edge of the pertinent K_S and k_3 values it is clear that values of $C^1_{\max}$ for case II provide no more than an ambiguous estimate of relative activity in which the contributions due to K_S and those due to k_3 can not be separately evaluated. It should be noted that past experience has shown that there is no basis for the assumption that in an extended series K_S is approximately constant and k_3 is the important variable or *vice versa.*[13]

While it is true that in the system depicted in equation (1) there is no ambiguity arising in the interpretation of C°, *i.e.*, the true zero-order coefficient, since it is directly proportional to k_3, it is obvious that valid comparisons cannot be made between C° values on one hand and $C^1_{\max}$ values on the other.

CONTRIBUTION No. 1787 FROM THE
GATES AND CRELLIN LABORATORIES OF CHEMISTRY
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA 4, CALIFORNIA

Bromomagnesium Salts of Dialkyl Phosphites as Intermediates in the Synthesis of Substituted Hydroxymethyl Phosphonic Acid Esters

BY OSCAR GAWRON, CHESTER GRELECKI, WILLIAM REILLY AND JAMES SANDS

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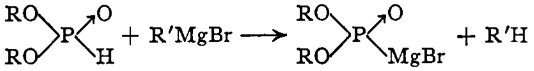
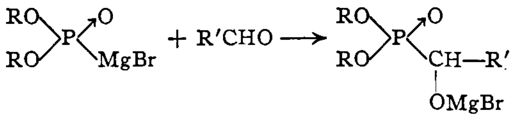
Recent reports[1-4] on the base-catalyzed condensation of dialkyl phosphites with carbonyl compounds to yield α-hydroxy phosphonates prompt us to report preliminary work on their synthesis by the use of bromomagnesium derivatives of dialkyl phosphites prepared *in situ.* These derivatives may be prepared by the addition of an ether solution of a Grignard reagent to an ether solution of a dialkyl phosphite according to the equation



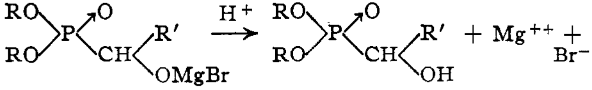
$$(RO)_2P(\rightarrow O)H + R'MgBr \longrightarrow (RO)_2P(\rightarrow O)MgBr + R'H$$

Refluxing the bromomagnesium derivative with an aldehyde or ketone and decomposing the reaction mixture with saturated ammonium chloride solution or dilute acid yields after drying and vacuum distillation the α-hydroxyphosphonate.

The reactions leading to the formation of the α-hydroxyphosphonates may be written in a manner analogous to the reaction of Grignard reagents with carbonyl compounds.



$$(RO)_2P(\rightarrow O)MgBr + R'CHO \longrightarrow (RO)_2P(\rightarrow O)CH(OMgBr){-}R'$$



$$(RO)_2P(\rightarrow O)CH(R')OMgBr \xrightarrow{H^+} (RO)_2P(\rightarrow O)CH(R')OH + Mg^{++} + Br^-$$

The acidity of dialkyl phosphites is well known,[5] magnesium salts,[6] in addition to others, having been prepared and while cognizance of this is taken in the replacement of alkoxy groups of dialkyl phosphites by alkyl groups from Grignard reagents,[7] apparently no previous attempt has been made to prepare and utilize halomagnesium derivatives for synthetic purposes.[8]

The *in situ* prepared bromomagnesium salts are stable on refluxing in diethyl ether, do not react with alkyl halides (*n*-butyl bromide and methyl iodide) on refluxing in diethyl ether and react with oxides and acyl halides in addition to ketones and aldehydes. These and other reactions are under investigation.

