ARTICLE

OBC
www.rsc.org/obc

An efficient synthesis of 2-amino alcohols by silica gel catalysed opening of epoxide rings by amines

Asit K. Chakraborti,* Santosh Rudrawar and Atul Kondaskar
Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), Sector 67, S. A. S. Nagar 160 062, Punjab, India.
E-mail: akchakraborti@niper.ac.in

Received 13th January 2004, Accepted 9th March 2004
First published as an Advance Article on the web 29th March 2004

Silica gel (60–120 mesh) efficiently catalyses the opening of epoxide rings by amines at rt under solvent-free conditions providing an easy method for the synthesis of 2-amino alcohols. Aromatic and aliphatic amines react with cyclohexene oxide with exclusive formation of the *trans*-2-aryl/alkylaminocyclohexanols in high yields. A complementary regioselectivity is exhibited by aromatic and aliphatic amines during the reaction with styrene oxide. The epoxide ring of non-styrenoidal unsymmetrical alkene oxide undergoes selective nucleophilic attack at the sterically less hindered carbon by aniline.

2-Amino alcohols are versatile intermediates in the synthesis of a vast range of biologically active natural and synthetic products,[1] unnatural amino acids,[2] and chiral auxiliaries.[3] The classical approach for the synthesis of 2-amino alcohols, involving nucleophilic opening of epoxides by amines,[4] which requires the treatment under heating[5] and works less well with poorly nucleophilic amines, lacks appreciable regioselectivity and poses problems in dealing with sensitive epoxides due to the potential side reactions at high temperatures, and needs excess amine. Various protocols have been developed for activating epoxides rendering them to be more susceptible to nucleophilic cleavage by amine. These include the use of alumina,[6] metal amides and triflamide,[7] alkali metal perchlorates and tetrafluoroborate,[8] metal triflates,[9] metal alkoxides,[10] zirconium sulfophenyl phosphonate,[11] metal halides,[12] microwave irradiation,[13] hexafluoro-2-propanol (HFIP) under reflux,[14] ionic liquid,[15] $^{n}Bu_3P$,[16] and $Yb(OTf)_3$ in supercritical CO_2 under high pressure at 55 °C.[17] However, these methodologies suffer from one or more disadvantages such as long reaction times, elevated temperatures, high pressure, moderate yields and regioselectivities, use of air and moisture sensitive catalysts, use of halogenated solvents, requirement of stoichiometric amounts of catalyst, use of costly reagents/catalysts, the need to use special apparatus, rearrangement to allylic alcohols,[18] potential hazards in handling pyrophoric/moisture sensitive reagents in the preparation of the catalyst, and in most of the cases being applicable to aromatic amines only. Therefore, the development of a better catalyst is in high demand.

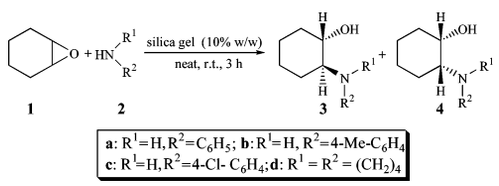
The tight legislation on the release of waste and toxic emissions, to control environmental pollution, has induced a paradigm shift in the development of new synthetic methodologies. Thus, besides the usual requisites of mildness and selectivity, the issue of environmentally friendly reaction conditions has become increasingly important in designing alternate synthetic routes for fine chemicals. Considering the potential industrial applications of the epoxide ring opening reaction by amines, we felt that the use of an easily available, less costly, non-toxic catalyst and solvent-free reaction condition should fulfil the 'triple bottom line'[19] philosophy of green chemistry. This led us to search for a heterogeneous catalyst as it would offer several intrinsic advantages such as the ease of product separation, catalyst reuse, minimization of the amount of salt and waste production, and prevention of corrosion by avoiding contact with hazardous acids. We considered the case of organic reactions run on the surfaces of solids such as alumina[20] and silica gel.[21] Herein we report that silica gel (60–120 mesh), routinely used for chromatography, efficiently catalyses the opening of epoxide rings by amines at rt in the absence of solvent.

