The Dehydration Reactions by Means of Esters of Phosphoric Acid

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Dehydration reactions of primary nitroparaffins and aldoximes by means of organic reagents, such as isocyanates, carbodiimides, ketene acetals and vinylogs, have been described in preceding papers[1-3]. In the present study, dehydration reactions using esters of phosphoric acid have been investigated in order to extend the scope of dehydrating reagents.

In general, the dehydrating reagents can be classified in three classes according to their abilities of dehydration: The first class involves well known strong dehydrating reagents, such as sulfuric acid and phosphorus pentoxide, which remove the hydrogen atom and the oxygen atom at the ratio of 2:1 irrespective of the structures of the compounds to be dehydrated. The second class involves very weak dehydrating reagents, such as calcium chloride and sodium sulfate, which can not remove a water molecule other than that included in the form of water, such as the water of crystallization or adhering water. The third class involves organic dehydrating reagents, such as carboxylic acid anhydrides, carboxylic acid chlorides, isocyanates, carbodiimides and vinylogs, which show that moderate dehydrating abilities and selective intramolecular or intermolecular dehydration of organic compounds are affected with these reagents.

These three classes of dehydrating reagents can be modified by strengthening or weakening their respective dehydrating abilities. For example, it is possible to weaken the strong dehydrating ability of sulfuric acid or phosphorus pentoxide till it is moderate. Recently, it was reported[4] that polyphosphoric acid which is considered to be a mixture of hydrates of phosphorus pentoxide is a very useful dehydrating reagent under moderate conditions.

Esters of phosphoric acid used as dehydrating reagents in the present study are prepared by the reaction of phosphorus pentoxide with alcohols instead of phosphoric acid in the preparation of polyphosphoric acid:

$$n\ P_2O_5 + m\ ROH \rightarrow P{-}R\ (n{-}m),$$

where P—R (n—m) denotes an ester of phosphoric acid prepared by the reaction of n mol. of phosphorus pentoxide with m mol. of alcohol ROH. In general, the molar ratio of phosphorus pentoxide to monohydric alcohols is favorable when it is more than 1/3.

Esters of phosphoric acid are prepared very readily by adding alcohols to phosphorus pentoxide with vigorous agitation. In the preparation of these esters, it is desirable to make the reaction mixture as homogeneous as possible. For this purposes the addition of a pre-formed ester of phosphoric acid to phosphorus pentoxide in advance is favorable, just as shown in the preparation of polyphosphoric acid by the reaction of phosphorus pentoxide with phosphoric acid instead of water.

Monohydric alcohols, such as methyl, ethyl, *n*-propyl, isopropyl and *tert*-butyl alcohols, and also dihydric alcohol, and ethylene glycol, react with phosphorus pentoxide to give viscous esters of phosphoric acid, except in the case of *tert*-butyl alcohol. This does not form a homogeneous ester with phosphorus pentoxide, but the product separates into two layers, probably because of the branched structure of the alcohol. The esters of phosphoric acid thus formed, except that from *tert*-butyl alcohol, show nearly the same reactions. As an example of the dehydration reactions, the dehydrations using P—Et (2—5) prepared from 2 mol. of phosphorus pentoxide and 5 mol. of ethyl alcohol are described.

The reactions of benzaldoxime and heptanaldoxime with P—Et (2—5) give corresponding nitriles in quantitative yields without any accompanying side reactions:

$$RCH{=}NOH + P{-}Et\ (2{-}5) \rightarrow RC{\equiv}N$$

On the other hand, it was reported that the same dehydration reaction of an aldoxime could scarcely be observed with polyphosphoric acid and an acid amide formed by the Beckmann rearrangement of the aldoxime was mainly obtained because of the strong acid character of polyphosphoric acid. The yield of benzonitrile is maximum when benzaldoxime reacts with P—Et (2—5) for 15 min. and then it decreases with the time of heating as shown in Table I.

The dehydration of cyclohexanol to cyclohexene results by a simple treatment with

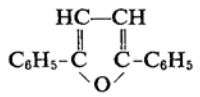
1) T. Mukaiyama and T. Hoshino, *J. Am. Chem. Soc.*, **82**, 5339 (1960).
2) T. Mukaiyama and T. Hata, This Bulletin, **33**, 1382 (1960).
3) T. Mukaiyama and T. Hata, ibid., **33**, 1712 (1960).
4) F. D. Popp and W. E. McEwen, *Chem. Revs.*, **58**, 321 (1958).

esters of phosphoric acid in a yield higher than when other dehydrating reagents, such as a catalytic amount of phosphoric acid, are used[5].

