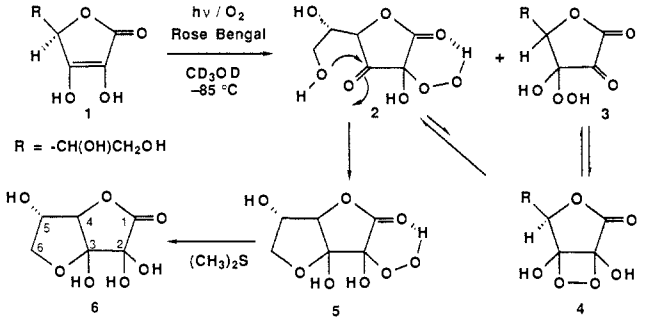
Table I. ^{13}C NMR Chemical Shifts of Photooxygenation Products of L-Ascorbic Acid[a,b]

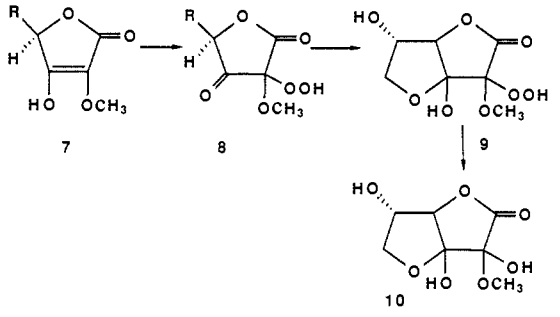
compds	C-1	C-2	C-3	C-4	C-5	C-6
2	169.68	90.81	204.03	84.27	71.12	62.18
3	161.07	185.45	98.56	81.01	68.94	62.18
5	170.32	99.08	105.91	88.86	74.24	76.80
6	173.96	92.38	106.87	88.67	74.34	76.86
8	169.12	93.10	201.89	84.10	71.67	62.81
9	168.19	100.58	106.46	88.96	73.77	77.34
10	171.47	93.68	106.42	88.61	73.61	76.22
11B[c]	157.75	156.96	170.01	76.89	70.76	70.30

[a] Chemical shifts are in ppm downfield from internal Me_4Si. [b] Solvent: CD_3OD at −80 °C, using the Bruker WP 200 (50 MHz for ^{13}C NMR). [c] Solvent: Acetone-d_6, at room temperature, C-1 and C-2 chemical shifts are interchangeable. Other peaks were assigned by the DEPT ^{13}C NMR technique and 2-D NMR (homo and heteronuclear) by using Bruker AM 500 (125 MHz for ^{13}C NMR) and AF 200 (50 MHz for ^{13}C NMR) spectrophotometers (Benn, R.; Günther, H. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 350).

Scheme I



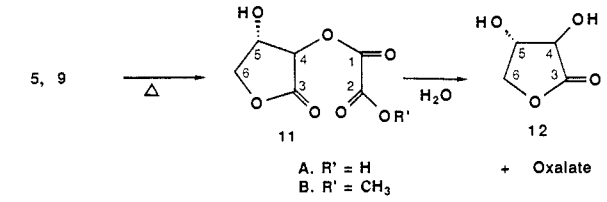
Scheme II



Isomer **2** finally cyclizes to the more stable hydroperoxide hemiketal **5**. Product **5** is slowly reduced by dimethyl sulfide to dehydroascorbic acid (DHA) **6**,[12] identified by comparison of its ^1H and ^{13}C NMR spectra with an authentic sample.[13] Structural assignments were aided by the preparation and photooxidation of many related compounds. The results of these studies will be reported in another place.[14]

Reaction of 2-*O*-methyl-L-ascorbic acid **7**[15] with $^1O_2$ at −85 °C gave hydroperoxy ketone **8** (Scheme II), which rearranged within 3 h at −78 °C to hemiketal **9**. This compound was reduced by dimethyl sulfide to give **10**. The structures of **9** and **10** were assigned on the basis of spectral data, and that of **10** confirmed

