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Iodonitrene: a direct metal-free electrophilic aminating reagent

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The use of conventional nitrenoids and/or metal nitrenes as electrophilic aminating reagents requires a pre-activated nitrogen atom, which makes transfer of an unprotected NH-group a difficult challenge. Iodonitrene, which is generated *in situ* from phenyliodine(III) diacetate and an ammonia surrogate, represents a new type of reactive electrophilic aminating reagent. The novel reactivity of iodonitrene not only resulted in direct NH-group transfer to nucleophilic atoms such as sulfur and nitrogen, but also led to the development of new reactions such as diazine synthesis *via* decarboxylation and contractive synthesis of cyclobutanes *via* nitrogen extrusion. We highlight the contemporary advances in the application of iodonitrene and discuss the current limitations and future prospects.

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1. Introduction

Direct access to nitrogen-containing functional groups is indispensable in the preparation of biologically important molecules. Amination methods such as nucleophilic substitution, reductive amination, and metal-catalyzed amination reactions (e.g. allylic substitution, hydroamination, and C–N cross-coupling reactions) are widely used for amine synthesis.^{1,2} Electrophilic amination requires the use of electrophilic aminating reagents, such as metal–nitrene equivalents, or oxaziri-



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logical activities.

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dines as nitrogen sources, resulting in a net addition of an amino group to the electron-rich functionalities of the substrate.^{3–8} Conventionally, the dirhodium-nitrene chemistry enables intramolecular amination of the inert C(sp³)-H bond to form a C–N bond *via* intermolecular nitrene transfer,⁹ and this condition was applied to the synthesis of *NH*-sulfoximines from sulfoximes¹⁰ and the direct preparation of *NH*-aziridines and anilines from alkenes and arenes,^{11,12} which have been broadly applied to organic synthesis (Scheme 1A).¹³ On the other hand, iodonitrene¹⁴ generated *in situ* from the reaction between hypervalent iodine(III) reagents and ammonia or its surrogates has recently been introduced as a promising electrophilic aminating reagent (Scheme 1B). The synthesis of *NH*-sulfoximines (Bull, Luisi and co-workers, 2016),¹⁴ the synthesis of diazirines from unprotected amino acids (Reboul and co-workers, 2019),¹⁵ and the contractive synthesis of cyclobutanes

from pyrrolidines (Antonchick and coworkers, 2021)¹⁶ revealed the novel reactivity of iodonitrene distinguishing it from the precedent metal-nitrene chemistry. The use of iodonitrene as an electrophilic aminating reagent not only provides a reactive nitrene species ready for nitrogen transfer, but also circumvents the use of metals and activated explosive reagents, such as *O*-mesitylenesulfonyl-hydroxylamine (MSH).¹⁷ Bull, Luisi and co-workers disclosed the evidence of iodonitrene and possible intermediates (PhI=NH),¹⁴ for instance, iminoiodane **1a** and the unprecedented iodonitrene **1b** (PhI=N⁺) *via* mass spectrometric analysis and isotopic labeling using ¹⁵N¹⁸ (Scheme 1C). However, no evidence of any reactive intermediates was found throughout the NMR studies.¹⁹

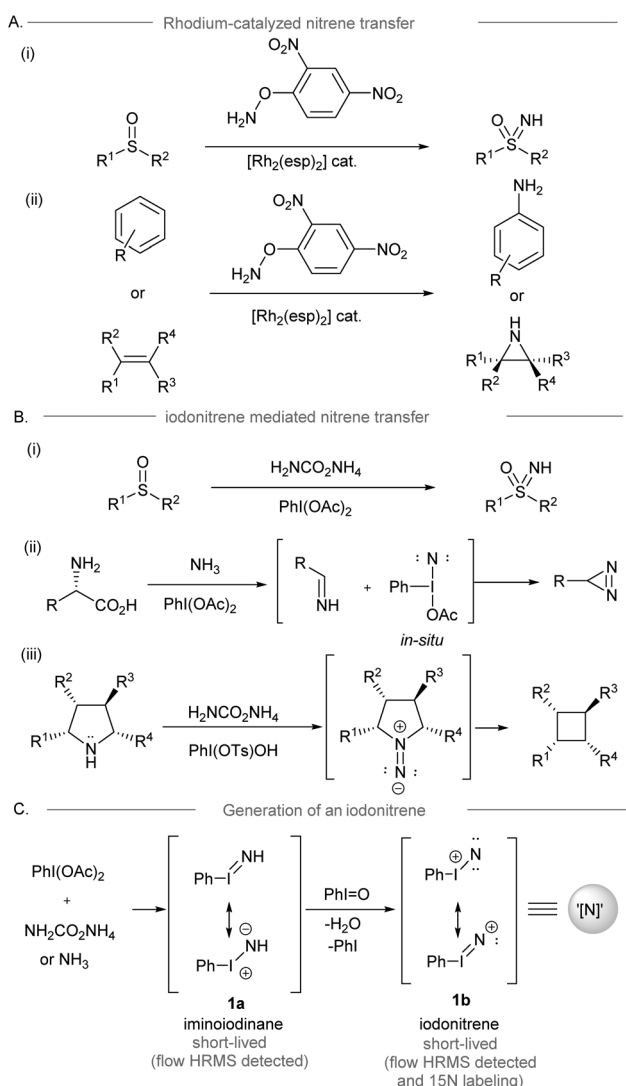
Our group^{20–27} is engaged in the novel method development using hypervalent iodine(III) chemistry.^{28–35} Despite a personal account and a review on *NH*-sulfoximines which was reported by the Bull group and the Luisi group,^{36–38} no review has been published, to the best of our knowledge, discussing the chemistry of iodonitrene. We are motivated to provide a concise minireview, highlighting iodonitrene and its application in organic synthesis. This minireview could be useful to synthetic scientists in method development and natural product synthesis and the pharmaceutical industry. Finally, we discuss the directions and prospects for the innovation of new reactions and potential applications in organic synthesis.

