Reaction of Epoxides with Metaphosphoric Acid Derivatives†

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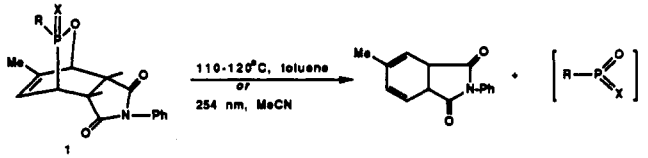
Ethyl metaphosphate ($EtOPO_2$), eliminated in the thermolysis of the bridged cyclic phosphonate *endo*-3-ethoxy-6-methyl-*N*-phenyl-2,3-oxaphosphabicyclo[2.2.2]oct-5-ene-8,9-dicarboximide 3-oxide, has been found to cause ring opening of epoxides, resulting in formation of 2-ethoxy-4-substituted 1,3,2-dioxaphospholane 2-oxides as major products. *N,N*-Diethyl metaphosphoramidate (Et_2NPO_2) reacted similarly. With ethyl metathiophosphate (EtOP(S)O), the 1,3,2-oxathiaphospholane 2-oxide ring was formed. Products of these reactions were characterized by ^{31}P NMR spectroscopy and by GC–MS. These reactions are presumed to be initiated by electrophilic attack of the metaphosphate on the epoxide oxygen to form a cyclic oxonium ion.

As a consequence of our discovery of a method to obtain derivatives of metaphosphoric acid by an uncomplicated fragmentation process,[1,2] we are able to carry out studies of this highly reactive species toward organic compounds. The accumulated evidence[3] is strong that metaphosphates have an exceedingly short but real lifetime and possess the expected planarity at phosphorus.[4] Mechanistic studies of our fragmentation process, to be reported elsewhere,[5] confirm their existence under the conditions we employ. We report now the results of the first study of the reaction of metaphosphates with epoxides.[6]

Our synthetic method for metaphosphates involves the fragmentation by thermal[1] or photochemical[2] means of derivatives of the 2,3-oxaphosphabicyclo[2.2.2]octene ring system. A considerable variety of metaphosphate derivatives is available from these processes. Thus, in **1**, R may be RO,[1,2] R_2N,[2,7,8] or RNH;[8] X is usually O but may also be S.[9]

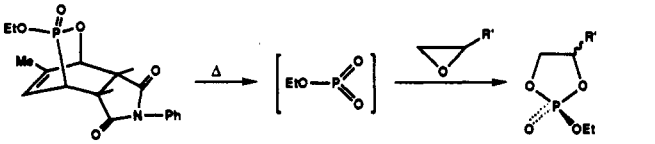


1

It is well-established[3] that metaphosphates are highly electrophilic in solution; they are efficient phosphorylating agents toward hydroxy and amino compounds and can even effect electrophilic substitution on activated aromatic rings (anilines[10] and *N*-methylpyrrole[1]). It is for these reasons that we considered epoxides as possible reactants with metaphosphates; many cases are known[11] where electrophiles, including other forms of low-coordination phosphorus compounds,[6] cause epoxide ring opening with consequent formation of cyclic or polymeric products. We first observed that the inclusion of epoxides in the medium for the photochemical generation of metaphosphates did not lead to any trapping products, and this approach has not been further employed. The thermal process, however, clearly led to identifiable reaction products, and these are the major subject of this report.

Results and Discussion

Reaction of Ethyl Metaphosphate with Epoxides. The course of the epoxide–metaphosphate reaction is easily followed by ^{31}P NMR spectroscopy. The starting material used in the first part of this study was **1a** with ^{31}P δ 24.90, which, as shown previously,[1] provides ethyl metaphosphate (**2**). At the conclusion of a heating period of 6 h in toluene, most of the starting material was destroyed, and when an



1a **2** **3** **4** (*cis, trans*)

epoxide was present initially in the medium, major new ^{31}P NMR signals appeared in the range δ 15.8–17.9 with minor signals at δ 0–1. Signals in the δ 16–18 range are unique to cyclic phosphates with five ring members,[12] and therefore structure **4**, a 1,3,2-dioxaphospholane 2-oxide, can be assigned.

The weak signals near δ 0 can be attributed to noncyclic, probably polymeric phosphates; these have not been further examined, since the emphasis in our study has been placed on the major, cyclic products. An important conclusion made in every case was that the epoxides were indeed effective traps for the metaphosphate; when trapping is incomplete, metaphosphates are known[3] to condense to give polyphosphates with characteristic ^{31}P NMR signals in the δ −10 and −20 regions, but these were absent in all of the spectra taken. The signal for the major product on expansion was revealed to be a nearly 1:1 composite of two signals, and this was true in every case studied except for the product from 2-phenyloxirane. However, all products could be resolved by gas chromatography into two very close-lying peaks (Table I). The products therefore are suggested to be a mixture of diastereoisomers, which is consistent with the cyclic structure postulated. Such isomerism is well-known for this ring system. The isomers are represented by **5** and **6**.

To prove that the two GC peaks signified the isomerism of the product, analysis by GC–MS was performed. Each

