tated from such solutions. It contains a half molecule of water per monomer unit which cannot be removed by long heating *in vacuo*.

3. α-Acetamidoacrylic acid may be copolymerized with acrylonitrile.

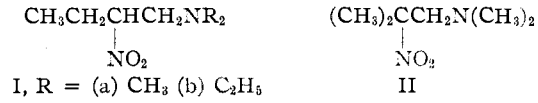
URBANA, ILLINOIS RECEIVED MAY 15, 1950

[CONTRIBUTION FROM NOYES CHEMICAL LABORATORIES, UNIVERSITY OF ILLINOIS]

Alkylation of Nitroparaffins with Amines and Their Derivatives

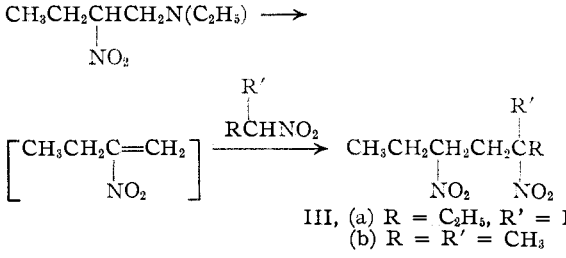
BY H. R. SNYDER AND WILLIAM E. HAMLIN

Certain amines have been employed in the alkylation of simple nitroparaffins[1,2,3] and nitro esters[4] but no general procedure for carbon-alkylation of nitroparaffins by amines has been developed as yet. It seems possible that the amines employed, which are Mannich bases, may serve as sources of unsaturated compounds and that the apparent alkylations are actually condensations of the Michael type. This consideration suggests that the Mannich bases of 1-nitropropane (I), which can undergo the elimination of secondary amine, might be used in the alkylation of other nitroparaffins, whereas the Mannich bases of 2-nitropropane (II) should be inert. It was found that 1-nitropropane and 2-



I, R = (a) CH_3 (b) C_2H_5 II

nitropropane were alkylated by the Mannich bases (Ia and Ib) to yield 3,5-dinitroheptane (IIIa) and 2-methyl-2,4-dinitrohexane (IIIb),[5] respectively. Apparently the use of a basic

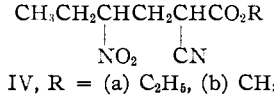


III, (a) R = C_2H_5, R' = H
(b) R = R' = CH_3

catalyst is not necessary in the alkylation of 1-nitropropane and, in fact, may increase the decomposition of the Mannich base. It was found that N-(2-nitrobutyl)-dimethylamine (Ia), which was prepared in the course of this investigation, is more stable in storage than the corresponding diethylamine (Ib).

3,5-Dinitroheptane was catalytically reduced to 3,5-diaminoheptane and a benzenesulfonamide derivative was prepared. Application of the Nef reaction to the dinitro compound yielded a very small amount of 3,5-heptanedione which was identified as its copper salt. Catalytic reduction of 2-methyl-2,4-dinitrohexane yielded the corresponding diamino compound from which a phenylthiourea derivative was prepared.

The Mannich base of 1-nitropropane (Ib) was also found to alkylate ethyl and methyl cyanoacetate to yield the corresponding α-cyano-γ-nitrocaproates (IV), but resinification was considerable. The use of sodium hydroxide catalyst was found to be undesirable. Ethyl α-cyano-γ-nitrocaproate has been prepared previously from 2-nitro-1-butene and cyanoacetic ester.[6]



IV, R = (a) C_2H_5, (b) CH_3

It would be expected that an amine exchange reaction similar to those of ketonic Mannich bases[7] could also occur with the Mannich base of 1-nitropropane. Actually, N-(2-nitrobutyl)-piperidine was obtained along with resinous material when N-(2-nitrobutyl)-dimethylamine (Ia) was refluxed with excess piperidine.

The quaternary ammonium salt formed by the addition of methyl iodide to the Mannich base of 1-nitropropane would also be expected to be a good alkylating agent. Unfortunately, all attempts to prepare this salt failed, apparently because it decomposed in the presence of methyl iodide; the reaction mixtures had the odor and lachrymatory property of 2-nitro-1-butene.

