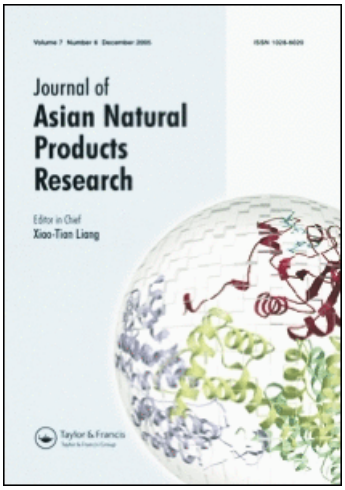


Journal of Asian Natural Products Research

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

Three New Diterpenoids from *Mallotus apelta* Muell.Arg.

Xiao-Fang Cheng[a]; Zhong-Liang Chen
[a] Department of Natural Products Chemistry, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, China

To cite this Article Cheng, Xiao-Fang and Chen, Zhong-Liang(1999) 'Three New Diterpenoids from *Mallotus apelta* Muell.Arg.', Journal of Asian Natural Products Research, 1: 4, 319 — 325
To link to this Article: DOI: 10.1080/10286029908039881
URL: http://dx.doi.org/10.1080/10286029908039881

JANPR, Vol. 1, pp. 319–325
Reprints available directly from the publisher
Photocopying permitted by license only

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

XIAO-FANG CHENG and ZHONG-LIANG CHEN*

Department of Natural Products Chemistry, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 200031, China

(Received 1 February 1999; Revised 17 March 1999; In final form 29 March 1999)

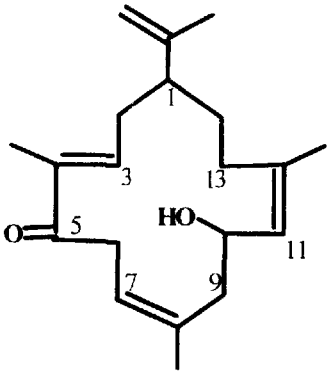
Three new diterpenoids, 10-hydroxy-cembrene-5-one, 6-hydroxy-cembrene-5,10-dione and 2α,4β,15,16-tetrahydroxyl-dolabradane were isolated from the petroleum ether fraction of the alcoholic extract of *Mallotus apelta* Muell.Arg. Their structures were determined by spectral methods.

Keywords: *Mallotus apelta* Muell.Arg.; Euphorbiaceae; Diterpenoids; 10-hydroxy-cembrene-5-one; 6-hydroxy-cembrene-5,10-dione; 2α,4β,15,16-tetrahydroxyl-dolabradane

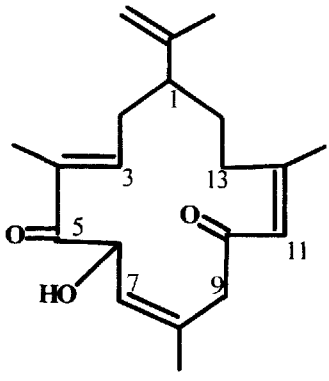
INTRODUCTION

Mallotus apelta Muell.Arg. (Euphorbiaceae) has been widely used in Chinese traditional medicine for the treatment of chronic hepatitis in South China [1]. In our earlier paper [2,3], we reported the isolation and identification of malloapeltine, 4,5,4′-trimethyl-ellagic acid and two new diterpenoids from *Mallotus apelta*. This paper deals with the structure elucidation (Fig. 1) of three other diterpenoid compounds.

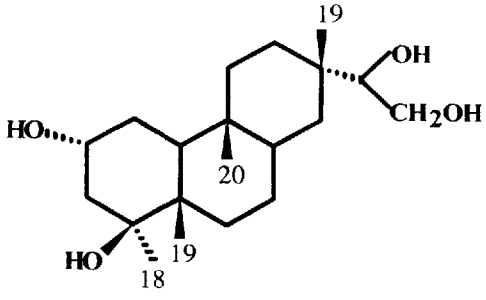
* Corresponding author. Tel.: 021-6434833, ext. 332. Fax: 86-21-64370269.
E-mail: zlchen@server.shcnc.ac.cn.



