TETRAZOLES. 31.* KINETICS OF THE REACTION OF NITRILES WITH ALKYLAMMONIUM AZIDES. FORMATION OF 5-SUBSTITUTED TETRAZOLES

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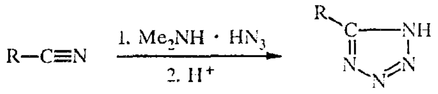
5-Substituted tetrazoles are formed by the reaction of nitriles with mono-, di-, and trialkylammonium azides in aprotic dipolar solvents and alcohols. Tetraalkylammonium azides do not react with nitriles. The formation of 5-substituted tetrazoles occurs by a 1,3-dipolar cycloaddition mechanism. Electron-accepting substituents increase the reactivity of nitriles significantly while the structure of the alkylammonium azide and the solvent polarity have no significant effect on the reaction rate.

Continuing our investigations on the mechanism of formation of 5-substituted tetrazoles, we have studied the kinetics of the reaction of nitriles of various structure with alkylammonium azides in aprotic dipolar solvents and in alcohols. It was established previously that 5-phenyl-tetrazole is formed in 71-77% yield by the reaction of benzonitrile with methyl-, dimethyl-, or trimethylammonium azide in DMF at 100°C [2]. The rate of this reaction does not depend significantly on the structure of the alkyl-ammonium azide. The rate constants ($\times 10^4$) for the reaction of benzonitrile with the indicated alkylammonium azides in DMF at 100°C were 1.0, 3.4, and 2.0 liter mole^{-1} sec^{-1} respectively. Benzonitrile does not react under these conditions with the quaternary ammonium salts tetramethyl- and tetrabutylammonium azides.

The reaction of dimethylammonium azide with the nitriles (Ia-g) in DMF also leads to the formation of 5-substituted tetrazoles in 80-90% yield.



I a-g II a-g

I, II a R = $(CH_3)_2N(CH_2)_2$; b R = $C_6H_5CH_2$; c R = $CH_3CO_2CH_2$; d R = C_6H_5; e R = $CH_3O_2CCH_2$; f R = $CNCH_2$; g R = $C_6H_5OCH_2$

The kinetics of this reaction were studied at 80-120°C. The second order rate constants are given in Table 1.

Analysis of the kinetic data (Table 1) by the method of Exner [3] and the existence of a correlation between the logarithm of the rate constant and the Taft induction constants [4] for the substituents (Table 2) indicate that the conversion into 5-substituted tetrazoles of all the nitriles studied occurs by the same mechanism.

It was suggested previously [5] that an imino azide is formed in the first stage of the reaction of nitriles with salts of hydrazoic acid as a result of attack by the azide ion at the carbon atom of the nitrile group. This is followed by cyclization to the tetrazole. According to an alternative proposal in [2] this reaction proceeds by a 1,3-dipolar cycloaddition mechanism. The following data support such a mechanism of forming 5-substituted tetrazoles. Dimethylammonium azide is practically unionized according to electrochemical measurements at concentrations of $\sim 6 \times 10^{-1}$ M [2]. It follows from this that the complex $(CH_3)_2NH\text{-}HN_3$ (III) is involved in the reaction of nitriles with dimethylammonium azide. Comparison of the geometry and

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[*] For Communication 30 see [1].

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TABLE 1. Rate Constants for the Reaction of Nitriles (Ia-f) with Dimethylammonium Azide in DMF

Compound	$k \times 10^4$ liter $mole^{-1}$ sec^{-1}				
	80°C	90°C	100°C	110°C	120°C
I a	0,03	0,05	0,08	0,11	0,20
I b	0,26	0,52	1,19	1,38	2,28
I c	0,65	1,65	3,66	6,98	12,31
I d	0,78	1,61	3,44	7,88	16,40
I e	7,83	25,25	36,65	49,65	67,39
I f	300	700	1600	3300	4500

TABLE 2. Parameters of the Taft Equation $\log k = \rho\sigma^* + \log k_0$ for the Reaction of Nitriles (Ia-f) with Dimethylammonium Azide in DMF

Tempara-ture, °C	ρ	$-\lg k_0$	r	s
80	3,35 ± 0,34	5,99 ± 0,28	0,96	0,34
90	3,37 ± 0,34	5,69 ± 0,25	0,96	0,28
100	3,41 ± 0,33	5,43 ± 0,26	0,96	0,29
110	3,60 ± 0,28	5,34 ± 0,21	0,97	0,20

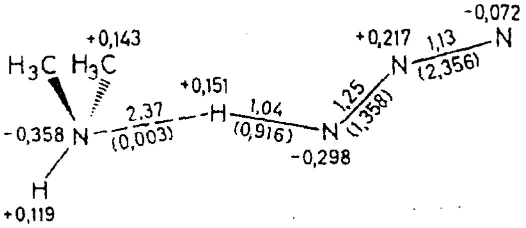

Fig. 1. Charges on atoms and bond lengths (Å) (bond indexes according to Weyberg) in the complex of dimethylamine with hydrazoic acid calculated by MNDO/M.

electronic structure of the azide fragment of complex (III), of hydrazoic acid, and of organic azides shows the similarity of this fragment in the structures indicated (Fig. 1) [6]. At the same time it is well known that hydrazoic acid and organic azides are typical 1,3-dipoles in 1,3-dipolar cycloaddition reactions [7]. Consequently there is a basis for considering that dimethylammonium azide may act as a 1,3-dipole when reacting with nitriles. The results obtained in the present work confirm this hypothesis. The constant ρ in the Taft equation has a high absolute value for the reaction of nitriles (Ia-f) with dimethylammonium azide (Table 2), which is characteristic of processes occurring by a 1,3-dipolar cycloaddition mechanism such as the formation of 1,5-disubstituted tetrazoles from nitriles and organic azides [8]. Activation parameters for the reaction of nitriles with dimethylammonium azide are also characteristic for the transition state of a 1,3-dipolar cycloaddition. Thus $\Delta H^{\#} = 56$ kJ $mole^{-1}$, $\Delta S^{\#} = 200$ J $mole^{-1}$ K^{-1}. These values are in good agreement with data predicted from nonempirical quantum chemical calculations [9].

