H, t, J = 6.5 Hz), 1.31–1.58 (2 H, m), 2.51–2.89 (1 H, m), 3.01 (3 H, br s), 3.32–3.74 (2 H, m); IR ν 3400, 2950, 1590, 1470 cm^{-1}.

The alcohol (*R*)-(+)-**2a** (950 mg, 5.9 mmol) was treated similarly to give 430 mg (82%) of (*R*)-(−)-2-amino-1-butanol: 90% ee;[13] $[\alpha]^{20}_D$ −9.2° (neat); spectral characteristics as reported above.

Lipase-Catalyzed Transesterification of 2-[*N*-(Alkoxycarbonyl)amino] 1-Alcohols 2a,c. The following procedure is representative. To a magnetically stirred solution of 2-[*N*-(ethoxycarbonyl)amino]-1-butanol (**2a**; 3.22 g, 20 mmol) in ethyl acetate (120 mL) at 25 °C was added steapsin (0.2 g, 2200 U) supported on Celite 577 (1.0 g), and the reaction mixture was stirred at 25 °C.

Periodically 1-μL aliquots of the liquid phase were withdrawn and analyzed by gas chromatography. After 48 h, approximately 50% conversion was reached and the reaction stopped. The solid enzyme was filtered off and the solution evaporated to dryness. Flash chromatography on SiO_2 with *n*-hexane/ethyl acetate (1:1) afforded 1.3 g (40%) of (*S*)-(−)-**2a** [$[\alpha]^{20}_D$ −32.2° (*c* 2, ethanol)] and 1.65 g (40%) of (*R*)-(+)-**3a**; [$[\alpha]^{20}_D$ +27.6° (*c* 2, ethanol)].

The ester (*R*)-(+)-**3a** (1.3 g, 6.4 mmol) was treated as described above to give 440 mg (77%) of (*R*)-(−)-2-amino-1-butanol: 95% ee;[13] $[\alpha]^{20}_D$ −9.6° (neat); spectral characteristics as already described.

The alcohol (*S*)-(−)-**2a** (1.0 g, 6.2 mmol) was treated as described above to give 430 mg (78%) of (*S*)-(+)-2-amino-1-butanol; 92% ee;[13] $[\alpha]^{20}_D$ +9.3° (neat); spectral characteristics as described above.

Lipase-Catalyzed Transesterification of 2-Amino-1-butanol (1a). To a magnetically stirred solution of (*RS*)-2-amino-1-butanol (**1a**; 2.0 g, 22.5 mmol) in ethyl acetate (120 mL) at 25 °C was added steapsin (1.0 g, 11 000 U) and the reaction mixture stirred at 25 °C.

Periodically, 1-μL aliquots of the liquid phase were withdrawn and analyzed by gas chromatography. After 72 h, about 35% conversion was reached and the reaction stopped. The enzyme, which appeared as a gummy substance, was filtered off and the solution evaporated to dryness. Flash chromatography on SiO_2 with *n*-hexane/ethyl acetate (1:1) afforded 810 mg (27%) of racemic 2-(acetylamino)-1-butanol [^{1}H NMR δ 0.95 (3 H, t, J = 7.2 Hz), 1.40–1.70 (2 H, m), 2.00 (3 H, s), 3.1–4.2 (4 H, m), 6.80 (1 H, br s); IR ν 3290, 1650, 1560 cm^{-1}] and 1.0 g (50%) of racemic 2-amino-1-butanol.

Acknowledgment. We thank Dr. Silvia Spera of Istituto G. Donegani for her valuable help and discussion concerning NMR analysis.

Registry No. (*R*)-**1a**, 5856-63-3; (*S*)-**1a**, 5856-62-2; (±)-**1a**, 13054-87-0; (*R*)-**1c**, 35320-23-1; (*S*)-**1c**, 2749-11-3; (±)-**1c**, 6168-72-5; (*R*)-**2a**, 110418-25-2; (*S*)-**2a**, 110418-29-6; (±)-**2a**, 110455-82-8; (*R*)-**2c**, 110418-26-3; (*S*)-**2c**, 83197-71-1; (±)-**2c**, 110455-83-9; (*S*)-**3a**, 110418-22-9; (*R*)-**3a**, 110418-27-4; (±)-**3a**, 110455-84-0; (*S*)-**3b**, 110418-23-0; (±)-**3b**, 110455-85-1; (*S*)-**3c**, 110418-24-1; (*R*)-**3c**, 110418-28-5; (±)-**3c**, 110507-76-1; triacylglycerol lipase, 9001-62-1; pancreatin, 8049-47-6; (±)-2-(acetylamino)-1-butanol, 71501-68-3.

