## References and Notes

(1) G. L. Nelson and E. A. Williams, "Progress in Physical Organic Chemistry", Vol. 12, R. W. Taft, Ed., Wiley, New York, N.Y., 1976, pp 234–282.
(2) (a) G. K. Hamer, I. R. Peat, and W. F. Reynold, *Can. J. Chem.*, **51**, 897 (1973); (b) G. H. Hamer, I. R. Peat, and W. F. Reynolds, *ibid.*, **51**, 915 (1973); see also N. Inamoto, S. Masuda, W. Nakanishi, and Y. Ideda, *Chem. Lett.*, 759 (1977).
(3) T. B. Posner and C. D. Hall, *J. Chem. Soc., Perkin Trans. 2*, 729 (1976).
(4) D. A. Happer, *Aust. J. Chem.*, **29**, 2607 (1976).
(5) C. D. Ritchie and W. F. Sager, "Progress in Physical Organic Chemistry", Vol. 2, S. G. Cohen, A. Streitwieser, Jr., and R. W. Taft, Ed., Wiley, New York, N.Y., 1964, pp 334–337.
(6) H. O. Krabbenhoft, *J. Org. Chem.*, in press.
(7) (a) J. B. Stothers, "Carbon-13 NMR Spectroscopy," Academic Press, New York, N.Y., 1972, pp 196–205; (b) G. C. Levy and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists", Wiley, New York, N.Y., 1972, pp 80–85.
(8) For a recent report dealing with the ambident nature of heteroatoms see W. P. Meyer and J. C. Martin, *J. Am. Chem. Soc.*, **98**, 1231 (1976).
(9) Pertinent data for five meta-substituted $\beta,\beta$-dichlorostyrenes have also been obtained;[6] inclusion of these points in the analysis gives $\rho = 3.51$ and $r = 0.996$.
(10) The $\alpha$-*tert*-butylstyrene system (**3**) gives only poor correlations upon Hammett analysis, presumably on account of severe effects precluding the attainment of coplanarity[2a] of the aryl and the 2-(3,3-dimethyl)butenyl groups.
(11) See also the related discussion in ref 5.
(12) S. Ehrenson, R. T. C. Brownlee, and R. W. Taft, "Progress in Physical Organic Chemistry", Vol. 10, A. S. Streitwieser, Jr., and R. W. Taft, Ed., Wiley, New York, N.Y., 1973, Chapter 1.
(13) Ideally, the minimum basis set should also include data for the $NR_2$ (R = H or $CH_3$) and F substituents in order to minimize accidental correlatiins between substituent $\sigma_I$ and $\sigma_R$ values.[12] However, the absence of these two data points should not be serious since an entire range of substituents (i.e., $OCH_3$ to $NO_2$) is utilized.
(14) Correlations of good precision are those for which $f \leq 0.1$.[12]
(15) The fact that satisfactory correlations are achieved with three different sets of substituent constants is not uncommon;[12] see also J. Hine, "Structural Effects in Equilibria in Organic Chemistry", Wiley, New York, N.Y., 1975, pp 79–81.
(16) The material described in this note was presented at the International Symposium on the Chemistry of Strained Rings, Binghamton, N.Y., May 27–29, 1977.
(17) (a) L. A. Errede and J. P. Cassidy, *J. Org. Chem.*, **28**, 1059 (1963); (b) V. M. Naiden and A. V. Dombrovskii, *J. Gen. Chem. USSR (Engl. Transl.)*, **32**, 1256 (1962); **1**, 2037 (1965); (c) R. Brown, Ph.D. Thesis, University of Maryland, 1968 [*Diss. Abstr. B*, **29**, 3670 (1969)]; A. Merz, *Angew Chem., Int. Ed. Engl.*, **16**, 57 (1977); (d) D. Seyferth, H. D. Simmons, Jr., and G. Singh, *J. Organomet. Chem.* **3**, 337 (1965); (e) A. J. Speziale and K. W. Ratts, *J. Am. Chem. Soc.*, **84**, 854 (1962).


