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Kinetics of the Reaction of 1-R-3,5-Dinitrobenzenes with 4-Chlorophenol in DMF in the Presence of Potassium Carbonate

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Abstract—The effect of substituent in 1-R-3,5-dinitrobenzenes on the rate and activation parameters of their reactions with 4-chlorophenol in dimethylformamide in the presence of potassium carbonate was studied by the competing reactions technique. Analysis of the activation parameters revealed predominant contribution of the enthalpy factor to variation of the Gibbs energy of activation.

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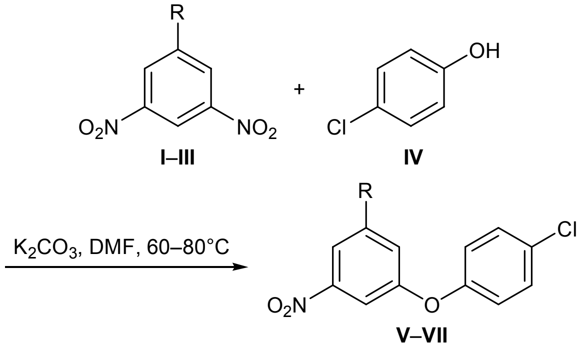
Diaryl ethers are extensively used in various fields of synthetic chemistry, in particular in the synthesis of herbicides [1], antibiotics [2], and other biologically active compounds [3]. Therefore, development of new methods for the synthesis of diaryl ethers and improvement of known procedures [4], as well as studies on the mechanisms of these processes, seem to be important.

It is known that the rate of bimolecular S_NAr reactions is determined by the nature of nucleophile, substrate, departing group, and solvent and that it is usually controlled by the enthalpy factor [5, 6]. Variation of the departing group in 1-nitro-3-X-arenes could result in entropy control over S_NAr reactions with phenols in the presence of potassium carbonate in DMF [7]. With a view to estimate the effect of substituent on the reactivity in bimolecular S_NAr processes, the kinetics of reactions of 1-R-3,5-dinitrobenzenes with 4-chlorophenol in the presence of potassium carbonate (Scheme 1) were studied by the competing reactions technique in dimethylformamide in the temperature range from 60 to 80°C.

Scheme 1.



I, **V**, R = NO_2; **II**, **VI**, R = CN; **III**, **VII**, R = CF_3.

The reactions resulted in replacement of one nitro group in the substrate by 4-chlorophenoxy group, and the products were characterized using NMR spectroscopy and mass spectrometry. From the relative reaction rates (Table 1) it follows that the reactivity of the nitro group in **I**–**III** decreases in the series $NO_2 > CN > CF_3$ and that the difference in the relative reaction rates decreases as the temperature rises.

The Hammett ρ values for the reactions of dinitrobenzenes **I**–**III** with 4-chlorophenol (**IV**) in DMF in

Table 1. Relative rate constants k_{rel}[a] for the reactions of 1-R-3,5-dinitrobenzenes **I**–**III** with 4-chlorophenol in DMF in the presence of K_2CO_3

R	$\Sigma\sigma_m$ [8]	k_{rel}		
		60°C	70°C	80°C
NO_2	1.42	19.4±1.1	17.3±1.5	15.1±1.6
CN	1.27	3.4±0.2	3.3±0.1	3.1±0.3
CF_3	1.14	1	1	1

[a] The relative rate constant k_{rel} was calculated assuming k_{rel} = 1 for compound **III** on the basis of the data in Table 5.

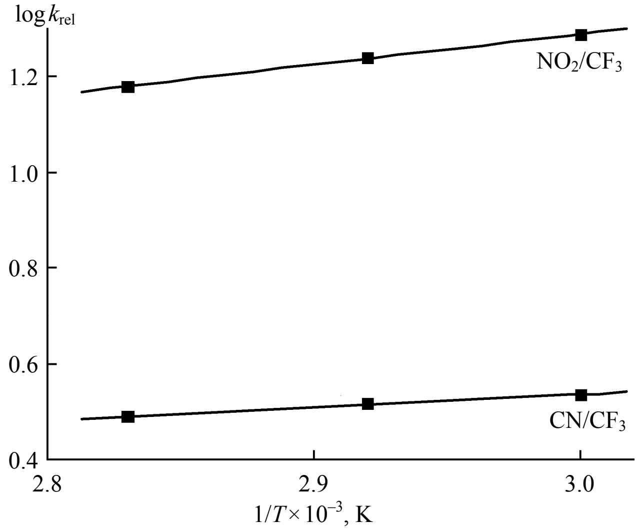


Fig. 1. Semilog plots of the relative rate constants versus reciprocal temperature for the reactions of 1-R-3,5-dinitrobenzenes **I–III** with 4-chlorophenol in DMF in the presence of K_2CO_3.

