Role of Remote Heteroatoms and Nature of the Reducing Agents on the Stereochemical Course of Reductions of the Carbon–Nitrogen π-Bond of a New Class of Tetrahydropyridines

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Total syntheses of the tetrahydropyridine derivatives (**3a—f**) and the steroid analogue (**1b**) are reported. Catalytic reductions of the above imines have been found to be highly stereoselective, yielding only the *trans*-amine in most cases. Lithium aluminium hydride reductions of the above imines (**3a—e**), (**1b**), and (**3f—g**), however, showed *cis*-stereoselectivity; the imines (**3a—b**) and (**1b**) afforded only the *cis*-amines under these conditions. Sodium borohydride reductions of the imines (**3a—g**) gave conflicting results, the imines (**3a—b**) and (**3f—g**) furnishing stereoselectively the *trans*-amines. Metal–ammonia reductions of the imines (**3a—b**) and (**3f**), having a carbocyclic B ring, gave a stereoisomeric mixture of amines; similar reduction of the imines (**3c—d**) with an oxygen atom in ring B, provided, interestingly, the corresponding *trans*-amines as the predominant product (84—94%). Reasons for the different stereochemical results observed in the reductions of the imines (**3a—g**) with various reducing agents have been briefly discussed. The stereochemical assignments of the amines (**14**)—(**15**) and (**16**)—(**17**) were secured from their ^{1}H and ^{13}C n.m.r. spectra, and also from ^{1}H n.m.r. spectra of their *N*-acetyl derivatives.

Heterosteroids, and particularly those containing nitrogen, possess a wide range of physiological activity.[1] The equilenin-like 15-aza-steroid is reported[2] to have antibacterial activity. A unique group of 15-aza-D-homosteroids, possessing an α,β-unsaturated imine function and showing antibacterial and antifungal activity, have also recently been isolated,[3] and a partial synthesis[4] of a member of this class of steroidal imines has been disclosed by Barton and his associates.

The synthesis of the 15-aza-C-homoequilenin derivative (**1a**), as well as the unique pyrrole derivatives (**2**) has recently been reported[5] from our laboratory and reductions of these imines with metal hydrides or by a catalytic procedure was shown[5] to be stereospecific in the *trans*-sense.

We now report the complete synthesis and characterisation of the 15-aza-C,D-bishomoequilenin (steroid nomenclature) derivative (**1b**), as well as the unique tetrahydropyridine derivatives where the pyridine ring is fused to seven-membered heterocyclic and carbocyclic rings such as (**3a—e**). The main objective of this work was to investigate in detail the stereochemistry of reduction of the above imines (**1b**) and (**3a—e**) with various reducing agents. Such reductions of the related six-membered analogues (**3f—g**) were also undertaken to find out the conformational effects of the six- and seven-membered rings on the stereochemical outcome of the reductions of these imines.

Preparation of the Imines (**3a—g**) *and* (**1b**).—Preparation of the propionic acid derivatives (**4a**), (**4c—f**), and (**5**) has already been reported.[5] The unknown propionic acids (**4b**) and (**4g**) were available by the standard procedure,[5] starting from the known α-methyl ketones (**6a**)[6] and (**6b**)[7] (see Scheme 1). Homologation of the above propionic acids (**4a—g**) finally provided the required butyric acids (**8a—g**; R^1 = H) (see Scheme 2). All the diazo ketones (**7a—g**) were characterised on the basis of their i.r. spectra; the butyric esters (**8a—g**; R^1 = Me) showed expected spectral behaviour, and some were characterised through elemental analyses. All the butyric acids (**8a—g**; R^1 = H) were crystalline solids except (**8b**; R^1 = H) which was obtained as an oil and further characterised as its methyl ester (**8b**; R^1 = Me).

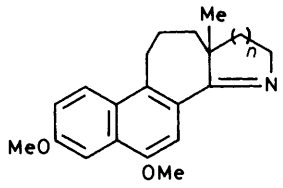
Synthesis of the imines (**3a—g**) (Scheme 2) in good yields (see Experimental section) involved a modified Curtius rearrangement[2,5,8] of the above oxo acids (**8a—g**; R^1 = H). Preparation of the tetracyclic imine (**1b**) involved homologation of the known[5] propionic acid (**5**) to the oxo acid (**11**) (Scheme 3), conversion of the latter into the azide (**12**), and then formation of the isocyanate (**13**) as shown in Scheme 3. To avoid demethylation, the isocyanate (**13**) was hydrolysed by base to furnish the desired steroidal imine (**1b**) in excellent overall yield.

Results and Discussion

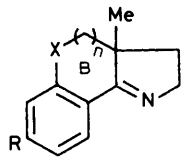
Chemical and Catalytic Reductions of the Imines (**3a—g**) *and* (**1b**).—The saturated amines, obtained through reduction of the above imines by various procedures, were characterised thoroughly by elemental analysis and ^{1}H and ^{13}C n.m.r. spectroscopy. The ratio (Table 1) of stereoisomeric amines was established by g.l.c.

Catalytic Reduction.—Catalytic reductions of the imines over Pd–C (10%) gave the corresponding *trans*-amines as the only product (see Table 1). Similar reduction of the tetracyclic imine (**1b**) afforded a non-homogeneous material. Reduction of (**1b**) in presence of PtO_2, however, provided again the corresponding *trans*-amine (**16**) as the only product. The above stereochemical course of catalytic reductions of the imines (**3a—g**) and (**1b**) clearly indicates that the α-face is sterically less hindered. Attempted catalytic reduction of the imine (**3e**) over Pd–C (10%) in methanol or in acetic acid gave back the imine (**3e**) probably due to poisoning of the catalyst.

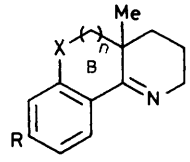
Reduction by metal hydrides. It has recently been demonstrated[9] that substantial stereochemical differences exist in the hydride reduction of cyclic ketones and carbon–nitrogen π-bonds. Reductions of the amines (**3a—g**) and (**1b**) with lithium aluminium hydride (LAH) in ether gave stereoselectively (Table



(1)
a; $n = 1$
b; $n = 2$



(2)
R = H or Me; X = CH_2, O or S
n = 1 or 2



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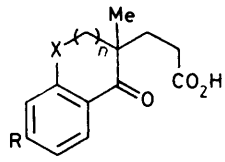
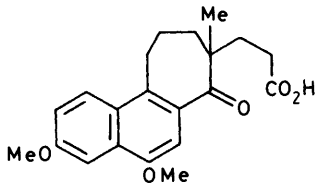
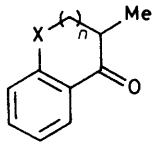


(4)

	R	X	n
a;	OMe	CH_2	2
b;	H	CH_2	2
c;	OMe	O	2
d;	H	O	2
e;	H	S	2
f;	OMe	CH_2	1
g;	H	S	1



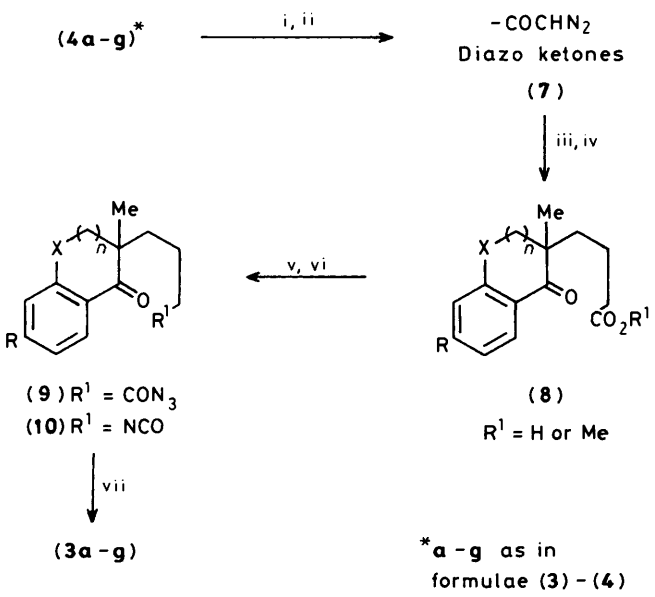
(5)



i, ii, iii → (4b) and (4g)

(6)
a; X = CH_2, n = 2
b; X = S, n = 1

Scheme 1. *Reagents:* i, CH_2=CHCN, OH^-; ii, OH^-; iii, H^+



Scheme 2. *Reagents:* i, $(COCl)_2$; ii, CH_2N_2; iii, $PhCO_2Ag$, MeOH; iv, OH^-, H^+; v, $ClCO_2Et$, NEt_3, NaN_3; vi, toluene/heat; vii, HCl, AcOH, reflux

1) the corresponding *cis*-amines (**15a**—**g**) and (**17**) respectively in excellent yields. This *cis*-stereoselectivity may be rationalised through the transition state (A) (Scheme 4) similar to carbon–oxygen π-bond reduction[10] with LAH. The carbon–nitrogen π-bond of the imines is expected to be polarised by lithium ion as shown by (B) in Scheme 4. The incipient positive charge, thus developed, is stabilised by resonance as depicted by (B) and (C) in Scheme 4. The α-face of the canonical form (C) is relatively more hindered (from stereomodels) because of its concave nature; and delivery of the hydride ion to the β-face may then account for the observed *cis*-stereoselectivity.*

Sodium borohydride ($NaBH_4$) reductions of the imines (**3a**—**g**) in methanol gave conflicting stereochemical results (Table 1). The *trans*-stereoselectivity in the reductions of the imines (**3a**—**b**) and (**3f**—**g**) may be explained by preferential attack of the hydride ion from the less hindered α-face as shown † in Scheme 5 (reactant-like transition state). It may be mentioned in this connection that the imine (**3a**) on reduction with $NaBH_4$ in isopropyl alcohol or with triacyloxy borohydride[11] gave again the *trans*-(**14a**) and the *cis*-amine (**15a**) in a ratio of *ca.* 85:15 and 95:5 respectively. Although practically no stereoselectivity was observed in the $NaBH_4$ reduction of the imines (**3c**—**d**) having an oxygen atom in the heterocyclic B-ring, it is significant that a similar reduction of the imine (**3e**), having a sulphur atom in ring B, showed *cis*-stereoselectivity (Table 1, entry 5). Although electronic interaction between the C=N group and the heteroatom (especially in the case of S) and other possible polar factors may affect the stereochemistry of reductions of C=N in (**3c**—**d**) and (**3e**), steric control on approach of the hydride ion to C=N seems to be of major importance. Introduction of a

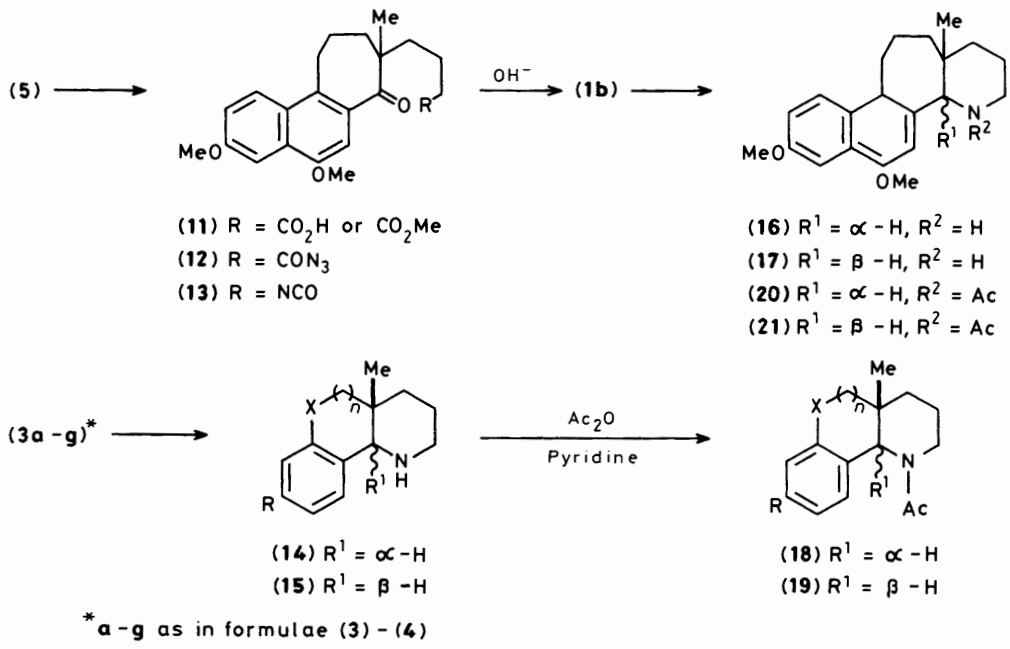
* The slightly diminished stereoselectivity for the LAH reductions of the imines (**3c**—**d**) may be due to some unspecified steric and electronic effects exerted by the oxygen atom in ring B.