Experimental

Ethane Evolution from Ethylmagnesium Bromide and Diethyl Phosphite.—A solution of 1.38 g. (0.010 mole) of diethyl phosphite in 6 ml. of anhydrous ether was placed in a 3-necked flask of 20-ml. capacity. The flask was connected *via* a small cold-water condenser to two gas burets arranged in series. After displacement of air by ether vapors, 6.65 ml. (0.010 mole) of a 1.50 *M* solution of ethylmagnesium bromide in anhydrous ether was added dropwise with shaking over a period of 20 minutes at room temperature. The evolved gas was collected in the first buret and then transferred to the second buret where its volume was measured at room temperature and atmospheric pressure. The confining liquid in both burets was 85% phosphoric acid. Blank determinations indicated essentially complete absorption of ether vapors. The volume of gas collected, reduced to standard conditions, was 218 ml. (97.4% of theory).[9]

***In situ* Preparation of the Bromomagnesium Salt of Dibutyl Phosphite.**—Into a 3-necked flask, equipped with sealed stirrer, dropping funnel, reflux condenser and calcium chloride drying tubes, a solution of 38.8 g. (0.2 mole) of dibutyl phosphite in 50 ml. of anhydrous ether was placed. A solution of 0.2 mole of ethylmagnesium bromide in 100 ml. of anhydrous ether was then added dropwise with stirring and cooling in an ice-salt mixture. Toward the end of the addition, the reaction mixture separated into two layers, the lower a thick oil. In the case of diethyl phosphite a pasty mass separated which on continued stirring dispersed and two layers formed. The intact reaction mixture or that prepared by reverse addition under the same conditions was used as a source of the bromomagnesium salt in subsequent experiments.

Attempts to isolate the bromomagnesium derivative of diethyl phosphite by separation of the lower layer, washing with ether and drying in high vacuum yielded a white, hygroscopic powder whose analysis consistently failed to agree with the calculated values and from which no empirical formula could be calculated.

Anal. Calcd. for $C_4H_{10}O_3BrMgP$: C, 19.82; H, 4.11; Br, 33.12; Mg, 9.95; P, 12.83. Found: C, 13.65; H, 5.61; Br, 26.56; Mg, 18.90; P, 11.50.

Stability of the Bromomagnesium Salt of Dibutyl Phosphite to Reflux in Ether.—After preparation of the bromomagnesium salt, using the quantities and conditions indicated above, the cooling bath was removed and the reaction mixture was refluxed for three hours. After standing overnight at room temperature decomposition of the salt was effected by shaking the reaction mixture with 100 ml. of cold

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(1) A. E. Arbuzov and M. M. Azanovskaya, *Doklady Akad. Nauk S. S. R.*, **58**, 1961 (1947); *C. A.*, **46**, 8606 (1952).

(2) V. S. Abramov, *Doklady Akad. Nauk. S. S. R.*, **73**, 487 (1950); *C. A.*, **45**, 2855 (1951).

(3) A. N. Pudovik, *Doklady Akad. Nauk. S. S. R.*, **73**, 499 (1950); *C. A.* **45**, 2856 (1951).

(4) E. K. Fields, U. S. 2,579,810 (Dec. 25, 1951).

(5) G. M. Kosolapoff, "Organophosphorus Compounds," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 193.

(6) T. Milobendzki and T. Knoll, *Chem. Polsk.*, **15**, 79 (1917); *C. A.*, **13**, 2867 (1919).

(7) G. M. Kosolapoff and R. M. Watson, THIS JOURNAL, **73**, 4101 (1951), use a Grignard to dialkyl phosphite ratio of 3.3:1 for the preparation of phosphinous acids intermediate in a synthesis of phosphinic acids.

(8) During the preparation of this manuscript, A. N. Pudovik, *Zhur. Obschchei Khim.*, **22**, 109 (1952); *C. A.*, **46**, 11099 (1952), prepared, *in situ*, the bromomagnesium salts of diethyl and dibutyl phosphite and treated these with 1-alkoxy-5-chloro-3-pentenes and 1-alkoxy-3-chloro-4-pentenes to give the corresponding 1-alkoxy-5-(dialkylphosphono)-3-pentenes.

