anhydride was added and the reaction mixture was heated gently on a steam bath. After cooling the reaction mixture was put in a 25° bath for 0.5 hr before the run was begun. Because of limited solubility of reactants in acetic acid almost all reaction mixtures were heterogeneous.

Analysis of Reaction Mixtures.—All analyses were carried out by vapor phase chromatography using a 6-ft column packed with 20% Carbowax 20M on a 70-80 mesh ABS support. The temperature was programmed from 80 to 200° at a rate of 7.5°/min. The helium flow rate was 60 ml/min. Standards of vinyl acetate and all the saturated products were prepared and used to calculate the concentration of the various products.

Registry No.—Ethylene, 74-85-1; $Pd(OAc)_2$, 3375-31-3; $Tl(OAc)_3$, 2570-63-0; $HAuCl_4$, 16903-35-8; $TlCl_3$, 13453-32-2.

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(+)-Limonene Oxidation with Selenium Dioxide–Hydrogen Peroxide

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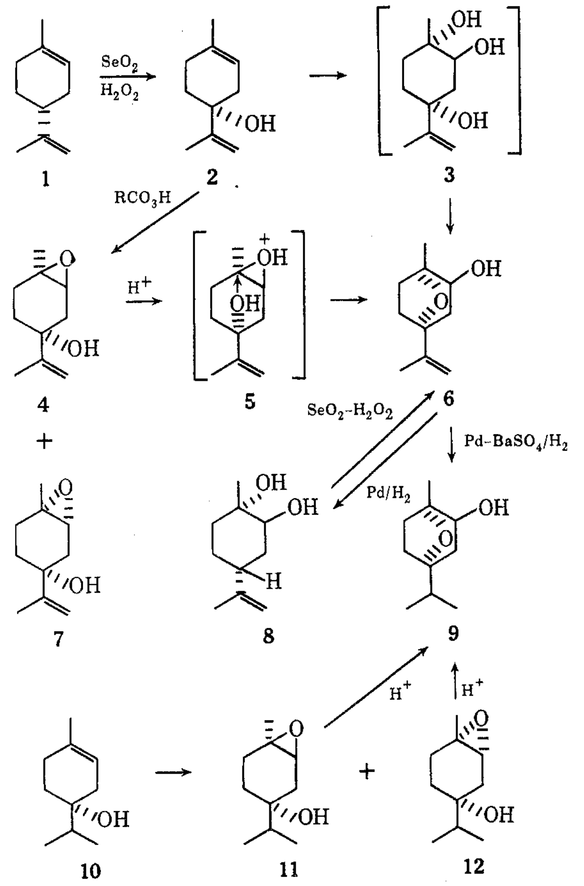
(+)-Limonene oxidation with selenium dioxide–hydrogen peroxide has afforded (+)-1-hydroxyneodihydrocarveol (**8**) as the main product plus (−)-carvone, (−)-*cis*-carveol, (−)-*trans*-carveol, (−)-1,8-*p*-menthadien-4-ol (**2**), and three other alcohols. One of the alcohols, (−)-1,4-epoxyneoisodihydrocarveol (**6**), is a new compound whose structure was determined and whose mechanism for formation was explored. (−)-1,8-*p*-Menthadien-4-ol (**2**) was oxidized with *m*-chloroperbenzoic acid to produce the previously unreported (−)-4-hydroxy-*trans*-8-*p*-menthene oxide (**4**), and (−)-4-hydroxy-*cis*-8-*p*-menthene oxide (**7**). The trans oxide **4**, but not the cis isomer **7**, was converted to **6** with acetic acid. Terpinen-4-ol (**10**) was similarly oxidized with peracid, and both the cis and trans isomers (**11** and **12**) afforded a 1,4-epoxide (**9**) upon treatment with dilute sulfuric acid.

Selenium dioxide oxidation of (+)-limonene has been studied by several workers,[2a-d] and the products identified involved oxidation at all allylic positions except carbon-3 (menthol series). Most of these oxidation products are constituents of natural products such as citrus essential oils,[2e] of which (+)-limonene is the major constituent. As part of a program to explore conversion of (+)-limonene to more valuable fine chemicals, we studied (+)-limonene oxidation with hydrogen peroxide and only a catalytic amount of selenium dioxide.[3] Among the oxidation products was a new 1,4-epoxide derivative (**6** in Scheme I) whose structure was determined and whose mechanism for formation was explored.