the presence of K_2CO_3 were determined from the $\log k_{rel}$—$\sum\sigma_m$ dependences [8]:

$$\log k_{rel}(60°C) = 4.61(\sum\sigma_m) - 5.28;$$
$$r = 0.998, s = 0.05, n = 3;$$

$$\log k_{rel}(70°C) = 4.43(\sum\sigma_m) - 5.07,$$
$$r = 0.998, s = 0.05, n = 3;$$

$$\log k_{rel}(80°C) = 4.22(\sum\sigma_m) - 4.83,$$
$$r = 0.998, s = 0.05, n = 3.$$

The ρ values are linearly related to temperature, and they decrease as the temperature rises. The absolute values of ρ are fairly high, which is typical of stepwise processes; they also suggest considerable electron density redistribution in the transition state. Positive ρ values indicate acceleration of the process as the electron-acceptor power of the substituent in the substrate increases. Insofar as the latter factor implies acceleration of nucleophilic attack due to enhancement of the electrophilicity of the carbon atom linked to the nitro group but the stage involving abstraction of the leaving group is thus decelerated, the observed large positive ρ values suggest that the rate-determining step is formation of transition state (cf. [9]).

Table 2. Variation of the activation parameters for the reactions of 1-R-3,5-dinitrobenzenes **I–III** with 4-chlorophenol in DMF in the presence of K_2CO_3

R	$\Delta\Delta H^{\neq}$,[a] kJ/mol	$\Delta\Delta S^{\neq}$,[a] J mol^{-1} K^{-1}	$T\Delta\Delta S^{\neq}$,[a,b] kJ/mol	$\Delta\Delta G^{\neq}$,[a,b] kJ/mol
NO_2	–12.5±0.7	–12.8±0.05	–4.4	–8.1
CN	–5.1±0.6	–5.2±0.04	–1.8	–3.3
CF_3	0	0	0	0

[a] The differences in the activation parameters $\Delta\Delta H^{\neq} = \Delta H^{\neq}(NO_2$ or CN$) - \Delta H^{\neq}(CF_3)$, $\Delta\Delta S^{\neq} = \Delta S^{\neq}(NO_2$ or CN$) - \Delta S^{\neq}(CF_3)$, and $\Delta\Delta G^{\neq} = \Delta G^{\neq}(NO_2$ or CN$) - \Delta G^{\neq}(CF_3)$ were calculated by the Eyring equation: $\log k_{rel} = (-\Delta\Delta H^{\neq}/T + \Delta\Delta S^{\neq})/4.576$ [10].

[b] At 70°C.

Temperature dependences of the logarithms of the relative rate constants were determined for each electrophile (Fig. 1), and they were used to estimate the differences in the activation parameters $\Delta\Delta H^{\neq}$, $\Delta\Delta S^{\neq}$, and $\Delta\Delta G^{\neq}$, depending on the substituent in the substrate, according to the modified Eyring equation [10] (Table 2).

$$\log k(NO_2/CF_3) = 652.3/T - 0.7;$$
$$r = 0.998, s = 0.004, n = 3;$$

$$\log k(CN/CF_3) = 269.1/T - 0.3;$$
$$r = 0.992, s = 0.004, n = 3.$$

Analysis of the activation parameters of the examined reaction showed that increase in the substrate electrophilicity is accompanied by reduction of the enthalpy, entropy, and Gibbs energy of activation. Here, the contribution of the enthalpy factor to variation of the Gibbs energy of activation predominates (Table 2).

