Erbium(III) Triflate is a Highly Efficient Catalyst for the Synthesis of β-Alkoxy Alcohols, 1,2-Diols and β-Hydroxy Sulfides by Ring Opening of Epoxides

Renato Dalpozzo,[a] Monica Nardi,*[a] Manuela Oliverio,[b] Rosina Paonessa,[b] Antonio Procopio[b]

[a] Dipartimento di Chimica, Università della Calabria, ponte Bucci cubo 12/c, 87030 Arcavacata di Rende (Cs), Italy
Fax +39(0984)493077; E-mail: nardi@unical.it

[b] Dipartimento Farmacobiologico, Università della Magna Graecia, Complesso Ninì Barbieri, 88021 Roccelletta Di Borgia (CZ), Italy

Received 25 May 2009; revised 19 June 2009

Dedicated to Professor Giovanni Sindona on the occasion of his 60th birthday

Abstract: Chemo- and stereoselectivity in the ring-opening reaction of epoxides with erbium(III) triflate are described. Epoxides can be cleaved under neutral conditions with alcohols and thiols in the presence of catalytic amounts of Lewis acid, affording the corresponding β-alkoxy alcohols and β-hydroxy sulfides in high yields. In water, epoxide ring opening occurs to produce the corresponding diols in good yields

Key words: epoxides, Lewis acids, nucleophilic additions, ring opening, green chemistry

Epoxides play an increasingly pivotal role in organic synthesis as versatile synthetic intermediates. Their ring-opening reaction is an important process in organic transformations that is widely applied in pharmaceutical[1] and natural product chemistry.[2] The inherent polarity and strain of the three-membered oxirane ring make them susceptible to reaction with a wide number of reagents, including nucleophiles, acids, bases, reducing and oxidizing agents.[3]

Epoxide ring-opening reactions to give β-amino alcohols,[4] 1,2-diacetates,[5] and carbonyl compounds,[6] as well as hydrolysis,[7] alcoholysis,[8] and thiolysis[9] are convenient, practical and widely employed strategies for the synthesis of important classes of intermediates in organic chemistry.

In spite of their respective features, the reported methods for the preparation of 1,2-diol, β-alkoxy alcohols and β-hydroxy sulfides, in particular, suffer from drawbacks in one way or another. The widespread applicability of such reactions in most cases is, however, restricted by the handling of toxic and/or expensive reagents, intolerance to highly sensitive groups, the formation of unwanted by-products and, for thiolysis in particular, the need to adopt an appropriate pH value that ensures good regioselectivity and minimizes the formation of side-products.

Recently, organic reactions using reusable and water-tolerant catalysts have received much attention. Furthermore, employing simple catalysts with high activity, under solvent-free conditions is an ideal green methodology.[10]

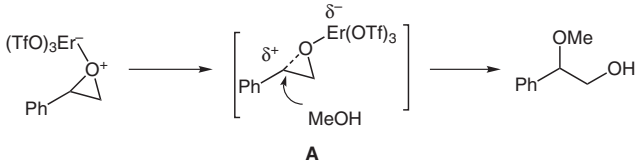
In the course of our research program on Lewis acid catalyzed reactions, we found that erbium triflate is a very useful, environmentally friendly catalyst for several acid-catalyzed reactions.[11] Moreover, erbium(III) triflate works under almost neutral conditions,[12] and is therefore tolerant towards many organic functional groups.

Owing to its unique qualities, erbium triflate has already proven to be a highly efficient and regioselective catalyst for many reactions involving epoxides, such as the rearrangement to carbonyl compounds,[13] the synthesis of acetonides,[14] the conversion into 1,2-diacetates,[15] and the preparation of β-amino alcohols.[16]

In this paper, we wish to report that erbium(III) triflate [$Er(OTf)_3$] can act as a mild and efficient Lewis acid catalyst for the regio- and stereoselective ring opening of epoxides with both oxygen and sulfur nucleophiles such as water, primary, secondary, tertiary or aromatic alcohols and thiols.

The reaction of styrene oxide (**1a**) with methanol in the presence of only 0.1 mol% $Er(OTf)_3$ proceeded smoothly under mild conditions with excellent conversion in a short reaction time. When the reaction was performed in the absence of $Er(OTf)_3$, **1a** was recovered entirely unreacted, whereas higher catalyst amounts (1 mol%) allowed **1a** to rearrange to the carbonyl compound.[13] Almost equimolecular amounts of reagents or slight excess of alcohol form a homogeneous mixture, so the reaction can be considered to be solvent-free.

