HETEROCYCLIC NITRO COMPOUNDS

XIX.* KINETICS OF THE METHYLATION OF 3(5)-NITRO-1,2,4-TRIAZOLES WITH DIMETHYL SULFATE

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UDC 547.792:541.127

The effect of a substituent in the triazole ring and of the composition of the solvent on the reaction rate was established as a result of a study of the kinetics of methylation of sodium salts of 3(5)-nitro-1,2,4-triazoles in water and water–dioxane mixtures. The relationships found are due to the different degree of dissociation of intimate ion pairs of anions of nitrotriazoles with sodium and the specific character of the solvation of the anions by water.

We have previously shown that the methylation of 3(5)-nitro-1,2,4-triazoles with dimethyl sulfate proceeds extremely selectively to give exclusively 1-methyl-3-nitro derivatives [2]. In the present research we undertook a study of the kinetics of this reaction in water (buffer solutions, pH 9.22) and water–dioxane mixtures.

We selected 3-nitro-1,2,4-triazole (I), 3-nitro-5-methyl-1,2,4-triazole (II), 3-nitro-5-carbomethoxy-1,2,4-triazole (III), and 3,5-dinitro-1,2,4-triazole (IV) as the objects of this investigation. The nitrotriazoles were introduced into the reaction in the form of their sodium salts. The course of the reaction was monitored by spectrophotometry from the consumption of the anions of the nitrotriazoles.

The kinetic investigation was complicated by the simultaneous hydrolysis of dimethyl sulfate, which, on the one hand, led to a decrease in its effective concentration, and, on the other, to a decrease in the pH of the medium, even in the case of buffer solutions. The methylation rate constants were therefore calculated for the initial sections of the kinetic curves until the change in the pH of the medium was small and did not influence the decrease in the concentration of the anions of the nitrotriazoles. In the determination of the reaction order in each of the components we used the method of initial rates [3], determining them by numerical differentiation by means of five-point formulas [4, 5]. The experiments for the determination of the reaction order showed that the concentration order in each of the components is unity, i.e., the overall reaction order is two.

The methylation rate constants were calculated by the method in [6] for parallel reactions with the aid of data [7] on the hydrolysis of dimethyl sulfate. We modified the formula [6] for the calculation of the constants:

$$k_e = \frac{k_h \ln \frac{[NT]_0}{[NT]} e^{k_h \tau}}{n[NT]_0 (e^{k_h \tau} - 1)},$$

where k_e is the experimental methylation rate constant, k_h is the rate constant for the hydrolysis of dimethyl sulfate, $[NT]_0$ is the initial nitrotriazole concentration, $[NT]$ is the instantaneous nitrotriazole concentration, τ is the time, and n is the ratio of the initial dimethyl sulfate and nitrotriazole concentrations.

The kinetic data are presented in Tables 1 and 2.

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* See [1] for communication XVIII.

Lensovet Leningrad Technologic Institute. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1564-1568, November, 1974. Original article submitted October 25, 1973.

TABLE 1. Kinetics of the Methylation of Nitrotriazoles with Dimethyl Sulfate in 90% (by volume) Dioxane–10% Water

Compound	T, K	$k_e \cdot 10^3$, liters/mole · sec	E_A, kcal/mole	lg A	$\Delta H^{\neq}_{25}$, kcal/mole	$\Delta S^{\neq}_{25}$, eu
I	298	0,376	21,8	12,4	21,2	−3,5
	308	1,23				
	318	3,74				
	328	10,6				
II	298	0,185	21,1	11,7	20,5	−7,1
	308	0,585				
	318	1,72				
	328	4,73				
III	298	9,64	16,7	10,2	16,1	−13,9
	308	24,0				
	318	56,3				
	328	125				
IV	298	580	16,2	11,6	15,6	−7,6
	308	1400				
	318	3210				
	328	6970				

TABLE 2. Kinetics of the Methylation of Nitrotriazoles with Dimethyl Sulfate in Water (buffer solution, pH 9.22)

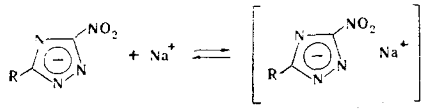
Compound	T, K	$k_e \cdot 10^2$, liters/mole · sec	E_A, kcal/mole	lg A	$\Delta H^{\neq}_{25}$, kcal/mole	$\Delta S^{\neq}_{25}$, eu
I	298	1,66	20,3	13,0	19,7	−0,9
	308	5,02				
	318	14,2				
	328	37,5				
II	298	1,82	19,8	12,7	19,2	−2,4
	308	5,36				
	318	14,7				
	328	38,1				
IV	298	0,389	21,0	12,9	20,5	−1,3
	308	1,23				
	318	3,58				
	328	9,83				

Upon examination of the experimental data, one's attention is first of all drawn to the unusual order of the reactivity of the nitrotriazole when the methylation is carried out in 90% dioxane. Judging from the acidities of nitrotriazoles [8], one should have expected decreases in the methylation rate in the order II > I > III > IV. In fact, the reverse dependence is observed (Table 1). As the percentage of water in the system increases, the rate constants level off (Table 3), and this is followed by reveral of the order of reactivities: in water II > I > IV. In this case, however, the difference in the methylation rate constants of II and IV is small (a factor of about four), although the acidity of dinitrotriazole IV is higher by seven orders of magnitude than the acidity of II [8].

A linear relationship is observed between the logarithm of the methylation rate constants and the pK_A values of the nitrotriazoles (Fig. 1), and the slopes in dioxane and water have opposite signs.

Thus the order of nucleophilic reactivities of the nitrotriazoles depends to the greatest degree on the character of the solvent and the state of the reacting particles in solutions.

