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THE DITERPENES OF *GOODENIA RAMELII* F. MUELL

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Abstract—The ether extract of *Goodenia ramelii* has yielded 19-(β-carboxy-n-propionyloxy)(−)-kaur-16-en-3α-ol (I) and a new diterpene triol shown to be (14*R*)-8β,13-epoxyeperuan-14,15,18-triol (III). The 14-epimer of III was obtained from stereoselective reaction of osmium tetroxide with 18-hydroxy-13-epi-(−)-manoyl oxide (VI) and the configuration of the 14-position firmly established. Unexpectedly the major product from reaction of osmium tetroxide with 13-epi-(−)-manoyl oxide requires approach of the reagent from the opposite side of the vinyl group to the side predominately attacked during epoxidation with perbenzoic acid.

DISCUSSION

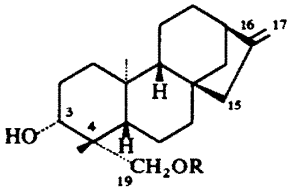
Goodenia strophiolata F. Muell, a shrub existing in the drier area of southerly Western Australia, is a source of large quantities of diterpenoids.[1] We have examined an extract of *Goodenia ramelii* F. Muell, which occurs in a more northerly region and have obtained the succinate ester, 19-(β-carboxy-n-propionyloxy)(−)-kaur-16-en-3α-ol, previously obtained in much greater yield from *G. strophiolata*. The parent diol II has been reported from *Beyeria leschenaultii*.[2]

In addition, the saponified neutral fraction from *G. ramelii* has yielded a new diterpene triol, $C_{20}H_{36}O_4$, which we have assigned structure III. The NMR spectrum of III indicated the presence of four Me groups at quarternary positions (9·24, 9·15, 8·88 and 8·71 τ). The latter two signals correspond to Me protons deshielded by vicinal oxygen and are assigned to the 8- and 13- Me groups. In addition a quartet centred at 6·75 τ (J = 11·0 c/s) is the signal expected[3] for the 18-protons. A three proton multiplet at 6·37 τ was assigned to the 14- and 15- protons. The NMR spectrum of the triacetate IV showed peaks due to the 14- and 15- protons as quartets of an ABX system (τ_A, 5·97; τ_B 5·53; τ_X, 5·02; J_{AB} = 12·1 c/s, J_{AX} = 2·6 c/s, J_{BX} = 8·8 c/s) and the absence of further splitting at 5·02 τ suggested that the vicinal diacetoxy system is attached to a carbon bearing no protons.

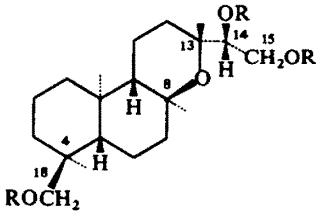
The presence of a 1:2 glycol system in III follows from formation of the acetonide derivative and since cleavage with sodium periodate gave the nor-aldehyde which was reduced with sodium borohydride to give the diol V.

Chemical evidence for the 13-epi-(−)-manoyl oxide skeleton was obtained by synthesis of the diol V from the readily available 18-hydroxy-13-epi-(−)-manoyl oxide (VI)[4]. Treatment of VI with osmium tetroxide gave a triol VII which differed from the natural triol, but which on oxidation with sodium periodate followed by sodium borohydride reduction gave the diol V identical to that obtained from the natural triol III. The triol obtained from osmium tetroxide oxidation of 18-hydroxy-13-epi-(−)-manoyl oxide can only differ from the natural triol in the stereochemistry at C-(14). Oxidation of 18-acetoxy-13-epi-(−)-manoyl oxide (VIII)[4] with perbenzoic acid gave a 3:1 mixture of the epimeric epoxides from which the major component IX could be

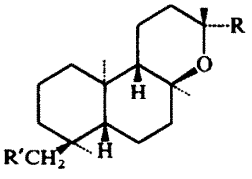
obtained by chromatography. Treatment of IX under reflux with acetic acid and subsequent saponification gave a 2:1 mixture of the triols III and VII further demonstrating their 14-epimeric relationship. Fractional crystallization gave the triol III identical to the natural material.

