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N-Bromoamides as versatile catalysts for aziridination of olefins using chloramine-T

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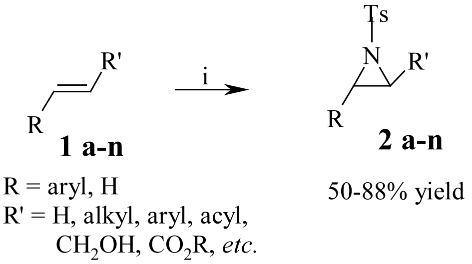
Abstract—N-Bromoamides catalyze effectively the aziridination of electron-deficient as well as electron-rich olefins using chloramine-T (N-chloro-N-sodio-p-toluenesulfonamide) as a nitrogen source under ambient conditions to afford the corresponding aziridines in good to excellent yields. © 2003 Elsevier Science Ltd. All rights reserved.

The aziridine ring is a versatile building block for organic synthesis, not only because the ring opening of aziridines provides a convenient entry to the stereoselective preparation of functionalized amino compounds but also because the exocyclic N-substituent controls the properties and reactivity of the three-membered ring. The stabilities and overall profiles of the chemical reactivities of these heterocycles are attributable not only to the combined effects of bond shortening and angle compression but also to the presence of the electron rich nitrogen atom.[1] Many biologically active compounds such as amino acids, β-lactam antibiotics and alkaloids have been derived from aziridines.[2]



1 a-n

2 a-n

R = aryl, H
R' = H, alkyl, aryl, acyl,
CH$_2$OH, CO$_2$R, *etc.*

50-88% yield

Scheme 1. *Reagents and conditions*: (i) NBS or N-bromoacetamide (20 mol%), anhydrous chloramine-T (1 equiv.), CH$_3$CN, 25°C.

The preparation of aziridines is generally achieved by non-catalytic methods.[3] Among the methods available in the literature, the direct aziridination of alkenes with nitrene precursors constitutes the most efficient and convenient method for the synthesis of aziridines.[4] However, these methods suffer from certain drawbacks such as the use of heavy transition metals as catalysts, low yields possibly due to competing C–H abstraction and insertion processes, and the expense and inconvenience of PhI=NTs as a nitrene source. It has recently been reported that halogenated compounds such as phenyltrimethylammonium tribromide,[5] iodine[6] or pyridinium bromide perbromide[7] can be employed as catalysts for aziridination of olefins using chloramine-T as the nitrogen source. However, these procedures have drawbacks such as (i) significant amounts of the allylic amination products are often produced for activated substrates such as cyclohexene; (ii) sometimes a large excess of olefin is required to obtain reasonable yields of the aziridine. In this paper, we wish to report the use of nonmetallic reagents such as N-bromoamides as the catalysts for the aziridination of a variety of olefins including α,β-unsaturated carbonyl compounds using chloramine-T as the nitrogen source (Scheme 1).

Under the reaction conditions [1 equiv. of olefin, 1 equiv. of anhydrous chloramine-T, 20 mol% of NBS (N-bromosuccinimide), MeCN, 25°C] a variety of olefins **1a–n** were successfully aziridinated under ambient conditions to afford the corresponding aziridines **2a–n** in good to excellent yields (Scheme 1). It may be noted that the aziridination of styrene was achieved in a reasonable yield (60%) even with 10 mol% of NBS

Keywords: aziridines; olefins; catalysts.

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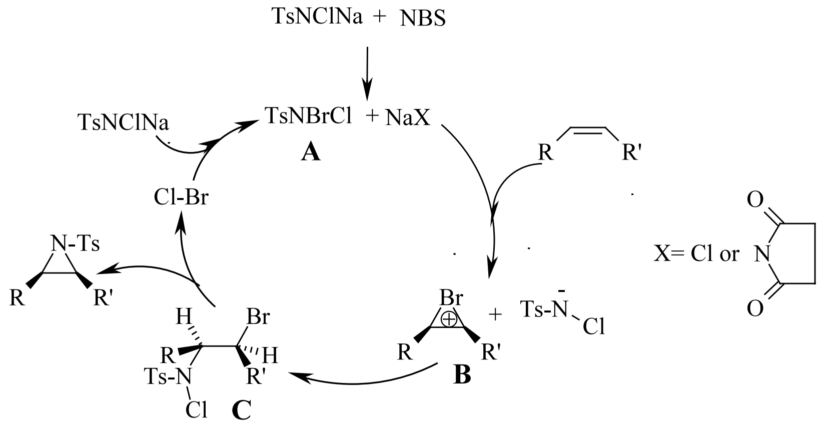

