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$NaIO_4$/LiBr-mediated aziridination of olefins using chloramine-T

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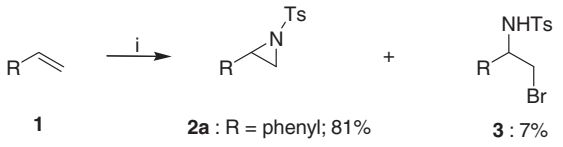
ABSTRACT

A new milder protocol for aziridination of a variety of olefins has been described. The process employs catalytic amount of sodium metaperiodate ($NaIO_4$) as an oxidant and LiBr and chloramine-T as the bromine and nitrogen sources, respectively. Interestingly, the formation of aziridine products in all the cases studied takes place presumably through a process of 1,2-aminobromination of alkenes.

Aziridines with a strained ring are of paramount importance in organic synthesis since they are valuable precursors of amino sugars, alkaloids, and substituted α-amino acids[1] or present in natural products such as mitomycins[2] and azinomycins[3] that exhibit potent biological activity. A variety of catalytic[4] as well as non-catalytic[5] routes have been established for the direct aziridination of alkenes. Recent studies mention the use of several halogenated compounds[6] in the aziridination of olefins with chloramine-T as the nitrogen source. However, these methods suffer from certain drawbacks: (i) the use of heavy transition metals as catalysts, (ii) low yields possibly due to competing C–H abstraction and insertion processes, (iii) the expense and inconvenience of PhI=NTs as a nitrene source, and (iv) formation of significant amounts of allylic amination products in the case of cyclohexene. During the course of our study on $NaIO_4$-mediated oxidative transformations of alkenes, we demonstrated the regiospecific halohydroxylation[7] and iodoazidation[8] of olefins in the presence of water or NaN_3, respectively. This prompted us to explore the possibility of employing chloramine-T[9] as the nitrogen nucleophile in the 1,2-aminobromination of alkenes mediated by $NaIO_4$–LiBr combination. In this communication, we describe a novel milder method that involves a reaction of $NaIO_4$/LiBr/H^+/chloramine-T combination with olefins; thus affording aziridines **2** in good yields (Scheme 1).

Using styrene as a test substrate, the reaction conditions were optimized to determine the optimal condition for aziridination, Table 1. When styrene was treated with $NaIO_4$, LiBr, and chloramine-T (all 1 equiv) in CH_3CN at 25 °C, the corresponding *N*-tosylaziridine (**2a**) was obtained in 20% yield; however, the yield could be significantly improved to 65% when 2 equiv of chloramine-T was used. Interestingly, lowering the molar ratio of $NaIO_4$ (30 mol %) resulted in a dramatic improvement in the yield of **2a** (81%) along with the formation of **3** as a minor product. However, further lowering of the concentration of either H_2SO_4 or LiBr had a deleterious effect on the yield (entries 4 and 7). In general, higher chloramine-T concentration (2 equiv) gave better yields. After several experimentation, it was finally found that a combination of $NaIO_4$ (30 mol %); olefin/LiBr/chloramine-T (1:1:2 equiv), and conc. H_2SO_4 (30 mol %), in CH_3CN, 25 °C, 12 h turned out to be the best reaction condition in achieving a good conversion of alkenes with excellent product selectivity. The reaction mixture became homogeneous as it proceeded. In the absence of either $NaIO_4$ or LiBr, no reaction occurred; also the reaction failed when other amine sources such as *p*-$TsNH_2$ and *p*-$TsNCl_2$ were used. A brief comparison of solvents demonstrated that CH_3CN was the most suitable



1 **2a** : R = phenyl; 81% **3** : 7%

2k : R = cyclohexyl; 58% **4** : 30%

Scheme 1. Reagents and conditions: (i) $NaIO_4$ (30 mol %); olefin/LiBr/chloramine-T = 1:1:2 (equiv), conc. H_2SO_4 (30 mol %), CH_3CN, 25 °C, 12 h.

