

LABDANE DITERPENES FROM *BRICKELLIA KELLERMANII**

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Key Word Index—*Brickellia kellermanii*; Compositae; diterpenes; labdane derivatives.

Abstract—From the aerial parts of *Brickellia kellermanii* three previously unknown labdane diterpenoids were isolated. They were named kellermanoldione (15,16-epoxy-6 β -hydroxy labda-8(17),13(16),14-trien-3, 12-dione), kellermandiolone (15,16-epoxy-3 β ,6 β -dihydroxy labda-8(17),13(16),14-trien-12-one) and kellermandioldione (15,16-epoxy-6 β -19-dihydroxy labda-8(17),13(16),14-trien-3,12-dione). The structure elucidation of these compounds was based on spectroscopic and chemical evidences. Kellermanoldione and kellermandiolone were chemically correlated and their absolute configuration established by X-ray analysis of *p*-bromobenzoyl kellermandiolone. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Most of the diterpenoids so far isolated from *Brickellia* species are labdanes [1]. Occasionally *ent*-labdane [1], pimarane [2] and clerodane [3] diterpenoids have been reported from this genus. We have undertaken the chemical investigation of *Brickellia kellermanii* Grenm., a shrub to which Mexican folk medicine attributes noteworthy antidiarrhoeic properties. This paper describes the structure elucidation of the new labdane derivatives, kellermanoldione (1), kellermandiolone (2) and kellermandioldione (9), isolated from this species together with the previously described 5,7,4'-trihydroxy-3,6-dimethoxy flavone [4].

RESULTS AND DISCUSSION

Kellermanoldione (1) was isolated as a crystalline solid whose mass spectrum ($[M]^+$ at m/z 330) and ^{13}C NMR data were consistent with a molecular formula of $\text{C}_{20}\text{H}_{26}\text{O}_4$. The ^1H and ^{13}C NMR spectra of 1 (Tables 1 and 2) revealed the presence of an exomethylene ^1H : δ 4.96 *br s*, H-17; δ 4.73 *br s* H-17'; ^{13}C : δ 143.9 *s*, C-8; δ 111.2 *t*, C-17) and three tertiary methyl groups. These structural features strongly suggested a labdane-type skeleton for this compound. The presence of the exomethylene group was proved by conversion of 1 to the spiroepoxide 5, characterized in its ^1H NMR spectrum by an AB system at δ 2.40 (H-17) and 2.21 (H-17'), as well as by the ^{13}C NMR signals at δ 57.2 *s* (C-8) and δ 47.4 *t* (C-17).

The IR spectrum of 1 showed absorptions for an α,β -unsaturated ketone (1680 cm^{-1}) and a β -substituted furan ring (1508, 872 cm^{-1}). The chemical shift of the furan protons in the ^1H NMR spectrum (δ 6.79 *dd*, H-14; δ 7.47 *dd*, H-15 and δ 8.12 *dd*, H-16) indicated that the keto group must be conjugated with the furan ring [5], therefore it is likely to be located at C-12. The fragments at m/z 95 $[\text{C}_5\text{H}_3\text{O}_2]^+$ and 67 $[\text{C}_4\text{H}_3\text{O}]^+$ [6] as well as the UV maximum at 248 nm ($\log \epsilon$ 3.56) [7] and the ^{13}C NMR signals for C-12–C-16, confirmed this assumption.

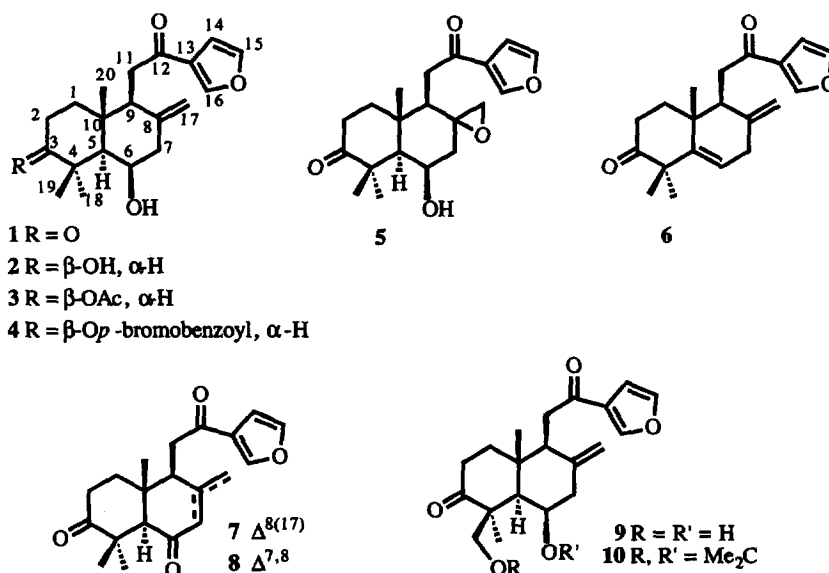
The ^1H – ^1H COSY spectrum of 1 established that the secondary hydroxyl present in the molecule (IR 3609 cm^{-1} ; ^1H : δ 4.38 *br dd*; ^{13}C : δ 69.3 *d*) was bonded to C-6. The β -axial orientation of this group was deduced from the H-6 coupling constants ($J = 5$ and 3 Hz). These assumptions were supported by chemical evidence, since compound 1 could not be esterified, but its dehydration took place easily to give 6, whose ^1H NMR spectrum (see Experimental) showed the signal for the vinylic H-6 at δ 5.60 as a triplet. Oxidation of 1 produced the 6-oxo derivative 7 which was isomerized into the α,β -unsaturated ketone 8 by the action of acidic bentonite [8].