Table 1 Reactions of **1** with various amines in the presence of silica gel[a]

Entry	Amine	Product[b]	Yield (%)[c]
1	**2a**	**3a**	90[d]
2	**2b**	**3b**	87
3	**2c**	**3c**	92
4	**2d**	**3d**	90

[a] The epoxide (2.5 mmol) was treated with the amine (2.5 mmol) in the presence of the silica gel (60–120 mesh, 25 mg, 10% w/w) at rt under nitrogen in the absence of solvent. [b] The ^1H and ^{13}C NMR analyses confirmed the *trans* stereochemistry of the product. [c] Isolated yields of the corresponding *trans*-2-aryl/alkylaminocyclohexanol. [d] A 12% yield of the amino alcohol was formed (GCMS) in carrying out the reaction in the absence of silica gel and the unreacted epoxide and the amine remained intact (GCMS).

To optimize the best reaction conditions cyclohexene oxide **1** (2.5 mmol) was taken as a symmetrically substituted epoxide and treated with various amines **2** (2.5 mmol) in the presence of chromatographic silica gel (60–120 mesh) (Scheme 1).



Scheme 1 Reaction of **1** with **2** in the presence of silica gel.

Complete conversion took place in 3 h (GCMS) at rt in the absence of solvent (Table 1). The requirement of the catalytic effect of the silica gel in opening the epoxide was established by the fact that no significant amino alcohol formation was observed in the absence of silica gel and the unreacted epoxide and the amine remained unchanged (GCMS). The reaction worked with aromatic amines with varying electronic nature *e.g.* aniline (**2a**), 4-methylaniline (**2b**), and 4-chloroaniline (**2c**) as well as with aliphatic amine such as pyrrolidine (**2d**).[22] On each occasion, the resultant 2-aryl/alkylaminocyclohexanol, was identified as the *trans* diastereoisomer **3** on the basis of NMR.[8,9e,12h] The catalyst was recovered by filtration after

DOI: 10.1039/b400588k

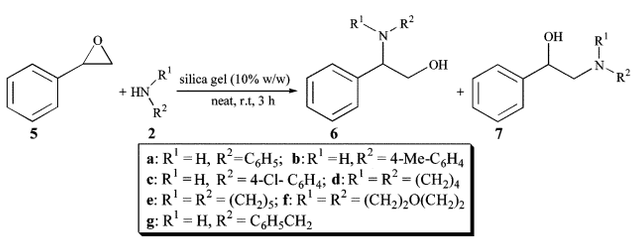
Table 2 Regioselectivity during the reaction of **5** with various amines in the presence of silica gel[a]

Entry	Amine	Yield (%)[b]	Ratio **6** : **7**[c]
1	**2a**	93	95 : 5[d]
2	**2b**	84	91 : 9
3	**2c**	88	98 : 2
4	**2d**	100	28 : 72
5	**2e**	100	17 : 83
6	**2f**	100	31 : 69
7	**2g**	100	22 : 78

[a] The epoxide **5** (2.5 mmol) was treated with the amine (2.5 mmol) in the presence of silica gel (60–120 mesh, 30 mg, 10% w/w) at rt under nitrogen in the absence of solvent for 1.5 h. [b] Isolated yields. [c] Determined by GCMS/^{1}H NMR. [d] The corresponding amino alcohols **6** and **7** were obtained in 94% yields in a ratio of 95 : 5 in CH_2Cl_2.

diluting the reaction mixture with Et_2O and was reused, after activation by heating at 100 °C under vacuum (~5 mmHg) for 10 h, without any significant loss of catalytic activity.

The regioselectivity of the silica gel catalysed reaction was evaluated during the reaction of styrene oxide **5**, a representative unsymmetrical epoxide, with various amines (Scheme 2) and the results are summarized in Table 2.



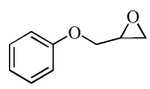
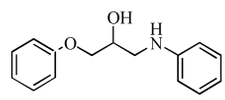
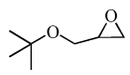
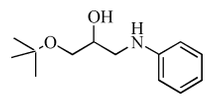
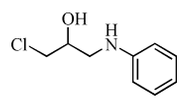
Scheme 2 Regioselective cleavage of **5** with various amines.

In all of the cases, the corresponding amino alcohols were obtained in excellent yields. For reaction with aromatic amines, the two regioisomers eluted at different retention time and the regioselectivity was determined by GCMS. In the MS, the regioisomer **6** exhibited a daughter ion at *m*/*z* ($M^+ - 31$) due to the loss of CH_2OH and the diagnostic feature in the mass spectra of **7** was the ion peak at *m*/*z* ($M^+ - 106$) arising out of the loss of PhCHO.

