Rearrangement of Rosifoliol Epoxides: Transformation of Eudesmane to Valencane Sesquiterpene Types

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A study has been made of the rearrangement of derivatives of the eudesmane sesquiterpene, (+)-rosifoliol (3), to valencane structures. This biogenetically significant methyl migration has been accomplished *via* Lewis acid-catalysed epoxide opening.

The recognition by Robinson[1] that the structure of (−)-eremophilone (1) could be rationalised in biogenetic terms as resulting from rearrangement of a regular eudesmane precursor, such as (2), was of fundamental importance to the development of subsequent theories of terpene biosynthesis.[2] Some 25 years later the structural relationship of (+)-valencene (5) and (−)-agarospirol (6) could be rationalised on the basis of alternate rearrangements of a hypothetical eudesmane precursor. A proposed[3] structure (3) for this key biosynthetic intermediate in valencane biosynthesis was later assigned to the natural sesquiterpene (+)-rosifoliol which was isolated by Southwell[4] from the Australian native raspberry *Rubus rosifolius*. A subsequent *X*-ray analysis[5] provided interesting information concerning the steric interactions and conformation of (+)-rosifoliol (3) in the crystalline state. The *cis*-1,3-diaxial methyl–methyl interaction, which is thought to favour the methyl migration, is relieved somewhat by co-operative alteration of the torsion angles around the ring junction.

same initial protonation from the α-face of (3) with concomitant bond migration would give (−)-agarospirol (6). A transformation[4] of biosynthetic significance is the conversion of (+)-rosifoliol (3) into (−)-dihydroagarofuran (7), after treatment with mercuric acetate followed by sodium borohydride. This process from (3) to (7) *in vivo* represents the trapping of a C-1 carbonium ion, illustrated in the Scheme, by intramolecular attack by the tertiary alcohol at C-11.

Unfortunately rearrangement of eudesmenes using mineral acid or Lewis acid catalysis have been disappointing in terms of the biomimetic synthesis of eremophilane sesquiterpenes through C-15 methyl migration to a carbonium ion centre generated at C-1 from either a tertiary alcohol or a 1,10-double bond.[6] Indeed reaction of (+)-rosifoliol (3) with toluene-*p*-sulphonic acid in benzene at room temperature, afforded mainly (−)-δ-selinene (21).[4] Recent investigations[7] into the biosynthesis of the 10-*epi*-eremophilane sesquiterpene, capsidiol (9), have confirmed the methyl migration postulated by


(1)   (2)

(3)   (4)   (5)

(7)   (6)
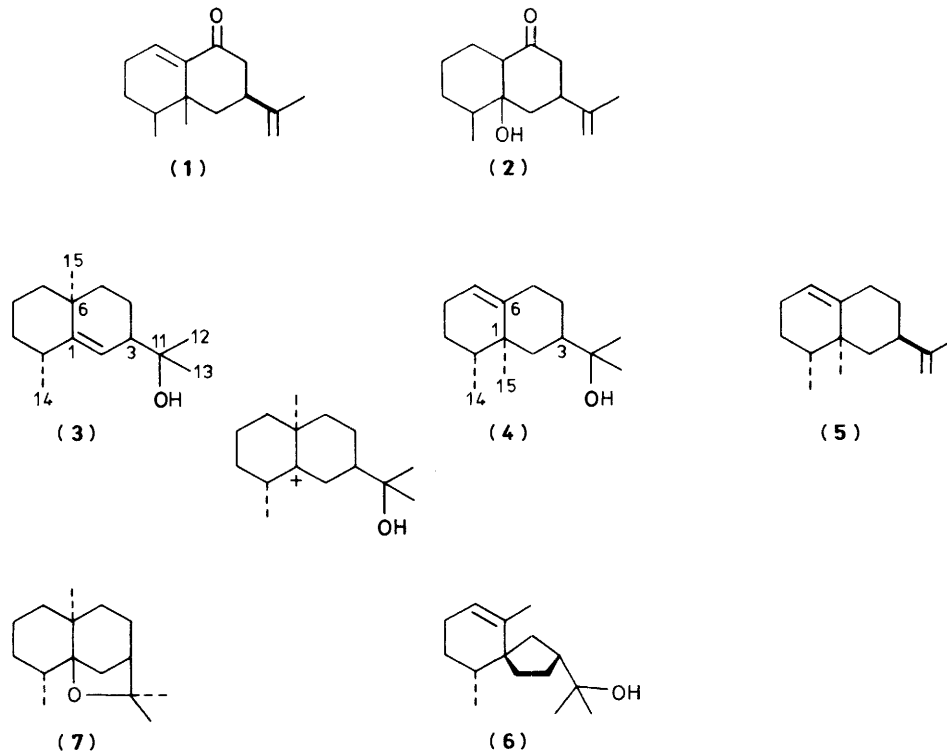
Scheme

From a biogenetic viewpoint protonation of the double bond in (3) from the β-face followed by methyl migration would afford (+)-valerianol (4) and thence to (+)-valencene (5) whereas the

Robinson and suggested the intermediacy of the epoxide (8). Rearrangements *in vitro* of the corresponding 1,10-epoxides (10) and (11) did not give the desired 1,2 migration of the methyl

group upon cleavage of the epoxide ring,[8] however the eudesmane–eremophilane transformation has been achieved by formic acid treatment of epoxydihydroalantolactone (12) which gave (13) amongst the products.[9] Our objective, therefore, was to utilise epoxide derivatives of (+)-rosifoliol (3) to investigate the biomimetic transformation of the eudesmane to the valencane sesquiterpene skeleton.