2. Electrophilic amination of sulfur-containing compounds

Sulfur-containing compounds possess significant biological profiles and appear as important elements in drug discovery.³⁹ For instance, sulfoximines are present as essential functional groups in drug candidates such as compound AZD6738 (Scheme 2, inset) from AstraZeneca.⁴⁰ Directing the transfer of the NH group from iodonitrene to sulfoxides gives *NH*-sulfoximines in one step. With the oxidizing power of the hypervalent iodine(III) reagent, oxidation of the sulfur atom could take place before and/or after the nitrogen transfer from iodonitrene. In this section, the direct *NH*-group transfer to sulfoxides and sulfonamides is discussed. Moreover, the sequential *NH*-group transfer accompanied by the oxidation of sulfides, thiols, and sulfonamides is elaborated.

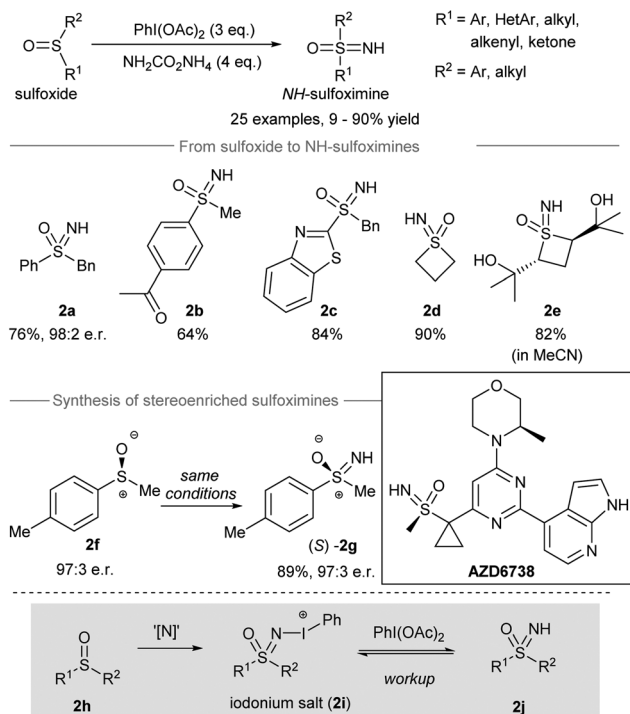
2.1 Direct *NH* transfer to sulfoxides

In 2016, Luisi, Bull and co-workers reported the direct transfer of the *NH*-group from iodonitrene to sulfoxides to afford *NH*-sulfoximines¹⁴ (Scheme 2). Under the standard conditions, the iodonitrene generated *in situ* from the reaction between phenyliodine(III) diacetate (PIDA) and ammonium carbamate⁴¹ promoted a *NH*-group transfer to produce various *NH*-sulfoximines. Both aryl-substituted and alkyl-substituted sulfoxides carrying different reactive groups, such as ketones, free alcohols, and benzothiazoles, gave sulfoxides **2a–2e** from decent to good yields. When methyl *p*-tolylsulfoxide **2f** was used as the starting material, the stereospecific *NH*-group transfer took



Scheme 1 (A) Rhodium catalyzed amination reactions involving dirhodium nitrene transfer.^{10–12} (B) Some examples of amination reactions using iodonitrenes as electrophilic aminating reagents.^{9,15} (C) The proposed mechanism of iodonitrene formation.⁹





Scheme 2 Direct *NH*-group transfer to sulfoxides producing *NH*-sulfoximines.¹⁴

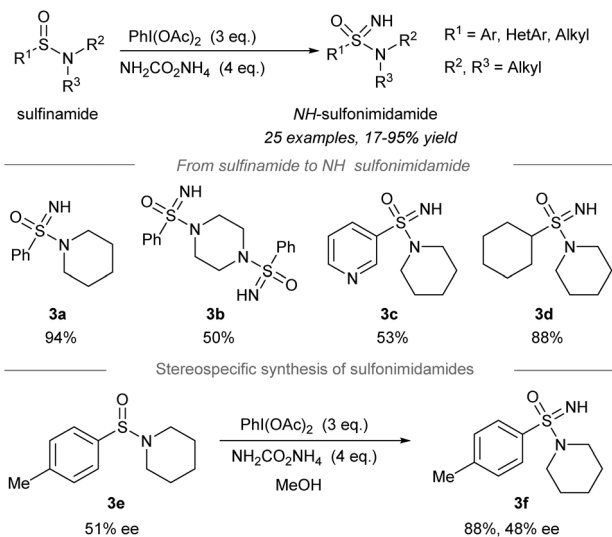
place under standard conditions and gave sulfoximine (S)-2g in 89% yield with 97:3 er. Mechanistically, the authors proposed that the nitrene transfer from iodonitrene (*i.e.* “[N]”) to sulfoxide 2h may generate an iodonium salt 2i. Further oxidation of 2i by free phenyliodine(III) diacetate followed by workup afforded *NH*-sulfoximines 2j.

