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Highly efficient and versatile chemoselective addition of amines to epoxides in water catalyzed by erbium(III) triflate

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Abstract

$Er(OTf)_3$ is proposed as a highly efficient and reusable catalyst for the opening of epoxides in water with aliphatic as well as aromatic amines leading to the synthesis of β-amino alcohols. The aqueous conditions employed in the present method will make it 'environmentally friendly' and potentially useful for industrial applications.

Keywords: Lewis acid catalysis; Erbium(III) triflate; Epoxide; Aminolysis; β-Aminoalcohol

β-Amino alcohols are versatile intermediates in the synthesis of a wide range of biologically active natural and synthetic products.[1–4]

The classical approach, involving the ring opening of epoxides with an excess of amines at elevated temperature, results inadequate for poorly nucleophilic amines,[5] critical to certain functional groups, and also to the control of regioselectivity.[5c,d]

So, to obviate these problems, various methodologies to carry out epoxide opening under milder conditions[6] were developed such as the use of alumina,[7] amides and triflamide,[8] metal alkoxides,[9] metal triflates,[10] various other metal salts,[11] alkali metal perchlorates/tetrafluoroborate,[12] rare earth metal halides,[12] silica under high pressure[13] and many other methods aiming to lower the environmental impact of the process.[14]

However, these methodologies still suffer from one or more disadvantages such as long reaction times, elevated temperatures, high pressures, the use of moisture/air sensitive and costly catalysts and/or stoichiometric amounts of catalysts, potential undesirable side reactions[15,16] moderate yields and/or poor regioselectivities, and additionally in most of the cases, the activity was proved towards aromatic amines or the aliphatic ones only.

Thus, there have been incessant efforts to develop methodologies for the opening of epoxide rings by amines as evidenced by the copious recent reports. 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, and considering the widespread applications of the resultant β-amino alcohols, we felt that a method of choice should be the one that uses a catalyst easily available and less costly, less toxic, operable under environmentally friendly conditions and, if possible, reusable so as to fulfill the 'triple bottom line' philosophy of green chemistry.[4b,17]

As a part of our research to develop Lewis acid-catalyzed methods, we found that erbium(III) compounds are a very useful, environmentally friendly catalyst for several acid-catalyzed reactions.[18] Moreover, erbium(III) triflate works under almost neutral conditions,[19] therefore it is tolerant towards many organic functions. In particular,

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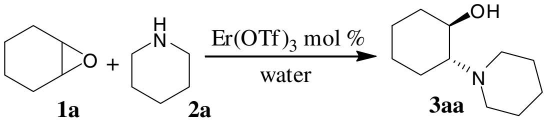
erbium triflate has proved to be a highly efficient and regioselective catalyst for the rearrangement of epoxides to carbonyl compounds.[20] In this context, we have examined erbium triflate as a Lewis acid for the aminolysis of epoxides in water. The use of water as a solvent not only is advantageous being the most 'green' solvent available but also allows a simple, efficient and robust system for the reuse of the catalyst extracted with organic solvents.[21] Some examples of the preparation of β-amino alcohols in water were already reported,[22] although the reactions of aromatic amines with the epoxides resulted to be extremely slow and gave the desired products in very poor yields. Therefore, herein we would like to report a mild, practical and efficient method for the opening of epoxides with aliphatic as well aromatic amines using $Er(OTf)_3$ to promote the reaction, extending what was previously published as simple procedure in water.

Initially, ring opening of cyclohexene oxide **1a** was investigated with piperidine **2a** in water (Scheme 1) at different temperatures and mol % of catalyst to set the better reaction conditions (Table 1). The reaction was carried out with a very simple procedure in 1 mol % of catalyst aqueous solution without adding any organic solvent. The β-amino alcohol **3aa** was extracted from the aqueous solution by diethyl ether. Only little improvement was recorded raising the catalyst up to 5 mol % (Table 1, entry 2), meanwhile quantitative yield was collected in only 2 h performing the reaction at 60 °C (Table 1, entry 3). Noteworthy, only 85% of β-amino alcohol was obtained when the reaction was conducted under the same conditions but without any catalyst (Table 1, entry 4). The trans stereochemistry of the β-amino alcohols **3aa** was deduced from the coupling constants of the ring protons in ^1H NMR spectrum.

