Development of One-Pot and Multicomponent Reactions towards Sulfones and Sulfonamides

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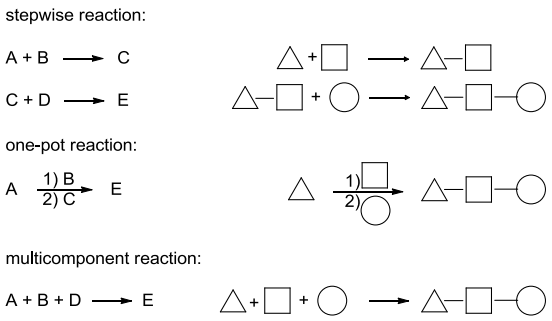
1. Introduction

"Many new synthetic processes have been discovered as a result of a perceived need in connection with specific problems involving novel or complicated structures and a deliberate search for suitable methodology." With these words E. J. Corey points out the challenges modern synthetic chemists are facing today.[1] The need for new pharmaceutical and agrochemical compounds is continuously rising, due to the growing and aging population. Therefore, organic chemistry in particular has to develop innovative, efficient and environmental friendly strategies to form e.g. carbon-carbon and carbon-heteroatom bonds using sustainable processes. Notably, the need for larger and more diverse substance libraries for drug research is a monumental task chemists are currently coping with.

B. M. Trost summarized it almost 25 years ago: "The limitations of raw materials, combined with environmental concerns, necessitate our rethinking of strategies toward complex organic synthesis."[2]

One strategy is the utilization of one-pot reactions or multicomponent reactions, MCR (scheme 1.1). These are characterized by a high atom-economy, low waste production and great efficiency. Especially for the pharmaceutical industry in constant need of more compound libraries to identify new biological active molecules, this approach is of great interest. By developing a general method to form certain classes of compounds, based on variation of only one of the components, access to hundreds of unknown molecules is granted.



Scheme 1.1. Comparison of the different Reaction Types.

The classic stepwise reaction is based on the isolation and purification of each intermediate molecule, causing a high material usage, waste production and high energy consumption. An improvement is the one-pot reaction, which is also a stepwise reaction, but neglects isolating intermediate products and proceeds without further purifications. MCR elegantly combines all required components, affording the desired product in only one step. In this context, compared to the latter, they are the most atom-economic and efficient way towards new molecules.

1.1 Sulfonyl-Containing Compounds

The sulfonyl-group (-SO_2-) is an important motif in organic chemistry and is found in a large variety of biologically active compounds.[3–5] Functional groups like sulfones, sulfinic and sulfonic acids, sulfonylureas and especially sulfonamides are one of the most common structures found in drugs. To date, there are more than 100 accredited drugs containing a sulfonyl-group[6,7] and approximate 10% of the blockbuster drugs in 2012 were bearing the sulfonamide moiety.[8,9] Hence, SO_2-functionalities are a key feature in constructing new drugs.

Therefore, development of new, generally applicable, preferably simple synthetic methods, which generate a broad scope of unknown substances of this group of compounds in a short period of time, is of great interest.

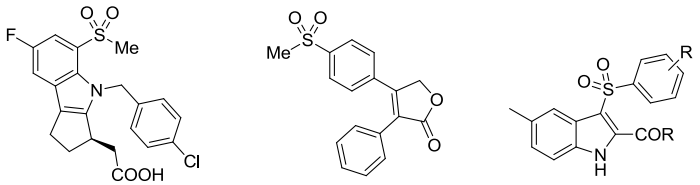
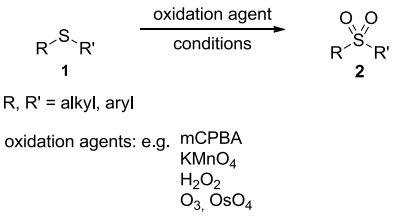


Figure 1.1. Biologically Active Sulfones.

1.1.1 Sulfones

As briefly discussed in above, sulfones are important building blocks in organic, pharmaceutical and medicinal chemistry.[4,5,10,11] The sulfonyl moiety is often found in drugs, like the COX-2 inhibitor Vioxx[12] or the prostaglandin D_2 antagonist Laropiprant[13] (figure 1.1). Furthermore, compounds containing a sulfone fragment, show antifungal, antibacterial or antitumor activities, and even inhibit HIV-1 transcriptase, such as indonylsulfones[14] (figure 1.1).

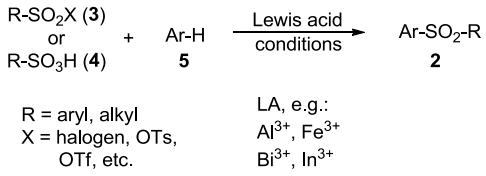
Due to their importance several procedures for their preparation exist. The most common are oxidation of sulfides or sulfoxides (scheme 1.2) and the sulfonylation of arenes (scheme 1.3),[10,11] although both have obvious disadvantages.



Scheme 1.2. General Oxidation Reaction to Sulfones.

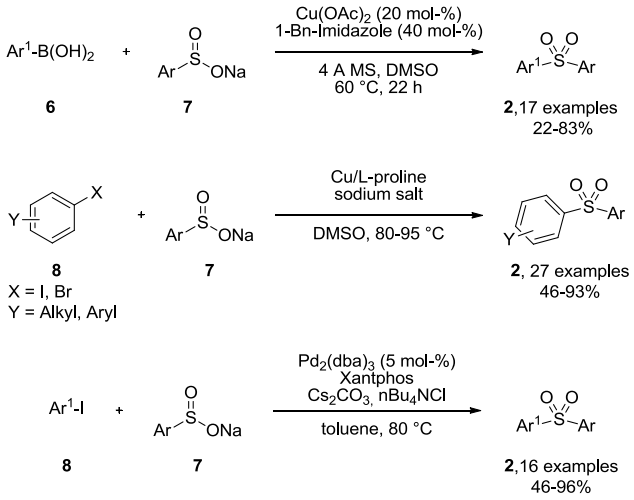
Sulfur is already present in the starting materials, and not introduced in a later stage of the synthesis. In case of the sulfides, many are commercially available; however specific substituted sulfones usually require individual preparation (scheme 1.2).[15–17] Access to sulfonyl halides (mostly chlorides) is limited

(scheme 1.3) and their synthesis requires harsh reaction conditions, restricting the amount of potential functional moieties.[18–22] Furthermore, both pathways may involve harmful or toxic oxidation agents and long reaction times. The sulfonylation approach, which is comparable to a Friedel-Crafts-type reaction, is usually carried out at elevated temperatures and depending on the reaction mechanism equimolar amounts of Lewis acids are required.[23]



Scheme 1.3. General Reaction for the Sulfonylation to Sulfones.

A milder alternative are transition metal-catalyzed reactions (scheme 1.4). Recently several groups have developed Pd- or Cu-catalyzed cross-coupling reactions between arylsulfinic acid salts and aryl halides or boronic acids.[24–26]



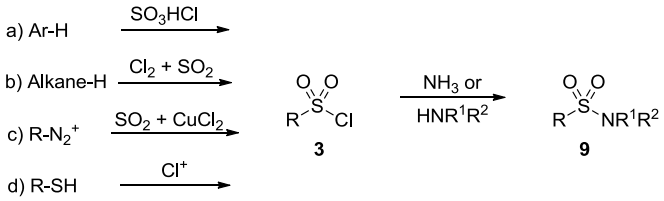
Scheme 1.4. Transition Metal-Catalyzed Synthesis of Diarylsulfones.

These methods are an improvement in comparison to the classical approaches (schemes 1.2 and 1.3), because they have a wider scope, due to the high availability of aryl halides. The sulfonyl-moiety is still included in the starting material, sulfinic acid sodium salts. Even though some are commercially available, the majority has to be prepared from the corresponding sulfonyl chlorides. These are, as mentioned above, difficult to prepare.

1.1.2 Sulfonamides

As previously mentioned the sulfonamide moiety is one of the most popular motifs in medicinal chemistry and is found in many drugs.[4,5,7] Interestingly, despite its huge importance, only one general preparation routine exists: reaction of the corresponding sulfonyl chlorides with amines or ammonia.[27,28] With this simple method, a variety of sulfonamides can be prepared in good to excellent yields. However, this

approach is hampered by the availability and the preparation of the corresponding sulfonyl chlorides. Due to the commonly harsh reaction conditions, such as the sulfonylation and chlorination of arenes or the sulfoxidation and sulfonylation of alkanes (scheme 1.5a and b), several difficulties within the synthetic pathway occur.[27–30] Functional group tolerance in these very acidic and oxidative conditions is low, and therefore excludes often highly functionalized sulfonyl chlorides. Alternatively sulfonyl chlorides can be prepared starting from diazonium salts[31] or via oxidative chlorination of thiols[32,33] (scheme 1.5c and d). However, the chlorosulfonylation of diazonium salts has to be carried out under extremely acidic conditions and the salts are potentially explosive. The oxidative chlorination of thiols, on the other hand, is performed under relatively mild conditions, but either routes c) or d) include a sulfur-containing starting material. Simple and general applicable methods for the synthesis of sulfonamides, not deriving from sulfonyl chlorides are extensively unknown up to date.



Scheme 1.5. Preparation Methods towards Sulfonamides.

1.2 Hypervalent Iodoniumspecies

Hypervalent iodoniumspecies[34–38] are generally categorized in two classes: Iodine(III)- and iodine(V)-compounds. Iodine(V)-species like IBX and Dess-Martin-Periodane are common, selective and mild oxidation agents, especially in total synthesis. In recent years, the research regarding iodine(III)-compounds became more popular. Commonly, they are classified by the ligands or carbon species that are attached to the iodine:

(1) Iodosylarenes ArIO and its acyclic derivatives $ArIX_2$, which are strong oxidizing agents, have a broad range of application in organic synthesis as oxygenation reagents and for oxidative functionalization of organic reagents.

(2) Five membered iodine heterocycles, like benziodoxoles or benziodoazoles, which are more stable than their acyclic analogues and are commonly used as strong oxidizing agents.

(3) Iodonium Salts $R^1R^2I^+X^-$, which have diverse reactivity patters due to the exceptional leaving group properties of the ArI-fragment.

(4) & (5) Iodonium ylides $ArI=CR_2$ and iodonium imides ArI=NR, which are carbene and nitrene precursors, respectively.

1.2.1 Diaryliodonium Salts

Although diaryliodonium salts are known for more than 100 years, they recently regained interest. The general structure of diaryliodonium salts is shown in figure 1.2.[34] In general, compounds of the molecular formula $ArIL_2$, where L is usually a more electronegative group, have a T-shaped structure. This derives from the bonding situation/characteristics. The overall structure is trigonal bipyramidal. A covalent bond between the arene and iodide as well as two free electron pairs are located at the equatorial positions. The other two ligands are binding in the axial positions, resulting in a 3c-4e$^-$-bond system, delocalized over the one double occupied 5p orbital of iodide and the ligands. In this case, the highest electron density is located at the end of the linear L-I-L triad, resulting in a soft electrophilic iodide.[39]

Concerning iodonium salts, one ligand is significantly more electronegative, ensuing an ionic compound. Herein the iodide-carbon bonds are equivalent and possess a more covalent than hypervalent character. Also the triad angle C-I-C is larger, affording more stable compounds, showing, for example high melting points over 200 °C.

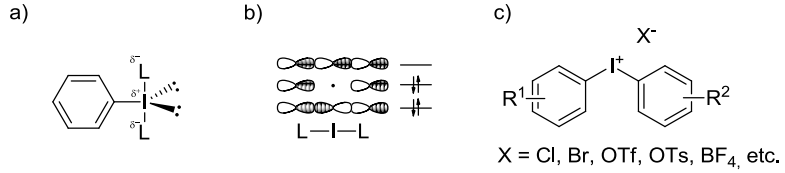
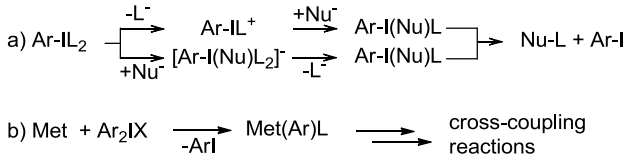


Figure 1.2. a) T-shaped Form determined by X-Ray Structure. b) Orbitals in the Hypervalent Bond. c) General Structure of Diaryliodonium Salts.

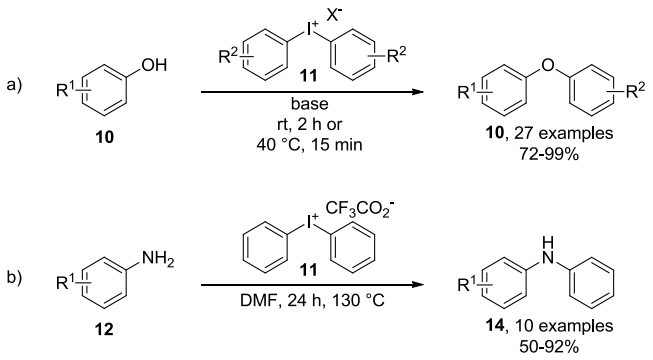
Due to their strongly electrophilic character and the extraordinary leaving group Ar-I, iodonium salts react with numerous nucleophiles. The general reactivity pattern is shown in scheme 1.6 and can be divided into two groups, reactions with nucleophiles (scheme 1.6a) and metal-catalyzed reactions (scheme 1.6b). 1.6a may process either as a mono- or bimolecular reaction. The latter is commonly proposed. Initial Nu-I bond formation is followed by release of one ligand. Subsequent nucleophilic substitution by the free ligand anion or reductive elimination yields the product Nu-L and releases Ar-I. The product, Nu-L is yielded via nucleophilic substitution of the free ligand anion, or alternatively, by reductive elimination. Metal-catalyzed reactions take advantage of iodonium salts as more reactive electrophiles than the corresponding aryl iodides. Oxidative addition of the salt to the metal centre results in a metal-aryl-ligand complex (scheme 1.6b), which reacts further to yield cross-coupling products.[34,39]

As iodonium salts are also exploited as radical source, radical mechanism were investigated, but excluded based on product distribution studies and radical inhibitors.



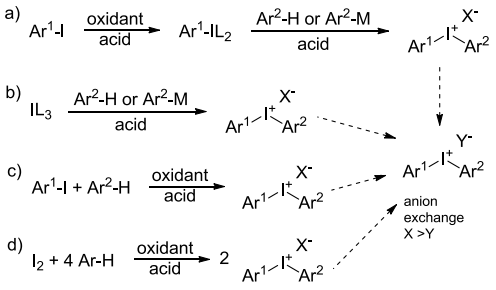
Scheme 1.6. General Reactivity of Iodonium Salts in a) Reactions with Nucleophiles, b) Metal-Catalyzed Reactions.

The usage of iodonium salts as electrophiles with heteroatom nucleophiles is gaining more interest, because of the transition-metal free conditions and broad scope such as diarylether synthesis or arylation of anilines shows (scheme 1.7).[40,41]



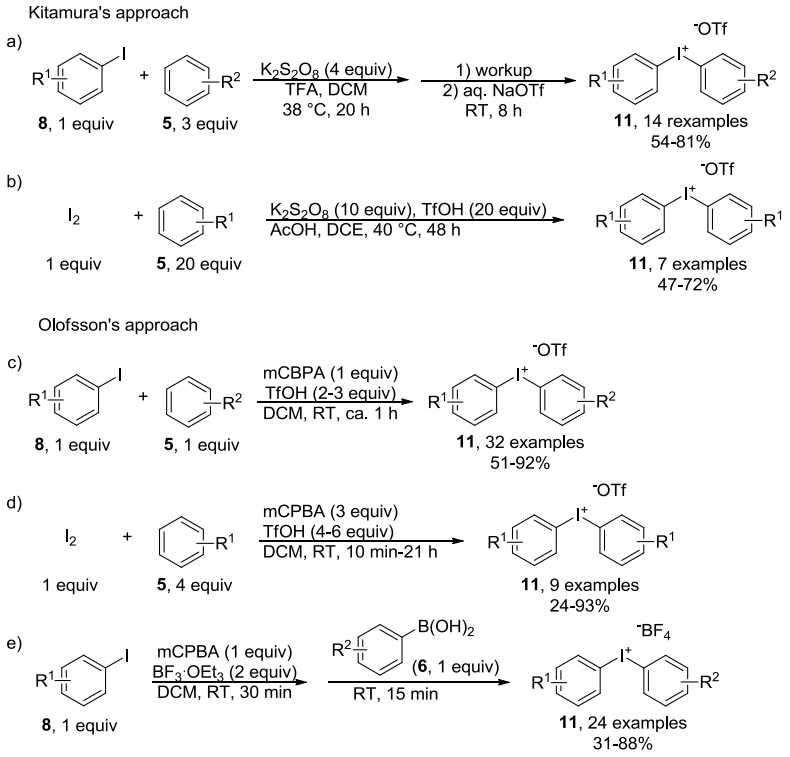
Scheme 1.7. Metal-Free Heteroatom Couplings using Iodonium Salts as Electrophiles.

A huge variety of synthetic strategies towards iodonium salts exist. General methods are summarized in scheme 1.8. Typical procedures usually involve several steps. Either oxidation of an aryl iodide to iodine(III) is performed prior to ligand exchange (scheme 1.8a) or depending on the properties of the iodonium salt an additional anion exchange is required. A shorter way of preparation of iodonium salts starts from an inorganic iodine(III)-species (scheme 1.8b). However, many one-pot procedures have been developed recently. They involve the oxidation and ligand exchange reaction in one step and the iodonium salts are generated directly from arenes and iodoarenes or molecular iodine (scheme 1.8c and d).[34]



Scheme 1.8. Synthetic Strategies for Preparing Diaryliodonium Salts.

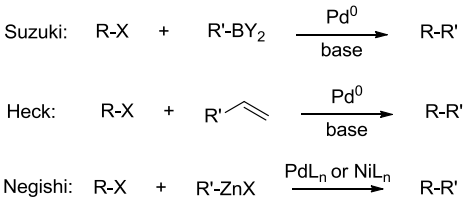
In the last years, the groups of Olofsson and Kitamura independently developed one-pot procedures for diaryliodonium salts.[42–46] Kitamura's approach is based on several routes containing potassium persulfate (scheme 1.9a and b). For reasons of simplicity two selected examples are briefly discussed. 1.9a requires excess reagents and is limited to electron-deficient aryl iodides and alkylarenes. The improved version 1.9b is the reaction between elemental iodine and arenes. Even though it is restricted to benzene, *tert*-butylbenzene and halobenzenes, it circumvents the use of partially expensive aryl iodides in contrast to 1.8a. The group of Olofsson developed a more general synthesis for iodonium salts using *meta*-chloroperbenzoic acid (*m*CPBA) as oxidizing agent for the iodoarenes to (diacyloxy)iodoarenes (scheme 1.9c-e). The scope is very broad, for both types of reactions, either starting from aryl iodides and arenes or elemental iodide and arenes. The limitations are very electron-rich or electron-deficient aryl groups.



Scheme 1.9. Kitamura's and Olofsson's One-Pot Approaches to Diaryliodonium Salts.

1.3 Transition Metal-Catalyzed Cross-Coupling Reactions

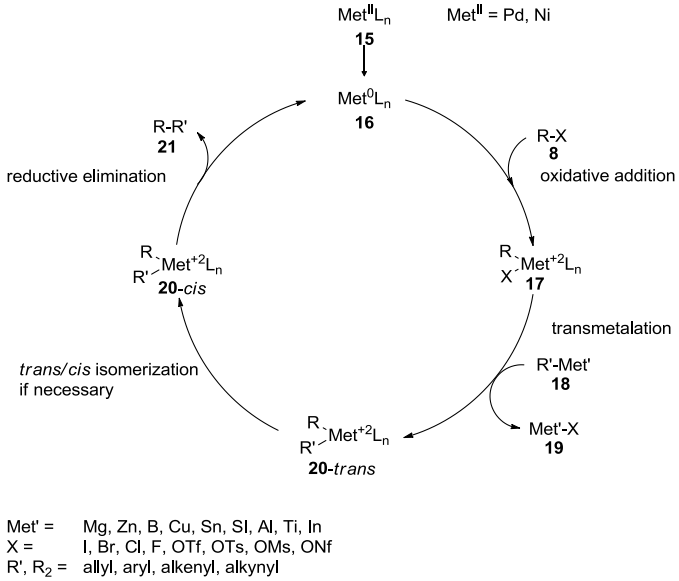
Transition metal-catalyzed cross-coupling reactions became one of the most powerful tools in synthetic chemistry throughout the last decades, manifested with the Nobel-Prize in chemistry for Suzuki, Heck and Negishi in 2010.



Scheme 1.10. Palladium-Catalyzed Cross-Coupling Reactions.

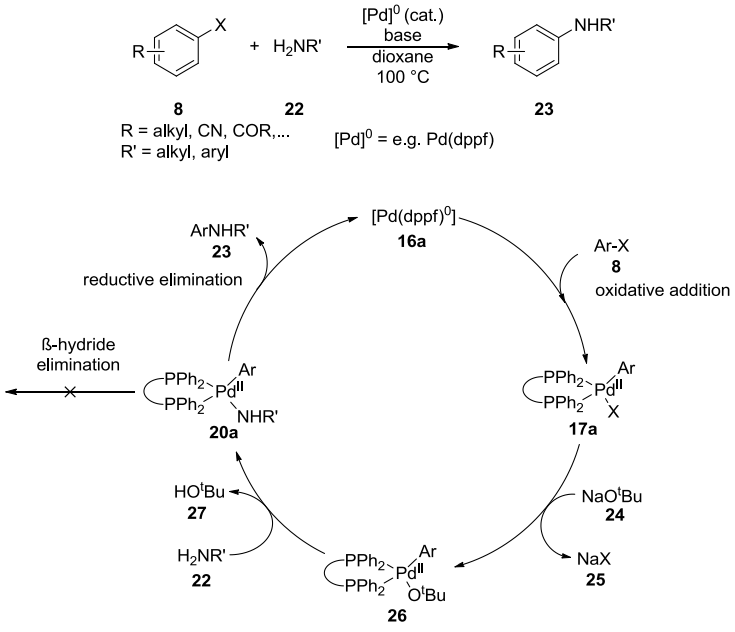
Usage covers a manifold of different carbon-carbon and carbon-heteroatom coupling reactions. In terms of the key steps the general catalytic cycle is similar, independent of the transition metal (scheme 1.11). Due to relevancy, only palladium- and nickel-catalyzed couplings are depicted. In a preliminary step, a Met(II)-precursor **15** is reduced *in situ* to the catalytic active Met(0)-species **16**. In cases of Met(0)-complexes, like $Pd(dba)_2$ or $Ni(cod)_2$ this step is redundant. The following step is the oxidative addition of electrophile R-X **8** into a Met-L-bond, yielding the organometallic species RXMetL **17**. Subsequent transmetalation leads to complex RR'MetL **20**. Final reductive elimination provides the desired cross-

coupling product R-R' **21** and regenerates the active catalyst Met^0L_n **16**. If the coupling partners are *trans* located, a *trans-cis*-isomerization occurs prior to the final reductive elimination leading to the product.



Scheme 1.11. General Catalytic Cycle for Transitionmetal-Catalyzed Cross-Coupling Reactions.

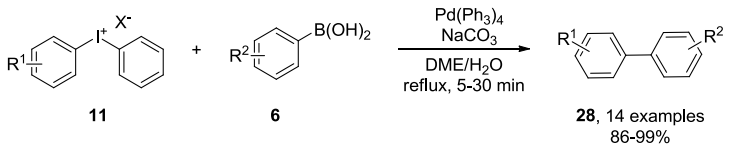
But not only carbon-carbon bonds can be generated via cross-coupling reactions. The Hartwig-Buchwald amination is a well known example for a carbon-heteroatom cross-coupling. The reaction between an aryl halide **8** and amine **22** also pursues via the general catalytic cycle yielding aryl amines **23** (scheme 1.12). Noteworthy, β-hydride elimination can be surpressed by usage of chelatating ligands, specific for this reaction.



Scheme 1.12. Hartwig-Buchwald Amination: General Reaction and Catalytic Cycle.

1.3.1 Palladium-Catalyzed Cross-Coupling Reactions

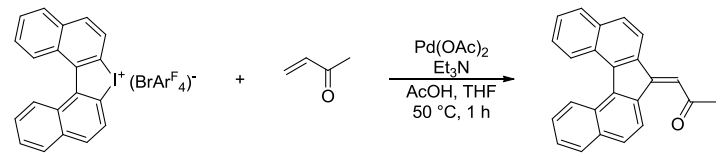
Various types of Pd-catalyzed cross-coupling reactions are distinguished, depending on the nature of the utilized transition metal and electrophile. The probably most popular ones, are the Heck, Negishi and Suzuki coupling reactions (scheme 1.10), and in case of carbon-heteroatom cross-couplings the Hartwig-Buchwald amination (scheme 1.12). Recently, the variety of electrophiles started to increase. First, mostly halides and their chemical equivalents were used, now also iodonium salts are applied. In scheme 1.13 a Suzuki-like Pd-catalyzed cross-coupling with an iodonium salt is shown.[47]



Scheme 1.13. Pd-Catalyzed Cross-Coupling with Iodonium Salts as Electrophiles.

This reaction proceeds via the general catalytic cycle (scheme 1.11), starting with the oxidative addition of the iodonium salt into a Pd-ligand-bond, followed by transmetalation of the boronic acid and ligand exchange, yielding the desired cross-coupling product after reductive elimination.

Another example for iodonium salts in cross-coupling reactions is depicted in scheme 1.14. This Heck-type reaction developed by Kina *et al.* provides a fluorene derivative **30** in excellent yield and under very mild conditions.[48]

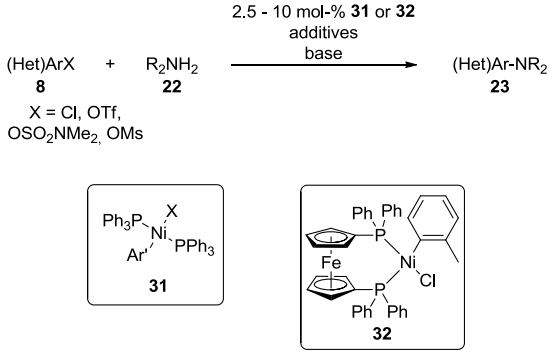


Scheme 1.14. Heck-type Cross-Coupling Reaction with an Iodonium Salt as Electrophile.

1.3.2 Nickel-Catalyzed Cross-Coupling Reactions

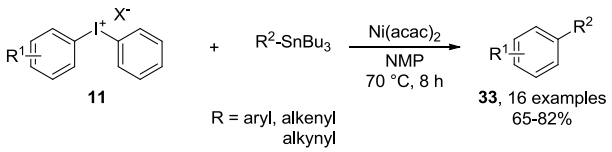
The Negishi-coupling is the oldest known nickel-catalyzed cross-coupling reaction. Although nickel is, as palladium and platinum, a d^{10}-metal, the catalytic power of nickel was not investigated in the same manner as the latter. Nickel reveals several unique features: It is smaller in atomic diameter and therefore more nucleophilic and in an economic point of view, less expensive than palladium or platinum. Because of the nucleophilicity transition metal-catalysts containing nickel are of higher reactivity for less reactive substrates like aryl chlorides or triflates. However, the most potent nickel-catalysts like $Ni(cod)_2$ are sensitive to air and moisture and therefore difficult to handle without special equipment. This could have been a reason for neglecting Ni^{2+} in catalysis. Additionally the *in situ* reduction of Ni^{2+}-salts to Ni(0)-species is more demanding in comparison to Pd^{2+} reduction and also limited in terms of reducing agents. Therefore nickel-salts are commonly used in reactions with potent reducing agents as coupling reagents,

such as organometallic compounds. Throughout the last years, first Yang *et al*.[49–51] and then Buchwald *et al.*[52] developed a novel type of Ni(0)-precursors, which are easy to prepare and more importantly, air stable and moisture insensitive (scheme 1.15).



Scheme 1.15. Ni(0)-Precursors developed by Yang *et al.* Buchwald *et al.* and their General Application.

But prior to this achievement, very simple Ni(0)-catalysts, like $Ni(acac)_2$ were used in cross-coupling reactions. An example is depicted in scheme 1.16, a Stille-like coupling exploiting iodonium salts as electrophiles.[53]

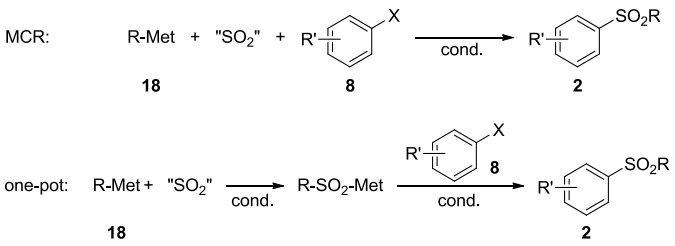


Scheme 1.16. Ni-catalyzed cross-coupling with iodonium electrophiles.

2. Objectives

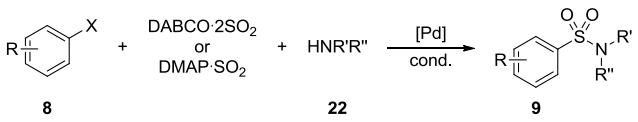
As previously described, sulfones and sulfonamides are very important building blocks in medicinal chemistry and pharmaceutical industry. Innovative and atom-economical synthetic approaches for both, sulfones and sulfonamides, are to be developed in the course of this thesis. Herein the introduction of the sulfonyl-moiety is to be considered the core step. In comparison to literature this results in a huge improvement, as the majority of published procedures emanate from sulfur or sulfur dioxide containing starting materials.

The initial point for the synthesis of sulfones is the reaction between an aryl halide, a SO_2-source and an organometallic compound (scheme 2.1). We envision the formation of sulfones from already accessible compounds via transition metal catalysis. A suitable reaction should be able to be carried out as either MCR or one-pot reaction preforming the sulfinate.



Scheme 2.1. Possible Pathways to Arylsulfones.

A second project is establishing a multicomponent reaction to sulfonamides. The basic idea is the palladium-catalyzed reaction between an aryl halide, an amine and DABCO·2SO_2 or DMAP·SO_2 as sulfur dioxide source (scheme 2.2).



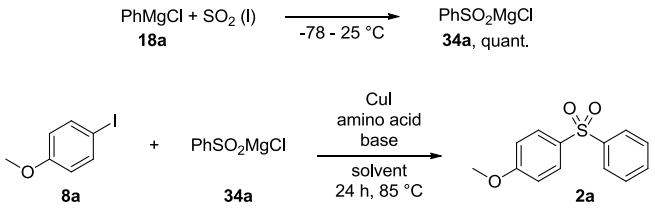
Scheme 2.2. Envisioned Reaction to form Sulfonamides.

3. Arylsulfone Synthesis based on Organometallic Reagents and Iodonium Salts

3.1 Introduction

As mentioned in the introduction, arylsulfones are important building blocks[10,11] in medicinal chemistry.[54–61] Due to the limited preparation methods, a straightforward, easy and general pathway to synthesize arylsulfones from readily available starting materials was desired. Furthermore, the sulfonyl-moiety should be introduced during the reaction sequence and not be included in the starting materials. There are several strategies of inserting a sulfonyl-group described in literature, for example gaseous SO_2[62–65] or known sulfur dioxide surrogates, like DABCO·2SO_2 (DABSO)[66] or DMAP·SO_2.[67]

As initial experiment a copper-catalyzed reaction between benzenesulfinic acid magnesium chloride salt (**34a**) and 4-iodoanisole (**8a**) with an amino acid ligand and a base was chosen (scheme 3.1). $PhSO_2MgCl$ (**34a**) is prepared from the corresponding phenyl Grignard (**18a**) reagent in quantitative yield. Thus, the aim was to develop a one-pot-sequence, starting from organometallic reagents and generating the sulfinate *in situ.*



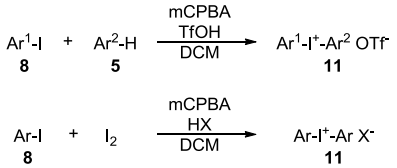
Scheme 3.1. Copper-Catalyzed Sulfonylation of 4-Iodoanisole.

After varying different amino acids, salen-derivatives or chelating agents as ligands and several bases to determine optimized conditions, the resulting yields were below 55%. An increase to 70% could only be achieved with prolonged reaction times up to 50 h. Unfortunately the results could not be reproduced with other substrates. Therefore, a different strategy had to be investigated. As sulfinic acid salts should be kept as nucleophiles, because of the broad variety of organometallic reagents, diaryliodonium salts were chosen as electrophilic agents. They are known to be powerful arylation agents[34–38,42,46,68–73] frequently employed in metal-catalyzed[74–89] and, more importantly in metal-free arylation reactions.[40,41,90–100]

3.2 Synthesis of the Starting Materials

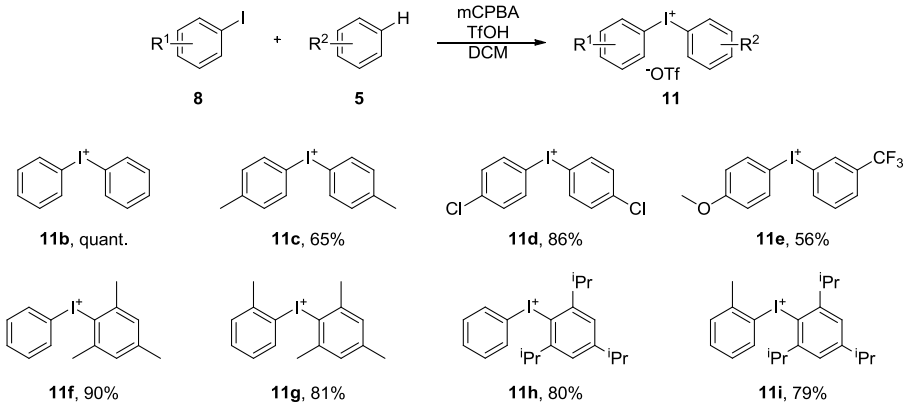
3.2.1 Synthesis of Diaryliodonium Salts

Diaryliodonium salts as electrophilic agents were chosen owing either to their commercial availability, like different diphenyliodonium salts **11** or simple preparation. Most of the symmetrical and unsymmetrical salts can be easily prepared via the reaction between an aryl iodide and an arene or I_2 and excess arene (scheme 3.2) after known literature procedures.[45,46,69,79,80,101–106]

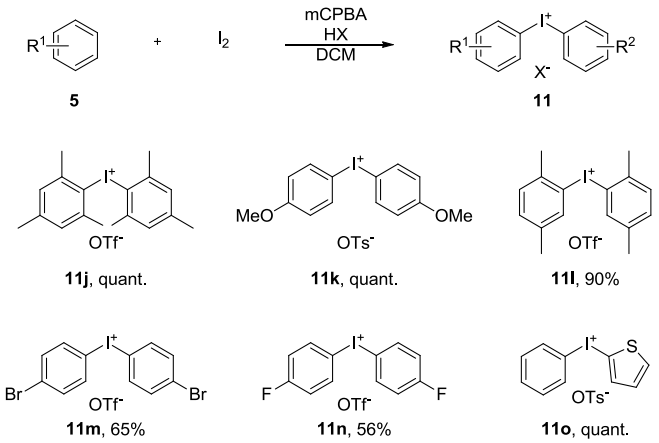


Scheme 3.2. General Routes to Diaryliodonium Salts.

Throughout this thesis a manifold of symmetrical, unsymmetrical and hetero-atom containing salts were prepared; mainly according to procedures from Olofsson *et al*.,[45,46,69,101–104] MacMillan *et al*.[79,105,106] and Gaunt *et al*.[80] The preparation protocols are quite simple, mostly one-pot procedures. All compounds are added in a specific manner, allowed to react, followed by removal of all volatile components and precipitation of the desired diaryliodonium salt from diethyl ether. After drying and recrystallization the analytically pure products are obtained in high to excellent yields (schemes 3.3 and 3.4).

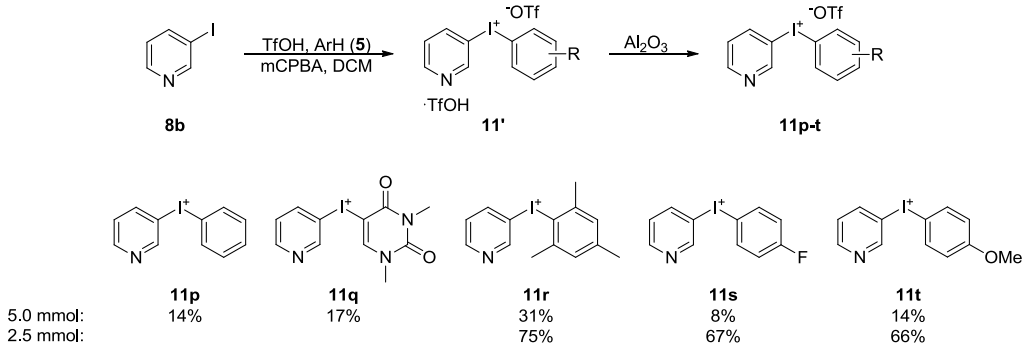


Scheme 3.3. Synthesized Diarylsulfones from Aryl Iodides and Arenes.
Conditions: 1.0 equiv 8, 1.1 equiv 5, 1.1 equiv *m*CPBA, 1.5 equiv TfOH, 0.2 M in DCM; yields after given after recrystallization.



Scheme 3.4. Synthesized Symmetrical Diarylsulfones from Elemental Iodide and (Hetero)Arenes. Conditions: 4.0-10 equiv 5, 1.0 equiv I_2, 2.0 equiv TfOH and 4.0 eqiuv *m*CPBA in DCM (0.2 M) at 25 °C for 0.5-16 h. For details see exp. section.

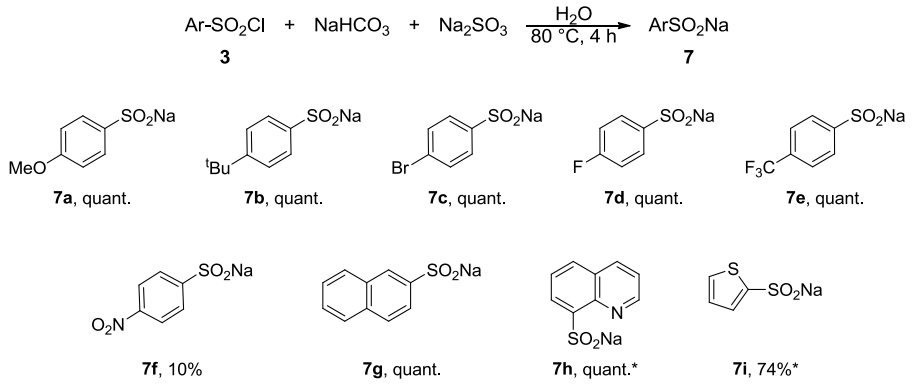
Accessing unsymmetrical, pyridine-containing salts follows a strategy in analogy to the above, but requires an extra step (scheme 3.5).[107] Due to protonation of the pyridine moiety during the reaction, an additional step is necessary, deprotonation of the iodonium salt by diluting it over an Al_2O_3-flash column. But this procedure has a clear dependence on the reaction scale. Olofsson *et al.*[107] performed the procedure only at a 0.5 mmol scale, by upgrading to 5.0 mmol, the yield decreased dramatically, compared to the literature (scheme 3.5, first row). By down-scaling to 2.5 mmol the yields increased up to 8-fold.



Scheme 3.5. Synthesized Pyridine-Containing Iodonium Salts. Conditions: 1.0 equiv 8b, 1.1 equiv 5, 4.0 equiv TfOH and 1.5 equiv *m*CPBA in DCM (0.2 M).

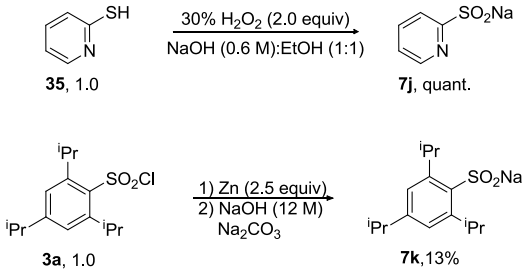
3.2.2 Synthesis of Arylsulfinic Acid Sodium Salts

Even though the commercial availability of sodium sulfinates is limited, a simple and very effective protocol to generate sulfinates from sulfonyl chlorides exists (scheme 3.6).[108] Due to the harsh reaction conditions to generate sulfonyl chlorides, only commercially available compounds were used for this transformation. Nearly all of them could be obtained in quantitative yields after recrystallization, except the *p*-NO_2-benzene sodium sulfinate (**7g**), which was only isolated in 10% yield; probably due to the electronic properties of the nitro-group.



Scheme 3.6. Synthesis of Arylsulfinic Acid Sodium Salts.
Conditions: 1.0 equiv 3, 2.0 equiv $NaHCO_3$ and 2.0 equiv Na_2SO_3 in H_2O (1.0 M) at 80 °C for 4 h.
***Na_2CO_3 instead of $NaHCO_3$.**

Sodium pyridine-2-sulfinate (**7j**) and sodium 2,4,6-triisoproylbenzene sulfinate (**7k**) were synthesized from different protocols, the first one from the corresponding thiole **35**[109] and the latter was first reduced by zinc, prior treatment with sodium salts (scheme 3.7).[110]



Scheme 3.7. Synthesis of Sodium Pyridine-2-Sulfinate and Sodium 2,4,6-Triisopropylbenzenesulfinate.

3.3 Preparation of Diarylsulfones based on Benzenesulfinic Acid Sodium Salts and Diaryliodonium Salts

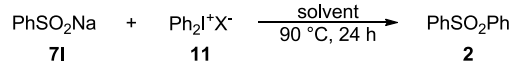
This section has been published in *Organic Letters*, **2013**, *1*, pp. 188-191 and discusses an efficient, high-yielding, and transition metal-free synthesis of diaryl sulfones from arylsulfinic acid sodium salts and diaryliodonium salts. The mild reaction conditions tolerate a range of functional groups, and unsymmetrical diaryliodonium salts show high chemoselectivity.

3.3.1 Optimizing the Reaction Conditions

In preliminary studies, we investigated the reaction of both commercially available benzenesulfinic acid sodium salt (**7l**) with diphenyliodonium triflate (**11b**). To our delight this reaction takes place in the absence of any transition metal-catalyst or additional base. While a variety of solvents can be used for this reaction (table 3.1, entries 1-7), best results were obtained with polar aprotic solvents such as *N*,*N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), or *N*-methyl-2-pyrrolidone (NMP). This might be due to the improved solubility of the sulfinic acid sodium salts in polar solvents. In apolar solvents (entries 4-6), the reaction mixture continuously stays a suspension (entries 1-3). While slightly higher yields were obtained in NMP and DMSO, we chose DMF as our solvent for further investigations, because the removal of the latter is considerably easier.

Interestingly, this reaction is quite insensitive to air and moisture. When the reaction was setup and run without an inert atmosphere using commercial grade DMF (entry 7), **2b** was isolated in almost equally good yield. The nature of the counterion had no influence on the yield and different diphenyliodonium salts worked as efficiently (entries 8-11).

Table 3.1. Survey of Solvents and Influence of the Counterion.[a]



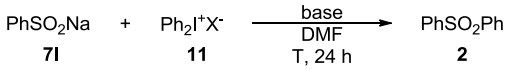
entry	solvent	salt	X	yield [%][b]
1	THF	**11b**	OTf^-	77[c]
2	1,4-dioxane	**11b**	OTf^-	65
3	toluene	**11b**	OTf^-	59
4	DMSO	**11b**	OTf^-	94
5	NMP	**11b**	OTf^-	96
6	DMF	**11b**	OTf^-	94
7	DMF	**11b**	OTf^-	90[d]
8	DMF	**11u**	Cl^-	95
9	DMF	**11v**	PF_6^-	96
10	DMF	**11w**	BF_4^-	96
11	DMF	**11x**	OTs^-	96

[a]reaction conditions: 1.0 equiv **7l** and 1.1 equiv **11** in 1.0 mL solvent at 90 °C for 24 h. [b]isolated yield of analytically pure product. [c]reaction performed at 80 °C. [d]reaction run without exclusion of air or moisture.

After determining the best solvent, we investigated other parameters, like the influence of additional base and reaction temperature. As shown in table 3.2, by both lowering and heightening the reaction

temperature, the yield decreases (entries 1 and 2). Also additional KO^{t}Bu lowers the yield down to 30%, independent from the nature of the counterion (entries 3-7), probably due to a side-reaction between ^{t}BuOH and the iodonium salts.

Table 3.2. Influence of Reaction Temperature and Additional Base.[a]



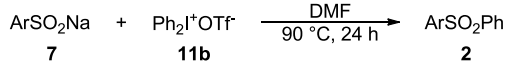
entry	X	T (°C)	Base	yield [%][b]
1	OTf^-	60	-	65
2	OTf^-	120	-	47
3	OTf^-	90	KO^{t}Bu	74
4	Cl^-	90	KO^{t}Bu	64
5	PF_6^-	90	KO^{t}Bu	69
6	BF_4^-	90	KO^{t}Bu	70
7	OTs^-	90	KO^{t}Bu	64

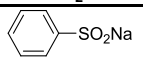
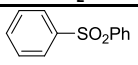
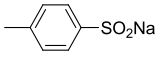
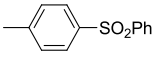
[a]reaction conditions: 1.0 equiv **7l** and 1.1 equiv **11** in 1.0 mL solvent at indicated temperature for 24 h. [b]isolated yields of analytically pure products.

