

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

**ADDITION REACTIONS OF THE PHOSPHORUS HALIDES. V.
THE FORMATION OF AN UNSATURATED PHOSPHONIC ACID**

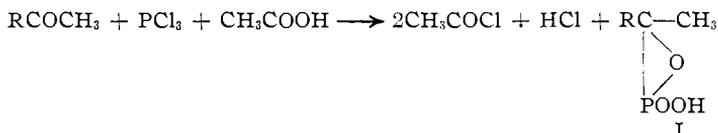
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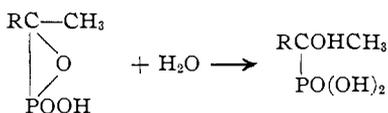
Introduction

Hydroxyphosphonic acids are obtained by treating most aldehydes and ketones with phosphorus trichloride in the presence of glacial acetic acid, pouring the mixture into water and evaporating the solution to dryness.¹ In the case of certain ketones considerable amounts of an unsaturated phosphonic acid are also formed. The isolation of an unsaturated acid from acetophenone has been described in an earlier paper.² Further study has now enabled us to establish the probable mechanism of the formation of this unsaturated compound and has also revealed some interesting transformations of this new type of phosphonic acid.

A study of the addition of phosphorus trichloride to benzaldehyde has shown that the first step seems to be a reversible combination of the two substances. In the presence of acetic acid or acetic anhydride, the primary addition compound is transformed into a phosphonic acid (I) or some derivative of a phosphonic acid (an acid chloride or anhydride). The following equation represents a similar reaction with a methyl ketone.

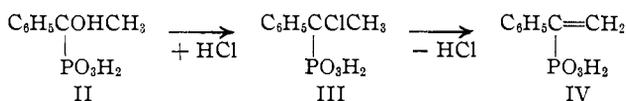


The general behavior of the reaction mixture with ketones, acetic acid, and phosphorus trichloride is in agreement with the inference that a phosphonic acid is thus formed. The first product which separates from the acetyl chloride and excess acetic acid is a gum which is only slowly transformed into the crystalline hydroxyphosphonic acid by boiling with water.



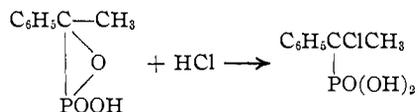
The similar hydrolysis of the phosphonic acid derived from acetophenone is complicated by several other reactions which lead to the formation of an unsaturated phosphonic acid. The following transformations take place with great ease.

¹ THIS JOURNAL, 42, 2337 (1920).² *Ibid.*, 43, 1928 (1921).



These reactions were established by preparing and studying each of the three acids in question.

The chloro acid (III) is obtained in excellent yields when the reaction mixture is directly saturated with dry hydrogen chloride. Apparently the oxygen ring of the phosphonic acid can be opened by hydrogen chloride.



On hydrolysis in water solution at *room temperature*, the chloro acid yields the hydroxy acid (II); indeed, this is the only way of obtaining this hydroxy-phosphonic acid. This hydrolysis is readily reversible, the chloro acid being formed by the action of conc. hydrochloric acid on the hydroxy acid. The chloro acid readily passes into the unsaturated phosphonic acid (IV), either by heating it alone or in aqueous solution. Strangely enough, the reaction in solution is accelerated by the presence of considerable amounts of hydrochloric acid. Both steps in the above scheme for the conversion of the hydroxy acid into the unsaturated acid are thus established. Further evidence for this mechanism lies in the fact that when the hydroxy-phosphonic acid is heated in pure water no change occurs; when it is heated in the presence of hydrochloric acid, a quantitative conversion into the unsaturated acid takes place.

It thus appears that the phosphonic acid which is formed when phosphorus trichloride, acetophenone and acetic acid react, is partially transformed into the α -chloro acid by the hydrogen chloride evolved. On pouring the reaction mixture into water and evaporating the solution to dryness, the major portion of the phosphonic acid is slowly hydrolyzed to the hydroxy-phosphonic acid, which, in turn, is transformed into the chloro acid by the hydrogen chloride present. The chloro acid formed either in the initial reaction or in aqueous solution loses hydrogen chloride as the solution is heated and gives the unsaturated acid which is the final product actually obtained.

