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Straightforward Strategies for the Preparation of NH-Sulfoximines: A Serendipitous Story

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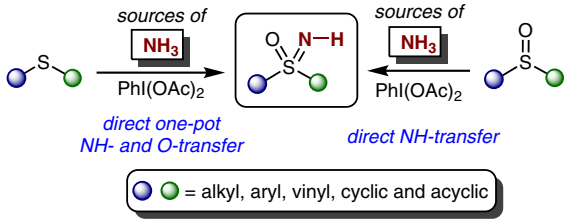

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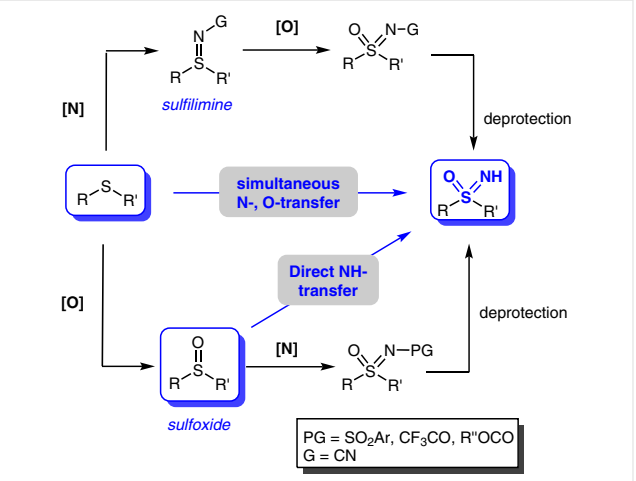
Abstract Sulfoximines are emerging as valuable new isosteres for use in medicinal chemistry, with the potential to modulate physicochemical properties. Recent developments in synthetic strategies have made the unprotected 'free' NH-sulfoximine group more readily available, facilitating further study. This account reviews approaches to NH-sulfoximines, with a focus on our contribution to the field. Starting from the development of catalytic strategies involving transition metals, more sustainable metal-free processes have been discovered. In particular, the use of hypervalent iodine reagents to mediate NH-transfer to sulfoxides is described, along with an assessment of the substrate scope. Furthermore, a one-pot strategy to convert sulfides directly into NH-sulfoximines is discussed, with N- and O-transfer occurring under the reaction conditions. Mechanistic evidence for the new procedures is included as well as relevant synthetic applications that further exemplify the potential of these approaches.

Key words NH-sulfoximines, N-transfer, hypervalent iodine, nitrenoids, catalysis

1 Introduction

Since the discovery of the first sulfoximine in 1949,[1] the chemistry of sulfoximines has developed from a rather niche area into a field with wide and expanding applications.[2–7] The sulfoximine group is chemically stable, is stable to hydrolysis, and has stable configuration. As such, the utility of the sulfoximine functional group encompasses chiral auxiliaries,[3] ligands in asymmetric catalysis,[4] and directing groups for C–H functionalization,[5] as well as agrochemicals[6] and medicinal chemistry.[7] Much of the development over the last decade has been facilitated by the introduction of new and more practical synthetic methodologies.[8–10] These advances in the field brought about an increasing interest in sulfoximines in life sciences and drug discovery.[11–14] Examples of some biologically relevant molecules bearing the sulfoximine moiety are shown in Figure 1.

Our understanding of the potential of the sulfoximine group in drug discovery is growing. Compounds containing NH-sulfoximines from Bayer (BAY1000394 and BAY1143572) and AstraZeneca (AZD6738) are paving the way in current clinical trials.[12] While there remain relatively few published studies on sulfoximine properties relevant to medicinal chemistry, high metabolic stability, hydrogen-bond acceptor/donor capabilities and desirable physico-



Scheme 1 Strategies for accessing NH-sulfoximines

chemical properties have been observed.[7,13,14] As isosteres for sulfones, the sulfoximine group often provides improved solubility, and also presents further complexity with an additional attachment point. In a recent study, Bolm and co-workers from Boehringer Ingelheim reported the analysis of a series of matched molecular pairs to compare sulfoximines against other sulfur functionalities on various simple substrates.[13] Sirvent and Lücking from Bayer evaluated the sulfoximine functionality as an isostere for amines by incorporation into analogues of marketed drugs and advanced clinical candidates with favorable comparison of the physical and biological properties.[14]

From NH-sulfoximines, the nitrogen atom offers potential to introduce further molecular diversity through an increasingly broad array of transformations, as exemplified by N-trifluoromethylation,[15] arylation,[16] aroylation,[17] alkynylation,[18] alkylation,[19] propargylation,[20] cyanation,[21] thioetherification,[22,23] and intramolecular halocyclization reactions.[24] Racemic NH-sulfoximines can also be subjected to catalytic kinetic resolution.[25]

As a consequence of the importance of the sulfoximine functionality, the development of strategies for the synthesis and incorporation of this structural motif is still a vigorous research area. To access NH-sulfoximines, different synthetic approaches are now available (Scheme 1). Either the

Biographical Sketches

James A. Bull is a University Research Fellow in the Department of Chemistry at Imperial College London. He obtained his M.Sci. degree from the University of Cambridge, then spent a year at GlaxoSmithKline. He returned to the University of Cambridge to obtain his Ph.D. in organic chemistry under the supervision of Professor Steven V. Ley (2006). He then spent two years undertaking postdoctoral research with Professor André B. Charette at Université de Montréal. In 2009, he joined Imperial College London as a Ramsay Memorial Research Fellow. In 2011, he was awarded an EPSRC Career Acceleration Fellowship, and in 2016 was awarded a University Research Fellowship from The Royal Society. His research focuses on the development of efficient synthetic and catalytic methods to access novel structural motifs and heterocycles of interest in drug discovery.

Leonardo Degennaro is an Assistant Professor at the University of Bari "A. Moro". He obtained his master's degree in Chemistry and Pharmaceutical Technology at the University of Bari in 1999, and in 2003 his Ph.D. in Chemical Applied and Enzymatic Synthesis. In 2002, he was a visiting scholar at the Institute of Organic and Molecular Inorganic Chemistry, University of Groningen (The Netherlands) under the supervision of Prof. B. L. Feringa. In 2006, he was appointed Assistant Professor in Organic Chemistry at the Faculty of Pharmacy of the University of Bari. In 2011, he became a visiting assistant professor at the Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University (Japan), working in the group of Prof. J.-i. Yoshida. His research activity concerns the development of new stereoselective syntheses, organometallic chemistry, the reactivity of small heterocycles, flow chemistry, and the study of dynamic phenomena at the molecular level.

Renzo Luisi is an Associate Professor of Organic Chemistry at the University of Bari "A. Moro", Italy. He obtained an M.Sci. (summa cum laude) in Chemistry and Pharmaceutical Technology at the University of Bari (Italy) in 1996. In 2000, he obtained his Ph.D. in Chemical Sciences, and in 2001 was hired as Assistant Professor at the University of Bari. Four years later, in 2005, he was appointed Associate Professor of Organic Chemistry at the same University. In 2014, he received his national habilitation to full professor. He has been a visiting scholar at the University of Illinois (USA) working in the group of Prof. P. Beak, and a visiting professor at the University of Manchester (UK), Brown University (RI, USA) and the University of North Carolina (Charlotte, USA). His main research interests include organometallic chemistry (mainly lithium and boron chemistry), the synthesis and reactivity of small heterocycles, asymmetric synthesis and dynamic NMR spectroscopy. In 2010, he was awarded with a special funding program for young scientists from the Italian Ministry of Education and Research to start independent research in the field of sustainable chemistry and microreactor technology.

