not absolutely pure. The compounds are not water soluble to any appreciable extent but are readily soluble in methanol, ethanol and chloroform. None of these compounds has a definite melting point, but they begin to decompose above 220° and decomposition is complete at 300°.

TABLE I

ARSENOSO COMPOUNDS DERIVED FROM HETEROCYCLIC AMINES

R-*p*-Arsenosobenzamido-Compound	As analysis, % Calcd.	Found	N analysis, % Calcd.	Found	MTD[a] mouse
2-R-Thiazole[b]	25.45	25.2	9.55	9.4	7.5
2-R-4-Methylthiazole	24.3	24.1	9.11	9.1	3.5
2-R-Thiazoline[c]	25.3	25.0	9.48	9.3	30.0
2-R-Pyridine[d]	26.0	26.1	9.74	9.8	2.0
2-R-Pyrimidine[e]	25.9	25.8	14.56	14.4[f]	30.0
2-R-4-Methylpyrimidine[e]	24.7	24.9	13.9	13.7[f]	3.5
2-R-4,6-Dimethylpyrimidine[e]	23.6	23.6	13.3	13.0[f]	3.5
R-*p*-Dichloroarsylbenzamido-					
2-R-Thiazole	21.45	21.4	8.0	7.9	..
2-R-Thiazoline[g]	21.3	21.3	7.8	7.8	..

[a] Maximal tolerated dose for intraperitoneal injection in twenty gram mice, expressed as the number of milligrams/kilogram, and determined by Dr. H. J. Robinson, Merck Institute for Therapeutic Research, Rahway, N. J. [b] 2-Aminothiazole was generously supplied by Dr. D. F. Robertson, Merck & Co., Rahway, N. J. [c] 2-Aminothiazoline was generously supplied by Dr. George W. Raiziss, Dermatological Research Laboratories, Philadelphia, Pa. [d] Previously synthesized by Doak, *et al.*, ref. 5a. [e] 2-Aminopyrimidine, 2-amino-4-methylpyrimidine and 2-amino-4,6-dimethylpyrimidine were generously supplied by Dr. Jackson P. English, American Cyanamid Co., Stamford, Conn., and Dr. E. H. Northey, Calco Chemical Division of the American Cyanamid Co., Bound Brook, N. J. [f] The customary difficulties in determining the nitrogen content of pyrimidines was experienced. The values represent the average of the two highest determinations. The other nitrogen determinations and the arsenic determinations are the average of three or more determinations. [g] The dichloroarsylbenzamide compounds of pyridine, 4-methylthiazole and the pyrimidines were not isolated.

Pharmacological Activity.—We are grateful to Dr. H. J. Robinson of the Merck Institute for Therapeutic Research for carrying out preliminary tests on these compounds. Our own preliminary studies against *T. equiperdum* infections in mice have not proved encouraging. Dr. Robinson found that although the compounds are highly active *in vitro* against *T. equiperdum* and *Dirofilaria immitis*, their high toxicity *in vivo* for the host makes their use undesirable. The results with the 2-*p*-arsenosobenzamidopyridine agree with those of Eagle, *et al.*,[5c] who reported the MTD for mice as 2.3 mg./kg. and although the compound possessed a high treponemicidal activity it had a low chemotherapeutic index.

Summary

The *p*-arsenosobenzoyl derivatives of 2-aminothiazole, 2-aminothiazoline, 2-aminopyridine, 2-amino-4-methylthiazole, 2-aminopyrimidine, 2-amino-4-methylpyrimidine and 2-amino-4,6-dimethylpyrimidine were synthesized. The *p*-dichloroarsylbenzoyl derivatives of 2-aminothiazol- and 2-aminothiazoline have been prepared.

Preliminary pharmacological tests with these compounds have not indicated favorable chemotherapeutic activity.

