Convenient Procedure for the Reduction of β-Enamino Ketones: Synthesis of γ-Amino Alcohols and Tetrahydro-1,3-oxazines

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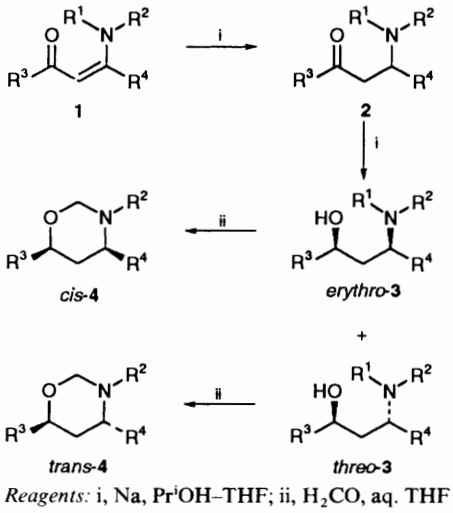
γ-Amino alcohols **3** can be easily synthesized in very good yields by reduction of enaminones **1** with Na in Pr^{i}OH–tetrahydrofuran. The reaction is fast, easy to perform, inexpensive and the easily accessible starting materials provide a convenient entry to γ-amino alcohols. The relative configuration assignment of the diastereoisomeric γ-amino alcohols obtained has been established by ^{1}H and ^{13}C NMR studies and unequivocally assigned by their cyclic tetrahydro-1,3-oxazine derivatives **4**.

Considerable attention has been devoted in organic synthesis to the preparation of γ-amino alcohols as well as the isolation and stereochemical determination of their diastereoisomers,[1] since γ-amino alcohols are a very common unit in natural products,[2] and have interesting pharmacological properties as analgesics.[3]

The γ-amino alcohol syntheses cited in the literature commonly utilize reductions of enaminones,[4] isoxazoles or isoxazolines,[5] β-amino carbonyl compounds,[6] ketopyridines,[7] α,β-unsaturated ketones, aldehydes or esters,[8] and α-cyano esters[9] by use of metal hydride or catalytic hydrogenation, but all of these methods suffer from certain restrictions. Greenhill[4a] pointed out that the reduction of β-enamino ketones takes place with difficulty, but these compounds can be reduced in low yields to γ-amino alcohols by catalytic hydrogenation. However, in many cases no reduction was observed and under more forcing conditions either nitrogen[4b] or oxygen[4f] is split from the molecule. Rare examples of reduction of organic compounds such as 5,6-dihydro-1,3-oxazine[6a] or 3,5-dimethylisoxazole[5a] to γ-amino alcohols with metals are reported in the literature.

For some time we have been studying the β-enamino ketone unit, obtaining an easy access to this class of compounds by a regioselective synthesis,[10] and their regio- and stereo-selective functionalization.[11] We now report the synthesis of γ-amino alcohols **3** by reduction of β-enamino ketones **1** with sodium in Pr^{i}OH–tetrahydrofuran (THF) as reported in Scheme 1.



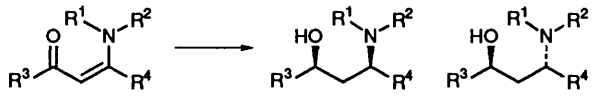
Scheme 1 *Reagents:* i, Na, Pr^{i}OH–THF; ii, H_2CO, aq. THF

The γ-amino alcohols are obtained in high yields as a mixture of *erythro* and *threo* isomers (or *cis* and *trans* isomers in the case of cyclic enaminones **1b**, **c**, **n**, **o**), where the *erythro* diastereoisomer is generally the main product (see Table 1). In the case of cyclic enaminones **1c**, **o** the prevalent *cis*-amino alcohols (*cis*-**3c**, **o**) are obtained in high yields. It is noteworthy that *cis*-3-aminocyclohexanol (*cis*-**3b**) is formed as the predominant isomer (*cis*/*trans* = 3.3) similarly to the catalytic reduction of the 3-acetamidophenol[12] (H_2/Ni Raney, high temperature and pressure, yield 56%, *cis*/*trans* = 4), and contrary to the results obtained in the catalytic reduction of 3-aminocyclohexenone where the *trans*-3-aminocycloexanone is obtained as predominant isomer (H_2/Ni Raney, 70 °C, 20 atm, yield 75%, *cis*/*trans* = 0.5).[4f] This reaction works well either with nonalkylated β-enamino ketones (**1a–c**) or *N*-monoalkylated (**1d–o**) or *N*-dialkylated ones (**1p**, **q**). In some cases the diastereoisomers can be quantitatively separated by column chromatography. The reaction is particularly easy to perform and special apparatus and conditions (high pressure, expensive catalysts and hydrogen atmosphere) are not required. The β-enamino ketones are easily accessible starting materials and can be prepared in high yields by simple condensation of β-diketones with amines[13] or regiospecifically obtained by the acylation of lithium imines with esters.[10] The reduction is complete in 30–120 min at room temperature. A lowering in the temperature from 20 to 0 °C does not lead to any appreciable variation in the diastereoisomeric ratio. At temperatures below 0 °C the reaction is too slow. In general, the standard conditions used were effective for all of the compounds listed in Table 1. The diastereoisomer ratio was determined by HPLC–MS or calculated by integration of the ^{1}H NMR data from the crude reduction residue. If lithium metal is used instead of sodium a vigorous evolution of hydrogen is observed and only 40% of enaminone **1o** is reduced to β-amino ketone **2o** (21%) and γ-amino alcohol **3o** (9%).

The reduction could be explained through a mechanism of electron transfer from the metal to the conjugate system of enaminone **1** and the successive abstraction of hydrogen from Pr^{i}OH (hydrogen source). The corresponding β-amino ketone **2**, intermediate of the reaction, is *in situ* reduced to γ-amino alcohol **3**. The β-amino ketone **2**, in several cases, has been detected in the reaction mixture by GLC–MS (< 5%) and can be isolated (**2m–o**) in moderate yields (near 20%) if the reaction is stopped at half the time required for the complete reduction.

In the first phase of this work, in order to find a useful procedure for the reduction of β-enamino ketones, we tried the reduction with some classic reducing systems ($NaBH_4$–MeOH; $LiAlH_4$–THF), but we obtained only the unaltered starting material. With *N*-dialkyl enaminones and $LiAlH_4$–THF in more forcing conditions we obtained only degradation of the starting material, but no relevant product was isolated. We also tried new efficient and powerful reducing systems such as $NaBH_4$ in the presence of acids ($CeCl_3$,[14] $ZnCl_2$,[15] $FeCl_3$,[16]

Table 1 Reduction of β-enamino ketones **1** to *erythro*- and *threo*-γ-amino alcohols **3**



1	R^1	R^2	R^3	R^4	3	Yield (%)	*erythro*/*threo*
1a	H	H	Me	Me	**3a**	76[a]	0.8
1b	H	H	$[CH_2]_3$		**3b**	81[a]	3.3[c]
1c	H	H	$CH_2CMe_2CH_2$		**3c**	92[a]	16.0[c,d]
1d	H	Me	Me	Me	**3d**	94[a]	1.4
1e	H	Me	Me	$Ph[CH_2]_2$	**3e**	88[a]	2.0
1f	H	Me	Ph	Me	**3f**	74[a]	1.2
1g	H	Bn	Me	Me	**3g**	84[a]	2.2
1h	H	Pr^i	Me	Me	**3h**	92[b]	2.2
1i	H	c-C_6H_{11}	Me	Me	**3i**	94[b]	2.4
1j	H	Ph	Me	Me	**3j**	95[b]	1.7
1k	H	Ph	Et	Me	**3k**	93[a]	1.4
1l	H	Ph	$Ph[CH_2]_2$	Me	**3l**	89[a]	1.4
1m	H	Ph	Ph	Me	**3m**	82[b]	2.0
1n	H	Ph	$[CH_2]_3$		**3n**	87[b]	2.0[c]
1o	H	Ph	$CH_2CMe_2CH_2$		**3o**	78[b]	10.0[c,d]
1p	Et	Et	Me	Me	**3p**	67[a]	0.5
1q	$[CH_2]_4$		Me	Me	**3q**	93[a]	0.8

[a] Yields of γ-amino alcohol isolated as mixture of the *erythro* and *threo* isomers. [b] Global yields of the pure *erythro* and *threo* isomers separately isolated. [c] *cis*/*trans* Diastereoisomeric ratio. [d] The ratio of diastereoisomers was determined by HPLC–MS.

