HETEROCYCLIC NITRO COMPOUNDS

XIV.* KINETICS OF THE NUCLEOPHILIC SUBSTITUTION OF A NITRO GROUP BY A HYDROXYL GROUP IN 3(5)-NITRO-1,2,4-TRIAZOLES

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The kinetics of the substitution of a nitro group by a hydroxyl group in 1-methyl-3-nitro-, 1-methyl-5-nitro-, and 3-nitro-4-methyl-1,2,4-triazoles as well as in a series of 1-methyl-3-R-5-nitro-1,2,4-triazoles were studied. The activation parameters of the reaction were determined. There is a linear correlation dependence between log k and the σ_m substituent constants in the investigated series.

High selectivity of the substitution of a nitro group in the 5 position of the triazole ring was observed in an investigation of the reaction of 3(5)-nitro-1,2,4-triazoles with nucleophilic reagents [2,3]. For a quantitative evaluation of this phenomenon, we undertook a study of the kinetics of the reaction of 3(5)-nitro derivatives of 1,2,4-triazole with the hydroxide ion with the idea of following the effect of substituents and the position of the nitro group in the ring on the reaction rate.

As objects for the investigation, we selected 1-methyl-3-nitro-1,2,4-triazole (I), 1-methyl-5-nitro-1,2,4-triazole (II), 3-nitro-4-methyl-1,2,4-triazole (III), and a series of 1-methyl-3-R-5-nitro-1,2,4-triazoles, where R = NO_2 (IV), CH_3 (V), C_6H_5 (VI), Cl (VII), COO^- (VIII), and $COOCH_3$ (IX). The kinetic trend of the reaction was monitored by measuring the nitrite ion concentration by a photocolorimetric method [4]. Depending on the rate of the reaction, the experiments were carried out either in borate buffer solutions with pH 9-11 (for IV, VII, and IX) or in 0.1-1.5 M solutions of sodium hydroxide at substrate concentrations of 10^{-3} to 10^{-4} M, which ensured that the reaction was pseudo-first-order.

First-order reaction with respect to nitrotriazole was proved by construction of the semilogarithmic anamorphosis of the dependence of the substrate concentration on the time. First-order reaction with respect to the nucleophile was established on the basis of measurements of the rate at various hydroxide ion concentrations (Table 1). Thus the reaction rate can be expressed by the formula

$$v = k_2[\mathrm{HetNO_2}][\mathrm{OH^-}]$$

The rate constants of the reaction of nitrotriazoles with hydroxide ion at various temperatures and activation parameters are presented in Table 2.

In the case of 1-methyl-3-methoxycarbonyl-5-nitro-1,2,4-triazole (IX), it was found that hydrolysis of the ester group to form acid VIII occurred simultaneously with cleavage of the nitro group when the kinetic experiments were carried out in borate buffer (pH 10.16). Under these conditions, the replacement of the nitro group in acid VIII proceeds at a negligibly low rate as compared with IX, and the rate constant for substitution of the nitro group in IX was therefore calculated from the initial section of the kinetic curves via the method used for parallel pseudo-first-order reactions.

In examining the results presented in Table 2, one should note the strong effect of the position of the nitro group in the triazole ring on the rate of substitution. The rate of replacement of the nitro group in the

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*See [1] for communication XIII.

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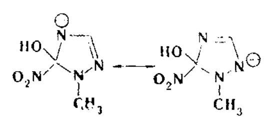
TABLE 1. Effect of the Hydroxide Ion Concentration on the Rate Constant of the First-Order Reaction of IV with Hydroxide Ion in Buffer Solutions at 25.1°C

$[HetNO_2]\cdot 10^4$, M	$[OH^-]\cdot 10^5$, M	$k_1\cdot 10^4$, sec^{-1}	$k_2=k_1/[OH^-]$, liter/mole · sec
5,087	1,492	4,48	30,0
6,049	2,798	8,32	29,8
3,099	5,185	15,5	29,9

TABLE 2. Rate Constants and Activation Parameters of the Reaction of 3(5)-Nitro-1,2,4-triazoles with Hydroxide Ion

