Reactivity of Organophosphates. III. Bond Fission in Phosphoryl Transfer Induced by Electrophilic Attack on Vinyl Phosphates

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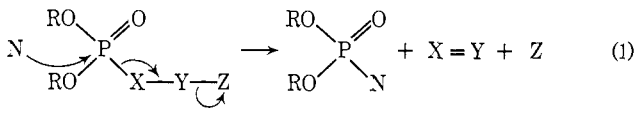
Abstract: The reaction of diethyl α-phenylvinyl phosphate (**5**) with HCl in aqueous dioxane produced diethylphosphoric acid and acetophenone with predominant C–O bond cleavage as shown by oxygen-18 labeling. The reaction of **5** with bromine in aqueous dioxane led to α-bromoacetophenone and diethylphosphoric acid, also with C–O bond cleavage. Reaction of **5** with bromine in ethanol followed by hydrolysis gave bromoacetophenone and diethylphosphoric acid. Reaction of diphenyl α-ethoxyvinyl phosphate (**6**) with benzoic acid formed ethyl acetate and benzoyl diphenyl phosphate, with C–O bond cleavage as shown by oxygen-18 labeling. All of these reactions of vinyl phosphates are interpreted as involving initial electrophilic attack on the double bond, followed by nucleophilic addition to the resulting α-phosphoryloxy carbonium ion. The adducts then cleave to products with C–O bond fission. The formation of the product from the adduct of **6** with benzoic acid is proposed to involve predominant displacement on carbonyl carbon by phosphoryl oxygen to give the mixed anhydride. It is suggested that C–O bond cleavage should be considered as a possible pathway in any cleavage of a vinyl phosphate initiated by electrophilic attack on the olefinic linkage.

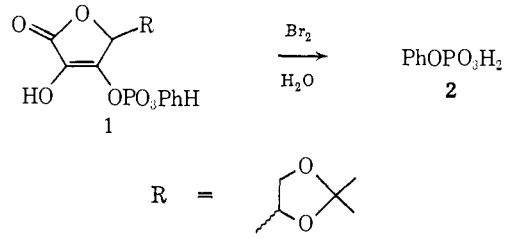
The transfer of the phosphoryl group is an important chemical process in biological systems. A significant example is the conversion of adenosine diphosphate (ADP) to adenosine triphosphate (ATP) by the reaction of vinyl phosphates, in particular phosphoenolpyruvate (PEP).[3] Numerous chemical model systems of this transformation have been examined, and a general scheme for chemical phosphorylations has been presented (eq 1),[4] where Y–Z can



(1)

be the carbon–carbon double bond of a vinyl phosphate, and electron transfer toward Z can be promoted by electrophilic attack or oxidation.

Examples of chemical systems which have been examined include the bromination of 3-phenylphosphoryl-5,6-isopropylidine-L-ascorbic acid (**1**) in aqueous solution to form monophenylphosphoric acid (**2**), or bromination of **1** in ethanol to form ethyl phenyl phosphate.[5] Similarly, the acid-catalyzed hydrolysis of L-ascorbic acid 3-phosphate has been examined,[6]



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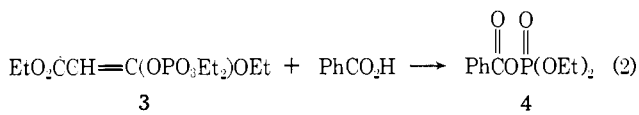
and all of these results were interpreted[7] as involving P–O bond cleavage according to the scheme in eq 1.

The acid-catalyzed hydrolyses of vinyl phosphates were proposed[8] to involve P–O bond cleavage on the basis of kinetic comparisons, and on the basis of the formation of anhydrides from the reaction of vinyl phosphates with acids, for example, the reaction of diethyl α-ethoxy-β-carboethoxyvinyl phosphate (**3**) with benzoic acid to form benzoyl diethyl phosphate (**4**) (eq 2).[9] The general scheme shown in eq 3 was proposed[8] for these reactions, and this suggestion has been widely accepted.[10]



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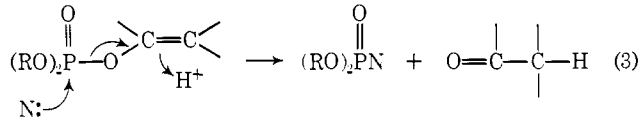

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The related oxidation of quinol phosphates according to eq 4 has also received considerable attention as a

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(2) E. P. Lyznicki, Jr., and T. T. Tidwell, *J. Amer. Chem. Soc.*, **94**, 3676 (1972).

