

Isothiocyanates and Their Synthetic Producers. VIII. The Synthesis and the Study of Spectral Features of Substituted Monothiourethanes

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A thioacylation of the proper amines to yield 20 substituted monothiourethanes, 16 of which were so far not reported, is described. Interpretation of infrared spectra of compounds thus synthesized makes it possible to ascribe in the case of aromatic monothiourethanes 3 characteristic absorption bands at 1520, 1360 and 930 cm^{-1} to the $-\text{NH}-\overset{\text{I}}{\text{C}}=\text{S}$ group.

Ultraviolet absorption spectra of monothiourethanes reveal in the 220–360 nm region an intense absorption band that could be associated with the so called „N“ conjugation of the chromophore system $-\text{NH}-\overset{\text{I}}{\text{C}}=\text{S}$.

The influence of the substituent on the localization and character of the absorption bands is discussed.

Our preceding papers [1–4] referred to the synthesis and physicochemical properties of the synthetic producers of isothiocyanates of 3,5-disubstituted tetrahydro-1,3,5-thiadiazine-2-thiones type.

Recently, aromatic thiourethanes were reported to display a significant biological activity [5, 6]; they were shown to release isothiocyanates even under mild conditions, *e.g.* in solutions and consequently, they belong also to the synthetic producers of the mentioned substances. Of various methods the best was found to be the thioacylation of amines [7, 8].

So far, there have been published only few papers dealing with infrared and ultraviolet absorption spectra of monothiourethanes. A more detailed study on infrared spectra of thiocarbonyl compounds whose $>\text{C}=\text{S}$ group is attached through one carbon atom to one or two nitrogen atoms was reported by Rao and Venkataraghavan [9]. Infrared spectra of monothiourethanes are mentioned in connection with the study of addition mechanism of alcohols to substituted phenylisothiocyanates [9, 10]; nevertheless, appropriate vibration frequencies of characteristic groups are not given.

This paper deals with the synthesis and study of physicochemical properties, namely ultraviolet and infrared absorption spectra of substituted monothiourethanes.

The biological activity of these substances will be the subject of another paper.

Experimental

Preparation of substituted monothiourethanes

The proper amine (0.02 mole) was dissolved in 50 ml of a suitable organic solvent (acetone, chloroform) and to this solution *O*-aryl or *O*-alkylester thiocarbonic acid chloride (0.01 mole) was dropwise added at a room temperature. After the addition of amine was completed the mixture was stirred for one hour and then poured into ice-cold water. The precipitated product was filtered off with suction, washed with water, dried and crystallized from the appropriate solvent (Table 1).

The synthesized monothiourethanes and their physicochemical constants are listed in Table 1.

Infrared absorption spectra of monothiourethanes were measured with a double-beam UR-20 Zeiss spectrophotometer in the 700–3600 cm^{-1} range in p.a. grade chloroform; concentration 0.1 M, cell thickness 0.17 mm. Ethanol and moisture were removed from chloroform by passing it through a silica gel column. The polystyrene film was used for calibration of wavenumbers.

Ultraviolet absorption spectra were taken with a VSU-1 Zeiss spectrophotometer in methanol; concentration 4×10^{-5} M, cell thickness 10 mm. P.a. grade methanol was dried with anhydrous potassium carbonate and distilled, the fraction 65.5–65.8°C being collected.

Results and Discussion

The synthesis of substituted monothiourethanes was carried out by reacting the proper amines with thioacyl chlorides. Both substrate and reagent were prepared according to the literature.

Of various methods to prepare monothiourethanes the most convenient was found to be the thioacylation [6]. Since this reaction proceeds by a $\text{S}_{\text{N}}2$ mechanism, its rate depends on the basicity of the reacting amine. The strong basic amines, *i.e.* aliphatic or aromatic with electron-donating substituents are known to react fairly good. Assuming this reaction mechanism, the yields listed in Table 1 are not consistent with the structure of reactants.