Figure 1. Proposed catalytic cycle for NBS-catalyzed aziridination of olefins.

under identical conditions. The results of the aziridinations are summarized in Table 1.†

As can be seen from Table 1, a variety of aromatic and aliphatic olefins undergo the reaction affording the corresponding aziridines in good to excellent yields. Allylic alcohols and allyl bromide also reacted very well under these reaction conditions to afford the corresponding aziridines in excellent yields. Notably, cyclohexene and cyclooctene afforded the corresponding aziridines in good yields without allylic amination. Aziridination of α,β-unsaturated carbonyl compounds is of great interest because such aziridines can act as synthons for the synthesis of biologically active compounds. It may also be noted that previously reported catalytic systems such as PTAB[5] and I_2[6] were not effective against α,β-unsaturated systems. In this respect, it is remarkable that NBS catalyzes the aziridination of α,β-unsaturated esters as well as ketones to afford efficiently the corresponding aziridines in 50–70% yields. However, methyl cinnamate and acrylamide failed to give aziridines under these conditions. Furthermore 1,2-disubstituted olefins also undergo the reaction successfully. The stereochemistry of the 1,2-disubstituted aziridines was found to be *trans* as confirmed by ^{1}H NMR spectroscopy (J=4.5 Hz). When *N*-bromoacetamide was used as the catalyst for the aziridination instead of NBS, the corresponding aziridines were obtained in only moderate yields (Table 1).

Although mechanistic aspects of the aziridination are not yet clear, we believe that NBS acts as the source for the generation of the Br^+ species. A proposed catalytic pathway is shown in Figure 1. Initially, NBS may react with the chloramine-T to give the species A, which then reacts with the olefin to afford the bromonium ion B. The bromonium ion B can then undergo stereospecific opening by the $TsNCl^-$ species to give the β-bromo-*N*-chloro-*N*-toluenesulfonamide (C). Cyclization of C would then lead to the formation of the aziridine. The reaction between chloramine-T and Br–Cl would regenerate species A, thus completing the catalytic cycle.

In conclusion, NBS is a versatile catalyst for the aziridination of olefins; in particular, it is active in catalyzing the aziridination of electron-deficient olefins, and is complementary to existing methods.

