STEREOCHEMISTRY OF NITROGEN HETEROCYCLES.

69.* ^{13}C NMR SPECTRA OF STEREOISOMERIC 10-METHYL-5-OXYGEN-SUBSTITUTED trans-DECAHYDROQUINOLINES

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The ^{13}C NMR spectra of 5-keto- and 5a- and 5e-hydroxy-10-methyl- and 1,10-dimethyl-trans-decahydroquinolines have been recorded and interpreted. The increments of the oxo and hydroxy groups in the 10-methyldecahydroquinoline and the isostructural 10-methyldecaline systems were compared. The difference between the increments of aza-cyclic and the carbocyclic systems appears at the γ-positions relative to the electronegative substituents ($C_{(7)}$ and $C_{(9)}$) and at the antiperiplanar γ-positions relative to nitrogen ($C_{(5)}$ and $C_{(7)}$). The increments of the oxo and the equatorial hydroxy groups in the aza ring are more shielded than in the carbon ring (at $C_{(7)}$, 2 ppm; at $C_{(9)}$, 1 ppm), while the increments of the axial hydroxy group are more deshielded (at $C_{(5)}$, 1.5-2.0 ppm; at $C_{(9)}$, 1.0-1.5 ppm). The more the respective carbon atoms of the heterocycle are hydrogenated, the stronger are the deshielding β-effect and the shielding γ-effect of the methyl group on nitrogen.

Piperidine and decahydroquinoline derivatives are convenient model compounds for the study of the steric aspect of the dependence of the ^{13}C NMR chemical shift (CS) of saturated cyclic amines on steric structure. The effects of alkyl substituents have been well studied for a number of cyclic amines [2, 3], but the effects of polar substituents have been studied but little.

We have studied the ^{13}C NMR spectra of the stereoisomers of 5-keto and 5-hydroxy derivatives of 10-methyl- and 1,10-dimethyl-trans-decahydroquinolines (compounds I and III); synthesis and proof of structure have been previously described [4-6]. We have considered the dependence of the effects of polar substituents on their steric orientation.

The chemical shifts of decahydroquinoline derivatives are practically the same in $CHCl_3$ and $CDCl_3$; the former as a rule are 0.05 ppm smaller. This makes it possible to directly compare our data for $CHCl_3$ with the literature data for $CDCl_3$ (Table 1).

Carbon signals were assigned on the basis of spectra with incomplete suppression of interaction with protons (off-resonance) and of comparison with CS; the latter (Table 1) were calculated on the basis of compounds I and II (the signals for which have been previously assigned [2, 3]), and of substituent effects in configurationally similar oxygen-substituted methyl decalines.

Decahydroquinoline (I) was synthesized by reduction of 10-methyl-5-keto-trans-decahydroquinoline (IV), by the method for synthesizing 2-methyldecahydroquinoline [7]. The identity of (I) synthesized by us with that described in [8] was confirmed by comparison of their physicochemical and spectral properties.

For assignment of the carbon signals in the spectrum of decahydroquinoline (I) (Eliel [3]), we obtained several deuterosubstituted materials; these enabled us to assign nearly all the spectral signals except those close in CS to $C_{(4)}$ and $C_{(5)}$ (δ, 40.53 and 39.88 ppm). In connection with the difference in substituent effects between acyclic and carbocyclic systems, we needed more complete interpretation of spectra, especially of the unsubstituted compounds. Since our method of preparing (I) (reduction of ketone (IV)) permitted us to deuterate the ring selectively at positions 5 and 6, we obtained the deuterated derivative (II). Deuteration was carried out until the signals at 21.48 $C_{(6)}$ and 39.88 ppm had disappeared (Table 1). Thus the signal at 39.88 ppm should be assigned to $C_{(5)}$, and that at 40.53 ppm

*For Communication 68, see [1].

