Ytterbium Triflate and High Pressure-mediated Ring Opening of Epoxides with Amines

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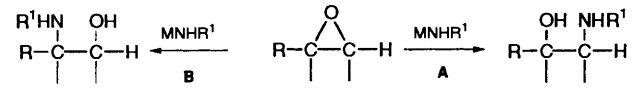
Ring opening of epoxides with amines in THF takes place very readily in the presence of catalytic amounts of ytterbium triflate to give the corresponding β-amino alcohols in good to high yields. With tri- and tetra-substituted epoxides, the use of an excess (2–3 equiv.) of the amine is needed. The $Yb(OTf)_3$-catalysed reaction of epoxides with amines in CH_2Cl_2 is quite complex; the yield of amino alcohols is generally lower and depends upon the addition order of the catalyst, amine and epoxide. The ring opening is accomplished also under high pressures in the absence of $Yb(OTf)_3$. Ring opening with a combination of $Yb(OTf)_3$ in CH_2Cl_2 and high pressure is more effective than the use, independently, of either $Yb(OTf)_3$ or the high-pressure method. Oxetanes and β-lactones undergo ring opening in the presence of $Yb(OTf)_3$.

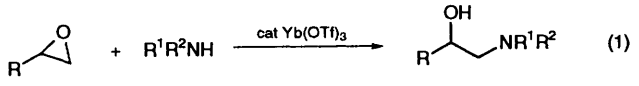
There are a number of limitations to the ring opening of epoxides by amines (R_2NH; the first generation of amine nucleophiles). For example, the low nucleophilicity of amines requires elevated temperatures, the reactivity of sterically bulky amines is low and the regiocontrol of the ring opening is not so easy.[1] To overcome these problems, several metal amides have been developed (R_2NM; the second generation of amine nucleophiles) (Scheme 1). Basic reagents such as lithium[2] and magnesium[3] amides and lead amide[4] attack the less hindered carbon atoms with moderate to high regioselectivity (type **A**).



Scheme 1 Regioselectivity of metal amides. Type **A**: M = Li, Mg, Al, Pb, Me_3Si ($AlCl_3$), CuLn. Type **B**: M = Al, Me_3Sn

A major drawback associated with lithium amides is that the hydrogen α to the epoxide ring is abstracted by the amide base and thus the corresponding allylic alcohol is frequently obtained as a major product.[2] Aminostannanes Me_3SnNR_2 provide type **B** ring opening,[5] whereas the Lewis acid-mediated reaction of Me_3SiNEt_2 gives type **A** cleavage. Diethylaluminium amides[7] and Al_2O_3 mediated amination[8] generally afford type **A** ring opening. $Ti(OPr^i)_4$-mediated ring opening of 2,3-epoxy alcohols and their derivatives proceeds regioselectively at C-3.[9] More recently, we have reported that the amine cuprate reagents attack the less hindered carbon atom of epoxides to give 1,2-amino alcohols in good yields (type **A**).[10]

Although some metal amides provide satisfactory results in the ring-opening reaction, it seemed desirable to develop a new reagent system in which ring opening would take place with amine in the presence of a catalyst (R_2NH-catalyst: the third generation of amine nucleophiles). Earlier, type **A** ring opening with a Ph_4SbOTf (Tf = CF_3SO_2)[11] and $CoCl_2$[12] catalyst has been reported. The reaction of epoxides with amines was promoted by a stoichiometric amount of $LiClO_4$ and related salts.[13] We now report that ytterbium triflate-catalysed ring opening of epoxides with amines takes place very readily, to give the corresponding β-amino alcohols in good to high yields [eqn. (1)]. The results are summarized in Table 1.

