Isothiocyanates. XXX. Synthesis, Ultraviolet and Infrared Spectra of 3-Substituted Rhodanines

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Received December 7, 1970

The synthesis of twenty-five 3-substituted rhodanines is reported; eight of them are so far not described in the literature. The effect of substituents in position 3 on the shift of the C=O absorption band in the i.r. spectra is studied. 3-Substituted rhodanines reveal in u.v. spectra two intensive absorption bands associated with the "N" and "S" conjugation.

Our preceding papers [1—3] referring to the quantitative study of nucleophilic addition reactions of isothiocyanates (ITC) deal with the reactivity of alkyl and particularly aryl isothiocyanates with —OH ions, amino groups (of various amines and amino acids), and thioglycolate. Results thus obtained together with further analogous ones from investigation of the reactivity of ITC with other thiols indicated the enormously high reactivity of ionized thiols when compared with amino groups of similar compounds (addition of amino groups in nonprotonized form). In this very case isothiocyanates gave with thioglycolate *N*-substituted thiocarbamoylmercaptoacetic acids or corresponding 3-substituted rhodanines as final products, depending on reaction conditions. *N*-Substituted thiocarbamoylmercaptoacetic acids could be quantitatively transformed into corresponding rhodanines (cyclization in acid medium). Similarly, isothiocyanates could be obtained from rhodanines upon alkaline hydrolysis of these five-membered rings to give *N*-substituted thiocarbamoylmercaptoacetic acids, which are unstable under the given reaction conditions.

In this connection it seemed useful to examine the some time ago described preparation of 3-substituted rhodanines from isothiocyanates and thioglycolic acid and investigate the recently described types of aliphatic and particularly aromatic ITC. Physicochemical properties of rhodanines including their stability and reactions in various media in relation to their structure is important, because these compounds belong to the group of so-called synthetic producers of ITC, *i.e.* substances liberating biologically active ITC.

This paper deals with the preparation of 3-substituted rhodanines and their i.r. and u.v. spectra.

Table 1

3-Substituted rhodanines

No.	R	Formula	*M*	Calculated/found		Yield [%] Method of preparation	M.p. [°C] B.p. [°C/Torr]
				% N	% S		
I	methyl-	$C_4H_5NOS_2$	147.22	—	—	35.2 *B*	69—70
II	ethyl-	$C_5H_7NOS_2$	161.25	—	—	43.1 *B*	128/4[c]
III	*n*-butyl-	$C_7H_{11}NOS_2$	189.30	—	—	70.2 *B*	145/4[c]
IV	benzyl-	$C_{10}H_9NOS_2$	223.32	—	—	68.6 *A*	82.5—83
V	4-bromobenzyl-	$C_{10}H_8BrNOS_2$	302.21	—	—	68.1 *B*	95—96
VI	α-phenylethyl-	$C_{11}H_{11}NOS_2$	237.34	—	—	48.3 *B*	108—109[b]
VII	β-phenylethyl-	$C_{11}H_{11}NOS_2$	237.34	—	—	44.2 *B*	106.5—107
VIII	phenyl-	$C_9H_7NOS_2$	209.29	—	—	12.0 *A* 38.6 *B*	112—114
IX	4-bromophenyl-	$C_9H_6BrNOS_2$	288.20	—	—	67.1 *B*	162—163
X	4-tolyl-	$C_{10}H_9NOS_2$	223.32	—	—	58.6 *B*	166.5—168
XI	4-ethoxyphenyl-	$C_{11}H_{11}NO_2S_2$	253.34	—	—	50.8 *B*	185—188
XII	4-dimethylaminophenyl-	$C_{11}H_{12}N_2OS_2$	252.36	10.70 10.96	25.41 25.74	45.5 *B*	204—206[a]
XIII	4-nitrophenyl-	$C_9H_6N_2O_3S_2$	254.29	—	—	14.5 *B*	226—228[a]
XIV	4-acetylphenyl-	$C_{11}H_9NO_2S_2$	251.33		—	50.2 *B*	146—147
XV	4-methoxyphenyl-	$C_{10}H_9NO_2S_2$	239.32	—	—	10.5 *A* 55.3 *B*	153.5—154

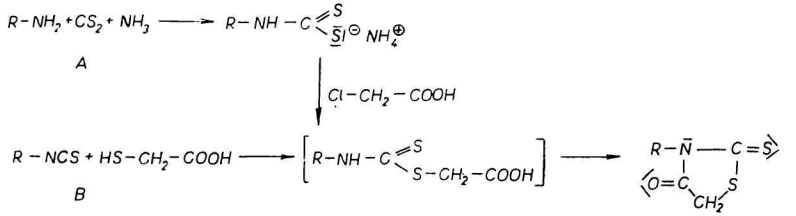
Table 1 (Continued)