Scheme III



by comparison with an authentic sample.[16]

On heating to room temperature, **9** is converted to oxalate **11B**, which was separated by column chromatography on silica gel[17] (Scheme III). Hydroperoxide **5** gave the analogous oxalate lactone **11A**.[17] Both **11A** and **11B** are easily hydrolyzed under mildly acidic conditions to L-threonolactone **12** and oxalate.[18] This reaction provides a chemical analogy for the metabolic formation of oxalate from oxygenation of ascorbate[19,20] instead of via the diketogulonate (DKG) pathway.[1,21]

Acknowledgment. Supported by NIH Grant no, GM20080.

(12) **6**: ^1H NMR (acetone-d_6, at −60 °C) δ 5.6 (brd, OH), 4.55 (1 H, d), 4.46 (1 H, q), 4.18 (1 H, m), 4.06 (1 H, m). For general information on dehydroascorbic acid, see: (a) Sapper, H.; Pleyer-Weber, A.; Lohmann, W. *Z. Naturforsch.* **1982**, *37C*, 129. (b) Kang, S.; Sapper, H.; Lohmann, W. *Ibid.* **1982**, *37C*, 1064. (c) Hvslef, J.; Hope, H.; Murray, B. D. *Carbohydr. Res.* **1986**, *147*, 11. (d) Hvoslef, J.; Pedersen, B. *Acta Chem. Scand.* **1979**, *B33*, 503.

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(14) Kwon, B. M.; Foote, C. S., in preparation.

(15) **7**: ^{13}C NMR (acetone-d_6) 172.60, 160.91, 122.91, 76.59, 70.21, 63.21, 60.11 ppm (Lu, P; Lillard, D. W., Jr.; Seib, P. A.; Kramer, K. J.; Liang, Y. *J. Agric. Food Chem.* **1984**, *32*, 21).

(16) Hydroperoxide **9**: ^1H NMR (MeOH-d_4, −70 °C) all peaks are broad, δ 5.4 (OH), 4.51 (1 H, C_4-H), 4.37 (1 H, C_5-H), 4.21 (1 H, C_6-H), 4.10 (1 H, C_6-H), 3.58 (3 H, CH_3). 2-methyl dehydroascorbic acid **10**: ^1H NMR (MeOH-d_4, at −20 °C) δ 5.4 (OH), 4.53 (1 H, C_4-H), 4.37 (1 H, C_5-H), 4.30 (1 H, C_6-H), 4.17 (1 H, C_6-H), 3.45 (3 H, CH_3) (Hvoslef, J.; Pedersen, B. *Acta Chem. Scand.* **1980**, *34B*, 285).

(17) Reaction of **11A** with diazomethane gave **11B**, separated by column chromatography (65% yield): ^1H NMR (acetone-d_6) δ 8 (brd, OH, D_2O exchangeable), 5.66 (d, 1 H, J = 8.1 Hz), 4.87 (q, 1 H, J = 8.0 Hz), 4.51 (m, 1 H), 4.22 (m, 1 H); MS, *m/e* 204 (M^+). Anal. Calcd for $C_7H_8O_7$: C, 41.19; H, 8.88. Found: C, 41.21; H, 8.92.

(18) After hydrolysis of **11B**, the reaction mixture was treated with diazomethane, and dimethyl oxalate was detected by GC, ^1H NMR ($CDCl_3$): δ 3.89. L-threonolactone **12** was crystallized from acetonitrile and ethyl ether, mp 65 °C, lit.[22] mp 66 °C.

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Intermediate in the Ene Reaction of Singlet Oxygen with 1,4-Diphenyl-*cis*-2-butene and 2-Butene

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Isotope effect measurements are a powerful tool for distinguishing between concerted and stepwise reaction pathways.[1] Large intermolecular primary deuterium isotope effects provide strong evidence for hydrogen abstraction in the rate-determining step of the reaction. However, high *intra*molecular (product) and simultaneous low *inter*molecular (i.e., competition, kinetic) isotope effects are evidence for an intermediate,[1] with an isotope effect on the second (product-determining) but not the first (rate-determining) step.

