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Publication Date

1950-02-06

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Contract No. W-7405-eng-48A-I

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D. C. Morrison

February 6, 1950

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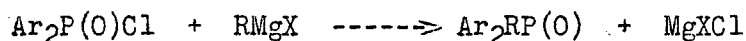
The Action of Grignard Reagents on Diaryl Phosphinyl Chlorides. (1)

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February 6, 1950

In connection with work on incorporation of radioactive phosphorus into organic molecules, it was found necessary to study the action of Grignard reagents on the chlorides of aromatic phosphinic acids. This reaction has not previously been examined. The product of this reaction is an unsymmetrical alkyl diaryl phosphine oxide of the type RAr_2Po , and is apparently formed by simple replacement of the halogen atom by an alkyl group according to the equation:



This class of compounds has usually been prepared by four types of reactions:

1. Pyrolysis of triaryl alkyl phosphonium hydroxides when Ar_3RPOH forms ArH and Ar_2RPO (2).

2. Arbusov rearrangement of $Ar_2P.OR$ with RI (3).

3. Reaction (with rearrangement) of Ar_2PCl with $NaOR$ (3). This reaction works directly only for the methyl and benzyl derivatives and for all others apparently the intermediate alkoxy diaryl phosphines must be isolated. This is then isomerized by heating (higher alkyl) or standing (lower alkyl) with the corresponding alkyl iodide. The latter step is the modification of the Arbusov rearrangement which leads to these oxides.

(1) The work described in this paper was sponsored by the Atomic Energy Commission. It was supported in part by a grant from the Henry, Laura and Irene B. Dernham Fund of the American Cancer Society and the Christine Breon Fund.

(2) Michaelis and Soden, Ann. 229 295 (1885)

(3) Arbusov, J. Russ. Phys. Chem. Soc. 42 395 (1910). Chem. abs. 5 1397.

4. Oxidation of the corresponding unsym. phosphines (4).

The reaction of the aromatic phosphinyl chlorides with the alkyl Grignard reagent proceeds smoothly to give fair to good yields of the phosphine oxides. The melting points of the oxides which were prepared in this way checked reasonably well with literature values given previously. These and the analytical results are given in the table. The phosphinyl chlorides were not isolated as such, but were used as obtained in toluene solution by the action of thionyl chloride on the free acid in this solvent. One of the phosphine oxides which was prepared was not previously described in the literature. This is diphenyl butyl phosphine oxide, and for characterization it was converted into the dinitro derivative and analyzed. The yield of isopropyl derivative was somewhat lower than the others, which may be explained by the fact that the halide is secondary.

The possibility of forming a similar class of phosphine oxides by the reaction of Grignard reagents with aromatic phosphonyl chlorides ($\text{ArP}(\text{O})\text{Cl}_2$) has not been examined. This reaction may produce the other class of mixed alkyl aryl oxides of the type R_2ArPO .

As a control experiment the action of ethyl magnesium bromide on diphenyl phosphinic acid was tried to see if the acid chloride is actually a necessary intermediate. No phosphine oxide was obtained in this experiment, and therefore, the direct replacement of the hydroxyl of the acid by the Grignard alkyl radical does not seem to be possible under the conditions used. The acid was recovered unchanged.

This reaction of the diaryl phosphinyl chlorides can be compared to the reaction of Grignard reagents with sulfonyl chlorides which furnishes sulfones (5). Unlike the latter, however, no halogenation, nor reduction of the phosphorus was observed in the reaction with phosphinyl chlorides. This may be due to the fact that both

(4) Michaelis and Link, Ann. 207 193 (1881)

(5) Gilman and Fothergill, This Journal, 51 3501 (1929). Earlier work is referred to here and the mechanism of the reaction is discussed.

the phosphine oxides and the phosphinic acids are very difficult to reduce and are unusually stable compounds.

EXPERIMENTAL

Preparation of Diaryl Phosphinic Acids.- The acids used as starting materials were obtained by either of the methods of Kosolapov (6,7). Generally, the method involving the use of diethylamino phosphoryl chloride gave better yields (7). The acids, for purification, were recrystallized from water and air-dried. The diphenyl acid had M.P. 192-193 while the di-p tolyl acid melted at 135.5-136.5.

Preparation of the Phosphine Oxides.- Since the experimental conditions for these preparations are all very similar, only a description of the method used for obtaining ethyl diphenyl phosphine oxide is given. Runs were usually carried out in 0.001-0.01 mol amounts.

0.22 gms (0.001 mols) of the diphenyl acid was dissolved in toluene and 0.5 ml of thionyl chloride (0.007 mol) was added. This amount of thionyl chloride is a large excess over the theoretical amount but ensures utilization of all the acid in forming the phosphinyl chloride. For larger runs a smaller excess was employed. The solution in toluene was heated under reflux for one to two hours and the excess thionyl chloride then removed by distilling away about half the toluene. The cooled solution of diaryl phosphinyl chloride was then diluted with benzene. It was transferred to a separatory funnel and added dropwise to a large excess of Grignard reagent at room temperature. The Grignard reagent was made from 0.25 gms (0.011 mols) of magnesium and 2.5 ml (0.032 mols) of ethyl bromide. This large excess of Grignard was more convenient to prepare and handle on the small scale used here. The time of addition of the phosphinyl chloride solution was one-half hour. The resulting solution was then heated to reflux for one to two hours.

(6) G. M. Kosolapov, This Journal, 64 2982 (1942).

(7) G. M. Kosolapov, This Journal, 71 369 (1949).