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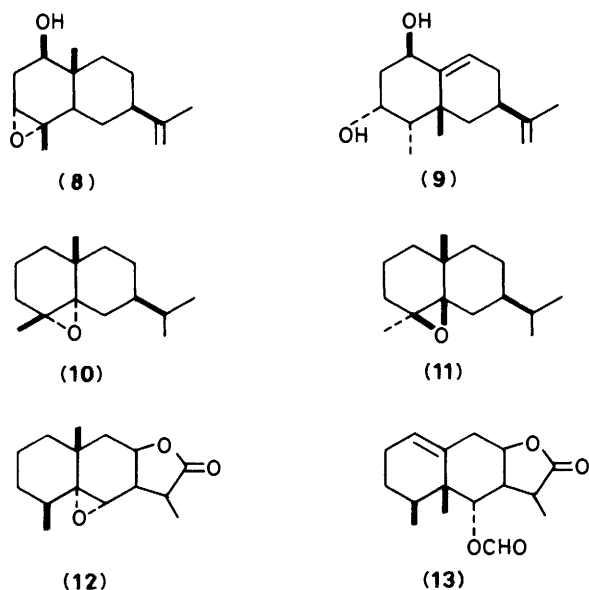
(+)-Rosifoliol (3) was readily epoxidised with m-chloroperbenzoic acid in ether to give a mixture of the epoxides (14) and (15) in the ratio 3:2 in which the major isomer was assigned as the β-epoxide. A minor by-product was 6α-hydroxydihydroagarofuran (16). Assignment of the stereochemistry of epoxidation could be made on the basis of intramolecular H-bonding in the β-epoxide which gave rise to distinctive


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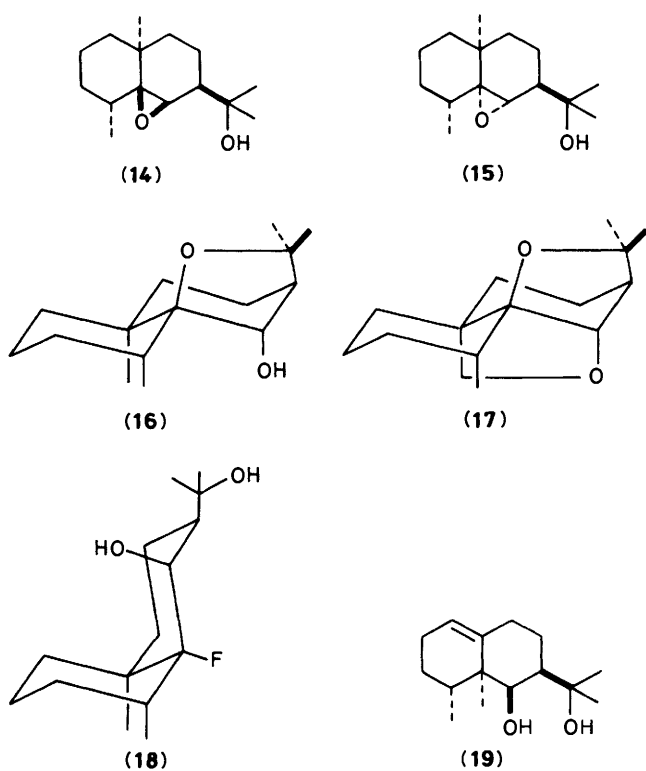
differences in the mode of cleavage of the isopropylol moiety in the mass spectra fragmentation. The minor product (16) exhibited an intense molecular ion together with the absence of significant contributions from m/z $M - 58$, $M - 59$, and 59 fragment ions typical of an isopropylol unit. The i.r. spectrum and the presence of a 1 H oxymethine doublet (δ 4.38, J 5 Hz) in the ^{1}H n.m.r. spectrum indicated a secondary alcohol function. It could readily be shown that (16) was an artifact produced by intramolecular attack of the hydroxy group on the α-epoxide (15). In order to establish the stereochemistry of the hydroxy substituent, (16) was treated with Pb(OAc)$_4$–I$_2$ in cyclohexane.[10] This produced a major product which was assigned structure (17) on the basis of n.m.r. data from which it could be deduced that the insertion reaction, leading to the tetrahydrofuran, involved the tertiary methyl group since (17) retained the secondary methyl substituent. Attempted epoxidation of (3) in either dichloromethane or benzene was difficult to control and proceeded beyond the epoxide stage to other products, the spectral data of which suggested further rearrangements to valencane or spirovetivane types. The complexity of these reactions precluded full characterisation of the products.

Treatment of rosifoliol α-epoxide (15) with formic acid at room temperature for 16 h gave no reaction, however boron trifluoride–diethyl ether in diethyl ether at −10 °C gave (16) in almost quantitative yield. Thus the tertiary alcohol function required protection to avoid premature trapping of the carbonium ion produced on opening of the epoxide ring. In the case of the β-epoxide (14) which has the cis relationship of the epoxide and isopropylol functions, a complex mixture of products was obtained on boron trifluoride treatment from which the fluorohydrin (18) was isolated. Incorporation of fluoride was indicated by n.m.r. data[11] and the structure (18) was proved by X-ray analysis.[12] The isolation of fluorohydrins from epoxides has precedent in both the steroid[13] and sesquiterpene[14] series. A second product from this reaction of boron trifluoride with (14) could only be assigned tentatively the valencene structure (19) on the basis of n.m.r. data.

