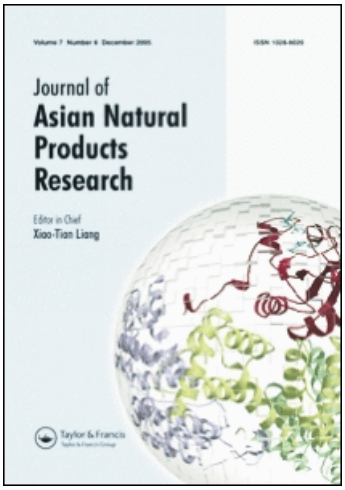

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TWO NEW DITERPENOIDS FROM *MALLOTUS APELTA* MUELL.ARG.

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Two new diterpenoids, malloapeltene (6,8-dihydroxy-cembrene-5-one) and malloapeltin (4α,15,16-trihydroxy-dolabradane) were isolated and characterized from the petroleum ether fraction of the alcoholic extract of *Mallotus apelta* Muell.Arg. Their structures were determined by spectral methods.

Keywords: Mallotus apelta Muell.Arg.; Euphorbiaceae; Diterpenoids; 4α,15,16-trihydroxy-dolabradane; Malloapeltin; Malloapeltene

INTRODUCTION

Mallotus apelta Muell.Arg. belonging to the Euphorbiaceae family has been widely used in Chinese traditional medicine for the treatment of chronic hepatitis in South China [1]. In our earlier paper [2], we reported the isolation and identification of malloapeltine and 4,5,4′-trimethyl-ellagic acid. Further work has afforded two new diterpenoids, malloapeltene (6,8-dihydroxy-cembrene-5-one) and malloapeltin (4α,15,16-trihydroxy-dolabradane), whose structures were identified by spectral methods.

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RESULTS AND DISCUSSION

The alcoholic extract from the roots of *M. apelta* was fractionated with petroleum ether and ethyl acetate [1]. The petroleum ether part was chromatographed on silica gel column eluted with cyclohexane-ethyl acetate, yielding compounds **1** and **2**. Compound **1** was identified as 6,10-dihydroxyl-cembrene-5-one and compound **2** was identified as 4α,15,16-trihydroxy-dolabradane.

Compound **1**, white needles ($CHCl_3$), mp 114–116°C, $[\alpha]_D + 160.84$. ^{13}C NMR and DEPT exhibited total 20 carbons including four tertiary methyl groups, eight vinylic carbon signals between δ110 and 150, one carbonyl at δ200.71, two hydroxyl-linking carbon signals between δ60 and 80, four methylene and one methline between δ30 and 50. Considering the HREIMS, its molecular formula was settled as $C_{20}H_{30}O_3$, $\Omega = 6$. Through ^1H–^1H COSY, HMQC and HMBC experiments, the planar structure of compound **1** was determined to be a cembrene-type macrocyclic diterpene [3,4] with one carbonyl group and two hydroxyl substitution in the ring. In ^1H NMR spectrum, the hydrogen at δ6.369 (dd, $J = 2.5$, 10.2 Hz) suffered about 1 ppm down field shift due to the conjugation effect of the carbonyl group. Correspondingly, the HMBC spectrum showed the correlation of the hydrogen at δ6.369 with the carbonyl signal (δ_C200.71), and also with C-1 (44.73), C-2 (δ_C34.60), CH_3-18 (δ_C11.81), which settled it to C-4, and the carbonyl was assigned to C-5. The hydrogen signal at δ5.307 (d, $J = 10.2$ Hz) of CHOH (δ_C 69.02) showed doublet peaks because of the *ortho* coupling of H-7 (δ5.107(d, $J = 10.2$ Hz)) and the HMBC spectrum also displayed its correlation with the carbonyl, and with C-7 (δ_C126.30), C-8 (δ_C137.00). The deshielding effect of the vinyl and carbonyl resulted in much down shift of the hydrogen signal and the hydroxy group was thus assigned to C-6. Another hydrogen signal at 4.61(m) of –CHOH (δ_C65.12) exhibited ddd peaks. The ^1H–^1H COSY spectrum showed its *ortho* correlation with the hydrogen signals of $-CH_2$ ($\delta_H = 2.662$ dd, $J = 4.2$, 12.8 Hz; $\delta_H = 2.142$ m) and the H-11 ($\delta_H = 5.127$, $J = 7.9$ Hz). Then, this hydroxyl group was assigned to C-10. The ^1H NMR, ^{13}C NMR data and cross peaks in HMBC spectrum of compound **1** were summarized in Table I.

In the 2D NOESY experiment, the H-3 at δ6.369 was correlated with the CH_3-18 (δ_H1.817), H-6 (δ5.307), H-7 (δ5.107), and there were also correlations among CH_3-18 (δ1.817) and H-6 (δ5.307), H-7 (δ5.107). The CH_3-20 (δ_H1.796) was correlated with the H-10 (δ4.613) but not with the H-11 (δ5.127). Summarily, the structure of compound **1** was settled as shown.

