Compounds with Bridgehead Nitrogen. Part 49.[1] The Synthesis and Stereochemistry of Perhydropyrido[3,2,1-*j,k*][3,1]benzoxazepines and of *r*-3a,*t*-11a,*c*-14a, *t*-14b, *t*-22a,*t*-22b-Perhydrodiquino[1,8a,8-*c,d*:1',8a',8'-*j,k*][1,8,3,10]dioxadiazacyclotetradecine

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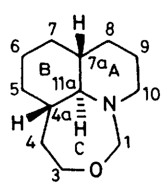
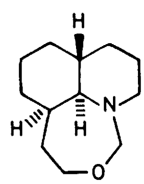
Ring closure of the diastereoisomeric 2-decahydroquinolin-8-ylethanols with formaldehyde gave *r*-4a,*c*-7a,*t*-11a-, *r*-4a,*t*-7a,*t*-11a, and *r*-4a,*c*-7a,*c*-11a-perhydropyrido[3,2,1-*j,k*][3,1]benzoxazepines, but instead of the fourth isomer a dimer, *r*-3a,*t*-11a,*c*-14a,*t*-14b,*t*-22a,*t*-22b-perhydrodiquino[1,8a,8-*c,*-*d*:1',8a',8'-*j,k*][1,8,3,10]dioxadiazacyclotetradecine, was obtained. Comparison of ^{13}C n.m.r. shifts of the conformationally locked isomers with those of perhydropyrido[1,2-*c*][1,3]oxazepine showed different average perhydro-1,3-oxazepine ring conformations in the various structures so that an estimate of the position of conformational equilibrium ($CDCl_3$ solution) of the bicyclic compound from this data could not be made. The ^{13}C n.m.r. spectrum of perhydropyrido[1,2-*c*][1,3]oxazepine in $CDCl_3$—$CFCl_3$, however, showed a ratio of *ca.* 5:1 *trans*-fused:*O*-inside-*cis*-fused conformers at −80 °C.

The stereochemistry of reduced heterocyclic compounds possessing seven-membered rings is complicated by the flexibility of the system. In fused ring derivatives the mobility of the ring is reduced and a knowledge of the stereochemistry of such compounds may assist our understanding of the less restricted ring systems. Accordingly the perhydropyrido[3,2,1-*j,k*][3,1]-benzoxazepines (**1**)—(**4**) were chosen for study.


(**1**)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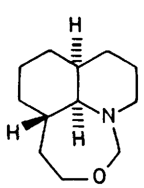
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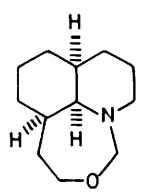
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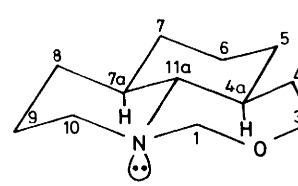
Synthesis of Compounds.—The isomeric perhydropyrido-[3,2,1-*j,k*][3,1]benzoxazepines (**1**)—(**4**) were obtained by a sequence starting from the reaction between morpholinocyclohexene and acrolein followed by treatment of the resultant alkylated enamine with dilute hydrochloric acid to give 3-(2-oxocyclohexyl)propanal.[2]

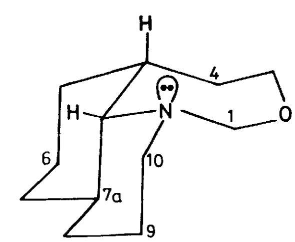
The cyclisation of 3-(2-oxocyclohexyl)propanal to 5,6,7,8-tetrahydroquinoline by treatment with hydroxylamine hydrochloride was based on the method used for the preparation of 6,7,8,9-tetrahydro-5*H*-cyclohepta[*b*]pyridine.[3] The preparation of 2-(5,6,7,8-tetrahydroquinolin-8-yl)ethanol was accomplished by the reaction between 8-lithio-5,6,7,8-tetrahydroquinoline and ethylene oxide based on the method[4] used for the synthesis of 3-(2-pyridyl)propan-1-ol.

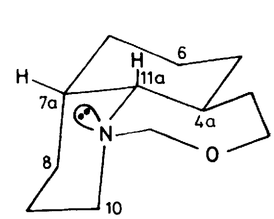
The reduction of 2-(5,6,7,8-tetrahydroquinolin-8-yl)ethanol can give four diastereoisomers, the amount of each produced depending on the mode of reduction. Two of the isomers were produced by reduction with sodium in ethanol and two different isomers by catalytic hydrogenation. The individual diastereoisomers of 2-decahydroquinolin-8-ylethanol were not isolated, but the isomer mixture from each mode of reduction was treated with formaldehyde to give the perhydropyrido[3,2,1-*j,k*][3,1]benzoxazepines (**1**)—(**4**) which were separated by column chromatography over alumina.

