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Studies on Heteroaromaticity. XXXVII.[1] 1,3-Dipolar Cycloaddition of a Nitrilimine Possessing a Nitrofuran Ring

Tadashi SASAKI and Toshiyuki YOSHIOKA

Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University, Chikusa-ku, Nagoya

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In continuation of our previous reports concerning the 1,3-dipolar cycloaddition of nitril oxides,[2] nitrones,[3] and diazoalkanes[4] possessing a nitrofuran ring, this note deals with similar reactions of a nitrilimine also possessing a nitrofuran ring. Such a nitrilimine has not been reported yet.

Many procedures have been reported for the preparation of reactive nitrilimines.[5] Among them, the most probable access to nitrilimines is by the action of tertiary bases on hydrazidoyl halides as reported by Huisgen.[6] We treated 5-nitro-2-furoylhydrazide (I) with phosphorus pentachloride according to his procedure. However, the expected hydrazidoyl chloride (II) could not be isolated and intractable polymers were produced instead. Recently Gladstone[7] demonstrated the intermediate formation of nitrilimines in lead tetraacetate-oxidation of benzaldehyde arylhydrazones by the 1,3-dipolar cycloaddition to acrylonitrile.

We treated readily available 5-nitro-2-furfural phenylhydrazone (III) with lead tetraacetate in a tetrahydrofuran(THF)-benzene mixture in the presence of dipolarophilic acrylonitrile at room temperature. The crude product was purified on column chromatography to afford pale yellow crystals; the structure was assigned as 5-cyano-3-(5-nitro-2-furyl)-1-phenylpyrazole (IV) on the basis of analytical and spectral data. The structure was further confirmed by the treatment of III with cyanoacetylene under similar reaction conditions affording the same product IV. This indicates the initial formation of a pyrazoline (V) by the 1,3-dipolar cycloaddition of a nitrilimine (VI) to acrylonitrile followed by heteroaromatization[1] to afford IV. When acetic acid was used as the solvent in the above reactions, the yield was lowered to 10%. Attempts to isolate a sideproduced hydrazidic acetate were unsuccessful, though this type of compound is generally believed to be produced from nitrilimine and acetic acid.[6] Treatment with styrene instead of acrylonitrile in the above reactions afforded 3-(5-nitro-2-furyl)-1,5-diphenylpyrazole (VII), which could not be obtained, however, from phenylacetylene and III in the presence of lead tetraacetate; the reaction afforded intractable oils. Similar reactions with acrylic and methacrylic acid afforded 3-(5-nitro-2-furyl)-1-phenylpyrazole (VIII) and 5-methyl-3-(5-nitro-2-furyl)-1-phenylpyrazole (IX) respectively, in good yields. Their analytical and spectral data were compatible with the above structures. The results indicate that the above reactions involve decarboxylation of the initial 1 : 1 adducts (X) by radical mechanism of lead tetraacetate and its oxidative heteroaromatization.[1]

Contrary to this, when methyl acrylate, methacrylate and allyl bromide were used as dipolarophiles, deep-red colored products, XI, XII and XIII, respectively, were produced. Their analytical and spectral data supported their pyrazoline structures; especially in the UV spectra strong bathochromic shifts were observed in the pyrazoline derivatives compared with the corresponding pyrazole derivatives.

The direction of addition of nitrilimine VI in the formation of IV and VIII was concluded to be the same irrespective of the polarization of used dipolarophiles, and in good accordance with the results obtained from nitril oxides[2,8] and other

1) Part XXXVI of this series: T. Sasaki, T. Yoshioka and Y. Suzuki, *Yuki Gosei Kagaku Kyokai Shi*, **28**, 469 (1970).

2) a) T. Sasaki and T. Yoshioka, This Bulletin, **40**, 2608 (1967); b) T. Sasaki and T. Yoshioka, *ibid.*, **42**, 826 (1969).

3) T. Sasaki and T. Yoshioka, *ibid.*, **41**, 2964 (1968).

4) T. Sasaki and A. Kojima, *ibid.*, **41**, 1658 (1968); *J. Heterocycl. Chem.*, **5**, 243 (1968).

