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Contribution of Ring Strain and the Stereoelectronic Effect to the Hydrolysis of Cyclic Five-Membered Ring Phosphorus Esters

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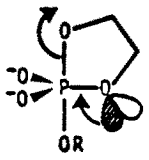
ABSTRACT

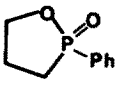
The rate of base catalyzed hydrolysis of cyclic five-membered ring 2-oxo-2-phenyl-1,2-oxaphospholan, 1, and 2-oxo-2-phenyl-1,3,2-dioxaphospholan, 2, and their acyclic analogues ethyl ethylphenylphosphinate, 3, and diethyl phenylphosphonate, 4, were measured. The cyclic ester 1 hydrolyzes 6.2×10^3 times faster than 3, corresponding to an activation free energy difference of 5.2 kcal/mol. This provides a good estimate of the magnitude of ring strain in these cyclic esters. In contrast, cyclic ester 2 hydrolyzes 1.5×10^6 times faster than its acyclic analog 4, corresponding to an activation free energy difference of 8.4 kcal/mol. This later energy difference is thought to be derived from both a ring strain effect (~ 5.2 kcal/mol) and a stereoelectronic effect (~ 3.2 kcal/mol).

INTRODUCTION

The rate of base catalyzed hydrolysis of cyclic five-membered ring phosphorus esters methyl ethylene phosphate and methyl propylphostonate is known to be about 10^6 and 3×10^5 (corresponding to an activation free energy difference of 8.0 - 8.5 kcal/mol) faster than that of their acyclic analogues, respectively.[1,2] The large rate enhancement for hydrolysis of cyclic esters has been previously attributed mainly to the relief of ring strain in forming a pentacovalent trigonal bipyramidal phosphorane transition/intermediate.[1,2] However, the origin of this large rate difference has been the subject of much debate.[1, 3-7] This is largely because the measurement of enthalpic strain is sill uncertain, ranging from 7 to 9 kcal/mol in an earlier report[8] and 5.5 kcal/mol for a later report.[9] By using the latter value, Westheimer and coworkers[3] had suggested that release of ring strain in forming a trigonal bipyramid (tbp) phosphorane intermediate accounted at most for 5 - 6 kcal/mol out of the 8.5 kcal/mol difference in activation free energy between the base catalyzed hydrolysis of methyl ethylene phosphate (MEP) and that of trimethyl phosphate. (The difference in energy of activation is comparable - about 7.5 kcal/mol[2b]). Furthermore, as Gerlt et al. pointed out[3], in the case of the cyclic diester, ethylene phosphate, which hydrolyzes 10^8 times faster than its acyclic analog, a ring strain argument could not be used to explain why the five-membered ring cyclic transition state/intermediate was still nearly 6 kcal/mol lower in energy than that of the equally strain free acyclic pentacovalent transition state.

In the cyclic triester transition state, however, the two lone pairs on the basal ring oxygen (assumed sp_3 hybridized) are oriented partially antiperiplanar (app) to the apical ring ester bond leaving group. Based upon a series of molecular orbital calculations, our laboratory has earlier[10-12] suggested that this app lone pair orientation could significantly facilitate P-O ester bond cleavage and that proper orbital overlap (stereoelectronic effect)[13,14] could be responsible for a significant lowering of transition state energies.





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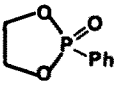

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Thus, we have prepared 2-oxo-2-phenyl-1,2-oxaphospholan, 1, and 2-oxo-2-phenyl-1,3,2-dioxaphospholan, 2 and their acyclic analogues ethyl ethylphenylphosphinate, 3, and diethyl phenylphosphonate 4, and measured the rates and activation parameters of their alkaline hydrolysis, hoping to pinpoint the magnitude of the ring strain effect and the stereoelectronic effect in related systems.

RESULTS

Product Study. All compounds 1 - 4 were hydrolyzed in 0.001 - 0.5 M NaOH, 50% aqueous dioxane and monitored by ^{31}P NMR as described previously[15]. The products were established by comparison of the ^{31}P chemical shifts with literature chemical shifts[16,17] or the chemical shift of hydrogen ethyl phenylphosphonate derived from the hydrolysis of diethyl phenylphosphonate under the same condition. All yielded the expected P-O cleavage product.

