Condensed Pyrazoles. 1. Nitro and Nitroso Derivatives of Pyrazolo[1,5-*a*]pyridine

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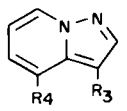
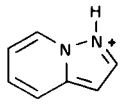
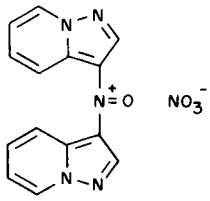
Grandberg and his co-workers (1) have reported that nitration of pyrazolo[1,5-*a*]pyridine (**1**) by refluxing mixed nitric acid-sulfuric acid yields 3-nitropyrazolo[1,5-*a*]pyridine (**2**), m.p. 146°. We have carried out a study seeking reagent-dependent orientation in the nitration of **1** (compare our previous results with arylpyrazoles (2,3), acetanilides (4), and arylpyrimidines (5)). Our results indicate very strongly that the compound, m.p. 146°, obtained by Grandberg and co-workers is actually the 3,4-dinitro species **3**.





1a

1 $R_3 = R_4 = H$
2 $R_3 = NO_2$, $R_4 = H$
3 $R_3 = R_4 = NO_2$
5 $R_3 = NO$ $R_4 = H$



4

Thus, reaction of **1** with fuming nitric acid in acetic anhydride at 0° gave a mixture of a compound, m.p. 186°, and a second product, m.p. 205°. The elemental analysis and mass spectrum of the compound, m.p. 186°, proved it to be a mononitro compound, and its nmr spectrum confirmed that this material is the 3-nitro species **2** (see discussion below). The product with m.p. 205° had elemental analyses, mass spectra, and infrared spectra demanding its formulation as a diaryloxidoammonium nitrate, and the nmr spectrum was consistent with its assignment as di(3-pyrazolo[1,5-*a*]pyridyl)oxidoammonium nitrate (**4**) (see below). Species of this general class have been obtained previously (6), but the easy isolation and stability of **4** merit comment: it was unaffected by attempted oxidation with hydrogen peroxide, or by attempted catalytic reduction with hydrogen and palladised charcoal.

Nitration of **1** by mixed nitric and sulfuric acids at 0° yielded the mononitro species **2** as sole conversion product of **1**; the mononitro compound **2** was also accessible by nitrosation of **1** with sodium nitrite in acetic acid, yielding 3-nitrosopyrazolo[1,5-*a*]pyridine **5**, followed by peroxyacetic acid oxidation. Mixed acids nitration of **1** or of **2** at room temperature yielded a dinitropyrazolo[1,5-*a*]pyridine, m.p. 149°, whose nmr spectrum (see discussion below) required its assignment as 3,4-dinitropyrazolo[1,5-*a*]pyridine (**3**).

Nuclear Magnetic Resonance Assignments.

Data assembled in the Table show that the 3- and 4-protons in **1** show characteristic chemical shifts and interproton couplings, which are absent in species carrying substituents at these positions. The expected deshielding influences of the 3-nitro group are evident, while the second *peri* nitro group causes minor reversals of the deshielding effects, probably reflecting anisotropy changes accompanying mutual rotations of the nitro groups out of the aromatic plane. For the diaryloxidoammonium **4**, some of the proton signals were not resolvable into assignable splitting patterns, but distinct assignable low-field signals from the 2-proton and the 7-proton, and the absence of 2-3 proton coupling, define the structure unequivocally.

Comments on the Reactivity of Pyrazolo[1,5-*a*]pyridine.

Ready dinitration of other pyrazole derivatives under mild conditions similar to those we have used with **1** is known (2,3), and all-valence electron (CNDO/2) (7) calculations for **1** and for its conjugate acid **1a** (see Table II) indicate high total electron densities at the 3- and the 4-positions of each of these species. The bond lengths and bond angles employed are listed in Table III; these parameters give a calculated dipole moment (2.50 D) in better agreement with experiment (2.18 D) than those employed in the similar calculations for pyrazolo-[1,5-*a*]pyridine recently published by Paudler and Chasman (8). Assuming a general correspondence between