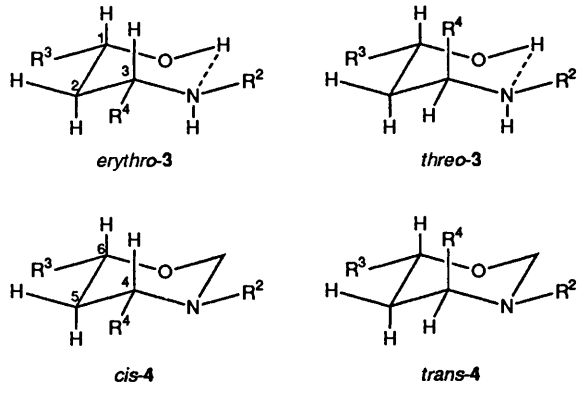


Fig. 1 Prevailing conformations for the *erythro*- and *threo*-γ-amino alcohols **3** and for *cis*- and *trans*-tetrahydro-1,3-oxazines **4**

H_2SO_4,[17] *etc.*) but no appreciable results have been obtained. $NaBH_4$–I_2 in THF[18] only gives γ-amino alcohol **3j**, but with a lower yield (52%) and a more complex reaction mixture than with our procedure. The poor reactivity of β-enamino ketones towards reducing hydrides, already well known,[4a] is due to the poor electrophilicity of the carbonyl group of the enaminone.[19] Consequently the hydride acts as a base, extracting an acidic proton from the enaminonic system. As a proof of this, *N*-acylated enamino ketones, which are more electrophilic,[19] are easily reduced by $NaBH_4$, giving γ-hydroxy enamides, useful intermediates for the preparation of β-hydroxy ketones[20] and α,β-unsaturated ketones.[19]

The relative configuration assignment of the γ-amino alcohols **3** was ascertained by ^1H NMR and ^{13}C NMR spectra of the mixture or of the isolated pure isomers.[21] In all the compounds we observed for the *threo*-isomer the NCH and OCH ^1H NMR signals at lower field and O–C, N–C ^{13}C NMR signals at higher field respectively compared with the *erythro* diastereoisomer (see Experimental section). For instance, the ^1H NMR spectrum of *erythro*-**3d** shows signals at δ 3.88 (J_{aa} 10.1, J_{ae} 2.2 Hz, OCH) and δ 2.66 (J_{aa} 13.8, J_{ae} 2.9 Hz, NCH). The diastereoisomeric *threo*-**3d** shows signals at δ 4.05 (J_{aa} 9.2, J_{ae} 2.8 Hz, OCH) and δ 2.85 (J_{ea} 4.9, J_{ee} 4.0 Hz, NCH). In addition, while for the *erythro*-**3d** two triplets at δ 1.40 (*J* 2.9 Hz) and δ 1.17 (*J* 10.6 Hz) are present for the 2-H^e and 2-H^a respectively, double doublets are present at δ 1.30 (*J* 5.6, 2.8 Hz) and δ 1.57 (*J* 9.2, 3.5 Hz) for the 2-H^e and 2-H^a, respectively, in the case of the isomer *threo*-**3d**.

These spectroscopic data show that the prevailing conformations for the isomers *erythro*- and *threo*-**3** are those shown in Fig. 1. The γ-amino alcohols show a tendency to form rings completed by intramolecularly hydrogen bonds.[21] Both the diastereoisomers **3** assume a chair conformation with an intramolecular hydrogen bond as depicted in Fig. 1. The attribution of the relative configurations of γ-amino alcohols was unequivocally assigned by a spectroscopic study of their cyclic tetrahydro-1,3-oxazine derivatives **4**. The condensation of some γ-amino alcohols, either as pure diastereoisomers (**3i**, **j**, **m**) or as mixture of *erythro* and *threo* isomers (**3d**, **e**, **g**), with formaldehyde affords tetrahydro-1,3-oxazines **4** in good yield with retention of the original stereochemistry of the starting materials (see Scheme 1 and Table 2).

For these tetrahydro-1,3-oxazines (**4d**, **e**, **g**, **i**, **j**, **m**) the ^1H NMR chemical shift, the multiplicity of the signals, the coupling constants and the two-dimensional ^1H NMR data [the rotating-frame NMR (ROESY) experiment was performed on *cis*- and *trans*-**4j**] are in good agreement with the structures depicted in Fig. 1. For the *trans*-**4** isomers, with respect to *cis*-**4**, we observed a relevant shift to higher field in the ^{13}C NMR spectra for C-6 (Δδ 4.9–5.7 ppm), C-2 (Δδ 5.9–11.0 ppm) and 4-Me (Δδ 2.3–3.9 ppm) signals (γ-effect).

In conclusion γ-amino alcohols **3** can be easily synthesized in very good yields by reduction of enaminones **1** with Na in Pr^iOH–THF at room temperature. The reaction is fast, easy to perform, inexpensive and the readily available starting materials provide a convenient entry to γ-amino alcohols.

Experimental

^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 200 or a Varian VXR 300 spectrometer for $CDCl_3$ solutions. Chemical shifts are given in ppm from Me_4Si. Coupling

Table 2 Synthesis of tetrahydro-1,3-oxazines **4** by condensation of γ-amino alcohols **3** with formaldehyde

3 **4**

3	R^2	R^3	R^4	4	Yield (%)
3d[a]	Me	Me	Me	*cis*-**4d**	46
				trans-**4d**	32
3e[a]	Me	Me	$Ph[CH_2]_2$	*cis*-**4e**	51
				trans-**4e**	27
3g[a]	Bn	Me	Me	*cis*-**4g**	51
				trans-**4g**	23
erythro-**3j**	$c\text{-}C_6H_{11}$	Me	Me	*cis*-**4i**	87
threo-**3i**				*trans*-**4i**	91
erythro-**3j**	Ph	Me	Me	*cis*-**4j**	89
threo-**3j**				*trans*-**4j**	82
erythro-**3m**	Ph	Ph	Me	*cis*-**4m**	92
threo-**3m**				*trans*-**4m**	87

[a] A mixture of the pure *erythro* and *threo* diastereoisomers, as obtained from the reduction of enamines **1**, was used as starting material.

constants are given in Hz. Mass spectra were determined by the electron-impact method on a VG 7070 instrument. GLC–MS analyses were performed on a Hewlett-Packard 59970 work station formed by an HP-5890 gas chromatograph equipped with a methyl silicone capillary column and by an HP-5970 mass detector. HPLC–MS analyses were performed on a HP-1090 liquid chromatography and by an HP-5988 mass spectrometer. IR spectra were recorded on a Perkin-Elmer 1600 FTIR apparatus. THF was dried by being refluxed over sodium wire until the blue colour of benzophenone ketyl persisted, and was then distilled into a dry receiver under nitrogen. Commercial compounds (Aldrich) were distilled and dried over molecular sieves (4 Å) before use.

The starting enaminones **1a–d, f, p** were synthesized from 1,3-diketones and the corresponding ammonium acetate or amine acetate.[22] The enaminones **1g, h, i, q** were synthesized according to Singh and Tandon's procedure.[13a] The enaminones **1j, m, n, o** were synthesized according to Boatman and Hauser's procedure.[13b] The enaminones **1e, k, l** were prepared by alkylation of the γ- or α'-dianion of the enaminones **1d, j** according to our procedure.[11]

Reduction of β-*Enamino Ketones* **1** *to* γ-*Amino Alcohols* **3**.—A typical procedure follows: the β-enamino ketone **1** (2 mmol) was dissolved in a mixture of Pr^iOH (2 cm^3) and THF (5 cm^3) and the solution was treated with an excess of sodium wire (0.276 g, 12 mmol) and magnetically stirred at room temperature for the time required for the complete reduction (30–120 min). It was useful to monitor the reaction by TLC or gas chromatography and thus determine when reduction was complete. After removal of the excess of the unchanged sodium the reaction mixture was poured into saturated aq. ammonium chloride (5 cm^3) and extracted with dichloromethane. The organic layer was dried, and evaporated under reduced pressure, and the residue obtained was submitted to HPLC–MS analysis for the determination of the conversion yields and the ratio of the two diastereoisomers. Column chromatographic separation of the crude material [hexane–ethyl acetate (1:1)] furnish the pure γ-amino alcohols **3** in a mixture or as separated diastereoisomers. Reaction yields are given in Table 1. If the reaction is stopped after half the time required for the complete reduction, the β-amino ketones **2m–o** can be isolated in yields ~ 20%. Spectral and analytical data follow.

