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$PhI(OAc)_2/I_2$ induced aziridination of alkenes with $TsNH_2$ under mild conditions

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ABSTRACT

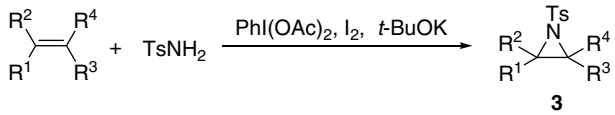
The aziridination of alkenes with the direct use of *p*-toluenesulfonamide ($TsNH_2$) was achieved by using $PhI(OAc)_2$ and I_2 under mild conditions. The reaction affords aziridines in moderate to good yields, and offers good manipulability by avoiding the use of the expensive metal catalyst and the unstable and explosive PhI=NTs.

Aziridines are important three-membered heterocyclic substructures in many biologically natural products, and are useful intermediates in organic synthesis.[1] As the powerful substrates, they can undergo various nucleophilic ring-opening reactions to afford the expected amine derivatives.[1,2] Metal-catalyzed transfer of nitrene to olefins is a well-established protocol for the preparation of aziridines.[3] *N*-Tosyliminophenyliodinane (PhI=NTs) has been widely used as the nitrene source,[4] but it suffers from its unstability, explosibility, and commercial unavailability. Although chloramine-T,[5] bromamine-T,[6] azides,[7] and nitrido complexes[8] can also be used in the aziridination of olefins, the direct aziridination from sulfonamides has attracted more and more attention recently.[9] In most of the cases, heavy metal catalysts are required to realize the aziridination. Che et al. reported an efficient metal-free aziridination using hypervalent iodine,[10] but the reaction is restricted to the use of aminophthalimide and aminobenzooxazolone. More recent work by Minakata described a metal-free aziridination from sulfonamides using *t*-BuOI.[11] As a part of our program to develop the synthetic application of sulfonamides in the presence of hypervalent iodine,[12] we report herein the results regarding the aziridination of alkenes with the direct use of *p*-toluenesulfonamide ($TsNH_2$) induced by $PhI(OAc)_2$ and I_2 under mild conditions (Scheme 1).

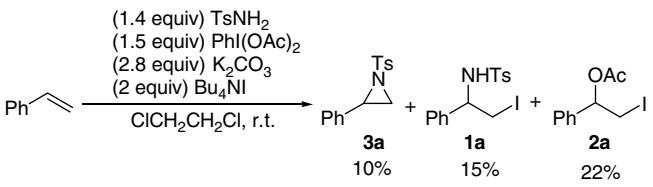
The aziridination of styrene with $TsNH_2$ was chosen to establish the reaction conditions. No aziridination was observed with the using of $PhI(OAc)_2$ and K_2CO_3 in $ClCH_2CH_2Cl$. However, when 0.2 equiv of tetrabutylammonium iodide (TBAI) was added as the phase-transfer catalyst, trace aziridine **3a** was detected from the reaction. When 2 equiv of Bu_4NI were used, aziridine **3a** could be isolated in 10% yield (Scheme 2). Control experiments showed that no aziridine was formed when Bu_4NBr or Bu_4NCl was used.

Compounds **1a** and **2a** were isolated as the byproducts of the reaction. Compound **2a** was supposed to be generated from the iodoacetoxylation of styrene via an acetyl hypoiodite (AcOI) intermediate, which was formed from the reaction of $PhI(OAc)_2$ with Bu_4NI. It was well known that acetyl hypoiodite could also be formed from the reaction of $PhI(OAc)_2$ with I_2.[13] So iodine (I_2) was used instead of Bu_4NI in the further reaction as shown in Table 1.

