result of coupling of this radical with a protonated ketyl (path a), and not a 3 + 2 radical cycloaddition reaction (path b) follows from yield *vs.* concentration studies. In the latter case, the yield of oxazolidine would be expected to increase with increasing ketone concentration.[8] The coupling mechanism predicts the oxazolidine yield to be essentially independent of ketone concentration. In fact, when the initial benzophenone concentration was varied from 0.02 to 0.09 *M*, the yield of oxazolidine IVa remained constant at 46% showing that the coupling mechanism is operative.

The failure of imine II to undergo 2 + 2 photocycloaddition with excited aryl ketones is noteworthy. Irradiation of benzophenone and 2,4-dimethyl-2-pentene, the hydrocarbon analog of II, gives a mixture of the two possible oxetanes in 94% yield;[9] thus, the azomethine nitrogen of II is exerting the controlling influence.

Other investigators have shown that irradiation of alcohol solutions of aryl ketones and *diaryl-N*-alkylimines results in reduction of imine.[10] The protonated ketyl derived from ketone by hydrogen abstraction from solvent presumably delivers a hydrogen atom to the azomethine double bond of the imine, and the resulting α-aminoalkyl radical gives amine by disproportionation.[10] In the present case the α-aminoalkyl radical formed would not benefit from aryl stabilization, and it is perhaps not surprising that reduction of the imine double bond does not compete favorably with the self- or cross-coupling reactions of the ketyl radical. Competition between reduction and coupling with 2-azaallyl (*i.e.*, cross coupling) is further complicated by the fact that the latter reaction may well be occurring within the initial solvent cage.[11]

[8] Only ~50% of the imine consumed forms oxazolidine suggesting radical VII is being partitioned between "oxazolidine" and "non-oxazolidine" pathways. The latter does not involve benzophenone since all the consumed benzophenone can be accounted for in terms of IIIa + IVa.

[9] A. A. Baum, unpublished results.

[10] (a) M. Fischer, *Chem. Ber.*, **100**, 3599 (1967); (b) A. Padwa, W. Bergmark, and D. Pashayan, *J. Amer. Chem. Soc.*, **91**, 2653 (1969).

[11] See, for example, S. A. Weiner, *J. Amer. Chem. Soc.*, **93**, 425 (1971).

Anthony A. Baum,* Linda A. Karnischky
Union Carbide Corporation, Tarrytown Technical Center
Tarrytown, New York 10591

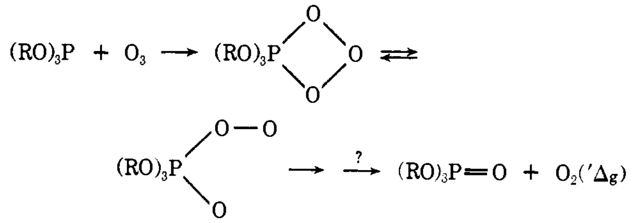
Received January 16, 1973

Mechanisms in Phosphite Ozonide Decomposition to Phosphate Esters and Singlet Oxygen

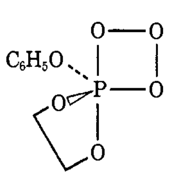
Sir:

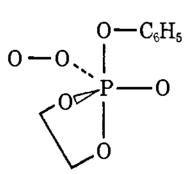
Phosphite ozonides[1–6] represent a particularly convenient and readily accessible source of singlet excited molecular oxygen, a synthetically useful intermediate with potential environmental and biological importance.[7–9] We wish to report here evidence for the involvement of two mechanisms in the decomposition of these ozonides to phosphate esters and oxygen. The data[10] presented below indicate that ozonides derived from phosphites with small rings or bicyclic structures decompose by simple extrusion of oxygen from the adduct without rearrangement about phosphorus. The decomposition of these phosphite ozonides shows virtually no substituent sensitivity, as is evident by the similarity in the decomposition rates of compounds **1–8** ($k = 1.4 \pm 0.4 \times 10^{-4}$ sec^{-1} at $-5°$ in CH_2Cl_2). On the other hand, those phosphite ozonides without geometrical constraints appear to decompose by a much lower energy pathway and display substantial substituent sensitivity consistent with a requirement for prior rearrangement *via* pseudorotation.

