MECHANISM OF THE ADDITION OF ALCOHOLS TO SUBSTITUTED PHENYLISOTHIOCYANATES

ELECTRICAL EFFECTS OF THE SUBSTITUENTS ON THE REACTION*

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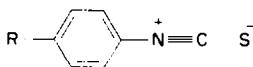Indian Institute of Science, Bangalore-12, India

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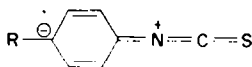Indian Institute of Science, Bangalore-12, India

Abstract—The addition reaction of alcohols to substituted phenylisothiocyanates is found to be a second-order reaction. The reaction is catalysed by triethylamine. First-order rate constants of the addition reaction have been determined in excess of ethanol, for a number of substituted phenyliso-thiocyanates and the rate data give a satisfactory linear correlation with Hammett σ constants of groups. While the energies of activation vary randomly with substitution, the entropies of activation bear a linear relationship to the energies of activation. Infra-red spectra indicate that the thiourethanes which are the products of the addition reaction exist in the thioamide form. The most prominent resonance form which can satisfactorily explain both the kinetic and infrared data, has been suggested.

INTRODUCTION

Browne and Dyson[1] studied the addition reaction of ethanol to substituted phenyl-isothiocyanates. Although they studied this reaction with a number of substituted phenylisothiocyanates there was no satisfactory correlation of the kinetic data with the electrical properties of the substituents. Caldow and Thompson[2] have recently reported the infra-red band intensities of the isothiocyanate group in a few sub-stituted phenylisothiocyanates. Electron-withdrawing groups are found to favour the —NCS band intensity, A, i.e. bond dipole,[3] as shown in Fig. 1, where log A is plotted against the Hammett σ constants of substituents.[4] The more prominent reso-nance forms of substituted phenylisothiocyanates may therefore be represented by I, II and III. Resonance forms II and III are probably more important since they

| I | II | III |
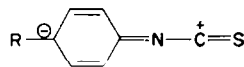
[1] D. W. Browne and G. H. Dyson, *J. Chem. Soc.* 3285 (1931).
[2] G. L. Caldow and H. W. Thompson, *Spectrochim. Acta* 13, 212 (1958).
[3] C. N. R. Rao and R. Venkataraghavan, *Canad. J. Chem.* 39, 1757 (1961).
[4] D. H. McDaniel and H. C. Brown, *J. Org. Chem.* 23, 420 (1958).

clearly point out the interaction of the substituents through the benzene ring. On the basis of these resonance forms one would expect that the nucleophilic reaction of alcohols with isothiocyanates will be facilitated by electron-withdrawing groups. We have now investigated the kinetics and energetics of the addition of alcohols to
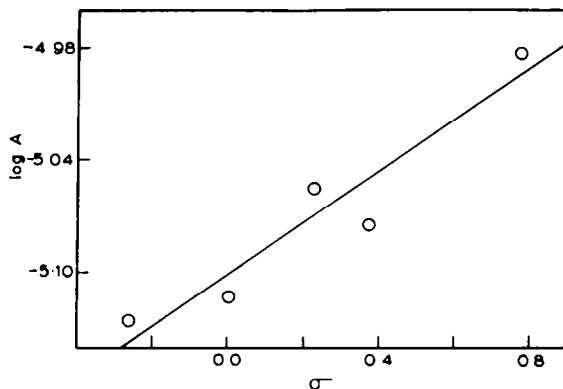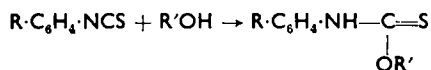

FIG. 1. Plot of the logarithm of infra-red band intensity of the —NCS group (ν_{Max} = 2130 cm^{-1}) in substituted phenylisothiocyanates versus Hammett σ constants.
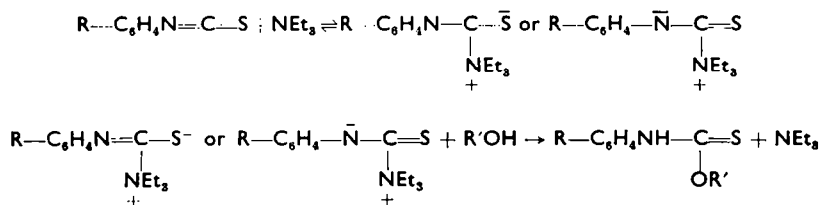
substituted phenylisothiocyanates in detail, with a view to understand the mechanism of the reaction.