The Mannich base of 2-nitropropane, N-(2-nitroisobutyl)-dimethylamine (II), is not structurally capable of producing an unsaturated intermediate which is considered necessary for condensation with nitroparaffins. The assumed unreactivity was tested by heating the amine (II) with excess 2-nitropropane in the presence of sodium hydroxide. There was no evidence of reaction. An amine exchange reaction with piperidine also failed.

Recently the acid catalyzed amine exchange reaction of 1-methylgramine with piperidine was reported.[8] N-(2-Nitroisobutyl)-dimethylamine

(1) Reichert and Posemann, *Arch. Pharm.*, **275**, 67 (1937).
(2) Snyder and Katz, THIS JOURNAL, **69**, 3140 (1947).
(3) Snyder and Pellegrini, unpublished work.
(4) Weisblat and Lyttle, THIS JOURNAL, **71**, 3079 (1949); **69**, 2118 (1947).
(5) Since the completion of this work Bahner and Kite have reported the synthesis of these two compounds by addition of 1-nitropropane and 2-nitropropane to 2-nitro-1-butene (THIS JOURNAL, **71**, 3597 (1949)); in that report the second compound is erroneously named as 3,5-dinitro-3-methylhexane.
(6) Bahner, U. S. Patent 2,426,158 [*C. A.*, **41**, 7410 (1947)].
(7) Snyder and Brewster, THIS JOURNAL, **70**, 4231 (1948).
(8) Snyder and Eliel, *ibid.*, **70**, 4233 (1948).

and 1-methylgramine are similar in the respect that neither is capable of undergoing an amine exchange reaction of the normal type. When the hydrochloride of the Mannich base (II) was treated with excess piperidine, a trace of N-(2-nitroisobutyl)-piperidine was detected by means of its picrate derivative.

The methiodide of N-(2-nitroisobutyl)-dimethylamine, which readily formed, was found to be quite stable; it did not carbon-alkylate ethyl acetamidocyanoacetate or oxygen-alkylate α-naphthol when the procedure of Baw[9] was followed.

Experimental[10]

N-(2-Nitrobutyl)-dimethylamine (Ia).—The method of preparation was patterned after that of Johnson[11] and of Blomquist and Shelley[12] for the preparation of similar compounds. To a stirred solution of 175.5 g. (1 mole) of 25% dimethylamine was added dropwise 83 g. (1 mole) of 38% formalin so that the temperature did not rise above 25°. After the addition was completed the mixture was stirred for an additional hour at room temperature. Then 89 g. (1 mole) of redistilled 1-nitropropane was added and stirring was continued for three hours. Fifteen grams of sodium chloride was dissolved in the mixture. The organic layer was separated and dried over magnesium sulfate. The product was distilled under a nitrogen atmosphere at *ca.* 20 mm. pressure. The fraction boiling at 77–85° was collected; yield 92.1 g. (70%). A portion of this fraction was redistilled from a 6-in. column packed with glass helices, attached to a variable take-off condenser. A sample boiling at 94° (15 mm.), $n^{20}D$ 1.4338, was collected for analysis by titration with standard acid.

Anal. Calcd. for $C_6H_{14}N_2O_2$: mol. wt., 146. Found: mol. wt., 147, 152.

3,5-Dinitroheptane: From N-(2-Nitrobutyl)-diethylamine (Ib).—The sodium salt of 1-nitropropane was prepared by crushing 2.2 g. (0.06 mole) of sodium hydroxide under 10 ml. of 1-nitropropane. This slurry was added to a solution of 10 g. (0.06 mole) of N-(2-nitrobutyl)-diethylamine[12] in 50 ml. of redistilled 1-nitropropane, and the mixture was heated with stirring at 90–100°. A slow current of nitrogen was passed through the mixture to eliminate the diethylamine formed in the reaction. After twenty-eight hours the reaction was stopped. The cooled mixture was acidified with 50 ml. of 10% acetic acid, and extracted with three 50-ml. portions of ether. The combined ether extract was washed with four 25-ml. portions of water and dried over anhydrous magnesium sulfate. Ether and excess 1-nitropropane were distilled at water-pump pressure. The residue was distilled at reduced pressure, and 7.0 g. of a yellow oil boiling at 103–122° (4 mm.) was collected. Redistillation yielded 2.0 g. (18%) of an oil boiling at 115–116° (4 mm.), $n^{20}D$ 1.4506. The product was distilled once again at reduced pressure and the fraction $n^{20}D$ 1.4500 was analyzed.