3-*Anilino*-1-*phenylbutan*-1-*one* **2m** (R^1 = H, R^2 = R^3 = Ph, R^4 = Me). Oil (Found: C, 80.5; H, 7.3; N, 5.6. $C_{16}H_{17}NO$ requires C, 80.30; H, 7.16; N, 5.85%); ν_{max}(neat)/cm^{-1} 3370, 1665, 1590, 1490, 750 and 695; δ_H(200 MHz; $CDCl_3$) 1.34 (3 H, d, *J* 6.4, Me), 3.08 (1 H, dd, *J* 16.5 and 7.5, 2-H), 3.34 (1 H, dd, *J* 16.5 and 4.2, 2-H), 3.37 (1 H, br s, NH), 4.10–4.37 (1 H, m, 3-H), 6.60–6.80 (3 H, m, Ph), 7.15–7.27 (2 H, m, Ph), 7.40–7.62 (3 H, m, Ph) and 7.90–8.00 (2 H, m, Ph); δ_C(75.46 MHz; $CDCl_3$) 21.55 (C-4), 44.96 (C-2), 46.14 (C-3), 114.06, 118.10, 128.69, 129.14, 129.90, 133.72, 137.68, 147.34 and 199.76 (CO); *m*/*z* (%) 239 (M^+, 35), 224 (2), 120 (100), 105 (22) and 77 (18).

3-*Anilinocyclohexanone* **2n** (R^1 = H, R^2 = Ph, R^3R^4 = $[CH_2]_3$). Oil (Found: C, 76.3; H, 8.1; N, 7.1. $C_{12}H_{15}NO$ requires C, 76.16; H, 7.99; N, 7.4%); ν_{max}(neat)/cm^{-1} 3350, 2900, 1695, 1590, 1485, 750 and 690; δ_H(200 MHz; $CDCl_3$) 1.60–1.85 (2 H, m), 1.95–2.55 (5 H, m), 2.78–2.90 (1 H, m), 3.63 (1 H, br s, NH), 3.72–3.87 (1 H, m, CHN), 6.55–6.80 (3 H, m, Ph) and 7.00–7.35 (2 H, m, Ph); δ_C(75.46 MHz; $CDCl_3$) 22.12, 31.05, 41.12, 48.54, 52.27 (CN), 113.28, 117.86, 129.38, 146.44 and 209.52 (CO); *m*/*z* (%) 189 (M^+, 95), 146 (67), 132 (100), 119 (88) and 93 (46).

3-*Anilino*-5,5-*dimethylcyclohexanone* **2o** (R^1 = H, R^2 = Ph, R^3R^4 = $CH_2CMe_2CH_2$). Oil (Found: C, 77.2; H, 8.7; N, 6.6. $C_{14}H_{19}NO$ requires C, 77.38; H, 8.81; N, 6.45%); ν_{max}(neat)/cm^{-1} 3350, 1700, 1600, 1460, 750 and 700; δ_H(200 MHz; $CDCl_3$) 0.99 and 1.12 (6 H, two s, 2 × Me), 1.50 (1 H, t, *J* 12.4), 2.00–2.32 (4 H, m), 2.87 (1 H, ddt, *J* 13.4, 4.6 and 1.8), 3.54 (1 H, br s, NH), 3.82 (1 H, tt, *J* 11.7 and 4.3, CHN), 6.55–6.75 (3 H, m, Ph) and 7.15–7.25 (2 H, m, Ph); δ_C(75.46 MHz; $CDCl_3$) 25.98 (Me), 31.88 (Me), 33.44 (C-5), 45.68, 48.28, 49.02 (C-3), 54.32, 113.26, 117.92, 129.44, 146.37 and 209.11 (CO); *m*/*z* (%) 217 (M^+, 80), 160 (100), 146 (47), 119 (98) and 93 (46).

4-Aminopentan-2-ol **3a**[5a] (mixture of the *erythro* and *threo* isomers in the ratio 0.8:1). Oil (Found: C, 58.1; H, 12.8; N, 13.7. Calc. for $C_5H_{13}NO$: C, 58.21; H, 12.70; N, 13.58%); ν_{max}(neat)/cm^{-1} 3350br, 1560, 1450, 1370 and 1130; δ_H(200 MHz; $CDCl_3$) 1.08–1.23 (6 H, m), 1.35–1.60 (2 H, m, 3-H_2), 2.69 (3 H, br s, OH, NH_2), 3.01 [0.4 H, dqd, *J* 10.8, 6.4 (q) and 2.8, *erythro* CHN], 3.36 (0.6 H, quint d, *J* 6.5 and 3.8, *threo* CHN), 3.96 [0.4 H, dqd, *J* 10.2, 6.1 (q) and 2.1, *erythro* CHO] and 4.11 [0.6 H, dqd, *J* 7.7, 6.4 (q) and 3.7, *threo* CHO]; δ_C(75.46 MHz; $CDCl_3$) *erythro*: 22.40, 23.80, 44.58 (C-3), 46.62 (C-4) and 68.81 (C-2); *threo*: 23.43, 23.58, 44.56 (C-3), 45.90 (C-4) and 65.12 (C-2); *m*/*z* (%) 103 (M^+, 5), 88 (86), 70 (60) and 59 (100).

3-Aminocyclohexanol **3b**[4f] (mixture of the *cis* and *trans* isomers in the ratio 3.3:1). Oil (Found: C, 62.8; H, 11.5; N, 12.0. Calc. for $C_6H_{13}NO$: C, 62.57; H, 11.38; N, 12.16%); ν_{max}(neat)/cm^{-1} 3300br, 1590, 1440, 1350 and 1030; δ_H(200 MHz; $CDCl_3$) 1.05–2.00 (8 H, m), 2.30 (3 H, br s, OH, NH_2), 2.84 (0.8 H, tt, *J* 9.3 and 3.7, *cis* 3-H), 3.09 (0.2 H, tt, *J* 9.5 and 3.8, *trans* 3-H), 3.64 (0.8 H, tt, *J* 9.3 and 3.6, *cis* 1-H) and 4.70 (0.2 H, m, *trans* 1-H); δ_C(75.46 MHz; $CDCl_3$) *cis*: 19.16, 34.38, 34.99, 42.72 (C-2), 48.43 (C-3) and 68.70 (C-1); *trans*: 20.26, 32.82, 35.73, 43.74 (C-2), 45.46 (C-3) and 66.35 (C-1); *m*/*z* (%) 115 (M^+, 9), 98 (22), 82 (15), 72 (100) and 56 (60).

cis-3-*Amino*-5,5-*dimethylcyclohexanol* cis-**3c**. Oil (Found: C, 66.9; H, 11.8; N, 9.5. $C_8H_{17}NO$ requires C, 67.09; H, 11.96; N, 9.78%); ν_{max}(neat)/cm^{-1} 3300br, 1560, 1450, 1350 and 1030; δ_H(200 MHz; $CDCl_3$) 0.79 and 0.86 (6 H, two s, 2 × Me), 0.70–1.20 (3 H, m), 1.36–1.62 (2 H, m), 1.98–2.10 (1 H, m), 2.40 (3 H, br s, OH, NH_2), 2.76 (1 H, tt, *J* 11.7 and 3.8, 3-H^{ax}) and 3.65 (1 H, tt, *J* 11.4 and 4.2, 1-H^{ax}); δ_C(75.46 MHz; $CDCl_3$) 25.91 (Me), 31.68 (C-5), 32.98 (Me), 45.74, 45.97, 47.68 (C-2), 48.87 (C-3) and 65.91 (C-1); *m*/*z* (%) 143 (M^+, 1), 125 (7), 84 (29) and 72 (100).