It is noteworthy that 2-methoxy-2-phenylethanol (**3aa**) was almost exclusively obtained, proving the high degree of regioselectivity achieved in this reaction (Table 1). On the other hand, upon the addition of amines to **1a**, a mixture of regioisomers was generally obtained where the formation of either isomer could prevail depending from the nature of the amine.[16]

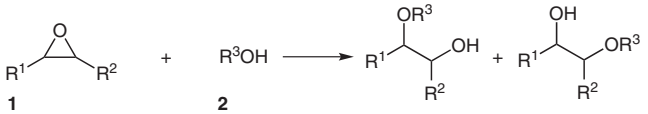


A

Scheme 1

SYNTHESIS 2009, No. 20, pp 3433–3438
Advanced online publication: 21.08.2009
DOI: 10.1055/s-0029-1216956; Art ID: Z11109SS

Table 1 Alcoholysis and Hydrolysis of Epoxides by $Er(OTf)_3$ at Room Temperature[a]



1
a: R^1 = Ph, R^2 = H
b: R^1–R^2= -$(CH_2)_4$-
c: R^1 = $PhOCH_2$, R^2 = H
d: R^1 = $AllOCH_2$, R^2 = H
e: R^1 = Bu, R^2 = H

2
a: R^3 = Me
b: R^3 = Et
c: R^3 = *i*-Pr
d: R^3 = *t*-Bu
e: R^3 = C_6H_{11}
f: R^3 = Ph
g: R^3 = Bn
h: R^3 = H

3

4

Entry	Epoxide	R^3OH[b]	Product	Time (min)	Yield (%)[c]	**3/4**
1	**1a**	**2a**	**aa**	30	100	100:0
2		**2b**	**ab**	45	100	100:0
3		**2c**	**ac**	90	100	100:0
4		**2d**	**ad**	90	80	100:0
5		**2e**	**ae**	180	100	100:0
6		**2f**[d]	**af**	1440	100	100:0
7		**2g**	**ag**	60	75	100:0
8		**2h**[e]	**ah**	30	100	–
9	**1b**	**2a**	**ba**	45	100	
10		**2b**	**bb**	45	100	
11		**2c**	**bc**	60	100	
12		**2d**	**bd**	120	67	
13		**2e**	**be**	360	95	
14		**2f**[d]	**bf**	2880	80	
15		**2g**	**bg**	60	100	
16		**2h**[e]	**bh**	60	100	
17	**1c**	**2a**	**ca**	30	100	0:100
18		**2b**	**cb**	45	90	0:100
19		**2c**	**cc**	60	90	0:100
20		**2d**	**cd**	150	59	0:100
21		**2e**	**ce**	580	85	0:100
22		**2f**[d]	**cf**	2880	70	0:100
23		**2g**	**cg**	90	70	0:100
24		**2h**[e]	**ch**	60	100	–
25	**1d**	**2a**	**da**	90	75	0:100
26		**2b**	**db**	90	70	0:100
27		**2c**	**dc**	90	70	0:100
28		**2d**	**dd**	220	76	0:100
29		**2e**	**de**	120	80	0:100
30		**2f**[d]	**df**	1440	70	0:100
31		**2g**	**dg**	90	70	0:100
32		**2h**[e]	**dh**	90	75	–
33	**1e**	**2a**	**ea**	90	75	0:100
34		**2b**	**eb**	90	70	0:100
35		**2c**	**ec**	90	70	0:100
36		**2d**	**ed**	180	65	0:100
37		**2e**	**ee**	120	90	0:100
38		**2f**[d]	**ef**	1440	90	0:100
39		**2g**	**eg**	120	70	0:100
40		**2h**[e]	**eh**	60	100	–

[a] Catalyst: 0.1 mol% (entries 1–8) or 1 mol% (entries 9–40).
[b] Alcohol: 1.2 mol per mole of **1**. Solvent-free.
[c] Isolated yield based on epoxides.
[d] Et_2O as solvent.
[e] H_2O–MeCN mixture.

The present results appear to have come about as an obvious consequence of the involvement of a carbonium ion intermediate that is formed by a Lewis acid assisted ring-opening reaction.[17] The Er(OTf)$_3$-catalyzed ring opening of an unsymmetrically polarized epoxide proceeds via cleavage of the C–O bond in a manner that gives the best stabilization of the developing positive charge (structure **A**, Scheme 1). Thus, the benzylic position is the favored site for the nucleophilic attack of methanol (**2a**), which gives rise to the formation of 2-methoxy-2-phenylethan-1-ol (**3aa**) with essentially complete regioselectivity.

