again, this implies a substantial degree of polar character in the transition state of ozonation.

The above discussion rules out a mechanism involving hydrogen-atom abstraction (Scheme Ic). Therefore, we will discuss the data below in terms of the two remaining mechanisms we favor.

The electronic effects discussed above, as well as the thermochemical calculations of Nangia and Benson[12] support a hydride abstraction mechanism. Nangia and Benson also disfavor the insertion route both because of the entropy differences cited above and because of the high-energy requirements (20–26 kcal mol^{-1}) that they estimate is required in achieving a pentavalent carbon transition state.[12] We observe energies of activation no greater than 14.6 kcal mol^{-1}. Additionally, one might expect the preexponential term for the insertion of ozone into a C–H bond to be lower than those of 1,3-dipolar additions of ozone to a C–C double bond, typically 10^6–10^7.[20] In fact the values measured herein are higher by about one-half of a log A unit.

Other evidence, however, seems to favor an insertion mechanism over a hydride abstraction. First, reactions of ozone with hydrocarbons occur with net retention of configuration.[5-8] Second, the polarity of the solvent has less effect on the reaction rates than might be expected for a reaction producing ionic intermediates. Data presented in Table II illustrate this point: even for the least-reactive substrates, going from CCl_4 to CH_3CN increases the rate constants by less than a factor of 3. Our value for the rate constant for ozonation of tetrahydrofuran in water[31] is roughly equal to our value measured in CCl_4. Erickson et al.[9] have determined relative reactivities for the ozonation of several ethers in acetone and propyl acetate; their values are similar to those we observe in acetonitrile. Taillefer et al.[14] have noted that the rate of ozonation of an acetal varies by less than a factor of 2 when hexane, Freon-11, ethyl acetate, or acetone is used as the solvent.

A possible rationalization for these data in terms of the hydride abstraction mechanism involves the observation of Hellmann and Hamilton[6] that the percent retention of configuration is higher in more viscous solvents. They suggest that the intermediate is a solvent-caged radical pair.[6] The intermediacy of a solvent-caged ion pair might also account for the small polar solvent effect, suggesting only minor solvation of reaction intermediates and rationalizing the observed retention of configuration. However, we do not favor this explanation without further experimental support.

In summary, of the two mechanisms we consider most likely, the retention of configuration[5-8] and the small solvent effects are most consistent with an insertion mechanism (Scheme Ib), while the relatively high log A values and the thermochemical calculations of Nangia and Benson[12] are more consistent with an initial hydride abstraction (Scheme Id). Neither mechanism can be ruled out with finality, and further experimental tests of these two mechanisms are needed.

Acknowledgment. This work was supported by grants from NIH (HL-16029) and NSF and a contract from the National Foundation for Cancer Research.

Registry No. 1,2,3-Trioxolane, 6669-36-9; tetrahydrofuran, 109-99-9; butyl ether, 142-96-1; isopropyl ether, 108-20-3; ethyl ether, 60-29-7; tetrahydropyran, 142-68-7; 1,2-dimethoxyethane, 110-71-4; *tert*-butyl methyl ether, 1634-04-4; 1,4-dioxane, 123-91-1; 2-chloroethyl ether, 111-44-4; 2,3-dimethylbutane, 79-29-8; cyclohexane, 110-82-7; pivaldehyde, 630-19-3; 2-phenylethanal, 122-78-1.

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Regioselective Phosphoranylation and Cyclodehydration of Triols with Diethoxytriphenylphosphorane

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Abstract: Diethoxytriphenylphosphorane (DTPP) selectively diphosphoranylates the vicinal diol functional group in 1,2,4-triols affording thermodynamically stable 2,2,2-triphenyl-1,3,2-dioxaphospholanes. When subjected to thermolysis conditions, these dioxaphospholanes dissociate to form transient betaines which subsequently collapse, via 3-exo-tet extrusion of triphenylphosphine oxide, to epoxides. The structures of the 2,2,2-triphenyl-1,3,2-dioxaphospholanes are readily assessed from ${}^nJ_{^{31}P-^{13}C}$ (n = 2, 3) coupling constants and ^{31}P chemical shifts. Alkyl and aryl substituents attached to the dioxaphospholane ring also induce pronounced substituent shielding effects on the ^{31}P resonance of the phospholanes. These effects are useful in corroborating the structural assignments of the dioxyphosphoranes.