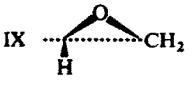


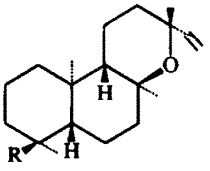
I R = —$COCH_2CH_2CO_2H$
II R = H



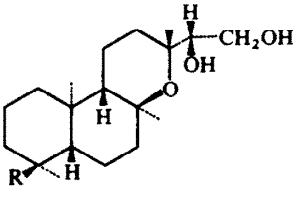
III R = H
IV R = Ac



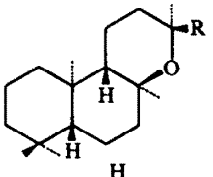
	R	R′
V	CH_2OH	OH
IX		OAc

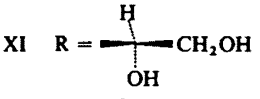


VI R = CH_2OH
VIII R = CH_2OAc



VII R = CH_2OH
XII R = Me





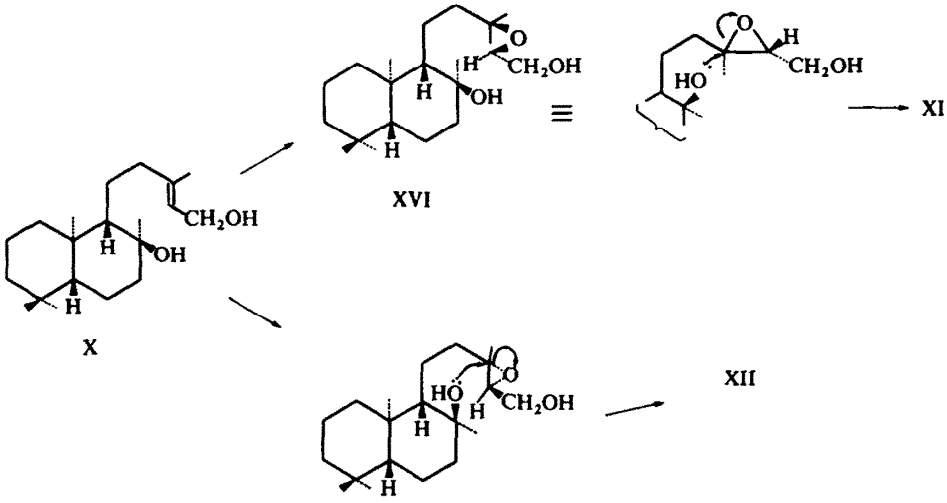
XIII R = CHO
XIV R = CO_2H
XV R = CO_2Me

The absolute stereochemistry at C-(14) was elucidated as a result of some parallel work in our laboratory which involved oxidation of eperu-13-en-8β, 15-diol[4] X with monoperphthalic acid. After chromatography on alumina, the diols XI and XII were obtained.

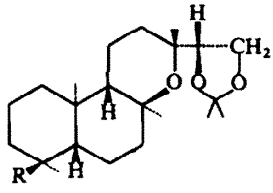
The structure of the diol XI was established to periodate oxidation to the nor-aldehyde XIII which was further oxidized to the corresponding acid XIV with the

Jones reagent.[5] Methylation gave XV which had physical constants and spectral behaviour that showed it to be the enantiomer of methyl manoylate.[6, 7, 8]

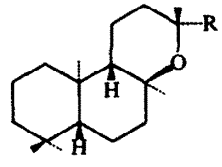
The diol XII was identical to material obtained by osmium tetroxide oxidation of 13-epi-(−)-manoyl oxide.

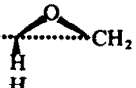


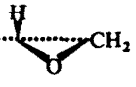
The two diols XI and XII can be considered to arise from the intermediate epoxides XVI and XVII respectively by nucleophilic attack from the 8β-OH. Thus from rear-side attack the epoxide XVII would yield an α(axial) glycol side chain (i.e. 13-epi-(−)-manoyl oxide skeleton) with retention of configuration at C-14. The diol XII

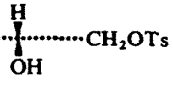


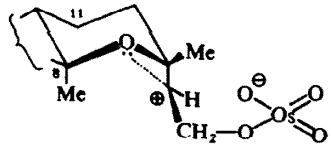
XVIII R = CH_2OH
XIX R = CHO
XX R = Me



XXI R = 

XXII R = 

XXIII R = 



XXIV

must then have the 14-*S* stereochemistry. Likewise the epoxide XVI would give an equatorial side chain ((−)-manoyl oxide skeleton) and consequently XI has the 14-*R* stereochemistry.

