means of a Dean–Stark trap. The solution was decanted from a small amount of gum and allowed to stand for 12 hr. at 25°. The crystalline product was collected and combined with a second crop obtained by concentration of the mother liquor: yield 30.2 g. (92%), m.p. 103.5–108°. Recrystallization from ethyl alcohol gave **3** of m.p. 107–108.5°: infrared (KBr, cm.$^{-1}$), 3230 (NH), 1750 and 1670 (C=O), 1110 (ether).

The **hydrochloride** of **3,** prepared by treatment of a sample in methanol with excess methanolic HCl, was recrystallized from methanol–ether; m.p. 172.5–174.5°.

3-(1-Methyl-3-pyrrolidinyl)indole (7).—A solution of 22.8 g. (0.10 mole) of N-methyl-3-indolylsuccinimide in dioxane was added to a heated suspension of 15.2 g. (0.40 mole) of lithium aluminum hydride in 400 ml. of dioxane at a rate which maintained reflux. The mixture was refluxed for 21 hr., cooled in ice, and treated carefully with ice water until a white solid was obtained. Filtration and evaporation of the filtrate *in vacuo* gave a pale yellow oil which slowly crystallized; yield 17.0 g. (85%). It was recrystallized from ethyl acetate to give a white product of m.p. 111.5–113°; infrared (CCl_4 cm.$^{-1}$), 3550 (NH).

2-(3-Indolyl)-1-pyrroline (VI).—A suspension of 19.8 g. (0.10 mole) of 3-(β-cyanopropionyl)indole[5] (V) in 250 ml. of methanol was hydrogenated at an initial pressure of 3 atm. over Raney nickel catalyst. After 2.5 hr. 2 moles of hydrogen had been absorbed. Continued hydrogenation for 3 days produced no further absorption, even after substitution of fresh catalyst. Removal of the catalyst and concentration *in vacuo* gave a crystalline solid which was triturated in ether and filtered to yield 15.6 g. (85%) of buff-colored material, m.p. 180.5–182.5° dec. An analytical sample was recrystallized from acetone then acetonitrile; m.p. 183–184.5° dec.; lit.[7] m.p. 182.5–183.5°; infrared ($CHCl_3$, cm.$^{-1}$), 3470 (NH).

Anal. Calcd. for $C_{12}H_{12}N_2$: C, 78.23; H, 6.57; N, 15.21. Found: C, 78.00; H, 6.50; N, 15.27.

3-(2-Pyrrolidinyl)indole (VII). A. By Hydrogenation of VI.—A suspension of 3.7 g. (0.02 mole) of VI in 100 ml. of methanol was hydrogenated at 40° and 3 atm. over 0.2 g. of platinum oxide, the theoretical amount of hydrogen being absorbed in 16 hr. Removal of the catalyst and concentration under reduced pressure left a white crystalline solid which was recrystallized from acetonitrile to give 2.0 g. (54%) of VII, m.p. 138–140°. A sample was recrystallized again from acetonitrile and had m.p. 140–142°; lit. m.p. 145.8–146.6°,[8] 141–143°[7]; infrared (KBr, cm.$^{-1}$), 3280 (NH).

Anal. Calcd. for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58; N, 15.04. Found: C, 77.50; H, 7.64; N, 15.19.

B. By Reduction of VI with Sodium Borohydride.—A solution of 3.7 g. (0.02 mole) of VI in 100 ml. of absolute methanol was treated with 1.5 g. (0.04 mole) of sodium borohydride in portions during 5–10 min. The solution was refluxed for 1 hr., cooled, and treated with 27 ml. of 6 *N* NaOH then 200 ml. of water. After 16 hr. a white crystalline solid was collected and dried *in vacuo* over P_2O_5; yield 2.1 g. (57%), m.p. 139.5–141°. After recrystallization from acetonitrile, the material had m.p. 141.5–142.5° alone or when mixed with VII obtained by catalytic reduction of V. Its infrared spectrum was superimposable on that of the material from A.

Acknowledgment.—We are indebted to Mr. David Whitehead and staff for the infrared data, to Mr. R. M. Downing and Mrs. C. Kalinowski for the elemental analyses, and to Mr. R. B. Babel for the preparation of several of the necessary intermediates.

