

THE SYNTHESIS OF CERTAIN ORGANOPHOSPHORUS COMPOUNDS
CONTAINING THE TRICHLOROMETHYL GROUP

by

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TITLE

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PREVIEW

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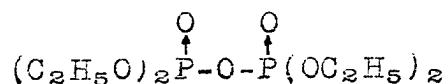
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INTRODUCTION

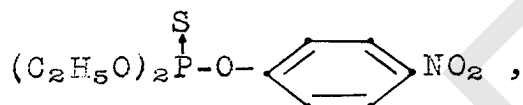
The work of Professor Carl Michaelis and his students in Germany from 1860 to the early 1900's provides the foundation for the chemistry of organophosphorus compounds. In the period that overlaps the latter part of Michaelis's work and extends to the present day, the work of Professor Aleksandr Arbusov and his students in Russia furnishes the background for many of the presently used synthetic methods. The contributions of many other workers appear in the literature since the first work was reported by Lassaigne in 1820. The upturn of interest in organophosphorus compounds in recent times and the great impetus given to industrial research in this field may be traced to the work of Gerhard Schrader.

During the 1930's, the Germans, led by Schrader¹, were investigating the use of phosphorus compounds as insecticides. The toxicity of these compounds was developed to such an extent that by the close of World War II certain of them were produced on a large scale in Germany for possible use as war gases. At the end of the war the organophosphorus technical knowledge of Germany was acquired by the Allied Governments as spoils of war. This technical knowledge, together with the obvious potentialities of the phosphorus insecticides, motivated American industry to investigate further the chemistry of these compounds. Nearly all of the major chemical companies now have organophosphorus research programs.

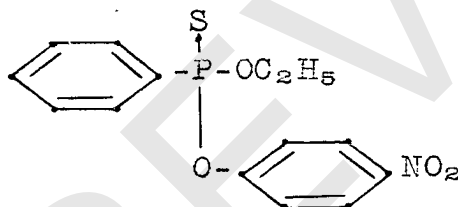
These compounds are used extensively in American agriculture and are also finding more and more use as plasticizers, oil additives, flotation agents and surface coating stabilizers.⁴ Among the several important phosphorus insecticides manufactured at present are tetraethyl pyrophosphate (TEPP),



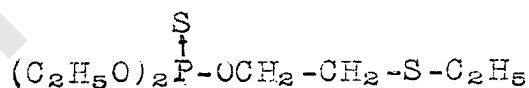
O, O-diethyl O-p-nitrophenyl thiophosphate (Parathion),



and O-ethyl O-p-nitrophenyl phenylthiophosphonate (EPN),



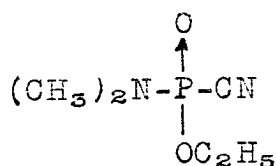
The first systemic insecticide to obtain the approval of the U. S. Department of Agriculture is a phosphorus containing compound O, O-Diethyl O-2-(ethylmercaptoethyl) thiophosphate (Systox).



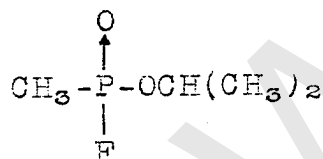
Tricresyl phosphate is used as a gasoline additive and is also a good plasticizer because it imparts fire retarding properties to the plastic. Triphenyl phosphate and tri(2-ethylhexyl) phosphate are also employed as plasticizers. Triphenyl phosphite is useful as an antioxidant and other phosphites

find uses as oil stabilizers, surface coatings, and finishes.

The governments of the major world powers are interested in organophosphorus compounds as potential war gases.^{3,10} Among the first compounds produced as war gases are N,N-dimethyl O-ethyl phosphorocyanidic amide (Tabun) and isopropyl methylphosphonic fluoride (Sarin).²



Tabun

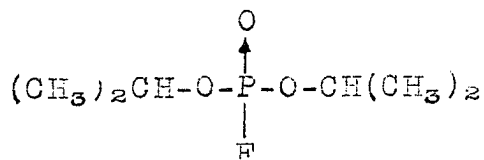


Sarin

In general the fluoroesters of phosphonic acids (such as Sarin), show the higher toxicity necessary for use as lethal agents. These substances act upon the body enzyme cholinesterase and render it incapable of its normal function of hydrolyzing the acetylcholine formed at the nerve endings. A minute quantity of the more toxic compounds, if inhaled or otherwise absorbed, kills within minutes. Typical symptoms are watering of the eyes and mouth, cramps, muscular twitching, miosis and dizziness. This property of mammalian toxicity is exhibited in varying degrees by most of the insecticides and other commercially important organophosphorus compounds, and is the major deterrent to their more extensive use. Estimates of the number of deaths which have resulted from careless handling of these insecticides run into the hundreds.

