Isothiocyanates. XXXIX. Synthesis, infrared and ultraviolet spectra of some phenyl isothiocyanates having a heterocyclic substituent

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The synthesis, infrared and ultraviolet spectra of 4-(1-pyrrolidinyl)-, 2- and 4-(1-piperidino)-, 2- and 4-(1-morpholinyl)-, and 4-[1-(4-methyl)piperazinyl]phenyl isothiocyanates are described.

It was pointed out in papers [1—4] that some isothiocyanates having a heterocyclic substituent exhibit cytostatic effect. Studying the substances showing biological activities we prepared compounds listed in Table 1.

The synthesis of isothiocyanates using the thiophosgene method afforded the derivative *I* in a high yield; the yields of other derivatives were lower. The thiophosgene method was used also for the synthesis with —NCS group in the *o*-position (compounds *V* and *VI*). To the authors' knowledge, it was impossible to prepare isothiocyanates by thiophosgene method in case an amino group was in the *o*-position with such a group with which it could form hydrogen bonds excepting the derivatives in which the hydrogen bond did not form for steric reasons.

Table 1

Characterization of the synthesized X-phenyl isothiocyanates

No.	X	Formula	*M*	Calculated/found % N	Calculated/found % S	Yield [%]	M.p., B.p. °C/torr
I	4-(1-Pyrrolidinyl)	$C_{11}H_{12}N_2S$	204.28	13.71 13.65	15.69 15.76	83	101—102
II	4-(1-Piperidino)	$C_{12}H_{14}N_2S$	218.31	12.83 12.90	14.68 14.61	34	55—56
III	4-(1-Morpholinyl)	$C_{11}H_{12}N_2OS$	220.28	12.71 12.99	14.55 14.48	39	84—85
IV	4-[1-(4-Methyl)piperazinyl]	$C_{12}H_{15}N_3S$	233.33	18.01 18.22	13.74 13.89	36	115—117
V	2-(1-Morpholinyl)	$C_{11}H_{12}N_2OS$	220.28	12.71 12.70	14.55 14.53	38	67—68
VI	2-(1-Piperidino)	$C_{12}H_{14}N_2S$	218.31	12.83 12.83	14.68 14.66	40	148—150/5

The synthesized compounds show characteristic absorption band assigned to the asymmetric vibrations of the —NCS group at 2000—2200 cm^{-1}. From among other absorption bands we present bands at 2900 cm^{-1} ascribed to the vibrations of aliphatic CH_2 bonds and the region of 1600 cm^{-1}, where the absorption bands associated with skeleton vibrations of an aromatic ring occur.

The ultraviolet spectra of derivatives display a characteristic absorption band in the region 300—320 nm; this band belongs to the $\pi-\pi^*$ transitions of the whole conjugated system and is visible in all aromatic isothiocyanates [7]. The spectra (their absorption maxima and intensity) are similar in all derivatives.

The absorption maxima of the derivatives *I* and *V* split into $\lambda_1 = 305$ nm, $\lambda_2 = 318$ nm; this occurs also in the case of some aromatic isothiocyanates [7]. The u.v. spectra of the derivative *VI* differ very much from those of other investigated derivatives. This is probably due to the *o*-substitution, where the increased interaction between a nitrogen and a carbon atom of the —NCS group could take place. But the —NCS group retains its original structures: this is confirmed by the i.r. spectra of the derivative with a characteristic absorption band at 2000 cm^{-1}.

Experimental

Infrared spectra were measured on a double-beam UR-20 Zeiss, Jena spectrophotometer in the 3600—800 cm^{-1} region. Chloroform solutions (2.5×10^{-2} M) were measured. The apparatus was calibrated against a polystyrene foil.

Ultraviolet spectra were obtained on a recording Specord UV VIS spectrophotometer in the region 200—400 nm. The concentration of dioxan solutions was 3×10^{-5} M.

The i.r. and u.v. spectral data are in Table 2.

Table 2

I.r. and u.v. spectral data of the synthesized derivatives

No.	$\tilde{\nu}_s$(NCS) [cm^{-1}]	$\tilde{\nu}_{arom}$ [cm^{-1}]	$\tilde{\nu}_{as}$(NCS) [cm^{-1}]	$\tilde{\nu}_s(CH_2)$ [cm^{-1}]	$\tilde{\nu}_{as}(CH_2)$ [cm^{-1}]	λ [nm] log ε		
I	925	1620	2055	2848	2920	305		318
			2132	2880	2945	4.46		4.46
			2176		2972			
II	925	1608	2080	2815	2944	316		
			2100	2860		4.51		
			2125					
			2180					
III	944	1610	2070	2840	2905	300		
			2125	2870		4.39		
			2180					
IV	920	1610	2080	2750	2929	303		
			2125	2810		4.42		
			2180	2834				
				2850				
V	925	1600	2080	2830	2905	305		318
	950		2100	2866		4.53		4.53
			2160					
VI	915	1602	2080	2750	2945	253	279	305
	948		2120	2815		4.19	3.96	3.69
			2155	2860				
			2186					

Condensation of the appropriate cyclic bases with *o*- and *p*-chloronitrobenzene yielded the intermediates. We did not succeed in the condensation with *m*-chloronitrobenzene. Reduction of the nitro derivatives with tin in acid medium [5, 6] led to the formation of amines which were isolated as hydrochlorides.

Phenyl isothiocyanates having a heterocyclic substituent

Thiophosgene (0.11 mole; 12.5 g, 8.3 ml) was added to chloroform (200 ml). The hydrochloride salt of amine (0.1 mole) in water (200 ml) was added to the vigorously stirred mixture. Then 10% NaOH solution was gradually added in small portions to the emulsion until neutral. The stirring was continued for about 1 hour. The chloroform layer was separated, washed with water, dried with anhydrous sodium sulfate, and vacuum distilled. The residue was recrystallized from petroleum ether or vacuum distilled. The synthesized isothiocyanates and their characterizations are in Table 1.

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