Anal. Calcd. for $C_7H_{14}N_2O_4$: C, 44.21; H, 7.37; N, 14.74. Found: C, 44.11; H, 7.37; N, 15.00.

A sample of this product on standing and cooling crystallized; it melted at 30.5–31.5° (lit.[5] 33°).

From N-(2-Nitrobutyl)-dimethylamine (Ia).—A solution of 10 g. (0.07 mole) of N-(2-nitrobutyl)-dimethylamine and 50 ml. of 1-nitropropane was heated with stirring under a stream of nitrogen for eight and one-half hours at 110–120°. Amine evolution was copious, and the solution gradually became dark-colored. The cooled solution was extracted with three 20-ml. portions of ether. The combined ether extract was washed with three 10-ml. portions of 5% hydrochloric acid, three 10-ml. portions of 5% sodium bicarbonate, three 20-ml. portions of water and dried over anhydrous magnesium sulfate. The ether and excess 1-nitropropane were distilled at water-pump pressure. The residue was distilled at 86–90° (0.3 mm.); yield 4.5 g. (34%), $n^{20}D$ 1.4521.

Approximately 3 g. of 3,5-dinitroheptane (IIIa) was dissolved in a solution of 4 g. of sodium hydroxide in 60 ml. of water. This solution was added dropwise with stirring to a solution of 12 ml. of concd. sulfuric acid in 80 ml. of water, cooled by means of an ice-bath. The mixture was extracted with three 20-ml. portions of ether, and the combined ether extract was dried over anhydrous magnesium sulfate. Evaporation of the ether yielded a few drops of a liquid identified as 3,5-heptanedione by means of its copper salt; m. p. 205° (lit.[13] m. p. 206°).

3,5-Diaminoheptane.—A solution of 3.9 g. (0.02 mole) of 3,5-dinitroheptane (IIIa) in 25 ml. of absolute ethanol was shaken with platinum oxide at room temperature under hydrogen at 45 p. s. i. Complete hydrogenation could not be effected. The solution was filtered and the alcohol was distilled at reduced pressure and room temperature. A yield of 1.3 g. (48%) of a fraction boiling at 82–88° (*ca.* 18 mm.) was sufficient for redistillation from a microdistillation apparatus. The second of three fractions, $n^{20}D$ 1.4507, was submitted for analysis.

Anal. Calcd. for $C_7H_{18}N_2$: C, 64.56; H, 13.93. Found: C, 64.27; H, 13.47.

The benzenesulfonamide derivative crystallized from ethanol as white needles, m. p. 150.5–151.5°.

Anal. Calcd. for $C_{19}H_{26}N_2O_4S_2$: C, 55.58; H, 6.38. Found: C, 56.04; H, 6.66.

2-Methyl-2,4-dinitrohexane (IIIb).—The sodium salt of 2-nitropropane was prepared by crushing 2.8 g. (0.07 mole) of solid sodium hydroxide in the presence of excess nitroparaffin. The slurry was transferred to the reaction flask, and 50 ml. of 2-nitropropane and 10 g. (0.07 mole) of N-(2-nitrobutyl)-dimethylamine (Ia) were added. The heterogeneous mixture was heated with stirring under a stream of nitrogen at 120°. After eight hours the evolution of dimethylamine was greatly diminished. The mixture was cooled, acidified with 50 ml. of 10% acetic acid, and extracted with four 10-ml. portions of ether. The combined ether extract was washed with two 20-ml. portions of 5% sodium carbonate, four 20-ml. portions of water, and dried over anhydrous magnesium sulfate. The ether and excess 2-nitropropane were distilled at water-pump pressure. The residue was distilled at reduced pressure, and 7.3 g. (55%) of a light yellow oil boiling at 88–92° (0.3 mm.) was collected. A small portion was redistilled at reduced pressure, and the second of three fractions, $n^{20}D$ 1.4536, was submitted for analysis.

