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SESQUITERPENOID ALCOHOLS FROM *CHRYSANTHEMUM MORIFOLIUM*

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Key Word Index—*Chrysanthemum morifolium*; Compositae; flowers; chrysanthediol; sesquiterpene alcohols.

Abstract—Three new sesquiterpenes, chrysanthediol A, chrysanthediacetate B and chrysanthediacetate C, and the known one, β-dictyopterol were isolated from the neutral alcoholic extract of flowers of *Chrysanthemum morifolium*. Their structures and stereochemistries were elucidated using various NMR techniques. Copyright © 1997 Elsevier Science Ltd

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INTRODUCTION

We have previously reported the isolation and characterization of 29 compounds from the flowers of *Chrysanthemum morifolium* [1, 2]. Further investigation of the neutral constituents of this species has led to the isolation of three new sesquiterpenes: chrysanthediol A (**1**), chrysanthediacetate B (**2**) and chrysanthediacetate C (**3**).

RESULTS AND DISCUSSION

Compound **1**, isolated as an oil, showed in its mass spectrum a very weak $[M]^+$ at m/z 236 consistent with the molecular formula $C_{15}H_{24}O_2$. Further fragment ions at m/z 218 $[M-18]^+$ and 200 $[M-18-18]^+$, revealed the presence of two hydroxyl groups. This was confirmed by the IR spectrum (3410 cm^{-1}). The ^1H NMR ($CDCl_3$) spectrum (Table 1) showed the presence of one vinylic proton at δ 5.16 (H-3), two olefinic methyl groups at δ 1.72 and 1.61 (Me-13, Me-15), four exomethylene protons at δ 4.68, 4.81, 5.38 and 5.44 (H_2-12, H_2-14), and two carbinolic methine protons at δ 3.84 and 4.19 (H-1, H-9). The ^{13}C NMR spectrum (Table 2) showed the signals of two methyl groups, six methylene groups, four methine groups and three quaternary carbon atoms, suggesting the presence of two terminal and one trisubstituted double bond. ^1H–^1H COSY and ^{13}C–^1H COSY experiments established the partial structures **A** and **B**. Correlation of each unit was indicated by analysis of the COLOC spectrum. The methine carbon atom C-7 (δ 39.8) in unit **A** showed correlations with H-12 (δ 4.68 and 4.81) in unit **B**. The quaternary carbon atom C-3 (δ 122.7) in unit **A** was correlated with H-5 (δ 2.00) and the methyl group at H-4 (δ 1.61). These results indicate a planar structure for **1**. The relative stereochemistry was determined by a nuclear Overhauser effect (NOE) difference experiment. NOEs were observed between (i) H-3 and Me-15; (ii) H-1 and H-9; and (iii) H-9 and H-1, H_2-12 and Me-13. From these spectral data, the structure of chrysanthediol A was established as **1**.

The ^1H and ^{13}C NMR spectra of the mixture of compounds B and C, showed no acetyl group signals, indicating the presence of a pair of stereoisomers of a sesquiterpendiol. We isolated chrysanthediacetates B (**2**) and C (**3**) by means of peracetylation.

The mass spectrum of **2**, obtained as an oil, showed $[M]^+$ at m/z 320, which is in accordance with the formula $C_{19}H_{28}O_4$; the presence of 19 carbon atoms was confirmed by the ^{13}C NMR spectrum. The IR and ^{13}C NMR ($CDCl_3$) spectra showed the presence of two ester carbonyl groups (1735 cm^{-1}, δ 170.2 *s* and 169.6 *s*). The ^1H NMR spectrum (Table 1) showed an olefinic methyl group at δ 1.83 *s* (Me-13), three exomethylene protons at δ 4.68, 4.70, 5.14, 5.17, 5.02 and 5.23 (H_2-12, H_2-14, H_2-15), and two carbinolic methine protons at δ 5.36 and 5.05 (H-3, H-9). The ^{13}C NMR spectrum (Table 2) showed the signals of one methyl, three exomethylene, two carbinolic methine, five methylene, one methine and two acetyl groups. The ^1H–^1H COSY and ^{13}C–^1H COSY spectra showed

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Table 1. ^{1}H NMR spectral data of compounds **1**–**3** (400 MHz, $CDCl_3$)