Formation and Decomposition of Certain β -Bromo-phosphonic Acids

The unsaturated acid obtained from acetophenone (phenyl-vinyl-phosphonic acid) readily adds 2 atoms of bromine in water or chloroform solution. The resulting dibromo acid (V) loses hydrogen bromide on heating and gives an unsaturated β -monobromo acid (VI). The corresponding

The latter reaction seems to be favored by a rise in temperature, as the yield of bromostyrene was lowered from 68 to 16% by warming the materials on the steam-bath. The hydrolysis of the dibromo acid by pure water was likewise found to be greatly accelerated by application of heat. The concentration of hydroxyl ion is apparently without much effect within certain limits, as the same yield was obtained with cold sodium hydroxide as with cold sodium carbonate. It should be noted, however, that when the hydroxyl-ion concentration is very low (about 10^{-13} in a water solution of the acid) little or no cleavage of the molecule takes place; instead, the dihydroxy acid is formed.

Experimental

α -Phenyl- α -chloro-ethyl-phosphonic Acid, $C_6H_5CCl(PO_3H_2)CH_3$.—Ten g. of acetophenone and 14.2 g. of phosphorus trichloride were mixed; after 2 hours 25 g. of glacial acetic acid was added and the mixture was allowed to stand overnight. Dry hydrogen chloride was then passed into the mixture for 20 minutes. Crystals soon began to form and in 2 hours the mixture was a hard cake. This was broken up and as much of the liquid as possible removed on a suction filter. The residue was recrystallized from ether; yield, 16 g., or 82%. The compound crystallized in long white needles which melted at 174–175°.

Analysis. Calc. for $C_8H_{10}PO_3Cl$: Cl, 16.1. Found: 15.9.

A small amount of the acid may also be obtained by merely allowing the reaction mixture to stand several days without passing in hydrogen chloride. Sufficient hydrogen chloride is produced in the initial reaction to form some of the chloro acid.

α -Phenyl- α -hydroxyethyl-phosphonic Acid, $C_6H_5COH(PO_3H_2)CH_3$.—The α -chloro acid just described is readily hydrolyzed by water even at room temperature. In order to isolate the hydroxy acid it is necessary to allow the aqueous solution to evaporate without heating it. Ten g. of the chloro acid was dissolved in 200 cc. of water and after standing for 2 days the solution was evaporated at room temperature by a current of air. A mass of white crystals was obtained which were spread on a watch glass, in a vacuum desiccator containing potassium hydroxide, and when dry were recrystallized from a mixture of chloroform and ether; m. p., 154–155°; yield, 7.5 g. of recrystallized acid or 81%.

Analyses. Calc. for $C_8H_{11}PO_4$: P, 15.4. Found: 15.3, 15.4.

The compound did not decolorize bromine water. It was not affected by being heated in water solution or in benzene solution for more than 8 hours. It could be converted into the α -chloro acid as follows. Three g. was dissolved in 15 cc. of conc. hydrochloric acid which was then saturated with hydrogen chloride. After standing for hours the mixture became almost solid. After the crystals were dried over potassium hydroxide in a vacuum and recrystallized they were identical with those of the α -chloro acid (m. p. 172–174°); yield, 3.2 g., or 96%.

Heated above its melting point, the compound lost water and gave α -phenyl-vinyl-phosphonic acid² (m. p. 112–113°) in 98% yield.

Conversion of the Chloro Acid into the Unsaturated Acid.—When the α -chloro acid is heated above its melting point, it loses hydrogen chloride, and α -phenyl-vinyl phosphonic acid, described in an earlier paper,² is formed. Ten g. of chloro acid yielded 7.5 g. of recrystallized unsaturated acid, m. p. 112–113°, a yield of 90%. The same transformation takes place slowly and incompletely in hot aqueous solution; this reaction could be readily followed by titrating aliquot samples with bromine water. A solution

of 5 g. of chloro acid in 250 cc. of water was boiled under a reflux condenser; 8% of unsaturated acid was formed in 16 hours, and 17% in 24 hours. Further boiling produced no change. The greater part of the compound had apparently decomposed as the solution gave a strong phosphate test. The transformation of the chloro acid into the unsaturated acid is thus slow and attended by decomposition in hot aqueous solution. The presence of considerable amounts of hydrogen chloride, however, so accelerates the formation of the unsaturated acid that the reaction is almost quantitative in conc. hydrochloric acid. Thus, 0.7 g. of chloro acid was dissolved in 25 cc. of conc. hydrochloric acid; the solution was heated under a reflux condenser for 6 hours, at the end of which time 95% of the chloro acid had been converted into the unsaturated acid.