Anal. Calcd. for $C_7H_{14}N_2O_4$: C, 44.21; H, 7.37; N, 14.74. Found: C, 44.21; H, 7.26; N, 15.01.

2-Methyl-2,4-diaminohexane.—The procedure for the preparation of 3,5-diaminoheptane was followed. The reduction was incomplete. A yield of 22% of a fraction boiling at 71–72° (*ca.* 18 mm.), $n^{20}D$ 1.4438, was collected.

Anal. Calcd. for $C_7H_{18}N_2$: C, 64.56; H, 13.93. Found: C, 63.82; H, 13.80.

The phenylthiourea derivative of 2-methyl-2,4-diaminohexane was prepared. The white solid was recrystallized from ethanol, m. p. 152.5–153.5°.

Anal. Calcd. for $C_{21}H_{28}N_4S_2$: C, 62.96; H, 7.04. Found: C, 63.39; H, 7.45.

Ethyl α-Cyano-γ-nitrocaproate (IVa).—To a solution of 10 g. (0.06 mole) of N-(2-nitrobutyl)-diethylamine (Ib) in 40 ml. of dry xylene was added 6.3 g. (0.06 mole) of redistilled ethyl cyanoacetate. The solution was heated with stirring at 95–100° and a slow stream of nitrogen was passed through the apparatus to eliminate the diethylamine formed in the reaction. After fifteen hours the amine evolution had practically ceased and the solution

(9) Baw, *Quart. J. Indian Chem. Soc.*, **3**, 101 (1926) [*C. A.*, **20**, 3695 (1926)].

(10) All melting points are corrected.

(11) Johnson, THIS JOURNAL, **68**, 12 (1946).

(12) Blomquist and Shelley, *ibid.*, **70**, 147 (1948).

(13) Fischer and Bartholomäus, *Ber.*, **45**, 1983 (1912).

had become dark-colored. To the cooled solution was added 60 ml. of ether. The ethereal solution was washed with four 25-ml. portions of 10% hydrochloric acid, four 15-ml. portions of 5% sodium bicarbonate, four 25-ml. portions of water and dried over anhydrous magnesium sulfate. The solvents and unchanged ester were distilled at water-pump pressure. The residue was distilled at reduced pressure, and 2 g. (16%) of a yellow oil boiling at 130–150° (2 mm.), $n^{20}D$ 1.4500, was collected. The crude product was redistilled at reduced pressure from a micro-distillation apparatus, and the middle of three fractions was submitted for analysis, $n^{20}D$ 1.4522 (lit.[6] b. p. 135° (1 mm.), $n^{20}D$ 1.451).

Anal. Calcd. for $C_9H_{14}N_2O_4$: N, 13.08. Found: N, 13.16.

The use of an equimolar amount of sodium hydroxide in the reaction as described above caused extreme resinification and no pure product could be isolated.

Methyl α-Cyano-γ-nitrocaproate (IVb).—A solution of 10 g. (0.06 mole) of N-(2-nitrobutyl)-diethylamine (Ib) and 5.5 g. (0.06 mole) of methyl cyanoacetate in 50 ml. of dry benzene was heated with stirring under a stream of nitrogen at 90–95°. The reaction was complete after eight hours. The solution was cooled and 50 ml. of ether was added. Traces of amine were removed by extraction with 20 ml. of 5% hydrochloric acid. Then the ether solution was washed with 20 ml. of 5% sodium bicarbonate, six 25-ml. portions of water and dried over anhydrous magnesium sulfate. The solvents were distilled at water-pump pressure. The residue was distilled at reduced pressure, and 2.9 g. (23%) of a yellow oil boiling at 119–122° (0.7 mm.) was collected. The crude product was redistilled twice and a sample, $n^{20}D$ 1.4561, was analyzed.

