Effect of solvent on the kinetics of arylsulfonylation of *N*-alkylated anilines in a water—propan-2-ol system

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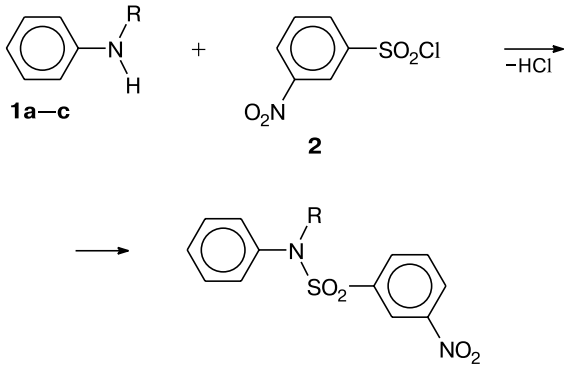
The effect of the composition of a water—propan-2-ol solvent on the kinetics of arylsulfonylation of *N*-ethyl-, *N*-isopropyl-, and *N*-butylanilines with 3-nitrobenzenesulfonyl chloride at 298 K was studied. The reaction rate constant increases monotonically with an increase in the water fraction in the solvent from 5 to 30 wt.%. The apparent activation parameters of the reaction of *N*-butylaniline with 3-nitrobenzenesulfonyl chloride were calculated. No considerable changes in the activation parameters of the reaction were observed on going from pure propan-2-ol to a 10% aqueous solution, which indicates that the mechanism remains unchanged upon solvent change. Propan-2-ol with a water content of 5—30 wt.% can be used in the synthesis of arylsulfonylation products of the amines under study in 98—99% yield.

Key words: arylsulfonylation, *N*-alkylated anilines, kinetics, 3-nitrobenzenesulfonyl chloride, water—propan-2-ol system.

We have previously[1,2] studied the kinetics of arylsulfonylation of *N*-alkylated anilines and *N*-isobutylanilines substituted at the benzene ring with 3-nitrobenzenesulfonyl chloride in several organic solvents at 298 K. It was found that the rate constants of all the reactions under study lie in an interval of $(0.16—29.24) \cdot 10^{-2}$ L mol^{-1} s^{-1}. Therefore, it seems of interest to search for mixed solvents accelerating the reactions of *N*-alkylarylamines with aromatic sulfonyl chlorides. Our previous studies[3] of the similar reaction of aromatic amines with 3- and 4-nitrobenzenesulfonyl chlorides showed that the arylsulfonylation rate constant increases substantially when water-organic solvents (water—propan-2-ol, water—dioxane, water—acetonitrile) are used. Interest in water as a component of solvents is caused by its amphiprotic nature and profitable use in practice of organic synthesis.

In the present work, we studied the kinetics of the reaction of *N*-substituted anilines with 3-nitrobenzenesulfonyl chloride (Scheme 1) and calculated the activation parameters of the reaction and the yields of the target product at different initial concentrations of the reactants and solvent compositions.

Scheme 1



1: R = Et (**a**), Pr^i (**b**), Bu (**c**)

Experimental

The kinetics of the reaction of amines **1a—c** with sulfonyl chloride **2** was studied by conductometry using an E7-14 electric conduction meter equipped with an OK-9023 circular platinum electrode. The initial concentration of alkylarylamine in the working solution was twice as large as the initial concentration of the arylsulfonylating agent, being $1 \cdot 10^{-2}$ mol L^{-1}.

In a water—propan-2-ol solvent, the reaction of amines **1a—c** with sulfonyl chloride **2** is accompanied by the hydrolysis and alcoholysis of the latter (Scheme 2).