The IR absorption at 1703 cm^{-1} and the ^{13}C NMR signal at δ 214.9 revealed the presence of a second keto group in 1. This group was located at C-3 as shown by comparison of the ^{13}C NMR signals of the ring A carbon atoms of kellermanoldione with the corresponding ones of the labdane derivatives, 2-oxo- and 3-oxo-manoyl oxides [9].

Reduction of 1 with NaBH_4 afforded the diol 2 whose ^1H NMR spectrum showed the signal for the proton under the newly formed hydroxyl group (H-3) at

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δ 3.20 as a doublet of doublets. The J values exhibited by this proton (10.8 and 4.6 Hz) indicated axial-axial and axial-equatorial relationships with its neighbouring protons (H-2, H-2'). Therefore, H-3 is α -oriented and the C-3-OH group has a β -equatorial disposition. The presence of the C-3-OH group was supported by the formation of the monoacetyl derivative 3, in whose ^1H NMR spectrum (see Experimental) the H-3 signal appeared at δ 4.43.

All the above data pointed towards structure 1 for kellermandione. The labdane absolute configuration proposed for this compound was consistent with previous reports on the chemistry of the genus [10–12], except for the case of *B. lemmonii* from which *ent*-labdanes have been described [1]. The presence of both enantiomeric series in *Brickellia* made it necessary to establish unequivocally the absolute configuration of 1. This was achieved by single-crystal X-ray analysis of its *p*-bromobenzoyl derivative (4). The results (Fig. 1) confirmed that 1 is a labdane.

The second compound isolated from this species was identical, in all respects, to the above mentioned dihydro derivative 2. We have named this compound kellermandiolone.

Kellermandioldione (9), the more polar compound isolated from *B. kellermanii*, showed similar spectroscopic characteristics to those of 1, except for the presence in its ^1H and ^{13}C NMR spectra of signals attributed to a hydroxymethylene (^1H : δ 4.07 *d*, 12 Hz; δ 3.51 *d*, 12 Hz; ^{13}C : δ 66.1 *t*) and two tertiary methyl groups. The above was supported by the fragments at m/z 328 [$\text{M} - \text{H}_2\text{O}$] $^+$; 316 [$\text{M} - \text{CH}_2\text{O}$] $^+$ and 298 [$\text{M} - \text{H}_2\text{O} - \text{CH}_2\text{O}$] $^+$, in the mass spectrum. Comparison of the ^{13}C NMR data of 1 and 9 showed a $\Delta\delta$ = 5.1 ppm for C-4 which located the hydroxymethylene moiety at that position. The β -orientation proposed for this functionality was based on the chemical shift of the hydroxymethylene protons [13]

and proved by the presence of a 4σ -coupling (W-coupling) between H-5 and one of the methylene protons in the ^1H NMR spectrum of its acetone (10). Inspection of Dreiding models showed that only the β -axial disposition of the $-\text{CH}_2\text{O}-$ group permits the involved protons (H-5, H-19) to adopt the required W-arrangement. Additional evidence for the correctness of structures 9 and 10 was supplied by the NOESY spectrum of 10 (Fig. 2).

EXPERIMENTAL

Plant material. Aerial parts of *B. kellermanii* (346.8 g) were collected in Chiapas State, México. A voucher specimen (MEXU-536568) is deposited at the Herbarium of the Instituto de Biología, UNAM.