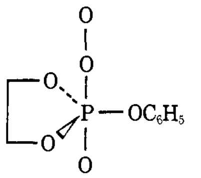
Previous work on these ozone adducts may be interpreted to support an overall mechanism for the decomposition reaction as shown below. Thompson's ^{31}P nuclear resonance data[1] provide strong evidence for pentacovalent phosphorus intermediates. Evidence for a rapid preequilibration of ring-closed and ring-opened ozonides is derived from thermochemical analyses of Benson and Shaw,[12] which indicate a maximum oxygen–oxygen bond strength of 2 kcal/mol compared with activation energies in the decomposition step of ~15 kcal/mol.[2,3] Our results add to this simple description and indicate that the decomposition step is deceptively complex and best described in terms of two mechanisms.



The similarity of the rates of decomposition for phosphite ozonides **1–8** suggests that one mechanism is operative in these cases. Support for this idea may be obtained by noting that the five-membered ring and the bicyclic phosphites are constrained to decompose from a limited range of geometries. Pseudorotations of the ozonides of phosphites **2–8** lead to several chemically distinguishable species, illustrated for compound **6**.


6a


6b


6c

Of these species, only **6a** or an ozonide ring opened

---

[1] Q. E. Thompson, *J. Amer. Chem. Soc.*, **83**, 845 (1961).

[2] (a) R. W. Murray and M. L. Kaplan, *ibid.*, **91**, 5358 (1969); (b) *ibid.*, **90**, 537 (1968).

[3] E. Koch, *Tetrahedron*, **26**, 3503 (1970).

[4] (a) E. Wasserman, R. W. Murray, M. L. Kaplan, and W. A. Yager, *J. Amer. Chem. Soc.*, **90**, 4160 (1968); (b) R. W. Murray and M. L. Kaplan, *ibid.*, **90**, 4161 (1968).

[5] (a) P. D. Bartlett and G. D. Mendenhall, *ibid.*, **92**, 210 (1970); (b) P. D. Bartlett and A. P. Schaap, *ibid.*, **92**, 6055 (1970).

[6] M. E. Brennan, *Chem. Commun.*, 956 (1970).

[7] D. R. Kearns, *Chem. Rev.*, **71**, 395 (1971).

[8] A. M. Trozzolo, *Ann. N. Y. Acad. Sci.*, **171** (1970).

[9] C. S. Foote, *Accounts Chem. Res.*, **1**, 104 (1968).

[10] Phosphites not commercially available were prepared by standard methods.[11] Ozonides were prepared by addition of phosphite to solutions of ozone in methylene chloride maintained at $-78°$. All ozonides have been shown to produce singlet oxygen (presumably $^1\Delta_g$) by the characteristic bleaching effect on rubrene.

[11] (a) G. M. Kosolopoff, "Organophosphorus Compounds," Wiley, New York, N. Y., 1950; (b) W. J. Lucas, F. W. Mitchell, Jr., and C. N. Scully, *J. Amer. Chem. Soc.*, **72**, 5491 (1950); (c) P. C. Crofts, J. H. H. Markes, and H. N. Rydon, *J. Chem. Soc.*, 4250 (1958).

[12] S. Benson and R. Shaw, *Org. Peroxides*, **1**, 105 (1970).

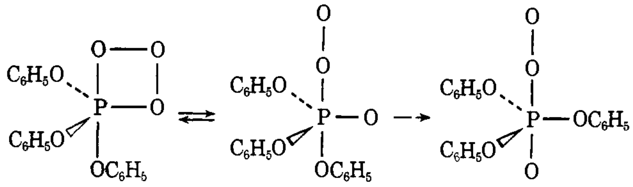
Table I. Rate Constants for Oxygen Evolution from Phosphite Ozonides in Methylene Chloride

Phosphite	Temp,[a] °C	No. of runs	Rate constant[b] ×10⁶ sec
1 1-Ethyl-4-phospha-3,5,8-trioxabicyclo[2.2.2]octane	−5	4	97.5
2 *o*-Phenylene phenyl phosphite	−5	3	110
3 *o*-Phenylene ethyl phosphite	−5	3	129
4 *o*-Phenylene 2-methylbutyl phosphite	−5	2	118
5 *o*-Phenylene pentafluorophenyl phosphite	−5	3	187
6 Ethylene phenyl phosphite	−5	3	150
7 Ethylene 2,2,2-trifluoroethyl phosphite	−5	6	170
8 Ethylene pentafluorophenyl phosphite	−5	3	140
9 Tris(pentafluorophenyl) phosphite	−5	3	415
10 Triphenyl phosphite	−5	5	7400
	−45	3	27.0
11 Tris(2,2,2-trifluoroethyl) phosphite	−5	4	1910
	−45	3	7.8
12 Trimethylene phenyl phosphite	−45	3	3260
13 Trimethylene pentafluorophenyl phosphite	−45	4	520
14 Trimethylene 2,2,2-trifluoroethyl phosphite	−45	3	2330

[a] All data could not be obtained at a single temperature. It is possible to compare ozonide stabilities through entries common to both temperatures employed. [b] Rates were obtained from measurement of oxygen evolution. Least-squares analysis of data shows good first-order dependence. Several decomposition rates have been measured previously.[2,3,6] Where temperatures are sufficiently similar to allow comparison, our rates are in satisfactory agreement with those previously reported.

