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# Efficient Copper-Mediated Reactions of Nitrenes Derived from Sulfonimidamides

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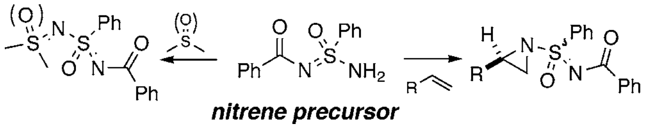
## ABSTRACT



**Sulfonimidamides lead efficiently to nitrenes and have been converted to sulfimides, sulfoximines, and aziridines in good yields, through a copper-mediated multicomponent reaction. The stereogenic sulfur atom and the trivalent nitrogen atom present in the molecules open the way to asymmetric synthesis, whose first results are presented.**

Because nitrogen-containing molecules are ubiquitous, selective nitrogen atom insertions into organic substrates are essential tools that can be used by synthetic chemists.[1] Among all the available methods, metal-mediated aminations and nitrene-derived reactions are of great interest. The latter method allows the formation of C−N and S═N[2] bonds via insertion or transfer. In particular, olefin aziridination can be achieved from both nitrido−metal and imido−metal complexes. The former has been pioneered by Groves[3] and Carreira.[4] Nitrogen sources for the latter are diverse, but the most widely used are chloramine-T[5] and iminoiodanes,[6] which are more convenient and versatile. Thus, a variety of catalytic systems are suitable for the decomposition of the hypervalent iodine derivatives: metal porphyrins,[7] salen[8] and terpyridine[9] complexes, non-heme iron compounds,[10] rhodium[11] and copper salts,[12] etc. Yet, the range of iodanes allowed is very narrow (basically limited to compounds originating from a few sulfonamides). DuBois' announcement that in situ-generated iminoiodanes obtained from carbamates and sulfamate esters could be used in rhodium-catalyzed multicomponent C−H insertions[13] and aziridination[14] triggered several reports focusing on the development of one-pot processes.[15] In addition, contrary to the case with carbenes, the enantioselective versions of those processes are much less efficient, notably because they are highly substrate-dependent.[16] As a consequence, this aspect remains

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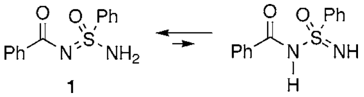
a challenge worth investigating, and there is a real need for new systems. Because of our previous work on chiral sulfur functions,[17] we decided to replace the sulfonamide/sulfamate moiety of the nitrene with a stereogenic sulfur-containing one. To the best of our knowledge, this approach to chiral nitrenes had never been reported, and our first choice was to use a sulfinamide. Such compounds led to oxidation when treated with iodosobenzene, the standard method for preparing iminoiodanes.[18] We thus decided to switch to a more oxidized function. We report herein the results we gathered using sulfonimidamides (**1**).

The first problem we faced was the known interconversion between the two nitrogen atoms of sulfonimidamides (Scheme 1).[19] We anticipated that this tautomerization should be hampered by the presence of an additional carbonyl group on the imido nitrogen. The equilibrium would be presumably displaced toward **1**, with the required free amino group.[20]

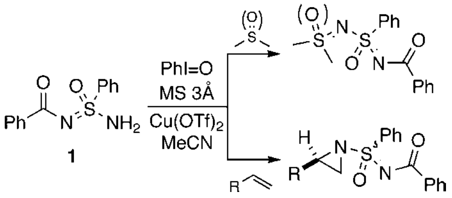
**Scheme 1.** Proton Exchange on Sulfonimidamides



When submitted to iodosobenzene diacetate in the presence of a base, **1** gave a yellowish precipitate, which decomposed upon drying. We assumed that the iodinane could indeed be formed but was too sensitive to be isolated easily. Dauban and Dodd reported similar problems with some of their substrates and introduced one of the above-mentioned multicomponent procedures.[15a]

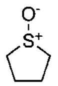
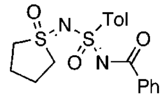
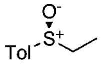
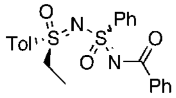
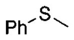
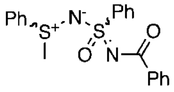
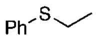
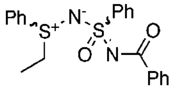
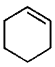
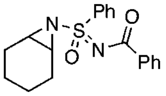
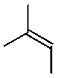
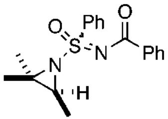
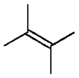
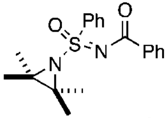
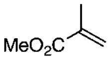
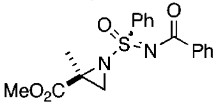
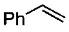
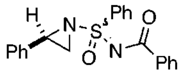
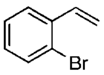
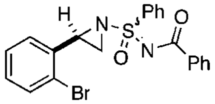
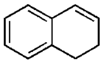
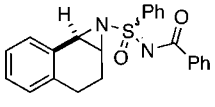
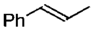
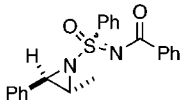
We thus adopted the same procedure, using the less expensive and less sensitive copper(II) salt instead of the copper(I) one. Sulfonimidate **1** was added together with iodosobenzene in five small lots (one every 15 min) to a slurry of a nitrene trap (sulfur function or olefin), 3 Å MS, and copper(II) triflate (10 mol %) at room temperature (Scheme 2).

