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ScienceDirect
Journal of Molecular Catalysis A: Chemical 270 (2007) 89–92
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
www.elsevier.com/locate/molcata

Highly regio- and stereoselective ring-opening of epoxides and aziridines with sodium azide using ammonium-12-molybdophosphate☆

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Received 6 December 2006; accepted 22 January 2007
Available online 26 January 2007

Abstract

Epoxides and aziridines undergo ring-opening readily with NaN_3 in the presence of ammonium-12-molybdophosphate to afford the corresponding 2-azidoalcohols and 2-azidoamines in high yields with good regio- and stereoselectivity under mild reaction conditions.

Keywords: Epoxide; Aziridine; 2-Azidoalcohol; 2-Azidoamine; Ammonium-12-molybdophosphate; Regioselectivity

Epoxides [1] and aziridines [2] are the most useful synthetic intermediates in organic synthesis. Because of their ring strain and high reactivity, their reactions with various nucleophiles lead to high regio- and stereoselective ring-opening products [3,4]. Among these, the azidolysis of epoxides and aziridines are the most important for preparation of azidoalcohols [5] and azidoamines [6]. The vicinal azidoalcohols are precursors of aminoalcohols [7] which are well known as β-blockers and present in various natural products and different bioactive compounds [8]. They are also useful for the synthesis of amino sugars and carbocyclic nucleosides [9]. 1,2-Azidoamines are precursors of vicinal diamines which have various applications in organic synthesis [10]. A valuable synthetic route to 2-azidoalcohols and 2-azidoamines consists of ring-opening of epoxides and aziridines, respectively, with azide ion.

The conventional method for the preparation of azidohydrins employing NaN_3 and NH_4Cl requires a longer reaction time (12–48 h) and generates side products [8]. The recent methods for azidolysis of epoxides [11] and aziridines [11f,12] utilize a combination of NaN_3 or $TMSN_3$ in the presence of a Lewis acid or a transition metal complex. Although these methods are useful for the synthesis of 2-azidoalcohols and 2-azidoamines many of them suffer from different disadvantages, such as high temperature longer reaction times, unsatisfactory yields and poor regioselectivity. Thus, an improved protocol for the preparation of these azido compounds is highly desirable.

In continuation of our work [13] on the development of useful synthetic methodologies, we have recently observed that ammonium-12-molybdophosphate (AMP) $(NH_4)_3[PMo_{12}O_{40}]$ [14] can efficiently be applied for cleavage of epoxides and aziridines with NaN_3 to form the corresponding 1,2-azidoalcohols and 1,2-azidoamines, respectively, in the following (Scheme 1).

Different epoxides and *N*-tosyl aziridines underwent ring-opening easily with NaN_3 in the presence of AMP at room temperature (Table 1). The products were formed in excellent yields. The conversion was complete in 3–5 h. Both the epoxides and aziridines yielded the products with equal ease.

In the present conversion, the ring cleavage of epoxides and aziridines occurred with high regio- and stereoselectivity. 2-Phenyl epoxides and *N*-tosyl-2-phenyl aziridines formed the products by opening at the benzylic position and 2-alkyl epoxides and *N*-tosyl-2-alkyl aziridines formed the products by cleavage at the terminal position. The ring-opening of bicyclic epoxides and aziridines with NaN_3 furnished the azo-compounds with *trans*-configuration indicating the conversion to be *anti*-stereoselective. In the ^1H NMR spectra, the ring protons of **2h** appeared at δ 3.35 (1H, ddd, $J = 9.8, 9.2, 4.2$ Hz) [>C*H*(OH)] and 3.12 (1H, ddd, $J = 9.5, 9.2, 4.2$ Hz) [>C*H*N_3] while those of **2n** at δ 3.73 (1H, m) [>C*H* (NHTs)] and 3.34 (1H, ddd, $J = 9.5, 9.2, 4.1$ Hz) [>C*H*N_3].

☆ Part 129 in the series, "Studies on novel synthetic methodologies", "IICT Communication No. 070209".

