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Calcium trifluoromethanesulfonate-catalysed aminolysis of epoxides

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Abstract—Aminolysis of epoxides catalysed by calcium trifluoromethanesulfonate under mild reaction conditions is described. The novel method is very efficient in the synthesis of wide variety of β-amino alcohols with high regio- and stereoselectivity.

1. Introduction

The aminolysis of epoxides is a classical route to β-amino alcohols, an important class of compounds both in organic as well as medicinal chemistry. Usually, the preparation involves heating an epoxide in a protic solvent with excess amine. The non-catalytic aminolysis procedure is satisfactory in many cases.

However, it suffers from many disadvantages, either high temperatures or prolonged reaction times. Chini and co-workers[1,2] described the catalytic activity of metal salts: $LiClO_4$, $NaClO_4$, $Mg(ClO_4)_2$, $Zn(OTf)_2$, $LiBF_4$ and $CaCl_2$ on the aminolysis of various epoxides. Their high yielding procedure for aminolysis of epoxides involves stirring eqimolar quantities of epoxide, amine and metal salt as catalyst in acetonitrile as solvent at room or at reflux temperature. However, the first example of catalytic aminolysis of epoxides was described by Malguzzi and Giordano.[3] They found that $AlCl_3$, $FeCl_3$, $CuCl_2$, $MgCl_2$ and some other metal salts catalysed the aminolysis of glycidylarylethers, but only with large excess of isopropylamine. Other authors described many different catalysts for the aminolysis of epoxides: LiOTf,[4] $CoCl_2$,[5] $Ln(OTf)_3$ (Ln=Yb, Nd, Gd),[6,7] $SmCl_3$,[8] $Cu(OTf)_2$,[9] $Sn(OTf)_2$,[9] Ph_4SbOTf,[10] $[(CH_3)_2CHO]_2AlOOCCF_3$,[11] chromatographic alumina,[12] and $CeCl_3{\cdot}7H_2O$–NaI.[13] Neef and co-workers[14] described the catalytic activity of $(NH_4)_2[Ce(NO_3)_6]$ in the aminolysis of some steroidal epoxides with 2-chloroaniline. Some of these catalysts are very expensive and/or unavailable as the most efficient lanthanide triflates. On the other hand, some catalysts were effective only in the aminolysis of epoxides with aromatic amines.[5,9]

2. Results and discussion

We have found that calcium trifluoromethanesulfonate efficiently catalyses aminolysis of wide variety of epoxides **1**–**6** with simple aliphatic amines,[15] benzylamine, dibenzylamine, aniline and its derivates **7**–**10**. Our method involves stirring equimolar quantities of epoxide and amine in acetonitrile as solvent in the presence of 10–50 mol% $Ca(OTf)_2$ as homogeneous catalyst, usually at room temperature, Scheme 1.

Calcium triflate was easily prepared by reaction of 2 equiv. of trifluoromethanesulfonic acid with calcium carbonate suspended in toluene at room temperature. Aminolysis of reactive terminal epoxides with reactive aliphatic amines could be carried out using 10 or 25 mol% of catalyst. In some cases reaction could be carried out in dichloromethane or diethylether, but acetonitrile proved to be the best solvent for this reaction. Results are summarised in Table 1.

Primary and secondary aliphatic amines react very rapidly at room temperature. Aniline and its derivates with electron donating substituents also react quite fast. However, anilines with electron accepting substituents, as well as sterically hindered anilines, react very slowly, and aminolysis at room temperature required prolonged reaction times. Products were purified by preparative chromatography on silica gel but in almost all cases the resulting crude β-amino

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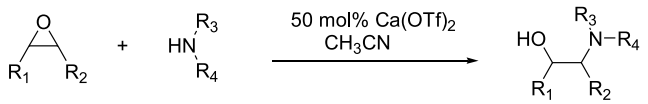

Scheme 1.

alcohols showed single spot on TLC chromatogram and could be used without further purification. Aminolysis of glycidylphenylether (**1**) with 4-nitroaniline (**8**) was performed at reflux temperature of solvent, and β-amino alcohol **18** was isolated in 37% yield by preparative chromatography together with unreacted reactants.

