evident that under similar conditions of *p*H and of buffer composition all of the lignins possess comparable mobilities. The differences observed are, however, significant, and this is illustrated in Fig. 5 (line 3) in which the diagrams of a mixture of oak native and cork lignins are reproduced. Two well defined peaks are to be recognized, the mobilities being characteristic of the respective components.

TABLE III

ELECTROPHORETIC MOBILITY OF VARIOUS LIGNINS IN GLYCINE–NaCl BUFFER, *p*H 10.7

Lignin samples	Mobility, cm.²/v. sec. × 10⁵ Ascending	Descending
Indulin	− 9.9	− 9.7
White Scots pine	−10.2	−10.1
Bagasse	− 9.8	− 9.1
Maple	− 9.3	− 8.3
Oak	− 8.7	− 8.2
Cork	− 9.5	− 8.9

In view of the complexity of the lignin molecule, and the possibility of variations in structure, it was noteworthy to find that the majority of lignins do give patterns characteristic of electrophoretically homogeneous compounds, the most significant exception being the white Scots pine lignin. It was of particular interest to observe here that this lignin, whether native or enzymatically liberated presents identical patterns and, on mixing the samples, the electrophoretic patterns did not change. Therefore, it must be assumed that this lignin is a mixture of electrophoretically distinct lignins, the ease of extraction of the components being the same both before and after enzymatic decay. As a result it is justifiable to assume that the electrophoretic analysis reflects the relative concentration of the components in the total lignin of the woody tissue.

The electrophoretic analyses of our various lignin samples have thus yielded results which could not be obtained, as yet by any other method. As in the case of proteins, electrophoresis supplies us with valuable information on the purity and homogeneity of the lignin preparations. The main limitations to a wider application of this method to lignin lies in the comparatively close mobility of all the samples thus far investigated.

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

The Synthesis of 4-Methyl-, 5-Methyl-, 6-Methyl- and 4,6-Dimethyltryptophans

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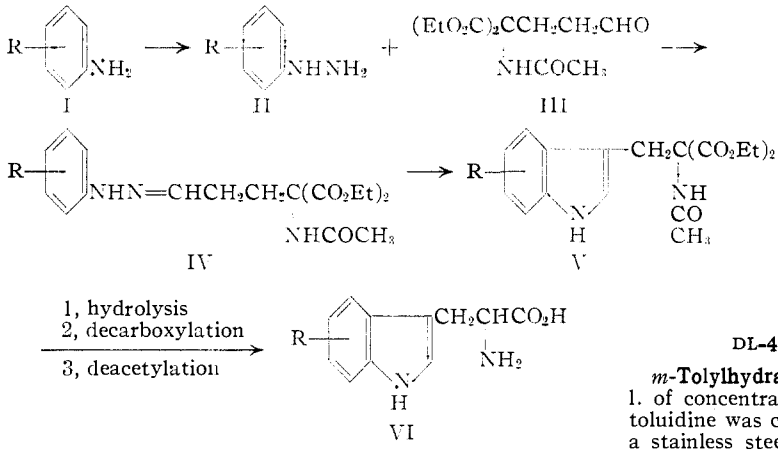
Procedures are described for the synthesis of 4-methyl-, 5-methyl-, 6-methyl- and 4,6-dimethyl-DL-tryptophans by the Fischer cyclization of the properly substituted phenylhydrazones of γ,γ-dicarbethoxy-γ-acetamidobutyraldehyde.

All the syntheses reported in this paper make use of the general procedure established by Moe and Warner[1,2] for the preparation of DL-tryptophan. The reaction sequence, which has also been used[3] for the synthesis of DL-5-fluorotryptophan, is given by formulas I–VI.