Isolation of the constituents of *B. kellermanii*. Dried and ground plant material was extracted with Me_2CO to give, after evapn of the solvent, 41 g of extract. Of this extract 34 g were decolourized with activated charcoal and chromatographed over a silica gel column eluted with mixts of hexane–EtOAc of increasing polarity. Frs eluted with hexane–EtOAc (17:3) contained 1, which was purified by crystallization from EtOAc–hexane (1.09 g). The first frs eluted with hexane–EtOAc (4:1) contained 2, which was purified by crystallization from EtOAc–hexane. The mother liquors of 2 were combined with the subsequent frs eluted with the same polarity, which contained a mixt. of 2 and a flavonoid. These frs were chromatographed over a silica gel column eluted with hexane– Me_2CO (9:1). 207.8 mg of 2 and 165.2 mg of the flavonoid were obtained. The flavonoid was identified as 5,7,4'-trihydroxy-3,6-dimethoxyflavone by comparison of its physical and spectroscopic constants, as well as of its triacetyl derivative, with those reported in lit. [4]. Compound 9 (66.8 mg) was isolated from frs eluted with hexane–EtOAc (11:9) and (2:3), after CC (silica

Table 1. ^1H NMR spectral data of compounds **1**, **2**, **4**, **5**, **9** and **10** (CDCl_3 , 300 MHz, TMS as int. standard)

H	1*	2	4†	5*	9	10‡
1	1.86 <i>ddd</i> 13, 6, 3	1.56§	1.64 <i>dt</i> 13, 3.6	1.86 <i>ddd</i> 13, 6, 3	1.82 <i>ddd</i> 13, 6, 4	1.76 <i>d</i> 7.5
1'	1.63 <i>td</i> 13, 4.6	1.30§	1.47 <i>dd</i> 13, 4.8	1.55§	1.70 <i>ddd</i> 13, 10.5, 8.5	1.73 <i>dd</i> 8.5, 6
2	2.74 <i>dd</i> § 15, 6	1.67§	1.7-1.9 <i>m</i> §	2.6-2.9 <i>m</i> §	2.47§	2.58 <i>ddd</i> 17, 7.5, 6
2'	2.34 <i>ddd</i> 15, 4.6, 3	1.67§	1.7-1.9 <i>m</i> §	2.6-2.9 <i>m</i> §	2.47 <i>m</i> §	2.31 <i>dd</i> 17.2, 8.5
3		3.20 <i>dd</i> 10.8, 4.6	4.70 <i>dd</i> 11, 4.8			
5	1.63 <i>d</i> 1.8	1.15 <i>d</i> 2	1.31 <i>d</i> 1.5	1.59 <i>d</i> 1.6	1.93 <i>d</i> 1.5	1.81 <i>s</i>
6	4.38 <i>br dd</i> 5, 3	4.41 <i>br s</i>	4.45 <i>br s</i>	4.47 <i>br s</i>	4.35 <i>br dd</i> 5, 3	4.25 <i>dd</i> 6, 3
7	2.54 <i>br dd</i> 14	2.47 <i>br d</i> 13	2.52 <i>br d</i> 14	2.50§	2.47 <i>m</i> §	2.44 <i>m</i> §
7'	2.39 <i>dd</i> 14, 3.2	2.36 <i>dd</i> 13, 3	2.35 <i>dd</i> 14, 3	1.6§	2.47 <i>m</i> §	2.34 <i>dd</i> 13.5, 3
9	2.75§	2.64 <i>br d</i> 10	2.75 <i>br d</i> 10	2.6-2.9 <i>m</i> §	2.77 <i>br d</i> 10.2	2.75 <i>d</i> 8.5
11	3.12 <i>dd</i> 17.4, 10.4	3.02 <i>dd</i> 17, 10	3.04 <i>dd</i> 17, 10	2.6-2.9 <i>m</i> §	3.10 <i>dd</i> 17.5, 10.2	3.11 <i>dd</i> 16, 8.5
11'	2.79 <i>dd</i> 17.4, 3.4	2.74 <i>dd</i> 17, 3.5	2.76 <i>dd</i> 17, 3.3	2.6-2.9 <i>m</i> §	2.77 <i>dd</i> 17.5, 3.2	2.70 <i>dd</i> 16, 3
14	6.79 <i>dd</i> 1.9, 0.8	6.75 <i>dd</i> 1.9, 0.8	6.76 <i>dd</i> 2, 0.9	6.76 <i>dd</i> 1.8, 0.8	6.76 <i>dd</i> 1.8, 0.9	6.75 <i>dd</i> 1.9, 0.8
15	7.47 <i>dd</i> 1.9, 1.5	7.42 <i>dd</i> 1.9, 1.5	7.42 <i>dd</i> 2, 1.5	7.47 <i>dd</i> 1.8, 1.5	7.43 <i>dd</i> 1.8, 1.5	7.42 <i>dd</i> 1.9, 1.4
16	8.12 <i>dd</i> 1.5, 0.8	8.01 <i>dd</i> 1.5, 0.8	8.07 <i>dd</i> 1.5, 0.9	8.08 <i>dd</i> 1.5, 0.8	8.09 <i>dd</i> 1.5, 0.9	8.07 <i>dd</i> 1.4, 0.8
17	4.96 <i>br s</i>	4.88 <i>br s</i>	4.91 <i>s</i>	2.40 <i>d</i> 3.3	4.68 <i>br s</i>	4.83 <i>br s</i>
17'	4.73 <i>br s</i>	4.64 <i>br s</i>	4.69 <i>s</i>	2.21 <i>d</i> 3.3	4.93 <i>br s</i>	4.53 <i>br s</i>
18	1.22 <i>s</i>	1.10 <i>s</i>	1.13 <i>s</i>	1.23 <i>s</i>	1.15 <i>s</i>	1.28 <i>s</i>
19	1.42 <i>s</i>	1.17 <i>s</i>	1.40 <i>s</i>	1.47 <i>s</i>	4.07 <i>d</i> 12	3.98 <i>d</i> 12.4
19'					3.51 <i>d</i> 12	3.50 <i>d</i> 12.4
20	1.27 <i>s</i>	1.06 <i>s</i>	1.06 <i>s</i>	1.48 <i>s</i>	1.12 <i>s</i>	1.06 <i>s</i>

