[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

# THE REACTION OF DIALKYL CHLOROPHOSPHATES WITH ARYLMAGNESIUM HALIDES

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*Received March 28, 1951*

The direct preparation of aromatic and aromatic-heterocyclic phosphonic acids [$ArPO(OH)_2$] can be carried out by the Friedel and Crafts reaction (1) by way of the halophosphines, using phosphorus trichloride and aluminum chloride. The catalyst is not necessary, if dialkylanilines or antipyrine are treated with phosphorus oxychloride (2). For the synthesis of definite isomers, the Friedel and Crafts method is, however, at best uncertain (3). Only one case has been reported where a sufficiently activated heterocyclic halide has lent itself to the synthesis with esters of phosphorous acid, which is so useful in the aliphatic series (4). The reaction of N,N-diethylamidodichlorophosphate with arylmagnesium halides at room temperature has been considered for, but not applied to, the preparation of aromatic phosphonic acids. More circuitous methods which involve the oxidation of aromatic derivatives of trivalent phosphorus or the tedious separation from diarylphosphinic acids ($Ar_2PO_2H$) have been reviewed in a recent monograph (5).

We are reporting a new Grignard method by which aromatic phosphonic acids of definitely predictable structure may be prepared unaccompanied by triarylphosphine oxides or phosphines which are the main products from the action of phosphorus halides on Grignard reagents. Triarylphosphine oxides are formed under the conditions of our reaction only if certain structural postulates are satisfied.

Dialkyl chlorophosphates were chosen as reagents for the Grignard synthesis of dialkyl arylphosphonates because their lone chlorine atom could be expected to be eliminated first with the establishment of a carbon-to-phosphorus linkage while the ester groups would remain unaffected if the arylmagnesium halide had been largely consumed. We have found that the reaction stops regularly with the formation of dialkyl arylphosphonates if the arylmagnesium halide group is protected sterically by one *ortho* substituent. A chlorine atom, a methyl or a phenyl group, or an adjacent aromatic ring may fulfill this blocking function. In this manner, *o*-chlorobenzene-, *o*-toluene-, *o*-biphenyl-, and naphthalene-1-phosphonic acid have been obtained from the corresponding Grignard reagents.

In the absence of an *ortho*-substituent the addition of dialkyl chlorophosphates to arylmagnesium halides caused a reaction which could not be arrested before the triarylphosphine oxide stage was reached. The yields of these products, based on the amount of aryl halide used, were between 33% and 75%. Phenylmagnesium bromide and diethyl chlorophosphate furnished triphenylphosphine oxide, and the corresponding aromatic phosphine oxides were obtained also from *p*-chlorophenyl-, *p*-tolyl-, *p*-biphenyl-, 2-thienyl-, and 2-naphthyl-magnesium bromide.

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It would appear from our results with sterically hindered arylmagnesium halides that the formation of phosphine oxides in the absence of an *ortho*-substituent could be interpreted as an addition of the Grignard reagent to the dialkyl arylphosphonate first formed. The next intermediate would be an alkyl diarylphosphinate [$Ar_2PO(OR)$], and Kosolapoff (3) has actually obtained ethyl diphenylphosphinate from the reaction of diethyl benzenephosphonate with phenylmagnesium bromide. By contrast we have never been able to isolate a diarylphosphinic acid in these experiments.

Since it had been shown that the "reversed" (6) addition of dilute solutions of arylmagnesium halides to phosphorus oxychloride limits the reaction of disubstitution to about 50% and permits the isolation of corresponding yields of phosphinic acids, we applied a similar procedure to the reaction of sterically unhindered arylmagnesium halides with dialkyl chlorophosphates. Benzenephosphonic acid and *p*-chlorobenzenephosphonic acid were obtained from phenylmagnesium bromide and its *p*-chloro derivative, respectively. This bears out the prediction that the ester groups of a dialkyl chlorophosphate have a lower affinity to Grignard reagents than that shown by its chlorine atom.

In two instances tested, sterically hindered and unhindered aryllithium compounds gave aromatic phosphonates when added to diethyl chlorophosphate. This is particularly interesting in view of the recent observation of Robins and Christensen (7) that addition of *p*-dimethylaminophenyllithium to phosphorus oxychloride yields bis(*p*-dimethylaminophenyl)phosphinic acid and tris(*p*-dimethylaminophenyl)phosphine oxide.

*Acknowledgement.* We are grateful to the Virginia-Carolina Chemical Corporation for support of this work, and to Drs. William P. Boyer and J. Roger Mangham of that company for many helpful suggestions.

## EXPERIMENTAL[2]

*Preparation of tertiary phosphine oxides and phosphonic acids.* With the exception of the preparation of benzenephosphonic acid and *p*-chlorobenzenephosphonic acid by the "reversed" Grignard reaction and Kosolapoff's modification of the Friedel and Crafts synthesis, the preparation of tri-*p*-chlorophenylphosphine oxide and *o*-toluenephosphonic acid may be considered typical and may serve to illustrate the procedure used for the preparation of the tertiary phosphine oxides and of the phosphonic acids.