Table I lists the products identified from selenium dioxide–hydrogen peroxide oxidation of (+)-limonene under four sets of reaction conditions. Increasing the proportion of oxidizing agents increased the yield of most products (reaction 2). Decreasing the catalytic amount of selenium dioxide (reaction 3) decreased the percentage of all oxidation products except (−)-*cis*-carveol, (+)-1-hydroxyneodihydrocarveol (**8**), and 1,8-*p*-menthadien-7-ol. Stopping the reaction at the end of the initial exothermic period (reaction 4) resulted in decreased yield of all oxidation products. For most products yield was best with high proportions of oxidizing agents and a long reaction time (reaction 2).

One of the main oxidation products of this reaction is a previously unreported compound, (−)-1,4-epoxyneoisodihydrocarveol[4] (**6** in Scheme I). The ir spectrum suggested that this compound contained either two hydroxyl groups or one hydroxyl group and an ether linkage [1045 (C–OH), 1118 cm^{-1} (C–O–C or *t*-OH)].[5] A high-resolution mass spectrum showed the empirical formula to be $C_{10}H_{16}O_2$. The low-resolution mass spectrum showed a major fragment due to loss of one water molecule (M − 18), but a second molecule

SCHEME I



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[1] One of the laboratories of the Southern Region, Agricultural Research Service, U. S. Department of Agriculture. References to specific commercial products do not constitute endorsement.

[2] (a) J. Verghese, *Perfum. Essent. Oil Rec.*, 876 (1968); (b) Y. Sakuda, *Bull. Chem. Soc. Jap.*, **42**, 3348 (1969); (c) A. F. Thomas and W. Bucher, *Helv. Chim. Acta*, **53**, 770 (1970); (d) E. N. Trachtenberg and J. R. Carver, *J. Org. Chem.*, **35**, 1646 (1970); (e) G. L. K. Hunter and M. G. Moshonas, *J. Food Sci.*, **31**, 167 (1966).

[3] M. Fieser and L. Fieser, "Reagents for Organic Synthesis," Vol. 2, Wiley, New York, N. Y., 1969, p 362.

[4] See E. E. Royals and J. C. Leffingwell, *J. Org. Chem.*, **31**, 1937 (1966), for nomenclature.

[5] R. N. Jones, "National Research Council Bulletin," No. 6, Ottawa, Canada.

TABLE I

PRODUCTS FROM D-LIMONENE OXIDATION WITH SeO_2–H_2O_2

	Compd	Glc peak area %			
		1[a]	2[b]	3[c]	4[d]
1	(+)-Limonene	68.7	47.1	74.6	92.4
2	(−)-Carvone	1.4	3.7	0.8	0.2
3	(−)-*trans*-Carveol	4.2	3.1	1.9	0.4
4	(−)-*cis*-Carveol	0.9	2.0	0.9	0.2
5	(−)-1,4-Epoxyneoisodihydrocarveol (**6**)	1.8	4.5	0.8	0.2
6	(+)-1-Hydroxyneodihydrocarveol (**8**)	10.2	22.1	13.7	4.2
7	(−)-1,8-*p*-Menthadien-4-ol (**2**)	6.2	9.3	2.7	0.8
8	1,8-*p*-Menthadien-7-ol	0.8	2.6	1.1	0.3
9	1,8-*p*-Menthadien-10-ol	4.5	3.2	2.7	0.5
10	α,*p*-Dimethylstyrene	Tr	0.2	0.5	0.2
11	Hydrocarbon (unidentified)	0.9	1.7	0.5	0.2

[a] Reaction conditions: 32 mmol SeO_2, 0.66 mol H_2O_2, 0.6 mol (+)-limonene, 4 hr. [b] 32 mmol SeO_2, 0.66 mol H_2O_2, 0.3 mol (+)-limonene, 4 hr. [c] 16 mmol SeO_2, 0.66 mol H_2O_2, 0.6 mol (+)-limonene, 4 hr. [d] 32 mmol SeO_2, 0.66 mol H_2O_2, 0.6 mol (+)-limonene, 20 min.

of water was not lost as is the case with the 1,2 diol **8**.[6] The nmr spectrum in dimethyl sulfoxide-d_6 showed two methyl singlets at δ 1.30 and 1.70 ppm assigned to the tertiary methyl and terminal allylic methyl groups, respectively, a one-proton multiplet centered at 3.5 ppm assigned to the carbon at position 2 bearing the hydroxyl group, and two one-proton singlets at 4.70 and 4.85 ppm asigned to the vinyl hydrogens on the terminal double bond. The hydroxyl hydrogen appeared as a one-proton doublet at 4.99 ppm. Upon addition of a trace of sulfuric acid, this doublet collapsed to a singlet appearing at 5.8 ppm.[7] Reduction of **6** with hydrogen and a 10% palladium on carbon catalyst afforded **8**, formed by hydrogenolysis of the allylic carbon–oxygen bond at C-4. Surprisingly, the double bond was not reduced under these conditions. Reduction of **6** with hydrogen and 5% palladium on barium sulfate afforded the known saturated derivative 1,4-epoxyneoisocarvomenthol (**9**), which was also prepared from terpinen-4-ol (**10**) by a procedure similar to that previously described.[8]

