

Bi(OTf)₃- and Bi(TFA)₃-Catalyzed Ring Opening of Epoxides with Anilines under Microwave Irradiation

Ahmad R. Khosropour,* Mohammad M. Khodaei,* and Kazem Ghazati
 Department of Chemistry, Faculty of Science, Razi University, Kermanshah 67149, Iran

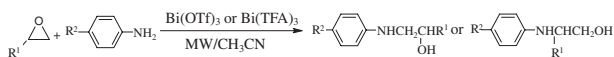
(Received November 25, 2003; CL-031140)

A facile and environmentally friendly methodology for ring opening of epoxides with anilines has been developed in the presence of catalytic amounts of bismuth (III) triflate or bismuth (III) trifluoroacetate using microwave-assisted heating. The ease of this procedure allowed preparation of the β -aminoalcohols quickly and efficiently.

β -Aminoalcohols as versatile building blocks both in organic and pharmaceutical sciences,^{1–3} have attracted attention of synthetic chemists. The most important synthetic routes to such compounds are the ring opening of epoxides with amines by acid catalyzed conditions.^{4–11} However, these methods often involve the use of expensive reagents, extended reaction times, drastic reaction conditions, unsatisfactory yields especially with aliphatic epoxides and entailed undesirable side reactions due to polymerization or rearrangement of oxiranes. Acid catalyzed ring opening of epoxides with anilines is limited and requires the careful control of acidity to prevent side reactions. Therefore, the introduction of a new and efficient method for this transformation is still in demand.

The applications of Bi(OTf)₃ and Bi(TFA)₃ as environmentally friendly reagents for organic synthesis have been extensively investigated.¹² This Lewis acid is easily available, inexpensive, easy to handle and relatively insensitive to air and small amounts of moisture.¹³ Also, we have reported that Bi(OTf)₃ or Bi(TFA)₃ are extraordinarily efficient catalysts for conversion of epoxides to thiiranes and 1,3-dioxolanes.¹⁴

Microwave activation as a non-conventional energy source has become an important method that can be used to carry out a wide range of reactions within short reaction times and in high yield and regioselectivity.¹⁵ There are no precedents of aminolysis of epoxides with anilines under microwave irradiation, and so we attempted this reaction in the presence of bismuth salts such as Bi(OTf)₃ and Bi(TFA)₃. Combination of bismuth salts and microwave irradiation served well in this reaction as well (Scheme 1). When an acetonitrile solution of epoxide and aniline was irradiated with microwave in the presence of a catalytic amount of the bismuth salts, ring-opening proceeded smoothly to afford the desired β -aminoalcohols in good to excellent yields (Table 1).



Scheme 1.

A variety of epoxides were converted to the β -aminoalcohols efficiently and chemoselectivity irrespective of functional groups like PhO-, RO-, ClCH₂-, and allyl ether. The presence of electron-donating and -withdrawing groups on aniline ring

Table 1. Bi(OTf)₃ or Bi(TFA)₃-catalyzed chemoselective opening of epoxides with anilines under microwave irradiation¹⁶

Entry	Products ^a	Yield/% ^b / Time/s	
		Bi(OTf) ₃	Bi(TFA) ₃
1		82/105	80/90 ^c
2		80/105	78/90 ^c
3		90/140	85/105
4	PhOCH ₂ CH(OH)CH ₂ NH-C ₆ H ₅	92/80	82/150
5	PhOCH ₂ CH(OH)CH ₂ NH-C ₆ H ₄ -CH ₃	86/90	78/135 ^c
6	PhOCH ₂ CH(OH)CH ₂ NH-C ₆ H ₄ -Br	90/85	87/120 ^f
7	PhOCH ₂ CH(OH)CH ₂ NH-C ₆ H ₄ -NO ₂	89/170	82/165 ^f
8	HOCH ₂ CHNH-Ph-C ₆ H ₅	96/20 ^c	90/20 ^d
9	HOCH ₂ CHNH-Ph-C ₆ H ₄ -CH ₃	93/25 ^c	92/20 ^d
10	HOCH ₂ CHNH-Ph-C ₆ H ₄ -Br	88/25 ^c	90/40 ^d
11	CH ₂ =CHCH ₂ OCH ₂ CH(OH)CH ₂ NH-C ₆ H ₅	80/150	79/150
12	CH ₃ (CH ₂) ₅ CH(OH)CH ₂ NH-C ₆ H ₅	79/140	75/165
13	CH ₃ (CH ₂) ₂ CH ₂ OCH ₂ CH(OH)CH ₂ NH-C ₆ H ₅	82/105	80/195
14	ClCH ₂ CH(OH)CH ₂ NH-C ₆ H ₅	85/110	84/195

^a All products were characterised by ¹H NMR, ¹³C NMR, and IR.
^b Isolated and unoptimized yields. ^c 1 mol %. ^d 3 mol %. ^e 4 mol %.
^f 6 mol %.

