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NORPINGUISONE METHYL ESTER AND NORPINGUISANOLIDE, PINGUISANE-TYPE NORSESQUITERPENOIDS FROM *PORELLA ELEGANTULA*

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Key Word Index—*Porella elegantula*, Jungermanniales, Hepaticae; norpinguisone methyl ester, norpinguisanolide; methyl 4-oxonorpinguisan-12-oate; pinguisane-type norsesquiterpene, superoxide release inhibitor

Abstract—Two new pinguisane-type norsesquiterpenoids were isolated from the liverwort *Porella elegantula* Norpinguisone methyl ester, which showed 50% inhibition at 35 μg/ml of the release of superoxide from guinea pig peritoneal macrophage, and norpinguisanolide were identified together with the previously known α-pinguisene, norpinguisone and perrottetianal The structures were established by 2D NMR spectroscopy and chemical evidence. The previously reported pinguisone methyl ester was shown to be methyl 4-oxonorpinguisan-12-oate

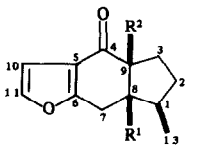
INTRODUCTION

The *Porella* species (Jungermanniales) of liverworts produce various terpenoids [1] and in particular, elaborate a number of pinguisane-type sesquiterpenes [2–5]. Although the pinguisane-type sesquiterpenes consist of a unique structure fused with a furan ring, their physiological properties have not been studied [6, 7]. In pursuit of biologically interesting substances in the liverworts [8–11], we have re-investigated *Porella elegantula* [12] which is indigenous to New Zealand and have isolated two new pinguisane-type norsesquiterpenes, norpinguisone methyl ester (**1**), as superoxide release inhibitor, and norpinguisanolide (**2**) In this paper, we report the structures of the two new sesquiterpenes, and propose a revised structure for norpinguisone methyl ester (**3**) previously isolated from *Porella vernicosa* [2].

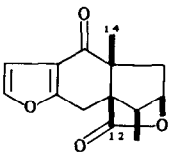
RESULTS AND DISCUSSION

A combination of column chromatography on silica gel and Sephadex LH-20 of an ether extract of *P. elegantula* has resulted in the isolation of the two new norsesquiterpenoids, norpinguisone methyl ester (**1**) and norpinguisanolide (**2**), along with the previously known α-pinguisene (**13**) [4], norpinguisone (**12**) [2] and perrottetianal (**14**) [13].

The IR, ^{1}H NMR and mass spectra of compound **1** were completely identical with those of the known norpinguisone methyl ester (**3**). However, analysis of the 2D long-range ^{13}C–^{1}H COSY of **1** for full assignment of its ^{13}C NMR data (Table 1) did not support the conclusion that compound **1** had the same structure as **3**. Namely, the carbon signal for the ketone at δ197 32 showed a distinct correlation with the proton signal due to a tertiary methyl group at δ1.12, which was further correlated with the C-3 (δ33 27), C-8 (δ61 83) and C-9 (δ58 46) signals through two or three bonds These results implied that the assignments of the methoxycarbonyl group at C-14 and the tertiary methyl group at C-12 in **3** must be reversed for compound 1. Moreover, additional evidence was obtained from the following chemical reactions. reduction of **1** with lithium aluminium hydride (LAH) furnished a sole diol (**4**), the mass spectrum of which revealed intensive retro-Diels–Alder fragment ions at *m/z*



1 R^1 = CO_2Me, R^2 = Me
3 R^1 = Me, R^2 = CO_2Me
12 R^1 = R^2 = Me



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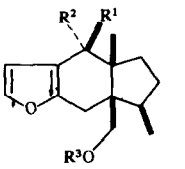
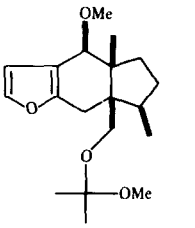


