26. V. T. Klimko and A. P. Skoldinov, Zh. Obshch. Khim., 29, 4027 (1959).
27. R. Rüegg, H. Lindlar, M. Montavon, G. Saucy, S. Schaeren, U. Schwieter, and O. Isler, Helv. Chim. Acta, 42, 847 (1959).
28. J. N. Zaganiaris, Berichte, 71, 2002 (1938).

SYNTHESIS AND SPECTRAL EXAMINATION OF THE POSITION OF TAUTOMERIC EQUILIBRIUM IN 2-THIOXO-4-QUINAZOLONE

L. M. Yun, S. Yangibaev, Kh. M. Shakhidoyatov, V. Ya. Alekseeva, and K. A. V'yunov

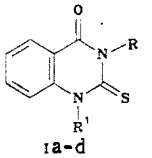
UDC 547.856.1.07:543.422.6:541.623

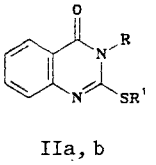
2-Thioxo-4-quinazolone and its derivatives mono- and dimethylated at ring atoms $N_{(1)}$ and $N_{(3)}$ and the exocyclic sulfur have been synthesized. Using model compounds, UV spectroscopy has been used to show that 2-thioxo-4-quinazolone exists in the thioketo-form, no appreciable amounts of the thiol or enol isomers being present.

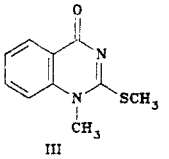
2-Thioxo-4-quinazolones display biological activity, and are therefore of practical importance [1, 2]. These compounds are also of interest from the theoretical point of view, since they could exist in a variety of tautomeric forms. No studies of the position of the prototropic equilibrium in thioxoquinoxalines have been carried out, as a result of the nonavailability of a complete set of methylated models, the electronic structures of which reduplicate the structures of the probable tautomeric forms.

We have examined the alkylation of 2-thioxo-4-quinazolone (Ia) with methyl tosylate in dimethyl formamide, which gives a mixture of compounds alkylated at $N_{(1)}$ (Ib), $N_{(3)}$ (Ic), and the exocyclic sulfur (IIa), the last product predominating in the reaction mixture [3]. The separation of the mixture of isomeric compounds (Ib), (Ic), and (IIa) was difficult, and we were able to separate preparatively only (IIa), the model compounds (Ib) and (Ic) being obtained by fusing 1-methyl- and 3-methyl-4-quinazolones with sulfur [4]. The course of alkylation was established from the PMR spectra, in which 2-methylthio-4-quinazolone (IIa) gives rise to a singlet signal for the methylene protons at 2.58 ppm, whereas (Ib) and (Ic) give signals for methyl protons at 3.70 and 3.35 ppm, respectively.

When monomethylated 2-thioxo-4-quinazolones (Ib) and (IIa) were methylated with methyl iodide in alcoholic alkali, dialkyl derivatives (IIb) and (III) were isolated. Compound (Id) was obtained by condensing N-methylanthranilic acid with methyl isothiocyanate.


Ia-d


IIa, b


III

Ia $R=R^1=H$; b $R=H$, $R^1=CH_3$; c $R=CH_3$, $R^1=H$; d $R=R^1=CH_3$; II a $R=H$, $R^1=CH_3$; b $R=R^1=CH_3$

The UV spectrum of (Ia) contained two bands at 218 and 292 nm, due to $\pi \rightarrow \pi^*$ transitions in the amide and thioamide groupings, respectively. Maxima similar in intensity and position are seen in the spectra of (Ib-d), the carbonyl and thiocarbonyl groups in which are unchanged as compared with (Ia).

Leningrad Lensovet Institute of Technology, Leningrad 198013, and the Institute for the Chemistry of Plant Compounds, Academy of Sciences of the Uzbek SSR, Tashkent 700170. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1236-1238, September, 1986. Original article submitted June 17, 1985; revision submitted November 6, 1985.