Kinetic data. The rate of hydrolysis of 1-4 was followed by UV spectroscopy, unless otherwise noted. The data is collected in Table I. Each run was repeated at least twice and the rate constants were calculated on a PDP-11 computer using a nonlinear least-squares analysis of the data.

Activation Parameters. The activation parameters for hydrolysis of 1 - 4 were calculated from the temperature dependence of the rate constants and collected in Table II.

Table I. Second-Order Base Catalyzed Rate Constants for Hydrolysis of 1-4 at 25.4 °C in 50% dioxane/water (v/v).

Compound	k_2, $mol^{-1}\ s^{-1}$	k_c/k_a([a])
1	0.659	6.2×10^3
2	109.0	1.5×10^6
3	0.000105	
4	0.0000718	

[a] rate constant ratio for cyclic (k_c) and acyclic (k_a) esters

Table II. Activation Parameters for the Base-Catalyzed Hydrolysis of 1-4.

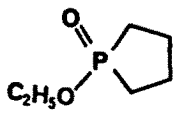
compd.	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, e.u.	$\Delta S_c^{\ddagger} - \Delta S_a^{\ddagger}$([a])
1	4.2 ± 0.7	-45.4 ± 2	-7.3
2	3.6 ± 0.8	-37.2 ± 3	+8.2
3	11.5 ± 0.5	-38.1 ± 1	
4	9.6 ± 0.8	-45.4 ± 2	

[a] Entropy of activation difference between cyclic (c) and acyclic compounds (a) in e.u.

DISCUSSION.

Previous Studies. Phospholan 1 was previously prepared by Mathey and Thavard[18] and Singh[19] by a different method; however, kinetics for its hydrolysis were not reported. 2 was previously synthesized by Revel and Navech[20], but again kinetics for its hydrolysis were not given.

Rate Enhancement of Cyclic Five-membered Ring Phosphinates. Cyclic five-membered ring phosphinates, except a highly strained bicyclic system,[21] hydrolyze at a comparable rate to their acyclic analogues[1,22]. For example, 5 hydrolyzes in base only 2 - 4xfaster than the corresponding acyclic analogue 6[22].



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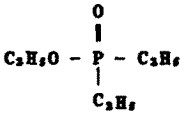

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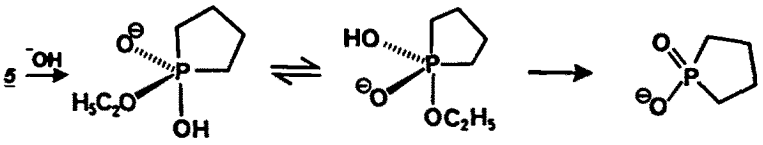
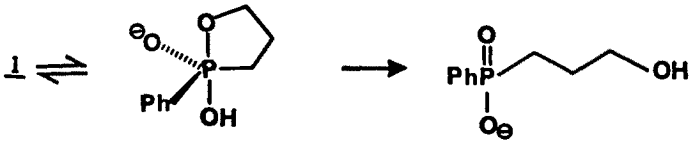
This difference was elegantly explained by Westheimer and coworkers[1,22] by assuming that hydroxide attack on 5 forms a pentacovalent tbp intermediate 7, which places the five-membered ring in an apical-equatorial position to release the ring strain energy of such a five-membered ring. (Discussed further below). However such an intermediate violates the "electronegativity rule," whereby an electropositive atom such as the ring carbons prefer the equatorial position of a trigonal bipyramid phosphorane[1,23,24].



7 8

In the reaction of 5, pseudorotation[1] of 7 then yields 8, which expels the ethoxy group from an apical position. (According to the principle of microscopic reversibility, apical attack at tetracoordinated phosphorus will be accompanied by apical leaving[1] from the phosphorane.) Apparently, the energy gained in release of ring strain in forming 7 or 8 is largely counterbalanced by the loss in energy associated with the resultant placement of the alkyl group in an axial position, and as a result a "normal" hydrolysis rate is observed[1,2].