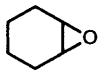
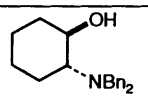
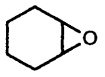
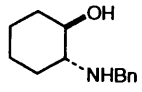
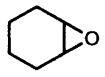
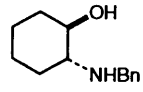
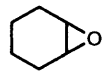
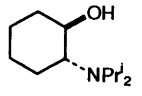
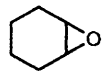
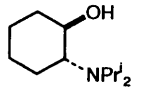
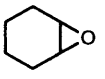
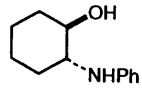
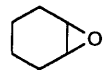
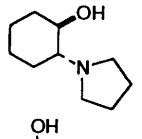
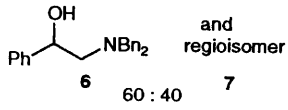
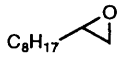
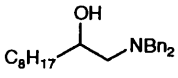
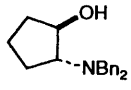
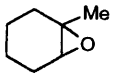
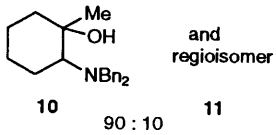
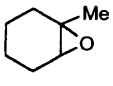
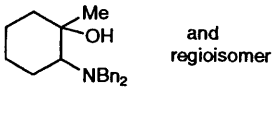
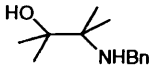


Results and Discussion

The $Yb(OTf)_3$-catalysed ring opening of epoxides with amines proceeded very smoothly, giving type **A** amino alcohols in good to high yields. The results are summarized in Table 1. The reaction of cyclohexene oxide with dibenzylamine in the presence of 10 mol% of $Yb(OTf)_3$ in THF at reflux for 12 h gave the corresponding *trans* β-amino alcohol **1** in essentially quantitative yield (entry 1). The reaction failed to proceed in the presence of $Yb(OPr^i)_3$, $Yb(NBn_2)_3$, $Yb(CN)_3$, YbF_3 or $La(OPr^i)_3$. The use of $YbCl_3$ was less effective, giving the β-amino alcohol in 65% yield. Accordingly, the use of the triflate derivative is essential for high yields. In fact, the triflates of Y, La, Pr, Sm, Eu, Dy, Er or Yb were very effective, affording the β-amino alcohol in >95% yield. Less satisfactory results were obtained with $Ho(OTf)_3$ (88%), $Gd(OTf)_3$ (45%) and $Nd(OTf)_3$ (70%). The effect of the amount of $Yb(OTf)_3$ upon chemical yield was investigated in the ring opening of cyclohexene oxide (entry 1); 99% yield with 10 mol% catalyst, 98% yield with 5 mol% catalyst and 75% yield with 1 mol% catalyst.

Whilst this study was being conducted, related work was published by Chini's group[14] and the following is their procedure. A mixture of cyclohexene oxide with Pr^i_2NH in CH_2Cl_2 in the presence of 10 mol% of $Yb(OTf)_3$ was stirred for 18 h at room temperature, to give the desired product **3** (90%). We repeated this procedure exactly: (1) to a mixture of the epoxide and the amine in $CHCl_2$ was added the catalyst, and the mixture was stirred for 18 h;[14] this gave the desired product in only 19% yield. We then modified the addition order of the reagent and substrate: (2) to the catalyst dissolved in CH_2Cl_2 was added the epoxide followed by the amine. The mixture was stirred for 18 h but, in this case, a complex mixture of products was obtained! We realized that the addition order plays an important role in obtaining the desired product in the case of the reaction in CH_2Cl_2. Accordingly, we carried out a further experiment with a change in the addition order; (3) to the catalyst dissolved in CH_2Cl_2 was added the amine, followed by the epoxide. We obtained the desired product **3** in 18% yield. Although we failed to obtain a chemical yield as high as that reported in the literature,[14] experiments (1) (the authors' procedure) and (3), in fact, gave the desired product, whilst experiment (2) did not. Taken together, it seems that in the absence of amine $Yb(OTf)_3$ reacts with the epoxide very rapidly in CH_2Cl_2 to give a mixture of unwanted products, whilst in its presence this reaction is prevented. Interestingly, the chemical yield of the reaction between cyclohexene oxide and diisopropylamine by our procedure, which uses THF as a solvent,

