ethyl)phosphonic acid (1.05 mmol) was added to a solution of the *dried* steroid (1.0 mmol) in anhydrous dichloromethane (20 mL). Diisopropylethylamine (2.1 mmol) was added (via syringe) to the well-stirred mixture. The homogeneous solution was kept for 15 h at 20 °C (in the dark, in the case of a conjugated di- or triunsaturated steroid). The solvent was evaporated, and the residue was triturated with ether (3 × 15 mL) to remove the α-bromostyrene byproduct and any unreacted steroid. The residual fine powder was dried for a few minutes at 20 °C (0.5 torr). This trialkylammonium phosphate salt was dissolved in a 2:1 v/v chloroform/methanol mixture (45 mL). The solution was treated with 3:48:47 v/v chloroform/methanol/1 N aqueous HCl reagent (15 mL) in order to liberate the free phosphoric acid under the mildest conditions. The two-phase system was stirred for a few min. The lower organic phase was separated and resubmitted to the same acidification procedure. Finally the lower organic phase was washed (twice) with a 3:48:47 v/v chloroform/methanol/water mixture (10 mL). The organic phase was evaporated at 20 °C (1 torr), and the residue was triturated with ether (10 mL) to remove any unreacted steroid that may have remained as contaminant. The steroid phosphate was dried at 20 °C for 6 h (0.5 mm). TLC and ^{31}P NMR spectroscopy disclosed that the steroid phosphates thus obtained were of at least 97% purity. The nonconjugated unsaturated compounds were recrystallized (cf. Table I) without significant changes in physical properties. The conjugated unsaturated compounds were submitted to ultraviolet absorption spectrometry and elemental analysis without crystallization. The presence of two very weak ^{31}P NMR signals at about −11 ppm (to high field from 85% H_3PO_4) that are observable in some of the steroid phosphate samples are attributable to trace amounts of sterol pyrophosphates formed in a secondary reaction.

The reaction time was reduced to 8 h in the synthesis of the labile $\Delta^{5,7,9}$-cholestatriene 3β-*O*-phosphate (**4**). Testosterone phosphate (**7**) is relatively hydrophilic; therefore, minimum volumes of the acidification reagent and the washing mixture were employed in its isolation.

Acknowledgment. This research was supported by the National Institutes of Health (Grant GM 20672).

Registry No. 1, 4358-16-1; **2**, 85135-01-9; **3**, 84284-80-0; **4**, 85135-02-0; **5**, 85135-03-1; **6**, 24352-60-1; **7**, 1242-14-4; cholesterol, 57-88-5; epicholesterol, 474-77-1; $\Delta^{5,7}$-cholestadien-3β-ol, 434-16-2; $\Delta^{5,7,9}$-cholestatrien-3β-ol, 51982-45-7; stigmasterol, 83-48-7; ergosterol, 57-87-4; testosterone, 58-22-0; $\Delta^{5,7,9}$-cholestatrien-3β-ol acetate, 1255-91-0; (1-phenyl-1,2-dibromoethyl)phosphonic acid, 85135-04-2.

Reactions of Oxaphospholenes. 2.[1] Hydrolysis of Neopentyl Esters, Phenyl Esters, and Amides

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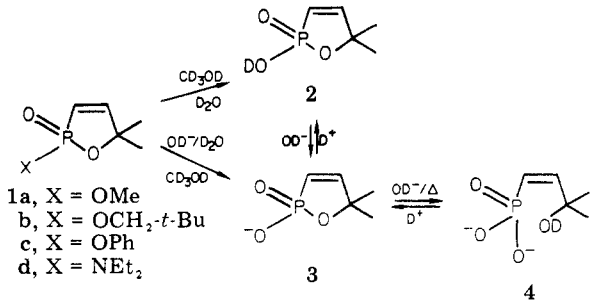
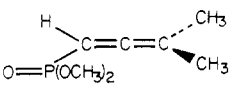
The neopentyl (**1b**) and phenyl (**1c**) esters of 2-hydroxy-5,5-dimethyl-1,2-oxaphosphol-3-ene 2-oxide (**2**) as well as the corresponding diethyl amide (**1d**) were synthesized, and their hydrolytic behavior was examined. Comparisons were made with the hydrolytic behavior of the methyl ester **1a** and allenic phosphonate **5**. The hydrolyses of **1a–c** in initially neutral aqueous methanol exhibited autocatalytic kinetics owing to acid catalysis by hydrolysis product **2**. Amide **1d** hydrolyzed only in the presence of added acid catalyst; allene phosphonate **5** was inert to both neutral and acidic conditions. The hydrolyses of **1b–d** in basic aqueous methanol proceeded via ring-opened intermediates **8b–d**, which then reclosed to the conjugate base of **2**. Phosphonate **5** lost only one methyl group during basic hydrolysis, but it simultaneously underwent isotope exchange of the olefinic hydrogen.

