pode predominating, and that the synthetic acid is the racemic form of the same acid.

WASHINGTON, D. C.

[CONTRIBUTION FROM THE PEARSON MEMORIAL LABORATORY OF TUFTS COLLEGE]

STUDIES IN THE DIPHENYL SERIES. III. SOME PHOSPHORUS DERIVATIVES OF DIPHENYL

BY DAVID E. WORRALL

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It has been shown in previous communications[1] that 4-chlorodiphenyl condenses smoothly with arsenic and antimony chlorides in the presence of sodium. The resulting tri-arylated metalloids in general have properties similar to the corresponding phenyl compounds and are useful for the preparation of derivatives containing one, two or three diphenyl groups. The study of biphenylated substances has been extended to phosphorus, the results of which are presented in the present communication.

Tri-biphenylphosphine was obtained by the action of sodium on 4-chlorodiphenyl and phosphorus trichloride dissolved in benzene.

$$3C_6H_5C_6H_4Cl + PCl_3 + 6Na = (C_6H_5C_6H_4)_3P + 6NaCl$$

The procedure followed gave directly a yield of approximately 55% of fairly pure material. The total amount of product formed was about 75% of the theoretical. Ether[2] has been used previously in similar condensations, but the results obtained in this Laboratory indicate the superiority of benzene.

Certain differences in behavior become apparent on comparing the chemical properties of tri-biphenylphosphine with the corresponding arsenic and antimony derivatives. The heats of formation of the halides of these elements increase with rising atomic weight. Therefore it was not surprising that the halogen addition products of tri-biphenylstibine were easily formed. Tri-biphenylarsine gave more trouble and the di-iodide was not isolated. Chlorine and bromine formed addition products that separated from solution with chloroform of crystallization, as was true in the stibine series. These substances, possibly because of the presence of chloroform and insolubility in water, are much less sensitive toward moisture than the corresponding phenyl derivatives. There was every indication, using tri-biphenylphosphine, that a reaction took place with chlorine and bromine, although no apparent change was observed with iodine. Yet only oils were obtained. This failure to obtain crystalline products presumably was due to the extreme hygroscopicity of the phosphorus derivatives, followed by partial hydrolysis.

$$(C_6H_5C_6H_4)_3PBr_2 + H_2O = (C_6H_5C_6H_4)_3PO + 2HBr$$

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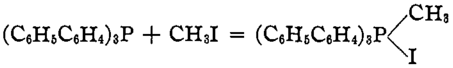
[1] Worrall, THIS JOURNAL, **52**, 664 (1930).

[2] Michaelis and Reese, *Ber.*, **15**, 1610 (1882).

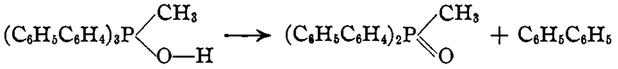
Tri-biphenylphosphine exhibits a much stronger tendency to form salts of the ammonium type than either of the corresponding arsenic and antimony compounds. Thus methyl iodide acts not at all with tri-biphenylstibine and only slowly at elevated temperatures with tri-biphenylarsine. The reaction with tri-biphenylphosphine takes place almost instantly at room temperature.



$$(C_6H_5C_6H_4)_3P + CH_3I = (C_6H_5C_6H_4)_3P\begin{array}{l}\diagup CH_3\\ \diagdown I\end{array}$$

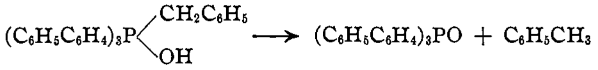
Similar reactions take place with allyl bromide and benzyl bromide, as well as ethyl chloro-acetate.

The resulting products, after treatment with silver oxide or alkali, form bases that undergo further change.[3] Thus methyl tri-biphenylphosphonium hydroxide decomposes into diphenyl and methyl di-biphenylphosphine oxide.



