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TRITERPENOIDS FROM *MALLOTUS REPANDUS*: THREE NEW δ-LACTONES*

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Key Word Index—*Mallotus repandus*; Euphorbiaceae; triterpenoids; 3α- and 3β-hydroxy-13α-ursan-28, 12β-olide.

Abstract—The leaves of *Mallotus repandus* contain friedelin, 3β-hydroxy-13α-ursan-28,12β-olide (**1**), its benzoate (**2**) and ursolic acid. The stems contain friedelin, lupeol, α-amyrin, **2** and 3α-hydroxy-13α-ursan-28, 12β-olide (**3**), 21α-hop-22(29)-ene-3β,30-diol and ursolic acid. **1–3** are new compounds.

INTRODUCTION

Of the six *Mallotus* species found in Hong Kong, three have been investigated for triterpenoids, two by us [1] [*] and the third in India [2]. We describe here our work on the fourth, *M. repandus*, which has recently been reported to contain the isocoumarin, bergenin [3].

RESULTS AND DISCUSSION

The petrol extract of the leaves on chromatography on alumina yielded in succession friedelin, compound **2**, sitosterol and compound **1**, and that of the stems, friedelin, lupeol, α-amyrin, compound **2**, sitosterol, compound **3** and 21α-hop-22(29)-ene-3β,30-diol. The last compound has only been isolated once by us from *Rhodomyrtus tomentosa* [4]. Ursolic acid was isolated from the subsequent ethanolic extracts of both the stems and leaves.

Compound **1**, $C_{30}H_{48}O_3$ (M^+, *m/e* 456), contained an OH group (ν_{max} 3490) and a δ-lactone function (ν_{max} 1745, 1120 cm^{-1}). It formed a monoacetate (**4**) and a monobenzoate, each of which indicated the OH group in **1** to be secondary and equatorial by an axial proton at δ 4.87 (*m*, $W_{\frac{1}{2}}$ = 18 Hz) and δ 4.60 (*m*, $W_{\frac{1}{2}}$ = 16 Hz) respectively in its NMR spectrum. Chromic acid oxidation of **1** yielded a six-membered ring ketone (**5**), $C_{30}H_{46}O_3$.

Compound **2**, $C_{37}H_{52}O_4$, contained an ester group (ν_{max} 1720, 1273), a δ-lactone function (ν_{max} 1740, 1115) and a monosubstituted benzene ring [ν_{max} 3040, 1600, 1580, 712, 690 cm^{-1}, δ 7.48 (3H, *m*) and 8.00 (2H, *m*)], and was found to be identical with the benzoate of **1**. Its MS was almost identical with that of **1**. The parent ion appeared at *m/e* 438 instead of 560, indicating the loss of a molecule of C_6H_5COOH from the molecular ion. Hydrolysis of **2** under mild conditions gave **1** and benzoic acid.

Compound **3**, $C_{30}H_{48}O_3$ (M^+, *m/e* 456), possessed an OH group (ν_{max} 3490) and a δ-lactone ring (ν_{max} 1745, 1120 cm^{-1}). It formed a monoacetate (**6**), which showed a secondary axial OAc group by a signal at δ 4.89 (1H, *m*, $W_{\frac{1}{2}}$ = 8 Hz). The MS of **3** was very similar to that of **1**. On chromic acid oxidation, **3** yielded a keto-lactone, identical with **5**. Compounds **1** and **3** were thus epimers, differing only in the configuration of the secondary OH function. $NaBH_4$ reduction of **5** gave **1** as the sole product, further confirming the latter to be the equatorial isomer.

Compounds **2–6** each showed in its NMR spectrum a signal at δ 3.94, 3.94, 4.03 or 3.98 respectively (each 1H, *m*, $W_{\frac{1}{2}}$ = 9 Hz) indicating an equatorial proton on a carbon atom adjacent to the oxygen function of the lactone ring. The absence of signals at δ 2.5–3.5 in each of these spectra showed that the C=O functions of the lactone ring was attached to a tertiary carbon atom, and the presence of seven partly perturbed Me signals suggested an ursane type skeleton.