Possible pathways for formation of **6** from (+)-limonene have been explored. The main product of selenium dioxide–hydrogen peroxide oxidation of (+)-limonene, (+)-1-hydroxyneodihydrocarveol (**8**), was oxidized to **6** under the same conditions used to obtain **6** from (+)-limonene. An intermediate, 1,4-dihydroxyneoisodihydrocarveol (**3**), probably formed in this reaction, can then be dehydrated to **6** just as in the formation of 1,4-cineole from 1,4-dihydroxy-*p*-menthane.[9] Chromium trioxide–pyridine oxidation of **8** also afforded **6**.

An alternate pathway for formation of **6** from (+)-limonene involves initial oxidation at C-4 to afford 1,8-*p*-menthadien-4-ol (**2**). Treatment of **2** with selenium dioxide and hydrogen peroxide did yield **6** in addition to the major product α,*p*-dimethylstyrene. Since selenium dioxide–hydrogen peroxide can oxidize an olefin to the corresponding 1,2 diol,[10] **3** is a possible intermediate in the formation of **6** from **2**. An intermediate 1,2 epoxide has been implicated in 1,2-diol formation from an olefin in this oxidation reaction.[10] Thus, **6** also can be obtained from **2** through a 1,2-epoxy-4-ol, *e.g.*, **4**.

Limonene 1,2-epoxide (1:1 mixture of cis and trans isomers)[11] is another possible intermediate in the oxidation of limonene to 1,4 epoxide **6**. Treatment of limonene 1,2-epoxide with selenium dioxide–hydrogen peroxide afforded **6** in small yield with **8** being the major product. In the conversion of limonene 1,2-epoxide to **6**, 4-hydroxy-8-*p*-menthene oxide is a likely intermediate. We prepared the previously unreported cis and trans isomers, **7** and **4**, respectively, of this suggested intermediate by epoxidation of the endocyclic double bond in **2** with peracid. The trans isomer **4** was readily converted to **6** upon treatment with acetic acid, but the cis isomer **7** decomposed under the same conditions and no starting material or **6** could be separated from the reaction mixture by gc. A concerted acid-catalyzed 1,2-epoxide opening and 1,4-epoxide formation, as illustrated in intermediate **5**, is sterically favorable in the trans isomer (**4**), but not in the cis isomer (**7**). If the peracid oxidation of **2** was allowed to stand for a longer time, only cis isomer **7** and 1,4 epoxide **6** were isolated, apparently because enough acid was present in the reaction mixture to convert the trans epoxide to **6**. Structures of **4** and **7** were assigned on the basis of the conversion of **4** to 1,4 epoxide **6**, on the relative gc retention times as compared to the saturated analogs,[12] and on the fact that the cis isomer **7** was reduced with palladium and hydrogen to 4-hydroxycarvomenthol.[12]

Of the three discussed pathways for formation of **6** from (+)-limonene, that involving initial oxidation to **8** seems the most probable. Thus, **8** is the major reaction product in all cases in Table I. The ratio of a secondary reaction product to a primary product should increase with time, and in (+)-limonene oxidation the ratio of secondary product **6** to primary product **8** shows a greater increase with time (**6**:**8** = 0.05 in run 4 and 0.18 in run 1 of Table I) than does that of **6** to primary product **2** (**6**:**2** = 0.25 in run 4 and 0.30 in run 1). Limonene 1,2-epoxide is the least likely intermediate considered because none was found among the products even under the shortest reaction time used (run 4); epoxidation of olefins with selenium dioxide and hydrogen peroxide has been reported, however.[13]

Oxidation of (+)-limonene to (−)-carvone and (−)-*cis*- and (−)-*trans*-carveols in this study indicates attack primarily at the 1,2 double bond[4] rather than allylic oxidation at C-6[14] to form these oxidation products. The (−)-*cis*- and (−)-*trans*-carveols are probably not intermediates in (−)-carvone formation, since the latter is of higher optical purity. Furthermore, the ratio of carvone to carveols does not increase with time (carvone:carveols = 0.33 in run 4 and 0.28

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[6] G. L. K. Hunter and M. G. Moshonas, *Anal. Chem.*, **37**, 378 (1965).