Several groups have reported isotope effects in the ene reaction of singlet oxygen with olefins, but intra- and intermolecular effects have never been measured in the same system with the same techniques. Stephenson et al.[2] have shown the stereochemical

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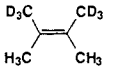
Table I. Isotope Effects for the Ene Reaction of 1,4-Diphenyl-*cis*-2-butene[a] with Singlet Oxygen

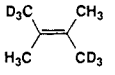
reaction type	substrate	conversion, %	k_H/k_D
intermolecular	**2**-d_0/**2**-d_4	38	1.04 ± 0.04
		54	1.09 ± 0.04
		64	1.08 ± 0.05
intramolecular	**2**-d_2	80	1.50 ± 0.04

[a] Mixture, 92% cis, 8% trans. However, the trans isomer is 20 times less reactive than the cis. No isomerization of the cis isomer was observed.

dependence of product isotope effects in the singlet oxygen reaction with *cis*- and *trans*-tetramethylethylene-d_6 (**1**). The results were

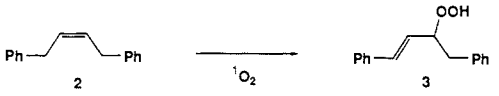


cis 1: k_H/k_D = 1.04-1.09



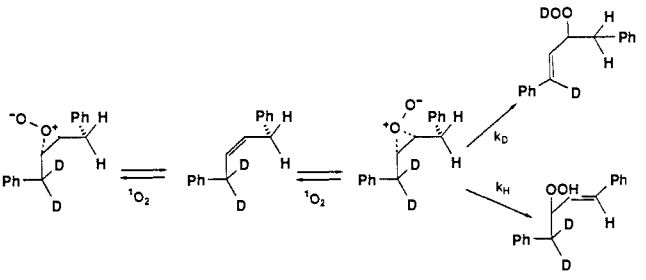
trans 1: k_H/k_D = 1.38-1.41

interpreted as suggesting irreversible formation of an intermediate with "structural requirements not dissimilar to those of the perepoxide". Earlier work by Nickon et al. was interpreted on the basis of a concerted mechanism,[3] Kopecky[4] found low intermolecular kinetic isotope effects (k_H/k_D = 1.08, 1.13) for *Z* and *E* d_0 versus d_6 dimethylstilbenes, and more recently, Gollnick[5] compared d_0 versus d_{12} 2,3-dimethylbutene and found k_H/k_D = 1.11. We now report both intermolecular (kinetic) and intramolecular (product) isotope effects on the reaction of singlet oxygen with 1,4-diphenyl-*cis*-butene (**2**)[6] and intramolecular effects with the 2-butenes.



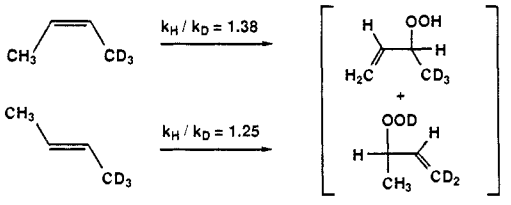
A mixture of equal amounts of **2**-d_0 and **2**-d_4 with 1.5×10^{-4} M mesoporphyrin IX in acetone-d_6 in an NMR tube at 0 °C reacts smoothly on irradiation with a 650-W tungsten–halogen lamp. The trans allylic hydroperoxide **3** is the only product. The reaction was interrupted at various conversions and analyzed by integration of the ^{1}H NMR spectrum (nitromethane was external standard), The results are shown in Table I. A very small kinetic isotope effect (average k_H/k_D = 1.07) was found in the intermolecular competition between **2**-d_0 and **2**-d_4. This effect is in the range of intermolecular kinetic isotope effects previously reported for tetramethylethylene and other alkenes and interpreted as supporting a concerted mechanism.[4,5] In contrast, there is a significant product isotope effect (average k_H/k_D = 1.50) in the intramolecular reaction using **2**-d_2, where methylene groups in the cis configuration compete. The magnitude of this effect is similar to those previously reported from *trans*-2,3-dimethylbutene-d_6[1b] and other alkenes in which hydrogen and deuterium compete in a cis relationship.