In order to extend this simple procedure, we decided to investigate the ring-opening reaction of styrene oxide (**1a**) using several other alcohols (**2b–g**) and water (**2h**) (Table 1, entries 2–8). Among the tested compounds, small alcohols and water generally gave the best yields and the shortest reaction times. As the alkyl group of the alcohol became bulkier, the reaction times increased, thus, the ring-opening reaction with *tert*-butanol produced β-hydroxy ether (**3ad**) in only low yield (Table 1, entry 4).

Nucleophilic attack of the alcohol on the benzylic site of the epoxide might be controlled by steric constraints and it is quite clear that a bulky alkyl group on the alcohol retards the reaction due to bulkiness. It is worth noting that, on the other hand, crowded amines did not decrease yield but inverted the regiochemistry.[16]

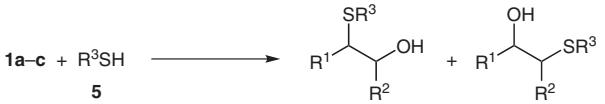
In addition, an electronic effect seemed to affect epoxide ring opening. In fact, attack of the less nucleophilic phenol (**2f**) produced the β-hydroxy ether (**3af**) after very long reaction times (Table 1, entry 6). However, this reaction was carried out in ethereal solution, because the reagents did not dissolve each other, so the influence of solvent could be invoked to explain this behavior.

In order to increase the merit of the present method, the procedure was then applied successfully to various 1,2-epoxides (**1b–e**) and, as expected because of the mild conditions employed, it was found to be compatible with substrates containing delicate functionalities (Table 1, entries 9–40). Yields and reaction times followed a trend similar to those obtained with styrene oxide.

In these reactions 1 mol% of catalyst was employed in order to ensure comparable reaction times and yields. It is well-established that rearrangement is much slower with aliphatic epoxides.[13]

As expected, the aliphatic oxiranes gave major products with the opposite regiochemistry to those obtained from aromatic epoxides: in the former, steric factors predominate over electronic effects.

Table 2 Thiolysis of Epoxides in Acetonitrile Using 1 mol% of Er(OTf)$_3$ at Room Temperature



Entry	Epoxide	R^2SH[a]	Product	Time (min)	Yield (%)[b]	**6/7**
1	**1a**	**5a**	**aa**	30	98	100:0
2		**5b**[c]	**ab**	1220	100	100:0
3		**5c**	**ac**	45	100	98:2
4		**5d**	**ad**	560	100	100:0
5		**5e**	**ae**	60	100	45:55
6		**5f**	**af**	30	100	43:57
7	**1b**	**5a**	**ba**	120	65	
8		**5b**[c]	**bc**	90	70	
9		**5c**	**bd**	90	70	
10		**5d**	**be**	560	86	
11		**5e**	**bf**	120	75	
12		**5f**		120	60	
13	**1c**	**5a**	**ca**	90	75	0:100
14		**5b**[c]	**cb**	90	68	0:100
15		**5c**	**cc**	98	78	0:100
16		**5d**	**cd**	560	83	0:100
17		**5e**	**ce**	120	85	0:100
18		**5f**	**cf**	120	85	0:100

[a] Thiol: 1.1 mol per mole of **1**.
[b] Isolated yield based on epoxides.

The same reaction was then extended to ring opening of epoxides with thiols to produce β-hydroxysulfides. Reaction conditions ware slightly modified in order to ensure homogeneity of the mixture, by adding a little acetonitrile as solvent.

Significantly, the reaction with **1a** did not show rearrangement to the carbonyl compound with 1 mol% of catalyst.

Yields were always found to be good to excellent and regioselectivity was complete in the aliphatic epoxide **1c**. In contrast, styrene oxide (**1a**) showed significant loss of selectivity with long-chain thiols (Table 2, entries 5–6).

In conclusion, erbium(III) triflate provides a genuinely 'green', economically convenient, practical and regioselective method for alcoholysis of epoxides under solvent-free conditions. Hydrolysis and thiolysis need low amounts of solvent, without diminishing the merit of the protocol. The present procedure does not need sophisticated equipment, and uses a non-toxic catalyst. The catalyst can be easily and consistently recovered,[13–16] so significant release into the environment can be avoided.

