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Lewis Acid-Catalysed Rearrangement/Reduction of 1-Phenyloxiranemethanamines: Synthesis of β-Phenethylamines

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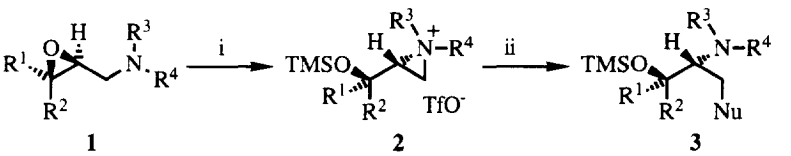
Abstract: A range of 1-phenyloxiranemethanamines has been prepared and their reactions with sodium cyanoborohydride under boron trifluoride catalysis have been investigated. In general the products were the corresponding 2-amino-3-phenylpropan-1-ols derived from Lewis acid-mediated ring opening of the epoxide in an *aza*-Payne manner and benzylic reduction of the intermediate aziridinium species.

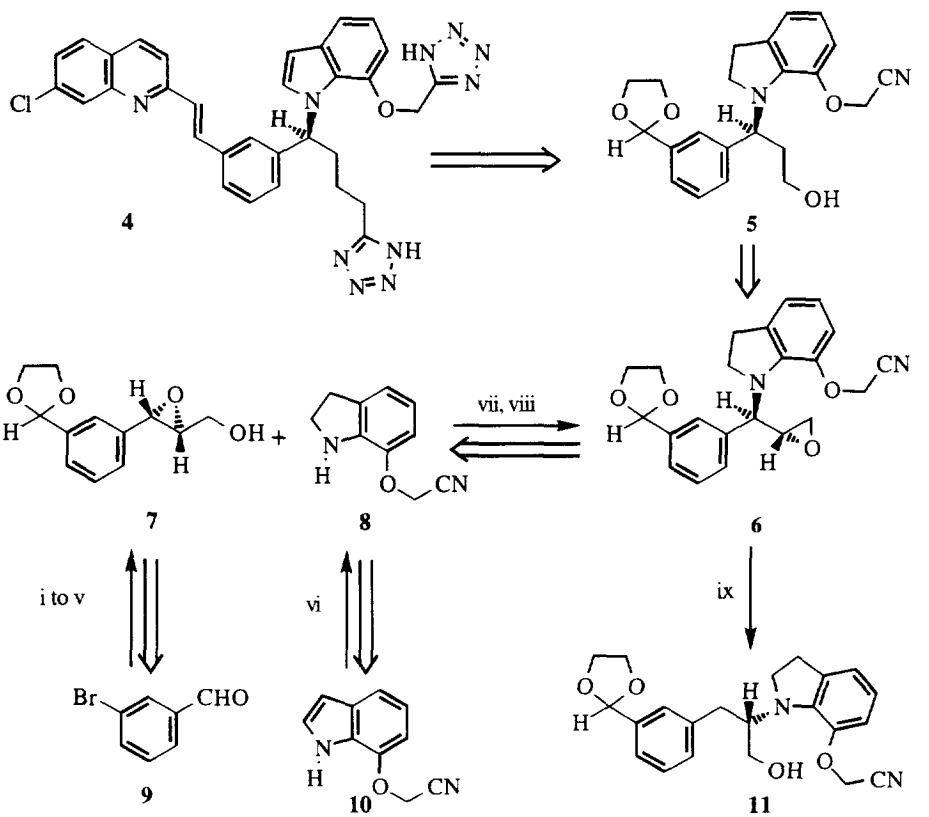
Enantiopure 2,3-epoxy alcohols, readily available by Sharpless asymmetric epoxidation methodology,[1] have been employed as valuable synthons for polyfunctionalised systems such as 2,3-aziridinyl alcohols[2] or 1,2-aziridinyl-3-ols,[3] aryl ether diols,[4] 3-amino-1,2-diols[5] and *N*-Boc-α-amino acids.[6] Recently, the Lewis acid-catalysed isomerisation of 2,3-epoxy amines **1** into the corresponding 2-trimethylsiloxymethylaziridinium ions **2** and reaction of the latter with nitrogen nucleophiles to give 1-substituted 2,3-diamino alcohols **3** has been reported (Scheme1).[7] This work prompted us to report our findings on the Lewis acid-catalysed reductions of 1-phenyloxiranemethanamines, which apparently proceed by a similar type of rearrangement to give 3-phenyl-2-aminopropanols.



1 **2** **3**

Scheme 1 *Reagents and conditions:* i, TMSOTf, -78°C, 10min; ii, nucleophile, -78°C - room temp., 3-5 days.

During the course of an investigation into the asymmetric synthesis of the leukotriene LTD_4 receptor antagonist LY290154 **4**,[8] the indolinopropanol **5** was targeted as a useful intermediate for the synthesis of **4** and it was thought that **5** could be derived from the oxiranemethanamine **6** *via* a Lewis acid-catalysed reduction of the epoxide. The Lewis acid-mediated reduction of unsymmetrical epoxides generally yields the product derived from reduction at the more hindered carbon, as reaction with the Lewis acid catalyst can generate an incipient carbocation at this position. The synthesis of **6** was accomplished in 7 steps from 3-bromobenzaldehyde **9** *via* the oxiranemethanol **7** (Scheme 2). The indoline **8** was prepared from reduction of the corresponding indole **10**[9] using standard conditions[10] and was added to the epoxide **7** under Lewis acid catalysis to give the amino diol, which was readily converted to **6**. Subsequent reduction of **6** with sodium cyanoborohydride and boron trifluoride in THF did not give the expected 3-aminopropanol **5**, but rather the isomeric 2-amino derivative **11**.

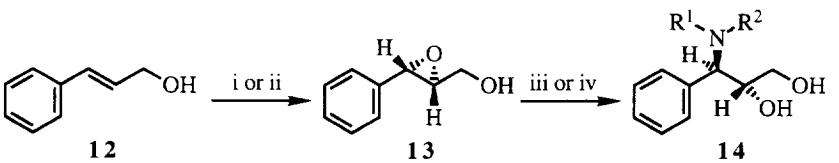


Scheme 2 *Reagents and conditions:* i, $(CH_2OH)_2$, TsOH, PhMe, Δ, 92%; ii, BuLi, THF, -78°C, then DMF, 93%; iii, $(EtO)_2P(O)CH_2CO_2Et$, NaH, THF, 95%; iv, $LiAlH_4$, Et_2O, -5°C, 81%; v, Sharpless, 54%; vi, $NaBH_3CN$, AcOH, 12 to 25°C, 70%; vii, $Mg(ClO_4)_2$, MeCN, 64%; viii, $PrSO_2Cl$, Et_3N, THF then NaOMe, MeOH, 70%; ix, $NaBH_3CN$, $BF_3.OEt_2$, THF, Δ, 37%.

Formation of **11** presumably involves intramolecular opening of the acid-complexed oxirane by the indoline, followed by reductive cleavage of the aziridinium intermediate thus produced, and is similar to the mechanism proposed by Rayner *et al.* for the **1** → **3** transformation shown in Scheme 1. There is further mechanistic precedence for the formation of **11** in the triethylaluminium-mediated rearrangement of primary 2,3-epoxy amines into 1,2-aziridinyl-3-ols,[3] and in the work of Sharpless and Masamune in which an equilibrating mixture of epoxy alcohols, resulting from a Payne rearrangement, was shown to lead to one ring opened product when treated with an appropriate nucleophile, as a consequence of selective attack.[11]

The conversion of **6** into **11** is an example of an unusual but potentially useful method for the preparation of α-hydroxymethyl *N*-substituted β-phenethylamines of modest complexity, and to explore the possible scope of the transformation we examined the reactivity of a number of structurally more simple α-amino epoxides towards Lewis acid-catalysed reductive ring opening. The experimental parameters were studied initially with racemic substrates and then with enantiomerically pure material to establish the chiral integrity of the rearrangement/reduction step.

Preparation of the required α-amino epoxides in either racemic or homochiral form was straightforward *via* the amino diols **14** (Schemes 3 and 4). Various methods have been advocated for the Lewis acid-catalysed regioselective ring opening of the oxirane **13** with nitrogen nucleophiles, and titanium(IV) isopropoxide and



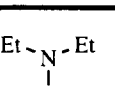
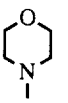
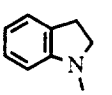
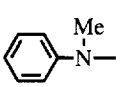
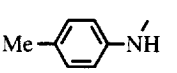
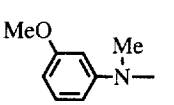
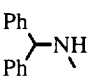
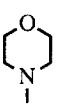
12 **13** **14**

Scheme 3 *Reagents and conditions:* i, mCPBA, DCM, 0°C;
ii, *t*-BuOOH, $Ti(O^iPr)_4$, (+)-DET, 4Å mol. sieves, DCM, -20°C;
iii, R^1R^2NH, $Ti(O^iPr)_4$, DCM; iv, R^1R^2NH, $Mg(ClO_4)_2$, MeCN.

magnesium perchlorate have been claimed to be the most effective catalysts. Both were used in the present study and the results are summarised in Table 1. Catalysis by titanium(IV) isopropoxide was generally satisfactory, and the amino diols **14** were obtained in moderate to excellent yields in almost all cases.

