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^{13}C NMR SPECTRA OF 5-SUBSTITUTED 8-MERCAPTOQUINOLINES

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The increments of the substituents were determined from the ^{13}C NMR spectra of 5-substituted quinolines. It is shown that the increments correlate with those in benzenes, as well as with the Swain—Lupton constants. The ^{13}C chemical shifts of some 5-substituted 8-mercapto-, 8-(methylthio)-, and 8-hydroxyquinolines were investigated. Their values are in satisfactory agreement with the additive contribution of the increments of the substituents. The deviations from additivity are associated with the steric hindrance to interaction of the substituents with the ring.

In a continuation of our studies of the electronic structures of quinoline and its derivatives in the present investigation we examined the ^{13}C NMR spectra of 5-methyl-, 5-fluoro-, 5-chloro-, 5-bromo-, 5-iodo-, 5-(methylthio)-, 5-(pentylthio)-, 5-methoxy-, and 8-mercaptoquinoline (I-VIII) and 8-(methylthio)quinoline (IX-XVI), 5,8-dimercaptoquinoline (XVII), and 5-(ethylthio)-8-(methylthio)quinoline (XVIII), as well as 5-(methylthio)-, 5-(ethylthio)-, and 5-(propylthio)-8-hydroxyquinoline (XIX-XXI). The ^{13}C NMR spectra of quinoline (XXII) and 8-mercapto-, 8-(methylthio)-, 8-hydroxy-, and 5-(methylthio)quinoline (XXIII-XXVI) were previously examined in [1, 2]. The increments of the substituents in the 5 position of the quinoline ring were determined from the ^{13}C NMR spectra of 5-methyl-, 5-fluoro-, 5-chloro-, 5-bromo-, 5-iodo-, 5-amino-, and 5-mercaptoquinoline (XXVII-XXXIII). The ^{13}C chemical shifts, the assignment of which was made on the basis of the spectra without decoupling of the protons (with the Overhauser nuclear effect) and the spectra with extraresonance suppression of the ^{13}C—^{1}H spin—spin coupling, are presented in Tables 1-3.

TABLE 1. ^{13}C Chemical Shifts of 5-Substituted Quinolines

Compound	δ, ppm								
	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}
XXVIII	151,6	121,5	129,0	158,2	110,6	129,2	125,9	149,5	119,4
XXIX	151,3	122,1	132,7	131,6	126,9	129,4	129,4	149,3	126,6
XXX	151,3	122,5	135,5	122,3	130,7	129,8	129,9	149,4	127,9
XXXI	151,5	123,1	140,6	99,2	138,1	130,8	131,0	149,2	130,8
XXVII	150,2	121,0	132,5	134,9	127,3	129,4	128,9	149,1	127,9
XXVI	151,1	121,3	133,0	137,5	124,5	129,7	127,7	149,0	127,7
XXXIII	151,0	121,6	133,8	129,0	129,9	129,5	128,8	149,0	128,2
XXII	150,7	121,6	136,4	128,4	127,0	129,9	129,9	148,8	128,8
XXXII	150,6	119,8	131,0	145,5	109,2	130,8	118,6	150,3	119,1

TABLE 2. ^{13}C Chemical Shifts of 5-Substituted 8-Mercapto-quinolines

Com-pound	δ, ppm									
	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C—R
II	150,4	121,9	130,2	155,8	110,7	126,2	128,9	143,8	120,1	
III	149,8	122,5	133,4	127,5	126,6	126,6	134,9	143,9	126,5	
IV	150,1	123,1	136,6	117,9	130,4	127,3	135,8	144,5	128,4	
V	150,3	123,7	141,4	93,6	137,7	128,2	137,2	144,3	130,6	
VIII	150,0	120,9	131,7	153,3	105,0	127,3	124,5	144,6	121,9	56,0 (5-OCH₃)
VI	149,8	121,9	134,2	132,6	126,4	127,3	133,4	144,3	128,4	17,7 (5-SCH₃)
VII	149,6	122,0	134,9	130,7	130,2	127,0	134,9	144,3	129,0	
I	149,1	121,5	133,6	131,6	127,3	127,1	132,5	144,3	128,6	18,7 (5-CH₃)
XVII	149,8	122,2	135,0	123,6	130,9	127,0	135,0	144,3	129,2	

