Hydrogenolysis of Unsaturated Phosphate Esters

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A series of unsaturated phosphate esters has been synthesized and subjected to hydrogenolysis over Adams catalyst. It has been demonstrated that direct hydrogenolysis of vinylic esters occurs yielding the phosphoric acid and the alkene; the alkene is then further reduced to the alkane. It has also been shown that migration of a "distant" olefinic linkage to a site subject to hydrogenolysis occurs at a rate such that cleavage product may be obtained. Moreover, it has been shown that benzylic ester linkages are subject to facile hydrogenolysis over Adams catalyst but not homobenzylic ester linkages.

It had previously been reported that diethyl isopropenyl phosphate (I) absorbed 2 mol of hydrogen over Adams catalyst yielding as the observed product diethylphosphoric acid; when palladium was used as the catalyst, only 1 mol of hydrogen was absorbed and diethyl isopropyl phosphate was observed to be the product.[1] In the course of our investigations on the hydrogenolysis of aryl phosphate esters[2,3] it was observed that diethyl 1-cyclohexenyl phosphate (II) underwent hydrogenolysis over Adams catalyst with the formation of cyclohexane. With this observation it became of interest to investigate in detail the hydrogenolysis of saturated and unsaturated aliphatic phosphate esters. If a generality of reaction could be established here it would further extend the already well-known scheme of nonhydrolytic phosphate ester cleavages involving aryl and benzylic linkages.[2-6]

To test the generality of this reaction and to elucidate the sequence of reaction steps the series of vinylic phosphate esters I–V was prepared and subjected to standard hydrogenolysis conditions. In all cases direct observation of hydrocarbon product and any intermediates was attempted. In addition, reactions using deuterium were performed on the vinylic esters, their hydrocarbon cleavage products, and possible intermediates to help establish the sequence of reaction steps.

Several other molecular systems were also synthesized and subjected to hydrogenolysis conditions. First, a fully saturated compound was investigated in a consideration of two possible reaction sequences, i.e., cleavage followed by reduction as compared to initial reduction followed by cleavage. Moreover, as deuterium interchange was noted with possible intermediates containing sites of unsaturation, and as structural isomerization under hydrogenation conditions is well known,[7] it was of interest to prepare and investigate a phosphate ester with an olefinic site distant from a possible site of hydrogenolysis. Finally, benzylic and homobenzylic esters were investigated.

Experimental Section

Reagents. All reagents used in the preparation of the phosphate esters or their precursors were purchased from Aldrich Chemical Co. and used without further purification. Absolute ethanol, used as a standard solvent for the hydrogenolyses, was purchased from Commercial Solvents Corp. and used without further purification. The platinum oxide catalyst ($83 \pm 0.5\%$) was a generous gift of Engelhard Minerals and Chemicals Corp. Deuterium was from Matheson Corp. and was in excess of 99.5 atom % D.

General Synthesis of Diethyl Vinyl Phosphates. The standard reaction technique used for the Perkow reaction was followed.[8,9] To 0.20 mol of triethyl phosphite heated to 120° was added in small portions 0.20 mol of the appropriate α-chloro ketone. The reaction mixture was maintained at 120° for 1 hr after completion of the addition and then raised to 170° for an additional 1 hr, whereupon the product was vacuum distilled. Yield and analytical data are given below for each compound. Satisfactory ir,

NMR, and mass spectra were obtained for all compounds, and elemental analyses for those not previously reported.[10]

Diethyl 2-Propenyl Phosphate (I):[1] yield 47%; bp 64° (0.9 Torr); mass spectrum, parent peak m/e 194 (25%), base peak m/e 99.

Diethyl 1-Cyclohexenyl Phosphate (II):[9] yield 35%; bp 105° (0.15 Torr); mass spectrum, parent peak m/e 234 (54%), base peak m/e 99.

Diethyl 1-Cyclopentenyl Phosphate (III): yield 78%; bp 83° (0.09 Torr); mass spectrum, parent peak m/e 220 (33%), base peak m/e 137. Anal. Calcd for $C_9H_{17}O_4P$: C, 48.88; H, 7.85. Found: C, 49.09; H, 7.73.

