

KINETICS OF THE REACTION OF BENZOYL ISOTHIOCYANATES WITH METHANOL IN NONAQUEOUS MEDIA

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Kinetics of nucleophilic reactions of benzoyl isothiocyanates with methanol in dioxane and acetonitrile have been studied by UV spectroscopic method. On the basis of statistical treatment of kinetic data the series investigated has been classified as isentropic. Correlation of $\log k'$ with σ_p constants gave a straight line with the positive slope ρ . This indicates that electron-accepting substituents increase the rate of the above reaction.

In our previous work we were concerned with the physicochemical properties and structure of benzoyl isothiocyanates¹. After information about the configuration and electronic structure of benzoyl isothiocyanates had been obtained, it was of interest to find to what extent the reactivity of the isothiocyanato group toward nucleophiles is affected by mesomeric interaction of the carbonyl with NCS group. Kinetics of nucleophilic addition reactions of acyl isothiocyanates with alcohols have not yet been studied. So far, only the results of the study of the reaction of alcohols with aromatic and aliphatic isothiocyanates have been reported^{2,3}. The aim of this work was to get information about the reactivity of benzoyl isothiocyanates and to characterize the reaction series as to its isokinetic behaviour.

EXPERIMENTAL

Compounds studied. Benzoyl isothiocyanate^{4,5} (I), b.p. 77–78°C/0.34 Torr. UV spectrum (dioxane): λ_{\max_1} 252 nm, $\log \epsilon_1$ 4.16; λ_{\max_2} 280 nm, $\log \epsilon_2$ 3.90. 4-Chlorobenzoyl isothiocyanate^{6,7} (II), m.p. 46–47°C (light petroleum). UV spectrum (dioxane): λ_{\max_1} 268 nm, $\log \epsilon_1$ 4.12; λ_{\max_2} 286 nm, $\log \epsilon_2$ 3.92. 3-Methylbenzoyl isothiocyanate^{7,8} (III), b.p. 83°C/1 Torr. UV spectrum (dioxane): λ_{\max_1} 255 nm, $\log \epsilon_1$ 4.05; λ_{\max_2} 284 nm, $\log \epsilon_2$ 3.41. 4-Methylbenzoyl isothiocyanate^{7,9} (IV), b.p. 107–109°C/0.5 Torr. UV spectrum (dioxane): λ_{\max_1} 264 nm, $\log \epsilon_1$ 4.16; λ_{\max_2} 286 nm, $\log \epsilon_2$ 3.92. 4-Methoxybenzoyl isothiocyanate^{6,10} (V), b.p. 110–112°C/0.25 Torr. m.p. 28 to 30°C. UV spectrum (dioxane): λ_{\max_1} 251 nm, $\log \epsilon_1$ 4.11; λ_{\max_2} 283 nm, $\log \epsilon_2$ 3.86. 4-Cyanobenzoyl isothiocyanate¹ (VI), m.p. 54–55°C (light petroleum). UV spectrum (dioxane): λ_{\max} 292 nm, $\log \epsilon$ 4.29.

Products. N-Substituted O-methyl monothiourethanes were prepared by refluxing the corresponding acyl isothiocyanate (0.05 mol) with methanol (0.1 mol) in dioxane. The crude product was recrystallized from an appropriate solvent. N-(Benzoyl)-O-methylmonothiourethane¹¹,

m.p. 97–98°C (light petroleum). UV spectrum (dioxane): $\lambda_{\max 1}$ 236 nm, $\log \epsilon_1$ 3.83; $\lambda_{\max 2}$ 271 nm, $\log \epsilon_2$ 4.08. N-(4-Methylbenzoyl)-O-methylmonothiourethane¹², m.p. 93–95°C (n-heptane-ethanol). UV spectrum (dioxane): $\lambda_{\max 1}$ 234 nm, $\log \epsilon_1$ 3.88, $\lambda_{\max 2}$ 270 nm, $\log \epsilon_2$ 4.21. N-(3-Methylbenzoyl)-O-methylmonothiourethane, m.p. 63–65°C (ethanol). UV spectrum (dioxane): $\lambda_{\max 1}$ 240 nm, $\log \epsilon_1$ 3.90; $\lambda_{\max 2}$ 273 nm, $\log \epsilon_2$ 4.10. For C₁₀H₁₁NO₂S (209.3) calculated: 57.33% C, 5.30% H, 6.69% N; found: 57.49% C, 5.15% H, 6.51% N. N-(4-Chlorobenzoyl)-O-methylmonothiourethane, m.p. 88–90°C (ethanol). UV spectrum (dioxane): $\lambda_{\max 1}$ 250 nm, $\log \epsilon_1$ 3.88; $\lambda_{\max 2}$ 272 nm, $\log \epsilon_2$ 4.16. For C₉H₈ClNO₂S (229.7) calculated: 47.01% C, 3.49% H, 6.09% N; found: 47.23% C, 3.47% H, 6.35% N. N-(4-Cyanobenzoyl)-O-methylmonothiourethane, m.p. 84–85°C (n-heptane-ethanol). UV spectrum (dioxane): λ_{\max} 270 nm, $\log \epsilon$ 4.18. For C₁₀H₈N₂O₂S (220.3) calculated: 49.02% C, 3.62% H, 12.70% N; found: 49.12% C, 3.71% H, 12.55% N. N-(4-Methoxybenzoyl)-O-methylmonothiourethane, m.p. 82–84°C (n-heptane-ethanol). UV spectrum (dioxane): $\lambda_{\max 1}$ 238 nm, $\log \epsilon_1$ 3.87; $\lambda_{\max 2}$ 277 nm, $\log \epsilon_2$ 4.07. For C₁₀H₁₁.NO₃S (225.3) calculated: 53.26% C, 4.92% H, 6.21% N; found: 53.30% C, 4.98% H, 6.02% N.