† A linear acyclic transition state has been used by Wigfield[12] to suggest a new concept in the stereoselective reductions of cyclohexanones with $NaBH_4$.

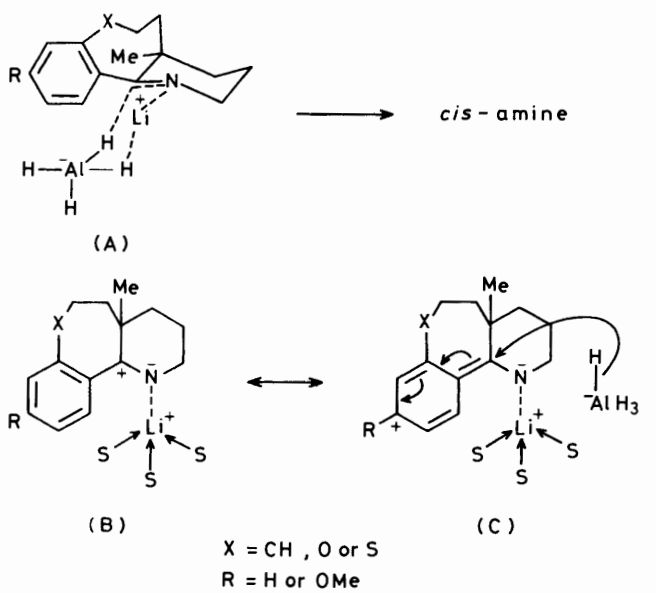
Table 1. Stereochemical results for reductions of the imines (**3a**—**g**) and (**1b**) with various reducing agents

		Ratio of the *trans*/*cis*-amine (**14**)/(**15**)				
Entry	Imine	Pd–C/H_2	LAH/Ether	$NaBH_4$/MeOH	$LiBH_4$/Diglyme	Na–NH_3 (**1**)
1	(**3a**)	89/11	0/100	92/8		56/44
2	(**3b**)	100/0	0/100	82/18	40/60	31/69
3	(**3c**)	100/0	19/81	59/41		94/6
4	(**3d**)	100/0	21/79	51/49	19/82	84/16
5	(**3e**)		10/90	20/80		
6	(**3f**)	97/3	3/97	90/10		55/45
7	(**3g**)		13/87	83/17	63/37	
8	(**1b**)	100/0[a]	0/100			

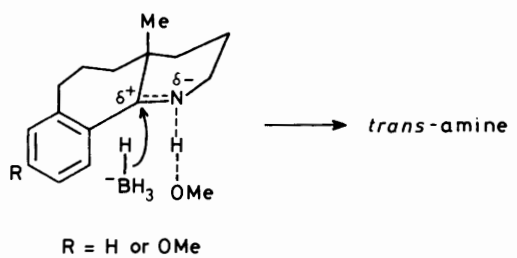
[a] Reduction by PtO_2 and H_2.



Scheme 3.



Scheme 4.



Scheme 5.

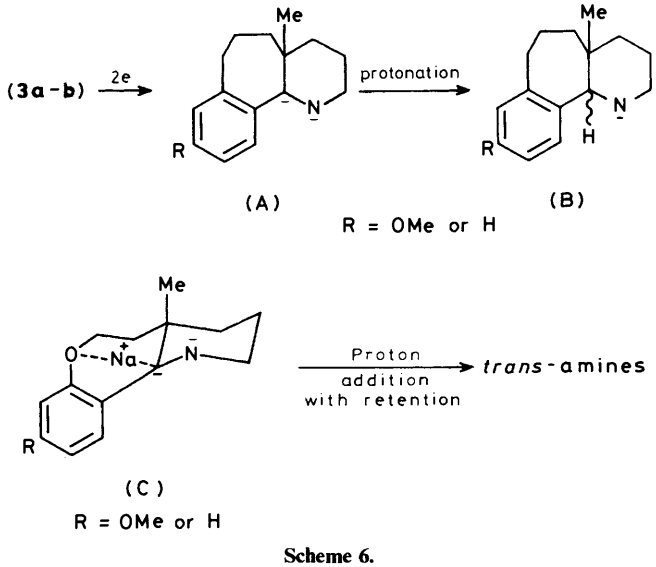
sulphur relative to an oxygen atom may deform[13] the seven-membered B-ring in (**3e**) due to variation of bond lengths and angles (C–S 1.82 Å and C–S–C angle of *ca.* 100°). This deformation may alter the ring geometry so as to bend the imine nitrogen down. This environmental change around C=N may now favour attack of the hydride ion from the β-face to give the *cis*-product (**15e**) as the major isomer. That the C=N of the imine (**3e**) is more out of the plane of the benzene ring than that of the oxa-imine (**3d**) is shown from their u.v. absorption maxima at $\lambda_{max.}$ 265 (ε 4 620) and 240 nm (ε 6 012) respectively. The imine (**3g**), having a sulphur atom in the six-membered B-ring showed practically the same stereoselectivity (entry 7,

Table 2. ^{1}H N.m.r. signals for the angular methyl group and the benzylic hydrogen atom at the ring-fusion of the *trans*- and the *cis*-amines

Amines	Stereochemistry	Angular methyl singlet (δ in p.p.m.)	Benzylic hydrogen singlet (δ in p.p.m.)
(14a)	*trans*	0.60	3.78
(15a)	*cis*	0.70	3.27
(14b)	*trans*	0.64	3.91
(15b)	*cis*	0.70	3.35
(14c)	*trans*	0.72	3.90
(15c)	*cis*	0.85	3.27
(14d)	*trans*	0.72	3.99
(15d)	*cis*	0.87	3.32
(14e)	*trans*	0.82	4.17
(15e)	*cis*	0.82	3.47
(14f)	*trans*	0.80	3.52
(15f)	*cis*	0.88	3.29
(14g)	*trans*	0.90	3.53
(15g)	*cis*	0.96	3.23
(16)	*trans*	0.70	4.18
(17)	*cis*	0.77	3.45

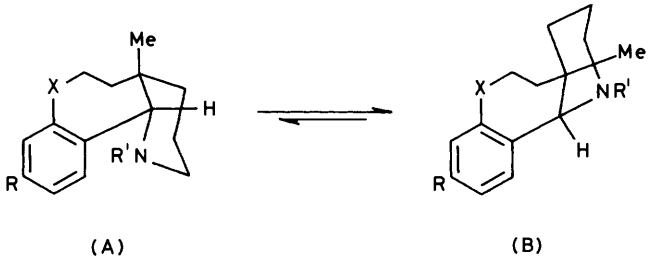
Table 1) as the carbocyclic analogue (**3f**) on reduction with $NaBH_4$. The imines (**3b**) and (**3d**) when reduced with $LiBH_4$ in diglyme furnished the corresponding *cis*-amines (**15b**) and (**15d**) as the major products in contrast to the *trans*-selectivity observed when $NaBH_4$ was used (entries 2 and 4, Table 1). This observation probably supports our earlier proposal (Scheme 4) that polarisation of the C=N by lithium ion favours *cis*-reduction.

Reduction by sodium metal in liquid ammonia. The stereochemical course of the reductions of the imines (**3a**—**d**) and (**3f**) with sodium in liquid ammonia using ammonium chloride as the proton source is informative, and the results are summarised in Table 1. Reduction of the imines (**3a**) and (**3f**), having a suitably placed aromatic methoxy group gave, in each case, a 44:56 mixture (entries 1 and 6 in Table 1) of the corresponding *cis*- and the *trans*-amine respectively. The related imine (**3b**), lacking the methoxy group, afforded the *cis*-amine (**15b**) as the major product (entry 2, Table 1). The geometry, stability and therefore the reactivity[14] of the benzylic carbanion (A)* (Scheme 6) seem to play a significant role on the stereochemical outcome of the reductions of the imines (**3a**—**b**) and (**3f**). Indiscriminate protonation of the resonance-destabilised and more reactive tetrahedral[15] carbanion like [(A; R = OMe) in Scheme 6], derived from (**3a**) and (**3f**), probably results in no stereoselectivity. Slower rate of protonation of the resonance-stabilised and therefore the less reactive trigonal[16] carbanion [(A; R = H) in Scheme 6] from the imine (**3b**) possibly accounts for the formation of one isomer (**15b**) in greater proportion. The heterocyclic imines (**3c**—**d**) on similar metal–ammonia reduction, interestingly, showed high *trans*-stereoselectivity (entries 3 and 4, Table 1). This stereochemical result must be linked with the presence of an oxygen atom† in ring-B of the imines (**3c**—**d**). An attractive explanation for the above *trans*-stereoselectivity may be that protonation of the intermediate benzylic carbanion proceeds with retention of configuration *via* a bridged transition state as shown by (C)‡ in Scheme 6.



Scheme 6.

Stereochemistry of the Amines.—The chemical shifts for the angular methyl groups and the benzylic hydrogen singlets in ^{1}H n.m.r. spectra for all the *trans*- and the *cis*-amines (in pairs) are tabulated in Table 2. A significant highfield signals (δ 3.23—3.47) for the benzylic hydrogen atoms of the *cis*-amines compared to those of the corresponding *trans*-isomers (δ 3.52—4.18) are informative, and this has been exploited for elucidation of the stereochemistry of the stereoisomeric amines. Further unambiguous support for the stereochemical assignments was available from the ^{1}H n.m.r. spectra (Tables 3 and 4) of the stereoisomeric acetyl derivatives (**18**)—(**19**) and (**20**)—(**21**) prepared from the amines. The angular methyl groups of the *trans*-acetyl derivatives (**18**) and the parent amines (**14**) showed signals more or less at the same field§ (see Tables 2 and 3). The related *cis*-acetyl derivatives (**19**), however, exhibited angular methyl singlets (Table 4) at significantly lower field (δ 1.09—1.33) compared to those of the corresponding *trans*-acetyl derivatives (δ 0.59—1.01); and this observation may be rationalised by considering two possible conformers (A) and (B) for the *cis*-acetyl compounds as shown in Scheme 7, and the conformer (B) probably contributes more to the equilibrium mixture (Scheme 7). Each *trans*-acetyl compound exhibited two sharp singlets of unequal intensity for each of the acetyl methyl



Scheme 7. Two conformers for the *cis*-acetyl compounds (**19a**—**e**)

* Dianion formation[17] can undoubtedly take place in the metal–ammonia reductions of diaryl ketones and, perhaps, with monoaryl ketones.