It is known that oppositely charged ions associate into intimate ion pairs or even covalent compounds in solvents with low dielectric permeabilities that solvate anions weakly (dioxane, ε 2.3) [9, 11]. In this connection, it might be assumed that in dioxane–water systems with a low water content the anions of nitrotriazoles are associated to a considerable degree in intimate ion pairs with a sodium ion



(1)

The reaction rate (V) in such cases is expressed [10] as

TABLE 3. Relationship between the Methylation Rate Constants of Nitrotriazoles and the Composition of the Water–Dioxane Mixture (at 25°C)

Water content, vol. % / Compound	$k_e \cdot 10^3$, liters/mole · sec					
	10	30	45	60	80	100
I	0,376	0,695	2,78	6,52	12,5	16,6
II	0,185	0,316	1,26	5,16	11,8	18,2
IV	580	424	210	73,5	17,3	3,89

$$V = k_i c_i \alpha + k_{ip} c_{ip} (1-\alpha),$$

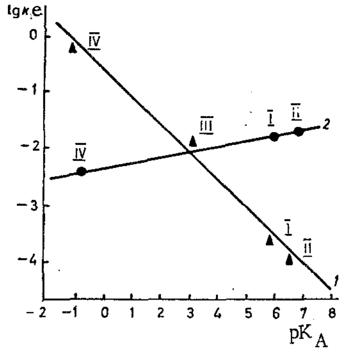


Fig. 1. Dependence of log k_e on the pK_A values of nitrotriazoles I-IV (at 25°C): 1) in 90% dioxane; 2) in water.

where k_i and k_{ip} are the rate constants with the ion and the ion pair, respectively, c_i and c_{ip} are the concentrations of the ions and ion pairs, and α is the degree of dissociation.

As a rule, $k_i \gg k_{ip}$ in reactions involving the participation of ions [11]. On the basis of this, the order of reactivities of nitrotriazoles in dioxane containing a low percentage of water is determined primarily by the concentration of the free anions of the nitrotriazoles, i.e., by the position of equilibrium (1), which is shifted to the left as the basicity of the anion decreases. The correlation between log k_e and pK_A (Fig. 1, line 1) in this case reflects the relationship between the ionization constants of the nitrotriazoles and the dissociation constants of the ion pairs in equilibrium (1). Thus the experimental methylation rate constant in systems containing a small amount of water is a complex value that includes the constant of equilibrium (1). An additional factor that may lead to an increase in the reaction rate in dioxane is bonding of the water molecules by dioxane, which hinders solvation of the anion by water [12]. Equilibrium (1) is shifted to favor dissociation as the percentage of water in the system and the dielectric permeability increase; this should increase the reaction rate [11]. At the same time, another factor – specific solvation of the anions of the nitrotriazoles by water – begins to come into play, and the degree of their solvation depends on the size of the anion and the magnitude of delocalization of the negative charge. Solvation, by hindering the approach of the attacking reagent, naturally reduces the reaction rate. These factors have different effects on the reactivities of mononitro-(I, II) and dinitrotriazoles (IV). The increase in the methylation rate on passing from dioxane to water for I and II is associated with a shift to the left of equilibrium (1) and an increase in the concentration of the free anions I and II, although their solvation also increases in this case. The sodium salt of IV is apparently already sufficiently dissociated in solutions with low water content; the decrease in the methylation rate of IV as the water content increases is therefore induced primarily by the increase in the specific solvation of the anion of IV.

However, it should be noted that, despite the decrease in the methylation rate of IV in water, it remains anomalously high as compared with the rate that might have been expected from the acid–base properties of IV. In our opinion, this is explained by the fact that, as a consequence of greater delocalization of the negative charge in the anion of IV than in the anions of I and II, the latter are solvated to a greater degree than IV. The lesser specific solvation of the anion of IV also leads to an unusually high methylation rate in water, although, in conformity with the effect of the substituents, it nevertheless remains lower than for the anions of I and II. A similar phenomenon also occurs in a number of polynitroalkanes, for which anomalously high reactivity of the anion of trinitromethane as compared with the anions of gem-dinitro compounds is noted; this anomalously high reactivity is due to its low capacity for solvation by water [13].

The assumptions expressed above are confirmed by an examination of the activation parameters of the reaction (Tables 1 and 2). The activation entropies for methylation are larger in water than in dioxanes for all of the compounds; this is probably associated with disruption of the orderliness during destruction of the hydrate shell on passing to less polar final products.

EXPERIMENTAL

Starting I-IV were synthesized by the method in [2, 14] and were additionally purified by three recrystallizations from alcohol. The dimethyl sulfate was freshly vacuum distilled prior to use. Doubledistilled water and column-rectified dioxane were used for the preparation of the solutions. Analytically pure grade sodium hydroxide and boric acid were used.

Compounds I-III were converted to their salts by the addition of an equivalent amount of sodium hydroxide to solutions of them; dioxane containing 10% (by volume) of water was used.

The change in the concentration of the anions of the nitrotriazoles was followed from the decrease in the optical density at 280-320 nm with an SF-4A spectrophotometer.

At I-IV working concentrations of $0.5\text{-}1 \cdot 10^{-4}$ M the reaction mixture was studied in the thermostatted cuvettes of the spectrophotometer. When reactions were carried out with I-IV concentrations above $1 \cdot 10^{-4}$ M, the reaction solutions were studied in vessels in an ultrathermostat, from which samples were selected and diluted to the concentrations necessary for the spectrophotometric measurements.

The error in the measurements, determined by the methods of mathematical statistics, was 5%.

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