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DRIMANE-TYPE SESQUITERPENOIDS FROM THE LIVERWORT *MAKINOA CRISPATA**

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Key Word Index—*Makinoa crispata*; Metzgeriales; Hepaticae; crispatanolide; 7α-chloro-6β-hydroxyconfertifoline; 6β,7α-dihydroxyconfertifoline; 6β,7β-epoxyconfertifoline; drimane-type sesquiterpenoid; chemosystematics.

Abstract—Three new drimane-type sesquiterpenoids, 7α-chloro-6β-hydroxyconfertifoline, 6β,7α-dihydroxyconfertifoline and 6β,7β-epoxyconfertifoline were isolated from the liverwort *Makinoa crispata* together with the previously known eudesmane-type sesquiterpene lactone, crispatanolide and a sacculatane-type diterpene dialdehyde, perrottetianal A. The stereostructures of the new compounds were established by 2D NMR and CD spectroscopy and chemical evidence. The present chemical results support Schuster's phylogenic classification of the two orders, Metzgeriales and Jungermanniales.

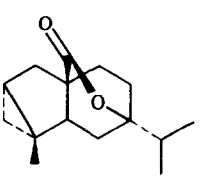
INTRODUCTION

Previously, we reported the isolation and structure elucidation of a novel sesquiterpene lactone, crispatanolide (**1**) from the liverwort *Makinoa crispata* [2]. In pursuit of pharmacologically interesting substances in the liverworts, we have reinvestigated *Makinoa crispata*, and have isolated three new drimane-type sesquiterpenes, 7α-chloro-6β-hydroxyconfertifoline (**2**). 6β,7α-dihydroxyconfertifoline (**3**) and 6β,7β-epoxyconfertifoline (**4**). In this paper, we wish to report on the isolation and structure determination of the three new drimane-type sesquiterpenoids.

RESULTS AND DISCUSSION

A combination of column chromatography on silica gel and Sephadex LH-20 of the ethyl acetate extract of *M. crispata* has resulted in the isolation of the three new drimane-type sesquiterpenoids, 7α-chloro-6β-hydroxyconfertifoline (**2**), 6β,7α-dihydroxyconfertifoline (**3**), 6β,7β-epoxyconfertifoline (**4**), along with the known crispatanolide (**1**) [2] and perrottetianal A (**5**) [3].

7α-Chloro-6β-hydroxyconfertifoline (**2**) has the molecular formula $C_{15}H_{21}O_3Cl$ ($[M]^+$ at *m/z* 284.1189), and its IR and UV spectra displayed the presence of an α,β-conjugated γ-lactone (1755 and 1645 cm^{-1}; λ_{max} 220.5$_{nm}$) and a hydroxyl group (3440 cm^{-1}). The ^1H and ^{13}C NMR spectra (Tables 1 and 2) indicated the presence of three tertiary methyl groups (δ_H1.06, 1.26 and 1.53), one methine group bearing a hydroxyl group [δ_H 4.54(s), δ_C71.8], one methine group bearing chlorine atom [δ_H4.63(*d*, *J* = 2.0 Hz), δ_C52.5] and a fused α,β-conjugated γ-lactone [δ_H4.83(*d*, *J* = 17.3 Hz), 4.88 (*dd*, *J* = 17.3, 2.0 Hz); δ_C68.7, 121.6, 172.9, 174.3] and as well as of three methylenes, one methine and two quaternary carbons. These spectral features revealed that **2** might be a drimane-type sesquiterpene lactone, confertifoline (**6**) or isodrimenin (**7**) with a hydroxyl and a chlorine group. Tanaka *et al.* [4] reported that the ^{13}C NMR spectrum of isodrimenin (**7**) showed the olefinic atoms at δ_C159.9 (C-8) and 150.9 (C-9). The ^{13}C NMR spectrum of **2** showed the olefinic C-atoms at δ_C121.6 (C-8) and 174.3 (C-9). In addition, the ^1H–^1H COSY, ^{13}C–^1H COSY and long-range ^{13}C-^1H COSY spectra (Table 3) of **2** suggested that **2** was 7-chloro-6-hydroxyconfertifoline. The characteristic fragment ions (Scheme 1) in the mass spectrum of **2** further supported the above structure. The stereochemistry of **2** was established by NOE difference spectra (Scheme 2). The NOEs were observed (i) between H-13 and H-14, (ii) H-11 and H-13, (iii) H-5 and H-15, (iv) H-5 and H-6 and (v) H-14 and H-15. The absolute configuration of **2** was determined by the following chemical degradations. Oxidation of **2** with Jones reagent gave a ketone (**8**). The CD spectrum of **8** had a positive Cotton effect at 316 nm ([θ] + 7504) based on α-axial haloketone rule [5]. Reduction of **8** with zinc–acetic acid yielded a dechloro compound, which was identical with (+)-fragrolide (**9**) [6] isolated from *Cinnamosma fragrans* in all respects. Acetylation of **2** gave momacetates **10** and **11**. The former acetate was identical in all respects with **10** [6] derived from cinnamosmolide (**12**) treated with thionyl