(3) For recent studies of the scope of this reaction and leading references, see A. E. Woods, V. B. Chatman, and R. A. Clark, *Biochem. Biophys. Res. Commun.*, **46**, 1 (1972); J. A. Stubbe and G. L. Kenyon, *Biochemistry*, **11**, 338 (1972).

(4) V. M. Clark and D. W. Hutchinson, *Progr. Org. Chem.*, **7**, 75 (1968).

(5) V. M. Clark, J. W. B. Hershey, and D. W. Hutchinson, *Experientia*, **22**, 425 (1966).

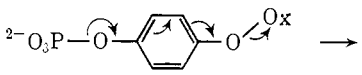
(6) H. Nomura, M. Kuwayama, T. Ishiguro, and S. Morimoto, *Chem. Pharm. Bull.*, **19**, 341 (1971).

(7) Specialist Report, "Organophosphorous Chemistry," No. 3, Chemical Society, London, 1972, p 141.

(8) (a) F. Lichtenthaler, *Chem. Rev.*, **61**, 607 (1961); (b) F. W. Lichtenthaler and F. Cramer, *Chem. Ber.*, **95**, 1971 (1962).

(9) F. Cramer and K.-G. Gärtner, *ibid.*, **91**, 704 (1958).

(10) (a) T. C. Bruice and S. J. Benkovic, "Bio-Organic Mechanisms," Vol. II, W. A. Benjamin, New York, N. Y., 1966, pp 106–108; (b) G. Hilgetag and H. Teichmann, *Z. Chem.*, **11**, 1 (1971); (c) C. A. Bunton and L. Robinson, *J. Amer. Chem. Soc.*, **91**, 6072 (1969).



$$PO_3^- + O{=}\langle\rangle{=}O + Ox^- \quad (4)$$

model of biological phosphorylations,[11] which could involve release of metaphosphate ion (PO_3^-),[12] or its equivalent, as an active phosphorylating agent by P–O cleavage. With various chemical oxidizing systems this reaction has been found to proceed with only 10–35% P–O cleavage, but enzymatic catalysis of the reaction has been shown to increase P–O cleavage to be the essentially exclusive mode of reaction.[11b]

In contrast to the mode of cleavage depicted in eq 1 and 3, vinyl carboxylates have been proposed to undergo alkyl–oxygen cleavage following electrophilic attack on the vinyl group by protons[13] or mercuric ions,[14] and similar addition–elimination sequences with alkyl–oxygen cleavage have been suggested for the reaction of vinyl carboxylates with carboxylic acids.[15a] The reaction of isopropenyl acetate with anhydrous HBr was proposed to involve an addition–elimination sequence with acyl–oxygen cleavage,[15b] whereas the reaction of vinyl phosphates with chlorine or HCl was found to involve addition–elimination with alkyl–oxygen cleavage.[16] Accordingly, it appeared desirable to examine the position of bond scission in various cleavage reactions of vinyl phosphates by the use of oxygen-18 labeling,[17] in order to define more exactly the reaction pathways followed by these important species.

Results

The hydrolysis of diethyl α-phenylvinyl phosphate (**5**) in a 1:1 mixture of 0.25 *M* HCl and aqueous dioxane at 70° gave acetophenone and diethylphosphoric acid (eq 5). The latter product was isolated

$$\underset{\mathbf{5}}{PhC(OPO_3Et_2){=}CH_2} \xrightarrow[H_2O]{HCl} PhCCH_3 + (EtO)_2PO_2H \quad (5)$$

after esterification to diethyl methyl phosphate with diazomethane. The incorporation of oxygen from the solvent into the phosphoric acid during the hydrolysis was examined by carrying out the reaction of the unlabeled ester **5** in water enriched with ^{18}O, and by reacting **5** labeled in the vinyl oxygen with unlabeled water. The isotope incorporations, presented in Table I, were measured from the mass spectra of diethyl methyl phosphate isolated from the reaction mixture, and indicate little or no incorporation of solvent oxygen in the product phosphoric acid. Acetophenone is known[19] to undergo facile exchange of oxygen with solvent water under these conditions and could not be used to monitor the isotope exchange. Control experiments showed that diethylphosphoric acid did not undergo appreciable exchange under the reaction and work-up conditions.