(9) Pudovik, footnote 8, using almost identical quantities as described above, on addition of diethyl phosphite to ethylmagnesium bromide found the evolution of ethane to be 32.4%.

saturated ammonium chloride solution. The ether layer was then separated, dried over anhydrous sodium sulfate and vacuum distilled to yield 31.0 g. (79%) of dibutyl phosphite, b.p. 89–91° (3 mm.), $n^{19.5}D$ 1.4246.

Diethyl 2-Hydroxypropane-2-phosphonate.—To 0.1 mole of the bromomagnesium derivative of diethyl phosphite, 5.8 g. (0.1 mole) of acetone in 25 ml. of anhydrous ether was added. The reaction mixture was then refluxed for three hours and after standing overnight at room temperature was decomposed in the manner previously indicated. After separation of the ether layer and drying over anhydrous sodium sulfate, vacuum distillation yielded 8.0 g. (41%) of product, b.p. 145–148° (20 mm.), m.p. 14–16°, literature[10] b.p. 145° (20 mm.), m.p. 14–15°.

Diethyl Ester of α-Hydroxybenzylphosphonic Acid.—To 0.1 mole of the bromomagnesium derivative of diethyl phosphite, 10.6 g. (0.1 mole) of benzaldehyde in 25 ml. of anhydrous ether was added. The reaction mixture was refluxed for three hours and then worked up as previously indicated. After removal of some unreacted phosphite and benzaldehyde by vacuum distillation, the residue in the still flask was recrystallized from benzene–petroleum ether to give 15 g. (61.5%) of crude product. After several recrystallizations, pure product, m.p. 83–84°, was obtained; lit.[11] m.p. 83–84°.

Acknowledgment.—This investigation was supported in part by a research grant (C-1347) from the National Cancer Institute of the National Institutes of Health, Public Health Service.

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(10) C. Marie, *Ann. Phys. Chem.*, [8] **3**, 335 (1904).

(11) M. I. Kabachnik and P. A. Rossiskaya, *Bull. acad. sci. U. R. S. S., Classe sci. Chim.*, 364 (1945); *C. A.*, **40**, 4688 (1946).

DEPARTMENT OF CHEMISTRY
DUQUESNE UNIVERSITY
PITTSBURGH, PA.

Reaction of Triphenyltin Hydride with Methyllithium

BY HENRY GILMAN AND SANDERS D. ROSENBERG

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Triethylsilane has been treated with methyllithium,[1] *n*-propyllithium, *n*-butyllithium, phenyllithium and lithium ethoxide.[2] In each reaction the products were lithium hydride and the corresponding substituted triethylsilane. This type

$$(C_2H_5)_3SiH + RLi \longrightarrow (C_2H_5)_3SiR + LiH$$

$$(C_2H_5)_3SiH + C_2H_5OLi \longrightarrow (C_2H_5)_3SiOC_2H_5 + LiH$$

of reaction was extended to the aromatic series when triphenylsilane was treated with methyllithium and phenyllithium to form lithium hydride and triphenylmethylsilane and tetraphenylsilane, respectively,[3] and appeared to be general for hydrides of Group IV-B elements when it was shown that triphenyltin hydride[3] and triphenylgermane[4] yielded lithium hydride and tetraphenyltin and tetraphenylgermanium, respectively, when reacting with phenyllithium. Benkeser and Riel[5] treated four substituted triarylsilanes with methyllithium to form, in each case, the triarylmethylsilane and lithium hydride.

Recently it was reported that when triphenyltin hydride reacts with methyllithium the products are triphenyltin-lithium and methane.[6] The reactive intermediate, triphenyltin-lithium, was identified by reaction with triphenyltin bromide to form hexaphenylditin in 49% yield.

$$(C_6H_5)_3SnH + CH_3Li \longrightarrow (C_6H_5)_3SnLi + CH_4$$

It may not be valid to generalize that the reaction of trisubstituted tin hydrides with methyllithium will be the same as that of trisubstituted silanes. The latter when treated with methyllithium form trisubstituted methylsilanes.[1,3,5] But because of this apparent anomalous result[6] and our interest in the organometallic complex, triphenyltin-lithium,[7] the reaction was repeated in this Laboratory.