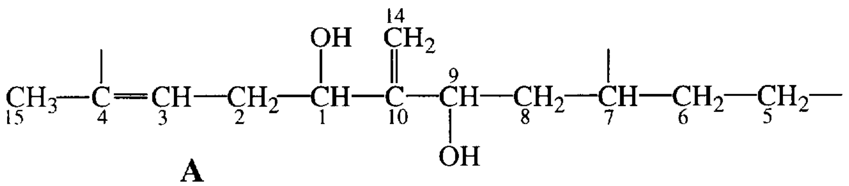
H	**1**	**2**	**3**
1a	3.84 *dd* (6.4, 10.2 Hz)	2.25 *m*	2.39 *ddd* (*J* = 17.2, 4.4, 3.0 Hz)
1b	–	2.05 *m*	2.07 *m*
2a	2.74 *m*	2.05 *m*	2.26 *m*
2b	2.21 *m*	2.05 *m*	1.90 *m*
3	5.16 *t*	5.36 *dd* (*J* = 7.7, 5.6 Hz)	5.24 *dd* (*J* = 10.9, 4.8 Hz)
5a	2.0 *m*	2.31 *ddd* (*J* = 14.5, 6.6, 5.1 Hz)	2.22 *m*
5b	2.0 *m*	1.97 *m*	1.89 *m*
6a	1.30 *m*	1.65 *m*	1.68 *m*
6b	1.30 *m*	1.53 *m*	1.56 *m*
7	2.0 *m*	2.18 *m*	2.10 *m*
8a	1.95 *m*	1.87 *ddd* (*J* = 13.7, 11.9, 3.8 Hz)	1.78 *ddd* (*J* = 12.7, 8.4, 3.0 Hz)
8b	1.30 *m*	1.65 *m*	1.60 *m*
9	4.19 *d* (*J* = 4.2 Hz)	5.05 *dd* (*J* = 11.7, 4.0 Hz)	4.83 *dd* (*J* = 11.2, 5.4 Hz)
12a	4.68 *brs*	4.70 *brs*	4.66 *brs*
12b	4.81 *brs*	4.68 *brs*	4.63 *brs*
13	1.72 *brs*	1.83 *brs*	1.63 *brs*
14a	5.44 *brs*	5.17 *brs*	5.20 *brs*
14b	5.38 *brs*	5.14 *brs*	5.14 *brs*
15a	1.61 *s*	5.23 *brs*	5.22 *brs*
15b	–	5.12 *brs*	5.08 *brs*
OAc	–	2.01 *s* 1.96 *s*	2.01 *s* 1.96 *s*

three partial units **C**–**E** (Tables 3 and 4). ^{1}H–^{1}H long-range COSY and COLOC experiments revealed some connections between the partial structures. Cross-peaks were observed between the following: (i) C-7 (δ 40.6) and H_2-12 (δ 4.70, 4.68); (ii) C-3 (δ 76.0) and H-15 (δ 5.12); (iii) C-9 (δ 78.4) and H-14 (δ 5.14); (iv) H-15 (δ 5.12) and H_2-5 (δ 2.31, 1.97); (v) H-3 (δ 5.36) and H-15 (δ 5.23); (vi) H-14 (δ 5.14) and H_2-1 (δ 2.25, 2.05); (vii) H-14 (δ 5.17) and H-1 (δ 2.25). The above spectral evidence established the planar structure. The relative stereochemistry was determined by NOE difference experiments. NOEs were observed between the following: (i) H-7 and H-9 and H-3; (ii) H-9 and H-7. From the above spectral data, the structure of chrysantheliacetate B was established as **2**.

Compound **3** displayed almost identical IR, and NMR spectra as **2**. The only significant difference between the ^{1}H NMR spectra of the two compounds was the coupling constants observed for H-3: δ 5.36 *dd* 7.7, 5.6 (*J* = Hz) in **2** and 5.24 *dd* (*J* = 10.9, 4.8 Hz) in **3**. No cross-peak was observed between H-3 and H-5 in the ^{1}H–^{1}H COSY spectrum of **3**, whereas

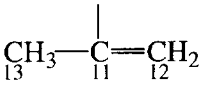
Table 2. ^{13}C NMR spectral data of compounds **1**–**4** (100 MHz, $CDCl_3$)

C	**1**	**2**	**3**	**4**
1	69.5 *d*	24.8 *t*	28.9 *t*	79.3 *d*
2	35.2 *t*	29.7 *t*	29.6 *t*	31.5 *t*
3	122.7 *d*	76.0 *d*	72.8 *d*	34.2 *t*
4	135.1 *s*	145.2 *s*	146.9 *s*	148.7 *s*
5	39.1 *t*	30.4 *t*	33.1 *t*	47.6 *d*
6	31.8 *t*	31.2 *t*	29.9 *t*	26.5 *t*
7	39.8 *d*	40.6 *d*	39.3 *d*	45.3 *d*
8	34.4 *t*	34.4 *t*	38.1 *t*	28.9 *t*
9	74.2 *d*	78.4 *d*	76.8 *d*	37.0 *t*
10	155.8 *s*	145.3 *s*	147.8 *s*	40.2 *s*
11	153.6 *s*	148.1 *s*	147.9 *s*	150.3 *s*
12	109.8 *t*	110.5 *t*	110.6 *t*	108.3 *t*
13	19.6 *q*	19.4 *q*	18.5 *t*	20.9 *q*
14	110.9 *t*	116.9 *t*	112.3 *t*	10.2 *q*
15	16.3 *q*	116.6 *t*	115.6 *t*	106.8 *t*
OAc	–	170.2 *s*, 169.6 *s*, 21.3 *q*	170.2 *s*, 169.7 *s*, 21.3 *q*	–