In order to preclude the hydroxy function, which is present in (14) and (15), from participating in the rearrangement processes (+)-rosifoliol (3) was converted (83%) into the methyl ether (20) using n-butyl-lithium in tetrahydrofuran followed by methyl iodide. Treatment of (20) with formic acid or Lewis acids afforded the polymerisable olefin (−)-δ-selenine (21).[15] Using m-chloroperbenzoic acid in diethyl ether (20) yielded a 3:1 mixture of epoxides. The major isomer exhibited a relatively sharp oxymethine singlet at C-2 ($Wh/2$ 3 Hz) which is consistent with the dihedral angle between the 2-H and the 3-H of close to 90° found on inspection of the Dreiding model of the α-epoxide (22). By comparison the β-epoxide (23) was found to have a broader downfield oxymethine signal ($Wh/2$ 6 Hz).

Preliminary investigation showed that ethyl aluminium dichloride (EtAlCl$_2$) was the Lewis acid which gave the least complex mixture of products from the α-epoxide (22). Treatment of (22) with catalytic amounts of EtAlCl$_2$ in benzene gave a reproducible mixture of six components five of which were identified after careful chromatographic separation. The major product has been assigned structure (24) which is enantiomeric with cogeijerene reported by Sutherland.[16] The u.v. and i.r. spectra of the EtAlCl$_2$ product agree with those published for cogeijerene except for the low optical rotation quoted in the literature. This may be attributed to the unexpected facile polymerisation of the diene (24). A further product which proved to be extremely prone to polymerisation was identified as the triene (25) from consideration of n.m.r. and u.v. data. A possible intermediate in the formation of (24) and (25) is the diene (26), and a third compound which was also isolated from the reaction of (22) with EtAlCl$_2$ could be assigned this structure, (26), on the basis of analysis (C$_{16}$H$_{26}$O), u.v.

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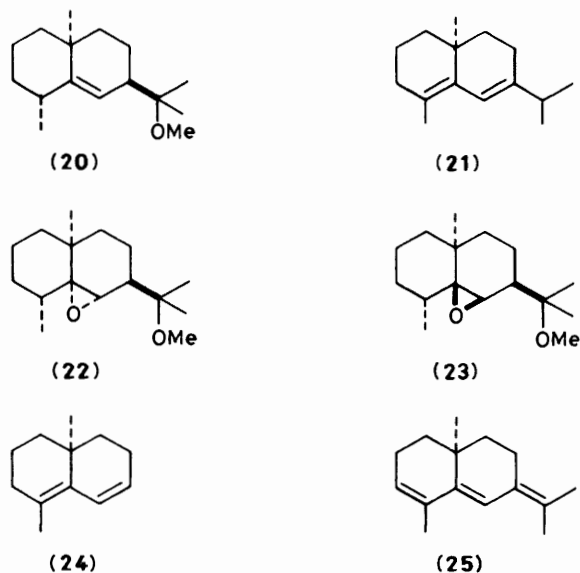
maxima (λ 240 nm, ε 21 800) and the n.m.r. data. The n.m.r. results showed retention of the methoxyisopropyl and angular methyl groups, as well as the presence of one vinyl-CH_3 and two vinyl-H resonances but the absence of the epoxide ring methine and the secondary methyl group.

Although products (24), (25), and (26) serve to illustrate one reaction pathway resulting from Lewis acid treatment of epoxides, greater interest in the case of (22) would be the isolation of rearranged products such as (27) or (28). Two components of the reaction of (22) with EtAlCl$_2$ in benzene were shown to be isomers of composition $C_{16}H_{28}O_2$ and could be assigned structures (27) and (28) respectively. From i.r. and n.m.r. data it was clear that the products were secondary alcohols in which the oxymethine resonances (δ 3.65 and 3.46 in the isomers) exhibited strong vicinal coupling (J 10 Hz) indicating a *trans* relationship for 2-H and 3-H. The presence in each isomer of only one vinyl-H signal, the presence of secondary and tertiary methyl resonances, and the absence of signals due to vinyl-CH_3 groups indicated that the rearranged products were (27) and (28) rather than the spirovetivane structure (29). The valencenes were formed in the ratio 5:2 and assigned structures (27) and (28) respectively although the

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(27) $\triangle^{6.7}$

(28) $\triangle^{5.6}$

(29)
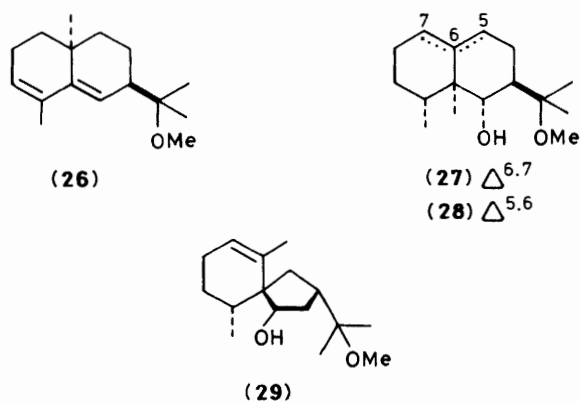
structural dinstinction between the isomers could not be made unambiguously on the basis of Eu(fod)$_3$-induced chemical shifts. The observation that the methyl migration is preferred over ring contraction during EtAlCl$_2$-induced rearrangement of the α-epoxide (22) suggests that the pathway involves considerable carbonium ion character at C-1 in the first stage

during the fission of the C–O bond of the epoxide–EtAlCl$_2$ complex. Thus the polarisation of the C–O must be well developed before the C(6)–C(15) bond breaks with the migration of the methyl group. The intermediacy of a carbonium ion-like transition state during rearrangement of (22) is consistent with the large number of products observed.

