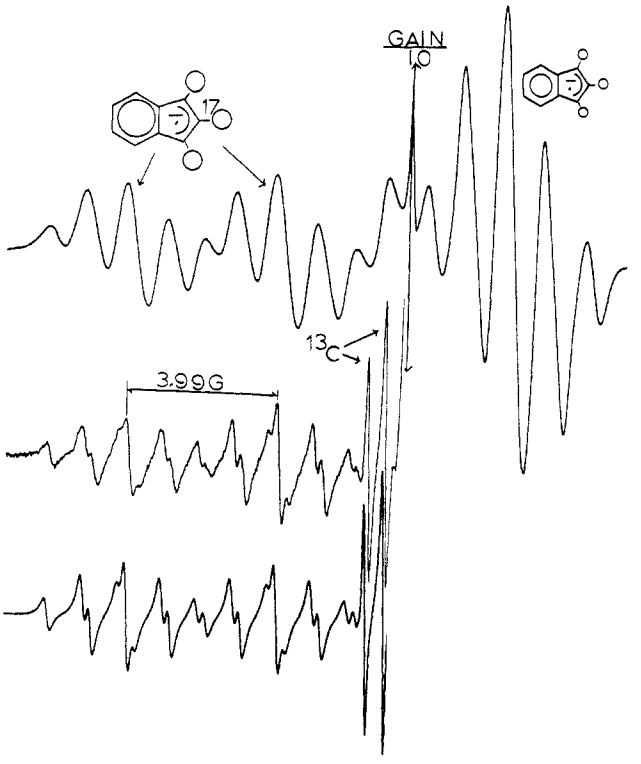

Figure 1. ESR spectra of an HMPA solution of the ninhydrin anion radical with 0.2 M added $H_2{}^{17}O$ recorded at 298 °C. Both spectra were recorded from the same anion radical solution. The top spectrum was recorded from a portion of the solution 4 min after the simultaneous addition of the $H_2{}^{17}O$ and 0.2 M neutral ninhydrin, and it shows the low field portion of the spectrum of the ^{17}O labeled anion radical and the unlabeled species. The gain was reduced by a factor of 10 at the vertical arrow. Computer simulation of this spectrum shows that the ^{17}O labeled anion radical represents 25% of the total anion radical. Line broadening is due to the rapid electron exchange between the neutral molecule and anion radical. The center spectrum was recorded 11 h after the addition of the $H_2{}^{17}O$. Neutral ninhydrin was not added to this portion of the solution, and no ^{17}O labeled anion radical could be observed within 1 h of the water addition. After 11 h, the ^{17}O labeled species only represents 3.5% of the total anion radical, and it yields ESR line heights that are comparable to those for the ^{13}C labeled materials that are present in natural abundance. The unlabeled anion radical is not shown and is off scale by more than a factor of 100. The spectrum shown on the bottom is a computer simulation and was generated by combining three spectra: (1) $C_9H_4O_2{}^{17}O$, A_H = 1.16 G, 2 H's, A_H = 0.93, 2 H's, A_o = 3.99 (anisotropic effects in the oxygen splitting not accounted for). (2) $C_8{}^{13}CH_4O_3$ (^{13}C on one of two equivalent positions), A_c = 3.15 G. (3) $C_8{}^{13}CH_4O_3$ (^{13}C on one of two equivalent positions), A_c = 2.20 G.

counter ion with the oxygen atom. The lack of ion association and hydrogen bonding generally results in smaller charge densities and higher spin densities on the oxygen atoms with correspondingly larger A_O's, Table I.

The reaction is functional even for ketyls, which are not stable in water. The ^{17}O labeled ketyl anion radicals can be prepared by simply adding a molar deficient amount of the $H_2{}^{17}O$ to the anion radical solution. The water probably first protonates the ketyl producing ^{17}O labeled hydroxide ion. This hydroxide ion can then add to the neutral ketone and follow a path that is analogous to that shown in Scheme I.

A number of side reactions can be envisioned that would lower the overall efficiency of the production of labeled anion radical, such as electron transfer from the hydroxide addition complex to neutral ketone followed by dimerization of the remaining radical.[6] Despite this, strong well resolved ESR spectra of ^{17}O labeled semiquinones, ketyls, and presumably semidiones can be recorded by use of this technique.

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Chemistry of Singlet Oxygen. 50. Hydroperoxide Intermediates in the Photooxygenation of Ascorbic Acid

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Ascorbic acid (vitamin C)[1] is an important aqueous antioxidant.[2] Tocopherol (a lipid-soluble antioxidant) is a powerful quencher for singlet oxygen,[3,4] and this is also true of ascorbic acid.[5] It is known that the double bond in ascorbic acid is cleaved on photooxygenation to give oxalate.[6] Careful studies of the mechanism of photooxygenation have not yet been carried out nor have initial products been determined. In this paper, we report the formation of unstable hydroperoxide intermediates and their decomposition to give oxalate esters. Spectral data for all compounds are summarized in Table I.

