New Triterpenoids of *Mallotus repandus*

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Three new triterpenoids—3α-hydroxy-13α-ursan-28,12β-olide 3-benzoate (**1**), 3α-hydroxy-28β-methoxy-13α-ursan-28,12β-epoxide 3-benzoate (**2**), and 3α-hydroxy-13α-ursan-28-oic acid (**3**)—and four known compounds were isolated from the stem and root bark of *Mallotus repandus*.

In Taiwan, the stems of *Mallotus repandus* (Willd.) Mueller-Arg. (Euphorbiaceae) have been used as an anti-inflammatory drug. Diterpenoids, triterpenoids, bergenin, cyano-γ-pyridone, and tannins have been reported to occur in this plant.[1,2] In a search for bioactive constituents from this plant, three new triterpenoids, 3α-hydroxy-13α-ursan-28,12β-olide 3-benzoate (**1**); 3α-hydroxy-28β-methoxy-13α-ursan-28,12β-epoxide 3-benzoate (**2**); and 3α-hydroxy-13α-ursan-28-oic acid (**3**), and four known compounds, 3-oxo-13α-ursan-28,12β-olide; 3α-hydroxy-13α-ursan-28,12β-olide; ursolic acid; and bergenin, were isolated from the stem and root bark of *M. repandus*. In the present paper the characterization of **1**, **2**, and **3** is reported.

The high-resolution MS of **1** revealed $[M]^+$ at *m/z* 560.3865, which corresponded to the molecular formula $C_{37}H_{52}O_4$. Its IR spectrum showed absorption bands characteristic of an ester group, a δ-lactone function, and an aromatic ring (1600 cm^{-1}). The ^1H and ^{13}C NMR spectral features of **1** suggested an ursane triterpene. The ^1H NMR spectrum of **1** indicated signals for two secondary and five tertiary methyl groups, an axial methine proton at δ 4.80 on C-3 bearing a OCOR group, an equatorial methine proton at δ 3.93 on C-12 adjacent to the oxygen function of the lactone ring, and a phenyl group.[2] In addition, the presence of two methine carbon signals at δ 75.6 and 83.4, and two carbonyl carbon signals at δ 166.4 and 176.9, suggested that **1** was a lactone of an ursane triterpene similar to 3β-hydroxy-13α-ursan-28,12β-olide 3-benzoate except that it exhibited different chemical shifts of H-3 and C-3 from those of 3β-hydroxy-13α-ursan-28,12β-olide 3-benzoate.[2] Thus, **1** was characterized as 3α-hydroxy-13α-ursan-28,12β-olide 3-benzoate. The ^{13}C NMR assignments of **1** (Table 1) were made by performing ^1H-decoupled, DEPT, 2D NMR correlation experiments and by comparing the corresponding data for ursan-3α,19α,20β-triol and methyl ursolate.[3,4]

The HR FABMS of **2** revealed $[M - 1]^+$ at *m/z* 575.4088, which corresponded to the molecular formula $C_{38}H_{55}O_4$. Its IR spectrum showed absorption bands characteristic of an ester group and an aromatic ring. The ^1H and ^{13}C NMR data of **2** also suggested an ursane triterpene. The ^1H NMR spectrum of **2** was similar to that of **1**, except for absence of a signal at δ 3.93 (corresponding to H-12α in **1**) and contained signals for a methine proton at δ 3.16, an aliphatic proton at 5.25 (s), and methoxyl protons at δ 3.37. The ^{13}C NMR spectrum of **2** (Table 1) is also similar to that of **1**, except for the absence of signals at δ 83.4 and 176.9 (corresponding to C-12 and C-28 in **1**) and presence of signals for a methoxyl carbon at δ 56.0, an oxygenated carbon at δ 76.6, and an oxygenated tertiary carbon at δ 101.5. This suggested that the C, D, and E rings of **2** are different from those of **1**. In the HMBC spectrum, the carbon signal at δ 101.5 was correlated with the methine proton signal at δ 3.16 and the methoxyl proton signal at δ 3.37, respectively, and the aliphatic proton signal at δ 5.25 was correlated with the methoxyl carbon at δ 56.0 (Figure 1). The NOESY spectrum of **2** indicated correlations between H-12, H-13, and H-28 and Me-27, H-13, and H-28

