Isothiocyanates. XLV. 3-Substituted rhodanines prepared from isothiocyanates containing sulfur beside the functional group

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Synthesis of 3-substituted rhodanines derived from (3-isothiocyanatophenyl)alkyl sulfides and sulfones is described in this work. Infrared and ultraviolet spectra as well as rate constants of the formation of rhodanines by addition od thioglycolic acid to the appropriate isothiocyanates have been measured. The results are compared with those obtained in a similar reaction with (4-isothiocyanatophenyl)alkyl sulfides and sulfones.

It is evident from the work of *Carter* and co-workers [1] that 3-substituted rhodanines show high fungicidal activity. This activity increases when an aromatic ring bound directly to nitrogen is incorporated into the molecule, mainly, if this aromatic ring is substituted in *p*-position. We utilized this knowledge in our previous work [2] and prepared 3-substituted rhodanines from (4-isothiocyanatophenyl)alkyl sulfides and sulfones.

3-Substituted rhodanines can be prepared by two basic procedures: dithiocarbamate [3—5] and isothiocyanate [2, 6]. It is a cyclization reaction resulting in the formation of a five-membered rhodanine ring in both cases.

The subject of this work was the synthesis of 3-substituted rhodanines (not described yet) from (3-isothiocyanatophenyl)alkyl sulfides and sulfones, interpretation of their i.r. and u.v. spectra, and determination of the rate constants of thioglycolic acid addition to these isothiocyanates.

The synthesized rhodanines are present in Table 1. All the prepared derivatives were yellow crystalline compounds crystallized from ethanol and glacial acetic acid, respectively. The yields varied from 30 to 48%.

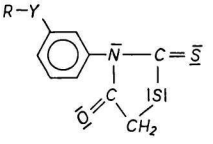
The i.r. spectra of all the synthesized rhodanines (Table 2) showed intensive absorption bands belonging to the stretching vibration of C=O group in the 1769—1754 cm^{-1} range. When Y = SO_2, a shift to higher wavenumbers (Table 2) was observed. It was in accordance with the electron-withdrawing effect of the SO_2 group. With all the sulfones an intensive absorption band $\nu_{as}(SO_2)$ was observed in the 1333—1327 cm^{-1} region and an absorption band of high intensity $\nu_s(SO_2)$ at 1156—1151 cm^{-1}.

The u.v. spectra (Table 2) of the synthesized 3-substituted rhodanines showed two absorption bands of significant intensities (log ε above 4) in the measured region 200—400 nm. The first band could be attributed to "N" conjugation (thioamide band) and the second one at ~300 nm to "S" conjugation (dithiocarbamate band).

The kinetics of the rhodanine formation was followed spectrophotometrically. The rate constants were calculated from the rhodanine increase in the region of its second absorption maximum. It is evident from our previous observations [7] that when the

Table 1

The synthesized 3-substituted rhodanines



No.	R	Y	Formula	*M*	Calculated/found			Yield [%]	M.p. [°C]
					% S	% C	% H		
I	Methyl	S	$C_{10}H_9NOS_3$	255.4	37.60	47.10	3.53	48.1	127
					37.83	46.93	3.68		
II	Ethyl	S	$C_{11}H_{11}NOS_3$	269.3	35.60	49.00	4.08	32.3	88
					35.87	49.19	4.01		
III	*n*-Octyl	S	$C_{17}H_{23}NOS_3$	353.6	27.20	57.78	6.56	28.5	97—99
					26.97	57.62	6.38		
IV	Methyl	SO_2	$C_{10}H_9NO_3S_3$	287.4	33.47	41.79	3.16	42.3	134—137
					33.32	41.65	3.01		
V	Ethyl	SO_2	$C_{11}H_{11}NO_3S_3$	301.4	31.80	43.90	3.66	39.5	105
					31.56	43.79	3.52		
VI	*n*-Octyl	SO_2	$C_{17}H_{23}NO_3S_3$	385.6	24.95	52.96	6.01	32.3	74—77
					24.63	52.82	5.89		

Table 2

Infrared and ultraviolet spectra of the prepared 3-substituted rhodanines

No.	$\lambda_{max\,I}$ [nm]	log ε	$\lambda_{max\,II}$ [nm]	log ε	ν(C=O) [cm^{-1}]	$\nu_{as}(SO_2)$ [cm^{-1}]	$\nu_s(SO_2)$ [cm^{-1}]
I	260	4.62	298	4.37	1760	—	—
II	258	4.91	296	4.37	1764	—	—
III	257	4.35	296	4.18	1754	—	—
IV	257	4.20	297	4.25	1769	1333	1156
V	257	4.63	296	4.35	1767	1330	1152
VI	256	4.08	297	4.18	1758	1327	1151

reaction of isothiocyanate with thioglycolic acid was accomplished in alkali medium under the conditions of pseudo-unimolecular reaction, *N*-substituted thiocarbamoylmercaptoacetic acids were formed quantitatively. Cyclization of these acids to the appropriate rhodanines occurred only after acidifying. However, at lower pH (~7.5) it was not possible to register the formation of the addition product because 3-substituted rhodanines were formed immediately. We studied the kinetics of formation of these rhodanines.

