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FURTHER SECO-LABDANES FROM *HEBECLINIUM MACROPHYLLUM*

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Key Word Index—*Hebeclinium macrophyllum*; Compositae; diterpenes; seco-labdane derivatives; stereospecific reactions; absolute configuration.

Abstract—A reinvestigation of the aerial parts of *Hebeclinium macrophyllum* afforded in addition to known compounds several further seco-labdane derivatives; all being epimeric pairs at C-5. The structures were elucidated by high field NMR techniques. The stereochemistry was assigned by NOE difference spectroscopy and the absolute configurations were deduced from the Cotton-effects of the natural compounds and of chemical transformation products.

INTRODUCTION

The genus *Hebeclinium* (tribe Eupatorieae) is placed in the subtribe Hebecliniinae [1]. So far only one species has been studied chemically. A seco-labdane was isolated, in addition to a nerolidol derivative [2]. We have now reinvestigated a much larger sample of the same species.

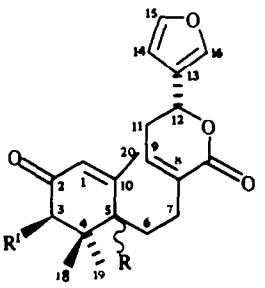
RESULTS AND DISCUSSION

The extract of the aerial parts of *Hebeclinium macrophyllum* (L.) DC, collected in Costa Rica, afforded several common compounds (see Experimental) and the seco-labdane derivatives **1a/b**–**5a/b**. These diterpenes were also present in the extract of a collection from Equador. However, only the structure of hebeclinolide (**1a/b**) could be elucidated [2] as the amount of the other diterpenes was insufficient for further investigations and the stereochemistry of **1** could not be determined.

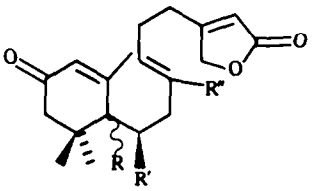
The lactones **2a** and **2b** were separated as their acetates. The ^{1}H NMR spectra (Table 1) clearly indicated that these ketones were isomers differing from **1a/b** by an additional oxygen function which could only be placed at C-3 as the pair of broadened doublets for H-3 were replaced by singlets at δ5.14 and 5.44 respectively. The spectra of **2a**Ac and **2b**Ac mainly differed in the signals of H-3, H-5-H-7 and OAc indicating that they were epimers at C-3 or C-5. NOE difference spectroscopy allowed the assignment of the relative configuration and of the methyls at C-4. Thus in the case of **2a**Ac a 10% NOE between H-3 and H-5 required equatorial orientations of the substituents at these centres. By irradiation of the signal at δ1.08 (H-19) NOE's with H-3 (5%), H-5 (5%) and H-18 (5%) were observed. A W-coupling between H-18 (0.84 *s*) and H-3 indicated the axial orientation of the methyl group. Similarly NOE's between H-3, H-6 (5%), H-6′ (2%) and H-19 (3%), between H-18 and H-5 (5%) and between H-19, H-5 (4%), H-3 (4%), H-6 (3%) and H-6′ (2%) (always the first proton is the irradiated one) as well as a W-coupling between H-18 and H-3 established axial orientation of H-3 and of the large substituent at C-5 in the acetate of **2b**. The absolute configuration followed from the negative Cotton-effects in both acetates following the helicity rule [3] for α,β-unsaturated, transoid ketones. The configuration at C-12 was determined with the reaction products of **1a/b** (s. below). The ^{13}C NMR spectra (Table 2) also agreed with the proposed structures.

