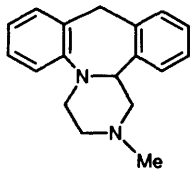
Stereoselective Construction of Vicinal Diamines. Part 1. Synthesis of Fused Pyrazines

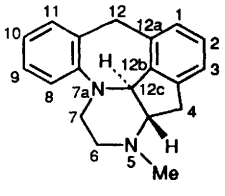
Barry S. Orlek,* Gary T. Borrett and Duncan M. Smith
SmithKline Beecham Pharmaceuticals, The Pinnacles, Harlow, Essex CM19 5AD, UK

A stereoselective approach to the construction of *trans*-1,2-diaminoindanes **8a**, **b** and *trans*-1,2-diaminotetralins **9a**, **b** is described. The *trans*-adducts **4** and **5**, derived from the addition of *N,N*-dichlorourethane to indene and 1,2-dihydronaphthalene, react with aryl amines to give *trans*-diamines **8a**, **b** and **9a**, **b** *via* the protonated oxazoline intermediates **13** and **14**. Elaboration of vicinal diamines **8a**, **b** and **9a**, **b** affords the diazabenzocycloheptafluorene **2** and dibenzopyrazinobenzazepine **3**, respectively.

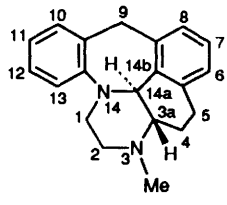
As part of a study designed to investigate the relationship between the conformation and biological activity of the antidepressant drug mianserin **1**,[1] the synthesis of conformationally restricted analogues **2**† and **3** was undertaken.



1

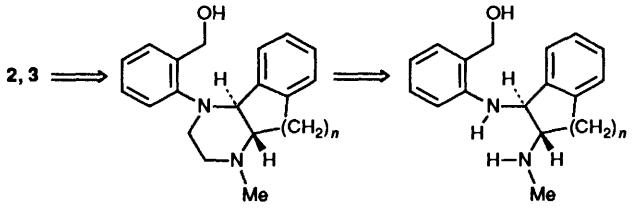


2



3

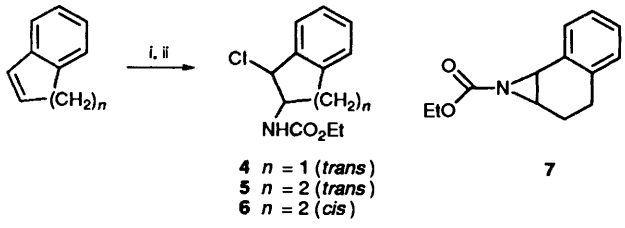
Retrosynthetic analysis suggested that the target structures **2** and **3** might be accessible from suitably functionalised *trans*-1,2-diaminoindane and 1,2-diaminotetralin precursors (Scheme 1).



n = 1, 2

Scheme 1

A key task which dictated overall strategy was the stereoselective construction of the *trans* vicinal diamine functionality. In view of the disadvantages associated with many established procedures, an alternative approach[2] was developed. It was envisaged that indene and 1,2-dihydronaphthalene could serve as precursors for 1,2-diamines *via* a two stage sequence involving addition of *N,N*-dichlorourethane followed by reaction with aryl amines. The addition of *N,N*-dichlorourethane to indene at ambient temperature followed by *in situ* reduction of the intermediate *N*-chlorourethane is known[3] to give the *trans*-adduct **4**. Examination of the addition of *N,N*-dichlorourethane to 1,2-dihydronaphthalene revealed high selectivity (96:4) in favour of the *trans*-adduct **5** which was obtained in good yield (66%) after crystallisation. The stereochemical assignment of the major product was facilitated by its conversion into the *N*-ethoxycarbonylaziridine **7**[4] upon treatment with sodium hydride in *N,N*-dimethylformamide (Scheme 2).



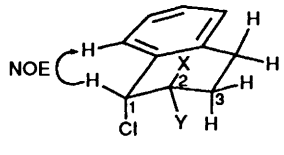
4 *n* = 1 (*trans*)
5 *n* = 2 (*trans*)
6 *n* = 2 (*cis*)

7

Scheme 2 *Reagents:* i, *N,N*-dichlorourethane, ii, sodium metabisulfite

The ^{1}H NMR spectra of adducts **5** and **6** displayed small coupling constants (*J*/Hz) of 4 and 3, respectively for the C-1 proton. In the case of the *trans*-isomer **5** the small coupling constant points to a *trans*-diaxial relationship between the substituents at C-1 and C-2. A significant nuclear Overhauser enhancement (NOE) was observed in the aromatic region of the spectrum of adduct **5** upon irradiation of the proton at C-1, and the axial proton at C-3 revealed coupling constants (J_{ae} 3 Hz, J_{ae} 7 Hz, J_{aa} 10 Hz and J_{gem} 14 Hz) which were consistent with the presence of an equatorial hydrogen at C-2. In the isomer **6** a comparable enhancement in the aromatic region was obtained due to irradiation of the C-1 proton, again suggesting an equatorial orientation for this proton. The presence of an axial proton at C-2 in this isomer was evident from the magnitude of the coupling constants (J_{ae} 9 Hz, J_{aa} 9 Hz, J_{aa} 13 Hz and J_{gem} 13 Hz) for the axial C-3 proton (Fig. 1).

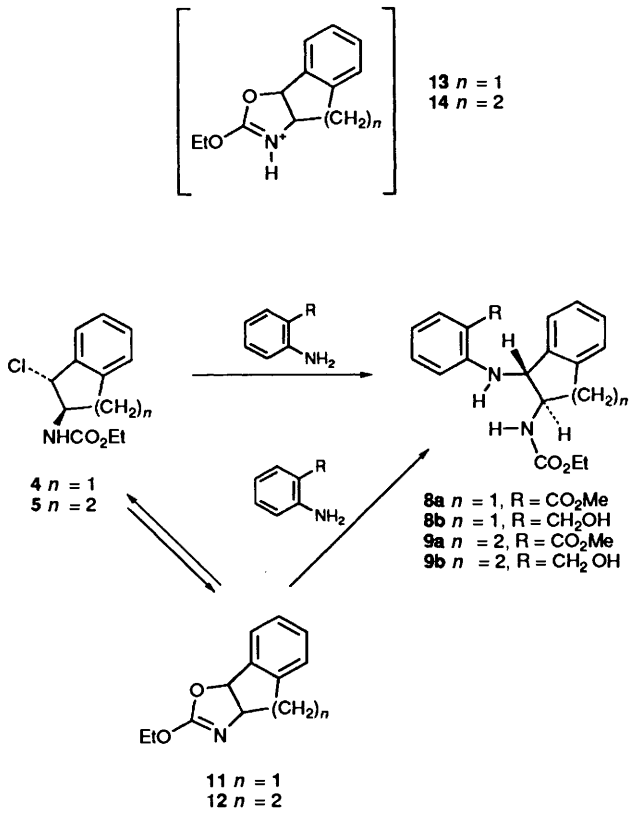
The behaviour of *trans*-adducts **4** and **5** towards suitably functionalised aryl amines was studied over a range of conditions (Scheme 3). Treatment of compounds **4** and **5** with an excess of methyl anthranilate afforded good yields of the *trans*-



5 X = $NHCO_2Et$; Y = H
6 X = H; Y = $NHCO_2$ Et

Fig. 1 Stereochemistry of adducts **5** and **6**

† For convenience only one stereoisomer is shown in diagrams.



