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°, and then allowed to stand overnight. The greenish oil containing white flakes of solid was filtered; the solid melted at 77° (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° 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°. 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°). The product (1.6 g.) melted at 135–138° 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 $C_{12}H_9O_2NCl_2$: 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°, and melted at 238°. This material slowly dissolved in cold aqueous bicarbonate (5%).

Anal. Calcd. for $C_{12}H_8O_2NCl_2Br$: C, 41.3; H, 2.3. Found: C, 46.76; H, 4.02.

This substance (0.6 g.) dissolved instantly in cold ammonium 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° with decomposition and which dissolved readily in bicarbonate solution with evolution of carbon dioxide.

Anal. Calcd. for $C_{12}H_{11}O_4N_2Br$ (monobromomonocarboxy amide): C, 46.40; H, 3.54. Found: C, 46.38; H, 3.53.

Sodio ethyl phthalimidomalonate[10] (16.35 g.) and β-chloropropionaldehyde acetal[11] were mixed and slowly heated to 160°. 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° 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°.

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).

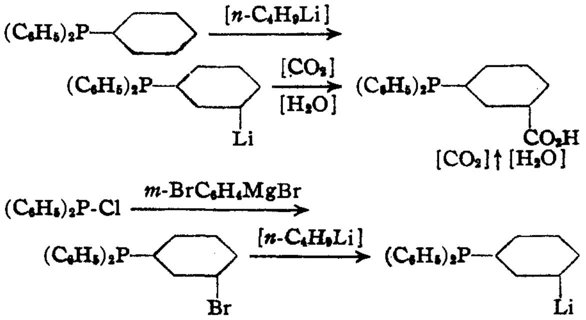
MINNEAPOLIS 14, MINNESOTA RECEIVED MARCH 2, 1945

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

The Metalation of Triphenylphosphorus, and Some Observations on the Formation of Tetraphenylphosphonium Bromide[1]

BY HENRY GILMAN AND GEORGE E. BROWN

The metalation of triphenylamine by *n*-butyllithium takes place in a *meta* position[2a] and not *ortho* as might have been predicted on the basis of earlier general observations.[2b,c] It was subsequently established[2d] 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



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.

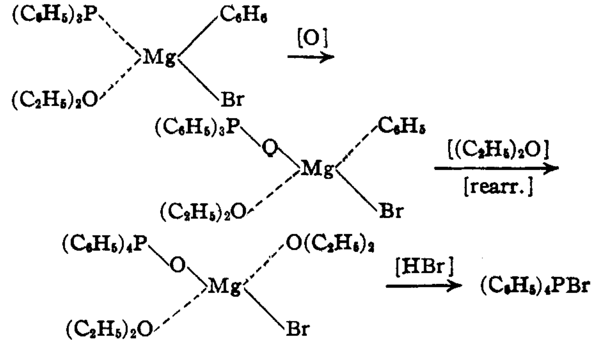
---

[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, **62**, 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).

It is quite probable, on the basis of analogy with related amines,[3] that diphenylphosphine, phenylphosphine, and P-alkylphenylphosphines will be metalated by *n*-butyllithium in an *ortho* position.

In another study, Dodonow and Medox[4] observed that tetraphenylphosphonium bromide is formed in a 72.7% yield when a mixture of triphenylphosphorus and phenylmagnesium bromide is first treated with oxygen and then hydrolyzed by hydrobromic acid. To account for this unusual reaction they postulated the prior formation of a coördinate of triphenylphosphorus, phenylmagnesium bromide and ether which then underwent essentially the following transformations:



It is highly unlikely that triphenylphosphorus oxide is first formed independently, because triphenylphosphorus is not readily oxidized in the absence of a catalyst or carrier.[5] Even if triphenylphosphorus oxide were formed initially, we have observed that this oxide does not react appreciably with phenylmagnesium bromide. It is also improbable that the Grignard reagent was first oxidized and reacted as C_6H_5OMgBr[5b] with the triphenylphosphorus because the separate oxidation of phenylmagnesium bromide gives yields of phenol which generally are of the order of 25%, whereas our yield of tetraphenylphosphonium bromide was 82.6%. Furthermore, we found that although phenyllithium with triphenylphosphorus in ether was oxidized to give tetraphenylphosphonium bromide (subsequent to hydrolysis by hydrobromic acid), lithium phenoxide and triphenylphosphorus gave none of the phosphonium compound under corresponding conditions.

Inasmuch as our yields of the phosphonium compound when phenyllithium was used were 31 and 30%, respectively, as contrasted with the much higher yields when phenylmagnesium bromide was used, there is indirect evidence for the formation of a coördinate complex. It has been shown that phenylmagnesium bromide has a much greater tendency to form coördination compounds than phenyllithium.[6] The non-formation of the onium compound when phenylsodium and benzene were treated with triphenylphosphorus may also point to the non-formation of any appreciable quantity of coördination compound inasmuch as neither phenylsodium nor benzene[6] might be expected to assist the formation of coördinate types in this reaction. However, the absence of onium formation with phenylsodium may also be due in part to the fact that the phenylsodium was present as a suspension[7] in the benzene. Incidentally, it should be mentioned that no onium compound was isolated in the reaction of triphenylphosphorus oxide and phenyllithium.

