30:70 ratio of (*E*)-**7** and (*Z*)-**7**.

Reaction of 5 with Bromine at Room Temperature. In a dry NMR tube was placed via syringe 0.50 ml of a 2.0 M solution of **5** in CCl_4 (*E*/*Z* ratio of 85:15). To this solution was added via syringe 0.50 ml of a 2.0 M solution of Br_2 in CCl_4. The Br_2 color disappeared immediately. Analysis of the reaction mixture by NMR immediately after reaction showed that a 74:26 ratio of (*E*)-**7** and (*Z*)-**7**, respectively, were formed and all starting material was consumed.

Similarly, a 50:50 mixture of (*E*)-**5** and (*Z*)-**5** gave a 70:30 ratio of (*E*)-**7** and (*Z*)-**7**, respectively.

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Registry No.—(*E*)-**1**, 52516-83-3; (*Z*)-**1**, 52516-84-4; (*E*)-**2**, 40726-02-1; (*Z*)-**2**, 40726-01-0; (*E*)-**3**, 53477-23-9; (*Z*)-**3**, 53477-24-0; (*E*)-**4**, 35741-84-5; (*Z*)-**4**, 35741-83-4; (*E*)-**5**, 58241-19-3; (*Z*)-**5**, 58241-20-6; (*E*)-**6**, 58241-21-7; (*Z*)-**6**, 58241-22-8; (*E*)-**7**, 58241-23-9; (*Z*)-**7**, 58241-24-0; 1,2-dibromoethane, 106-93-4; (3-chlorobutyl)dichloromethylsilane, 18145-84-1; *p*-bromoanisole, 104-92-7; 4-bromotoluene, 106-38-7; HF, 7664-39-3; carbon tetrachloride, 56-23-5; CBr_3H, 75-25-2; bromine, 7726-95-6; bromo(3-bromobutyl)methyl(*p*-tolyl)silane, 58241-25-1; bromo(3-bromo-1-methylpropyl)methyl(*p*-tolyl)silane, 58241-26-2.

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Stereospecific Synthesis of 6,*c*-10-Dimethyl(*r*-5-*C*¹)spiro[4.5]dec-6-en-2-one and Its Conversion into (±)-α-Vetispirene[1]

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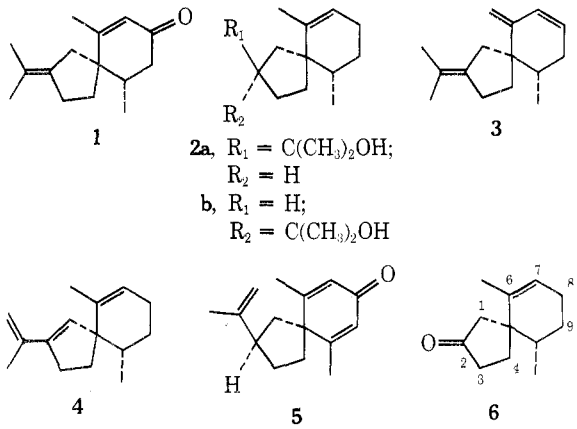
A stereospecific synthesis of the spiro enone **6** and its conversion into (±)-α-vetispirene is described. The photochemical rearrangement of the methoxy dienone **7** was employed as a key step to establish the spiro[4.5]decane ring system.

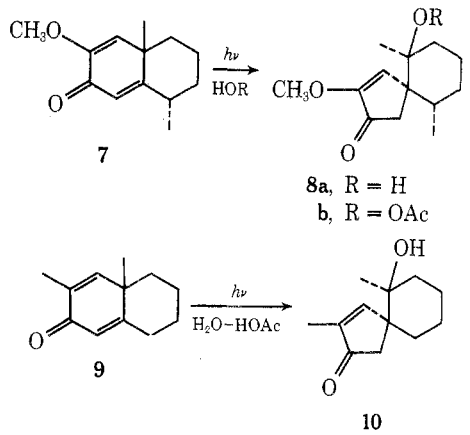
Interest in the synthesis of spirovetivane sesquiterpenes has been aroused since Marshall and co-workers reported that β-vetivone is a member of this group rather than a hydroazulene derivative as originally reported.[2] Recently, total syntheses of (±)-β-vetivone (**1**),[2c,3a-e] (−)-β-vetivone,[3f] (±)-hinesol (**2a**),[3e,4a] (±)-agarospirol (**2b**),[5] (−)-agarospirol,[3f] (±)-β-vetispirene (**3**),[3e,4b,6] and (±)-α-vetispirene (**4**)[3e,4b] have been reported.[7] In addition, relay syntheses of anhydro-β-rotunol (**5**)[8] from β-rotunol[9] and from nootkatone[10] have appeared. Several general approaches to the spiro[4.5]decane ring skeleton of these compounds also have been published.[11]

An attractive approach to various spirovetivane sesquiterpenes appeared to involve the synthesis of the spiro[4.5]dec-6-en-2-one **6** having the carbonyl group in the five-

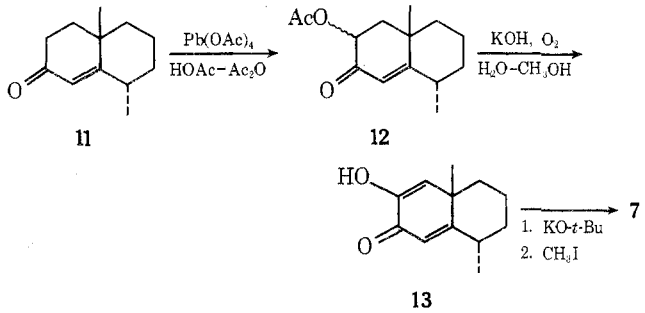
membered ring in the proper position for introduction of an appropriate three-carbon side chain. In this paper we report the stereospecific synthesis of 6[12] and its ready conversion into (±)-α-vetispirene (4).[13]



The route to 6 involved photochemical rearrangement of the 2-methoxy cross-conjugated cyclohexadienone 7 as a means of establishing the spiro[4.5]decane system. Kropp has shown that the 2-methyl dienone 9 yields largely the spiro hydroxy ketone 10 on irradiation in aqueous acetic acid.[14] It

