oxide, and subsequent alkaline hydrolysis of the acetamido groups.

The relative insolubility of 1,1,1-trichloro-2,2-bis-(*p*-benzamidophenyl)-ethane[3] made it desirable to attempt the preparation of a soluble derivative of the parent amine of this compound. 1,1,1-Trichloro-2,2-bis-(*p*-phthalamidophenyl)-ethane[4] appeared suitable, but we did not succeed in purifying the product from the partial hydrolysis of the corresponding phthalimido compound.

Experimental

1-(*p*-Acetamidophenyl)-ethyl Bromide.—This halide, previously described by Rousset,[5] was obtained from 1-(*p*-acetamidophenyl)-ethanol[5] which, in turn, could be prepared by reduction of *p*-acetamidoacetophenone with aluminum isopropoxide in the customary manner. A solution of 30 g. of 1-(*p*-acetamidophenyl)-ethanol in 300 cc. of dry chloroform was cooled to −10° in an ice–salt-bath. Phosphorus tribromide (10 cc.) was dropped in with constant stirring, the temperature being kept below 0°, and the solution was then allowed to warm to room temperature. Stirring was discontinued, the mixture allowed to stand overnight, the chloroform and excess phosphorus tribromide removed under reduced pressure, and the residue poured into 100 cc. of ice and water. The oil formed was extracted into ether; drying and evaporation of the ether extract yielded 24 g. (58%) of platelets which were recrystallized from ethanol. The crystals melted at 93–95° and darkened on standing.

α,α′-bis-(*p*-Acetamidophenyl)-ethyl Ether.—To 0.5 g. of sodium finely dispersed under xylene, was added a solution of 3.7 g. of 1-(*p*-acetamidophenyl)-ethanol in 50 cc. of dry ether at room temperature with mechanical stirring. When the spontaneous refluxing had ceased, a solution of 5 g. of 1-(*p*-acetamidophenyl)-ethyl bromide in 50 cc. of ether was added, and the mixture stirred overnight. It was washed with 50 cc. of water, the ether solution was dried over sodium sulfate, and the solvents were evaporated in a vacuum. The residual oil solidified on cooling and was crystallized from ethanol-acetone. It weighed 3 g. (44%) and melted at 109–111°.

Anal. Calcd. for $C_{20}H_{24}N_2O_3$: N, 8.23. Found: N, 8.51.

α,α′-bis-(*p*-Aminophenyl)-ethyl Ether.—A solution of 14 g. of α,α′-bis-(*p*-acetamidophenyl)-ethyl ether in 150 cc. of 15% ethanolic potassium hydroxide was refluxed for ten hours. The ethanol was distilled under reduced pressure, the residue taken up in water, and the solution acidified. The oil formed was separated and the acid solution extracted with ether which removed 4 g. of unhydrolyzed starting material. The aqueous layer was then made alkaline, the oil extracted into ether, dried, and fractionated. Six grams (57%) of a pale yellow oil boiling at 110–114° (70 mm.) was collected.

The **monohydrochloride** formed readily on treatment of an acetone solution of the oil with ethereal hydrogen chloride. It was recrystallized from ethanol–ether and melted at 186–187°.

Anal. Calcd. for $C_{16}H_{20}N_2O.HCl$: N, 9.57. Found: N, 9.73.

1,1,1-Trichloro-2,2-bis-(*p*-phthalimidophenyl)-ethane.—A suspension of 100 g. of phthalanil and 50 g. of chloral in 500 cc. of 100% sulfuric acid was allowed to stand at room temperature for three days with occasional shaking. The solid gradually disappeared leaving a clear yellow-brown solution. This was poured onto 2000 g. of crushed ice, and the colorless precipitate thus formed was filtered. It weighed 112 g. (87%). Recrystallization from ethanol yielded colorless crystals, m. p. 97–99°.

Anal. Calcd. for $C_{30}H_{17}Cl_3N_2O_4$: N, 4.87. Found: N, 4.76.

(4) Suggested by Dr. Randolph T. Major.

(5) Rousset, *Bull. soc. chim.*, [3] **11**, 321 (1892).

Hydrolysis of the phthalimido groups patterned upon the method of Kuhara and Fukui[6] using a barium hydroxide-barium chloride solution led to an alkali-soluble product which, however, resinified during its isolation.

Succinanil and chloral could not be condensed under the same conditions.

(6) Kuhara and Fukui, *Am. Chem. J.*, **26**, 454 (1901).

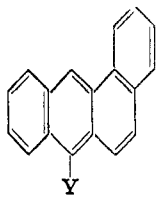
COBB CHEMICAL LABORATORY
UNIVERSITY OF VIRGINIA
CHARLOTTESVILLE, VA.

