3-*n*-Propyl-2,2'-biquinoline.—This was prepared in a manner similar to the above procedure using the same molar quantities of *o*-aminobenzaldehyde and *n*-butyl 2-quinolyl ketone. The yield of pure product crystallizing from petroleum ether and melting at 49–50° was 1.5 g. or 33.5%.

Anal. Calcd. for $C_{21}H_{18}N_2$: C, 84.53; H, 6.08. Found: C, 84.65; H, 6.00.

3-Phenyl-2,2'-biquinoline.—Using the same molar quantities of *o*-aminobenzaldehyde and benzyl 2-quinolyl ketone as above, 3 g. of pure product was obtained, crystallizing from dilute methanol and melting at 147–148°, yield 60.2%.

Anal. Calcd. for $C_{24}H_{16}N_2$: C, 86.72; H, 4.85. Found: C, 86.42; H, 4.89.

3-Carboethoxy-2,2'-biquinoline.—The procedure was the same as in the previous case, using the same molar quantities of *o*-aminobenzaldehyde and ethyl quinaldoylacetate. The pure product (3.4 g.), crystallizing from dilute ethanol, melted at 109–110°; yield 69.1%.

Anal. Calcd. for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91. Found: C, 76.60; H, 4.89.

***o*-Aminoacetophenone.**—This was prepared by the catalytic reduction of *o*-nitroacetophenone, resulting from the air-oxidation of *o*-nitroethylbenzene.[9]

4-Methyl-2,2'-biquinoline.—A mixture of 2 g. of *o*-aminoacetophenone, 2.6 g. of 2-acetylquinoline, 25 ml. of ethanol, 1.2 g. of sodium hydroxide and 150 ml. of water was refluxed for 24 hr. The residue from the ether extraction of the reaction mixture was extracted with petroleum ether. After removal of the solvent, the residue was recrystallized from ethanol; yield 0.2 g., m.p. 171–172°, or 5.0%.

Anal. Calcd. for $C_{19}H_{14}N_2$: C, 84.41; H, 5.22. Found: C, 84.40; H, 5.33.

(9) W. S. Emerson, *et al.*, *ibid.*, **69**, 706 (1947).

4-Phenyl-2,2'-biquinoline.—A mixture of 3 g. of *o*-aminobenzophenone (prepared by the method of Hewett, *et al.*),[10] 3 g. of 2-acetylquinoline and 3 ml. of piperidine was heated for 24 hr. at 160°. The reaction mixture was treated with cold methanol, and the resulting precipitate crystallized from benzene–petroleum ether; yield 1 g. (17.2%) of pure product melting at 203°.

Anal. Calcd. for $C_{24}H_{16}N_2$: C, 86.72: H, 4.85. Found: C, 86.89; H, 4.95.

4-Phenyl-2-bromoquinoline.—A mixture of 10 g. of 4-phenylcarbostyril (prepared by the method of Hauser and Reynolds,[11] 20 g. of PBr_3 and 13 g. of $POBr_3$ was heated for 5 hr. at 140–150°. The reaction mixture was poured on ice and made alkaline with sodium hydroxide solution. The resulting precipitate was removed by filtration and crystallized from methanol; yield 8.5 g., m.p. 94–95°.

Anal. Calcd. for $C_{15}H_{10}NBr$: Br, 28.13. Found: Br, 28.09.

4,4'-Diphenyl-2,2'-biquinoline.—A mixture of 11.3 g. of 4-phenyl-2-bromoquinoline and 15 g. of Cu powder was heated at 260–280° for 2 hr. The reaction mixture was then finely powdered, and repeatedly extracted with concentrated hydrochloric acid. The solution was made alkaline, and the resulting precipitate removed by filtration, dried and extracted with benzene. The yield of pure product, crystallizing from benzene, was 0.5 g. or 3.1%, m.p. 362°.

Anal. Calcd. for $C_{30}H_{20}N_2$: C, 88.20; H, 4.94. Found: C, 87.85; H, 4.82.

(10) C. L. Hewett, *et al.*, *J. Chem. Soc.*, 293 (1948).

(11) C. R. Hauser and G. A. Reynolds, THIS JOURNAL, **70**, 2402 (1948).

PHILADELPHIA, PA.