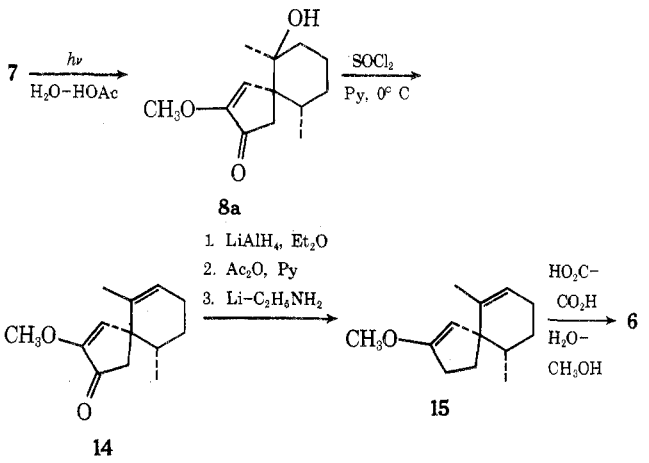


was anticipated that a methoxyl substituent would exert an influence similar to that of a methyl substituent on the course of the photochemical rearrangement and that 7 would also yield spiro[4.5]decane derivatives, e.g., 8, on irradiation in protic solvents.[15] The synthesis of 6 from 8 would then require (1) the appropriate manipulation of the 2-methoxy-1-en-3-one system to obtain the ketone function at C-2, and (2) the introduction of the 6,7 double bond via an elimination reaction involving the C-6 oxygen function. The methoxy dienone 7 was prepared from the octalone 11.[16] Treatment of 11 with lead tetraacetate in acetic acid containing acetic anhydride yielded the acetoxy enone 12 (as a mixture of C-2 epimers) in 44% yield.[17] Compound 12 was hydrolyzed and air oxidized to the 2-hydroxy dienone 13 which was methylated by treatment with potassium *tert*-butoxide in *tert*-butyl alcohol followed by addition of methyl iodide to produce 7 in 60% yield.[18]



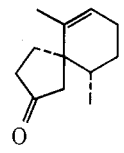
Two somewhat different routes were employed for the conversion of 7 into 6. The first of these is shown in Scheme I. Irradiation of a 1% solution of 7 in 45% aqueous acetic acid

Scheme I



for 5 h using a 450-W Hanovia high-pressure mercury lamp housed in a quartz probe followed by chromatography of the crude photolysis mixture on silica gel afforded the spiro hydroxy ketone 8a in 28% yield. The spectral properties of the product were consistent with the assigned structure. They were quite similar to those reported for 10[14a] if the expected changes resulting from introduction of the C-10 methyl group and substitution of the methoxyl group for the C-2 methyl group were taken into account. In addition to 8a, significant quantities of unchanged starting material and the hydroxy dienone 13 were isolated. The yield of 8a was not improved by the use of a Pyrex probe to house the Hanovia lamp or by carrying out the irradiation with a Hanau NK6/20 lamp which emits most of its light at 2537 Å. The use of longer irradiation periods led to the isolation of increased quantities of 13, which apparently is produced by light-catalyzed hydrolysis of the enol ether function of 7.[19]

On treatment of 8a with thionyl chloride in pyridine at 0 °C, the spiro dienone 14 was isolated as the exclusive product in 36% yield. Compound 14 was converted into the enol ether 15 (82% overall yield) by reduction of the carbonyl group with lithium aluminum hydride in ether (inverse addition), acetylation of the resulting mixture of allylic alcohols with acetic anhydride in pyridine, and reductive cleavage of the epimeric mixture of allylic acetates with lithium in ethylamine.[20,21] Examination of models of the allylic anion that would be expected to be involved as an intermediate in the reductive cleavage reaction indicates that protonation at the 3 position leading to 15 should be more favorable sterically than protonation at the 1 position which would yield the corresponding 2,3 isomer. Hydrolysis of 15 with oxalic acid in aqueous methanol afforded 6 in quantitative yield. The product showed ir absorption (film) at 1742 cm^{-1} for a cyclopentanone and lower frequency bands in locations similar to those reported by Marshall and Johnson[2c] for the enone 16, the epimer of 6 having the 1-methylene group and the 10-methyl group trans. The NMR spectrum (CCl_4) of 6 showed a doublet (J = 6 Hz) at δ 0.93 for the 10-methyl group, a doublet (J = 1.5 Hz) at δ 1.65 for the 6-methyl group, and broad absorption ($W_{1/2}$ ca. 8 Hz) at δ 5.38 for the C-7 olefinic proton. Interestingly, the 1-methylene protons of 6 appear to have almost identical chemical shifts for they give rise to a "singlet" at δ 2.15 at 60 MHz. This absorption appeared as two closely spaced peaks (separation <1 Hz) at 100 MHz and could be attributed to peaks 2 and 3 of an AB quartet centered at δ 2.15. In contrast, the 1-methylene protons of 16 appear as a well-separated AB quartet.[2c]



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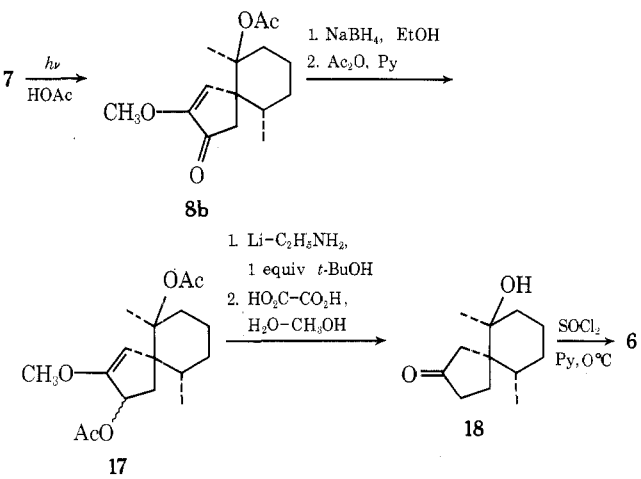
Although the above route proved to be a feasible approach to **6**, the low yields obtained in the photolysis and dehydration steps prompted investigation of another pathway which is shown in Scheme II. The conversion of **7** into a spirocyclic

Scheme II

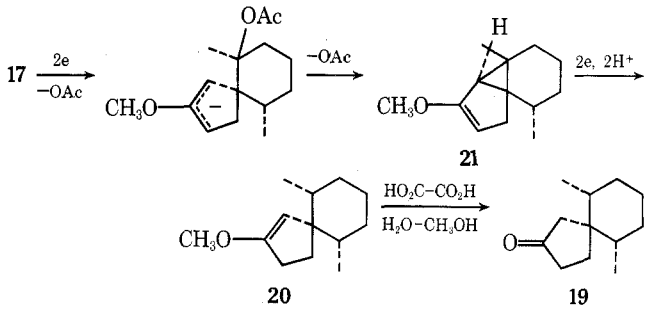


system proceeded much more smoothly when the irradiation was carried out in glacial rather than aqueous acetic acid. The absence of water eliminated the hydrolysis of **7** to **13** and the efficiency of the photochemical rearrangement process was improved significantly as well. Thus the acetoxy ketone **8b** was obtained in 89% yield when a dilute solution of the dienone in glacial acetic acid was irradiated for 3 h using a 450-W Hanovia lamp housed in a Pyrex probe. Again, the spectral properties of **8b** clearly supported the assigned spirocyclic structure.

