

REACTIONS OF AROMATIC ISOTHIOCYANATES WITH BENZALDEHYDES

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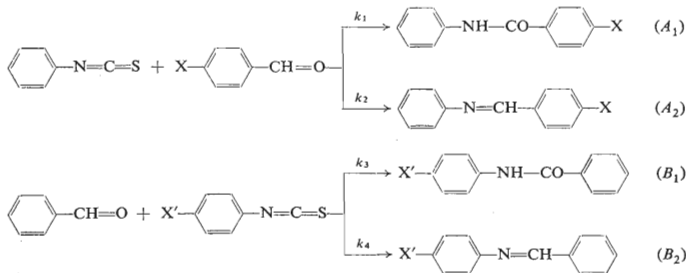
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Received January 17th, 1974

Reactions of phenyl isothiocyanate (*I*) with 4-*X*-C₆H₄CHO (*II*) and of benzaldehyde (*III*) with 4-*X'*-C₆H₄NCS (*IV*) (*X* = H, Br, Cl, NO₂, CH₃, OCH₃, and N(CH₃)₂, and *X'* = H, Br, COCH₃, CH₃, COOC₂H₅, and OCH₃) give both corresponding azomethines (*V*) and anilides (*VI*). Relative amounts of the products depend on substituent effects upon the reaction centers —CH=O and —N=C=S, respectively. From the rate constants and gas chromatographic data the mechanism of formation of these products is suggested.

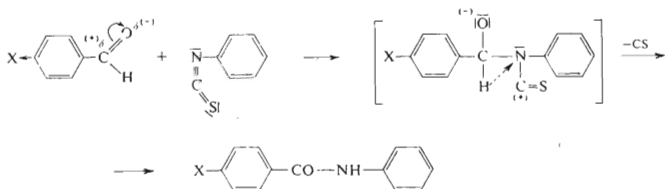
In previous works¹⁻³ we were concerned with the reaction of aryl, aralkyl, and alkyl isothiocyanates with various nucleophilic reagents. The reaction of isothiocyanates with aldehydes and other carbonyl compounds, which we find to give products *V* and *VI*, has not previously been studied. Formation of products *V* was established in the reaction of phenyl isothiocyanate⁴ and heterocumulenes of the type R—NSO (ref.⁵) with aromatic and heterocyclic aldehydes. In these reactions, formation of the anilides *VI* was not observed^{4,5}.

In the reaction of starting compounds *I* and *II* with *III* and *IV*, respectively, at an elevated temperature in the absence of a catalyst and a solvent, a mixture of products *V* and *VI* is formed. The relative amounts of both products depend on the substituent attached to the *para* position of compounds *II* and *IV*, respectively

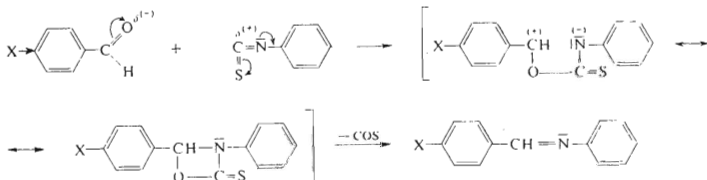


The relative amounts of the products of the reactions (A) and (B) obtained after a 5 h-reaction time are presented in Table I. A quantitative analysis of the reaction mixtures was made by gas chromatography. The formation of both types of the products in reactions (A) and (B) can be explained by nucleophilic addition reaction of the aldehydic group with the isothiocyanato one. The reaction course, and also the relative amounts of the products, depend on which of the components acts predominantly as a nucleophile and which acts as an electrophile. This reaction is an example of the "pure" influencing of the —NCS and —CH=O groups by electronic effects of the substituents. Kinetic measurements of the reactions (A) and (B) showed that at the molar ratio of the starting compounds equal to 1 : 1, the reactions are of second order.

In the reaction of 4-substituted benzaldehydes *II* with compound *I*, the electron-attracting groups increase the electrophilicity of the —CH=O group to such an extent that the main reaction is nucleophilic addition of the —NCS group of the compound *I* via free electron pair of the nitrogen (Scheme 1). In agreement with this, the slope of the dependence of the rate constants k_1 of the reaction (A) on σ_p constants is negative ($\rho = -0.545$). This reaction probably involves the migration of H^- followed by the abstraction of the C=S fragment. Substitution of the compound *II* by electron-donating substituents decreases the reactivity of the C=O group so that



SCHEME 1



SCHEME 2

the NCS group acts as an electrophile and the oxygen of the carbonyl group acts as a nucleophile. The reaction gives products *V* (Scheme 2). The slope of the dependence of k_2 on σ_p constants is positive and equals to 0.935. It seems likely that the reaction proceeds through a cyclic mechanism, similar to the reaction of phenyl isocyanate with aldehydes⁵. The suggested mechanism is supported by the fact that also the reaction of 4-substituted isothiocyanates *IV* with benzaldehyde (*III*, reaction (*B*)) leads under identical conditions to the products *V* and *VI*. Their relative amounts are also substituent-dependent and their ratio is essentially the reverse of that of the products of the reaction (*A*).

The rate of formation of the products *V* and *VI* in the reactions (*A*) and (*B*) was followed by gas chromatography. The rate constants obtained (Table I, Fig. 1) are in a good agreement with the suggested mechanism of the reactions (*A*) and (*B*).

