ice water and acidified with dilute hydrochloric acid to give 1.17 g. (10%) of XVIII after filtration, as a yellow powder, m.p. 171–173°. One recrystallization from 95% ethanol gave dense yellow needles; m.p. 172–176° dec.

Anal. Calcd. for $C_{10}H_9O_2N$: C, 68.56: H, 5.18; N, 8.00; mol. wt., 175. Found: C, 68.78; H, 5.43; N, 8.30; mol. wt., 173.

An alcoholic solution of XVIII gave a deep red color with ferric chloride suggesting the presence of a phenolic hydroxyl group.[49] Although most oximes also give a red color with ferric chloride solution,[50] 2-indanone, XV, and 1,3-dioximino-2-indanone failed to give any color test with this reagent. The infrared spectrum potassium bromide showed a moderate OH band at 2.97 μ, and a strong band at 6.07 μ (C=N). Ultraviolet: $^{95\%}_{\max}$ 234 mμ (ϵ 3000), *ca.* 262 mμ[51] (ϵ 8000), 287 mμ (ϵ 4000), 303 mμ (ϵ 2700).

The picrate of XVIII was obtained as fluffy yellow needles after one recrystallization from 95% ethanol; m.p. 178–179° dec.

Anal. Calcd. for 2 $C_{10}H_9O_2N{:}C_6H_3O_7N_3$: C, 53.89; H, 3.65; N, 12.09. Found: C, 53.71; H, 3.72; N, 11.74.

Treatment of VI with n-butyl nitrite in potassium ethoxide. A solution of potassium ethoxide was prepared by dissolving 2.79 g. (0.014 g.-atom) of potassium in 95 ml. of absolute ethanol, under nitrogen, with stirring and external cooling (ice bath). VI (18.0 g., 0.714 mole) dissolved in 25 ml. of absolute ethanol was added in one portion. To the brown solution was added dropwise 9.35 ml. (8.26 g., 0.080 mole) of *n*-butyl nitrite over a 15-min. period. At first addition, the solution turned blood red, but after stirring for 3 hr. at 0°, the solution had turned green. The ethanolic solution was evaporated to dryness to yield a dark green residue which was dissolved in a minimum amount of carbon tetrachloride, and then reprecipitated with excess petroleum ether (b.p. 30–60°). The residue was suction-filtered, washed with petroleum ether (avoiding exposure to air a much as possible by keeping the residue covered with ether), and dried *in vacuo* to give a green potassium salt in 19.8 g. yield (87% based on $C_{17}H_{14}NO_3K$). Its infrared spectrum (potassium bromide) showed strong, broad bands at 2.99–3.15 μ (OH,CH) and 6.10–6.17 μ (C=N).

The potassium salt (1.0 g., 0.0031 mole) was dissolved in 20 ml. of ethanol and the whole externally cooled to 0°. Dilute hydrochloric acid was added dropwise with stirring to *p*H 1 during which time a grayish yellow residue appeared. Water (200 ml.) was added and the insoluble crude material (0.7 g., 80%) was filtered and washed with water. Successive crystallizations from 95% ethanol, and methanol gave XIX as soft yellow needles, m.p. range 109–126°.

Anal. Calcd. for $C_{17}H_{15}O_3N$: C, 72.58; H, 5.38; N, 4.98. Found: C, 72.77; H, 5.47; N, 5.14.

XIX gave a positive ferric chloride test and its infrared spectrum showed bands at 2.96 μ (m) (OH), and 6.06 μ (s) (C=N). Ultraviolet:
$\lambda^{95\%\ C_2H_5OH}_{\max}$ 227 mμ[52] (ϵ 41,900), *ca.* 262 mμ[51] (ϵ 12,400), 289 mμ (ϵ 4900), 303 mμ (ϵ 3300).