DL-2-Amino-4-(4-pyridyl)butyric Acid

FREDERICK LEONARD[1a] AND WALTER TSCHANNEN

Department of Medicinal Chemistry, Geigy Research, Division of Geigy Chemical Corporation, Ardsley, New York

Received August 10, 1965

The Michael addition products of acylamidomalonates or acylamidocyanoacetates with acrylonitrile,[2a–c] methyl methacrylate,[2c,d] acrylamide,[2c] acrolein,[3] methyl vinyl ketone,[4] and methyl vinyl sulfone[5] have proved to be useful intermediates for the preparation of amino acids. We report in this communication the successful basic-resin catalyzed addition of ethyl acetamidomalonate to another activated α,β-olefinic system, 4-vinylpyridine, and hydrolysis of the addition product to the new, unnatural, basic amino acid, DL-2-amino-4-(4-pyridyl)butyric acid dihydrochloride (**1**). Compound **1** was found to have no inhibitory effects *in vitro* against standard strains of *Mycobacterium tuberculosis*, bacteria, and fungae.

Experimental Section[6]

DL-2-Amino-4-(4-pyridyl)butyric Acid Dihydrochloride.—A mixture of 21.7 g. (0.1 mole) of diethyl acetamidomalonate, 11.6 g. (0.11 mole) of 4-vinylpyridine, 10 g. of Amberlite 400 (OH form), and 50 ml. of absolute ethanol was heated at 60–70° (stirring) for 20 hr. The mixture was filtered and concentrated *in vacuo* to a heavy syrup which did not crystallize; yield 24 g.

The crude malonate (24 g.) was refluxed for 12 hr. with 6 *N* HCl. The reaction mixture was concentrated to dryness *in vacuo*. The crystalline residue was extracted twice with boiling ethanol (reflux) and recrystallized from methanol–ether; yield 12.5 g. (49.4% over-all), m.p. 223–224°. A second recrystallization from methanol did not change the melting point.

Anal. Calcd. for $C_9H_{14}Cl_2N_2O_2$: C, 42.71; H, 5.58; N, 11.07. Found: C, 43.02; H, 5.78; N, 10.84.

(1) To whom inquiries should be addressed at Psychopharmacology Service Center, National Institute of Mental Health, Bethesda, Md. 20014

(2) (a) W. E. Hanby, S. G. Waley, J. Watson, and E. J. Ambrose, *J. Chem. Soc.*, 3239 (1950); (b) N. F. Albertson and S. Archer, *J. Am. Chem. Soc.*, **67**, 2043 (1945); (c) K. Shimo and S. Wakamatsu, *J. Org. Chem.*, **26**, 3788 (1961); (d) H. R. Snyder, J. F. Shekleton, and C. D. Lewis, *J. Am. Chem. Soc.*, **67**, 310 (1945).

(3) D. T. Warner and O. A. Moe, *ibid.*, **70**, 2765 (1948); J. W. Cornforth, R. Cornforth, C. E. Daldgleisch, and A. Neuberger, *Biochem. J.*, **48**, 591 (1957).

(4) H. Gershon and A. Scala, *J. Org. Chem.*, **26**, 2347 (1961); F. Leonard and W. Tschannen, *J. Med. Chem.*, **8**, 287 (1965).

(5) T. Kaneko and T. Inui, *Nippon Kagaku Zasshi*, **76**, 396 (1955); *Chem. Abstr.*, **51**, 17747 (1957).

(6) Microanalyses were performed by Mr. J. Deonorine of these laboratories. All melting points were determined on a Thomas–Hoover melting point apparatus and are corrected.

5-Nitro- and 5-Aminogramines

JOSEPH I. DEGRAW, VERNON H. BROWN, AND W. A. SKINNER

Department of Pharmaceutical Chemistry, Stanford Research Institute, Menlo Park, California

Received August 5, 1965

As part of a program designed to detect physiological activity in organic compounds, we have prepared a series of 5-nitro- and 5-aminogramines. Previous work has shown that gramine compounds can exert a variety of physiological actions in animals including antiserotonin activity,[1,2] hypotension,[3] and oxytocic activity.[3–6]

(1) E. N. Shaw and D. W. Woolley, *J. Pharmacol. Exptl. Therap.*, **116**, 154 (1956).

(2) G. Ehrhart and I. Hennig, *Arch. Pharm.*, **294**, 550 (1961).

(3) D. K. DeJongh and E. C. Van Proosdij-Hartzema, *J. Pharmacol. Exptl. Therap.*, **105**, 130 (1952).

(4) E. G. Van Proosdij-Hartzema and D. K. DeJongh, *Arch. Intern. Pharmacodyn.*, **98**, 335 (1954).

(5) A. M. Akkerman and H. Veldstra, *Rec. trav. chim.*, **73**, 629 (1954).

(6) A. M. Akkerman, D. K. DeJongh, and H. Veldstra, *ibid.*, **70**, 899 (1951).