† The oxygen atom in ring-B in place of $-CH_2-$ is expected not to bring about any significant conformational change in ring-B or in any part of the molecule.

‡ This representation involving alkoxy oxygen atom, the benzylic carbanion, and the sodium cation is mainly supported from steric reasons. Cation-bridging between an alkoxide ion and carbanionic centre has been proposed[18] to explain high stereoselectivity in the metal–ammonia reduction of some α,β-unsaturated carbonyl compounds.

§ This is quite expected as the *trans*-amines and their acetyl derivatives have the same rigid conformation.

Table 3. ^{1}H N.m.r. signals (δ in p.p.m.) for the angular methyl, the acetyl methyl, the aromatic methoxy, and the benzylic hydrogen atom at the ring-fusion of the *trans*-acetyl derivatives (amides)

trans-Amides	Angular methyl singlet(s)	Acetyl methyl singlet(s)	Aromatic methoxy singlet(s)	Benzylic hydrogen singlet(s)
(18a)	0.60	2.16	3.73	5.40
	0.59	1.83	3.71	4.76
(18b)	0.62	2.18	—	5.54
	0.61	1.86		4.89
(18c)	0.78	2.18	3.78	5.54
		1.84		4.96
(18d)	0.76	2.20	—	5.67
		1.82		5.07
(18f)	1.01	2.17	3.80	4.63
	0.98	1.59	3.76	4.12
(20)	0.62	2.24	3.95	5.77
		1.88	3.94	5.12

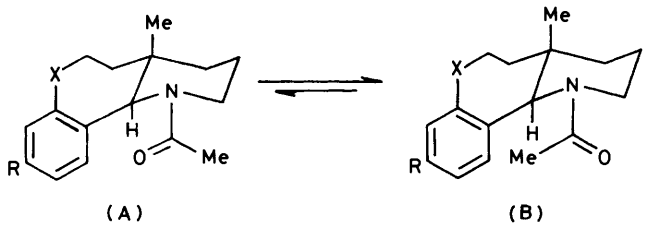
Table 4. ^{1}H N.m.r. signals (δ in p.p.m.) for the angular methyl, the acetyl methyl, the aromatic methoxy, and the benzylic hydrogen atom at the ring-fusion of the *cis*-acetyl derivatives (amides)

cis-Amides	Angular methyl singlet(s)	Acetyl methyl singlet(s)	Aromatic methoxy singlet(s)	Benzylic hydrogen singlet(s) (broad)
(19a)	1.12	2.18	3.82	4.85
		1.91		
(19b)	1.18	2.19		4.80
		1.91		
(19c)	1.22	1.97	3.76	4.98
(19d)	1.26	1.96		4.98
(19e)	1.33	2.24		5.53
		1.88		
(19f)	1.15	2.27	3.79	5.53
	1.09	2.21	3.78	4.52
(21)	1.24	2.17	3.96	4.98
		1.91	3.94	

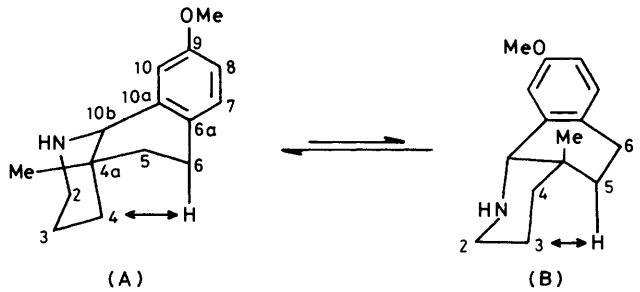
group and the benzylic hydrogen atom* at the ring fusion (Table 3). The multiple signals exhibited by the angular methyl, acetyl methyl, and the benzylic hydrogen atom of the stereoisomeric acetyl derivatives (Tables 3 and 4) may be rationalised by the restricted rotation[19] around the C–N amide bond at room temperature. This is supported by the fact that the multiple signals observed for each of the angular methyl, the benzylic hydrogen atom, and the acetyl methyl group of the *cis*-acetyl compound (**19f**) in $(CD_3)_2SO$ at 30 °C, collapsed at 80 °C to a single peak.

The stereochemistry of the isomeric amines was finally corroborated from the ^{13}C n.m.r. spectra and these are collected in Table 5. It is clearly evident from the data (Table 5) that the angular methyl carbon signals of the *cis*-amines (**15a**), (**15c**), and (**15f**) are diagnostically shifted downfield by 8—11 p.p.m. relative to those of the corresponding *trans*-isomers (**14a**), (**14c**), and (**14f**), and this is analogous to that reported[20,21] for octahydrophenanthrenes. Based on this fact, the ring-fusion stereochemistry of the sulphur analogue (**15e**) could be established as *cis*.

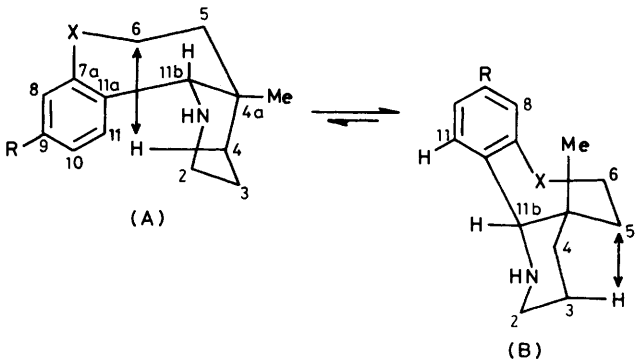
* Of the two singlets for the benzylic hydrogen atom of the *trans*-acetyl compound, the singlet at higher field is more intense, and this probably reflects a greater proportion of the rotamer (B) in equilibrium (Scheme 8).



Scheme 8. Two rotamers for the *trans*-acetyl compounds (**18a—d**)



Two conformers for the *cis*-amine (**15f**)



Scheme 9. Two conformers for the *cis*-amines (**15a**), (**15c**), and (**15e**)

The following important observations in the ^{13}C chemical shifts (Table 5) of the *cis*-amines (**15a**), (**15c**), (**15e**), and (**15f**) are informative and deserve special comments.

(i) While C-4 of the *cis*-amine (**15f**) was shielded by 9.5 p.p.m., the C-5 signals of (**15a**) and (**15c**) experienced an upfield shift by *ca.* 11 p.p.m. when compared with those of the corresponding *trans*-isomers (**14f**), (**14a**), and (**14c**) respectively. These observations definitely reflect the predominance of different conformers [(A) and (B) in Scheme 9] in *cis*-[6:6] and *cis*-[7:6] systems in the equilibrium mixtures. It is evident that in conformer (A), a γ_g interaction exists between C-4 and C-6 whereas C-3 and C-5 are involved in a similar interaction in the (B) conformer. It can, therefore, be presumed that the *cis*-amine (**15f**), having 6:6 ring fusion, exists predominantly in conformation (A), and the *cis*-amines (**15a**) and (**15c**), having 7:6 ring fusion, exist mainly in conformation (B) in the equilibrium mixtures. (ii) All the *cis*-amines (**15a**), (**15c**), and (**15f**) exhibited a significant downfield shift of the signal arising from the aromatic methine carbon *ortho* to the piperidine ring [C-10 in (**15f**) and C-11 in both (**15a**) and (**15c**)] by 5.4—6.1 p.p.m. relative to their *trans*-counterparts. The reason for deshielding of this aromatic methine carbon is not clearly understood. This effect may, however, be considered as diagnostic in determining the stereochemistry at the ring-fusion of this class of amines. (iii) One more important observation is that the benzylic carbon (C-11b), adjacent to the nitrogen atom of the *cis*-amines (**15a**) and (**15c**) experienced deshielding by 10—12 p.p.m. compared to that of the *trans*-amines (**14a**) and (**14c**) respectively. The above downfield shift of the benzylic carbon of the *cis*-amines (**15a**) and (**15c**) may possibly be attributed to *syn*-periplanar interaction between C(11b)-H and the aromatic C(11)-H which is expected to be present in the predominant conformer (B) of (**15a**) and (**15c**). Although the *trans*-isomer of the sulphur analogue (**14e**) is not available in the pure form, it can be seen from ^{13}C n.m.r. spectrum of the *cis*-isomer (**15e**) that its benzylic carbon adjacent to the nitrogen atom also resonated downfield (δ 74.9 p.p.m.) close to those of (**15a**) and (**15c**), thereby indicating that the *cis*-isomer (**15e**) also exists predominantly in conformation (B). In this connection, Dreiding molecular models of the two possible conformers of the *cis*-amine (**15f**) showed no *syn*-periplanar interaction as was observed for (**15a**) and (**15c**) mentioned above.

Experimental

M.p.s were determined on a sulphuric acid bath. U.v. spectra were measured for solutions in ethanol with a Unicam SP 500 spectrophotometer, i.r. spectra for solutions in $CHCl_3$ with a Perkin-Elmer 297 instrument, and n.m.r. spectra for solutions in $CDCl_3$ (unless otherwise stated) with a Varian T-60, a JEOL JNM FX-100 and a Varian XL-200 spectrophotometers (tetramethylsilane as internal standard). G.l.c. was carried out on a Hewlett-Packard-5710A chromatograph using 1% OV-225 (0.6 × 183 cm) column (unless otherwise stated). Extracts were dried over Na_2SO_4. Ether refers to diethyl ether and light petroleum refers to the fraction of b.p. 40—60 °C. Basic Brockmann alumina (B.D.H.) and silica gel (60—120 mesh, B.D.H.) were used for column chromatographic experiments.

6-Carboxyethyl-6-methyl-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (**4b**).—Condensation of the ketone (**6a**)[6] (5.1 g) with acrylonitrile followed by alkaline hydrolysis as described earlier[5] gave the crystalline acid (**4b**) (7.02 g, 95%), m.p. 62—63 °C (ether–light petroleum); $\nu_{max.}$ 1 710 and 1 675 cm^{-1}; δ(60 MHz) 7.32—6.85 (4 H, m), 2.85—2.52 (2 H, m), 2.47—2.12 (2 H, m), 2.05—1.42 (6 H, m), and 1.17 (3 H, s) (Found: C, 72.95; H, 7.5. $C_{15}H_{18}O_3$ requires C, 73.15; H, 7.37%).

2-Carboxyethyl-2-methyl-2H-1-thiopyran-4(3H)-one (**4g**).—Condensation of the known ketone (**6b**)[7] with acrylonitrile followed by alkaline hydrolysis afforded the crystalline acid (**4g**) (0.81 g, 74%), m.p. 120—122 °C (ether–light petroleum); $\nu_{max.}$ 1 710 and 1 675 cm^{-1} (Found: C, 62.65; H, 5.65. $C_{13}H_{14}O_3S$ requires C, 62.39; H, 5.64%).