Anal. Calcd. for $C_8H_{12}N_2O_4$: N, 14.00. Found: N, 14.26.

N-(2-Nitrobutyl)-piperidine by Amine Exchange.—The procedure was patterned after that of Snyder and Brewster[7] for amine exchange reactions. A solution of 5 g. (0.03 mole) of N-(2-nitrobutyl)-dimethylamine (Ia) and 14.5 g. (0.15 mole) of piperidine was heated under reflux. Nitrogen was passed through the solution and the reaction appeared to be complete after two and one-half hours. The solution was cooled and 1 ml. of 10% sodium hydroxide was added. Then the solution was extracted with three 10-ml. portions of ether. The combined ether extract was washed with three 10-ml. portions of water, and dried over anhydrous magnesium sulfate. The ether and excess piperidine were distilled at water-pump pressure. The dark-colored residue was distilled at reduced pressure, and 1.3 g. (23%) of an almost colorless liquid, $n^{20}D$ 1.4707, boiling at 73–78° (0.3 mm.) (lit.[14] b. p. 128–133° (18 mm.)) was collected. There was *ca.* 2 g. of resinous material left in the distillation flask. The molecular weight was determined by titration according to the method of Cerf.[14]

Anal. Calcd. for $C_9H_{18}N_2O_2$: mol. wt., 186. Found: mol. wt., 177, 184.

N-(2-Nitroisobutyl)-dimethylamine (II) as an Alkylating Agent.—The Mannich base, N-(2-nitroisobutyl)-dimethylamine, prepared according to the procedure of Johnson,[11] was used in an attempt to alkylate 2-nitropropane by the method used to prepare 2-methyl-2,4-dinitrohexane. No evidence of reaction was detected. An attempted amine exchange of the Mannich base (II) with piperidine according to the method used to effect the exchange with (Ia) also failed.

N-(2-Nitroisobutyl)-dimethylamine Hydrochloride.—To a solution of 10 g. (0.07 mole) of N-(2-nitroisobutyl)-dimethylamine in 25 ml. of absolute alcohol was added a solution of 10 ml. of concentrated hydrochloric acid in 25 ml. of absolute alcohol. A white solid precipitated when the solution was cooled and was collected on a filter. Addition of ether to the filtrate yielded another crop of crystals. The combined solid was washed with a little absolute alcohol followed by a little absolute ether. The yield of crude hydrochloride was 8 g. (62%). After three recrystallizations from absolute ethanol it melted at 165–166° (dec.).

Anal. Calcd. for $C_6H_{15}ClN_2O_2$: C, 39.45; H, 8.27. Found: C, 39.68; H, 8.48.

N-(2-Nitroisobutyl)-piperidine.—The procedure used was an adaptation of that of Snyder and Eliel[8] for the amine exchange reaction of 1-methylgramine with piperidine. A solution of 5 g. (0.03 mole) of N-(2-nitroisobutyl)-dimethylamine hydrochloride and 12.7 g. (0.15 mole) of redistilled piperidine in 25 ml. of *n*-hexanol was refluxed for eight hours. There was only a little amine evolution. The solution deposited crystals when cooled. Ether was added and the suspension was extracted with four 25-ml. portions of 10% hydrochloric acid followed by four 20-ml. portions of 5% hydrochloric acid. The combined acid extract was made alkaline with 40% sodium hydroxide, and was extracted with three 20-ml. portions of ether. The combined ether extract was dried over anhydrous magnesium sulfate. The ether was evaporated and the residue was distilled at water-pump pressure (*ca.* 30 mm.), yielding 2.5 g. of a liquid boiling at 97–115°. It was redistilled at reduced pressure and *ca.* 1 g. of a liquid boiling at 55–70° (4 mm.)[15] was collected. A picrate was prepared from this fraction and after two recrystallizations from ethanol melted at 142.5–143.5°. Admixture with an authentic sample of N-(2-nitroisobutyl)-piperidine picrate showed no depression of the melting point. Since it has not been reported in the literature, the picrate obtained from the amine exchange reaction was submitted for analysis.

