N-Alkyl derivatives of 3,3-bis(p-toluenesulfonamidophenyl)-2-butanone (Nos. 19 and 20). A mixture of 300 ml. of pyridine, 38.7 g. (0.12 mole) of 3,3-bis(*p*-aminophenyl)-2-butanone dihydrochloride[7] and 57.2 g. (0.3 mole) of *p*-toluenesulfony chloride was stirred for 45 min. at 27° and poured into water. The product was extracted into chloroform and the chloroform was washed successively with 20% sulfuric acid, 5% sodium carbonate solution, and water. The dried (magnesium sulfate), filtered chloroform solution was evaporated and the residue was dissolved in 10% sodium hydroxide solution and filtered. The filtrate was acidified with acetic acid to give a pink solid which was collected and dried. There was obtained 86.6 g. (95%) of product, m.p. 75–80°, which could not be recrystallized but which was suitable for use in subsequent reactions.

A 25% solution of the sulfonamide (1 mole equivalent) in ethanol was treated with 1*N* sodium hydroxide (3 mole equivalents) and the requisite alkyl iodide (3 mole equivalents) and stirred at 75° for 3 hr. It was partially evaporated and then extracted with benzene. The benzene layer was washed with water, dried (magnesium sulfate) and evaporated. The residue was recrystallized.

3,3-Bis(p-N-alkylaminophenyl)-2-butanones (Nos. 21 and 22). The appropriate sulfonamide derivative in two volumes of 80% sulfuric acid was heated at 155–160° for 5 min. The cooled solution was poured into water, made alkaline with 20% sodium hydroxide solution, and the product was extracted into ether. The washed, dried (potassium carbonate) ether extract was evaporated and the residue was recrystallized or converted to a salt.

3,3-Bis(p-fluorophenyl)-2-butanone (No. 23). A stirred solution of 16.4 g. (0.05 mole) of 2,2-bis(*p*-aminophenyl)-3-butanone dihydrochloride[7] in 25 ml. of 37% hydrochloric acid and 25 ml. of water was treated dropwise with a solution of 7.2 g. (0.105 mole) of sodium nitrite in 15 ml. of water at 0°. The excess nitrite was neutralized with urea and to the solution there was added 15.2 g. (0.14 mole) of sodium fluoborate in 30 ml. of water. The resulting precipitate was filtered, washed successively with 6 ml. of water, 3 ml. of methanol, and 10 ml. of ether and dried to give 17.0 g. (76%) of salt, m.p. 139° dec.

The diazonium fluoborate was decomposed by heating with a free yellow flame, and the residue was dissolved in chloroform, washed with dilute hydrochloric acid, 10% sodium hydroxide and water, and then dried (sodium sulfate). The filtered chloroform solution was fractionally distilled.

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γ-(*p*-Aminophenyl)butyric Acid

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The preparation of γ-(*p*-aminophenyl)butyric acid was reported by van der Scheer[1] in 1934 through reduction of γ-(*p*-nitrophenyl)butyric acid. The nitrated derivative was obtained from γ-phenylbutyric acid which in turn had been prepared from phenylethyl bromide by the malonic ester synthesis described by Fischer.[2]

Starting with γ-phenylbutyric acid which had been prepared through Clemmensen reduction[3] of β-benzoylpropionic acid, the procedure of van der Scheer gave the amino acid in an over-all yield of 6%. The nitration of γ-phenylbutyric acid to γ-(*p*-nitrophenyl)butyric acid was accomplished in only 20% yield, the formation of the *ortho* isomer predominating. Although van der Scheer reported a yield of 70% for the preparation of the γ-(*p*-aminophenyl)butyric acid by zinc dust–hydrochloric acid reduction of the nitro compound, the yield obtained in several reactions was not over 40%.

The need for considerable quantities of γ-(*p*-aminophenyl)butyric acid led to the development of the two-step synthesis described herein which affords the amino acid in an over-all yield of 43%. Acetanilide is succinoylated by the procedure described in the literature[4] to give β-(*p*-acetylaminobenzoyl)propionic acid in 60% yield. Treatment of this keto acid by the Huang-Minlon[5] modification of the Wolff-Kishner reaction effected both reduction of the carbonyl group and hydrolysis of the acetamido group in one step to form the γ-(*p*-aminophenyl)butyric acid.

Previous attempts to effect this combined hydrolysis-reduction through the Clemmensen reaction were not successful.

EXPERIMENTAL[6]

A mixture of β-(*p*-acetylaminobenzoyl)propionic acid[4] (77 g., 0.33 mole), 76 g. of potassium hydroxide, 55 ml. of hydrazine hydrate (85%), and 400 ml. of triethylene glycol were heated under reflux for 1.5 hr. The condenser was then removed and the temperature of the solution raised to 195° during which time excess hydrazine hydrate was expelled. (*Caution*—Hood). Refluxing was then continued for an additional 4 hr. at this temperature. The cooled solution was diluted with 400 ml. of water and made weakly acidic (to Alkacid paper) by the addition of 6*N* hydrochloric acid, about 200 ml. being required. The acid which precipitated was removed by filtration, washed with cold water, and dried in a vacuum desiccator over anhydrous calcium chloride; yield 42.8 g., 73%, m.p. 115–120°. Recrystallization of the analytical sample from water gave white plates, m.p. 130–132°. The melting point was not depressed when mixed with an authentic sample of γ-(*p*-aminophenyl)-butyric acid.[7]

Anal. Calcd. for $C_{10}H_{13}O_2N$: C, 67.02; H, 7.31; N, 7.82. Found: C, 66.96; H, 7.55; N, 7.76.

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(6) All melting points are uncorrected.

(7) van der Scheer reported a melting point of 130–131°.