2.2 Direct *NH* transfer to sulfinamides

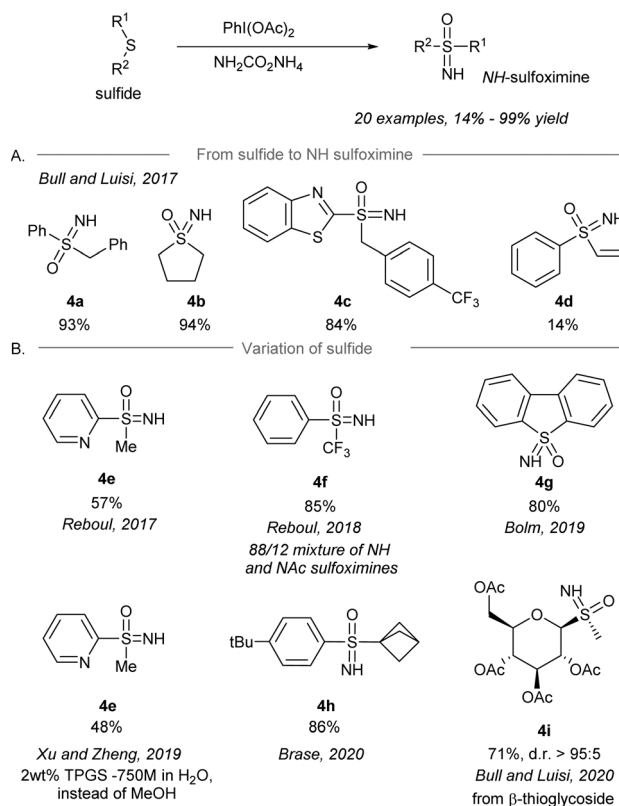
Later, one-pot conversion of sulfinamides to sulfonimides *via* transfer of the electrophilic *NH*-group was reported by Stockman, Lücking, and co-workers (Scheme 3).⁴² Under the optimized conditions, sulfonimides (3a to 3d) were formed from sulfinamides in good to high yields. The replacement of the aryl substituents of tertiary sulfonamides by the 3-pyridinyl group (3c) or cyclohexyl group (3d) was tolerated. Importantly, the *NH*-group transfer to chiral sulfinamide 3e (51% ee) proceeded stereospecifically to give *NH*-sulfonimide 3f with 48% ee.

2.3 One-pot *NH*- and *O*-transfer to sulfides

After the pioneering synthesis of *NH*-sulfoximines from sulfides using iodonitrene as an electrophilic aminating reagent by Bull and Luisi in 2016,¹⁴ the synthesis of *NH*-sulfoximines from the corresponding sulfides *via* a one-pot *NH*- and *O*-transfer was realized by several research groups using iodonitrene chemistry (Scheme 4). In 2017, Bull and Luisi first reported the one-pot *NH*- and *O*-transfer to sulfides to give *NH*-sulfoximines (Scheme 4A).⁴³ Aryl-, alkyl- and benzothiazole-substituted (R^1) sulfides gave the corresponding *NH*-sulfoxi-



Scheme 3 Direct *NH*-group transfer in the synthesis of *NH*-sulfonimides from sulfinamides.⁴²



Scheme 4 (A) Direct *NH*-sulfoximation of sulfides by an iodonitrene. (B) Variation of sulfides as the starting materials.⁴³⁻⁴⁹

mines in high yield (4a–4c, 84%–94% yield). However, the low yield of vinyl substituted sulfoximine 4d is suggested to be the result of a possible polymerization of the substrate.

Shortly after Bull and Luisi's work, other research groups reported variants of the transformation with modification of

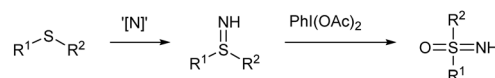


substrates and/or conditions (Scheme 4B), for instance pyridinyl sulfides **4e** (Reboul's group),^{44,50} *S*-perfluoroalkylated sulfides **4f** (Reboul's group),⁵¹ thiophene-derived sulfides **4g** (Bolm's group),⁴⁸ bicyclo[1.1.1]pentyl sulfides **4h** (Bräse's group),⁵³ and β -thioglycosides **4i** (Bull and Luisi's group).⁵⁴ Besides, sulfoximation of sulfides could be achieved to afford **4e** under aqueous micellar conditions using the surfactant TPGS-750-M as an additive.⁴⁹

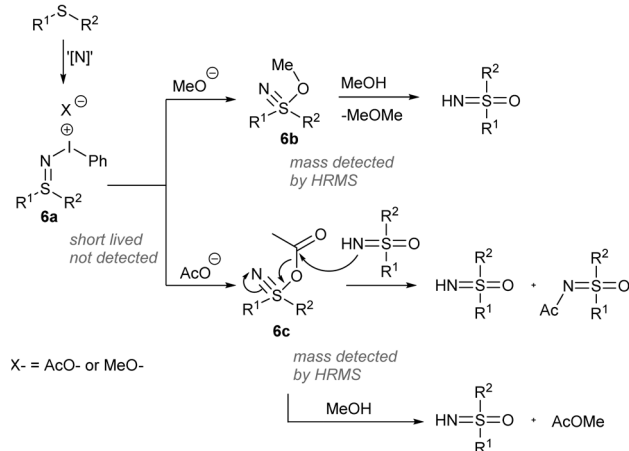
After the report of the direct sulfoximation of sulfides, a tandem *NH*-sulfoximation/*C*(sp²)-*H* amination of sulfides to give dibenzothiazines⁵² was developed by Chen and co-workers in 2018 (Scheme 5). Treatment of [1,1'-biaryl]-2-sulfides with PIDA and ammonium phosphate trihydrate afforded the *NH*- and *O*-transfer products *NH*-sulfoximines, which after intramolecular *C*(sp²)-*H* functionalization provided dibenzothiazines.^{55,56} The variation of the substituents R¹ and R² gave the desired dibenzothiazine products **5a** and **5b** in high yield. A phenyl group on R³ (**5c**) significantly reduced the yield of the reaction to 45% yield. Heterocyclic dibenzothiazines such as **5d** and **5e** were also compatible with the reaction conditions. The authors proposed that the oxidation of the newly formed *NH*-sulfoximine **5f** with PIDA gave **5g**, which cyclized to give dibenzothiazine **5h** (Scheme 5).