Homologation of the Oxo Acids (**4a—g**) *and* (**5**): *Typical Procedure for the Preparation of 4-(3-Carboxypropyl)-4-methyl-3,4-dihydro-1-benzoxepin-5(2H)-one* (**8d**; R^1 = H).—The crystalline propionic acid (**4d**)[5] (4 g) was converted into its dry sodium salt by a reported[22] procedure, and an ice-cold solution of this in dry benzene (50 ml) and pyridine (0.3 ml) was treated with oxalyl chloride (3 ml). The stirred reaction mixture was kept at 0 °C for 30 min, at room temperature (30 °C) for 30 min, and then finally at 55—60 °C for 1 h. The resulting precipitate was filtered off, and the solvent was removed under reduced pressure. A solution of the resulting acid chloride in dry ether (60 ml) was then added slowly to an ice-cold and stirred ethereal solution of diazomethane (from 11.2 g of nitrosomethyl urea) containing dry triethylamine (1 ml). The reaction mixture was left at 0—5 °C for 20 h and then filtered. The ether solution was concentrated and the resulting diazo ketone was purified by passage through basic alumina (15 g) to furnish the diazo ketone (**7d**) (2.46 g, 56%) as yellow viscous oil, $\nu_{max.}$ 2 105, 1 675, and 1 640 cm^{-1}; this was directly used in the next step.

To a refluxing and stirred solution of the above diazo ketone (2.46 g) in dry methanol (25 ml) was added dropwise a freshly prepared[23] solution of silver benzoate in dry triethylamine (10%; 0.4 ml) during 30 min. The reaction mixture was then refluxed for 1 h. The cooled reaction mixture was filtered and the residue was washed thoroughly with ether. The combined filtrate and washings were evaporated and the residue was dissolved in ether (75 ml). Work-up afforded the methyl ester (**8d**; R^1 = Me) (2.27 g) as an oil, b.p. 159—160 °C (bath)/0.1 mmHg; $\nu_{max.}$ 1 730 and 1 675 cm^{-1}; δ(60 MHz; CCl_4) 7.60—6.73 (4 H, m), 4.16 (2 H, t, *J* 9 Hz), 3.55 (3 H, s), 2.26—1.80 (4 H, m), 1.70—1.33 (4 H, m), and 1.18 (3 H, s).

The above methyl ester (2.17 g) was hydrolysed by heating it under reflux for 3 h with a solution of KOH (1 g) in methanol (19 ml) and water (1 ml). Work-up gave the crystalline butyric acid (**8d**; R^1 = H) (2.05 g, quantitative), m.p. 106—107 °C (ether–light petroleum); $\nu_{max.}$ 1 710 and 1 675 cm^{-1} (Found: C, 68.5; H, 6.95. $C_{15}H_{18}O_4$ requires C, 68.69; H, 6.92%).

4-(3-Carboxypropyl)-8-methoxy-4-methyl-3,4-dihydro-1-benzoxepin-5(2H)-one (**8c**; R^1 = H) *and the Corresponding Methyl Ester* (**8c**; R^1 = Me).—The known propionic acid (**4c**)[5] (0.96 g) was converted as before into the diazo ketone (**7c**) as viscous oil (0.61 g, 59%), $\nu_{max.}$ 2 110, 1 665, and 1 635 cm^{-1}. Rearrangement of this diazo ketone (0.45 g) as before finally furnished the crystalline methyl ester (**8c**; R^1 = Me) (0.45 g), m.p. 75—76 °C (ether–light petroleum); $\nu_{max.}$ 1 730 and 1 665 cm^{-1}; δ(100 MHz) 7.56 (1 H, d, *J* 9 Hz), 6.60 (1 H, dd, *J* 9 and 2.5 Hz), 6.43 (1 H, d, *J* 2.5 Hz), 4.32—4.16 (2 H, m), 3.78 (3 H, s), 3.58 (3 H, s), 2.30—1.84 (4 H, m), 1.84—1.36 (4 H, m), and 1.20 (3 H, s) (Found: C, 66.5; H, 7.45. $C_{17}H_{22}O_5$ requires C, 66.65; H, 7.24%).

Alkaline hydrolysis of the above keto ester (**8c**; R^1 = Me) (1 g) gave the butyric acid (**8c**; R^1 = H) (0.95 g, quantitative), m.p. 80—81 °C (ether–light petroleum); $\nu_{max.}$ 1 710 and 1 665 cm^{-1} (Found: C, 65.55; H, 6.85. $C_{16}H_{20}O_5$ requires C, 65.74; H, 6.90%).

6-(3-Carboxypropyl)-6-methyl-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (**8b**; R^1 = H), *and the Methyl Ester* (**8b**; R^1 = Me).—The keto acid (**4b**)[5] (3.5 g) afforded the diazo

Table 5. ^{13}C Chemical shifts* of stereoisomeric amines

	(14a)[c]	(15a)	(14c)	(15c)[d]	(15e)[e]		(14f)[f]	(15f)[g]
C-2	47.1	49.1	47.2	47.8	47.4	C-2	47.3	46.7
C-3	22.5	22.3	22.6	21.9	22.4	C-3	22.8	22.6
C-4	41.3	42.0	40.6	40.0	41.4	C-4	36.3	26.8
C-4a	34.4	34.7	33.1	32.9	33.2	C-4a	31.7	31.2
C-5	46.6	35.8	46.2	35.7	37.3	C-5	38.7	38.2
C-6	23.7	24.3	68.9	68.8	29.9	C-6	25.7	26.0
C-7	35.8	36.0	—	—	—	C-6a	136.9	136.8
C-7a	142.5	144.7	158.6[a]	159.4[a]	144.0	C-7	113.5	113.0
C-8	114.5	115.8	108.6	108.4	132.3[a]	C-8	157.7	158.1
C-9	157.7	158.4	158.8[a]	160.0[a]	127.0[b]	C-9	110.9	111.9
C-10	109.9	109.7	106.4	106.7	126.6[b]	C-10	125.4	130.8
C-11	126.7	132.8	127.0	132.5	133.4[a]	C-10a	130.5	130.9
C-11a	133.9	133.3	127.6	125.3	135.1	C-10b	62.9	62.6
C-11b	63.3	75.6	61.9	72.4	74.9	Angular Me	14.3	25.1
Angular Me	17.9	25.9	16.7	25.6	25.6	OMe	54.8	54.8
OMe	58.8	54.9	54.9	54.6	—			

* Spectra were recorded in $CDCl_3$ and the chemical shifts are expressed on the δ scale with $SiMe_4$ as internal standard. [a,b] Assignments may be reversed. [c] Used as a 92:8 mixture of (**14a**) and (**15a**). [d] Used as a 81:19 mixture of (**15c**) and (**14c**). [e] Used as a 4:1 mixture of (**15e**) and (**14e**). [f] Used as a 9:1 mixture of (**14f**) and (**15f**). [g] Used as a 97:3 mixture of (**15f**) and (**14f**).

ketone (**7b**) (2.25 g, 58%), $\nu_{max.}$ 2 110, 1 680, and 1 640 cm^{-1}. Rearrangement of this diazo ketone (2.25 g) as before furnished the butyric ester (**8b**; R^1 = Me) (2.17 g), b.p. 160—165 °C (bath)/0.1 mmHg; $\nu_{max.}$ 1 725 and 1 680 cm^{-1}; δ(60 MHz; CCl_4) 7.30—6.83 (4 H, m), 3.55 (3 H, s), 2.72 (2 H, t, *J* 9 Hz), 2.28—1.32 (10 H, m), and 1.12 (3 H, s) (Found: C, 74.35; H, 8.15. $C_{17}H_{22}O_3$ requires C, 74.42; H, 8.0%).

Alkaline hydrolysis of the above ester (**8b**; R^1 = Me) (2.17 g) finally gave the acid (**8b**; R^1 = H) (1.98 g, 96%) as an oil, $\nu_{max.}$ 1 710 and 1 680 cm^{-1}, and this was directly used in the next step.

6-(3-*Carboxypropyl*)-2-*methoxy*-6-*methyl*-6,7,8,9-*tetrahydro*-5H-*benzocyclohepten*-5-*one* (**8a**; R^1 = H) *and the Methyl Ester* (**8a**; R^1 = Me).—The propionic acid (**4a**)[5] (0.4 g) afforded the diazo ketone (**7a**) as a viscous yellow oil (0.24 g, 56%), $\nu_{max.}$ 2 110, 1 665, and 1 635 cm^{-1}. Rearrangement of this diazo ketone (0.56 g) by the usual procedure furnished the homologated ester (**8a**; R^1 = Me) (0.56 g), b.p. 165—170 °C (bath)/0.05 mmHg; $\nu_{max.}$ 1 725 and 1 665 cm^{-1}; δ(60 MHz) 7.25 (1 H, d, *J* 8 Hz), 6.78 (1 H, d, *J* 2.5 Hz), 6.76—6.53 (1 H, m), 3.80 (3 H, s), 3.61 (3 H, s), 2.91—2.53 (2 H, m), 2.38—2.06 (2 H, m), 2.05—1.42 (8 H, m), and 1.17 (3 H, s).

The above ester (**8a**; R^1 = Me) (0.23 g) on alkaline hydrolysis gave the desired acid (**8a**; R^1 = H) (0.20 g), m.p. 126—128 °C (ether–light petroleum); $\nu_{max.}$ 1 710 and 1 665 cm^{-1} (Found: C, 70.2; H, 7.95. $C_{17}H_{22}O_4$ requires C, 70.32; H, 7.64%).

8-(3-*Carboxypropyl*)-3,5-*dimethoxy*-8-*methyl*-8,9,10,11-*tetrahydro*-7H-*cyclohepta*[a]*naphthalene* (**11**; R = CO_2H) *and the Methyl Ester* (**11**; R = CO_2Me).—The tricyclic keto acid (**5**)[5] (4 g) provided a diazo ketone (2.8 g, 65.5%) as yellow gummy material; $\nu_{max.}$ 2 105, 1 665, and 1 625 cm^{-1}. Rearrangement of this diazo ketone as before afforded the crystalline keto ester (**11**; R = CO_2Me) (1.88 g), m.p. 74—75 °C (ether–light petroleum); $\nu_{max.}$ 1 725 and 1 670 cm^{-1}; δ(60 MHz) 7.90 (1 H, d, *J* 9 Hz), 7.55 (1 H, d, *J* 2.5 Hz), 7.13 (1 H, dd, *J* 9 and 2.5 Hz), 6.72 (1 H, s), 4.00 (3 H, s), 3.93 (3 H, s), 3.63 (3 H, s), 3.30—2.87 (2 H, m), 2.40—1.14 (10 H, m), and 1.23 (3 H, s) (Found: C, 71.9; H, 7.45. $C_{23}H_{28}O_5$ requires C, 71.85; H, 7.34%).

Alkaline hydrolysis of the above ester (2.65 g) gave the desired butyric acid (**11**; R = CO_2H) (2.54 g, quantitative), m.p. 105—106 °C (ether–light petroleum); $\nu_{max.}$ 1 710 and 1 670 cm^{-1} (Found: C, 71.15; H, 7.3. $C_{22}H_{26}O_5$ requires C, 71.33; H, 7.07%).

