Reduction of 21. To a solution of lithium (~20.0 mg) in liquid NH_3 (~50 mL) at reflux was added **21** (74.4 mg, 0.38 mmol) in ether (4 mL) containing *tert*-butyl alcohol (169 mg). After another small portion of lithium was added, stirring was continued at -33 °C for 0.5 h. The usual workup (addition of NH_4Cl, evaporation of NH_3, Et_2O extraction) yielded a residue which was taken up in acetone and treated with Jones reagent. After standard workup, the residue was purified by VPC (column B, 120 °C) to give **23**, having NMR and IR spectra identical with those of an authentic sample.

^{18}O Labeling of 10. A mixture of **10** (285.2 mg), 98% $H_2{}^{18}O$ (0.40 mL), and THF (5.8 mL), through which dry HCl gas had been bubbled for 0.5 min, was allowed to stand at 25 °C for 6 days. The mixture was neutralized with $NaHCO_3$, diluted with H_2O, and extracted with Et_2O. The residue after removal of solvent was combined with that from a smaller scale run (53.5 mg) and was flash chromatographed using 90:10 hexanes/Et_2O to give **10** (302 mg, 90%). Mass spectrometric analysis indicated that the value of $(M + H)^+_{227}/(M + H)^+_{225}$ was 0.218 (i.e., **10** contained 17.9% ^{18}O).

Photolysis of ^{18}O-Labeled 10. The labeled furanone (290 mg) was dissolved in anhydrous benzene (85 mL) and was irradiated as described above for 74 h at which time very little **10** remained. The benzene was removed by distillation and the residue was flash chromatographed using 92.5:7.5 hexanes/Et_2O. Enone **21** was eluted in fractions 12-17, furanones **10** and **8** in fractions 20-27. These were further purified by preparative VPC (column A, 150-160 °C) before analysis by mass spectrometry. The ratio of $(M + H)^+_{199}/(M + H)^+_{197}$ for **21** was 0.015 (1.5% ^{18}O); the ratio of these ions in the spectrum of **21** obtained from unlabeled **10** was 0.013. The value of $(M + H)^+_{171}/(M + H)^+_{169}$ found for **8** was 0.212, and the value of $(M + H)^+_{227}/(M + H)^+_{225}$ from recovered **10** was 0.216, indicating essentially no loss of label from these compounds.

A small amount of labeled furanone **8** was treated with unlabeled hydrochloric acid in THF for 3 days as described above for **10**. Mass spectrometric analysis indicated that most of the ^{18}O had been washed out.

Photolysis of 2. A solution of **2** (100 mg) in C_6H_6 (70 mL) was irradiated through Vycor. TLC analysis (silica gel plates, 98:2 CH_2Cl_2/MeOH) indicated little starting material after 1.75 h and the formation of one major and several minor products. The residue after removal of solvent was flash chromatographed using 99:1 CH_2Cl_2/MeOH to give **3**, mp 150.5-152 °C (lit.[7] mp 149-150 °C) and having a NMR spectrum identical with that reported.[7] Irradiation through Pyrex gave a slower reaction but comparable results.

Photolysis of Bullatenone (30). A solution of **30**[4] (138 mg) in C_6H_6 (90 mL) was irradiated through Pyrex for 9 h. TLC as above indicated one faster R_f product. Flash chromatography using 99.5:0.5 CH_2Cl_2/MeOH gave recovered **30** (20.5 mg) and **31** (101.6 mg, 86%), mp 189-191 °C: IR 3028 (w), 2980 (m), 1764 (s), 1378 (m), 1362 (m), 1120 (s), 1007 (m) cm^{-1}; NMR (60 Mz) δ 7.27 (s, 5 H), 3.62 (s, 1 H), 1.40 (s, 3 H), 0.85 (s, 3 H); CI mass spectrum, m/z 377.1717 [$(M + H)^+$, calcd for $C_{24}H_{25}O_4$, 377.1753].

The dimer was the only product detected when the concentration of the furanone irradiated was lowered to 0.25 mg/mL.

Acknowledgment. This research was supported by the National Science Foundation. We thank Professor Albert Padwa for helpful discussion and Phyllis Wilson for technical assistance.

Reactions of 1,2-Oxaphospholenes. 4.[1] Responses toward Oxidations, Cycloadditions, and Conjugate Additions

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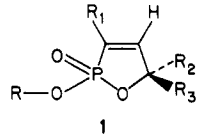
Received May 21, 1985

In contrast to the more normal reactivity of the carbon-carbon double bond in vinyl phosphonates, the oxaphospholene double bond in 5,5-dimethyl-2-phenyl-1,2-oxaphosphol-3-ene 2-oxide (**7**) has proven to be quite resistant to a broad spectrum of reagents including typical electrophiles, most electrophilic and nucleophilic epoxidizing reagents, and organometallic nucleophiles as well as representative Diels-Alder dienes and 1,3-dipoles. Four exceptions to this trend were *N*-bromoacetamide (NBA), ozone, lithium dimethylcuprate, and sodium naphthalene. Reaction of **7** with NBA involved formation of a bromonium ion followed by methyl migration, ring opening, and dehydrobromination to give (3-keto-2-methyl-1-butenyl)phenylphosphinic acid, characterized as its methyl ester **14**. Ozonolysis of **7** proceeded with cleavage of the double bond, affording (after a series of decarboxylations and oxidations) acetone, phenylphosphonic acid, and 1-carboxy-1-methylethyl phenylphosphonate (**21**). The latter two acids were characterized as their methyl esters. Reactions of **7** with the cuprate gave, instead of methylation, the two-electron reduction product (3-methyl-2-butenyl)phenylphosphinic acid (**24**), also characterized as its methyl ester. Reduction of **7** with naphthalene sodium also gave **24**, in support of the stepwise two-electron reduction mechanism suggested in the case of the cuprate. Finally, in a related reaction, treatment of the 4-bromo derivative of **7** with magnesium or the cuprate led via ring opening to (3-methyl-1,2-butadienyl)phenylphosphinic acid (**8**), the original precursor of **7**, and its 4-bromo derivative.