TABLE 3. ^{13}C Chemical Shifts of 5-Substituted 8-(Methylthio)-quinoline and 8-Hydroxyquinoline

Com-pound	δ, ppm									
	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C—R
X	150,4	122,2	130,0	155,9	110,8	122,8	135,7	145,9	119,5	15,0 (8-SCH₃)
XI	149,8	122,8	133,3	127,1	126,9	122,5	140,3	145,9	126,2	14,6 (8-SCH₃)
XII	149,8	123,2	135,8	117,3	130,5	123,0	141,2	145,9	127,3	14,6 (8-SCH₃)
XIII	150,1	123,8	140,9	93,0	137,9	124,2	142,6	146,0	130,0	14,7 (8-SCH₃)
XVI	150,0	121,2	131,6	153,2	105,2	124,7	130,3	146,5	121,5	56,1 (5-OCH₃) 15,4 (8-SCH₃)
XIV	149,8	122,2	134,0	131,7	127,7	123,4	139,7	146,2	128,0	18,0 (5-SCH₃) 14,9 (8-SCH₃)
XVIII	149,6	122,4	134,7	129,2	131,1	123,0	140,6	146,2	129,2	
XV	149,5	122,3	134,6	129,6	130,7	122,9	140,3	146,2	129,0	
IX	148,9	121,7	133,1	130,5	127,6	123,1	138,0	146,0	127,9	18,6 (5-CH₃) 14,7 (8-SCH₃)
XIX	148,6	122,5	134,8	124,5	131,7	111,1	152,9	139,5	129,3	19,6 (5-SCH₃)
XX	149,0	123,1	135,6	122,5	135,9	111,3	154,0	139,9	131,1	
XXI	148,5	122,5	134,9	122,5	135,4	111,1	153,5	139,5	130,5	

TABLE 4. Increments of the Substituents (Δδ) in 5-Substituted Quinolines

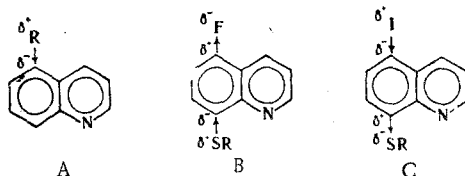| Substituent	Δδ, ppm						
	$\Delta\delta_\alpha$ (C_5)	$\Delta\delta'_o$ (C_6)	$\Delta\delta''_o$ (C_{10})	$\Delta\delta_p$ (C_8)	$\Delta\delta_m$ (C_7)	$\Delta\delta''_m$ (C_9)	$\Delta\delta$ (C_4)
F (XXVIII)	+29,8	−16,4	−9,4	−4,0	−0,7	+0,7	−7,4
Cl (XXIX)	+3,2	−0,1	−2,2	−0,4	−0,5	+0,5	−3,7
Br (XXX)	−6,1	+3,7	−0,9	0	−0,1	+0,6	−0,9
I (XXXI)	−29,2	+11,1	+2,0	+1,1	+0,9	+0,4	+3,6
CH₃ (XXVII)	+6,5	+0,3	−0,9	−1,0	−0,5	+0,3	−3,9
SCH₃ (XXVI)	+9,1	−2,5	−1,1	−2,2	−0,2	+0,2	−3,4
SH (XXXIII)	+0,6	+2,9	−0,6	−1,1	−0,4	+0,2	−2,6
NH₂ (XXXII)	+17,1	−17,8	−9,7	−11,3	+0,9	+1,5	−5,4

