METHYL ESTER OF PHENYLNITROMETHANE

IN THE 1,3-DIPOLAR CYCLOADDITION REACTION

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According to the classification of Huisgen [1], nitro compounds are regarded as being 1,3-dipoles of the type

Recently it was shown by us [2] that nitro derivatives are capable of entering into the 1,3-dipolar cycloaddition reaction via the system of bonds

$$> \stackrel{\mathbf{1}}{\mathbf{C}} = \stackrel{\mathbf{2}}{\stackrel{\mathbf{N}}{\mathbf{N}}} \stackrel{\mathbf{3}}{\rightarrow} \stackrel{\mathbf{0}}{\stackrel{\mathbf{0}}{\mathbf{O}}}$$

The behavior of the methyl ester of phenylnitromethane (I) in this reaction was studied in the present paper. The reaction of (I) with methyl acrylate and acrylonitrile leads to the formation of crystalline products (II) and (III), to which, on the basis of the data of the elemental and spectral analyses (Figs. 1 and 2), we have assigned the structure of the corresponding N-methoxy-3-phenylisoxazolidine derivatives. In studying the properties of the obtained heterocycles we discovered that their treatment with $LiAlH_4$ leads, besides the usual reduction of the nitrile and ester functions, to a conversion of the isoxazolidine ring to the isoxazoline ring. Besides possessing independent interest, this reaction can serve as a convenient way of proving the structure of the addition products.

Thus, from (II) we obtained 3-phenyl-5-hydroxymethylisoxazoline (IV) in quantitative yield, which proved to be identical with the product obtained by an independent synthesis [3]. From (III) under analogous conditions is formed 3-phenyl-5-aminomethylisoxazoline (V), the desamination of which leads to the formation of (IV). The high yields of (IV) and (V) suggest that the substituents in (II) and (III) occupy the same positions, and these compounds should now be assigned the structure of N-methoxy-3-phenyl-5-carbomethoxyisoxazolidine and N-methoxy-3-phenyl-5-nitriloisoxazolidine, respectively. The direction of the addition is also confirmed by the hydrolysis $(20\% H_2SO_4$ solution, 20°) of (II) to β -benzoyllactic acid





The sole product that we were able to isolate from the reaction of (I) with styrene was 3,5-diphenyl-1,2,4oxadiazole (VI). It proved that (VI) is also formed by simply allowing (I) to stand for a long time.* In our opinion, the formation of (VI) can be explained by the 1,3-dipolar addition of (I) to benzaldoxime (the decomposition product of (I) according to the scheme $R-CH = NOOCH_3 \rightarrow R-CH = NOH + CH_2O$), followed by spontaneous aromatization of the addition product. This assumption was confirmed by the fact that (VI) is easily formed when (I) is reacted with excess benzaldoxime





As a result, it was shown that compounds containing the CN double bond can also serve as dipolarophiles for the O-esters of nitro compounds. Since nitronium esters are usually unstable and decompose easily to the corresponding oximes, then in each case it is possible to expect secondary reaction of the nitronium ester with the oxime. It is obvious that the direction of the reaction and the ratio of the obtained products will depend both on the stability of the O-ester and on the relative reactivity of different dipolarophiles toward it. Thus, for example, after isolating (II) or (III) from the corresponding reaction mixtures there remained an oil, which, on the basid of the data of thin-layer chromatography on Al_2O_3 , still contains a certain amount of (II) or (III) and, in each case, (VI) and benzaldoxime. We estimated the amount of (II) and (III) in the oily residues from the amount of (IV) and (V), isolated after reacting the oils with LiAlH₄. The total yields of (II) and (III) are respectively equal to 68 and 60.7%. The question of whether (II) and (III) are the cis- or the trans-isomers will be the subject of a later study.

EXPERIMENTAL

N-Methoxy-3-phenyl-5-carbomethoxyisoxazolidine (II). A mixture of 1 g of freshly prepared (I) and 2.85 g of methyl acrylate was kept for 4 days at 20°, after which it was diluted with ether and washed with 5% NaOH solution. The ether extracts were dried over MgSO₄, the ether and excess methylacrylate were removed, and the residual oil was chromatographed on an Al₂O₃ column (eluent benzene). After removal of the benzene, the oil crystal-lized when rubbed, after which the crystals were separated and recrystallized from hexane, m.p. 60-61°. The yield of (II) was 0.53 g (34%). Found: C 60.68, 60.48; H 6.42, 6.48; N 6.19, 6.09%. C₁₂H₁₅NO₄. Calculated: C 60.74; H 6.37; N 5.91%.

Reaction of (II) with LiAlH₄. With stirring, a solution of 0.2 g of (II) in 10 ml of absolute ether was added in drops to a suspension of 0.2 g of LiAlH₄ in 20 ml of absolute ether, after which the mixture was kept at ether boil for 3 h. Then 1 ml of water and 10 ml of 20% H_2SO_4 solution were added, the water layer was extracted 3 times with ether, and the combined ether extracts were dried over MgSO₄. After evaporation of the ether, (IV) (m.p. 78°) was obtained in quantitative yield. The mixed melting point with the product obtained by an independent synthesis was not depressed.

N-Methoxy-3-phenyl-5-nitriloisoxazolidine (III). A solution of 1 g of freshly prepared (I) in 1.75 g of acrylonitrile was kept for 4 days at 20°. After removal of the acrylonitrile, the residual oil crystallized when cooled and

^{*} Arndt and Rose [4] described the preparation of (VI) by treating (I) with hot hydrochloric acid solution, but they did not explain the mechanism of its formation.



Fig. 2. Infrared spectrum of (III).

rubbed. The crystals of (III) were separated and recrystallized from hexane, m.p. 96°. Yield 0.62 g (45.7%). Found: C 65.05; 64.93; H 5.90, 5.94; N 13.99, 14.21%. C₁₁H₁₂N₂O₂. Calculated: C 64.71; H 5.92; N 13.72%.

Reaction of (III) with LiAlH₄. The reaction was run in the same manner as the reaction of (II) with LiAlH₄. After adding the water and dilute H₂SO₄ solution, the aqueous layer was washed twice with ether and then, with ice, cooling, made alkaline with 20% NaOH solution. The reaction product was extracted with ether from the alkaline solution, the ether extracts were dried over MgSO₄ and, after evaporation of the ether, we obtained 0.15 g (86.9% yield) of (V). (V) was characterized as the phenyl isocyanate derivative, m.p. 194[•] (with decomp.). Found: C 68.95, 68.73; H 5.88, 5.79; N 14.23, 14.39% C₁₇H₁₇N₃O₂. Calculated: C 69.13; H 5.80; N 14.22%. The desamination of (V) (NaNO₂, 10% CH₃COOH solution) gave (IV).

SUMMARY

1. The methyl ester of phenylnitromethane reacts by the 1,3-dipolar addition scheme with compounds, containing an activated double bond, with the formation of 5-substituted 3-phenyl-N-methoxyisoxazolidine derivatives.

2. The reaction of the N-methoxyisoxazolidines with $LiAlH_4$ leads to their conversion to the corresponding isoxazoline derivatives.

3. The methyl ester of phenylnitromethane enters into the 1,3-dipolar addition reaction across the C = N bond in oximes. As the result of spontaneous aromatization, the formed adduct is converted to the oxadiazole derivative.

LITERATURE CITED

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-tocover English translations appears at the back of this issue.