0009-3122/86/2209-1001$12.50

TABLE 1. 2-Thioxo-4-quinazolone (Ia) and Its Methylated Analogs (Ib-III)

Compound	mp, °C	UV spectrum, λ_{max}, nm (log ε)		Found, %				Empirical formula	Calculated, %			
		C_2H_5OH	C_2H_5OH + KOH	C	H	N	S		C	H	N	S
Ia	298—300	218 (4,17); 292 (4,27)	224 (4,07); 299 (4,05)	53,8	3,2	15,8	18,0	$C_8H_6N_2OS$	53,7	3,4	15,7	17,9
Ib	239—240	220 (4,05); 291 (4,19)	225 (4,14); 279 (4,23)	56,4	4,3	14,4	16,7	$C_9H_8N_2OS$	56,2	4,2	14,6	16,6
Ic	259—260	219 (4,14); 291 (4,22)	223 (4,31); 268 (3,64)	56,5	4,4	14,5	16,4	$C_9H_8N_2OS$	56,2	4,2	14,6	16,6
Id	175—176	219 (4,55); 292 (3,74)	—	58,0	4,9	14,0	15,7	$C_{10}H_{10}N_2OS$	58,2	4,8	13,6	15,5
IIa	210	232 (4,12); 275 (3,87)	240 (4,14); 285 (3,85)	56,5	4,3	14,6	16,8	$C_9H_8N_2OS$	56,2	4,2	14,6	16,6
IIb	78—79	232 (4,17); 280 (3,86)	—	58,4	4,6	13,7	15,4	$C_{10}H_{10}N_2OS$	58,2	4,8	13,6	15,5
III	159—160	203 (4,12); 254 (4,16)	—	58,4	4,9	13,8	15,6	$C_{10}H_{10}N_2OS$	58,2	4,8	13,6	15,5

When the exocyclic sulfur atom is alkylated (IIa), the UV spectrum shows a bathochromic shift of the first maximum, by 11 nm (λ_{max} 232 nm), and a hypsochromic shift of the second maximum by 16 nm. Similar changes in the bands for $\pi \rightarrow \pi^*$ transitions are seen in 2-thiohydantoins, which incorporate the grouping —(O)CNHC(S)NH— which is also present in 2-thioxo-4-quinazolone [5]. In the formation of the S-methylated derivative of (IIb), it is theoretically possible for two types of C=N bonds to be formed, involving atoms $N_{(1)}$ and $N_{(3)}$. Comparison of the UV spectra of 1,3- and 2,3-dimethyl derivatives (Id) and (IIb) shows that the positions of the maxima are identical and the intensities of the bands similar for (IIa, b), indicating the formation on alkylation of a compound with a nonconjugated system of C=O and C=N bonds. The conjugated grouping O=C—N_3=C(SR) results in a more complex spectrum (III), since a new band appears with a lower intensity and an absorption maximum at 315 nm, apparently corresponding to $\pi \rightarrow \pi^*$ transitions in the thiocarbonyl group [5].

In the spectrum of the monoanion of (Ia), two absorption bands are seen at 224 and 299 nm, i.e., the maxima are shifted bathochromically with respect to their positions in the neutral molecule. This is due to charge delocalization occurring in the (Ia) anion, the possibility of such a process having been demonstrated by IR spectroscopy in thioamides [6]. This charge delocalization takes place for the most part in the thioamide group, and therefore the positions of the absorption maxima in the spectra of the monoanions of (Ia) and (Ib) change over the range 280-300 nm, and the electronic structure of the anion approximates in the limiting case to that of (III). When a proton is detached from $N_{(1)}$ (compounds Ib and IIa), delocalization of charge takes place in the heterocyclic moiety ot the molecule $S=C_{(2)}-N_{(1)}=C_{(6)}$, the latter being conjugated with the aromatic nucleus. This is the reason for the appearance of absorption with a maximum at 307 nm in the spectrum of the anion of (Ia).

Examination of the UV spectra shows that dissociation of the 2-thioxo-4-quinazolone molecule begins with the cleavage of a proton from $N_{(3)}$, the basicity of which is evidently higher than that of $N_{(1)}$. The compounds (I) exist in the thioketo-form. The hydrogen atoms are located at the ring $N_{(1)}$ and $N_{(3)}$ atoms, as confirmed by the spectra of the model compounds (Ib) and (Ic). No appreciable amounts of the thiol form are present in solution, since migration of a proton to the exocyclic sulfur would result in a bathochromic shift of the first maximum in the region 215-225 nm, and a hypsochromic shift in the region 285-295 nm, such as occurs in the spectrum of the 2-methyl compound (IIa).

EXPERIMENTAL

UV spectra were obtained on a Hitachi EPS-3T in alcohol (c 10^{-4}-10^{-5} M), and PMR spectra on a JNM-4H-100 instrument in $CDCl_3$ and CF_3COOH, internal standard TMS (δ scale). Compounds (I-III) were purified by recrystallization from alcohol, hexane, and acetic acid, and their purities were established by thin-layer chromatography on Silufol UV-254 in the systems benzene—acetone (4:1) or chloroform—methanol (15:1).