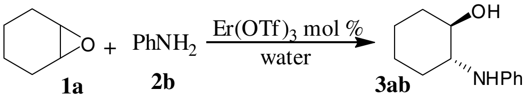
The use of water as a solvent allows a simple and efficient system for the reuse of the catalyst. In fact, after the completion of reaction, the aqueous solution containing the catalyst was extracted with organic solvent, fresh substrate was added and the process was repeated for three cycles with consistent activity (Table 1, entries 5–7).



Scheme 1.

Table 1
Aminolysis of cyclohexene oxide **1a** by aniline **2b**

Entry	Catal. mol (%)	*T* (°C)	*t* (h)	Yield (%)
1	1.0	rt	24	28
2	5.0	rt	24	55
3	5.0	60	8	95
4	—	60	24	Trace
5	1° Recycl.	60	24	92
6	2° Recycl.	60	24	89
7	3° Recycl.	60	24	90



Scheme 2.

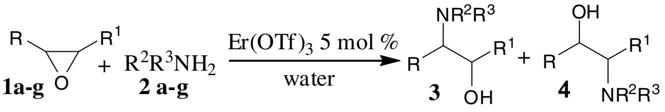
Table 2
Aminolysis of cyclohexene oxide **1a** by piperidine **2a**

Entry	Catal. mol (%)	*T* (°C)	*t* (h)	Yield (%)
1	1.0	rt	16	88
2	5.0	rt	8	90
3	5.0	60	2	>99
4	—	60	2	85
5	1° Recycl.	60	2	95
6	2° Recycl.	60	2	92
7	3° Recycl.	60	2	90

To extend this simple procedure to aromatic amines and optimize the best reaction conditions, cyclohexene oxide **1a** was treated with aniline **2b** in 1 mol % of aqueous solution of $Er(OTf)_3$ at room temperature (Scheme 2). Very poor yields were obtained not only under these experimental conditions but also by using 5 mol % of catalyst (Table 2, entries 1 and 2). However, still, a satisfactory result was registered after 8 h when the reaction was performed at 60 °C in 5 mol % of catalyst aqueous solution (Table 2, entry 3). As expected, no reaction was obtained without any catalyst also after prolonged reaction time (Table 2, entry 4). The trans stereochemistry of the β-amino alcohols **3ab** (Table 1, entry 1) was deduced from the coupling constants of the peaks at 3.27 ppm (ddd, $J = 10.5, 9.4, 4.1$ Hz, CH-NHPh) and 3.35 ppm (ddd, $J = 10.2, 9.7, 4.3$ Hz, CH-OH) in the ^1H NMR spectrum.

Again, after the completion of the reaction, the aqueous solution containing the catalyst was extracted with organic solvent, fresh substrate was added and the process was repeated for three cycles with still good activity (Table 2, entries 5–7).

As reported above,[19] a water solution of $Er(OTf)_3$ is only weakly acidic, nevertheless, it may be possible that the true catalyst is TfOH, released from the hydrolysis of $Er(OTf)_3$. However, the observation that TfOH is not as effective as $Er(OTf)_3$ to catalyze the epoxide opening (1 equiv aniline, 1 equiv cyclohexene epoxide, 10% TfOH, 25 °C, 7 h, 23%) suggests that a Lewis acid is likely involved in activating the epoxide. Encouraged by our results in the nucleophilic opening reaction catalyzed by 5 mol % $Er(OTf)_3$ in water, we studied the scope and limitations of this reaction treating structurally diverse amines with various aliphatic and aromatic epoxides (Scheme 3).



Scheme 3.