The hydroxy acid, while stable in pure water, is transformed by being heated in hydrochloric acid into the unsaturated acid; 0.6 g. in 20 cc. of conc. hydrochloric acid was 97% converted into the unsaturated acid by boiling.

Preparation of α -Phenyl-vinyl-phosphonic Acid.—If the usual procedure for preparing an hydroxy-phosphonic acid is employed with acetophenone, the unsaturated acid is the main product. In a typical experiment, 20 g. of acetophenone, 30 g. of phosphorus trichloride and 50 g. of glacial acetic acid were allowed to react in the usual way. The resulting mixture was poured into 200 cc. of water and evaporated to dryness four times, 100 cc. of water being added after each evaporation. The crude solid thus obtained was dried on a porous plate; it weighed 29 g. (95% yield) and contained 88% of unsaturated acid. Recrystallization from ether and chloroform yielded the pure unsaturated acid.

A better method of preparation is the following. One hundred g. of acetophenone, 89 cc. of phosphorus trichloride and 240 g. of glacial acetic acid were allowed to react. After 2 hours the mixture was saturated with hydrogen chloride, and 12 hours later the crude chloro acid was collected on a filter, and placed in a beaker in an oil-bath. The temperature of the bath was raised to 180°; hydrogen chloride was given off. When the effervescence had ceased, the mixture was cooled. The hard crystalline cake was almost pure (though somewhat colored) unsaturated acid. It weighed 104 g. Recrystallization from chloroform and ether gave the pure acid (m. p. 112–113°) in a yield of 80 to 90% based on the acetophenone employed.

It is interesting to note that an aqueous solution of the unsaturated acid was unchanged after boiling it for 35 hours.

α,β -Dibromo- α -phenyl-ethyl-phosphonic Acid, $C_6H_5CBr(PO_3H_2)CH_2Br$.—Fifteen g. of the unsaturated acid was dissolved in 200 cc. of chloroform. A solution of bromine in carbon tetrachloride was added while the mixture was kept in the sunlight. The bromine color was rather rapidly discharged, and crystals soon began to deposit. After a permanent color was obtained the solvent was evaporated in a current of air and the solid recrystallized from chloroform and ether. There was thus obtained 24 g. (84% yield); m. p. 186–188°.

Analysis. Calc. for $C_8H_9PO_3Br_2$: Br, 46.5. Found: 46.2.

Decomposition of the Dibromo Acid.—Ten g. of the acid was dissolved in 100 cc. of saturated sodium carbonate solution at 0°. The mixture became turbid at once. After 2 hours, it was extracted with ether and 3.6 g. of α -bromostyrene was obtained, (68% yield). In another experiment 70 g. was dissolved in sodium carbonate solution at room temperature and the mixture heated for a short time on the steam-bath. There was obtained by extraction with ether only 6 g. (16%) of α -bromostyrene. The α -bromostyrene was identified by its boiling point (110–112° at 35 mm.), its analysis, and its odor. Similar experiments in which *cold* conc. sodium hydroxide solution was used showed that 67 to 73% of the dibromo acid had decomposed to give α -bromostyrene.

α,β -Dihydroxy- α -phenyl-ethyl-phosphonic Acid, $C_6H_5COH(PO_3H_2)CH_2OH$.—Ten

g. of the dibromo acid was dissolved in 25 cc. of water and the solution evaporated on the steam-bath. After 2 days crystals began to form in the reddish gum which then soon solidified. The crystals were dried in a desiccator over potassium hydroxide and recrystallized from ether and carbon tetrachloride or from acetone. After recrystallizing, 5.5 g. of material was obtained; m. p. 143–145°; yield 87%. The compound contained no halogen and did not decolorize bromine water.

Analyses. Calc. for $C_8H_{11}O_3P$: P, 14.2. Found: 14.2; 14.1.

The formation of this acid from the dibromo acid could be conveniently followed by titrating aliquot portions of an aqueous solution of the latter by the Volhard method. A solution of the dibromo acid (0.3 g. in 25 cc.) titrated as soon as possible showed 11% hydrolysis; after standing for 2 hours it showed 19%, and after 6 hours, 69%. In a similar experiment, a solution was heated to boiling for 1 hour and at the end of that time 99% hydrolysis had taken place.

α -Phenyl- β -bromo-vinyl-phosphonic Acid, $C_8H_5C(PO_3H_2)=CHBr$.—Ten g. of the dibromo acid was heated above its melting point in an evacuated flask; large quantities of hydrogen bromide were evolved. The mixture was cooled after the evolution of gas had ceased, and 12 hours later a large quantity of crystals had deposited. Several recrystallizations from carbon tetrachloride yielded 7 g. of substance, melting at 133–135°; yield, 90%.