A Cyclization Approach to Functionalized Seven-Membered Carbocycles

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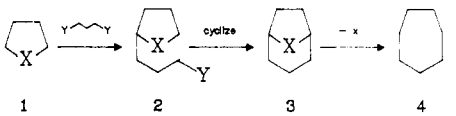
Functionalized seven-membered carbocycles are prepared by dialkylative cyclization of masked butadienes with 2-alkylidene-1,3-dihalopropanes. 3-Sulfolenes are essential intermediates acting as aids to constrain the conformation of the butadiene part during the cyclization step.

Seven-membered carbocyclic compounds are generally more difficult to prepare by cyclization reactions than their lower homologues (ring sizes of five and six) because of conformational flexibility and entropic reasons.[1] One attractive way to solve these problems is to make use of the rigidity of a preexisting ring to lessen the conformational flexibility during the cyclization process. As illustrated in Scheme I, one can imagine a bicyclo[3.2.*n*] system **3** to be synthesized by attaching a three-carbon unit to a cyclic compound **1** containing a four-carbon unit via a 2,2′-dialkylation process. Because of the conformational rigidity of the preexisting ring, the disfavored entropic effect usually encountered for seven-membered ring cyclization (from **2** to **3**) should be minimized. The bridge of the bicyclic compound **3** (noted as X) can be removed afterward to yield the desired seven-membered product **4**. The prerequisite for the success of this strategy is to have a good conformationally constrained four-carbon unit containing a readily removable functional group that facilitates the connection of a three-carbon unit to the molecule at correct positions.

Scheme I



3-Sulfolenes appear to be qualified candidates for conformationally constrained four-carbon units because they are susceptible to smooth deprotonation/alkylation reactions[2] and the activating group, SO_2, can normally be removed by mild thermolysis.[3] More importantly, the

(1) For a review of a cycloaddition approach to seven-membered rings, see: Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 1.

(2) (a) Chou, T. S.; Tso, H. H.; Chang, L. J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 515. (b) Chou, T. S.; Tso, H. H.; Chang, L. J. *J. Chem. Soc., Chem. Commun.* **1984**, 1323. (c) Chou, T. S.; Tso, H. H.; Chang, L. J. *J. Chem. Soc., Chem. Commun.* **1985**, 236. (d) *Chou*, T. S.; Tso, H. H.; Lin, L. C. *J. Org. Chem.* **1986**, *51*, 1000. (e) Chou, T. S.; Tso, H. H.; Tao, Y. T.; Lin, L. C. *J. Org. Chem.* **1987**, *52*, 244.

(3) (a) Mock, W. L. *J. Am. Chem. Soc.* **1975**, *97*, 3666. (b) McGregor, S. D.; Lemal, D. L. *Ibid.* **1966**, *88*, 2858. (c) Kellogg, R. M.; Prins, W. L. *J. Org. Chem.* **1974**, *39*, 2366.

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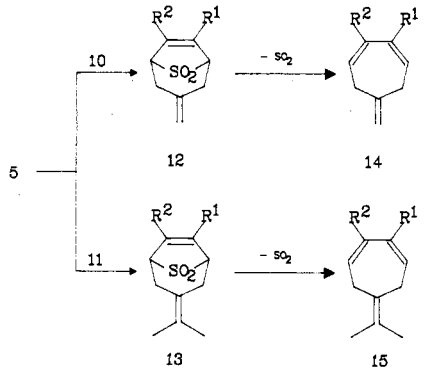
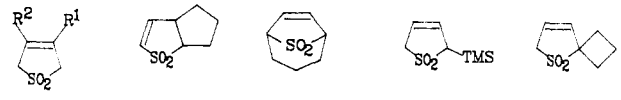
Table I. Dialkylative Cyclization and SO_2 Extrusion of 3-Sulfolenes