RECEIVED OCTOBER 1, 1946

The Conjugation of Peptides with 1,2-Benzanthryl-10-isocyanate[1]

BY LARRY Q. GREEN AND HUGH J. CREECH

In connection with immunological studies[2] of hydrocarbon–protein conjugates,[3] it was found desirable to have as inhibitors some compounds with greater water solubilities than the amino acid conjugates[4] employed previously. It was thought that the use of di- and tripeptides or of dicarboxylic amino acids as components of the conjugates might solve this problem. Accordingly, 1,2-benzanthryl-10-isocyanate was coupled to glycylglycine, triglycine and glutamic acid in aqueous dioxane solution. As was the case with the glycine and ε-amino caproic acid conjugates prepared from this isocyanate, the new compounds were obtained only in an amorphous condition. Although the compounds were not isolated in an absolutely pure state because of their susceptibility to decomposition, they were suitable for the immunological tests.



I. Y = —NHCONHCH$_2$CONHCH$_2$COOH
II. Y = —NHCONHCH$_2$CONHCH$_2$CONHCH$_2$COOH
III. Y = —NHCONHCHCH$_2$CH$_2$COOH
COOH

Experimental[5]

Glycylglycine, charring point 225°, was prepared by the hydrolysis of 2,5-diketopiperazine.[6] A solution of 375 mg. of this compound in 5 cc. of water adjusted to *p*H 9 with sodium hydroxide was added slowly with stirring to a solution of 500 mg. of 1,2-benzanthryl-10-isocyanate in 50 cc. of purified dioxane. After ten minutes at room temperature, 150 cc. of water was added to the light yellow suspension and the mixture was heated to 40° whereupon most of the precipitate went into solution. Normal

(1) Aided by a grant from the International Cancer Research Foundation. This article was prepared at the present address of one of us (H. J. C.), The Lankenau Hospital Research Institute and The Institute for Cancer Research, Philadelphia 30, Pa.

(2) Manuscripts in course of preparation; also, Creech and Franks, *Am. J. Cancer*, **30**, 555 (1937).

(3) Creech and Jones, THIS JOURNAL, **63**, 1661, 1670 (1941).

(4) Fieser and Creech, *ibid.*, **61**, 3502 (1939).

(5) Analyses by Miss E. Werble.

(6) Fischer, *Ber.*, **34**, 2868 (1901).

hydrochloric acid was added to the filtrate causing the formation at *p*H 3 of a gelatinous yellow precipitate which was washed twice with a liter of slightly acidified water. The precipitate was removed and dried in a vacuum desiccator; the slightly brown powder was ground and washed with ether.[7] The **1,2-benzanthryl-10-carbamidoacetoglycine** (I) thus obtained in 82% yield darkened at 210° and had not completely melted at 260°.

Anal. Calcd. for $C_{23}H_{19}O_4N_3$: C, 68.9; H, 4.78; N, 10.45. Found: C, 67.8; H, 4.88; N, 10.43.

Chloroacetylglycylglycine, prepared from 2,5-diketopiperazine and chloroacetyl chloride,[8] was treated with ammonium hydroxide to give triglycine[9] which turned yellow at 215° and melted with decomposition at 240°. This compound was conjugated with the isocyanate under conditions similar to those used above to form **1,2-benzanthryl-10-carbamidoacetoglycylglycine** (II) obtained in 68% yield as a slightly brown powder which darkened at 200° and decomposed at 250°.

Anal. Calcd. for $C_{25}H_{22}O_5N_4$: C, 65.6; H, 4.84. Found: C, 66.36, 66.15; H, 4.78, 4.81.

For the preparation of α-(1,2-benzanthryl-10-carbamido)-glutaric acid (III), 1(+)-glutamic acid was employed. The procedures of coupling and isolation were the same as those used before. The brown product, obtained in 44% yield, darkened slightly at 235°, softened at 247° and melted at 252–254° with decomposition.

Anal. Calcd. for $C_{24}H_{20}O_5N_2$: C, 69.2; H, 4.83; N, 6.74. Found: C, 68.92; H, 4.90; N, 6.46.

(7) Attempts to crystallize this compound from aqueous dioxane or from other solvents were not successful; usually such attempts led to serious decomposition.

(8) Fischer, *Ber.*, **39**, 2931 (1906).

(9) Fischer, *ibid.*, **37**, 2500 (1904).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF MARYLAND
COLLEGE PARK, MD.