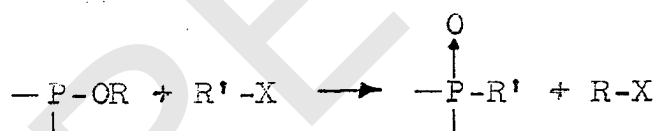
The toxicity of these compounds would seem to preclude

their use in medicine. However, reports have appeared concerning the use of diisopropyl phosphorfluoridate (DFP),

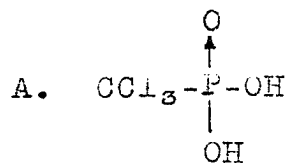


in surgical medicine. There is evidence also that phosphanilic acid (p-aminophenylphosphonic acid) possesses chemotherapeutic properties similar to the sulfa drugs.⁵

Since the trichloromethyl group was present in several important compounds (DDT, chloral, chloreton) it seemed of interest to investigate the synthesis and reactions of some phosphorus compounds containing this group. Until recent years the Michaelis-Arbusov reaction was the only known reliable method of obtaining a trichloromethyl phosphorus compound. The overall reaction has been represented thus:⁶



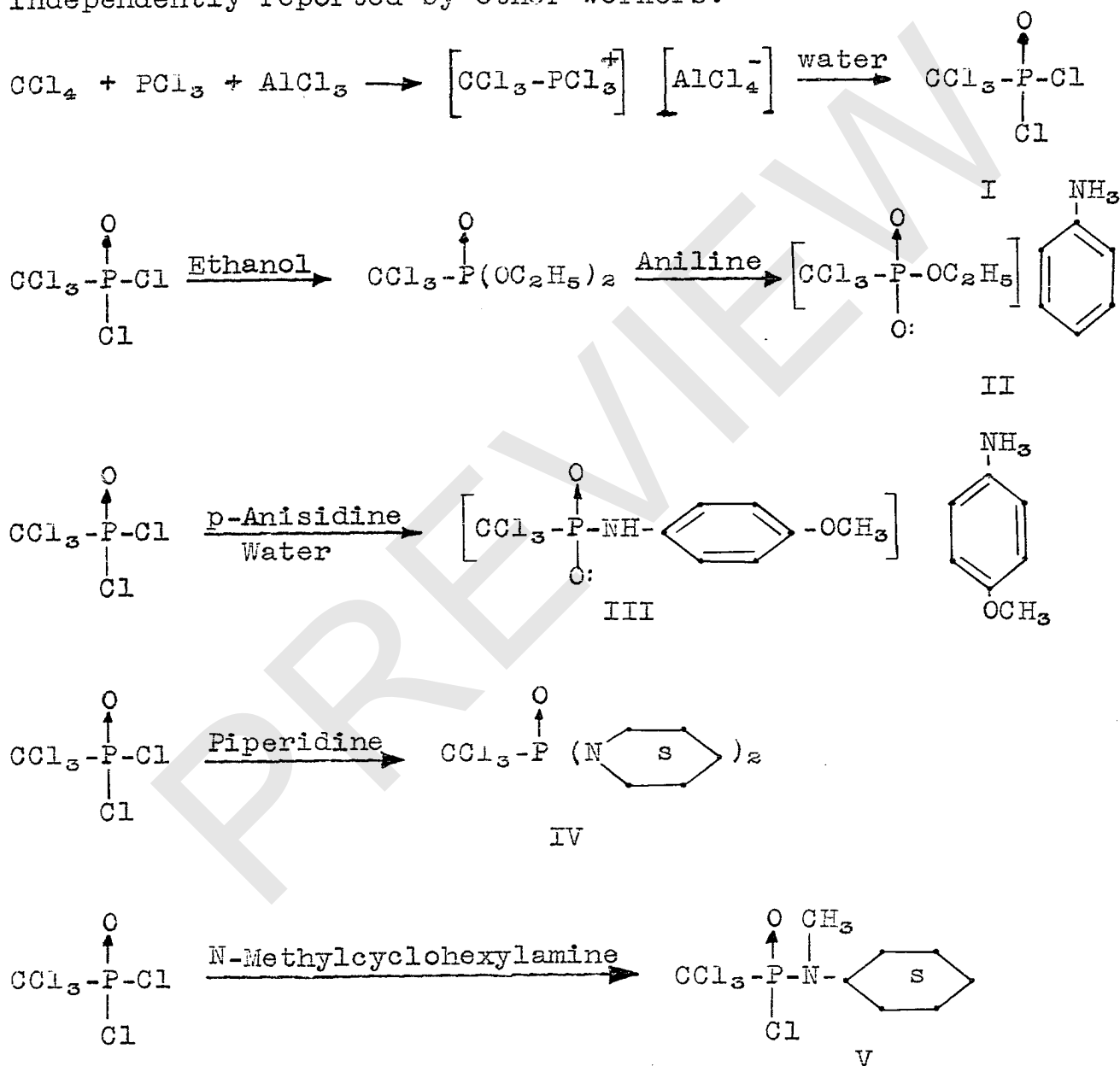
Many trivalent phosphorus esters have been used, although tertiary phosphites were most commonly employed. The organic halide used was any alkyl halide or aryl-alkyl halide, provided the halogen was not directly attached to the ring. The reaction did not require a solvent, was mildly exothermic, gave a clean product and was nearly quantitative in many cases. When the starting ester was a trialkylphosphite and the organic halide was carbon tetrachloride, the product was an ester of trichloromethylphosphonic acid (A).⁷