We recently described[1] the hydrolytic behavior of oxaphospholene ester **1a**. In 50% aqueous methanol **1a** hydrolyzed to free acid **2** (which served to autocatalyze the reaction). Complete hydrolysis required 5.5 h at 68 °C, with <10% hydrolysis occurring after 18 h at 25 °C. By



contrast, **1a** was converted instantaneously to salt **3** in aqueous methanolic KOH. In both these reactions the oxaphospholene ring remained intact; i.e., hydrolysis occurred with exocyclic cleavage. Only when **3** was heated to 70 °C in the presence of excess hydroxide was endocyclic cleavage observed to give **4**. Because the reaction of **1a** with *methoxide* led to salt **3** in addition to degenerate transesterification, we surmised that the exocyclic hydrolyses (**1a** → **2** and **1a** → **3**) occurred at least in part by alkyl–oxygen cleavage; only with elevated temperatures or potent nucleophiles did products arise from attack at phosphorus (e.g., ring-opening via phosphoryl–oxygen cleavage). If our conclusions were correct, it should be possible by altering the alkoxy group in **1a** to suppress exocyclic alkyl–oxygen cleavage and activate exocyclic phosphoryl–oxygen cleavage. Exocyclic alkyl–oxygen cleavage should be eliminated sterically in the neopentyl ester **1b** and structurally (because of hybridization) in phenyl ester **1c**. Furthermore, the phenoxy group in **1c** should be a considerably better nucleofuge than either methoxy (**1a**) or neopentoxy (**1b**). We have now prepared these two phosphonate esters and examined their hydrolytic behavior. We have also examined phosphonamide **1d** and, for comparison's sake, dimethyl allenic phosphonate ester **5**.[3]

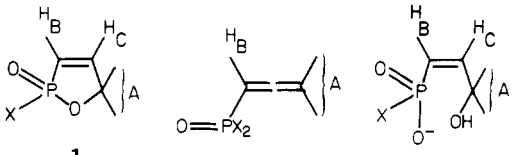


5

(1) Part 1: Macomber, R. S.; Krudy, G. A. *J. Org. Chem.* **1981**, *46*, 4038.

0022-3263/83/1948-1420$01.50/0

Table I. ^{1}H NMR Spectral Data for Compounds in This Study[a]



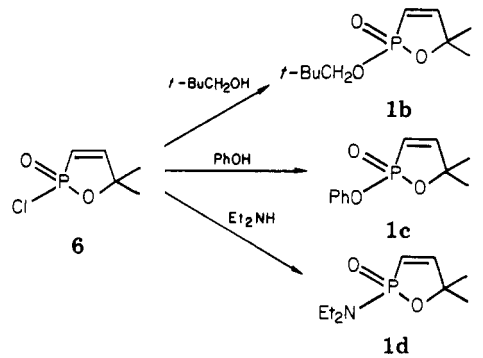
1 5 8

cmpd	X	H_A	H_B	H_C	H_X
1b	$OCH_2C(CH_3)_3$	1.50	6.17 (33, 8)	7.35 (49, 8)	0.92 (0), 3.67 (7)[b]
1c	OPh	1.03, 1.49	6.27 (34, 8)	7.27 (49, 8)	7.0-7.5 (m)
1d	$N(CH_2CH_3)_2$	1.45	5.94 (33, 8)	7.14 (47, 8)	1.07 (7), 3.00 (12, 7)[b]
5	OCH_3	1.79 (8, 3)	5.25 (m)		3.73 (11)
8b	$OCH_2C(CH_3)_3$	1.33	5.49 (11, 14.5)	6.31 (45, 14.5)	0.89 (s), 3.46 (5.5)
8d	$N(CH_2CH_3)_2$	1.33	*c*	*c*	*c*
5a	OCH_3, O^-	1.72 (6, 3)[d]	*d*		3.51 (11)

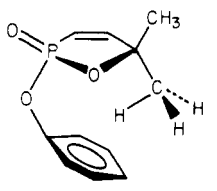
[a] δ in ppm downfield from DSS in 50:50 D_2O/CD_3OD;[6] coupling constants (in hertz) in parentheses. See ref 1 for spectra of 1a, 2, 3, 4, and methanol. [b] In D_2O/CD_3OD neopentyl alcohol exhibits C-H singlets at δ 0.87 and 3.20; diethylamine exhibits a triplet (J = 7 Hz) at δ 1.06 and a quartet (J = 7 Hz) at δ 2.58; diethylammonium ion shows a triplet (J = 7.5 Hz) at δ 1.28 and a quartet (J = 7.5 Hz) at δ 3.05. [c] Unable to determine because of presence of 1d and 3; see text. [d] See text regarding H/D exchange.

