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# LABDANE TYPE DITERPENOIDS FROM THE LIVERWORT *FRULLANIA HAMACHILOBA**

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**Key Word Index**—*Frullania hamachiloba*; Jungermanniales; hamachilobenes A–E; manoyloxide; labdane-type diterpenoids; γ-cyclocostunolide; chemosystematics

**Abstract**—Five new labdane-type diterpenoids named hamachilobenes A-E have been isolated from the epiphytic liverwort *Frullania hamachiloba*, together with γ-cyclocostunolide and their absolute stereostructures determined to be manoyloxide derivatives by a combination of NMR and CD spectra.

## INTRODUCTION

Epiphytic liverworts *Frullania* species are rich sources of sesquiterpene lactones and/or bibenzyl derivatives [2–6]. Several *Frullania* species including eudesmane- or eremophilane-type sesquiterpene lactones cause the intense allergenic contact dermatitis [2]. *Frullania hamachiloba* grows on the trunk and twig of deciduous trees and its colour is reddish brown or yellowish brown. This species is morphologically quite different from the other *Frullania* species [Dr S. Hattori, personal communications]. This phenomenon prompted us to investigate its chemical constituents.

## RESULTS AND DISCUSSION

Air-dried and ground material was extracted with ether to give a green oil which was chromatographed on silica gel and Sephadex LH-20 to afford five new diterpene acetates named hamachilobenes A–E (**1**–**5**), together with the previously known sesquiterpene lactone, γ-cyclocostunolide (**14**) [2].

### *Hamachilobene* A (**1**)

The molecular formula ($C_{24}H_{38}O_6$) of **1** was suggested by CIMS. The IR spectrum indicated the presence of a hydroxyl and an acetoxyl group. The $^1$H NMR spectrum (Table 1) contained the signals of five tertiary methyls, two acetyl methyls, a terminal vinyl group, two protons (δ4.48, *dd*, $J=11.7$, 4.9 Hz, H-3; δ5.37, *dd*, $J=12.2$, 2.0 Hz, H-6) on carbon bearing acetoxyl group and a methine (δ3.60, *d*, $J=2.4$ Hz) with hydroxyl group. The presence of two acetoxyl groups was confirmed by the reduction of **1** with lithium aluminium hydride to give a triol (**6**). The $^{13}$C NMR spectrum (see Experimental) of **1** contained 24 carbons; terminal vinylic carbons; three methine carbons attached to oxygen, two quaternary carbons bearing oxygen, two acetyl groups and in addition, seven methyls, four methylenes, two methines and two quaternary carbons. Oxidation of **1** with pyridinium chlorochromate (PCC) gave an acetoxyketone (**2**) (1745, 1733, 1235 cm$^{-1}$; δ169.9, 170.8, 202.2), whose IR spectrum showed the absence of the absorption band of a hydroxyl group, indicating that an additional oxygen function of **1** was an ether and it was connected with two quaternary carbons ($\delta_C$ 74.4, 76.2), thus **1** was suggested to be a tricyclic diterpene diacetate with a terminal vinylic, a secondary hydroxyl and an ether groups. A two dimensional proton–proton correlated COSY and spin decoupling experiments of **1** suggested the presence of the partial structure –C(5)$H_{ax}$–C(6)$H_{ax}$OAc–C(7)$H_{eq}$OH– and –C(3)$H_{ax}$OAc–C(2)$H_2$–. Consideration of these chemical and spectral data led to the conclusion that the structure of **1** was depicted as manoyloxide-type diterpenes (**7**) which are widely distributed in higher plants [7]. The relative configuration of **1** was established by means of extensive difference NOE spectroscopy. NOEs between C(4)$Me_{eq}$ and C(3)-$H_{ax}$ established the position of the equatorial acetoxyl group at C-3. The most important resonances observed are indicated in Fig. 1 and complete assignment of $^1$H NMR signals of **1** was possible (Table 1). Thus, the stereostructure of hamachilobene A was established to be 3β,6α-diacetoxy-7α-hydroxymanoyloxide (**1**) or its enantiomer. The absolute configuration will be discussed later.

