

# Activation Parameters of the Reactions of 4-Nitrophenyl Benzoates and *S*-Phenyl Benzothioate with 4-Chlorophenol in Dimethylformamide in the Presence of Potassium Carbonate

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Received June 2, 2008

**Abstract**—The kinetics of transesterification of 4-nitrophenyl benzoates and *S*-phenyl benzothioate with 4-chlorophenol in dimethylformamide in the presence of potassium carbonate were studied. Variation of the substrate reactivity and activation parameters of the process is discussed with respect to the substituent in the benzoic acid fragment.

**DOI:** 10.1134/S1070428009040095

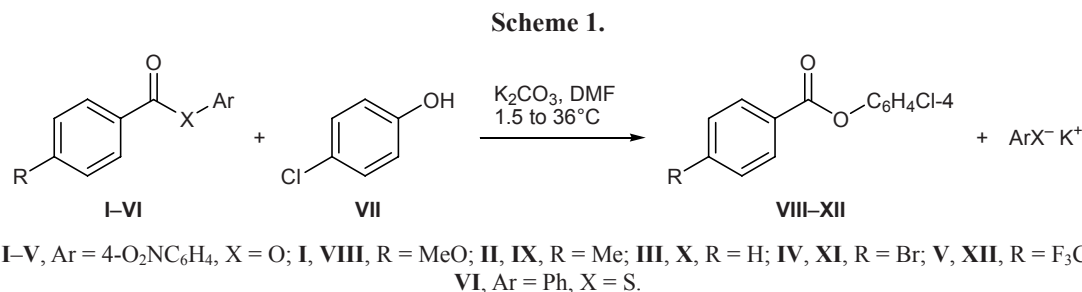
The reactivity of aryl benzoates in transesterification processes is determined by several factors, including electrophilicity of the carbonyl carbon atom, nucleophile nature, and solvation [1–5]. The electrophilicity of the carbonyl carbon atom depends in turn on the nature of substituents in fragments attached thereto. We previously studied [4, 5] the effect of substituents in the benzoyl group on the reactivity of substituted 4-nitrophenyl benzoates toward 4-chlorophenol and benzenethiol in the presence of potassium carbonate in dimethylformamide. We found that donor substituents in the benzoyl fragment, as might be expected [6], reduce the reactivity and that electron-withdrawing groups enhance it. Presumably, the reaction involves several steps, and the reaction rate is not determined by removal of departing group [4, 5]. Although dissociation of the bond with departing group occurs at the stage that is not rate-determining, the nature of departing group may be expected to affect the rate and activation parameters of transesterification [7].

It is known that the enthalpy and entropy of activation can change to a much stronger extent than the energy of activation [8]. In reactions of carbonyl compounds with nucleophiles, characterized by similar  $\Delta G^\ddagger$  values, either enthalpy or entropy contribution may predominate [9, 10]. Despite numerous published data on the activation parameters of reactions of carbonyl compounds with nucleophiles [11], only a few publications are available on activation parameters of

transesterification processes. The reaction of 4-nitrophenyl acetate with 4-chlorophenoxide ion in aqueous medium was reported to be characterized by the following activation parameters:  $\Delta H^\ddagger = 51.4$  kJ/mol,  $\Delta S^\ddagger = -75.7$  J mol<sup>-1</sup> K<sup>-1</sup>,  $\Delta G^\ddagger = 74.0$  kJ/mol [11]. In going to 90% aqueous DMSO, the activation parameters of the same reaction insignificantly decreased:  $\Delta H^\ddagger = 38.1$  kJ/mol,  $\Delta S^\ddagger = -69.9$  J mol<sup>-1</sup> K<sup>-1</sup>,  $\Delta G^\ddagger = 59.0$  kJ/mol [12]. Variations of the enthalpy of activation  $\Delta H^\ddagger$ , entropy of activation  $\Delta S^\ddagger$ , and Gibbs energy of activation  $\Delta G^\ddagger$  are very important for elucidating specific features of transesterification reactions in relation to the reactant structure.