γ-(1,2,3,4-*Tetrahydro*-6-*methoxy*-2-*methyl*-1-*oxo*-2-*naphthyl*)-*butyric Acid* (**8f**; R^1 = H) *and the Methyl Ester* (**8f**; R^1 = Me).—The known[5] keto acid (**4f**) (2 g) provided the diazo ketone (**7f**) (1.35 g, 62%), $\nu_{max.}$ 2 105, 1 665, and 1 600 cm^{-1}, and this on rearrangement as before afforded the butyric ester (**8f**; R^1 = Me) (1.29 g), b.p. 180—185 °C (bath)/0.2 mmHg; $\nu_{max.}$ 1 725 and 1 665 cm^{-1}; δ(60 MHz) 7.80 (1 H, d, *J* 9 Hz), 6.72 (1 H, d, *J* 2.5 Hz), 6.53 (1 H, dd, *J* 9 and 2.5 Hz), 3.77 (3 H, s), 3.53 (3 H, s), 3.01—2.66 (2 H, m), 2.33—2.03 (2 H, m), 2.00—1.67 (2 H, m), 1.67—1.18 (4 H, m), and 1.12 (3 H, s).

The above ester (2.15 g) on alkaline hydrolysis furnished the desired butyric acid (**8f**; R^1 = H) (1.92 g, 80%), m.p. 109—110 °C (ether–light petroleum); $\nu_{max.}$ 1 705 and 1 665 cm^{-1} (Found: C, 69.75; H, 7.5. $C_{16}H_{20}O_4$ requires C, 69.55; H, 7.30%).

4-(3-*Carboxypropyl*)-4-*methyl*-3,4-*dihydro*-1-*benzothiepin*-5(2H)-*one* (**8e**; R^1 = H).—The acid chloride of the known[5] propionic acid (**4e**) was prepared by heating under reflux for 2 h a solution of (**4e**) (1.1 g) and oxalyl chloride (2 ml) in light petroleum (5 ml). The crude acid chloride, obtained after removal of the solvent, was converted as before into the diazo ketone (**7e**) as a yellow oil (0.98 g, 82%); $\nu_{max.}$ 2 110, 1 680, and 1 635 cm^{-1}. Rearrangement of this diazo ketone (0.98 g) finally furnished the methyl ester (**8e**; R^1 = Me) (0.94 g) as viscous oil, b.p. 155—160 °C (bath)/0.1 mmHg; $\nu_{max.}$ 1 715 and 1 680 cm^{-1}; δ(60 MHz; CCl_4) 7.33—7.13 (4 H, m), 3.60 (3 H, s), 3.03—2.73 (2 H, m), 2.33—1.77 (4 H, m), 1.63—1.33 (4 H, m), and 1.21 (3 H, s).

Alkaline hydrolysis of the above ester (0.76 g) provided the desired butyric acid (**8e**; R^1 = H) (0.70 g, 96%), m.p. 81—82 °C (ether–light petroleum); $\nu_{max.}$ 1 710 and 1 680 cm^{-1} (Found: C, 64.55; H, 6.5. $C_{15}H_{18}O_3S$ requires C, 64.74; H, 6.52%).

2-*Carboxypropyl*-2-*methyl*-2H-1-*thiopyran*-4(3H)-*one* (**8g**; R^1 = H).—The propionic acid derivative (**4g**) (0.4 g) was converted as before into the diazo ketone (**7g**) as a viscous oil (0.31 g, 70%) ($\nu_{max.}$ 2 110 and 1 675 cm^{-1}) and this on rearrangement provided the homologated ester (**8g**; R^1 = Me) (0.23 g); $\nu_{max.}$ 1 725 and 1 675 cm^{-1}; δ(60 MHz) 8.01—7.80

(1 H, m), 7.23—6.80 (3 H, m), 3.53 (3 H, s), 3.05 (2 H, s), 2.36—1.93 (6 H, m), and 1.26 (3 H, s).

Alkaline hydrolysis of the above ester (0.22 g) gave the butyric acid (**8g**; R^1 = H) (0.18 g, 86%), m.p. 129—130 °C (ether–light petroleum); $\nu_{max.}$ 1 710 and 1 675 cm^{-1} (Found: C, 63.6; H, 6.2. $C_{14}H_{16}O_3S$ requires C, 63.63; H, 6.10%).

Preparation of the Cyclic Imines (**3a**—**g**) *and* (**1b**).—The conversion of the oxo butyric acids (**8a**—**g**) and (**11**; R = CO_2H) into the above cyclic imines was achieved by following the procedure reported[5] earlier for the preparation of the pyrrole derivative from the oxo propionic acid (**4d**).

2,3,4,4a,5,6-*Hexahydro*-4a-*methyl*[1]*benzoxepino*[5,4-b]*pyridine* (**3d**).—The butyric acid (**8d**; R^1 = H) (1.2 g) gave, initially, a mixture of the acid azide (**9d**) and the isocyanate (**10d**) as a viscous oil (1.7 g) ($\nu_{max.}$ 2 280, 2 140, 1 710, and 1 675 cm^{-1}). Heating a solution of this mixture in toluene for 2 h at 100 °C gave the crude isocyanate (**10d**) (1.2 g) ($\nu_{max.}$ 2 280 and 1 675 cm^{-1}). Acid hydrolysis of this isocyanate and work-up of the reaction mixture as reported[5] earlier furnished the desired pyridine derivative (**3d**) (0.79 g, 80% based on butyric acid used), b.p. 130—135 °C (bath)/0.1 mmHg; $\nu_{max.}$ 1 630 and 1 603 cm^{-1}; $\lambda_{max.}$ 240 nm (ε 6 012); δ(100 MHz) 7.44 (1 H, dd, *J* 8 and 1.5 Hz), 7.32—6.76 (3 H, m), 4.48—4.04 (2 H, m), 4.00—3.40 (2 H, m), 2.08—1.84 (2 H, m), 1.80—1.52 (4 H, m), and 1.08 (3 H, s) (Found: C, 78.25; H, 8.1. $C_{14}H_{17}NO$ requires C, 78.10; H, 7.96%).

2,3,4,4a,5,6-*Hexahydro*-9-*methoxy*-4a-*methyl*[1]*benzoxepino*[5,4-b]*pyridine* (**3c**).—The oxo acid (**8c**; R^1 = H) (0.6 g) was converted into the isocyanate (**10c**) (0.6 g) ($\nu_{max.}$ 2 275 and 1 665 cm^{-1}). Acid hydrolysis of this isocyanate finally afforded the pyridine derivative (**3c**) (0.32 g, 64%), b.p. 130—135 °C (bath)/0.1 mmHg, m.p. 82—83 °C (light petroleum); $\nu_{max.}$ 1 625 and 1 600 cm^{-1}; *m/z* 245 (M^+) and 230 ($M^+ - 15$); $\lambda_{max.}$ 257 nm (ε 8 189); δ(100 MHz) 7.36 (1 H, d, *J* 9 Hz), 6.51 (1 H, dd, *J* 9 and 2 Hz), 6.34 (1 H, d, *J* 2 Hz), 4.48—3.38 (4 H, m), 3.76 (3 H, s), 2.20—1.40 (6 H, m), and 1.09 (3 H, s) (Found: C, 73.25; H, 7.8. $C_{15}H_{19}NO_2$ requires C, 73.44; H, 7.81%).

2,3,4,4a,6,7-*Hexahydro*-4a-*methylbenzo*[6,7]*cyclohepta*[5,6-b]*pyridine* (**3b**).—The butyric acid (**8b**; R^1 = H) (1.14 g) was converted into the acid azide and this then treated to afford the isocyanate (**10b**) (1.10 g) ($\nu_{max.}$ 2 280 and 1 680 cm^{-1}). Acid hydrolysis of this crude isocyanate finally gave the pyridine derivative (**3b**) (0.74 g, 80%), b.p. 135—140 °C (bath)/0.1 mmHg; $\nu_{max.}$ 1 630 cm^{-1}; $\lambda_{max.}$ 227 nm (ε 5 248); δ(200 MHz) 7.28—7.00 (4 H, m), 4.16—3.86 (1 H, m), 3.82—3.54 (1 H, m), 2.92—2.60 (2 H, m), 2.18—1.78 (4 H, m), 1.78—1.38 (4 H, m), and 0.92 (3 H, s) (Found: C, 84.35; H, 9.15. $C_{15}H_{19}N$ requires C, 84.46; H, 8.98%).

2,3,4,4a,6,7-*Hexahydro*-9-*methoxy*-4a-*methylbenzo*[6,7]*cyclohepta*[5,6-b]*pyridine* (**3a**).—The butyric acid (**8a**; R^1 = H) (0.5 g) after three steps as before furnished the desired pyridine derivative (**3a**) (0.27 g, 65%), b.p. 115—120 °C (bath)/0.05 mmHg; $\nu_{max.}$ 1 625 and 1 600 cm^{-1}; $\lambda_{max.}$ 247 nm (ε 7 036); δ(60 MHz) 7.00 (1 H, d, *J* 8 Hz), 6.65 (1 H, d, *J* 2.5 Hz), 6.50—6.43 (1 H, m), 3.90—3.16 (5 H, m), 2.90—2.43 (2 H, m), 2.10—1.20 (8 H, m), and 0.85 (3 H, s) (Found: C, 78.8; H, 9.25. $C_{16}H_{21}NO$ requires C, 78.97; H, 8.70%).

2,3,4,4a,5,6-*Hexahydro*-4a-*methyl*[1]*benzothiepino*[5,4-b]*pyridine* (**3e**).—The oxo acid (**8e**; R^1 = H) (0.5 g) by the usual procedure[5] gave the pyridine derivative (**3e**) (0.29 g, 70%), b.p. 155—160 °C (bath)/0.1 mmHg, m.p. 53—54 °C (ether–light petroleum); $\nu_{max.}$ 1 630 cm^{-1}; $\lambda_{max.}$ 265 nm (ε 4 620); δ(200 MHz) 7.42—7.36 (1 H, m), 7.28—7.16 (3 H, m), 4.06—3.66 (2 H, m), 3.12—2.80 (2 H, m), 2.28—2.12 (1 H, m), 1.98—1.70 (4 H, m), 1.62—1.46 (1 H, m), and 1.00 (3 H, s) (Found: C, 72.5; H, 7.6. $C_{14}H_{17}NS$ requires C, 72.70; H, 7.41%).

2,3,4,4a,5,6-*Hexahydro*-8-*methoxy*-4a-*methylbenzo*[h]*quinoline* (**3f**).—The butyric acid (**8f**; R^1 = H) (0.9 g) was converted as before into the crystalline quinoline derivative (**3f**) (0.57 g, 77%), b.p. 135—140 °C (bath)/0.1 mmHg, m.p. 60—61 °C (light petroleum); $\nu_{max.}$ 1 625 and 1 600 cm^{-1}; $\lambda_{max.}$ 264 nm (ε 16 210); *m/z* 229 (M^+), 214 ($M^+ - 15$), and 201 ($M^+ - 28$); δ(200 MHz) 7.96 (1 H, d, *J* 9 Hz), 6.80 (1 H, dd, *J* 9 and 2.5 Hz), 6.64 (1 H, d, *J* 2.5 Hz), 4.05—3.89 (1 H, m), 3.82 (3 H, s), 3.81—3.61 (1 H, m), 3.19—2.97 (1 H, m), 2.88—2.72 (1 H, m), 1.92—1.42 (6 H, m), and 1.11 (3 H, s) (Found: C, 78.45; H, 8.5. $C_{15}H_{19}NO$ requires C, 78.56; H, 8.35%).

