hr. On cooling, in most cases the cyclization product was obtained crystalline, otherwise the solvent was evaporated *in vacuo* and the residue left for crystallization. The products were recrystallized from ethanol and the yields were usually in the range of 50–80%; only in the case of compounds No. 9, 10 and 12 were they 10–15%.

2-Phenylimino-3-methyl-1,3,4-thiadiazoline was prepared by the above procedure from 2-methyl-4-phenylthiosemicarbazide and by methylation of 2-phenylamino-1,3,4-thiadiazole with methyl iodide.[1] Crystallization from ethanol afforded the pure substance with m.p. and mixed m.p. 260° (lit.[1] m.p. 258°).

Anal. Calcd. for $C_9H_9N_3S$: N, 21.98. Found: N, 21.80.

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2-Imidazolone- and 2-Imidazolidonepropionic Acids

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The importance of oxygenated imidazoles in the metabolism of histidine[1] has led us to synthesize 2-imidazolonepropionic acid and the corresponding imidazolidone for metabolic studies. The method was analogous to that of Dittmer, *et al.*[2] involving the synthesis of 5-aminolevulinic acid and its condensation with potassium cyanate. The overall yield of imidazolone from methyl 5-chlorolevulinate was 50%. High pressure reduction of the imidazolone[2] was unnecessary; the solubility of the imidazolidone in acetic acid facilitated smooth reduction with Adam's catalyst at atmospheric pressure.

EXPERIMENTAL[3]

Methyl 5-chlorolevulinate was prepared from methyl 4-chloro-4-oxobutyrate by the method described by Neuberger and Scott,[4] b.p. 92–94° (2 mm.), 99–101° (3 mm.), 128–131° (23 mm.) and n_D^{25} 1.4536. Infrared peaks in cm.$^{-1}$ ($CHCl_3$) follow: strong—1733, 1437, 1399, 1356, 1325, 1240–1200, 1172–1168; moderate—2924, 1087, 1021–1017, 992, 966–962; weak—3520–2420, 3229–3150, 1620, 889–881, 867–866, 842–837.

The *2,4-dinitrophenylhydrazone*, after several recrystallizations from methanol, was obtained as yellow-orange flat elongated plates, m.p. 109–112°.

Anal. Calcd. for $C_{12}H_{13}N_4O_6Cl$: C, 41.81; H, 3.80; Cl, 10.29. Found: C, 41.79; H, 3.95; Cl, 10.19.

Methyl 5-phthalimidolevulinate, although reported,[4] was prepared by the method of Dittmer[2] in 60–75% yields. Recrystallization from alcohol was far more convenient than from water.

2-Imidazolone-4(5)-propionic acid. Crude methyl 5-phthalimidolevulinate (29.15 g., 0.106 mole) was refluxed with 300 ml. of 6*N* hydrochloric acid for 8 hr., cooled, and filtered from phthalic acid.[5] The filtrate was concentrated *in vacuo* and again three times from water, finally on the oil pump, to yield 20.36 g. of gummy crystals. The crude amino acid hydrochloride was added to 40 ml. of water and filtered from 0.95 g. of 5-phthalimidolevulinic acid. To the solution potassium cyanate (15.0 g., 0.185 mole, in 25 ml. of water) was added as rapidly as possible without allowing the solution to warm up, maintaining the *p*H around 5 by the addition of acetic acid. The precipitating solution was shaken intermittently until gas evolution ceased and was then warmed over steam for an hour. After chilling, the light tan product was collected: 12.74 g. (77%), m.p. 251–253° dec. The product was combined with 1.0 g. of product from a previous run, dissolved in 70 ml. of hot sodium bicarbonate solution, filtered, and acidified while hot with 6*N* hydrochloric acid until precipitation ceased (*p*H 3). After chilling, filtration provided 11.50 g. of nearly white crystals, which began to decompose (black) at 253–255° and melted from 255–257°. This sample was used for analysis, but recrystallization from 30% alcohol provided a whiter product, though in poorer yield and no better melting point. Acetic acid provided white crystals dec. (black) 263–263.5° but recovery was moderate.

Anal. Calcd. for $C_6H_8N_2O_3$: C, 46.15; H, 5.16; N, 17.95. Found: C, 46.24; H, 5.27; N, 17.81.

Infrared bands in cm.$^{-1}$ (Nujol) follow: strong—1699–1691, 1625–1598; moderate—3369, 3280, 3165, 1414, 1350, 1303, 1242, 775; mod. to weak—1221, 1194, 1020, 794, 753–742, 735–732; weak—1960–1909, 1085, 1058, 1003, 919, 910.

Ultraviolet (water): end absorption, 220 mμ, log ϵ 3.77[6]; in acid, λ_{max} 310 mμ, log ϵ 2.33, plus end absorption, 220 mμ, log ϵ 3.29; in base, λ_{max} 296 mμ, log ϵ 2.66, plus end absorption, 230 mμ, log ϵ 3.28.

2-Imidazolidone-4(5)-propionic acid. 2-Imidazolone-4(5)-propionic acid (11.50 g.) as a slurry in 280 ml. of acetic acid was added to 1.50 g. of Adam's catalyst (prereduced in 20 ml. of acetic acid) and stirred under hydrogen at atmospheric pressure for 16 hr. when uptake ceased at the theoretical amount. Solution had occurred when about 80% reduced. The solution was filtered and concentrated *in vacuo* to a solid, which was dissolved in about 10 ml. of hot water. Chilling afforded 9.38 g. of hard, tiny, colorless crystals, insoluble in acetone, m.p. 159–160°. Recrystallization did not raise the melting point. Recrystallization proceeds well from acetic acid, in which it is less soluble. Concentration of the mother liquor to 3 ml. yielded another 0.65 g., m.p. 152–156°.

Anal. Calcd. for $C_6H_{10}N_2O_3$: C, 45.56; H, 6.37; N, 17.72. Found: C, 45.74; H, 6.20; N, 17.69.

Infrared in cm.$^{-1}$ (Nujol): strong—1709, 1652, 1290–1269, 1197; moderate—3335, 3251, 2658, 2565–2512, 1497, 1408, 1345, 1306, 1167, 1107, 904, 764; weak—1886–1873, 1033, 964, 877, 806.

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(1) D. D. Brown and M. W. Kies, *J. Am. Chem. Soc.*, **80**, 6147 (1958); D. D. Brown and M. W. Kies, *J. Biol. Chem.*, **234**, 3182 (1959); H. Tabor, *Pharmacol. Revs.*, **6**, 229 (1954).

(2) K. Dittmer, M. F. Ferger, and V. du Vigneaud, *J. Biol. Chem.*, **164**, 19–28 (1946).

(3) Analyses were performed by W. C. Alford, Analytical Laboratory, National Institutes of Health, Bethesda, Md. Infrared spectra were run by O. Silva, NIMH, National Institutes of Health, on a Perkin-Elmer Double Beam Model 21. Ultraviolet spectra were run by L. S. Pijanowski, Department of Chemistry, University of Florida, Gainesville, Fla. Melting points were determined under a microscope on a Fisher-Johns Melting Point Apparatus and are uncorrected.

(4) A. Neuberger and J. J. Scott, *J. Chem. Soc.*, 1820–1825 (1954).

(5) Reflux time should be increased; work-up of such precipitates afforded 5-phthalimidolevulinic acid, m.p. 160–161°, from 5–20%.

(6) Ref. 2 reports almost identical spectra for the homologous valeric, caproic and octanoic acids.