Compound 1



Compound 2



Compound 3

FIGURE 1

RESULTS AND DISCUSSION

Compound **1** was isolated as colorless oil. HREIMS revealed $[M]^+$ at m/z 302.2253 (calcd. 302.2246), which corresponded to the formula $C_{20}H_{30}O_2$, $\Omega = 6$. ^{13}C-NMR and DEPT spectra displayed a total of twenty carbon signals, including eight olefinic carbon signals and one carbonyl signal. According to the unsaturation of $\Omega = 6$, compound **1** still possessed one ring in the skeleton. Because of the absence of aromatic ring absorption in the IR spectrum, it might be a macrocyclic diterpenoid compound with four methyl groups.

According to HMBC and HMQC spectra, the four methyl group singlet peaks were all assigned to have direct connection with four quaternary

vinylic carbons ($-C_3=C_4-CH_3$-18; $-C_7=C_8$ CH_3-19; $-C_{11}=C_{12}-CH_3$-20; $H_2C_{16}=C_{15}-CH_3$-17). The carbonyl group C-5 was conjugated with one vinyl group ($-C_3=C_4-CH_3$-18). One methylene group (δ 40.95) between the carbonyl group C-5 and the vinyl group ($-HC_7=C_8-CH_3$-19) led to one of its protons shifted much downfield to δ 3.87. Further information from HMBC could join the four sections together one by one. All the data of ^{1}H-NMR, ^{13}C-NMR and HMBC were summarized in Table I.

The 2D-NOESY spectra of compound **1** gave the cross peaks between H-3 and CH_3-18; H-7 and CH_3-18 (weak); H-10 and CH_3-20; H-16 and CH_3-17. So the configurations of those vinyl groups were $-C_3=C_4-$, E; $-C_7=C_8-$, Z; $-C_{11}=C_{12}-$, Z.

At last, the structure of compound **1** was characterized to be 10-hydroxy-cembrene-5-one [4,5].

Compound **2** was obtained as a pale-yellow oil. EIMS and HREIMS gave the molecular formula as $C_{20}H_{28}O_3$, $\Omega = 7$. The structure was settled by comparing with the former reported macrocyclic diterpenoid, the only difference was the 10-hydroxy group in the former one changed into a carbonyl group here. The structure was then confirmed by ^{1}H-NMR, ^{13}C-NMR, HMQC and HMBC spectra. All the data were summarized in Table II.

TABLE I ^{1}H-NMR, ^{13}C-NMR and HMBC data of compound **1** (δ ppm, in CD_3COCD_3)

Position	*^{1}H-NMR*	*^{13}C-NMR*	*HMBC*
1		46.15, d	H-2, H-3
2	2.39, m	35.60, t	CH_3-18
	2.08, m		
3	6.49, m	145.97, d	H-2, CH_3-18
4		137.24, s	H-2, CH_3-18
5		201.28, s	H-3, H-6, CH_3-18
6	3.87, m	40.95, t	
	2.79, br		
7	5.13, br	122.58, d	H-6, H-10, CH_3-19
8		135.25, s	H-9, CH_3-19
9	2.45, br	49.62, t	H-11
	2.06, m		
10	4.81, m	65.73, d	H-11, H-9
11	5.09, d, $J = 7.1$ Hz	129.32, d	H-9, CH_3-20
12		140.61, s	CH_3-20
13		34.82, t	CH_3-20
14		32.83, t	H-2
15		149.22, s	CH_3-17
16	5.11, m	112.21, t	CH_3-17
17	1.71, s	19.71, q	H-16
18	1.68, s	11.87, q	H-3
19	1.68, s	16.52, q	H-7
20	1.76, s	20.25, q	H-11

TABLE II ^{1}H-NMR, ^{13}C-NMR and HMBC data of compound **2** (δ ppm, in CD_3COCD_3)

Position	*^{1}H-NMR*	*^{13}C-NMR*	*HMBC*
1		45.82, d	H-3, H-16, CH_3-17
2		36.77, t	H-3
3	6.72, dd, J = 5.6, 11.1 Hz	145.89, d	H-6, CH_3-18
4		136.13, s	H-6, H-9, CH_3-18
5		201.63, s	H-3, H-6, H-7, CH_3-18
6	5.57, d, J = 10.3 Hz	70.23, d	H-7
7	5.35, d, J = 10.3 Hz	130.48, d	H-6, H-9, CH_3-19
8		136.02, s	H-7, H-9, CH_3-19
9	3.24, d, J = 13.7 Hz 2.93, d, J = 13.7 Hz	57.95, t	H-7, CH_3-19
10		198.43, s	H-9, H-11
11	6.17, s	119.10, d	H-9, CH_3-20
12		160.00, s	H-11, CH_3-20
13		36.27, t	H-11, CH_3-20
14		27.70, t	
15		148.44, s	H-16, CH_3-17
16	4.76, s 4.85, s	112.77, t	CH_3-17
17	1.75, s	19.01, q	H-16
18	1.91, s	12.34, q	H-3
19	1.88, s	16.85, q	H-7, H-9
20	2.16, s	22.30, q	H-11