4-(Methylamino)pentan-2-ol **3d**[8b] (mixture of the *erythro* and *threo* isomers in the ratio 1.4:1). Oil (Found: C, 61.4; H, 13.1; N, 11.7. Calc. for $C_6H_{15}NO$: C, 61.49; H, 12.90; N, 11.95%); ν_{max}(neat)/cm^{-1} 3300br, 1440, 1135 and 1065; δ_H(200 MHz;

$CDCl_3$) 0.99–1.65 (8 H, m), 2.33 (3 H, s, NMe), 2.66 [0.6 H, dqd, *J* 13.8, 6.6 (q) and 2.9, *erythro* CHN], 2.85 [0.4 H, dqd, *J* 6.7 (q), 4.9, 4.0, *threo* CHN], 3.63 (2 H, br s), 3.88 [0.6 H, dqd, *J* 10.1, 6.2 (q) and 2.2, *erythro* CHO] and 4.05 [0.4 H, dqd, *J* 9.2, 6.1 (q), 2.8, *threo* CHO]; δ_C(75.46 MHz; $CDCl_3$) *erythro*: 20.72 (C-5), 24.36 (C-1), 33.11 (NMe), 45.11 (C-3), 56.51 (C-4) and 69.30 (C-2); *threo*: 19.86 (C-5), 24.04 (C-1), 34.31 (NMe), 41.01 (C-3), 53.92 (C-4) and 65.31 (C-2); *m/z* (%) 117 (M^+, 3), 102 (8), 84 (3) and 58 (100).

4-(*Methylamino*)-6-*phenylhexan*-2-*ol* **3e** (mixture of the *erythro* and *threo* isomers in the ratio 2:1). Oil (Found: C, 75.5; H, 10.4; N, 6.5. $C_{13}H_{21}NO$ requires C, 75.32; H, 10.20; N, 6.76%); ν_{max}(neat)/cm^{-1} 3300br, 1445, 1360, 1125, 740 and 690; δ_H(200 MHz; $CDCl_3$) 1.18 (3 H, d, *J* 6.1, CMe), 1.20–2.20 (4 H, m), 2.39 (2.1 H, s, *erythro* NMe), 2.42 (0.9 H, s, *threo* NMe), 2.45–2.90 (5 H, m), 3.96 [0.7 H, dqd, *J* 10.1, 6.1 (q) and 2.0, *erythro* CHO], 4.16 [0.3 H, dqd, *J* 9.3, 6.1 (q) and 2.7, *threo* CHO] and 7.15–7.38 (5 H, m, Ph); δ_C(75.46 MHz; $CDCl_3$) *erythro*: 23.98 (C-1), 31.96, 32.85 (NMe), 35.18, 41.05 (C-3), 59.67 (C-4), 69.14 (C-2), 125.95, 128.22, 128.47 and 141.76; *threo*: 23.77 (C-1), 31.65, 33.80 (NMe), 35.01, 37.34 (C-3), 58.10 (C-4), 65.17 (C-2), 126.02, 128.17, 128.29 and 141.56; *m/z* (%) 207 (M^+, 3), 148 (63), 102 (100), 91 (71) and 58 (86).

3-(*Methylamino*)-1-*phenylbutan*-1-*ol* **3f** (mixture of the *erythro* and *threo* isomers in the ratio 1.2:1). Oil (Found: C, 73.5; H, 9.4; N, 8.05. $C_{11}H_{17}NO$ requires C, 73.70; H, 9.56; N, 7.81%); ν_{max}(neat)/cm^{-1} 3280br, 1665, 1590, 1440, 745 and 690; δ_H(200 MHz; $CDCl_3$) 1.10 (d, *J* 6.2, CMe), 1.12 (d, *J* 6.4, CMe), 1.75–2.20 (2 H, m, 2-H_2), 2.38 and 2.40 (3 H, two s, NMe), 2.60–2.95 (1 H, m, CHN), 3.8 (2 H, br s, NH, OH), 4.91 (0.67 H, dd, *J* 10.4, 2.6, *erythro* CHO), 5.06 (0.33 H, dd, *J* 7.4 and 3.7, *threo* CHO) and 7.10–7.45 (5 H, m, Ph); δ_C(75.46 MHz; $CDCl_3$) *erythro*: 20.71 (C-4), 32.77 (NMe), 45.98 (C-2), 56.62 (C-3), 75.72 (C-1), 126.07, 127.15, 128.68 and 146.08; *threo*: 19.95 (C-4), 30.04 (NMe), 42.27 (C-2), 53.52 (C-3), 72.32 (C-1), 126.22, 127.40, 128.80 and 142.81; *m/z* (%) 179 (M^+, 11), 120 (45), 77 (19) and 58 (100).

4-(*Benzylamino*)*pentan*-2-*ol* **3g** (mixture of the *erythro* and *threo* isomers in the ratio 2.2:1). Oil (Found: C, 74.6; H, 9.85; N, 7.0. $C_{12}H_{19}NO$ requires C, 74.57; H, 9.91; N, 7.25%); ν_{max}(neat)/cm^{-1} 3250br, 1440, 1360, 1115, 740 and 690; δ_H(200 MHz; $CDCl_3$) 1.13 (d, *J* 6.2, *erythro* Me), 1.17 (d, *J* 6.6, *threo* Me), 1.18 (d, *J* 6.3, *erythro* Me), 1.22 (d, *J* 6.6, *threo* Me), 1.20–1.85 (2 H, m), 2.92 [dqd, *J* 11.2, 6.0 (q) and 2.9, *erythro* CHN], 3.05–3.25 (m, *threo* CHN), 3.70–4.30 (5 H, m) and 7.15–7.35 (5 H, m); δ_C(75.46 MHz; $CDCl_3$) *erythro*: 20.98 (C-5), 23.82 (C-1), 45.01 (C-3), 50.71 (PhCH_2), 54.06 (C-4), 68.97 (C-2), 127.19, 128.21, 128.50 and 139.45; *threo*: 19.68 (C-5), 23.62 (C-1), 40.82 (C-3), 51.04 (C-4), 51.42 (PhCH_2), 64.83 (C-2), 127.21, 128.23, 128.52 and 139.48; *m/z* (%) 193 (M^+, 1), 178 (4), 134 (51) and 91 (100).

erythro-4-(*Isopropylamino*)*pentan*-2-*ol* erythro-**3h**. Oil (Found: C, 66.0; H, 13.1; N, 9.9. $C_8H_{19}NO$ requires C, 66.16; H, 13.19; N, 9.64%); ν_{max}(neat)/cm^{-1} 3250br, 1440, 1360 and 1150; δ_H(200 MHz; $CDCl_3$) 0.99–1.55 (14 H, m), 2.84 [1 H, dqd, *J* 11.5, 6.5 (q) and 2.7, CHN], 2.92 (1 H, sept, *J* 6.2, NC*H*Me_2), 3.94 [1 H, dqd, *J* 10.2, 6.2 (q) and 1.9, CHO] and 5.30 (2 H, br s); δ_C(75.46 MHz; $CDCl_3$) 22.08, 22.48, 24.35, 25.06, 45.63 (C-3), 45.85, 52.03 (C-4) and 69.46 (C-2); *m/z* (%) 145 (M^+, 2), 130 (14), 86 (100) and 72 (18).

threo-4-(*Isopropylamino*)*pentan*-2-*ol* threo-**3h**. Oil (Found: C, 66.1; H, 13.3; N, 9.8%); ν_{max}(neat)/cm^{-1} 3300br, 1430, 1365 and 1130; δ_H(200 MHz; $CDCl_3$) 0.99–1.60 (14 H, m), 2.91 (1 H, sept, *J* 6.2, NC*H*Me_2), 3.16 [1 H, dqd, *J* 6.5 (q), 5.7 and 3.4, CHN], 4.10 [1 H, dqd, *J* 8.4, 6.3 (q) and 3.0, CHO] and 5.50 (2 H, br s); δ_C(75.46 MHz; $CDCl_3$) 20.77, 23.41, 23.72, 24.05, 41.96 (C-3), 45.97, 48.47 (C-4) and 65.61 (C-2); *m/z* (%) 145 (M^+, 3), 130 (17), 86 (100) and 72 (19).

erythro-4-(*Cyclohexylamino*)*pentan*-2-*ol* erythro-**3i**. Oil (Found: C, 71.5; H, 12.7; N, 7.4. $C_{11}H_{23}NO$ requires C, 71.30; H, 12.51; N, 7.56%); ν_{max}(neat)/cm^{-1} 3250br, 1445, 1370, 1165 and 1130; δ_H(200 MHz; $CDCl_3$) 0.87 (3 H, d, *J* 6.2, Me), 0.90 (3 H, d, *J* 6.2, Me), 0.80–1.80 (14 H, m), 2.25–2.46 (1 H, m), 2.74 [1 H, dqd, *J* 11.0, 6.2 (q) and 2.8, CHN] and 3.74 [1 H, dqd, *J* 10.3, 6.2 (q) and 1.8, CHO]; δ_C(75.46 MHz; $CDCl_3$) 21.57 (C-5), 23.68 (C-1), 24.18, 24.71, 25.77, 32.53, 34.67, 45.18 (C-3), 50.82 (C-4), 53.02 and 68.64 (C-2); *m/z* (%) 185 (M^+, 16), 170 (38), 142 (51) and 126 (100).