The monomethylated amino acids under consideration have been previously prepared by alkylation with the corresponding gramines[4,5] or from the alkyl indole-3-aldehyde *via* the well-known hydantoin synthesis.[6] The present research was directed toward a synthetic route adaptable to larger scale preparations and one in which the starting materials would be more readily available. In general, the appropriate toluidine or xylidine (I) was diazotized and the diazonium salt was reduced to the hydrazine (II) with stannous chloride. The reaction of II with γ,γ-dicarbethoxy-γ-acetamidobutyraldehyde[1] (III) provided the hydrazone (IV) in excellent yields. This intermediate was used for cyclization without purification. The diethyl alkylskatylacetamidomalonate (V) was obtained by cyclization of IV in boiling aqueous sulfuric acid. The highest yields of VI were obtained when the hydrolyses and decarboxylation were carried out in three steps by a suitable modification of the procedures of Snyder and Smith[7] and of Rydon.[4]

The synthesis of DL-5-methyltryptophan utilized *p*-toluidine as the raw material, and the reaction sequence outlined above presented no difficulty. Although it has been reported[8] that the reactive position in a *m*-substituted arylhydrazone, under

(1) O. A. Moe and D. T. Warner, THIS JOURNAL, **70**, 2763 (1948).
(2) O. A. Moe and D. T. Warner, *ibid.*, **70**, 2765 (1948).
(3) H. Rinderknecht and C. Niemann, *ibid.*, **72**, 2296 (1950).
(4) H. N. Rydon, *J. Chem. Soc.*, 705 (1948).
(5) M. E. Jackman and S. Archer, THIS JOURNAL, **68**, 2105 (1946).
(6) W. Robson, *J. Biol. Chem.*, **62**, 495 (1924).
(7) H. R. Snyder and C. W. Smith, THIS JOURNAL, **66**, 350 (1944).
(8) C. Hollins, "Synthesis of Nitrogen Ring Compounds," Ernest Benn, Ltd., London, 1924, p. 96.



the conditions of the Fischer ring closure, is "probably that one which is para to the substituent group," in the present work both isomers were formed. This result is in agreement with the work of several previous authors.[9a-e]

Fractional crystallization of the reaction product (V), obtained in the sequence in which I was *m*-toluidine, yielded approximately equal quantities of the two isomers which were identified by comparison of their melting points with those reported[4] for diethyl 6-methyl- and diethyl 4-methylskatylacetamidomalonate. Since a relatively large quantity of the mixture remained after each isolation of one of the isomers, it was impossible to make a precise determination of the ratio of the two products. Both were hydrolyzed and decarboxylated to yield DL-4-methyl- and DL-6-methyltryptophan, respectively. The infrared spectrum of DL-6-methyltryptophan prepared by this procedure was identical with that of an authentic sample.

The geometric similarity of the two ortho positions in the 3,5-dimethylphenylhydrazone of III excludes the possibility of isomer formation in the ring closure. As a result, it was possible to obtain a much higher yield of a single cyclization product (diethyl 4,6-dimethylskatylacetamidomalonate (VII)). The crude substituted indole (VII) contained traces of highly colored impurities which could not be removed in the usual manner (Norit treatment, chromatography, etc.). Of the recrystallization solvents investigated, carbon tetrachloride appeared to remove the maximum amount of these colored materials. However, a sample recrystallized from this solvent did not have the composition of VII. The analytical results approached values which would be expected if VII contained one mole of the solvent (carbon tetrachloride). Further investigation showed that the carbon tetrachloride could be removed quantitatively by recrystallization of the solvated compound (VIII) from an ethanol–water mixture or by heating VIII under reduced pressure. Unfortunately, a comparison of the infrared spectra of VII and VIII gave no information as to how the carbon tetrachloride was complexed with VII. This solvent association may be similar to that noted by Koelsch[9e] in the recrystallization of 2,6-dicarbethoxy-3-(β-carbethoxyethyl)-indole from ethanol to give a product having the composition of the indole derivative plus 0.5 mole of ethanol. Compound VII was hydrolyzed and decarboxylated in the usual manner to yield DL-4,6-dimethyltryptophan.

(9) (a) K. Schofield and R. S. Theobald, *J. Chem. Soc.*, 796 (1949); (b) B. M. Barclay and N. Campbell, *ibid.*, 530 (1945); (c) S. G. P. Plant, *ibid.*, 2493 (1929); (d) C. F. Koelsch, *J. Org. Chem.*, **8**, 295 (1943); (e) S. W. Fox and M. W. Bullock, THIS JOURNAL, **73**, 2756 (1951).