Aziridine **3a** was obtained in 18% yield when 1 equiv of I_2 was introduced into the reaction (Table 1, entry 2). The increase of the amount of I_2 decreased the yield of aziridine (entry 3). The result obtained with 0.5 equiv of I_2 was comparable to that with 1 equiv of I_2 (entry 4), but the reaction could not be completed when the amount of I_2 was decreased to 0.25 equiv (entry 5). When the amounts of $TsNH_2$ and K_2CO_3 (ratio 1:2) were increased, the yield of aziridine **3a** increased (entries 6 and 7). The ratio of $TsNH_2$ with K_2CO_3 in 1:2 was essential to the reaction (entries 7–10). No aziridine was detected from the reaction in the absence of base. Aziridine **3a** was isolated in 76% yield when 3 equiv of $PhI(OAc)_2$ were used (entry 11). Furthermore, the control



Scheme 1. $PhI(OAc)_2/I_2$ induced aziridination of alkenes with *p*-toluenesulfonamide.



Scheme 2. $PhI(OAc)_2/Bu_4NI$ induced aziridination of styrene with *p*-toluenesulfonamide.

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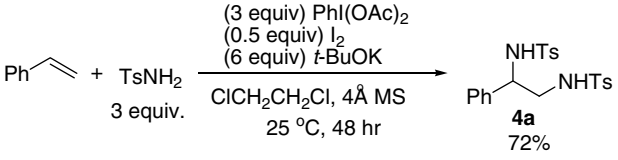
Table 1
The screening experiments of reaction conditions[a]

Entry	$TsNH_2$ (equiv)	$PhI(OAc)_2$ (equiv)	I_2 (equiv)	Base (equiv)	Solvent	Temp. (°C)	**1a**[b] (%)	**2a**[b] (%)	**3a**[b] (%)
1	1.4	1.5	0	K_2CO_3 (2.8)	$ClCH_2CH_2Cl$	25	0	0	0
2	1.4	1.5	1	K_2CO_3 (2.8)	$ClCH_2CH_2Cl$	25	32	41	18
3	1.4	1.5	2	K_2CO_3 (2.8)	$ClCH_2CH_2Cl$	25	16	65	9
4	1.4	1.5	0.5	K_2CO_3 (2.8)	$ClCH_2CH_2Cl$	25	31	30	21
5	1.4	1.5	0.25	K_2CO_3 (2.8)	$ClCH_2CH_2Cl$	25	13	21	7
6	2	1.5	0.5	K_2CO_3 (4)	$ClCH_2CH_2Cl$	25	35	7	43
7	3	1.5	0.5	K_2CO_3 (6)	$ClCH_2CH_2Cl$	25	24	6	56
8	3	1.5	0.5	K_2CO_3 (3)	$ClCH_2CH_2Cl$	25	32	7	35
9	3	1.5	0.5	K_2CO_3 (0)	$ClCH_2CH_2Cl$	25	31	48	0
10	3	1.5	0.5	K_2CO_3 (9)	$ClCH_2CH_2Cl$	25	21	10	12
11	3	3	0.5	K_2CO_3 (6)	$ClCH_2CH_2Cl$	25	13	5	76
12	3	4	0.5	K_2CO_3 (6)	$ClCH_2CH_2Cl$	25	12	8	72
13	3	3	0.5	K_2CO_3 (6)	$ClCH_2CH_2Cl$, 4 Å MS	25	10	Trace	83
14	3	3	0.5	*t*-BuOK (6)	$ClCH_2CH_2Cl$, 4 Å MS	25	12	Trace	88
15	3	3	0.5	KOH (6)	$ClCH_2CH_2Cl$, 4 Å MS	25	10	Trace	35
16	3	3	0.5	Et_3N (6)	$ClCH_2CH_2Cl$, 4 Å MS	25	0	0	0
17	3	3	0.5	*t*-BuOK (6)	EtOAc, 4 Å MS	25	23	12	44
18	3	3	0.5	*t*-BuOK (6)	Toluene, 4 Å MS	25	11	Trace	78
19	3	3	0.5	*t*-BuOK (6)	THF, 4 Å MS	25	0	0	0
20	3	3	0.5	*t*-BuOK (6)	DMF, 4 Å MS	25	0	0	0
21	3	3	0.5	*t*-BuOK (6)	DMSO, 4 Å MS	25	0	0	0
22	3	3	0.5	*t*-BuOK (6)	CH_3CN, 4 Å MS	25	0	0	0
23	3	3	0.5	*t*-BuOK (6)	$ClCH_2CH_2Cl$, 4 Å MS	0	24	15	28
24	3	3	0.5	*t*-BuOK (6)	$ClCH_2CH_2Cl$, 4 Å MS	50	Trace	5	Trace[c]

