3. W. Mathes, W. Sauermilch, and T. Klein, Chem. Ber., 84, 452 (1951).
4. E. Frainnet, R. Bourhis, F. Simouin, and F. Moulines, J. Organomet. Chem., 105, 17 (1976).
5. L. Ya. Leitis, G. V. Glemite, M. V. Shimanskaya, A. A. Avot, and I. I. Ioffe, Izv. Akad. Nauk Latv. SSR, Ser. Khim., No. 5, 559 (1969).
6. É. Ya. Lukevits, Yu. P. Romadan, S. A. Giller, and M. G. Voronkov, Dokl. Akad. Nauk SSSR, 145, 806 (1962).

STRUCTURAL ANALYSIS OF 2,3,6-TRISUBSTITUTED 1,4-DIHYDRO-4-OXOQUINOLINES BY MEANS OF ^{13}C AND ^{15}N NMR SPECTROSCOPY

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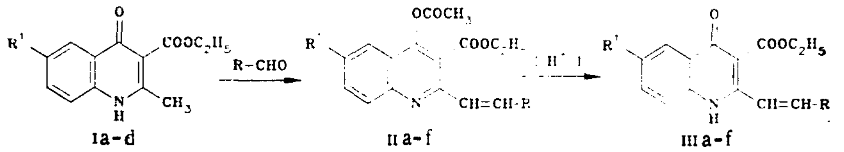
UDC 547.831.9:543.422.25

2,6-Substituted 1,4-dihydro-4-oxoquinoline-3-carboxylic acid ethyl esters were synthesized, and the effect of substituents on the migration of a hydrogen atom from the nitrogen atom to the oxygen atom was studied by ^{13}C and ^{15}N NMR spectroscopy. The presence of a 4-nitrophenylvinyl or 5-nitro-2-furylvinyl system in the 2 position of the compounds stabilizes their 4-oxoquinoline form.

Electron-acceptor substituents in the 2 position of 4-pyridones and 4-quinolones, by increasing the positive charge on the nitrogen atom, promote the migration of a hydrogen atom to the oxygen atom, and the corresponding 4-hydroxypyridines or 4-hydroxyquinolines are formed as a result [1]. A similar effect was expected from the introduction into the 2 position of 6-substituted 1,4-dihydro-4-oxoquinoline-3-carboxylic acid ethyl esters III of 4-nitrophenylvinyl and 5-nitro-2-furylvinyl systems, which have a pronounced negative conjugation effect.

However, the quinolone structure of IIIc, which was proved by PMR and IR spectroscopy [11.9 ppm (1H, s, NH) and 1630 cm^{-1} ($\nu_{C=O}$)], indicates the opposite (as compared with the expected) effect of the conjugated system containing a nitro group [2].

In order to make a detailed study of this phenomenon we synthesized IIIa-f by condensation of 2-methyl-1,4-dihydro-4-oxoquinoline-3-carboxylic acid ethyl esters Ib-d with 4-nitrobenzaldehyde and 5-nitro-2-furfural in acetic anhydride with subsequent hydrolysis of the acetyl group of the intermediate 4-acetoxy derivatives IIa-f of quinolines in an acidic medium.



I a $R^1=H$; b $R^1=OCH_3$; c $R^1=Cl$; d $R^1=Br$; II, III a $R=4\text{-}NO_2C_6H_4$, $R^1=H$; b $R=4\text{-}NO_2C_6H_4$, $R^1=OCH_3$; c $R=4\text{-}NO_2C_6H_4$, $R^1=Cl$; d $R=4\text{-}NO_2C_6H_4$, $R^1=Br$; e $R=$ 5-nitro-2-furyl, $R^1=H$; f $R=$ 5-nitro-2-furyl, $R^1=OCH_3$

The ranges of the locations of the ^{13}C signals of the quinoline ring of Ia, II, and IIIa-f and the model compound 2-methyl-1,4-dihydro-4-oxoquinoline (Table 1) correspond to the literature data for substances with similar structures. The diverse structures of the investigated compounds made it possible to refine the assignment of the chemical shifts of the $C_{(5)}$ and $C_{(8)}$ atoms, which differ from the data in [3].

The shift of the resonance signals of the $C_{(2)}$, $C_{(4)}$, and $C_{(6)}$ atoms to weak or strong field basically corresponds to the character of the inductive effect of the substituents. Thus the signal of the $C_{(4)}$ atom in Ia and IIIa-f under the influence of the oxo group is

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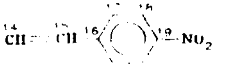
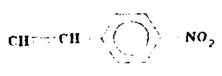
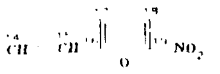
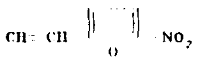
Institute of Organic Synthesis, Academy of Sciences of the Latvian SSR, Riga 226006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1381-1384, October, 1988. Original article submitted May 8, 1987; revision submitted September 15, 1987.