AUGUSTA, GA. RECEIVED JUNE 16, 1949

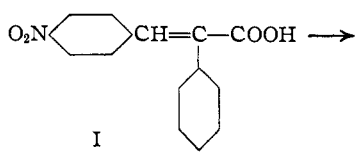
[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

The Preparation of Three Aminodiiodophenyl-phenylpropionic Acids

BY T. R. LEWIS, MARGARET G. PRATT, E. D. HOMILLER, B. F. TULLAR AND S. ARCHER

Several years ago a program was initiated in this Laboratory the goal of which was the discovery of a superior radiopaque to be used in clinical cholecystography. As a part of this study, three isomeric aminodiiodophenylphenylpropionic acids were prepared for pharmacological evaluation. The synthesis of these acids is the subject of the present report.

A common structural feature which is shared by the cholecystographic agents examined clinically up to now is the diiodohydroxyphenyl group. It has been suggested that the presence of the hydroxyl in a gall-bladder contrast medium is necessary for visualization of this organ.[1] The utility of our compounds has been determined by Hoppe[2] who has found that the amino may replace the hydroxyl group without impairing the usefulness of the drug.[3] It is our belief that the sole function of these radicals is to facilitate the introduction of the iodine atoms into the benzene ring. The diiodo acid, III, was prepared according to the equations

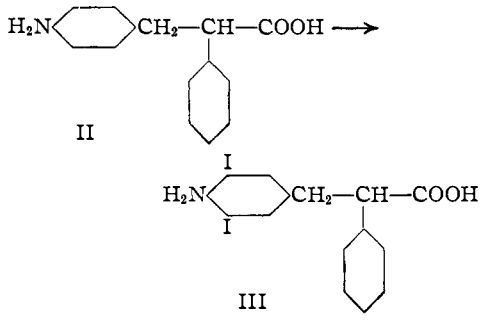


I

(1) Epstein, Natelson and Kramer, *J. Am. Roentgenol.*, **56**, 202 (1946).

(2) Hoppe and Archer, *Federation Proc.*, **8**, 303 (1949).

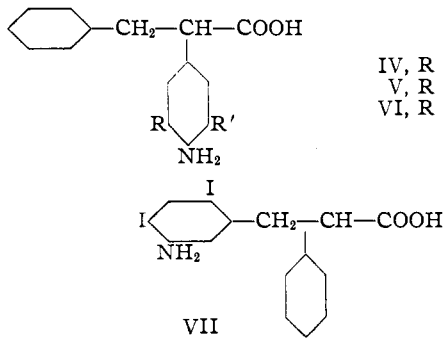
(3) Other work in this Laboratory has demonstrated that neither the amino nor hydroxyl group is essential for good visualization.



The *p*-nitrobenzaldiacetate was prepared by a slight modification of the standard method.[4] A readily separable mixture of *cis* and *trans* isomers was obtained by modification of known methods.[5,6] Under optimum conditions the combined yield of isomers was 80–85%.[7]

Reduction of the pure higher melting form of I in the presence of Raney nickel catalyst afforded the amino acid, II, in 97% yield. The crude mixed isomers yielded the same substance of comparable purity in 90% of the theoretical amount. The iodination was carried out in dilute acetic acid with iodine monochloride. Analytically pure III was obtained as tan needles after recrystallization from methanol in 64% yield. After our work had been completed the acid, III, was reported by Barnett and coworkers.[8]

The isomeric diiodo acid, V, was synthesized by a similar series of reactions. A mixture of



isomeric α-*p*-nitrophenylcinnamic acids was obtained in about 80% yield. Buckles[7] obtained only one isomer in 13% yield with the aid of triethylamine. Catalytic reduction of the nitro acid resulted in a quantitative yield of the saturated amino acid, IV.

When the iodination of this compound was performed under conditions which were satisfactory for the formation of the isomeric acid, III, the product, V, was obtained in very small amounts (15–25% yield). The material was contaminated with tarry by-products which were difficult to remove. When iodinated in hydrochloric acid solution, IV gave two products which were separated by chloroform extraction. The soluble product proved to be the desired diiodo acid, V. The insoluble material, which could not be recrystallized and melted at 182°, contained ionic chlorine. When dissolved in sodium hydroxide and the solution carefully acidified a new substance separated. The analytical data indicated that this was the monoiodo acid, VI, and the substance from which it was obtained was the corresponding hydrochloride salt.