Stereochemistry of Perhydropyrido[3,2,1-j,k][3,1]*benzoxazepines.*—An examination of Dreiding models suggests (**1a**), (**2a**), (**3a**), and (**4a**), shown in the Figure as the most favourable conformations of the isomeric perhydropyrido[3,2,1-*j,k*][3,1]-benzoxazepines (**1**)—(**4**).

The assignment of configurations and preferred conform-


(**1a**)


(**2a**)


(**3a**)

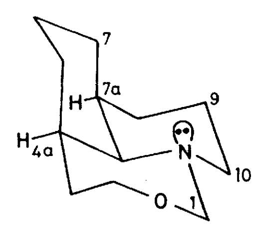

(**4a**)

Figure. The predicted conformations of the perhydropyrido[3,2,1-*j,k*][3,1]benzoxazepines (**1**)—(**4**)

Table 1. ^{1}H N.m.r. spectra of the isomeric perhydropyrido[3,2,1-*j,k*][3,1]benzoxazepines (**1**), (**3**), and (**4**) and perhydrodiquino[1,8a,8-*c,d*:1′,8a′,8′-*j,k*][1,8,3,10]dioxadiazacyclotetradecine (**9**) in $CDCl_3$

Chemical shifts

Compound	1-'*eq*'	1-'*ax*'	3-'*eq*'	3-'*ax*'	10-*eq*	10-*ax*	4a	6-ax	11a
(**1**)	4.25		3.85	3.52	2.90	2.53	—	—	—
(**3**)	4.48		3.85	3.52	2.73	2.78	1.95		2.43
								5-*ax*	
(**4**)	4.11	3.96	3.80	3.72	2.82	2.15		1.94	2.08
	8-'*eq*'	8-'*ax*'	10-'*eq*'	10-'*ax*'	6-*eq*	6-*ax*	3a	22a	22b
	19-'*eq*'	19-'*ax*'	21-'*eq*'	21-'*ax*'	17-*eq*	17-*ax*	14a	11a	14b
(**9**)	4.43	4.06	3.95	3.40	3.00	2.64	2.23		2.17

Coupling constants[a]

Compound	$J_{1\text{-}'ax',1\text{-}'eq'}$	$J_{3\text{-}'ax',3\text{-}'eq'}$	$J_{3\text{-}'ax',4\text{-}'ax'}$	$J_{3\text{-}'ax',4\text{-}'eq'}$	$J_{3\text{-}'eq',4\text{-}'ax'}$	$J_{3\text{-}'eq',4\text{-}'eq'}$	$J_{10\text{-}ax,10\text{-}eq}$	$J_{10\text{-}ax,9\text{-}ax}$	$J_{10\text{-}ax,9\text{-}eq}$	$J_{10\text{-}eq,9\text{-}ax}$	$J_{10\text{-}eq,9\text{-}eq}$	$J_{11a,4a}$	$J_{11a,7a}$
(**1**)		−11.9	11.9	4.0	5.5	1.8	−11.0	11.0	4.9	4.5	2.5		
(**3**)		−11.3	11.3	3.2	3.8	3.8	−12.0	12.0	3.4			10.7	4.8
(**4**)	−10.7	−11.9	11.9	4.8	4.0	1.9	−10.6					*ca.* 6.0	*ca* 6.0
	$J_{8\text{-}'ax',8\text{-}'eq'}$	$J_{10\text{-}'ax',10\text{-}'eq'}$	$J_{10\text{-}'ax',11\text{-}'ax'}$	$J_{10\text{-}'ax',11\text{-}'eq'}$	$J_{10\text{-}'eq',11\text{-}'ax'}$	$J_{10\text{-}'eq',11\text{-}'eq'}$	$J_{6\text{-}ax,6\text{-}eq}$	$J_{6\text{-}ax,5\text{-}ax}$	$J_{6\text{-}ax,5\text{-}eq}$	$J_{6\text{-}eq,5\text{-}ax}$	$J_{6\text{-}eq,5\text{-}eq}$	$J_{22b,3a}$	$J_{22b,22a}$
	$J_{19\text{-}'ax',19\text{-}'eq'}$	$J_{21\text{-}'ax',21\text{-}'eq'}$	$J_{21\text{-}'ax',22\text{-}'eq'}$	$J_{21\text{-}'ax',22\text{-}'eq'}$	$J_{21\text{-}'eq',22\text{-}'ax'}$	$J_{21\text{-}'eq',22\text{-}'eq'}$	$J_{17\text{-}ax,17\text{-}eq}$	$J_{17\text{-}ax,16\text{-}ax}$	$J_{17\text{-}ax,16\text{-}eq}$	$J_{17\text{-}eq,16\text{-}ax}$	$J_{17\text{-}eq,16\text{-}eq}$	$J_{14b,14a}$	$J_{14b,11a}$
(**9**)	−10.7	−11.6	11.6	3.3	3.0	3.0	−11.7	11.3	3.2	5.6	2.5—3.0	9.7	5.6

[a] Geminal coupling constants are assumed to be negative.