entry	R^1	R^2	sulfolene	halide	dialkylation intermediate	yield, %	7-membered product	yield, %
1	H	H	**5a**	**10**	**12a**	60		
2	Me	H	**5b**	**10**	**12b**	51		
3	Me	Me	**5c**	**10**	**12c**	64	**14a**	92
4	Cl	H	**5d**	**10**	**12d**	22	**14b**	95
5	$-(CH_2)_4-$		**5e**	**10**	**12e**	67	**14c**	96
6	H	H	**5a**	**11**	**13a**	71		
7	Me	H	**5b**	**11**	**13b**	74	**15a**	96
8	Me	Me	**5c**	**11**	**13c**	75	**15b**	97
9	Cl	H	**5d**	**11**	**13d**	69	**15c**	97
10	$-(CH_2)_4-$		**5e**	**11**	**13e**	86	**15d**	99

Scheme II



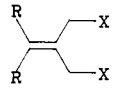
double deprotonation/alkylation reactions of 3-sulfolene **5a** occur sequentially at positions 2 and 5 in a regioselective manner giving the 2,5-disubstituted sulfolenes.[4] However,



5 6 7 8 9

the attempted dialkylative cyclization of **5a** with 1,3-diiodopropane disappointingly gave only the fused bicyclic product **6** instead of the anticipated bridged bicyclic product **7**.[4] On the other hand, the deprotonation/alkylation reaction of the silylated sulfolene **8** with 1,3-diiodopropane proceeded in a 2,2-disubstitution manner giving the spirosulfolene **9**, where the trimethylsilyl group served as a directing group for the regioselective cyclization.[5]

We then searched for other possible three-carbon units and found that the 2,5-dialkylative cyclization of **5a** (1 equiv) with the diiodide **10** [1 equiv, prepared from 3-chloro-2-(chloromethyl)propene with NaI] under normal conditions [−78 °C, 2 equiv of lithium hexamethyldisilazide (LiHMDS)] proceeded cleanly to give the bicyclo[3.2.1] sulfone **12a**. Reactions of **10** with other substituted 3-



10 R=H, X=I
11 R=Me, X=Br

sulfolenes gave similar results (Scheme II; Table I). The readily available dibromide **11**[6] was found to be an equally good three-carbon unit for this dialkylative cyclization purpose. Its reactions with 3-sulfolenes gave the bicyclo[3.2.1] products **13** in even better yields (Table I). The high tendency of these reactions to yield bridged bicyclic products was especially noticeable when **11** (1 equiv) was treated with **5a** (1 equiv) and LiHMDS (1 equiv). This reaction gave mainly the cyclic product **13a** and recovered starting material. Use of 1,3-diiodopropane instead of **11** under similar conditions was found to give mainly the monoalkylated product 2-(iodopropyl)-3-sulfolene.[4]

The difference in the modes of reactions between 1,3-diiodopropane and the bisallylic halides **10** and **11** toward 3-sulfolenes requires some discussion. In an earlier paper,[4] we tried to explain the failure of 2,5-dialkylative cyclization with 1,3-diiodopropane on the basis that the lone pair of electrons of the second anion generated at the monoalkylated stage would be trans to the pendant iodopropyl group, which precluded the formation of **7**. Such a rationale now appears unsatisfactory for the current results, since the cyclization stage leading to the formation of **12** and **13** would encounter the same problem. We therefore speculate that the second anion generated at the monoalkylated stage might exist in sp^2 hybrid instead of the aforementioned sp^3 hybrid, and it was only the steric hindrance of the bulky sulfone functionality that blocked the iodopropyl group from approaching the anion at the 5-position, causing the failure of bridging. Whereas the π-orbital of the S=O bond of the 3-sulfolene can be aligned with that of the C=C bond of the halide **10** or **11** to cause a favorable interaction so that the haloalkylidenepropyl group tends to underlie the sulfolene ring leading to the formation of **12** and **13**.