Magnesium perchlorate was a much less effective catalyst when simple dialkylamines were used, presumably because it is a stronger acid and complexed essentially irreversibly with the more basic dialkylamines. Preparation of compound **14i** was a repeat of the morpholine ring-opening experiment using homochiral oxirane **13a**. Both the ^1H and ^{13}C NMR data for **14i** were identical to those of the analogous racemate **14b**. The chiral integrity of **14i** was determined by ^1H NMR spectroscopy using the commercially available chiral solvating agent[12] (1*R*)-(-)-2,2,2-trifluoro-1-(9-anthryl)ethanol (TFAE). Method development on the racemic product indicated that preparation of a *ca.* 5:1 TFAE : amino diol **14b** mixture caused chemical shift non-equivalence (0.03 ppm) of the benzylic methine proton doublet. This method was subsequently used to assay the homochiral diol **14i**, and indicated that the enantiomeric excess was > 98%.

Table 1. *Lewis acid-catalysed ring opening of 3-phenyloxiranemethanol* **13** *with amines.*

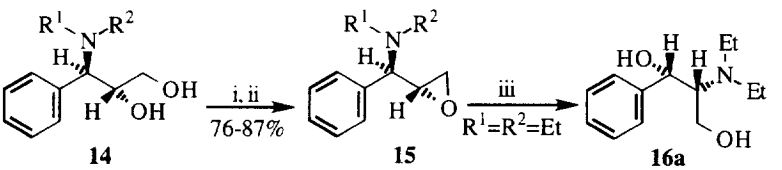
Product	Amine	Yield, % with $Mg(ClO_4)_2$	Yield, % with $Ti(O^iPr)_4$
14a		0†	77
14b		0†	45
14c		0†	59
14d		77	78
14e		53	77
14f		75	89
14g*		57	63
14h		18	18
14i		-	32‡

† Only unreacted starting material could be recovered from these reactions.

* This amine was prepared according to the method described by Crochet and Blanton.[13]

‡ This product was derived from enantiomerically pure epoxy alcohol **13a**.

The amino diols **14** were converted into the corresponding 1-phenyloxiranemethanamines **15** by a two step, one-pot procedure in excellent yield (Scheme 4). The first step was the synthesis of the mono-*n*-propanesulfonyl ester of **14** by reaction with the sulfene derived from *n*-propanesulfonyl chloride. Subsequent treatment of the ester with sodium methoxide gave the oxirane **15**. In general these compounds were purified by column chromatography, but the diethylamino epoxide **15a** was unstable to this method of purification and hence for future reactions was used without further purification. The decomposition product from the chromatographic purification of **15a** was identified as the isomeric amino diol **16a**. This product is presumably formed by acidic silica gel-catalysis of the *aza*-Payne rearrangement/hydrolysis, and is apparently much more facile for this particular epoxy amine than it is for the other derivatives. This hydrolysis product is potentially quite interesting, because if homochiral material were used then the corresponding homochiral amino diol should be obtained, and it has been reported recently that chiral 2-amino-1,3-diols have found use as ligands for enantioselective Reformatsky reactions.[14]



14 **15** **16a**

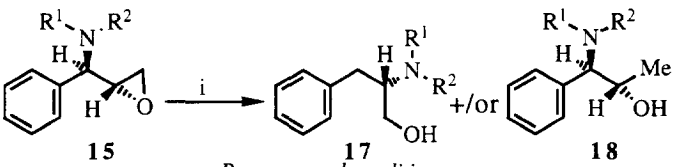
Scheme 4 *Reagents and conditions:* i, $PrSO_2Cl$, Et_3N, DCM, -10°C; ii, NaOMe, MeOH, 25°C; iii, SiO_2 chromatography.

The results for the reduction of epoxy amines **15** with sodium cyanoborohydride catalysed by boron trifluoride etherate in THF are summarised in Table 2. The diethylamino and pyrrolidino derivatives, **15a** and **15c**, respectively, gave particularly polar products under these reaction conditions and it appeared that some form of boron complex had been generated in each case. This was supported by the presence of several strong bands in the infrared spectra at *ca.* 2200-2370 cm^{-1} compatible with the presence of B-H bonds. Attempts to hydrolyse these products using both acidic and basic conditions were unsuccessful. It was surprising to observe that the indolino system **15d** gave only the amino alcohol **18d**, in contrast to the result with the epoxy amine **6**. Mixtures of both rearranged and non-rearranged products, **17** and **18**, respectively, were obtained with the *p*-toluidino and diphenylmethylamino compounds **15f** and **15h**. The only products recovered from the Lewis acid-catalysed reduction of the morpholino, *N*-methylanilino and *N*-methyl-3-methoxyphenylamino compounds, **15b**, **15e** and **15g** respectively, were those derived from the rearrangement/reduction route, namely **17b**, **17e** and **17g**. The result with **15g** was in some ways unexpected, as with the aromatic amines **15e** and **15f** products derived by cyclisation on to the aromatic ring might have been expected rather than products arising from cleavage of the intermediate aziridinium species. It was for this reason that the electron rich aromatic amine **15g** was prepared, *i.e.* to ascertain whether the alternative cyclisation reaction pathway might be favoured; clearly, however, the rearrangement process is particularly effective in the case of **15g**.

The homochiral epoxy amine **15i** rearranged in a similar fashion to its racemic counterpart **15b** to give the amino alcohol **17i**. The chiral purity of **17i** could not be established from a chiral ^1H NMR experiment using the shift reagent TFAE because of the unresolved complexity of the aliphatic region in the ^1H NMR

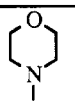
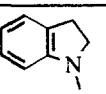
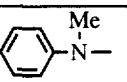
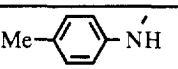
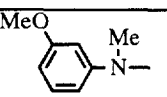
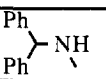
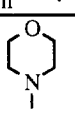
spectrum. Fortunately, however, capillary electrophoresis could be exploited for this compound. Chiral separation of the two enantiomers in racemic amino alcohol **17b** was achieved under reverse polarity conditions using 50mM pH 2.5 borax containing *ca.* 20 mg ml^{-1} sulfated β-cyclodextrin. Under the same conditions the enantiomeric excess of **17i** was determined as > 99.5%.

Table 2. *Lewis acid-catalysed reduction of 1-phenyloxiranemethanamines* **15**[a]



15 **17** **18**

Reagents and conditions:
i, $NaBH_3CN$, $BF_3.OEt_2$, THF, Δ, N_2.

Compound	Amine	Yield of 17, %	Yield of 18, %
15b		**48**	**0**
15d		**0**	**14**
15e		**48**	**0**
15f		**27**	**27**
15g		**65**	**0**
15h		**39**	**17**
15i		**51**	**0**

[a] Reaction of **15a** ($R^1 = R^2 = Et$) and **15c** (R^1, $R^2 = (CH_2)_4$) under the standard conditions gave complex mixtures of very polar products, and no **17** or **18**.

Experimental

General Procedures : Reactions requiring anhydrous conditions were performed using oven dried glassware and conducted under nitrogen. Anhydrous solvents were prepared according to the published procedure[15] and stored over activated 4Å molecular sieves. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1720X FT-IR spectrometer. NMR spectra were recorded on a JEOL EX270 instrument and were performed in $CDCl_3$ solutions using tetramethylsilane as the internal reference. Chiral ^1H NMR experiments were conducted on a Bruker AM300 spectrophotometer. Mass spectra were obtained using a Kratos MS-25 mass spectrometer with an ionisation potential of 70 eV at 200°C. Elemental analyses were performed on a Carlo Erba 1106 CHN elemental analyser. Distillations were performed using a bulb-to-bulb (Kugelrohr) apparatus (Büchi GKR-50 glass tube oven); all boiling points quoted relate to the oven temperature at which distillation commenced. Flash chromatography was performed on silica gel (Sorbsil C60, MPD 60Å, 40-60 microns) according to the published procedure.[16] TLC was performed on aluminium backed plates pre-coated with silica (0.2 mm, $60F_{254}$) and developed using standard visualising agents: UV fluorescence (254 and 366 nm) and iodine. R_f values are quoted to the nearest 0.05. Optical rotations were determined using a JASCO DIP-370 digital polarimeter at 589 nm (Na D-line), with a path length of 1 dm. Concentrations (*c.*) are quoted in g / 100 ml. Chiral capillary electrophoresis was run on an ABI model 270-HT instrument.

