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An efficient method for the cleavage of aziridines using hydroxyl compounds

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Abstract

A variety of *N*-activated aziridines were opened with water, primary, allylic, and propargyl alcohols at rt in high yield using a catalytic amount of $Sn(OTf)_2$ or $BF_3{\cdot}OEt_2$.

The Lewis acid-induced ring-opening of *N*-substituted aziridines with several nucleophiles such as $TMSN_3$, TMSCN, and amines has been very well studied,[1–5] but aziridine ring-opening with hydroxyl compounds, to the best of our knowledge, is unknown. In this communication, we report our efforts in this direction where aziridines were cleaved with primary, allylic, and propargyl alcohols at rt in the presence of a catalytic amount of $Sn(OTf)_2$ or $BF_3{\cdot}OEt_2$. We further report that the cleavage is also effected with water.

While working on the $Sn(OTf)_2$-induced cleavage reaction of *N*-tosyl aziridines with TMSCN in MeOH as solvent, we discovered that the products were β-amino ethers resulting from an opening of the aziridines with MeOH. The role of TMSCN in these reactions was ruled out as they also proceeded in its absence. So, in a typical procedure, a solution of *N*-tosyl aziridine (1 mmol) and $Sn(OTf)_2$ (10 mol%) in MeOH (1 mL) was stirred at rt for 1 h. The excess MeOH was removed and the crude product was chromatographed over silica gel to provide pure β-amino ether[6] in 99% yield (Table 1, entry 1). The *trans* stereochemistry of the product (entry 1) was deduced from the coupling constants ($J=9$, 9 and 3.9 Hz) of the peak at δ 2.86 (C*H*–OMe) in its ^1H NMR spectrum. We carried out this ring-opening reaction with MeOH in the presence of other Lewis acids such as $CuCl_2$ (24 h, 6% yield), $SnCl_2$ (24 h, 8% yield), $FeCl_3$ (24 h, 32% yield), $LiClO_4$ (24 h, 10% yield), $Cu(OTf)_2$ (24 h, 3% yield), and $AlCl_3$ (12 h, 35%), but very poor yields of the product were obtained as indicated. Some other Lewis acids such as ZnI_2, $ZnCl_2$, and $CoCl_2$ failed to give any product (12 h, rt). However, the reaction was very efficient with $BF_3{\cdot}OEt_2$ (entry 1). Since both $Sn(OTf)_2$ and $BF_3{\cdot}OEt_2$ turned out to be highly effective for the aziridine opening with MeOH, the reaction was extended to the use of several other hydroxyl compounds.

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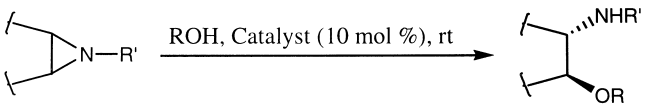
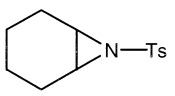
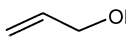
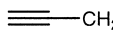
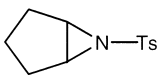
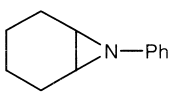
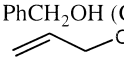
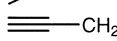
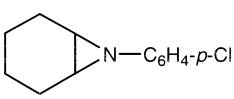
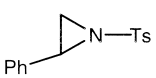
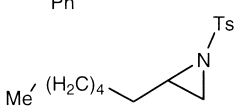
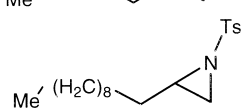
Table 1
Cleavage of aziridines with hydroxyl compounds in the presence of a catalytic amount of $Sn(OTf)_2$ and $BF_3{\cdot}OEt_2$[a]



Entry	Aziridine	ROH	$Sn(OTf)_2$		$BF_3.OEt_2$	
			Time	Yield (%)	Time	Yield (%)
1.		MeOH	1 h	99	20 min	99
2.		EtOH	30 h	99	3 h	99
3.			1 h	99	1 h	92
4.			30 min	99	30 min	98
5.		$PhCH_2OH$ (CH_2Cl_2)	20 h	90	2 h	94
6.		H_2O (MeCN)	15 h	89	5 h	90
7.		MeOH	5 h	99	2 h	99
8.		EtOH	65 h	98	9 h	99
9.		MeOH	10 min	76	10 min	92
10.		EtOH	10 min	68	10 min	94
11.		n-PrOH	15 min	65	15 min	90
12.		$PhCH_2OH$ (CH_2Cl_2)	24 h	66	2 h	86
13.			15 min	86	5 min	91
14.			15 min	85	5 min	93
15.		H_2O (THF)	20 min	92	20 min	90
16.		MeOH	10 min	99	10 min	99
17.		EtOH	10 min	99	10 min	99
18.		MeOH	30 min	98[b]	15 min	99[b]
19.		EtOH	30 min	94[b]	15 min	99[b]
20.		MeOH	8 h	96[c]	2.5 h	97[c]
21.		EtOH	24 h	92[d]	14 h	98[d]
22.		MeOH	30 h	76[e]	4 h	96[e]
23.		EtOH	96 h	74[f]	20 h	96[f]