In 2D-NOESY spectra, H-3 correlated with CH_3-18, H-6 in space, so the configuration of $-C_3=C_4-$ was E. H-6 correlated with H-3 and CH_3-18. One of H-9 (δ 3.24) correlated with H-7 and H-11 at the same time. But no through-space interactions appeared for CH_3-19/H-7, and CH_3-20/H-11. Weak interactions of H-7 and H-11 to CH_3-18 and to each other were displayed, too. Thus both the configuration of $-C_7=C_8-$ and $-C_{11}=C_{12}-$ were Z. Compound **2** was named 6-hydroxy-cembrene-5,10-dione [4,5].

Compound **3**, white powder. EIMS provided only the ion peak of M^+-H_2O(322), ^{13}C-NMR and DEPT spectra provided all twenty carbon signals: four methyl groups, eight methylenes, four methylidynes. Considering the information from EIMS, ^{13}C-NMR and DEPT, its molecular formula was asserted as $C_{20}H_{36}O_4$, $\Omega = 3$. There are four hydroxyl-linking carbon signals between δ 60–80. It is thus a tricyclic diterpenoid compound.

The structure of compound **3** was established to be a dolabradane-type diterpenoid by HMBC and HMQC experiment. In the HMBC spectrum, the protons of CH_3-18 (δ 1.26) and CH_3-19 (δ 0.89) correlated simultaneously with the hydroxyl-linking carbon C-4 (δ 73.48), quaternary carbon C-5 (δ 42.25), while only the protons of CH_3-19 correlated with C-10 when it

transferred from C-4 to C-5. It was impossible for protons of CH_3-18, which was linked to C-4 to give correlation with C-10. The hydroxyl group linked to C-4 correlated with CH_3-18, not with CH_3-19. Protons of CH_3-20 correlated with the quaternary carbon C-9 (δ 35.15), C-8 (δ 41.81) and C-10 (δ 44.15). The hydroxyl group linked to C-2 (δ 64.83) correlated with the two methylene signals C-1, C-3 *ortho* to C-2, and only the position C-2 could provide the opportunities for the hydroxy group. The hydroxyl groups at δ 4.32 and δ 4.26 were linked to C-15 (δ 80.40) and C-16 (δ 61.91) respectively, correlated with the two carbon signals simultaneously, establishing their connectivity. Strong correlation between CH_3-17 (δ 0.81) and C-15; CH_3-17 (δ 0.81) and C-13 (δ 35.76) were displayed, too. The data of compound **3** were all summarized in Table III.

2D-NOESY showed significant through-space interactions for CH_3-20/CH_3-19, CH_3-20/CH_3-17. So the configuration of CH_3-17, CH_3-19 and CH_3-20 were all β, while CH_3-18 was α and 4-OH was β. No cross peak was shown between H-2 and CH_3-18, which suggested that 2-OH might have α-configuration. Compound **3** was named 2α,4β,15,16-tetrahydroxyldolabradane.

TABLE III ^{1}H-NMR, ^{13}C-NMR and HMBC data of compound **3** (δ ppm, in DMSO-d_6)

Position	^{13}*C-NMR*	^{1}*H-NMR*	*HMBC*
1	28.28, t		
2	64.83, d	3.92, br	
3	43.44, t		
4	73.48, s		
5	42.25, s		
6	32.29, t		
7	25.69, t		
8	41.81, d		
9	35.15, s		
10	44.15, d		
11	36.08, t		
12	36.35, t		
13	35.76, s		
14	29.11, t		
15	80.40, d	3.99, br	C-14, C-17
16	61.91, t	3.22, br	
		3.42, br	
17	19.63	0.81, s	C-15, C-13, C-14
18	26.39	1.26, s	C-3, C-4, C-5
19	14.67	0.89, s	C-4, C-5, C-6, C-10
20	12.17	0.66, s	C-9, C-8, C-10
2-OH		4.16, br	C-1, C-2, C-3
4-OH		3.69, s	C-4, CH_3-18
15-OH		4.32, d	C-13, C-15, C-16
16-OH		4.26, d	C-15, C-16