threo-4-(*Cyclohexylamino*)*pentan*-2-*ol* threo-**3i**. Oil (Found: C, 71.5; H, 12.6; N, 7.3%); ν_{max}(neat)/cm^{-1} 3250br, 1445, 1370, 1130 and 1090; δ_H(200 MHz; $CDCl_3$) 0.94 (3 H, d, *J* 6.3, Me), 0.95 (3 H, d, *J* 6.2, Me), 0.85–1.80 (14 H, m), 2.27–2.45 (1 H, m), 3.03 [1 H, dqd, *J* 6.3 (q), 5.7 and 3.7, CHN], 3.90 [1 H, dqd, *J* 8.3, 6.2 (q) and 3.1, CHO]; δ_C(75.46 MHz; $CDCl_3$) 20.25 (C-5), 23.38 (C-1), 24.79, 24.92, 25.82, 33.46, 33.70, 41.54 (C-3), 47.22 (C-4), 53.09 and 64.78 (C-2); *m/z* (%) 185 (M^+, 8). 170 (17), 142 (42) and 126 (100).

erythro-4-Anilinopentan-2-ol *erythro*-**3j**.[4c] Oil (Found: C, 73.6; H, 9.4; N, 7.9. Calc. for $C_{11}H_{17}NO$: C, 73.70; H, 9.56; N, 7.81%); ν_{max}(neat)/cm^{-1} 3350br, 1600, 1490, 1310, 1125, 745 and 690; δ_H(200 MHz; $CDCl_3$) 1.17 (3 H, d, *J* 6.3, Me), 1.21 (3 H, d, *J* 6.2, Me), 1.50–1.80 (2 H, m, 3-H_2), 3.56 (2 H, br s), 3.71 (1 H, sext, *J* 6.3, CHN), 4.05 (1 H, sext, *J* 6.2, CHO), 6.64–6.87 (3 H, m) and 7.15–7.32 (2 H, m); δ_C(300 MHz; $CDCl_3$) 21.93 (C-5), 24.48 (C-1), 46.19 (C-3), 50.34 (C-4), 68.44 (C-2), 115.69, 119.30, 129.82 and 147.47; *m/z* (%) 179 (M^+, 30), 164 (8), 120 (100) and 77 (18).

threo-4-Anilinopentan-2-ol *threo*-**3j**.[4c] Oil (Found: C, 73.8; H, 9.7; N, 7.7%); ν_{max}(neat)/cm^{-1} 3300br, 1590, 1490, 1300, 745 and 690; δ_H(200 MHz; $CDCl_3$) 1.21 (3 H, d, *J* 6.4, Me), 1.23 (3 H, d, *J* 6.2, Me), 1.59 (1 H, ddd, *J* 14.7, 8.2 and 3.5, 3-H), 1.72 (1 H, ddd, *J* 14.7, 7.9 and 4.2, 3-H), 3.15 (2 H, br s), 3.65–3.85 (1 H, m, CHN), 4.03–4.17 (1 H, m, CHO), 6.64–6.86 (3 H, m) and 7.13–7.28 (2 H, m); δ_C(75.46 MHz; $CDCl_3$) 21.15 (C-5), 23.91 (C-1), 45.44 (C-3), 46.33 (C-4), 65.23 (C-2), 113.78, 117.64, 129.30 and 147.41; *m/z* (%) 179 (M^+, 55), 164 (12), 121 (23) and 120 (100).

5-*Anilinohexan*-3-*ol* **3k** (mixture of the *erythro* and *threo* isomers in the ratio 1.4:1). Oil (Found: C, 74.4; H, 10.1; N, 7.4. $C_{12}H_{19}NO$ requires C, 74.57; H, 9.91; N, 7.25%); ν_{max}(neat)/cm^{-1} 3350br, 1590, 1485, 1305, 740 and 675; δ_H(200 MHz; $CDCl_3$) 0.96 (3 H, t, *J* 7.4, *Me*CH_2), 1.19 (1.8 H, d, *J* 6.3, *erythro Me*CHN), 1.22 (1.2 H, d, *J* 6.2, *threo Me*CHN), 1.43–1.72 (4 H, m), 3.40 (2 H, br s), 3.65–3.90 (2 H, m, CHO, CHN), 6.60–6.85 (3 H, m) and 7.10–7.30 (2 H, m); δ_C(75.46 MHz; $CDCl_3$) *erythro*: 10.29 (C-1), 21.98 (C-6), 31.30 (C-2), 43.92 (C-4), 50.41 (C-5), 73.69 (C-3), 115.67, 119.29, 129.82 and 147.48; *threo*: 10.57 (C-1), 21.75 (C-6), 31.12 (C-2), 43.83 (C-4), 46.79 (C-5), 70.92 (C-3), 114.29, 118.09, 129.90 and 148.09; *m/z* (%) 193 (M^+, 14), 120 (100), 93 (12) and 77 (16).

5-*Anilino*-1-*phenylhexan*-3-*ol* **3l** (mixture of the *erythro* and *threo* isomers in the ratio 1.4:1). Oil (Found: C, 80.4; H, 8.7; N, 5.0. $C_{18}H_{23}NO$ requires C, 80.26; H, 8.61; N, 5.20%); ν_{max}(neat)/cm^{-1} 3350br, 1580, 1480, 740 and 680; δ_H(200 MHz; $CDCl_3$) 1.22 (1.8 H, d, *J* 6.5, *erythro Me*CHN), 1.27 (1.2 H, d, *J* 6.6, *threo Me*CHN), 1.65–1.95 (4 H, m), 2.65–2.97 (2 H, m, CH_2Ph), 3.60 (2 H, br s), 3.68–4.05 (2 H, m, CHO, CHN), 6.70–6.92 (3 H, m) and 7.20–7.43 (7 H, m); δ_C(75.46 MHz; $CDCl_3$) *erythro*: 22.04 (C-6), 32.27, 40.22, 44.46 (C-4), 50.70 (C-5), 71.82 (C-3), 115.85, 119.55, 126.27, 128.76, 128.91, 129.84, 142.68 and 147.32; *threo*: 21.77 (C-6), 32.69, 39.98, 44.19 (C-4), 46.86 (C-5), 69.11 (C-3), 114.44, 118.36, 126.35, 128.57, 129.55, 129.67, 142.54 and 147.93; *m/z* (%) 269 (M^+, 10), 120 (100), 91 (20) and 77 (11).

erythro-3-Anilino-1-phenylbutan-1-ol *erythro*-**3m**.[4c] Oil (Found: C, 79.85; H, 8.0; N, 5.6. Calc. for $C_{16}H_{19}NO$: C, 79.63;

H, 7.94; N, 5.80%); ν_{max}(neat)/cm^{-1} 3350br, 1580, 1480, 1300, 740 and 690; δ_H(200 MHz; $CDCl_3$) 1.21 (3 H, d, *J* 6.3, Me), 1.84 [1 H, dt, *J* 14.4 and 4.4 (t), 2-H], 1.94 [1 H, dt, *J* 14.4 and 8.7 (t), 2-H], 3.69 (2 H, br s), 3.76 [1 H, dqd, *J* 8.3, 6.2 (q) and 4.8, CHN], 4.96 (1 H, dd, *J* 8.7, 4.4, CHO), 6.60–6.85 (3 H, m) and 7.15–7.40 (7 H, m); δ_C(75.46 MHz; $CDCl_3$) 21.91 (C-4), 46.71 (C-2), 50.16 (C-3), 74.64 (C-1), 115.70, 119.40, 126.24, 127.99, 128.69, 129.86, 145.13 and 147.31; *m*/*z* (%) 241 (M^+, 27), 120 (100) and 77 (37).