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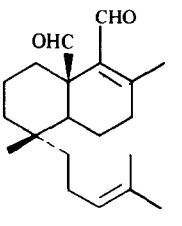

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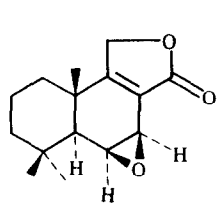
*Part 32 in the series 'Chemosystematics of Bryophytes' For Part 31, see ref. [1].



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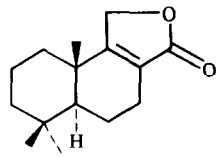

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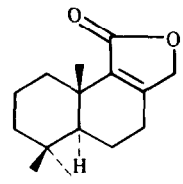

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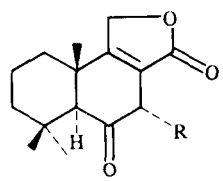
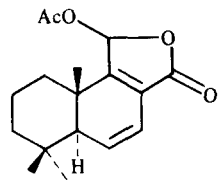


8 R = Cl
9 R = H



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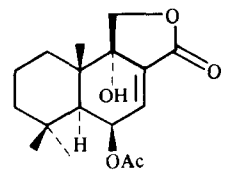

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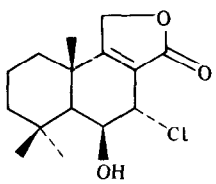
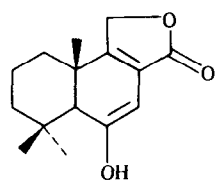
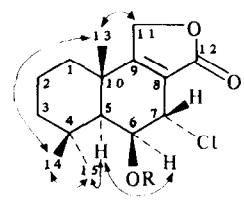


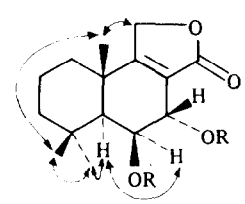
2 *m/z* 284 (16%)



m/z 248 (73%)

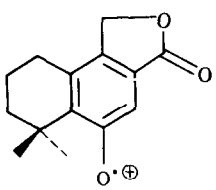


2 R = H
10 R = Ac

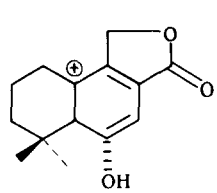


3 R = H
13 R = Ac
14 R = Bz

Scheme 2

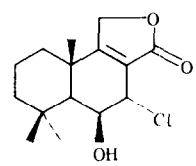


m/z 231 (46%)



m/z 233 (94%)

Scheme 1



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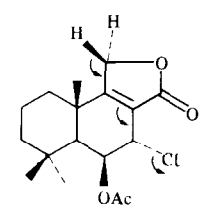

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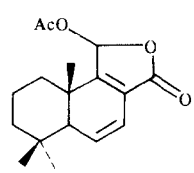

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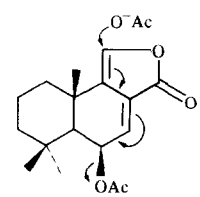

Scheme 3

chloride ($SOCl_2$). We suggest that **11** might be obtained by the reaction mechanism as shown in Scheme 3. On the basis of the above chemical and spectral data, the absolute stereostructure of **2** was established to be 7α-chloro-6β-hydroxyconfertifoline.