The stereoselectivity of this method was *anti* as demonstrated by the reaction of cyclohexene oxide (**6**) with benzylamine which gave exclusively *trans*-1,2-amino alcohol **30**. Aminolysis of styrene oxide (**5**) with benzyl- and dibenzylamine gave mixtures of regioisomers **28a**,**b** and **29a**,**b**. In both cases the ratio of β-amino alcohols **28a**, **29a** products of S_N2 reaction vs. **28b**, **29b** products of S_N1 reaction was around 85:15 as determined by HPLC. This result is similar to that obtained with LiOTf but quite different to that obtained with $Zn(OTf)_2$ which causes predominant formation of β-amino alcohols by S_N1 reaction.[4] Calcium triflate proved to be a much more active catalyst than LiOTf and also cheaper and more easily available. The catalyst could be regenerated from the water layer after work-up of the reaction mixture.

3. Conclusion

In summary, this new method for the synthesis of a wide variety of β-amino alcohols by the aminolysis of 1,2-epoxides appears to have great synthetic applications in consideration of its efficiency, simplicity, regio- and stereoselectivity.

4. Experimental

IR spectra were recorded on a Perkin–Elmer Spectrum One spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on a Varian XL-GEM 300 for $CDCl_3$ solutions, shifts are given in ppm downfield from TMS as an internal standard. HPLC analyses were performed with a Thermo Separation Products (San Jose, USA) instrument equipped with vacuum degasser SCM 1000, quaternary gradient pump P 4000, autosampler AS 3000, scanning UV/VIS detector UV 3000 HR and ChromQuest 251 software. TLC analyses were performed on Merck's (Darmstadt, Germany) DC-alufolien with Kieselgel 60_{254}. Elemental analyses were done in Central Analytical Service (CAS) at Ruđer Bošković Institute.

4.1. General procedure and caracterisation of β-amino alcohols 11–30

To a solution of the epoxide (10 mmol) and amine (10 mmol) in 30 ml of acetonitrile calcium trifluoromethanesulfonate* (1.7 g, 5 mmol, 50 mol%) was

Table 1. Aminolysis of epoxides with amines using calcium trifluoromethanesulfonate as catalyst, Scheme 1

Entry	Epoxide R_1, R_2	Amine R_3, R_4	β-Amino alcohol[a]	Time[b] (h)	Yield[c] (%)
1	$PhOCH_2$, H (**1**)	2-Pr, H[d]	**11**	5	98
2	$PhOCH_2$, H (**1**)	2-Pr, H[e]	**11**	2	96
3	$PhOCH_2$, H (**1**)	2-Pr, H	**11**	0.5	99
4	$PhOCH_2$, H (**1**)	2-Pr, H[f]	**11**	0.3	96
5	$PhOCH_2$, H (**1**)	*tert*-C_4H_9, H	**12**	24	92
6	$PhOCH_2$, H (**1**)	Et, Et	**13**	0.5	87
7	$PhOCH_2$, H (**1**)	Bn, Bn	**14**	24	97
8	$PhOCH_2$, H (**1**)	Bn, H	**15**	5	87
9	$PhOCH_2$, H (**1**)	Ph, H	**16**	28	68
10	$PhOCH_2$, H (**1**)	4-$CH_3OC_6H_4$, H (**7**)	**17**	20	90 (41)[g]
11	$PhOCH_2$, H (**1**)	4-$O_2NC_6H_4$, H (**8**)	**18**	45[h]	37
12	$PhOCH_2$, H (**1**)	2,6-$(CH_3)_2C_6H_3$, H (**9**)	**19**	78	95
13	$PhOCH_2$, H (**1**)	*tert*-C_4H_9, Bn (**10**)	**20**	48	94
14	$PhOCH_2$, H (**1**)	Ph, Bn	**21**	72	83
15	Me, H (**2**)	Bn, Bn	**22**	5	87
16	Me, H (**2**)	Bn, H	**23**	4	85
17	$ClCH_2$, H (**3**)	Bn, Bn	**24**	5	91
18	$ClCH_2$, H (**3**)	Bn, H	**25**	4	97
19	*n*-C_6H_{13}, H (**4**)	Bn, Bn	**26**	24	95
20	*n*-C_6H_{13}, H (**4**)	Bn, H	**27**	20	90
21	Ph, H (**5**)	Bn, Bn	**28a**,**b**	24	80
22	Ph, H (**5**)	Bn, H	**29a**,**b**	22	99 (38[i])[g]
22	$-(CH_2)_4-$ (**6**)	Bn, H	**30**	27	91