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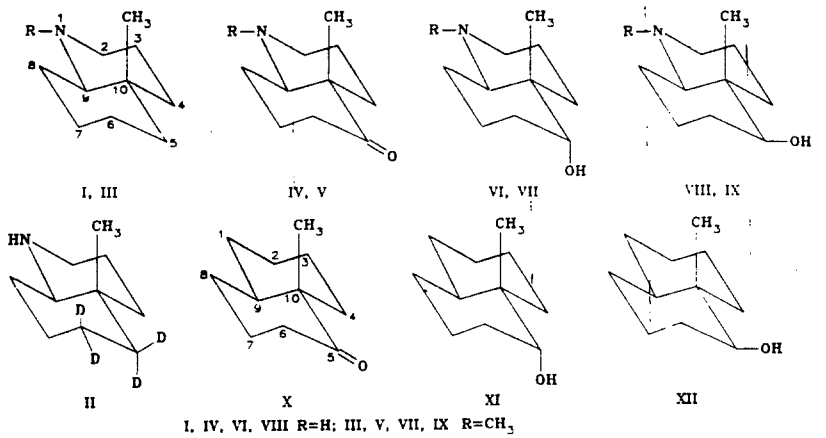
to $C_{(4)}$. Since the δ-effect of the methyl on N is small (about 0.2 ppm), it may be assumed that the CS of $C_{(4)}$ and $C_{(5)}$ in decahydroquinoline (III) will differ but little from the shifts of those atoms in (I). On this basis the signal at 40.70 ppm in (III) can be assigned to $C_{(4)}$, and that at 40.30 ppm to $C_{(5)}$.



The presence of polar substituents in (IV)-(IX) facilitates the interpretation of their spectra. Thus for aminoketone (IV) the downfield signal at 214.7 ppm naturally belongs to the carbonyl $C_{(5)}$. From analysis of spectra with incomplete decoupling of protons and comparisons with the spectrum of (I) we may confidently assign the doublet signal at 63.8 ppm to $C_{(9)}$, the triplet at 47.3 ppm to $C_{(2)}$, the singlet at 48.8 ppm to $C_{(10)}$, and the quartet at 15.7 ppm to the methyl at $C_{(10)}$. If we take acount of the α-effect of the oxo at 13.5 ppm for $C_{(6)}$ in 10-methyl-5-keto-trans-decaline (X) [9, 10] we can assign the triplet at 36.8 ppm to $C_{(6)}$ (the decaline ring is numbered so that the substituent numbers will be the same as in the aza and carbo systems).

It is known that the effect of oxo on the other carbon atoms of decaline and decahydroquinoline is small [9-11], except for the effect on the carbon in peri position to the bicyclic system (cis effect); for $C_{(4)}$ in ketone (X) it is 9.6 ppm. Correspondingly the signal at 31.5 can be assigned to $C_{(4)}$.

Assignments for aminoketone (V) were made similarly; here the quartet at 43.3 ppm undoubtedly belongs to the methyl at nitrogen, while the quartet at 17.6 belongs to the methyl at $C_{(10)}$.

The ^{13}C NMR spectra of decahydroquinolines and their N-alkyl derivatives have been compared by Eliel and Vierhapper [3, 12]. These authors noted that in addition to the deshielding effect of the substituent at nitrogen on the α-carbon of the piperidine ring, the $C_{(8)}$ signal undergoes an upfield shift (−3.6 ± 0.2 ppm). When this effect is taken into account, the signals at 27.5 ppm of the secondary ketone (IV) and that at 24.0 ppm of the tertiary amine (V) can be assigned to $C_{(8)}$.

It is known that in trans-decahydroquinoline replacement of the hydrogen at methyl by methyl causes shielding of $C_{(3)}$ by 1.5 ± 0.4 ppm; on the other hand the CS of $C_{(7)}$ is practically unchanged (0.1 ± 0.2 ppm) [12]. Thus in N-substituted amine (I) and N-methyl substituted (III) the signal shifts of $C_{(5)}$ are respectively 26.1 and 26.14 ppm, and those of $C_{(3)}$ are 23.1 and 22.2 ppm. It can therefore be assumed that the very similar signals at 23.1 and 22.9 ppm should belong to $C_{(7)}$ of aminoketones (IV) and (V) respectively. Furthermore the CS of $C_{(3)}$ of unsubstituted aminoketone (IV) should be about 1 ppm larger than in N-methyl substituted (V), viz., 22.2 and 21.1 ppm, respectively.