A mechanism of the one-pot synthesis of *NH*-sulfoximines from sulfides was suggested by Bull, Luisi, and co-workers (Scheme 6), based on direct nitrene *NH*-group transfer to sulfides and subsequent *O*-transfer from PIDA to afford sulfoximines⁴³ (Scheme 6A). Later, an investigation by Reboul and co-workers⁴⁴ revealed that iodonitrene could be generated when PIDA was reacted with either ammonium carbamate or

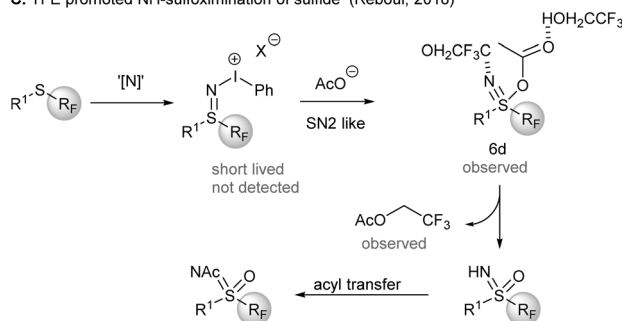
A. Proposed mechanism (Bull and Luisi, 2017)



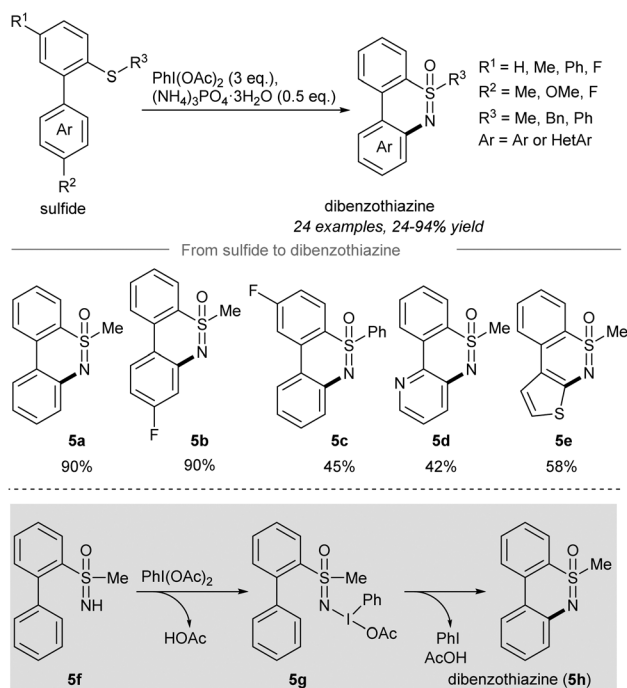
B. Mechanistic study (Reboul, 2017)



C. TFE promoted *NH*-sulfoximation of sulfide (Reboul, 2018)



Scheme 6 Mechanistic investigation of direct *NH*-sulfoximation of sulfides.^{42,45,46}



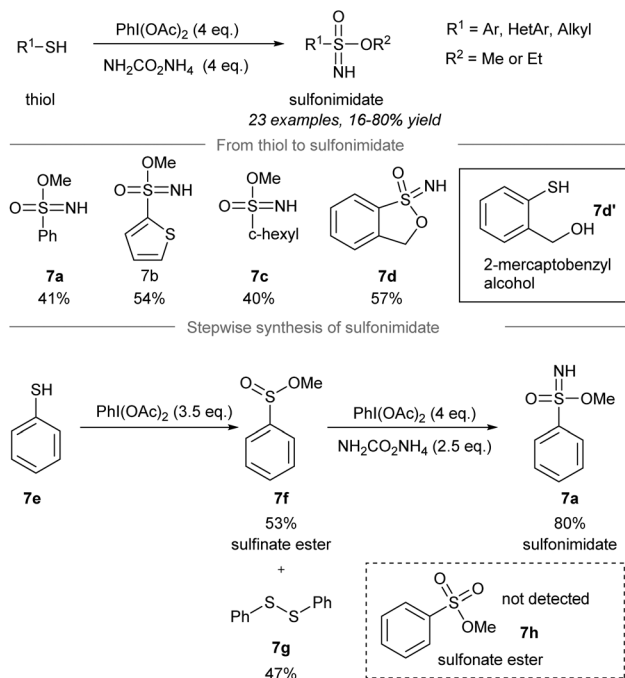
Scheme 5 Synthesis of dibenzothiazines from sulfides through tandem *NH*-sulfoximation/*C*(sp²)-*H* amination.⁵²

ammonium carbonate (Scheme 6B). Although the sulfilimine **6a** formed initially was short-lived and not detected, nucleophilic addition of methoxide or acetate to sulfilimines gave **6b** and **6c**, respectively, which could be detected by HRMS. The rate enhancement of the sulfoximation of *S*-perfluoroalkylated sulfides could be ascribed to the *H*-bonding between 2,2,2-trifluoroethanol (TFE) and the observed sulfanitrile intermediate **6d** (Scheme 6C). The attack of TFE on the acetate of **6d** produced trifluoroethyl acetate. Acetyl group transfer from trifluoroethyl acetate to the reaction product *NH*-sulfoximines furnished *N*-Ac sulfoximines.