5) R. Huisgen, R. Grashey and J. Sauer, "Cycloaddition Reactions of Alkenes," in "The Chemistry of Alkenes," ed. by S. Patai, Interscience Publ., New York (1964), pp 812—822 and references cited therein.

6) R. Huisgen, M. Seidl, G. Wallvillich and H. Knupfer, Tetrahedron, **17**, 3 (1962).

7) W. A. F. Gladstone, *Chem. Commun.*, **1969**, 179.

8) R. A. Firestone, *J. Org. Chem.*, **33**, 2285 (1968), and references cited therein.

nitrilimines.[8] The same holds in the reactions with α,β-unsaturated acids, esters and olefins.

We reported the thermal 1,3-dipolar cycloaddition of aromatic hydroxamoyl chloride with indene and acenaphthylene affording the corresponding isoxazolidines.[9] Treatment of III with indene and acenaphthylene in the presence of lead tetraacetate at room temperature afforded indenopyrazole (XIV or XIV′) and acenaphthopyrazole (XV) after oxidative heteroaromatization of the expected pyrazolines. The pyrazole structure present in XIV or XIV′ and XV was demonstrated by their UV spectra and by the absence of C-4 and C-5 methine proton in the NMR spectra.[9] There are two possible structures for the indenopyrazole, either 3-(5-nitro-2-furyl)-1-phenylindeno[2,3-*d*]pyrazole (XIV) or its [3,2-*d*]pyrazole (XIV′). Assuming a similar trend in the direction of addition of nitrilimines to nitrile oxides,[9] we tentatively assigned XIV preferentially to XIV′.

However, no cycloaddition of VI to acetonitrile, benzonitrile, benzaldehyde and *m*-nitrobenzaldehyde was observed.

Experimental[10]

5-Cyano-3-(5-nitro-2-furyl)-1-phenylpyrazole (IV). *From Acrylonitrile.* To a solution of 1 g (4.5 mmol) of 5-nitrofurfural phenylhydrazone III[11] and 1.1 g (25 mmol) of acrylonitrile in 60 m*l* of a THF-benzene (1 : 5) mixture was added 4 g (9 mmol) of lead tetraacetate at room temperature with stirring. The reaction mixture was further stirred at room temperature for 3 days. After filtering off undissolved parts, the solvents were removed under reduced pressure. The residual crude product was purified on a silica-gel (Mallinckrodt, 100 mesh) column using chloroform as the eluent to afford 0.58 g (55%) of pale yellow crystals IV, mp 165—167°C (from ethanol). IR (KBr) cm^{-1}: 2260 (CN). UV λ_{max}^{EtOH} mμ (ε): 290 (shoulder, 8650) and 344 (18400). NMR ($CDCl_3$) τ: 2.59 (s, C-4-H of pyrazole ring).[12]

Found: C, 60.03; H, 2.53; N, 19.63%. Calcd for $C_{11}H_8N_4O_3$: C, 60.00; H, 2.88; N, 19.99%.

From Cyanoacetylene. Similar treatment of 1.6 g (25 mmol) of cyanoacetylene[13] instead of 1.1 g (25 mmol) of acrylonitrile in the above reaction afforded 0.57 g (55%) of IV.

3-(5-Nitro-2-furyl)-1,5-diphenylpyrazole (VII). Similar treatment of 2.0 g (25 mmol) of styrene instead of 1.1 g of acrylonitrile afforded 0.33 g (20%) of pale yellow crystals VII, mp 155—157°C (ethanol). UV λ_{max}^{EtOH} mμ (ε): 236(23600) and 358(18400). NMR ($CDCl_3$) τ: 3.01 (s, C-4-H of pyrazole ring).[12] Found: C, 69.19; H, 3.59; N, 12.67%. Calcd for $C_{19}H_{13}N_3O_3$: C, 68.87; H, 3.96; N, 12.68%.