threo-3-Anilino-1-phenylbutan-1-ol *threo*-**3m**.[4c] Oil (Found: C, 79.7; H, 7.7; N, 5.6%); ν_{max}(neat)/cm^{-1} 3325br, 1590, 1485, 1305, 740 and 690; δ_H(200 MHz; $CDCl_3$) 1.21 (3 H, d, *J* 6.2, Me), 1.88 (1 H, ddd, *J* 14.3, 8.4 and 4.0, 2-H), 2.02 (1 H, ddd, *J* 14.3, 7.7 and 3.5, 2-H), 3.40 (2 H, br s), 3.64–3.84 (1 H, m, CHN), 5.00 (1 H, dd, *J* 7.7 and 4.0, CHO), 6.60–6.83 (3 H, m) and 7.10–7.40 (7 H, m); δ_C(75.46 MHz; $CDCl_3$) 21.72 (C-4), 45.88 (C-2), 47.13 (C-3), 72.30 (C-1), 114.84, 118.69, 126.18, 127.87, 128.99, 129.83, 145.27 and 147.73; *m*/*z* (%) 241 (M^+, 21), 120 (100) and 77 (30).

cis-3-*Anilinocyclohexanol* cis-**3n**. Oil (Found: C, 75.5; H, 8.8; N, 7.5. $C_{12}H_{17}NO$ requires C, 75.35; H, 8.96; N, 7.32%); ν_{max}(neat)/cm^{-1} 3350br, 1600, 1500, 1030, 900 and 730; δ_H(200 MHz; $CDCl_3$) 1.05–1.45 (4 H, m), 1.80–2.10 (3 H, m), 2.25–2.40 (1 H, m), 2.50 (2 H, br s), 3.36 (1 H, tt, *J* 10.1 and 3.8, CHN), 3.77 (1 H, tt, *J* 9.8 and 4.1, CHO), 6.55–6.75 (3 H, m) and 7.10–7.28 (2 H, m); δ_C(75.46 MHz; $CDCl_3$) 21.53, 32.58, 35.34, 42.39 (C-2), 50.77 (C-3), 69.77 (C-1), 113.76, 117.75, 129.79 and 147.57; *m*/*z* (%) 191 (M^+, 83), 148 (100), 132 (48), 118 (42), 106 (71), 93 (45) and 77 (30).

trans-3-*Anilinocyclohexanol* trans-**3n**. Oil (Found: C, 75.5; H, 9.1; N, 7.2%); ν_{max}(neat)/cm^{-1} 3300br, 1600, 1500, 1320, 980, 755 and 695; δ_H(200 MHz; $CDCl_3$) 1.20–1.40 (1 H, m), 1.45–1.88 (5 H, m), 1.90–2.07 (2 H, m), 2.50 (2 H, br s, NH, OH), 3.76 (1 H, tt, *J* 9.0 and 3.7, CHN), 4.08–4.19 (1 H, m, CHO), 6.55–6.78 (3 H, m) and 7.11–7.25 (2 H, m); δ_C(75.46 MHz; $CDCl_3$) 19.41, 32.17, 33.23, 39.80 (C-2), 47.30 (C-3), 66.96 (C-1), 113.20, 117.10, 129.29 and 146.96; *m*/*z* (%) 191 (M^+, 79), 148 (100), 132 (41), 118 (37), 106 (75), 93 (47) and 77 (32).

cis-3-*Anilino*-5,5-*dimethylcyclohexanol* cis-**3o**. Oil (Found: C, 76.7; H, 9.8; N, 6.2. $C_{14}H_{21}NO$ requires C, 76.67; H, 9.65; N, 6.39%); ν_{max}(neat)/cm^{-1} 3300br, 1600, 1470, 1030, 770 and 710; δ_H(200 MHz; $CDCl_3$) 0.91 (1 H, t, *J* 12.3), 0.97 (1 H, q, *J* 11.6), 0.99 (3 H, s, Me), 1.03 (3 H, s, Me), 1.10 (1 H, t, *J* 11.9), 1.67–1.86 (2 H, m), 2.32–2.46 (1 H, m), 3.10 (2 H, br s), 3.47 (1 H, tt, *J* 11.7 and 4.0, CHN), 3.85 (1 H, tt, *J* 11.4 and 8.6, CHO), 6.57–6.78 (3 H, m) and 7.13–7.28 (2 H, m); δ_C(75.46 MHz; $CDCl_3$) 26.32, 32.17, 33.47, 43.39, 46.13, 48.05, 48.48, 67.13 (C-1), 113.84, 117.89, 129.86 and 147.63; *m*/*z* (%) 219 (M^+, 55), 160 (34), 148 (100), 118 (27) and 93 (27).

trans-3-*Anilino*-5,5-*dimethylcyclohexanol* trans-**3o**. Oil (Found: C, 76.8; H, 9.7; N, 6.2%); ν_{max}(neat)/cm^{-1} 3350br, 1600, 1500, 750 and 690; δ_H(200 MHz; $CDCl_3$) 0.97 (3 H, s, Me), 1.21 (3 H, s, Me), 0.90–2.20 (6 H, m), 3.30 (2 H, br s), 3.90 (1 H, tt, *J* 10.3 and 3.7, CHN), 4.28 (1 H, quint, *J* 3.6, CHO), 6.58–6.75 (3 H, m) and 7.12–7.22 (2 H, m); δ_C(75.46 MHz; $CDCl_3$) 29.25, 32.27, 33.66, 40.51, 45.21, 45.53, 46.44, 68.32 (C-1), 113.61, 117.58, 129.80 and 147.77; *m*/*z* (%) 219 (M^+, 47), 160 (38), 148 (100), 118 (33) and 93 (21).

4-*Diethylaminopentan*-2-*ol* **3p** (mixture of the *erythro* and *threo* isomers in the ratio 0.5:1). Oil (Found: C, 68.0; H, 13.45; N, 8.6. $C_9H_{21}NO$ requires C, 67.87; H, 13.29; N, 8.79%); ν_{max}(neat)/cm^{-1} 3350br, 1430, 1370 and 1140; δ_H(200 MHz; $CDCl_3$) 0.83–1.28 (12 H, m, 4 × Me), 1.50–2.05 (2 H, m, 3-H_2), 2.10–2.80 (4 H, m), 2.96–3.16 (0.3 H, m, *erythro* CHN), 3.28 [0.7 H, dqd, *J* 10.6, 6.7 (q) and 3.4, *threo* CHN], 3.84–3.97 (0.3 H, m, *erythro* CHO), 4.03 [0.7 H, qt, *J* 6.4 (q) and 4.3 (t), *threo* CHO] and 5.20 (1 H, br s, OH); δ_C(75.46 MHz; $CDCl_3$) *erythro*: 12.83 (C-5), 13.39, 23.68 (C-1), 40.81 (C-3), 44.08, 52.27 (C-4) and 69.30 (C-2); *threo*: 13.23, 16.77 (C-5), 22.93 (C-1), 38.56 (C-3), 42.47, 50.71 (C-4) and 66.48 (C-2); *m*/*z* (%) 159 (M^+, 3), 144 (7) and 100 (100).

4-*Pyrrolidinopentan*-2-*ol* **3q** (mixture of the *erythro* and *threo* isomers in the ratio 0.8:1). Oil (Found: C, 68.6; H, 12.05; N, 9.2. $C_9H_{19}NO$ requires C, 68.74; H, 12.18; N, 8.91%); ν_{max}(neat)/cm^{-1} 3500br, 1450, 1370 and 1140; δ_H(200 MHz; $CDCl_3$) 1.05–1.22 (6 H, m), 1.25–1.53 (2 H, m, 3-H_2), 1.65–1.80 (4 H, m), 2.45–2.75 (4.5 H, m), 3.14 [0.6 H, dqd, *J* 10.4, 6.5 (q) and 3.2, *threo* CHN], 3.90–4.15 (0.4 H, m, *erythro* CHO), 4.16 [0.6 H, dqd, *J* 9.5, 6.5 (q) and 3.0, *threo* CHO] and 6.0 (1 H, br s, OH); δ_C(75.46 MHz; $CDCl_3$) *erythro*: 12.94 (C-5), 23.81, 24.25 (C-1), 42.48 (C-3), 47.15, 56.08 (C-4) and 69.87 (C-2); *threo*: 18.10 (C-5), 23.81, 24.01 (C-1), 41.42 (C-3), 52.09, 58.11 (C-4) and 65.28 (C-2); *m*/*z* (%) 157 (M^+, 11), 142 (23), 97 (35) and 98 (100).

