CHEMISTRY OF ETHYLENEIMINE

XII.* TRANSFORMATIONS OF 1-CHLORO-1-CYANO-2-(2,2-DIMETHYLHYDRAZINO)ETHANE IN THE PRESENCE OF SODIUM HYDRIDE

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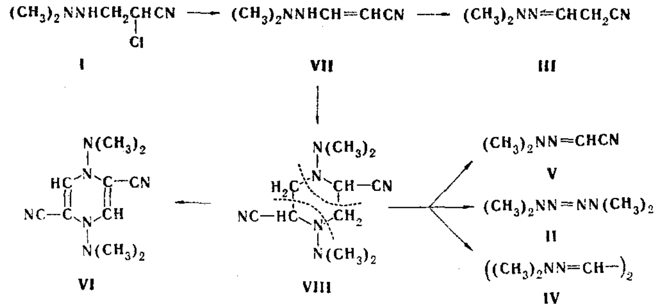
Tetramethyltetrazene, cyanoacetaldehyde N,N-dimethylhydrazone, glyoxal N,N-bis(dimethylhydrazone), glyoxylic acid nitrile N,N-dimethylhydrazone, and 1,4-dimethylamino-2,5-dicyanodihydropyrazine are formed by reaction of 1-chloro-1-cyano-2-(2,2-dimethylhydrazino)ethane with sodium hydride.

It is known [2] that cyclization of α-haloalkylamines with alkaline agents gives aziridines. We have previously [3] obtained 1-chloro-1-cyano-2-(2,2-dimethylhydrazino)ethane (I), which is a member of the α-haloalkylhydrazine class.

In the present research we studied the reaction of hydrazine I with sodium hydride in tetrahydrofuran (THF). The reaction mixture was heated at 70°C for 4 h, and the products were isolated by preparative gas–liquid chromatography (GLC). The formation of aziridine systems is not observed in this case. Tetramethyltetrazene (II), cyanoacetaldehyde N,N-dimethylhydrazone (III), glyoxal N,N-bis(dimethylhydrazone) (IV), and glyoxylic acid nitrile N,N-dimethylhydrazone (V) were obtained as the chief products of the reaction of hydrazine I with sodium hydride.



In addition, we also detected small amounts of 1,4-bis(dimethylamino)-2,5-dicyano-1,4-dihydropyrazine (VI) during separation of the reaction mixture with a column filled with silica gel. A comparison of the physicochemical constants and IR and PMR spectra of the compounds obtained as a result of the reaction and prepared by alternative synthesis confirms the structures of the indicated compounds.

It might be assumed that the reaction intermediate is enehydrazine VII, which is isomerized to hydrazone III or dimerizes to give 1,4-dimethyl-2,5-dicyanopiperazine (VIII). We were unable to isolate

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piperazine VIII from the reaction mixture, possibly because of the peculiar retrograde decomposition of VIII to give hydrazone V and oxidation to pyrazine VI. (A similar transformation of the products of reduction of dihydropyrazines was previously reported in [4].) The mechanism of this reaction requires thorough study, inasmuch as the formation of hydrazone III can also be explained by disintegration of piperazine VIII at the 3 and 5 bonds. The presence in the reaction mixture of tetrazene II and hydrazone IV, which may be formed by reaction of the products of the retrograde decomposition of VIII, constitutes evidence for more profound transformations of the intermediates.

EXPERIMENTAL

The IR spectra of liquid films and suspensions of the compounds in mineral oil or hexachlorobutadiene were obtained with a UR-20 spectrometer. The PMR spectra of carbon tetrachloride solutions of the compounds were recorded with a Perkin–Elmer R-12 A spectrometer (60 MHz) with tetramethylsilane as the internal standard. The mass spectra were recorded with an MKh-1303 mass spectrometer at an ionizing voltage of 70 eV. Preparative GLC was carried out with a Pye Unicam-105 chromatograph with a flame-ionization detector and a 3 m by 6 mm column filled with 10% E-301 silicone elastomer on Fluoropack-80 (with 0.4-0.315 mm particles); the nitrogen flow rate was 90 ml/min, the temperature was programmed from 120 to 215°, the temperature-rise rate was 4 deg/min, and the sample dose was 0.2 ml.

Reaction of 1-Chloro-1-cyano-2-(2,2-dimethylhydrazino)ethane with Sodium Hydride. A solution of 29.4 g (0.2 mole) of hydrazine I was added dropwise at 0° to a suspension of 4.8 g (0.2 mole) of sodium hydride in absolute THF. At the end of the spontaneous heating period, the mixture was stirred at room temperature for 4 h, after which the precipitate was removed by filtration, and the filtrate was subjected to separation by preparative GLC. Information on the compounds isolated in this way is presented below.

Tetramethyltetrazene (II). As indicated above, the isolated preparation had the same specific retention volume as a genuine sample [5] during analysis by GLC on stationary polyethylene glycol-2500 and Apiezon-M phases (10% on Fluoropack-80). IR spectrum, cm^{-1}: 2800 and 2830 [$N(CH_3)_2$]; 1634 ($N=N$). PMR spectrum:* 7.28 [s, $N(CH_3)_2$, $J_{C^{13}H} = 135.5$ Hz).