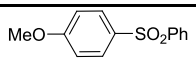
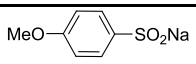
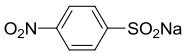
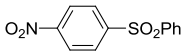
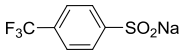
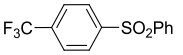
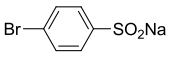
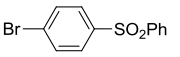
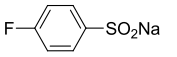
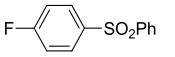
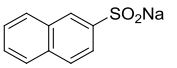
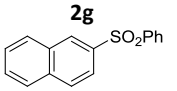
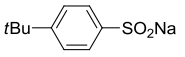
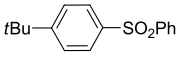
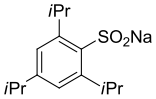
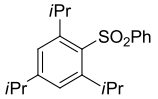
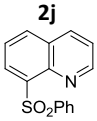
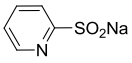
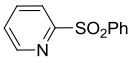
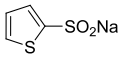
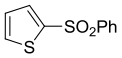
3.3.2 Variation of the Arylsulfinic Acid Salt

With the optimized conditions in hand, we turned to explore the scope of this reaction. As shown in table 3.3, various arylsulfinic acid sodium salts **7** are suitable substrates regardless of their electronic or steric properties. Simple, commercially available salts like benzenesulfinic acid sodium salt **7l** and tosyl sulfinate **7m** afforded the corresponding diarylsulfones **2b** and **2c** in almost quantitative yields (entries 1 and 2). Both electron-rich and electron-poor sulfinic acid sodium salts **7a**, **7g** and **7f** lead to the desired diarylsulfones **2a**, **2d** and **2e** in excellent yields (entries 3-5). Reaction of the halo-substituted substrates **7c** and **7d** delivered diarylsulfones **2f** and **2g** (entries 6 and 7), whereas the bromo-substituted species could be easily further modified using cross-coupling chemistry. Steric hindrance, often problematic in metal-catalyzed coupling reactions,[111] does not pose a problem. The sterically very hindered (1,3,5-triisopropyl)-benzenesulfinic acid sodium salt (**7k**) was phenylated in 61% yield (entry 10). This method can be extended to heteroarylsulfinic acids sodium salts **7h-i** to synthesize arylheteroaryl sulfones **2k-m**, which are of particular interest for the development of new drugs[112,113] (entries 11-13). Only alkylsulfinic acid sodium salts, such as methanesulfinic acid sodium salt (**7n**) did not react under these conditions (entry 14).

Table 3.3. Phenylation of (Hetero)Arylsulfinic Acid Salts.[a]



entry	$ArSO_2Na$	$ArSO_2Ph$	yield [%][b]
1	 **7l**	 **2b**	94
2	 **7m**	 **2c**	96

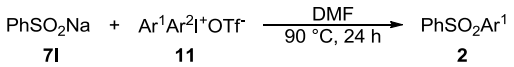
3	 **7a**	 **2a**	**90**
4	 **7g**	 **2d**	81
5	 **7f**	 **2e**	83
6	 **7c**	 **2f**	90
7	 **7d**	 **2g**	83
8	 **7g**	 **2h**	63
9	 **7b**	 **2i**	54[c]
10	 **7k**	 **2j**	61
11	 **7h**	 **2k**	90
12	 **7j**	 **2l**	40
13	 **7i**	 **2m**	83[d]
14	$MeSO_2Na$ **7n**	**-**	-

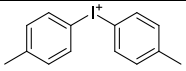
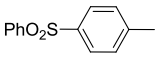
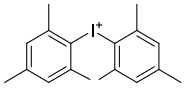
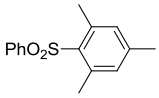
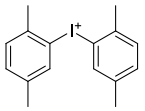
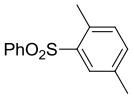
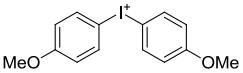
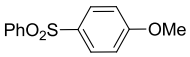
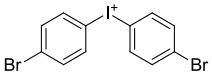
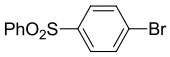
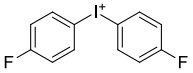
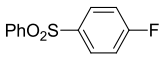
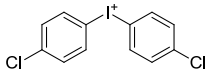
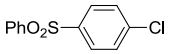
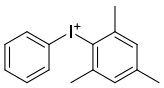
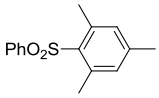
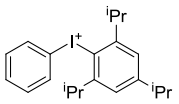
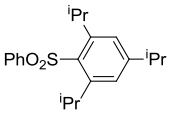
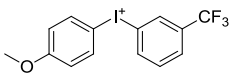
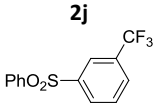
[a]reaction conditions: 1.0 equiv **7** and 1.1 equiv **11b** in 1.0 mL DMF at 90 °C for 24 h. [b]isolated yields of analytically pure product. [c]reaction performed with 1.1 equiv. **7** and 1.0 equiv. **11b**. [d]reaction run with 1.1 equiv. **7** and 1.0 equiv. **11b** in DMSO.

3.3.3 Variation of the Diaryliodonium Salt

Next we examined the reactivity of other symmetrical and unsymmetrical diaryliodonium salts. The reaction of benzenesulfinic acid sodium salt (**7l**) with various symmetrical diaryliodonium salts **11** furnished the phenylarylsulfones of type **2** in moderate to excellent yields (table 3.4, entries 1-7). Steric hindrance in the diaryliodonium salt was not a problem. Reaction of *ortho*- or bis(*ortho*)-substituted salts **11j** and **11l** delivered the diarylsulfones **2n** and **2o** in very high yields (entries 2 and 3). Halogen-substituted substrates **11m**, **11n** and **11d** efficiently arylated **7l** (entries 5-7). Unsymmetrical salts **11f** and **11h** selectively transferred the bulky ortho-substituted aryl moiety, furnishing products **2n** and **2j** (entries 8 and 9). In the case of the unsymmetrical diaryliodonium salt **11e**, the electron-poor trifluoro-methylphenyl moiety was transferred with excellent chemoselectivity (entry 10). Thus, unsymmetrical diaryliodonium salts could be used as an alternative in cases where the symmetric salt is expensive or difficult to prepare.

Table 3.4. Arylation of Benzenesulfinic Acid Sodium Salt (7l).[a]

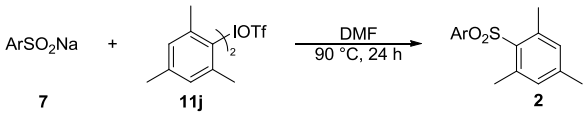


entry	$Ar^1Ar^2I^+$	$PhSO_2Ar^1$	yield [%][b]
1	 **11c**	 **2c**	92
2	 **11j**	 **2n**	91
3	 **11l**	 **2o**	84
4[c]	 **11k**	 **2a**	87
5	 **11m**	 **2f**	61[d]
6	 **11n**	 **2g**	47[d]
7	 **11d**	 **2p**	96
8	 **11f**	 **2n**	88
9	 **11h**	 **2j**	94
10	 **11e**	 **2q**	78

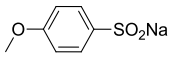
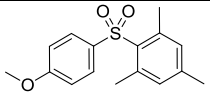
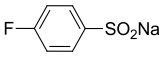
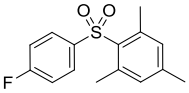
[a]reaction conditions: 1.0 equiv of **7l** and 1.1 equiv of **11** in 1.0 mL of DMF for 24 h at 90 °C. [b]isolated yields of analytically pure products. [c]tosylate as counterion. [d]reaction run in NMP.

Furthermore, we varied both, the iodonium salt and the sulfinate. Through this approach, more complex diarylsulfones are provided, which, depending on the substitutes can be further functionalized. As proof of principle, we run the reaction of sterically hindered iodonium salt **11j** with both electron-rich and –poor sulfinates **7a** and **7d** achieving diarylsulfones **2r** and **2s** in very high yields (table 3.5).

Table 3.5. Arylsulfones Deriving from Dimesityliodonium Triflate (11j).[a]



7 11j 2

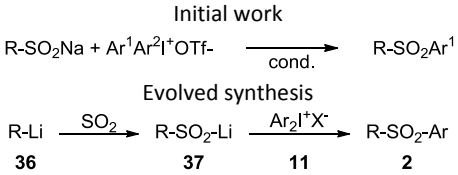
entry	$ArSO_2Na$	$ArSO_2Ph$	yield [%][b]
1	 **7a**	 **2r**	83
2	 **7d**	 **2s**	82

[a]reaction conditions: 1.0 equiv **7** and 1.1 equiv **11j** in 1.0 mL DMF at 90 °C for 24 h. [b]isolated yields of analytically pure products.

3.4 Preparation of Diarylsulfones based on Arylsulfinic Acid Lithium Salts and Diaryliodonium Salts

This section has been published in *Organic Letters*, **2013**, *15*, pp. 4972-4975 and discusses an efficient, transition metal-free arylation of lithium sulfinates, which are readily accessible from reactions of organolithium reagents with sulfur dioxide. Based on this method, a practical four-step-protocol for the direct transformation of (hetero)arenes and (hetero)aromatic halides into diarylsulfones was developed.

While a wide variety of different diaryliodonium salts is readily available or can be prepared efficiently,[34,35,38,40,42,46,68–73,79–81,94,99,100,114] the availability of sulfinic acid sodium salts is rather limited as previously described.[115] In order to expand the scope of our method, we were interested in the use of more easily accessible sulfinic acid salts. We envisioned, that the corresponding sulfinic acid lithium salts **37** should display a similar reactivity (scheme 3.8). These lithium sulfinates can be prepared in a very straightforward manner from the reaction of organolithium compounds **36** with sulfur dioxide. Considering the huge variety of well known organolithium reagents,[116,117] this approach would allow a modular synthesis of arylsulfones using sulfur dioxide[63,66,118,119] as source for the sulfonyl moiety.

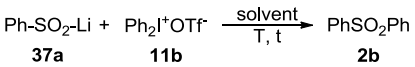


Scheme 3.8. Routes to Arylsulfones based on Diaryliodonium salts.

3.4.1 Optimizing the Reaction Conditions

We started our initial studies with benzenesulfinic acid lithium salt (**37a**), which could be easily prepared in quantitative yield from the reaction of phenyllithium (**36**) and sulfur dioxide with subsequent removal of the solvents. As expected the reaction between the lithium salt **37a** and diphenyliodonium triflate (**11b**) proceeded efficiently and furnished diphenylsulfone (**2b**). Best results were obtained in polar aprotic solvents DMF, DMSO und NMP (table 3.6, entries 1-3). Other solvents, such as THF or 1,4-dioxane, led to lower yields (entries 4 and 5). As with arylsulfinic acid sodium salts, this reaction is insensitive to air and moisture. Performing the reaction without exclusion of those, using commercial grade DMF or DMSO, **2b** was isolated in identical yields (entries 1 and 2 in parentheses).

Table 3.6. Survey of Solvents, Reaction Time and Temperature[a].

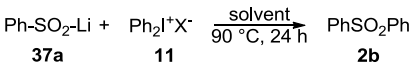


entry	temperature		90 °C[b]		60 °C[b]
	solvent	time	24 h	48 h	24 h
1	DMSO		80% (79%)[c]	95%	68%
2	DMF		84% (86%)[c]	87%	77%
3	NMP		83%	78%	77%
4	Dioxane		47%	-	-
5	THF		26%	-	-
6	DMF		83%[d]	-	-

[a]reaction conditions: 1.5 equiv **37a** and 1.0 equiv **11b** in 1.0 mL solvent at indicated temperature indicated time. [b]isolated yields of analytically pure products. [c]reaction run without exclusion of air or moisture. [d]performed as one-pot-reaction/ without isolating the salt **37a**.

Since we were also interested in developing a practical protocol for the direct transformation of organolithium reagents into sulfones, we merged the single steps into an one-pot sequence. Reaction of PhLi (**36a**) with sulfur dioxide (typically 10 equiv), followed by removal of solvents and excess SO_2, subsequent treatment of the obtained crude lithium sulfinate with Ph_2IOTf (**11b**) in DMF furnished diphenylsulfone (**2a**) in 83% yield (entry 6).[120] In the case of sulfinic acid lithium salts, the nature of the diphenyliodonium counterion X^-, has pronounced effect on the yield (table 3.7). While reactions with non-nucleophilic counterions, such as OTf^-, BF_4^- or PF_6^-, furnished the product **2b** in >80% yield (table 3.6, table 3.7 entries 1 and 2), the yield decreased significantly if the more nucleophilic counterions Cl^- and OTs^- were employed (entries 3 and 4).[100] This finding might be due to a possible side reaction, where the salt is reduced to its corresponding aryl halide, like chloro- or tosylbenzene, which was determined by GC-MS.

Table 3.7. Survey of the Counterion[a]

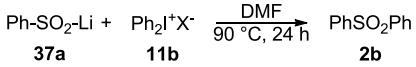


entry	solvent / counterion X^-	DMSO[b]	DMF[b]	NMP[b]
1	PF_6	92%	86%	83%
2	BF_4	83%	91%	83%
3	Cl	69%	60%	32%
4	OTs	80%	65%	60%

[a]reaction conditions: 1.5 equiv **37a** and 1.0 equiv **11** in 1.0 mL solvent at 90 °C for 24 h. [b]isolated yield of analytically pure product.

To finish the optimization reactions, we investigated the influence of the ratio of the starting components. As shown in table 3.8, it has quite an impact. By increasing the excess of $PhSO_2Li$ from 1.2 to 1.5 equivalents, the yield increases 20%, whereas the raise to 2.0 equivalents does not make a difference (entries 1-3). Inverting the ratio even gains quantitative yield (entry 4). However, the purity of the lithium sulfinate **37a** is only assumed. Due to this, this result is not reliable and depends on the quality of the sulfinate used. Therefore, even though the yield is not as high, we chose to use the sulfinate in excess.

Table 3.8. Survey of Equivalents.[a]



37a **11b** **2b**

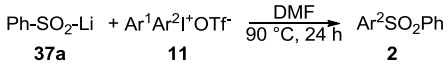
entry	equiv $PhSO_2Li$	equiv. $Ph_2I^+OTf^-$	yield (%)[b]
1	1.2	1.0	69
2	1.5	1.0	89
3	2.0	1.0	89
4	1.0	1.5	quant.

[a]reaction conditions: equivalents of compounds as indicated, in 1.0 mL DMF at 90 °C for 24 h. [b]isolated yields of analytically pure product.

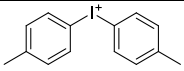
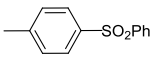
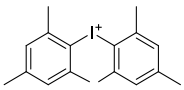
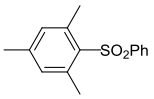
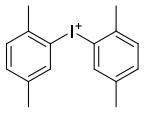
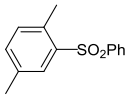
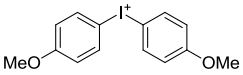
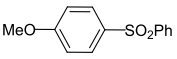
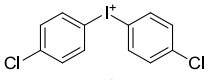
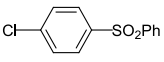
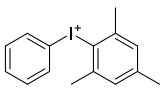
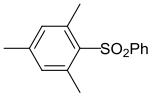
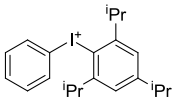
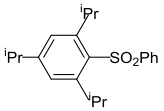
3.4.2 Variation of the Iodonium Salt

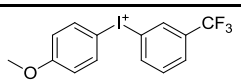
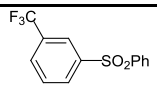
With the optimized reaction conditions at hand, we investigated the reaction of benzenesulfinic acid lithium salt (**37a**) with different diaryliodonium salts **11** (table 3.9). Various symmetrical diaryliodonium salts arylated **37a** in good to excellent yields (entries 1-5). Unsymmetrical iodonium salts **11f** and **11h** selectively transferred the sterically more demanding aryl moiety (entries 6 and 7).[121] In case of the unsymmetrical iodonium reagent **11e**, a preferential transfer of the electron-poor trifluoromethylphenyl group was observed (entry 8).

Table 3.9. Arylation of Benzenesulfinic Acid Lithium Salt (37a).[a]



37a **11** **2**

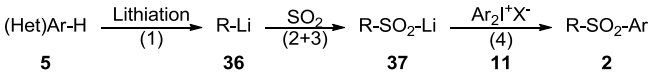
entry	$Ar^1Ar^2I^+$	$PhSO_2Ar^1$	yield [%][b]
1	 **11c**	 **2c**	80
2	 **11j**	 **2n**	67
3	 **11l**	 **2o**	76
c	 **#**	 **2a**	74
5	 **11k**	 **2p**	78
6	 **11d**	 **2n**	73
7	 **11h**	 **2j**	81

8[c]	 **11e**	 **2q**	76[d]

[a]reaction conditions: 1.5 equiv **37a** and 1.0 equiv **11** in 1.0 mL DMF for 24 h at 90 °C. [b]isolated yields of analytically pure products. [c]tosylate as counterion. [d]together with 6% **2a**.

3.4.3 Direct Lithiation Approach to Diarylsulfones

One of the most atom-economical[2] routes to organolithium reagents is the direct lithiation/ deprotonation of acidic C-H functionalities.[116,117] In combination with our method, it allows the direct transformation of simple, readily available arenes or heteroarenes into the corresponding sulfones. This four-step, one-pot reaction sequence consists of: (1) generation of the organolithium reagent from the corresponding arene or heteroarene **5** using the appropriate lithiation reagents and conditions;[116,117] (2) reaction of the lithium reagent with SO_2; (3) removal of solvents and excess SO_2; and (4) reaction of the sulfinate with the diaryliodonium salt (scheme 3.9 and table 3.10).

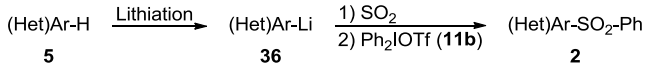


Scheme 3.9. General direct Lithiation Approach to Diarylsulfones.

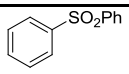
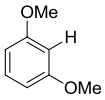
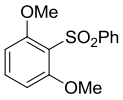
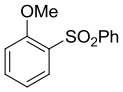
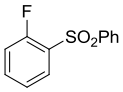
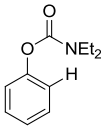
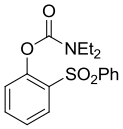
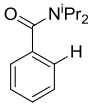
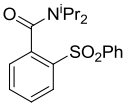
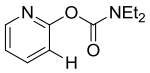
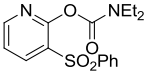
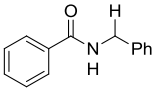
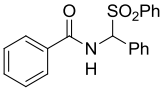
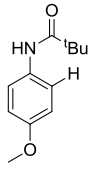
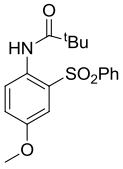
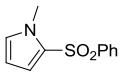
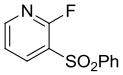
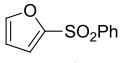
Using this procedure diphenylsulfone (**2b**) was obtained in 52% yield starting from benzene (**5a**) (table 3.10, entry 1), which is, compared to the test system 30% less. This is due to non-complete deprotonation of benzene, proved by isolating also alkylarylsulfone **38b** as side-product. More importantly, different arenes bearing "directing metalation groups" (DMG),[117,122] which simplify ortho-lithiation, could be transformed directly into diarylsulfones. Excellent DMG's like carbamate **5e** and tertiary amide **5f**, were functionalized to the corresponding diarylsulfones **2w** and **2x** (entries 5 and 6). Interestingly, pyridine-derivative **5g**, bearing the same DMG like benzene **5e**, did not afford the desired product (entry 7), maybe due to the electron-poor nature of pyridines. As aniline-derivatives do not possess a high ability for ortho-lithiation, the transformation to diarylsulfone **2aa** only turned out in moderate yield (entry 9). Additionally, different heteroarenes could be functionalized in a similar manner (entries 10-15). *N*-methylpyrrole (**5j**), pyridine **5k**, furan (**5l**) and thiophene (**5m**) were transformed in good to high yields (entries 10-13). Even by upscaling the reaction, the yields could be reproduced (entries 13 and 14). In case of 2-bromothiophene (**5n**), the yield decreased extremely in comparison to unsubstituted thiophene (entry 14). A possible explanation is the competitive halogen-lithium-exchange, though the diarylsulfone **2m** was only isolated in traces. Also the further functionalization of sulfone **2m** did not take place; only the starting material was regained (entry 15). However, also ferrocene (**2o**) was converted into to corresponding sulfone **2ag** (entry 16). Sadly, a double deprotonation/substitution sequence did not take place, only the single substituted compound was isolated (entry 17). Furthermore, lateral lithiation, as in case of benzamide **5h** (entry 8) or deprotonation of highly functionalized heteroaromatics, like caffeine (**2p**) (entry 18) did not turned out as we envisioned. Mentionable is that also a conversion of BOC-

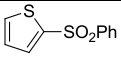
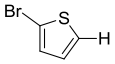
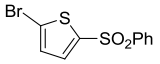
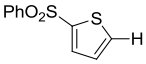
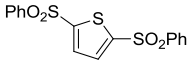
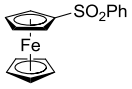
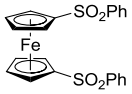
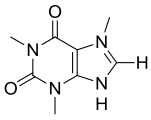
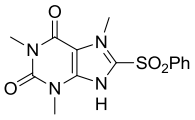
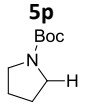
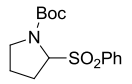
protected pyrrolidine **5q** to the corresponding sulfone was not possible. By trying to isolate the crude lithium sulfinate, it decomposed the moment it was exposed to air.

Table 3.10. Direct Lithiation Approach to Diarylsulfones.[a]



5 **36** **2**

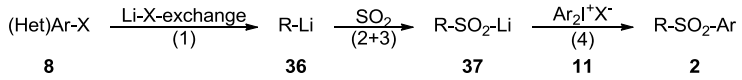
entry	(Het)Ar-H	lithiation reagent	(Het)Ar-SO_2-Ph	yield [%][b]
1	 **5a**	*n*BuLi, TMEDA	 **2b**	52
2	 **5b**	*n*BuLi	 **2t**	79
3	 **5c**	*n*BuLi, TMEDA	 **2u**	61
oc	 **5d**	*n*BuLi, TMEDA	 **2v**	73
5	 **5e**	*s*BuLi, TMEDA	 **2w**	47
6	 **5f**	*s*BuLi, TMEDA	 **2x**	68
7	 **5g**	*s*BuLi, TMEDA	 **2y**	-
8	 **5h**	LDA	 **2z**	-
9	 **5i**	*t*BuLi	 **2aa**	30%
10	 **5j**	*n*BuLi, TMEDA	 **2ab**	51 (51)[c]
11	 **5k**	LDA	 **2ac**	55
12	 **5l**	*n*BuLi	 **2ad**	61

13	 **5m**	*n*BuLi	 **2m**	85 (82)[c]
14	 **5n**	LDA	 **2ae**	33
15	 **2m**	*n*BuLi	 **2af**	-
16	 **5o**	*t*BuLi	 **2ag**	42
17	 **5o**	*n*BuLi, TMEDA	 **2ah**	-
18	 **5p**	LDA	 **2ai**	-
19	 **5q**	*s*BuLi, TMEDA	 **2aj**	-

[a]reaction conditions: sulfinate **36** (prepared from 1.5 equiv **5**) and 1.0 equiv **11** in 1.0 mL DMF for 24 h at 90 °C. [b]isolated yields of analytically pure products. [c]2.0 mmol **11** used.

3.4.4 Halogen-Lithium Exchange Approach to Diarylsulfones

The halogen-lithium exchange is another efficient method for the preparation of organolithium reagents.[116,117] This method is also compatible with our four step one-pot approach as described above (scheme 3.10).

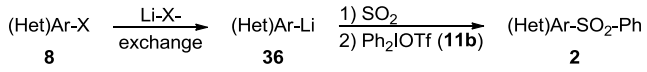


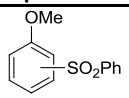
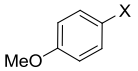
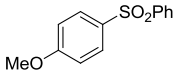
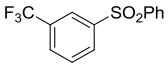
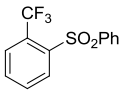
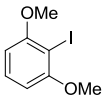
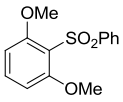
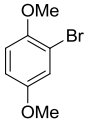
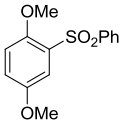
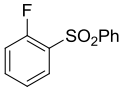
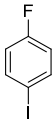
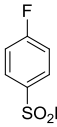
Scheme 3.10. Halogen-Lithium-Exchange Approach to Diarylsulfones.

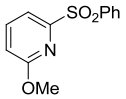
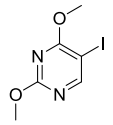
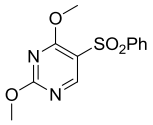
Diverse anisole- and dimethoxybenzene-derivatives are excellent substrates for the exchange protocol (table 3.11). For example, aryllithium reagents prepared from 2-bromoanisole (**8c**) and 3-bromoanisole (**8d**), respectively, are treated with SO_2, followed by removal of solvents and excess SO_2; the reaction of the remaining crude lithium sulfinates with diphenyliodonium triflate (**11b**) furnishes diarylsulfones **2u** and **2ak** in 97% and 92% yield (entries 1 and 2). In a similar manner, other bromo- or iodoanisole derivatives react, but with decreasing yields (entries 3 and 4). A conclusion of these experiments is the dependence of the reactivity on the position of the methoxy-group. Due to the coordinating attribute of the methoxy group, *ortho*-bromoanisole, gives the best results, following by *meta*- and then *para*-substituted anisoles (entries 1-4). It is comparable to the *ortho*-lithiation. Furthermore, the size of the halogen substituent matters, by comparing bromo- and iodoanisole **8e** and **8a** (entries 3 and 4). The bigger the substituent, the worse the yield, 78% vs. 53%. But if the aryl halide is electron-poor, like in case of **8f-i**,

this effect reverses (entries 5-8). The influence of ortho-substituents is also clearly shown in entries 9 and 10. Whereas the sulfone **2t** generated starting from 1,3-dimethoxy-2-iodobenzene (**8j**) achieves 74% yield, sulfone **2am** based on 1,4-dimethoxy-2-bromobenzene (**8k**) yields only 42%. Further different double substituted benzene-derivatives respond well to the four-step sequence (entries 5-11) achieving very good yields. In comparison to that bromobenzene (**8n**) provides only poor yield (entry 13). Unlike as for the deprotonation protocol, heteroaromatic substrates are not very suitable substrates for the exchange protocol. In case of pyridine **8o** only 36% yield is provided and with the uracile-derivative **8p** only 22% (entries 14 and 15).

Table 3.11. Halogen-Lithium-Exchange Approach to Diarylsulfones.[a]



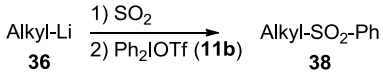
entry	(Het)Ar-X	exchange reagent	product	yield [%][b]
		*n*BuLi		
1	**8c: *o*-Br**		**2u**	97
2	**8d: *m*-Br**		**2ak**	92
				
3	**8e: X = Br**	*n*BuLi	**2a**	78
4	**8a: X = I**	*t*BuLi		53
		*n*BuLi		
5	**8f: X = Br**		**2q**	74
6	**8g: X = I**			83
		*n*BuLi		
7	**8h: X = Br**		**2al**	38%
8	**8i: X = I**			64%
				
9		*n*BuLi		74
	8j		**2t**	
				
10		*n*BuLi		42 (53)[c]
	8k		**2am**	
				
11		*n*BuLi		62
	8l		**2v**	
				
12		*n*BuLi		-
	8m		**2g**	
				
13		*n*BuLi		27

	8n		**2b**	
14		*t*BuLi		36
	8o		**2an**	
15		*n*BuLi		22
	8p		**2ao**	

[a]reaction conditions: sulfinate **37** (prepared from 1.5 equiv **8**) and 1.0 equiv **11b** in 1.0 mL DMF for 24 h at 90 °C. [b]isolated yields of analytically pure products. [c]2.0 mmol **11b** used.

3.4.5 Alkylarylsulfones

As subsequent step, we wanted to know, if alkylarylsulfones could be generated from alkyllithium reagents, SO_2 and iodonium salts based on our one-pot protocol. Due to findings in previous experiments, where alkylarylsulfones were isolated as side-products, we assumed it should be possible. So we performed our one-pot sequence with commercially available alkyllithium reagents and to our delight, it turned out very well. Starting from primary, secondary or tertiary alkyllithium reagents **36b-e**, the desired alkylarylsulfones **38a-d** were obtained in 76-93% yield (scheme 3.11).



36b: MeLi
36c: *n*BuLi
36d: *t*BuLi
36e: *s*BuLi

38a: 84 %
38b: 89 %
38c: 76 %
38d: 93 %

Scheme 3.11. Synthesis of Arylalkyl Sulfones.
Conditions: 1.5 equiv 36 and 1.0 equiv 11b in 1.0 mL DMF for 24 h at 90 °C.

3.5 Preparation of Sulfones from Organomagnesium Reagents

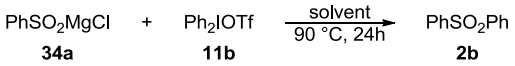
This and the next section has been published in *The Journal of Organic Chemistry*, **2015**, *80*, pp. 2582-2600 and discusses the limitation and scope of our previous developed four-step protocol, starting from organomagnesium and –zinc species.

Though the lithiation approach is an improvement to our initial protocol based on sulfinic acid sodium salts, it is inherently limited by the low functional group tolerance of organolithium reagents. As shown in tables 3.10 and 3.11, the direct functionalization of sensitive heteroaromatics, such as the pyridine derivatives **8o** and **5k**, leads to the desired heteroaryl sulfones in low to moderate yields. Therefore we investigated similar reactions with organomagnesium reagents. Various procedures for the synthesis of these Grignard reagents exist. In addition, highly functionalized organomagnesium reagents, bearing sensitive groups, can be prepared efficiently.[123–129] We envisioned that the higher functional group compatibility of Grignard reagents should lead to a broader scope of our established one-pot sequence.[130]

3.5.1 Optimizing the Reaction Conditions

In initial experiments with different phenyl magnesium sulfinates we observed a pronounced effect of the Grignard counterions. We started our experiments with a study of the influence of different solvents and Grignard counterions (tables 3.12 and 3.13). As model system, we chose the reaction between benzenesulfinic acid magnesium salts **34a-d**, prepared from different phenylmagnesium halides **18a-d**, and diphenyliodonium triflate (**11b**). Due to the previous findings, the influence of the iodonium salt counterions was not investigated. An initial solvent screening (table 3.12) gave similar results as the earlier ones. For the reaction with the benzenesulfinic acid magnesium salt **34a** best results were obtained with DMSO (entry 1). Other polar aprotic solvents, such as DMF or NMP, led to lower yields (entries 2 and 3). Aprotic unpolar solvents, like THF or 1,4-dioxane do not fit the reaction at all (entries 4-6).

Table 3.12. Solvent Screening.[a]



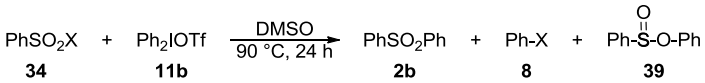
entry	solvent	yield [%][b]
1	DMSO	41 (75)[c]
2	DMF	37 (40)[c]
3	NMP	18
4	THF	-
5	1,4-dioxane	-
6	toluene	-

[a]reaction conditions: 1.3 equiv benzenesulfinic acid salt **34a**, 1.0 equiv iodonium salt **11** in 1.0 mL solvent at 90 °C for 24 h at a 0.5 mmol scale. [b]isolated yields of analytically pure products. [c]reaction run for 48 h.

An interesting matter is the influence of the counterion of the Grignard reagent and presence of salt (table 3.13). Depending on the Grignard preparation, either through insertion of magnesium (with or without

LiCl) or halogen-metal exchange, the yields are changing dramatically. Unfortunately, the yield decreases for sulfinates prepared from other "Knochel"-type phenyl-Grignards (table 3.13).[114,131–136]

Table 3.13 Influence of Counterion.[a]

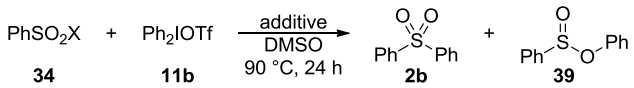


entry	X	yield [%][b]	
		insertion	exchange
1	MgCl (**34a**)	75	-[c]
2	MgCl·LiCl (**34b**)	62	55
3	MgBr·LiCl (**34c**)	31	-[c]
4	MgI·LiCl (**34d**)	22	-[c]

[a]reaction conditions: 1.3 equiv benzenesulfinic acid salt **34**, 1.0 equiv iodonium salt **11b** in 1.0 mL DMSO at 90 °C for 24 h at a 0.5 mmol scale. [b]isolated yields of analytically pure products. [c]reaction was not performed.

The presence of additional LiCl in the reaction mixture leads to a slightly lower yield (entry 2). Changing the Grignard counterion from chloride to bromide or iodide has a marked effect on the reaction yield. In the case of the sulfinate prepared from PhMgI·LiCl the yield drops to 22% (entry 4). Analysis of the reaction mixture via GC-MS shows the formation of considerable amounts of halobenzenes **8m** and **8p** and in case of bromides as counterions also the sulfoxide **39** is formed. These side-products can be formed in a competing arylation of the halide counterions.[75,114,133–136] Considering this side-reactions, a decreased yield in the presence of more nucleophilic counterions or excess lithium chloride should be expected. Unfortunately, various additives or cosolvents could not suppress this side-reaction and improve the overall yield (table 3.14).

Table 3.14. Survey of Cosolvent and Additives.[a]

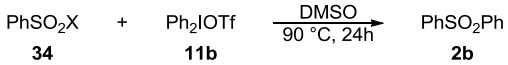


entry	X	additive	yield [%] A : B
1	MgCl·LiCl	dioxane, 10 vol-%	59 : 0
2	MgCl·LiCl	TMEDA, 2.0 equiv	-
3	MgCl·LiCl	2,2'-oxybis(*N,N*-dimethylethanamine)	40 : 0
4	MgBr·LiCl	dioxane, 10 vol-%	32 : 31
5	MgBr·LiCl	TMEDA, 2.0 equiv	0 : 30
6	MgBr·LiCl	2,2'-oxybis(*N,N*-dimethylethanamine)	0 : 33

[a]reaction conditions: 1.3 equiv benzenesulfinic acid salt **34**, 1.0 equiv iodonium salt **11b** and additive as indicated in 1.0 mL solvent at 90 °C for 24 h at a 0.5 mmol scale. [b]isolated yields of analytically pure products.

The only option to enhance the yield of the desired sulfone, is the use of a three-fold excess of the iodonium reagent. By employing a great excess of the iodonium salt, the yield can be increased considerably for all types of Grignard reagent (table 3.15, entries 5-8).

Table 3.15. Survey of Equivalents and Time.[a]



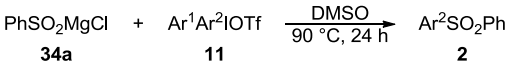
entry	X	equiv sulfinate 34b	equiv Ph_2IOTf (11b)	yield [%][b]
1	MgCl	1.3	1.0	75 (75)[c]
2	MgCl	1.5	1.0	70 (68[c],57[d])
3	MgCl	2.0	1.0	65
4	MgCl	1.0	1.5	68
5	MgCl	1.0	3.0	90
6	MgCl·LiCl	1.0	3.0	81
7	MgBr·LiCl	1.0	3.0	40
8	MgI·LiCl	1.0	3.0	37

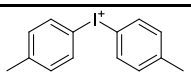
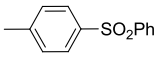
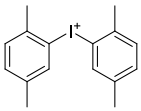
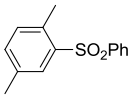
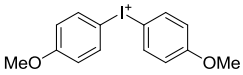
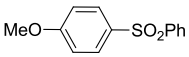
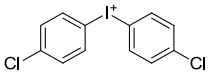
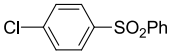
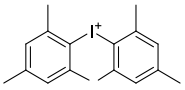
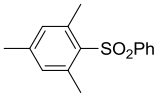
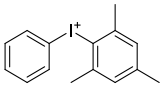
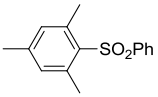
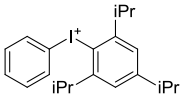
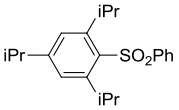
[a]reaction conditions: equiv benzenesulfinic acid salt **34** and **11b** as indicated in 1.0 mL DMSO at 90 °C for 24 h at a 0.5 mmol scale. [b]isolated yields of analytically pure products. [c]reaction run for 48 h. [d]reaction performed without exclusion of air and moisture.

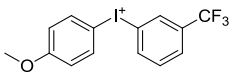
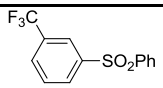
3.5.2 Variation of the Iodonium Salt

Though an excess of the iodonium salt was proven to be favored for the arylation reaction, the first experiments regarding the variation of those were performed before having this insight. As shown in table 3.16, in most cases the latter found conditions are the more successful. Especially sterically demanding and electron-rich salts give up to three times higher yields (entries 5-7).

Table 3.16. Arylation of Benzenesulfinic Acid Magnesium Salt 34a.[a]



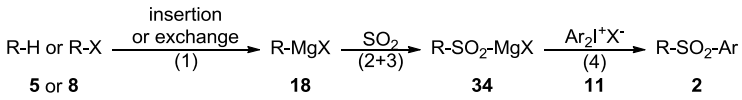
Entry	Ar^1Ar^2IOTf	product	yield [%][b]
1	 **11c**	 **2c**	62
2	 **11l**	 **2o**	56
3	 **11k**	 **2a**	27 (62)[c]
4	 **11d**	 **2p**	52 (74)[c]
5	 **11j**	 **2n**	25 (80)[c]
6	 **11f**	 **2n**	47 (80)[c]
7	 **11h**	 **2j**	42 (98)[c]

8	 **11e**	 **2q**	81[d]

[a]reaction conditions: 1.5 equiv benzene sulfinic acid salt **34a**, 1.0 equiv salt **11** in 1.0 mL DMSO at 90 °C for 24 h at a 0.5 mmol scale. [b]isolated yields of analytically pure products. [c]1.0 equiv salt **34** and 3.0 equiv salt **11**. [d]6% of **2a** as side-product.

3.5.3 Direct Magnesation Approach or Variation of the Sulfinate

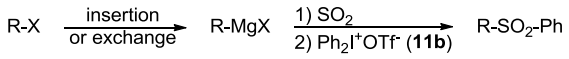
As mentioned before, Grignard reagents can be prepared by various protocols (see above). To our delight, two of those methods, the direct insertion of magnesium into organic halides (in the presence or absence of lithium chloride)[131] and the magnesium-halogen exchange[137] are compatible with our arylation protocol. Therefore we were able to develop a similar one-pot, four-step synthesis of arylsulfones via *in situ* generated organomagnesium reagents. Generation of the organomagnesium species (1), followed by the reaction of the Grignard reagent with SO_2 and removal of excess SO_2 and solvent exchange and treatment of the obtained crude magnesium sulfinate (2+3) with a diaryliodonium salt leads to the desired arylsulfones (4) (scheme 3.12 and table 3.17).

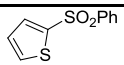
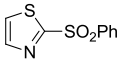
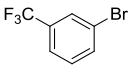
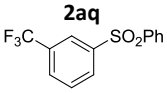


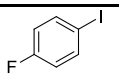
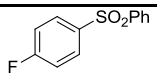
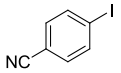
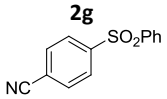
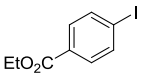
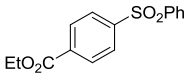
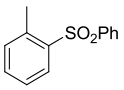
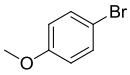
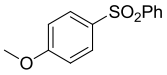
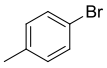
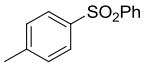
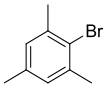
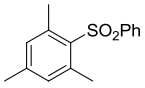
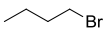
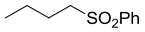
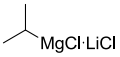
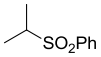
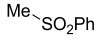
Scheme 3.12. General Magnesation Approach to Diarylsulfones.

As a first result, we observed that the exchange protocol-based sequence gives higher yields than the insertion-based one (table 3.17). This may be due to the aryl bromides, which are normally used for the insertion reaction, because their reactivity suits best for this kind of preparation of Grignard reagents. Whereas, applying the halogen-metal exchange, the resulting sulfinate bears a chloride as halide counterion, which is, like our preliminary experiments have shown, favored. Nevertheless, a lot of substrates could be transformed into various diarylsulfones.

Table 3.17. Direct Magnesation Approach to Arylsulfones.[a]



entry	R-X	metalation reagents	$PhSO_2Ar$	yield [%][b]
1[b,c]	 **8r**	*i*PrMgCl·LiCl	 **2m**	73
2	 **8s**	*i*PrMgCl·LiCl	 **2ap**	-
3	 **8t**	*i*PrMgCl·LiCl	 **2aq**	-
4[b,c]	 **8f**	*i*PrMgCl·LiCl	 **2q**	38

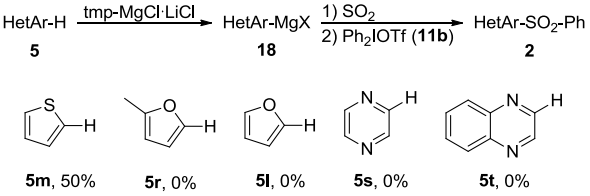
5[b,c]	 **8m**	*i*PrMgCl·LiCl	 **2g**	66
6[b,c]	 **8u**	*i*PrMgCl·LiCl	 **2ar**	49
7[b,c]	 **8v**	*i*PrMgCl·LiCl	 **2as**	46[g]
8[b,c,d]	 **8w: X = I**	a) *i*PrMgCl·LiCl		49
9	**8x: X = Br**	b) Mg, LiCl	**2at**	21
10[c,d]	 **8e**	Mg, LiCl	 **2a**	35
11[c,d]	 **8y**	Mg, LiCl	 **2c**	69
12[c,d]	 **8z**	Mg, LiCl	 **2n**	-
13[c,d]	 **40a**	Mg	 **38b**	17
14[f,e]	 **18e**	-	 **38e**	72
15[f,]	Me-MgCl **18f**	-	 **38a**	51

[a]reaction conditions: for halogen-metal-exchange: 1.0 equiv **8**, 3.0 equiv **11b** in 1.0 mL DMSO for 24 h at 90 °C; for insertion: 1.5 equiv **8** and 1.0 equiv **11b** in 1.0 mL DMSO for 24 h at 90 °C. [b]isolated yields of analytically pure products. [c]Grignard reagent was prepared by halogen-metal exchange with *i*PrMgCl·LiCl. [d]Grignard reagent was prepared by insertion of magnesium with the Knochel-method. [e]commercial available reagent. [f]1.3 equiv **8**.

2-Bromothiophene (**8r**) was converted to the corresponding diarylsulfone **2m** in 73% yield (entry 1). But unfortunately, other heteroarenes like 2-bromothiazole (**8s**) or 3-bromopyridine (**8t**) did not react under these conditions (entries 2 and 3). Also electron-poor arenes like **8f** and **8m** and arenes bearing sensitive groups **8t** and **8u** delivered the diarylsulfones **2q**, **2g**, **2at** and **2as** in moderate yields (entries 4-7), though the latter ones were more promising. In direct comparison, the first statement is proven. In case of the 2-substituted toluenes **8v** and **8w**, the exchange procedure (entry 9) gives more than twice the yield as the insertion protocol (entry 8). The insertion method only seems to work well with electron-poor arenes (entry 11), where 4-bromotoluene (**8y**) is converted into diarylsulfone **2c** in 69% yield. Furthermore, electron-rich arenes, like **8k** only give poor yields (entry 7) and sterically hindered substrates, e.g. mesitylbromide (**8z**), are not tolerated (entry 12). The reaction of alkyl organomagnesium reagents, prepared either *in situ* or obtained from commercial sources, leads to the desired alkylarylsulfones in 17-72% yield (entries 13-15).

3.5.4 Deprotonation Approach with tmp-Magnesium Bases

The deprotonation of acidic C-H-bonds with suitable magnesium amide bases is another very efficient approach for the synthesis of Grignard reagents.[138–140] Unfortunately, this procedure is not compatible with our arylation approach. Although thiophene (**5m**) could be transformed into the desired sulfone in 50% overall yield, the direct functionalization of several other heterocycles, such as furan or several nitrogen heterocycles, with tmp-MgCl·LiCl was not successful (scheme 3.13).



Scheme 3.13. Direct Metalation Approach by Deprotonation with tmp-MgCl·LiCl.

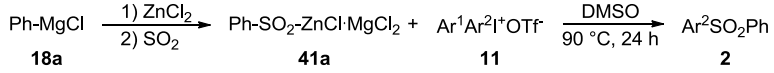
3.6 Preparation of Sulfones from Organozinc Species

Next we turned our attention to reactions with organozinc compounds. Organozinc reagents are known for their exceptional functional group compatibility and can be prepared via various efficient procedures.[123,125–129,141–143] Therefore one could expect a broader scope for our one-pot arylsulfone synthesis.