In the case of the β-epoxide (23), however, the *trans*-stereochemical relationship of the tertiary methyl substituent with the epoxide function would favour a more synchronised *trans*-concerted migration of the methyl group concomitant with the Lewis acid-induced ring opening. As predicted the β-epoxide (23) rearranged smoothly to give a 4:1 mixture of isomeric products subsequently assigned as the 2β-hydroxy-valencenes (30) and (31) in 70% yield. The presence of D$_2$O exchangeable protons in both isomers (δ 4.17 and 4.38) in addition to vinyl-H signals (δ 5.35 and 5.55; J 5 Hz) secondary methyl (δ 0.89 and 0.86; J 7 Hz), three tertiary methyl (δ 0.88, 1.19, 1.32/0.84, 1.21, 1.33) and methoxy signals (δ 3.21 and 3.17) suggested that rearrangement to the valencenes (30) and (31) had occurred. The chemical shifts of the equatorial oxymethine protons, 2-H (δ 4.03 and 4.04) were downfield of the axial counterparts in (27) and (28) by 0.5 p.p.m. which is consistent with predicted values.[17] The small vicinal coupling between 2-H and 3-H indicated an equatorial–axial (or equatorial–equatorial) relationship and is in accord with Dreiding models of (30) and (31). Again a distinction between (30) and (31) could not be

(30) $\triangle^{6.7}$

(31) $\triangle^{5.6}$
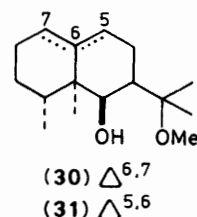
made unambiguously by Eu(fod)$_3$-induced chemical shifts since the angle factor of the McConnell-Robertson relationship[18] is very close to the crucial 54° where Eu changes sign. As in the case of the 2α-hydroxy series the n.m.r. data was in support of the valencane structures and not in accord with spiro-structures which would result from the alternative rearrangement process. Intuitively, the assignment of the major isomer as (30) agrees with the preferred extended relationship of the epoxide ring with the migrating methyl group and the C–H bond broken in the concluding step of the rearrangement process leading to the 2β-hydroxyvalencenes from the β-epoxide (23). The favoured formation of the $\triangle^{5.6}$ isomer from the concerted rearrangement process would also reflect the predominance of the $\triangle^{5.6}$ isomers in nature.[19] Since both α- and β-epoxides (22) and (23) gave different products which could be separated by chromatography it was decided to use the mixture of epoxides for the isolation of the products (24), (25), (26), (27), (28), (30), and (31) on a preparative scale, thus dispensing with the difficult separation of the epoxides bearing in mind the scarcity of (+)-rosifoliol (3). Although acetylation of (30)/(31) could be effected, it was found that oxidation could not be achieved even by a number of methods (Jones reagent, pyridinium chlorochromate, pyridinium dichromate, or t-butyl hypochlorite).

Thus, we have succeeded in effecting the biomimetic transformation of (+)-rosifoliol (3) into valencene derivatives through rearrangement of the α- and β-epoxides (22) and (23). Comparison of both the efficiency and product complexity in each case illustrates the great stereochemical requirements for the *in vivo* processes involved in the biosynthesis of eremophilane and valencane sesquiterpenes.

Experimental

I.r. spectra, calibrated against polystyrene at 1 603 cm⁻¹, were recorded on a Perkin-Elmer 197 spectrophotometer as liquid film or Nujol mull and u.v. spectra were obtained in EtOH solution using Varian Cary 118X or Pye Unicam SP8-100 instruments. ¹H N.m.r. spectra were recorded with Varian SC300 (300 MHz), Perkin-Elmer R32 (90 MHz), and R34 (220 MHz) instruments and ¹H, ¹⁹F n.m.r. spectra were measured using a Bruker WP80 machine. 360 MHz Spectra were measured by Dr. I. Sadler (Edinburgh). Mass spectra were obtained using AEI MS902 and MS45 instruments. Melting points were determined on a Buchi 510 and are uncorrected as are boiling points. Optical rotations were measured using a Thorn Automation–NPL Automatic Polarimeter type 243 calibrated against a standard camphor solution using a 1 cm cell. Gas-liquid chromatography was carried out using a Carlo-Erba Strumentazione instrument using a 40 ft wall-coated open tubular OV 101 column and a Pye Unicam 204 instrument using a 40 ft wall-coated open tubular F.F.A.P. column with temperature programme 100—220 °C (10 °C/5 min). T.l.c. was carried out on silica gel (Fluka GF 254) and examined by u.v. light at 254 and 366 nm or by staining in iodine vapour. Preparative chromatography was performed on aluminium oxide Fluka type 507C. Flash column chromatography was carried out on Kieselgel 60H (Merck). (+)-Rosifoliol (3), m.p. 81—82 °C, was isolated[4] from the shrub *Rubus rosifolius* collected from north-eastern N.S.W., Australia. Petroleum refers to light petroleum and ether to diethyl ether throughout.

Epoxidation of (+)-*Rosifoliol* (3).—A solution of (+)-rosifoliol (3) (190 mg, 0.86 mmol) in dry ether (10 ml) was treated with *m*-chloroperbenzoic acid (365 mg, 2.11 mmol) in ether (10 ml) at room temperature for 16 h in the dark. The solution was diluted with ether (50 ml), washed with aqueous sodium bisulphite (15 ml), aqueous sodium hydrogen carbonate (2 × 15 ml), and brine (15 ml), and then dried (MgSO₄) and evaporated to dryness to give a colourless oil (206 mg). Chromatography of this oil over alumina and elution with 5% ether in petroleum gave (−)-6α-hydroxydihydroagarofuran (16) (8 mg, 4%), m.p. 147—148 °C (Found: C, 75.6; H, 11.3. C₁₅H₂₆O₂ requires C, 75.6; H, 11.0%); [α]_D²⁰ −82.5° (c 0.2 EtOH); ν_max. 3 380, 1 290, 1 240, 1 162, 1 140, 1 110, 952, 935, and 921 cm⁻¹; δ_H (300 MHz; CDCl₃) 1.21 (3 H, s, 15-Me), 1.22 (3 H, d, J 8 Hz, 10-Me), 1.30 (3 H, s, 12- or 13-Me), 1.32 (3 H, s, 13- or 12-Me), 1.60 (1 H, s, OH), 1.84 (1 H, m), and 2.08 (1 H, m), 4.38 (1 H, d, J 4 Hz, 2-H); m/z 238.1936 (M⁺, C₁₅H₂₆O₂, 18%), 223.1700 (C₁₄H₂₃O₂, 7), 126.1050 (C₈H₁₅O, 100).