The bicyclic sulfones **12** and **13** can be converted to the corresponding cycloheptadienes by extrusion of SO_2. Thus, treatment of **12** and **13** with $LiAlH_4$[7] in THF smoothly brought about the formation of the seven-membered carbocycles **14** and **15** (Table I). Compounds **14** and **15** were obtained very cleanly. The purity of each was estimated to exceed 98% by GC (Carbowax 20M column, 3 m) and/or HPLC (LiChrosorb column, hexane) analyses. However, we were unable to obtain satisfactory microanalytical data for these products, probably owing to their instability. Nevertheless, the ^1H NMR, IR, and MS spectral data are in total agreement with the assigned structures. High-temperature thermolysis of the bicyclic sulfones resulted in double-bond isomerization, presumably via a 1,5-hydrogen-shift process. For example, thermolysis of **12e** on a preparative GC (Carbowax 20M column) at 220 °C yielded **16** as the only product. These seven-membered carbocyclic conjugated dienes[8] are expected to be versatile intermediates in organic synthesis.

Since substituted 3-sulfolenes are readily accessible by the cycloaddition reactions of the corresponding dienes with SO_2,[9] the sequence described herein exemplifies that

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(5) Tso, H. H.; Chou, T. S.; Lee, W. C. *J. Chem. Soc., Chem. Commun.* **1987**, 934.
(6) Marshall, J. A.; Faubl, H.; Warne, T. M., Jr. *J. Chem. Soc., Chem. Commun.* **1967**, 753.
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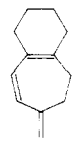
(8) Pattenden, G. In *Comprehensive Organic Chemistry*; Barton, D. H. R., Ollis, W. D., Eds.; Pergamon: Oxford, 1979; Vol. 1, Chapters 2, 3.
(9) Turk, S. D.; Cobb, R. L. In *1,4-Cycloaddition Reactions*; Hamer, J., Ed.; Academic: New York, 1967; Chapter 2.



18

functionalized seven-membered carbocycles can be prepared by the dialkylative cyclization reactions from butadienes and a suitable three-carbon unit aided by the use of conformationally constrained intermediates, 3-sulfolenes.

Experimental Section

^1H NMR spectra were determined on a Bruker AW-80 or a Bruker MSL-200 NMR spectrometer as solutions in $CDCl_3$. IR spectra were determined on a Perkin-Elmer 882 infrared spectrophotometer. Mass spectra were recorded on a Hewlett-Packard 5995B gas chromatograph/mass spectrometer. Elemental analyses were performed at the microanalysis laboratory of National Taiwan University, Taipei, on a Perkin-Elmer 240C EA instrument. 3-Sulfolene **5a** was purchased from Fluka Chemical AG, while other sulfolenes **5b–d**[9] and **5e**[10] were prepared from the proper butadienes and SO_2 according to literature procedures. All reactions were carried out under an atmosphere of dry nitrogen. All solvents were freshly distilled before use.

Dialkylative Cyclization Reactions of 3-Sulfolenes 5. To a mixture of a 3-sulfolene (**5a–e**, 1 mmol), 2-alkylidene-1,3-dihalopropane (**10** or **11**, 1 mmol), and hexamethylphosphoramide (HMPA, 4 mmol) in dry THF (10 mL) at −78 °C was added LiHMDS [2 mmol, prepared in THF (3 mL) from hexamethyldisilazane (3.2 mmol) and *n*-BuLi (2 mmol) at −10 °C for 10 min and then at room temperature for 30 min] dropwise during a period of 30 min. The resulting mixture was stirred at −78 °C for 2 h, whereupon an excess of EtOAc (10 mL) was added. The resulting mixture was then gradually warmed to room temperature. The solvent was removed under reduced pressure, and the crude oil was chromatographed on a silica gel column (EtOAc/hexane, 1:1) to give the bicyclic sulfone **12** or **13**. Analytical samples were obtained by HPLC (LiChrosorb column, EtOAc/hexane, 1:2). Yields of the products are listed in Table I.

3-Methylene-8-thiabicyclo[3.2.1]-6-octene 8,8-dioxide (12a): white solid; mp 114–115 °C; IR (KBr) 1685, 1647, 1294, 1185, 1125, 1112, 899, 760 cm^{-1}; NMR (200 MHz) δ 2.54 dd, 2 H, J = 4.5, 16 Hz), 3.19 (dd, 2 H, J = 2, 16 Hz), 3.60 (br s, 2 H), 4.87 (s, 2 H), 6.45 (br s, 2 H); MS, m/z 170 (M^+), 106, 91 (100), 78, 65, 51. Anal. Calcd for $C_8H_{10}O_2S$: C, 56.45; H, 5.92. Found: C, 56.49; H, 5.85.