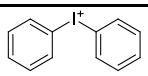
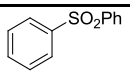
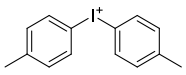
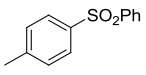
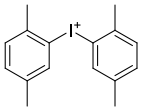
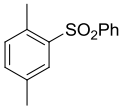
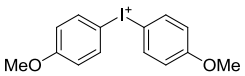
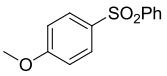
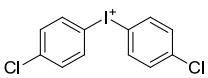
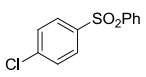
3.6.1 Variation of the Iodonium Salt

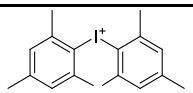
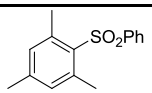
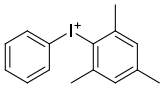
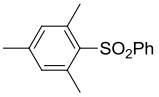
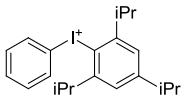
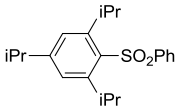
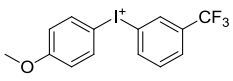
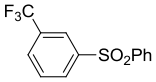
We started our investigations with the reaction between benzenesulfinic acid zinc salt **41a** and various diaryliodonium salts **11**. The zinc sulfinate **41a** was prepared from phenylmagnesium chloride **18a** via transmetalation with $ZnCl_2$ and subsequent reaction with sulfur dioxide. Although this procedure leads to the formation of stoichiometric amounts of halide ions, our optimized conditions from the corresponding transformation with Grignard reagents (DMSO, 1.5 equiv RSO_2Met, 1.0 equiv Ar_2IOTf) proved to be suitable for reactions with the benzenesulfinic acid zinc salt. The reaction of benzenesulfinic acid zinc salt (**41a**) with various symmetrical diaryliodonium salts **11** furnished the phenylarylsulfones of type **2** in moderate to excellent yields (table 3.18). Reaction of *para* –or bis(*ortho-meta*)-substituted salts **11c** and **11l** delivered the diarylsulfones **2c** and **2o** in high yields (entries 2 and 3). Also electron-rich salts, like **11k** and halogen-bearing substrates **11d** arylated sulfinate **41a** in high yields (entries 4 and 5). But steric hindrance is a limitation, the bis(1,3,5-trimethylbenzne)iodonium salt **11j** only turned out the diarylsulfone **2n** in 34% yield (entry 6). In case of the asymmetric diaryliodonium salts **11f**, **11h** and **11e**, either the more bulky substituent or the electron-poor one were transferred (entries 7-9).

Table 3.18. Arylation of Benzenesulfinic Acid Zinc Salt 41a.[a]



18a **41a** **11** **2**

entry	$Ar^1Ar^2I^+OTf^-$	Ar^1SO_2Ph	yield [%][b]
1	 **11b**	 **2b**	67
2	 **11c**	 **2c**	75
3	 **11l**	 **2o**	74
4[d]	 **11k**	 **2a**	70
5	 **11d**	 **2p**	64

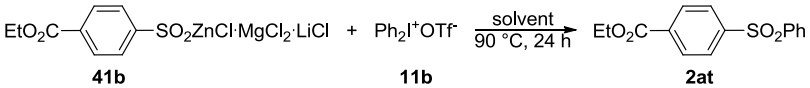
6	 **11j**	 **2n**	34
7	 **11f**	 **2n**	59
8	 **11h**	 **2j**	46
9	 **11e**	 **2q**	76[d]

[a]reaction conditions: 1.5 equiv benzene sulfinic acid salt **41a**, 1.0 equiv salt **11** in 1.0 mL DMSO at 90 °C for 24 h at a 0.5 mmol scale. [b]isolated yields of analytically pure products. [c]1.0 equiv salt **41a** and 3.0 equiv salt **11.** [d]5% of **2a** were isolated as by-product.

3.6.2 Survey of Solvents and Influence of Stoichiometry

We next examined the scope of our one-pot arylsulfone synthesis with different organozinc reagents obtained via transmetalation or direct zinc insertion in the presence of LiCl.[137] Unfortunately the above mentioned reactions conditions for benzenesulfinic acid zinc salt **41a** proved unsuitable for various other aryl and alkyl zinc reagents. Therefore, we decided to investigate the reaction of the zinc sulfinate **41b** in more detail. The ester-substituted zinc sulfinate **41b** was prepared from the corresponding aryl iodide **8u** via magnesium-halide exchange with *i*PrMgCl·LiCl, transmetalation with $ZnCl_2$ and subsequent reaction with SO_2. With this specific synthesis of the zinc sulfinate, we were able to examine *worst case* reaction conditions in the presence of a great excess of halide ions (table 3.19). Indeed the reaction of 1.5 equivalents of the sulfinic acid zinc salt **41b** with 1.0 equivalent diphenyliodonium triflate (**11b**) in different polar aprotic solvents furnished the desired sulfone in low yields (entries 1-3). Performing the reaction in DMSO with 3.0 equivalents of the iodonium salt **11b** did not affect the yield (entry 4). However, the yield could be improved dramatically by performing the reaction in NMP or DMF and employing a 3-fold excess of the iodonium salt (entries 5 and 6).

Table 3.19. Survey of Solvents and Influence of Stoichiometry.[a]



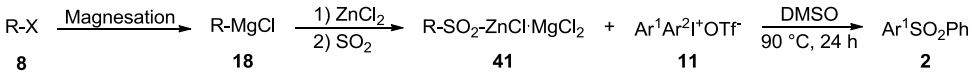
41b **11b** **2at**

entry	equiv Ar-SO_2-ZnX (41b)	equiv $Ph_2I^+OTf^-$ (11b)	solvent	yield [%][b]
1	1.5	1.0	DMSO	37 (57)[c]
2	1.5	1.0	NMP	8
3	1.5	1.0	DMF	15
4	1.0	3.0	DMSO	43
5	1.0	3.0	NMP	75
6	1.0	3.0	DMF	85

[a]reaction conditions: equiv of **41b** and **11b** as indicated in 1.0 mL solvent for 24 h at 90 °C at a 0.5 mmol scale. [b]isolated yields of analytically pure products. [c]preformed organo zinc reagent.

3.6.3 Variation of the Sulfinic Acid Zinc Salt

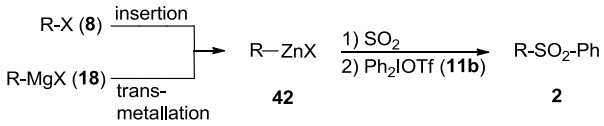
To close the investigation according to the scope of our method, we performed the reaction starting from different (hetero)aryl halides with diphenyliodonium triflate (**11b**) (table 3.20) applying our optimized five-step protocol (scheme 3.14).

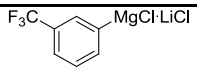
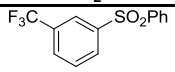
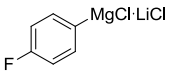
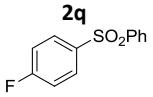
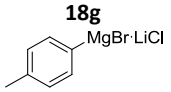
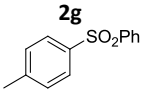
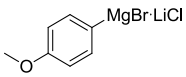
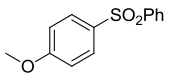
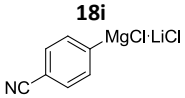
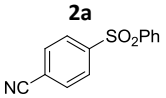


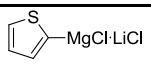
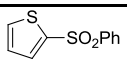
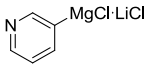
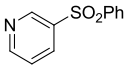
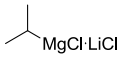
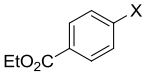
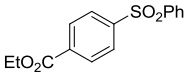
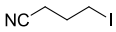
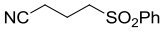
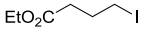
Scheme 3.14. General Zincation Approach to Arylsulfones.

Most of the sulfinates were generated *in situ* from the corresponding organomagnesium species via transmetalation with $ZnCl_2$ and subsequent treatment with SO_2. The resulting diarylsulfones were obtained in moderate to good yields (entries 1-8). Electron-poor aryl halides **18f**, **18g** and **18h** delivered the corresponding phenylarylsulfones **2g**, **2q** and **c** in good yields, 63%, 74% and 73%, respectively (entries 1-3). However, electron-rich arenes like **18i** obtain the desired product **2a** only in 44% yield (entry 4). To our delight, different heteroaromatic species, such as 2-bromothiophene (**18k**) and 3-bromopyridine (**18l**) led to the diarylsulfones **2au** and **2ar** in good yields (entries 6 and 7). The arylation of zinc sulfinates generated from the corresponding iodide by zinc insertion also obeys our four-step protocol. For alkyl zinc sulfinates it suits very well. Unlike the reaction with magnesium sulfinates iodide as counterion is tolerated for alkyl zinc sulfinates (entries 11 and 12). With functionalized alkyl sulfinates you get up to 84% yield (entry 12), aromatic sulfinates deriving from aryl iodides on the other hand are not favored (entry 10). Directly compared, considering our first model system, the transmetalation protocol is more efficient, 85% vs. 41%.

Table 3.20. Zincation Approach to Diarylsulfones.[a]



entry	R-X	R-SO_2Ph	yield [%][b]
1[c]	 **18f**	 **2q**	74
2[c]	 **18g**	 **2g**	63
3[c,d]	 **18h**	 **2c**	65
4[c,d]	 **18i**	 **2a**	44
5	 **18j**	 **2as**	73

6	 **18k**	 **2m**	59
7	 **18l**	 **2ar**	51
8[c]	 **18e**	 **38e**	64
9[c]	 **18m**: X = MgCl·LiCl	 **2at**	85
10	**8u**: X =I		41
11	 **40b**	 **38f**	64
12	 **40c**	 **38g**	84

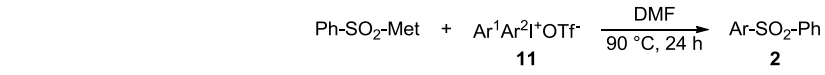
[a]reaction conditions: 1.0 equiv **18** or **40**, 3.0 equiv **11b** in 1.0 mL DMF for 24 h at 90 °C. [b]isolated yields of analytically pure products. [c]reaction carried out in DMSO. [d]1.5 equiv (hetero)arylhalide, 1.0 equiv **11b**.

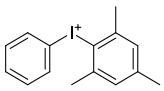
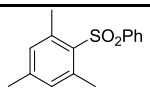
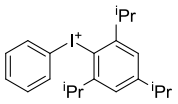
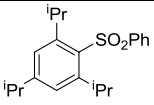
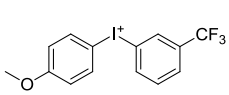
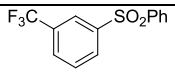
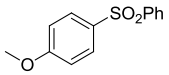
3.7 Selectivity Studies

To finish our investigations regarding diarylsulfones from organometallic regents, we finally performed chemoselectivity studies with various asymmetric diaryliodonium salts. As seen in our previous experiments with benzenesulfinic acid salts, we wanted to explore the influence of the *ortho*-effect and transition metal-catalysis.

First we treated the benzenesulfinic acid salts **7l**, **37a**, **34a** and **41a** with three different diaryliodonium salts (table 3.21). In case of the salts **11f** and **11h** (entries 1 and 2), the sterically demanding arene was transferred exclusively.[121] In another example, preferentially the electron-poor arene bearing a trifluoro-methyl group was transferred (entry 3). But in the case of the lithium and zinc sulfinate also the electron-poor arene arylated, whereas with the magnesium sulfinate also 4-iodoanisole as by-product was isolated almost quantitatively.

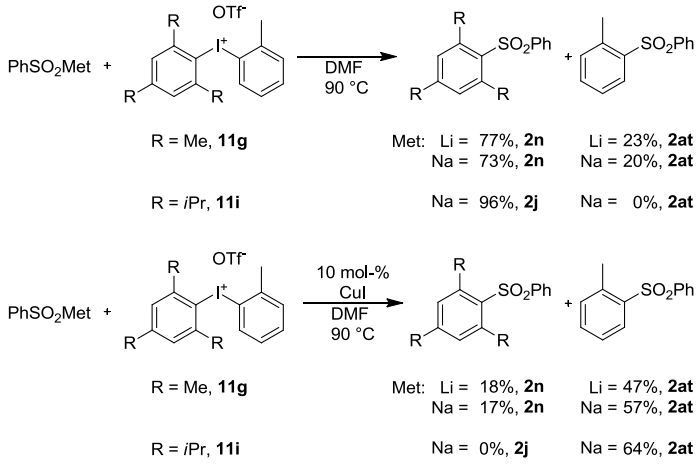
Table 3.21. Selectivity Studies with Sterically Different Demanding Aryl Substituents.[a]



Entry	$Ar^1Ar^2I^+OTf^-$	Ar-SO_2-Ph		Met = [b]			
				Na	Li	Mg[c]	Zn
1			**2n**	88%	79%	80%	59%
	11f	$PhSO_2Ph$	**2b**	-	-	-	-
2			**2j**	94%	81%	98%	46%
	11h	$PhSO_2Ph$	**2b**	-	-	-	-
3			**2q**	78%	71%	81%	76%
	11e		**2a**	<2%	6%	<2%	5%

[a]reaction conditions: 1.5 equiv **sulfinate** and 1.0 equiv **11** in 1.0 mL DMF for 24 h at 90 °C at a 0.5 mmol scale. [b]isolated yields of analytically pure products. [c]reactions carried out in DMSO.

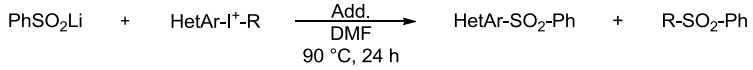
To explore the influence of transition metal-catalysis, we performed a reaction with simple asymmetric iodonium salts **11g** and **11i**. Previous results have been replicated by inverting the selectivity when adding catalytic amounts of CuI (scheme 3.15). This result is consistent with the *ortho*-effect, which predicts, that the sterically more demanding group is preferably transferred, if no catalyst is added.[121] However, the outcome with CuI was worse. In the uncatalyzed reaction, we got near 100% conversion and the sterically hindered group was transferred to yield diarylsulfone **2n** as main product. Adding CuI, the product ratio changes, but the conversion drops to about 65%. A possible explanation for the low conversion can be copper-catalyzed side-reactions, like homo-couplings, or reductions. Besides, we did not optimize the reaction conditions.



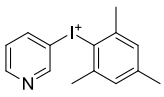
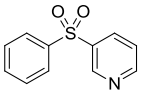
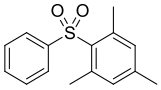
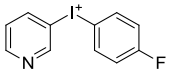
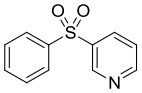
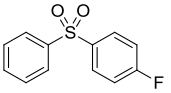
Scheme 3.15. Selectivity Studies. Reaction conditions: see experimental section.

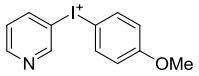
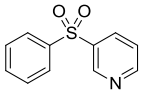
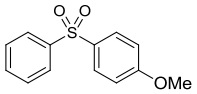
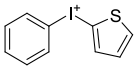
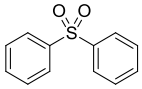
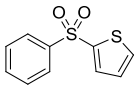
Furthermore, we were interested in the reaction of heteroaromatic iodonium salts and if we can selectively transfer the heteroatom-bearing arene, to expand the scope. We synthesized various asymmetric iodonium salts (**11r-o** and **11t**) bearing different electronic attributes (table 3.22). The results were not as we predicted; only in case of **11r** (entry 1) a clear inversion of chemoselectivity could be observed. Uncatalyzed, the sterically demanding 1,3,5-trimethylbenzene-group was transferred in 70% yield. By adding CuI, the pyridine-containing diarylsulfone **2ar** was the main product. In case of the other pyridine-bearing salts **11s** and **11t** no obvious effect was detected, it got even worse adding the catalyst. With electron-rich arenes, preferably the heteroaromatic group is transferred and obviously, adding a transition metal does not have an influence on the preferable transferred group. In case of iodonium salt **11s**, the yield even decreases by adding CuI (entry 2). Regarding the thiophene-derivative **11o**, adding CuI, did not change the chemoselectivity, but it at least lead to a mixture of both possible products (entry 4).

Table 3.22. Selectivity Studies of Heteroatom-Containing asymmetric Diaryliodonium Salts.[a]



37a 11 A B

entry	HetAr-I$^+$-R	add	A	B
1	 **11r**		 **2ar**	 **2n**
		-	12%	70%
		CuI	62%	29%
2	 **11s**		 **2ar**	 **2g**
		-	69%	22%
		CuI	24%	-

3	 **11t**		 **2ar**	 **2a**
		-	41%	7%
		CuI	40%	-
4	 **11o**		 **2b**	 **2m**
		-	75%	-
		CuI	44%	28%

[a]reaction conditions: 1.5 equiv **37a**, 1.0 equiv **11** if indicated 10 mol-% CuI in 1.0 mL DMF for 24 h at 90 °C on a 0.5 mmol scale.
[b]isolated yields of analytically pure products.

4. Nickel-Catalyzed Approach to Diarylsulfones

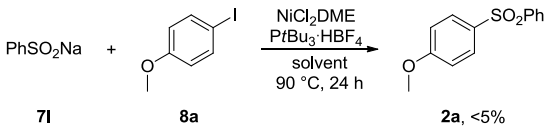
For this project, special thanks go to my bachelor students Vanessa Luciano and Marcella Drost, who contributed more than 50% of the herein discussed experiments under my supervision.

4.1 Introduction

After establishing a method concerning the synthesis of arylsulfones from sulfinic acid salts and iodonium salts, a more atom-economic and sustainable route to diarylsulfones was to be investigated. There are several drawbacks regarding to the protocol depicted in chapter 3. Even though the conversion rate and yields are high, an aryl iodide deriving from the iodonium salt is always generated as by-product due to the reaction mechanism. Furthermore, the access to sulfinic acids is limited. Although, this thesis describes a very elegant approach of preparation, starting from (hetero)aryl halides or (hetero)arenes, the access is still restricted to compounds which can be transferred into organometallic reagents. Moreover, not every molecule is suitable for our established method, e.g. highly functionalized heteroaromatics, like caffeine.

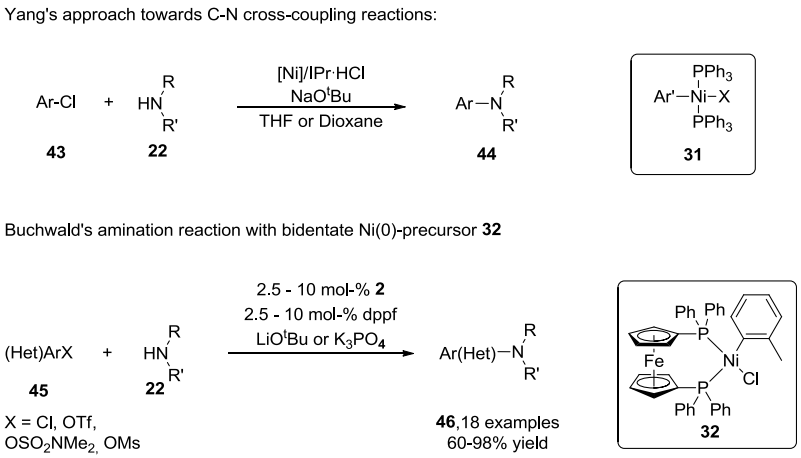
As starting point, the electrophile should be changed from iodonium salts into aryl halides, preferably aryl chlorides, to circumvent the generation of the aryl iodide caused by the salt. Nickel-catalysts are known for their reactivity towards aryl chlorides and tosylates, so a nickel-catalyzed cross-coupling reaction was chosen to be investigated. Unfortunately, there are only a few known reactions with sulfur nucleophiles, such as the conversion from thiols to sulfides[144–146] or thioetherification C-S coupling.[147] In both cases, sulfides are obtained as products; nickel-catalyzed cross-coupling reactions yielding sulfones are, to the best of our knowledge, unknown.

Thus, in analogy to a Hartwig-Buchwald-amination (see scheme 1.12), a nickel carbon-sulfur cross-coupling reaction was envisioned. Unfortunately, a Ni(II)-catalyst only provided traces of the desired product (scheme 4.1). Switching to Ni(0) as catalytic active species seemed to be necessary.



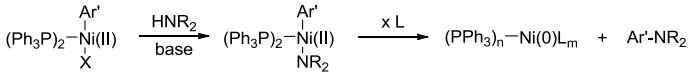
Scheme 4.1. Ni(II)-Catalyzed C-S-Coupling Reaction.

Ni(0)-catalysts are usually air and moisture sensitive. Fortunately, Yang *et al.*[49–51,148] and more recently Buchwald *et al.*[52] developed Ni(0)-precursors, air-stable and moisture insensitive and very effective regarding amination reactions, starting from aryl chlorides or tosylates (scheme 4.2). These Ni(0)-precursors are Ni(II)-(σ-aryl) complexes which are activated *in situ*, by base and an additional ligand. In scheme 4.3 a possible pathway for the activation of this complex is shown.



Scheme 4.2. Yang's and Buchwald's Nickel-Catalyzed Amination Reactions.

It is assumed that in a first step the halide ion is abstracted by base and substituted by the amine as ligand. Then, induced by another ligand or base, reductive elimination takes place, were the Ni(0)-catalyst is generated and a tertiary amine is formed. The secondary amine, which is needed for the C-N cross-coupling is regenerated during the catalytic cycle by base (not shown).

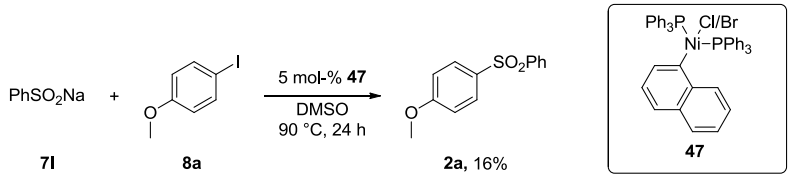


Scheme 4.3. Possible Pathway for Activation of Ni(II)-(σ-aryl) Complexes

Based on the studies of Yang and Buchwald, developing a nickel-catalyzed sulfonylation cross-coupling reaction seemed promising. As test system the reaction between benzenesulfinic acid sodium salt (**7l**) and 4-iodoanisole (**8b**) was chosen (scheme 4.1).

4.2 Optimizing the Reaction Conditions

The nickel-catalyzed reaction between benzenesulfinic acid sodium salt (**7l**) and 4-iodoanisole (**8a**), with Yang's Ni(naphtyl)(PPh$_3$)$_2$Cl/Br-complex **47** as Ni(0)-precursor catalyst, provided 16% yield and indicated, that the nickel-catalyzed sulfonylation of aryl halides is a feasible approach. Thus, reaction parameters were to be optimized.

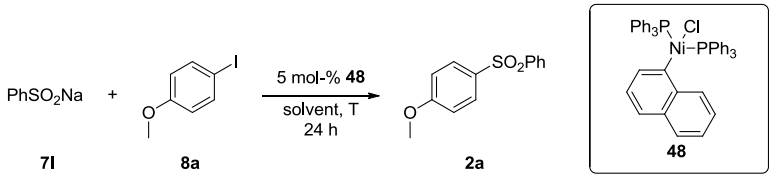


Scheme 4.4. Ni-Catalyzed Sulfonylation of Aryl Halides.

4.2.1 Solvent and Temperature Screening

In a first step a solvent and temperature screening was performed (table 4.1). Similar to our previous method, aprotic polar solvents like DMSO, NMP and DMF led to an increase in yield, whereas non-polar solvents are of opposite effect (see chapter 3). Additionally the temperature dependence is shown in table 4.1. Optimum results were obtained in NMP at 120 °C (entry 3).

Table 4.1. Solvent and Temperature Screening.[a]

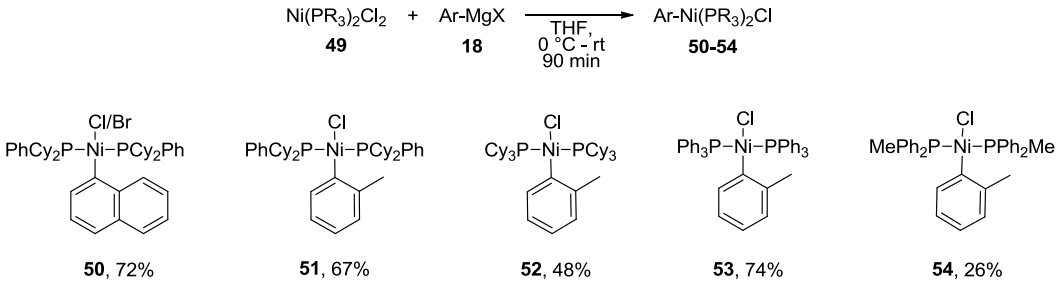


entry	solvent	90 °C[b]	120 °C[b]
1	DMSO	15%	43%
2	DMF	8%	39%
3	NMP	33%	83% (74%)[c]
4	Dioxane	-	-
5	Toluene	-	-
6	THF	-	-

[a]reaction conditions: 1.1 equiv **7l**, 1.0 equiv **8a** and 5 mol-% catalyst **48** in 2.0 mL solvent at indicated temperature for 24 h. [b]isolated yields of analytically pure products. [c]reaction run at 105 °C.

4.2.2 Evaluation of the Optimum Catalyst

The next distinct step is identifying an optimized catalyst. Several air-stable nickel(0)-precursor catalysts were prepared and tested. In scheme 4.5 the catalysts synthesized in our lab are depicted and table 4.2 summarizes the testing results.



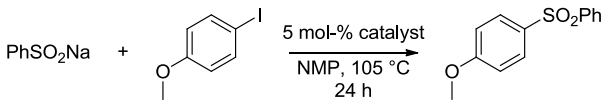
Scheme 4.5. Synthesized Ni(0)-precursors.

The catalysts were synthesized according to Buchwald's procedure, starting with the corresponding bis(phosphine) nickel dichloride **49** and an aryl Grignard reagent **18**.[52]

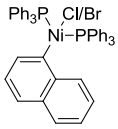
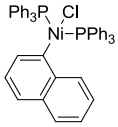
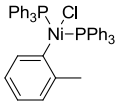
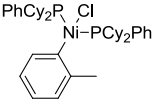
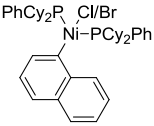
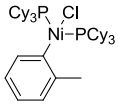
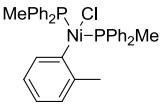
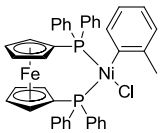
The oxidation state of the catalyst was probed by test reactions with $NiCl_2$ and $NiCl_2$-DME. In both cases, only traces of the desired product were isolated (entries 1 and 2), indicating that a Ni(0)-catalysis is crucial. Afterwards both, the aryl component and the phosphine ligands were varied. In case of the nickel(0)-precursors bearing two triphenylphosphine ligands **47**, **48** and **53**, the nature of arene and halide does not have a mentionable impact (entries 3-5). Substitution of two or three benzenes by cyclohexanes decreases

the yield drastically (entries 6-8), leading to the hypothesis, that the steric demand of the phosphine ligand and the resulting cone angle may not be neglected. As subsequent step, a less hindered precursor **54** was synthesized and the basic assumption, "the smaller the ligand the better the yield", was proven (entry 9). For reasons of completeness, a bidentate Ni(0)-precursor **32**, Buchwald found to be superior was tested. The low yield of 9% was to be expected, based on the steric demand of **32** (entry 10).

Table 4.2. Survey of Catalysts.[a]



7l **8a** **a**

Entry	catalyst	yield [%][b]
1	$NiCl_2 \cdot 6H_2O + PBu_3 \cdot HBF_4$	<5
2	$NiCl_2DME + PBu_3 \cdot HBF_4$	<5
3	 **47**	79
4	 **48**	74
5	 **53**	71
6	 **51**	18
7	 **54**	14
8	 **50**	8
9	 **52**	86
10	 **32**	9

[a]reaction conditions: 1.1 equiv **7l**, 1.0 equiv **8a** and 5 mol-% catalyst in 2.0 mL NMP at 105 °C for 24 h. [b]isolated yields of analytically pure products.

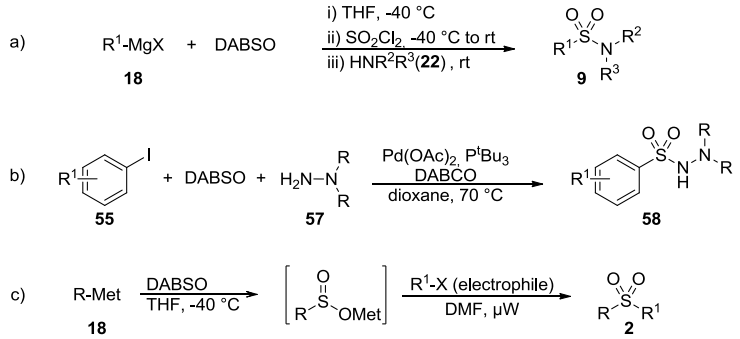
This catalyst screening leads to the conclusion that the cone angles of the phosphine ligands[149] greatly influence yields. This was probed by the bidentate ligands. If the cone angle is as large as in PCy_3 (179°) the yield is very low (entry 8). Utilizing PPh_3 which has a cone angle of 145°, the yield increases up to 71% (entry 5). By adding tri-furylphosphine (cone angle 134°) as additional ligand, the yield increases further. Unfortunately, it was not possible, to synthesize the corresponding catalyst with this ligand. But by replacing one phenyl-ligand with a methyl-group, the yield rises from 71% (entry 5) to 86% (entry 9).

Based on this results, further steps are the synthesis of the corresponding nickel-catalyst with PMe_3 (cone angle 118°) as ligand and another approach is to investigate phosphide ligands which also reveals smaller cone angles.

5. Application of SO_2 Surrogates to form Arylsulfones

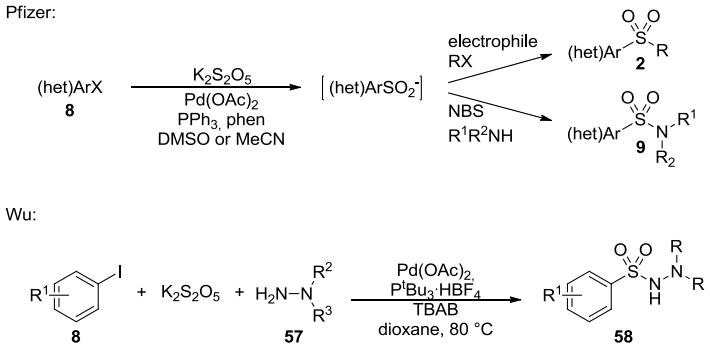
5.1 Introduction

Despite sulfur dioxide is a highly toxic gas, it is a versatile reagent in organic synthesis.[150–152] It is utilized in numerous distinct pericyclic transformations, such as chelotropic reactions with dienes, hetero-Diels-Alder cycloadditions and ene-reactions.[153–155] SO_2 has been applied in the synthesis of arylsulfonyl chlorides,[156–158] in Friedel-Crafts-type sulfinylations,[159] in alkene isomerization[160,161] and in copolymerization with alkenes or alkynes.[162] Additionally, SO_2 is exerted for the synthesis of sulfinates and sulfones from nucleophilic organometallic reagents, like our established method, described in chapter 3.[120,163–165] Recently, Vogel and coworkers have developed SO_2-induced multicomponent reactions for the stereoselective synthesis of polyfunctional molecules.[67,166,167] Although SO_2 shows a diverse reactivity profile and can be used for the preparation of a large range of compounds, the difficulties associated with handling a toxic and corrosive gas severely restrict the utility of SO_2 as a reagent for organic synthesis.



Scheme 5.1. Exploiting DABSO as SO_2-Surrogate.

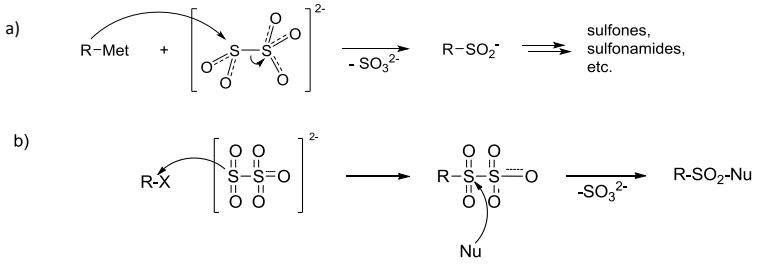
Olah, already in the 70's, and more recently Willis have shown, that stable, solid tertiary amine-SO_2 complexes can be used to replace gaseous SO_2.[66,118,130,168–174] Especially the 1,4-diaza-bicyclo[2.2.2]-octane-*bis*(sulfur dioxide) complex (DABCO·2SO_2 or DABSO), introduced by Willis, has already found applications in various processes (scheme 5.1).[66,118,130,172–176] However, the handling of gaseous SO_2, with all associated difficulties, is still necessary for the preparation of those complexes. In the last two years Wu *et al.* and a group from Pfizer developed palladium-catalyzed reactions, which exploit potassium metabisulfite ($K_2S_2O_5$) as sulfur dioxide equivalent (scheme 5.2).[177,178] Considering the availability and price of potassium or sodium metabisulfite,[13] these salts would be ideal replacements for gaseous sulfur dioxide.



Scheme 5.2. Exploiting Potassium Metabisulfite as SO_2-surrogate.

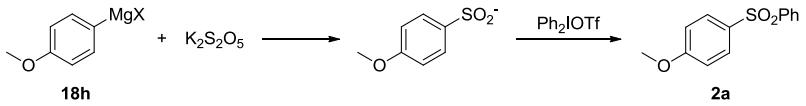
5.2 $Na_2S_2O_5$ and $K_2S_2O_5$ as SO_2-surrogates

$Na_2S_2O_5$ and $K_2S_2O_5$, also known as food additives E 223 and E 224, are widely used as antioxidants, disinfectants and preservative agents. The metabisulfite anion consists of a SO_2- and a SO_3-group linked through a long and labile S-S-bond and the negative charge mainly is localized on the SO_3-group.[179,180] The labile nature of the S-S-bond and the partial charge separation was targeted as described herein. On the one hand, highly nucleophilic organometallic reagents should be able to cleave the S-S-bond by reaction with the more electrophilic SO_2-subunit and nucleophilic substitution of the more negatively charged SO_3-group, furnishing the corresponding sulfinates and SO_3^{2-} (scheme 5.3a). This reactivity can be expected due to the fact that metabisulfites react with water to form two molecules of bisulfate. On the other hand, the metabisulfite anion can act as nucleophile and attack an electrophile, e.g. an alkyl halide, forming a disulfide-species. Subsequent cleavage by a nucleophile, yields a sulfonyl-containing compound (scheme 5.3b).



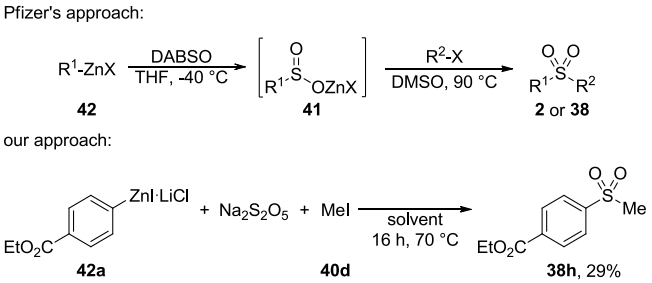
Scheme 5.3. Proposed Reaction of Organometallic Reagents with the Metabisulfite Anion.

The above mentioned possible reaction mechanisms for the metabisulfite anion cause two different approaches. In a first experiment, potassium metabisulfite was exploited as electrophile in a substitution reaction with a Grignard reagent as nucleophile. Subsequent treatment with an iodonium salt to trap the sulfinate was expected to lead to the sulfone (scheme 5.4). Unfortunately, this compound could not be isolated or detected.



Scheme 5.4. Exploiting the Metabisulfite Anion as Electrophile.

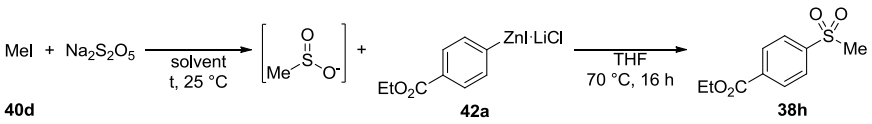
In analogy to Pfizer's approach (scheme 5.5), an organozinc reagent was used as nucleophile to react with metabisulfite as electrophile. The proof of principle reaction between (4-(ethoxycarbonyl)phenyl)zinc(II) iodide·LiCl (**42a**), MeI (**40d**) and $Na_2S_2O_5$ worked as multicomponent reaction and yielded 29% of the alkylaryl sulfone **38h**. Regarding this success, further experiments were conducted.



Scheme 5.5. Pfizer's and our Approach towards Sulfones from Organozinc Reagents and Metabisulfites.

5.2.1 Investigating the Reaction Parameters

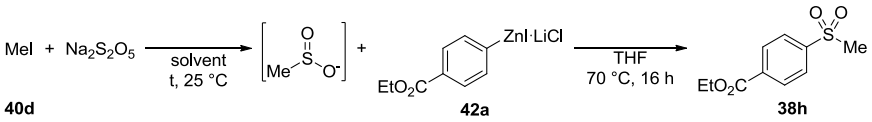
Although, the test system was set up as multicomponent reaction, the corresponding one-pot reaction was investigated prior, to unravel the reaction mechanism, consisting of two steps. Formation of the disulfide intermediate was followed by a nucleophilic attack of an aryl zinc reagent (scheme 5.6). In the course of the optimization experiments, the aryl zinc reagent was always used to trap the intermediate state, as the isolation of it is a separate point of investigation.



Scheme 5.6. Test System for the One-Pot Reaction to Alkylaryl Sulfones.

In a first step, different solvents were screened. As inferred from table 5.1, aprotic polar solvents, in particular NMP, result in high yields (entries 1-3). Even upon addition of TBAF to THF to increase the solubility of the metabilsulfite, yields were insuffient (entry 4). Other protic polar solvents, like MeCN or MeOH did not yield the desired alkyl sulfone either.

Table 5.1. Solvent Screening[a]



40d **42a** **38h**

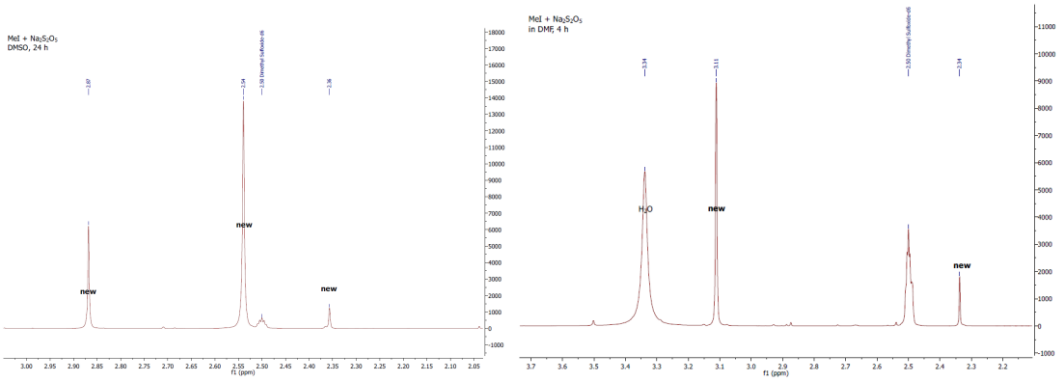
entry	solvent	yield [%][b]
1	DMSO	62
2	NMP	91
3	DMF	60
4	THF	-
5	MeCN	-
6	MeOH	-
7	acetone	-
8	sulfolane	-

[a]reaction conditions: 1.0 equiv **42a**, 2.0 equiv $Na_2S_2O_5$, 2.5 equiv. **40d** in 2.0 mL overall solvent, for 16 h at 70 °C. [b]isolated yields of analytically pure products.

5.2.1.1 Isolating the Intermediate

As subsequent step, the intermediate was to be isolated and the addition of arylzinc was omitted. The test reactions were carried out in d_6-DMSO, degassed d_6-DMSO, DMF and NMP. D_6-DMSO as solvent allowed direct monitoring by NMR. Concerning DMF and NMP based reactions, the solvent was evaporated under reduced pressure and then the samples were resolved in d_6-DMSO and sunjected to NMR. Even though the best solvent for the reaction was found to be NMP, its evaporation posed a problem and the resulting NMR-spectra were to be discarded.

The intermediate was formed in DMF at 25 °C within 4 h. In DMSO 24 h are required and isolation is more demanding due to solvent separation. Subsequent elemental analysis revealed impurities most likely owing to unreacted educts. Furthermore the NMR-signals of both intermediates, isolated from DMF and DMSO, are different (Scheme 5.7). DMSO procedure cause appearance of new signals at δ = 2.87 ppm and 2.36 ppm, whereas utilization of DMF caused new signals at δ = 3.11 ppm and 2.34 ppm. The high-field signal is identical, thus it was assumed to be the intermediate signal. However, the other new NMR signal still lacks explanation.



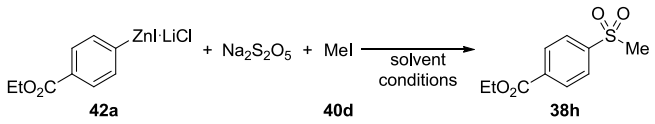
Scheme 5.7. Comparison of Intermediates of the Reaction run in DMSO and DMF.

This results only proof, formation of a new compound, but the isolation process still needs to be optimized.

5.2.1.2 Comparison of MCR and One-Pot Procedure

As mentioned above, this reaction works either as multicomponent or as one-pot reaction, thus a comparative study was set up. We found one-pot reactions reveal higher yields than MCRs as summarized in table 5.2. Additionally, solvent dependence was probed and NMP gave best results. Moreover, the reaction time in NMP was accessed. By increasing the reaction time from 24 h to 36 h, the yield drops from 90% to 30%, assumingly based on the preformation of the sulfinate.

Table 5.2. One-Pot vs. MCR.[a]



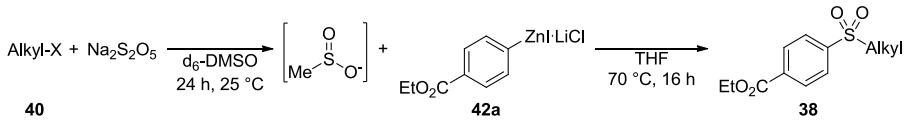
entry	reaction type	DMSO[b]	NMP[b]	DMF[b]
1	one-pot	62%	91 (30[c])%	60%
2	MCR	49%	60-71%	-

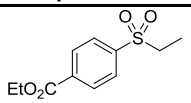
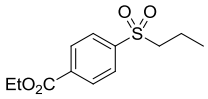
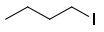
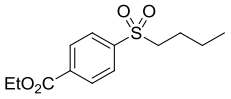
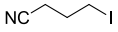
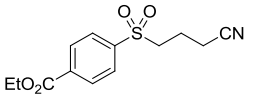
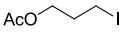
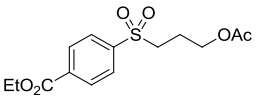
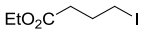
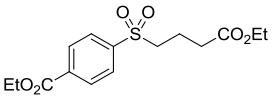
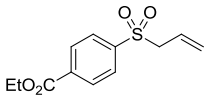
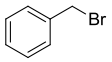
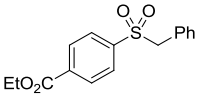
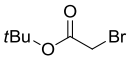
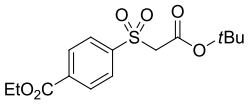
[a]reaction conditions: MCR: 1.0 equiv **42a**, 2.0 equiv $Na_2S_2O_5$ and 2.5 equiv **40d** in 2.0 mL solvent, for 16 h at 70 °C. one-pot: 2.5 equiv. **40d**, 2.0 equiv $Na_2S_2O_5$ for 24 h at 25 °C, then 1.0 equiv **42a** was added, 16 h 70 °C. [b]isolated yields of analytically pure product. [c]reaction run for 36 h.

5.2.2 Exploring the Scope

Despite the fact that optimized generally applicable reaction conditions were not evaluated, experiments with d_6-DMSO, in order to monitor the progress of the formation of the intermediate sulfinate were conducted. In general, after 24 h the starting alkyl halide signal vanished, and new peaks in the NMR-spectra were detected. At this point, the arylzinc reagent **42a** was added and the reaction stirred for additional 16 h at 70 °C. Unfortunately the results are not consistent. Although the starting material was completely consumed in all cases, not every reaction yielded the alkylarylsulfone of type **38** (table 5.3Table 5.3). In case of ethyl iodide (**40e**), the desired sulfone could only be isolated via a MCR (entry 1). By using propyl iodide (**40f**), both protocols worked, and as previously stated, the one-pot procedure was found to be superior (entry 2). With other alkyl iodides **40g** and **40b** good results were achieved (entries 3 and 4), but with **40h** and **40c**, a reaction after addition of the zinc reagent did not take place. Possible explanations are the electronic properties of the alkyl chain. Reactions in the presence of electron poor ether- and ester-substituents in contrast to the electron-rich nitrile. In case of alkyl bromides, only very reactive species like allyl bromide (**40j**) react with the zinc reagent to sulfone **38o** (entry 7). Other alkyl bromides are consumed during the first step, but do not react any further. Moreover, an attempt to form the alkyl iodide *in situ* through an excess NaI, failed.

Table 5.3. Examples.[a]



entry	alkyl-X	product	yield [%][b]
1	 **40e**	 **38i**	- (37)[c]
2	 **40f**	 **38j**	51 (30)[c]
3	 **40g**	 **38k**	75
4	 **40b**	 **38l**	57
5	 **40h**	 **38m**	-
6	 **40c**	 **38n**	-
7	 **40j**	 **38o**	43
8	 **40k**	 **38p**	-
9	 **40l**	 **38q**	-

[a]reaction conditions: 2.0 equiv. **40**, 2.5 equiv $Na_2S_2O_5$ for 24 h at 25 °C, then 1.0 equiv **42a** was added, 16 h at 70 °C. [b]isolated yield of analytically pure products. [c]reaction run as MCR: 1.0 equiv **42a**, 2.5 equiv $Na_2S_2O_5$ and 2.5 equiv **40** in 2.0 mL solvent, for 16 h at 70 °C.