Procedure. Kinetics of the reaction of benzoyl isothiocyanates with methanol have been followed on a UV spectrometer, Model PE-402, by measuring the decrease in the concentration of a given isothiocyanate at an appropriate wavelength. Benzoyl isothiocyanates were used in $5 \cdot 10^{-5}$ M concentrations, methanol in $5 \cdot 10^{-3}$ M concentration. This insured that the reaction proceeded as a pseudomonomolecular one. Measurements were carried out in thermostatted 1 cm-cells in the 68–85°C region (the temperature was kept with an accuracy of $\pm 0.3^\circ$ C). Dioxane was used as a solvent. In addition, acetonitrile was employed as the solvent in the case of benzoyl- and 4-chlorobenzoyl isothiocyanates. The value of the apparent rate constant k' was obtained from the slope of the linear $\log \Delta E$ vs time plot. The actual constant k was obtained by dividing the apparent rate constant k' by the concentration of methanol. The reaction products were verified by comparing their UV spectra with the spectra of the corresponding final products under identical conditions. The calculation of activation parameters¹³, regression dependences as well as the confirmation of the validity^{14–16} of the isokinetic relationship was performed by a statistical method.

TABLE I

Rate Constants (k' in min^{-1} and k in $\text{l mol}^{-1} \text{min}^{-1}$) for the Reaction of Substituted Benzoyl Isothiocyanates I–VI with Methanol in Dioxane

No	Isothiocyanate	$10^2 k'$			k		
		68°C	75°C	85°C	68°C	75°C	85°C
I	benzoyl	0.69	0.95	1.40	1.39	1.91	2.80
II	4-chlorobenzoyl	1.52	2.08	2.99	3.04	4.15	5.98
III	3-methylbenzoyl	0.54	0.94	1.38	1.07	1.88	2.76
IV	4-methylbenzoyl	0.42	0.62	0.85	0.85	1.24	1.70
V	4-methoxybenzoyl	0.29	0.38	0.57	0.58	0.76	1.15
VI	4-cyanobenzoyl	6.11	8.21	10.62	12.23	16.43	21.24

RESULTS AND DISCUSSION

Because of a high instability of benzoyl isothiocyanates in aqueous media we have decided to examine kinetics of their nucleophilic addition reaction with methanol in organic solvents. As the reaction does not proceed at a measurable rate at temperatures below 60°C, kinetic measurements had to be carried out at the higher temperatures. As a consequence of this fact, the solvent used should fit the following conditions: it had to dissolve benzoyl isothiocyanates, be miscible with methanol, have b.p. higher than 85°C and absorb UV light in the region below 250 nm. These criteria have been fulfilled by dioxane and acetonitrile.

The linear dependence of $\log k'_{85^\circ\text{C}}$ on $\log k'_{68^\circ\text{C}}$ ($q = 0.934$, $r = 0.99$) which was obtained from the results of kinetic measurements of the reaction (Tables I and II) confirms to a certain extent the validity of the isokinetic relationship for the model series under study. The reaction series has been also tested by statistical method suggested by Exner¹⁴⁻¹⁶ (Table III). The first group comprised kinetic results obtained for all the benzoyl isothiocyanates investigated, whereas in the second group the results of the statistical treatment of five 4-substituted benzoyl isothiocyanates were included, excluding thus 3-methylbenzoyl isothiocyanate. With regard to experimental possibilities and solvents, a broader temperature region which would ensure the greater accuracy of statistical results, could not be used. On the basis of the values of s_{00} and s_0 and after carrying out F-test one can speak about the validity of the isokinetic relationship for the first group, although the accuracy is not too high ($s_{00} = 0.028$). From the values of the isokinetic temperature and standard deviation for the isoentropic nature of the reaction series ($\beta = 1573$ and $s_s \approx s_{00}$) one can regard the reaction series as isoentropic¹⁷ (Fig. 1). As 3-methylbenzoyl isothio-

TABLE II

Activation Parameters (E_A , ΔH^\ddagger in kcal mol⁻¹ and $\log A$, ΔS^\ddagger in cal grad⁻¹ mol⁻¹) of the Reaction of Substituted Benzoyl Isothiocyanates I—VI with Methanol in Dioxane