This is not the case, however, in the hydrolysis of cyclic five-membered ring cyclic phosphinate 1. As shown in Table I, phosphinate 1, with the P-O ester bond incorporated into the ring, hydrolyzes in base 6.2 x 10^3 faster than the corresponding acyclic analogue 3. This, of course, is predictable based upon the general preference rules governing nucleophilic attack at tetracoordinate phosphorus, i.e., in forming the tbp intermediate, a five-membered ring tends to span the ring in an apical - equatorial position (to release the ring strain), 9 and



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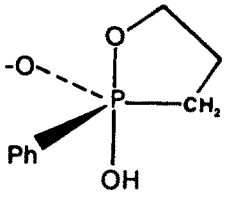
the more electronegative ligand will prefer to seek an apical position (apicophilicity rule)[1,23-25]. Thus, in 1 the release of ring strain is fully achieved without violation of the apicophilicity rule and a significant rate enhancement is observed.

Estimation of Ring Strain Contribution to Rate Acceleration. The enthalpies of hydrolysis of ethylene phosphate and diethyl phosphate, as indicated by Gerlt et al[3], are 6.4 kcal/mol and 1.8 kcal/mol respectively. The difference in the enthalpic energy is thus only 4.6 kcal/mol of strain in the cyclic five-membered ring phosphodiesters. Unfortunately sufficiently accurate thermochemical measurements of ring strain in five-membered ring phosphate triesters are unavailable. In methyl ethylene phosphate, reported enthalpic strain varies between 7 to 9 kcal/mol in an earlier report[26,27] and 5.5 kcal/mol[9] for a later report.

In this ethylene phosphate diester five-membered ring system the 4.6 kcal/mol of ring strain is insufficient to explain the total 10^8 fold rate acceleration relative to its acyclic analog (corresponding to an activation energy difference of 10-11 kcal/mol).[3] We suggested that much of the 6 kcal/mol difference in energies of the acyclic vs. cyclic transition states could be attributed to a stereoelectronic effect[10-12]. In the triester five-membered ring system, the situation is not as clear. Methyl ethylene phosphate hydrolyzes 10^6 (from ref 28) and ethyl ethylene phosphate 2×10^7 (from ref 29) times faster than their acyclic analogues, corresponding to 8.3 - 10 kcal/mol difference in activation energies. Because estimated ring strain is as high as 9 kcal/mol, it could be responsible for essentially all of the rate enhancement for hydrolysis of methyl or ethyl ethylene phosphate. If this is the case, a stereoelectronic effect would not need to be invoked in order to explain the rate acceleration.

Hydrolysis of 1 and 2 in base, however, potentially provides a good test for the relative importance of ring strain and the stereoelectronic effect contributions to the rate accelerations in these systems. Both 1 and 2 will presumably form tbp phosphorane intermediates 9 and 10, respectively.



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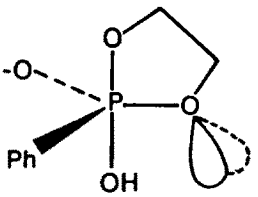

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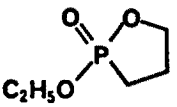

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However, there are no basal ring oxygen lone pairs in 9 to participate in a stereoelectronic effect aiding in the expulsion of the leaving group. The rate difference in the catalyzed base hydrolysis between 1 and 3 thus could provide a good estimate for ring strain effects alone. (However, see below for a possible complication in this analysis.) Hydrolysis of 2 will presumably reflect both ring strain and the stereoelectronic effect. Significantly, the difference in rate between 1 and 3 is 6.2×10^3, corresponding to an activation free energy difference of 5.2 kcal/mol. This is comparable to the reported ring strain value, 5.5 kcal/mol obtained from a measurement of the heat of hydrolysis of methyl ethylene phosphate by Kaiser et al.[9] It is also comparable to the ring strain estimate in ethylene phosphate[3].