### *Hamachilobene* B (**2**)

The spectral data displayed the presence of two acetoxyl and a ketone groups (1745, 1733 cm$^{-1}$; $\delta_H$2.07, 2.19 s; $\delta_C$202.2). Reduction of **2** with lithium aluminium hydride gave two triols **6** and **8**, respectively. The spectral data and physical constants of the former triol was identical to those of **6** derived from **1**, indicating that **2** was dehydro derivative of **1**. In fact, hamachilobene B was completely identical to **2** obtained from **1** by PCC oxidation, in all respects.

*Part 24 in the series of 'Chemosystematics of Bryophytes'. For Part 23, see [1].

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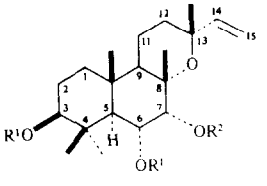
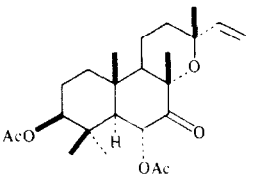
Table 1. $^1$H NMR spectral data for hamachilobenes A–E (**1**–**5**) (ppm from internal TMS)*

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| H-3 | 4.48 *dd* | 4.44 *dd* | 4.43 *dd* | 4.44 *dd* | 3.26 *dd* |
| | (11.7, 4.9)† | (11.7, 4.9) | (11.7, 4.9) | (10.7, 4.9) | (11.3, 4.4) |
| H-5 | 2.08 *d* | 1.60 *d* | 1.46 *d* | 1.26 *d* | |
| | (12.2) | (12.2) | (11.7) | (10.8) | |
| H-6 | 5.37 *dd* | 5.62 *d* | 5.27 *dd* | 3.81 *ddd* | 1.79 *m* |
| | (12.2, 2.0) | (13.2) | (11.2, 9.8) | (10.8, 10.8, 9.8) | |
| H-7 | 3.60 *d* | | 3.58 *dd* | 4.89 *d* | 4.94 *t* |
| | (2.4) | | (9.8, 2.4)‡ | (10.8) | (2.5) |
| H-14 | 5.87 *dd* | 5.88 *dd* | 5.85 *dd* | 5.80 *dd* | 5.81 *dd* |
| | (17.6, 10.7) | (17.6, 10.7) | (17.6, 10.7) | (17.1, 10.8) | (17.6, 10.7) |
| $H_a$-15 | 4.97 *dd* | 4.96 *dd* | 4.93 *dd* | 4.89 *d* | 4.87 *dd* |
| | (10.7, 0.98) | (10.7, 1.5) | (10.7, 1.5) | (10.8) | (10.7, 1.5) |
| $H_b$-15 | 5.06 *d* | 5.22 *dd* | 5.13 *dd* | 5.15 *dd* | 5.08 *dd* |
| | (17.6) | (17.6, 1.5) | (17.6, 1.5) | (17.6, 2.0) | (17.6, 1.5) |
| C-4-Me | 0.88 *s* | 0.97 *s* | 0.95 *s* | 1.02 *s* | 0.75 *s* |
| C-4-Me | 1.04 *s* | 1.06 *s* | 0.96 *s* | 1.15 *s* | 0.91 *s* |
| C-8 Me | 1.39 *s* | 1.56 *s* | 1.35 *s* | 1.34 *s* | 1.33 *s* |
| C-10 Me | 0.92 *s* | 1.18 *s* | 0.95 *s* | 0.89 *s* | 0.82 *s* |
| C-13 Me | 1.28 *s* | 1.28 *s* | 1.23 *s* | 1.17 *s* | 1.23 *s* |
| OAc | 2.05 *s* | 2.07 *s* | 2.05 *s* | 2.06 *s* | 2.08 *s* |
| | 2.13 *s* | 2.19 *s* | 2.10 *s* | 2.15 *s* | |

*All signals were assigned by spin decoupling, 2D-COSY ($^1$H–$^1$H) and difference NOE experiments.
†Figures in parentheses are coupling constants in Hz, run at 400 MHz in $CDCl_3$.
‡The coupling disappeared on addition of $D_2O$.