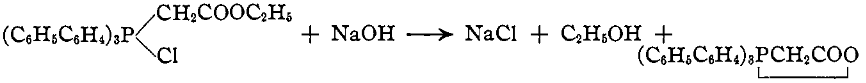
$$(C_6H_5C_6H_4)_3P\begin{array}{l}\diagup CH_3\\ \diagdown O{-}H\end{array} \longrightarrow (C_6H_5C_6H_4)_2P\begin{array}{l}\diagup CH_3\\ \diagdown\!\!\diagdown O\end{array} + C_6H_5C_6H_5$$

A similar change takes place with allyl tri-biphenylphosphonium hydroxide. On the contrary, the benzyl bromide addition product changes on warming with alkali into toluene and a tri-arylated phosphine oxide.



$$(C_6H_5C_6H_4)_3P\begin{array}{l}\diagup CH_2C_6H_5\\ \diagdown OH\end{array} \longrightarrow (C_6H_5C_6H_4)_3PO + C_6H_5CH_3$$

This same phosphine oxide is obtained from the ethyl chloro-acetate derivative under the same conditions. Tri-biphenylphosphobetaine may be isolated by working at low temperatures.



$$(C_6H_5C_6H_4)_3P\begin{array}{l}\diagup CH_2COOC_2H_5\\ \diagdown Cl\end{array} + NaOH \longrightarrow NaCl + C_2H_5OH + (C_6H_5C_6H_4)_3\underline{PCH_2COO}$$

A striking difference in the properties of tri-arylated phosphines is the non-reactivity with phosphorus trichloride, a reaction so useful in the arsenic and antimony series (using the corresponding halide) for obtaining mono- and di-arylated derivatives.

Experimental

Tri-biphenylphosphine.—To 9 g. of granulated sodium suspended in 200 cc. of dry benzene were added 25 g. of 4-chloro-diphenyl and 6.1 g. of recently distilled phosphorus trichloride. A crystal of antimony was added and the mixture was heated to boiling under a reflux condenser. A lively reaction resulted that continued for perhaps half an hour after removal of the flame. Following this, heat was again applied for an hour and the hot mixture filtered by suction. The residue was thoroughly washed with warm benzene, the mixed filtrates concentrated to approximately 75 cc. and alcohol added to faint turbidity. A thick paste formed on stirring. It was filtered and washed thoroughly with cold alcohol; yield, 12 g. of cream-colored material pure enough for most purposes.

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[3] See Michaelis and Soden, *Ann.*, **229**, 310 (1884).

Anal. Calcd. for $C_{36}H_{27}P$: P, 6.3. Found: P, 6.3.

The orange-colored filtrate from the last operation deposited a tar on further concentration containing an appreciable amount of unchanged chlorodiphenyl as well as tri-biphenylphosphine. No traces were found of diphenyl. By working up the residues, several grams of the desired product was obtained, but it was of an inferior quality difficult to purify and scarcely worth the time necessary to isolate it. The yield of tri-biphenylphosphine was not improved by longer heating during the preparation; neither was it increased by using an excess of phosphorus trichloride. Unchanged chlorodiphenyl always appeared just as in the original preparation containing an excess of sodium.

Ether was found unsuitable as a solvent in the preparation of tri-biphenylphosphine. For example, 25 g. of chlorodiphenyl with appropriate amounts of sodium and phosphorus trichloride was mixed with 200 cc. of dry ether. The ether apparently was attacked by phosphorus trichloride, for while the reaction was much more vigorous than with benzene and started without preliminary heating, the black tarry mass after evaporation of the ether contained somewhat less than three grams of tri-biphenylphosphine. Over 10 g. of chlorodiphenyl was recovered by steam distillation, while the amount of unchanged sodium present in the residues was much greater than in the preparation involving the use of benzene.