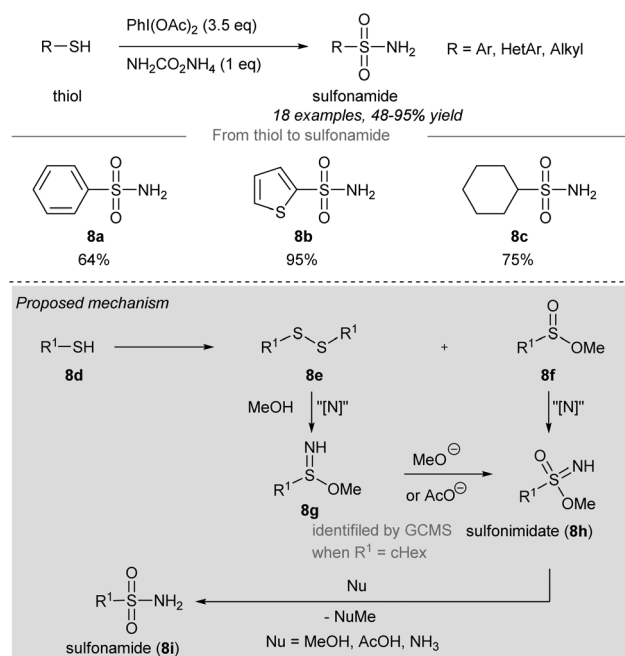
2.4 One-pot *NH*- and *O*-transfer to thiols

In 2018, Luisi, Bull and co-workers disclosed a one-pot chemoselective *NH*-, *O*- and *OR*-transfer to thiols using iodonitrenes to give sulfonimides and sulfonamides⁵⁷ (Scheme 7 and 8). By reducing the amount of ammonium carbamate, the product distribution could be changed from sulfonimides (4 equiv. of ammonium carbamate) (Scheme 7) to sulfonamides (1 equiv. of ammonium carbamate) (Scheme 8).





Scheme 7 Synthesis of sulfonimidates from thiols through a one-pot *NH*-, *O*-, *RO*-transfer.⁵⁷



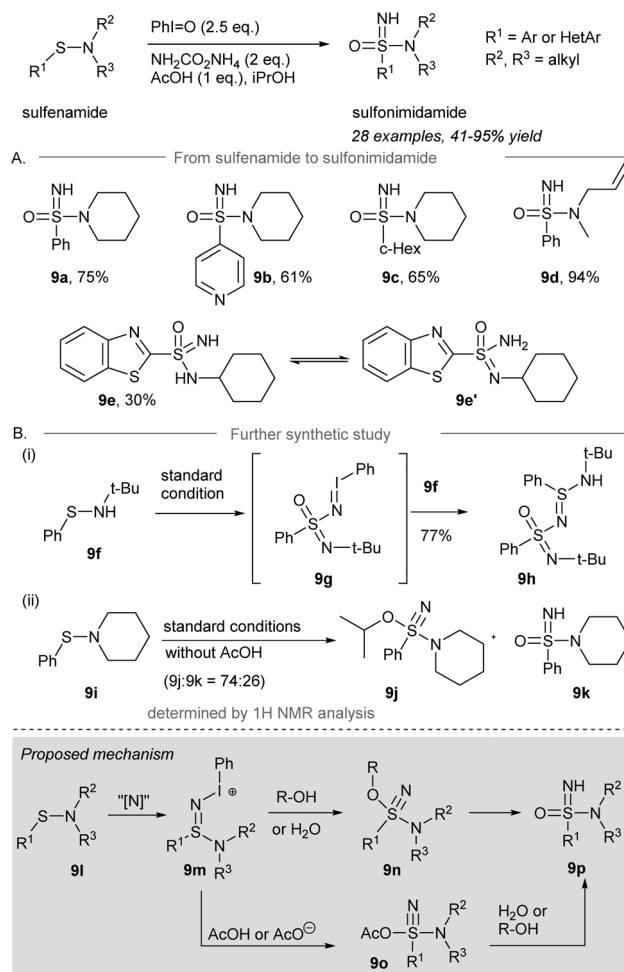
Scheme 8 Synthesis of sulfonimidates and sulfonamides from thiols through a one-pot *NH*-, *O*-, *RO*-transfer.⁵⁷

To prepare sulfonimidates, phenylthiol, thiophene-2-thiol and cyclohexanethanol were converted to the corresponding sulfonimidates 7a–7c in moderate yields under the standard conditions (Scheme 7). Interestingly, 2-mercaptobenzylalcohol 7d' was transformed into cyclization product 7d in 57% yield. Treatment of phenylthiol 7e with an excess of phenyliodine(III)

diacetate afforded a mixture of methyl sulfinate ester 7f and diphenyl disulfide 7g. However, sulfonate ester 7h was not observed. Exposure of methyl benzenesulfinate 7f to the *in situ* generated iodonitrene in acetonitrile afforded sulfonimide 7a. Phenylthiol, thiophene-2-thiol and cyclohexanethiol afforded the corresponding sulfonamides 8a–8c in good to excellent yields (Scheme 8).

Based on the experimental evidence, the authors suggested a possible mechanism of these reactions (Scheme 8, grey box). Intermediate 8g was detected by GCMS when R was a cyclohexyl group, which was reacted with methoxide or acetate to give sulfonimide 8h as the product. Sulfonimide 8h could be converted to sulfonamide 8i by reaction with existing nucleophiles, including methanol, acetic acid, and ammonia.

In 2019, Bull and co-workers reported the direct one-pot *NH*- and *O*-transfer from sulfonamides to sulfonimidamides (Scheme 9A).⁵⁸ Treatment of sulfonamides with 2.5 equivalents of iodosylbenzene and 2 equivalents of ammonium carbamate in the presence of 1 equivalent of AcOH as an additive gave sulfonimidamides in good yield. Phenyl-sulfenamide, 4-pyridi-



Scheme 9 (A) Synthesis of sulfonimidamides from sulfonamides through one-pot *NH*- and *O*-transfer.⁵⁸ (B) Further synthetic study of sulfonimidation.



nyl-sulfenamide, and cyclohexyl-sulfenamide performed well under the standard conditions to give the corresponding sulfonimidamides **9a–9c** in decent yield. A secondary sulfenamide containing an *NH* moiety gave sulfonimidamide **9e** in 30% isolated yield, along with the corresponding sulfinamide as the major side product.