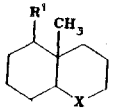
We considered spectra with incomplete proton quenching, and CS calculations by the additive scheme based on decahydroquinolines (I) and (III); we used the increments of the axial and the equatorial hydroxy groups in configurationally similar 10-methyl-5-hydroxy-trans-decaline systems ((XI) and (XII) [13], Table 2). We can confidently assign the carbon signals of the axial and equatorial alcohols (VI), (VII) and (VIII), (IX) (Table 1) aside from the similar $C_{(6)}$ and $C_{(8)}$ signals of alcohol (VI) (28.5 and 28.9 ppm), and the $C_{(3)}$ and $C_{(7)}$ signals of alcohols (VIII) (22.4 and 22.7 ppm) and (IX) (21.8 and 22.2 ppm).

Comparison of calculated and observed spectra show that the use as references of (I) and (III) and the increments obtained from the spectra of the isostructural hydroxydecalines

TABLE 1. Chemical Shifts of ^{13}C Nuclei of 1-R-5-R^1-10-Methyl-trans-decahydroquinolines (I)-(IX)

Compound	R	R^1	Solvent	δ, ppm										
				$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(8)}$	$C_{(9)}$	$C_{(10)}$	10-CH_3	N-CH_3
I	H	H_2	$CHCl_3$	48,2	23,1	40,7	40,0	21,5	26,1	29,0	64,5	34,0	15,6	
			$CDCl_3$**	48,13	22,97	40,53***	39,88***	21,48	25,97	28,88	64,31	33,94	15,6	
II	H	D_2	$CHCl_3$	48,17	23,03	40,63	—	—	25,79	28,91	64,46	33,84	15,52	
			$CDCl_3$	48,26	23,09	40,72	—	—	25,82	28,97	64,55	33,90	15,55	
III	CH_3	H_2	$CDCl_3$**	59,19	22,15	40,70***	40,30***	21,19	26,14	25,08	71,92	34,10	17,35	43,11
IV	H	=O	$CHCl_3$	47,3	22,2;	31,5;	214,6;	36,8;	23,1	27,5;	63,8;	48,8;	15,7;	
				47,2	*22,4*	*31,1*	*213,5*	*36,8*	*25,1*	*27,4*	*64,8*	*48,4*	*15,6*	
V	CH_3	=O	$CHCl_3$	58,3	21,1;	31,6;	213,8;	36,4;	22,9	24,0;	71,0;	49,3;	17,6;	43,3
				58,2	*21,4;*	*31,1*	*213,8*	*36,5*	*25,1*	*23,5*	*72,2*	*48,5*	*17,3*	
VIII	H	OHeq	$CHCl_3$	47,6	(22,4)	36,4;	77,8;	30,2;	(22,7);	27,9	62,7;	39,3;	10,0;	
				47,8	*22,7*	*35,5*	*77,5*	*29,8*	*23,3*	*27,8*	*62,9*	*39,3*	*9,7*	
IX	CH_3	OHeq	$CHCl_3$	58,8	(21,8);	36,3;	78,1	29,8;	(22,2);	24,3;	70,7;	39,8;	11,7;	43,7
				58,8	*21,8*	*35,9*	*77,8*	*29,5*	*23,3*	*23,9*	*70,1*	*39,4*	*11,5*	
VI	H	OHax	$CHCl_3$	47,6	22,8	33,4	74,7	(28,5)	19,8	(28,9)	57,1;	38,2;	16,2;	
				47,7	*22,6*	*33,4*	*77,1*	*27,9*	*19,3*	*28,5*	*56,2*	*38,4*	*16,0*	
VII	CH_3	OHax	$CHCl_3$	58,77	21,77	33,76	75,32	28,46	19,70	24,85	65,26	38,48	17,92	43,27
			$CDCl_3$	58,81;	21,82;	33,80;	75,39;	28,51;	19,73;	24,91;	65,22;	38,54;	17,95;	43,23
				58,7	*21,7*	*33,4*	*73,4*	*27,6*	*19,3*	*24,6*	*63,4*	*38,5*	*17,8*	

*Signals that can vary with location are in parentheses, calculated CS are in italics.
**Data of [3].
***Our asignment (given in text).