The goal of the present work was to examine the effect of the leaving group nature on the reactivity of 4-nitrophenyl benzoate and *S*-phenyl benzothioate in transesterification with 4-chlorophenol (K<sub>2</sub>CO<sub>3</sub>, DMF) and analyze the ratio of the enthalpy and entropy contributions to the energy barrier of this reaction. The difference in the basicities of the leaving groups in 4-nitrophenyl benzoate (**III**) and *S*-phenyl benzothioate (**VI**) amounts to 1.64 pK units (pK = 12.34 and 10.7 for 4-nitrophenol and benzenethiol, respectively, in DMF [13]); presumably, this difference is sufficient to affect the reaction rate and its activation parameters (cf. [14, 15]).

Aryl benzoates **I–VI** reacted with 4-chlorophenol (**VII**) in DMF in the presence of K<sub>2</sub>CO<sub>3</sub> in the temperature range from 1.5 to 36°C to give the corresponding 4-chlorophenyl benzoates **VIII–XII** (Scheme 1). The



products are stable under these conditions [4, 5]. The apparent rate constants for the reactions of esters **III** and **VI** with nucleophile **VII** at different temperatures are given in Table 1. In the examined temperature range, the transesterification of 4-nitrophenyl benzoate was faster than the reaction with *S*-phenyl benzothioate. Both the rate constants and the difference between them increase as the temperature rises. The apparent rate constants at 1.5 and 36°C differ by more than an order of magnitude. In going from 4-nitrophenyl benzoate to *S*-phenyl benzothioate the apparent rate constants decrease by a factor of 3.6 to 4.7 (Table 1).

The effect of leaving group in transesterification is determined by such factors as its basicity and polarizability of the atom therein attached to the carbonyl carbon atom, as well as by solvation of the leaving and entering groups [14, 15]. Taking into account p*K* values of 4-nitrophenol and benzenethiol in DMF (12.34 and 10.7, respectively [13]), phenylsulfanyl group should be expected to favor transesterification process to a stronger extent, as compared to 4-nitrophenoxy group, for benzenethiol is stronger acid than 4-nitrophenol. However, the observed reactivity ratio of aryl benzoates **III** and **VI** does not fit the relation between the basicities of the leaving groups.

It is known that the reactivity ratio of esters derived from phenols and benzenethiols in transesterification depends on the nature of oxygen-centered nucleophile [14–18]. For example, the ratio of the rate constants for transesterification of *S*-(4-nitrophenyl) benzothioate and 4-nitrophenyl benzoate with 4-chlorophenoxide ion in anhydrous ethanol at 25°C ( $k_S/k_O = 6.1$ )

[14] approaches the corresponding value found in 10% aqueous DMSO ( $k_S/k_O = 6.6$ ) [15]. However, in the reaction with hydroxide ion as nucleophile in 10% DMSO the rate constant ratio for *S*-(4-nitrophenyl) benzothioate and 4-nitrophenyl benzoate changed to the opposite ( $k_O/k_S = 1.4$ ) [15]. This relation ( $k_O > k_S$ ) corresponds to the apparent rate constant ratio found for 4-nitrophenyl benzoate and *S*-phenyl benzothioate toward hydroxide ion ( $k_O/k_S = 18.9$ ) in [7] and in the present work (Table 1). Obviously, the basicity of the leaving group is not the main factor responsible for the substrate reactivity in the transesterification process under study. The above data are quite consistent with the assumption [4] that elimination of leaving group is not the rate-determining stage.

The polarizability of the sulfur atom in phenylsulfanyl group is higher than that of the oxygen atom in 4-nitrophenoxy group. Therefore, dissociation of the C(O)–SAr bond in *S*-phenyl benzothioate (**VI**) should be more facile than dissociation of the C(O)–OAr bond in 4-nitrophenyl benzoate (**III**), and the latter should be less reactive than the former toward 4-chlorophenol. On the other hand, increased difference in the polarizabilities of nucleophile and substrate could lead to reduced efficiency of their mutual interaction [14]. Presumably, this factor is responsible for the observed ratio in the reactivities of *S*-phenyl benzothioate (**VI**) and 4-nitrophenyl benzoate (**III**) toward 4-chlorophenol (**VII**) in DMF in the presence of K<sub>2</sub>CO<sub>3</sub>.