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Synthesis of 6-*n*-Amylindole and 6-*n*-Amyltryptophan

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The Reissert method has been utilized for the preparation of 6-*n*-amylindole from 2-nitro-4-(1-pentenyl)-toluene. 6-*n*-Amyltryptophan was prepared by saponification, decarboxylation and deacetylation of diethyl 6-*n*-amylskatylacetamidomalonate, obtained by the alkylation of diethyl acetamidomalonate with 6-*n*-amylgramine.

In a search for a useful synthetic route to 6-*n*-amyltryptophan it was necessary to investigate the preparation of 6-*n*-amylindole. Although this substance could be obtained by an application of the Tyson[2] ring closure to 2-methyl-5-*n*-amylformanilide, the yield was not high and attention was turned to a reaction sequence, outlined in formulas I–IX, utilizing a Reissert[3] indole cyclization.

n-Valeryl chloride was distilled from a mixture of benzoyl chloride and *n*-valeric acid according to the procedure of Brown[4] or prepared by the action of thionyl chloride on *n*-valeric acid. Nitration of the mixture obtained from the Friedel–Crafts reaction of *n*-valeryl chloride and toluene yielded two isomeric nitro compounds from which I was separated by recrystallization from low-boiling petroleum ether. A Meerwein–Ponndorf–Verley reduction of I provided the carbinol II in excellent yields. The unsaturated compound III was obtained when II was distilled from a trace of *p*-toluenesulfonic acid. The condensation of III with diethyl oxalate in the presence of potassium ethoxide gave good yields of an unidentified compound X when the procedure described by Blaikie and Perkin[5] was suitably modified. Acidification of an aqueous solution of V brought about the precipitation of crude X.

The anomalous solubility of X in chloroform and sharp melting point of the purified material led initially to the belief that X was the pyruvic acid derivative VI. However, an alkaline hygroscopic residue remained after ignition of an analytical sample of X and a platinum-wire flame test indicated the presence of potassium in the sample. The analytical results approached values which would be expected if X is assumed to be an equimolar mixture of V and VI. Further evidence for this assumption was established when it was found that VI was isolated quantitatively by ether extraction from a dilute hydrochloric acid slurry of X.

Ferrous sulfate in dilute ammonium hydroxide has been used by a number of authors[6–8] for the reductive cyclization of various substituted *o*-nitro-

(1) Procter and Gamble Fellow, 1951–1952.

(2) F. Tyson, THIS JOURNAL, **63**, 2024 (1941); **72**, 2801 (1950).

(3) A. Reissert, *Ber.*, **30**, 1030 (1897).

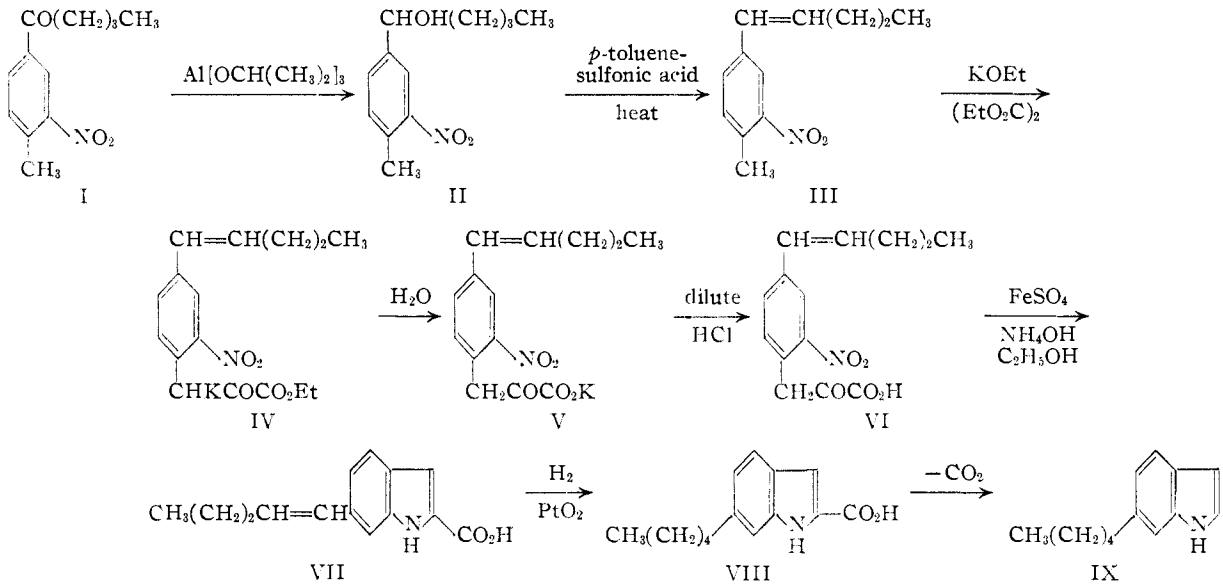
(4) H. Brown, THIS JOURNAL, **60**, 1325 (1938).