4 R^1 = R^3 = H, R^2 = OH
5 R^2 = R^3 = H, R^1 = OMe
6 R^1 = OMe, R^2 = H, R^3 = Ac



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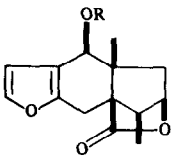
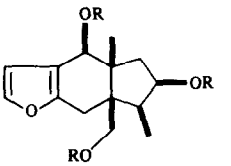
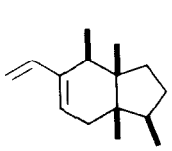


8 R = H
9 R = COC_6H_4-*p*-Br



10 R = H
11 R = Ac



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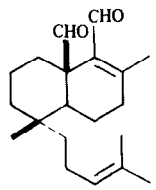

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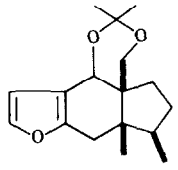

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110 and 109 typical to the pinguisanes [2] The NOE was observed between the signal due to a proton (δ4.34) geminal to the hydroxy group and the tertiary methyl signal, indicating that the LAH reduction occurred from a less hinder convex β-side and thus yielded an α-oriented hydroxy group Treatment of the diol **(4)** with 2,2-dimethoxy-propane in the presence of *p*-toluenesulphonic acid afforded two products **5** and **7**, neither of which corresponded to the acetonide **(15)**. Compound **7** contained a dimethyl ketal group, which was presumably formed between the stereochemically hindered primary alcohol at C-12 and 2,2-dimethoxypropane [14], and was instantly converted to compound **5** on exposure to 1 N HCl The acetate **(6)** available from **5** upon acetylation was subjected to difference NOE experiments and thereby the NOEs were observed as shown in Fig 1. The NOEs for the signals due to the acetoxymethylene at C-12 were observed upon irradiation of the C-13 and C-14 methyl signals, and the doublet methylene signals of H-7, respectively This suggested that the CO_2Me and Me groups in **1** must be located at C-8 and C-9, respectively, and that these groups took the same spatial arrangement as that of the Me-13 group In addition, detection of the NOE between the signal (δ3 95) due to a proton adjacent to the methoxyl group and the β-proton signal on the furan ring substantiated the C-4 position of the ketone function in **1** It should be emphasized that the configuration for the OMe group at C-4 in **6** was inverted to be β in the course of the methylation since there was no NOE between the proton signals at C-4 and the Me signal at C-14 An inversion of the configuration on C-4 was reasonably rationalized as being due to a SN_2 type displacement of the oxonium ion formed between a secondary hydroxyl

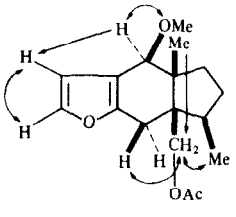

Fig 1 The observed NOEs for compound **6** (indicated by arrows)

group and 2,2-dimethoxypropane in the presence of an acid catalyst by methanol generated *in situ* from the reagent [15]. This unusual reaction was presumably attributable to the fact that both hydroxyl groups of the diol **(5)** were not in a position to form an acetonide. Consequently, the structure of norpinguisone methyl ester was represented as **1**, and hence the structure of the previously reported [2] norpinguisone methyl ester **(3)** was revised to be methyl 4-oxonorpinguisan-12-oate

