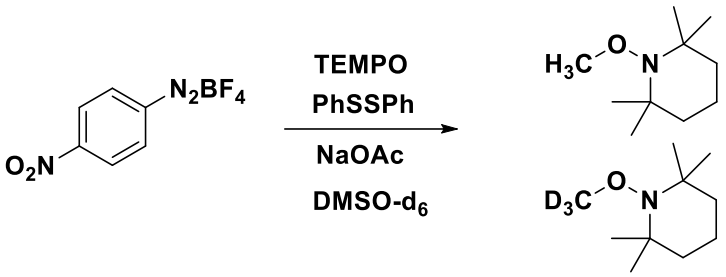
Best	Formula	Score	Mass	Mass (MFG)	Diff (ppm)	Diff (abs. ppm)	Diff (mDa)	ID Source	Score (MFG)	DBE
✓	C8 H11 O S2	96.18	187.0252	187.0251	-0.49	0.49	-0.09	MFG	96.18	3.5

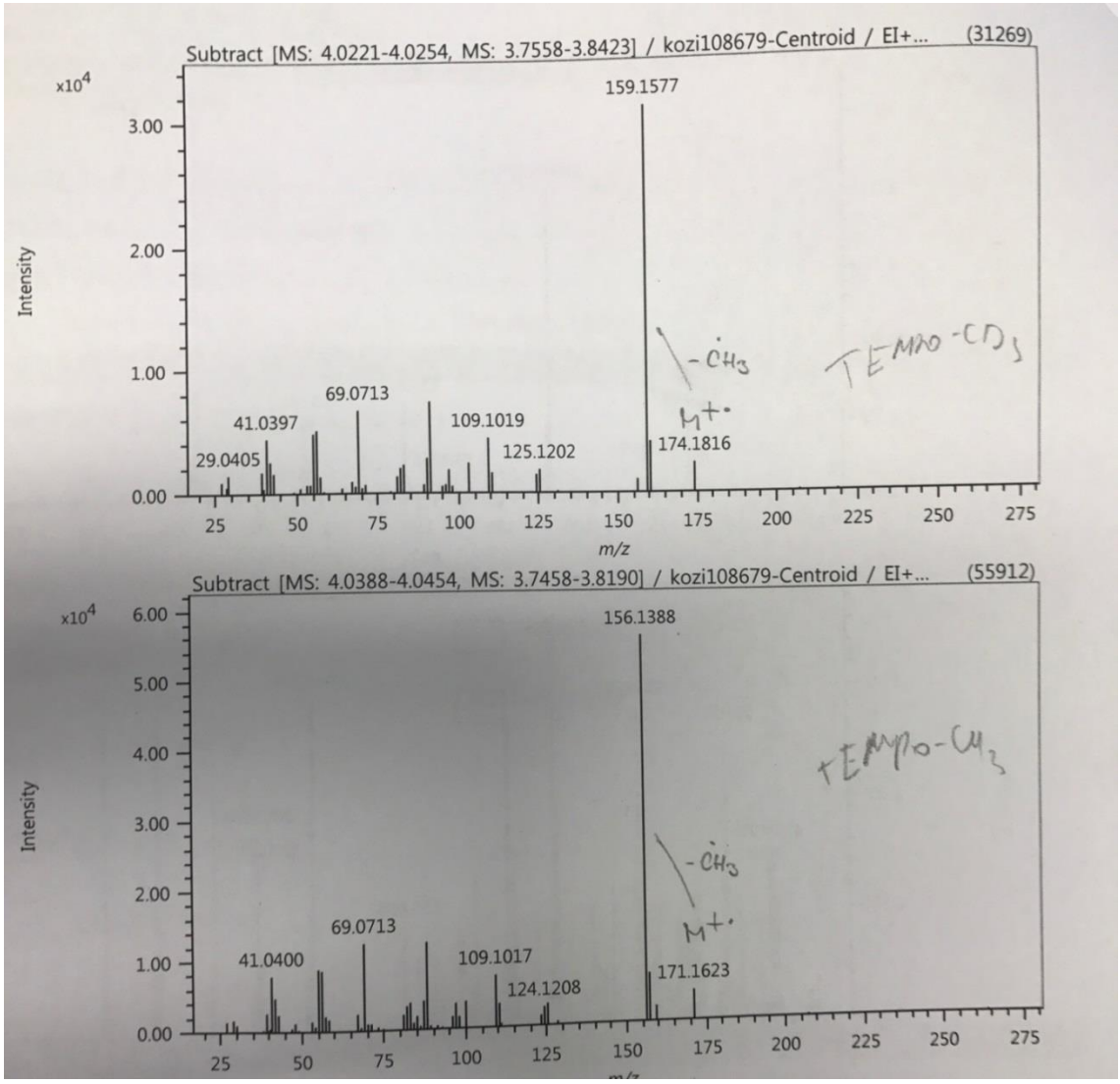
Species	Ion Formula	m/z	Height	Score (MFG)	Score (MS)	Score (MFG, MS/MS)	Score (mass)	Score (iso. abund)	Score (iso. spacing)
M*+	C8 H11 O S2	187.0246	21004.3	96.18	96.18		99.91	93.26	92.24

m/z	m/z (Calc)	Diff (ppm)	Diff (mDa)	Height	Height (Calc)	Height %	Height % (Calc)	Height Sum %	Height Sum% (Calc)
187.0245	187.0246	0.34	0.1	21768	21004.3	100	100	85.7	82.7
188.0278	188.0274	-2.28	-0.4	1877.4	2183.7	8.6	10.4	7.4	8.6
189.0227	189.0211	-8.96	-1.7	1625.9	2025.1	7.5	9.6	6.4	8
190.025	190.0238	-6.6	-1.3	129.6	187.9	0.6	0.9	0.5	0.7





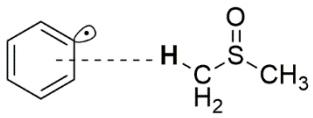




Calculations

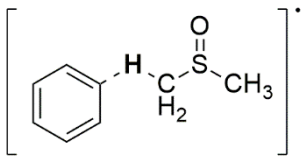
Geometries and energies were calculated using Gaussian G09W.[21a] DFT calculations were performed using M06-2X functional,[21b] and 6-31+G(d,p) basis set. Geometry optimizations and single point calculations were done using the polarized continuum model to account for solvation effects.

Calculated geometries of the optimized structures and transition states:



solvated complex

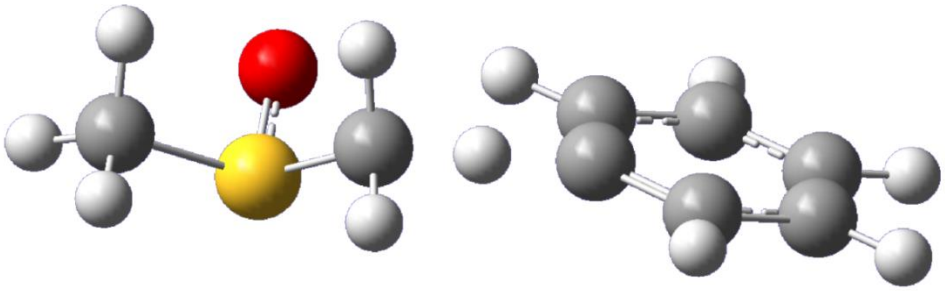
C	-3.75654000	-0.35292600	-0.17780300
C	-3.39646500	0.99452800	-0.24593100
C	-2.05530100	1.37374700	-0.09357500
C	-1.14888500	0.35898900	0.12264900
C	-1.44364500	-0.98519200	0.19797400
C	-2.79071000	-1.33851600	0.04167800
H	-4.79731100	-0.63707500	-0.29706000
H	-4.15411900	1.75379500	-0.41643200
H	-1.75810100	2.41696100	-0.14347800
H	1.17871000	1.62544600	1.07466900
H	-0.66435000	-1.72206400	0.37143000
H	-3.08238300	-2.38372300	0.09150300
C	2.17728200	1.42647200	0.68214700
H	2.49817800	2.24910300	0.04000800
H	2.88418200	1.26552800	1.49923400
S	2.06244100	-0.08797600	-0.29437700
O	1.74965700	-1.20170500	0.70616100
C	3.82056300	-0.25402500	-0.67649400
H	3.94354000	-1.18709500	-1.22722900
H	4.13499500	0.58892300	-1.29527700
H	4.38254600	-0.28700900	0.25950600

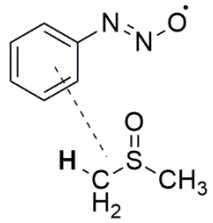


transition state

C	-3.72533200	-0.42086800	-0.10887600
C	-3.43064800	0.94387600	-0.13590800
C	-2.10633700	1.37761200	-0.01126800
C	-1.12199800	0.41427600	0.13688100
C	-1.37559600	-0.94768700	0.16739800
C	-2.70606900	-1.36345200	0.04139200
H	-4.75476000	-0.75179000	-0.20499000
H	-4.22790500	1.67184000	-0.25369900
H	-1.86363500	2.43632000	-0.02984800
H	0.18409400	0.82706700	0.27221300

H	-0.56247700	-1.65921500	0.28513400
H	-2.94401200	-2.42309800	0.06108700
C	1.42657200	1.16914300	0.39646000
H	1.52862400	2.13947200	-0.09035200
H	1.63949900	1.16863600	1.46710800
S	2.30201600	-0.12796500	-0.46626900
O	1.95360500	-1.41821300	0.27776500
C	3.97928700	0.30274300	0.05879900
H	4.65304400	-0.44349900	-0.36468700
H	4.22959000	1.29450700	-0.32298700
H	4.01756700	0.27904000	1.14992200

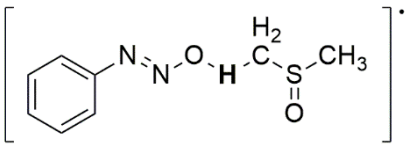




solvated complex

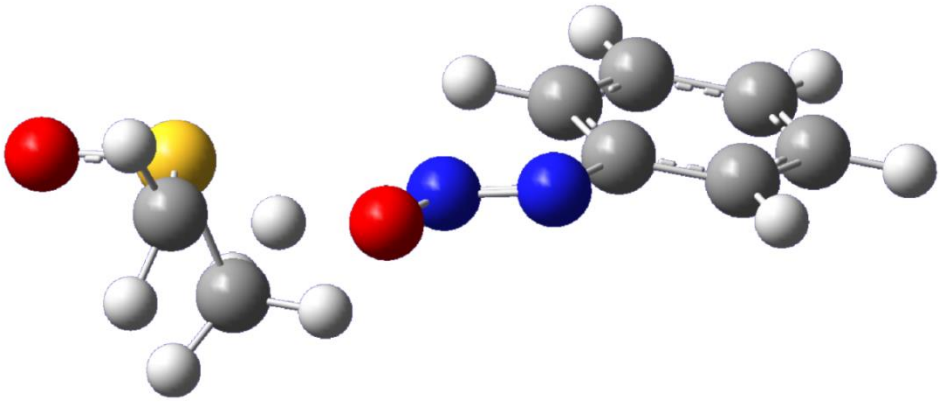
C	-1.90524600	-1.46853900	1.38567200
C	-1.74940300	-0.12792600	1.04812700
C	-1.67297500	0.23012400	-0.30258100
C	-1.76033000	-0.73671200	-1.30359300
C	-1.91583700	-2.07630900	-0.95327300
C	-1.98839400	-2.44488700	0.38919700
H	-1.96403100	-1.75130100	2.43165000
H	-1.69198600	0.63241600	1.82137200
H	-1.70035100	-0.42984300	-2.34294600
H	-1.98067900	-2.82989900	-1.73113700
H	-2.11013600	-3.48815600	0.66122600
N	-1.51623200	1.57213600	-0.76170900
N	-1.30014400	2.42815400	0.09815600
O	-1.12911600	3.61977100	0.03557500
H	0.94576300	1.00043300	1.11986700

C	1.75730500	1.13738100	0.40030200
H	2.37919900	1.98160100	0.69992300
H	1.37087400	1.28666000	-0.61155200
S	2.80213300	-0.33570400	0.41109000
O	3.82479800	-0.13098300	-0.70656700
C	1.57388200	-1.48282800	-0.24643800
H	2.05852900	-2.45385300	-0.35424400
H	0.73791900	-1.55768700	0.45428200
H	1.23593200	-1.11325700	-1.21754800



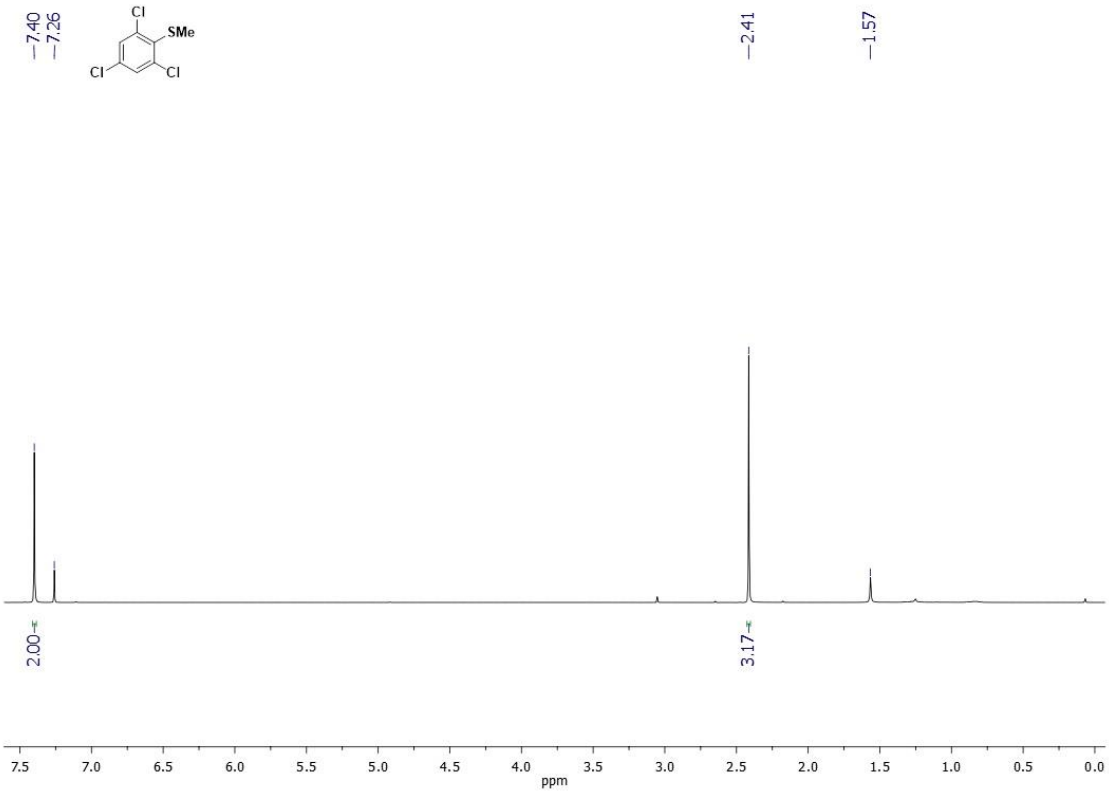
transtion state

C	2.69438100	-1.72231000	-0.39732800
C	1.69265600	-0.75783900	-0.42283400
C	2.00977400	0.56433400	-0.09041000
C	3.31659600	0.91988600	0.24146300
C	4.31251700	-0.05479300	0.26976600
C	4.00276200	-1.37607900	-0.04791400
H	2.45578200	-2.74865900	-0.65728100
H	0.67905900	-1.02103700	-0.70724800
H	3.53578300	1.95592200	0.47989300
H	5.32823400	0.21992400	0.53476900
H	4.77812700	-2.13540000	-0.03199200
N	1.06277000	1.63584300	-0.08595100
N	-0.11065600	1.25595000	-0.08463700
O	-0.96336400	2.28147500	-0.09327900
H	-2.07099100	1.71392400	-0.08586700
C	-3.15663900	1.04535300	-0.14425200
H	-3.62860400	1.39198200	-1.06401800
H	-3.71548500	1.27970400	0.76421300
S	-2.73461800	-0.69740600	-0.28393600
O	-4.10830000	-1.36921500	-0.34410800
C	-2.14150200	-0.95160500	1.40072200
H	-1.93345400	-2.01746900	1.50191200
H	-1.22537600	-0.37572200	1.54782000
H	-2.92393600	-0.64698700	2.09872400

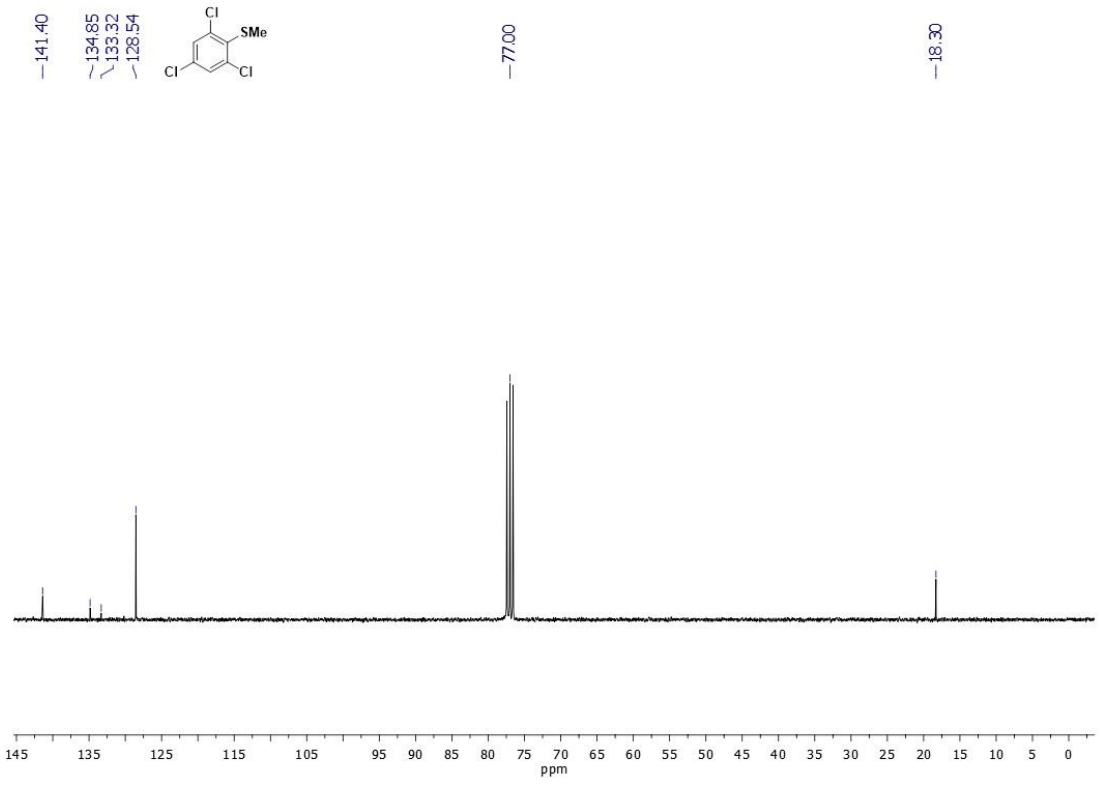


NMR spectra of selected compounds

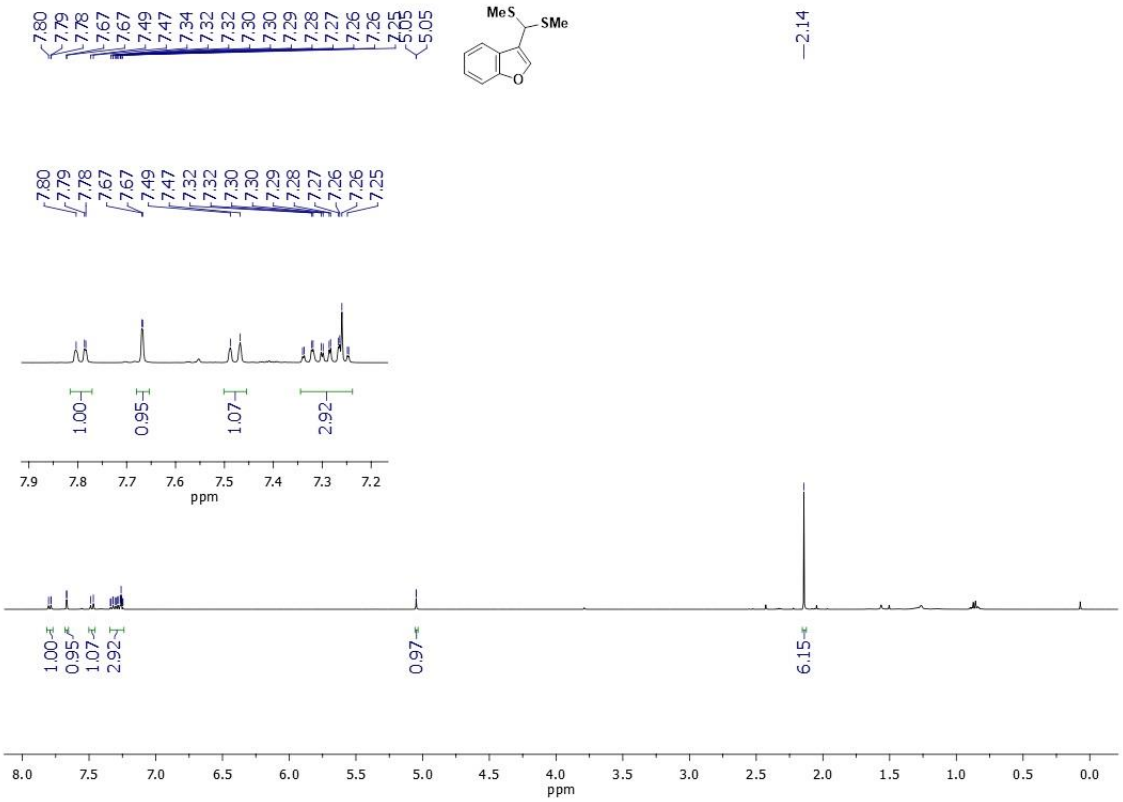
^{1}H-NMR (300 MHz, $CDCl_3$)



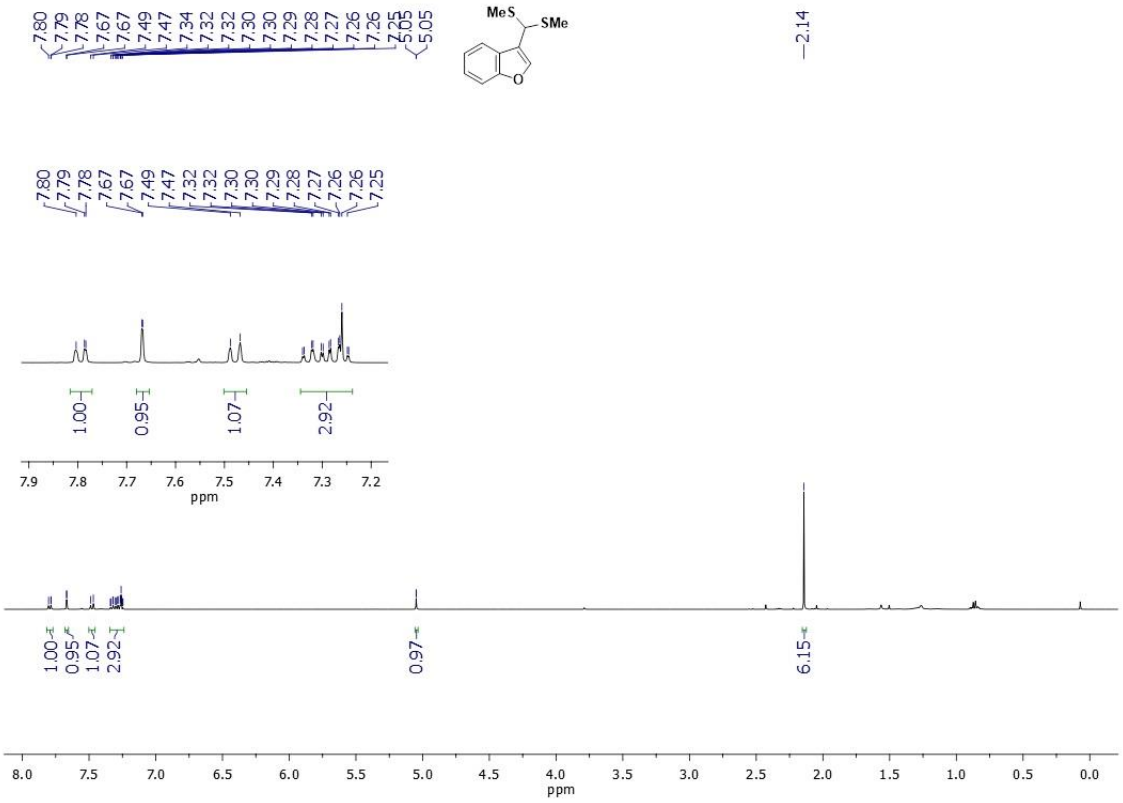
^{13}C-NMR (75 MHz, $CDCl_3$)



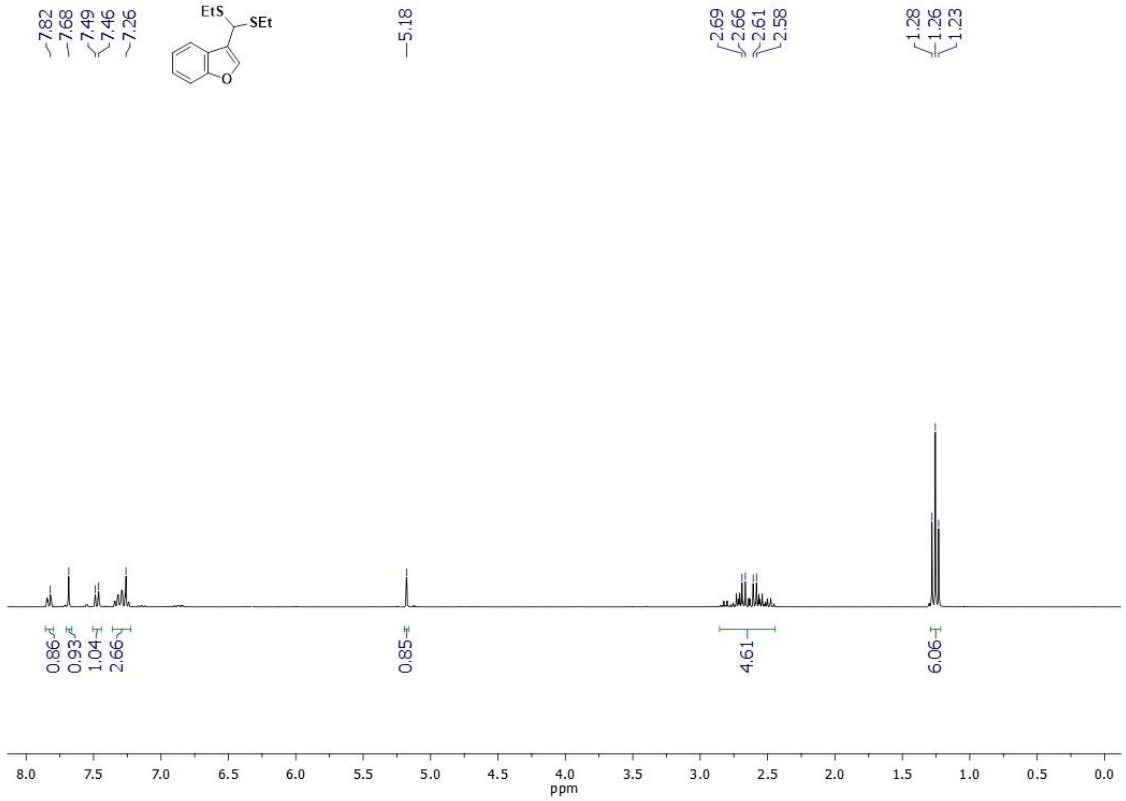
^{1}H-NMR (400 MHz, $CDCl_3$)