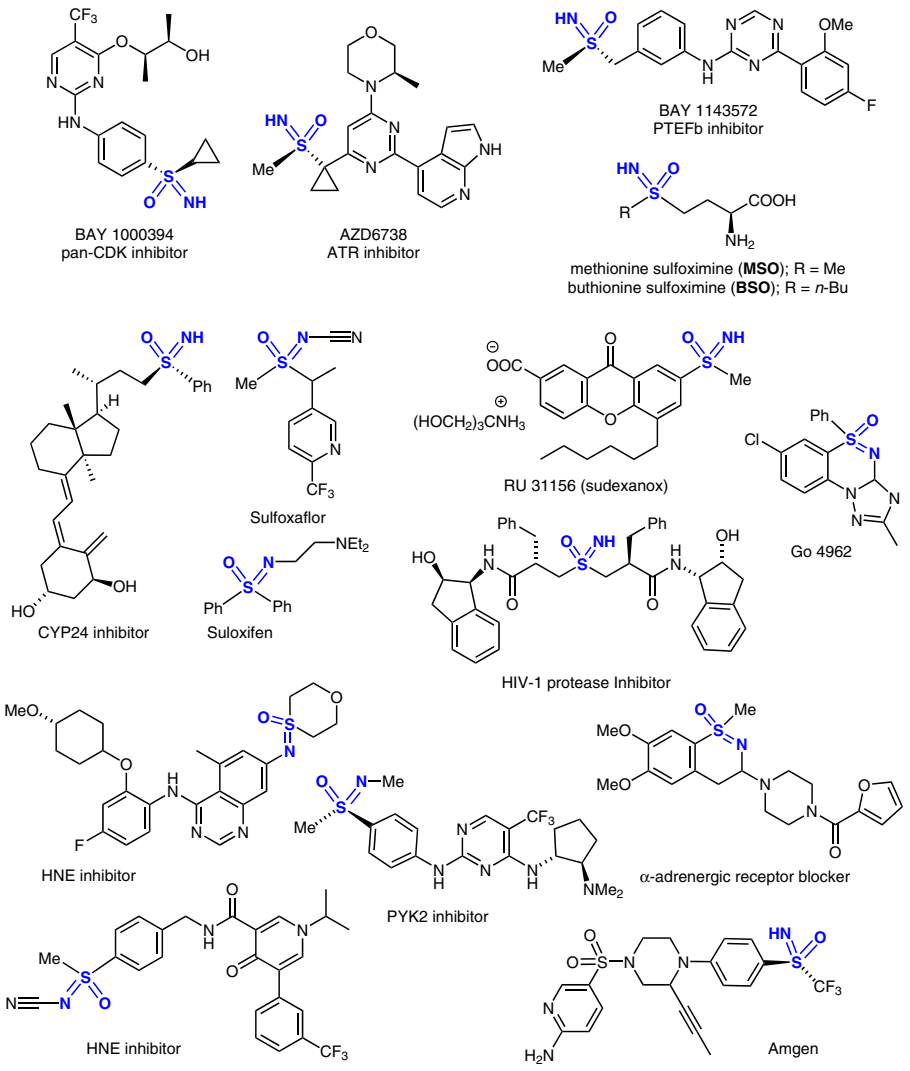


Figure 1 Examples of biologically relevant sulfoximine compounds

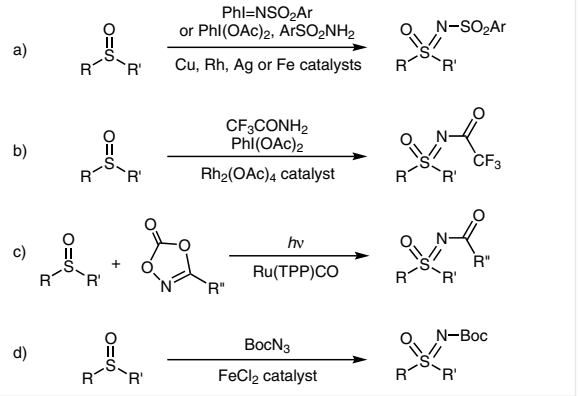
oxygen or the nitrogen group may be introduced first, affording the corresponding sulfoxide or sulfilimine,[26] respectively, using electrophilic reagents. Further oxidation of sulfilimines or imination of sulfoxides affords the sulfoximine. Commonly, a protected nitrogen group is involved, meaning three-step sequences are required to access the free NH-sulfoximine from sulfides.

In this account, we review methods for the synthesis of NH-sulfoximines through transition-metal-catalyzed and metal-free methods. In 2015, Bolm produced a comprehensive review on methods for sulfoximine synthesis.[8a] Here, we aim to highlight important advances for the preparation of NH-sulfoximines since 2015, with a focus on our own contributions. In particular, we recently reported straightforward strategies for the preparation of NH-sulfoximines by deprotection of easily removable N-protecting groups, the direct introduction of the NH group on sulfoxides, and the simultaneous transfer of O and NH groups on sulfides. Herein, we report our perspective on the progress of the work, how our strategies complement other available procedures, and underlying mechanistic investigations.

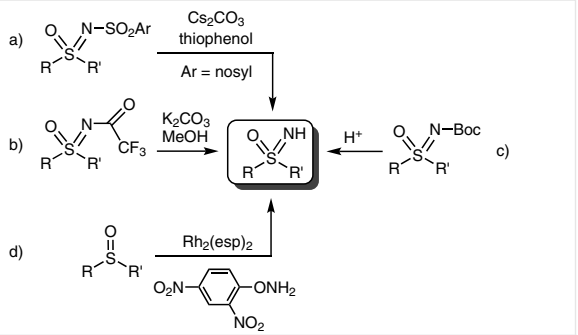
2 Strategies to Form NH-Sulfoximines Involving Transition-Metal Catalysts

When we first entered the field in 2015, there were several powerful methods available for transition-metal-catalyzed N-transfer to sulfoxides, being the most common route to protected sulfoximines (Scheme 2).[8a] The use of various transition-metal catalysts allows the generation and stabilization of metal-nitrenoid species responsible for

the N-transfer to the sulfur atom. The use of Cu, Rh, Ag and Fe catalysis has been employed for the transfer of sulfonamide groups by activated nitrogen species (e.g., PhI=NSO_2Ar) (Scheme 2, a).[27,28] Bolm reported the use of a combination of trifluoroacetamide and $PhI(OAc)_2$ in the presence of $Rh_2(OAc)_4$ as the catalyst for transferring the N–$COCF_3$ group to sulfoxides (Scheme 2, b).[28] The same author developed the *N*-acyl transfer to sulfoxides using 1,4,2-dioxazol-5-ones under Ru-catalyzed photochemical conditions (Scheme 2, c).[29] With these methods, removal of the nitrogen substituent could give access to free NH-sulfoximines. While *N*-tosyl groups are quite challenging to remove, it has been demonstrated that the nosyl (Ns) group could be removed by treatment with thiophenol and cesium carbonate (Scheme 3, a).[26b] On the other hand, *N*-trifluoroacetyl sulfoximines can be effectively N-deprotected by treatment with K_2CO_3/MeOH (Scheme 3, b).[28]



Scheme 2 Metal-based approaches to N-protected sulfoximines



Scheme 3 Strategies for accessing NH-sulfoximines

To date, there is only one direct transition-metal-catalyzed method for the preparation NH-sulfoximines. Richards reported a direct Rh-catalyzed method for NH-transfer to sulfoxides using *O*-(2,4-dinitrophenyl)hydroxylamine as the nitrogen source, and $Rh_2(esp)_2$ as the catalyst (Scheme 3, d).[30]

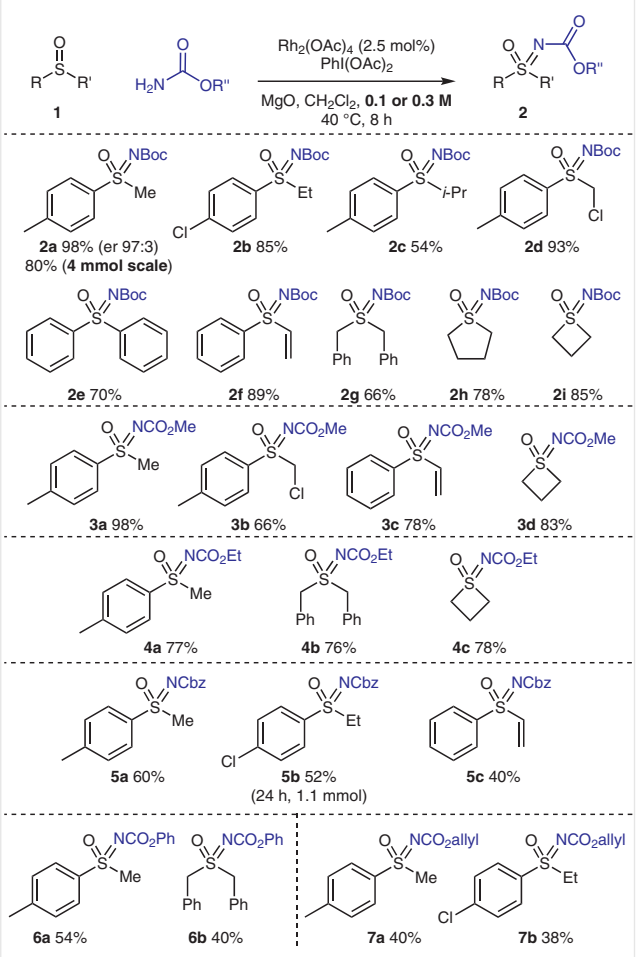
For the purposes of our initial investigations, we were interested in carbamate-protected sulfoximines. We envisioned that these would be stable to allow synthetic transformations prior to revealing the NH-sulfoximine, and would be straightforward to deprotect under well-understood conditions. In particular, sulfoximine carbamates bearing *N*-Boc and *N*-Cbz groups would present orthogonal N-deprotection strategies. However, we were surprised that similar catalytic methods to form carbamate-protected sulfoximines from carbamates were not available. Indeed, carbamate protecting groups were commonly installed through reaction of NH-sulfoximines formed by other methods.[12a] The only direct method, developed by Bach, used $FeCl_2$-catalyzed transfer of the *N*-Boc group to the sulfur atom of sulfoxides, using potentially explosive azides as the nitrogen source (Scheme 2, d).[31] Bach demonstrated the removal of the Boc group under acidic conditions using TFA (Scheme 3, c).

With the aim of providing new N-protected sulfoximines, we developed a Rh-catalyzed nitrogen transfer from *tert*-butyl, benzyl, methyl, ethyl, phenyl and allyl carbamates (Scheme 4).[32] We began our study exploring the use of $BocNH_2$ and $PhI(OAc)_2$ in the presence of $Rh_2(OAc)_4$ in order to generate an activated nitrenoid species (i.e., BocN=Rh) for the N-transfer to methyl tolylsulfoxide **1a**. Adapting Bolm's protocol,[28] using rhodium catalysis and magnesium oxide as the base,[33] we were delighted to observe the direct formation of the *N*-Boc sulfoximine **2a** in a very good yield when running the reaction at 40 °C. It is worth pointing out that the reaction required the metal catalysis; no reaction occurred in the absence of $Rh_2(OAc)_4$, and the reaction was performed under air without requiring anhydrous dichloromethane.