Experimental[10,11]

DL-4-Methyl- and 6-Methyltryptophan

***m*-Tolylhydrazine.**[12]—A solution in 2.25 l. of water of 0.75 l. of concentrated hydrochloric acid and 352.2 ml. of *m*-toluidine was cooled to 0° in a 5-gallon can equipped with a stainless steel paddle stirrer powered by a Mixmaster motor. To this solution was added as rapidly as possible a precooled solution of 235.2 g. of sodium nitrite in 0.9 l. of water. The temperature of the reaction mixture was not allowed to exceed 5°. After the addition of sodium nitrite solution was completed, the solution was saturated with 950 g. of sodium chloride. A cooled solution of 1608 g. of stannous chloride dihydrate in 0.75 l. of concentrated hydrochloric acid was slowly added to the saturated solution. After the initial frothing had subsided the rate of addition was increased (temperature maintained below 12°). Upon completion of the addition, the cooling bath was removed and the curdy precipitate was vigorously stirred for 1.5 hours. The reaction mixture was then heated to 80–90° and decolorized with Norit. The filtrate, which had a light yellow color, was cooled overnight in an ice-box and the white precipitate was collected by filtration. Suitable precautions were taken to protect the complex salt from overlong exposure to the atmosphere. The salt was decomposed with an excess of 25% sodium hydroxide solution. A yellow-green oil separated. The free *m*-tolylhydrazine was extracted with two 500-ml. portions of ether. After the ether extract had been dried with anhydrous sodium sulfate, the solvent was removed under reduced pressure. The residue was used in the succeeding step. For further purification the product may be distilled under reduced pressure. Pure *m*-tolylhydrazine (246 g., 62%) was obtained as a pale yellow oil boiling at 135–137° (20 mm.).

γ,γ-Dicarbethoxy-γ-acetamidobutyraldehyde (III).—One mole of this aldehyde in a benzene solution was prepared by the method of Moe and Warner[1] (procedure B).

γ,γ-Dicarbethoxy-γ-acetamidobutyraldehyde-*m*-tolylhydrazone.—To the benzene solution of III were added 24 ml. of glacial acetic acid and 135 g. of *m*-tolylhydrazine. This mixture was refluxed 7–8 hours and allowed to stand at room temperature for an additional 8-hour period. A light-colored oil separated from the solution when 2 l. of high-boiling petroleum ether was added. This heterogeneous mixture was set aside in an ice-box at 0–5° for 2 or 3 days. Occasional scratching of the flask was necessary to induce crystallization. After complete crystallization the light yellow crystals were collected by filtration, washed with 50 ml. of high-boiling petroleum ether and dried *in vacuo*; yield 330–350 g. (88–93%),[13] m.p. 72–76°. The crude product may be used for cyclization without further purification.

Cyclization of γ,γ-Dicarbethoxy-γ-acetamidobutyraldehyde-*m*-tolylhydrazone.—To a solution of 107 ml. of concentrated sulfuric acid and 2.3 l. of water was added 387 g. (1 mole) of IV (R = 3-methyl-) and the mixture was vigorously stirred at reflux temperature in a 5-l. Morton flask for 4.5 hours. After approximately one hour, the suspended liquid solidified. The product was collected by filtration of the cooled solution, washed with 0.5 l. of water and air-dried.

(10) All melting points are corrected.

(11) Microanalyses by Miss Emily Davis, Mrs. Jean Fortney, Miss Rachel Kopel, Mrs. Katherine Pih and Mr. Maurice Dare.

(12) This procedure was adapted from the one given for phenylhydrazine by L. Gattermann, "Practical Methods of Organic Chemistry," ed. 3, The Macmillan Co., New York, N. Y., 1920, p. 251.

(13) This yield was based on diethyl acetamidomalonate.