[a]The reaction was carried out using ROH as solvent except for entries 5, 6, 12, and 15 where 1.5 equiv. of ROH was used in the solvent shown in parenthesis. [b]HPLC and NMR indicated only single product formed by internal attack. [c]Ratio of products from terminal attack *vs* internal attack is 60:40 {$Sn(OTf)_2$} and 58:42 (BF_3). [d]Ratio of products from terminal attack *vs* internal attack is 61:39. [e]Ratio of products from terminal attack *vs* internal attack is 58:42 {$Sn(OTf)_2$} and 63:37 (BF_3). [f]Ratio of products from terminal attack *vs* internal attack is 63:37 {$Sn(OTf)_2$} and 58:42 (BF_3).

Ring-opening of the *N*-tosyl aziridine with EtOH took longer, but a quantitative yield of the product was obtained (entry 2). The results of the above reaction with allylic and propargyl alcohols were similar (entries 3 and 4). Ring-openings of the aziridine with benzyl alcohol and water were carried out in CH_2Cl_2 and MeCN and the products were obtained in high yields (entries 5 and 6). The reaction was then extended to a variety of aziridines with a variety of alcohols and the results are summarized in Table 1. In the case of the phenyl-substituted *N*-tosylaziridine (entries 18 and 19), only a single product was obtained due to internal attack of the alcohols (as confirmed by ^{1}H NMR and HPLC). Terminal attack was favoured in the case of the alkyl-substituted acyclic *N*-tosylaziridines, although the regioselectivity was not good (entries 20–23).[7] The aziridine ring-opening reaction with hydroxyl compounds was much faster with $BF_3{\cdot}OEt_2$ in comparison with $Sn(OTf)_2$. The main drawback of this method is that *secondary* and *tertiary* alcohols failed to open aziridines under the above conditions. It was also observed that *N*-alkyl substituted azirdines could not be opened with any of the Lewis acids.

Acknowledgements

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3. For opening of aziridine with TMSCN in the presence of lanthanoid tricyanides, see: (a) Matsubara, S.; Kodama, T.; Utimoto, K. *Tetrahedron Lett.* **1990**, *31*, 6379. (b) Osborn, H. M. I.; Sweeney, J. B. *Synlett* **1994**, 145.
4. For opening of aziridines with amines in the presence of Lewis acids, see: (a) Sekar, G.; Singh, V. K. *J. Org. Chem.* **1999**, *64*, 2537. (b) Meguro, M.; Asao, N.; Yamamoto, Y. *Tetrahedron Lett.* **1994**, *35*, 7395. (c). Meguro, M.; Yamamoto, Y. *Heterocycles* **1996**, *43*, 2473.
5. For rearrangement of acylaziridines to oxazolines using orthogonal Lewis acids, see: Ferraris, D.; Drury III, W. J.; Cox, C.; Lectka, T. *J. Org. Chem.* **1998**, *63*, 4568.
6. The amino ether (entry 1) was characterized as follows: white solid, mp 60–62°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.09 (m, 4H), 1.52 (m, 1H), 1.61 (m, 1H), 1.96 (m, 1H), 2.12 (m, 1H), 2.35 (s, 3 H), 2.78 (ddd, J = 9.5, 9.3, 3.4 Hz, 1H), 2.86 (ddd, J = 9, 9, 3.9 Hz, 1H), 3.12 (s, 3H), 5.03 (s, 1H), 7.22 (d, J = 8.3 Hz, 2H), 7.69 (d, J = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 23.4, 23.6, 28.6, 31.0, 55.8, 57.0, 81.3, 127.2, 129.5, 137.3, 143.0; mass (EI, m/z): 283 (M^+).
7. Ratios of the regioisomers were determined by HPLC and ^{1}H NMR spectra.