2-Thioxo-4-quinazolone (Ia) was obtained by fusing 4-quinolone with sulfur [4].

1-Methyl-2-thioxo-4-quinazolone (Ib). 1-Methyl-4-quinazolone (0.13 g, 0.8 mmole) was fused with sulfur (0.2 g, 6 mmole) at 220-230°C for 20 min. The mixture was then cooled, dissolved in 100 ml of 2 N sodium hydroxide, and excess sulfur filtered off. The filtrate was neutralized with dilute (1:1) acetic acid to pH 6.8. The solid which separated was filtered off, washed with 100 ml of water, and dried to give 0.13 g (84%) of product. IR spectrum: 3200, 3090 (NH), 1695 cm^{-1} (C=O).

3-Methyl-2-thioxo-4-quinazolone (Ic) was obtained similarly.

2-Methyl-2-thioxo-4-quinazolone (IIa). To a suspension of 3.56 g (20 mmole) of (Ia) in 100 ml of alcohol was added a solution of 1.12 g (20 mmole) of potassium hydroxide in 20 ml of alcohol. To the resulting solution of the salt was added 2.84 g (20 mmole) of methyl iodide. The mixture was boiled for 6 h, cooled, and the crystals which separated were twice recrystallized from alcohol to give 0.89 g (23%) of product. IR spectrum: 3170 (NH), 1680 (C=O), 1585 cm^{-1} (C=N).

1,3-Dimethyl-2-thioxo-4-quinazolone (Id). To a solution of 1.1 g (7 mmole) of N-methylanthranilic acid in 10 ml of acetic acid was added 0.5 g (7 mmole) of methyl isothiocyanate. The mixture was kept for 2 h at 100°C, cooled, and the crystals which separated filtered off and recrystallized from alcohol. Yield 0.46 g (33%). IR spectrum: 1680 cm^{-1} (C=O). PMR spectrum (CF_3COOH): 3.50 (3H, s, $N_{(3)}CH_3$); 3.72 (3H, s, $N_{(1)}CH_3$); 6.9-9.88 ppm (4H, m, C_6H_4).

2,3-Dimethyl-2-thioxo-4-quinazolone (IIb). A mixture of 0.96 g (5 mmole) of (IIa), 0.71 g (5 mmole) of methyl iodide, and 0.28 g (5 mmole) of KOH in 50 ml of anhydrous methanol was boiled for 4 h. The solvent was distilled off, and the residue washed with water, dried, and twice recrystallized to give 0.75 g (77%) of product. IR spectrum: 1685 (C=O), 1620 cm^{-1} (C=N).

1,2-Dimethyl-2-thioxo-4-quinazolone (III). To 1.7 g (5 mmole) of the potassium salt of (Ib) in 20 ml of anhydrous methanol was added 0.71 g (5 mmole) of methyl iodide, and the mixture kept for 3 h at 50°C. The solvent was distilled off, and the solid residue separated on a chromatrographic column (3 × 100 cm) packed with grade II alumina, eluted successively with hexane and a mixture of hexane and chloroform (1:1). Yield 0.06 g (6%) of 1,3-dimethyl-2-thioxo-4-quinazolone (Id) and 0.9 g (87%) of (III). IR spectrum: 1645 (C=O), 1605 cm^{-1} (C=N). PMR spectrum (CF_3COOH): 2.18 (3H, s, SCH_3); 3.71 (3H, s, $H_{(1)}CH_3$); 7.35 ppm (4H, m, C_6H_4).

LITERATURE CITED

1. N. B. Das and A. S. Mittra, J. Indian Chem. Soc., 56, 398 (1979).
2. H. K. Misra and A. K. SenGupto, Pest. Sci., 13, 177 (1982).
3. Kh. M. Shakhidoyatov, S. Yangibaev, L. M. Yun, and Ch. Sh. Kadyrov, Zh. Prikl. Spektrosk. No. 1, 112 (1982).
4. L. M. Yun, S. Yangibaev, Kh. M. Shakhidoyatov, and Ch. Sh. Kadyrov, Khim. Geterotsikl. Soedin., No. 2, 268 (1983).
5. K. A. Byunov, A. I. Ginak, and E. C. Sochilin, Zh. Prikl. Spektrosk., 16, 1037 (1972).
6. K. A. Byunov, A. I. Ginak, and E. G. Sochilin, Zh. Prikl. Spektrosk., 25, 866 (1976).