Table I. ^{18}O Content of $(EtO)_2P(O)OMe$ Obtained from Hydrolysis of $PhC(OPO_3Et_2){=}CH_2$ (**5**) (% excess ^{18}O)[a]

Reactant $PhC(OPO_3Et_2){=}CH_2$	Solvent H_2O[b]	Product $(EtO)_2P(O)OMe$
0.0 ± 0.3	3.3 ± 0.4	0.9 ± 0.3
6.9 ± 0.8[c]	0.0 ± 0.1	7.4 ± 0.6
0.0 ± 0.3	7.4 ± 0.9[c]	0.1 ± 0.3

[a] Deviations are the averages of at least four determinations of each sample. [b] Determined from authentic $(EtO)_2P(O)OMe$ prepared from diethyl chlorophosphate and labeled water. [c] These samples were prepared from the same batch of labeled water.

Reaction of **5** with bromine in aqueous dioxane gave bromoacetophenone and diethylphosphoric acid (eq 6).

$$\underset{\mathbf{5}}{PhC(OPO_3Et_2){=}CH_2} + Br_2 \xrightarrow{H_2O} PhCCH_2Br + (EtO)_2PO_2H + HBr \quad (6)$$

The reaction was carried out with ^{18}O-enriched water and the phosphoric acid product isolated as before as the methyl ester for analysis by mass spectrometry. The results, summarized in Table II, indicate no uptake of solvent oxygen in the product acid. The isolation procedure of the diethyl methyl phosphate was the same as in the acid-catalyzed hydrolysis, which was shown to involve no further exchange.

Table II. ^{18}O Content of $(EtO)_2PO_2Me$ Obtained from the Bromination of $PhC(OPO_3Et_2){=}CH_2$ (**5**) (% excess ^{18}O)[a]

Reactant $PhC(OPO_3Et_2){=}CH_2$	Solvent H_2O	Product $(EtO)_2PO_2Me$
0.0 ± 0.1	6.5 ± 0.3	0.0 ± 0.3

[a] Analyses as noted in Table I.

Bromination of **5** in ethanol also gave bromoacetophenone and diethylphosphoric acid, isolated as described above. No triethyl phosphate could be detected in the product, indicating that nucleophilic substitution did not occur on the phosphoryl grouping during this reaction (eq 7). Small amounts of acetophenone and benzoic acid were also formed during the brominations of **5**, apparently from the reactions of **5** with liberated HBr, and bromoacetophenone with bromine, respectively.

$$\underset{\mathbf{5}}{PhC(OPO_3Et_2){=}CH_2} + Br_2 \xrightarrow{EtOH} PhCCH_2Br + (EtO)_2PO_2H + HBr \quad (7)$$

The reaction of diphenyl α-ethoxyvinyl phosphate (**6**) with benzoic acid to benzoyl diphenyl phosphate (**7**) was carried out according to the known[20] procedure (eq 8). The reaction could be conveniently monitored when carried out in an nmr tube, and is complete as

(11) (a) V. M. Clark, D. W. Hutchinson, G. W. Kirby, and A. Todd, *J. Chem. Soc.*, 715 (1961); (b) J. Wodak, *J. Amer. Chem. Soc.*, **90**, 2991 (1968); (c) G. M. Blackburn and J. S. Cohen, *Top. Phosphorus Chem.*, **6**, 187 (1969).

(12) D. G. Gorenstein, *J. Amer. Chem. Soc.*, **94**, 2523 (1972).

(13) D. S. Noyce and R. M. Pollack, *ibid.*, **91**, 119, 7158 (1969).

(14) P. Abley, J. E. Byrd, and J. Halpern, *ibid.*, **94**, 1985 (1972).

(15) (a) H. H. Wasserman and P. S. Wharton, *ibid.*, **82**, 661, 1411 (1960); (b) E. A. Jeffrey and D. P. N. Satchell, *J. Chem. Soc.*, 2889 (1963).