A careful reinvestigation of the ^{1}H NMR spectrum of **1a/b** in deuteriobenzene indicated that again an epimeric mixture (*ca* 7:3) was present. This was supported by the ^{13}C NMR spectrum (Table 2) were a few signals were doubled. However, all attempts to separate this mixture were unsuccessful. While the negative Cotton-effect of the mixture indicated the same configurations of the main compound at C-5 as in **2a** the absolute configuration at C-12 had to be determined. As the CD bands of the two chiral chromophores are overlapping we tried to remove the chiral centre at C-5 by converting the unsaturated ketone to a saturated, symmetric one using 1,4-addition of dimethyl lithium cuprate. Suprisingly, this led to the formation of two lactones (**7a/b**) in which the Δ^8 double bond was absent. A new methyl doublet, an additional pair of doublets around δ2–3 and the absence of the signal of an olefinic proton required, together with the molecular formula ($C_{21}H_{28}O_4$), the formation of a new ring. The structures of **7a** and **7b** followed from the spectral data. In the ^{1}H NMR spectra in deuteriobenzene (Table 1) all signals could be assigned by spin decoupling. The stereochemistry was determined by the observed NOE's. In the case of **7a** clear effects were obtained between H-5, H-18 (2%), H-19 (3%) and H-20 (4%), between H-6β and H-3β (3%), between H-20, H-5 (4%), H-11α (10%) and H-19 (3%) as well as between H-21, H-7β (10%) and H-12 (10%) In the case of **7b**, NOE's between H-5 and H-20 (3%), between H-18, H-5 (5%) and H-6β (4%), between H-20, H-3β (3%), H-5 (10%) and H-9 (11%) as well as between H-21, H-7α (3%), H-11β (11%) and H-12 (8%) were observed. For the assignment of the methyl signals the W-couplings were useful [**7a**: H-20/H-1β, H-19/H-3β; **7b**: H-20/H-1α, H-19/H-3β]. Inspection of models showed that all data required in the case of **7a** the cyclohexanone ring in a chair and in the case of **7b** in a boat conformation. The ^{13}C NMR spectra (Table 2) nicely agreed with the structures.

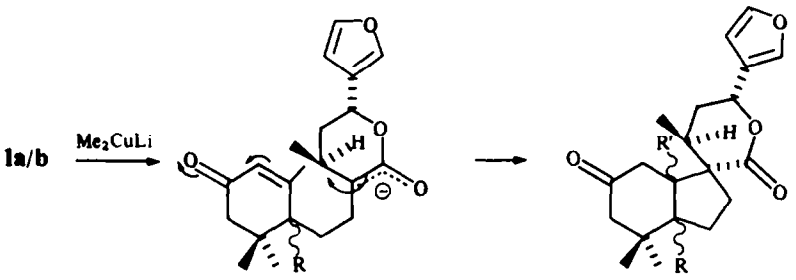
The formation of **7a** and **7b** clearly indicated that also hebeclinolide was an epimeric mixture at C-5. The



	1a	1b	2a	2b
R	αH	βH	αH	βH
R'	H	H	OH	OH

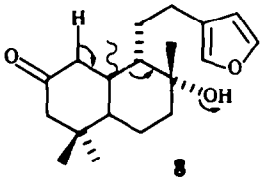


	3a	3b	4a	4b	5a	5b
R	αH	βH	αH	βH	αH	βH
R'	H	H	H	H	OAc	OAc
R"	CH_2OH	CH_2OH	CHO	CHO	Me	Me



6a R = αH
6b R = βH

	7a	7b
R	αH	βH
R'	αMe	βMe



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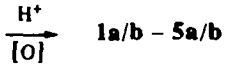

formation of these two lactones only can be explained if **1a** was first attacked regio- and stereospecifically at C-9 from the β-face leading to the anion **6a** which then was transformed by Michael-addition thermodynamically controlled to **7a**. Similar **1b** only gave **7b**, epimeric at C-5 and C-10. The ratio of **7a/7b** and **1a/1b** was nearly identical as followed from the ^{1}H NMR spectra. Having now in hand two saturated cyclohexanone derivatives the absolute configuration could be deduced from the observed Cotton-effects by application of the octant rule. As expected the main product (**7a**) showed a negative and the minor compound (**7b**) a positive Cotton-effect. It is very likely that the other diterpenes have the same absolute configuration.

The ^{1}H NMR spectra of **3a/b** and **4a/b** (Table 1) indicated that these compounds differed in a more pronounced manner from **1a/b** and **2a/b**. Signals *ca* δ4.8 and 5.9 indicated that the furane was replaced by a butenolide moiety. Furthermore the δ-lactone ring was absent. Again spin decoupling allowed the assignment of all signals. The downfield shift of the H-9 signal in the spectrum of **4a/b** required an aldehyde group at C-17 which was supported by a singlet at δ9.39. A broadened singlet at δ4.07 in the spectrum of **3a/b** showed that the corresponding alcohols were present. Though the ^{1}H NMR spectra gave no indication of the presence of epimers the very weak negative Cotton-effect in the case of **3a/b** favours the presence of mixtures of 5α-H and racemic compounds (**3a/b** and **4a/b**).