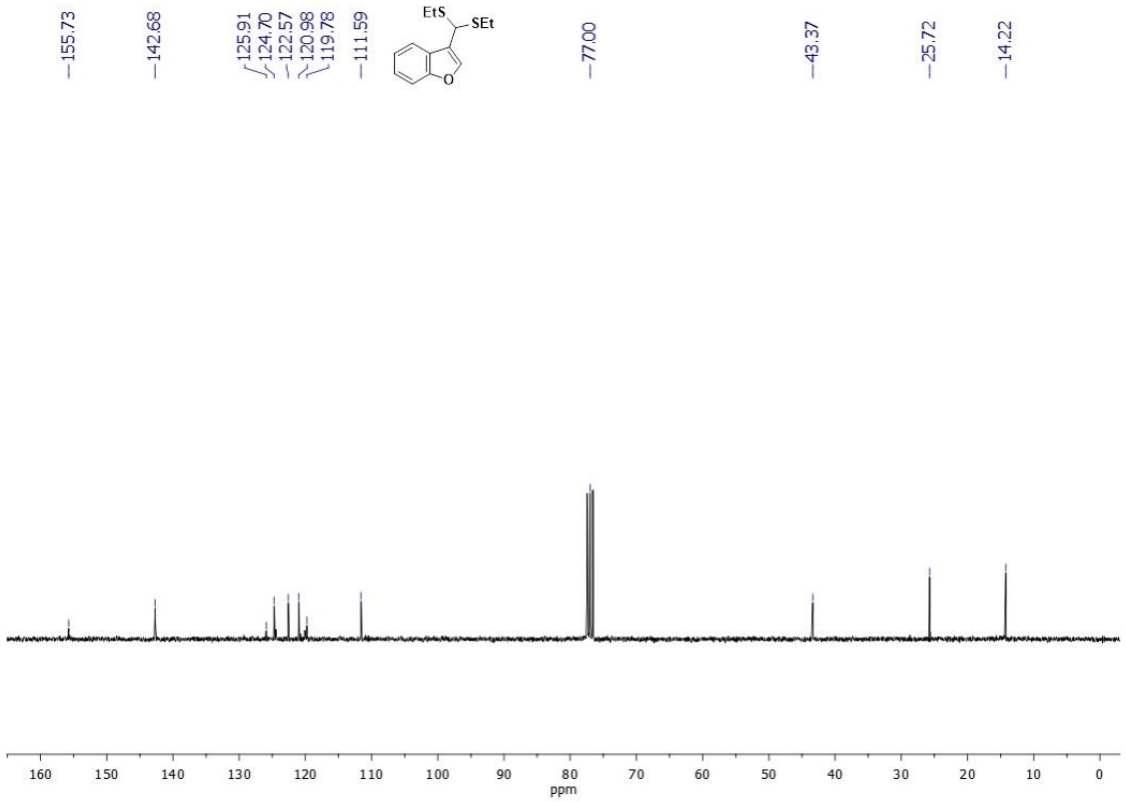
^{13}C-NMR (75 MHz, $CDCl_3$)



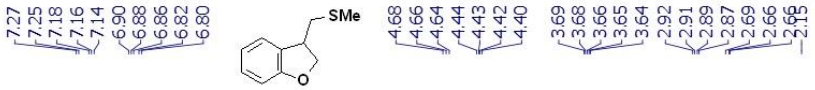
^{1}H-NMR (300 MHz, $CDCl_3$)

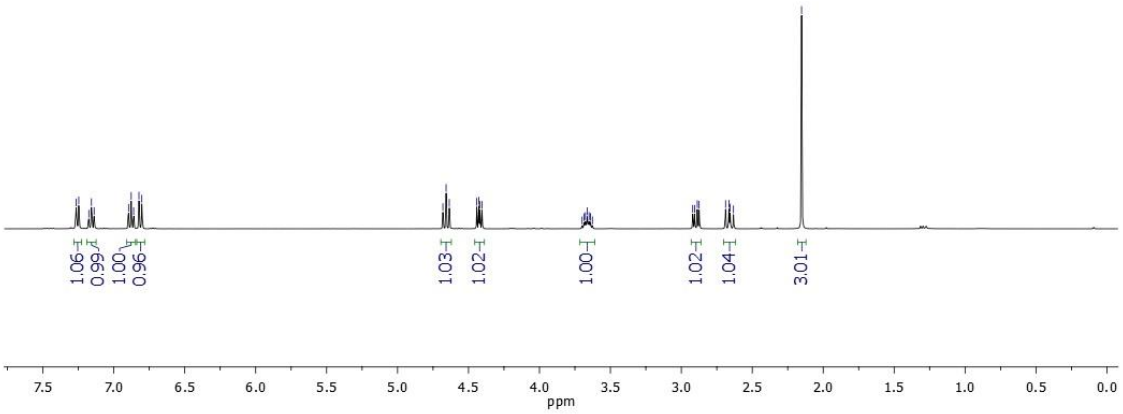


^{13}C-NMR (75 MHz, $CDCl_3$)

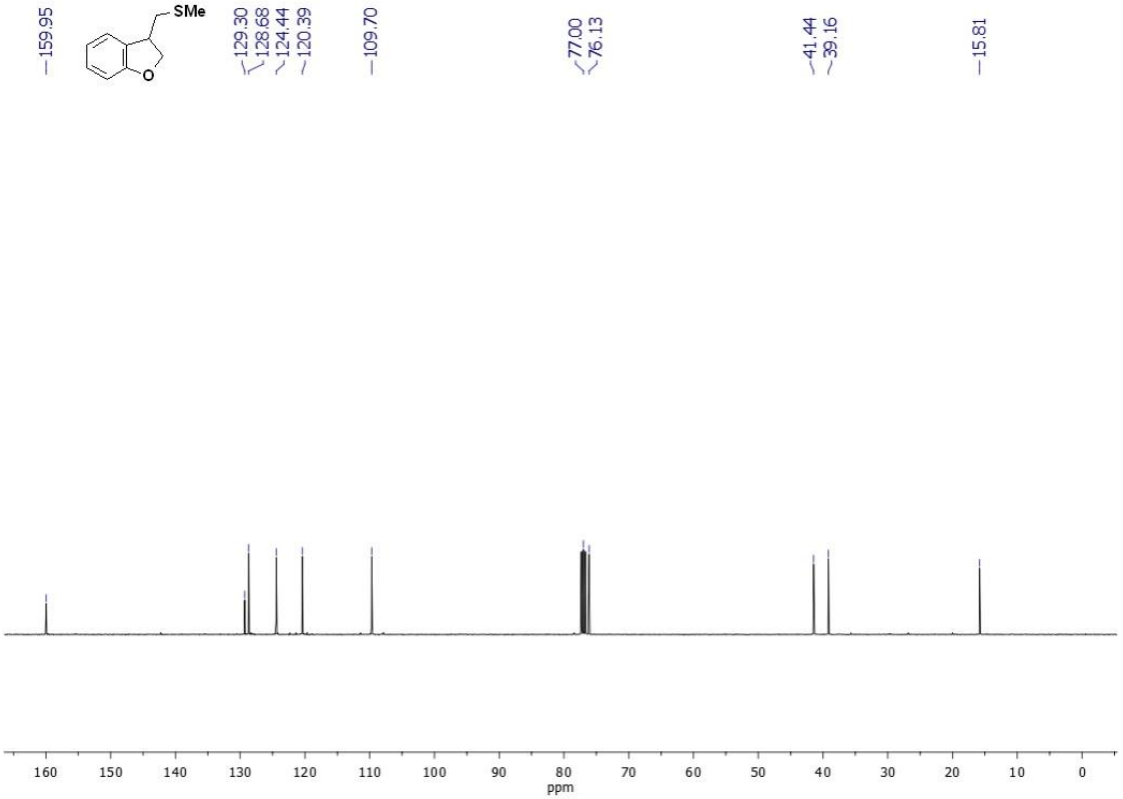


^{1}H-NMR (400 MHz, $CDCl_3$)





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



3.5. References

[1] a) *Patai's Chemistry of Functional Groups: The Thiol Group*, *Vol. 1 and 2* (Ed.: S. Patai), Wiley-VCH, **1974**; b) *Patai's Chemistry of Functional Groups: The Ether Linkage*, (Ed.: S. Patai), Wiley-VCH, **1967**, ch. 13; c) D. N. Jones in *Comprehensive Organic Chemistry*, *Vol. 3* (Eds.: D. H. R. Barton, D. W. Ollis), Pergamon, New York, **1979**.

[2] a) I. P. Beletskaya, V. P. Ananikov, *Chem. Rev.* **2011**, *111*, 1596–1636; b) C. C. Eichman, J. P. Stambuli, *Molecules*, **2011**, *16*, 590–608; c) V. Gomez-Benitez, O. Baldovino-Pantaleon, C. Herrera-Alvarez, R. A. Toscano, D. Morales-Morales, *Tetrahedron Lett.* **2006**, *47*, 5059–5062; d) O. Baldovino-Pantaleon, S. Hernandez-Ortega, D. Morales-Morales, *Inorg. Chem. Commun.* **2005**, *8*, 955–959; e) O. Baldovino-Pantaleon, S. Hernandez-Ortega, D. Morales-Morales, *Adv. Synth. Catal.* **2006**, *348*, 236–242; f) N. Taniguchi, *J. Org. Chem.* **2004**, *69*, 6904–6906; g) S.-i. Fukuzawa, D. Tanihara, S. Kikuchi, *Synlett*, **2006**, *13*, 2145–2147; h) P.-S. Luo, M. Yu, R.-Y. Tang, P. Zhong, J.-H. Li, *Tetrahedron Lett.* **2009**, *50*, 1066–1070; i) W. Fu, T. Liu, Z. Fang, Y. Ma, X. Zheng, W. Wang, X. Ni, M. Hu, T. Tang, *Chem. Commun.* **2015**, *51*, 5890–5893; j) N. Taniguchi, T. Onami, *J. Org. Chem*. **2004**, *69*, 915–920; k) S. Kumar, L. Engman, *J. Org. Chem.* **2006**, *71*, 5400–5403; l) N. Taniguchi, *J. Org. Chem.* **2007**, *72*, 1241–1245.

[3] a) H. H. Hodgson, *Chem. Rev.* **1947**, *40*, 251–277; b) R. Leuckart, *J. Prakt. Chem.* **1890**, *41*, 179–224.

[4] F. Mo, G. Dong, Y. Zhang, J. Wang, *Org. Biomol. Chem.* 2013, **11**, 1582–1593.

[5] a) J. Laquidara, *Chem. Eng. News* **2001**, *79*, 6; b) H. Spencer, *Chem. Brit.* **1977**, *13*, 240–241.

[6] Selected examples: a) T. Zincke, *Chem. Ber.* **1911**, *44*, 769–771; b) A. Luxen, L. Christiaens, *Tetrahedron Lett.* **1982**, *23*, 3905–3908; c) G. Petrillo, R. Novi, G. Garbarino, C. Dellerba, *Tetrahedron* **1986**, *42*, 4007–4016; d) F. Effenberger, H. Isak, *Chem. Ber.* **1989**, *122*, 545–551; e) J. A. Burns, J. C. Butler, J. Moran, G. M. Whitesides, *J. Org. Chem.* **1991**, *56*, 2648–2650; f) P. J. Hogg, *Trends Biochem. Sci.* **2003**, *28*, 210–214; g) M. Erlandsson, M. Hällbrink, *Int. J. Pept. Res. Ther.* **2005**, *11*, 261–265; h) O. Dmitrenko, C. Thorpe, R. D. Bach, *J. Org. Chem.* **2007**, *72*, 8298–8307; i) D. Witt, *Synthesis*, **2008**, *16*, 2491–2509; j) D. Kundu, S. Ahammed, C. R. Brindabad, *Green Chem.* **2012**, *14*, 2024–2030.

[7] a) M. Majek, A. Jacobi von Wangelin, *Chem. Commun.* **2013**, *49*, 5507–5509; b) X. Wang, G. D. Cuny, T. Noël, *Angew. Chem. Int. Ed.* **2013**, *52*, 7860–7864.

[8] J. P. Barham, G. Coulthard, K. J. Emery, E. Doni, F. Cumine, G. Nocera, M. P. John, L. E. A. Berlouis, T. McGuire, T. Tuttle, J. A. Murphy, *J. Am. Chem. Soc.* **2016**, *138*, 7402–7410.

[9] a) L. C. Schmidt, V. Rey, A. B. Penenory, *Eur. J. Org. Chem.* **2006**, *9*, 2210–2214; b) M. E. Buden, J. F. Guastavino, R. A. Rossi, *Org. Lett.* **2013**, *15*, 1174–1177; c) A. Dewanji, S. Murarka, D. P. Curran, A. Studer, *Org. Lett.* **2013**, *15*, 6102–6105. For applications of NaOAc in radical substitution reactions, see: d) U. M. V. Basavanag, A. Dos Santos, L. El Kaim, R. Gamez-Montano, L. Grimaud, *Angew. Chem. Int. Ed.* **2013**, *52*, 7194–7197; e) Y. Sawama, R. Nakatani, T. Imanishi, Y. Fujiwara, Y. Monguchi, H. Sajiki, *RSC Adv.* **2014**, *4*, 8657–8660; f) KOAc-mediated Meerwein alkenylation: C. Molinaro, J. Mowat, F. Gosselin, P. D. O'Shea, J.-F. Marcoux, R. Angelaud, I. W. Davies, *J. Org. Chem.* **2007**, *72*, 1856–1858.

[10] a) R. Francke, D. Little, *Chem. Soc. Rev.* **2014**, *43*, 2492–2521; b) A. Studer, D. P. Curran, *Angew. Chem. Int. Ed.* **2016**, *55*, 58–102.

[11] Base-mediated thiolations: a) A. Kumar, B. S. Bhakuni, Ch. D. Prasad, S. Kumar, S. Kumar, *Tetrahedron*, **2013**, *69*, 5383–5392; b) N. Mukherjee, T. Chatterjee, B. C. Ranu, *J. Org. Chem.* **2013**, *78*, 11110–11114; c) R.-Y. Tang, P. Zhong, Q.-L. Lin, *Synthesis* **2007**, *1*, 85–91.

[12] S. Shaaban, A. Jolit, D. Petkova, N. Maulide, *Chem. Commun.* **2015**, *51*, 13902–13905.

[13] K. G. Back, A. A. Thomas, *Am. Ind. Hyg. Assoc. J.* **1963**, *24*, 23–27.

[14] G. Landelle, A. Panossian, F. R. Leroux, *Curr. Top. Med. Chem.* **2014**, *14*, 941–951.

[15] a) A. L. J. Beckwith, C. J. Easton, A. K. Serelis, *J. Chem. Soc. Chem. Commun.* **1980**, 482–483; b) A. L. J. Beckwith, *Tetrahedron* **1981**, *37*, 3073–3100; c) A. L. J. Beckwith, C. H. Schiesser, *Tetrahedron* **1985**, *41*, 3925–3941; d) J. E. Baldwin, *J. Chem. Soc. Chem. Commun.* **1976**, 734–736; e) A. Srikrishna, *J. Chem. Soc. Chem. Commun.* **1987**, 587–588.

[16] a) F. Dénès, M. Pichowicz, G. Povie, P. Renaud, *Chem. Rev.* **2014**, *114*, 2587–2693; b) M. P. Bertrand, C. Ferreri in *Radicals in Organic Synthesis* (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, **2001**, 485–504.

[17] E. H. Krenske, W. A. Pryor, K. N. Houk, *J. Org. Chem.* **2009**, *74*, 5356–5360.

[18] ESI-MS spectra also documented the formation of TEMPO-CH_3 and TEMPO-CD_3 adducts from standard reactions performed in DMSO and DMSO-d_6, respectively.

[19] Electron affinity of the acetyloxy radical: X.-B. Wang, H.-K. Woo, L.-S. Wang, B. Minofar, P. Jungwirth, *J. Phys. Chem. A* **2006**, *110*, 5047–5050.

[20] a) A comprehensive review of radical reactions with arenediazonium salts: C. Galli, *Chem. Rev.* **1988**, *88*, 765–792. Diazotate radicals in the presence of weak carboxylate bases: b) R. Huisgen, G. Horeld, *Ann. Chem.* **1949**, *562*, 137–162; c) R. Huisgen, H. Nakaten, *Ann. Chem.* **1951**, *573*, 181; d) G. H. Williams in *Homolytic Aromatic Substitution*, Pergamon,

London, **1960**; e) T. Kauffmann, H. O. Friestad, H. Henkler, *Ann. Chem.* **1960**, *634*, 64; f) C. Rüchardt, E. Merz, *Tetrahedron Lett.* **1964**, *5*, 2431–2534; g) C. Rüchardt, B. Freudenberg, E. Merz, *Spec. Publ. Chem. Soc.* **1965**, 154; h) J. Besse, H. Zollinger, *Helv. Chim. Acta* **1981**, *64*, 529; i) R. M. Elofson, N. Cyr, J. K. Laidler, *Tetrahedron Lett.* **1990**, *31*, 7205; h) S. Kindt, K. Wicht, M. R. Heinrich, *Org. Lett.* **2015**, *17*, 6122–6125.

[21] a) This mechanism would require the deprotonation of the intermediate arenediazohydroxide by NaOAc which is very unlikely based on the reported pK_a value of 6-8 (H_2O): E. S. Lewis, M. P. Hanson, *J. Am. Chem. Soc.* **1967**, *89*, 6268–6272. b) For diazotates in acidic/basic water, see: O. Macháčková, V. Štěrba, *Collect. Czech. Chem. Commun.* **1972**, *37*, 3313–3327.

[22] a) M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, *Gaussian 09, Rev. E.01*, Gaussian Inc., Wallingford CT, **2009**; b) Y. Zhao, D. G. Truhlar, *Theor. Chem. Acc.* **2008**, *120*, 215–251.

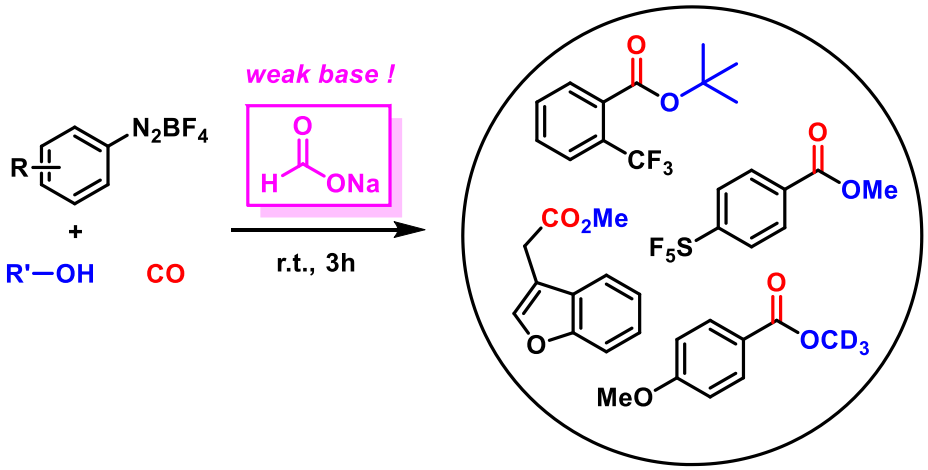
[23] a) J. F. Bunnett, *Acc. Chem. Res.* **1978**, *11*, 413–420; b) C. L. Øpstad, T.-B. Melø, H.-R. Sliwka, V. Partali, *Tetrahedron* **2009**, *65*, 7616–7619; c) K. L. Handoo, A. Kaul, *Indian J. Chem. B* **1992**, *31*, 561; d) R. A. Alonso, R. A. Rossi, *Tetrahedron Lett.* **1985**, *26*, 5763–5764; e) N. Kornblum, A. S. Erickson, *J. Org. Chem.* **1981**, *46*, 1037–1039.

[24] For selected works on dichalcogenide reactions, see: a) A. L. Stein, F. N. Bilheri, G. Zeni, *Chem. Commun.* **2015**, *51*, 15522–15525; b) G. Sartori, J. S. S. Neto, A. P. Pesarico, D. F. Back, C. W. Nogueiraa, G. Zeni, *Org. Biomol. Chem.* **2013**, *11*, 1199–1208; c) A. R. Rosario, K. K. Casola, C. E. S. Oliveira, G. Zeni, *Adv. Synth. Catal.* **2013**, *355*, 2960–2966.

[25] a) G. Pandey, K. S. Sesha Poleswara Rao, D. K. Palit, J. P. Mittal *J. Org. Chem.* **1996**, *61*, 6799–6804; b) G. Pandey, S. R. Gadre, *Acc. Chem. Res.* **2004**, *37*, 201–210.

Chapter 4

- Metal-free Radical Aromatic Carbonylations Mediated by Weak Bases -



Abstract: We report a new method of metal-free alkoxycarbonylation. This reaction involves the generation of aryl radicals from arenediazonium salts by a very weak base (HCO_2Na) under mild conditions. Subsequent radical trapping with carbon monoxide and alcohols gives alkyl benzoates. The conditions (metal-free, 1 equiv. base, MeCN, r.t., 3 h) tolerate various functional groups (I, Br, Cl, CF_3, SF_5, NO_2, ester). Mechanistic studies indicate the operation of a radical aromatic substitution mechanism.

This chapter has been published:
D. Koziakov, A. Jacobi von Wangelin, *Org. Biomol. Chem*. **2017**, *15*, 6715–6719.

Author contributions:
Denis Koziakov synthesized starting materials, did reactions, and wrote the manuscript.

4. Metal-free Radical Aromatic Carbonylations Mediated by Weak Bases

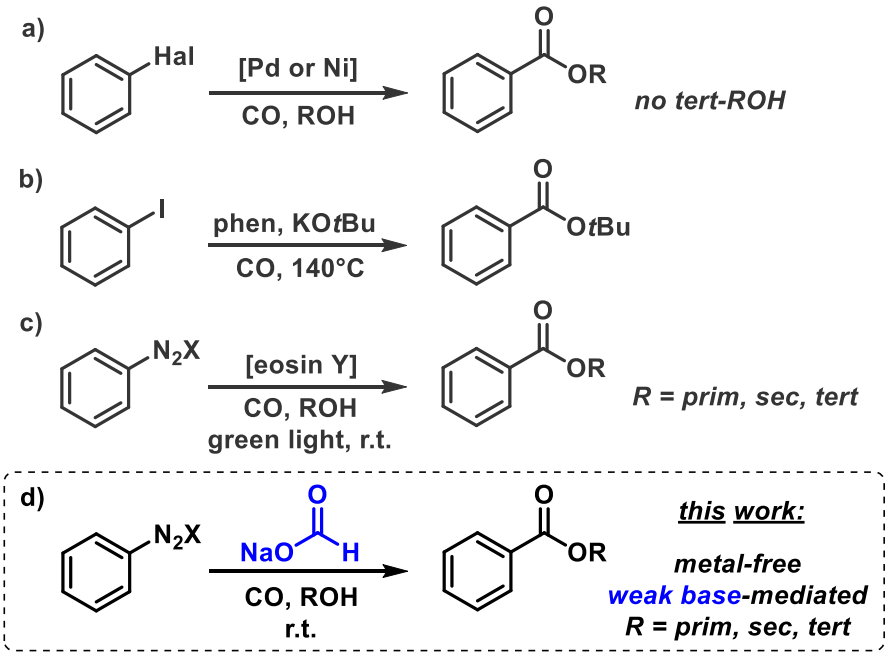
4.1. Introduction

Benzoates are key structural motifs of numerous fine chemicals, agrochemicals, pharmaceuticals, materials, and natural products.[1] The transition metal-catalyzed alkoxycarbonylation of aryl electrophiles with carbon monoxide and alcohols is the most versatile synthesis method for benzoates (Scheme 4.1a).[2] On the other hand, related metal-free carbonylations are rare.[3] Lei and co-workers reported a radical *tert*-butoxycarbonylation of aryl iodides mediated by KO*t*Bu/phenanthroline (Scheme 4.1b).[4] This reaction is most likely initated by single-electron transfer from extended heteroaromatic radical anions that form upon base-mediated thermal condensation. However, severe limitation arise from the exclusive production of *tert*-butyl benzoates, the harsh conditions, and the little mechanistic insight.[5] Our group and Xiao *et al*. simultaneously developed photoredox-catalyzed alkoxycarbonylations of arenediazonium salts with wide scope under mild conditions.[6] We believed that a robust and versatile method of alkoxycarbonylation would enable the reaction of easily accessible aryl electrophiles with various primary, secondary, and tertiary alcohols under mild conditions with the aid of a cheap initiator. Arenediazonium salts constitute an especially versatile class of aryl electrophiles that display distinct reactivity from aryl halides, can easily be prepared from anilines, and undergo ready degradation to aryl radicals in the presence of reductants and bases.[7] The formation of aryl radicals from arenediazonium salts with very weak bases under ambient conditions was demonstrated in the context of several radical aromatic substitution reactions.[7b,8] The application of arenediazonium salts to radical alkoxycarbonylations were recently realized in photoredox-catalyzed processes (Scheme 4.1c).[6] We surmised that the sequential combination of both reactivity concepts, *i)* the mild generation of aryl radicals from arenediazonium salts and very weak bases and *ii)* the facile trapping of aryl radicals with carbon monoxide and alcohols, would allow for an expedient method of alkoxycarbonylation of arenes and obviate the need for radical initiators, metal catalysts, inert conditions, or irradiation equipment (Scheme 4.1d).[9]

4.2. Results and Discussion

Following earlier work on radical aromatic substitutions,[6a,10] we investigated the efficacy of weak carboxylates as initiators[11] of radical carbonylations. We aimed at the use of inorganic bases as they are cheap, environmentally benign, and can be easily removed from the organic products. The initial model reaction of the white crystalline 4-nitrobenzenediazonium tetrafluoroborate (**1**) with CO and *tert*-butanol cleanly afforded the *tert*-butyl ester **2** (Table 4.1). It is

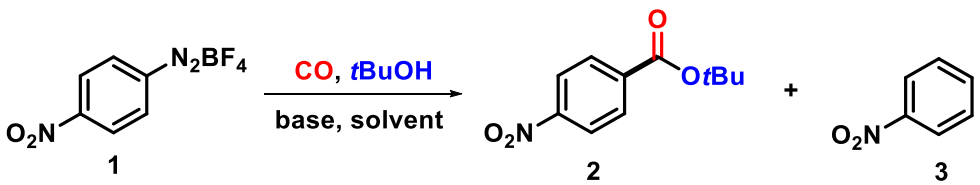
important to note that transition metal-catalyzed alkoxy-carbonylations mostly fail to deliver *tert*-butyl esters due to the steric bulk of the alcohol. Co-solvents were added to assist the dissolution of the arenediazonium salt **1**.



Scheme 4.1. Alkoxycarbonylation of aryl electrophiles.

A survey of inexpensive bases showed highest activity and selectivity with stoichiometric amounts of sodium formate which resulted in minimal hydrodediazonation toward **3**.[10b] No reaction was observed in the absence of base. Importantly, the reaction displayed no sensitivity toward air and moisture. The optimized conditions involved equimolar sodium formate and **1** (~0.1 M) in a mixture of *t*-butanol/acetonitrile (10/1) under pressurized CO (50 bar) for 3 h at room temperature to give *tert*-butyl 4-nitrobenzoate (**2**) in 80% yield (entry 1).

Table 4.1. Optimization experiments.[a]



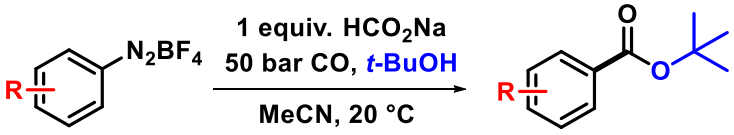
Entry	Base	Solvent (mL)	Equiv. *t*BuOH	Yield 2 / 3 [%]
1	**HCO_2Na**	**MeCN (0.4)**	**100**	**80 / 9**
2	AcONa	MeCN (0.4)	100	71 / 19
3	BzONa	MeCN (0.4)	100	71 / 10
4	K_2CO_3	MeCN (0.4)	100	71 / 8

5	HCO_2Na	MeCN (0.2)	100	76 / 9
6	HCO_2Na	MeCN (3)	1	8 / 3
7	NaH	MeCN (0.4)	100	24 / 15
8[b]	HCO_2Na	MeCN (0.2)	66	61 / 17
9[b]	*n*BuLi	MeCN (0.2)	66	22 / 18
10[b]	H_2NNMe_2	MeCN (0.2)	66	3 / 26
11[b]	HCO_2Na	AcMe (0.2)	66	58 / 18
12[b]	HCO_2Na	DMF (0.2)	66	26 / 25
13[b]	HCO_2Na	H_2O (0.2)	66	18 / 20
14[b]	HCO_2Na	MeCN (0)	66	40 / 18

[a] Conditions: 4-Nitrobenzenediazonium tetrafluoroborate (0.3 mmol), base (0.3 mmol), r.t., CO (50 bar), 12 h, GC yields *vs.* internal 1-dodecanenitrile; [b] CO (30 bar).

The optimized conditions were applied to a set of diverse arenediazonium salts (Table 4.2).