However, in case of aliphatic amines, the two regioisomers could not be separated by column chromatography. In the GCMS, both the regioisomers eluted at the same time but the presence of ion peaks at $M^+ - 31$ and $M^+ - 106$ indicated the formation of **6** and **7**. In the ^{1}H NMR, the benzylic proton of **6** and **7**, obtained from the reaction of **5** with aliphatic amines, appeared at ~ δ 3.9 and 4.7, respectively. The ratio of the two regioisomeric products was determined based on the methine and methylene proton signals corresponding to **6** and **7** and by comparison with the reported values (in the case of the product obtained with benzylamine,[8] and piperidine[23]).

A complementary regioselective outcome was displayed by the reactions with aromatic and aliphatic amines. The reaction of **5** with aromatic amines afforded the major regioisomer following the nucleophilic attack at the benzylic carbon (entries 1–3). The observed regioselectivity was in conformity with the results obtained for the Lewis acid catalysed epoxide ring opening reaction of **5** with aromatic amines.[10b,11,12f–h,17] No change in the product yield and regioselectivity was observed when the silica gel catalysed reaction of **5** with **2a** was carried out in a solvent such as CH_2Cl_2. Aliphatic amines exhibited a preference for nucleophilic attack at the terminal carbon with 17 : 83 to 31 : 69 selectivities (entries 4–7). The regioselective outcome of the silica gel catalysed reaction of **5** with aliphatic amines resembles the results obtained for the Lewis acid catalysed reactions.[7f,8,9a–d] The regioselective formation of **6**

Table 3 Reaction of various epoxides with **2a** in the presence of silica gel[a]

Entry	Epoxide	Product[b]	Yield (%)[c]
1			100
2			100
3			69[d]

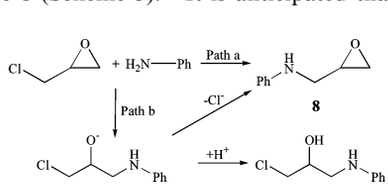
[a] The epoxide (2.5 mmol) was treated with **2a** (2.5 mmol) in the presence of silica gel (60–120 mesh, 10% w/w) at rt under nitrogen in the absence of solvent for 3 h. [b] Determined by GCMS and ^{1}H/^{13}C NMR. [c] Isolated yields of the corresponding amino alcohol. [d] The unreacted epichlorohydrine remained unchanged (GCMS).

during the reaction of **5** with aromatic amines may be accounted for by the fact that the phenyl group in **5** induces a carbocationic character at the benzylic carbon of the epoxide complexed with SiO_2 due to the resonance effect. Thus, the aromatic amines react selectively at the benzylic carbon of **5** due to their less nucleophilic property. The relatively more nucleophilic property of the aliphatic amines favors a more S_N2 process and drives the nucleophilic attack at the terminal carbon of **5**. The role of the carbocationic character, at the benzylic position in the transition state during the reaction of **5** with aromatic amines, in controlling the regioselectivity is further demonstrated by the observations that an increase in polarity of the reaction medium by the use of fluoro alcohols[14] and ionic liquids[15] leads to selective nucleophilic attack at the benzylic position in **5** by aromatic amines in the absence of metal catalyst.

To evaluate the generality of the regioselectivity for non-styrenoidal oxides, various unsymmetrical epoxides were treated with **2a** in the presence of silica gel (Table 3).

Quantitative yields of the corresponding amino alcohols were obtained during the reaction of glycidyl phenyl ether, and glycidyl *tert*-butyl ether (entries 1, 2) and in each case complete selectivity for nucleophilic attack at the less hindered carbon of the epoxide was observed. These observations suggest that the reversal of regioselectivity (nucleophilic attack at more hindered benzylic carbon) during the reaction of **5** with **2a** and other aromatic amines was controlled by the electronic factor of the phenyl group in **5**.

The reaction of epichlorohydrine (entry 3) exemplified the case of excellent chemoselectivity affording the amino alcohol corresponding to nucleophilic attack at the terminal carbon of the epoxide moiety. No product arising from nucleophilic displacement of the chlorine could be detected through GCMS analysis of the reaction mixture. As epichlorohydrine is an ambiphilic substrate, in principle, the reaction may proceed *via* two distinct pathways: (i) direct displacement of chlorine (path a) or (ii) initial attack on the epoxide (path b) followed by protonation of the amino alcohol or extrusion of the chlorine atom to give **8** (Scheme 3).[24] It is anticipated that the oxygen



Scheme 3 Reaction of epichlorohydrine with **2a**.

atoms in SiO_2 help the delocalisation of the negative charge of the alkoxide generated after the nucleophilic attack on the silica gel complexed epoxide. Thus, the free alkoxide anion is not available for subsequent elimination of the chloride anion.

