Syntheses of Cecropia Juvenile Hormones by Selective Side-chain Methylation of (*E,E*)-Farnesol[1)]

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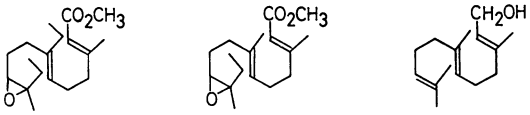
The stereoselective route to the title insect hormones (JH-1 & JH-2) depends crucially on the epoxidation of allylic alcohols with *t*-butyl hydroperoxide in the presence of oxobis(2,4-pentanedionato-*O,O'*)vanadium(IV). The oxidation of 2-methyl-1-hepten-3-ol exclusively produces the (2*R**,3*S**) isomer of the diastereomeric epoxy alcohols. This is converted into (*Z*)-6-methyl-5-undecene by the sequence involving oxirane reaction with lithium dibutylcuprate(I) and the removal of both hydroxyl groups of the resulting 1,2-diol. Extension of the series of reactions to the mono- and bisoxirane derived from (*E,E*)-farnesol gives JH-2 and JH-1, respectively.

Since C_{18}-Cecropia juvenile hormone (**1**), now called JH-1, was first synthesized in a nonstereoselective manner, no less than ten syntheses of **1** and the lower homolog, JH-2 (**2**), have appeared.[2)]



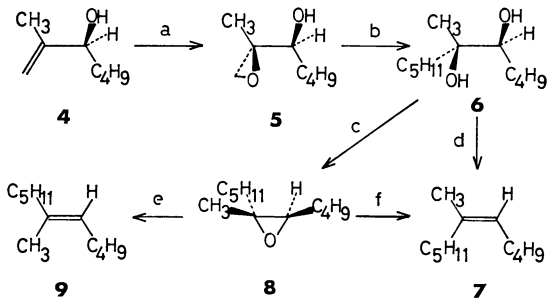
1 **2** **3**

Apparently of great interest are those routes which give only the required stereoisomer with the right configuration about each of the double bond. This paper presents a simple and efficient route starting from the readily available (*E,E*)-farnesol (**3**) and giving the desired products selectively.

The approach is based on a combination of catalyzed, stereoselective epoxidation of allylic alcohols and the transformation of the resulting glycidols into 3-alkylated 1,2-diols.

The principle is first illustrated with a simple example, then its application to syntheses of insect hormones being described.

Stereoselective Preparation of (Z)-6-Methyl-5-undecene (7) and Its Isomer (9). Sharpless *et al.* showed that catalytic epoxidation of cyclic allylic alcohols with *t*-butyl hydroperoxide proceeds with high degrees of stereoselectivity.[3)] The same technique can be successfully extended to a variety of acyclic allylic alcohols.[1)] Of special interest for the syntheses of **1** and **2** is the observation that epoxidation of the allylic alcohol **4** with $VO(acac)_2$–*t*-BuOOH reagent in benzene at room temperature produced (2*R**, 3*S**) epoxy alcohol **5** in 96% selectivity. This was improved (>99%) when the epoxidation was carried out in toluene at 0 °C. In contrast, *m*-chloroperbenzoic acid epoxidation of **4** gave a 62 : 38 mixture of (2*R**,3*S**) and (2*S**,3*S**) epoxy alcohols. The (2*R**,3*S**) structure of **5** was established, after acetylation, by GLPC comparison with the known data.[4,5)] Further study is required before stereochemical and mechanistic details can be understood.[6)] However, from the observation that cyclic allylic alcohols exhibit a strong preference for epoxidation *cis* to the hydroxyl group, we can assume that the preferred conformation of this allylic alcohol at the epoxidation transition state might be the one illustrated, close to that proposed in the case of cyclic allylic alcohols. The epoxy oxygen is then introduced on the same side as the hydroxyl group to give (2*R**,3*S**) epoxy alcohol **5**.[2,4,7)]



a) $VO(acac)_2$–*t*-BuOOH; b) Bu_2CuLi; c) BuLi, *p*-TsCl; d) $Me_2NCH(OMe)_2$, Ac_2O; e) NaI–AcOH, $SnCl_2$–$POCl_3$–C_5H_5N; f) $LiPPh_2$, MeI.