Elution with 20% ether in petroleum gave (+)-rosifoliol β-epoxide (14) (95 mg, 47%), m.p. 55—57 °C (Found: C, 75.6; H, 11.3. C₁₅H₂₆O₂ requires C, 75.6; H, 11.0%); [α]_D²⁰ +37.5° (c 0.2 in EtOH); ν_max. 3 350, 1 160, 940, 910, 850, 797, and 750 cm⁻¹; δ_H (300 MHz; CDCl₃) 1.10 (3 H, d, J 8 Hz, 10-Me), 1.12 (3 H, s, 15-Me), 1.24 (3 H, s, 12- or 13-Me), 1.34 (3 H, s, 13- or 12-Me), 1.78 (2 H, m), 1.88 (1 H, m), 2.10 (1 H, s, OH), and 3.13 (1 H, d, J 3 Hz, 2-H); m/z 220.1849 (C₁₅H₂₄O, 2%), 202.1712 (C₁₅N₂₂, 28), 187.1460 (C₁₄H₁₉, 21), 180.1534 (C₁₂H₂₀O, 40), 39.8425 (100).

Elution with 50% ether in petroleum gave (−)-rosifoliol α-epoxide (15) (67 mg, 33%), m.p. 66—67 °C (Found: C, 75.8; H, 10.7. C₁₅H₂₆O₂ requires C, 75.6; H, 11.0%); [α]_D²⁰ −14.1° (c 0.3 in EtOH); ν_max. 3 430, 1 160, 938, and 898 cm⁻¹; δ_H (300 MHz; CDCl₃) 1.06 (3 H, s, 15-Me), 1.09 (3 H, d, J 7 Hz, 10-Me), 1.24 (3 H, s, 12- or 13-Me), 1.26 (3 H, s, 13- or 12-Me), and 2.90 (1 H, s, 2-H); m/z 238.1923 (M⁺, C₁₅H₂₆O₂, 3%), 220.1817 (C₁₅H₂₄O, 4), 179.1428 (C₁₂H₁₉O, 38), 161.1324 (C₁₂H₁₇, 17), and 97.0650 (C₆H₉O, 100).

Lead Tetra-acetate–Iodine Treatment of (16).—A mixture of lead tetra-acetate (2.0 g), moist with acetic acid, and calcium

carbonate (600 mg) was refluxed in cyclohexane (30 ml) for 5 min. Iodine (480 mg) was added and the whole refluxed with irradiation (300 W lamp). After 1 h when the solution had almost decolourised, a solution of (16) (207 mg, 0.83 mmol) was added together with a further crystal of iodine and refluxing with irradiation continued for 3 h. The mixture was cooled, filtered through Celite (5 g), and washed with ether (3 × 10 ml). The organic phase was then washed with 10% aqueous sodium thiosulphate (3 × 10 ml), water, and brine, dried (MgSO₄), and concentrated. Elution from alumina with 2 and 5% ether in petroleum gave the bis-ether (17) (94 mg, 48%), m.p. 21—24 °C (Found: C, 76.3; H, 10.2. C₁₅H₂₄O₂ requires C, 76.2; H, 10.2%); [α]_D²⁰ −70° (c 2.2 in EtOH); ν_max. 1 300—800 cm⁻¹ complex 20 peaks); δ_H (300 MHz, CDCl₃) 1.16 (3 H, d, J 8 Hz, 10-Me), 1.21 (3 H, s, 12- or 13-Me), 1.32 (3 H, s, 13- or 12-Me), 3.76 (1 H, d, J 8.5 Hz, 15-H), 4.07 (1 H, dd, J 2.5, 8.5 Hz, 15-H_B), and 4.69 (1 H, d, J 5 Hz, 2-H); m/z 236.1786 (M⁺, C₁₅H₂₄O₂, 29%), 221.1540 (C₁₄H₂₁O₂, 100), 191.1436 (C₁₃H₁₉O, 81), and 161.1331 (C₁₂H₁₇, 24).