6β,7α-Dihydroxyconfertifoline (**3**) has the molecular formula, $C_{15}H_{22}O_4$ ($[M]^+$ at *m/z* 266.1500), and the IR, UV and NMR (Tables 1 and 2) spectra were similar to those of compound **2**. The ^1H NMR spectrum of **2** showed the presence of two hydroxyl groups [δ_H 4.16 (*br s*) and 4.36 (*br s*)] and two methines [δ_H 4.08 (*d*, J = 4.2 Hz) and 4.44 (*d*, J = 4.2 Hz)] bearing a hydroxyl group. Acetylation of **3** with acetic anhydride–pyridine and dimethylaminopyridine (DMAP) yielded a diacetate (**13**). The ^1H–^1H COSY, ^{13}C–^1H COSY, long-range ^{13}C–^1H COSY (Table 3) and NOE difference spectra (Scheme 2) of **13** showed that **3** was 6β,7α-dihydroxyconfertifoline.

The absolute configuration of **3** was determined by the CD spectrum of the dibenzoate derivative (**14**), obtained from **3** by treatment with DMAP and benzoyl chloride in pyridine. The CD spectrum of **14** had a strong positive

Table 1. ^{1}H NMR (400 MHz) spectral data for compounds **2**–**4**, **8**–**11**, **13** and **14**

H	2*	3†	4†	8*	9*	10*	11*	13*	14*
5	1.73 (*br s*)	1.59 (*br s*)	1.58 (*br s*)	3.04 (*br s*)	2.43 (*br s*)	1.92 (*br s*)	1.48 (*d*, 3.4)	1.66 (*br s*)	1.85 (*br s*)
6	4.54 (*br s*)	4.44 (*d*, 4.2)	3.84 (*d*, 4.4)			5.63 (*br s*)	5.85 (*dd*, 3.4, 6.1)	5.53 (*br s*)	5.87 (*br s*)
7	4.63 (*d*, 2.0)‡	4.08 (*dd*, 4.2, 2.0)	3.58 (*d*, 4.4)	4.52 (*d*, 2.0)	2.98 (*dd*, 15.1, 2.4)	4.54 (*br s*)	6.91 (*dd*, 6.1, 2.0)	5.45 (*d*, 1.7)	5.95 (*br s*)
					3.13 (*dd*, 15.1, 2.4)				
11	4.83 (*d*, 17.3),	4.79 (*d*, 17.3),	4.82 (*d*, 18.1)	4.83 (*d*, 17.3)	4.84 (*d*, 2.4)	4.83 (*d*, 17.3)	6.68 (*d*, 2.0)	4.81 (*d*, 17.3)	4.90 (*d*, 17.6)
	4.88 (*dd*, 17.3, 2.0)	4.93 (*dd*, 17.3, 2.0)	4.98 (*d*, 18.1)	4.89 (*dd*, 17.3, 2.0)		4.88 (*dd*, 17.3, 2.0)		4.88 (*dd*, 17.3, 1.7)	4.98 (*d*, 17.6)
13	1.53 (*s*)	1.54 (*s*)	1.37 (*s*)	1.35 (*s*)	1.31 (*s*)	1.51 (*s*)	1.44 (*s*)	1.55 (*s*)	1.70 (*s*)
14	1.26 (*s*)	1.25 (*s*)	1.20 (*s*)	1.21 (*s*)	1.18 (*s*)	1.08 (*s*)	1.14 (*s*)	1.01 (*s*)	1.04 (*s*)
15	1.06 (*s*)	1.02 (*s*)	1.18 (*s*)	1.05 (*s*)	1.04 (*s*)	1.05 (*s*)	1.02 (*s*)	1.03 (*s*)	1.07 (*s*)
the others	2.23 (*br s*, 6-OH)	4.16 (*br s*, OH),				2.07 (*s*, OAc)	2.08 (*s*, OAc)	2.07 (*s*, OAc)	7.42–7.60 (*m*, Bz)
		4.36 (*br s*, OH)						2.08 (*s*, OAc)	7.80–8.06 (*m*, Bz)

*Solvent $CDCl_3$.
†Solvent $(CD_3)_2CO$.
‡Coupling constant (J in Hz) are given in parentheses.