*Determined at 200 MHz.

†*p*-Bromobenzoyl signals: δ 7.88 (2H, *dd*, $J = 7$, 2 Hz, H-2', H-6'); 7.56 (2H, *dd*, $J = 7$, 2 Hz, H-3', H-5').‡Acetonide signals: δ 1.28 (3H, *s*); 1.24 (3H, *s*).

§Superimposed signals.

gel, hexane-EtOAc 3:2) and crystallization from EtOAc-hexane.

Kellermanoldione (1). Crystals, mp 155–157°, $[\alpha]_D - 80.83$ (CHCl_3 , c 0.24). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 248 (log ϵ 3.56) IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3609, 1702, 1680, 1648, 1562, 1508, 872; EI-MS m/z (rel. int.): 330 $[\text{M}]^+$ ($\text{C}_{20}\text{H}_{26}\text{O}_4$; 1.4); 312 $[\text{M} - \text{H}_2\text{O}]^+$ (2); 297 $[312 - \text{Me}]^+$ (3); 294 $[\text{M} - 2\text{H}_2\text{O}]^+$ (4); 95 $[\text{C}_5\text{H}_3\text{O}_2]^+$ (100); 67 $[\text{C}_4\text{H}_3\text{O}]^+$ (11).

Kellermadiolone (2). Crystals, mp 203–204°, $[\alpha]_D - 45.95$ (CHCl_3 , c 0.235). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 246 (log ϵ 3.44); IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3616, 1679, 1562, 1509, 934, 872; EI-MS m/z (rel. int.): 332 $[\text{M}]^+$ ($\text{C}_{20}\text{H}_{28}\text{O}_4$;

0.4); 314 $[\text{M} - \text{H}_2\text{O}]^+$ (2); 299 $(314 - \text{Me})^+$ (3); 294 $[\text{M} - 2\text{H}_2\text{O}]^+$ (4); 95 $[\text{C}_5\text{H}_3\text{O}_2]^+$ (100); 67 $[\text{C}_4\text{H}_3\text{O}]^+$ (12).

Kellermadioldione (9). Crystals, mp 169–170°, $[\alpha]_D - 67.74$ (CHCl_3 , c 0.126) UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm 249 (log ϵ 3.61); IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3265, 1705, 1667, 1649, 1562, 1514, 1466, 1425, 1322, 1157, 1074, 1051, 872; EI-MS m/z (rel. int.): 360 $[\text{M}]^+$ ($\text{C}_{20}\text{H}_{26}\text{O}_5$; 4); 328 $[\text{M} - \text{H}_2\text{O}]^+$ (8); 316 $[\text{M} - \text{CH}_2\text{O}]^+$ (5); 298 $[316 - \text{H}_2\text{O}]^+$ (9); 283 $[298 - \text{Me}]^+$ (5) 255 $[283 - \text{CO}]^+$ (2); 95 $[\text{C}_5\text{H}_3\text{O}_2]^+$ (100); 67 $[\text{C}_4\text{H}_3\text{O}]^+$ (5).