^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker WM300 instrument operating at 300 MHz and 75 MHz, respectively. Chemical shift (δ) are given in ppm from TMS as internal standard, coupling constants (*J*) are given in Hertz. Reactions were monitored by a GC-MS Shimadzu workstation fitted with a GC 2010 (30 m, QUADREX 007-5MS capillary column, operating in splitless mode; 1 mL/min flow of He as carrier gas) and a 2010 quadrupole mass-detector. Commercial reagents (Aldrich or Fluka) were used without further purification.

β-Hydroxy Ether Synthesis; General Procedure

To a solution of epoxide **1a–e** (1 mmol) in the appropriate alcohol **2a–d** or **2f**,**g** (1.2 mmol), $Er(OTf)_3$ (0.1 mmol) was added and the mixture was stirred at 25 °C (reaction was monitored by TLC). Sat. $NaHCO_3$ (30 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 15 mL). The organic layer was separated and dried with Na_2SO_4. Evaporation of the solvent followed by chromatography on a short silica gel column gave the corresponding product.

Phenol (**2e**) and **1a–e** gave heterogeneous mixtures, so Et_2O (2 mL) was added to ensure solubility. Upon completion, the solvent was removed by rotary evaporation and the residue treated as above.

1,2-Diol Synthesis; General Procedure

To a solution of **1a–e** (1 mmol) in MeCN–H_2O (1:1, 2 mL), $Er(OTf)_3$ (0.1 mmol) was added and the mixture was stirred at 25 °C (reaction monitored by TLC). After completion of the reaction, the solution was extracted with EtOAc (3 × 15 mL). The organic layer was separated and dried with Na_2SO_4. Evaporation of the solvent followed by chromatography on a short silica gel column gave the corresponding product.

β-Hydroxysulfide Synthesis; General Procedure

To a solution of **1a–c** (1 mmol) in MeCN (2 mL), the appropriate thiol **5a–f** (1.1 mmol) and $Er(OTf)_3$ (0.1 mmol) were added and the mixture was stirred at 25 °C (reaction monitored by TLC). After completion of the reaction, solvent was evaporated under reduced pressure. Sat. $NaHCO_3$ (30 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 15 mL). The organic layer was separated and dried with Na_2SO_4. Evaporation of the solvent followed by chromatography on a short silica gel column gave the corresponding product.

All known products were identified by comparison of their EI-MS and ^{1}H NMR spectral data with literature reported data: **3aa**,[8d] **3ab**,[8d] **3ac**,[8d] **3ad**,[8d] **3ae**,[17c] **3af**,[17c] **3ag**,[17c] **3ba**,[8d] **3bb**,[8d] **3bc**,[8d] **3bd**,[8d] **3be**,[17c] **3bf**,[17c] **3bg**,[17c] **4ca**,[8d] **4cb**,[8d] **4cc**,[8d] **4cd**,[8d] **4ce**,[17c] **4cf**,[17c] **4cg**,[17c] **4da**,[8d] **4db**,[8d] **4dc**,[8d] **4dd**,[8d] **4de**,[17c] **4df**,[17c] **4dg**,[17c] **4ea**,[17c] **4eb**,[17c] **4ec**,[17c] **4ed**,[17c] **4ee**,[17c] **4ef**,[17c] **4eg**,[17c] **6aa**,[18] **6ab**,[9i] **6ac**,[9j] **7ac**,[9j] **6ad**,[9j] **6ba**,[18] **6bb**,[9j] **6bc**,[9j] **6bd**,[9j] **6be**,[19] **6bf**,[19] **7cb**,[9j] **7cc**,[9j] and **7cd**.[9j]

Diols **3ah–eh** were identical to authentic compounds.

2-(Octylthio)-2-phenylethanol (6ae)

Colorless oil.

^{1}H NMR ($CDCl_3$): δ = 0.83–0.92 (m, 3 H), 1.18–1.29 (m, 8 H), 1.32–1.40 (m, 2 H), 1.45–1.65 (m, 2 H), 2.53 (t, *J* = 7.27 Hz, 2 H), 3.80–3.88 (m, 2 H), 3.93 (dd, *J* = 8.07, 6.06 Hz, 1 H), 7.25–7.31 (m, 5 H).

^{13}C NMR ($CDCl_3$): δ = 140.80 (C), 130.40 (2 × CH), 128.34 (CH), 125.49 (2 × CH), 66.39 (CH_2), 53.10 (CH), 32.56 (CH_2), 31.97 (CH_2), 29.88 (CH_2), 28.18 (CH_2), 24.97 (CH_2), 23.37 (CH_2), 21.75 (CH_2), 14.80 (CH_3).