Correlations between the enthalpy and entropy of activation ($\Delta\Delta H^{\neq} = 0.98\Delta\Delta S^{\neq} - 0.01$; $r = 0.999$, $s = 0.02$, $n = 3$) and between the enthalpy and Gibbs energy of activation ($\Delta\Delta H^{\neq} = 1.54\Delta\Delta G^{\neq} - 0.01$; $r = 0.999$, $s = 0.01$, $n = 3$) were found for the reactions of compounds **I–III** with 4-chlorophenol. The existence of such correlations suggests enthalpy–entropy compensation effect [11, 12]. The calculated compensation (isokinetic) temperature (976 K) considerably exceeds the experimental temperature (333–353 K), which may be regarded as an evidence in support of the chemical nature of the observed compensation effect.

Correlations were also found between the enthalpy, entropy, and Gibbs energy of activation, on the one hand, and Hammett substituent constants $\sum\sigma_m$ for 1-R-3,5-dinitrobenzenes (Table 3, Fig. 2). The slopes of the corresponding linear dependences are negative, for increase in electron-withdrawing power of the R substituent is accompanied by reduction of the activation parameters. The absolute values of the slopes (Table 3) characterize the sensitivity of the activation parameters to variation of substituent in the electrophile [13]. It is seen that the enthalpy and entropy of activation are more sensitive to variation of substituent in the electrophile than the Gibbs energy of activation.

The activation parameters $\Delta H^{\ne}$, $\Delta S^{\ne}$, and $\Delta G^{\ne}$ were calculated from those found for the reaction with compound **III** [7] and the corresponding differences for compounds **I**–**III** (Table 4). The dependences of $\Delta H^{\ne}$, $\Delta S^{\ne}$, and $\Delta G^{\ne}$ upon $\sum\sigma_m$ were also determined:

$$\Delta H^{\ne} = -44.8\sum\sigma_m + 241.3;$$
$$r = 0.997,\ s = 0.6,\ n = 3;$$
$$\Delta S^{\ne} = -45.8\sum\sigma_m + 230.5;$$
$$r = 0.998,\ s = 0.6,\ n = 3;$$
$$T\Delta S^{\ne} = -15.8\sum\sigma_m + 79.1;$$
$$r = 0.996,\ s = 0.3,\ n = 3;$$
$$\Delta G^{\ne} = -29.0\sum\sigma_m + 162.2;$$
$$r = 0.999,\ s = 0.3,\ n = 3.$$

These dependences made it possible to estimate the activation parameters for the reaction of 1,3-dinitrobenzene with 4-chlorophenol in the presence of potassium carbonate in DMF (Table 4; cf. [7]).

Thus the results of the present study have shown that nucleophilic replacement of one nitro group in 1-R-3,5-dinitrobenzenes by 4-chlorophenoxy group in DMF in the presence of K_2CO_3 is characterized by predominant contribution of the enthalpy factor to variation of the Gibbs energy of activation.

EXPERIMENTAL

The ^{1}H and ^{19}F NMR spectra were recorded on a Bruker AC-200 spectrometer using hexamethyldisiloxane and trifluoroacetic acid, respectively, as internal references. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT 8200 instrument. The reaction mixtures were analyzed by GLC on Hewlett–Packard HP 5890 and LKhM-7A instruments (thermal conductivity detector; linear oven temperature programming from 50 to 270°C at a rate of 10 deg/min; stationary phase 15% of SKTFT-803, SE-30, or VS-1 on Chromaton W; carrier gas helium, flow rate 60 ml/min). Quantitative analysis was performed by the internal normalization method, and the components were identified by adding the corresponding authentic samples.

Table 3. Absolute values of the slopes $|b|$ of the dependences of activation parameters a upon Hammett substituent constants $\sum\sigma_m$ for the reactions of 1-R-3,5-dinitrobenzenes **I**–**III** with 4-chlorophenol in DMF in the presence of K_2CO_3; $a = b\sum\sigma_m + c$

Activation parameter a	$\lvert b\rvert$	c	r	s	n
$\Delta\Delta H^{\ne}$	44.8	51.3	0.998	0.6	3
$\Delta\Delta S^{\ne}$	45.8	52.5	0.998	0.6	3
$T\Delta\Delta S^{\ne}$[a]	15.8	18.1	0.998	0.2	3
$\Delta\Delta G^{\ne}$[a]	29.0	33.2	0.998	0.4	3

[a] At 70°C.