Analyses. Calc. for $C_8H_5O_3BrP$: Br, 30.4. Found: 30.3; 30.2.

An aqueous solution of the acid did not decolorize bromine water, but did decolorize potassium permanganate solution.

Formation of Phenyl-acetylene.—The crude monobromo acid prepared as just described was dissolved in sodium carbonate solution and allowed to stand for a short time. The solution became turbid almost immediately. The liquid was distilled with steam, the distillate extracted with ether, the ethereal solution dried and distilled. From 120 g. of crude acid there was obtained 17 g. of phenyl-acetylene boiling at 140–142°; yield, 37%. The product was identified by its boiling point and reaction with ammoniacal silver nitrate solution.

Addition of Hydrogen Bromide to the Unsaturated Acid.—Fifteen g. of this substance was dissolved in 100 cc. of 82% hydrobromic acid and the mixture heated in a sealed tube at 100° for 17 hours. Fifteen g. of a product was obtained which melted over a wide range (110–140°). It was not found possible to isolate a pure product. The presence of α -phenyl- β -bromo-ethyl-phosphonic acid in this crude product is shown by its reaction with sodium carbonate. One g. of styrene was obtained from 15 g. of the crude acid; yield, 17%. The styrene was identified by its odor, reaction with bromine and polymerization. Very probably the crude monobromo acid contains some α -bromo acid as well as β -bromo acid; this would account for the difficulty in purification, and the low yield of styrene.

α,β -Dichloro- α -phenyl-ethyl-phosphonic Acid, $C_8H_5CCl(PO_3H_2)CH_2Cl$.—This acid was prepared from the unsaturated acid in the same manner as was the dibromo acid. An 83% yield was obtained of recrystallized compound melting at 175–178°.

Analysis. Calc. for $C_8H_7PO_3O_2$: Cl, 27.8. Found: 27.5.

Summary

1. The mechanism of the formation of an unsaturated phosphonic acid from acetophenone, phosphorus trichloride and acetic acid has been established by a study of the corresponding hydroxy- and chloro-phosphonic acids.

2. The hydroxy-phosphonic acid is very readily converted into the

chloro acid by the action of hydrochloric acid; the chloro acid in turn easily loses hydrogen chloride, forming the unsaturated compound.

3. Certain β -halogen phosphonic acids have been prepared from the unsaturated phosphonic acid.

4. These compounds easily lose hydrogen bromide and phosphoric acid when treated with sodium carbonate forming unsaturated hydrocarbons. Thus, phenyl acetylene, styrene, and α -bromostyrene were formed from the corresponding bromo-phosphonic acids.

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SOME DELTA KETONIC NITRILES AND THEIR RELATION TO CYCLIC COMPOUNDS

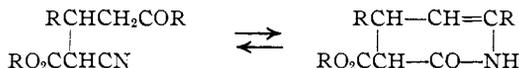
By E. P. KOHLER, ALICE GRAUSTEIN¹ AND D. R. MERRILL

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By adding cyano-acetic ester, cyano-acetamide, malononitrile, benzyl cyanide and similar substances to unsaturated ketones, it is possible to obtain a great variety of closely related δ -ketonic nitriles, which pass, more or less readily, into hydroxyridine derivatives. We are using these addition products to study the conditions under which the cyclic compounds are formed, the mechanism of the reactions which are involved, and, in particular, the transition from hydroxyridine to pyridine derivatives.

This paper deals with the substances that were obtained by adding methyl cyano-acetate to benzal-acetophenone and benzal-*p*-chloro-acetophenone. The products from the two ketones behave alike, but the cyclic compounds and the substitution products obtained from the *p*-chloro derivatives generally melt higher and are less soluble than those derived from the chlorine-free substance. It was frequently advantageous, therefore, to determine the most favorable conditions for a reaction first with the chloro ketone.

The simplest transformation of the open-chained addition products into cyclic compounds that we have found, is represented by the equation.



This rearrangement takes place with great ease when solutions of the addition products in indifferent media are saturated with hydrogen chloride or with hydrogen bromide. If the amount of solvent is small, the change into the cyclic compound is almost quantitative, and, when hydrogen bromide is used as agent, the reaction is completed in a few hours.

Owing to the ease with which substances like these pass into each other, it is sometimes difficult to distinguish between structural isomerism and

¹ Mrs. D., R. Merrill.