Efficient Ring Opening Reactions of *N*-Tosyl Aziridines with Amines and Water in Presence of Catalytic Amount of Cerium(IV) Ammonium Nitrate

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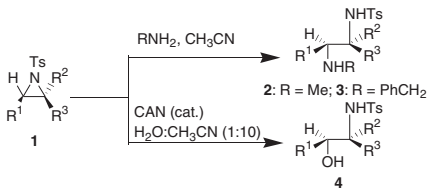
While methyl- and benzylamines opened *N*-tosyl aziridines **1** very efficiently in acetonitrile with complete regio- and stereoselectivity to give the corresponding diamines **2** and **3**, respectively, in excellent yields, similar openings with water could only be achieved in the presence of a catalytic amount of cerium(IV) ammonium nitrate under very mild conditions furnishing the amino alcohols **4**.

The importance of aziridinyl compounds as precursors of amines, diamines, amino alcohols and various other nitrogen containing products are attracting increasing attentions as organic chemists develop new methodologies for regio- and stereoselective opening of aziridine rings using various nucleophiles.[1–18] In this paper we describe efficient openings of *N*-tosyl aziridines **1** with methyl- and benzylamines in CH_3CN leading to the formation of diamines **2** and **3**. However, similar ring opening reactions with water required catalytic amounts of cerium(IV) ammonium nitrate (CAN)[19–21] that provided amino alcohols **4** in good yields under very mild conditions.

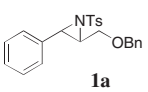
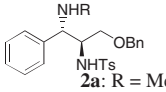
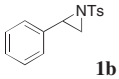
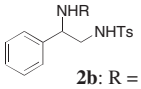
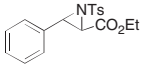
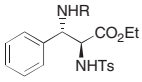
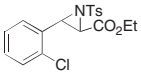
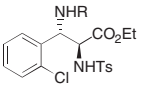
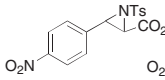
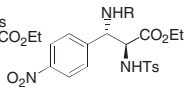
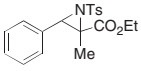
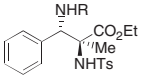


The starting aziridines **1a–f** were prepared from the corresponding epoxides in four steps: (a) ring opening of the epoxides with NaN_3 in MeOH : H_2O (8 : 1) in presence of NH_4Cl;[22] (b) reduction of the resulting azides to amines using Ph_3P in dry THF; (c) protection of the amines as tosylates using TsCl, Et_3N in CH_2Cl_2 and (d) treatment of *N*-tosyl amino alcohols with diethyl azodicarboxylate and Ph_3P in dry THF. The remaining aziridines **1g** and **1h** were made by reacting the respective olefins with chloramine-T and I_2 (cat.) in CH_3CN. The aziridines, thus prepared, were treated with $MeNH_2$·HCl or benzylamine, with equimolar amounts of Et_3N for the former, at 0 °C in dry CH_3CN under N_2 atmosphere. Reactions were continued at room temperature until the starting materials completely disappeared. Aqueous work-up was followed by chromatographic purification to furnish the diamines in excellent yields. Reactions with benzylamine were faster compared to those with methylamine. The results are summarized in Table 1.

Only one regioisomer was obtained in aryl-substituted aziridines when the reactions were carried out at room temperature and the ring openings occurred exclusively at the benzylic positions. The *N*-tosyl aziridine of styrene (**1b**, entry 2, Table 1) did not undergo any reaction when treated with $BnNH_2$ at room temperature even after long reaction hours. When the temperature was raised to 45 °C, two regioisomers were obtained in 4 : 1 ratio, the major one being formed by opening of the ring at the benzylic position. The selectivity was completely lost at refluxing temperature.

