<u>D)</u> With Aluminum Isopropoxide. A solution of 3.6 g (0.017 mole) of amino ketone I in 20 ml of isopropyl alcohol was added dropwise to a solution of 8.2 g (0.04 mole) of aluminum isopropoxide in 100 ml of anhydrous isopropyl alcohol, and the mixture was refluxed for 2 h. It was then cooled to 0°C and hydrolyzed with 100 ml of 1 N NaOH. The organic layer was separated, acidified to pH \sim 2 with hydrochloric acid, and vacuum evaporated to dryness. A solution of the residue in water was saturated with potassium carbonate, and the base was extracted with ether. The extract was dried with MgSO₄ and vacuum distilled to give 1.6 g (44%) of a mixture of amino alcohols IV and VII.

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SYNTHESIS OF 4-NITROISOXAZOLINE N-OXIDES*

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The reaction of some aliphatic diazo compounds with trans-l-phenyl-1,2-dinitroethylene gave the first representatives of 4-nitroisoxazoline N-oxides, which differ from the unknown 3-nitroisoxazoline N-oxides with respect to their individual physical and chemical properties.

The formation of 3-nitroisoxazoline N-oxides (I) by reaction of aliphatic diazo compounds (II) with gem-dinitroalkenes was described in [2]. The known reactions of II with vic-dinitroalkenes lead to pyrazoles that do not contain a nitro group or to 3,4-dinitro- Δ^1 -pyraz= olines [3]. It seemed of interest to study the possibility of the participation of the nitro group in vic-dinitroalkenes in cycloaddition reactions with diazoalkanes.

We found that the previously unknown 4-nitroisoxazoline N-oxides (IVa-d) are formed in rather high yields in the reaction of II containing various substituents in the benzene ring [for example, p-methoxyphenyl-(IIa) and p-bromophenylmethyl-(IIb)] such as p-nitrophenyl-methyldiazomethane (IIc) and o-bromodiphenyldiazomethane (IId) with trans-1-phenyl-1,2-dinitroethylene (III) at 20-25°C. In the case of diazo compound IIc a decrease in the yield of IVc is observed because of the effect of the electron-acceptor nitro group in the aromatic ring, and the corresponding 3,4-dinitro- Δ^1 -pyrazoline (V) is formed as a side product.

It is apparent that the trans configuration is retained in 4-nitroisoxazoline N-oxides IVa-d; this is characteristic for cycloaddition to trans-olefins under the given conditions [4]. Isomers of IV were not detected in the reaction mixtures.

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II, IV a $R=C_6H_5$, $R^1=p-CH_3OC_6H_4$; b $R=CH_3$, $R^1=p-BrC_6H_4$; c $R=CH_3$, $R^1=p-NO_2C_6H_4$; d $R=C_6H_5$, $R^1=p-BrC_6H_4$; V $R=CH_3$, $R^1=p-NO_2C_6H_4$; VI $R=C_6H_5$, $R^1=p-CH_3OC_6H_4$

The reactions of aliphatic diazo compounds with a C=C bond are extremely sensitive to steric factors [5]. In the given case it is therefore natural to expect addition of the α -carbon atom of the diazoalkane to the unsubstituted carbon atom of the dinitroalkene in accordance with the Auwers rule [6]. The formation of quite stable salts VI by the action of an alcohol solution of KOH on N-oxide IVa, which contains a labile hydrogen atom adjacent to the nitro group, confirms the structural specificity. Salts VI are reconverted to IV when they are acidified with dilute solutions of mineral acids. It must be noted that bromination or chlorination of these salts at -5 to 0°C in various solvents (H₂O, dry ether, or CCl₄) does not lead to individual substances. Decomposition of the halogenation products to give resinous substances is observed in solution.

Compounds IVa-d readily liberate iodine from KI solution and decolorize a solution of KMnO₄ in acetic acid; this is also typical for 3-nitroisoxazoline N-oxides (I) [7]. Reaction with an activated C=C bond to give nitroisoxazolizidines is characteristic for I [8]. However, we were unable to effect this reaction with IV; this can be explained by the steric effect of the bulky phenyl group in the 3 position of the isoxazoline ring and to a certain extent by a decrease in the activity of the 3-C atom with respect to the C=C bond of the alkene because of the remoteness of the nitro group from the 3-C atom of the heteroring.

The IR spectra of IVa-d do not differ substantially from the IR spectra [7] of N-oxides I: They contain the intense absorption bands of a C=N bond (1630-1640 cm⁻¹) that are characteristic for nitroisoxazoline N-oxides and bands of a nitro group (1500-1515, 1330-1340, and 835-860 cm⁻¹). The UV spectra display absorption maxima at 280-294 nm; this demonstrates a considerable hypsochromic shift as compared with the UV spectra [9] of I.

It should be noted that it is difficult to detect the signal of the CH_3 group in the PMR spectra because of the low solubility of IVa-d in the acceptable solvents. The signal of the CH group in the 4 position of the isoxazoline ring is shifted under the influence of the electron-acceptor NO_2 group to weak field and is found in the region of the signal of the aromatic ring; this is in agreement with the literature data [10]. The signal of the CH group in IVa was determined by comparison of the PMR spectrum of the corresponding potassium salt, which does not contain a hydrogen atom in the 4 position of the isoxazoline ring.