Table 1 Ring opening of epoxides with amines

Entry	Epoxide	Amine (R^1R^2NH)[a]	Condition[b,c]	Reaction time (h)	Product and yield[d]		
1		Bn_2NH	**A**	12		**1**	99
2		$BnNH_2$	**B**; 10 kbar	144 (6 days)		**2**	90
3		$BnNH_2$	**A**	10		**2**	86
4		Pr^i_2NH	**B**	18		**3**	19
5		Pr^i_2NH	**B**; 10 kbar	18		**3**	40
6		$PhNH_2$	**A**	10		**4**	94
7			**A**	10		**5**	93
8		Bn_2NH	**A**	0.3		**6** 60 : 40 **7**	98
9		Bn_2NH	**A**	1.5		**8**	92
10		Bn_2NH	**A**	12		**9**	85
11		Bn_2NH	**A**	24		**10** 90 : 10 **11**	56
12		Bn_2NH	**C**	72		**10** 80 : 20 **11**	80
13		$BnNH_2$	**C**	72		**12**	93

[a] Bn = CH_2Ph, Pr^i = $CH(CH_3)_2$. [b] Method **A**; THF/reflux, epoxide:amine = 1:2, Method **B**; CH_2Cl_2/room temp., epoxide:amine = 1:2, Method **C**; THF/reflux, epoxide:amine = 1:3. [c] $Yb(OTf)_3$ (10 mol%) was used in entries 1, 3–11. In entry 12, 20 mol% $Yb(OTf)_3$ was used. In entry 13, 30 mol% $Yb(OTf)_3$ was used. [d] Isolated yield.

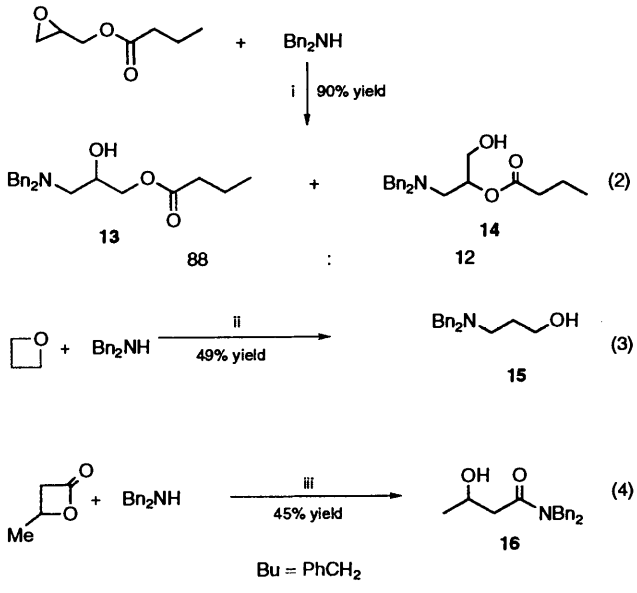
did not depend upon the addition order. Perhaps, in this case, THF coordinates strongly with $Yb(OTf)_3$, thus modifying its strong Lewis acidity and preventing undesirable side reactions of the epoxide. With THF as the medium the mixture has to be treated under reflux to induce reaction whilst in CH_2Cl_2 it proceeds at room temperature. The reason for our inability to reproduce the reported chemical yield (90%) of the reaction in CH_2Cl_2 is unclear.

The high pressure reaction[15] of cyclohexene oxide with benzylamine in CH_2Cl_2 at room temperature under 10 kbar afforded the corresponding β-amino alcohol **2** in 90% yield (entry 2). The reaction proceeded under essentially neutral

conditions without any additives, although a long reaction time was needed. In view of this, it occurred to us that a combination of high pressure and $Yb(OTf)_3$ catalyst might enhance the reaction rate of the epoxide ring opening: as shown in entries 3 and 4, of Table 1 this proved to be the case.