It appeared that in acetic acid solution the desired product, V, was being attacked further by the iodine monochloride thereby lowering the yield. It was hoped that removal of the diiodo acid from the reaction zone as soon as it was formed would result in improvement in both quantity and quality of the final product. Actually this proved to be the case, for when chloroform or tetrachloroethane was added to the reaction mixture iodination proceeded smoothly. The over-all yield of analytically pure material, based on α-nitrophenylcinnamic acid, was 64%.

It was of some pharmacological interest to obtain the optical antipodes of V. These were secured by iodination of the active forms of IV. *d*-Desoxyephedrine served as a satisfactory resolving agent for α-phenyl-β-aminophenylpropionic acid since there was a wide difference in solubility of the diastereomeric salts in ethyl acetate. The iodination of the optically active forms of IV was carried out as in the case of the *dl*-form.

The isomer VII was prepared by the same sequence that was used for III and V. The α-phenyl-*m*-nitrocinnamic acid was prepared by Koelsch's method.[6] No attempt was made to find optimum conditions for the iodination step. The position of the iodine atoms in the benzene ring was not determined but it is believed that the expression, VII, is the most probable structure for the compound.

Experimental[9]

α-Phenyl-*p*-nitrocinnamic Acid.—A mixture of 560 g. of *p*-nitrobenzaldiacetate, 340 g. of phenylacetic acid, 228 g. of fused sodium acetate and 560 ml. of acetic acid was refluxed for ten hours. At the end of this time the dark reaction mixture was cooled to 40° and slowly poured with stirring into three liters of water. After cooling to 5° the crystalline product was collected and the filtrate (A) reserved.

The filter cake was broken up and added to a solution of 80 g. of sodium hydroxide in four liters of water. The solution was clarified (Filtercel) and acidified with glacial acetic acid. The acid which separated was collected on a filter, washed with water and dried; yield, 387 g., m. p. 190–205°. The filtrate was combined with filtrate (A) above and acidified strongly with hydrochloric acid. In this way 40 g. of crude low melting isomer (m. p. 100–

(4) "Organic Syntheses," Coll. Vol. II, p. 441 (1941).

(5) Bakunin, *Gazz. chim. ital.*, **27**, II, 36 (1897); **31**, II, 83 (1901).

(6) Koelsch and Johnson, THIS JOURNAL, **65**, 565 (1943).

(7) Buckles and Housman, *ibid.*, **70**, 414 (1948), prepared the acid, I, in 66% yield using triethylamine instead of sodium acetate. They did not report the presence of the low melting isomer.

(8) Barnett, Robinson and Wilson, *J. Chem. Soc.*, 203 (1947).

(9) All melting points unless otherwise specified are uncorrected. Analyses were carried out under the supervision of Mr. M. E. Auerbach.

110°) was obtained; total yield, 427 g. or 70% of the theoretical. When the reflux period was doubled the combined yield of the desired product was increased to 80–85%. When recrystallized from ethanol, the higher melting form melted at 208–210°. The lower melting form was crystallized from dilute ethanol, m. p. 143–145°. Bakunin[5] reported 213–214° and 147°, respectively, as the melting points of these isomers.

β-*p*-Aminophenyl-α-phenylpropionic Acid.—A water solution of 427 g. of the crude mixed acids and 66 g. of sodium hydroxide was reduced at 70° and 1,000 p.s.i. in the presence of Raney nickel catalyst. After six hours the theoretical amount of hydrogen was absorbed. The catalyst was filtered off and the filtrate made acid to congo red with 400 ml. of hydrochloric acid. The solution was cooled in ice and filtered. The crystalline hydrochloride was washed with 20% hydrochloric acid and dried *in vacuo* at 50°; yield, 400 g. (90%), m. p. >270°. Neutralization of the filtrate afforded 20 g. of the amino acid, m. p. 204–205°.

Anal. Calcd. for $C_{15}H_{15}NO_2 \cdot HCl$: Cl, 13.07. Found: Cl, 12.95.

