

free products from the reaction of sodium alcoholate and phosphorus oxychloride in toluene. Using a similar method dialkyl phosphorofluoridates were also now prepared from phosphorus oxyfluoride and sodium alcoholates.

An advantage of the method described herein is the complete absence of any chlorine containing compounds. Since phosphorus oxyfluoride can be prepared with excellent yield the described method seems to be generally applicable for the preparation of any dialkyl phosphorofluoridates.

#### EXPERIMENTAL

**Phosphorus oxyfluoride.** Phosphorus oxychloride, 230 g. (1.5 mole) was placed in a four neck round bottom flask equipped with an efficient sealed mechanical stirrer, a feeder for antimony trifluoride powder, a thermometer, and a distillation column. The flask was then heated to 50°. The column was connected to a water cooled descending condenser and three traps cooled with ice water, dry ice-acetone, and liquid air. Antimony trifluoride 178.7 g. (1 mole) was added during 3 hr. to the reaction mixture while the temperature was maintained at 50–70°. The stirring mixture was then heated for an additional 2 hr. The reaction products distilled into the condenser system.

On redistilling the condensed products 20.5 g. phosphorus oxydichlorofluoride (5% based on  $\text{SbF}_3$ ), b.p. 53° and 98 g. phosphorus oxyfluoride (94% based on  $\text{SbF}_3$ ), b.p. -40° and a trace of phosphorus oxychlorodifluoride, b.p. +3° were obtained.

An analogous reaction, using phosphorus oxybromide was carried out in a similar manner, except that the further 2 hr. heating was carried out at 100°. Phosphorus oxyfluoride, b.p. -40° was again the main product. Phosphorus oxybromodifluoride (b.p. 30°) and phosphorus oxydibromofluoride (b.p. 110°) were also formed as low-yield products.

**Dialkyl phosphorofluoridate from phosphorus oxyfluoride with alcohols. Diisopropyl phosphorofluoridate.** (a) Absolute ether (250 ml.) was placed in a 500 ml. four neck round bottom flask equipped with a sealed mechanical stirrer, dropping funnel, thermometer, and feeding neck closed with a calcium chloride tube. The flask was cooled in a dry ice-acetone mixture. To the cooled ether solution 26 g. (0.25 mole) of phosphorus oxyfluoride, and then, with continuous stirring and cooling 30 g. (0.5 mole) of isopropyl alcohol were added. After the addition of the isopropyl alcohol was complete, the temperature of the solution was allowed to reach 20° and dry ammonia gas was introduced until the reaction mixture was neutral to litmus. The ammonium fluoride which separated was removed by filtration. The ether was stripped from the system and the product distilled to give 30.8 g. (67%) diisopropyl phosphorofluoridate, b.p. 60–61°/10 mm.

*Anal.* Calcd. for  $\text{C}_6\text{H}_{14}\text{FO}_2\text{P}$ : F, 10.32. Found: F, 11.0.

(b) A mixture of 60 g. (1 mole) of isopropyl alcohol and 250 ml. of ether was placed in a four-necked round-bottomed flask equipped with a sealed mechanical stirrer, gas inlet tube, dropping funnel, and thermometer. The solution was cooled with a dry ice-acetone mixture and then 52 g. (0.5 mole) of phosphorus oxyfluoride was added with stirring and cooling. The phosphorus oxyfluoride dissolved instantly. Anhydrous pyridine, 79 g. (1 mole) was added to the solution at about -40°. After the addition of the pyridine was complete, the mixture was allowed to reach room temperature about 20° while stirring was continued. When the stirring was stopped, the reaction mixture separated in two phases. The lower pyridine layer was discarded and the upper ethereal layer was distilled. After removing the ether, diisopropyl phosphorofluoridate (84.5 g., 93%) b.p. 60–61°/10 mm. was obtained.

*Anal.* Found: F, 10.6.

**Diethyl phosphorofluoridate** was similarly prepared according to method (b). The yield was 89%, b.p. 48–49°/10 mm.

*Anal.* Calcd. for  $\text{C}_4\text{H}_{10}\text{FO}_2\text{P}$ : F, 12.18. Found F, 12.4.

**Dimethyl phosphorofluoridate** was also obtained with method (b) in a similar way. Yield 91%, b.p. 58–59°/20 mm.

*Anal.* Calcd. for  $\text{C}_2\text{H}_6\text{FO}_2\text{P}$ : F, 14.85. Found: F, 14.65.