Although in the conversion of photoproduct **8a** into **6** the 6,7 double bond was introduced as the first step in the sequence, it appeared that a more efficient approach from **8b** would first involve modification of the A ring and then introduction of the B ring double bond as the last step in the sequence. Thus **8b** was converted into a mixture of epimeric diacetates **17** in 81% yield by reduction with sodium borohydride in anhydrous ethanol followed by acetylation of the epimeric mixture of hydroxy acetates with acetic anhydride in pyridine. Treatment of **17** with lithium in ethylamine containing 1 equiv of *tert*-butyl alcohol at −78 °C followed by hydrolysis of the crude reduction mixture with oxalic acid in aqueous methanol gave the hydroxy ketone **18** in 45% yield. A mixture of saturated ketones containing mainly cis-dimethyl compound **19**, which has been obtained as a degradation product of β-vetivone,[2c] was also isolated from this sequence. This product apparently arose from the enol ether **20** which could have been produced by *O*-alkyl cleavage of the tertiary acetate group. *O*-Alkyl cleavage reactions of tertiary acetates have been observed previously in metal–ammonia reductions.[22] However, in this case the pathway shown in Scheme III which involves the formation and reductive cleavage of the vinyl cyclopropane **21** provides a plausible mechanism for the conversion of **17** into **20**.

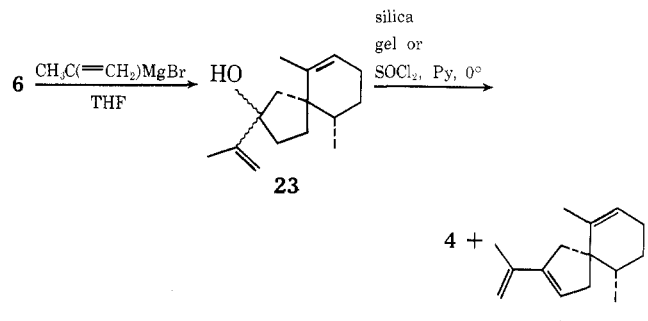
The enone **6** was prepared in ~65% yield by dehydration of **18** with thionyl chloride in pyridine at 0 °C.[23] Despite the occurrence of the side reaction involving hydrogenolysis of the tertiary acetate group in the reduction step, the overall yield

Scheme III



of **6** from **7** by the sequence shown in Scheme II was about 20%. This was more than twice the yield of **6** that was obtained by the route shown in Scheme I.

In order to prepare (±)-α-vetispirene (**4**) from the spiro enone **6** it was necessary to introduce an isopropenyl group at C-2 and to form the 1,2 double bond. It was found that this conversion could be accomplished directly by treatment of **6** with isopropenylmagnesium bromide in dry THF followed by chromatography of the crude reaction mixture on silica gel (Grace, grade 950, mesh size 60–200). In this way the desired natural product **4** and the isomeric triene **22** were obtained in an approximately 3:2 ratio in 35% yield from **6**. Alternatively, if the crude reaction mixture from the Grignard addition step was chromatographed on silica gel that had been prewashed with acetone a mixture of epimeric alcohols having spectral properties consistent with the structure **23** was isolated in approximately 40% yield. This mixture was dehydrated to give a 3:2 mixture of **4** and **22** either on being stirred in a hexane solution with unwashed silica gel or by reaction with thionyl chloride in pyridine at 0 °C.



The isomeric trienes were separated by preparative GLC using a Carbowax column. (±)-α-Vetispirene was eluted first from the column and it exhibited uv, ir, and NMR spectral properties identical with those of the authentic material.[24] The spectral properties of the triene **22** (see Experimental Section) were completely in accord with the assigned structure.

The intermediate spiro ketone **6** clearly has utility for the synthesis of other members of the spirovetivane family and studies along these lines are in progress.

Experimental Section[25]

***trans*-4a,8-Dimethyl-3-acetoxy-3,4,5,6,7,8-hexahydro-2(4a*H*)-naphthalenone (12).** To a solution of 72.6 g (0.41 mol) of **11**[16] in 800 ml of glacial acetic acid containing 60 ml of acetic anhydride was added 300 g (0.68 mol) of lead tetraacetate. The reaction mixture was heated at 60 °C with stirring under nitrogen for 36 h. Approximately 700 ml of acetic acid was then removed by distillation at reduced pressure using a water aspirator and 200 ml of water was added to the residue. The mixture was extracted with three 150-ml portions of ether and the combined ether extracts were neutralized by cautious addition of solid sodium bicarbonate until the evolution of carbon dioxide ceased. The ethereal solution was then washed with two 100-ml portions of water and dried over anhydrous sodium sulfate. Removal of the solvent in vacuo gave a yellow oil which on dis-

tillation under reduced pressure gave 31.0 g of a mixture of **11** and the corresponding cross-conjugated dienone, *trans*-4a,8-dimethyl-5,6,7,8-tetrahydro-2(4a*H*)-naphthalenone, bp 80–120 °C (0.25 mm), and 42.8 g (44%) of **12** as a mixture of the 3α and 3β isomers: bp 120–140 °C (0.25 mm); uv max (95% EtOH) 242 nm (ε 12 600); ir ($CHCl_3$) 1720 (acetate), 1691 (α,β-unsaturated ketone), and 1615 cm^{-1} (conjugated C=C); NMR (CCl_4) δ 1.05 (m, 3 H, 8-CH_3's), 1.25 (s, 2 H, 4a-CH_3), 1.42 (s, 1 H, 4a-CH_3), 2.03 (s, 3 H, 3-OAc), 5.25 (broad t, 1 H, 3α- and 3β-H), and 5.62 ppm (broad s, 1 H, 1-H).

Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.15, H, 8.53. Found: C, 70.89, H, 8.40.

***trans*-4a,8-Dimethyl-3-methoxy-5,6,7,8-hexahydro-2(4a*H*)-naphthalenone (7).** To a solution of 42.8 g (0.18 mol) of **12** in 300 ml of methyl alcohol was added a solution of 30.0 g (0.54 mol) of potassium hydroxide in 100 ml of water. While a slow stream of oxygen was being passed through the solution, it was stirred for 24 h at room temperature. Approximately 200 ml of methyl alcohol was removed by distillation in vacuo, and 150 ml of water was added to the residue. The aqueous phase was washed with three 50-ml portions of ether and acidified with dilute hydrochloric acid. The acidic mixture was extracted with three 75-ml portions of ether and the combined ether extracts were washed with a saturated solution of sodium chloride and dried over sodium sulfate. The ether was removed in vacuo to give 33.2 g (96%) of crude *trans*-4a,8-dimethyl-3-hydroxy-5,6,7,8-tetrahydro-2-(4a*H*)-naphthalenone (**13**). Recrystallization of this material from ether–hexane gave an analytical sample: mp 100.5–101.5 °C; uv max (95% EtOH) 250 nm (ε 14 000) and 288 (3350); NMR (CCl_4) δ 1.17 (d, J = 6 Hz, 3 H, 8-CH_3), 1.28 (s, 3 H, 4a-CH_3), 5.90 (s, 1 H, 4-H), 6.12 (d, J = 1.7 Hz, 1-H), and 6.45 ppm (broad s, 1 H, OH).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.85; H, 8.43.