Synthesis of Tetrahydro-1,3-*oxazines* **4**.—To a solution of a γ-amino alcohol **3** (as pure diastereoisomer or in admixture, 1 mmol) in THF (2 cm^3) at room temperature was added 37% aq. formaldehyde (1 mmol). The mixture was magnetically stirred for 20 h at room temperature. Solvent was removed and the residue was dried under reduced pressure. Column chromatographic separation of crude material [hexane–ethyl acetate (8:2)] furnished the pure corresponding tetrahydro-1,3-oxazine **4** as separated diastereoisomers. Reaction yields are given in Table 2. Spectral and analytical data follow.

cis-3,4,6-*Trimethyltetrahydro*-1,3-*oxazine* cis-**4d**. Oil (Found: C, 65.0; H, 11.8; N, 11.0. $C_7H_{15}NO$ requires C, 65.07; H, 11.70; N, 10.84%); ν_{max}(neat)/cm^{-1} 1440, 1365 and 1100; δ_H(200 MHz; $CDCl_3$) 1.10 (3 H, d, *J* 6.4, 4-Me), 1.18 (3 H, d, *J* 6.2, 6-Me), 1.25–1.50 (2 H, m, 5-H_2), 2.25 (3 H, s, 3-Me), 2.47–2.68 (1 H, m, 4-H), 3.46–3.63 (1 H, m, 6-H) and 3.99 and 4.43 (2 H, two d, J_{AB} 9.1, 2-H_2); δ_C(75.46 MHz; $CDCl_3$) 20.29 (4-Me), 22.01 (6-Me), 34.73 (C-5), 38.35 (3-Me), 56.05 (C-4), 73.83 (C-3) and 87.40 (C-2); *m*/*z* (%) 129 (M^+, 30), 114 (100), 86 (63), 72 (40), 70 (98) and 58 (48).

trans-3,4,6-*Trimethyltetrahydro*-1,3-*oxazine* trans-**4d**. Oil (Found: C, 65.25; H, 11.9; N, 10.6%); ν_{max}(neat)/cm^{-1} 1430, 1370 and 1130; δ_H(200 MHz; $CDCl_3$) 1.16 (3 H, d, *J* 6.1, 4-Me), 1.23 (3 H, d, *J* 7.1, 6-Me), 1.30–1.45 (1 H, m, 5-H^{eq}), 1.84 (1 H, ddd, *J* 13.4, 10.8 and 5.3, 5-H^{ax}), 2.55 (3 H, s, 3-Me), 2.85–3.04 (1 H, m, 4-H), 3.81 [1 H, dqd, *J* 10.8, 6.2 (q) and 2.6, 6-H^{ax}], 4.19 and 4.58 (2 H, two d, J_{AB} 10.6, 2-H); δ_C(75.46 MHz; $CDCl_3$) 18.02 (4-Me), 22.10 (6-Me), 32.96 (C-5), 40.86 (3-Me), 52.25 (C-4), 68.12 (C-6) and 79.74 (C-2); *m*/*z* (%) 129 (M^+, 26), 114 (100), 86 (57), 72 (38) and 70 (93).

cis-3,6-*Dimethyl*-4-*phenethyltetrahydro*-1,3-*oxazine* cis-**4e**. Oil (Found: C, 76.8; H, 9.7; N, 6.2. $C_{14}H_{21}NO$ requires C, 76.67; H, 9.65; N, 6.39%); ν_{max}(neat)/cm^{-1} 1450, 1380, 1125, 1000, 760 and 710; δ_H(200 MHz; $CDCl_3$) 1.21 (3 H, d, *J* 6.2, 6-Me), 1.30–1.80 (4 H, m), 2.35 (3 H, s, 3-Me), 2.68 (2 H, t, *J* 8.1, PhCH_2), 2.80 [1 H, dtd, *J* 11.0, 7.3 (t) and 3.5, 4-H], 3.58 [1 H, dqd, *J* 10.1, 6.4 (q) and 3.1, 6-H], 4.28 and 4.55 (2 H, two d, J_{AB} 9.9, 2-H) and 7.15–7.38 (5 H, m, Ph); δ_C(75.46 MHz; $CDCl_3$) 22.42 (6-Me), 32.27, 33.57, 34.16, 35.89, 58.98 (C-4), 73.86 (C-6), 87.62 (C-2), 126.33, 128.87, 129.04 and 142.70; *m*/*z* (%) 219 (M^+, 10), 114 (100), 91 (81), 84 (23) and 70 (97).

trans-3,6-*Dimethyl*-4-*phenethyltetrahydro*-1,3-*oxazine* trans-**4e**. Oil (Found: C, 76.5; H, 9.8; N, 6.2%); ν_{max}(neat)/cm^{-1} 1450, 1390, 1100, 995, 750 and 700; δ_H(200 MHz; $CDCl_3$) 1.16 (3 H, d, *J* 6.2, 6-Me), 1.19 [1 H, dt, *J* 14.0 and 2.3 (t)], 1.65–1.95 (2 H, m), 2.05–2.33 (1 H, m), 2.63 (3 H, s, 3-Me), 2.55–2.85 (3 H, m, 4-H, PhCH_2), 3.78 [1 H, dqd, *J* 11.3, 6.2 (q) and 2.6, 6-H], 4.26 and 4.61 (2 H, two d, J_{AB} 10.9, 2-H_2) and 7.13–7.37 (5 H, m, Ph); δ_C(75.46 MHz; $CDCl_3$) 22.58 (6-Me), 31.41, 33.40, 34.05, 41.73, 56.36, (C-4), 68.78 (C-6), 80.42 (C-2), 126.23, 128.82, 128.98 and 142.87; *m*/*z* (%) 219 (M^+, 5), 114 (100), 91 (46), 84 (15) and 70 (87).

cis-3-*Benzyl*-4,6-*dimethyltetrahydro*-1,3-*oxazine* cis-**4g**. Oil (Found: C, 75.9; H, 9.2; N, 7.0. $C_{13}H_{19}NO$ requires C, 76.06; H, 9.33; N, 6.82%); ν_{max}(neat)/cm^{-1} 1450, 1385, 1105, 1005, 740 and 705; δ_H(200 MHz; $CDCl_3$) 1.20 (3 H, d, *J* 6.6, 4-Me), 1.24 (3 H, d, *J* 6.1, 6-Me), 1.35–1.56 (2 H, m, 5-H_2), 3.02 [d quint, *J* 8.11 and 6.6 (1 H, quint), 4-H], 3.55 and 3.91 (2 H, two d, J_{AB} 13.6, CH_2Ph), 3.53–3.70 (1 H, m, 6-H), 4.07 and 4.39 (2 H, two d, J_{AB} 9.8, 2-H) and 7.15–7.40 (5 H, m, Ph); δ_C(75.46 MHz; $CDCl_3$) 20.37 (4-Me), 21.82 (6-Me), 37.66 (C-5), 48.71 (Ph-*C*H_2), 55.05 (C-4), 73.45 (C-6), 83.52 (C-2), 126.79, 128.22, 128.91 and 139.45; *m*/*z* (%) 205 (M^+, 22), 204 (24), 190 (100), 146 (54), 92 (60) and 91 (47).

trans-3-*Benzyl*-4,6-*dimethyltetrahydro*-1,3-*oxazine* trans-**4g**. Oil (Found: C, 76.1; H, 9.45; N, 6.6%); ν_{max}(neat)/cm^{-1} 1450, 1380, 1100, 1000, 745 and 700; δ_H(200 MHz; $CDCl_3$) 1.16 [1 H, dt, *J* 13.6, 2.0 (t), 5-H], 1.20 (3 H, d, *J* 6.2, 4-Me), 1.26 (3 H, d, *J* 7.1, 6-Me), 1.90 (1 H, ddd, *J* 13.6, 11.3 and 5.7, 5-H), 2.86–3.04 (1 H, m, 4-H), 3.85 [1 H, dqd, *J* 11.5, 5.7 (q) and 2.0, 6-H], 3.87 and 4.02 (2 H, two d, J_{AB} 13.7, CH_2Ph), 4.29 and 4.69 (2 H, two d, J_{AB} 11.0, 2-H_2) and 7.15–7.42 (5 H, m, Ph); δ_C(75.46 MHz; $CDCl_3$) 18.09 (4-Me), 22.21 (6-Me), 32.61 (C-5), 49.30 (Ph*C*H_2), 56.85 (C-4), 67.89 (C-6), 78.57 (C-2), 126.84, 128.23, 128.48 and 139.70; *m*/*z* (%) 205 (M^+, 15), 204 (15), 190 (77), 146 (27), 92 (31) and 91 (100).