Experimental

Triphenylphosphorus and *n*-Butyllithium.—A solution of 0.16 mole of *n*-butyllithium and 12.1 g. (0.05 mole) of triphenylphosphorus in a total volume of 250 cc. of ether was refluxed with stirring for 46 hours, and then carbonated by pouring upon Dry Ice. Subsequent to extraction with 5% potassium hydroxide, and acidification by hydrochloric acid, there was obtained 6 g. of semi-solid acidic material. This was dissolved in glacial acetic acid and placed in a refrigerator. Recrystallization from ethanol gave 0.9 g. (5.9%) of *m*-carboxyphenyldiphenylphosphorus, melting at 157°. Also, a small amount of benzoic acid was isolated from the acidic filtrate.

Anal. Calcd. for $C_{19}H_{15}O_2P$: P, 10.12; neut. equiv., 306.1. Found: P, 10.38 and 10.46; neut. equiv., 307.5.

There was a practically quantitative recovery of triphenylphosphorus when an ether solution of 0.25 mole of triphenylphosphorus and 0.25 mole of *n*-butyllithium was refluxed, with stirring, in a nitrogen atmosphere for one-half hour.

***m*-Carboxyphenyl-diphenylphosphorus.**—A benzene-ether solution of 0.03 mole of *m*-bromophenylmagnesium bromide was added slowly to a stirred cold ether solution of 6.6 g. (0.03 mole) of diphenylphosphorus chloride. The reaction was carried out in a nitrogen atmosphere. Subsequent to hydrolysis by dilute hydrochloric acid, the mixture was steam distilled to remove bromobenzene. No attempt was made to isolate the *m*-bromophenyl-diphenylphosphorus, and the dried ether extract was added to 0.06 mole of *n*-butyllithium. After stirring in a nitrogen atmosphere for one-half hour, the mixture was carbonated by Dry Ice. The yield of pure *m*-carboxyphenyldiphenylphosphorus (m. p. 157°) was 1 g. (10.9% based on the diphenylphosphorus chloride). A mixed m. p. determination with the acid obtained by the metalation of triphenylphosphorus showed no depression.

The diphenylphosphorus chloride was prepared in essential accordance with the directions of Michaelis[8] by heating a mixture of 26.2 g. (0.1 mole) of triphenylphosphorus and 17.9 g. (0.1 mole) of phenylphosphorus dichloride in a flask immersed in a metal bath at 280° for four hours and then at 300° for six hours. The yield of viscous liquid distilling at 316–320°, in a carbon dioxide atmosphere, was 6.5 g. (29.5%).

The phenylphosphorus dichloride was prepared by refluxing a mixture of 30 g. of aluminum chloride, 150 g. of benzene, and 200 g. of phosphorus trichloride for about thirty hours, at the end of which time there was no appreciable evolution of hydrogen chloride.[9]

***m*-Carboxyphenyl-diphenylphosphorus Oxide.**—An alkaline solution of 0.2 g. (0.0007 mole) of *m*-carboxyphenyl-

---

[3] Gilman, Brown, Webb and Spatz, THIS JOURNAL, **62**, 977 (1940).

[4] Dodonow and Medox, *Ber.*, **61**, 907 (1928).

[5] (a) Schönberg, *ibid.*, **68**, 163 (1935). (b) It is not excluded that the phenylmagnesium bromide might form transitorily a peroxidic type to act as an oxygen-carrier.

[6] Gilman and Jones, THIS JOURNAL, **62**, 1243 (1940).

[7] The limitation of solvents is inherent in the highly polar characteristics of the organosodium compounds.

[8] Michaelis and Link, *Ann.*, **207**, 193 (1881).

[9] Kamai, *J. Gen. Chem.* (U. S. S. R.), **2**, 524 (1932) [*C. A.*, **27**, 967 (1933)]; Michaelis, *Ber.*, **12**, 1009 (1879).

diphenylphosphorus was stirred for one hour with sufficient potassium permanganate to maintain a pink color. After removal of the manganese dioxide, the alkaline solution was decolorized and then acidified with hydrochloric acid. The oxide slowly crystallized from the aqueous solution, and recrystallization from ethanol gave 0.12 g. (57%) of product melting at 232°.