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(1) Quin, L. D.; Marsi, B. G. *J. Am. Chem. Soc.* **1985**, *107*, 3389.
(2) Quin, L. D.; Pete, B.; Szewczyk, J.; Hughes, A. N. *Tetrahedron Lett.* **1988**, *29*, 2627.
(3) Westheimer, F. H. *Chem. Rev.* **1981**, *81*, 313.
(4) Friedman, J. M.; Knowles, J. R. *J. Am. Chem. Soc.* **1985**, *107*, 6126. Freeman, S.; Friedman, J. M.; Knowles, J. R. *J. Am. Chem. Soc.* **1987**, *109*, 3166.
(5) Quin, L. D.; Jankowski, S. Unpublished results.
(6) Epoxides have been reported to react with related species. (a) PhP(O)=NPh: Bertrand, G.; Majoral, J. P.; Baceiredo, A. *Tetrahedron Lett.* **1980**, 5015. (b) $ArPS_2$ (presumably): Darling, S. M.; Liao, C. W., U. S. Patent 2,849,553 (*Chem. Abstr.* **1958**, *52*, 19112).
(7) Quin, L. D.; Szewczyk, J.; Szewczyk, K. M.; McPhail, A. T. *J. Org. Chem.* **1986**, *51*, 3341.
(8) Quin, L. D.; Bourdieu, C.; Quin, G. S. *Tetrahedron Lett.* **1990**, *31*, 6473.
(9) Quin, L. D.; Sadanani, N. D.; Wu, X.-P. *J. Am. Chem. Soc.*, **1989**, *111*, 6852.
(10) Clapp, C. H.; Westheimer, F. H *J. Am. Chem. Soc.* **1974**, *96*, 6710. Clapp, C. H.; Satterthwait, A.; Westheimer, F. H. *J. Am. Chem. Soc.* **1975**, *97*, 6873.
(11) Parker, R. E.; Isaak, N. S. *Chem. Rev.* **1959**, *59*, 737.
(12) Gallagher, M. J. In *Phosphorus-31 NMR Spectroscopy in Stereochemical Analysis*; Verkade, J. G., Quin, L. D., Eds.; VCH Publishers: Deerfield Beach, FL, 1987; pp 308–310.

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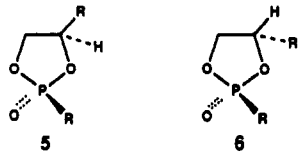


5 6

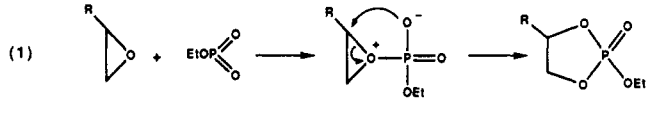
of these GC peaks had nearly the same fragmentation pattern. No MS data for these cyclic phosphates were found in the literature, and important characteristics of the spectra are summarized in Table II. In only one case (3, R = Ph) was a pronounced M^+ signal observed. Fragmentation by loss of C_2H_3 was frequently seen and is consistent with the literature on noncyclic ethyl phosphates.[13] Also observed for all compounds were signals of widely varying intensity for $P(OH)_4^+$ (m/z 99), $PO(OH)_2^+$ (m/z 81), and $P(OH)_2^+$ (m/z 65), which are commonly seen in phosphate ester fragmentation and are useful in confirming the assignment of phosphate structure.

In two cases (7 and 10), the expected 1,3,2-dioxaphospholane 2-oxides were synthesized by independent methods and found to be identical in their ^{31}P NMR, ^1H NMR, and GC–MS spectra with the products from the oxirane–metaphosphate reaction. The synthetic methods used for 2-ethoxy-4-methyl-1,3,2-dioxaphospholane 2-oxide (7) and the 4-phenyl derivative (10) are outlined in Scheme I.

Attempts to isolate the dioxaphospholane oxides from the oxirane–metaphosphate reactions were impeded by their instability in the reaction medium. However, in one case (7, from 2-methyloxirane) the product was isolated by distillation in low yield (~20%). Approximate yields in the reactions were calculated from the relative peak areas for the products on the ^{31}P NMR spectra. For compounds with similar substitution patterns around phosphorus, these areas may give a reasonably reliable indication of concentrations, but yields so calculated (all ~50–60%, Table I) must be considered only approximate at this time.

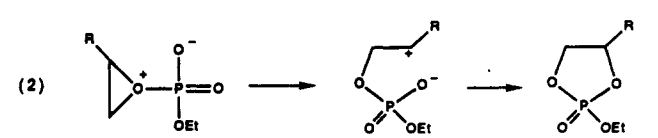
Mechanistic Considerations of the Ethyl Metaphosphate–Epoxide Reaction. There can be little doubt that the first event in the metaphosphate–epoxide reaction is the formation of a Lewis salt (11), since the metaphosphate is a powerful electrophile and is believed to coordinate to ethereal oxygen.[3]

Three pathways can be visualized for the formation of a 1,3-dioxaphospholane oxide from this intermediate.



11

This pathway from 11 is an internal nucleophilic substitution. However, in view of Baldwin's rules[14] of ring closure, this mechanism is unlikely even though it is mentioned in the literature[6b] to explain the formation of a 1,3,2-dithiaphospholane sulfide in the reaction of an epoxide with the presumed species $ArPS_2$ (from the reactant $(ArPS_2)_2$).



11 12

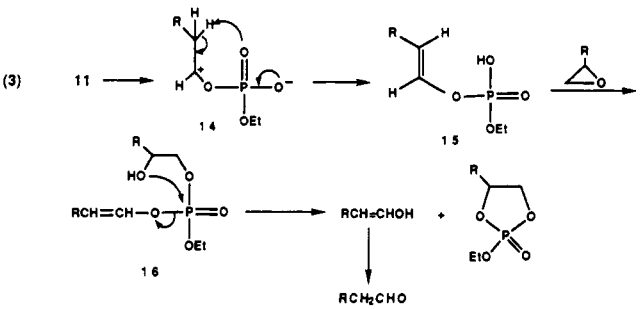
(13) Desmarchelier, J. M.; Wustner, D. A.; Fukuto, T. R. *Residue Rev.* **1976**, *63*, 77.
(14) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734, 736, 738.

Table I. Data for the Reactions of Ethyl Metaphosphate with Various 2-Substituted Oxiranes 3

R′	yields[a] (%)	δ ^{31}P	isomer[b] retention times (min)
Me	62	16.35; 16.58	11.43; 11.67[c]
t-Bu	65	16.67; 17.97	8.13; 8.49[c]
Ph	50	16.32	18.37; 18.63[c]
CH_2Br	40	15.77; 17.50	10.45; 10.69[d]
CH_2OMe	54	15.98; 16.37	9.33; 9.63[d]

[a] Approximate only, as provided by ^{31}P NMR peak areas. [b] Ratio 1:1. [c] Column DB1701, 30 m, 0.25 mm i.d. 80 °C for 2 min, then 10 °C/min. [d] Column DB5, 30 m, 0.25 mm i.d. 80 °C for 2 min, then 10 °C/min.