EXPERIMENTAL SECTION

General Experimental Procedure

IR recorded on Nicolet Magna-FTIR-750 type IR Instrument; ^{1}H NMR, ^{13}C NMR and HMQC were recorded on BrukerACF-300 type NMR Instrument at 400 and 100 MHz (in CD_3COCD_3 and DMSO-d_6) respectively. EIMS and HREIMS recorded on MAT-95 type MS Instrument.

Plant Material

Roots of *Mallotus apelta* Muell.Arg. were collected in Guangxi Province, China in August 1996. A voucher specimen is deposited in the herbarium of Guilin Institute of Medicinal Control.

Extraction and Isolation

Dried roots of *Mallotus apelta* Muell.Arg. were extracted with 95% EtOH. The combined extracts were concentrated almost to dryness under reduced pressure. Hot petroleum ether was added and the insoluble materials were removed by filtration. The filtrate was concentrated to get part 1. Part 1 was subjected to the silica gel column eluting with cyclohexane–ethyl acetate to obtain compound **1** (35 mg), **2** (100 mg) and **3** (30 mg) at cyclohexane–ethyl acetate (50 : 1), (30 : 1) and (2 : 3) respectively.

Compound **1**, MW 302, formula $C_{20}H_{30}O_2$. IR ν_{Max}^{KBr} (cm^{-1}): 3434.7 (–OH), 1712.5(–CO), 1670.1(–C=C–), 1446.4, 1384.7, 1074.2, 891.0. ^{1}H-NMR and ^{13}C-NMR see Table I. EIMS *m/z* (rel. int.): 302(3.93, M^+), 285(7.43), 271(3.53), 257(3.70), 233(6.96), 205(10.41), 187(14.59), 177(15.03), 149(24.29), 121(46.20), 107(48.57), 95(55.67), 81(43.64), 55(52.71), 43(100.0). HREIMS *m/z* M^+: 302.2253 (calcd. 302.2246).

Compound **2**, MW 316, formula $C_{20}H_{28}O_3$. IR ν_{Max}^{KBr} (cm^{-1}): 3446.2-(–OH), 3100, 1670.1(br, –CO), 1616.1(–C=C–), 1378.9, 1278.6, 1124.3, 1024.6, 894.8. ^{1}H-NMR and ^{13}C-NMR see Table II. EIMS *m/z* (rel. int.): 317(4.65), M^++1, 316(1.71), M^+, 271(8.68), 203(20.84), 189(26.72), 175(15.56), 161(21.25), 149(17.40), 135(23.06), 121(26.28), 107(25.92), 95(100), 82(37.54), 67(29.36), 53(20.84), 41(30.30). 299(HREIMS *m/z* (M^+): 316.2021 (calcd. 316.2039).

Compound **3**, MW 340, formula $C_{20}H_{36}O_4$. IR ν_{Max}^{KBr} (cm^{-1}): 3428.9-(–OH), 1454.1, 1022.1, 923.8, 667.3. ^{1}H-NMR and ^{13}C-NMR see Table III. EIMS *m/z* (rel. int.): 322(2.01, M^+-H_2O), 304(3.84), 289(7.54), 271(4.83),

252(17.78), 237(35.79), 203(30.04), 191(24.52), 177(45.20), 161(19.02), 147(26.11), 135(27.85), 121(40.25), 107(45.87), 95(54.63), 87(57.11), 67(30.78), 55(46.050), 43(100.0).

References

[1] X.Q. Shan and L.B. Feng. *Zhi Wu Xue Bao*, 1985, **27**(2): 192–195.
[2] X.F. Cheng, Z.M. Meng and Z.L. Chen. *Phytochemistry*, 1998, **49**(7): 2193–2194.
[3] X.F. Cheng, Z.L. Chen and Z.M. Meng. *J. Asian Nat. Prod. Res.*, 1999, **1**(3): 163–168.
[4] Koji Yamada and Kenjiro Ryu. *J. Nat. Prod.*, 1997, **60**(8): 798–803.
[5] L. Deniell. *J. Nat. Prod.*, 1997, **60**(8): 828–832.