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Reference Data

NMR Spectra and Stereochemistry of Perhydrooxazolo[3,4-*a*]pyridines*

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Low-temperature ^{13}C and ^{1}H NMR spectra show perhydrooxazolo[3,4-*a*]pyridine to exist in $CDCl_3$–$CFCl_3$ solution at 183 K as an equilibrium between 73% *trans*-fused and 27% *O*-inside *cis*-fused conformers. *cis*-(H-1, H-8a)-1-Alkylperhydrooxazolo-[3,4-*a*]pyridines (alkyl = methyl, ethyl, isopropyl) adopt equilibria heavily biased towards the *trans*-fused conformers, whereas the epimers adopt 18% *O*-inside *cis*-fused ⇌ 82% *trans*-fused conformational equilibria at 183 K in $CDCl_3$–$CFCl_3$. At 190 K in $CDCl_3$ *cis*-(H-6, H-8a)-6-ethylperhydrooxazolo[3,4-*a*]pyridine adopts an equilibrium containing *ca* 3% *trans*-fused conformer in equilibrium with 97% *O*-inside *cis*-fused conformer.

* Part 55 in the series 'Compounds with Bridgehead Nitrogen.' For Part 54, see Ref. 1.

INTRODUCTION

The conformational equilibria (e.g. **1a** ⇌ **1b**) in perhydrooxazolo[3,4-*a*]pyridines have been investigated by NMR spectroscopy[2–6] using model compounds to obtain shifts for the various conformers. Such estimates of the position of equilibrium are open to objection, since even remote substitution may exert an effect on the NMR parameter in question. Accordingly, low-temperature NMR spectra of the perhydrooxazolo[3,4-*a*]pyridines have been measured in order to provide direct estimates of equilibria positions.

RESULTS AND DISCUSSION

The low-temperature ^{13}C NMR spectra of **1**, **3** and **5** in $CDCl_3$–$CFCl_3$ at 183 K showed two sets of signals, assigned as in Table 1 to the *trans* conformers (**1a**, **3a** and **5a**) and the *O*-inside *cis* conformers (**1b**, **3b** and **5b**), largely on the basis of the upfield shifts of C-1 and C-7 due to γ-axial interactions. Estimates of equilibria in $CDCl_3$–$CFCl_3$ solutions based on integration of comparable signals (provided in the footnotes to Table 1) compare favourably with those reported previously.[2–6] The position of the **1a** ⇌ **1b** equilibrium was confirmed by the ^{1}H NMR spectrum of **1** recorded in CD_2Cl_2–CS_2 at 173 K (Table 2). Similar conformational equilibria positions to that adopted by **5** are indicated for **7** and **9** by the spectral data (Tables 1 and 2), which also show that **2**, **4**, **6** and **8** adopt exclusively the *trans*-fused conformations.

EXPERIMENTAL

Elemental analyses were carried out by the Butterworth Microanalytical Consultancy, Teddington, Middlesex. Melting points are uncorrected.

The ^{1}H NMR spectra were recorded as 10% solutions in the appropriate solvent with tetramethylsilane (TMS) as internal reference, on a Bruker WH270 spectrometer. Accumulated scans over 4K data points were normally 100, and the resultant FID was Fourier transformed over 8K data points after application of a trapezoidal window filter to the FID signal; the resultant peak-to-peak resolution was 0.1 Hz, with an error of ±0.7 Hz when the sweep width was *ca* 3 kHz (3012 Hz). The ^{13}C NMR spectra were recorded on a Jeol FX90Q (22.5 MHz) Fourier transform spectrometer as *ca* 10% solutions with TMS as internal reference; pulse length 6 μs, pulse interval 2 s, 2000 scans. ^{13}C chemical shifts are considered to be accurate to ±0.05 ppm and $^{1}J(CH)$ values to ±1.0 Hz.