Recently, we demonstrated the versatility of diethoxytriphenylphosphorane (DTPP) for the mild, selective cyclodehydration of various diols to cyclic ethers.[1] Our findings stimulated in intense interest in the origin and structural characteristics of the phosphoranylated intermediates which apparently preceded the requisite, but transitory, betaines.[1,2]

"Phosphorylation" of a nucleoside hydroxyl group is generally viewed as a critical step in oligonucleotide synthesis.[3] This process is uniquely different from the "phosphoranylation" methodology described here involving triols. Nevertheless, both processes involve formation of a new phosphorus–oxygen bond by combining a hydroxyl group with an organophosphorus reagent, and it seems plausible that fundamental knowledge on "site selective" *phosphoranylation* of polyols would be useful in predicting the preferred sites of *phosphorylation* within polyhydroxy substrates as well. Thus, it seemed reasonable, based on the conceptual similarity of the two processes, that results from phosphoranylation chemistry could serve as stimuli for development of new regioselective phosphorylation reagents. In fact, phosphoranylated intermediates have been shown to be essential in transphosphorylation of dinucleotides initiated by ribonucleases.[4]

Herein, we present pertinent details on the mechanism of phosphoranylation and cyclodehydration of triols as well as im-

(1) Robinson, P. L.; Barry, C. N.; Kelly, J. W.; Evans, S. A., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 5210–5219.
(2) Robinson, P. L.; Evans, S. A., Jr. *J. Org. Chem.* **1985**, *50*, 3860–3863.
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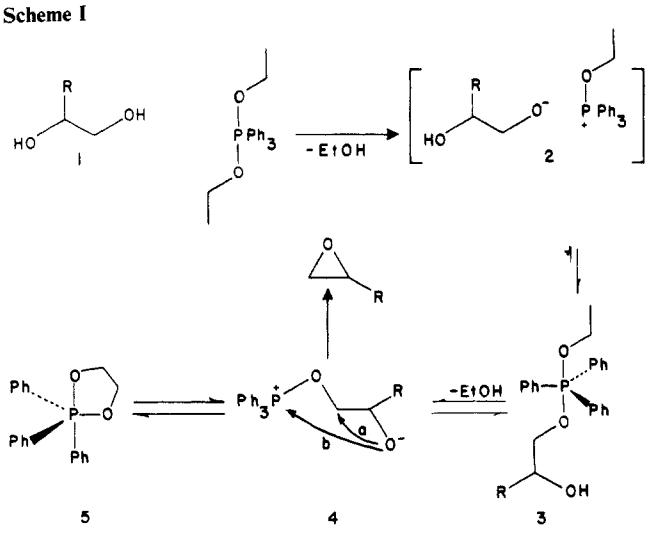
Scheme I



portant observations on the solution dynamics of dioxyphosphoranes.

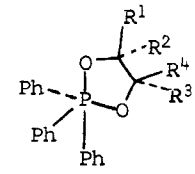
Results and Discussion

DTPP reacts with a 1,2-diol (cf. **1**) at 30 °C to afford two important intermediate dioxaphosphoranes, **3** and **5**, which are observable by ^{31}P NMR spectroscopy (Scheme I). Proton transfer from diol **1** to the apical ethoxy oxygen of DTPP[1] initiates the phosphorane interchange through ion pair **2**. Collapse of ion pair **2** to the unsymmetrical phosphorane **3** with diapical oxo ligands represents net phosphoranylation of the sterically least hindered C-1 carbinol group. Loss of ethanol from **3** affords the requisite betaine **4** capable of further collapse to either the cyclic ether (e.g., epoxide) via path a or the intermediate 2,2,2-triphenyl-1,3,2-dioxaphospholane **5** possessing oxo ligands in apical and equatorial orientations (via path b).

1,3,2-Dioxaphospholanes (cf. **5**) are thermodynamically stable at 25 °C, especially in aprotic solvents (e.g., benzene, toluene, dichloromethane).[5] Several acyclic dioxyphosphoranes having alkoxy ligands are also quite stable although aryloxyphosphoranes undergo rapid dissociation–recombination at ambient temperature.[6] Thermolysis temperatures between 40 and 100 °C initiate dissociation of generic dioxaphospholane **5** to betaine **4** where the C-1 carbinol is effectively phosphoranylated. Decomposition of betaine **4** gives either ketone by oxidative rearrangement in conformationally restricted systems[2] or cyclic ether[1] through *n*-exo-tet[7] cyclization in conformationally flexible acyclic substrates.

^{31}P NMR. The ^{31}P NMR shift data for several relatively stable triphenyl-1,3,2-dioxaphospholanes are described in Table I and deserve comment. The substituent steric shift effect which induces upfield shifts of the ^{31}P resonances in these systems appears to be conceptually analogous to substitutent effects (i.e., γ-steric effect) observed in ^{13}C NMR.[8-10] The conformational dynamics of the 1,3,2-dioxaphospholane ring system caused by the Berry pseudorotational phenomenon[11] tends to average these γ-substituent effects on the phosphorus atom. That is, substituents attached to the *apical carbinol carbon* will induce a slightly different effect on the phosphorus atom when compared to substituents attached to the *equatorial carbinol carbon*. This is so because the apical P–O bond is slightly longer than the equatorial P–O bond,[12] implying that while individual substituents attached to the 1,3,2-dioxaphospholane ring have at least a γ carbon/phosphorus interaction, their specific steric shift contributions are expected to be averaged by rapid Berry pseudorotation.[11b]

Table I. ^{31}P NMR Shifts of 1,3,2-Dioxaphospholanes[a]