No.	R	Formula	*M*	Calculated/found % N	Calculated/found % S	Yield [%] Method of preparation	M.p. [°C] B.t. [°C/Torr]
XVI	3-nitrophenyl-	$C_9H_6N_2O_3S_2$	254.29	— —	— —	51.4 *B*	195—196
XVII	4-carbethoxyphenyl-	$C_{12}H_{11}NO_3S_2$	281.36	4.97 5.12	22.79 23.07	54.2 *B*	114—115
XVIII	3-acetaminophenyl-	$C_{11}H_{10}N_2O_2S_2$	266.34	10.51 10.19	24.07 23.60	46.5 *B*	220—222[a]
XIX	1-naphthyl-	$C_{13}H_9NOS_2$	259.35	— —	— —	61.8 *B*	168
XX	2-naphthyl-	$C_{13}H_9NOS_2$	259.35	— —	— —	60.5 *B*	185—186
XXI	1-naphthylmethyl-	$C_{14}H_{11}NOS_2$	273.38	5.08 5.32	23.45 23.05	56.3 *B*	111
XXII	4-nitro-1-naphthyl-	$C_{13}H_8N_2O_3S_2$	304.35	9.20 9.01	21.07 21.39	39.5 *B*	86—88
XXIII	4-bromobiphenylyl-	$C_{15}H_{10}BrNOS_2$	364.30	3.84 3.69	17.60 17.58	49.5 *B*	188—190
XXIV	4-chlorobiphenylyl-	$C_{15}H_{10}ClNOS_2$	319.84	4.37 4.62	20.04 19.72	48.5 *B*	188.5—191
XXV	4-hydroxybiphenylyl-	$C_{15}H_{11}NO_2S_2$	301.39	4.64 4.59	21.27 21.39	43.3 *B*	265—266[a]

a) Melting points with decomposition.
b) Racemate.
c) Boiling points [°C/Torr].

Experimental

Two basic procedures were used to prepare 3-substituted rhodanines: *A*. dithiocarbamate [4] and *B*. isothiocyanate [5] method. 3-Substituted rhodanines were crystallized from ethanol excepting 3-(4-nitrophenyl)rhodanine and 3-(4-dimethylaminophenyl)-rhodanine which were crystallized from glacial acetic acid (Scheme 1).



Scheme 1

Infrared absorption spectra of the synthesized derivatives were measured with a double-beam UR-10 (Zeiss, Jena) spectrophotometer in the 700 to 3600 cm^{-1} range as 0.05 M solutions in chloroform. Ultraviolet absorption spectra were taken with a VSU-1 (Zeiss, Jena) spectrophotometer in the 220—360 nm range in 10-mm cells as 2.5×10^{-5} M to 5×10^{-5} M solutions in glacial acetic acid (0.1%) containing methanol in order to avoid decomposition. The physicochemical properties of 3-substituted rhodanines are listed in Table 1.

Results and Discussion

Of both possibilities to prepare rhodanines the isothiocyanate procedure (method *B*) has been found to be more effective. Rhodanine can be obtained in a 100% yield under strictly maintained conditions; this procedure is, however, convenient for a micro-scale preparation [8]. In many cases rhodanines synthesized by our procedure had the melting point within 2 to 3°C. This fact is in accordance with the literature [5, 6], nonetheless melting points of some derivatives differed from those referred. Thus the fundamental 3-phenylrhodanine is reported to have m.p. 195—197°C [5], 192—193°C [7], and 188—194°C [6].

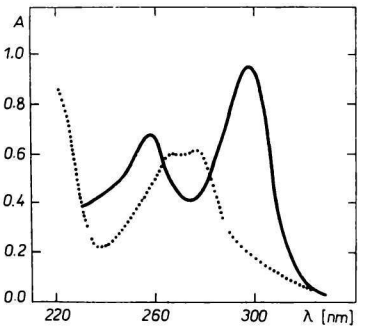


Fig. 1. Ultraviolet spectra of 3-phenylrhodanine (—) and phenyl isothiocyanate (. .) in methanol; $c = 5 \times 10^{-5}$ M.

