Oxidation of Aminoheterocycles to Nitroheterocycles with Peroxytrifluoroacetic Acid. I. Pyrazoles and Pyridines (1,2)

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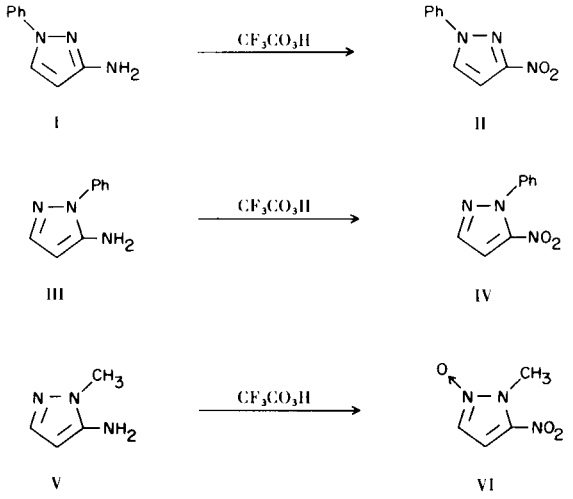
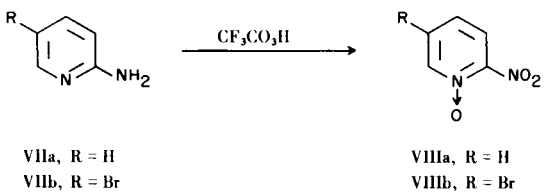
The oxidation of aminofurazans to nitrofurazans with anhydrous peroxytrifluoroacetic acid has been reported in a previous communication from this laboratory (3). The oxidation of other aminoheterocycles with this reagent has subsequently been attempted in order to determine the applicability of this reaction to the synthesis of nitroheterocycles that cannot be obtained by direct nitration.

3-Amino-1-phenylpyrazole (I) and 5-amino-1-phenyl pyrazole (III) were converted to 3-nitro-1-phenylpyrazole (II) and 5-nitro-1-phenylpyrazole (IV), respectively, when treated with an excess of anhydrous peroxytrifluoroacetic acid in dichloromethane. However, under the same conditions, 5-amino-1-methylpyrazole (V) gave 1-methyl-5-nitropyrazole 1-oxide (VI). 3-Aminopyrazole was degraded under these conditions.



2-Aminopyridine (VIIa) and 2-amino-5-bromopyridine (VIIb) were oxidized directly to 2-nitropyridine 1-oxide (VIIIa) and 5-bromo-2-nitropyridine 1-oxide (VIIIb), respectively. The conversion of VIIa to VIIIa has been accomplished previously (4), but a synthetic route involving four steps was necessary.



VIIa, R = H
VIIb, R = Br

VIIIa, R = H
VIIIb, R = Br

Attempted oxidations of melamine, 2-aminopyrimidine, and 5,5′-diamino-3,3′-bi-1,2,4-oxadiazolyl to the corresponding nitro compounds by peroxytrifluoroacetic acid failed. Thus, according to the limited evidence available, it appears that heterocycles that have an amino group on a carbon atom adjacent to two heteroatoms cannot be oxidized to the corresponding nitroheterocycles with peroxytrifluoroacetic acid.

EXPERIMENTAL (5)

3-Nitro-1-phenylpyrazole (II).

Trifluoroacetic anhydride (34 ml., 0.24 mole) was added dropwise with stirring to a slurry of 90% hydrogen peroxide (5.4 ml., 0.20 mole) in methylene chloride (100 ml.) at 0-10° (6). After the addition was completed the solution was allowed to warm to 20° and a solution of 3-amino-1-phenylpyrazole (4.77 g., 0.03 mole) (7) in 25 ml. of methylene chloride was added dropwise. During the addition the exothermic reaction caused the solution to reflux. The solution was refluxed two hours after the addition, cooled, and extracted first with water (2 x 100 ml.) then with aqueous sodium bicarbonate (100 ml.). The solution was dried over magnesium sulfate and evaporated to dryness under reduced pressure. The residue was crystallized from ethanol-water to give 2.68 g. (47%) of II, m.p. 98-99°.

Anal. Calcd. for $C_9H_7N_3O_2$: C, 57.14; H, 3.73; N, 22.21. Found: C, 56.77; H, 3.67; N, 21.77.

5-Nitro-1-phenylpyrazole (IV).

5-Amino-1-phenylpyrazole (4.77 g., 0.03 mole) was oxidized with peroxytrifluoroacetic acid according to the foregoing procedure. The product was crystallized first from ethanol-water followed by benzene-hexane to provide 1.2 g., (21%) of IV, m.p. 99-100°.

Anal. Calcd. for $C_9H_7N_3O_2$: C, 57.14; H, 3.73; N, 22.21. Found: C, 57.00; H, 3.66; N, 22.15.

1-Methyl-5-nitropyrazole 1-Oxide (VI).

A solution of 5-amino-1-methylpyrazole (3.0 g., 0.03 mole) (8) in 25 ml. of methylene chloride was added dropwise to a solution of peroxytrifluoroacetic acid (0.2 mole) in 100 ml. of methylene chloride. After the solution had refluxed two hours, the solvent was removed under reduced pressure. The viscous residue was dissolved in 100 ml. of water and the solution was neutralized with sodium bicarbonate. The neutral solution was evaporated to dryness under reduced pressure and the residue was extracted with methylene chloride. The methylene chloride extracts were dried

over magnesium sulfate and evaporated to an oil, which was extracted with hot heptane. The product crystallized when the heptane extracts were chilled in the freezer. The crystals were collected by filtration and dried to yield 0.41 g. (10%) of VI, m.p. 109°.

Anal. Calcd. for $C_4H_5N_3O_3$: C, 33.57; H, 3.52; N, 29.37. Found: C, 33.48; H, 3.94; N, 29.46.

2-Nitropyridine 1-Oxide (VIIIa).

2-Aminopyridine (2.82 g., 0.03 mole) was subjected to peroxytrifluoroacetic acid oxidation according to the procedure described for the preparation of II. The product was crystallized from ethanol to provide 0.83 g. (20%) of VIIIa, m.p. 89° [lit. (4) m.p. 85-86°].

Anal. Calcd. for $C_5H_4N_2O_3$: C, 42.86; H, 2.88; N, 20.00. Found: C, 42.87; H, 2.97; N, 19.51.

5-Bromo-2-nitropyridine 1-Oxide (VIIIb).

2-Amino-5-bromopvridine (5.19 g., 0.03 mole) was added cautiously in small portions to a solution of peroxytrifluoroacetic acid (0.2 mole) in 100 ml. of methylene chloride. The solution was refluxed for 20 hours, extracted with water (2 x 100 ml.), and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue was recrystallized from ethanol. The yield of VIIIb was 1.71 g. (26%), m.p. 156-157°.

Anal. Calcd. for $C_5H_3BrN_2O_3$: C, 27.42; H, 1.38; N, 12.79. Found: C, 27.51; H, 1.52; N, 12.65.

Acknowledgment.

The author is grateful to Dr. L. C. Smith for helpful criticism of the manuscript.

REFERENCES

(1) This work was performed under the auspices of the U. S. Atomic Energy Commission.

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Received November 3, 1969 Los Alamos, New Mexico 87544