Table 1. ^{13}C NMR Chemical Shift Values of **1**, **2**, and **3**[a,b]

carbon	**1** ($CDCl_3$)	**2** ($CDCl_3$)	**3** ($CDCl_3$)
1	40.5	41.1	37.6
2	21.6	21.3	29.0
3	75.6	75.5	72.6
4	38.0	37.2	38.4
5	57.4	59.7	54.3
6	19.3	19.4	19.2
7	32.4	32.6	34.2
8	38.5	38.7	39.3
9	49.8	52.7	49.0
10	37.2	37.1	38.4
11	39.4	37.5	20.7
12	83.4	76.6	29.0
13	39.1	41.1	44.3
14	35.9	34.2	40.3
15	27.9	28.3	29.3
16	32.4	32.2	33.7
17	51.4	40.7	49.0
18	49.8	50.2	54.2
19	39.0	41.3	39.1[c]
20	39.0	41.3	39.2[c]
21	30.0	29.9	37.2[d]
22	31.5	35.7	36.9[d]
23	14.3	14.6	15.0
24	34.6	35.9	31.1
25	23.3	21.0	23.3
26	20.4	24.0	31.6[d]
27	30.5	30.6	35.8
28	176.9	101.5	180.4
29	18.0	17.6	19.2
30	10.1	10.1	10.4
1′	166.4	166.3	
2′	130.9	130.9	
3′	129.5	129.5	
4′	128.3	128.3	
5′	132.7	132.7	
6′	128.3	128.3	
7′	129.5	129.5	
OMe		56.0	

[a] The number of protons directly attached to each carbon was verified by DEPT experiment. [b] Signals obtained by $^1H-^1H$ COSY, HMQC, HMBC, and NOESY techniques. [c] Assignments may be interchangeable. [d] Assignments may be revised.

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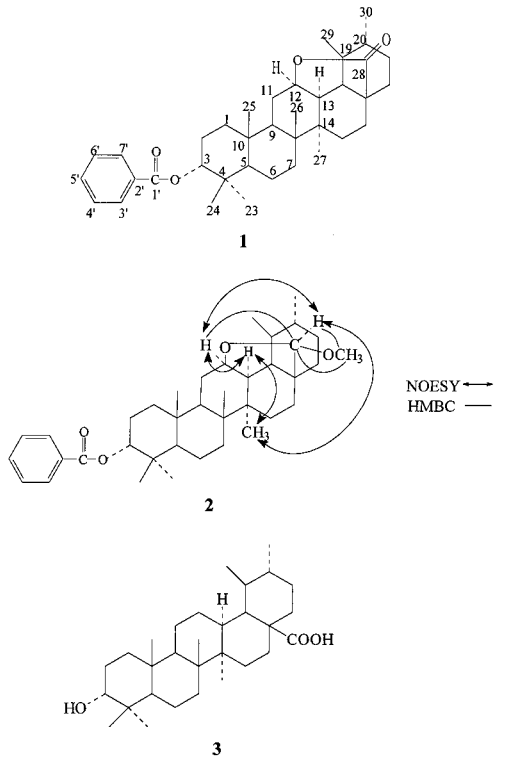

Figure 1. Structures of **1**, **2**, and **3**, and partial C/H long-range correlations and NOESY interactions of **2**.

(Figure 1). Thus, **2** was characterized as 3α-hydroxy-28*β*-methoxy-13α-ursan-28,12*β*-epoxide 3-benzoate. The ^{13}C NMR assignments of **2** (Table 1) were made by performing ^{1}H-decoupled, DEPT, 2D NMR correlation experiments and by comparing the corresponding data for **1**.

The HRMS of **3** revealed $[M]^+$ at *m/z* 458.3766, which corresponded to the molecular formula $C_{30}H_{50}O_3$. Its IR spectrum showed absorption bands characteristic of hydroxyl and carboxylic groups. The ^{1}H and ^{13}C NMR signals of **3** also indicated an ursane skeleton. The ^{1}H NMR spectrum of **3** contained signals for two secondary and five tertiary methyl groups, and an axial methine proton at δ 3.26 on C-3 bearing a hydroxyl group. The absence of any signal beyond δ 3.26 and any band near 1600 cm^{-1} in the IR spectrum suggested the saturated nature of this compound. Based on the above evidence, the chemical shift of H-3 and C-3 in the ^{1}H and ^{13}C NMR spectra of **3**, respectively, are identical to those of corresponding data for 3α-hydroxy-13α-ursan-28,12*β*-olide, and the NOESY spectrum of **3** indicated correlation between H-13 (δ 1.89, m) and Me-27 (δ 0.95, s). Thus, compound **3** was characterized as 3α-hydroxy-13α-ursan-28-oic acid (Figure 1). The ^{13}C NMR assignments of **3** (Table 1) were made by performing ^{1}H-decoupled, DEPT, 2D NMR correlation experiments and by comparing the corresponding data for ursan-3α,19α,20*β*-triol and methyl ursolate.[3,4]

Experimental Section

General Experimental Procedures. Melting points are reported uncorrected. Optical rotation was obtained on a JASCO model DIP-370 digital polarimeter; UV spectra were obtained on a JASCO model 7800 UV−vis spectrophotometer; IR spectra were recorded on a Hitachi model 260−30 spectrophotometer; ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian Unity-400 spectrometer; and MS were obtained on a JMS−HX mass spectrometer.

Plant Material. The stem and root bark of *Mallotus repandus* (1.4 kg) were collected at Kaohsiung Hsien, Taiwan, during July 1996, and a voucher specimen has been deposited in the authors' laboratory (voucher no. Ma-01).