[7] O. L. Chapman and R. W. King, *J. Amer. Chem. Soc.*, **86**, 1256 (1964).

[8] P. Garside, T. G. Halsall, and G. M. Hornby, *J. Chem. Soc. C*, 716 (1969).

[9] J. L. Simonsen, "The Terpenes," Vol. 1, University Press, Cambridge, England, 1953, p 304.

[10] W. Sonoda and S. Tsutsumi, *Bull. Chem. Soc. Jap.*, **38**, 958 (1965).

[11] See Royals and Leffingwell,[4] footnote 49.

[12] G. Ohloff and G. Uhde, *Helv. Chim. Acta*, **48**, 10 (1965).

[13] J. Itakura, H. Tanaka, H. Ito, and T. Matsubara, Japanese Patent 19,894 (1970); *Chem. Abstr.*, **73**, 109375*j* (1970).

[14] A. Blumann and O. Zeitschel, *Chem. Ber.*, **46**, 1178 (1913); H. E. Eschnazi, *Israel Res. Council Bull.*, 109 (1951).

in run 1 of Table I) as should be the case if the carveols were intermediates in carvone formation.

A comparison sample of 1,4-epoxyneoisocarvomenthol (**9**) was prepared by epoxidation of terpinen-4-ol (**10**) to 4-hydroxy-*trans*-carvomenthane epoxide (**11**) and 4-hydroxy-*cis*-carvomenthane epoxide (**12**) followed by acid-catalyzed epoxide opening of either **11** or **12** to **9**. Garside, *et al.*,[8] who prepared **9** from **10** by peracid oxidation, had proposed **11** as an intermediate in their reaction, but had not isolated it. We epoxidized **10** with *m*-chloroperbenzoic acid and isolated **11** and **12**,[12] both of which rearranged to **9** upon treatment with 0.1 *N* sulfuric acid. However, only the trans isomer (**11**) cleanly afforded **9**, while the cis isomer (**12**) also produced significant quantities of *p*-cymene and carvenone. The structures of **11** and **12** were confirmed by lithium aluminum hydride reduction of **11** to *trans-p*-menthane-1,4-diol as previously reported,[12] and the cis epoxide to 4-hydroxycarvomenthol[12] plus a small amount of *cis-p*-menthane-1,4-diol. The 4-hydroxycarvomenthol, thus prepared, was identical with that obtained by catalytic reduction of **7** described above.

Absolute configurations of the compounds, as shown in Scheme I, were determined by comparison of **8** and terpinen-4-ol (**10**) isolated in this study with previously reported samples of known configuration. Compound **8**, having mp 66.5–67.5° and $[\alpha]\mathrm{D}$ +41°, was the isomer previously obtained from peracid oxidation of (+)-limonene and has the 1*S*,2*S*,4*R* configuration.[15] Catalytic reduction of 1,8-*p*-menthadien-4-ol (**2**) afforded (4*R*)-terpinen-4-ol with $[\alpha]\mathrm{D}$ −36° of established configuration (reported $[\alpha]\mathrm{D}$ −34°).[12] The 1,8-*p*-menthadien-4-ol (**2**) obtained from this selenium dioxide and hydrogen peroxide oxidation reaction had $[\alpha]\mathrm{D}$ −43°, whereas the 1,8-*p*-menthadien-4-ol obtained previously from selenium dioxide oxidation of (+)-limonene either was optically inactive[2b,c] or slightly dextrorotatory.[2d] Presently accepted mechanisms for selenium dioxide oxidation of olefins to allylic alcohols[16] do not explain this formation of optically active 1,8-*p*-menthadien-4-ol (**2**) from (+)-limonene, because the proposed intermediate contains a 4,8 double bond, and should be attacked equally from either side of the molecule at C-4 to produce racemic 1,8-*p*-menthadien-4-ol.[2c] In the present case, stereospecific hydrogen removal and oxygen addition with inversion at C-4 must take place without racemization.

Experimental Section

Infrared spectra were obtained on thin liquid films with a Perkin-Elmer Infracord. Nuclear magnetic resonance spectra were obtained with a Varian A-60 spectrometer on samples dissolved in deuteriochloroform or dimethyl-d_6 sulfoxide containing tetramethylsilane as internal standard. Optical rotations were determined on absolute ethanol solutions with a Rudolph Model 62 polarimeter. Low-resolution mass spectra were determined at 70 eV with a Bendix Model 3012 Time-of-Flight mass spectrometer, and high-resolution mass spectra with an A. E. I. Picker ultrahigh-resolution mass spectrometer. Melting points were determined between glass plates on a Nalge block type melting point apparatus and are uncorrected.