(16) H. Gross and J. Freiburg, *Chem. Ber.*, **101**, 3201 (1968).

(17) The hydrolyses of certain vinyl phosphates with adjacent carboxylate functions have been examined with the use of O-18 labeling, and involve neighboring group participation by the carboxylate.[18]

(18) K. J. Schray and S. J. Benkovic, *J. Amer. Chem. Soc.*, **93**, 2522 (1971); J. F. Marecek and D. L. Griffith, *ibid.*, **92**, 917 (1970).

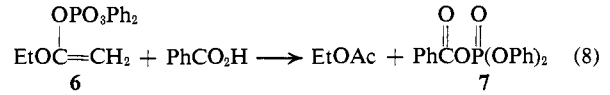
(19) D. Samuel and B. L. Silver, *Advan. Phys. Org. Chem.*, **3**, 123 (1965).

(20) H. H. Wasserman and D. Cohen, *J. Org. Chem.*, **29**, 1817 (1964); *J. Amer. Chem. Soc.*, **82**, 4435 (1960).

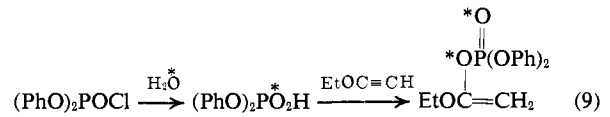
Table III. ^{18}O Distribution in the Reaction of $EtOC(OPO_3Ph_2)=CH_2$ with $PhCO_2H$ (% excess ^{18}O)[a]

Reactant $EtOC(OPO_3Ph_2)=CH_2$	Reactant $PhCO_2H$	Product $(PhO)_2PO_2Me$	Product $PhCONHC_6H_{11}$	Product EtOAc
9.73 ± 0.15[d]	0.00 ± 0.06	8.72 ± 0.24[b]	0.20 ± 0.06[c]	0.62 ± 0.06
0.00 ± 0.05	10.46 ± 0.20[d]	0.24 ± 0.05	4.37 ± 0.18	4.58 ± 0.13

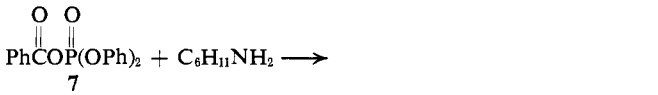
[a] Deviations are the average of the deviations from at least 10 scans of each peak. [b] Two separate preparations gave percentages within ±0.16% of the reported average. [c] Two separate preparations gave percentages within ±0.04% of the reported average. [d] These samples were prepared from the same batch of labeled water.



soon as the reagents can be mixed and the spectrum observed. A sample of **6** labeled with ^{18}O was prepared by the reaction of ethoxyacetylene and diphenylphosphoric acid-^{18}O obtained from diphenyl chlorophosphate and $H_2{}^{18}O$ (eq 9). This sequence would



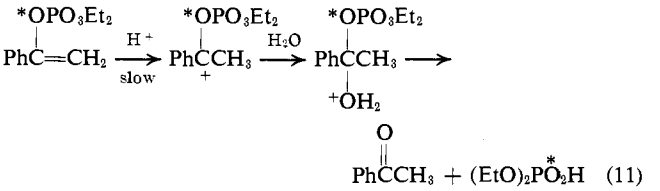
yield **6** with ^{18}O evenly distributed between the phosphoryl oxygen and the vinyl oxygen. Reaction of this sample of labeled **6** with benzoic acid gave **7** which was reacted with cyclohexylamine to the known[20] products, *N*-cyclohexylbenzamide and cyclohexylammonium diphenyl phosphate (eq 10). The ammonium



salt was acidified and treated with diazomethane to yield diphenyl methyl phosphate, and the products were analyzed for ^{18}O content. The results are summarized in Table III. Similarly the reaction of unlabeled **6** with labeled benzoic acid was carried out, and the isotopic distribution of the products of this reaction are also reported in Table III.