Diethyl 6-Methylskatylacetamidomalonate.—The cyclization product obtained above was dissolved in 1.5 l. of boiling 95% ethanol, treated with Norit, and allowed to stand undisturbed while cooling to room temperature overnight. The mother liquor was decanted from the light yellow solid and saved in order to allow recovery of the 4-methyl isomer. The solid, which had a melting point of 160–170°, was recrystallized from 600-ml. portions of 95% ethanol until the melting point was constant (180–181°)[14]; yield 55–60 g. (15.3–16.7%).[13] An additional 3–6 g. of pure product could be obtained by reducing the volume of the mother liquor from the final recrystallization to 200–300 ml.

Anal. Calcd. for $C_{19}H_{24}N_2O_5$: C, 63.31; H, 6.71; N, 7.76. Found: C, 62.89; H, 6.76; N, 7.93.

DL-N-Acetyl-6-methyltryptophan.—The malonic ester derivative (33.6 g., 0.097 mole) was converted to the dicarboxylic acid by a method previously described.[7] The crude oily dicarboxylic acid was separated by decantation and added to 144 ml. of water containing a trace of sodium hydrosulfite. This mixture was then refluxed for 2.5 hours. The monocarboxylic acid separated as a solid during the decarboxylation. After cooling the reaction mixture to 0°, the product was collected by filtration and recrystallized from a 25% ethanol–water mixture containing a trace of sodium hydrosulfite. The precipitate, which had a light pink color, was dried *in vacuo* with protection from light; yield 18–19 g. (71.5–75.2%), m.p. 190–191°.

Anal. Calcd. for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.90; H, 6.44; N, 10.62.

DL-6-Methyltryptophan.—N-Acetyl-6-methyltryptophan was hydrolyzed by refluxing 19 g. (0.073 mole) with 21.1 g. (0.38 mole) of potassium hydroxide in 264 ml. of water for 23 hours. After treatment with Norit, a solution of 21.6 ml. of glacial acetic acid and 21.6 ml. of water was added. Although a copious precipitate was obtained immediately, the acidified mixture was allowed to remain in the refrigerator overnight. The crude product was then collected by filtration, washed with cold water, and dried *in vacuo*. After drying, the DL-6-methyltryptophan was powdered and then suspended in absolute alcohol. When purified in this manner the product is white or light pink; yield 15 g. (94%), m.p. 260° (dec.) with softening at 245°.[14] The infrared spectrum of this compound and that of an authentic sample are identical.[15]

Diethyl 4-Methylskatylacetamidomalonate.—The mother liquor set aside above for the recovery of the 4-methyl isomer was heated to boiling and cooled to 0° overnight. The light yellow solid (m.p. 143–155°) was removed by filtration and recrystallized from 550-ml. portions of 95% ethanol until the melting point[14] reached 163–164°; yield 60–63 g. (16.7–17.5%).[13]

Anal. Calcd. for $C_{19}H_{24}N_2O_5$: C, 63.31; H, 6.71; N, 7.76. Found: C, 63.23; H, 6.89; N, 7.90.

DL-4-Methyltryptophan.—The ester (43.5 g., 0.121 mole) was saponified by refluxing with a solution of 43.5 g. (1.09 moles) of sodium hydroxide in 187 ml. of water and 280 ml. of 95% ethanol for 4 hours. After filtration to remove a little insoluble material, the cooled saponification mixture was acidified with 150 ml. of concentrated hydrochloric acid and extracted with five 300-ml. portions of ether. The ether extract was evaporated to dryness under reduced pressure. To the glassy residue of dicarboxylic acid was added 500 ml. of water and the mixture was refluxed under a nitrogen atmosphere for 2.5 hours. Heating was continued for 24 hours after the addition of 125 g. (0.396 mole) of barium hydroxide octahydrate. The hydrolysis mixture was poured into 2.5 l. of boiling water and the aqueous solution was titrated with 366 ml. of 2.187 *N* sulfuric acid. The barium sulfate was collected by filtration and washed well with hot water. The combined filtrates were treated with Norit and evaporated under reduced pressure to 500 ml. During the evaporation the amino acid precipitated. The yield of crude dry amino acid was 15 g. (57%). This product was dissolved in 4.5 l. of boiling water. After a Norit treatment, the filtrate was evaporated to 700 ml. under reduced pressure and the amino acid was collected by filtration; yield 12.5 g., m.p. 270–272.[14]

Anal. Calcd. for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.46. Found: C, 66.27; H, 6.43.