2,3,4,4a-*Tetrahydro*-4a-*methyl*[1]*benzothieno*[4,3-b]*pyridine* (**3g**).—The butyric acid (**8g**; R^1 = H) (1.05 g) was converted into the acid azide and this then gave the isocyanate (**10g**) as a viscous oil (1.17 g); $\nu_{max.}$ 2 275, 2 145, and 1 675 cm^{-1}. Acid hydrolysis and work-up[5] finally provided the pyridine derivative (**3g**) (0.68 g, 79%), m.p. 93—95 °C; $\nu_{max.}$ 1 625 cm^{-1}. Recrystallisation from ether–light petroleum provided an analytical sample, m.p. 95—96 °C; $\lambda_{max.}$ 260 nm (ε 7 468); δ(60 MHz) 8.03—7.83 (1 H, m), 7.01—6.76 (3 H, m), 3.90—3.50 (2 H, m), 3.08 (1 H, d, *J* 13 Hz), 2.35 (1 H, d, *J* 13 Hz), 1.77—1.43 (4 H, m), and 1.23 (3 H, s) (Found: C, 71.85; H, 7.05. $C_{13}H_{15}NS$ requires C, 71.87; H, 6.96%).

2,3,11,12,13,13a-*Hexahydro*-6,8-*dimethoxy*-13a-*methyl*-1H-*naphtho*[1′,2′:6,7]*cyclohepta*[1,2-b]*pyridine* (**1b**).—The tricyclic keto acid (**11**; R^1 = CO_2H) (0.4 g) was converted into the acid azide (**12**) (0.48 g) ($\nu_{max.}$ 1 710 and 1 665 cm^{-1}) which rearranged to the isocyanate (**13**) when heated in toluene (15 ml). Hydrolysis of the isocyanate (**13**) was effected with aqueous KOH (50%; 7 ml) under nitrogen at 100 °C for 2 h. Toluene was removed under reduced pressure and the residue was dissolved in cold HCl (6M). The acidic solution was extracted with ether–methylene dichloride (2 × 30 ml) to remove any neutral material and then made alkaline with solid Na_2CO_3; the separated product was extracted with ether–methylene dichloride (5 × 25 ml) and the extract worked up to afford the tetracyclic imine (**1b**) (0.33 g, 94%) as a foamy solid; $\nu_{max.}$ 1 620 and 1 595 cm^{-1}; *m/z* 323 (M^+) and 308 ($M^+ - 15$); δ(200 MHz) 7.99 (1 H, d, *J* 9 Hz), 7.63 (1 H, d, *J* 3 Hz), 7.23 (1 H, dd, *J* 9 and 3 Hz), 6.74 (1 H, s), 4.02 (3 H, s), 3.96 (3 H, s), 3.96—3.71 (2 H, m), 3.46—3.30 (1 H, m), 3.06—2.90 (1 H, m), 2.00—1.78 (5 H, m), 1.66—1.50 (2 H, m), 1.32—1.18 (1 H m), and 0.95 (3 H, s).

Chemical and Catalytic Reduction of the Imines (**3a**—**g**) *and* (**1b**), cis-1,2,3,4,4a,11b-*Hexahydro*-9-*methoxy*-4a-*methyl*-2H-*benzo*[6,7]*cyclohepta*[5,6-b]*pyridine* (**15a**), *the corresponding* trans-*Isomer* (**14a**), *and their* N-*Acetyl Derivatives* (**19a**) *and* (**18a**).—(a) *By reduction of the imine* (**3a**) *with lithium aluminium hydride* (LAH): *formation of the* cis-*amine* (**15a**) *and its* N-*acetyl derivative* (**19a**). The imine (**3a**) (0.11 g), reduced with LAH (0.05 g) in dry ether (15 ml) following the procedure reported[5] for a similar reduction of the related pyrrole derivative, furnished only (from g.l.c.) the *cis*-amine (**15a**) (0.09 g, 87%), b.p. 115—120 °C (bath)/0.1 mmHg; m.p. 83—84 °C (light petroleum); $\nu_{max.}$ 1 605 cm^{-1}; *m/z* 245 (M^+), 230 ($M^+ - 15$), and 202 ($M^+ - 43$); δ(200 MHz) 7.08 (1 H, d, *J* 9 Hz), 6.70—6.58 (2 H, m), 3.78 (3 H, s), 3.27 (1 H, s), 3.40—3.14 (2 H, m), 2.84—2.64 (2 H, m), 2.54—2.43 (1 H, m), 2.10—1.66 (8 H, m), and 0.70 (3 H, s) (Found: C, 78.25; H, 9.5. $C_{16}H_{23}NO$ requires C, 78.32; H, 9.45%).

A solution of the above amine (**15a**) (0.11 g) in pyridine was

acetylated with Ac_2O as described earlier[5] to give on work-up a viscous oil. Chromatographic purification of the latter over silica gel gave the acetyl derivative (**19a**) as oil (0.10 g, 82%), b.p. 185—190 °C (bath)/0.1 mmHg; $\nu_{max.}$ 1 622 cm^{-1}; δ(200 MHz) for the special features, see Table 4.

(b) *By* $NaBH_4$ *reduction of the imine* (**3a**)*; formation of a stereoisomeric mixture of the amines* (**14a**) *and* (**15a**). (i) A solution of the imine (**3a**) (0.13 g) in MeOH (4 ml) was reduced with an excess of $NaBH_4$ as described[5] previously to furnish a product (0.12 g, 92%), b.p. 110—115 °C (bath)/0.05 mmHg; $\nu_{max.}$ 1 605 cm^{-1}. G.l.c. of this material at 190 °C showed it to be a 92:8 mixture of the *trans*-(**14a**) and the *cis*-amine (**15a**) having R_t values of 4.6 and 3.5 min respectively. The special features of ^1H n.m.r. (60 MHz) spectrum of this mixture are the two angular methyl singlets at δ 0.60 and 0.70 and the two benzylic hydrogen singlets at δ 3.78 and 3.27 for the *trans*-(**14a**) and the *cis*-amine (**15a**) respectively (Found: C, 78.25; H, 9.5. $C_{16}H_{23}NO$ requires C, 78.32; H, 9.45%).

(ii) Use of isopropyl alcohol as a solvent in the above reduction of (**3a**) also gave a 85:15 mixture respectively of the *trans*-(**14a**) and the *cis*-amine (**15a**).

(iii) Reduction of the imine (**3a**) with sodium triacyloxyborohydride ($NaBH_4$ + tartaric acid) according to the prescribed[11] procedure furnished again in excellent yield a 95:5 mixture of the *trans*-(**14a**) and the *cis*-amine (**15a**) respectively.

Acetylation of the above mixture of amines (0.11 g) as before provided an oil (0.13 g) which on chromatography over silica gel (5.5 g) and elution of the chromatogram with ether–light petroleum (25:75) afforded the pure *trans*-acetyl compound (**18a**) (0.11 g, 86%) as colourless plates, m.p. 99—100 °C (ether–light petroleum); $\nu_{max.}$ 1 622 cm^{-1}; δ(100 MHz) for the special features, see Table 3 (Found: C, 75.04; H, 8.95. $C_{18}H_{25}NO_2$ requires C, 75.22; H, 8.77%).

(c) *By sodium–liquid ammonia reduction of the imine* (**3a**)*: formation of a stereoisomeric mixture of the amines* (**14a**) *and* (**15a**). Reduction of the imine (**3a**) (0.15 g) with sodium metal in liquid ammonia as described earlier[5] for the related system afforded an amine (0.14 g, 92.7%) as a 56:44 mixture (from g.l.c. and ^1H n.m.r.) of the *trans*-(**14a**) and the *cis*-amine (**15a**) respectively.

(d) *By catalytic reduction of the imine* (**3a**)*: formation of a mixture of* (**14a**) *and* (**15a**). A solution of the imine (**3a**) (0.05 g) in MeOH (5 ml) was hydrogenated over Pd–C (0.05 g, 10%) at 30 °C under ordinary pressure. After complete absorption of hydrogen (4 h), the reaction mixture was worked up to furnish a saturated amine (0.05 g) as a 89:11 mixture (from g.l.c.) of the *trans*-(**14a**) and the *cis*-amine (**15a**).

cis-1,2,3,4,4a,11b-*Hexahydro*-4a-*methylbenzo*[6,7]*cyclohepta*[5,6-b]*pyridine* (**15b**), *the* trans-*Isomer* (**14b**), *and their* N-*Acetyl Derivatives* (**19b**) *and* (**18b**).—(a) *By reduction with* LAH*: formation of the* cis-*amine* (**15b**) *and its acetyl derivative* (**19b**). Reduction of the imine (**3b**) (0.12 g) with LAH in ether afforded the pure *cis*-amine (**15b**) (0.11 g, 92%), b.p. 120—125 °C (bath)/0.1 mmHg; $\nu_{max.}$ 1 600 cm^{-1}; δ(200 MHz) 7.24—7.04 (4 H, m), 3.44—3.18 (2 H, m), 3.35 (1 H, s), 2.89—2.68 (2 H, m), 2.65—2.50 (1 H, m), 2.14—1.95 (1 H, m), 1.94—1.76 (1 H, m), 1.76—1.20 (6 H, m), and 0.70 (3 H, s) (Found: C, 83.5; H, 9.95. $C_{15}H_{21}N$ requires C, 83.67; H, 9.83%).

Acetylation of the above amine (**15b**) (0.09 g) furnished the *cis*-acetyl derivative (**19b**) (0.10 g, 93%), b.p. 180—185 °C (bath)/0.1 mmHg; $\nu_{max.}$ 1 625 cm^{-1}; δ(100 MHz) for the special features, see Table 4 (Found: C, 79.15; H, 9.2. $C_{17}H_{23}NO$ requires C, 79.33; H, 9.01%).

(b) *By catalytic reduction of the imine* (**3b**)*: formation of the* trans-*amine* (**14b**) *and its* N-*acetyl derivative* (**18b**). The imine (**3b**) (0.1 g) on catalytic reduction afforded the pure *trans*-amine (**14b**) (0.09 g, 90%), b.p. 120—125 °C (bath)/0.1 mmHg; δ(200 MHz) 7.58 (1 H, d, *J* 9 Hz), 7.30—7.06 (3 H, m), 3.91 (1 H, s), 3.35—3.22 (1 H, m), 2.98—2.64 (3 H, m), 1.92—1.36 (10 H, m), and 0.64 (3 H, s) (Found: C, 83.55; H, 9.9. $C_{15}H_{21}N$ requires C, 83.67; H, 9.83%).

Acetylation of (**14b**) (0.08 g) gave the *trans*-acetyl derivative (**18b**) (0.09 g, quantitative), b.p. 180—185 °C (bath)/0.1 mmHg, $\nu_{max.}$ 1 625 cm^{-1}; δ(100 MHz) for the special features, see Table 3 (Found: C, 79.25; H, 9.25. $C_{17}H_{23}NO$ requires C, 79.33; H, 9.01%).

(c) *By* $NaBH_4$ *reduction of the imine* (**3b**)*: formation of a mixture of the amines* (**14b**) *and* (**15b**). The imine (0.07 g) on reduction with $NaBH_4$ afforded a material (0.07 g, 96%) as an 82:18 mixture (from g.l.c. at 150 °C) of the *trans*-(**14b**) and the *cis*-amine (**15b**) having R_t values of 4.2 and 2.5 min respectively.

