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Kinetics of the Reactions of 4-Nitrochlorobenzene with Substituted Phenolates in an Aprotic Polar Solvent

V. I. Mil'to, V. Yu. Orlov, G. S. Mironov, and V. V. Kopeikin

Yaroslavl State University, Yaroslavl, 150000 Russia

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Abstract—The kinetics of 4-nitrochlorobenzene reactions with substituted phenolates in the medium of *N*,*N*-dimethylacetamide was studied. The Brønsted relation is fulfilled by substituted potassium phenolates: the nucleophilicity of phenolates increases with an increase in their basicity. The rate-limiting step in the reactions of 4-nitrochlorobenzene with substituted phenolates and potassium resorcinate is changed from the phenoxide anion to the phenoxide dianion. In the latter case, electron transfer from the resorcinate dianion with the generation of radical species can be responsible for the reaction rate.

INTRODUCTION

The replacement of an activated halogen or nitro group in benzene derivatives with substituted phenoxides is a widely used technique for the preparation of polyfunctional diaryl ethers—multipurpose chemical reagents [1–3]. A number of publications [4–6] were devoted to this reaction because of the practical value of the target products and interest in the theoretical aspects of this process (aromatic nucleophilic substitution reactions). However, some aspects of this problem are still understood incompletely. The aim of this work was to study the reaction kinetics of substituted phenolates with 4-nitrochlorobenzene (4-NCB) in a medium of the aprotic solvent *N*,*N*-dimethylacetamide (DMAC).

EXPERIMENTAL

The reaction kinetics of chlorine atom substitution in 4-NCB with potassium phenolates was studied in a thermostatically controlled flask equipped with a stirrer, a reflux condenser, a capillary for admitting nitrogen, and a thermostatically controlled dropping funnel. The initial reactant concentrations were equal to 4×10^{-2} mol/l; DMAC was used as a solvent. The flask was maintained at a constant temperature and purged with nitrogen; the solvent and 4-NCB were placed in the flask, and a potassium phenolate solution in DMAC was added from the thermostatically controlled funnel and stirred in a nitrogen atmosphere. In the course of experiments, samples were taken and cooled, and the product composition was determined. The concentration of phenolates was determined by nonaqueous titration (a pH-672 potentiometer with glass and silver–silver chloride electrodes; titrant, 0.01 mol/l HCl solution in water; a solvent, 2-propanol). 4-Nitrochlorobenzene was determined by GLC (Chrom-4 chromatograph with a flame-ionization detector; carrier gas, nitrogen; column length, 3 m; column diameter, 3 mm; stationary phase, polyethylene glycol adipate; solid support, NAW; column and injector temperatures, 170 and 280°C, respectively; internal standard, nitrobenzene).

Solvents of reagent grade were additionally dried with alkali metal hydroxides and calcium chloride and distilled in a vacuum.

The potassium salts of substituted phenols and resorcinol were prepared as described below. Phenol and a calculated amount of a 0.2 mol/l potassium methylate solution in methanol (the latter was prepared according to the procedure [7]) were placed in a flask equipped with a reflux condenser and a capillary for admitting nitrogen. The mixture was refluxed in a nitrogen atmosphere for 0.5–1.0 h; methanol was distilled at a reduced pressure. The resulting salt was dried at 20–40°C at a reduced pressure.

Balance experiments for the reaction of 4-NCB with potassium resorcinate were performed in a thermostatically controlled flask equipped with a stirrer, a reflux condenser, and a capillary for admitting nitrogen. The initial concentrations of 4-NCB and potassium resorcinate were equal to 3.12×10^{-2} and 2.5×10^{-2} mol/l, respectively; DMAC was a solvent.

The EPR spectra were recorded on an RE-1306 spectrometer with an operating frequency of 9580 MHz, a Klystron power of 10 MW, and a linear field scan. The measurements were performed in a quartz capillary 1 mm in diameter; Mn^{2+} in MgO was used as a standard sample.