The obtained rate constant values of the reactions of 3- and 4-substituted isothiocyanatophenyl sulfides and sulfones with thioglycolic acid are quoted in Table 3. The concentration of thioglycolic acid in the reaction medium was constant throughout (large excess); the reaction was thus pseudo-unimolecular. The rate constants were evaluated by using the equation of the first order reaction. The apparent rate constants (k') were calculated from the linear relationship of log ΔE against time.

Table 3

Rate constants of thioglycolic acid addition to the appropriate isothiocyanates

R	X	$k' \ 10^3$ [s^{-1}] 3-substituted derivative	$k \cdot 10^{-2}$ [l mol^{-1} s^{-1}] 3-substituted derivative	$t_{1/2}$ [s]	$k' \ 10^3$ [s^{-1}] 4-substituted derivative	$k \cdot 10^{-3}$ [l mol^{-1} s^{-1}] 4-substituted derivative	$t_{1/2}$ [s]
Methyl	S	4.73 ± 0.02	3.00	147.4	16.66 ± 0.060	1.06	41.7
Methyl	SO_2	33.71 ± 0.020	21.38	20.5	5.77 ± 0.010	1.83	121.5
Ethyl	S	6.84 ± 0.050	4.34	101.9	16.26 ± 0.073	1.03	42.5
Ethyl	SO_2	15.27 ± 0.002	9.69	45.2	7.55 ± 0.020	4.79	92.4
n-Octyl	S	0.130 ± 0.001	0.082	5330.7	0.210 ± 0.030	0.133	3300
n-Octyl	SO_2	0.122 ± 0.005	0.077	5670	—	—	—

The actual rate constants (k) were obtained by dividing the apparent rate constants (k') by the concentration of the ionized form of thioglycolic acid $^-S-CH_2COO^-$ at the given pH.

Comparison of the rate constants of the thioglycolic acid addition to 3- and 4-substituted isothiocyanatophenyl sulfides and sulfones showed that when the alkyl chain was shorter the sulfones were more reactive due to the $-I$ effect of the sulfone group. With lengthening of the alkyl chain the reactivity of the isothiocyanates decreased rapidly (the difference between the reactivity of sulfides and sulfones was negligible) due to steric hindrance [7]. The rate of addition of thioglycolic acid to (4-isothiocyanatophenyl)alkyl sulfides and sulfones was orderly higher than that of thioglycolic acid to (3-isothiocyanatophenyl)alkyl sulfides and sulfones.

Experimental

The isothiocyanates used for preparation of the 3-substituted rhodanines were prepared by thiophosgene method from the appropriate primary amines [8].

The i.r. spectra were measured on a double-beam UR-20 (Zeiss Jena) spectrophotometer in the region of 800—3600 cm^{-1}; concentration of compounds in chloroform was $2.5 \times \times 10^{-2}$ M, NaCl cells of 1.04 mm thickness were used.

The u.v. spectra were taken with a recording Specord UV-VIS (Zeiss Jena) spectrophotometer using cells of 10-mm thickness in the region of 200—400 nm (concentration $2.5-5.0 \times 10^{-5}$ M in methanol).

3-Substituted rhodanines

The appropriate isothiocyanate (0.01 mole) and thioglycolic acid (1.4 ml) were heated on a glycerine bath under reflux at 120—130°C for 1—2 hrs. The content of the flask was poured into water after the reaction was over. Slightly yellow crystalls of rhodanine were obtained. After sucking and washing with water, the crude product was crystallized from ethanol and glacial acetic acid, respectively.

Kinetic measurements

The rate constants of thioglycolic acid addition to the isothiocyanates were determined spectrophotometrically on a recording Specord UV-VIS spectrophotometer at 25 $\pm$ 0.2°C in the region of the second maximum of the forming rhodanines. The reaction mixture contained 0.1 M McIlvaine buffer (9.0 ml; pH = 7.5), 0.1 M water solution of thioglycolic acid (0.5 ml), and 0.001 M methanolic solution of the isothiocyanate (0.5 ml).

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