Discussion

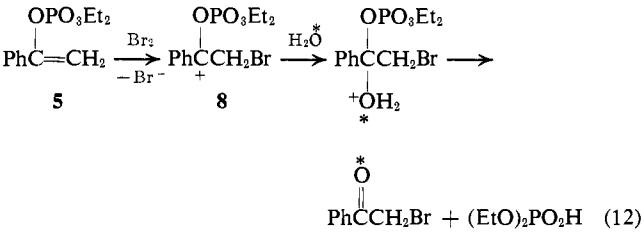
The isotope distributions in Table I show that the HCl-catalyzed hydrolysis of **5** (eq 5) occurs with predominant, and perhaps exclusive, C–O bond cleavage. These results, as well as the kinetic studies on α-arylvinyl phosphates,[10c,21] establish the reaction sequence shown in eq 11 as the pathway for hydrolysis



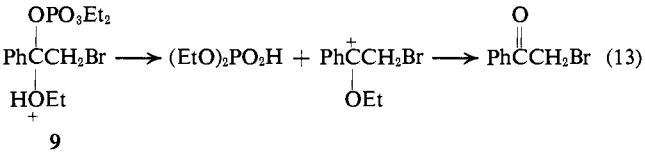
of this compound. Thus the possibility of nucleophilic attack of solvent on phosphorus concerted with proton addition (eq 3) is excluded, and the reaction follows the stepwise pathway analogous to that accepted for reactions of vinyl carboxylates.

This conclusion appears reasonable on several grounds. The rate of attack of water on phosphoryl phosphorus has been found to be much slower than the analogous attack on carbonyl carbon in the acid-catalyzed hydrolysis of vinyl phosphates compared to vinyl acetates,[21a] and triethyl phosphate compared to ethyl acetate.[22] The carbonium ion in eq 11 is stabilized by three potentially electron-donating substituents but a concerted pathway would skip the formation of this relatively favorable intermediate. Addition of water to this ion is analogous to the familiar path of hydrolysis of ketals.

The labeling studies for the bromination of **5** indicate C–O bond cleavage, and a possible pathway for this reaction in aqueous dioxane is shown in eq 12. The re-



action in ethanol could conceivably proceed to the same intermediate **8**, which on attack by ethanol could form **9**, which leads to the final products (eq 13)



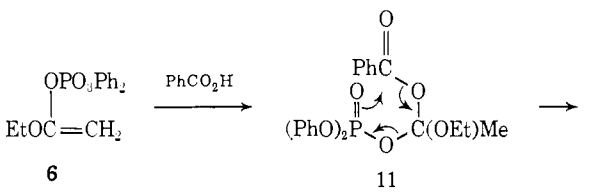
perhaps with the intervention of the diethyl ketal of bromoacetophenone. This result is in contrast to the formation of ethyl phenyl phosphate from bromination of **1** in ethanol.[5] However, **1** possesses a labile acidic proton not available in **5**, so by analogy with the proposals for oxidative cleavage of quinol phosphates,[11a,23] phenyl metaphosphate, $PhOPO_2$ (**10**), is a plausible candidate for the active phosphorylating agent from **1**. Formation of **10** could occur by routes analogous to those proposed, namely by bromine oxidation at the enolic oxygen,[11a] or by bromine addition at carbon.[23] Still a third possibility would be bromine oxidation at phosphoryl oxygen. Any of these routes are consistent with the fact that quinol mono- and diphosphates undergo cleavage to metaphosphates, whereas trisubstituted phosphates, such as **5**, do not.[11a]

The data in Table III decisively indicate that the conversion of the α-ethoxyvinyl phosphate **6** to benzoyl diphenyl phosphate (**7**) occurs with predominant C–O

(21) (a) R. D. Frampton, T. T. Tidwell, and V. A. Young, *J. Org. Chem.* **94**, 1271 (1972); (b) A. Arcoria, S. Fisichella, and F. Sardo, *J. Org. Chem.*, 37, 2612 (1972).

(22) E. P. Lyznicki, Jr., and T. T. Tidwell, *Can. J. Chem.*, in press.

(23) A. Lapidot and D. Samuel, *J. Amer. Chem. Soc.*, **86**, 1886 (1964).



6 11

$$EtOAc + (PhO)_2POCPh \quad (14)$$

7

cleavage of the phosphoryloxy group. Equation 14 shows a reasonable route for this process. The fraction of the recovered isotope from labeled diphenylphosphoric acid which appears in the product diphenyl methyl phosphate is 0.91, corresponding to 82% C–O cleavage. Similarly, the fraction of the recovered isotope from labeled benzoic acid which appears in the product ethyl acetate is 0.498 ± 0.014, corresponding to 100 ± 3% C–O cleavage. Thus the portion of C–O cleavage falls in the range 91 ± 9%, presumably by the route in eq 14 or a stepwise variant.