(5) K. Blaikie and W. Perkin, *J. Chem. Soc.*, **125**, 296 (1924).

(6) F. Mayer and E. Alken, *Ber.*, **55**, 2278 (1922).

(7) W. Kermack, W. Perkin and R. Robinson, *J. Chem. Soc.*, **119**, 1602 (1921).

(8) F. Bergel and A. Morrison, *ibid.*, 49 (1943).



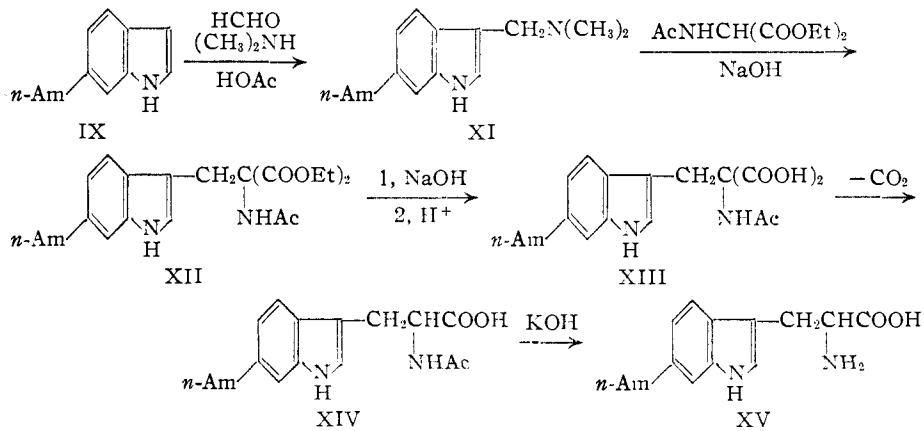
phenylpyruvic acids to the corresponding indole-2-carboxylic acids. An aqueous solution of these reagents was unsatisfactory for the conversion of VI to VII, but when the reduction was carried out in an ethanol–water mixture 6-(1-pentenyl)-indole-2-carboxylic acid was produced in good yield. The ammonium salt of VII was much more soluble in ethanol than in water, a fact which probably accounts for the relative ease with which ammonium 6-(1-pentenyl)-indole-2-carboxylate was removed from the precipitate of ferric and ferrous hydroxide in an ethanolic solution.

Hydrogenation over platinum oxide catalyst smoothly converted 6-(1-pentenyl)-indole-2-carboxylic acid (VII) to 6-*n*-amylindole-2-carboxylic acid (VIII). The decarboxylation of VIII was carried out in refluxing quinoline in the presence of a catalytic amount of copper chromium oxide catalyst.

Substituted indoles, as well as indole itself, have been found to undergo the Mannich reaction to yield the corresponding gramines.[9,10] Although all the reported gramine preparations have been carried out in aqueous solution, 6-*n*-amylgramine (XI) was obtained in only 53% yield when the Mannich reaction was attempted in this solvent. However, a 1:1 water–ethanol mixture of the reactants became homogeneous after one hour and the yield of purified XI was approximately 90%.

In an inert solvent, such as toluene or xylene, gramine reacts with a diethyl acylamidomalonate in the presence of a catalytic quantity of sodium hydroxide to yield the corresponding diethyl skatylacylamidomalonate.[11,12] The sodium hydroxide-catalyzed condensation of 6-*n*-amylgramine with diethyl acetamidomalonate was accompanied by a vigorous evolution of dimethylamine and yielded a viscous oil which was assumed to be diethyl 6-*n*-amylskatylacetamidomalonate (XII).

The crude condensation product XII was saponified in sodium hydroxide solution without further purification and no attempt was made to isolate the 6-*n*-amylskatylacetamidomalonic acid (XIII). Rather, an equivalent amount of dilute sulfuric acid was added to the saponification mixture and the decarboxylation was carried out by heating the solution. The purified product, N-acetyl-6-*n*-amyltryptophan (XIV), was obtained in a 70% yield (based on 6-*n*-amylgramine).