[a] β-Amino alcohols were fully caracterised because much of the data have not been given in the present literature.
[b] Determined by TLC analyses.
[c] Yield of products isolated by preparative chromatography.
[d] 10 mol% $Ca(OTf)_2$.
[e] 25 mol% $Ca(OTf)_2$.
[f] 100 mol% $Ca(OTf)_2$.
[g] Yield of recrystallised product is given in the parenthesis.
[h] Reaction was carried out at reflux temperature of acetonitrile.
[i] Yield of compound **29a**.

added and the reaction mixture was stirred at room temperature or at reflux temperature until TLC analysis indicated complete consumption of reactants. Then, the acetonitrile was evaporated and to the residue water (20 ml) was added and extracted with dichloromethane (3×20 ml). Organic extracts were collected, dried (Na_2SO_4) and evaporated. Crude products were separated by preparative chromatography on silica gel using eluents containing 0.5% of triethylamine.

**Preparation of calcium triflate*. To the suspension of calcium carbonate (143 g, 1.43 mol) in 1000 ml of toluene, trifluoromethanesulfonic acid (250 ml, 427.5 g, 2.86 mol) was added dropwise during 2 h. The reaction mixture was stirred at room temperature for an additional 3 h. Then, the product was filtered, washed with 300 ml of toluene and dried in high vacuum for 5 h. Calcium triflate (465 g, 97%) was obtained as a white or slightly yellowish powder which was used as catalyst without further purification.

4.1.1. 1-(*N*-Isopropyl)amino-3-phenoxy-2-propanol (11). Colourless crystals; mp 94–95.5°C; yield 2.04 g (98%). +AFs-Found: C, 68.9; H, 9.1; N, 6.7. $C_{12}H_{19}NO_2$ requires C, 68.87; H, 9.15; N, 6.69+ACUAXQA7- R_f (10% MeOH/CH_2Cl_2) 0.35; ν_{max} (KBr) 3310, 1600, 1585, 1490, 1445, 1355, 1295, 1240, 1170, 1110, 1085, 1035, 1020 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.31–7.25 (2H, m, Ph), 6.98–6.90 (3H, m, Ph), 4.06–4.01 (1H, m, C*H*–OH), 3.98–3.95 (2H, s, OCH_2), 2.91–2.62 (5H, m, CH_2-N*H*C*H*Me_2, O*H*), 1.09 (6H, d, *J*=6.2 Hz, CH(CH_3)$_2$); δ_C (300 MHz, $CDCl_3$) 158.5, 129.1, 120.5, 114.1, 70.5, 67.7, 49.4, 48.4, 22.4, 22.1.

4.1.2. 1-(*N*-*tert*-Butyl)amino-3-phenoxy-2-propanol (12). Colourless crystals; mp 98–99°C; yield 2.04 g (92%). +AFs-Found: C, 69.9; H, 9.5; N, 6.3. $C_{13}H_{21}NO_2$ requires C, 69.92: H, 9.48; N, 6.27+ACUAXQA7- R_f (20% MeOH/CH_2Cl_2) 0.29; ν_{max} (KBr) 3300, 1595, 1580, 1490, 1445, 1365, 1295, 1235, 1172, 1107, 1082, 1015 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.32–7.27 (2H, m, Ph), 6.99–6.92 (3H, m, Ph), 4.02–3.96 (3H, m, C*H*–OH, OCH_2), 3.08 (2H, s, N*H*, O*H*), 2.88–2.84 (1H, m, CH_2N), 2.71–2.67 (1H, m, CH_2N), 1.15 (9H, s, C(CH_3)$_3$); δ_C (300 MHz, $CDCl_3$) 158.5, 129.3, 120.7, 114.3, 70.4, 68.3, 50.3, 44.7, 28.8.

