Novel aziridination of olefins: direct synthesis from sulfonamides using *t*-BuOI†

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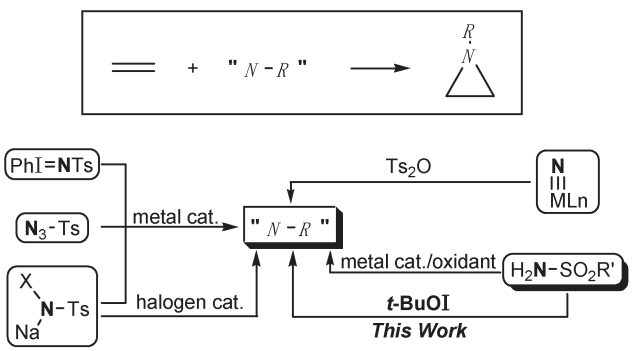
tert-Butyl hypoiodite (*t*-BuOI) was found to be a powerful reagent for synthesis of aziridines from olefins and sulfonamides. The aziridination of olefins was achieved by using sulfonamides with *t*-BuOI. Our preliminary findings represent the example of metal-free aziridination of olefins with readily accessible sulfonamides as a nitrogen source.

The aziridination of olefins is an extremely important transformation since aziridines are useful synthetic intermediates and are often present as substructures in natural products and frequently show diverse biological activities.[1] Among the various methods for the synthesis of aziridines, the transfer of a nitrogen atom onto an olefin is the shortest route and offers a method for the practical formation of aziridines. To generate an active nitrogen species for olefin aziridination, great progress has been made with combinations of nitrogen sources and catalysts and/or activators as shown in Scheme 1. The reagent [*N*-(*p*-toluenesulfonyl)imino]-phenyliodinane (PhI=NTs) has been extensively used as a primary nitrene source for transition metal-catalyzed aziridination[2] including asymmetric versions.[3] However, the reagent suffers from several drawbacks such as its commercial unavailability, the high cost of its source, and the fact that an equimolar amount of iodobenzene is generated. Although alternative nitrogen sources, azides,[4] chloramine-T,[5] bromamine-T,[6] nitrido complexes,[7] and combinations of sulfonamides and terminal oxidants[8] have been widely applied to olefin aziridination, catalytic or stoichiometric amounts of metals are required for the processes except for methods using chloramine-T and a halogen catalyst system.[9] The direct preparation of aziridines from sulfonamides and olefins without the use of heavy metal catalysts would enhance the scope and synthetic value of the reaction.[10] In this context we report herein on the unusual metal-free aziridination of olefins with readily accessible sulfonamides as a nitrogen source, in which *tert*-butyl hypoiodite (*t*-BuOI) plays an important role as a powerful oxidant. Although *t*-BuOI is known as an iodination reagent which can readily be prepared from *t*-BuOCl and NaI,[11] examples of using the reagent in organic transformations are rarely reported to date.[12]



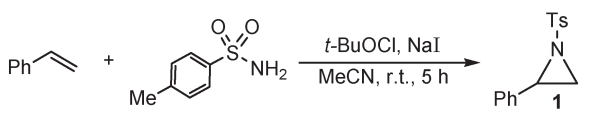
Scheme 1 Representative methods for generating active nitrogen species for olefin aziridination.

We began our investigation with styrene and *p*-toluenesulfonamide as a model aziridination. As illustrated in Table 1, treatment of *p*-toluenesulfonamide and styrene (2 equiv) with *t*-BuOI (1 equiv) at room temperature in acetonitrile provided *N*-(*p*-toluenesulfonyl)-2-phenylaziridine (**1**) in moderate yield (entry 1). Screening of the amount of *t*-BuOI required (entries 2–4) showed 1.5 mmol of *t*-BuOI to be optimal, to give aziridine **1** in excellent yield (entry 4). These results suggest that more than one equivalent of *t*-BuOI relative to *p*-toluenesulfonamide is required for the aziridination to be complete.

In order to confirm the superiority of the system, other representative iodinating reagents, bis(pyridine)iodine tetrafluoroborate (IPy_2BF_4), NIS and I_2, were evaluated to the aziridination. Since IPy_2BF_4 and I_2 did not give the desired aziridine and the efficiency was rather low to afford **1** in 18% yield by NIS, *t*-BuOI was found to be a powerful reagent for the reaction.

The scope of substrates in the aziridination by *t*-BuOI with *p*-toluenesulfonamide was then explored using a range of olefins under the optimized conditions (Table 2). The reaction of 1,2-dihydronaphthalene with *p*-toluenesulfonamide proceeded smoothly to afford the desired aziridine in good yield (entry 1). In the case of α-methylstyrene, the corresponding aziridine was

Table 1 Aziridination of styrene with *p*-toluenesulfonamide using *t*-BuOI[a]



Entry	*t*-BuOCl/mmol	NaI/mmol	Yield (%)[b]
1	0.5	0.5	46
2	1.0	1.0	84
3	1.2	1.2	93
4	1.5	1.5	95

[a] Reaction conditions: styrene (1.0 mmol), *p*-toluenesulfonamide (0.5 mmol), MeCN (3 mL), rt, 5 h. [b] Isolated yields based on *p*-toluenesulfonamide.