Were this mechanism followed, a *tert*-butyl substituent on the cationic center of 12 would likely undergo some methyl group migration,[15] and when the rearranged cation collapsed, a six-membered ring (a 1,3,2-dioxaphosphorinane oxide 13) would result (Scheme II). ^{31}P NMR provides a very sensitive technique for the detection of such products, which would have shifts several ppm upfield of phosphoric acid (vide infra). No such signals were detected in the reaction mixture from 2-*tert*-butyloxirane.



14 15 16

Here, structure 11 may undergo a typical rearrangement known for such oxonium salts formed from epoxides, a [1,2] hydride shift[11,16] to form 12. Usually, such species as 14 then decompose with the release of a carbonyl compound, but the pathway above envisions a [1,5] H shift (or proton elimination) that will give an enol phosphate 15. Attack of another molecule of epoxide on the hydroxy function created in 15 would then be a natural consequence (as seen in Scheme Ia) to give a hydroxyalkyl ester 16. This can easily undergo intramolecular displacement of the enolic group and give the cyclic product. An aldehyde is released as a coproduct, and indeed we have observed propionaldehyde in the reaction product from 2-methyloxirane with the aid of GC–MS. The amount is quite small, however, only 0.53% of theory. It is possible that the aldehyde might itself be consumed in a reaction with ethyl metaphosphate, for it is known[17] that carbonyl compounds can form enol phosphates with metaphosphates. The enol phosphate from propionaldehyde would be the same as that formed from the proposed [1,5] H shift for 14 and thus would also serve as a source of cyclic phosphate 7. Additional research is required to

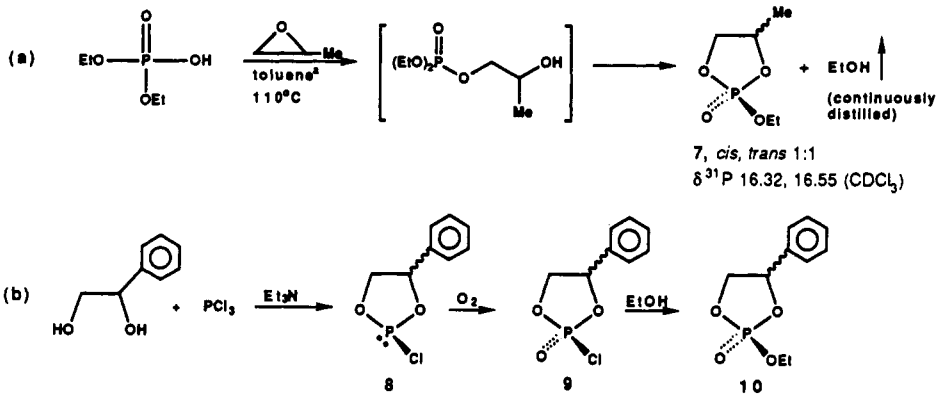
(15) See, for example: Bridgewater, A. J.; Cheung, H. T. A.; Vadasz, A.; Watson, T. R. *J. Chem. Soc., Perkin Trans. 1* **1980**, 556.
(16) (a) Rickborn, B.; Gerkin, R. M. *J. Am. Chem. Soc.* **1971**, *93*, 1693. (b) Milstein, D.; Buchman, O.; Blum, J. *Tetrahedron Lett.* **1974**, 2257. (c) Rao, A. S.; Paknikar, S. K.; Kritane, J. G. *Tetrahedron* **1983**, *39*, 2323. (d) Manioka, K.; Hasegawa, M.; Yamamoto, H.; Suzuki, K.; Shimazaki, M.; Tsuchihashi, G. *J. Am. Chem. Soc.* **1986**, *108*, 3827. (e) Maruoka, K.; Nagahara, S.; Ooi, T.; Yamamoto, H. *Tetrahedron Lett.* **1989**, *30*, 5607. (f) See also: Bartok, M.; Lang, K. L. In *Small Ring Heterocycles*; Hassner, A., Ed.; Interscience: New York, 1985; pp 65–68.
(17) Satterthwait, A. C.; Westheimer, F. H. *J. Am. Chem. Soc.*, **1980**, *102*, 4464. Satterthwait, A. C.; Westheimer, F. H. *J. Am. Chem. Soc.* **1981**, *103*, 1177.

Table II. Mass Spectral Data for 2-Ethoxy-1,3,2-dioxaphospholane 2-Oxides(3)[a]

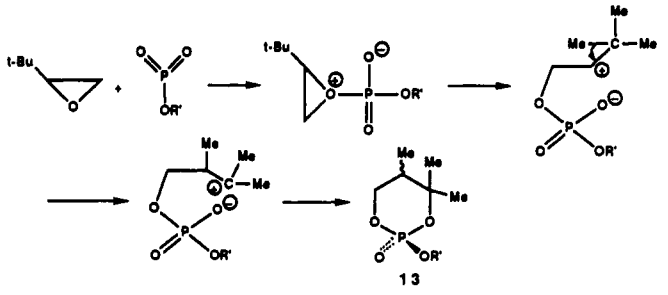
R′	mol formula	mol wt	base peak	M+[b] (RA)	other m/z (RA)
Me	$C_5H_{11}O_4P$	166	139[c]	0.35	99 (70.7), 81 (17.9), 65 (25.4)
t-Bu	$C_8H_{17}O_4P$	208	99	d	152 (87.5), 124 (55.2), 54 (86.5)
Ph	$C_{10}H_{13}O_4P$	228	102	25.06	200 (11), 119 (19.3), 105 (58.0)
CH_2Br	$C_5H_{10}BrO_4P$	244, 246[e]	137	f	219 (60.9), 217 (66.6), 123 (91.2), 57 (51.3)
CH_2OMe	$C_6H_{13}O_5P$	196	45	g	151 (7.0), 123 (13.2), 95 (9.5)