The yield is subject preponderantly to the possibility to isolate the pure product out of the reaction mixture and it depends mainly both upon the choice of a suitable solvent and the physicochemical properties of the reaction product. The potential yield increase of the single products would require a more detailed study of reaction conditions. Thus *e.g.* the yield of *N*-phenyl-*O*-phenylmonothiourethane was reported [5] to be 46%, whereas that by [7] 96% the same method, except solvent, being applied. When choosing solvents attention should be paid to the properties of the reaction products (monothiourethanes), since some of them are little stable in more polar solvent and undergo a rapid decomposition. Aromatic monothiourethanes *e.g.*, undergo decomposition due to the solvent even at room temperature affording isothiocyanate and phenol.

It is interesting that the melting points of some monothiourethanes are not constant and depend in a large extent upon the rate of heating. This phenomenon has been pointed out by Rivier [11]. Thus Dixon [12] found the melting point of *N*-phenyl-*O*-phenylmonothiourethane to be 149–150°C, Rieche and co-workers [7] 143°C, Teruhisa Noguchi and co-workers 154–156°C [13]. Numerous references differ in the m.p. of the mentioned substance even more.

Table 1
List of synthesized monothiourethanes
 $R-NH-CS-O-R_1$

Derivative	Substituent		Stoichiometric formula	<i>M</i>	Calculated/found		Yield [%]	M.p. [°C]
	R	R ₁			% N	% S		
<i>I</i>	phenyl	phenyl	C ₁₃ H ₁₁ NOS	229.14	—	—	46	142—143
<i>II</i>	tolyl	phenyl	C ₁₄ H ₁₃ NOS	243.33	5.76	13.2	65	benzene/light petroleum 130—132.5
<i>III</i>	4-methoxyphenyl	phenyl	C ₁₄ H ₁₃ NO ₂ S	259.33	5.92	13.51	62	<i>n</i> -heptane/ethanol 137—139.5
<i>IV</i>	4-ethoxyphenyl	phenyl	C ₁₅ H ₁₅ NO ₂ S	273.35	5.65	12.71	82	ethanol 144—146
<i>V</i>	4-dimethylamino-phenyl	phenyl	C ₁₅ H ₁₆ N ₂ OS	272.37	5.24	11.65	66	chloroform/ <i>n</i> -heptane 1 : 2 138—144
<i>VI</i>	4-bromophenyl	phenyl	C ₁₃ H ₁₀ BrNOS	308.20	10.28	11.75	85	chloroform/ <i>n</i> -heptane 1 : 2 142—146
<i>VII</i>	4-acetophenyl	phenyl	C ₁₅ H ₁₃ NO ₂ S	271.34	4.58	10.39	66	benzene/light petroleum 122—126
<i>VIII</i>	4-nitrophenyl	phenyl	C ₁₃ H ₁₀ N ₂ O ₃ S	274.2	5.17	11.81	45	ethanol 123—126
<i>IX</i>	4-biphenyllyl	phenyl	C ₁₉ H ₁₅ NOS	305.31	10.21	11.69	65	chloroform/ <i>n</i> -heptane 1 : 2 146—151
<i>X</i>	4-bromobiphenyllyl	phenyl	C ₁₉ H ₁₄ BrNOS	384.31	10.16	11.84	44	ethanol 138—142
					3.65	8.33		ethanol
					3.75	8.22		

Table 1 (Continued)

Derivative	R	Substituent	R ₁	Stoichiometric formula	M	Calculated/found		Yield [%]	M.p. [%]
						% N	% S		
XI	1-naphthyl		phenyl	C ₁₇ H ₁₃ NOS	280.37	4.99	11.43	57	168—170
						4.95	11.70		ethanol
XII	2-naphthyl		phenyl	C ₁₇ H ₁₃ NOS	280.37	4.99	11.43	67	142—146
						4.90	11.24		ethanol
XIII	4-bromophenyl		tolyl	C ₁₄ H ₁₂ BrNOS	322.23	4.35	9.96	68	170—172
						4.69	10.25		chloroform/ <i>n</i> -heptane 1 : 3
XIV	phenyl		butyl	C ₁₁ H ₁₅ NOS	209.31	—	—	48	53
						—	[14]*		
XV	<i>n</i> -butyl		phenyl	C ₁₁ H ₁₅ NOS	209.31	6.59	15.30	80	125—128/3 Torr
						6.70	15.07		
XVI	octyl		phenyl	C ₁₆ H ₂₃ NOS	265.42	5.28	12.10	63	45—47
						5.08	12.20		<i>n</i> -heptane
XVII	benzyl		phenyl	C ₁₄ H ₁₃ NOS	243.33	—	—	81	82.5
						—	[7]*		ethanol
XVIII	4-bromobenzyl		phenyl	C ₁₄ H ₁₂ BrNOS	322.23	4.34	9.50	59	110—115
						4.60	9.85		<i>n</i> -heptane
XIX	1-naphthylmethyl		phenyl	C ₁₈ H ₁₅ NOS	293.38	4.78	10.20	54	128—129
						5.01	10.53		<i>n</i> -heptane
XX	butyl		butyl	C ₉ H ₁₉ NOS	189.23	7.40	16.80	63	98—100/3 Torr
						7.23	16.75		