**Scheme 2.** Nitrene Formation from Sulfonimidamides



As we were more familiar with sulfur chemistry, we started our study by preparing the previously unknown *N*-sulfonimidoyl sulfoximines. Reaction with tetrahydrothiophene oxide proceeded smoothly and yielded 80% of the corresponding sulfoximine (Table 1, entry 1). This outcome validated our approach. Upon starting from a chiral enantiopure sulfoxide, we could isolate two diastereomers of the

**Table 1.** Reactions of Sulfonimidamide-Derived Cu−Nitrenes

| entry | substrate | product | yield (%)[a] | ds[b] |
|---|---|---|---|---|
| 1[c] |  |  | 80 | - |
| 2 |  |  | 54 | - |
| 3 |  |  | 63[d] | 52:48 |
| 4 |  |  | 53[e] | 60:40 |
| 5 |  |  | 60[f] | -[g] |
| 6 |  |  | 59[f] | 55:45 |
| 7 |  |  | 59[f] | - |
| 8 |  |  | 43[f] | 58:42 |
| 9 |  |  | 78 | 52:48 |
| 10 |  |  | 64 | 60:40 |
| 11 |  |  | 68 | 72:28 |
| 12 |  |  | 59 | 75:25 |

[a] All reactions were run at room temperature in MeCN in the presence of 3 Å MS, 1 equiv of **1**, and 10 mol % $Cu(OTf)_2$. PhIO was added in five different lots over 2 h. [b] Unless otherwise noted, diastereoselection was measured by NMR and HPLC. [c] *p*-Tolyl benzoyl sulfonimidamide was used. [d] Corresponding sulfoxide was also observed (5%). [e] Corresponding sulfoxide was also observed (3%). [f] Performed with 5 equiv of olefin. [g] Diastereomers could not be separated.

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sulfoximine (entry 2). The reaction proceeded with retention of optical purity of the sulfoxide's sulfur atom (both isolated products were enantiopure; they were racemic upon starting from the same racemic sulfoxide).[21] As it is customary with such imination,[2b,c] we assumed that the nitrene attacked the sulfur lone pair.

Sulfides are interesting targets for iminations, since the latter lead to chiral sulfimides. Here, methyl (respectively, ethyl) phenyl sulfide gave the corresponding sulfimides in acceptable yields (entries 3 and 4). Those products were accompanied by traces of sulfoxides arising from the direct oxidation of the sulfides by iodosobenzene.[22] The diastereoselectivities were low. Yet, it seems that the substitution pattern of the sulfide does bring some modifications.

For the aziridinations, we initially decided to use 5 equiv of the olefins. With aliphatic alkenes, we were able to isolate the corresponding aziridines in acceptable yields (entries 5−7). 2-Methyl-2-butene failed to give any selectivity (entry 6). Since some sulfonimidamides are bioactive,[23] we have an access to a new class of compounds, whose activity is under investigation. Nitrenes are electrophilic and generally less reactive toward electron-poor alkenes. This explains the loss in yield when an acrylate was used (entry 8).

A second class of olefins was much more promising: when an aromatic ring was attached to the double bond, the aziridines were obtained in higher yields and from only 1 equiv of the styrene derivatives (entries 9−12). The best yield was reached with styrene (78%, entry 9). The diastereoselectivities were also much better, nearing 50% de, which is acceptable for aziridinations. Our best result so far has been with *trans*-$\beta$-methylstyrene (3:1 ds, entry 12). Reduction of the catalyst loading to 5% led to diminished yields (40%), without loss of stereoselection. Copper(II) triflate is probably not the most active system to allow low loadings.

In conclusion, we have introduced a new class of nitrenes, which are more reactive than their parent sulfonamide-derived ones. In some cases, we could lower the amount of trapping agents used to only 1 equiv, thus broadening the scope of those intermediates. Besides, we have shown that the reactions proceed with some diastereoselectivity. Since the diastereoselectivities are very promising and seem to be a function of both steric and electronic effects, we can take advantage of the versatility provided by the presence of an additional group on the S═N nitrogen atom. Work toward the optimization of the selectivities, by fine-tuning the starting sulfonimidamide, trying different metals, and/or looking for potential matched pairs for double induction, as well as the extension of the reactivity to insertions is under way and will be reported in due course.

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**Supporting Information Available:** Experimental procedures and spectral data for all new compounds, evidence for purity, and proof of retention related to entry 2 of Table 1. This material is available free of charge via the Internet at http://pubs.acs.org.

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