6-Methyl-3-methylene-8-thiabicyclo[3.2.1]-6-octene 8,8-dioxide (12b): white solid; mp 90.5–91.5 °C; IR (KBr) 1644, 1634, 1293, 1174, 1109, 912, 840, 757 cm^{-1}; NMR (200 MHz) δ 1.93 (s, 3 H), 2.48 (d, 1 H, J = 16 Hz), 2.55 (d, 1 H, J = 16 Hz), 3.13 (d, 2 H, J = 16 Hz), 3.34 (br s, 1 H), 3.58 (s, 1 H), 4.83 (s, 2 H), 6.01 (br s, 1 H); MS, m/z 184 (M^+), 120, 105 (100), 92, 91, 83, 79. Anal. Calcd for $C_9H_{12}O_2S$: C, 58.67; H, 6.56. Found: C, 58.66; H, 6.68.

6,7-Dimethyl-3-methylene-8-thiabicyclo[3.2.1]-6-octene 8,8-dioxide (12c): white solid; mp 136–138 °C IR (KBr) 1644, 1300, 1184, 1108, 937, 801 cm^{-1}; NMR (200 MHz) δ 1.77 (s, 6 H), 2.47 (dd, 2 H, J = 4.5, 16 Hz), 3.02 (dd, 2 H, J = 2, 16 Hz), 3.27 (br s, 2 H), 4.75 (s, 2 H); MS, m/z 198 (M^+), 134, 119 (100), 106, 105, 91, 77. Anal. Calcd for $C_{10}H_{14}O_2S$: C, 60.57; H, 7.12. Found: C, 60.32; H, 7.12.

6-Chloro-3-methylene-8-thiabicyclo[3.2.1]-6-octene 8,8-dioxide (12d): white solid; mp 107–108 °C; IR (KBr) 1598, 1560, 1310, 1181, 1120, 896 cm^{-1}; NMR (200 MHz) δ 2.56 (d, 1 H, J = 16 Hz), 2.71 (d, 1 H, J = 16 Hz), 3.13 (d, 2 H, J = 16 Hz), 3.56 (br s, 1 H), 3.74 (s, 1 H), 4.92 (s, 1 H), 4.95 (s, 1 H), 6.31 (d, 1 H, J = 5 Hz); MS, m/z 206 (M^+ + 2), 204 (M^+), 142, 140, 105 (100), 103, 79, 77. Anal. Calcd for $C_8H_9ClO_2S$: C, 46.95; H, 4.43. Found: C, 46.87; H, 4.38.

1,3,4,5,6,7-Hexahydro-1,3-(2′-methylenepropano)isobenzothiophene 2,2-dioxide (12e): white solid; mp 140–141 °C; IR (KBr) 1654, 1298, 1184, 1137, 913 cm^{-1}; NMR (200 MHz) δ 1.65 (br s, 4 H), 2.06 (br s, 4 H), 2.46 (dd, 2 H, J = 4.5, 16 Hz), 3.01 (dd, 2 H, J = 2, 16 Hz), 3.28 (br s, 2 H), 4.75 (s, 2 H); MS, m/z 224 (M^+), 160, 117, 91, 85, 83 (100). Anal. Calcd for $C_{12}H_{16}O_2S$: C, 64.25; H, 7.19. Found: C, 64.19; H, 7.18.

3-Isopropylidene-8-thiabicyclo[3.2.1]-6-octene 8,8-dioxide (13a): white solid; mp 123.5–124 °C; IR (KBr) 1302, 1196, 1163, 1133, 758 cm^{-1}; NMR (80 MHz) δ 1.60 (s, 6 H), 2.89 (s, 4 H), 3.58 (br s, 2 H), 6.38 (br s, 2 H); MS, m/z 198 (M^+), 134, 133, 119, 105, 91 (100). Anal. Calcd for $C_{10}H_{14}O_2S$: C, 60.57; H, 7.12. Found: C, 60.55; H, 7.08.