ENTRY	R^1	R^2	R^3	R^4	δ ^{31}P (ppm)
1	H	H	H	H	-36.5
2	H	H	H	C_6H_5	-35.8
3	H	H	H	CH_3	-37.2
4	H	H	H	X[b]	-37.7
5	H	H	H	$-CH_2C_6H_5$	-37.4
6	C_6H_5	H	H	C_6H_5	-39.7
7	CH_3	H	H	CH_3	-40.3
8	CH_2	CH_2	CH_2	CH_2	-40.6
9	C_6H_5	C_6H_5	H	CH_3	-40.5
10	CH_3	CH_3	H	CH_3CH_2	-44.2
11	CH_3	CH_3	H(Y)[c]	Y(H)[c]	-44.5
12	CH_3	CH_3	CH_3	CH_3	-48.7

[a] Solvent for ^{31}P NMR determinations: 2 mL of toluene/1 mL of benzene-d_6. X = $CH_2CH_2OCH_3$. Y = $CH_3CH_2CH(CH_3)$-$CH_2CH_2OCH_3$.

Nevertheless, some potentially useful alkyl substituent shift parameters may be obtained. First, the dioxyphosphoranes having diapical oxo ligands exhibit ^{31}P shifts near δ -55 [$Ph_3P(OHex)_2$, δ -55.95; $Ph_3P(OEt)_2$, δ -55.0] while the 1,3,2-dioxaphospholanes described in Table I are 7–18 ppm less shielded.[13] This deshielding of the ^{31}P nucleus during the conversion from acyclic to monocyclic dioxyphosphorane has been previously reported[9b,14] and can be viewed as diagnostic. For substitution at C-4 and C-5 on the 1,3,2-dioxaphospholane ring, the alkyl substituent effect on the phosphorus nucleus is ca. -1 ppm for one alkyl group (cf. entries **3–5**), ca. -3.8 ppm for two alkyl groups (cf. entry **7**), ca. -7.7 ppm for three alkyl groups (cf. entries **10** and **11**), and ca. -12 ppm for four alkyl groups (entry **12**). Perhaps, surprisingly, one phenyl substituent has virtually no effect on the ^{31}P shift (entry **2**); however, steric crowding apparently increases with two phenyl substituents and this translates to a 3–4 ppm shielding effect (cf. entries **6** and **9**).[15]

Whereas 1,2-diols condense with DTPP to form acyclic, phosphoranylated intermediates which subsequently extrude ethanol to give 1,3,2-dioxaphospholanes **5**, their 1,3-, 1,4-, and

(5) Rameriz, F. *Bull. Soc. Chim. Fr.* **1970**, 3491.
(6) (a) Sigal, I. S.; Westheimer, F. H. *J. Am. Chem. Soc.* **1979**, *101*, 5329–5334. (b) Sigal, I. S.; Westheimer, F. H. *J. Am. Chem. Soc.* **1979**, *101*, 5334–5338.
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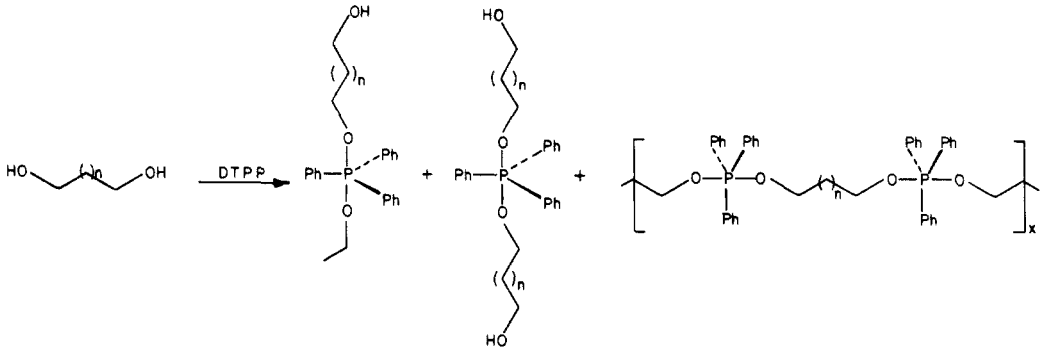
(15) The effect of C4,C5 substituents on the O–P–O angle in 1,3,2-dioxaphospholanes and the subsequent influence on the ^{31}P chemical shift has not been quantitatively assessed. It is, of course, known that changes in the O–P–O bond angle in a phosphate diester model relate to the ^{31}P NMR shifts [see: Gorenstein, D. G.; Kar, D. *Biochem. Biophys. Res. Commun.* **1975**, *65*, 1073–1080].