$$C_6H_{11}OH + P{-}Et\ (2{-}5) \rightarrow C_6H_{10}$$

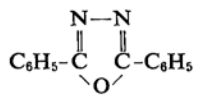
The reaction of dibenzoylethane with P—Et (3—4) gives 2, 5-diphenylfuran in a nearly quantitative yield:

$$C_6H_5COCH_2CH_2COC_6H_5 + P{-}Et\ (3{-}4) \rightarrow$$



Similarly, the reaction of dibenzoylhydrazine with P—Et (2—5) gives 2, 5-diphenyl-1, 3, 4-oxadiazole in a good yield:

$$C_6H_5CONHNHCOC_6H_5 + P{-}Et\ (2{-}5) \rightarrow$$



The results of the dehydrations of benzaldoxime and cyclohexanol with the other esters are listed in Tables I and II. It should be noted that the reactivities of the five esters are nearly the same irrespective of their nature, except the ester of *tert*-butyl alcohol. It is also noted that the yield increases as the molar ratio of phosphorus pentoxide to alcohols increases and the maximum yield is obtained when benzaldoxime reacts with P—Et (3—4). P—Et (3—4), being a highly viscous liquid, is made to react more smoothly with benzaldoxime in a separate layer of a benzene solution.

Moreover, the esters of phosphoric acid possess several obvious advantages over polyphosphoric acid: 1) Since esters of phosphoric acid are less acidic than polyphosphoric acid, side reactions other than dehydration do not take place as shown in the dehydration of benzaldoxime. 2) In contrast to polyphosphoric acid, esters of phosphoric acid are soluble in organic solvents, such as chloroform, and reactions of organic compounds are conducted in homogeneous systems. 3) By the change of the molar ratio of phosphorus pentoxide to alcohols, the dehydrating ability of the esters is properly controlled.

The dehydrations by means of esters of phosphoric acid are considered to proceed through the bond fission of the pyrophosphate linkage by an attack of compounds containing a hydroxyl group to form 2 mol. of phosphates, and it is established that tetraethyl pyrophosphate reacts with benzaldoxime to give benzonitrile in a 76% yield along with 2 mol. of diethyl phosphate (95% yield).

$$(EtO)_2POOPO(OEt)_2 + C_6H_5CH{=}NOH \rightarrow 2(EtO)_2POOH + C_6H_5C{\equiv}N$$

Dehydrations of aldoximes, cyclohexanol, dibenzoylethane and dibenzoylhydrazine are well conducted with esters of phosphoric acid and also mostly with polyphosphoric acid, but dehydration of an acid amide with these reagents does not succeed and, when benzamide reacts with P—Et (2—5), ethyl benzoate is obtained in an 18% yield instead of the dehydrated product, benzonitrile, probably because of a replacement reaction of the alkoxyl group of the esters with the amino group of the acid amide.

$$C_6H_5CONH_2 + P{-}Et\ (2{-}5) \rightarrow C_6H_5COOEt$$

Since esters of phosphoric acid contain alkoxyl groups and form a carboxylic ester by the reaction with an acid amide, polyphosphonic acid is prepared from phosphorus pentoxide and benzenephosphonic acid.

$$C_6H_5PO(OH)_2 + P_2O_5 \rightarrow \text{polyphosphonic acid}$$

When benzamide reacts with the polyphosphonic acid, the dehydrated product, benzonitrile, is obtained, as expected, in a 60% yield.

Experimental

Preparation of Esters of Phosphoric Acid [P—R(*n*—*m*)].—To *n* mol. of phosphorus pentoxide was added *m* mol. of a monohydric alcohol or *m*/2 mol. of a dihydric alcohol dropwise with continuous stirring. When unchanged phosphorus pentoxide remained in a viscous ester, the whole was further heated on a boiling water bath until phosphorus pentoxide was completely dissolved. In general, the resulting esters, P—R (*n*—*m*), are viscous homogeneous liquids, but the ester from *tert*-butyl alcohol separated into two layers. P—Me (*n*—*m*)

TABLE I. THE REACTIONS OF α-BENZALDOXIME WITH VARIOUS ALKYL ESTERS OF PHOSPHORIC ACID, P—R (*n*—*m*), AT 100°C

P—R (*n*—*m*)	Reaction time, min.	Benzonitrile, yield %
P—Et (2—5)	5	60
	15	92
	60	70
	120	48
P—Et (1—3)	15	48
P—Et (2—5)	15	92
P—Et (1—2)	15	92
P—Et (3—4)	15	98
P—Me (2—5)	15	68
P—*n*Pr (2—5)	15	90
P—iso Pr (2—5)	15	92
P—*t*Bu (2—5)	15	53
P—EG (3—4)	15	87

5) L. F. Fieser, "Experiments in Organic Chemistry", D. C. Heath & Co., Boston (1955), p. 61.

and P—EG (*n*—*m*), prepared by the reactions of phosphorus pentoxide with methyl alcohol and ethylene glycol, respectively, were dark brown liquids, but they showed similar reactions to the other esters.