Gas chromatographic analyses and separations were performed on F & M Model 500 and 700 gas chromatographs equipped with 0.20 in. i.d. × 20 ft stainless steel columns packed with 20% Carbowax 20M on 60/80 mesh Gas-Chrom P and using thermal conductivity detectors. Temperature programming was from 100 to 220° at 1°/min at a He flow rate of 100 ml/min and an injection port temperature of 245°. Peak areas were determined as height times width at half-height. When reaction product percentages are listed, they were determined by integrating the gc curve for the crude reaction mixture.

(+)-Limonene was obtained from distillation of Valencia orange essence oil,[17] bp 45–50° (1.5 mm), $[\alpha]^{29}\mathrm{D}$ +116.5° (*c* 1.24), and was shown to be greater than 99% pure by gc.

Selenium Dioxide–Hydrogen Peroxide Oxidation of (+)-Limonene.—Selenium dioxide (3.6 g, 32.4 mmol) and 75 g (0.66 mol) of 30% hydrogen peroxide were added to a stirred solution of 80 g (0.6 mol) of (+)-limonene in 100 ml of tetrahydrofuran (THF). The mixture was heated until a vigorous exothermic reaction ensued. After 10 min, the exothermic reaction began to subside and the mixture was heated to reflux. Three separate oxidations (see footnotes to Table I), varying the molar quantities of reagents, were conducted in this manner. A fourth reaction was also carried out in which the initial exothermic reaction was allowed to subside (20 min) and the mixture was not heated further.

In each case, the reaction products were isolated by removing the THF solvent at 30° and water pump pressure on a rotary evaporator (Buchi Rotavapor R, Type KRV 65/45) and the bulk of the (+)-limonene was then removed in the same apparatus at 40° and 1 mm pressure. Portions of the residual liquid were subjected to gc to separate individual products for identification. Carvone, $[\alpha]^{29}\mathrm{D}$ −54.5° (*c* 0.67), *cis*-carveol, $[\alpha]^{29}\mathrm{D}$ −12.8° (*c* 1.56), *trans*-carveol, $[\alpha]^{29}\mathrm{D}$ −90° (*c* 1.11), 1,8-*p*-menthadien-10-ol, and 1-hydroxyneodihydrocarveol [mp 66.5–67.5° and $[\alpha]^{29}\mathrm{D}$ +41.0° (*c* 1.86) after two crystallizations of a gc-purified sample from benzene–hexane[15b]] were all identified by comparison of their infrared spectra with those from authentic samples obtained previously at our laboratories.[2,17] Authentic samples of α,*p*-dimethylstyrene and 1,8-*p*-menthadien-7-ol were obtained from commercial sources. Quantitative estimates as listed in Table I have been corrected to include the limonene removed by distillation.

The ir, nmr, and mass spectra of 1,8-*p*-menthadien-4-ol (**2**) were identical with those already reported.[18] Both compounds **2** and **6** could be isolated in >90% purity by distillation of the residue after removing the bulk of the (+)-limonene: (−)-1,8-*p*-menthadien-4-ol (**2**), bp 34–36° (0.1 mm), gc purified sample showed $[\alpha]^{29}\mathrm{D}$ −43.0° (*c* 1.24); (−)-1,4-epoxyneoisodihydrocarveol (**6**), bp 58–65° (0.1 mm), gc-purified sample showed $[\alpha]^{29}\mathrm{D}$ −89.2° (*c* 1.35); ir 3490 (s), 2995 (s), 1650 (s), 1450 (s), 1380 (s), 1320 (w), 1270 (w), 1235 (w), 1220 (sh), 1200 (w), 1180 (w), 1118 (s), 1100 (sh), 1045 (s), 1035 (sh), 1010 (w), 985–975 (m, split), 950 (m), 900 (m), 875 (m), 815 (w), 755 $\mathrm{cm^{-1}}$ (w); mass spectrum *m/e* (rel intensity) 168 (9), 150 (14), 124 (11), 107 (26), 97 (11), 95 (20), 92 (14), 84 (20), 82 (12), 81 (13), 69 (30), 67 (11), 58 (13), 55 (16), 43 (100), 41 (40); high resolution *m/e* 168.1148 (calcd for $C_{10}H_{16}O_2$, 168.1149); nmr (Me_2SO-d_6) δ 1.30 (s, 3, *t*-CH_3), 1.70 (s, 3, $=CCH_3$), 3.50 (m, 1, CHOR), 4.70 and 4.85 (s, 2, $C=CH_2$), 4.99 (d, 1, J = 4 Hz, OH); the latter, with a trace H_2SO_4 added, shifted to δ 5.87 (s).[7] The monoacetate derivative of **6** was prepared with acetic anhydride and pyridine: ir 1730, 1240 $\mathrm{cm^{-1}}$ (-$COOCH_3$); mass spectrum *m/e* (rel intensity) 210 (3), 168 (3), 151 (9), 150 (8), 135 (6), 107 (10), 92 (8), 84 (8), 69 (17), 58 (3), 55 (7), 43 (100).