Scheme II

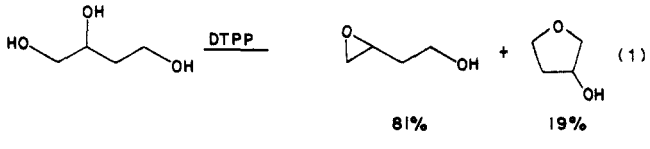


1,5-diol homologues [$HO(CH_2)_nOH$, n = 3–5] react with DTPP to afford *only* acyclic phosphoranes similar to **3** at ambient temperature. Apparently, the 6-, 7-, and 8-membered 1,3,2-dioxaphosphoranes derived from these diols (n = 3–5) are considerably less stable than their acyclic diapical dioxyphosphorane analogues.[13] The structural assignments of these acyclic dioxyphosphoranes rest largely on their ^{31}P NMR shifts as determined in the following comparisons. 2-Methoxyethanol reacts with DTPP to give (1,4-dioxapentyl)ethoxytriphenylphosphorane **6** [^{31}P δ −55.6 (37.2%], bis(1,4-dioxapentyl)triphenylphosphorane **7** [^{31}P δ −56.3 (6.3%)], and unchanged DTPP [^{31}P δ −55.0 (56.5%)]. These results indicate that oxo ligands having extended alkyl chains exert a small but consistent shielding effect on the phosphorane phosphorus nucleus.

Acyclic dioxyphosphoranes tend to oligomerize to other diapical phosphoranes upon standing in the presence of excess diol (Scheme II).[16] However, when these oligomeric phosphoranes are thermolyzed, they readily dissociate to the prerequisite betaines required for cyclic ether formation (n = 0, 2, 3). The 0.1–0.2-ppm shielding exhibited by the oligomeric dioxyphosphoranes would be in accord with expectations based on the slight increase in γ-steric interactions.

Triphenyl-1,3,2-dioxaphospholanes are also characterized by their ^{31}P–^{13}C coupling constants. In diapical dioxyphosphoranes [(e.g., DTPP, $Ph_3P(OHex)_2$)], the geminal and vicinal phosphorus–carbon couplings are readily observed: $^2J_{POC} \sim 7.5$ Hz and $^3J_{POCC} \sim 5.5$ Hz. In the triphenyl-1,3,2-dioxaphospholanes reported here, the geminal couplings were not observable; however, the vicinal couplings are readily identified and fall into the range of $^3J_{POCC}$ = ca. 5.5 Hz. The absence of an observable 2-bond coupling between carbon and phosphorus nuclei appears to be related to a diminution of the P–O–C bond angle in the five-membered ring.[17]

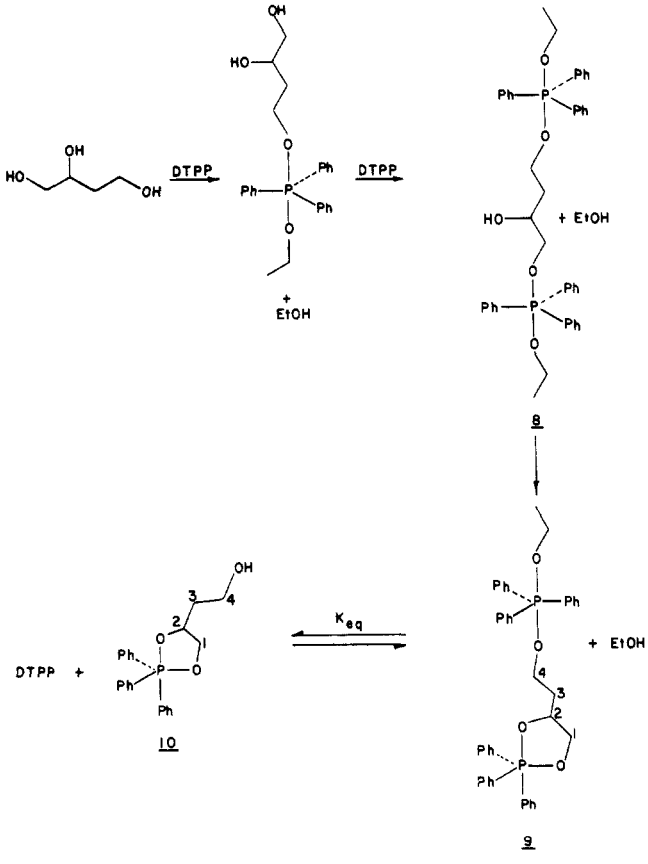
Phosphoranylation of Triols. 1,2,4-Butanetriol reacts with 1 equiv of DTPP (eq 1) at 40 °C to give 3,4-epoxy-1-butanol (**6**; 81%) and tetrahydro-3-furanol (**7**; 19%). This reaction is important because it serves as a simple model for studying the



81% 19% (1)

regiochemistry of phosphoranylation in polyols. ^{31}P NMR data suggest that the C-4 hydroxyl group is initially phosphoranylated (^{31}P δ −55.2). The primary C-1 hydroxyl group then reacts with another equivalent of DTPP to give the diphosphoranylated triol **8** (Scheme III). Subsequent loss of ethanol gives **9** (^{31}P δ −38.2 and −55.2). In **9**, the C-1 and C-2 carbinol groups are phosphoranylated by the same phosphorus atom comprising the 1,3,2-dioxaphosphorane ring. By contrast, the C-4 carbinol is

