Copper-Catalyzed Nitrogen Transfer Mediated by Iodosylbenzene PhI═O

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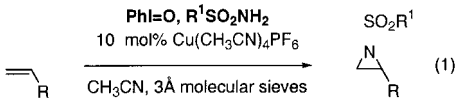
Transition metal-catalyzed functionalization of hydrocarbons is a fundamental process of paramount importance in organic synthesis. Among the numerous existing methodologies, catalyzed atom transfer to olefins plays a pivotal role since it allows access to aziridines,[1]amino alcohols,[2] diols,[2,3] and epoxides.[1,4] In the latter case, iodosylbenzene[5] (PhI═O) **1** has been extensively used as a primary oxygen atom source in combination with manganese, iron, ruthenium or chromium catalysts.[1,6] In a theoretical study, even copper complexes were found to transfer oxygen from **1** to cyclohexene.[7]

Copper complexes formed from the aza-analogue of **1**, that is [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane (PhI═NTs) display a high capacity to catalyze aziridination of olefins.[8] Among the many known metal-catalyzed nitrene-transfer reactions,[1] this process represents the method of choice and has been successfully applied to the total synthesis of natural or biologically active products.[9] The commercial availability of easy-to-handle copper-(I) and particularly -(II) complexes makes this reaction highly practical. Moreover, a wide array of olefins reacts to give *N*-(sulfonylated)aziridines in moderate to excellent yields. Finally, several iminoiodinanes, differing in the substituents attached to the sulfonyl group, have been developed as sources of nitrene for synthetic applications.[10] However, one of the major drawbacks of this reaction lies in the preparation and isolation of these iminoiodinanes which can be sometimes difficult to reproduce.

Since aziridines are useful intermediates in total synthesis,[11] their direct preparation from sulfonamides would enhance the scope and the synthetic value of the reaction. In this regard we have discovered that *an unusual copper-catalyzed nitrogen transfer to olefins can be mediated by the primary oxygen atom source iodosylbenzene* **1** [eq 1].



(1)

Initial experiments investigated the use of iodosobenzene-(diacetate) [$PhI(OAc)_2$] alone or in the presence of bases such as *t*-BuOK, CaO, *i*-$PrNEt_2$ for the copper-catalyzed aziridination of olefins starting from sulfonamides. Since all attempts were unsatisfactory, we decided to explore other hypervalent iodine -(III) reagents. Inspired by the papers of White[12] and Simandi,[13] we supposed that such a direct copper-catalyzed aziridination could be performed starting from iodobenzene dimethoxide [$PhI(OMe)_2$]. Indeed, sequential addition to this reagent, in acetonitrile and in the presence of 3 Å molecular sieves, of *p*-toluenesulfonamide and after 3 h,[14] of tetrakis(acetonitrile)copper(I) hexafluorophosphate and methyl methacrylate[15] gave rise to aziridine **2a** in 37% yield. Since preparation of $PhI(OMe)_2$ from **1** is rather tedious,[16] the reaction was attempted directly with PhI═O which is easily accessible in large quantity and with high purity by base treatment of commercially available $PhI(OAc)_2$.[17] Application of the same procedure then led to the expected product **2a** in 56% yield. Finally, because the course of formation of the intermediate iminoiodinanes is difficult to monitor, we decided to introduce all of the reagents at once at the beginning of the reaction. To our surprise, aziridine **2a** was isolated with nearly the same yield of 54%, while no epoxide was detected. This result prompted us to study the aziridination of various olefins under these "one-pot" conditions.

Typical experiments[18] were run with olefins as the stoichiometrically limiting component (except in entries 4 and 6, Table 1) in the presence of a catalytic amount of copper(I) salt and a slight excess of **1** and the sulfonamide. For the purpose of this study, we chose *p*-toluenesulfonamide, the precursor of the standard and easily prepared reagent PhI═NTs, as well as *p*-methoxybenzenesulfonamide and 2-(trimethylsilyl)ethanesulfonamide whose parent iminoiodinanes are not easily isolated. Results are shown in Table 1. Generally, yields are comparable to those obtained in the aziridinations using iminoiodinanes. Therefore, in addition to its practical interest, this new direct nitrene transfer appears to be at least as efficient as the classical procedure since preparation of PhI═NSO_2R is far from being quantitative. This is also apparent in the intramolecular version of the reaction,[10e] the results of which are summarized in Table 2. Moreover, it is

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(18) See Supporting Information for typical aziridination procedures with each sulfonamide.

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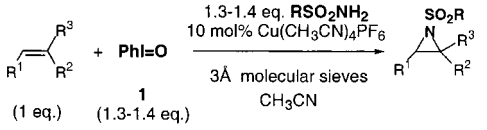
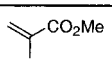
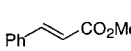
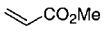
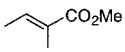
Table 1. Copper-Catalyzed Aziridination of Representative Olefins Mediated by PhI=O