Diethyl 1-Cycloheptenyl Phosphate (IV): yield 78%; bp 80° (0.01 Torr); mass spectrum, parent peak m/e 248 (40%), base peak m/e 155. Anal. Calcd for $C_{11}H_{21}O_4P$: C, 53.56; H, 8.53. Found: C, 53.23; H, 8.47.

Diethyl α-Styryl Phosphate (V): yield 39%; bp 106° (0.04 Torr); mass spectrum, parent peak m/e 256 (37%), base peak m/e 106. Anal. Calcd for $C_{12}H_{17}O_4P$: C, 56.06; H, 6.78. Found: C, 56.21; H, 6.64.

General Synthesis of Diethyl Alkyl Phosphates. To 0.12 mol of the alcohol in 100 ml of dry benzene was added slowly 0.1 mol of sodium hydride (ether washed) and the solution was stirred for 2 hr. To this was added dropwise 0.1 mol of diethyl phosphorochloridate and the reaction mixture was stirred for several hours. There was then added 50 ml of pentane, causing precipitation of the salt, which was filtered with suction. The solvent was removed at reduced pressure and the residual phosphate was vacuum distilled. Yield and analytical data are given below for each compound.

Diethyl Cyclohexyl Phosphate (VI):[11] yield 45%; bp 103° (0.65 Torr); mass spectrum, parent peak m/e 236 (1%), base peak m/e 155.

Diethyl Benzyl Phosphate (VII):[12] yield 25%; bp 101° (0.8 Torr); mass spectrum, parent peak m/e 244 (67%), base peak m/e 91.

Diethyl 2-Phenylethyl Phosphate (VIII):[12] yield 43%; bp 147° (0.25 Torr); mass spectrum, parent peak m/e 256 (3%), base peak m/e 106.

Diethyl 5-Pent-1-enyl Phosphate (IX): yield 16%; bp 85° (0.75 Torr); mass spectrum, parent peak m/e 222 (12%), base peak m/e 99. Anal. Calcd for $C_9H_{19}O_4P$: C, 48.65; H, 8.56. Found: C, 48.93; H, 8.64.

General Procedure for 1 Atm and 4 Atm Hydrogen Reactions. The reactors and experimental conditions for hydrogenation were as previously described.[3] For the analytical experiments the reaction flask was charged with 25 ml of absolute ethanol ca. 0.020 M in the compound to be investigated and ca. 0.020 M in a reference material for gas–liquid chromatographic (GLC) analysis. For the studies involving the isolation and identification of products the concentration of the reactant was increased to ca. 1 M.

Deuterium Incorporation Studies. All experiments using deuterium were performed at 1 atm pressure with solutions ca. 1 M in phosphate ester. The extent of deuterium incorporation was determined by collection of product or "unreacted" starting material using gas–liquid chromatography and its analysis by mass spectrometry. The resultant spectra were compared with those of the corresponding undeuterated materials.

Analysis. Gas–liquid chromatographic analysis (and preparative GLC) were performed using two columns: a 10 ft × 0.25 in. column of 20% Carbowax 20M on Chromosorb W was used for analysis of reactions of III whereas a 5 ft × 0.25 in. column of 20% Apiezon L on Chromosorb W was used for all other reaction sys-

tems. For quantitative analysis all products were compared for GLC relative response factors with a reference material; cyclohexane was used as the reference material for all reaction systems except those involving II and VI and the deuterium studies, where methylcyclohexane was used as the reference material.

All ir spectra were measured using a Perkin-Elmer Model 237-B spectrometer; NMR spectra were measured using a Varian EM360 spectrometer and mass spectra were measured using a Varian MAT CH-7 instrument.