No	Isothiocyanate	E_A	$\log A$	ΔH^\ddagger	ΔS^\ddagger
I	benzoyl	9.99	6.55	9.30	-30.83
II	4-chlorobenzoyl	9.62	6.65	8.93	-30.39
III	3-methylbenzoyl	13.20	8.56	12.59	-21.65
IV	4-methylbenzoyl	9.80	6.22	9.12	-32.34
V	4-methoxybenzoyl	9.84	6.06	9.15	-33.07
VI	4-cyanobenzoyl	7.79	6.09	7.10	-32.98

cyanate differed markedly in its ΔS^\ddagger and ΔH^\ddagger parameters from 4-substituted benzoyl isothiocyanates (Table II and Fig. 1) we have examined in more detail the second group of the compounds which comprised exclusively 4-substituted benzoyl isothiocyanates.

TABLE III

Tests on the Validity of the Isokinetic Relationship for the Series of Benzoyl Isothiocyanates

Symbols used: l the number of substances in the series, $\sum n$ the number of measurements, ΔT the temperature region in K, s standard deviations, s_{00} without the condition of the common point of intersection, s_0 isokinetic; differences in the reactivity s_R between reactions, s_∞ isoenthalpic; β the isokinetic temperature (in K), ψ the value of the isokinetic relationship at a given temperature region, ψ_n normalized with respect to the temperature region, s_s the standard deviation for testing the isoentropic relationship.

Group (substances)	$l(\sum n)$ ΔT	s_{00} s_0	s_R s_∞	ψ ψ_n	β s_s
1	6 (18)	0.0278	0.467	0.067	1 573
(I-VI)	17	0.0314	0.033	0.116	0.030
2	5 (15)	0.017	0.516	0.029	-22 253
(I-II, IV-VI)	17	0.015	0.018	0.055	0.014

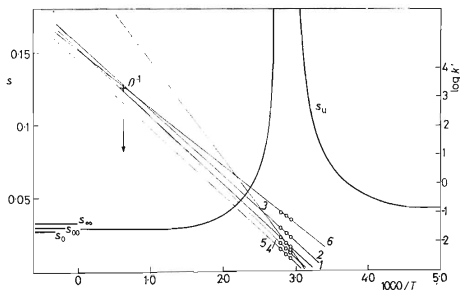


FIG. 1

Isokinetic Relationship for the Reaction of Substituted Benzoyl Isothiocyanates with Methanol

Lines 1-6 correspond to the linear dependence of $\log k'$ on $1000/T$ (in $u \text{ grad}^{-1}$) for the derivatives presented in Table I. The curve represents the dependence of the standard deviation s_u upon the presumed isokinetic temperature.

The results obtained for this group (Table III) demonstrate quite clearly the validity of the isokinetic relationship ($s_{00} > s_0$) at a given precision which is greater than in the former case ($s_{00} = 0.017$). Similarly high is also the significance of the relation (ψ_n lies in the region of statistically significant correlations). Based on the values of β and s_s , one can consider this series as being most likely the isoentropic one ($\beta = -22253$ and $s_s < s_{00}$). The same conclusion can be drawn also from comparison of ΔS^\ddagger for 4-substituted benzoyl isothiocyanates (Table II). As the isokinetic relationship is justified for this series, also Hammett equation may be expected to be fulfilled in this case. The $\log k'$ (at 68°C) vs σ_p dependence is a straight line, as shown in Fig. 2 ($\rho = 1.42$, $r = 0.99$). Its positive slope indicates that electron-accepting substituents increase the rate of the reaction. Changes in polarity of solvents do not affect significantly the reaction rate (Table IV).

The values of activation parameters (Table II), very small solvent effect (Table IV) and the sensitivity of the reaction toward substituent effects (Fig. 2) all indicate that the reaction could proceed by a concerted mechanism with formation of partial charges in the transition state.

TABLE IV

Rate Constants k ($1 \text{ mol}^{-1} \text{ min}^{-1}$) for the Reaction of Benzoyl Isothiocyanate (I) and 4-Chlorobenzoyl Isothiocyanate (II) with Methanol in Solvents of Varying Polarity at $68 \pm 0.3^\circ\text{C}$ and the Values of the Empirical Parameter E_T (kcal mol^{-1})

Solvent	E_T^a	$k, 1$	$k, 2$
Acetonitrile	46.0	1.79	4.62
Dioxane	36.0	1.39	3.04

^a Taken from ref. ¹⁸.

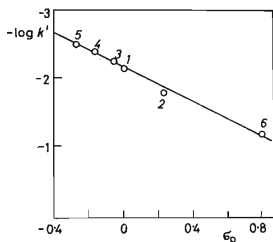


FIG. 2
Dependence of $\log k'$ (at 68°C) on Hammett σ_p Constants for the Reaction of Substituted Benzoyl Isothiocyanates with Methanol

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