* Model substances.

Table 2

Characteristic IR and UV data of monothiourethanes
 $R-NH-CS-O-R_1$

Derivative	R	Substituent R_1	$\nu(NH)$ [cm^{-1}]	$\nu(C-C)$ [cm^{-1}]	$\nu(NH-C=S)^a$ [cm^{-1}]	$\nu(NH-C=S)^b$ [cm^{-1}]	$\nu(NH-C=S)^c$ [cm^{-1}]	$\nu(C-O-C)$ [cm^{-1}]	λ_{max} [nm]	log ϵ
I	phenyl	phenyl	3395 vs 3420 split	1600 1497	1530	1380	932	1160 1170	278	4.38
II	tolyl	phenyl	3390 vs 3415 split	1595 1493	1527	1375	930	1160	280	4.21
III	4-methoxyphenyl	phenyl	3395 vs 3420 split	1600 1495	1525	1380	928	1160	282	4.23
IV	4-ethoxyphenyl	phenyl	3392 vs 3420 split	1600 1495	1520	1370	927	1160	283	4.23
V	4-dimethylaminophenyl	phenyl	3393 vs 3420 split	1494	1530	1355	950	1158	245 302	4.06 4.24
VI	4-bromophenyl	phenyl	3395 vs 3420 split	1595 1494	1518	1370	930	1167 1168	285	4.30
VII	4-acetophenyl	phenyl	3390 vs 3410 sh	1595 split 1608	1523	1365	930	1170	308	4.40
VIII	4-nitrophenyl	phenyl	3390 vs 3412 sh	1600 1495	1520	1368	930	1175	326	4.20
IX	4-biphenyl	phenyl	3395 vs 3420 split	1595 1493	1530	1380	930	1163	248 298	4.23 4.49
X	4-bromobiphenyl	phenyl	3395 vs 3415 split	1596 1492	1530	1375	930	1165	253 300	4.24 4.53

Table 2 (Continued)

Derivative	R	Substituent R ₁	$\nu(\text{NH})$ [cm ⁻¹]	$\nu(\text{C—C})$ [cm ⁻¹]	$\nu(\text{NH—C} \equiv \text{S})^a$ [cm ⁻¹]	$\nu(\text{NH—C} \equiv \text{S})^b$ [cm ⁻¹]	$\nu(\text{NH—C} \equiv \text{S})^c$ [cm ⁻¹]	$\nu(\text{C—O—C})$ [cm ⁻¹]	λ_{max} [nm]	log ϵ
XI	1-naphthyl	phenyl	3390 split 3415 vs	1600	1525	1350	920	1165	306 320	4.16 4.04
XII	2-naphthyl	phenyl	3395 vs 3415 split	1495 split 1505 1600 doublet	1535	1350	930	1162	270 300	4.45 4.24
XIII	4-bromophenyl	tolyl	1392 vs 3415 split	1595	1515	1375	930	1165	284	4.32
XIV	phenyl	butyl	3400 split 3424 vs	1600	1523	1335	—	1188	275	4.29
XV	<i>n</i> -butyl	phenyl	3410	1600 1490	1525	1345	—	1165	248	4.18
XVI	octyl	phenyl	3410	1600 1402	1525	1345	—	1160	248	4.15
XVII	benzyl	phenyl	3410	1600 1490	1525	1345	—	1140	250	4.14
XVIII	4-bromobenzyl	phenyl	3410	1600 1492	1520	1335	—	1140	250	4.17
XIX	1-naphthylmethyl	phenyl	3405	1600 1490	1520	1380	—	1140	250 270	4.13 3.99
XX	butyl	butyl	3415 vs 3445 split	—	1525	1340	—	1190	243	4.13

vs — very strong, sh — shoulder.