The ^{1}H NMR spectra of **5a** and **5b** (Table 1) again showed that these compounds were epimers. Spin decoupling allowed the assignment of all signals. The chemical shift of H-6 required the presence of an ester function at this carbon. An additional olefinic methyl signal further showed that no oxygen function was at C-17 while again a butenolide moiety was present. Accordingly, **5a** and **5b** were 6β-acetoxy derivatives of **3a/b** with no hydroxy group at C-17. The differences in the stereochemistry of **5a**

Table 1. ^{1}H NMR spectral data of compounds **1a/b–5a/b** and **7a/b** (400 MHz, $CDCl_3$, δ-values)

H	**1a/b** (C_6D_6)	**2aAc 2bAc**	**3a/b***	**4a/b†**	**5a‡ 5b‡**	**7a§** (C_6D_6) **7b§**
1	5.97 *br s*	5.92, 5.84 *q*	5.86 *br s*	5.85 *br s*	5.94, 6.01 *brs*	1.90, 2.78 *br d* 1.70 *br d*, 2.32 *d*
3	2.34 *br d*	5.14, 5.44 s	2.37 *br d*	2.34 *br d*	2.02 *d*, 2.41 *br d*	1.89 *br d*, 2.29 *d*
3′	2.12 br d		2.07 *d*	2.04 *d*	2.37 *br d*, 2.10 *d*	2.12, 1.92 *br d*
5	1.55 *dd*	2.30 *br d*, 2.04 *m*	1.89 *t*	1.92 *dd*	2.07 *d*, 2.21 *br d*	2.35 *br dd*, 1.48 *dd*
6	1.72 *m*	1.78, 2.04 *m*	1.59 *m*	1.66 *m*	5.49 *ddd*	2.06, 2.56 *dddd*
6′	1.41 *m*	1.69, 1.68 *m*		1.43 *m*		1.37 *dddd*, 1.61 *m*
7α	2.38 (2.24) *m*	2.58, 2.47 *m*	2.17 *t*	2.37*m*	2.36, 2.17 *dd*	2.23 *ddd*, 2.09 *br dd*
7β	2.14 *m*	2.42, 2.47 *m*		2.31 *m*	2.27, 2.10 *dd*	1.21, 1.06 *ddd*
9	5.74 *br dd*	6.69, 6.66 *br dd*	5.40 *br t*	6.41 *t*	5.14, 5.11 *t*	1.52, 1.80 *ddd*
11α	1.99 *br dd*	2.71, 2.69 *br dd*	2.34 *dt*	2.66 *m*	2.29, 2.28 *dt*	1.97, 1.80 *ddd*
11β	1.72*m*	2.62, 2.60 *ddd*				1.08, 1.15 *ddd*
12	4.84 (4.81) *dd*	5.42, 5.40 *dd*	2.49 *br t*		2.42 *br t*, 2.42 *t*	5.16, 5.12 *dd*
14	6.17 *br s*	6.45, 6.45 *br s*	5.86 *br s*	5.91 *t*	5.83, 5.83 *tt*	6.20, 6.32 *br s*
15	7.07 *dd*	7.42, 7.42 *dd*	—	—	—	7.09, 7.07 *dd*
16	7.15 *br s*	7.49, 7.49 *br s*	4.74 *d*	4.78 *d*	4.72 *d*	7.15 *br s*, 7.07 *dd*
18	0.89 *s*	0.84, 1.02 *s*	1.09 *s*	1.11 *s*	1.12, 1.00 *s*	0.75, 0.77*s*
19	0.87 *s*	1.08, 1.12 *s*	1.03 *s*	1.04 *s*	1.01, 1.25 *s*	0.91, 0.87 *s*
20	1.68 (1.66) *d*	2.07, 2.03 *s*	2.01 *d*	2.03 *d*	2.07, 2.05 *d*	1.19, 0.73 *s*
OAc	—	2.19, 2.20 *s*	—	—	1.89, 2.00 *s*	—