The increments of the substituents (Δδ) in XXVI–XXXI (Table 4), just as in 8-substituted quinolines [2], correlate satisfactorily with the increments in substituted benzenes ($\Delta\delta^B$) and with the Swain–Lupton parameters:

$$\Delta\delta_\alpha = 0.91\Delta\delta_\alpha{}^B - 0.73 \quad r = 0.99$$
$$\Delta\delta^*_\alpha = 0.83\Delta\delta_\alpha{}^B + 1.23 \quad r = 0.99$$
$$\Delta\delta_p = 1.45\Delta\delta_p{}^B + 2.16 \quad r = 0.86$$
$$\Delta\delta^*_p = 1.55\Delta\delta_p{}^B + 1.50 \quad r = 0.94$$

$$\overline{\Delta\delta_o} = 0.89\Delta\delta_o{}^B - 1.03 \quad r = 0.99$$
$$\overline{\Delta\delta^*_o} = 0.89\Delta\delta_o{}^B - 1.38 \quad r = 0.97$$
$$\Delta\delta_p = 3.0F + 20.0R + 0.9 \quad r = 0.95$$
$$\Delta\delta^*_p = 3.5F + 16.9R - 0.8 \quad r = 0.94$$

where $\Delta\delta^*$ are the increments of the substituents in 8-substituted quinolines, and $\overline{\Delta\delta_0} = (\Delta\delta_0' + \Delta\delta_0'')/2$ ($\Delta\delta_0'$ and $\Delta\delta_0''$ are the increments of the substituents attached to the C_6 and C_{10} atoms, respectively).

This result draws attention to the fact that steric hindrance to the coupling of the substituents, particularly such bulky substituents as CH_3, Cl, Br, and I, with the quinoline ring on the part of the γ-hydrogen atom exists in 5-substituted quinolines. In 8-substituted quinolines a similar effect is created by the polarizable unshared pair of electrons of the nitrogen atom [2]. It is possible that the certain decrease in the $\Delta\delta_p$ values of the substituents in 5-substituted quinolines is associated with this. The chemical shift of the C_5 atom in the spectra of XXVI-XXXIII is determined by steric hindrance and, evidently, the polarization of the C_5-R bond by the dipole of the quinoline ring. The decrease in $\Delta\delta_\alpha$ (6.5 ppm), i.e., the shift of the C_5 signal to strong field as compared with $\Delta\delta_\alpha$ for 8-methylquinoline (7.7 ppm), is associated with weakening of the coupling of the CH_3 group with the ring. In addition to this effect, polarization of the C_5-R bond (A) may make a certain contribution in XXVI-XXVIII, XXIX, and XXXIII in the same direction. In XXX and XXXI these effects affect the C_5 chemical shift in the opposite directions, and in the XXX molecule the effect of the contribution of resonance structure A to the ground state of the molecule is evidently greater than the effect of disruption of the conjugation of the substituent with the ring ($|\Delta\delta_\alpha| > |\Delta\delta_\alpha^B|$). The effect of disruption of the coupling of the substituent with the ring predominates in XXXI as a consequence of the large volume of the substituent. In 8-iodoquinoline, in which one can assume a smaller degree of steric hindrance, $\Delta\delta_\alpha = -25.9$ ppm, as compared with -29 ppm in the spectrum of the XXXI molecule, which may be a consequence of the contribution of structure A to the ground state of the molecule.

The deviations from the additive contribution of the substituents to the chemical shifts of some ring carbon atoms are appreciable in 5,8-disubstituted quinolines. The C_8 signal in the spectra of I and IX is shifted additionally to strong field (Table 5). In the II and X molecules, with allowance for the properties of the substituents, the changes in the ^{13}C chemical shifts may be due to polarization, which leads to resonance structure B. The changes in the C_5 and C_8 chemical shifts in V and XIII are the opposite of their changes in the spectra of the II and X molecules. This may be associated with polarization, which leads to resonance structure C, as a consequence of the smaller degree of electronegativity and the greater polarizability of the iodine atom as compared with the fluorine atom.

A   B   C

In connection with the changes in the ^{13}C chemical shifts in the spectra of I, II, V, IX, X, and XIII it may be noted that the deviations of $\Delta\delta$ from the additive scheme are in agreement with an increase in the conjugation of the substituent in the 5 position of the quinoline ring.

