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A SESQUITERPENE ESTER FROM *CELASTRUS HINDSII*

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Key Word Index—*Celastrus hindsii*; Celastracea; cytotoxicity; sesquiterpene esters; celahin-B; celahin-C.

Abstract—A new sesquiterpene ester, celahin C, together with a known related compound, celahin B, was isolated from *Celastrus hindsii*. The structure of the new ester was determined by 2D NMR spectra and by comparison with the structure of celahin B.

INTRODUCTION

In our studies on the antitumour constituents of the Celastraceae, we have isolated several cytotoxic sesquiterpene pyridine pyridone alkaloids from *Maytenus emarginata* (Gray) Hou [1–4]. Recently, we reported on the isolation and structural elucidation of one new and one known compound from *Celastrus hindsii* Benth. The former, celahinine A, is a sesquiterpene pyridine alkaloid and the latter, celahin A, a sesquiterpene polyester, respectively, with β-dihydroagarofuran skeletons [5]. Further investigation of *C. hindsii* has led to the isolation of one known (celahin B, **1**) and one new (celahin C, **2**) sesquiterpene polyol ester with β-dihydroagarofuran skeletons, and one compound with a similar skeleton, 1β-acetoxy-2β,8β,5α-tribenzoyloxy-4α,6α-dihydroxy-β-dihydroagarofuran (**3**) [6]. The structure of the new compound (**2**) was established by 2D NMR spectra, inculding ^{1}H–^{1}H COSY, ^{1}H–^{13}C COSY, ^{1}H–^{13}C long-range COSY, and 2D NOE studies.

RESULTS AND DISCUSSION

The alcoholic extract of the dried stems of *C. hindsii* was extracted successively with *n*-hexane and chloroform. Repeated column chromatography of the chloroform extract yielded three sesquiterpenes (**1**–**3**).

Compound **1** was obtained as an amorphous powder; its physical and spectral data were consistent with those reported in the literature [7] for celahin B (**1**). This sesquiterpene has a β-agarofuran skeleton with a benzoyl ester at the C-9 position and four acetyl esters at the C-1, C-2, C-6, and C-15 positions. An axial methyl is found at C-4 and represents a structural feature generally found in compounds from Celastraceae plants [3, 8]. As usually found in this class of skeleton [5, 8], H-6 has axial stereochemistry. From the NOESY spectrum of **1** (Fig. 1), the correlation between H-6 and H-1 suggested axial stereochemistry for both H-6 and H-1 in agreement with previous reports [5–8]. However, no correlation was found between H-6 and H-9 in the NOESY spectrum suggesting that H-9 is equatorial in compound **1**.

Celahin-C (**2**), amorphous powder, $C_{28}H_{36}O_{10}$, exhibited IR absorption at 3440 (OH) and 1725 (CO_2) cm^{-1}. The ^{1}H and ^{13}C NMR spectra of **2** were similar to those of **1**, except for the absence of one acetyl methyl and the upfield shifts of certain protons. The molecular ion of **2** (*m/z* 532) was 42 units (C_2H_2O) lower than that of **1** indicating the substitution of an OH group for an OAc group; the upfield chemical shift in the ^{1}H NMR spectrum of **2** may be due to the loss of the deshielding effect of this acetate. In the ^{1}H NMR spectrum of **2**, one proton signal showed an extreme upfield shift (δ5.68 in **1** to 4.70 in **2**) compared with the other proton signals; this shift suggested that the hydroxy group was at the C-1 position. Moreover, from the ^{1}H–^{1}H COSY spectrum of **2**, the correlated signals at δ5.46, 2.51, 2.28 and 2.15 were assigned as H-9, H-8a, H-8b and H-7, respectively; the signals at δ4.70, 5.31, 2.30, 1.85, 2.39 and 1.12 were assigned as H-1, H-2, H-3ax, H-3eq, H-4, and H-14, respectively; and the signals at δ4.84 and 4.43 were assigned as H-15a and H-15b, respectively (Table 1). The complete assignment of each carbon signal is shown in Table 2 and was based on the ^{13}C–^{1}H COSY spectrum of **2**.