Preparation of compound 2. NaBH_4 (28 mg) was slowly added to a stirred soln of **1** (55 mg) in MeOH

Table 2. ^{13}C NMR spectral data of compounds **1**, **2**, **4**, **5**, **9** and **10** (75 MHz, CDCl_3 , TMS as int. standard)

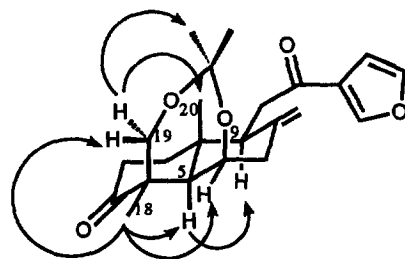
C	1*	2	4†	5*	9	10‡
1	39.8 <i>t</i>	39.6 <i>t</i>	39.3 <i>t</i>	39.8 <i>t</i>	37.3 <i>t</i>	36.9 <i>t</i>
2	34.6 <i>t</i>	27.9 <i>t</i>	24.4 <i>t</i>	33.6 <i>t</i>	35.4 <i>t</i>	35.0 <i>t</i>
3	215.3 <i>s</i>	78.8 <i>d</i>	81.5 <i>d</i>	215.3 <i>s</i>	215.0 <i>s</i>	215.2 <i>s</i>
4	48.8 <i>s</i>	39.8 <i>s</i> §	39.7 <i>s</i>	48.6 <i>s</i>	53.9 <i>s</i>	51.1 <i>s</i>
5	56.9 <i>d</i>	56.0 <i>d</i>	56.1 <i>d</i>	56.4 <i>d</i>	58.5 <i>d</i>	54.6 <i>d</i>
6	69.3 <i>d</i>	68.0 <i>d</i>	68.8 <i>d</i>	68.8 <i>d</i>	68.2 <i>d</i>	66.7 <i>d</i>
7	46.8 <i>t</i>	47.1 <i>t</i>	47.2 <i>t</i>	43.2 <i>t</i>	45.5 <i>t</i>	43.7 <i>t</i>
8	143.9 <i>s</i>	144.5 <i>s</i>	144.3 <i>s</i>	57.0 <i>s</i>	143.7 <i>s</i>	144.1 <i>s</i>
9	50.4 <i>d</i>	51.3 <i>d</i>	51.3 <i>d</i>	44.2 <i>d</i>	49.7 <i>d</i>	49.5 <i>d</i>
10	39.5 <i>s</i>	39.7 <i>s</i> §	39.3 <i>s</i>	38.6 <i>s</i>	39.2 <i>s</i>	38.9 <i>s</i>
11	36.3 <i>t</i>	36.2 <i>t</i>	36.3 <i>t</i>	34.1 <i>t</i>	36.6 <i>t</i>	36.5 <i>t</i>
12	193.3 <i>s</i>	193.8 <i>s</i>	193.6 <i>s</i>	193.1 <i>s</i>	193.4 <i>s</i>	193.6 <i>s</i>
13	127.9 <i>s</i>	128.1 <i>s</i>	128.1 <i>s</i>	127.2 <i>s</i>	127.9 <i>s</i>	128.1 <i>s</i>
14	108.7 <i>d</i>	108.7 <i>d</i>	108.8 <i>d</i>	108.5 <i>d</i>	108.7 <i>d</i>	108.7 <i>d</i>
15	144.3 <i>d</i>	144.2 <i>d</i>	144.3 <i>d</i>	144.4 <i>d</i>	144.4 <i>d</i>	144.3 <i>d</i>
16	146.8 <i>d</i>	146.7 <i>d</i>	146.7 <i>d</i>	147.1 <i>d</i>	146.9 <i>d</i>	146.7 <i>d</i>
17	111.2 <i>t</i>	110.3 <i>t</i>	110.6 <i>t</i>	47.4 <i>t</i>	111.3 <i>t</i>	109.5 <i>t</i>
18	25.9 <i>q</i>	28.1 <i>q</i>	28.3 <i>q</i>	26.2 <i>q</i>	23.8 <i>q</i>	24.9 <i>q</i>
19	23.9 <i>q</i>	16.6 <i>q</i>	18.2 <i>q</i>	23.9 <i>q</i>	66.1 <i>t</i>	67.0 <i>t</i>
20	17.1 <i>q</i>	17.5 <i>q</i>	17.6 <i>q</i>	17.3 <i>q</i>	16.9 <i>q</i>	16.4 <i>s</i>

*Determined at 50 MHz.

†*p*-Bromobenzoyl signals: δ 129.7 *s* (C-1'); δ 131.1 *d* (C-2', C-6'); δ 131.7 *d* (C-3', C-5'); δ 127.8 *s* (C-4').‡Acetonide signals: δ 24.4 *q*, δ 24.7 *q*.