Unexpectedly, *tert*-butylphenylsulfenamide **9f** was converted to **9h** in 77% yield under the standard conditions (Scheme 9B). It is rationalized that direct one-pot *NH*- and *O*-transfer to **9f** followed by activation by an excess of iodosylbenzene leads to the formation of iminoiodinane intermediate **9g**. Imination of **9g** by another equivalent of sulfenamide **9f** produced **9h**. When the reaction was performed in the absence of an acid, sulfenamide **9i** was converted into λ^6 -sulfanenitrile **9j** and sulfonimidamide **9k** in a ratio of 74:26 determined by ^1H NMR spectroscopy. The λ^6 -sulfanenitrile **9j** was fully characterized by HRMS and ^1H -, ^{13}C -NMR and IR spectroscopy.

The proposed mechanism is depicted in Scheme 9 (grey box). Sulfonamide **9l** is reacted with the iodonitrene to afford sulfenamidinium salt **9m**. Elimination of iodobenzene from **9m** forming the $\text{S}=\text{N}$ triple bond may occur before or at the same time as an attack of a nucleophile, being either $\text{R-OH}/\text{H}_2\text{O}$ to give alkoxy-amino- λ^6 -sulfanenitrile **9n** or AcOH to give sulfonimidamide **9o**. Finally, **9n** is converted to the desired sulfonimidamide **9p**. Alternatively, sulfonimidamide **9o** reacts with water from the solvent or the solubilization of iodosylbenzene produces sulfonimidamide **9p** under the standard conditions to give the corresponding sulfonimidamides **9a–9c** in decent yield, respectively.

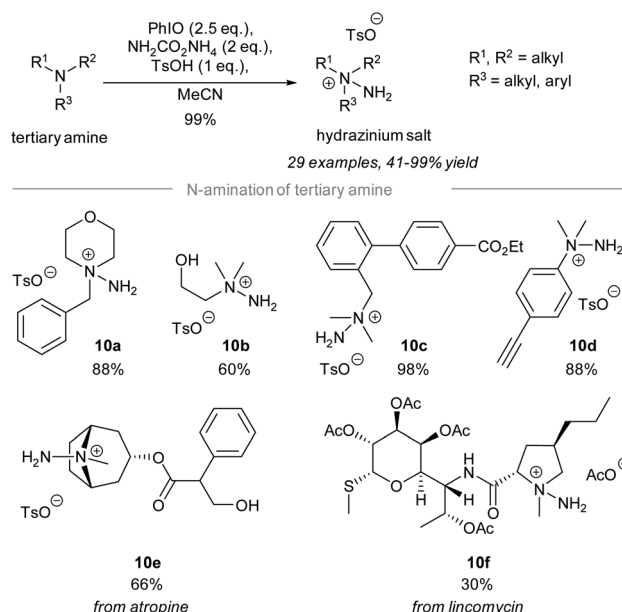
3. Selective electrophilic amination of tertiary amines

In 2021, Bull and Luisi disclosed the electrophilic amination of tertiary amines to give the corresponding hydrazinium salts (Scheme 10).⁵⁹ Treatment of tertiary amines with 2.5 equivalents of iodosylbenzene and 2 equivalents of ammonia carbamate in the presence of *p*-methylbenzenesulfonic acid gave hydrazinium salts. The study of the substrate scope revealed that many reactive functional groups are well-tolerated under the standard conditions.

For instance, the hydrazinium salts of primary alcohol **10b**, ethyl ester **10c**, and alkyne **10d** were prepared successfully in good yield using the reported protocol. Importantly, chemoselective electrophilic amination of the tertiary amino group on atropine and a lincomycin derivative took place to give the corresponding hydrazinium salts **10e** and **10f**, respectively.

4. Synthesis of terminal diazirines from amino acids through tandem decarboxylation/iodonitrene transfer

In 2019, Reboul and co-workers disclosed the synthesis of terminal diazirines from amino acids through a tandem de-



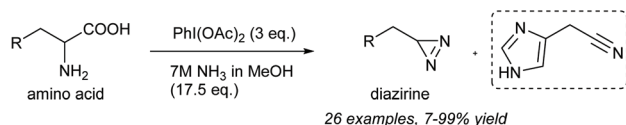
Scheme 10 Chemoselective electrophilic amination of tertiary amines.⁵⁹

carboxylation/iodonitrene transfer⁶⁰ (Scheme 11). Treatment of amino acids with phenyliodine(III) diacetate and 7M ammonia solution produces terminal diazirines as major products accompanied by a small number of undesired nitriles that resulted from over-oxidation. Amino acids such as *L*-histidine, *L*-tyrosine, *N*-Boc-*L*-tryptophan, *L*-citrulline, and 4-iodo-*L*-phenylalanine were converted to the corresponding diazirines **11a**, **11b**, **11d**, **11e**, and **11h** in high yield. However, unprotected *L*-tryptophan resulted in a volatile diazirine **11c** in 27% yield, which was not accurate for quantification. Besides, sulfurated amino acids such as cysteine (Cys)⁵⁷ and methionine (Met)⁵⁰ were incompatible with the reaction conditions due to possible side reactions with PIDA. Prior protection of sulfur, for instance, in (*S*)-trityl-*L*-cysteine and (*S*)-Bn-*L*-cysteine sulfoxide gave the corresponding terminal diazirines **11f** and **11g** in poor to moderate yield. Noteworthy, no sulfoximination⁴⁵ product was observed when the sulfoxides above were subjected to the standard conditions.