In the decade since we first discovered a general synthetic route to 1,2-oxaphosphol-3-enes from propargyl alcohols,[2] we have investigated in detail the mechanisms of the reactions involved.[3] Recently we began a systematic study of the chemistry of this novel phosphorus heterocyclic system. Our initial interest was focused on nucleophilic substitution at the phosphorus atom in **1**.[1,4]



1

(1) Paper 3 in the series: Macomber, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 4386.

(2) (a) Macomber, R. S. *J. Org. Chem.* **1971**, *36*, 2713. (b) Macomber, R. S.; Kennedy, E. R.; Florian, L. R.; Elder, R. C. *J. Org. Chem.* **1973**, *38*, 4177.

(3) (a) Macomber, R. S.; Kennedy, E. R. *J. Org. Chem.* **1976**, *41*, 3191. (b) Macomber, R. S. *J. Am. Chem. Soc.* **1977**, *99*, 3072. (c) Macomber, R. S.; Krudy, G. A.; Seff, K.; Diaz-Miron, L. E. R. *J. Org. Chem.* **1983**, *48*, 1425.

(4) (a) Macomber, R. S.; Krudy, G. A. *J. Org. Chem.* **1981**, *46*, 4038. (b) Macomber, R. S.; Krudy, G. A.; Amer, M. Z. *J. Org. Chem.* **1983**, *48*, 1420.

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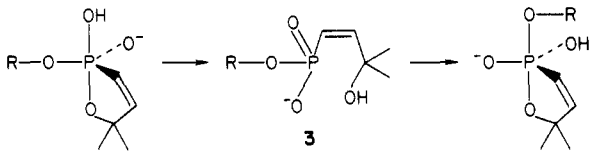
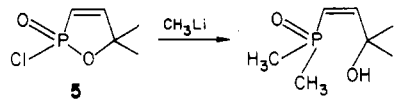
Oxaphospholenes such as 1 are cyclic phosphonate esters and can be regarded as phosphorus analogues of γ-lactones. Moreover, the double bond in "conjugation" with the phosphoryl group makes them close cousins of butenolides. Because of these similarities, we first investigated hydrolysis reactions of 1. A priori, hydrolysis could be expected to involve alkyl–oxygen cleavage, exocyclic phosphoryl–oxygen cleavage, or endocyclic phosphoryl–oxygen cleavage. Indeed, all three mechanisms were observed.[1,4] However, alkyl–oxygen cleavage was suppressed when R was sterically larger than methyl, and the nucleophile (e.g., hydroxide) then attacked phosphorus to give trigonal-bypyramid 2.



2 3 4

Westheimer's rules[5] suggested that 2 would be inhibited from pseudorotation and would collapse by ring opening (endocyclic cleavage) to 3, as was indeed observed.[1,4b] However, unlike systems lacking the double bond,[5] 3 was relatively unstable[1,4a] and reclosed to 4, which then collapsed to phosphonic acid 1 (R = H), the product of *net* exocyclic cleavage.[1,4b]

With nucleophiles stronger than hydroxide or methoxide, stable analogues of 3 could be isolated. Thus, treatment of chloro derivative 5 with excess methyllithium led exclusively to phosphene oxide 6.[4a] A similar reaction

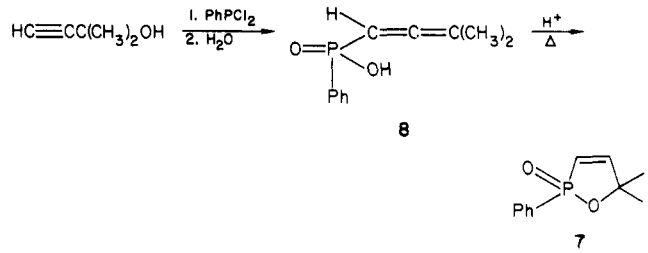


5 6

was observed with phenyl Grignard as nucleophile.[6] In no case, however, did we observe any evidence for Michael-type nucleophilic attack at C_4, the carbon β to the phosphoryl, although such reactions are known for acyclic vinyl phosphonates.[7] The present report describes our studies on the response of a prototype oxaphospholene system to conditions for oxidations, cycloadditions, and conjugate addition. To circumvent unwanted complications from exocyclic cleavage at the alkoxy group of 1, our test system in the present study has been cyclic phosphinate 7, prepared from 2-methyl-3-butyn-2-ol via acid-catalyzed cyclization of the isomeric allenic phosphinic acid 8.[3c] Although it might be argued that the *gem*-dimethyl groups could sterically interfere with some of the reactions described below, the relative inaccessibility of 1 with R_2 and/or R^3 = H and only hydrogen at the β-carbon[2,3] made 7 our first choice.

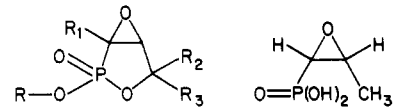
Results

(a) Epoxidation Studies. We began our work in this area by attempting to epoxidize the double bond in 1 to



8 7

give bicyclic oxide 9, which can be regarded as an analog of phosphonomycin 10.[8] However, preliminary studies[9a]

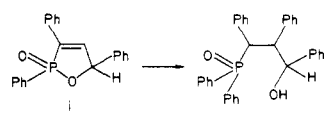


9 10

with a model system (1, R_1 = R = H; R_2 = R_3 = CH_3) suggested that the double bond in 1 was too electron deficient (by virtue of "conjugation" with the phosphoryl group, as further demonstrated through NMR studies[9b]) to react with electrophilic peracids such as *m*-chloroperbenzoic or peracetic acid. Our previous work[1-4] had shown that the oxaphospholene double bond was also completely inert toward common electrophiles such as Br^+ (from Br_2 in nonpolar media), HgX^+, H^+, RS^+, and RSe^+. Nonetheless, there had been one report[10a] of successful epoxidation (80% yield) of a 2-phospholene double bond with *N*-bromoacetamide (NBA) via the bromohydrin, so this is where we began the present study.