Oxidation of Limonene 1,2-Epoxide to 6.—To 80 g (0.52 mol) of limonene 1,2-epoxide[11] (FMC Corp., New York, N. Y.) in 100 ml of THF were added 0.66 mol of 30% hydrogen peroxide and 32 mmol of selenium dioxide following the above procedure (4-hr reflux) for (+)-limonene oxidation. Gc separation of the crude reaction mixture after removal of solvent afforded limonene 1,2-epoxide (6%), 1,4-epoxyneoisodihydrocarveol (**6**) (8%), and 1-hydroxyneodihydrocarveol (**8**) (86%) based on relative gc peak areas.

Oxidation of 1,8-*p*-Menthadien-4-ol (2) to 6.—To 0.90 g (6.0 mmol) of **2** in 50 ml of THF were added 4.0 mmol of 30% hydro-

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(15) (a) H. Schmidt, *Chem. Ber.*, **82**, 11 (1949); (b) W. F. Newhall, *J. Org. Chem.*, **29**, 185 (1964).

(16) J. P. Schaefer, B. Horvath, and H. P. Klein, *J. Org. Chem.*, **33**, 2647 (1968); E. N. Trachtenberg, C. H. Nelson, and J. R. Carver, *ibid.*, **35**, 1653 (1970); K. B. Sharpless and R. F. Lauer, *J. Amer. Chem. Soc.*, **94**, 7154 (1972).

(17) R. L. Coleman and P. E. Shaw, *J. Agr. Food Chem.*, **19**, 520 (1971).

(18) H. E. Eschinasi, *Israel J. Chem.*, **6**, 713 (1968); T. Sakai, K. Yoshihara, and Y. Hirose, *Bull. Chem. Soc. Jap.*, **41**, 1945 (1968); S. Kusumoto, A. Ohsuka, and M. Kotake, *ibid.*, **41**, 1950 (1968).

gen peroxide and 2.7 mmol of selenium dioxide following the above procedure for (+)-limonene oxidation. Gc separation of the crude reaction mixture after removal of solvent yielded 7% *p*-cymene, 56% *α*,*p*-dimethylstyrene, 17% starting material (**2**), and 20% 1,4-epoxyneoisodihydrocarveol (**6**).

Oxidation of (+)-1-Hydroxyneodihydrocarveol (8) to (−)-1,4-Epoxyneoisodihydrocarveol (6). A. With Selenium Dioxide–Hydrogen Peroxide.—To 3.0 g (17.4 mmol) of **8** in 50 ml of methylene chloride were added 8.0 mmol of 30% hydrogen peroxide and 1.4 mmol of selenium dioxide following the procedure for (+)-limonene oxidation. Gc separation of the crude reaction mixture after separation of the layers and removal of methylene chloride afforded a 9:1 mixture of starting material **8** and (−)-1,4-epoxyneoisodihydrocarveol (**6**), $[\alpha]^{29}\mathrm{D}$ −91.8° (*c* 0.98).

B. With Chromium Trioxide–Pyridine.—To 20 mg of **8** in 25 *μ*l of pyridine was added 500 *μ*l of a 10% solution of the CrO_3–pyridine complex[19] in methylene chloride, and the reaction mixture was kept for 18 hr at room temperature. The solution was decanted from a brown precipitate that had formed during the reaction, the solvent was removed under N_2 at 35°, and the residue was separated by gc to afford a 2:3 mixture of **6** and starting material **8**.