$$R \cdot C_6H_4 \cdot NCS + R'OH \rightarrow R \cdot C_6H_4 \cdot NH-\underset{\underset{OR'}{|}}{C}\!=\!S$$

(R = p or m substituent on the ring; R^1 = alkyl group)

RESULTS AND DISCUSSION

The addition reaction of alcohols to isothiocyanates was expected to be a second-order reaction. However the reaction with methanol in benzene medium was found to be extremely slow in the case of phenyl- and para-bromophenyl-isothiocyanates at 53·5°. Therefore, it was decided to catalyse the reaction in order to follow the kinetics. Triethylamine was found to catalyse the reaction. It was possible to obtain fairly satisfactory second-order plots with p-bromophenylisothiocyanate (Fig. 2). The effect of concentration of triethylamine on the second-order rate constant is shown in Fig. 3. The mechanism of the catalysis may be represented as follows.

$$R-\!-\!-C_6H_4N\!=\!C\!-\!S \; ; \; NEt_3 \rightleftharpoons R \cdot C_6H_4N-\underset{\underset{+}{\overset{|}{NEt_3}}}{C}-\bar{S} \text{ or } R-\!-\!C_6H_4-\bar{N}-\underset{\underset{+}{\overset{|}{NEt_3}}}{C}\!=\!S$$

$$R-C_6H_4N\!=\!C-S^- \text{ or } R-C_6H_4-\bar{N}-\underset{\underset{+}{\overset{|}{NEt_3}}}{C}\!=\!S + R'OH \rightarrow R-C_6H_4NH-\underset{\underset{OR'}{|}}{C}\!=\!S + NEt_3$$

The second-order reaction was still too slow in the case of phenyl- and p-methoxy-phenylisothiocyanates, probably because of the decrease in the electron-withdrawing power of the substituents. It was therefore decided to study the electrical effects of the substituents on the reaction in the first-order fashion, in excess of alcohol.
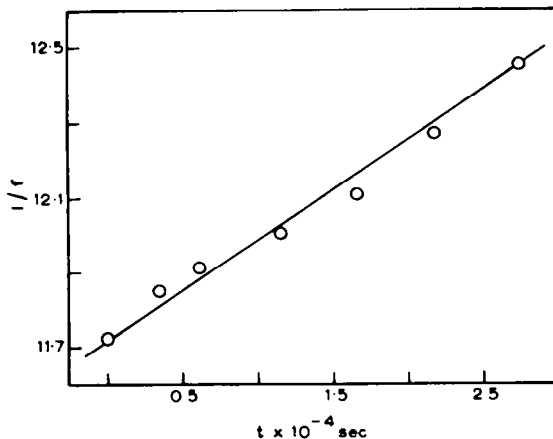
FIG. 2. Kinetics of addition of methanol (0·1 M) to *p*-bromophenylisothiocyanate (0·1 M) in presence of triethylamine catalyst (0·1 M) at 53·5°.
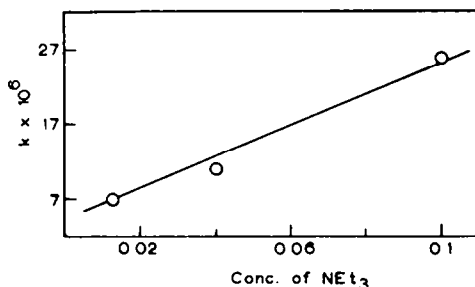*f* = concentration of isothiocyanate in moles per litre.

FIG. 3. Dependence of second-order rate constant (g.mole^{-1} l.sec.$^{-1}$) on triethylamine concentration (g.mole per litre).