DL-5-Methyltryptophan

γ,γ-Dicarbethoxy-γ-acetamidobutyraldehyde-*p*-tolylhydrazone.—This compound was prepared by the procedure for the *m*-tolylhydrazone from 0.5 mole of III[1] and 67 g. (0.55 mole) of *p*-tolylhydrazine.[6] The yield was quantitative[13] and the intermediate was sufficiently pure for cyclization.

Diethyl 5-Methylskatylacetamidomalonate.—A suspension of 200 g. (0.53 mole) of the hydrazone in a solution of 54 ml. of concentrated sulfuric acid and 1150 ml. of water was refluxed and stirred for 4.5 hours. The oil obtained by cooling the reaction mixture and decanting the aqueous acid crystallized after standing at room temperature for 3 days; yield 117 g. (60.7%). A portion of the crude product (91.0 g.) was dissolved in 450 ml. of boiling ethanol and treated twice with 5-g. portions of Norit. The alcoholic solution was diluted with 785 ml. of water and refrigerated overnight. The yield was 78.6 g. (86% recovery), m.p. 133–135°. A sample, purified for analysis by two recrystallizations from ethanol–water, melted at 135–137°.[14]

Anal. Calcd. for $C_{19}H_{24}N_2O_5$: C, 63.32; H, 6.71; N, 7.76. Found: C, 63.14; H, 6.83; N, 7.59.

5-Methylskatylacetamidomalonic Acid.—A suspension of 75 g. (0.21 mole) of the once-recrystallized ester in a solution of 43 g. (1.07 moles) of sodium hydroxide and 430 ml. of water was refluxed for 4 hours. After the removal of a little insoluble material by filtration, the filtrate was cooled to 0–5° and acidified with 112 ml. of cold concentrated hydrochloric acid. The solid malonic acid derivative was collected by filtration, ground in a mortar, washed with cold water, and dried over calcium chloride; yield 59 g. (92%). The product is unstable on storage and should be decarboxylated as soon as possible.

DL-N-Acetyl-5-methyltryptophan.—A suspension of 58.5 g. (0.19 mole) of the malonic acid derivative in 275 ml. of water was heated at reflux temperature for 2 hours. The mixture foamed badly as the temperature approached 100° and cooling was necessary in order to avoid loss through the reflux condenser. Solid sodium bicarbonate was added to the cooled suspension until solution was complete. After treatment with Norit the solution was cooled to 10° and acidified with concentrated hydrochloric acid. The oil which precipitated solidified when heated on the steam-bath. The solid was ground, washed with cold water and dried; yield 47.7 g. (96.6%) of light pink solid, m.p. 170–173°.

DL-5-Methyltryptophan.—DL-N-acetyl-5-methyltryptophan (47.7 g., 0.183 mole) was hydrolyzed by the method described above for the 6-methyl compound. The crude product (37 g.) was dissolved in 3 l. of boiling water. The solution obtained was treated with Norit and filtered while hot. After evaporation to a volume of 300 ml. under reduced pressure, the suspension was refrigerated overnight and the solid was collected by filtration; yield 24 g. (60.8%) of white amorphous powder. A small sample, recrystallized from ethanol–water, melted at 260–263° (dec.)[14] on a rapidly heated hot-stage apparatus which had been preheated to 210°.

Anal. Calcd. for $C_{12}H_{14}N_2O_2$: C, 66.01; H, 6.46; N, 12.84. Found: C, 65.88; H, 6.32; N, 12.77.

DL-4,6-Dimethyltryptophan

3,5-Dimethylaniline.—2,4-Dimethylaniline (Eastman Organic Chemicals White Label) was successively acetylated,[16]

(14) This table compares the melting points obtained experimentally with those reported by other authors.