Results

Esters **1b** and **1c** were prepared from the corresponding acid chloride **6**[1] in pyridine. Amide **1d** was similarly prepared from **6** and diethyl amine in ether. It is interesting to note from their ^{1}H NMR spectra that the ring methyl groups are equivalent in **2** and **3** but nonequivalent in the esters and amide.[1,3,4] The chemical shift difference in CCl_4 follows the order **1a** ($\Delta\delta$ = 0.05 ppm) = **1b** (0.05) < **1d** (0.06) < **1c** (0.24). The exceptionally large chemical shift difference in **1c** can be ascribed to significant transannular shielding by the phenyl ring of the *Z* methyl group, as in conformation **7**. In methanol or 50% aqueous methanol this difference decreases to <0.02 ppm for **1a**, **1b**, and **1d** (each shows only a slightly broadened singlet), while it *increases* to 0.46 ppm for **1c**! This indicates that association of methanol with the phosphoryl group in **1a**, **1b**, and **1d** renders the methyls effectively equivalent, while the same association increases the proportion of conformation **7** in the case of **1c**. Such shielding is not nearly as important when the phenyl is directly attached to phosphorus.[5]



6 1b 1c 1d



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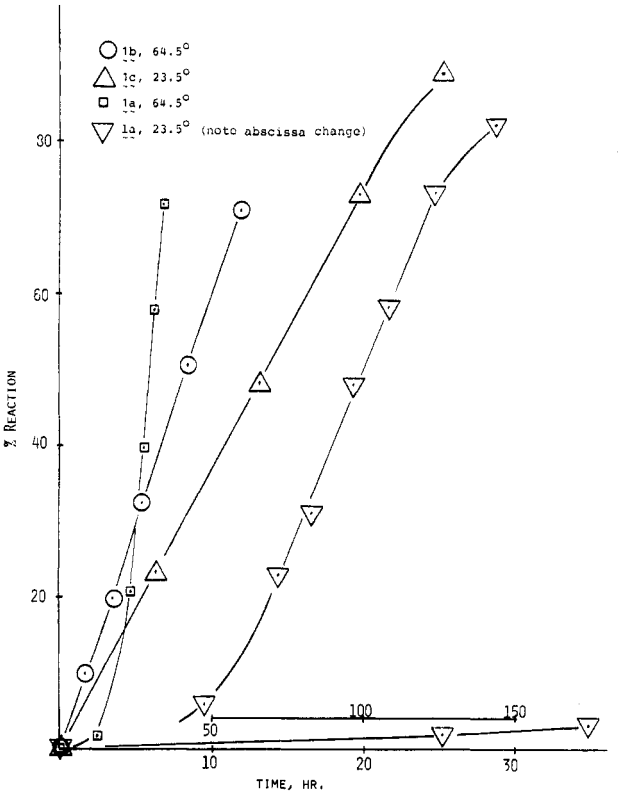


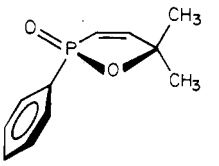
Figure 1. Percent hydrolysis of **1a**, **1b**, and **1c** in initially neutral 50% aqueous methanol as a function of time.

(2) Professor David Gorenstein has communicated his unpublished observation that reaction of **1a** with deuteriomethoxide in deuteriomethanol gave rapid formation of deuteriomethyl **1a** and slower formation of **3** and the trideuteriomethyl ether (25 °C).

(3) (a) Macomber, R. S.; Kennedy, E. R. *J. Org. Chem.* **1976**, *41*, 3191. (b) Krudy, G. A.; Macomber, R. S. *J. Org. Chem.* **1978**, *43*, 4556 and references therein.

(4) They are equivalent, however, in chloride **6**.[1]

(5) Compound i has $\Delta\delta$ = 0.10 ppm in CCl_4: Amer, M. Z., unpublished observation.



i

Table II. Rates and Rate Constants for the Hydrolyses of 1a-d and 5 in 50% Aqueous Methanol[6]

substrate	1a		1b	1c	1d	5
temp, °C	23.5	64.5	64.5	23.5	64.5	64.5
$[ester]_0$, M	0.49	0.61	0.46	0.53	0.30	0.51
rate,[a] M min^{-1}	7.3×10^{-5} [b]	2.4×10^{-3} [b]	4.6×10^{-4}	3.2×10^{-4}	[c]	[d]
$t_{1/2}$, h	101	6.0	8.4	13.2		
k_{uncat},[e] min^{-1}	1×10^{-5}	1×10^{-4}	1×10^{-4}	1×10^{-4}		
k_{cat},[e] M^{-1} min^{-1}	1.6×10^{-2}	1.5×10^{-1}	1.0×10^{-1}	6.2×10^{-2}	1.7×10^{-3} [f]	[g]

[a] Apparent zero-order rate. [b] Estimated from 10-80% completion. [c] No reaction detected after 25.3 h. [d] No reaction detected after 24.0 h. [e] $k_{obsd} = k_{uncat} + k_{cat}[H^+]$; see text. [f] Initial concentration of trifluoroacetic acid = 0.46 M. [g] No reaction detected after 20.3 h; initial concentration of trifluoroacetic acid = 0.74 M.

