[CONTRIBUTION FROM THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

The Preparation of γ-(*p*-Aminophenyl)-butyric and ε-(*p*-Aminophenyl)-caproic Acids

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In the course of investigations on the correspondence between immunological specificity and chemical constitution, the results of which will be published in another communication, it was necessary to prepare *p*-nitro and *p*-amino derivatives of γ-phenylbutyric and ε-phenylcaproic acids. As no record of these compounds was found in the literature a description of their preparation is hereby given.

γ-Phenylbutyric acid was prepared from phenylethyl bromide by the malonic ester synthesis as described by Fischer.[1] δ-Phenylbutyl alcohol was obtained from γ-phenylbutyric acid ethyl ester[2] by reduction with sodium in toluene by the modified method of Bouveault, described by Levene and Allen;[3] after pouring the reaction mixture into water the δ-phenylbutyl alcohol was extracted with ether and distilled *in vacuo*, after removal of the toluene and ether. The boiling point agreed with that given by v. Braun.

δ-Phenylbutyl Chloride.—One part of δ-phenylbutyl alcohol and two parts of thionyl chloride were boiled for one hour. Most of the thionyl chloride was removed by distillation at atmospheric pressure. The phenylbutyl chloride was distilled *in vacuo;* yield 98% of the weight of phenylbutyl alcohol used; b. p. 122–123° at 17 mm., the same as reported by J. v. Braun[4] who prepared it from benzoyl-δ-phenylbutylamine.

δ-Phenylbutylmalonic Ester.—This substance was prepared by the method described by Fischer for γ-phenylbutyric acid[1] by condensation of δ-phenylbutyl chloride and malonic ester; yield 145 g. from 135 g. of phenylbutyl chloride; b. p. 212–215° at 20–22 mm.

ε-Phenylcaproic Acid.—δ-Phenylbutylmalonic ester was converted into the free acid by the method used by Fischer for the preparation of phenylethylmalonic acid.[1] The acid was heated at 160–165° until no more carbon dioxide was given off and the resulting ε-phenylcaproic acid was distilled *in vacuo;* yield 14 g. from 24 g. of δ-phenylbutylmalonic ester; b. p. 192–196° at 20–22 mm. J. v. Braun[2] who prepared ε-phenylcaproic acid from ε-phenylamyl cyanide reports b. p. 180–190° at 17 mm.

γ-(*p*-Nitrophenyl)-butyric Acid.—Twenty grams of γ-phenylbutyric acid was slowly added to 140 cc. of concentrated nitric acid (sp. gr. 1.42) at 20–25°. The solution was kept at 25° for six hours and was then poured on ice. The next day the crystals were filtered off, washed with water and dried; yield 20 g. The crude product was recrystallized from 20 cc. of benzene and the crystals were filtered off after standing overnight in the ice box. Two more recrystallizations from benzene gave the maximum m. p. of 92–93°; yield 5 g. of hard prisms. The substance is soluble in alcohol, acetone, chloroform, ether and benzene, not soluble in water and petroleum ether.

Anal. After drying at 60° *in vacuo* over H_2SO_4, calcd. for $C_{10}H_{11}O_4N$: C, 57.39; H, 5.3; N, 6.7. Found: C, 57.61; H, 5.4; N, 6.41. 0.2216 g. dissolved in 75% alcohol neutralized 10.65 cc. of $N/10$ NaOH; calcd. 10.6 cc.

To determine the position of the nitro group, 1 g. of the substance was heated in a sealed tube with 20 cc. of dilute nitric acid (1:2.5) for four hours at 200°; 0.56 g. of *p*-nitrobenzoic acid or 70% of the theoretical yield was obtained, which showed the correct melting point without further recrystallization. *p*-Nitrophenylacetic acid oxidized in the same manner gave 75% of the theoretical yield of *p*-nitrobenzoic acid.

ε-(*p*-Nitrophenyl)-caproic Acid.—Thirty grams of ε-phenylcaproic acid was slowly added to 210 cc. of concentrated nitric acid (sp. gr. 1.42) at 20–25°. The solution was kept at 25° for twenty-four hours and was then poured on ice. After standing in the ice box until crystallization took place, the crystals were washed with cold water and dried *in vacuo* at ordinary temperature; yield 34 g. The substance was dissolved in 40 cc. of isoamyl alcohol and 100 cc. of petroleum ether (b. p. 30–60°) was added. An oil separated which dissolved upon heating. The crystals which separated at low temperature were washed with petroleum ether; yield 11 g. After a second recrystallization from a mixture of isoamyl alcohol and petroleum ether 8 g. of substance was obtained as prisms, m. p. 64–65°. The substance is soluble in alcohol, acetone, chloroform, ether and benzene, not soluble in water or petroleum ether.

Anal. After drying at 45° *in vacuo* over H_2SO_4, calcd. for $C_{12}H_{15}O_4N$: C, 60.73; H, 6.38; N, 5.91. Found: C, 60.75; H, 6.47; N, 5.90. 0.2216 g. neutralized 9.6 cc. of $N/10$ NaOH; calcd. 9.5 cc.

On oxidation of 1 g. of the substance with 30 cc. of dilute nitric acid (1:2.5) 0.52 g. of pure *p*-nitrobenzoic acid or 74% of the theoretical yield was obtained.