As shown in entries 6–13, the $Yb(OTf)_3$-catalysed ring opening is quite effective for epoxides including those bearing sterically demanding substituents. The ring opening of the monosubstituted epoxide was complete in 20 min in the presence of 10 mol% $Yb(OTf)_3$ in refluxing THF (entry 8). In the case of an aliphatic epoxide, regioselective ring opening took place exclusively at the less hindered epoxide carbon (entry 9). With a trisubstituted epoxide, the chemical yield decreased significantly (entries 11, 12); the use of 10 mol% of $Yb(OTf)_3$ and 2 equiv. of Bn_2NH in reluxing THF for 24 h gave a 56% yield; the yield increased to 80% on use of 20 mol% of $Yb(OTf)_3$ and 3 equiv. of Bn_2NH with a prolonged reaction time (72 h). With the tetrasubstituted epoxide, the reaction became very sluggish (entry 13) and the use of 3 equiv. of $BnNH_2$ and 30 mol% of $Yb(OTf)_3$ in refluxing THF for 72 h gave a 93% yield.

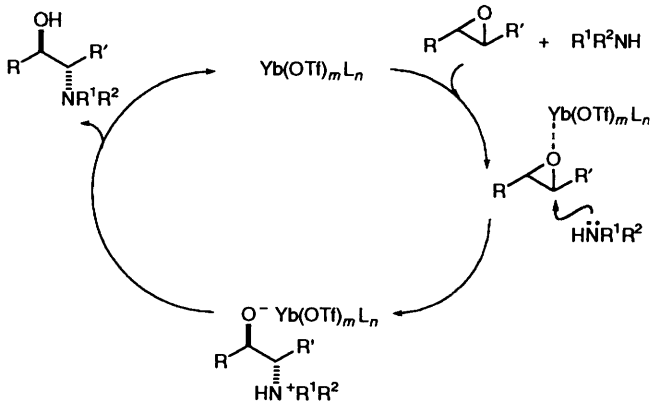
Accordingly, both methods **A** and **B** are useful for the synthesis of β-amino alcohols from epoxides under neutral conditions; the use of high pressure in such reactions can be useful. Efficient ring opening is induced in a $Yb(OTf)_3$-catalysed reaction, further applications of which are shown in eqns. (2)–(4).



Reagents and conditions: i, 10 mol% of $Yb(OTf)_3$, THF, reflux, 20 min; ii, 10 mol% of $Yb(OTf)_3$, THF, room temp., 48 h; iii, 10 mol% of $Yb(OTf)_3$, THF, reflux, 24 h; iv, 3 mol dm^{-3} aq. HCl

The minor product **14** in (2) was produced *via* a trans-esterification process. In fact, treatment of the major product **13** with 10 mol% $Yb(OTf)_3$ in THF at reflux for 12 h gave a mixture (83:17) of products in quantitative yield. The four-membered oxygen-containing compounds underwent ring-opening with dibenzylamine in the presence of 10 mol% of $Yb(OTf)_3$ (entries 3, 4). Consequently, we are now in a position to induce effective ring opening of epoxides, oxetanes and β-lactones using the third generation of amine nucleophiles [R_2NH/cat. $Yb(OTf)_3$], application of the high-pressure technique being used to accelerate the reaction.

A mechanistic rationale which accounts for the $Yb(OTf)_3$-catalysed ring opening is shown in Scheme 2, although it is highly speculative. The catalyst $Yb(OTf)_3$ itself, its THF coordination complex, or its amine complex $Yb(OTf)_mL_n$ could coordinate with an epoxide oxygen to assist the S_N2-type ring



Scheme 2

opening with amine nucleophiles. The resulting ring-opened intermediate would then undergo a rapid proton transfer to give the desired amino alcohol and a catalytic species.

Experimental

^1H NMR spectra were recorded on a JEOL GSX-270 spectrometer. The chemical shifts are expressed in ppm downfield from the tetramethylsilane internal standard. ^{13}C NMR spectra were recorded on a JEOL GSX-270 spectrometer. All *J* values are in Hz. IR spectra were recorded on a Hitachi Model 215. M.p.s were determined on a Yamato MP-21 capillary melting point apparatus. M.p.s and b.p.s are uncorrected. The Kugelrohr distillation temperatures are oven temperatures, not b.p.s.

Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under argon. All other solvents were dried and stored over 3 Å molecular sieves. Most commercially supplied chemicals were distilled and stored over molecular sieves.

The reaction of cyclohexene oxide with dibenzylamine is representative for method **A**. To a solution of $Yb(OTf)_3$ (57 mg, 0.10 mmol) in dry THF (1.0 cm^3), cyclohexene oxide (0.10 cm^3, 1.0 mmol) and dibenzylamine (0.38 cm^3, 2.0 mmol) were added under an Ar atmosphere. The refluxing mixture was stirred and the progress of the reaction was monitored with TLC. When cyclohexene oxide had been consumed, the reaction mixture was diluted with distilled water and extracted with ether (×3). The extract was washed with brine, dried (K_2CO_3) and evaporated under reduced pressure to provide the crude product which was purified by silica gel column chromatography (hexane–AcOEt 10:1) to give *trans*-2-(*N*,*N*-dibenzylamino)cyclohexanol **1** (292 mg, 99% yield).

The reaction of cyclohexene oxide with benzylamine is representative for method **B** at 10 kbar. A mixture of cyclohexene oxide (0.30 cm^3, 3.0 mmol), CH_2Cl_2 (1.0 cm^3) and benzylamine (0.65 cm^3, 6.0 mmol) in a Teflon capsule was placed in a high-pressure apparatus. The reaction was carried out at 10 kbar at room temperature. After an appropriate time, the pressure was released and the solvent was removed under reduced pressure. The product was purified by silica gel column chromatography (hexane–AcOEt, 1:3) to give *trans*-2-benzylaminocyclohexanol **2** (185 mg, 90%).

The reaction of cyclohexene oxide with diisopropylamine is representative for method **B**. To a CH_2Cl_2 (1.0 cm^3) solution of cyclohexene oxide (0.20 cm^3, 2.0 mmol) and diisopropylamine (0.42 cm^3, 3.0 mmol) in a Teflon capsule was added $Yb(OTf)_3$ (115 mg, 0.20 mmol). The stirred reaction mixture was left for an appropriate time and then diluted with distilled water to quench the reaction. The organic layer was extracted with CH_2Cl_2 (×3), and the extract dried (Na_2SO_4) and evaporated under

reduced pressure to give the crude product which was purified by silica gel column chromatography (hexane–AcOEt, 7:1) to give *trans*-2-(*N*,*N*-diisopropylamino)cyclohexanol **3** (38.0 mg, 19%).

The reaction of cyclohexene oxide with diisopropylamine is representative for method **B** at 10 kbar with $Yb(OTf)_3$. To a CH_2Cl_2 (1.0 cm^3) solution of cyclohexene oxide (0.20 cm^3, 2.0 mmol) and diisopropylamine (0.42 cm^3, 3.0 mmol) in a Teflon capsule was added $Yb(OTf)_3$ (115 mg, 0.20 mmol). The capsule was placed in a high-pressure apparatus and the reaction was carried out at 10 kbar at room temperature. The pressure was released after an appropriate time and the work-up procedure was similar to that of method **B**.

trans-2-(N,N-*Dibenzylamino*)*cyclohexanol* **1**. Colourless needles, m.p. 88.0–89.0 °C; δ 1.00–1.35 (4 H, m), 1.60–1.72 (1 H, m), 1.73–1.83 (1 H, m), 1.91–2.00 (1 H, m), 2.00–2.12 (1 H, m), 2.35 (1 H, ddd, *J* 3.5, 10.0, 11.5, N-CH), 3.37 (2 H, d, *J* 13.0), 3.50 (1 H, ddd, *J* 4.7, 10.0, 10.0, O-CH), 3.74 (1 H, br s), 3.85 (2 H, d, *J* 13.0) and 7.14–7.37 (10 H, m); ν_{max}(KBr) 3450, 1455, 1070, 760 and 700 (Found: C, 81.45; H, 8.7; N, 4.7. Calc. for $C_{20}H_{25}NO$: C, 81.31; H, 8.53; N, 4.74%).