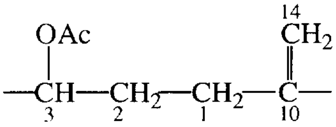
$\underset{15}{CH_3}-\underset{4}{\overset{|}{C}}=\underset{3}{CH}-\underset{2}{CH_2}-\underset{1}{\overset{OH}{\overset{|}{CH}}}-\underset{10}{\overset{\overset{14}{CH_2}}{\overset{\|}{C}}}-\underset{\underset{OH}{|}}{\overset{9}{CH}}-\underset{8}{CH_2}-\underset{7}{\overset{|}{CH}}-\underset{6}{CH_2}-\underset{5}{CH_2}-$

A



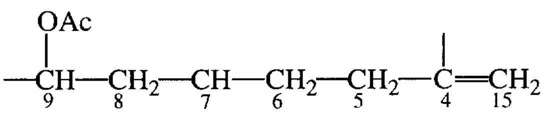
$\underset{13}{CH_3}-\underset{11}{\overset{|}{C}}=\underset{12}{CH_2}$

B



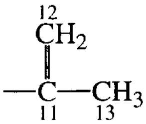
$-\underset{3}{\overset{OAc}{\overset{|}{CH}}}-\underset{2}{CH_2}-\underset{1}{CH_2}-\underset{10}{\overset{\overset{14}{CH_2}}{\overset{\|}{C}}}-$

C



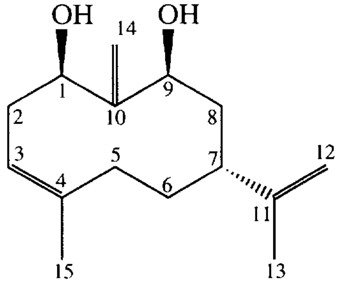
$-\underset{9}{\overset{OAc}{\overset{|}{CH}}}-\underset{8}{CH_2}-\underset{7}{CH}-\underset{6}{CH_2}-\underset{5}{CH_2}-\underset{4}{\overset{|}{C}}=\underset{15}{CH_2}$

D



$-\underset{11}{\overset{\overset{12}{CH_2}}{\overset{\|}{C}}}-\underset{13}{CH_3}$

E



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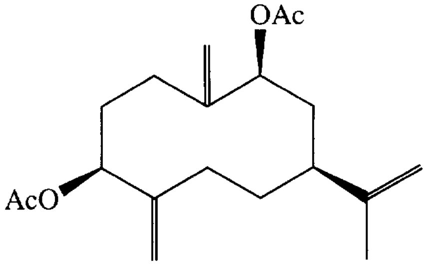

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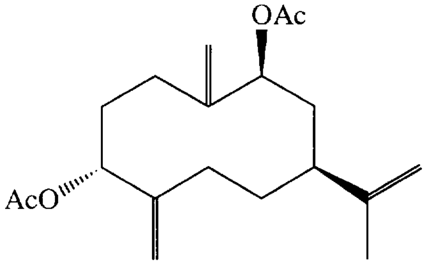

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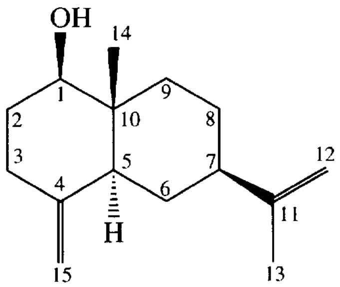

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Table 3. ^{13}C–^{1}H long-range correlations of compounds **1**–**3**

1		**2**		**3**	
^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
1α	10, 14	5	4	1	3, 10, 14
5	3, 4, 6	7α	12	5	4
7β	12, 13	9	14	7α	11, 12
12	7, 13	12	7, 13	12	7, 13
13	7, 11, 12	13	7, 11, 12	13	7, 11, 12
14	9	14	9	14	9
15	3, 4	15	3, 5	15	3, 5

Table 4. ^1H–^1H long-range correlations of compounds **2** and **3**

2		**3**	
^1H	^1H	^1H	^1H
3	1a, 1b, 15a	3	15b
5a	15b	9	14a
5b	15a, 15b	5a	15a, 15b
14a	1b	14a	1a
14b	1a, 1b	14b	1a, 1b

the spectrum of **2** showed an obvious cross-peak between H-3 and H-5. Thus, compound **3** was assigned as 3-*epi*-chrysanthediacetate B. This assumption was supported by ^1H–^1H and ^{13}C–^1H COSY and long-range ^1H–^1H, ^{13}C–^1H COSY experiments. The relative stereochemistry was determined by NOE difference experiments. NOEs were observed between the following: (i) H-9 and H-7 and H_2-8; (ii) H-3 and H-5 and H-2. Therefore, the structure of chrysanthediacetate C was established as **3**.