**Dialkyl phosphorofluoridate from phosphorus oxyfluoride with sodium alcoholates. Diisopropyl phosphorofluoridate.** In a four neck round bottom flask, equipped as described previously 50 ml. of toluene was added. The flask was cooled in  $\text{CO}_2$ -acetone and then 26 g. (0.25 mole) phosphorus oxyfluoride was condensed into the cold toluene. To this mixture a sodium isopropylate suspension, prepared by using 11.5 g. (0.5 mole) sodium and 30 g. (0.5 mole) isopropyl alcohol in 200 ml. toluene, was added with efficient stirring and Dry Ice-acetone cooling. Thereafter, the mixture was allowed to reach room temperature with continuous stirring. The separated sodium fluoride was removed by filtration and the filtrate was distilled yielding 27 g. (58%) of diisopropyl phosphorofluoridate, b.p. 82–85°/20 mm.

*Anal.* Calcd. for  $\text{C}_6\text{H}_{14}\text{FO}_2\text{P}$ : F, 10.32. Found: F, 10.45.

**Dimethyl phosphorofluoridate** was similarly prepared by the adding the equimolar quantity of sodium methylate as a methanolic solution to the phosphorus oxyfluoride solution. The yield was 77%, b.p. 58–60° at 20 mm.

*Anal.* Calcd. for  $\text{C}_2\text{H}_6\text{FO}_2\text{P}$ : F, 14.84. Found: 14.6.

**Diethyl phosphorofluoridate** was prepared according to the preparation of dimethyl phosphorofluoridate. In a manner described in the previous example 0.2 mole of sodium ethylate in alcoholic solution was added to 10.4 g. (0.1 mole) phosphorus oxyfluoride also in alcohol with dry ice-acetone cooling. On working up the reaction mixture 12.5 g. (80%) diethyl phosphorofluoridate, b.p. 47–49°/10 mm., was obtained.

*Anal.* Calcd. for  $\text{C}_4\text{H}_{10}\text{FO}_2\text{P}$ : F, 12.18. Found: F, 12.0.

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### Preparation of Pyridinedicarboxylic Acid *N*-Oxides

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Although the pyridinedicarboxylic acid *N*-oxides and several substituted pyridinedicarboxylic acid *N*-oxides are known<sup>1–7</sup> and were prepared, in most cases, by the usual peracid oxidation of the pyridinedicarboxylic acid, none of the corresponding pyridinedicarboxylic acid *N*-oxides are reported.

- (1) O. Diels and K. Alder, *Ann.*, **505**, 103 (1933).
- (2) O. Diels and H. Pistor, *Ann.*, **530**, 87 (1937).
- (3) E. Ghigi, *Ber.*, **75**, 1318 (1942).
- (4) G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, S133 (1949).
- (5) G. R. Clemo and H. Koenig, *J. Chem. Soc.*, S231 (1949).
- (6) E. C. Taylor, Jr., and A. J. Crovetti, *J. Org. Chem.*, **19**, 1633 (1954).
- (7) E. C. Taylor, Jr., and A. J. Crovetti, *J. Am. Chem. Soc.*, **78**, 214 (1956).

Initial attempts to prepare 2,6-pyridinedicarboxylic acid *N*-oxide by peracetic or performic acid oxidation of 2,6-pyridinedicarboxylic acid led to recovery of unreacted dicarboxylic acid, even when large excesses of peracid at elevated temperatures were used.<sup>8</sup> 2,5-Pyridinedicarboxylic acid also was unreactive to *N*-oxide formation by peracetic acid, although a small yield of *N*-oxide was isolated in one experiment when a 40-fold excess of peracid was used at 80–100°. These results might have been anticipated in the light of patents<sup>9</sup> which describe the use of 2,5- and 2,6-pyridinedicarboxylic acids as stabilizers for hydrogen peroxide, persulfuric and peracetic acids, although it was not demonstrated whether the stabilizing action was due to the pyridine diacid or the *N*-oxide.

2,5- and 2,6-Pyridinedicarboxylic acid *N*-oxide were prepared in good yields by oxidizing the sodium salts of the dicarboxylic acid in water-acetic acid solution with peracetic acid. Structures of the *N*-oxides were indicated by analyses and by decarboxylation to the known nicotinic and picolinic acid *N*-oxides. Although excess acetic acid was present, the relatively high dissociation constant<sup>10</sup> of the first carboxylic acid group of the pyridine diacid ensures that the species being oxidized was the mono-salt, probably in equilibrium with the disalt.

The low reactivity of the pyridine diacids toward electrophilic attack on the nitrogen atom is at least in part due to steric hindrance and/or Zwitterion formation, but an additional effect is the accumulation of electron withdrawing substituents on the pyridine nucleus, a phenomenon observed also by Taylor and Croveti.<sup>7</sup> It is suggested that all the above effects are removed or minimized by oxidizing the diacid as the mono- or disodium salt.

