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Microwave-induced clay-catalyzed ring opening of *N*-tosylaziridines: a green approach to achiral and chiral diamines

Upender K. Nadir* and Anamika Singh

Department of Chemistry, Indian Institute of Technology, Delhi, Hauz Khas, New Delhi 110016, India

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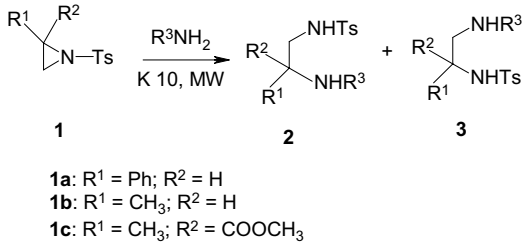
Abstract—*N*-Tosylaziridines react efficiently with amines in the presence of Montmorillonite K-10 as catalyst under microwave irradiation in solvent-free conditions to yield the corresponding achiral and chiral diamines regio- and stereoselectively, in a few minutes and in high yields.

Aziridines are useful intermediates in organic synthesis.[1–3] *N*-Arylsulfonylaziridines, in particular, have recently attracted considerable attention due to their susceptibility towards highly regio- and stereoselective nucleophilic ring opening[2a] and ring expansion reactions. The nucleophilic ring opening of aziridines has been used to prepare biologically active compounds such as amino acids,[2b,4] heterocycles[5] and alkaloids.[6] With nitrogen nucleophiles such as amines, aziridines yield vicinal diamines,[7] which are components of many biologically and medicinally important compounds.[8,9] A recent review describes ring opening reactions of aziridines with various nucleophiles.[10] Our interest in the synthesis[11] and useful transformations[12–15] of *N*-tosylaziridines led us to study their reactions with amines. We report, here, a facile, regioselective and high yielding ring opening of *N*-tosylaziridines with amines leading to mono-*N*-tosyl 1,2-diamines (Scheme 1).



Scheme 1. Regiochemistry of ring-opening of *N*-tosylaziridines with amines.

The demand for increasingly clean and efficient chemical synthesis is important from both economic and environmental points of view.[16] One commonly used method is the combination of microwave irradiation[17,18] and a solid support[19] like Montmorillonite K-10. This offers a number of advantages (a) solvents, which are often expensive, toxic and difficult to remove in the case of aprotic solvents with high boiling points, are avoided; (b) liquid extraction for isolation of products is not required; (c) reaction times are shortened; (d) yields are increased; (e) reactions are cleaner. When these solvent-free green conditions were used to carry out reactions of *N*-tosylaziridines with various amines, diamines were obtained in high yields (Table 1).

The reaction times were short (3–5 min) and the products were cleanly separated by extraction from the clay with minimal use of solvents. The aziridine opening reaction was also smooth with disubstituted substrates (**1c–e**) (Schemes 1 and 2). By conventional methods, the reaction of aziridines with amines takes several hours. Moreover, the regio- and stereoselectivity is variable, with or without a Lewis acid, particularly with aliphatic amines like benzyl and alkylamines.[20] The starting aziridines **1a** and **1f** were synthesized by a known three-step procedure;[21] **1c** was prepared using

Keywords: Microwave; Aziridines; Diamines; Clay.
* Corresponding author. Tel.: +91 11 26591518; fax: +91 11 26582037; e-mail: ukn@netearth.iitd.ac.in

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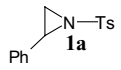
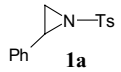
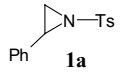
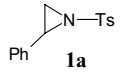
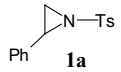
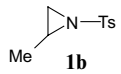
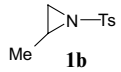
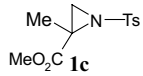
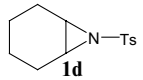
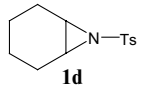
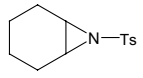
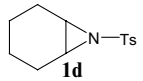
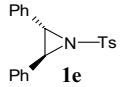
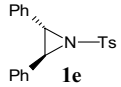
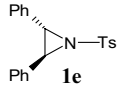
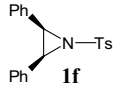
Table 1. Microwave-induced clay-catalyzed aziridine opening with amines under solvent-free conditions

Aziridines	Amines	Product(s) (ratio of **2**:**3**)[a]	Yield[b] (%) (time, min)
 **1a**	$C_6H_5NH_2$	**2a**	98 (3)
 **1a**	4-$MeC_6H_4NH_2$	**2b**	95 (5)
 **1a**	4-$MeOC_6H_4NH_2$	**2c**	94 (5)
 **1a**	$PhCH_2NH_2$	**2d**:**3d** (90:10)	92 (5)
 **1a**	*n*-$BuNH_2$[c]	**2e**:**3e** (56:44)	91 (3)
 **1b**	$C_6H_5NH_2$	**3f**	97 (3)
 **1b**	$PhCH_2NH_2$	**2g**:**3g** (10:90)	93 (5)
 **1c**	$C_6H_5NH_2$	**2h**	85 (3)
 **1d**	$C_6H_5NH_2$	**4a**	94 (3)
 **1d**	4-$MeC_6H_4NH_2$	**4b**	89 (5)
 **1d**	4$MeOC_6H_4NH_2$	**4c**	84 (5)
 **1d**	$PhCH_2NH_2$	**4d**	82 (5)
 **1e**	$C_6H_5NH_2$	**5a**	87 (5)
 **1e**	*n*-$BuNH_2$	**5b**	82 (5)
 **1e**	$PhCH_2NH_2$	**5c**	84 (5)
 **1f**	$C_6H_5NH_2$	No reaction	—

