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# Syntheses of Fused Heterocycles *via* Cycloaddition of Hetaryne. Studies on Heteroaromaticity. Part XLVII[1]

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In comparison with abundant examples for the cycloaddition reactions of dehydrobenzene (benzyne), only occasional reports have been made concerning the same reactions of dehydroaromatic heterocycles (hetarynes).[2] Recently, the electronic structures of hetarynes have been discussed using the extended Hückel theory,[3] by which the larger relative stability is predicted for 3-pyridyne compared with other pyridyne isomers.

These facts prompted us to report one-step syntheses of the fused bicyclic heteroaromatic ring system by the cycloaddition reactions of this hetaryne.

Expecting that the intermediate 3-pyridyne (II) might be trapped with dipolarophiles or dienophiles, the lead tetraacetate oxidation of 1-aminotriazolo-[4,5-*c*]pyridine (I)[4] was carried out in the presence of dienophilic five-membered heterocycles or some dipolarophiles.

These results are described in this note.

### Results and Discussion

Only one example of 1,2-cycloaddition of dehydroheterocycle is recorded;[5] cyclopentadiene adds to 3-pyridyne in a 1,2-fashion rather than in a 1,4-fashion of Diels-Alder reaction. On the other hand, attempts to add 3-pyridyne to anthracene remain unsuccessful.[6]

In contrast, lead tetraacetate oxidation of compound I was carried out in the presence of dimethylfulvene, norbornadiene, and furan at room temperature for 1 hr. Only the *endo*-oxide III (picrate, mp 178°C) was obtained from furan in a 74% yield, which was identified by the IR and NMR spectral comparison with those of an authentic sample prepared by heating 3-pyridinediazonium-4-carboxylate in furan.[7] A recent report described the lead tetraacetate oxidation of I in the presence of tetracyclone which affords 5,6,-7,8-tetraphenylisoquinoline.[4] Neither 1,2-cycloadducts nor 1,4-Diels-Alder adducts could be isolated from the reaction of 3-pyridyne with dimethylfulvene or norbornadiene.

Similarly, 1,3-dipolar cycloaddition reactions of 3-pyridyne with dipolarophiles were also attempted.

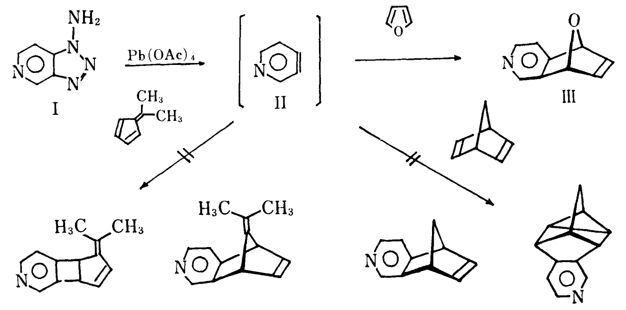

Chart 1.

There is only one example[2] known for a 1,3-addition of azide to a dehydroheterocyclic intermediate as shown by the following scheme.

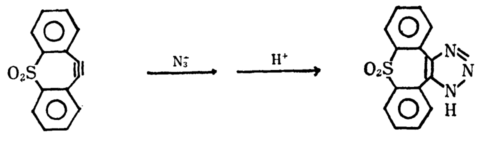

Chart 2.

Treatment of a mixture of I and *N*-phenylsydnone in 1 : 1.3 mol ratio with lead tetraacetate in tetrahydrofuran at room temperature led to the formation of 1,3-dipolar cycloadduct IV, mp 132—133°C, in a 30% yield. The NMR spectrum of IV shows signals of the ring protons at $\tau$ 0.60 (1*H*, s), 1.52 (1*H*, s), 1.77 (1*H*, d, $J$=7.0 Hz), and overlapping signals at $\tau$ 1.96—2.51 (1*H*-ring proton and 5*H*-phenyl protons, m). Similar oxidation of a mixture of compound I and benzaldehyde phenylhydrazone[8,9] in 1 : 1.1 mol ratio with an excess of lead tetraacetate afforded the expected cycloadduct V as pale yellow oil (picrate, mp 234—237°C) in a 15% yield. However, attempted cycloaddition of diphenyldiazomethane or benzonitrile oxide with 3-pyridyne was unsuccessful.

The orientation in the addition reaction of 1,3-dipolar *N*-phenylsydnone or diphenylnitrilimine with 3-pyridyne is not clear at present. However, the nucleophilic attack of the dipolar on 3-pyridyne might occur preferentially at the C-4 position as a consequence of its lower total electron density (3.97 against 4.35 electrons)[3] as shown by the following chart.

The structures of the 1,3-dipolar cycloadducts IV and V were tentatively assigned as 2-phenyl-2*H*-pyrazolo[4,3-*c*]pyridine and 1,3-diphenyl-1*H*-pyrazolo-

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[1] Part of series, XLVI., T. Sasaki and T. Yoshioka, This Bulletin, **43**, 2989 (1970).

[2] R. W. Hoffmann, "Dehydrobenzene and Cycloalkynes," Academic Press, New York, N. Y. (1967), p. 199, 303, 306.