When the pure α-phenyl-*p*-nitrocinnamic acid, m. p. 208–210°, was reduced and the filtrate from the reduction mixture made slightly acidic the free amino acid was secured in 97% of the theoretical yield, m. p. 200–203°.

β-(4-Amino-3,5-diiodophenyl)-2-phenylpropionic Acid.—A solution of 85 g. of the amino acid hydrochloride, II, in 750 ml. of acetic acid and 650 ml. of water was heated to 80°. Then a solution of 36 ml. of iodine monochloride in 120 ml. of acetic acid was added over a period of thirty minutes. After one hour more at this temperature the mixture was cooled to 60° and treated with 20 g. of sodium bisulfite. After cooling to zero degrees the whole was filtered. The product was washed with water and air-dried, wt. 110 g.

The crude acid was dissolved in 600 ml. of warm methanol, treated with 50 ml. of water previously saturated with sulfur dioxide and decolorized with Norite. Water was added to the filtrate to incipient turbidity and the solution cooled. The product was removed by filtration, washed with 70% methanol and dried; wt. 98 g. or 64% of the theoretical yield, m. p. 175–176.8° (cor.).

Anal. Calcd. for $C_{15}H_{13}I_2NO_2$: I, 51.48; N, 2.66. Found: I, 51.87; N, 2.70.

The compound obtained above was light tan. A white product was obtained in the following way. A 120-g. sample of the diiodo acid, m. p. 162–166°, was dissolved in acetone and treated with 25 g. of morpholine. The salt was collected and recrystallized from dilute ethanol. The first crop of needles was collected and dried, wt. 72 g. The melting point depended upon the rate of heating.

Anal. Calcd. for $C_{15}H_{13}I_2NO_2 \cdot C_4H_8NO$: $N_{A.P.}$, 2.44. Found: $N_{A.P.}$, 2.62.[10] The salt was dissolved in 1.5. liters of ethanol and to the solution there was added 200 ml. of 3% sodium hydrosulfite. The cloudy solution was filtered (Filtercel) and the filtrate further diluted with 750 ml. of water. It was saturated with sulfur dioxide and allowed to cool slowly. The next day the heavy white crystals of the pure acid were filtered and dried. The product, which weighed 65 g., melted at 175–176.2° (cor.).

***p*-Nitrophenylacetic Acid.**—The following is better suited for a large scale preparation than the one described in "Organic Syntheses."[11] In a 22-liter flask equipped with a stirrer and reflux condenser there was placed 7 liters of water. Then 7.5 liters of sulfuric acid was added carefully and, when the solution had cooled to 50°, 2500 g. of *p*-nitrobenzyl cyanide was added in one portion. The contents of the flask were heated (Glas-col mantle) until the inner temperature had reached 140–150° and the solution began to reflux. Heating was continued for another fifteen minutes. The total heating time was one and one-half hours. The clear solution was poured into 15 liters of water with vigorous stirring. The nitrophenylacetic acid was removed by filtration, washed with cold water and dried. The cream-colored solid weighed 2700 g. and melted at 151–153°. The yield was 97% of the theoretical.

α-*p*-Nitrophenylcinnamic Acid.—A mixture of 380 g. of *p*-nitrophenylacetic acid, 267 g. of benzaldehyde, 264 g. of fused sodium acetate and 1200 ml. of acetic anhydride was refluxed for twelve hours and poured into 3500 ml. of water. The cooled mixture was filtered and the solid (Fraction A) was saved. The filtrate was made strongly acid with hydrochloric acid and cooled. The pale yellow crystals (Fraction B) were collected.

Fraction A was heated in a sodium carbonate solution and the mixture filtered. The filtrate was extracted with benzene to remove some oily material and then acidified to give 410 g. of the higher melting acid (m. p. 210–213). After recrystallization from ethanol the product melted at 219–221°.[12]

Anal. Calcd. for $C_{15}H_{11}NO_4$: N, 5.20. Found: N, 4.92.

Fraction B, which weighed 44 g. and melted at 140–143° was crystallized from chloroform–ligroin until the melting point reached 150–152°.