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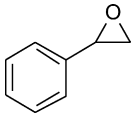
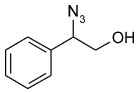
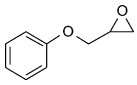
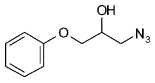
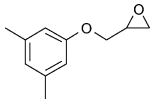
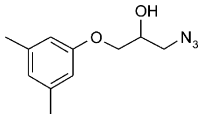
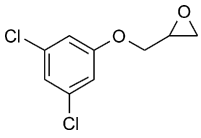
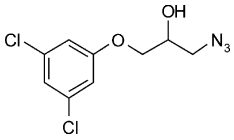
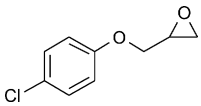
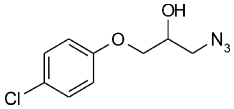
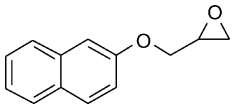
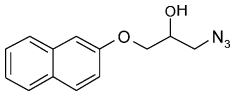
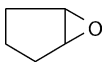
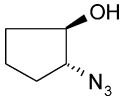
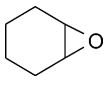
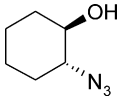
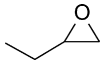
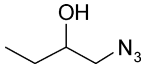
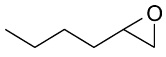
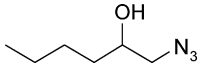
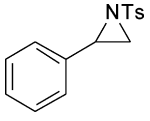
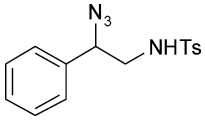
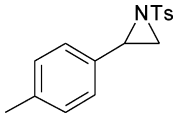
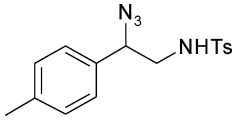
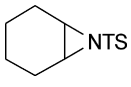
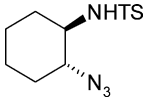
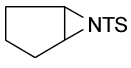
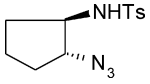
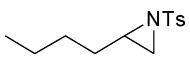
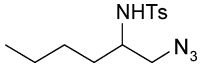
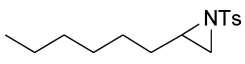
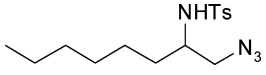
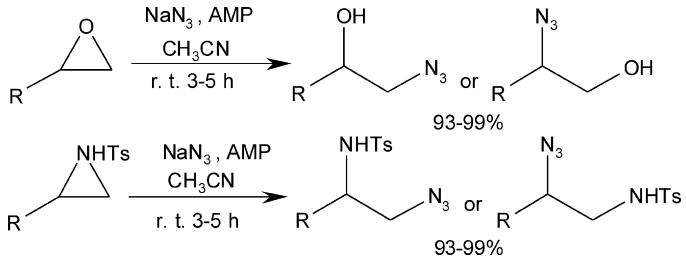
doi:10.1016/j.molcata.2007.01.040

Table 1
Ring-opening of epoxides and aziridines with NaN_3 using AMP

Entry	Epoxide/aziridine 1	Product 2	Isolated yield (%)
a			98
b			96
c			95
d			94
e			96
f			93
g			97
h			95
I			99
j			98
k			97
l			98
m			96
n			93
o			96
p			98

The structures of the products were established from their spectral (IR, ^1H NMR and MS) and analytical data.



Scheme 1.

In recent years, heteropoly acids and their salts have gained much importance in laboratories as well as in industries due to their impressive catalytic activity and ability to conduct the reactions in a clean manner [15]. The synthetic utilities of these catalysts has not yet been fully explored. The present catalyst, AMP (the ammonium salt of a heteropoly acid) is commercially available. It is highly efficient for the ring-opening of both epoxides and aziridines with NaN_3 at room temperature. The catalyst, AMP works under heterogeneous conditions and can conveniently be handled and separated from the reaction mixture by simple filtration.

In conclusion, we have developed a mild and simple method for the preparation of 1,2-azidoalcohols and 1,2-azidoamines by ring-opening of epoxides and aziridines, respectively, with NaN_3 using AMP as a heterogeneous catalyst. The high yields and excellent regio- and stereoselectivity are advantages of the present protocol.

1. Experimental

1.1. General procedure for the synthesis of 1,2-azidoalcohols and 1,2-azidoamines

To a mixture of epoxide (or *N*-tosyl aziridine) (1 mmol) and NaN_3 (1.5 mmol) in CH_3CN (5 ml) AMP (10 mol%) was added. The mixture was stirred at room temperature. After completion of the reaction, as monitored by TLC, water–EtOAc (1:1) (10 ml) was added and the mixture was shaken and filtered. The organic portion was separated from the filtrate and the aqueous portion was extracted with EtOAc (2×5 ml). The combined organic portions were concentrated and subjected to column chromatography (silica gel, hexane–EtOAc) to afford the corresponding azidoalcohols or azidoamines.