[a] Data presented are for the isomer of shortest retention time. [b] Percent relative to base peak as 100%. [c] $M^+ - C_2H_3$. [d] Not detected. A low-intensity peak at m/z 209 (0.4%) may be $M^+ + 1$. Also observed was $M^+ - CH_3$, m/z 193 (3.6%) and $M^+ - C_2H_3$, m/z 181 (0.6%). [e] For Br = 79 and Br = 81, respectively. [f] M^+ was not detected. The pair of signals (nearly 1:1) at 217 and 219 could be $M^+ - C_2H_3$. No other pair of signals due to Br isotopes were assignable. [g] M^+ was not detected. $M^+ - C_2H_3$ was detected at m/z 166 (6.4%).

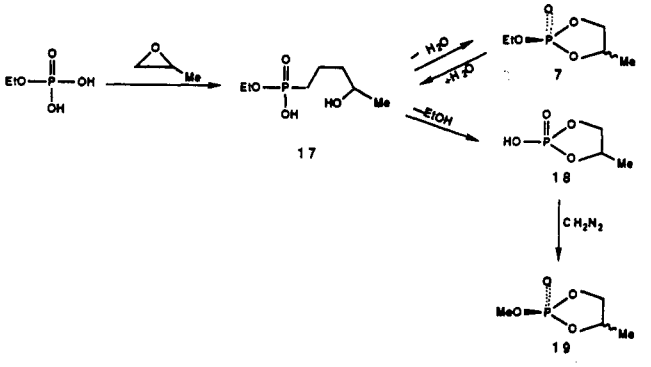
Scheme I



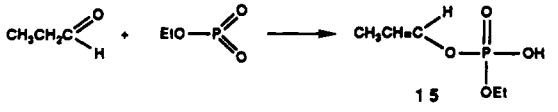
Scheme II



Scheme III

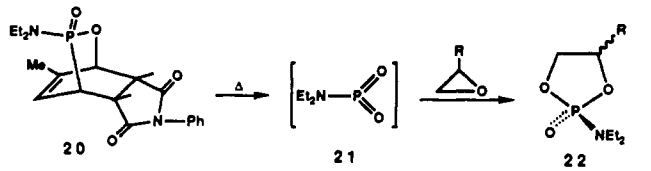


establish the importance of the enol phosphate as an intermediate in the metaphosphate–oxirane reaction, however.



We noted that the composition of the metaphosphate–epoxide reaction mixture underwent some changes on standing at room temperature for 2–4 days. For the 2-methyloxirane product, loss of 7 occurred, with formation of phosphates giving ^{31}P NMR shifts around δ 0 (unidentified, probably oligomeric from consecutive epoxide ring openings). Also, a low-intensity signal slightly downfield (δ 19.2) of the signals for ester 7 developed in the medium but later decreased. Such a phosphorus shift compels an assignment to this signal of a 1,3,2-dioxaphospholane 2-oxide derivative, and the acid 18 was suspected. Since direct hydrolysis of 7 to 18 by exocyclic cleavage is unlikely,[18] the slow formation of acid 18 can be accounted for by a ring-opening hydrolysis of ester 7 to form 17 (Scheme III); this intermediate can then recyclize to 7 (a source of water), but it can also cyclize to 18 by elimination of ethanol. The same observation of instability was made when 7 was prepared by a different process, the reaction of ethyl phosphate with 2-methyloxirane (Scheme III); the initial product 7 was hydrolyzed to acid 18 over a period of 2 days. To confirm the structure of acid 18, methylation with diazomethane was performed to convert it to the methyl ester 19. This was identical in ^{31}P NMR and GC–MS with an authentic sample.

Reaction of Epoxides with N- and S-Containing Metaphosphate Derivatives. We have extended the scope of the new reaction by showing that both an *N,N*-dialkyl metaphosphoramidate[7] (21, prepared from 20) and an alkyl metathiophosphate[9] (24, prepared from 23)[9] react with an epoxide (2-methyloxirane). The former reaction was quite straightforward; the ^{31}P NMR spectrum showed the only significant product to be the expected isomeric 1,3,2-dioxaphospholane 2-oxides (22) with ^{31}P δ 16.67 (unresolved, but revealed to be a 1:2 mixture by GC–MS).



(18) Gorenstein, D. G.; Chang, A.; Yang, J. *Tetrahedron Lett.* **1987**, *43*, 469. Taira, K.; Fanni, T.; Gorenstein, D. G. *J. Am. Chem. Soc.* **1984**, *106*, 1521.

Scheme IV

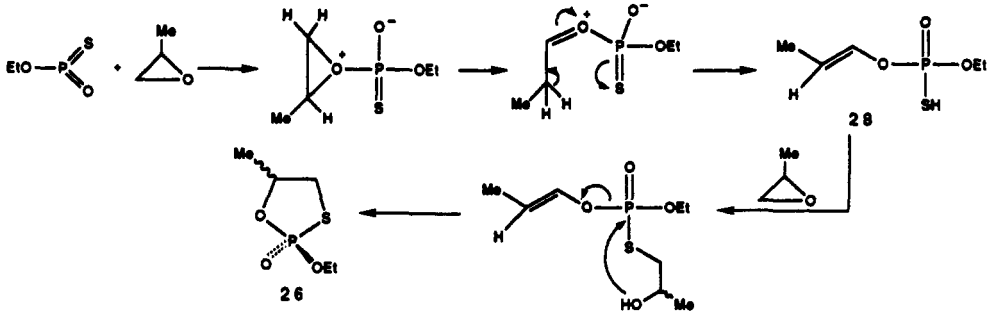
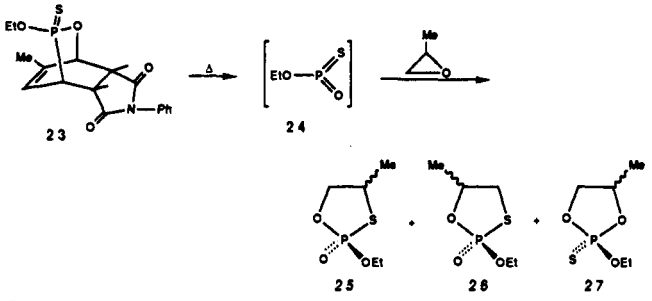