Treatment of the epoxy alcohol **5** with excess lithium dibutylcuprate(I) in ether at −26 °C for 2 h produced (5*R**,6*S**) diol **6** in 88% overall yield from **4**. As expected from earlier reports,[8)] dibutylcuprate-(I) exclusively attacked the unsubstituted carbon atom of the epoxide ring to furnish 1,2-diol as the sole product. Several methods for stereospecific deoxygenation of diols have been given;[9)] the one reported by Eastwood *et al.*[9c)] ($Me_2NCH(OMe)_2$, Ac_2O) afforded (*Z*)-6-methyl-5-undecene (**7**) in 80% yield. GLPC analysis of the olefin **7** displayed two peaks in the ratio 97 : 3. The major peak, having a shorter retention time, was ascribed to the *Z* isomer[10)] and this was supported by a vinyl methyl signal appearing at δ 1.65.[11)]

On the other hand, the geometrical isomer **9** was obtained from epoxide **8** by the Cornforth procedure[12)] in 80% yield, whose NMR spectrum supports the *E* configuration.[11)] The epoxide **8** was also converted into *Z* olefin **7** by treatment with lithium diphenylphosphide and then with methyl iodide (80% yield).[13)]

Stereospecific Synthesis of dl-*JH-2 (2).* Two methods of nonselective homologation of (*E,E*)-farnesol (**3**)

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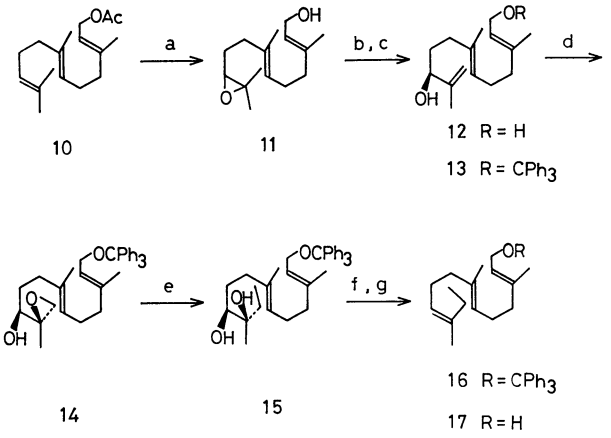
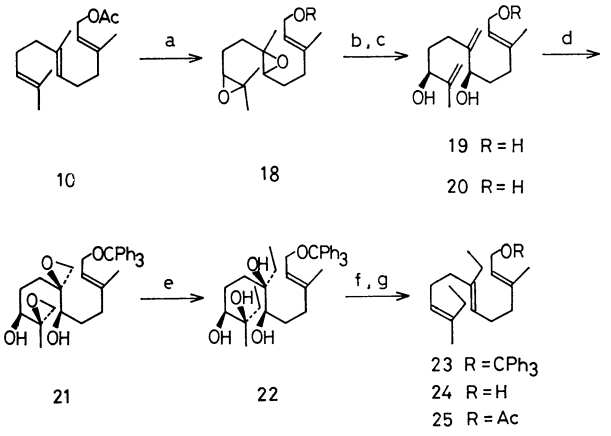
are known to afford a triene having the skeleton of JH-1 (**1**).[14,15] We now report a stereoselective route to hormones **1** and **2** which utilizes the series of reactions mentioned above.

The key intermediate in the synthesis of *dl*-JH-2 (**2**) is the allylic alcohol **13** prepared as follows. The epoxide **11**[16] was efficiently converted into bis-allylic alcohol **12** (90% yield) by reaction with diethyl-



a) NBS, NaOPr-*i*; b) Et_2Al-TMP; c) Ph_3CCl-*p*-TsOH; d) $VO(acac)_2$-*t*-BuOOH; e) Me_2CuLi; f) $(CH_3)_2NCH(OCH_3)_2$, Ac_2O; g) $HClO_4$.