Anal. Calcd. for $C_{15}H_{11}NO_4$: N, 5.20. Found: N, 5.25.

In another experiment, in which benzaldiacetate was generated *in situ* from benzaldehyde and acetic anhydride the yield of mixed *cis* and *trans* isomers was 80% after a sixteen-hour heating period. This product was reduced to the amino acid in 93% yield.

α-Aminophenyl-β-phenylpropionic Acid.—The reduction of 48.2 g. of the sodium salt of the higher melting acid was carried out at 350 p.s.i. Hydrogen was absorbed at room temperature and after the gas uptake had slackened the temperature was raised to 130° to complete the reaction. The operation required ninety minutes. The catalyst (Raney nickel) was removed and the filtrate then made faintly acidic. The solid that separated weighed 48.7 g. (98%) and melted at 200–203°. A small sample, after recrystallization from ethanol, melted at 202–204°.

Anal. Calcd. for $C_{15}H_{15}NO_2$: N, 5.81. Found: N, 5.76.

The hydrochloride was prepared by cooling a hot solution of the amino acid in 6 *N* hydrochloric acid. The white needles thus obtained melted above 250°.

Anal. Calcd. for $C_{15}H_{15}NO_2 \cdot HCl$: C, 74.66; H, 6.27. Found: C, 74.47; H, 6.08.

α-(4-Amino-3,5-diiodophenyl)-β-phenylpropionic Acid.—The filtered reduction mixture which originally contained 50 g. of α-*p*-nitrophenylcinnamic acid was acidified with 40 ml. of hydrochloric acid and maintained at 80°.

A mixture of 300 ml. of *sym*-tetrachloroethane (or an equal volume of chloroform), 67.0 g. of iodine monochloride and 180 ml. of 6 *N* hydrochloric acid was warmed to 50°. The solution of amino acid hydrochloride was added over a period of fifteen minutes at 50–55°. The mixture was heated at 55° for ten more minutes and cooled. The layers were separated and the organic phase washed with 250 ml. of 5% sodium hydrosulfite. After washing with water, 5 g. of Darco was added and the mixture stirrred at room temperature for one hour. After the charcoal was removed, the solution was diluted with three volumes of petroleum ether. The solid that separated was collected and dried. It weighed 79.6 g. and melted at 142.6–143.8° (cor.). It was taken up in a mixture of 350 ml. of ethanol and 125 ml. of water and decolorized. The filtrate deposited 65 g. of the diiodo acid, m. p. 141–145.4° (cor.). After recrystallization from benzene–ligroin there was obtained 57.4 g. of cream-colored needles, m. p. 144–146.2° (cor.). The yield was 64% based on the cinnamic acid.

Anal. Calcd. for $C_{15}H_{13}I_2NO_2$: I, 51.48. Found: I, 51.24.

A typical experiment in which the organic solvent was omitted from the reaction mixture gave a product from which two substances were isolated.

(10) Perchloric acid titration of the morpholine nitrogen. This salt was first prepared by M. E. Auerbach of this Laboratory.

(11) "Organic Syntheses," Coll. Vol. I, p. 406.

(12) Walther and Wetzlich, *J. prakt. Chem.*, [2] **61**, 181 (1900), reported the m. p. as 224.5°.

Seventy grams of the amino acid hydrochloride was added to a solution of 900 ml. of 4 *N* hydrochloric acid and 32 ml. of iodine monochloride over a period of two hours. After one-half hour 200 ml. of hydrochloric acid was added and about one hour later 950 ml. of water. The mixture was heated to 80° for one hour and diluted with 500 ml. of water. It was cooled to 35° and saturated with sulfur dioxide. The solid was filtered off and dried, wt. 107 g. It was heated with chloroform and filtered. The insoluble residue weighed 53 g. The chloroform solution was diluted with petroleum ether and cooled. A total of 35 g. of crude diiodo acid was collected which, after recrystallization from ethanol, amounted to 16.0 g. of crystals, m. p. 139–141°. The recrystallization was not smooth since a dark oil tended to separate and contaminate the product. The chloroform-insoluble fraction which melted at 182° (dec.) was probably the hydrochloride of VI.