Cotton effect at 232 nm ($[\theta]+77761$) arising from the interaction between two benzoyl groups [7]. Thus, the absolute stereochemistry of **3** was established as depicted in Scheme 2.

6β,7β-Epoxyconfertifoline (**4**) has the molecular formula $C_{15}H_{20}O_3$ ([M]$^+$ at m/z 248.1399) and the spectral data (IR, UV, NMR) were similar to those of **2** and **3**. The ^{1}H and ^{13}C NMR (Tables 1 and 2) of **4** showed the presence of an epoxy ring [δ_H3.58 (*d*, J=4.4 Hz) and 3.84 (*d*, J=4.4 Hz); δ_C41.3 and 55.5]. Basic treatment of **2** with sodium hydride in dimethylformamide at 0–5° yielded **4**, Based on the results, **4** was assigned to be 6β,7β-epoxyconfertifoline.

The configuration at C-7 of **2** is assumed to be *S*-oriented as in the case of **3** since it is likely that **2** would be biosynthetically formed by the opening of the epoxy ring of **4** caused by an attack of an anion (Cl^- or OH^-) upon C-7. More than 130 chlorine-containing compounds have been isolated from higher plants and ferns [8]. Many of them are chlorohydrins which were isolated together with the related epoxides [9]. At first, we thought **2** could be an artefact. However, the isolation of **2** was carried out using chlorine-free solvents and the presence of **2** in the ethyl acetate extract of fresh *M. crispata* was confirmed by GC-MS. Thus, it was concluded that the compound is a natural product. This is the first record of the isolation of a chlorine-containing compound from bryophytes.

There is chemically clear evidence that the Metzgeriales and the Jungermanniales originated from a common ancestor although the present species belonging to both orders are morphologically quite different. Drimane- and pinguisane-type sesquiterpenoids and sacculatane-type diterpenoids have been found in *Porella*, *Ptilidium*, *Lejeunea* and *Trichocoleopsis* species belonging to the Jungermanniales [10]. *Aneura pinguis* and *Pellia endiviifolia* belonging to the Metzgeriales produce drimane- and pinguisane-type sesquiterpenoids as well as sacculatane diterpenoids [10]. *Makinoa crispata* belonging to the Metzgeriales also elaborates drimane-type sesquiterpenoids and sacculatane-type diterpenoids along with eudesmane-type sesquiterpenoids which are widely distributed in the Jungermanniales. The chemical evidence regarding the Metzgeriales and the Jungermanniales supports Schuster's phylogenic classification of the two orders. In the modern classification of the Hepaticae, the Jungermanniales and Metzgerales are united within the subclass Jungermanniae [11].

EXPERIMENTAL

Mps: uncorr. The solvents used for spectral measurements were TMS–$CDCl_3$ or TMS–$(CD_3)_2CO$ [^{1}H NMR (400 MHz); ^{13}C NMR (100 MHz)]; $CHCl_3$ or Me_2CO ($[\alpha]_D$); EtOH (CD and UV). TLC, GC and GC-MS were carried out as previously reported [12].

Plant material. Makinoa crispata (Steph.) Miyake was collected in Tokushima, Japan in October 1987 and identified by Dr M. Mizutani. A voucher specimen was deposited at the Herbarium of the Institute of Pharmacognosy, Tokushima Bunri University.