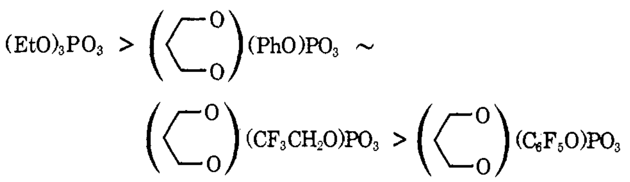
structure[13] would appear to be an appropriate phosphate precursor. In pseudorotamer **6b** the incipient phosphate ester ligands are planar with bond angles far removed from that of the product, while **6c** and other pseudorotamers suffer from the relatively high-energy diequatorial disposition of a five-membered ring.[14] The other member of this series, the ozonide of bicyclic phosphite **1**, clearly has available *only* geometries approximating **6a**. Thus, we postulate the simplest possible mechanism, one involving ring opening of the ozonides of compounds **1–8** followed by rate-determining cleavage of the phosphorus–oxygen bond from geometries approximated by **6a**.

It is interesting to note that the ozonides of compounds **1–8** show decomposition rates remarkably insensitive to substituents; large variations in apical and equatorial ligands (see **6a** for geometry) are tolerated without significant rate variation. It is possible that a portion of the stability of these ozonides is due to the known fact that cyclic structures tend to operate against the conversion of pentacoordinate phosphorus to phosphate.[15a] However, this explanation of the data does not account for the substantial substituent sensitivity noted in the decomposition of the ozonides of compounds **9–14**; and we conclude that a second mechanism is available to this group of compounds. We postulate that the accessibility of conformations[13] such as **10c**, generally unavailable to the geometrically con-



10a **10b** **10c**

strained ozonides of **1–8**, accounts for both the faster rates and the substituent effects of ozonides of **9–14**. Conformation **10c** is doubly attractive as a reactive intermediate since little structural reorganization is required to reach phosphate and because it necessarily takes advantage of the preferred apical geometry of leaving groups.[15] It would also be expected that the relative rates of decomposition would depend on the affinity of the ester ligands for equatorial positions. This is obvious from the trends[16] $(EtO)_3PO_3 > (PhO)_3PO_3 \sim (CF_3CH_2O)_3PO_3 > (C_6F_5O)_3PO_3$ and



Thus electronegative groups,[17] which tend to avoid the equatorial positions,[15] retard the rate, as does the presence of the six-membered ring which prefers apical-equatorial disposition, although not strongly.[14a]

The postulate of prior pseudorotation in the unconstrained phosphite ozonides accounts then for the substituent effects noted for compounds **9–14** while allowing phosphite ozonides such as **1–8**, which are denied this second mechanism, to remain substituent insensitive.

We conclude that in the absence of steric constraints, phosphite ozonides will decompose from geometries represented by **10c**. Structural factors which do not allow this low-energy pathway lead to relatively stable ozonides which decompose by the substituent-insensitive route discussed above. The results suggest that because of the symmetry of species such as **10c**, ozonization of phosphites of the types **9–14** need not lead to complete retention of configuration in the phosphate as do other oxidations studied in these systems.[19,20] In addition the results shown for compounds **1–8** make it apparent that attempts to develop phosphite ozonides

---

(13) We are not prepared to speculate about the electronic distribution in the ring-opened ozonide at this point. If dipolar, however, it seems most likely that the –O–O ligand would be assigned a positive charge with a negative charge on the –O ligand. Thus, we prefer to write the –O–O ligand in an apical position when possible.

(14) (a) B. C. Chang, W. E. Conrad, D. B. Denny, D. Z. Denny, R. Edelman, R. L. Powell, and D. W. White, *J. Amer. Chem. Soc.*, **93**, 4004 (1971); (b) D. Gorenstein and F. H. Westheimer, *ibid.*, **92**, 634 (1970); (c) D. Gorenstein, *ibid.*, **92**, 644 (1970); (d) E. A. Dennis and F. H. Westheimer, *ibid.*, **88**, 3432 (1966); (e) G. O. Doak and R. Schmutzler, *Chem. Commun.*, 476 (1970); (f) D. Houalla, R. Wolf, D. Gagnaire, and J. B. Robert, *ibid.*, 443 (1969).