The C-14 stereochemistry in the triol VII was related to that of the diol XII by formation of the acetonide XVIII followed by chromium trioxide–pyridine oxidation to the aldehyde XIX. Wolff–Kishner reduction of XIX yielded the acetonide XX identical to a sample prepared from XII.

Hence the triol VII from osmium tetroxide oxidation of 18-hydroxy-13-epi-(−)-manoyl oxide has the 14-*S* configuration and the natural triol III the 14-*R* configuration.

The direction of approach of the reagent in the osmium tetroxide reaction and particularly the stereoselectivity of the reaction were unexpected. A comparison with the stereochemical outcome in perbenzoic acid oxidation has been made in the following manner. Oxidation of 13-epi-(−)-manoyl oxide with perbenzoic acid gave a separable 3:1 mixture of epoxides XXI and XXII. The minor product was synthesized stereospecifically from the monotosylate XXIII obtained by the selective tosylation of the diol XII. This was achieved by treatment with sodium methoxide which caused displacement of the tosylate group in XXIII by the anion generated from the OH group at C(14) to give the epoxide XXII in which the stereochemistry at C(14) of the original diol XII is retained. Base-catalyzed hydrolysis of XXII gave the diol XII.

Thus perbenzoic acid oxidation occurred largely from the side opposite to that for osmium tetroxide oxidation. It has been shown[9] that the neighbouring ether oxygen in 3β-methoxycholest-4-ene does not direct the approach of peracids and it is therefore unlikely that the ether function in epimanoyl oxide influences the stereochemical outcome in this case. Consequently the epoxidation of 13-epi-(−)-manoyl oxide is considered to be sterically controlled and the major product XXI reflects the steric preference for attack on the vinyl group.

Clearly other factors prevail for the osmium tetroxide oxidation if the same conformational preference exists in the solvent employed in this reaction. The stereoselective formation of the diol XII from 13-epi-(−)-manoyl oxide can be rationalized by considering the reagent to attack C-(15), forming a carbonium ion at C-(14) which is stabilized by participation of the neighbouring ether oxygen (e.g. XXIV). Cyclization to the osmate ester would then be directed to give the 14-*S* configuration. Transition states permitting participation by the oxygen atom and leading to a product with the 14-*R* configuration appear to be sterically unfavoured. A similar two step mechanism has been proposed by Waters[10] to explain osmium tetroxide oxidation of aromatic hydrocarbons. The assumption of a charged transition state is also supported by the results of Criegee. *et al.*[11] which showed that the oxidation of α-pinene is faster in polar solvents.[12] However, Dewar[13] has concluded from molecular orbital calculations that osmium tetroxide addition takes place in one step via a cyclic transition state.

EXPERIMENTAL

Analyses were carried out by the Australian Microanalytical Service, Melbourne. Rotations were normally determined for $CHCl_3$ solns in 1-dm tubes at room temp (19–25°). Light petroleum refers to a fraction of b.p. 55–65°. IR spectra were measured with a Perkin–Elmer Infracord 337 for the range 4000–400 cm^{-1} and CS_2 solvent was used for the data quoted. All identities were confirmed by comparison of IR spectra (CS_2

or Nujol mulls). M.ps are uncorrected and were determined on a Kofler block unless designated (cap.). The latter values are for sealed evacuated capillaries. NMR spectra were determined on a Varian A-60 spectrometer for $CDCl_3$ or $CHCl_3$ solns containing TMS as internal standard. All chemical shifts are quoted on the τ-scale.[14]

(a) *Isolation of constituents*

Dried milled leaves and terminal branches of *G. ramelii* (13 Kg) collected 70 miles north of Kalgoorlie, W. A., in October 1964 were exhausted with cold ether. The extract was repeatedly washed with 8% $NaHCO_3$ aq and then 5% NaOH aq. Isolation of the acids from the former soln gave a residue (30 g) which was filtered through activated charcoal (120 g) in ether. 19-(β-Carboxy-n-propionyloxy) (−)-kaur-16-en-3α-ol (I, 4 g) was obtained and crystallized from aqueous MeOH as needles, m.p. and mixed m.p. with an authentic sample from *G. strophiolata*[1] 155–157°, $[\alpha]_D$ −78° (*c*, 1·7 in EtOH). Saponification of I with 5% KOH in aqueous MeOH gave II, which crystallized from AcOEt as prisms, m.p. and mixed m.p. 184–185° (lit[2] m.p. 184–185°).