4.1.3. 1-(*N*,*N*-Diethyl)amino-3-phenoxy-2-propanol (13). Viscous yellow oil; yield 1.93 g (87%). +AFs-Found: C, 69.9; H, 9.5; N, 6.3. $C_{13}H_{21}NO_2$ requires C, 69.92; H, 9.48; N, 6.27+ACUAXQA7- R_f (20% MeOH/CH_2Cl_2) 0.26; ν_{max} (liquid film) 3413, 1600, 1588, 1457, 1386, 1300, 1246, 1172, 1078 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.31–7.25 (2H, m, Ph), 6.97–6.92 (3H, m, Ph), 4.05–3.96 (4H, m, OCH_2C*H*–O*H*), 2.73–2.51 (6H, m, CH_2N(CH_2CH_3)$_2$), 1.05 (6H, t, *J*=7.1 Hz, CH_2CH_3); δ_C (300 MHz, $CDCl_3$) 158.5, 129.1, 120.5, 114.2, 70.0, 65.7, 55.6, 46.9, 11.5.

4.1.4. 1-(*N*,*N*-Dibenzyl)amino-3-phenoxy-2-propanol (14). Colourless crystals; mp 63–64.7°C; yield 3.36 g (97%). +AFs-Found: C, 79.5; H, 7.3; N, 4.0. $C_{23}H_{25}NO_2$ requires C, 79.51; H, 7.25; N, 4.03+ACUAXQA7- R_f (CH_2Cl_2) 0.52; ν_{max} (KBr) 3430, 1600, 1492, 1450, 1245, 1105, 1077 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.31–7.21 (12H, m, Ph), 6.92 (1H, t, *J*=7.1 Hz, Ph), 6.82 (2H, d, *J*=8.0 Hz, Ph), 4.11–4.05 (1H, m, C*H*–OH), 3.84 (2H, d, *J*=4.7 Hz, OCH_2), 3.76 (2H, d, *J*=13.2 Hz, CH_2Ph), 3.51 (2H, d, *J*=13.5 Hz, CH_2Ph), 3.24 (1H, s, O*H*), 2.64 (2H, d, *J*=6.6 Hz, CH_2N); δ_C (300 MHz, $CDCl_3$) 158.6, 138.5, 129.3, 129.0, 128.3, 127.2, 120.8, 114.4, 70.1, 66.4, 58.6, 56.0.

4.1.5. 1-(*N*-Benzyl)amino-3-phenoxy-2-propanol (15). Colourless crystals; mp 67–69°C; yield 2.24 g (87%). +AFs-Found: C, 74.7; H, 7.5; N, 5.4. $C_{16}H_{19}NO_2$ requires C, 74.68; H, 7.44; N, 5.44+ACUAXQA7- R_f (10% MeOH/CH_2Cl_2) 0.37; ν_{max} (KBr) 3300, 1598, 1585, 1490, 1450, 1245, 1125, 1080 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.36–7.26 (7H, m, Ph), 6.97–6.83 (3H, m, Ph), 4.10–4.04 (1H, m, C*H*–OH), 3.93 (2H, d, *J*=5.2 Hz, OCH_2), 3.81 (2H, d, *J*=1.9 Hz, CH_2Ph), 2.97 (2H, s, O*H*, N*H*), 2.89–2.73 (2H, m, CH_2N); δ_C (300 MHz, $CDCl_3$) 158.2, 139.0, 129.0, 128.0, 127.8, 126.7, 120.5, 114.1, 70.1, 67.8, 53.2, 51.0.

4.1.6. 1-(*N*-Phenyl)amino-3-phenoxy-2-propanol (16). Colourless oil; yield 1.65 g (68%). +AFs-Found: C, 74.0; H, 7.0; N, 5.8. $C_{15}H_{17}NO_2$ requires C, 74.05; H, 7.04; N, 5.76+ACUAXQA7- R_f (5% 2-PrOH/CH_2Cl_2) 0.57; ν_{max} (liquid film) 3391, 1601, 1497, 1457, 1245, 1109, 1080 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.33–7.11 (4H, m, Ph), 7.05–6.84 (3H, m, Ph), 6.79–6.65 (3H, m, Ph), 4.30–4.18 (1H, m, C*H*–OH), 4.02–3.93 (2H, m, OCH_2), 3.65–3.55 (2H, m, O*H*, N*H*), 3.41–3.21 (2H, m, CH_2N); δ_C (300 MHz, $CDCl_3$) 158.2, 147.6, 129.4, 129.2, 121.1, 118.1, 114.3, 113.3, 69.8, 68.5, 46.6.