The first-order rate constants of a number of substituted phenylisothiocyanates were determined in excess of ethanol. Typical first-order data may be seen in Fig. 4. In Fig. 5 are shown Arrhenius plots for a few isothiocyanates. All the rate data have been summarized in Table 1. A plot of $\log k/k_0$ *vs.* the Hammett σ constants of substituents is shown in Fig. 6. The equation for the least-square line is found to be,

$$\log k/k_0 = 0{\cdot}342 + 1{\cdot}705\sigma.$$

The correlation coefficient and standard deviation are 0·960 and 0·253 respectively and are quite satisfactory. The correlation of these rate data with the σ^+ constants[5] was much poorer, with a correlation coefficient of 0·915 and a standard deviation of 0·364.

The energy of activation of the first-order reaction does not vary systematically with the substituent constants (Fig. 7). This is not unexpected since ρ is generally temperature-dependent. However, the entropies of activation calculated from the absolute rate theory,

$$k = \frac{RT}{Nh} e^{-\Delta H^{\ddagger}/RT} e^{\Delta S^{\ddagger}/R}$$

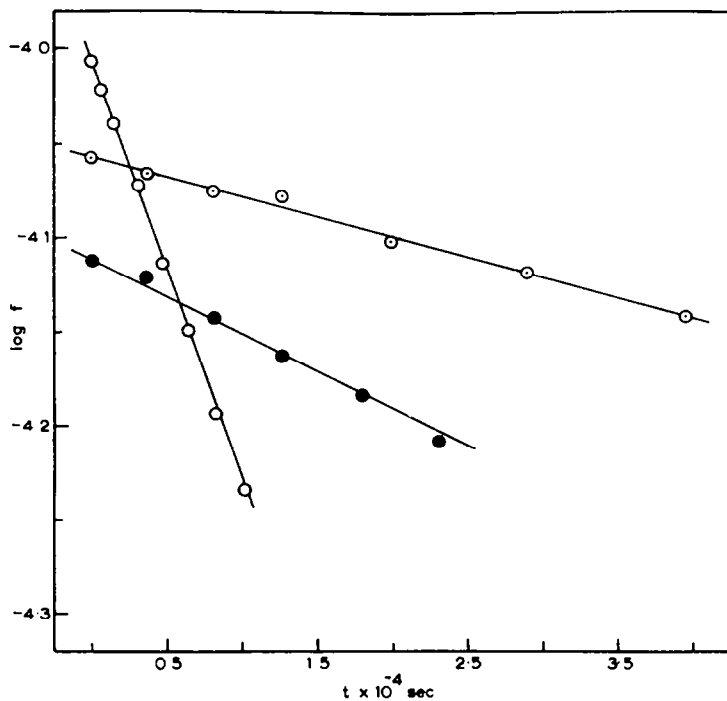[5] H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.* **80**, 4979 (1958).

FIG. 4. Kinetics of the addition of ethanol to substituted phenylisothiocyanates at 53·5°.

f = concentration of isothiocyanates in moles per ml.

○—p-bromophenyl isothiocyanate

●—phenylisothiocyanate

⊙—p-methoxyphenylisothiocyanate

TABLE 1. FIRST-ORDER RATE DATA FOR THE ADDITION OF ETHANOL TO
SUBSTITUTED PHENYL ISOTHIOCYANATES ($R—C_6H_4NCS$)