[3] W. Adams, A. Grimison, and R. Hoffmann, *J. Amer. Chem. Soc.*, **91**, 2570 (1969).

[4] G. W. J. Fleet and I. Fleming, *J. Chem. Soc.*, *C*, **1969**, 1758.

[5] T. Kauffmann, J. Hansen, K. Udeloft, and R. Winthwein, *Angew. Chem.*, **76**, 590 (1964).

[6] T. Kauffmann, *ibid.*, **77**, 557 (1965).

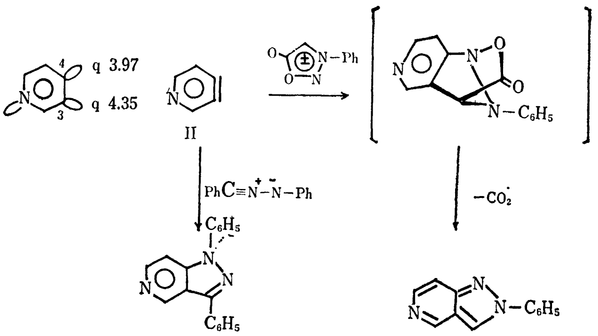
[7] T. Kauffmann and F. P. Boettcher, *Chem. Ber.*, **95**, 949 (1962).

[8] The nitrilimines have been trapped during the oxidation of aldehyde hydrazones; W. A. F. Gladstone, J. B. Aylward, and R. O. C. Norman, *J. Chem. Soc.*, *C*, **1969**, 2587.

[9] T. Sasaki and T. Yoshioka, This Bulletin, **43**, 1254 (1970).

[4,3-*c*]pyridine, respectively. Such a fused ring system as pyrazolo[4,3-*c*]pyridine is the first in the fused heterocyclic series.

Attempted 1,3-dipolar cycloaddition reactions of 3-pyridinediazonium-4-carboxylate with dipolarophilic nitrilimines were unsuccessful.



V IV

Chart 3.

Thus, it can be concluded that the cycloaddition reactivity of 3-pyridyne is generally much lower than that of benzyne, since the stereospecific 2+4 cycloaddition, the 2+2 nonconcerted cycloaddition, and the 1,3-cycloaddition for benzyne have been reported to give the corresponding cycloadducts in excellent yields.[2,10)]

## Experimental[11)]

*Lead Tetraacetate Oxidation of 1-Aminotriazolo[4,5-*c*]pyridine in the Presence of Furan.* Compound I (390 mg) was dissolved in furan (5.1 g) and this solution was dropwise added to a stirred suspension of lead tetraacetate (1.4 g) in dichloromethane (20 m*l*) at 20°C. The reaction was always instantaneous and exothermic with evolution of nitrogen. Work-up involved filtration, evaporation of the solution, and chromatography (silicic acid, 100 mesh, Mallinckrodt) of the residue using benzene as an eluent.

Colorless oil of an *endo*-oxide III (317 mg, 75%) was obtained from the eluent; picrate, mp 178°C (lit,[7)] mp 178°C).

Found: C, 48.28; H, 2.69; N, 14.97%. Calcd for $C_{15}H_{10}O_8N_4$ (picrate): C, 48.13; H, 2.69; N, 14.97%.

*Reaction of 3-Pyridyne with* N*-Phenylsydnone.* A solution of compound I (400 mg) and *N*-phenylsydnone (670 mg) in tetrahydrofuran (40 m*l*) was added dropwise to a stirred suspension of lead tetraacetate (1.2 g) in tetrahydrofuran (20 m*l*) at 20—25°C. After 1 hr, work-up as described above afforded an adduct IV (168 mg, 30%) as colorless prisms, mp 132—133°C.

Found: C, 73.56; H, 4.71; N, 21.74%. Calcd for $C_{12}H_9N_3$: C, 73.83; H, 4.65; N, 21.53%.

*Reaction of 3-Pyridyne with 1,3-Diphenylnitrilimine.* A solution of benzaldehyde phenylhydrazone (226 mg) and I (135 mg) in dichloromethane (20 m*l*) was added during 50 min to a stirred suspension of lead tetraacetate (1.5 g) in dichloromethane (50 m*l*) at below 10°C. The resulting thick suspension was further stirred at room temperature for 1 hr. Work-up as above afforded an adduct V (80 mg) as pale yellow oil; picrate, mp 234—237°C.

Found: C, 57.86; H, 3.29; N, 16.51%. Calcd for $C_{24}H_{16}N_6O_7$ (picrate): C, 57.60; H, 3.22; N, 16.80%.

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10) For leading reference, see M. Jones, Jr., and R. H. Levin, *J. Amer. Chem. Soc.*, **91**, 6411 (1969).

11) The melting points were measured with a Yanagimoto micromelting point apparatus and are uncorrected. Microanalyses were performed on a Yanagimoto C.H.N.-Corder, Model MT-1. The NMR spectra were taken with a JEOLCO., Model JNM-MH-60 NMR spectrometer and with a Varian A-60 spectrometer with tetramethylsilane as an internal standard. The chemical shifts are expressed in $\tau$ values. The IR spectra were taken with a JASCO Model IR-S spectrometer.