The crude product (33.0 g) from above was dissolved in 200 ml of *tert*-butyl alcohol and a solution of potassium *tert*-butoxide in *tert*-butyl alcohol (prepared from 28.5 g of potassium and 1 l. of *tert*-butyl alcohol) was added in a thin stream with stirring under nitrogen. The mixture was stirred for 2 h at room temperature and 142.0 g of methyl iodide was added. The mixture was stirred for 1 h at room temperature and then heated at reflux for 30 min. Approximately 500 ml of *tert*-butyl alcohol was removed by distillation and the residue was diluted with 700 ml of water and extracted with four 100-ml portions of ether. The combined ether extracts were washed with one 50-ml portion of 10% aqueous sodium hydroxide and dried over anhydrous sodium sulfate. Removal of the solvent in vacuo afforded an oil which solidified on standing. Recrystallization from ether–hexane gave 23.0 g (64%) of **7**: mp 82.5–83.0 °C; uv max (95% EtOH) 251 nm (ε 11 300) and 285 (3300); ir ($CHCl_3$) 1655 (α,β-unsaturated ketone), 1635 cm^{-1} (conjugated C=C); NMR (CCl_4) δ 1.10 (d, J = 6 Hz, 3 H, 8-CH_3), 1.25 (s, 3 H, 4a-CH_3), 3.57 (s, 3 H, 3-OCH_3), 5.74 (s, 1 H, 4-H), and 5.90 ppm (d, J = 1.7 Hz, 1-H).

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69, H. 8.79. Found: C, 75.44; H, 8.61.

Irradiation of 7. A. In Aqueous Acetic Acid. A solution of 12.0 g of **7** in 1.5 l. of 45% aqueous acetic acid was irradiated for 5 h using a 450-W Hanovia lamp housed in a Pyrex probe. A stream of nitrogen was bubbled through the solution for 10 min prior to and during the entire irradiation period. The solvent was removed by lyophilization and the residue was chromatographed on 240 g of silica gel. Elution with 300 ml of each of hexane and 5, 10, 20, and 30% ether–hexane yielded only traces of material and further elution with 300 ml each of 40 and 50% ether–hexane gave 1.23 g of **13**. Elution with 900 ml each of 60 and 70% ether–hexane gave oily products having no clearly defined spectral characteristics while elution with 1200 ml of 80% ether–hexane gave 2.35 g of **7**. Finally, elution with 1 l. of ether and 600 ml of 50% methanol–ether gave 2.93 g (28%, based upon unrecovered starting material) of **8a**: bp 120–125 °C (bath temperature) (0.05 mm); uv max (95% EtOH) 258 mm (ε 8300); ir ($CHCl_3$) 1711 (conjugated cyclopentenone), 1626 (conjugated C=C), 1460, 1381, and 1351 cm^{-1}; NMR ($CDCl_3$) δ 0.72 (d, J = 6 Hz, 3 H, 10-CH_3), 1.05 (s, 3 H, 6α-CH_3), 2.16 and 2.72 (AB quartet, J_{AB} = 19.5 Hz, 2 H, 4-CH_2), 3.75 (s, 3 H, 2-OCH_3), and 6.33 ppm (s, 1 H, 1-H).

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.94, H, 8.93. Found: C, 69.38, H, 8.70

B. In Glacial Acetic Acid. A solution of 1.00 g (0.0049 mol) of **7** in 290 ml of glacial acetic acid (freshly distilled from molecular sieves) was irradiated with a 450-W Hanovia lamp for 3 h using a Pyrex probe. The solution was agitated with a stream of nitrogen for 10 min prior to and during the entire irradiation period. The solution was washed into a 500-ml round-bottom flask with benzene and frozen, and the solvents were removed by lyophilization to leave light tan crystals. Recrystallization from ether gave 1.15 g (89%) of **8b** as white crystals: mp 123–124 °C; ir ($CHCl_3$) 1720 (ester C=O), 1710 (conjugated cyclopentenone), 1626 (conjugated C=C), 1460, 1370, 1255, 1222, 1169, 1128, 1024, 977, 940, and 755 cm^{-1}; NMR ($CDCl_3$) δ 0.72 (d, J = 6.5 Hz, 3 H, 10-CH_3), 1.37 (s, 3 H, 6-CH_3), 2.03 (s, 3 H, 6-OAc), 2.16 and 2.69 (AB quartet, J_{AB} = 19.5 Hz, 2 H, 4-CH_2), 3.77 (s, 3 H, 2-OCH_3), and 6.22 (s, 1 H, 1-H).

Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.67; H, 8.27. Found: C, 67.52; H, 8.35.

6,*c*-10-Dimethyl-2-methoxy(*r*-5-*C*^{1})spiro[4.5]dec-1,6-dien-3-one(14).[26] While the temperature was maintained below 7 °C with an ice–salt bath, 8 ml of thionyl chloride was added slowly to a solution of 2.26 g (0.101 mol) of **8a** in 40 ml of pyridine with stirring under nitrogen. The reaction mixture was allowed to warm to room temperature and stirred for 30 min. It was then cooled below 20 °C and 5 ml of water was added dropwise with stirring while the temperature was maintained below 20 °C. An additional 50 ml of water was added and the mixture was extracted with three 50-ml portions of ether. The combined ethereal extracts were washed with a saturated solution of sodium chloride and dried over anhydrous sodium sulfate. The ether was removed in vacuo to give 0.76 g (36%) of **14**: bp 110–115 °C (bath temperature) (0.05 mm); uv max (95% EtOH) 256 nm (ε 7900); ir ($CHCl_3$) 1712 (conjugated cyclopentenone), 1632 (conjugated C=C), 1380, 1349, and 982 cm^{-1}; NMR (CCl_4) δ 0.90 (d, J = 6 Hz, 3 H, 10-CH_3), 1.52 (broad s, 3 H, 6-CH_3), 2.20 and 2.32 (AB quartet, J_{AB} = 19 Hz, 2 H, 4-CH_2), 5.52 (m, 1 H, 7-H), and 6.22 (s, 1 H, 1-H); mass spectrum (70 eV) *m/e* 206 (M^+); exact mass calcd, 206.1307; found, 206.1351.