Experimental procedures: (2S,3S)-3-Phenyloxiranemethanol **13a**. Prepared according to the published procedure[17] (68%; lit. 89%). Physical and spectroscopic data were in accordance with the reported values. $[\alpha]_D^{26}$ -52.9 (*c.* 1.03, $CHCl_3$); (lit.[17] $[\alpha]_D^{25}$ -49.6 (*c.* 2.40, $CHCl_3$)).

Preparation of 3-amino-3-phenylpropane-1,2-diols **14**. *Method A: Using magnesium perchlorate as the catalyst.*

A stirred solution of 3-phenyloxiranemethanol (**13**)[18] (1.50 g, 10.0 mmol) and magnesium perchlorate (2.23 g, 10.0 mmol) in dry acetonitrile (30 ml) under nitrogen at room temperature was treated dropwise with a solution of the appropriate amine (10.0 mmol) in dry acetonitrile (30 ml). The resulting solution was stirred at room temperature until the reaction was complete by TLC inspection. The mixture was quenched with saturated $NaHCO_3$ (aq) (400 ml) and extracted with ethyl acetate (3 x 100 ml). The combined organic phases were washed with brine (200 ml), dried (Na_2SO_4) and the solvent removed *in vacuo* to give the crude product.

Method B: Using titanium(IV) isopropoxide as the catalyst. A stirred solution of epoxide **13** (1.50 g, 10.0 mmol) and titanium(IV) isopropoxide (5.95 ml, 20.0 mmol) in dry dichloromethane (30 ml) under nitrogen at room temperature was treated dropwise with a solution of the appropriate amine (12.0 mmol) in dry dichloromethane (30 ml). The mixture was stirred at room temperature for 2 h, quenched with a solution of 10% NaOH in brine (30 ml) and the resulting suspension was stirred for an additional period of 12 h. The mixture was filtered through a short pad of Celite and the filtrate extracted with 0.1-1.0 M HCl (4 x 100 ml). The resulting aqueous phase was washed once with dichloromethane (100 ml), basified to pH 11-14 with 1 M NaOH and extracted with dichloromethane (3 x 100 ml). Concentration *in vacuo* of the combined, dried (Na_2SO_4) organic phases provided the crude product.

The crude products from Methods A and B were purified either by recrystallisation or column chromatography. The following compounds were prepared according to this methodology:

3-(N,N-Diethylamino)-3-phenylpropane-1,2-diol **14a**. *Method A:* No reaction with diethylamine.

Method B: Diethylamine gave the title compound **14a** (77%) as a colourless oil after Kugelrohr distillation, b.p. 135°C at 0.1 mmHg; R_f (1:9 methanol/dichloromethane) 0.10. (Satisfactory elemental analysis could not be obtained for this material); ν_{max} (thin film)/cm^{-1} 3372 (OH), 1601; δ_H (270 MHz; $CDCl_3$) 1.08 (6H, t, J = 7.1 Hz, $NCH_2C\underline{H}_3$), 2.11 (2H, m, $NC\underline{H}_2CH_3$), 2.67 (2H, m, $NC\underline{H}_2CH_3$), 3.67 (1H, dd, J = 7.3, 10.9 Hz, C(1)$\underline{H}$), 3.75 (1H, dd, J = 5.0, 10.6 Hz, C(1)$\underline{H}$), 3.84 (1H, d, J = 9.2 Hz, C(3)$\underline{H}$), 4.26 (1H, m, C(2)$\underline{H}$), 7.21-7.40 (5H, m, ArC$\underline{H}$); δ_C (67.8 MHz; $CDCl_3$) 12.58 ($NCH_2\underline{C}H_3$), 43.49 ($N\underline{C}H_2CH_3$), 67.24 ($\underline{C}$-1), 67.32, 68.45 ($\underline{C}$-2 and $\underline{C}$-3), 127.49, 127.92, 129.51 (Ar-$\underline{C}$H), 134.45 (Ar *ipso*-$\underline{C}$); *m/z* 206 (M^+-17, 1%), 162 (100).

3-(4-Morpholino)-3-phenylpropane-1,2-diol **14b.** *Method A:* No reaction with morpholine.

Method B: Morpholine gave the title compound **14b** (45%) as colourless crystals from ethyl acetate and hexane, m.p. 96-97°C; R_f (ethyl acetate) 0.15. (Found: C, 66.03; H, 8.00; N, 5.78. $C_{13}H_{19}NO_3$ requires C, 65.80; H, 8.07; N, 5.90%); ν_{max} (Nujol)/cm^{-1} 3343 (OH), 1496; δ_H (270 MHz; $CDCl_3$) 2.48 (4H, m, C(3')$\underline{H}_2$ and C(5')$\underline{H}_2$ (morpholine)), 3.44 (1H, d, J = 7.3 Hz, C(3)$\underline{H}$), 3.56 (1H, dd, J = 6.1, 11.1 Hz, C(1)$\underline{H}$), 3.60-3.67 (5H, m, C(1)$\underline{H}$ + C(2')$\underline{H}_2$ and C(6')$\underline{H}_2$ (morpholine)), 4.29 (1H, m, C(2)$\underline{H}$), 7.21-7.40 (5H, m, ArC$\underline{H}$); δ_C (67.8 MHz; $CDCl_3$) 50.68 ($\underline{C}$-3' and $\underline{C}$-5' (morpholine)), 66.13 ($\underline{C}$-2' and $\underline{C}$-6' (morpholine)), 66.81 ($\underline{C}$-1), 68.11 ($\underline{C}$-3), 73.28 ($\underline{C}$-2), 127.91, 128.18, 129.36 (Ar-$\underline{C}$H), 134.27 (Ar *ipso*-$\underline{C}$); *m/z* 206 (M^+-31, 2%), 176 (100).

3-Phenyl-3-(1-pyrrolidino)propane-1,2-diol **14c**. *Method A:* No reaction with pyrrolidine.

Method B: Pyrrolidine gave the title compound **14c** (59%) as a pale brown solid, m.p. 53.5-56°C; R_f (1:9 methanol/dichloromethane) 0.05. (Satisfactory elemental analysis could not be obtained for this material); ν_{max} (thin film)/cm^{-1} 3392 (OH), 1603; δ_H (270 MHz; $CDCl_3$) 1.73 (4H, m, C(3')$\underline{H}_2$ and C(4')$\underline{H}_2$ (pyrrolidine)), 2.54 (4H, m, C(2')$\underline{H}_2$ and C(5')$\underline{H}_2$ (pyrrolidine)), 3.21 (2H, br s, 2 x O$\underline{H}$), 3.36 (1H, dd, J = 6.6, 11.2 Hz, C(1)$\underline{H}$), 3.41 (1H, d, J = 5.3 Hz, C(3)$\underline{H}$), 3.48 (1H, dd, J = 5.0, 11.2 Hz, C(1)$\underline{H}$), 4.23 (1H, m, C(2)$\underline{H}$), 7.26-7.37 (5H, m, ArC$\underline{H}$); δ_C (67.8 MHz; $CDCl_3$) 22.82 ($\underline{C}$-3' and $\underline{C}$-4' (pyrrolidine)), 51.66 ($\underline{C}$-2' and $\underline{C}$-5' (pyrrolidine)), 65.43 ($\underline{C}$-1), 70.96, 71.98 ($\underline{C}$-2 and $\underline{C}$-3), 127.60, 127.96, 129.24 (Ar$\underline{C}$H), 136.53 (Ar *ipso*-$\underline{C}$); *m/z* 219 (M^+-2, 1%), 160 (100).