Although a 23-hour reflux period in 10% potassium hydroxide was sufficient for the complete hydrolysis of N-acetyl-4-methyl-, N-acetyl-6-methyl- and N-acetyl-4,6-dimethyltryptophans to the corresponding amino acids,[13] this procedure was unsatisfactory for the preparation of 6-*n*-amyl-

(9) H. Kuhn and O. Stein, *Ber.*, **70**, 567 (1937).

(10) H. R. Snyder and F. Pilgrim, THIS JOURNAL, **70**, 3788 (1948).

(11) E. Howe, A. Zambito, H. R. Snyder and M. Tishler, *ibid.*, **67**, 38 (1945).

(12) A. Butenandt, H. Hellman and E. Renz, *Z. physiol. Chem.*, **284**, 163 (1949).

(13) H. R. Snyder, H. Beilfuss and J. Williams, THIS JOURNAL in press.

tryptophan (XV) from XIV. Even when the deacetylation of XIV was carried out with 10% potassium hydroxide for a period of three days approximately one-third of the material XIV was recovered unchanged. This resistance to hydrolysis was not a function of solubility for the potassium salt of XIV was completely soluble in the hot basic solution. Unreacted XIV was separated from XV as the water-soluble ammonium salt, since the ammonium salt of the amino acid did not form under the conditions utilized and the free amino acid was obtained in yields as high as 80%, based on the acetyl derivative consumed.

Experimental[14,15]

n-Valeryl Chloride.—The acid chloride was distilled very rapidly from a mixture of 1030 ml. of benzoyl chloride and 415 g. of *n*-valeric acid and the fraction having a boiling point of 90–135° was collected; yield 385–425 g. (73–80%). This product was saturated with hydrogen chloride but was sufficiently pure for use in the following reaction.

n-Valeryl chloride was also prepared by allowing a mixture of 200 g. of *n*-valeric acid and 169 ml. (278 g.) of thionyl chloride to stand at room temperature for 4 hours, at 70–90° for 2 hours and at room temperature again overnight. The yield of the acid chloride after distillation was 173.5 g. (74%), b.p. 118–120°.

p-Methylvalerophenone was prepared in 75% yield by a modification of the procedure of Layraud[16] by the dropwise addition (over 2 hours) of 384 g. of *n*-valeryl chloride (b.p. 90–135°) to a stirred mixture of 1840 ml. of toluene and 454 g. of aluminum chloride, followed by a 2.5-hour reflux period.

3-Nitro-4-methylvalerophenone.—In order to ensure a successful nitration with a large quantity of the ketone it was necessary to carry out the reaction in a 5-l. Morton flask equipped with a stainless steel paddle stirrer. Air was bubbled through 1650 ml. of nitric acid (sp. gr. 1.49) for a 1.5-hour period. The pretreated acid was very vigorously stirred and after the temperature had reached −5° *p*-methylvalerophenone (422 g.) was added over a 50-minute period (temperature maintained below 10°). The reaction mixture was poured onto 10–12 l. of cracked ice with stirring and the nitration product was extracted from the aqueous acid with ether. After washing the ether extract with 10% sodium bicarbonate until the washings no longer gave a positive test for an organic acid, the ether solution was washed 3 times with water and dried over sodium sulfate. The ether was evaporated on the steam-bath and to the residue was added 1 l. of low-boiling petroleum ether. The resultant heterogeneous mixture partially solidified after refrigeration for a 24-hour period. 3-Nitro-4-methylvalerophenone was collected and separated from the oil, probably 2-methyl-5-nitrovalerophenone, and solvent by filtration through a sintered glass funnel. Most of the oily isomer was removed by applying suction for approximately 15 minutes; yield 250–275 g. If filtration was continued for a longer period of time the low-melting solid liquefied and separation could not be effected in this manner. The crude solid (112 g.) was heated with 1 l. of low-boiling petroleum ether and treated with 5 g. of Norit. To the filtrate was added 400 ml. of hot low-boiling petroleum ether and the solution was refrigerated overnight. The light yellow crystals were collected by filtration and recrystallized from 1400-ml. portions of the same solvent until the melting point was constant (46–48°). The total yield of purified 3-nitro-4-methylvalerophenone was 175–200 g. (33–38%), m.p. 46–48°.

