[Contribution from the Cobb Chemical Laboratory, University of Virginia]

THE REACTION OF DIALKYL CHLOROPHOSPHATES WITH ARYLMAGNESIUM HALIDES. II

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In a study of the reaction of arylmagnesium halides and dialkyl chlorophosphates (1) we observed that dialkyl arylphosphonates were formed only when the reactivity of the Grignard reagent was curtailed by the presence of an adjacent group while sterically unhindered arylmagnesium halides reacted with the chlorophosphate esters to give triarylphosphine oxides in satisfactory yields when the dialkyl chlorophosphate was added to the Grignard reagent. The influence of the size of the hindering groups on this divergent course of the reaction had not been investigated. We have found that *o*-methoxyphenylmagnesium bromide, when treated with dibutyl chlorophosphate, gives over 65% of dibutyl *o*-methoxyphenylphosphonate from which the corresponding *o*-methoxyphenylphosphonic acid was obtained by acid hydrolysis. On the other hand, addition of diethyl chlorophosphate to *o*-fluorophenylmagnesium bromide gave a mixture of reaction products from which no more than 10% of alkali-soluble *o*-fluorophenylphosphonic acid could be elaborated. An alkali-insoluble fraction, presumably tri-(*o*-fluorophenyl)phosphine oxide could not be characterized.

The reaction of phenylmagnesium bromide with diethyl chlorophosphate, which yields triphenylphosphine oxide, could be pictured to proceed stagewise in analogy to the reaction of esters of carboxylic acids with Grignard reagents which furnishes tertiary alcohols. In this reaction some authors, notably Boyd and Hatt (2), prefer the formation of an intermediate ketone since they were successful in showing pinacol formation in Grignard reactions involving esters. Pinacols are known to form in ether solution by the interaction of a ketone and the binary system (MgX_2 + Mg). Conversely, Morton and Peakes (3) prefer the older interpretation of Grignard (4) because they were able to obtain better yields of tertiary carbinol from the action of a Grignard reagent on an ester rather than on a ketone.

The formation of diethyl phenylphosphonate as an intermediate in our reaction which would then react further with phenylmagnesium bromide to give triphenylphosphine oxide was ruled out because Kosolapoff (5) had shown that the reaction of this ester with phenylmagnesium bromide when forced in hot toluene for six hours gives a 33% yield of ethyl diphenylphosphinate only. By contrast we have obtained good yields of triphenylphosphine oxide from phenylmagnesium bromide and diethyl chlorophosphate even at 0° in a matter of minutes. A guide to the possible mechanism of the reaction was provided by the observation of Swain and Boyles (6) that the reduction of diisopropyl ketone by *n*-propylmagnesium bromide (7) could be greatly inhibited by complexing the

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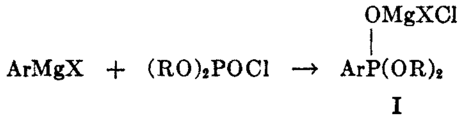
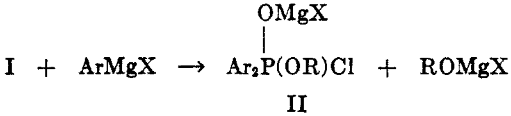
ketone with magnesium bromide and allowing the complex to react with the Grignard reagent. It appeared possible that a similar mechanism of complexing of diethyl phenylphosphonate could explain both the course of our reaction and that observed by Kosolapoff. Operating on the assumption that the complex (I) formed from the addition of diethyl chlorophosphate to phenylmagnesium bromide was equivalent to the complexed state of the ketone of Swain and Boyles, we added diethyl phenylphosphonate to an ethereal suspension of freshly prepared magnesium bromide. A white precipitate formed immediately but disappeared as it was swept into solution. No ethyl diphenylphosphinate was obtained from this reaction but triphenylphosphine oxide was isolated in a yield of 55.5%.