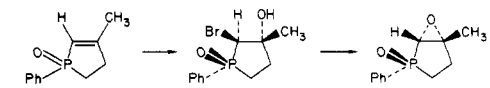
Cyclic phosphinate 7 was completely inert toward NBA at 25 °C in the following deuteriated solvents: acetonitrile (4 days), aqueous acetonitrile (1:1, v/v, 1 day), methanol (3 days), and methanol–TFA (2:1, v/v, 15 h). In aqueous solution there was a clean reaction (which could be monitored by ^1H NMR), as the initially neutral medium became increasingly acidic. The product was reasonably stable at 25 °C in acidic water and could be extracted into chloroform, where it decomposed after a few days (more rapidly when neat). The ^1H NMR spectrum (Experimental Section) was consistent *not* with the desired bromohydrin, but rather with rearranged and ring-opened ketophosphinate 11 (Scheme I). Only one of two possible diastereomers could be detected at 80 MHz, and we assign to it the stereochemistry shown, based on analogy to the bromination of the phospholene,[10a] and the (assumed) migration of the trans methyl group. The decomposition of 11 gave 12, the product of trans-dehydrobromination

(5) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70.
(6) Campbell, I. G. M.; Raza, S. M. *J. Chem. Soc. C* **1971**, 1836.
(7) Kirby, A. J.; Warren, S. G. "The Organic Chemistry of Phosphorus"; Elsevier: New York, 1967. It has also been reported[6] that reaction of i with phenyl Grignard gave ii, though attack at the double bond probably occurred after ring opening.



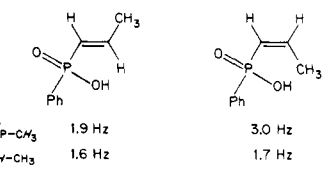
i ii

(8) Kahan, F. M.; Kahan, J. S.; Cassidy, P. J.; Kropp, H. *Ann. N.Y. Acad. Sci.* **1974**, *235*, 364.
(9) (a) Macomber, R. S. *J. Org. Chem.* **1978**, *43*, 1832. (b) Macomber, R. S.; Krudy, G. A. *J. Org. Chem.* **1978**, *43*, 4656. (c) Macomber, R. S. *Synth. Commun.* **1977**, *7*, 405.
(10) (a) It was reported (Smith, D. G.; Smith, D. J. H. *Tetrahedron Lett.* **1973**, 1249) that bromination of iii occurred cis to the phosphonyl oxygen:



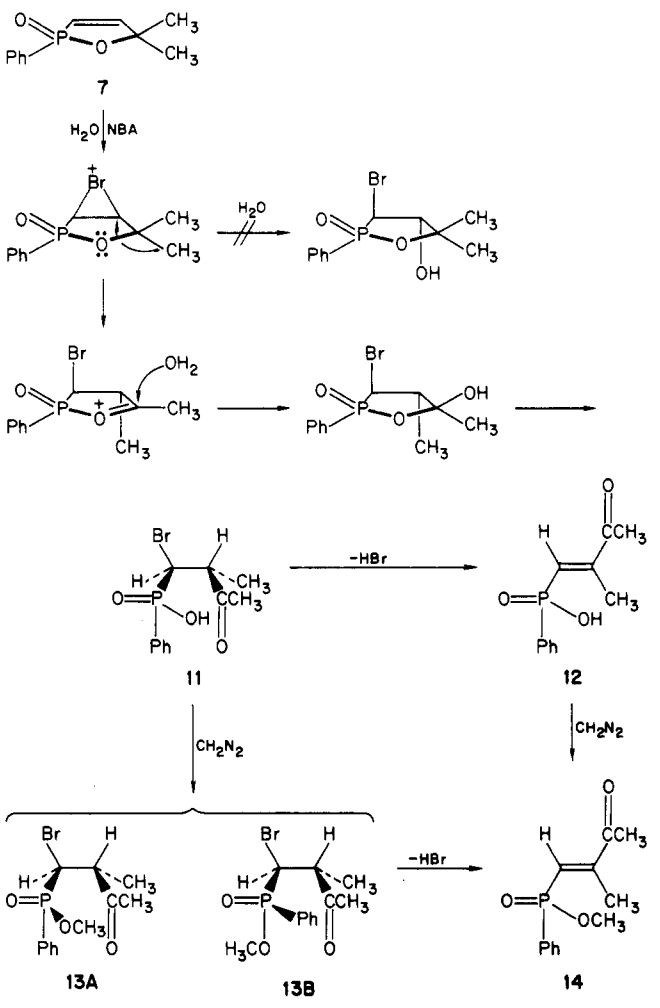
iii iv v

(b) Gareev, R. D.; Pudovic, A. N. *Zh. Obshch. Khim.* **1979**, *49*, 503 report the following coupling constants:



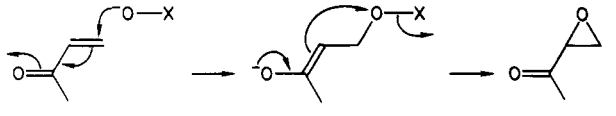
$^4J_{P-CH_3}$ 1.9 Hz 3.0 Hz
$^4J_{H-CH_3}$ 1.6 Hz 1.7 Hz

Scheme I

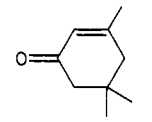


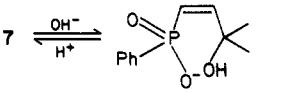
(vide infra). Although **11** and **12** were themselves too labile to permit isolation in pure form, these products could be esterified with diazomethane.[9c] Compound **11** provided two diastereomers (because of the newly created dissymmetry of phosphorus) of phosphinate **13** in nearly equal amounts. The fact that the two diastereomers could be readily detected in this case offers support for the conclusion that only a single diastereomer of **11** was formed. However, attempts to separate and purify the diastereomers of **13** led instead to a single product resulting from dehydrobromination of either **13A** or **13B**, the same product from esterification of **12**. We assign to this final product structure **14** on the basis of complete spectral analysis (Experimental Section). The *E* stereochemistry is proposed on the basis of coupling constants[10b] ($^3J_{cis\text{-}PCH_3}$ = 6.5 Hz; $^4J_{cis\text{-}PCH_3}$ = 2.9 Hz; $^4J_{trans\text{-}HCH_3}$ = 1.2 Hz) as well as the presumed trans stereochemistry of the elimination and the (assumed) greater thermodynamic stability of the *E* isomer.

There are several other reagents known to epoxidize double bonds in conjugation with electron-withdrawing groups. They may be classified as nucleophilic oxidants whose reactions proceed via an initial Michael-type addition.