(15) (a) F. H. Westheimer, *Accounts Chem. Res.*, **1**, 70 (968); (b) K. Mislow, *ibid.*, **3**, 321 (1970); (c) F. Ramirez, *ibid.*, **1**, 168 (1968).

(16) In these series we take advantage of the work of Murray and Kaplan[2] who have shown that triethyl phosphite ozonide has only a short lifetime even at −95° and is thus much less stable than any ozonide studied herein.

(17) Calculations of the electronegativities of the groups CF_3CH_2O– and C_6H_5O–, performed by known methods,[18] suggest that their electronegativities are quite similar.

(18) (a) J. E. Huheey, *J. Phys. Chem.*, **69**, 3284 (1965); (b) A. F. Clifford, *ibid.*, **63**, 1227 (1959).

(19) (a) For N_2O_4 oxidation, see D. Z. Denny, G. Y. Chen, and D. B. Denny, *J. Amer. Chem. Soc.*, **91**, 6838 (1969); (b) for *tert*-butyl hydroperoxide oxidation, see M. U. Hague, C. N. Coughlin, J. H. Horgis, and W. G. Bentrude, *J. Chem. Soc. A*, 1786 (1970).

(20) D. B. Denny informs us that in two cases, both cyclic trialkyl phosphites, one five-membered and one six-membered, retention of configuration was found in ozone oxidation. This might indicate that pseudorotation to species like **10c** could be rate determining. Additional examples are necessary to support this conclusion.

as room-temperature stable sources of singlet oxygen are likely to go unrewarded.

Acknowledgment. This work received financial support from a Merck award for Young Faculty Development and a Camille and Henry Dreyfuss Teacher–Scholar Grant. We would also like to acknowledge a Frederick P. Whitaker Fellowship provided in support of the graduate study of David E. McClure during the year of 1971–1972.

L. M. Stephenson,* D. E. McClure
Department of Chemistry, Stanford University
Stanford, California 94305
Received November 22, 1972

Reaction of α,α'-Dibromo Ketones with Organocopper Reagents. A New Method for α Alkylation of Ketones[1]

Sir:

We recently observed that 2-bromocyclododecanone reacts with lithium dimethylcuprate(I) in diethyl ether giving cyclododecanone in 95% yield after acidic work-up, giving 2-deuteriocyclododecanone in 88% yield after D_2O work-up, and giving 2-methylcyclododecanone in 67% yield after exposure to excess methyl iodide.[2] These results suggested the intermediacy of a metal (lithium or copper) enolate.[3] We were intrigued by the possibility that α,α'-dibromo ketones might also react with organocopper reagents leading initially to enolates in which internal displacement of bromide would produce cyclopropanones (or allene oxide or oxyallyl carbonium ion structures)[4] as in the Favorskii rearrangement. Further reaction with the organocopper reagent might produce a new enolate **2**,[5] and exposure of this species to various electrophiles would yield α-substituted and/or α,α'-disubstituted ketones (eq 1). We report herein the successful execution of this synthetic scheme and its application to α-secondary and α-tertiary alkylation of ketones.

Seven symmetrical cyclic (**1a–c**) and acyclic (**1d–f**) α,α'-dibromo ketones have been treated separately with 5 mol equiv of lithium dimethylcuprate(I) (concentration *ca.* 0.25 *M*) at −78° in diethyl ether during 0.5 hr[6] to give the corresponding α-methyl ketones consistently in good to excellent yields after −78° methanol quench and then aqueous work-up; no dimethylation is observed[7–9] (see Table I).

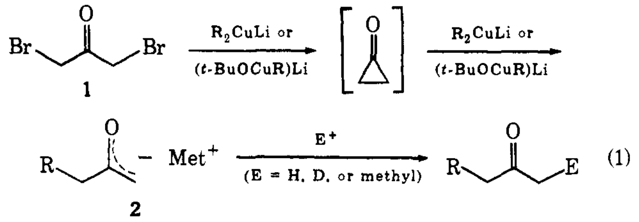


Table I. α-Methyl Ketones from α,α'-Dibromo Ketones and Lithium Dimethylcuprate(I) in Diethyl Ether at −78° (See Equation 1)