The neutral fraction (30 g) was filtered through activated charcoal (120 g) in ether to give a dark viscid oil which was saponified with 5% KOH in aqueous MeOH. Removal of the MeOH by steam distillation followed by extraction with $CHCl_3$ gave an oil (8 g) which when filtered through neutral alumina (180 g) in ether gave (14*R*)-8β, 13-*epoxyeperuan*-14,15,18-*triol* (III, 3 g). Recrystallization from benzene gave needles m.p. 164–165°, $[\alpha]_D$ −21° (*c*, 1·9 in EtOH). (Found: C, 70·7; H, 10·9. $C_{20}H_{36}O_4$ requires: C, 70·5; H, 10·7%.)

(b) *Derivatives of* (14*R*)-8β,13-*epoxyeperuan*-14,15,18-*triol* (III)

(i) The triacetate IV, prepared with Ac_2O in pyridine at room temp overnight, crystallized from benzene–light petroleum as needles, m.p. 106–107°, $[\alpha]_D$ +15° (*c*, 1·1) (Found: C, 67·3; H, 9·3 $C_{26}H_{42}O_7$ requires: C, 67·0; H, 9·1%.)

(ii) The triol III (100 mg) in acetone (25 ml) containing conc HCl (2 drops) was allowed to stand at room temp for 40 hr. The soln was dried over anhyd K_2CO_3, filtered and evaporated to give a crystalline residue. Recrystallization from light petroleum gave the acetonide (85 mg) as needles, m.p. 125–126° $[\alpha]_D$ −25° (*c*, 1·3) (Found: C, 72·2; H, 10·4; $C_{23}H_{40}O_4$ requires: C, 72·6; H, 10·6%.)

Periodate oxidation of (14*R*)-8β, 13-*epoxyeperuan*-14,15,18-*triol* (III)

The triol III (250 mg) in aqueous MeOH was oxidized with sodium periodate (750 mg) at room temp for 7 days. Concentration of the soln under reduced press and isolation of the product with ether gave the aldehyde (190 mg) which crystallized from light petroleum as prisms, m.p. 135–136°, $[\alpha]_D$ −97° (*c*, 1·5). ν_{max} 3630 (OH), 1725 cm^{-1} (aldehyde CO). The *semicarbazone*, prepared with semicarbazide hydrochloride and AcONa in aqueous MeOH, crystallized from aqueous EtOH as needles, m.p. 254–255°, $[\alpha]_D$ −91° (*c*, 1·4 in DMF) (Found: C, 65·7; H, 9·6; N, 11·5. $C_{20}H_{35}O_3N_3$ requires: C, 65·7; H, 9·7; N, 11·5%.)

(d) 8β, 13-*Epoxy*-15-*noreperuan*-14,18-*diol* (V)

The aldehyde (210 mg) in MeOH (20 ml) was reduced with $NaBH_4$ (250 mg) at room temp for 2 hr. Dilution with water and extraction with ether gave 8β, 13-*epoxy*-15-*noreperuan*-14,18-*diol* (V, 160 mg) which crystallized from acetone–light petroleum as needles, m.p. 124–125°, $[\alpha]_D$ −97° (*c*, 1·5). (Found: C, 73·6; H, 10·6. $C_{19}H_{34}O_3$ requires: C, 73·5; H, 11·0%.) The NMR spectrum showed singlets at 9·25, 9·13, 8·85 and 8·72 τ (4 tertiary Me groups) and two overlapping quartets centred at 6·75 τ (*J*, 11 c/s) and 6·62 τ (*J*, 10·5 c/s) due to the C-18 and C-14 protons respectively.

(e) (14*S*)-8β, 13-*Epoxyeperuan*-14,15,18-*triol* (VII)

Compound VI[4] was acetylated with Ac_2O in pyridine at room temp overnight to give VIII.