For example, *tert*-butyl hydroperoxide (with Triton B catalyst) has been used to epoxidize conjugated carbonyl compounds[11] and even acyclic vinyl phosphonates.[12] Unfortunately, heterocycle **7** was completely inert to a tenfold excess of the reagent, being recovered unchanged after **5** days at 60 °C in methanol solution. Because this bulky reagent also failed to epoxidize the congested ketone isophorone, **15**,[11] our search shifted to sterically less demanding oxidants. Both sodium hypochlorite[13] and the sodium salt of hydrogen peroxide[14] are known to epoxidize α,β-unsaturated carbonyl compounds. Once again, however, no epoxidation was observed either in the case of hypochlorite (fourfold excess, 60 °C, 2 days, aqueous solution) or sodium hydrogen peroxide (threefold excess, 25 °C, 12 h, methanolic solution). In both bases, however, the hydroxide ion present caused ring opening of the heterocycle to **16**,[15] which reclosed to **7** upon acidification of the reaction mixture.[4a] These results suggest that the double bond in *acyclic phosphinate* **16** was also inert toward epoxidation under these conditions.



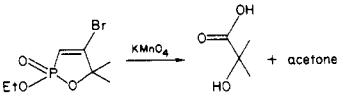


(b) Oxidations and Cycloadditions. Oxaphospholenes do undergo complex oxidations in the presence of aqueous permanganate,[2a,16] suggesting that perhaps **7** could be made to react with oxidants whose mode of reaction involved initial cycloaddition. The prime example of such a reagent is ozone, which is known to epoxidize (rather than cleave) double bonds in certain types of substrates.[17]

Compound **7** did indeed react with ozone in deuteriochloroform, though slowly at −38 °C. To avoid unwanted side reactions (vide infra) the reaction mixture was *not* subjected to further oxidative or reductive workup. Instead, the crude reaction mixture was separated by distillation (25 °C, 0.2 torr) into a volatile fraction and a nonvolatile fraction.[18] The volatiles comprised acetone (identified by NMR and GLC), deuteriochloroform, and a minor as-yet-unidentified component which exhibits a proton singlet at δ 8.03 (vide infra).

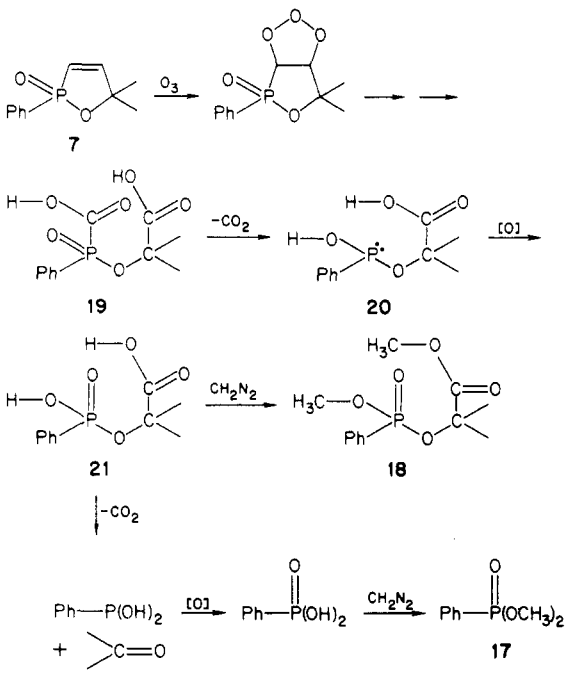
The nonvolatile fraction consisted of two acids which were esterified with diazomethane[9c] and separated by column chromatography. Their structures, assigned on the

(11) Yang, N. C.; Finnegan, R. A. *J. Am. Chem. Soc.* **1958**, *80*, 5845.
(12) Griffin, C. E.; Kundu, S. K. *J. Org. Chem.* **1969**, *34*, 1532.
(13) (a) Marmor, S. *J. Org. Chem.* **1963**, *28*, 250. (b) Arcoria, A.; Ballistreri, F. P.; Cantone, A.; Musumara, G.; Tripolone, M. *Gazz. Chim. Ital.* **1980**, *110*, 267.
(14) Wasson, R. L.; House, H. O. "Organic Syntheses"; Wiley: New York, 1963; Coll. Vol. I, p 552.
(15) ^{1}H NMR of **16** (D_2O, internal DSS): δ 1.39 (s, 6 H), 5.71 (dd, J_{PH} = 16.0, J_{HH} = 14.4 Hz, 1 H), 6.41 (dd, J_{PH} = 40, J_{HH} = 14.4 Hz, 1 H), 7.4–7.9 (m, 5 H). This spectrum is virtually superimposable on the one where the phenyl group is substituted by an O^-.[4a]
(16) In most cases these oxidations gave complex mixtures of products, but in one case two of the non-phosphorus-containing products were identified (Pudovik, A. N.: Khussainova, N. G. *Zh. Obshch. Khim.* **1980**, *50*, 1690):

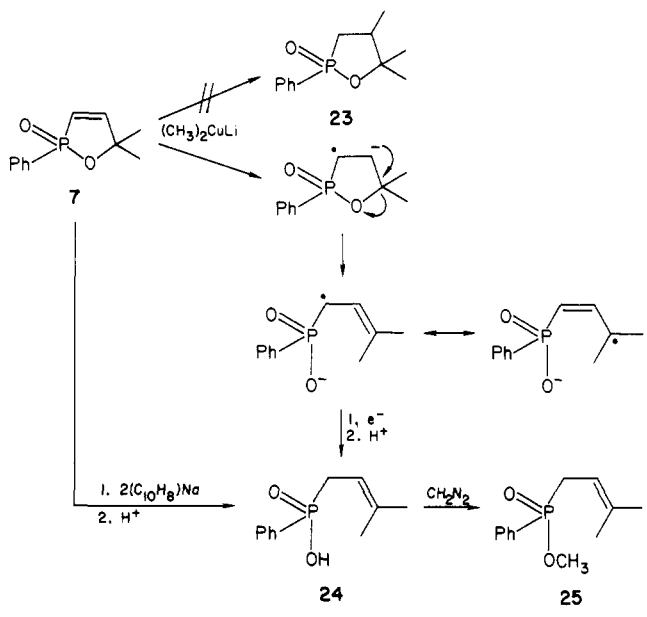


(17) Bailey, P. S.; Hwang, H. H.; Chiang, C.-Y. *J. Org. Chem.* **1985**, *50*, 231.
(18) It should be noted that this distillation did *not* cause any significant changes in the ^{1}H NMR spectra of the products, or their ratios.