aluminum 2,2,6,6-tetramethylpiperidide,[17] followed by tritylation of the primary hydroxyl group (88% yield). The trityl ether **13** was oxidized to the epoxy alcohol **14**[18] by the $VO(acac)_2$–*t*-BuOOH reagent and the resulting crude **14** was methylated to furnish the diol **15**[18] (81% yield after preparative TLC purification), which was found to be homogeneous upon TLC analysis. Application of the Eastwood procedure[9c] gave the triene trityl ether **16** stereospecifically in 55% yield. Removal of the protecting group by perchloric acid furnished the desired homofarnesol **17** almost quantitatively. The homogeneity of **17** was indicated by TLC analysis, its infrared and NMR spectra being identical with those obtained for homofarnesol.[19] The synthesis of JH-2 (**2**) from **17** has been reported.[19]



a) MCPBA, K_2CO_3; b) $LiNEt_2$; c) Ph_3CCl-*p*-TsOH; d) $VO(acac)_2$-*t*-BuOOH; e) $(CH_3)_2CuLi$; f) $(CH_3)_2OCH_3)_2$, Ac_2O; g) $HClO_4$.

Synthesis of dl-*JH-1 (1).* (*E,E*)-Farnesol (**3**) was transformed by the van Tamelen-McCormick procedure[15] into the triene trityl ether **20**. The conversion of the intermediate **20** into the bishomofarnesol **24** was accomplished by the sequence of steps described above. The IR and NMR spectra of **24** were entirely analogous to those reported,[15,19] its structure and homogeneity being further confirmed, after acetylation, by TLC and GLPC comparison with an authentic sample of the acetate **25**.[21] The transformation of **24** into JH-1 (**1**) has been reported.[15,19]

Experimental

IR spectra were determined on a Shimadzu IR-27-G spectrometer, mass spectra on a Hitachi RMU-6L mass spectrometer, and NMR spectra on a Varian EM-360 or JEOL-C-60-H spectrometer; chemical shifts are given in δ with tetramethylsilane as an internal standard. Microanalyses were carried out at the Elemental Analyses Center of Kyoto University, and GLPC analyses on a Yanagimoto GCG-550F. All experiments were carried out under an atmosphere of dry nitrogen or argon, preparative thin layer chromatography on silica gel 60 PF_{254} (Merck, Art. 7747) plates, and preparative column chromatography on silica gel 60 (Merck, Art. 7734).

(2R,3S*)-2-Methyl-1,2-epoxyheptan-3-ol (5).* *t*-Butyl hydroperoxide (90%, 600 mg, 6.0 mmol) was added dropwise over a period of 10 min at room temperature to a solution of 2-methyl-1-hepten-3-ol (**4**) (512 mg, 4.0 mmol) and oxobis-(2,4-pentanedionato-*O,O'*)vanadium(IV) (32 mg, 0.12 mmol) in benzene (15 ml). After being stirred at ambient temperature for 2 h, the resulting solution was poured into saturated aqueous sodium sulfite. The mixture was vigorously stirred for 20 min and extracted with ether. The ethereal phase was washed with water, dried (anhydrous sodium sulfate), and concentrated *in vacuo* to give the epoxy alcohol **5** as a pale yellow liquid: bp 80 °C (bath temp, 1 Torr); TLC, R_f 0.55 (3:1 hexane–ethyl acetate); IR (neat), 3400 (s), 1470 (m), and 1110 cm^{-1} (m); NMR (CCl_4), 1.28 (3H, s, CH_3–CO), 2.61 (2H, dd, CH_2–O), and 3.32—3.67 (1H, m, CH–OH).

A small aliquot was acetylated by stirring with acetic anhydride in pyridine. GLPC analysis (10% PEG 20 Mesh, 110 °C, 1.0 kg/cm^2) of the resulting acetates showed a peak at 6.5 min (96%), corresponding to the (2*R**,3*S**) epoxy acetate, and a small peak at 5.8 min (4%), corresponding to the (2*S**,3*S**) isomer: bp 80 °C (bath temp, 1 Torr); TLC, R_f 0.53 (1:1 hexane–ether); IR (neat), 1735(s), 1360 (m), 1230—1240(s), and 1110 cm^{-1}(m); NMR (CCl_4), 1.21 (3H, s, CH_3–CO), 1.91 (3H, s, CH_3–CO_2), 2.50 (2H, dd, CH_2–O), and 4.32 (1H, t, CH–O); MS (*m/e*), 186 (7), 156 (14), 144 (23), 127 (100), and 114 (52).

Found: C, 64.4; H, 9.5%. Calcd for $C_{10}H_{18}O_3$: C, 64.5; H, 9.7%.

(5R,6S*)-6-Methylundecane-5,6-diol (6).* Lithium dibutylcuprate(I) was prepared by the addition of 32.0 mmol (16.2 ml of 1.98 M hexane solution) of butyllithium to a vigorously stirred suspension of 3.04 g (16.0 mmol) of copper(I) iodide in 40 ml of ether at −26 °C. After being stirred at this temperature for 20 min, the crude epoxy alcohol **5** dissolved in 20 ml of ether was added at the same temperature. Stirring was continued for 2 h, then the product was isolated by quenching the reaction mixture in ether, filtering through a pad of Celite 545, extracting with ether, drying over sodium sulfate, and concentrating to give an

oil. Preparative TLC (3:1 hexane–ethyl acetate) afforded 663 mg (82% yield from **4**) of the (5*R**,6*S**) diol **6**, which showed a single spot of R_f 0.60 upon TLC analysis (3:1 hexane–ethyl acetate): bp 120 °C (bath temp, 1 Torr); IR (neat), 3450(s), 1470(m), and 1035 cm^{-1}(s); NMR ($CDCl_3$), 3.10—3.36 (1H, m, CH–OH); MS (*m/e*), 182 (18), 157 (36), 115 (36), 63 (100), and 57 (100).

Found: C, 71.2; H, 13.0%. Calcd for $C_{12}H_{26}O_2$: C, 71.2; H, 13.0%.

(Z)-6-Methyl-5-undecene (7). *A. From Diol 6*: A mixture of the (5*R**,6*S**) diol **6** (606 mg, 3.0 mmol) and *N,N*-dimethylformamide dimethyl acetal (3.0 ml) was stirred at room temperature for 17 h. After removal of the volatile material *in vacuo*, the resulting dioxolane derivative was heated in acetic anhydride (3.0 ml) at 130 °C for 17 h. The reaction mixture was allowed to cool to room temperature, poured into water, and the product was extracted with pentane. After being washed with saturated aqueous sodium hydrogencarbonate, saturated brine, and water, the organic phase was dried (Na_2SO_4), and concentrated. Column chromatography using pentane as an eluent gave (*Z*)-6-methyl-5-undecene (**7**) (403 mg, 80% yield) as a clear oil: bp 130 °C (bath temp, 24 Torr); TLC, R_f 0.80 (hexane); IR (neat), 1660—1675(w), 1385(m), and 840 cm^{-1}(w); NMR (CCl_4), 1.65 (3H, s, CH_3–C=), and 5.03 (1H, bt, CH=); MS (*m/e*), 168(12), 114(10), 94(31), 68(72), and 55(100).

Found: C, 85.8; H, 14.6%. Calcd for $C_{12}H_{24}$: C, 85.6; H, 14.4%.

B. From Oxirane 8: According to the procedure of Vedejs and Fuchs,[13] lithium diphenylphosphide in tetrahydrofuran (0.83 M) was prepared from chlorodiphenylphosphine (0.92 ml, 5.0 mmol) and lithium wire (140 mg, 20.0 mmol) in THF (5 ml). A solution of the oxirane **8** (184 mg, 1.0 mmol) in THF (5 ml) was added over a period of 5 min to the solution of lithium diphenylphosphide in THF (3.0 ml, 2.5 mmol) at ambient temperature. The resulting mixture was stirred at the same temperature for 17 h. Methyl iodide (0.27 ml, 4.3 mmol) was then added and the mixture was allowed to stand at room temperature for 1 h. After aqueous workup, the organic phase was dried (Na_2SO_4), and freed of the solvent. The residual liquid was subjected to column chromatography with pentane as an eluent to give pure olefin **7** (132 mg, 80% yield).

(E)-6-Methyl-5,6-epoxyundecane (8). A 1.83 M hexane solution of butyllithium was added dropwise at 0 °C to an ethereal solution (2 ml) of the diol **6** (202 mg, 1.0 mmol) containing a trace of 1,10-phenanthroline until the initially colorless solution turned orange. After 10 min, hexamethylphosphoric triamide (1 ml) and *p*-toluenesulfonyl chloride (229 mg, 1.2 mmol) were successively added and then the whole mixture was stirred at ambient temperature for 6 h. The crude product obtained on extractive workup was purified by preparative TLC (benzene) which furnished 166 mg (90% yield) of the oxirane **8**. GLPC analysis (10% PEG 20 Mesh, 90 °C, 1.0 kg/cm^2) showed the oxirane to be >97% pure: bp 86 °C (bath temp, 2 Torr); TLC, R_f 0.65 (benzene); IR (neat), 1470(s), 1376(m), and 1120 cm^{-1} (w); NMR ($CDCl_3$), 1.18 (3H, s, CH_3–CO), and 2.30—2.67 (1H, bt, CH–O); MS (*m/e*), 184(2), 155(6), 127(10), 114(18), and 58(100).

Found: C, 78.2; H, 13.3%. Calcd for $C_{12}H_{24}O$: C, 78.3; H, 13.0%.

(E)-6-Methyl-5-undecene (9). The oxirane **8** (80 mg, 0.44 mmol) was added to a cooled (−16 °C) solution of sodium iodide (150 mg, 1.0 mmol) and sodium acetate (15 mg, 0.18 mmol) in acetic acid (0.6 ml). After 1 h, the mixture was warmed to room temperature and poured into ether and aqueous sodium hydrogencarbonate. The ethereal solution was washed with a little sodium hydrogensulfite and water, dried (Na_2SO_4), and freed of the solvent. The resulting iodohydrin was added to a cooled (0 °C) solution of tin(II) chloride (230 mg, 1.21 mmol) in pyridine (0.9 ml). Phosphoryl chloride (0.06 ml, 0.40 mmol) in pyridine (0.2 ml) was then added with cooling, and the mixture was allowed to stand at room temperature overnight. After being diluted with hexane, the organic phase was washed with 1 M hydrochloric acid, and water, dried (Na_2SO_4), and concentrated. The crude product was subjected to column chromatography with hexane as an eluent. The olefin **9** (62 mg, 80% yield) was obtained as a colorless oil: bp 130 °C (bath temp, 24 Torr); TLC, R_f 0.80 (hexane); IR (neat), 1665—1675(w) and 840—860 cm^{-1}(sh); NMR (CCl_4), 1.59 (3H, s, CH_3–C=) and 5.05 (1H, bt, CH=); MS (*m/e*), 168 (16), 112(10), 96(30), 59(78), and 55(100).

Found: C, 85.7; H, 14.5%. Calcd for $C_{12}H_{24}$: C, 85.6; H, 14.4%.

(2E,6E)-3,7,12-Trimethyl-2,6,11-dodecatriene-1,10-diol (12). Diethylaluminum 2,2,6,6-tetramethylpiperidide was prepared *in situ* from diethylaluminum chloride (1.7 ml of 1.0 M benzene solution) and 1.68 mmol of lithium 2,2,6,6-tetramethylpiperidide in benzene (5 ml) at 0 °C for 30 min.[17] To this slurry was added dropwise the epoxy alcohol **11**[16] (80 mg, 0.34 mmol) dissolved in 4 ml of benzene at the same temperature. After being stirred for 2 h, 5 ml of 1 M hydrochloric acid was added. Ethereal extracts were dried (Na_2SO_4) and freed of the solvent. The remaining liquid was subjected to preparative TLC (5: 2 ether–hexane) to give pure **12** (71 mg, 90% yield); TLC, R_f 0.41 (2:1 ether–hexane); IR (neat), 3300—3420(s), 1650—1675(m), 1450 (m), 1000(m), and 895 cm^{-1}(m); NMR ($CDCl_3$), 1.59 (3H, s, CH_3–C= on C-3), 1.67 (3H, s, CH_3–C=, C-11), 3.86 (1H, bt, CH–OH), 3.97 (2H, d, CH_2–OH), 4.69 (2H, dd, CH_2=), and 4.82—5.40 (2H, m, CH=).

Microanalysis was performed after trimethylsilylation of both hydroxyl groups:

Found: C, 66.1; H, 11.2%. Calcd for $C_{21}H_{42}O_2Si_2$: C, 65.9; H, 11.1%.

(10R,11S*)-(2E,6E)-3,7,11-Trimethyl-1-trityloxy-2,6-tridecadiene-10,11-diol (15).* The diol **12** (71 mg, 0.31 mmol) was converted into the primary mono(trityl ether) **13** by reaction with trityl chloride (92 mg, 0.33 mmol) in 2 ml of pyridine at 50 °C for 2.5 h. Preparative TLC (1 : 1 hexane–ether) gave purified **13** (130 mg, 88% yield).

t-Butyl hydroperoxide (90%, 32 mg, 0.33 mmol) was added to a mixture of oxobis(2,4-pentanedionate-*O,O'*)-vanadium(IV) (11 mg, 0.04 mmol), the allylic alcohol **13** (130 mg, 0.27 mmol), and benzene (3 ml) as described above, yielding the epoxy alcohol **14** as a pale yellow liquid: TLC, R_f 0.68 (1 : 1 hexane–ether); NMR ($CDCl_3$), 1.23 (3H, s, CH_3–CO), 1.62 (3H, s, CH_3–C= on C-7), 1.95 (3H, s, CH_3–C=, C-3), 2.25—2.70 (2H, m, CH_2–O, C-12), 3.19 (1H, m, CH–O), 3.31—3.70 (2H, bd, CH_2–O, C-1), 5.03—5.52 (2H, m, CH=), and 7.00—7.40 (15 H, m, aromatic).

The crude epoxy alcohol **14** in ether (1 ml) was added at −26 °C to a solution of lithium dimethylcuprate(I) (0.56 mmol) in ether (3 ml) and the whole mixture was stirred at 0 °C for 12 h. According to the procedure described above, the trityl ether **15** (113 mg, 81% yield from **13**) was obtained as a pale yellow liquid after purification by preparative TLC (1 : 1 hexane–ether): TLC, R_f 0.54 (1 : 1 hexane–ether); IR (neat), 3410—3490(s), 1480(m), 1450 (s), 1380(m), and 1050 cm^{-1}(s); NMR ($CDCl_3$), 1.12 (3H, t, CH_3–CH_2), 1.45 (3H, s, CH_3–C= on C-7), 1.62 (3H, s,

CH_3–C= on C-3), 3.15—3.56 (1H, m, CH–OH), 4.94—5.53 (2H, m, CH=), and 7.05—7.45 (15H, m, aromatic).

Microanalysis was performed with the 10,11-*O*-isopropylidene-1-trimethylsilyl ether derivative:

Found: C, 69.1; H, 11.3%. Calcd for $C_{22}H_{42}O_3Si$: C, 69.1; H, 11.1%.

*(2E,6E,10Z)-3,7,11-Trimethyl-2,6,10-tridecatrien-1-ol (**17**).* The diol **15** (113 mg, 0.22 mmol) was transformed into the triene trityl ether **16** (56 mg, 55% yield) as described above for **7**: TLC, R_f 0.54 (3 : 1 petroleum ether–benzene); IR (neat), 1490(w), 1055(s), and 790 cm^{-1}(s); NMR ($CDCl_3$, 100 MHz), 0.95 (3H, t, J=8 Hz, CH_3–CH_2), 1.65 (6H, s, CH_3–C= on C-7 and C-11), 1.88—2.40 (12H, m, methylenes except C-1), 1.96 (3H, s, CH_3–C= on C-3), 3.60 (2H, d, J=7 Hz, CH_2–O), 5.09 (2H, bt, CH= on C-6, 10), 5.44 (1H, bt, CH= on C-2), and 7.16—7.68 (15H, m, aromatic).