Each compound was subjected to the same series of solvolysis reactions;[6] first methanol, then neutral 50% aqueous methanol, and finally basic and/or acidic 50% aqueous methanol.

The reactions were followed by ^1H NMR, and the relevant parameters are given in Table I. As we found previously with **1a**,[1] compounds **1b**, **1d**, and **5** were completely unchanged after 24 h in methanol at 23.5 °C; **1c** was slowly converted to **1a**. In neutral 50% aqueous methanol,[6] esters **1b** and **1c**, like **1a**, hydrolyzed cleanly to **2** and the corresponding alcohol (phenol) without any detectable intermediates. In the concentration ranges studied, plots of percent hydrolysis vs. time (zero-order kinetics) were surprisingly linear for **1b** (correlation coefficient 0.9998) and **1c** (0.9993), as shown in Figure 1. Ester **1a** exhibited an upturn in rate, becoming nearly linear only after 10% reaction.[7] The phenomenological *rates* for these processes (Table II) show relative reactivity of **1b** (1.0 < **1a** (5.2) < **1b** (23). Because these pseudo-zero-order rates were somewhat sensitive to initial ester concentration as well as the concentration of added acids,[7] a more appropriate kinetic model would involve two competing hydrolysis reactions, one uncatalyzed and the other specific acid catalyzed by ionization of hydrolysis product **2**,[8] i.e., $k_{obsd} = k_{uncat} + k_{cat}[H^+]$. The autocatalytic nature of these hydrolyses was most evident from the monotonic increase in the instantaneous *first-order* rate constant (k_{obsd}) with time (Figure 2).[7] Values of k_{cat} were determined as follows: the magnitude of k_{obsd} was graphically estimated as the slope (tangent) of the appropriate line in Figure 2 at each experimental point. These values of k_{obsd} were then plotted against $[H^+]$, which was determined from the observed concentration of **2** and its pK_a.[8] The least-squares slope of this line gave k_{cat} (Table II). In each case the $k_{cat}[H^+]$ term swamped k_{uncat}, so only upper-limit estimates of k_{uncat} are given in Table II. Although **1b** and **1c** fit this kinetic model quite well, the induction period in the case of **1a** was not as well correlated.

Amide **1d** and allenic phosphonate **5** were both inert in aqueous methanol as indicated in Table II. The addition of 1.5 equiv of trifluoroacetic acid brought about slow hydrolysis of **1d** (k_{cat} given in Table II), but **5** remained unaffected. Thus, the relative reactivity (k_{cat}) follows the order **5** < **1d** < **1b** < **1a** < **1c**.

As with **1a**,[1] esters **1b** and **1c** reacted instantaneously with KOH in 50% aqueous methanol. But in contrast to **1a**, these hydrolysis did *not* proceed directly to **3** but rather involved at least one intermediate. For example, **1b** was

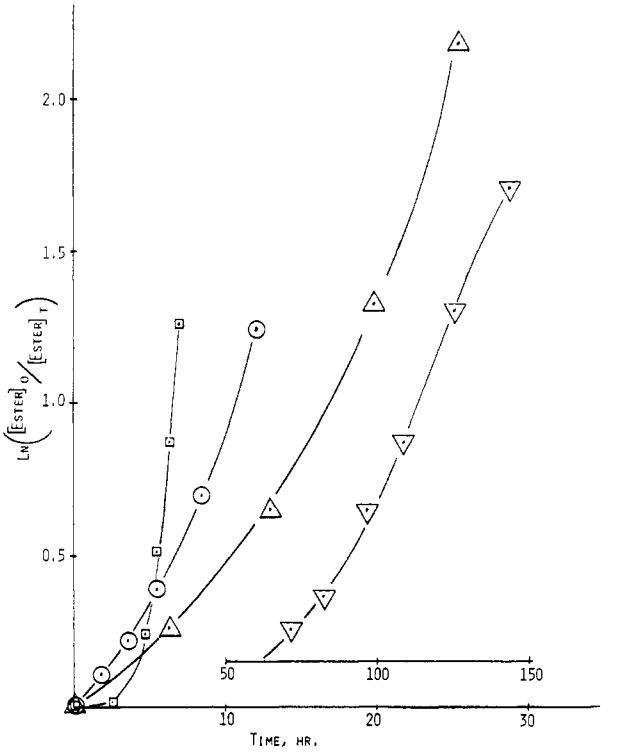
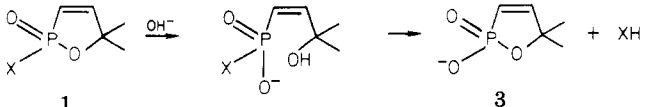