Boron Trifluoride Treatment of (14).—A solution of (+)-rosifoliol β-epoxide (14) (130 mg, 0.55 mmol) in dry ether (50 ml) was treated with boron trifluoride–ether (320 mg, 2.25 mmol) at −10 °C. After 16 h the solution was washed with 5% aqueous sodium hydrogen carbonate (2 × 10 ml), dried (MgSO₄), and concentrated. The crude product (120 mg) was chromatographed over grade 3 alumina. Elution with 20% ether in petroleum gave (18) (22 mg, 14%) which was crystallised from hexane as white needles, m.p. 150 °C; ν_max. 3 350, 3 200, 1 180, 1 018, 998, 970, and 955 cm⁻¹; δ_H (360 MHz; CDCl₃) 1.0 (1 H, br), 1.03 (3 H, d, J 1.2 Hz, 15-Me), 1.12 (3 H, dd, J 2.1, 7.6 Hz, 10-Me), 1.24 (1 H, t, J 3.4 Hz), 1.28 (3 H, s, 12- or 13-Me), 1.38 (3 H, s, 13- or 12-Me), 1.53 (1 H, s, OH), 1.77 (1 H, s, OH), 2.15 (2 H, m), 2.28 (1 H, m), and 4.05 (1 H, d, J 9 Hz, 2-H); δ_F (80 MHz; CDCl₃) 85.003 (Wh/2 21.6, CF) ¹H decoupled: Wh/2 0.88 Hz; m/z 243.1750 (C₁₄H₂₄FO₂, 1.4%), 240.1885 (C₁₅H₂₅FO, 2.6), 225.1658 (C₁₄H₂₂FO, 5), 222.1784 (C₁₅H₂₃F, 5), 220.1816 (C₁₅H₂₄O, 4), 207.1537 (C₁₄H₂₀F, 2), 205.1587 (C₁₄H₂₁O, 5), 202.1723 (C₁₅H₂₂, 3), 187.1477 (C₁₄H₁₉, 4), 182.1463 (C₁₂H₁₉F, 21), and 162.1401 (C₁₂H₁₈, 100). Elution with 5% ethanol in ether gave a colourless oil (24 mg, 18%) tentatively assigned as (19), ν_max. 3 380, 1 155, 975, 905, and 818 cm⁻¹, δ_H (360 MHz; CDCl₃) 0.89 (3 H, d, J 7 Hz, 10-Me), 0.90 (3 H, s, 15-Me), 1.21 (3 H, s, 13- or 12-Me), 1.37 (3 H, s, 13- or 12-Me), 1.56 (1 H, s, OH), 2.09 (2 H, br), 2.3 (1 H, m), 4.08 (1 H, s, 2-H), and 5.37 (1 H, d, J 5.3, 7-H).

Boron Trifluoride Treatment of (15).—A solution of (+)-rosifoliol α-epoxide (15) (151 mg, 0.63 mmol) in ether (20 ml) was treated with boron trifluoride–ether (0.6 ml, 4.23 mmol) at −10 °C. After 16 h the solution was diluted with ether (30 ml), washed with 10% aqueous sodium hydrogen carbonate, dried (MgSO₄), and concentrated to give the product (150 mg) which was crystallised to give (16); this was identical with the product prepared previously.

Rosifoliol Methyl Ether (20).—(+)-Rosifoliol (3) (200 mg, 0.9 mmol) in dry tetrahydrofuran (3.0 ml) was added to n-butyl-lithium in hexane (1.6M; 1 ml, 1.6 mmol). Methyl iodide (0.5 ml, 1.14 g, 8.03 mmol) was added and, after 16 h at room temperature, the solution was diluted with ether (10 ml), washed with water (5 ml) and brine (5 ml), dried (MgSO₄), and concentrated to give a colourless oil. Chromatography on alumina (6.0 g) and elution with petroleum gave (+)-rosifoliol methyl ether (20) as a colourless oil (124 mg, 54.8%) (Found: C, 81.3; H, 11.9. C₁₆H₂₈O requires C, 81.3; H, 11.7%); [α]_D²⁰ +80° (c 1.9 in EtOH); ν_max. 2 940, 1 640, 1 470, 1 380, 1 365, 1 150, 1 120, 1 080, 1 025, 940, 860, and 840 cm⁻¹; δ_H (220 MHz;

CDCl$_3$) 1.09 (3 H, s, 15-Me), 1.10 (3 H, s, 12- or 13-Me), 1.12 (3 H, s, 13- or 12-Me), 1.15 (3 H, d, J 8 Hz, 10-Me), 2.24 (1 H, ddd, J 3, 3, 4 Hz, 3-H), 2.49 (1 H, m), 3.21 (3 H, s, OMe), and 5.37 (1 H, d, J 3 Hz, 2-H); m/z 204.1877 (C$_{15}$H$_{24}$, 90%), 202.1718 (C$_{15}$H$_{22}$, 30), 200.1560 (C$_{15}$H$_{20}$, 17), 189.1663 (C$_{14}$H$_{21}$, 94), and 161.1324 (C$_{12}$H$_{17}$, 100).

Formic Acid Treatment of (**20**).—(+)-Rosifoliol methyl ether (**20**) (25 mg, 0.11 mmol) was treated with formic acid (30 mg, 0.65 mmol) at 70 °C for 30 min, after which the mixture was diluted with ether (10 ml). The solution was washed with 5% aqueous sodium hydrogen carbonate (5 ml) and brine (2 ml), dried (MgSO$_4$), and concentrated to give (−)-δ-selenine (**21**) (20 mg, 0.1 mmol, 91%).[19]

Ethyl Aluminium Dichloride Treatment of (**20**).—(+)-Rosifoliol methyl ether (**20**) (20 mg, 0.09 mmol) in cyclohexane (0.1 ml) was treated with ethyl aluminium dichloride (25% solution in hexane; 0.02 ml, 0.04 mmol) under nitrogen at room temperature. After 16 h the resultant wine-red solution was quenched with 10% aqueous ammonium chloride, diluted with ether, washed with brine, dried (MgSO$_4$), and concentrated to give a colourless oil (18 mg) shown by g.l.c. to be 77% (−)-δ-selinene (**21**).[19]

