hydride and 10 ml. of water in 50 ml. of isopropyl alcohol was stirred for 18 hr. at 25°. After 2 ml. of aqueous 6*N* hydrochloric acid had been added dropwise, the solution was concentrated to give a residue which was diluted with water and extracted with ether. The organic phase was washed with dilute ammonia and with water and was concentrated. Recrystallization of the dried residue from dichloromethane–petroleum ether afforded 300 mg. (78%) of long needles; m.p. 111–113°; infrared spectrum: 3.00 (OH and NH), 6.10, 6.50 μ (secondary amide).

Anal. Calcd. for $C_{11}H_{15}NO_2$ (193.24): C, 68.37; H, 7.82; N, 7.25. Found: C, 68.76; H, 7.95; N, 7.15.

3-Isopropoxy-1-isoindolinone from phthalimide. To a solution of 441 mg. (0.003 mole) of phthalimide in 300 ml. of isopropyl alcohol was added 468 mg. (0.012 mole) of sodium borohydride. After the mixture had been stirred for 18 hr. at 25°, 3 ml. of aqueous 6*N* hydrochloric acid was added dropwise. The solution was kept at 25° for 24 hr. to ensure completion of isopropyl ether formation. After 10 ml. of 6*N* ammonia had been added, the solution was concentrated to give a residue which was extracted with ether. The organic phase was washed with dilute ammonia and with water and was concentrated to give a product which was dissolved in 10 ml. of isopropyl alcohol containing 1 ml. of aqueous 3*N* potassium hydroxide. After 10 min. at reflux temperature to ensure hydrolysis of traces of phthalide, the solution was concentrated to give a residue which was diluted with 5 ml. of water. After 15 hr. at 0°, the precipitate was collected, washed with water, and dried to give 200 mg. (35%); m.p. 125–128°. Recrystallization from water gave heavy prismatic needles, m.p. 133–134° (*cf.* ref. 5: 125°); infrared spectrum: 3.05 (NH), 5.90, 6.00 μ (amide).

Anal. Calcd. for $C_{11}H_{13}NO_2$ (191.22): C, 69.09; H, 6.85; N, 7.33. Found: C, 69.10; H, 6.79; H, 7.30.

Phthalide (V) *from phthalimide.* To a solution of 588 mg. (0.004 mole) of phthalimide and 20 ml. of water in 100 ml. of isopropyl alcohol was added 624 mg. (0.016 mole) of sodium borohydride. After the mixture had been stirred for 20 hr. at 25°, 5 ml. of aqueous 6*N* hydrochloric acid was added dropwise. The solution was concentrated to give a residue which was dissolved in 7 ml. of hot water. After 15 hr. at 0°, the precipitate was collected, washed with water, and dried. A benzene solution of the 1 g. of solid (which contained boric acid) was poured through a column of 30 g. of aluminum oxide. The residue from concentration of the benzene eluate was recrystallized from dichloromethane–petroleum ether to give 320 mg. (60%) of small transparent plates; m.p. 72–73°[7]; infrared spectrum: 5.70 μ (lactone).

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Pyridine 1-Oxides. VIII. Hydrolysis of 4-Nitro-3-picoline[1]

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During the course of our investigations of pyridine 1-oxides, it was noticed that freshly distilled 4-nitro-3-picoline,[3] when left at room temperature for several days partially exposed to the atmosphere, slowly deposited a light yellow solid. This observation had not been made by Herz and Tsai.[3] Suction filtration of the mixture gave unchanged 4-nitro-3-picoline as the filtrate, but separation of the solid material in this manner seemed to accelerate the formation of more solid in the filtrate. The rate of solid formation was increased by the presence of water but not by bubbling oxygen through the oil. The yellow solid was insoluble in ethanol but very soluble in water; the *p*H of the solution was 3. By contrast, 4-nitro-3-picoline is very soluble in ethanol but insoluble in water.