The mechanism of the interaction of arylmagnesium halides with dialkyl chlorophosphates may therefore be pictured by the following equations (*a–c*). The alternate formation of complex I by reaction of diethyl phenylphosphonate with magnesium bromide is shown in equation (*d*). The difference between the outcome of our reaction, and that of the interaction of diethyl phenylphosphonate with phenylmagnesium bromide (5) may lie in the difference between the composition of complex II, and of that probably present in the latter reaction (*e*). It is to be expected that II will be more reactive towards Grignard reagents (equation *c*) than complex III.

(*a*)


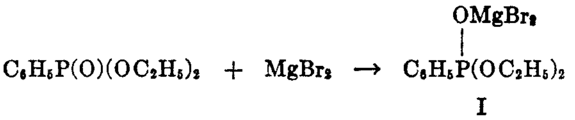
$$\mathrm{ArMgX} + (\mathrm{RO})_2\mathrm{POCl} \rightarrow \underset{\mathrm{I}}{\mathrm{Ar}\overset{\mathrm{OMgXCl}}{\overset{|}{\mathrm{P}}}(\mathrm{OR})_2}$$

(*b*)


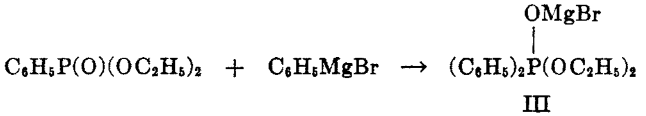
$$\mathrm{I} + \mathrm{ArMgX} \rightarrow \underset{\mathrm{II}}{\mathrm{Ar}_2\overset{\mathrm{OMgX}}{\overset{|}{\mathrm{P}}}(\mathrm{OR})\mathrm{Cl}} + \mathrm{ROMgX}$$

(*c*)

$$\mathrm{II} + \mathrm{ArMgX} \rightarrow \mathrm{Ar}_3\mathrm{P(Cl)(OMgX)} \xrightarrow{\mathrm{HOH}} \mathrm{Ar}_3\mathrm{PO} + \mathrm{MgXCl}$$

(*d*)


$$\mathrm{C_6H_5P(O)(OC_2H_5)_2} + \mathrm{MgBr_2} \rightarrow \underset{\mathrm{I}}{\mathrm{C_6H_5}\overset{\mathrm{OMgBr_2}}{\overset{|}{\mathrm{P}}}\mathrm{(OC_2H_5)_2}}$$

(*e*)


$$\mathrm{C_6H_5P(O)(OC_2H_5)_2} + \mathrm{C_6H_5MgBr} \rightarrow \underset{\mathrm{III}}{\mathrm{(C_6H_5)_2}\overset{\mathrm{OMgBr}}{\overset{|}{\mathrm{P}}}\mathrm{(OC_2H_5)_2}}$$

EXPERIMENTAL

o-Methoxyphenylphosphonic acid. A solution of *o*-anisylmagnesium bromide prepared from 3.0 g. (0.125 g.-atom) of magnesium and 23.4 g. (0.125 mole) of *o*-bromoanisole in 75 ml. of dry ether was treated dropwise with a solution of 28.6 g. (0.125 mole) of dibutyl chlorophosphate in 30 ml. of ether under an atmosphere of nitrogen. After stirring for 30 minutes at room temperature the mixture was poured onto acidified ice and worked up. A pale yellow oil (39.7 g.) was obtained from which 19.6 g. (65.4%) of colorless dibutyl *o*-methoxyphenylphosphonate was isolated by distillation, b.p. 176° (0.65 mm.). Hydrolysis of 12.0 g. of this ester with 150 ml. of concentrated hydrochloric acid for 17 hours and concentration of the hydrolysate under reduced pressure gave a viscous clear oil which deposited crystals on treatment with ethyl acetate. After several recrystallizations from methanol-ethyl acetate the acid melted at 201–202°.

Anal. Calc'd for $C_7H_9O_4P$: C, 44.69; H, 4.82.