Table III. Partial Mass Spectral Data for the Diastereomers of 2-Ethoxy-5-methyl-1,3,2-oxathiaphospholane 2-Oxide (26) and 2-Ethoxy-4-methyl-1,3,2-oxathiaphospholane 2-Oxide (25)[a]

	m/z	isomers of 26		m/z	isomers of 25	
GC ret. (min)		13.90	~14.01		13.84	14.06
ratio		4	4		1	1
	182	18.1	19.9	182	29.1	26.7
	154	100	100	154	100	100
	139	16.8	17.8	139	63.6	63.1
	138	30.1	31.2	138	46.6	44.7
	121	35.2	33.1	141	40.7	61.2
	93	45.7	45.7	115	62.2	44.9
	74	53.4	53.6	114	42.6	46.4
	65	26.3	25.0	97	23.1	25.3
	41	50.8	48.9	60	75.9	83.2

[a] Obtained for peaks on GC analysis (DB1701 column, 30 m, 0.25 mm i.d.; 80 °C for 2 min, ramp 10 °C/min). Samples from reaction of 2-methyloxirane with ethyl metathiophosphate or *O,O*-diethyl phosphorothioate were nearly identical.

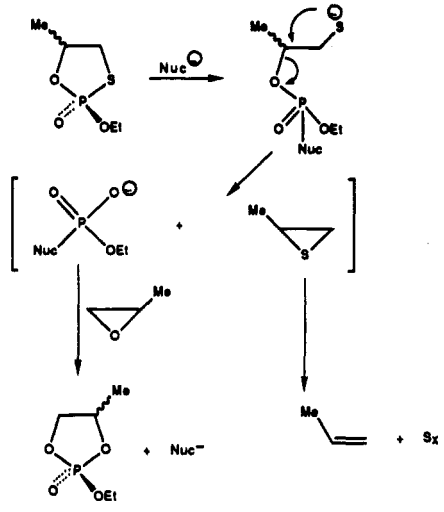
From the reaction with ethyl metathiophosphate (**24**), three products (each diastereomeric) can be visualized:



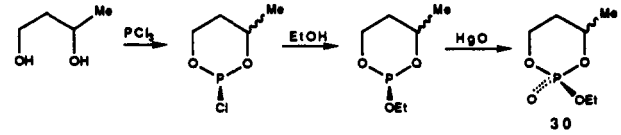
However, only products with the sulfur atom in the ring (**25** and **26**) were observed; the ^{31}P NMR spectrum contained signals at δ 44.85, 43.95, 42.15, and 41.29 (ratio 1.0:1.0:4.0:4.0), which are in the expected region for diastereomeric 1,3,2-oxathiaphospholane 2-oxides (the shift for the O-methyl analogue of **26** is reported[19] to be δ 38). Had a thiophosphoryl derivative (**27**) been formed, a shift at much lower field (possibly δ 80–90) would have been observed. GC–MS (Table III) showed that there were four compounds with very close retention times (13.90–14.06 min), each giving the expected m/z value of 182 for M^+ of $C_5H_{11}O_3PS$. The intensities were similar to those seen on the ^{31}P NMR spectrum; the two more intense compounds are assigned structure **26** (with 1:1 cis–trans isomers) and the less intense are assigned the regioisomeric structure **25** (also 1:1 cis–trans isomers). As expected, there were some major differences in the fragmentation patterns for **25** and **26**, although both gave the same base peak of m/z 154 by loss of C_2H_4.

(19) Nuretdinova, O. N.; Guseva, F. F.; Arbuzov, B. A. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1976**, 2625.

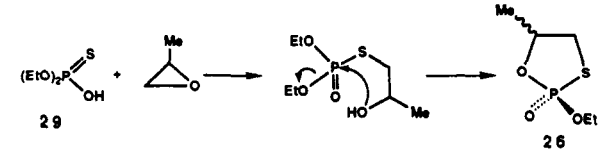
Scheme V



Scheme VI



Assignment of the major product as having the methyl group in the 5-position is based on the concept of the attack of a nucleophile at the least substituted position of an alkyl oxirane,[11] an event that would be consistent with mechanism (3) suggested for ethyl metaphosphate attack on an epoxide (as in Scheme IV, intermediate **28**). Proof for the structure assignments given to the regioisomers comes from another reaction that we have performed. We reacted *O,O*-diethyl phosphorothioate (**29**) with 2-methyloxirane and found by GC–MS (Table III) the same ratio of regioisomers (and of their diastereomers) as from the metathiophosphate reaction. The same four ^{31}P NMR signals from δ 41–45 were also observed. In this reaction, nucleophilic attack by sulfur can be expected to occur at the least substituted carbon, as is known to be true from an analogous reaction.[20] The oxathiaphospholane



oxides were quite unstable, and isolation was not successful. The instability seems to be associated with the formation of a sulfur-free product; on standing there was a definite increase in the amount of byproducts with ^{31}P NMR δ 16.35 and 16.38, which are obviously due to the diastereomeric 1,3,2-dioxaphospholane 2-oxides (**7**). This

can be explained by a mechanism such as that in Scheme V, which resembles proposals of other authors.[19-21]