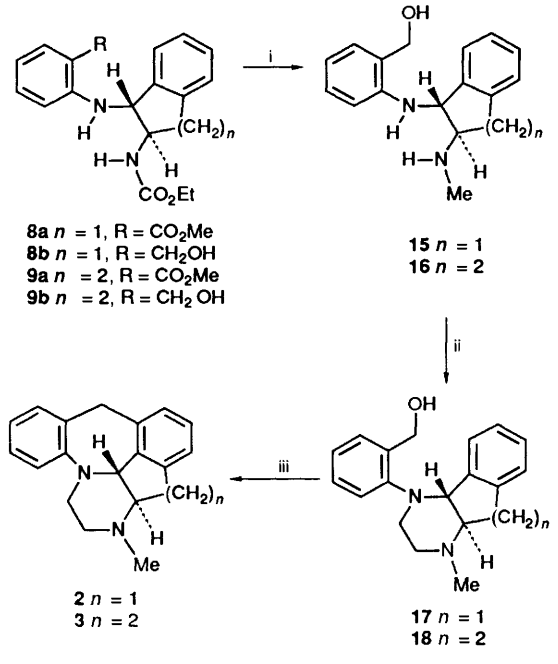
Scheme 3

diamine derivatives **8a** and **9a** respectively. In the former case a small proportion (8%) of the *cis*-isomer could be isolated when the reaction was carried out on a large scale. The stereochemistry of **8a** could be assigned by ^{1}H NMR spectroscopy since it has been shown[5] that in 1,2-disubstituted indanes the shift difference between the protons at C-3 is larger for *trans* substitution. In the case of **8a** these signals appear at δ 2.80 and 3.44 whereas the corresponding resonances in the *cis*-isomer are observed at δ 3.04 and 3.29. The stereochemistry of **9a** could not be assigned unambiguously by ^{1}H NMR spectroscopy, but spectra of elaborated structures provided clear evidence of *trans* substitution.

Reaction of compounds **4** and **5** with one equivalent of *o*-aminobenzyl alcohol in *N*,*N*-dimethylformamide (DMF), using barium carbonate as a mild acid mop, produced moderate yields of the alcohols **8b** and **9b**, which were identical to the products resulting from selective reduction of the ester function in **8a** and **9a** respectively. It was of interest that when the reaction of compounds **4** and **5** with *o*-aminobenzyl alcohol was carried out using the more basic combination of potassium carbonate and DMF, yields of **8b** and **9b** dropped considerably. The crude product derived from **4** contained a second component of similar polarity which comprised 30% of the total and gave rise to a characteristic doublet (J 7 Hz) at δ 5.9 in the ^{1}H NMR spectrum. Treatment of compound **4** with potassium carbonate in aqueous ethanol afforded the same compound in good yield and facilitated its identification as the oxazoline **11**. Similarly, the alkylation product derived from adduct **5** was found to contain an impurity identified as the oxazoline **12**. On treatment with potassium carbonate in aqueous ethanol adduct **5** afforded mainly the oxazoline **12**, although a small proportion (14%) of the aziridine **7** was also formed. Use of potassium hydrogen carbonate in this reaction reduced the yield of aziridine and led to an increased yield (79%) of oxazoline **12**. Conversion of *N*-(2-halogenoethyl)amides into oxazolines under basic conditions is well documented.[6] The reaction proceeds *via* a rate-determining internal S_N2 displacement (requiring an anti-periplanar arrangement of functional groups) to give an oxazolinium cation, followed by deprotonation. Consistent with the role assigned to the base in this mechanism is the observation that oxazoline formation from adducts **4** and **5** is favoured by mild bases. By contrast it has been shown that the formation of aziridines from cyclic β-iodo carbamates,[4] which generally requires more basic conditions,[2] involves proton abstration from the carbamate nitrogen followed by a rate-determining cyclisation step.[7]

The pH-dependence of the alkylation reactions and the recovery of the oxazolines **11** and **12** under more basic conditions point to the intermediacy of oxazolinium cations **13** and **14**. In support of this proposal is the finding that oxazolines **11** and **12** reacted readily with methyl anthranilate in the presence of toluene-*p*-sulfonic acid to give good yields of the diamine derivatives **8a** and **9a**. By contrast it has been shown[2] that oxazoline **11** reacts very sluggishly in the absence of an acid catalyst. These results are in accord with reports[7] of acid-catalysed ring openings of 2-alkyl-2-oxazolines by amines to give *N*-(2-aminoethyl)carboxamides. The proposed mechanism also accounts for the *trans* stereochemistry of the alkylation products. Further evidence for the facile interconversion between β-chloro carbamates **4** and **5** and the corresponding oxazolines was provided by the observation that **11** and **12** were readily transformed into β-chloro carbamates **4** and **5** in ethereal HCl.

Elaboration of the vicinal diamine precursors **8a**, **b** and **9a**, **b** to give the required target structures proceeded in a straightforward manner (Scheme 4). Amino alcohols **15** and **16**



Scheme 4 *Reagents and conditions:* i, $LiAlH_4$, Et_2O; ii, dibromoethane. NEt_3, 100 °C; iii. H_3PO_4, 90 °C

were obtained by lithium aluminium hydride reduction. Treatment of **15** and **16** with dibromoethane afforded the piperazines **17** and **18** respectively. Subsequent cyclisation in phosphoric acid produced target structures **2** and **3**.

The *trans*-diamine stereochemistry of the final products **2** and **3** was evident from the magnitude of the coupling between the bridgehead protons (J 10 Hz and J 9.7 Hz respectively, Tables 1 and 2). In the case of diamine **2** further confirmation was

Table 1 ^{1}H NMR Spectroscopic data for diazabenzocycloheptafluorene **2**[a]

Protons	δ	Multiplicity (J/Hz)
4a-H	2.20	ddd (J 10, 10, 6)
CH_3-N	2.35	s
6ax-H	2.50	ddd (J 12, 12, 3)
4ax-H	2.62	dd (J 14, 11)
6eq-H	2.86	m overlapping
4eq-H	2.88	m overlapping
12eq-H	3.45	d (J 13)
7ax-H	3.69	ddd (J 14.5, 11, 3)
7eq-H	3.87	ddd (J 14, 3, 3)
12ax-H	4.37	d (J 13)
12c-H	4.48	d (J 10)

[a] 250 MHz spectrum in $CDCl_3$. Spectroscopic assignments confirmed using spin–spin decoupling and COSY.