Figure 2. First-order plots of the data in Figure 1. The same legend applies.

immediately and cleanly converted by reaction with 1.5 equiv of KOH to a product that exhibited a spectrum (Table I) virtually identical with that of ring-opened salt **4**,[1] except that the neopentyl group was still *attached* (the methylene showed 5.5-Hz coupling to phosphorus). We, therefore, assign structure **8b** to this intermediate.



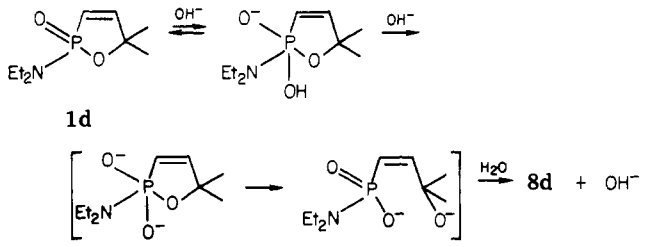
1 8a, X = OCH_3; b, X = OCH_2-*t*-Bu; c, X = OPh; d, X = NEt_2 3

At 23.5 °C **8b** was subsequently converted to **3** (*not* **4**) and neopentyl alcohol with a first-order rate constant of 2.5×10^{-4} min^{-1} (23.5 °C) and 2.8×10^{-3} min^{-1} (64.5 °C). Amide **1d** behaved similarly, though much more slowly. As it disappeared, intermediate **8d** was formed *without* release of diethylamine, followed subsequently by the appearance of **3** and diethylamine (Figure 3). The rate of disappearance of **1d** was best accommodated by a rate law first order in **1d** and *second* order in OH^- ($k = 8.5 \times 10^{-3}$ M^{-2} min^{-1}), though the *stoichiometry* remained one to one. This suggests a ring-opening sequence as shown (see Discussion).

(6) Deuterated solvents were used; 50% aqueous methanol reflects the volume proportions before mixing.

(7) This type of autocatalytic behavior is described in: Moore, J. W.; Pearson, R. G. "Kinetics and Mechanism"; Wiley: New York, 1981; p 26. For its application to a phosphinate thermolysis, see: Haake, P.; Diebert, C. E. *J. Am. Chem. Soc.* **1971**, *93*, 6931.

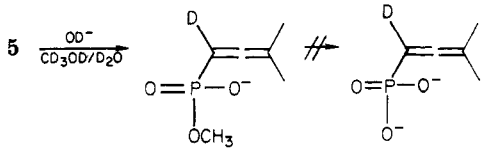
(8) The pK_a of **2** was found to be 1.70 in water (23.5 °C) and 2.66 in 50% aqueous methanol (23.5 °C).[6]



1d

The phenyl ester (**1c**) was somewhat more complicated, perhaps owing to the extra acidity of the released phenol. The ester itself was consumed instantaneously by 2 equiv of KOH. Its absorptions were replaced by those of **2** and **3** as well as at least one additional compound (*gem*-dimethyl absorption at δ 1.49 and 1.51). Although the aromatic protons made the olefenic region quite complex, peaks were present in the region δ 5.2–6.6 that could be attributed to **8c**. Addition of 2 more equiv of KOH converted the mixture to **3** and phenoxide. It should be remembered that we were unable to detect **8a** during our previous work,[1] although a similar intermediate had been proposed by Buck et al.[9] Because OPh is a far better nucleofuge than OMe, it seems unlikely that **8a** would be more reactive than **8c** (or **8b** for that matter). These observations help resolve the discrepancy between our work[1] and that of Buck,[9] for it is now clear that the ring-opened structures are anionic and survive only in basic media (see Discussion).

Allenic ester **5** reacted with hydroxide more slowly than esters **1a**, **1b**, and **1c** but more rapidly than amide **1d**. This reaction was first order in both **5** and OH^-, with rate constant of 6.3×10^{-2} min^{-1} M^{-1} (36 °C). Significantly, only one methoxy was cleaved, giving half-ester **5a** (Table I), which was inert toward further hydrolysis (68 h, 64.5 °C).