An alternative route to that shown in eq 14 would involve formation of the addition intermediate **11** followed by cleavage to products with attack of carbonyl oxygen on phosphoryl phosphorus. Another alternative would involve direct attack of the carboxylic acid on phosphorus, as in eq 3. Either of these pathways would involve P–O cleavage, which is shown by the data in Table III to occur to the extent of 0–13%. The arguments given previously that direct displacement on phosphorus would be a relatively unfavorable process suggest that the intermediate **11** also intervenes in any reaction involving P–O cleavage.

The formation of **11** is also in agreement with the formation of addition intermediates in the reactions of α-ethoxyvinyl phosphate **3** with electrophiles,[16] and the possibility of the reactions of vinyl phosphates with carboxylic and phosphoric acids proceeding by addition–elimination was indeed briefly pointed out previously.[16] The related reaction of α-ethoxyvinyl carboxylates with carboxylic acids has also been demonstrated to occur by such an addition–elimination sequence by isotopic labeling.[15a]

Several factors might tend to favor displacement by phosphoryl oxygen on carbonyl carbon as depicted in eq 14 over the alternative displacement by carbonyl oxygen on phosphoryl phosphorus. These include the relative weakness of the carbon–phosphate bond in a reaction which presumably has some polar character, the possible resistance of phosphorus to formation of a five-coordinate transition state, and the greater nucleophilicity of phosphoryl over carbonyl oxygen.[24]

In conclusion, it has been demonstrated that reactions of fully substituted vinyl phosphates initiated by a variety of electrophiles occur with C–O cleavage. The electrophile-induced cleavage of vinyl phosphates shown in eq 3 is not required by the available data for any example, and attractive alternative mechanisms are available. It is suggested that the addition–elimination pathway should receive prime consideration as a possible mechanism for any cleavage of vinyl phosphates initiated by electrophilic attack.

(24) C. G. Swain and C. B. Scott, *J. Amer. Chem. Soc.*, 75, 141 (1953).

Experimental Section

General. Nmr spectra were determined using Varian A-60 and T-60 instruments with tetramethylsilane as an internal standard. Gas chromatography (vpc) was performed with Varian-Aerograph 90P-3 and 1820-1 instruments and the conditions specified. Water containing excess ^{18}O was obtained from Bio-Rad Laboratories.

Mass Spectral Analyses. Analyses on diethyl α-phenylvinyl phosphate (**5**) and its precursors and reaction products were carried out using a Perkin-Elmer Hitachi RMU instrument at 70 eV. Peak intensities were taken as the measured peak heights, and percentages of excess ^{18}O were taken as the ratio of the mass spectral ions (M + 2)/M with the ratio for the unlabeled compound subtracted out.[25] Analyses on the precursors and reaction products of diphenyl α-ethoxyvinyl phosphate were carried out at 70 eV using an AEI-MS902 instrument equipped with a Vacumetrics, Inc., proportional mass counter. Results of the analyses are given in Tables I–III. The agreement between results from repeated runs with the same reactants, between parallel experiments with different reactants labeled, and between analyses of different samples prepared from the same source of isotope lends confidence in the validity of the method of analysis.

Diethyl α-phenylvinyl phosphate (5)[21] was prepared by the reaction of chloroacetophenone and triethyl phosphite, and was purified by short-path distillation at 120–125° (0.05 Torr). Chloroacetophenone-^{18}O was prepared by heating a mixture of normal material (1.55 g, 0.010 mol), 7 ml of purified dioxane, 2.5 ml of water (7.0 atom per cent excess ^{18}O), and 0.20 ml of concentrated HCl at 70° for 1 hr. The mixture was extracted with chloroform, and the extracts were washed, dried, and evaporated to give solid chloroacetophenone which analyzed for 7.1 ± 0.4% excess ^{18}O. Triethyl phosphite (1.70 g, 0.010 mol) was added and the solution heated at 110° for 4 hr. Distillation gave labeled **5**.