Table 2 ^{1}H NMR spectroscopic data for dibenzopyrazinobenzazepine **3**[a]

Protons	δ	Multiplicity (J/Hz)
4eq-H	1.79	ddd (J 11.3, 8.5, 2.2)
4ax-H	1.94	ddd (J 11.3, 10.7, 7.1)
3a-H	2.14	ddd (J 9.7, 8.7, 7.0)
CH_3-N	2.32	s
2ax-H	2.51	ddd (J 11.3, 13.5, 2.6)
5eq-H	2.56	ddd (J 14.4, 7.1, 2.2)
5ax-H	2.75	ddd (J 14.4, 10.7, 8.5)
2eq-H	2.94	ddd (J 11.3, 2.7, 2.7)
1eq-H	3.12	ddd (J 13.5, 2.6, 2.7)
9eq-H	3.37	d (J 12.9)
1ax-H	3.40	ddd (J 13.5, 13.5, 2.7)
14a-H	3.70	d (J 9.7)
9ax-H	4.84	d (J 12.9)

[a] 270 MHz spectrum in $CDCl_3$. Spectrum assigned using COSY and coupling constants obtained from the resolution enhanced spectrum.

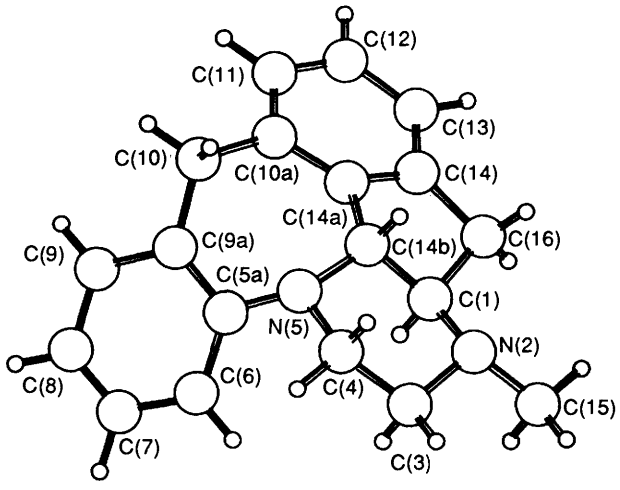


Fig. 2 Crystal structure of **2** showing crystallographic numbering system used

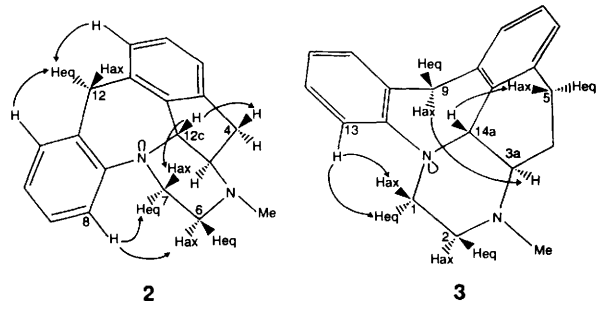


Fig. 3 Comparison of the conformation of structures **2** and **3** showing nuclear Overhauser enhancements

provided by an X-ray structure analysis (Fig. 2). A salient feature of the crystal state conformation of **2** is the *cis* junction between the dihydroazepine and piperazine rings. The conformation of the dihydroazepine ring is characterised by a *syn* relationship between the pseudoaxial hydrogen on C-12 and the hydrogen on C-12c.* The piperazine ring adopts a chair conformation. ^{1}H NMR spectroscopic data (Table 1) point to a similar conformation in solution. The chemical shift δ 4.48 of the methine proton 12c-H is consistent with a *cis* ring junction. By contrast, the appearance of the corresponding signal at δ 4.08 in the spectrum of mianserin[8] has been attributed to the *trans* diaxial shielding effect of the adjacent nitrogen lone pair. NOE (Fig. 3) between 8-H and 7eq-H and 6ax-H provides further evidence for the *cis* junction. The enhancement between 8-H and 6ax-H is consistent with a chair conformation for the piperazine ring. The 12-H signal at δ 4.37 shows line broadening which points to an axial orientation. This effect is due to long range coupling to aromatic protons, and is largest for benzylic protons which are perpendicular to the plane of the aromatic ring.[9] The observed NOE on the 12-H signal at δ 3.45 upon irradiation of the aromatic region confirms the equatorial assignment for this proton. The ^{1}H NMR spectrum of structure **3** (Table 2) indicated a solution conformation similar to that of mianserin. The shielding of the methine proton 14a-H is consistent with a *trans* junction between the dihydroazepine and piperazine rings. This orientation brings 1ax-H and 13-H into close proximity and the deshielding of 1ax-H relative to 1eq-H can probably be ascribed to the resulting Van der Waals deshielding effect.[8] Irradiation of the aromatic region produced NOE at 1ax-H and 1eq-H but not at 2ax-H (Fig. 3). The absence of NOE between the pseudoaxial proton at C-9 and the methine proton 14a-H is consistent with an *anti* relationship. A small NOE was observed between 9ax-H and 3a-H. Irradiation of 14a-H produced a large NOE on 5ax-H indicating a *syn* relationship between these protons.

* The crystallographic numbering of these atoms is C(10) and C(14b), respectively.

Experimental

Melting points were obtained on a Kofler hot stage apparatus and are uncorrected. NMR spectra were recorded on a Varian CFT-20, a JEOL GX-270, a Bruker WM-250 or a Bruker AM-400 spectrometer using tetramethylsilane as internal standard with coupling constants (J) measured in Hz. Mass spectra were obtained on an AEI MS9 (70 ev) or a JEOL DX303 (70 ev) spectrometer and IR spectra on a Perkin-Elmer 197 spectrometer. All evaporations of solvent were carried out under reduced pressure, and organic solutions were dried over sodium sulfate. Silica gel used for column chromatography was Merck Kieselgel 60. Standard work-up for lithium aluminium hydride reductions involved quenching with wet ether followed by water and then filtration to remove precipitated aluminium salts. Light petroleum refers to the fraction with b.p. 60–80 °C.

trans-1-*Chloro*-2-*ethoxycarbonylamino*-1,2,3,4-*tetrahydronaphthalene* **5**.—Freshly-distilled 1,2-dihydronaphthalene (10.0 g, 0.077 mol) in dry toluene (75 cm^3) was treated dropwise

under nitrogen with *N,N*-dichlorourethane (10 cm^3, 0.085 mol) dissolved in the same dry solvent (25 cm^3) at a rate adjusted to maintain the temperature at 35–40 °C. After stirring at room temp. for a further 2 h the reaction was cooled in ice and quenched with sodium metabisulfite (200 cm^3 of a 20% aqueous solution) keeping the temperature below 10 °C. The reaction was stirred vigorously at ice temp. for 4 h and then extracted with ethyl acetate. The extract was washed with water, while maintaining a neutral pH by addition of sodium hydrogen carbonate, then brine, dried and evaporated to dryness. After trituration with pentane a 94:6 mixture of *trans*- and *cis*-1-chloro-2-ethoxycarbonylamino-1,2,3,4-tetrahydronaphthalene (15.4 g, 79%) was obtained. Crystallisation afforded pure *trans*-isomer **5** (12.8 g, 66%), m.p. 122–124 °C (from pentane–ether) (Found: C, 61.5; H, 6.5; Cl, 14.3; N, 5.5. $C_{13}H_{16}ClNO_2$ requires C, 61.5; H, 6.4; Cl, 14.0; N, 5.5%); ν_{max}(KBr)/cm^{-1} 3260 (NH) and 1685 (C=O); δ_H(270 MHz; $CDCl_3$) 1.22 (3 H, t, *J* 7.5, CH_3), 1.90 (1 H, dq, *J* 14 and 6, 3-Heq), 2.50 (1 H, dddd, *J* 3, 7, 10 and 14, 3-Hax), 2.75–3.05 (2 H, m, 4-H), 4.10 (2 H, q, *J* 7.5, CH_2CH_3), 4.30 (1 H, m, 2-H), 4.95 (1 H, br, NH), 5.06 (1 H, d, *J* 4, 1-H) and 7.1–7.45 (4 H, m, aromatic); δ_C(68 MHz; $CDCl_3$) 14.54, 23.08, 24.4, 52.04, 58.51, 61.09, 126.76, 128.62, 129.11, 131.22, 133.71, 135.07 and 155.89.

