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Montmorillonite clay catalyzed cleavage of aziridines with alcohols

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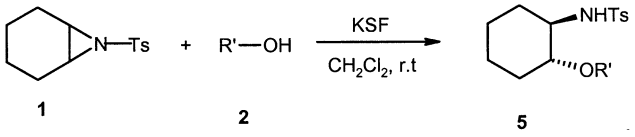
Abstract—A variety of *N*-tosyl aziridines react smoothly with alcohols in the presence of montmorillonite KSF or Amberlyst-15 at ambient temperature to afford the corresponding β-amino ethers in excellent yields with high selectivity. © 2002 Elsevier Science Ltd. All rights reserved.

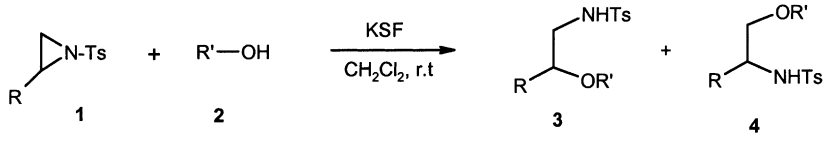
Aziridines are versatile building blocks for the synthesis of many biologically interesting molecules such as amino acids,[1] heterocycles[2] and alkaloids.[3] They are well known carbon electrophiles capable of reacting with various nucleophiles and their ability to undergo regioselective ring opening reactions contributes to their synthetic value.[4] As a result, several methods have been reported for the regioselective ring opening of aziridines with various nucleophiles such as organometallic reagents,[5] silyl nucleophiles,[6] Wittig reagents,[7] amines,[8] halides,[9] and alkenes[10] to generate ring-opened products, but procedures for their opening with alcohols are scarce.[11] Moreover, no attempt has been made to recycle the catalyst in order to make the process more economic and eco-friendly. In recent years, the use of solid acidic catalysts such as clays, ion-exchange resins and zeolites has received considerable attention in different areas of organic synthesis[12] because of their simplicity in operation, environmental compatibility, reusability, greater selectivity, non-corrosiveness and ready availability at low cost. Particularly, clay catalysts make the reaction processes convenient, more economic, environmentally benign and act as both Bronsted and Lewis acids in their natural and ion-exchanged forms, enabling them to function as efficient catalysts for various transformations.[13]

In this paper, we wish to describe our results on the regioselective ring opening of aziridines with alcohols using the reusable solid acid, montmorillonite clay. Thus, treatment of styrene *N*-tosyl aziridine with allyl alcohol in the presence of montmorillonite KSF clay at ambient temperature gave the corresponding β-amino ether in 90% yield (Scheme 1; R = Ph; R′ = allyl).

In general, treatment of aryl-*N*-tosylaziridines with alcohols gave predominantly the ring-opened product **3** with preferential attack at the benzylic position together with a trace amount of **4**. However, alkyl-*N*-tosyl aziridines gave predominantly the ring-opened product **4** resulting from terminal attack with only a minor amount of **3** due to internal attack of the alco-



Scheme 2.



R= aryl, hexyl; R' = allyl, benzyl, propargyl,alkyl

Scheme 1.

Keywords: solid acids; aziridines; alcohols; β-amino ethers.

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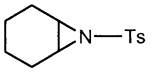
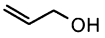
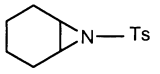
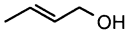
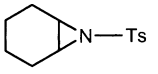
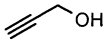
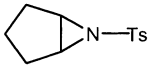
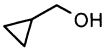
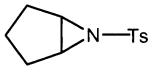
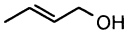
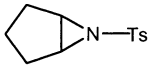
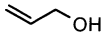
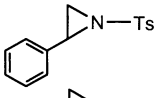
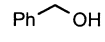
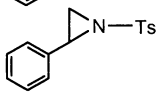
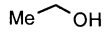
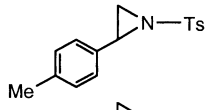
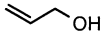
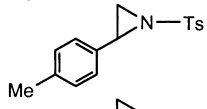
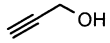
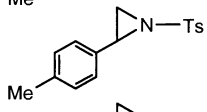
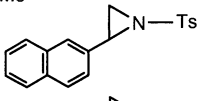
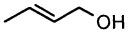
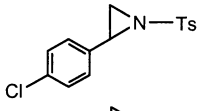
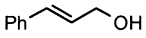
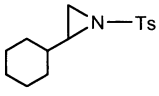
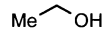
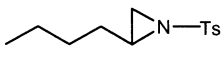
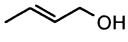
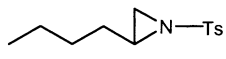
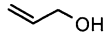
hols, as has been observed by others in most aziridine ring opening reactions. A variety of alcohols reacted to give the respective β-aryl ethers in high yields. The ratios of the products **3** and **4** were determined from the ^{1}H NMR spectra of the crude products. In all cases, the reactions proceeded efficiently in high yields at ambient temperature. Furthermore, the reaction of cycloalkyl-*N*-tosyl aziridines with alcohols afforded the corresponding β-aminoethers **5** in high yields (Scheme 2).