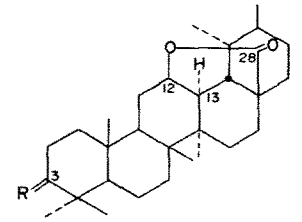
The MS of **1**, **3**, **4** and **6** each showed a strong fragment at *m/e* 189, and prominent peaks at *m/e* 207, 207, 249, 249 respectively, indicating the location of the secondary OR group (R = H in **1** and **3**, and Ac in **4** and **6**) in rings A or B, and the lactone function in C, D and/or E. Attempted hydrolysis of the lactone ring in **1** under mild conditions was unsuccessful. However, refluxing **1** with 40% KOH in diethylene glycol for 2 days led to the isolation of ursolic acid (**7**).

Thus the secondary OH function in **1** and **3** was in the 3-position, and the lactone function must have been derived from the 28β-COOH and 12β-OH group. Inspection of the model indicated that a C-28 → C-12-olide was not possible with a 13β-H configuration, and moreover the formation of ursolic acid as the hydrolysis product of **2** could be explained by the *trans*-elimination of H_2O from the 12β-OH and 13α-H. Hence **1** was 3β-hydroxy-13α-ursan-28,12β-olide, **2** the corresponding 3β-yl benzoate, and **3** the 3α-hydroxy compound.

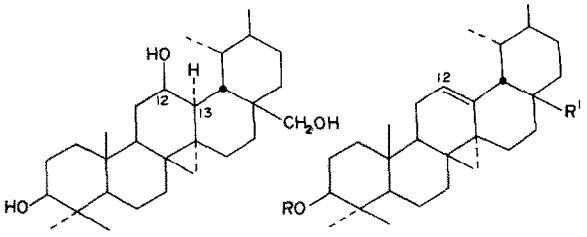
Reduction of **1** with $LiAlH_4$ in boiling dioxan for 6 days gave an amorphous triol (**8**), $C_{30}H_{52}O_3$ (reduction under milder conditions was unsuccessful). Attempted preparation of the triacetate by refluxing **8** with acetic

* Part 14 in the series "An examination of the Euphorbiaceae of Hong Kong." For Part 13, see Hui, W. H. and Li, M. M. (1976) *Phytochemistry* **15**, 985.

anhydride and C_5H_5N led to the isolation of uvaol diacetate (**9**), further confirming the ready *trans-diaxial* elimination of the 12β-OH and 13α-H.



1 R = α-H, β-OH
2 R = α-H, β-OBz
3 R = α-OH, β-H
4 R = α-H, β-OAc
5 R = O
6 R = α-OAc, β-H



8

7 R = H R' = COOH
9 R = Ac R' = CH_2OAc

This investigation describes the isolation of the third naturally occurring pentacyclic triterpene-δ-lactone. The other two are phillyrigenin (3β-27-dihydroxy-taraxastan-28,20β-olide) [5, 6] and larreagenin A (3β-hydroxy-29-nor-urs-13(18)-en-28,20β-olide) [7]. Compounds **1–3** also represent the first examples of members of the ursane series with a *cis* C/D ring junction.

EXPERIMENTAL

IR spectra were recorded for KBr discs; NMR spectra in $CDCl_3$ were determined at 60 MHz using TMS as internal standard, and optical rotations in $CHCl_3$ solns. Petrol had bp 60–80°. Known compounds were determined by TLC, mmp, IR and MS comparisons with authentic samples.

Extraction and isolation of compounds. Milled air-dried leaves and stems of *M. repandus* (Willd.) Muell.-Arg. were separately extracted 2X at room temp. with petrol for 7 days. Each of the combined extracts was distilled to a small vol. and chromatographed on alumina. Each of the plant materials was then extracted 2X with 95% EtOH at room temp. for 7 days. Each of the combined extracts was distilled to dryness, and repeatedly extracted with Et_2O. The combined ethereal sols were shaken with 1M NaOH. The aq. layers on acidification gave a solid in each case.

Leaves. The extract from the leaves (4 kg) in petrol was chromatographed on alumina (1.2 kg). Elution with petrol gave friedelin (0.3 g), mp 260–261°, IR ν_{max} cm^{-1}: 1715, with petrol–C_6H_6 (1:1), plates of compound **2**, (0.01 g), mp 340–342° (from petrol–$CHCl_3$), $[\alpha]_D$ + 32.0° (Found · C, 79.3; H, 8.9 $C_{37}H_{52}O_4$ requires C, 79.2; H, 9.3%), then sitosterol (0.8 g), mp 138–140°, and with C_6H_6 needles of compound **1**, (0.013 g), mp 385–386° (from MeOH), $[\alpha]_D$ + 17.0° (Found: M^+ 456. $C_{30}H_{48}O_3$ requires M^+ 456). The acidic solid (4.0 g) from the EtOH extract was treated with CH_2N_2 in Et_2O, and the product was chromatographed on alumina (100 g). Elution with petrol–C_6H_6 yielded methyl ursolate (0.1 g), mp 170°, MS: M^+, *m/e* 470, IR ν_{max} cm^{-1}: 3350 (OH), 1740, 1200 (COOMe), 1640, 820 (C=CH).