Extraction and Isolation. The stem and root bark (1.4 kg) of *M. repandus* were chipped and extracted with Me_2CO at room temperature. The Me_2CO extract was chromatographed over Si gel. Elution with cyclohexane−EtOAc (10:1) yielded **1** (50 mg); cyclohexane−$CHCl_3$ (9.5: 0.5) yielded 3-oxo-13a-ursan-28,12*β*-olide; cyclohexane−$CHCl_3$ (4: 1) yielded **2** (8 mg); $CHCl_3$ yielded **3** (10 mg) and 3α-hydroxy-13α-ursan-28,12*β*-olide (15 mg); $CHCl_3$−MeOH (9: 1) yielded ursolic acid (5 mg); and EtOAc−MeOH (9: 1) yielded bergenin (110 mg). These known compounds were identified by spectroscopic methods and comparison with authentic data[2] or sample.

3α-Hydroxy-13α-ursan-28,12*β*-olide 3-benzoate (1): colorless needles (MeOH); mp 260−262 °C; $[\alpha]^{27}_D$ −33° ($CHCl_3$, *c* 1.0); IR ν_{max} (KBr) cm^{-1} 1734, 1715; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.81 (3H, d, J = 6.4 Hz, Me-30), 0.87 (3H, d, J = 6.4 Hz, Me-29), 0.88 (3H, s, Me-23), 0.98 (3H, s, Me-27), 0.93 (3H, s, Me-24), 1.19 (3H, s, Me-26), 1.20 (3H, s, Me-25), 1.79 (1H, m, H-13α), 3.93 (1H, m, $W_{1/2}$= 9 Hz, H-12α), 4.80 (1H, m, $W_{1/2}$= 16 Hz, H-3*β*), 7.36 (2H, m, H-4′ and -6′), 7.47 (1H, m, H-5′), 7.96 (2H, m, H-3′ and -7′); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; EIMS (70 ev) *m/z* 560 $[M]^+$ (7), 455 $[M - C_6H_5CO]^+$ (4), 438 $[M - C_6H_5COOH]^+$ (15), 423 $[438 - Me]^+$ (7), 370 (9), 314 (15), 187 (10), 123 (17), 105 (100); HREIMS *m/z* 560.3865 (calcd for $C_{37}H_{52}O_4$, 560.3855).

3α-Hydroxy-28*β*-methoxy-13α-ursan-28,12*β*-epoxide 3-benzoate (2): colorless powder (MeOH−$CHCl_3$); mp 155−157 °C; $[\alpha]^{27}_D$ 179° ($CHCl_3$, *c* 0.05); IR ν_{max} (KBr) cm^{-1} 1716, 1603; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.77 (3H, d, J = 6.4 Hz, Me-30), 0.79 (3H, d, J = 6.4 Hz, Me-29), 0.84 (3H, s, Me-23), 0.86 (3H, s, Me-24), 0.90 (3H, s, Me-27), 1.00 (3H, s, Me-26), 1.03 (3H, s, Me-25), 1.75 (1H, m, H-13α), 3.16 (1H, m, $W_{1/2}$= 9 Hz, H-12α), 3.37 (3H, s, OMe), 4.81 (1H, m, $W_{1/2}$= 16 Hz, H-3*β*), 5.25 (1H, s, H-28α), 7.36 (2H, m, H-4′ and -6′), 7.47 (1H, m, H-5′), 7.96 (2H, m, H-3′ and -7′); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; FABMS (negative) *m/z* 575 $[M - 1]^-$ (0.2), 545 $[M - OMe]^-$ (0.3), 455 $[M - Me - C_6H_5CO]^-$ (0.2), 423 $[M - Me - C_6H_5COOH]^-$ (1), 395 $[423 - CO]^-$ (1), 189 (4), 123 (11), 105 (34), 69 (90), 55 (100); HRFABMS *m/z* 575.4088 (calcd for $C_{38}H_{55}O_4$, 575.4100).

3α-Hydroxy-13α-ursan-28-oic acid (3): colorless needles ($CHCl_3$); mp 155−157 °C; $[\alpha]^{27}_D$ +53° ($CHCl_3$, *c* 0.05); IR ν_{max} (KBr) cm^{-1} 3339, 1688; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.79 (3H, s, Me-23), 0.87 (3H, d, J = 6.4 Hz, Me-30) 0.89 (3H, d, J = 6.4 Hz, Me-29) 0.95 (3H, s, Me-27), 1.01 (3H, s, Me-24), 1.14 (3H, s, Me-25), 1.23 (3H, s, Me-26), 1.83 (m, H-13α), 3.26 (1H, m, $W_{1/2}$= 16 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; EIMS (70 ev) *m/z* 458 $[M]^+$ (0.3), 440 $[M - H_2O]^+$ (2), 395 $[400 - COOH]^+$ (1), 307 (21), 203 (11), 189 (14), 175 (23), 163 (22), 152 (39), 123 (48), 107 (54), 95 (80), 55 (100); HREIMS *m/z* 458.3766 (calcd for $C_{30}H_{50}O_3$, 458.3759).

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References and Notes

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