Table 2. ^{13}C N.m.r. spectra of the isomeric perhydropyrido[3,2,1-*j,k*][3,1]benzoxazepines (1), (3), and (4) and perhydrodiquino[1,8a,8-*c,d*:1′,8a′,8′-*j,k*][1,8,3,10]dioxadiazacyclotetradecine (9) in $CDCl_3$

Compd.	(1)		(3)		(4)			(9)	
Nucleus	δ	^1J	δ	^1J	δ	^1J	Nucleus	δ	^1J
C-1	85.7	151 (t)	83.5	155 (t)	85.3	149 (t)	C(8)[C(19)]	84.3	147 (t)
C-11a	72.3	130 (d)	67.1	133 (d)	67.1	128 (d)	C(22b)[C(14b)]	67.1	*ca.* 132 (d)
C-3	68.4	143 (t)	67.5	142 (t)	65.5	144 (t)	C(10)[C(21)]	69.5	141 (t)
C-10	54.3	132 (t)	44.8	133 (t)	53.2	132 (t)	C(6)[C(17)]	54.1	131 (t)
C-7a	41.7	*ca.* 130 (d)	36.8	125 (d)	38.7	127 (d)	C(3a)[C(14a)]	37.6	*ca.* 125 (d)
C-4a	39.8	*ca.* 128 (d)	35.6	(d)	42.2	125 (d)	C(22a)[C(11a)]	37.0	*ca.* 125 (d)
C-4	38.7	128 (t)	34.2	123 (t)	32.8	125 (t)	C(11)[C(22)]	33.6	*ca.* 125 (t)
C-5	32.8	130 (t)	29.8	123 (t)	27.1	126 (t)	C(3)[(14)]	33.3	*ca.* 123 (t)
C-8	32.8	128 (t)	25.0	123 (t)	31.0	123 (t)	C(4)[C(15)]	33.1	*ca.* 125 (t)
C-7	33.2	128 (t)	32.1	*ca.* 126 (t)	25.7	126 (t)	C(1)[C(12)]	32.6	*ca.* 125 (t)
C-9	26.7	126 (t)	26.8	128 (t)	21.6	128 (t)	C(5)[C(16)]	26.8	126 (t)
C-6	25.5	128 (t)	20.8	*ca.* 126 (t)	26.0	126 (t)	C(2)[C(13)]	21.3	128 (t)

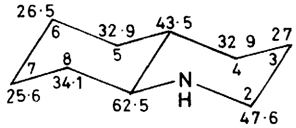
ations of the perhydropyrido[3,2,1-*j,k*][3,1]benzoxazepines (1)—(4) were based on 270 MHz ^{1}H n.m.r. (Table 1) and ^{13}C n.m.r. (Table 2) spectral data.

(i) r-4a,c-7a,t-11a-*Perhydropyrido*[3,2,1-j,k][3,1]*benzoxazepine* (1).—The first isomer eluted in the chromatographic separation of the two isomeric perhydropyrido[3,2,1-*j,k*][3,1]-benzoxazepines obtained by the sodium in ethanol reduction route was assigned the *r*-4a, *c*-7a, *t*-11a configuration (1).

The 270 ^{1}H n.m.r. spectrum of this isomer showed a singlet at δ 4.25 (2 H) assigned to the C-1 methylene protons. The signals at δ 3.85 and 3.52 were assigned to the pseudo-equatorial and pseudo-axial C(3) methylene protons respectively. The coupling of 11.9 Hz between 3-H-′*ax*′ and 4-H-′*ax*′ is of the order of magnitude expected for a vicinal coupling between antiperiplanar protons. This and the values of the other $J_{3,4}$ couplings is consistent with a staggered geometry around the C(3)–C(4) bonds [O–C(3)–C(4)–C(5) dihedral angle of *ca.* 60°].