TABLE 1. Chemical Shifts in the ^{13}C and ^{15}N NMR Spectra for 1,4-Dihydro-4-oxoquinoline Derivatives, δ, ppm (d_6-DMSO)

Compound	Substituents in the quinoline ring			^{15}N (J_{NH})	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(8)}$	$C_{(9)}$	$C_{(10)}$	$C_{(11)}$	$C_{(12)}$	$C_{(13)}$	$C_{(14)}$	$C_{(15)}$	$C_{(16)}$	$C_{(17)}$	$C_{(18)}$	$C_{(19)}$	$C_{(20)}$
	$C_{(3)}$	$C_{(2)}$	$C_{(6)}$																				
—	H	CH_3	H	−246,2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Ia*	$\overset{11}{C}OO\overset{12}{C}H_2\overset{13}{C}H_3$	$\overset{14}{C}H_3$	H	−215,1	148,9	114,8	173,5	117,9	123,5	132,0	125,0	139,2	124,7	166,7	60,2	14,0	18,0	—	—	—	—	—	—
IIa*	$COOCH_2CH_3$		H	−85,01**	—	—	153,2**	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
IIIa*	$COOCH_2CH_3$		H	−255,9 (94,6)	144,7	115,3	173,9	118,6	124,0	132,7	125,0	139,5	124,9	166,0	60,8	14,2	121,2	134,7	141,5	128,4	124,2	147,5	—
IIIb	$COOCH_2CH_3$		$\overset{20}{O}CH_3$	—	143,9	114,3	173,3	104,7	156,3	120,5	123,1	134,1	126,2	166,5	60,7	14,1	124,5	134,4	141,7	128,5	124,3	147,6	55,5
IIIc	$COOCH_2CH_3$		Cl	—	145,3	115,5	172,8	121,2	128,9	132,9	124,1	138,3	126,0	166,0	60,9	14,1	124,1	135,2	141,5	128,6	124,3	147,8	—
IIId	$COOCH_2CH_3$		Br	—	145,2	115,6	172,6	121,3	116,7	135,4	127,1	138,5	126,4	165,9	60,8	14,0	123,9	135,4	141,4	128,5	124,3	147,7	—
IIIe	$COOCH_2CH_3$		H	—	143,4	115,8	173,9	118,6	124,1	132,8	124,9	139,5	124,9	166,1	60,8	14,0	123,5	122,6	153,1	114,8	115,3	151,8	—
IIIf	$COOCH_2CH_3$		OCH_3	—	142,5	114,8	173,3	104,6	156,4	120,6	123,8	134,2	126,2	166,5	60,9	14,1	123,3	122,4	153,3	115,0	115,4	151,9	55,5

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*^{13}C chemical shifts from the data in [2].

**The spectrum was recorded from a solution in $CdCl_3$.

TABLE 2. Effect of the Substituent Attached to the $C_{(6)}$ Atom on the Chemical Shifts in the ^{13}C NMR Spectra of 1,4-Dihydro-4-oxoquinolines

Compound	R^1	Increments, ppm								
		$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(8)}$	$C_{(9)}$	$C_{(10)}$
IIIa	H	0,0	—	—	—	—	—	—	—	—
IIIb	OCH_3	−0,8	−1,0	−0,6	−13,9	32.3	−12.2	−1.9	−5.4	1.3
IIIc	Cl	−0,6	0.2	−1.1	2.6	4.9	0.2	−0.9	−1.2	1.1
IIId	Br	−0,5	0.3	−1.3	2,7	−7.3	2.7	2.1	−1.0	1.5
IIIe	H	0,0	—	—	—	—	—	—	—	—
IIIf	OCH_3	−0,9	−1,0	−0,6	−14,0	32,3	−12.2	1.1	−5,3	1,3

TABLE 3. Effect of the Substituent Attached to the $C_{(2)}$ Atom on the Chemical Shifts in the ^{13}C and ^{15}N NMR Spectra of 1,4-Dihydro-4-oxoquinolines

Compound	Increments, ppm									
	$N_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(8)}$	$C_{(9)}$	$C_{(10)}$
Ia	0,0	—	—	—	—	—	—	—	—	—
IIIa	−10,0	−4,2	0,5	0,4	0,7	0,5	0,7	0,0	0,3	0.2
IIIe	—	−5,5	1,0	0,4	0,7	0,6	0,8	0,1	0,3	0.2

shifted 19-21 ppm to weak field as compared with the chemical shift of the $C(_4)$ atom bonded to the acetoxy group in IIa; this is yet another confirmation of the quinoline structure of the analyzed compounds.

The increments of the chemical shifts for the quinolines that differ with respect to the nature of the substituent in the 6 and 2 positions, i.e., 4-quinolones IIIa-f, calculated on the basis of the data in Table 1 (see Tables 2 and 3) constitute evidence only for the slight effect of the halogen atoms and the methoxy group on the increase in the electron density on the $C(_4)$ atom and the opposite effect of the 4-nitrophenylvinyl and 5-nitro-2-furyl vinyl systems.

The shift of the ^{15}N chemical shifts in the spectra of IIIa to stronger field when the methyl group is replaced by a 4-nitrophenylvinyl system (Table 1), which constitutes evidence for an increase in the electron density on the nitrogen atom and, consequently, strengthening of the N—H bond, is easily observed.