Fractional crystallisation of mother liquors afforded the pure *cis*-isomer **6**, m.p. 139–141 °C (from ethanol–ether) (Found: C, 61.5; H, 6.4; Cl, 14.0; N, 5.6. $C_{13}H_{16}ClNO_2$ requires C, 61.5; H, 6.4; Cl, 14.0; N, 5.5 %); ν_{max}(KBr)/cm^{-1} 3300 (NH) and 1693 (C=O); δ_H(270 MHz; $CDCl_3$) 1.28 (3 H, t, *J* 8, CH_3), 1.95 (1 H, dq, *J* 13 and 4, 3-Heq), 2.17 (1 H, tt, *J* 9 and 13, 3-Hax), 3.0 (2 H, m, 4-H), 4.15 (2 H, q, *J* 8, CH_2CH_3), 4.24 (1 H, m, 2-H), 5.19 (1 H, br d, NH), 5.35 (1 H, d, *J* 3, 1-H) and 7.1–7.35 (4 H, m, aromatic); δ_C(68 MHz; $CDCl_3$) 14.62, 24.00, 28.43, 50.52, 61.10, 63.09, 126.46, 129.00, 129.05, 130.64, 134.97, 135.05 and 155.77.

1,2-(N-*Ethoxycarbonylimino*)-1,2,3,4-*tetrahydronaphthalene* **7**.—To a suspension of sodium hydride (0.10 g, 4.30 mmol) in dry *N,N*-dimethylformamide (DMF) (20 cm^3) cooled under nitrogen in an ice–salt bath was added dropwise a solution of compound **5** (1.0 g, 3.9 mmol) in the same dry solvent (15 cm^3). After stirring below 0 °C for 1 h the mixture was allowed to warm to room temp. over 2 h. The reaction was poured onto ice and extracted into ether. The organic extracts were washed exhaustively with water, dried and concentrated. Extraction of the residue into cold pentane afforded the unstable imine **7** as a colourless oil (0.71 g, 84%); ν_{max}(film)/cm^{-1} 1720 (C=O); δ_H(270 MHz; $CDCl_3$) 1.27 (3 H, t, *J* 7, CH_3), 1.63 (1 H, m, 3-H), 2.42 (1 H, m, 3-H), 2.57 (1 H, br dd, *J* 16 and 6, 4-H), 2.80 (1 H, ddd, *J* 16, 14 and 5, 4-H), 3.22 (1 H, br d, *J* 6, 2-H), 3.46 (1 H, d, *J* 6, 1-H), 4.16 (2 H, q, *J* 7, OCH_2) and 7.0–7.45 (4 H, m, aromatic); *m/z* 217 (M^+; 30%), 188 (10), 172 (8), 160 (42), 144 (55), 134 (52), 128 (100), 117 (70) and 91 (40) (Found: M^+, 217.1094. $C_{13}H_{15}NO_2$ requires *M*, 217.1086).

cis-2-*Ethoxy*-3a,8b-*dihydro*-4H-*indeno*[2,1-d]*oxazole* **11**.—A solution of *trans*-1-chloro-2-ethoxycarbonylaminoindane **4** (4.0 g, 0.017 mol) in ethanol (125 cm^3) was treated with potassium carbonate (2.4 g, 0.018 mol) and diluted with water (50 cm^3). After stirring at room temp. for 20 h the reaction was concentrated under high vacuum and diluted with water and extracted into ether. The extracts were washed with brine, dried and evaporated to give oxazoline **11** (3.3 g, 97%), m.p. 53–54 °C (from pentane–ether) (Found: C, 70.7; H, 6.4; N, 6.8. $C_{12}H_{13}NO_2$ requires C, 70.9; H, 6.45; N, 6.9%); ν_{max}(Nujol)/cm^{-1} 1665 (C=N); δ_H(270 MHz: $CDCl_3$) 1.30 (3 H, t, *J* 7, CH_3), 3.14 (1 H, dd, *J* 17 and 2, 3-H), 3.37 (1 H, dd, *J* 17 and 7, 3-H), 4.20 (1 H, dq, *J* 12 and 7, $OCHCH_3$), 4.22 (1 H, dq, *J* 12 and 7, $OCHCH_3$), 4.88 (1 H, dt, *J* 7 and 2, 2-H), 5.93 (1 H, d, *J* 7, 1-H) and 7.2–7.5 (4 H, m, aromatic); δ_C(20 MHz; $CDCl_3$) 14.21, 40.03, 66.50, 66.81, 87.06, 125.57, 126.37, 127.23, 129.82, 139.10, 142.42 and 162.03.

cis-2-*Ethoxy*-3a,4,5,9b-*tetrahydronaphth*[2,1-d]*oxazole* **12**.—A solution of *trans*-1-chloro-2-ethoxycarbonylamino-1,2,3,4-tetrahydronaphthalene **5** (1.0 g, 4.0 mmol) in ethanol (100 cm^3) was treated dropwise with a solution of potassium hydrogen carbonate (0.44 g, 4.4 mmol in 30 cm^3 water) over a period of 3 h. After stirring for a further 30 min the reaction mixture was concentrated under high vacuum, diluted with water, then extracted into ether. The extracts were washed with brine, dried and concentrated to give an oil (0.87 g). Flash chromatography on silica gel using light petroleum–ethyl acetate (6:1) as eluent followed by bulb-to-bulb distillation (180 °C/0.4 mmHg) afforded pure compound **12** (0.69 g, 79%) (Found: C, 71.5; H, 7.0; N 6.4. $C_{13}H_{15}NO_2$ requires C, 71.9; H, 7.0; N, 6.45%) ν_{max}(film)/cm^{-1} 1660 (C=N); δ_H(270 MHz; $CDCl_3$) 1.33 (3 H, t, *J* 7, CH_3), 1.95 (2 H, m, 3-H), 2.55 (1 H, ddd, *J* 15.5, 5 and 5, 4-Heq), 2.84 (1 H, ddd, *J* 15.5, 7 and 7, 4-Hax), 4.26 (2 H, q, *J* 7, OCH_2), 4.47 (1 H, m, 2-H), 5.60 (1 H, d, *J* 1-H) and 7.05–7.45 (4 H, m, aromatic); δ_C(68 MHz; $CDCl_3$) 14.30, 25.50, 28.93, 61.86, 66.53, 79.46, 126.66, 128.37, 128.60, 130.44, 132.20, 139.60 and 162.71; *m/z* 217 (M^+; 18%), 189 (14), 118 (13), 146 (30), 145 (30), 144 (72), 143 (13), 130 (37), 129 (48), 128 (100), 127 (15), 120 (12), 119 (20), 118 (14), 117 (76), 116 (32), 115 (51) and 91 (31).