The two remaining distinguishable signals in the spectrum were a doublet of doublets and a doublet of triplets centred at δ 2.9 and δ 2.53 assigned to the C(10) equatorial and axial protons respectively. The vicinal coupling constants between these protons (Table 1) are consistent with the chair conformation of ring A. Signals from 11a-H, observed in the spectra of the other isomers, were hidden under the methylene envelope (δ to high field of 2.00). This highfield shift is clear evidence for the stereochemistry (1a). In such a structure the 11a-H is expected to be shielded by the antiperiplanar nitrogen lone pair [5] and by the two vicinal equatorial C-5 and C-7 methylene groups.[6]

The ^{13}C n.m.r. data of *r*-4a,*c*-7a,*t*-11a-perhydropyrido[3,2,1-*j,k*][3,1]benzoxazepine (1) are given in Table 2. The C-3, C-1, C-10, and C-11a signal assignments were based on the known electronegativity effects on chemical shifts [7,8] and the variations in $^1J_{^{13}C\text{-}H}$ couplings with adjacent heteroatoms.[9] The signal arising from C-11a was readily distinguished by its appearance in the undecoupled spectrum as a doublet. The remaining assignments were based on a comparison of the observed shifts (Table 2) with those calculated for the hypothetical conformer (6) from the ^{13}C shifts of *trans*-decahydroquinoline (5) adjusted



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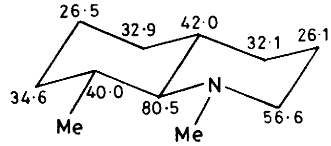
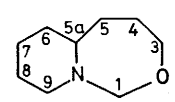


(6)

for the effects of the *N*-methyl [7] and 8-methyl substituents.[10] The observed ^{13}C chemical shifts (see Table 2) for the isomer (1) are in reasonable agreement with the calculated values for compound (6), especially since the effect of the remainder of the hexahydro-1,3-oxazepine ring on the chemical shifts has not been taken into account. Thus the ^{13}C n.m.r. data along with all the other data including clearly defined absorption in the 2 800—2 600 cm^{-1} region of the i.r. spectrum [11] are in complete agreement with isomer (1) existing in conformation (1a).

(ii) r-3a,t-11a,c-14a,t-14b,t-22a,t-22b-*Perhydrodiquino*[1,8a,-8-c,d:1′,8a′,8′-j,k][1,8,3,10]*dioxadiazacyclotetradecine*.—The second compound eluted in the chromatographic separation of the mixture of compounds obtained by the sodium in ethanol reduction route was initially thought to be one of the isomers of (1)—(4). Indeed all the spectroscopic data were consistent with this expectation. The compound was, however, a crystalline solid (m.p. 98—100 °C), insoluble in acetonitrile, whereas the other three isomers were all colourless mobile liquids readily soluble in acetonitrile.



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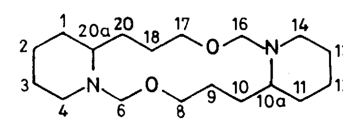

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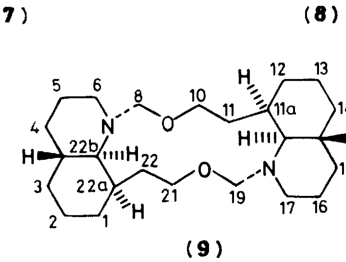


(9)

Since the related perhydropyrido[1,2-*c*][1,3]oxazepine (7) crystallises as the dimer, perhydropyrido[1,6-*c*:1′,6′-*j*][1,8,3,10]dioxadiazacyclotetradecine (8),[12] it seemed probable that the crystalline product was dimeric. In fact, the field desorption mass spectrum of the compound gave M^+ at 390 (13.9%) with M^+ + 1 at 391 (13.4%) confirming the dimeric nature of the substance ($C_{24}H_{42}N_2O_2$ 390) which was assigned the structure shown in (9) on the spectral data outlined below.

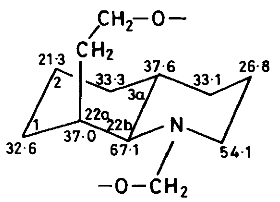
The 270 MHz n.m.r. spectrum of compound (9) showed a doublet of triplets at δ 3.0 and a well resolved triplet of doublets at δ 2.64 assigned to the C-6 equatorial and axial protons respectively. The values of the vicinal couplings between these methylene protons are consistent with a chair conformation for ring A.

The C-8 methylene protons absorbed as a lowfield AB quartet at δ 4.43 and δ 4.06 showing the largest N–CH_2–O *chemical*-shift difference (0.37 p.p.m.) of the four compounds.

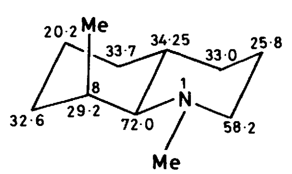
The signals at δ 3.95 and δ 3.40 were readily assigned to the C-10 equatorial and axial protons respectively. The observed splittings are in accord with an approximate axial–equatorial relationship between the C-10 and C-11 methylene bonds.

In addition, two other sets of signals were observed in the 270 ^{1}H n.m.r spectrum of compound (**9**): a two-proton broad multiplet at δ 2.23 and an approximation to a doublet of doublets at δ 2.17 (1 H). Inspection of Dreiding models of the dimer suggests assignment of these signals to the three ring junction protons 3a-H, 22a-H, and 22b-H. 22b-H Is expected to absorb as a doublet of doublets with one large coupling ($J_{22b,3a}$) and one smaller coupling ($J_{22b,22a}$). Analysis of the signals at δ 2.17 gave two splittings of 9.7 and 5.6 Hz which may approximate to these vicinal coupling constants. This confirms the *trans* A/B ring fusion and the axial orientation of the C-22 methylene group.