3-(1-Indolinyl)-3-phenylpropane-1,2-diol **14d**. *Method A:* Indoline (reaction time 90 min) gave the title compound **14d** (77%) as beige needles from ethyl acetate and hexane, m.p. 124.5-125.5°C; R_f (3:7 ethyl acetate/hexane) 0.05. (Found: C, 75.52; H, 7.05; N, 5.12. $C_{17}H_{19}NO_2$ requires C, 75.81; H, 7.11; N, 5.20%); ν_{max} (Nujol)/cm^{-1} 3392 (OH), 1601; δ_H (270 MHz; $CDCl_3$) 2.85 (2H, m, C(3')$\underline{H}_2$ (indoline)), 3.26 (1H, m, C(2')$\underline{H}$ (indoline)), 3.47 (1H, dt, J = 5.0, 5.3 Hz, C(2')$\underline{H}$ (indoline)), 3.77 (1H, dd, J = 5.8, 11.4 Hz, C(1)$\underline{H}$), 3.90 (1H, dd, J = 3.8, 11.4 Hz, C(1)$\underline{H}$), 4.53 (1H, m, C(2)$\underline{H}$), 4.71 (1H, d, J = 8.9 Hz,

C(3)H), 6.69 (1H, t, *J* = 7.3 Hz, ArCH), 6.77 (1H, d, *J* = 8.2 Hz, ArCH), 7.02 (1H, d, *J* = 7.3 Hz, ArCH), 7.09 (1H, t, *J* = 7.6 Hz, ArCH), 7.27-7.38 (5H, m, ArCH); δ_C (67.8 MHz; $CDCl_3$) 28.23 (C-3' (indoline)), 47.59 (C-2' (indoline)), 61.26 (C-3), 64.55 (C-1), 70.50 (C-2), 106.85, 117.40, 127.22, 127.91, 128.61, 128.95 (ArCH), 129.25, 135.96, 150.76 (Ar *ipso*-C); *m/z* 269 (M^+, 3%), 91 (100).

Method B: Indoline gave **14d** (78%) which had identical physical and spectroscopic properties to those described above.

3-(N-Methyl-N-phenylamino)-3-phenylpropane-1,2-diol **14e**. *Method A:* *N*-Methylaniline (reaction time 4 h) gave the title compound **14e** (53%) as colourless needles after column chromatography (1:4 → 1:1 ethyl acetate/hexane) and recrystallisation from ethyl acetate/hexane, m.p. 117-118.5°C; R_f (1:1 ethyl acetate/hexane) 0.30. (Found: C, 74.84; H, 7.46; N, 5.43. $C_{16}H_{19}NO_2$ requires C, 74.68; H, 7.44; N, 5.44%); ν_{max} (Nujol)/cm^{-1} 3371 (OH), 1597; δ_H (270 MHz; $CDCl_3$) 2.58 (3H, s, CH_3), 3.81 (1H, dd, *J* = 5.3, 11.2 Hz, C(1)H), 3.92 (1H, dd, *J* = 3.6, 11.2 Hz, C(1)H), 4.46 (1H, m, C(2)H), 4.98 (1H, d, *J* = 9.6 Hz, C(3)H), 6.80 (1H, t, *J* = 7.3 Hz, ArCH), 6.92 (2H, d, *J* = 7.9 Hz, ArCH), 7.22-7.37 (7H, m, ArCH); δ_C (67.8 MHz; $CDCl_3$) 32.89 (CH_3), 64.31 (C-1), 65.02 (C-3), 70.26 (C-2), 114.59, 118.22, 127.75, 128.28, 128.57, 129.90 (ArCH), 136.86, 150.19 (Ar *ipso*-C); *m/z* 257 (M^+, 3%), 196 (100).

Method B: *N*-Methylaniline gave **14e** (77%) which had identical physical and spectroscopic properties to those described above.

3-[N-(4-Methylphenylamino)]-3-phenylpropane-1,2-diol **14f**. *Method A:* *p*-Toluidine (reaction time 3 h) gave the title compound **14f** (75%) as a colourless solid after column chromatography (1:1 ethyl acetate/hexane) and recrystallisation from ethyl acetate/hexane, m.p. 112-113°C; R_f (1:1 ethyl acetate/hexane) 0.20. (Found: C, 74.61; H, 7.39; N, 5.36. $C_{16}H_{19}NO_2$ requires C, 74.68; H, 7.44; N, 5.44%); ν_{max} (Nujol)/cm^{-1} 3317 (NH and OH), 1602; δ_H (270 MHz; $CDCl_3$) 2.18 (3H, s, CH_3), 3.58 (1H, dd, *J* = 5.3, 11.5 Hz, C(1)H), 3.68 (1H, dd, *J* = 3.8, 11.4 Hz, C(1)H), 4.01 (1H, m, C(2)H), 4.61 (1H, d, *J* = 5.3 Hz, C(3)H), 6.50 (2H, d, *J* = 8.6 Hz, ArCH), 6.90 (2H, d, *J* = 7.9 Hz, ArCH), 7.22-7.37 (5H, m, ArCH); δ_C (67.8 MHz; $CDCl_3$) 20.33 (CH_3), 60.99 (C-3), 63.61 (C-1), 73.93 (C-2), 114.12, 127.15, 127.66, 128.81, 129.65 (ArCH), 127.26, 139.28, 144.47 (Ar *ipso*-C); *m/z* 257 (M^+, 4%), 195 (100).

Method B: *p*-Toluidine gave **14f** (89%) which had identical physical and spectroscopic properties to those described above.

3-[N-(3-Methoxyphenylamino)-N-methyl]-3-phenylpropane-1,2-diol **14g**. *Method A:* *N*-Methyl-*m*-anisidine **16**[12] (reaction time 1 h) gave the title compound **14g** (57%) as a colourless solid after column chromatography (1:9 → 1:1 ethyl acetate/hexane) and recrystallisation from ethyl acetate/hexane, m.p. 86-87.5°C; R_f (1:1 ethyl acetate/hexane) 0.30. (Found: C, 71.12; H, 7.29; N, 4.78. $C_{17}H_{21}NO_3$ requires C, 71.06; H, 7.37; N, 4.87%); ν_{max} (Nujol)/cm^{-1} 3306 (OH), 1599; δ_H (270 MHz; $CDCl_3$) 2.35 (2H, br s, 2 x OH), 2.54 (3H, s, NCH_3), 3.72-3.77 (4H, m, C(1)H and OCH_3), 3.87 (1H, dd, *J* = 3.0, 11.2 Hz, C(1)H), 4.42 (1H, m, C(2)H), 4.96 (1H, d, *J* = 9.9 Hz, C(3)H), 6.35 (1H, dd, *J* = 2.2, 8.1 Hz, ArCH), 6.43 (1H, t, *J* = 2.3 Hz, ArCH), 6.54 (1H, dd, *J* = 2.3, 8.3 Hz, ArCH), 7.16 (1H, t, *J* = 8.1 Hz, ArCH), 7.23-7.36 (5H, m, ArCH); δ_C (67.8 MHz; $CDCl_3$) 32.80 (NCH_3), 55.06 (OCH_3), 64.13 (C-1), 64.17 (C-3), 70.35 (C-2),

100.68, 102.44, 107.06, 127.57, 128.21, 128.45, 129.92 (ArCH), 137.20, 151.50, 160.68 (Ar *ipso*-C); *m/z* 287 (M^+, 3%), 226 (100).

Method B: *N*-Methyl-*m*-anisidine **16** gave **14g** (63%) after column chromatography (1:9 → 1:1 ethyl acetate/hexane). The product had identical physical and spectroscopic properties to those described above.

3-(N,N-Diphenylmethylamino)-3-phenylpropane-1,2-diol **14h**. *Method A:* Diphenylmethylamine (reaction time 3 h) gave the title compound **14h** (18%) as a yellow solid after column chromatography (1:4 → 2:3 ethyl acetate/hexane) and Kugelrohr distillation, b.p. 160°C at 0.3 mmHg; m.p. 33.5-36°C; R_f (ethyl acetate) 0.60. (Satisfactory elemental analysis could not be obtained for this material); ν_{max} (thin film)/cm^{-1} 3393 (NH and OH), 1600; δ_H (270 MHz; $CDCl_3$) 2.99 (3H, br s, 2 x OH and 1 x NH), 3.45 (1H, dd, J = 5.8, 11.4 Hz, C(1)H), 3.57 (1H, dd, J = 4.0, 11.2 Hz, C(1)H), 3.61 (1H, d, J = 6.3 Hz, C(3)H), 3.76 (1H, m, C(2)H), 4.59 (1H, s, $CHPh_2$), 7.07-7.35 (15H, m, ArCH); δ_C (67.8 MHz; $CDCl_3$) 63.47, 63.67 (C-1 and $CHPh_2$), 64.75 (C-3), 73.51 (C-2), 127.08, 127.28, 127.46, 127.73, 127.92, 128.55, 128.72, 128.81 (ArCH), 138.63, 141.51, 143.22 (Ar *ipso*-C); *m/z* 273 (M^+-60, 4%), 167 (100).

Method B: Diphenylmethylamine gave **14h** (18%) after column chromatography (20% → 40% ethyl acetate/hexane) and Kugelrohr distillation. The product had identical physical and spectroscopic properties to those described above.