*Tri-p-chlorophenylphosphine oxide.* To an ice-cooled Grignard solution prepared in an atmosphere of nitrogen from 2.4 g. (0.1 mole) of magnesium and 19.1 g. (0.1 mole) of *p*-chlorobromobenzene in 80 cc. of dry ether, a solution of 5.7 g. (0.033 mole) of diethyl chlorophosphate[3] in 50 cc. of ether was added dropwise with rapid stirring and after removal of the ice-bath. A vigorous reaction set in immediately. When approximately half of the diethyl chlorophosphate had been added a heavy brown oil separated from the reaction mixture and refluxing diminished and finally stopped. As the remainder of the reagent was added the brown oil gradually went back into solution. The mixture was refluxed for an additional two hours, cooled, and decomposed by slowly pouring it onto a mixture of

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[2] All melting points are corrected.

[3] The dialkyl chlorophosphates were prepared from the corresponding dialkyl hydrogen phosphites by the method of McCombie, Saunders, and Stacey, *J. Chem. Soc.*, 380 (1945). The dialkyl hydrogen phosphites are available from the Virginia-Carolina Chemical Corporation, Richmond, Virginia.

crushed ice and dilute hydrochloric acid. The organic layer was separated and the aqueous layer was extracted twice with ether, the ether extracts combined, dried over sodium sulfate, and evaporated. The residual oil deposited 6.4 g. (54%) of colorless crystals which, after recrystallization from dilute ethanol, melted at 178°.

TABLE I

PROPERTIES OF ARYLPHOSPHONIC ACIDS AND PHOSPHINE OXIDES

| COMPOUND | M.P., °C. | YIELD, % | EMPIRICAL FORMULA | ANALYSES | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Calculated | | | Found | | |
| | | | | C | H | P | C | H | P |
| *o*-Toluenephosphonic acid* | 139–141[a,c] | 50.4 | $C_7H_9O_3P$ | 48.84 | 5.27 | 17.99 | 48.52 | 5.29 | 18.28 |
| Naphthalene-1-phosphonic acid* | 199–200 | 45 | $C_{10}H_9O_3P$ | 57.70 | 4.36 | 14.89 | 57.86 | 4.47 | 15.05 |
| *o*-Biphenylphosphonic acid | 203–205[b] | 31.4 | $C_{12}H_{11}O_3P$ | 61.54 | 4.73 | 13.22 | 61.65 | 4.47 | 13.25 |
| 2-Chlorobenzenephosphonic acid | 181–183 | 26.1 | $C_6H_6ClO_3P$ | 37.42 | 3.14 | | 37.02 | 2.72 | |
| Benzenephosphonic acid* | 161–163[c] | 40.5 | $C_6H_7O_3P$ | 45.58 | 4.46 | 19.59 | 45.30 | 4.32 | 19.69 |
| 4-Chlorobenzenephosphonic acid* | 186–187[c] | 48 | $C_6H_6ClO_3P$ | | | | | | |
| *p*-Toluenephosphonic acid* | 188–190[d] | 55 | $C_7H_9O_3P$ | | | | | | |
| Triphenylphosphine oxide* | 156.5–158 | 73 | $C_{18}H_{15}OP$ | 77.68 | 5.43 | 11.13 | 78.11 | 5.73 | 11.24 |
| Tri-*p*-tolylphosphine oxide* | 143–144[c] | 75.5 | $C_{21}H_{21}OP$ | | | | | | |
| Tri-*β*-naphthylphosphine oxide | 248–249 | 66 | $C_{30}H_{21}OP$ | 84.09 | 4.94 | 7.23 | 82.64 | 4.64 | 7.18 |
| Tri-2-thienylphosphine oxide | 129–130 | 75 | $C_{12}H_9OPS_3$ | 48.63 | 3.06 | 10.45 | 48.85 | 3.38 | 10.46 |
| Tri-*p*-chlorophenylphosphine oxide* | 178 | 54 | $C_{18}H_{12}Cl_3OP$ | 56.65 | 3.17 | 8.12 | 56.80 | 3.02 | 8.24 |
| Tri-*p*-biphenylphosphine oxide* | 233–234[c] | 33 | $C_{36}H_{27}OP$ | | | | | | |

[a] Prepared by addition of diethyl chlorophosphate to *o*-tolylmagnesium bromide, or by addition of *o*-tolyllithium to diethyl chlorophosphate. [b] Di-*n*-butyl chlorophosphate was used in the preparation of this compound. [c] Identified by mixture melting point with an authentic sample. [d] Prepared by addition of *p*-tolyllithium to diethyl chlorophosphate and subsequent hydrolysis. Neut. equiv. Calc'd, 172.12; Found, 173.78, 174.92. Identified as the dianilide, m.p. 207–208.5°. *This compound has been reported in the literature. For exhaustive treatment of references, see Kosolapoff (5).