The assignment of the signals in the ^{13}C n.m.r. spectrum of perhydrodiquino[1,8a,8-*c,d*:1′,8a′,8′-*j,k*][1,8,3,10]dioxadiazacyclotetradecine (**9**) was assisted by reference to the shifts observed[13] for compound (**10**).



(9a)



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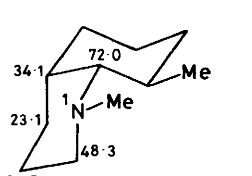

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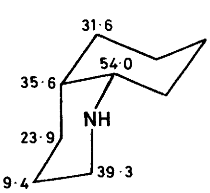


(12)

A comparison of the ^{13}C shifts of the decahydroquinoline carbon nuclei in isomer (**1a**) with those in the dimer (**9**) [see structure (**9a**)] confirms the presence in (**9**) of the axial methylene at C-22a. Thus C-2 and C-3a are shielded (4.2 and 4.1 p.p.m. respectively) relative to the corresponding nuclei in (**1a**) as a consequence of the γ-substituent effect.[10] The C-5 and C-6 shifts are very similar to those for C-9 and C-10 in compound (**1a**) confirming the *trans* AB geometry.

(iii) r-4a,t-7a,t-11a-*Perhydropyrido*[3,2,1-j,k][3,1]*benzoxazepine* [3).—The first isomer eluted from the chromatographic separation of the mixture obtained *via* the catalytic reduction of 2-(5,6,7,8-tetrahydroquinolin-8-yl)ethanol was assigned the *r*-4a,*t*-7a,*t*-11a configuration (**3**).

The 270 MHz n.m.r. spectrum of (**3**) showed a distinctive doublet of doublets at δ 2.43 which was assigned to the 11a-proton. In conformation (**3a**) the nitrogen lone pair and 11a-H are not *trans*-diaxial as in (**1a**), leading to a relative deshielding. The magnitude of the two couplings involving the 11a-proton (10.7 and 4.8 Hz) are of the order expected for vicinal $J_{ax,ax}$ and $J_{ax,eq}$ couplings and indicate conformation (**3a**). [These 11a-H parameters are also consistent with (**2a**) but this structure is ruled out, in particular by the ^{13}C-10 shift—see below.]

The sharply resolved doublet of triplets at δ 3.85 and the triplet of doublets at δ 3.52 were assigned to the 3-H-′*eq*′ and 3-H-′*ax*′ respectively. The magnitudes of the couplings $J_{3'ax',4'eq'}$, $J_{3'eq',4'ax'}$, and $J_{3'eq',4'eq'}$ (Table 1) suggest a near staggered relationship between the C-3 and C-4 methylene bonds.

The two overlapping signals at δ 2.78 and 2.73 were assigned to the C(10) axial and equatorial protons respectively. These signals approximate to a triplet of doublets (axial proton) overlapping a broad doublet (equatorial proton). The very small negative chemical shift difference (0.05 p.p.m.) is due to the deshielding of 10-H_{ax} by the C(1)–O bond and support conformation (**3a**) rather than (**2a**).

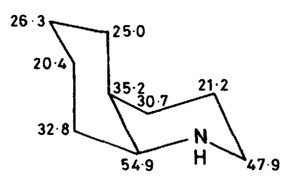
The ^{13}C chemical shift assignments were aided by comparison with shifts for (**11**) estimated from those for *N*-outside-*cis*-decahydroquinoline (**12**)[7] adjusted for the two methyl substituent effects.[7,10] The most notable feature of the ^{13}C n.m.r. spectrum of isomer (**3**) is the highly shielded signal for C-10 [δ 44.8, *cf.* 54.3 and 54.1 (in (**1a**) and (**9a**) respectively] and for C-8 [δ 25.0, *cf.* 32.8 and 33.1 in (**1a**) and (**9a**) respectively] arising from γ-interactions in the *cis*-fused structure (**3a**). These shieldings indicate structure (**3a**) rather than (**2a**). The absence of absorption in the 2 800—2 600 cm^{-1} region of the i.r. spectrum[11] supports the assignment of the *cis*-A/C ring fusion.

(iv) r-4a, c-7a, c-11a-*Perhydropyrido*[3,2,1-j,k][3,1]*oxazepine* (**4**).—The *r*-4a,*c*-7a,*c*-11a configuration (**4**) was assigned to the second isomer obtained by the catalytic hydrogenation route.