The interaction of phosphorus trichloride and chlorodiphenyl in benzene solution with sodium was decidedly sluggish, provided carefully purified and dried material was used. Several hours of heating to boiling under a reflux condenser failed to cause any tarnishing of sodium or color changes in the benzene layer, but the addition of a crystal of antimony trichloride to the hot mixture immediately caused blackening of sodium around the added crystal. Heat was also evolved as a circle of black slowly spread over the sodium and eventually the reaction was vigorous enough to cause the mixture to boil. No such effect was observed on adding a drop of arsenic trichloride. Occasionally the desired reaction did take place after the preliminary heating without the addition of antimony chloride. That the catalytic effect was not due to moisture or the mere presence of a solid was indicated by the absence of the reaction on adding pieces of porous tile moistened with water. Hydrogen, of course, was evolved and flakes of solid sodium hydroxide formed in the ether until the water was destroyed, but the sodium did not become black.

Tri-biphenylphosphine is easily soluble in hot glacial acetic acid, chloroform or benzene, separating from the latter in snow-white aggregates of tiny slender needles. It melts sharply at 172°.

Tri-biphenylphosphine Oxide.—To 5 g. of tri-biphenylphosphine dissolved in 40 cc. of dry chloroform was added 0.5 g. of redistilled bromine, slightly less than the chemical equivalent. Bromine was instantly absorbed while heat sufficient to cause boiling of the solvent was liberated. Crystal formation did not take place on standing and evaporation of the solvent left a yellow sirup. Undoubtedly the bromine addition product was formed, but perhaps due to partial hydrolysis from incomplete drying of the components, it was not obtained in a form suitable for analysis. The dibromide must be extremely hygroscopic as the oil puffed up like a balloon, due to the escape of hydrogen bromide, when placed in a vacuum desiccator over sulfuric acid and the air exhausted by means of a water pump. If the oil was heated in air over a flame, a crystalline residue of the oxygen compound quickly appeared as hydrogen bromide was evolved. In either case the residue was crystallized from alcohol containing a little ammonia and dried *in vacuo*. Flat needle-like crystals melting at 233–234° were obtained.

Anal. Calcd. for $C_{36}H_{27}PO$: P, 6.1. Found: P, 6.1.

While it may be unsafe to infer from the analytical data above that the substance was not tri-biphenylphosphonium hydroxide (P, 5.9), the behavior on heating, in which no change indicating loss of water was observed, substantiated the belief that it was an oxide. The oxide is much less soluble in benzene and more soluble in alcohol than tri-biphenylphosphine. Iodine did not react with tri-biphenylphosphine.

Tri-biphenylphosphine Sulfide.—Obtained by the action of carbon disulfide saturated with sulfur on tri-biphenylphosphine, as hydrogen sulfide is without action; microscopic plates melting at 241–242° with preliminary softening.

Anal. Calcd. for $C_{36}H_{27}PS$: S, 6.1. Found: S, 5.9.

Action of Phosphorus Trichloride.[4]—Three grams of tri-biphenylphosphine and 30 cc. of phosphorus trichloride were heated in a sealed tube to 225–250° for one hundred hours. A crystalline product melting at 228–230° was extracted by alcohol from the resulting black tar, apparently impure tri-biphenylphosphine oxide. The melting point was not lowered by mixing with a known sample of the oxide. No indications were obtained of the presence of monobiphenyl or di-biphenylchlorophosphines.

Tri-biphenylphosphonium Salts.—On mixing 5 g. of tri-biphenylphosphine with 25 cc. of methyl iodide, the substance promptly dissolved with considerable heat evolution. A quantitative yield of tri-biphenylphosphonium methyl iodide separated in a few minutes. Similar products were obtained by heating the phosphine for a few hours under a reflux condenser with equal amounts of the halogen derivatives listed below. Approximately 5 volumes of benzene were added in all cases to control the temperature and to facilitate the separation of the products, which are relatively insoluble in it. The phosphonium salts were recrystallized from alcohol.