Compound **4**, which has been previously isolated from *Dictyopteris divaricata*, was identified by comparison of its spectroscopic data with literature values [3, 4].

EXPERIMENTAL

General. ^1H and ^{13}C NMR spectra: Bruker AM-400 and Varian Gemini-300. Chemical shifts are reported in δ; int. standards were $CHCl_3$ (δ 7.27) and $CDCl_3$ (δ 77.0).

Plant material. Chrysanthemum morifolium Ramat was collected in Tonglu, Zhejiang province, in autumn. A voucher specimen is deposited at the Herbarium of the Department of Phytochemistry, Shanghai Institute of Materia Medica, Academia Sinica, Shanghai, People's Republic of China.

Extraction and isolation. Air-dried flowers (5 kg) were extracted with 70% EtOH (3 × 5 l) at 70°. After filtration, the solvent was evapd to dryness under red. pres. and the residue dissolved in H_2O and extracted with 3 × 1 l of Et_2O to give an Et_2O extract (60 g). The H_2O layer was again extracted with *n*-BuOH and the extract washed with 3 × 1 l of 5% NaOH to obtain a neutral *n*-BuOH-sol. part (25 g). This was subjected to chromatography over silica gel with $CHCl_3$ and MeOH mixts of increasing polarity and rechromatography on Sephadex LH-20 (MeOH) to give compounds **4** (80 mg), **1** (23 mg) and a mixt. (50 mg) of **2** and **3**. Compounds **2** (15 mg) and **3** (20 mg) were obtained subsequently after peracetylation.

Chrysanthediol A (**1**). Oil. $[\alpha]_D^{17}$ −23.16° (CH_3OH; *c* 0.475). EI-MS (*m/z*): 218, 203, 185, 175, 161, 147, 133, 119, 107, 93, 79. IR ν_{max}^{KBr} cm^{-1}: 3410, 2980, 1640, 890. ^1H NMR: Table 1. ^{13}C NMR: Table 2.

Chrysanthediacetate B (**2**). Oil. $[\alpha]_D^{17}$ +45.53° (CH_3OH; *c* 0.797). EI-MS (*m/z*): 320, 278, 261, 218, 200, 185, 157, 131. IR ν_{max}^{KBr} cm^{-1}: 2930, 1735, 1645, 1245, 900. ^1H NMR: Table 1. ^{13}C NMR: Table 2.

Chrysanthediacetate C (**3**). Oil. $[\alpha]_D^{17}$ −46.64° (CH_3OH; *c* 0.729). EI-MS (*m/z*): 320, 278, 260, 218, 200, 157, 131. IR ν_{max}^{KBr} cm^{-1}: 2935, 1735, 1650, 1240, 900. ^1H NMR: Table 1. ^{13}C NMR: Table 2.

β-Dictyopterol (**4**). Oil. $[\alpha]_D^{17}$ +18.89° (CH_3OH; *c* 0.745). IR $[\nu]_{max}^{KBr}$ cm^{-1}: 3400, 2918, 1710, 1649. HRMS: 220.1851 (calc. 220.356). EI-MS (*m/z*): 220, 203, 187, 159, 107, 93. ^1H NMR (C_6D_0): δ 4.84 (1H, *brs*, 12a-H), 4.82 (1H, *brs*, 12b-H), 4.76 (1H, *brs*, 15a-H), 4.54 (1H, *brs*, 15b-H), 3.09 (1H, *dd*, J = 11.4, 4.7 Hz, 1α-H), 2.16 (1H, *dddd*, J = 13.4, 5.0, 2.3 Hz, 3β-H), 1.92 (2H, *m*, 9β, 3α-H), 1.81 (1H, *tt*, J = 11.0, 4.0 Hz, 7α-H), 1.68 (3H, *brs*, 13-Me), 1.60 (2H, *m*, 8β, 2β-H), 1.55 (2H, *m*, 6β-H, 5α-H), 1.48 (1H, *m*, 2α-H), 1.32 (2H, *m*, 8α, 6α-H), 0.95 (1H, *m*, 9α-H), 0.68 (3H, *s*, 14-Me). ^{13}C NMR: Table 2.

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