Table 1. ^{13}C NMR spectra ($CDCl_3$–$CFCl_3$)[a] of perhydrooxazolo[3,4-*a*]pyridines

		Chemical shifts, (ppm)							
Compound	Temperature (K)	C-1	C-3	C-5	C-6	C-7	C-8	C-8a	Alkyl
1	273	69.0	86.9	47.7	25.0	22.5	25.7	60.8	
1a[b]	183	71.6	85.8	47.4	24.5	23.6	26.5	61.8	
1b	183	62.9	88.5	47.1	24.8	18.5	22.5	57.4	
2	301[a]	71.5	86.0	53.3	37.6	30.9	26.5	62.35	27.3, 11.65
2	185	71.5	85.6	52.85	37.3	30.6	26.3	62.1	27.25, 11.9
3	301	64.0	88.4	53.1	37.4	22.8	25.5	58.1	27.1, 11.4
3a[c]	190	71.6	85.6	52.9	37.4	30.5	19.8	62.1	27.3, 11.6
3b	190	62.9	88.6	52.9	37.4	22.6	24.8	57.4	27.3, 11.6
4	301	76.1	86.0	48.4	24.1	24.6	24.9	64.5	17.6
5	298	76.8	85.9	48.2	24.9	23.0	25.8	68.4	18.0
5a[d]	183	78.9	85.5	47.8	24.4	23.5	26.2	68.4	17.9
5b	183	75.9	86.8	48.4	24.4	18.5	30.0	64.4	19.1
6	298	81.4	85.8	48.4	24.8	24.2	24.8	64.5	24.5, 10.3
7	298	81.9	85.8	48.0	24.8	22.9	26.2	66.3	26.1, 10.4
8	298	85.2	85.2	48.1	24.3	23.7	24.4	63.8	29.3, 18.8, 20.3
9	298	85.5	85.7	47.9	23.5	23.0	24.2	64.2	31.2, 18.5, 19.1

[a] Ambient temperature spectra of all the compounds in $CDCl_3$–$CFCl_3$ and in $CDCl_3$ provide very similar chemical shift values.
[b] 73% **1a** ⇌ 27% **1b** at 183 K.
[c] 3% **3a** ⇌ 97% **3b** at 190 K.
[d] 82% **5a** ⇌ 18% **5b** at 183 K.

Reference Data

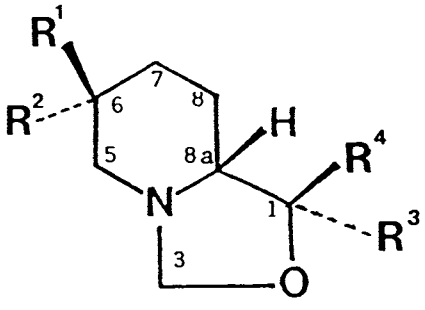
Table 2. ^{1}H NMR spectra of perhydrooxazolo[3,4-*a*]pyridines

			Chemical shifts, δ (ppm)													
Compound	Solvent	Temperature (K)	1'eq'	1'ax'	3'eq'	3'ax'	5eq	5ax	6eq	6ax	7eq	7ax	8eq	8ax	8a	Alkyl
1[a]	CD_2Cl_2–CS_2	300	3.74	3.34	4.40	3.81	2.85	2.20							2.42	
1a	CD_2Cl_2–CS_2	173	3.92	3.38	4.50	3.68	3.02	2.01							2.12	
1b	CD_2Cl_2–CS_2	173	3.48	3.55	4.27	4.33	2.50	2.72							3.38	
2	$CDCl_3$	301	3.95	3.46	4.59	3.78	3.06	1.74	—	1.58	1.80	1.00	1.90	1.32	2.21	1.28, 0.92
3	$CDCl_3$	301	3.62	3.48	4.40	4.33	2.73	2.30	—	1.49	1.78	1.05	1.64	1.97	3.23	1.26, 0.90
6	$CDCl_3$	301	3.90		4.60	3.73	3.04	2.02			1.85				2.23	1.44, 0.96
7[a]	$CDCl_3$	301		3.58	4.54	3.95	2.90	2.07			1.82				2.24	1.53, 1.02
8	$CDCl_3$	301	3.69		4.58	3.83	3.03	2.12	1.57	1.57	1.87	1.29	1.69	1.43	2.39	1.76, 0.98, 0.89
9[a]	$CDCl_3$	301		3.42	4.42	3.89	2.93	2.18							2.24	0.98, 0.95