In general, the reaction rate of aminolysis in water depends on the structure of the epoxide and on the nucleophilicity. The data in Table 3 clearly show that the reaction of aliphatic and aromatic amines with different epoxides in water gives the corresponding β-amino alcohols in high yield and in a regioselective manner, attaching the less substituted carbon of oxirane (GC/MS). The reaction of epichlorohydrine **1e** (Table 3, entry 20) provided an example of excellent chemoselectivity, affording the amino alcohol corresponding to nucleophilic attack at the terminal carbon of the epoxide moiety. Therefore, no product arising from the nucleophilic displacement of the chlorine could be detected through GC/MS analysis of the reaction mixture.

In some cases, the β-amino alcohols precipitated from the solution and were separated by a simple filtration. Otherwise, they were extracted from the aqueous solution by diethyl ether. All the compounds were fully characterized by GC/MS, and ^{1}H NMR by a comparison with the known compounds.[4b,10f,g,22h]

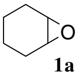
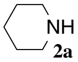
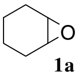
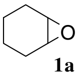
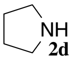
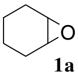
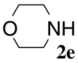
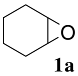
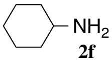
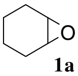
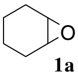
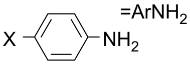
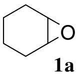
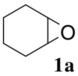
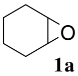
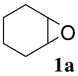
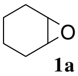
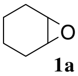
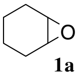
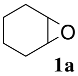
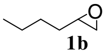
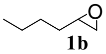
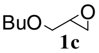
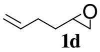
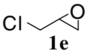
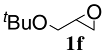
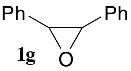
Under the same experimental conditions, the aryl asymmetric oxiranes underwent cleavage by a variety of amines in a regioselective fashion which strongly depend on the nature of nucleophile. Thus, next we planned to evaluate the regioselectivity of the Er(OTf)$_3$-catalyzed ring opening reaction of styrene oxide **1h**, which was chosen as representative unsymmetrical epoxide, with amines (Scheme 4).

In all cases the reactions were completed within 2–8 h at 60 °C (Table 4), affording high yields of the amino alcohols. The major regioisomeric alcohol formed during the reaction of **1h** with aromatic amines was isolated by column chromatography of the crude product isolated from the reaction mixture. However, the regioisomeric amino alcohol formed by the reaction of **1h** with aliphatic amines could not be separated by column chromatography. In each case, the regioselectivity was determined by GC/MS analysis of the crude product mixture. As reported by other authors, the aromatic epoxides gave the major product with the opposite regiochemistry with respect to the aliphatic oxiranes: in these latter ones, steric factors predominate over the electronic ones, meanwhile for aromatic substrates the opposite regiochemistry suggests that electronic factors prevail over steric factors.

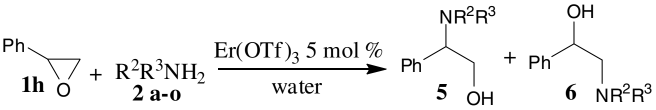
The product from nucleophilic attack at the benzylic carbon showed a fragment of m/z [M$^+$−31] due to the loss of CH$_2$OH, whereas, the characteristic feature in the mass spectra of the products from the reaction at the terminal carbon of the epoxide ring was the ion peak at m/z [M$^+$−106] due to the loss of PhCHO. The formation of the amino alcohol by nucleophilic attack at the terminal carbon of **1h** was further determined by the absorption of the benzylic methine proton at 4.70 ppm in the ^{1}H NMR spectra. The structure of the products was confirmed by GC/MS and ^{1}H NMR by comparison with the known compounds.[4b,10f,14b,22g]

For example, in the reactions with aromatic amines, the benzylic proton of **5** and **6** appeared at δ 4.6 and 5.2,

Table 3
Reactions of aliphatic epoxides with aliphatic and aromatic amines at 60 °C in deionized water