# Epoxidation of Allenic Phosphonic Acids. Intramolecular Trapping of Allene Oxides[1]


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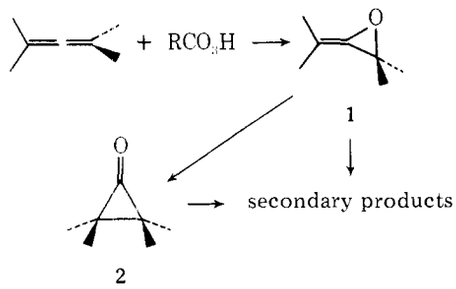
The epoxidation of allenes has intrigued several groups of investigators over the last decade. Allenes readily react with peracids to give complex mixtures of products which can be rationalized as arising from allene oxides (**1**) and their cyclopropanone isomers (**2**).[2] The rearrangement of **1** to **2**, as well

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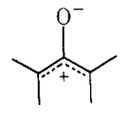
as some of the subsequent reactions of **1** and **2**, have been postulated to involve oxyallyl zwitterion **3**[3] (or its conjugate acid), although recent CNDO/2 calculations suggest another



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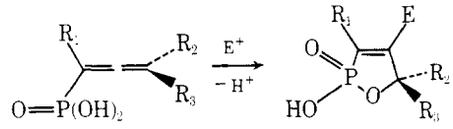
lower energy path for the rearrangement.[4] In two cases, the allene oxides themselves have been isolated.[5] For example, the monoepoxide of 1,3-di-*tert*-butylallene can be isolated, and it rearranges cleanly to 2,3-di-*tert*-butylcyclopropanone with a half-life of ca. 5 h at 100 °C.[5a] The gas-phase reaction of allenes with ground state oxygen atoms has also been rationalized in terms of allene oxides, cyclopropanones, and oxallyl radicals.[6]

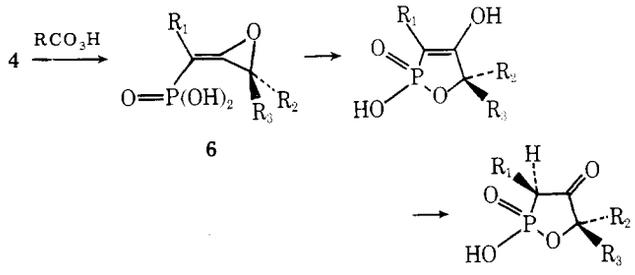
We recently reported that allenic phosphonic acids (**4**) react with electrophiles such as Brönsted acids, bromine, or mercuric salts to form oxaphospholene.[1,7,8]




4 5

a, $R_1 = H$; $R_2 = R_3 = CH_3$
b, $R_1 = R_2 = tert$-butyl; $R_3 = H$

From these studies it seemed likely that reaction of **4** with peracids would lead to allene oxide **6**, which might rapidly and cleanly isomerize to 4-keto-1,2-oxaphospholane **7**.[9]

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## Results and Discussion

When a 20% excess of peracetic acid[10] was added to an aqueous solution of **4a**[7] at 25 °C, $^1H$ NMR indicated 50% consumption of the starting material after 1.8 h. Two major products were formed: acetone ($\delta$ 2.21 (s))[11] and A [$\delta$ 1.44 (s, 6 H), 2.84 (d, $J$ = 14 Hz, 2 H)[13]] in the ratio 1:3. After 6.3 h, 20% of the starting material remained, and two additional products, B [$\delta$ 1.38 (s, 6 H), 3.39 (d, $J$ = 22 Hz, 2 H)[13]] and C [$\delta$ 2.98 (d, $J$ = 22 Hz)[13]], had formed such that the four products were present in essentially equal amounts.[14] After 24 h, starting material (10%) remained, along with A (7%), acetone (20%), B (37%), and C (26%).

Reaction of **4a** with a threefold excess of *m*-chloroperbenzoic acid[15] in chloroform[16] resulted in complete conversion to a stable[17] mixture of A and acetone (3:1) after 5.6 h at 25 °C. Extraction with water gave a solution of A, which hydrolyzed quantitatively to B with a half-life of 20 h at 25 °C. Addition of 1.2 equiv of peracetic acid to the solution of B gave C and acetone in essentially equal amounts, with a comparable half-life. Unfortunately, attempts to isolate A, B, and C from these aqueous solutions gave viscous oils whose NMR spectra suggested that polymerization had occurred.