Results and Discussion

The diethyl vinyl phosphates I–V were subjected to hydrogenation in ethanol solution over Adams catalyst at 1 and 4 atm pressure of hydrogen. The products and yields (as determined by GLC) are listed in Table I. With the exception of I, where a true quantitative determination could not be made owing to volitalization of the product from the reaction mixture, quantitative or near quantitative cleavage of the vinylic ester group was observed. This is interesting as it points to the extremely facile nature of the hydrogenolysis process as compared to other possible reactions, such as olefin reduction and hydrogen exchange (vide infra). With reaction systems of II–V attempts were made to observe and isolate cleaved olefinic intermediate; GLC collection of the entire region of expected elution was performed and the effluent subjected to mass spectral analysis. No olefinic material could be observed even under these extremely sensitive conditions of analysis. Changing to a saturated hydrocarbon solvent, useful in slowing the reduction of aromatics,[2,3] again proved unsuccessful. Either the free olefinic hydrocarbon *is not* an intermediate, *or* it is formed in only low concentrations and is reduced to the alkane with a high rate. Several experiments were performed to consider these possibilities.

First, in a consideration of the possibility of initial *reduction* of the vinylic phosphate, the fully saturated system VI was prepared and subjected to the identical conditions as used for II. After 1 week using conditions of 1 atm pressure of hydrogen, diethyl cyclohexyl phosphate exhibited *no* cleavage and could be recovered unchanged. After 1 week under conditions of 4 atm pressure of hydrogen only 5% cleavage (to cyclohexane) could be observed. From this it may be concluded that initial reduction of the vinylic ester followed by hydrogenolysis does not occur.

Second, in a consideration of the possibility of the free alkene being an intermediate, but present at any one time in only low concentration, evidence of an indirect nature was gathered. Several experiments were performed using deuterium in deuterated alcohol (CH₃OD, CD₃OD, CH₃CH₂OD) and cyclohexane solvents. In these solvents with Adams catalyst and deuterium it was observed that the alkenes to be considered as intermediates underwent significant deuterium incorporation *in excess* of that expected by addition to the olefinic linkage. That this deuterium-for-hydrogen exchange occurred with the *alkene* and not its reduction product was shown by further experiments of the same type with the alkane itself; within experimental error no deuterium incorporation could be observed for the fully saturated compounds under these reaction conditions. Thereby, were the product alkane (from vinylic phosphate cleavage with deuterium) to exhibit incorporation of more than *three* atoms of deuterium it *could* be indicative of alkene intermediacy. For compound II, studied in CH₃OD and CD₃OD solution, use of deuterium for the cleavage reaction resulted in formation of cyclohexane exhibiting various quantities of deuterium incorporation, up to *seven* atoms of deuterium in significant amount. Similarly, for compound IV, studied in cyclohexane solution, incorporation of up to seven atoms of deuterium in

Table I

$$(CH_3CH_2O)_2\overset{O}{\overset{\|}{P}}{-}OR \xrightarrow{H_2, \text{PtO}_2} (CH_3CH_2O)_2PO_2H + R'H$$

R	Compd	Yield R'H (24 hr reaction time),[a] %	
		1 atm H₂	4 atm H₂
	I	>15[b]	>6[b]
	II	97.6	100.0
	III	97.3	100.0
	IV	96.7	100.0
	V	5.6	100.0
		94.4	0
	VI	0[c]	5[c]
	VII	8.6	86.0
		60.0	<1
	VIII	No hydrocarbon product	
	IX	5.0	<1

[a] Yields as measured by GLC using a calibrated internal reference. [b] Quantities as determined by GLC; these represent minimum values as significant amounts of material are lost due to volatilization of product during isolation. [c] One week reaction time.

significant amount was observed in the cycloheptane product.

It is critical to note here that excess deuterium incorporation can only arise with the alkene itself or a cleaved alkene–catalyst complex; mass spectral analysis of unreacted vinyl phosphate ester after reaction was allowed to proceed to more than 20% completion showed within experimental error *no deuterium incorporation*. This constitutes firm evidence that the overall mechanism of reaction involves first hydrogenolysis of the vinyl ester linkage (without catalyst-mediated hydrogen exchange) yielding the phosphoric acid and the alkene followed by reduction of the alkene to the alkane accompanied by catalyst-mediated hydrogen exchange. It should again be noted that the alkene might not be "free" but rather associated at all times after generation, prior to reduction, with the catalyst surface upon which exchange occurs. To consider this problem, fundamental to studies of catalytic surface reactions, further competitive kinetic experiments are being designed.