In Fig. 1 is graphically represented the dependence of the rate constants k ($\text{mol}^{-1} \cdot \text{min}^{-1}$) of the formation of the products A_1 and A_2 on σ_p substituents. The dependence of the reaction rates k_1 and k_2 of the reactions of 4-X-C₆H₄CHO on σ_p constants is linear; the 4-nitro- and 4-dimethylamino derivative deviate generally from this linearity. In accordance with the suggested mechanism of formation of the azomethines or the anilides, σ_p of the dimethylamino group gives linear correlation in the formation of the anilides, and σ_p of the nitro group fits the correlation found for the formation of the azomethines (Table I, Fig. 1). In both compounds the strong electron-donating or electron-attracting effect of the substituent is enhanced, which reflects in the higher rate constants (Table I). Similar relations were observed also with the reaction (*B*). However, the dependence of the rate constants k_3 and k_4 on σ_p was not linear.

After finding these relationships, we performed the reaction of phenyl isocyanate with compound *III* with the aim of ascertaining whether the products *V* and *VI* are

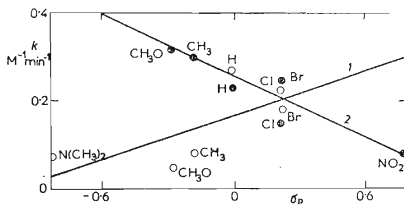


FIG. 1

Dependence of the Rate Constants k of the Reaction (*A*) on σ_p
 1 Formation of the Product A_1 , 2 Formation of the Product A_2 .

TABLE I

The Rate Constants k ($\text{mol}^{-1} \text{min}^{-1}$) of the Reactions (A) and (B) and the Yields of the Products (% after 5 h)

X	k_1	% A ₁	k_2	% A ₂	X'	k_3	% B ₁	k_4	% B ₂
H ^a	2.66	17.37	2.30	4.56	H	2.66	17.37	2.30	4.56
Br	1.76	12.90	2.37	14.74	Br	1.39	12.15	3.00	23.50
Cl	2.19	17.50	1.35	10.32	COCH ₃	2.84	18.35	32.53	79.23
NO ₂	12.27	57.93	0.74	5.74	CH ₃	1.08	17.20	6.25	6.50
CH ₃ O	0.43	3.22	3.15	9.91	COOC ₂ H ₅	3.22	19.16	11.89	50.79
(CH ₃) ₂ N	0.66	22.98	10.35	41.08	OCH ₃	2.66	25.15	0.61	7.12
CH ₃	3.79	7.49	2.96	17.18					

^a The rate constants k ($\text{mol}^{-1} \text{min}^{-1}$) of the reaction of III with phenyl isocyanate: $k_{\text{benzanilide}} = 0.29$, $k_{\text{azomethine}} = 2.61$.

formed also in this case. In contrast to the earlier study in which only the azomethine formation was observed, after carrying out the reaction over a period of 8 hours, we found 5.24% of benzanilide to be present in the reaction mixture. Comparison of the amounts of the azomethines formed in the reactions of I with III and of phenyl isocyanate with III revealed that the former reaction, when carried out under identical conditions (8 h), gives a lesser amount of the azomethine (9.23%), compared to the latter reaction (18.9%). This indicated that the carbon atom of the NCO group bears a higher partial positive charge and acts then to a greater extent as an electrophile.

EXPERIMENTAL

4-Substituted phenyl isothiocyanates (4-methyl-, 4-methoxy-, 4-bromo-, 4-acetyl-, and 4-ethoxy-carbonyl-) were prepared by the thiophosgene method from appropriate amines⁶. The aldehydes were commercial samples. All of the compounds were recrystallised or distilled prior to using in kinetic measurements.

The reactions of 4-substituted phenyl isothiocyanates with benzaldehyde and 4-substituted benzaldehydes with phenyl isothiocyanate were carried out with equimolar amounts of the components at 140°C. After 5 h, the mixture was poured onto water, the solids were removed by filtration with suction and recrystallised from ethanol. The obtained crystalline substances which did not melt within a narrow temperature range, were identified by gas chromatography as a mixture of 1,2- and 3,4-isomers, respectively. For that reason, the rate of the formation of individual substances was further followed.

Gas Chromatographic Analysis of Formation of Benzanilides and Azomethines

The individual components of the reaction mixtures were determined with a Hewlett-Packard, Model 7620 A, chromatograph equipped with a flame-ionisation detector. The two columns

used (183×0.2 cm) were filled with 10% UCW-98 (column I) and 10% OV-17 (column II) on Diatoport (80–100 mesh). The working conditions were as follows. Column I — the temperature 200°C , the injection port and detector temperature 260°C , the nitrogen flow rate 33.5 ml/min. Column II — the temperature 180°C , the injection port and detector temperature 250°C , the nitrogen flow rate 33.5 ml/min. The results of the analyses were obtained from the records made with a Hewlett-Packard integrator, Model 3370 B. Along with quantitative changes of individual reaction components, the retention times (t_R) of the starting isothiocyanates and aldehydes and those of the reaction products (isolated for this purpose and used as standards) were also determined.

The rates of the reactions (A) and (B) were measured at $140 \pm 0.2^\circ\text{C}$. The samples were withdrawn periodically (1 h) from the reaction flasks and analysed. The time-dependence of the concentrations of the products formed (in wt.%) was obtained from gas chromatographic data. This dependence was linear; the products other than those described above were not formed. The rate constants k ($\text{M}^{-1} \text{min}^{-1}$) were calculated from second-order rate equation. The rate constant of the reaction of phenyl isothiocyanate with benzaldehyde was determined similarly.

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Translated by J. Heflejš.