We have previously shown[18] that phosphonic acids can be esterified with diasomethane (**8**) and under certain conditions carboxylic acids in water may be similarly esterified.[19] The solutions of A, B, and C were separately treated with **8** (large excesses being required for aqueous solutions). Although A and C led to complex mixtures of products, B was esterified

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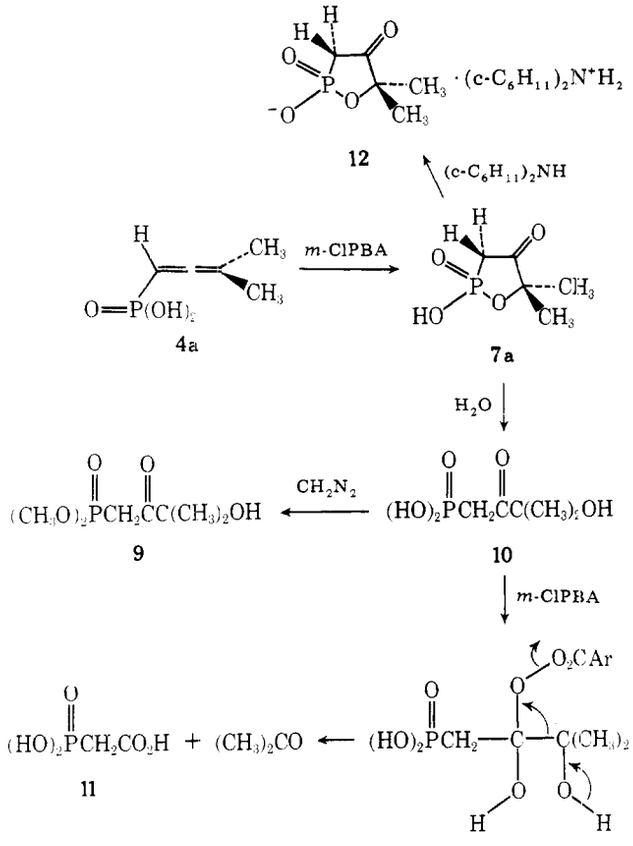
Scheme I

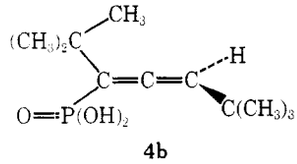


relatively cleanly to give a colorless liquid to which we assign structure **9** based on its $^1$H NMR spectrum [($CDCl_3$) $\delta$ 1.38 (s, 6 H), 3.47 (d, $J$ = 23 Hz, 2 H), 3.85 (d, $J$ = 11.5 Hz, 6 H), 4.30 (bs, 1 H)] and other data given in the Experimental Section. This assignment then suggests structures **7a, 10,** and **11** for A, B, and C, respectively.[20] More direct evidence for the formation of **7a** came from the isolation of its dicyclohexylamine salt **12**,[21] the properties of which are described in the Experimental Section.

While it is not surprising that compounds **7a, 10,** and **11,** tend to polymerize (or at least associate strongly),[22] it was unexpected that neither **7a, 10,** or even **9** give typical carbonyl derivatives such as 2,4-dinitrophenylhydrazones. This may be due to their neopentyl nature. It is also interesting that the 4-keto group in **7a** greatly facilitates hydrolytic ring opening,[23] while 1,2-oxaphosphol-3-enes show no tendency to ring open even in TFA at 75 °C.[1,7,8]

Two additional observations are worthy of comment at this point. When the dimethyl ester of **4a**[7,18] was allowed to react with 2.5 mol equiv of *m*-chloroperbenzoic acid (necessary for complete consumption of starting material), acetone was the only identifiable product. When cyclization of **6** is prevented by protection of the POH groups, further oxidation of the intermediate to acetone ensues. This also explains the presence of acetone in the original reaction of **4a** with peracid (vide supra).