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(49) The unexpected yellow color and positive phenolic hydroxyl test of 3-hydroxyisoquinoline should be noted [J. H. Boyer and L. T. Wolford, *J. Org. Chem.*, 21, 1297 (1956)].

(50) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, *The Systematic Identification of Organic Compounds*, 4th ed., Wiley, New York, 1956, p. 113.

(51) Inflection.

(52) Very broad band.

[CONTRIBUTION FROM THE PROTECTIVE DEVELOPMENT DIVISION OF THE U. S. ARMY CHEMICAL RESEARCH AND DEVELOPMENT LABORATORIES]

A New Synthetic Route to α-Isonitrosoacetonitriles. The Chlorination of Isonicotinaldehyde Oxime

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A new synthetic route to aromatic and heteroaromatic α-isonitrosoacetonitriles has been found which involves chlorination of the appropriate aldoxime followed by reaction with excess alkali cyanide. The synthesis of a number of α-isonitrosoacetonitriles is presented; in addition, the chlorination of one of the aldoximes is described in detail. It was found that chlorination of isonicotinaldehyde oxime gave isonicotinohydroxamic chloride hydrochloride, which on neutralization with base yielded isonicotinohydroxamic chloride and 3,4-di(4-pyridyl)furoxan. The nitrile *N*-oxide of isonicotinonitrile is a logical intermediate in the synthesis of α-isonitroso-4-pyridineacetonitrile and 3,4-di(4-pyridyl)furoxan; however, no evidence of its formation was found.

During a Beckmann rearrangement study it was necessary to prepare a number of aromatic and heteroaromatic α-isonitrosoacetonitriles. Compounds of this oxime class have been prepared heretofore from the appropriate acetonitrile and alkyl nitrite[1] or nitric oxide,[2] from ω,ω′-dibromoaceto compounds by action of hydroxylamine and alkali,[3] or by boiling the appropriate glyoxime with sodium carbonate.[3] In addition a method limited to aliphatic compounds has been described which involves an oxidation of the reaction product of aldoximes and alkali cyanides.[4] We found the isonitrosation of acetonitriles described by Meyer[1]

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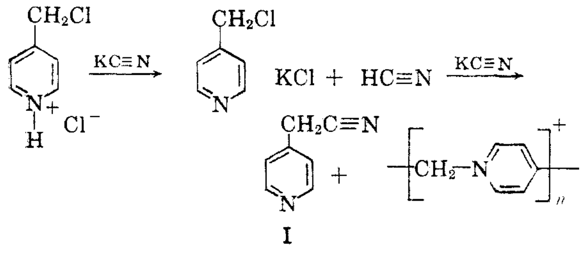
(1) V. Meyer, *Ann.*, 250, 163 (1889).

(2) E. L. Reilly, U. S. Pat. 2,749,358 (1956); *Chem. Abstr.*, 51, 1269 (1957).

(3) (a) A. Russanov, *Ber.*, 24, 3504 (1891). (b) M. R. Zimmerman, *J. Pr. Chem.*, 66, 353 (1902).

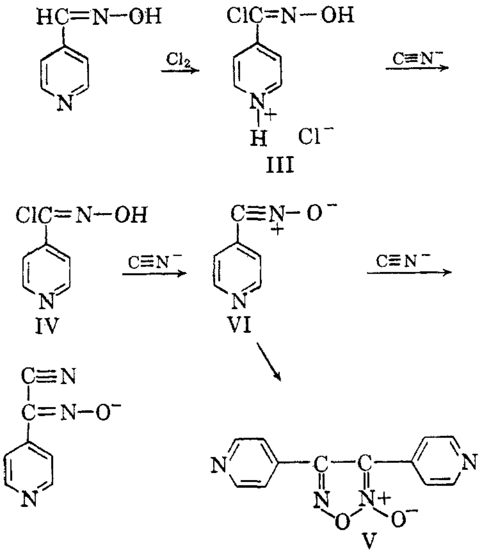
(4) L. W. Kissinger and H. E. Ungnade, *J. Org. Chem.*, 25, 1471 (1960).