Anal. Calcd. for $C_{19}H_{15}O_3P$: P, 9.63. Found: P, 10.12 and 10.09.

p-Bromophenyl-diphenylphosphorus.—An ether solution of 0.1 mole of p-bromophenylphosphorus dichloride[10] was added slowly to a vigorously stirred solution of 0.22 mole of phenylmagnesium bromide in ether. After refluxing for two hours, the mixture was hydrolyzed by dilute hydrochloric acid, and the ether extract dried. On distillation there was obtained 23 g. (67%) of compound distilling at 205–210° (4 mm.).

Anal. Calcd. for $C_{18}H_{14}BrP$: C, 63.3; H, 4.11; P, 9.09. Found: C, 63.6; H, 4.20; P, 9.23.

p-Carboxyphenyl-diphenylphosphorus.—A solution of 6.82 g. (0.02 mole) of p-bromophenyldiphenylphosphorus in a mixture of 30 cc. of ether and 20 cc. of benzene was added to 0.02 mole of n-butyllithium in 60 cc. of ether. After stirring for one-half hour, the mixture was carbonated by Dry Ice and then, by conventional procedures, there was obtained 3.5 g. (57%) of product which melted at 156° after crystallization from glacial acetic acid.

Anal. Calcd. for $C_{19}H_{15}O_2P$: P, 10.13. Found: P, 10.24 and 10.32.

The melting point of p-carboxyphenyl-diphenylphosphorus was depressed on adding an equal quantity of m-carboxyphenyl-diphenylphosphorus.

Tetraphenylphosphonium Bromide.—In essential accordance with the procedure of Dodonow and Medox,[4] a filtered solution of phenylmagnesium bromide (prepared from 9.56 g. of bromobenzene) was added to 4 g. of triphenylphosphorus; the total volume of solution was 75 cc. Dry oxygen was passed over the surface of the vigorously stirred solution for one and one-half hours, and a solid soon started to form. Then a solution of hydrobromic acid (9.5 cc. of 45% hydrobromic acid and 20.5 cc. of water) was added. The yield of tetraphenylphosphonium bromide dihydrate was 82.6%.

From a corresponding experiment using 4 g. of triphenylphosphorus and phenyllithium (prepared from 9.56 g. of bromobenzene and 0.9 g. of lithium) there was obtained a 31% yield of the phosphonium dihydrate. A duplicate run gave a 30% yield.

To a suspension of phenylsodium (prepared from 10 g. of diphenylmercury and 9 g. of sodium wire) in benzene was added 4 g. of triphenylphosphorus. After stirring for one-half hour, oxygen was passed into the flask for five hours prior to the addition of hydrobromic acid. No tetraphenylphosphonium bromide was isolated.

Triphenylphosphorus Oxide with Phenyllithium and with Phenylmagnesium Bromide.—A suspension of 5.56 g. (0.02 mole) of triphenylphosphorus oxide was added to a solution of phenyllithium prepared from 0.03 mole of bromobenzene. After refluxing for four hours there was present some RLi compound as evidenced by color test I.[11] Hydrolysis by a hydrobromic acid solution yielded no tetraphenylphosphonium bromide, and 72% of the triphenylphosphorus oxide was recovered.

In a corresponding experiment with phenylmagnesium bromide,[12] no tetraphenylphosphonium bromide was obtained.

Incidental to the possible preparation of a sample of m-carboxyphenyl-diphenylphosphorus or its oxide by oxidation of a nuclear methyl group, 1.5 g. of potassium permanganate was added to a finely divided suspension of 2.22 g. (0.01 mole) of triphenylphosphorus in water. The suspension was stirred for eight hours, filtered, dried, and the solid extracted with ether. The yield of triphenylphosphorus oxide was 2.73 g. (98.3%).

Triphenylphosphorus and Lithium Phenoxide.—A solution containing 0.025 mole of lithium phenoxide was prepared by adding an ether solution of phenol to a filtered solution of n-butyllithium until the mixture gave no color test I.[11] Then a solution of 6.55 g. (0.025 mole) of triphenylphosphorus in ether was added, and the mixture was refluxed with stirring for three hours. Subsequent to hydrolysis by hydrobromic acid, no tetraphenylphosphonium bromide was isolated and 95% of the triphenylphosphorus was recovered.

Summary

Triphenylphosphorus is metalated in a *meta* position by n-butyllithium in ether. Supporting evidence is presented for the intermediate formation of a coördination complex in the preparation of tetraphenylphosphonium bromide by the oxidation of a mixture of triphenylphosphorus and phenylmagnesium bromide (or phenyllithium), followed by hydrolysis with hydrobromic acid.

AMES, IOWA RECEIVED FEBRUARY 3, 1945

---

[10] Michaelis, *Ann.*, **293**, 237 (1896).

[11] Gilman and Schulze, THIS JOURNAL, **47**, 2002 (1925).

[12] See, also, ref. 4 and Gilman and Vernon, *ibid.*, **48**, 1063 (1926), for other experiments of triphenylphosphorus oxide and Grignard reagents.