Addition of alkali to the aqueous solution of the solid followed by extraction with benzene and then with chloroform (see Experimental) effected a separation of the yellow solid into two crystalline compounds. Both exhibited absorption bands at 1645 cm.$^{-1}$ in the infrared characteristic of the carbonyl stretching band in pyridones (1650–1630 cm.$^{-1}$ [4]) Microanalytical data then allowed the assignment of the structure 3-methyl-4-pyridone (I. R = —CH_3) to the lower melting solid (m.p. 92–94°) and the structure 1-(3′-methyl-4′-pyridyl)-3-methyl-4-pyridone (II. R = —CH_3) to the higher melting solid (m.p. 197–198°). An authentic sample of 3-methyl-4-pyridone was made for comparison by catalytic reduction of 4-hydroxy-3-picoline-1-oxide, which in turn was prepared by alkaline hydrolysis of 4-chloro-3-picoline 1-oxide.

Recrystallization of the original yellow solid from methanol yielded two different crystalline compounds, of which one was obtained pure by hand separation of the crystals. This proved to be the nitric acid salt of 3-methyl-4-pyridone (I. R = —CH_3); an authentic sample was prepared independently by treatment of 3-methyl-4-pyridone with dilute nitric acid. The origin of the nitric acid is not known with certainty, although it seems probable that it must have arisen by air oxidation of the nitrous acid formed during the hydrolysis of 4-nitro-3-picoline and of III (see below).

It has been reported by den Hertog[5] that 4-nitropyridine behaves similarly upon standing. Analogous products (I and II. R = H) were obtained and the suggestion was made that these products arose as outlined on page 3002.

It appears that the above displacement and hydrolytic reactions may be general for 4-nitropyridines, and care should be taken in storing and handling such compounds to exclude all traces of moisture.

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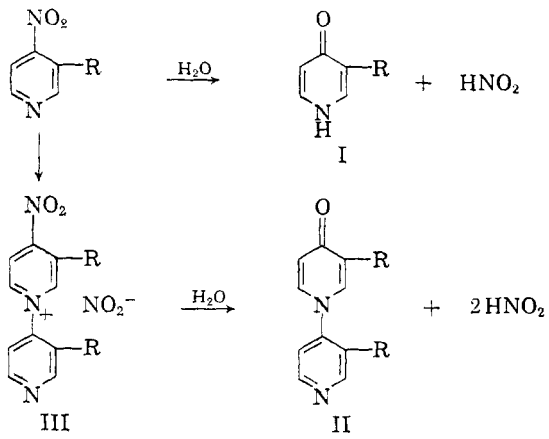

EXPERIMENTAL

4-Hydroxy-3-picoline 1-oxide. To a solution of 2.0 g. of potassium hydroxide in 20 ml. of water was added 2.0 g. of 4-chloro-3-picoline-1-oxide,[6] and the yellow solution was heated under reflux for 16 hr. Dilute hydrochloric acid (6*N*) was slowly added to *p*H 7 and the sodium silicate which separated was filtered and washed with water. The combined filtrates were acidified to *p*H 4 with hydrochloric acid and evaporated to dryness. Extraction of the residue with 100 ml. of absolute ethanol and evaporation of the ethanol extract yielded an amorphous tan solid which was triturated with cold ethanol. Filtration yielded 0.52 g. (30%) of 4-hydroxy-3-picoline-1-oxide, m.p. 215–216°. This material is reported to melt at 224°.[6]

1-(3'-Methyl-4'-pyridyl)-3-methyl-4-pyridone (II, R = —CH_3). The light yellow solid (1.87 g., m.p. 145–150° dec.) which had spontaneously precipitated from a sample of 10 g. of 4-nitro-3-picoline[3] on standing was collected by filtration and washed with ethanol. It was then dried, dissolved in 50 ml. of water and sodium carbonate added to *p*H 10. The resulting solution was evaporated to dryness under reduced pressure, the residue refluxed with 300 ml. of benzene for 30 min. and then filtered hot. Evaporation of the filtrates to dryness yielded 0.72 g. of a yellow solid, m.p. 165–175°. Sublimation at 140°/0.3 mm. removed a small amount of 3-methyl-4-pyridone, m.p. 91–94° (see below), and sublimation at 170°/0.3 mm. then yielded white crystals, m.p. 197–198°.

