C-ACYLATION OF RHODANINE DERIVATIVES

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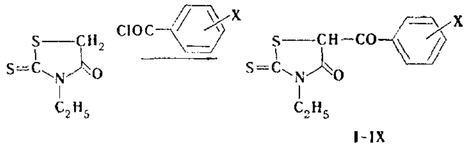
The corresponding 5-aroyl derivatives were obtained by reaction of aromatic carboxylic acid chlorides with 3-ethylrhodanine, and their chemical and physicochemical properties were studied. It is shown that they are completely enolized and stabilized by intramolecular hydrogen bonding; the side-chain carbonyl group undergoes enolization. Methylation with diazomethane gives O-ethers – α-methoxyarylidene derivatives of 3-ethylrhodanine – and S-ethers, which exist as dipolar ions.

3-Ethylrhodanine reacts with aromatic carboxylic acid chlorides to give the corresponding 5-aroyl derivatives (I-IX) in high yields (Table 1).



The reaction proceeds in dioxane in the presence of calcium hydroxide at 80-95°C. 3-Ethyl-5-methylrhodanine reacts similarly. The latter reacts with benzoyl chloride to give 3-ethyl-5-methyl-5-benzoylrhodanine (X). The reaction with aliphatic acid chlorides does not proceed under these conditions.

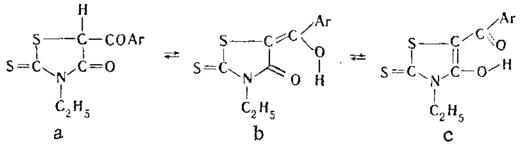
All of the aroyl derivatives except X are quite strong acids – the pK_a values, determined by potentiometric titration in a mixture of 75% acetone and 25% water (by volume) [1] for I, IV, V, VIII, and IX are, respectively, 4.06, 4.38, 4.32, 4.81, and 3.43. In alkaline solution they form stable anions which undergo hydrolytic cleavage only under rather severe conditions, considerably more severe than the conditions for the hydrolysis of benzylidene derivatives of rhodanine [2]. In this case, benzoic acids and products of the cleavage of the rhodanine ring are formed. In some cases, we were also able to isolate 3-ethylrhodanine. Consequently, the carbonyl carbon of the side chain primarily undergoes attack by the hydroxide ion.

In the bromination of III at 0° in $CHCl_3$, the aroyl group is displaced to give p-bromobenzoic acid and, probably, a bromo derivative of 3-ethylrhodanine.

Compounds I-IX form intensely colored chelates with metal salts – for example, Fe^{2+} gives a green chelate, while Cu^{2+} gives a red-brown chelate.

The aroyl derivatives of 3-ethylrhodanine can exist in several tautomeric forms (a-c).

The IR spectra of I-IX contain bands of a double bond at 1600-1626 cm^{-1}, of a thioamide grouping at 1242-1246, 1125-1134, and 1100-1105 cm^{-1}, and of other groups (Table 1). In contrast to model compound



Lensovet Leningrad Technological Institute. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1491-1495, November, 1972. Original article submitted January 6, 1971.

TABLE 1. Aroyl Derivatives of 3-Ethylrhodanine (I-IX)

Comp.	X	mp, °C	Crystallization solvent	Empirical formula	Found, %		Calc., %		Yield, %
					N	S	N	S	
I	H	89,5	Petroleum ether	$C_{12}H_{11}NO_2S_2$	5,1	24,2	5,3	24,1	86
II	*p*-Cl	129	Ethanol–water	$C_{12}H_{10}ClNO_2S_2$	4,7	21,2	4,7	21,3	90
III	*p*-Br	133—134	Cyclohexane	$C_{12}H_{10}BrNO_2S_2$	4,2	18,8	4,1	18,8	82
IV	*p*-CH_3	107—108	" "	$C_{13}H_{13}NO_2S_2$	5,1	22,8	5,0	22,9	85
V	*m*-CH_3	99—100	,, ,,	$C_{13}H_{13}NO_2S_2$	5,0	23,0	5,0	22,9	89
VI	*p*-NO_2	178	,, ,,	$C_{12}H_{10}N_2O_4S_2$	9,0	20,7	9,1	20,6	85
VII	*m*-NO_2	131—132	Acetone–water	$C_{12}H_{10}N_2O_4S_2$	9,0	20,4	9,0	20,6	87
VIII	*p*-OCH_3	141—141,5	Ethanol–water	$C_{13}H_{13}NO_3S_2$	4,8	21,7	4,7	21,6	90
IX	*p*-$COOC_4H_9$	75—76	Cyclohexane	$C_{17}H_{19}NO_4S_2$	3,8	17,6	3,8	17,5	91

TABLE 1 (continued)