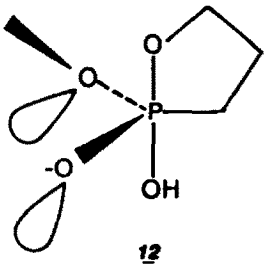
The ring strain will consist of both angle strain and eclipsing strain. The relief of eclipsing is presumably less important because in the ground state the cyclic five-membered ring could principally pucker at any ring atom. In fact the 3,3-dimethyl substituted analogue of 1 is known to exist in a conformation puckered at ring oxygen in solution, and at C-3 carbon in the solid state[19]. X-ray analysis shows methyl ethylene phosphate (MEP) puckers at ring carbon[30]. In methyl ethylene

phosphate, x-ray analysis[30] has shown the O-P-O bond angle to be 99°. This appears to be typical for five-membered ring phosphorus compounds in contrast to acyclic tetracoordinate phosphorus compounds. Therefore we can assume that there is ~ 10° of bond angle strain in 1 and 2 as in the case of methyl ethylene phosphate. Furthermore, the preferred O-P-O angle in the tbp transition state in five-membered rings is about 90°[1,23,24]. Using angle-bending force constraints, Usher et al.[31] calculated a relief of ring strain of 3 - 6 kcal/mol associated with the formation of a tbp intermediate in agreement with the experimental value.

Estimation of Stereoelectronic Effect. With a more confident value, 5.2 kcal/mol of ring strain in hand, one can estimate the contribution of the stereoelectronic effect to the rate acceleration in five-membered ring phosphate esters.

The rate difference in base hydrolysis between 2 and 4, 1.48×10^6, corresponds to a difference in free energy of activation of 8.4 kcal/mol. This is a comparable rate acceleration to that of MEP and suggests that the phenyl ring does not contribute any unusual steric energy to the system. Assuming the value of ring strain in dioxa and oxa phospholan 2 and 1 is nearly the same, one can subtract the ring strain effect, 5.2 kcal/mol, leaving a value of 3.2 kcal/mol extra stabilization of the cyclic vs. acyclic transition states unexplained if ring strain arguments alone are used. As suggested by Gerlt et al.,[3] this extra stabilization may be a result of solvation differences on the reactants and transition states. Alternatively, Verkade[32] had proposed that the amount of π bonding between the phosphorus atom and the ester oxygen could be less in the cyclic than in the acyclic esters. This effect would be diminished in the transition state although no satisfactory explanation for the observed behavior can be substantiated at present. We would like to suggest that the stereoelectronic effect is responsible for this 3.2 kcal/mol difference.

The one remaining complication in this analysis which cannot be entirely discounted is the possibility that eclipsing interaction differences casts in doubt our assumption that ring strain effects in 1 and 2 are comparable. It is certainly possible that eclipsing interactions in P-CH_2CH_2- are greater in the cyclic transition state for hydrolysis of 1 than in the acyclic transition state for hydrolysis of 3. However, ethyl propylphostonate 11 hydrolyzes in base 3×10^5 times faster than its acyclic analog[29]. Because this is comparable to the rate acceleration in MEP (10^6), ethyl ethylene phosphate (2×10^7) and 2 (1.5×10^6), eclipsing interactions resulting from substitution of the ring oxygen by a methylene appear to be minor. In fact, it is rather surprising that the rate acceleration for hydrolysis of the phostonate is nearly as great as that of MEP if our arguments about the significance of the stereoelectronic effect are correct. Obviously, as in 1 phostonate 11 does not have an app lone pair on a ring atom to stereoelectronically aid in expulsion of the endocyclic P-O ester bond (the phostonate proceeds with complete endocyclic cleavage in keeping with the pseudorotation rules of Westheimer[1]). An important difference between phosphinate 1 and phostonate 11 is the potential availability of an electron lone pair on the exocyclic alkoxyl oxygen in the latter. In the transition state 12 for cleavage of the endocyclic ester bond in the hydrolysis of 11, two lone pairs in 12 can be