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 72.0; H, 6.0; N, 14.0. Found: C, 71.7; H, 6.1; N, 14.2.

3-Methyl-4-pyridone (I, R = —CH_3). Method A. The residue from the benzene extraction above was refluxed with chloroform and filtered hot. Evaporation of the chloroform filtrate to dryness yielded 0.27 g. of an oil which solidified on standing to a light yellow solid, m.p. 90°. Recrystallization from a mixture of ethanol, ether and petroleum ether (b.p. 40–60°) (1:5:25) gave light tan crystals, m.p. 92–94°.

Anal. Calcd. for C_6H_7NO: C, 66.0; H, 6.5; N, 12.8. Found: C, 66.1; H, 6.5; N, 12.6.

Method B. A solution of 0.25 g. of 4-hydroxy-3-picoline-1-oxide in 100 ml. of methanol was hydrogenated in the presence of 0.25 g. of 10% palladium-on-carbon catalyst and under 3 atm. of hydrogen at 43° for 8 hr. Removal of the catalyst by filtration and evaporation of the alcoholic filtrate gave a tan oil which solidified after extraction with boiling benzene; yield, 0.18 g. (82%), m.p. 92°. This material was identical in every respect with the product obtained by Method A above, as judged by a mixed melting point determination and comparison of infrared spectra.

Nitric acid salt of 3-methyl-4-pyridone. Method A. The yellow solid which had spontaneously precipitated from 4-nitro-3-picoline upon standing was collected by filtration, washed with ethanol and ether, and recrystallized from methanol. A product consisting of yellow crystals, m.p. 163° dec. and orange-yellow plates, m.p. 180° dec., was obtained. Hand separation of the crystals allowed the isolation in pure form of the plates, m.p. 180°d., which were recrystallized from methanol.

Anal. Calcd. for $C_6H_8N_2O_4$: C, 41.9; H, 4.7; N, 16.3. Found: C, 42.1; H, 4.6; N, 16.1.

The yellow crystals melting at 163° dec., appeared on the basis of microanalysis to be a mixture of the nitric acid salts of 3-methyl-4-pyridone and 1-(3'-methyl-4'-pyridyl)-3-methyl-4-pyridone. They were not further characterized.

Method B. Addition of 3.0 ml. of dilute nitric acid to 0.03 g. of 3-methyl-4-pyridone in water, followed by evaporation to dryness, yielded light yellow crystals, m.p. 180° dec., identical in every respect with the material prepared by Method A above.

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Preparation of 1-Phenyl-2-methyl-2-hydrazinopropane Hydrochloride and Its Isopropyl Derivative

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In view of the current interest in hydrazine derivatives of β-phenethylamine and the recent paper by Biel and co-workers[1] on the chemistry and structure activity relationships of aralkylhydrazines as central stimulants, we have prepared in our laboratory 1-phenyl-2-methyl-2-hydrazinopropane hydrochloride and *N*-(1-phenyl-2-*t*-butyl)-N^1-isopropylhydrazine hydrochloride to elucidate further the relationship between structure and pharmacological activity. The compounds were tested for hypotensive activity in dogs and cats. *N*-(1-Phenyl-2-*t*-butyl)-N^1-isopropylhydrazine hydrochloride produced only transient depressor responses in anesthetized dogs following intravenous injections of doses of 2 to 8 mg./kg. The compound, 1-phenyl-2-methyl-2-hydrazinopropane hydrochloride in doses up to 4.5 mg./kg. possesses intense vasopressor activity in anesthetized dogs.

N-Formyl-2-phenyl-*t*-butylamine (II) was prepared with slight modification of the procedure given by Ritter and Kalish.[2] We obtained the amide as a white solid with 92% yield. The authors[2] reported the amide as a viscous liquid and obtained 62% yield. The amide was hydrolyzed to the amine

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