(d) *By* $LiBH_4$ *reduction of the imine* (**3b**)*: formation of a mixture of* (**14b**) *and* (**15b**). To a solution of the imine (**3b**) (0.1 g) in dry diglyme (2 ml) was added $LiBH_4$ (0.07 g) in one lot, and the reaction mixture was stirred at room temperature (30 °C) for 22 h. The resulting mixture was then poured into water (30 ml) and left for 1 h. The product was then extracted with ether (4 × 20 ml) and the combined organic extract was washed with water. Removal of the dry solvent afforded a saturated amine (0.08 g, 80%) as a 40:60 mixture (from g.l.c. at 150 °C) of the *trans*-(**14b**) and the *cis*-amine (**15b**) respectively.

(e) *By sodium–liquid ammonia reduction of the imine* (**3b**)*: formation of a mixture of the amines* (**14b**) *and* (**15b**). Sodium–liquid ammonia reduction of the imine (**3b**) (0.06 g) afforded a reduced amine (0.06 g, quantitative) as a 31:69 mixture (from g.l.c. and ^1H n.m.r.) of the *trans*-(**14b**) and the *cis*-amine (**15b**) respectively. The characteristic features of its ^1H n.m.r. (200 MHz) spectrum are the two benzylic hydrogen singlets at δ 3.91 and 3.35 and the two angular methyl singlets at δ 0.64 and 0.70 for the *trans*-(**14b**) and the *cis*-amine (**15b**) respectively.

cis-1,2,3,4,4a,5,6,11b-*Octahydro*-4a-*methyl*[1]*benzoxepino*-[5,4-b]*pyridine* (**15d**), *the* trans-*Isomer* (**14d**), *and their* N-*Acetyl Derivatives* (**18d**) *and* (**19d**).—(a) *By reduction with* LAH*: formation of a mixture of* (**14d**) *and* (**15d**) *and the pure* N-*acetyl derivative* (**19d**). Reduction of the imine (**3d**) (0.13 g) with LAH in ether as before furnished an amine (0.11 g, 91%), b.p. 120—125 °C (bath)/0.1 mmHg; $\nu_{max.}$ 1 603 cm^{-1}. G.l.c. at 150 °C of this material showed it to be a 79:21 mixture of the *cis*-(**15d**) and the *trans*-amine (**14d**) of R_t values of 3.6 and 4.5 min respectively. The special features of its ^1H n.m.r. (200 MHz) spectrum are the two benzylic hydrogen singlets at δ 3.99 and 3.32 and two angular methyl singlets at δ 0.72 and 0.87 for the *trans*-(**14d**) and the *cis*-amine (**15d**) respectively.

Acetylation of the above mixture (0.09 g) as before afforded the crystalline *cis*-acetyl derivative (**19d**) (0.08 g, 72%), m.p. 99—101 °C (ether–light petroleum); $\nu_{max.}$ 1 630 cm^{-1}; δ(100 MHz) for characteristic features, see Table 4 (Found: C, 74.0; H, 8.3. $C_{16}H_{21}NO_2$ requires C, 74.10; H, 8.16%).

(b) *By* $NaBH_4$ *reduction of the imine* (**3d**)*: formation of a mixture of the amines* (**14d**) *and* (**15d**). Reduction of (**3d**) (0.08 g) with $NaBH_4$ provided a saturated amine (0.078 g, 97%) as a 49:51 mixture (from g.l.c.) of the *cis*-(**15d**) and the *trans*-amine (**14d**) respectively. The special features of its ^1H n.m.r. (200 MHz) spectrum are the two benzylic hydrogen singlets at δ 3.99 and 3.32 and two angular methyl singlets at δ 0.72 and 0.87 respectively for the *trans*-(**14d**) and the *cis*-amine (**15d**).

(c) *By* $LiBH_4$ *reduction of the imine* (**3d**)*: formation of a mixture of* (**14d**) *and* (**15d**). The imine (**3d**) (0.1 g) on reduction with $LiBH_4$ by the procedure described for (**3b**) furnished a saturated amine (0.085 g, 85%) as a 19:82 mixture (from g.l.c. at 150 °C) of the *trans*-(**14d**) and the *cis*-amine (**15d**) respectively.

(d) *By catalytic reduction of the imine* (**3d**)*: formation of the* trans-*amine* (**14d**) *and its* N-*acetyl derivative* (**18d**). Catalytic hydrogenation of (**3d**) (0.15 g) as before afforded the pure (from

g.l.c.) *trans*-amine (**14d**) (0.14 g, 96%), b.p. 120—125 °C (bath)/0.1 mmHg; $\nu_{max.}$ 1 603 cm^{-1}; δ(200 MHz) 7.43 (1 H, d, *J* 8 Hz), 7.24—6.94 (3 H, m), 4.28 (1 H, m), 3.99 (1 H, s), 3.70 (1 H, t, *J* 12 Hz), 3.34—3.20 (1 H, br d, *J* 12 Hz), 2.70 (1 H, m), 2.12—1.93 (1 H, m), 1.82—1.43 (6 H, m), and 0.72 (3 H, s) (Found: C, 77.25; H, 8.95. $C_{14}H_{19}NO$ requires C, 77.38; H, 8.81%).

The above amine (0.12 g) on acetylation gave a viscous oil (0.13 g) ($\nu_{max.}$ 1 630 cm^{-1}). Chromatography of this material over silica gel and elution of the chromatogram with ether–light petroleum (1:4) gave the *trans*-acetyl derivative (**18d**), b.p. 180—185 °C (bath)/0.1 mmHg; δ(100 MHz) for special features, see Table 3 (Found: C, 74.0; H, 8.25. $C_{16}H_{21}NO_2$ requires C, 74.10; H, 8.16%).

(e) *By sodium–liquid ammonia reduction of the imine* (**3d**): *formation of a mixture of* (**14d**) *and* (**15d**). Reduction of the imine (**3d**) (0.06 g) with sodium metal in liquid ammonia gave a product (0.05 g, 88%) as a 84:16 mixture (from g.l.c. and ^1H n.m.r.) of the *trans*-(**14d**) and the *cis*-amine (**15d**) respectively.

cis-1,2,3,4,4a,5,6,11b-*Octahydro*-9-*methoxy*-4a-*methyl*[1]-*benzoxepino*[5,4-b]*pyridine* (**15c**), *the* trans-*Isomer* (**14c**), *and their* N-*Acetyl Derivatives* (**19c**) *and* (**18c**).—(a) *By* LAH *reduction of the imine* (**3c**): *formation of a mixture of the amines* (**15c**) *and* (**14c**). The imine (**3c**) (0.12 g) on LAH reduction afforded a reduced amine (0.11 g, 91%), b.p. 120—125 °C (bath)/0.1 mmHg as a 19:81 mixture (from g.l.c. at 190 °C) of the *trans*-(**14c**) and the *cis*-amine (**15c**) having R_t values of 6.68 and 5.59 min respectively. The special features of its ^1H n.m.r. (200 MHz) spectrum are the two benzylic hydrogen singlets at δ 3.90 and 3.27 and the two angular methyl singlets at δ 0.72 and 0.85 respectively for (**14c**) and (**15c**).

Acetylation of the above amine mixture (0.20 g) as before gave a viscous oil (0.21 g) which on chromatography over silica gel furnished the *cis*-acetyl derivative (**19c**) (0.16 g, 73%), b.p. 180—190 °C (bath)/0.1 mmHg; $\nu_{max.}$ 1 630 cm^{-1}; δ(100 MHz) for the special features, see Table 4 (Found: C, 70.4; H, 8.2. $C_{17}H_{23}NO_3$ requires C, 70.56; H, 8.01%).

(b) *By* $NaBH_4$ *reduction of the imine* (**3c**): *formation of a mixture of the amines* (**14c**) *and* (**15c**). Reduction of the imine (**3c**) (0.05 g) with $NaBH_4$ as before[5] afforded a saturated amine (0.04 g, 87%) as a 59:41 mixture (from g.l.c. and ^1H n.m.r.) of the *trans*-(**14c**) and the *cis*-amine (**15c**) respectively.

(c) *Sodium–liquid ammonia reduction of the imine* (**3c**): *formation of a mixture of the amines* (**14c**) *and* (**15c**). Reduction[5] of the imine (**3c**) (0.06 g) with sodium metal in liquid ammonia afforded an amine (0.05 g, 83%) as a 94:6 mixture (from g.l.c. and ^1H n.m.r.) of the *trans*-(**14c**) and the *cis*-amine (**15c**).

(d) *By catalytic reduction of the imine* (**3c**): *formation of the* trans-*amine* (**14c**) *and its* N-*acetyl derivative* (**18c**). The imine (**3c**) (0.15 g) on catalytic hydrogenation as before afforded the *trans*-amine (**14c**) (0.15 g, quantitative), b.p. 125—130 °C (bath)/0.1 mmHg; δ(200 MHz) 7.31 (1 H, d, *J* 9 Hz), 6.68 (1 H, dd, *J* 9 and 3 Hz), 6.58 (1 H, d, *J* 3 Hz), 4.26 (1 H, m), 3.90 (1 H, s), 3.78 (3 H, s), 3.70 (1 H, m), 2.70 (1 H, m), 1.80—1.40 (6 H, m), and 0.72 (3 H, s) (Found: C, 72.75; H, 8.7. $C_{15}H_{21}NO_2$ requires C, 72.84; H, 8.56%).

Acetylation of the above amine (0.12 g) as before provided the *trans*-acetyl derivative (**18c**) (0.13 g, 98%), m.p. 170—172 °C (acetone–light petroleum); $\nu_{max.}$ 1 630 cm^{-1}; δ(100 MHz) for special features, see Table 3 (Found: C, 70.35; H, 8.2. $C_{17}H_{23}NO_3$ requires C, 70.56; H, 8.01%).

Stereoisomeric Mixture of 1,2,3,4,4a,5,6,11b-*Octahydro*-4a-*methyl*[1]*benzothiepino*[5,4-b]*pyridine* (**15e**) *and* (**14e**), *and the Pure* cis-*Acetyl Derivative* (**19e**).—(a) *By* LAH *reduction of the imine* (**3e**): *formation of a mixture of the amines* (**15e**) *and* (**14e**), *and the pure* cis-*acetyl compound* (**19e**). Reduction of (**3e**) (0.13 g) with LAH as before afforded a saturated amine (0.08 g, 61%), b.p. 150—160 °C (bath)/0.1 mmHg as a 9:1 mixture (from ^1H n.m.r.) of the *cis*-(**15e**) and the *trans*-amine (**14e**), the special features of its ^1H n.m.r. (100 MHz) spectrum are the two benzylic hydrogen singlets at δ 4.17 and 3.47 for the *trans*-(**14e**) and the *cis*-amine (**15e**) respectively (Found: C, 71.95; H, 8.4. $C_{14}H_{19}NS$ requires C, 72.07; H, 8.21%).

Acetylation of the above mixture (0.05 g) as before afforded the *cis*-acetyl derivative (**19e**) (0.05 g, 77%), m.p. 99—100 °C identical with that reported below.

(b) *By* $NaBH_4$ *reduction of the imine* (**3e**). Reduction of the imine (**3e**) (0.14 g) with $NaBH_4$ gave an amine (0.11 g, 79%) as a 1:4 mixture (from ^1H n.m.r. at 200 MHz) of the *trans*-(**14e**) and the *cis*-amine (**15e**) respectively.