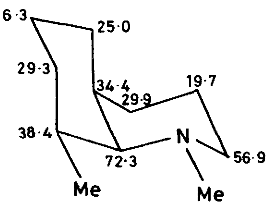
In the 270 MHz ^{1}H n.m.r. spectrum of (**4**) the multiplet centred at δ 3.80 was assigned to the C-3 equatorial proton and the triplet of doublets at δ 3.72 assigned to the axial proton. The coupling constants between the C-3 and C-4 methylene protons abstracted from these signals (Table 1) are consistent with the normal axial–axial (dihedral angle 180°) and axial–equatorial (60°) couplings. 11a-H absorbed at δ 2.08 and gave $J_{11a,4a} = J_{11a,7a}$ of *ca.* 6.0 Hz consistent with (**4a**). In addition, a quartet of doublets at δ 1.94 was assigned to 5*ax*-H deshielded by the C(3)–O and C(11a)–N bonds in (**4a**). The large chemical-shift difference ($\Delta_{10ax,10eq}$ = 0.67 p.p.m.) observed between the C-10 methylene protons confirmed the *trans*-A/C ring fusion.

The ^{13}C shift assignments in (**4a**) were based on those shown in (**14**) calculated from the shifts in *N*-inside-*cis*-decahydroquinoline (**13**).[7] The shieldings of C-7 and C-9 relative to the corresponding shifts in (**1a**) and (**3a**) indicate the γ-interactions with C-9 and the heteroatoms and confirm structure (**4a**). The *trans*-A/C ring fusion is supported by strong Bohlmann bands[11] in the i.r. spectrum.

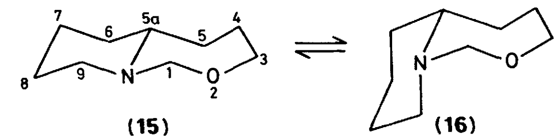
Conformational Equilibrium in Perhydropyrido[1,2-c][1,3]-*oxazepine* (**7**).—Comparison of the ^{13}C shifts (recorded in $CDCl_3$ at 25 °C) of perhydropyrido[1,2-*c*][1,3]oxazepine (**7**) (see Table 3) with those in the locked *trans*-fused (**1a**) and the locked *cis*-fused (**3a**) show that an estimate of the position of *cis*⇌*trans* conformational equilibrium [(**15**)⇌(**16**)] in (**7**) cannot be based on such comparisons. For example, although comparison of C-9 (δ 50.8) in (**7**) with δ 54.3 in (**1a**) and δ 44.8 in (**3a**) might be taken as indicating a (**15**)⇌(**16**) equilibrium containing *ca.* 70% (**15**), a comparison of the C-1 shifts [δ 87.5 in (**7**), 85.7 in (**1a**) and 83.5 in (**3a**)] shows the shifts for (**7**) lying outside the range spanned by (**1a**) and (**3a**). This is not unexpected since the additional ring fusion in (**1a**) and (**3a**) must



(13)



(14)



(15) (16)

influence the average seven-membered ring conformations in the various structures and so make comparisons inappropriate.

The ^{13}C n.m.r. spectrum of (7) in $CDCl_3$–$CFCl_3$ at −80 °C using gated decoupling so that no nuclear Overhauser enhancements are involved showed absorption for both conformers (**15**) and (**16**) (see Table 3), and integration of the signals from C-1, C-3, and C-5a enabled an estimate of the equilibrium position to be made as *ca.* 5:1 *trans*-fused (**15**)–*cis*-fused (**16**) at that temperature. If entropy changes are assumed to be negligible then at 25 °C the equilibrium should contain *ca.* 26% *cis*-fused conformer (**16**).

Table 3. ^{13}C N.m.r. spectra of perhydropyrido[1,2-*c*][1,3]oxazepine (**7**)

Carbon nucleus	(7)[a] Chemical shift (δ)	(7)[b] Chemical shift (δ)	(7)[c] Chemical shift (δ) *trans* (15)	(7)[c] Chemical shift (δ) *cis* (16)
C-1	87.8	87.5	88.1	84.5[c]
C-3	70.3	70.2	70.8	69.2
C-4	29.6	29.3	29.7	28.1
C-5	33.5	33.3	34.0	31.5
C-5a	62.5	62.3	63.8	60.0
C-6	31.5	31.5	32.2	28.1
C-7	23.3	23.1	24.9	19.0
C-8	26.7	26.4	26.3	26.3
C-9	51.1	50.9	53.9	43.9

[a] Solvent $CDCl_3$—$CFCl_3$ at ambient temperature. [b] Solvent $CDCl_3$ at ambient temperature. [c] Solvent $CDCl_3$—$CFCl_3$ at −80 °C.