Compound	M.p., °C. Obsd.	Reptd.	Ref.
Diethyl 6-methyskatylacetamidomalonate	180–181	172–173	4
Diethyl 4-methylskatylacetamidomalonate	163–164	161	4
DL-6-Methyltryptophan	260 dec. softens 245	258–260	4
DL-4-Methyltryptophan	270–272	265–267	4
Diethyl 5-methylskatylacetamidomalonate	135–137	136	4
DL-5-Methyltryptophan	260–263	264	4
		259–263	6
		284–288	5

(15) The infrared absorption spectra were observed and interpreted by Miss Elizabeth Petersen and Miss Helen Miklas.

(16) L. F. Fieser, "Experiments in Organic Chemistry," ed. 2, D. C. Heath and Company, New York, N. Y., 1941, pp. 164–165.

nitrated,[17] hydrolyzed[18] and deaminated in a mixture of hypophosphorous acid and ethanol,[19] to give 3,5-dimethylnitrobenzene in 62% over-all yield. Catalytic reduction of this compound in the presence of Raney nickel catalyst furnished 3,5-dimethylaniline; yield 90%, b.p. 99–100° (20 mm.).

3,5-Dimethylphenylhydrazine.—3,5-Dimethylaniline (20 g.) (0.165 mole) was diazotized and reduced according to the procedure of Borsche and Groth.[20] The complex salt obtained was decomposed with 10% sodium hydroxide. The hydrazine separated as an oil which solidified upon stirring and cooling of the mixture to 0°. The product was then collected by filtration and dried over phosphorus pentoxide; yield 16.5 g. (74%), m.p. 80–82°. 3,5-Dimethylphenylhydrazine is sensitive to air and light; therefore suitable precautions must be taken to avoid decomposition during its filtration and drying.

γ,γ-Dicarbethoxy-γ-acetamidobutyraldehyde-3,5-dimethylphenylhydrazone.—A benzene solution of 73.8 g. (0.27 mole) of III[1] and 38 g. (0.28 mole) of 3,5-dimethylphenylhydrazine was refluxed 1.5 hours. After this mixture was allowed to stand overnight, the product was precipitated by the addition of high-boiling petroleum ether. The oil which separated from solution was crystallized by refrigeration for 5–6 hours. The crystalline product was collected by filtration and dried; yield 95 g. (90%),[13] m.p. 88–93°. A small sample purified for analysis by recrystallization from an ethanol–water mixture melted at 90–91°.

Anal. Calcd. for $C_{20}H_{29}N_3O_5$: C, 61.36; H, 7.47; N, 10.49. Found: C, 61.55; H, 7.49; N, 10.51.

Diethyl 4,6-Dimethylskatylacetamidomalonate.—A suspension of 45 g. (0.115 mole) of the hydrazone in a solution of 15 ml. of concentrated sulfuric acid and 300 ml. of water was refluxed and vigorously stirred for 4.75 hours. Cooling the reaction mixture to room temperature in a water-bath caused the oily product to solidify. The aqueous acid was decanted and the solid was dissolved in 250 ml. of hot ethanol. This solution was treated with Norit and water was added to incipient cloudiness. The product first separated as an oil which solidified during overnight refrigeration. The yield of dark-yellow solid, collected by filtration and air-dried, was 30 g. (77%), m.p. 98–108°. Most of the color was removed by two recrystallizations from 200-ml. portions of carbon tetrachloride. The yield of solvated product (VIII) was 33 g., m.p. 63.5–65° (softening at 61°). Identification of this compound is described in the following section. Two recrystallizations of VIII (31.5 g.) from an ethanol–water mixture raised the melting point to 115–117.5°, yield 18.5 g. A sample purified for analysis by further recrystallizations from the same solvent pair had a melting point of 115–116°.

Anal. Calcd. for $C_{20}H_{26}N_2O_5$: C, 64.14; H, 7.00; N, 7.48. Found: C, 64.30; H, 6.92; N, 7.46.