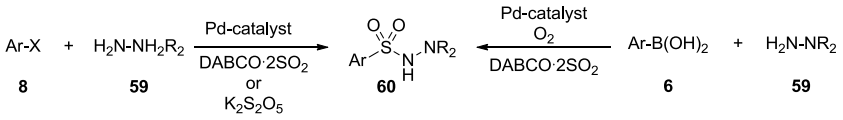
Our results show the one-pot procedure to be favored, yet general conditions could not be established. Clarifying the separate steps by isolating the intermediate product and investigating the mechanism in detail should lead to a better understanding and inplementation of a universal protocol.

6. Multicomponent Reaction Approach to Sulfonamides

6.1 Introduction

In analogy to sulfones, sulfonamides are of wide interest in medicinal chemistry and therefore the pharmaceutical industry.[3–5] As already introduced, the preparation of sulfonamides often proceeds via sulfonyl chlorides, either as starting material or intermediates. Most of the educts have to be synthesized under harsh conditions and are not commercially available.

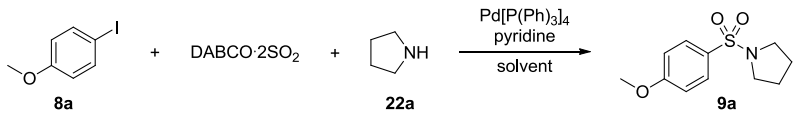
Recently, the groups of Willis and Wu published aminosulfonylation reactions starting from aryl halides[118,172,177] and aryl boronic acids.[177] These methods allow the simple preparation of *N*-aminosulfonamides generated from a SO_2-source and starting materials not containing a sulfur moiety. Unfortunately, these approaches are restricted to hydrazines as nitrogen-nucleophiles and are not compatible with amines. Therefore, the many sulfonamides can only be prepared in an intricately fashion.[172]



Scheme 6.1. Aminosulfonylation of Aryl halides and Arylboronic Acids.

Surprisingly, a manifold of studies concerning the bonding of sulfur dioxide to metal-complexes and the insertion in metal-carbon-bonds exist, but only few examples for transition metal-catalyzed reactions with SO_2 are reported.[181–187]

In order to create new, innovative routes to sulfonamides with a general applicability and broad scope, multicomponent reaction were investigated. MCR's by definition possess a large range of possible products. Therefore the reaction between an aryl halide, an amine, instead of hydrazines, and DABSO as sulfur dioxide source was carried out (scheme 6.2). In a first experiment, with $Pd[P(Ph_3)_4]$ as catalyst and pyridine as base, the desired sulfonamide could be isolated. With this result, the development of a MCR to prepare sulfonamides was investigated, starting from 4-iodoanisole (**8a**), DABSO and pyrrolidine (**22a**).

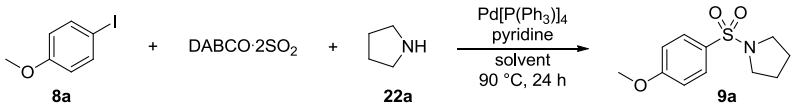


Scheme 6.2. Proof of Principle MCR to generate Sulfonamides.

6.2 Optimizing the reaction conditions

The MCR between 4-iodoanisole (**8a**), pyrrolidine (**22a**) and DABSO under palladium-catalysis served as proof of principle and was chosen as test system (scheme 6.2). As first step a solvent screening was conducted. As shown in table 6.1 only DMSO delivered the desired sulfonamide, but with $Pd[P(Ph_3)_4]$ as catalyst the yield was not satisfying.

Table 6.1. Solvent Screening.[a]



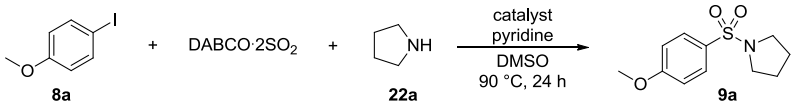
8a **22a** **9a**

entry	Solvent	yield [%][b]
1	DMSO	26
2	DCE	-
3	1,4-dioxane	-
4	DMF	-
5	THF	-
6	toluene	-
7	DMPU	-
8	MeCN	-
9	NMP	-

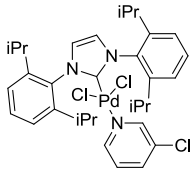
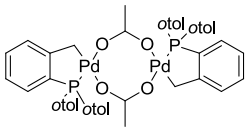
[a]reaction conditions: 1.0 equiv 4-iodoanisole, 2.0 equiv DABSO, 4.0 equiv pyrrolidine, 2.0 equiv pyridine, 5 mol-% $Pd[PPh_3]_4$ in 2.0 mL solvent at 90 °C for 24 h. [b]isolated yield of analytically pure product.

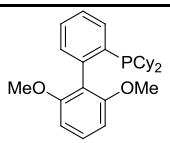
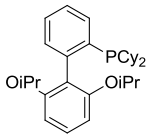
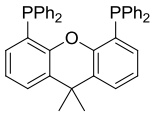
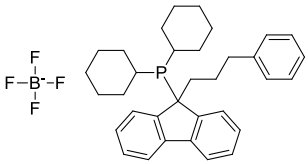
As subsequent step, different palladium-catalysts and ligands were tested. As inferred from table 6.2, various palladium-catalysts are active even in the absence of ligands, but only provide moderate yields. Other transition metal-catalysts were also probed (not shown), with unsatisfying results. Adding ligands to the reaction mixture had either a decreasing effect on the yield (entries 8-10) or none at all (entry 11).

Table 6.2. Survey of Catalysts and different Ligands.[a]



8a **22a** **9a**

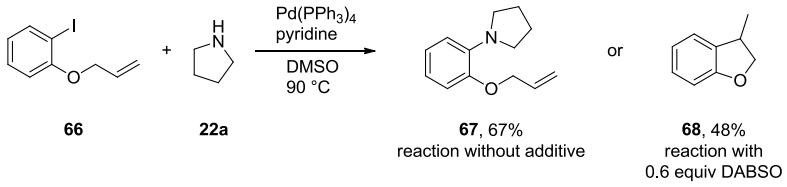
entry	catalyst	ligand	yield [%][b]
1	-	-	<5
2	$Pd[P(Ph)_3]_4$	-	26
3	$Pd(OAc)_2$	-	46
4	Pd/C	-	25
5	 **60**	-	42
6	 **61**	-	40
7	$Pd(dba)_2$	-	39

8	$Pd(OAc)_2$	 **62**	13
9	$Pd(OAc)_2$	 **63**	27
10	$Pd(OAc)_2$	 **64**	25
11	$Pd(OAc)_2$	 **65**	49

[a]reaction conditions: 1.0 equiv **8a**, 2.0 equiv DABSO, 4.0 equiv **22a**, 2.0 equiv pyridine, 5.0 mol-% catalyst and 10 mol-% ligand in 2.0 mL DMSO at 90 °C for 24 h. [b]isolated yield of analytically pure product.

These results lead to the assumption that a typical transition metal-catalyzed cross-coupling reaction does not take place, but proceeds via a radical mechanism. To verify this, a "radical clock"[188] experiment (scheme 6.3) was set up.

The reaction of allylphenolether **66** and pyrrolidine (**22a**) without a SO_2-source, under typical reaction conditions for transition metal-catalyzed reactions, lead to the predicted product of a palladium-catalyzed amination.[111] Adding DABSO caused cyclic product is formation (scheme 6.3). This indicates that in presence of a sulfur dioxide source an aryl radical species has to be generated and reacts as a "radical clock" **68** in a 5-exo-dig cyclization reaction with the olefin. The insertion mechanism of SO_2 could not be clarified with these experiments.

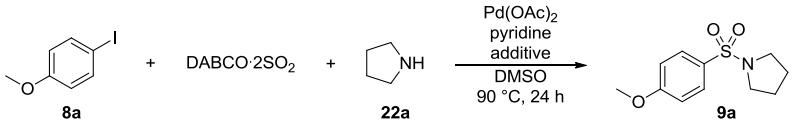


Scheme 6.3. Radical Clock Experiments.

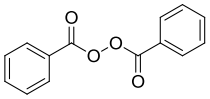
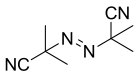
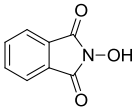
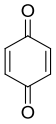
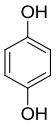
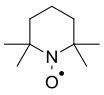
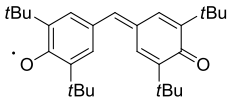
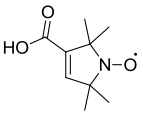
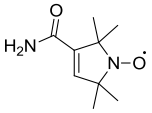
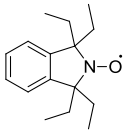
Due to the fact, that the reaction between 4-iodoanisole (**8a**), DABSO and pyrrolidine (**22a**) processes via a radical pathway, a set of radical scavengers and stable radicals as additives were applied, to investigate their influence on the yield (table 6.3). Addition of radical starters, like dibenzoylperoxide (**69**) or AIBN (**70**) (entries 2 and 3) had either a decreasing or no influence in terms of yield. Identical results were found for electron acceptors or donors, respectively (entries 4-6). With the notable exception of 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO, **74**) (entry 6), no improvement was observed regarding stable radicals

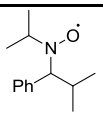
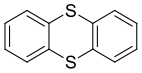
(entries 7-12). With the addition of TEMPO (**74**) the yield could be increased up to 57% and be reproduced.

Table 6.3. Survey of different Additives, stable Radicals and Scavengers.[a]



8a **22a** **9a**

entry	Additive	yield [%][b]
1	-	46
2	 **69**	18
3	 **70**	40
4	 **71**	45
5	 **72**	45
6	 **73**	50
7	 **74**	54-57(-)[d]
8	 **75**	49
9	 **76**	39
10	 **77**	48
11	 **78**	17

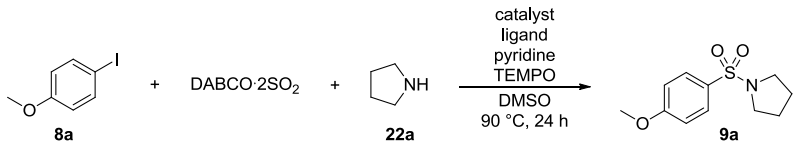
12	 **79**	24
13	 **5o**	23
14	 **80**	45

[a]reaction conditions: 1.0 equiv **8a**, 2.0 equiv DABSO, 4.0 equiv **22a**, 2.0 equiv pyridine, 10 mol-% $Pd(OAc)_2$ and 20 mol-% additive in 2.0 mL DMSO at 90 °C for 24 h. [b]calculated yields according to an internal standart. [c]isolated yield of analytically pure product. [d]reaction run without exclusion of air and moisture.

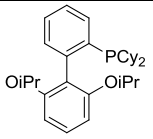
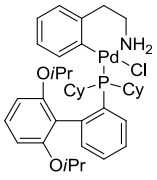
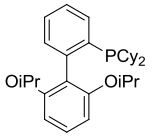
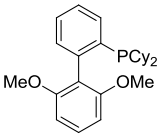
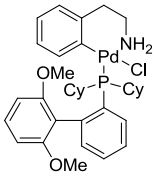
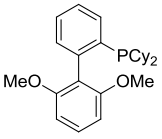
Unfortunately, the reaction still only takes place with $Pd(OAc)_2$ in strong Lewis-basic solvents, like DMSO. As TEMPO **74** leads to an increase in yield, a second survey of catalysts was carried out (table 6.4).

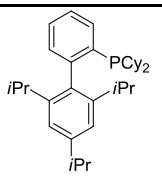
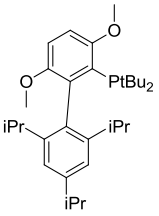
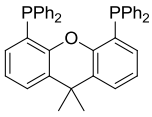
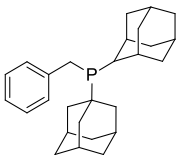
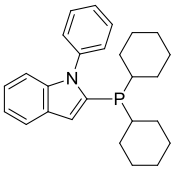
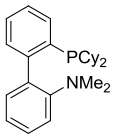
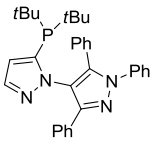
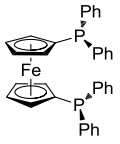
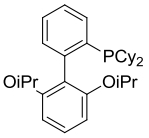
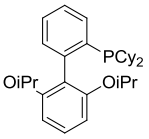
$Pd(OAC)_2$ with a set of different ligands developed by Buchwald (entries 1-12), as well as other palladium-species (entries 14-21) were tested. Best results were obtained with RuPhos and SPhos (entries 1 and 3) and both their G1 adducts (entries 2 and 4). The remaining ligands did not affect the yield. RuPhos as ligand to various palladium-catalysts had a negative impact on the yields (entries 13 and 14).

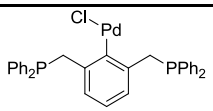
Table 6.4. Survey of Ligands and different Palladium-Catalysts.[a]



8a **22a** **9a**

entry	catalyst	ligand	yield [%][b]
1	$Pd(OAc)_2$	 **63**	57
2	 **81**	 **63**	67
3	$Pd(OAc)_2$	 **62**	70
4	 **82**	 **62**	43

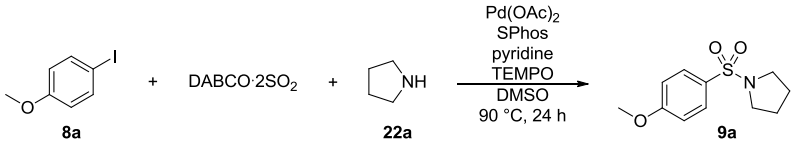
5	$Pd(OAc)_2$	 **83**	45
6	$Pd(OAc)_2$	 **84**	45
7	$Pd(OAc)_2$	 **64**	44
8	$Pd(OAc)_2$	 **85**	45
9	$Pd(OAc)_2$	 **86**	48
10	$Pd(OAc)_2$	 **87**	48
11	$Pd(OAc)_2$	 **88**	44
12	$Pd(OAc)_2$	 **89**	16
13	$Pd_2(dba)_3$	 **63**	44
14	$PdCl_2$	 **63**	44

15	 **90**	31

[a]reaction conditions: 1.0 equiv **8a**, 2.0 equiv DABSO, 4.0 equiv **22a**, 2.0 equiv pyridine, 20 mol-% TEMPO (**74**), 10 mol-% ligand and 5 mol-% cat. in 2.0 mL solvent at 90 °C for 24 h. [b]isolated yield of analytically pure product.

As a next step different ratios of the starting materials and the base were examined (table 6.5). Reducing the amount of all three components, DABSO, amine and base, best results were achieved (entry 5).

Table 6.5 Further Investigations regarding SPhos and TEMPO.[a]



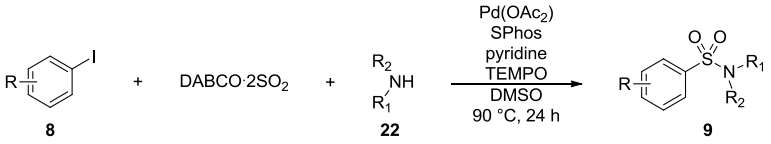
entry	equiv SO_2	equiv NHR_2	equiv Py	yield [%][b]
1	1.0	3.0	1.0	45
2	1.5	1.5	0.75	20
3	2.0	2.0	1.0	30
4	3.0	1.5	2.0	40
5	3.0	3.0	1.5	60
6	3.0	3.0	3.0	36
7	3.0	5.0	2.0	18

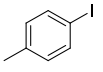
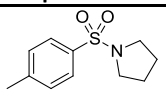
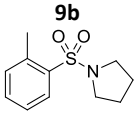
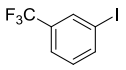
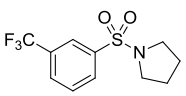
[a]reaction conditions: 1.0 equiv **8a**, equiv DABSO, pyrrolidine **22a** and pyridine as indicated, 20 mol-% TEMPO, 10 mol-% SPhos and 5 mol-% $Pd(OAc)_2$ in 2.0 mL DMSO at 90 °C for 24 h. [b]isolated yield of analytically pure product.

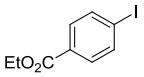
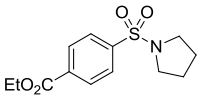
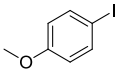
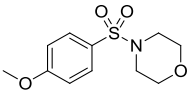
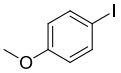
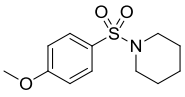
6.3 Exploring the Scope

With optimized reaction conditions at hand, the scope was examined by varying both, the amine and aryl iodide (table 6.6). Unfortunately, these experiments revealed that the established reactions conditions are not generally applicable. Only one more example afforded an acceptable yield of the desired sulfonamide (entry 1). All remaining combinations, only resulted poor yields.

Table 6.6. Exploring the Scope and Limitations.[a]



entry	aryl iodide	R_1R_2NH	product	yield [%][b]
1	 **8aa**	 **22a**	 **9b**	53
2[c]	 **8w**	 **22a**	 **9c**	17
3[c]	 **8g**	 **22a**		-

			9d	
4	 **8v**	 **22a**	 **9e**	18
5	 **8a**	 **22b**	 **9f**	-
6	 **8a**	 **22c**	 **9g**	15

[a]reaction conditions: 1.0 equiv **8**, 1.5 equiv DABSO, 3.0 equiv **22**, 1.5 equiv pyridine, 20 mol-% TEMPO, 10 mol-% SPhos and 5 mol-% $Pd(OAc)_2$ in 2.0 mL DMSO at 90 °C for 24 h. [b]isolated yield of analytically pure product. [c]4.0 equiv **22a** and 2.0 equiv.DABSO used.

Based on these results, mechanistic studies are to be expanded. The postulated possible steps need to be further investigated. We envision to establish a multicomponent reaction approach to sulfonamides after fully understanding the reaction mechanism.

7. Summary and Outlook

This PhD-thesis focusses on developing new methods towards the preparation of sulfones and sulfonamides. The primary target was to setup efficient, generally applicable procedures, preferably one-pot protocols or multicomponent reactions and aditionally to introduce the sulfonyl-moiety during the reaction, either as gaseous sulfur dioxide or via a SO_2-surrogate, like DABSO or metabisulfite.

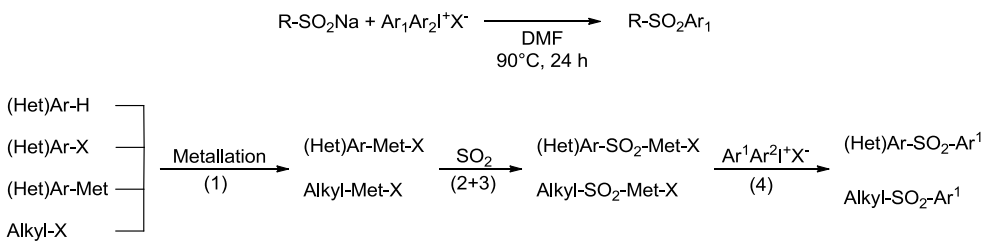
7.1 Arylsulfone Synthesis based on Organometallic Reagents and Iodonium Salts

We successfully established a synthesic pathway to arylsulfones starting from sulfinic acid sodium, lithium, magnesium and zinc salts (scheme 7.1). This reaction has a very broad scope and both aryl and alkyl sulfinates can be arylated in an efficient manner (scheme 7.2). Moreover, reactions with unsymmetrical diaryliodonium salts reveal high chemoselectivity (scheme 7.3).

Based on the reaction with arylsulfinic acid sodium salts and iodonium salts a simple route to diarylsulfones was developed. However, the sulfonyl group was still contained in one educt. In order to be able to insert the sulfonyl moiety during the synthesis, we designed a practical one-pot-protocol for the direct transformation of (hetero)aromatic and aliphatic halides as well as (hetero)arenes into arylsulfones, inserting the sulfonyl moiety during the synthesis. This innovative protocol consists of:

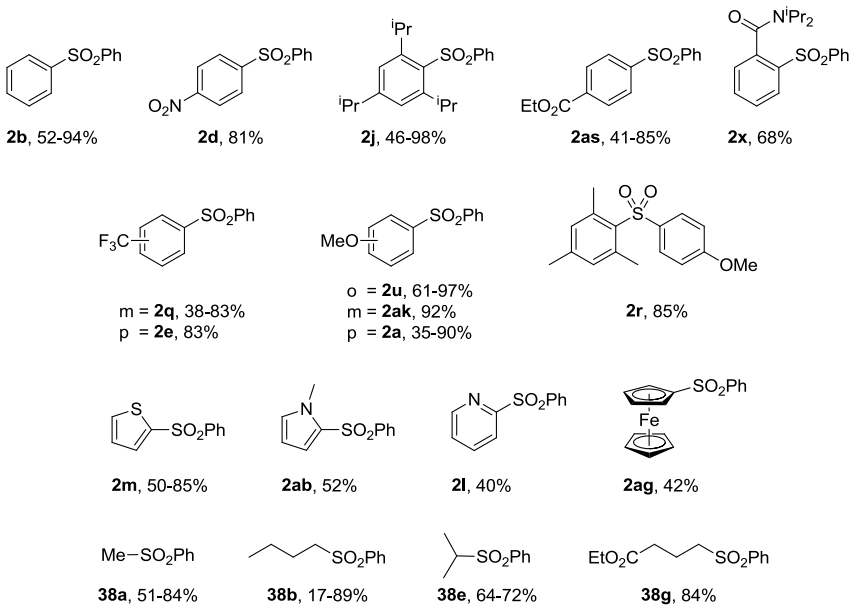
(1) generation of the organometallic reagent via metal-halide-exchange, direct metal insertion or deprotonation;
(2) reaction of the organometallic reagent with sulfur dioxide;
(3) removal of excess sulfur dioxide; and
(4) treatment of the formed crude metal sulfinates with a diaryliodonium salt (scheme 7.1).

Various aryl- and heteroarylsulfones can be prepared utilizing this straightforward procedure. Reactions with magnesium and zinc sulfinates are inherently limited due to side-reactions of their halide counterions with the iodonium salts which may be circumvented by employing an excess of iodonium salt.



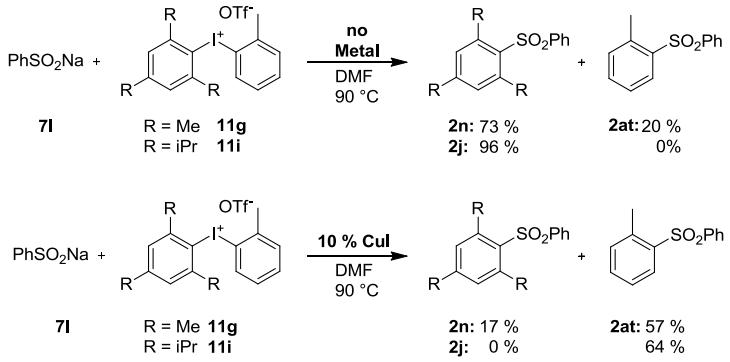
Scheme 7.1. Initially Developed Method and evolved Four-Step One-Pot Synthesis.

The broad scope of our method is depicted in scheme 7.2. It has a high functional group tolerance, electron-rich and –poor arenes can be converted easily to diarylsulfones, heteroaromatics do not pose a problem; and last but not least, alkylarylsulfones are accessible.



Scheme 7.2. Selected Examples synthesized in the course of this Thesis.

In reactions with unsymmetrical diaryliodonium salts an interesting chemoselectivity was observed. The sterically more demanding aryl groups were transferred preferentially (scheme 7.3). An excellent selectivity was observed with, e.g. the very bulky tri(isopropyl)phenyl group. This chemoselectivity could be reversed by the addition of transition metals. In the presence of catalytic amounts of CuI transfer of the less bulky aryl group is preferred.

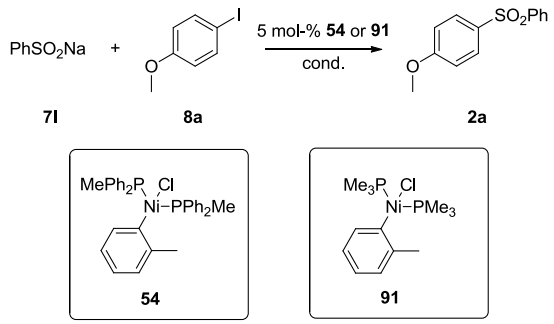


Scheme 7.3. Selected Examples for the Selectivity Studies perfomed during this Thesis.

7.2 Nickel-Catalyzed Approach to Diarylsulfones

A new transition metal-catalyzed approach yielding diarylsulfones starting from aryl halides and sulfinates should be developed (scheme 7.4).

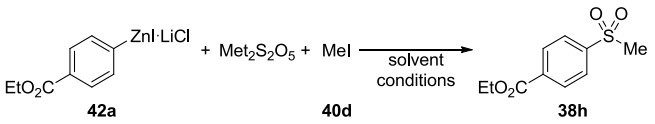
Our initial studies evaluated nickel-catalysts to suit the reaction best. Results of our optimization studies showed a strong dependence of the yield on the cone angles described by the ligands attached to the central nickel-atom. Thus, a Ni-catalyst with small phosphine ligands such as **54** was chosen. Following this thesis, a $NiPMe_3$-complex **91** is to be tested, which is assumed to give excellent results and lead to a general applicability of the method. Furthermore, diphosphine ligands seem promising due to their small cone angles and are also under investigation.



Scheme 7.4. Nickel-Catalyzed Approach to Diarylsulfones.

7.3 Application of SO_2-Surrogates to form Arylsulfones

In a third project the use of SO_2-surrogates, especially deriving from metabisulfites ($S_2O_5^-$) was exploited. The goal was to develop an one-pot or even multicomponent reaction of alkyl halides, "SO_2" and an organozinc species (scheme 7.5). Up to date general conditions could not be found. Therefore, mechanistic studies are performed and the individual steps will be investigated to point to possible improvements, to clarify the reaction mechanism and to develop a general protocol.

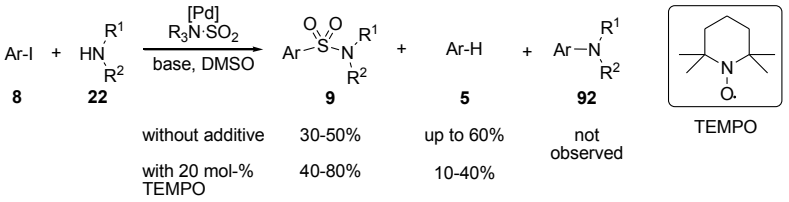


Scheme 7.5. Application of SO_2-Surrogates to form Arylsulfones.

7.4 Multicomponent Reaction Approach to Sulfonamides

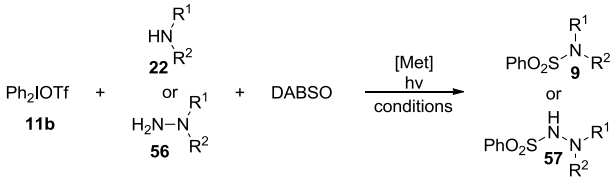
The aim was to establish a transition metal-catalyzed multicomponent reaction to form sulfonamides. We envisioned a three component reaction between an amine, an aryl halide and DABSO as SO_2-source and accomplished to evolve a novel palladium-catalyzed aminosulfonylation reaction starting from amines, accordingly (scheme 7.6). To the best of our knowledge, only examples with hydrazines are mentioned in literature.

A key component for the reaction and at the same time a restriction is the strong Lewis acidic solvent DMSO. We showed that only the dehalogenated arene is a side-product and its formation can be surpressed by adding TEMPO, a stable nitroxide. Formation of the classic cross-coupling product **92** was not observed. Additional experiments with a "radical clock" lead to the conclusion that this cross-coupling reaction does not proceed via the classical pathway, but through a radical mechanism. As subsequent step, the mechanistic studies will be expanded. We expect the development of a generally applicable multicomponent approach to sulfonamides after in depth understanding of the reaction mechanism.



Scheme 7.6. Palladium-Catalyzed 3-Component Reaction to Sulfonamides.

An alternative way for the application of metabisulfite and DABSO as SO_2-source is a photo-catalyzed cross-coupling (scheme 7.7). This reaction between an iodonium salt, hydrazines or eventually amines and a SO_2-surrogate yields sulfonamides and is under current investigation in our lab.



Scheme 7.7. Transition Metal-Catalyzed Photoreaction towards Sulfonamides.

8. Experimental Part

8.1 General

All reactions were carried out with magnetic stirring and, if air or moisture sensitive, in flame dried glassware under an argon atmosphere. Syringes were used to transfer solvents and reagents, and were purged with argon prior to use. All yields refer to isolated yields of compounds estimated to be > 95% pure as determined by ^{1}H-NMR.

8.1.1 Solvents

Anhydrous solvents were either purchased from commercial suppliers and stored over MS4Å or dried according to standard methods by distillation over drying agents as stated below. Both were under an atmosphere of Argon. Solvents for column chromatography were technical standard.

Dichloromethane was distilled from CaH_2.
Diethyl ether was predried over KOH and then distilled from sodium benzophenone ketyl under argon.
DMF was purchased from *Alfa Aesar* and stored under an argon atmosphere.
1,4-Dioxane was purchased from *Sigma-Aldrich* and stored under an argon atmosphere.
NMP was purchased from *Acros Organics* and stored under an argon atmosphere.
Pyridine was purchased from *Acros Organics* and stored under an argon atmosphere.
Toluene was predried over $CaCl_2$ and distilled from CaH_2 and stored under an argon atmosphere.
THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under argon.

8.1.2 Chromatography

Thin layer chromatography was performed using aluminum plates coated with SiO_2 (*Merck* 60, F-254). The spots were visualized by ultraviolet light or by staining of the TLC-plate with the dye-solution below:

- iodide absorbed on silica gel
- cerium ammoniummolybdate (CAM)

(Flash) Column chromatography was performed with Silica 0.04-0.063 mm/ 230-400 mesh from *Merck*.

8.1.3 Analytical Data

NMR spectroscopy NMR spectra were recorded on *Bruker AM-250* (^{1}H: 250 MHz), *Avance 300* (^{1}H: 300 MHz, ^{13}C: 75 MHz), *Avance-400* (^{1}H: 400 MHz, ^{13}C: 100 MHz) or *AV-500* (^{1}H: 500 MHz, ^{13}C: 126 MHz). Chemical shifts are reported as δ-values relative to the residual $CDCl_3$-peak (δ = 7.26 ppm for ^{1}H and δ = 77.16 ppm for ^{13}C), d_6-DMSO (δ = 2.50 ppm for ^{1}H and δ = 39.52 ppm for ^{13}C) or MeOD (δ = 3.31 ppm for ^{1}H and δ = 49. ppm for ^{13}C). Coupling constants (*J*) are given in Hz and multiplicities of the signals are

abbreviated as follows: s = singlet; d = doublet; t = triplet; q = quartet; sept = septet; m = multiplet; dd = doublet of doublets and dt = doublet of triplets.

Mass Spectrometry Mass spectra (MS) were measured on a VG Plattform II - spectrometer using ESI (electrospray ionisation) techniques at the Department of Chemistry.

High Resolution Mass Spectra (MALDI-HRMS) were measured on a MALDI LTQ Orbitrap XL using MALDI (Matrix-assisted Laser Desorption/Ionization) techniques at the Department of Chemistry.

Melting Points were measured on an *OptiMelt MPA 100* from *Stanford Research* and are uncorrected.

Infrared Spectroscopy Spectra were recorded from 4000-400 cm-1 on a *Spectrum Two (FT-IR)* IR spectrometer from *PerkinElmer*. Samples were measured neat (ATR, Smiths Detection DuraSampl IR II Diamond ATR). The absorption bands were reported in wave numbers (cm^{-1}). For the characterization the following abbreviations were used: s (strong), m (medium), w (weak).

8.1.4 Reagents

Commercial available starting materials were purchased and used without further purification.

Following compounds were prepared to literature procedures: phenyl diethylcarbamate (**5e**),[189] *N,N*-diisopropylbenzamide (**5f**),[190] pyridin-2-yl diethylcarbamate (**#**), *N*-benzylbenzamide (**5g**),[190] *N*-(4-methoxyphenyl)pivalamide (**5i**),[193] 1-methyl-1*H*-pyrrole (**5j**),[194] 2-bromo-6-methoxypyridine (**8o**), [191] 5-iodo-2,4-dimethoxypyrimidine (**8p**),[192].[195]

***i*PrMgCl·LiCl** was purchased as a solution in THF from *Rockwood Lithium*.

MeMgCl·LiCl was purchased as a solution in THF from *Rockwood Lithium*.

***n*BuLi** was purchased as a solution in hexane from *Rockwood Lithium*.

***s*BuLi** was purchased as a solution in cyclohexane from *Rockwood Lithium*.

***t*BuLi** was purchased as a solution in pentane from *Rockwood Lithium*.

MeLi was purchased as a solution in Et_2O from *Rockwood Lithium*.

PhLi was purchased as a solution in Et_2O from *Rockwood Lithium*.

$ZnCl_2$ was purchased as a solution in THF from *Rockwood Lithium*.

***m*CBPA** was dried under high vacuum for 1 h prior to use. It was assumed an activity between 75% and 60%, depending on the purity of the commercially available chemical.

Noncommercial organomagnesium reagents were prepared either by direct magnesium insertion or magnesium insertion in the presence of LiCl into the corresponding aryl halide. Zinc reagents were prepared either by transmetalation with $ZnCl_2$ of the corresponding organomagnesium reagent or by insertion of zinc in the presence of LiCl.

The content of organometallic reagents was determined either by the method of *Paquette* (organolithium or –magnesium reagents) or the method of *Knochel* (organomagnesium or – zinc reagents) prior to use.

SO_2 (sulfur dioxide 3.8 from *Gerling, Holz & Co*) was used directly without further purification.

SO_2 is a toxic and corrosive gas! It should be handled with care only in a well-ventilated fume-hood with the necessary precaution! It is possible to obtain the crude metal sulfinates by passing a stream of sulfur dioxide through the solution of the organometallic reagent. However, with this technique a great excess of SO_2 is introduced into the reaction and has to be removed afterwards. In general better and more reproducible yields were obtained by using a defined amount of liquid SO_2. Therefore SO_2 was condensed into a dry and Ar-filled Schlenk-flask, cooled to -78 °C. Because of its high heat of evaporation, liquid and cooled SO_2 can be easily handled, measured and transferred with syringes. For small scale reactions, we recommend this procedure.
For the removal of excess SO_2 we employed the two following procedures. (For the removal of excess SO_2 (gaseous or liquid) appropriate measures to trap and destroy SO_2 should be taken, e.g. passing the SO_2 stream through an aq. NaOH solution.)

Procedure A: After warming the reaction mixture to 25 °C within 90 min the solvents and excess SO_2 were removed under reduced pressure. The residue was coevaporated with CH_2CL_2 (2 x 1.5 mL).

Procedure B: Excess SO_2 was removed by passing Ar through the solution for 30 min. Diaryliodonium salt **11** (0.50 mmol, 1.0 equiv) and DMF (1.0 mL) were added directly to the remaining solution/suspension. The flask was charged with a small distillation head and heated to 90 °C. After the lower boiling solvents (hexanes, pentane, cyclohexane and/or THF, Et_2O) were distilled off (typically within 1 h), the flask was capped with a rubber septum and heated for the remaining time. (As alternative the flask can be capped directly with a rubber septum pierced with a 20G needle and heated to 90 °C for 24 h. Low boiling solvents are evaporated directly into the atmosphere! This should be only done in a closed, well-ventilated fume-hood!)

Preparation of Benzenesulfinic Lithium Salt 37a

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with Phenyllithium (**36a**) (32.2 mL, 50 mmol, 1.55 M solution in Et_2O, 1.0 equiv) and cooled to -40 °C. At this temperature, liquid SO_2 (1.1 mL, 55 mmol, 1.1 equiv) was added and the reaction mixture was allowed to warm to 25 °C within 90 min. It was then concentrated under reduced pressure and excess Et_2O was coevaporated two times with CH_2Cl_2 (150 mL) to get the solid benzenesulfinic lithium salt (**37a**) (11.32 g).*

*Note: The theoretical amount of lithium salt **37a** (formula weight: 148.11 g/mol) from 32.3 mL Phenyllithium (**36a**) is 7.41 g. The material obtained (11.32 g) should therefore contain 65% of **37a** (assuming 100% conversion). A purity of 65% of this material was thus assumed in later calculations.

Preparation of Benzenesulfinic Magnesium Chloride Salt 34a

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with phenylmagnesium chloride (**18a**) (70 mL, 74.2 mmol, 1.06 M solution in THF, 1.0 equiv) and cooled to -40 °C. At this temperature, liquid SO_2 (2.0 mL, 100 mmol, 1.3 equiv) was added and the reaction mixture was allowed to warm to 25 °C within 90 min. It was then concentrated under reduced pressure and excess THF was coevaporated two times with CH_2Cl_2 (150 mL) to get the solid benzenesulfinic magnesium chloride salt (**34a**) (21.18 g).*

*Note: The theoretical amount of magnesium chloride salt **34a** (formula weight: 200.93 g/mol) from 74.2 mL phenylmagnesium chloride (**18a**) is 14.9 g. The material obtained (21.18 g) should therefore contain 70% of **34a** (assuming 100% conversion). A purity of 70% of this material was thus assumed in later calculations.

8.2 Typical Procedures

8.2.1 Typical Procedure for the Preparation of Sulfones from Arylsulfinic Acid Sodium Salts (TP 1)

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with diaryiodonium salt **11** (1.1 equiv), arylsulfinic acid sodium salt **7** (1.0 equiv) and DMF (2.0 mL/mmol sodium salt, 0.5 M). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc) afforded the analytically pure product.

8.2.2 Typical Procedure for the Preparation of Sulfones from Benzenesulfinic Lithium Salt (TP 2)

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with benzenesulfinic acid lithium salt **37** (1.5 equiv), diaryliodonium salt **11** (1.0 equiv) and DMF (2.0 mL/mmol iodonium salt, 0.5 M). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc) afforded the analytically pure product.

8.2.3 Typical Procedure for the Preparation of Sulfones from Alkyllithium Reagents (TP 3)

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with alkyllithium **36** (1.5 equiv) cooled to -78 °C and then liquid SO_2 (10 equiv) was added and the mixture was warmed to 25 °C within 90 min. After removal of SO_2 and solvents according to procedure A, diphenyliodonium triflate **11** and (1.0 equiv) and DMF (2.0 mL/mmol iodonium salt, 0.5 M) were added. The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc) afforded the analytically pure product.

8.2.4 Typical Procedure for the Preparation of Sulfones from Benzenesulfinic Acid Magnesium Chloride Salt (TP 4)

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with benzenesulfinic acid magnesium chloride salt (**34a**) (1.5 equiv or 1.0 equiv), diaryliodonium salt **11** (1.0 equiv or 3.0 equiv, repectively) and DMSO (2.0 mL/mmol limiting factor, 0.5 M). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc) afforded the analytically pure product.

8.2.5 Typical Procedure for the Preparation of Sulfones from Grignard Reagents (TP 5)

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with a corresponding Grignard reagent (**18**) (solution in THF, 1.5 equiv or 1.0 equiv) in THF (total volume 1.5 mL), cooled to -40 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents according to procedure A, diphenyliodonium triflate **11b** (1.0 equiv or 3.0 equiv, respectively) and DMSO (2.0 mL/mmol limiting factor, 0.5 M) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc) afforded the analytically pure product.

8.2.6 Typical Procedure for the Preparation of Sulfones from *in situ* generated Benzenesulfinic Acid Zinc Salt (TP 6)

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with phenylmagnesium chloride (**18a**) (0.53 M solution in THF, 1.4 mL, 0.75 mmol, 0.5 equiv) and $ZnCl_2$ (0.7 M solution in THF, 1.1 mL, 0.8 mmol, 1.6 equiv) was added drop wise. After stirring at 25 °C for 30 min, the mixture was cooled to -40 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents according to procedure A, to the crude benzenesulfinic zinc salt (**41**), diaryliodonium salt **11** (1.0 equiv) and DMSO (2.0 mL/mmol iodonium salt, 0.5 M) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc) afforded the analytically pure product.

8.2.7 Typical Procedure for the Preparation of Sulfones from Organozinc Reagents (TP 7)

To a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with a corresponding organozinc reagent (**41**) (solution in THF, 0.5 mmol, 1.0 equiv) in THF (total volume 1.5 mL), cooled to -40 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents, diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol, 3.0 equiv) and DMF (2.0 mL/mmol organozinc reagent, 0.5 M) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc) afforded the analytically pure product.

8.2.8 Typical Procedure for the Synthesis of Iodonium Salts from Aryl Iodides and Arenes (TP 8)

In an oven-dried round-bottom flask equipped with a magnetic stirrer *m*CPBA (1.1 equiv) was dissolved in CH_2Cl_2 (5.0 mL/mmol aryl iodide, 0.2 M), before addition of an aryl iodide **8** (1.0 equiv) and an arene **5** (1.0 equiv). After cooling to 0 °C, TfOH (1.5 equiv) was added drop wise and the mixture was allowed to stir for a specific time at 25 °C. Then, all volatile compounds were removed under reduced pressure and the residue was diluted with Et_2O (5.0 mL/mmol aryl iodide, 0.2 M) and put in an ultrasonic bath for 15 min. After crystallization at -20 °C for 16 h, the solid was filtrated and washed three times with Et_2O (20 mL). Drying under high vacuum afforded the analytically pure products.

8.2.9 Typical Procedure for the Synthesis of Iodonium Salts from elemental Iodide and Arenes (TP 9)

In an oven-dried round-bottom flask equipped with a magnetic stirrer *m*CPBA (4.0 equiv) was dissolved in CH_2Cl_2 (5.0 mL/mmol iodide, 0.2 M), before addition of I_2 (1.0 equiv) and an arene **5** (4.0-10.0 equiv). After cooling to 0 °C, TfOH (1.5 equiv) was added drop wise and the mixture was allowed to stir for a specific time at 25 °C. Then, all volatile compounds were removed under reduced pressure and the residue was diluted with Et_2O (5.0 mL/mmol aryl iodide, 0.2 M) and put in an ultrasonic bath for 15 min. After crystallization at -20 °C for 16 h, the solid was filtrated and washed three times with Et_2O (20 mL). Drying under high vacuum afforded the analytically pure products.

8.2.10 Typical Procedure for the Synhtesis of Pyridine Iodonium Salts (TP 10)

In an oven-dried round-bottom flask equipped with a magnetic stirrer 3-iodopyridine (**8b**) (1.0 equiv) was dissolved in CH_2Cl_2 (4.0 mL/mmol iodopyridine, 0.25 M), and TfOH (4.0 equiv) was added drop wise and strirred at 25 °C for 5 min. Then, *m*CPBA (1.5 equiv) and a (hetero)arene **5** (1.1 equiv) were added and the reaction mixture was heated to 60 °C and stirred at this temperature for 30 min. After cooling to 25 °C, the mixture was concentrated under reduced pressure and diluted with Et_2O (4.0 mL/mmol **8a**, 0.25 M) and stirred at 0 °C for 30 min. Then, the solid was filtrated and washed three times with Et_2O (5.0 mL). After drying under reduced pressure a deprotonation of the pyridine salt was performed by diluting the intermediate over a basic Alox flash column. It was dissolved in a mixture of CH_2Cl_2:MeOH (5:1, 2.0 mL/mmol) and then put on a column (Ø = 6 cm/mmol) consisting of sand (H = 0.5 cm) and basic Al_2O_3 (6.0 g/mmol) and diluted with CH_2Cl_2:MeOH (20:1, 160 ml/mmol). Concentration in vacuo yielded the analytically pure product.

8.2.11 Typical Procedure for the Synthesis of Sodium Sulfinates (TP 11)

In a round bottom flask, equipped with a magnetic stirrer and a reflux condenser, a sulfonyl chloride **3** (1.0 equiv), $NaHCO_3$ (2.0 equiv) and Na_2SO_3 (2.0 equiv) in H_2O (1.0 mL/mmol sulfonyl chloride **3**, 1.0 M) were heated at 80 °C for 4 h. After the removal of all volatile compounds under reduced pressure, the residue is washed three times with EtOH (15 mL), where as the last time, it is put into the ultrasonic bath for 5 min and then allowed to crystallize. After recrystallization out of EtOH, the product is afforded. The purities are given separately for each compound.

8.2.12 Typical Procedure for the MCR to Sulfonamides (TP 12)

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with an aryl iodide **8** (1.0 equiv), an amine **22** (3.0 equiv), DABSO (1.5 equiv), $Pd(OAc)_2$ (5 mol-%), SPhos (**62**) (10 mol-%), pyridine (2.0 equiv) and TEMPO (**74**) (20 mol-%) in DMSO (1.0 mL/mmol aryl iodide **8**, 1.0 M) and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous HCl-solution (1.0 M, 10 mL) was added and the aqueous layer was extracted three times with EtOAc (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution

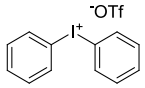
(10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc) afforded the analytically pure product.

8.3 Experimental Procedures

8.3.1 Starting Materials

All starting materials were prepared according to literature and their analytical data is consistent with it.