The scope of this reaction was widely explored, with examples shown in Scheme 4. Several *N*-Boc sulfoximines **2a–i** were prepared in good to excellent yields. Under optimized reaction conditions, it was also possible to transfer methyl and ethyl carbamates to the sulfur atom of sulfoxides to afford sulfoximines **3a–d** and **4a–c**, respectively. In the case of four-membered thietane 1-oxide, 5 mol% of the Rh catalyst was needed for the N-transfer of the carbamates leading to thietane sulfoximines **2i**, **3d** and **4c** (Scheme 4). The stereospecificity of the transfer of the *N*-Boc group to the sulfur was demonstrated by performing the reaction on enantioenriched (*S*)-**1a** (*er* 97:3). The reaction occurred with complete retention of configuration and preservation of the *er* in *N*-Boc-sulfoximine **2a**.[32,34]

Slightly different reaction conditions were needed for the transfer of benzyl, phenyl and allyl carbamates, which may undergo unfavorable coordination between the π-system in the carbamate substituents and the catalyst. These substrates were less reactive, but this could be somewhat ameliorated by running the reaction at an increased 0.3 M concentration of sulfoxide. Under these optimized conditions, *N*-benzyloxycarbonyl sulfoximines **5a–c**, *N*-phenyl-

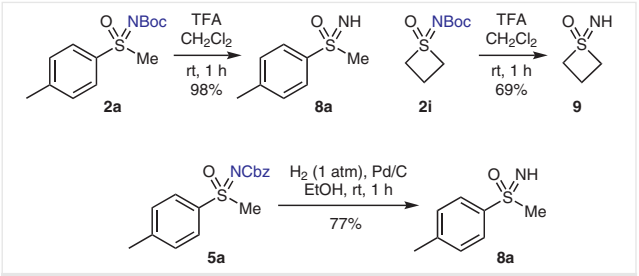
oxycarbonyl sulfoximines **6a**,**b** and *N*-allyloxycarbonyl sulfoximines **7a**,**b** could be prepared in acceptable yields (Scheme 4).



Scheme 4 Examples of Rh-catalyzed N-transfer of carbamates

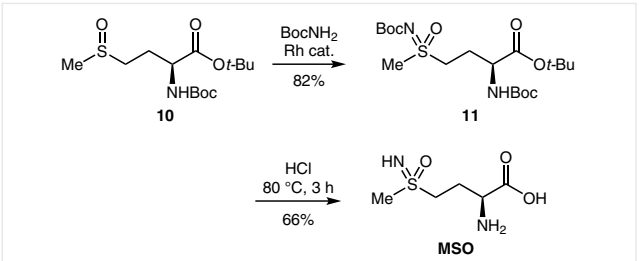
The usefulness of N-protected sulfoximines was demonstrated by further manipulations: *N*-Boc and *N*-Cbz sulfoximines **2b** and **5b** underwent smooth Pd- and Fe-catalyzed cross-coupling reactions.[32] The possibility to generate free NH-sulfoximines was demonstrated with the deprotection of *N*-Cbz- and *N*-Boc-sulfoximines **2a**, **5a** and **2i** (Scheme 5). By using standard acidic conditions, the Boc group was removed from *N*-Boc sulfoximines **2a** and **2i**, in good to excellent yields, affording the corresponding NH-sulfoximines **8a** and **9**, respectively. By using hydrogenolysis conditions (Scheme 5), the corresponding NH-sulfoximine **8a** was obtained in 77% yield from *N*-Cbz sulfoximine **5a**.

This synthetic strategy for the preparation of N-protected sulfoximines was effectively employed for the preparation of the target molecule methionine sulfoximine (**MSO**).[32,35] *N*-Boc sulfoximine **11**, formed from protected



Scheme 5 Deprotection of N-protected sulfoximines

methionine sulfoxide **10** (a 1:1 mixture of diastereoisomers) by Rh-catalyzed *N*-Boc transfer, was fully deprotected under acidic conditions affording MSO in 54% yield over the two steps (Scheme 6).



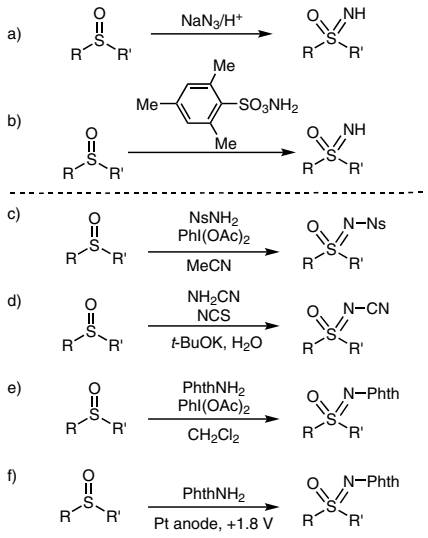
Scheme 6 Preparation of methionine sulfoximine (**MSO**)

This carbamate transfer protocol appears to be a general and convenient procedure for the preparation of sulfoximine carbamates. Our approach complements well with other available strategies to N-protected sulfoximines, and may facilitate synthetic planning by allowing flexible removal of protecting groups to access NH-sulfoximines.

3 Metal-Free Strategies to Prepare NH-Sulfoximines

The use of transition-metal catalysts such as rhodium can be expensive on large scale, and presents toxicological issues in the late-stage preparation of pharmaceutical products. In order to render the preparation of sulfoximines more sustainable, several transition-metal-free strategies have been developed (Scheme 7). For the direct preparation of NH-sulfoximines from sulfoxides, one of the oldest but still used procedures relies on the use of NaN_3 under acidic conditions (Scheme 7, a).[36] However, the harsh reaction conditions and the hazards related to the development of HN_3 makes this strategy unattractive. Interestingly, the use of flow technology has been suggested as a possible solution for the safer use of azides.[9b] However, even under flow conditions, this strategy was not compatible with enantioenriched starting materials. The use of the Eaton's reagent (phosphorus pentoxide, in methanesulfonic acid) and NaN_3

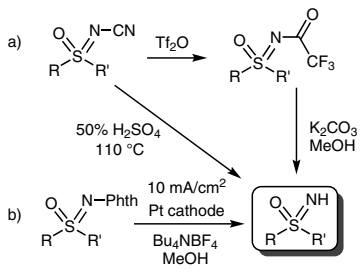
has recently been proposed by Liang for accessing NH-sulfoximines.[37] Another old strategy for the preparation of NH-sulfoximines uses *O*-mesitylene sulfonylhydroxylamine (MSH) for the direct transfer of the NH group to a sulfoxide (Scheme 7, b). However, MSH is an unstable reagent that needs to be prepared before use.[38]



Scheme 7 Reported metal-free strategies for the preparation of NH-sulfoximines

Several alternative milder metal-free iminations of sulfoxides have been developed leading to N-protected sulfoximines (Scheme 7). In one of the earlier reports, Bolm developed a metal-free transfer of the *p*-nitrobenzenesulfonylamide ($NsNH_2$) to the sulfur of sulfoxides in the presence of $PhI(OAc)_2$ as the oxidant (Scheme 7, c).[39] Very recently, Bolm reported a metal-free synthesis of *N*-cyanosulfoximines by N-transfer from cyanamide (NH_2CN) in presence of *N*-chlorosuccinimide (NCS) as the oxidant and potassium *tert*-butoxide as the base (Scheme 7, d).[40] Yudin introduced two metal-free methodologies leading to *N*-phthalimidosulfoximines. One simple protocol relies on the use of *N*-aminophthalimide ($PhthNH_2$) in the presence of $PhI(OAc)_2$ as the oxidant in dichloromethane (Scheme 7, e).[41] Yudin also developed a 'green' and mild electrochemical sulfoxide imination using $PhthNH_2$ as the iminating agent (Scheme 7, f).[42]

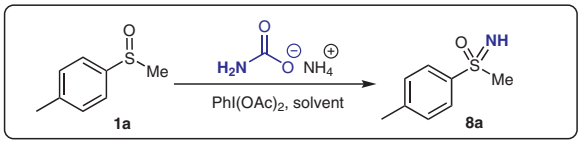
Removal of these N-protecting groups has been demonstrated in isolated examples. Deprotecting the CN group needed two additional steps to reveal the NH-sulfoximine consisting of treatment with Tf_2O followed by basic hydrolysis (Scheme 8, a).[43] The direct removal of the cyano group is also possible under rather forcing conditions: 50% aqueous sulfuric acid at 110 °C.[44] Yudin proved that the *N*-phthalimido group could be removed electrochemically using a Pt cathode in the presence of a methanolic solution of an ammonium salt (Scheme 8, b).[42]



Scheme 8 Removal of the N-protecting groups in selected sulfoximines

We considered that development of a safe, metal-free and direct method for the NH-transfer to sulfoxides, particularly using convenient inexpensive nitrogen sources, would offer considerable value. Building on our previous work on the Rh-catalyzed transfer of alkyl carbamates to sulfoxides (Scheme 4), we explored the possibility of using a carbamic salt as the nitrogen source, expecting the NH-sulfoximine to be formed directly due to the driving force for decarboxylation to occur, either before or after the N-transfer.

Ammonium carbamate was chosen as an inexpensive and easily handled nitrogen source, and was tested in metal-catalyzed (Rh and Fe) as well as metal-free N-transfer reactions. To our delight, we were able to obtain the desired NH-sulfoximine.[45] However, unexpectedly and serendipitously, we found that the reaction proceeded efficiently without requiring a transition-metal catalyst. This metal-free protocol opened up new perspectives in the field of the direct preparation of NH-sulfoximines as well as in N-transfer methodologies. The reaction was optimized using sulfoxide **1a**, and could be conducted under different reaction conditions (Scheme 9).