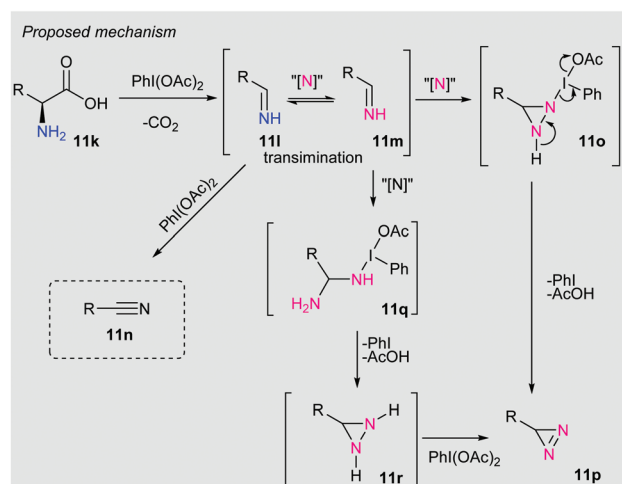
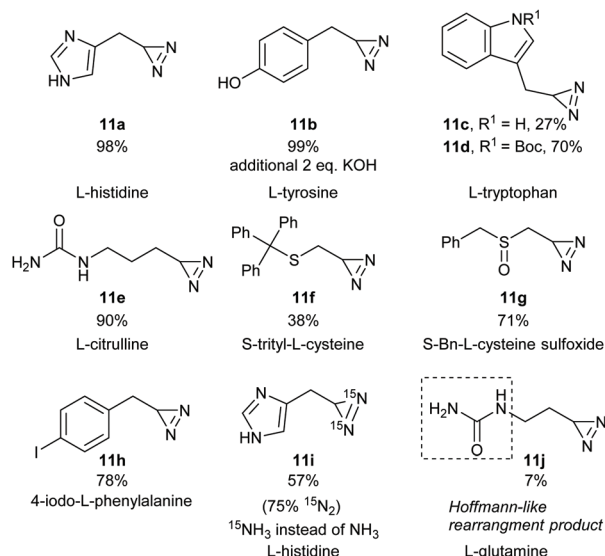
Treatment of *L*-histidine with PIDA and ^{15}N -labeled ammonia afforded $^{15}\text{N}_2$ -diazirine **11i** in 57% yield with 75% ^{15}N -label incorporated. This implied that both nitrogen atoms of the newly installed diazirine group originated from the ammonia solution. Primary amides, such as *L*-glutamine, gave diazirines in low yield due to sublimation. In particular, a Hofmann-like rearrangement of *L*-glutamine took place to give urea **11j** in 7% yield. This rearrangement could be alleviated by prior *N*-ethylation of *L*-glutamine.

The authors proposed a possible reaction mechanism (Scheme 11, grey box). Amino acid **11k** is subjected to decarboxylation upon treatment with phenyliodine(III) diacetate to give an imine **11l**.^{61,62} The imine **11l** formed could be oxidized to nitrile **11n** in the presence of an excess amount of





From amino acids to diazirines



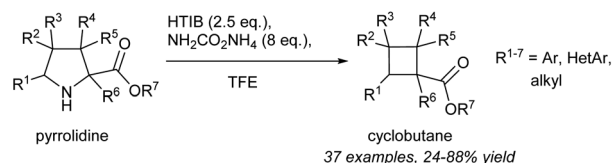
Scheme 11 Synthesis of terminal diazirines from amino acids through a tandem decarboxylation/iodonitrene transfer.⁶⁰

oxidant. Transimination⁶³ of imine **11l** takes place with the iodonitrene to give **11m**,¹⁴ which reacts with the second moiety of the iodonitrene *via* insertion to give the diaziridine intermediate **11o**.⁶⁴ Subsequent oxidation with the release of iodobenzene and acetic acid affords the desired diazirine **11p**.⁶⁵ Another possible pathway involves the nucleophilic addition of ¹⁵NH₃ to give **11q**,⁶⁶ followed by cyclization into diaziridine **11r**. Oxidation of diaziridine **11r** by phenyliodine (III) diacetate afforded diazirine **11p**.

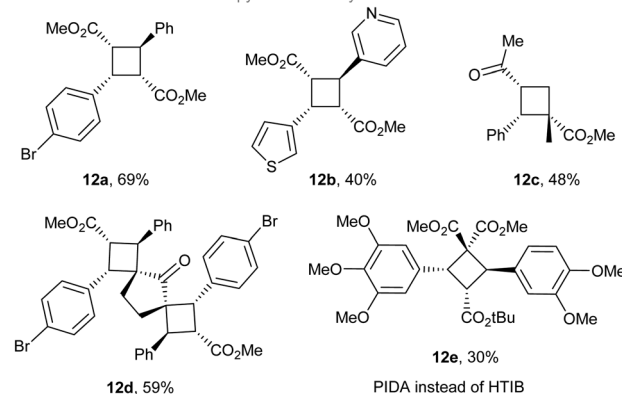
Very recently, Reboul's chemistry on direct diazirine synthesis from amino acids was used to prepare a diazirine tag for chemical proteomics.⁶⁷

5. Stereoselective and contractive synthesis of cyclobutanes from pyrrolidines

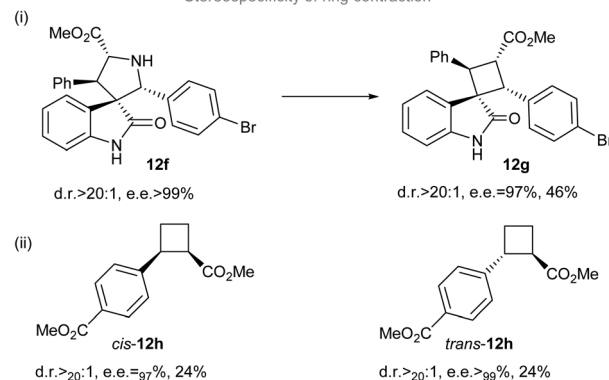
In 2021, stereoselective and contractive synthesis of cyclobutanes from the corresponding pyrrolidines was reported by Antonchick and co-workers¹⁶ (Scheme 12). Iodonitrene, which was generated *in situ* from the reaction between 2.5 equivalents of hydroxy(tosyloxy)iodobenzene (HTIB) and 8 equivalents of