**1** $R^1$ = Ac, $R^2$ = H
**6** $R^1$ = $R^2$ = H



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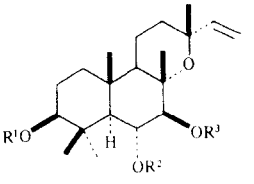
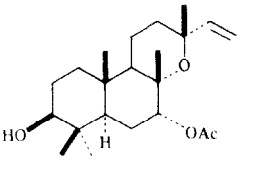
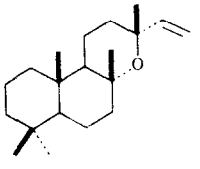


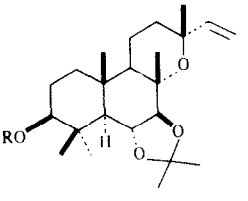
**3** $R^1$ = $R^2$ = Ac, $R^3$ = H
**4** $R^1$ = $R^3$ = Ac, $R^2$ = H
**8** $R^1$ = $R^2$ = $R^3$ = H
**9** $R^1$ = $R^2$ = $R^3$ = Ac
**12** $R^1$ = Ac, $R^2$ = $R^3$ = H
**13** $R^1$ = Ac, $R^2$ = $R^3$ = *p*ClBz



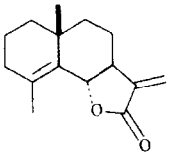
**5**



**7**



**10** R = H
**11** R = Ac



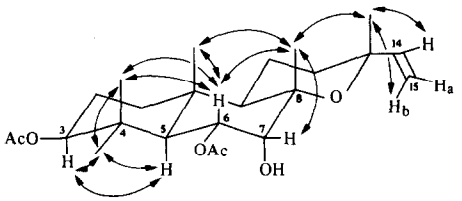
**14**

*Hamachilobene* C (**3**)

CIMS of **3** indicated the same molecular ion at *m/z* 423 $[M+1]^+$ as that of **1**. The $^1$H NMR and $^{13}$C NMR closely resembled those of **1**, except for the chemical shifts of two protons (H-6 and H-7). 2D-COSY and spin decoupling experiments exhibited the presence of the partial structures $-C(5)H_{ax}-C(6)H_{ax}OAc-C(7)H_{ax}OH-$ and $-C(3)H_{ax}-C(2)H_2-$. The above spectral evidence suggested that **3** might be the stereoisomer at C-7 of **1**. This assumption was confirmed as follows. Acetylation of **3** gave a triacetate **9**, followed by reduction with lithium aluminium hydride to afford a triol whose spectral data were in accordance with those of the major triol (**8**) obtained from **2**. All signals of $^1$H NMR spectra were assigned by 2D-COSY, spin decoupling and difference NOE's experiments as indicated in Table 1.

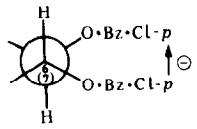
*Hamachilobene* D (**4**)

CIMS gave the same molecular ion at *m/z* 423 as those of **1** and **3**. The $^1$H NMR signals was very similar to those of **1** and **3**, except for the chemical shifts of three protons (H-3, H-6 and H-7), showing that **4** was the isomer of **3**. 2D-COSY and spin decoupling experiments confirmed the position of the functional groups and their relative stereochemistry and thus the structure of hamachilobene



1

Fig. 1. NOEs observed by difference NOE spectra.



13

Fig. 2 A negative exciton chirality between two benzoate chromophores.

D was formulated as **4**. This assumption was further confirmed by the chemical transformation of **4**. Acetylation of **4** yielded a triacetate, the spectral data of which were in agreement with those of **9**, obtained from **3**.