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.48; H, 8.60.

2-Methoxy-6,*c*-10-dimethyl(*r*-5-*C*^{1})spiro[4.5]deca-1,6-dienone (15).[26] A solution of 0.152 g (0.004 mol) of lithium aluminum hydride in 10 ml of anhydrous ether was added dropwise with stirring under nitrogen to a solution of 0.298 g (0.0014 mol) of **14** in 30 ml of ether at 0 °C. The reaction mixture was stirred for 2 h at 0 °C and for 1 h at room temperature. A saturated aqueous solution of sodium potassium tartrate was then added dropwise with stirring until no new precipitate was produced on the introduction of fresh reagent. The reaction mixture was filtered with suction and the filter cake was washed with ether. The ethereal filtrate and washings were dried over anhydrous sodium sulfate. The solvent was removed in vacuo to yield 0.281 g (93%) of an oil. The spectral properties of this material showed that it was a ca. 1:1 mixture of C-3 epimers of 3-hydroxy-2-methoxy-6,*c*-10-dimethyl(*r*-5-*C*^{1})spiro[4.5]deca-1,6-diene:[26] ir ($CHCl_3$) 3590 (OH) and 1649 cm^{-1} (C=C); NMR (CCl_4) δ 0.80 and 0.88 (pair of d's, J = 6 Hz, 3 H, 10-CH_3's), 1.30 and 1.47 (pair of d's J = 1.5 Hz, 3 H, 6-CH_3's), 3.60 (s, 3 H, 2-OCH_3), 4.33 (s, 1 H, 1-H), 4.58 (broad t, J = 5 Hz, 1 H, 3-H's), and 5.32 ppm (broad s, 1 H, 7-H); exact mass calcd, 208.146; found, 208.142.

A solution of 0.511 g (0.0025 mol) of the above mixture of alcohols in 20 ml of dry pyridine was treated with 3.7 g of acetic anhydride and stirred at room temperature under nitrogen for 24 h. Water (4 ml) was added and stirring was continued for 1.5 h at room temperature. Forty milliliters of water was then added and the mixture was extracted with two 50-ml portions of ether. The ethereal solution was washed with aqueous sodium bicarbonate and saturated sodium chloride solutions and dried over sodium sulfate. Removal of the solvent in vacuo gave 0.566 g (92%) of a colorless oil. The spectral properties of this material showed that it was a ca. 1:1 mixture of the C-3 epimers of 3-acetoxy-2-methoxy-6,*c*-10-dimethyl(*r*-5-*C*^{1})spiro[4.5]deca-1,6-diene.[26] This material showed ir ($CHCl_3$) 1726 (OAc), 1648 (C=C), 1366, and 1025 cm^{-1}; NMR (CCl_4) δ 0.85 and 0.90 (pair of d's, J = 6 Hz, 3 H, 10-CH_3's), 1.52 and 1.60 (pair of d's, J = 1.5 Hz, 3 H, 6-CH_3's), 1.97 (s, 3 H, 3-OAc), 3.58 (s, 3 H, 2-OCH_3), 4.55 (s, 1 H, 1-H), 5.36 (m, 1 H, 7-H), and 5.40 and 5.56 ppm (pairs of t's, 1 H, 3-H's); exact mass calcd, 250.157; found, 250.150.

A solution of 0.40 g (0.0057 g-atom) of lithium in ca. 20 ml of dry ethylamine was added dropwise with stirring under nitrogen to a solution of 0.316 g (0.0013 mol) of the above mixture of allylic acetates in 20 ml of dry ethylamine at 16 °C. The addition was continued until the blue color of the metal–amine solution persisted for ca. 20 s after the introduction of a fresh drop of reagent. Then 1 g of ammonium chloride was added immediately. The ethylamine was allowed to evaporate and the residue was washed with 200 ml of ether. Removal of the ether gave 0.24 g (99%) of **15** as a yellow oil, bp 85–90 °C (bath temperature) (0.5 mm), which contained greater than 95% one component on GLC (column A).[25] Compound **15** showed the following spectral properties: ir ($CHCl_3$) 1645 (C=C), 1450, 1376, and 1352 cm^{-1}; NMR (CCl_4) δ 0.78 (d, J = 6 Hz, 3 H, 10-CH_3), 1.49 (d, J = 1.5 Hz, 3 H, 6-CH_3), 3.45 (s, 3 H, 2-OCH_3), 4.13 (t, J = 1 Hz, 1 H, 1-H), and 5.20 (m, 1 H, 7-H); exact mass calcd, 192.151; found, 192.154.

3,*t*-6-Diacetoxy-2-methoxy-*c*-6,*c*-10-dimethyl(*r*-5-*C*^{1})spiro[4.5]dec-1-ene (17).[26] A solution of 6.04 g (0.023 mol) of acetoxy ketone **8b** and 0.863 g (0.023 mol) of sodium borohydride in 60 ml of absolute ethanol was stirred in a 100-ml round-bottom flask at room

temperature for 48 h. Acetone (5 ml) was added, and the solution was stirred for 2 h. The solvents were removed in vacuo, and 100 ml each of ether and water were added to the residue. The layers were separated, the aqueous layer was extracted several times with 20-ml portions of ether, and the combined organic layers were washed with water and dried. Removal of the solvent in vacuo afforded 5.95 g (98%) of a mixture of C-3 epimers of *t*-6-acetoxy-3-hydroxy-2-methoxy-*c*-6,*c*-10-dimethyl(*r*-5-*C*¹)spiro[4.5]dec-1-ene. Recrystallization from ether gave an analytical sample: mp 89–90 °C; ir ($CHCl_3$) 3420 (OH), 1725 (ester C=O), 1648 (C=C), 1447, 1366, 1250, 1168, 1143, 1061, 1040, 827, and 756 cm^{-1}; NMR ($CDCl_3$) δ 0.70 and 0.85 (pair of d's, J = 6.5 Hz, 3 H, 10-CH_3's); 1.33 and 1.47 (pair of s's, 3 H, 6-CH_3's), 1.99 and 2.01 (pair of s's, 3 H, 6-OAc), 3.67 (s, 3 H, 2-OCH_3), 4.43 and 4.46 (pair of s's, 1 H, 1-H), and 4.57 (m, 1 H, 3-H's); exact mass calcd, 268.167; found, 268.163.

Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.16; H, 8.96. Found: C, 67.23; H, 9.02.