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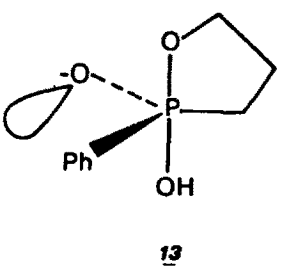

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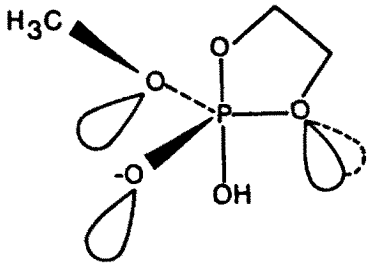
oriented app to the apical P-O bond, while in 13 there is only one lone pair on the basal oxyanion

to stereoelectronically assist in cleavage of the apical bond. As demonstrated by Deslongchamps[14], there appears to be a leveling effect on the magnitude of the stereoelectronic acceleration afforded by increasing numbers of app lone pairs. Two lone pairs will likely be nearly as effective as three and thus in the transition state 14 for hydrolysis of methyl ethylene phosphate, the third lone pair may be unnecessary. This could explain why phostonate 11 and methyl ethylene phosphate hydrolyze 3 x 10^5 and 10^6 times faster than their acyclic analogues, respectively, while cyclic phosphinate 1 hydrolyzes only 6.2 x 10^3 times faster than its acyclic analog. Note that the k_c/k_a rate ratio for ethyl ethylene phosphate is 70 times larger than the rate ratio for ethyl propylphostonate[29]. This could be a reflection of eclipsing interaction differences or a real measure of a stereoelectronic effect. This analysis, of course, is entirely speculative, and it is not very profitable to push it much further.



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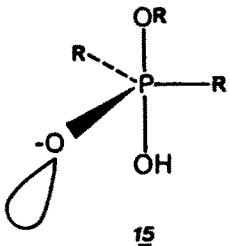

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Activation Parameters. We have earlier pointed out that much of the kinetic acceleration in the hydrolysis of five-membered ring cyclic esters is entropically derived and could be a reflection of a stereoelectronic effect[10-12]. In the cyclic ester the lone pairs on oxygen are already "frozen" in the proper geometry, while in an acyclic ester freezing two rotational degrees of freedom about the two basal ester bonds in the transition state is required to obtain a proper orbital overlap. Thus in 2 and 4 the difference in entropy of activation, +8.2 e.u. (Table II), accounts for ~ 10^2 (2.5 kcal/mol) of the rate acceleration for the cyclic ester. Most significantly, the entropy of activation for cyclic phosphinate 1 is 7.3 e.u. more negative (Table II) than the entropy of activation for its acyclic analog 3. Obviously there is no stereoelectronic advantage to constraining the conformation about the P-C bonds in the acyclic transition state 15. It is presumably the stereoelectronic requirement to constrain the conformation about P-O bond in 15 so as to orient the oxygen lone pair app to the leaving group that is responsible for the unfavorable 8.2 e.u. entropy of activation difference in 1 and 3. Jencks[33] has previously demonstrated that restriction of rotation about a single bond indeed is entropically unfavorable by as much as 8 e.u. Also, in acyclic analogues 3 and 4, the rate of hydrolysis is essentially the same; however, the entropy of activation for 4 is 2 kcal/mol less favorable than 3. This is compensated by an enthalpic, presumably stereoelectronic advantage of ca. 2 kcal/mol. Indeed in numerous instances in acyclic and six-membered ring systems[10-14,34,35], the stereoelectronic effect may be masked by this trade-off between enthalpic and entropic energy contributions.

CONCLUSION

Thus, we believe we have been able to isolate the effect of ring strain in the hydrolysis of cyclic five-membered ring phosphorus esters. The magnitude of the ring strain effect is likely to be in the range of 4 - 6 kcal/mol for related cyclic five-membered rings. One of the early reported values for ring strain, of ca. 8.5 kcal/mol, appears to be too high compared to our analysis and other reports. There may well be a ca. 3 kcal/mol stereoelectronic effect in the cyclic five-membered ring phosphorus ester systems. It seems quite reasonable that as demonstrated in the accompanying paper, there could well be a 3 kcal/mol stereoelectronic effect for the base catalyzed hydrolysis of methyl ethylene phosphate relative to its acyclic analogue.