3-Nitro-4-methylphenyl-*n*-butylcarbinol.—In a reaction flask equipped with an 8-inch packed column and a variable take-off distilling head was placed a solution of 10.6 g. of redistilled aluminum isopropoxide, 11.0 g. of 3-nitro-4-methylvalerophenone and 150 ml. of absolute isopropyl alcohol. After heating of the reaction mixture to gentle boiling, the column was heated to approximately 63°. The take-off head was adjusted so that the mixture of acetone and isopropyl alcohol distilled at a rate of 10–14 drops per minute. After 2.5 hours a negative test for acetone was obtained with 2,4-dinitrophenylhydrazine reagent. The excess isopropyl alcohol was distilled under reduced pressure and the viscous yellow residue was hydrolyzed at room temperature in a stirred solution of 18.2 ml. of concentrated hydrochloric acid and 91 ml. of water. After extraction of the yellow oil with ether, the ether extract was washed with 1% hydrochloric acid and water. This solution was dried over sodium sulfate, the ether was evaporated on the steam-bath and the light yellow oily residue was distilled under reduced pressure. The yield after distillation was 10.6 g. (95.5%), b.p. 130–131° (0.3 mm.), $n^{20.5}D$ 1.5354. When used to prepare 2-nitro-4-(1-pentenyl)-toluene it was not necessary to distil the crude 3-nitro-4-methylphenyl-*n*-butylcarbinol.

Anal. Calcd. for $C_{12}H_{17}NO_3$: C, 64.53; H, 7.68; N, 6.27. Found: C, 64.62; H, 7.77; N, 6.55.

2-Nitro-4-(1-pentenyl)-toluene.—A mixture of 10 g. of 3-nitro-4-methylphenyl-*n*-butylcarbinol and 0.085 g. of *p*-toluenesulfonic acid monohydrate was distilled as rapidly as possible under reduced pressure; yield 8.74 g. (95%). The distillate, which contained a trace of the acid catalyst, was dissolved in 100 ml. of ether and the ether solution was washed with 10% sodium bicarbonate and water. The ether solution, dried over sodium sulfate, yielded 8.19 g. (89%) of redistilled product, b.p. 108–109° (0.3 mm.), $n^{20}D$ 1.5563–1.5598. The progressive rise in the refractive indices was probably due to the presence of the two *cis–trans* isomers.

Anal. Calcd. for $C_{12}H_{15}NO_2$: C, 70.20; H, 7.37; N, 6.82. Found: C, 70.49; H, 7.37; N, 6.89.

2-Nitro-4-(1-pentenyl)-phenylpyruvic Acid.—A 2-fold excess of absolute ethanol was slowly added to a stirred mixture of 150 ml. of absolute benzene and 9.72 g. of potassium. When the potassium had completely reacted the excess solvents were evaporated under reduced pressure. After the addition of 300 ml. of absolute ether and 33.9 ml. of diethyl oxalate, 51.2 g. of 2-nitro-4-(1-pentenyl)-toluene was added dropwise. The red potassium salt of ethyl 2-nitro-4-(1-pentenyl)-phenylpyruvate precipitated after approximately 40 minutes. After the reaction mixture had been stirred and heated at the reflux temperature for a 20-hour period, the potassium salt was collected by filtration, washed with absolute ether, and immediately dissolved in 800 ml. of water. The filtrate was washed 3 times with water and the combined aqueous solutions were heated to approximately 70°. The cooled solution was extracted twice with ether and enough concentrated hydrochloric acid was added to the aqueous phase to make the total concentration of acid about 2%. 2-Nitro-4-(1-pentenyl)-phenylpyruvic acid was extracted from the acidic solution with ether. The ether extract was washed with water, dried over magnesium sulfate and evaporated on the steam-bath. The oily residue was dissolved in boiling benzene and hot hexane was added to incipient cloudiness. From the refrigerated mixture 28.5 g. of product, m.p. 113–119°, was collected by filtration. An additional 7 g. of crude product was obtained by the addition of boiling hexane to the concentrated filtrate. The latter material was recrystallized from benzene–hexane; yield 5 g. (m.p. 117–119°). The total yield of product, sufficiently pure for reductive cyclization, was 33.5 g. (49%). An analytical sample of this material was prepared by further recrystallizations from a benzene–hexane mixture; m.p. 118–119°.

Anal. Calcd. for $C_{14}H_{15}NO_5$: C, 60.63; H, 5.45; N, 5.05; neut. equiv., 277.3. Found: C, 60.71; H, 5.49; N, 5.29; neut. equiv., 281.3.