Anal. Calcd. for $C_{15}H_{14}INO_2 \cdot HCl$: Cl, 8.80. Found: Cl, 8.63. Twenty grams of this material was dissolved in 15% sodium hydroxide and carefully neutralized. The oil that separated soon solidified. It was recrystallized from dilute methanol several times and then melted at 116.8–117.7° (cor.).

Anal. Calcd. for $C_{15}H_{14}INO_2$: I, 34.55. Found: I, 34.60.

α-(4-Acetamido-3,5-diiodophenyl)-β-phenylpropionic Acid.—Thirty grams of α-(4-amino-3,5-diiodophenyl)-β-phenylpropionic acid and 250 ml. of acetic anhydride containing 0.5 ml. of sulfuric acid was refluxed for ninety minutes and poured into water. The semi-solid product was washed with water by decantation and then dissolved in 100 ml. of 10% sodium hydroxide solution. After filtration the solution was made acid with acetic acid. The crystals were filtered and recrystallized from ethanol. There was obtained 19 g. of acetyl body, m. p. 215–217°. After another recrystallization it melted at 221.2–223.5° (cor.).

Anal. Calcd. for $C_{17}H_{15}I_2NO_3$: C, 38.16; H, 2.83; I, 47.44. Found: C, 38.37; H, 3.04; I, 47.60.

Resolution of *dl*-α-(4-Aminophenyl)-β-phenylpropionic Acid.—A solution of 240 g. of the *dl*-amino acid and 160 g. of *d*-desoxyephedrine in 2500 ml. of ethyl acetate was allowed to stand at 25° for one hour. The crystals were filtered and recrystallized from ethyl acetate. In this way 129 g. of a pure diastereomeric salt, m. p. 148–150°, was secured. A 120-g. sample was dissolved in 2500 ml. of boiling water and slowly acidified with 50 ml. of acetic acid. On cooling, 70 g. of pure *d*-α-(4-aminophenyl)-β-phenylpropionic acid deposited. The acid melted at 186–188°; $[\alpha]^{25}D$ (5% in H_2O) +102°.

Anal. Calcd. for $C_{15}H_{15}NO_2$: neutral equivalent, 241.1. Found: neutral equivalent, 240.2.

The ethyl acetate filtrate from the original crystallization was concentrated to dryness *in vacuo*. The residue was dissolved in water and made strongly basic. The desoxyephedrine was gathered with ether. In this way 100 g. of the resolving agent was recovered. The aqueous solution was acidified and the crude *l*-amino acid was filtered off.

The product was dissolved in 1600 ml. of boiling ethyl acetate and 104 g. of *l*-desoxyephedrine added. On cooling a salt separated which was recrystallized from the same solvent. It weighed 115 g. and melted at 148–150°. Thirty three grams of this salt was converted to 19 g. of the *l*-amino acid, which melted at 186–188°, $[\alpha]^{25}D$ (5% in water) −103°.

Anal. Calcd. for $C_{15}H_{15}NO_2$: neutral equivalent, 241.1. Found: neutral equivalent, 239.5.

***d*-α-(4-Amino-3,5-diiodophenyl)-β-phenylpropionic Acid.**—The *d*-amino acid (70 g.) was iodinated according to the procedure described for the *dl* compound. However, the diiodo acid was separated from the chloroform solution by extraction with ammonium hydroxide in which the ammonium salt of the diiodo acid was insoluble. It was collected, washed with acetone and dried, wt. 125 g. It was dissolved in water containing a few ml. of ammonium hydroxide and slowly acidified with acetic acid. The product was collected, dried and recrystallized from chloroform–petroleum ether. There was recovered 87 g. (63%) of pure material, m. p. 118.4–119.8° (cor.), $[\alpha]^{25}D$ (1.5% in 95% ethanol) +88.5°.

Anal. Calcd. for $C_{15}H_{13}I_2NO_2$: C, 36.54; H, 2.66; I, 51.48. Found: C, 36.39; H, 2.79; I, 51.75.