*Hamachilobene* E (**5**)

Compound **5** had the molecular ion at *m/z* 364 and an acetoxyl group, a secondary hydroxyl group (3600 $cm^{-1}$; $\delta_H$3.26, *dd*, $J = 11.2$, and 2.5 Hz) which disappeared on addition of $D_2O$; $\delta_C$74.6, *d*) and a terminal vinylic group. The $^{13}C$ NMR showed the presence of 22 carbon atoms. Comparison of the spectral data of **5** with those of **1–4** suggested that **5** also was manoyloxide with one secondary hydroxyl and one acetoxyl group. The location and the relative stereochemistry of these functional groups were established by the same methods as those carried out on the above new diterpenoids and the structure of the fifth compound was elucidated as **5**.

*The absolute configuration of hamachilobenes* (**1–5**)

The absolute configuration of the new manoyloxides were established by CD spectra of dibenzoate (**13**) of **8** derived from **2**. Treatment of **8** with dry acetone in the presence of dry copper sulphate to give an acetonide (**10**), followed by acetylation with acetic anhydride in pyridine to afford a monoacetoxy acetonide (**11**), which was treated with 60% acetic acid to furnish a monoacetoxy diol (**12**). The resulting diol was esterified with *p*-chlorobenzoyl chloride to give a dibenzoate (**13**). The relative stereostructure of the resulting benzoate was confirmed to be the same as that of the original manoyloxides by the extensive NMR experiments. CD spectrum of **13** showed the negative Cotton effect at 263 nm, indicating that the absolute configurations of **13** at C-6 and C-7 were *R* and *S*, respectively [8] (Fig. 2]. Thus, the absolute stereostructures of hamachilobenes (A–E) were established as (3*S*,6*R*)-diacetoxy-(7*R*)-hydroxymanoyloxide (**1**),(3*S*,6*R*)-diacetoxy-7-oxomanoyloxide (**2**), (3*S*,6*R*)-diacetoxy-(7*S*)-hydroxymanoyloxide (**3**), (3*S*,7*S*)-diacetoxy-(6*R*)-hydroxymanoyloxide (**4**) and (3*S*)-hydroxy-(7*R*)-acetoxymanoyloxide (**5**), respectively.

Liverworts often elaborate sesqui- and diterpenoids enantiomeric to those found in higher plants [2] and as a very rare phenomenon, the epiphytic liverworts, *Frullania* species biosynthesize both antipodes, like sesquiterpene lactones, (+)-frullanolide from *F. dilatata* and (−)-frullanolide from *F. tamarisci* and *F. nisquallensis* [2]. The present manoyloxides and highly oxidized manoyloxides isolated from the liverwort, *Ptychantus striatus* [2, 9] have the same absolute configuration as those found in higher plants. On the other hand, (−)-manool [10], jungermannol [2, 11], labda-12,14-diene-7,8-diol [12] and labda-7,13*E*-diene-15-ol [13] found in the other liverworts possess enatiomeric configurations like those found in higher plants. On the basis of the above results, it is obvious that liverworts produce both normal and enantiomeric series of diterpenoids. In a previous paper [3], we showed that there are five chemotypes of *Frullania* species. The present species is, however, very specific, since the major component is labdane-type diterpenoids and a sesquiterpene lactone is found as a minor component. The present *Frullania* species is thus classified as a sixth chemotype; labdane-sesquiterpene lactone type. The above conclusion is correlated with the morphological difference between *F. hamachiloba* and the other typical *Frullania* species.

## EXPERIMENTAL

All mps uncorr. The solvents used for spectral measurement were: TMS–$CDCl_3$ [$^1H$ NMR (400 Mz); $^{13}C$ NMR (100 MHz)]; $CHCl_3$ (IR and $[\alpha]_D$) and MeOH (CD). CIMS were measured using methane as reaction gas. GC/MS were carried out at 70 eV using SE-30 (1%) column, temp. programmed from 50 to 270° at 5°/min, injec. temp. 270°; He 30 ml/min.

*Plant material. Frullania hamachiloba* Steph. was collected in Mt. Kenzan in 1984 and identified by Dr S. Hattori and voucher specimen was deposited at the Institute of Pharmacognosy, Tokushima Bunri University.