^{1}H–^{13}C long-range correlation (HMBC) was used to confirm the location of the acetyl ester groups. Thus, the carbonyl signals at δ_C165.4, 170.0, and 170.5 were correlated with the proton signals at δ_H8.04 (benzoyl-H) and

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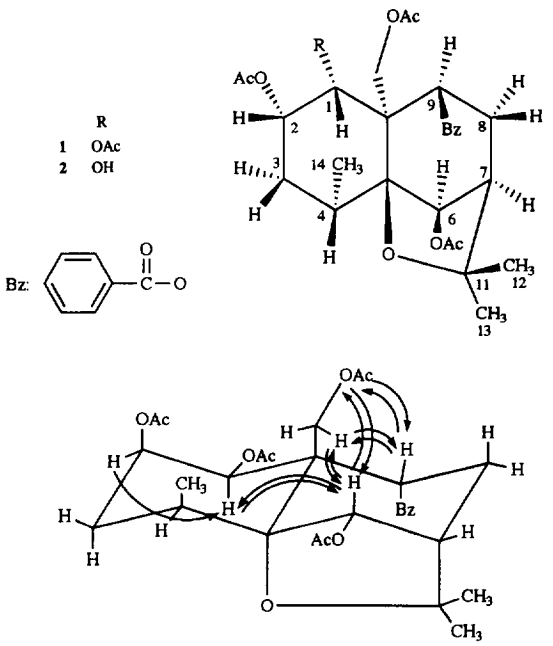

Fig. 1. NOESY correlations in celahin-B (1).

Table 1. ^{1}H NMR data* (300 MHz) for celahin B (1) and C (2)

H	1	2
1	5.68 (*d*, 3.5)	4.70 (*d*, 3.6)
2	5.56 (*m*)	5.31 (*m*)
3a	2.40 (*m*)	2.30 (*m*)
3e	1.79 (*m*)	1.85 (*m*)
4	2.39 (*m*)	2.39 (*m*)
6	5.95 (*s*)	5.83 (*s*)
7	2.20 (*d*, 2.8)	2.15 (*m*)
8a	2.50 (*m*)	2.51 (*m*)
8b	2.22 (*m*)	2.28 (*m*)
9	5.39 (*d*, 7.2)	5.46 (*d*, 7.3)
12	1.43 (*s*)	1.47 (*s*)
13	1.40 (*s*)	1.47 (*s*)
14	1.16 (*d*, 7.5)	1.12 (*d*, 5.3)
15a	5.03 (*d*, 12.8)	4.84 (*d*, 12.6)
15b	4.34 (*d*, 12.7)	4.43 (*d*, 12.6)
OAc	1.52 (C-1)†	1.28
OAc	2.06 (C-6)†	2.08 (C-6)
OAc	2.08 (C-2)	2.20 (C-15)†
OAc	2.22 (C-15)	—
Bz: H-2,6	8.02 (*m*)	8.04 (*m*)
Bz: H-3,5	7.41 (*m*)	7.44 (*m*)
Bz: H-4	7.52 (*m*)	7.55 (*m*)

*Measured in $CDCl_3$ (multiplicities, J in Hz).
†Assignments by ^{1}H–^{13}C long-range correlation.

Table 2. ^{13}C NMR (75.47 MHz) data* for celahin B (1) and C (2)