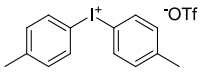
Diphenyliodonium triflate (11b)[46]



Diphenyliodonium triflate (**11b**) was prepared according to TP 8 from iodobenzene (**8p**) (20 mmol, 2.6 mL), benzene (**5a**) (22 mmol, 2.0 mL), *m*CPBA (75% active, 22 mmol, 5.1 g) and TfOH (60 mmol, 5.3 mL) in CH_2Cl_2 (100 mL). The reaction time was 3 h. After recrystallization, quantitative yields of a beige solid were achieved.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.02 – 7.93 (m, 4H), 7.69 – 7.59 (m, 2H), 7.53 – 7.42 (m, 4H).

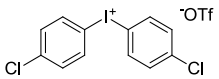
Di-p-tolyliodonium triflate (11c)[46]



Di-*p*-tolyliodonium triflate (**11c**) was prepared according to TP 8 from 4-iodotoluene (**8aa**) (10 mmol, 2.2 g), toluene (**8w**) (11 mmol, 1.2 mL), *m*CPBA (75% active, 11 mmol, 2.53 g) and TfOH (20 mmol, 1.8 mL) in CH_2Cl_2 (50 mL). The reaction time was 10 min. Recrystallization yielded a colorless solid (2.96 g, 65%).

^{1}H NMR (250 MHz, DMSO): δ = 8.09 (d, *J* = 8.3 Hz, 4H), 7.32 (d, *J* = 8.1 Hz, 4H), 2.33 (s, 6H).

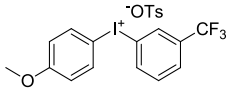
Bis(4-chlorophenyl)iodonium triflate (11d)[46]



Bis(4-chlorophenyl)iodonium triflate (**11d**) was prepared according to TP 8 from 4-iodo-1-chlorobenzene (**8ab**) (10 mmol, 2.38 g), chlorobenzene (**8ac**) (11 mmol, 1.1 mL), *m*CPBA (75% active, 11 mmol, 2.53 g) and TfOH (30 mmol, 1.8 mL) in CH_2Cl_2 (50 mL). The reaction time were 16 h. Recrystallization yielded a colorless solid (4.31 g, 86%).

^{1}H NMR (250 MHz, DMSO): δ = 8.33 – 8.20 (m, 4H), 7.69 – 7.58 (m, 4H).

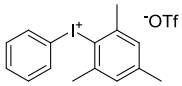
(4-Methoxyphenyl)(3-(trifluoromethyl)phenyl)iodonium tosylate (11e)[101]



(4-Methoxyphenyl)(3-(trifluoromethyl)phenyl)iodonium tosylate (**11e**) was prepared according to TP 8 from 3-iodobenzotrifluoride (**8g**) (5.0 mmol, 0.7 mL), anisole (**5c**) (5.5 mmol, 0.6 mL), *m*CPBA (75% active, 7.5 mmol, 1.73 g) and $TsOH \cdot H_2O$ (7.5 mmol, 1.5 g) in CH_2Cl_2 (25 mL). The reaction time was 30 min. Recrystallization yielded a colorless solid (2.73 g, 56%).

^{1}H NMR (250 MHz, MeOD): δ = 8.52 (s, 1H), 8.37 (d, *J* = 8.2 Hz, 1H), 8.21 – 8.08 (m, 2H), 7.97 (d, *J* = 7.9 Hz, 1H), 7.75 – 7.63 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.13 – 7.02 (m, 2H), 3.85 (s, 3H), 2.36 (s, 3H).

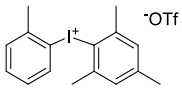
Mesityl(phenyl)iodonium triflate (11f)[46]



Mesityl(phenyl)iodonium triflate (**11f**) was prepared according to TP 8 from iodobenzene (**8q**) (10 mmol, 1.1 mL), mesitylene (**5v**) (11 mmol, 1.5 mL), *m*CPBA (75% active, 11 mmol, 2.53 g) and TfOH (17 mmol, 1.5 mL) in CH_2Cl_2 (50 mL). The reaction time was 3 h. Recrystallization yielded a colorless solid (4.25 g, 90%).

^{1}H NMR (250 MHz, DMSO): δ = 8.03 – 7.92 (m, 2H), 7.69 – 7.57 (m, 1H), 7.56 – 7.44 (m, 2H), 7.22 (s, 2H), 2.60 (s, 6H), 2.29 (s, 3H).

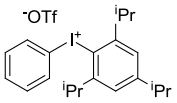
Mesityl(o-tolyl)iodonium triflate (11g)[46]



Mesityl(*o*-tolyl)iodonium triflate (**11g**) was prepared according to TP 8 from 2-iodotoluene (**8v**) (10 mmol, 1.3 mL), mesitylene (**5v**) (11 mmol, 1.5 mL), *m*CPBA (65% active, 10 mmol, 2.65 g) and TfOH (17 mmol, 1.5 mL) in CH_2Cl_2 (50 mL). The reaction time was 3 h. Recrystallization yielded a colorless solid (3.95 g, 81%).

^{1}H NMR (250 MHz, $CDCl_3$): (250 MHz, $CDCl_3$) δ 7.51 – 7.39 (m, 3H), 7.21 – 7.13 (m, 1H), 7.12 (s, 2H), 2.60 (s, 9H), 2.36 (s, 3H).

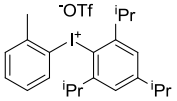
Phenyl(2,4,6-triisopropylphenyl)iodonium triflate (11h)[100]



Phenyl(2,4,6-triisopropylphenyl)iodonium triflate (**11h**) was prepared according to TP 8 from iodobenzene (**8q**) (10 mmol, 1.3 mL), 1,3,5-triisopropylbenzene (**5u**) (11 mmol, 2.7 mL), *m*CPBA (75% active, 11 mmol, 2.53 g) and TfOH (15 mmol, 1.3 mL) in CH_2Cl_2 (50 mL). The reaction time was 3 h. Recrystallization yielded a colorless solid (4.42 g, 80%).

^{1}H NMR (250 MHz, DMSO): δ = 7.97 – 7.89 (m, 2H), 7.69 – 7.58 (m, 1H), 7.59 – 7.48 (m, 2H), 7.31 (s, 2H), 3.46 – 3.35 (m, 2H), 3.08 – 2.88 (m, 1H), 1.31 – 1.15 (m, 18H).

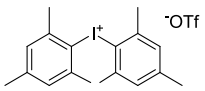
o-Tolyl(2,4,6-triisopropylphenyl)iodonium triflate (11i)[88]



o-Tolyl(2,4,6-triisopropylphenyl)iodonium triflate (**11i**) was prepared according to TP 8 from 2-iodotoluene (**8v**) (9.0 mmol, 1.2 mL), 1,3,5-triisopropylbenzene (**5u**) (10 mmol, 2.4 mL), *m*CPBA (65% active, 10 mmol, 2.65 g) and TfOH (15 mmol, 1.3 mL) in CH_2Cl_2 (40 mL). The reaction time was 2 h. Recrystallization yielded a colorless solid (3.85 g, 79%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.50 – 7.41 (m, 2H), 7.28 – 7.22 (m, *J* = 6.1 Hz, 2H), 7.21 – 7.13 (m, 2H), 3.27 – 3.09 (m, 2H), 3.06 – 2.89 (m, 1H), 2.66 (s, 3H), 1.29 (d, *J* = 6.9 Hz, 6H), 1.23 (d, *J* = 6.7 Hz, 12H).

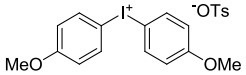
Dimesityliodonium triflate (11j)[46]



Dimesityliodonium triflate (**11j**) was prepared according to TP 9 from mesitylene (**5v**) (41 mmol, 5.7 mL), I_2 (10 mmol, 2.54 g), *m*CPBA (75% active, 30 mmol, 6.9 g) and TfOH (20 mmol, 1.76 ml) in CH_2Cl_2 (50 mL). The reaction time was 1 h. Recrystallisation yielded a colorless solid in quantitative yield.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.04 (s, 4H), 2.49 (s, 12H), 2.31 (s, 6H).

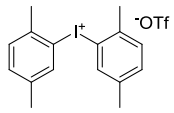
Bis(4-methoxyphenyl)iodonium tosylate (11k)[70]



Bis(4-methoxyphenyl)iodonium tosylate (**11k**) was prepared according to TP 9 from anisole (**5c**) (28 mmol, 3.1 mL), I_2 (8.0 mmol, 2.03 g), *m*CPBA (75% active, 20 mmol, 4.6 g) and $TsOH \cdot H_2O$ (28 mmol, 5.49 g) in CH_2Cl_2 (40 mL). The reaction time was 16 h. Column chromatography (CH_2Cl_2:MeOH 20:1) yielded the analytically pure product as yellow solid in quantitative yield.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.9 Hz, 4H), 7.59 (d, *J* = 8.1 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 4H), 3.78 (s, 6H), 2.31 (s, 3H).

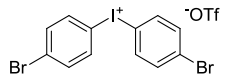
Bis(2,5-dimethylphenyl)iodonium triflate (11l)[46]



Bis(2,5-dimethylphenyl)iodonium triflate (**11l**) was prepared according to TP 9 from *p*-xylene (**5x**) (100 mmol, 12.3 mL), I_2 (10 mmol, 2.54 g), *m*CPBA (75% active, 40 mmol, 9.2 g) and TfOH (20 mmol, 1.76 ml) in CH_2Cl_2 (50 mL). The reaction time was 16 h. Recrystallisation yielded a colorless solid with a purity of 90%.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.75 – 7.67 (m, 2H), 7.38 – 7.29 (m, 4H), 2.56 (s, 6H), 2.33 (s, 6H).

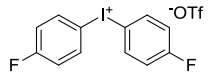
Bis(4-bromophenyl)iodonium triflate (11m)[46]



Bis(4-bromophenyl)iodonium triflate (**11m**) was synthesized according to TP 9 from bromobenzene (**8n**) (100 mmol, 10.5 mL), I_2 (10 mmol, 2.54 g), *m*CPBA (75% active, 40 mmol, 9.2 g) and TfOH (20 mmol, 1.8 ml) in CH_2Cl_2 (50 mL). The reaction time was 20 min. Recrystallization yielded the product as orange solid (2.90 g, 50%).

^{1}H NMR (250 MHz, DMSO): δ = 8.17 (d, *J* = 8.7 Hz, 4H), 7.76 (d, *J* = 8.7 Hz, 4H).

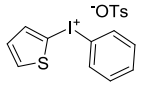
Bis(4-fluorophenyl)iodonium triflate (11n)[46]



Bis(4-fluorophenyl)iodonium triflate (**11n**) was synthesized according to TP 9 from fluorobenzene (**8ab**) (80 mmol, 7.5 mL), I_2 (8 mmol, 2.03 g), *m*CPBA (75% active, 32 mmol, 7.36 g) and TfOH (16 mmol, 1.4 ml) in CH_2Cl_2 (40 mL). The reaction time were 16 h. Recrystallization yielded the product as orange solid (2.09 g, 56%).

^{1}H NMR (250 MHz, DMSO): δ = 8.39 – 8.25 (m, 4H), 7.50 – 7.33 (m, 4H).

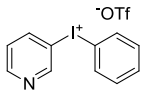
Phenyl(thiophen-2-yl)iodonium tosylate (11o)[70]



Phenyl(thiophen-2-yl)iodonium tosylate (**11o**) was prepared according to TP 8 from Koser's reagent (2.0 mmol, 784.4 mg) and thiophene (**5m**) (2.0 mmol, 0.2 mL) in TFE (50 mL) for 24 h at 25 °C. Recrystallization yielded a colorless solid in quantitative yield.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.00 – 7.90 (m, 2H), 7.81 – 7.75 (m, 1H), 7.59 – 7.52 (m, 1H), 7.52 – 7.41 (m, 3H), 7.38 – 7.28 (m, 2H), 7.08 – 6.96 (m, 3H), 2.31 (s, 3H).

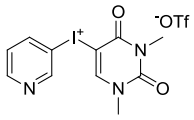
Phenyl(pyridin-3-yl)iodonium triflate (11p)[107]



Phenyl(pyridin-3-yl)iodonium triflate (**11p**) was prepared according to TP 10 from 3-iodopyriridine (**8b**) (4.88 mmol, 1.0 g), benzene (**5a**) (5.4 mmol, 0.5 mL), TfOH (19.5 mmol, 1.72 mL) and *m*CPBA (70% active, 7.3 mmol, 1.81 g) in CH_2Cl_2 (20 mL). After deprotonation, a colorless solid was obtained (291.4 mg, 9%).

^{1}H NMR (400 MHz, MeOD): δ = 9.23 (d, *J* = 2.1 Hz, 1H), 8.83 (dd, *J* = 4.8, 1.3 Hz, 1H), 8.64 – 8.60 (m, 1H), 8.27 – 8.22 (m, 2H), 7.76 – 7.70 (m, 1H), 7.59 – 7.53 (m, 3H).

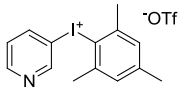
(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)(pyridin-3-yl)iodonium(11q)[107]



(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)(pyridin-3-yl)iodonium (**11q**) was prepared according to TP 10 from 3-iodopyriridine (**8b**) (3.2 mmol, 665.5 mg), *N*,*N*-dimethyluracil (**5y**) (3.6 mmol, 500 mg), TfOH (13.0 mmol, 1.1 mL) and *m*CPBA (70% active, 4.9 mmol, 1.0 g) in CH_2Cl_2 (20 mL). After deprotonation, a colorless solid was obtained (267.4 mg, 16%).

^{1}H NMR (400 MHz, MeOD): δ = 9.19 (d, *J* = 2.1 Hz, 1H), 8.94 (s, 1H), 8.84 (dd, *J* = 4.8, 1.3 Hz, 1H), 8.59 (ddd, *J* = 8.3, 2.2, 1.5 Hz, 1H), 7.59 – 7.56 (m, 1H), 3.49 (s, 3H), 3.34 (s, 3H).

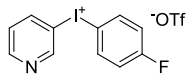
Mesityl(pyridin-3-yl)iodonium triflate (11r)[107]



Mesityl(pyridin-3-yl)iodonium triflate (**11r**) was prepared according to TP 10 from 3-iodopyriridine (**8b**) (2.44 mmol, 500 mg), mesitylene (**5v**) (2.7 mmol, 0.4 mL), TfOH (9.8 mmol, 0.86 mL) and *m*CPBA (70% active, 3.7 mmol, 902.3 mg) in CH_2Cl_2 (10 mL). After deprotonation, a colorless solid was obtained (882.6 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.99 (d, *J* = 2.1 Hz, 1H), 8.79 (dd, *J* = 4.7, 1.2 Hz, 1H), 8.33 (ddd, *J* = 8.3, 2.3, 1.4 Hz, 1H), 7.54 (dd, *J* = 8.3, 4.8 Hz, 1H), 7.26 (s, 2H), 2.68 (s, 6H), 2.37 (s, 3H).

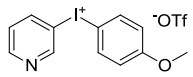
(4-Fluorophenyl)(pyridin-3-yl)iodonium triflate (11s)[107]



(4-Fluorophenyl)(pyridin-3-yl)iodonium triflate (**11s**) was prepared according to TP 10 from 3-iodopyridine (**8b**) (2.44 mmol, 500 mg), fluorobenzene (**8ab**) (2.7 mmol, 0.3 mL), TfOH (9.8 mmol, 0.86 mL) and *m*CPBA (70% active, 3.7 mmol, 902.3 mg) in CH_2Cl_2 (10 mL). After deprotonation, a colorless solid was obtained (740.2 mg, 67%).

^{1}H NMR (400 MHz, MeOD): δ = 9.32 (d, *J* = 1.8 Hz, 1H), 8.90 (d, *J* = 4.8 Hz, 1H), 8.77 (d, *J* = 8.4 Hz, 1H), 8.35 – 8.28 (m, 2H), 7.71 (dd, *J* = 8.3, 5.0 Hz, 1H), 7.34 (t, *J* = 8.7 Hz, 2H).

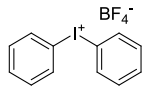
(4-Methoxyphenyl)(pyridin-3-yl)iodonium triflate (11t)[107]



(4-Methoxyphenyl)(pyridin-3-yl)iodonium triflate (**11t**) was prepared according to TP 10 from 3-iodo-pyridine (**8b**) (1.46 mmol, 300 mg), anisole (**5c**) (1.8 mmol, 0.2 mL), TfOH (5.8 mmol, 0.52 mL) and *m*CPBA (70% active, 2.56 mmol, 630.9 mg) in CH_2Cl_2 (10 mL). After deprotonation, a colorless solid was obtained (441.8 mg, 66%).

^{1}H NMR (250 MHz, MeOD): δ = 9.19 (d, *J* = 2.2 Hz, 1H), 8.82 (dd, *J* = 4.8, 1.4 Hz, 1H), 8.56 (ddd, *J* = 8.3, 2.3, 1.4 Hz, 1H), 8.19 – 8.10 (m, 2H), 7.56 (ddd, *J* = 8.3, 4.8, 0.6 Hz, 1H), 7.14 – 7.02 (m, 2H), 3.86 (s, 3H).

Diphenyliodonium tetrafluoridoborate (11w) [99]

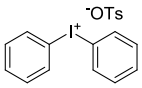


In an oven-dried round-bottom flask equipped with a magnetic stirrer *m*CPBA (75% active, 1.1 equiv, 11 mmol, 2.53 g) was dissolved in CH_2Cl_2 (35 mL), before addition of iodobenzene (**8p**) (1.0 equiv, 10 mmol, 1.3 mL), boron trifluoride diethyl etherate (2.0 equiv, 20 mmol, 2.5 mL) and stirred at 25 °C for

30 min. After cooling to 0 °C, phenyl boronic acid (**6a**) (1.1 equiv, 11 mmol, 1.22 g) was added mixture was allowed to stir for 15 min at 25 °C. The reaction mixture was filtered over a pad of silica (15 g) and diluted with CH_2Cl_2:MeOH (20:1, 360 mL), then concentrated under reduced pressure diluted with Et_2O (30 mL), stirred for 30 min and then filtered and washed twice with Et_2O (30 mL). After drying under high vacuum, the analytically pure product was afforded as a beige solid (3.32 g, 90%).

^{1}H NMR (250 MHz, d_6-DMSO): δ = 8.30 – 8.21 (m, 4H), 7.72 – 7.62 (m, 2H), 7.60 – 7.46 (m, 4H).

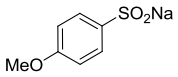
Diphenyliodonium tosylate (11x)[100]



A solution of diphenyliodonium tetrafluoridoborate (**11w**) (3.6 mmol, 1.33 g) was dissolved in CH_2Cl_2 (15 mL) and extracted with aq. NaOTs-solution (30 mL, 1.1 M in H_2O). Then, the aqueous phase was extracted twice with CH_2Cl_2 (15 mL). Afterwards the organic layers were concentrated under reduced pressure. This procedure is repeated five times. Then the anion exchange is quantitative and yields a colorless solid.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.99 – 7.87 (m, 4H), 7.87 – 7.79 (m, 4H), 7.60 – 7.40 (m, 2H), 7.39 – 7.27 (m, 4H), 2.39 (s, 3H).

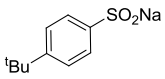
Sodium 4-methoxybenzenesulfinate (7a)[108]



Sodium 4-methoxybenzenesulfinate (**7a**) was prepared according to TP 11 from 4-methoxybenzene sulfonyl chloride (**3b**) (10 mmol, 2.06 g), $NaHCO_3$ (20 mmol, 1.68 g) and Na_2SO_3 (20 mmol, 2.5 g) in H_2O (10 mL). After recrystallization out of EtOH, a colorless solid in quant. yield was obtained (purity 95%).

^{1}H NMR (250 MHz, DMSO): δ = 7.47 – 7.32 (m, 2H), 6.92 – 6.81 (m, 2H), 3.74 (s, 3H).

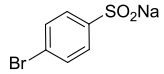
Sodium 4-(tert-butyl)benzenesulfinate (7b)[108]



Sodium 4-(*tert*-butyl)benzenesulfinate (**7b**) was prepared according to TP 11 from 4-*tert*-butylbenzene sulfonyl chloride (**3c**) (10 mmol, 2.33 g), $NaHCO_3$ (20 mmol, 1.68 g) and Na_2SO_3 (20 mmol, 2.5 g) in H_2O (10 mL). After recrystallization from MeOH, a colorless solid in quant. yield was obtained (purity 80%).

^{1}H NMR (250 MHz, DMSO): δ 7.55 – 7.30 (m, 4H), 1.27 (s, 9H).

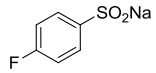
Sodium 4-bromobenzenesulfinate (7c)[108]



Sodium 4-bromobenzenesulfinate (**7c**) was prepared according to TP 11 from 4-bromobenzene sulfonyl chloride (**3d**) (10 mmol, 2.06 g), $NaHCO_3$ (20 mmol, 1.68 g) and Na_2SO_3 (20 mmol, 2.5 g) in H_2O (10 mL). After recrystallization from EtOH, a colorless solid in quant. yield was obtained (purity 90%).

^{1}H NMR (250 MHz, DMSO): δ = 7.56 – 7.48 (m, 2H), 7.48 – 7.39 (m, 2H).

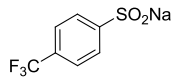
Sodium 4-fluorobenzenesulfinate (7d)[108]



Sodium 4-fluorobenzenesulfinate (**7d**) was prepared according to TP 11 from 4-fluorobenzene sulfonyl chloride (**3e**) (10 mmol, 1.95 g), $NaHCO_3$ (20 mmol, 1.68 g) and Na_2SO_3 (20 mmol, 2.5 g) in H_2O (10 mL). After recrystallization out of EtOH, a colorless solid in quant. yield was obtained.

^{1}H NMR (250 MHz, DMSO): δ = 7.55 – 7.41 (m, 2H), 7.16 – 7.05 (m, 2H).

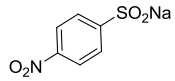
Sodium 4-(trifluoromethyl)benzenesulfinate (7e)[108]



Sodium 4-(trifluoromethyl)benzenesulfinate (**7e**) was prepared according to TP 11 from 4-trifluoromethyl benzene sulfonyl chloride (**3f**) (2.0 mmol, 500 mg), $NaHCO_3$ (4.0 mmol, 504.2 mg) and Na_2SO_3 (4.0 mmol, 336.0 mg) in H_2O (5.0 mL). After recrystallization from EtOH, a colorless solid in quant. yield was obtained.

^{1}H NMR (250 MHz, MeOD): δ = 7.83 (m, 2H), 7.79 – 7.69 (m, 2H).

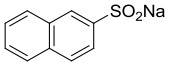
Sodium 4-nitrobenzenesulfinate (7f)[108]



Sodium 4-nitrobenzenesulfinate (**7f**) was prepared according to TP 11 from 4-nitrobenzene sulfonyl chloride (**3g**) (10 mmol, 2.22 g), $NaHCO_3$ (20 mmol, 1.68 g) and Na_2SO_3 (20 mmol, 2.5 g) in H_2O (10 mL). After recrystallization from MeOH, an orange solid was obtained (209 mg, 10%).

^{1}H NMR (250 MHz, DMSO): δ = 8.23 – 8.15 (m, 2H), 7.76 – 7.65 (m, 2H).

Sodium naphthalene-2-sulfinate (7g)[108]



Sodium naphthalene-2-sulfinate (**7g**) was prepared according to TP 11 from naphthalene-2-sulfonyl chloride (**3h**) (10 mmol, 2.27 g), $NaHCO_3$ (20 mmol, 1.68 g) and Na_2SO_3 (20 mmol, 2.5 g) in H_2O (10 mL). After recrystallization from MeOH, a colorless solid in quant. yield was obtained.

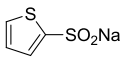
^{1}H NMR (250 MHz, DMSO): δ = 8.14 (s, 1H), 8.00 – 7.93 (m, 1H), 7.93 – 7.89 (m, 1H), 7.89 – 7.83 (m, 1H), 7.71 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.56 – 7.48 (m, 2H).

Sodium quinoline-8-sulfinate (7h)[108]

Sodium quinoline-8-sulfinate (**7h**) was prepared according to TP 11 from 8-quinoline sulfonyl chloride (**3i**) (5.0 mmol, 1.14 mg), Na_2CO_3 (9.0 mmol, 953.9 mg) and Na_2SO_3 (11.5 mmol, 1.45 g) in H_2O (5.0 mL). After recrystallization from EtOH, a colorless solid in quant. yield was obtained (purity 90%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.91 (dd, *J* = 4.3, 1.8 Hz, 1H), 8.38 – 8.31 (m, 1H), 8.26 (dt, *J* = 8.5, 2.7 Hz, 1H), 7.95 (dt, *J* = 7.4, 3.7 Hz, 1H), 7.68 (dt, *J* = 8.7, 4.4 Hz, 1H), 7.52 (dd, *J* = 8.3, 4.3 Hz, 1H).

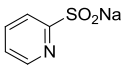
Sodium thiophene-2-sulfinate (7i)[108]



Sodium thiophene-2-sulfinate (**7i**) was prepared according to TP 11 from thiophene-2-sulfonyl chloride (**3j**) (5.0 mmol, 913.3 mg), Na_2CO_3 (9.0 mmol, 953.9 mg) and Na_2SO_3 (11.5 mmol, 1.45 g) in H_2O (5.0 mL). After recrystallization from EtOH, a colorless solid was obtained (630 mg, 74%).

^{1}H NMR (250 MHz, DMSO): δ = 7.42 – 7.37 (m, 1H), 6.99 – 6.91 (m, 2H).

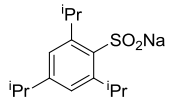
Sodium pyridine-2-sulfinate (7j)[109]



In a round-bottom flask 2-mercaptopyridine (**35**) (1.0 equiv, 4.5 mmol, 528 mg) were dissolved in aqueous NaOH-solution (0.6 M solution in H_2O, 20 mL) and EtOH (20 mL). Then H_2O_2 (30 w-% in H_2O, 2.0 equiv, 1.0 mL) was added. The reaction was monitored via TLC and finished after 20 min. After concentrating, the residue was crystallized from EtOH and delivered a colorless solid in quant. yield.

^{1}H NMR (250 MHz, DMSO): δ = 8.39 (ddd, *J* = 4.7, 1.7, 0.9 Hz, 1H), 7.77 (td, *J* = 7.5, 1.7 Hz, 1H), 7.69 – 7.62 (m, 1H), 7.21 (ddd, *J* = 7.3, 4.8, 1.4 Hz, 1H).

Sodium 2,4,6-triisopropylbenzenesulfinate (7k)[110]

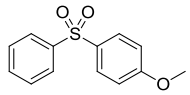


In a round bottom flask zinc (2.5 equiv, 12.5 mmol, 817.0 mg) was suspended in 75 °C hot water (10 mL), then triisopropylbenzene sulfonyl chloride (**3a**) (1.0 eqiuv, 5.0 mmol, 1.55 g) was added in portions, before the mixture stirred at 90 °C for 1 h. After cooling to 25 °C, NaOH (12 M solution in H_2O, 1.0 mL) and Na_2CO_3 (1.0 g) were added. Afterwards it was filtered over a pad of celite and diluted with hot water (10 mL). After concentrating to about half the volume under reduced pressure, the solution was cooled to 4 °C and sodium 2,4,6-triisopropylbenzenesulfinate (**7k**) crystallized. After filtrating the crystals and washing with water, the residue was recrystalized from EtOH. The product was yielded as colorless solid (201 mg, 13%).

^{1}H NMR (250 MHz, MeOD): δ = 7.10 (s, 1H), 7.00 (s, 1H), 4.58 – 4.30 (m, 2H), 2.92 – 2.74 (m, 1H), 1.36 – 1.15 (m, 18H).

8.3.2 Target Molecules

1-(4-Methoxyphenylsulfonyl)benzene (2a)



1-(4-Methoxyphenylsulfonyl)benzene (**2a**) was synthesized from commercial arylsulfinic acid sodium salts (**7a**, **7l**), crude benzenesulfinic acid lithium salt (**37a**), and from 4-methoxyphenyllithium (**36f**) prepared by halogen-lithium-exchange of 4-bromoanisole (**8e**) with *n*BuLi, and 4-iodoanisole (**8a**) with *t*BuLi, respectively.[196,197] Furthermore **2a** was prepared from benzenesulfinic acid magnesium and zinc (**34a** and **41a**) salts and bromo(4-methoxyphenyl)magnesium·LiCl (**18i**) and bromo(4-methoxyphenyl)zinc·LiCl (**42c**) which was prepared by transmetalation with $ZnCl_2$ of the latter.[137,198]

1-(4-Methoxyphenylsulfonyl)benzene (**2a**) was also prepared via a nickel-catalyzed amination reaction.

From 4-methoxybenzenesulfinic acid sodium salt (7a): 1-(4-Methoxyphenylsulfonyl)benzene (**2a**) was synthesized according to TP 1 from diphenyliodonium triflate (**11b**) (0.55 mmol, 236.6 mg) and 4-methoxybenzenesulfinic acid sodium salt (**7a**) (0.5 mmol, 102.2 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as colorless solid (111.7 mg, 90%).

From benzenesulfinic acid sodium salt (7l): 1-(4-Methoxyphenylsulfonyl)benzene (**2a**) was also prepared according to TP 1 from bis(4-methoxyphenyl)iodonium tosylate (**11k**) (0.55 mmol, 248.8 mg) and benzenesulfinic acid sodium salt (**7l**) (0.5 mmol, 82.2 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as colorless solid (108.0 mg, 87%).

From benzenesulfinic acid lithium salt (37a): According to TP 2 **2a** was synthesized from benzenesulfinic acid lithium salt (**37a**) (65w-%, 170.9 mg, 0.75 mmol) and bis(4-methoxyphenyl)iodonium tosylate (**11k**) (256.2 mg, 0.50 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 9:1 → 1:1) yielded the product as colorless solid (91.5 mg, 74%).

From 4-bromoanisole (8e) and *n*BuLi: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with 4-bromoanisole (**8e**) (0.1 mL, 1.5 equiv, 0.75 mmol) in dry THF (1.0 mL) and cooled to -78 °C and then *n*BuLi (0.38 mL, 2.13 M solution in hexanes, 0.80 mmol, 1.6 equiv) was added drop wise. The mixture was allowed to stir at this temperature for 2 h, before liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed according to procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as a colorless solid (96.9 mg, 78%).

From 4-iodoanisole (8a) and *t*BuLi: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with 4-iodoanisole (**8a**) (175.5 mg, 1.5 equiv, 0.75 mmol) in dry THF (1.0 mL) and cooled to -78 °C and then *t*BuLi (0.48 mL, 1.64 M solution in pentane, 0.80 mmol, 1.6 equiv) was added drop wise. The mixture was allowed to warm to -50 °C within 2 h, before liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed according to procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as a colorless solid (65.2 mg, 53%).

From benzenesulfinic acid magnesium chloride salt (34a): 1-methoxy-4-(phenylsulfonyl)benzene (**2a**) was prepared according to TP 4 from benzenesulfinic acid magnesium chloride salt (**34a**) (55w-%, 91.3 mg, 0.25 mmol) and bis(4-methoxyphenyl)iodonium tosylate (**11k**) (380.1 mg, 0.75 mmol) in DMSO (0.5 mL).

Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (38.4 mg, 62%).

From bromo(4-methoxyphenyl)magnesium·LiCl (18i): 1-methoxy-4-(phenylsulfonyl)benzene (**2a**) was also prepared according to TP 5 from bromo(4-methoxyphenyl)magnesium·LiCl (**18i**) (0.9 M solution in THF, 0.83 mL, 0.75 mmol, 1.5 equiv) and diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (43.3 mg, 35%).

From *in situ* generated benzenesulfinic acid zinc salt (41a): 1-methoxy-4-(phenylsulfonyl)benzene (**2a**) was also prepared according to TP 6 from *in situ* generated benzenesulfinic acid zinc salt (**41a**) (assume 0.75 mmol) and bis(4-methoxyphenyl)iodonium tosylate (**11k**) (256.2 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (86.0 mg, 70%).

From bromo(4-methoxyphenyl)magnesium·LiCl (18i) and $ZnCl_2$: To a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum charged with bromo(4-methoxy-phenyl)magnesium·LiCl (**18i**) (0.9 M solution in THF, 0.85 ml; 0.75 mmol, 1.5 equiv) was added $ZnCl_2$ (0.7 M solution in THF, 1.1 mL, 0.80 mmol, 1.6 equiv) and stirred at 25 °C for 30 min. After cooling to -40 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents, diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMSO (1.0 mL) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the analytically pure product as a colorless solid (55.1 mg, 44%).

Nickel-catalyzed amination: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with 4-iodoanisole (**8a**) (1.0 equiv, 0.5 mmol, 117.2 mg), benzenesulfinic acid sodium salt (**7l**) (1.1 equiv, 0.55 mmol, 90.4 mg) and Ni(*o*-tolyl)$(PMePh_2)_2Cl$ (**54**) (5 mol-%, 29.3 mg) in NMP (2.0 mL). The reaction mixture was heated to 105 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed three times with dist. H_2O (15 mL) and once with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the analytically pure product (107.5 mg, 86%).

m.p.: 92 – 93 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.97 – 7.79 (m, 4H), 7.59 – 7.40 (m, 3H), 7.04 – 6.86 (m, 2H), 3.83 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ = 163.50, 142.50, 133.24, 132.95, 130.00, 129.31, 127.42, 114.63, 55.76.

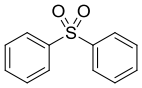
MS: m/z: calc. for $C_{13}H_{12}O_3S+Na^+$ 271.04, found 271.08.

IR (cm^{-1}): 1590 (s), 1576 (s), 1496 (s), 1464 (m), 1445 (s), 1315 (s, -SO_2-), 1297 (s), 1260 (s), 1185 (m), 1147 (s, -SO_2-), 1104 (s), 1071 (s), 1019 (s), 998 (s), 832 (s), 802 (s), 755 (m), 728 (s), 709 (s), 686 (s), 628 (m), 576 (s), 552 (s), 453 (m).

R_f (cyclohexane:EtOAc 9:1): 0.13.

Analytical data are consistent with literature.[199]

Diphenylsulfone (2b)



1-(Phenylsulfonyl)benzene (**2b**) was synthesized starting from commercial benzenesulfinic acid sodium salt (**7l**), crude benzenesulfinic lithium salt (**37a**), from phenyllithium (**36a**) or from phenyllithium prepared by lithiation of benzene (**5a**) with *n*BuLi,[117] and various phenyl-Grignard reagents (**18**) and phenylzinc chloride (**42b**), prepared via transmetalation with *i*PrMgCl·LiCl.[137,198]

From benzenesulfinic acid sodium salt (7l): Diphenylsulfone (**2b**) was synthesized according to TP 1 from diphenyliodonium triflate (**11b**) (0.55 mmol, 236.6 mg) and benzenesulfinic acid sodium salt (**7l**) (0.5 mmol, 82.2 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as colorless solid (102.4 mg, 94%).

From benzenesulfinic lithium salt (37a): According to TP 2 **2b** was prepared from benzenesulfinic acid lithium salt (**37a**) (65w-%, 170.9 mg, 0.75 mmol) and diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as colorless solid (91.3 mg, 84%).

From phenyllithium (36a): A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with phenyllithium (**36a**) (0.65 mL, 1.55 M solution in Et_2O, 0.75 mmol, 1.5 equiv) and cooled to -78 °C and then liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C, excess SO_2 and solvents were removed according to procedure A. Then diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMF (1.0 mL) were added and the mixture was stirred at 90 °C for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 4:1) yielded the product as colorless solid (90.0 mg, 83%).

From benzene (5a) and *n*BuLi: To a solution of *n*BuLi (0.34 mL, 2.45 M solution in hexane, 0.8 mmol, 1.6 equiv) and TMEDA (0.11 mL, 0.75 mmol, 1.5 equiv) in a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was added benzene (**5a**) (67 µL, 0.75 mmol, 1.5 equiv). The mixture

was allowed to stir at 25 °C for 3 h. After removal of excess SO_2 and solvents by procedure A, diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL) were added and the mixture was stirred at 90 °C for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) afforded the analytically pure product as colorless solid (56.6 mg, 52%).

From bromobenzene (8n) and *n*BuLi: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with bromobenzene (**8n**) (0.1 mL, 1.5 equiv, 0.75 mmol) in dry THF (1.0 mL) and cooled to -78 °C and then *n*BuLi (0.35 mL, 2.45 M solution in hexanes, 0.83 mmol, 1.65 equiv) was added drop wise. The mixture was allowed to warm to -30 °C within 1 h and then recooled to 78 °C, before liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed according to procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**#**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as a colorless solid (29.4 mg, 27%).

From benzenesulfinic acid magnesium chloride salt (34a): According to TP 4 **2b** was synthesized from benzenesulfinic acid magnesium chloride salt (**34a**) (70w-%, 186.6 mg, 0.65 mmol) and diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 20:1 → 4:1) yielded the product as colorless solid (82.0 mg, 75%).

From benzenesulfinic acid magnesium chloride salt·LiCl (34b): According to TP 4 **2b** was synthesized from benzenesulfinic acid magnesium chloride salt·LiCl (**34b**) (56w-%, 217.2 mg, 0.50 mmol) and diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 4:1) yielded the product as colorless solid (87.5 mg, 81%).

From benzenesulfinic acid magnesium bromide salt·LiCl (34c): According to TP 4 **2b** was synthesized from benzenesulfinic acid magnesium bromide salt·LiCl (**34c**) (62w-%, 232.1 mg, 0.50 mmol) and diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 4:1) yielded the product as colorless solid (42.6 mg, 40%).

From benzenesulfinic acid magnesium iodode salt·LiCl (34d): According to TP 4 **2b** was synthesized from benzenesulfinic acid magnesium iodode salt·LiCl (**34d**) (65w-%, 257.5 mg, 0.50 mmol) and diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 4:1) yielded the product as colorless solid (40.0 mg, 37%).

From *in situ* generated benzenesulfinic acid zinc salt (41a): According to TP 6 **2b** was prepared from crude benzenesulfinic acid zinc salt (**41a**) (assume 0.75 mmol) and diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (72.8 mg, 67%).

m.p.: 122 - 124 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.96-7.93 (m, 4H), 7.58-7.47 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ = 141.73, 133.30, 129.40, 127.77.

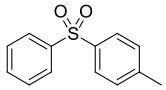
MS: m/z: calc. for $C_{12}H_{10}O_2S+Na^+$ 241.03, found 241.08.

IR (cm^{-1}): 3070 (w), 2923 (w), 1581 (w), 1477 (w), 1447 (m), 1308 (s, -SO_2-), 1294 (s). 1181 (m), 1151 (s,-SO_2-), 1103 (s), 1068 (m), 1023 (m), 997 (m), 935 (w), 759 (s), 726 (s), 682 (s), 582 (s), 557 (s), 427 (w).

R_f (Cyclohexane:EtOAc 9:1): 0.18.

Analytical data are consistent with literature. [199]

1-Methyl-4-(phenylsulfonyl)benzene (2c)



1-Methyl-4-(phenylsulfonyl)benzene (**2c**) was synthesized starting from commercial available sulfinic acid sodium salts **7l** and **7m**; from benzenesulfinic acid lithium (**37a**), magnesium (**34a**) and zinc (**41a**) salts, as well as from *p*-tolylmagnesium chloride (**18h**) and *p*-tolylzinc chloride (**42d**), generated from **18h** and $ZnCl_2$.[137,198]

From *p*-toluenebenzenesulfinic acid sodium salt (7m): 1-Methyl-4-(phenylsulfonyl)benzene (**2c**) was prepared according to TP 1 from diphenyliodonium triflate (**11b**) (0.55 mmol, 236.6 mg) and *p*-toluene-benzenesulfinic acid sodium salt (**7m**) (0.5 mmol, 93.8 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as colorless solid (111.4 mg, 96%).

From benzenesulfinic acid sodium salt (7l): 1-Methyl-4-(phenylsulfonyl)benzene (**2c**) was also synthesized according to TP 1 from di-*p*-tolyliodonium triflate (**11c**) (0.55 mmol, 252.0 mg) and benzenesulfinic acid sodium salt (**7l**) (0.5 mmol, 82.2 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as colorless solid (107.0 mg, 92%).

From benzenesulfinic acid lithium salt (37a): 1-Methyl-4-(phenylsulfonyl)benzene (**2c**) was prepared according to TP 2 from benzenesulfinic acid lithium salt (**37a**) (65w-%, 170.9 mg, 0.75 mmol) and di-*p*-tolyliodonium triflate (**11c**) (229.1 mg, 0.50 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as colorless solid (93.3 mg, 80%).

From benzenesulfinic acid magnesium chloride salt (34a): According to TP 4 1-methyl-4-(phenylsulfonyl)benzene (**2c**) was synthesized from benzenesulfinic acid magnesium chloride salt (**34a**) (70w-%, 215.3 mg, 0.75 mmol) and di-*p*-tolyliodonium triflate (**11c**) (229.1 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 20:1 → 4:1) yielded the product as colorless solid (72.2 mg, 62%).

From *p*-tolylmagnesium chloride·LiCl (18h): 1-methyl-4-(phenylsulfonyl)benzene (**2c**) was also synthesized according to TP 5 from *p*-tolylmagnesium·chlride·LiCl (**18h**) (1.1 M solution in THF, 0.46 mL, 0.5 mmol, 1.0 equiv), diphenyliodonium triflate (**11b**) (643.3 mg, 1.5 mmol, 3.0 equiv) and SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (80.6 mg, 69%).

From *in situ* generated benzenesulfinic acid zinc salt (41a): 1-methyl-4-(phenylsulfonyl)benzene (**2c**) was also synthesized according to TP 6 from *in situ* generated benzenesulfinic acid zinc salt (**41a**) (assume 0.75 mmol) and di-*p*-tolyliodoniumiodonium triflate (**11c**) (229.1 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (86.6 mg, 75%).

From *p*-tolylmagnesium bromide·LiCl (18h) and $ZnCl_2$: To a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum charged with *p*-tolylmagnesium bromide·LiCl (**18h**) (0.9 M solution in THF, 0.85 ml, 0.75 mmol, 1.5 equiv) was added $ZnCl_2$ (0.7 M solution in THF, 1.1 mL, 0.83 mmol, 1.65 equiv) and stirred at 25 °C for 30 min. After cooling to -40 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents, diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMSO (1.0 mL) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 20:1 → 4:1) afforded the analytically pure product as a colorless solid (76.0 mg, 65%).

m.p.: 127 – 129 °C.

^{1}H-NMR (250 MHz, $CDCl_3$): δ = 7.98 – 7.89 (m, 2H), 7.86 – 7.79 (m, 2H), 7.58 – 7.44 (m, 3H), 7.29 (d, *J* = 8.0 Hz, 2H), 2.39 (s, 3H).

^{13}C-NMR (63 MHz, $CDCl_3$): δ = 144.27, 142.19, 138.85, 133.09, 130.03, 129.33, 127.86, 127.63, 21.67.

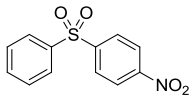
MS: m/z: calc. for $C_{13}H_{12}O_2S+Na^+$ 255.05, found 255.09.

IR (cm^{-1}): 1592 (w), 1447 (m), 1305 (m, -SO_2-), 1293 (m), 1152 (s, -SO_2-), 1105 (s), 1070 (m), 1043 (w), 1018 (w), 997 (w), 815 (m), 757 (w), 724 (s), 703 (m), 686 (s), 650 (s), 573 (s), 545 (s), 487 (m), 445 (w).

R_f (cyclohexane:EtOAc 9:1): 0.27.

Analytical data are consistent with literature.[199]

1-(4-Nitrophenylsulfonyl)benzene (2d)



1-(4-Nitrophenylsulfonyl)benzene (**2d**) was synthesized according to TP 1 from diphenyliodonium triflate (**11b**) (0.55 mmol, 236.6 mg) and 4-nitrobenzenesulfinic acid sodium salt (**7b**) (0.5 mmol, 139.5 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as yellowish powder (104.6 mg, 81%).

m.p.: 143 – 145 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.37 – 8.28 (m, 2H), 8.17 – 8.08 (m, 2H), 8.02 – 7.91 (m, 2H), 7.67 – 7.59 (m, 1H), 7.60 – 7.51 (m, 2H).

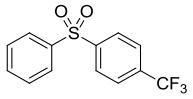
^{13}C-NMR (101 MHz, $CDCl_3$): δ = 150.48, 147.50, 140.16, 134.25, 129.82, 129.10, 128.16, 124.65.

MS: m/z: calc. for $C_{12}H_9NO_4S+H^+$ 264.03, found 263.95.

R_f (Cyclohexane:EtOAc 9:1): 0.30.

Analytical data are consistent with literature.[200]

1-(Trifluoromethyl)-4-(phenylsulfonyl)benzene (2e)



1-(Trifluoromethyl)-4-(phenylsulfonyl)benzene (**2e**) was synthesized according to TP 1 from diphenyl-iodonium triflate (**11b**) (0.55 mmol, 236.6 mg) and 4-triflouromethylbenzenesulfinic acid sodium salt (**7e**) (0.5 mmol, 122.2 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as colorless solid (118.4 mg, 83%).

m.p.: 90 – 101 °C.

^{1}H-NMR (250 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 8.2 Hz, 2H), 8.02 – 7.89 (m, 2H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.67 - 7.49 (m, 3H).

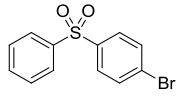
^{13}C-NMR (101 MHz, $CDCl_3$): δ = 145.38, 140.71, 134.97 (q, *J* = 33.1 Hz), 133.91, 129.67, 128.34, 128.03, 126.57 (q, *J* = 3.7 Hz), 123.23 (q, *J* = 273.1 Hz).

MS: m/z: calc. for $C_{13}H_9F_3O_2S+Na^+$ 309.02, found 309.07.

