

frozen in an ice-bath, then supported inside a transparent Dewar flask by a bored stopper and stirred. Temperature readings were taken after one-minute or half-minute intervals timed with a stop watch. The temperature readings were plotted against time and the "break" located by graphical extrapolation of the linear portions of the heating curves in the presence and absence of solid. The values of the freezing point depression thus obtained (Table VII) were in each case the result of at least two checking determinations.

TABLE VII

DETERMINATION OF  $K_m$  CONSTANT OF POLYALLYL ACETATE AND POLYALLYL CHLORIDE

Sample	Concn. in g./kg. $C_6H_5$	Depression of f. p., °C.	Mol. wt.	$\eta_{sp}/c_{bm}^a$ $C_6H_5$ soln., 27°	$K_m$
PAAc 197	34.8	0.20°	890	0.289	$3.2 \times 10^{-4}$
PAAc 197	47.0	.28	860	.289	$3.4 \times 10^{-4}$
PAAc 208	54.0	.24	1150	.376	$3.3 \times 10^{-4}$
PA Chloride	49.9	.53	480	.168	$3.5 \times 10^{-4}$
	39.5	.43	470		

<sup>a</sup>  $c_{bm}$  = concentration in basal moles per liter.<sup>14</sup>

**Viscometric Determinations.**—The viscosities were measured in benzene as solvent, in a thermostat operating at  $27.0 \pm 0.15^\circ$ . A modified Ostwald pipet was used. In orienting experiments it was established that no disturbances were created by vibration of the bath nor by slight disorientation of the viscometer, and that for solutions up to 3% polymer the time of flow was reproducible as closely as the stop watch could be read (0.2%), and varied by about one per cent. per degree centigrade. It was also established that the specific viscosity was a linear function of concentration up to a solute concentration of 34 g. per liter. The results are expressed in terms of the constant  $K_m$  of the Staudinger equation,<sup>15</sup>

$$K_m = \eta_{sp}/c_{bm} \times M$$

where  $c_{bm}$  = concentration in basal moles per liter,  $M$  = molecular weight of the polymer, and

$$\eta_{sp} = (\eta_2 - \eta_1)/\eta_1$$

Here  $\eta_1$  and  $\eta_2$  are the viscosities of the solvent and of the solution, respectively.

(15) Staudinger, "Die Hochmolekulare organische Verbindungen," Berlin, 1932, p. 56.

## Summary

The decomposition of benzoyl peroxide in allyl acetate as solvent is very nearly unimolecular, the rate constant at  $80^\circ$  varying from 0.191 to  $0.235 \text{ hr.}^{-1}$  over a tenfold range of initial peroxide concentration. The concentration of monomer is a linear function of the concentration of peroxide over the entire course of a polymerization, *i. e.*,  $dM/dP$  is constant throughout. The value of  $dM/dP$  shows some dependence upon the initial peroxide concentration, changing from 28.8 with 1.01% by weight of peroxide to 15.6 with 9.95% by weight of peroxide, but the average degree of polymerization of the polymer is  $13.7 \pm 0.4$  in all cases.

The constancy of  $dM/dP$  during a polymerization is interpreted as meaning that the polymerization chain is broken by collision of a growing free radical with a monomer molecule to yield a new, stabler free radical which is usually incapable of propagating the chain. This process is designated as "degradative chain transfer."

A discussion is presented showing that unimolecular reactions in an expanding or contracting medium are best treated in terms of concentrations per unit weight, and not per unit volume of the medium. In the present case it is also convenient to treat certain bimolecular reactions in terms of weight-concentrations of the species whose change in concentration is being considered.

Further work is in progress directed toward a fuller interpretation of the polymerization of allyl acetate by peroxides.

The polymerization of allyl chloride at  $80^\circ$  by benzoyl peroxide yields a polymer containing an average of 6.3 monomer units per molecule. On an average 5.8 such molecules are produced by each peroxide molecule decomposing.

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## Certain Compounds Related to Tryptophan

BY LEE IRVIN SMITH AND A. WALTER SOGN<sup>1</sup>

Recently, new and convenient syntheses for *dl*-tryptophan, starting with gramine, have been published.<sup>2</sup> In this paper work is reported which deals with a different approach to the synthesis of the amino acid. The synthesis was successful insofar as the tryptophan nucleus was concerned, but amination of the final product, ethyl  $\alpha$ -car-

bethoxy- $\beta$ -(3-indole)-propionate (VIII) could not be achieved.