The above mixture (0.08 g) on acetylation afforded the *cis*-acetyl derivative (**19e**) (0.09 g), m.p. 99—100 °C (ether–light petroleum); $\nu_{max.}$ 1 630 cm^{-1}; δ(200 MHz) for the special features of ^1H n.m.r. spectrum, see Table 4 (Found: C, 69.55; H, 7.8. $C_{16}H_{21}NOS$ requires C, 69.79; H, 7.69%).

cis-1,2,3,4,4a,5,6,10b-*Octahydro*-8-*methoxy*-4a-*methylbenzo*-[h]*quinoline* (**15f**), *the* trans-*Isomer* (**14f**) *and their* N-*Acetyl Derivatives* (**19f**) *and* (**18f**).—(a) *By reduction of the imine* (**3f**) *with* LAH: *formation of* (**15f**) *and its acetyl derivative* (**19f**). Reduction of the imine (**3f**) (0.12 g) with LAH in ether[5] furnished an amine (0.10 g, 84%), b.p. 130—135 °C (bath)/0.1 mmHg, m.p. 55—57 °C, and this was shown to be a 97:3 mixture (from g.l.c. at 190 °C) respectively of the *cis*-(**15f**) and the *trans*-amine (**14f**). Recrystallisation of this material provided an analytical sample of the *cis*-amine (**15f**), m.p. 59—60 °C (light petroleum); δ(200 MHz) 7.19 (1 H, d, *J* 9 Hz), 6.78 (1 H, dd, *J* 9 and 3 Hz), 6.68 (1 H, d, *J* 3 Hz), 3.80 (3 H, s), 3.29 (1 H, s), 3.14—3.03 (1 H, m), 2.92—2.70 (3 H, m), 2.49—2.33 (1 H, m), 1.76—1.60 (2 H, m), 1.57—1.37 (3 H, m), 1.29—1.16 (1 H, m), and 0.88 (3 H, s) (Found: C, 77.7; H, 9.3. $C_{15}H_{21}NO$ requires C, 77.88; H, 9.15%).

Acetylation of the amine (**15f**) (0.07 g) as before gave the *cis*-acetyl derivative (**19f**) (0.07 g, 94%), m.p. 84—86 °C (ether–light petroleum); $\nu_{max.}$ 1 640 cm^{-1}; δ(200 MHz) for the special features, see Table 4 (Found: C, 74.8; H, 8.4. $C_{17}H_{23}NO_2$ requires C, 74.69; H, 8.48%).

(b) *By catalytic reduction of the imine* (**3f**): *formation of the* trans-*amine* (**14f**). The imine (**3f**) (0.12 g) on catalytic hydrogenation as before gave the amine (**14f**) (0.12 g, quantitative), b.p. 130—135 °C (bath)/0.1 mmHg, m.p. 37—39 °C, and this was shown to be a 97:3 mixture (from g.l.c. at 190 °C) of the *trans*-(**14f**) and the *cis*-amine (**15f**) respectively. Recrystallisation of this product furnished the pure *trans*-amine (**14f**), m.p. 38—39 °C (light petroleum); δ(200 MHz) 7.46 (1 H, d, *J* 8 Hz), 6.74 (1 H, dd, *J* 9 and 2.5 Hz), 6.65 (1 H, d, *J* 2.5 Hz), 3.78 (3 H, s), 3.52 (1 H, s), 3.40—3.26 (1 H, m), 3.02—2.70 (3 H, m), 1.92—1.28 (7 H, m), and 0.80 (3 H, s) (Found: C, 77.75; H, 9.3. $C_{15}H_{21}NO$ requires C, 77.88; H, 9.15%).

(c) *By* $NaBH_4$ *reduction of the imine* (**3f**): *formation of a mixture of the amines* (**14f**) *and* (**15f**) *and the* trans-*acetyl derivative* (**18f**). Reduction of the imine (**3f**) (0.10 g) with $NaBH_4$ furnished an oil (0.1 g, quantitative) and this was found to be a 9:1 mixture (from g.l.c. at 190 °C) of the *trans*-(**14f**) and the *cis*-amine (**15f**) having R_t values of 3.65 and 2.79 min respectively. The special features of its ^1H n.m.r. (200 MHz) spectrum are the two benzylic hydrogen singlets at δ 3.52 and 3.29 and two angular methyl singlets at δ 0.80 and 0.88 for the *trans*-(**14f**) and the *cis*-amine (**15f**) respectively.

Acetylation of the above mixture of amines (0.1 g) as before afforded a gummy solid (0.12 g), and this on recrystallisation furnished the pure *trans*-acetyl derivative (**18f**) (0.08 g, 67%), m.p. 121—122 °C (ether–light petroleum); $\nu_{max.}$ 1 640 and 1 610 cm^{-1}; δ(200 MHz) for special features, see Table 3

(Found: C, 74.45; H, 8.8. $C_{17}H_{23}NO_2$ requires C, 74.69; H, 8.48%).

(d) *By sodium–liquid ammonia reduction of* (**3f**). Reduction of (**3f**) (0.06 g) with sodium metal in liquid ammonia gave in near quantitative yield a 55:45 mixture (from g.l.c.) of the *trans*-(**14f**) and the *cis*-amine (**15f**) respectively.

cis-1,2,3,4,4a,13b-*Hexahydro*-10,12-*dimethoxy*-4a-*methylnaphtho*[a]*cyclohepta*[7,8-b]*pyridine* (**17**), *the* trans-*Isomer* (**16**), *and their* N-*Acetyl Derivatives* (**21**) *and* (**20**).—(a) *By* LAH *reduction of the imine* (**1b**)*: formation of the* cis-*amine* (**17**) *and its* N-*acetyl derivative* (**21**). The tetracyclic imine (**1b**) (0.10 g) on LAH reduction as before afforded the *cis*-amine (**17**) (0.09 g, 97%), m.p. 119—123 °C. Recrystallisation provided pure *cis*-amine (**17**), m.p. 123—124 °C (ether–light petroleum); $\nu_{max.}$ 1 622 and 1 595 cm^{-1}; δ(200 MHz) 8.06 (1 H, d, *J* 9 Hz), 7.59 (1 H, d, *J* 3 Hz), 7.20 (1 H, dd, *J* 9 and 3 Hz), 6.73 (1 H, s), 4.01 (3 H, s), 3.95 (3 H, s), 3.45 (1 H, s), 3.44—3.24 (3 H, m), 2.94—2.74 (2 H, m), 2.16—1.84 (2 H, m), 1.70—1.40 (6 H, m), and 0.77 (3 H, s) (Found: C, 77.3; H, 8.65. $C_{21}H_{27}NO_2$ requires C, 77.50; H, 8.36%).

Acetylation of the *cis*-amine (**17**) (0.05 g) gave the *cis*-acetyl derivative (**21**) (0.06 g, 93%), m.p. 206—207 °C (acetone); $\nu_{max.}$ 1 625 cm^{-1}; δ(100 MHz) for the special features, see Table 4 (Found: C, 75.0; H, 8.0. $C_{23}H_{29}NO_3$ requires C, 75.15; H, 7.95%).

(b) *By catalytic reduction of the imine* (**1b**)*: formation of the* trans-*amine* (**16**) *and its acetyl derivative* (**20**). The imine (**1b**) on hydrogenation over PtO_2 (0.07 g) in MeOH gave the *trans*-amine (**16**) as a gum solid which showed decomposition on crystallisation; $\nu_{max.}$ 1 622 cm^{-1}; δ(200 MHz) 8.04 (1 H, d, *J* 9 Hz), 7.62 (1 H, d, *J* 3 Hz), 7.28 (1 H, s), 7.21 (1 H, dd, *J* 9 and 3 Hz), 4.18 (1 H, s), 4.04 (3 H, s), 3.96 (3 H, s), 3.71—3.45 (1 H, m), 3.39—3.21 (1 H, m), 2.94—2.65 (2 H, m), 2.04—1.10 (9 H, m), and 0.70 (3 H, s). It was shown to be homogeneous by g.l.c. having an R_t value of 52.5 min whereas the *cis*-amine (**17**) had an R_t value of 42 min.

The above amine (0.20 g) on acetylation afforded the crystalline *trans*-acetyl derivative (**20**) (0.19 g, 84%), m.p. 209—210 °C (acetone–light petroleum); $\nu_{max.}$ 1 625 cm^{-1}; δ(100 MHz) for the special features, see Table 3 (Found: C, 74.9; H, 8.15. $C_{23}H_{29}NO_3$ requires C, 75.17; H, 7.95%).

cis-1,2,3,4,4a,10b-*Hexahydro*-4a-*methyl*[1]*benzothieno*[4,3-b]*pyridine* (**15g**) *and the* trans-*Isomer* (**14g**).—(a) *By reduction of the imine* (**3g**) *with* LAH*: formation of a mixture of the amines* (**15g**) *and* (**14g**). The imine (**3g**) (0.1 g) on LAH reduction afforded a reduced amine (0.09 g, 90%), b.p. 130—135 °C (bath)/0.1 mmHg as a 87:13 mixture (from g.l.c. at 190 °C on a Shimadzu GC-9A chromatograph using OV-17 column) of the *cis*-(**15g**) and the *trans*-amine (**14g**) having R_t values of 6.34 and 7.21 min respectively. The special features of its ^1H n.m.r. spectrum (100 MHz) are the two benzylic hydrogen singlets at δ 3.53 and 3.23, and the two angular methyl singlets at δ 0.90 and 0.96 respectively for the *trans*-(**14g**) and the *cis*-amine (**15g**).

(b) *By* $NaBH_4$ *reduction of the imine* (**3g**)*: formation of the* trans-*amine* (**14g**). Reduction of the imine (**3g**) (0.125 g) with $NaBH_4$ furnished a saturated amine (0.115 g, 91%) as a 83:17 mixture (from g.l.c. at 190 °C) of the *trans*-(**14g**) and the *cis*-amine (**15g**) respectively. Recrystallisation of this material provided an analytical sample of the *trans*-amine (**14g**), m.p. 53—54 °C (light petroleum); δ(100 MHz) 7.64—7.48 (1 H, m), 7.26—6.96 (3 H, m), 3.54 (1 H, s), 3.46—3.22 (1 H, m), 3.06 (1 H, d, *J* 12 Hz), 2.90—2.62 (1 H, m), 2.50 (1 H, d, *J* 12 Hz), 1.86—1.32 (5 H, m), and 0.90 (3 H, s) (Found: C, 71.1; H, 8.0. $C_{13}H_{17}S$ requires C, 71.21; H, 7.81%).

(c) *By* $LiBH_4$ *reduction of the imine* (**3g**)*: formation of a mixture of the amines* (**15g**) *and* (**14g**). The imine (**3g**) (0.1 g) on reduction with $LiBH_4$ in diglyme by the procedure described for (**3b**) provided a saturated amine (0.085 g, 85%) as a 37:63 mixture (from g.l.c. at 190 °C) of the *cis*-(**15g**) and the *trans*-amine (**14g**) respectively. The special features of its ^1H n.m.r. spectrum (100 MHz) are the two benzylic hydrogen singlets at δ 3.23 and 3.53, and the two angular methyl singlets at δ 0.96 and 0.90 respectively for (**15g**) and (**14g**).

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