4.1.7. 1-(*N*-4-Methoxyphenyl)amino-3-phenoxy-2-propanol (17). Colourless crystals; mp 78–80.5°C; yield 2.47 g (90%) of crude product, 1.11 g (41%) of recrystallised product from 10 ml of diethylether. +AFs-Found: C, 70.3; H, 7.0; N, 5.1. $C_{16}H_{19}NO_3$ requires C, 70.31; H, 7.01; N, 5.12+ACUAXQA7- R_f (5% 2-PrOH/CH_2Cl_2) 0.42; ν_{max} (KBr) 3258, 1599, 1495, 1442, 1267, 1233, 1170, 1017 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.35–7.28 (2H, m, Ph), 7.04–6.93 (3H, m, Ph), 6.82 (2H, d, *J*=8.8 Hz, Ph), 6.69 (2H, d, *J*=8.8 Hz, Ph), 4.26 (1H, s, C*H*–OH), 4.06–4.04 (2H, m, OCH_2), 3.77 (3H, s, OCH_3), 3.61 (2H, s, N*H*, O*H*), 3.42–3.36 (1H, m, CH_2N), 3.28–3.22 (1H, m, CH_2N); δ_C (300 MHz, $CDCl_3$) 158.2, 152.5, 141.7, 129.4, 121.1, 114.8, 114.7, 114.3, 69.9, 68.5, 55.6, 47.7.

4.1.8. 1-(*N*-4-Nitrophenyl)amino-3-phenoxy-2-propanol (18). Yellow crystals; mp 97.5–99.5°C; yield 1.06 g (37%). +AFs-Found: C, 62.5; H, 5.6; N, 9.7. $C_{15}H_{16}N_2O_4$ requires C, 62.49; H, 5.59; N, 9.72+ACUAXQA7- R_f (5% 2-PrOH/CH_2Cl_2) 0.37; ν_{max} (KBr) 3391, 1603, 1497, 1473, 1243, 1187, 1113, 1045 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.05 (2H, d, *J*=9.1 Hz, Ph), 7.34–7.27 (2H, m, Ph), 7.04–6.84 (3H, m, Ph), 6.57 (2H, d, *J*=9.1 Hz, Ph), 5.15 (1H, s, O*H*), 4.31 (1H, m, C*H*–OH), 4.17–4.02 (2H, m, OCH_2), 3.57–3.36 (2H, m, CH_2NH), 3.00–2.99 (1H, m, N*H*); δ_C (300 MHz, $CDCl_3$) 157.9, 153.3, 137.8, 129.5, 126.3, 121.4, 114.3, 111.2, 69.4, 68.3, 45.6.

4.1.9. 1-(*N*-2,6-Dimethylphenyl)amino-3-phenoxy-2-propanol (19). Pale yellow oil; yield 2.58 g (95%). +AFs-Found: C, 75.2; H, 7.8; N, 5.1. $C_{17}H_{21}NO_2$ requires C, 75.25; H, 7.80; N, 5.16+ACUAXQA7- R_f (5%

2-PrOH/CH_2Cl_2) 0.56; ν_{max} (liquid film) 3391, 1599, 1497, 1476, 1378, 1245, 1173, 1080, 1042 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.34–7.27 (3H, m, Ph), 7.08–6.91 (5H, m, Ph), 4.11–4.09 (1H, m, C*H*OH), 4.07–4.05 (2H, m, OCH_2), 3.61 (2H, s, O*H*, N*H*), 3.35–3.30 (1H, m, CH_2N), 3.20–3.14 (1H, m, CH_2N), 2.38 (6H, s, CH_3); δ_C (300 MHz, $CDCl_3$) 158.4, 129.4, 129.3, 128.9, 128.1, 123.0, 121.1, 114.3, 70.1, 68.9, 50.9, 18.2.