Scheme III



phosphoranylated by an equivalent of DTPP and gives a pentavalent phosphorus having two oxo ligands oriented diapically in the trigonal-bipyramidal conformer. When a sufficient concentration of ethanol is generated, ethanol effectively transfers a proton to the C-4 oxygen of **9** thereby liberating ethoxytriphenylphosphonium ion, which is subsequently trapped by ethoxide ion. This process gives DTPP and cyclic triphenyl-1,3,2-dioxyphospholane **10**. The equilibrium between **9** and **10** at 30 °C is controlled by the concentration of ethanol (see Scheme III). If 1,2,4-butanetriol is treated with 2.0 equiv of DTPP (25 °C) and removal of ethanol is accomplished utilizing 4 Å molecular sieves, the equilibrium constant [K_{eq} = **9**/**10**] is shifted from unity without molecular sieves to K_{eq} = 2.3 in the presence of molecular sieves. At 30 °C, there is insufficient thermal energy to initiate decomposition of the betaines derived from phosphoranes **9** and **10**, thus virtually no cyclic ethers are formed. The data in Table II show the ^{31}P shift assignments of intermediates and progress of reaction between equimolar quantities of DTPP and 1,2,4-butanetriol at 40 °C as a function of time.

The ^{31}P resonance (δ −37.5) has been assigned to **10** by analogy with the triphenyl-1,3,2-dioxaphospholane (**11**) derived from 4-methoxy-1,2-butanediol which exhibits a ^{31}P resonance at δ −37.7. This chemical shift is consistent with the ^{31}P shift of other

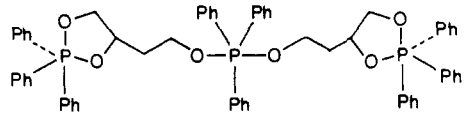
(16) This is understandable since some diols are only partially soluble in the DTPP reaction mixture and consequently there is excess DTPP initially.

(17) For a recent review detailing spin–spin coupling interactions involving phosphorus and other nuclei, see: Gorenstein, D. G. *Prog. NMR Spectrosc.* **1983**, 1–98.

Table II. ^{31}P NMR Shifts and Concentrations of **9** and **10** vs. Time

time (h)	^{31}P δ	Ph_3PO (%) (27.3)	**9** (%) (−38.21)	**9** (%) (−55.12)	**10** (%)[a] (−37.5)	$Ph_3P(OEt)_2$ (%) (−55.0)
0.33		1.4	5.6	12.6	0.7	79.7
1.0		2.2	10.5	12.8	5.4	69.0
2.66		4.4	16.5	21.7	25.6	31.8

[a] The integrated intensity of the ^{31}P resonances at δ −38.21 for **9** also includes the resonance for presumably a small quantity (ca. 5%) of



However, the resolution at 101 MHz is not sufficient to separately integrate the two ^{31}P resonances for an accurate assessment of the relative product ratios.

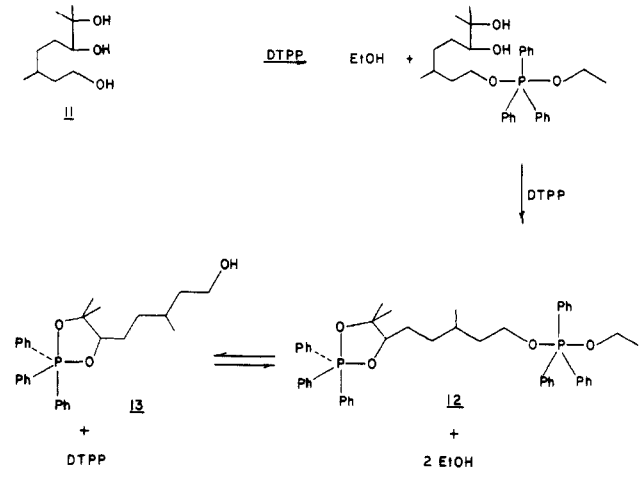
monosubstituted 2,2,2-triphenyl-1,3,2-dioxaphospholanes (Table I). The ^{13}C NMR spectrum of **10** [^{13}C NMR: δ (C1) 69.3, (C2) 64.7, (C3) 37.5 ($^3J_{POCC}$ = 6.2 Hz); (C4) 59.4] is similar to the ^{13}C NMR spectrum of **11** [^{13}C NMR: δ (C1) 69.5, (C2) 68.8, (C3) 35.0 ($^3J_{POCC}$ = 6.0 Hz), (C4) 64.3, (OCH_3) 58.6]. The ^{13}C NMR shift assignments are made by using DEPT and off-resonance decoupling NMR techniques.

The equilibrium concentration of **10** is diminished when one uses 2.0 equiv of DTPP. Excess DTPP reacts with **10** to shift the equilibrium toward **9**. The C-4 carbinol carbon of **10** *does not* couple with phosphorus whereas the C-4 carbinol carbon of **9** does couple with the phosphorus nucleus of the acyclic phosphorane. These data serve to confirm the assignments of **10**. Finally, the major product, 3,4-epoxy-1-butanol, is realized upon thermolysis of phosphorane **10**.