cis-3-*Cyclohexyl*-4,6-*dimethyltetrahydro*-1,3-*oxazine* cis-**4i**. Oil (Found: C, 73.2; H, 11.9; N, 7.3. $C_{12}H_{23}NO$ requires C, 73.04; H, 11.75; N, 7.10%); ν_{max}(neat)/cm^{-1} 1450, 1390, 1215, 1100 and 990; δ_H(200 MHz; $CDCl_3$) 1.10 (3 H, d, *J* 6.4, 4-Me), 1.16 (3 H, d, *J* 6.2, 6-Me), 1.27 [1 H, dt, *J* 13.0 and 10.9 (t), 5-H], 1.48 [1 H, dt, *J* 13.0 and 3.0 (t), 5-H], 0.80–1.90 (10 H, m, [CH_2]$_5$), 2.79 (1 H, tt, *J* 11.2 and 3.0, NCH), 2.85 [1 H, dqd, *J* 10.9, 6.4 (q) and 3.0, 4-H], 3.50 [1 H, dqd, *J* 10.9, 6.2 (q) and 3.0, 6-H] and 3.98 and 4.64 (2 H, two d, J_{AB} 11.4, 2-H_2); δ_C(75.46 MHz; $CDCl_3$) 20.37 (4-Me), 22.12 (6-Me), 26.78, 26.85, 27.26, 28.08, 32.91, 42.24, 52.76, 55.41 (C-4), 73.89 (C-6) and 80.78 (C-2); *m*/*z* (%) 197 (M^+, 78), 182 (97), 154 (100), 138 (55), 112 (37) and 82 (76).

trans-3-*Cyclohexyl*-4,6-*dimethyltetrahydro*-1,3-*oxazine* trans-**4i**. Oil (Found: C, 72.9; H, 11.6; N, 7.3%); ν_{max}(neat)/cm^{-1} 1450, 1390, 985 and 830; δ_H(200 MHz; $CDCl_3$) 1.06–1.35 (6 H, m), 1.10 (3 H, d, *J* 6.2, 6-Me), 1.22 (3 H, d, *J* 7.1, 4-Me), 1.50–2.05 (6 H, m), 2.55–2.70 (1 H, m, NC*H*[CH_2]$_5$), 3.21 (1 H, quint, *J* 6.8, 4-H), 3.76 [1 H, dqd, *J* 11.5, 6.2 (q) and 2.6, 6-H] and 4.48 and 4.54 (2 H, two d, J_{AB} 12.6, 2-H); δ_C(75.46 MHz; $CDCl_3$) 19.24 (4-Me), 22.89 (6-Me), 26.26, 26.41, 26.52, 32.33, 33.70, 35.58, 47.64, 60.36 (C-4), 68.28 (C-6) and 76.49 (C-2); *m*/*z* (%) 197 (M^+, 32), 182 (78), 154 (100), 138 (24) and 82 (48).

cis-4,6-*Dimethyl*-3-*phenyltetrahydro*-1,3-*oxazine* cis-**4j**. Oil (Found: C, 75.2; H, 9.1; N, 7.6. $C_{12}H_{17}NO$ requires C, 75.35; H, 8.96; N, 7.32%); ν_{max}(neat)/cm^{-1} 1595, 1490, 1250, 1095, 995, 765 and 700; δ_H(200 MHz; $CDCl_3$) 1.04 (3 H, d, *J* 6.4, 4-Me), 1.29 (3 H, d, *J* 6.2, 6-Me), 1.44 [1 H, dt, *J* 13.3 and 11.0 (t), 5-H], 1.63 [1 H, dt, *J* 13.3 and 3.0 (t), 5-H], 3.30 [1 H, dqd, *J* 11.0, 6.4 (q) and 3.0, 4-H], 3.72 [1 H, dqd, *J* 11.0, 6.2 (q) and 3.0, 6-H], 4.43 and 4.76 (2 H, two d, J_{AB} 9.3, 2-H_2) and 7.07–7.37 (5 H, m, Ph); δ_C(75.46 MHz; $CDCl_3$) 20.77 (4-Me), 21.63 (6-Me), 40.03 (C-5), 53.76 (C-4), 73.39 (C-6), 85.66 (C-2), 124.51, 125.90, 128.69 and 147.08; *m*/*z* (%) 191 (M^+, 95), 176 (98), 132 (100), 119 (88), 104 (99) and 77 (90).

trans-4,6-*Dimethyl*-3-*phenyltetrahydro*-1,3-*oxazine* trans-**4j**. Oil (Found: C, 75.3; H, 8.7; N, 7.5%); ν_{max}(neat)/cm^{-1} 1595, 1490, 1185, 1000, 745 and 695; δ_H(200 MHz; $CDCl_3$) 1.21 (3 H, d, *J* 6.2, 4-Me), 1.31 [1 H, dt, *J* 13.2 and 2.0 (t), 5-H], 1.45 (3 H, d, *J* 7.1, 6-Me), 1.80 (1 H, ddd, *J* 13.2, 11.5 and 5.7, 5-H), 3.91–4.10 (2 H, m, 4- and 6-H), 4.90 and 5.05 (2 H, two d, J_{AB} 11.2, 2-H_2), 6.90 (1 H, t, *J* 7.3, *p*-HPh), 7.09 (2 H, d, *J* 7.7, *o*-HPh) and 7.23–7.34 (2 H, m, *m*-HPh); δ_C(75.46 MHz; $CDCl_3$) 17.02 (4-Me), 22.06 (6-Me), 35.73 (C-5), 52.58 (C-4), 68.06 (C-6), 74.70 (C-2), 118.64, 120.25, 129.01 and 150.36; *m*/*z* (%) 191 (M^+, 96), 176 (100), 132 (87), 119 (60), 104 (88) and 77 (72).

cis-4-*Methyl*-3,6-*diphenyltetrahydro*-1,3-*oxazine* cis-**4m**. Oil (Found: C, 80.5; H, 7.6; N, 5.75. $C_{17}H_{19}NO$ requires C, 80.60; H, 7.56; N, 5.53%); ν_{max}(neat)/cm^{-1} 1600, 1500, 1090, 760 and 710; δ_H(200 MHz; $CDCl_3$) 1.13 (3 H, d, *J* 6.4, 3-Me), 1.77–1.92 (2 H, m, 5-H_2), 3.56 [1 H, d quint, *J* 7.7 and 6.4 (quint), 4-H], 4.65 (1 H, dd, *J* 10.2 and 4.4, 6-H), 4.71 and 5.02 (2 H, two d, J_{AB} 9.7, 2-H_2) and 7.10–7.45 (10 H, m, Ph); δ_C(75.46 MHz; $CDCl_3$) 20.97 (4-Me), 39.97 (C-5), 54.38 (C-4), 79.33 (C-6), 85.27 (C-2), 124.46, 125.81, 125.92, 127.13, 127.65, 128.81, 142.19 and 147.18; *m*/*z* (%) 253 (M^+, 92), 238 (35), 132 (97), 119 (100), 104 (99) and 77 (99).

trans-4-*Methyl*-3,6-*diphenyltetrahydro*-1,3-*oxazine* trans-**4m**. Oil (Found: C, 80.7; H, 7.5; N, 5.8%); ν_{max}(neat)/cm^{-1} 1590, 1490, 1180, 1030, 750 and 690; δ_H(200 MHz; $CDCl_3$) 1.50–1.70 (1 H, m, 5-H), 1.71 (3 H, d, *J* 7.1, 4-Me), 2.27 [1 H, td, *J* 12.7 (t) and 8.5, 5-H], 4.21 (1 H, quint, *J* 6.8, 4-H), 5.05 (1 H, dd, *J* 12.0 and 2.3, 6-H), 5.21 and 5.36 (2 H, two d, J_{AB} 11.4, 2-H), 7.12 (1 H, t, *J* 7.0, *p*-HPh) and 7.32–7.60 (9 H, m, Ph); δ_C(75.46 MHz; $CDCl_3$) 17.16 (4-Me), 35.98 (C-5), 53.32 (C-4), 74.37 (C-6), 75.09 (C-2), 119.17, 120.72, 125.99, 127.67, 128.48, 129.18, 142.56 and 150.62; *m*/*z* (%) 253 (M^+, 94), 238 (42), 132 (97), 119 (96), 104 (100) and 77 (99).

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