Compound **2** had the molecular formula $C_{14}H_{14}O_4$ (M^+ at *m/z* 246 0890), and its IR and UV spectra displayed the presence of a conjugated carbonyl group (1680 and 1605 cm^{-1}, 212 nm) and a γ-lactone moiety (1780 cm^{-1}) The ^1H and ^{13}C NMR spectra (Tables 1 and 2) indicated the presence of a fused furan ring [δ6.69 (*d*, J = 1 7 Hz) and 7 42 (*dd*, J = 1 7, 0 1 Hz)], one tertiary methyl (δ1 24) and one secondary methyl [δ1 03 (*d*, J = 6 4 Hz)] group as well as of two CH_2, one CH, two quarternary carbons, and one CH bearing an oxygen-function These spectral features revealed that **2** belonged to a pinguisane-type norsesquiterpene with a γ-lactone unit. This was additionally supported by the observation of an intensive retro-Diels–Alder fragment ion at *m/z* 108 typical to the norpinguisones **1** and **12**, and a base peak at *m/z* 192 derived from putative successive β-cleavages followed by aromatization (Fig 2) Thus, compound **2** had a furano-cyclohexanone ring characteristic of **1** The 2D long-range ^{13}C–^1H COSY spectrum of **2** was measured to clarify the location of the γ-lactone moiety As shown in Table 3, the carbonyl signal at C-4 showed only correlation with the proton signal due to Me-14 which had further cross peaks with the C-3, C-8 and C-9 carbon signals In addition, the signal due to a lactone carbonyl group showed a correlation with the H-2 and H-7β proton signals These results suggested the presence of a 5-membered 12, 2-olide and the tertiary methyl group at C-9 Reduction of **2** with LAH followed by acetylation yielded a triacetate **(11)** (1730 and 1740 cm^{-1}; δ2 06, 2 09 and 2 14). The results of difference NOE experiments are shown in Fig 3 The NOEs for the AB type signals

Table 1 ^{13}C NMR spectral data for compounds **1** and **2***

C	1	2
1	39 87	47 23
2	29 53	82 61
3	33 27	39 38
4	197 32	195 34
5	116 75	118 15
6	163 21	161 43
7	25 14	19 66
8	61 83	59 96
9	58 46	50 36
10	107 09	107 36
11	144 44	144 09
12	173 16	175 35
13	15 58	10 07
14	20 64	21 93
CO_2Me	51 63	

*All assignments were confirmed by the C-H and long-range C-H COSYs

Table 2 ^{1}H NMR (400 MHz) spectral data for compounds **1**, **2**, **8**, and **11**

H	1	2	8	11
1	2 10 (*m*)	2.11 (*q*, 6.4)	2.41 (*q*, 6.6)	2.32 (*dq*, 7 7, 7 3)
2α	1 81 (*dddd*, 12.7, 9.8, 6 6, 3 0)*	4.61 (*dd*, 1 9, 0 1)	4.64 (*d*, 2.4)	5 38 (*ddd*, 7.7, 7 7, 4 2)
2β	1 55 (*dddd*, 12 7, 9 5, 9 5, 3 4)			
3α	2 72 (*ddd*, 13 2, 9 8, 3 4)	2 79 (*dd*, 14.0, 1.9)	2.21 (*dd*, 13 6, 2 4)	2.30 (*dd*, 14 4, 7 7)
3β	2 10 (*m*)	1.83 (*dd*, 14.0, 0.1)	1.81 (*d*, 13 6)	1.58 (*dd*, 14.4, 4 2)
4			4.71 (*t*, 1 9)	5 56 (*t*, 1 5)
7α	3 28 (*d*, 18.8)	2 92 (*d*, 18 5)	2 61 (*ddd*, 18 2, 1.9, 1 0)	2 61 (*dd*, 17.5, 1 5)
7β	3 53 (*d*, 18 8)	3 48 (*dd*, 18.5, 0 1)	3 18 (*ddd*, 18.2, 1.9, 1.0)	2 74 (*dd*, 17 5, 1 5)
10	6.64 (*d*, 2.0)	6 69 (*d*, 1 7)	6.41 (*d*, 1 9)	6.18 (*d*, 1.8)
11	7 35 (*d*, 2 0)	7.42 (*dd*, 1 7, 0.1)	7.35 (*dt*, 1.9, 1 0)	7 26 (*d*, 1.8)
12				4 16 (*d*, 14.4)
				4.25 (*d*, 14.4)
13	0 91 (*d*, 6 8)	1.03 (*d*, 6.4)	1 03 (*d*, 6.6)	0 96 (*d*, 7.3)
14	1 12 (*s*)	1.24 (*s*)	0 97 (*s*)	1 10 (*s*)
CO_2Me	3 77 (*s*)			
Ac				2.06, 2 09 and 2 14 (each *s*)

*Coupling constants (J in Hz) are given in parentheses.

