

SYNTHESIS AND PROPERTIES OF 4-SUBSTITUTED 4-ISOTHIOCYANATOBENZOPHENONES

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Dedicated to Professor Dr Š. Krasnec on the occasion of his 60th birthday.

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The 4'-substituted 4-isothiocyanatobenzophenones *I*–*VI* have been synthesised from the corresponding amines by action of thiophosgene. The infrared and ultraviolet spectra of these compounds were measured and the kinetics of the addition of both OH ions and the amino group of glycine to the functional NCS group have been investigated. The absorption maxima of $\nu_{as}(\text{NCS})$ and $\nu(\text{CO})$ as well as the rate constants were correlated with Hammett's σ_p constants.

In continuation of our previous studies of isothiocyanates of the diphenylsubstituted types, *viz.* the isothiocyanates of substituted biphenyls¹, *p*-terphenyls², diphenylmethanes³, diphenyl sulphides and diphenyl sulphones⁴, diphenyl oxides⁵, azobenzenes⁶, and stilbenes⁷, the present paper is devoted to the synthesis of 4-isothiocyanatobenzophenones bearing in 4'-position the substituents CH₃O, CH₃, H, Br, NCS, and NO₂, respectively. These derivatives we used for investigating the influence of the substituent effect on the character of the isothiocyanate group, and by an analysis of their infrared spectra and kinetic data we judged of the transfer of the electronic effects through the benzophenone system.

EXPERIMENTAL

Compounds used. The 4'-substituted 4-aminobenzophenones were prepared by the following literature methods: 4-Aminobenzophenone and 4-amino-4'-methylbenzophenone according to ref.⁸ and ⁹ respectively, 4-amino-4'-bromobenzophenone by reduction of 4-nitro-4'-bromobenzophenone¹⁰ according to ref.⁹, 4,4'-diaminobenzophenone according to ref.^{11,12}, 4-amino-4'-nitrobenzophenone by reduction of 4,4'-dinitrobenzophenone with sodium hydrogen sulphide in medium of pyridine according to ref.¹², and finally 4-amino-4'-methoxybenzophenone according to ref.¹³.

Preparation of the isothiocyanatobenzophenones: To a mixture of chloroform (40 ml), thiophosgene (25 g; 0.22 mol) and water (100 ml) are added with stirring powdered CaCO₃ (1 g) and gradually 0.2 mol of the corresponding aminobenzophenone dissolved in chloroform (150 to 250 ml). During the addition ($\frac{1}{2}$ –1 h) the pH is kept weakly alkaline on phenolphthalein and the

liberated HCl is neutralised by addition of powdered CaCO_3 . The reaction mixture is then stirred for further 3–4 h at 25–30°C. After the reaction is over, the mixture is filtered and the separated chloroform layer dried over CaCl_2 and subsequently filtered. The chloroform is removed by heating on a water bath and the residue purified by extraction with light petroleum followed by chromatography on aluminium oxide and active charcoal and, if necessary, by additional recrystallisation from light petroleum. The synthesised isothiocyanates are presented in Table I together with their yields, analysis and physical constants.

Spectral measurements. Infrared absorption spectra were measured on a Zeiss (Jena) double-beam spectrophotometer, Model UR 10, with a LiF prism for the 3600–1800 cm^{-1} region and a NaCl prism for the 1800–700 cm^{-1} region, using 0.1M chloroform solutions in NaCl cells of 0.145 mm thickness. The frequencies of the more important absorption maxima are given in Table II. The accuracy of the instrument in the region of $\nu(\text{CO})$ is $\pm 1 \text{ cm}^{-1}$ and in the region of $\nu_{\text{as}}(\text{NCS}) \pm 3 \text{ cm}^{-1}$. The correlation of the $\nu(\text{CO})$ frequencies with Hammett's σ_p constants (ρ 6.96, r 0.96) as well as the correlation of the frequencies of the first maximum of the $\nu_{\text{as}}(\text{NCS})$ absorption band (ρ -14.8, r 0.92) are given in Fig. 1.