*Anal.* Calc'd for $C_{18}H_{12}Cl_3OP$: C, 56.64; H, 3.17; P, 8.11.
Found: C, 56.80; H, 3.02; P, 8.24.

*o-Toluenephosphonic acid.* To a cooled and stirred Grignard solution prepared in an atmosphere of nitrogen from 2.4 g. (0.1 mole) of magnesium and 18.8 g. (0.1 mole) of *o*-

bromotoluene was added in small portions 17.2 g. (0.1 mole) of diethyl chlorophosphate in 50 cc. of ether. When approximately one-half of the reagent had been added the ether began to reflux and continued to boil for about 15 minutes after completion of the addition. Refluxing was continued for an additional two hours and the reaction mixture was cooled, decomposed by pouring the cold solution onto a mixture of crushed ice and dilute hydrochloric acid, and worked up as described in the preceding experiment. Yield, 11.5 g. (50.4%) of diethyl *o*-toluenephosphonate, b.p. 148–150°/14 mm. The oil was hydrolyzed with 50 cc. of concentrated hydrochloric acid and the hydrolysate concentrated to a syrupy consistency. It deposited colorless crystals which, after several recrystallizations from benzene, had m.p. 139–141°.

*Anal.* Calc'd for $C_7H_9O_3P$: C, 48.84; H, 5.27; P, 17.99.
Found: C, 48.52; H, 5.29; P, 18.28.

*Benzenephosphonic acid.* The acid was prepared by the "reversed" Grignard synthesis patterned on the directions of Kosolapoff (6). The Grignard solution from 7.8 g. (0.05 mole) of bromobenzene in 60 cc. of dry ether was diluted to 200 cc. with ether and added dropwise over a period of 2.25 hours to a gently refluxing and stirred solution of 8.5 g. (0.05 mole) of diethyl chlorophosphate in 200 cc. of ether. After standing overnight the reaction mixture was decomposed with ice and dilute hydrochloric acid and worked up. The oily ester was hydrolyzed with 50 cc. of concentrated hydrochloric acid and the hydrolysate was evaporated to dryness. The crystalline residue weighed 3.2 g. (40.5%), and, after two recrystallizations from ethyl acetate, melted at 161–163°. It was identified by mixture melting point with an authentic sample prepared by hydrogenolysis (palladium-on-carbon catalyst) of *p*-chlorobenzenephosphonic acid.

*Anal.* Calc'd for $C_6H_7O_3P$: C, 45.58; H, 4.46; P, 19.59.
Found: C, 45.30; H, 4.32; P, 19.69.

*p-Toluenephosphonic acid.* To a stirred and refluxing solution of 8.6 g. (0.05 mole) of diethyl chlorophosphate in 200 cc. of dry ether, there was added dropwise during 2.5 hours a filtered ethereal solution of *p*-tolyllithium prepared from 8.5 g. (0.05 mole) of *p*-bromotoluene and 0.80 g. (0.10 mole) of lithium in 200 cc. of dry ether. Soon after the addition of *p*-tolyllithium was started a white precipitate separated from the mixture and increased in quantity during the reaction period. The flask was cooled in an ice-bath and cold dilute hydrochloric acid was added dropwise with stirring. The organic layer was separated and the aqueous layer was extracted twice with ether, the ether extracts were combined, and worked up in the usual manner. Distillation of the residual oil gave 6.3 g. (55%) of diethyl *p*-toluenephosphonate, b.p. 122°/1 mm., which was hydrolyzed with concentrated hydrochloric acid overnight; 3.2 g. of fine white needles, m.p. 188.5–190°, were deposited from the cooled and concentrated hydrolysate [Literature, m.p. 187.5–189° (1)].

## SUMMARY

The addition of dialkyl chlorophosphates to *ortho*-substituted arylmagnesium halides yields esters of aromatic phosphonic acids, whereas sterically unhindered Grignard compounds are converted to triarylphosphine oxides. Reversed Grignard reactions with sterically unhindered arylmagnesium halides and dialkyl chlorophosphates produce aromatic phosphonic acids. Aryllithium derivatives behave like the corresponding Grignard reagents.

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## REFERENCES

(1) KOSOLAPOFF AND HUBER, *J. Am. Chem. Soc.*, **69**, 2020 (1947); see there for references of early work.

(2) ATHERTON AND TODD, *J. Chem. Soc.*, 674 (1947).
(3) KOSOLAPOFF, *J. Am. Chem. Soc.*, **72**, 5508 (1950).
(4) KOSOLAPOFF, *J. Am. Chem. Soc.*, **69**, 1002 (1947).
(5) KOSOLAPOFF, *Organophosphorus Compounds*, John Wiley and Sons, New York, 1950, pp. 121–179.
(6) KOSOLAPOFF, *J. Am. Chem. Soc.*, **64**, 2982 (1942).
(7) ROBINS AND CHRISTENSEN, *J. Org. Chem.*, **16**, 324 (1951).