Extraction and isolation. The fresh *M. crispata* was homogenized with EtOAc (10 l) by a mixer. The resultant EtOAc extract was evapd *in vacuo* to give a green oil (19.9 g). The crude extract was chromatographed on silica gel using a *n*-hexane–EtOAc gradient to provide five fractions. From fr. 1(20% EtOAc–*n*-hexane), pure crispatanolide (**1**) (552 mg) [2] was obtained as

Table 2. ^{13}C NMR (100 MHz) spectral data for compounds **2–4**, **7–10**, **13** and **14**

C	2*‡	3†	4†	7*§	8*	9*	10*	13*‡	14*
1	38.6	38.3	37.7	35.1	35.4	35.7	38.6	38.4	38.7
2	18.5	18.6	18.5	18.6	18.0	17.9	18.4	18.2	18.5
3	42.6	42.9	43.1	41.9	41.8	42.5	42.6	42.9	43.1
4	33.4	33.3	33.6	33.2	32.2	32.5	33.3	33.3	33.6
5	48.3	49.0	50.5	52.3	49.9	62.7	47.5	49.6	50.5
6	71.8	71.3	70.2	18.3	200.7	205.7	72.0	69.0	70.2
7	52.5	66.5	64.7	25.2	57.1	37.7	49.0	63.7	64.7
8	121.6	123.0	120.2	159.9	122.5	121.8	121.7	119.8	120.2
9	174.3	173.8	175.8	150.9	173.9	172.4	173.1	175.4	175.8
10	37.3	37.2	37.2	34.8	41.8	40.0	37.4	37.1	37.2
11	68.7	68.2	68.4	172.4	67.9	68.2	68.3	68.3	68.4
12	172.9	169.8	171.7	70.8	169.8	170.1	171.5	171.8	171.7
13	22.6	21.8	23.0	20.1	21.6[a]	21.6[b]	22.6[c]	22.2	23.0
14	23.5	23.2	23.0	21.4	22.3[a]	21.8[b]	23.0[c]	22.7	23.0
15	33.2	33.1	33.2	33.4	31.6	32.4	32.9	32.9	33.2
OAc							21.1	20.6	128.4, 128.6
or							169.5	21.1	128.8, 129.9
OBz								168.4	131.1, 133.3
								168.8	164.4, 165.3

*Solvent $CDCl_3$,
†Solvent $(CD_3)_2CO$.
‡Assignments were confirmed by the ^{13}C-^1H and long-range ^{13}C-^1H COSYs.
§Ref. N. Tanaka *et al.* [4].
[a–c]Assignments may be interchanged.

Table 3. C–H correlation in the long-range C–H COSY of compounds **2** and **13**

C	Correlated H
1	H-2, H-3
2	H-1, H-3
3	Me-13, Me-15
4	Me-14, Me-15, H-5
5	Me-15, H-3
6	H-7
7	H-6
8	H-6, H-7, H-11
9	Me-13, H-7, H-11
10	Me-13, H-5, H-6
11	
12	
13	H-1, H-5
14	Me-15, H-3, H-5
15	Me-14, H-3, H-5

colourless plates (from Et_2O–*n*-hexane; mp 109–111°). From fr. 2 (25% EtOAc–*n*-hexane), pure perrottetianal A (**5**) (1.02 g) [3] was obtained as a colourless oil. The crude products of fr. 3 (30% EtOAc–*n*-hexane) were further purified by prep. TLC (*n*-hexane–EtOAc, 4:1) to give 6β,7β-epoxyconfertifoline (**4**) (14 mg). Fr. 4 (40% EtOAc–*n*-hexane) was recrystallized from EtOAc–*n*-hexane to give pure 7α-chloro-6β-hydroxyconfertifoline (**2**) (347 mg). Fr. 5 (50% EtOAc–*n*-hexane) was recrystallized from EtOAc–*n*-hexane to give pure 6β,7α-dihydroxyconfertifoline (**3**) (92 mg).