(2R,3S)-3-(4-Morpholino)-3-phenylpropane-1,2-diol **14i**. *Method B:* Reaction of (2*S*,3*S*)-3-phenyloxiranemethanol **13a** with morpholine using the same conditions and purification protocol as for the racemate **13** gave **14i** in 32% yield as colourless crystals. It had identical physical and spectroscopic properties to (**14b**) with the exception of m.p. 108-109°C and $[\alpha]_D^{25}$ -23.5 (*c.* 0.81, $CHCl_3$).

Preparation of 1-phenyloxiranemethanamines **15**. To a stirred solution of the appropriate 3-amino-3-phenylpropane-1,2-diol **14** (7.00 mmol) in dry dichloromethane (50 ml) under a nitrogen atmosphere at -10°C was added triethylamine (2.05 ml, 14.7 mmol) in one portion followed by *n*-propanesulfonyl chloride (0.79 ml, 7.00 mmol) in dry dichloromethane (10 ml) dropwise. The mixture was stirred for 20 min when TLC showed formation of the primary *n*-propanesulfonyloxy derivative. The resulting mixture was then treated dropwise with a solution of sodium (0.42 g, 18.3 g atoms) in dry methanol (30 ml) and stirred below 0°C until TLC showed complete conversion to the epoxide. The reaction mixture was quenched with brine (200 ml) and extracted with dichloromethane (3 x 100 ml). Concentration *in vacuo* of the combined, dried (Na_2SO_4) organic phases gave the crude product which was purified by column chromatography.

The following compounds were obtained by this procedure:

N,N-Diethyl-1-phenyloxiranemethanamine **15a**. The amino diol **14a** (reaction time 30 min for epoxide formation) gave the title compound **15a** (78%) as a brown oil which was used and characterised crude because of its tendency to decompose during column chromatography or Kugelrohr distillation; R_f (1:9 methanol/dichloromethane) 0.75; ν_{max} (thin film)/cm^{-1} 1603; δ_H (270 MHz; $CDCl_3$) 0.99 (6H, t, J = 7.1 Hz, NCH_2CH_3), 2.49-2.78 (5H, m, NCH_2CH_3 and C(3)H), 2.90 (1H, dd, J = 3.6, 5.3 Hz, C(3)H), 3.16 (1H, m, C(2)H), 3.28 (1H, d, J = 2.0 Hz, C(1)H), 7.23-7.41 (5H, m, ArCH); *m/z* 206 (M^++1, 7%), 116 (100).

Purification of crude **15a** by column chromatography (1:9 ethyl acetate/hexane → ethyl acetate → 1:9 methanol/dichloromethane) gave *2-(N,N-diethylamino)-3-phenylpropane-1,3-diol* **16a** (33%) as a pale yellow oil after Kugelrohr distillation, b.p. 125°C at 0.1 mmHg; R_f (1:9 methanol/dichloromethane) 0.10. (Satisfactory elemental analysis could not be obtained for this material); ν_{max} (thin film)/cm^{-1} 3392 (OH), 1603; δ_H (270 MHz; $CDCl_3$) 0.97 (6H, t, *J* = 7.1 Hz, $NCH_2C\underline{H}_3$), 2.42 (2H, m, $NC\underline{H}_2CH_3$), 2.69 (2H, m, $NC\underline{H}_2CH_3$), 2.93 (2H, br s, O<u>H</u>), 2.98 (1H, m, C(2)<u>H</u>), 3.61 (1H, dd, *J* = 7.8, 10.7 Hz, C(1)<u>H</u>), 3.69 (1H, dd, *J* = 5.6, 10.9 Hz, C(1)<u>H</u>), 4.87 (1H, d, *J* = 5.9 Hz, C(3)<u>H</u>), 7.23-7.37 (5H, m, Ar<u>C</u>H); δ_C (67.8 MHz; $CDCl_3$) 14.34 ($NCH_2\underline{C}H_3$), 43.74 ($N\underline{C}H_2CH_3$), 58.24 (<u>C</u>-2), 65.84, 72.67 (<u>C</u>-1and <u>C</u>-3), 126.16, 127.53, 128.28 (Ar<u>C</u>H), 143.34 (Ar *ipso*-<u>C</u>); *m/z* 206 (M^+-17, 1%), 116 (100).

N-(1-Oxiranyl-1-phenylmethyl)morpholine **15b.** The amino diol **14b** (reaction time 75 min for epoxide formation) gave the title compound **15b** (87%) as colourless crystals after column chromatography (1:4 ethyl acetate/hexane) and recrystallisation from ethyl acetate/hexane, m.p. 62-63.5°C; R_f (1:9 ethyl acetate/hexane) 0.50. (Found: C, 71.09; H, 7.76; N, 6.30. $C_{13}H_{17}NO_2$ requires C, 71.21; H, 7.81; N, 6.39%); ν_{max} (thin film)/cm^{-1} 1602; δ_H (270 MHz; $CDCl_3$) 2.49 (4H, m, C(3')<u>H</u>$_2$ and C(5')<u>H</u>$_2$ (morpholine)), 2.66 (1H, dd, *J* = 2.6, 4.9 Hz, C(3)<u>H</u>), 2.76 (1H, d, *J* = 7.6 Hz, C(1)<u>H</u>), 2.92 (1H, dd, *J* = 3.8, 5.1 Hz, C(3)<u>H</u>), 3.12 (1H, m, C(2)<u>H</u>), 3.70 (4H, m, C(2')<u>H</u>$_2$ and C(6')<u>H</u>$_2$ (morpholine)), 7.26-7.36 (5H, m, Ar<u>C</u>H); δ_C (67.8 MHz; $CDCl_3$) 48.82 (<u>C</u>-3' and <u>C</u>-5' (morpholine)), 52.08 (<u>C</u>-3), 53.93 (<u>C</u>-1), 66.99, (<u>C</u>-2' and <u>C</u>-6' (morpholine)), 73.19 (<u>C</u>-2), 127.80, 128.46, 128.50 (Ar<u>C</u>H), 138.90 (Ar *ipso*-<u>C</u>); *m/z* 219 (M^+, 4%), 176 (100).

N-(1-Oxiranyl-1-phenylmethyl)pyrrolidine **15c**. The amino diol **14c** (reaction time 30 min for epoxide formation) gave the title compound **15c** (76%) as colourless crystals after column chromatography (3:7 ethyl acetate/hexane) and Kugelrohr distillation, b.p. 95°C at 0.2 mmHg; R_f (1:1 ethyl acetate/hexane) 0.40. (Satisfactory elemental analysis could not be obtained for this material); ν_{max} (thin film)/cm^{-1} 1603; δ_H (270 MHz; $CDCl_3$) 1.77 (4H, m, C(3')<u>H</u>$_2$ and C(4')-<u>H</u>$_2$ (pyrrolidine)), 2.50 (4H, m, C(2')<u>H</u>$_2$ and C(5')<u>H</u>$_2$ (pyrrolidine)), 2.67 (1H, dd, *J* = 2.4, 5.1 Hz, C(3)<u>H</u>), 2.67 (1H, d, *J* = 7.6 Hz, C(1)<u>H</u>), 2.91 (1H, dd, *J* = 3.8, 5.1 Hz, C(3)<u>H</u>), 3.18 (1H, m, C(2)<u>H</u>), 7.24-7.40 (5H, m, Ar<u>C</u>H); δ_C (67.8 MHz; $CDCl_3$) 23.08 (<u>C</u>-3' and <u>C</u>-4' (pyrrolidine)), 48.57 (<u>C</u>-2' and <u>C</u>-5' (pyrrolidine)), 52.90 (<u>C</u>-3), 55.13 (<u>C</u>-1), 73.16 (<u>C</u>-2), 127.53, 128.07, 128.28 (Ar<u>C</u>H), 140.49 (Ar *ipso*-<u>C</u>); *m/z* 203 (M^+, 3%), 70 (100).