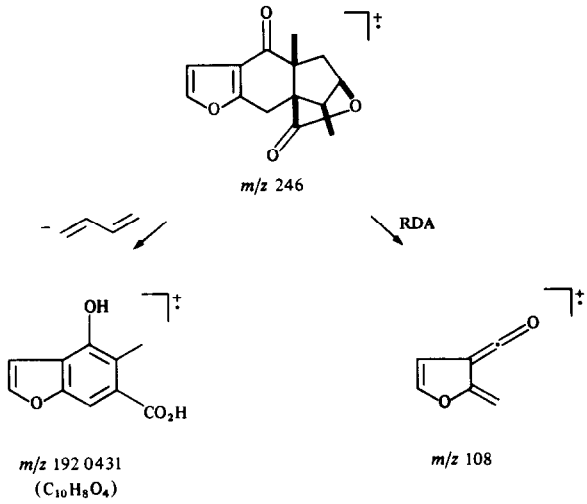

Fig 2 Mass spectral fragmentation of compound **2**.

Table 3. C-H correlation in the long-range C-H COSY of compound **2**

C	Correlated H
1	Me-13, H-3β, H-7β
2	Me-13, H-3β
3	Me-14
4	Me-14
5	H-10, H-11, H-7α,β
6	H-10, H-11, H-7α,β
7	
8	Me-13, Me-14, H-2, H-7α,β
9	Me-14, H-3α, H-2, H-7α
10	H-11
11	H-10
12	H-2, H-7β
13	
14	H-3α,β

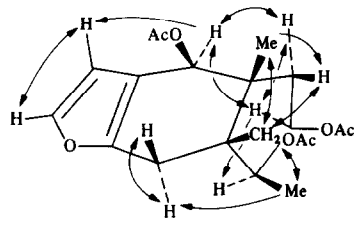

Fig 3 The observed NOEs for compound **11** (indicated by arrows)

due to the acetoxymethylene appeared at δ4.16 and 4.25 and were observed upon irradiation of the signals due to the Me-13, Me-14, H-3β and H-7β, respectively, indicating that the CH_2OAc was located at C-8 and took the same spatial arrangement as those of the Me-13 and Me-14. Furthermore, this was supported from the observation of the NOEs between the triplet signals due to a proton attached to the carbon bearing an acetoxy group at C-4 and the signals due to H-2, H-3α and H-10 that the OAc group at C-4 in **11** took a β-orientation and thus the ketone function in **2** was placed at C-4. The evidence revealed that the structure of norpinguisanolide was shown as **2** including its relative stereochemistry. The absolute configuration of **2** was examined by the CD

spectrum of the *p*-bromobenzoate derivative **(9)** of **2**, which was obtained from sodium borohydride reduction followed by *p*-bromobenzoylation The β-configuration of the hydroxy group at C-4 in **8** was confirmed by a NOESY experiment The CD spectrum of **9** had a first negative Cotton effect ($\Delta\varepsilon$ −2 5) at 250 nm arising from the interaction between the bromobenzoyl group at C-4 and the furan chromophore [16] indicating the C-14 was represented as *S* Thus, the absolute stereochemistry of norpinguisanolide was depicted as **2** The five-membered-ring lactone moiety existing in **2** is surrounded by the two methyl groups and placed under a stereo-chemically hindered environment. In fact, we failed in ring opening of the γ-lactone by the usual basic conditions, since **2** was resistant to alkaline hydrolysis

Norpinguisone methyl ester **(1)** exhibited 50% inhibition at 35 μg/ml of the release of superoxide from the guinea pig peritoneal macrophage induced by formyl methionyl leucyl phenylalanine (FMLP) [17], whereas norpinguisanolide (**2**) had no activity even at a high concentration as 50 μg/ml Recently, it has been made clear [18, 19] that superoxide plays an important role in various diseases such as rheumatoid arthritis and myocardinal ischemia, and superoxide release inhibitors could be effective for preventing or curing such a disease The relationship between the structure of the pinguisane-type sesquiterpene and its activity is now under investigation