Identification of VIII.—A sample of VIII was recrystallized from carbon tetrachloride and placed in a tared weighing bottle (net weight 2.2975 g.). Excess solvent was then removed at room temperature by drying under reduced pressure (1.0 mm.). At approximately one-hour intervals the sample was weighed and returned to the desiccator until a weight was observed (1.2350 g.) that remained constant at a pressure of 1 mm. for a period of 5 hours. A portion of this carefully dried sample (0.9828 g.) was heated at 56.5° (pressure 1 mm.) until it reached a constant weight (0.6966 g.). The weight loss was 0.2862 g. If VIII is assumed to contain one mole of carbon tetrachloride, which is lost upon heating, per mole of diethyl 4,6-dimethylskatylacetamidomalonate, the weight loss required is 0.2862 g. The composition was verified by a Parr bomb fusion analysis of VIII for chlorine.[21] The melting point of a mixture of VII and the product obtained after heating showed no depression. An attempt to establish, by means of the infrared spectrum, the manner in which the solvent was coordinated with the molecule was unsuccessful.[15]

Anal. Calcd. for $C_{20}H_{26}N_2O_5 \cdot CCl_4$: Cl, 26.84. Found: Cl, 27.32.

DL-N-Acetyl-4,6-dimethyltryptophan.—A suspension of 37.5 g. (0.10 mole) of the ester (m.p. 115–117.5°) in a solution of 25.20 g. (0.63 mole) of sodium hydroxide and 225 ml. of water was heated at reflux temperature for 4 hours. After the addition of 1870 ml. of water the mixture was cooled to 5° and 800 ml. of 0.781 *N* sulfuric acid was added dropwise. The neutralized solution of the dicarboxylic acid was refluxed for 2.5 hours and treated with Norit. The precipitate of gray needles was collected by filtration. The product was dried over phosphorus pentoxide; yield 16.4 g., m.p. 207–211°. An additional 4.5-g. portion of material was recovered by evaporation of the mother liquor to 0.5 l. under reduced pressure. The total yield was 20.9 g. (76.5%). The crude product (13 g.) was recrystallized from boiling water (1820 ml.) containing a trace of sodium hydrosulfite; yield 11.5 g., m.p. 210–211°.

Anal. Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.66; H, 6.61; N, 10.22. Found: C, 65.57; H, 6.66; N, 10.03.

DL-4,6-Dimethyltryptophan.—A solution of 18.3 g. (0.067 mole) of the N-acetylamino acid, 255 ml. of water and 20.8 g. (0.371 mole) of potassium hydroxide was heated at reflux temperature for 23 hours. To the hot solution was then added 104 ml. of boiling water and 21.3 ml. (0.376 mole) of glacial acetic acid. After overnight refrigeration, the amino acid was collected by filtration and dried over calcium chloride; yield 12.5 g. (81%). The product (11.5 g.) was purified by dissolving it in a solution of 8.50 g. (0.152 mole) of potassium hydroxide in 288 ml. of water and treating the mixture with Norit. To the hot filtrate was added 138 ml. of boiling 95% ethanol. After acidification with 8.75 ml. (0.155 mole) of glacial acetic acid, the solution was slowly cooled to 0°. The product was collected by filtration and washed with 50-ml. portions of water, ethanol and ether; yield 10 g. (87%), m.p. 315–317° (dec., melting point bath preheated to 290°).

Anal. Calcd. for $C_{13}H_{16}N_2O_2$: C, 67.19; H, 6.94; N, 12.06. Found: C, 67.35; H, 6.96; N, 11.95.

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(17) P. Jacobson, *Ann.*, **427**, 142 (1922).

(18) C. Willgerodt and F. Schmierer, *Ber.*, **38**, 1472 (1905).

(19) H. R. Snyder and L. Carpino, unpublished work.

(20) W. Borsche and H. Groth, *Ann.*, **549**, 238 (1941).

(21) This analysis was performed by Clark Microanalytical Laboratory, Urbana, Illinois.