6-Methyl-3-isopropylidene-8-thiabicyclo[3.2.1]-6-octene 8,8-dioxide (13b): white solid; mp 121–122 °C; IR (KBr) 1556, 1305, 1195, 1118, 829, 747 cm^{-1}; NMR (200 MHz) δ 1.60 (s, 3 H), 1.62 (s, 3 H), 1.92 (s, 3 H), 2.73–3.04 (m, 4 H), 3.33 (s, 1 H), 3.60 (s, 1 H), 5.98 (br s, 1 H); MS, m/z 212 (M^+), 148, 105 (100), 91, 79. Anal. Calcd for $C_{11}H_{16}O_2S$: C, 62.20; H, 7.60. Found: C, 61.93; H, 7.60.

6,7-Dimethyl-3-isopropylidene-8-thiabicyclo[3.2.1]-6-octene 8,8-dioxide (13c): white solid; mp 151–152 °C; IR (KBr) 1656, 1292, 1195, 1103, 861 cm^{-1}; NMR (200 MHz) δ 1.62 (s, 6 H), 1.82 (s, 6 H), 2.77 (d, 2 H, J = 16 Hz), 2.88 (dd, 2 H, J = 3, 16 Hz), 3.33 (br s, 2 H); MS, m/z 226 (M^+), 162, 161, 119 (100), 105, 91, 77. Anal. Calcd for $C_{12}H_{18}O_2S$: C, 63.68; H, 8.02. Found: C, 63.69, H, 8.11.

6-Chloro-3-isopropylidene-8-thiabicyclo[3.2.1]-6-octene 8,8-dioxide (13d): pale yellow solid; mp 115–116 °C; IR (KBr) 1600, 1311, 1192, 1122, 974, 875, 860 cm^{-1}; NMR (200 MHz) δ 1.64 (s, 6 H), 2.73–3.17 (m, 4 H), 3.51 (br s, 1 H), 3.75 (br s, 1 H), 6.26 (d, 1 H, J = 4.5 Hz); Hz); MS, m/z 234 (M^+ + 2), 232 (M^+), 169, 167, 127, 125 (100), 91, 77. Anal. Calcd for $C_{10}H_{13}ClO_2S$: C, 51.61; H, 5.63. Found: C, 51.64; H, 5.64.

1,3,4,5,6,7-Hexahydro-1,3-(2′-isopropylidenepropano)isobenzothiophene 2,2-dioxide (13e): white solid; mp 119–119.5 °C; IR (KBr) 1648, 1293, 1193, 1141, 1090, 777 cm^{-1}; NMR (200 MHz) δ 1.63 (s, 6 H), 1.52–1.87 (m, 4 H), 1.93–2.27 (m, 4 H), 2.75 (d, 2 H, J = 16 Hz), 2.89 (d, 2 H, J = 3.5 Hz), 3.33 (br s, 2 H); MS, m/z 252 (M^+), 188, 187 (100), 173, 105, 91. Anal. Calcd for $C_{14}H_{20}O_2S$: C, 66.63; H, 7.99. Found: C, 66.36; H, 8.00.

Sulfur Dioxide Extrusion Reactions of Bicyclic Sulfones 12 and 13. To a suspension of $LiAlH_4$ (equal amount by weight of the bicyclic sulfone used) in dry THF (10 mL/100 mg of $LiAlH_4$) was added a solution of bicyclic sulfone **12** or **13** in THF. The mixture was heated to 50 °C for 30 min, and the excess of $LiAlH_4$ was destroyed by adding aqueous ether. The resulting solution was dried (Na_2SO_4), filtered, and evaporated under reduced pressure to give essentially pure product **14** or **15**. Yields of the products are listed in Table I.

2,3-Dimethyl-6-methylene-1,3-cycloheptadiene (14a): colorless oil; IR (neat) 1646, 1421, 1371, 1173, 1076, 1064, 880, 866, 780 cm^{-1}; NMR (80 MHz) δ 1.78 (s, 6 H), 2.71 (d, 4 H, J = 6 Hz), 4.51 (s, 2 H), 5.76 (t, 2 H, J = 6 Hz); MS, m/z 134 (M^+), 128, 119 (100), 105, 91, 77.