Table 4.2. Carbonylation of arenediazonium salts with *tert*-butanol.[a]

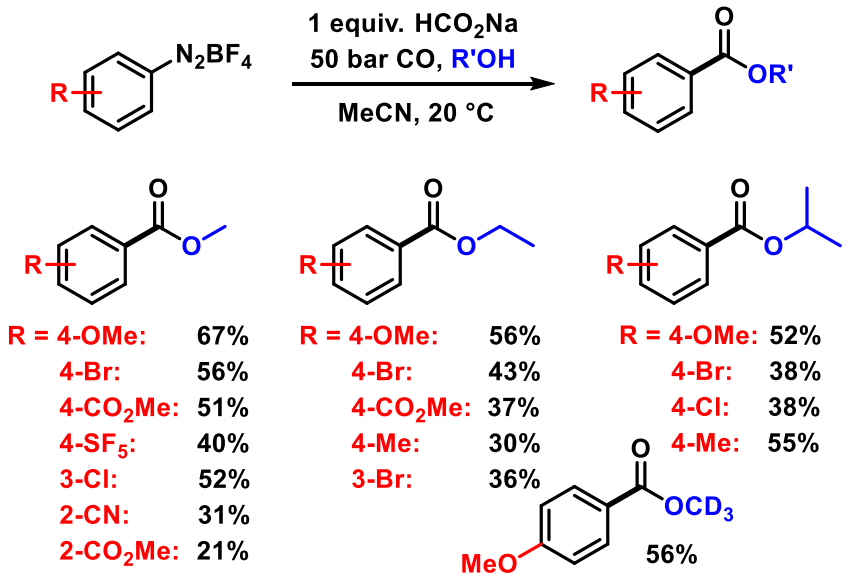


Aryl	Yield [%]	Aryl	Yield [%]
4-O_2N-C_6H_4	75	4-MeO-C_6H_4	44
4-Br-C_6H_4	63	3-Br-C_6H_4	52
4-Cl-C_6H_4	66	3-Cl-C_6H_4	60
4-I-C_6H_4	42	2-MeO-C_6H_4	49
4-F_3C-C_6H_4	50	2-F_3C-C_6H_4	54
4-Me-C_6H_4	61	2-O_2N-C_6H_4	<5
4-MeO_2C-C_6H_4	56	2-MeO_2C-C_6H_4	<5
4-F_5S-C_6H_4	51	1-naphthyl	54

[a] Conditions: arenediazonium tetrafluoroborate (0.9 mmol), HCO_2Na (0.9 mmol), *t*BuOH (9 mL), MeCN (1.2 mL), CO (50 bar), r.t., 3 h.

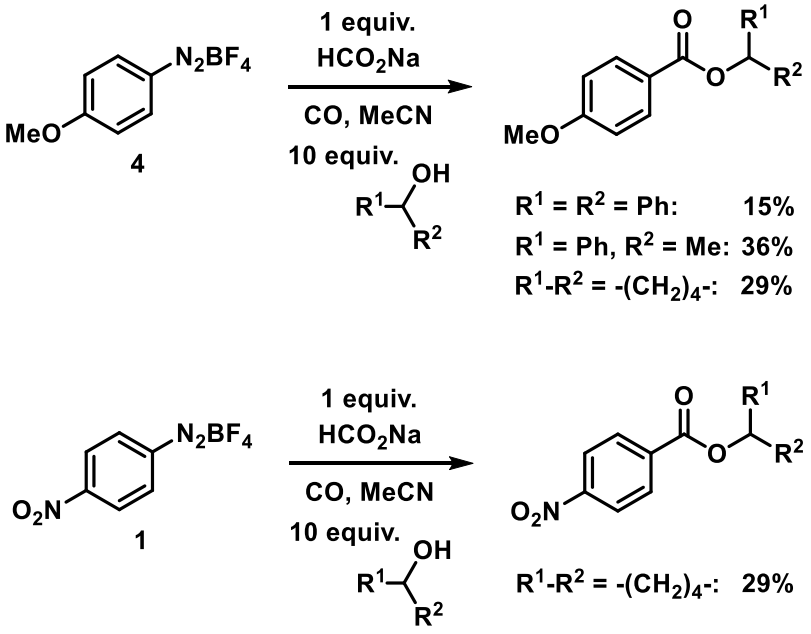
Halides, esters, CF_3, SF_5, and naphthyl substituents were tolerated. Especially the high chemoselectivity in the presence of aryl halide entities under the reaction conditions is a major advantage over metal-catalyzed protocols. With 2-nitro and 2-carboxymethyl substituents, only very little product formation was observed. Under similar conditions, methanol, ethanol, and *i*-propanol were reacted as simplest representatives of *n*- and *s*-alcohols (Scheme 4.2).

Generally, alkoxycarbonylations of **4** afforded the highest yields with MeOH, EtOH, and *i*PrOH while the more electrophilic **1** showed higher reactivity with *t*BuOH. Despite the good solubility of arenediazonium salts in these alcohols, the addition of acetonitrile as co-solvent was shown to lower the rate of the hydrodediazonation pathway.[10b] Generally, the yields of ethyl and *i*-propyl esters were slightly lower than those of the methyl esters which is a consequence of the higher propensity of the former to engage in hydrogen atom transfer reactions.



Scheme 4.2. Methyl, ethyl, and *i*-propyl benzoate syntheses.

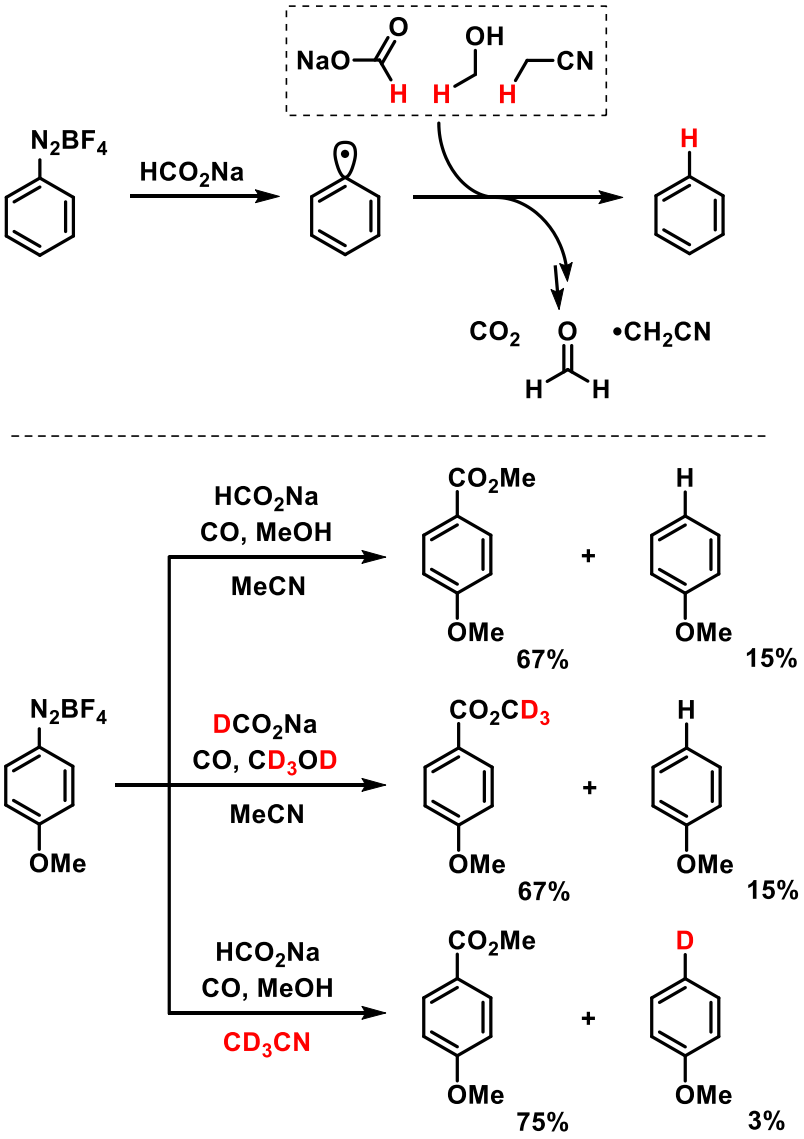
Likewise, other *sec*-alcohols gave the benzoates in moderate yields and the corresponding ketones from competing alcohol oxidation (Scheme 4.3).



Scheme 4.3. Alkoxycarbonylations with *sec*-alcohols.

For short-chain alcohols, the resultant oxidized by-products are volatile and therefore require no laborious separation from the benzoates. In the case of tertiary alcohols, H atom transfer operated exclusively from the α-position of acetonitrile.

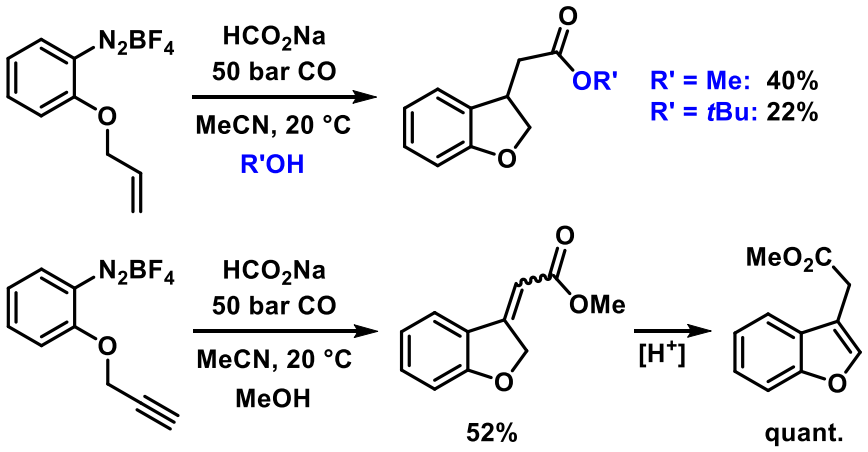
Deuterium labelling in the methoxycarbonylation of 4-methoxybenzenediazonium tetrafluoroborate (**4**) with d_4-methanol, sodium d_1-formate, and d_3-acetonitrile, respectively, revealed the significant deuterium atom transfer from the solvent in methoxycarbonylations (Scheme 4.4). This trend was supported by experiments with d_3-MeCN, *t*-BuCN, and d_6-acetone as co-solvents which enhanced the selectivity of the alkoxycarbonylation.



Scheme 4.4. Competing hydrodediazonation by α-H atom transfer.

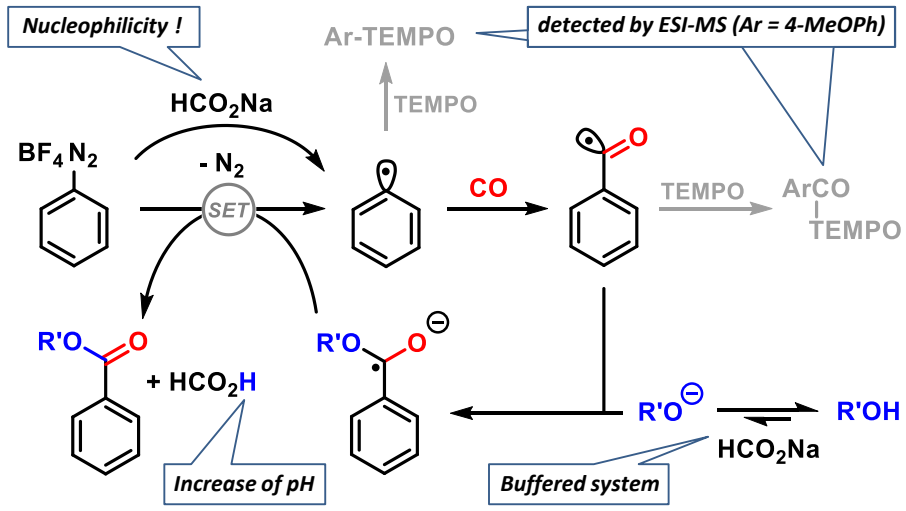
A methodological extension of the alkoxycarbonylation was realized with tethered alkenes and alkynes (Scheme 4.5). Reactions of 2-

allyloxybenzenediazonium tetrafluoroborate afforded 2,3-dihydrobenzofuran-3-yl acetates by a sequence of aryl radical formation, intramolecular 5-*exo* ring closure, and alkoxycarbonylation. The related propargyl derivative cleanly gave the benzofuran-3-yl acetate after acid-mediated olefin isomerization during workup.[6b] The latter reaction constitutes an inexpensive alternative to the palladium-catalyzed Heck olefination of the same substrate.[12]



Scheme 4.5. Sequential cyclization-alkoxycarbonylation reactions.

Key mechanistic studies were performed that support the notion of a radical pathway involving intermediate aryl and acyl radicals (Scheme 4.6).



Scheme 4.6. Postulated mechanism of the formate-mediated alkoxycarbonylation of arenediazonium salts.

The initiation of the arenediazonium ion degradation to reactive aryl radicals by very weak bases was already reported earlier.[7b,8] Nucleophilic attack of the formate onto the diazonium terminus most likely generates a diazoformate adduct which decomposes to an aryl radical.[8] Consistent with this ionic initiation step, the use of sodium trifluoroacetate instead of sodium formate

gave identical reactivity with **1**, whereas the much less electrophilic **4** was unreactive with the less nucleophilic NaO_2CCF_3. With the radical trap 2,2,6,6-tetramethyl piperidinyloxyl (TEMPO), rapid formation of the aryl and aroyl adducts was observed under reaction conditions. We postulate that the employed base affects the acid-base equilibrium of the alcohol toward the more nucleophilic alkoxide. However, acid-catalysis could enhance the electrophilicity of the aroyl radical. The direct attack of the alcohol/alkoxide onto the aroyl radical distinguishes this mechanism from carbonylations of organo-halides (mostly iodides) which operate *via* the acyl halide intermediate.[9] Both reactivity patterns can most effectively be provided by a buffered system comprising of a weak base. The potentially good reducing power of the intermediate aroyl radical and dioxa-substituted benzyl radical suggests the operation of a radical chain mechanism.[13] Besides the initial aryl radical formation, the base sodium formate could induce (minor) deprotonation to give the alcoholate $R'O^-$ and/or the intermediate ketyl-type radical anion. The consumption of the base was indirectly proven by a steady decrease of the pH over the course of the reaction (to pH 4 upon completion).

4.3. Conclusion

We have developed a new alkoxycarbonylation protocol that affords alkyl benzoates from arenediazonium salts, carbon monoxide, and alcohols. This method provides a useful alternative to metal-catalyzed carbonylation reactions. The competition of hydrogen atom transfer can be reduced by the choice of alcohols and solvents. The radical reaction mechanism is most likely initiated by the ionic reaction between the aryl electrophile and sodium formate under mild conditions. The intermediacy of aryl and aroyl radicals was shown by radical trapping experiments. Further applications of the concept of weak base-initiated radical cascade processes to other substrates are actively being pursued in our laboratories.

4.4. Experimental Section

General

Chemicals and Solvents. Commercial chemicals (≥98% purity) were used as obtained from Sigma-Aldrich or Fisher. Solvents (anhydrous, ≥99%) were used without further purification. Acetonitrile was stored over molecular sieves (Sigma-Aldrich). Methanol, ethanol, and *iso*-propanol were distilled under an inert atmosphere of nitrogen gas and stored over molecular sieves. Carbon monoxide (4.7) was used.

Analytical thin-layer chromatography. TLC was performed using aluminium plates with silica gel and fluorescent indicator (DC60 F254, Merck). Thin layer chromatography plates were visualized by exposure to UV light.

Column chromatography. Flash column chromatography with silica gel (60 Å, 0.035-0.070 mm) from *Acros Organics*. Pentane or mixtures thereof with ethyl acetate were used as eluents. Product yields were determined as isolated by column chromatography or for optimization and screening purposes by quantitative GC-FID measurements. 1-Dodecanenitrile was used as internal standard; the yield was calculated from a linear calibration curve that was set up from at least five data points of various concentrations of authentic product material.

Gas chromatography with mass-selective detector. *Agilent* 6890N Network GC-System, mass detector 5975 MS. Column: BPX5 (30m x 0.25 mm x 0.25, from *SGE*, carrier gas: H_2. Standard heating procedure: 50°C (2 min), 25°C/min -> 300°C (5 min).

Gas chromatography with FID. *Agilent* 7820A GC-Systems. Column: HP 5 19091J 413 (30 m x 0.32 mm x 0.25 µm) from *Agilent*, carrier gas: N_2. GC-FID was used for reaction optimization screening (Calibration with internal standard 1-dodecanenitrile and analytically pure samples).

NMR. ^{1}H, ^{19}F, and ^{13}C nuclear magnetic resonance spectra were recorded on a *Bruker* Avance 300 (300 MHz ^{1}H; 75 MHz ^{13}C; 282 MHz ^{19}F) and *Bruker* Avance 400 (400 MHz ^{1}H, 101 MHz ^{13}C) spectrometers. Chemicals shifts are reported in ppm (δ) relative to solvent residual peak as internal reference. Coupling constants (*J*) are reported in Hertz (Hz). Following abbreviations are used for spin multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sep = septet, m = multiplet, dd = doublet of doublet, dt = doublet of triplet, td = triplet of doublet, tt = triplet of triplet.

High resolution mass spectrometry (HRMS). The spectra were recorded by the Central Analytics Lab at the Department of Chemistry, University of Regensburg, on a MAT SSQ 710 A from *Finnigan*.

General procedure for the synthesis of arenediazonium salts

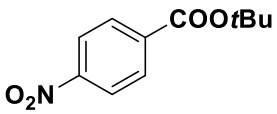
The parent aniline (30 mmol) was dissolved in 32% aqueous tetrafluoroboric acid (12 mL) at room temperature. Afterwards, an aqueous solution of sodium nitrite (30 mmol) in water (4 mL) was added dropwise at 0 °C over 5 min. The resulting mixture was stirred for 40 min and the precipitate was collected by filtration and re-dissolved in minimum amount of acetone. Then, diethyl ether was added until precipitation of diazonium tetrafluoroborate, which is filtered, washed several times with diethyl ether and dried.

General procedure for alkoxycarbonylation

A rolled rim bottle (20 mL) was charged with a magnetic stir bar, the arenediazonium salt (0.9 mmol), sodium formate (0.9 mmol), acetonitrile (1.2 mL for reactions with *t*-BuOH, 9 ml for other alcohols), alcohol (9 mL of *t*-BuOH, 45 mmol of other alcohols) and capped with a snap-on lid. The snap-on lid was punctured with a needle. The reactor was sealed, placed on a magnetic stirrer, and slowly filled with CO (50 bar). After 3 h of stirring, water (5 mL) was added to give an emulsion, which was extracted with ethyl acetate (3 x 5 mL). The organic phases were washed with brine (5 mL) and dried ($MgSO_4$). The solvent was evaporated *in vacuo*; the residue was purified by flash column chromatography (silica gel) using pentane/ethyl acetate mixtures (from 100/0 to 100/20) as eluent to obtain pure product.

Reactions with *tert*-butanol

***Tert*-butyl 4-nitrobenzoate**



$C_{11}H_{13}NO_4$, 223.23 g/mol

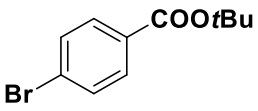
Yield 142.9 mg, 0.64 mmol, 71% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.26 (d, *J* = 8.9 Hz, 2H), 8.14 (d, *J* = 8.9 Hz, 2H), 1.62 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 163.7, 150.2, 137.4, 130.5, 123.3, 82.6, 28.1.

LR MS (EI, 70 eV, m/z): 222.8 [M^+]

***Tert*-butyl 4-bromobenzoate**



$C_{11}H_{13}BrO_2$, 257.13 g/mol

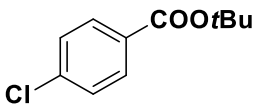
Yield 146.6 mg, 0.57 mmol, 63% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.84 (d, *J* = 8.6 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2H), 1.58 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 165.0, 131.4, 131.0, 130.8, 127.4, 81.4, 28.1.

LR MS (EI, 70 eV, m/z): 257.9 [M^+]

***Tert*-butyl 4-chlorobenzoate**



$C_{11}H_{13}ClO_2$, 212.67 g/mol

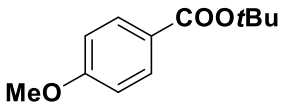
Yield 125.5 mg, 0.59 mmol, 66% (isolated)

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.91 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 1.58 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 164.8, 138.7, 130.8, 130.4, 128.4, 81.4, 28.1.

LR MS (EI, 70 eV, m/z): 212.0 [M^+]

***Tert*-butyl 4-methoxybenzoate**



$C_{12}H_{16}O_3$, 208.26 g/mol

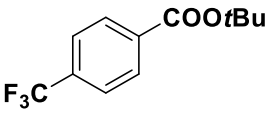
Yield 83.3 mg, 0.40 mmol, 44% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.94 (d, *J* = 9.0 Hz, 2H), 6.89 (d, *J* = 8.9 Hz, 2H), 3.84 (s, 3H), 1.58 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 165.6, 162.9, 131.3, 124.4, 113.3, 80.5, 55.3, 28.2.

LR MS (EI, 70 eV, m/z): 208.1 [M^+]

***Tert*-butyl 4-(trifluoromethyl)benzoate**



$C_{12}H_{13}F_3O_2$, 246.23 g/mol

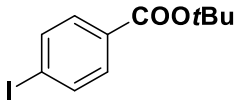
Yield 110.8 mg, 0.45 mmol, 50% (isolated)

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 8.09 (d, *J* = 8.1 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 1.61 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 164.5, 135.2, 133.9 (q, *J* = 32.5 Hz), 129.8, 125.2 (q, *J* = 3.8 Hz), 122.4, 81.9, 28.1

LR MS (EI, 70 eV, m/z): 246.0 [M^+]

***Tert*-butyl 4-iodobenzoate**



$C_{11}H_{13}IO_2$, 304.13 g/mol

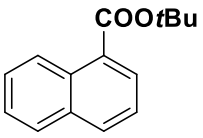
Yield 115.6 mg, 0.38 mmol, 42% (isolated)

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.77 (d, *J* = 8.6 Hz, 2H), 7.68 (d, *J* = 8.6 Hz, 2H), 1.58 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 165.2, 137.5, 131.5, 130.9, 100.0, 81.5, 28.1.

LR MS (EI, 70 eV, m/z): 304.0 [M^+]

***Tert*-butyl 1-naphthoate**



$C_{15}H_{16}O_2$, 228.29 g/mol

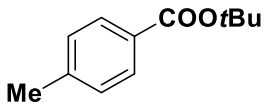
Yield 111.9 mg, 0.49 mmol, 54% (isolated)

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 8.88 (d, *J* = 8.7 Hz, 1H), 8.10 (dd, *J* = 7.2 Hz, *J* = 1.2 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.64-7.58 (m, 1H), 7.51 (quint, *J* = 7.7 Hz, 2H), 1.70 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 167.1, 133.8, 132.6, 131.2, 129.6, 129.2, 128.4, 127.4, 126.0, 125.8, 124.5, 81.5, 28.3.

LR MS (EI, 70 eV, m/z): 228.1 [M^+]

***Tert*-butyl 4-methylbenzoate**



$C_{12}H_{16}O_2$, 192.26 g/mol

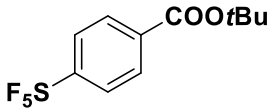
Yield 105.7 mg, 0.55 mmol, 61% (isolated)

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.87 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 2.40 (s, 3H), 1.59 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 165.9, 142.9, 129.4, 129.3, 128.9, 80.7, 28.2, 21.6.

LR MS (EI, 70 eV, m/z): 192.1 [M^+]

***Tert*-butyl 4-(pentafluoro-λ^6-sulfanyl)benzoate**



$C_{11}H_{13}F_5O_2S$, 304.28 g/mol

Yield 140.0 mg, 0.46 mmol, 51% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.06 (d, *J* = 8.7 Hz, 2H), 7.79 (d, *J* = 8.9 Hz, 2H), 1.60 (s, 9H).

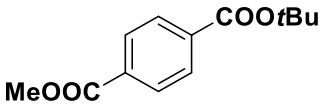
^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 163.9, 156.5 (quint, *J* = 17.6 Hz), 134.8, 129.8, 125.9 (quint, *J* = 4.7 Hz), 82.2, 28.0.

^{19}F-NMR (282 MHz, $CDCl_3$): δ_F [ppm] = 82.7, (quint, *J* = 150.0 Hz, 1F), 61.9 (d, *J* = 150.0 Hz, 4F).

LR MS (EI, 70 eV, m/z): 304.1 [M^+]

HR MS (CI, m/z): found: 305.06080 [MH^+] (calculated: 305.06292)

Tert-butyl methyl terephthalate



$C_{13}H_{16}O_4$, 236.27 g/mol

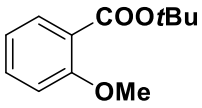
Yield 118.1 mg, 0.50 mmol, 56% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.08-7.99 (m, 4H), 3.92 (s, 3H), 1.58 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 166.3, 164.8, 135.7, 133.3, 129.31, 129.29, 81.6, 52.3, 28.0.

LR MS (EI, 70 eV, m/z): 236.0 [M^+]

Tert-butyl 2-methoxybenzoate



$C_{12}H_{16}O_3$, 208.26 g/mol

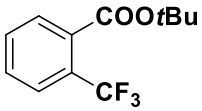
Yield 91.6 mg, 0.44 mmol, 49% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.72 (dd, *J* = 7.9 Hz, *J* = 1.8 Hz, 1H), 7.41 (td, *J* = 7.9 Hz, *J* = 1.8 Hz, 1H), 6.94 (quint, *J* = 3.6 Hz, 2H), 3.87 (s, 3H), 1.57 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 165.3, 159.0, 132.8, 131.3, 121.7, 119.9, 111.9, 80.8, 55.8, 28.2.

LR MS (EI, 70 eV, m/z): 208.1 [M^+]

Tert-butyl 2-(trifluoromethyl)benzoate



$C_{12}H_{13}F_3O_2$, 246.23 g/mol

Yield 101.0 mg, 0.41 mmol, 45% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.74-7.68 (m, 2H), 7.62-7.50 (m, 2H), 1.59 (s, 9H).

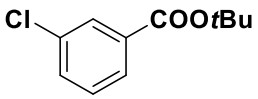
^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 166.3, 133.2 (d, *J* = 2.1 Hz), 131.6, 130.5, 129.9, 128.1 (q, *J* = 32.1 Hz), 126.4 (q, *J* = 5.2 Hz), 123.5 (q, *J* = 273.3 Hz), 82.9, 27.8.

^{19}F-NMR (282 MHz, $CDCl_3$): δ_F [ppm] = -59.4.

LR MS (EI, 70 eV, m/z): 246.2 [M^+]

HR MS (CI, m/z): found: 247.09515 [MH^+] (calculated: 247.09404)

***Tert*-butyl 3-chlorobenzoate**



$C_{11}H_{13}ClO_2$, 212.67 g/mol

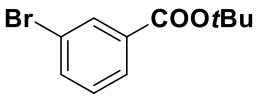
Yield 114.8 mg, 0.54 mmol, 60% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.94 (t, *J* = 1.8 Hz, 1H), 7.86 (dt, *J* = 7.7 Hz, *J* = 1.3 Hz, 1H), 7.48 (dd, *J* = 8.0 Hz, *J* = 1.1 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 1.59 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 164.4, 134.2, 133.7, 132.4, 129.4, 127.5, 81.6, 28.1.

LR MS (EI, 70 eV, m/z): 212.0 [M^+]

***Tert*-butyl 3-bromobenzoate**



$C_{11}H_{13}BrO_2$, 257.13 g/mol

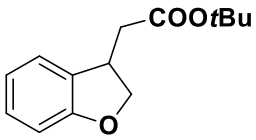
Yield 120.9 mg, 0.47 mmol, 52% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.10 (t, *J* = 1.8 Hz, 1H), 7.91 (dt, *J* = 7.8 Hz, *J* = 1.3 Hz, 1H), 7.64 (dd, *J* = 8.0 Hz, *J* = 1.1 Hz, 1H), 7.28 (t, *J* = 7.9 Hz, 1H), 1.59 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 164.3, 135.3, 133.9, 132.4, 129.7, 128.0, 122.2, 81.7, 28.1.

LR MS (EI, 70 eV, m/z): 258.0 [M^+]

***Tert*-butyl 2-(2,3-dihydrobenzofuran-3-yl)acetate**



$C_{14}H_{18}O_3$, 234.30 g/mol

Yield 46.9 mg, 0.20 mmol, 22% (isolated)

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.14 (q, *J* = 7.6 Hz, 2H), 6.86 (td, *J* = 7.4 Hz, *J* = 0.8 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 4.74 (t, *J* = 9.1 Hz, 1H), 4.26 (dd, *J* = 9.8 Hz, *J* = 6.6 Hz, 1H), 3.89 – 3.79 (m, 1H), 2.71 (dd, *J* = 16.2 Hz, *J* = 5.3 Hz, 1H), 2.51 (dd, *J* = 16.2 Hz, *J* = 9.3 Hz), 1.46 (s, 9H).

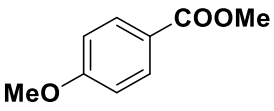
^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 171.1, 159.8, 129.3, 128.5, 124.2, 120.5, 109.6, 81.0, 76.7, 40.7, 38.4, 28.1.

LR MS (EI, 70 eV, m/z): 234.1 [M^+]

HR MS (EI, m/z): found: 234.12516 [M^+] (calculated: 234.12505)

Reactions with other alcohols

Methyl 4-methoxybenzoate



$C_9H_{10}O_3$, 166.18 g/mol

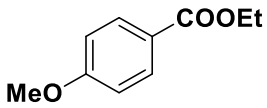
Yield 96.4 mg, 0.58 mmol, 64% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.98 (d, *J* = 9.0 Hz, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H), 3.83 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 166.8, 163.2, 131.5, 122.5, 113.5, 55.3, 51.8.