as the most convenient general method for α-isonitrosoacetonitriles; however, certain heteroaromatic compounds such as 4-pyridineacetonitrile (I) were neither prepared easily nor available commercially. The synthesis of I presented a special problem due to intermolecular alkylation.[5] In such cases it was found that α-isonitrosoacetonitriles may be synthesized more conveniently by chlorination of the aldoxime followed by reaction with excess cyanide. Details for the synthesis of α-isonitroso-4-pyridineacetonitrile (II) are given in the Experimental. In addition this new method was applied successfully to the synthesis of α-isonitroso-6-methyl-2-pyridineacetonitrile, α-isonitroso-2-pyridineacetonitrile, α-isonitroso-4-quinolineacetonitrile, α-isonitroso-*p*-chlorophenylacetonitrile, and α-isonitrosophenylacetonitrile.



It was noted that chlorination of picolinaldehyde and isonicotinaldehyde oximes had been reported previously by Wiley and Wakefield.[6] The products were described as, "white solids, insoluble in solvents and very soluble in water." The authors[6] postulated that hydroxamic chlorides were formed only momentarily and that the isolated materials were actually hydrochlorides of the nitrile *N*-oxides. Addition of alkali was thought to give the water soluble nitrile *N*-oxides which formed furoxans; alternatively, the hydrochlorides dimerized on standing and addition of alkali liberated the furoxans.[6] It was attractive to examine these interesting postulates since it is reasonable to assume that the nitrile *N*-oxide is a probable precursor in the formation of both the α-isonitrosoacetonitrile and the furoxan (Scheme I).

As reported,[6] isonicotinaldehyde oxime on chlorination gave a colorless solid (III); addition of alkali to aqueous solutions of III yielded a precipitate (IV) which dissolved in excess base to give yet another solid product (V). High water solubility, elemental analysis, and adequate analogy from literature on the chlorination of aldoximes[7] support assignment of a hydroxamic chloride hydrochloride structure to III. Elemental analysis of IV corresponds to calculated values for either the nitrile *N*-oxide hydrochloride or the hydroxamic chloride; however, poor water solubility favors assignment of the covalent hydroxamic chloride structure. Assignment of a furoxan structure to V is in agreement with molecular weight determination and elemental analysis.



The infrared absorption spectra of III, IV, and V are given in Fig. 1. Only the spectrum of V shows features corresponding to those reported for furoxans[8] and none of the spectra contains absorption bands characteristic of both the triple bonds and *N*-oxide linkage of the nitrile oxide.[6] The nitrile

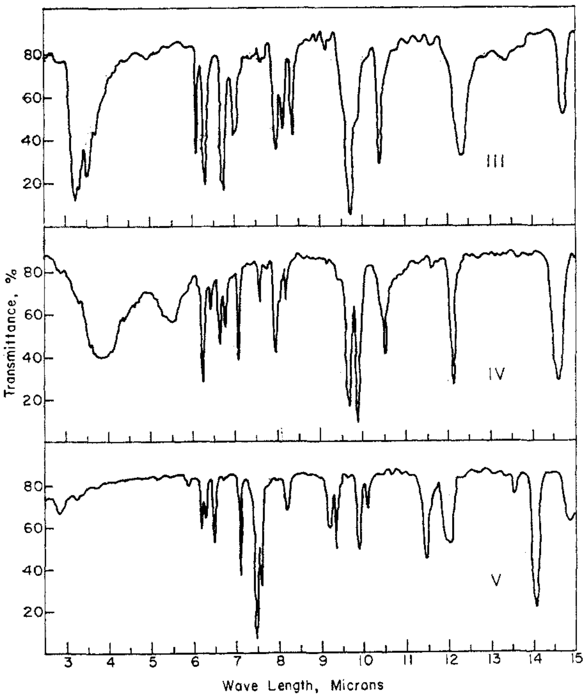


Fig. 1. Infrared absorption spectra of isonicotinohydroxamic chloride hydrochloride (III), isonicotinohydroxamic chloride (IV), and 3,4-di(4-pyridyl)furoxan(V)

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(5) E. J. Poziomek, R. M. Poirier, and J. Stockinger, unpublished results.