Ring Opening of Oxazolines with HCl.—(a) *Reaction of compound* **11** *with HCl*. Oxazoline **11** (0.2 g, 1.0 mmol) was dissolved in saturated ethereal HCl. After 15 min the reaction mixture was cooled in ice and treated with saturated sodium hydrogen carbonate solution. The aqueous phase was back-extracted into ether and the combined organic layers washed with brine, dried and concentrated to give a product identical to authentic *trans*-1-chloro-2-ethoxycarbonylaminoindane **4**, δ_H(60 MHz; $CDCl_3$) 1.22 (3 H, t, *J* 7, CH_3), 2.78 (1 H, dd, *J* 16 and 5, 3-H), 3.46 (1 H, dd, *J* 16 and 7, 3-H), 4.09 (2 H, q, *J* 7, OCH_2), 4.2–4.6 (1 H, m, 2-H), 4.95 (1 H, br s, NH), 5.13 (1 H, d, *J* 5, 1-H) and 7.15 (4 H, m, aromatic).

(b) *Reaction of compound* **12** *with HCl*. Oxazoline **12** (0.2 g, 0.9 mmol) was dissolved in saturated ethereal HCl. After 30 min evaporation of volatiles afforded a product identical to authentic *trans*-1-chloro-2-ethoxycarbonylamino-1,2,3,4-tetrahydronaphthalene **5**.

trans-2-*Ethoxycarbonylamino*-1-(2-*methoxycarbonylanilino*)-*indane* **8a**.—*Method A. Alkylation of adduct* **4**. *trans*-1-Chloro-2-ethoxycarbonylaminoindane **4** (80 g, 0.33 mol) was treated with methyl anthranilate (290 g, 1.92 mol) and stirred under nitrogen at 65–70 °C for 5 h. The resulting viscous mixture was diluted with toluene and washed exhaustively with hydrochloric acid (5 mol dm^{-3}). Further washing with water and brine followed by evaporation of solvent afforded a crude product (103 g) consisting of the *trans*-product **8a** together with 8% of the *cis*-isomer as judged by ^1H NMR spectroscopy. Crystallisation from light petroleum–ethyl acetate afforded pure *trans*-isomer **8a** (70.6 g, 60%), m.p. 110–111 °C (Found: C, 67.9; H, 6.15; N, 7.9. $C_{20}H_{22}N_2O_4$ requires C, 67.8; H, 6.3; N, 7.9%); ν_{max}(KBr)/cm^{-1} 3330 (NH) and 1695 (br, C=O); δ_H(270 MHz; $CDCl_3$) 1.22 (3 H, t, *J* 7, CH_3), 2.80 (1 H, dd, *J* 16 and 6, 3-H), 3.44 (1 H, dd, *J* 16 and 7, 3-H), 3.80 (3 H, s, CH_3), 4.10 (2 H, q, *J* 7, OCH_2), 4.35 (1 H, m, 2-H), 4.80 [2 H (overlapping signals) d, *J* 5, 1-H; NH exchanges with D_2O], 6.65 (1 H, m, aromatic), 7.1–7.5 (6 H, m, aromatic) and 7.93 (2 H, m, overlapping aromatic and NH); δ_C(100 MHz; $CDCl_3$) 14.56, 37.33, 51.47, 58.30, 60.88, 63.15, 110.36, 112.16, 115.27, 125.02, 125.21, 127.45, 128.57, 131.66, 134.77, 141.55, 150.61, 156.23 and 168.88; *m/z* 354 (M^+,

5%), 266 (20), 265 (100), 250 (5), 234 (10), 233 (38), 232 (12), 205 (8), 204 (8) and 130 (30). Mother liquors afforded a second crop containing the *cis*-product. Recrystallisation from light petroleum–ether produced pure *cis*-isomer (1.5 g), m.p. 123–124 °C (Found: C, 67.6; H, 6.3; N 7.85. $C_{20}H_{22}N_2O_4$ requires C, 67.8; H, 6.3; N, 7.9%); ν_{max}(KBr)/cm^{-1} 3330 (NH), 1695 (br, C=O); δ_H(270 MHz; $CDCl_3$) 1.12 (3 H, t, *J* 7, CH_3), 3.04 (1 H, dd, *J* 16 and 4, 3-H), 3.29 (1 H, dd, *J* 16 and 6, 3-H), 3.84 (3 H, s, CH_3), 4.02 (1 H, q, *J* 7, OCH_2), 4.78 (1 H, br m, 2-H), 5.04 (1 H, br s, NH), 5.10 (1 H, dd, *J* 6 and 6, 1-H, collapses to a doublet with D_2O), 6.68 (1 H, m, aromatic), 6.95 (1 H, m, aromatic), 7.28 (3 H, m, aromatic), 7.40 (2 H, m, aromatic), 7.94 (1 H, m, aromatic) and 8.1 (1 H, d, *J* 6, NH exchanges with D_2O); δ_C(68 MHz; $CDCl_3$) 14.52, 38.11, 51.61, 54.61, 59.66, 60.76, 110.78, 112.43, 115.82, 124.50, 125.24, 127.49, 128.60, 131.64, 134.77, 140.17, 141.35, 150.71, 150.81; 156.43 and 169.07; *m/z* 354 (M^+, 8%), 265 (100), 250 (5), 233 (32) and 130 (30).

Method B. Alkylation of oxazoline **11**. A solution of the oxazoline **11** (0.81 g; 4.0 mmol) in dry toluene (3 cm^3) was treated with methyl anthranilate (0.66 g; 4.4 mmol) and toluene-*p*-sulfonic acid (10 mg, 0.05 mmol) and stirred at room temp. for 5 h. The reaction was diluted with ether and washed with dilute hydrochloric acid (2.5 mol dm^{-3}) and brine. After drying and evaporation of solvent, purification by chromatography on silica gel using light petroleum–ethyl acetate (9:1) as eluent afforded **8a** (1.0 g, 72%) identical by NMR spectroscopy to the product obtained by Method A.