LR MS (EI, 70 eV, m/z): 166.1 [M⁺]

Ethyl 4-methoxybenzoate



$C_{10}H_{12}O_3$, 180.20 g/mol

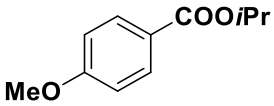
Yield 90.1 mg, 0.50 mmol, 56% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.99 (d, *J* = 9.0 Hz, 2H), 6.90 (d, *J* = 9.0 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H) 3.84 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 166.3, 163.2, 131.5, 122.8, 113.5, 60.6, 55.3 14.3.

LR MS (EI, 70 eV, m/z): 180.1 [M⁺]

Isopropyl 4-methoxybenzoate



$C_{11}H_{14}O_3$, 194.23 g/mol

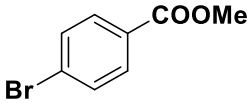
Yield 91.3 mg, 0.47 mmol, 52% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.98 (d, *J* = 8.9 Hz, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 5.22 (sep, *J* = 6.3 Hz, 1H) 3.84 (s, 3H), 1.34 (d, *J* = 6.3 Hz, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 165.8, 163.1, 131.4, 123.3, 113.4, 67.9, 55.3 21.9.

LR MS (EI, 70 eV, m/z): 194.1 [M⁺]

Methyl 4-bromobenzoate



$C_8H_7BrO_2$, 215.05 g/mol

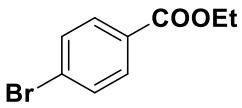
Yield 107.5 mg, 0.50 mmol, 56% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.87 (d, *J* = 8.6 Hz, 2H), 7.55 (d, *J* = 8.6 Hz, 2H), 3.89 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 166.3, 131.6, 131.0, 128.9, 128.0, 52.2.

LR MS (EI, 70 eV, m/z): 214.0 [M^+]

Ethyl 4-bromobenzoate



$C_9H_9BrO_2$, 229.07 g/mol

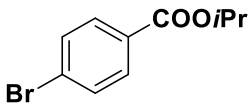
Yield 107.5 mg, 0.50 mmol, 56% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.89 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 165.8, 131.6, 131.0, 129.3, 127.8, 61.2, 14.2.

LR MS (EI, 70 eV, m/z): 230.0 [M^+]

Isopropyl 4-bromobenzoate



$C_{10}H_{11}BrO_2$, 243.10 g/mol

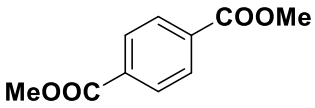
Yield 82.7 mg, 0.34 mmol, 38% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.89 (d, *J* = 8.6 Hz, 2H), 7.57 (d, *J* = 8.6 Hz, 2H), 5.24 (sep, *J* = 6.3 Hz, 1H), 1.36 (d, *J* = 6.3 Hz, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 165.4, 131.6, 131.0, 129.8, 127.7, 68.7, 21.9.

LR MS (EI, 70 eV, m/z): 241.9 [M^+]

Dimethyl benzene-1,4-dicarboxylate



$C_{10}H_{10}O_4$, 194.19 g/mol

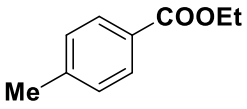
Yield 89.3 mg, 0.46 mmol, 51% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.06 (s, 4H), 3.91 (s, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 166.1, 133.8, 129.4, 52.3.

LR MS (EI, 70 eV, m/z): 194.0 [M^+]

Ethyl 4-methylbenzoate



$C_{10}H_{12}O_2$, 164.20 g/mol

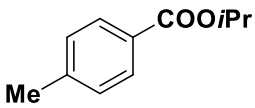
Yield 44.3 mg, 0.27 mmol, 30% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.94 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 166.7, 143.4, 129.5, 129.0, 127.7, 60.7, 21.6, 14.3.

LR MS (EI, 70 eV, m/z): 164.0 [M^+]

Isopropyl 4-methylbenzoate



$C_{11}H_{14}O_2$, 178.23 g/mol

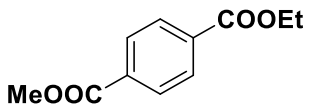
Yield 89.1 mg, 0.50 mmol, 55% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.93 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.24 (sep, *J* = 6.3 Hz, 1H), 2.40 (s, 3H), 1.36 (d, *J* = 6.2 Hz, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 166.1, 143.2, 129.5, 128.9, 128.1, 68.0, 21.9, 21.6.

LR MS (EI, 70 eV, m/z): 178.0 [M^+]

Methyl ethyl benzene-1,4-dicarboxylate



$C_{11}H_{12}O_4$, 208.21 g/mol

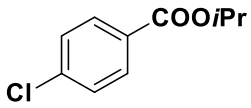
Yield 68.7 mg, 0.33 mmol, 37% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.08 (s, 4H), 4.38 (q, *J* = 7.1 Hz, 2H), 3.93 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 166.2, 165.7, 134.2, 133.7, 129.4, 61.4, 52.4, 14.2.

LR MS (EI, 70 eV, m/z): 208.1 [M^+]

Isopropyl 4-chlorobenzoate



$C_{10}H_{11}ClO_2$, 198.65 g/mol

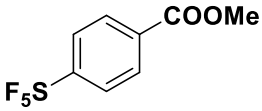
Yield 67.5 mg, 0.34 mmol, 38% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.96 (d, *J* = 8.6 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 5.23 (sep, *J* = 6.3 Hz, 1H), 1.36 (d, *J* = 6.3 Hz, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 165.2, 139.0, 130.9, 129.3, 128.5, 68.7, 21.9.

LR MS (EI, 70 eV, m/z): 198.0 [M^+]

Methyl 4-(pentafluoro-λ^6-sulfanyl)benzoate



$C_8H_7F_5O_2S$, 262.19 g/mol

Yield 94.4 mg, 0.36 mmol, 40% (isolated)

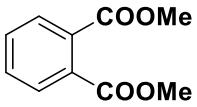
^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.13 (d, *J* = 8.9 Hz, 2H), 7.83 (d, *J* = 8.9 Hz, 2H), 3.96 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 165.3, 156.9 (quint, *J* = 17.7 Hz), 133.0, 130.0, 126.2 (quint, *J* = 4.7 Hz), 52.6.

^{19}F-NMR (282 MHz, $CDCl_3$): δ_F [ppm] = 82.4, (quint, *J* = 149.0 Hz, 1F), 61.9 (d, *J* = 149.0 Hz, 4F).

LR MS (EI, 70 eV, m/z): 262.0 [M^+]

Dimethyl benzene-1,2-dicarboxylate



$C_{10}H_{10}O_4$, 194.19 g/mol

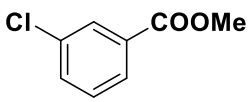
Yield 36.9 mg, 0.19 mmol, 21% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.72 (dd, *J* = 5.7 Hz, *J* = 3.3 Hz, 2H), 7.53 (dd, *J* = 5.7 Hz, *J* = 3.3 Hz, 2H), 3.90 (s, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 168.0, 131.9, 131.1, 128.8, 52.6.

LR MS (EI, 70 eV, m/z): 193.9 [M^+]

Methyl 3-chlorobenzoate



$C_8H_7ClO_2$, 170.59 g/mol

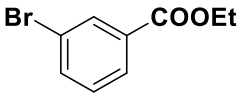
Yield 80.2 mg, 0.47 mmol, 52% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.01 (t, *J* = 1.9 Hz, 1H), 7.91 (dt, *J* = 7.8 Hz, *J* = 1.3 Hz, 1H), 7.51 (dd, *J* = 8.0 Hz, *J* = 1.1 Hz, 1H), 7.37 (t, *J* = 7.9 Hz, 1H), 3.91 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 165.8, 134.4, 132.9, 131.8, 129.63, 129.62 127.6, 52.4.

LR MS (EI, 70 eV, m/z): 170.0 [M^+]

Ethyl 3-bromobenzoate



$C_9H_9BrO_2$, 229.07 g/mol

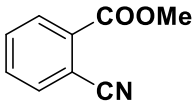
Yield 73.3 mg, 0.32 mmol, 36% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.17 (t, *J* = 1.8 Hz, 1H), 7.97 (dt, *J* = 7.8 Hz, *J* = 1.3 Hz, 1H), 7.66 (dd, *J* = 8.0 Hz, *J* = 1.0 Hz, 1H), 7.31 (t, *J* = 7.9 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 165.2, 135.7, 132.5, 132.3, 129.9, 128.1, 122.4, 61.4, 14.2.

LR MS (EI, 70 eV, m/z): 228.0 [M^+]

Methyl 2-cyanobenzoate



$C_9H_7NO_2$, 161.16 g/mol

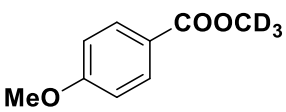
Yield 45.1 mg, 0.28 mmol, 31% (isolated)

^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.17 – 8.11 (m, 1H), 7.84 – 7.78 (m, 1H), 7.73 – 7.68 (m, 2H), 4.00 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 164.5, 134.8, 132.7, 132.4, 132.3, 131.1, 117.5, 112.9, 52.8.

LR MS (EI, 70 eV, m/z): 161.0 [M^+]

Methyl-d_3 4-methoxybenzoate



$C_9H_7D_3O_3$, 169.19 g/mol

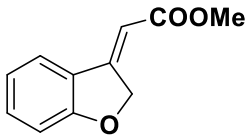
Yield 84.6 mg, 0.50 mmol, 56% (isolated)

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.99 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 3.85 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 166.8, 163.3, 131.5, 122.6, 113.6, 55.4, 51.0 (q, *J* = 22.3 Hz).

LR MS (EI, 70 eV, m/z): 169.1 [M^+]

Methyl 2-(benzofuran-3(2*H*)-ylidene)acetate



$C_{11}H_{10}O_3$, 190.20 g/mol

Yield 89.4 mg, 0.47 mmol, 52% (isolated)

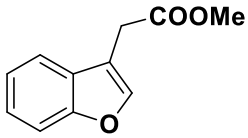
^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.52 (dd, *J* = 7.9 Hz, *J* = 1.2 Hz, 1H), 7.37 (td, *J* = 7.8 Hz, *J* = 1.3 Hz, 1H), 7.01 – 6.94 (m, 2H), 6.18 (t, *J* = 3.1 Hz, 1H), 5.52 (d, *J* = 3.1 Hz, 2H), 3.77 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 167.5, 165.4, 156.2, 133.6, 124.0, 122.2, 121.1, 111.4, 103.9, 76.6, 51.4.

LR MS (EI, 70 eV, m/z): 190.0 [M^+]

HR MS (EI, m/z): found: 190.06253 [M^+] (calculated: 190.06245)

Methyl 2-(benzofuran-3-yl)acetate



$C_{11}H_{10}O_3$, 190.20 g/mol

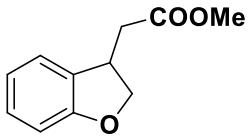
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.63 (s, 1H), 7.59 – 7.55 (m, 1H), 7.50 – 7.46 (m, 1H), 7.24 – 7.23 (m, 2H), 3.74 (s, 1H), 3.72 (d, *J* = 0.6 Hz, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 171.1, 155.1, 142.8, 127.5, 124.5, 122.6, 119.6, 113.0, 111.5, 52.2, 29.5.

LR MS (EI, 70 eV, m/z): 190.0 [M^+]

HR MS (EI, m/z): found: 190.06293 [M^+] (calculated: 190.06245)

Methyl 2-(2,3-dihydrobenzofuran-3-yl)acetate



$C_{11}H_{12}O_3$, 192.21 g/mol

Yield 69.2 mg, 0.36 mmol, 40% (isolated)

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.15 (t, *J* = 7.6 Hz, 2H), 6.87 (t, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 4.75 (t, *J* = 9.1 Hz, 1H), 4.25 (dd, *J* = 9.2 Hz, *J* = 6.9 Hz, 1H), 3.93 – 3.87 (m, 1H), 3.73 (s, 3H), 2.84 – 1.76 (m, 1H), 2.65 – 2.55 (m, 1H).

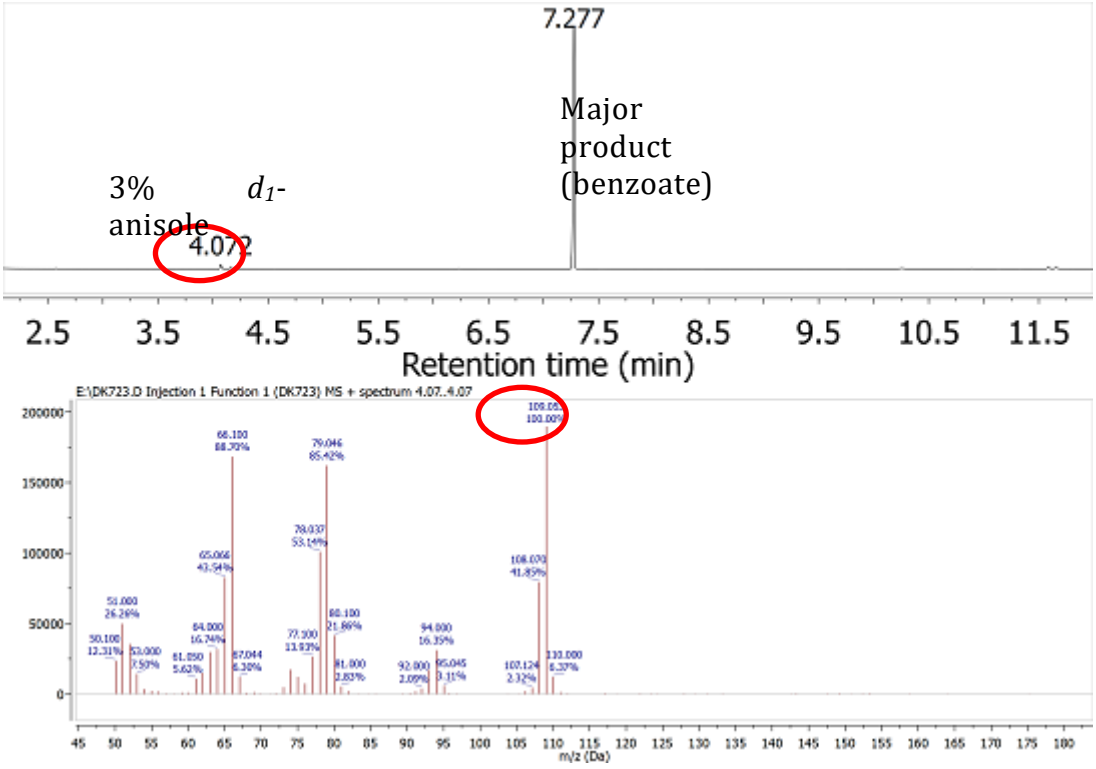
^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 172.2, 159.8, 129.0, 128.7, 124.2, 120.6, 109.7, 76.7, 51.8, 39.2, 38.3.

LR MS (EI, 70 eV, m/z): 192.0 [M^+]

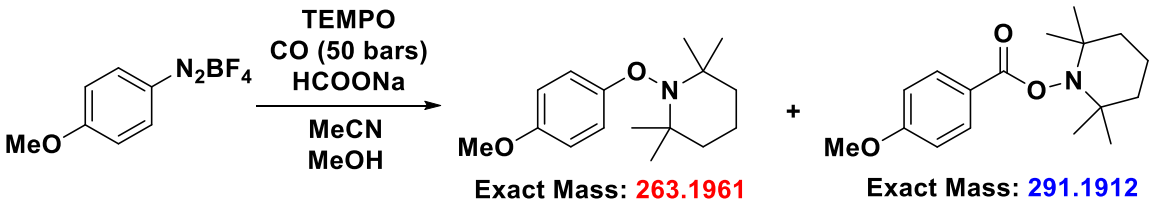
HR MS (EI, m/z): found: 192.07782 [M^+] (calculated: 192.07810)

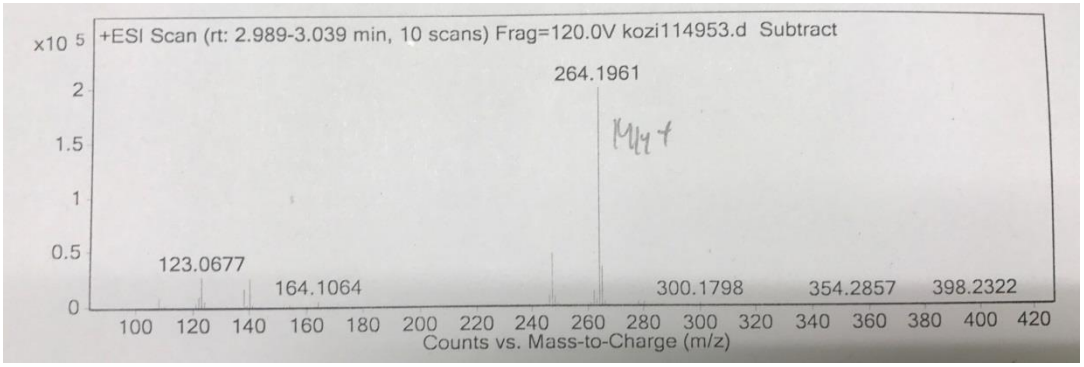
Deuteration experiment in CD_3CN (Scheme 4.4)

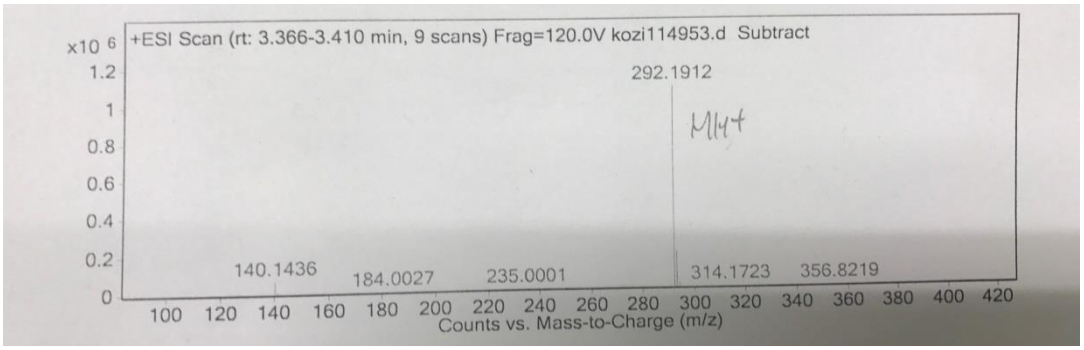
GC-MS spectrum of deutero anisole (4.072 min) in crude reaction mixture:



Mass spectra of radical trapping experiments with TEMPO

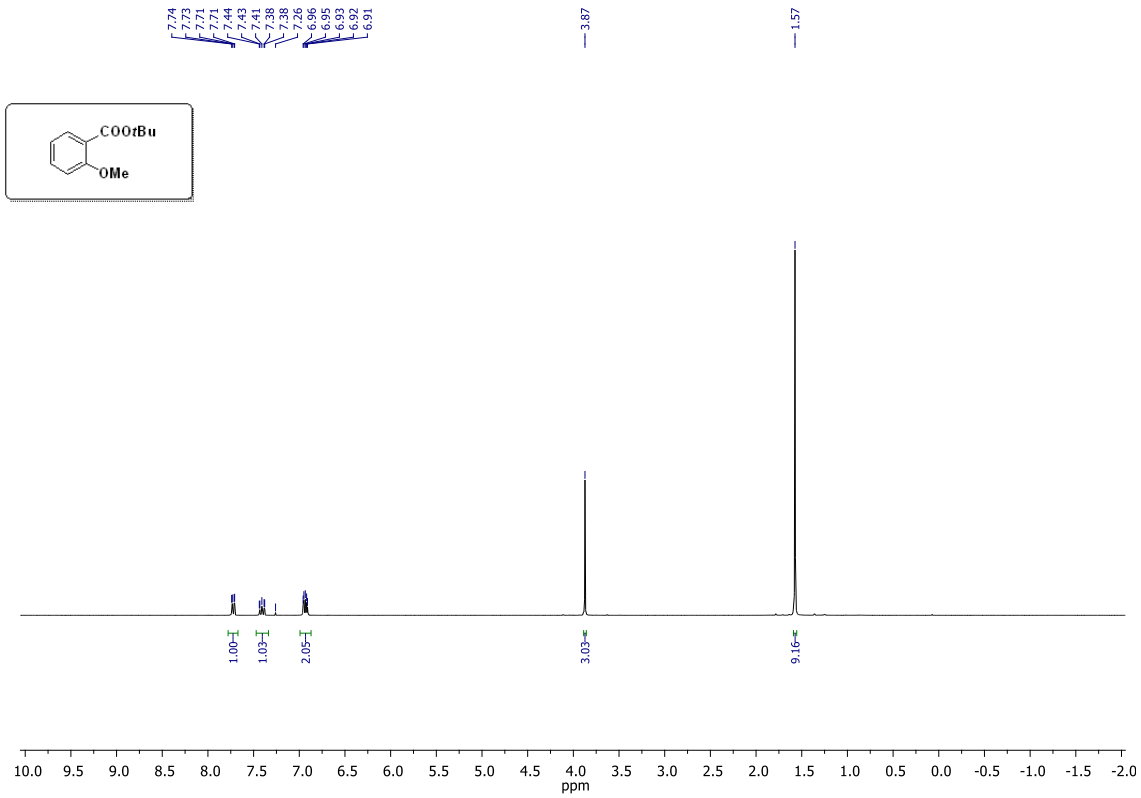




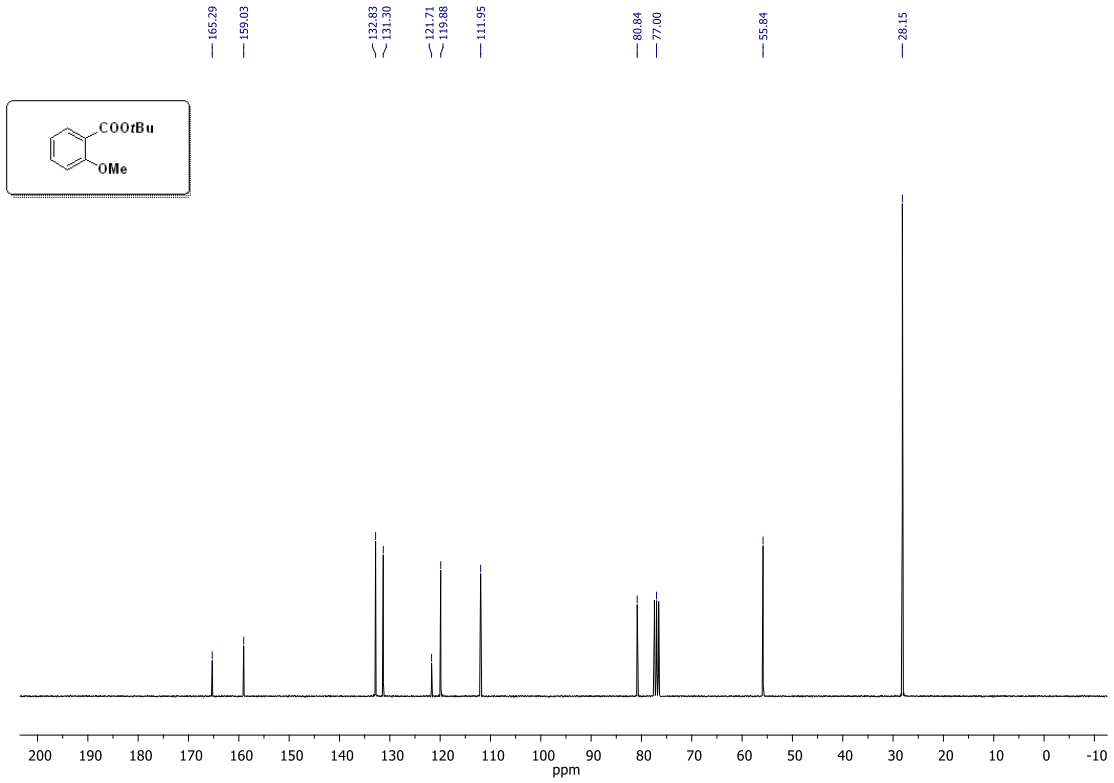


NMR spectra of selected compounds

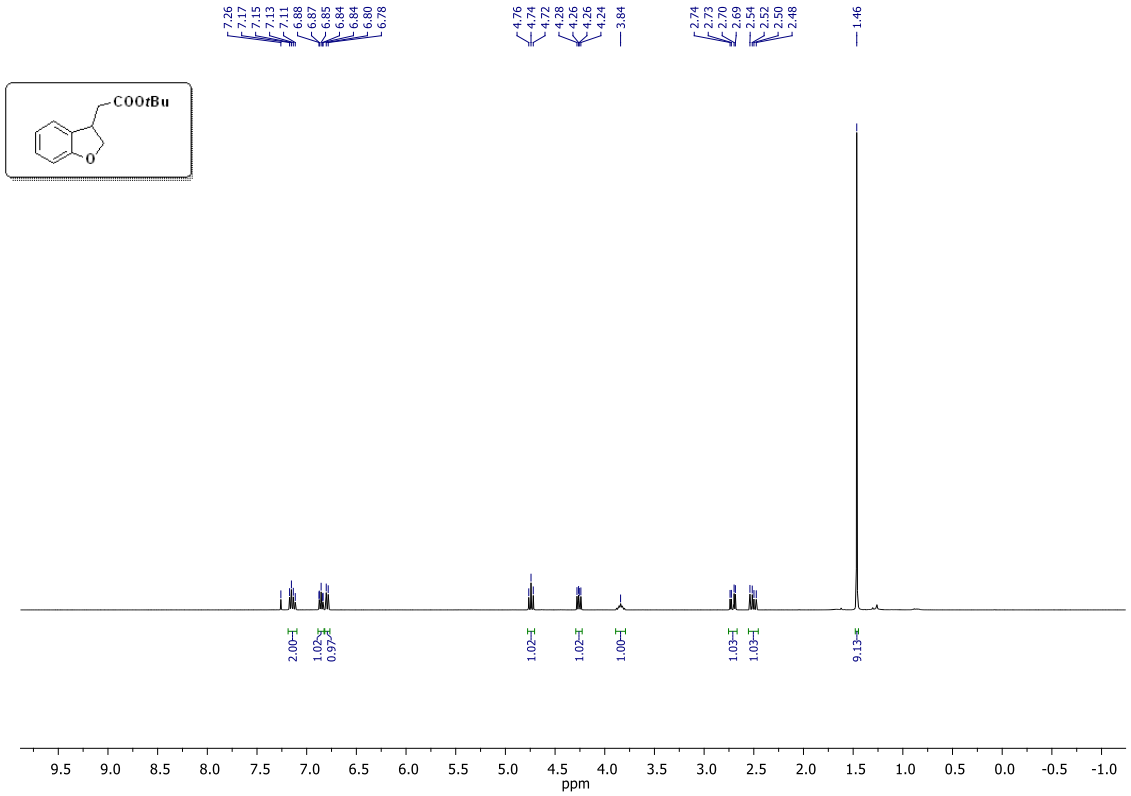
^{1}H-NMR (300 MHz, $CDCl_3$)



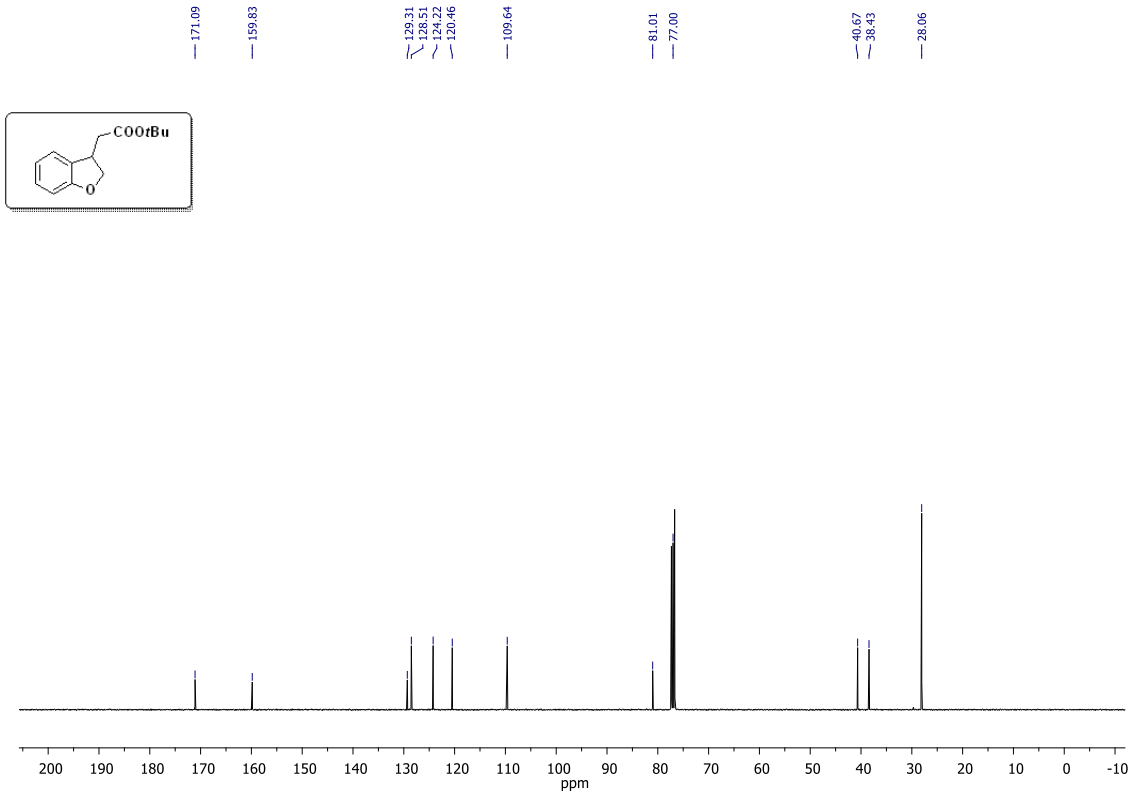
^{13}C-NMR (75 MHz, $CDCl_3$)