3-(5-Nitro-2-furyl)-1-phenylpyrazole (VIII). Acrylic acid (2.0 g, 27 mmol) was dissolved in a mixture of 20 m*l* of THF and 30 m*l* of benzene. To this solution was added 1.0 g (4.5 mmol) of III and then a solution of 3.1 g (8.5 mmol) of lead tetraacetate in 30 m*l* of benzene with stirring at room temperature. Work up as above afforded 0.65 g (90%) of pale yellow crystals VIII, mp 124—126°C (ethanol). UV λ_{max}^{EtOH} mμ (ε): 264(13200) and 364(20600). NMR ($CDCl_3$) τ: 2.13 (d, 1H, J=3.0 Hz, C-5-H of pyrazole ring) and 3.20 (d, 1H, J=3.0 Hz, C-4-H of pyrazole ring).[12]

Found: C, 60.99; H, 3.41; N, 16.48%. Calcd for $C_{13}H_9N_3O_3$: C, 61.17; H, 3.55; N, 16.47%.

5-Methyl-3-(5-nitro-2-furyl)-1-phenylpyrazole. (IX). Similar treatment of 0.8 g of III, 1.5 g of methacrylic acid and 3.2 g of lead tetraacetate in 15 m*l* of THF and 60 m*l* of benzene afforded 0.62 g (88%) of pale yellow crystals IX, mp 121—123°C (ethanol). UV λ_{max}^{EtOH} mμ (ε): 252(17400) and 358(18200). NMR ($CDCl_3$) τ: 3.46 (s, C-4-H of pyrazole ring) and 7.65 (s, C–CH_3).

Found: C, 62.25; H, 3.99; N, 15.48%. Calcd for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.12; N, 15.61%.

5-Methoxycarbonyl-3-(5-nitro-2-furyl)-1-phenyl-2-pyrazoline (XI). When 2 g of methyl acrylate was used instead of methacrylic acid in the above reaction, 40% yield of deep red colored crystals XI, mp 138—140°C (ethanol) was obtained. UV λ_{max}^{EtOH} mμ (ε): 245 (8700), 296(11700) and 452(19500). NMR ($CDCl_3$) τ: 5.18 (double d, J=8.0 and 10.0 Hz, C-5-H of pyrazoline ring),[14] 6.30 (s, –$COOCH_3$) and 6.45 (m, –CH_2–).[14]

Found: C, 57.51; H, 4.15; N, 13.28%. Calcd for $C_{15}H_{13}N_3O_5$: C, 57.14; H, 4.16; N, 13.33%.

5-Methyl-5-methoxycarbonyl-3-(5-nitro-2-furyl)-1-phenyl-2-pyrazoline (XII). Deep red colored crystals, mp 165—167°C (ethanol). Yield was 50%. UV λ_{max}^{EtOH} mμ (ε): 304(10000) and 450(19500). NMR ($CDCl_3$) τ: 6.35 (s, –CH_2–), 6.38 (s, –$COOCH_3$) and 8.18 (s, C-5-CH_3 of pyrazoline ring).[14]

Found: C, 58.23; H, 4.64; N, 12.70%. Calcd for $C_{16}H_{15}N_3O_5$: C, 58.35; H, 4.59; N, 12.76%.

5-Bromomethyl-3-(5-nitro-2-furyl)-1-phenyl-2-pyrazoline (XIII). Deep red colored crystals, mp 121—122°C (ethanol). Yield: 60%. UV λ_{max}^{EtOH} mμ (ε): 250(8800), 300(10800) and 460(20000). NMR ($CDCl_3$) τ: 5.15 (m, C-5-H of pyrazoline ring)[14] and 6.5 (m, –CH_2– of pyrazoline ring and CH_2Br).

Found: C, 47.69; H, 3.12; N, 11.64%. Calcd for $C_{14}H_{12}N_3O_3Br$: C, 48.01; H, 3.45; N, 12.00%.

3-(5-Nitro-2-furyl)-1-phenyl-indeno[2,3-d]pyrazole (XIV). Pale yellow crystals, mp 238—240°C (ethanol). Yield: 15%. UV λ_{max}^{EtOH} mμ (ε): 270(23000) and 365 (21000). NMR (DMSO-d_6) τ: no signal due to methine

9) T. Sasaki, T. Yoshioka and Y. Suzuki, *Yuki Gosei Kagaku Kyokai Shi*, **27**, 998 (1969).