The trityl ether **16** thus obtained was treated with 3 ml of 5% perchloric acid in tetrahydrofuran at 0 °C for 1.5 h. After being diluted with ether, the mixture was washed with water, saturated sodium hydrogencarbonate, and saturated brine, dried (Na_2SO_4), and concentrated *in vacuo*. Chromatography on silica gel (1 : 1 hexane–ether) gave the purified homofarnesol **17** (28 mg, 99% yield) which exhibited appropriate physical properties:[19] TLC, R_f 0.41 (2 : 1 ether–hexane); IR (neat), 3250—3380(s), 1665(m), 1450(s), 1380(s), and 1000—1020 cm^{-1} (s); NMR ($CDCl_3$, 100 MHz), 0.95 (3H, t, J=7 Hz, CH_3–CH_2), 1.58 (3H, s, CH_3–C=, C-3), 1.65 (6H, s, CH_3–C=, C-7, 11), 1.85—2.16 (11H, m, methylenes except C-1 and OH), 4.05 (2H, d, J=7 Hz, CH_2–OH), 4.89—5.14 (2H, m, CH=, C-6, 10), and 5.35 (1H, bt, CH=, C-2); MS (*m/e*), 236(2), 218(2), 160(5), 83(71), and 55(100).

*(2E,6E,10Z)-7-Ethyl-3,11-dimethyl-2,6,10-tridecatrien-1-ol (**24**).* According to the same procedure as aforementioned, compound **24** was obtained in 25% overall yield from the diol **20**.[15] The bisoxirane **21**:[18] TLC, R_f 0.68 (ethyl acetate); NMR ($CDCl_3$), 1.23 (3H, s, CH_3–CO), 1.95 (3H, s, CH_3–C=), 2.25—2.80 (4H, m, CH_2–O, C-7, C-12), 3.19 (2H, m, CH–OH), 3.31—3.70 (2H, bd, CH_2–O, C-1), 5.13—5.52 (1H, bt, CH=), and 7.00—7.40 (15H, m, aromatic). The tetrol **22**: TLC, R_f 0.60 (ethyl acetate); NMR ($CDCl_3$), 1.65 (3H, s, CH_3–C=), 2.90—3.35 (2H, m, CH–OH), 3.60 (2H, d, CH_2–O, C-1), 5.46 (1H, bt, CH=), and 7.10—7.55 (15H, m, aromatic). The bishomofarnesol **24** so obtained was spectrometrically identical with the reported data:[14,17] TLC, R_f 0.54 (1 : 1 hexane–ether); IR(neat), 3280—3370(s), 1665(w), 1450(s), 1380(m), and 1000—1020 cm^{-1}(s); NMR ($CDCl_3$, 100 MHz), 0.95 (6H, t, J=7 Hz, CH_3–CH_2), 1.65 (3H, s, CH_3–C= on C-3), 1.90—2.35 (13H, m, methylenes except C-1 and OH), 4.12 (2H, d, J=7 Hz, CH_2–OH), 5.04 (2H, bt, CH=, C-6, 10), and 5.40 (1H, t, J=7 Hz, CH=, C-2); MS (*m/e*), 232(3), 203(3), 175(5), 149(12), 83(50). and 55(100).

The structure and homogeneity of the alcohol **24** were further confirmed, after acetylation, by TLC and GLPC comparison with an authentic sample of acetate **25**. TLC analysis showed a single spot of R_f 0.24 (3 : 1 hexane–ether). The substance was found to be >93% pure by GLPC analysis (10% PEG 20 Mesh, 165 °C, 45 ml/min, 14.1 min retention time).

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18) Both the (10*R**,11*S**) configuration of **14**, and the (6*R**,7*S**,10*R**,11*S**) or (6*R**,7*S**,10*S**,11*R**) configuration of **21** were assumed on the stereochemical outcome of the previous example, as well as on the stereochemistry of the double bonds of the products **17** and **24**, since NMR analyses were not sufficiently effective. The stereochemical analysis of **21** was complicated by the fact that no stereochemical data were available allowing inference on the relative arrangement of the 6 and 10 positions in the MCPBA epoxidation step (**10**→**18**).

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