Compound **2**. Colourless plates (from EtOAc–*n*-hexane), mp 194.5–196°; $[\alpha]_D$ +36.0° (Me_2CO; *c* 0.88); HRMS: $[M]^+$ (found 284.1189; Calcd. for $C_{15}H_{21}O_3Cl$; 284.1198); EIMS *m/z* (rel. int.): 284 $[M]^+$ (16), 266 $[M-H_2O]^+$ (19), 249 (41), 248 $[M-HCl]^+$ (73), 233 $[M-HCl-Me]^+$ (94), 231 (46), 220 (41), 215 (34), 91 (63), 85 (100), 69 (66); UV λ_{max} nm (ε): 220.5 (9923); IR ν_{max}^{KBr} cm^{-1}: 3440 (OH), 1755 (lactone C=O), 1645 (C=C), 1440, 1250, 1195, 1020, 995, 790; ^1H and ^{13}C NMR: see Tables 1 and 2.

Compound **3**. Colourless needles (from EtOAc–*n*-hexane), mp 212–215°; $[\alpha]_D$ +47.9° (Me_2CO; *c* 0.73); HRMS: $[M]^+$ (found: 266.1500; calcd. for $C_{15}H_{22}O_4$; 266.1518); EIMS *m/z* (rel. int.): 266 $[M]^+$ (10), 248 $[M-H_2O]^+$ (18), 233 (26), 230 (22), 215 (21), 204 (26), 179 (37), 164 (54), 153 (96), 142 (100), 135 (54), 85 (95); UV λ_{max} nm (ε): 220.5 (9923); IR ν_{max}^{KBr} cm^{-1}: 3540, 3490 (OH), 1735 (lactone C=O), 1650 (C=C), 1385, 1200, 1040, ^1H and ^{13}C NMR: see Tables 1 and 2.

Compound **4**. Colourless needles (from Et_2O): mp 138–140°; $[\alpha]_D$ +16.7° (Me_2CO; *c* 0.65); HRMS: $[M]^+$ (found: 248.1399; calcd. for $C_{15}H_{20}O_3$; 248.1385); EIMS *m/z* (rel. int.): 248 $[M]^+$ (8), 233 (18), 163 (18), 151 (38), 135 (26), 109 (24), 105 (26), 95 (42), 91 (35); UV λ_{max} nm (ε): 220.0 (9585); IR ν_{max}^{KBr} cm^{-1}: 1755 (lactone C=O), 1645 (C=C), 1440, 1195, 1020, 995, ^1H and ^{13}C; see Tables 1 and 2.

Oxidation of **2** *with* CrO_3. To a soln of **2** (41 mg) in Me_2CO (5 ml) was added Jones reagent (8 M CrO_3–H_2SO_4) (0.2 ml) at 0–5°. The mixture was stirred at 0–5° for 30 min, and then added to ice-H_2O. The reaction mixture was extracted with EtOAc, and the extract was washed with H_2O, dried over $MgSO_4$, and concd to crude crystals (39 mg), which were recrystallized from Et_2O–*n*-hexane to give 7α-chloro-6-oxoconfertifoline (**8**) (28 mg) as colourless needles; mp 162.0–163.5°; $[\alpha]_D$ +193.5° ($CHCl_3$; *c* 0.47); HRMS: $[M]^+$ (found: 282.1008; calcd. for $C_{15}H_{19}O_3Cl$; 282.0993); EIMS *m/z* (rel. int.) 282 $[M]^+$ (19), 267 (24), 246 (44), 203 (32), 163 (45), 105 (33), 91 (30), 43 (100); UV λ_{max} nm (ε): 219.5

(8895); IR ν_{max}^{KBr} cm^{-1}: 1775 (lactone C=O), 1730 (C=O), 1665 (C=C), 1345, 1125, 1025, 995; CD: $[\theta]_{316\,nm}+7504$, $[\theta]_{248}+8186$, $[\theta]_{221}+6594$; ^1H and ^{13}C NMR: see Tables 1 and 2.