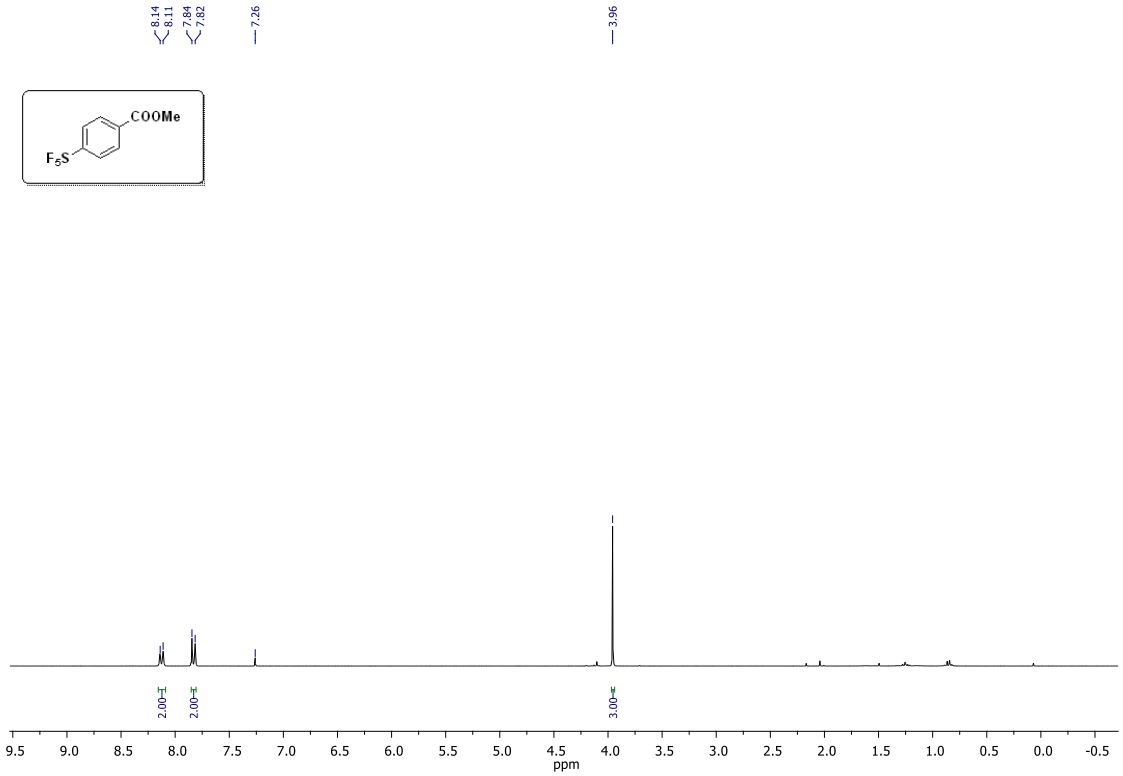
^{1}H-NMR (400 MHz, $CDCl_3$)



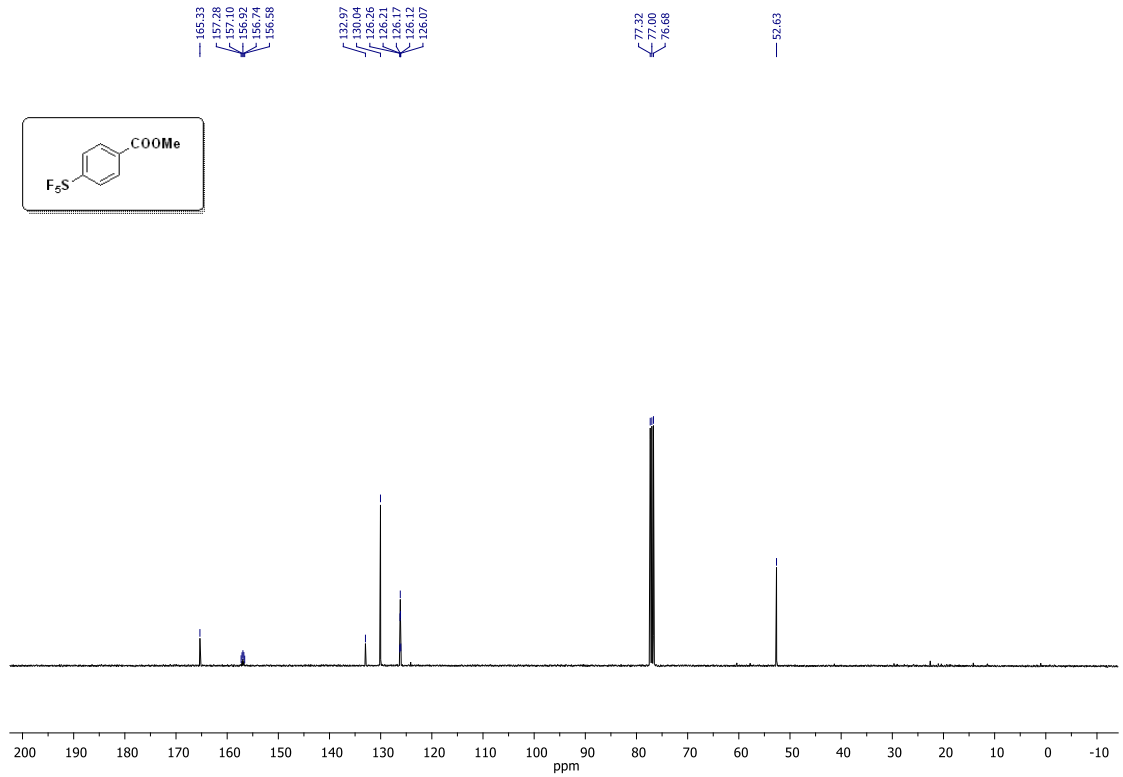
^{13}C-NMR (101 MHz, $CDCl_3$)



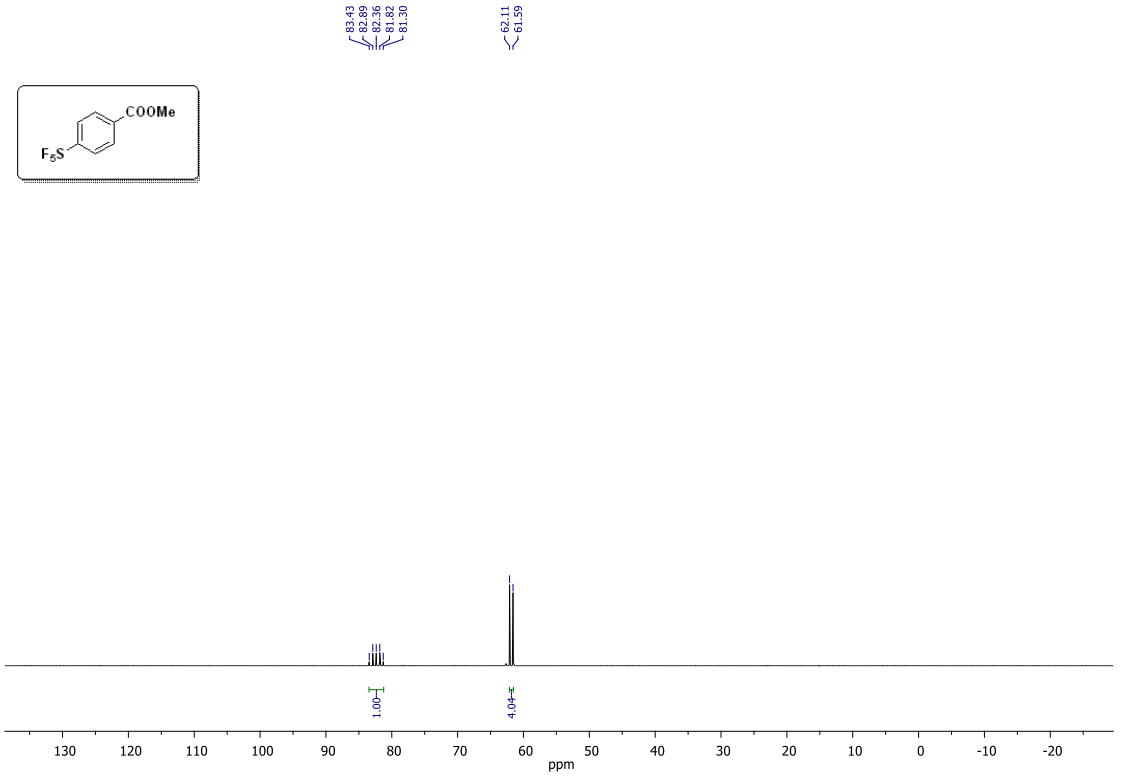
^{1}H-NMR (300 MHz, $CDCl_3$)



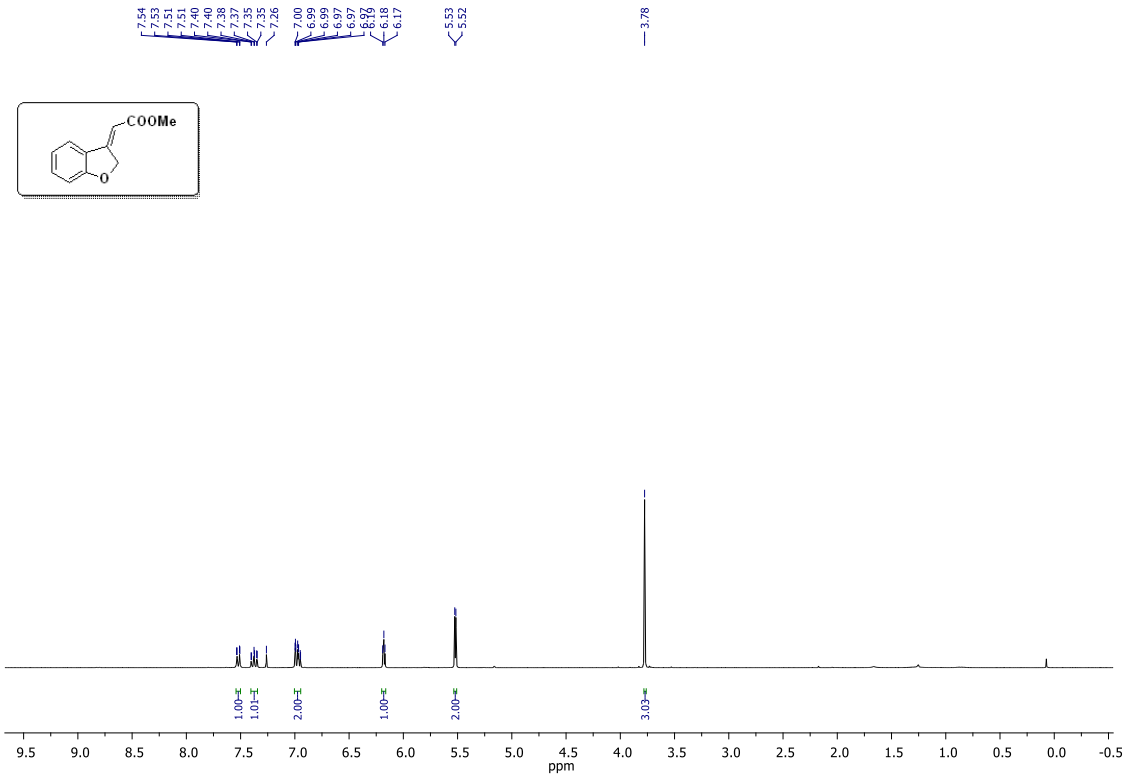
^{13}C-NMR (101 MHz, $CDCl_3$)



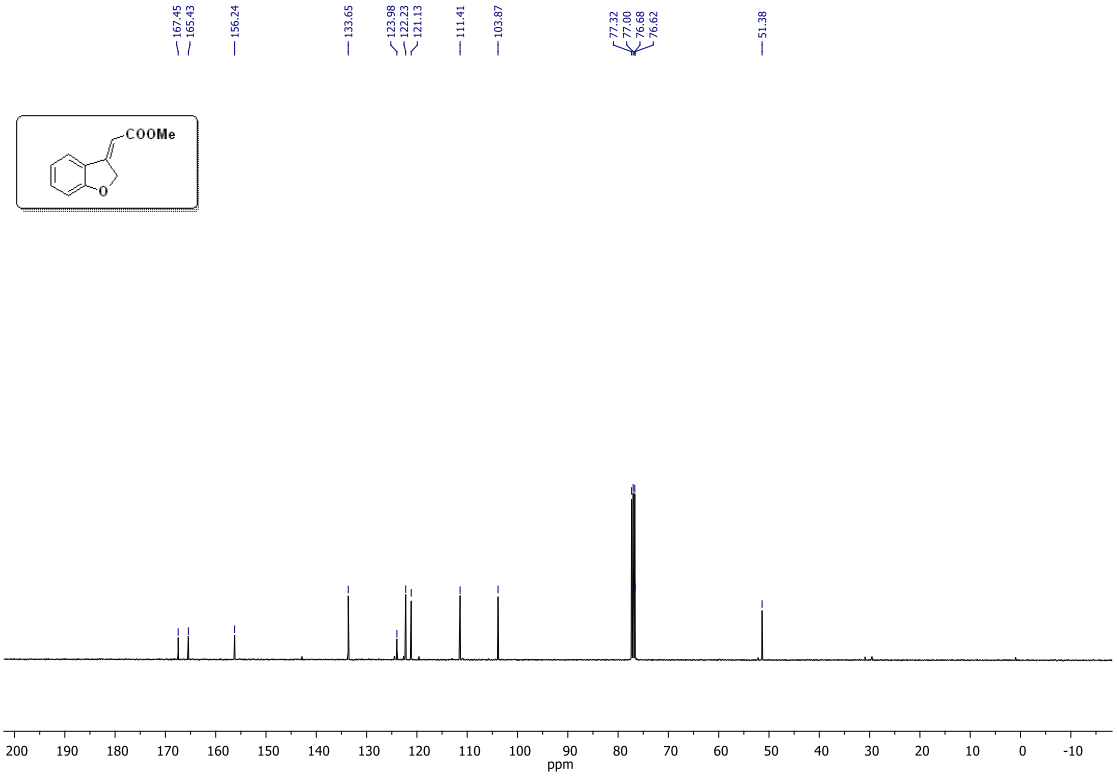
^{19}F-NMR (282 MHz, $CDCl_3$)



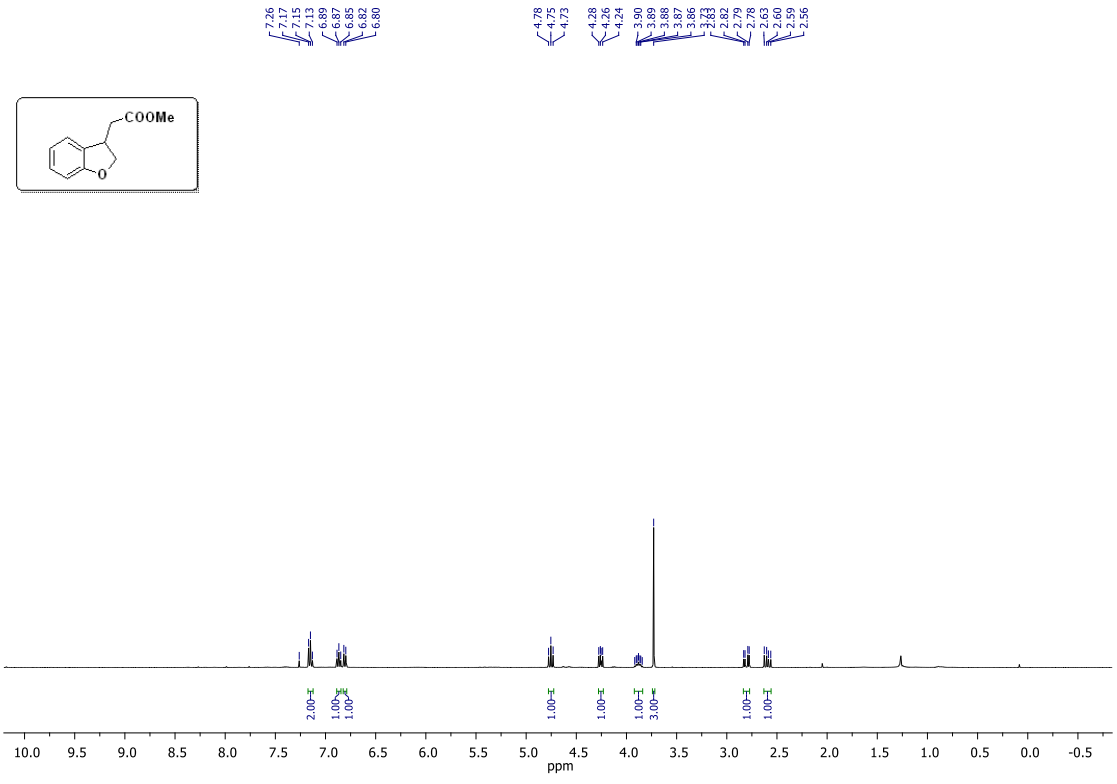
^{1}H-NMR (300 MHz, $CDCl_3$)



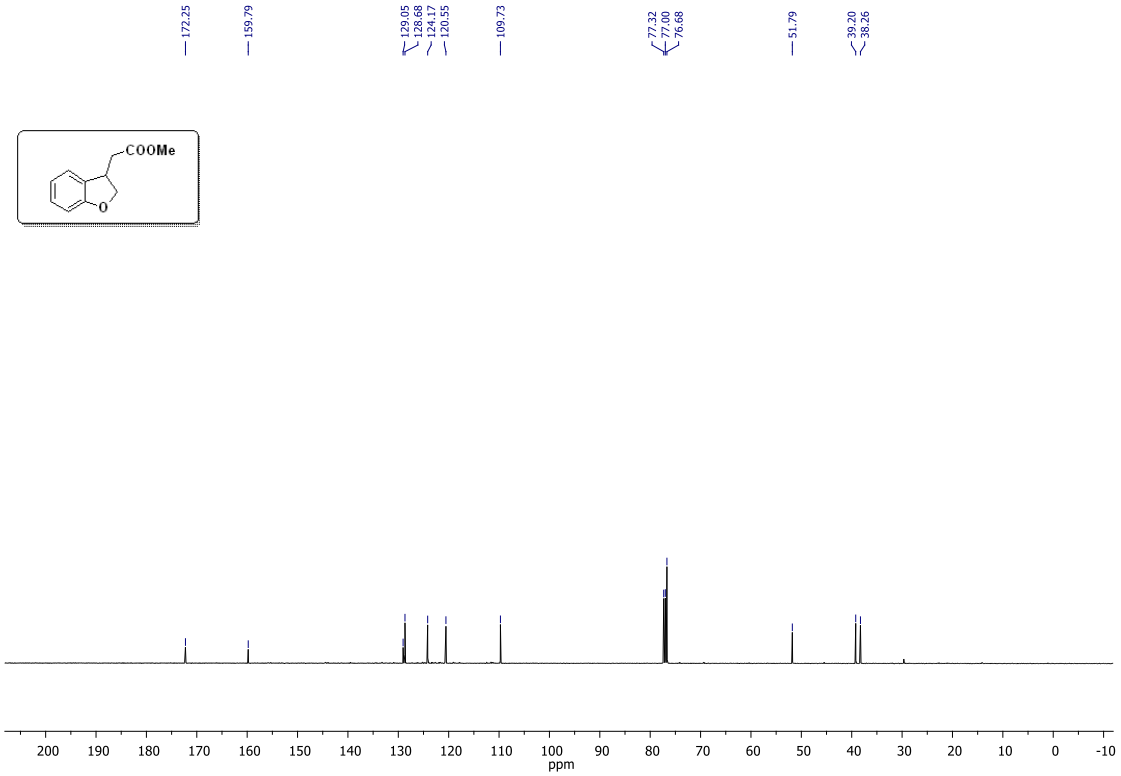
^{13}C-NMR (101 MHz, $CDCl_3$)



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



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



4.5. References

[1] W. Riemenschneider, H. M. Bolt in *Ullmann's Encyclopedia of Industrial Chemistry*, Vol. 13, Wiley-VCH, Weinheim, **2012**, 245.

[2] A. Brennführer, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2009**, *48*, 4114–4133.

[3] a) P. Song, P. Yu, J.-S. Lin, Y. Li, N.-Y. Yang, X.-Y. Liu, *Org. Lett.* **2017**, *19*, 1330–1333; b) T. Kawamoto, A. Sato, I. Ryu, *Chem. Eur. J.* **2015**, *21*, 14764–14767; c) S. Fukuoka, *Ind. Eng. Chem. Res.* **2016**, *55*, 4830–4835; d) K. Nagahara, I. Ryu, M. Komatsu, N. Sonoda, *J. Am. Chem. Soc.* **1997**, *119*, 5465–5466.

[4] H. Zhang, R. Shi, A. Ding, L. Lu, B. Chen, A. Lei, *Angew. Chem. Int. Ed.* **2012**, *51*, 12542–12545.

[5] a) C.-L. Sun, H. Li, D.-G. Yu, M. Yu, X. Zhou, X.-Y. Lu, K. Huang, S.-F. Zheng, B.-J. Li, Z.-J. Shi, *Nat. Chem.* **2010**, *2*, 1044–1049; b) E. Shirakawa, K.-I. Itoh, T. Higashino, T. Hayashi, *J. Am. Chem. Soc.* **2010**, *132*, 15537–15539; c) W. Liu, H. Cao, H. Zhang, H. Zhang, K. H. Chung, C. He, H. Wang, F. Y. Kwong, A. Lei, *J. Am. Chem. Soc.* **2010**, *132*, 16737–16740; d) S. Zhou, G. M. Anderson, B. Mondal, E. Doni, V. Ironmonger, M. Kranz, T. Tuttle, J. A. Murphy, *Chem. Sci.* **2014**, *5*, 476–482; e) F. Cumine, S. Zhou, T. Tuttle, J. A. Murphy, *Org. Biomol. Chem.* **2017**, *15*, 3324–3336; f) K. J. Emery, T. Tuttle, A. R. Kennedy, J. A. Murphy, *Tetrahedron* **2016**, *72*, 7875–7887; g) J. P. Barham, G. Coulthard, K. J. Emery, E. Doni, F. Cumine, G. Nocera, M. P. John, L. E. A. Berlouis, T. McGuire, T. Tuttle, J. A. Murphy, *J. Am. Chem. Soc.* **2016**, *138*, 7402–7410; h) J. P. Barham, G. Coulthard, R. G. Kane, N. Delgado, M. P. John, J. A. Murphy, *Angew. Chem. Int. Ed.* **2016**, *55*, 4492–4496.

[6] a) M. Majek, A. Jacobi von Wangelin, *Angew. Chem. Int. Ed.* **2015**, *54*, 2270–2274; b) W. Guo, L.-Q. Lu, Y. Wang, Y.-N. Wang, J.-R. Chen, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2015**, *54*, 2265–2269.

[7] a) H. H. Hodgson, *Chem. Rev.* **1947**, *40*, 251–277; b) C. Galli, *Chem. Rev.* **1988**, *88*, 765–792; c) H. Bonin, E. Fouquet, F.-X. Felpin, *Adv. Synth. Catal.* **2011**, *353*, 3063–3084; d) J. G. Taylor, A. V. Moro, C. R. D. Correia, *Eur. J. Org. Chem.* **2011**, *8*, 1403–1428; e) F. Mo, G. Dong, Y. Zhang, J. Wang, *Org. Biomol. Chem.* **2013**, *11*, 1582–1593.

[8] a) S. Kindt, K. Wicht, M. R. Heinrich, *Org. Lett.* **2015**, *17*, 6122–6125; b) S. K. Fehler, G. Pratsch, C. Ostreicher, M. C. D. Fürst, M. Pischetsrieder, M. R. Heinrich, *Tetrahedron* **2016**, *72*, 7888–7893; c) S. Kindt, K. Wicht, M. R. Heinrich, *Angew. Chem. Int. Ed.* **2016**, *55*, 8744–8747; d) N. Hegmann, L. Prusko, M. R. Heinrich, *Org. Lett.* **2017**, *19*, 2222–2225; e) J. Hofmann, E. Gans, T. Clark, M. R. Heinrich, *Chem. Eur. J.* **2017**, *23*, 1–11; f) D. Koziakov, M. Majek, A. Jacobi von Wangelin, *Org. Biomol. Chem.* **2016**, *14*, 11347–11352; g) M. Gomberg, W. E. Bachmann, *J. Am. Chem. Soc.* **1924**, *46*,

2339–2343; h) W. S. M. Grieve, D. H. Hey, *J. Chem. Soc.* **1934**, 1797–1806; i) R. Huisgen, L. Krause, *Ann. Chem.* **1951**, *574*, 157–171; j) T. Kauffmann, H. O. Friestad, H. Henkler, *Ann. Chem.* **1960**, 634, 64–78; k) C. Rüchardt, E. Merz, *Tetrahedron Lett.* **1964**, *5*, 2431–2436; l) C. Rüchardt, B. Freudenberg, E. Merz, *Spec. Publ. Chem. Soc.* **1965**, 154; m) J. Besse, W. Schwarz, A. Zollunger, *Helv. Chim. Acta* **1981**, *64*, 504–512; n) F. P. Crisostomo, T. Martin, R. Carrillo, *Angew. Chem. Int. Ed.* **2014**, *53*, 2181–2185; o) U. Costas-Costas, E. Gonzalez-Romero, C. Bravo-Diaz, *Helv. Chim. Acta* **2001**, *84*, 632–648.

[9] a) C. Chatgilialoglu, D. Crich, M. Komatsu, I. Ryu, *Chem. Rev.* **1999**, *99*, 1991–2070; b) I. Ryu, *Chem. Soc. Rev.* **2001**, *30*, 16–25; c) I. Ryu, *J. Synth. Org. Chem. Jpn.* **2016**, *74*, 826–831; d) S. Sumino, A. Fusano, T. Fukuyama, I. Ryu, *Acc. Chem. Res.* **2014**, *47*, 1563–1574; e) B. T. Sargent, E. J. Alexanian, *J. Am. Chem. Soc.* **2016**, *138*, 7520–7523; f) L. Lu, D. Cheng, Y. Zhan, R. Shi, C.-W. Chiang, A. Lei, *Chem. Commun.* **2017**, *53*, 6852–6855; g) F. Jin, Y. Zhong, X. Zhang, H. Zhang, Q. Zhao, W. Han, *Green Chem.* **2016**, *18*, 2598–2603; h) Y. Nishii, T. Nagano, H. Gotoh, R. Nagase, J. Motoyoshiya, H. Aoyama, Y. Tanabe, *Org. Lett.* **2007**, *9*, 563–566.

[10] a) M. Majek, A. Jacobi von Wangelin, *Chem. Commun.* **2013**, *49*, 5507–5509; b) M. Majek, F. Filace, A. Jacobi von Wangelin, *Chem. Eur. J.* **2015**, *21*, 4518–4522.

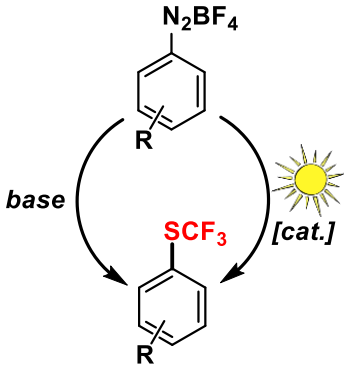
[11] Carboxylates as radical initiators in polymerizations: a) H. R. Kricheldorf, A. Stricker, D. Langanke, *Macromol. Chem. Phys.* **2001**, *202*, 2963–2970; b) R. F. Storey, J. W. Sherman, *Macromolecules* **2002**, *35*, 1504–1512.