EXPERIMENTAL

Mps uncorr ^{1}H (400 and 90 MHz) and ^{13}C NMR (100 MHz) $CDCl_3$, TMS as int standard CC silica gel (Merck, 70–230 mesh and Wakogel C-300) TLC precoated silica gel plates F_{254} (Merck, 0 25 mm) Spots were visualized by UV (254 nm) and $CeSO_4$–30% H_2SO_4

Plant material The liverwort, *Porella elegantula* were collected in New Zealand in November, 1986 and identified by Dr E O Campbell A voucher specimen has been deposited at the Herbarium of Institute of Pharmacognosy, Tokushima Bunri University

Extraction and isolation Air-dried and powdered plants (37 g) were extracted with Et_2O (310 ml) at room temp for 12 days The resultant Et_2O extract was evapd *in vacuo* to give a crude extract (1 32 g), which was divided by CC on silica gel using a *n*-hexane–EtOAc gradient into 8 fractions frs 1,2 (*n*-hexane–EtOAc, 9 1), frs 3,4 (*n*-hexane EtOAc, 4 1), frs 5,6 (*n*-hexane–EtOAc, 3 2), fr 7 (*n*-hexane–EtOAc, 2 3), fr 8 (EtOAc, 100%) Fr 1 afforded α-pinguisene (**13**) (107 mg) Fr 2 (186 mg) was chromatographed by CC on silica gel (*n*-hexane–EtOAc, 1 1) to afford norpinguisone (**12**) (53 mg) Frs 3,4 (321 mg) was chromatographed on Sephadex LH-20 (40 ml) eluting with *n*-hexane–CH_2Cl_2 (4 1), followed by CC on silica gel (C-300) (CH_2Cl_2–EtOAc, 100%→1 1) to give norpinguisone methyl ester (**1**) (145 mg) and perrottetianal A (14) (67 mg) Fr 6 (116 mg) was purified by Sephadex LH-20 (MeOH–CH_2Cl_2, 7 3) to give norpinguisanolide **(2)** (87 mg)

Norpinguisone methyl ester **(1)** Colourless oil, $[\alpha]_D^{16}$ −60 2 ($CHCl_3$, *c* 0 91), MS *m/z* (rel int) 262 1206 $[M]^+$ (calc 262 1205 for $C_{15}H_{18}O_4$) (27), 203 (39), 108 (100), 80 (37), UV λ_{max}^{EtOH} nm (ε) 208 (9500), 268 (4700), IR $\nu_{max}^{CHCl_3}$ cm^{-1} 1724 (ester), 1640 (conj C=O), 1620 (C=C), ^{1}H and ^{13}C NMR see Tables 2 and 1

Reduction of **1** *with* $LiAlH_4$ To a suspension of powdered $LiAlH_4$ (53 mg, 1 39 mmol) in dry Et_2O (2 ml) was added dropwise a soln of **1** (18 mg, 0 07 mmol) in Et_2O (0 5 ml) The reaction mixture was stirred at room temp for 1 hr and then under reflux for 30 min After cooling to 0° excess EtOAc, 5 drops of H_2O and 1 drop of 1 N HCl were added successively and then the ppt was filtered *in vacuo* and washed well with EtOAc The filtrate was washed successively with 1 N HCl, 5% $NaHCO_3$ soln and brine, and dried over $MgSO_4$ The evapn of solvent afforded an oil, which was purified by CC on silica gel (CH_2Cl_2 EtOAc, 3 1) to yield the diol **(4)** (10 9 mg) as a colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3340 (OH), 1502 (furan) MS *m/z* (rel int) 218 $[M-18]^+$ (46), 110 (100), 109 (95), ^{1}H NMR (90 MHz) δ 1 04 (3H, *d*, *J* = 6 8 Hz Me-13), 1 18 (3H, *s*, Me-14), 2 45 (1H, *d*, *J* = 17 6 Hz, H-7), 2 78 (1H, *d* *J* = 17 6 Hz, H-7), 3 57 (1H, *d*, *J* = 11 0 Hz, H-12), 3 86 (1H, *d*, *J* = 11 0 Hz, H-12), 4 34 (1H, *br s*, H-4), 6 36 (1H *d*, *J* = 2 0 Hz, H-10), 7 24 (1H, *d*, *J* = 2 0 Hz, H-11)