In conclusion, this study demonstrates that chromatographic silica gel (60–120 mesh) is a highly efficient, mild, and reusable catalyst for opening of epoxides with amines. The mild reaction conditions, excellent regio-, diastereo-, and chemo-selectivity, and applicability for aromatic and aliphatic amines offer specific advantages. The low cost and apparent non-toxic nature of silica gel and the solvent-free reaction conditions are consistent with increasing environmental concerns[25] and will make the present method potentially useful for industrial applications.

Typical procedure. *trans*-2-(phenylamino)cyclohexanol (3a)

Silica gel (60–120 mesh, 25 mg, 10% w/w) was added to a magnetically stirred mixture of **1** (0.25 ml, 2.5 mmol) and **2a** (0.225 ml, 2.5 mmol) at rt under nitrogen. After completion of the reaction (3 h, GCMS), the reaction mixture was diluted with Et_2O (15 ml) followed by addition of a few drops of water (to settle down the catalyst). The catalyst was separated by decantation of the supernatant ethereal solution, was washed with Et_2O (10 ml) and the combined ethereal solutions were dried (Na_2SO_4) and concentrated under vacuum to afford *trans*-2-(phenylamino)cyclohexanol **3a** (0.428 g, 90%); IR (neat): 3354, 2931, 2858, 1601, 1500, 1448, 1319 and 1067; NMR δ_H (300 MHz, $CDCl_3$) 6.7–7.2 (m, 5 H), 3.33 (ddd, *J* 4.2, 10.4 and 10.5, 1 H), 3.13 (ddd, *J* 3.9, 10.0 and 10.1, 1 H), 2.9 (m, D_2O exchangeable, 2 H), 2.10–2.16 (m, 2 H), 1.72–1.78 (m, 2 H) and 1.03–1.42 (m, 4 H); NMR δ_C (300 MHz, $CDCl_3$) 147.81, 129.34, 118.38, 114.40, 74.55, 60.17, 33.15, 31.62, 25.02 and 24.27; *m*/*z* (EI) 191 (M^+); identical (^1H and ^{13}C NMR, and MS) with an authentic sample.[12h] The recovered catalyst was activated by heating at 100 °C under vacuum (~5 mmHg) for 10 h and reused for the reaction of a fresh batch of **1** (2.5 mmol) and **2a** (2.5 mmol) affording **3a** in 86% yields. This general procedure was followed for the other reactions. On each occasion, the product was identified by comparing the spectral data (IR, NMR, MS) with those reported in the literature, wherever applicable. New spectral data were obtained in the following cases.

2-(4-Methylphenyl)aminocyclohexanol (3b)[12d]

IR (neat): 3389, 2932, 2859, 1616, 1517, 1298 and 1067; NMR δ_H (300 MHz, $CDCl_3$) 6.98 (d, *J* 7.7, 2 H), 6.62 (d, *J* 7.7, 2 H), 3.26–3.34 (m, 1 H), 3.01–3.10 (m, 1 H), 2.23 (s, 3 H), 2.07–2.12 (m, 2 H), 1.67–1.75 (m, 2H), 1.23–1.42 (m, 3 H) and 0.94–1.06 (m, 1 H); δ_C (300 MHz, $CDCl_3$) 145.06, 129.25, 126.57, 114.15, 73.38, 59.75, 32.99, 30.83, 24.34, 23.86 and 19.93; *m*/*z* (EI) 205 (M^+), 162, 146 (100%).

2-(4-Chlorophenyl)aminocyclohexanol (3c)[26]

IR (neat): 3386, 2931, 2858, 1511, 1242 and 1035; NMR δ_C (300 MHz, $CDCl_3$) 146.15, 128.82, 122.23, 115.13, 73.93, 59.86, 32.23, 31.09, 24.55 and 24.02.

2-Pyrrolidin-1-yl-cyclohexanol (3d)[9c]

IR (neat): 3422, 2938, 1640, 1484, 1085 and 738; NMR δ_C (300 MHz, $CDCl_3$) 69.97, 65.35, 47.94, 33.33, 24.55, 24.00, 23.42 and 22.15; *m*/*z* (EI) 169 (M^+), 140 and 110 (100%).