The polarity of the solvent has practically no effect on the rate of the reaction of phenoxyacetonitrile (Ig) with dimethylammonium azide (Table 3). This is in good agreement with known data on the effect of the solvent nature on the rate of reactions occurring by a 1,3-dipolar cycloaddition mechanism [10]. Finally it is noted that tetraalkylammonim azides do not react with nitriles since under the experimental conditions they form an azide ion which is not a 1,3-dipole.

The agreement of the data shown suggests that the formation of 5-substituted tetrazoles from nitriles and alkylammonium azides can occur by a 1,3-dipolar cycloaddition mechanism. However, it is impossible to exclude completely the possibility of forming 5-substituted tetrazoles by a two-stage mechanism. Evidently such a mechanism exists for substrates in which the nitrile group is directly bound to a strongly electron-accepting substituent such as trifluoroacetonitrile [11] and oxalic acid nitrile [12].

TABLE 3. Rate Constants for the Reaction of Phenoxyacetonitrile (Ig) with Dimethylammonium Azide in Various Solvents, 70°C

Solvent	$k \cdot 10^4$, liter·mol^{-1}·s^{-1}	Solvent	$k \cdot 10^4$, liter·mol^{-1}·s^{-1}
Dimethylformamide	11,40	Propanol	18,40
Acetonitrile	11,90	Propan-2-ol	10,30
Sulfolan	11,27	t-butanol	11,40
Methyl ethyl ketone	7,31		

EXPERIMENTAL

The concentration of nitriles in the kinetic measurements were checked by GLC on a TSvet 100 chromatograph. The detector was a catherometer and the carrier gas was helium. The temperature of the detector and evaporator was 200-250°C, carrier gas supply 50 ml min^{-1}. The stationary phase was Chemasorb AW-HMDS coated with 15% PFMS when determining the running concentrations of nitriles (Ia-e) and Chromaton N-AW, DMCS coated with 5% XE-60 for nitriles (If, g).

Kinetic Measurements. The kinetics of the reaction of nitriles with alkylammonium azides were studied in a thermostatted reactor (±0.1°C) fitted with an efficient reflux condenser and magnetic stirrer. The total concentration of reactants in solution was ~1.2 M. Test samples of the reaction solution were withdrawn with a micropipette at definite time intervals and placed in special test tubes from which a portion was taken with a Hamilton microsyringe and injected into the evaporator of the chromatograph. The concentration of nitrile was calculated from the area of the chromatographic peak by the absolute calibration method of [13]. Rate constants were calculated from the equation for a second order reaction under conditions of equal initial reactant concentration. The mean rate constant was taken from 3-4 measurements. The error of determining the rate constant was ±10 rel.%.

The nitriles (Ia-g) had characteristics after purification corresponding to literature data [14]. Solvents were purified as described in [10]. Data of elemental analysis for C, H, and N of the alkylammonium azides and tetrazoles corresponded to calculated values.

Dimethylammonium Azide. Dimethylamine hydrochloride (41.0 g: 0.5 mole) and sodium azide (32.5 g: 0.5 mole) were stirred in DMF (100 ml) for 4 h at 70°C. The suspension was cooled to 25°C and the sodium chloride filtered off. The filtrate was placed in a flask made of heat-stable glass and cooled in liquid nitrogen. The precipitated solid was filtered off, washed on the filter with dry hexane, and dried over anhydrous magnesium sulfate. Dimethylammonium azide (18 g: 41%) was obtained after crystallization from propan-2-ol. The remaining alkylammonium aizdes were obtained by a similar procedure.

5-(2-Dimethylaminoethyl)tetrazole. β-Dimethylamino-propionitrile (9.8 g: 0.10 mole) and dimethylammonium azide (11.3 g: 0.13 mole) were stirred in DMF (25 ml) for 8 h at 110°C. The solution was cooled to 25°C and kept at this temperature for 6 h, the precipitated solid was filtered off, washed on the filter with methylene chloride, and dried in an air stream. Yield was 11.2 g (80%), mp 200°C (water–ethanol, 1:1).

5-Phenyltetrazole. Benzonitrile (10.3 g: 0.1 mole) and dimethylammonium azide (8.8 g: 0.1 mole) were stirred in DMF (50 ml) for 7 h at 110°C. The solution was cooled to 15°C, water (100 ml) poured in, and 15% hydrochloric acid was added dropwise with stirring to pH 2-3. The precipitated solid was filtered off, washed on the filter with cold water (2 × 30 ml), and dried in an air stream. Yield was 12.0 g (82%), mp 214°C (water–ethanol, 1:2). The remaining 5-substituted tetrazoles were obtained analogously. All the compounds had characteristics corresponding to the literature data in [15-18].

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