Peracid Oxidation of 1,8-*p*-Menthadien-4-ol (2).—To 0.8 g (5.2 mmol) of **2** in 10 ml of methylene chloride cooled in an ice bath were added 0.9 g (5.2 mmol) of *m*-chloroperbenzoic acid (K & K Laboratories, Inc., Plainview, N. Y.) in 10 ml of methylene chloride followed by 25 ml of saturated aqueous sodium carbonate solution. The reaction mixture was kept in the ice bath and stirred for 4 hr, the layers were separated, and the organic layer was concentrated under N_2. Separation of the residue by gc afforded 12% starting material (**2**) and 67% (−)-4-hydroxy-*cis*-8-*p*-menthene oxide (**7**): $[\alpha]^{29}\mathrm{D}$ −81.2° (*c* 1.23); ir 3600 (s), 3050 (s), 1655 (m), 1450 (s), 1420 (w), 1380 (m), 1360 (w), 1340 (m), 1305 (w), 1265 (w), 1240 (m), 1225 (w), 1215 (w), 1200 (w), 1140 (w), 1130 (w), 1115 (m), 1095 (m), 1090 (m), 1085 (m), 1060 (s), 1135 (m), 1120 (m), 1005 (w), 985 (m), 970 (w), 905 (s), 855 (s), 840 (s), 775 cm^{-1} (s); mass spectrum *m/e* (rel intensity) 168 (21), 107 (10), 97 (11), 95 (11), 84 (29), 83 (19), 82 (7), 81 (14), 71 (19), 69 (82), 55 (40), 44 (64), 43 (100), 41 (81); high resolution *m/e* 168.1149 (calcd for $C_{10}H_{16}O_2$, 168.1149); nmr ($CDCl_3$) δ 1.35 (s, 3, *t*-CH_3), 1.78 (s, 3, $=CCH_3$), 3.2 (m, 1, CHOR), 4.90 and 5.02 (2 singlets, 2, $C=CH_2$); and 17% (−)-4-hydroxy-*trans*-8-*p*-menthene oxide (**4**): $[\alpha]^{29}\mathrm{D}$ −88.4° (*c* 1.13); ir 3450 (s), 2950 (s), 1645 (m), 1440 (s), 1420 (m), 1380 (m), 1360 (m), 1305 (m), 1260 (m), 1230 (w), 1215 (s), 1118 (m), 1090 (m), 1060 (s), 1040 (m), 1018 (m), 1005 (w), 975 (m), 950 (m), 905 (s), 845 (s,) 785 (m), 718 cm^{-1} (m); mass spectrum *m/e* (rel intensity) 168 (2), 153 (2), 150 (3), 110 (9), 107 (14), 97 (8), 95 (12), 84 (16), 83 (11), 82 (12), 81 (9), 71 (11), 69 (26), 67 (12), 58 (11), 55 (20), 53 (9), 44 (19), 43 (100), 41 (49), 39 (28); high resolution *m/e* 168.1143 (calcd for $C_{10}H_{16}O_2$, 168.1149); nmr ($CDCl_3$) δ 1.27 (s, 3, *t*-CH_3), 1.67 (s, 3, $=CCH_3$), 2.92 (m, 1, CHOR), 4.80 and 4.94 (singlets, 2, $C=CH_2$).

When the peracid reaction mixture was removed from the ice bath after 4 hr, allowed to stir at room temperature 20 hr longer, and worked up as described above, the products isolated by gc were about equal quantities of **7** and 1,4-epoxyneoisodihydrocarveol (**6**).

Rearrangement of 4-Hydroxy-*trans*-8-*p*-menthene Oxide (4) to 6.—When 4 *μ*l of **4** was treated with 20 *μ*l of 9:1 acetic acid–water and in 5 min injected onto the gc column, a 2:1 mixture of starting material **4** and **6** was obtained. When 4-hydroxy-*cis*-8-*p*-menthene oxide (**7**) was treated under the same conditions, no starting material, or **6**, or other gc-volatile products could be isolated.

Reduction of 1,4-Epoxyneoisodihydrocarveol (6) to 8.—To 50 *μ*l of **6** in 0.5 ml of absolute EtOH was added 50 mg of 10% Pd/C and the mixture was shaken at 50 psi hydrogen for 24 hr in a Parr hydrogenation apparatus. The catalyst was removed by filtration, the filtrate was concentrated to small volume, and the residue was separated by gc to afford **8**, $[\alpha]^{29}\mathrm{D}$ +39.5° (*c* 1.32), as the only product isolated, which was identified by ir comparison with an authentic sample.[2e]

Reduction of 7 to 4-Hydroxycarvomenthol.—Catalytic reduction of **7** with 10% Pd/C by the above procedure afforded, by gc separation, 4-hydroxycarvomenthol (identified by ir comparison to the authentic sample prepared below by $LiAlH_4$ reduction of **11**), and *cis*- and *trans*-*p*-menthan-4-ol, which were identified by comparison of their ir spectra to published spectra for these two alcohols.[20]

Reduction of 6 to 1,4-Epoxyneoisocarvomenthol (9).—When hydrogenation of **6** was carried out as described above except that 5% Pd on $BaSO_4$ catalyst was used, the product isolated by gc was identified as **9** by comparison of its ir and mass spectra to those of an authentic sample prepared as described below.