Equally interesting is the observation that **4b** was totally inert toward *m*-chloroperbenzoic acid after 5 days at 42 °C,



**4b**

even though 1,3-di-*tert*-butylallene reacts readily.[5a] The phosphoryl substituent apparently deactivates both $\pi$ bonds, the closer by induction and the further sterically, thereby precluding epoxidation. Oxaphospholene **5a** was also inert toward peracid (73 °C, 24 h).

## Experimental Section

**General.** The instrumentation and general methods were as previously described.[7,8,22]

**Reaction of 4a with *m*-Chloroperbenzoic Acid.** To a suspension of 590 mg (4.00 mmol) of **4a**[7] in 25 mL of dry chloroform at 24 °C was added a solution of 2.00 g (10.1 mmol) of peracid[15] in 25 mL of dry chloroform at once. The reaction could be followed by $^1$H NMR as described in the text. The initially heterogeneous mixture[16] became essentially homogeneous after 2 h, remaining so through the end of the reaction. After a total of 5 h, the solution was decanted from a small amount of insoluble material and extracted with 4 × 5 mL of water.[24] To this aqueous solution of **7a** was added 1.00 g (5.5 mmol) of dicyclohexylamine, and the resulting mixture was shaken overnight at 24 °C, then evaporated to dryness at <0.1 mm and 40 °C. The residue was recrystallized from benzene and dried (130 °C, 0.01 mm) to give 285 mg (21%) of **12:** mp 168–170 °C; $^1$H NMR ($CDCl_3$) $\delta$ 0.6–2.3 [envelope with sharp singlet at 1.43, 28 H (theoretical 25)], 2.51 (d, $J$ = 13 Hz) and 2.5–3.0 (envelope) (totalling 4 H), 8.3 (bs, 2 H); IR ($CHCl_3$) 3200–2200 (v br), 1735 (vs), 1455, 1230, 1080, 980, 820 cm$^{-1}$. Anal. Calcd for $C_{17}H_{32}NO_4P$: C, 59.09; H, 9.34. Found: C, 59.10; H, 9.51.[25]

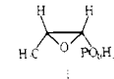
**Isolation of 9.** A solution of ca. 1.0 g of **7a** in 24 mL of water was prepared as described above. It was heated to 51 °C for 19h causing quantitative hydrolysis to **10.** This reaction can be monitored by $^1$H NMR as described in the text. Ethereal diazomethane (330 mL of a 1% solution) was added, the ether phase was separated, dried, and evaporated, and the crude **9** was distilled to give 300 mg of a colorless liquid, bp 70 °C (0.05 mm). This product was further purified by HPLC (silica gel, chloroform) to give 95% pure **9,** the $^1$H NMR data for which are given in the text: IR ($CHCl_3$) 3400 (broad), 1725, 1250 cm$^{-1}$; MS (20 eV) *m/e* (rel abundance) 211 (1), 192 (6), 151 (19), 150 (68), 124 (15), 111 (100), 110 (34), 80 (25).

**Acknowledgment.** The HPLC purification of **9** was performed by Mr. Bruce Downs; Messrs. Stephen Gee and John Sullivan prepared the **4a** used in this work.

**Registry No.**—**4a,** 1831-37-4; **7a,** 65378-71-4; **9,** 65378-72-5; **10,** 65378-73-6; **12,** 65378-74-7.

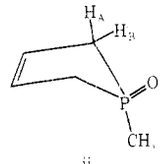
## References and Notes

(1) Paper 7 in the series on formation and cyclization of allenic phosphonic acids; Paper 6: R. S. Macomber, *J. Org. Chem.*, **42,** 3297 (1977).
(2) See, for example, J. K. Crandall, W. H. Machleder, and S. A. Sojka, *J. Org. Chem.*, **38,** 1149 (1973), and references therein.
(3) A. Liberles, S. Kang, and A. Greenburg, *J. Org. Chem.*, **38,** 1923 (1973).
(4) M. E. Zandler, C. E. Choc, and C. K. Johnson, *J. Am. Chem. Soc.*, **96,** 3317 (1974).
(5) (a) R. L. Camp and F. D. Greene, *J. Am. Chem. Soc.*, **90,** 7349 (1968); (b) J. K. Crandall and W. H. Machleder, *J. Heterocycl. Chem.*, **6,** 777 (1969).
(6) J. J. Havel, *J. Am. Chem. Soc.*, **96,** 530 (1974).
(7) R. S. Macomber and E. R. Kennedy, *J. Org. Chem.*, **41,** 3191 (1976).
(8) R. S. Macomber, *J. Am. Chem. Soc.*, **99,** 3072 (1977).
(9) The obvious similarity of **6** and its isomers to the antibiotic phosphomycin (i) suggests that these compounds may possess similar physiological properties.