It has previously[4] been shown that for aniline acylation with benzenesulfonyl chloride the conversion of the sulfonyl chloride due to solvolysis in methanol does not exceed 2—3%, whereas in other alcohols (ethanol, propanol, *etc.*) alcoholysis occurs more slowly. Therefore, when calculating the arylsulfonylation rate constant, we neglected the alcoholysis of sulfonyl chloride **2**. The rate constant of hydrolysis of sulfonyl chloride **2** (k_h) was

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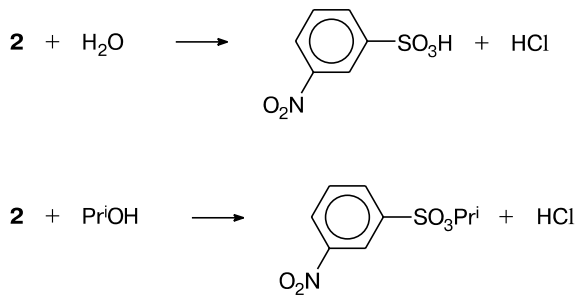
Scheme 2



determined during a special kinetic experiment and then taken into account in the calculation of the reaction rate constant (k_{ac}) (see Scheme 1).

The kinetics of the reaction of amines **1a—c** with sulfonyl chloride **2** is described by a kinetic equation of the second order

$$-dc_{sc}/d\tau = k_{ac}c_{am}c_{sc} + k_h c_{sc}, \quad (1)$$

where c_{am} and c_{sc} are the current concentrations of amine and acid chloride, respectively; τ is time.

The arylsulfonylation rate constant with allowance for hydrolysis of sulfonyl chloride **2** at $c_{am}^0 = 2c_{sc}^0$ was calculated by the equation

$$k_{ac} = \frac{k_h[e^{-k_h\tau}(c_{sc}^0 - x) - c_{sc}^0]}{2c_{sc}^0(c_{sc}^0 - x)(1 - e^{-k_h\tau})}, \quad (2)$$

where $(c_{sc}^0 - x) = c_{sc}^0 \cdot (æ_\infty - æ_\tau)/(æ_\infty - æ_0)$; $æ_0$, $æ_\tau$, and $æ_\infty$ are the conductions of the reaction mixture at the initial moment τ_0, at the time moment τ, and after the end of the reaction, respectively; c_{sc}^0 is the initial concentration of sulfonyl chloride; x is the change in the sulfonyl chloride concentration to the moment τ.

Amines (Aldrich) with the main substance content 98—99% were used without additional purification. Compound **2** (pure grade) was recrystallized from heptane. Propan-2-ol (reagent grade) was distilled on a column under atmospheric pressure. All solutions containing water were prepared using bidistilled water.

The physicochemical constants of the reactants (m.p., b.p.) after purification corresponded to published data.[5]

Results and Discussion

It has previously[2] been shown that *N*-alkylated anilines with an isostructural alkyl substituent are least reactive in arylsulfonylation. For instance, in *N*-isopropylaniline (**1b**) the reaction center is screened by two Me groups, due to which the attack to the nucleophilic center of amine by the arylsulfonylating agent is hindered. We expected an increase in the reactivity of this aliphatic-aromatic amine in arylsulfonylation with a change in the solvent nature; however, for the water-alcoholic solvents under study with the water content 5—50 wt.% hydrolysis occurred much more rapidly than arylsulfonylation and, hence, it was impossible to calculate the reaction rate constants (see Scheme 1). The steric factor exerts, most likely, the decisive effect on the kinetics of arylsulfonylation of *N*-isopropylaniline and, therefore, a substantial increase in k_{ac} cannot be attained even by a change in the solvent nature.

Then we studied the reaction of amines **1a,c** with the *N*-alkyl substituent of normal structure. The k_{ac} and k_h values for the reaction of these amines with sulfonyl chloride **2** in a water—propan-2-ol solvent at different water contents in the mixture are presented in Table 1.