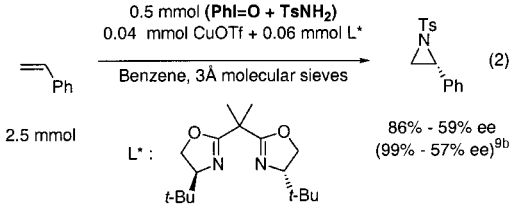


Entry	Substrate	Aziridine	% Yield[a,b]
1		**2a** : R = *p*-MePh **2b** : R = Ses **2c** : R = *p*-MeOPh	56 (58)[16] 43 (60)[11d] 59 (-)
2		**3a** : R = *p*-MePh **3b** : R = Ses **3c** : R = *p*-MeOPh	75 (-) 68 (68)[11d] 78 (-)
3		**4a** : R = *p*-MePh **4b** : R = Ses **4c** : R = *p*-MeOPh	47 (40)[11a] 53 (39)[11d] 40 (60)[11a]
4		**5a** : R = *p*-MePh	45 (45)[16]
5		**6a** : R = *p*-MePh **6b** : R = Ses	44 (42)[16] 48 (47)[11d]
6		**7a** : R = *p*-MePh **7b** : R = Ses **7c** : R = *p*-MeOPh	70 (74)[11a] 46 (34)[11d] 70 (98)[11a]
7		**8a** : R = *p*-MePh **8b** : R = Ses	76 (-) 63 (67)[11d]
8		**9a** : R = *p*-MePh **9b** : R = *p*-MeOPh	60 (-) 62 (95)[11a]

[a] Isolated yield after flash chromatography. [b] Value in parentheses for yield reported in the literature starting from PhI=NSO_2R under comparable conditions. [c] 5 equiv of olefin and 1 equiv of (PhI=O + RSO_2NH_2) were used.

noteworthy that portionwise addition of **1** and the sulfonamide to the olefin allowed isolation of aziridines in better yields, particularly in the case of the highly reactive intermediate iminoiodinanes.

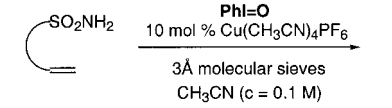
Because the reaction was also found to occur in dichloromethane or benzene, asymmetric copper-catalyzed aziridination was performed. By applying the experimental procedure described by Evans to styrene,[8b] aziridine **3a** was obtained with an ee of 59% comparable to that obtained previously [eq 2].

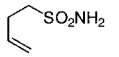
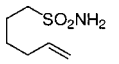
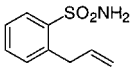
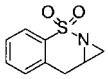


From a mechanistic point of view, this nitrene-transfer reaction contradicts the previous assumption which postulated that copper-catalyzed aziridination could be hampered by metal-catalyzed hydrolysis of iminoiodinanes to sulfonamides and **1**. Indeed, PhI=O-mediated aziridination occurred even in the presence of water.[19] Therefore, we propose that metal-catalyzed degradation of iminoiodinanes leads to iodobenzene and, via nitrenoid **13**, the starting sulfonamide. This hypothesis led us to suppose, according to the mechanistic pathway in Scheme 1,[20] that an excess of the sulfonamide was not necessary to perform the reaction. Indeed, use of an equimolar amount of methyl methacrylate and $TsNH_2$ in the presence of a slight excess (1.4 equiv) of **1** led to aziridine **2a** with the same yield of 56%.

(19) Aziridination of styrene in the presence of 3 equiv of water without molecular sieves led to approximatively a 50% yield of aziridine.

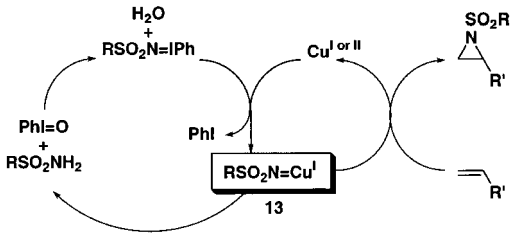
Table 2. Intramolecular Copper-Catalyzed Reactions Mediated by PhI=O



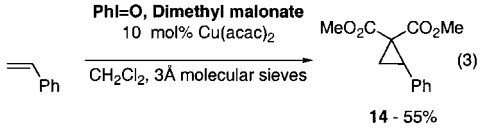
Substrate	% Yield[a,b]	Product
	**10** : 62 (38)	
	**11** : 51 (51)	
	**12** : 69 (60)	

[a] Isolated yield after flash chromatography. [b] Value in parentheses for yield reported using classical methodology.[10e]

Scheme 1



The most striking feature of this process is the nitrogen-transfer mediated by an oxo donor. Control experiments run on methyl methacrylate, styrene, and cyclohexene in the absence of sulfonamide did not allow isolation of epoxides in significative amounts (less than 10%), confirming that these reactions are sluggish,[7,21] while aziridination was found to occur even with copper(II) salts. Since copper complexes do not significantly catalyze oxygen transfer, it seemed worthwhile to test the generality of the pathway depicted in Scheme 1, starting from acidic hydrogen-containing products. We thus decided to attempt cyclopropanation of styrene directly from dimethyl malonate.[22] To our satisfaction, a copper-catalyzed carbene transfer was observed under stoichiometric conditions starting from **1** leading to cyclopropane **14** in 55% yield [eq 3].



In conclusion, we have developed *a direct copper-catalyzed nitrogen transfer mediated by the powerful oxygen atom donor PhI=O*. This unique reaction greatly simplifies the procedure for copper-catalyzed aziridination of olefins and enhances its efficiency.

Supporting Information Available: Experimental details and characterization for all new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) A test experiment conducted on stilbene, which was the most reactive substrate towards copper-mediated epoxidation of olefins by **1**, confirmed this assumption since an NMR study of the crude reaction revealed a 10:1 ratio of aziridine and epoxide.

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