had no effect on this reaction (Entries 1–3, 4–7, and 8–10). When cyclohexene oxide was treated with aniline in the presence of Bi(OTf)₃ and Bi(TFA)₃ under microwave irradiation, *trans*-2-(anilino)cyclohexan-1-ol was regioselectively obtained in 82%

and 89% yields, respectively (Entries 1 and 2). This reaction proceeded indeed rapidly to finish within 105 second of irradiation. The reactions of styrene oxide with aniline gave rise to the formation of β -aminoalcohol derived from α -attack of aniline (Entries 8-10). These high reactivity and selectivity are similar to those observed in the case of strong Lewis acids.^{10a,b,11}

Very recently, Cepanec has reported that the epoxide-opening reaction with nitroaniline gave unsatisfactory result in spite of the prolonged reaction time.⁵ In sharp contrast to this, our protocol promoted by microwave irradiation furnished the desired β -aminoalcohol in a good yield even in the short reaction time (<175 s) (Entry 7).

In conclusion, the present microwave-assisted procedure provides an efficient and very simple methodology for the preparation of 2-anilinoalkanols using Bi(OTf)₃ or Bi(TFA)₃ as very cheap, low toxic, and oxygen and moisture tolerant catalysts in very short reaction times. In addition, high selectivity described in this report is another merit of this method.

All of the products refer to pure 2-anilinoalkanols. The apparatus used for these reactions was a Samsung domestic microwave oven (900 W) without any modification.

We are thankful to the Razi University Research Council for partial support of this work.