It was found that triphenyltin hydride and methyllithium react to form triphenylmethyltin (18%), tetraphenyltin (25%) and lithium hydride in accordance with results cited previously.[1–5] In a check run the yield of triphenylmethyltin was 15% and of tetraphenyltin, 25%. No gas evolution was noted in either run and the characteristic yellow-tan color, denoting triphenyltin-lithium, was not evident. It is interesting to note the formation of tetraphenyltin, possibly as a consequence of disproportionation, even under these mild conditions.[3]

$$(C_6H_5)_3SnH + CH_3Li \longrightarrow (C_6H_5)_3SnCH_3 + (C_6H_5)_4Sn + LiH$$

We are also presenting at this time a method for the quantitative analysis of tin in organotin compounds.[8]

Experimental

Triphenyltin Hydride.—This preparation was carried out as described by Wittig and co-workers[6] except that triphenyltin iodide was used in place of triphenyltin bromide. Two runs were made and in both the yield of triphenyltin hydride, distilling at 151° (0.05 mm.), was 1.8 g. (51.6%). It was found that if triphenyltin chloride was substituted for triphenyltin iodide no reaction took place under corresponding conditions.

Reaction of Triphenyltin Hydride with Methyllithium.—The methyllithium used in this reaction was prepared[9] by refluxing for one hour, 1.42 g. (0.01 mole) of freshly opened methyl iodide (Eastman Kodak Co., white label) with 0.08 g. (0.01 g. atom plus 10%) of lithium metal in 100 ml. of ether. The lithium iodide thus formed was allowed to settle out and the clear methyllithium solution was used.

A 250-ml. flask was equipped with a magnetic stirrer, a 100-ml. graduated dropping funnel, a nitrogen inlet tube and a gas outlet tube. The gas outlet tube was attached to a gas bubble counter filled with concentrated sulfuric acid; the counter was, in turn attached to a Dumas tube filled with fine cupric oxide; this tube was attached to water- and carbon dioxide-absorption tubes used in micro carbon and hydrogen quantitative analysis.[10]

About 50 ml. of ether was placed in the flask, gentle stirring was begun, and a very slow stream (*ca.* one bubble every three seconds) of nitrogen gas was passed through the entire system for one hour. The long burner under the Dumas tube was turned on during the sweep-through of the gas. The absorption tubes were then weighed.

After the absorption tubes were returned to their positions 1.6 g. (0.0046 mole) of triphenyltin hydride was added to the reaction flask and 0.0046 mole of methyllithium in 35 ml. of ether was placed in the dropping funnel. The same rate of nitrogen sweep-through and stirring as before were

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(1) H. Gilman and S. P. Massie, THIS JOURNAL, **68**, 1128 (1946).

(2) R. N. Meals, *ibid.*, **68**, 1880 (1946).

(3) H. Gilman and H. W. Melvin, *ibid.*, **71**, 4050 (1949).

(4) O. H. Johnson and D. M. Harris, *ibid.*, **72**, 5566 (1950).

(5) R. A. Benkeser and F. J. Riel, *ibid.*, **73**, 3472 (1951).

(6) G. Wittig, F. J. Meyer and G. Lange, *Ann.*, **571**, 12 (1951).

(7) H. Gilman and S. D. Rosenberg, THIS JOURNAL, **74**, 531 (1952).

(8) A qualitative test for tin in organotin compounds has been described recently by H. Gilman and T. N. Goreau, *J. Org. Chem.*, **17**, 1470 (1952).

(9) H. Gilman, E. A. Zoellner and W. M. Selby, THIS JOURNAL, **55**, 1252 (1933).

(10) J. B. Niederl and V. Niederl, "Micromethods of Quantitative Organic Analysis," 2nd Edition, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 111.