Scheme II



Scheme III



basis of spectral data (see Experimental Section), were dimethyl phenylphosphonate (**17**) and mixed phosphonate **18**. The relative yields of these products were dependent on reaction conditions. Thus, the starting material in 3.0 mL of a 1.0 M solution of **7** was completely consumed after 20 min at −35 °C to give a 5:1 ratio of **21** to phenylphosphonic acid. By contrast, with a comparable flow of ozone, 3.0 mL of a 3.3 M solution required 105 min at −38 °C and provided a 1:1 ratio of the two compounds. Further, it was found that **18** slowly (over several weeks at ambient temperature) afforded the unidentified volatile product (vide supra).

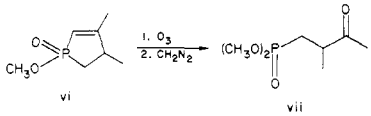
Exactly how, in the absence of an oxidative workup, the olefinic C–H groups were oxidized to C–O–H has not yet been clarified. Nonetheless, we suggest (Scheme II) that the primary ozonide eventually collapsed to dicarboxylic acid **19**. This compound decarboxylated to mixed diacid **20**, which was readily oxidized by ozone or other peroxides present in the reaction mixture to **21** (isolated as its diester **18**). Diacid **21** was also unstable with respect to decarboxylation, giving acetone and phenylphosphinic acid. The latter suffered oxidation to phenylphosphonic acid, which was isolated as its dimethyl ester **17**. Clearly, from the structure of the products and the time dependence of their yields, the presumed ozonide intermediate(s) must fragment more rapidly than they are formed. It is for this reason that further oxidative or reductive workups were not investigated (vide supra). There is one report of an ozonolysis in a comparable system, with analogous results.[19]

Observation of this oxidative fragmentation does serve as direct evidence that the oxaphospholene double bond is capable of undergoing cycloadditions with at least one reactive 1,3-dipole. It is also known that cyclic vinylphosphonates can participate as dienophiles in the Diels–Alder reaction.[20] By comparison, we found no evidence that diazomethane undergoes a similar cycloaddition with **7** (6 days at −2 °C, 12 h at 25 °C). Moreover, **7** could be recovered unchanged from melts with two common Diels–Alder dienes, anthracene, and 1,3-diphenylisobenzofuran.[21] We are forced to conclude that the double bond in **7** is not sufficiently electron deficient and/or the *gem*-dimethyl groups and phosphorus substituents are too sterically demanding for the molecule to undergo cycloadditions with typical dienes and 1,3-dipoles.[22]

(c) Attempted Michael Addition. From the results described above, it appeared that the phosphorus atom was more electrophilic than the β-carbon toward typical organometallic nucleophiles, as well as oxygen nucleophiles. However, there is one class of reagents, the organocuprates, which exhibits a preference to undergo Michael addition to double bonds conjugated with electron-withdrawing groups, rather than attacking the withdrawing group itself.[23] Moreover, it has been reported that lithium dimethylcuprate undergoes just such an attack on butenolide **22**.[24] We therefore undertook to examine the reaction of **7** with this cuprate.

When the cuprate, formed in the usual way from methyllithium and cuprous iodide,[23] was allowed to react with

(19) Compound vi affords vii upon ozonolysis:

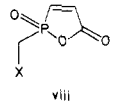


Hunger, K.; Hasserodt, U.; Korte, F. *Tetrahedron* **1964**, *20*, 1593.

(20) Darling, S. D.; Subramanian, N. *Tetrahedron Lett.* **1975**, 3279.

(21) We previously reported (Krudy, G. A. Ph.D. Dissertation, University of Cincinnati, 1982) that **1** (R_1 = R = H, R_2 = R_3 = CH_3) was similarly inert toward these two dienes, as well as 2,3-dimethyl-1,3-butadiene and cyclopentadiene.

(22) It should be noted that viii

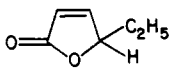


has been reported to undergo a Diels–Alder reaction with 2,3-dimethyl-1,3-butadiene (Khairullin, V. K.; Kimitrieva, G. V.; Pudokik, A. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1971**, 1249, 1254). Apparently the carbonyl group (coupled with the absence of the *gem*-dimethyl groups) renders the double bond both more electron deficient and more sterically accessible.

(23) House, H. O.; Umen, M. J. *J. Org. Chem.* **1973**, *38*, 3893 and references therein.

(24) Vigneron, J. P.; Meric, R.; Dhaenens, M. *Tetrahedron Lett.* **1980**, *21*, 2057.

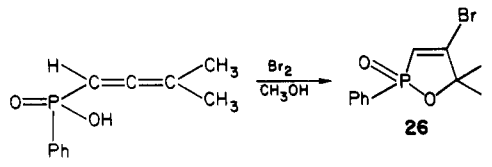
(25) We thank David Cunningham of this Department for carrying out these determinations.