5a **5b**

It is interesting to note that **5a** underwent H/D exchange in the olefinic position, as shown by the disappearance of its absorption and collapse of the methyl signal to a doublet (J_{PH} = 6.5 Hz).[10]

Discussion

The relative reactivity of compounds **1a–d** is well accommodated by the series of reactions shown in Scheme **I** (in basic media O*H becomes O^-). Reaction 1, direct S_N2 attack at carbon with alkyl–oxygen cleavage, occurs only with **1a**, $k_1 \approx k_2$.[1,2] Reaction 2 involves nucleophilic attack at phosphorus to form trigonal bipyramid **9**, with nucleophile and ring oxygen apical.[11] Pseudorotation (reaction 3) or its equivalent (reactions 5 and –6) places the OR apical (**9a**) so it can depart (reaction 4) to give the product of *exocyclic* phosphoryl–oxygen cleavage, **2** (**3** in basic media). Intermediate **9** is thus partitioned between **9a** and *endocyclic* phosphoryl–oxygen cleavage product **8**. Because **8** is only observed in basic media, reaction 5 must

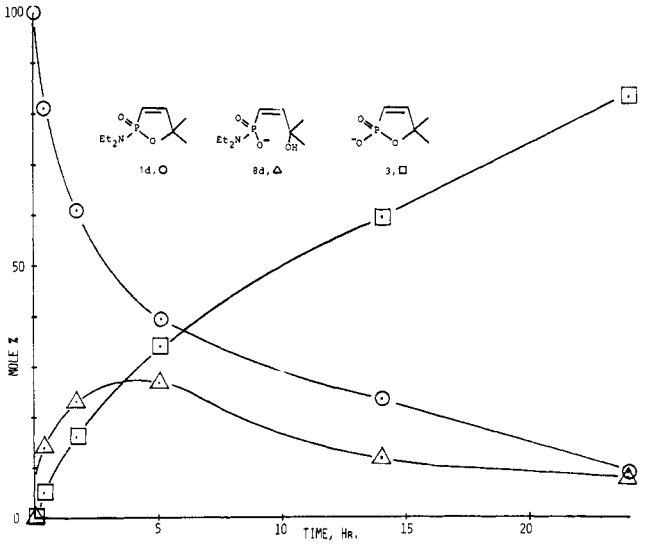
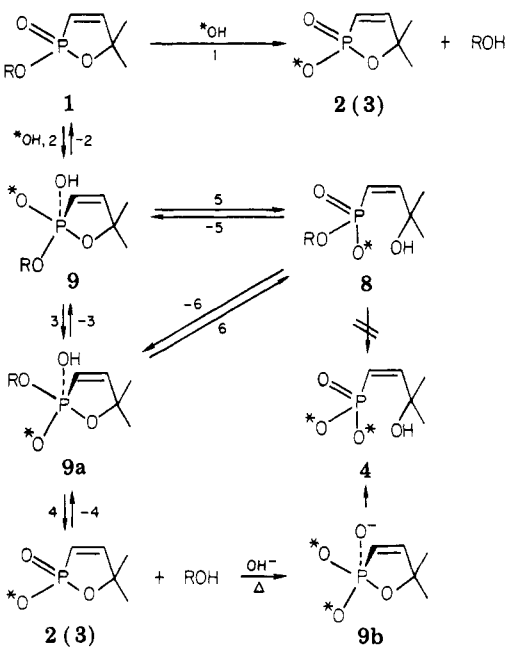


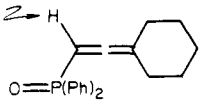
Figure 3. Reaction of amide **1d** with 2 molar equiv of KOH in 50% aqueous methanol at 23.5 °C.

Scheme I



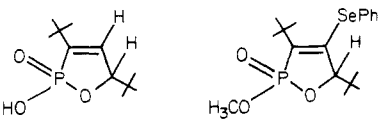
(9) van Aken, D.; Castelijns, A. M. C. F.; Buck, H. M. *Recl. Trav. Chim. Pays-Bas.* **1980**, *99*, 322.

(10) When the reaction was carried out in CH_3OH/H_2O, the methyls in **5a** exhibited a doublet of doublets (J = 6, 3 Hz). Similar H/D exchange in ii has been reported: Horner, L.; Binder, V. *Phosphorus Relat. Group V Elem.* **1971**, *1*, 17.



ii

(11) Single-crystal X-ray structural analysis of iii[12a] and iv[12b] both show endocyclic C–P–O angles of 97 ± 0.5°. Therefore in any trigonal-bipyramidal structure, the ring oxygen must be apical and the ring carbon must be equatorial.



iii iv

(12) (a) Elder, R. C.; Florian, L. R.; Kennedy, E. R.; Macomber, R. S. *J. Org. Chem.* **1973**, *38*, 4177. (b) Macomber, R. S.; Krudy, G. A.; Seff, K. *J. Org. Chem.*, accompanying paper in this issue.