2-(4-Chlorophenyl)amino-2-phenylethanol (6c)

IR (neat): 3396, 2931, 1600, 1496, 1314 and 813; NMR δ_H (300 MHz, $CDCl_3$) 7.13–7.39 (m, 5 H), 7.00 (d, *J* 8.8, 2 H), 6.46 (d, *J* 8.8, 2 H), 4.41–4.45 (dd, *J* 4.1 and 6.9, 1 H), 3.90–3.95 (dd, *J* 4.1 and 10.8, 1 H) and 3.71–3.77 (dd, *J* 6.9 and 10.8, 1 H); NMR δ_C (300 MHz, $CDCl_3$) 145.62, 139.50, 128.81, 128.67, 127.55, 126.56, 122.23, 114.90, 66.86 and 59.93; *m*/*z* (EI) 247 (M^+) and 216 (100%). $C_{14}H_{14}ClNO$ requires: C, 67.88; H, 5.70; N, 5.65%; found: C, 67.86; H, 5.71; N, 5.64%.

1-Phenoxy-3-phenylaminopropan-2-ol (Table 3, entry 1)[13a,15]

IR (neat): 3391, 3056, 2926, 2872, 1600, 1495, 1243 and 1041; NMR δ_C (300 MHz, $CDCl_3$) 158.22, 147.86, 129.37, 129.12, 121.01, 117.75, 114.37, 113.14, 69.80, 68.44 and 46.45; *m*/*z* (EI) 243 (M^+) and 106 (100%).

1-*tert*-Butoxy-3-phenylaminopropan-2-ol (Table 3, entry 2)

IR (neat): 3385, 3051, 2973, 1601, 1500, 1243 and 1078; NMR δ_H (300 MHz, $CDCl_3$) 7.16 (m, 2 H), 6.70 (m, 1 H), 6.62 (d, *J* 8.2, 2 H), 3.93 (m, 1 H), 3.44–3.49 (dd, *J* 3.9 and 8.9, 1 H), 3.35–3.41 (dd, *J* 6.3 and 8.9, 1 H), 3.24–3.30 (dd, *J* 4.2 and 12.5, 1 H), 3.09–3.15 (dd, *J* 6.9 and 12.5, 1 H) and 1.20 (s, 9 H). NMR δ_C (300 MHz, $CDCl_3$) 148.34, 129.14, 117.52, 113.09, 73.33, 69.20, 64.02, 46.86 and 24.43. *m*/*z* (EIMS) 223 (M^+) and 106 (100%). $C_{13}H_{21}NO_2$ requires: C, 69.92; H, 9.48; N, 6.27%; found: C, 69.90; H, 9.49; N, 6.26%.

1-Chloro-3-phenylaminopropan-2-ol (Table 3, entry 3)[8]

IR (neat): 3404, 3062, 2952, 1602, 1505, 1318, 1259, 1090 and 753; NMR δ_H (300 MHz, $CDCl_3$) 7.19 (m, 2 H), 6.75 (m, 1 H), 6.66 (d, *J* 7.9, 2 H), 4.05–4.10 (m, 1 H), 3.61 (m, 2 H), 3.36–3.41 (dd, *J* 4.4 and 13.3, 1 H) and 3.20–3.27 (dd, *J* 7.1 and 13.3, 1 H); NMR δ_C (300 MHz, $CDCl_3$) 147.31, 129.20, 118.23, 113.35, 69.47, 47.25 and 42.02; *m*/*z* (EI) 185 (M^+), 168 and 106 (100%).

References and notes

1 (*a*) D. R. Gehlert, D. J. Goldstein and P. A. Hipskind, *Annu. Rep. Med. Chem.*, 1999, 201; (*b*) E. J. Corey and F. Zhang, *Angew. Chem., Int. Ed. Engl.*, 1999, **38**, 1931; (*c*) C. W. Johannes, M. S. Visser, G. S. Weatherhead and A. H. Hoveyda, *J. Am. Chem. Soc.*, 1998, **120**, 8340; (*d*) B. L. Chng and A. Ganesan, *Bioorg. Med. Chem. Lett.*, 1997, **7**, 1511; (*e*) G. A. Rogers, S. M. Parsons, D. C. Anderson, L. M. Nilsson, B. A. Bahr, W. D. Kornreich, R. Kaufman, R. S. Jacobs and B. Kirtman, *J. Med. Chem.*, 1989, **32**, 1217; (*f*) J. De Cree, H. Geukens, J. Leempoels and H. Verhaegen, *Drug Dev. Res.*, 1986, **8**, 109.