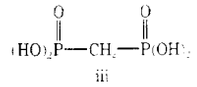


(10) Commercially available "40%" material from FMC Corp., 45.5% by iodometric titration.
(11) Addition of authentic acetone increased the intensity of this signal. Separation of the volatile products and solvent by vacuum transfer then treatment with 2,4-dinitrophenylhydrazine gave the 2,4-DNP of acetone, mp 126.0–126.8 °C (lit.[12] 125 °C).
(12) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds", 5th ed, Wiley, New York, N.Y., 1964.
(13) When the reaction is carried out in $D_2O$ this signal is rapidly lost due to exchange.
(14) Assuming the $\delta$ 2.98 doublet is 2 H (vide infra).
(15) Eastman 85% min; 88% by iodometric titration.
(16) Phosphonic acid **4a** is sparingly soluble in chloroform. But the initial suspension becomes homogeneous as the reaction proceeds.

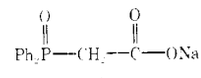
(17) After 24 h at room temperature there was a slight decrease in the amount of A and a comparable increase in the amount of acetone.
(18) R. S. Macomber, *Synth. Commun.*, **7(6)**, 405 (1977).
(19) E. J. Eisenbraun, R. N. Morris, and G. Adolphen, *J. Chem. Educ.*, **47**, 710 (1970).
(20) Analogous compounds show very similar chemical shifts and P–H coupling constants: ii [K. Moedritzer and P. A. Berger, *J. Org. Chem.*, **42**, 2023 (1977)]; iii and iv [Sadtler Research Labs NMR Standard Spectra 7770, 7771]



ii $\delta_A$ 2.59 ($J_{PA}$ = 14 Hz), $\delta_B$ 2.47 ($J_{PB}$ = 8 Hz)



iii $\delta_{CH_2}$ 2.61 ($^2J_{PH}$ = 21 Hz)



iv $\delta_{CH_2}$ 3.59 ($^2J_{PH}$ = 14 Hz)

(21) This technique has been used to isolate salts of other phosphonic acids: R. Rabinowitch, *J. Org. Chem.*, **28**, 2975 (1963).
(22) Compound **5b** was found to form a phosphonic anhydride under certain hydrolysis conditions: R. C. Elder, L. R. Florian, E. R. Kennedy, and R. S. Macomber, *J. Org. Chem.* **38**, 4177 (1973).
(23) The dicyclohexylamine salt of **7a** is stable in water, suggesting that the hydrolytic ring opening is acid catalyzed.
(24) Less than 20 mg of *m*-chlorobenzoic acid is extracted into the water.
(25) Elemental analysis performed by Integral Microanalytical Labs.

## Procedure for the Permethylation of Ketones Using Potassium Hydride and Methyl Iodide

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*Received October 11, 1977*

The classical method for the synthesis of permethylated ketones is sequential reaction of the ketone with portions of sodamide and methyl iodide.[1] More recent methods utilize such bases as sodium alkoxides[2] or sodium hydride.[3] In most cases, the overall yield for the replacement of all enolizable hydrogens does not exceed 50%.

We recently required a sample of 2,2,6,6-tetramethylcyclohexanone. The excellent procedure discovered by Charles Brown for using potassium hydride to prepare potassium ketone enolates[4] together with a report[5] that KH reacts with methyl iodide only sluggishly at 50 °C suggested a simple route. Treatment of cyclohexanone with a fourfold excess of KH and methyl iodide at 25 °C might lead directly to the desired ketone. Indeed, with slight modifications of this procedure, the results were sufficiently gratifying that we applied the method to a variety of ketones and report our results here.