Comp.	λ_{max} (lg ε), nm		IR spectra in CCl_4*	δ_{OH} in $CHCl_3$, ppm
	n-hexane	ethanol		
I	265 (4,0), 285 (3,95), 388 (4,48)	275 (4,17), 395 (4,40)	1644, 1605, 1597, 1572, 1500 1370, 1246, 1132, 1102	10,7
II	275 (4,14), 395 (4,43)	275 (4,13), 400 (4,47)	1645, 1600, 1590, 1487, 1358 1241, 1133, 1100	—
III	265 (4,21), 398 (4,46)	278 (4,18), 392 (4,5)	1647, 1610, 1600, 1572, 1484 1366, 1245, 1125, 1100	10,1
IV	275 (4,1), 392 (4,46)	272 (4,12), 396 (4,38)	1648, 1601, 1575, 1506, 1366 1245, 1131, 1101	11,1
V	270 (3,9), 284 (3,9), 386 (4,36)	274 (4,16), 390 (4,48)	1650, 1600, 1583, 1368, 1250 1132	10,3
VI	265 (4,14), 295 (3,89), 400 (4,33)	275 (4,30), 410 (4,17)	1650, 1616, 1590, 1531, 1496 1355, 1242, 1131, 1101	—
VII	282 (3,98), 386 (4,34)	274 (4,26), 385 (4,44)	1655, 1606, 1579, 1542, 1353 1246, 1125, 1105	9,5
VIII	290 (4,18), 398 (4,46)	275 (4,25), 398 (4,45)	1636, 1626, 1593, 1583, 1563 1506, 1361, 1262, 1241, 1129 1101	—
IX	282 (3,6), 400 (4,20)	276 (3,46), 388 (4,4)	1740, 1658, 1610, 1600, 1572 1374, 1280, 1245, 1134, 1100	10,0

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*Recorded with an IKS-22 spectrometer with a NaCl prism (d 0.1 mm).

X, the IR spectrum of which contains two carbonyl group bands (ν_{CO} 1736 and 1693 cm^{-1}), there is only one intense band at 1636-1658 cm^{-1} in the spectra of I-IX in this region. Its position changes in conformity with the nature of the substituent in the benzene ring – electron-donor substituents shift it to lower frequencies, while electron-acceptor substituents shift it in the opposite direction. A broad low-intensity band is observed in the region of OH group absorption. The positions of both bands (ν_{CO} and ν_{OH}) change only slightly as the solution concentration changes and depend only slightly on the nature of the solvent (CCl_4, $CHCl_3$, dioxane, and dimethyl sulfoxide). The latter and the chemical shifts (9.49-11.07 ppm) and pK_a values are evidence for enolization of one of the carbonyl groups of I-IX and for their stabilization by strong intramolecular hydrogen bonding.

The side-chain carbonyl group apparently undergoes enolization (structure b), since the IR spectra do not contain the absorption band characteristic for the thiazoline ring at 1553 cm^{-1} that is observed in the spectrum of 2-thioketo-3-ethyl-4-chloro-5-formylthiazoline (XI) [3]. This is also indicated by the UV spectra of I-IX (Table 1). The introduction of an aroyl group into the 3-ethylrhodanine molecule leads to deepening of the color by about 100 nm (λ_{max} of 3-ethylrhodanine in n-heptane and alcohol is 295 nm). This deepening of the color can occur when I-IX exist primarily in the form of structure b. The smaller effect of the substituents on the position of λ_{max} than is observed in the benzylidene derivatives of rhodanine [4] may be explained by cross conjugation with the hydroxyl group attached to the double bond of the side chain. The absence of significant solvatochromism on passing from n-hexane to ethanol (Table 1) serves as a confirmation of the presence of strong intramolecular hydrogen bonding.

Substances XIV and XV, respectively, which are sparingly soluble in nonpolar solvents, were isolated in 10-13% yields along with the expected O-ethers (XII and XIII) when ether solutions of I and III were

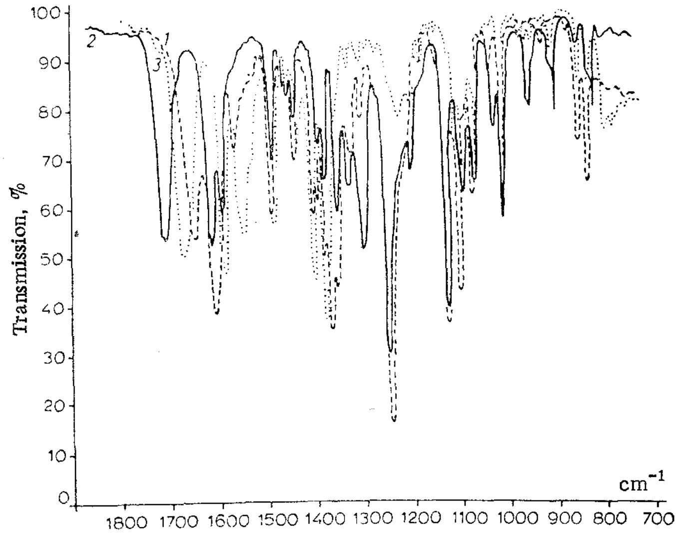


Fig. 1. IR spectra of I, XII, XIV in $CHCl_3$ (d 0.1 mm, c 20 mg/ml): 1) I; 2) XII; 3) XIV.