Treatment of **4** *with 2,2-dimethoxypropane* A mixture of **4** (10 9 mg) and 2,2-dimethoxypropane (2 ml) was stirred in the presence of *p*-toluenesulphonic acid (5 pieces) at room temp overnight Na_2CO_3 was added and stirring was continued for 30 min After filtering and washing with Et_2O, the evapn of the filtrate gave an oil (9 6 mg), which was purified by CC on silica gel (CH_2Cl_2–EtOAc, 4 1) to furnish compounds **5** (2 7 mg) and **7** (3 5 mg) **5** MS *m/z* (rel int) 218 $[M-32]^+$ (32), 124 (100) ^{1}H NMR (90 MHz) δ 1 10 (3H, *d*, *J* = 6 3 Hz, Me-13), 1 23 (3H, *s*, Me-14), 2 36 (1H, *d*, *J* = 19 5 Hz, H-7), 2 84 (1H, *d*, *J* = 19 5 Hz, H-7), 3 43 (1H, *d*, *J* = 12 0 Hz, H-12), 3 47 (3H, *s*, OMe), 3 67 (1H, *d*, *J* = 12 0 Hz, H-12), 3 88 (1H, *s*, H-4), 6 35 (1H, *d*, *J* = 2 3 Hz, H-10), 7 26 (1H, *d*, *J* = 2 3 Hz, H-11), **7** ^{1}H NMR (90 MHz) δ 1 01 (3H, *d*, *J* = 6 8 Hz, Me-13), 1 07 (3H, *s* Me-14), 1 30 (6H, *s*), 2 54 (2H, *br s*, H-7), 3 13 (3H *s*, OMe), 3 26 (1H, *d*, *J* = 7 0 Hz, H-12), 3 38 (1H, *d*, *J* = 7 0 Hz, H-12) 3 50 (3H, *s* OMe), 3 82 (1H, *br s*, H-4), 6 34 (1H, *d*, *J* = 1 8 Hz H-10), 7 26 (1H, *d*, *J* = 1 8 Hz, H-11)

Acetylation of **5** A mixture of **5** (2 7 mg), Ac_2O and pyridine (0 3 ml) was allowed to stand overnight at room temp The usual work-up afforded the acetate (**6**) (2 8 mg) as colourless oil, ^{1}H NMR (400 MHz) δ 0 95 (3H, *s*, Me-14), 0 99 (3 H, *d*, *J* = 6 4 Hz, Me-13), 2 06 (3H, *s*, OAc), 2 54 (2H, *d*, *J* = 2 8 Hz H-7), 3 60 (3H, *s*, OMe), 3 95 (1H, *t*, *J* = 2 8 Hz, H-4), 6 39 (1H, *d*, *J* = 2 2 Hz, H-10), 7 25 (1H, *d*, *J* = 2 2 Hz, H-11)

Acid treatment of **7** To a soln of **7** (2 0 mg) in MeOH (1 ml) was added 3 drops of 1 N HCl and the mixture was allowed to stand at room temp for 10 min The usual work-up afforded an oil (1 1 mg), the ^{1}H NMR spectrum and TLC behaviour of which were identical with those of compound **5**

Norpinguisanolide **(2).** Colourless plates (from *n*-hexane), mp 132-134 0°, $[\alpha]_D^{22}$ −125 0° ($CHCl_3$, *c* 0 47) MS *m/z* (rel int) 246 0890 $[M]^+$ (calc 246 0892 for $C_{14}H_{14}O_4$) (98), 192 0431 (calc 192 04323 for $C_{10}H_8O_4$) (100), 108 (70), UV λ_{max}^{EtOH} nm (ε) 212 (13 100), 263 (8700), IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3410 (furan), 1780 (γ-lactone), 1680 (conj C=O), 1605 (C=C), 1515 and 904 (furan), ^{1}H and ^{13}C NMR see Tables 2 and 1