*H-17 4.07 *br s*; †H-17 9.39 *s*; ‡H-14 1.67, 1.65 *br s*; §H-21 0.72, 0.71 *d*;

J[Hz]: Compounds **1a/b**: 1,20 = 1; 3,3′ = 11α, 11β = 17; 5,6 = 5,6′ = 9,11β = 5; 9,11α = 14,15 = 15,16 = 1.5; 11α, 12 = 11; 11β,12 = 4.5; compounds **2a/b**: 1,20 = 14,15 = 15,16 = 1.5; 9,11α = 2.5; 9,11β = 5.5; 11α, 11β = 17.5; 11α, 12 = 11; 11β, 12 = 4.5; (2*a*: 5,6 = 7); compounds **3a/b** and **4a/b**: 1,20 = 14,16 = 1.5; 3,3′ = 17.5; 5,6 = 5; 9,11 = 7 (compounds **3a/b**: 6,7 = 8.5; 11,12 = 7; compounds **4a/b**: 5,6′ = 5); compounds **5a/b**: 1,20 = 12,14 = 14,16 = 1.5; 3α, 3β = 17.5; 7,7′ = 14; 9,11 = 11,12 = 7; (compound **5a**: 5,6 = 6,7′ = 3.5; 6,7 = 9.5; compound **5b**: 5,6 = 2.5; 6,7 = 10; 6,7′ = 3); compound **7a**: 1α, 1β = 12.5; 3α, 3β = 7α, 7β = 13.5; 5,6α = 9.5; 5,6β = 10.5; 6α,6β = 13; 6α, 7α = 10; 6α, 7β = 6β, 7α = 4.5; 6β, 7β = 11α, 12 = 12; 9,11α = 4; 9,11β = 3; 9,21 = 7; 11α, 11β = 14; 11β, 12 = 5; 14, 15 = 15,16 = 1.5; compound **7b**: 1α, 1β = 16.5; 3α, 3β = 18; 5,6α = 11; 5,6β = 8.5; 6α, 6β = 12; 6α, 7α = 6β, 7β = 9,21 = 7; 6α, 7β = 13; 7α, 7β = 11α, 12 = 12.5; 9,11α = 3.5; 9,11β = 3; 11α, 11β = 14; 11β, 12 = 4.5; 14,15 = 15,16 = 1.5.

Table 2. ^{13}C NMR spectral data of compounds **1a/b**, **2a/bAc**, **5a/b** and **7a/b** (67.9 MHz, $CDCl_3$, δ-values)

C	**1a/b**	**2a/2bAc**	**5a/ 5b**	**7a*** **7b†**
1	125.2 *d*	125.8, 124.1 *d*	125.8, 125.5 *d*	49.6,§ 50.4 *t*§
2	199.3 *s*	192.8, 192.7 *s*	198.9, 198.6 *s*	211.6, 211.7 *s*
3	47.1 *t*	81.2, 77.2 *d*	47.0, 47.8 *t*	46.1,§ 50.1 *t*§
4	36.3 *s*	42.1, 40.7 *s*	36.0, 35.5 *s*	37.7, 33.2 *s*
5	50.9 *d*	50.7, 53.3 *d*	54.7, 54.4 *d*	54.0, 58.6 *d*
6	29.2 *t*	27.3, 28.7 *t*	69.2, 71.4 *d*	25.8, 26.5 *t*
7	31.0 *t*	33.1, 31.5 *t*§	25.6 *t*	32.8‡, 35.6 *t*‡
8	132.9 *s*	132.6, 132.5 *s*	133.4, 133.3 *s*	61.4, 60.5 *s*
9	143.7 *d*	143.7, 143.7 *d*	127.5, 128.0 *d*	32.2 *d*
10	165.1 (164.7) *s*	162.0, 164.2 *s*	159.4, 160.5 *s*	52.6, 48.5 *s*
11	30.1 *t*	30.4, 30.5 *t*§	27.3, 28.4*t*	31.8‡, 33.6 *t*‡
12	70.4 *d*	72.4, 72.4 *d*	46.3, 42.5 t	72.2, 71.7 *d*
13	123.8 *s*	123.8, 123.8 *s*	174.0 *s*	125.0, 125.1 *s*
14	108.5 *d*	108.0, 108.6 *d*	115.7 *d*	108.5 *d*
15	143.7 *d*	140.0, 140.0 *d*	169.5, 169.5 *s*	143.7 *d*
16	139.9 (138.6) *d*	139.1, 138.9 *d*	73.0 *t*	139.4 *d*
17	171.8 (171.7) *s*	164.7, 164.6 *s*	16.2, 16.3 *q*	175.6, 171.1 *s*
18	27.1 *q*	15.1, 22.7 *q*	29.6, 25.7 *q*	31.2, 31.8 *q*
19	24.5 *q*	22.8, 23.9 *q*‡	26.3, 30.7 *q*	26.8, 25.1 *q*
20	24.6 *q*	24.6, 24.3 *q*‡	27.3, 28.0 *q*	30.1, 30.5 *q*
OAc	—	170.4, 170.4 *s*	169.6, 169.9 *s*	
		20.7, 20.7 *q*	21.0, 21.1 *q*	