4.1.10. 1-(*N*-*tert*-Butyl-*N*-benzyl)amino-3-phenoxy-2-propanol (20). Colourless viscous oil; yield 2.94 g (94%). +AFs-Found: C, 76.7; H, 8.7; N, 4.5. $C_{20}H_{27}NO_2$ requires C, 76.64; H, 8.68; N, 4.47+ACUAXQA7- R_f (5% 2-PrOH/CH_2Cl_2) 0.47; ν_{max} (liquid film) 3440, 1600, 1490, 1450, 1390, 1360, 1245, 1170, 1040 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.41–7.31 (7H, m, Ph), 7.01–6.96 (1H, m, Ph), 6.89 (2H, m, Ph), 3.96–3.91 (1H, m, CH_2Ph), 3.81 (2H, d, OCH_2), 3.68–3.63 (1H, m, CH_2Ph), 3.59–3.55 (1H, m, C*H*–OH), 3.41 (1H, s, O*H*), 2.86–2.77 (2H, m, CH_2N), 1.25 (9H, s, C(CH_3)$_3$); δ_C (300 MHz, $CDCl_3$) 158.4, 141.5, 128.9, 128.1, 127.8, 126.5, 120.3, 114.1, 69.7, 66.8, 55.3, 53.4, 27.9, 27.0.

4.1.11. 1-(*N*-Phenyl-*N*-benzyl)amino-3-phenoxy-2-propanol (21). Colourless oil; yield 2.76 g (83%). +AFs-Found: C, 79.3; H, 7.0; N, 4.2. $C_{22}H_{23}NO_2$ requires C, 79.25; H, 6.95; N, 4.20+ACUAXQA7- R_f (CH_2Cl_2) 0.45; ν_{max} (liquid film) 3390, 1595, 1492, 1450, 1385, 1355, 1243, 1195, 1110, 1075, 1035 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.53–6.94 (15H, m, Ph), 4.86–4.84 (2H, m, OCH_2), 4.58–4.54 (1H, m, C*H*–OH),), 4.24–4.13 (2H, m, CH_2Ph), 3.96–3.75 (2H, m, CH_2N), 3.07–3.15 (1H, m, O*H*); δ_C (300 MHz, $CDCl_3$) 158.1, 148.2, 138.1, 129.3, 129.0, 128.3, 126.6, 126.4, 120.9, 116.8, 114.3, 112.6, 69.3, 67.9, 55.0, 53.8.

4.1.12. 1-(*N*,*N*-Dibenzyl)amino-2-propanol (22). Colourless oil; yield 2.20 g (87%). +AFs-Found: C, 80.0; H, 8.3; N, 5.5. $C_{17}H_{21}NO$ requires C, 79.96; H, 8.29; N, 5.49+ ACUAXQA7- R_f (5% 2-PrOH/CH_2Cl_2) 0.59; ν_{max} (liquid film) 3450, 1600, 1580, 1450, 1370, 1328, 1248, 1120, 1075, 1030 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.28–7.21 (10H, m, Ph), 3.79 (1H, s, C*H*–OH), 3.75 (2H, s, CH_2Ph), 3.37–3.32 (2H, m, CH_2Ph), 3.11 (1H, s, O*H*), 2.37–2.35 (2H, m, CH_2N), 1.02 (3H, d, J=5.6 Hz, CH_3,); δ_C (300 MHz, $CDCl_3$) 141.2, 131.7, 131.1, 130.9, 129.9, 129.8, 65.8, 63.9, 61.1, 55.5, 22.7.

4.1.13. 1-(*N*-Benzyl)amino-2-propanol (23). Pale yellow oil; yield 1.40 g (85%). +AFs-Found: C, 72.7; H, 9.1; N, 8.5. $C_{10}H_{15}NO$ requires C, 72.69; H, 9.15; N, 8.48+ ACUAXQA7- R_f (10% MeOH/CH_2Cl_2) 0.24; ν_{max} (liquid film) 3350, 1600, 1582, 1492, 1450, 1370, 1250, 1105, 1028 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.26–7.18 (5H, m, Ph), 3.79–3.74 (1H, m, C*H*–OH), 3.71–3.68 (2H, m, CH_2Ph), 3.01 (2H, s, O*H*, N*H*), 2.57–2.37 (2H, m, CH_2N), 1.07 (3H, d, J=6.3 Hz, CH_3); δ_C (300 MHz, $CDCl_3$) 141.8, 130.3, 130.0, 128.9, 67.4, 58.4, 55.5, 23.0.