2 (*a*) P. O'Brien, *Angew Chem., Int Ed. Engl.*, 1999, **38**, 326; (*b*) G. Li, H.-T. Chang and K. B. Sharpless, *Angew Chem., Int Ed. Engl.*, 1996, **35**, 451.

3 D. J. Ager, I. Prakash and D. R. Schaad, *Chem. Rev.*, 1996, **96**, 835.

4 (*a*) S. C. Bergmeier, *Tetrahedron*, 2000, **56**, 2561; (*b*) D. M. Hodgson, A. R. Gibbs and G. P. Lee, *Tetrahedron*, 1996, **52**, 14361; (*c*) R. M. Hanson, *Chem. Rev.*, 1991, **91**, 437; (*d*) O. Mitsunobu, in *Comprehensive Organic Synthesis*, ed. E. Winterfeldt, Pergamon Press, New York, 1996, Vol 6, Pt 1.3.4.1; (*e*) A. S. Rao, S. K. Paknikar and J. G. Kirtane, *Tetrahedron*, 1983, **39**, 2323.

5 (*a*) P. A. Crooks and R. Szyudler, *Chem. Ind. (London)*, 1973, 1111; (*b*) J. A. Deyrup and C. L. Moyer, *J. Org. Chem.*, 1969, **34**, 175; (*c*) M. Freifelder and G. R. Stone, *J. Org. Chem.*, 1961, **26**, 1477; (*d*) M. Mousseron, J. Jullien and Y. Jolchine, *Bull. Soc. Chim. Fr.*, 1952, 757; (*e*) R. E. Lutz, J. A. Freekand and R. S. Murphy, *J. Am. Chem. Soc.*, 1948, **70**, 2015.

6 G. H. Posner and D. Z. Rogers, *J. Am. Chem. Soc.*, 1977, **99**, 8208.

7 (*a*) Et_2AlNHR: L. E. Overman and L. A. Flippin, *Tetrahedron Lett.*, 1981, **22**, 196; (*b*) silicon amides: A. Papini, I. Ricci, M. Taddei, G. Seconi and P. Dembach, *J. Chem. Soc., Perkin Trans. 1*, 1984, 2261; (*c*) R_2NMgBr: M. C. Carre, J. P. Houmounou and P. Caubere, *Tetrahedron Lett.*, 1985, **26**, 3107; (*d*) R'_3PbNR_2: J.-I. Yamada, M. Yumoto and Y. Yamamoto, *Tetrahedron Lett.*, 1989, **30**, 4255; (*e*) Cu amide: Y. Yamamoto, N. Asao, M. Meguro, N. Tsukade, H. Nemoto, N. Adayari, J. G. Wilson and H. Nakamura, *J. Chem. Soc., Chem. Commun.*, 1993, 1201; (*f*) $LiNTf_2$: J. Cossy, V. Bellosta, C. Hamoir and J.-R. Desmurs, *Tetrahedron Lett.*, 2002, **43**, 7083.

8 M. Chini, P. Crotti and F. Macchia, *Tetrahedron Lett.*, 1990, **31**, 4661.

9 (*a*) Ph_4SbOTf: M. Fujiwara, M. Imada, A. Baba and H. Matsuda, *Tetrahedron Lett.*, 1989, **30**, 739; (*b*) $Ln(OTf)_3$: M. Chini, P. Crotti, L. Favero, F. Machhia and M. Pineschi, *Tetrahedron Lett.*, 1994, **35**,