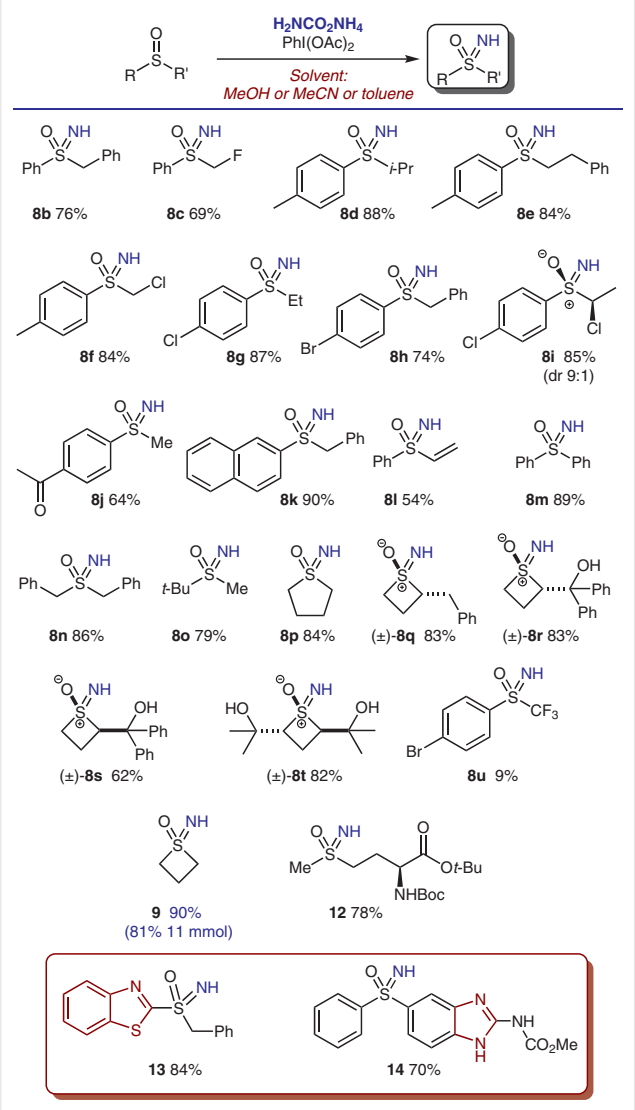
Conditions	Yield
a) toluene, $H_2NCO_2NH_4$ (2 equiv), $PhI(OAc)_2$ (2 equiv), MgO, 35 °C, 16 h	90%
b) MeCN, $H_2NCO_2NH_4$ (2.5 equiv), $PhI(OAc)_2$ (1.5 equiv), 25 °C, 3 h	90%
c) MeOH, $H_2NCO_2NH_4$ (4 equiv), $PhI(OAc)_2$ (3 equiv), 25 °C, 30 min	96%
Conditions c), 10 mmol scale	91%

Scheme 9 Metal-free protocols for the formation of NH-sulfoximines

Indeed, the reaction could be run in toluene, acetonitrile and methanol. Using toluene as the solvent (Scheme 9, conditions a), mixing ammonium carbamate with bisacetoxyiodobenzene and magnesium oxide at 35 °C for 16 hours led to sulfoximine **8a** in 90% yield. The heterogeneous nature of the reaction in toluene affected the rate of dissolution of ammonium carbamate; therefore, to reduce the reaction time, more polar solvents were employed. Acetonitrile and methanol were both successful, providing full conversion in

the absence of the base (Scheme 9, conditions b or c). However, a higher yield (96%) and a shorter reaction time (30 min) were achieved in methanol (Scheme 9, conditions c). This protocol is very simple and easy to perform in an open flask, and is scalable, as demonstrated by performing the reaction on a 10 mmol scale (**1a**: 91% yield of **8a**). To highlight the practical nature of this method, we prepared a video of the protocol.[46]

The scope of the reaction has been widely investigated, mainly using MeOH as the solvent (Scheme 10).[45] Different protocols and solvents can also be used depending on the solubility of the starting sulfoxide.



Scheme 10 Scope of the NH-transfer reaction to sulfoxides

As reported in Scheme [10,45] the NH-transfer occurred on various sulfoxides leading to the corresponding NH-sulfoximines **8b–t** in good to excellent yields. We found that the protocol was compatible with aryl- and alkyl-substituted sulfoxides (e.g., **8b–o**), as well as with cyclic sulfoxides (as in the cases of **8p–t**). A lower yield was observed with phenyl vinyl sulfoxide, leading to **8l** in 54% yield. A trifluoromethylsulfoxide provided **8u** in only 9% yield due to the lower nucleophilicity of the sulfoxide. Concerning the stereochemical outcome of the NH-transfer methodology, complete stereoselectivity was observed in sulfoximines **8q–t** derived from diastereomerically pure cyclic sulfoxides. Similarly, the 9:1 diastereomeric ratio of an α-chlorinated sulfoxide was retained in sulfoximine **8i**. The reaction on enantioenriched sulfoxides resulted in enantioenriched sulfoximines (*S*)-**8a**, (*R*)-**8b** and (*R*)-**8h** (er > 97:3), with complete retention of the configuration from the starting materials.[45] The scalability of the procedure was also demonstrated with thietanesulfoximine **9**, prepared on an 11 mmol scale in 81% yield.

Functional group compatibility of this NH-transfer to form sulfoximines is important to ensure synthetic efficiency, and in later-stage applications. In particular, for applications in medicinal chemistry, compatibility with heterocycles is crucial. The conditions were shown to be tolerant of various functional groups in the sulfoxides, including free hydroxy groups in sulfoximines **8r–t** (Scheme 10). Furthermore, protected methionine sulfoxide smoothly underwent NH-transfer providing protected MSO derivative **12** in good yield (Scheme 10). To give an indication of the tolerance of the reaction to a much wider array of possible sulfoxide substrates, the procedure was subjected to the Glorius robustness screen.[45,47] The standard reaction with sulfoxide **1a** was performed in the presence of stoichiometric quantities of various functionalized additives (Figure 2). The majority of the heterocycles tested were found to be compatible giving the product **8a** in yields ranging from 85–95%. Importantly, heterocycles with basic nitrogen groups were found to be compatible with the reaction. Very high yields were observed in the presence of pyridine, pyrimidine, quinoline, imidazole, thiazole, benzoxazole and benzothiazole. According to this robustness screen, sulfoxides bearing benzothiazole and imidazole groups were expected to provide very good yields of the corresponding sulfoximines. Therefore, sulfoximine **13**, bearing a benzothiazole substituent, was targeted, and was successfully prepared in 84% yield. Similarly, oxfendazole, an anthelmintic containing benzimidazole, was shown to undergo NH-transfer furnishing the corresponding sulfoximine **14** in 70% yield (Scheme 10).

On the other hand, electron-rich heterocycles such as indole, furan and thiophene were tolerated less well, leading to a poor recovery of the added heterocycle. The pyrrole group required N-protection with electron-withdrawing substituents such as the Boc group in order to be tolerated

in the reaction. Various other functional groups were tested, and the NH-transfer protocol proved to be compatible with alkene, alkyne, alkyl amine, phenol, ester, aldehyde, and nitrile functionalities. The results in Figure 2 demonstrate a high degree of compatibility of the reaction conditions for a wide range of pharmaceutically relevant functionalities.

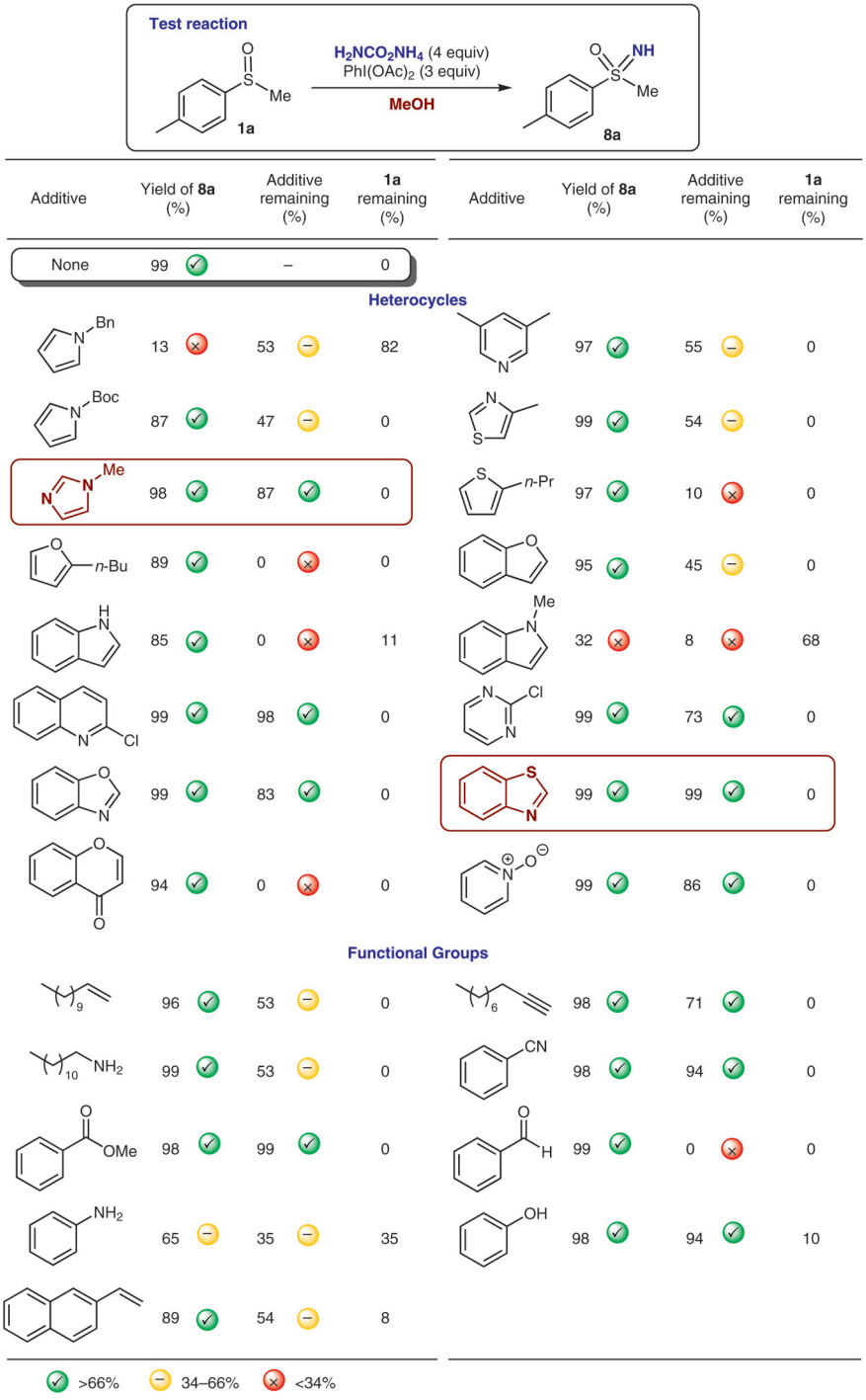
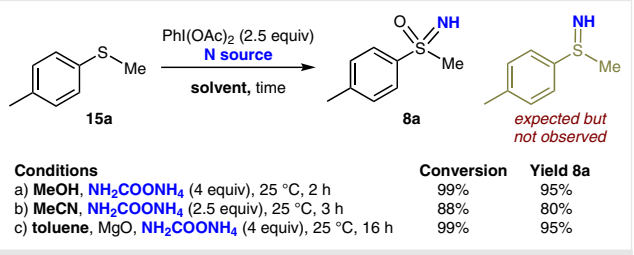