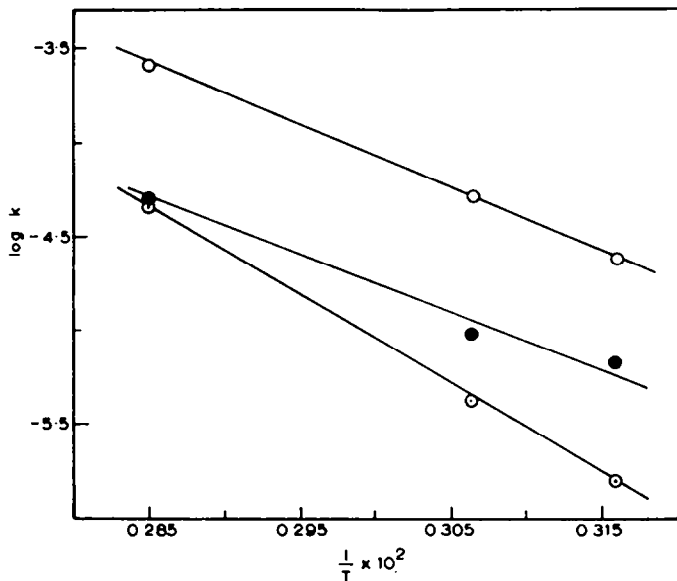| Substituent R	Temperature °K	k, sec^{-1} × 10^5	Energy of activation, E, k.cal.mole^{-1}	Entropy of activation, ΔS ‡ cal.deg.$^{-1}$ at 326·5°K
p-NO$_2$	316·5	12·55		
	326·5	94·16	35·7	37·1
p-COCH$_3$	316·5	4·54		
	326·5	10·54	17·4	−22·8
m-Cl	316·5	—		
	326·5	17·04	—	—
p-Br	316·5	2·42		
	326·5	5·30	15·6	−29·8
p-Cl	316·5	—		
	326·5	4·84	—	—
H	316·5	0·69		
	326·5	0·95	13·1	−40·2
p-CH$_3$	316·5	0·36		
	326·5	0·92	14·9	−35·8
p-OCH$_3$	316·5	0·16		
	326·5	0·42	21·7	−15·7
p-N(CH$_3$)$_2$	316·5	—		
	326·5	0·17	—	—

FIG. 5. Typical Arrhenius plots of the first-order rate data

○—p-bromophenylisothiocyanate

●—phenylisothiocyanate

○—p-methoxyphenylisothiocyanate

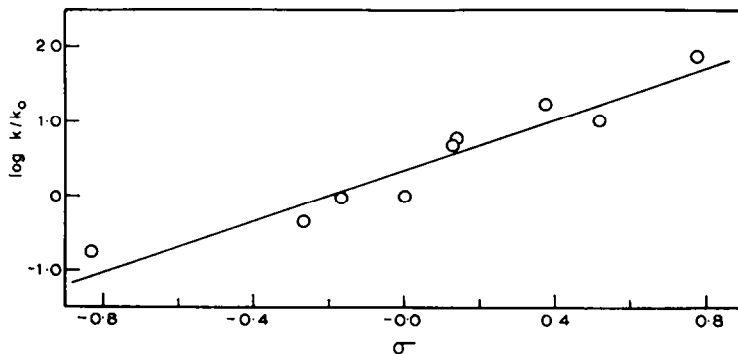The data of Browne and Dyson at the boiling temperature of alcohol have also been included.

FIG. 6. Correlation of the first-order data with Hammett σ values of groups.

vary linearly with the energies of activation (Fig. 8). This is obviously a special case of the Hammett equation[6]

$$\Delta\Delta H^{\ddagger} = \Delta E = \left(\frac{\rho + \lambda T}{\lambda}\right)\Delta\Delta S^{\ddagger}$$

where λ is a constant.

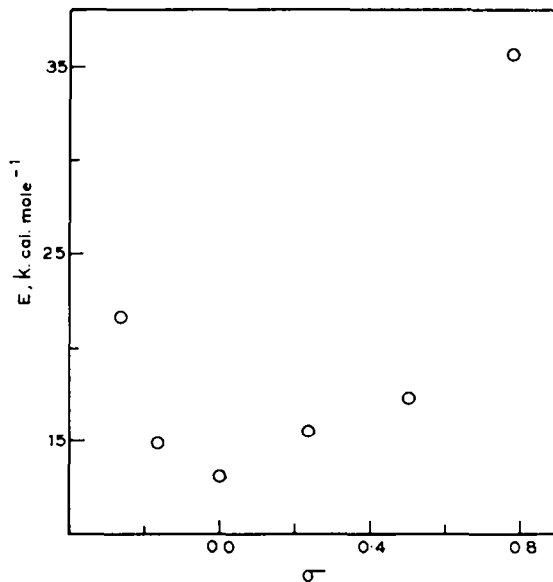[6] J. E. Leffler, J. Chem. Phys. 23, 2199 (1955).