The results of elementary analysis of IVa-d are in agreement with the calculated values, and their individuality was proved by thin-layer chromatography (TLC).

The data presented above demonstrate the common character and certain differences in the properties of the 4- (IV) and 3-nitroisoxazoline N-oxides (I).

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The UV spectra of ethanol solutions of the compounds were recorded with an SF-4 spectrophotometer. The PMR spectra of solutions of the compounds in acetone or DMSO were recorded with an RS-60 spectrometer with hexamethyldisiloxane as the internal standard. The individuality of the compounds was monitored by TLC on Silufol-254; the R_f values are presented for a methanol-chloroform system (2:1).

<u>4-Nitroisoxazoline N-Oxides (IVa-d)</u>. A solution of 0.01 mole of the appropriate diazoalkane in 30-40 ml of hexane, benzene, or ether was added to a solution of 0.01 mole of dinitroalkene III in 30-40 ml of ether, and the mixture was maintained at 20-25°C for 10-24 h. The solvent was then removed by vacuum distillation, and the residue was recrystallized from ethanol to give yellow crystals of IVa (69%) with mp 121-122°C (dec.). Found: C 67.9; H 4.6; N 7.3%. $C_{22}H_{18}N_2O_5$. Calculated: C 67.7; H 4.6; N 7.2%. PMR spectrum (in acetone), δ : 3.76 (OCH₃), 7.18 ppm [14H (aromatic) and 1H]. Compound IVa had R_f 0.81. Compound IVb was obtained in 67% yield and had mp 141°C (dec.). Found: C 50.7; H 3.4; Br 21.5; N 7.5%. $C_{16}H_{13}BrN_2O_4$. Calculated: C 50.9; H 3.4; Br 21.2; N 7.4%. PMR spectrum (in DMSO), δ : 7.38 ppm (aromatic H + 1H). Compound IVb had R_f 0.78. Compound IVc was obtained in 48% yield and had mp 170°C (dec.). Found: C 56.2; H 3.6; N 12.0%. $C_{16}H_{13}N_3O_6$. Calculated: C 56.0; H 3.8; N 12.2%. PMR spectrum (in acetone), δ : 7.41 [4H (aromatic) + 1H] and 8.21 ppm [5H (aromatic)]. Compound IVd was obtained in 83% yield and had mp 153°C (dec.). Found: C 57.5; H 3.6; Br 23.8; N 6.3%. $C_{21}H_{15}BrN_2O_4$. Calculated: C 57.4; H 3.4; Br 23.6; N 6.3%. PMK

In the case of diazo compound IIc the residue after removal of the solvent was washed thoroughly with a large amount of ethanol, and the filtrate was vacuum evaporated to give 3,4-dinitro- Δ '-pyrazoline V, with mp 104°C (dec.), in 20% yield. Found: C 51.5; H 3.4; N 18.7%. C₁₆H₁₃N₅O₆. Calculated: C 51.7; H 3.5; N 18.8%. IR spectrum: 1565, 1523, and 1354 cm⁻¹. UV spectrum: 262 nm (log ϵ 4.19). PMR spectrum (in tetrachlorethylene), δ : 1.58 (CH₃), 6.46 (CH), and 7.88 ppm [9H (aromatic)].

Action of Methyl Acrylate on 4-Nitroisoxazoline N-Oxides. A 3.5 mmole sample of methyl acrylate was added to a solution of 2 mmole of IVa or IVb in 10 ml of benzene, and the mixture was heated at 60-65°C for 140 h. The starting N-oxide IVa or IVb was isolated after removal of the volatile substances in vacuo.

Potassium Salt (VI) of 3,5-Diphenyl-4-nitro-5-(p-methoxyphenyl)isoxazoline N-Oxide . A 0.5-g (1 mmole) sample of IVa was added in small portions at 20-25°C to a methanol solution of 0.15 g (2 mmole) of KOH. The salt was precipitated from the reaction mixture by cooling to 0-5°C. The shiny yellow plates were purified by reprecipitation from aqueous solution by the addition of methanol. The yield of product with mp 48°C (dec.) was 0.35 g (73%). Found: C 61.5; H 4.0; N 6.4%. $C_{22}H_{17}KN_2O_5$. Calculated: C 61.7; H 3.9; N 6.5%. IR spectrum: 1635, 1510, and 1380 cm⁻¹. The UV spectrum of the product was similar to the UV spectrum of the starting IVa.

Halogenation of Salt VI. An ether solution of bromine was added to a suspension of salt VI in dry ether at -5 to 0° C or a weak stream of chlorine was bubbled through the suspension until the yellow salt disappeared completely. After a few minutes, vigorous gas evolution was observed. Removal of the solvent gave a mixture of resinous products, the identification of which was difficult.

The same results were obtained when the halogenation was carried out in water or dry CCl₄.

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