MS (EI): *m*/*z* (%) = 266 (1) [M$^+$], 145 (68), 107 (100), 103 (20), 91 (14), 79 (58), 77 (32).

2-(Hexylthio)-2-phenylethanol (6af)

Colorless oil.

^{1}H NMR ($CDCl_3$): δ = 0.81–0.92 (m, 3 H), 1.20–1.40 (m, 6 H), 1.45–1.65 (m, 2 H), 2.40 (t, *J* = 7.27 Hz, 2 H), 3.80–3.88 (m, 2 H), 3.95 (dd, *J* = 7.67, 6.06 Hz, 1 H), 7.23–7.25 (m, 5 H).

^{13}C NMR ($CDCl_3$): δ = 140.59 (C), 129.80 (2 × CH), 128.22 (CH), 125.51 (2 × CH), 71.50 (CH_2), 53.00 (CH), 32.95 (CH_2), 32.05 (CH_2), 30.58 (CH_2), 29.24 (CH_2), 23.26 (CH_2), 15.00 (CH_3).

MS (EI): *m*/*z* (%) = 238 (1) [M$^+$], 132 (74), 117 (61), 107 (100), 84 (43), 79 (71).

2-(Octylthio)-1-phenylethanol (7ae)

Colorless oil.

^{1}H NMR ($CDCl_3$): δ = 0.83–0.92 (m, 3 H), 1.18–1.29 (m, 8 H), 1.32–1.40 (m, 2 H), 1.45–1.65 (m, 2 H), 2.42 (t, *J* = 7.27 Hz, 2 H), 2.72 (dd, *J* = 13.72, 9.69 Hz, 1 H), 2.92 (dd, *J* = 13.72, 3.63 Hz, 1 H), 4.71 (ddd, *J* = 9.69, 3.64, 2.42 Hz, 1 H), 7.23–7.25 (m, 5 H).

^{13}C NMR ($CDCl_3$): δ = 143.30 (C), 129.75 (2 × CH), 127.61 (CH), 125.44 (2 × CH), 71.90 (CH), 34.14 (CH_2), 31.97 (CH_2), 30.38, 29.88 (CH_2), 28.18 (CH_2), 24.97 (CH_2), 23.37 (CH_2), 21.75 (CH_2), 14.80 (CH_3).

MS (EI): *m*/*z* (%) = 266 (6) [M$^+$], 235 (100), 145 (3), 123 (21), 121 (21), 103 (34), 91 (84), 77 (13).

2-(Hexylthio)-1-phenylethanol (7af)

Colorless oil.

^{1}H NMR ($CDCl_3$): δ = 0.81–0.92 (m, 3 H), 1.20–1.40 (m, 6 H), 1.45–1.65 (m, 2 H), 2.52 (t, *J* = 7.27 Hz, 2 H), 2.70 (dd, *J* = 9.63, 9.29 Hz, 1 H), 2.92 (dd, *J* = 13.72, 3.63 Hz, 1 H), 4.73 (dd, *J* = 9.69, 3.63 Hz, 1 H), 7.23–7.25 (m, 5 H).

^{13}C NMR ($CDCl_3$): δ = 143.35 (C), 130.57 (2 × CH), 127.71 (CH), 125.28 (2 × CH), 73.33 (CH), 33.05 (CH_2), 32.95 (CH_2), 32.05 (CH_2), 30.58 (CH_2), 29.24 (CH_2), 23.26 (CH_2), 15.00 (CH_3).

MS (EI): *m*/*z* (%) = 238 (9) [M$^+$], 207 (100), 122 (31), 117 (3), 107 (3), 103 (38), 91 (88), 77 (17).

1-(Cyclohexylthio)-3-phenoxypropan-2-ol (7ca)

Colorless oil.

^{1}H NMR ($CDCl_3$): δ = 1.22–1.34 (m, 6 H), 1.71–1.76 (m, 4 H), 1.96–1.98 (m, 1 H), 2.73 (dd, *J* = 13.72, 6.86 Hz, 1 H), 2.88 (dd, *J* =

13.72, 5.25 Hz, 1 H), 3.99–4.08 (m, 3 H), 6.89–6.93 (m, 3 H), 7.25–7.29 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 159.31 (C), 130.05 (2 × CH), 121.99 (CH), 116.45 (2 × CH), 71.00 (CH_2), 68.77 (CH), 45.65 (CH), 34.61 (CH_2), 28.33 (2 × CH_2), 26.50 (2 × CH_2), 25.21 (CH_2).