RESULTS AND DISCUSSION

The interaction of 4-NCB with substituted phenolates in the medium of DMAC results in the formation

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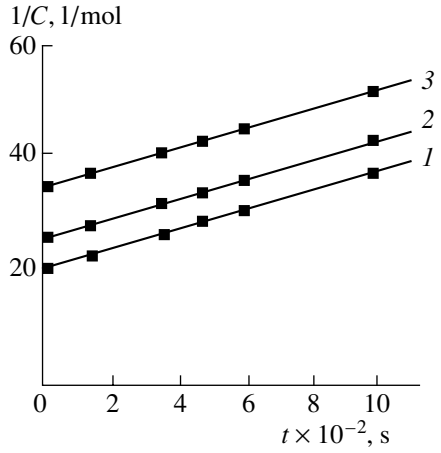


Fig. 1. Reciprocals of reactant concentrations as functions of time in the reaction of 4-nitrochlorobenzene with potassium phenolate at the 1 : 1 ratio between the reactants and initial reactant concentrations of (*1*) 0.05, (*2*) 0.04, and (*3*) 0.03 mol/l (60°C).

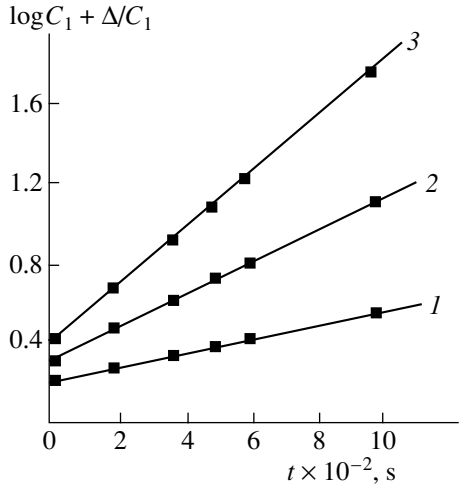
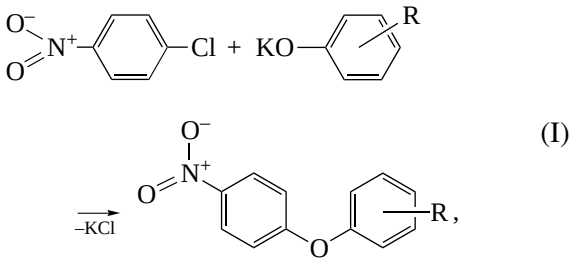


Fig. 2. $\log[(C_1 + \Delta)/C_1]$ as a function of time in the reaction of 4-nitrochlorobenzene with potassium phenolate with an excess of the latter at 60°C and initial concentrations (mol/l): 4-NCB, 0.04; potassium phenolate, (*1*) 0.06, (*2*) 0.08, and (*3*) 0.1.

of the nitro derivatives of diphenyl oxide. The reaction takes place according to the following scheme:



(I)

where R = 3-NH_2, 3-CH_3, H, 4-Cl, 4-Br, or 3-NO_2.

We found using GLC and TLC that the reaction is not complicated by side processes. The yield of nitro-substituted diphenyl oxides was as high as 93–96 mol %.

The reaction of 4-NCB with potassium phenolate was chosen as a model reaction. The reciprocal of 4-NCB concentration linearly depended on time at an equimolecular ratio between the reactants and at different initial reactant concentrations. This fact is indicative of a second-order reaction (Fig. 1). Table 1 (experiment nos. 1–3) summarizes the experimental rate constants. Another method [8] was also used, according to which the rate constant (k) at a constant initial concentration of one of the reactants (4-NCB, C_1^0) and at different initial concentrations of the other (potassium phenolate, C_2^0) was found from the equation

$$\log[(C_1 + \Delta)/C_1] - \log[(C_2 + \Delta)/C_2] = \Delta kt/2.303,$$

Table 1. Rate constants of the reaction of 4-nitrochlorobenzene with potassium phenolate at various initial reactant concentrations (60°C)

Experiment no.	Initial concentration ×10², mol/l		$\Delta = (C_2^0 - C_1^0) \times 10^2$, mol/l	$k \times 10^2$, l mol^{-1} s^{-1}
	4-NCB (C_1^0)	potassium phenolate (C_2^0)		
1	3.0	3.0	0	4.95 ± 0.12
2	4.0	4.0	0	5.00 ± 0.10
3	5.0	5.0	0	5.00 ± 0.14
4	4.0	6.0	2.0	4.78 ± 0.15
5	4.0	8.0	4.0	5.11 ± 0.10
6	4.0	10.0	6.0	5.20 ± 0.12

where $\Delta = C_2^0 - C_1^0$; t is time; and C_1 and C_2 are the current concentrations of 4-NCB and potassium phenolate, respectively).