Fig. 7. Plot of energy of activation *versus* Hammett σ values of groups.
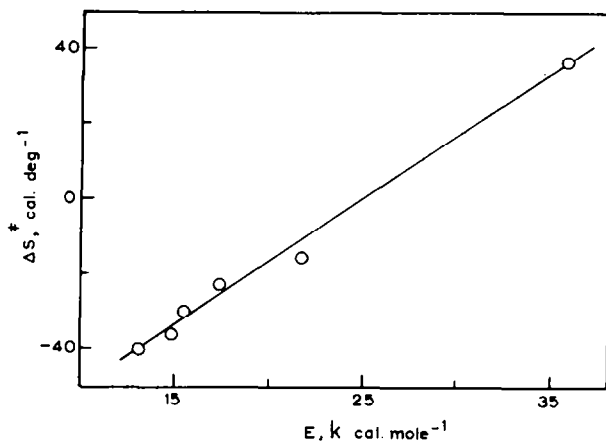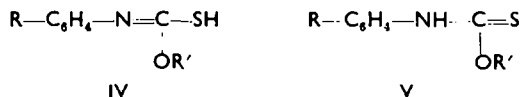

Fig. 8. Relation between entropy of activation and energy of activation.

The thiourethanes which are the products of the addition reaction can exist in two tautomeric forms,

R—C_6H_4—N=C—SH   R—C_6H_4—NH—C=S
        | |
        OR′   OR′

IV   V

Infra-red spectra of several substituted phenylthiourethanes in chloroform solution indicate no S—H stretching vibration. Bands due to the N—H stretching and the "—N—C=S bands" due to mixed vibrations[7] could however be identified. Apparently, the thiourethanes exist mostly as thioamides (V).

[7] C. N. R. Rao and R. Venkataraghavan, *Spectrochim. Acta* (in press).

The data on the kinetics clearly show that electron-withdrawing groups favour the addition of alcohols to isothiocyanates, just as anticipated on the basis of the infra-red intensity data. Resonance forms II and III of isothiocyanates can satisfactorily explain both the kinetics and infra-red data. Since the attack is by the alkoxide ion, it is quite reasonable that the proton would go to the most electronegative element, while the alkoxy group attaches itself to the carbon. This is supported by the thioamide structure of the thiourethanes which would actually mean that form III should be favoured more than II.

EXPERIMENTAL

The substituted phenylisothiocyanates were prepared by the oxidation of the corresponding ammonium dithiocarbanates[8] or by the reaction of the corresponding anilines with thiophosgene.[9] All the compounds were purified before use. Dry methanol, ethanol and benzene were used in all the reactions.

Kinetics were studied at 53·5° and 43·5° using boiling acetone and carbon disulphide baths. The reaction vessel was similar to the one used by Lieber, *et al.*[10]. During any one experiment the temp does not vary more than $\pm 0.3°$.

The amount of the isothiocyanate in a reaction mixture was analysed by gravimetric method employing benzidine as the reagent.[1] This analytical precedure is very tedious and was chosen in the absence of any other analytical method suitable for these studies. The rates determined are therefore not as precise as one would have liked them to be.

Second-order rates were determined in benzene media with methanol as the reactant, in presence of triethylamine catalyst. First-order rates were determined in excess of ethanol and in the absence of triethylamine.

Infra-red spectra of thiourethanes were recorded in chloroform solution employing a Grubb-Parson double beam spectrometer and Perkin-Elmer spectrometer, model 137-B.

[8] F. B. Dains, R. Q. Brewester and C. P. Olander, *Organic Synthesis* Coll Vol. 1; p. 447. John Wiley, New York (1946).

[9] G. M. Dyson and H. J. George, *J. Chem. Soc.* 125, 1702 (1924).

[10] E. Lieber, C. N. R. Rao and T. S. Chao, *J. Amer. Chem. Soc.* 79, 5962 (1957).

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