It is seen that k_{ac} increases monotonically with an increase in the water content in the binary solvent, and

Table 1. Rate constants of acylation of amines **1a,c** with sulfonyl chloride **2** (k_{ac}) and hydrolysis of sulfonyl chloride **2** (k_h) in a water—propan-2-ol solvent at different water contents in the mixtures (298 K)

ω_{H_2O} (wt.%)	X_{H_2O}*	$k_{ac} \cdot 10^2$/L mol^{-1} s^{-1}		$k_h \cdot 10^4$ /s^{-1}
		1a	**1c**	
0	0.00	5.00±0.01	3.21±0.02	—
5	0.15	—	5.21±0.04	1.26±0.04
10	0.27	10.60±0.30	7.44±0.09	1.63±0.02
15	0.37	—	9.45±0.04	1.69±0.01
20	0.45	16.00±0.10	11.20±0.08	2.09±0.03
25	0.52	—	13.10±0.25	2.19±0.02
30	0.59	21.50±0.60	15.20±0.25	2.35±0.01

* Mole fraction (here and in Table 2).

Table 2. Results of calculation of the yield of the arylsulfonylation product (α_{ac}) and the content of 3-nitrobenzenesulfonic acid admixture (α_h) in the water—propan-2-ol solvent at different water contents in the mixtures (298 K)

ω_{H_2O} (wt.%)	X_{H_2O}	c_{sc}^0 /mol L^{-1}	α_{ac} (%)		α_h (%)	
			1a	**1c**	**1a + 2**	**1c + 2**
5	0.15	0.005	—	60.64	—	39.36
	0.15	0.1	—	94.66	—	5.34
	0.15	0.5	—	98.57	—	1.43
10	0.27	0.005	69.05	62.45	30.95	37.55
	0.27	0.1	96.25	95.05	3.75	4.95
	0.27	0.5	99.05	98.69	0.95	1.31
15	0.37	0.005	—	66.31	—	33.69
	0.37	0.1	—	95.77	—	4.22
	0.37	0.5	—	98.89	—	1.11
20	0.45	0.005	71.82	65.49	28.18	34.51
	0.45	0.1	96.71	95.63	3.29	4.37
	0.45	0.5	99.16	98.85	0.84	1.15
25	0.52	0.005	—	67.52	—	32.48
	0.52	0.1	—	96.00	—	4.00
	0.52	0.5	—	98.96	—	1.04
30	0.59	0.005	74.67	68.92	25.33	31.08
	0.59	0.1	97.15	96.23	2.85	3.77
	0.59	0.5	99.28	99.02	0.72	0.98

the increase reaches almost 5 times on going from neat propan-2-ol to a 30% aqueous solution (see Table 1).

The apparent activation parameters of the reaction of amine **1c** with sulfonyl chloride **2** in a 10% aqueous propan-2-ol were estimated: E_a = 17.4±3.4 kJ mol^{-1}, $-\Delta S^{\neq}$ = 216.6±11.4 J mol^{-1} K^{-1}. Comparison of the obtained results and data for the series of alkylarylamines in pure propan-2-ol[2] (E_a = 17—30 kJ mol^{-1}, $\Delta S^{\neq}$ = 180—227 J mol^{-1} K^{-1}) suggest that the mechanism of the reaction under study remains unchanged upon this change of the solvent.

The yield of the arylsylfonylation product (α_{ac}) and the content of 3-nitrobenzenesulfonic acid admixture (α_h) in the binary solvents under study were calculated using the kinetic data (see Table 1) by solving the system of differential equations (3) and (4) using the fourth-order Runge—Kutta method.

$$\begin{cases} d\alpha_{ac}/d\tau = 2k_{ac}c_{sc}^{0}(1 - \alpha_{ac} - \alpha_h)^2 & (3) \\ d\alpha_h/d\tau = k_h(1 - \alpha_{ac} - \alpha_h) & (4) \end{cases}$$

The results of calculations of α_{ac} and α_h upon the completion of the reaction of alkylarylamines **1a,c** with sulfonyl chloride **2** are presented in Table 2.

The data in Table 2 show that the water—propan-2-ol solvent with the water content 5—30 wt.% can be used in the synthesis of the arylsulfonylation products of amines **1a,c** in 98—99% yield.

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