R_f (Cyclohexane:EtOAc 9:1): 0.26.

Analytical data are consistent with literature.[201]

1-Bromo-4-(phenylsulfonyl)benzene (2f)



From 4-bromobenzenesulfinic acid sodium salt (7c): 1-Bromo-4-(phenylsulfonyl)benzene (**2f**) was synthesized according to TP 1 from diphenyliodonium triflate (**11b**) (0.55 mmol, 236.6 mg) and 4-bromobenzenesulfinic acid sodium salt (**7c**) (0.5 mmol, 135.3 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as yellow solid (133.0 mg, 90%).

From benzenesulfinic acid sodium salt (7l): 1-bromo-4-(phenylsulfonyl)benzene (**2f**) was also prepared according to TP 1 from bis(4-bromophenyl)iodonium triflate (**11m**) (0.5 mmol, 323.4 mg) and benzenesulfinic acid sodium salt (**7l**) (0.5 mmol, 82.2 mg) in NMP (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as yellow solid (90.6 mg, 61%).

m.p.: 98 – 99 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.98 – 7.87 (m, 2H), 7.84 – 7.76 (m, 2H), 7.68 – 7.61 (m, 2H), 7.61 – 7.54 (m, 1H), 7.55 – 7.46 (m, 2H).

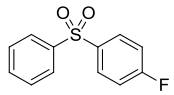
^{13}C-NMR (101 MHz, $CDCl_3$): δ = 141.30, 140.83, 133.59, 132.74, 129.55, 129.33, 128.59, 127.79.

MS: m/z: calc. for $C_{12}H_9BrO_2S+Na^+$ 318.94, found 318.99.

R_f (Cyclohexane:EtOAc 9:1): 0.29.

Analytical data are consistent with literature.[199]

1-(4-Fluorophenylsulfonyl)benzene (2g)



1-fluoro-4-(phenylsulfonyl)benzene (**2g**) was synthesized starting from 4-fluorobenzenesulfinic acid sodium salt (**7d**), benzenesulfinic acid sodium salt (**7l**), from 1-fluoro-4-iodobenzene (**8m**) and *i*PrMgCl·LiCl and $ZnCl_2$ by halogen-metal-exchange and transmetalation, respectively.[137,198]

From 4-fluorobenzenesulfinic acid sodium salt (7d): 1-(4-Fluorophenylsulfonyl)benzene (**2g**) was synthesized according to TP 1 from diphenyliodonium triflate (**11b**) (0.55 mmol, 236.6 mg) and 4-fluorobenzenesulfinic acid sodium salt (**7d**) (0.5 mmol, 96.1 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as colorless solid (97.8 mg, 83%).

From benzenesulfinic acid sodium salt (7l): 1-(4-Fluorophenylsulfonyl)benzene (**2g**) was also prepared according to TP 1 from bis(4-fluorophenyl)iodonium triflate (**11n**) (0.55 mmol, 256.4 mg) and benzenesulfinic acid sodium salt (**7d**) (0.5 mmol, 82.2 mg) in NMP (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as colorless solid (55.0 mg, 47%).

From 1-fluoro-4-iodobenzene (8m) and *i*PrMgCl·LiCl: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *i*PrMgCl·LiCl (1.04 M solution in THF, 0.53 mL, 0.55 mmol, 1.1 equiv) in THF (in total 1.5 mL solvent) and cooled to 0 °C. Then 1-fluoro-4-iodobenzene (**8m**) (58 µL, 0.50 mmol, 1.0 equiv) was added drop wise. After complete addition the mixture was stirred at this temperature for 1 h. Then it was cooled to -40 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents, diphenyliodonium triflate (**11b**) (643.3 mg, 1.5 mmol, 3.0 equiv) and DMSO (1.0 mL) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the analytically pure product as a colorless solid (78.1 mg, 66%).

From 1-fluoro-4-iodobenzene (8m), *i*PrMgCl·LiCl and $ZnCl_2$: To a solution of *i*PrMgCl·LiCl (1.04 M solution in THF, 0.53 mL, 0.55 mmol, 1.1 equiv) cooled to 0 °C was added 1-fluoro-4-iodobenzene (**8m**) (58 µL, 0.5 mmol, 1.0 equiv). After stirring 1 h at this temperature, $ZnCl_2$ (0.7 M solution in THF, 0.79 mL, 0.55 mmol, 1.1 equiv) was added and the mixture was allowed to warm to 25 °C. After cooling to -40 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents, diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol, 3.0 equiv) and DMF (1.0 mL) were added and the mixture was stirred at 90 °C for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the product as a colorless solid (75.1 mg, 63%).

m.p.: 112 – 113 °C.

^{1}H-NMR (250 MHz, $CDCl_3$): δ = 8.15 – 7.74 (m, 4H), 7.65 – 7.42 (m, 3H), 7.18 (t, *J* = 8.4 Hz, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ = 165.58 (d, *J* = 255.9 Hz), 141.63, 137.85 (d, *J* = 3.3 Hz), 133.45, 130.62 (d, *J* = 9.6 Hz), 129.51, 127.71, 116.73 (d, *J* = 22.7 Hz).

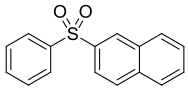
MS: m/z: calc. for $C_{12}H_9FO_2S+Na^+$ 259.02, found 259.06.

R_f (cyclohexane:EtOAc 9:1): = 0.23.

IR (cm^{-1}): 1585 (m), 1491 (m), 1447 (m), 1315 (m, -SO_2-), 1291 (s), 1233 (s), 1150 (s, -SO_2-), 1101 (s), 1068 (m), 1012 (w), 998 (w), 955 (w), 838 (s), 817 (m), 756 (m), 728 (s), 709 (m), 686 (s), 653 (s), 570 (s), 543 (s), 474 (w), 453 (w), 406 (w.)

Analytical data are consistent with literature.[199]

2-(Phenylsulfonyl)naphthalene (2h)



2-(Phenylsulfonyl)naphthalene (**2h**) was prepared according to TP 1 from diphenyliodonium triflate (**11b**) (0.55 mmol, 236.6 mg) and 2-naphtalenesulfinic acid sodium salt (**7g**) (0.5 mmol, 107.1 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as colorless solid (84.4 mg, 63%).

m.p.: 119 – 121 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.58 (s, 1H), 8.05 – 7.96 (m, 3H), 7.93 (d, *J* = 8.7 Hz, 1H), 7.90 – 7.83 (m, 2H), 7.68 – 7.47 (m, 5H).

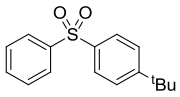
^{13}C-NMR (101 MHz, $CDCl_3$): δ = 141.66, 138.42, 135.01, 133.15, 132.22, 129.63, 129.40, 129.27, 129.14, 129.09, 127.91, 127.71, 127.62, 122.69.

MS: m/z: calc. for $C_{16}H_{12}O_2S+Na^+$ 291.05, found 291.09.

R_f (Cyclohexane:EtOAc 9:1): 0.20.

Analytical data are consistent with literature.[202]

1-(4-tert-Butylphenylsulfonyl)benzene (2i)



1-(4-*tert*-Butylphenylsulfonyl)benzene (**2i**) was synthesized according to TP 1 from diphenyliodonium triflate (**11b**) (0.5 mmol, 215.1 mg) and 4-*tert*-butylbenzenesulfinic acid sodium salt (**7f**) (0.55 mmol, 165.3 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as colorless solid (73.4 mg, 54%).

m.p.: 127 - 128 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.97 - 7.94 (m, 2H), 7.87 - 7.84 (m, 2H), 7.57 – 7.47 (m, 5H), 1.30 (s, 9H).

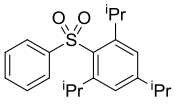
^{13}C-NMR (101 MHz, $CDCl_3$): δ = 157.21, 142.10, 138.69, 133.12, 129.34, 127.74, 127.66, 126.44, 35.31, 31.16.

MS: m/z: calc. for $C_{16}H_{18}O_2S+Na^+$ 297.09, found 297.19.

R_f (cyclohexane:EtOAc 9:1): 0.31.

Analytical data are consistent with literature.[203]

1,3,5-Triisopropyl-2-(phenylsulfonyl)benzene (2j)



1,3,5-Triisopropyl-2-(phenylsulfonyl)benzene (**2j**) was prepared starting from 1,3,5-triisopropylbenzene-sulfinic acid sodium salt (**7k**), benzenesulfinic acid sodium (**7l**), lithium (**37a**), magnesium (**34a**) and zinc (**41a**) salts.

From 1,3,5-triisopropylbenzenesulfinic acid sodium salt (7k): 1,3,5-Triisopropyl-2-(phenylsulfonyl)-benzene (**2j**) was synthesized according to TP 1 from diphenyliodonium triflate (**11b**) (0.55 mmol, 236.6 mg) and 1,3,5-triisopropylbenzenesulfinic acid sodium salt (**11b**) (0.45 mmol, 161.3 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as colorless solid (84.5 mg, 61%).

From benzenesulfinic acid sodium salt (7l): 1,3,5-Triisopropyl-2-(phenylsulfonyl)benzene (**2j**) was prepared according to TP 1 from (phenyl)(2,4,6-triisopropylphenyl) iodonium triflate (**11h**) (0.55 mmol, 311.5 mg) and benzenesulfinic acid sodium salt (**7l**) (0.5 mmol, 82.2 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1) yielded the product as colorless solid (162.0 mg, 94%).

From benzenesulfinic acid lithium salt (37a): 1,3,5-Triisopropyl-2-(phenylsulfonyl)benzene (**2j**) was prepared according to TP 2 from benzenesulfinic acid lithium salt (**37a**) (65w-%, 170.9 mg, 0.75 mmol) and (phenyl)(2,4,6-triisopropylphenyl) iodonium triflate (**11h**) (278.2 mg, 0.50 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as colorless solid (139.9 mg, 81%).

From benzenesulfinic acid magnesium chloride salt (34a): 1,3,5-triisopropyl-2-(phenylsulfonyl)benzene (**2j**) was prepared according to TP 4 from benzenesulfinic acid magnesium chloride salt (**34a**) (55w-%, 182.7 mg, 0.5 mmol) and (phenyl)(2,4,6-triisopropylphenyl) iodonium triflate (**11h**), (834.6 mg, 1.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 20:1 → 9:1) yielded the product as colorless solid (169.0 mg, 98%).

From *in situ* generated benzenesulfinic acid zinc salt (41a): 1,3,5-triisopropyl-2-(phenylsulfonyl)benzene (**2j**) was also prepared according to TP 6 from *in situ* generated benzenesulfinic acid zinc salt (**41a**) (assume 0.75 mmol) and (phenyl)(2,4,6-triisopropylphenyl)iodonium triflate (**11h**) (278.2 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 20:1 → 9:1) yielded the product as colorless solid (78.7 mg, 46%).

m.p.: 122 – 123 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.81 – 7.69 (m, 2H), 7.58 – 7.42 (m, 3H), 7.16 (s, 2H), 4.18 (hept, *J* = 6.7 Hz, 2H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.25 (d, *J* = 6.9 Hz, 6H), 1.13 (d, *J* = 6.8 Hz, 12H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ = 153.99, 151.45, 145.46, 132.37, 132.33, 129.07, 125.76, 124.15, 34.35, 29.54, 24.72, 23.69.

MS: m/z: calc. for $C_{21}H_{28}O_2S+Na^+$ 367.17, found 367.22.

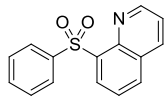
EA:	calc.:	C 73.21	H 8.19	S 9.31
	found:	C 73.09	H 8.18	S 9.28.

IR (cm^{-1}): 2960 (m), 2929 (m), 2870 (w), 1597 (m), 1464 (m), 1444 (m), 1422 (m), 1384 (w), 1336 (m, -SO_2-), 1292 (s, -SO_2-), 1256 (m), 1147 (s, -SO_2-), 1090 (m), 1072 (m), 1035 (m), 933 (w), 886 (m), 760 (m), 691 (m), 651 (s), 6223 (m), 573 (s), 556 (s), 528 (m).

R_f (CCyclohexane:EtOAc 9:1): 0.50.

Analytical data are consistent with literature.[163]

8-(Phenylsulfonyl)quinoline (2k)



8-(Phenylsulfonyl)quinoline (**2k**) was synthesized according to TP 1 from diphenyliodonium triflate (**11b**) (0.55 mmol, 236.6 mg) and 8-quinolinesulfinic acid sodium salt (**7h**) (0.5 mmol, 120.0 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as colorless solid (120.4 mg, 90%).

m.p.: 188 – 190 °C.

^{1}H-NMR (250 MHz, $CDCl_3$): δ = 8.96 (dd, *J* = 4.0, 1.3 Hz, 1H), 8.73 (d, *J* = 7.3 Hz, 1H), 8.22 (dd, *J* = 7.5, 6.1 Hz, 2H), 8.19 – 8.02 (m, 2H), 7.69 (t, *J* = 7.8 Hz, 1H), 7.56 – 7.38 (m, 4H).

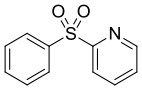
^{13}C-NMR (63 MHz, $CDCl_3$): δ = 151.25, 143.89, 142.04, 138.09, 136.36, 134.68, 132.97, 131.90, 129.31, 129.06, 128.39, 125.61, 122.1.

MS: m/z: calc. for $C_{15}H_{11}NO_2S+H^+$ 270.05, found 270.11.

R_f (cyclohexane:EtOAc 4:1): 0.11.

Analytical data are consistent with literature.[163]

2-(Phenylsulfonyl)pyridine (2l)



2-(Phenylsulfonyl)pyridine (**2l**) was synthesized according to TP 1 from diphenyliodonium triflate (**11b**) (0.55 mmol, 236.6 mg) and 2-pyridinesulfinic acid sodium salt (**7j**) (0.5 mmol, 87.0 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 1:1) yielded the product as colorless solid (44.0 mg, 40%).

m.p.: 92 - 93 °C.

^{1}H-NMR (250 MHz, $CDCl_3$): δ = 8.72 – 8.63 (m, 1H), 8.25 – 8.17 (m, *J* = 7.9, 0.9 Hz, 1H), 8.12 – 8.03 (m, 2H), 7.93 (td, *J* = 7.8, 1.7 Hz, 1H), 7.67 – 7.49 (m, 3H), 7.46 (ddd, *J* = 7.6, 4.7, 1.1 Hz, 1H).

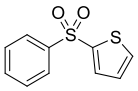
^{13}C-NMR (63 MHz, $CDCl_3$): δ = 159.10, 150.62, 139.16, 138.20, 133.87, 129.25, 129.11, 127.00, 122.33.

MS: m/z: calc. for $C_{11}H_9NO_2S+Na^+$ 242.02, found 242.09.

R_f (cyclohexane:EtOAc 4:1): 0.11.

Analytical data are consistent with literature.[200]

2-(Phenylsulfonyl)thiophene (2m)



2-(Phenylsulfonyl)thiophene (**2m**) was synthesized starting from 2-thiophenesulfinic acid sodium salt (**7i**), from thiophene (**5m**) and *n*BuLi,[117] from 2-bromothiophene (**8r**) and *i*PrMgCl·LiCl and $ZnCl_2$ by halogen-metal-exchange and transmetalation[137,198] and from thiophene (**5m**) by deprotonation with tmp-MgCl·LiCl.[140]

From 2-thiophenesulfinic acid sodium salt (7i): 2-(Phenylsulfonyl)thiophene (**2m**) was synthesized according to TP 1 from diphenyliodonium triflate (**11b**) (0.50 mmol, 215.1 mg) and 2-thiophenesulfinic acid sodium salt (**7i**) (0.55 mmol, 98.5 mg) in DMSO (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as colorless solid (93.6 mg, 83%).

From thiophene (5m) and *n*BuLi: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *n*BuLi (0.34 mL, 2.45 M solution in hexanes, 0.83 mmol, 1.5 equiv) and cooled to -78 °C. Then thiophene (**5m**) (0.06 mL, 0.75 mmol, 1.5 equiv) was added drop wise and the mixture was allowed to warm to 0 °C and stirred at this temperature for 2 h. Then it was recooled to -78 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed by procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture

was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as a colorless solid (95.6 mg, 85%).

From 2-bromothiophene (8r) and *i*PrMgCl·LiCl: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *i*PrMgCl·LiCl (1.04 M solution in THF, 0.53 mL, 0.55 mmol, 1.1 equiv) in THF (in total 1.5 mL solvent) and cooled to -20 °C. Then 2-bromothiophene (**8r**) (48 µL, 0.50 mmol, 1.0 equiv) was added drop wise. After complete addition the mixture was stirred at this temperature for 30 min. Then it was cooled to -40 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents, diphenyliodonium triflate (**11b**) (643.3 mg, 1.5 mmol, 3.0 equiv) and DMSO (1.0 mL) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1) afforded the analytically pure product as a colorless solid (81.3 mg, 73%).

From thiophene (5m) and tmp-MgCl·LiCl: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with thiophene (**5m**) (59 µL, 0.75 mmol, 1.5 equiv) in THF (0.5 mL) and then tmp-MgCl·LiCl (0.72 M in THF, 1.2 mL, 0.83 mmol, 1.65 equiv) was added drop wise. After complete addition the mixture was stirred at 25 °C for 24 h. After cooling to -40 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents according to Procedure A, diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMSO (1.0 mL) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the analytically pure product as a colorless solid (51.5 mg, 50%).

From 2-bromothiophene (8r), *i*PrMgCl·LiCl and $ZnCl_2$: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *i*PrMgCl·LiCl in THF (in total 1.5 mL solvent) (1.04 M solution in THF, 0.53 mL, 0.55 mmol, 1.1 equiv) and cooled to -20 °C. Then 2-bromothiophene (**8r**) (48 µL, 0.50 mmol, 1.0 equiv) was added drop wise. After complete addition the mixture was stirred at this temperature for 30 min, then $ZnCl_2$ (0.7 M solution in THF, 0.9 mL, 0.55 mmol, 1.1 equiv) was added and the mixture was allowed to warm to 25 °C. After recooling to -40 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of

excess SO_2 and solvents according to Procedure A, diphenyliodonium triflate (**11b**) (643.3 mg, 1.5 mmol, 3.0 equiv) and DMSO (1.0 mL) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1) afforded the analytically pure product as a colorless solid (66.4 mg, 59%).

m.p.: 123 – 125 °C.

^{1}H-NMR (250 MHz, $CDCl_3$): δ = 8.08 – 7.89 (m, 2H), 7.73 – 7.62 (m, 2H), 7.62 – 7.44 (m, 3H), 7.08 (dd, *J* = 4.9, 3.8 Hz, 1H).

^{13}C-NMR (63 MHz, $CDCl_3$): δ = 143.27, 142.29, 133.98, 133.51, 133.43, 129.45, 127.97, 127.47.

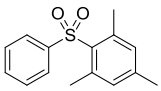
MS: m/z: calc. for $C_{10}H_8O_2S_2$+Na^+ 246.99, found 247.03.

IR (cm^{-1}): 3093 (w), 1503 (w), 1445 (m), 1398 (m), 1343 (w, -SO_2-), 1314 (s, -SO_2-), 1302 (s), 1228 (m), 1147 (s, -SO_2-), 1002 (m), 1081 (m), 11067 (m), 1014 (s), 998 (m), 923 (w), 855 (m), 753 (m), 722 (s), 682 (s), 660 (s), 590 (s), 567 (s), 451 (w), 437 (m).

R_f (cyclohexane:EtOAc 9:1): 0.18.

Analytical data are consistent with literature.[200]

1,3,5-Trimethyl-2-(phenylsulfonyl)benzene (2n)



1,3,5-Trimethyl-2-(phenylsulfonyl)benzene (**2n**) was prepared starting from crude benzenesulfinic acid sodium (**7l**), lithium (**37a**), magnesium (**34a**) and zinc (**41a**) salts.

From benzenesulfinic acid sodium salt (7l): 1,3,5-Trimethyl-2-(phenylsulfonyl)benzene (**2n**) was prepared according to TP 1 from dimesityliodonium triflate (**11j**) (0.55 mmol, 297.0 mg) and benzenesulfinic acid sodium salt (**7l**) (0.5 mmol, 82.2 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 9:1) yielded the product as white solid (118.4 mg, 91%).

From benzenesulfinic acid sodium salt (7l): 1,3,5-Trimethyl-2-(phenylsulfonyl)benzene (**2n**) was also synthesized according to TP 1 from (2,4,6-trimethylphenyl)(phenyl)iodonium triflate (**11f**) (0.55 mmol, 259.7 mg) and benzenesulfinic acid sodium salt (**7l**) (0.5 mmol, 82.2 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as white solid (114.0 mg, 88%).

From benzenesulfinic acid lithium salt (37a): 1,3,5-Trimethyl-2-(phenylsulfonyl)benzene (**2n**) was prepared according to TP 2 from benzenesulfinic acid lithium salt (**37a**) (65w-%, 170.9 mg, 0.75 mmol) and

dimesityliodonium triflate (**11j**) (257.2 mg, 0.5 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as colorless solid (87.3 mg, 67%).

From benzenesulfinic acid lithium salt (37a): 1,3,5-Trimethyl-2-(phenylsulfonyl)benzene (**2n**) was also synthesized according to TP 2 from benzenesulfinic acid lithium salt (**37a**) (65w-%, 170.9 mg, 0.75 mmol) and (2,4,6-trimethylphenyl)(phenyl)iodonium triflate (**11f**) (236.1 mg, 0.5 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 →9:1) yielded the product as colorless solid (94.5 mg, 73%).

From benzenesulfinic acid magnesium chloride salt (34a): 1,3,5-trimethyl-2-(phenylsulfonyl)benzene (**2n**) was prepared according to TP 4 from benzenesulfinic acid magnesium chloride salt (**34a**) (55w-%, 182.7 mg, 0.5 mmol) and dimesityliodonium triflate (**11j**) (771.5 mg, 1.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 20:1 → 4:1) yielded the product as colorless solid (104.0 mg, 80%).

From benzenesulfinic acid magnesium chloride salt (34a): 1,3,5-trimethyl-2-(phenylsulfonyl)benzene (**2n**) was prepared according to TP 4 from benzenesulfinic acid magnesium chloride salt (**34a**) (55w-%, 182.7 mg, 0.5 mmol) and (2,4,6-trimethylphenyl)(phenyl)iodonium triflate (**11f**) (708.3 mg, 1.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 20:1 → 4:1) yielded the product as colorless solid (103.8 mg, 80%).

From *in situ* generated benzenesulfinic acid zinc chloride salt (41a): 1,3,5-trimethyl-2-(phenylsulfonyl)benzene (**2n**) was also prepared according to TP 6 from *in situ* generated benzenesulfinic acid zinc salt (**41a**) (assume 0.75 mmol) and dimesityliodonium triflate (**11j**) (257.2 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 20:1 → 9:1) yielded the product as colorless solid (44.6 mg, 34%).

From *in situ* generated benzenesulfinic acid zinc chloride salt (41a): 1,3,5-trimethyl-2-(phenylsulfonyl)benzene (**2n**) was also prepared according to TP 6 from *in situ* generated benzenesulfinic acid zinc salt (**41a**) (assume 0.75 mmol) and (2,4,6-trimethylphenyl)(phenyl)iodonium triflate (**11f**) (236.1 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 20:1 → 9:1) yielded the product as colorless solid (77.4 mg, 59%).

m.p.: 79 – 80 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.82 - 7.75 (m, 2H), 7.56 - 7.52 (m, 1H), 7.49 - 7.44 (m, 2H), 6.94 (s, 2H), 2.59 (s, 6H), 2.30 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ = 143.69, 143.50, 140.22, 133.93, 132.68, 132.32, 129.00, 126.32, 22.91, 21.13.

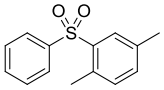
MS: m/z: calc. for $C_{15}H_{16}O_2S+Na^+$ 283.08, found 283.40.

IR (cm^{-1}): 1600 (m), 1447 (s), 1348 (m), 1290 (s), 1145 (s), 1093 (s), 1072 (m), 1050 (m), 1030 (s), 999 (m), 855 (s), 761 (s), 645 (s), 585 (s), 572 (s), 530 (s) 495 (m).

R_f (Cyclohexane:EtOAc 9:1): 0.32.

Analytical data are consistent with literature. [199]

1,4-Dimethyl-2-(phenylsulfonyl)benzene (2o)



1,4-Dimethyl-2-(phenylsulfonyl)benzene (**2o**) was prepared starting from benzenesulfinic acid sodium (**7l**), lithium (**37a**), magnesium (**34a**) and zinc (**41a**) salts.

From benzenesulfinic acid sodium salt (7l): 1,4-Dimethyl-2-(phenylsulfonyl)benzene (**2o**) was prepared according to TP 1 from bis(2,5-dimethylphenyl)iodonium triflate (**11l**) (0.55 mmol, 297.2 mg) and benzenesulfinic acid sodium salt (**7l**) (0.5 mmol, 82.2 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as colorless solid (103.9 mg, 84%).

From benzenesulfinic acid lithium salt (37a): 1,4-Dimethyl-2-(phenylsulfonyl)benzene (**2o**) was prepared according to TP 2 from benzenesulfinic acid lithium salt (**37a**) (65w-%, 170.9 mg, 0.75 mmol) and bis(2,4-dimethylphenyl)iodonium triflate (**11l**) (243.1 mg, 0.50 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as colorless solid (94.2 mg, 76%).

From benzenesulfinic acid magnesium chloride salt (34a): According to TP 4 1,4-dimethyl-2-(phenylsulfonyl)benzene (**2o**) was synthesized from benzenesulfinic acid magnesium chloride salt (**34a**) (70w-%, 215.3 mg, 0.75 mmol) and bis(2,4-dimethylphenyl)iodonium triflate (**11l**) (243.2 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (68.5 mg, 56%).

From *in situ* generated benzenesulfinic acid zinc salt (41a): 1,4-dimethyl-2-(phenylsulfonyl)benzene (**2o**) was also synthesized according to TP 6 from *in situ* generated benzenesulfinic acid zinc salt (**41a**) (assume 0.75 mmol) and bis(2,4-dimethylphenyl)iodonium triflate (**11l**) (243.2 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (90.6 mg, 74%).

m.p.: 112 – 114 °C.

^{1}H-NMR (250 MHz, $CDCl_3$): δ = 8.04 (s, 1H), 7.90 – 7.82 (m, 2H), 7.60 – 7.44 (m, 3H), 7.32 – 7.26 (m, 1H), 7.10 (d, *J* = 7.7 Hz, 1H), 2.39 (d, *J* = 10.6 Hz, 6H).

^{13}C-NMR (63 MHz, $CDCl_3$): δ = 141.68, 138.56, 136.59, 134.95, 134.46, 133.03, 132.74, 129.89, 129.10, 127.70, 21.01, 19.81.

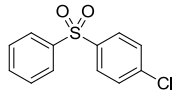
MS: m/z: calc. for $C_{14}H_{14}O_2S+Na^+$ 269.06, found 269.10.

IR (cm^{-1}): 3096 (w), 2923 (w), 1490 (w), 1450 (m), 1292 (s, -SO_2-), 1201 (w), 1154 (s, -SO_2-), 1143 (s, -SO_2-), 1092 (m), 1055 (m), 999 (w), 900 (w), 884 (w), 821 (m), 764 (m), 723 (s), 693 (m), 595 (s), 579 (s), 523 (s), 494 (m), 472 (w), 457 (m), 435 (w).

R_f (cyclohexane:EtOAc 9:1): 0.29.

Analytical data are consistent with literature.[199]

1-(4-Chlorophenylsulfonyl)benzene (2p)



1-(4-Chlorophenylsulfonyl)benzene (**2p**) was prepared starting from benzenesulfinic acid sodium (**7l**), lithium (**37a**), magnesium (**34a**) and zinc (**41a**) salts.

From benzenesulfinic acid sodium salt (7l): 1-(4-Chlorophenylsulfonyl)benzene (**2p**) was prepared according to TP 1 from bis(4-chlorophenyl)iodonium triflate (**11d**) (0.55 mmol, 274.5 mg) and benzenesulfinic acid sodium salt (**7l**) (0.5 mmol, 82.2 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as white solid (120.9 mg, 96%).

From benzenesulfinic acid lithium salt (37a): 1-(4-Chlorophenylsulfonyl)benzene (**2p**) was prepared according to TP 2 from benzenesulfinic acid lithium salt (**37a**) (65w-%, 170.9 mg, 0.75 mmol) and bis(4-chlorophenyl)iodonium triflate (**11d**) (249.5 mg, 0.5 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as colorless solid (98.2 mg, 78%).

From benzenesulfinic acid magnesium chloride salt (34a): 1-chloro-4-(phenylsulfonyl)benzene (**2p**) was prepared according to TP 4 from benzenesulfinic acid magnesium chloride salt (**34a**) (55w-%, 182.7 mg, 0.5 mmol) and bis(4-chlorophenyl)iodonium triflate (**11d**) (748.6 mg, 1.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 20:1 → 9:1) yielded the product as colorless solid (110.3 mg, 74%).

From *in situ* generated benzenesulfinic acid zinc salt (41a): 1-chloro-4-(phenylsulfonyl)benzene (**2p**) was prepared according to TP 6 from *in situ* generated benzenesulfinic acid zinc salt (**41a**) (assume 0.75 mmol) and bis(4-chlorophenyl)iodonium triflate (**11d**) (249.5 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 20:1 → 9:1) yielded the product as colorless solid (80.5 mg, 64%).

m.p.: 96 – 97 °C.

^{1}H-NMR (250 MHz, $CDCl_3$): δ = 8.02 – 7.79 (m, 4H), 7.63 – 7.43 (m, 5H).

^{13}C-NMR (63 MHz, $CDCl_3$): δ = 141.40, 140.34, 140.03, 133.55, 129.74, 129.54, 129.26, 127.78.

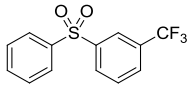
MS: m/z: calc. for $C_{12}H_9ClO_2S+Na^+$ 274.99, found 275.04.

IR (cm^{-1}): 1575 (m); 1474 (m), 1447 (m), 1391 (m), 1311 (s, -SO_2-), 1280 (m), 1177 (w), 1152 (s, -SO_2-), 1107 (s), 1085 (s), 1070 (s), 1028 (w), 10017 (m), 998 (m), 827 (m), 764 (s), 748 (s), 718 (s), 700 (m), 685 (s), 608 (s), 531 (s), 493 (s), 468 (m), 436 (m).

R_f (Cyclohexane:EtOAc 9:1): 0.29.

Analytical data are consistent with literature.[199]

1-(Trifluoromethyl)-3-(phenylsulfonyl)benzene (2q)



1-(Trifluoromethyl)-3-(phenylsulfonyl)benzene (**2q**) was prepared starting from benzenesulfinic acid sodium (**7l**), lithium (**37a**), magnesium (**34a**) and zinc (**41a**) salts, and from [3-(trifluoromethyl)phenyl]-lithium (**36g**) synthesized by halogen-lithium-exchange of 3-bromobenzotrifluoride (**8f**) and 3-iodobenzotrifluoride (**8g**) with *n*BuLi,[204,205] and from [3-(trifluoromethyl)phenyl]-magnesium and –zinc (**18h** and **42d**), prepared via insertion and transmetalation of 3-iodobenzotrifluoride (**8g**), respectively.[137,198]

From benzenesulfinic acid sodium salt (7l): 1-(Trifluoromethyl)-3-(phenylsulfonyl)benzene (**2q**) was prepared according to TP 1 from (4-methoxyphenyl)(3-trifluoromethylphenyl)iodonium tosylate (**11e**) (0.55 mmol, 302.7 mg) and benzenesulfinic acid sodium salt (**7l**) (0.5 mmol, 82.2 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as colorless needles (111.7 mg, 78%).

From benzenesulfinic acid lithium salt (37a): 2q was prepared according to TP 2 from benzenesulfinic acid lithium salt (**37a**) (65w-%, 170.9 mg, 0.75 mmol) and (4-methoxyphenyl)(3-trifluoromethylphenyl)-iodonium tosylate (**11e**) (275.2 mg, 0.50 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as colorless solid (108.8 mg, 76%) and **2a** (7.4 mg, 6%) as by-product.

From 3-bromobenzotrifluoride (8f) and *n*BuLi: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *n*BuLi (0.38 mL, 2.13 M solution in hexanes, 0.8 mmol, 1.6 equiv) in dry Et_2O (1.0 mL) and cooled to 0 °C. At this temperature 3-bromobenzotrifluoride (**8f**) (0.1 mL, 0.75 mmol, 1.5 equiv) was added drop wise and the mixture stirred for 1 h at 0 °C. Then it was cooled to -78 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed according to procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the

solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as a colorless solid (106.3 mg, 74%).

From 3-iodobenzotrifluoride (8g) and *n*BuLi: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *n*BuLi (0.38 mL, 2.13 M solution in hexanes, 0.8 mmol, 1.6 equiv) in dry Et_2O (1.0 mL) and cooled to -78 °C. At this temperature 3-iodobenzotrifluoride (**8g**) (0.1 mL, 0.75 mmol, 1.5 equiv) was added drop wise and the mixture stirred for 1 h at -78 °C. Then liquid SO_2 (0.1 mL, 5.0 mmol, 10 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed according to procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as a colorless solid (118.9 mg, 83%).

From benzenesulfinic acid magnesium chloride salt (34a): According to TP 4 1-(phenylsulfonyl)-3-(trifluoromethyl)benzene (**2q**) was synthesized from benzenesulfinic acid magnesium chloride salt (**34a**) (70w-%, 215.3 mg, 0.75 mmol) and (4-methoxyphenyl)(3-trifluoromethyl)(phenyl)iodonium tosylate (**11e**) (275.2 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 20:1 → 4:1) yielded the product as colorless solid (115.9 mg, 81%).

From 3-bromobenzotrifluoride (8f) and *i*PrMgCl·LiCl: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *i*PrMgCl·LiCl (1.04 M solution in THF, 0.53 mL, 0.55 mmol, 1.1 equiv) in THF (in total 1.5 mL solvent) and cooled to -20 °C. Then 3-bromobenzotrifluoride (**8f**) (72 µL, 0.50 mmol, 1.0 equiv) was added drop wise. After complete addition the mixture was stirred at this temperature for 30 min. Then it was cooled to -40 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents, diphenyliodonium triflate (**11b**) (643.3 mg, 1.5 mmol, 3.0 equiv) and DMSO (1.0 mL) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1) afforded the analytically pure product as a colorless solid (53.3 mg, 38%).

From *in situ* generated benzenesulfinic acid zinc salt (41a): 1-(phenylsulfonyl)-3-(trifluoromethyl)benzene (**2q**) was also synthesized according to TP 6 from *in situ* generated benzenesulfinic acid zinc salt (**41a**) (assume 0.75 mmol) and (4-methoxyphenyl)(3-trifluoromethyl)(phenyl) iodonium tosylate (**11e**) (275.2 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (94.1 mg, 76%) and **2a** (6.1 mg, 5%) as by-product.

From 3-iodobenzotrifluoride (8g), *i*PrMgCl·LiCl and $ZnCl_2$: To a solution of *i*PrMgCl·LiCl (1.04 M solution in THF, 0.53 mL, 0.55mmol, 1.1 equiv) cooled to -20 °C was added 3-iodobenzotrifluoride (**8g**) (72 µL, 0.5 mmol, 1.0 equiv). After stirring 30 min at this temperature, $ZnCl_2$ (0.7 M solution in THF, 0.79 mL, 0.55 mmol, 1.1 equiv) was added and the mixture was allowed to warm to 25 °C. After cooling to -40 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents, diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol, 3.0 equiv) and DMF (1.0 mL) were added and the mixture was stirred at 90 °C for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the product as a colorless solid (105.8 mg, 74%).

m.p.: 83 – 84 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.22 (s, 1H), 8.13 (d, *J* = 7.9 Hz, 1H), 8.02 – 7.92 (m, 2H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.71 – 7.49 (m, 4H).

^{13}C-NMR (126 MHz, CDCl3): δ = 141.94 (q, *J* = 292.8 Hz), 133.91, 132.16 (q, *J* = 33.6 Hz), 131.10, 130.27, 130.04 (q, *J* = 3.3 Hz), 129.72, 128.01, 126.47, 124.82 (q, *J* = 3.7 Hz), 123.22 (q, *J* = 273.0 Hz).

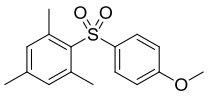
MS: m/z: calc. for $C_{13}H_9FO_2S+Na^+$ 309.02, found 309.06.

IR (cm^{-1}): 3064 (w), 1737 (w), 1609 (w), 1586 (w), 1480 (w), 1449 (w), 1432 (w), 1323 (s, -SO_2-), 1306 (s, -SO_2-), 1180 (m), 1155 (s, -SO_2-), 1124 (s, -SO_2-), 1109 (s), 1067 (s), 998 (w), 930 (m), 842 (w), 821 (w), 803 (m), 757 (m), 731 (s), 686 (s), 649 (m), 634 (m), 584 (s), 553 (s), 500 (m), 459 (w), 424 (w), 407 (w).

R_f (cyclohexane:EtOAc 9:1): 0.20.

Analytical data are consistent with literature.[206]

2-(4-Methoxyphenylsulfonyl)-1,3,5-trimethylbenzene (2r)



2-(4-Methoxyphenylsulfonyl)-1,3,5-trimethylbenzene (**2r**) was prepared according to TP 1 from dimesityliodonium triflate (**11j**) (0.55 mmol, 259.7 mg) and 4-methoxybenzenesulfinic acid sodium salt (**7a**) (0.5 mmol, 102.2 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as colorless solid (120.6 mg, 83%).

m.p.: 138 - 140 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.77 – 7.69 (m, 2H), 6.95 – 6.90 (m, 4H), 3.84 (s, 3H), 2.60 (s, 6H), 2.28 (s, 3H).

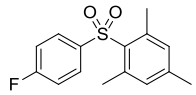
^{13}C-NMR (101 MHz, $CDCl_3$): δ = 162.92, 143.16, 139.94, 135.46, 134.71, 132.30, 128.64, 114.17, 55.73, 22.98, 21.12.

MS: calc. for $C_{16}H_{18}O_3S+Na^+$ 313.09, found 313.15.

R_f (cyclohexane:EtOAc 9:1): 0.18.

Analytical data are consistent with literature.[207]

2-(4-Fluorophenylsulfonyl)-1,3,5-trimethylbenzene (2s)



2-(4-Fluorophenylsulfonyl)-1,3,5-trimethylbenzene (**2s**) was prepared according to TP 1 from dimesityliodonium triflate (**11j**) (0.55 mmol, 259.7 mg) and 4-fluorobenzenesulfinic acid sodium salt (**7d**) (0.5 mmol, 95.9 mg) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as colorless solid (114.0 mg, 82%).

m.p.: 88 - 90 °C.

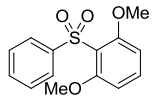
^{1}H-NMR (250 MHz, $CDCl_3$): δ = 7.86 – 7.74 (m, 2H), 7.20 – 7.08 (m, 2H), 6.95 (s, 2H), 2.58 (s, 6H), 2.29 (s, 3H).

^{13}C-NMR (63 MHz, $CDCl_3$): δ = 167.09, 163.03, 143.70, 140.12, 136.83 (d, *J* = 372.6 Hz), 132.43, 129.13 (d, *J* = 9.3 Hz), 116.25 (d, *J* = 22.6 Hz), 22.91, 21.12.

MS: calc. for $C_{16}H_{18}O_3S+Na^+$ 301.07, found 301.10.

R_f (cyclohexane:EtOAc 9:1): 0.34.

1,3-Dimethoxy-2-(phenylsulfonyl)benzene (2t)



1,3-Dimethoxy-2-(phenylsulfonyl)benzene (**2t**) was synthesized from (2,6-dimethoxyphenyl)-lithium (**36h**) which was prepared by lithiation of 1,3-dimethoxybenzene (**5b**) with *n*BuLi and halogen-lithium-exchange of 2-iodo-1,3-dimethoxybenzene (**8j**) with *n*BuLi.[208,209]

From 1,3-dimethoxybenzene (5b) and *n*BuLi: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with 1,3-dimethoxybenzene (**5b**) (0.1 mL, 0.75 mmol, 1.5 equiv) in dry THF (1.0 mL) and cooled to 0 °C. At this temperature *n*BuLi (0.34 mL, 2.45 M solution in hexanes, 0.83 mmol, 1.65 eqiuv) was added drop wise and the mixture stirred at 25 °C for 3.5 h. Then it was cooled to -30 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added at once. The mixture was allowed to

warm to 25 °C within 90 min and then excess SO_2 was removes according to procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 1:1) yielded the product as a colorless solid (110.3 mg, 79%).

From 2-iodo-1,3-dimethoxybenzene (8j) and *n*BuLi: To a solution of 2-iodo-1,3-dimethoxybenzene (**8j**) (198.1 mg, 0.75 mmol, 1.5 equiv) in dry hexanes (3.5 mL) in a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was added *n*BuLi (0.40 mL, 2.13 M solution in hexanes, 0.85 mmol, 1.65 equiv) and the mixture stirred at 25 °C for 16 h. After cooling to -78 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents according to Procedure A, to the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 4:1 → 1:1) yielded the product as a colorless solid (103.0 mg, 74%).

m.p.: 110 - 112 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 7.5 Hz, 2H), 7.55 - 7.42 (m, 3H), 7.39 (t, *J* = 8.4 Hz, 1H), 6.55 (d, *J* = 8.5 Hz, 2H), 3.75 (s, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ = 159.64, 144.64, 135.06, 132.43, 128.32, 127.35, 118.11, 105.44, 56.58.

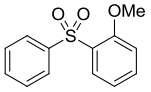
MS: m/z: calc. for $C_{14}H_{14}O_4S+Na^+$ 301.05, found 301.30.

IR (cm^{-1}): 2977 (w), 2945 (w), 1577 (s),1476 (s), 1427 (s), 1318 (m, -SO_2-), 1305 (s, -SO_2-), 1290 (m), 1254 (s), 1188 (w), 1150 (s, -SO_2-), 1107 (s), 1088 (s), 1043 (m), 1023 (m), 780 (s), 754 (s), 713 (m), 695 (s), 649 (m), 612 (m), 572 (s), 560 (s), 496 (m), 472 (m).

R_f (Cyclohexane:EtOAc 9:1): 0.05.

Analytical data are consistent with literature.[164]

1-(2-Methoxyphenylsulfonyl)benzene (2u)



1-(2-methoxyphenylsulfonyl)benzene (**2u**) was synthesized from 2-methoxyphenyllithium (**36i**) which was prepared by lithiation of anisole (**5c**) with *n*BuLi[210] and halogen-lithium-exchange of 2-bromoanisole (**8c**) with *n*BuLi.[196]

From anisole (5c) and *n*BuLi: To a solution of anisole (**5c**) (0.82 mL, 0.75 mmol, 1.5 equiv) and TMEDA (0.22 mL, 1.5 mmol, 3.0 equiv) in dry Et_2O in a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was added *n*BuLi (0.61 mL, 2.45 M solution in hexanes, 1.5 mmol, 3.0 equiv) drop wise. The mixture was allowed to stir at 25 °C for 30 min and then cooled to -78 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed by procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as a colorless solid (75.7 mg, 61%).

From 2-bromoanisole (8c) and *n*BuLi: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *n*BuLi (0.33 mL, 2.45 M solution in hexanes, 0.80 mmol, 1.6 equiv) and cooled to -78 °C. Then 2-bromoanisole (**8c**) (0.1 mL, 0.75 mmol, 1.5 equiv) was added drop wise and the reaction mixture stirred at this temperature for 1 h, before liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. The mixture was allowed to warm to 25 °C within 90 min and then excess SO_2 and solvents were removed according to procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as a colorless solid (120.2 mg, 97%).

m.p.: 142 – 145 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.16 (dd, *J* = 7.9, 1.7 Hz, 1H), 8.00 - 7.94 (m, 2H), 7.58 - 7.52 (m, 2H), 7.51 - 7.45 (m, 2H), 7.13 - 7.08 (m, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 3.75 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ = 157.23, 141.68, 135.64, 133.01, 130.02, 129.16, 128.60, 125.41, 120.67, 112.61, 55.97.

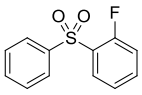
MS: m/z: calc. for $C_{13}H_{12}O_3S+Na^+$ 271.04, found 271.40.

IR (cm^{-1}): 1584 (m), 1479 (m), 1466 (m), 1452 (m), 1434 (m), 1304 (s, -SO_2-), 1280 (s), 1243 (m), 1180 (w), 1147 (s, -SO_2-), 1091 (s), 1059 (m), 1034 (m), 1014 (m), 799 (m), 164 (s), 733 (s), 717 (s), 692 (s), 584 (s), 559 (s), 537 (s), 509 (s), 469 (w), 448 (w).

R_f (cyclohexane:EtOAc 9:1): 0.09.

Analytical data are consistent with literature.[211]

1-(2-Fluorophenylsulfonyl)benzene (2v)



1-(2-Fluorophenylsulfonyl)benzene (**2v**) was synthesized starting from (2-fluorophenyl)lithium (**36i**), prepared from fluorobenzene (**8ad**) and *n*BuLi or fluoro-3-iodobenzene (**8l**) and *n*BuLi via deprotonation or halogen-metal-exchange, respectively.[117]

From fluorobenzene (8ad) and *n*BuLi: To a solution of fluorobenzene (**8ad**) (0.07 mL, 0.75 mmol, 1.5 equiv) and TMEDA (0.13 mL, 0.85 mmol, 1.65 equiv) in dry THF (0.75 mL) in a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was cooled to -50 °C and then added *n*BuLi (0.35 mL, 2.45 M solution in hexanes, 0.85 mmol, 1.65 equiv) drop wise. The mixture was allowed to stir at this temperature for 7 h and then cooled to -78 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed by procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as a colorless solid (86.4 mg, 73%).