TABLE I ^{1}H NMR, ^{13}C NMR data and HMBC correlation of compound **1** in $CDCl_3$, δ ppm

No	^{1}H NMR *Data*	^{13}C NMR	HMBC
1	2.000 (m)	44.73	
2	2.341 (m)	34.60	
3	6.369 (dd, J=2.5, 10.2 Hz)	146.18	CH_3-18, C_2, C_5, C_1
4	—	134.50	
5	—	200.71	
6	5.307 (d, J=10.2 Hz)	69.02	C_5, C_7, C_8,
7	5.107 (d, J=10.1 Hz)	126.30	C_5, CH_3-19
8	—	137.00	
9	2.662 (dd, J=4.2, 12.8 Hz)	48.51	C_7, C_8, C_{10}, CH_3-19
	2.142 (m)		
10	4.613 (m)	65.12	
11	5.127 (J=7.9 Hz)	126.66	
12	—	142.33	
13	1.740 (m)	33.42	
	2.11 (m)		
14	1.309 (m)	31.60	
	1.529 (m)		
15	—	147.10	
16	4.741 (s)	111.89	C_1, C_{15}, CH_3-17,
	4.817 (s)		
17	1.678 (s)	18.98	C_1, C_{15}, C_{16}
18	1.817 (s)	11.81	
19	1.817 (s)	15.76	
20	1.796 (s)	19.68	

Compound **2**, mp 194–196°C, $[\alpha]_D$ +28.04 was obtained as amorphous white powder. The molecular formula was determined as $C_{20}H_{36}O_3$ by HREIMS and ^{13}C NMR data, Ω=3. ^{13}C NMR and DEPT spectra exhibit the presence of 20 carbons, including 4 tertiary methyl groups, 9 methylenes, 3 methines and 4 quaternary carbons. No vinylic and carbonyl groups existed in the structure. So, it was a tricyclic diterpenoid. There were three hydroxyl-linked carbon signals between δ60–80 ppm, the one at δ73.75 was a quaternary carbon. According to ^{1}H–^{1}H COSY, the other two at δ61.75 (–CH_2OH) and δ80.22 (–CHOH) are *ortho* to each other on the side chain.

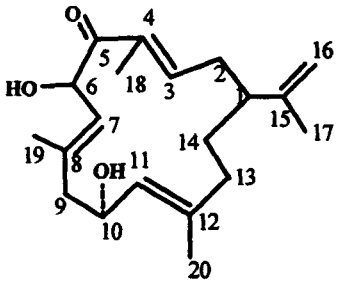
In the ^{1}H NMR and HMBC spectra of compound **2**, the signal of hydroxyl group was very clear. The HMBC spectrum shows the correlation of the hydroxyl group at δ3.829 (s) not only with its linking carbon signal at δ73.75, but also with a methyl group at δ22.95 (δ_H1.164, s), a methylene at δ36.61 and a quaternary carbon at δ42.16 *ortho* to the carbon at δ73.75. The methyl group at δ_H1.164 (δ_C22.95) showed just the same correlation as the hydroxyl group at δ3.829 in the HMBC spectrum, which indicated that it was linked to the carbon at δ73.75, too. The methyl group at δ0.939 (s)

TABLE II ^{1}H NMR and ^{13}C NMR spectral data and HMBC correlation of compound **2** (in DMSO-d_6, δ ppm)

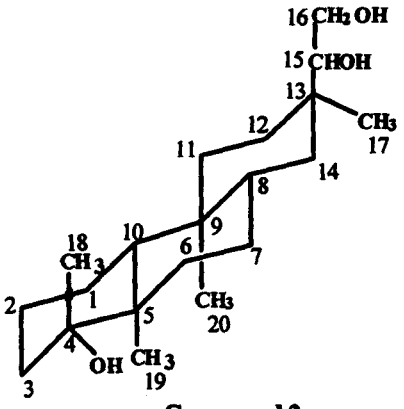
No	^{13}C NMR *Data*	^{1}H NMR *Data*	*Cross peaks in* HMBC *spectrum*
1	20.18		H_{10}
2	25.66		
3	36.61		C_4-OH
4	73.75		C_4-OH
5	42.16		C_4-OH
6	32.19		
7	22.95		
8	41.56		
9	36.61		
10	50.40		
11	35.10		
12	35.62		
13	36.26		
14	29.08		
15	80.22	2.973(1H, dd, $J=2.5$, 8.5 Hz)	
16	61.75	3.194(1H, t, $J=8.5$, 10.8 Hz)	
		3.469(1H, dd, $J=2.5$, 10.8 Hz)	
17	19.60	0.810(3H, s)	C_{12}, C_{13}, C_{14}, C_{15}
18	22.95	1.164(3H, s)	C_3, C_4, C_5, C_4-OH
19	15.00	0.939(3H, s)	C_4, C_{10}, C_5, C_6,
20	12.07	0.661(3H, s)	C_8, C_{10}, C_9, C_{11}