*C-21 18.6 *q*; † 17.8 *q*; ‡§ may be interchangeable.

and **5b** could not be deduced from the couplings of H-5 and H-6. However, by NOE difference spectroscopy the stereochemistry of the two isomers and also the conformations could be determined. Clear effects were observed for **5a** between H-6, H-18 (6%), H-17 (6%) and H-5 (4%), between H-18, H-3α (2%), H-3β (4%) and H-6 (8%) as well as between H-19, H-3α (2%) and H-5 (6%). These results and a W-coupling between H-19 and H-3β required a conformation in which H-19 and the large substituent at C-5 were axial and the acetoxy methyl was shielded by the enone system. The observed NOE's in the case of **5b** indicated that again the large substituent at C-5 was axial while now H-19 was equatorial as followed from the W-coupling between H-18 and H-3α. NOE's were observed between H-6 and H-19 (6%) as well as between H-19, H-5 (4%), H-6 (9%) and H-3α (2%). The chemical shift of the acetate methyl now was normal (δ2.00 *s*). Accordingly, all data agreed with the presence of 6β-acetoxy derivatives differing in the configuration at C-5. In agreement with this assumption the Cotton-effects were of opposite sign. The ^{13}C NMR spectra (Table 2) further supported the structures. Small shift differences were visible in the spectra of the epimers which, however, gave no clear indications concerning the conformations.

Most likely the diterpenes were formed by fragmentation of the labdane derivative **8** followed by oxidation at different positions (see Scheme). The already introduced name hebeclinolide should be valid for **1a**. The desacetoxy derivative of **5a** we have named hebemacrophyllide.

The chemistry of this *Hebeclinium* species shows no relationship to that of other investigated genera which are placed in the subtribe Hebecliniinae. While from *Decachaeta* guaianolides were reported [4] from *Peteravenia* species kaurane, isokaurane and beyerane derivatives were isolated [5]. Clearly, further investigations are necessary to get a better picture of the relationships within this group of genera.

EXPERIMENTAL

The aerial parts (900 g, collected near Tilaran, Costa Rica, voucher 108546, deposited in the Herbarium of the University of Costa Rica) was extracted with MeOH–Et_2O–petrol (1:1:1) and the extract obtained was separated as reported previously [6]. The less polar CC fractions gave by PTLC (silica gel PF 254) 30 mg caryophyllene, 15 mg germacrene D, 30 mg γ-cadinene, 16 mg β-farnesene and 15 mg caryophyllen-1,10-epoxide. The fractions obtained with Et_2O gave 16 mg phytol and 6 mg 9-angeloyloxy-10,11-epoxy-4,5-dehydronerolidol [7]. The polar CC fractions (Et_2O–MeOH, 9:1) were separated by HPLC (RP 8, MeOH–H_2O, 13:7, *ca* 100 bar) affording 6 mg **3a/b** (R_f 5.3 min.), 7 mg **4a/b** (R_f 5.8 min.), 120 mg **1a/b** (R_f 7.7 min.) and two mixtures (A: R_f 6.0 min. and B: R_f 6.8 min.). Fraction A was acetylated with Ac_2O (1 hr, 70°). PTLC (Et_2O–petrol, 7:3, three developments) gave 12 mg **2b**Ac (R_f 0.6) and 22 mg **2a**Ac (R_f 0.5). PTLC of fraction B (Et_2O, two developments) gave 12 mg **5b** (R_f 0.8) and 18 mg **5a** (R_f 0.7). Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material. Comparison of the crude ^{1}H NMR spectra of the mixtures obtained from the Equador collection [2] indicated that the same diterpenes were present.