Hydrolysis of 5. A solution of 0.503 g (2.0 mmol) of **5** in 4 ml of purified dioxane and 4 ml of 0.25 *N* HCl was heated in a sealed ampoule at 70° for 310 min. The solution was cooled, brought to pH 10 with 10% KOH, and extracted with three 50-ml portions of $CHCl_3$. The extracts were dried and evaporated to give 0.122 g of acetophenone. The aqueous layer was acidified with 0.1 *N* HCl to pH 2 and continuously extracted with ether. The ether extract was dried with $MgSO_4$ and evaporated to give 0.104 g (0.67 mmol) of diethylphosphoric acid, which was esterified with ethereal diazomethane. Pure diethyl methyl phosphate for mass spectral analysis was obtained by vpc (10 ft × 3/8 in. SE-52 on Chromosorb W, 155°, 120 ml/min). Experiments were run with normal ester in labeled acid solution prepared from labeled water and concentrated HCl, or with labeled ester in normal acid.

A control experiment was carried out with labeled diethylphosphoric acid prepared from reacting 1.00 g (6.0 mmol) of diethyl chlorophosphate and 0.60 g (33 mmol) of water (7.0 atom per cent excess ^{18}O) at room temperature for 1.5 hr. A portion of the labeled acid was treated under the reaction conditions, and after conversion to diethyl methyl phosphate showed no change in isotopic composition. Similarly, treatment of unlabeled diethylphosphoric acid with labeled water under the reaction conditions gave no uptake of isotope.

Reaction of 5 with Bromine in Ethanol. Bromine (0.50 ml, 9.4 mmol) was added to a solution of 2.01 g (7.8 mmol) of **5** in 30 ml of absolute ethanol at room temperature over a period of 20 min. The bromine color rapidly disappeared in an exothermic reaction throughout the addition. After 0.5 hr a solution of 20% KOH was added, and the basic solution was extracted with three 50-ml aliquots of chloroform. The combined organic extracts were dried, evaporated, and distilled (0.2 Torr with bath at 90°) to give 0.347 g of distillate (with a characteristic lachrymatory odor) which was shown by nmr to consist of equal amounts of bromoacetophenone and acetophenone. No signals attributable to triethyl phosphate were observed. Further distillation and vpc separation gave pure acetophenone. The distillation residue consisted of 0.7 g of unreacted **5**.

The aqueous layer above was acidified to pH 2 with HCl and extracted six times with 50-ml portions of ether. The ether extracts were dried, evaporated, and treated with diazomethane to yield diethyl methyl phosphate, which was found by vpc to contain about 5% of methyl benzoate.

Reaction of 5 with Bromine in Aqueous Dioxane. Bromine was

(25) C. G. Swain, G.-I. Tsuchihashi, and L. J. Taylor, *Anal. Chem.*, 35, 1415 (1963).

added slowly to a solution of 1.04 g (4.1 mmol) of **5** in a solution of 6 ml of water and 5 ml of dioxane until the bromine was no longer rapidly decolorized. Product isolation as in the reaction in ethanol gave 0.56 g (69%) of crude bromoacetophenone and a mixture of esterified acids shown by vpc (10 ft × 3/8 in. SE-52 on Chromosorb W, 155°, 120 ml/min) to consist of 80% diethyl methyl phosphate and 20% methyl benzoate. Both products were isolated and identified by comparison with authentic specimens.

Reaction of 0.487 g (1.9 mmol) of **5** with bromine in 3 ml of dioxane and 4.1 g of water containing ^{18}O was carried out by the procedure above.

Diphenylphosphoric acid was prepared by stirring 10 g of diphenyl chlorophosphate (Aldrich) overnight with an equimolar amount of water in a flask equipped with a drying tube. The resultant oil crystallized on standing, and was treated with 100 ml of benzene which was distilled away to remove excess water and HCl. The residue was recrystallized from a mixture of 5 ml of chloroform and 45 ml of hexane. A second recrystallization gave long white needles, mp 66–68° (lit.[26] mp 70° (anhydrous), lit.[27] 68°, lit.[28] 51–52° (dihydrate)). Labeled material was prepared by the use of ^{18}O-enriched water. The acid was converted to its methyl ester for isotopic analysis by treatment with ethereal diazomethane.