Reactions of α-Benzaldoxime with Esters of Phosphoric Acid.—A solution of α-benzaldoxime (5.0 g., 0.05 mol.) in 10 ml. dry benzene was added to 7.5 g. of P—Et (3—4) and the mixture was heated at 90°C with continuous stirring for 15 min. After removal of benzene, 4.2 g. (98% of the theoretical) of benzonitrile, b. p. 65~66°C (8 mmHg), was obtained. The results of the dehydration of α-benzaldoxime with P—R (*n*—*m*) are summarized in Table I.

Reaction of Heptanaldoxime with P—Et (3—4).—A solution of heptanaldoxime (2.6 g., 0.02 mol.) in 10 ml. dry benzene was added to 25 g. of P—Et (3—4). The mixture was heated on a boiling water bath for 30 min. with continuous stirring. After removal of benzene, 1.8 g. (80%) of heptanenitrile, b. p. 71~73°C (20 mmHg), was obtained.

Reactions of Cyclohexanol with Esters of Phosphoric Acid.—Cyclohexanol (6.0 g., 0.06 mol.) was added to 8.0 g. of P—Et (2—5) and the mixture was heated at 90°C with continuous stirring for 2 hr. 4.5 g., (92%) of cyclohexene, b. p. 47°C (200 mmHg), was obtained. The results of the dehydration of cyclohexanol with P—R (*n*—*m*) are summarized in Table II.

Reaction of Dibenzoylethane with P—Et (3—4).—Dibenzoylethane (1.0 g., 0.004 mol.) was added to P—Et (3—4) (5.0 g.) and the mixture was heated at 100°C with continuous stirring until the viscous mixture became brownish yellow in color. Then the mixture was poured into 150 ml. of ice water with vigorous stirring and the precipitate was collected by filtration. It was recrystallized from 95% ethanol and 0.86 g. (93%) of 2,5-diphenylfuran, m. p. 88~90°C, was obtained.

TABLE II. THE REACTIONS OF CYCLOHEXANOL WITH VARIOUS ALKYL ESTERS OF PHOSPHORIC ACID AT 100°C

P—R (*n*—*m*)	Reaction time, hr.	Cyclohexene, yield, %
P—Et (2—5)	1.0	68
	1.5	92
	2.0	88
	3.0	93
P—Me (2—5)	2.0	88
P—*n*Pr (2—5)	2.0	99
P—iso Pr (2—5)	2.0	99
P—*t*Bu (2—5)	2.0	52

Reaction of Dibenzoylhydrazine with P—Et (3—4).—A solution of 1.0 g. (0.004 mol.) of dibenzoylhydrazine in 10 ml. dimethylformamide was added to 10 g. of P—Et (3—4). Then, the mixture was heated at 100°C for 2 hr. and poured into 200 ml. of ice water with vigorous stirring. The precipitate was collected by filtration and recrystallized from benzene to give 0.6 g. (65%) of 2,5-diphenyl-1,3,4-oxadiazole, m. p. 136°C.

Reaction of α-Benzaldoxime with Tetraethyl Pyrophosphate.—A mixture of tetraethyl pyrophosphate (2.9 g., 0.01 mol.) and α-benzaldoxime (1.21 g., 0.01 mol.) was heated at 95°C for 14 hr. and 0.78 g. (76%) of benzonitrile, b. p. 42~44°C (2 mmHg), and 2.92 g. (95%) of diethyl phosphate, b. p. 120~123°C (0.02 mmHg), were obtained.

Reaction of Benzamide with Polyphosphonic Acid.—To fused benzenephosphonic acid (2.0 g., 0.013 mol.) was added phosphorus pentoxide (3.0 g., 0.021 mol.) little by little with stirring during a period of 20 min. To the viscous polyphosphonic acid thus prepared was added benzamide (1.0 g., 0.008 mol.) with continuous stirring. After heating the mixture for 30 min. at 130°C, it was cooled at room temperature. Then it was dissolved in 20 ml. of water and extracted twice with 20 ml. of chloroform. The chloroform layers were combined and distilled under reduced pressure to give 0.5 g. (60%) of benzonitrile, b. p. 87~89°C (25 mmHg).

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