3β-Hydroxyhebeclinolide acetate (**2a**Ac). Colourless crystals, mp. 112°; IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1760, 1240 (OAc), 1735 (γ-lactone), 1700 (C=CC=O); MS *m/z* (rel. int.): 386.173 [M]$^+$ (1.4) (calc. for $C_{22}H_{26}O_6$: 386.173), 344 [M – ketene]$^+$ (2.6), 326 [M – HOAc]$^+$ (1.9), 311 [326 – Me]$^+$ (7.3), 272 [$C_{16}H_{16}O_4$, RDA]$^+$ (6.6), 209 [$C_{12}H_{17}O_3$]$^+$ (21), 177 [$C_{10}H_{19}O_3$]$^+$ (32), 149 [209 – HOAc]$^+$ (89), 95 [$C_5H_3O_2$]$^+$ (100); CD (MeCN): $\Delta\varepsilon_{351} - 0.21$, $\Delta\varepsilon_{333} - 0.50$, $\Delta\varepsilon_{324} - 0.59$, $\Delta\varepsilon_{315} - 0.52$.

5-epi-3β-Hydroxyhebeclinolide acetate (**2b**Ac). Colourless oil; IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1755, 1245 (OAc), 1735 (γ-lactone), 1695 (C=CC=O); MS *m/z* (rel. int.): 386.173 [M]$^+$ (0.5) (calc. for $C_{22}H_{26}O_6$: 386.173), 344 (4), 326 (3.5), 311 (3.6), 272 (1.3), 209 (11), 177 (13), 149 (55), 95 (100); CD (MeCN): $\Delta\varepsilon_{327} - 0.38$.

17-Hydroxyhebemacrophyllide (**3a/b**). Colourless oil; IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1785 (γ-lactone), 1670 (C=CC=O); MS *m/z* (rel. int.): 332.199 [M]$^+$ (1.5) (calc. for $C_{20}H_{28}O_4$: 332.199), 317 [M – Me]$^+$ (1.6), 314 [M – H_2O]$^+$ (2.1), 235 [$C_{15}H_{23}O_2$]$^+$ (3.0), 217 [235 – H_2O]$^+$ (3.7), 207 [235 – CO]$^+$ (5.6), 151 [$C_{10}H_{15}O$]$^+$ (100), 138 [$C_9H_{14}O$]$^+$ (58), 123 [138 – Me]$^+$ (59), 98 [$C_5H_6O_2$]$^+$ (28), 95 [$C_5H_3O_2$]$^+$ (96); CD (MeCN): $\Delta\varepsilon_{330} - 0.03$.

17-Oxo-hebemacrophyllide (**4a/b**). Colourless oil; IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1790 (γ-lactone), 1695 (C=CC=O); MS *m/z* (rel. int.): 330.183 [M]$^+$ (1.8) (calc. for $C_{20}H_{26}O_4$: 330.183), 315 [M – Me]$^+$ (1.0), 233 [$C_{15}H_{21}O_2$]$^+$ (2.3), 205 [233 – CO]$^+$ (2.2), 177 [205 – CO]$^+$ (6.2), 151 [$C_{10}H_{15}O$]$^+$ (89), 138 [$C_9H_{14}O$]$^+$ (23), 123 [151 – CO]$^+$ (21), 95 [$C_5H_3O_2$]$^+$ (62), 83 [C_5H_7O]$^+$ (100).