trans-2-(*Benzylamino*)*cyclohexanol* **2**. Colourless oil; δ 0.97–1.07 (1 H, m), 1.15–1.31 (3 H, m), 1.64–1.76 (2 H, m), 1.98 (1 H, m), 2.14 (1 H, m), 2.31 (1 H, ddd, *J* 4.0, 9.4, 11.4, N-CH), 2.70 (2 H, br s), 3.21 (1 H, ddd, *J* 4.0, 9.4, 9.4, O-CH), 3.68 (1 H, d, *J* 13.0), 3.93 (1 H, d, *J* 13.0) and 7.20–7.40 (5 H, m).

trans-2-(N,N-*Diisopropylamino*)*cyclohexanol* **3**. The ^1H NMR spectra was in good agreement with reported data.[13]

trans-2-(*Anilino*)*cyclohexanol* **4**. Colourless needles, m.p. 57.0–58.0 °C; δ 1.05 (1 H, m), 1.20–1.48 (3 H, m), 1.73 (2 H, m), 2.12 (2 H, m), 2.87 (1 H, br s), 3.13 (1 H, ddd, *J* 4.1, 9.0, 10.9, N-CH), 3.35 (1 H, ddd, *J* 4.0, 9.0, 10.0, O-CH), 6.74 (3 H, m) and 7.18 (2 H, m); ν_{max}(KBr)/cm^{-1} 3390, 1590, 1510, 1490, 1320, 1060, 740 and 685 (Found: C, 75.2; H, 9.1; N, 7.4. Calc. for $C_{12}H_{17}NO$; C, 75.35; H, 8.96; N, 7.32%).

trans-2-(*Pyrrolidin*-1-*yl*)*cyclohexanol* **5**. Colourless oil, b.p. 130–140 °C (5 mmHg, Kugelrohr); δ 1.10–1.32 (4 H, m), 1.64–1.82 (7 H, m), 2.10 (1 H, m), 2.45 (1 H, ddd, *J* 3.3, 9.5, 11.0, N-CH), 2.54 (2 H, m), 2.68 (2 H, m), 3.35 (1 H, ddd, *J* 4.1, 9.5, 9.5, O-CH) and 4.04 (1 H, br s); ν_{max}(neat)/cm^{-1} 3470, 1455, 1360, 1300, 1120 and 1085 (Found: C, 70.6; H, 11.3; N, 8.3. Calc. for $C_{10}H_{19}NO$: C, 0.96; H, 11.2; N, 8.28%).

2-(N,N-*Dibenzylamino*)-1-*phenylethanol* **6**. Colourless oil; δ 2.64 (2 H, d, *J* 7.5), 3.48 (2 H, d, *J* 14.0), 3.78 (1 H, br s), 3.91 (2 H, d, *J* 14.0), 4.70 (1 H, t, *J* 7.5) and 7.15–7.40 (15 H, m); ν_{max}(neat)/cm^{-1} 3430, 755 and 700 (Found: C, 83.0; H, 7.4; N, 4.5. Calc. for $C_{22}H_{23}NO$: C, 83.24; H, 7.30; N, 4.41%).

2-(N,N-*Dibenzylamino*)-2-*phenylethanol* **7**. Colourless oil; δ 3.03 (1 H, br s), 3.15 (2 H, d, *J* 13.0), 3.61 (1 H, dd, *J* 5.0, 10.5), 3.93 (2 H, d, *J* 13.0), 3.93 (1 H, dd, *J* 5.0, 10.5), 4.14 (1 H, dd, *J* 10.5, 10.5) and 7.23–7.46 (15 H, m) ν_{max}(neat)/cm^{-1} 3450, 1600, 1495, 1450 and 1080 (Found: C, 82.9; H, 7.5; N, 4.3. Calc. for $C_{22}H_{23}NO$: C, 83.24; H, 7.30; N, 4.41%).