Found: C, 44.76; H, 4.71.

o-Fluorophenylphosphonic acid. A solution of 0.1 mole of *o*-fluorophenylmagnesium bromide was prepared from 4.1 g. (0.171 mole) of magnesium and 18.9 g. (0.108 mole) of *o*-fluorobromobenzene by the entrainment method using a total of 7.0 g. (0.065 mole) of ethyl bromide and 90 ml. of ether. To this solution was added 21.9 g. (0.127 mole) of diethyl chlorophosphate in 15 ml. of ether, and after stirring and refluxing for 1.5 hours, the cooled mixture was decomposed with 5% hydrochloric acid and worked up. The resulting 25.8 g. of orange-colored oil was fractionated, the major portion (95%) boiling at 135° (0.55 mm.). The distillate was refluxed with 150 ml. of concentrated hydrochloric acid for 12 hours and the water-soluble, oily reaction product was extracted with sodium carbonate solution. The cleared alkaline solution was acidified, evaporated to dryness under reduced pressure, and the solid residue was extracted exhaustively with benzene. Concentration of the benzene extract gave 1.0 g. (5.7%) of colorless crystals, m.p. 135–137.5°. An analytical sample was prepared by recrystallization from ethyl acetate-petroleum ether.

Anal. Calc'd for $C_6H_6FO_3P$: C, 40.92; H, 3.43.

Found: C, 40.74; H, 3.70.

Reaction of complexed diethyl phenylphosphonate with phenylmagnesium bromide. To a suspension of 5.1 g. (0.2105 g.-atom) of magnesium in 70 ml. of dry ether was added, under an atmosphere of nitrogen with stirring and cooling, 33.6 g. (0.2105 mole) of bromine. After the addition of the bromine was completed the mixture was stirred for 2.5 hours when a test sample gave no more change in color on treatment with solid sodium bisulfite. Diethyl phenylphosphonate (20.0 g., 0.0935 mole) was added over a period of 45 minutes and the solution was stirred for another hour. The clear dark solution was added slowly to a stirred solution of phenylmagnesium bromide prepared from 4.5 g. (0.185 g.-atom) of magnesium and 29.3 g. (0.1851 mole) of bromobenzene in 70 ml. of ether. Since no visible reaction occurred at this point, 30 ml. of ether was distilled off until a solid precipitate appeared. Dry benzene (160 ml.) was added and distillation was continued until the ether was removed. After refluxing for six hours the mixture was decomposed with acidified ice and worked up as usual. Triphenylphosphine oxide (14.3 g., 55.5%) was collected by crystallization from ethyl acetate. It sintered at 152°, m.p. 154–156°. A mixture melting point with an authentic sample showed no depression.

Tri-o-anisylphosphine oxide. A solution of 3.0 g. (0.02 mole) of phosphorus oxychloride in 30 ml. of ether was added dropwise at 0° to a solution of *o*-anisylmagnesium bromide prepared from 1.2 g. (0.05 g.-atom) of iodine-activated magnesium and 9.4 g. (0.105 mole) of *o*-bromoanisole in 80 ml. of ether. The ether began to reflux and a brown layer separated. After stirring for a few minutes the mixture was decomposed with acidified ice and worked up. The reaction product was recrystallized from dilute ethanol. Colorless crystals, m.p. 216–217°.

Anal. Calc'd for $C_{21}H_{21}O_4P$: C, 68.47; H, 5.74.

Found: C, 68.44; H, 5.76.

SUMMARY

o-Anisylmagnesium bromide reacts with dibutyl chlorophosphate to give a 65.4% yield of dibutyl *o*-methoxyphenylphosphonate. From the corresponding reaction of *o*-fluorophenylmagnesium bromide and diethyl chlorophosphate less than 10% of diethyl *o*-fluorophenylphosphonate and a considerable amount of

an alkali-insoluble oil, presumably tri-(*o*-fluorophenylphosphine) oxide is obtained.

Reaction of diethyl phenylphosphonate with magnesium bromide gives a reactive complex which furnishes with phenylmagnesium bromide, triphenylphosphine oxide. A mechanism for the reaction of dialkyl chlorophosphates with arylmagnesium halides is proposed.

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