correlated with the carbon at δ73.75, 50.40 (–CH) and 42.16(quaternary carbon), which suggested this methyl group to be linked to the quaternary carbon at δ42.16. By considering the above-mentioned facts, one of the methyl groups usually at C-4 has now changed to C-5 (δ_C42.16). Another methyl group at δ_H0.661 (δ_C12.07) correlates with the carbon at δ50.40 (–CH), δ41.56 (–CH) and δ36.61(quaternary carbon), but not with C-5 (δ_C42.16), which settled it to C-9 (δ36.61, quaternary carbon) instead of C-10. The connectivities between the CH_3-17 and C-15 (δ_C80.22–CHOH) assigned it to C-13. Finally, compound **2** was determined to be a dolabradane-type diterpenoid with three hydroxyl groups substituted at C-4, C-15 and C-16. Its ^{13}C NMR and ^{1}H NMR data and HMBC correlation were summarized in Table II.

The results from differential NOESY experiment ascertained the stereochemistry of compound **2**. Irradiation of CH_3-19 (δ0.939) resulted in the enhancement of CH_3-20 (δ0.661 2.24%) and C_4-OH (δ3.829 3.40%), irradiation of CH_3-20 cause the enhancement of CH_3-19 (δ0.939) and CH_3-17 (δ0.810). So the stereochemistry of C_4-OH (δ3.829), CH_3-17 (δ0.810) and CH_3-20 (δ 0.661), were all α-configuration. While irradiation of CH_3-18(β-) only cause the enhancement of C_4-OH (δ3.829, 9.33%). Irradiation of H-15 (δ2.973) resulted in the enhancement of CH_3-17 (δ0.810, s).



Compound 1



Compound 2

EXPERIMENTAL

General Experimental Procedures

Mp were tested on BuCHI 510 (uncorrected). UV and IR spectra were recorded on Shimadzu M-250 and Perkin-Elmer 559-B spectrophotometer. ^{1}H NMR, ^{13}C NMR and HMQC were recorded on BrukerACF-300 type NMR instrument at 300 and 75 MHz, respectively in DMSO-d_6. EI-MS and HREIMS were taken on MAT-711. Optical rotations were measured on JASCO DIP-181 polarimeter. TLC was performed on silica gel F_{254} glass or alumina plates (Merck) using solvent system cyclohexane-ethyl acetate (1 : 1).

Plant Material

Roots of *M. apelta* Muell.Arg. were collected in Guangxi Province in August 1997. A voucher specimen is deposited in the herbarium of Guilin Institute of Medicinal Control.

Extraction and Isolation

Dried roots (10 kg) of *M. apelta* Muell.Arg. were extracted with 95% EtOH under room temperature. The combined extracts were concentrated almost to dryness under reduced pressure. Hot petroleum ether was added and the insoluble materials was removed by filtration. The filtrate was concentrated and subjected to the silica gel column eluting with cyclohexane-ethyl acetate to obtain compound **1** (75 mg) at (4 : 1) and compound (62 mg) **2** at (1 : 1).

TABLE III Differential NOESY spectrum of MA10

Irradiation	*Enhancement*					
	CH_3-17 (0.810)	CH_3-18 (1.164)	CH_3-19 (0.939)	CH_3-20 (0.661)	CH-15 (2.973)	C_4-OH (3.829)
CH_3-20	0.65	—	3.3	—	—	—
CH_3-18	—	—	—	—	—	9.33
CH_3-19	—	—	—	2.24	—	3.40
CH-15	0.12	—	—	—	—	

Compound **1**, $C_{20}H_{30}O_3$, 6,8-dihydroxyl-cembrene-5-one was obtained as white needles, mp 114–116°C; $[\alpha]_D$ + 160.84 ($CHCl_3$, *c* 0.166); UV (MeOH) λ_{max} nm (log ϵ): 209.0 (4.82), 236.0 (4.52); IR (MeOH) ν_{max}: 3461.7, 3411.5 (–OH), 3079.8 (=CH), 1664.3 (–CO), 1625.0 (–C=CH), 1380.8, 1280.5, 1022.1, 894.8 cm^{-1}; ^1H NMR and ^{13}C NMR (see Table I). HREIMS m/z (M^+) 318.2197(cal. 318.2195). EIMS m/z (rel. int): 318(M^+, 5.4), 278(4.7), 255(6.6), 121(55.6), 97(100), 56(84.0).

Compound **2**, $C_{20}H_{36}O_3$, 4α,15,16-trihydroxyl-dolabradane, amorphous white powder, mp 194–196 $[\alpha]_D$ + 28.04 (MeOH; *c* 0.428); UV (MeOH) λ_{max} nm (log ϵ): 205.0 (3.86); IR (KBr) ν_{max}: 3371.0 (–OH), 1467.6, 1384.7, 1371.2, 1080.0, 1026.0, 919.9 cm^{-1}; ^1H NMR and ^{13}C NMR (see Table I); HREIMS m/z (M^+) 324.2695 (cal. 324.2665). EIMS m/z (rel. int): 324(M^+, 59.0), 309(20.5), 263(54.7), 245(100), 163(27.3), 95(44.4); Difference NOE (see Table III).

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