1-(N,N-*Dibenzylamino*)*decan*-2-*ol* **8**. Colourless oil; δ 0.86 (3 H, t, *J* 6.8), 1.18–1.34 (14 H, m), 2.42 (2 H, d, *J* 7.0), 3.37 (2 H, d, *J* 13.0), 3.68 (1 H, m), 3.86 (2 H, d, *J* 13.0) and 7.21–7.37 (10 H, m); ν_{max}(neat)/cm^{-1} 3450, 1495 and 1370 (Found: C, 81.5; H, 10.0; N, 4.1. Calc. for $C_{24}H_{35}NO$: C, 81.53; H, 9.98; N, 3.96%).

2-(N,N-*Dibenzylamino*)*cyclopentanol* **9**. Colourless needles, m.p. 47.5–48.5 °C; δ 1.33–1.98 (7 H, m), 2.93 (1 H, ddd, *J* 7.5, 7.5, 7.5), 3.50 (2 H, d, *J* 13.5), 3.77 (2 H, d, *J* 13.5), 4.06 (1 H, ddd, *J* 7.5, 7.5, 7.5) and 7.17–7.42 (10 H, m); ν_{max}(neat)/cm^{-1} 3400, 1500, 1455, 1080 and 1035 (Found: C, 80.95; H, 8.3; N, 5.0. Calc. for $C_{19}H_{23}NO$; C, 81.10; H, 8.24; N, 4.98%).

Compounds **10** and **11** were obtained as inseparable mixtures. For the purpose of separation and identification, the mixtures were treated with acetic anhydride and pyridine to give **10** and **11′** which were easily separated by silica gel column chromatography.

2-(N,N-*Dibenzylamino*)-1-*methylcyclohexanol* **10**. Colourless needles, m.p. 94.7–95.9 °C; δ 1.41–1.51 (1 H, m), 1.26 (3 H, s), 1.55–1.71 (2 H, m), 1.77–1.89 (2 H, m), 2.61 (1 H, dd, *J* 3.5, 12.0, N-CH), 3.28 (1 H, br s), 3.41 (2 H, d, *J* 13.5), 3.85 (2 H, d, *J* 13.5) and 7.22–7.35 (10 H, m); ν_{max}(KBr)/cm^{-1} 3505, 1140, 750 and 700 (Found: C, 81.3; H, 8.8; N, 4.5. Calc. for $C_{21}H_{27}NO$: C, 81.51; H, 8.80; N, 4.52%).

2-(N,N-*Dibenzylamino*)-2-*methylcyclohexyl acetate* **11′**. White needles, m.p. 78.5–79.3 °C; δ 1.16 (3 H, s), 1.22–1.50 (3 H, m), 1.50–1.81 (5 H, m), 1.94 (1 H, m), 2.09 (3 H, s), 3.79 (2 H, d, *J* 14.5), 3.89 (2 H, d, *J* 14.5), 5.21 (1 H, dd, *J* 4.0, 8.5, O-CH) and 7.03–7.22 (10 H, m); ν_{max}(KBr)/cm^{-1} 1730, 1500, 1255, 760 and 720 (Found: C, 78.4; H, 8.3; N, 4.0. Calc. for $C_{23}H_{29}NO_2$: C, 78.59; H, 8.32; N, 3.99%).

3-*Benzylamino*-2,3-*dimethylbutan*-2-*ol* **12**. The ^1H NMR spectra were in good agreement with reported data.[13]

Further applications of the $Yb(OTf)_3$-mediated ring opening of three- and four-membered ring oxygen-containing compounds was carried out similarly.

The $Yb(OTf)_3$ mediated isomerization of an ester was carried out as follows. To a solution of pure 3-(*N*,*N*-dibenzylamino)-2-hydroxylpropyl butyrate **13** (68.0 mg, 0.20 mmol) in THF (1.0 cm^3) was added $Yb(OTf)_3$ (11.5 mg, 0.02 mmol) and the mixture was refluxed for 12 h. The reaction was stopped by the addition of distilled water to the mixture. The organic layer was extracted with ether (× 3) and the combined extracts were washed with brine, dried (K_2CO_3) and evaporated under reduced pressure. The product was purified by a silica gel column chromatography (hexane–AcOEt, 10:1) to give a 83:17 mixture of the starting butyrate **13** and 3-(*N*,*N*-dibenzylamino)-1-hydroxypropan-2-yl butyrate **14** in essentially quantitative yield.