Kinetic measurements. The ultraviolet spectra were taken on a spectrophotometer Jasco (Japan), Model ORD/UV-5, using $1.5\text{--}3.5 \cdot 10^{-5}\text{M}$ methanolic solutions at $25 \pm 1^\circ\text{C}$; cell thickness 1 cm. The molar solubilities of the derivatives in water and 10% methanol were determined at 25°C by the method of saturating from above¹⁴. The kinetics of the addition reaction of OH^- ions were followed according to ref.¹⁵ on a spectrophotometer Zeiss VSU-1, using reaction mixtures of the composition 9.9 ml of methanol, 10 ml of 0.2M-NaOH and 0.1 ml of $0.5\text{--}1 \cdot 10^{-2}\text{M}$ methanolic isothiocyanate solution at $25 \pm 0.2^\circ\text{C}$ in cells of 1 cm thickness.

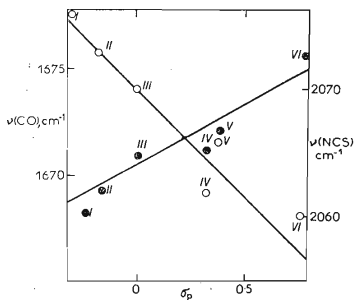


FIG. 1

Dependence of $\nu(\text{CO})$ of the Keto Group of 4'-Substituted 4-Isothiocyanatobenzophenones (●) and of $\nu_{\text{as}}(\text{NCS})$ (○) on Hammett's σ_p Substituent Constants^{20,21}

Designation of the derivatives as in Table I.

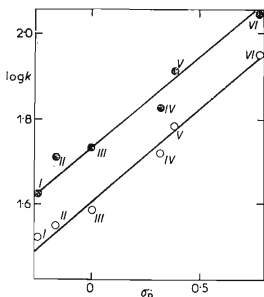


FIG. 2

Dependence of the Logarithms of the Rate Constants of the Reaction of 4'-Substituted 4-Isothiocyanatobenzophenones with Glycine (●) and OH^- Ions (○) on Hammett's σ_p Substituent Constants^{20,21}

Designation of the derivatives as in Table I.

The kinetics of the addition reactions of glycine were measured according to ref.¹⁵ on a spectrophotometer Zeiss VSU-1, using reaction mixtures consisting of 9.9 ml of methanol, 8 ml of 0.1M borate buffer (pH 9.8), 2 ml of $5 \cdot 10^{-3}$ M glycine solution, and 0.1 ml of $0.5-1 \cdot 10^{-2}$ M methanolic solution of the isothiocyanate at $25 \pm 0.2^\circ\text{C}$ in cells of 1 cm thickness. The characteristic data of the ultraviolet spectra, the solubilities, and the rate constants of the addition of hydroxyl ions and glycine are given in Table II and Fig. 2.

RESULTS AND DISCUSSION

The yield of the isothiocyanates depends to a high degree on the character of the substituent. The electron acceptor effect of the substituent (nitro and isothiocyanate group, respectively) decreases the basicity and thus also the reactivity of the amino group and the yield of the isothiocyanates. Contrasting with this, in the case of activating substituents (methyl and methoxy group, respectively) are the yields higher (about 70%). From the infrared spectra of the investigated isothiocyanates it follows that $\nu_{\text{sym}}(\text{NCS})$ in the region of 940 cm^{-1} does not markedly change with the character of the substituent. The carbonyl group is characterised by a maximum in the region of 1670 cm^{-1} . This maximum depends on the character of the substituent, but the slope of the dependence of the σ_p substituent constant, when compared with other substituents¹⁶⁻¹⁸, shows a relatively small value (ρ 6.96). The lower value of the slope is also connected with the standard effect of the NCS group in all