Compound VIII (1·46 g) in pyridine (25 ml) was treated with OsO_4 (1·12 g) at room temp for 44 hr. A soln of $NaHSO_3$ (5 g) in water (30 ml) and pyridine (20 ml) was added and the mixture shaken for 3 hr. Isolation of the neutral product with ether gave an oil (1·4 g) which was chromatographed on alumina (100 g). Elution with benzene–ether (4:1) gave (14*S*)-18-*acetoxy*-8β,13-*epoxyeperuan*-14,15-*diol* (1·3 g) which crystallized from benzene–light petroleum as needles, m.p. 113–114°, $[\alpha]_D$ −36° (*c*, 1·8). (Found: C, 69·2; H, 10·0. $C_{22}H_{38}O_5$ requires: C, 69·1; H, 10·0%.) The acetoxy diol (1·10 g) in 5% NaOH–MeOH (50 ml) was heated under reflux for 2 hr. Dilution with water and extraction with $CHCl_3$ gave (14*S*)-8β,13-*epoxyeperuan*-14,15,18-*triol* (VII, 1·05 g) which crystallized from $CHCl_3$ as needles, m.p. 175–176°, $[\alpha]_D$ −31°

(*c*, 1·5 in EtOH). (Found: C, 70·3; H, 10·6. $C_{20}H_{36}O_4$ requires: C, 70·5; H, 10·7%). The NMR spectrum of VII in pyridine showed peaks at 9·23 (6H) and 8·67 τ (6H), (4 tertiary Me groups).

The same triol VII (270 mg) was obtained from OsO_4 oxidation of 18-hydroxy-13-epi-(−)-manoyl oxide (500 mg).

Sodium periodate oxidation of VII using the conditions described under (c) gave 8β,13-epoxy-14-oxo-15-noreperuan-18-ol, m.p. and mixed m.p. with the product obtained from the natural triol 135–136° (section c). Reduction of the aldehyde with $NaBH_4$ in MeOH gave V, m.p. and mixed m.p. with the diol described under (d) 123–124°.

(f) *Epoxidation of* 18-*acetoxy*-13-*epi*-(−)-*manoyl oxide* (VIII)

Compound VIII (2·90 g) in $CHCl_3$ (20 ml) was treated with excess of a perbenzoic acid–$CHCl_3$ soln at 0° for 5 days. The reaction mixture was washed with 5% Na_2CO_3 aq and water. Removal of the solvent gave an oil which when filtered through alumina in light petroleum gave the *epoxide* IX (1·0 g) which crystallized from aqueous MeOH as needles, m.p. 104–105°, $[\alpha]_D$ −34° (*c*, 1·6). (Found: C, 72·8; H, 10·1. $C_{22}H_{36}O_4$ requires: C, 72·5; H, 10·0%). ν_{max} 3040, 820 cm^{-1} (epoxide), 1740 cm^{-1} (acetate). The NMR spectrum showed a 3 proton multiplet at 7·03 τ due to the epoxide protons.

(g) (14*R*)-8β,13-*Epoxyeperuan*-14,15,18-*triol* (III)

The epoxy acetate IX (460 mg) in AcOH (15 ml) was heated under reflux for 2 hr. The reaction mixture was diluted with water and the neutral product isolated with ether. The product in aqueous MeOH (50 ml, 1:9) was heated under reflux with KOH (2·5 g) for 2 hr. Concentration of the soln, dilution with water and extraction with ether gave an oil (300 mg) which was indicated on the basis of the NMR spectrum to be a mixture of III and VII in the ratio 2:1. Repeated recrystallization from benzene gave III as needles, m.p. and mixed m.p. with the natural triol, 161–162° $[\alpha]_D$ −21° (*c*, 1·1).

(h) *Oxidation of eperu*-13-*en*-8β,15-*diol* (X) *with monoperphthalic acid*

Compound X[4] (3·6 g) in dry ether (200 ml) was allowed to stand with monoperphthalic acid (115 ml of 0·38 M soln in ether) at 0° for 3 days. The ether soln was washed successively with 5% K_2CO_3 aq and water, and the solvent removed to give an oil which was chromatographed on alumina (250 g, Act IV). Elution with benzene ether (9:1) gave (14*R*)-8β,13-*epoxy*-enantio-*labdan*-14,15-*diol* (XI, 1·65 g) which crystallized from light petroleum as needles, m.p. 105–106°, $[\alpha]_D$ −7° (*c*, 3·0). (Found: C, 73·7; H, 11·0. $C_{20}H_{36}O_3$ requires: C, 74·0; H, 11·2%.) Elution with benzene–ether (4:1 and 2:1) gave XII (1·07 g) which crystallized from light petroleum as needles, m.p. 108–109°, $[\alpha]_D$ −21° (*c*, 2·0). (Found: C, 73·5; H, 11·2. $C_{20}H_{36}O_3$ requires: C, 74·0; H, 11·2%.)

(i) (14*S*)-14,15-*Isopropylidenedioxy*-8β,13-*epoxy*-*eperuane* (XX)

Compound XII (112 mg) in acetone (10 ml) with conc HCl (5 drops) was allowed to stand at room temp for 24 hr. The soln was poured into 8% $NaHCO_3$ aq and extracted with ether to give XX (120 mg) which crystallized from MeOH as plates, m.p. 95–96°, $[\alpha]_D$ −12° (*c*, 1·5). (Found: C, 75·9; H, 11·0. $C_{23}H_{40}O_3$ requires: C, 75·8; H, 11·1%.)

(j) *Osmium tetroxide oxidation of* 13-*epi*-(−)-*manoyl oxide*

13-Epi-(−)-manoyl oxide (350 mg) in pyridine (15 ml) was treated with OsO_4 (350 mg) at room temp for 60 hr. $NaHSO_3$ (3 g) in water (30 ml) and pyridine (20 ml) was added and after 4 hr the mixture poured into water. Isolation of the neutral product with ether and recrystallization from light petroleum gave XII (310 mg) as needles, m.p. and mixed m.p. with the product described under (h), 108–109° (lit.[15] m.p. 106–107°). The acetonide prepared as in (i) had m.p. and mixed m.p. 95–96°.

(k) *Periodate oxidation of* (14*R*)-8β,13-*epoxy*-enantio-*labdan*-14,15-*diol* (XI)

Compound XI (246 mg) in dioxan (60 ml) was treated with a soln of sodium periodate (1·0 g) in water (15 ml) at room temp for 4 days. The soln was concentrated under reduced press, poured into water and extracted with ether to give XIII as an oil (225 mg), characterized as the semicarbazone m.p. 225–227° (aq EtOH) (lit.[8] m.p. for enantiomer 225–227·5°).

A similar oxidation of XI (200 mg) using periodic acid (0·8 g) in MeOH (50 ml) and water (12 ml) gave the *dimethyl acetal* (158 mg). Recrystallization from aqueous MeOH gave plates m.p. 99–100°, $[\alpha]_D$ −12° (*c*, 1·0). (Found: C, 74·3; H, 11·1 $C_{21}H_{38}O_3$ requires: C, 74·5; H, 11·3%.)

(l) *Methyl* 8β,13-*epoxy*-15-*nor*-enantio-*labdan*-14-*oate* (XV)

The aldehyde XIII (200 mg) in acetone (15 ml) was oxidized with a slight excess of Jones[5] reagent at room temp for 90 min. The soln was reduced with MeOH, concentrated, poured into 5% Na_2CO_3 aq and washed with ether. Isolation of the acidic fraction from the aqueous phase with 2N HCl and ether gave XIV (215 mg). Recrystallization from aqueous MeOH gave solvated needles m.p. 45–47° (lit.[8] m.p. 45–47 for solvated form of enantiomer). Methylation with diazomethane in ether gave *methyl* 8β,13-*epoxy*-15-*nor*-enantio-*labdan*-14-*oate* (XV). Recrystallization from aqueous MeOH gave needles, m.p. 84–85°, $[\alpha]_D$ −12° (*c*, 1·2). (Found: C, 74·8; H, 10·7. $C_{20}H_{34}O_3$ requires: C, 74·5; H, 10·6%.) (Lit.[8] m.p. 83–85°, $[\alpha]_D$ +14° for enantiomer.) The IR and NMR spectra were identical to those of methyl manoylate.[6,7]

(m) (14*S*)-14,15-*Isopropylidenedioxy*-8β,13-*epoxyeperuane* (XX)

To a suspension of VII (816 mg) in acetone (30 ml) was added conc HCl (3 drops) and the mixture shaken until homogeneous (30 min). The soln was allowed to stand a further 14 hr at room temp then dried over anhyd K_2CO_3, the residue washed with ether and the combined filtrates evaporated to give (14*S*)-14,15-*isopropylidenedioxy*-8β,13-*eperuan*-18-*ol* (XVIII, 931 mg). Recrystallization from benzene–light petroleum gave plates, m.p. 170–172°, $[\alpha]_D$ −24° (*c*, 1·4). (Found: C, 72·2; H, 10·5. $C_{23}H_{40}O_4$ requires: C, 72·6; H, 10·6%.)

Compound XVIII (610 mg) in pyridine (25 ml) was oxidized with CrO_3 (650 mg) for 2 hr at room temp. The reaction mixture was poured into 3%KOH aq and extracted with ether. The ether extract was washed with 5% H_2SO_4 and water, dried and evaporated to give (14S)-14,15-*isopropylidenedioxy*-8β,13-*epoxyeperuan*-18-*al* (XIX, 561 mg). Recrystallization from aqueous MeOH gave plates, m.p. 129–130° (cap.), $[\alpha]_D$ −13° (*c*, 1·4).

The aldehyde XIX (217 mg) in diethylene glycol (25 ml) was heated under reflux with hydrazine hydrate (1 ml, 80%) for 2 hr. The soln was cooled, NaOH (2·0 g) added and the soln boiled without a condenser until the temp reached 210°. Refluxing was then continued for 4 hr. Dilution with water and extraction with ether gave XX (189 mg). Recrystallization from MeOH gave plates m.p. and mixed m.p. with the sample described under 95–96°.

(n) *Epoxidation of* 13-*epi*-(−)-*manoyl oxide*

13-epi-(−)-manoyl oxide (225 mg) in $CHCl_3$ (30 ml) was treated with an excess of perbenzoic acid and allowed to stand at 6° for 12 days. The reaction mixture was washed with 5% Na_2CO_3 aq and water, dried over Na_2SO_4 and evaporated to give a solid residue (220 mg), the NMR spectrum of which indicated the presence of a mixture of XXI and XXII in the ratio 3:1. The product was chromatographed on neutral alumina (30 g). Elution with light petroleum gave unchanged starting material (20 mg), m.p. and mixed m.p. 98–100°. Elution with benzene–light petroleum (1:19) gave (14*S*)-8β,13; 14,15-*diepoxyeperuane* (XXII, 41 mg) which crystallized from aqueous EtOH as needles, m.p. 104–105°, $[\alpha]_D$ −26° (*c*, 1·4). (Found: C, 78·4; H, 11·0. $C_{20}H_{34}O_2$ requires: C, 78·4; H, 11·2%). Elution with benzene–light petroleum (1:9 and 1:4) gave (14*R*)-8β, 13; 14,15-*diepoxyeperuane* (XXI, 117 mg) which crystallized from aqueous EtOH as plates m.p. 128–129°, $[\alpha]_D$ −18° (*c*, 1·2). (Found: C, 78·2; H, 10·9. $C_{20}H_{34}O_2$ requires: C, 78·4; H, 11·2%.)

(o) (14*S*)-8β,13; 14,15-*diepoxyeperuane* (XXII)

To XII (1·04 g) in dry benzene (6 ml) and pyridine (0·4 ml) was added toluene-*p*-sulphonyl chloride (0·90 g) and the soln allowed to stand at 6° for 48 hr. The mixture was poured into water and the neutral fraction isolated with ether to give an oil (1·51 g), which was chromatographed on silicic acid (80 g). Elution with benzene–ether (30:1) gave the *monotosylate* XXIII (1·10 g) which crystallized from light petroleum as plates, m.p. 101–103°, $[\alpha]_D$ −38° (*c*, 2·6). (Found: C 67·4; H, 8·7. $C_{27}H_{42}O_5S$ requires: C, 67·8; H, 8·9%.) Elution with ether gave unchanged XII (0·12 g).

The monotosylate XXIII (176 mg) in dry MeOH (5 ml) was cooled to 0° and MeONa (from 0·17 g Na) in MeOH (15 ml) added. After 12 hr at 6° the mixture was concentrated under reduced press, diluted with water and extracted with ether to give XXII (101 mg). Recrystallization from aqueous MeOH gave needles, m.p. and mixed m.p. with the material described under (n) 104–105°.

(p) *Hydrolysis of* (14*S*)-8β,13; 14,15-*diepoxyeperuane* (XXII)

The epoxide XXII (195 mg) in DMSO (20 ml) was heated with 10% KOH aq (2 ml) at 100° for 12 hr. The mixture was poured into water and extracted with ether to give XII (190 mg) which crystallized from light petroleum as needles, m.p. and mixed m.p. with the material described under (h) 108–109°.

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