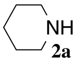
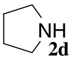
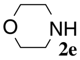
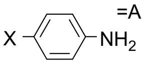
Entry	Epoxide	Amine	t (h)	Yield[a] (%)
1	 **1a**	 **2a**	2	>99
2	 **1a**	BuNH$_2$ **2c**	5	80
3	 **1a**	 **2d**	2	>99
4	 **1a**	 **2e**	2	>99
5	 **1a**	 **2f**	4	93
6	 **1a**	PhCH$_2$NH$_2$ **2g**	2	>99
7	 **1a**	 **2b** :X=H	8	95
8	 **1a**	**2h**: X = CH$_3$	8	92
9	 **1a**	**2i**: X = OCH$_3$	8	90
10	 **1a**	**2j**: X = OH	8	92
11	 **1a**	**2k**: X = Cl	8	95
12	 **1a**	**2l**: X = Br	8	92
13	 **1a**	**2m**: X = NO$_2$	8	90
14	 **1a**	**2n**: Y = CH$_3$	8	92
15	 **1a**	**2o**: Z = CH$_3$	8	90
16	 **1b**	**2b**	8	87 100:0
17	 **1b**	**2h**	8	85 100:0
18	 **1c**	**2h**	8	92 100:0
19	 **1d**	**2b**	8	82 100:0
20	 **1e**	**2b**	8	90 100:0
21	 **1f**	**2b**	8	87 100:0
22	 **1g**	**2b**	8	78

[a] Isolated yields; all the compounds, when necessary, were purified by flash chromatography and the major product was fully characterized by the comparison of their spectral data with the known compounds.[4b,10f,g,22h]



Scheme 4.

Table 4
Reactions of styrene oxide **1h** with aliphatic and aromatic amines at 60 °C in deionized water

Entry	Amine	*t* (h)	Yield[a] (%) **5**:**6**
1	 **2a**	2	>99 0:100
2	$BuNH_2$ **2c**	2.5	93 10:90
3	 **2d**	2.0	97 10:90
4	 **2e**	2.0	95 4:96
5	$PhCH_2NH_2$ **2g**	2.5	90 25:75
6	 $=ArNH_2$ **2b** :X=H	8	95 85:15
7	**2h**: $X = CH_3$	8	93 90:10
8	**2i**: $X = OCH_3$	6	94 88:12
9	**2j**: $X = OH$	6	93 87:13
10	**2k**: $X = Cl$	8	94 95:5
11	**2l**: $X = Br$; $Y, Z = H$	8	92 92:18
12	**2m**: $X = NO_2$; $Y, Z = H$	8	88 93:7
13	**2n**: $Y = CH_3$; $X, Z = H$	6	93 88:12
14	**2o**: $Z = CH_3$; $X, Y = H$	6	92 90:10

[a] Isolated yields; all the compounds, when necessary, were purified by flash chromatography and the major product was fully characterized by the comparison of their spectral data with the known compounds.[4b,10f,14b,22g]

respectively, in the ^1H NMR. During the reaction with aniline, the GC/MS revealed the product to be a mixture of **5** and **6** in a ratio of 85:15 on the basis of the daughter ions at m/z 213–31 and 213–106 corresponding to **5** and **6**, respectively. The signals at δ 3.7–4.1 (m, 4H), 4.46–4.54 (m, 1H), 6.4–7.5 (m, 10H) in the ^1H NMR of the product could be assigned to 2-phenylamino-2-phenylethanol **5** and the values at δ 3.3–3.6 (m, 2H), 4.61 (br s, 2H), 4.87–4.95 (m, 1H), 6.5–7.9 (m, 10H) to 2-phenylamino-1-phenylethanol **6**. A 85:15 ratio could be determined for **5**:**6** taking into consideration the integral values of the corresponding benzylic protons.