A solution of 2.78 g (0.0104 mol) of the above mixture in 40 ml of dry pyridine was treated with 8 g (0.078 mol) of acetic anhydride, and the solution was stirred under nitrogen at room temperature for 20 h. The reaction mixutre was then cooled to 0 °C, 16 ml of water was added carefully, and stirring was continued for 2 h. The mixture was then poured into 100 ml of ether, the layers were separated, and the aqueous layer was extracted with 50 ml of ether. The combined organic layers were washed with water and dried, and the solvents were removed in vacuo, leaving 3.3 g of pale yellow oil. Chromatography of this material on 60 g of silica gel using hexane–ether as eluent afforded 2.66 g (83%) of a mixture of 3-epimers of the diacetate **17** (20% ether in hexane): ir (film) 1730 (ester C=O), 1650 (C=C), 1446, 1369, 1245, 1170, 1145, 1033, 943, and 831 cm^{-1}; NMR (CCl_4) δ 0.72 and 0.81 (pair of d's, J = 6 Hz, 3 H, 10-CH_3's), 1.32 and 1.40 (pair of s's, 3 H, 6-CH_3's), 1.93 and 1.97 (pair of s's, 6 H, C-3 and C-6 OAc's), 3.63 (s, 3 H, 2-OCH_3), 4.60 (s, 1 H, 1-H), and 5.47 (pair of d's, J = 4.4 Hz, 1 H, 3-H's).

Anal. Calcd for $C_{17}H_{26}O_5$: C, 65.81; H, 8.39. Found: C, 65.99; H, 8.36.

***t*-6-Hydroxy-*c*-6,*c*-10-dimethyl(*r*-5-*C*¹)spiro[4.5]decan-2-one (18).**[26] In a 250-ml round-bottom flask equipped with magnetic stirrer, dropping funnel, and dry ice condenser 125 ml of ethylamine (freshly distilled from lithium) was collected under nitrogen. The ethylamine was cooled to −78 °C in a dry ice–acetone bath, and a solution of 1.00 g (0.00323 mol) of **17** and 0.239 g (0.00323 mol) of dry *tert*-butyl alcohol in 25 ml of dry ether was added. Then 0.1355 g (0.0194 g-atom) of lithium was added in small, freshly cut pieces. The mixture was stirred for 1.5 h, until the blue color of the lithium in ethylamine solution persisted. After 5 min of additional stirring, the mixture was filtered through glass wool into a flask containing 1 g of solid ammonium chloride, and the flask and funnel were rinsed with dry ether. The solvents were removed in vacuo, 50 ml each of ether and water were added to the residue, and the layers were separated. The aqueous layer was extracted with 50 ml of ether, the combined organic layers were washed with brine and dried, and the ether was removed to leave 0.64 g of an oil which on the basis of NMR and GLC analysis (column A)[25] appeared to be a 2:1 mixture of the desired hydroxy enol ether resulting from cleavage of the allylic acetoxyl group and the corresponding enol ether resulting from reductive cleavage of both the allylic and tertiary acetoxyl groups. This mixture showed the following spectral properties: ir (film) 3460 (OH), 1649 (C=C), 1460, 1365, 1226, 1036, 920, and 805 cm^{-1}; NMR ($CDCl_3$) δ 0.78 (d, J = 6 Hz, C-6 and C-10 CH_3's), 1.09 (s, C-10 CH_3), 3.61 (s, 3 H, OCH_3), and 4.31 ppm (s, 1 H, vinyl H).

A solution prepared from 0.51 g (0.0024 mol) of the crude mixture from above, 0.11 g (0.00122 mol) of oxalic acid, and 22 ml of 60% aqueous methanol was stirred at room temperature for 30 min. Saturated sodium bicarbonate (12 ml) was added and the mixture was extracted with 50 ml of 1:1 benzene–ether. The organic extracts were washed and dried, and the solvents were removed in vacuo to give 0.466 g of yellow oil. Chromatography on silica gel using hexane–ether as eluent afforded 0.151 g of ca. 4:1 mixture of **19** and the corresponding trans dimethyl ketone. The major component of this mixture was collected by GLC (column B)[25] and exhibited identical spectral properties with those reported for **19** by Marshall and Johnson.[2c]

Further elution with 25% ether in hexane gave 0.227 g (43%) of **18**: ir (film) 3470 (OH), 1735 (C=O), 1476, 1458, 1406, 1378, 1254, 1170, 1072, and 919 cm^{-1}; NMR ($CDCl_3$) δ 0.83 (d, J = 6.5 Hz, 3 H, 10-CH_3), 1.15 (s, 3 H, 6-CH_3), and 2.93 (s, 1 H, 6-OH).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.47; H, 10.20. Found: C, 73.26; H, 10.37.

6,*c*-10-Dimethyl(*r*-5-*C*¹)spiro[4.5]dec-6-en-2-one (6). A. From 18. A solution of 0.224 g (0.00114 mol) of the hydroxy ketone **18** in 4 ml of dry pyridine was placed in a 10-ml round-bottom flask under nitrogen and was cooled to 0 °C in an ice–salt bath. The solution was then treated with 0.5 ml of thionyl chloride dropwise while the temperature was maintained below 5 °C. After the addition was complete the solution was stirred at 0 °C for 75 min, and 6 ml of water was then added dropwise while the temperature of the reaction mixture was maintained between 5 and 15 °C. The mixture was extracted well with 50 ml of ether, the extracts were washed with brine and dried, and the ether was removed to give 0.124 g (61%) of the ketone **6**. Distillation using a micro-Hickman apparatus afforded an analytical sample: bp 83–85 °C (bath temperature) (0.7 mm); ir (film) 1742 (C=O), 1450, 1407, 1377, 1159, 899, and 799 cm^{-1}; NMR (CCl_4) δ 0.90 (d, J = 6 Hz, 3 H, 10-CH_3), 1.65 (d, J = 1.5 Hz, 3 H, 6-CH_3), 2.15 (AB quartet, J_{AB} = 19 Hz, 2 H, 1-CH_2), and 5.37 (s, $W_{1/2}$ = 8 Hz, 1 H, 7-H).

Anal. Calcd for $C_{12}H_{18}O$: C, 80.90; H, 10.11. Found: C, 80.69; H, 10.12.

B. From 15. A solution of 0.260 g (0.0013 mol) of **15** in 10 ml of methanol containing 4 ml of water and 0.051 g (0.0005 mol) of oxalic acid was stirred at room temperature for 30 min. A saturated aqueous solution of sodium bicarbonate (5 ml) was added and the mixture was extracted with three 25-ml portions of 1:1 benzene–ether. The organic extracts were dried over sodium sulfate, and the solvent removed in vacuo to yield 0.253 g (100%) of **6** as a pale yellow oil, bp 85–88 °C (bath temperature) (1 mm), which was greater than 95% one component by GLC (column A)[25] and exhibited the same spectral properties as those recorded above.