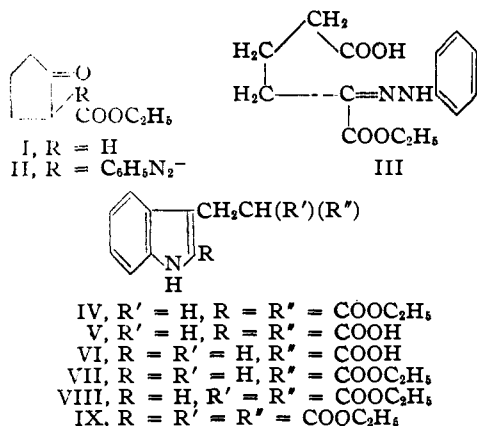
In the synthesis, IV was the key compound. This substance was prepared from ethyl  $\alpha$ -keto-cyclopentanone carboxylate I, which was coupled with diazotized aniline to obtain II. The azo compound was subjected to hydrolytic cleavage whereby the phenylhydrazone of ethyl hydrogen  $\alpha$ -keto adipate, III, resulted and action of acid upon III caused a Fischer indole synthesis to occur with production of IV.

This series of reactions was first reported by Kalb, Schweizer and Schimpf,<sup>3</sup> but the procedure

(1) Abstracted from a thesis by A. W. Sogn, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the M.S. degree, November, 1942.

(2) (a) Snyder, Smith and Stewart, *THIS JOURNAL*, **66**, 200 (1944); (b) Snyder and Smith, *ibid.*, **66**, 350 (1944); (c) Albertson, Archer and Suter, *ibid.*, **66**, 500 (1944); (d) **67**, 36 (1945); (e) Howe, Zam-bito, Snyder and Tishler, *ibid.*, **67**, 38 (1945); (f) Elks, Elliott and Hems, *J. Chem. Soc.*, 624 (1944); (g) 626 (1944); (h) 629 (1944).

(3) Kalb, Schweizer and Schimpf, *Ber.*, **59**, 1858 (1926).



of Manske and Robinson<sup>4</sup> was much more convenient. The yield of IV, based upon I, was 46%. In order to prepare the way for amination via a bromo derivative, IV was to be converted directly into IX by action of ethyl carbonate according to the procedure of Wallingford and his associates<sup>5</sup> or into VIII via V, VI, and VII. Surprisingly enough, IV was completely inert toward ethyl carbonate in the presence of sodium ethoxide; no IX was obtained, and starting material was recovered almost completely. The alternate, but longer route was then explored. The diester IV was hydrolyzed by action of alkali to the diacid V in 93% yield<sup>3</sup>; V was decarboxylated to VI and, without isolation, VI was esterified to VII in over-all yields of 78%. The ester VII was readily carbethoxylated to VIII (yield 52%). This ester VIII has previously been prepared by different methods and reported to melt at 89–90°<sup>6</sup> and at 60°.<sup>2a</sup> The substance VIII obtained in this work melted at 77–78°. Further, hydrolysis of VIII to the corresponding diacid has also been reported,<sup>2a, 6</sup> but no diacid could be obtained in the present work; hydrolysis of VIII according to the method reported<sup>6</sup> led only to the mono acid, β-(3-indole)-propionic acid, which melted at 134°.

Bromination of the ester VIII, in various solvents, and in the presence of potassium acetate as a buffer, led to no definite bromo compound. Bromine readily reacted with VIII, and hydrobromic acid was evolved, but removal of the solvent left a residue of an oil which could not be crystallized. Nor could this crude bromo compound be aminated by action of ammonia. The product was an oily substance, often colored, from which no solid material could be obtained except a small amount of unchanged VIII. Attempts to hydrolyze the bromination product by action of acids led to nothing but black, tarry material.<sup>7</sup>

(4) (a) Manske and Robinson, *J. Chem. Soc.*, 240 (1927); (b) Jackson and Manske, *This Journal*, **52**, 5029 (1930).

(5) Wallingford, Homeyer and Jones, *ibid.*, **63**, 2056 (1941).

(6) Maurer and Moser, *Z. physiol. Chem.*, **161**, 131 (1926).

(7) Elks, Elliott and Hems (ref. 2g.) brominated the ester IX; the product was the 5-bromo compound, and no bromination occurred at

Unsuccessful attempts were made to convert the acid V into its acid chloride by action of thionyl chloride, but although a product was obtained, the analytical values were unsatisfactory. Bromination of this substance gave a high melting solid, which was not a mono bromo derivative and which gave no amino acid derivative when it reacted with ammonia.

Attempts were made to alkylate phthalimidomalonic ester with β-chloropropionic aldehyde acetal. It was hoped that the phenylhydrazone of the resulting aldehyde compound would, by a Fischer indole synthesis, lead directly to *dl*-tryptophan.<sup>8</sup> However, no alkylation could be achieved; either no reaction at all occurred, or else the reaction mixture developed dark spots which rapidly spread throughout the mass and only tarry decomposition products resulted.

