about every 50 ml. of solution had been collected. Six fractions were thus collected. Evaporation of fractions 1, 2, 3 and 6 gave no residue. The fourth fraction gave a mixture with m. p. 75–88°. The fifth fraction gave crystals, m. p. 104.5–108.5°, and after recrystallization there was obtained 25 mg., m. p. 108.0–109.8°, identical with 9,10-dihydroanthracene.

Dehydrogenation of 9,10-Dihydroanthracene.—In a test-tube connected to a reflux condenser were placed 1.00 g. of 9,10-dihydroanthracene and 100 mg. of palladium–charcoal catalyst. The tube was placed in a bath at 200° for a few minutes, during which time 6 ml. of gas was collected (blank). The temperature was raised to 300° and kept at 300–340° for three hours, during which time an additional 118 ml. of gas was collected (83%). The reaction mixture was cooled, dissolved in benzene, filtered, and the anthracene removed by means of maleic anhydride. There was obtained 1.24 g. of adduct equivalent to 0.8 g. of anthracene (80%). After the excess maleic anhydride had been removed, the remaining material was treated with trinitrobenzene; whereupon 70 mg. of the 1,2,3,4-tetrahydroanthracene complex, m. p. 128–131°, was obtained, mixed melting point, no depression.

Reaction between 2-Cyclohexenone and Anthracene.—In a preliminary experiment, cyclohexenone was refluxed with palladium–charcoal, but no hydrogen was evolved.[25] A mixture of 2.95 g. anthracene, 3.84 g. cyclohexenone, and 300 mg. of palladium–charcoal was heated in a sealed tube for seven and one-half hours at 295–325°. The tube was cooled in dry-ice, opened (pressure), and the contents dissolved in benzene and filtered. The benzene solution was extracted with 5% sodium hydroxide solution and the alkaline extract made to 500 ml. A 20-ml. aliquot was titrated with potassium bromate–potassium bromide solution.[26] The titration indicated 1.74 g. of phenol present in the total reaction mixture. The tribromophenol formed in the titration was filtered and recrystallized from ethanol, m. p. 91–92° (literature reports 95°). The benzene solution remaining after the alkaline extraction was treated with maleic anhydride and 1.64 g. endoanthracene maleic anhydride was precipitated and filtered. The excess maleic anhydride was extracted from the filtrate, the benzene was evaporated, and the residue was distilled. The distillate (2.45 g.) was dissolved in 20 ml. of ethanol and treated with 2 g. of picric acid. There was obtained 1.52 g. of orange-yellow crystals, m. p. 110–113°, identical with the picrate of 1,2,3,4-tetrahydroanthracene. The mother liquor was passed through a column of activated alumina. The first fraction gave 50 mg. of 1,2,3,4-tetrahydroanthracene. The second fraction contained some tetrahydroanthracene, some dihydroanthracene, and some other material that may have resulted from the polymerization of cyclohexenone. After removal of about 135 mg. of 9,10-dihydroanthracene, m. p. 107–109°, mixed melting point, no depression, the remaining material was treated with trinitrobenzene. There separated 0.386 g. of 1,2,3,4-tetrahydroanthracene trinitrobenzene complex, m. p. 128–130.5°, mixed melting point, no depression. The mother liquor was not investigated further.

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Summary

When anthracene and tetralin are heated together at 1 atmosphere pressure in the presence of a palladium catalyst, a 30% yield of 1,2,3,4-tetrahydroanthracene can be obtained.

When anthracene and tetralin are heated together in a sealed tube in the presence of a palladium catalyst, the reaction resembles a catalytic hydrogenation of anthracene and a 61% yield of 1,2,3,4-tetrahydroanthracene along with small amounts of 9,10-dihydroanthracene, and 1,2,3-4,5,6,7,8-octahydroanthracene are obtained. This type of hydrogenation of anthracene can also be achieved with 2-cyclohexenone.

The dehydrogenation of 9,10-dihydroanthracene in the liquid phase results in expulsion of less than the theoretical quantity of hydrogen and formation of some 1,2,3,4-tetrahydroanthracene.

1,2,3,4-Tetrahydroanthracene can be conveniently prepared in good yield by refluxing an ethanol solution of anthracene or 9,10-dihydroanthracene with Raney nickel.

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[25] Compare Ruzicka, ref. 5a, who by heating 3-methylcyclohexene-2-one for two days with selenium at 260° obtained only a 15% yield of *m*-cresol.

[26] United States Pharmacopeia, X.

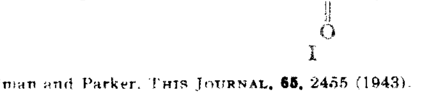
[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF INDIANA UNIVERSITY]

Amino Acids. III. α-Amino-*n*-butyric Acid and α-Amino-isobutyric Acid

BY JOHN H. BILLMAN AND EARL E. PARKER

The method used for the synthesis of alanine[1] from 2-amino-*n*-propanol has now been extended to the preparation of α-amino-*n*-butyric acid and α-amino-isobutyric acid from 2-amino-*n*-butanol and 2-amino-2-methyl-*n*-propanol.