$Er(OTf)_3$ was found to be better than other recently reported catalysts in terms of conversion and reaction times. Moreover, due to the mild acidic nature of $Er(OTf)_3$, it works effectively for epoxide ring opening reaction with aliphatic as well as aromatic amines.[23]

In comparison with $Sc(OTf)_3$,[10f] which was one of the most versatile and reactive catalyst recently proposed in the epoxide ring opening with amines, the $Er(OTf)_3$ required prolonged reaction times in the case of the aromatic amines, but showed to be more active with aliphatic ones.

In conclusion, $Er(OTf)_3$ is a highly efficient and reusable catalyst for the opening of epoxides in water with aliphatic as well as aromatic amines leading to the synthesis of β-amino alcohols. The procedure of these reactions is very simple and presents some specific advantages such as low toxicity and low cost, mild reaction conditions in short times and excellent stereo-, regio- and chemoselectivity. The aqueous conditions employed in the present method will make it 'environmentally friendly' and potentially useful for industrial applications.

References and notes

1. (a) Corey, E. J.; Zhang, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 1931–1934; (b) Johannes, C. W.; Visser, M. S.; Weatherhead, G. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 8340–8347; (c) Rogers, G. A.; Parsons, S. M.; Anderson, D. C.; Nilsson, L. M.; Bahr, B. A.; Kornreich, W. D.; Kaufman, R.; Jacobs, R. S.; Kirtman, B. *J. Med. Chem.* **1989**, *32*, 1217–1230; (d) Radesca, L.; Bowen, W. D.; Paolo, L. D.; de Costa, B. R. *J. Med. Chem.* **1991**, *34*, 3058–3065.
2. (a) O'Brien, P. *Angew. Chem., Int. Ed.* **1999**, *38*, 326–329; (b) Li, G.; Chang, H.-T.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **1996**, *35*, 451–454.
3. (a) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835–876; (b) Bloom, J. D.; Dutia, M. D.; Johnson, B. D.; Wissner, A.; Burns, M. G.; Largis, E. E.; Dolan, J. A.; Claus, T. H. *J. Med. Chem.* **1992**, *35*, 3081–3084.
4. (a) Auvin-Guette, C.; Rebuffat, S.; Prigent, J.; Bodo, B. *J. Am. Chem. Soc.* **1992**, *114*, 2170–2174; (b) Pujala, S. B.; Chakaborti, A. K. *J. Org. Chem.* **2007**, *2*, 3713–3722. and references cited therein.
5. (a) Lutz, R. E.; Freek, J. A.; Murphy, R. S. *J. Am. Chem. Soc.* **1948**, *70*, 2015–2023; (b) Freifelder, M.; Stone, G. R. *J. Org. Chem.* **1961**, *26*, 1477–1480; (c) Deyrup, J. A.; Moyer, C. L. *J. Org. Chem.* **1969**, *34*, 175–179; (d) Crooks, P. A.; Szyudler, R. *Chem. Ind. London* **1973**, 1111–1112; (e) Rao, A. S.; Paknikar, S. K.; Kirtane, J. G. *Tetrahedron* **1983**, *39*, 2323–2367; (f) Hanson, R. M. *Chem. Rev.* **1991**, *91*, 437–475; (g) Sello, G.; Orsini, F.; Bernasconi, S.; Di Gennaro, P. *Tetrahedron: Asymmetry* **2006**, *17*, 372–376.
6. (a) Sundrarajan, G.; Vijayakrishna, K.; Varghese, B. *Tetrahedron Lett.* **2004**, *45*, 8253–8256; (b) Surendra, K.; Krishnaveni, N. S.; Rao, K. R. *Synlett* **2005**, 506–510.
7. (a) Posner, G. H.; Rogers, D. Z. *J. Am. Chem. Soc.* **1977**, *99*, 8208–8214; (b) Xue, W. M.; Kung, M. C.; Kozlov, A. I.; Popp, K. E.; Kung, H. H. *Catal. Today* **2003**, *85*, 219–224.
8. (a) Fiorenzo, M.; Ricco, A.; Tadder, M.; Tassi, D. *Synthesis* **1983**, 640–641; (b) Crandall, J. K.; Apparu, M. *Org. React.* **1983**, *29*, 345–443; (c) Kissel, C. L.; Rickborn, B. *J. Org. Chem.* **1972**, *37*, 2060–2063; (d) Yamamoto, Y.; Asao, N.; Meguro, M.; Tsukade, N.; Nemoto, H.; Adayari, N.; Wilson, J. G.; Nakamura, H. *J. Chem. Soc., Chem. Commun.* **1993**, 1201–1203; (e) Cossy, J.; Bellosta, V.; Hamoir, C.; Desmurs, J.-R. *Tetrahedron Lett.* **2002**, *43*, 7083–7086.