Epoxidation of (+)-*Rosifoliol Methyl Ether* (**20**).—A solution of (**20**) (180 mg, 0.76 mmol) in dry ether (10 ml) was treated with *m*-chloroperbenzoic acid (180 mg, 1.04 mmol) in dry ether (10 ml) for 16 h at room temperature in the dark. The solution was diluted with ether (20 ml), washed with 10% aqueous sodium bisulphite (10 ml), 5% aqueous sodium hydrogen carbonate (2 × 10 ml), and brine (10 ml), dried (MgSO$_4$), and concentrated to give a colourless oil containing two products in the ratio 1 : 3 by g.l.c. and ^{1}H n.m.r. integration. Chromatography on alumina and elution with 2% ether in petroleum gave (+)-rosifoliol methyl ether β-epoxide (**23**) (10 mg, 5%) (Found: C, 76.2; H, 11.2. C$_{16}$H$_{28}$O$_2$ requires C, 76.1; H, 11.2%); $[\alpha]_D^{20}$ +25° (*c* 2.6 in EtOH); $\nu_{max.}$ 2 940, 1 470, 1 385, 1 365, and 1 080 cm^{-1}; δ_H (220 MHz; CDCl$_3$) 1.12 (3 H, d, J 8 Hz, 10-Me), 1.13 (3 H, s, 15-Me), 1.17 (3 H, s, 12- or 13-Me), 1.26 (3 H, s, 13- or 12-Me), 2.13 (1 H, m), 2.99 (1 H, s, 2-H), and 3.20 (3 H, s, OMe).

Elution with further 2% ether in petroleum gave an epoxide mixture (**22**)/(**23**) (87 mg) followed by the α-epoxide (**22**) (30 mg, 16%) (Found: C, 75.9; H, 10.9. C$_{16}$H$_{28}$O$_2$ requires C, 76.1; H, 11.2%); $[\alpha]_D^{20}$ −5° (*c* 2.1 in EtOH); $\nu_{max.}$ 2 940, 1 470, 1 460, 1 385, 1 370, 1 080 and 900 cm^{-1}; δ_H (220 MHz; CDCl$_3$) 1.09 (3 H, s, 15-Me), 1.12 (3 H, d, J 8 Hz, 10-Me), 1.18 (3 H, s, 12- or 13-Me), 1.20 (3 H, s, 13- or 12-Me), 1.92 (1 H, t, J 9 Hz, 3-H), 2.90 (1 H, s, 2-H), and 3.23 (3 H, s, OMe); m/z 252.2082 (C$_{16}$H$_{28}$O$_2$, 1.2%), 220.1827 (C$_{15}$H$_{24}$O, 11), 205.1589 (C$_{14}$H$_{21}$O, 8), 202.1715 (C$_{15}$H$_{22}$, 5), 177.1296 (C$_{12}$H$_{17}$O, 29), and 73.0613 (C$_4$H$_9$O, 100).

Ethyl Aluminium Dichloride Treatment of (**22**).—The α-epoxide (**22**) (10.5 mg, 0.04 mmol) in dry benzene (1 ml) was treated at room temperature to cautious additions of ethyl aluminium dichloride (8% in benzene). With the addition of each drop of reagent the solution developed a transient yellow colouration. The addition was stopped when the yellow colour persisted and the reaction was immediately terminated by adding water and shaking. The organic layer was dried (MgSO$_4$) and concentrated to reveal a pale yellow oil ($\nu_{max.}$ 3 440, 1 610, and 1 080 cm^{-1}). G.l.c. showed the presence of six products constituting 31, 24, 8, 16, 6, and 6% of the oil in order of elution.

Ethyl Aluminium Dichloride Treatment of (**23**).—The β-epoxide (**23**) (6 mg, 0.02 mmol) in dry benzene was treated with ethyl aluminium dichloride in benzene as above and, after work-

up, afforded a colourless oil ($\nu_{max.}$ 3 480 and 1 070 cm^{-1}). G.l.c. and ^{1}H n.m.r. showed 70% of two isomers (**30**) and (**31**) present in the ratio of 4 : 1.

Ethyl Aluminium Dichloride Treatment of the Epoxide Mixture (**22**)/(**23**).—A solution of the mixture of the (80%) and (20%) epoxides (**22**)/(**23**) (580 mg, 2.3 mmol) in dry benzene (10 ml) was treated at room temperature to cautious additions of ethyl aluminium dichloride as above. After addition of 1.3 ml of reagent (0.8 mmol) the solution was worked up to give a pale yellow oil (440 mg) which was chromatographed on alumina. Elution with petroleum gave (−)-epicogeigerene (**24**) (87 mg, 23%) (Found: C, 88.8; H, 11.1. Calc. for C$_{12}$H$_{18}$: C, 88.8; H, 11.1%); $[\alpha]_D^{20}$ +51.5° (*c* 0.7 in EtOH); $\nu_{max.}$ 2 910, 1 640br, 1 455, 1 375, 1 150, and 880 cm^{-1}; $\lambda_{max.}$ 242 (ε 17 200), 236sh (10 600), and 251sh nm (12 300), δ_H (220 MHz; CDCl$_3$) 0.97 (3 H, s, angular-Me), 1.67 (3 H, s, vinyl-Me), 5.65 (1 H, m, 3-H), and 6.35 (1 H, d, J 10 Hz, 2-H); m/z 162.1404 (C$_{12}$H$_{18}$, 45%), 147.1174 (C$_{11}$H$_{15}$, 100), 105.0711 (C$_8$H$_9$, 42), and 91.0547 (C$_7$H$_7$, 33). Further elution with petroleum gave the readily polymerisable triene (**25**) (18 mg, 4%); $[\alpha]_D$ +51.5° (*c* 0.7 in EtOH); $\nu_{max.}$ 2 910, 1 640br, 1 455, 1 375, 1 150, and 880 cm^{-1}; $\lambda_{max.}$ 283 (ε 15 000), 295 (12 300), and 273sh nm (11 200); δ_H (220 MHz; CDCl$_3$) 0.92 (3 H, s, 15-Me), 1.73 (3 H, s, 14-Me), 1.80 (6 H, s, 12- and 13-Me), 5.60 (1 H, m, 2-H), and 6.32 (1 H, s, 9-H); m/z 202.1706 (C$_{15}$H$_{22}$, 5%), 200.1560 (C$_{15}$H$_{10}$, 7), 187.1474 (C$_{14}$H$_{19}$, 5), and 185.1328 (C$_{14}$H$_{17}$, 8).