Reduction of **8** with Zn–AcOH. To a soln of **8** in AcOH (4 ml) was added Zn (200 mg) and the reaction mixture was stirred at room temp. for 12 hr. The excess Zn was removed by filtration, washed with EtOAc. The solvent was concd to afford a crude product (29 mg), which was purified by prep. TLC (C_6H_6–EtOAc, 4:1) to furnish **9** (7 mg) as colourless needles; mp 165.5–167.0° (lit. [6]; mp 165–167°). This compound was identical with fragrolide (**9**) [6] in all respects ($[\alpha]_D$, IR, UV, ^1H NMR). ^1H and ^{13}C NMR: see Tables 1 and 2.

Acetylation of **2**. A mixture of **2** (22 mg), Ac_2O (1 ml), DMAP (20 mg) and pyridine (2 ml) was stirred at room temp. for 12 hr, poured into water, and extracted with $CHCl_3$. The $CHCl_3$ was washed successively with 1 M HCl, H_2O, 5% $NaHCO_3$, and H_2O, dried, and evapd *in vacuo*. The residue (29 mg) was subjected to prep. TLC (C_6H_6–EtOAc, 7:1) to afford 6β-acetoxy-7α-chloroconfertifoline (**10**) and 11-acetoxy-6,7-dehydroconfertifoline (**11**) (7 mg), respectively. Compound (**10**): colourless needles; mp 177.5–179° (lit. [6], mp 178°); $[\alpha]_D+43.2°$ ($CHCl_3$; *c* 0.37) (lit. [6], $[\alpha]_D+46.7°$). This compound was identical with **10** derived from cinnamosmolide (**12**) [5] in all respects (IR, UV, ^1H NMR). ^1H and ^{13}C NMR: see Tables 1 and 2. Compound **11**: EIMS *m/z* (rel. int.): 290 $[M]^+$ (1). 149 (26), 85 (23), 69 (16), 43 (100); UV λ_{max} nm (ε): 213 (10274), 250.5 (3257); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770, 1745 (C=O), 1360, 1230, 1180, 940; ^1H NMR; see Table 1.

Acetylation of **3**. A mixture of **3** (30 mg), Ac_2O (1 ml) and pyridine (1 ml) was stirred at room temp. for 24 hr. The usual work-up afforded the diacetate (**13**) (29 mg) as colourless needles from Et_2O. Mp 215–218° (decomp.); $[\alpha]_D+62.3°$ (Me_2CO; *c* 0.82); EIMS *m/z* (rel. int.): 290 $[M-AcOH]^+$ (7), 248 (69), 233 (18), 166 (20), 162 (21), 43 (100); UV λ_{max} nm (ε): 219 (11490); IR ν_{max}^{KBr} cm^{-1}: 1765, 1735 (C=O), 1670 (C=C), 1360, 1230, 1205, 1020, 1010; (found: C, 65.39; H, 7.45. $C_{19}H_{26}O_6$ requires C, 65.12; H, 7.48); ^1H and ^{13}C: see Tables 1 and 2.

Benzoylation of **3**. A mixture of **3** (12 mg), benzoyl chloride (0.5 ml), DMAP (0.1 g) and pyridine (4 ml) was stirred at room temp. for 48 hr. The usual work-up afforded oil (607 mg), which was purified by CC on silica gel (C_6H_6–EtOAc, 4:1) to give the dibenzoate (**14**) (11 mg) as a colourless oil. $[\alpha]_D+101.4°$ ($CHCl_3$; *c* 0.22); UV λ_{max} nm (ε): 282 (1695), 275 (2260), 232.5 (33867); IR ν_{max}^{neat} cm^{-1}: 1765, 1725 (C=O), 1680 (C=C), 1600, 1585, 1240, 1085, 1020; CD: $[\theta]_{232\,nm}+77761$; ^1H and ^{13}C NMR: see Tables 1 and 2.

Treatment of **2** *with* NaH. To a soln of **2** (10 mg) in dry DMF (3 ml) was added 60% NaH (5 mg) and the mixture stirred at 0–5° for 1 hr. The usual work-up afforded oil (8 mg), which was purified by prep. TLC (*n*-hexane–EtOAc, 3:1) to give the pure product (1 mg), the ^1H NMR spectrum and TLC behaviour of which were identical with those of 6β,7β-epoxyconfertifoline (**4**).

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