#### EXPERIMENTAL

2,6-Pyridinedicarboxylic acid, 2,5-pyridinedicarboxylic acid monohydrate and picolinic acid *N*-oxide were obtained from Aldrich Chemical Co.; melting points are uncorrected.

*2,6-Pyridinedicarboxylic acid N-oxide.* 2,6-Pyridinedicarboxylic acid (5.01 g., 0.03 mole) was dissolved in 45 g. of 6.67% aqueous sodium hydroxide, and to this was added 10 g. of 45% peracetic acid in acetic acid, concurrently with 20 g. 10% aqueous sodium hydroxide. After heating at 60° for 1 hr. an additional 5 g. peracetic acid solution was added and the solution was warmed on the steam bath for 1 hr. The solution was cooled, acidified with conc. HCl, and filtered, and the white crystals were dried to yield 4.0 g. (73% yield) of 2,6-pyridinedicarboxylic acid *N*-oxide, m.p. 155–157°. Mixed m.p.'s with 2,6-pyridinedicarboxylic acid and with picolinic acid *N*-oxide were depressed (146° and 116°, respectively).

(8) We are indebted to Mr. P. S. Starcher of this department for these observations.

(9) F. P. Greenspan and D. G. MacKellar, U. S. Patent 2,609,391 (Sept. 2, 1952); F. P. Greenspan, U. S. Patent 2,624,655 (Jan. 6, 1953); F. P. Greenspan and D. G. MacKellar, U. S. Patent 2,663,621 (Dec. 22, 1953).

(10) V. D. Canic, *Ber. Chem. Ges. Belgrad*, 20, 29 (1955), as reported in *Chem. Zentr.* 128, 381 (1957).

*Anal.* Calcd. for C<sub>7</sub>H<sub>7</sub>O<sub>3</sub>N: C, 45.91; H, 2.75; N, 7.65; acid equiv., 91.5. Found: C, 45.54; H, 3.06; N, 7.94; acid equiv., 93.

The decarboxylation of 2,6-pyridinedicarboxylic acid *N*-oxide was accomplished by immersing a test tube containing the *N*-oxide (4.0 g.) in a bath held at 155°; as the contents melted, vigorous gas evolution was observed and the temperature rose to 163°. After 4 min., the test tube was cooled. The resulting solid mass was dissolved in hot methanol and filtered while hot, and the filtrate was allowed to cool. The crystals obtained were recrystallized again from methanol, m.p. and mixed m.p. with authentic picolinic acid *N*-oxide, 153–154°.

*2,5-Pyridinedicarboxylic acid N-oxide.* Conditions similar to those for oxidation of 2,6-pyridinedicarboxylic acid were used; 15.0 g. of 2,5-pyridinedicarboxylic acid monohydrate gave 14 g. (86%) 2,5-pyridinedicarboxylic *N*-oxide as light tan crystals, m.p. 241–244°, mixed m.p. with starting material, 216–218°.

*Anal.* Calcd. for C<sub>7</sub>H<sub>5</sub>O<sub>3</sub>N: C, 45.91; H, 2.75; N, 7.65; acid equiv. 91.5. Found: C, 46.08; H, 3.20; N, 7.73; acid equiv., 91.9.

The decarboxylation of 2,5-pyridinedicarboxylic acid *N*-oxide was accomplished by heating the above product in ethylene glycol at 150° for 30 min., to give nicotinic acid *N*-oxide, m.p. 246–248° (methanol). Mixed m.p.'s of this product with starting dicarboxylic acid *N*-oxide and with nicotinic acid (m.p. 234°) were depressed (199–208° and 187–230°, respectively). Acid equiv.: calcd. for C<sub>6</sub>H<sub>5</sub>O<sub>2</sub>N: 139; found: 143.

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### Rearrangement of 4-Amino-6-chloro-1-methylpyrazolo(3,4-d)pyrimidine in Basic Solution<sup>1</sup>

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When 4-amino-6-chloro-1-methylpyrazolo(3,4-d)pyrimidine (I)<sup>4</sup> was refluxed in dilute alkaline solution, the expected 4-amino-6-hydroxy-1-methylpyrazolo(3,4-d)pyrimidine (IV) was not obtained. Instead, the isomeric 6-amino-4-hydroxy-1-methylpyrazolo(3,4-d)pyrimidine (II) was formed in 68% yield. The product was identified by comparison of ultraviolet absorption spectra, as well as by the R<sub>f</sub> values of authentic samples of both 4-amino-6-hydroxy-1-methylpyrazolo(3,4-d)pyrimidine<sup>4</sup> and 6-amino-4-hydroxy-1-methylpyrazolo(3,4-d)pyrimidine<sup>4</sup> previously prepared.

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(4) C. C. Cheng and R. K. Robins, *J. Org. Chem.*, 23, 852 (1958).