C	1	C–H connectivities†	2	C–H connectivities†
1	71.5 (*d*)	H-3, H-15	69.6 (*d*)‡	H-3, H-15
2	69.5 (*d*)§	H-1, Me-Ac-2	73.3 (*d*)‡	—
3	29.7 (*t*)	H-2	29.7 (*t*)	H-3
4	33.1 (*d*)	H-14	33.1 (*d*)	H-14
5	89.2 (*s*)	H-9, H-15, H-14	89.3 (*s*)	H-9, H-15
6	78.1 (*d*)	—	78.3 (*d*)	—
7	48.8 (*d*)	H-9	48.8 (*d*)	H-9
8	34.8 (*t*)	H-6, H-9	34.3 (*t*)	H-6, H-9
9	69.5 (*d*)§	—	69.3 (*d*)‡	—
10	53.3 (*s*)	H-1, H-15	54.6 (*s*)	H-1, H-15
11	82.7 (*s*)	H-6, H-12	82.6 (*s*)	H-6, H-12, H-13
12	30.3 (*q*)	H-12	31.9 (*q*)	H-12
13	25.9 (*q*)	H-13	26.0 (*q*)	H-13
14	17.7 (*q*)	—	17.9 (*q*)	—
15	65.4 (*t*)	H-1, H-15	65.2 (*t*)	H-1, H-15
MeCOO–C	169.3 (C-1)	H-1, Me-Ac-1	170.0 (C-6)	H-6
	169.9 (C-6)	H-6, Me-Ac-6	170.5 (C-15)	Me-Ac-15
	169.9 (C-2)	—	171.4 (C-2)¶	—
	170.5 (C-15)	Me-Ac-15	—	—
BzCO	165.3	H-9	165.4 (C-9)	H-9
BzC-2,6	128.3		128.6	
BzC-3,5	130.1		129.5	
BzC-4	133.4		133.1	
BzC-1	129.1		129.5	
AcMe	20.3		14.1	
	21.3		21.4	
	21.3		21.7	
	21.7		—	

*Multiplicities were obtained from DEPT spectra.
†^{1}H–^{13}C long-range correlation (HMBC) corresponding to 2-bond or 3-bond connectivities.
‡Assignments of these signals could be interchangeable.
§This signal was correlated with two protons (H-2 and H-9) in the ^{1}H–^{23}C COSY spectrum.
¶Assignment of this signal explained in text.

5.46 (H-9), at 2.08 (acetyl methyl) and 5.83 (H-6), and at 2.20 (acetyl methyl) and 4.84, 4.43 (H-$15_{a,b}$), respectively. These correlations suggested that the one benzoyl ester and two acetyl esters were positioned at C-9, C-6, and C-15, respectively. Although no distinct correlation was found between the remaining carbonyl carbon (δ_c171.4) and any proton signal in **2**, the last acetyl ester must be located at C-2, since, as in **1**, only this position remains unassigned. Therefore, the structure of celahin-C (**2**) has been completely established.

EXPERIMENTAL

Plant material. The stems of *C. hindsii* were collected in September 1992 in Taishung Hsien, Taiwan. A voucher specimen is deposited at the National Research Institute of Chinese Medicine, Taipei Hsien, Taiwan.

General experimental procedures. ^{1}H and ^{13}C NMR: at 300.13 and 75.46 MHz, respectively; HMBC: established by coupling constants of 8 Hz; EIMS: JEOL SX-102A; CC: silica gel (Merck 70–230 mesh); TLC: precoated silica gel (Merck 60F-254) plates; HPLC: prep. silica gel column.

Isolation. The dried stems of *C. hindsii* (5.2 kg) were extracted exhaustively with EtOH. The crude EtOH extract (200 g) was chromatographed on silica gel (2.5 kg) eluting with hexane–EtOAc and EtOAc to give 8 frs. Fr. 5 (eluting with hexane–EtOAc 3:1) was further separated by HPLC (silica gel, hexane–EtOAc 1:2.5) to yield **1** (5 mg, 0.000079%), **2** (4 mg, 0.000063%), **3** (15 mg, 0.00024%).

Celahin-B (**1**). Amorphous, IR ν_{max} cm^{-1}: 1735, 1600, 1280, 710; EIMS *m/z* (rel. int.): 574 $[M]^+$ (4), 532 (70), 410 (15), 202 (39), 173 (14), 105 (100); ^{1}H and ^{13}C NMR: Tables 1 and 2.

Celahin-C (**2**). Amorphous, mp 85–90°. $[\alpha]_D$ + 26.67° ($CHCl_3$; *c* 0.1); UV λ_{max} nm (log ε) 245 (3.19), 275 (2.95), 282 (2.92); IR ν_{max} cm^{-1}: 3440, 1725, 1660, 1275, 710; EIMS *m/z* (rel. int.): 532 $[M]^+$ (3), 517 (4), 490 (15), 430 (10), 309 (7), 215 (16), 202 (15), 173 (23), 105 (100); ^{1}H and ^{13}C NMR: Tables 1 and 2.

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