Figure 2 Robustness test



Conditions	Conversion	Yield 8a
a) **MeOH**, NH_2COONH_4 (4 equiv), 25 °C, 2 h	99%	95%
b) **MeCN**, NH_2COONH_4 (2.5 equiv), 25 °C, 3 h	88%	80%
c) **toluene**, MgO, NH_2COONH_4 (4 equiv), 25 °C, 16 h	99%	95%

Scheme 11 Metal-free NH-transfer with sulfides

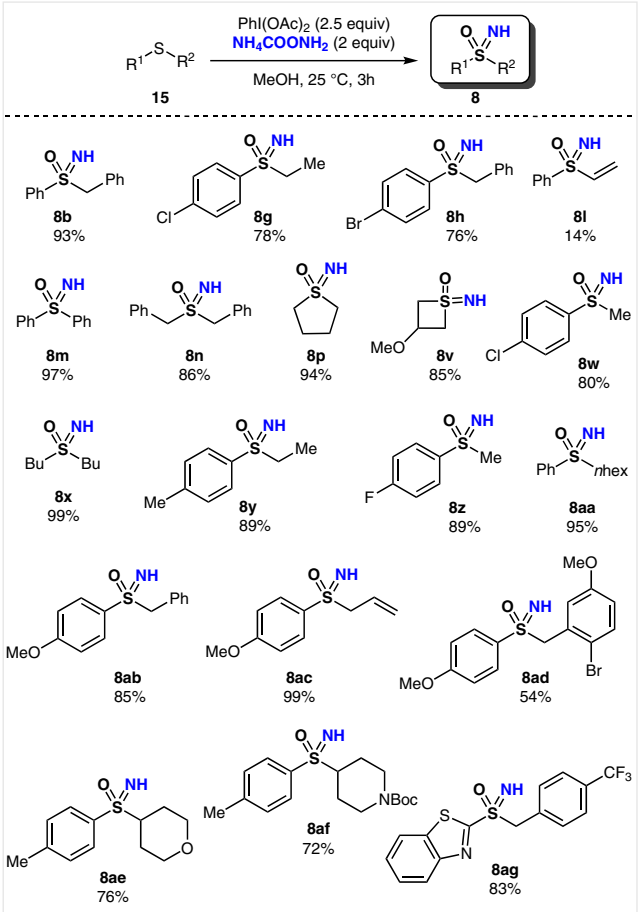
Next, we considered the use of this straightforward direct NH-transfer procedure with sulfides as substrates.[48] Aiming to develop a method for the direct preparation of NH-sulfilimines by imination of the sulfur atom, sulfide **15a** was reacted under the same conditions employed for the imination of sulfoxides (Scheme 11). Surprisingly, by using $PhI(OAc)_2$ and $NH_2CO_2NH_4$ in methanol, sulfoximine **8a** was obtained in very high yield rather than the expected sulfilimine. Considering that most preparations of NH-sulfoximines are based on multistep syntheses starting from sulfides (Scheme 1), the availability of a selective strategy for N- and O-transfer in the same reaction to generate NH-sulfoximines was extremely attractive, and promised a considerable advance. In preliminary experiments on sulfide **15a**, the efficacy of the protocol used for the imination of sulfoxides was proven. The use of ammonium carbamate (NH_2COONH_4) in the presence of $PhI(OAc)_2$ (2.5 equiv) at 25 °C, in MeOH, toluene or acetonitrile, led to exclusive formation of the corresponding sulfoximine **8a** (Scheme 11).

This straightforward protocol was tested with several sulfides verifying the robustness of the methodology (Scheme 12).[48] The reaction tolerated aryl-, alkyl-, cycloalkyl-, benzyl- and alkenyl-substituted sulfides. Various functional groups (OMe, CF_3, *N*-Boc, allyl) and heterocycles were also found to be compatible with this protocol.

The wide scope and functional group tolerance makes this strategy useful for the direct introduction of the sulfoximine moiety in organic molecules. Currently, this approach affords racemic sulfoximine products. The direct enantioselective synthesis of sulfoximines from sulfides presents an important future aim.

4 Mechanistic Evidence for the Direct Synthesis of NH-Sulfoximines from Sulfoxides and Sulfides

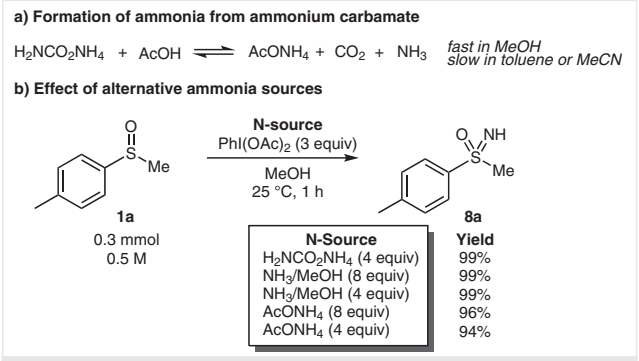
The mechanisms of these direct NH-transfer methods mediated by hypervalent iodine reagents were intriguing



Scheme 12 Scope of the NH-transfer reaction with different sulfides

and by no means clear. This prompted us to undertake considerable investigations to provide mechanistic insights. In the NH-transfer to sulfoxides, our approach involved chemical experiments combined with NMR and HRMS investigations to prove the role of ammonium carbamate and to determine the structures of the most likely intermediates.[45]

Ultimately the role of ammonium carbamate was shown to simply be as a convenient source of ammonia. As reported in Scheme 13, using methanol as the solvent, a fast ligand exchange reaction with $PhI(OAc)_2$ releases acetic acid, which decomposes the ammonium carbamate to ammonia and ammonium acetate.[49] The role of ammonia, as the effective nitrogen source, was further demonstrated by using alternative sources of ammonia such as a solution of ammonia in methanol and ammonium acetate (Scheme 13, b).[45] In all cases, complete conversion of sulfoxide **1a** into the corresponding sulfoximine **8a** was observed.

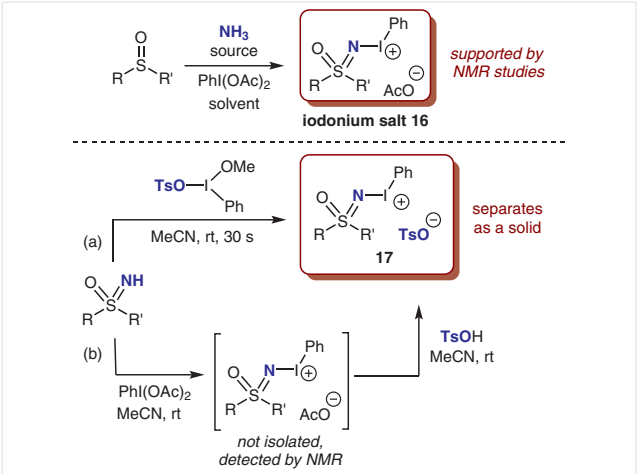


Scheme 13 Ammonia sources for NH-transfer to sulfoxides

The reactions monitored by NMR in deuterated toluene, acetonitrile or methanol were found to undergo complete conversion in each case, and a faster reaction in MeOH and MeCN over toluene.[45] However, NMR experiments did not provide evidence about likely intermediates; the iodonium salt **16** was the only detectable species (Scheme 14), which collapsed to the NH-sulfoximine over time. The hypervalent iodonium salt could also be prepared by simply mixing the NH-sulfoximine with $PhI(OAc)_2$. At this stage, it seemed most likely that the sulfoximine product could be reacting very rapidly with excess $PhI(OAc)_2$ while the reaction is progressing to give the iodonium salts. However, HRMS studies indicated this may not be the full story. The iodonium salts were found to be labile when aged for a prolonged time in solution, or under basic work-up conditions giving the corresponding NH-sulfoximine.