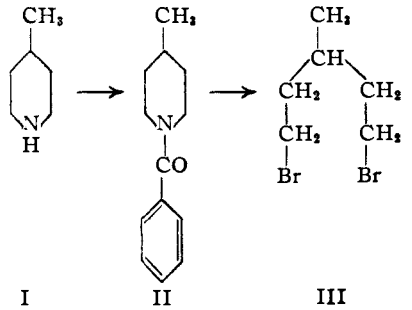
RECEIVED JULY 23, 1946

1,5-Dibromo-3-methylpentane

BY NELSON J. LEONARD AND ZENO W. WICKS[1]

1,5-Dibromo-3-methylpentane (III) has not been prepared previously. This compound is of interest as an intermediate in the synthesis of certain heterocycles,[2] and as a building unit for certain saturated isoprenoid molecules in which synthesis may be effected by combination of alternating symmetrical six- and four-carbon units rather than the customary unsymmetrical five- and five-carbon units.

4-Methylpiperidine (I) was converted to 1-benzoyl-4-methylpiperidine (II) by a Schotten–Baumann reaction with benzoyl chloride,[3] and this, in turn, by a von Braun reaction with phosphorus pentabromide, gave III.[4]



I II III

1-Benzoyl-4-methylpiperidine (II).—To a mixture of 340 g. of I (3.4 moles), 180 g. of sodium hydroxide (4.5 moles), and 1400 ml. of water, 476 g. of benzoyl chloride (3.4 moles) was added with stirring at 35–40° during one hour. The non-aqueous layer and the ether extracts of the aqueous layer were combined and evaporated to dryness. The solid residue was recrystallized from ethanol as colorless prisms; m. p. 83.5–84°; yield, 635 g. (92%).

Anal. Calcd. for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.92; H, 8.26; N, 6.72.

1,5-Dibromo-3-methylpentane (III).—During cooling and stirring, 575 g. of phosphorus tribromide (2.15 moles) was added to 426.5 g. of II (2.10 moles), followed by 325 g. of bromine (2.13 moles). The reaction mixture was distilled under reduced pressure from 65 (30 mm.) to 112° (20 mm.), until a yellow solid collected in the condenser and extensive decomposition occurred in the distilling flask. The total distillate was poured onto ice, the mixture stirred for several hours and allowed to stand overnight. The oily layer was separated and boiled with 625 ml. of 40% hydrobromic acid solution under reflux for four hours. After steam distillation, the oily layer in the distillate was separated and washed twice with 10% sodium carbonate, once with water, dried over Drierite, then distilled *in vacuo*. The product boiled at 97–98.5° (10 mm.); yield, 333 g. (65%); $n^{20}D$ 1.5073; d^{20}_4 1.607.

Anal. Calcd. for $C_6H_{12}Br_2$: C, 29.53; H, 4.96; Br, 65.51; MR_D, 45.44. Found: C, 29.68; H, 5.19; Br, 65.38; MR_D, 45.21.

(1) Present address: Interchemical Corporation, New York, N. Y.

(2) *Cf.* Prelog and Seiwerth, *Ber.*, **72**, 1638 (1939).

(3) "Organic Syntheses," Coll. Vol. I, 1941, p. 101; Adams and Leonard, THIS JOURNAL, **66**, 257 (1944).

(4) "Organic Syntheses," Coll. Vol. I, 1941, p. 428.

NOYES CHEMICAL LABORATORY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS

RECEIVED JULY 26, 1946

Osmotic and Activity Coefficients of Lithium Nitrate Solutions

BY R. A. ROBINSON

Vapor pressure measurements of lithium nitrate solutions have been made by the isopiestic method[1] at 25° up to a concentration of 3.8 *M*. The range has now been extended by further measurements in more concentrated solution. Lithium nitrate was prepared by double recrystallization from the salt obtained from a sample of lithium carbonate which had been purified by the method outlined by Caley and Elving.[2]

TABLE I

m_{LiNO_3}	m_{NaCl}	m_{LiNO_3}	m_{NaCl}	m_{LiNO_3}	m_{NaCl}
3.316	3.676	3.500	3.877	3.607	3.996
3.864	4.273	4.661	5.136	4.750	5.221
5.292	5.796	5.554	6.061	5.614	6.132
m_{LiNO_3}	$m_{H_2SO_4}$	m_{LiNO_3}	$m_{H_2SO_4}$	m_{LiNO_3}	$m_{H_2SO_4}$
5.456	4.246	6.925	5.161	8.682	6.202
9.522	6.691	10.33	7.124	11.22	7.635
11.78	7.909	11.94	8.012	12.29[a]	8.161
13.36	8.757	13.72	8.966		

[a] In equilibrium with saturated solution.

(1) R. A. Robinson, THIS JOURNAL, **57**, 1165 (1935).

(2) H. S. Booth, "Inorganic Syntheses," Vol. I, McGraw-Hill Book Co., Inc., New York, N. Y., 1939.