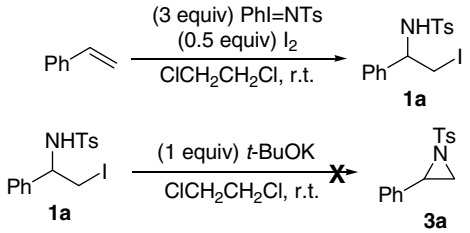
[a] All reactions were conducted in 1 mmol scale.
[b] Isolated yield based on styrene.
[c] Product **4a** was isolated in 62% yield.

experiment showed that no aziridination occurred in the absence of $PhI(OAc)_2$. When 4 Å MS was added as the additive, the yield of **3a** increased to 83% (entry 13). *t*-BuOK was also a good base for the reaction (entry 14), while a significantly lower yield was obtained with the using of KOH as the base (entry 15). When Et_3N was used, no aziridine was formed in the reaction (entry 16). No product was detected when THF, DMF, DMSO, or CH_3CN was used as solvent while the reaction could proceed in AcOEt and toluene with varied efficiency (entries 17–22). Drastic decrease in the yield of aziridine occurred when the reaction was cooled to 0 °C (entry 23), or warmed up to 50 °C (entry 24). A diamination product **4a** was isolated in 62% yield when the reaction was warmed up to 50 °C. Diamination **4a** could also be formed when the reaction was left for a longer time (48 h) at room temperature (Scheme 3). Masuyama et al. reported a diamination reaction of alkenes by using chloramine-T in the presence of tin(II) iodide at a higher temperature (50 °C).[5a]

In order to get some clues of the reaction pathway, the reaction of styrene with *N*-tosyliminophenyliodinane in the presence of iodine was carried out. No aziridine **3a** was formed, but the reaction gave byproduct **1a** in 62% yield. Byproduct **1a** was treated with *t*-BuOK, but no intramolecular cyclization was observed (Scheme 4).



Scheme 3. $PhI(OAc)_2/I_2$ induced diamination of styrene.

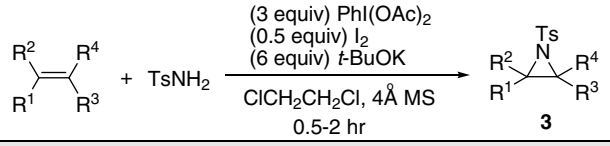


Scheme 4. Control experiments.

The scope of the $PhI(OAc)_2/I_2$ induced aziridination of alkenes was explored under the optimized conditions (Table 2).[14] These reactions proceeded smoothly and afforded the corresponding aziridines in moderate to good yields. The electronic nature of the substituents on the styrene could be either electron-donating or electron-withdrawing (entries 2–4). When *E*- and *Z*-stilbene were employed, *cis*-aziridine **3e** was isolated as the major isomer in both cases (entries 5 and 6). The reaction of *E*-1-(3-chloroprop-1-enyl)-benzene also gave a *cis*-aziridine (entry 7), but a mixture of cis and trans products was obtained in the case of *E*-cinnamyl propionate (entry 8). Indene and 1,2-dihydronaphthalene were also good substrates for the aziridination (entries 9 and 10). For the reactions of cyclic and acyclic aliphatic olefins, 1 equiv of I_2 was required to accelerate the reactions (entries 11–16).