Benzoic acid-^{18}O was prepared by stirring benzoyl chloride with a slight excess of ^{18}O-enriched water in dioxane for 4 days, followed by evaporation of the solvent and sublimation.

Diphenyl α-ethoxyvinyl phosphate (6) was prepared by the reaction of diphenylphosphoric acid with excess ethoxyacetylene (Chemical Samples Co.) in dichloromethane or CCl_4 by the published procedure:[20] nmr (CCl_4) δ 1.14 (t, 3, J = 7 Hz, Me), 3.70 (q, 2, J = 7 Hz, OCH_2), 3.5–3.9 (m, 2, vinyl H), and 7.10 (s, 10, Ar). The vinyl and methylene resonances overlap, but the overlap is somewhat reduced in solvent benzene.

Reaction of 6 and benzoic acid[20] could be carried out in an nmr tube in CCl_4 solvent. As soon as an equimolar amount of benzoic acid had been added the aliphatic absorptions moved about 0.05 ppm upfield, the vinyl absorption disappeared, the aromatic absorption (now 15H) became several multiplets, and a new absorption due to the acetyl methyl appeared at δ 1.96. This spectrum is assigned to benzoyl diphenyl phosphate (**7**)[20] and ethyl acetate. In preparative experiments (in CH_2Cl_2), addition of 2 equiv of cyclohexylamine gave an exothermic reaction. After the reaction mixture had stood overnight a white precipitate of *N*-cyclohexylammonium diphenyl phosphate was collected and recrystallized from 1-propanol, mp 191–193° (lit.[20] mp 192°). The filtrate was distilled leaving a residue which was sublimed (120° (0.05 Torr)) to yield *N*-cyclohexylbenzamide, mp 145–148° (lit.[29] mp 149°). This melting point was apparently incorrectly transcribed in ref 20.

Methylation of diphenylphosphoric acid was accomplished by dissolving the cyclohexylammonium salt in boiling water and adding an equivalent amount of HCl just as the salt began to reprecipitate from the cooling solution. The solution was stirred and ethereal diazomethane was added. The product was extracted into ether which was dried and evaporated, leaving diphenyl methyl phosphate for mass spectral examination. Alternatively, the salt was dissolved in hot ethanol which was acidified on cooling, followed by alternate acidification with HCl and neutralization with diazomethane. Isotopic analyses of products from the two procedures were the same within experimental error, but higher recoveries of product were realized by the former method.

The last portion of the distillate from the filtrate from the isolation of the phosphate salt consisted of a mixture of ethyl acetate and CH_2Cl_2. The ethyl acetate was isolated by vpc (10 ft × 3/8 in. SE-30 on Chromosorb W, 80°, 65 ml/min) for mass spectral analysis.

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Electrophilic Reactions at Single Bonds. IX.[1a] Intermolecular Hydrogen Exchange and Alkylation (Alkylolysis) of Alkanes with Alkylcarbenium Fluoroantimonates[1b,c]

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Abstract: Intermolecular hydrogen exchange and alkylation of alkanes with their parent carbenium ion salts, such as the dimethyl-, trimethyl-, dimethylethyl-, and dimethylisopropylcarbenium fluoroantimonates, were studied under stable ion conditions in SO_2ClF and SO_2 solution (by nmr and glc methods). From the study of the temperature-dependent ^1H nmr spectra, the energies of activation, E_a, for the exchange reaction between the trimethylcarbenium ion and 2-methylpropane as well as 2-deuterium-2-methylpropane were determined. The highly hindered dimethyl-*tert*-butylcarbenium ion shows no hydrogen exchange with its parent hydrocarbon, 2,2,3-trimethylbutane (triptane). The intermolecular hydrogen exchange reactions are always accompanied by alkylation of alkanes by the carbenium ions, even though the former reactions are much faster. All data are in accord with reactions involving electrophilic attack by the carbenium ions on the C–H or C–C bonds *via* triangular three-center bonded carbonium ion transition states.

Intermolecular hydride transfers from isoalkanes to trivalent carbenium ions in acid-catalyzed media are well known from the work of Bartlett, Nenitzescu, and Schmerling, and have been reviewed.[2] More recently, we were able to develop superacid solvent systems allowing us to study stable carbocations and

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