N-(1-Oxiranyl-1-phenylmethyl)indoline **15d**. The amino diol **14d** (reaction time 90 min for epoxide formation) gave the title compound **15d** (81%) as a yellow oil after column chromatography (1:19 ethyl acetate/hexane); R_f (1:1 ethyl acetate/hexane) 0.75. (Found: C, 80.84; H, 6.82; N, 5.74. $C_{17}H_{17}NO$ requires C, 81.24; H, 6.82; N, 5.57%); ν_{max} (thin film)/cm^{-1} 1606; δ_H (270 MHz; $CDCl_3$) 2.59 (1H, dd, *J* = 2.6, 5.0 Hz, C(3)<u>H</u>), 2.78 (1H, dd, *J* = 3.6, 5.0 Hz, C(3)<u>H</u>), 2.92 (2H, t, *J* = 8.4 Hz, C(3')<u>H</u>$_2$ (indoline)), 3.36 (1H, m, C(2)<u>H</u>), 3.48 (2H, m, C(2')<u>H</u>$_2$ (indoline)), 4.17 (1H, d, *J* = 6.9 Hz, C(1)<u>H</u>), 6.24 (1H, d, *J* = 7.9 Hz, Ar<u>C</u>H), 6.57 (1H, dt, *J* = 0.7, 7.3 Hz, Ar<u>C</u>H), 6.89 (1H, dt, *J* = 0.7, 7.8 Hz, Ar<u>C</u>H), 7.01 (1H, dd, *J* = 0.7, 7.3 Hz, Ar<u>C</u>H), 7.19-7.32 (3H, m, Ar<u>C</u>H), 7.39-7.44 (2H, m, Ar<u>C</u>H); δ_C (67.8 MHz; $CDCl_3$) 28.45 (<u>C</u>-2' (indoline)), 46.72 (<u>C</u>-3), 50.04 (<u>C</u>-3' (indoline)), 52.69 (<u>C</u>-1), 62.53 (<u>C</u>-2), 107.33, 117.46, 124.40, 127.10, 127.56, 127.80, 128.43 (Ar<u>C</u>H), 129.54, 138.17, 151.05 (Ar *ipso*-<u>C</u>); *m/z* 251 (M^+, 12%), 221 (100).

N-Methyl-N-phenyl-1-phenyloxiranemethanamine **15e**. The amino diol **14e** (reaction time 1 h for epoxide formation) gave the title compound **15e** (78%) as a pale yellow oil after column chromatography (1:19 ethyl acetate/hexane); R_f (1:1 ethyl acetate/hexane) 0.70. (Found: C, 80.44; H, 7.14; N, 5.92. $C_{16}H_{17}NO$ requires C, 80.30; H, 7.16; N, 5.85%); ν_{max} (thin film)/cm^{-1} 1599; δ_H (270 MHz; $CDCl_3$) 2.57 (1H, dd, *J* = 2.6, 4.6 Hz, C(3)H), 2.80 (1H, dd, *J* = 4.0, 5.0 Hz, C(3)H), 2.89 (3H, s, NCH$_3$), 3.42 (1H, m, C(2)H), 4.64 (1H, d, *J* = 5.9 Hz, C(1)H), 6.73 (1H, t, ArCH), 6.79 (2H, d, *J* = 8.3 Hz, ArCH), 7.15-7.41 (7H, m, ArCH); δ_C (67.8 MHz; $CDCl_3$) 34.16 (NCH$_3$), 45.48 (C-3), 52.76 (C-1), 64.75 (C-2), 113.15, 117.40, 127.30, 127.42, 128.45, 129.13 (ArCH), 138.72, 149.76 (Ar *ipso*-C); *m/z* 239 (M$^+$, 10%), 209 (100).

N-(4-Methylphenyl)-1-phenyloxiranemethanamine **15f.** The amino diol **14f** (reaction time 30 min for epoxide formation) gave the title compound **15f** (81%) as colourless crystals after column chromatography (1:19 ethyl acetate/hexane) and recrystallisation from hexane, m.p. 55-56.5°C; R_f (1:1 ethyl acetate/hexane) 0.70. (Found: C, 80.26; H, 7.05; N, 5.90. $C_{16}H_{17}NO$ requires C, 80.30; H, 7.16; N, 5.85%); ν_{max} (thin film)/cm^{-1} 3371 (NH), 1618; δ_H (270 MHz; $CDCl_3$) 2.18 (3H, s, NCH$_3$), 2.67 (1H, dd, *J* = 2.8, 4.8 Hz, C(3)H), 2.73 (1H, dd, *J* = 4.0, 4.6 Hz, C(3)H), 3.34 (1H, m, C(2)H), 4.13 (1H, br s, NH), 4.52 (1H, d, *J* = 4.6 Hz, C(1)H), 6.46 (2H, d, *J* = 8.2 Hz, ArCH), 6.89 (2H, dd, *J* = 0.7, 8.6 Hz, ArCH), 7.24-7.41 (5H, m, ArCH); δ_C (67.8 MHz; $CDCl_3$) 20.31 (NCH$_3$), 44.76 (C-3), 54.83 (C-1), 57.94 (C-2), 114.21, 126.99, 127.73, 128.70, 129.54 (ArCH), 127.31, 139.35, 144.60 (Ar *ipso*-C); *m/z* 239 (M$^+$, 26%), 196 (100).

N-(3-Methoxyphenyl)-N-methyl-1-phenyloxiranemethanamine **15g**. The amino diol **14g** (reaction time 30 min for epoxide formation) gave the title compound **15g** (79%) as a pale brown oil after column chromatography (1:19 ethyl acetate/hexane); R_f (1:1 ethyl acetate/hexane) 0.75. (Found: C, 75.82; H, 7.17; N, 5.00. $C_{17}H_{19}NO_2$ requires C, 75.81; H, 7.11; N, 5.20%); ν_{max} (thin film)/cm^{-1} 1609; δ_H (270 MHz; $CDCl_3$) 2.55 (1H, dd, *J* = 2.6, 4.6 Hz, C(3)H), 2.76 (1H, t, *J* = 4.5 Hz, C(3)H), 2.86 (3H, s, NCH$_3$), 3.39 (1H, m, C(2)H), 3.70 (3H, s, OCH$_3$), 4.62 (1H, d, *J* = 6.3 Hz, C(1)H), 6.28-6.33 (2H, m, ArCH), 6.39 (1H, d, *J* = 8.6 Hz, ArCH), 7.09 (1H, t, *J* = 8.3 Hz, ArCH), 7.20-7.39 (5H, m, ArCH); δ_C (67.8 MHz; $CDCl_3$) 34.05 (NCH$_3$), 45.27 (C-3), 52.56 (OCH$_3$), 54.79 (C-1), 64.49 (C-2), 99.52, 101.87, 105.95, 127.15, 127.31, 128.34, 129.69 (ArCH), 138.60, 151.05, 160.57 (Ar *ipso*-C); *m/z* 269 (M$^+$, 15%), 239 (100).

N-(Diphenylmethyl)-1-phenyloxiranemethanamine **15h.** The amino diol **14h** (reaction time 30 min for epoxide formation) gave the title compound **15h** (76%) as a colourless oil after column chromatography (1:19 ethyl acetate/hexane) and Kugelrohr distillation, b.p. 140°C at 0.2 mmHg; R_f (1:1 ethyl acetate/hexane) 0.80. (Found: C, 83.77; H, 6.66; N, 4.43. $C_{22}H_{21}NO$ requires C, 83.78; H, 6.71; N, 4.44%); ν_{max} (thin film)/cm^{-1} 3319 (NH), 1600; δ_H (270 MHz; $CDCl_3$) 2.13 (1H, br s, NH), 2.67 (2H, m, C(3)H), 3.17 (1H, m, C(2)H), 3.72 (1H, d, *J* = 4.6 Hz, C(1)H), 4.69 (1H, s, CHPh$_2$), 7.14-7.38 (15H, m, ArCH); δ_C (67.8 MHz; $CDCl_3$) 44.98 (C-3), 55.29 (CHPh$_2$), 59.64 (C-1), 63.07 (C-2), 126.86, 127.10, 127.26, 127.71, 127.78, 127.92, 128.27, 128.54 (ArCH), 139.57, 143.02, 144.04 (Ar *ipso*-C); *m/z* 297 (M$^+$-18, 0.5%), 167 (100).

(1S,2R)-N-(1-Oxiranyl-1-phenylmethyl)morpholine **15i**. The amino diol **14i** was converted to the title compound **15i** in 84% yield as colourless crystals using exactly the same conditions and purification procedure as for the preparation of the analogous racemate **15b**. It had identical physical and spectroscopic properties to (**15b**), with the exception of m.p. 71-74.5°C and $[\alpha]_D^{25}$ +29.4 (*c.* 0.37, $CHCl_3$).

Preparation of 2-amino-3-phenylpropan-1-ols **11** and **17**.

To a stirred solution of the appropriate 1-phenyloxiranemethanamine **6** or **15** (5.00 mmol) and sodium cyanoborohydride (0.95 g, 15.0 mmol) in dry tetrahydrofuran (50 ml) under a nitrogen atmosphere at room temperature was added sequentially and dropwise bromocresol green (catalytic) and boron trifluoride etherate (2 ml) in dry tetrahydrofuran (20 ml) dropwise until an orange-yellow solution (from blue) was obtained. The resulting solution was stirred until TLC showed that the reaction was complete, with more $BF_3.OEt_2$ solution being added periodically to maintain the acidity. The reaction mixture was quenched with 1 M Na_2CO_3 (200 ml) and extracted with ethyl acetate (3 x 100 ml). Concentration *in vacuo* of the combined, dried (Na_2SO_4) organic phases provided the crude product which was purified by column chromatography.