The amino alcohols were benzoylated with benzoyl chloride and anhydrous sodium carbonate in benzene to yield the N-benzoylamino alcohol I.



$$R-\overset{R^1}{\underset{NH_2}{C}}-CH_2OH \longrightarrow R-\overset{R^1}{\underset{NH-\underset{\overset{\|}{O}}{C}-C_6H_5}{C}}-CH_2OH \qquad (1)$$

I

The yield of crude 2-benzoylamino-*n*-butanol was 89–91% while the yield of pure 2-benzoylamino-2-methyl-*n*-propanol was 78–79%.

A number of oxidizing agents were tried in order to ascertain whether any of them possessed advantages over alkaline permanganate for the oxidation of the benzoylated amino alcohols to the corresponding amino acids II. Among those examined and found to react were lead dioxide,

$$R-\overset{R^1}{\underset{NH-\underset{\overset{\|}{O}}{C}-C_6H_5}{C}}-CH_2OH \xrightarrow{[O]} R-\overset{R^1}{\underset{NH\underset{\overset{\|}{O}}{C}-C_6H_5}{C}}-CO_2H$$

II

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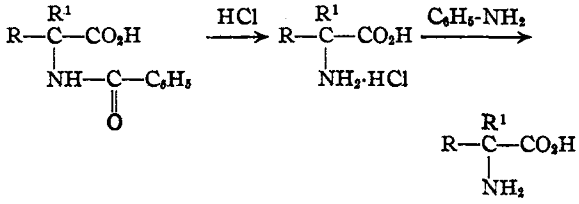
[1] Billman and Parker, THIS JOURNAL, **65**, 2455 (1943).

sodium dichromate and sulfuric acid, chromic acid, ammonium persulfate, and nitric acid. None of them were as good as alkaline permanganate.

The yields of α-benzoylamino-*n*-butyric acid and α-benzoylamino-isobutyric acid, containing very small amounts of benzoic acid as impurity, were 67–72% and 91–93%, respectively.

The benzoylated amino acids were hydrolyzed to yield approximately the theoretical amounts of the amino acid hydrochlorides. The yields of pure α-amino-*n*-butyric acid and α-aminoisobutyric acid obtained upon liberation from their hydrochlorides were 72 and 86%, respectively.



$$\mathrm{R{-}\overset{R^1}{\underset{NH-\underset{O}{\underset{\|}{C}}-C_6H_5}{\underset{|}{C}}}{-}CO_2H} \xrightarrow{\mathrm{HCl}} \mathrm{R{-}\overset{R^1}{\underset{NH_2\cdot HCl}{\underset{|}{C}}}{-}CO_2H} \xrightarrow{\mathrm{C_6H_5\text{-}NH_2}} \mathrm{R{-}\overset{R^1}{\underset{NH_2}{\underset{|}{C}}}{-}CO_2H}$$

The authors wish to thank Eli Lilly and Company for assistance in this work.

Experimental

2-Benzoylamino-*n*-butanol.—In a liter 3-necked flask equipped with a dropping funnel, a thermometer, and an efficient stirrer were placed 500 cc. of benzene, 25 g. of anhydrous sodium carbonate and 18.3 g. of pure 2-amino-*n*-butanol. The mixture was vigorously stirred and cooled to 10°. A solution containing 28.1 g. of benzoyl chloride and 100 cc. of benzene was then added drop by drop at such a rate that the temperature did not exceed 10°. After forty-five minutes, a second 25 g. of sodium carbonate was added. The mixture was stirred for four hours, then the bath was removed and stirring continued for four additional hours.

The dropping funnel was then replaced by a condenser and the reaction refluxed until no odor of benzoyl chloride could be detected. The hot mixture was filtered to remove the inorganic material. This residue was extracted with two 100-cc. portions of hot benzene. The combined filtrates were reduced to 400 cc. and chilled in the refrigerator. The crystals of 2-benzoylamino-*n*-butanol were filtered off and washed with cold benzene. A small second crop was obtained by evaporating the filtrate to 150 cc. The product weighed 34–35 g. (89–91%) and melted at 97–98°.

Recrystallization from toluene yielded a product melting at 98–99°. Calcd.: N, 7.25. Found: N, 6.98.

α-Benzoylamino-*n*-butyric Acid.—In 400 cc. of water containing 2 g. of sodium hydroxide was suspended 32.5 g. of crude 2-benzoylamino-*n*-butanol. To this vigorously stirred mixture was added 36 g. of potassium permanganate at such a rate that the temperature did not exceed 40°. Stirring was continued until most of the permanganate had been consumed and the temperature had fallen to room temperature. The manganese dioxide was filtered off and the excess of permanganate reduced with saturated sodium bisulfite solution. The mixture was again filtered, acidified with concentrated hydrochloric acid, and chilled in the refrigerator. The benzoylamino-*n*-butyric acid weighed 23.7–25.1 g. and melted at 139–40°. This was a 67–72% yield of crude material.