γ-(*p*-Aminophenyl)-butyric Acid.—Ten grams of finely ground γ-(*p*-nitrophenyl)-butyric acid was suspended in 350 cc. of normal hydrochloric acid and 25 g. of zinc dust added in small portions with constant vigorous stirring. The nitro compound disappeared gradually within one hour. The solution which was still acid to Congo red was filtered and 25 g. of sodium acetate added. The precipitate was filtered, redissolved in 100 cc. of water by addition of a slight excess of ammonia and the zinc removed with hydrogen sulfide. The aminophenylbutyric acid was precipitated by making the solution weakly acid to Congo red with hydrochloric acid; yield, 6.8 g. It was recrystallized from 20 volumes of boiling water as large platelets,

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(1) E. Fischer, *Ber.*, **39**, 2211 (1906).

(2) J. v. Braun, *ibid.*, **44**, 2867 (1911).

(3) P. A. Levene and C. H. Allen, *J. Biol. Chem.*, **27**, 433 (1916).

(4) J. v. Braun, *Ber.*, **43**, 2837 (1910).

m. p. 130–131°. The substance is easily soluble in hot water, alcohol and acetone, less soluble in chloroform, insoluble in cold water, benzene, ether and petroleum ether.

Anal. After drying at 100° *in vacuo* over H_2SO_4, calcd. for $C_{10}H_{13}O_2N$: C, 67.00; H, 7.32; N, 7.82. Found: C, 66.78; H, 7.11; N, 7.72.

ε-(*p*-Aminophenyl)-caproic Acid.—Ten grams of ε-(*p*-nitrophenyl)-caproic acid reduced in the same manner as the nitrophenylbutyric acid yielded 7.5 g. of crude ε-(*p*-nitrophenyl)-caproic acid. It was recrystallized from 80 volumes of boiling water. Long narrow microscopic platelets, m. p. 108–109°. The substance is soluble in hot water, alcohol and acetone, less soluble in chloroform and benzol, insoluble in cold water, ether and petroleum ether.

Anal. After drying at 100° *in vacuo* over H_2SO_4, calcd. for $C_{12}H_{17}O_2N$: C, 69.52; H, 8.27; N, 6.76. Found: C, 69.46; H, 8.36; N, 6.64.

NEW YORK, N. Y.
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COMMUNICATIONS TO THE EDITOR

ANOMALOUS FRIEDEL-CRAFTS REACTIONS WITH FURANS

Sir:

The compound formed by interaction of benzene, 2-furoic acid and aluminum chloride is α-naphthoic acid and not 3-phenyl-2,3-dihydro-2-furoic acid [THIS JOURNAL, **49**, 565 (1927)]. The formation of α-naphthoic acid, probably through an endoxy compound as a consequence of 1,4-addition, may be general with related types. Other catalysts and experimental conditions, with a miscellany of compounds, are being investigated.

In the reaction between 2-furfural, isopropyl chloride and aluminum chloride in carbon disulfide [*ibid.*, **55**, 4197 (1933)], the isopropyl group is introduced into a β-position despite the availability of an α-position. Bromination of the corresponding acid gives a 5-bromo-β-isopropyl-2-furoic acid identical with that obtained by the oxidation of the bromoaldehyde obtained from 5-bromo-2-furfural, isopropyl chloride and aluminum chloride. The same acid is obtained by hydrolysis of the ester resulting by interaction of ethyl 5-bromo-2-furoate, isopropyl chloride and aluminum chloride.

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IOWA STATE COLLEGE M. MCCORKLE
AMES, IOWA N. O. CALLOWAY
RECEIVED DECEMBER 26, 1933

THE MUTAROTATION OF α-*d*-GLUCOSE IN DEUTERIUM WATER

Sir:

In a previous communication [THIS JOURNAL, **55**, 5056 (1933)] it has been reported that the mutarotation of α-*d*-glucose in 60% heavy water at 18° has a velocity coefficient of 0.00290 as compared to 0.00546 found under identical conditions in ordinary distilled water. With the production of 100% deuterium water (D_2O) in this Laboratory, it became possible to determine the velocity coefficient of the mutarotation of α-*d*-glucose in this medium. A 0.6030-g. sample of pure α-*d*-glucose was dissolved in 3.3210 g. of D_2O of d_4^{20} 1.1055 and the rotation of the solution (d_{20}^{20} 1.175) was read at certain intervals of time in a 2-dm. semi-micro tube with sodium light at 20°. The first reading (α_0 38.50°) was taken seven minutes after the addition of D_2O. The results obtained are shown in Table I.

TABLE I

Time, minutes	α	$k_1 + k_2 = \frac{1}{t}\log\frac{\alpha_\infty - \alpha_0}{\alpha_\infty - \alpha}$
0	α_0 = 38.50	.....
15	37.05	0.00221
50	34.09	.00221
90	31.29	.00220
120	29.50	.00221
180	26.72	.00220
300	23.06	.00222
697	19.35	.00222
1440	α_∞ = 18.83	Mean 0.00221

The velocity coefficient for α-*d*-glucose in ordinary distilled water is given by Hudson and Dale [THIS JOURNAL, **39**, 320 (1917)] as $k_1 + k_2 = 0.00635$ at 20°, and as $k_1 + k_2 = 0.00225$ at 10°. A comparison of these values with the mean value for $k_1 + k_2$ in Table I shows that the velocity of the mutarotation of α-*d*-glucose in pure D_2O at 20° is identical with that found in ordinary distilled water at 10°. In this case, therefore, the effect of the deuterium water on the velocity of the mutarotation is equivalent to a drop of 10° in the temperature. The specific rotation of the equilibrium solution in D_2O is $[\alpha]_D^{20}$ 18.83° ×