Substrate	Product	% yield[a]
cis-2,6-Dibromocyclohexanone (*cis*-**1a**)	2-Methylcyclohexanone	70[b] (95[c])
trans-2,6-Dibromocyclohexanone (*trans*-**1a**)	2-Methylcyclohexanone	98[b]
2,8-Dibromocyclooctanone (**1b**)	2-Methylcyclooctanone	80[c]
cis-2,12-Dibromocyclododecanone (*cis*-**1c**)	2-Methylcyclododecanone	97
4,6-Dibromo-5-nonanone (**1d**)	4-Methyl-5-nonanone	70
1,3-Dibromo-1,3-diphenyl-2-propanone (**1e**)	1,3-Diphenyl-2-butanone	72[d]
2,4-Dibromo-2,4-dimethyl-3-pentanone (**1f**)	2,2,4-Trimethyl-3-pentanone	54[e]

[a] The yield was determined by analytical vpc using an internal standard. [b] The variation in yield as a function of substrate stereochemistry is not yet understood. [c] Reaction temperature −78° for 5 min, then 25° for 1 hr before methanol quench. [d] 18% dimer: 1,3,4,6-tetraphenyl-2,5-hexanedione. [e] Reaction was performed in pentane at −50°.

Evidence pointing to a cyclopropanone (or allene oxide or oxyallyl carbonium ion)[4] intermediate in the reaction of α,α'-dibromo ketone **1e**, for example, with

---

[1] Part of this work was presented at the 8th Middle Atlantic Regional Meeting of the American Chemical Society, Washington, D. C., Jan 14–17, 1973, Abstract H3.

[2] (a) Alkylation of α-bromo ketones and of α,α'-dibromo ketones in low yields using lithium dialkylcuprates(I) has recently been reported: J. E. Dubois, C. Lion, and C. Moulineau, *Tetrahedron Lett.*, 177 (1971); J. E. Dubois and C. Lion, *C. R. Acad. Sci. Paris, Ser. C*, 272, 1377 (1971). (b) Zinc reduction of 2-bromocyclododecanone followed by addition of methyl iodide has been reported to form 2-methylcyclododecanone: T. A. Spencer, R. W. Britton, and D. S. Watt, *J. Amer. Chem. Soc.*, **89**, 5727 (1967).

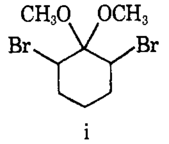
[3] The low reactivity of this enolate toward methyl iodide and other normally reactive electrophiles suggests that it is a copper rather than a lithium enolate; for some comments on copper enolate chemistry, see H. O. House and W. F. Fischer, Jr., *J. Org. Chem.*, **34**, 3615 (1969).

[4] Much attention has been devoted recently to the intermediates formed in reductive elimination of bromine from α,α'-dibromo ketones using (a) electrochemistry: A. J. Fry and R. Scoggins, *Tetrahedron Lett.*, 4079 (1972); J. P. Dirlam, L. Eberson, and J. Casanova, *J. Amer. Chem. Soc.*, 94, 240 (1972); (b) zinc–copper couple: H. M. R. Hoffmann, K. E. Clemens, E. A. Schmidt, and R. H. Smithers, *J. Amer. Chem. Soc.*, 94, 3201 (1972); H. M. R. Hoffmann, T. A. Nour, and R. H. Smithers, *J. Chem. Soc., Chem. Commun.*, 963 (1972); and (c) iron carbonyls: R. Noyori, K. Yokoyama, S. Makino, and Y. Hayakawa, *J. Amer. Chem. Soc.*, 94, 1772 (1972); R. Noyori, *et al.*, *ibid.*, **94**, 7202 (1972).

[5] For a discussion of nucleophilic attack on cyclopropanones, see N. J. Turro, *Accounts Chem. Res.*, **2**, 25 (1969).

(6) All reactions were performed routinely on a 1–2 mmol scale and in several cases on a 10–15 mmol scale with the usual precautions for rigorous exclusion of air and moisture. Cuprous iodide was purchased from Fischer Chemical Co. and was continuously extracted with THF in a Soxhlet extractor for about 12 hr and then dried under vacuum at 25°; the cuprous iodide thus purified remained pure on standing for several months, and aliquots were used for reaction with organolithium reagents to generate organocuprates(I).

(7) It should be noted that 1,3-dibromoalkanes are much less reactive than α,α'-dibromo ketones toward organocuprates(I); dibromide i, for example, is inert to lithium dimethylcuprate(I).



i

(8) For an excellent discussion with leading references of the importance of ketones in organic chemistry and the difficulties in controlling α alkylation of ketones, see H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, New York, N. Y., 1972, Chapter 9.

(9) It should be noted that, in contrast to nucleophilic attack of an enolate ion or an enamine on an electrophilic methyl group, lithium dimethylcuprate(I) reaction with α,α'-dibromo ketones involves an electrophilic substrate and a nucleophilic methyl group; this difference may allow methylation of certain complex ketones not easily methylated by the enolate or enamine approach.