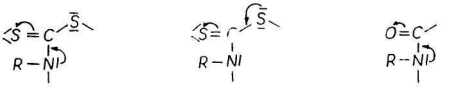
Table 2

Characteristic u.v. and i.r. maxima of 3-substituted rhodanines

No.	$\lambda_{max\ I}$ [nm]	log ε	$\lambda_{max\ II}$ [nm]	log ε	$\tilde{\nu}$(C=O) [cm^{-1}]
I	258	4.22	294	4.29	1742
II	260	4.19	294	4.27	1730
III	260	4.31	296	4.39	1725
IV	260	4.23	296	4.29	1742
V	260	4.29	292	4.32	1741
VI	258	4.01	296	4.16	1728
					1742 sh
VII	262	4.11	296	4.18	1738
VIII	258	4.13	296	4.27	1754
IX	256	4.23	296	4.39	1738
					1758 sh
X	256	4.06	296	4.28	1749
XI	250	4.21	296	4.37	1751
XII	266	4.41	294	4.23	1744
XIII	250	4.27	294	4.29	1758
XIV	252	4.48	296	4.37	1755
					1695*
XV	252	4.14	296	4.35	1750
XVI	254	4.35	296	4.27	1758
XVII	256	4.28	296	4.20	1727
XVIII	250	4.32	296	4.11	1741
XIX	252	4.28	292	4.34	1750
XX	264	4.28	290	4.19	1746
XXI	258	4.20	294	4.23	1742
XXII	248	4.28	296	4.05	1750
XXIII	260	4.47	—	—	1742
XXIV	262	4.41	—	—	1745
XXV	—	—	284	4.30	1740

* $\tilde{\nu}$(C=O) due to the C=O group of acetyl.
sh — shoulder.
$\lambda_{max\ III}$ of compound *XX* — 276 nm (4.26) and of *XXI* — 282 nm (4.26).

Characteristic u.v. data of 3-substituted rhodanines are given in Table 2. 3-Substituted rhodanines reveal two strong absorption bands (log ε 4—4.5; Fig. 1), the first of them being located at about 250 nm, whereas the second at about 290 nm. As follows from the structure of these substances, the corresponding absorption bands could be associated — similarly as is the case with dithiocarbamates and thiadiazines — to the so-called "N" (*I*) (thioamide band) and "S" conjugation (*II*) (dithiocarbamate band) [9]. The third conjugated system (*III*) (Scheme 2) in the molecule is formed by the



II III

Scheme 2

amido grouping, which cannot be seen in the investigated range of spectrum (approx. 290 to 300 nm), since it is overlapped by the II. absorption band. The interpretation of u.v. spectra of various model substances [10] corroborated that the single bands are correctly ascribed to the appropriate conjugated system. 3-Substituted 2-thiohydantoins, which are considered to be such substances, do not contain dithiocarbamate grouping and display therefore only one absorption band at 260 nm. Polycondensed hydrocarbons attached to the rhodanine skeleton reveal in their spectra absorption bands due to aromatic rings (so-called α, β, and γ bands) (Table 2, compounds *XX* and *XXI*). Derivatives *XXIV*, *XXV*, and *XXVI* (Table 2) show only one strong absorption band as a result of overlapping of the rhodanine absorption bands by those of aromatic substituents.

The effect of substituent in the position 3 differently influences positions I ($\sim$ 250 nm) and II ($\sim$ 295 nm) of the absorption maximum. When comparing u.v. spectra of *e.g.* 3-phenylrhodanine, 3-(4-nitrophenyl)rhodanine and 3-(4-dimethylaminophenyl)rhodanine (Table 2, compounds *VIII*, *XII*, and *XIII*) it becomes evident that electron acceptor substituents shifted the I. absorption band hypsochromically, whereas electron donor substituents bathochromically. In contrast, the II. absorption band remains practically substituent unaffected.

3-Substituted rhodanines show in their spectra a strong absorption about 1725—1758 cm^{-1} (Table 2) due to stretching vibrations of the cyclic carbonyl group. Electron donor substituents in position 3 of the rhodanine ring shift the $\tilde{\nu}$(C=O) absorption bands towards lower wave numbers (*e.g.* the $\tilde{\nu}$(C=O) of 3-(4-dimethylaminophenyl)-rhodanine is 1744 cm^{-1}) and electron acceptor substituents towards higher wave numbers (*e.g.* the $\tilde{\nu}$(C=O) of 3-(4-nitrophenyl)rhodanine is 1758 cm^{-1}). Stretching vibrations of C—H bonds of an aromatic ring appear at 3005—3095 cm^{-1} and those of alkyl groups at 2800—3000 cm^{-1}. The intensity of the latter increases with the number of carbon atoms in the alkyl chain. Thus 3-methylrhodanine has a weak band at 2950 cm^{-1}, 3-ethylrhodanine a medium band at 2945 cm^{-1} and 3-*n*-butylrhodanine strong bands at 2882, 2942, and 2970 cm^{-1}.

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Translated by Z. Votický