MS (EI): *m*/*z* (%) = 266 (15) [M^+], 245 (25), 173 (21), 155 (100), 133 (53), 94 (61), 83 (81), 55 (63).

1-(Octylthio)-3-phenoxypropan-2-ol (7ce)
Colorless oil.

^{1}H NMR ($CDCl_3$): δ = 0.86 (t, *J* = 6.45 Hz, 3 H), 1.27–1.28 (m, 8 H), 1.33–1.35 (m, 2 H), 1.55–1.59 (m, 2 H), 2.54 (t, *J* = 7.27 Hz, 2 H), 2.73 (dd, *J* = 13.72, 7.27 Hz, 1 H), 2.85 (d, *J* = 6.06 Hz, 1 H), 4.00–4.10 (m, 3 H), 6.82–6.99 (m, 3 H), 7.22–7.32 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 159.12 (C), 130.15 (2 × CH), 123.20 (CH), 116.39 (2 × CH), 71.18 (CH_2), 70.40 (CH), 33.44 (CH_2), 32.62 (CH_2), 32.01 (CH_2), 29.62 (CH_2), 28.13 (CH_2), 25.04 (CH_2), 21.75 (CH_2), 15.61 (CH_2), 14.00 (CH_3).

MS (EI): *m*/*z* (%) = 296 (16) [M^+], 278 (19), 203 (67), 185 (100), 159 (6), 145 (5), 133 (66), 107 (20), 105 (14), 94 (40), 77 (26), 69 (27), 57 (27), 43 (51).

1-(Hexylthio)-3-phenoxypropan-2-ol (7cf)
Colorless oil.

^{1}H NMR ($CDCl_3$): δ = 0.81–0.92 (m, 3 H), 1.53–1.63 (m, 2 H), 2.54 (t, *J* = 7.27 Hz, 2 H), 2.71 (dd, *J* = 13.72, 7.27 Hz, 1 H), 2.82 (dd, *J* = 13.72, 4.84 Hz, 1 H), 4.10 (m, 3 H), 6.91 (m, 3 H), 7.25 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 159.13 (C), 130.20 (2 × CH), 121.0 (CH), 116.36 (2 × CH), 71.14 (CH_2), 68.53 (CH), 34.75 (2 × CH_2), 33.76 (CH_2), 30.41 (CH_2), 23.28 (CH_2), 15.52 (CH_2), 13.97 (CH_3).

MS (EI): *m*/*z* (%) = 268 (22) [M^+], 250 (29), 175 (72), 157 (100), 133 (74), 107 (24), 94 (54), 77 (43), 43 (99).

References

(1) (a) Smith, J. G. *Synthesis* **1984**, 629. (b) Luly, J. R.; Yi, N.; Soderquist, J.; Stein, H.; Cohen, J.; Perun, T. J.; Plattner, J. J. *J. Med. Chem.* **1987**, *30*, 1609. (c) Corey, E. J.; Cheng, X.-M. *The Logic of Chemical Synthesis*; Wiley: New York, **1989**. (d) Jones, R. J.; Rapoport, H. *J. Org. Chem.* **1990**, *55*, 1144. (e) Jaramillo, C.; Chiara, J. L.; Martinlomas, M. *J. Org. Chem.* **1994**, *59*, 3135. (f) Stead, P.; Marley, H.; Mahmoudian, M.; Webb, G.; Noble, D.; Ip, Y. T.; Piga, E.; Rossi, T.; Roberts, S.; Dawson, M. J. *Tetrahedron: Asymmetry* **1996**, *7*, 2247. (g) Amantini, D.; Fringuelli, F.; Piermatti, O.; Tortoioli, S.; Vaccaro, L. *ARKIVOC* **2002**, *(xi)*, 293.

(2) (a) Corey, e. J.; Clark, D. A.; Goto, G.; Marfat, A.; Mioskowski, C.; Samuelsson, B.; Hammarstorm, S. *J. Am. Chem. Soc.* **1980**, *102*, 3663. (b) Corey, E. J.; Clark, D. A.; Goto, G. *Tetrahedron Lett.* **1980**, *21*, 3143.

(3) (a) Jacobsen, E. N. *Acc. Chem. Res.* **2000**, *33*, 421. (b) Taylor, S. K. *Tetrahedron* **2000**, *56*, 1149.