The above procedure was used in order to synthesise the following compounds:

(2S)-2-(7-Cyanomethoxyindolin-1-yl)-3-[3-(1,3-dioxolan-2-yl)phenyl]propan-1-ol **11**. The epoxy amine **6** (reaction time 3.5 h at reflux) gave the title compound **11** (37%) as a pale yellow oil after column chromatography (2:3 ethyl acetate/hexane); R_f (1:1 ethyl acetate/hexane) 0.25, $[\alpha]_D^{25}$ -67.8 (*c.* 0.9, $CHCl_3$). (Satisfactory elemental analysis could not be obtained for this material); ν_{max} (thin film)/cm^{-1} 3474 (OH), 2250 (CN), 1605; δ_H (270 MHz; $CDCl_3$) 2.70 (1H, dd, *J* = 8.4, 13.5 Hz, C(3)H), 2.78 (1H, dd, *J* = 5.6, 13.5 Hz, C(3)H), 3.03 (2H, m, C(3')H_2, (indoline)), 3.53 (2H, m, C(2')H_2, (indoline)), 3.65 (2H, m, C(1)H_2), 4.04 (4H, m, C(4")H_2, C(5")H_2 (dioxolane)), 4.60 (3H, m, C(2)H, OCH_2CN), 5.78 (1H, s, C(2") H (dioxolane)), 6.70 (2H, m, ArCH), 6.83 (1H, m, ArCH), 7.7 (1H, m, ArCH), 7.24 (3H, m, ArCH).

Attempted synthesis of 2-(N,N-diethylamino)-3-phenylpropan-1-ol **17a**. The epoxy amine **15a** gave none of the title compound **17a**, but only yielded an unidentifiable boron complex.

2-(4-Morpholino)-3-phenylpropan-1-ol **17b**. The epoxy amine **15b** (reaction time 30 min at reflux) gave the title compound **17b** (48%) as colourless crystals after column chromatography (1:49 methanol/dichloromethane) and recrystallisation from ethyl acetate/hexane, m.p. 75.5-77°C; R_f (1:9 methanol/dichloromethane) 0.65. (Found: C, 70.28; H, 8.63; N, 6.10. $C_{13}H_{19}NO_2$ requires C, 70.56; H, 8.65; N, 6.33%); ν_{max} (thin film)/cm^{-1} 3446 (OH), 1603; δ_H (270 MHz; $CDCl_3$) 2.35 (1H, dd, *J* = 9.2, 12.9 Hz, C(3)H), 2.63 (4H, m, C(3')H_2 and C(5')H_2 (morpholine)), 2.83 (1H, m, C(2)H), 2.93 (1H, dd, *J* = 4.3, 12.9 Hz, C(3)H), 3.24 (1H, br s, OH), 3.37 (2H, m, C(1)H), 3.69 (4H, m, C(2')H_2 and C(6')H_2 (morpholine)), 7.11-7.29 (5H, m, ArCH); δ_C (67.8 MHz; $CDCl_3$) 31.86 (C-3), 48.48 (C-1), 59.57 (C-3' and C-5' (morpholine)), 67.30 (C-2), 67.39 (C-2' and C-6' (morpholine)), 126.24, 128.54, 128.84 (ArCH), 138.91 (Ar *ipso*-C); *m/z* 221 (M^+, 0.5%), 130 (100).

Attempted synthesis of 3-phenyl-2-(1-pyrrolidino)propan-1-ol **17c**. The epoxy amine **15c** gave none of the title compound **17c**, but only yielded an unidentifiable boron complex.

Attempted synthesis of 2-(1-indolinyl)-3-phenylpropan-1-ol **17d**; *preparation of 1-(1-indolinyl)-1-phenylpropan-2-ol* **18d**. The epoxy amine (**15d**) (reaction time 30 min) gave a brown oil after column chromatography (1:4 ethyl acetate/hexane) which was found to be a mixture of products using ^{1}H-NMR, but one spot by TLC. On standing, a colourless solid formed within the brown oil and was obtained by crystallisation from diethyl ether. The colourless crystals isolated were identified as *1-(1-indolinyl)-1-phenylpropan-2-ol* **18d** (14%) and this was the only identifiable product (none of the title compound **17d** was isolated), m.p. 93.5-95.5°C; R_f (1:4 ethyl acetate/hexane) 0.35. (Found: C, 80.49; H, 7.37; N, 5.34. $C_{17}H_{19}NO$ requires C, 80.60; H, 7.56; N, 5.53%); ν_{max} (thin film)/cm^{-1} 3294 (OH), 1606; δ_H (270 MHz; $CDCl_3$) 1.33 (3H, d, C$\underline{H}_3$, J = 6.3 Hz, C(3)$\underline{H}$), 1.66 (1H, br s, O$\underline{H}$), 2.90 (2H, m, C(3')$\underline{H}_2$ (indoline)), 3.36 (2H, m, C(2')$\underline{H}_2$ (indoline)), 4.33 (1H, d, J = 7.9 Hz, C(1)$\underline{H}$), 4.48 (1H, m, C(2)$\underline{H}$), 6.48 (1H, d, J = 8.3 Hz, ArC$\underline{H}$), 6.57 (1H, t, J = 7.1 Hz, ArC$\underline{H}$), 7.00 (2H, m, ArC$\underline{H}$), 7.18-7.38 (5H, m, ArC$\underline{H}$); δ_C (67.8 MHz; $CDCl_3$) 20.51 ($\underline{C}H_3$), 28.29 ($\underline{C}$-3' (indoline)), 48.20 ($\underline{C}$-2' (indoline)), 66.33, 67.01 ($\underline{C}$-1 and $\underline{C}$-2), 106.72, 116.98, 124.40, 127.10, 127.76, 128.55, 128.97 (Ar$\underline{C}$H), 129.31, 136.69, 151.27 (Ar *ipso*-$\underline{C}$); *m/z* 253 (M^+, 7%), 208 (100).

2-(N-Methyl-N-phenylamino)-3-phenylpropan-1-ol **17e**. The epoxy amine **15e** (reaction time 30 min) gave the title compound **17e** (48%) as a colourless oil after column chromatography (3:7 ethyl acetate/hexane) and Kugelrohr distillation, b.p. 115°C at 0.1 mmHg; R_f (3:7 ethyl acetate/hexane) 0.40. (Found: C, 79.45; H, 7.86; N, 5.91. $C_{16}H_{19}NO$ requires C, 79.63; H, 7.94; N, 5.80%); ν_{max} (thin film)/cm^{-1} 3401 (OH), 1598; δ_H (270 MHz; $CDCl_3$) 2.05 (1H, br s, O$\underline{H}$), 2.65 (1H, dd, J = 8.4, 13.7 Hz, C(3)$\underline{H}$), 2.79 (3H, s, C$\underline{H}_3$), 2.83 (1H, dd, J = 5.9, 13.9 Hz, C(3)$\underline{H}$), 3.59 (1H, dd, J = 5.0, 11.2 Hz, C(1)$\underline{H}$), 3.69 (1H, dd, J = 9.4, 11.1 Hz, C(1)$\underline{H}$), 4.15 (1H, m, C(2)$\underline{H}$), 6.76 (1H, dt, J = 1.0, 6.8 Hz, ArC$\underline{H}$), 6.86 (2H, dd, J = 1.0, 8.9 Hz, ArC$\underline{H}$), 7.07-7.31 (7H, m, ArC$\underline{H}$); δ_C (67.8 MHz, $CDCl_3$) 30.62 ($\underline{C}H_3$), 34.67 ($\underline{C}$-3), 61.73 ($\underline{C}$-1), 63.36 ($\underline{C}$-2), 114.86, 118.22, 126.29, 128.43, 128.86, 129.08 (Ar$\underline{C}$H), 138.33, 150.96 (Ar *ipso*-$\underline{C}$); *m/z* 241 (M^+, 10%), 150 (100).