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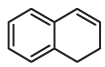
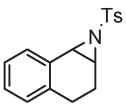
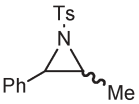
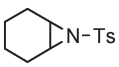
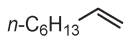
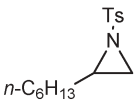
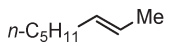
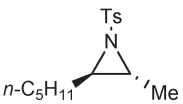
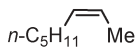
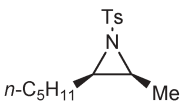
† Electronic supplementary information (ESI) available: Procedure of synthesis and experimental data of *aziridines*. See DOI: 10.1039/b606499j

Table 2 Olefin aziridination using the present system[a]

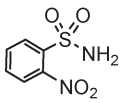
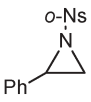
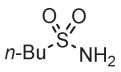
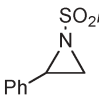
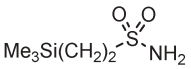
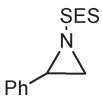
Entry	Olefin	Aziridine	Yield (%)[b]
1			76[c]
2			81[d,e]
3			66[f,g]
4			58[h]
5			77
6			63
7			82

[a] Reaction conditions: *p*-toluenesulfonamide (0.5 mmol), olefin (1.0 mmol), *t*-BuOCl (1.5 mmol), NaI (1.5 mmol), MeCN (3 mL), rt, 96 h. [b] Isolated yields based on *p*-toluenesulfonamide. [c] Reaction time: 0.5 h. [d] Reaction time: 2 h. [e] ^{1}H-NMR yield. [f] Reaction time: 5 h. [g] *Cis*/*trans* = 41/59. [h] *t*-BuOCl and NaI: 1 mmol.

produced in high yield (entry 2). When *cis*-β-methylstyrene was employed, a mixture of diastereomers was formed (entry 3). The present reaction system was also found to be applicable to the aziridination of aliphatic olefins. Cyclic and acyclic terminal olefins such as cyclohexene and 1-octene underwent aziridination in good to moderate yields (entries 4 and 5). It is noteworthy that the reaction of *trans*-2-octene proceeded with complete stereoselectivity, giving a *trans*-substituted aziridine as the sole product (entry 6). In contrast to *cis*-β-methylstyrene (entry 3), the aziridination of *cis*-2-octene was stereoselective and gave the corresponding *cis*-aziridine exclusively in good yield (entry 7). These complete stereoselective and stereospecific aziridinations are fully consistent with a reaction pathway involving a cyclic iodonium intermediate.

Some other sulfonamides function as competent nitrogen sources in the present aziridination, as summarized in Table 3. When aziridination was performed with *o*-nitrobenzenesulfonamide (*o*-$NsNH_2$), the desired product was formed in moderate yield (entry 1). An alkylsulfonamide, *n*-butanesulfonamide, was found to be applicable to the reaction, giving an *N*-butanesulfonylaziridine in high yield (entry 2). Although arenesulfonyl groups attached to the nitrogen of aziridines can be removed under reducing conditions, undesirable reactions such as the ring-opening of the aziridine sometimes occurs.[13] To obtain

Table 3 Aziridination of styrene with sulfonamides using *t*-BuOI[a]

Entry	Amide	Time/h	Product	Yield (%)[b]
1		12		66[c]
2		5		92
3		3		97

[a] Reaction conditions: sulfonamide (0.5 mmol), styrene (1.0 mmol), *t*-BuOCl (1.5 mmol), NaI (1.5 mmol), MeCN (3 mL), rt. [b] Isolated yields based on a sulfonamide. [c] *t*-BuOCl and NaI: 1 mmol.

N-unsubstituted aziridines more readily, we attempted to synthesize *N*-[2-(trimethylsilyl)ethanesulfonyl]aziridines (*N*-SES-aziridine), whose SES group can easily be deprotected under mild conditions.[14] Treatment of styrene with 2-(trimethylsilyl)ethanesulfonamide ($SESNH_2$) in the presence of *t*-BuOI led to the production of *N*-SES-aziridine in 97% yield (entry 3).

In summary, an efficient and convenient method for the synthesis of aziridines from olefins and sulfonamides using *t*-BuOI has been developed.[15] Our preliminary findings represent the first example of the metal-free aziridination of olefins using readily available sulfonamides as a nitrogen source. Mechanistic considerations and expanding the generality of the reaction are currently underway.

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15 General procedure for the synthesis of aziridines. To a mixture of the sulfonamide (0.5 mmol), the olefin (1.0 mmol) and NaI (1.0–1.5 mmol) in MeCN (3 mL) was added *t*-BuOCl (1.0–1.5 mmol). The mixture was allowed to stir in the dark at room temperature for indicated time under an atmosphere of nitrogen, quenched with 0.3 M aqueous $Na_2S_2O_3$ (3 mL), extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate).