A Synthesis of (±)-β-Vetivone and Its Related Spirovetivanes *via* the Base-catalyzed Spiroannelation of Phenolic Tosylates

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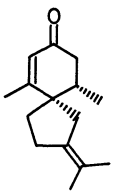
(±)-β-Vetivone was synthesized by the base-catalyzed spiroannelation of 2-[2-(4-hydroxy-2-methylphenyl)-ethyl]-3-methyl-3-butenyl *p*-toluenesulfonate followed by methylation and subsequent isomerization of the side chain double bond. The reactivities of the related tosylates, 4-(4-hydroxy-2-methylphenyl)-2-isopropylbutyl *p*-toluenesulfonate, 3-hydroxy-2-[2-(4-hydroxy-2-methylphenylethyl]-3-methylbutyl *p*-toluenesulfonate, and 2,3-epoxy-2-[2-(4-hydroxy-2-methylphenyl)ethyl]-3-methylbutyl *p*-toluenesulfonate have been discussed.

β-Vetivone (**1**),[1] a fragrance principle of vetiver oil, solavetivone (**2**),[2] hinesolone (**3**),[3] and the related alcohols **4** and **5**,[4] aroma substances from flue-cured Virginia tobacco, are spirovetivane-type sesquiterpenes bearing a 2-cyclohexenone group. Reported attempts to synthesize these sesquiterpenes[5] involve complex intermediates and many steps. Therefore, adequate use of promising intermediates for the synthesis of the desired terpenes would be important.

One of the attractive approaches to the spirovetivane may involve the preparation of 2-alkyl-6-methylspiro-[4.5]deca-6,9-dien-8-one *via* the base-catalyzed annelation of the corresponding phenols by the Winstein's method.[6] The spiroannelation has often been used for the synthesis of spiro[*n*.5]dienones,[7] but has not been employed yet for the spirovetivane synthesis.[8]

Phenolic tosylates **6a**—**c** and **7a** are considered to be promising precursors in obtaining **8** and **9**, which can be transformed to (±)-**1** and its related compounds **10a**—**c** by introducing methyl group at C-10. The isopropenyl group at C-2 of **8b** may be modified to isopropylidene, 1-(hydroxymethyl)vinyl, and 1,2-dihydroxy-1-methylethyl groups, leading to **1**, **4**, and **5**, respectively.



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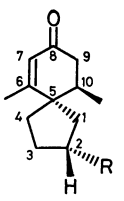
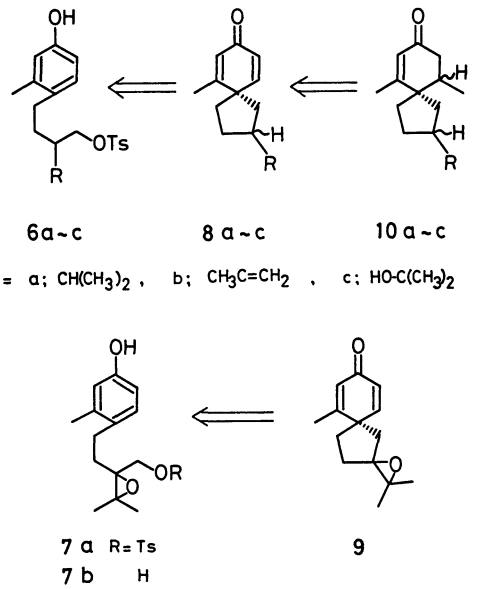


2 R; $C(CH_3)=CH_2$
3 $C(OH)(CH_3)_2$
4 $C(OH)(CH_2OH)CH_3$
5 $C(CH_2OH)=CH_2$

In this paper, we describe spiroannelation of 2-substituted butyl tosylates **6a**—**c** and **7a** leading to the corresponding spirodienones **8a**—**c** and **9** as well as a synthesis of (±)-β-vetivone (**1**).

Results and Discussion

Preparation of Phenolic Tosylates 6a—c and 7a. The lactone **11**, prepared from 3-(4-methoxy-2-methylbenzoyl)propanoic acid[9] by reduction and following lactonization, was treated with lithium diisopropylamide (LDA) in THF at −78 °C followed by addition of acetone, affording a C-2 epimeric mixture of **12** in quantitative yield. Dehydration of the alcohol **12** with thionyl chloride and subsequent hydrogenation of the resultant isopropylidene derivative **13** with Pt and then Pd on charcoal gave the carboxylic acid **14** in 98% yield. Treatment of **14** with boron tribromide in dichloromethane and next with diazomethane provided **15** in 87% yield. The desired **6a** was obtained by reduction of **15** with lithium aluminum hydride (LAH) followed by tosylation in 92% yield.



6a~c **8a~c** **10a~c**

R= a; $CH(CH_3)_2$, b; $CH_3C=CH_2$, c; $HO\text{-}C(CH_3)_2$

7a R=Ts
7b H

9

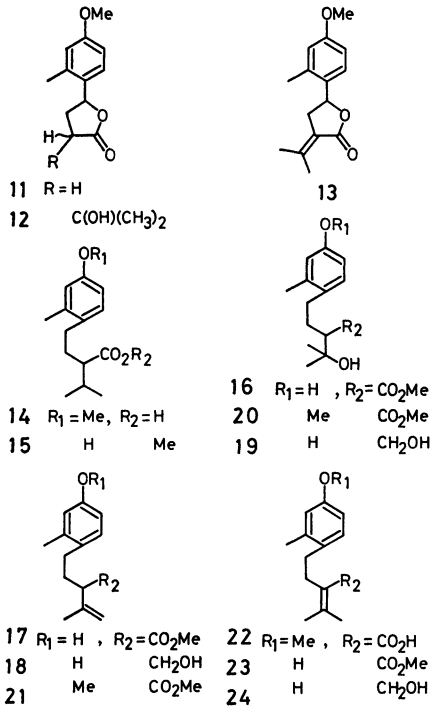
The arrow (⇐) indicates a reverse-synthesis.

Similarly, methyl 4-(4-hydroxy-2-methylphenyl)-butanoate was converted into **16** in 86% yield. Dehydration of **16** with thionyl chloride afforded β,γ-unsaturated ester **17** as a sole product, which was then reduced with LAH to give **18**. Subsequent tosylation of **18** provided **6b** in 68% yield (from **16**).

On the other hand, the monotosylate **6c** was prepared by selective tosylation of the primary hydroxyl group of **19**, obtained by reduction of **16** with LAH in THF, on treatment with tosyl chloride in dry pyridine at −30 °C for 6 h in 86% yield.

The alcohol **20**, prepared by coupling reaction of methyl 4-(4-methoxy-2-methylphenyl)butanoate with acetone, was dehydrated with thionyl chloride to give **21** in 89% yield. The olefin **21** was isomerized to the α,β-unsaturated acid **22** using wet potassium *t*-butoxide in *t*-butylalcohol. Successful conversion of the acid **22**

into the phenolic ester **23** was carried out by demethylation with boron tribromide followed by esterification with diazomethane in 78% yield (from **21**). Thus, another tosylate **7a** was obtained in 82% yield by reduction of **23** with LAH followed by epoxidation of **24** with monoperoxyphthalic acid.

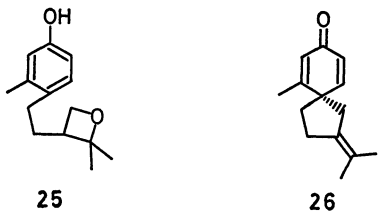


Spiroannelation of Phenolic Tosylates ***6a—c*** *and* ***7a.*** The base-catalyzed spiroannelation of **6a** was performed by treatment with *t*-BuOK in refluxing *t*-butyl alcohol, providing C-2 epimers of **8a** in 83% yield after chromatography (SiO_2). Similarly, the tosylate **6b** gave **8b** in 74% yield.[10]

On the other hand, the hydroxy tosylate **6c** could lead to the corresponding spiro compound **8c** only in 17% yield, but it gave the oxetane **25** (67%) as a major product. Treatment of **6c** with sodium methoxide in methanol resulted in **8c** (7%) and **25** (74%). Other combinations of solvents and bases such as NaH–benzene, *t*-BuOK–DMSO, *t*-BuOK–THF, K_2CO_3–acetone, and BuLi–THF did not improve the yield of **8c**. The predominant formation of oxetane may be due to the faster intramolecular S_N2 reaction of the tertiary hydroxyl group toward the tosyloxyl group. The epoxy tosylate **7a** was similarly spiroannelated with *t*-BuOK in refluxing *t*-butyl alcohol, providing **9** in 45% yield. The low yield of **9** would arise from instability of the dienone in high temperature and strong base.

Conversion of ***8a—c*** *to (±)-β-Vetivone and Its Related Compounds.* The dienones **8a**, **8b**, and **8c** underwent methylation at the C-10 carbon with lithium dimethylcuprate(I). However, the epoxy dienone **9** did not afford the desired methylated compound, but it gave complex mixtures.[11] Thus, **8a** was allowed to react with lithiumdimethylcuprate(I) at −25 °C to give **10a** in 85% yield. Similarly, **8b** and **8c** provided **10b** and **10c** in 75 and 63% yield, respectively. The compound **10b** was subsequently converted into (±)-β-vetivone and (±)-10-epi-β-vetivone (1:1 by HPLC) in 80% yield by isomerization of the terminal double bond with rhodium trichloride[12] in ethanol at 110 °C. The pure (±)-**1** was separated by HPLC and identified by the spectroscopic comparison with the authentic data.[5f]

The compound **10c** as an epimeric mixture at C-2 and C-10 was converted into (±)-**1** and (±)-10-epi-**1** (1:1 by HPLC) in 72% yield by dehydration with thionyl chloride.[3,5a,5b,5j,5k] Similarly, the alcohol **8c** was transformed to the olefinic dienone **26** in 75% yield, which had been converted into (±)-**1** by Pesaro.[5h]



Experimental

Boiling points are indicated by an air-bath temperature and uncorrected. Melting points are taken on a Thomas-Hoover capillary melting point apparatus and uncorrected. IR spectra were obtained on a JASCO IRA-1 spectrometer. ^1H NMR spectra were measured at 60 MHz with a Hitachi R-24 or at 100 MHz with a JEOL FX-100. The chemical shift values are expressed in δ (ppm) downfield from Me_4Si as an internal standard.

*4-(4-Methoxy-2-methylphenyl)butanolide (**11**).* The mixture of 3-(4-methoxy-2-methylbenzoyl)propanoic acid (669 mg, 3 mmol) dissolved in 6.5 ml of 2% aq NaOH and $NaBH_4$ (65 mg, 1.7 mmol) was stirred at room temperature for 24 h, acidified with 10% H_2SO_4 under cooling with an ice bath, and then heated at 80 °C for 15 min. The organic phase was extracted with $CHCl_3$. The extract was washed with saturated $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated *in vacuo* to give a residue which was chromatographed (SiO_2, hexane:benzene=5:1) to provide **11** (608 mg, 98%) as colorless crystals: mp 52—54 °C (hexane–benzene); IR (neat) 1777 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.27 (s, 3H, CH_3), 1.6—2.8 (m, 4H, CH_2), 3.72 (s, 3H, CH_3O), 5.4—5.8 (m, 1H, CH), 6.5—7.3 (m, 3H, ArH). Found: C, 69.87; H, 6.58%. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84%.

*2-(1-Hydroxy-1-methylethyl)-4-(methoxy-2-methylphenyl) butanolide (**12**).* The lactone **11** (722 mg, 3.5 mmol) was added dropwise to a THF solution of LDA, which was prepared by treatment of $NH(CHMe_2)_2$ (1 ml, 7 mmol) dissolved in 4.5 ml of THF with BuLi (5.3 mmol) at −78 °C under N_2. After stirring at −78 °C for 30 min, acetone (0.25 ml, 3.5 mmol) was added and stirred for 30 min. The mixture was quenched with 2 ml of saturated NH_4Cl and the organic phase was taken up in AcOEt. The extract was washed with saturated $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated *in vacuo* to give a residue (970 mg), which was chromatographed (SiO_2, benzene:hexane:AcOEt=10:2:1), providing **12** (970 mg, quant) as a colorless liquid: bp 115—117 °C (0.01 mmHg); IR (neat) 3466 (OH), 1761 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (s, 6H, CH_3), 2.29 (s, 3H, CH_3), 1.8—3.0 (m, 3H, CH_2, CH) 3.41 (s, 1H, OH), 3.77 (s, 3H, CH_3O), 5.4—5.8 (m, 1H, CH), 6.5—7.3 (m, 3H, ArH). Found: C, 68.06; H, 7.53%. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63%.

*2-Isopropylidene-4-(4-methoxy-2-methylphenyl)butanolide (**13**).* Thionyl chloride (0.09 ml, 1.3 mmol) was added dropwise to a solution of **12** (300 mg, 1.1 mmol) dissolved in 0.5 ml of pyridine and 1.5 ml of CH_2Cl_2. The reaction mixture was stirred at 0 °C for 20 min and then at room temperature for 4 h. After addition of a few pieces of ice, the organic phase was extracted with ether. The extract was washed with 5% HCl and water, dried (Na_2SO_4), and concentrated under reduced pressure, providing 275 mg of the residue which was chromatographed (SiO_2, hexane: benzene: AcOEt=10: 4: 1) to give **13** (275 mg, 98%): bp 105—107 °C (0.003 mmHg); IR (neat) 1745 (C=O), 1668 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.84 (s, 3H, CH_3), 2.29 (s, 6H, CH_3), 2.4—3.6 (m, 2H, CH_2), 3.75 (s, 3H, CH_3O), 5.51 (dd, J_1=7 Hz, J_2=8 Hz, 1H, CHO). 6.5—7.4 (m, 3H, ArH). Found: C, 73.19; H, 7.57%. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37%.

*2-Isopropyl-4-(4-methoxy-2-methylphenyl)butanoic Acid (**14**).* The lactone **13** (400 mg, 1.6 mmol) dissolved in 20 ml of MeOH was hydrogenated with PtO_2 (40 mg) at room temperature for 12 h and then Pd/C (40 mg) for 6 h to give **14** (388 mg, 96%): bp 111—113 °C (0.01 mmHg); IR (neat) 3500—2400 (CO_2H), 1702 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (d, J=6 Hz, 6H, CH_3), 1.4—2.9 (m, 6H, CH_2, CH) 2.26 (s, 3H, CH_3), 3.74 (s, 3H, CH_3O), 6.4—7.3 (m, 3H, ArH), 9.3—10.4 (br s, 1H, CO_2H). Found: C, 71.97; H, 9.03%. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%.

*Methyl 4-(4-Hydroxy-2-methylphenyl)-2-isopropylbutanoate (**15**).* Boron tribromide (0.25 ml, 2.64 mmol) was added dropwise to a solution of **14** (335 mg, 1.32 mmol) dissolved in 3.5 ml of dry CH_2Cl_2 at −70 °C. The mixture was stirred for 1 h at −70 °C and 0 °C for 1 h, quenched with water, and extracted with AcOEt. The usual work-up gave yellow liquid, which was subsequently esterified with diazomethane and chromatographed (SiO_2, benzene: hexane: AcOEt=6: 2: 1) to afford **15** (283 mg, 86%) as an oil: bp 92—94 °C (0.005 mmHg); IR (neat) 3380 (OH), 1732, 1710 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (d, J=6 Hz, 6H, CH_3), 2.14 (s, 3H, CH_3), 1.4—2.6 (m, 6H, CH_2, CH), 3.63 (s, 3H, CH_3O), 6.3—6.9 (m, 4H, ArH, OH). Found: C, 71.99; H, 9.06%. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%.

4-(4-Hydroxy-2-methylphenyl)-2-isopropylbutyl p-*Toluenesulfonate (**6a**).* A solution of sublimated *p*-TsCl (309 mg, 1.62 mmol) in 1.5 ml of dry pyridine was added dropwise to a solution of 4-(4-hydroxy-2-methylphenyl)-2-isopropyl-1-butanol (240 mg, 1.08 mmol) dissolved in 1.5 ml of dry pyridine at −30 °C. After stirring at −30 °C for 10 min and at 0 °C for 6 h, the mixture was quenched with water and then worked up to give an oil, which was chromatographed (SiO_2, benzene: AcOEt=2: 1) to yield **6a** (381 mg, 94%) as a pale yellow oil: IR (neat) 3470 (OH), 1354, 1175 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82 (d, J=7 Hz, 6H, CH_3), 1.2—2.0 (m, 4H, CH_2, CH), 2.14 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.2—2.6 (m, 2H, CH_2), 4.04 (d, J=4 Hz, 2H, CH_2O), 5.11 (br s, 1H, OH), 6.4—7.0 (m, 3H, ArH), 7.28 (d, J=8 Hz, 2H, ArH), 7.77 (d, J=8 Hz, 2H, ArH). Found: C, 67.09; H, 7.58%. Calcd for $C_{21}H_{28}O_4S$: C, 66.99; H, 7.50%.

*Methyl 3-Hydroxy-2-[2-(4-hydroxy-2-methylphenyl)ethyl]-3-methylbutanoate (**16**).* The compound **16** was obtained as a colorless oil in 86% yield by alkylation of methyl 4-(4-hydroxy-2-methylphenyl)butanoate in the same reaction conditions as employed for **12** using a mixed solvent (HMPA: THF=1: 10); bp 123—126 °C (0.01 mmHg); IR (neat) 3320 (OH), 1707 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (s, 6H, CH_3), 2.19 (s, 3H, CH_3), 1.5—2.7 (m, 7H, CH_2, CH, OH), 3.73 (s, 3H, CH_3O), 6.4—7.1 (m, 3H, ArH). Found: C, 67.49; H, 8.08%. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33%.

*Methyl 2-[2-(4-Hydroxy-2-methylphenyl)ethyl]-3-methyl-3-butenoate (**17**):* Bp 123—125 °C (0.009 mmHg); IR (neat) 3440 (OH), 1733 (C=O), 1644 (C=C) cm^{-1}; NMR ($CDCl_3$) δ 1.75 (br s, 3H, CH_3), 2.29 (s, 3H, CH_3), 1.5—2.8 (m, 5H, CH_2, OH), 3.09 (t, J=7 Hz, 1H, CH), 3.68 (s, 3H, CH_3O), 4.8—5.0 (m, 2H, CH_2=), 6.8—7.2 (m, 3H, ArH). Found: C, 72.56; H, 8.25%. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12%.

*2-[2-(4-Hydroxy-2-methylphenyl)ethyl]-3-methyl-3-buten-1-ol(**18**).* Reduction of **17** with $LiAlH_4$ in dry THF provided **18** as an oil in 90% yield: bp 118—121 °C (0.015 mmHg); IR (neat) 3320 (OH), 1644 (C=C) cm^{-1}; NMR ($CDCl_3$) δ 1.69 (s, 3H, CH_3), 1.1—1.8 (m, 2H, CH_2), 2.16 (s, 3H, CH_3), 2.0—2.8 (m, 5H, CH_2, CH, OH), 3.54 (d, J=7 Hz, 2H, CH_2O), 4.8—5.1 (m, 2H, CH_2=), 6.4—7.1 (m, 3H, ArH). Found: C, 76.26; H, 9.00%. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15%.

2-[2-(4-Hydroxy-2-methylphenyl)ethyl]-3-methyl-3-butenyl p-*Toluenesulfonate (**6b**):* IR (neat) 3460 (OH), 1649 (C=C), 1358, 1178 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 1.58 (s, 3H, CH_3), 1.2—1.8 (m, 2H, CH_2), 2.12 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.0—2.7 (m, 3H, CH_2, CH), 3.96 (d, J=7 Hz, 2H, CH_2O), 4.7—5.0 (m, 2H, CH_2=), 5.67 (br s, 1H, OH), 6.4—7.0 (m, 3H, ArH), 7.23 (d, J=8 Hz, 2H, ArH), 7.70 (d, J=8 Hz, 2H, ArH). Found: C, 67.43; H, 7.07%. Calcd for $C_{21}H_{26}O_4S$: 67.35; H, 7.00%.

*2-[2-(4-Hydroxy-2-methylphenyl)ethyl]-3-methyl-1,3-butanediol (**19**):* Mp 111—113 °C (benzene: AcOEt=5: 1); IR (neat) 3320 (OH); NMR (acetone-d_6) δ 1.16 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.3—1.9 (m, 3H, CH_2, CH), 2.23 (s, 3H, CH_3), CH_3), 2.3—2.8 (m, 2H, CH_2), 2.88 (br. s, 1H, OH), 3.7—4.0 (m, 2H, CH_2O), 4.0—4.2 (m, 1H, OH), 6.4—7.1 (m, 3H, ArH), 7.89 (br s, 1H, OH). Found: C, 70.61; H, 9.53%. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30%.

3-Hydroxy-2-[2-(4-hydroxy-2-methylphenyl)ethyl]-3-methylbutyl p-*Toluenesulfonate (**6c**):* IR (neat) 3400 (OH), 1352, 1177 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 1.15 (s, 6H, CH_3), 1.3—2.0 (m, 3H, CH_2, CH), 2.12 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 2.2—2.8 (m, 2H, CH_2), 3.90 (br s, 2H, OH), 4.19 (d, J=3 Hz, 2H, CH_2O), 6.3—6.9 (m, 3H, ArH), 7.27 (d, J=8 Hz, 2H, ArH), 7.54 (d, J=8 Hz, 2H, ArH). Found: C, 64.13; H, 7.23%. Calcd for $C_{21}H_{28}O_5S$: C, 64.26; H, 7.19%.

*Methyl 3-Hydroxy-2-[2-(4-methoxy-2-methylphenyl)ethyl]-3-methylbutanoate (**20**):* Bp 103—105 °C (0.01 mmHg); IR (neat) 3460 (OH), 1728 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.20 (s, 6H, CH_3), 1.5—2.1 (m, 2H, CH_2), 2.23 (s, 3H, CH_3), 2.2—2.7 (m, 3H, CH_2, CH), 2.78 (br s, 1H, OH), 3.69 (s, 3H, CH_3O), 3.71 (s, 3H, CH_3), 6.5—7.1 (m, 3H, ArH). Found: C, 68.48; H, 8.50%. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H. 8.63%.

*Methyl 2-[2-(4-methoxy-2-methylphenyl)ethyl]-3-methyl-3-butenoate (**21**):* Bp 81—83 °C (0.003 mmHg); IR (neat) 1733 (C=O), 1646 (C=C) cm^{-1}; NMR ($CDCl_3$) δ 1.75 (br s, 3H, CH_3), 1.7—2.2 (m, 2H, CH_2), 2.26 (s, 3H, CH_3), 2.3—2.7 (m, 2H, CH_2), 3.07 (t, J=7 Hz, 1H, CH), 3.67 (s, 3H, CH_3O), 3.73 (s, 3H, CH_3O), 4.8—5.0 (m, 2H, CH_2=), 6.5—7.1 (m, 3H, ArH). Found: C, 73.29; H, 8.64%. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45%.

*2-[2-(4-Methoxy-2-methylphenyl)ethyl]-3-methyl-2-butenoic Acid (**22**).* The mixture of **21** (1.37 g, 5.22 mmol) and *t*-BuOK (2.59 g, 23.1 mmol) in 8 ml of dry *t*-BuOH and 18 ml of dry THF was refluxed for 30 h. After evaporation of the solvent *in vacuo*, the residue was mixed with 10 ml of water and then acidified with 5% HCl. The usual work-up gave 1.32 g of a solid, which was recrystallized from hexane/benzene (10/1) affording **22** (1.25 g, 96%) as colorless crystals: mp 108—110 °C; IR (nujol) 3400—2000 (CO_2H), 1687 (C=O), 1652 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.77 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.58 (br s, 4H, CH_2), 3.73 (s, 3H, CH_3O), 6.5—7.2 (m, 3H, ArH), 11.16 (br s, 1H, CO_2H).

Found: C, 72.55; H, 8.12%. Calcd for $C_{15}H_{20}O_3$: C, 72.55: H, 8.12%.

*Methyl 2-[2-(4-Hydroxy-2-methylphenyl)ethyl]-3-methyl-2-butenoate (**23**)*: Mp 81—82 °C (hexane: benzene=15: 1); IR (Nujol) 3330 (OH), 1682 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.74 (s, 3H, CH_3), 1.98 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.54 (br s, 4H, CH_2), 3.70 (s, 3H, CH_3O), 6.40 (br s, 1H, OH), 6.5—7.1 (m, 3H, ArH). Found: C, 72.56; H, 8.19%. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12%.

*2-[2-(4-Hydroxy-2-methylphenyl)ethyl]-3-methyl-2-buten-1-ol (**24**)*: Mp 119—121 °C (CH_2Cl_2); IR (Nujol) 3340 (OH), 1653 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.67 (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 1.9—2.9 (m, 6H, CH_2, OH), 4.13 (s, 2H, CH_2O), 6.4—7.1 (m, 3H, ArH). Found: C, 76.33; H, 9.20%. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15%.

*2,3-Epoxy-2-[2-(4-hydroxy-2-methylphenyl)ethyl]-3-methyl-1-butanol (**7b**)*. An ethereal solution of monoperoxyphthalic acid (0.5 ml, *ca.* 0.5 mmol) was added to an ice-cooled solution of **24** (43 mg, 0.2 mmol) in 0.5 ml of ether with stirring. After stirring at 5 °C for 10 h, the reaction mixture was quenched with saturated $NaHCO_3$ and then extracted with ether. The extract was washed with brine, dried (Na_2SO_4), and concentrated *in vacuo* to give an oil, which was chromatographed (SiO_2, benzene: AcOEt=5: 1) affording **7b** (42 mg, 91%) as a colorless oil: bp 112—114 °C (0.009 mmHg); IR (neat) 3340 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 1.5—2.9 (m, 6H, CH_2, OH), 3.78 (s, 2H, CH_2O), 6.4—7.1 (m, 3H, ArH). Found: C, 71.16; H, 8.31%. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53%.

*2,3-Epoxy-2-[2-(4-hydroxy-2-methylphenyl)ethyl]-3-methylbutyl p-Toluenesulfonate (**7a**)*: Mp 79—81 °C (hexane: benzene=5: 1); IR (Nujol) 3250 (OH), 1365, 1168 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (s, 6H, CH_3), 2.16 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 1.5—2.8 (m, 4H, CH_2), 4.15 (s, 2H, CH_2O), 6.00 (br s, 1H, OH), 6.4—7.1 (m, 3H, ArH), 7.30 (d, J=9 Hz, 2H, ArH), 7.79 (d, J=9 Hz, ArH). Found: C, 64.63; H, 6.60%. Calcd for $C_{21}H_{26}O_5S$: C, 64.59; H, 6.71%.

*2-Isopropyl-6-methylspiro[4.5]deca-6,9-dien-8-one (**8a**)*. Sublimated *t*-BuOK (16 mg, 0.14 mmol) in 1.2 ml of dry BuOH was added dropwise to a solution of **6a** (45 mg, 0.12 mmol) in 0.8 ml of dry *t*-BuOH under N_2 and the mixture was refluxed for 12 h. After cooling to room temperature, the mixture was quenched with water and then worked up to afford a yellow oil, which was chromatographed (SiO_2, benzene: AcOEt=10: 1) to give **8a** (21 mg, 86%) as a pale yellow oil: bp 60—61 °C (0.01 mmHg); IR (neat) 1660 (C=O), 1625, 1604 (C=C) cm^{-1}; NMR ($CDCl_3$) δ 0.92 (d, J=6 Hz, 3H, CH_3), 0.96 (d, J=6 Hz, 3H, CH_3), 1.99, 2.01 (2s, 3H, CH_3), 1.1—2.3 (m, 8H, CH_2, CH), 5.9—6.2 (m, 2H, CH=), 6.87 (d, J=10 Hz, 1H, CH=). Found: C, 82.24; H, 9.92%. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87%.

*2-Isopropenyl-6-methylspiro[4.5]deca-6,9-dien-8-one (**8b**)*: Bp 65—68 °C (0.007 mmHg); IR (neat) 1659 (C=O), 1624, 1602 (C=C) cm^{-1}; NMR ($CDCl_3$) δ 1.77 (br s, 3H, CH_3), 2.02, 2.04 (2s, 3H, CH_3), 1.5—2.3 (m, 6H, CH_2), 2.4—3.2 (m, 1H, CH), 4.7—4.9 (m, 2H, CH_2=), 5.9—6.2 (m, 2H, CH=), 6.91 (d, J=10 Hz, CH=). Found: C, 83.15; H, 9.12%. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97%.

*2-(1-Hydroxy-1-methylethyl)-6-methylspiro[4.5]deca-6,9-dien-8-one (**8c**)*: IR (neat) 3380 (OH), 1650 (C=O), 1614 (C=C) cm^{-1}; NMR ($CDCl_3$) δ 1.25 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 2.00, 2.02 (2s, 3H, CH_3), 1.4—2.4 (m, 7H, CH_2, CH), 2.73 (br s, 1H, OH), 5.9—6.2 (m, 2H, CH=), 6.99 (d, J=10 Hz, 1H, CH=). Found: C, 76.21; H, 8.97%. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15%.

*3-[2-(4-Hydroxy-2-methylphenyl)ethyl]-2,2-dimethyloxetane (**25**)*: Mp 78—80 °C (hexane: benzene=15: 1); IR (neat) 3280 (OH) cm^{-1}; NMR ($CDCl_3$) δ 1.34 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.6—2.0 (m, 2H, CH_2), 2.20 (s, 3H, CH_3), 2.1—3.0 (m, 3H, CH_2, CH), 4.09 (dd, J_1=6 Hz, J_2=7 Hz, 1H, CH_2O), 4.51 (dd, J_1=7 Hz, J_2=8 Hz, 1H, CH_2O), 6.4—7.0 (m, 3H, ArH), 7.60 (br s, 1H, OH). Found: C, 76.34; H, 9.17%. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15%.

*2,2,6-Trimethyl-1-oxadispiro[2.1.5.2]dodeca-6,9-dien-8-one (**9**)*: Bp 75—77 °C (0.008 mmHg); IR 1662 (C=O), 1624, 1603 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 2.01, 2.04 (2s, 3H, CH_3), 1.5—2.9 (m, 6H, CH_2), 6.0—6.3 (m, 2H, CH=), 6.90 (d, J=11 Hz, 1H, CH=). Found: C, 77.02; H, 8.37%. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.13%.

*2-Isopropyl-6,10-dimethylspiro[4.5]dec-6-en-8-one (**10a**)*. An ethereal solution of lithium dimethylcuprate (I) (1.0 mmol) was added to a solution of **8a** (70 mg, 0.34 mmol) in 1.5 ml of dry ethre over 20 min period under N_2 at −20——25 °C. The mixture was stirred for 1.5 h and quenched with water and 5% HCl. The usual work-up gave an oil, which was chromatographed (SiO_2, benzene: AcOEt=10: 1) providing **10a** (61 mg, 81%) as a slightly yellow oil: bp 56—57 °C (0.01 mmHg); IR (neat) 1669 (C=O), 1614 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (d, J=7 Hz, 6H, CH_3), 0.96—1.03 (m, 3H, CH_3), 1.93, 1.95, 1.96, 1.97 (4s, 3H, CH_3), 1.1—2.8 (m, 11H, CH_2, CH), 5.70 (br s, 1H, CH=). Found: C, 81.84; H, 10.98%. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98%.

*2-Isopropenyl-6,10-dimethylspiro[4.5]dec-6-en-8-one (**10b**)*: Bp 65—67 °C (0.008 mmHg); IR (neat) 1667 (C=O), 1612 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00, 1.04 (2d, J=7 Hz, 3H, CH_3), 1.78 (br s, 3H, CH_3), 1.99, 2.00, 2.01, 2.02 (4s, 3H, CH_3), 1.30—2.80 (m, 10H, CH_2, CH), 4.75 (br s, 2H, CH_2=), 5.75 (br s, 1H, CH=). Found: C, 82.49; H, 10.35%. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16%.

*2-(1-Hydroxy-1-methylethyl)-6,10-dimethylspiro[4.5]dec-6-en-8-one (**10c**)*: IR (neat) 3420 (OH), 1654 (C=O), 1612 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90—1.07 (m, 3H, CH_3), 1.25 (s, 6H, CH_3), 1.92—2.00 (m, 3H, CH_3), 1.30—2.62 (m, 11H, CH_2, CH, OH), 5.73 (br s, 1H, CH=). Found: C, 76.19; H, 10.24%. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24%.

*2-Isopropylidene-6,10-dimethylspiro[4.5]dec-6-en-8-one (dl-β-Vetivone) (**1**) and Its C-10 Epimer.* A mixture of **10b** (14 mg, 0.064 mmol) and $RhCl_3 \cdot 2H_2O$ (1.3 mg, 0.05 mmol) in 0.05 ml of dry EtOH was heated in a glass tube at 110 °C for 8 h. The mixture was filtered and the precipitate was rinsed several times with ether. The combined filtrates were concentrated *in vacuo* and the residue was chromatographed (SiO_2, benzene: AcOEt=10: 1) to give (±)-**1** and its C-10 epimer (11 mg, 80%). HPLC separation of the epimeric mixture (μ-Porasil, 4φ-30 cm, ether: hexane=1: 10, flow rate 2 ml/min, 1000 psi) and further purification through a short silica gel column to remove a paraffin provided (±)-**1** (3 mg, retention time 10.8 min) as an oil and 10-epi-(±)-**1** (3 mg, retention time 12.7 min); (±)-**1**: IR (CCl_4) 1670, 1658 (shoulder), 1612 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (d, J=7 Hz, 3H, CH_3), 1.73—1.51 (m, 6H, CH_3), 1.89 (d, J=1.5 Hz, 3H, CH_3), 2.2—1.8 (m, 3H, CH, CH_2), 2.6—2.2 (m, 5H, CH_2), 2.63 (dd, J_1=17 Hz, J_2=5 Hz, 1H, CH_2CO), 5.78 (br s, 1H, CH=). 10-epi-(±)-**1**: IR (CCl_4) 1670, 1657 (shoulder), 1612 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (d, J=7 Hz, 3H, CH_3), 1.62 (br s, 6H, CH_3), 1.90 (d, J=1.5 Hz, 3H, CH_3), 2.0—1.7 (m, 3H, CH, CH_2), 2.6—2.0 (m, 5H, CH_2), 2.59 (dd, J_1=17 Hz, J_2=6 Hz, 1H, CH_2CO), 5.78 (br s, 1H, CH=).

*2-Isopropylidene-6-methylspiro[4.5]deca-6,9-dien-8-one (**26**)*. Thionyl chloride (0.014 ml, 0.19 mmol) was added to an ice-cooled solution of **8c** (35 mg, 0.16 mmol) in 0.15 ml of dry pyridine and 0.3 ml of dry CH_2Cl_2 under N_2. After 10 min stirring, the reaction mixture was warmed to room temperature for 3.5 h. The mixture was quenched with a few pieces

of ice and the organic substances were worked up to give an oil, which was chromatographed (SiO_2, benzene: AcOEt=5: 1) providing **26** (24 mg, 75%) as colorless crystals: mp 80—82 °C (pentane) (lit. 82—83 °C)[5h]; IR (neat) 1662 (C=O), 1627, 1605 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.67 (br. s, 6H, CH_3), 2.00, 2.02 (2s, 3H, CH_3), 1.5—2.8 (m, 6H, CH_2), 5.9—6.3 (m, 2H, CH=), 6.92 (d, J=10 Hz, 1H, CH=).

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