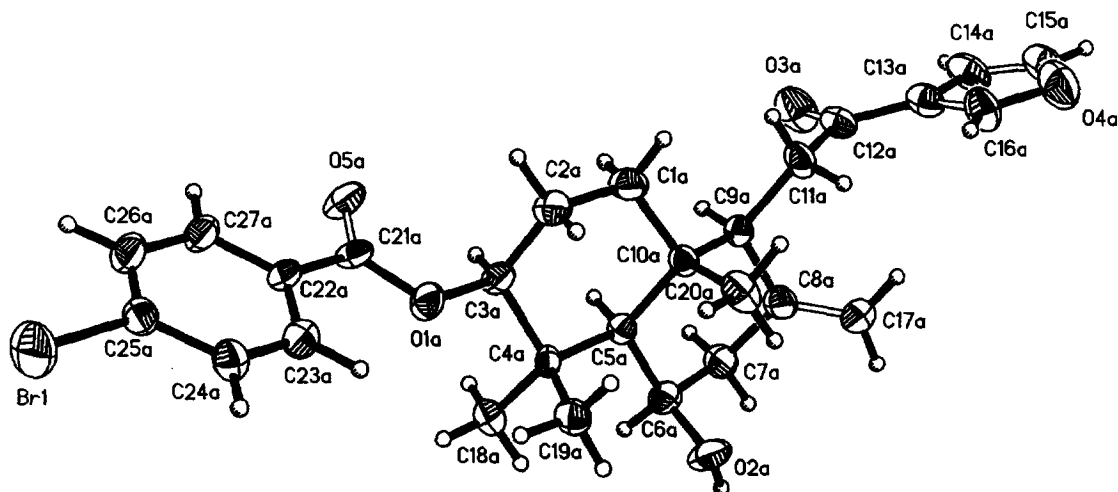
§Superimposed signals.

(10 ml) at 0°. The reaction mixt. was left to stand for 20 min, neutralized (HOAc) and the solvent eliminated by air flow. Then H_2O was added and the mixt. was extracted with EtOAc and dried over anhyd. Na_2SO_4 . After crystallization from EtOAc–hexane, compound **2** was obtained as crystals, mp 196–199°, $[\alpha]_D - 45.95$ (CHCl_3 , *c* 0.235), UV $\lambda_{\text{max}}^{\text{MeOH}}$ 246 nm ($\log \epsilon$ 3.44); IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3616, 1679, 1562, 1509, 934, 872; EI-MS *m/z* (rel. int.): 332 $[\text{M}]^+$ ($\text{C}_{20}\text{H}_{28}\text{O}_4$; 0.4); 314 $[\text{M} - \text{H}_2\text{O}]^+$ (2); 299 $[314 - \text{Me}]^+$ (3); 294 $[\text{M} - 2\text{H}_2\text{O}]^+$ (4); 95 $[\text{C}_5\text{H}_3\text{O}_2]^+$ (100); 67 $[\text{C}_4\text{H}_3\text{O}]^+$ (12).

Fig. 2. Selected NOESY correlations for compound **10**.

Preparation of compound 3. A soln of **2** (38 mg) in pyridine (0.5 ml) and Ac_2O (0.5 ml) was heated on a steam bath for 1 hr. After the usual work up, 29.2 mg of **3** were obtained as crystals, mp 177–178°. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3590, 1723, 1680, 1562, 1509, 872; ^1H NMR (80 MHz, CDCl_3): δ 4.43 (1H, *m*, H-3); 4.43 (1H, *m*, H-6); 3.05 (1H, *dd*, $J = 17, 10$ Hz, H-11), 6.73 (1H, *dd*, $J = 2, 1$ Hz, H-14), 7.41 (1H, *t*, $J = 2$ Hz, H-15), 8.04 (1H, *dd*, $J = 2, 1$ Hz, H-16), 4.87 (1H, *br s*, H-17); 4.63 (1H, *br s*, H-17'); 1.10 (3H, *s*, H-18); 1.27 (3H, *s*, H-19); 1.01 (3H, *s*, H-20); 2.06 (3H, *s*, AcO); EI-MS *m/z* (rel. int.): 374 $[\text{M}]^+$ ($\text{C}_{22}\text{H}_{30}\text{O}_5$; 0.4); 356 $[\text{M} - \text{H}_2\text{O}]^+$ (0.6); 296 $[\text{M} - \text{HOAc} - \text{H}_2\text{O}]^+$ (4); 281 $[296 - \text{Me}]^+$ (7); 95 $[\text{C}_5\text{H}_3\text{O}_2]^+$ (100); 43 $[\text{Ac}]^+$ (58).