The characteristic infrared data of the synthesized monothiourethanes are listed in Table 2. All investigated monothiourethanes display an intensive absorption band due to the N—H vibrations at $\sim 3400\text{ cm}^{-1}$ that, in case of aromatic substituents (Fig. 1a, derivatives I—VIII), is split the more intensive maximum being shifted toward the lower wavenumber range. This band is not split in the spectra of derivatives where the nitrogen atom is aralkyl substituted (Fig. 1b, Table 2, derivatives XV—XIX). The nature of the substituent is of no significant effect on the position of this absorption band. Monothiourethanes do not show any absorption in the $2400\text{--}2700\text{ cm}^{-1}$ region, characteristic of the SH vibrations, and it could be therefore assumed that they do not occur in tautomeric isothio-form.

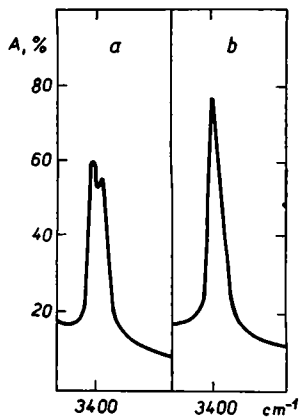


Fig. 1. Infrared spectra $\nu(-\text{NH})$ of some substituted monothiourethanes, measured in chloroform; conc. 0.1 M; NaCl cell thickness 0.17 mm.

- a) *N*-phenyl-*O*-phenylmonothiourethane; b)
N-benzyl-*O*-phenylmonothiourethane.

The $900\text{--}1600\text{ cm}^{-1}$ range is of great importance for the substances under investigation since there are three absorption bands, belonging to the mixed vibrations $\text{NH}-\text{C}=\text{S}$, in the spectra. According to Rao [9], these bands cannot be localized precisely and their position depends upon the type of the proper compound. In thiocarbonyl compounds attached to nitrogen atom they use to appear in regions as follows: $-\text{NH}-\text{C}=\text{S}$ (a) at $1395\text{--}1570\text{ cm}^{-1}$, band $-\text{NH}-\text{C}=\text{S}$ (b) at $1260\text{--}1420\text{ cm}^{-1}$ and band $-\text{NH}-\text{C}=\text{S}$ (c) at $940\text{--}1140\text{ cm}^{-1}$.

When comparing infrared absorption spectra of the synthesized monothiourethanes it becomes evident that in the case of those containing aromatic substituents the $-\text{NH}-\text{C}=\text{S}$ absorption band is observed in the $1515\text{--}1535\text{ cm}^{-1}$ region (Fig. 2, Table 2). It was possible to localize those bands just by contrasting them with spectra of the proper aromatic amines having no bands in this region. In the case of monothiourethanes containing alicyclic or aliphatic substituents attached to nitrogen atoms (Table 2, derivatives XIV—XX) the absorption band $-\text{NH}-\text{C}=\text{S}$ (c) does not occur in the $900\text{--}1000\text{ cm}^{-1}$ region. There are many absorption bands

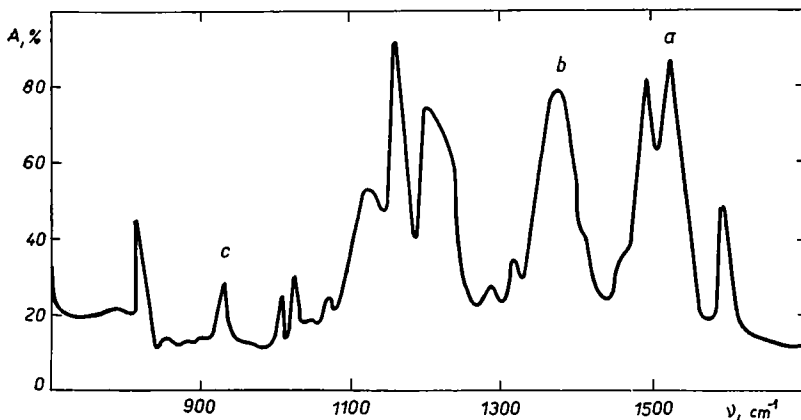


Fig. 2. Infrared absorption spectrum of *N*-(4-tolyl)-*O*-phenylmonothiourethane, measured in chloroform; conc. 0.1 M; NaCl cell thickness 0.17 mm.