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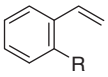
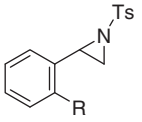
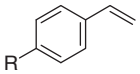
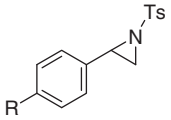
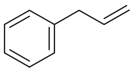
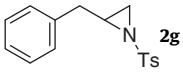
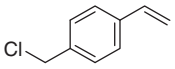
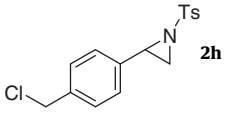
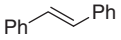
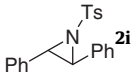
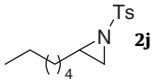
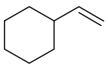
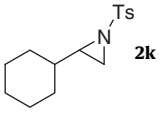
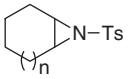
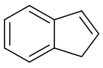
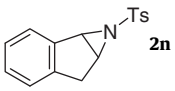
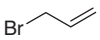
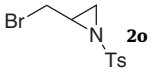
Table 1
$NaIO_4$-mediated aziridination of styrene with chloramine-T and LiBr[a]

Entry	$NaIO_4$ (equiv)	LiBr (equiv)	Chloramine-T[b] (equiv)	Conc. H_2SO_4 (mol %)	Yield **2a**[c] (%)
1	1	1	1.1	30	20
2	1	1	2	30	65
3	0.3	1	1.1	30	40
4	0.3	1	1.1	10	25
5	0.3	1	2	30	81[d]
6	0.5	1	2	30	62
7	1	0.3	2	30	35

Reaction conditions: [a]experiments were conducted with styrene (1 equiv as substrate) in dry CH_3CN as solvent; temp = 25 °C; time = 12 h; [b]anhydrous chloramine-T was used;[9] [c]isolated yield after column chromatographic purification; [d]7% of 1-phenyl-1-(*p*-toluenesulfonamido)-2-bromoethane **3** was isolated.

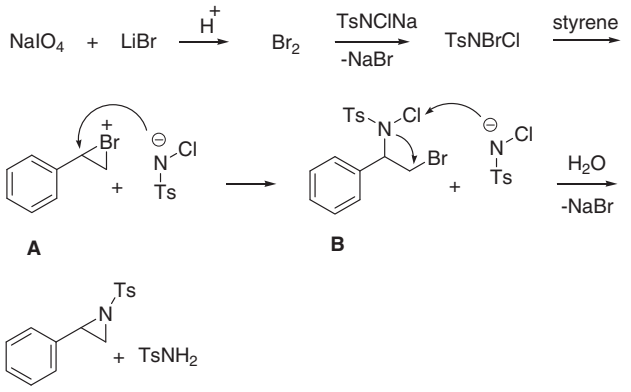
Table 2
Scope of the aziridination reaction mediated by $NaIO_4$–LiBr–chloramine-T combination[a]

Entry	Substrate (**1**)	Product[b] (**2**)	Yield[c] (%)	Mp (°C)
1				
		2a	81 (R = H)	92–94
		2b	79 (R = Cl)	Gum
2				
		2c	77 (R = Cl)	115–116
		2d	75 (R = F)	136–138
		2e	72 (R = Br)	127–129
		2f	40 ($R = CH_3$)	130–131
3		 **2g**	80	Gum
4		 **2h**	65	101–103
5		 **2i**	64	140–142
6		 **2j**	60	Gum
7		 **2k**	58[d]	94–95
8				
		2l	60 (*n* = 1)	55–57
		2m	48 (*n* = 3)	122–123
9		 **2n**	52	164–166
10		 **2o**	60	75–78

Reaction conditions: [a]alkenes (3 mmol), LiBr (3 mmol), chloramine-T (6 mmol), $NaIO_4$ (30 mol %), H_2SO_4 (30 mol %), 25 °C, 12 h; [b]products were characterized by mp, IR, ^1H and ^{13}C NMR and elemental analysis; [c]isolated yield after chromatographic purification; [d]30% of aminobrominated product (**4**) was formed.

solvent for aziridination as other solvents like CH_2Cl_2, $CHCl_3$, THF, and Et_2O were found to be ineffective.

Encouraged by these results, substrate scope of $NaIO_4$-mediated aziridination was next examined using the conditions optimized for the aziridination of styrene. As can be seen from Table 2, a wide array of aromatic, cyclic, and acyclic olefins afforded the corresponding aziridines, **2a–o** in good isolated yields.[10] With styrene derivatives, the reaction proceeded well giving aziridines **2a–i** in



Scheme 2. Plausible mechanistic pathway for $NaIO_4$-mediated aziridination.