3-(N,N-*Dibenzylamino*)-2-*hydroxypropyl butyrate* **13**. Colourless oil; δ 0.91 (3 H, t, *J* 7.0), 1.58 (2 H, sext, *J* 7.0), 2.23 (2 H, t, *J* 7.0), 2.48 (1 H, dd, *J* 4.5, 13.0, N-CH_2), 2.56 (1 H, dd, *J* 8.5, 13.0, N-CH_2), 3.26 (1 H, br s), 3.46 (2 H, d, *J* 13.5), 3.81 (2 H, d, *J* 13.5). 3.93 (1 H, dd, *J* 5.5, 13.0, O-CH_2), 3.94 (1 H, dddd, *J* 4.5, 5.5, 5.5, 8.5, O-CH), 4.11 (1 H, dd, *J* 5.5, 13.0, O-CH_2) and 7.22–7.38 (10 H, m); ν_{max}(neat)/cm^{-1} 3450, 1745, 1500, 1460 and 1185 (Found: C, 73.7; H, 8.2; N, 4.1. Calc. for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97; N, 4.10%).

3-(N,N-*Dibenzylamino*)-1-*hydroxypropan*-2-*yl butyrate* **14**. Colourless oil; δ 0.94 (3 H, t, *J* 7.0), 1.64 (2 H, sext, *J* 7.0), 2.28 (2 H, t, *J* 7.0), 2.67 (1 H, dd, *J* 5.8, 12.7, N-CH_2), 2.27 (1 H, dd, *J* 6.5, 12.7, N-CH_2), 3.55 (2 H, d, *J* 13.0), 3.64 (2 H, d, *J* 4.9 Hz, O-CH_2), 3.70 (2 H, d, *J* 13.0), 5.04 (1 H, ddt, *J* 4.9, 5.8, 6.5, O-CH) and 7.22–7.38 (10 H, m); ν_{max}(neat)/cm^{-1} 3550, 1740, 1600, 1500 and 1190 (Found: C, 74.0; H, 8.0; N, 4.2. Calc. for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97; N, 4.10%). The elemental analysis and IR spectroscopy were carried out on the title compound which was contaminated with small amounts of 3-(*N*,*N*-dibenzylamino)-2-hydroxypropyl butyrate.

3-(N,N-*Dibenzylamino*)*propanol* **15**. Colourless oil; δ 1.76 (2 H, quint., *J* 5.5), 2.65 (2 H, t, *J* 5.5, CH_2-N), 3.58 (4 H, s), 3.65 (2 H, t, *J* 5.5, CH_2-O), 4.65 (1 H, br s) and 7.22–7.38 (10 H, m); ν_{max}(neat)/cm^{-1} 3380, 1505, 1480 and 1080 (Found: C, 79.6; H, 8.3; N, 5.5. Calc. for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49%).

N,N-*Dibenzyl*-3-*hydroxy-butanamide* **16**. White crystals, m.p. 72.5–73.4 °C; δ 1.22 (3 H, d, *J* 6.0), 2.45 (1 H, dd, *J* 9.0, 16.0), 2.59 (1 H, dd, *J* 2.3, 16.0), 4.28 (1 H, ddq, *J* 2.3, 6.0, 9.0, O-CH), 4.39 (1 H, d, *J* 17.0), 4.49 (1 H, d, *J* 17.0), 4.53 (1 H, d, *J* 14.5), 4.70 (1 H, d, *J* 14.5) and 7.11–7.42 (10 H, m); ν_{max}(KBr)/cm^{-1} 3310, 1625, 1460, 766 and 700 (Found: C, 76.1; H, 7.5; N, 4.95. Calc. for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94%).

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