From fluoro-2-iodobenzene (8l) and *n*BuLi: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *n*BuLi (0.38 mL, 2.13 M solution in hexanes, 0.8 mmol, 1.6 equiv) in dry THF (1.5 mL) and cooled to -78 °C. Then fluoro-2-iodobenzene (**8l**) (0.09 mL, 0.75 mmol, 1.5 equiv) was added drop wise and the mixture was allowed to stir at this temperature for 30 min. Then liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed by procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as a colorless solid (65.3 mg, 62%).

m.p.: 102 – 104 °C.

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.14 – 8.09 (m, 1H), 8.06 – 7.98 (m, 2H), 7.64 – 7.51 (m, 4H), 7.35 – 7.30 (m, 1H), 7.13 – 7.09 (m, 1H).

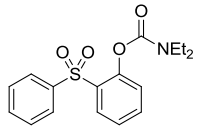
^{13}C-NMR (101 MHz, $CDCl_3$) δ 160.65, 141.08, 136.08 (d, *J* = 8.5 Hz), 133.79, 129.91, 129.25, 128.61 (d, *J* = 161.5 Hz), 128.30 (d, *J* = 2.1 Hz), 124.74 (d, *J* = 3.9 Hz), 117.43 (d, *J* = 21.2 Hz).

MS: m/z: calc. for $C_{12}H_9FO_2S$ +Na^+ 259.07, found 259.02.

R_f (cyclohexane:EtOAc 9:1): 0.22.

Analytical data are consistent with literature.[212]

2-(Phenylsulfonyl)phenyl diethylcarbamate (2w)



[2-[[(Diethylamino)carbonyl]oxy]phenyl]-lithium (**36k**) was synthesized according to literature by lithiation of phenyl diethylcarbamate (**5e**) with *s*BuLi.[213]

To a solution of *s*BuLi (0.70 mL, 1.2 M solution in cyclohexane, 0.83 mmol, 1.65 equiv) and TMEDA (0.12 mL, 0.83 mmol, 1.65 equiv) in a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was added phenyl diethylcarbamate (**5e**) (154.0 mg, 0.75 mmol, 1.5 equiv) at -78 °C. The mixture stirred for 1 h at this temperature and then liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. The reaction was allowed to warm to 25 °C within 90 min. After removing excess SO_2 by procedure A, to the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMF (1.0 mL) and the reaction was stirred at 90 °C for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 50:1 → 9:1) yielded the product as a colorless solid (77.8 mg, 47%).

m.p.: 92 - 93 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.15 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.88 – 7.80 (m, 2H), 7.65 – 7.52 (m, 2H), 7.52 - 7.42 (m, 2H), 7.37 (td, *J* = 7.8, 1.1 Hz, 1H), 7.21 (dd, *J* = 8.2, 0.9 Hz, 1H), 3.43 (q, *J* = 7.1 Hz, 2H), 3.23 (q, *J* = 7.1 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 152.37, 149.43, 141.47, 134.94, 133.29, 132.70, 130.05, 129.04, 127.37, 125.45, 125.11, 42.18, 41.91, 14.27, 13.28.

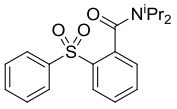
MS: m/z: calc. for $C_{17}H_{19}NO_4S$+H^+ 334.10, found 334.45.

HRMS: m/z: calc. for $C_{17}H_{19}NO_4S$+K^+ 372.06664, found 372.06664.

IR (cm^{-1}): 2983 (w), 1723 (s), 1468 (w), 1448 (w), 1410 (m), 1382 (w), 1321 (s, -SO_2-), 1257 (s), 1201 (s), 1141 (s, -SO_2-), 1093 (s), 1060 (m), 1040 (w), 999 (w), 950 (m), 838 (w), 824 (w), 788 (w), 771 (m), 750 (w), 731 (s), 718 (m), 691 (s), 586 (s), 567 (s), 507 (m).

R_f (Cyclohexane:EtOAc 4:1): 0.17.

2-(Phenylsulfonyl) diisopropylbenzamide (2x)



[2-[[Bis(1-methylethyl)amino]carbonyl]phenyl]-lithium (**36l**) was synthesized according to literature by lithiation of *N*,*N*-diisopropylbenzamide (**5f**) by *s*BuLi.[214]

To a solution of *s*BuLi (0.70 mL, 1.2 M solution in cyclohexane, 0.83 mmol, 1.65 equiv) and TMEDA (0.12 mL, 0.83 mmol, 1.65 equiv) in a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was added *N*,*N*-diisopropylbenzamide (**5f**) (154.0 mg, 0.75 mmol, 1.5 equiv) in dry THF (1.0 mL) at -78 °C. The mixture stirred for 1 h at this temperature and then liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. The reaction was allowed to warm to 25 °C within 90 min. After removing excess SO_2 by procedure B, diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMF (1.0 mL) were added and the reaction was stirred at 90 °C for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 4:1) yielded the product as a colorless solid (117.5 mg, 68%).

m.p.: 198 - 200 °C.

^{1}H-NMR (400 MHz, CDCl3): δ = 8.11 - 8.07 (m, 2H), 8.05 (d, *J* = 7.4 Hz, 1H), 7.58 - 7.44 (m, 5H), 7.22 (d, *J* = 6.8 Hz, 1H), 3.68 - 3.50 (m, 2H), 1.69 (d, *J* = 6.8 Hz, 3H), 1.55 (d, *J* = 6.8 Hz, 3H), 1.30 (d, *J* = 6.6 Hz, 3H), 1.09 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ = 167.91, 141.66, 138.52, 137.69, 133.56, 133.31, 130.36, 129.06, 129.01, 128.54, 127.03, 51.49, 46.00, 20.63, 20.52, 19.91, 19.56.

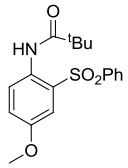
MS: m/z: calc. for $C_{19}H_{23}NO_3S+Na^+$ 368.13, found 368.30.

HRMS: m/z: calc. for $C_{19}H_{23}NO_3S+H^+$ 346.14714, found 346.14703.

IR (cm^{-1}): 1628 (s), 1476 (w), 1442 (m), 1371 (m), 1340 (m, -SO_2-), 1317 (s, -SO_2-), 1297 (w), 1212 (w), 1186 (w), 1153 (s, -SO_2-), 1130 (m, -SO_2-), 1105 (m), 1090 (w), 1058 (w), 1035 (w), 782 (m), 759 (m), 730 (m), 710 (m), 688 (m), 656 (w), 590 (s), 568 (s), 533 (w), 502 (w).

R_f (Cyclohexane:EtOAc 9:1): 0.07.

N-(4-methoxy-2-(phenylsulfonyl)phenyl)pivalamide (2aa)

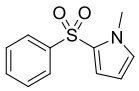


(5-methoxy-2-pivalamidophenyl)lithium (**36m**) was prepared via lithiation of *N*-(4-methoxyphenyl)-pivalamide (**5i**) with *t*BuLi. [122]

A solution of *N*-(4-methoxyphenyl)pivalamide (**5i**) (155.5 mg, 0.75 mmol, 1.5 equiv) in dry THF (1.0 mL) in a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was cooled to -78 °C and then *t*BuLi (1.72 mL, 1.6 M solution in pentane, 2.7 mmol, 3.6 equiv) was added drop wise. The mixture was allowed to stir at this temperature, warm to -20 °C within 1 h, before recooling to -78 °C and then liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed by procedure A. To the crude sulfinic acid lithium salt was added diphenyl-iodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as a colorless solid (59.3 mg, 30%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.99 – 7.76 (m, 1H), 7.68 – 7.35 (m, 5H), 6.88 – 6.79 (m, 2H), 3.79 – 3.75 (s, 3H), 1.29 (s, 9H).

1-Methyl-2-(phenylsulfonyl)-1H-pyrrole (2ab)



(1-Methyl-1*H*-pyrrol-2-yl)-lithium (**36n**) was prepared by lithiation of *N*-methylpyrrole (**5j**) with *n*BuLi.[214,215]
A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *N*-methylpyrrole (**5j**) (66 µL, 0.75 mmol, 1.5 equiv) and TMEDA (0.12 mL, 0.83 mmol, 1.65 equiv) and then *n*BuLi (0.34 mL, 2.45 M solution in hexanes, 0.83 mmol, 1.5 equiv) was added drop wise and the mixture was heated to 55 °C for 15 min. The mixture was then cooled to -78 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed according to procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced

pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as a pale pink solid (55.9 mg, 51%).

m.p.: 79 - 81 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.91 - 7.86 (m, 2H), 7.58 - 7.54 (m, 1H), 7.53 - 7.48 (m, 2H), 7.04 (dd, *J* = 4.0, 1.9 Hz, 1H), 6.76 (t, *J* = 2.2 Hz, 1H), 6.17 (dd, *J* = 4.0, 2.6 Hz, 1H), 3.70 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 142.30, 133.00, 129.80, 129.34, 128.00, 127.30, 119.01, 108.48, 35.76.

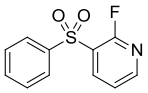
MS: m/z: calc. for $C_{11}H_{11}NO_2S+H^+$ 222.06, found 222.80.

HRMS: m/z: calc. for $C_{11}H_{11}NO_2S+H^+$ 222.05833, found 222.05796.

IR (cm^{-1}): 3122 (w), 2969 (w), 1513 (w), 1468 (w), 1441 (m), 1396 (w), 1326 (m, -SO_2-), 1297 (s, -SO_2-), 1155 (s, -SO_2-), 1128 (s, -SO_2-), 1098 (m), 1051 (m), 1014 (m), 998 (m), 952 (w), 766 (s), 752 (s), 725 (s), 688(s), 631 (s), 595 (s), 566 (m), 546 (s), 486 (m).

R_f (cyclohexane:EtOAc 9:1): 0.18.

2-Fluoro-3-(phenylsulfonyl)pyridine (2ac)



(2-Fluoro-3-pyridinyl)-lithium (**36o**) was prepared by lithiation of 2-fluoropyridine (**5k**) by LDA.[216]
A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum, charged with diisopropylamine (0.12 mL, 0.85 mmol, 1.65 equiv) in dry THF (1.0 mL) was cooled to -78 °C and then *n*BuLi (0.35 mL, 2.45 M solution in hexanes, 0.85 mmol, 1.65 equiv) was added drop wise. After stirring for 15 min at this temperature, the mixture was stirred for another 15 min at 0 °C. After recooling the *in situ* prepared LDA to -70 °C, 2-fluoropyridine (**5k**) (65 µL, 0.75 mmol, 1.5 equiv) was added drop wise and stirred at this temperature for 4 h. Then and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed according to procedure A. To the crude sulfinic acid lithium salt were added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 4:1 → 1:1) yielded the product as a colorless solid (65.0 mg, 55%).

m.p.: 90 - 92 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.56 - 8.51 (m, 1H), 8.43 - 8.38 (m, 1H), 8.05 - 8.00 (m, 2H), 7.68 - 7.64 (m, 1H), 7.59 - 7.54 (m, 2H), 7.43 - 7.39 (m, 1H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 158.87 (d, *J* = 245.4 Hz), 152.90 (d, *J* = 15.1 Hz), 140.96, 139.74, 134.42, 129.52, 128.63, 125.41 (d, *J* = 30.3 Hz), 122.23 (d, *J* = 4.7 Hz).

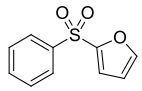
MS: m/z: calc. for $C_{11}H_8FNO_2S+Na^+$ 260.02, found 260.50.

HRMS: m/z: calc. for $C_{11}H_8FNO_2S+H^+$ 238.03325, found 238.03340.

IR (cm^{-1}): 1586 (m), 1568 (w), 1448 (m), 1420 (m), 1326 (m, -SO_2-), 1300 (m), 1228 (w), 1177 (w), 1156 (s, -SO_2-), 1134 (m, -SO_2-), 1091 (m), 1067 (m), 1044 (w), 995 (w), 852 (m), 812 (w), 750 (m), 725 (s), 681 (s), 567 (m), 558 (s), 537 (s), 512 (m), 468 (w), 441 (m).

R_f (Cyclohexane:EtOAc 9:1): 0.15.

2-(Phenylsulfonyl)furan (2ad)



Furan-2-yllithium (**36p**) was prepared via deprotonation of furan (**5l**) with *n*BuLi. [117]

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *n*BuLi (0.33 mL, 2.45 M solution in hexanes, 0.8 mmol, 1.6 equiv) and cooled to -78 °C. Then furan (**5l**) (0.06 mL, 0.75 mmol, 1.5 equiv) was added drop wise and the mixture was allowed to warm to 0 °C and stirred at this temperature for 2 h. Then it was recooled to -78 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed by procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1) yielded the product as a colorless solid (63.5 mg, 61%).

m.p.: 70 - 71 °C.

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.03 – 7.98 (m, 2H), 7.65 – 7.60 (m, 1H), 7.58 – 7.51 (m, 3H), 7.21 (dd, *J* = 3.5, 0.8 Hz, 1H), 6.51 (dd, *J* = 3.5, 1.8 Hz, 1H).

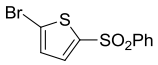
^{13}C-NMR (126 MHz, $CDCl_3$) δ 147.60, 133.91, 133.33, 129.46, 128.05, 127.82, 117.58, 111.76.

MS: m/z: calc. for $C_{10}H_8O_3S+H^+$ 209.01, found 209.80.

R_f (cyclohexane:EtOAc 9:1): 0.18.

Analytical data are consistent with literature.[217]

2-Bromo-5-(phenylsulfonyl)thiophene (2ae)



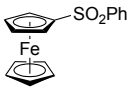
(5-Bromothiophen-2-yl)lithium (**36q**) was prepared via deprotonation of 2-bromothiophene (**8r**) with LDA.[117]

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum, charged with diisopropylamine (0.12 mL, 0.85 mmol, 1.65 equiv) in dry THF (1.0 mL) was cooled to -78 °C and then *n*BuLi (0.35 mL, 2.45 M solution in hexanes, 0.85 mmol, 1.65 equiv) was added drop wise. After stirring for 15 min at this temperature, the mixture was stirred for another 15 min at 0 °C. After recooling the *in situ* prepared LDA to -78 °C, 2-bromothiophene (**8r**) (0.06 mL, 0.75 mmol, 1.5 equiv) was added drop wise, warmed to 0 °C and stirred at this temperature for 4 h. It was recooled to -78 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After removing excess SO_2 by procedure B, diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMF (1.0 mL) were added and the reaction was stirred at 90 °C for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as colorless solid (50.7 mg, 33%).

^{1}H NMR (250 MHz, $CDCl_3$) δ 8.02 – 7.91 (m, 2H), 7.64 – 7.48 (m, 3H), 7.45 (d, *J* = 4.0 Hz, 1H), 7.05 (d, *J* = 4.0 Hz, 1H).

Analytical date is consistent with literature.[218]

(Phenylsulfonyl)-ferrocene (2ag)



Ferrocenyllithium (**36r**) was prepared according to literature by lithiation of ferrocene (**5o**) with *t*BuLi.[219]
A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with ferrocene (**5o**) (153.5 mg, 0.83 mmol, 1.65 equiv) in dry THF (10 mL) and cooled to 0 °C. At this temperature *t*BuLi (0.46 mL, 1.64 M solution in pentane, 0.75 mmol, 1.5 equiv) was added drop wise and the mixture was stirred for 15 min. After warming to 25 °C, the mixture was recooled to -78 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. The reaction mixture was allowed to warm to 25 °C within

90 min. After removing excess SO_2 by procedure B, diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMF (1.0 mL) were added. The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as an orange solid (68.8 mg, 42%).

m.p.: 140 - 145 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 7.5 Hz, 2H), 7.54 – 7.47 (m, 1H), 7.44 (t, *J* = 7.4 Hz, 2H), 4.69 (s, 2H), 4.51 (s, 5H), 4.41 (s, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ = 143.25, 132.68, 129.14, 126.83, 90.40, 71.28, 70.91, 69.41.

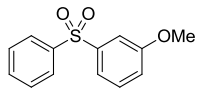
MS: m/z: calc. for $C_{16}H_{14}FeO_2S+Na^+$ 349.00, found 349.20.

IR (cm^{-1}): 2921 (w), 1581 (w), 1448 (m), 1411 (w), 1299 (s, -SO_2-), 1184 (m), 1152 (s, -SO_2-), 1140 (s, -SO_2-), 1104 (m), 1084 (m), 1071 (m), 1019 (m), 998 (m), 819 (m), 761 (s), 723 (s), 687 (s), 638 (w), 611 (m), 585 (s), 560 (s), 545 (s), 494 (m), 478 (s), 451 (m)

R_f (Cyclohexane:EtOAc 9:1): 0.26.

Analytical data are consistent with literature.[211]

1-Methoxy-3-(phenylsulfonyl)benzene (2ak)



(3-Methoxyphenyl)lithium (**36s**) was prepared by halogen-lithium-exchange from 3-bromoanisole (**8d**) and *n*BuLi.[196]

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *n*BuLi (0.33 mL, 2.45 M solution in hexanes, 0.80 mmol, 1.6 equiv) and cooled to -70 °C. Then 3-bromoanisole (**8d**) (0.1 mL, 0.75 mmol, 1.5 equiv) was added drop wise and the reaction mixture stirred at this temperature for 1 h, before liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. The mixture was allowed to warm to 25 °C within 90 min and then excess SO_2 and solvents were removed according to procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure.

Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as a colorless solid (114.7 mg, 92%).

m.p.: 89 - 91 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.98 - 7.91 (m, 2H), 7.59 - 7.54 (m, 1H), 7.53 - 7.48 (m, 3H), 7.46 - 7.43 (m, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.07 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H), 3.84 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 160.15, 142.83, 141.68, 133.33, 130.52, 129.40, 127.78, 120.06, 119.68, 112.37, 55.82.

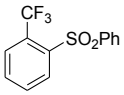
MS: m/z: calc. for $C_{13}H_{12}O_3S+Na^+$ 271.04, found 271.13.

IR (cm^{-1}): 1592 (m), 1474 (m), 1447 (s), 1421 (m), 1298 (s, -SO_2-), 1245 (s), 1181 (m), 1148 (s, -SO_2-), 1099 (s), 1069 (m), 1026 (s), 992 (m), 925 (w), 865 (m), 842 (w), 790 (s), 755 (w), 723 (s), 678 (s), 609 (s), 571 (s), 526 (s), 471 (m); 458 (m), 421 (w).

R_f (cyclohexane:EtOAc 9:1): 0.15.

Analytical data are consistent with literature.[220]

1-(2-(Trifluoromethyl)phenylsulfonyl)benzene (2al)



1-(2-(trifluoromethyl)phenylsulfonyl)benzene (**2al**) was prepared starting from (2-(trifluoromethyl)-phenyl)lithium (**36t**) generated out of 2-bromobenzotrifluoride (**8h**) and 2-iodobenzotrifuoride (**8i**) via halogen-metal-exchange with *n*BuLi. [204,205]

From 2-bromobenzotrifluoride (8h) and *n*BuLi: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *n*BuLi (0.38 mL, 2.13 M solution in hexanes, 0.8 mmol, 1.6 equiv) in dry Et_2O (1.0 mL) and cooled to 0 °C. At this temperature 2-bromobenzotrifluoride (**8h**) (0.11 mL, 0.75 mmol, 1.5 equiv) was added drop wise and the mixture stirred for 1 h at 0 °C. Then it was cooled to -78 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed according to procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as a colorless solid (54.3 mg, 38%).

From 2-iodobenzotrifluoride (8i) and *n*BuLi: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *n*BuLi (0.38 mL, 2.13 M solution in hexanes, 0.8 mmol, 1.6 equiv) in dry Et_2O (1.0 mL) and cooled to -78 °C. At this temperature 2-iodobenzotrifluoride (**8i**) (0.11 mL, 0.75 mmol, 1.5 equiv) was added drop wise and the mixture stirred for 1 h at -78 °C. Then liquid SO_2 (0.1 mL, 5.0 mmol, 10 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed according to procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded the product as a colorless solid (91.7 mg, 64%).

m.p.: 89 - 91°C.

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.47 (d, *J* = 7.9 Hz, 1H), 7.90 - 7.84 (m, 3H), 7.83 - 7.76 (m, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.61 - 7.55 (m, 1H), 7.54 - 7.48 (m, 2H).

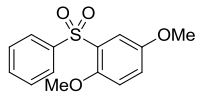
^{13}C-NMR (126 MHz, $CDCl_3$) δ = 140.68 (d, *J* = 179.2 Hz), 133.66, 133.47, 132.68, 132.5, 129.15, 128.90, 128.67 (q, *J* = 6.3 Hz), 127.93, 125.86, 122.59 (d, *J* = 274.4 Hz).

MS: m/z: calc. for $C_{13}H_9F_3O_2S+Na^+$ 309.02$^+$, found 309.10.

R_f (cyclohexane:EtOAc 9:1): 0.24.

Analytical date is consistent with literature.[221]

1-(2,5-Dimethoxyphenylsulfonyl)benzene (2am)



(2,5-Dimethoxyphenyl)-lithium (**36u**) was prepared according to literature by halogen-lithium-exchange of 1-bromo-2,4-dimethoxybenzene (**8k**) and *n*BuLi.[220]

To a solution of 1-bromo-2,4-dimethoxybenzene (**8k**) (0.11 mL, 0.75 mmol, 1.5 equiv) in dry THF (1.0 mL) in a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was added *n*BuLi (0.56 mL, 1.2 mmol, 2.4 equiv) drop wise at 25 °C and then stirred for 2 h. After cooling to -78 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed according to procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol, 1.0 equiv) and DMF (1.0 mL). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The

combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 1:1) yielded the product as a colorless solid (58.4 mg, 42%).

m.p.: 107 - 109 °C.

^{1}H-NMR: (500 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 8.8 Hz, 1H), 7.96 – 7.92 (m, 2H), 7.56 – 7.51 (m, 1H), 7.49 – 7.44 (m, 2H), 6.58 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.38 (d, *J* = 2.3 Hz, 1H), 3.84 (s, 3H), 3.72 (s, 3H).

^{13}C-NMR: (101 MHz, $CDCl_3$): δ = 165.77, 158.77, 142.25, 132.73, 131.87, 128.56, 128.19, 121.49, 104.76, 99.59, 55.97, 55.86.

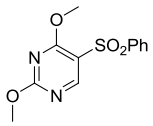
MS: m/z: calc. for $C_{14}H_{14}O_4S+Na^+$ 301.05, found 302.30.

HRMS: m/z: calc. for $C_{14}H_{14}O_4S+H^+$ 279.06856, found 279.06858.

IR (cm^{-1}): 1578 (m), 1489 (w), 1458 (m), 1432 (w), 1408 (w), 1321 (m, -SO_2-), 1299 (S, -SO_2-), 1251 (m), 1210 (s), 1144 (s), 1145 (s, -SO_2-), 1091 (s), 1064 (s), 1020 (s), 938 (w), 920 (m), 840 (w), 829 (m), 813 (w), 792 (w), 765 (m), 733 (s), 708 (m), 691 (s), 658 (m), 641 (m), 592 (s), 555 (s), 528 (s), 470 (w), 454 (m).

R_f (Cyclohexane:EtOAc 9:1): 0.08.

2,4-Dimethoxy-5-(phenylsulfonyl)pyrimidine (2ao)

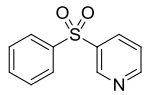


(2,4-dimethoxypyrimidin-5-yl)lithium (**36w**) was prepared via halogen-metal-exchange of 5-iodo-2,4-dimethoxypyrimidine (**8p**) with *n*BuLi.[117]

A solution of 5-iodo-2,4-dimethoxypyrimidine (**8p**) (200.0 mg, 0.75 mmol, 1.5 equiv) in dry THF (1.0 mL) in a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was cooled to -78 °C and then added *n*BuLi (0.38 mL, 2.13 M solution in hexanes, 0.80 mmol, 1.60 equiv) drop wise. The mixture was allowed to stir at this temperature for 1 h and then liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added. After warming to 25 °C within 90 min, excess SO_2 and solvents were removed by procedure A. To the crude sulfinic acid lithium salt was added diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and 1.0 mL DMF. The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 4:1 → 1:1) yielded the product as a colorless solid (30.3 mg, 22%).

^{1}H NMR (250 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.03 – 7.93 (m, 2H), 7.67 – 7.57 (m, 1H), 7.57 – 7.46 (m, 2H), 4.03 (s, 3H), 3.99 (s, 3H).

3-(Phenylsulfonyl)pyridine (2aq)



Pyridin-3-ylzinc(III) chloride (**42f**) was prepared via halogen-metal-exchange and transmetalation of 3-bromopyridine (**8t**) with *i*PrMgCl·LiCl and $ZnCl_2$.[137,198]

To a solution of *i*PrMgCl·LiCl (1.04 M solution in THF, 0.53 mL, 0.55mmol, 1.1 equiv) in THF (1.0 mL) at 25 °C was added 3-bromopyridine (**8t**) (49 µL, 0.5 mmol, 1.0 equiv). After stirring 30 min at this temperature, $ZnCl_2$ (0.7 M solution in THF, 0.79 mL, 0.55 mmol, 1.1 equiv) was added and the mixture stirred another 30 min. After cooling to -40 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents according to procedure A, diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol, 3.0 equiv) and DMF (1.0 mL) were added and the mixture was stirred at 90 °C for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 4:1 → 1:1) afforded the product as a colorless solid (56.0 mg, 51%).

m.p.: 120 - 122 °C.

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 9.14 (d, *J* = 2.2 Hz, 1H), 8.79 (dd, *J* = 4.9, 1.5 Hz, 1H), 8.27 – 8.22 (m, 1H), 7.99 - 7.94 (m, 2H), 7.64 – 7.60 (m, 1H), 7.57 – 7.53 (m, *J* = 10.6, 4.8 Hz, 2H), 7.48 (dd, *J* = 8.1, 4.9 Hz, 1H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 153.34 (d, *J* = 2.8 Hz), 148.47 (d, *J* = 1.7 Hz), 140.74, 138.66, 135.76 (d, *J* = 1.9 Hz), 134.05, 129.77, 127.96, 124.17.

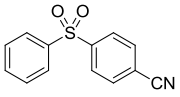
MS: m/z: calc. for $C_{11}H_9NO_2S+H^+$ 220.04, found 219.80.

IR (cm^{-1}): 1570 (m), 1473 (w), 1445 (w), 1417 (m), 1303 (s, -SO_2-), 1234 (w), 1197 (m), 1158 (s, -SO_2-), 1129 (-SO_2-), 1113 (s), 1094 (m), 1074 (m), 1017 (m), 999 (m), 823 (m), 768 (m), 742 (s), 703 (s), 686 (s), 617 (s), 589 (s), 567 (s), 488 (m), 458 (m), 418 (m).

R_f (hexanes:EtOAc 4:1): 0.11.

Analytical data are consistent with literature.[212]

4-(Phenylsulfonyl)benzonitrile (2ar)



4-(phenylsulfonyl)benzonitrile (**2ar**) was prepared starting from (4-cyanophenyl)magnesium chloride and zinc chloride (**18j** and **42g**) generated out of 4-iodobenzonitrile (**8u**) via halogen-metal-exchange and transmetalation with *i*PrMgCl·LiCl and $ZnCl_2$, respectively.[137,198]

From 4-iodobenzonitrile (8u) and *i*PrMgCl·LiCl: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with 4-iodobenzonitrile (**8u**) (114.5 mg, 0.5 mmol, 1.0 equiv) in THF (1.0 mL) and cooled to -10 °C. Then *i*PrMgCl·LiCl (1.04 M solution in THF, 0.53 mL, 0.55 mmol, 1.1 equiv) was added drop wise. After complete addition the mixture was stirred at this temperature for 1 h. Then it was cooled to -40 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents, diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol, 3.0 equiv) and DMSO (1.0 mL) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1) afforded the analytically pure product as a colorless solid (59.1 mg, 49%).

From 4-iodobenzonitrile (8u), *i*PrMgCl·LiCl and $ZnCl_2$: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with 4-iodobenzonitrile (**8u**) (114.5 mg, 0.5 mmol, 1.0 equiv) in THF (0.5 mL) and cooled to -10 °C. Then *i*PrMgCl·LiCl (1.04 M solution in THF, 0.53 mL, 0.55 mmol, 1.1 equiv) was added drop wise. After complete addition the mixture was stirred at this temperature for 1 h and then added $ZnCl_2$ (0.7 M solution in THF, 0.9 mL, 0.55 mmol, 1.1 equiv) and stirred for another hour. Then it was cooled to -40 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents, diphenyliodonium triflate (**11b**) (643.3 mg, 1.5 mmol, 3.0 equiv) and DMSO (1.0 mL) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1) afforded the analytically pure product as a colorless solid (88.3 mg, 73%).

m.p.: 120 - 122 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 – 8.04 (m, 2H), 7.97 – 7.94 (m, 2H), 7.82 – 7.78 (m, 2H), 7.65 – 7.61 (m, 1H), 7.57 – 7.53 (m, 2H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 146.03, 140.28, 134.18, 133.22, 129.80, 128.43, 128.15, 117.29, 117.09.

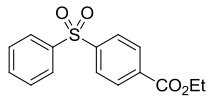
MS: m/z: calc. for $C_9H_{12}O_2S+H^+$ 244.04, found 244.12.

IR (cm^{-1}): 2237 (w), 1447 (m), 1396 (m), 1322 (s, -SO_2-), 1311 (s, -SO_2-), 1290 (s), 1150 (s, -SO_2-), 1100 (s), 1070 (s), 1015 (m), 998 (s), 851 (s), 840 (s), 801 (m), 786 (m), 756 (s), 729 (s), 707 (s), 687 (s), 623 (s), 570 (s), 540 (s), 519 (s), 471 (m), 401 (w).

R_f (hexanes:EtOAc 4:1): 0.30.

Analytical date is consistent with literature.[222]

Ethyl 4-(phenylsulfonyl)benzoate (2as)



Ethyl 4-(phenylsulfonyl)benzoate (**2as**) was prepared starting from [4-(ethoxycarbonyl)phenyl]iodo-zinc·LiCl (**42a**), which was generated from ethyl 4-iodobenzoate and *i*PrMgCl·LiCl, $ZnCl_2$ or zinc and LiCl by halogen-metal-exchange, transmetalation or direct insertion, respectively.[137,198]

From ethyl 4-iodobenzoate (8v) and *i*PrMgCl·LiCl: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *i*PrMgCl·LiCl in THF (1.04 M solution in THF, 0.59 mL, 0.72 mmol, 1.43 equiv) (in total 1.5 mL) and cooled to -20 °C. Then ethyl 4-iodobenzoate (**8v**) (109 µL, 0.65 mmol, 1.3 equiv) was added drop wise. After complete addition the mixture was stirred at this temperature for 30 min. Then it was cooled to -40 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents according to procedure A, diphenyliodonium triflate (**11b**) (643.3 mg, 1.5 mmol, 3.0 equiv, respectively) and DMSO (1.0 mL) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 20:1 → 4:1) afforded the analytically pure product as a colorless solid (67.0 mg, 46%).

From ethyl 4-iodobenzoate (8v) and *i*PrMgCl·LiCl·and $ZnCl_2$: To a solution of *i*PrMgCl·LiCl in THF (1.04 M solution in THF, 0.53 mL, 0.55 mmol, 1.1 equiv) cooled to -20 °C was added ethyl 4-iodobenzoate (**8v**) (83 µL, 0.5 mmol, 1.0 equiv). After stirring 30 min at this temperature, $ZnCl_2$ (0.7 M solution in THF, 0.79 mL, 0.55 mmol, 1.1 equiv) was added and the mixture was allowed to warm to 25 °C. After cooling to -40 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 3 h. After removal of excess SO_2 and solvents, diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol, 3.0 equiv) and DMF (1.0 mL) were added and the mixture was stirred at 90 °C for 24 h. After cooling to

25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the product as a colorless solid (123.4 mg, 85%).

From [4-(ethoxycarbonyl)phenyl]iodo-zinc (42a)·LiCl: According to TP 7 ethyl 4-(phenylsulfonyl)benzoate (**2as**) was prepared from [4-(ethoxycarbonyl)phenyl]iodo-zinc·LiCl (**42a**) (0.84 M solution in THF, 0.89 mL, 0.75 mmol), SO_2 (0.1 mL, 5.0 mmol) and diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the product as a colorless solid (59.2 mg, 41%).

m.p.: 92 - 94 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.19 – 8.11 (m, 2H), 8.07 – 7.88 (m, 4H), 7.63 – 7.48 (m, 3H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 165.14, 145.52, 141.04, 134.81, 133.72, 130.54, 129.58, 127.98, 127.80, 61.87, 14.36.

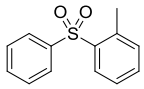
MS: m/z: calc. for $C_{15}H_{14}O_4S+Na^+$ 331.05, found 313.10.

HRMS: m/z: calc. for $C_{15}H_{14}O_4S+2H^+$ 292.07176, found 292.07193.

IR (cm^{-1}): 3024 (w), 3009 (w), 2925 (w), 1712 (s), 1474 (w), 1402 (m), 1367 (m), 1312 (s, -SO_2-), 1269 (s), 1155 (s, -SO_2-), 1110 (s), 1088 (s), 1020 (s), 980 (s), 962 (s), 878 (m), 865 (m), 783 (s), 754 (s), 730 (m), 719 (m), 689 (s), 562 (s), 528 (s), 507 (s), 460 (m), 431 (s).

R_f (hexanes:EtOAc 9:1): 0.19.

1-Methyl-2-(phenylsulfonyl)benzene (2at)



1-methyl-2-(phenylsulfonyl)benzene (**#**) was synthesized starting from *o*-tolylmagnesium bromide·LiCl (**18o**) and *o*-tolylmagnesium chloride·LiCl (**18p**) generated from 2-iodotoulene (**8w**) and *i*PrMgCl·LiCl by halogen-metal-exchange.[198]

From 2-iodotoluene (8w) and *i*PrMgCl·LiCl: A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *i*PrMgCl·LiCl (1.04 M solution in THF, 0.77 mL, 0.8 mmol, 1.6 equiv) in THF (in total 1.5 mL solvent) and cooled to 0 °C. Then 2-iodotoluene (**8w**) (0.1 mL, 0.75 mmol, 1.5 equiv) was added drop wise. After complete addition the mixture was stirred at this temperature for 1 h. Then it was cooled to -40 °C and liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents according to procedure A, diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and DMSO (1.0 mL) were

added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1) afforded the analytically pure product as a colorless solid (57.7 mg, 49%).

From *o*-tolylmagnesium bromide·LiCl (18o): 1-methyl-2-(phenylsulfonyl)benzene (**2at**) was synthesized according to TP 5 from *o*-tolylmagnesium bromide·LiCl (**18o**) (0.9 M solution in THF, 0.85 mL, 0.75 mmol, 1.5 equiv), diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) and SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1) afforded the analytically pure product as a colorless solid (24.7 mg, 21%).

m.p.: 73 – 75 °C.

^{1}H-NMR (250 MHz, $CDCl_3$): δ = 8.21 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.90 – 7.81 (m, *J* = 3.7, 2.7 Hz, 2H), 7.62 – 7.44 (m, 4H), 7.44 – 7.34 (m, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 7.4 Hz, 1H), 2.44 (s, 3H).

^{13}C-NMR (63 MHz, $CDCl_3$): δ = 141.49, 139.00, 138.13, 133.72, 133.13, 132.80, 129.56, 129.14, 127.77, 126.59, 20.29.

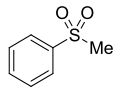
MS: m/z: calc. for $C_{13}H_{12}O_2S+Na^+$ 255.05, found 255.08.

IR (cm^{-1}): 3061 (w), 1472 (m), 1446 (m), 1386 (w), 1305 (s, -SO_2-), 1203 (w), 1155 (s, -SO_2-), 1137 (s, -SO_2-), 1091 (m), 1058 (m), 1043 (m), 997 (m), 934 (w), 806 (m), 760 (m), 723 (s), 702 (s), 688 (s), 591 (s), 567 (s), 540 (s), 497 (m), 474 (w), 458 (m), 428 (m).

R_f (Cyclohexane:EtOAc 9:1): 0.24.

Analytical data are consistent with literature.[223]

1-(Methylsulfonyl)benzene (38a)



1-(Methylsulfonyl)benzene (**38a**) was prepared starting from methyllithium (**36b**) and methylmagnesium chloride (**18f**).

From methyllithium (36b): 1-(Methylsulfonyl)benzene (**38a**) was prepared according to TP 3 from methyllithium (**36b**) (0.63 mL, 1.2 M solution in Et_2O, 0.75 mmol), SO_2 (0.1 mL, 5.0 mmol), diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as colorless solid (65.5 mg, 84%).

From methylmagnesium chloride (18f): (Methylsulfonyl)benzene (**18f**) was prepared according to TP 5 from MeMgCl (**18f**) (2.44 M solution in THF, 0.31 mL, 0.75 mmol, 1.5 equiv), SO_2 (0.1 mL, 5.0 mmol) diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol, 1.0 equiv) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the analytically pure product as a colorless solid (39.5 mg, 51%).

m.p.: 88 - 90 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.97 - 7.93 (m, 2H), 7.69 - 7.64 (m, 1H), 7.61 - 7.55 (m, 2H), 3.05 (s, 3H).

^{13}C-NMR (126 MHz, CDCl3): δ = 140.70, 133.84, 129.50, 127.48, 44.62.

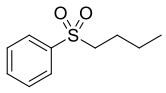
MS: m/z: calc. for $C_7H_8O_2S+Na^+$ 179.01, found 179.70.

IR (cm^{-1}): 3021 (w), 2928 (w), 1983 (w), 1829 (w), 1584 (w), 1478 (w), 1448 (m), 1408 (w), 1328 (m, -SO_2-), 1283 (s), 1176 (w), 1142 (s, -SO_2-), 1084 (s), 1024 (w), 1000 (w), 961 (m), 931 (m), 851 (w), 757 (m), 744 (s), 687 (s), 525 (s), 448 (m), 411 (w).

R_f (Cyclohexane:EtOAc 9:1): 0.18.

Analytical data are consistent with literature.[224]

1-(Butylsulfonyl)benzene (38b)



1-(Butylsulfonyl)benzene was prepared starting from *n*butyllithium (**36c**) and *n*butylmagngesium chloride·LiCl (**18q**).

From *n*BuLi (36c): 1-(Butylsulfonyl)benzene (**38b**) was prepared according to TP 3 from *n*butyllithium (**36c**) (0.31 mL, 2.45 M solution in hexanes, 0.75 mmol), SO_2 (0.1 mL, 5.0 mmol), diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as colorless oil (88.4 mg, 89%).

From *n*butylmagnesium chloride·LiCl (18q): 1-(Butylsulfonyl)benzene (**38b**) was prepared according to TP 5 from *n*butylmagnesium chloride·LiCl (**18q**) (1.5 M solution in THF, 0.5 mL, 0.75 mmol), diphenyliodonium triflate (**11b**) (215.1 mg, 0.5 mmol) and SO_2 (0.1 mL, 5.0 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the analytically pure product as a colorless oil (16.7 mg, 17%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.97 - 7.87 (m, 2H), 7.69 - 7.63 (m, 1H), 7.60 - 7.54 (m, 2H), 3.13 - 3.04 (m, 2H), 1.75 - 1.64 (m, 2H), 1.39 (sext, *J* = 5.7 Hz, 2H), 0.89 (t, *J* = 7.4 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ = 139.40, 133.72, 129.37, 128.18, 56.22, 24.75, 21.67, 13.61.

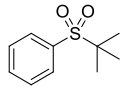
MS: m/z: calc. for $C_{10}H_{14}O_2S+H^+$ 199.06, found 199.60.

IR (cm^{-1}): 2961 (m), 2936 (w), 2874 (w), 1465 (w), 1447 (m), 1406 (w), 1328 (w, -SO_2-), 1298 (s, -SO_2-), 1234 (m), 1184 (m), 1142 (s, -SO_2-), 1085(s), 1024 (w), 999 (w), 916 (w), 798 (m), 747 (s), 728 (s), 688 (s), 590 (s), 560 (s), 531 (s), 488 (m), 470 (m), 436 (m).

R_f (cyclohexane:EtOAc 9:1): 0.19.

Analytical data are consistent with literature.[225]

1-(tert-Butylsulfonyl)benzene (38c)



1-(*tert*-Butylsulfonyl)benzene (**38c**) was prepared according to TP 3 from *t*butyllithium (**36e**) (0.46 mL, 1.64 M solution in pentane, 0.75 mmol), SO_2 (0.1 mL, 5.0 mmol), diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded the product as colorless solid (75.5 mg, 76%).

m.p.: 93 - 95 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.98 - 7.84 (m, 2H), 7.71 - 7.60 (m, 1H), 7.59 - 7.47 (m, 2H), 1.34 (s, 9H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 135.48, 133.67, 130.61, 128.84, 59.93, 23.76.

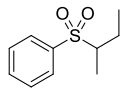
MS: m/z: calc. for $C_{10}H_{14}O_2S+Na^+$ 221.06, found 221.14.

IR (cm^{-1}): 3062 (w), 2979 (w), 2923 (w), 2853 (w), 1583 (w), 1476 (w), 1449 (m), 1379 (w, -SO_2-), 1276 (s), 1200 (w), 1156 (w, -SO_2-), 1129 (s, -SO_2-), 1076 (s), 1022 (w), 997 (w), 943 (w), 801 (w), 765 (m), 725 (s), 696 (s), 638 (s), 590 (m), 566 (s), 519 (m), 458 (w).

R_f (cyclohexane:EtOAc 9:1): 0.19.

Analytical data are consistent with literature.[226]

1-(sec-Butylsulfonyl)benzene (38d)



1-(*sec*-Butylsulfonyl)benzene (**38d**) was prepared according to TP 3 from *s*butyllithium (**36d**) (0.63 mL, 1.2 M solution in cyclohexane, 0.75 mmol), SO_2 (0.1 mL, 5.0 mmol), diphenyliodonium triflate (**11b**) (215.1 mg, 0.50 mmol) in DMF (1.0 mL). Purification by chromatography (cyclohexane:EtOAc 9:1 → 4:1) yielded the product as colorless oil (92.2mg, 93%).

^{1}H-NMR: (400 MHz, $CDCl_3$): δ = 7.91 - 7.85 (m, 2H), 7.68 - 7.62 (m, 1H), 7.60 - 7.53 (m, 2H), 3.02 - 2.89 (m, 1H), 2.07 - 1.95 (m, 1H), 1.50 - 1.36 (m, 1H), 1.27 (d, *J* = 6.9 Hz, 3H), 0.98 (t, *J* = 7.5 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ = 137.58, 133.66, 129.18, 129.15, 61.68, 22.64, 12.72, 11.29.

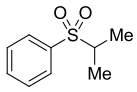
MS: m/z: calc. for $C_{10}H_{14}O_2S+Na^+$ 221.06, found 221.50.

IR (cm^{-1}): 2975 (m), 2939 (w), 1440 (m), 1296 (s, -SO_2-), 1263 (m) 1241 (m), 1138 (s, -SO_2-), 1085 (s), 1071 (m), 1060 (m), 1020 (m), 999 (w), 847 (w), 764 (s), 727 (s), 691 (s), 614 (m), 590 (s), 572 (s), 540 (s), 499 (m), 456 (m), 422 (w).

R_f (cyclohexane:EtOAc 9:1): 0.21.

Analytical data are consistent with literature.[199]

(Isopropylsulfonyl)benzene (38e)



(Isopropylsulfonyl)benzene (**38e**) was prepared starting from isopropylmagnesium chloride·LiCl (**38e**) and isopropylzinc chloride·LiCl·$MgCl_2$ (**42h**) generated by transmetalation of the latter with $ZnCl_2$.[137]

From isopropylmagnesium chloride·LiCl (38e): According to TP 5 (isopropylsulfonyl)benzene (**38e**) was prepared from isopropylmagnesium chloride·LiCl (**38e**) (1.04 M solution in THF, 0.48 ml, 0.5 mmol), SO_2 (0.1 mL, 5.0 mmol) and diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol) in DMSO (1.0 mL). Purification by column chromatography (hexanes:EtOAc 20:1 → 9:1) afforded the analytically pure product as a colorless oil (66.7 mg, 72%).

From isopropylmagnesium chloride·LiCl (38e) and $ZnCl_2$: To a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum charged with *i*PrMgCl·LiCl (**38e**) (1.04 M solution in THF, 0.48 ml, 0.5 mmol, 1.0 equiv) was added $ZnCl_2$ (0.7 M solution in THF, 0.86 mL, 0.6 mmol, 1.2 equiv) and stirred at 25 °C for 30 min. After cooling to -40 °C, liquid SO_2 (0.1 mL, 5.0 mmol, 10.0 equiv) was added and the mixture was allowed to warm to 25 °C within 90 min. After removal of excess SO_2 and solvents according to procedure A, diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol, 3.0 equiv) and DMSO (1.0 mL) were added and the reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl-solution (10 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 20:1 → 9:1) afforded the analytically pure product as a colorless oil (58.8 mg, 64%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.83 (m, 2H), 7.67 – 7.62 (m, 1H), 7.59 – 7.53 (m, 2H), 3.19 (hept, *J* = 6.7 Hz, 1H), 1.28 (d, *J* = 6.9 Hz, 6H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 137.07, 133.72, 129.17, 129.16, 55.66, 15.81.