4.1.14. 1-(*N*,*N*-Dibenzyl)amino-3-chloro-2-propanol (24). Pale yellow oil; yield 2.64 g (91%). +AFs-Found: C, 70.5; H, 7.0; N, 4.8. $C_{17}H_{20}NOCl$ requires C, 70.46; H, 6.96; N, 4.83+ACUAXQA7- R_f (CH_2Cl_2) 0.52; ν_{max} (liquid film) 3420, 1600, 1582, 1450, 1370, 1245, 1155, 1030 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.37–7.27 (10H, m, Ph), 3.94–3.86 (1H, m, C*H*–OH), 3.82–3.77 (2H, m, CH_2Ph), 3.56–3.52 (2H, m, CH_2Ph), 3.46 (2H, d, J=5.2 Hz, ClCH_2,), 2.65–2.60 (3H, m, CH_2N, O*H*); δ_C (300 MHz, $CDCl_3$) 137.5, 128.8, 128.1, 127.1, 67.4, 58.3, 56.2, 47.1.

4.1.15. 1-(*N*-Benzyl)amino-3-chloro-2-propanol (25). Viscous yellow oil; yield 1.93 g (97%). +AFs-Found: C, 60.1; H, 7.1; N, 7.0. $C_{10}H_{14}NOCl$ requires C, 60.15; H, 7.07; N, 7.01+ACUAXQA7- R_f (10% MeOH/CH_2Cl_2) 0.28; ν_{max} (liquid film) 3300, 1600, 1585, 1450, 1360, 1252, 1165, 1030 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.60–7.27 (5H, m, Ph), 4.43 (1H, m, C*H*–OH), 4.31–3.99 (2H, m, CH_2Ph), 3.60–3.44 (2H, m, ClCH_2), 3.09–2.69 (4H, m, CH_2N, O*H*, N*H*); δ_C (300 MHz, $CDCl_3$) 130.2, 129.8, 128.9, 128.8, 66.1, 58.1, 57.7, 46.0.

4.1.16. 1-(*N*,*N*-Dibenzyl)amino-2-octanol (26). Yellow oil; yield 3.08 g (95%). +AFs-Found: C, 81.2; H, 9.6; N, 4.3. $C_{22}H_{31}NO$ requires C, 81.18; H, 9.60; N, 4.30+ ACUAXQA7- R_f (5% 2-PrOH/CH_2Cl_2) 0.74; ν_{max} (liquid film) 3460, 1600, 1580, 1450, 1370, 1290, 1245, 1120, 1030 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.33–7.17 (10H, m, Ph), 3.81–3.75 (2H, m, CH_2Ph), 3.66 (1H, m, C*H*–OH), 3.37–3.35 (2H, m, CH_2Ph), 3.30 (s, 1H, O*H*), 2.39–2.37 (2H, m, CH_2N), 1.24 (10H, s), 0.88–0.84 (3H, m); δ_C (300 MHz, $CDCl_3$) 138.4, 128.9, 128.3, 127.2, 127.1, 66.9, 59.7, 58.3, 52.5, 34.7, 31.7, 29.3, 25.6, 22.5, 14.0.

4.1.17. 1-(*N*-Benzyl)amino-2-octanol (27). Colourless oil which crystallised upon standing at room temperature to give colourless waxy crystals; mp 32–35°C; yield 2.12 g (90%). +AFs-Found: C, 76.5; H, 10.7; N, 5.9. $C_{15}H_{25}NO$ requires C, 76.55; H, 10.71; N, 5.95+ACUAXQA7- R_f (10% MeOH/CH_2Cl_2) 0.36; ν_{max} (liquid film) 3300, 1600, 1580, 1435, 1280, 1140, 1115, 1030 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.37–7.33 (5H, m, Ph), 3.85–3.74 (2H, m, CH_2Ph), 3.64 (1H, s, C*H*–OH), 2.92 (2H, s, O*H*, N*H*), 2.74–2.70 (1H, m, CH_2N), 2.51–2.44 (1H, m, CH_2N), 1.43–1.29 (10H, m), 0.90–0.88 (3H, m); δ_C (300 MHz, $CDCl_3$) 139.1, 127.9, 127.7, 126.6, 69.0, 54.4, 53.1, 34.9, 31.4, 29.0, 25.2, 22.2, 13.7.