[12] F. A. Siqueira, J. G. Taylor, C. R. D. Correia, *Tetrahedron Lett.* **2010**, *51*, 2102–2105.

[13] a) A. Studer, D. P. Curran, *Nat. Chem.* **2014**, *6*, 765–773; b) A. Studer, D. P. Curran, *Angew. Chem. Int. Ed.* **2016**, *55*, 58–102.

Chapter 5

- Radical Aromatic Trifluoromethylthiolation: Photoredox Catalysis vs. Base Mediation -



Abstract: The radical trifluoromethylthiolation of arenediazonium salts with commercial bis(trifluoromethyl) disulfide was studied under base-mediated dark and photoredox-catalytic conditions. While the operationally simple base protocol afforded the sulfides in moderate yields, photoredox catalysis with only 0.5 mol% $[Ru(bpy)_3]Cl_2$ gave up to 90% yield within 3 h.

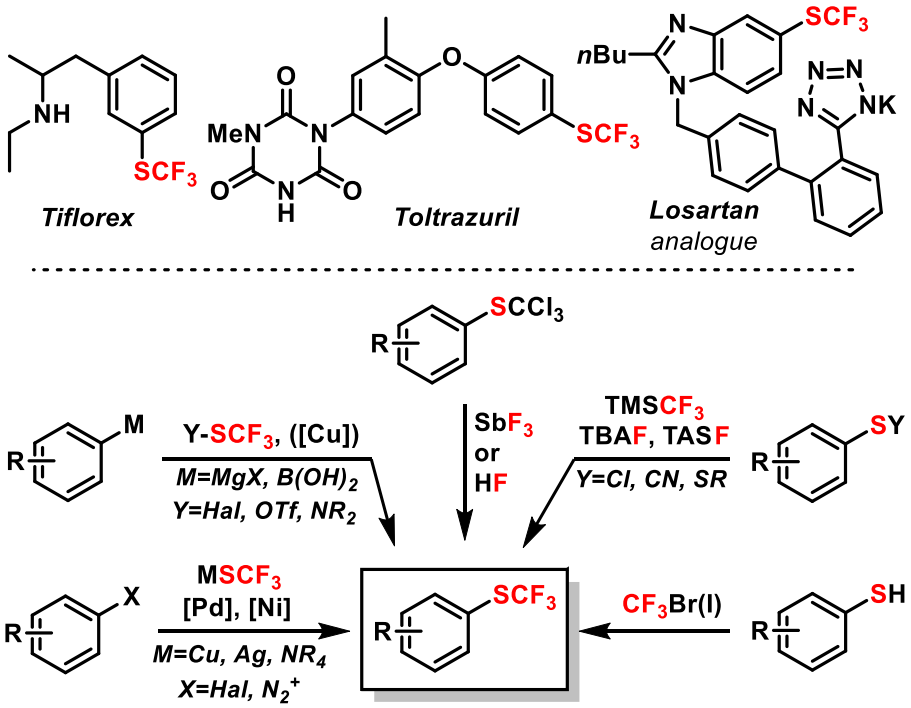
This chapter has been submitted:
D. Koziakov, M. Majek, A. Jacobi von Wangelin, *Eur. J. Org. Chem*. **2017**.

Author contributions:
Denis Koziakov synthesized starting materials, did reactions, and wrote the manuscript. Michal Majek synthesized 1,2-bis(trifluoromethyl) disulfide.

5. Radical Aromatic Trifluoromethylthiolation: Photoredox Catalysis *vs.* Base Mediation

5.1. Introduction

Even though fluorine containing compounds are the least spread among naturally occurring organic halides,[1] fluorine-containing substituents have recently emerged as a widespread and significant component in pharmaceuticals,[2] agrochemicals,[3] and materials[4]. Beside the introduction of fluorides, trifluoromethyl, and other perfluoroalkyl units, the trifluoromethylsulfanyl (SCF_3) group has attracted great attention for its exceptional physical and chemical properties. Several well-known drugs, comprising SCF_3, are depicted in the Scheme 5.1.[5]

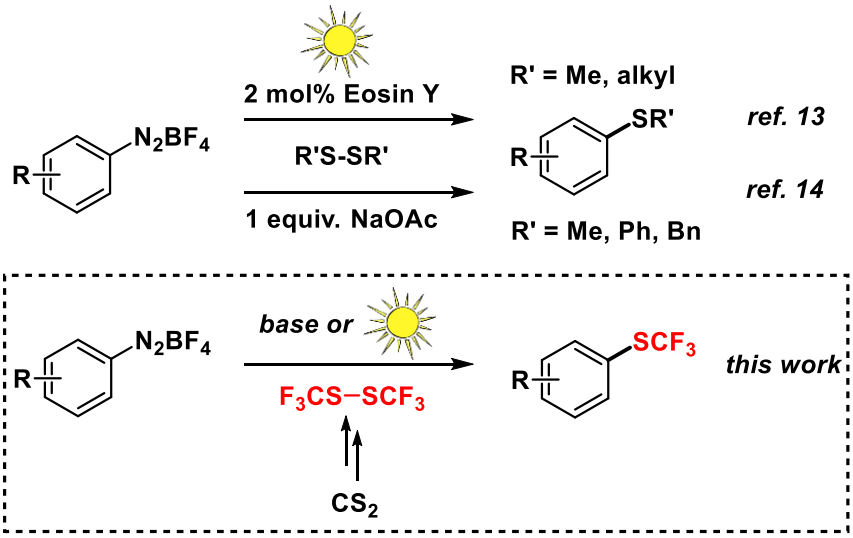


Scheme 5.1. Important synthesis routes to aryl trifluoromethyl sulfides.

The trifluoromethylsulfanyl group (SCF3) is a chemically stable, relatively polar and strongly electron-withdrawing substituent that imparts very high lipophilicity to an organic molecule. Despite its polarity (σ_p=0.48, cf. 0.23 (Cl), 0.53 (CF_3), 0.66 (CN)), SCF_3 exhibits the highest Hansch lipophilicity constant among standard heteroatomic organic substituents (π_p=1.44, cf. 0.88 (CF_3), 0.14 (F), 1.68 (*t*Bu)).[6] The synthetic procedures for the decoration of aromatic residues with the trifluoromethylsulfanyl substituents are manifold (Scheme 5.1): *i)* substitution of electron-rich arenes (ArH,[7] ArM, M=Mg,[8] B[9]) with electrophilic SCF_3 reagents; *ii)* transition metal-mediated trifluoromethylsulfanylation of electrophilic aryl halides with formally anionic SCF_3 species such as $AgSCF_3$ or Me_4NSCF_3,[10] *iii)* reaction of aryl-S precursors with trifluoromethylation reagents;[11] *iv)* halogen-fluorine exchange reactions

of polyhalogenoalkyl thioethers.[12] Electrophilic SCF_3-containing reagents include the easy-to-handle trifluoromethane-sulfenyl trifluoroacetate, the disulfide $(CF_3S)_2$, the gaseous $ClSCF_3$, $PhN(Me)SCF_3$, and hypervalent aryliodane reagents comprising the SCF_3 group. Copper, silver, and ammonium trifluoromethyl thiolates are commonly employed as SCF_3 nucleophiles.

We have recently reported on the photoredox-catalyzed synthesis of arylsulfides from arenediazonium salts and disulfides in the presence of eosin Y under green light irradiation (Scheme 5.2, top).[13] Later, we have developed a weak base-mediated protocol of very similar scope.[14] Most of the examples reported involved unfunctionalized dialkyl and diaryldisulfides. Here, we report the extension of these operationally facile radical aromatic thiolation methods to include the synthesis of trifluoromethylsulfanyl benzenes (Scheme 5.2, bottom). Both, dark reactions in the presence of weak base and photoredox catalytic conditions were studied.

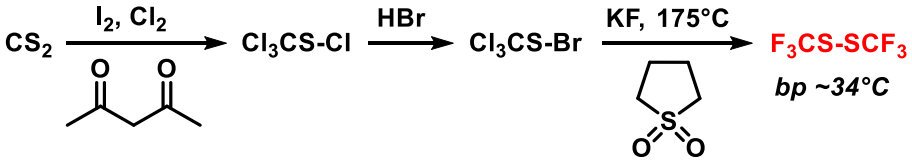


Scheme 5.2. Radical thiolations by photoredox catalysis and base mediation.

5.2. Results and Discussion

Bis(trifluoromethyl) disulfide, $F_3CS\text{-}SCF_3$, is a commercial reagent that can also be freshly prepared on lab scale by a literature procedure. The synthesis involves three sequential halogenation steps starting from carbon disulfide (Scheme 5.3). However, the low boiling points and toxicity of the intermediates and the product (~34 °C) require special precautions. Trichloromethylsulfenyl chloride was synthesized by chlorination of CS_2 with elemental chlorine.[15] The major side reaction is the decomposition of sulfur dichloride to disulfur dichloride which can be suppressed by the addition of acetylacetone.[16] Halogen exchange with aqueous HBr afforded trichloromethylsulfenyl bromide which underwent fluorination and dimerization by action of KF in hot sulfolane.[17] Pure 1,2-bis(trifluoromethyl) disulfide could be stored in a freezer over longer

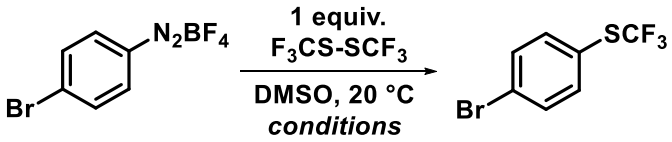
periods of time without decomposition (^{19}F NMR, 282 MHz, $CDCl_3$: 45.8 ppm). Our attempt to replace sulfolane with DMSO as the reaction solvent in the final step led to rapid decomposition and gas evolution even below 150 °C.



Scheme 5.3. Synthesis of 1,2-bis(trifluoromethyl) disulfide.

Initial optimization experiments (Table 5.1) were performed with equimolar 4-bromobenzenediazonium tetrafluoroborate and $(F_3CS)_2$.

Table 5.1. Base-mediated and photoredox-catalyzed trifluoromethylthiolation. [a]



Entry	Procedure	Base (equiv.)	Photocatalyst (mol%)	Yield in % [b]
1 [c]	-	-	-	0
2 [c]	**A**	NaOAc (1)	-	40
3 [c]	**B**	-	Eosin Y (2)	0
4	**B**	-	Eosin Y (2)	66
5 [c]	**C**	-	$[Ru(bpy)_3]Cl_2$ (0.5)	0
6	**C**	-	$[Ru(bpy)_3]Cl_2$ (0.5)	69
7 [d]	**C**	-	$[Ru(bpy)_3]Cl_2$ (0.5)	59

[a] Conditions: 4-Bromobenzenediazonium tetrafluoroborate (0.3 mmol), DMSO (1.5 mL), under N_2, 6 h. Procedure A: NaOAc (0.3 mmol), 20 °C; B: eosin Y (0.012 mmol), irradiation with green LED (525 nm, 3.8 W), 20 °C; C: $[Ru(bpy)_3]Cl_2{\cdot}6H_2O$ (0.012 mmol, bpy = 2,2'-bipyridine), irradiation with blue LED (450 nm, 3.8 W), 20 °C. [b] GC yields *vs.* internal 1-dodecanenitrile. [c] dark reaction. [d] 0.5 equiv. $(F_3CS)_2$.

The dark reactions in the absence of base gave no conversion (entries 1, 3, 5). With sodium acetate (NaOAc) as weak base, moderate conversion to 4-bromotrifluoromethylsulfanyl benzene was observed (procedure **A**, entry 2). Significantly higher yields were obtained from photoredox-catalytic reactions with eosin Y (**B**: 2 mol%, 525 nm) and $[Ru(bpy)_3]Cl_2{\cdot}6H_2O$ (**C**: 0.5 mol%, 450

nm), respectively, under LED (3.8 W) irradiation (entries 4, 6). Employment of 0.5 equiv. $(F_3CS)_2$ resulted in slightly lower yields (entry 7).

A reaction profile analysis documented the rapid onset of trifluoromethylthiolation for all three procedures (>90% relative product formation within the first 3 h) and the highest reaction rate of the photoredox catalysis with only 0.5 mol% $[Ru(bpy)_3]Cl_2$ (Figure 5.1).

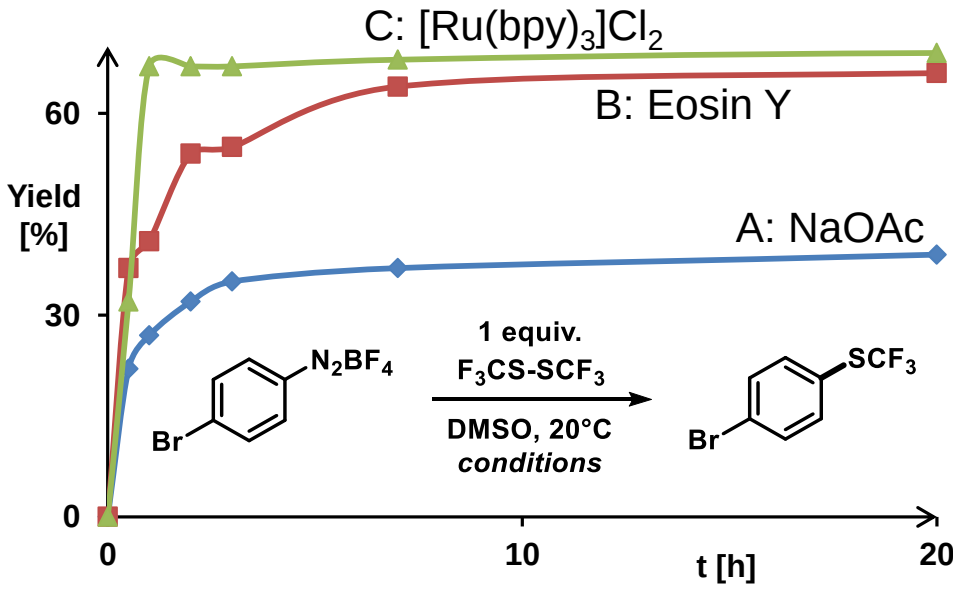
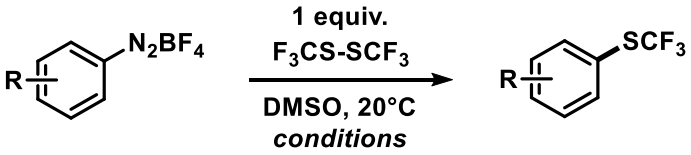


Figure 5.1. Reaction profiles of procedures **A**-**C** (for conditions, see Table 5.1).

Then, we subjected a set of five arenediazonium salts to a comparative study of trifluoromethylthiolation under the three reaction conditions **A**-**C** (Table 5.2). In all cases, the majority of product formation occurred in the first 3 h of the reaction. Photoredox catalysis conditions with $[Ru(bpy)_3]Cl_2 \cdot 6H_2O$ fared best for all substrates tested; eosin Y was only slightly less active. While being the operationally simplest strategy, the weak base mediated procedure gave significantly lower yields.

Table 5.2. Comparison of procedures **A**-**C** for selected arenediazonium salts.[a]

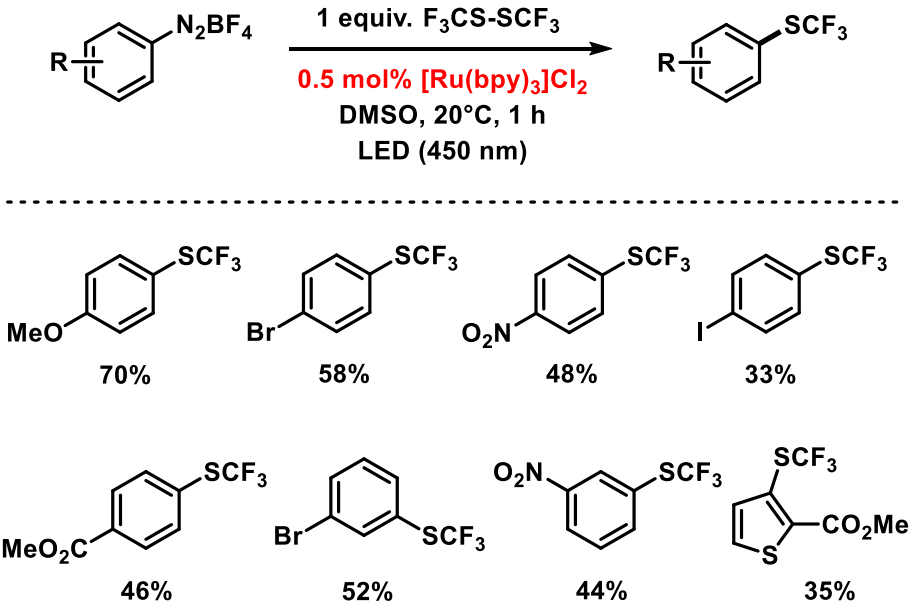


Entry	Ar-SCF_3	**A** Yield in %[b] 3 h (24 h)	**B** Yield in %[b] 3 h (24 h)	**C** Yield in %[b] 3 h (24 h)
1	4-Br	35 (40)	55 (66)	67 (68)

2 [c]	4-Br	30 (33)	50 (56)	57 (59)
3	4-OMe	75 (76)	77 (77)	77 (79)
4	4-NO_2	28 (34)	53 (67)	61 (71)
5	4-F	27 (31)	73 (81)	89 (89)
6	Ph	27 (33)	59 (60)	68 (69)

[a] Conditions: Arenediazonium tetrafluoroborate (0.3 mmol), DMSO (1.5 mL), under N_2, 24 h. Procedure **A**: NaOAc (0.3 mmol), 20 °C.; **B**: eosin Y (0.006 mmol), green LED (525 nm, 3.8 W), 20 °C; **C**: $[Ru(bpy)_3]Cl_2 \cdot 6H_2O$ (0.0015 mmol), blue LED (450 nm, 3.8 W), 20 °C. [b] GC yields *vs.* internal 1-dodecanenitrile. [c] 0.5 equiv. $(F_3CS)_2$.

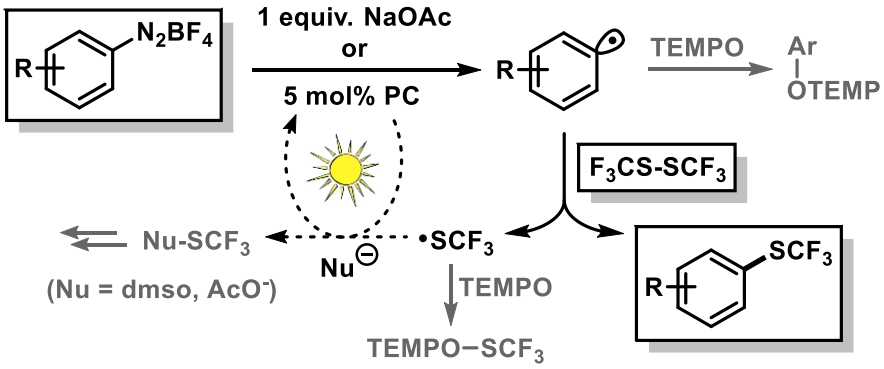
The optimized conditions were then applied to eight different arenediazonium salts in the presence of $[Ru(bpy)_3]Cl_2$ under irradiation with blue light (450 nm, one external 3.8 W LED per reaction). Moderate to good yields of the desired aryl trifluoro-methylsulfides were isolated after only 1 h reaction (Scheme 5.4).



Scheme 5.4. Ru-catalyzed photoredox-trifluoromethylthiolation (isolated yields).

Based on literature reports from our group and others,[13,14] we postulate a radical mechanism that is initiated by the reductive activation of the arenediazonium salt[18] (Scheme 5.5). With the weak base sodium acetate, this most likely involves the formation of the diazoacetate adduct which thermally decomposes to give the aryl radical Ar•. Under photocatalytic conditions, single electron transfer (SET) occurs with the excited photocatalyst PC (eosin Y or $[Ru(bpy)_3]Cl_2$). Ar• undergoes rapid reaction with the good non-bonding electron donor $(SCF_3)_2$. Cleavage of the resultant disulfide radical generates the trifluoromethylthiyl radical F_3CS• which

readily engages in hydrogen atom transfer (HAT) or possibly recombines with suitable nucleophiles. Back-electron transfer (formally from the elusive $[NuSCF_3]^{\bullet-}$) could be a potential pathway of photocatalyst regeneration. Upon addition of TEMPO, both radical intermediates as TEMPO adducts were observed by mass spectrometry.



Scheme 5.5. Postulated reaction mechanism.[13,14]

5.3. Conclusion

We have developed three related synthetic protocols that enable the straight-forward trifluoromethylthiolation of readily available arenediazonium salts with the commercial disulfide $(F_3CS)_2$. Weak base-mediated reactions in the presence of one equiv. NaOAc are operationally most simple but afforded only moderate yields. The photoredox-catalyzed protocols gave significantly higher yields of the Ar-SCF_3 products. With only 0.5 mol% $[Ru(bpy)_3]Cl_2 \cdot 6H_2O$, very good yields were obtained after irradiation with blue light at room temperature for 1 h.

5.4. Experimental Section

General

Chemicals and Solvents. Commercial chemicals (≥98% purity) were used as obtained from Acros, Sigma-Aldrich, Merck, Alfa Aesar, TCI or Fisher. Solvents (anhydrous, ≥99%) were used without further purification. DMSO was dried over molecular sieves (certified <0.005% water content, Sigma-Aldrich).

Analytical thin-layer chromatography. TLC was performed using aluminium plates with silica gel and fluorescent indicator (DC60 F254, Merck). Thin layer chromatography plates were visualized by exposure to UV light.

Column chromatography. Flash column chromatography with silica gel (60 Å, 0.035-0.070 mm) from *Acros Organics*. Pentane or mixtures thereof with ethyl acetate were used as eluents. Product yields were determined as isolated by column chromatography or for optimization and screening purposes by

quantitative GC-FID measurements. 1-Dodecanenitrile was used as internal standard; the yield was calculated from a linear calibration curve that was set up from at least five data points of various concentrations of authentic product material.

Gas chromatography with mass-selective detector. *Agilent* 6890N Network GC-System, mass detector 5975 MS. Column: BPX5 (30m x 0.25 mm x 0.25, from *SGE*, carrier gas: H_2. Standard heating procedure: 50°C (2 min), 25°C/min -> 300°C (5 min).

Gas chromatography with FID. *Agilent* 7820A GC-Systems. Column: HP 5 19091J 413 (30 m x 0.32 mm x 0.25 µm) from *Agilent*, carrier gas: N_2. GC-FID was used for reaction optimization screening (Calibration with internal standard 1-dodecanenitrile and analytically pure samples).

NMR. ^{1}H, ^{19}F, and ^{13}C nuclear magnetic resonance spectra were recorded on a *Bruker* Avance 300 (300 MHz ^{1}H; 75 MHz ^{13}C; 282 MHz ^{19}F) and *Bruker* Avance 400 (400 MHz ^{1}H, 101 MHz ^{13}C, 376 MHz ^{19}F) spectrometers. Chemicals shifts are reported in ppm (δ) relative to solvent residual peak as internal reference. Coupling constants (*J*) are reported in Hertz (Hz). Following abbreviations are used for spin multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

General procedure for the synthesis of arenediazonium salts

The parent aniline (30 mmol) was dissolved in 32% aqueous tetrafluoroboric acid (12 mL) at room temperature. Afterwards, an aqueous solution of sodium nitrite (30 mmol) in water (4 mL) was added dropwise at 0 °C over 5 min. The resulting mixture was stirred for 40 min and the precipitate was collected by filtration and re-dissolved in minimum amount of acetone. Then, diethyl ether was added until precipitation of diazonium tetrafluoroborate, which is filtered, washed several times with diethyl ether and dried.

General procedure for base-induced trifluoromethylthiolation

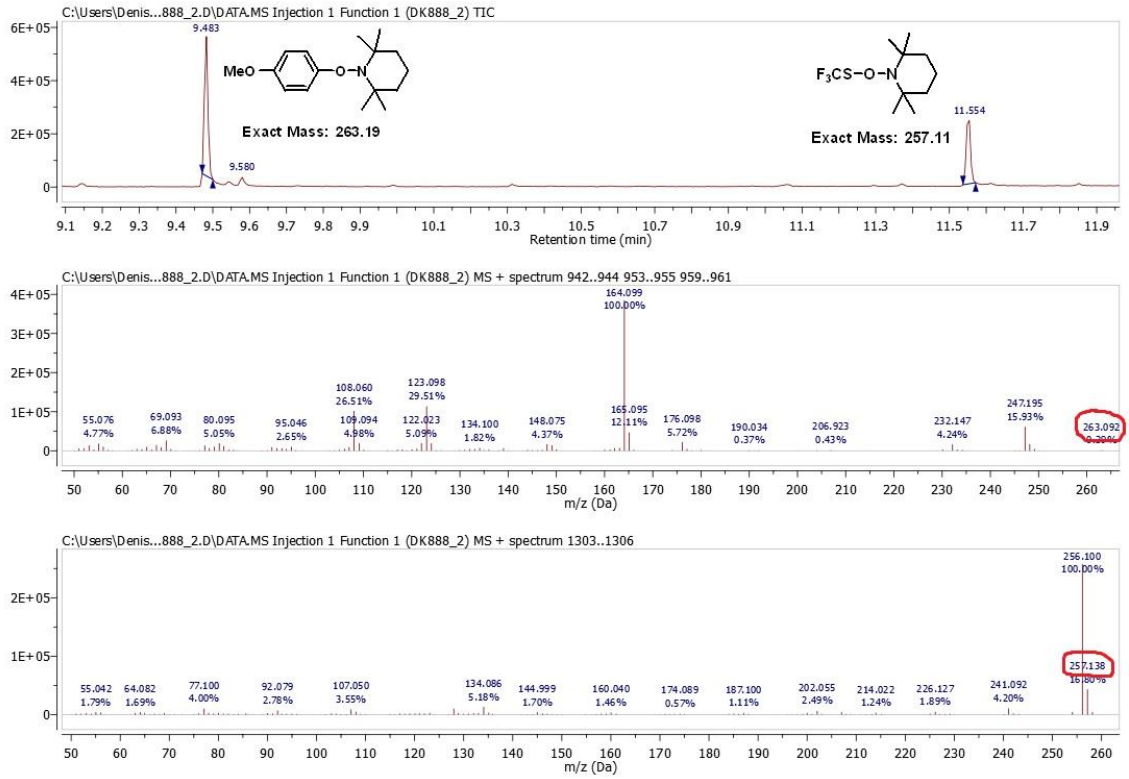
A vial (5 mL) was charged with a magnetic stir bar, the arenediazonium salt (0.9 mmol), 1,2-bis(trifluoromethyl)disulfane (0.9 mmol), and sodium acetate (0.9 mmol) and capped with a rubber septum. The vial was purged with N_2 (5 min). Dry DMSO (4.5 mL) was added. After 8 h of stirring water (5 mL) was added to give an emulsion, which was extracted with diethylether (3 x 5 mL). The organic phases were washed with brine (5 mL) and dried over $MgSO_4$. The solvent was evaporated *in vacuo*, and the residue was purified by flash column chromatography (silica gel) using pentane/ethyl acetate mixtures (from 100/0 to 100/20) as eluent to obtain pure product.

General procedure for photo-catalytic trifluoromethylthiolation

A vial (5 mL) was charged with a magnetic stir bar, the arenediazonium salt (0.9 mmol) and photocatalyst (0.018 mmol, 4.0 mol% of Eosin Y or 0.0045 mmol, 0.5 mol% or $[Ru(bpy)_3]Cl_2 \cdot 6H_2O$). Dry DMSO (4.5 mL) was added. The vial was purged with N_2 (5 min). 1,2-bis(trifluoromethyl)disulfane (0.9 mmol) was added the reaction vessel was sealed with a rubber septum. The reaction mixture was irradiated in case of Eosin Y with green light (LED, λmax = 525 nm, 3.8 W) for 6 h, in case of Ru catalyst with blue light (LED, λmax = 450 nm, 3.8 W) for 1 h. After the irradiation was discontinued, water (5 mL) was added to give an emulsion, which was extracted with diethylether (3 x 5 mL). The organic phases were washed with brine (5 mL) and dried over $MgSO_4$. The solvent was evaporated *in vacuo*, and the residue was purified by flash column chromatography (silica gel) using pentane/ethyl acetate mixtures (from 100/0 to 100/20) as eluent to obtain pure product.