trans-2-*Ethoxycarbonylamino*-1-(2-*methoxycarbonylanilino*)-1,2,3,4-*tetrahydronaphthalene* **9a**.—*Method A—Alkylation of adduct* **5**. A mixture of *trans*-1-chloro-2-ethoxycarbonylamino-1,2,3,4-tetrahydronaphthalene **5** (19.0 g, 0.075 mol) and methyl anthranilate (60 cm^3) was heated under nitrogen at 60 °C for 5 h. The reaction was diluted with ether and washed exhaustively with 2.5 mol dm^{-3} hydrochloric acid, followed by saturated aqueous sodium hydrogen carbonate and brine. After drying and evaporation of solvent, trituration with ether–light petroleum yielded **9a** (17.4 g, 63%), m.p. 116–118 °C (from ethyl acetate–light petroleum) (Found: C, 68.1; H, 6.7; N, 7.8. $C_{21}H_{24}N_2O_4$ requires C, 68.5; H, 6.6, N, 7.6%); ν_{max}(KBr)/cm^{-1} 3340 (NH), 1710 (C=O) and 1695 (C=O); δ_H(270 MHz; $CDCl_3$) 1.22 (3 H, t, *J* 7, CH_3), 1.92 (1 H, m, 3-H), 2.26 (1 H, m, 3-H), 2.88 (2 H, m, 4-H), 3.78 (3 H, s, OCH_3), 4.05–4.25 (3 H, m, overlapping 2-H and OCH_2), 4.64 (1 H, br s, sharpens to a doublet *J* 5 with D_2O), 4.7 (1 H, d, *J* 9, carbamate NH), 6.63 (1 H, m, aromatic), 7.1–7.35 (5 H, m, aromatic) and 7.9 (2 H, m, aromatic and NH); δ_C(68 MHz; $CDCl_3$) 14.58, 22.78, 24.10, 47.94, 51.46, 54.35, 60.89, 110.00, 111.96, 115.18, 126.82, 127.92, 129.12, 131.14, 131.69, 134.47, 135.11, 135.37, 149.90, 156.37 and 169.02; *m/z* 368 (M^+, 8%), 279 (100), 238 (43), 220 (42), 194 (55), 165 (18), 144 (30), 128 (65) and 117 (52).

Method B. Alkylation of oxazoline **12**. A solution of the oxazoline **12** (0.24 g, 1.1 mmol) in dry toluene (5 cm^3) was treated with methyl anthranilate (0.18 g, 1.2 mmol) and toluene-*p*-sulfonic acid (21 mg, 0.11 mmol) and stirred at room temp. for 4 h. The reaction was diluted with ether, washed with dilute hydrochloric acid (2.5 mol dm^{-3}) followed by saturated aqueous sodium hydrogen carbonate and brine, then dried and concentrated. Trituration with pentane yielded **9a** (0.33 g, 83%), m.p. 114–117 °C (from pentane–ether), identical by NMR spectroscopy to the product obtained by Method A.

trans-2-*Ethoxycarbonylamino*-1-(2-*hydroxymethylanilino*)-*indane* **8b**.—A solution of the adduct **4** (1.2 g, 5.0 mmol) and *o*-aminobenzyl alcohol (0.62 g, 5.0 mmol) in dry DMF (10 cm^3) containing finely ground barium carbonate (0.49 g, 2.5 mmol) was heated at 85 °C under nitrogen for 10 h. After dilution with water the reaction was extracted into ether. Concentration of the dried extracts followed by purification on silica gel using cyclohexane–ethyl acetate as eluent afforded **8b** (0.75 g, 51%), m.p. 119–120 °C (from light petroleum–ether) (Found: C, 69.8; H, 7.0; N, 8.6. $C_{19}H_{22}N_2O_3$ requires C, 69.9; H, 6.8; N, 8.6%); ν_{max}(KBr)/cm^{-1} 3380 (NH, OH) and 1695 (C=O), δ_H(80 MHz; $CDCl_3$), 1.17 (3 H, t, *J* 7, CH_3), 2.80 (1 H, dd, *J* 16 and 7, 3-H), 3.35 (1 H, dd, *J* 8 and 16, 3-H), 4.03 (2 H, q, *J* 7, OCH_2), 4.4 (1 H, m, 2-H), 4.65 (2 H, s, CH_2OH), 4.84 (1 H, d, *J* 6, 1-H), 4.95 (1 H, br, NH, exchanges slowly with D_2O) and 6.5–7.5 (8 H, m, aromatic); δ_C(20 MHz; $CDCl_3$) 14.33, 36.61, 59.09, 60.92, 63.85, 64.33, 111.45, 116.88, 124.44, 124.82, 127.12, 128.05, 129.21, 139.53, 142.38, 147.00 and 156.67; *m/z* 326 (M^+, 15%), 280 (8), 237 (100), 218 (35), 132 (23), 130 (22) and 117 (45).

trans-2-*Ethoxycarbonylamino*-1-(2-*hydroxymethylanilino*)-1,2,3,4-*tetrahydronaphthalene* **9b**.—A solution of *trans*-1-chloro-2-ethoxycarbonylamino-1,2,3,4-tetrahydronaphthalene **5** (12.80 g, 0.05 mol) and *o*-aminobenzyl alcohol (6.20 g, 0.05 mol) in dry DMF (50 cm^3) was treated with finely ground barium carbonate (5.40 g, 0.028 mol) and stirred under nitrogen at 85 °C for 10 h. The reaction mixture was diluted with water and extracted into ether. The extract was washed with water, dried and concentrated to a brown foam (15.6 g). Chromatography on silica gel using light petroleum–ethyl acetate (75:25) as eluent afforded **9b** (7.5 g, 43%), m.p. 134–135 °C (from pentane–ether) (Found: C, 70.6, H, 7.2, N, 8.2. $C_{20}H_{24}N_2O_3$ requires C, 70.6, H, 7.1, N, 8.2%); ν_{max}(KBr)/cm^{-1} 3380 and 3340 (NH and OH) and 1685 (C=O); δ_H(80 MHz; $CDCl_3$) 1.18 (3 H, t, *J* 7, CH_3), 1.5–2.5 (3 H, m, overlapping signals, 3-H and OH exchanges with D_2O), 2.9 (2 H, m, 4-H), 4.05 (2 H, q, *J* 7, OCH_2), 4.15 (1 H, m, 2-H), 4.58 (2 H, s, CH_2OH), 4.75 (1 H, d, *J* 9, 1-H overlapping with carbamate NH which exchanges with D_2O) and 6.5–7.5 (7 H, m, aromatic); δ_C(20 MHz; $CDCl_3$) 14.38, 24.72, 25.33, 49.53, 56.11, 60.86, 64.19, 110.83, 116.51, 124.06, 126.50, 127.48, 128.70, 129.24, 129.53, 129.94, 135.58, 135.79, 146.58 and 156.53; *m/z* 340 (M^+, 16%), 322 (8), 251 (100), 232 (12), 194 (35), 146 (20), 128 (55), 120 (28) and 91 (25).