EXPERIMENTAL SECTION:

^{31}P NMR were recorded on a Bruker WP-80 spectrometer at 32.4 MHz NMR, and ^1H NMR on a 60 MHz Varian A-60 or EM-360 spectrometers. Chemical shifts in parts per million for ^1H spectra are referenced to

internal Me_4Si and for ^{31}P NMR are referenced to external 85% H_3PO_4. Infrared spectra were obtained on a Perkin Elmer spectrometer. Mass spectra were obtained on an AEI MS-30 spectrometer. Melting points were taken on a Thomas-Hoover apparatus and uncorrected.

Chemicals were generally of highest purity. Baker analyzed 60-200 mesh silica gel was used for chromatography after being activated at 130 °C overnight. Triethylamine, phenyl phosphonic dichloride, and ethylene glycol were distilled before use.

2-oxo-2-phenyl-1,2-oxaphospholan, 1. To a stirred solution of 0.05 mol (9.0 g, 6.8 mL) phenyl dichlorophosphine and 0.05 mol of triethyl amine in 50 mL of anhydrous ether, 0.05 mol (3.8 g, 3.6 mL) of 1,3-propanediol in 40 mL of ether was added dropwise with cooling in ice and under a nitrogen atmosphere. After the addition, the reaction mixture was allowed to stir for another 1 h. The amine salt was then filtered off and the filtrate was concentrated in vacuo to give a slightly yellow liquid. P-31 NMR ($CDCl_3$, 155.6 ppm; lit.[19]: 152.8 ppm). Without further purification, the crude product was heated neat under reflux at 150 °C under a nitrogen atmosphere overnight. After cooling to room temperature, the residue was extracted with chloroform (x2 100mL). The ^{31}P NMR of crude product showed mainly two peaks at 57.8 and 14.8 ppm. This was distilled (0.1 mm, 142 °C) and chromatographed (85:10:5 of EtOAc-hexane-MeOH) to give a pure colorless liquid, 1 (yield: 40%). ^{31}P ($CDCl_3$: 57.7 ppm (lit[19]: 58.7 ppm). ^{13}C NMR ($CDCl_3$): 24.05 9d, J_{PC} = 82.1 Hz), 27.76, 70.53 (d, J_{POC} = 4 Hz), 128.34, 129.03, 131.12, 131.76, 132.63. ^1H NMR ($CDCl_3$): 1.70-2.8 (m, 4H, $-CH_2CH_2P$), 4.0-4.9 (m, 2 H, OCH_2), 7.2-8.1 (m, aromatic, 5H).

2-oxo-2-phenyl-1,3,2-dioxaphospholan, 2. To 0.02 mol (2.82 mL) of phenyl phosphonic dichloride in 50 mL of anhydrous ether, 0.02 mol (1.08 mL) of ethylene glycol and 0.04 mol of triethyl amine was added dropwise over 1 h. The reaction mixture was allowed to stir for another 1 h. Then the amine salt was filtered off and the filtrate was concentrated in vacuo to give a colorless liquid. The ^{31}P NMR ($CDCl_3$) of crude product showed mainly one peak at 36.1 ppm (lit.[20]: 36.0 ppm). After column chromatography, the product crystallized during storage at 4°, which was recrystallized from chloroform/petroleum ether to give a white granular crystal, m.p. 53 - 55°. ^{13}C NMR ($CDCl_3$): 66.59 (2C), 122.41, 129.19, 131.91, 132.10, 132.41. ^1H NMR ($CDCl_3$): 4.55 (distorted AB, m, 2H, CH_2), 4.70 (distorted AB, m, 2H, CH_2).