only be significant[13] when **9** is first converted to its conjugate base. Once formed, **8** (as its conjugate base) does *not* hydrolyze to **4** for the same reasons that **5a** is inert to further hydrolysis: the charge on O* electrostatically inhibits attack at phosphorus and renders the phosphonate moiety a poor nucleofuge. Instead **8** (conjugate base) reenters the manifold of trigonal-bipyrimidal intermediates (reactions −5 or −6), proceeding toward the thermodynamically most stable **2** (or **3**). In comparing neopentyl ester **1b** with phenyl ester **1c**, the order of reactivity is determined both by reaction 4, where phenoxy is the better leaving group, and by the steric retardation of reaction 2 by the neopentyl group. In basic media **1b** is converted completely to kinetic product **8b** ($k_5 > k_3$). Amide **1d** is less reactive than all the esters (even in acidic media), a surprising observation in view of the generally high reactivity of phosphonamides under acidic conditions.[14] This may be due to the electronegativity-increasing effect of the five-membered ring on the phosphoryl group, causing electron withdrawal from the neighboring nitrogen, thereby decreasing the fraction of N-protonation. The fact that **1d** is *not* rapidly converted to **8d** under basic conditions demonstrates the extent to which the nitrogen decreases the electrophilicity of the phosphorus.

The fact that none of the intermediates **8b–d** hydrolyze to **4**, and that **4** rises only from **3** when heated in excess base, suggests that **4** arises only from the fully ionized (or perhaps monoprotonated) intermediate **9b**. Such an intermediate would not have been formed during the relatively low base concentrations used in the present work.

Finally, a comment on the reactivity of allenic phosphonate **5**. Of all the esters it was by far the least reactive: inert in neutral and acidic media and losing only one alkyl group during (slow) basic hydrolysis. Regarding this as the somewhat more "normal" behavior of acyclic phosphonates, it is easy to see how incorporation of the phosphorus into a five-membered ring drastically affects its proclivity toward nucleophilic substitution.[15,16]

Experimental Section

General procedures and instrumentation were as described previously.[1,3] Esters **1a**[1,3a,17] and **5**[3a,17] were prepared by our published methods. Elemental analyses were performed by Integral Microanalytical Laboratories, Inc., Raleigh, NC, and Dr. Ruth Holman, Merrell-Dow, Cincinnati, OH. TLC was performed on 0.25-mm EM plates.

5,5-Dimethyl-2-neopentoxy-1,2-oxaphosphol-3-ene 2-Oxide (1b). To a solution of 910 mg (5.5 mmol) of acid chloride **6**[1] in 25 mL of dry pyridine was added a solution of 484 mg (5.5 mmol) of neopentyl alcohol in 1.0 mL of dry pyridine. After 24 h at −20 °C, the mixture was filtered, the solid pyridine hydrochloride was washed with 2 mL of methylene chloride, and the combined filtrate and washings were evaporated at 35 °C and 0.10 mm. The oily semisolid was taken up in 20 mL of ether, filtered, and again evaporated (35 °C, 0.10 mm). Bulb-to-bulb distillation (0.13 mm, pot 150 °C) afforded 605 mg (51%) of the ester as a clear colorless oil, which solidified upon standing at −20 °C. Sublimation (0.08 mm, 70 °C) gave material with mp 42–44 °C. ^{1}H NMR (CCl_4) δ 0.95 (s, 9 H), 1.43 (s, 3 H), 1.48 (s, 3 H), 3.69 (d, J = 7 Hz, 2 H), 5.95 (dd, J = 30, 8 Hz, 1 H), 6.95 (dd, J = 46, 8 Hz, 1 H); IR (CCl_4) 2980 (s), 1595 (m), 1480 (m), 1460 (m), 1370 (s), 1330 (s), 1260 (vs), 1180 (s), 1040 (vs), 970 (vs), 940 (vs), 880 (s), 850 (s) cm^{-1}; MS (70 eV), m/e 218 (18, M$^+$), 162 (35), 149 (100), 148 (65), 135 (71), 131 (29), 115 (93), 113 (42), 80 (43), 69 (48), 65 (40), 58 (25), 53 (32); R_f (ethyl acetate) 0.39. Anal. Calcd for $C_{10}H_{19}O_3P$: C, 55.05; H, 8.72. Found: C, 54.95; H, 8.82.[18] This material could not be recrystallized from CCl_4.