Preparation of compound 4. *p*-Bromobenzoyl chloride (44 mg) was added to a soln of **2** (61.1 mg) in dry pyridine (3 ml). The reaction mixt. was heated on a steam bath for 24 hr. *p*-Bromobenzoyl chloride (27 mg) was added. After 72 hr the reaction mixt. was diluted with EtOAc, washed with aq. 5% HCl, then with satd NaHCO_3 soln and H_2O and dried over anhyd. Na_2SO_4 , evapd and purified by CC (silica gel, hexane–EtOAc, 3:1). Crystallization from EtOAc–hexane gave 55.6 mg of **4**, mp 246–247°. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3613, 1713, 1681, 1648, 1591, 1285, 1275, 1159, 1118, 1104, 1070, 1013, 873, FAB-MS (*m*-nitrobenzyl alcohol) *m/z*: 517 $[\text{MH} + 2]^+$ (4); 516 $[\text{M} + 2]^+$ (3); 515 $[\text{MH}]^+$ (6); 514 $[\text{M}]^+$ (1); 499 $[517 - \text{H}_2\text{O}]^+$ (<1); 497 $[517 - \text{H}_2\text{O}]^+$

Fig. 1. ORTEP drawing of compound **4**.

(<1); 482 [MH - Me]⁺ (<1); 481 [M - Me]⁺ (<1); 315 [MH - C₇H₅⁷⁹BrO₂]⁺ (5); 313 [MH - C₇H₅⁸¹BrO₂]⁺ (1.5); 297 [315 - H₂O]⁺ (15); 281 [481 - C₇H₅⁷⁹BrO₂]⁺ (1.8); 279 [MH - C₇H₅⁸¹BrO₂]⁺ (1.8); 185 [C₇H₅⁸¹BrO]⁺ (36); 183 [C₇H₅⁷⁹BrO]⁺ (35); 154 [m-nitrobenzylalcohol]⁺ (100); 95 [C₅H₃O₂]⁺ (55).

Preparation of compound 5. *m*-Chloroperbenzoic acid (51 mg) was added to a soln of **1** (39.3 mg) in CHCl₃ (10 ml). After 24 hr the reaction mixt. was neutralized with satd NaHCO₃ soln, washed with H₂O and dried over anhyd. Na₂SO₄. The crude product was purified by CC (silica gel, CHCl₃) and crystallization (EtOAc-hexane) to obtain 30.2 mg of **5**, mp 186–187°; IR $\nu_{\text{max}}^{\text{nujol}}$ cm⁻¹: 3400, 1686, 1665, 1655, 1561, 1509, 1458, 1157, 1081, 1035, 873; EI-MS *m/z* (rel. int.): 346 [M]⁺ (C₂₀H₂₆O₅; 2); 331 [M - Me]⁺ (1); 328 [M - H₂O]⁺ (1); 318 [M - CO]⁺ (1); 310 [M - 2H₂O]⁺ (1); 95 [C₅H₃O₂]⁺ (100); 67 [C₄H₃O]⁺ (5).

Preparation of compound 6. SOCl₂ (0.5 ml) was dropwise added to a soln of **1** (62.6 mg) in pyridine (1 ml) at 0°. The residue obtained after the usual work up was purified by CC (silica gel, hexane-EtOAc 4:1). After crystallization (hexane-EtOAc) 37.4 mg of **6** were obtained as crystals mp 141–143°; UV $\lambda_{\text{max}}^{\text{MeOH}}$ 247 nm (log ϵ 3.54); IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 1705, 1680, 1561, 1509, 872; ¹H NMR (80 MHz, CDCl₃): δ 5.60 (1H, *br t*, H-6); 3.10 (1H, *dd*, *J* = 17, 10 Hz, H-11), 6.77 (1H, *dd*, *J* = 2, 1 Hz, H-14), 7.47 (1H, *t*, *J* = 2 Hz, H-15), 8.06 (1H, *br t*, *J* = 2, 1 Hz, H-16), 4.89 (1H, *br s*, H-17); 4.56 (1H, *br s*, H-17') 1.23 (3H, *s*, H-18); 1.28 (3H, *s*, H-19); 0.82 (3H, *s*, H-20); EI-MS *m/z* (rel. int.): 312 [M]⁺ (C₂₀H₂₄O₃; 0.6); 297 [M - Me]⁺ (18); 279 [297 - H₂O]⁺ (2); 95 [C₅H₃O₂]⁺ (100); 67 [C₄H₃O]⁺ (8).