Table 4. Activation parameters of the reactions of 1-R-3,5-dinitrobenzenes **I**–**III** with 4-chlorophenol in DMF in the presence of K_2CO_3

R	$\Delta H^{\ne}$,[a] kJ/mol	$\Delta S^{\ne}$,[a] J mol^{-1} K^{-1}	$T\Delta S^{\ne}$,[a,b] kJ/mol	$\Delta G^{\ne}$,[a,b] kJ/mol
NO_2	177.5±9.9	165.2±0.9	56.6	120.9
CN	184.9±22.2	172.8±1.3	59.3	125.6
CF_3[c]	190	178	61	129
H[d]	209.5	198	67.9	141.6

[a] The activation parameters $\Delta H^{\ne}$, $\Delta S^{\ne}$, and $\Delta G^{\ne}$ were determined from those found for compound **III** and the corresponding differences given in Table 2.

[b] At 70°C.

[c] Data of [7].

[d] Calculated from the dependences of the activation parameters upon $\sum\sigma_m$ for $\sigma_m = 0.71$: $\Delta H^{\ne} = -44.8\sum\sigma_m + 241.3$ ($r = 0.997$, $s = 0.6$, $n = 3$), $\Delta S^{\ne} = -45.8\sum\sigma_m + 230.5$ ($r = 0.998$, $s = 0.6$, $n = 3$), $T\Delta S^{\ne} = -15.8\sum\sigma_m + 79.1$ ($r = 0.996$, $s = 0.3$, $n = 3$), $\Delta G^{\ne} = -29.0\sum\sigma_m + 162.2$ ($r = 0.999$, $s = 0.3$, $n = 3$).

Table 5. Relative rate constants of competing reactions of 1-R-3,5-dinitrobenzenes **I**–**III** with 4-chlorophenol in DMF in the presence of K_2CO_3

R_1/R_2	k_{rel}[a]		
	60°C	70°C	80°C
NO_2/CN	5.66±2%	5.26±9%	4.89±2%
CN/CF_3	3.43±6%	3.29±5%	3.09±11%

[a] Average values from at least three measurements.

Dimethylformamide was distilled under reduced pressure over calcium hydride. Potassium carbonate was calcined in a muffle furnace and ground prior to use. Commercial 1,3,5-trinitrobenzene (**I**) and 4-chlorophenol (**IV**) were purified according to standard procedures. 3,5-Dinitrobenzonitrile (**II**) and 3,5-dinitrobenzotrifluoride (**III**) were synthesized by known methods, and their physical constants were consistent with those given in [14, 15].

Diphenyl ethers V–VII (*general procedure*). A flask maintained at a constant temperature was purged with argon and charged with required amounts

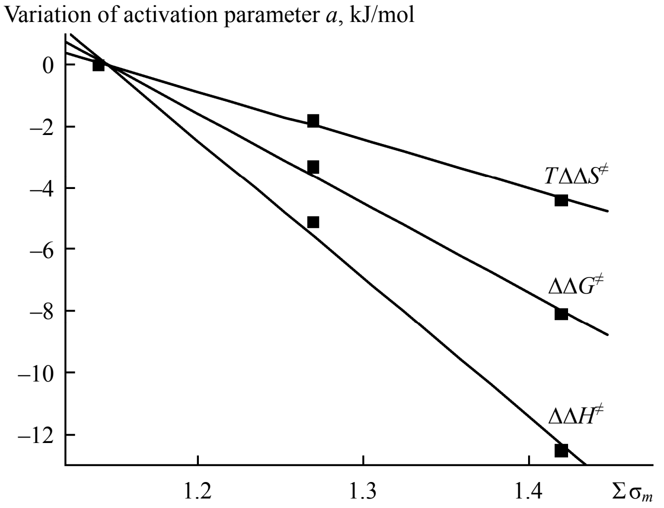


Fig. 2. Dependence of the activation parameters (a) on the Hammett substituent constants $\sum\sigma_m$ for the reactions of 1-R-3,5-dinitrobenzenes **I**–**III** with 4-chlorophenol in DMF in the presence of K_2CO_3; $a = b\sum\sigma_m + c$; σ_m values were taken from [8].

of substrate **I**–**III**, 4-chlorophenol, potassium carbonate, and dimethylformamide. The mixture was stirred for 3 h at 60°C, cooled to room temperature, diluted with 10 ml of water, and neutralized with 10% hydrochloric acid. The precipitate was filtered off, washed with water, and dried.