Ethyl ethylphenylphosphinate, 3. To 0.03 mol of phenyl phosphonous dichloride in 20 mL of anhydrous ether, a solution of 0.06 mol of absolute ethanol and 0.06 mol of pyridine in 40 mL of ether was added dropwise at 0 - 5° over 1 h. The resulting mixture was allowed to stir for another 1 h. Then the amine salt was filtered off and the filtrate was concentrated in vacuo to give a crude phosphonite, ^{31}P NMR: 153.9 ppm. The crude phosphonite was used without further purification for the following reaction. Thus, the crude phosphonite with a catalytic amount of EtI in xylene was heated under reflux under a N_2 atmosphere. The reaction was monitored by ^{31}P NMR until all the phosphonite disappeared. The solvent was removed by distillation and the residue was chromatographed to give a colorless liquid. ^{31}P NMR ($CDCl_3$): 43.8 ppm; ^1H NMR($CDCl_3$): 0.96 (t, J = 7 Hz, 3H, CH_3), 1.95 doublet of quartets, J = 7 Hz, J = 14 Hz, 2H, PCH_2), 3.95 (m, 2H, OCH_2), 7.35-8.15 (m, 5H, aromatic).; IR ($CDCl_3$) 3700, 3640, 3400, 2940, 2400, 1510, 1440, 1220, 1122, 1043 cm^{-1}. (Lit[37]: bp 140° C (10mm)). Diethyl phenylphosphonate, 4. To an ice cooled solution of 20 mL of absolute ethanol and 10 mL of pyridine, 0.04 mol (5.6 mL) of phenyl phosphonic dichoride was added dropwise with vigorous stirring and under a N_2 atmosphere. The reaction mixture was mixed with ethyl acetate to precipitate out the pyridinium salt. The salt was then filtered off and the filtrate was poured into 30 mL of water and extracted with chloroform (30 mL x2). The organic layer was washed with anhydrous $MgSO_4$ and concentrated in vacuo to give a colorless liquid. ^{31}P NMR ($CDCl_3$): 18.7 ppm (lit[38]: 16.9.; ^1H NMR ($CDCl_3$): 1.32 (t, J = 7 Hz, 6H, CH_3), 4.16 (quintet, J_{POCH} = 7 Hz, J = 7 Hz, 4H, OCH_2), 7.30-8.20 (m, 5H, aromatic).; IR ($CDCl_3$): 2950, 2300, 1510, 1430, 1210, 1110, 1010.; MS, m/e: 214 (2.8), 157.3 (76.3), 141.4 (38.9), 140.4 (68.4), 92.6 (20.6), 76.6 (32.4), 31.9 (32.1).

Recyclization of 1-hydroxylpropylphenylphosphinic acid. To a solution of 0.3 g of 1-hydroxylpropylphenylphosphinic acid and 1 mL of pyridine in 3 mL of $CHCl_3$, 0.8 g of toluene sulfonyl chloride was added all at once. The reaction was immediately monitored by ^{31}P NMR and showed mainly the cyclized product at 56.9 ppm.

Kinetic Studies. Kinetic measurements were carried out on a Cary 210 UV-visible spectrophotometer equipped with an automatic sample changer. The cells were maintained at a constant temperature by means of a thermostated cuvette holder. Time vs. absorbance data were taken and then calculated by a PDP 11/03 computer. The pseudo first order rate constant, k_{obsd}, was determined by an iterative, nonlinear least squares computer program. Occasionally, the computer generated rate constant was checked against the slope of a $\ln(A_\infty - A_0)$ vs. time plot. Reactions were followed for at least 3 half lives. With this data the computer program would iteratively fit the rate constant, initial A_0, and final, A_∞ absorbance. The calculated and observed A_∞ generally agreed to within 3%.

Reactions were followed at wavelengths ranging from 260 - 275 nm. Temperature control ranged from 9.5 - 66.3 °C. All of the hydroxide reactions on the esters gave good first-order kinetics. Duplicate runs generally agreed within 3%. Unless otherwise specified, kinetic runs were carried out in 50% dioxane/water (V/V). Activation parameters were also calculated by an iterative non-linear least squares program. Errors are linear estimates of the standard deviations[18].

Product Study of Alkaline Hydrolysis. Product analysis was made by ^{31}P and ^1H NMR and confirmed by recyclization of the hydrolysis product of 2.

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