6-(1-Pentenyl)-indole-2-carboxylic Acid.—2-Nitro-4-(1-pentenyl)-phenylpyruvic acid, 13 g., was dissolved in a solution of 66.5 ml. of concentrated ammonium hydroxide, 95 ml. of water and 190 ml. of ethanol. To the stirred solution was added 84.5 g. of ferrous sulfate in 95 ml. of hot water and the resultant mixture was refluxed for 0.5 hour. The reaction mixture was diluted with 450 ml. of hot ethanol, treated with Norit, filtered and the precipitate of ferric hydroxide was washed with hot ethanol; the ethanol solution was concentrated to a small volume. The cooled concentrate was acidified with an equal volume of 5% hydrochloric acid and extracted with ether. Evaporation of the ether extract after washing it with water gave a light gray

(14) All melting points are corrected.

(15) Microanalyses by Miss Emily Davis, Mrs. Jean Fortney, Miss Rachel Kopel, Mrs. Katherine Pih, Mrs. Esther Fett and Mr. Joseph Nemeth.

(16) E. Layraud, *Bull. soc. chim. France*, [3] **35**, 227 (1906).

crystalline product. This material was dissolved in ethanol, treated with Norit and recrystallized from a water–ethanol mixture. Two additional recrystallizations of the product from 250-ml. portions of toluene yielded 7 g. (65%) of 6-(1-pentenyl)-indole-2-carboxylic acid, m.p. 200–202° dec.

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.33; H, 6.59; N, 6.11. Found: C, 73.56; H, 6.55; N, 6.24.

6-*n*-Amylindole-2-carboxylic Acid.—A solution of 12.7 g. of 6-(1-pentenyl)-indole-2-carboxylic acid and 150 ml. of ethanol which contained 0.2 g. of platinum oxide was shaken on a low pressure hydrogenation apparatus for 45 minutes. After collection of the catalyst by filtration, dilution of the filtrate with water yielded 12.8 g. of pink crystalline product. A yield of 12 g. (94%) of 6-*n*-amylindole-2-carboxylic acid, m.p. 168–169°, was obtained by recrystallization of this material from a benzene–hexane mixture.

Anal. Calcd. for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.71; H, 7.52; N, 6.18.

6-*n*-Amylindole.—Nitrogen was bubbled through a refluxing mixture of 12 g. of 6-*n*-amylindole-2-carboxylic acid, 34 ml. of redistilled quinoline and a trace of copper chromite for a 2-hour period. The cooled reaction mixture was taken up in ether and the ether solution was washed 9 times with 5% hydrochloric acid, 2 times with water, 2 times with 2.5% potassium hydroxide and 3 times with water. The residue which remained after evaporation of the dried ether extract was added to 67 ml. of low-boiling petroleum ether and the mixture was filtered to remove a little insoluble material. The filtrate was cooled in a salt–ice mixture and the product was collected by filtration. An additional recrystallization of the waxy solid from a similar quantity of the same solvent yielded 6.7 g. (69%) of 6-*n*-amylindole, m.p. 53–55°. This product was sufficiently pure for the preparation of 6-*n*-amylgramine.

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.37; H, 9.15; N, 7.48. Found: C, 83.34; H, 9.12; N, 7.63.

6-*n*-Amylgramine.—6-*n*-Amylindole, 2 g., was added to a stirred and cooled solution of 2.29 g. of 25% dimethylamine, 1.51 g. of glacial acetic acid, 0.80 g. of 40% formaldehyde, 10 ml. of water and 15 ml. of ethanol. The mixture was stirred at room temperature for 3.25 hours. After the light yellow solution had been allowed to stand at room temperature for a total of 20 hours, the reaction mixture was treated with Norit. Most of the ethanol was removed by distillation under reduced pressure after the addition of 90 ml. of water and the residue was poured into a stirred solution of 1.5 g. of sodium hydroxide in 16 ml. of water. The basic solution became cloudy and a white solid precipitated. After the mixture had been stirred for 1 hour at room temperature and 1 hour at 0°, the white precipitate of 6-*n*-amylgramine was collected by filtration, washed with water and air-dried. One recrystallization of this material from low-boiling petroleum ether yielded 2.25 g. (88%) of product; m.p. 92–95°. The analytical sample, prepared by further recrystallizations from the same solvent, had a melting point of 94.5–95.5°.