Interestingly, similar hypervalent iodonium salts were recently reported by Bolm, and used as sources of sulfoximines for N–C bond-forming reactions.[18b] In the Bolm work, the sulfinimidoyl iodonium salts, of general structure **17**, precipitated from acetonitrile by mixing a NH-sulfoximine with methoxy(tosyloxy)iodobenzene (Scheme 14, path a). Considering this report, and surprised by some spectroscopic discrepancies, we found that sulfinimidoyl iodonium salt **17** could be obtained by mixing the NH-sulfoximine with $PhI(OAc)_2$ in acetonitrile and adding tosic acid. A white solid, corresponding to iodonium salt **17**, suddenly separated from the solution. Running the experiment in deuterated acetonitrile allowed us to conclude that, in solution, a fast ligand exchange around the hypervalent iodine occurs, and that the most stable (or insoluble) complex, the tosylate salt, separated as the solid.[50]

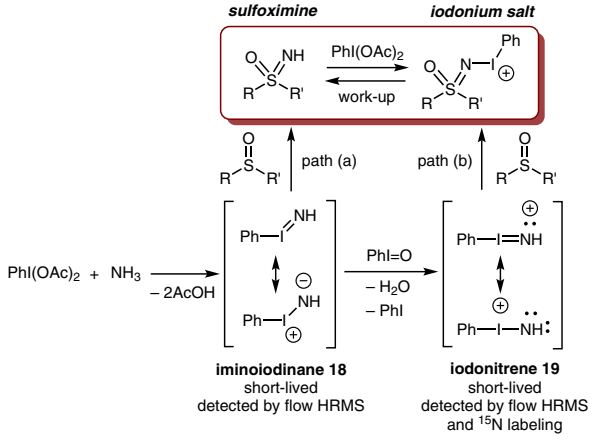
Flow HRMS analysis provided additional evidence to probe the mechanism of the NH-transfer reaction.[45,51] In fact, signals consistent with an iminoiodinane (PhI=NH) as well as an unprecedented iodonitrene ($PhI=N^+$) species[52] were observed after mixing a solution of $PhI(OAc)_2$ and ammonium carbamate or acetate. Addition of the sulfoxide resulted only in the formation of hypervalent iodonium salt



Scheme 14 Isolation of sulfinimidoyl iodonium salts

16. The identity of the iodonitrene ($PhI=N^+$) was also confirmed via HRMS by labeling experiments using ^{15}N-labeled ammonium acetate.[45]

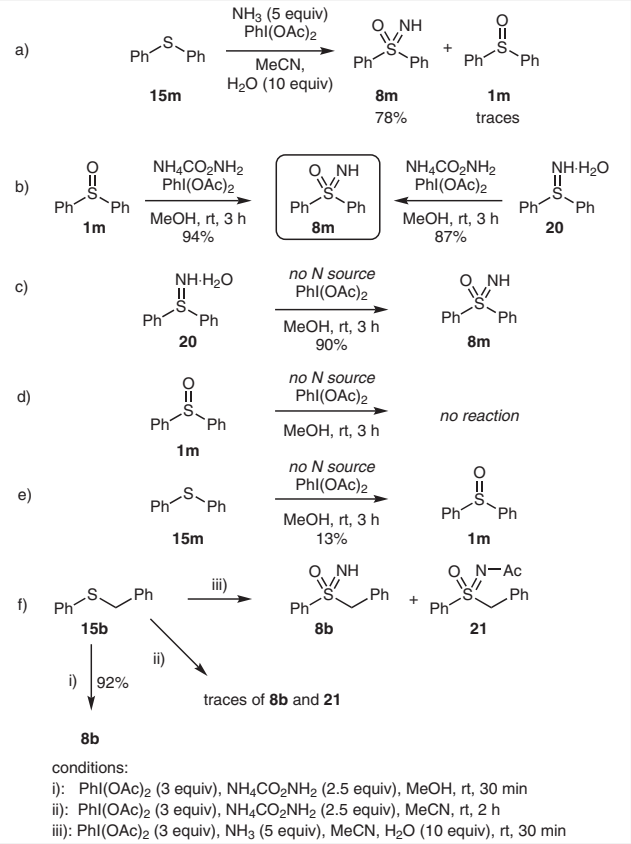
To summarize the mechanistic studies, it is likely that the nitrogen source provides a sufficient concentration of ammonia which reacts with $PhI(OAc)_2$ forming either iminoiodinane **18** or iodonitrene **19** that react with the sulfoxide (Scheme 15). Assuming the involvement of **18** [Scheme 15, path (a)], the formation of the sulfoximine may occur by direct attack of the sulfoxide at nitrogen with displacement of iodobenzene,[53] or by attack at the iodine center with subsequent reductive elimination leading to the sulfoximine.[54] With iodonitrene **19** [path (b)], the direct nucleophilic attack of the sulfur at the electrophilic nitrogen would directly furnish the iodonium salt according to NMR and MS observations. In both pathways, the nucleophilicity of the sulfoxide plays a role.



Scheme 15 Two possible pathways for the formation of NH-sulfoximines

In the reaction forming sulfoximines from sulfides,[48] the mechanism for both NH- and O-transfer with the same reagents posed an even bigger question. Building on the data obtained in the reaction of sulfoxides, a similar electrophilic nitrene or nitrenoid species would likely be involved. However, mechanistic differences, including the sequence of introduction of the heteroatoms, could be envisaged. Firstly, we observed that two equivalents of the oxidant were required. When less oxidant was used, only the starting material and the product sulfoximine were present and intermediate species were not observed. This indicates that a more reactive intermediate species is formed. Therefore, we performed a series of experiments to establish whether N or O is transferred first. It is worth pointing out that mechanistic aspects related to this process, have also been reported recently by Reboul and co-workers.[55] In Scheme 16, a combination of the data from the chemical investigations reported by ourselves[48] as well as by Reboul are presented.

By using diphenyl sulfide (**15m**) in the presence of ammonia and $PhI(OAc)_2$ in acetonitrile and water, diphenyl sulfoximine (**8m**) could be obtained in 78% yield (Scheme 16, a). Complete selectivity, for the formation of sulfoximine **8m**, was also observed starting either from diphenyl sulfoxide (**1m**) (Scheme 16, b), or diphenylsulfilimine **20**. From sulfilimine **20**, reaction with $PhI(OAc)_2$ in the absence of the nitrogen source led to sulfoximine **8m** resulting from an oxidation process (Scheme 16, c). However, either sulfoxide **1m**, or sulfide **15m** in the absence of the nitrogen source gave little or no reaction, which appears crucial to the excellent chemoselectivity of the processes (Scheme 16, d and e). Further useful insights were obtained by studying the reactivity of benzyl phenyl sulfide (**15b**). On reacting **15b** with $PhI(OAc)_2$, a complex mixture was obtained, in striking contrast, with a 92% yield of sulfoximine **8b** in the presence of ammonium carbamate [Scheme 16, f, conditions (i)]. Interestingly, Reboul demonstrated that water could be playing a role in the reaction; in acetonitrile, no reaction occurred when water was removed from the reaction mixture [Scheme 16, f, conditions (ii)]. However, it is not necessary to be the source of the sulfoximine oxygen. By contrast, in the presence of 10 equivalents of water and using acetonitrile as the reaction solvent, a 1:1 mixture of sulfoximine **8b** and the corresponding *N*-acyl derivative **21** was observed [Scheme 16, f, conditions (iii)]. These results support the hypothesis that the nitrogen is likely transferred first, and that the corresponding sulfilimine is further oxidized to intermediates that are broken down by the methanol solvent or by water.



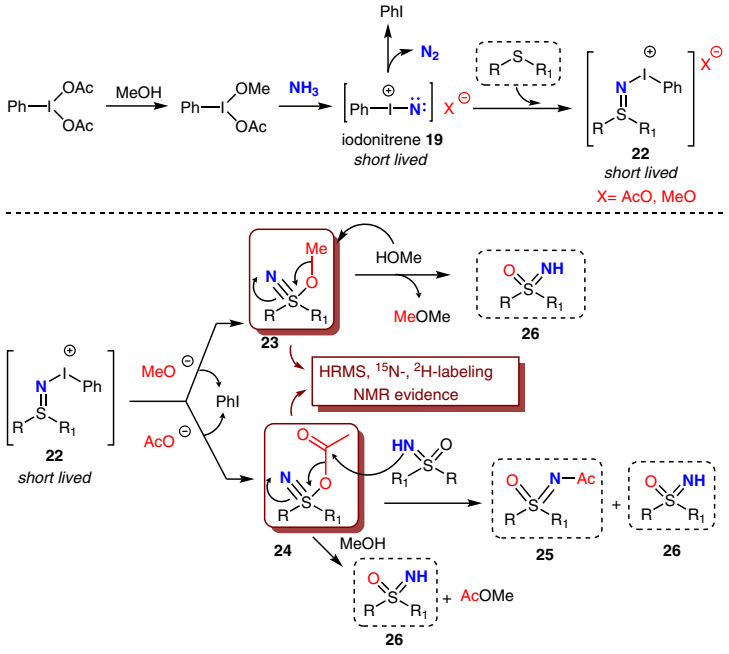
Scheme 16 Mechanistic aspects for the N-transfer to sulfoxides

Based on labeling experiments, HRMS and ^{1}H, ^{13}C and ^{15}N NMR investigations, Reboul proposed the mechanism reported in Scheme 17.[55] The previously proposed iodonitrene **19** is likely to be the N-donor to the sulfur,[45,48] leading to a short lived sulfilimine iodonium species **22**. Intermediate **22** is attacked by a methoxy or acetate anion with formation of methoxy- or acetoxy-λ^6-sulfanenitrile **23** or **24**, respectively. Interestingly, intermediates **23** and **24** have been characterized by HRMS, isotopic labeling and multinuclear magnetic resonance.[55]

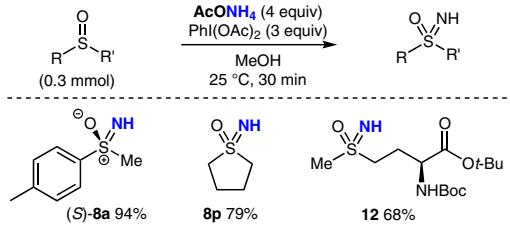
Methoxy-λ^6-sulfanenitrile **23** could undergo nucleophilic attack by methanol with formation of dimethyl ether and the corresponding sulfoximine **26**. Similarly, acetoxy-λ^6-sulfanenitrile **24** may behave as an acetylating agent either toward the sulfoximine or methanol leading to *N*-acyl-sulfoximine **25** and NH-sulfoximine **26** (Scheme 17). This mechanism supports the hypothesis that the oxygen is derived from methanol or acetate.