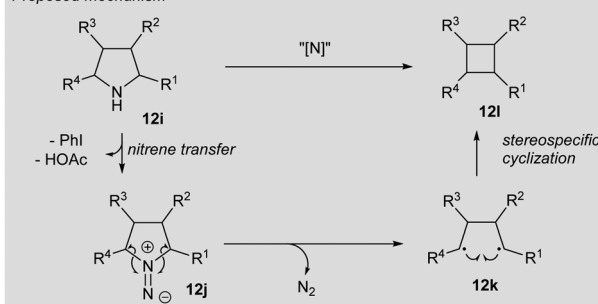
From pyrrolidines to cyclobutanes



Stereospecificity of ring contraction



Proposed mechanism



Scheme 12 Stereospecific contraction synthesis of cyclobutanes from pyrrolidines.⁵⁹



ammonium carbamate, acted as an electrophilic aminating reagent and converted the pyrrolidines into the corresponding cyclobutanes in a stereoselective manner. *meso*-Cyclobutanes carrying α -aryl and/or α -heterocyclic substituents, such as **12a** and **12b**, could be prepared in decent yield from the corresponding pyrrolidines under the standard conditions. The pyrrolidine possessing an α -quaternary center could be converted to the corresponding cyclobutane **12c** in 48% yield. Furthermore, double ring contraction of bipyrrrolidines with an additional amount of HTIB (*i.e.* 5 equiv.) provided polyspirocyclobutane **12d** in 59% yield. The contractive synthesis of cyclobutane **12e** was effected by HTIB instead of PIDA and it acted as an essential intermediate to the preparation of the cytotoxic cyclobutane natural product piperarborenine B.^{68–70}

When optically-pure spirooxindole **12f** was subjected to the standard conditions, spirocyclobutane **12g** was formed with excellent stereocontrol (*dr* > 20 : 1, *ee* = 97%) validating the stereospecificity of the ring contraction. More importantly, the stereospecific nature of the ring contraction was further substantiated by the formation of cyclobutanes *cis*-**12h** and *trans*-**12h**. Although both ring contractions afforded low yields (*i.e.* 24%), the outstanding diastereo- and enantiocontrol for *cis*-**12h** (*dr* > 20 : 1, *ee* > 97%) and *trans*-**12h** (*dr* > 20 : 1, *ee* > 99%) indicated a memory of chirality for the developed novel ring contraction allowing access to enantiopure novel cyclobutane derivatives.

The proposed reaction mechanism is depicted (Scheme 12, grey box). Treatment of pyrrolidine **12i** with the *in situ* generated iodonitrene species leads to electrophilic amination, affording 1,1-diazene **12j** as a possible intermediate. The reactive 1,1-diazene **12j** proceeds further to give 1,4-biradical **12k** *via* dinitrogen extrusion. The intramolecular cyclization of 1,4-biradical **12k** leads to C–C bond formation to give cyclobutane **12l**.

6. Summary and outlook

This review provides an overview of iodonitrene chemistry and illustrates its development since 2016. Through the discovery of iodonitrene as an *in situ* generated reactive species from the reaction between hypervalent iodine(III) and ammonia, iodonitrene has been used extensively as an electrophilic aminating reagent in the amination of sulfides and sulfoxides. Until 2019, the unprecedented synthesis of diazirines from unprotected amino acids was achieved by Reboul making use of hypervalent iodine(III) as an oxidant for decarboxylation and an iodonitrene as a source of nitrogen. Diazirines generated by this method can be used as a tag once they are incorporated into bioactive compounds and could be used for various biological investigations. Later, our group reported the stereospecific contractive synthesis of cyclobutanes from pyrrolidines featuring iodonitrene-promoted electrophilic amination of the N-atoms of pyrrolidines followed by nitrogen extrusion. Taking into account the reaction we described above, iodonitrene not only serves as an

electrophilic aminating reagent, but also shows the oxidation properties of hypervalent iodine(III). This makes iodonitrene a very interesting reagent for the development of new methods.

Iodonitrene acts as a convenient and easily manageable reagent in organic synthesis. Besides its metal-free nature, the use of iodonitrene provides comparable reactivity to rhodium-carbene in the synthesis of NH-sulfoximines from sulfoxides but requires no use of a transition metal. This provides a fascinating opportunity that rhodium-catalyzed nitrene transfer reactions might be accomplished by iodonitrene chemistry, for instance, in the amination of arenes and alkenes. One major issue that needs to be addressed is the stoichiometric amounts of hypervalent iodine(III) reagent necessary to react with ammonia or its surrogate in order to generate iodonitrene. Inspired by the organocatalytic reactions developed by us and others, hypervalent iodine(III) formed from catalytic quantities of aryl iodides and *m*-CPBA as a stoichiometric oxidant might react with ammonia to give iodonitrenes, avoiding the use of stoichiometric amounts of hypervalent iodine(III). Furthermore, the prospect of asymmetric iodonitrene transfer might be enabled by iodonitrenes prepared from chiral hypervalent iodine(III) compounds. New method development involving the use of iodonitrene continues to be an active research area. We envision that synthetic application of the reported iodonitrene chemistry, such as the preparation of diazirine tags and the synthesis of bioactive natural products, will be flourished as practically useful chemistry applied widely in the synthetic community and the pharmaceutical industry.

Conflicts of interest

There are no conflicts to declare.

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