Reaction of Ethyl Metaphosphate with 1-Methyloxetane. Other small-ring cyclic ethers are known to be sensitive to attack by electrophiles, leading us to inquire if the oxetane and tetrahydrofuran systems would be attacked by a metaphosphate. When 2-methyloxetane was included in the metaphosphate generation medium employing **1a** at 120 °C, evidence was obtained from the ^{31}P NMR spectrum that complete trapping by the ether did occur; there were no signals for polyphosphates, and the major product gave a complex pattern in the noncyclic phosphate region (δ 0–2). Small signals at δ −7.5 and −4.8 seem to match those expected for the cis and trans isomers of 4-methyl-1,3,2-dioxaphosphorinane 2-oxide (**30**, prepared as seen in Scheme VI) since values of δ −7.40 and −5.02 were observed for an authentic sample. Since the amount of these isomers was quite small, no further attention was given to this process. The failure to form major amounts of cyclic products may be of mechanistic significance, since it implies a major difference from the special chemistry of oxiranes. An attempt to react tetrahydrofuran with thermally generated ethyl metaphosphate was not successful and led only to polyphosphate formation from condensations of the untrapped metaphosphate.

Experimental Section

General Procedures. Melting points are corrected; boiling points are uncorrected. For ^{31}P NMR spectra, 85% H_3PO_4 was used as external reference with positive signs downfield, negative upfield. ^1H NMR spectra were recorded at 80 MHz. GC analyses were performed with DB1701 or DB5 30 m × 0.25 mm columns, with peak analysis by mass spectrometry. Compounds **1a**,[1] **7**,[20] **19**,[22] **20**,[8] **29**,[14] and **30**[21] were prepared according to the published procedures.

Generation of Ethyl Metaphosphate from 1a in the Presence of Epoxides. (a) General Procedure. A solution of reagent **1a** (0.2 mmol) and the appropriate epoxide (0.6 mmol) in dry toluene (3 mL) was heated in a sealed tube at 120 °C for 5–6 h. Then, the solvent was evaporated in vacuo. The residue was dissolved in $CDCl_3$ and analyzed by use of ^{31}P NMR and GC–MS (Tables I and II). All attempts to separate reaction products by column chromatography on silica gel (Merck, grade 60, 60 Å) or Florisil (Fisher, 100–200 mesh) failed.

(b) Isolation of *trans*- and *cis*-2-Ethoxy-4-methyl-1,3,2-dioxaphospholane 2-Oxide (7). A solution of **1a** (0.413 g, 1.19 mmol) and 2-methyloxirane (0.318 g, 5.48 mmol) in dry toluene was heated in a sealed tube at 120 °C for 6 h. After evaporation of the solvent in vacuo, Kugelrohr distillation (160 °C/0.1 mm) gave **7**[20] as a colorless oil (0.036 g): ^{31}P NMR ($CDCl_3$) δ 16.35, 16.58 (ratio 1:1, corresponding to those of authentic samples), and −2.01 (15%) attributed to unidentified phosphates; ^1H NMR ($CDCl_3$) δ 1.34 (t, $^3J_{HH}$ 7.0 Hz, 3 H), 1.43 (dd, $^3J_{HH}$ 6.0 Hz, $^4J_{PH}$ 2.1 Hz, 3 H), 3.9–4.9 (m, 5 H).

Authentic *trans*- and *cis*-2-Ethoxy-4-methyl-1,3,2-dioxaphospholane 2-Oxide (7). A solution of **1a** (0.639 g, 1.84 mmol) and ethanol (0.0944 g, 2.05 mmol) in dry toluene (3 mL) was heated in a sealed tube at 120 °C, and the reaction progress was monitored by ^{31}P NMR. When the signal at δ 27.77 attributed to the starting material was replaced by a signal at δ 1.54 for diethyl phosphate, a solution of 2-methyloxirane (0.267 g, 4.60 mmol) in toluene (0.5 mL) was added and heating was continued at 110 °C for 5 h. Then, the reaction mixture was diluted with toluene (25 mL) and concentrated to half of its volume by slow distillation (~1 h) under atmospheric pressure. The residue was evaporated to dryness in vacuo. Kugelrohr distillation (150 °C (0.05 mm)) afforded **7**[20] as a colorless oil (0.028 g): ^{31}P NMR ($CDCl_3$) δ 16.43, 16.67 (1:1), and δ −1.38 (17%) attributed to unidentified noncyclic phosphate. The GC–MS data matched those obtained for the metaphosphate–oxirane reaction product.

***trans*- and *cis*-2-Chloro-4-phenyl-1,3,2-dioxaphospholane (8).** To a stirred solution of phosphorus trichloride (20.59 g, 0.15 mol) in chloroform (100 mL) was added 2-phenyl-1,2-ethanediol (20.1 g, 0.15 mol) gradually in small portions at room temperature. Hydrogen chloride was evolved copiously. The reaction mixture was heated at 40 °C for 15 min and then distilled to give 4.63 g (15.7%) of **8**, bp 120–125 °C (1.5 mm). The residue polymerized vigorously with decomposition (Caution!): ^{31}P NMR ($CDCl_3$) δ 174.0 and 171.2 (ratio 1:2). Anal. Calcd for $C_8H_8ClO_2P$: C, 47.43; H, 3.98. Found: C, 48.07; H, 3.99.

2-Chloro-4-phenyl-1,3,2-dioxaphospholane 2-Oxide (9). Dry oxygen was passed through a solution of 2-chloro-4-phenyl-1,3,2-dioxaphospholane (**8**; 3.22 g, 0.015 mol) in dry benzene (50 mL) until the slightly exothermic reaction ceased (2 h). Benzene was evaporated in vacuo to afford **9** as a colorless oil (3.5 g, ~100%): ^{31}P NMR ($CDCl_3$) δ 21.26. Attempts at distillation of the crude chloride were unsuccessful.