Table 1. KSF clay catalyzed ring opening of aziridines with alcohols[14]

Entry	Aziridine	Alcohol	Reaction time (h)	Yield[a] (%)	Ratio[b] **3:4**
a			5.0	89	--
b			4.5	85	--
c			6.5	90	--
d			7.0	81	--
e			5.5	83	--
f			6.0	85	--
g			4.0	87	92:8
h			3.5	90	96:4
i			3.0	88	97:3
j			3.5	90	95:5
k			4.0	89	92:8
l			5.0	87	94:6
m			5.5	83	95:5
n			6.0	81	7:93
o			7.5	90	10:90
p			8.5	87	12:88

[a]Isolated and unoptimized yields.

[b]Ratio of products from internal attack *vs* terminal attack.

In the case of cycloalkyl aziridines, the stereochemistry of the ring product **5a** was found to be *trans* from the coupling constants of the ring protons at δ 2.85 ppm (ddd, $J=3.5$, 9.5, 9.5 Hz, 1H) for (CHN) and the signal at δ 3.05 ppm for (CHOR) showed a similar kind of splitting pattern (ddd, $J=4.0$, 9.5, and 9.5 Hz, 1H) in its ^{1}H NMR spectrum. The method is clean and highly regioselective, affording β-amino ethers in excellent yields. The reaction conditions are mild and no side or decomposition products are observed. All the products were fully characterized by ^{1}H, ^{13}C NMR, IR and mass spectroscopic data. Several examples illustrating this simple and practical method for the synthesis of β-aminoethers are summarized in Table 1. Similar yields and selectivity were also obtained with Amberlyst-15 under the present reaction conditions. However, in the absence of catalyst, the reaction did not yield any product even under reflux. Finally, the clay was recovered by filtration, washed with methanol and recycled in subsequent reactions (after activation at 120°C for 4–5 h) with only a gradual decrease in activity; for example, styrene-*N*-tosyl aziridine and propargyl alcohol gave 92, 87 and 82% yields, respectively, over three cycles. These results clearly show the advantage of this method over Lewis acid catalyzed procedures.

In conclusion, this paper describes a simple and efficient method for the preparation of β-amino ethers from *N*-tosyl aziridines using solid acid catalysis. The notable features of this method are mild reaction conditions, selectivity, simplicity in operation and low cost and reusability of the catalyst, which makes it a simple, economic and environmentally benign process.

Acknowledgements

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14. *Experimental procedure*: A mixture of *N*-tosyl aziridine (5 mmol), the alcohol (7 mmol) and montmorillonite KSF (1.5 g Aldrich Co) or Amberlyst-15 (1.5 g) in dichloromethane (10 mL) was stirred at ambient temperature for the appropriate time (see Table 1). After completion of the reaction, as indicated by TLC, the reaction mixture was filtered and washed with dichloromethane (10 mL). The combined organic layers were concentrated in vacuo and the resulting product was purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane, 1:9) to afford the pure β-amino ether. Spectral data for selected products:
5a: **2-Allyloxy-1-(4-methylphenylsulfonamido)cyclohexane**: Liquid, ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.5–1.30 (m, 4H), 1.45–1.65 (m, 2H), 1.85–1.95 (m, 1H), 2.05–2.10 (m, 1H), 2.40 (s, 3H), 2.85 (ddd, 1H, $J=3.5$, 9.5, 9.5 Hz), 3.05 (ddd, 1H, $J=4.0$, 9.5, 9.5 Hz), 3.75 (dd, 1H, $J=6.5$, 10.3 Hz), 3.90 (dd, 1H, $J=7.0$, 10.5 Hz), 5.05 (m, 2H), 5.25 (brs, 1H, NH), 5.65–5.80 (m, 1H), 7.20 (d, 2H, $J=8.0$ Hz), 7.68 (d, 2H, $J=8.0$ Hz); EIMS: m/z: 309 [M$^+$]. IR (KBr) ν: 3340, 2928, 2850, 1580, 1150, 1080, 833 cm^{-1}.
3h: ***N*-(2-Ethoxy-2-phenylethyl)-4-methyl-1-benzene sulfonamide**: Liquid, ^{1}H NMR (200 MHz, $CDCl_3$): δ 1. 08 (t, 3H, $J=6.8$ Hz), 2.40 (s, 3H), 2.85 (ddd, 1H, $J=2.9$, 9.5, 11.8 Hz), 3.18 (ddd, 1H, $J=3.7$, 9.5, 11.8 Hz), 3.25 (m, 1H), 3.28 (m, 1H), 4.30 (dd, 1H, $J=3.7$, 9.5 Hz), 4. 98 (brs, NH, 1H), 7.20 (d, 2H, $J=8.0$ Hz), 7.25–7.38 (m, 5H), 7.68 (d, 2H, $J=8.0$ Hz). EIMS: m/z: 319 [M$^+$]. IR (KBr) ν: 3340, 2928, 2850, 1580, 1150, 1080, 833 cm^{-1}.