The ^{31}P resonances at δ −38.2 and −55.12 have been assigned to diphosphorane **9**. The fact that the triphenyl-1,3,2-dioxyphospholane ^{31}P resonance of **9** is shifted upfield of that of **10** is consistent with the notion that increasing substitution tends to enhance substituent shielding effects at the phosphorus nucleus. Supporting structural evidence for phosphorane **9** comes from performing an inverse-gated-decoupled ^{31}P NMR experiment. The results show that the integration of the ^{31}P resonance at δ −55.12 (unsymmetrical diapical phosphorane) is always equal or greater (see footnote *a* in Table II) than the integration of the resonance corresponding to the triphenyl-1,3,2-dioxaphospholane resonance at δ −38.2. Furthermore, we only observe these mixed acyclic phosphoranes in significant concentrations by ^{31}P NMR when there are no energetically lower lying phosphoranes possible, as is the case here. Perhaps the most convincing experimental evidence for **9** comes from the observation that one can perturb the equilibrium **9** ⇌ **10** toward **9** by simply removing ethanol. This implies that ethanol reversibly converts **9** to **10** and the ^{13}C NMR spectrum of **9** [^{13}C NMR: δ (C1) 69.0, (C2) 64.4, (C3) 36.4 (br s), (C4) 58.7 ($^2J_{POC}$ = 5.5 Hz)], is clearly supportive. One observes coupling of C-4 carbinol with phosphorus and this is similar to the ^{13}C NMR assignment of **11**. Carbon-3 in **9** shows a broad signal as the result of two different vicinal ^{31}P–^{13}C coupling constants, unlike C-3 in **10** which is coupled to only one phosphorus nucleus and is a resolved doublet.

Phosphoranes **9** and/or **10** are precursor(s) to both 3,4-epoxy-1-butanol (80–84%) and tetrahydro-3-furanol (20–16%). The main question to be answered is whether the cyclization selectivity observed is kinetic or thermodynamic in nature. Cyclodehydration of 1,4-pentanediol and 1,2-propanediol with DTPP affords 2-methyltetrahydrofuran ($k_{cycl\text{-}5}$ = 1.77 × 10^{-7} mol L^{-1} s^{-1}) and propylene oxide ($k_{cycl\text{-}3}$ = 4.44 × 10^{-8} mol L^{-1} s^{-1}) at 45 °C. The relative ratio of rates for ring formation, $k_{cycl\text{-}5}/k_{cycl\text{-}3}$, is 4.0, hence the product selectivity observed in the cyclodehydration of 1,2,4-butanetriol is opposite of that expected based on competitive rates for 3 and 5 membered ring formation.[18] Here, 3,4-epoxy-1-butanol predominates over tetrahydro-3-furanol, ca. 4:1. We believe that the product selectivity observed in the cyclodehydration of 1,2,4-butanetriol is derived from the thermodynamic stability of the intermediate 1,3,2-dioxaphospholane. Upon thermolysis of **9** and/or **10**, the C-2 oxygen–phosphorus bond is cleaved, leading to the betaine in which the C-1 oxygen is bonded to a triphenylphosphonium group and the C-2 atom bound to an oxy anion. The C-2 oxy anion extrudes triphenylphosphine oxide from C-1, affording 3,4-epoxy-1-butanol.

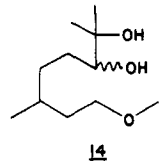
Scheme IV



These intermediate 1,3,2-dioxaphospholanes provide a means for selectivity by creating an oxy anion at C-2 while simultaneously placing an excellent leaving group on C-1. The major product, 3,4-epoxy-1-butanol, is derived from a 3-exo-tet cyclization. Tetrahydro-3-furanol results from phosphoranyl transfer to C-4 in **10** ultimately generating a C-1 oxy anion. Consequently, a 5-exo-tet displacement of triphenylphosphine oxide affords the minor product, tetrahydro-3-furanol.

3,7-Dimethyl-1,6,7-octanetriol (**11**) reacts with DTPP to afford largely 3,7-dimethyl-6,7-epoxyoctan-1-ol (85%). We envision initial phosphoranylation of the C-1 hydroxyl of **11** (which, incidentally, facilitates solubilization of triol **11**) followed by phosphoranylation of the C-6 and C-7 hydroxyls affording diphosphoranylated intermediate **12** (Scheme IV). Ethanol then transfers a proton to the C-1 oxygen which gives **13** and regenerates DTPP. Thus, similar to the 1,2,4-butanetriol case, an equilibrium is established between phosphoranes **12** and **13**, both of which when thermolyzed give the cyclic ether.

The assignment of dioxyphosphorane **13** as a mixture of two diastereomers, ^{31}P δ −44.5 and −44.6, was made by converting the C-1 hydroxyl group of 3,7-dimethyl-1,6,7-octanetriol into diastereoisomeric methyl ethers **14**. The triphenyl-1,3,2-dioxaphosphoranes from erythro and threo diol **14** were prepared and diastereomeric ^{31}P resonances were observed at δ −44.5 and −44.6.



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(18) These data are consistent with the expectations suggested in the following: (i) Stirling, C. J. M. *Pure Appl. Chem.* **1984**, *56*, 1781–1796. (ii) Stirling, C. J. M. *J. Chem. Ed.* **1973**, *50*, 844–845.