(±)-α-Vetispirene (4). To a mixture of 1.37 g (0.057 g-atom) of magnesium in 50 ml of dry THF (freshly distilled from $LiAlH_4$) containing a trace of iodine and 15 drops of carbon tetrachloride was added dropwise with stirring under nitrogen 10.18 g (0.084 mol) of freshly distilled isopropenyl bromide. The rate of addition of the halide was adjusted to maintain gentle reflux of the solution during the addition period. When the addition was complete the reaction mixture was allowed to cool to room temperature and then cooled to 3 °C in an ice bath. A solution of 1.13 g (0.0063 mol) of the spiro enone **6** in 6.0 ml of dry THF was added dropwise with stirring under nitrogen while the temperature of the reaction mixture was maintained below 5 °C. When the addition was complete the reaction mixture was stirred at room temperature for 2 h. An aqueous saturated solution of ammonium chloride (50 ml) was then added dropwise at such a rate that the temperature did not go above 50 °C. When the addition was complete the mixture was cooled to room temperature and extracted with two 100-ml portions of ether. The combined ether extracts were washed with 2% aqueous sodium bicarbonate and a saturated solution of sodium chloride and dried over magnesium sulfate. The ether was removed under reduced pressure and the residue was chromatographed on silica gel (Grace, grade 950, mesh size 60–200). Elution of the column with pentane yielded 0.24 g (35% based upon unrecovered **6**) of a colorless oil which by GLC analysis (column C) was found to be composed of (±)-α-vetispirene (**4**) and the isomeric triene **22** in a 3:2 ratio. Further elution of the column with 5% ether–pentane yielded 0.53 g of the starting ketone **6**. None of the expected mixture of epimeric alcohols **21** resulting from simple addition of the Grignard reagent to the ketone was isolated.

In another run starting with 0.15 g of **6**, the crude reaction product was chromatographed on silica gel that had been prewashed with acetone and the acetone removed from the column by elution with hexane before addition of the sample. Elution of the column with 3% ether–hexane gave 0.06 g (~60% based upon unrecovered **6**) of a mixture of epimeric alcohols (**23**). Further elution of the column with ether–hexane mixture gave 0.07 g of the starting ketone **6**. The mixture of alcohols showed the following spectral properties: ir (film) 3450 (OH), 1638 (C=C), 1450, 1376, 898, and 800 cm^{-1}; NMR (CCl_4) δ 0.90 and 1.00 (pair of d's, J = 1.5 Hz, 3 H, 6-CH_3's), 1.83 [d, J =0.5 Hz, 3 H, -C(CH_3)=CH_2], 4.73 [m, 1 H, -C(CH_3)=CH_2], 4.99 [m, 1 H, J = 0.5 Hz, -C(CH_3)=CH_2], and 5.26 (broad s, $W_{1/2}$ = 8 Hz, 1 H, 7-H); mass spectrum (70 eV) *m/e* 220 (M^+), 202 ($M^+ - H_2O$), 187 ($M^+ - H_2O$, CH_3), and 178 ($M^+ - CH_3CH{=}CH_2$).

When a solution of approximately 0.100 g of the mixture of the alcohols **23** in 20 ml of pentane was stirred with **6**.0 g of unwashed silica gel for 16 h, GLC analysis of the recovered product revealed that dehydration of **23** to produce a 3:2 mixture of **4** and **22** had occurred.

Thionyl chloride (0.092 ml) was added dropwise with stirring under nitrogen to a solution of 0.09 g (0.0004 mol) of the alcohol mixture **23** in 2 ml of dry pyridine while the temperature was maintained at −5 °C with an ice–salt bath. After the addition was complete the solution was stirred at −5 °C for 35 min. Water (5 ml) was added dropwise with stirring while the temperature was maintained below 0 °C. The reaction mixture was extracted with three 10-ml portions of ether and the combined ethereal extracts were washed with 10 ml of a saturated solution of aqueous sodium chloride and dried over sodium sulfate. Removal of the ether by fractional distillation gave 0.065 g (~80%)

of a colorless oil which by GLC analysis (column C) contained **4** and **22** in a ca. 3:2 ratio.

The isomeric trienes were separated by preparative GLC (column B). (±)-α-Vetispirene was eluted from the column first and the sample exhibited uv, ir, and NMR spectral properties identical with those of an authentic sample.[24] The synthetic compound showed the following spectral properties: uv max (95% EtOH) 238 nm (ε 20 600); ir (CCl_4) 3085, 1774, 1630, 884 (C=CH_2); 3045, 3018, 1660, 1597 (CH=C<, conjugated); 1379, 1200, 1076, 1060, and 841 cm^{-1}; NMR (CCl_4) δ 0.86 (d, $J \simeq 6$ Hz, 3 H, 10-CH_3), 1.54 (d, $J = 2$ Hz, 3 H, 6-CH_3), 1.91 [d, $J = 1$ Hz, 3 H, C(CH_3)=CH_2], ~2.50 (10-line multiplet, 2 H, 3-CH_2), 4.86 (br s, 2 H, =CH_2), 5.32 (m, 1 H, 7-H), and 5.45 (br s, $W_{1/2} = 3.5$ Hz, 1 H, 1-H); mass spectrum (70 eV) *m/e* 202 (M^+). The material was shown to be homogeneous on GLC columns A,[25] C,[25] and D.[25] The triene **22** showed uv max (95% EtOH) 237 nm (ε 16 333); ir (CCl_4) 3090, 1770, 1635, 887 (C=CH_2), 3050, 3025, 1655, 1602 (-CH=C<), 1470, 1455, 1382, 1265, and 976 cm^{-1}; NMR (CCl_4) δ 0.85 (d, $J = 6$ Hz, 10-CH_3), 1.56 (d, $J = 2$ Hz, 3 H, 6-CH_3), 1.88 [br s, 3 H, C(CH_3)=CH_2], 4.82 [br s, 2H, C(CH_3)=CH_2], 5.23 (m, 1 H, 7-H), 5.63 (br s, $W_{1/2} = \sim 6$ Hz, 1 H, 3-H); exact mass calcd, 202.1722; found, 202.1728.