Experimental

Elemental analyses were carried out by the Analytical Section, Department of Chemistry, Portsmouth Polytechnic, and Butterworth Micro-Analytical Consultancy, Teddington, Middlesex. I.r. spectra were recorded on Perkin-Elmer 237 and 297 grating instruments as 0.2M-solutions in deuteriochloroform using 0.2-mm matched cells. The ^1H n.m.r. spectra were determined on a Bruker WH 270 spectrometer as 10% solutions with tetramethylsilane as internal reference. The error in the measurement of the chemical shifts was ±0.02 p.p.m. and for the coupling constant ±0.25 Hz.

The ^{13}C n.m.r. spectra of compounds (**1**), (**3**), (**4**), and (**9**) were obtained from the P.C.M.U. at Harwell on a Bruker 90 F.T. spectrometer operating at 25.2 MHz; spectral width 6024 Hz (decoupled) and 3012 Hz (undecoupled) with 4096 memory points; pulse width 11 μs; pre-delay time 143 μs; number of scans accumulated 1 000—2 000 (decoupled) or 20 000—40 000 (undecoupled). Samples were dissolved in equal volumes of $CDCl_3$ with tetramethylsilane as internal reference. $^1J_{^{13}C\text{-}H}$ Couplings are considered to be accurate to ±1.0 Hz and chemical shifts to ±0.05 p.p.m. The low temperature ^{13}C n.m.r. spectrum of compound (**7**) was obtained on a Jeol FX 900 spectrometer (City of London Polytechnic). Ether refers to diethyl ether throughout.

3-(2-*Oxocyclohexyl*)*propanal*.—To a solution of freshly distilled 1-morpholinocyclohexene (2 mol, 334 g) in dry ether (150 ml) at 0 °C was added slowly during 1 h a solution of acrolein (2 mol, 132 ml) in dry ether (2 l), under nitrogen. The resulting solution was stirred for 1 h at room temperature before hydrochloric acid (100 ml concentrated hydrochloric acid made up to 550 ml with distilled water) was added and stirred for a further 0.5 h. The ether layer was separated and washed with saturated aqueous sodium hydrogen carbonate (3 × 300 ml). The ethereal solution was dried (Na_2SO_4), concentrated, and the residue distilled *in vacuo* to give 3-(2-oxocyclohexyl)propanal (102 g, 33%) as a colourless oil, b.p. 90—92 °C at 0.2 mmHg (lit.,[14] 141.5 °C at 22 mmHg).

5,6,7,8-*Tetrahydroquinoline*.—A solution of 3-(2-oxocyclohexyl)propanal (0.66 mol, 102 g) in absolute ethanol (100 ml) was added to a refluxing solution of hydroxylamine hydrochloride (0.66 mol, 46 g) in absolute ethanol (500 ml). The solution rapidly became dark and eventually black. This solution was refluxed for 2 h, after which the ethanol was removed under reduced pressure. The residue was basified with 30% aqueous sodium hydroxide and the solution extracted with ether (3 × 400 ml). The combined ethereal solutions were dried (Na_2SO_4), concentrated, and the crude black residue distilled *in vacuo* to give 5,6,7,8-tetrahydroquinoline (35 g, 40%) as a colourless oil, b.p. 62—64 °C at 0.25 mmHg (lit.,[15] 92—93 °C at 12 mmHg).

2-(5,6,7,8-*Tetrahydroquinolin*-8-*yl*)*ethanol*.—A solution of 5,6,7,8-tetrahydroquinoline (1.0 mol, 133 g) in dry ether (150 ml) was added during 0.75 h to a solution of phenyl-lithium, formed *in situ* by the addition of bromobenzene (1.06 mol, 167 g) to a rapidly stirred suspension of lithium metal (14 g) in dry ether (1.5 l) under nitrogen. The resulting red-brown solution of 8-lithio-5,6,7,8-tetrahydroquinoline was stirred for an additional 1 h. The reaction mixture was cooled to 0 °C with ice, and ethylene oxide (1 mol, 44 g) in sodium dried ether (50 ml) added slowly with stirring during 0.75 h. The red solution this formed was stirred for 1 h and 6M-hydrochloric acid added until the pH of the solution was 1—2. The aqueous layer was separated and basified with saturated aqueous sodium carbonate and extracted with chloroform. The combined extracts were dried (K_2CO_3), concentrated and distilled *in vacuo* to give 2-(5,6,7,8-*tetrahydroquinolin*-8-*yl*)*ethanol* (45 g, 25%), b.p. 110—112 °C at 0.1 mmHg (Found: C, 64.2; H, 8.6; N, 8.0. $C_{11}H_{15}NO$ requires C, 64.4; H, 8.5; N, 7.9%).