Preparation of (−)-1,4-Epoxyneoisocarvomenthol (9) from Terpinen-4-ol (10).—Epoxidation of **10** with 1 equiv of *m*-chloroperbenzoic acid by the above described procedure for peracid oxidation of **2** afforded, by gc analysis, 26% starting material, 62% 4-hydroxy-*cis*-carvomenthene epoxide (**12**), and 12% 4-hydroxy-*trans*-carvomenthene epoxide (**11**). The relative retention times and mass spectra matched those reported for these two epoxides.[12]

The cis epoxide **12** (shorter gc retention time) was reduced with $LiAlH_4$ as described previously[12] to afford, by gc separation, 4-hydroxycarvomenthol whose mass spectrum was identical with that published for this compound,[12] and a trace of *cis*-*p*-menthane-1,4-diol, mp 116–117.5°, whose ir and mass spectra were identical with those of an authentic sample prepared as described previously from ascaridole.[21] The trans epoxide **11** (longer gc retention time) was reduced with $LiAlH_4$, as described previously, to *trans*-*p*-menthane-1,4-diol,[12] whose ir spectrum was identical with that of a comparison sample prepared below.

The comparison sample was prepared by adding to 0.5 g of **10** a mixture of 1.0 g of $Hg(OAc)_2$ in 30 ml of water and 30 ml of THF, and after 10 min, 30 ml of 3 *N* NaOH and 30 ml of 0.5 *M* $NaBH_4$ in 3 *N* NaOH were added.[22] The reaction mixture was filtered, the filtrate was saturated with NaCl, the layers were separated, the upper organic layer was concentrated to dryness, and the crystalline residue was recrystallized three times from hexane to yield *trans*-*p*-menthane 1,4-diol, mp 135–136.5°.

After treatment of *ca.* 10 *μ*l of 4-hydroxy-*trans*-carvomenthane epoxide (**11**) with 100 *μ*l of THF and 50 *μ*l of 0.1 *N* H_2SO_4 for 5 min and injection of the mixture onto the gc the only product isolated was **9** $[\alpha]^{29}\mathrm{D}$ −76.2° (*c* 1.35).[8] Similar treatment of 4-hydroxy-*cis*-carvomenthene epoxide (**12**) afforded a smaller quantity of **9** with significant amounts of *p*-cymene and carvenone also identified. Carvenone was identified by ir comparison with that of an authentic sample,[23] and the *p*-cymene by ir and mass spectral comparison with that of a sample purchased commercially.

Reduction of 1,8-*p*-Menthadien-4-ol (2) to Terpinen-4-ol (10).[24]—A 500-*μ*l sample of **2**, bp 34–36° (0.1 mm), in 1 ml of absolute ethanol was shaken with 10% Pd on carbon under 60 psi hydrogen for 4 hr in a Parr hydrogenation apparatus. The catalyst was allowed to settle and portions of the solution were separated by gc to afford terpinen-4-ol (**10**), $[\alpha]^{29}\mathrm{D}$ −36° (*c* 1.44), as the main product with some starting material and *p*-menthan-4-ol also identified.

Registry No.—**1**, 5989-27-5; **2**, 38630-70-5; **4**, 38630-71-6; **6**, 38630-72-7; **6** monoacetate, 38630-73-8; **7**, 38630-74-9; **8**, 38630-75-0; **9**, 38630-76-1; **10**, 20126-76-5; SeO_2, 7446-08-4; H_2O_2, 7722-84-1; (−)-carvone, 6485-40-1; (−)-*cis*-carveol, 2102-59-2; (−)-*trans*-carveol, 2102-58-1; 1,8-*p*-menthadien-10-ol, 3269-90-7.

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[19] J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).

[20] B. M. Mitzner, V. J. Mancini, S. Lemberg, and E. T. Theimer, *Appl. Spectrosc.*, **22**, 34 (1968).

[21] O. Wallach, *Justus Liebigs Ann. Chem.*, **392**, 59 (1912).

[22] H. C. Brown and P. Geoghegan, Jr., *J. Amer. Chem. Soc.*, **89**, 1522 (1967).

[23] Kindly furnished by Dr. Ross Sheldon, Glidden-Durkee Co., Jacksonville, Fla.

[24] J. C. Leffingwell, U. S. Patent 3,609,197 (Sept 28, 1971).