Anal. Calcd. for $C_{16}H_{23}N_2$: C, 78.63; H, 9.90; N, 11.47. Found: C, 78.67; H, 9.99; N, 11.38.

Diethyl 6-*n*-Amylskatylacetamidomalonate.—Purified nitrogen was bubbled through a refluxing mixture of 7.04 g. of 6-*n*-amylgramine (m.p. 92–95°), 6.57 g. of diethyl acetamidomalonate, 0.35 g. of powdered sodium hydroxide and 30 ml. of absolute toluene for a 5-hour period. Although initially a copious quantity of dimethylamine was evolved the evolution of this gas practically ceased at the end of the heating period. The reaction mixture was filtered and the toluene was removed from the filtrate by evaporation under reduced pressure. The residue, a light yellow viscous oil, was saponified without further purification.

N-Acetyl-6-*n*-amyltryptophan.—The oil obtained above was refluxed in a solution of 11.56 g. of sodium hydroxide and 230 ml. of water for a 4-hour period. The light yellow reaction mixture which contained a little insoluble material was treated with Norit, and 850 ml. of water was added to the filtrate. The diluted solution was cooled to 5–10° and titrated with 368 ml. of 0.781 *N* sulfuric acid. Pink crystals of N-acetyl-6-*n*-amyltryptophan precipitated when this solution was refluxed for a period of 2.5 hours. After refrigeration of the decarboxylation mixture overnight, the product was collected by filtration and air-dried, yield 8.2 g. (90%). The crude material was taken up in 80 ml. of absolute ethanol, treated with Norit and recrystallized from a mixture of 50 ml. of absolute ethanol and hexane. (The hexane was added to incipient cloudiness.) The yield of light pink crystalline product was 6.38 g. (70%), m.p. 208–209° (placed in the melting point bath at 200°).

Anal. Calcd. for $C_{18}H_{24}N_2O_3$: C, 68.31; H, 7.64; N, 8.86. Found: C, 68.18; H, 7.66; N, 8.75.

6-*n*-Amyltryptophan.—A solution of 1 g. of N-acetyl-6-*n*-amyltryptophan, 12 ml. of water and 1.00 g. of potassium hydroxide was refluxed in a copper round-bottomed flask for a 22-hour period. When a sample of the solution was examined only the unchanged acetyl derivative could be recovered. The major portion of the solution was returned to the copper flask and to it was added 4.9 g. of N-acetyl-6-*n*-amyltryptophan, 59 ml. of water and 5.03 g. of potassium hydroxide. The resulting solution was heated at reflux temperature for 3 days, treated with Norit, titrated with 118 ml. of 0.781 *N* sulfuric acid and refrigerated overnight. The product, collected by filtration, had a melting point of 225–270°. This material was added to a solution of 12 ml. of concentrated ammonium hydroxide in 240 ml. of water. The mixture was shaken intermittently for a period of 0.5 hour and the insoluble amino acid was collected by filtration. Unreacted N-acetyl-6-*n*-amyltryptophan was recovered from the filtrate by the procedure described in the following paragraph. The partially purified amino acid was dissolved in a solution of 5.46 g. of potassium hydroxide and 72 ml. of water. The solution thus obtained was treated with Norit and titrated with 106.5 ml. of 0.781 *N* sulfuric acid. After refrigeration of this mixture, the product was collected by filtration and slurried with approximately 50 ml. of hot absolute ethanol. The purified 6-*n*-amyltryptophan was collected by filtration and washed with small portions of absolute ethanol; yield 3.4 g. (80% on the basis of unrecovered N-acetyl-6-*n*-amyltryptophan). The product had a melting point of 288–292° (dec., melting point bath preheated to 282°).

Anal. Calcd. for $C_{16}H_{22}N_2O_2$: C, 70.03; H, 8.08; N, 10.21. Found: C, 70.18; H, 8.28; N, 10.46.

The ammonium hydroxide solution was acidified with glacial acetic acid and allowed to stand at room temperature for 0.75 hour. The precipitate of crude N-acetyl-6-*n*-amyltryptophan, collected by filtration, had a melting point of 206–209°, weight 1.75 g. This material was recrystallized by the procedure described for the purification of N-acetyl-6-*n*-amyltryptophan, weight 1.03 g. The melting point of a mixture of this compound and an authentic sample of N-acetyl-6-*n*-amyltryptophan showed no depression.

URBANA, ILL.