			Coupling constants (Hz)							
Compound	Solvent	Temperature (K)	1'eq', 1'ax'	1'eq', 8a	1'ax', 8a	3'eq', 3'ax'	5eq, 5ax	5ax, 6ax	5ax, 6eq	8a, 8ax
1[a]	CD_2Cl_2–CS_2	300	−6.8	6.8	10.3	−2.5				
1a	CD_2Cl_2–CS_2	173	−6.7	6.7		0	−9.7			
1b	CD_2Cl_2–CS_2	173				−5.8				
2	$CDCl_3$	301	−6.6	6.6	9.4	−0.8	−10.3	10.3		
3	$CDCl_3$	301	−7.2	7.2	9.7	−5.6	−10.6	10.6		
6	$CDCl_3$	301		6.9		−1.3	−10.6	11.3	3.4	10.0
7[a]	$CDCl_3$	301			8.1	−2.5	−11.3	8.9	3.8	10.6
8	$CDCl_3$	301		6.7		−1.1	−11.3	9.7		11.9
9[a]	$CDCl_3$	301			8.75	−2.8	−10.6	8.8		

[a] Spectra represent average of *trans*-⇌*cis* conformational equilibria.

Compounds **1** and **4**–**9** were prepared by modifications of published routes.[2,3]



1 $R^1 = R^2 = R^3 = R^4 = H$

2 $R^1 = Et$, $R^2 = R^3 = R^4 = H$

3 $R^1 = R^3 = R^4 = H$, $R^2 = Et$

4 $R^3 = Me$, $R^1 = R^2 = R^4 = H$

5 $R^4 = Me$, $R^1 = R^2 = R^3 = H$

6 $R^3 = Et$, $R^1 = R^2 = R^4 = H$

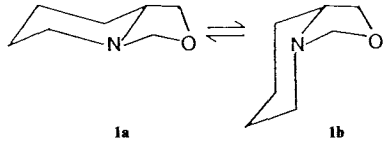
7 $R^4 = Et$, $R^1 = R^2 = R^3 = H$

8 $R^3 = i\text{-Pr}$, $R^1 = R^2 = R^4 = H$

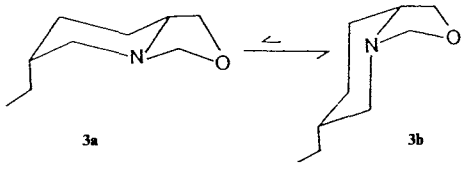
9 $R^4 = i\text{-Pr}$, $R^1 = R^2 = R^3 = H$

5-Ethyl-2-piperidylcarbinol

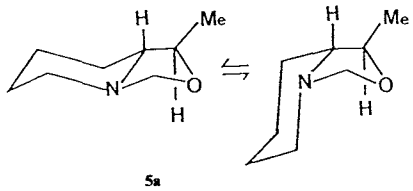
2-(5-Ethylpyridyl)carbinol (0.3 M, 40 g) was dissolved in glacial acetic acid (100 ml) and reduced with hydrogen at 60 lb in^{-2} in a Parr hydrogenator in the presence of Adams platinum oxide catalyst (1 g). When the reduction was complete the catalyst was filtered off and the acetic acid removed *in vacuo*. The residue was basified with 30% aqueous sodium hydroxide solution and extracted with diethyl ether (3 × 200 ml). The combined extracts were dried (Na_2SO_4), concentrated and the residue was distilled *in vacuo* to yield a mixture of the 5-ethyl-2-piperidylcarbinols (33 g, 79%) as a colourless oil, b.p. 89–90 °C at 0.04 mmHg (found, C 67.2, H 12.15, N 9.6; $C_8H_{17}NO$ requires C 67.1, H 12.0, N 9.8%).