5,5-Dimethyl-2-phenoxy-1,2-oxaphosphol-3-ene 2-Oxide (1c). To a solution of 1.13 g (6.8 mmol) of acid chloride **6** in 3 mL of dry pyridine was added a solution of 640 mg (6.8 mmol) of phenol in 1 mL dry pyridine. After standing at −20 °C for 2 days, the solution was filtered from solid pyridine hydrochloride and evaporated at 25 °C and 0.10 mm. The resulting semisolid was taken up in 12 mL of methylene chloride, washed first with 1 N hydrochloric acid and then with saturated sodium carbonate, dried over magnesium sulfate, and stripped. The resulting oil was twice distilled bulb-to-bulb (0.08 mm, pot 140 °C) to give 750 mg (50%) of a clear colorless oil, which crystallized upon standing at −20 °C; mp 33–35 °C; ^{1}H NMR (CCl_4) δ 1.23 (s, 3 H), 1.42 (s, 3 H), 6.07 (dd, J = 33, 8.5 Hz, 1 H), 6.93 (dd, J = 48.5, 8.5 Hz, 1 H), 7.0–7.2 (m, 5 H); IR (CCl_4) 3070 (w), 3000 (m), 2950 (w), 1590 (s), 1490 (s), 1370 (m), 1330 (s), 1280 (vs), 1210 (vs), 1180 (s), 1080 (m), 1030 (m), 1010 (m), 970 (vs), 940 (vs), 865 (m), 850 (m), 700 (m) cm^{-1}; MS (70 eV), m/e 224 (M$^+$, 91), 209 (39), 183 (38), 145 (30), 143 (20), 142 (36), 131 (23), 113 (40), 95 (46), 94 (100), 85 (26), 83 (34), 77 (24), 66 (100), 65 (100), 63 (30), 55 (36), 51 (30), 50 (23), 47 (21), 40 (40), 39 (91); R_f (ethyl acetate) 0.38. Anal. Calcd for $C_{11}H_{13}O_3P$: C, 58.93; H, 5.98. Found: C, 58.40, H, 5.98.[18] Attempts to recrystallize this material from CCl_4 gave only **2**.

2-(Diethylamino)-5,5-dimethyl-1,2-oxaphosphol-3-ene 2-Oxide (1d). Under nitrogen a solution of 0.70 g (4.2 mmol) of **6** in 25 mL of anhydrous ether was rapidly added, at room temperature, to a stirred solution of 2.10 g (29 mmol) of diethyl amine in 10 mL of anhydrous ether. The mixture was stirred under nitrogen at room temperature for 2 days, filtered, stripped of solvent and excess amine, leaving the crude product as an oil. Two distillations [89–91 °C (0.21 mmHg)] afforded 0.75 g (88%) of amide as a colorless oil, which solidified on standing: mp 40–42 °C; ^{1}H NMR (CCl_4) δ 1.08 (t, J = 7 Hz, 6 H), 1.42 (s, 3 H), 1.48 (s, 3 H), 3.03 (dq, J = 12, 7 Hz, 4 H), 5.85 (dd, J = 30, 8 Hz, 1 H), 7.00 (dd, J = 44, 8 Hz, 1 H); IR (CCl_4) 2970 (s), 2930 (m), 2870 (m), 1590 (w), 1455 (m), 1375 (s), 1360 (m), 1340 (sh), 1320 (s), 1240 (vs), 1205 (s), 1170 (s), 1060 (m), 1030 (vs), 960 (vs), 915 (vs), 550 (s), 820–740 (m), 695 (s) cm^{-1}; MS (70 eV), m/e 203 (M$^+$), 72 (base). Exact mass calcd for $C_9H_{18}NO_2P$ 203.1076, found 203.1090. Anal. Calcd for $C_9H_{18}O_2PN$: C, 53.20; H, 8.87. Found: C, 52.87; H, 9.08.[18]

Registry No. **1a**, 59474-17-8; **1b**, 85152-44-9; **1c**, 85152-45-0; **1d**, 85152-46-1; **5**, 17166-43-7; **5a**, 85152-49-4; **6**, 75779-67-8; **8b**, 85152-47-2; **8c**, 85152-50-7; **8d**, 85152-48-3.

(13) If formed in neutral or acidic media, **8** is far too reactive to exist in detectable concentration (reaction −5, Scheme I, is very fast).
(14) Rahil, J.; Haake, P. *J. Am. Chem. Soc.* **1981**, *103*, 1723.
(15) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70.
(16) Note added in proof: Hydrolysis of **1a** in the presence of imidazole occurs via both alkyl–oxygen cleavage to **3** and endocyclic cleavage to **8a**. Macomber, R. S. *J. Am. Chem. Soc.*, in press.
(17) Macomber, R. S. *Synth. Commun.* **1977**, *7*, 405.
(18) These compounds are quite hygroscopic, and **1c** is especially prone toward hydrolysis in air. Special care was required to obtain satisfactory elemental analyses.