TABLE 2. Increment of Functional Groups in the  Structure

Compound	X	R^1	Functional group	Increments of functional groups at C atoms, ppm									
				$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(8)}$	$C_{(9)}$	$C_{(10)}$	10-CH_3
X	CH_2	=O	=O	−1,0	−0,7	−9,6	173,5	15,3	−1,0	−1,6	0,3	14,4	0,0
IV	NH	=O	=O	−0,9	−0,9	−9,2	174,6	15,3	−3,0	−1,5	−0,7	14,8	0,1
V	NCH_3	=O	=O	−0,9	−1,0	−9,1	173,5	15,2	−3,2	−1,1	−0,9	15,2	0,2
XII	CH_2	OH_e	OH_e	−0,4	−0,4	−4,8	37,5	8,3	−2,8	−1,2	−1,6	5,3	−5,9
VIII	NH	OH_e	OH_e	−0,6	−0,7	−3,7	37,8	8,7	−3,4	−1,1	−1,8	5,3	−5,6
IX	NCH_3	OH_e	OH_e	−0,4	−0,4	−4,4	37,8	7,6	−3,9	−0,8	−1,2	5,7	−5,6
XI	CH_2	OH_a	OH_a	−0,5	−0,5	−7,3	33,1	6,4	−6,8	−0,5	−8,3	4,4	0,4
VI	NH	OH_a	OH_a	−0,6	−0,3	−7,3	34,7	7,0	−6,3	−0,1	−7,4	4,2	0,6
VII	NCH_3	OH_a	OH_a	−0,5	−0,4	−6,9	35,0	7,2	−6,4	−0,2	−6,6	4,4	0,2
III	NCH_3	H	1-CH_3	11,0	−1,0	0,0	0,3	−0,4	0,0	−3,9	7,4	0,1	1,8
V	NCH_3	=O	1-CH_3	11,0	−1,1	0,1	−0,8	−0,4	−0,2	−3,5	7,2	0,5	0,9
IX	NCH_3	OH_e	1-CH_3	11,2	−0,6	0,1	0,3	−0,4	−0,5	−3,6	8,0	0,5	1,7
VII	NCH_3	OH_a	1-CH_3	11,2	−1,0	0,4	0,6	0,0	−0,1	−4,0	8,2	0,3	1,7

(XI) and (XII) [13] gives very good similarity. In all cases the calculated shift coincides with that observed, as a rule within 1 ppm, and only for aminoalcohol (VII) does the difference increase to 2.2 ppm at $C_{(5)}$ and $C_{(9)}$. But the interpretation of these signals either according to multiplicity or the magnitude of the CS values is not in doubt. Use of the hydroxyl increments from cyclohexanol [14] gives significantly poorer results; the difference between calculated and observed CS reaches 3-5 ppm. Similar results, only a little better, were obtained using the increments from 2-methylcyclohexanol [15].

From the assignment of the ^{13}C NMR spectra of the stereoisomers of 10-methyl-5-keto and 5-hydroxy-trans-decahydroquinolines and their N-methyl derivatives we were able to calculate the increments of the 5-keto, 5-hydroxy, and 1-methyl groups in a number of decahydroquinolines. The increments of polar functional groups are mainly the same in azacyclic and carbocyclic systems (see Table 2). But there are also differences, due apparently to the incomplete additivity of the effects of those substituents at position 5 and of the amino group of the decahydroquinoline ring. Thus ketones (IV) and (V) show an increase in the shielding γ-effect at $C_{(7)}$ (−2.0 to −2.2 ppm) and $C_{(9)}$ (−1.0 to −1.2 ppm). (The minus sign indicates the increment change in the aza ring with respect to the increment in the carbon ring). Axial alcohols (VI) and (VII) show amplification of the deshielding α-effect at $C_{(5)}$ (1.6-1.9 ppm) and a weakening of the shielding γ-effect at $C_{(9)}$ (0.9-1.7 ppm). For equatorial alcohols (VIII) and (IX) the difference from the carbosystem is less significant; we can observe only a small increase in the shielding γ-effect for $C_{(7)}$ (−0.6 to −1.1 ppm).