TABLE I

Nmr Assignments in Pyrazolo[1,5-*a*]pyridines
(Chemical shifts in ppm from internal TMS,
major (ortho) couplings in Hz)

Proton	Compound Solvent	1 DMSO-d_6	2 for 1, 2,	3 and 3	4 TFA-d
2		8.00	9.20	9.14	9.45
3		6.62	---	---	---
4		7.72	8.58	---	a
5		7.17	8.20	8.58	a
6		6.85	7.68	7.57	a
7		8.70	9.32	9.37	9.08
J_{23}		2.0	---	---	---
J_{45}		9.0	8.0	---	b
J_{56}		6.5	7.5	7.0	b
J_{67}		7.0	6.5	7.0	5.5

(a) A 3-proton multiplet was observed between 450-530 Hz from TMS. (b) Couplings not resolved.

TABLE II

CNDO/2 Electron Densities for Pyrazolo[1,5-*a*]pyridine **1** And Its Conjugate Acid **1a**

Carbon and Nitrogen	1	1a
N(1)	5.191	5.043
C(2)	3.853	3.824
C(3)	4.162	4.124
C(4)	4.059	4.046
C(5)	3.933	3.898
C(6)	4.040	4.016
C(7)	3.902	3.877
N(8)	5.034	4.928
C(9)	3.856	3.803
Hydrogen		
H(1)	----	0.802
H(2)	0.995	0.958
H(3)	0.992	0.930
H(4)	0.989	0.952
H(5)	1.004	0.940
H(6)	0.982	0.922
H(7)	1.002	0.927

total electron density and reactivity towards electrophiles (as was evident for monosubstituted benzenes (9)), the total densities of 4.162 electron and 4.059 electron at the 3- and 4-positions of **1**, and 4.124 electron and 4.046 electron at the 3- and 4-positions of **1a**, suggest that these positions should be at least as reactive as the para position of phenol (where the total electron density is 4.021 (9)). Although the reactivity of the conjugate acid **1a** will surely be lessened by Coulombic repulsion, it is evident that the reaction conditions chosen by Grandberg and co-workers were inordinately severe for a π-excessive species such as pyrazolo[1,5-*a*]pyridine, whether it is undergoing reaction as the conjugate acid or as the free base. We are unable to account for the Russian workers' failure to obtain elemental analyses identifying their product of m.p. 146° (which is surely identical with our **3**, m.p. 149°) as a dinitro species.

TABLE III

Bond Lengths & Bond Angles for the CNDO/2 Calculations

Bond	1	1a
1-2	0.132 nm	0.130 nm
2-3, 3-9, 4-9, 4-5, 5-6, & 6-7	0.140	0.140
7-8	0.134	0.140
8-9	0.134	0.140
8-1	0.145	0.150
Angle		
9-8-1	105°	108°
8-1-2	112	106
1-2-3	107	110
2-3-9	109	108
3-9-8	109	108
8-4-9	115	120
9-4-5, 4-5-6, 5-6-7,	----	----
6-7-8	120	120
7-8-9	125	120

All C-H bonds have length 0.108 nm. The N-H bond is 0.100 nm. All C-H bonds and the N-H bond bisect the bond angles linking the C or N atom to the ring.

EXPERIMENTAL

The following equipment was employed: Melting points, Fisher-Johns apparatus, ir spectra, Beckman IR-8 spectrometer (potassium chloride disk technique), nmr spectra, Varian A-60D spectrometer, elemental analyses, Hewlett-Packard Model 185 CHN Analyzer. Mass spectra were obtained by Dr. L. Y. Foo using the DuPont Model 21-491 instrument at the Halifax Laboratories of the National Research Council. CNDO/2 Calculations were carried out using Program 91 of the Quantum Chem-

istry Program Exchange on the IBM 360/50 system at the University of New Brunswick, Fredericton.

Nitrations of Pyrazolo[1,5-*a*]pyridine.

Using Nitric Acid in Acetic Anhydride.