The log( $k/T$ ) and 1/ $T$  values for each aryl benzoate give rise to a linear relation (see figure). These relations were used to calculate (according to the Eyring

**Table 1.** Apparent rate constants for the reactions of 4-nitrophenyl benzoate (**III**) and *S*-phenyl benzothioate (**VI**) with 4-chlorophenol in the presence of K<sub>2</sub>CO<sub>3</sub> (DMF, 1.5–36°C)

Compound no.	$k_{ap} \times 10^2, {}^a \text{ l mol}^{-1} \text{ s}^{-1}$			
	1.5°C	15°C	24°C	36°C
<b>III</b>	2.2±0.2	8.2±0.5	15±2	35±3
<b>VI</b>	0.61±0.04	2.1±0.2	3.9±0.3	7.4±0.2

<sup>a</sup> Average values from the results of at least three parallel runs.

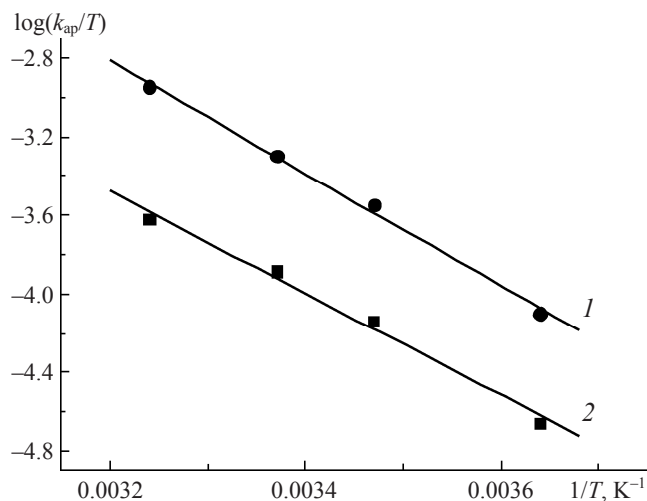
equation [19]) the activation parameters  $\Delta H^\ddagger$ ,  $\Delta S^\ddagger$ , and  $\Delta G^\ddagger$  which reflect variation in the reactivity in energy units (Table 2). Compounds **III** and **VI** fit isoselective relationship with an isoselective temperature  $T_{\text{iso}}$  of 178 K. The latter was determined as the crossing point of the straight lines shown in figure [20]. The temperature range examined in the present work is considerably higher than  $T_{\text{iso}}$ .

The data in Table 2 show that in going from 4-nitrophenyl benzoate (**III**) to *S*-phenyl benzothioate (**VI**) the enthalpy of activation  $\Delta H^\ddagger$  decreases by 5.1 kJ/mol and the entropy of activation  $\Delta S^\ddagger$  decreases by  $29 \text{ J} \times \text{mol}^{-1} \text{ K}^{-1}$ ; simultaneously, the Gibbs energy of activation  $\Delta G^\ddagger$  increases by 3.3 kJ/mol (Table 2). The change of the latter parameter is determined mainly by variation of the enthalpy of activation. The enthalpies, entropies, and Gibbs energies of activation, found in the present work, fall into the ranges typical of transesterification processes (cf. [12]).

It is known that substituent-related change in the entropy depends on the solvation factor [21, 22]. Considering the leaving group as substituent in 4-nitrophenyl benzoate (**III**) and *S*-phenyl benzothioate (**VI**), we presumed that the lower entropy of activation in the reaction with *S*-phenyl benzothioate (**VI**) than in the reaction with 4-nitrophenyl benzoate (**III**) is the result of stronger difference in nonspecific solvation of the initial and transition states in the reaction with **VI**. Decrease in the enthalpy and entropy of activation in going from benzoate **III** to benzothioate **VI** leads to increase in the Gibbs energy of activation and is responsible for the observed reactivity series of aryl benzoates with respect to the leaving group nature.

Table 3 contains the enthalpies, entropies, and Gibbs energies of activation for the reactions of 4-nitrophenyl benzoates with 4-chlorophenol in the presence of potassium carbonate in dimethylformamide. The parameters  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$  change over fairly broad ranges, whereas the range of variation of  $\Delta G^\ddagger$  is typical of reactions of carbonyl compounds with nucleophiles [11, 12]. The enthalpy and entropy of activation are highly sensitive to the substituent in the benzoyl fragment. Increase in the electron-acceptor power of the substituents is accompanied by appreciable reduction of both enthalpy and entropy contributions to the overall energy barrier.