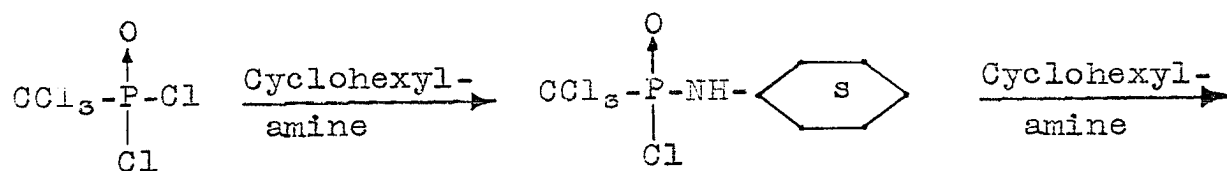


These esters are not too useful for further reactions because the conditions necessary for the hydrolysis of the ester frequently result in cleavage of the trichloromethyl group also. With regard to the scope of reactions, the acid chloride is undoubtedly the most versatile of the trichloromethyl phosphorus compounds. This compound, trichloromethylphosphonic dichloride, is the subject of the following investigation.

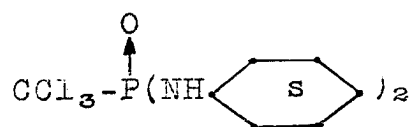
GRAPHICAL SUMMARY

Roman numerals accompanying the compounds correspond to those used in the discussion and experimental sections. All numbered compounds are new. Compounds I, II and VIII are independently reported by other workers.^{18,19}

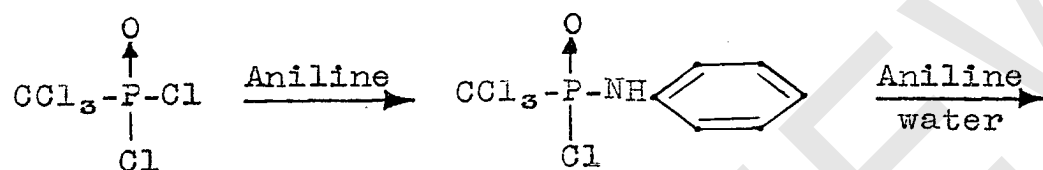




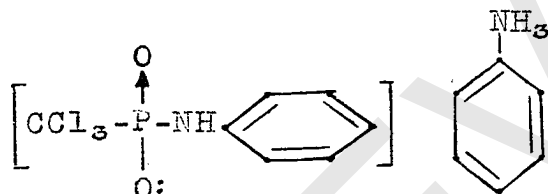
VI



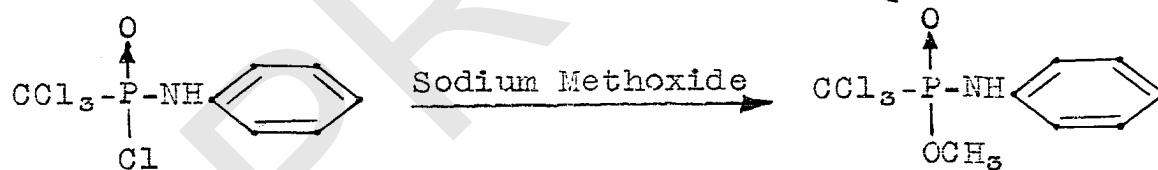
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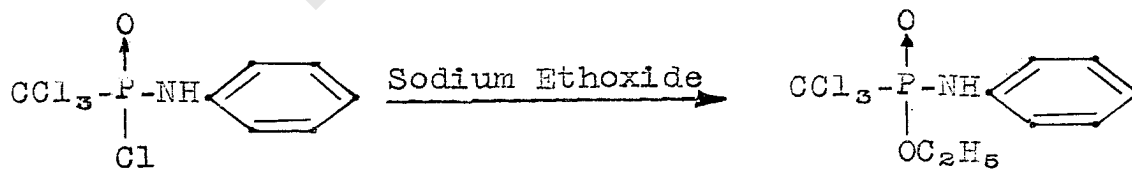
VIII



IX

Diazomethane
or
Methylsulfate

X



XI