present in the 1000–1140 cm^{-1} range and the accurate localization of band *c* would require a special and more detailed study. All monothiourethanes display in the 1140–1190 cm^{-1} range very intensive absorption bands belonging to the stretching frequencies $\nu(\text{C}-\text{O}-\text{C})$ of thio-ester bonds.

Ultraviolet absorption spectra of some substituted monothiourethanes are shown in Fig. 3. Values of absorption maxima and molar absorptivity logarithms are listed in Table 2. As seen from the spectral data, the investigated compounds reveal a strong absorption band ($\log \epsilon \sim 4$) in the 220–360 nm range. This absorption

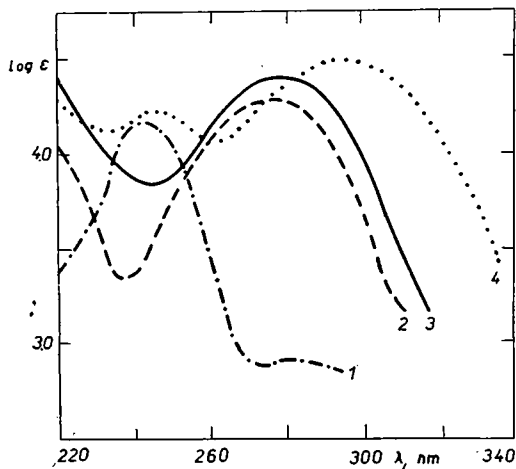


Fig. 3. Ultraviolet absorption spectra of substituted monothiourethanes, measured in methanol.

1. *N*-butyl-*O*-butylmonothiourethane; 2. *N*-phenyl-*O*-butylmonothiourethane; 3. *N*-phenyl-*O*-phenylmonothiourethane; 4. *N*-biphenyl-*O*-phenylmonothiourethane.

band is probably due to the $\pi \rightarrow \pi^*$ transition associated with an electron transfer as a result of the $p-\pi$ conjugation between the free electron pair at nitrogen or oxygen atom and the double bond of the thionic group. Considering the structure of monothiourethanes it can be assumed that the above-mentioned absorption band belongs either to the „N“ or to the „O“ conjugation of the molecule:



To clear this fact a dependence of substituents on the position of that band was investigated. It has been found this absorption band to be susceptible towards the change in character of substituent at nitrogen, whereas that attached to oxygen does not effect its position. Thus *e.g.* *N*-phenyl-*O*-phenylmonothiourethane (derivative I) and *N*-phenyl-*O*-butylmonothiourethane reveal absorption at 278 nm ($\log \epsilon$ 4.38) and 275 nm ($\log \epsilon$ 4.29), respectively, that of *N*-butyl-*O*-butylmonothiourethane is hypsochromically shifted to 243 nm ($\log \epsilon$ 4.13). From the above it is apparent that the examined absorption band can be ascribed to the „N“ conjugation in the molecule of monothiourethanes; the „O“ conjugation is of no effect in this region. These results are consonant with those of our previous paper referring to the study of ultraviolet absorption spectra of tetrahydro-1,3,5-thiadiazine-2-thiones and some model compounds containing the $-\text{NC}(:\text{S})$ grouping [15].

From the data listed in Table 2 it is obvious that the hypsochromic effect can be observed in spectra of those substances where the nitrogen atom is bearing a substituent of alkyl or aralkyl type (compounds *XV*, *XVI*, *XVII*, *XVIII*).

Substituents with fused benzene rings (compounds *XI*, *XII*, *XIX*) show more complex bands due to the absorption of the aromatic rings, and, as a result, an overlapping of absorption bands belonging to the conjugated system of monothiourethane can occur.

In the case of both biphenyl- and dimethylaminophenyl derivatives of monothiourethanes two absorption bands appear in their ultraviolet spectra; that at 245 nm can be ascribed to the modified benzene system.

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