Deviations of a character that differs from additivity of the increments are noted in the spectra of VI, XIV, XVII, and XIX. A peculiarity of these compounds is the steric hindrance to conjugation of the substituents in the 5 position on the part of 4- and 6-H. In these compounds the coupling of the substituents, just as in the I, II, V, IX, X, and XIII molecules, tends to increase the conjugation of the SH and SCH_3 groups in the 5 position with the ring. However, in this case the steric hindrance on the part of 6-H apparently increases. As a result of this, the SH and SCH_3 groups are evidently not located in the plane of the quinoline ring, by which one can explain the additional (above and beyond the additive sum of the increments) shift of the C_5 signals to strong field of the C_6, C_8, and C_{10} signals to weak field.

The fact that in VI, XIV, XVII, and XIX this effect is associated with changes in the increments of the SH and SCH_3 groups in the 5 position follows from the deviations of the C_6 chemical shifts from the additive scheme. The effect of the OH, SH, and SCH_3 groups in the 8 position of the quinoline ring on the C_6 chemical shift is slight ($\Delta\delta_m'$, Table 4). Similar changes in the increments of the SCH_3 group as a consequence of disruption of the conjugation are observed in the case of 7-substituted 8-(methylthio)quinolines [3].

TABLE 5. Deviations of the ^{13}C Chemical Shifts of 5,8-Disubstituted Quinolines from the Additive Contribution of the Substituents

Compound	C_5	C_6	C_7	C_8	C_9	C_{10}
I	0,2	0,1	0,2	−1,9	−0,1	0,4
X	0,1	0,1	0,4	−1,6	−0,1	0,3
II	1,1	0,2	−0,5	−2,5	−1,0	0,4
XI	2,2	0	0,3	−0,9	0,4	0,4
III	−0,6	−0,2	−0,3	0,1	−0,7	−0,4
XII	0	−0,2	−0,2	0,1	−0,4	−0,1
IV	−0,9	−0,2	0	0,4	−0,2	0,2
XIII	−0,5	−0,4	−0,1	0,6	−0,5	−0,3
V	−2,1	−0,3	−0,1	0,7	−0,2	−0,5
XIV	−1,7	−0,4	0,1	0,9	−0,2	−0,5
VI	−1,4	2,0	0,1	0,2	0	0,4
XV	−1,3	3,0	0,4	1,3	0,2	0,6
IX	−1,9	1,1	0	0,7	0	0,7
XIX	−3,1	4,2	−0,2	1,8	0,5	0,1

The signal of the SCH₃ group also undergoes a shift to weak field in the spectra of VI and XIV as compared with XXVI (Tables 2 and 3). The magnitude of this shift is even greater in the case of the XIX molecule. This is evidently not associated with the differences in the properties of the OH, SH, and SCH₃ groups (for example, in the spectra of XIV and XVI the ^{13}C chemical shifts of the SCH₃ group in the 8 position virtually coincide). As compared with XIV, large deviations in $\Delta\delta$ from the additive contribution of the substituents to the ^{13}C chemical shifts of the quinoline ring (C_5, C_6, C_8, and C_{10}) are also noted in the spectrum of the XIX molecule. This effect of the OH group in XIX may be due to the greater disruption of the conjugation of the SCH₃ group with the ring as compared with XIV.

An increase in the size of the S-alkyl group in the 5 position (XVI, XVIII, XX, and XXI) leads to an even greater (as compared with the VI, XIV, VII, and XIX molecules) shift of the C_5 signal to strong field and of the C_6, C_8, and C_{10} signals to weak field (Table 3), i.e., the degree of disruption of the conjugation of the substituent increase. The 5-S-alkyl group in, for example, nickel 5-propylthio-8-mercaptoquinolinate is not located in the plane of the molecule, according to x-ray diffraction data [4]. Only the addition of the first CH₂ group (the S-ethyl group in XVIII and XX), which increases the volume of the substituent near 6-H, has an appreciable effect as the size of the S-alkyl substituent is increased. Further lengthening of the alkyl chain naturally does not have a significant effect on the ^{13}C chemical shifts of the ring carbons (Table 3).