(4) See among others: (a) Zhao, P. Q.; Xu, L. W.; Xia, C. G. *Synlett* **2004**, 846. (b) Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Melchiorre, P.; Sambri, L. *Org. Lett.* **2004**, *6*, 3973. (c) Mirkani, V.; Tangestaninejad, S.; Yadollahi, B.; Alipanah, L. *Catal. Lett.* **2005**, *101*, 93. (d) Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Melchiorre, P.; Sambri, L. *Org. Lett.* **2005**, *7*, 1983. (e) Ertürk, E.; Demir, A. S. *ARKIVOC* **2008**, *(ii)*, 160.

(5) See among others: (a) Tatarova, L. E.; Korchagina, D. V.; Volko, K. P.; Salakhutdinov, N. F.; Barkhash, V. A. *Russ. J. Org. Chem.* **2003**, *39*, 1076; Chem. Abstr. 2004, 140, 271015. (b) Fan, R. H.; Hou, X. L. *Tetrahedron Lett.* **2003**, *44*, 4411. (c) Fogassy, G.; Pinel, C.; Gelbard, G. *Catal. Commun.* **2009**, *10*, 557.

(6) See among others: (a) Bathia, K. A.; Eash, K. J.; Leonard, N. M.; Oswald, M. C.; Mohan, R. S. *Tetrahedron Lett.* **2001**, *42*, 8129. (b) Serrano, D. P.; van Grieken, R.; Melero, J. A.; García, A. *Appl. Catal., A* **2007**, *319*, 171.

(7) See among others: (a) Reddy, M. A.; Surendra, K.; Bhanumathi, N.; Rao, K. R. *Tetrahedron* **2002**, *58*, 6003. (b) Boruwa, J.; Borah, J. C.; Kalita, B.; Barua, N. C. *Tetrahedron Lett.* **2004**, *45*, 7355. (c) Salehi, P.; Dabiri, M.; Zolfigol, M. A.; Fard, M. A. B. *Phosphorus, Sulfur Silicon Relat. Elem.* **2004**, *179*, 1113. (d) Sengul, M. E.; Menzek, A.; Sahin, E.; Arik, M.; Saracoglu, N. *Tetrahedron* **2008**, *64*, 7289. (e) Cavdar, H.; Saracoglu, N. *Tetrahedron* **2009**, *65*, 985.

(8) See among others: (a) Kantam, M. L.; Jeyalakshmi, K. A. K.; Likhar, P. R. *Catal. Lett.* **2003**, *89*, 95. (b) Mirkhani, V.; Tangestaninejad, S.; Yadollahi, B.; Alipanah, L. *Tetrahedron* **2003**, *59*, 8213. (c) Moghadam, M.; Tangestaninejad, S.; Mirkhani, V.; Shaibani, R. *Tetrahedron* **2004**, *60*, 6105. (d) Kim, B. H.; Piao, F.; Lee, E. J.; Kim, J. S.; Jun, Y. M.; Lee, B. M. *Bull. Korean Chem. Soc.* **2004**, *25*, 881. (e) Firouzabadi, H.; Iranpoor, N.; Jafari, A. A.; Makarem, S. *J. Mol. Catal. A: Chem.* **2006**, *250*, 237. (f) Robinson, M. W. C.; Buckle, R.; Mabbett, I.; Grant, G. M.; Graham, A. E. *Tetrahedron Lett.* **2007**, *48*, 4723. (g) Leitao, A. J. L.; Salvador, J. A. R.; Pinto, R. M. A.; Sà e Melo, M. L. *Tetrahedron Lett.* **2008**, *49*, 1694.

(9) See among others: (a) Fringuelli, F.; Pizzo, F.; Tortoioli, S.; Vaccaro, L. *Adv. Synth. Catal.* **2002**, 344. (b) Fringuelli, F.; Pizzo, F.; Tortoioli, S.; Vaccaro, L. *J. Org. Chem.* **2003**, *68*, 8248. (c) Fringuelli, F.; Pizzo, F.; Tortoioli, S.; Vaccaro, L. *Green Chem.* **2003**, *5*, 436. (d) Fan, R.-H.; Hou, X.-L. *J. Org. Chem.* **2003**, *68*, 726. (e) Pironti, V.; Colonna, S. *Green Chem.* **2005**, *7*, 43. (f) Wu, J.; Xia, H.-G. *Green Chem.* **2005**, *7*, 708. (g) Reddy, M. S.; Srinivas, B.; Sridhar, R.; Narender, M.; Rao, K. R. *J. Mol. Catal. A: Chem.* **2006**, *255*, 180. (h) Azizi, N.; Saidi, M. R. *Catal. Commun.* **2006**, *7*, 224. (i) Su, W.; Chen, J.; Wu, H.; Jin, C. *J. Org. Chem.* **2007**, *72*, 4524. (j) Chakraborti, S. A. K. *J. Mol. Catal. A: Chem.* **2007**, *263*, 137. (k) Gao, P.; Xu, P.-F.; Zhai, H. *Tetrahedron Lett.* **2008**, *49*, 6536. (l) Yang, M.-H.; Yan, G.-B.; Zheng, Y.-F. *Tetrahedron Lett.* **2008**, *49*, 6471.