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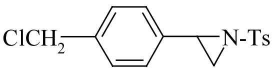
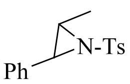
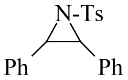
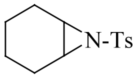
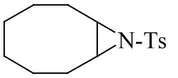
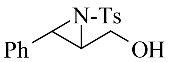
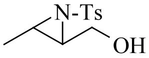
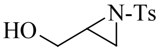
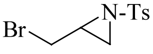
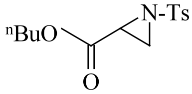
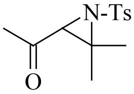
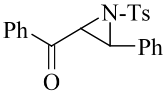
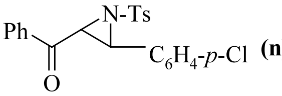
[†] **General experimental procedure**: A 25 ml RB flask was charged with olefin **1a**–**n** (1 mmol), anhydrous chloramine-T (0.228 g, 1 mmol), NBS or *N*-bromoacetamide (20 mol%) and acetonitrile (5 ml). The resulting reaction mixture was stirred at 25°C (monitored by TLC). After completion, the reaction mixture was diluted with EtOAc (15 ml) and washed with water and brine. The organic layer was dried over anhydrous Na_2SO_4, concentrated under reduced pressure to afford crude product, which was purified by column chromatography on silica gel using pet. ether and EtOAc as eluent to afford pure aziridines **2a**–**n**.
***trans*-*N*-(*p*-Tolylsulfonyl)-2-benzoyl-3-phenylaziridine (2m)**: **mp**: 143–145°C (recrystallized from $CHCl_3$); **^{1}H NMR** (200 MHz, $CDCl_3$): δ 2.39 (s, 3H), 4.29 (d, J=4.12 Hz, 1H), 4.52 (d, J=4.12 Hz, 1H), 7.22 (d, J=8.54 Hz, 2H), 7.34 (s, 5H), 7.44–7.62 (m, 3H), 7.71 (d, J=8.34 Hz, 2H), 8.06 (d, J=8.54 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 21.28, 47.08, 50.02, 127.25, 127.39, 128.39, 128.64, 129.27, 132.69, 133.83, 135.67, 136.33, 144.16, 190.07; **MS** *m*/*z* (% rel. intensity): 377 (M^+, 7), 278 (9), 222 (86), 167 (27), 105 (100), 91 (46), 77 (68), 65 (23). **Anal.**: $C_{22}H_{19}NO_3S$ requires C, 70.00; H, 5.07; N, 3.71; S, 8.50; found C, 70.12; H, 5.10; N, 3.81; S, 8.42%.
***trans*-*N*-(*p*-Tolylsulfonyl)-2-benzoyl-3-(4-chlorophenyl)aziridine (2n)**: **mp**: 150–152°C (recrystallized from pet. ether–EtOAc); **^{1}H NMR** (200 MHz, $CDCl_3$): δ 2.38 (s, 3H), 4.25 (d, J=4.11 Hz, 1H), 4.48 (d, J=4.11 Hz, 1H), 7.20–7.28 (m, 6H), 7.42–7.61 (m, 3H), 7.69 (d, J=8.44 Hz, 2H), 8.03 (d, J=8.42 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 21.50, 46.49, 50.17, 127.62, 128.87, 129.49, 131.51, 134.08, 135.00, 136.02, 137.21, 144.49, 189.99; **MS** *m*/*z* (% rel. intensity): 411 (M^+, 6), 307 (3), 278 (6), 255 (100), 227 (12), 201 (19), 165 (39), 139 (13), 105 (45), 90 (26), 77 (50). **Anal.**: $C_{22}H_{18}ClNO_3S$ requires C, 64.15; H, 4.40; Cl, 8.61; N, 3.40; S, 7.79; found C, 64.32; H, 4.32; Cl, 8.55; N, 3.41; S, 7.71%.

Table 1. NBS-catalyzed aziridination of olefins at 25°C[a]

Sr. No.	Olefin (1)	t/h	Product (2)	Yield[b,c] (%)	mp[d] (^{0}C)
1.	Styrene	8	 **(a)**	65 (55)	88-89 (88-89)
2.	4-Chloromethylstyrene	6	 **(b)**	67 (53)	100-102
3.	*trans*-*β*-Methylstyrene	6	 **(c)**	68[e]	73-75 (72-74)
4.	*cis*-Stilbene	12	 **(d)**	75 (72)	155-157 (156)
5.	Cyclohexene	10	 **(e)**	82 (75)	55-56 (56)
6.	Cyclooctene	11	 **(f)**	79	123-124 (123)
7.	Cinnamyl alcohol	14	 **(g)**	73[e]	Gum
8.	Crotyl alcohol	5	 **(h)**	88	Gum
9.	Allyl alcohol	8	 **(i)**	68	Gum
10.	Allyl bromide	3	 **(j)**	87	76-77 (77)
11.	*n*-Butyl acrylate	24	 **(k)**	51	Gum
12.	Mesitylene	8	 **(l)**	70 (66)	Gum
13.	Chalcone	28	 **(m)**	53[e] (55)	143-145
14.	4-Chlorochalcone	30	 **(n)**	50[e]	150-152

a) reaction conditions: NBS (20 mole %), Chloramine-T (1 mmol), olefin (1 equiv.), CH_3CN (5 ml), 25 ^{0}C.
b) isolated product after column chromatography.
c) yields in parentheses refer to the corresponding aziridines using *N*-bromoacetamide as catalyst.
d) Numbers in parentheses refer to mp's reported in the literature.[4c,7]
e) The *trans* isomer is formed exclusively (confirmed by *J* values in ^{1}H-NMR spectrum).

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