2-Chloro-6-methylene-1,3-cycloheptadiene (14b): colorless oil; IR (neat) 1647, 1632, 979, 892, 790 cm^{-1}; NMR (80 MHz) δ 2.87 (br s, 1 H), 2.97 (br s, 3 H), 4.67 (s, 2 H), 5.80–6.10 (m, 3 H); MS, m/z 142 (M^+ + 2), 140 (M^+), 105 (100), 79, 77.

6-Methylene-3′,4′,5′,6′-tetrahydro-2,3-benzo-1,3-cycloheptadiene (14c): colorless oil; IR (neat) 1642, 1261, 1096, 877, 818 cm^{-1}; NMR (80 MHz) δ 1.59 (br s, 4 H), 2.20 (br s, 4 H), 2.76 (d, 4 H, J = 6 Hz), 4.51 (s, 2 H), 5.67 (t, 2 H, J = 6 Hz); MS, m/z 160 (M^+), 145, 91 (100), 77.

2-Methyl-6-isopropylidene-1,3-heptadiene (15a): colorless oil; IR (neat) 1613, 1261, 1095, 1020, 861, 805 cm^{-1}; NMR (80 MHz) δ 1.63 (s, 6 H), 1.76 (s, 3 H), 2.74–3.04 (m, 4 H), 5.60–5.91 (m, 3 H); MS, m/z 148 (M^+), 133, 105 (100), 92, 91.

2,3-Dimethyl-6-isopropylidene-1,3-cycloheptadiene (15b): colorless oil; IR (neat) 1685, 1261, 1098, 1022, 810 cm^{-1}; NMR (200 MHz) δ 1.55 (s, 6 H), 1.28 (s, 6 H), 2.63 (d, 4 H, J = 5.5 Hz), 5.67 (t, 2 H, J = 5.5 Hz); MS, m/z 162 (M^+), 147, 119 (100), 105, 91.

2-Chloro-6-isopropylidene-1,3-cycloheptadiene (15c): colorless oil; IR (neat) 1630, 1260, 1105, 1068, 867, 799 cm^{-1}; NMR (80 MHz) δ 1.63 (s, 6 H), 2.72–3.20 (m, 4 H), 5.83–6.21 (m, 3 H); MS, m/z 170 (M^+ + 2), 168 (M^+), 126, 125, 117, 91 (100).

6-Isopropylidene-3′,4′,5′,6′-tetrahydro-2,3-benzo-1,3-cycloheptadiene (15d): Colorless oil; IR (neat) 1654, 1261, 1095, 801 cm^{-1}; NMR (200 MHz) δ 1.54 (br s, 10 H), 2.12 (br s, 4 H), 2.67

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(d, 4 H, J = 6 Hz), 5.59 (t, 2 H, J = 6 Hz); MS, m/z 188 (M^+, 100), 173, 145, 115, 91.

Preparation of 5-Methylene-3′,4′,5′,6′-tetrahydro-1,2-benzo-1,3-cycloheptadiene (16). A solution of compound **12e** in EtOAc (20% by weight) was injected on a GC (injection temperature 220 °C, oven temperature 180 °C, detector temperature 250 °C) with a Carbowax 20M (3-m) column. The chromatogram showed the existence of only one component **16**, which was collected with a dry ice trap: colorless oil; IR (neat) 1611, 1448, 879, 792 cm^{-1}; NMR (80 MHz) δ 1.55 (br s, 4 H), 2.08 (br s, 4 H), 2.14 (d, 2 H, J = 10 Hz), 2.47 (d, 2 H, J = 10 Hz), 4.74 (s, 1 H), 4.85 (s, 1 H), 5.56 (d, 1 H, J = 13 Hz), 6.10 (d, 1 H, J = 13 Hz); MS, m/z 160 (M^+, 100), 145, 131, 117, 91, 77. Anal. Calcd for $C_{12}H_{16}$: C, 89.93; H, 10.07. Found: C, 89.76; H, 10.24.

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Registry No. **5a**, 77-79-2; **5b**, 1193-10-8; **5c**, 18214-56-7; **5d**, 7311-87-7; **5e**, 55370-42-8; **10**, 17616-43-2; **11**, 26430-96-6; **12a**, 110417-28-2; **12b**, 110417-29-3; **12c**, 110417-31-7; **12d**, 110417-31-7; **12e**, 110417-32-8; **13a**, 110417-33-9; **13b**, 110417-34-0; **13c**, 110417-35-1; **13d**, 110417-36-2; **13e**, 110417-37-3; **14a**, 110417-38-4; **14b**, 110417-39-5; **14c**, 110417-40-8; **15a**, 110417-41-9; **15b**, 110417-42-0; **15c**, 110417-43-1; **15d**, 110417-44-2; **16**, 110417-45-3.