2-(N-(4-Methylphenylamino))-3-phenylpropan-1-ol **17f**. The epoxy amine (**15f**) (reaction time 4 h) gave two products by TLC and after work-up. Column chromatography (1:49 methanol/dichloromethane) gave *1-(N-(4-methylphenyl))-1-phenylpropan-2-ol* **18f** (27%) as a yellow oil after Kugelrohr distillation, b.p. 115°C at 0.4 mmHg; R_f (1:49 methanol/dichloromethane) 0.45. (Found: C, 79.44; H, 7.90; N, 5.72. $C_{16}H_{19}NO$ requires C, 79.63; H, 7.94; N, 5.80%); ν_{max} (thin film)/cm^{-1} 3397, 3349 (NH and OH), 1618; δ_H (270 MHz; $CDCl_3$) 1.09 (3H, d, J = 6.6 Hz, C(3)$\underline{H}$), 2.17 (3H, s, C$\underline{H}_3$), 4.12 (1H, m, C(2)$\underline{H}$), 4.31 (1H, d, J = 4.0 Hz, C(1)$\underline{H}$), 6.46 (2H, d, J = 8.2 Hz, ArC$\underline{H}$), 6.88 (2H, d, J = 7.9 Hz, ArC$\underline{H}$), 7.21-7.31 (5H, m, ArC$\underline{H}$); δ_C (67.8 MHz; $CDCl_3$) 19.18, 20.29 (($\underline{C}$-3) and $\underline{C}H_3$ (4-methylphenyl)), 63.36 ($\underline{C}$-1), 70.46 ($\underline{C}$-2), 113.86, 127.39, 127.64, 128.45, 129.56 (Ar$\underline{C}$H), 126.76, 139.12, 144.71 (Ar *ipso*-$\underline{C}$); *m/z* 241 (M^+, 6%), 196 (100).

Further elution gave the title compound **17f** (27%) as a yellow oil after Kugelrohr distillation, b.p. 125°C at 0.4 mmHg; R_f (1:49 methanol/dichloromethane) 0.35. (Found: C, 79.31; H, 7.89; N, 5.74. $C_{16}H_{19}NO$ requires C, 79.63; H, 7.94; N, 5.80%); ν_{max} (thin film)/ cm^{-1} 3392 (NH and OH), 1618; δ_H (270 MHz; $CDCl_3$) 2.24 (3H, s, C$\underline{H}_3$), 2.79 (1H, dd, *J* = 7.3, 13.5 Hz, C(3)$\underline{H}$), 2.88 (2H, br s, N$\underline{H}$ and O$\underline{H}$), 2.91 (1H, dd, *J* = 5.1, 13.7 Hz, C(3)$\underline{H}$), 3.46 (1H, dd, *J* = 6.8, 12.0 Hz, C(1)$\underline{H}$), 3.65-3.74 (2H, m, C(1)$\underline{H}$ and C(2)$\underline{H}$), 6.60 (2H, d, *J* = 8.3 Hz, ArC$\underline{H}$), 7.00 (2H, d, *J* = 7.9 Hz, ArC$\underline{H}$), 7.15-7.31 (5H, m, ArC$\underline{H}$); δ_C (67.8 MHz; $CDCl_3$) 20.34 (C$\underline{H}_3$), 37.25 (C-3), 56.32 (C-2), 63.09 (C-1), 114.30, 126.40, 128.48, 129.25, 129.88 (ArCH), 127.49, 137.92, 144.67 (Ar *ipso*-C); *m/z* 241 (M^+, 14%), 150 (100).

2-(N-(3-Methoxyphenylamino)-N-methyl)-3-phenylpropan-1-ol **17g**. The epoxy amine **15g** (reaction time 30 min) gave the title compound **17g** (65%) as a pale brown oil after column chromatography (1:4 ethyl acetate/hexane); R_f (1:4 ethyl acetate/hexane) 0.35. (Found: C, 75.16; H, 7.81; N, 5.04. $C_{17}H_{21}NO_2$ requires C, 75.25; H, 7.80; N, 5.16%); ν_{max} (thin film)/cm^{-1} 3421 (OH), 1610; δ_H (270 MHz; $CDCl_3$) 2.20 (1H, br s, O$\underline{H}$), 2.66 (1H, dd, *J* = 8.3, 13.9 Hz, C(3)$\underline{H}$), 2.76 (3H, s, NC$\underline{H}_3$), 2.80 (1H, dd, *J* = 6.3, 13.5 Hz, C(3)$\underline{H}$), 3.57 (1H, dd, *J* = 5.1, 11.4 Hz, C(1)$\underline{H}$), 3.66 (1H, dd, *J* = 9.2, 11.2 Hz, C(1)$\underline{H}$), 3.72 (3H, s, OC$\underline{H}_3$), 4.11 (1H, m, C(2)$\underline{H}$), 6.31 (1H, dd, *J* = 2.3, 7.9 Hz, ArC$\underline{H}$), 6.35 (1H, t, *J* = 2.3 Hz, ArC$\underline{H}$), 6.45 (1H, dd, *J* = 2.3, 8.3 Hz, ArC$\underline{H}$), 7.07-7.24 (6H, m, ArC$\underline{H}$); δ_C (67.8 MHz; $CDCl_3$) 30.66 (NC$\underline{H}_3$), 34.72 (C-3), 54.97 (OC$\underline{H}_3$), 61.76 (C-1), 62.98 (C-2), 100.97, 102.73, 107.42, 126.20, 128.36, 128.81, 129.61 (ArCH), 138.33, 152.31, 160.50 (Ar *ipso*-C); *m/z* 271 (M^+, 10%), 180 (100).

2-(N-Diphenylmethylamino)-3-phenylpropan-1-ol **17h**. The epoxy amine (**15h**) (reaction time 4 h) gave two products by TLC and after work-up. Column chromatography (3:7 ethyl acetate/hexane) gave initially *1-(N-diphenylamino)-1-phenylpropan-2-ol* **18h** (17%) as a colourless oil after Kugelrohr distillation, b.p. 140°C at 0.3 mmHg; R_f (3:7 ethyl acetate/hexane) 0.55. (Found: C, 83.00; H, 7.36; N, 4.36. $C_{22}H_{23}NO$ requires C, 83.24; H, 7.30; N, 4.41%); ν_{max} (thin film)/ cm^{-1} 3406 (NH and OH), 1600; δ_H (270 MHz; $CDCl_3$) 1.04 (3H, d, *J* = 6.2 Hz, C(3)$\underline{H}$), 2.27 (2H, br s, N$\underline{H}$ and O$\underline{H}$), 3.54 (1H, d, *J* = 5.0 Hz, C(1)$\underline{H}$), 3.97 (1H, m, C(2)$\underline{H}$), 4.67 (1H, s, C$\underline{H}$Ph$_2$), 7.08-7.38 (15H, m, ArC$\underline{H}$); δ_C (67.8 MHz; $CDCl_3$); 18.98 (C-3), 63.58, 65.21 (C-1 and C$\underline{H}$Ph$_2$), 70.23 (C-2), 126.99, 127.08, 127.17, 127.45, 127.67, 128.16, 128.45, 128.48 (ArCH), 139.52, 142.93, 144.22 (Ar *ipso*-C); *m/z* 272 (M^+-45, 23%), 167 (100).

Further elution gave the title compound **17h** (39%) as a colourless oil after Kugelrohr distillation, b.p. 135°C at 0.1 mmHg; R_f (3:7 ethyl acetate/hexane) 0.40. (Found: C, 82.92; H, 7.38; N, 4.36. $C_{22}H_{23}NO$ requires C, 83.24; H, 7.30; N, 4.41%); ν_{max} (thin film)/cm^{-1} 3402 (NH and OH), 1600; δ_H (270 MHz; $CDCl_3$) 2.28 (2H, br s, N$\underline{H}$ and O$\underline{H}$), 2.72 (1H, dd, *J* = 5.5, 10.4 Hz, C(3)$\underline{H}$), 2.77-2.88 (2H, m, C(2)$\underline{H}$ and C(3)$\underline{H}$), 3.30 (1H, dd, *J* = 4.6, 10.9 Hz, C(3)$\underline{H}$), 3.56 (1H, dd, *J* = 3.5, 10.7 Hz, C(1)$\underline{H}$), 4.90 (1H, s, C$\underline{H}$Ph$_2$), 7.03-7.32 (15H, m, ArC$\underline{H}$); δ_C (67.8 MHz; $CDCl_3$) 38.17 (C-3), 57.31 (C$\underline{H}$Ph$_2$), 62.82 (C-1), 63.90 (C-2), 126.25, 126.97, 127.01, 127.08, 127.28, 128.41, 129.20 (ArCH), 138.45, 143.43 (Ar *ipso*-C); *m/z* 286 (M^+-31, 4%), 167 (100).

(2S)-2-(4-Morpholino)-3-phenylpropan-1-ol **17i**. The epoxy amine **15i** was converted to the title compound **17i** in 51% yield as colourless needles using exactly the same conditions and purification procedure

as for the preparation of the analogous racemate **17b**. It had identical physical and spectroscopic properties to **17b**, with the exception of m.p. 69-70.5°C and $[\alpha]_D^{25}$ -4.6 (*c*. 1.12, $CHCl_3$).

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