References and Notes

- G. K. Jnaneshwara, V. H. Deshpande, M. Lalithambika, T. Ravindranathan, and A. V. Bedekar, *Tetrahedron Lett.*, **39**, 459 (1998).
- a) J. Takehara, S. Hashiguchi, A. Fujii, S. I. Inoue, T. Ikaria, and R. Nayori, *J. Chem. Soc., Chem. Commun.*, **1996**, 233. b) D. J. Ager, I. Prakash, and D. Schaad, *Chem. Rev.*, **96**, 835 (1996). c) C. Auvin-Guette, S. Rebuffat, Y. Prigent, and B. Bodo, *J. Am. Chem. Soc.*, **114**, 2170 (1992).
- H. E. Carter, F. J. Glick, W. P. Norris, and G. E. Phillips, *J. Biol. Chem.*, **170**, 285 (1947).
- J. S. Yadav, B. V. S. Reddy, A. K. Basak, and A. Venkat Narsaiah, *Tetrahedron Lett.*, **44**, 1047 (2003).
- I. Cepanec, M. Litvić, H. Mikuldas, A. Bartolincić, and V. Vinković, *Tetrahedron*, **59**, 2435 (2003).
- a) Y. Harrak and M. D. Pujol, *Tetrahedron Lett.*, **43**, 819 (2002). b) N. R. Swamy, G. Kondaji, and K. Nagaiah, *Synth. Commun.*, **32**, 2307 (2002). c) T. Ollevier and G. Lavie-Compin, *Tetrahedron Lett.*, **43**, 7891 (2002).
- M. Curini, F. Epifano, M. C. Marcotullio, and O. Rosati, *Eur. J. Org. Chem.*, **2001**, 4149.
- S. Rampalli, S. S. Chandhari, and K. G. Akamanchi, *Synthesis*, **2000**, 78.
- S. Chandrasekhar, T. Ramachandar, and S. Jaya Prakash, *Synthesis*, **2000**, 1817.
- a) G. Sekar and V. K. Singh, *J. Org. Chem.*, **64**, 287 (1999). b) M. Chini, P. Crotti, L. Favero, F. Macchia, and M. Pineschi, *Tetrahedron Lett.*, **35**, 433 (1994). c) M. Meguro, N. Asao, and Y. Yermamoto, *J. Chem. Soc., Perkin Trans. I*, **1994**, 2597. d) M. Fujiwara, M. Imada, A. Baba, and H. Matsuda, *Tetrahedron Lett.*, **30**, 739 (1989).
- J. Auge and F. Leroy, *Tetrahedron Lett.*, **37**, 7715 (1996).
- a) J. V. Yadav, B. V. S. Reddy, P. N. Reddy, and M. S. Rao, *Synthesis*, **2003**, 1387. b) I. Mohammadpoor-Baltork and A. R. Khosropour, *Monatsh. Chem.*, **133**, 189 (2002). c) S. Repichet, A. Zwick, L. Vendier, C. Le Roux, and J. Dubac, *Tetrahedron Lett.*, **43**, 993 (2002). d) M. N. Leonard, L. C. Wieland, and R. S. Mohan, *Tetrahedron*, **58**, 8373 (2002).
- I. Mohammadpoor-Baltork, A. R. Khosropour, H. Aliyan, *J. Chem. Res., Synop.*, **7**, 780 (2001). and cited therein.
- a) I. Mohammadpoor-Baltork and A. R. Khosropour, *Molecules*, **6**, 996 (2001). b) I. Mohammadpoor-Baltork and A. R. Khosropour, *Synth. Commun.*, **22**, 3411 (2001).
- R. S. Pottorf, N. K. Chadha, M. Katkevics, V. Ozola, E. Suna, H. Ghane, T. Regberg, and M. R. Player, *Tetrahedron Lett.*, **44**, 175 (2003).
- Experimental Procedure: To a solution of epoxides (1 mmol) and anilines (1 mmol) in CH₃CN (2 mmol) was added Bi(OTf)₃ (0.02 mmol) or Bi(TFA)₃ (0.05 mmol). The mixture was irradiated with microwave oven for the appropriate time according to Table. After completion of the reaction, as indicated by TLC or GLC, the solvent was evaporated and washed with 0.5N HCl (25 mL). The mixture was extracted with CH₂Cl₂ (3 × 10 mL) and the organic layer was dried with Na₂SO₄. The solvent was evaporated and the crude product purified by plate or column chromatography on a silica gel to afford the pure β -aminoalcohols in 75–96% yields. Spectroscopic data for compounds: **2**: *trans*-2-(4-Methylanilino)cyclohexan-1-ol: Viscous liquid, IR (KBr, cm⁻¹) 3618–3104 (NH and OH), 1603, 1502, ¹H NMR (CDCl₃, 200 MHz) δ 1.09 (m, 1H), 1.47 (m, 3H), 1.72 (m, 2H), 2.09 (m, 2H), 2.33 (s, 3H), 3.01–3.27 (ddd, 1H, *J* = 11, 11, 6.2), 3.31–3.53 (m, 1H), 3.57–4.22 (bs, 2H), 6.78–7.02 (m, 4H, Ar-H), ¹³C NMR (CDCl₃, 200 MHz) δ 24.7, 25.4, 31.4, 31.8, 33.6, 60.9, 74.8, 115.2, 119.3, 129.8, 147.7, Analysis calcd. for C₁₃H₁₉NO; C, 76.06; H, 9.33; N, 6.82. Found: C, 76.35; H, 9.11; N, 6.61%. **11**: 1-Anilino-3-(2-propenoxy)-2-propanol: viscous liquid; IR (NaCl, cm⁻¹) 3510–3115 (NH and OH), 3009, 1598, 1500, 1068, ¹H NMR (CDCl₃, 200 MHz) δ 3.15(dd, *J* = 9.9, 10 Hz, 2H), 3.26 (dd, 5, 7 Hz, 2H), 3.52 (m, 2H), 3.81(bs, 1H), 4.08(d, *J* = 9 Hz, 2H), 5.23 (d, *J* = 12 Hz, 2H), 5.98 (m, 1H), 6.62 (d, *J* = 10 Hz, 2H), 7.15 (d, 10 Hz, 2H), ¹³C NMR (CDCl₃, 200 MHz) δ 47.4, 69.4, 72.8, 73.9, 113.9, 117.9, 118.5, 129.7, 134.7, 142.7, Analysis calcd. for C₁₂H₁₇NO₂; C, 69.54; H, 8.27; N, 6.76. Found: C, 69.30; H, 8.39; N, 6.68%. **12**: 1-Anilino-2-octanol: viscous liquid; IR (NaCl, cm⁻¹): 3598–3100 (NH and OH), 1592, 1495, ¹H NMR (CDCl₃, 200 MHz) δ 0.92 (t, *J* = 7 Hz, 3H), 1.24–1.86 (m, 10H), 3.21 (dd, *J* = 10, 10 Hz, 2H), 3.32 (dd, *J* = 8, 4 Hz, 1H), 3.91 (m, 1H), 6.68–7.35 (m, 5H), ¹³C NMR (CDCl₃, 200 MHz) δ 14.5, 23.0, 26.0, 29.8, 32.2, 35.5, 51.0, 70.7, 114.0, 118.7, 129.7, 151.6, Analysis calcd. for C₁₄H₂₃NO; C, 75.97; H, 10.47; N, 6.33. Found: C, 75.71; H, 10.66; N, 6.48%. **14**: 1-Anilino-3-chloro-2-propanol: viscous liquid; IR (NaCl cm⁻¹): 3504–3100 (NH and OH), 1594, 1497, 1090, ¹H NMR (CDCl₃, 200 MHz) δ 3.24 (m, 2H), 3.45 (dd, *J* = 10.1, 4.8 Hz, 1H), 3.72 (d, *J* = 8 Hz, 2H), 4.12 (m, 1H), 6.74 (m, 3H), 7.19 (m, 2H), ¹³C NMR (CDCl₃, 200 MHz) δ 47.7, 48.1, 70.2, 113.9, 118.9, 129.9, 148.0, Analysis calcd. for C₉H₁₂ClNO; C, 58.23; H, 6.51; N, 7.54. Found: C, 58.02; H, 6.68; N, 7.69%.