moderate to good yields (entries 1–4). The better results however were achieved with allylbenzene (80%) and unsubstituted styrene (81%). Monosubstituted terminal olefins, one of the most challenging substrates, such as 1-octene produced a reasonably good yield (60%) of the corresponding *N*-tosyl aziridine. Allyl bromide also reacted very well (60%) under the reaction conditions without allylic amination. Notably, cyclic alkenes were also transformed to the corresponding aziridines **2l–m** in moderate yields (entry 8). In contrast, electron-deficient olefins such as α,β-unsaturated esters and ketones exhibited only low reactivity and yielded their aziridine derivatives in only 10–20% yield. No byproduct other than *p*-tosamide was detected by TLC or NMR in all the substrates examined. Although the exact nature of the species involved in the reaction is not known, our earlier studies[7] had shown that 1 equiv of $NaIO_4$ was sufficient to oxidize 8 equiv of Br^- ions, ($IO_4^- + 8H^+ + 8e^- \rightarrow 4H_2O + I^-$). Hence, only 30 mol % of $NaIO_4$ was required to bring about 100% conversions. From the above facts and the evidence provided by the cyclic voltammetry study, it is believed that Br_2, generated by the $NaIO_4$-mediated oxidation of LiBr in acidic condition, reacts with chloramine-T to give the reactive species TsNBrCl, which then subsequently adds onto styrene to form bromonium ion **A**. The stereospecific opening of **A** with $TsNCl^-$ at the benzylic position occurs to give β-bromo-*N*-chloro-*N*-toluenesulfonamide (**B**). Finally, cyclization of **B** with another molecule of chloramine-T results in the formation of aziridine, along with the generation of 1 mole of $TsNCl_2$; the hydrolysis of which leads to isolation of $TsNH_2$ as the by product (Scheme 2).

In conclusion, a mild one-pot procedure for the preparation of *N*-tosyl-2-substituted aziridines is reported. The method employs catalytic amount of $NaIO_4$ as an oxidant and LiBr and chloramine-T as the bromine and nitrogen sources, respectively. Further experiments to define the nature of the species involved in the process and the stereochemical aspects of the reaction are in progress.

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10. *General experimental procedure for aziridination of olefins*:
To a stirred solution of olefin (3 mmol) in dry CH_3CN (25 mL), anhydrous chloramine-T (1.365 g, 6 mmol), LiBr (0.257 g, 3 mmol), $NaIO_4$ (0.192 g 30 mol %), and concd H_2SO_4 (0.088 g, 30 mol %) were added at 25 °C. The resulting reaction mixture was stirred at 25 °C (monitored by TLC). After completion, the reaction mixture was diluted with EtOAc (15 mL) and washed with water followed by aq saturated $Na_2S_2O_3$ (2 × 15 mL) solution. The organic layer was dried over anhyd Na_2SO_4, concentrated under pressure to afford crude product, which was purified by column chromatography on silica gel using pet. ether and EtOAc (10:1) as eluent to afford pure aziridines **2a–o**.
N-(p-Toluenesulfonyl)-2-benzylaziridine (**2g**): Yield: 80%; gum; IR ($CHCl_3$, cm^{-1}): 675, 770, 840, 915, 1090, 1130, 1250, 1355, 1370, 1400, 1480, 2880, 2910, 2980, 3280; ^1H NMR (200 MHz, $CDCl_3$) δ 2.14 (d, J = 4.5 Hz, 1H), 2.43 (s, 3H), 2.65–2.78 (m, 3H), 2.82–2.93 (m, 1H), 7.01–7.07 (m, 2H), 7.12–7.26 (m, 5H), 7.68 (d, J = 8.4 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): 21.4, 32.5, 37.2, 40.9, 126.2, 127.7, 28.2, 128.5, 129.3, 134.4, 136.8, 143.9; Anal. Calcd for $C_{16}H_{17}NO_2S$ requires C, 66.87%; H, 5.96%; N, 4.87%. Found: C, 66.80%; H, 6.01%; N, 4.90%.
N-(p-Toluenesulfonyl)-2-bromomethylaziridine (**2o**): Yield: 60%; mp: 75–78 °C; IR ($CHCl_3$, cm^{-1}): 1093, 1119, 1292, 1328, 1403, 1597, 2926, 2981, 3029, 3132, 3150, 3175, 3200, 3277; ^1H NMR (200 MHz, $CDCl_3$) δ 2.45 (s, 3H), 3.50–3.65 (m, 1H), 3.75–3.80 (m 1H), 4.10–4.30 (m, 1H), 5.01–5.25 (m, 1H), 7.35 (d, J = 8.2 Hz, 2H), 7.85 (d, J = 8.2 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 21.3, 32.8, 47.2, 49.92, 126.9 129.7, 136.6, 143.7; Anal. Calcd for $C_{10}H_{12}BrNO_2S$ requires C, 41.39%; H, 4.17%; N, 4.83%. Found: C, 41.35%; H, 4.19%; N, 4.80%.