(6) R. H. Wiley and B. J. Wakefield, *J. Org. Chem.*, **25**, 546 (1960).

(7) For historical references on the chlorination of aldoximes see ref. 6.

(8) J. H. Boyer, U. Toggweiler, and G. A. Stoner, *J. Am. Chem. Soc.*, **79**, 1748 (1957).

N-oxide of isonicotinonitrile is a logical intermediate in the formation of II and V; however, no evidence of its synthesis was found.

EXPERIMENTAL[9–11]

α-Isonitroso-4-pyridineacetonitrile (II). Chlorine was passed into a methanolic solution of isonicotinaldehyde oxime (30 g., 0.25 mole) at 5–10° for 15 min.; a precipitate formed within 5 min. Other suitable solvents were ether or ethanol. The chlorination product was filtered, then was added to a methanolic solution of potassium cyanide (51 g., 0.80 mole) with vigorous stirring. (The reaction with cyanide and subsequent operations were performed in a very efficient hood to protect the operator from exposure to hydrogen cyanide gas.) The mixture was heated at 60° for 1 hr. with occasional stirring, cooled, filtered, and the filtrate treated with 10% hydrochloric acid to *p*H 5. The resulting mixture was filtered; the residue was washed twice with 200-ml. portions each of water to give 20.0 g. (54.4%) of a tan solid, m.p. 276–278° dec. Its infrared spectrum and melting point were identical to those of a sample prepared by the isonitrosation of 4-pyridineacetonitrile.[5]

Anal. Calcd. for $C_7H_5N_3O$: C, 57.1; H, 3.4; O, 10.9. Found: C, 57.4; H, 3.7; O, 11.0.

Other α-isonitroso analogs were prepared in essentially the same manner as described for II; these are listed in the next section. All of the compounds were either white or tan solids. If it were found that the chlorination product of the carboxaldoxime was soluble in the reaction medium the excess solvent was distilled using a rotating type evaporator and the residue was used directly in the reaction with alkali cyanide. If the final product were soluble in methanol, the reaction mixture was evaporated to dryness, the residue was pulverized with water, and the mixture was filtered. The resulting solid was then recrystallized from water or a combination of water-alcohol.

α-Isonitroso-6-methyl-2-pyridineacetonitrile, 19.0 g. (47%), m.p. 209–210° dec.

Anal. Calcd. for $C_8H_7N_3O$: C, 59.6; H, 4.4; N, 26.1. Found: C, 59.2; H, 4.5; N, 25.4.

α-Isonitroso-2-pyridineacetonitrile, 2.6 g. (11%) m.p. 218–221°. No attempt was made to increase the yield though it is thought that it could be increased substantially. The infrared spectrum and melting point were identical to those of a sample prepared by isonitrosation of 2-pyridineacetonitrile.[5]

Anal. Calcd. for $C_7H_5N_3O.{}^1/_2H_2O$: C, 53.8; H, 3.8; O, 15.4. Found: C, 53.3; H, 3.8; O, 15.0.

α-Isonitroso-4-quinolineacetonitrile, 6.0 g. (48%) m.p. 255–257°.

Anal. Calcd. for $C_{11}H_7N_3O\cdot H_2O$: C, 61.4; H, 4.2. Found: C, 61.3; H, 3.9.

α-Isonitroso-p-chlorophenylacetonitrile, 5.0 g. (9.3%) m.p. 107–109° (reported, ref. 3b, 111–112°). The preparation of this compound was not repeated; however it is felt that the yield could be increased.