6β-Acetoxyhebemacrophyllide (**5a**). Colourless oil; IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1790 (γ-lactone), 1745, 1245 (OAc), 1675 (C=CC=O); MS *m/z* (rel. int.): 374.209 [M]$^+$ (1.0) (calc. for $C_{22}H_{30}O_5$: 374.209), 314 [M – HOAc]$^+$ (13), 258 [$C_{16}H_{18}O_3$, RDA]$^+$ (20), 195 [$C_{11}H_{15}O_3$]$^+$ (27), 151 [$C_{10}H_{15}O$]$^+$ (20), 138 [$C_9H_{14}O$]$^+$ (100), 123 (82), 98 (35); CD (MeCN): $\Delta\varepsilon_{370} + 0.22$, $\Delta\varepsilon_{354} + 0.53$, $\Delta\varepsilon_{340} + 0.63$, $\Delta\varepsilon_{329} + 0.45$, $\Delta\varepsilon_{316} + 0.27$.

5-epi-6β-Acetoxyhebemacrophyllide (**5b**). Colourless oil; IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1785 (γ-lactone), 1745, 1240 (OAc), 1670 (C=CC=O); MS *m/z* (rel. int.): 374.209 [M]$^+$ (4.0) (calc. for $C_{22}H_{30}O_5$: 374.209), 314 (18), 258 (20), 195 (32), 151 (22), 138 (100), 123 (92), 98 (39), CD (MeCN): $\Delta\varepsilon_{375} - 0.18$, $\Delta\varepsilon_{357} - 0.36$, $\Delta\varepsilon_{343} - 0.34$, $\Delta\varepsilon_{329} - 0.22$, $\Delta\varepsilon_{317} - 0.1$.

Reaction of **1a** *and* **1b** *with* Me_2CuLi. To 1.5 ml of a soln of Me_2CuLi in Et_2O (prepared from 200 mg Cu_2I_2 in 8.8 ml Et_2O with 1.2 ml of a 1.6 m MeLi solution) 16 mg **1a/b** in 2 ml Et_2O were added at 0°. After 30 min. dil HCl was added. The crude mixture showed in its ^{1}H NMR spectrum the presence of *ca* 70% **7a** and 30% **7b**. PTLC (Et_2O–petrol, 5:1) gave 4 mg **7b** (R_f 0.49) and 9 mg **7a** (R_f 0.36).

7a: Colourless crystals, mp 174–76°; IR $\nu_{max}^{CHCl_3}$, cm^{-1}: 1725 (γ-lactone), 1715 (C=O); MS *m/z* (rel. int.): 344.199 [M]$^+$ (4.9) (calc. for $C_{21}H_{28}O_4$: 344.199), 221 [$C_{13}H_{17}O_3$]$^+$ (17), 193 [$C_{11}H_{13}O_3$]$^+$ (26), 152 [$C_{10}H_{16}O$]$^+$ (24), 121 [C_8H_9O]$^+$ (38), 94 [C_6H_6O]$^+$ (100); CD (MeCN): $\Delta\varepsilon_{293} - 1.14$.

7b: Colourless crystals, mp 120–22°; IR $\nu_{max}^{CHCl_3}$, cm^{-1}: 1725 (γ-lactone), 1715 (C=O); MS *m/z* (rel. int.): 344.199 [M]$^+$ (5.4) (calc. for $C_{21}H_{28}O_4$: 344.199), 221 (16), 193 (17), 152 (21), 121 (44), 94 (100); CD (MeCN): $\Delta\varepsilon_{317} + 0.12$, $\Delta\varepsilon_{307} + 0.26$, $\Delta\varepsilon_{297} + 0.28$, $\Delta\varepsilon_{288} + 0.23$, $\Delta\varepsilon_{279} + 0.15$.

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REFERENCES

1. King, R. M. and Robinson, H. (1980) *Phytologia* **46**, 446.
2. Bohlmann, F. and Grenz, M. (1977) *Chem. Ber.* **110**, 1321.
3. Snatzke, G. (1965) *Tetrahedron* **21**, 413, 421.

4. Castro, V., Ciccio, F., Alvarado, S., Bohlmann, F., Schmeda-Hirschmann, G. and Jakupovic, J. (1983) *Liebigs Ann. Chem.* 974.
5. Ellmauerer, E., Jakupovic, J., Bohlmann, F. and Scott, R. (1986) *J. Nat. Prod.* (in press).
6. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1979.
7. Bohlmann, F. and Zdero, C. (1976) *Chem. Ber.* **109**, 1436.