Preparation of compound 7. Jones reagent was dropwise added to a soln of **1** (50 mg) in Me₂CO (7 ml) at 0°. After the usual work up, compound **7** (46 mg) was obtained as crystals (EtOAc-hexane) mp 177–178°; [α]_D + 7.61 (CHCl₃, *c* 0.21); UV $\lambda_{\text{max}}^{\text{MeOH}}$ 238 nm (log ϵ 4.09); IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 1711, 1680, 1562, 1508, 898, 872; ¹H NMR (80 MHz, CDCl₃): δ 6.76 (1H, *dd*, *J* = 1.5, 1 Hz, H-14), 7.4 (1H, *t*, *J* = 1.5 Hz, H-15), 8.04 (1H, *dd*, *J* = 1.5, 1 Hz, H-16), 4.84 (1H, *br s*, H-17); 4.58 (1H, *br s*, H-17'); 1.21 (3H, *s*, H-18); 1.48 (3H, *s*, H-19); 1.03 (3H, *s*, H-20); EI-MS *m/z* (rel. int.): 328 [M]⁺ (C₂₀H₂₄O₄; 8); 313 [M - Me]⁺ (13); 285 [313 - CO]⁺ (6); 233 [M - C₅H₃O₂]⁺ (30); 215 [233 - H₂O]⁺ (11); 95 [C₅H₃O₂]⁺ (100); 67 [C₄H₃O]⁺ (20).

Preparation of compound 8. Jones reagent was dropwise added to a soln of **1** (54 mg) in Me₂CO (10 ml) at 0°. The reaction mixt. containing **7** (comparative TLC) was filtered through bentonite ('Tonsil' [8]). The filtrate contained a mixt. of **7** and **8**, which were sep'd by CC (silica gel, hexane-EtOAc 9:1). 13 mg of **7** and 28 mg of **8** were obtained. Compound **8**, mp 181–183° (hexane-EtOAc); IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 1709, 1676, 1634, 1562, 1508, 873; ¹H NMR (80 MHz, CDCl₃): δ 6.78 (1H, *br s*, H-14), 7.46 (1H, *t*, *J* = 1.5 Hz, H-15), 8.06

(1H, *br s*, H-16), 1.75 (3H, *br s*, H-17); 1.32 (3H, *s*, H-18); 1.41 (3H, *s*, H-19); 1.16 (3H, *s*, H-20); EI-MS *m/z* (rel. int.): 328 [M]⁺ (C₂₀H₂₄O₄; 9); 313 [M - Me]⁺ (12); 285 [313 - CO]⁺ (5); 233 [M - C₅H₃O₂]⁺ (26); 215 [233 - H₂O]⁺ (11); 95 [C₅H₃O₂]⁺ (100); 67 [C₄H₃O]⁺ (35).

Preparation of compound 10. 1.5 g of bentonite were added to a soln of compound **9** (48.9 mg) in Me₂CO (10 ml). The suspension was stirred for 1.5 hr then filtered and evap'd. The residue was crystallized from EtOAc-hexane to give 55.6 mg of the acetone **10** as crystals, mp 162–163°; IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 1684, 1651, 1562, 1509, 1383, 1237, 1159, 1076, 1039, 873; EI-MS *m/z* (rel. int.): 386 [M]⁺ (C₂₃H₃₀O₅; 4); 371 [M - Me]⁺ (1); 356 [M - CH₂O]⁺ (<1); 328 [M - Me₂CO]⁺ (18); 310 [M - H₂O]⁺ (13); 283 [298 - Me]⁺ (7); 255 [283 - CO]⁺ (4); 95 [C₅H₃O₂]⁺ (100); 67 [C₄H₃O]⁺ (11).

X-ray data of compound 4. Monoclinic crystal system. space group C2 with *a* = 59.897(3) Å, *b* = 5.989(1) Å, *c* = 14.135(1) Å, *V* = 4949.0 (5) Å³, *Z* = 8, *D*_{calc} = 1.384 g cm⁻³, CuK α radiation (λ = 1.54178 Å). Diffraction measurements were made on a Siemens P4/PC diffractometer using CuK α radiation. Of 3435 reflexions, 3391 were unique. The structure was solved by direct methods (SIR 92) [14] and refined by full-matrix least squares using Siemens SHELXTL PLUS (PC version) [15]. The function $S[w(|F_o|^2 - |F_c|^2)^2]$ was minimized, in which $w = 1.0/[s|F_o|^2 + 0.0008|F_c|^2]$. 2778 unique observed reflexions (*F* > 4 σ (*F*)) corrected by Lorentz polarization and absorption (face-indexed method) effects, were used and the number of variables was 602. Final *R* = 0.475, *R*_w = 0.0603, *S* = 1.13. The maximum negative and positive peaks in the final difference map were -0.34 and 0.33 eÅ⁻³, respectively. Absolute configuration was established by the method of Rogers [16] (η = 1.01 (16)).

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