Reduction of **2** *with* $NaBH_4$ To a soln of **2** (12 9 mg) in MeOH (3 ml) was added $NaBH_4$ (30 mg) and the reaction mixture was stirred at room temp for 2 hr EtOAc (25 ml) and 1 N HCl (10 ml) were added successively and stirring was continued for 5 min The upper layer was washed with brine, and dried over $MgSO_4$ The evapn of solvent *in vacuo* yielded compound **8** (10 8 mg) as an oil, ^{1}H NMR see Table 2

Reduction of **2** *with* $LiAlH_4$ To a suspension of $LiAlH_4$ (25 mg) in dry Et_2O (2 ml) was added a soln of **2** (4 8 mg) in dry Et_2O (0 5 ml) at room temp and then the reaction mixture was refluxed for 1 hr The work-up similar to that for **1** afforded the diol **(10)** (2 0 mg) as an oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3600 (OH), 3350 (OH), ^{1}H NMR (90 MHz) δ 0 94 (3 H, *d*, *J* = 7 0 Hz, Me-13), 0 95 (3 H, *s*, Me-14), 1 67 (1H, *dd*, *J* = 13 6, 4 3 Hz H-3β), 2 54 (1H, *dd*, *J* = 13 6, 6 6 Hz, H-3α), 3 44 (1H, *d*, *J* = 11 4, H-12), 3 67 (1H, *d*, *J* = 11 4 Hz, H-12), 4 25 (2H, *m*, H-2 and 4) 6 31 (1H, *d*, *J* = 1 8 Hz, H-10), 7 26 (1H, *d* *J* = 1 8 Hz, H-11)

Acetylation of **10** A mixture of **10** (2 0 mg), Ac_2O (3 drops) and pyridine (5 drops) was allowed to stand at room temp overnight The usual work up afforded the triacetate **(11)** (2 1 mg) as an oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 1740, 1730 (OAc), 1230, MS *m/z* (rel int). 318 $[M-60]^+$ (15), 161 (39), 110 (62), 43 (100), ^1H NMR see Table 2.

p-*Bromobenzoylation* of **8** A mixture of **8** (14 5 mg), *p*-bromobenzoyl chloride (60 mg) and pyridine (2 ml) was allowed to stand at room temp overnight The usual work-up afforded an oil, which was purified by CC on silica gel (CH_2Cl_2, 100%) to give the compound **9** as crystals, Colourless prisms (from Et_2O), mp 114–115°, UV λ_{max}^{EtOH} nm (ε) 208 (2290), 248 (17 500), CD (EtOH) $\Delta\varepsilon$ 250 nm −2 5, $\Delta\varepsilon$ 227 nm −1 9, ^1H NMR (90 MHz) δ1.08 (3 H, *d*, *J* = 6 6 Hz, Me-13), 1.16 (3H, *s*, Me-14), 1 80 (1H, *d*, *J* = 14.2 Hz, H-3β), 2.34 (1H, *dd*, J = 14.2, 2.2 Hz, H-3α), 2.62 (1H, *q*, *J* = 6 6 Hz, H-1), 2 66 (1H, *dd*, *J* = 18 6, 1 8 Hz, H-7α), 3 34 (1H, *dd*, *J* = 18.6, 1 8 Hz, H-7β), 4.65 (1H, *d*, *J* = 2 2 Hz, H-2), 6.16 (1H, *d*, *J* = 1 9 Hz, H-10), 6 21 (1H, *t*, *J* = 1 8 Hz, H-4), 7 32 (1H, *d*, *J* = 1 9 Hz, H-11), 7 62 and 7 95 (each 2H, *d*, *J* = 8 6 Hz)

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