In summary, we have developed a $PhI(OAc)_2$ and I_2 induced aziridination of alkenes with the direct use of *p*-toluenesulfonamide under mild conditions. The procedure offers good manipulability by avoiding the use of the expensive metal catalyst and the unstable and explosive PhI=NTs. The further investigation of the scope, mechanism, synthetic applications, and asymmetric reactions is ongoing and will be reported in due course.

Table 2
$PhI(OAc)_2/I_2$ induced aziridination of alkenes with *p*-toluenesulfonamide[a]



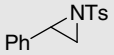
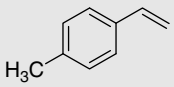
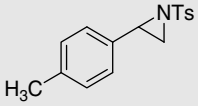
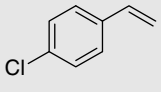
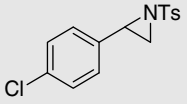
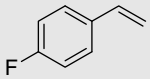
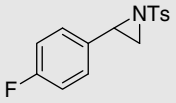
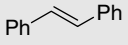
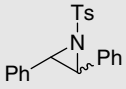
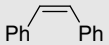
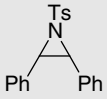
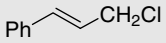
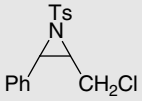
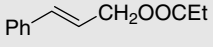
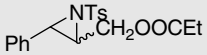
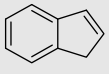
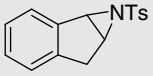
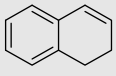
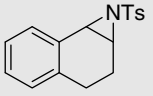
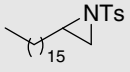
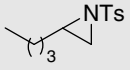
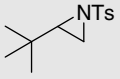
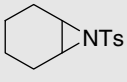
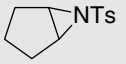
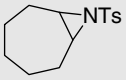
Entry	Alkene	Aziridine	**3**[b] (%)
1			**3a** (88)
2			**3b** (65)
3			**3c** (78)
4			**3d** (58)
5			**3e** (74) trans/cis = 15:85[c]
6			**3e** (88) trans/cis <5:95[c]
7			**3f** (56) trans/cis <5:95[c]
8			**3g** (75) trans/cis = 56:44[c]
9			**3h** (68)
10			**3i** (65)
11			**3j** (62)[d]
12			**3k** (58)[d]
13			**3l** (52)[d]
14			**3m** (62)[d]

Table 2 (*continued*)

Entry	Alkene	Aziridine	**3**[b] (%)
15			**3n** (48)[d]
16			**3o** (52)[d]

[a] All reactions were conducted in 1 mmol scale.
[b] Isolated yield based on styrene.
[c] The ratio determined by ^1H NMR.
[d] One equivalent of I_2 was used.

Acknowledgements

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References and notes

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14. Representative experimental procedure and spectroscopic data for **3a**: A solution of $TsNH_2$ (513 mg, 3 mmol) in anhydrous $ClCH_2CH_2Cl$ was treated with *t*-BuOK (672 mg, 6 mmol) and 4 Å MS. After 10 min, $PhI(OAc)_2$ (966 mg, 3 mmol) was added, and the resulted mixture was stirred at room temperature for 1 h. Styrene (104 mg, 1 mmol) and I_2 (127 mg, 0.5 mmol) were added. After styrene disappeared (determined by TLC, about 0.5 h), the mixture was filtered with Celite. The crude product was purified by flash column chromatography to provide the corresponding product. 2-phenyl-1-tosylaziridine **3a**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.2 Hz, 2H), 7.20–7.40 (m, 7H), 3.75 (dd, J = 7.2, 4.4 Hz, 1H), 2.90 (d, J = 7.2 Hz, 1H), 2.40 (s, 3H), 2.35 (d, J = 4.5 Hz, 1H).