The trisubstituted aziridine **1f** did not undergo any reaction

Table 1. Opening of *N*-tosyl aziridines (**1**) with amines RNH_2 in CH_3CN

Entry	Starting Aziridines	Product Diamines	Reaction conditions[a] [Time (h); Yield (%)]
1.	 **1a**	 **2a**: R = Me **3a**: R = Bn	A [10; 82] B [4; 98]
2.	 **1b**	 **2b**: R = Me **3b**: R = Bn	A [12; 81] B [12; no reaction]
3.	 **1c**	 **2c**: R = Me **3c**: R = Bn	A [12; 84] B [3; 73]
4.	 **1d**	 **2d**: R = Me **3d**: R = Bn	A [8; 90] B [5; 92]
5.	 **1e**	 **2e**: R = Me **3e**: R = Bn	A [10; 78] B [4; 92]
6.	 **1f**	 **2f**: R = Me **3f**: R = Bn	A [12; no reaction] B [8;[b] 70]
7.	 **1g**	 **2g**: R = Me **3g**: R = Bn	A [12, no reaction] B [7; 87]
8.	 **1h**	 **2h**: R = Me **3h**: R = Bn	A [12, no reaction] B [3;[c] 92]

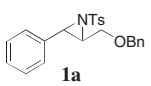
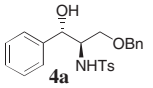
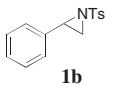
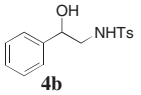
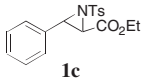
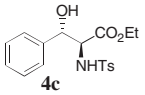
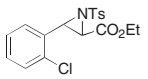
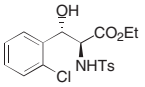
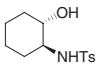
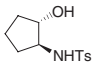
[a] A: $MeNH_2$·HCl (10 eq), Et_3N (10 eq), CH_3CN, 0 °C to rt; B: $PhCH_2NH_2$ (10 eq), CH_3CN, 0 °C to rt. [b] reaction went to completion only under refluxing condition. [c] reaction was carried out at 55 °C.

with methylamine. However, with benzylamine, the opening could be achieved only under refluxing condition to give the expected diamine **3f**. No double ring opening was observed in any of these reactions.[5] The aziridines with aliphatic substituents **1g** and **1h** did not undergo any reaction with $MeNH_2$.

The structural assignments were made on the basis of ^1H NMR studies and decoupling experiments. The diamine **2a**, for example, showed connectivity among the C*H*$_2$OBn, C*H*(CH$_2$OBn) and N*H*Ts protons determined by irradiating the C*H*(CH$_2$OBn) signal that caused decoupling of the protons attached to it. This was further supported by two-dimensional double quantum filtered correlation spectroscopy (DQF COSY) experiment.[23] The structures of other diamines were similarly assigned.

Next, six of these aziridines **1a**–**d**, **1g**, and **1h** were taken in water–CH_3CN (1 : 10), cooled to 0 °C and treated with catalytic amounts of CAN (0.1–0.2 eq). This led to facile opening of the aziridine rings with hydroxyl group to furnish the amino alcohols **4a**–**d**, **4g**, and **4h** in good yields. The results are summarized in Table 2. Here, once again, only one regioisomer was obtained in aryl-substituted aziridines. The structural assignments were made in the same way as they were done for the diamines. Both ^1H NMR decouplings and DQF COSY experiments were utilized to prove the observed regioselectivities.

Table 2. Opening of *N*-tosyl aziridines (**1**) with water using catalytic amount of CAN[a]

Entry	Starting Aziridines	Product Amino alcohols	Time (h); Yield (%)
1.	 **1a**	 **4a**	2.5; 82
2.	 **1b**	 **4b**	2; 85
3.	 **1c**	 **4c**	8; 75
4.	 **1d**	 **4d**	5 (50 °C); 72
5.	 **1g**	 **4g**	7;[b] 88
6.	 **1h**	 **4h**	7;[b] 61

[a] CAN (0.1 eq), H_2O:CH_3CN (1:10), 0 °C to rt (50 °C in entry 4). [b] 0.2 eq CAN was used.

The ring openings with amines and water occurred presumably via S_N2 mechanism and the stereochemistries were assigned accordingly. This was further confirmed by converting the amino alcohols to their corresponding oxazolidinone derivatives on treatment with 1,1′-carbonyldiimidazole. The ^3J couplings of 8–10 Hz between the C4-*H* and C5-*H* of these five membered rings (9 Hz, for example, for the oxazolidinone from **4c**) confirmed the *cis* orientations of the ring protons[24] and that, in turn, supported the assigned stereochemistries of the products.

In conclusion, the methods described here for efficient ring openings of *N*-tosyl aziridines with amines and particularly, the CAN-catalyzed openings with water under very mild conditions will find useful applications in the synthesis of various diamines and amino alcohols. Further work is under progress.

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