4.1.18. 2-(*N*,*N*-Dibenzyl)amino-1-phenyl-1-ethanol (28a). Crude products **28a**,**b** were obtained as a yellow oil. Compound **28a** was isolated by preparative chromatography as colourless oil; yield 2.54 g (80%). +AFs-Found: C, 83.3; H, 7.3; N, 4.4. $C_{22}H_{23}NO$ requires C, 83.24; H, 7.30; N, 4.41+ACUAXQA7- R_f (CH_2Cl_2) 0.50; ν_{max} (liquid film) 3437, 1602, 1585, 1453, 1372, 1243, 1175, 1073, 1028 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.68–7.35 (15H, m, Ph), 5.01–4.97 (1H, m, C*H*–OH), 4.17–4.13 (2H, m, CH_2Ph), 4.05 (1H, s, O*H*), 3.76–3.72 (2H, m, CH_2Ph), 2.94–2.91 (2H, m, CH_2N); δ_C (300 MHz, $CDCl_3$) 141.9, 138.0, 128.7, 128.2, 128.1, 127.9, 127.1, 127.0, 125.6, 69.3, 61.4, 57.9. From the collected fractions with R_f=0.67 regioisomer **28b** was isolated but contaminated with considerable amount of **28a**.

4.1.19. 2-(*N*-Benzyl)amino-1-phenyl-1-ethanol (29a). From the yellow-orange coloured crude product (2.24 g, 99%) colourless crystals of pure **29a** was obtained by

recrystallisation from 4 ml of toluene; mp 98–100°C, lit.[2] mp 100–102°C, lit.[16] mp 102–103°C; yield 0.87 g (38%). +AFs-Found: C, 79.3; H, 7.6; N, 6.1. $C_{15}H_{17}NO$ requires C, 79.26; H, 7.54; N, 6.16+ACUAXQA7- R_f (10% MeOH/CH_2Cl_2) 0.38; ν_{max} (KBr) 3290, 1600, 1580, 1450, 1375, 1255, 1182, 1100, 1025 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.49–7.32 (10H, m, Ph), 4.81–4.77 (1H, m, C*H*–OH), 3.85–3.75 (2H, m, CH_2Ph), 3.25 (2H, s, O*H*, N*H*), 2.90–2.74 (2H, m, CH_2N); δ_C (300 MHz, $CDCl_3$) 142.3, 139.2, 128.0, 127.9, 127.7, 127.0, 126.7, 125.4, 71.4, 56.1, 53.0.

4.1.20. *trans*-2-(*N*-Benzyl)amino-cyclohexanol (30). Colourless oil which crystallised upon standing to give colourless needles; mp 65–68°C; yield 1.87 g (91%); +AFs-[Found: C, 76.1; H, 9.5; N, 6.7. $C_{13}H_{19}NO$ requires C, 76.06; H, 9.33; N, 6.82%]+AF0AOw- R_f (1,2-dichloroethane/MeOH/Et_3N, 8:1.8:0.2) 0.39; ν_{max} (liquid film) 3296, 1603, 1499, 1451, 1430, 1242, 1154, 1100, 1029 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.36–7.19 (5H, m, Ph), 3.85 (1H, d, J=12.8 Hz, CH_2Ph), 3.59 (1H, d, J=12.8 Hz, CH_2Ph), 3.47 (2H, s, N*H*, O*H*), 3.19–3.13 (1H, m, C*H*–OH), 2.33–2.25 (1H, m, C*H*–N), 2.06–2.02 (1H, m, C*H*–N), 1.85–1.81 (1H, m), 1.62 (2H, m), 1.21–1.11 (3H, m), 1.04–0.97 (1H, m); δ_C (300 MHz, $CDCl_3$) 139.5, 127.9, 127.7, 126.5, 72.6, 62.4, 50.3, 33.5, 29.4, 24.3, 24.0.

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