α-Amino-*n*-butyric Acid Hydrochloride.—In a typical experiment 25.1 g. of crude α-benzoylamino-*n*-butyric acid was suspended in 200 cc. of 18% hydrochloric acid and refluxed eight hours. The mixture was cooled to room temperature and the benzoic acid filtered off. The filtrate was then evaporated to dryness under reduced pressure. A small portion of water was added and the process repeated. The operation was repeated again with water and three more times with absolute alcohol. A theoretical yield of 17 g. of α-amino-*n*-butyric acid hydrochloride was obtained. Calcd.: N, 10.05. Found: N, 10.04.

α-Amino-*n*-butyric Acid.—The α-amino-*n*-butyric acid hydrochloride (17 g.) was dissolved by warming it with 100 cc. of 95% alcohol. The mixture was filtered and treated with 20 cc. of pure aniline. It was then chilled in the refrigerator for several hours. The product was filtered off and washed with absolute alcohol to free it of aniline. The yield of halogen free α-amino-*n*-butyric acid was 9 g. or 72% of the theoretical. *Anal.* Calcd.: N, 13.6. Found: (Van Slyke) N, 13.8.

2-Benzoylamino-2-methyl-*n*-propanol.—In a liter 3-necked flask equipped with a dropping funnel, a thermometer, and an efficient stirrer were placed 400 cc. of benzene, 50 g. of anhydrous sodium carbonate and 18.3 g. of pure 2-amino-2-methyl-*n*-propanol. The mixture was vigorously stirred and cooled to 10° with an ice-bath. A solution containing 28.1 g. of benzoyl chloride and 100 cc. of benzene was then added at such a rate that the temperature did not exceed 10°. After the mixture had been stirred for four hours, the bath was removed and stirring continued for two more hours.

The dropping funnel was then replaced by a condenser and the mixture refluxed until all of the benzoyl chloride had reacted. The hot mixture was then filtered to remove the inorganic material. This residue was extracted with two 100-cc. portions of hot benzene. The combined filtrates were reduced to 400 cc. and the solution chilled. The crystals of 2-benzoylamino-2-methyl-*n*-propanol were filtered off and washed with two small portions of cold benzene. This filtrate was reduced to 100 cc. and 200 cc. of petroleum ether added. The gummy solid that was obtained was recrystallized from benzene and yielded a small amount of crystals of the same purity as the original batch. The total yield was 30.2–30.5 g. (78–79%) of material melting 88–89°. *Anal.* 7.10% nitrogen. A sample that was recrystallized three times from benzene melted 89–90°. *Anal.* Calcd.: N, 7.25. Found: N, 7.24.

α-Benzoylamino-isobutyric Acid.—In 400 cc. of water containing 4 g. of sodium hydroxide was suspended 38.6 g. of 2-benzoylamino-2-methyl-*n*-propanol. To this vigorously stirred mixture was added 42.1 g. of potassium permanganate at such a rate that the temperature did not exceed 40°. Stirring was continued until most of the permanganate had been consumed and the temperature had fallen to that of the room. The manganese dioxide was filtered off and the excess of permanganate reduced with methyl alcohol. The mixture was again filtered and acidified with concentrated hydrochloric acid and chilled. The α-benzoylamino-isobutyric acid was filtered off and the filtrate neutralized with bicarbonate and evaporated to 150 cc. under reduced pressure. The solution was acidified and yielded from 1 to 4 g. of product. The total yield was 37.6–38.6 g. (91–93%) of material melting over a one or two degree range between 193 and 198°.

α-Amino-isobutyric Acid Hydrochloride.—In a typical experiment 37.8 g. of α-benzoylamino-isobutyric acid was suspended in 300 cc. of 18% hydrochloric acid and refluxed for eight hours. The mixture was worked up by the same procedure as for isolating α-amino-*n*-butyric acid hydrochloride; yield 25.4 g. (99%).

α-Aminoisobutyric Acid.—The aminoisobutyric acid hydrochloride (24.8 g.) was dissolved in 150 cc. of hot 95% alcohol, treated with 24 cc. of pure aniline, and chilled in the refrigerator. The product was filtered off and washed with absolute alcohol to free it of aniline. The yield of α-aminoisobutyric acid was 15.7 g. or 86% of the theoretical. *Anal.* Calcd.: N, 13.59. Found: (Van Slyke) N, 13.48.

Summary

A new method has been developed for the synthesis of α-amino-*n*-butyric acid and α-amino-isobutyric acid from the corresponding amino alcohols.

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