The observed differences between azacyclic and carbocyclic systems are apparently not random, because there is a definite relation between the position of the polar group and the localization of the deviations. In the first place, all the differences appear at atoms that are in γ-position with respect to substitutents ($C_{(7)}$ or $C_{(9)}$) or nitrogen (anitiperiplanar $C_{(5)}$ and $C_{(7)}$), i.e., where the substituents or nitrogen provide shielding. In the second place, for the equatorial alcohols and ketone, which have similar effects, the deviations from the carbocyclic values are negative, whereas for the axial alcohols, which produce very different effects, the deviations are positive.

To compare the effects of methyl at position 1 in the azacyclic and carbocyclic systems seemed impossible because there are no data for the latter system. It was possible, however, to observe a dependence of methyl increments in the azacyclic system on the degree of substitution of carbon; the carbons carrying more hydrogen atoms showed more distinct deshielding β-effect and shielding γ-effect. Thus, the deshielding β-effects are +11.1 ± 0.1 ppm at $C_{(2)}H_2$ and +7.7 ± 0.5 ppm at $C_{(9)}H$; the shielding γ-effects are −0.9 ± 0.2 ppm at $C_{(3)}H_2$ and about zero (= 0.3 ± 0.2 ppm) at the quaternary $C_{(10)}$. At the same time, in the similar azacyclic system but without methyl at position 10 (1-methyl-trans-decahydroquinoline) the first three effects are practically the same (11.0, 7.5, −1.2 ppm), but at the $C_{(10)}H$ carrying more hydrogen the deshielding γ-effect increases to −1.2 ppm.

From these data it can be concluded that the substituent increment values are similar in the isostructural azacyclic and carbocyclic systems, and can be used to calculate carbon CS in azaheterocyclic systems. But for some carbon atoms there are substantial differences in increments, due to the nonadditivity of the effects of polar substituents and heterocyclic nitrogen. Although the reasons for this nonadditivity are not yet clear (as also the nature of the deshielding effects), our data can be used to calculate more accurately the carbon CS in azacyclic systems with polar substituents.

EXPERIMENTAL

^{13}C NMR spectra were recorded* with a WP-80 spectrometer (20.155 MHz) at room temperature. Solution concentrations were 20-25%. Internal standard was HMDS (chemical shift relative to TMS, 1.91 ppm). Chemical shifts are given on a scale of δ from TMS.

Elemental analysis for C, H, and N agreed with the calculated values.

10-Methyl-trans-decahydroquinoline ((I), $C_{10}H_{19}N$). To 2.5 g (0.015 mole) of decahydroquinoline (III) (mp 56°C) were added 2.3 g (0.045 mole) of hydrazine hydrate, 2.4 g of powdered NaOH, and 15 g of triethylene glycol. The reaction mixture was heated under reflux for 1.5 h at 140-145°C. The reflux condenser was replaced by a descending condenser, and

*The spectra were recorded by coworkers of the Laboratory of Physical Research Methods, of the Institute of Chemical Sciences of the Academy of Sciences of the Kazakh SSR, viz., V. B. Rozhnov, E. I. Khokhlova, and N. V. Chernova, to whom the authors express their thanks.

water and hydrazine hydrate were distilled off while the bath temperature was raised from 150° to 200°C. The mixture was cooled and the reaction product was extracted with ether. Drying and vacuum distillation yielded 2.0 g (87% of theory) of compound (I), bp 222°C; n_D^{20} 1.4918; R_f 0.11 (Al_2O_3 III st. act.; eluent, water-saturated ether). Hydrochloride ($C_{10}H_{19}N \cdot HCl$). Mp, 220-221°C (from isopropanol). Picrate ($C_{10}H_{19}N \cdot C_6H_3N_3O_7$). Mp 224-225°C (from ethanol); according to [7], mp is 222-223°C.

5,5,6,6,D_4-10-Methyl-trans-decahydroquinoline (II) was obtained by the procedure described above, from decahydroquinoline (I) previously deuterated at $C_{(6)}$; reagents were ND_2–$ND_2 \cdot D_2O$, NaOD, and $(D-O-CH_2-CH_2-O-CH_2)_2$.

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