22

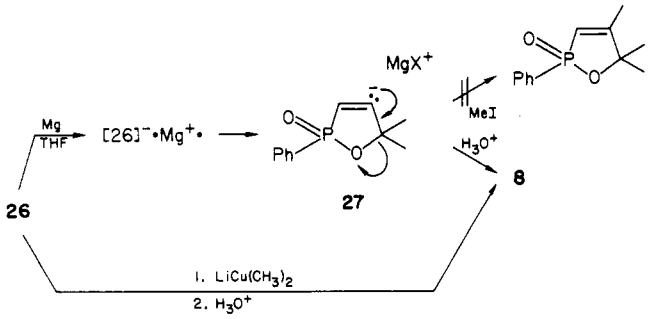
7 (see Experimental Section), a single product was formed in 90% yield (by ^1H NMR). Surprisingly, the product was *not* the expected 4-methyl adduct **23**. Rather, ring-opened phosphinic acid **24** (isolated as its methyl ester **25** in 65% overall yield) was the only product (Scheme III). This suggested that the cuprate served not as a source of a nucleophilic methyl group, but rather as a two-electron reducing agent. Further evidence for the stepwise sequence of one-electron reductions was obtained from the reaction of **7** with excess of sodium naphthalene, which also afforded **24** as the only product (69% isolated yield). House has suggested[23] that cuprates will *reduce* certain conjugated carbonyl compounds (rather than undergoing Michael addition) when their reduction potential in an aprotic medium is *less* negative than ca. −1.1 V (vs. SCE). Michael addition, on the other hand, occurs with substrate reduction potentials in the range −1.1 to −2.4 (vs. SCE). By using normal pulse voltammetry (DMF solution, tetramethylammonium nitrate supporting electrolyte, platinum electrodes), no reduction peak for **7** could be detected to −2.7 V (vs. SCE) at which point the solvent itself began to reduce. Similar results were observed during a cyclic voltammetric study of **7**. Thus, it appears that House's generalizations about α,β-unsaturated carbonyl compounds do not seem to extend to this particular functional group. Alternatively, it may be that ring opening of the radical anion derived from **7** is so fast, that complexation with the copper and delivery of the methyl group is precluded.

Finally, an attempt was made to examine the fate of carbanionic charge at C_4 of the oxaphospholene system. The precursor for this study, 4-bromo derivative **26**, was prepared by bromination of allene **8**.[3c]



8 26

Treatment of **26** with 1.2 equiv of magnesium in THF, followed by methyl iodide, gave a single product (70% yield, 30% recovered starting material), allenic phosphinic acid **8**. Once again, the charged intermediate **27** underwent ring opening during reduction. Perhaps even more interesting was that exactly the same result was observed when **26** was allowed to react with lithium dimethylcuprate.



26 27 8

Conclusions

The findings described here and in our previous work demonstrate that the polar double bond in oxaphospholenes is quite *unreactive* toward a variety of reagents including electrophiles, nucleophilic oxidants, dienes, 1,3-dipoles, and most organometallic reagents. Exceptions to this generalization are (1) NBA, which gives a rearranged ring-opened ketophosphinate, (2) ozone, which cleavages the double bond, and (3) lithium dimethylcuprate or sodium naphthalene, which serve as two-electron reducing agents. The reactivity of the double bond in **7** is thus somewhat lower than that of the corresponding bond in acyclic vinyl phosphonates. Moreover, the presence of the ring oxygen provides a ready pathway for ring opening under a variety of conditions. The extent to which the *gem*-dimethyl groups and the phosphorus substituents in **7** sterically protect the double bond and thereby sterically inhibit its reactivity will be tested by examining oxaphospholenes with only one substituent at C_5 and with other substituents at phosphorus. This work is currently underway.

Experimental Section

General Data. The instruments used in this work included the following: IBM NR-80 and Nicolet NT 300 (NMR); Kratos MS-80/DS 55 (MS); Perkin-Elmer 599 (IR). NMR spectra were run on $CDCl_3$ solutions; chemical shifts are reported in parts per million downfield from internal Me_4Si. IR spectra were run on CCl_4 solutions (unless otherwise noted) and are calibrated against polystyrene. All melting points are uncorrected. Ethereal diazomethane was prepared with Aldrich's Diazald Kit. Flash chromatography[26] was performed with silica gel 60 (230–400 mesh) from EM Reagents; TLC was performed with silica gel 60 F on precoated plastic sheets from EM Reagents.

Preparation of 5,5-Dimethyl-2-phenyl-1,2-oxaphosphol-3-ene 2-Oxide (7). (3-Methyl-1,2-butadienyl)phenylphosphinic acid (**8**) was prepared as previously described[3c] from 2-methyl-3-butyn-2-ol (5.85 g) and dichlorophenylphosphine (4.20 g). The crude acid, suspended in 30 mL of water, was heated to 100 °C for 40 h and then neutralized with solid sodium bicarbonate. The crude oxaphospholene was extracted into 100 mL of methylene chloride. Rotary evaporation followed by double sublimation (100 °C at 0.2 mm) afforded 3.39 g (71% from the phosphine) of white crystals: mp 66–69 °C (lit.[27] 58–60 °C); ^1H NMR δ 1.58 (s, 3 H), 1.67 (s, 3 H), 6.18 (dd, J_{HH} = 8.2 Hz, J_{PH} = 33.5 Hz, 1 H), 7.08 (dd, J_{HH} = 8.2 Hz, J_{PH} = 40.1 Hz, 1 H), 7.4–8.0 (m, 5 H); IR 3030 (w), 2990 (m), 1540 (m), 1490 (s), 1460 (m), 1370 (m), 1320 (s), 1240 (vs), 1230 (vs), 1190 (m), 1170 (s), 1120 (s), 1060 (m), 960 (vs), 920 (vs), 850 (s), 820 (s), 810 (m), 710 (s), 690 (s), 620 (m), 580 (s) cm^{-1}.

Reaction of 7 with NBA. A solution of 208 mg (1.00 mmol) of **7** and 190 mg (1.40 mmol) of NBA in 8 mL of water was stirred in the dark for 80 h at 25 °C. The resulting acidic (pH 1) light brown solution was extracted with 2 × 10 mL of $CHCl_3$, and the combined extracts were dried ($MgSO_4$) and evaporated to give **11** (223 mg, 75%) as an unstable pale yellow oil: ^1H NMR δ 1.23 (d, J_{HH} = 6.9 Hz, 3 H), 2.06 (s, 3 H), 2.90 (m, 1 H), 4.41 (dd, J_{PH} = 6.6 Hz, J_{HH} = 4.7 Hz, 1 H), 7.2–7.9 (m, 5 H); IR ($CDCl_3$) 2950 (m), 1720 (vs), 1440 (s), 1260 (s), 1250 (s), 1180 (s), 1110 (s), 960 (s), 860 (s), 800 (s) cm^{-1}.