In the transesterification of 4-nitrophenyl benzoates having electron-donating substituents the contribution of the enthalpy component to the energy of activation predominates, so that their reactivity is enthalpy-con-



Plots of  $\log(k_{\text{ap}}/T)$  versus reciprocal temperature ( $1/T$ ) for the reactions of (1) 4-nitrophenyl benzoate (**III**) and (2) *S*-phenyl benzothioate (**VI**) with 4-chlorophenol in the presence of  $\text{K}_2\text{CO}_3$  in DMF: (1)  $\log(k_{\text{ap}}/T) = -2862(1/T) + 6$ ;  $r = 0.998$ ,  $s = 0.4$ ,  $n = 4$ ; (2)  $\log(k_{\text{ap}}/T) = -2596(1/T) + 5$ ;  $r = 0.995$ ,  $s = 0.5$ ,  $n = 4$ .

trolled. In going to 4-nitrophenyl benzoates with electron-withdrawing substituents, the enthalpy contribution appreciably decreases due to increase in the electrophilicity of the carbonyl carbon atom [3, 23–25]. Simultaneously, the entropy of activation decreases as a result of substituent-related change of solvation, and the entropy contribution to the energy barrier increases, which suggests enhanced ordering of the transition state. The observed variation in the ratio of the enthalpy ( $\Delta H^\ddagger$ ) and entropy contributions ( $T\Delta S^\ddagger$ ) to the energy barrier, depending on the substituent nature, is not typical of reactions of carbonyl compounds with nucleophiles (cf. [9, 10]).

Thus the revealed relations in the variation of rate constants ( $k_{\text{O}} > k_{\text{S}}$ ) allowed us to presume that the basicity of the leaving group is not the main factor responsible for the reactivity of aryl benzoates toward 4-chlorophenol in the transesterification process. Analysis of the activation parameters showed that the ratio

**Table 2.** Activation parameters of the reactions of 4-nitrophenyl benzoate (**III**) and *S*-phenyl benzothioate (**VI**) with 4-chlorophenol in the presence of  $\text{K}_2\text{CO}_3$  in DMF

Comp. no.	$\Delta H^\ddagger$ , kJ/mol	$-\Delta S^\ddagger$ , $\text{J mol}^{-1} \text{ K}^{-1}$	$-T\Delta S^\ddagger$ , <sup>a</sup> kJ/mol	$\Delta G^\ddagger$ , <sup>a</sup> kJ/mol
<b>III</b>	$54.8 \pm 2.2$	$76.1 \pm 0.6$	22.6	77.4
<b>VI</b>	$49.7 \pm 3.5$	$105.1 \pm 0.8$	31.0	80.7

<sup>a</sup> At 24°C.

**Table 3.** Activation parameters<sup>a</sup> of the reactions of 4-nitrophenyl benzoates (I–V) with 4-chlorophenol in the presence of K<sub>2</sub>CO<sub>3</sub> in DMF

Compound no.	$\Delta H^\ddagger$ , kJ/mol	$-\Delta S^\ddagger$ , J mol <sup>-1</sup> K <sup>-1</sup>	$-T\Delta S^\ddagger$ , <sup>b</sup> kJ/mol	$\Delta G^\ddagger$ , <sup>b</sup> kJ/mol
I	61.2±2.7	71.4±3.1	21.2	82.4
II	55.6±3.5	80.5±3.2	23.9	79.5
III	54.8±2.2	76.1±0.6	22.6	77.4
IV	25.6±7.5	158.2±30.3	47.0	72.6
V	4.9±0.8	212.9±30.4	63.2	68.1

<sup>a</sup> The activation parameters  $\Delta H^\ddagger$ ,  $\Delta S^\ddagger$ , and  $\Delta G^\ddagger$  were estimated from the corresponding values found for 4-nitrophenyl benzoate (III) and differences  $\Delta\Delta H^\ddagger = \Delta H^\ddagger(\text{R}) - \Delta H^\ddagger(\text{H})$ ,  $\Delta\Delta S^\ddagger = \Delta S^\ddagger(\text{R}) - \Delta S^\ddagger(\text{H})$ , and  $\Delta\Delta G^\ddagger = \Delta G^\ddagger(\text{R}) - \Delta G^\ddagger(\text{H})$  for compounds I, II, IV, and V [4].