Table I

Data on the Salts

	Cryst. form	M. p., °C.	Analyses			Remarks
			Calcd.		Found	
Methyl iodide	Sparkling plates	135–136 with foaming	20.1	I	20.0	Colors on standing
Allyl bromide	Narrow plates	195–196	13.1	Br	13.2	Forms in few minutes
Benzyl bromide	Plates	Softens above 269. Melts at 277	12.1	Br	12.2	Cryst. from alcohol and water
Ethyl chloroacetate	Square plates	164–165	5.8	Cl	5.7	Reaction slow

These salts are easily converted into the corresponding bases by moist silver oxide or sodium hydroxide; these however, undergo further change into phosphine oxides.

Di-phenyl Methylphosphine Oxide.—Obtained by heating an alcohol solution of tri-biphenylphosphonium methyl iodide with moist silver oxide. The odor of diphenyl quickly became apparent. The mixture was then filtered and the residue extracted with a fairly large volume of hot alcohol. Lustrous slender needle-like crystals melting at 223–224° with preliminary softening separated on cooling.

Anal. Calcd. for $C_{25}H_{21}PO$: P, 8.4. Found: P, 8.5.

Di-biphenyl Allylphosphine Oxide.—Obtained from the corresponding phosphonium salt by the action of hot alcoholic potash. The product after the removal of diphenyl by steam distillation was crystallized from alcohol diluted with water. It showed a

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[4] Challenger and Pritchard observed the formation of triphenylphosphine oxide in the action of triphenylphosphine on phosphorus trichloride, *J. Chem. Soc.*, **125**, 870 (1924). According to Stilp ("Dissertation," Rostock, **1910**), this same oxide may form the principal product when sodium and bromobenzene react with phosphorus trichloride.

strong tendency to separate out from solution as an oil, but on standing in a cool place microscopic crystals were obtained softening above 160° and melting to a cloudy liquid at 192–193°. The analysis indicated the presence of alcohol of crystallization. This assumption is substantiated by the fact that on heating the substance in a test-tube, it melts with foaming and a combustible gas is evolved.

Anal. Calcd. for $C_{27}H_{23}PO \cdot C_2H_5OH$: P, 7.0. Found: P, 7.0.

The phosphine oxide may be obtained free from alcohol by drying the crystals in vacuo over sulfuric acid.

Tri-biphenyl benzylphosphonium bromide reacted differently with alcoholic potash. Toluene was set free, recognizable by its odor, while tri-biphenylphosphine oxide melting at 233–234° crystallized out in a few minutes.

Tri-biphenyl Phosphobetaine.—Tri-biphenylphosphine oxide also formed when the phosphonium salt obtained by the action of ethyl chloro-acetate was warmed with alcoholic potash. If, however, the solutions were mixed at the temperature of melting ice and subsequently poured into ice water, the betaine formed. It was washed free from alkali before recrystallization from alcohol. A pale yellow precipitate of brilliant diamond-shaped plates was obtained, melting at 109–110° with preliminary softening.

Anal. Calcd. for $C_{38}H_{29}PO_2$: P, 5.9. Found: P, 5.9.

It changes into tri-biphenylphosphine oxide on standing at room temperature.

Summary

Tri-biphenylphosphine has been obtained by the action of sodium in benzene on chlorodiphenyl and phosphorus trichloride and its chemical properties were investigated. Phosphonium salts were formed with methyl iodide, allyl bromide, benzyl bromide and ethyl chloro-acetate, which on warming in alkaline solution decomposed into phosphine oxides and hydrocarbons.

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[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

DIARSYLS. III. DIARYLDI-IODODIARSYLS[1]

BY F. F. BLICKE AND F. D. SMITH

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Arsenobenzenes, in the form of salvarsan and its analogs, have been made the subject of intensive investigations. Especially important from a chemotherapeutic standpoint are the oxidation products of these compounds.

It has been shown by experiments in vitro that, in general, the parasiticidal action of arseno compounds is relatively low compared with that of compounds of the arsine oxide type. Furthermore, when an arseno compound is introduced into an infected animal, there is a fairly long latent period during which there is no evidence of any parasiticidal action.

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[1] This investigation was made possible by the generous financial assistance of Parke, Davis and Company and we wish to express our sincere appreciation for the aid which has been given us.