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Studies of Heteroaromaticity. XXIII.[1] 1,3-Dipolar Cycloaddition Reactions of 5-Nitrofuronitrile Oxide and *m*-Nitrobenzonitrile Oxide with Benzyne

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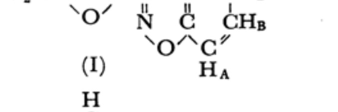
Many papers have been published on the electrophilic addition of benzyne to nitrosobenzene,[2] acridine,[3] acetylene derivatives,[4] and on the 1,3-dipolar cycloaddition reactions of benzyne with diazoketones and acyl azides.[5] Also, several kinds of reactive dienes are known as trapping agents of benzyne.[6] However, it seems rather surprising that there has been no report which deals with its 1,3-dipolar cycloaddition reactions with nitrile oxides.

In the course of our studies on the dipolar reactivity of 5-nitro-2-furohydroxamoyl chloride,[7] we have reported that the thermal 1,3-dipolar cycloaddition procedure using hydroxamoyl chlorides has a big advantage over the corresponding nitrile oxide method, especially in the reactions with acetylenic dipolarophiles. Since benzyne is regarded as a cyclic acetylene, we attempted to apply the same procedure to benzyne. The product obtained was yellow crystals and the structure was confirmed to be 3-(5-nitro-2-furyl)benzisoxazole (I) by the elemental analyses and spectral data; the NMR spectrum in $CDCl_3$ showed signals at 1.17τ (multiplet, 1H) and 2.33 (multiplet, 3H), besides those of nitrofuran ring protons at 2.50 (doublet, 1H, $J=3.8$ cps) and at 2.64 (doublet, 1H, $J=3.8$ cps).[8] We assigned the signal at 2.33τ to H_B aromatic protons and that at 1.17τ to an H_A proton of the benzene ring. The increased deshielding of H_A compared with that of H_B is explained by the strong paramagnetic anisotropic effect of a neighbouring ether oxygen. The presence of the ultraviolet absorption maximum in ethanol at 327 mμ ($\varepsilon=10300$) indicates that the structure of this product is similar to 3-(5-nitro-2-furyl)-5-substituted isoxazole (II).[7]

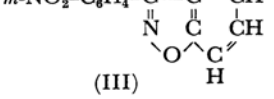
Similar treatment of *m*-nitrobenzhydroxamoyl chloride also afforded the corresponding 3-(*m*-nitrophenyl)benzisoxazole (III) in 10% yield. These yields are much lower compared with those in the cases with diazoketones and acyl azides,[5] and these low yields may be explained by the weak electrophilicity of the nitrile oxides formed under the reaction conditions.

Whereas 1,2-dimethoxyethylene is known to be a suitable solvent[9] for the generation of benzyne by the above method, it was used in place of dichloromethane. However, the yields could not be improved so much.

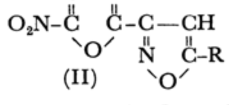
The reaction path may involve the initial coordination of the electronegative oxygen of the nitrile oxide with a triple bond of benzyne to form an oxygen-carbon bonding, followed by cyclization to benzisoxazole as indicated below:



(I)



(III)



(II)

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[1] Part XXII of this series: T. Sasaki and M. Ando, This Bulletin, **41**, 2215 (1968).

[2] G. N. Steinhoff and M. C. Henry, *J. Org. Chem.*, **29**, 2808 (1964).

[3] Private communication from Dr. F. Yoneda (Keio University).

[4] M. Stiles and U. Burckhard, *J. Org. Chem.*, **27**, 4715 (1962).

[5] W. Ried and M. Schön, *Chem. Ber.*, **98**, 3124 (1965); *Ann.*, **689**, 141 (1965).

[6] G. Wittig and A. Krebs, *Chem. Ber.*, **94**, 3260 (1961); G. Wittig and W. R. Hoffmann, *ibid.*, **95**, 2718 (1962); E. Wolthuis, *J. Org. Chem.*, **26**, 2215 (1961); F. M. Beringer and S. J. Huang, *ibid.*, **29**, 445 (1964).

[7] T. Sasaki and T. Yoshioka, This Bulletin, **40**, 2604 (1967).

[8] T. Sasaki, S. Eguchi and K. Kojima, *J. Heterocyclic Chem.*, **5**, 243 (1968).

[9] L. F. Fieser and M. Fieser, "Reagents for Orrganic Synthesis," John Wiley and Sons, Inc., New York, N. Y. (1967), p. 268.

This mechanism is rather interesting when compared with that of benzonitrile oxide with nitrosobenzene[10] and of nitrosobenzene with benzyne,[2] in both of which the reactions are thought to be initiated by a carbon-nitrogen bonding, while the Diels-Alder reaction of benzyne with styrene is recently reported.[11]

Experimental[12]

3-(5-Nitro-2-furyl)benzisoxazole. 5-Nitro-2-furohydroxamoyl chloride,[7] 1.31 g (7 mmol), was dissolved in a mixture of 1 m*l* of isoamyl nitrite and 40 m*l* of dichloromethane. The solution was warmed to 55—60°C and a solution of 1.23 g (9 mmol) of anthranilic acid and 1.2 m*l* of triethylamine in 18 m*l* of acetone was added slowly to this stirred solution at the same temperature in 1 hr. The reaction mixture was refluxed for further 2 hr until the evolution of nitrogen gas had completely ceased. After the solvents were removed under reduced pressure, the residue was dissolved in chloroform and chromatographed on a silica-gel column, using chloroform as the eluent. The first fraction afforded 0.1 g (10%) of yellow crystals, mp 176°C, after recrystallization from ethanol. The main products eluted from other fractions were intractable tars.

Found: C, 57.63; H, 2.62; N, 12.12%. Calcd for $C_{11}H_6O_4N_2$: C 57.40; H, 2.63; N, 12.17%

3-(*m*-Nitrophenyl)benzisoxazole. Similarly, 10% yield of this compound was obtained, mp 176°C. UV λ_{max}^{EtOH} mμ (ε): 285 (6500), 224 (19500).

Found: C, 64.62; H, 3.35; N, 11.45%. Calcd for $C_{13}H_8O_3N_2$: C, 65.00; H, 3.36; N, 11.66%.

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[10] T. Minisci, R. Galli and A. Quilico, *Tetrahedron Letters*, **1963**, 785.

[11] W. L. Dilling, *ibid.*, **1966**, 939.

[12] The melting points were determined on a Yanagimoto electric micromelting point apparatus and are uncorrected. All the ultraviolet and infrared spectra were recorded on a JASCO Model ORD/UV-5 optical rotary dispersion recorder and on a JASCO Model IR-S infrared spectrophotometer respectively. The NMR spectra were taken on a Varian A-60 apparatus, with tetramethylsilane as an internal standard, and the chemical shifts are presented in terms of τ values.