Continued elution with petroleum gave (**26**) (103 mg, 19%) (Found: C, 82.2; H, 11.0. C$_{16}$H$_{26}$O requires C, 82.0; H, 11.0%); $[\alpha]_D^{20}$ +260° (*c* 2.7 in EtOH); $\nu_{max.}$ 2 960, 2 940, 2 910, 1 620, 1 470, 1 455, 1 380, 1 365, 1 140, 1 080, 870, and 790 cm^{-1}; $\lambda_{max.}$ 240 (ε 21 800), 235sh (15 400), and 247sh nm (14 100); δ_H (220 MHz; CDCl$_3$) 0.95 (3 H, s, 6-Me), 1.10 (3 H, s, 12- or 13-Me), 1.17 (3 H, s, 13- or 12-Me), 2.05 (1 H, m, 8-H$_A$), 2.24 (1 H, m, 8-H$_B$), 2.44 (1 H, m, 3-H), 3.23 (3 H, s, OMe), 5.55 (1 H, m, 9-H), and 5.57 (1 H, d, J 4 Hz, 2-H); m/z 234.1974 (C$_{16}$H$_{26}$O, 1%), 219.1749 (C$_{15}$H$_{23}$O, 2), 202.1721 (C$_{15}$H$_{22}$, 7), and 73.0562 (C$_4$H$_9$O, 100).

Elution with 1% ether in petroleum gave (**27**) (50 mg, 9%) (Found: C, 76.4; H, 11.2. C$_{16}$H$_{28}$O$_2$ requires C, 76.1; H, 11.2%); $\nu_{max.}$ 3 430, 2 980, 2 940, 2 850, 1 465, 1 385, 1 375, 1 065, and 1 035 cm^{-1}; δ_H (220 MHz; CDCl$_3$) 1.01 (3 H, s, 15-Me), 1.10 (3 H, d, J 7 Hz, 14-Me), 1.15 (3 H, s, 12- or 13-Me), 1.30 (3 H, s, 13- or 12-Me), 3.25 (3 H, s, OMe), 3.65 (1 H, d, J 10 Hz, 2-H), 5.22 (1 H, d, J 5 Hz, 5-H), and 5.34 (1 H, s, OH); m/z 220.1820 (C$_{15}$H$_{24}$O, 3%), 205.1597 (C$_{14}$H$_{21}$O, 1), 202.1724 (C$_{15}$H$_{22}$, 3), and 73.0659 (C$_4$H$_9$O, 100).

Further elution with 1% ether in petroleum gave (**28**) (14 mg, 3%) as a colourless oil contaminated with the isomer (**27**) (31% by g.l.c.). Spectra obtained by difference: $\nu_{max.}$ 3 430, 2 980, 2 940, 2 850, 1 465, 1 385, 1 375, 1 130, and 1 060 cm^{-1}; δ_H (220 MHz; CDCl$_3$) 0.99 (3 H, s, 15-Me), 1.14 (3 H, d, J 7 Hz, 14-Me), 1.15 (3 H, s, 12- or 13-Me), 1.20 (3 H, s, 13- or 12-Me), 2.25 (1 H, br d, J 11 Hz, 3-H), 3.25 (3 H, s, OMe), 3.46 (1 H, d, J 11 Hz, 2-H), 5.43 (1 H, s, OH), and 5.46 (1 H, br s, 7-H).

Elution with 5% ether in petroleum afforded (**30**) as a colourless oil (12 mg, 2%) (Found: C, 76.0; H, 11.14. C$_{16}$H$_{28}$O$_2$ requires C, 76.1; H, 11.2%), $[\alpha]_D^{20}$ −17.0° (*c* 0.9 in EtOH), $\nu_{max.}$ 3 480, 2 970, 2 930, 2 850, 2 830, 1 465, 1 380, 1 365, 1 070, and 1 045 cm^{-1}; δ_H (220 MHz, CDCl$_3$) 0.88 (3 H, s, 15-Me), 0.89 (3 H, d, J 7 Hz, 14-Me), 1.19 (3 H, s, 12- or 13-Me), 1.32 (3 H, s, 13- or 12-Me), 3.21 (3 H, s, OMe), 4.03 (1 H, s, 2-H), 4.17 (1 H, s, OH), and 5.35 (11 H, d, J 5 Hz, 7-H); m/z 252.2083 (C$_{16}$H$_{26}$O$_2$, 0.2%), 234.1990 (C$_{16}$H$_{26}$O, 0.2), 220.1844 (C$_{15}$H$_{24}$O, 7), 205.1593 (C$_{14}$H$_{21}$O, 7), 202.1720 (C$_{15}$H$_{22}$, 7), and 73.0633 (C$_4$H$_9$, 100).

Further elution with 5% ether in petroleum gave a small amount of (**31**) (4 mg, 0.7%) as a colourless oil, $\nu_{max.}$ 3 480 and

1 070 cm^{-1}; δ_H (300 MHz; CDCl$_3$) 0.84 (3 H, s, 15-Me), 0.86 (3 H, d, J 7 Hz, 14-Me), 1.21 (3 H, s, 12- or 13-Me), 1.33 (3 H, s, 13- or 12-Me), 3.17 (3 H, s, OMe), 4.04 (1 H, s, 2-H), 4.38 (1 H, s, OH), and 5.55 (1 H, br d, J 5 Hz).

Acknowledgements

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