Authentic *trans*- and *cis*-2-Ethoxy-4-phenyl-1,3,2-dioxaphospholane 2-Oxide (10). A solution of ethanol (1.83 g, 0.039 mol) and triethylamine (4.02 g, 0.039 mol) in benzene (100 mL) was cooled to 5 °C, and a cold solution of crude 2-chloro-4-phenyl-1,3,2-dioxaphospholane 2-oxide (**9**; 8.7 g, 0.039 mol) was added dropwise with vigorous stirring. Then, the reaction mixture was allowed to warm to room temperature, and stirring was continued for 2 h. The amine salt was filtered off and the filtrate was evaporated in vacuo to give a yellow oil. The oil was extracted with dry hexane (2 × 200 mL) and the layers were combined and concentrated under reduced pressure. The residue was distilled in vacuo to afford **10** as a yellow oil (1.3 g, 14.4%) bp, 120–125 °C (1.5 mm). The viscous residue decomposed violently (Caution!): ^{31}P NMR ($CDCl_3$) δ 16.32; ^1H NMR ($CDCl_3$), δ 1.40 (t, $^3J_{HH}$ 7.2 Hz, 3 H), 3.7–5.1 (m, 4 H), 5.4–5.8 (m, 1 H). The GC–MS data matched those for the metaphosphate–oxirane reaction product. Anal. Calcd for $C_{10}H_{13}O_4P$: C, 52.63; H, 5.74. Found: C, 53.07; H, 5.77.

Generation of *O*-Ethyl Phosphoric Acid Monoester from Heating 1a and Water. To a solution of **1a** (0.0836 g, 0.241 mmol) in toluene (3 mL) was added water (0.0045 g, 0.25 mmol) and the mixture heated in a sealed tube at 120 °C for 6 h. Toluene was then evaporated in vacuo and replaced by ether (2 mL). A white precipitate was filtered off, and the filtrate was concentrated under reduced pressure to give the crude *O*-ethyl phosphoric acid monoester as a pale yellow oil, 0.0320 g (~100%; ^{31}P NMR ($CDCl_3$) δ 1.72 (also a minor impurity with δ 0.62)); the anilinium salt was formed by adding a solution of aniline in ethanol. The precipitated solid was filtered off and recrystallized from ethanol–ether, 0.026 g (49.0%): mp 163–164 °C (lit.[25] mp 164–166 °C); ^1H NMR ($CDCl_3$) δ 1.16 (t, $^3J_{HH}$ = 7.2 Hz, 3 H, CH_3), 3.7–4.2 (m, 3 H, $-NH_3^+$), 4.26 (dq, $^3J_{HH}$ = 7.2 Hz, $^3J_{PH}$ = 7.2 Hz, 2 H, CH_2), 6.85–7.35 (m, 5 H, Ph–N); ^{31}P NMR (D_2O) δ 2.45.

Generation of *trans*- and *cis*-2-Ethoxy-4-methyl-1,3,2-dioxaphospholane 2-Oxides (7) by the Reaction of *O*-Ethyl Phosphoric Acid Ester with 2-Methyloxirane. To a solution of **1a** (0.0765 g, 0.220 mmol) in toluene (3 mL) was added water (0.0050 g, 0.228 mmol) and the mixture heated in a sealed tube at 120 °C for 6 h. Toluene was then evaporated and replaced by ether (2 mL). A white solid was filtered off. The filtrate was evaporated to dryness in vacuo. The residue of *O*-ethyl phosphoric acid monoester was dissolved in toluene (3 mL), and the solution was treated with 2-methyloxirane (0.0290 g, 0.499 mmol). After being heated in a sealed tube at 120 °C for 4 h, the reaction mixture was concentrated in vacuo to afford a crude mixture of *trans*- and *cis*-**7** as a yellow oil (0.044 g; ^{31}P NMR ($CDCl_3$) δ 16.67 and 16.43, ratio 1:1).

Heating of 1a with 2-Methyloxirane. Detection of Propionaldehyde. A solution of **1a** (0.157 g, 0.451 mmol) and 2-methyloxirane (0.0819 g; 1.410 mmol) in toluene (1.5 mL) was

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heated in a sealed tube at 120 °C for 4.5 h. The reaction mixture was analyzed by GC-MS and contained 0.01% of propionaldehyde (0.00014 g, 0.0024 mmol). Relative to the original concentration of **1a**, the yield of propionaldehyde can be estimated as 0.53%.

Proof of 2-Hydroxy-4-methyl-1,3,2-dioxaphospholane 2-Oxide (18) Formation from 7. The reaction mixture prepared previously containing *O*-ethyl phosphoric acid monoester was dissolved in $CDCl_3$ (1.5 mL), left at room temperature for 48 h, and then analyzed (^{31}P NMR ($CDCl_3$) δ 19.07 (**18**), 16.67, and 16.43 (both **7**), with a broad complex signal at −2.0 to +2.0). The solvent was evaporated in vacuo and replaced by ether (5 mL). To the resultant solution was added a solution of diazomethane (0.0369 g, 0.880 mmol) in ether (40 mL). After 5 h at room temperature, the reaction mixture had ^{31}P ($CDCl_3$) δ 17.81, 17.54, 16.67, 16.44, and a broad complex signal at −2.0 to +2.0. The observed intensity of the signals with δ 17.81 and 17.54 increased considerably after a mixture of the authentic[24] isomeric methyl esters **19** (δ 17.66 and 17.43) was added to the sample.