*Extraction and isolation. F. hamachiloba* was dried for 3 days, mechanically ground and extracted with $Et_2O$ for 1 month. The ether extract was filtered and removal of the solvent gave the green oil (6.42 g). A small amount of the extract was analysed by TLC, GC and GC/MS. The presence of monoterpenoids, α-pinene, β-phellandrene, limonene, α-terpinene and myrcene, and sesquiterpene hydrocarbons, *trans*-β-farnesene, α-cubebene and β-caryophyllene were confirmed by comparison of mass spectra with those of authentic samples, as very minor components. The remaining material (6.40 g) was chromatographed on silica gel using *n*-hexane and EtOAc gradient. Fraction (284 mg) eluted by *n*-hexane–EtOAc (95:5) was rechromatographed on Lobar column using the same solvent as described above to give γ-cyclocostunolide (**14**) (11 mg) [2]. Fractions eluted by n-hexane–EtOAc (7:3) and (1:1) were combined and the viscous oil (1.80 g) was rechromatographed on Sephadex LH-20 using $CHCl_3$–MeOH (1:1) to afford diterpene mixtures (420 mg) and (107 mg). The former mixtures were further chromatographed on silica gel using $C_6H_6$–EtOAc gradient to afford hamachilobenes A (**1**) (40 mg) and B (**2**) (17 mg). The latter mixtures were

again chromatographed on Lobar column using $C_6H_6$–EtOAc (90:10) to give hamachilobenes C (**3**) (30 mg), D (**4**) (21 mg) and E (**5**) (15 mg), respectively. *Hamachilobene* A (**1**): mp 136–138°; $[\alpha]_D$ +38.9° (*c* 0.36); IR $\nu_{max}$ $cm^{-1}$: 3540, 1730, 1250, 1025; $^{13}C$ NMR: $\delta$15.9, 16.8, 21.2, 21.9, 25.2, 28.9 29.9 (each Me); 14.8, 23.0, 34.5, 36.4 ($CH_2$), 47.4, 49.2 (CH), 71.3, 75.5, 80.3 (CH–O), 37.1, 37.3 (C), 74.4, 76.2 (C–O), 110.8 (=$CH_2$), 146.4 (=CH), 170.4, 170.8 (COO); CIMS *m/z*: 423 $[M+1]^+$, 405, 362, 345, 303, 285 (base), 267, 203, 81, 44. *Hamachilobene* B (**2**): mp 154–156° $[\alpha]_D$ +37.8° (*c* 0.26); IR $\nu_{max}$ $cm^{-1}$: 1745, 1733, 1235, 1017; CD $\Delta\varepsilon_{284\ nm}$ −2.2; $^{13}C$ NMR: $\delta$15.9, 16.3, 21.0, 21.1, 24.5, 29.8, 30.1 (each Me), 15.5, 22.8, 33.2, 36.4 ($CH_2$); 52.7, 57.4 (CH), 74.0, 79.7 (CH–O), 37.2, 38.4 (C), 74.7, 79.9 (C–O), 111.8 (=$CH_2$), 146.3 (=CH), 169.9, 170.8 (COO), 202.2 (C=O); EIMS *m/z* 420 $[M]^+$, 392, 360, 332, 264, 254, 203, 189, 175, 161, 151, 147, 135, 122, 107, 98, 95, 85, 81 (base), 69, 55, 44. *Hamachilobene* C (**3**): 94–95° $[\alpha]_D$ +19.1° (*c* 1.46); IR $\nu_{max}$ $cm^{-1}$: 3580, 1725, 1245, 1020; $^{13}C$ NMR: 16.6, 16.9, 21.2, 21.7, 22.0, 29.1, 29.7 (each Me), 15.2, 23.0, 34.4, 36.4 ($CH_2$), 51.6, 56.3 (CH), 80.0, 84.0 (CH–O), 37.5, 37.8 (C), 73.6, 77.3 (C-O), 110.4 (=$CH_2$), 147.1 (=CH), 170.9, 171.0 (COO); CIMS *m/z*: 423 $[M+1]^+$, 362, 345, 303, 285 (base), 276, 267, 257, 232. *Hamachilobene* D (**4**): mp 144–146°; $[\alpha]_D$ +46.4° (*c* 0.58); IR $\nu_{max}$ $cm^{-1}$: 3570, 1725, 1250, 1020; $^{13}C$ NMR: $\delta$16.4, 16.6, 21.2 (x2), 22.5, 29.5, 30.4 (each Me), 15.2, 23.1, 34.6, 36.5 ($CH_2$), 52.4, 58.6 (CH), 71.2, 80.4, 86.4 (CH–O), 37.1, 38.4 (C), 73.3, 76.0 (C–O), 110.6 (=$CH_2$), 147.1 (=CH), 170.9, 172.2 (COO); CIMS *m/z*: 423 $[M+1]^+$, 407, 345, 303, 285 (base), 267, 257, 203, 151, 123, 81, 44. *Hamachilobene* E (**5**): mp 90–92°; $[\alpha]_D$ 0° (*c* 0, 76); IR $\nu_{max}$ $cm^{-1}$: 3600, 1725, 1245, 1018; $^{13}C$ NMR: $\delta$15.2 (x2), 21.6, 25.2, 27.8, 28.8 (each Me); 14.9, 24.3, 27.2, 35.2, 37.1 ($CH_2$), 47.8, 49.4 (CH), 74.6, 78.7 (CH–O), 36.5, 38.3 (C), 73.5, 84.1 (C–O), 109.7 (=$CH_2$), 147.5 (=CH), 170.4 (COO); CIMS *m/z*: 365 $[M+1]^+$, 349, 305, 287 (base),269, 201, 135, 81.