1a **1b**



3a **3b**



5a **5b**

6-Ethylperhydro-oxazolo[3,4-*a*]pyridine

The mixture of isomeric 2-(5-ethylpiperidyl)-carbinols (0.16 M, 23 g) was shaken with an excess of 36% aqueous formaldehyde solution (20 ml) for 0.5 h. The solution was basified with 30% sodium hydroxide solution and extracted with diethyl ether (3 × 60 ml). The extracts were combined, dried (Na_2SO_4), concentrated and the residue was distilled *in vacuo* to give a mixture of 6-ethylperhydrooxazolo[3,4-*a*]pyridines (20.7 g, 83%) as a colourless oil, b.p. 87–90 °C at 6.5 mmHg. Isomer separation (4 g of mixture) was achieved by column chromatography over Grade IV Woelm neutral alumina (400 g). Elution was begun with light petroleum (b.p. 40–60 °C) (1 l) followed by diethyl ether–light petroleum (5:95). Sixty fractions (15 ml) of the latter solvent were collected before the eluate was detected. The progress of the elution was monitored by ^{1}H NMR spectroscopy. Evaporation of the next 100 fractions gave *trans*-(H-6, H-8*a*)-6-ethylperhydro-oxazolo[3,4- *a*]pyridine (found, C 69.8, H 11.1; N 8.8; $C_9H_{17}NO$ requires C 69.6, H 11.0, N 9.0%). The following 200 fractions yielded a mixture of isomers but the next 100 fractions gave, on evaporation, *cis*-(H-6, H-8a)-6-ethylperhydrooxazolo[3,4-*a*]pyridine (found, C 69.7, H 10.8, N 9.0; $C_9H_{17}NO$ requires C 69.6, H 11.0, N 9.0%).

Acknowledgements

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Reference Data

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2. T. A. Crabb and R. F. Newton, *Tetrahedron* **24**, 1997 (1968).
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^{13}C NMR Chemical Shift Assignments for Some Carbazole Derivatives

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^{13}C NMR chemical shift assignments have been made for a series of 1-substituted carbazoles, 8-substituted 1,2,3,4-tetrahydrocarbazoles, 1-substituted benzo[*a*]carbazoles and 6-substituted dibenzo[*c,g*]carbazoles. Single examples were examined of other classes of substituted carbazoles: 3-butylcarbazole and its tetrahydro precursor 6-butyl-1,2,3,4-tetrahydrocarbazole, 8-butyl- and 8,10-diethylbenzo[*a*]carbazoles and their 5,6-dihydro precursors, dibenzo[*a,i*]carbazole and its 5,6,7,8-tetrahydro precursor, benzo[*c*]carbazole and its 6-chloro derivatives and 5,6-dihydrobenzo[*c*]carbazole and 5,6,8,9-tetrahydrodibenzo[*c,g*]carbazole and their *N*-methyl derivatives. In addition, the *N*-(1-pyrrolidinomethyl) derivatives of carbazole, 1,2,3,4-tetrahydrocarbazole, benzo[*c*]carbazole and dibenzo[*c,g*] carbazole were also studied.

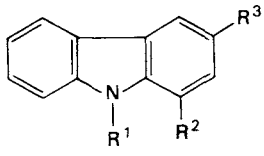
KEY WORDS ^{13}C NMR Chemical shift assignments Carbazole derivatives.

INTRODUCTION

Although several publications are available on the ^{13}C NMR chemical shift assignments of carbazoles, these mainly deal with *N*-substituted or symmetrically substituted compounds,[1–4] and the amount of data for unsymmetrical *C*-substituted derivatives is limited.[5,6] We now report the analyses of the ^{13}C NMR spectra of a range of unsymetrically substituted carbazoles, including some benzo and dibenzo derivatives, which allow considerable insight into the pattern of chemical shifts in these compounds.