The chemical shifts of triphosphoranylated **12** [^{31}P δ −55.1 and −44.9] are assigned by analogy with those in **9**. The unsymmetrical diapical phosphorane phosphorus at δ −55.1 and the triphenyl-1,3,2-dioxaphosphorane phosphorus, δ −44.9, have equal integrated intensities indicating these resonances originate from **12**. It is noteworthy that the ^{31}P chemical shifts for the triphenyl-1,3,2-dioxaphospholane segments of **12** and **13** are consistent with the shift in entry 10 (Table I).

Summary. These results are of immense value in providing a basis for predicting the regiochemistry of phosphoranylation within polyols as well as prediction of product(s) expected from the cyclodehydration process. 3-Exo-tet cyclizations will dominate in polyol systems where the formation of triphenyl-1,3,2-dioxaphospholanes are allowed. This cyclization preference occurs despite the kinetically favored phosphoranylation of the least sterically hindered hydroxyl groups.

Experimental Section

1,2,4-Butanetriol and tetrahydro-3-furanol were purchased from the Aldrich Chemical Co. 3,7-Dimethyl-1,6,7-octanetriol and diethyl peroxide were prepared previously.[1] 3,4-Epoxy-1-butanol was prepared according to procedures reported by Barker and Hartman.[19] Gas chromatographic analyses were carried out on a Hewlett-Packard Model 5754B research gas chromatograph with stainless-steel columns packed with 20% Carbowax 20M on Chromsorb W-HP-AW-DMCS (120–200 mesh). Preparative HPLC was accomplished with a Waters LC500A preparative chromatograph. NMR spectra (^{13}C, ^{31}P) were obtained on a Bruker WM-250 spectrometer and/or a Bruker AC200 spectrometer. Phosphorus-31 NMR spectra are referenced to external H_3PO_4 (85%), and ^{13}C NMR spectra are referenced to internal tetramethylsilane (Me_4Si).

General Procedure for Phosphorane Preparation. In a dry sealable 10-mm NMR tube under argon was added 3 mmol of diol (triol) followed by 3.0 mL of 1.0 M DTPP (3 mmol) in toluene. To this solution 1.0 mL of benzene-d_6 (lock solvent) was added. The tube was sealed with a flame at −78 °C under vacuum and allowed to warm to 25 °C at which time the 10-mm tube was placed in the probe of the NMR.

Diethoxytriphenylphosphorane (DTPP), ca. 1.0 M. Diethoxytriphenylphosphorane was easily prepared by dissolving 68.6 g (0.30 mol) of PPh_3 in 195 mL of anhydrous toluene to which was added 27.0 g (0.30 mol) of diethyl peroxide while the toluene solution was stirred in an ice bath under N_2. (We urge all investigators to always exercise caution when working with peroxides.[20]) The solution is then heated in an oil bath at 70 °C for 48 h. The final concentration of the solution was determined from the initial amount of Ph_3P, the total volume of solution, and the yield of DTPP as determined by an inverse gated decoupled ^{31}P NMR experiment.

4-Methoxy-1,2-butanediol. 1,2,4-Butanetriol (10.61 g, 0.10 mol) was combined with 12.29 mL (0.10 mol) of 2,2-dimethoxypropane in 50 mL of anhydrous benzene. A catalytic amount of *p*-toluenesulfonic acid (100 mg) was added, and the reaction was allowed to reflux overnight with removal of the azetrope with a Dean-Stark trap. The acetonide was purified by distillation (69–72 °C (4 mmHg)) to give a clear liquid (70%). The acetonide (7.3 g, 0.05 mol) was added to a mixture containing sodium hydride (1.4 g) in anhydrous ether, and this mixture was allowed to stir for 3 h. Iodomethane (3.11 mL) was added, and the resulting suspension was stirred overnight at ambient temperature. Sodium iodide was removed by filtration, and the ether was removed under reduced pressure. Tetrahydrofuran (10 mL) and 10.0 mL of hydrochloric acid (1.0 M HCl) were added to the residue, and this mixture was stirred at ambient temperature overnight. The mixture was neutralized with a saturated solution of sodium carbonate, and the volume was reduced (reduced pressure). The oily residue was continuously extracted with ether to give a yellow oil. Chromatographic purification of the oil (230–400 mesh silica gel; ethyl acetate as eluant) gave homogeneous 4-methoxy-1,2-butanediol: bp 117–118 °C (12 mmHg) (lit.[21] bp 116 °C (12 mmHg)); ^{13}C NMR ($CDCl_3$) δ (Cl) 66.5, (C2) 70.3, (C3) 32.8, (C4) 69.9, and (OCH_3) 58.6 (^{13}C assignments made by DEPT); ^1H NMR ($CDCl_3$) δ 4.15 (br s, 2 H, OH), 3.82 (m, 1 H, H–C2), 3.38–3.65 (m, 6 H), and 1.71 (s, 3 H, OCH_3).