*Reduction of* **1** *with* $LiAlH_4$. To a suspension of $LiAlH_4$ (10 mg) in dry $Et_2O$ was added **1** (5 mg) in dry $Et_2O$ dropwise at 0° and stirred for 30 min. Work-up as usual gave a triol (**6**) (4 mg) as white powder: CIMS *m/z*: 339 $[M+1]^+$, 323, 303 (base); $^1H$ NMR: $\delta$0.82, 0.95, 1.29, 1.03, 1.31 (each 3H, s, Me), 2.07 (1H, *d*, *J* = 11.0 Hz, H-5), 3.18, (1H, *s*, OH), 3.20 (1H, *m*, H-3), 3.50 (1H, *s*, OH), 3.62 (1H, *d*, *J* = 2.9 Hz, 7H), 3.69 (1H, *ddd*, *J* = 13.9, 11.0, 2.9 Hz, H-6), 4.96 (1H, *d*, *J* = 11 Hz, $H_a$-15), 5.06 (1H, *d*, *J* = 17.6 Hz, $H_b$-15), 5.88 (1H, *dd*, *J* = 17.6, 11.0 Hz, H-14).

*Oxidation of* **1** *with pyridinium chlorochromate* (PCC). To PCC (100 mg) in $CH_2Cl_2$ (2 ml) was added **1** (7 mg) in $CH_2Cl_2$ and stirred for overnight at room temp. The resulting mixture was filtered and removal of the solvent gave the residue which was purified by prep. TLC to afford a diacetoxyketone (2 mg) whose physical and spectral data were identical to those of the natural hamachilobene B (**2**).

*Reduction of* **2** *with* $LiAlH_4$. Compound **2** (13 mg) was treated in the same manner as described above. Work-up as usual gave a triol mixtures which were purified by prep. TLC to afford the triols **6** (0.8 mg) and **8** (2 mg). The former product was identical to **6** prepared from **1** in all respects. Triol (**8**): white powder; CIMS *m/z*: 339 $[M+1]^+$, 323, 303, 285, 275, 207, 123, 81, 42 (base); $^1H$ NMR: $\delta$ 0.87, 0.96, 1.24, 1.30, 1.31 (each 3H, *s*, Me), 1.15 (1H, *d*, *J* = 10.3 Hz, H-5), 2.58 (1H, *d*, *J* = 2.2 Hz, 6-OH), 2.63 (1H, *d*, *J* = 2.9 Hz, 7-OH), 3.20 (1H, *m*, H-3), 3.47 (1H, *dd*, *J* = 9.5, 2.2 Hz, H-7), 3.74 (1H, *ddd*, *J* = 10.3, 9.5, 2.2 Hz, H-6), 4.93 (1H, *dd*, *J* = 10.3, 1.5 Hz, $H_a$-15), 5.12 (1H, *dd*, *J* = 17.6, 1.5 Hz, $H_b$-15), 5.85 (1H, *dd*, *J* = 17.6, 10.3, H-14).