***l*-α-(4-Amino-3,5-diiodophenyl)-β-phenylpropionic Acid.**—Seventeen grams of the *l*-amino acid gave 13.0 g. of the *l*-diiodo acid, m. p. 118–120° (cor.), $[\alpha]^{25}D$ (1.5% in 95% ethanol) −88.4°. The specimen of the iodinated product which was first obtained melted at 102.5–103.5° (cor.). The rotation and analytical data were the same as that obtained for the higher melting form. Apparently this was an unstable polymorph since on standing it changed to the higher melting form. Once the latter was obtained we were unable to secure the low-melting compound.

Anal. Calcd. for $C_{15}H_{13}I_2NO_2$: C, 36.54; H, 2.66; I, 51.48. Found: C, 36.68; H, 2.70; I, 51.60.

α-Phenyl-*m*-nitrocinnamic Acid.—A mixture of 16.0 g. of *m*-nitrobenzaldehyde, 13.6 g. of phenylacetic acid, 16.0 g. of fused sodium acetate and 51 ml. of acetic anhydride was refluxed for sixteen hours. The whole was poured into water, cooled and filtered. The solid (Fraction A) was dissolved in 200 ml. of 3% sodium hydroxide solution, extracted with benzene and acidified with 11 ml. of acetic acid. In this way 21.1 g. of a crystalline solid, m. p. 130–140°, was obtained. The filtrate was combined with the one obtained above and acidified strongly with hydrochloric acid. The solid that separated weighed 2.2 g. and melted at 160–170° (Fraction B). The combined yield, 23.3 g., was 87% of the theoretical. This material was suitable for use in the reduction step.

Fraction A was twice recrystallized from ethanol. Seven grams of pure isomer, m. p. 183.8–185.2° (cor.), was obtained. Fraction B was purified in the same way, m. p. 193–196°.[13]

β-*m*-Aminophenyl-α-phenylpropionic Acid.—A solution of 48.2 g. of the nitrocinnamic acid in 500 ml. of 0.4 *N* sodium hydroxide was reduced at 70° using Raney nickel catalyst. Slight acidification of the filtrate from the catalyst resulted in the deposition of a gummy solid. The *p*H was adjusted to 7 and the suspension warmed on the steam-bath. The gum gradually solidified. It was filtered and dried. It weighed 46.4 g. (96%) and melted at 129–132°. After recrystallization from water the product melted at 131–132°.

Anal. Calcd. for $C_{15}H_{15}NO_2$: C, 74.66; H, 6.27. Found: C, 74.62; H, 6.07.

β-(5-Amino-2,4-diiodophenyl)-α-phenylpropionic Acid.—The amino acid (49.0 g.) was dissolved in 800 ml. of acetic acid and heated to 80°. A solution of 23 ml. of iodine monochloride in 150 ml. of acetic acid was added over a period of forty minutes. The mixture was heated at 80–90° for an additional hour, cooled and filtered. The filter cake was washed with acetic acid and then ether. The crude material amounted to 90 g. After two recrystallizations from dilute ethanol (sulfur dioxide was used to decolorize the solution in the first crystallization) the pure diiodo acid melted at 205–205.4° (cor.) and weighed 26.5 g.

Anal. Calcd. for $C_{15}H_{13}I_2NO_2$: I, 51.48; N, 2.84. Found: I, 51.90; N, 2.76.

Summary

1. The preparation of β-(4-amino-3,5-diiodophenyl)-α-phenylpropionic acid, α-(4-amino-3,5-diiodophenyl)-β-phenylpropionic acid and β-(5-amino-2,4-diiodophenyl)-α-phenylpropionic acid has been described.

2. The resolution of α-(4-aminophenyl)-β-phenylpropionic acid has been achieved and the resulting optical antipodes converted to the corresponding diiodo derivatives.

RENSSELAER, NEW YORK RECEIVED MARCH 14, 1949

(13) Bakunin (ref. 5) reported 181–182° and 195–196° as the melting points of the isomers.