Anal. Calcd. for $C_8H_5ClN_2O\cdot 2H_2O$: C, 44.3; H, 4.2; O, 22.2. Found: C, 44.1; H, 4.0; O, 22.1.

α-Isonitrosophenylacetonitrile, 14.0 g. (38%) m.p. 132–133° (reported, ref. 3b, 129°). The infrared spectrum and melting point of this compound were identical to that of a sample prepared by the isonitosation of phenylacetonitrile.[5]

Anal. Calcd. for $C_8H_6N_2O$: C, 65.7; H, 4.1; O, 11.0. Found: C, 65.5; H, 4.0; O, 11.2.

Isonicotinohydroxamic chloride hydrochloride (III). The chlorination product of isonicotinaldehyde oxime described in the preparation of II was filtered to give 48.0 g. (83%) of a white crystalline solid, m.p. 192–193° dec.

Anal. Calcd. for $C_6H_6Cl_2N_2O$: C, 37.3; H, 3.1; Cl, 36.7. Found: C, 37.8; H, 3.1; Cl, 36.0.

Isonicotinohydroxamic chloride (IV). To 27.0 g. (0.14 mole) of III in a minimum amount of cold water was added an aqueous solution of sodium hydroxide (5.6 g. 0.14 mole). The mixture was filtered immediately to give 14 g. (53%) of colorless solid, m.p. 155–156°.

Anal. Calcd. for $C_6H_5ClN_2O\cdot 1^3/_4H_2O$: C, 38.3; H, 4.5; Cl, 18.4. Found: C, 38.4; H, 4.2; Cl, 18.4.

A portion of the product was triturated with methanol and the mixture was filtered to give a colorless solid, m.p. 139–141.5° dec., whose infrared absorption spectrum corresponded to the higher melting hydrate.

Anal. Calcd. for $C_6H_5ClN_2O$: C, 46.0, H, 3.2; Cl, 22.6. Found: C, 45.5; H, 3.3; Cl, 22.1.

3,4-Di(4-pyridyl)furoxan (V). To a mixture of 10.5 g. (0.067 mole) of IV in water was added an aqueous solution of sodium carbonate monohydrate (6.7 g., 0.067 mole). A yellow-orange solution resulted and was stirred for 30 min. at room temperature. A precipitate formed and the mixture was filtered to give 3.0 g. (17.3%) of a grey-tan solid, m.p. 163–168° dec.

Anal. Calcd. for $C_{12}H_8N_4O_2\cdot H_2O$: C, 55.8; H, 3.9. Found: C, 55.2; H, 4.1.

The preparation of the furoxan was repeated a number of times in an attempt to repeat the work of Wiley and Wakefield,[6] who reported a m.p. of 140–141°. Reaction of either III or IV with alkali hydroxides or carbonates at temperatures between 0° to 100° gave white to tan solids whose melting points fell between 133° and 174°. Infrared absorption spectra were similar irrespective of melting point and the elemental analyses indicated various degrees of hydration. It was found that the furoxan was insoluble in water or ether, slightly soluble in hot acetone or methanol, and soluble in hot benzene or dioxane. A portion of the solid whose elemental analyses were given in the previous paragraph was recrystallized from benzene to give a white crystalline solid (needles) m.p. 182–184° dec.

Anal. Calcd. for $C_{12}H_8N_4O_2$: C, 60.0; H, 3.4; N, 23.3; O, 13.3; mol. wt., 240. Found: C, 60.2; H, 3.5; N, 23.7; O, 13.1; mol. wt., 236.

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(9) Melting points are uncorrected.

(10) Infrared spectra were obtained from potassium bromide discs by means of a Perkin-Elmer Infracord (Model 137) spectrophotometer.

(11) Carboxaldoximes were commercially available with exception of *p*-chlorobenzaldoxime. This was prepared from the carboxaldehyde using hydroxylamine in ethanol-water (m.p. 109°; lit.[6] 107–109°).