9. (a) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557–1560; (b) Vidal-Ferran, A.; Moyano, A.; Pericas, M. A.; Riera, A. *J. Org. Chem.* **1997**, *62*, 4970–4982; (c) Sagawa, S.; Abe, H.; Hase, Y.; Inaba, T. *J. Org. Chem.* **1999**, *64*, 4962–4965; (d) Rampalli, S.; Chaudhari, S. S.; Akamanchi, K. G. *Synthesis* **2000**, 78–80.
10. (a) Fujiwara, M.; Imada, M.; Baba, A.; Matsuda, H. *Tetrahedron Lett.* **1989**, *30*, 739–742; (b) Cepanec, I.; Litvić, M.; Mikuldaš, H.; Bartolinčić, A.; Vinković, V. *Tetrahedron* **2003**, *59*, 2435–2439; (c) Meguro, M.; Asao, N.; Yamamoto, Y. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2597–2601; (d) Hou, X.-L.; Wu, J.; Dai, L.-X.; Xia, L.-J.; Tang, M.-H. *Tetrahedron: Asymmetry* **1998**, *9*, 1747–1752; (e) Auge, J.; Leroy, F. *Tetrahedron Lett.* **1996**, *37*, 7715–7716; (f) Placzek, A. T.; Donelson, J. L.; Trivedi, R.; Gibbs, R. A.; De, S. K. *Tetrahedron Lett.* **2005**, *46*, 9029–9034; (g) Sekar, G.; Singh, V. K. *J. Org. Chem.* **1999**, *64*, 287–289; (h) Chini, M.; Crotti, P.; Favero, L.; Macchia, F.; Pineschi, M. *Tetrahedron Lett.* **1994**, *35*, 433–436; (i) Ollevier, T.; Lavie-Compin, G. *Tetrahedron Lett.* **2004**, *45*, 49–52; (j) Khodaei, M. M.; Khosropour, A. R.; Ghozati, K. *Tetrahedron Lett.* **2004**, *45*, 3525–3529.
11. (a) Reddy, R.; Reddy, M. A.; Bhanumathi, N.; Rama Rao, K. *Synthesis* **2001**, 831–832; (b) Iqbal, J.; Pandey, A. *Tetrahedron Lett.* **1990**, *31*, 575–576; (c) Chandrasekhar, S.; Ramachandar, T.; Prakash, S. J. *Synthesis* **2000**, 1817–1818; (d) Ollevier, T.; Lavie-Compin, G. *Tetrahedron Lett.* **2002**, *43*, 7891–7893; (e) McCluskey, A.; Leitch, S. K.; Garner, J.; Caden, C. E.; Hill, T. A.; Odell, L. R.; Stewart, S. G. *Tetrahedron Lett.* **2005**, *46*, 8229–8232; (f) Fagnou, K.; Lautens, M. *Org. Lett.* **2000**, *2*, 2319–2321; (g) Chakraborti, A. K.; Kondaskar, A. *Tetrahedron Lett.* **2003**, *44*, 8315–8319; (h) Zhao, P.-Q.; Xu, L.-W.; Xia, C.-G. *Synlett* **2004**, 846–850; (i) Rodriquez, J. R.; Navarro, A. *Tetrahedron Lett.* **2004**, *45*, 7495–7498; (j) Kamal, A.; Ramu, R.; Amerudin Azhar, M.; Ramesh Khanna, G. B. *Tetrahedron Lett.* **2005**, *46*, 2675–2677; (k) Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Eur. J. Org. Chem.* **2001**, 4149–4152.
12. (a) Chini, M.; Crotti, P.; Macchia, F. *Tetrahedron Lett.* **1990**, *31*, 4661–4664; (b) Chini, M.; Crotti, P.; Macchia, F. *J. Org. Chem.* **1991**, *56*, 5939–5942; (c) Chini, M.; Crotti, P.; Flippin, L. A.; Macchia, F. *J. Org. Chem.* **1991**, *56*, 7043–7048.