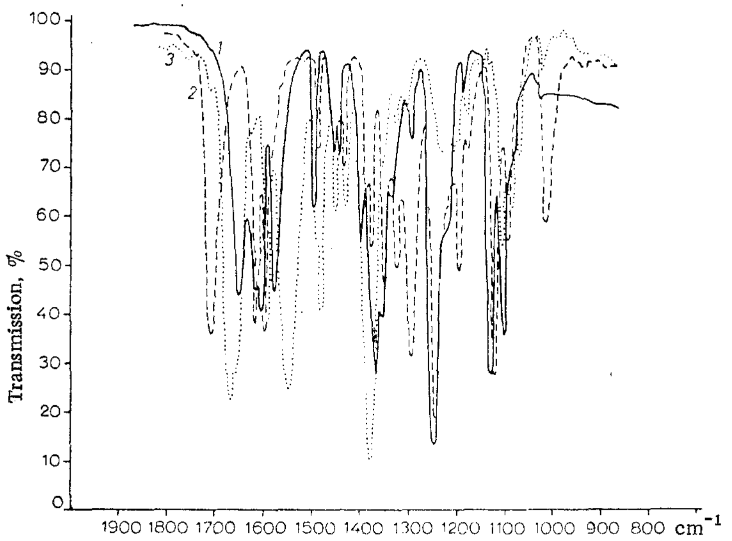
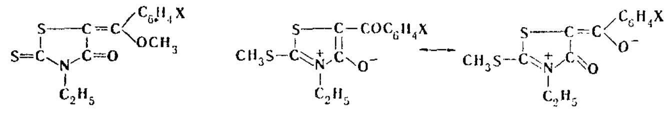


Fig. 2. IR spectra of III, XIII, XV in $CHCl_3$ (d 0.1 mm, c 20 mg/ml): 1) III; 2) XIII; 3) XV.

treated with diazomethane. The structures of the methylation products were established by means of the UV and IR spectra. A hypsochromic shift of 40-43 nm in hexane and of 36-40 nm in ethanol, as compared with the starting materials, is observed in the UV spectra of the nonpolar-solvent-soluble XII and XIII; this may be a consequence of rupture of the hydrogen-bonded ring. The absorption band of the carbonyl group is observed at 1710 cm^{-1} in the IR spectra and can be assigned to ν_{CO} absorption of the rhodanine ring [ν_{CO} of 3-ethylrhodanine is observed at 1718 cm^{-1}, while ν_{CO} of 2-thioketo-3-ethyl-4-chloro-5-formylthiazoline (XI) is observed at 1677 cm^{-1}]. The character of the spectra of the O-methyl derivatives is close to that of the spectrum of 5-ethoxymethylene-3-ethylrhodanine and 3-ethylrhodanine, from which it can be concluded that they have the α-methoxyarylidene structure.



XII, XIII XIV, XV

XII, XIV X=H; XIII, XV X=p-Br

A dipolar ion structure should be assigned to the methylation products (XIV and XV), which are somewhat more deeply colored than the starting compounds; the IR spectra of XIV and XV do not contain the absorption bands of the thioamide grouping (1248, 1130, and 1100 cm^{-1}). The absorption band of the carbonyl groups in XIV is broadened and is found at 1668 cm^{-1} (Fig. 1, ν_{CO} of the dipolar ion obtained from 5-phenylrhodanine is observed at 1685 cm^{-1} [5]). The absorption band of the carbonyl group in the IR spectrum of XV is also broadened and split into two bands (Fig. 2) which correspond to polarized carbonyl groups. The formation of dipolar ions during the diazomethane methylation of the aroyl derivatives of 3-ethylrhodanine can be explained by the fact that the latter, which are rather strong acids, are ionized in ether solution; the electron density in the anion is concentrated both on the oxygen atoms and on sulfur, and the reaction proceeds at the most sterically accessible centers.

Thus, the 5-aroyl derivatives of 3-ethylrhodanine are completely enolized and exist primarily in the α-hydroxyarylidene structure, stabilized by intramolecular hydrogen bonding, in solutions in nonpolar solvents.