Anal. Calcd. for $C_{15}H_{21}N_5O_9$: C, 43.37; H, 5.10. Found: C, 43.53; H, 5.11.

During the course of the investigation the picrate of N-(2-nitroisobutyl)-dimethylamine was prepared. It was insoluble in alcohol, but had a limited solubility in acetone. A sample recrystallized from purified acetone melted at 167.5–168.5° (dec.).

Anal. Calcd. for $C_{12}H_{17}N_5O_9$: C, 38.40; H, 4.57. Found: C, 38.92; H, 4.91.

N-(2-Nitroisobutyl)-dimethylamine Methiodide.—To a solution of 20 g. (0.13 mole) of N-(2-nitroisobutyl)-dimethylamine in 20 ml. of absolute ethanol was added 36 g. (0.25 mole) of methyl iodide. The solution was kept in a stoppered flask for thirty-six hours. The crystals which formed were collected on a filter. After one recrystallization from methanol the yield was 24.3 g. (65%) of the methiodide. A portion of the crystals was recrystallized three times from methanol and the melting point was found to be 194.5–195.5°.

Anal. Calcd. for $C_7H_{17}IN_2O_2$: C, 29.17; H, 5.94. Found: C, 29.29; H, 5.89.

N-(2-Nitroisobutyl)-trimethylammonium Picrate.—To a solution of *ca.* 0.2 g. of N-(2-nitroisobutyl)-trimethylammonium iodide in 10 ml. of water was added 2 ml. of a saturated aqueous solution of picric acid which had been made alkaline with 10% sodium hydroxide. Yellow crystals precipitated immediately and were separated by filtration. After three recrystallizations from ethanol the salt melted at 212–213° (dec.).

Anal. Calcd. for $C_{13}H_{19}N_5O_9$: C, 40.12; H, 4.92. Found: C, 40.42; H, 4.86.

Summary

The Mannich base of 1-nitropropane has been shown to alkylate 1-nitropropane, 2-nitropropane, ethyl and methyl cyanoacetate, and to undergo amine exchange with piperidine.

N-(2-Nitroisobutyl)-dimethylamine was found to be unreactive as an alkylating agent for 2-

(14) Cerf, *Bull. soc. chim. France*, [5] **4**, 1451, 1460 (1937).

(15) An authentic sample of N-(2-nitroisobutyl)-piperidine[11] was prepared which boiled at 94–96° (3 mm.).

nitropropane. A trace of N-(2-nitroisobutyl)-piperidine was obtained by means of an acid catalyzed amine exchange.

This investigation has revealed no exception to the proposal that alkylation of nitroparaffins by amines must proceed through an elimination–addition mechanism.

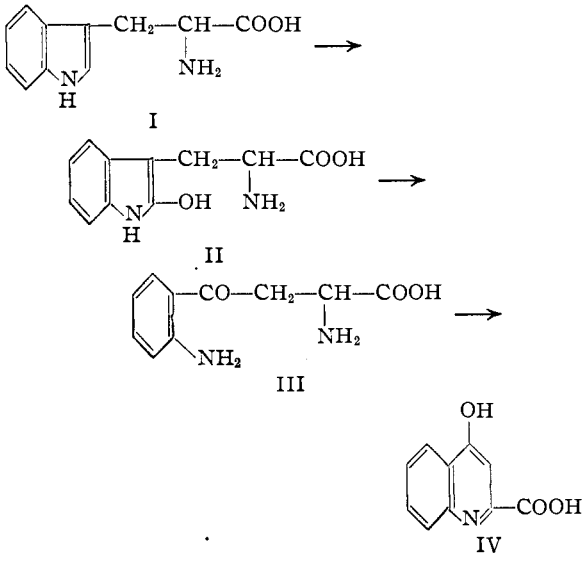
URBANA, ILLINOIS RECEIVED MARCH 16, 1950