The spectral and analytical data of some representative azidocompounds are given below.

2a: IR (KBr)—υ_{max} 3528, 2103, 1680, 1592 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.42–7.23 (5H, m), 4.65 (1H, t, $J = 6.0$ Hz), 3.71 (2H, d, $J = 6.0$ Hz), 1.84 (1H, brs); FABMS: *m/z* 164 $[M+H]^+$; Anal. Calcd. for $C_8H_9N_3O$: C, 58.90; H, 5.52; N, 25.77%. Found: C, 58.81, H, 5.62; N, 25.83%.

2e: IR (KBr)—υ_{max} 3408, 2104, 1599, 1451 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.23 (2H, d, $J = 8.0$ Hz), 6.81 (2H, d, $J = 8.0$ Hz), 4.14 (1H m), 3.95 (2H, d, $J = 6.0$ Hz), 3.61–3.42 (2H, m), 2.62 (1H, d, $J = 6.0$ Hz); FABMS: *m/z* 230, 228 $[M+H]^+$; Anal. Calcd. for $C_9H_{10}ClN_3O_2$: C, 47.47; H, 4.40; N, 18.46%. Found: C, 47.54; H, 4.48, N, 18.39%.

2h: IR (KBr)—υ_{max} 3429, 2100, 1603, 1452 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 3.35 (1H, ddd, $J = 9.8$, 9.2, 4.2 Hz), 3.12 (1H, ddd, $J = 9.5$, 9.2, 4.2 Hz), 2.31 (1H, brs), 2.12–195 (2H, m), 1.83–1.68 (2H m), 1.43–1.16 (4H m); FABMS: *m/z* 142 $[M+H]^+$; Anal. Calcd. for $C_6H_{11}N_3O$: C, 51.06; H, 7.80; N, 29.79%. Found: C, 51.14; H, 7.86; N, 29.71%.

2l: IR (KBr)—υ_{max} 3284, 2106, 1598, 1451 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.72 (2H, d, $J = 8.0$ Hz), 7.28 (2H, d $J = 8.0$ Hz), 7.18–7.06 (4H, m), 5.29 (1H, t, $J = 6.0$ Hz), 4.54 (1H, dd, $J = 7.0$, 6.0 Hz), 3.21–2.92 (2H, m), 2.42 (3H, s) 2.31 (3H, s); FABMS: *m/z* 331 $[M+H]^+$; Anal. Calcd. for $C_{16}H_{18}N_4O_2S$: C, 58.18; H, 5.45; N, 16.97%. Found: C, 58.24; H, 5.42; N, 16.88%.

2n: IR (KBr)—υ_{max} 3280, 2102, 1599, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.78 (2H, d, $J = 8.0$ Hz), 7.32 (2H, d, $J = 8.0$ Hz), 5.79 (1H, d, $J = 6.0$ Hz), 3.73 (1H, m), 3.34 (1H, ddd, $J = 9.5$, 9.2, 4.1 Hz), 2.47 (3H, s) 2.01–1.88 (2H, m), 1.73–1.52 (3H, m) 1.43 (1H, m); FABMS: *m/z* 281 $[M+H]^+$; Anal. Calcd. for $C_{12}H_{16}N_4O_2S$: C, 51.43; H, 5.71; N, 20.00%. Found: C, 51.48; H, 5.73; N, 20.08%.

2o: IR (KBr)—υ_{max} 3281, 2101, 1599, 1451 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.81 (2H, d, $J = 8.0$ Hz), 7.32 (2H, d, $J = 8.0$ Hz), 5.54 (1H, d, $J = 6.0$ Hz), 3.32–3.14 (3H, m), 2.42 (3H, s), 1.51–1.32 (2H, m), 1.22–0.98 (4H, m), 0.75 (3H, t, $J = 7.0$ Hz); FABMS: *m/z* 297 $[M+H]^+$; Anal. Calcd. for $C_{13}H_{20}N_4O_2S$: C, 52.70; H, 6.76; N, 18.92%. Found: C, 52.76; H, 6.71; N, 18.86%.

Acknowledgments

The authors thank CSIR and UGC, New Delhi for financial assistance.

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