The observed linear dependence of $\log(C_1 + \Delta)/C_1$ on t (Fig. 2) suggests that this reaction is a second-order reaction. The rate constants of the process were found from the slopes of the above straight lines (Table 1, experiment nos. 4–6). The variation of initial reactant concentrations has almost no effect on the rate constant.

The effect of temperature on the rate of the model reaction was studied at 50–80°C. The Arrhenius dependence is linear over this range, and the activation energy calculated from it is equal to 57.44 ± 2.62 kJ/mol. Table 2 summarizes the rate constants.

The effect of the nature of substituents in potassium phenolates on the rate of reaction (I) was studied. It was found that the reaction is of the second order for all reactant pairs regardless of the nature and position of substituents. Table 3 summarizes the rate constants found from the time dependence of the reciprocal of 4-NCB concentration.

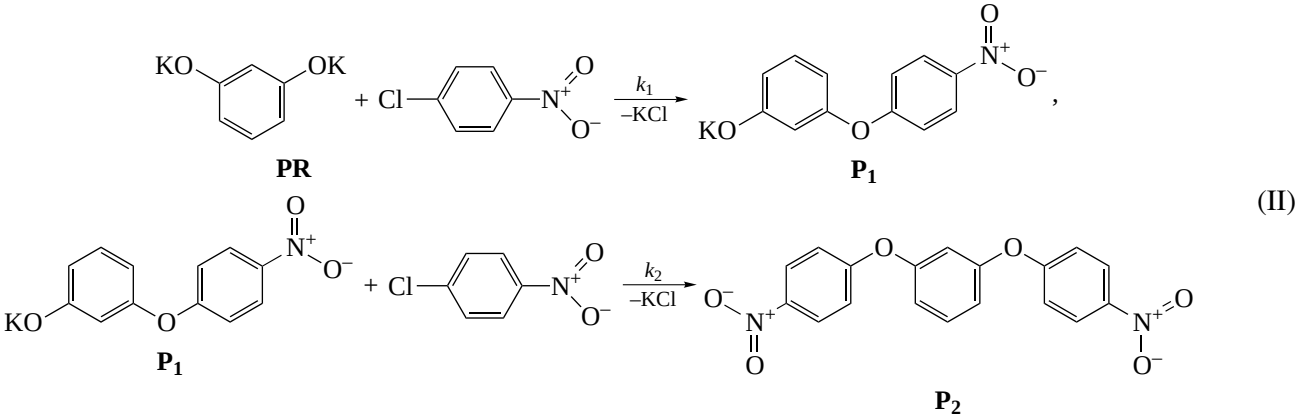
The experimental data satisfactory correlate with the Hammett σ-constants according to the equation

$$\log k = (-1.31 \pm 0.10) + (-1.89 \pm 0.08)\sigma.$$

The correlation coefficient is $r = 0.997$; the standard deviation is $s = 0.16$. This fact indicates the adequacy of the mechanism over the entire reaction series. The σ^0-constants were used in the correlation because in the test series a substituent occupies a *meta* or *para* position, which excludes direct polar conjugation.

The rate constants for substituted potassium phenolates suggest that the Brønsted relation is fulfilled: the nucleophilicity of phenolates increases with their basicity [10].

Bisphenolates (nucleophiles with two reaction sites) are used in the synthesis of polynuclear aromatic compounds containing bridging oxide groups. We decided on the synthesis of 4,4'-dinitrodiphenyl ether of resorcinol by the reaction of potassium resorcinate with 4-NCB as a test reaction for kinetic studies. Analysis of balance experiments showed that the reaction occurs according to the following scheme:



(II)