433; (*c*) Yb(OTf)$_3$: M. Meguro, N. Asao and Y. Yamamoto, *J. Chem. Soc., Perkin Trans. 1*, 1994, 2597; (*d*) LiOTf: J. Auge and F. Leroy, *Tetrahedron Lett.*, 1996, **37**, 7715; (*e*) Cu(OTf)$_2$ and Sn(OTf)$_2$: G. Sekar and V. K. Singh, *J. Org. Chem.*, 1999, **64**, 287.
10 (*a*) Ti(OPr^i)$_4$: S. Sagava, H. Abe, Y. Hase and T. Inaba, *J. Org. Chem.*, 1999, **64**, 4962; (*b*) DIPAT (diisopropoxyaluminium trifluoroacetate): S. Rampalli, S. S. Chaudhari and K. G. Akamanchi, *Synthesis*, 2000, 78.
11 M. Curini, F. Epifano, M. C. Marcotullio and O. Rosati, *Eur. J. Org. Chem.*, 2001, 4149.
12 (*a*) $CoCl_2$: J. Iqbal and A. Pandey, *Tetrahedron Lett.*, 1990, **31**, 575; (*b*) $TaCl_5$: S. Chandrasekhar, T. Ramchander and S. J. Prakash, *Synthesis*, 2000, 1817; (*c*) $SmCl_3$: X.-L. Fu and S.-H. Wu, *Synth. Commun.*, 1997, **27**, 1677; (*d*) $CeCl_3$: L. R. Reddy, M. A. Reddy, N. Bhanumathi and K. R. Rao, *Synthesis*, 2001, 831; (*e*) $BiCl_3$: T. Ollevier and G. Lavie-Compin, *Tetrahedron Lett.*, 2002, **43**, 7891; (*f*) $ZnCl_2$: L. D. Pachón, P. Gamez, J. J. M. van Bassel and J. Reedijk, *Tetrahedron Lett.*, 2003, **44**, 6025; (*g*) VCl_3: G. Sabitha, G. S. K. K. Reddy, K. B. Reddy and J. S. Yadav, *Synthesis*, 2003, 2298; (*h*) $ZrCl_4$: A. K. Chakraborti and A. Kondaskar, *Tetrahedron Lett.*, 2003, **44**, 8315.
13 (*a*) R. Gupta, S. Paul, A. K. Gupta, P. L. Kachroo and A. Dandia, *Ind. J. Chem.*, 1997, **36B**, 281; (*b*) M. M. Mojtahedi, M. R. Saidi and M. Bolourtchian, *J. Chem. Res. (S)*, 1999, 128.
14 U. Das, B. Crousse, V. Kesavan, D. Bonnet-Delpon and J.-P. Bégué, *J. Org. Chem.*, 2000, **65**, 6749.
15 J. S. Yadav, B. V. S. Reddy, A. K. Basak and A. V. Narsaiah, *Tetrahedron Lett.*, 2003, **44**, 1047.
16 R.-H. Fan and X.-L. Hou, *J. Org. Chem.*, 2003, **68**, 726.
17 M. Shi and Y. Chen, *J. Fluorine Chem.*, 2003, **122**, 219.
18 Metal alkylamides induce the rearrangement of epoxides to allylic alcohols. (*a*) J. Yamada, Y. Yomoto and Y. Yamamoto, *Tetrahedron Lett.*, 1989, **30**, 4255; (*b*) J. K. Crandall and M. Apparu, *Org. React.*, 1983, **29**, 345; (*c*) J. K. Whitesel and S. W. Felman, *J. Org. Chem.*, 1980, **45**, 755; (*d*) C. L. Kissel and B. Rickborn, *J. Org. Chem.*, 1972, **37**, 2060.
19 J. Elkington, http://www.sustainability.co.uk/sustainability.httm.
20 G. W. Kabalka and R. M. Pagni, *Tetrahedron*, 1997, **53**, 7999.
21 (*a*) A. McKillop and D. W. Young, *Synthesis*, 1979, 401; (*b*) A. McKillop and D. W. Young, *Synthesis*, 1979, 481.
22 The reported catalysts such as $CoCl_2$, Cu(OTf)$_2$, HFIP, zirconium sulfophenyl phosphonate, $TaCl_5$, $CeCl_3$–NaI, VCl_3, and $BiCl_3$ are not effective for reactions with aliphatic amines.
23 S. A. Anderson, J. T. Ayers, K. M. DeVries, F. Ito, D. Mendenhall and B. C. Vanderplas, *Tetrahedron: Asymmetry*, 1999, **10**, 2655.
24 D. E. McClure, B. H. Arison and J. J. Baldwin, *J. Am. Chem. Soc.*, 1979, **101**, 3666.
25 R. L. Garrett, in *Designing Safer Chemicals*, R. L. Garrett and S. C. De Vilto, eds., American Chemical Society Symposium Series 640, Washington DC, 1996, Chapter 1.
26 X.-L. Hou, J. Wu, L.-X. Dai, L.-J. Xia and M.-H. Tang, *Tetrahedron: Asymmetry*, 1998, **9**, 1747.