(10) (a) Grieco, P. A. *Organic Synthesis in Water*; Blackie Academic and Professional: London, **1998**. (b) Tundo, P.; Ananstas, P. T. *Green Chemistry: Challenging Perspectives*; Oxford University Press: Oxford, **1999**. (c) Li, C.-J.; Chan, T.-H. *Comprehensive Organic Reactions in Aqueous Media*, 2nd ed.; Wiley: Hoboken, **2007**. (d) Kobayashi, S.; Sugiura, M.; Kitagawa, H.; Lam, W. W.-L. *Chem. Rev.* **2002**, *102*, 2227. (e) Kobayashi, S.; Menabe, K. *Acc. Chem. Res.* **2002**, *35*, 209.

(11) (a) Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Nardi, M.; Procopio, A.; Tagarelli, A. *Synthesis* **2004**, 496. (b) Procopio, A.; Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Nardi, M.; Romeo, G. *Org. Biomol. Chem.* **2005**, *3*, 4129. (c) De Nino, A.; Dalpozzo, R.; Procopio, A.; Tagarelli, A.; Nardi, M.; Russo, B. *Synthesis* **2006**, 332. (d) Dalpozzo, R.; De Nino, A.; Nardi, M.; Russo, B.; Procopio, A. *Synthesis* **2006**, 1127. (e) Procopio, A.; Dalpozzo, R.; De Nino, A.; Nardi, M.; Oliverio, M.; Russo, B. *Synthesis* **2006**, 2608. (f) Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Nardi, M.; Procopio, A.; Russo, B.; Tagarelli, A. *ARKIVOC* **2006**, *(vi)*, 181. (g) Procopio, A.; Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Nardi, M.; Oliverio, M.; Russo, B. *Carbohydr. Res.* **2007**, *342*, 2125. (h) Procopio, A.; Gaspari, M.; Nardi, M.; Oliverio, M.; Romeo, R. *Tetrahedron Lett.* **2008**, *49*, 1961.

(12) A 0.1 M aqueous solution of $Er(OTf)_3$ is only weakly acidic (pH ca. 5.9), and the aqueous layer from workup is even less acidic (pH ca. 6.6).

(13) Procopio, A.; Dalpozzo, R.; De Nino, A.; Nardi, M.; Sindona, G.; Tagarelli, A. *Synlett* **2004**, 2633.

(14) Procopio, A.; Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Nardi, M.; Russo, B. *Adv. Synth. Catal.* **2005**, *347*, 1447.

(15) Dalpozzo, R.; De Nino, A.; Nardi, M.; Russo, B.; Procopio, A. *ARKIVOC* **2006**, *(vi)*, 67.

(16) Procopio, A.; Gaspari, M.; Nardi, M.; Oliverio, M.; Rosati, O. *Tetrahedron Lett.* **2008**, *49*, 2289.

(17) (a) Posner, G. H.; Rogers, D. Z. *J. Am. Chem. Soc.* **1977**, *99*, 8214. (b) Otera, J.; Yoshinago, Y.; Hirakawa, K. *Tetrahedron Lett.* **1985**, *26*, 3219. (c) Iranpoor, N.; Salehi, P. *Synthesis* **1994**, 1152. (d) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936. (e) Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *J. Org. Chem.* **1999**, *64*, 6094. (f) Iranpoor, N.; Adibi, H. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 675. (g) Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307. (h) Schneider, C.; Sreekanth, A. R.; Mai, E. *Angew. Chem. Int. Ed.* **2004**, *43*, 5691.

(18) Iranpoor, N.; Mohammadpour Baltork, I.; Shiriny Zardaloo, F. *Tetrahedron* **1991**, *47*, 9861.

(19) Yadav, J. S.; Reddy, B. V. S.; Bayshya, G. *Chem. Lett.* **2002**, 906.