5 Further Applications

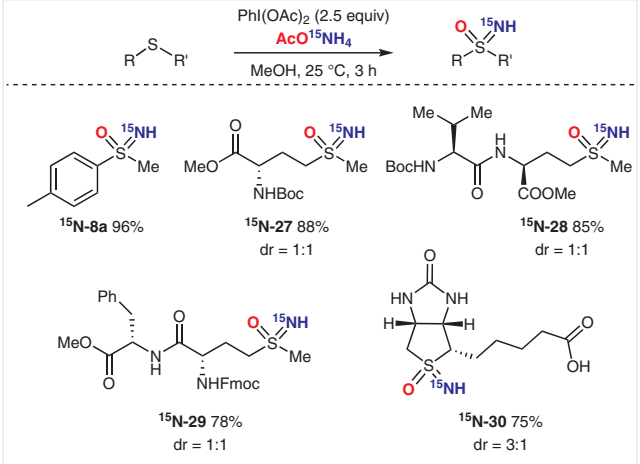
In this section, we report further interesting applications of the strategies described herein for the preparation of NH-sulfoximines. Firstly, the potential to use alternative nitrogen sources, such as cheap and easy to handle ammonium acetate, was demonstrated in the preparation of sulfoximines (*S*)-**8a**, **8p** and the MSO precursor **12** in good yields (Scheme 18).[45]



Scheme 17 Proposed mechanism for the N,O-transfer to sulfides



Scheme 18 Preparation of NH-sulfoximines (*S*)-**8a**, **8p** and the MSO precursor **12**



Scheme19 Preparation of ^{15}NH-sulfoximines **^{15}N-27–30**

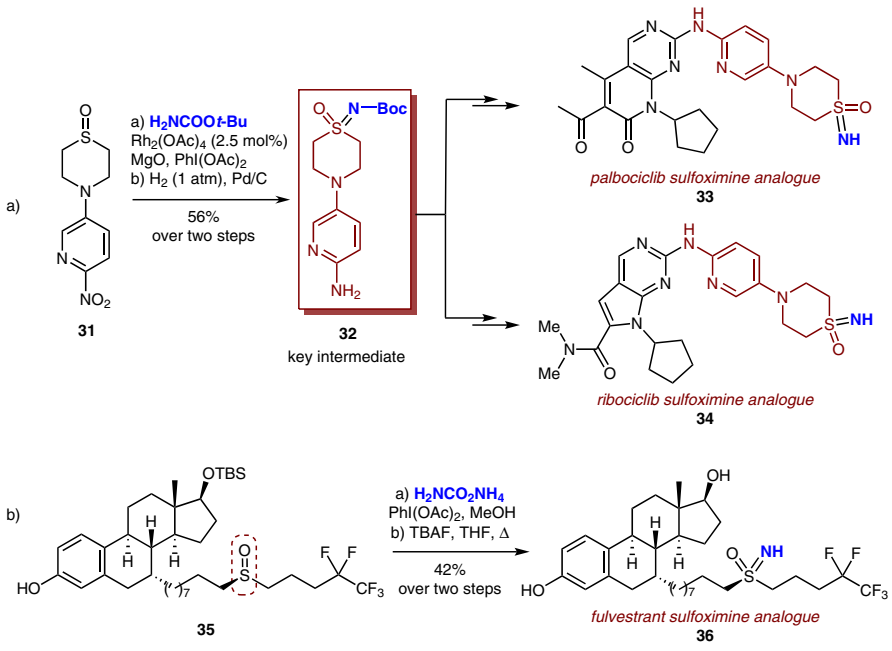
The preparation of ^{15}N-labeled sulfoximines from biologically relevant sulfides was readily achieved by exploiting the functional group compatibility of the NH- and O-transfer strategy. Using ^{15}N-labeled ammonium acetate as the nitrogen source, the reaction with protected methionine, dipeptides, and biotin afforded the corresponding ^{15}NH-sulfoximines **^{15}N-27–30** in good yields as mixtures of diastereoisomers (Scheme 19).[48]

Lücking employed the Rh-catalyzed strategy for the preparation of sulfoximine carbamates in the synthesis of sulfoximine analogue of palbociclib and ribociclib, which are selective CDK4/6 inhibitors used in cancer therapy. *N*-Boc sulfoximine **32** was the key intermediate in the preparation of analogues **33** and **34** obtained after facile removal of the Boc group (Scheme 20, a).[14]

The strategy for the direct NH-transfer to a sulfoxide has been applied by Lücking for the preparation of the sulfoximine analogues of fulvestrant, a selective estrogen receptor degrader (SERD) that both antagonizes and degrades ER-α and is active in patients on antihormonal agents experiencing disease progression. The synthesis of analogue **36** was accomplished in two steps including a stereospecific N-transfer with ammonium carbamate and PhI(OAc)$_2$ followed by TBS deprotection (Scheme 20, b).[14]

6 Conclusion

In this account, we have collected our recent achievements in the development of straightforward strategies for accessing NH-sulfoximines, and reviewed these in the context of the field. Both metal-based and metal-free ap-



Scheme 20 Preparation of the sulfoximine-containing analogues of drug compounds

proaches have been described, as well as useful synthetic applications. The rhodium-catalyzed synthesis of sulfoximine carbamates allows the introduction of orthogonal and easily removable protecting groups into a molecule. From a sustainability point of view, the metal-free approach avoids the use of expensive transition-metal-catalysts and offers synthetic efficiency toward free NH-sulfoximines. The metal-free protocols are suitable for converting both sulfoxides and sulfides directly into sulfoximines, and appear to be widely applicable. In addition, the protocols tolerate functionality in the substrate, and are suitable for both the late-stage introduction of the sulfoximine moiety and for ^{15}N-labeling. From a mechanistic point of view, the available spectroscopic and spectrometric measurements suggest iodonitrene or iminoiodinane species as reactive and short-lived intermediates. In the near future, it is expected that these strategies will lead to further progress in sulfoximine chemistry, drug discovery programs, as well as in other N-transfer reactions.

Acknowledgment

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References

(1) Bentley, H. R.; McDermott, E. E.; Pace, J.; Whitehead, J. K.; Moran, T. *Nature* **1949**, *163*, 675.
(2) Reggelin, M.; Zur, C. *Synthesis* **2000**, 1.
(3) (a) Koep, S.; Gais, H.-J.; Raabe, G. *J. Am. Chem. Soc.* **2003**, *125*, 13243. (b) Shen, X.; Miao, W.; Ni, C.; Hu, J. *Angew. Chem. Int. Ed.* **2014**, *53*, 775. (c) Frings, M.; Atodiresei, I.; Wang, Y.; Runsink, J.; Raabe, G.; Bolm, C. *Chem. Eur. J.* **2010**, *16*, 4577. (d) Shen, X.; Liu, Q.; Zhang, W.; Hu, J. *Eur. J. Org. Chem.* **2016**, 906.
(4) (a) Bolm, C.; Verrucci, M.; Simic, O.; Cozzi, P. G.; Raabe, G.; Okamura, H. *Chem. Commun.* **2003**, 2826. (b) Langner, M.; Bolm, C. *Angew. Chem. Int. Ed.* **2004**, *43*, 5984. (c) Langner, M.; Remy, P.; Bolm, C. *Chem. Eur. J.* **2005**, *11*, 6254.
(5) (a) Yadav, M. R.; Rit, R. K.; Sahoo, A. K. *Org. Lett.* **2013**, *15*, 1638. (b) Yadav, M. R.; Rit, R. K.; Sahoo, A. K. *Chem. Eur. J.* **2012**, *18*, 5541. (c) Rit, R. K.; Yadav, M. R.; Ghosh, K.; Shankar, M.; Sahoo, A. K. *Org. Lett.* **2014**, *16*, 5258. (d) Ghosh, K.; Rit, R. K.; Ramesh, E.; Sahoo, A. K. *Angew. Chem. Int. Ed.* **2016**, *55*, 7821. (e) Cheng, Y.; Dong, W.; Parthasarathy, K.; Bolm, C. *Org. Lett.* **2017**, *19*, 726.
(6) Gnamm, C.; Jeanguenat, A.; Dutton, A. C.; Grimm, C.; Kloer, D. P.; Crossthwaite, A. J. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 3800.
(7) Lücking, U. *Angew. Chem. Int. Ed.* **2013**, *52*, 9399.
(8) (a) Bizet, V.; Hendriks, C. M. M.; Bolm, C. *Chem. Soc. Rev.* **2015**, *44*, 3378. (b) Worch, C.; Mayer, A. C.; Bolm, C. In *Organosulfur Chemistry in Asymmetric Synthesis*; Toru, T.; Bolm, C., Eds.; Wiley-VCH: Weinheim, **2008**, 209.
(9) For the use of flow chemistry in sulfoximine synthesis, see: (a) Lebel, H.; Piras, H.; Borduy, M. *ACS Catal.* **2016**, *6*, 1109. (b) Gutmann, B.; Elsner, P.; O'Kearney-McMullan, A.; Goundry, W.; Roberge, D. M.; Kappe, C. O. *Org. Process Res. Dev.* **2015**, *19*, 1062.
(10) For the cross-coupling of sulfoximine-containing building blocks, see: (a) Steinkamp, A.-D.; Wiezorek, S.; Brosge, F.; Bolm, C. *Org. Lett.* **2016**, *18*, 5348. (b) Sirvent, J. A.; Bierer, D.; Webster, R.; Lücking, U. *Synthesis* **2017**, *49*, 1024. (c) Battula, S. R. K.; Rama Kishore Putta, V. P.; Subbareddy, G. V.; Chakravarthy, I. E.; Saravanan, V. *Org. Biomol. Chem.* **2017**, *15*, 3742. (d) Cho, G. Y.;