TABLE I
Survey of the Synthetised 4'-Substituted 4-Isothiocyanatobenzophenones

Number Substituent	M.p., $^\circ\text{C}$ (yield, %)	Formula (m.w.)	Calculated/Found	
			% N	% S
<i>I</i> CH_3O	122-123 (65)	$\text{C}_{15}\text{H}_{11}\text{NO}_2\text{S}$ (269.3)	5.26 5.23	11.9 11.65
<i>II</i> CH_3	109-110 (78)	$\text{C}_{15}\text{H}_{11}\text{NOS}$ (253.3)	5.53 5.55	12.65 12.86
<i>III</i> H	78 (46)	$\text{C}_{14}\text{H}_9\text{NOS}$ (239.3)	5.95 5.92	13.36 13.47
<i>IV</i> Br^a	108-109 (50)	$\text{C}_{14}\text{H}_8\text{BrNOS}$ (318.8)	4.41 4.40	10.06 10.29
<i>V</i> NCS	117.5 (31)	$\text{C}_{15}\text{H}_8\text{N}_2\text{S}_2\text{O}$ (296.4)	9.45 9.57	21.64 21.61
<i>VI</i> NO_2	115 (14)	$\text{C}_{14}\text{H}_8\text{N}_2\text{O}_3\text{S}$ (284.3)	9.85 9.62	11.27 11.06

^a % Br: Calculated: 25.07%; found: 25.18%.

TABLE II
Physico-Chemical Data of 4'-Substituted 4-Isothiocyanatobenzophenones

Num-ber	$\nu(\text{CO})$ cm^{-1}	$\nu_{\text{as}}(\text{NCS})$ cm^{-1}	λ_{max} (log ϵ) methanol, nm	Solubility ^a		k_{NH_2} ^b	k_{OH^-} ^c
				H ₂ O	10% methanol		
I	1 668	2 076	274–277 (4.74)	0.312	0.88	41.9 ± 0.83	33.3 ± 0.66
II	1 669	2 073	292–295 (4.50)	0.37	2.29	51.7 ± 1.02	35.5 ± 0.71
III	1 671	2 070	296–302 (4.44)	2.54	3.09	54.4 ± 1.08	38.6 ± 0.76
IV	1 671	2 062	295–298 (4.37)	0.43	1.25	66.2 ± 1.32	52.4 ± 1.04
V	1 672	2 066	304–308 (4.69)	0.45	0.99	82.5 ± 1.64	61.2 ± 1.22
VI ^d	1 676	2 060	275–277 (4.59)	0.33	2.22	110.3 ± 2.2	87.3 ± 1.65

^a At 25°C, values given in $\text{M}^{-1} \cdot 10^5$; ^b borate buffer of pH 9.8 with 50% methanol at 25°C, in $\text{l mol}^{-1} \text{min}^{-1}$; ^c 0.2M-NaOH with 50% methanol, 25°C, values in $\text{l mol}^{-1} \text{min}^{-1}$; ^d $\nu(\text{NO}_2)$ 1360 cm^{-1} , 1549 cm^{-1} .

derivatives. The frequency of the first maximum of $\nu_{\text{as}}(\text{NCS})$ in the region 2070 cm^{-1} is dependent on the character of the substituent, as this was the case with all previously by us studied systems. The value of the slope ($\rho - 14.8$) remains behind the value¹⁹ valid for the basic benzenoid system ($\rho - 54.8$) and also behind further diphenyl systems with a value of $\rho \sim -20$. From the foregoing it follows that the transfer of electronic effects through the carbonyl group is limited, and this ρ value is the lowest of all up to now by us investigated systems, where the maximum transfer asserted itself with stilbene derivatives⁷ ($\rho - 23.7$) and the minimum transfer with diphenyl oxides⁵ ($\rho - 15.8$). In the case of the carbonyl group with its considerable hindrance of the electronic effect one has to take into consideration already the fact that for benzophenones is the correlation coefficient of the dependence in question lower (r 0.92) than for the other by us investigated systems, where the correlation coefficient was generally higher than 0.97.

The now synthesised isothiocyanates are characterised by their ultraviolet spectra which show absorption maxima in the region of 270–300 nm without any sharp peaks. From the determined values (Table II) and also from the graphical correlation of the addition rates of OH^- and glycine with the σ constants follows in both cases a linear relation at which the correlation coefficient for the addition of the hydroxyl ions is higher (r 0.94) than the correlation coefficient for the addition of glycine (r_{NH_2} 0.89). From comparison of the slope ρ for the basic series of the benzenoid isothiocyanates¹⁵ (ρ_{NH_2} 0.84) with the corresponding value for the now investigated series of compounds (ρ_{NH_2} 0.41) it follows that the transfer of electronic effects is limited, similarly as this follows from the correlation of the infrared spectra.

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