Thus the inclusion in the 2 position of quinolines IIIa-f of systems with a negative conjugation effect promotes redistribution of the electron density, which stabilizes their 4-oxoquinoline form.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in Nujol were obtained with a Perkin-Elmer 580B spectrometer. The ^1H NMR spectra of solutions in d_6-DMSO were measured with a Bruker WH-90 spectrometer (90 MHz) with tetramethylsilane (TMS) as the internal standard, the ^{13}C NMR spectra of solutions in d_6-DMSO were recorded with a Bruker WH-360 spectrometer (90.5 MHz) with TMS as the internal standard, and the ^{15}N NMR spectra of solutions in d_6-DMSO or $CDCl_3$ were obtained with a Bruker WH-360 spectrometer (36.5 MHz) with nitromethane as the external standard. The elementary analysis of the compounds was carried out with a model 1106 Carlo Erba apparatus.

Compounds Ia-d, IIa-d, and IIIa were synthesized by the method in [2], IIIe, f was synthesized by the method in [4], and the 2-methyl-1,4-dihydro-4-oxoquinoline was the reagent provided by the Aldrich Chemical Co.

2-[2-(4-Nitrophenyl)vinyl]-6-methoxy-1,4-dihydro-4-oxoquinoline-3-carboxylic Acid Ethyl Ester (IIIb). A suspension of 1.2 g (2.75 mmole) of ethyl 2-[2-(4-nitrophenyl)vinyl]-4-acetoxy-6-methoxyquinoline-3-carboxylate (IIb) was refluxed for 20 min in 20 ml of concentrated HCl, after which the mixture was cooled, and the precipitate was removed by filtration, washed with water until the wash water was neutral, and dissolved in hot DMF. The solution was filtered, and the filtered solution was added with stirring to a threefold volume of water. The precipitated crystals were removed by filtration to give 0.85 g (78%) of IIIb with mp 282°C (dec.). IR spectrum: 3180, 3220 (NH); 1720, 1700 ($COOC_2H_5$); 1630 (quinolone C=O); 1515, 1340 cm^{-1} (NO_2). ^1H NMR spectrum: 1.27 (3H, t, $CH_2C\underline{H}_3$). 3.84 (3H, s, CH_3O), 4.29 (2H, q, $C\underline{H}_2CH_3$). 7.20-8.31 (9H, m, C_9H_3N, CH=CH, C_6H_4), 11.75 ppm (1H, s, NH). Found: C 63.2; H 4.5; N 6.7%. $C_{21}H_{18}N_2O_5$. Calculated: C 64.0; H 4.6; N 7.1%.

Ethyl 2-[2-(4-Nitrophenyl)vinyl]-6-bromo-1,4-dihydro-4-oxoquinoline-3-carboxylate (IIId). This compound was obtained in 83% yield by the method presented for IIIb and had mp 290°C (dec.). IR spectrum: 3120, 3220 (NH); 1720 ($COOC_2H_5$); 1630 (quinolone C=O); 1515, 1345 cm^{-1} (NO_2). ^1H NMR spectrum: 1.27 (3H, t, $CH_2C\underline{H}_3$), 4.31 (2H, q, $C\underline{H}_2CH_3$), 7.36-8.31 (9H, m, C_9H_3N, CH=CH, C_6H_4), 11.91 ppm (H, s, NH). Found: C 54.5; H 3.5; N 6.4%. $C_{20}H_{14}BrN_2O_5$. Calculated: C 54.2; H 3.4; N 6.3%.

Ethyl 2-[2-(4-Nitrophenyl)vinyl]-6-chloro-1,4-dihydro-4-oxoquinoline-3-carboxylate (IIIc). This compound was obtained in 87% yield by the method presented for IIIb and had mp 290°C (dec.). IR spectrum: 3180, 3220 (NH); 1720 ($COOC_2H_5$); 1630 (quinolone C=O); 1515, 1345 cm^{-1} (NO_2). ^1H NMR spectrum: 1.27 (3H, t, $CH_2C\underline{H}_3$), 4.31 (2H, q, $C\underline{H}_2CH_3$), 7.38-8.31 (9H, m, C_9H_3N, CH=CH, C_6H_4), 11.91 ppm (H, s, NH). Found: C 60.0; H 3.8; N 6.8%. $C_{20}H_{15}ClN_2O_5$. Calculated: C 60.2; H 3.8; N 7.0%.

LITERATURE CITED

1. J. Elguero, C. Marzin, A. R. Katritzky, and P. Linda, The Tautomerism of Heterocycles, Academic Press, New York (1976), p. 88.
2. L. I. Kononov, G. A. Veinberg, É. É. Liepin'sh, I. V. Dipan, N. M. Sukhova, and É. Lukevits, Khim. Geterotsikl. Soedin., No. 7, 931 (1988).
3. G. M. Coppola, A. D. Kahle, and M. J. Shapiro, Org. Magn. Reson., 17, 242 (1981).
4. N. M. Sukhova, T. V. Lapina, and M. Yu. Lidak, Khim. Geterotsikl. Soedin., No. 11, 1521 (1983).