The selective reactivity of the vinyl phosphate ester linkage is worthy of note; while it undergoes facile hydrogenolysis, compared to ordinary alkenes it is quite unreactive toward reduction and catalyzed hydrogen exchange. This interesting nature of the linkage is to be a topic of further investigation.

Several other points may be raised by these experiments with deuterium. First, as it appears that catalyst-mediated exchange of hydrogens (and possibly thereby isomerization) occurs with ordinary olefinic linkages under these conditions at a rate competitive with reduction, there exists the possibility that a "distant" olefinic linkage in an alkyl

phosphate ester might be induced to migrate to a position from which cleavage might occur. To test this possibility the diethyl 5-pent-1-enyl phosphate (IX) was prepared and subjected to the standard conditions of hydrogenolysis. Unlike the result observed with VI, also an alkyl ester, with IX it is found that cleavage to yield pentane does occur at 1 atm pressure of hydrogen, albeit to a relatively low extent (5%), the remaining material being the reduced phosphate ester; complete reaction is obtained within 6 hr. Only reduction is observed at 4 atm pressure of hydrogen over extended periods of time.

Moreover, these results raise questions concerning the required location of the site of unsaturation if cleavage is to occur. The capability of a vinyl phosphate ester to undergo cleavage *without* isomerization is shown by the hydrogenolysis of compound I and the lack of deuterium incorporation into the unreacted vinyl phosphate esters. This does not eliminate the possibility that a more distant olefinic site might also be subject to hydrogenolysis; allylic and benzylic phosphate linkages are subject to hydrogenolysis over palladium catalysts, and in the present effort have been found to be subject to cleavage over Adams catalyst as well. Efforts to investigate the nature of allylic and benzylic ester cleavage over Adams catalyst have not proven fruitful; with the ester linkage being primary or secondary they are capable of undergoing hydrogen exchange (and isomerization) both prior to and after hydrogenolysis yielding no data of significance (for the current question) from their cleavage with or without deuterium. Tertiary esters would be unsatisfactory as they cleave by other routes.[13]

Summary

Vinyl phosphate esters undergo hydrogenolysis over Adams catalyst to yield the phosphoric acid and the alkene, the latter being reduced to the alkane. Olefinic linkages in other positions can undergo migration to the vinylic (or allylic) site by hydrogen exchange on the catalytic surface; once the site of unsaturation is in the vinylic ester position no further hydrogen exchange occurs. Benzylic, but not homobenzylic, phosphate esters also undergo hydrogenolysis over Adams catalyst.

References and Notes

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Addition of Trichloroacetic Acid to 8-Methylcamphene

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The reaction of 8-methylcamphene (5) with haloacetic acids gives a mixture of isobornyl esters which on hydrolysis followed by dehydration with phosphorus oxychloride in pyridine affords a mixture of 8-methylcamphene (5), 9-methylcamphene (8), and 10-methylcamphene (7). Authentic samples of 8-methylisoborneol (15) and 10-methylisoborneol (19) on dehydration with phosphorus oxychloride in pyridine gave 10-methylcamphene (7) and 8-methylcamphene (5), respectively, demonstrating that dehydration occurs by way of a Wagner–Meerwein shift without the intervention of 3,2-alkyl shifts.

The facile and sequential conversion of 8-camphenecarboxylic acid (1) to lactone 2, endo lactone 3, and exo lactone 4[2] led us to investigate the action of acids on 8-methylcamphene (5) in order to determine whether similar alkyl shifts would provide a simple entry to the β-santalene ring system.[3]

A mixture of 8-methylcamphenes 5 and 6[4] was obtained in 36% overall yield by the sequence shown in Chart I. Gas chromatographic analysis indicated the presence of *anti*-5 and *syn*-6 in a ratio of 93:7.[5]

The action of stannic chloride on 5 and 6 gave recovered starting material or polymer depending on conditions, while sulfuric acid produced polymers. Oxalic acid or cupric acetate in acetic acid[6] gave no rearrangement,[7] while pyruvic acid at 160° for 6 hr afforded 7% of isomerized olefins.[7] Subsequent to the completion of this work Vaughan[8]

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