Okamura, H.; Bolm, C. *J. Org. Chem.* **2005**, *70*, 2346. (e) Tota, A.; Fanelli, F.; Falcicchio, A.; Luisi, R.; Degennaro, L. *Chem. Heterocycl. Compd.* **2017**, *53*, 322.
(11) (a) Goldberg, F. W.; Kettle, J. G.; Xiong, J.; Lin, D. *Tetrahedron* **2014**, *70*, 6613. (b) Goldberg, F. W.; Kettle, J. G.; Kogej, T.; Perry, M. W. D.; Tomkinson, N. P. *Drug Discovery Today* **2015**, *20*, 11.
(12) (a) Lücking, U.; Jautelat, R.; Krüger, M.; Brumby, T.; Lienau, P.; Schäfer, M.; Briem, H.; Schulze, J.; Hillisch, A.; Reichel, A.; Wengner, A. M.; Siemeister, G. *Chem. Med. Chem.* **2013**, *8*, 1067. (b) Siemeister, G.; Lücking, U.; Wengner, A. M.; Lienau, P.; Steinke, W.; Schatz, C.; Mumberg, D.; Ziegelbauer, K. *Mol. Cancer Ther.* **2012**, *11*, 2265. (c) Foote, K. M.; Lau, A.; Nissink, J. W. M. *Future Med. Chem.* **2015**, *7*, 873. (d) Foote, K. M.; Nissink, J. W. M.; Turner, P. (AstraZeneca) WO2011154737 A1, **2011**.
(13) Frings, M.; Bolm, C.; Blum, A.; Gnamm, C. *Eur. J. Med. Chem.* **2017**, *126*, 225.
(14) Sirvent, J. A.; Lücking, U. *Chem. Med. Chem.* **2017**, *12*, 487.
(15) Teng, F.; Cheng, J.; Bolm, C. *Org. Lett.* **2015**, *17*, 3166.
(16) Sedelmeier, J.; Bolm, C. *J. Org. Chem.* **2005**, *70*, 6904.
(17) (a) Priebbenow, D. L.; Bolm, C. *Org. Lett.* **2014**, *16*, 1650. (b) Muneeswara, M.; Kotha, S. S.; Sekar, G. *Synthesis* **2016**, *48*, 1541.
(18) (a) Chen, X. Y.; Wang, L.; Frings, M.; Bolm, C. *Org. Lett.* **2014**, *16*, 3796. (b) Wang, H.; Cheng, Y.; Becker, P.; Raabe, G.; Bolm, C. *Angew. Chem. Int. Ed.* **2016**, *55*, 12655.
(19) Cheng, Y.; Dong, W.; Wang, L.; Parthasarathy, K.; Bolm, C. *Org. Lett.* **2014**, *16*, 2000.
(20) Cheng, H.; Wen, J.; Bolm, C. *Chem. Eur. J.* **2017**, DOI: 10.1002/chem.201700953.
(21) Teng, F.; Yu, J. T.; Zhou, Z.; Chu, H.; Cheng, J. *J. Org. Chem.* **2015**, *80*, 2822.
(22) Bohnen, C.; Bolm, C. *Org. Lett.* **2015**, *17*, 3011.
(23) Zhu, H.; Yu, J.-T.; Cheng, J. *Chem. Commun.* **2016**, *52*, 11908.
(24) Wang, H.; Frings, M.; Bolm, C. *Org. Lett.* **2016**, *18*, 2431.
(25) Dong, S.; Frings, M.; Cheng, H.; Wen, J.; Zhang, D.; Raabe, G.; Bolm, C. *J. Am. Chem. Soc.* **2016**, *138*, 2166.
(26) (a) Tomooka, C. S.; Carreira, E. M. *Helv. Chim. Acta* **2002**, 3773. (b) Mancheno, O. G.; Bolm, C. *Chem. Eur. J.* **2007**, *13*, 6674. (c) Lebel, H.; Piras, H.; Bartholoméüs, J. *Angew. Chem. Int. Ed.* **2014**, *53*, 7300.
(27) (a) Wang, J.; Frings, M.; Bolm, C. *Chem. Eur. J.* **2014**, *20*, 966. (b) Müller, J. F. K.; Vogt, P. *Tetrahedron Lett.* **1998**, *39*, 4805. (c) Cren, S.; Kinahan, T. C.; Skinner, C. L.; Tye, H. *Tetrahedron Lett.* **2002**, *43*, 2749. (d) Lacôte, E.; Amatore, M.; Fensterbank, L.; Malacria, M. *Synlett* **2002**, 116. (e) Cho, G. Y.; Bolm, C. *Org. Lett.* **2005**, *7*, 4983.
(28) Okamura, H.; Bolm, C. *Org. Lett.* **2004**, *6*, 1305.
(29) (a) Bizet, V.; Buglioni, L.; Bolm, C. *Angew. Chem. Int. Ed.* **2014**, *53*, 5639. (b) Bizet, V.; Bolm, C. *Eur. J. Org. Chem.* **2015**, 2854.
(30) Miao, J.; Richards, N. G. J.; Ge, H. *Chem. Commun.* **2014**, *50*, 9687.
(31) (a) Bach, T.; Körber, C. *Tetrahedron Lett.* **1998**, *39*, 5015. (b) Bach, T.; Körber, C. *Eur. J. Org. Chem.* **1999**, 1033.
(32) Zenzola, M.; Doran, R.; Luisi, R.; Bull, J. A. *J. Org. Chem.* **2015**, *80*, 6391.
(33) For optimization of in situ iminoiodinane formation using MgO, see: Espino, C. G.; Du Bois, J. *Angew. Chem. Int. Ed.* **2001**, *40*, 598.
(34) Johnson, C. R.; Kirchhoff, R. A.; Corkins, H. G. *J. Org. Chem.* **1974**, *39*, 2458.
(35) (a) For related studies, see: Buglioni, L.; Bizet, V.; Bolm, C. *Adv. Synth. Catal.* **2014**, *356*, 2209. (b) Also see: Marzag, H.; Schuler, M.; Tatibouët, A.; Reboul, V. *Eur. J. Org. Chem.* **2017**, 896.
(36) Johnson, C. R.; Haake, M.; Schroeck, C. W. *J. Am. Chem. Soc.* **1970**, *92*, 6594.
(37) Wang, J.; Zhang, J.; Miao, K.; Yun, H.; Shen, H. C.; Zhao, W.; Liang, C. *Tetrahedron Lett.* **2017**, *58*, 333.
(38) (a) Mendiola, J.; Rincon, J. A.; Mateos, C.; Soriano, J. F.; de Frutos, O.; Niemeier, J. K.; Davis, E. M. *Org. Process Res. Dev.* **2009**, *13*, 263. (b) Tamura, Y.; Minamikawa, J.; Sumoto, K.; Fujii, S.; Ikeda, M. *J. Org. Chem.* **1973**, *38*, 1239.
(39) Cho, G. Y.; Bolm, C. *Tetrahedron Lett.* **2005**, *46*, 8007.
(40) Dannenberg, C. A.; Fritze, L.; Krauskopf, F.; Bolm, C. *Org. Biomol. Chem.* **2017**, *15*, 1086.
(41) Krasnova, L. B.; Hili, R. M.; Chernoloz, O. V.; Yudin, A. K. *ARKIVOC* **2005**, *(iv)*, 26.
(42) Siu, T.; Yudin, A. K. *Org. Lett.* **2002**, *4*, 1839.
(43) Mancheno, O. M.; Bolm, C. *Org. Lett.* **2007**, *9*, 3809.
(44) Stoss, P.; Satzinger, G. *Tetrahedron Lett.* **1973**, *14*, 267.
(45) Zenzola, M.; Doran, R.; Degennaro, L.; Luisi, R.; Bull, J. A. *Angew. Chem. Int. Ed.* **2016**, *55*, 7203.
(46) Bull Group Chemistry: https://youtu.be/4KpDQnGHi28
(47) (a) Collins, K. D.; Glorius, F. *Nat. Chem.* **2013**, *5*, 597. (b) Collins, K. D.; Rühling, A.; Glorius, F. *Nat. Protoc.* **2014**, *9*, 1348. (c) Collins, K. D.; Glorius, F. *Acc. Chem. Res.* **2015**, *48*, 619.
(48) Tota, A.; Zenzola, M.; Chawner, S. J.; St John-Campbell, S.; Carlucci, C.; Romanazzi, G.; Degennaro, L.; Bull, J. A.; Luisi, R. *Chem. Commun.* **2017**, *53*, 348.
(49) Silva, L. F.; Lopes, N. P. *Tetrahedron Lett.* **2005**, *46*, 6023.
(50) R. Luisi and J. A. Bull groups, unpublished results.
(51) Iacobucci, C.; Reale, S.; De Angelis, F. *Angew. Chem. Int. Ed.* **2016**, *55*, 2980.
(52) Ivanov, A. S.; Popov, I. A.; Boldyrev, A. I.; Zhdankin, V. V. *Angew. Chem. Int. Ed.* **2014**, *53*, 9617.
(53) Ochiai, M.; Kaneaki, T.; Tada, N.; Miyamoto, K.; Chuman, H.; Shiro, M.; Hayashi, S.; Nakanishi, W. *J. Am. Chem. Soc.* **2007**, *129*, 12938.
(54) Dohi, T.; Kita, Y. *Hypervalent Iodine*, In *Iodine Chemistry and Applications*; John Wiley & Sons: Hoboken, **2015**, Chap. 7, 103-15.
(55) Lohier, J.-F.; Glachet, T.; Marzag, H.; Gaumont, A.-C.; Reboul, V. *Chem. Commun.* **2017**, *53*, 2064.