Registry No.—**4,** 51196-11-3; **6,** 58406-60-3; **7,** 58355-87-6; **8a,** 58406-61-4; **8b,** 58384-56-8; **11,** 58407-30-0; 3α-**12,** 58355-88-7; 3β-**12,**58355-89-8; **13,** 58355-90-1; **14,** 58355-91-2; **15,** 58355-92-3; *c*-3-**17,** 58355-93-4; *t*-3-**17,** 58406-62-5; **18,** 58355-94-5; **22,** 58355-95-6; *c*-3-OH-**23,** 58355-96-7; *t*-3-OH-**23,** 58406-63-6; *c*-3-hydroxy-2-methoxy-6,*c*-10-dimethyl(*r*-5-C^1)spiro[4.5]deca-1,6-diene, 58355-97-8; *t*-3-hydroxy-2-methoxy-6,*c*-10-dimethyl(*r*-5-C^1)spiro[4.5]deca-1,6-diene, 58406-64-7; 3c-acetoxy-2-methoxy-6,*c*-10-dimethyl(*r*-5-C^1)spiro[4.5]deca-1,6-diene, 58355-98-9; *t*-3-acetoxy-2-methoxy-6,*c*-10-dimethyl(*r*-5-C^1)spiro[4.5]deca-1,6-diene, 58406-65-8; *t*-6-acetoxy-*c*-3-hydroxy-2-methoxy-*c*-6,*c*-10-dimethyl(*r*-5-C^1)spiro-[4.5]dec-1-ene, 58355-99-0; *t*-6-acetoxy-*t*-3-hydroxy-2-methoxy-*c*-6,*c*-10-dimethyl(*r*-5-C^1)spiro[4.5]dec-1-ene, 58406-66-9.

References and Notes

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(7) The synthetic approaches reported by Dauben and Hart[3e] and by Yamada and co-workers[3c,4b] are particularly useful since they proceed via intermediates suitable for conversion into a variety of these substances.

(8) Anhydro-β-rotunol in a stress metabolite recently isolated from blight infected potato tubers; see D. T. Coxon, K. R. Price, and B. Howard, *Tetrahedron Lett.*, 2921 (1974).

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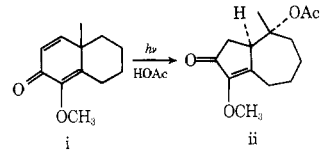
(12) For a preliminary report describing the synthesis of **6,** see D. Caine and J. B. Dawson, *Chem. Commun.*, 1232 (1970).

(13) α-Vetispirene was first isolated from oil vetiver by Andersen and coworkers; see N. H. Andersen, M. S. Falcone, and D. D. Syrdal, *Tetrahedron Lett.*, 1759 (1970).

(14) (a) P. J. Kropp, *J. Am. Chem. Soc.*, **86,** 4053 (1964). (b) For reviews on the photochemistry of cross-conjugated cyclohexadienones, see P. J. Kropp, *Org. Photochem.*, **1,** 1 (1967); K. Schaffner, *Adv. Photochem.*, **4,** 81 (1966).

(15) (a) We have found that the 4-methoxy dienone i yields the 5/7-fused acetoxy ketone ii on irradiation in glacial acetic acid, and that similar behavior is exhibited by 6/5-fused dienones related to i.[15b] These results, which showed



i ii

that the photochemical behavior of 4-methoxy dienones is similar to that of the corresponding methyl compounds,[15c] provided strong indications that the rearrangement of **7** would proceed in the desired manner. (b) D. Caine and F. N. Tuller, *J. Am. Chem. Soc.*, **93,** 6311 (1971); *J. Org. Chem.*, **38,** 3663 (1973); (c) D. Caine and J. B. Dawson, *J. Org. Chem.*, **29,** 3108 (1964); P. J. Kropp, *ibid.*, **29,** 3110 (1964).

(16) (a) J. A. Marshall and D. J. Schaffer, *J. Org. Chem.*, **30,** 3642 (1965); (b) D. Caine and F. N. Tuller, *ibid.*, **34,** 222 (1969).

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(21) For the employment of similar procedure for the conversion of α-methoxy conjugated enones into enol ethers, see ref 15b and R. E. Ireland, D. R. Marshall, and J. W. Tilley, *J. Am. Chem. Soc.*, **92,** 4754 (1970).

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(23) (a) An exocyclic double bond isomer was reported to be formed as a minor product in the preparation of the spiro enone **16** by dehydration of a spiro hydroxy ketone related to **18** with thionyl chloride in pyridine.[23b] However, in several runs we did not obtain evidence for the formation of the exocyclic double bond isomer of **6** under similar conditions. It is possible that this isomer was formed but was isomerized to **6** or selectively decomposed under our isolation conditions.
Several other methods of dehydration of **18** were investigated. For example, reaction of this hydroxy ketone with (carboxysulfanoyl)triethylammonium hydroxide inner salt methyl ester[23c] in acetonitrile at 40 °C gave a 96% yield of olefinic product. However, examination of the NMR spectrum of this material revealed that it was a ca. 2:1 mixture of **6** and the corresponding exocyclic methylene derivative. Unfortunately, we could not effect the separation of the components of this mixture by distillation or column chromatography on silica gel or alumina. On standing at room temperature in chloroform in the presence of a trace of trifluoroacetic acid the 2:1 mixture of **6** and its isomer was converted into an approximately 8:1 mixture of the two compounds. However, under the reaction conditions acid-catalyzed rearrangement of **6** into the octalone **11**[12] occurred to some extent. Therefore, this method of dehydration was not investigated further. (b) J. A. Marshall and P. C. Johnson, *J. Am. Chem. Soc.*, **89,** 2750 (1967). (c) E. M. Burgess, H. R. Penton, Jr., and E. A. Taylor, *J. Org. Chem.*, **38,** 26 (1973).

(24) We are grateful to Professor Niels H. Andersen for making copies of the ir, NMR, and uv spectra of natural α-vetispirene available to us.

(25) Melting points and boiling points are uncorrected. Infrared spectra were taken on Perkin-Elmer Model 457 or 137 infrared spectrophotometers. Ultraviolet spectra were taken on a Cary Model 14 or a Beckman DBGT recording spectrophotometer using 1-cm matched quartz cells. NMR spectra were determined at 60 MHz with a Varian A-60 or a Varian T-60 spectrometer. Signals are reported in parts per million (δ) downfield from internal tetramethylsilane. Mass spectra were obtained using a Hitachi Perkin-Elmer RMU-7 or a Varian M-66 spectrometer. Microanalyses were obtained by Galbriath Laboratories, Inc., Knoxville, Tenn., or by Atlantic Microlab, Inc., Atlanta, Ga. Gas–liquid chromatography was carried out using a Perkin-Elmer 881 or an Aerograph A-90-P3 gas chromatograph. The following columns were used: A (6 ft × 0.125 in., 10% Carbowax K-20 on Chromosorb W); B (10 ft × 0.25 in., 20% Carbowax K-20M on Chromosorb W); C (6 ft × 0.125 in., 20% Carbowax K-20M on Chromosorb W); D (6 ft × 0.125 in., 10% SE-30 on Chromosorb W).

(26) For an explanation of the nomenclature used here, see ref 2c, footnote 16d.