After ca. 12 h at 25 °C, neat **11** was converted cleanly to **12**, another oil which defied attempted purification: ^1H NMR δ 2.02 (dd, J_{PH} = 2.9 Hz, J_{HH} = 1.5 Hz, 3 H), 2.34 (s, 3 H), 6.8 (dq, J_{PH} = 16.5 Hz, J_{HH} = 1.5 Hz, 1 H), 7.3–7.9 (m, 5 H); IR ($CDCl_3$) 2920 (m), 1680 (vs), 1440 (s), 1250 (m), 1210 (s), 1170 (s), 1120 (s), 960 (s), 800 (s) cm^{-1}.

Reaction of 223 mg of crude **11** with excess ethereal diazomethane,[9c] followed by evaporation left 210 mg (90%) of a 55/45 mixture of two diastereomers of **13**. The major isomer exhibited the following ^1H NMR: δ 1.43 (d, J_{HH} = 6.95 Hz, 3 H), 2.15 (s, 3 H), 3.1 (m, 1 H), 3.78 (d, J_{PH} = 10.9 Hz, 3 H), 4.6 (m, 1 H), 7.4–8.0 (m, 5 H). The minor isomer exhibited peaks at δ 1.37 (d, J_{HH} = 6.95 Hz, 3 H), 2.25 (s, 3 H), 3.1 (m, 1 H), 3.71 (d, J_{PH} = 10.9 Hz, 3 H), 4.6 (m, 1 H), 7.4–8.0 (m, 5 H). The IR spectrum ($CDCl_3$)

(26) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(27) Midharlova, T. S.; Skvortsov, N. K.; Ignat'ev, V. M.; Ionin, B. I.; Petrov, A. A. *Dokl. Akad. Nauk SSSR* **1978**, *241*, 1095.

of the mixture gave bands at 2990 (w), 1720 (s), 1440 (s), 1360 (m), 1260 (s), 1180 (m), 1120 (s), 1040 (s), 900 (m), and 790 (s) cm^{-1}. Although the product mixture was stable at 25 °C, all attempts to separate the mixture (or heating it to 80 °C in the presence of a catalytic amount of pyridine) led instead to elimination product **14**. Thus, when 210 mg of the mixture was subjected to flash chromatography[26] (20 cm × 2 mm column, 85% EtOAc, 15% petroleum ether), pure **14** (98 mg, 41% from **7**) eluted as a colorless oil (after evaporation): ^1H NMR δ 2.13 (dd, J_{PH} = 2.9 Hz, J_{HH} = 1.2 Hz, 3 H), 2.35 (s, 3 H), 3.71 (d, J_{PH} = 11.3 Hz, 3 H), 6.67 (dq, J_{PH} = 15.7 Hz, J_{HH} = 1.2 Hz, 1 H), 7.3–7.9 (m, 5 H); ^{13}C NMR δ (J_{PC}, Hz) 14.6 (6.5), 25.9, 51.1 (6.4), 127.6 (134.4), 128.8 (13.0), 130.6 (135.5), 131.4 (10.4), 132.6 (2.8), 153.9, 199; IR ($CDCl_3$) 2940 (w), 1690 (vs), 1440 (s), 1370 (w), 1220 (vs), 1120 (s), 1040 (s), 930 (m), 800 (s), 550 (s) cm^{-1}; MS, *m/e* 238.0771 (calcd for $C_{12}H_{15}O_3P$ 238.0760), 195, 155 (base), 77, 43.

Compound **14** was also formed by treatment of **12** with excess ethereal diazomethane.[9c]

Ozonolyses of 7. A stream of ozone (3.4% in oxygen, 0.01 ft^3/m) was bubbled through a solution of 208 mg of **7** in 3 mL of $CDCl_3$ at −38 °C for 105 min.[28] The resulting solution was distilled (0.2 mm, 25 °C) to give a volatile fraction and a nonvolatile residue. The former fraction was found (^1H NMR and GC) to consist of $CDCl_3$, acetone (δ 2.17 (s)), and an unidentified minor component (δ 8.03 (s)). The latter fraction was allowed to react with a slight excess of ethereal diazomethane,[9c] rotary evaporated, and subjected to flash chromatography[26] (15 cm × 1.5 cm, 20% petroleum ether, 80% ethyl acetate) to give 70 mg (26%) of 1-carbomethoxy-1-methylethyl methyl phenylphosphonate (**18**) and 50 mg (27%) of dimethyl phenylphosphonate (**17**). The NMR and IR data for the latter compound matched those previously published;[29] MS, *m/e* 186.0428 (theoretical for $C_8H_{11}O_3P$ 186.0446). The former compound (homogeneous by TLC) exhibited the following spectral data: ^1H NMR δ 1.69 (s, 6 H), 3.74 (s, 3 H), 3.76 (d, J_{PH} = 11.4 Hz, 3 H), 7.45–7.95 (m, 5 H); IR: 1750 (m), 1440 (w), 1260 (s), 1137 (s), 1055 (s), 1040 (s), 1025 (s), 1000 (s); MS, *m/e* 213 (base), 173, 155, 141, 124, 77.[30]