[CONTRIBUTION FROM THE INSTITUTE OF POLYTECHNICS, UNIVERSITY OF CITY OSAKA]

Studies on Amino Acids. III. The Synthesis of α-Hydroxytryptophan

BY MUNIO KOTAKE, TAKEO SAKAN AND TOSHIO MIWA

Y. Kotake,[1] *et al.*, have demonstrated the presence of kynurenine, as well as kynurenic acid, in the urine of rabbits which have been fed tryptophan. They have postulated the following sequence of reactions in the intermediary metabolism of tryptophan.



I

II

III

IV

α-Hydroxytryptophan, which is postulated as an intermediary in the above scheme, was isolated by Wieland and Witkop[2] from the hydrolysis product of phalloidin, a toxic principle found in a poisonous mushroom, *Amanita phalloides*. The yield of amino acid was too small to permit biological experiments. Later, Butenandt[3] was able to show that this compound possesses a hereditary-controlling gene hormone activity, though weaker than kynurenine, in producing the color of eyes of *Drosophila melanogaster;* in this respect α-hydroxytryptophan acts as pro-kynurenine.

Previous attempts to synthesize α-hydroxytryptophan proved unsuccessful.[4,5] The optically active α-hydroxytryptophan which has been obtained by oxidizing L-tryptophan with peracetic acid under controlled conditions is proved, recently, by Witkop[6] to be identical with that obtained from phalloidin.

In our investigations, we found that *o*-nitrophenylacetic acid ethyl ester undergoes the Michael condensation with diethyl methylenemalonate in the presence of sodium ethoxide. The product was treated with 48% hydrobromic acid and decarboxylation took place, giving an acid compound with formula $C_{11}H_{11}O_6N$. When the condensation product was treated with ethyl nitrite and sodium ethoxide, a corresponding oximino ester was produced with 60% yield.

Since *o*-nitrophenylsuccinic acid was obtained by hydrolyzing this ester with hydrochloric acid, the oximino ester must have the structural formula (VI) and thus the chemical structure of the condensation product must be (V). The acid with the empirical formula $C_{11}H_{11}O_6N$ is therefore shown to be *o*-nitrophenylglutaric acid (VII).

On reducing the oximino ester (VI) at 0° with stannous chloride and hydrochloric acid in glacial acetic acid, the amino ester crystallized out with tin chloride as a double salt. After removing the tin with hydrogen sulfide, the product was hydrolyzed with hydrochloric acid and concentrated in an atmosphere of carbon dioxide. The hydrochloride of the amino acid was obtained in a crystalline form, which after recrystallization from water decomposes at 208°. The free amino acid, decomposition point 248–249°, was obtained from this hydrochloride.

The analytical results obtained for this compound closely agree with the data calculated for α-hydroxytryptophan and furthermore a violet color shown by the ninhydrin test characterizes the compound as an α-amino acid. In the Millon and Folin–Denis reactions the compound gave a yellowish-orange and a dark blue color, respectively. An aromatic amine, which was liberated only when the amino acid was warmed with alkali, could be diazotized and coupled with β-naphthol to produce a dye. The positive "Pine splint reaction" was shown when the amino acid was dry distilled with zinc dust. These facts indicate the presence of oxindole residue in the molecule. The results obtained by these tests agree with those reported by Wieland for the α-hydroxytryptophan, which has been isolated from phalloidin. The amino acid we have

(1) Y. Kotake, *Z. physiol. Chem.*, **195**, 158 (1931).
(2) Wieland and Witkop, *Ann.*, **543**, 171 (1940).
(3) Butenandt, *Naturwiss.*, **28**, 447 (1940).
(4) Fischer and Smeykal, *Ber.*, **56**, 2368 (1923).
(5) Julian, Pikl and Wantz, THIS JOURNAL, **57**, 2026 (1935).
(6) Witkop, *Ann.*, **558**, 98 (1947).