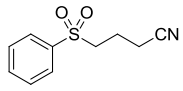
MS: m/z: calc. for $C_9H_{12}O_2S+Na^+$ 207.05, found 207.10.

IR (cm^{-1})**:** 2981 (w), 2939 (w), 1468 (m), 1447 (m), 1389 (w), 1298 (s, -SO_2-), 1261 (s), 1167 (m), 1138 (s -SO_2-), 1086 (s), 1051 (s), 1024 (m), 1000 (m), 876 (m), 793 (m), 764 (s), 728 (s), 690 (s), 581 (s), 568 (s), 534 (s), 514 (s), 477 (w), 447 (m).

R_f (hexanes:EtOAc 9:1): 0.13.

Analytical data are consistent with literature.[227]

4-(Phenylsulfonyl)butanenitrile (38f)



According to TP 7 4-(phenylsulfonyl)butanenitrile (**38f**) was synthesized from (3-cyanopropyl)iodo-zinc·LiCl (**42i**) (1.38 M solution in THF, 0.38 mL, 0.5 mmol), SO_2 (0.1 mL, 5.0 mmol) and diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol) in DMF (1.0 mL). Purification by column chromatography (hexanes:EtOAc 4:1 → 1:1) afforded the product as a colorless solid (66.1 mg, 64%).

m.p.: 70 - 72 °C.

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.00 – 7.85 (m, 2H), 7.74 – 7.67 (m, 1H), 7.66 – 7.55 (m, 2H), 3.25 – 3.19 (m, 2H), 2.63 – 2.56 (m, 2H), 2.18 – 2.11 (m, 2H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = δ 138.78, 134.47 – 134.29 (m), 129.74, 128.16, 118.20, 54.42, 19.24, 16.36 (d, *J* = 2.3 Hz).

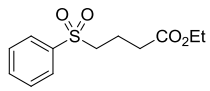
MS: m/z: calc. for $C_{10}H_{11}NO_2S+Na^+$ 232.04, found 232.09.

IR (cm^{-1}): 2935 (w), 2247 (m), 1479 (w), 1444 (m), 1426 (m), 1408 (m), 1304 (s, -SO_2-), 1272 (s), 1210 (m), 1154 (m, -SO_2-), 1142 (s, -SO_2-), 1084 (s), 1053 (m), 1024 (s), 1000 (m), 931 (w), 876 (m), 779 (m), 738 (s), 718 (s), 688 (s), 605 (s), 550 (s), 526 (s), 463 (m).

R_f (hexanes:EtOAc 4:1): 0.1.

Analytical data are consistent with literature.[228]

Ethyl 4-(phenylsulfonyl)butanoate (38g)



According to TP 7 ethyl 4-(phenylsulfonyl)butanoate (**38g**) was prepared from (4-ethoxy-4-oxobutyl)iodozinc·LiCl (**42j**) (0.89 M solution in THF, 0.56 mL, 0.5 mmol), SO_2 (0.1 mL, 5.0 mmol) and diphenyliodonium triflate (**11b**) (645.3 mg, 1.5 mmol) in DMF (1.0 mL). Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the product as a colorless oil (107.1 mg, 84%).

^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.88 (m, 2H), 7.69 – 7.64 (m, 1H), 7.60 – 7.54 (m, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.20 – 3.16 (m, 2H), 2.44 (t, *J* = 7.1 Hz, 2H), 2.06 – 2.00 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.21, 139.06, 133.94, 129.50, 128.21, 60.85, 55.31, 32.37, 18.44, 14.30.

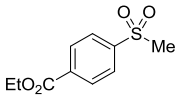
MS: m/z: calc. for$C_{12}H_{16}O_4S+Na^+$ 279.09, found 278.80.

IR (cm^{-1}): 3065 (w), 2980 (w), 2931 (w), 1727 (s), 1585 (w), 1569 (w), 1447 (m), 1375 (m), 1354 (s, -SO_2-), 1299 (s), 1237 (s), 1186 (m), 1143 (s, -SO_2-), 1086 (s), 1029 (s), 935 (w), 842 (w), 791 (m), 738 (s), 689 (s), 587 (m), 562 (m), 530 (s), 486 (w), 447 (w).

R_f (hexanes:EtOAc 4:1): 0.22.

Analytical data are consistent with literature.[229]

Ethyl 4-(methylsulfonyl)benzoate (38h)

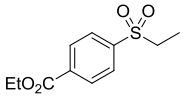


A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with methyl iodide (**40d**) (2.0 equiv, 1.0 mmol, 0.1 mL) and $Na_2S_2O_5$ (2.5 equiv, 1.25 mmol, 238.0 mg) in NMP (2.0 mL). After complete consumption of the iodide (monitored by NMR), (4-(ethoxycarbonyl)-phenyl)zinc(II) iodide (**42a**) (0.87 M solution in THF, 1.0 equiv, 0.5 mmol, 0.6 ml) was added and the reaction mixture was heated to 70 °C and stirred at this temperature for 16 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed three times with dist. H_2O (15 mL) and once with sat. aqueous NaCl-solution (10 mL) dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 20:1 → 9:1) afforded the analytically pure product (104.0 mg, 91%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 – 8.21 (m, 2H), 8.05 – 8.00 (m, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.08 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H).

Analytical date is consistent with literature.[230]

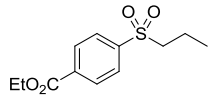
Ethyl 4-(ethylsulfonyl)benzoate (38i)



A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with ethyl iodide (**40e**) (2.5 equiv, 1.25 mmol, 0.1 mL), $Na_2S_2O_5$ (2.5 equiv, 1.25 mmol, 238.0 mg) and (4-(ethoxycarbonyl)phenyl)zinc(II) iodide (**42a**) (0.87 M solution in THF, 1.0 equiv, 0.5 mmol, 0.6 ml) in DMSO (1.4 mL). The reaction mixture was heated to 70 °C and stirred at this temperature for 16 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed three times with dist. H_2O (15 mL) and once with sat. aqueous NaCl-solution (10 mL) dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1 → 1:1) afforded the analytically pure product (45.3 mg, 37%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 – 8.21 (m, 2H), 8.01 – 7.95 (m, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.14 (q, *J* = 7.4 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.4 Hz, 3H).

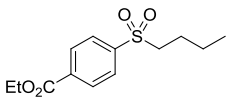
Ethyl 4-(propylsulfonyl)benzoate (38j)



A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *n*propyl iodide (**40f**) (2.0 equiv, 1.25 mmol, 0.1 mL) and $Na_2S_2O_5$ (2.5 equiv, 1.25 mmol, 238.0 mg) in d_6-DMSO (2.0 mL). After complete consumption of the iodide (monitored by NMR), (4-(ethoxycarbonyl)-phenyl)zinc(II) iodide (**42a**) (0.87 M solution in THF, 1.0 equiv, 0.5 mmol, 0.6 ml) in THF (0.4 mL) was added. The reaction mixture was heated to 70 °C and stirred at this temperature for 16 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed three times with dist. H_2O (15 mL) and once with sat. aqueous NaCl-solution (10 mL) dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the analytically pure product (65.8 mg, 51%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 – 8.18 (m, 2H), 8.02 – 7.94 (m, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.13 – 3.05 (m, 2H), 1.79 – 1.67 (m, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.00 (t, *J* = 7.4 Hz, 3H).

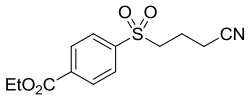
Ethyl 4-(butylsulfonyl)benzoate (38k)



A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with *n*butyl iodide (**40g**) (2.0 equiv, 1.0 mmol, 0.10 mL) and $Na_2S_2O_5$ (2.5 equiv, 1.25 mmol, 238.0 mg) in d_6-DMSO (1.0 mL). After complete consumption of the iodide (monitored by NMR), (4-(ethoxycarbonyl)-phenyl)zinc(II) iodide (**42a**) (0.87 M solution in THF, 1.0 equiv, 0.5 mmol, 0.6 ml) in THF (0.4 mL) was added and the reaction mixture was heated to 70 °C and stirred at this temperature for 16 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed three times with dist. H_2O (15 mL) and once with sat. aqueous NaCl-solution (10 mL) dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1 → 1:1) afforded the analytically pure product (101.2 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 – 8.20 (m, 2H), 8.02 – 7.95 (m, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.14 – 3.05 (m, 2H), 1.74 – 1.63 (m, 2H), 1.45 – 1.36 (m, 5H), 0.89 (t, *J* = 7.3 Hz, 3H).

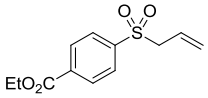
Ethyl 4-((3-cyanopropyl)sulfonyl)benzoate (38l)



A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with 4-iodobutanenitrile (**40j**) (2.0 equiv, 1.0 mmol, 0.1 mL) and $Na_2S_2O_5$ (2.5 equiv, 1.25 mmol, 238.0 mg) in d_6-DMSO (1.4 mL). After complete consumption of the iodide (monitored by NMR), (4-(ethoxycarbonyl)-phenyl)zinc(II) iodide (**42a**) (0.87 M solution in THF, 1.0 equiv, 0.5 mmol, 0.6 ml) was added and the reaction mixture was heated to 70 °C and stirred at this temperature for 16 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL) and sat. aqueous NaCl-solution (10 mL) dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 4:1 → 1:1) afforded the analytically pure product (79.6 mg, 57%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 – 8.24 (m, 2H), 8.02 – 7.98 (m, 2H), 4.48 – 4.39 (m, 2H), 3.28 – 3.22 (m, 2H), 2.61 (t, *J* = 7.0 Hz, 2H), 2.20 – 2.12 (m, 2H), 1.46 – 1.40 (m, 3H).

Ethyl 4-(allylsulfonyl)benzoate (38o)

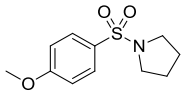


A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with allyl bromide (**40j**) (2.0 equiv, 1.0 mmol, 0.1 mL) and $Na_2S_2O_5$ (2.5 equiv, 1.25 mmol, 238.0 mg) in d_6-DMSO (2.0 mL). After complete consumption of the bromide (monitored by NMR), (4-(ethoxycarbonyl)-

phenyl)zinc(II) iodide (**42a**) (0.87 M solution in THF, 1.0 equiv, 0.5 mmol, 0.6 ml) was added and the reaction mixture was heated to 70 °C and stirred at this temperature for 16 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL) and sat. aqueous NaCl-solution (10 mL) dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (hexanes:EtOAc 9:1 → 4:1) afforded the analytically pure product (54.4 mg, 43%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.27 – 8.15 (m, 2H), 8.02 – 7.89 (m, 2H), 5.92 – 5.68 (m, 1H), 5.39 – 5.26 (m, 1H), 5.13 (dd, *J* = 17.0, 1.0 Hz, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.88 – 3.78 (m, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

1-((4-Methoxyphenyl)sulfonyl)pyrrolidine (9a)

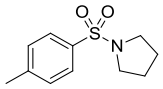


1-((4-methoxyphenyl)sulfonyl)pyrrolidine (**9a**) was synthesized according to TP 12 from 4-iodoanisole (**8a**) (0.5 mmol, 117 mg), pyrrolidine (**22a**) (2.0 mmol, 0.16 mL), DABSO (1.0 mmol, 240.3 mg), $Pd(OAc)_2$ (10 mol-%, 11.2 mg), SPhos (20 mol-%, 41.1 mg), pyridine (1.0 mmol, 0.1 mL) and TEMPO (20 mol-%, 15.6 mg) in DMSO (2.0 mL). Purification by chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (84.6 mg, 70%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.80 – 7.71 (m, 2H), 7.03 – 6.93 (m, 2H), 3.87 (s, 3H), 3.28 – 3.14 (m, 4H), 1.82 – 1.67 (m, 4H).

Analytical date is consistent with literature.[231]

1-Tosylpyrrolidine (9b)

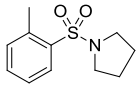


1-Tosylpyrrolidine (**9b**) was synthesized according to TP 12 from 4-iodotoluene (**8aa**) (0.5 mmol, 109 mg), pyrrolidine (**22a**) (1.5 mmol, 0.12 mL), DABSO (0.75 mmol, 180.2 mg), $Pd(OAc)_2$ (5 mol-%, 5.6 mg), SPhos (10 mol-%, 20.5 mg), pyridine (**#**) (1.0 mmol, 0.1 mL) and TEMPO (20 mol-%, 15.6 mg) in DMSO (2.0 mL). Purification by chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (59.2 mg, 53%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.76 – 7.67 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 3.32 – 3.15 (m, 4H), 2.43 (s, 3H), 1.85 – 1.67 (m, 4H).

Analytical date is consistent with literature.[66]

1-(o-Tolylsulfonyl)pyrrolidine (9c)

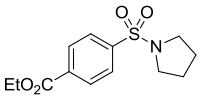


1-(o-tolylsulfonyl)pyrrolidine (**9c**) was synthesized according to TP 12 from 2-iodotoluene (**8w**) (0.5 mmol, 63 µL), pyrrolidine (**22a**) (2.0 mmol, 0.16 mL), DABSO (1.0 mmol, 240.3 mg), $Pd(OAc)_2$ (10 mol-%, 11.2 mg), pyridine (1.0 mmol, 0.1 mL) and TEMPO (20 mol-%, 15.6 mg) in DMSO (2.0 mL). Purification by chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (17.6 mg, 17%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.93 – 7.88 (m, 1H), 7.47 – 7.39 (m, 1H), 7.35 – 7.28 (m, 2H), 3.34 – 3.28 (m, 4H), 2.64 (s, 3H), 1.93 – 1.87 (m, 4H).

Analytical date is consistent with literature.[66]

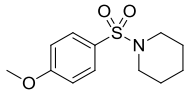
Ethyl 4-(pyrrolidin-1-ylsulfonyl)benzoate (9e)



Ethyl 4-(pyrrolidin-1-ylsulfonyl)benzoate (**9e**) was synthesized according to TP 12 from ethyl 4-iodobenzoate (**8v**) (0.5 mmol, 84 µL), pyrrolidine (**22a**) (1.5 mmol, 0.12 mL), DABSO (0.75 mmol, 180.2 mg), $Pd(OAc)_2$ (5 mol-%, 5.6 mg), SPhos (10 mol-%, 20.5 mg), pyridine (1.0 mmol, 0.1 mL) and TEMPO (20 mol-%, 15.6 mg) in DMSO (2.0 mL). Purification by chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (24.5 mg, 18%).

^{1}H NMR (250 MHz, $CDCl_3$) δ 8.25 – 8.12 (m, 2H), 8.00 – 7.84 (m, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 3.33 – 3.12 (m, 4H), 1.83 – 1.69 (m, 4H), 1.41 (t, *J* = 7.1 Hz, 3H).

1-((4-Methoxyphenyl)sulfonyl)piperidine (9g)

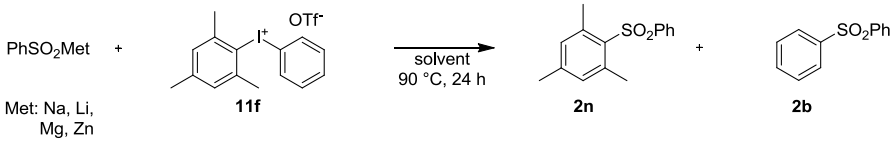


1-((4-methoxyphenyl)sulfonyl)piperidine (**9g**) was synthesized according to TP 12 from 4-iodoanisole (**#**) (0.5 mmol, 117 mg), piperdine (**9c**) (1.5 mmol, 0.15 mL), DABSO (0.75 mmol, 180.2 mg), $Pd(OAc)_2$ (5 mol-%, 5.6 mg), SPhos (10 mol-%, 20.5 mg), pyridine (1.0 mmol, 0.1 mL) and TEMPO (20 mol-%, 15.6 mg) in DMSO (2.0 mL). Purification by chromatography (hexanes:EtOAc 9:1 → 4:1) yielded the product as colorless solid (19.6 mg, 15%).

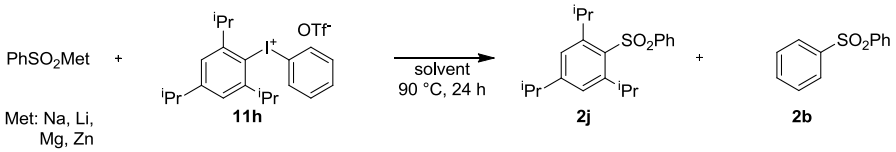
^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.75 – 7.62 (m, 2H), 7.02 – 6.93 (m, 2H), 3.87 (s, 3H), 3.02 – 2.89 (m, 4H), 1.70 – 1.56 (m, 4H), 1.47 – 1.34 (m, 2H).

Analytical date is consistent with literature.[178]

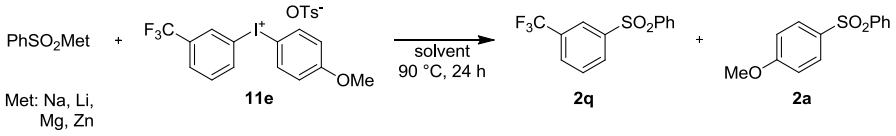
8.3.3 Selectivity Studies



A dry Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with phenyl(2,4,6-trimethylphenyl)iodonium triflate (**11f**) and a benzenesulfinic acid salt (**7l**, **34a**, **37a** or **41a**) (0.5 mmol, 1.0 equiv) in 1.0 mL solvent (equiv and solvents according to TP 1, 2, 4 and 6). After heating to 90 °C, the reaction mixture was stirred at this temperature for 24 h. After cooling to 25 °C, sat. aq. NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded only **2n** as a colorless solid in all cases. Yields are given in chapter 3.5.

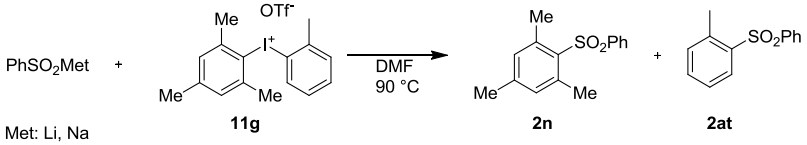


A dry Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with phenyl(2,4,6-triisopropylphenyl)iodonium triflate (**11h**) and a benzenesulfinic acid salt (**7l**, **34a**, **37a** or **41a**) (0.5 mmol, 1.0 equiv) in 1.0 mL solvent (equiv and solvents according to TP 1, 2, 4 and 6). After heating to 90 °C, the reaction mixture was stirred at this temperature for 24 h. After cooling to 25 °C, sat. aq. NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded only **2j** as a colorless solid in all cases. Yields are given in chapter 3.5.



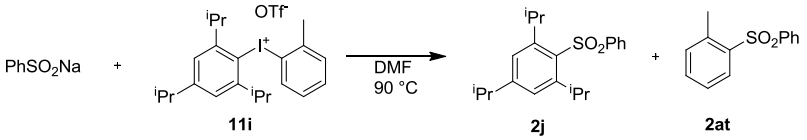
A dry Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with (4-methoxyphenyl)(3-(trifluoromethyl)phenyl)iodonium tosylate (**11e**) and a benzenesulfinic acid salt (**7l**, **34a**, **37a** or **41a**) (0.5 mmol, 1.0 equiv) in 1.0 mL solvent (equiv and solvents according to TP 1, 2, 4 and 6). After heating to 90 °C, the reaction mixture was stirred at this temperature for 24 h. After cooling to 25 °C,

sat. aq. NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded two products, **2q** and **2a**, as colorless solids. Yields are given in chapter 3.5.



A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with (2-methylphenyl)(2,4,6-trimethylphenyl)iodonium triflate (**11q**) and benzenesulfinic acid sodium or lithium salts (**7l** or **37a**) (equiv according to TP 1 and 2) in 1.0 mL DMF After heating to 90 °C, the reaction mixture was stirred at this temperature for 24 h. After cooling to 25 °C, sat. aq. NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 20:1 → 9:1) yielded two products, **2n** and **2at**, as colorless solids. Yields are given in chapter 3.5.

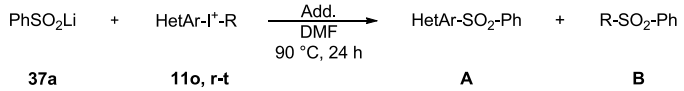
In the second experiment the same setup was made, only 10 mol-% CuI (0.05 mmol, 9.5 mg) were added to the reaction mixture. After stirring at 90 °C for 24 h, the reaction was cooled to 25 °C, sat. aq. NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Isolation by column chromatography (cyclohexane:EtOAc 100:1 → 9:1) afforded also two products, **2n** and **2at**, as colorless solids.



In the other selectivity experiment, a dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with (2-methylphenyl)(2,4,-triisopropylphenyl)iodonium triflate (**11i**) (0.55 mmol, 313.2 mg, 1.1 equiv) and benzenesulfinic acid sodium salt (**7l**) (0.5 mmol, 82.2 mg, 1.0 equiv) in DMF (1.0 mL). After heating to 90 °C, the reaction mixture was stirred at this temperature for 24 h. After cooling to 25 °C, sat. aq. NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column

chromatography (cyclohexane:EtOAc 20:1 → 4:1) yielded only product **2j** (173.8 mg, 96%) as colorless solid.

In the next experiment the same setup was made as above, only 10 mol-% CuI (0.05 mmol, 9.5 mg) were added to the reaction mixture. After stirring at 90 °C for 24 h, the reaction was cooled to 25 °C, sat. aq. NH_4Cl-solution (10 mL) was added and the aqueous layers were extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Isolation by column chromatography (cyclohexane:EtOAc 20:1 → 9:1) afforded the other sulfone **2at** (74.0 mg, 64%) as colorless solid.



Metal-free

The metal-free reactions were made according to TP 2:

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with benzenesulfinic acid lithium salt **37a** (1.5 equiv), pyridine-3-yl-iodonium salts **11r-t** (1.0 equiv) and DMF (2.0 mL/mmol iodonium salt, 0.5 M). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) afforded the analytically pure products **A** and **B**, as colorless solids. Yields are given in section 3.5.

Metal-catalyzed reactions

The metal-catalyzed reactions were prepared according to TP 2 with additional 10 mol-% CuI (9.5 mg):

A dry, Ar-flushed Schlenk-flask equipped with a magnetic stirrer and a rubber septum was charged with benzenesulfinic acid lithium salt **37a** (1.5 equiv), pyridine-3-yl-iodonium salts **11r-t** (1.0 equiv), CuI (10 mol-%, 9.5 mg) and DMF (2.0 mL/mmol iodonium salt, 0.5 M). The reaction mixture was heated to 90 °C and stirred at this temperature for 24 h. After cooling to 25 °C, sat. aqueous NH_4Cl-solution (10 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were washed with dist. H_2O (15 mL), dried over Na_2SO_4 and the solvents were removed under reduced pressure. Purification by column chromatography (cyclohexane:EtOAc 9:1 → 4:1) afforded the analytically pure products **A** and **B**, as colorless solids. Yields are given in section 3.5.

9. Appendix

9.1 Abbreviations

° C	degree Celsius
Ac	acetyl
Ad	adamantyl
AIBN	Azobisisobutyronitrile
Alk	alkyl
Ar	aryl
aq	aqueous
BiPhos	5-(di-*tert*-butylphosphino)-3',5'-diphenyl-1'H-1,4'-bipyrazole
Bn	benzyl
Bz	benzoyl
Bu	butyl
CAM	Cerium ammoniummolybdate
cod	cycloocta-1,5-diene
cond	conditions
Cy	cyclohexyl
d	dublett
DABCO	1,4-diazabicyclo[2.2.2]octane
DABSO	1,4-diazabicyclo[2.2.2]octane·2SO_2
DavePhos	2'-(dicyclohexylphosphino)-*N,N*-dimethyl-[1,1'-biphenyl]-2-amine
dba	dibenzylidenacetone
DCE	dichloroethane
DCM	dichloromethane
dd	dublett of dubletts
DMAP	4-dimethylaminopyridine
DME	dimethoxyethanol
DMF	*N,N*-dimethylformamid
DMG	direct metallating group
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(*1H*)-pyrimidinone
DMSO	dimethylsulfoxide
dppf	1,1'-bis(diphenylphosphino)ferrocene
dt	dublett of tripletts
e.g.	exempli gratia (lat.), for example
equiv	equivalents
et al.	et alii (lat.), and others
Et_2O	diethylether
etc.	et cetera (lat.), and so on
EtOAc	ethylacetate
exp	experimental
g	gramm

GC	gas chromatography
h	hour
het	hetero
HRMS	high resolution mass spectrometry
Hz	Hertz
IBX	2-iodoxybenzoic acid
*i*Pr	iso-propyl
IPr·HCl	1,3-Bis(2,6-diisopropylphenyl)imidazolium Chloride
IR	infra red
J	joule
L	liter
LA	Lewis Acid
M	molar, mega
m	milli, meta, multiplett
m.p.	melting point
MALDI	Matrix-assisted laser desorption/ionization
MCR	multi component reaction
*m*CPBA	*meta*-chloroperbenzoic acid
Me	methyl
MeCN	acetonitrile
Met	metal
min	minute
MS	mass spectrometry, molecular sieve
NBS	*N*-bromosuccinimde
nBu	*n*butyl
NMP	*N*-methylpyrrolidone
NMR	nuclear magnetic resonance
o	ortho
OTf	triflate
OTS	tosylate
p	para
PEPPSI	pyridine-enhanced precatalyst preparation stabilization and initiation
Ph	phenyl
phen	phenantrene
pp.	pages
ppm	parts per million
q	quartett
quant	quantitative
R_f	retention factor
rt	room temperature
RuPhos	2-Dicyclohexylphosphino-2',6'-diisopropoxybiphenyl
s	singlett, sec
sat.	saturated
sept	septett
SPhos	2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl
t	time, triplett, tert

T	temperature
TBAB	tetrabutyl ammonium bromide
TBAF	tetrabutyl ammonium flouride
TEMPO	2,2,6,6-tetramethylpiperidinyloxyl
TFA	trifluoro acetic acid
TFE	trifluoro ethanol
TfOH	trifluoromethanesulfonic acid
THF	tetrahydrofuran
TMEDA	tetramethylethylenediamine
TP	typical procedure
XantPhos	(9,9-dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphine)

9.2 References

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9.4 Deutsche Zusammenfassung (German Summary)

9.4.1 Einleitung und Zielsetzung

Die Sulfonyl-Gruppe (-SO_2-) ist ein weit verbreitetes Strukturmotiv in der organischen Chemie und Bestandteil vieler biologisch aktiver Moleküle, insbesondere Arzneistoffen (Abb. 9.1). Zwei der am häufigsten auftretenden Gruppen sind Sulfone und Sulfonamide, die in über 100 zugelassenen Medikamenten und 10% der meistverkauften Medikamente sind. Insofern kommt der Entwicklung neuer Synthesemethoden eine große Bedeutung zu. Dabei stehen besonders einfache, wirtschaftliche und zeitsparende Vorgehensweisen im Vordergrund, die eine große Bandbreite an neuen Substanzen generieren können. Ein Ansatz hierfür sind Multikomponenten- oder Eintopfreaktionen.

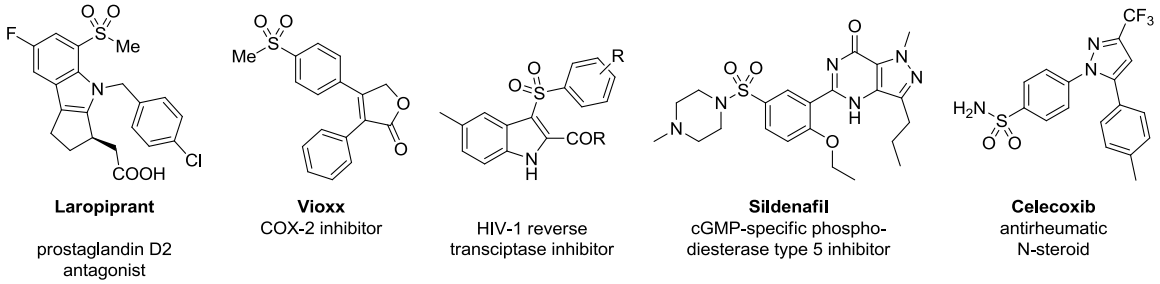

Abbildung 9.1. Biologisch aktive Sulfone und Sulfonamide.

Aufgrund der Wichtigkeit dieser zwei Strukturklassen, sollen im Rahmen der hier vorliegenden Doktorarbeit neue Syntheserouten für Sulfone und Sulfonamide entwickelt werden. Besonderes Augenmerk wird auf die die Einführung der SO_2-Einheit während der Reaktionsführung gelegt. Im Vergleich zu bereits existierenden Verfahren ist dies ein enormer Fortschritt, da die Mehrheit der bekannten Routen auf Schwefel- oder Schwefeldioxid-haltige Startmaterialien zurückgreift.

In dieser Arbeit ist der Ausgangspunkt Sulfonsynthese die Reaktion zwischen einem Arylhalogenid, einer SO_2-Quelle und einem Organometallreagenz (Abb. 9.2). Die Darstellung der Sulfone soll über eine Übergangsmetall-katalysierte Route erfolgen, die von einfachen, leicht zugänglichen Edukten ausgeht. Desweiteren sollte dieser Weg sowohl als Multikomponentenreaktion als auch als Eintopfreaktionen, mit der Bildung der Sulfinate *in situ*, ablaufen.

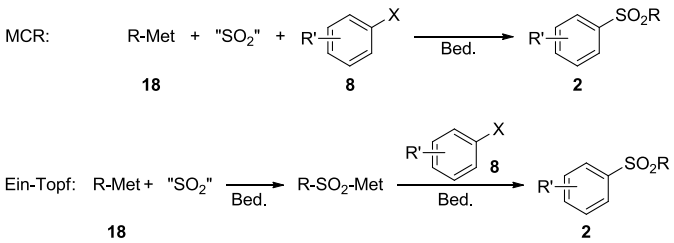

Abbildung 9.2. Mögliche Syntheserouten zu Arylsulfonen.

Als zweites Projekt soll eine Multikomponentenreaktion zur Synthese von Sulfonamiden ausgehend von einer Palladium-katalysierte Reaktion zwischen einem Arylhalogenid, einem Amin und DABCO·2SO_2 oder DMAP·SO_2 als Schwefeldioxid-Quelle (Abb. 9.3) etabliert werden.

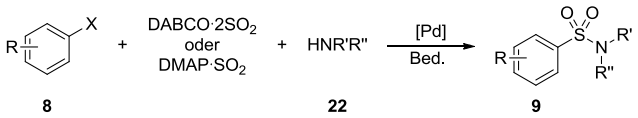

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Abbildung 9.3. Vorgeschlagene Reaktion zu Darstellung von Sulfonamiden.

9.4.2 Synthese von Arylsulfonen ausgehend von Organometallreagenzien und Iodoniumsalzen

Es gelang uns einen syntheischen Zugang zu Arylsulfonen basierend auf von Natrium-, Lithium-, Magnesium- und Zinksulfinaten zu finden (Abb. 9.4). Diese Reaktion besitzt eine sehr große Anwendungsbandbreite und setzt sowohl Aryl- als auch Alkylsulfinate effizient um (Abb. 9.5). Außerdem weisen Reaktionen mit unsymmetrischen Diaryliodoniumsalzen hohe Chemoselektivitäten auf (Abb. 9.6).

Auf der Grundlage auf der Reaktion zwischen Natriumsulfinaten und Iodoniumsalzen wurde eine simple Route zur Synthese von Diarylsulfonen abgeleitet, jedoch war hierbei die Sulfonylgruppe noch Bestandteil eines der Edukte. Um die SO_2-Einheit während der Reaktion einführen zu können, wurde ein praktisches Eintopf-Protokoll entwickelt, welches die direkte Umsetzung von (hetero)aromatischen und alkylischen Halogeniden zu Arylsulfonen gestattet. Diese innovative Methode besteht aus folgenden vier Schritten (Abb. 9.4):

1) Generierung des Organometallreagenzes via Halogen-Metall-Austausch, direkte Metallinsertion oder Deprotonierung
2) Reaktion des Organometallreagenzes mit SO_2 zum Sulfinat
3) Entfernen des SO_2-Überschusses und flüchtiger Komponenten
4) Umsetzung des nicht aufgereinigten Sulfinates mit einem Iodoniumsalz.

Diverse Aryl- und Heteroarylsulfone können mittels dieses direkten Verfahrens hergestellt werden. Reaktionen mit Magnesium- und Zinksulfinaten sind jedoch aufgrund von Nebenreaktionen zwischen den Halogenid-Gegenionen inhärent limitiert. Dies kann aber durch einen Überschuss an Iodoniumsalz umgangen werden.

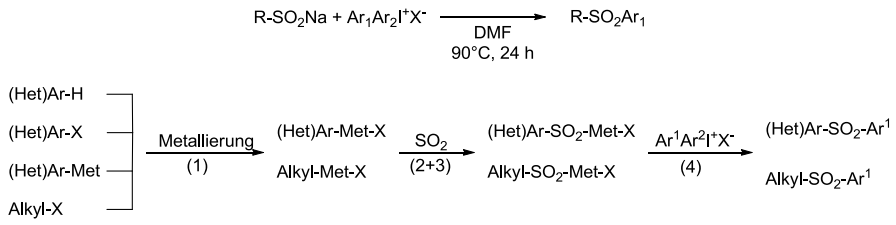

Abbildung 9.4. Ursprüngliche Methode und Weiterentwicklung zur 4-stufigen Eintopfsynthese.

Die große Bandbreite unserer Methode ist in Abbildung 9.5 gezeigt. Die hohe Toleranz gegenüber funktionellen Gruppen führt zur Umsetzung von elektronenarmen und –reichen Arylen als auch Heteroaromaten zu Diarylsulfonen. Außerdem bietet dieser Weg Zugang zu Alkylarylsulfonen.

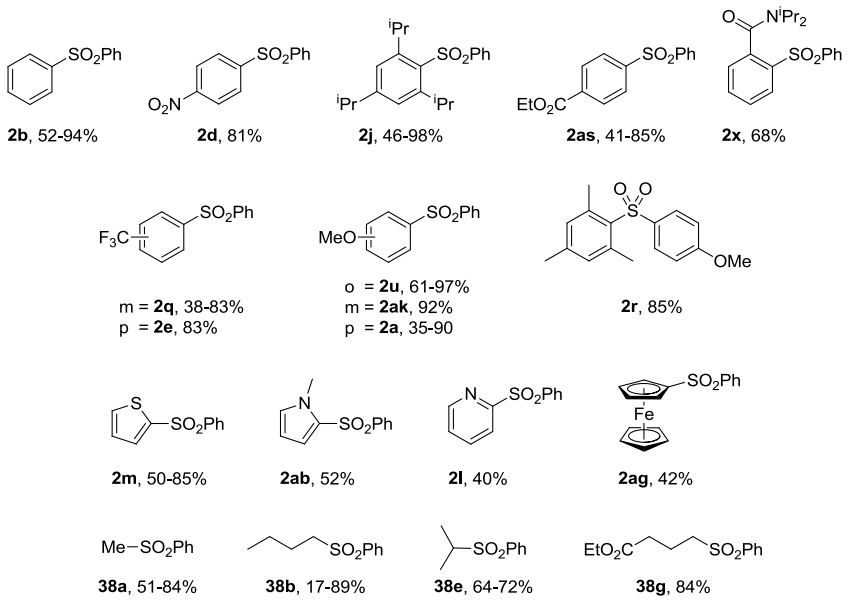

Abbildung 9.5. Ausgewählte Substanzen, die im Rahmen dieser Arbeit synthetisiert wurden.

In Reaktionen mit unsymmetrischen Diaryliodoniumsalzen wurde eine interessante Chemoselektivität beobachtet. Sterisch anspruchsvollere Arylgruppen werden bevorzugt übertragen (Abb. 9.6). Ein exzellentes Beispiel dafür ist die Triisopropylphenyl-Gruppe. Die Chemoselektivität kann durch Zugabe eines Übergangsmetall-Katalysators umgekehrt werden. In Anwesenheit katalytischer Mengen CuI wird die sterisch weniger anspruchsvolle Gruppe transferiert.

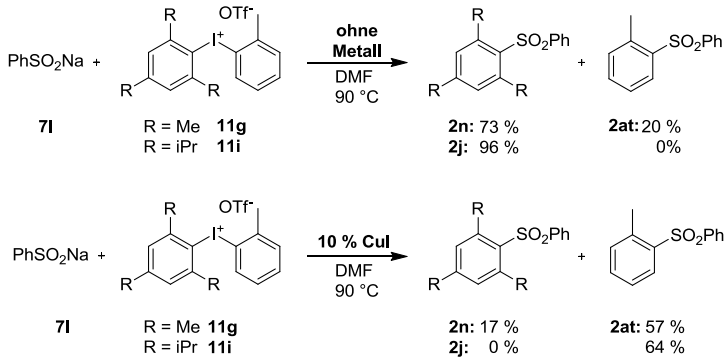

Abbildung 9.6. Ausgewählte Beispiele zu Selektivitätsstudien.

9.4.3 Nickel-katalysierter Ansatz zur Synthese von Diarylsulfonen

Es soll ein neuartiger Übergangsmetall-katalysierter Ansatz zur Darstellung von Diarylsulfonen ausgehend von Arylhalogeniden und Sulfinaten entwickelt werden (Abb. 9.7).

Erste Experimente deuten auf Nickel-Katalysatoren als gute Wahl für die Reaktion. Optimierungsreaktionen zeigten eine starke Abhängigkeit der Ausbeute in Hinsicht auf die Bisswinkel der an das zentrale Nickelatom koordinierten Liganden. Da die bis dato besten Ergebnisse mit dem Komplex **54** erzielt wurden, wird der $NiPMe_3$-Komplex **91** momentan in unserem Labor weiteren Studien unterzogen. Bislang ist davon auszugehen, dass dieser Katalysator hervorragende Ergebnisse liefert und zu einer allgemein gültigen Methode führt. Außerdem werden Diphosphin-Liganden getestet, die sich durch noch kleinere Bisswinkel auszeichnen.

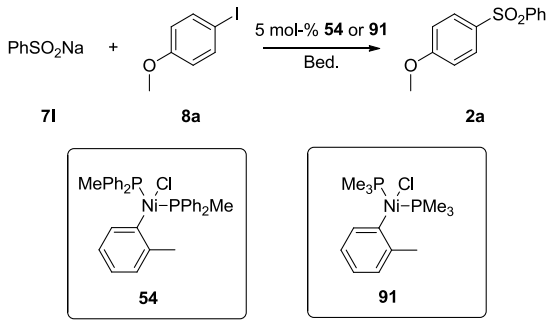

Abbildung 9.7. Nickel-katalysierter Ansatz zur Synthese von Diarylsulfonen.

9.4.4 Anwendung von SO_2-Surrogaten zur Herstellung von Arylsulfonen

In einem weiteren Projekt sollte die Anwendbarkeit von SO_2-Surrogaten, insbesondere Metabisulfiten ($S_2O_5^-$), untersucht werden. Ziel war eine Eintopf- oder sogar Multikomponentenreaktion zu entwickeln, die von Alkylhalogeniden, „SO_2“ und Organozinkreagenzien (Abb. 9.8) ausgeht. Trotz in Kapitel 5 diskutierten Teilerfolgen, konnte noch keine allgemeingültige Route gefunden werden. Durch Aufklärung des Reaktionsmechanismus soll so ein generell anwendbares Protokoll entstehen.

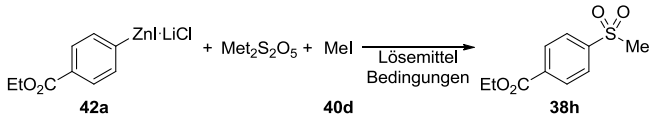

Abbildung 9.8. Anwendung von SO_2-Surrogaten zur Darstellung von Arylsulfonen.

9.4.5 Multikomponenten Reaktion zur Darstellung von Sulfonamiden

Zielsetzung war die Etablierung einer Übergangsmetall-katalysierten Multikomponenten Reaktion zur Darstellung von Sulfonsäureamiden. Eine Reaktion zwischen Aminen, Arylhalogeniden und DABSO als SO_2-Quelle wurde in Form einer Palladium-katalysierten Aminosulfonylierung entwickelt (Abb. 9.9). Dies ist eine enorme Verbesserung, da soweit nur Reaktionen ausgehend von Hydrazinen, aber nicht Aminen literaturbekannt sind.

Eine Kernkomponente und zugleich Einschränkung in der Reaktionsführung ist das benötigte stark Lewis-saure Solvenz DMSO. Ferner wurde gezeigt, dass nur das dehalogenierte Aren als Nebenprodukt entsteht,

dessen Bildung kann aber durch den Zusatz von TEMPO, einem stabilen Radikal, unterdrückt werden. Das klassische Kreuzkupplungs-Produkt **92** wurde nicht beobachtet. Weitere Experimente mit einer sogenannten „Radikaluhr" führten zu der Annahme, dass diese Kreuz-Kupplung nicht über einen klassischen, sondern radikalischen Mechanismus verläuft. Als nächste Schritte werden die mechanistischen Studien ausgedehnt. Wir erhoffen uns durch das Verständnis des Mechanismus, eine generell anwendbare Multikomponenten Reaktion zur Synthese von Sulfonamiden entwickeln zu können.

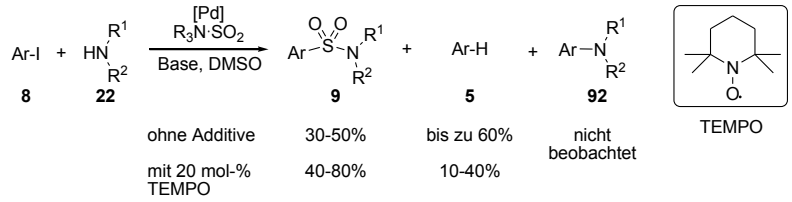

Abbildung 9.9. Palladium-katalysierte 3-Komponenten Reaktion zu Sulfonamiden.

Eine mögliche Alternative zur Nutzung von Metabilsulfit oder DABSO als SO_2-Ersatz ist eine photokatalysierte Kreuz-Kupplung (Abb. 9.10). Die Reaktion von Iodoniumsalzen, Hydrazinen oder sogar Aminen und einer SO_2-Quelle zu Sulfonamiden, wird momentan auch untersucht.

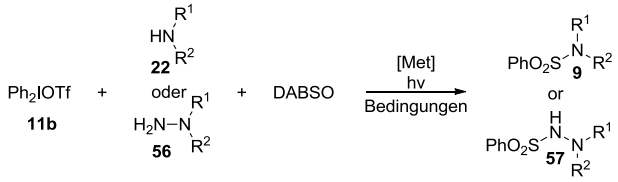

Abbildung 9.10. Übergangsmetall-katalysierte Photoreaktion zur Darstellung von Sulfonamiden.

9.5 Curriculum Vitae

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EDUCATION

Goethe Universität
PhD Student in the Institute for Organic Chemistry and Chemical Biology 2015
PhD thesis: *One-Pot and Multicomponent Reactions towards Sulfones and Sulfonamides*
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Goethe Universität
Academic Degree Master of Science (grade: 1,8, good) 2011
Masterthesis: *Synthesis and reaktivity of quinoline and pyridine sulfonates* (grade: 1,3, very good)
Under supervision of Dr. G. Manolikakes
Academic Degree Bachelor of Science (Note: 1,8, good) 2009
Bacherlorthesis: *Iminium Catalysis – Synthesis of the catalysts and their application* 2008
(Note: 1,0, very good)
In the group of Prof. Dr. M. Rüping

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Allgemeine Hochschulreife

TEACHING EXPERIENCE

Supervisor in the Lab Course „Organische Chemie für Chemiker und Biochemiker“ **2011-2014**

Supervision of the Bachelor Thesis: **2013-2014**
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Nickel – katalysierte Synthese von Arylsulfonen

PUBLICATIONS

Umierski, Natalie; Manolikakes, Georg *Organic Letters* **2013,** *15*, 188-191. *Metal-free synthesis of diaryl sulfones from arylsulfinic acid salts and diaryliodonium salts.*

Umierski, Natalie; Manolikakes, Georg *Organic Letters* **2013,** 15, 4972-4975. *Arylation of Lithium Sulfinates with Diaryliodonium Salts: A Direct and Versatile Access to Arylsulfones.*

Margraf, Natalie; Manolikakes, Georg *Journal of Organic Chemistry,* **2015***, 80,* 2582-2600. *One-Pot Synthesis of Arylsulfones from Organometallic Reagents and Iodonium Salts.*

POSTER

Umierski, Natalie; Manolikakes, Georg *Orchem* **2014**, Weimar *One-Pot Transitionmetal-free Synthesis of Sulfones from Sulfinic Acid Salts with Diaryliodonium Salts.*

Umierski, Natalie; Georg Manolikakes *Frühjahrssymposium* **2014**, Jena *One-Pot Metal-free Synthesis of Sulfones from Sulfinic Acid Salts with Diaryliodonium Salts.*

Umierski, Natalie; Georg Manolikakes *Wissenschaftsforum Chemie* **2013**, Darmstadt *One-Pot Metal-free Synthesis of Sulfones from Lithium and Sodium Sulfinic Acid Salts with Diaryliodonium Salts.*

Umierski, Natalie; Beliakin, Michael; Georg Manolikakes *Frühjahrssymposium* **2012**, Rostock

AWARDS

Travel Grant of the German Chemical Society	2014
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