Selective Reduction of **8a**.—A solution of **8a** (1.0 g, 2.88 mmol) in dry tetrahydrofuran (THF) (6 cm^3) was cooled below −10 °C under nitrogen and treated dropwise with lithium triethylborohydride (10 cm^3 of a 1 mol dm^{-3} solution in THF). Stirring was continued overnight at room temp. The reaction mixture was then cooled below 0 °C and treated with water (1 cm^3) followed by 5 mol dm^{-3} hydrochloric acid (25 cm^3). After stirring for 0.5 h the mixture was diluted with pentane. The aqueous layer was washed with ether, basified with 40% sodium hydroxide and extracted into ether. The organic layers were washed with brine and dried. Evaporation of solvent afforded *trans*-2-ethoxycarbonylamino-1-(2-hydroxymethylanilino)indane **8b** (0.75 g, 81%), m.p. 115–117 °C (from ether–pentane). Reduction of **9a** under similar conditions afforded **9b**.

trans-1-(2-*Hydroxymethylanilino*)-2-*methylaminoindane* **15**.—A solution of **8a** (17.3 g, 0.049 mol) in dry ether (360 cm^3) was added dropwise to a suspension of lithium aluminium hydride (9.0 g, 0.24 mol) in dry ether (280 cm^3) under nitrogen over 1.5 h. After stirring overnight at room temp., standard work-up followed by crystallisation from ethyl acetate–light petroleum afforded the amino alcohol **15** (11.7 g, 89%), m.p. 113–114 °C (Found: C, 75.8; H, 7.5; N, 10.3. $C_{17}H_{20}N_2O$ requires C, 76.1; H, 7.5; N, 10.4%); ν_{max}(Nujol)/cm^{-1} 3380 and 3290 (OH, NH); δ_H(270 MHz; $CDCl_3$) 2.38 (2 H, br s, NH and OH—exchanges with D_2O), 2.47 (3 H, s, CH_3), 2.72 (1 H, dd, *J* 15 and 8, 3-H), 3.21 (1 H, dd, *J* 15 and 7, 3-H), 3.35 (1 H, q, *J* 7, 2-H), 4.63 (2 H, s, OCH_2), 4.83 (1 H, dd, *J* 7 and 7, 1-H, collapses to a doublet with D_2O), 5.08 (1 H, d, *J* 7, NH exchanges with D_2O), 6.68 (1 H, m, aromatic), 6.91 (1 H, m, aromatic), 7.07 (1 H, m, aromatic) and

7.1–7.2 (5 H, m, aromatic); δ_C(68 MHz; $CDCl_3$) 35.31, 36.89, 64.24, 64.99, 69.75, 111.96, 117.32, 124.68, 125.22, 125.54, 127.43, 128.37, 129.83, 130.16, 140.81, 144.01 and 147.99; *m/z* 268 (M^+, 25%), 238 (12), 237 (14), 236 (12), 225 (15), 194 (18), 146 (100) and 144 (47). Reduction of **8b** under similar conditions also afforded **15**.

trans-1-(2-*Hydroxymethylanilino*)-2-*methylamino*-1,2,3,4-*tetrahydronaphthalene* **16**.—A suspension of the ester **9a** (17.4 g, 0.047 mol) in dry ether (400 cm^3) was added to lithium aluminium hydride (10.0 g, 0.26 mol) in dry ether (400 cm^3) under nitrogen over 1.5 h. Overnight stirring at room temp. followed by standard work up and crystallisation from ethyl acetate afforded **16** (11.4 g, 85%), m.p. 123–124 °C (Found: 76.6; H, 7.8; N, 9.95. $C_{18}H_{22}N_2O$ requires C; 76.6; H, 7.85; N, 9.9%); ν_{max}(Nujol)/cm^{-1} 3335 and 3050 (NH, OH); δ_H(270 MHz; $CDCl_3$) 1.75 (1 H, m, 3-H), 2.10 (1 H, m, 3-H), 2.45 (3 H, s, CH_3), 2.48 (2 H, br s, OH and NH exchanges with D_2O), 2.90 (3 H, m, 2-H and 4-H), 4.50 (1 H, t, *J* 8, 1-H, collapses to a doublet with D_2O), 4.64 (2 H, ABq, *J* 12, OCH_2), 4.90 (1 H, d, *J* 8, NH exchanges with D_2O), 6.67 (1 H, t, *J* 8, aromatic), 6.82 (1 H, d, *J* 8, aromatic), 7.15 (5-H, m, aromatic) and 7.35 (1 H, m, aromatic); *m/z* 282 (M^+, 20%), 225 (8), 206 (16), 194 (23) and 159 (100). Reduction of **9b** under similar conditions also afforded **16**.

trans-2,3,4,4a,9,9a-*Hexahydro*-4-[2-(*hydroxymethyl*)*phenyl*]-1-*methyl*-1H-*indeno*[1,2-b]*pyrazine* **17**.—A solution of the *trans*-diamine **15** (11.6 g, 0.043 mol) in 1,2-dibromoethane (70 cm^3) containing triethylamine (25 cm^3) was added dropwise to stirring 1,2-dibromethane (130 cm^3) at 100 °C over 1.5 h. This was followed by dropwise addition of triethylamine (25 cm^3) over 30 min. The reaction was cooled to 50 °C then diluted with ether (800 cm^3) and stirred for 1 h. After filtration the solution was concentrated, and addition of ethyl acetate assisted crystallisation of the piperazine **17** (6.9 g, 54%), m.p. 166–167 °C (Found: C, 77.6; H, 7.6; N, 9.4. $C_{19}H_{22}N_2O$ requires C, 77.5; H, 7.5; N, 9.5%); ν_{max}(Nujol)/cm^{-1} 3160 (OH); δ_H(400 MHz; $CDCl_3$) 2.42 (3 H, s, CH_3), 2.47 (1 H, ddd, *J* 11.4, 11.4 and 3.7, 2-Hax), 2.53 (1 H, ddd, *J* 11.1, 9.1 and 6.3, 9a-H), 2.80 (1 H, dd, *J* 14.0 and 11.1, 9-Hax), 3.02 (1 H, ddd, *J* 11.4, 3.0 and 2.0, 2-Heq), 3.06 (1 H, dd, *J* 14.0 and 6.3, 9-Heq), 3.08 (1 H, ddd, *J* 11.8, 11.4 and 3.0, 3-Hax), 3.19 (1 H, ddd, *J* 11.8, 3.7 and 2.0, 3-Heq), 4.29 (1 H, d, *J* 9.1, 3-Heq), 4.64 (1 H, dd, *J* 13.3 and 5.4, CHO), 4.98 (1 H, d, 13.3, CHO), 5.26 (1 H, br s, OH), 6.15 (1 H, d, 9.2 aromatic), 6.87 (1 H, t, 9.1, aromatic) and 7.06–7.46 (6 H, m, aromatic); δ_C(100 MHz; $CDCl_3$) 34.23, 43.21, 57.08, 57.23, 64.73, 66.70, 74.34, 122.76, 123.56, 124.90, 126.29, 126.38, 127.05, 128.51, 128.60, 137.85, 139.64, 141.22 and 149.34; *m/z* 294 (M^+, 20%), 178 (12), 158 (10), 135 (62) and 116 (100).

trans-1,2,3,4,4a,5,6,10b-*Octahydro*-1-[2-(*hydroxymethyl*)-*phenyl*]-4-*methylbenzo*[f]*quinoxaline* **18**.—1,2-Dibromoethane (55 cm^3) was heated to 100 °C and treated with a solution of the *trans*-diamine **16** (4.0 g, 0.014 mol) in 1,2-dibromoethane (23 cm^3) containing triethylamine (8.2 cm^3) over 1.5 h. Further triethylamine (8.2 cm^3) was added over 0.5 h. After dilution with ether and filtration, the filtrate was evaporated to dryness and triturated with light petroleum–ether to give the title compound **18** (1.8 g, 41%), m.p. 153–155 °C (from ethyl acetate) (Found: C, 77.8; H, 7.9; N, 9.3. $C_{20}H_{24}N_2O$ requires C, 77.9; H, 7.8; N, 9.1%); ν_{max}(Nujol)/cm^{-1} 3100 (OH); δ_H(270 MHz; $CDCl_3$) 1.8–2.3 (3 H, m), 2.38 (3 H, s, NCH_3), 2.55 (1 H, m), 2.75–3.25 (4 H, m), 3.42 (1 H, m), 4.36 (1 H, d, *J* 9), 4.85 (1 H, d, *J* 13), 5.14 (1 H, d, *J* 13), 6.85–7.15 (7 H, m, aromatic) and 7.25 (1 H, m, aromatic); δ_C(68 MHz; $CDCl_3$) 27.14, 43.07, 55.08, 55.35, 61.25, 64.38, 65.06, 121.64, 124.46, 125.76, 126.14, 126.55, 126.96, 127.95, 128.99, 134.52, 136.87 and 137.78; *m/z* 308 (M^+, 28%), 178 (12), 172 (15), 136 (23), 135 (45) and 130 (100).