### Experimental Part<sup>9</sup>

**Ethyl β-(2-Carboethoxyindole-3)-propionate, IV.**—The procedure was essentially that of Manske and Robinson.<sup>4</sup> The product, purified by distillation under reduced pressure (b. p. 207–210° (2–2.5 mm.)); the pressure should be 3.5 mm. or below) formed a light yellow solid (65 g. from 63 g. of I) melting at 91°. Recrystallization from a mixture of benzene (50 cc.) and petroleum ether (25 cc., b. p. 77–115°) gave 47 g. of a product melting at 94–95°. An additional 5.2 g. was obtained by concentrating the filtrates. The total amount of purified product, 53.2 g., is 46%.

**β-(2-Carboxyindole-3)-propionic Acid, V.**—The procedure was essentially that of Kalb, Schweizer, and Schimpf.<sup>3</sup> The product (26.2 g. from 35 g. of IV, 93%) melted at 194°.

**β-(3-Indole)-propionic Acid VI and the Ethyl Ester, VII.**—The acid V (41 g.) was heated at 225° for thirty minutes. The resulting crude acid VI (which melted at 133.5° after crystallization from water) was refluxed for three hours with dry ethanol (100 cc.) containing sulfuric acid (5 cc.). The ester VII weighed 30 g. (78% based upon V), boiled at 171° (4 mm.), and solidified to a solid which melted at 43–45°.

**Ethyl α-Carboethoxy-β-(3-indole)-propionate, VIII.**—Sodium (1.7 g.) was dissolved in dry ethanol (25 cc.) and excess ethanol was removed by distillation under reduced pressure. The ester VII (16 g.), dissolved in ethyl carbonate (52 g.) was added, and the mixture was stirred for thirty minutes while it was heated under reduced pressure (200 mm.) so that alcohol, but not ethyl carbonate, distilled. Additional ethyl carbonate (10 cc.) was added and the mixture was gently refluxed, first under atmospheric pressure for two hours and then under reduced pressure for thirty minutes. Acetic acid (4 cc.) and water (200 cc.) were added and the mixture was extracted with ether several times. The combined extracts were washed with aqueous bicarbonate, then with water, and dried (sodium sulfate). The solvent and excess ethyl carbonate were removed by distillation under reduced pressure and the residue was fractionated. The ester VIII was collected at 190–195° (5 mm.); the distillate solidified and was recrystallized from ethanol (10 cc.). It formed large prisms (11 g., 52%) which melted at 77–78°.

*Anal.* Calcd. for C<sub>16</sub>H<sub>19</sub>O<sub>4</sub>N: C, 66.41; H, 6.61. Found: C, 66.64; H, 6.79.

**Bromination of VIII. A.**—The ester VIII (1 g.) and potassium acetate (350 mg.) were dissolved in acetic acid (5 cc.) and the cooled solution was brominated by addition

the carbon atom of the malonic ester grouping. These Authors obtained unchanged material as the only identifiable product of the reaction between IX and sulfonyl chloride.

(8) This synthesis was suggested by Dr. C. F. Koelsch.

(9) Microanalyses by S. T. Rolfsen.

of a solution of bromine (560 mg.) in acetic acid (5 cc.). Bromine was absorbed rapidly and potassium bromide precipitated. The mixture was poured into excess concentrated ammonium hydroxide at  $-5^{\circ}$ , and then allowed to stand overnight. The greenish oil containing white flakes of solid was filtered; the solid melted at  $77^{\circ}$  (VIII) and weighed 250 mg. No other solid material could be obtained from the oil. **B.** The ester VIII (1 g.) in chloroform (5 cc.) was cooled to  $0^{\circ}$  and brominated by addition of a solution of bromine (560 mg.) in chloroform (5 cc.). The solvent was removed under reduced pressure and cold ammonium hydroxide was added to the oily residue. The result was the same as that described in A. When this bromination was repeated at room temperature, evaporation of the solvent left a dark oily material which contained small amounts of VIII.

**Action of Thionyl Chloride upon V.**—The acid V (2 g.) was added to a solution of thionyl chloride (10 cc.) in benzene (10 cc.) containing pyridine (1 drop). There was little reaction until the solution was warmed to  $60^{\circ}$ . Benzene and thionyl chloride were removed by distillation under reduced pressure; three successive 10-cc. portions of benzene were added and removed in the same way. The solid residue was crystallized from a mixture of benzene (15 cc.) and petroleum ether (15 cc., b. p.  $77-115^{\circ}$ ). The product (1.6 g.) melted at  $135-138^{\circ}$  with decomposition. It was insoluble in water and in cold aqueous bicarbonate (5%), but dissolved in the carbonate on warming. It was soluble in benzene and in chloroform.

*Anal.* Calcd. for  $C_{12}H_{11}O_2NCl_2$ : C, 53.40; H, 3.33. Found: C, 55.46; H, 3.98.