Comp.	t, °C	k_2, liter/mole · sec	ΔH_{25}, kcal/mole	ΔS_{25} eu	lg k_{25}
I	62,4 70,2 80,0	$7{,}65\cdot 10^{-6}$ $1{,}51\cdot 10^{-5}$ $4{,}47\cdot 10^{-5}$	24,6	−9,0	−7,242
II	10,1 20,0 30,3 40,1	$8{,}45\cdot 10^{-4}$ $2{,}30\cdot 10^{-3}$ $7{,}17\cdot 10^{-3}$ $1{,}82\cdot 10^{-2}$	17,5	−10,7	−2,390
III	9,6 20,0 29,9 40,4	$7{,}37\cdot 10^{-5}$ $2{,}34\cdot 10^{-4}$ $6{,}78\cdot 10^{-4}$ $1{,}90\cdot 10^{-3}$	18,0	−13,6	−3,396
IV	10,0 17,4 25,0 34,7 42,0	8,78 17,2 30,1 57,1 123	13,5	−6,5	1,484
V	9,8 24,8 39,7	$7{,}38\cdot 10^{-4}$ $3{,}61\cdot 10^{-3}$ $1{,}49\cdot 10^{-2}$	17,1	−12,3	−2,436
VI	9,4 23,0 36,9	$2{,}34\cdot 10^{-3}$ $9{,}19\cdot 10^{-3}$ $3{,}22\cdot 10^{-2}$	16,0	−13,8	−1,962
VII	9,8 19,9 32,9 40,0	0,122 0,314 0,865 1,68	14,5	−11,5	−0,224
VIII	10,0 24,6 39,5	$9{,}52\cdot 10^{-4}$ $4{,}94\cdot 10^{-3}$ $1{,}08\cdot 10^{-2}$	13,9	−23,2	−2,464
IX	24,9	0,20	—	—	−0,700

5 position at 25° is greater by a factor of 71,000 than in the 3 position (I and II), and this difference is due almost completely to the difference in the activation energies. In the light of these results, the high selectivity of the reactions of nucleophilic reagents with methyldinitrotriazole IV, which leads to the formation of 5-substituted nitro compounds [2,3], becomes understandable. This same circumstance makes it possible to disregard the rate of substitution of a nitro group in the 3 position of IV and to calculate the rate constant for replacement of the nitro group in the 5 position by the usual method.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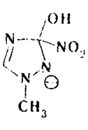
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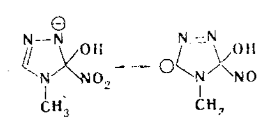
IIIA

Such a large difference in the reactivity can apparently be explained by the different degree of stability of the intermediate activated complexes (A), which are formed in the first step of the substitution reaction. It is easy to demonstrate that the possibility of delocalization of the charge of the attacking reagent is greater in 1-methyl-5-nitro-1,2,4-triazole (II), since hetero atoms $N_{(2)}$ and $N_{(4)}$ participate in delocalization in the intermediate complex (IIA) with the nucleophile. Only heteroatom $N_{(2)}$ (IA) participates in charge delocalization in 1-methyl-3-nitro-1,2,4-triazole (I). In 4-methyl-3-nitro-1,2,4-triazole (III), the delocalization of the negative charge in the intermediate complex can be realized with participation of the nitrogen heteroatom and $C_{(5)}$ (IIIA). Since the electronegativity of nitrogen is greater than that of carbon, the contribution of the structure with a negative charge on carbon during stabilization of the intermediate complex is lower than the contribution of the structure with a charge on nitrogen. This may explain the increase in the rate of the reaction of III as compared with I and the decrease as compared with II.

Barlin [5] previously arrived at this conclusion on examining the reactivity of 1-methyl-5-bromo- and 4-methyl-5-bromo-1,2,4-triazoles, 1- and 2-methyl-5-bromotetraazoles, and 1-methyl-2-bromo-5-nitro- and 1-methyl-5-bromo-4-nitroimidazoles [5]. The data that we obtained for the relative reactivities in different positions of the ring are in agreement with the previously published results of quantum-chemical calculation, which predict the greatest nucleophilic reactivity in the 5 position of the triazole ring [6,7].

As expected, an increase in the electronegativity of the substituent in the 3 position leads to an increase in the reaction rate (II and IV-IX). The change in the rate is due chiefly to differences in the activation enthalpies, since the activation entropies are close in the series under consideration. In the case of R = COO^- (VIII), the substrate is a negatively charged ion, and its reaction with the hydroxide ion, because of electrostatic repulsion, is associated with more significant steric requirements for the transition state, which is indicated by the more negative activation entropy.