3,7-Dimethyl-1-methoxy-6,7-octanediol. Citronellol (11.66 mL, 0.064 mol) was added to a suspension of sodium hydride (2.4 g, 0.1 mol) in 50.0 mL of diethyl ether, and the reaction mixture was magnetically stirred under a nitrogen atmosphere (4 h). Methyl iodide (6.18 mL) was added, and the reaction was allowed to stir overnight. The sodium iodide and sodium hydride were removed by filtration, and the organic layer was concentrated under reduced pressure to give an oil. A solution containing 88% formic acid (39 mL, 0.88 mol) and 30% H_2O_2 (9.9 mL) was prepared, and crude methoxy citronellol (0.064 mol) was added dropwise while maintaining a temperature range of 40–45 °C. The mixture was kept at 40 °C for 1 h and then stirred overnight at ambient temperature. The volume of the reaction mixture was reduced under reduced pressure, and the remaining solution was treated with an ice-cold solution of NaOH (5.0 g in 10.0 mL of H_2O) at such a rate to maintain a temperature under 45 °C. When the exothermicity ceased the solution was warmed to 45 °C and extracted with 7 × 150 mL portions of ethyl acetate. The product was purified by distillation at reduced pressure: bp 148–150 °C (0.6 mmHg). Anal. Calcd for $C_{11}H_{21}O_3$: C, 64.7; H, 11.8. Found: C, 64.6; H, 11.6.

Determination of the Relative Rates of Three- vs. Five-Membered Ring Closure. Diol (0.003 mol) was added to a dry sealable 10-mm NMR tube under argon. The tube was cooled to −78 °C and 3.0 mL of 1.1 M DTPP was added along with 0.50 mL of benzene-d_6 (lock solvent). The tube was sealed off with a flame under vacuum at −78 °C. The tube was removed from the dry ice/acetone bath and allowed to warm for 10 min before it was placed in the NMR probe at 45 °C. After 5 min, inverse-gated-decoupled ^{31}P NMR spectra were obtained at 15-min intervals for 4 h. A 5-s delay between pulses was used to eliminate NOE effects. In these reactions, the presence of the triphenylphosphine oxide ^{31}P NMR resonance at δ 27 was used to measure the rate of ether formation.

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Registry No. 1 ($R^1 = R^2 = R^3 = R^4 = H$), 107-21-1; **1** ($R^1 = R^2 = R^3 = H$; $R^4 = Ph$), 93-56-1; **1** ($R^1 = R^2 = R^3 = H$; $R^4 = Me$), 57-55-6; **1** ($R^1 = R^2 = R^3 = H$; $R^4 = CH_2CH_2OCH_3$), 90325-06-7; **1** ($R^1 = R^2 = R^3 = H$; $R^4 = Bz$), 17131-14-5; **1** ($R^1 = R^4 = Ph$; $R^2 = R^3 = H$), 492-70-6; **1** ($R^1 = R^4 = Me$; $R^2 = R^3 = H$), 513-85-9; **1** (R^1, $R^4 = (CH_2)_4$; $R^2 = R^3 = H$), 931-17-9; **1** ($R^1 = R^2 = Ph$; $R^3 = H$; $R^4 = Me$), 52183-00-3; **1** ($R^1 = R^2 = Me$; $R^3 = H$; $R^4 = Et$), 7795-80-4; **1** ($R^1 = R^2 = Me$; R^3, $R^4 = CH_2CH_2CH(CH_3)CH_2CH_2CH(CH_3)CH_2CH_2OCH_3$, (H)), 65760-61-4; **1** ($R^1 = R^2 = R^3 = R^4 = Me$), 76-09-5; **5** ($R^1 = R^2 = R^3 = R^4 = H$), 34736-69-1; **5** ($R^1 = R^2 = R^3 = H$; $R^4 = Ph$), 104762-37-0; **5** ($R^1 = R^2 = R^3 = H$; $R^4 = Me$), 104762-38-1; **5** ($R^1 = R^2 = R^3 = H$; $R^4 = CH_2CH_2OCH_3$), 104762-39-2; **5** ($R^1 = R^2 = R^3 = H$), 104762-40-5; **5** ($R^1 = R^4 = Ph$; $R^2 = R^3 = H$), 104833-17-2; **5** ($R^1 = R^4 = Me$; $R^2 = R^3 = H$), 104778-48-5; 5,5-diethylcyclopentadiene, 61111-73-7; spiro[4.4]nonadiene, 766-29-0; 1,1-dimethylcyclohexane, 590-66-9.

(19) Hartman, F. C.; Barker, R. *J. Org. Chem.* **1963**, 28, 1004–1008.

(20) **Diethyl peroxide**: See ref 1 for full experimental details on the preparation and purification of diethyl peroxide. After crude diethyl peroxide has been prepared, *we recommend that purification by distillation should be done at temperatures of 25–28 °C and pressures between 70 and 80 Torr.* It is best to store diethyl peroxide over 4-Å molecular sieves at −20 °C. Under these conditions it is stable indefinitely. See also the following for early preparative information: Chang, B. C.; Conrad, W. E.; Denney, D. B.; Denney, D. Z.; Edelman, R.; Powell, R. L.; White, D. W. *J. Am. Chem. Soc.* **1971**, *93*, 4004.

(21) See: Beilstein, Band I 519i, III 2344c.