As a consequence of steric hindrance, substitution of quinoline in the 5 position gives rise to a substantial change in the C_4 chemical shift (I-XXI and XXVI-XXXIII). The latter is determined primarily by two factors, viz., the van der Waals interaction between the bulky substituent in the 5 position and 4-H and by the polarization of the C_4-H bond by the electrostatic field of the polar C_5-R group. In the case of the CH₃ group (I, IX, and XXVII) the shift of the C_4 signal to strong field is due to the first reason. According to the calculation, for the D and E conformations the $\Delta\delta$ values for C_4 are −2.7 and −10.5 ppm, respectively. In the case of XXXII, in addition to this effect ($\Delta\delta$ = −5.4 ppm for the F conformation), the dipole induced in the C_4-H bond by the electrostatic field of the polar C_5-R bond also makes a contribution to the strong-field shift of the C_4 signal. The latter determines the shift of the C_4 signal in the spectra of VI-VIII, XIV-XXI, XXVI, and XXXIII. In the spectra of the 5-halo derivatives (except for the 5-iodo derivatives) the C_4 signal also undergoes a strong-field shift; as the size of the halogen atom increases, i.e., as the steric hindrance and the associated van der Waals interaction increase, the strong-field

D   E   F
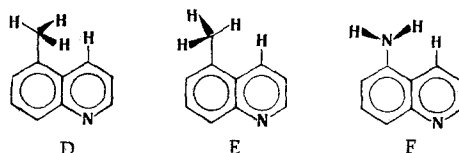
shift of the C_4 signal decreases in the order F > Cl > Br. In the case of 5-iodo derivatives (V, XIII, and XXXI) the C_4 signal is even shifted to weak field.

In addition to these data it is expedient to cite the chemical shift of the 4-H proton, which in the case of quinoline is 2.0 ppm, as compared with 1.69, 1.57, 1.61, and 1.78 ppm in the spectra of II-V, respectively. It is noteworthy that the 4-H and C_4 chemical shifts in the spectra of III-V change in the opposite direction, and it may be assumed that the decrease in the shielding of C_4 in the order F > Cl > Br > I is not associated with anisotropy of the C_5—Hal bond.

In our examination of the changes of the C_4 chemical shifts with respect to the induced dipole, i.e., the polarization of the C_4—H bond by the electrostatic field of the C_5—Hal bond, calculation within the point-charge approximation conveys the order of the decrease in the shift of the C_4 signal to weak field: F > Cl > Br > I. However, in this order, in connection with the identical direction in space of the group dipole moment, the calculation does not lead to a shift in the C_4 signal to weak field relative to XXII.

In connection with this problem it is interesting to digress to a small extent and examine the results of the calculation of 8-(methylthio)quinoline in the sp and spd bases of the AO of the sulfur atom [the CNDO/2 (complete neglect of differential overlap/2) approximation]. The inclusion of the d orbitals in the AO basis and an increase in their diffuse character (d') lead to a decrease in the electron density on the nitrogen atom ($q_N = -0.159$ in the sp basis, $q_N = -0.151$ in the spd basis, and $q_N = -0.145$ in the spd' basis).

Relative to the halogen atoms, which have vacant d orbitals, the spatial orientation of the C_4 atom is similar to the orientation of the nitrogen atom relative to the sulfur atom. In conformity with the material set forth above it may be assumed that the interaction of the vacant d orbitals of the iodine atom, which are more diffuse than the d orbitals of the sulfur atom, with the filled orbitals in the region of C_4 is the reason for the shift of the signal of this carbon atom to weak field. Proceeding from the expression $\Delta\delta/\Delta q = 200$ ppm/e, for $\Delta\delta = 4.2$ ppm in the spectrum of XXXI we obtain $\Delta q = 0.02$ e, which is completely compatible with the results of the calculation presented above.

EXPERIMENTAL

The ^{13}C NMR spectra of solutions in $CDCl_3$ were obtained by the method in [1]. The 8-mercaptoquinoline derivatives were synthesized by previously described methods [5].

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