Allylic Hydroperoxide Rearrangement: β-Scission or Concerted Pathway?

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The rearrangements of the allylic hydroperoxides derived from oleic acid have been studied. Two hydroperoxides are formed by singlet-oxygen oxidation of oleic acid *trans*-9-hydroperoxyoctadec-10-enoic acid (**5**) and *trans*-10-hydroperoxyoctadec-8-enoic acid (**6**). These hydroperoxides can be separated by reverse-phase chromatography. Rearrangement of ^{18}O-labeled hydroperoxides (**5** or **6**) under a $^{32}O_2$ atmosphere led to no incorporation of ^{16}O into the rearrangement products. Similarly, rearrangement of ^{16}O-labeled hydroperoxides (**5** or **6**) under a $^{36}O_2$ atmosphere led to no incorporation of ^{18}O into the rearrangement products. The hydroperoxide **5** rearranges to a mixture of **5** and *trans*-11-hydroperoxyoctadec-9-enoic acid and alcohols and ketones resulting from Russell termination steps. The results are discussed in terms of a concerted rearrangement of allylic peroxyl radicals proceeding through a five-membered-ring transition state.

Allylic hydroperoxides undergo structural rearrangement. This rearrangement has been known since 1957, when Schenck reported that the tertiary C-5 α-hydroperoxide of cholesterol rearranges to its α-allylic isomer.[1-6] At least three mechanisms for the allylic hydroperoxide rearrangement have been proposed.[7-9] These three mechanisms are outlined in Figure 1 and involve the following. (1) Formation of a cyclic five-membered-ring peroxide with a free radical at position 4 of the ring (see structure **1** of Figure 1). This mechanism amounts to a stepwise reaction pathway with **1** being a true intermediate in the rearrangement. (2) Formation of a cyclic five-membered-ring transition state, **2**, that links the two allylic hydroperoxyl radicals. This mechanism is a concerted mechanism in which **2** is not an authentic reaction intermediate, but rather is a transition state. (3) β-Fragmentation of an allylic peroxyl radical to form molecular oxygen and an allyl carbon radical, **3**, which can recombine with oxygen at either end of the radical to give the starting and rearranged peroxyl radicals. Each of these mechanisms involves intermediate peroxyls, and consistent with this is the fact that free-radical initiators facilitate the reaction and phenolic inhibitors stop the rearrangement.[7,8]

Several experiments have been carried out to determine the mechanism of the allylic hydroperoxide rearrangement. For example, Brill has attempted to trap the proposed radical intermediate, **1** by carrying out the rearrangement under high pressures of O_2 or with allylic systems designed to undergo further molecular rearrangements at the intermediate radical stage.[8] No oxygen entrapment or other evidence for radical intermediate **1** could be presented to support the stepwise mechanism involving a cyclic peroxide radical. Furthermore, when authentic radicals like **1** are generated, they are found to react by addition of molecular oxygen and cyclic peroxide hydroperoxides (OOH at C-4) can be isolated.[9] It thus seems reasonable to rule out further consideration of the stepwise rearrangement mechanism involving intermediate **1**.

The remaining mechanisms could be distinguished by an appropriate experiment involving the use of isotopically labeled oxygen to determine if fragmentation of the peroxyl radical intermediate occurs. Thus, if a β-scission pathway is followed, a rearrangement carried out under $^{36}O_2$ should show incorporation of $^{36}O_2$ into the hydroperoxide products. We report here the results of such a study of the allylic hydroperoxides formed from singlet-oxygen oxidation of oleic acid.

Results

Synthesis and Purification of Allylic Hydroperoxides. Singlet-oxygen oxidation of oleic acid **4** yields only two allylic hydroperoxides. Thus, photolysis of methylene blue photosensitizer and oleic acid in methanol under $^{32}O_2$ gave two hydroperoxide products[10-12] (Figure 2). These

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