trans-4a,5,6,7,12,12c-*Hexahydro*-5-*methyl*-4H-5,7a-*diazabenzo*[5,6]*cyclohepta*[1,2,3,4-def]*fluorene* **2**.—To orthophosphoric acid (7 cm^3 of an 88% solution) stirring at 90 °C was added alcohol **17** (6.8 g, 0.023 mol). After 1 h the reaction was poured into an ice–chloroform mixture and the pH was adjusted to 8 by addition of 40% aqueous sodium hydroxide while maintaining the temperature below 45 °C. The chloroform layer was separated and the aqueous phase was extracted twice more with chloroform. The combined extracts were washed with water, dried and concentrated. Flash chromatography on silica gel using light petroleum–acetone (7:3) as eluent followed by crystallisation from ethyl acetate–pentane afforded the title compound **2** (5.6 g, 88%), m.p. 151–2 °C (Found: C, 82.4, H, 7.3; N, 10.3. $C_{19}H_{20}N_2$ requires C, 82.6; H, 7.3; N, 10.1%); δ_C(68 MHz; $CDCl_3$) 33.3, 38.3, 43.7, 50.1, 54.2, 68.6, 71.9, 118.1, 120.3, 122.9, 124.4, 127.2, 127.4, 129.2, 135.5, 136.4, 139.0, 139.2 and 146.5; *m/z* 276 (M^+, 100%), 261 (30), 247 (10), 232 (75), 219 (30), 218 (30), 204 (15) and 118 (25).

trans-1,2,3,3a,4,5,9,14a-*Octahydro*-3-*methyldibenzo*[b,e,f]-*pyrazino*[3,2,1-jk][1]*benzazepine* **3**.—To 88% orthophosphoric acid (46 cm^3) heated at 90–100 °C was added alcohol **18**. The mixture was stirred for 3 h at this temperature and then poured onto ice. After adjusting the pH to 7 with 40% aqueous sodium hydroxide the product was extracted into chloroform and the dried extract was concentrated. Chromatography on silica gel using 30% acetone in light petroleum as eluent followed by recrystallisation from ethyl acetate yielded target structure **3** (1.45 g, 33%), m.p. 128–129 °C (Found: C, 70.5; H, 6.5; N, 6.7. $C_{20}H_{22}N_2$ requires C, 70.9; H, 6.45; N, 6.9%). δ_C(68 MHz) 26.60, 27.41, 38.85, 43.35, 50.95, 55.54, 64.48, 119.40, 123.22, 125.33, 126.29, 126.55, 126.62, 127.19, 136.00, 136.95, 139.29, 139.36 and 150.09; *m/z* 290 (M^+, 80%), 275 (19), 246 (79) and 234 (100) (Found: M^+ 290.1778, $C_{20}H_{22}N_2$ requires *M* 290.1783).

Crystal Data for Compound **2**.—$C_{19}H_{20}N_2$, *M* = 276.37. Triclinic, *a* = 10.348(1), *b* = 10.542(1), *c* = 13.710(1) Å, α = 100.43(1), β = 93.93(1), γ = 96.45(1)°; *v* = 1455.5 $Å^3$ (determined and refined from the setting angles of 23 reflections), space group $P\bar{1}$, *z* = 4 (cell volume suggested two independent molecules in the assymmetric unit), ρ = 1.26 g cm^{-3}.

Data collection and processing. Y-290 four-circle diffractometer, molybdenum radiation (graphite monochromator); data collected for reflections with $\theta \leqslant 25°$ and of the 5138 measured 3228 had $I \geqslant 3\sigma(I)$ and were used in the refinement.

Structure analysis and refinement. Structure was solved using the centro-symmetric direct method routine of SHELX; all non-hydrogen atoms being revealed at the first attempt. Parameters for each molecule were refined in a separate least squares block. After convergence with anisotropic thermal parameters for C and N a difference map showed the position of all hydrogen atoms. Further refinement with the hydrogen atoms included in calculated position (but not refined) resulted in a final *R* value of 6.8%. The two independent molecules appear to have the same geometry *i.e.* the deviation of any individual dimension from the mean with its pair is not appreciably larger than 5* standard deviation. Tables of fractional coordinates, bond lengths and angles and thermal parameters for compound **2** have been deposited with the Cambridge Crystallographic Database.†

Acknowledgements

The authors wish to thank Dr. J. Everett for helpful discussions on the NMR work. The X-ray structure determination was

† For full details of the deposition scheme see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1993, issue 1.

carried out by the late Professor T. J. King (Nottingham), and the authors thank Dr. M. J. Begley for his assistance in preparing the data for publication.

References

1 R. N. Brogden, R. C. Heel, T. M. Speight and G. S. Avery, *Drugs*, 1978, **16**, 273.
2 For a preliminary account of this work see B. S. Orlek, *Tetrahedron Lett.*, 1986, 1699. References to other methods for preparing vicinal diamines are cited therein.
3 B. J. Walker and P. J. Wrobel, *J. Chem. Soc., Chem. Commun.*, 1980, 462.
4 A. Hassner and C. Heathcock, *J. Org. Chem.*, 1964, **29**, 3640.
5 C. F. Huebner, E. M. Donoghue, C. J. Novak, L. Dorfman and E. Wenkert, *J. Org. Chem.*, 1970, **35**, 1149.
6 (*a*) J. Sicher, M. Tichy, F. Sipos and M. Pankova, *Collect. Czech. Chem. Commun.*, 1961, **26**, 2418; (*b*) S. Winstein and R. Boschan, *J. Am. Chem. Soc.*, 1950, **72**, 4669; (*c*) H. W. Heine, *J. Am. Chem. Soc.*, 1957, **79**, 908.
7 (*a*) W. Seeliger, E. Aufderhaar, W. Diepers, R. Feinauer, R. Nehring, W. Thier and H. Hellman, *Angew. Chem., Int. Ed. Engl.*, 1966, **5**, 875 and references therein; (*b*) M. J. Fazio, *J. Org. Chem.*, 1984, **49**, 4889.
8 C. W. Funke, *Recl. Trav. Chim. Pays-Bas*, 1982, **101**, 437.
9 F. Sternhell, *Rev. Pure and Appl. Chem.*, 1964, **14**, 15.

Paper 3/00733B
Received 5*th February* 1993
Accepted 25*th February* 1993