<sup>b</sup> At 24°C.

of the enthalpy and entropy contributions to the overall energy barrier changes to the opposite one with variation of the substituent nature.

### EXPERIMENTAL

The reaction mixtures were analyzed by gas–liquid chromatography on an LKhM-72 instrument equipped with a thermal conductivity detector; linear oven temperature programming from 50 to 270°C at a rate of 10 deg/min; SKTFT-803 column, stationary phase 15% of VS-1 on Chromaton W; carrier gas helium, flow rate 60 ml/min. The components were quantitated using internal normalization technique with hexamethylbenzene as reference and were identified by comparison with authentic samples. Commercial dimethylformamide was distilled under reduced pressure first over calcium hydride and then over molecular sieves and was stored over molecular sieves under argon. Commercial potassium carbonate was ground, bolted through a 0.5-mm sieve, calcined in a muffle furnace, and again ground and bolted through a 0.5-mm sieve. Commercial 4-chlorophenol was purified according to standard procedures. Aryl benzoates were synthesized as described in [4, 5]; their physical constants were consistent with published data.

**The stability of compound X under the transesterification conditions** was checked as follows. A flask was purged with argon and charged with 0.40 or 0.47 mmol of potassium carbonate and a solution of 0.14 mmol of compound X and 0.14 mmol of 4-nitrophenol or 0.16 mmol of X and 0.16 mmol of benzenethiol in 2 ml of DMF. The mixture was maintained for 1 h at 36°C, a mixture of 2 ml of chloroform and 2 ml of 10% hydrochloric acid was added to terminate the reaction, and the organic phase was separated, washed with 2 ml of water, dried over CaCl<sub>2</sub>,

and analyzed by GLC. According to the GLC data, the mixture contained compound X (recovery 97%) and 4-nitrophenol (recovery 68%) or compound X (recovery 96%) and benzenethiol (recovery 93%).

**Kinetic study of the reactions of 4-nitrophenyl benzoate (III) and S-phenyl benzothioate (VI) with 4-chlorophenol (VII) in the presence of potassium carbonate in dimethylformamide.** Insofar as potassium carbonate is almost insoluble in DMF [26], the use of the direct kinetic method was complicated due to heterogeneity of the reaction system. The state of nucleophile generated from 4-chlorophenol and potassium carbonate in the two-phase system (K<sub>2</sub>CO<sub>3</sub>–DMF) was studied in [27, 28]. According to the procedure described in [29] we estimated parameters ensuring that the reaction rate depended neither on the K<sub>2</sub>CO<sub>3</sub> surface area accessible to contact with the reactant nor on the rate of transition of nucleophilic complex to solution: K<sub>2</sub>CO<sub>3</sub>–4-chlorophenol ratio ≥1.4:1, K<sub>2</sub>CO<sub>3</sub> grain size ≤ 0.5 mm, speed of stirring ≥750 rpm, and time for generation of nucleophilic complex ≥30 min. These settings were applied while determining the apparent rate constants for the reactions of esters III and VI with 4-chlorophenol in the presence of K<sub>2</sub>CO<sub>3</sub> in dimethylformamide.

A flask was purged with argon and charged with K<sub>2</sub>CO<sub>3</sub> (grain size ≤0.5 mm) and a solution of 4-chlorophenol in 2 ml of DMF was added to attain a K<sub>2</sub>CO<sub>3</sub>–4-chlorophenol ratio of ≥1.4:1. The mixture was stirred using a magnetic stirrer (≥750 rpm) for 30 min at a required temperature. The initial reactant concentrations were (2–6) × 10<sup>-2</sup> M. A solution of the corresponding aryl benzoate in 2 ml of DMF, adjusted to the same temperature, was added, and the mixture was stirred. Samples were withdrawn at definite time intervals and poured into a mixture of chloroform with 10% hydrochloric acid. The organic phase was sepa-

rated, dried, and analyzed by GLC using artificial mixtures for quantitation (internal standard hexamethylbenzene). The rate constants were calculated by the second-order equation:

$$k = \{2.303/[\tau(a - b)]\} \log \{[b(a - x)]/[a(b - x)]\},$$

where  $a$  and  $b$  are the initial reactant concentrations (M),  $x$  is the concentration of the product (M), and  $\tau$  is the reaction time (s).

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