After cooling it was hydrolyzed by a mixture of ice and hydrochloric acid.

The organic layer was separated and the aqueous layer extracted with ether. This extract was combined with the organic layer and the ether removed by distillation. The remaining benzene and toluene were removed by steam distillation and this operation was continued for several hours in order to remove also small amounts of any other volatile material. The cooled residue was extracted with ether several times and these extracts combined. The ethereal solution was extracted with cold aqueous sodium carbonate solution to extract any acidic material. It was then dried and evaporated. The residue was either crystalline or became so on standing. For decolorization it was heated in acetone solution with decolorizing charcoal for about one-half hour. The cooled solution was filtered to remove charcoal and the acetone boiled off of the filtrate on a steam bath. The product was then recrystallized affording fair to good yields of the phosphine oxide. Recrystallization can be done, in the case of the ethyl derivative, from ether.

With the other phosphine oxides recrystallization was effected from ether-petroleum ether (B.P. 30°-60°) or from acetone-water. The more soluble fractions obtained in this manner contained small amounts of oily impurities together with a little of the oxide. In some cases (benzyl, isobutyl diphenyl phosphine oxides) repeated recrystallizations were necessary in order to obtain a specimen of satisfactory melting point or analysis.

The butyl diphenyl phosphine oxide showed no unusual properties when compared to other members of the series, except perhaps in melting point. The M.P. of 89.5° is the lowest of the group.

Nitration of Butyl Diphenyl Phosphine Oxide.- For characterization this compound was converted into its di-nitro derivative, purified and analyzed. The nitrating mixture used was a mixture of two to two and one-half volumes of concentrated sulfuric acid with one volume of fuming nitric acid. A large excess of this acid was cooled to 0° and to it was added the oxide in small portions at a

time. The solution thus formed was left in an ice bath for one to two hours and then poured slowly into ice water. This resulted in precipitation of a light-colored product. The liquid was extracted with ether and the ether solution of nitro oxide was extracted repeatedly with water to remove acids. Evaporation of the ether solution left a residue which was recrystallized from ether and from ether-petroleum ether. The crystals first obtained are usually yellow but after a number of recrystallizations the product is nearly white. By analogy with previous work, it was thought that this substance is probably a meta-dinitro compound. This was shown to be the case in the nitration of triphenyl phosphine oxide by Challenger and Wilkinson (8).

Reaction of Diphenyl Phosphinic Acid and Ethyl Magnesium Bromide.- This reaction was carried out in order to determine whether or not the acid chloride is an essential intermediate or if the hydroxyl group of the acid can be directly replaced by the alkyl group by heating with excess Grignard reagent. The former was found to be the case. Ethyl magnesium bromide in ether solution and in five-fold molar excess was treated slowly with the solid acid. This caused effervescence, doubtless due to evolution of ethane, and the acid dissolved immediately. No precipitate formed. This mixture was then heated to reflux for three and one-half hours. After one and three-quarters hours of heating, a crystalline precipitate began to form and increased in amount on further heating. Finally a thick sludge of this material was produced. The slurry was cooled and hydrolyzed by ice-hydrochloric acid. The ether layer was separated and the aqueous layer extracted with ether. The two ether layers were combined and most of the solvent removed by distillation. Sodium carbonate was then added together with water and the mixture steam distilled until nothing further passed over. The carbonate solution was cooled and extracted with ether. This extract upon evaporation left

(8) Challenger and Wilkinson, J. C. S. 125 2675 (1924).

virtually no residue, thus showing that no diphenyl ethyl phosphine oxide had been formed. The carbonate solutions was acidified with hydrochloric acid and then either cooled in ice or saturated with sodium chloride (It was previously found that an aqueous solution of the sparingly soluble diphenyl phosphinic acid yields a nearly complete recovery of the acid as a crystalline precipitate when saturated with salt) when a crystalline deposit of the acid was obtained. This had M.P. 192° - 193° .

Summary.- The reaction of Grignard reagents with diaryl phosphinyl chlorides was studied. This reaction was shown to lead to alkyl diaryl phosphine oxides. The direct replacement of hydroxyl group in a free diaryl phosphinic acid by the Grignard reagent is not feasible. The dinitro derivative of one of these phosphine oxides, not previously reported, was prepared for characterization.

Acknowledgement.- The author is indebted to Professor Melvin Calvin and to Drs. K. G. Scott, R. M. Lemmon and W. M. Garrison for advice during the course of this work and to Dr. J. G. Hamilton for making available the use of his laboratory.

TABLE

Compound	M.P. <u>Lit.</u>	M.P. Uncor <u>Found</u>	C <u>Calc</u>	C <u>Found</u>	H <u>Calc</u>	H <u>Found</u>	Yield <u>%</u>
Ph ₂ EtPO	121	123 - 124	73.04	72.68	6.52	6.56	67.2
Ph ₂ (isoPr)PO	145 - 146	144 - 146	73.77	73.91	6.97	6.81	44.6
Ph ₂ (isoBu)PO	137.5-138	132.5-134	74.42	74.12	7.37	7.29	75.2
Ph ₂ (PhCH ₂)PO	192 - 193	189 - 190	78.08	77.72	5.82	5.82	69.0
Me(p-Tolyl) ₂ PO	143	145.5-146.5	73.77	73.93	6.97	7.12	63.8
Ph ₂ BuPO		89.5	74.42	74.28	7.37	7.33	68.0
Bu(NO ₂ .Ph) ₂ PO	-	124 - 125.5	55.17	55.50	5.46	5.04	74.1

Microanalyses by C. W. Koch and V. H. Tashinian.