To pyrazolo[1,5-*a*]pyridine (10) (0.50 g.) in acetic anhydride (15 ml.) at 0° was added, dropwise, a solution (cooled to 0°) of fuming nitric acid (90%, 1 ml.) in acetic anhydride (5 ml.). The resulting solution was stirred for 1 hour and allowed to reach room temperature, poured into water and heated to boiling, and allowed to cool overnight. The precipitated material was collected by filtration and washed with ice water, and extracted with hot chloroform. The chloroform-soluble fraction was crystallized from chloroform yielding yellow needles of 3-nitropyrazolo[1,5-*a*]pyridine (0.41 g., 60%), m.p. 186°; m/e: 163 (100%, M^+), 147 (40%, $M^+ - O$), 117 (60%, $M^+ - NO_2$); ν max 1520 and 1340 cm^{-1} (C-nitro).

Anal. Calcd. for $C_7H_5N_3O_2$: C, 51.54; H, 3.09; N, 25.76. Found: C, 51.10; H, 3.31; N, 25.60.

The residue from the chloroform extraction was washed thoroughly with benzene; simple filtration provided brilliant green needles of di(3-pyrazolo[1,5-*a*]pyridyl)oxidoammonium nitrate (0.16 g.), m.p. 205°; m/e: 264 (15%, M^+ for dipyrazolopyridyloxidoammonium ion); 237 (100%, $M^+ - HCN$); 210 (100%, $M^+ - 2HCN$); ν max 1510 (nitroso); 1430 and 840 cm^{-1} (nitrate).

Anal. Calcd. for $C_{14}H_{10}N_6O_4$: C, 51.54; H, 3.09; N, 25.76. Found: C, 51.60; H, 3.05; N, 25.70.

Using Mixed Nitric-Sulfuric Acids.

At 0°.

Pyrazolo[1,5-*a*]pyridine (0.50 g.) was dissolved in concentrated sulfuric acid (d 1.84, 5 ml.) at 0°; to this solution, a mixture of fuming nitric acid (90%, 0.3 g.) and concentrated sulfuric acid (2 ml.), also at 0°, was added. The mixture was stirred at 0° for 1 hour and poured onto crushed ice. The precipitate was collected and crystallized from chloroform, giving 3-nitropyrazolo[1,5-*a*]-pyridine (0.54 g., 78%) identical with the chloroform-soluble fraction obtained from the nitric acid-acetic anhydride treatment described above.

At Room Temperature (20°).

Using conditions as at 0°, except that an excess of fuming nitric acid (0.8 g. rather than 0.3 g.) was used, gave 3,4-dinitropyrazolo[1,5-*a*]pyridine (0.47 g., 53%), m.p. 149°, as yellow needles from methanol; ν max 1515 and 1300 cm^{-1} (C-nitro).

Anal. Calcd. for $C_7H_4N_4O_4$: C, 40.40; H, 1.94; N, 26.92. Found: C, 40.60; H, 2.05; N, 27.00.

Reaction using the 3-nitro compound as substrate similarly yielded the dinitro compound in 80% yield.

Using a Nitrosation-Oxidation Sequence.

A solution of sodium nitrite (0.60 g.) in water (2.5 ml.) was slowly added to a stirred solution of pyrazolo[1,5-*a*]pyridine (0.70 g.) in acetic acid (5 ml.); the temperature was kept in the range 12-15°. After 15 minutes, the resulting brown solution was poured into water, and the green precipitate was collected and washed with water. Crystallization from acetone gave bright bluish-green needles of 3-nitrosopyrazolo[1,5-*a*]pyridine (0.52 g., 60%), m.p. 145-147°.

Anal. Calcd. for $C_7H_5N_3O$: C, 57.14; H, 3.43; N, 28.56. Found: C, 57.60; H, 3.27; N, 28.30.

The 3-nitrosopyrazolo[1,5-*a*]pyridine (0.50 g.) was dissolved in acetic acid (15 ml.) and hydrogen peroxide (30%, 3.5 ml.) was added. The mixture was heated to boiling for 1 minute, cooled, and poured into water (60 ml.), yielding a yellow precipitate. Collection and crystallization from chloroform yielded 3-nitropyrazolo[1,5-*a*]pyridine (0.50 g., 90%), m.p. 186°, identical with the material obtained above.

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