The logarithms of the rate constants for the examined series (II and IV-IX) correlate satisfactorily with the σ_m substituent constants:

$$\lg k_{25}=5.05\ \sigma_m-2.17\ (r=0.996,\ s=0.14).$$

The correlations with the σ_p constants are less satisfactory.

The good correlation of the rate constants with the σ_m substituent constants means that the inductive and resonance effects of the substituents in the 3 position are transmitted to the reaction center in the 5 position, analogous to the effect of substituents in the meta position of the benzene ring.

EXPERIMENTAL

The nitro derivatives of 1,2,4-triazole (I-V and VII-IX) used in this study were synthesized by the methods described in [8-10] and were additionally crystallized.

1-Methyl-3-phenyl-5-nitro-1,2,4-triazole (VI). A solution of 7 g (0.04 mole) of 1-methyl-3-phenyl-5-amino-1,2,4-triazole [11] in 225 ml of 6% sulfuric acid, heated to 50-55°, was added slowly to a cooled (0°) solution of 65 g (0.094 mole) of sodium nitrite in 150 ml of water. The mixture was heated at 60-65° for 30 min, and the precipitate was removed by filtration, washed with hot water, and dried to give 7 g (85%) of a product with mp 160° (twice from carbon tetrachloride). Found: C 52.4; H 3.6; N 27.4%; M 197. $C_9H_8N_4O_2$. Calculated: C 52.9; H 3.9; N 27.4%; M 204.

Sulfanilic Acid. Chemically pure sulfanilic acid was recrystallized twice from distilled water with activated charcoal and dried at 120° to constant weight.

R Salt (Disodium 2-Naphthol-3,6-disulfonate). This compound was obtained and purified by the method in [12].

All of the reagents and solvents used in this study were checked for the absence of nitrite ion.

Method Used to Determine the Nitrite Ion. A 100-ml volumetric flask was charged with 3 ml of 0.036 M sulfanilic acid solution in 2.5 N hydrochloric acid and 20-25 ml of distilled water. The test solution containing the nitrite ion was introduced into the flask with a calibrated pipette, 23-25 ml of borate buffer with pH 12.65 was introduced after 7-8 min, and 5 ml of 0.02 M solution of the R salt was added immediately. After 10-15 min, 10 ml of 0.7 N sodium hydroxide was introduced into the flask, the solution was diluted to the mark with water after 10 min, and the mixture was thermostatted at 21° and subjected to colorimetry with an FÉK-M photocolorimeter using a green-light filter (absorption maximum 530 nm) and cuvettes with a solution working-layer thickness of 50 mm.

The resulting colored solutions were stable and did not change their optical densities for 24 h. The amount of nitrite ion was determined from a calibration graph. This method made it possible to determine nitrite ion concentrations from $1\cdot10^{-6}$ to $5\cdot10^{-5}$ M with an error of ±2%.

Method Used to Carry Out the Kinetic Experiments. The kinetic experiments were carried out in a thermostatted glass apparatus equipped with a stirrer with a glycerol seal, a thermometer, and a tube for introducing the reagent. A definite volume (200-250 ml) of the solution of the base was poured into the apparatus, the mixture was thermostatted and stirred, and a thermostatted solution of the nitro compound was introduced with a calibrated pipette. There was no heat effect during mixing of the reagents. At definite time intervals, samples of the reaction mass were removed and analyzed for nitrite ion content.

In the case of nitro compounds with solubilities too low for the preparation of a working solution (VI, for example), the reverse order of mixing of the reagents was used: a solution of alkali was added to a dilute solution of the nitro compound.

The yield of nitrite ion for an "infinitely" long time or artificial acceleration of the reaction on heating was 100 ± 2%. The error in the determination of the pseudo-first-order rate constant (k_1), with a confidence probability $\alpha = 0.95$, was ±2.6%. The error in the second-order rate constant ($k_2 = k_1/[OH^-]$), with allowance for the error in determining $[OH^-]$ in buffer solutions, was ±6% but appreciably lower in reactions in alkali solutions, the concentration of which was determined by titration.

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