Reaction of 7 with Lithium Dimethylcuprate. Into a 100-mL flask charged with 2.4 g (13 mmol) of cuprous iodide, 40 mL of anhydrous ether, and a dry nitrogen atmosphere at 0 °C was syringed 16.5 mL (24.8 mmol) of 1.5 M methyllithium in ether.[24] After 30 min a solution of 832 mg (4.00 mmol) of **7** in 30 mL of anhydrous ether was added dropwise over an additional 30 min. The originally tan solution became progressively yellow, and precipitate formed during the addition. After 3.5 h at 0 °C, the ether suspension was added portionwise to 160 mL of 2.4 M hydrochloric acid. The resulting pink suspension was filtered, the ether layer was separated, and the aqueous layers were saturated with sodium chloride and extracted with 3 × 100 mL ether. The combined ether solutions were dried (magnesium sulfate) and rotary evaporated to give 625 mg of a brown oil. ^1H NMR indicated the presence of (3-methyl-2-butenylphenylphosphinic acid (**24**, theoretical yield 840 mg): δ 1.32 (d, J = 3 Hz, 3 H), 1.61 (d, J = 6 Hz, 3 H), 2.63 (dd, J_{HH} = 8.1 Hz, J_{PH} = 17.8 Hz, 2 H), 5.05 (m, 1 H), 7.3–7.9 (m, 5 H). This material proved difficult to purify, so it was esterified with diazomethane[9c] and subjected to flash chromatography (15 cm × 3 cm, 10% petroleum ether, 90% ethyl acetate), affording 580 mg (65% overall) of methyl (3-methyl-2-butenyl)phenylphosphinate (**25**) as a pale yellow liquid homogeneous by TLC. ^1H NMR: δ 1.39 (d, J_{HH} = 3.4 Hz, 3 H), 1.66 (d, J_{HH} = 4.9 Hz, 3 H), 2.70 (dd, J_{HH} = 7.8 Hz, J_{PH} = 18.4 Hz, 2 H), 3.64 (d, J_{PH} = 11.0 Hz, 3 H), 5.14 (m, 1 H), 7.4–7.9 (m, 5 H); ^{13}C NMR δ (J_{PC}, Hz) 17.67 (2.5), 25.66 (2.5), 30.48 (98.7), 51.00 (7.4), 112.39 (10.0), 128.38 (12.8), 130.2 (123.4), 131.82 (9.1), 132.10 (2.2), 136.82 (13.0); IR 2970 (m), 2940 (m), 2900 (m), 2840 (w), 1590 (w), 1440 (s), 1400 (w), 1370 (w), 1235 (vs), 1215 (vs), 1115 (s), 1040 (vs), 910 (m), 860 (m), 730 (s), 695 (s), 670 (m); MS, *m/e* 224.0959 (theoretical for $C_{12}H_{17}O_2P$ 224.0967), 157, 156 (base), 155, 142, 125, 91, 78, 77, 76, 69, 67, 51.

Reaction of 7 with Sodium Naphthalene. A dark green solution of sodium naphthalene was prepared by stirring a mixture of 1.28 g of naphthalene and 230 mg of sodium in 50 mL of dry THF for 45 min under argon. Approximately 20 mL of this solution was added dropwise to a solution of 104 mg of **7** in 30 mL of dry THF under argon at 0 °C, until the green color persisted for 30 min. The reaction mixture was added with stirring to 40 mL of 1.2 M HCl, then concentrated by rotary evaporation, filtered to remove the naphthalene, saturated with sodium chloride, and extracted with 2 × 100 mL of methylene chloride. Thorough evaporation of solvent under high vacuum left 72 mg (69%) of **24** as a pale yellow liquid. Its ^1H NMR was superimposable on the spectrum obtained for the cuprate reduction product (vide supra).

Preparation of 4-Bromo-5,5-dimethyl-2-phenyl-1,2-oxaphosphol-3-ene 2-Oxide. To a solution of 2.40 g (11.5 mmol) of **8**[3c] in 85 mL of methanol was added dropwise a solution of 1.2 mL of bromine in 40 mL of methanol. The solution was stirred for 48 h at 25 °C, evaporated and redissolved in 80 mL of CH_2Cl_2. This solution was washed with an equal volume of water, and evaporated to dryness. Recrystallization of the crude product from benzene/cyclohexane (1/2, v/v) afforded 3.16 g (95%) of **26** as colorless crystals: mp 82.5–85 °C; ^1H NMR δ 1.65 (s, 3 H), 1.73 (s, 3 H), 6.39 (d, J_{PH} = 26.7 Hz, 1 H), 7.5–7.8 (m, 5 H); IR 2990 (w), 1580 (s), 1460 (w), 1440 (m), 1380 (w), 1360 (w), 1260 (s), 1245 (s), 1130 (m), 1315 (m), 970 (s), 940 (s), 880 (s), 820 (m), 710 (m), 690 (m), 570 (s); MS, *m/e* 287.9762, 285.9776 (molecular ions and base, theoretical for $C_{11}H_{12}O_2PBr$ 287.9739, 285.9759) 273, 271, 209, 207, 195, 189,149, 143, 142, 141, 128, 77.

Reaction of 26 with Magnesium. A mixture containing 30 mg (1.2 mmol) of magnesium and 287 mg (1.00 mmol) of **26** in 12 mL of dry THF was heated to 50 °C, and 2 drops CH_3I was added to initiate the Grignard reaction. After 30 min an additional 10 mL of CH_3I was added and refluxing continued for 10 min to trap any remaining intermediate(s). The resulting mixture was poured over 20 mL of 1.2 M HCl. Evaporation of the organic solvents was followed by extraction with CH_2Cl_2. The extracts were washed with H_2O, dried, and evaporated to give 205 mg of a colorless oil which consisted of 30% **26** and 70% **8**, whose ^1H NMR and IR spectra matched those previously published:[3c] ^1H NMR δ 1.55 (dd, J_{PH} = 6.8 Hz, J_{HH} = 3.2 Hz, 6 H), 5.35 (m, 1 H), 7.3–7.9 (m, 5 H); IR (partial) 1960 cm^{-1}.

Reaction of 26 with Me_2CuLi. The cuprate (4.5 mmol in 26 mL of ether) was prepared as described above. A solution of 287 mg (1.00 mmol) of **26** in 20 mL of THF was added at 0 °C over 15 min. After 12 h of stirring the resulting green solution was poured over 50 mL of 1.2 N HCl. After filtration, the filtrate was partially evaporated to remove volatile organic solvents, saturated with NaCl, and extracted with CH_2Cl_2. The extracts were dried and evaporated to give 193 mg of a yellow oil consisting (by ^1H NMR) of 10% **26** and 90% **8**, whose spectra matched the ones above.

Acknowledgment. We thank the Research Council of the University of Cincinnati for a grant which partially supported this work.

(28) Because of the slow reaction of **7** with ozone, the solution remained blue throughout this period. The reaction was monitored by ^1H NMR on parallel samples, and this length of time was required for complete consumption of **7** at this concentration. See text.

(29) (a) Sidall, T. H.; Prohaska, C. A. *J. Am. Chem. Soc.* **1962**, *84*, 3467. (b) Mavel, G.; Mankowski-Favelier, R.; Tank, T. N. *J. Chim. Phys.* **1967**, *64*, 1692. (c) Christol, H.; Levy, M.; Marty, C. *J. Organomet. Chem.* **1968**, *12*, 459.

(30) Although the molecular ion (*m/e* 272) was absent from the spectrum, the base peak at *m/e* 213 had the correct composition for M − CO_2CH_3 (calcd 213.0681, found 213.0693).