The yield of 4,4'-dinitrodiphenyl ether of resorcinol (P_2) was as high as 96–98 mol %. The intermediate product P_1 was isolated and identified by IR and ^{1}H NMR spectroscopy. From the expression [8]

$$C_{P_1}^{\infty} = \frac{C_{PR}^{\infty} - (C_{PR}^{\infty})^{k_2/k_1}/(C_{PR}^{0})^{k_2/k_1 - 1}}{k_2/k_1 - 1},$$

where $C_{P_1}^{\infty}$ is the concentration of P_1 at the end of the reaction, mol/l; C_{PR}^{∞} is the concentration of potassium resorcinate at the end of the reaction, mol/l; and C_{PR}^{0} is the initial concentration of potassium resorcinate, mol/l, it was found that $k_2/k_1 = 2.2$. The rate constant of the reaction of 4-NCB with 4-nitrophenyl ether of potassium resorcinate (k_2) was found from the reciprocal concentration–time linear relations at different initial concentrations of the reactants (Table 4).

The reactant concentrations were determined by independent techniques: chromatography and potentiometry for the substrate and the reagent, respectively. Thus, $k_2 = 27.0 \times 10^{-2}$ l mol^{-1} s^{-1} and $k_1 = 12.3 \times 10^{-2}$ l mol^{-1} s^{-1}.

The temperature dependence of the rate constant of the reaction between 4-NCB and 4-nitrophenyl ether of potassium resorcinate is adequately described by the Arrhenius equation at 50–110°C; the activation energy was equal to 58.12 ± 2.44 kJ/mol. Table 5 summarizes the reaction rate constants.

To interpret the reactivity of substituted phenolates in the reactions with 4-NCB, we used the method of reactivity indices. The logarithms of the rate constants of the reaction of 4-NCB with substituted phenolates and potassium resorcinate correlated with the Kloppmann reactivity index (KRI) [11]. In the case under consideration, the index had the form (the covalent term of the general equation)

$$\mathrm{KRI} = \Delta_{\mathrm{orb}} = \frac{2(c_a c_b \beta)^2}{E_{\mathrm{HOMO}} - E_{\mathrm{LUMO}}},$$

where c_a and c_b are the electron densities of frontier orbitals at the reaction sites a and b, respectively; β is the resonance integral; E_{HOMO} is the energy of the highest occupied molecular orbital; and E_{LUMO} is the energy of the lowest unoccupied molecular orbital.

The logarithms of the rate constants of the reactions between 4-NCB and substituted phenolates satisfactorily correlated (r = 0.978) with the KRI (Fig. 3). The resorcinate dianion obviously does not match the correlation (it is not shown in Fig. 3): KRI = 0.05628.

It is likely that this deviation of the characteristics of the resorcinate dianion from the correlation dependence indicates that the rate-limiting step of the reaction is changed on going from the single-charge nucleophile to the double-charge species. Taking into account the fact that the resorcinate dianion has a high-energy HOMO close to the LUMO of 4-NCB, the observed anomalous behavior can be interpreted in terms of a single-electron transfer mechanism. This is supported by published data [12, 13]. According to these data, the lower the energy difference between the frontier orbitals of reactants, the higher the probability that electron transfer will be involved in the rate-limiting step of aromatic nucleophilic substitution.

To test this hypothesis, the reaction between potassium resorcinate and 4-NCB in DMAC was performed in an EPR spectrometer cell. The signals of radical species (Fig. 4, spectrum *1*) were detected in the initial resorcinate–DMAC system at 20°C. The amount of paramagnetic centers was 10^{17}–10^{18} spin. The g-factors were calculated by the equation

$$g = \frac{0.7158\nu}{\frac{0.7158}{\nu}/g_{\mathrm{st}} \pm \Delta H},$$

where ν is the klystron operating frequency, g_{st} is the g-factor of the standard sample (Mn^{2+} in MgO) equal to 1.9810, and ΔH is the difference between the resonance signal of the standard sample and the resonance signal of the test sample. The g-factor found (g_{iso} = 2.0000 ± 0.0003; ΔH = 9.7 + 0.2 G) allowed us to reliably assign the signal to radicals like $^{-}$O–Ar–O$^{\bullet}$ [14]. The shape of the EPR spectrum was changed on the addition of

Table 2. Temperature dependence of the rate constant of the reaction of 4-nitrochlorobenzene with potassium phenolate at an initial concentration of the reactants equal to 4.0×10^{-2} mol/l