[a] Ratio of isomers were determined by ^1H NMR of the crude products.
[b] Isolated, unoptimized yields.
[c] 3 equiv *n*-$BuNH_2$ was used.

dichloramine-T as nitrogen source and $Cu(acac)_2$ as catalyst;[11] **1d** and **1e** were accessed by the Sharpless and co-workers method.[22]

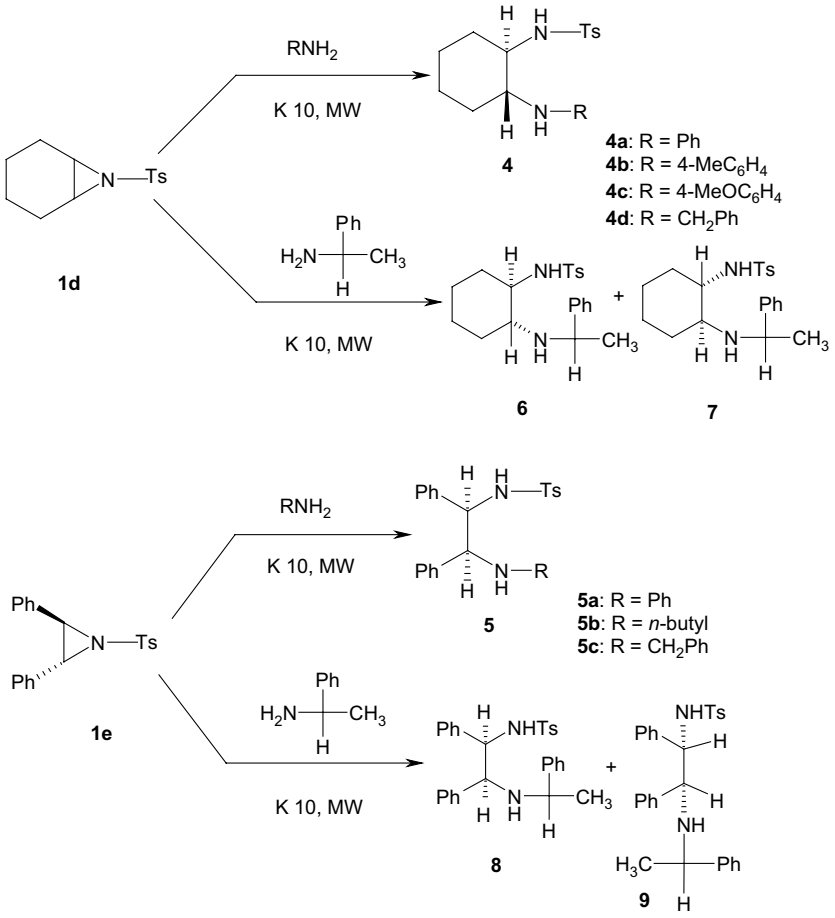
With arylamines (R^3 = aryl) the reaction was completely regiospecific and only one regioisomer **2** with **1a** and **3** with **1b** was obtained (Scheme 1). Benzylamines afforded a mixture of **2** and **3** (90:10) and *n*-butylamine led to a 56:44 mixture of **2** and **3**. Disubstituted aziridine **1e** gave **5b** with *n*-butylamine and **5c** with benzylamine. All the reactions proceeded in excellent overall yield. The regiochemical course of these reactions is in accord with our previous observations[13] that the nucleophile attacks at the more electrophilic centre, which, for aryl-substituted aziridines, is the substituted carbon, whereas for alkyl-substituted aziridines this is the unsubstituted carbon. In the case of aziridine **1c**, nucleophilic attack takes place at the substituted carbon (Scheme 1).

The reaction is completely stereoselective and only the *trans* product from **1d** and the *erythro* diastereomer **5a** from **1e** were produced (Scheme 2). All the products were either known or had the expected spectroscopic properties. The products from aziridine **1e** (**5a**–**c**) were presumed to be the *erythro* diastereomers, based on the fact that **1d** gave the *trans* isomer and from our general observations[23] on the reactions of nucleophiles with *N*-tosylaziridines. The lack of reactivity of aziridine **1f**, is also in accord with our previous observations.[23] To our knowledge, there has been no report on microwave-induced clay-catalyzed ring opening of *N*-tosylaziridines with amines.

Attempts to carry out these reactions in the absence of Montmorillonite K-10 did not yield the products indicating that the clay is acting as a catalyst. When the reactions were carried out at room temperature in the presence of a solvent and clay, the products were formed very slowly, showing that microwave irradiation has a major role to play in these reactions. It was found that the clay employed was reusable. Thus in the reaction of **1a** with aniline, in three successive runs, the yield of the product **2a** was 98%, 96% and 95%, respectively.

The reaction could also be extended to synthesize chiral diamines by treating racemic aziridines **1d** and **1e** with optically active α-methylbenzylamine to give a diastereomeric mixture (50:50) of the corresponding diamines (Scheme 2). Diastereomers **6** and **7** were separated by column chromatography whereas **8** and **9** could be separated by recrystallization.

In conclusion, this letter describes an efficient, easy, eco-friendly method for highly regio- and stereoselective preparation of vicinal mono-*N*-tosyl diamines from *N*-tosylaziridines using a solid support under microwave irradiation. The attractive features of this procedure are that it is quite general, proceeds rapidly, uses no toxic and/or expensive solvents, uses mild reaction conditions and the catalyst can be reused several times without significant loss of activity. All these factors combine to make it a 'Green' synthesis.



Scheme 2. Synthesis of achiral and chiral diamines.

Acknowledgements

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