*Acetylation of* **3**. Compound **3** (3 mg) was acetylated with $Ac_2O$–pyridine (each 0.5 ml) overnight. Work-up as usual gave a triacetate (**9**) (2.7 mg) as white powder: $^1H$ NMR: $\delta$0.92, 0.94, 0.96, 1.16, 1.37 (each, 3H, *s*, Me), 2.00 (3H, *s*, AcO), 2.05 (6H, *s*, 2xAcO), 4.42 (1H, *dd*, *J* = 11.7, 5.4 Hz, H-3), 5.05 (1H, *d*, *J* = 10.7 Hz, H-7), 5.34 (1H, *dd*, *J* = 11.2, 9.8 Hz, H-6), 4.90 (1H, *dd*, *J* = 10.7, 2.0 Hz, $H_a$-15), 5.19 (1H, *dd*, *J* = 17.6, 2.0 Hz, $H_b$-15), 5.80 (1H, *dd*, *J* = 17.6, 10.7 Hz, H-14).

*Acetylation of* **4**. **4** (3 mg) was treated in the same manner as described above to give a triacetate whose spectral data were identical to those of **9** prepared from **3**.

*Reduction of* **9** *with* $LiAlH_4$. **9** (5.6 mg) was reduced in the same manner described above to afford a triol (5.2 mg) whose spectral data were identical to those of **8**.

*Benzoylation of* **8**. To an $Me_2CO$ soln of **8** (7.2 mg) obtained from **2** and **9** was added dry $CuSO_4$ (1.5 mg) and the soln was refluxed at 60–70° for 10 hr. The resulting mixture was carefully filtered and the filtrate to give an acetonide (**10**) which was acetylated with $Ac_2O$–pyridine overnight. The reaction mixture was poured into $H_2O$ and extracted with $Et_2O$. Removal of the solvent gave an acetate (**11**) which was treated with 60% AcOH (2 ml) with stirring overnight, without further purification. The resulting mixture was extracted with $Et_2O$ and the extract was dried and evaporated to afford a diol (**12**). Without further purification **12** in pyridine (1 ml) was esterified with *p*-chlorobenzoylchloride (0.1 ml) at 40° for 3 days with stirring. Work-up as usual gave the residue which was chromatographed on Sephadex LH-20 ($CHCl_3$–MeOH 1:1) to afford a dibenzoate fraction. It was carefully purified by prep. TLC to furnish the dibenzoate (**13**) (1 mg) as white powder. **13**: EIMS *m/z*: 658 $[M+2]^+$, 656 $[M]^+$, 641, 503, 485, 329, 287, 269, 257, 232, 217, 199, 189, 151, 141, 121, 111, 95, 81, 69, 55, 44 (base): $^1H$ NMR: $\delta$ 0.88, 0.99, 1.07, 1.13, 1.52. (each 3H, *s*, Me), 2.01 (3H, *s*, AcO), 4.47 (1H, *dd*, *J* = 11.2, 4.9 Hz, H-3), 5.44 (1H, *d*, *J* = 10.3 Hz, H-7), 5.75 (1H, *dd*, *J* = 10.3, 11.2 Hz, H-6), 4.91 (1H, *dd*, *J* = 10.7, 1.5 Hz, $H_a$-15), 5.23 (1H, *dd*, *J* = 17.1, 1.5 Hz, $H_b$-15), 5.81 (1H, *dd*, *J* = 17.1, 10.7 Hz, H-14), 7.24 (4H, *d*, *J* = 8.3 Hz, 4xAr-H), 7.72 (4H, *d*, *J* = 8.3 Hz, 4xAr-H); CD $\Delta\varepsilon_{263}$ −11.4.

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