Bromination of this material (1 g.) in chloroform (10 cc.) by addition of bromine (560 mg.) in chloroform (5 cc.) led to a solid which, when recrystallized from a mixture of dioxane and petroleum ether, weighed 0.7 g., began to decompose at  $220^{\circ}$ , and melted at  $238^{\circ}$ . This material slowly dissolved in cold aqueous bicarbonate (5%).

*Anal.* Calcd. for  $C_{12}H_{11}O_2NCl_2Br$ : C, 41.3; H, 2.3. Found: C, 46.76; H, 4.02.

This substance (0.6 g.) dissolved instantly in cold am-

monium hydroxide (10 cc.). After the solution had stood overnight, most of the ammonia was removed by distillation under reduced pressure, the solution was acidified with hydrochloric acid and the white solid (0.4 g.) was removed. After crystallization from aqueous ethanol, it formed a chalky powder which melted at  $241-242^{\circ}$  with decomposition and which dissolved readily in bicarbonate solution with evolution of carbon dioxide.

*Anal.* Calcd. for  $C_{12}H_{11}O_2N_2Br$  (monobromomonocarboxy amide): C, 46.40; H, 3.54. Found: C, 46.38; H, 3.53.

Sodio ethyl phthalimidomalonate<sup>10</sup> (16.35 g.) and  $\beta$ -chloropropionaldehyde acetal<sup>11</sup> were mixed and slowly heated to  $160^{\circ}$ . After about forty-five minutes, localized dark spots appeared, and soon the whole mass became dark. Heating was continued for two hours, after which excess acetal was removed by distillation. Water (50 cc.) was added to the residue; there resulted a sticky black mass from which no solid could be obtained by crystallization from alcohol. The experiment was repeated except that a temperature of  $130^{\circ}$  was used. The result was the same except that a longer time was required for a reaction. When the materials were refluxed in xylene (25 cc.) for ninety-six hours, no reaction at all occurred; ethyl phthalimidomalonate was recovered. Likewise in alcohol very little reaction occurred; ethyl phthalimidomalonate was recovered, together with a very small amount of an unidentified solid melting at  $194^{\circ}$ .

### Summary

1. The synthesis of certain compounds related to tryptophan is described. It was not possible, however, to convert any of these compounds into the amino acid.

(10) Barger and Weichselbaum, "Org. Syntheses," **14**, 58 (1934).

(11) Witzemann, Evans, Hass and Schroeder, *ibid.*, **11**, 26 (1931).

MINNEAPOLIS 14, MINNESOTA RECEIVED MARCH 2, 1945

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

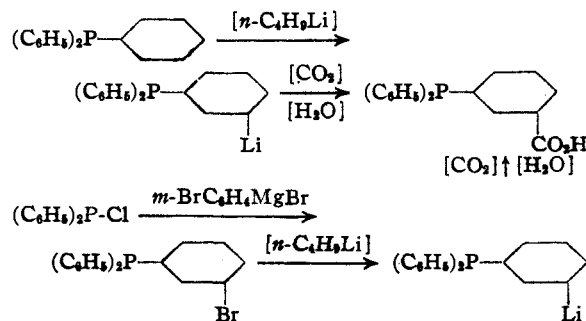
## The Metalation of Triphenylphosphorus, and Some Observations on the Formation of Tetraphenylphosphonium Bromide<sup>1</sup>

BY HENRY GILMAN AND GEORGE E. BROWN

The metalation of triphenylamine by *n*-butyllithium takes place in a *meta* position<sup>2a</sup> and not *ortho* as might have been predicted on the basis of earlier general observations.<sup>2b,c</sup> It was subsequently established<sup>2d</sup> that triphenylarsenic was also metalated in a *meta* position. Apparently there is a common orientation pattern of the related triaryl types, for we now find that triphenylphosphorus is also metalated in a *meta* position by *n*-butyllithium. The structure of the product was established by the following sequence of reactions

(1) Paper LX in the series: "The Relative Reactivities of Organometallic Compounds"; the preceding paper is by Gilman and Stuckwisch, *THIS JOURNAL*, **67**, 877 (1945). Taken from part of a thesis by G. E. Brown, Iowa State College (1941).

(2) (a) Gilman and Brown, *THIS JOURNAL*, **63**, 3208 (1940); (b) Gilman and Bebb, *ibid.*, **61**, 109 (1939); (c) Gilman, Stuckwisch, and Kendall, *ibid.*, **63**, 1758 (1941); (d) Gilman and Stuckwisch, *ibid.*, **63**, 3532 (1941).



There is probably no rearrangement in the halogen-metal interconversion reaction of *m*-bromophenyl-diphenylphosphorus, for a related reaction with *p*-bromophenyl-diphenylphosphorus gave on carbonation an acid unlike that obtained from the metalation of triphenylphosphorus.