2-*Decahydroquinolin*-8-*ylethanol*.—(*a*) Reduction by sodium in ethanol. A solution of 2-(5,6,7,8-tetrahydroquinolin-8-yl)ethanol (0.4 mol, 70.8 g) in absolute ethanol (750 ml) was boiled under reflux and sodium metal (120 g) added slowly during *ca.* 1.5 h. The solution was boiled under reflux for a further 2 h before being cooled to room temperature. The solution was acidified carefully with hydrochloric acid until its pH was 1, and was then basified with 30% aqueous sodium hydroxide, and extracted with ether (3 × 300 ml). The combined ether extracts were dried (Na_2SO_4), concentrated, and the residue distilled *in vacuo* to give a mixture of isomeric 2-*decahydroquinolin*-8-*ylethanols* (36 g, 50%) as a pale yellow oil, b.p. 119—121 °C at 0.07 mmHg (Found: C, 72.2; H, 11.7; N, 7.6. $C_{11}H_{21}NO$ requires C, 72.1; H, 11.55; N, 7.6%).

(*b*) *Catalytic hydrogenation.* 2-(5,6,7,8-Tetrahydroquinolin-8-ylethanol (0.4 mol, 70.8 g) was dissolved in glacial acetic acid (180 ml) and reduced with hydrogen at 98 lb in^{-2} in a Parr hydrogenator in the presence of Adams platinum oxide catalyst (1 g). When the reduction was complete, the catalyst was filtered off and the acetic acid removed *in vacuo*. The residue was basified with 30% aqueous sodium hydroxide. This solution was extracted with ether (3 × 300 ml), and the extracts were combined, dried (Na_2SO_4), concentrated, and the residue distilled *in vacuo* to yield a mixture of isomeric 2-*decahydroquinolin*-8-*ylethanols* (53 g, 72%), b.p. 106—108 °C at 0.4 mmHg (Found: C, 72.4; H, 11.5; N, 7.4. $C_{11}H_{21}NO$ requires C, 72.1; H, 11.55; N, 7.6%).

r-4a,c-7a,t-11a-*Perhydropyrido*[3,2,1-j,k][3,1]*benzoxazepine* (**1**) *and Perhydrodiquino*[1,8a,8-c,d:1′,8a′8′-j,k][1,8,3,10]*dioxadiazacyclotetradecine* (**9**).—The mixture of 2-decahydroquinolin-8-ylethanols (0.14 mol, 25.0 g) prepared by the sodium in ethanol reduction was shaken with excess of 36% aqueous formaldeyde (26 ml) for 1 h. The solution was basified with 30% aqueous sodium hydroxide, extracted with ether (4 × 75 ml), and the combined ether extracts dried (Na_2SO_4), concentrated, and the residue distilled *in vacuo* to give an oil (22 g, 81%), b.p. 97—102 °C at 1.2 mmHg. This (20 g) was chromatographed over a column of H-type grade 3 alumina (2 000 g) [elution with 25% ether in light petroleum (b.p. 40—60 °C); 150-ml fractions]. r-4a,c-7a,t-11a-*perhydropyrido*[3,2,1-j,k][3,1]*benzoxazepine* (**1**) (4 g) was eluted first b.p. 91—93 °C at 0.7 mmHg (Found: C, 73.6; H, 10.85; N, 7.1. $C_{12}H_{21}NO$ requires C, 73.8; H, 10.8; N, 7.2%) and *perhydrodiquino*[1,8a,8-c,d:1′,8a′,8′-j,k][1,8,3,10]*dioxadiazacyclotetradecine* (**9**) (3.2 g) was eluted second, m.p. 98—100 °C (Found: C, 73.8; H, 10.95; N, 7.4. $C_{24}H_{42}N_2O_2$ requires C, 73.8; H, 10.8; N, 7.2%).

r-4a,t-7a,t-11a- *and* r-4a,c-7a,c-11a-*Perhydropyrido*[3,2,1-j,k][3,1]*benzoxazepine* (**3**) *and* (**4**).—The mixture of 2-decahydroquinolin-8-ylethanols (0.14 mol, 25 g) prepared by catalytic reduction was ring closed with 36% aqueous formaldehyde solution (26 ml) and separated by column chromatography as above. The first isomer to be eluted was r-4a,t-7a,t-11a-*perhydropyrido*[3,2,1-j,k][3,1]*benzoxazepine* (**3**) (1.5 g), b.p. 83—86 °C at 0.2 mmHg (Found: C, 73.9; H, 10.85; N, 7.25. $C_{12}H_{21}NO$ requires C, 73.8; H, 10.8; N, 7.2%), followed by r-4a,c-7a,c-11a-*perhydropyrido*[3,2,1-j,k][3,1]*benzoxazepine* (**4**) (3.8 g), b.p. 98—100 °C at 1.0 mmHg (Found: C, 73.7; H, 10.6; N, 7.05. $C_{12}H_{21}NO$ requires C, 73.8; H, 10.8; N, 7.2%).

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