EXPERIMENTAL

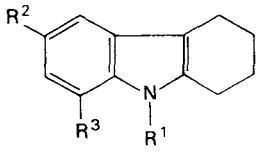
The compounds studied were prepared by procedures described elsewhere.[7,8] Thus, **3–11**, **16**, **17**, **31**, **36** and **37** were prepared via lithiation of the respective aminal derivatives **2**, **14**, **30** and **35**, and **19–21** were prepared from benzo[*a*]carbazole-1,11-dianion.[7] 6-Chlorobenzo[*c*]carbazole (**31**) was available only as a mixture containing a smaller amount of the 8-isomer, but the signals due to the major component were readily identi-



1 $R^1 = R^2 = R^3 = H$

2 $R^1 = CH_2N$(pyrrolidine); $R^2 = R^3 = H$

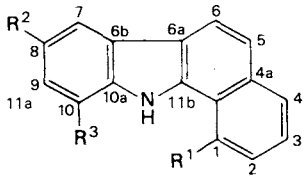
3 $R^1 = R^3 = H$; $R^2 = CH_3$
4 $R^1 = R^3 = H$; $R^2 = CH_2CH_2CH_2CH_3$
5 $R^1 = R^3 = H$; $R^2 = OH$
6 $R^1 = R^3 = H$; $R^2 = Cl$
7 $R^1 = R^3 = H$; $R^2 = NO_2$
8 $R^1 = R^3 = H$; $R^2 = CO_2H$
9 $R^1 = R^3 = H$; $R^2 = COC_6H_5$
10 $R^1 = R^3 = H$; $R^2 = COC_6H_4$–*p*–CH_3
11 $R^1 = R^3 = H$; $R^2 = C(OH)(C_6H_5)_2$
12 $R^1 = R^2 = H$; $R^3 = CH_2CH_2CH_2CH_3$



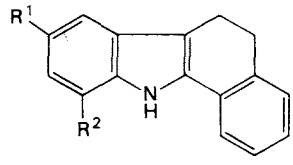
13 $R^1 = R^2 = R^3 = H$

14 $R^1 = CH_2N$(pyrrolidine); $R^2 = R^3 = H$

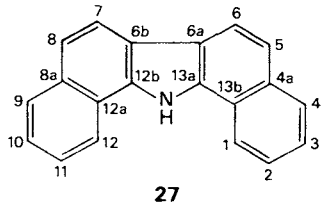
15 $R^1 = R^3 = H$; $R^2 = CH_2CH_2CH_2CH_3$
16 $R^1 = R^2 = H$; $R^3 = D$
17 $R^1 = R^2 = H$; $R^3 = CO_2H$



18 $R^1 = R^2 = R^3 = H$
19 $R^1 = D$; $R^2 = R^3 = H$
20 $R^1 = Cl$; $R^2 = R^3 = H$
21 $R^1 = CO_2H$; $R^2 = R^3 = H$
22 $R^1 = R^3 = H$; $R^2 = CH_2CH_2CH_2CH_3$
23 $R^1 = H$; $R^2 = R^3 = CH_2CH_3$



24 $R^1 = R^2 = H$
25 $R^1 = CH_2CH_2CH_2CH_3$; $R^2 = H$
26 $R^1 = R^2 = CH_2CH_3$



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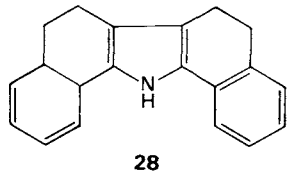

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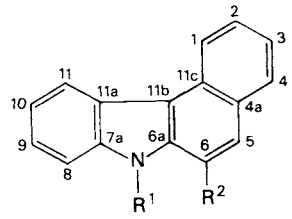

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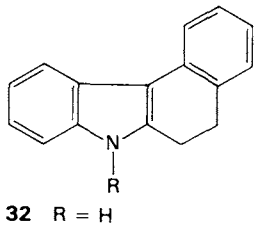
30 $R^1 = CH_2N$(pyrrolidine); $R^2 = H$

31 $R^1 = H$; $R^2 = Cl$



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