EXPERIMENTAL

5-(X-Aroyl)-3-ethylrhodanines (I-IX, Table 1). A 1.5-g (0.02 mole) sample of finely ground calcium hydroxide was added to a solution of 0.01 mole of 3-ethylrhodanine in 8 ml of dioxane, and 0.01 mole of the appropriate carboxylic acid chloride was added with stirring to the mixture. The mixture was then heated up slowly on a water bath. At 60-65° the mass turned red, and its temperature rose to 80-95°. Stirring was continued for another 1.5 h at this temperature, after which the mass was poured into 25 ml of 2 M hydrochloric acid. The resulting red-brown oil crystallized after a certain time had elapsed. The crystals were removed by filtration, washed with water, dried, and crystallized from a suitable solvent.

3-Ethyl-5-methyl-5-benzoylrhodanine (X). This compound was similarly obtained in 35% yield from 3-ethyl-5-methylrhodanine and had mp 54-56° (from petroleum ether). λ_{max}, nm (log ε), in alcohol: 223 (3.78), 262 (3.92), 295 (4.01); ν_{CO} in CCl_4: 1737 and 1693 cm^{-1}. Found %: N 4.8; S 23.1. $C_{13}H_{13}NO_2S_2$. Calculated %: N 5.0; S 22.9.

2-Thioketo-3-ethyl-4-chloro-5-formylthiazoline (XI). This compound was obtained via the method in [3]. λ_{max}, nm (log ε), in heptane: 233 (3.95), 297 (3.82), 360 (4.25), 372 (4.26); IR spectrum in $CHCl_3$: 1677 (ν_{CO}), 1555, 1379, 1360, 1245, 1142, 1102 cm^{-1}.

Bromination of 3-Ethyl-5-(p-bromobenzoyl)rhodanine (III). A solution of 0.8 g (5 mmole) of bromine in 50 ml of chloroform was added at 0° to a solution of 1.7 g (5 mmole) of III in 150 ml of chloroform. A colorless precipitate formed from the mixture as the bromine was added. At the end of the reaction, the precipitate was removed by filtration, washed with petroleum ether, and dried to give 0.81 g (80%) of p-bromobenzoic acid with mp 253°.

Diazomethane Methylation of 3-Ethyl-5-benzoylrhodanine (I). An ether solution of 0.5 g (0.011 mole) of diazomethane was added gradually at 0° to a suspension of 2 g (0.0075 mole) of I in 100 ml of ether. After 2 h, the precipitate was removed by filtration and washed several times with ether to give 0.2 g (10%) of 2-methyl-3-ethyl-5-benzoylthiazolium salt (XIV) with mp 204-205° (from ethanol), λ_{max}, nm (log ε), in alcohol: 258 (4.08), 392 (4.12). Found, %: N 5.1; S 22.8. $C_{13}H_{13}NO_2S_2$. Calculated, %: N 5.0; S 22.9. The ether was removed from the filtrate by distillation, and the residue was recrystallized several times from aqueous alcohol to give 1.3 g (62%) of 3-ethyl-5-(α-methoxybenzylidene)rhodanine (XII) with mp 112-114°. λ_{max}, nm (log ε), in alcohol: 287 (4.0), 362 (4.53). Found, %: N 5.1; S 23.1.

Similarly, 2 g of III gave 0.23 g (13%) of 2-methyl-3-ethyl-5-(p-bromobenzoyl)thiazolium salt (XV) and 1.4 g (81%) of 3-ethyl-5-(α-methoxy-p-bromobenzoyl)rhodanine (XIII). Compound XV had mp 186-187° (aqueous ethanol), λ_{max}, nm (log ε), in ethanol: 260 (4.3), 392 (4.36); in benzene: 410 (4.14). Found, %: N 3.9; S 18. Compound XIII had mp 110-111° (aqueous ethanol); λ_{max}, nm (log ε), in alcohol: 285 (4.1), 362 (4.45). Found, %: N 3.9; S 18.0.

3-Ethyl-5-ethoxymethylenerhodanine. This compound was obtained in 48% yield via the method in [6,7]. λ_{max}, nm (log ε), in alcohol: 288 (4.03), 352 (4.41). IR spectrum in CCl_4: 1714 (ν_{CO}), 1644 ($\nu_{C=CH}$), 1375, 1350, 1252, 1130, 1100 cm^{-1}.

LITERATURE CITED

1. A. Albert and E. Serjeant, Ionization Constants of Acids and Bases, Methuen (1962).
2. N. M. Turkevich and I. I. Kurnitskii, Ukr. Khim. Zh., 16, 454 (1950).
3. I. Ya. Kvitko and B. A. Porai-Koshits, Zh. Organ. Khim., 2, 169 (1966).
4. A. E. Lutskii, Zh. Obshch. Khim., 14, 487 (1944).
5. S. Abrahamsson and A. Westerdahl, Acta Chem. Scand., 21, 442 (1967).
6. C. P. Lo and W. J. Croxall, J. Am. Chem. Soc., 76, 4166 (1954).
7. C. P. Lo, J. Am. Chem. Soc., 80, 3466 (1958).