Temperature, °C	$k \times 10^2$, l mol^{-1} s^{-1}
50	2.50 ± 0.15
60	5.00 ± 0.10
70	10.00 ± 0.18
80	17.00 ± 0.33

Table 3. Rate constants of the reactions of 4-nitrochlorobenzene with substituted potassium phenolates at 60°C and an initial concentration of the reactants equal to 4.0×10^{-2} mol/l

Substituent R	σ [9]	$k \times 10^2$, l mol^{-1} s^{-1}
3-NH_2	−0.140	8.90 ± 0.16
3-CH_3	−0.076	6.80 ± 0.14
H	0	5.00 ± 0.10
4-Cl	0.267	1.50 ± 0.10
4-Br	0.270	1.45 ± 0.12
3-NO_2	0.700	0.25 ± 0.08

Table 4. Rate constant (k_2) of reaction (II) at various initial reactant concentrations (110°C)

Initial concentration ×10^2, mol/l		$k_2 \times 10^2$, l mol^{-1} s^{-1}
P_1	4-NCB	
3.0	3.0	27.27 ± 0.33
4.0	4.0	27.00 ± 0.21
5.0	5.0	26.82 ± 0.24

Table 5. Temperature dependence of k_2 at initial 4-NCB and P_1 concentrations of 4.0×10^{-2} mol/l

Temperature, °C	$k_2 \times 10^2$, l mol^{-1} s^{-1}
60	2.10 ± 0.16
75	5.00 ± 0.12
90	11.20 ± 0.14
110	27.00 ± 0.21

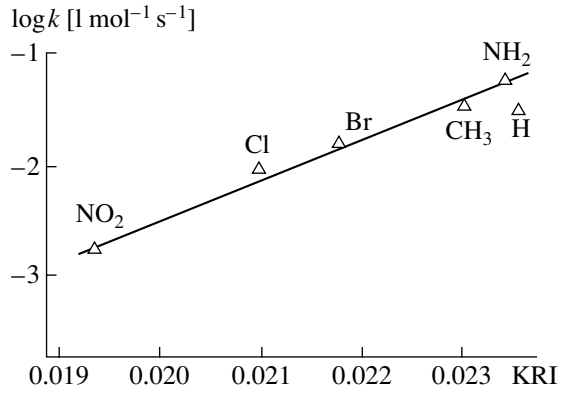


Fig. 3. log*k* as a function of reactivity indices for the reactions of 4-nitrochlorobenzene with substituted phenolates.

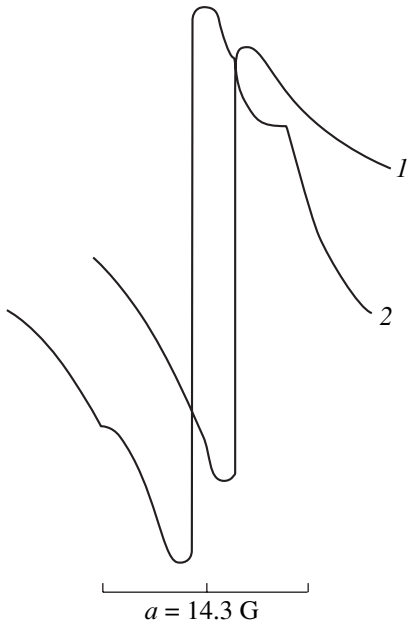


Fig. 4. EPR spectra of the (*1*) potassium resorcinate–DMAC and (*2*) potassium resorcinate–DMAC–4-nitrochlorobenzene systems at 20°C.

4-NCB to the system (Fig. 4, spectrum *2*). The new signal can be attributed to a radical anion like R–NO$^{\cdot-}$ [15], that is, in our case, the 4-NCB radical anion, which was described as a kinetically stable species [16]. Note that we failed to detect the signals of radical species when the reaction of 4-NCB with potassium phenolate was performed in the EPR spectrometer cell at 20°C.

Thus, we can conclude that the rate-limiting step in the reactions of 4-NCB with substituted phenolates and potassium resorcinate changes on going from the phenoxide anion to the phenoxide dianion. In the letter case, the reaction rate can be controlled by electron transfer from the resorcinate dianion with the generation of radical species.

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