Cyanoacetaldehyde N,N-Dimethylhydrazone (III). This compound had bp 58-60° (3 mm), n_D^{20} 1.4769, and (M^+) 111. IR spectrum, cm^{-1}: 2200 ($C\equiv N$); 2804 and 2844 [$N(CH_3)_2$]. PMR spectrum: 3.79 (1H, t, $J=5.1$ Hz, CH), 6.80 (2H, d, $J=5.1$ Hz, CH_2), and 7.21 [6H, s, $N-(CH_3)_2$]. Found: C 53.8; H 7.9; N 37.7%. $C_5H_9N_3$. Calculated: C 54.0; H 8.1; N 37.8%.

Glyoxal N,N-Bis(dimethylhydrazone) (IV). This compound had bp 103° (6 mm) and [M^+] = 142. IR spectrum, cm^{-1}: 1555 ($C=N$); 2800 and 2838 [$N(CH_3)_2$]. PMR spectrum: 3.09 (2H, s, CH) and 7.19 [12 H, s, $N(CH_3)_2$]. The product was identical to the compound obtained by a modified method [6]. A mixture of 28.8 g (0.3 mole) of glyoxal hydrate and 52.5 ml (0.7 mole) of dimethylhydrazine was heated at 100° for 30 min, after which it was subjected to vacuum rectification. The fraction with bp 98-100° (6 mm) [bp 105° (10 mm) [6]] was collected.

Glyoxylic Acid Nitrile N,N-Dimethylhydrazone (V). This compound had bp 110° (11 mm), mp 25° (mp 27-28° [7], and [M^+] 97. IR spectrum, cm^{-1}: 2225 ($C\equiv N$); 2810 and 2890 [$N(CH_3)_2$]. PMR spectrum: 4.27 (1H, s, CH) and 6.91 [6H, s, $N(CH_3)_2$]. Found: C 49.4; H 7.5; N 43.1%. $C_4H_7N_3$. Calculated: C 49.5; H 7.2; N 43.3%.

Isolation of 1,4-Bis(dimethylamino)-2,5-dicyano-1,4-dihydropyrazine (VI). The reaction mixture obtained by reaction of hydrazine I with sodium hydride by the method presented above was passed through a 1 M long column filled with silica gel with elution by 500 ml of THF. The product, which remained on the silica gel as a red-brown zone, was extracted from the sorbent with methanol in a Soxhlet apparatus. The alcoholic extract was cooled to give red needles with mp 205-206° (from ethanol); no melting-point depression was observed for a mixture of this product with 1,4-bis(dimethylamino)-2,5-dicyano-1,4-dihydropyrazine prepared by the method in [8].

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* The chemical shifts are presented on the τ scale in parts per million. The following abbreviations are used here and subsequently: s is singlet, d is doublet, t is triplet, and q is quartet.

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CHEMISTRY OF INDOLE

XLIV.* FORMATION OF CYCLIC AMIDES FROM NITRILES OF THE INDOLE AND INDOLENINE SERIES

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Under the conditions of the Ritter reaction (sulfuric acid), indolylacetonitrile is converted to a tricyclic lactam of the pyrrolo[2,3-b]indole series. Depending on their structure and the reaction conditions, nitriles of the indolenine series form linear amides or cyclic lactams.

We have shown in [2] that nitriles of 3-indolylpropionic acid are protonated primarily at the nitrile group in concentrated sulfuric acid and consequently undergo the Ritter reaction. However, the indole ring itself is capable of protonation in solutions of strong acids to give a carbonium ion with localization of the positive charge in the 2 position. This sort of protonation is responsible for the dimerization and polymerization of indole and gives rise to rearrangements with migration of an alkyl or aryl group bonded to the pyrrole ring [3].

It might have been assumed that the indole molecule is capable of producing the carbonium ion necessary for alkylation in the Ritter reaction. If this protonated molecule also contains a reactive nitrile group, an intramolecular Ritter reaction is possible. However, we did not observe intramolecular cyclization for 3-indolylpropionitriles. Thus 3-indolylpropionitrile, which does not have a substitutent attached to C_2, forms only an amide with a linear structure [2]. 2-Methyl-3-indolylacetonitrile (Ia) also gives only 2-methyl-3-indolylacetamide (IIa) on dissolving in sulfuric acid.

In the case of 3-indolylacetonitrile (Ib) the reaction proceeds ambiguously. An amide (IIb) is formed at room temperature, whereas a three-membered lactam (III) is obtained at higher temperatures. Compound IV is obtained with cyclohexene at high temperatures, i.e., cyclohexene also participates in the Ritter reaction.

The UV spectra of amides IIa, b are characterized by the absorption typical for indoles with the characteristic fine structure of the long-wave maximum. Insofar as the spectra of III and IV are concerned, they are characteristic for indoline systems (243-246 and 295-297 nm; for example, see [4]). The

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[*] See [1] for communication XLIII.

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