A small kinetic isotope effect and a substantial product isotope effect strongly suggest that there is an intermediate whose formation is rate-determining.[1] Formation of a peroxide or an exciplex with similar structural requirements accommodates the present and previous data. Schuster et al.[7] have reported similar conclusions based on an analysis of the activation parameters of the reaction. They argue for the intermediacy of both an exciplex and a perepoxide. Similar isotope effect arguments were also made for the reaction of several enophiles, where either the first or second step can be rate-determining depending on the reactivity of the enophile.[8]



The small but nonzero intermolecular isotope effect here and in similar alkenes[2] suggests reversible formation of the intermediate.[9] Beak has carefully analyzed the kinetics of such reversible processes and derived conditions where reversible formation of similar intermediates can give various isotope effects.[1a] Reactions of triazolinediones with deuteriated butene isomers have isotope effects in the same direction as with singlet oxygen, but larger.[10] *cis*-Butene-*1,1,1*-d_3 gives a large isotope effect (k_H/k_D = 5.36), while both *trans*-butene-*1,1,1*-d_3 and isobutylene-d_3 show a small but substantial effect, k_H/k_D = 1.29 and 1.25, respectively. The intermolecular isotope effect for this reaction is k_H/k_D = 1.02 ± 0,1. These results were explained by a reversibly formed aziridinium imide intermediate similar to the proposed perepoxide.

The deuteriated butene isomers[10,11] give similar results with singlet oxygen, although the isotope effects are smaller. The reaction of $^1O_2$ with *cis*- and *trans*-butenes-d_3 shows a substantial intramolecular isotope effect for both the cis and trans isomers. *cis*-Butene-*1,1,1*-d_3 has k_H/k_D = 1,38, close to that observed in



most cis relationships, whereas the trans isomer has an unexpectedly large isotope effect, 1.25, much larger than the effect observed with (*Z*)-2,3-bis-(trideuteriomethyl)-2-butene, k_H/k_D = 1.07. The substantial isotope effect observed for the trans isomer could be the result either of partial reversion of the intermediate to the starting materials or isomerization of the intermediate. However, if there is an open intermediate, it cannot return to starting material, since no isomerization of the starting olefin was observed. If one or both of these processes operate to a significant extent, an isotope effect is expected even for methyl groups on opposite sides of the double bond.

Acknowledgment. This work was supported by NSF Grant no. CHE86-11873.

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(6) The synthesis of *cis*-**2**-d_4 proceeds through the following steps: (a) Exchange of two hydrogens for deuterium in phenylacetic acid in an alkaline solution of D_2O at 100 °C. (b) $LiAlH_4$ reduction of the acid-d_2 followed by bromination and conversion to the alkyltriphenylphosphonium bromide. (c) Oxidation of 2-phenylethanol-*2,2*-d_2 with pyridinium chlorochromate to phenylacetaldehyde-*2,2*-d_2. (d) Wittig coupling of phenylacetaldehyde-d_2 with the corresponding ylide-d_2 to give *cis*-**2**-d_4 in 92% isomeric purity and 91% deuterium incorporation. MS for $C_{16}H_{12}D_4$ calcd 212.1503, found 212.1499. Wittig coupling of phenylacetaldehyde with the ylide-d_2 gave *cis*-**2**-d_2 in 92% isomeric purity and >98% deuterium incorporation. MS for $C_{16}H_{14}D_2$ calcd 210.1377, found 210.1356.

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(11) Analyzed by NMR. The only product detected during the photooxygenation of *cis*- or *trans*-butene-d_3 was the ene adduct. GC analysis showed no isomerization of starting material or formation of any products from dioxetanes. The butenes are too volatile to permit determination of the intermolecular isotope effect.