13. (a) Kotsuki, H.; Hayashida, K.; Shimanouchi, T.; Nishizawa, H. *J. Org. Chem.* **1996**, *61*, 984–990; (b) Chakraborti, A. K.; Rudrawar, S.; Kondaskar, A. *Org. Biomol. Chem.* **2004**, *2*, 1277–1280.
14. (a) Fan, R.-H.; Hou, X.-L. *J. Org. Chem.* **2003**, *68*, 726–730; (b) Mojtahedi, M. M.; Saidi, M. R.; Bolourtchian, M. *J. Chem. Res. (S)* **1999**, 128–129; (c) Gupta, R.; Paul, S.; Kachroo, P. L.; Dandia, A. *Ind. J. Chem.* **1997**, *36B*, 281–283; (d) Das, U.; Crousse, B.; Kesavan, V.; Bonnet-Delpon, D.; Begue', J.-P. *J. Org. Chem.* **2000**, *65*, 6749–6751; (e) Yadav, J. S.; Reddy, B. V. S.; Basak, A. K.; Narsaiah, A. V. *Tetrahedron Lett.* **2003**, *44*, 1047–1050; (f) Reddy, L. R.; Reddy, M. A.; Bhanumathi, N.; Rama Rao, K. *Synlett* **2000**, 339–340; (g) Azizi, N.; Saidi, M. R. *Org. Lett.* **2005**, *7*, 3649–3651.
15. Harris, C. E.; Fisher, G. B.; Beardsley, D.; Lee, L.; Goralsky, C. T.; Nicholson, L. W.; Singaram, B. *J. Org. Chem.* **1994**, *59*, 7746–7751.
16. Atkins, R. K.; Frazier, J.; Moore, L. L. *Tetrahedron Lett.* **1986**, *27*, 2451–2454.
17. Elkington, J. http://www.sustainability.co.uk/sustainability.htm.
18. (a) Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Nardi, M.; Procopio, A.; Tagarelli, A. *Synthesis* **2004**, 496–498; (b) Procopio, A.; Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Russo, B.; Sindona, G. *Adv. Synth. Catal.* **2004**, *346*, 1465–1470; (c) Dalpozzo, R.; De Nino, A.; Nardi, M.; Russo, B.; Procopio, A. *Synthesis* **2006**, *2*, 1127–1129; (d) De Nino, A.; Dalpozzo, R.; Maiuolo, L.; Procopio, A.; Tagarelli, A.; Bartoli, G. *Eur. J. Org. Chem.* **2004**, 2176–2180; (e) Procopio, A.; Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Nardi, M.; Romeo, G. *Org. Biomol. Chem.* **2005**, *3*, 4129–4133; (f) Procopio, A.; Dalpozzo, R.; De Nino, A.; Nardi, M.; Russo, B.; Tagarelli, A. *Synthesis* **2006**, *2*, 332–338; (g) Dalpozzo, R.; De Nino, A.; Nardi, M.; Russo, B.; Procopio, A.; Tagarelli, A. *Arkivok* **2006**, *vi*, 181–189; (h) Procopio, A.; Dalpozzo, R.; De Nino, A.; Nardi, M.; Oliverio, M.; Russo, B. *Synthesis* **2006**, *15*, 2608–2612; (i) Procopio, A.; Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Oliverio, M.; Russo, B.; Tocci, A. *Aust. J. Chem.* **2007**, *60*, 75–79; (j) Procopio, A.; Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Nardi, M.; Oliverio, M.; Russo, B. *Carbohydr. Res.* **2007**, *342*, 2125–2131.
19. A 0.1 M water solution of $Er(OTf)_3$ is only weakly acidic (pH ca. 5.9), and the aqueous layer from work-up is even less acidic (pH ca. 6.6).