Rose bengal-sensitized photooxygenation of ascorbic acid (**1**[7,8]) in CD_3OD at −85 °C gave a reaction mixture which was kept in liquid N_2 until analysis by ^{13}C NMR (−80 °C). Two isomeric hydroperoxy ketones, **2** and **3**, are formed in 65% and 35% yield, respectively.[9]

When the reaction mixture stood at −78 °C for 5 h, the carbonyl peaks of **2** and **3** decreased, and new peaks at 105.91 and 99.08 ppm appeared, corresponding to hydroperoxydehydroascorbic acid **5**.[10] On further standing for 30 h at −78 °C, the reaction mixture showed only peaks for **5**. Hydroperoxy ketone **3**, which lacks a C-3 carbonyl group, apparently also rearranges to hydroperoxide **5**. Scheme I below provides a reasonable working model for these reactions.

Addition of the hydroperoxide in **3** to the C-2 carbonyl group may produce intermediate dioxetane **4**[11] which opens to **2**. We did not detect dioxetane **4**, which is likely to be very unstable.

(1) For a general review of ascorbic acid, see: (a) *Vitamin C*; Counsell, J. N.; Hornig, D. H., Eds.; Applied Science Publisher: London; 1981. (b) "L-Ascorbic Acid: Chemistry, Metabolism and Uses"; *ACS Advances in Chemistry Series No. 200*; Seib, P. A., Tolbert, B. M., Eds.; American Chemical Society; Washington, DC, 1982. (c) Seib, P. A. *Int. J. Vit. Nutr. Res.* **1985**, *27*, 259. (d) Englard, S.; Seifter, S. *Ann. Res. Nutr.* **1986**, *6*, 365.

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(8) Typical procedure: 1 mmol of ascorbic acid in CD_3OD (4 mL) containing rose bengal was photolyzed at −85 °C with a Varian-Eimac 300 W Xenon lamp and a 0.1 M K_2CrO_4 filter solution (in NH_4OH–NH_4Cl at pH 10, cutoff <460 nm) until **1** was gone (TLC). The reaction mixture was monitored by ^{13}C NMR (−80 °C). Upon warming to room temperature, over 80% of oxalate **11A** and less than 20% of the autoxidation product, dehydroascorbic acid **6**, were formed.

(9) The product ratio was approximately determined by comparing the peak height of carbonyl groups in the ^{13}C NMR; peaks of **2** and **3** were assigned by comparison of their chemical shifts with similar compounds from oxidation of L-ascorbic acid (Matusch, R. *Z. Naturforsch.* **1977**, *32B*, 562).

(10) The structure was assigned by comparison with dehydroascorbic acid; see ref 13.

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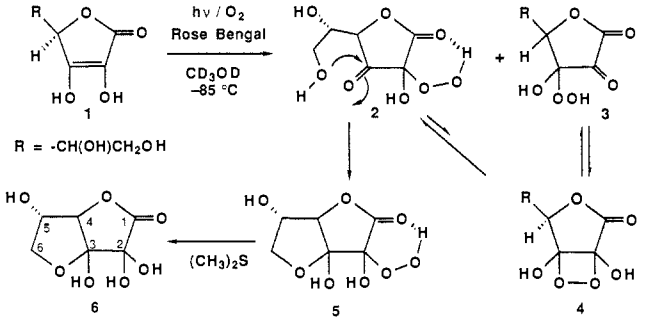
Table I. ^{13}C NMR Chemical Shifts of Photooxygenation Products of L-Ascorbic Acid[a,b]

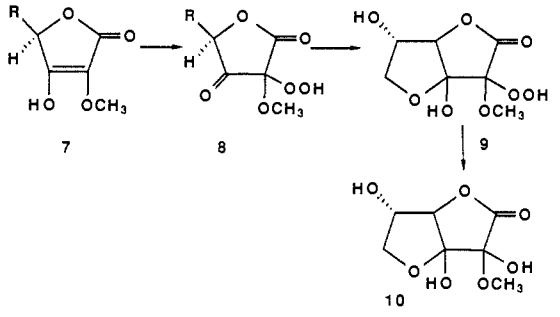
compds	C-1	C-2	C-3	C-4	C-5	C-6
2	169.68	90.81	204.03	84.27	71.12	62.18
3	161.07	185.45	98.56	81.01	68.94	62.18
5	170.32	99.08	105.91	88.86	74.24	76.80
6	173.96	92.38	106.87	88.67	74.34	76.86
8	169.12	93.10	201.89	84.10	71.67	62.81
9	168.19	100.58	106.46	88.96	73.77	77.34
10	171.47	93.68	106.42	88.61	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



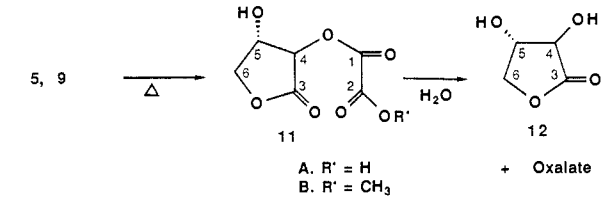
Scheme II



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]

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(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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(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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