4′-Chloro-3,5-dinitrodiphenyl ether (V) was synthesized from 2.13 g (10 mmol) of 1,3,5-trinitrobenzene (**I**) and 1.28 g (10 mmol) of 4-chlorophenol in the presence of 2.76 g (20 mmol) of K_2CO_3 in 10 ml of DMF. Yield of the crude product 2.68 g. Purification by column chromatography (silica gel, $CHCl_3$) gave 2.41 g (82%) of compound **V** with mp 133–134°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.05 m (2H, o′-H), 7.44 m (2H, *m*′-H, J = 9.0 Hz), 7.52 m (1H, 6-H), 8.06 m (1H, 2-H), 8.72 m (1H, 4-H). Found: *m*/*z* 294.00402 $[M]^+$. $C_{12}H_7ClN_2O_5$. Calculated: *M* 294.00434.

3-(4-Chlorophenoxy)-5-nitrobenzonitrile (VI) was synthesized from 0.17 g (0.88 mmol) of 3,5-dinitrobenzonitrile (**II**) and 0.11 g (0.86 mmol) of 4-chlorophenol in the presence of 0.3 g (2.2 mmol) of K_2CO_3 in 2 ml of DMF. Yield of the crude product 0.2 g. Purification by column chromatography (silica gel, $CHCl_3$) gave 0.14 g (59%) of compound **VI** with mp 78–79.5°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.03 m (2H, *o*′-H), 7.40 m (2H, *m*′-H, J = 9.0 Hz), 7.51 m (1H, 2-H), 7.94 m (1H, 4-H), 8.15 m (1H, 6-H). Found: *m*/*z* 274.01508 $[M]^+$. $C_{13}H_7ClN_2O_3$. Calculated: *M* 274.01452.

1-(4-Chlorophenoxy)-3-nitro-5-trifluoromethylbenzene (VII) was synthesized from 0.24 g (1.02 mmol) of 3,5-dinitrobenzotrifluoride (**III**) and 0.12 g (0.94 mmol) of 4-chlorophenol in the presence of 0.28 g (2.03 mmol) of K_2CO_3 in 2 ml of DMF. Yield of the crude product 0.26 g. Purification by column chromatography (silica gel, $CHCl_3$) gave 0.17 g (54%) of compound **VII** with mp 39–40.5°C; published data [13]: mp 47–48°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.25 m (2H, *o*′-H, J = 9.0 Hz), 7.45 m (2H, *m*′-H, J = 9.0 Hz), 7.52 m (1H, 6-H), 7.90 m (1H, 2-H), 8.65 m (1H, 4-H). ^{19}F NMR spectrum ($CDCl_3$): δ_F 98.78 ppm, s (3F, CF_3).

Determination of the relative rate constants of the reactions of dinitrobenzenes I–III with 4-chlorophenol in DMF in the presence of K_2CO_3. A flask maintained at a constant temperature was purged with argon and charged with substrate couple **I**/**II** or **II**/**III**, 4-chlorophenol, and K_2CO_3 at a ratio of 5 : 5 : 1 : 2, and dimethylformamide was added so that the substrate concentration $c_{\mathrm{I}} = c_{\mathrm{II}}$ be equal to ~10^{-1} M. The mixture was stirred as long as necessary (up to 90 min) at a required temperature (60, 70, or 80°C), and the process was terminated by adding a mixture of 5 ml of chloroform and 5 ml of 5% hydrochloric acid. The organic phase was separated, washed with 10 ml of water, and dried over anhydrous calcium(II) chloride. The solvent was removed, and the residue was weighed and analyzed by GLC. The relative rate constants were calculated by the following formula [16]:

$$k_{\mathrm{I}}/k_{\mathrm{II}} = (\log[A_{\mathrm{I}}^0] - \log[A_{\mathrm{I}}^{\tau}])/(\log[A_{\mathrm{II}}^0] - \log[A_{\mathrm{II}}^{\tau}]),$$

where A_{I}^0 and A_{II}^0 are the initial concentrations (mol/l) of compounds **I** and **II**, respectively; and A_{I}^{τ} and A_{II}^{τ} are the concentrations (mol/l) of the same compounds at a moment of time τ. The relative rate constants calculated from the results of at least three measurements are collected in Table 5.

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