20. (a) Procopio, A.; Dalpozzo, R.; De Nino, A.; Nardi, M.; Sindona, G.; Tagarelli, A. *Synlett* **2004**, 2633–2635; (b) Procopio, A.; Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Nardi, M.; Russo, B. *Adv. Synth. Catal.* **2005**, *346*, 1447–1450; (c) Dalpozzo, R.; De Nino, A.; Nardi, M.; Russo, B.; Procopio, A. *Arkivok* **2006**, *vi*, 67–73.
21. (a) Li, C.-J. *Chem. Rev.* **2005**, *105*, 3095–3166; (b) Firouzabadi, H.; Iranpoor, N.; Jafari, A. A. *Adv. Synth. Catal.* **2005**, *347*, 655–661; (c) Manabe, K.; Limura, S.; Sun, X.-M.; Kobayashi, S. *J. Am. Chem. Soc.* **2002**, *124*, 11971–11978; (d) Li, C. J.; Chang, T. H. *Organic Reactions in Aqueous Media*; Wiley: New York, 1997; (e) *Organic Synthesis in Water*; Grieco, P. A., Ed.; Blackie Academic and Professional: London, UK, 1998; (f) Ribe, S.; Wipf, P. *Chem. Commun.* **2001**, 299–307.
22. (a) Azizi, N.; Saidi, M. R. *Organometallics* **2004**, *23*, 1457–1458; (b) Azizi, N.; Saidi, M. R. *Tetrahedron* **2004**, *60*, 383–387; (c) Azizi, N.; Saidi, M. R. *Eur. J. Org. Chem.* **2003**, 4630–4633; (d) Azizi, N.; Saidi, M. R. *J. Organomet. Chem.* **2003**, *688*, 283–285; (e) Azizi, N.; Rajabi, F.; Saidi, M. R. *Tetrahedron Lett.* **2004**, *45*, 9233–9236; (f) Azizi, N.; Saidi, M. R. *Org. Lett.* **2005**, *7*, 3649–3651; (g) Bonollo, S.; Fringuelli, F.; Pizzo, F.; Vaccaro, L. *Green Chem.* **2006**, *8*, 960–964; (h) Azizi, N.; Saidi, M. *Tetrahedron* **2007**, *63*, 888–891.
23. *Experimental*: The general procedure for the β-amino alcohol synthesis can be described as follows: $Er(OTf)_3$ (30.7 mg, 5 mol %) was added to a magnetically stirred mixture of epoxide **1a**–**h** (1.0 mmol) and amine **2a**–**o** (1.1 mmol) in the deionized water (0.5 mL) at 60 °C for 2–8 h. After the completion of the reaction (GC/MS, TLC), the reaction mixture was extracted with diethyl ether or dichloromethane, dried over anhydrous sodium sulfate, filtered and concentrated under vacuum (rotary evaporator). The residue was purified by column chromatography on silica gel using chloroform as eluent. All the compounds were fully characterized by IR, GC/MS and ^{1}H NMR by a comparison with the known compounds.[4b,10f,g,14b,22h,g] After reaction workup the aqueous phase can be evaporated under reduced pressure to furnish the erbium salt in 90% recovered yield, as pale pink solid. The purity of recovered $Er(OTf)_3$ was confirmed by comparison with the IR spectrum of the commercial product and, after drying over P_2O_5 overnight, it was reused three times in the reaction of **1a** with recovered yields of **3ab** always almost 90%.