### Results and Discussion

**Reaction of KH with Methyl Iodide.** A suspension of KH (10 mmol) in tetrahydrofuran (THF) was maintained at 25 °C and treated with 10 mmol of methyl iodide. Evolution of a gas determined to be methane (GLC retention volume) began immediately. A total of 3.7 mmol of methane was formed in less than 1 min (as measured by a gas buret). No further methane was formed over a 2-h period. GLC analysis of the THF suspension confirmed the presence of the expected 6.3 mmol of residual methyl iodide. Additions of 10 mmol of cyclohexanone to the suspension resulted in the rapid evolution of 6.3 mmol of hydrogen, confirming the presence of 6.3 mmol of residual KH.

Evidently, KH does reduce methyl iodide at room temperature, but the reaction stops far short of completion. We have no direct evidence on the reason for the incomplete reduction, but the following experiment was particularly revealing.

A suspension of 15 mmol of KH in THF was treated with 5 mmol of 2,2,6-trimethylcyclohexanone. Hydrogen (5.0 mmol) was evolved over a 5-min period. Injection of 5 mmol of methyl iodide did not produce any gas evolution (<0.1 mmol). GLC analysis of a small aliquot of the reaction mixture revealed the presence of 4.9 mmol of 2,2,6,6-tetramethylcyclohexanone. At this point, the suspension was treated with an additional 10 mmol of methyl iodide and 3.6 mmol of methane was immediately formed. Again the presence of residual KH (6.4 mmol) and methyl iodide (6.4 mmol) was established.

Based on these results, we make the following points. The incomplete reduction of methyl iodide by KH is probably not due to inhibition by the product KI since KI is also formed (presumably in a similar state) by reaction of the ketone enolate with methyl iodide.[6] The incomplete reduction is probably not due to a trace amount of an inhibitor in the methyl iodide unless the inhibitor is removed by the ketone enolate. The incomplete reduction is not due to the presence of some 30% of a highly reactive form of KH unless this highly reactive form does not preferentially react with the ketone. Most importantly, from our point of view, the potassium enolate of 2,2,6-trimethylcyclohexanone is remarkably reactive to methyl iodide and this reaction is much faster than the reduction of methyl iodide with KH.

**Permethylation of ketones.** Based on the above results, our original concept was modified slightly so as to minimize competing reduction of methyl iodide. Cyclohexanone was added to a THF suspension containing 4.3 equiv of KH. Methyl iodide (4.3 equiv) was then added dropwise to the

**Table I. Methylation of Ketones with KH and Methyl Iodide at 25 °C**

| Ketone | Registry no. | Product | Registry no. | Yield[a] |
|---|---|---|---|---|
| Cyclobutanone | 1191-95-3 | 2,2,4,4-Tetramethylcyclobutanone | 4298-75-3 | (79) |
| Cyclopentanone | 120-92-3 | 2,2,5,5-Tetramethylcyclopentanone | 4541-35-9 | 100 (83) |
| Cyclohexanone | 108-94-1 | 2,2,6,6-Tetramethylcyclohexanone | 1195-93-3 | 96 (81) |
| Cycloheptanone | | 2,2,7-Trimethylcycloheptanone | 40514-75-8 | 75 |
| Cycloheptanone[b] | 502-42-1 | 2,2,7,7-Tetramethylcycloheptanone | 64342-79-6 | 62 (50) |
| Acetone | 67-64-1 | 2,2,4-Trimethyl-3-pentanone | 5857-36-3 | 90 |
| Acetone[b] | | 2,2,4,4-Tetramethyl-3-pentanone | 815-24-7 | 72 (60) |
| Acetophenone | 98-86-2 | 2,2-Dimethylpropiophenone | 938-16-9 | 100 (81) |
| 4-Heptanone | 123-19-3 | 3,3,5-Trimethyl-4-heptanone | 51220-07-6 | 86 (66) |

[a] GLC yields, isolated yields (distillation) in parentheses. [b] Reaction mixture refluxed for 1 h prior to addition of the final equivalent of methyl iodide.

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