Reaction of *N,N*-Diethyl Metaphosphoramidate with 2-Methyloxirane. A solution of **20** (0.0928 g, 0.247 mmol) and 2-methyloxirane (0.032 g, 0.551 mmol) in 3 mL of toluene was heated in a closed tube for 4.5 h at 120 °C. The solvent was then removed by evaporation and the residue was taken up in $CDCl_3$. The ^{31}P NMR spectrum contained only one signal for a reaction product (δ 16.9), along with a small signal for unreacted starting material. Analysis by GC showed the product to consist of a 1:2 mixture of isomers with retention times of 11.3 and 11.7 min, respectively. The mass spectra of the GC peaks were nearly identical. For both the base peak had m/z 178 ($M^+ - CH_3$). For the former, M^+ (calcd for $C_7H_{16}NO_3P$ 193, found 193) had 14.3% relative abundance and for the latter 12.9%. Other strong signals included m/z 150 ($M^+ - CH_3 - C_2H_4$), 138, and 110.

Generation of *trans*- and *cis*-2-Ethoxy-5-methyl-1,3,2-oxathiaphospholane 2-Oxides (26) and -2-Ethoxy-4-methyl-1,3,2-oxathiaphospholane 2-Oxides (25) by Heating 23 and 2-Methyloxirane. A solution of **23** (0.097 g, 0.269 mmol) and 2-methyloxirane (0.0390 g, 0.671 mmol) in toluene (3 mL) was heated in a sealed tube at 120 °C for 4 h. Evaporation of the solvent in vacuo gave a yellow oil (0.121 g) that was dissolved in $CDCl_3$ (1.5 mL) having ^{31}P NMR δ 44.85, 43.95, 42.15, and 41.29 for isomers of **26** and **25**, respectively, with others at 16.68, 16.44, and −2.03 (broad) in the ratio 1.0:1.0:4.0:4.0:9.0:9.0:23.0, respectively. GC-MS data are given in Table III.

Generation of *trans*- and *cis*-2-Ethoxy-5-methyl-1,3,2-oxathiaphospholane 2-Oxides (26) and -2-Ethoxy-4-methyl-1,3,2-oxathiaphospholane 2-Oxides (25) from *O,O*-Diethyl Phosphorothioate (29) and 2-Methyloxirane. To a solution of **29** (0.0839 g, 0.493 mmol) at 0 °C in toluene (2.5 mL) was added dropwise with stirring a solution of 2-methyloxirane (0.030 g, 0.518 mmol) in toluene (25 mL). The reaction mixture was allowed to warm to room temperature, the solvent evaporated in vacuo, and the residue dissolved in $CDCl_3$; ^{31}P NMR δ 45.47 and 44.50 for the isomers of **26** and 42.79 and 42.09 for isomers of **25**, with others at 30.98, 29.58, 0.69, and 0.059 in the ratio 1.0:1.2:2.0:2.5:9.8:1.0:2.0:5.5. Some unreacted **29** was also present (δ 67.48).

To prepare a sample for GC-MS measurements, a mixture of **29** (0.158 g, 0.927 mmol) and 2-methyloxirane (0.0554 g, 0.954 mmol) was maintained at room temperature for 4 h. GC-MS data are given in Table III.

Reaction of 2-Methyloxetane with Ethyl Metaphosphate. A mixture of 0.464 g (0.644 mmol) of 2-methyloxetane (refluxed over NaH and distilled) and **1a** (0.0860 g, 0.248 mmol) in 3 mL of toluene was heated for 6 h at 120 °C. Toluene was removed and the residue dissolved in $CDCl_3$. The ^{31}P NMR spectrum contained strong complex signals at δ −0.5 to −1.8 and very weak signals at δ −4.8 and −7.5, attributed to cyclic esters **30** (cis-trans). When the same reaction was conducted in acetonitrile, no signals for **30** were observed.

***trans*- and *cis*-2-Ethoxy-4-methyl-1,3,2-dioxaphosphorinane 2-Oxide (30).** A solution of 2-ethoxy-4-methyl-1,3,2-dioxaphosphorinane[23] (2.3 g, 0.014 mol) in benzene (25 mL) was added dropwise to a cooled (ice bath) and vigorously stirred suspension of yellow mercuric oxide (4.7 g, 0.021 mol) in benzene (100 mL). The mixture was stirred for 15 h and then filtered. The filtrate was concentrated in vacuo, and the residue was distilled under reduced pressure to give **30** as a colorless liquid (15.0 g, 59.5%): bp 100-110 °C (0.05 mm); ^{31}P NMR ($CDCl_3$) δ −5.02, −7.40 (ratio 0.07:1); ^1H NMR ($CDCl_3$) δ 1.38 (t, $^3J_{HH}$ 7.1 Hz, 3 H); 1.39 (dd, $^3J_{HH}$ 7.1 Hz, $^4J_{PH}$ 2.6 Hz, 3 H); 1.6-2.28 (m, 2 H); 4.15 (dq, $^3J_{HH}$ 7.1 Hz, $^3J_{PH}$ 5.6 Hz, 2 H); 4.2-4.8 (m, 3 H). Anal. Calcd for $C_6H_{13}O_4P$: C, 40.00; H, 7.27. Found: C, 39.57; H, 6.90.

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Absolute Configuration of Hydroazulenoid Diterpenes Based on Circular Dichroism

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The structure of a new hydroazulenoid diterpene, 9-*epi*-dictyol B (**1**), isolated from the brown alga *Glossophora kuntii*, was proposed on the basis of its spectral data and confirmed by chemical transformations. Absolute stereochemistry studies, based on the CD exciton chirality method, of the new diterpenoid 9-*epi*-dictyol B (**1**) as well as those of the previously reported dictyotadiol (**6**) led to the determination of the absolute configuration of the new compound 9-*epi*-dictyol B (**1**) and revisions of absolute configurations of previously reported diterpenoids dictyotriols C (**2**), D (**3**), and E (**4**), dictyol B (**5**), and dictyotadiol (**6**). The cause of previous erroneous results is discussed and indeed points to the extreme care which must be exercised by anyone using this method.

The exciton chirality method, a powerful tool for absolute configuration studies, has been successfully applied to a great number of synthetic and natural organic compounds,[1] and its utility has been expanded with new ap-

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