Radical trapping experiments with TEMPO

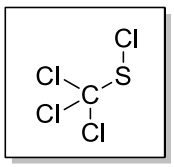
The model reaction of 4-methoxybenzenediazonium tetrafluoroborate with $(F_3CS)_2$ was performed according to the General Procedure (see before). After 5 min, 1 equiv. of 2,2,6,6-tetramethylpiperidin-1-yl-oxyl (TEMPO) was added, and the reaction quenched after another 20 min. Mass spectra of the organic phases were recorded, which displayed the TEMPO adducts of the two radical intermediates postulated to occur in the overall radical mechanism:



Preparation of 1,2-Bis-(trifluoromethyl)disulfide

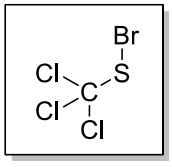
Caution! Trichloromethane sulfenyl chloride, trichloromethane sulfenyl bromide and 1,2-bis-(trifluoromethyl)disulfide are very toxic compounds by inhalation, and extreme caution should be taken while synthesizing or handling these compounds. A well ventilated fume cupboard should be utilized during all the operations with these materials, and all the contaminated glassware should be thoroughly rinsed with sodium hypochlorite. Moreover, 1,2-bis-(trifluoromethyl)disulfide, is an extremely volatile compound (b.p. ~ 34 °C) and due care should be taken when transferring this compound to any vessel.

Trichloromethane sulfenyl chloride



Three-necked, mechanically stirred, reaction flask was connected to a battery of washing flasks filled with aqueous NaOH (1 M). Reaction system was purged with nitrogen gas, and the reaction flask was charged with carbon disulfide (30.4 g, 24 ml, 0.40 mol). Acetylacetone (0.20 ml; 0.20 g; 2.0 mmol) and elemental iodine (80 mg; 0.63 mmol) were added to the reaction mixture at room temperature. Reaction mixture was cooled by an ice bath below 5 °C. Gaseous chlorine (47.0 g; 1.33 mol) was bubbled through the solution over a period of 3 h at such speed, that the temperature did not rise above 10 °C. Note, that towards the end of the reaction, the rate of consumption of the chlorine drops significantly, and the total consumption of chlorine had to be controlled by monitoring the total mass gain of the reaction mixture in periodic intervals, as overchlorination of product to thiophosgene can occur. Fractional distillation was performed to obtain cherry-red sulfur dichloride (59-62 °C; 30.7 g; 0.3 mol) as the first fraction, followed by the crude product as the second, colorless fraction (80-82 °C; 250 mbar). Trichloromethanesulfenyl chloride (35.9 g; 0.19 mol; 48 %) was isolated as colorless oil with a strong garlic smell. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 97.6 (**C**Cl_3); GC-MS (EI): m/z (relative intensity) = 185.8 (M^+), 148.9, 116.9, 83.9. Spectral data were consistent with the literature.[19]

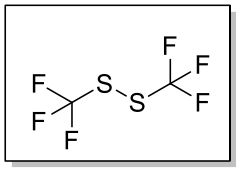
Trichloromethane sulfenyl bromide



62 % aqueous solution of HBr (20 ml; 0.26 mol) was added to trichloromethanesulfenyl chloride (35.9 g; 0.2 mol) without external cooling, and the two phase mixture as rapidly agitated for 17 h at room temperature. The organic phase was separated, and dried over magnesium sulfate. Solids were filtered off and the liquid phase was subjected to distillation at reduced pressure. The product distilled off as the first fraction (90-96 °C, 110 mbar). Trichloromethane sulfenyl bromide (35.9 g, 0.16 mol, 78 %) was isolated as a

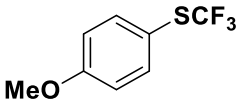
deep red oil with characteristic smell. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 93.1 (CCl_3); GC-MS (EI): m/z (relative intensity) = 229.7 (M^+), 150.8, 116.9, 78.9.

1,2-Bis-(trifluoromethyl)disulfide



A three necked round bottomed flask was equipped with a nitrogen gas inlet and a Vigreaux column. Condenser was attached to the Vigreaux column, and the condenser outlet was fed to a cooling trap (0 °C), and subsequently to another cooling trap (-78 °C). Second cooling trap was vented to the atmosphere *via* a bubble counter. Reaction vessel was charged with a suspension of KF (38.0 g; 0.65 mol) in sulfolane (210 ml). Gentle flow of nitrogen gas through the apparatus was initiated, and the reaction mixture was heated to 175 °C. Neat trichloromethane sulfenyl bromide (35.9 g, 0.16 mol) was added to the reaction mixture over a period of one hour at such rate, that no excessive gas formation was detected by the bubble counter. Care should be taken during the addition, as the reaction occurs after induction period, and rapid addition of sulfenyl bromide can lead to uncontrollable gas evolution. Reaction mixture was stirred at 175 °C for another 15 minutes, formation of condensate in the cooling traps ceased afterwards. Condensed gasses collected in the first cooling trap were identified as the product. Reaction residues were decomposed by a slow addition of the sludge to an aqueous solution of sodium hypochlorite, after the reaction mixture cooled down to room temperature. Note: We have noted, that significant weakening of glass walls of the reaction vessel occurred during the reaction. 1,2-Bis-(trifluoromethyl)disulfide (5.15 g, 25.5 mmol; 15 %) was isolated as a mobile colourless liquid with sharp garlic smell. ^{19}F NMR spectrum of product was measured using phenyl trifluoromethyl sulfide as an internal standard (δ =-43.2).[20] ^{19}F NMR (282 MHz, $CDCl_3$): δ = -45.8 (s, 6F). Spectral data were consistent with the literature.[21]

(4-Methoxyphenyl)(trifluoromethyl)sulfane



$C_8H_7F_3OS$, 208.20 g/mol

Yield 131.2 mg, 0.63 mmol, 70% (isolated)

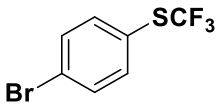
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.57 (d, *J* = 8.8 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 3.84 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 161.9, 138.3, 134.8, 129.6 (q, *J* = 308.1 Hz), 115.0, 55.4.

^{19}F-NMR (282 MHz, $CDCl_3$): δ_F [ppm] = -44.43.

LR MS (EI, 70 eV, m/z): 208 [M^+]

(4-Bromophenyl)(trifluoromethyl)sulfane



$C_7H_4BrF_3S$, 257.07 g/mol

Yield 134.2 mg, 0.52 mmol, 58% (isolated)

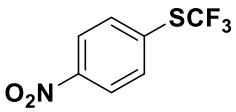
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.59-7.50 (m, 4H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 137.7, 132.8, 129.2 (q, J = 308.3 Hz), 126.0, 123.4 (q, J = 2.1 Hz).

^{19}F-NMR (376 MHz, $CDCl_3$): δ_F [ppm] = -43.25.

LR MS (EI, 70 eV, m/z): 256 [M^+]

(4-Nitrophenyl)(trifluoromethyl)sulfane



$C_7H_4F_3NO_2S$, 223.17 g/mol

Yield 96.4 mg, 0.43 mmol, 48% (isolated)

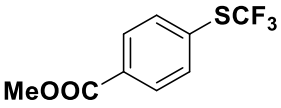
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 8.28 (d, J = 8.9 Hz, 2H), 7.83 (d, J = 8.7 Hz, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 149.1, 136.1, 132.5 (q, J = 2.3 Hz), 128.9 (q, J = 308.8 Hz), 124.3.

^{19}F-NMR (282 MHz, $CDCl_3$): δ_F [ppm] = -41.82.

LR MS (EI, 70 eV, m/z): 223 [M^+]

Methyl 4-((trifluoromethyl)thio)benzoate



$C_9H_7F_3O_2S$, 236.21 g/mol

Yield 95.7 mg, 0.41 mmol, 45% (isolated)

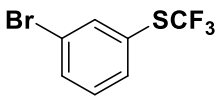
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 8.07 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.3 Hz, 2H), 3.93 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 166.0, 135.5, 132.1, 130.4, 129.8 (q, *J* = 2.0 Hz), 129.3 (q, *J* = 308.3 Hz), 52.4.

^{19}F-NMR (282 MHz, $CDCl_3$): δ_F [ppm] = -42.36.

LR MS (EI, 70 eV, m/z): 236 [M^+]

(3-Bromophenyl)(trifluoromethyl)sulfane



$C_7H_4BrF_3S$, 257.07 g/mol

Yield 120.3 mg, 0.47 mmol, 52% (isolated)

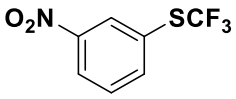
^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.82 (t, *J* = 1.7 Hz, 1H), 7.65-7.58 (m, 2H), 7.31 (t, *J* = 7.9 Hz, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 138.7, 134.8, 134.0, 130.8, 129.3 (q, *J* = 308.4 Hz), 126.2 (q, *J* = 2.1 Hz), 122.9.

^{19}F-NMR (376 MHz, $CDCl_3$): δ_F [ppm] = -42.86.

LR MS (EI, 70 eV, m/z): 256 [M^+]

(3-Nitrophenyl)(trifluoromethyl)sulfane



$C_7H_4F_3NO_2S$, 223.17 g/mol

Yield 88.4 mg, 0.40 mmol, 44% (isolated)

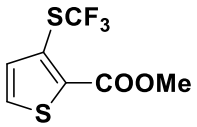
^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 8.55-8.51 (m, 1H), 8.37 (d, *J* = 8.3 Hz, 1H), 8.24 (d, *J* = 7.8 Hz, 1H), 8.0 (d, *J* = 7.7 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ_C [ppm] = 148.5, 141.8, 130.8, 130.4, 129.0 (q, *J* = 308.8 Hz), 126.7, 125.7.

^{19}F-NMR (282 MHz, $CDCl_3$): δ_F [ppm] = -42.53.

LR MS (EI, 70 eV, m/z): 223 [M^+]

Methyl 3-((trifluoromethyl)thio)thiophene-2-carboxylate



$C_7H_5F_3O_2S_2$, 242.23 g/mol

Yield 76.3 mg, 0.32 mmol, 35% (isolated)

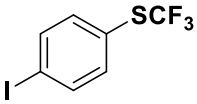
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H [ppm] = 7.59 (d, *J* = 5.3 Hz, 1H), 7.25 (d, *J* = 5.1 Hz, 1H), 3.91 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 161.8, 131.7, 130.6 (d, *J* = 2.2 Hz), 129.4 (q, *J* = 309.1 Hz), 129.3 (d, *J* = 2.2 Hz), 128.5, 52.5.

^{19}F-NMR (376 MHz, $CDCl_3$): δ_F [ppm] = -41.34.

LR MS (EI, 70 eV, m/z): 242 [M^+]

(4-Iodophenyl)(trifluoromethyl)sulfane



$C_7H_4F_3IS$, 304.07 g/mol

Yield 90.3 mg, 0.30 mmol, 33%

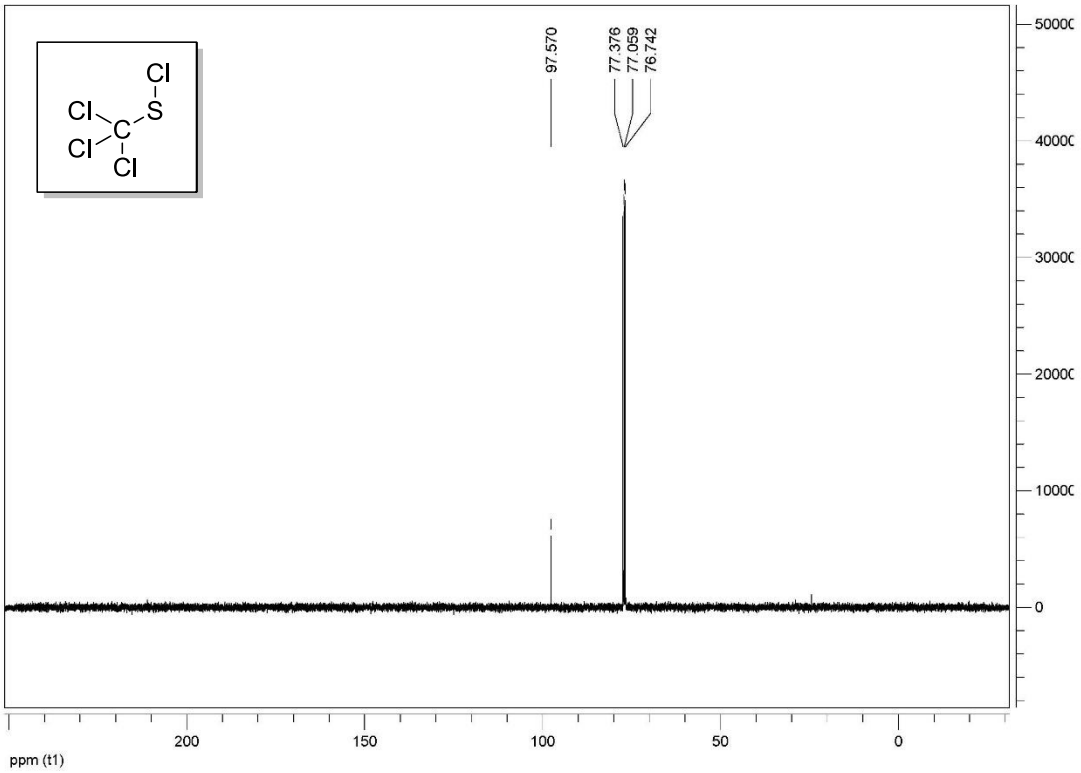
^{1}H-NMR (300 MHz, $CDCl_3$): δ_H [ppm] = 7.77 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H).

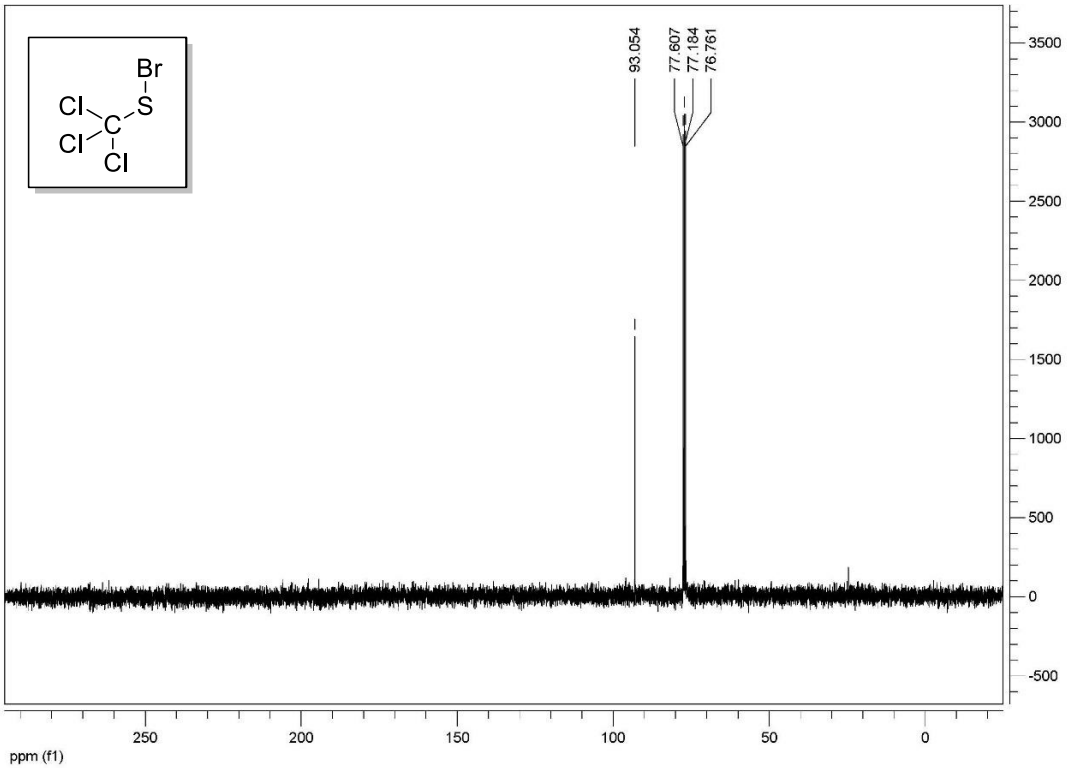
^{13}C-NMR (101 MHz, $CDCl_3$): δ_C [ppm] = 138.8, 137.7, 129.1 (q, *J* = 308.4 Hz), 124.2 (q, *J* = 2.1 Hz), 98.0.

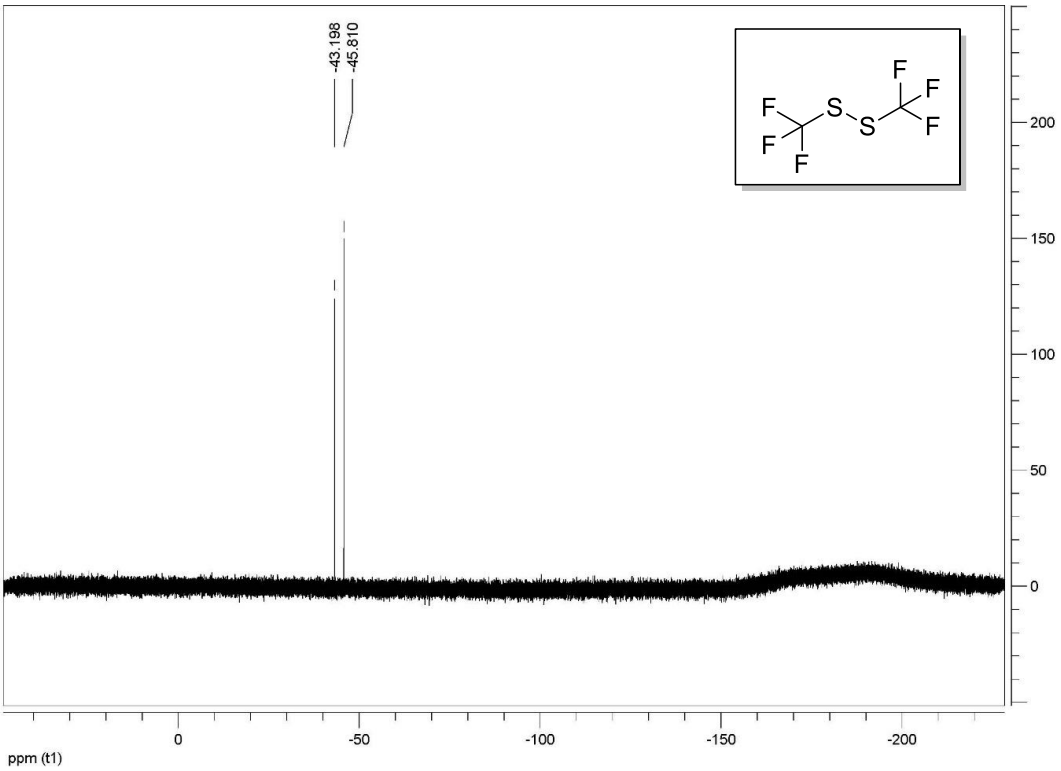
^{19}F-NMR (282 MHz, $CDCl_3$): δ_F [ppm] = -43.09.

LR MS (EI, 70 eV, m/z): 304 [M^+]

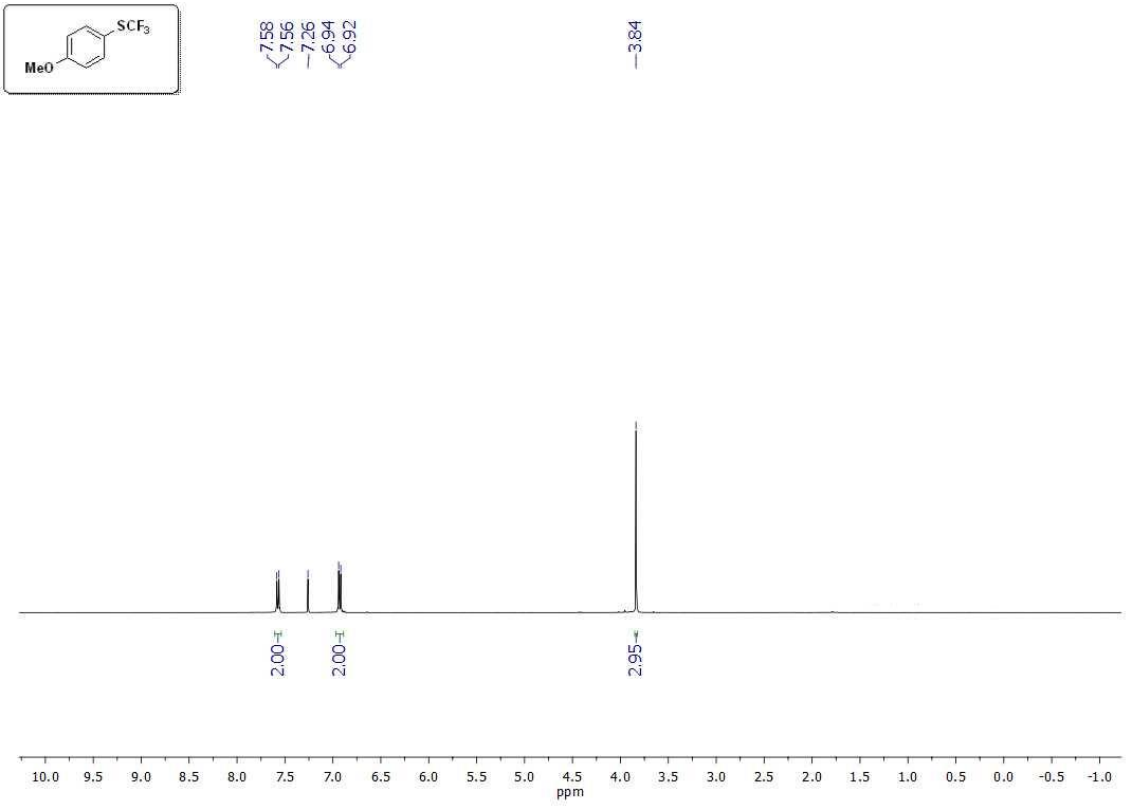
NMR spectra of selected compounds



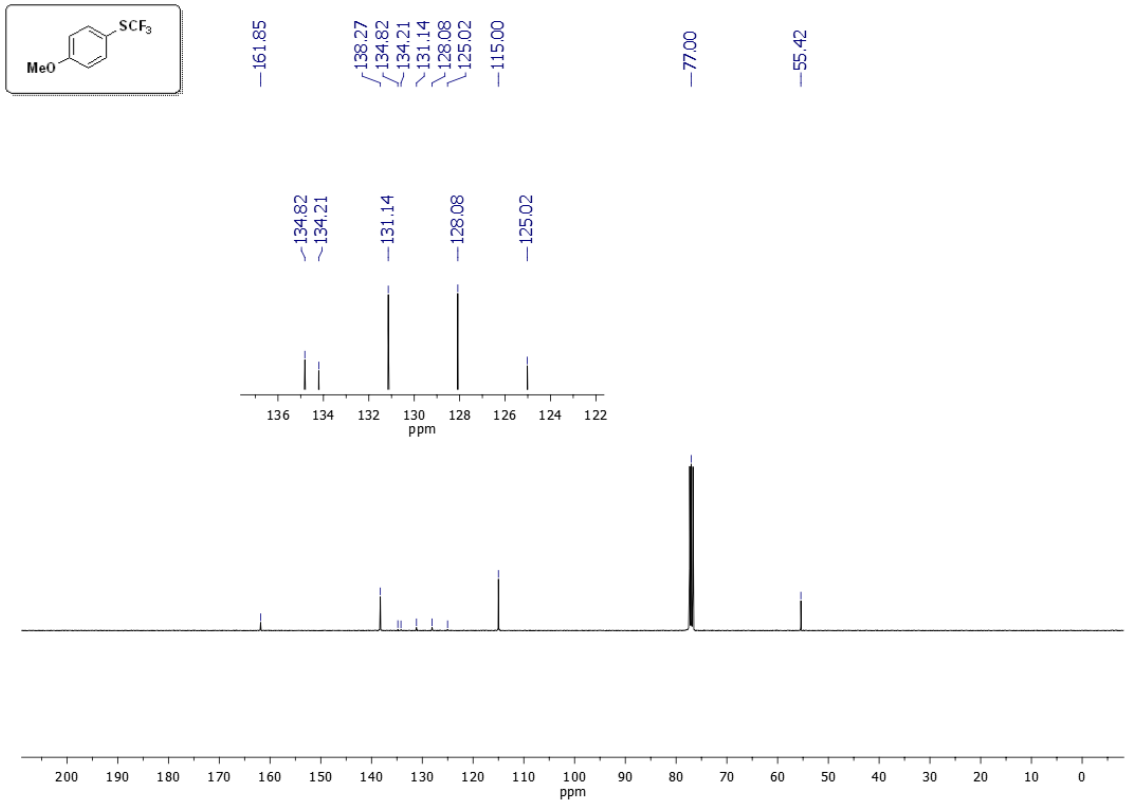




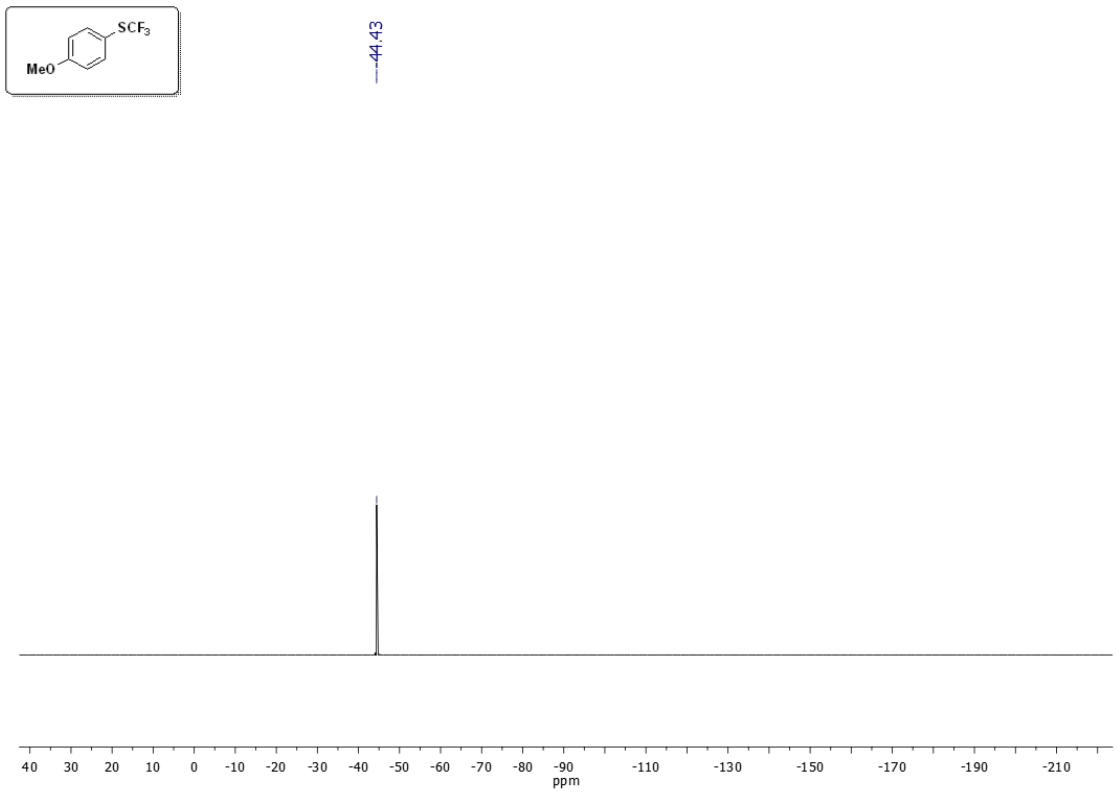
^{1}H-NMR (400 MHz, $CDCl_3$)



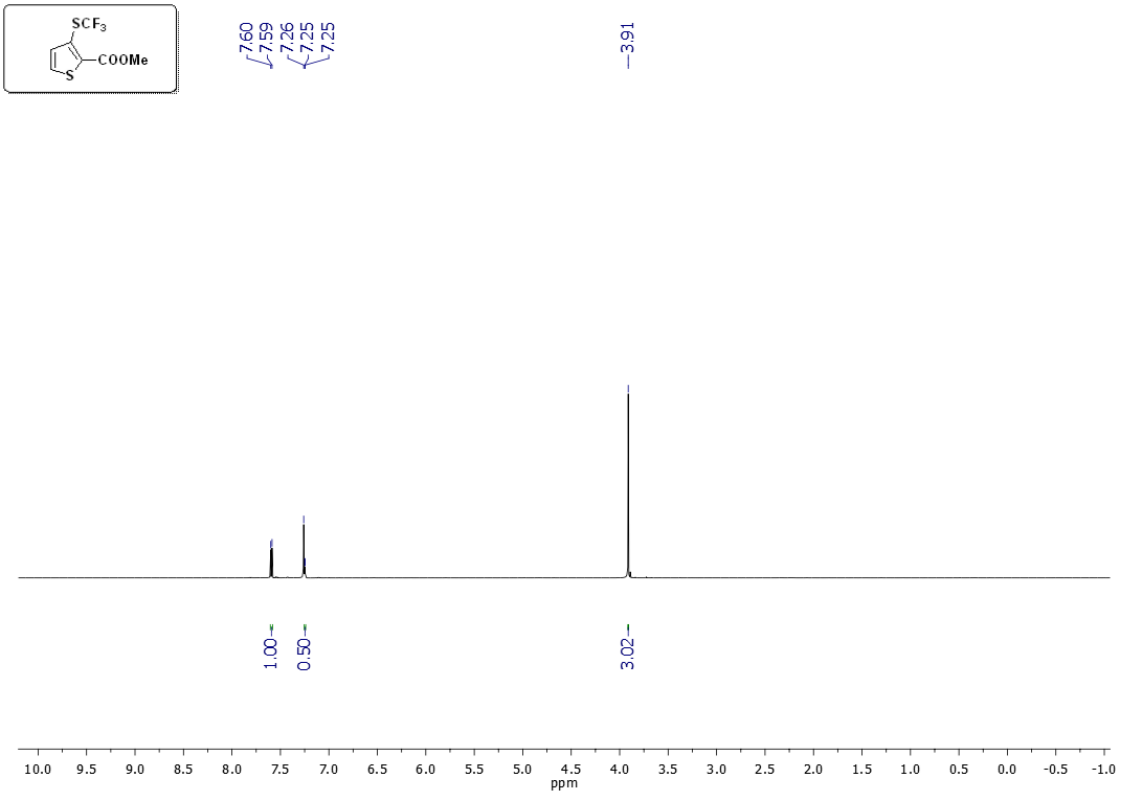
^{13}C-NMR (101 MHz, $CDCl_3$)