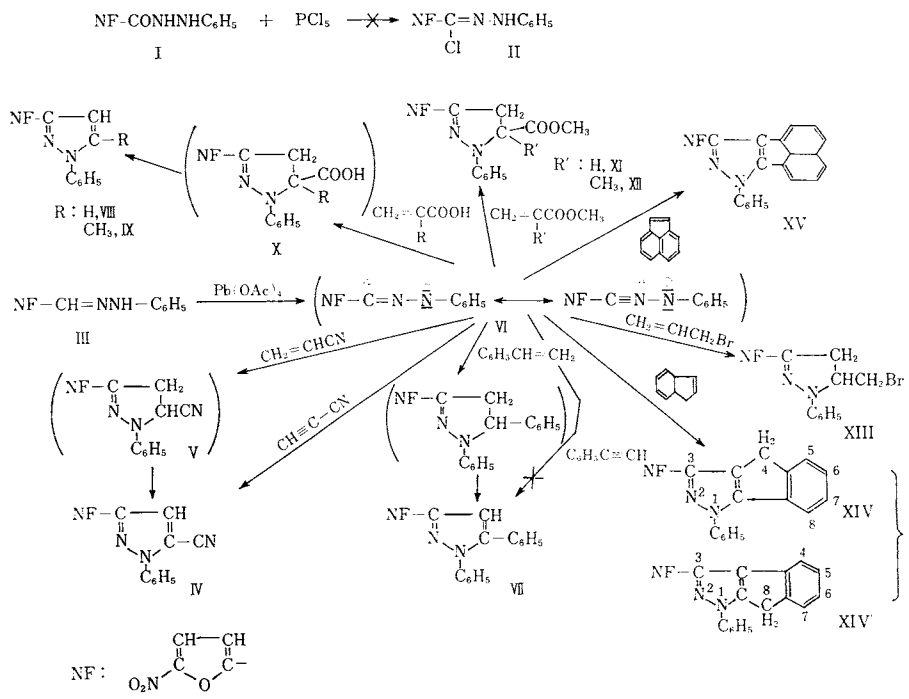
10) Melting points are uncorrected. Microanalyses were carried out with a Yanagimoto C.H.N. Corder MT-1 type. The ultraviolet absorption spectra (UV) were recorded on a Nippon Bunko optical rotary dispersion recorder, Model ORD/UV-5. The infrared spectra (IR) were obtained with a Nippon Bunko IR-S spectrophotometer. The NMR spectra were determined with a Varian A-60 spectrometer, using tetramethylsilane as the internal standard. The chemical shifts are recorded in τ-values.

11) T. Takahashi, H. Saikachi and S. Yoshina, *Yakugaku Zasshi*, **69**, 284 (1949).

12) I. L. Finar and D. M. Rackham, *J. Chem. Soc., B*, **1968**, 211.

13) French 1532848 (Cl. CO7c), 12, July, 1968. *Chem. Abstr.*, **71**, 229 (1969).

14) R. Sustman, R. Huisgen and H. Huber, *Chem. Ber.*, **100**, 1802 (1967).



proton in a range of 3—5 τ.[9]

Found: C, 69.82; H, 3.76; N, 12.10%. Calcd for $C_{20}H_{13}N_3O_3$: C, 69.96; H, 3.83; N, 12.24%.

3-(5-Nitro-2-furyl)-1-phenylacenaphtho[1,2-*d*]pyrazole (XV). Pale yellow crystals, mp 284—286°C (ethanol). Yield: 13%. UV λ_{max}^{EtOH} mμ (ε): 320(18000) and 375(19000). NMR (DMSO-d_6) τ: no signal at 3—5 τ.[9]

Found: C, 73.07; H, 3.31; N, 10.86%. Calcd for $C_{23}H_{13}N_3O_3$: C, 72.81; H, 3.45; N, 11.08%.