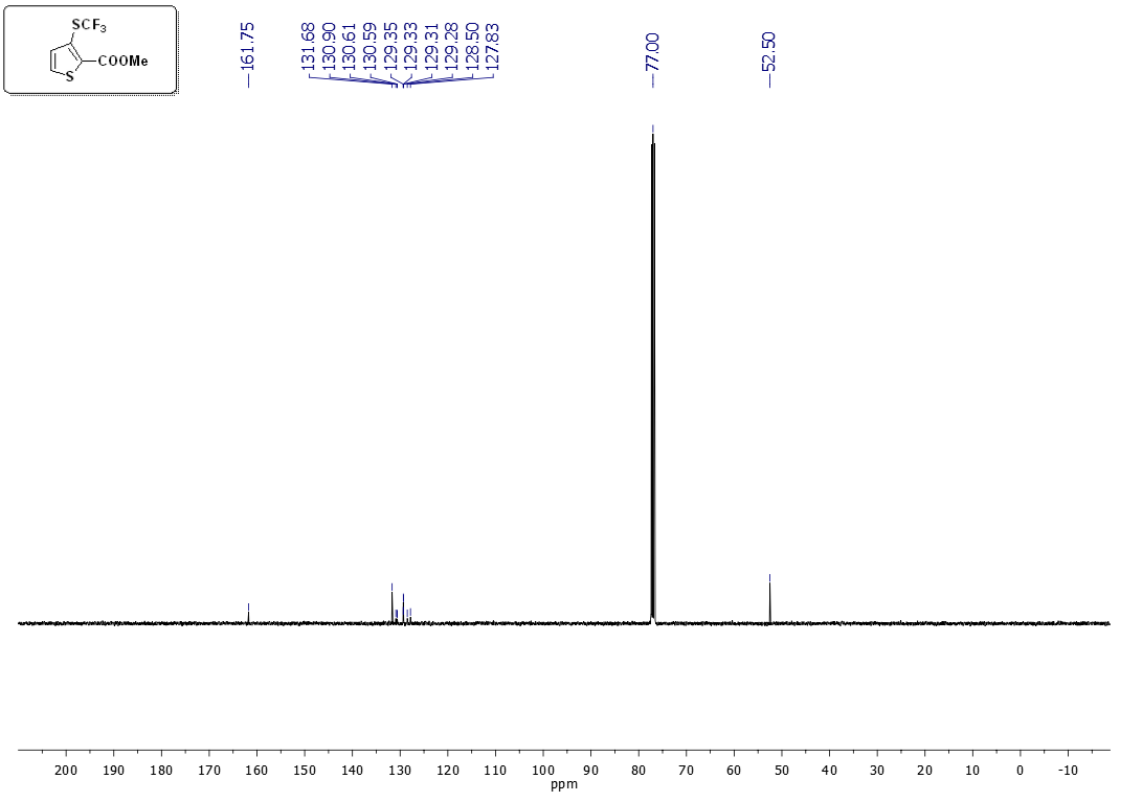
^{19}F-NMR (282 MHz, $CDCl_3$)



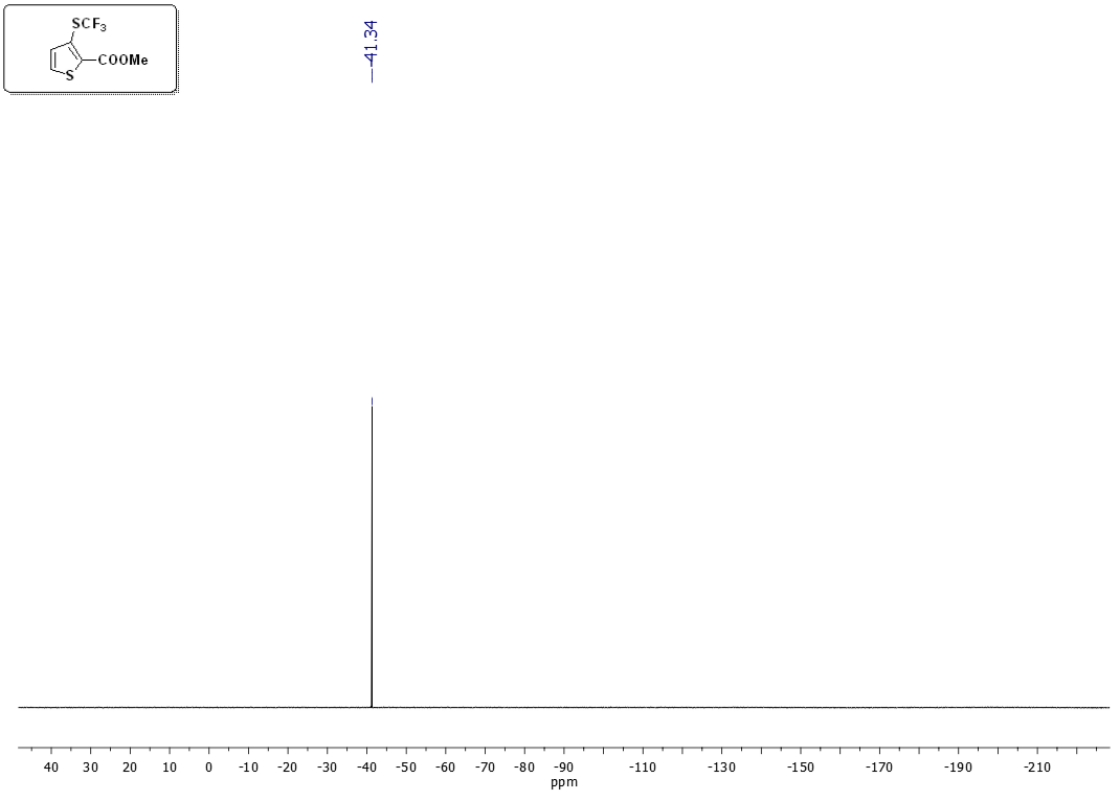
^{1}H-NMR (400 MHz, $CDCl_3$)



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



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



5.5. References

[1] D. B. Harper, D. O'Hagan, C. D. Murphy in *The Handbook of Environmental Chemistry*, *Vol. 3P* (Ed.: G. W. Gribble), Springer, Heidelberg, **2003**, 141–169.

[2] a) H. J. Böhm, D. Banner, S. Bendels, M. Kansy, B. Kuhn, K. Müller, U. Obst-Sander, M. Stahl, *ChemBioChem* **2004**, *5*, 637–643; b) K. L. Kirk, *Curr. Top. Med. Chem.* **2006**, *6*, 1447–1456; c) K. Müller, C. Faeh, F. Diederich, *Science* **2007**, *317*, 1881–1886; d) W. K. Hagmann, *J. Med. Chem.* **2008**, *51*, 4359–4369; e) D. O'Hagan, *Chem. Soc. Rev.* **2008**, *37*, 308–319; f) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320–330; g) J.-P. Begue, D. Bonnet-Delpon, *J. Fluorine Chem.* **2006**, *127*, 992–1012; h) F. M. D. Ismail, *J. Fluorine Chem.* **2002**, *118*, 27–33; i) C. Isanbor, D. O'Hagan, *J. Fluorine Chem.* **2006**, *127*, 303–319.

[3] a) P. Jeschke, *ChemBioChem* **2004**, *5*, 570–589; b) P. Maienfisch, R. G. Hall, *Chimia* **2004**, *58*, 93–99.

[4] a) F. Guittard, E. T. de Givenchy, S. Geribaldi, A. Cambon, *J. Fluorine Chem.* **1999**, *100*, 85–96; b) F. Babudri, G. M. Farinola, F. Naso, R. Ragni, *Chem. Commun.* **2007**, 1003–1022; c) M. Cametti, B. Crousse, P. Metrangolo, R. Milani, G. Resnati, *Chem. Soc. Rev.* **2012**, *41*, 31–42; d) R. Berger, G. Resnati, P. Metrangolo, E. Weber, J. Hulliger, *Chem. Soc. Rev.* **2011**, *40*, 3496–3508; e) C. M. Kassis, J. K. Steehler, D. E. Betts, Z. B. Guan, T. J. Romack, J. M. DeSimone, R. W. Linton, *Macromolecules* **1996**, *29*, 3247–3254; f) M. G. Dhara, S. Banerjee, *Prog. Polym. Sci.* **2010**, *35*, 1022–1077; g) S. Schlögl, R. Kramer, D. Lenko, H. Schröttner, R. Schaller, A. Holzner, W. Kern, *Eur. Polym. J.* **2011**, *47*, 2321–2330; h) D. Anton, *Adv. Mater.* **1998**, *10*, 1197–1205; i) H. Saito, E. Nakagawa, T. Matsushita, F. Takeshita, Y. Kubo, S. Matsui, K. Miyazawa, Y. Goto, *IEICE Transactions on Electronics* **1996**, *E79C*, 1027–1034; j) P. Kirsch, A. Hahn, *Eur. J. Org. Chem.* **2005**, 3095–3100; k) Y. Li, *Acc. Chem. Res.* **2012**, *45*, 723–733.

[5] Toltrazuril: a) A. Günther, K.-H. Mohrmann, M. Stubbe, H. Ziemann, *Bayer AG 1986,* DE3516630; b) P. Laczay, G. Vörös, G. Semjén, *Int. J. Parasitol* **1995**, *25*, 753–756; c) P. Pommier, A. Keïta, S. Wessel- Robert, B. Dellac, H. C. Mundt, *Rev. Med. Vet.* **2003**, *154*, 41. Tiflorex: a) J. N. André, L. G. Dring, G. Gillet, C. Mas-Chamberlin, *Br. J. Pharmacol.* **1979**, *66*, 506; b) T. Silverstone, J. Fincham, J. Plumley, *Br. J. Clin. Pharmacol.* **1979**, *7*, 353–356; c) M. J. Kirby, H. Carageorgiou-Markomihalakis, P. Turner, *Br. J. Clin. Pharmacol.* **1975**, *2*, 541–542. Losartan: L. M. Yagupolskii, I. I. Maletina, K. I. Petko, D. V. Fedyuk, R. Handrock, S. S. Shavaran, B. M. Klebanov, S. Herzig, *J. Fluorine Chem.* **2001**, *109*, 87–94.

[6] a) C. Hansch, A. Leo in *Substituent constants for correlation analysis in chemistry and biology*, (Ed.: G. L. Flynn), Wiley, New York, **1979**, 339; b) C. Hansch, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165–195; c) J.-A. Ma, D.

Cahard, *Chem. Rev.* **2008**, *108*, 1–43; d) J. Nie, H.-C. Guo, D. Cahard, J.-A. Ma, *Chem. Rev.* **2011**, *111*, 455–529; e) O. A. Tomashenko, V. V. Grushin, *Chem. Rev.* **2011**, *111*, 4475–4521; f) T. Furuya, A. S. Kamlet, T. Ritter, *Nature* **2011**, *473*, 470–477; g) T. Besset, C. Schneider, D. Cahard, *Angew. Chem. Int. Ed.* **2012**, *51*, 5048–5050; h) B. Manteau, S. Pazenok, J.-P. Vors, F. R. Leroux, *J. Fluorine Chem.* **2010**, *131*, 140–158.

[7] a) A. Haas, M. Lieb, Y. Zhang, *J. Fluorine Chem.* **1985**, *29*, 297–310; b) L. D. Tran, I. Popov, O. Daugulis, *J. Am. Chem. Soc.* **2012**, *134*, 18237–18240; c) S. Andreades, J. F. Harris, Jr., W. A. Sheppard, *J. Org. Chem.* **1964**, *29*, 898–900; d) R. M. Scribner, *J. Org. Chem.* **1966**, *31*, 3671–3682; e) T. S. Croft, *Phosphorus and Sulfur and the Relat. Elem.* **1976**, *2*, 129–132; f) T. S. Croft, *Phosphorus and Sulfur and the Relat. Elem.* **1976**, *2*, 133–139; g) A. Ferry, T. Billard, E. Bacqué, B. R. Langlois, *J. Fluorine Chem.* **2012**, *134*, 160–163.

[8] a) W. A. Sheppard, *J. Org. Chem.* **1964**, *29*, 895–898; b) F. Baert, J. Colomb, T. Billard, *Angew. Chem. Int. Ed.* **2012**, *51*, 10382–10385.

[9] a) X. Shao, X. Wang, T. Yang, L. Lu, Q. Shen, *Angew. Chem. Int. Ed.* **2013**, *52*, 3457–3460; b) C. Chen, Y. Xie, L. Chu, R.-W. Wang, X. Zhang, F.-L. Qing, *Angew. Chem. Int. Ed.* **2012**, *51*, 2492–2495; c) C. Chen, L. Chu, F.-L. Qing, *J. Am. Chem. Soc.* **2012**, *134*, 12454–12457.

[10] a) Z. Weng, W. He, C. Chen, R. Lee, D. Tan, Z. Lai, D. Kong, Y. Yuan, K.-W. Huang, *Angew. Chem. Int. Ed.* **2013**, *52*, 1548–1552; b) G. Teverovskiy, D. S. Surry, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2011**, *50*, 7312–7314; c) C.-P. Zhang, D. A. Vicic, *J. Am. Chem. Soc.* **2012**, *134*, 183–185; d) D. J. Adams, A. Goddard, J. H. Clark, D. J. Macquarrie, *Chem. Commun.* **2000**, 987–988; e) G. Danoun, B. Bayarmagnai, M. F. Gruenberg, L. J. Goossen, *Chem. Sci.* **2014**, *5*, 1312–1316; f) C. Matheis, V. Wagner, L. J. Goossen, *Chem. Eur. J.* **2016**, *22*, 79–82.

[11] a) C. Wakselman, M. Tordeux, *J. Chem. Soc., Chem. Commun.* **1984**, 793–794; b) C. Wakselman, M. Tordeux, *J. Org. Chem.* **1985**, *50*, 4047–4051; c) R. Goumont, N. Faucher, G. Moutiers, M. Tordeux, C. Wakselman, *Synthesis* **1997**, 691–695; d) A. Harsányi, É. Dorkó, Á. Csapó, T. Bakó, C. Peltz, J. Rábai, *J. Fluorine Chem.* **2011**, *132*, 1241–1246; e) V. N. Boiko, G. M. Shchupak, *J. Fluorine Chem.* **1994**, *69*, 207–212; f) T. Billard, S. Large, B. R. Langlois, *Tetrahedron Lett.* **1997**, *38*, 65–68; g) V. N. Movchun, A. A. Kolomeitsev, Y. L. Yagupolskii, *J. Fluorine Chem.* **1995**, *70*, 255–257; h) C. Wakselman, M. Tordeux, J.-L. Clavel, B. Langlois, *J. Chem. Soc., Chem. Commun.* **1991**, 993–994; i) B. Quiclet-Sire, R. N. Saicic, S. Z. Zard, *Tetrahedron Lett.* **1996**, *37*, 9057–9058; (j) N. Roques, *J. Fluorine Chem.* **2001**, *107*, 311; k) G. Blond, T. Billard, B. R. Langlois, *Tetrahedron Lett.* **2001**, *42*, 2473–2475; l) C. Pooput, M. M´edebielle, W. R. Dolbier, *Org. Lett.* **2004**, *6*, 301–303; m) C. Pooput, W. R. Dolbier, M. M´edebielle, *J. Org. Chem.* **2006**, *71*, 3564–3568.

[12] a) N. N. Yarovenko, A. S. Vasileva, *J. Gen. Chem. USSR* **1958**, *28*, 2537; b) E. A. Nodiff, S. Lipschutz, P. N. Craig, M. Gordon, *J. Org. Chem.* **1960**, 25, 60–65; c) A. E. Feiring, *J. Org. Chem.* **1979**, *44*, 2907–2910; d) J. M. Kremsner, M. Rack, C. Pilger, C. O. Kappe, *Tetrahedron Lett.* **2009**, *50*, 3665–3668; e) B. Gutmann, D. Obermayer, B. Reichart, B. Prekodravac, M. Irfan, J. M. Kremsner, C. O. Kappe, *Chem. Eur. J.* **2010**, *16*, 12182–12194; f) T. Umemoto, S. Ishihara, *J. Fluorine Chem.* **1998**, 92, 181–187.

[13] a) M. Majek, A. Jacobi von Wangelin, *Chem. Commun.* **2013**, *49*, 5507–5509; b) M. Majek, F. Filace, A. Jacobi von Wangelin, *Beilstein J. Org. Chem.* **2014,** *10,* 981–989; c) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322–5363.

[14] D. Koziakov, M. Majek, A. Jacobi von Wangelin, *Org. Biomol. Chem.* **2016**, *14*, 11347–11352.

[15] B. Rathke, *Justus Liebigs Ann. Chem.* **1873**, *167*, 195–211.

[16] C. C. Greco, E. N. Walsh, *U.S. Patent* 4092357, **1978**.

[17] R. E. A. Dear, E. E. Gilbert, *Synthesis* **1972**, 310.

[18] a) C. Galli, *Chem. Rev.* **1988**, *88*, 765–792; b) H. Bonin, E. Fouquet, F.-X. Felpin, *Adv. Synth. Catal.* **2011**, *353*, 3063–3084; c) F. Mo, G. Dong, Y. Zhang, J. Wang, *Org. Biomol. Chem.* **2013**, 11, 1582–1593.

[19] G. K. S. Prakash, J. Hu, J. Simon, D. R. Beller, G. A. Olah, *J. Fluorine Chem.* **2004**, *125*, 595–601.

[20] W.-Y. Fang, T. Dong, J.-B. Han, G.-F. Zha, C.-P. Zhang, *Org. Biomol. Chem.* **2016**, *14*, 11502–11509.

[21] D. M. Ceacareanu, M. R. C. Gerstenberger, A. Haas, *Chem. Ber.* **1983**, *116*, 3325–3331.

Chapter 6

- Appendix -

6. Appendix

6.1. List of abbreviations

Ar	Aryl
ATR	Attenuated Total Reflection
bpy	2,2'-bipyridine
cf.	Compare
d	Day
DCM	Dichloromethane
DFT	Density functional theory
DMF	*N*,*N*-Dimethylformamide
DMSO	Dimethylsulfoxide
EDG	Electron donating group
e.g.	For Example
EI	Electron impact
equiv.	Equivalent
ESI	Electrospray ionization
Et	Ethyl
et al.	And others
eV	Electronvolt
FID	Flame ionization
FT-IR	Fourier-Transform-Infrared spectroscopy
GC	Gas chromatography
h	Hour
HAT	Hydrogen Atom Transfer
HR	High resolution
Hz	Hertz
***i*Pr**	Isoropyl
LED	Light emitting diode
LR	Low resolution
Me	Methyl
MeCN	Acetonitrile
MeOH	Methanol
MHz	Megahertz
min	Minute
mmol	Millimole
MS	Mass spectrometry
nm	Nanometer
NMR	Nuclear magnetic resonance
PC	Photocatalyst
Ph	Phenyl
phen	Phenantroline
ppm	Parts per million
R	Alkyl rest
r.t.	Room temperature
s, sec	Secondary
SET	Single Electron Transfer
***t*Bu**	*tert*-Butyl
***t*-Bu**	*tert*-Butyl
TBA	Tetrabutylammonium iodide
TEMPO	2,2,6,6-tetramethylpiperidin-1-yl)-oxyl
TFA	Trifluoroacetic acid
TLC	Thin layer chromatography
UV	Ultraviolet radiation
VIS	Visible radiation
vs.	Versus

6.2. Summary

The aim of this thesis was the development of transition metal-free radical aromatic substitutions mediated by weak, inexpensive, and non-toxic inorganic bases.

In the beginning, the general preparation and properties of arenediazonium salts were given. An overview of existing reaction types of arenediazonium compounds from the old ones to the most modern was given. The major focus laid on the transformations of arenediazonium salts in the presence of weak bases. The key mechanistic steps were highlighted, where authors could propose a mechanism.

Chapters 3 and 4 dealt with the generation of aryl radicals from arenediazonium tetrafluoroborates by very weak bases. This strategy was applied to the preparation of aromatic sulfides, selenides, tellurides, as well as diverse *tert*-butyl, alkyl, and *i*-propyl benzoates. Unexpected heterocyclic products were synthesized from arenediazonium salts using this method. In order to prove the proposed mechanisms, mechanistic investigations were made, involving spectroscopic and computational techniques and deuterium labeling. The postulated mechanisms involved homolysis of the initially formed diazoacetate or diazoformate. Mechanistic studies in thiolation reactions indicated the operation of a radical aromatic substitution mechanism *via* aryl, acetyloxyl, thiyl, and dimsyl radicals. In the alkoxycarbonylation reactions the aryl radical reacted with carbon monoxide to provide the acyl radical, which was confirmed by trapping experiments.

Chapter 5 aimed to compare photoredox catalysis and base mediation in a radical aromatic trifluoromethylthiolation reaction. Three related synthetic protocols (two photocatalytic and one base-mediated) utilizing arenediazonium tetrafluoroborates as starting compounds were developed. Diverse aromatic trifluoromethyl sulfides were synthesized employing a photo-catalyzed protocol which afforded significantly higher yields.

6.3. Zusammenfassung

Das Ziel der vorliegenden Arbeit war die Entwicklung von übergangsmetallfreien radikalischen aromatischen Substitutionen, die durch schwache, kostengünstige und nicht-toxische anorganische Basen vermittelt werden.

Im ersten Kapitel werden allgemeine Methoden zur Herstellung von Arendiazoniumsalzen und deren Eigenschaften vorgestellt. Anschließend wird eine Übersicht präsentiert, in der bestehende Reaktionstypen von Arendiazonium-verbindungen unter Berücksichtigung ihrer Entwicklung von alt zu modern vorgestellt wurden. Das Hauptaugenmerk wurde dabei auf Transformationen von Arendiazoniumsalzen in Gegenwart von schwachen Basen gelegt. Wichtige mechanistische Schritte, in denen die Autoren einen Mechanismus vorschlagen konnten wurden hervorgehoben.

Die Kapitel 3 und 4 befassten sich mit der Erzeugung von Arylradikalen durch sehr schwache Basen ausgehend von Arendiazoniumtetrafluoroboraten. Diese Strategie wurde auf die Herstellung von aromatischen Sulfiden, Seleniden, Telluriden sowie diversen Benzoesäureestern angewendet. Unter Verwendung dieser Methode wurden unerwartete heterocyclische Produkte aus Arendiazoniumsalzen synthetisiert. Um die vorgeschlagenen Mechanismen zu beweisen, wurden mechanistische Untersuchungen durchgeführt, die spektroskopische und computergestützte Techniken, sowie Deuterium-Markierungen beinhalteten. Die postulierten Mechanismen beschrieben die Homolyse des anfänglich gebildeten Diazoacetats oder Diazoformiats. Mechanistische Studien in Thiolierungsreaktionen zeigten die Präsenz eines radikalischen aromatischen Substitutionsmechanismus unter Mitwirkung von Aryl-, Acetyloxyl-, Thiyl- und Dimsyl-Radikalen. Die Beobachtung der Reaktion zwischen dem Aryl Radikal und Kohlenmonoxid zum Acyl-Radikal bei den Alkoxycarbonylierungsreaktionen wurde durch Abfangexperimente bestätigt.

Kapitel 5 zielte darauf ab, die Photoredox-Katalyse und die Basenvermittlung in der radikalischen aromatischen Trifluormethylthiolierung zu vergleichen. Es wurden drei verwandte synthetische Protokolle (zwei photokatalytische und eine basenvermittelte) unter Verwendung von Arendiazoniumtetrafluoroboraten als Ausgangsverbindungen entwickelt. Verschiedene aromatische Trifluormethylsulfide wurden unter Verwendung eines photokatalysierten Protokolls synthetisiert. Dabei konnte eine signifikant höhere Ausbeute beobachtet werden.

6.4. Acknowledgments

In the first place I would like to thank my scientific supervisor Prof. Dr. Axel Jacobi von Wangelin for giving me an opportunity to study in Germany and be part of his wonderful scientific group. The door to Prof. Jacobi von Wangelin's office was always open whenever I ran into a trouble spot or had a question about my research or writing. He always could find time to discuss my research and other problems.

I would like to thank the experts who agreed and found time to be members of the examination committee Jun.-Prof. Dr. Ivana Fleischer (second reviewer), Prof. Dr. Frank-Michael Matysik (examiner), and Prof. Dr. Siavosh Mahboobi (chairperson).

I would like to express my appreciation to Dr. Michal Májek, who always gave me advice and shared his ideas with me. Michal was actively participating in my research, giving me valuable comments and helping me whenever I needed his help. He is also a very open-minded person, who likes to talk about different topics.

I would also like to thank two other members of my research group Dr. Tim Gieshoff and Dr. Matteo Villa. They were always willing to help me and most of the time they gave me instructions on how to use any equipment in our group.

I am very thankful to all the members of my research group for having a very nice time together, for the atmosphere of friendliness, for the desire to help in any situation.

I wish to express my very profound gratitude to my parents, relatives, and friends in Kazan for providing me with unfailing support and continuous encouragement throughout my years of study and through the process of researching and writing this thesis.

Finally, I would like to thank my friends Viktoria Filippova, Efrain Reyes-Rodriguez, and Ali Rami who made my life in Regensburg cheerful and unforgettable.

6.5. Curriculum Vitae

Personal Data

Name: Denis Koziakov
Date of Birth: November 3rd, 1991 in Kazan (Russian Federation)
Nationality: Russian

Education

2014 – 2017 Doctoral Thesis in Organic Chemistry, in the group of Prof. Dr. Axel Jacobi von Wangelin:
"Radical Aromatic Substitutions Mediated by Weak Bases"

2009 – 2014 Diploma (with honors) in chemistry, Kazan Federal University
Diploma Thesis:
"Synthesis and structure of novel sulfur-containing nitrogen heterocycles based on 3-pyrroline-2-one"

1999 – 2009 Gymnasium # 75, Kazan: Certificate of secondary education

List of publications

1) D. Koziakov, M. Majek, A. Jacobi von Wangelin, *Eur. J. Org. Chem*. **2017** (submitted).
2) D. Koziakov, A. Jacobi von Wangelin, *Org. Biomol. Chem*. **2017**, *15*, 6715–6719.
3) D. Koziakov, M. Majek, A. Jacobi von Wangelin, *Org. Biomol. Chem*. **2016**, *14*, 11347–11352.

Presentations (oral, poster)

1) GDCh-Wissenschaftsforum Chemie 2017, Berlin (poster)
2) International Society of Heterocyclic Chemistry Congress 2017, Regensburg (poster)
3) International Conference on Green and Sustainable Chemistry 2017, Melbourne, Australia (poster and oral)
4) ORCHEM 2016, Weimar (poster)
5) GDCh-Wissenschaftsforum Chemie 2015, Dresden (poster)

6.6. Eidesstatliche Erklärung

I. Ich erkläre hiermit an Eides statt, dass ich die vorliegende Arbeit ohne unzulässige Hilfe Dritter und ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe; die aus anderen Quellen direkt oder indirekt übernommenen Daten und Konzepte sind unter Angabe des Literaturzitats gekennzeichnet.

II. Bei der Auswahl und Auswertung haben mir die in den jeweiligen Kapiteln aufgeführten Personen in der beschriebenen Art und Weise unentgeldlich geholfen.

III. Weitere Personen waren an der inhaltlich-materiellen Herstellung der vorliegenden Arbeit nicht beteiligt. Insbesondere habe ich hierfür nicht die entgeltliche Hilfe eines Promotionsberaters oder anderer Personen in Anspruch genommen. Niemand hat von mir weder unmittelbar noch mittelbar geldwerte Leistungen für Arbeiten erhalten, die im Zusammenhang mit dem Inhalt der vorgelegten Dissertation stehen.

IV. Die Arbeit wurde bisher weder im In- noch im Ausland in gleicher oder ähnlicher Form einer anderen Prüfungsbehörde vorgelegt.

_____

Regensburg, den 13.10.2017