Stems. The stems (26 kg) extract was chromatographed on alumina (1.5 kg). Elution with petrol yielded first friedelin (0.15 g), then lupeol (0.07 g), mp 205–207°, MS: *m/e* 426 (M^+), IR ν_{max} cm^{-1}: 3360 (OH), 3080, 1640, 880 (C=CH_2), and finally α-amyrin (0.03 g), mp 185–187° (from petrol), $[\alpha]_D$ + 80.0°, MS: *m/e* 426 (M^+), IR ν_{max} cm^{-1}: 3350 (OH), 1655, 830 (C=CH). Elution with petrol–C_6H_6 (1:1) afforded plates of compound **2** (0.3 g), mp 340–342°, identical with the sample for the leaves, then sitosterol (1.0 g). Further elution with C_6H_6 gave compound **3** (0.05 g), mp 319–321° (from MeOH), $[\alpha]_D$ + 9.0° (Found: C, 78.6; H, 10.5; M^+ 456. $C_{30}H_{48}O_3$ requires C, 78.9; H, 10.6%; M^+ 456). Elution with C_6H_6–$CHCl_3$ (1:1) yielded fine needles of 21α-hop-22(29)-ene-3β,30-diol (0.01 g), mp 253–254 (from EtOAc), $[\alpha]_D$ + 6.5, MS: M^+ *m/e* 442, IR ν_{max} cm^{-1} 3300 (OH), 1650, 915 ($HOH_2C-\underset{|}{C}=CH_2$). The acidic solid from the EtOH extract was treated as that for the leaves. Methyl ursolate (0.03 g) was obtained.

Derivatives of **1**. (a) Acetate (**4**)—Acetylation of **1** with $(CH_3CO)_2O$ and C_5H_5N at boiling temp. gave **4**, mp 369–370° (from C_6H_6), $[\alpha]_D$ + 10.0° (Found: M^+ 498. $C_{32}H_{50}O_4$ requires M^+ 498), IR ν_{max} cm^{-1}: 1740, 1248 (OAc), 1745, 1120 (δ-lactone). (b) Benzoate (**2**)—Treatment of **1** with C_6H_5COCl in C_5H_5N at room temp. yielded a compound, mp 341–342°, identical with **2**.

Oxidation of **1**. Compound **1** (0.03 g) in C_6H_6 (60 ml) was stirred with a soln of CrO_3 (0.1 g) in H_2O (5 ml) and AcOH (10 ml) for 16 hr. The product was recrystallized from MeOH to give needles of **5** (0.015 g), mp 325–327°, $[\alpha]_D$ + 55.0° (Found: M^+ 454. $C_{30}H_{46}O_3$ requires M^+ 454), IR ν_{max} cm^{-1}: 1720 (C=O), 1745, 1120 (δ-lactone).

Hydrolysis of **2**. Compound **2** (0.09 g) was refluxed with 5% KOH (40 ml) for 2 hr, and then Et_2O extracted. The alkaline layer on acidification, gave needles of benzoic acid (0.01 g), mp 120–121°. The Et_2O layer yielded needles (0.06 g), mp 385–386°, $[\alpha]_D$ + 17.0° (Found: C, 78.8; H, 11.0; M^+ 456. $C_{30}H_{48}O_3$ requires C, 78.9, H, 10.6%; M^+ 456), identical with **1**.

Reactions of **3**. (a) Compound **3** (0.03 g), was acetylated as for **1**, to give the product (0.025 g) mp 337–339°, (from petrol). (b) Compound **3** (0.03 g) in C_6H_6 was treated with CrO_3 in aq. AcOH as for **1**. The product (0.014 g), mp 325–327°, was identical with **5**.

Reduction of **5**. Compound **5** (0.025 g) was stirred with $NaBH_4$ (0.1 g) in $(Me)_2CHOH$ (25 ml) for 4 hr. The product was recrystallized from MeOH to give needles of **1** (0.02 g), mp 384–386°.

Hydrolysis of **1**. (a) Compound **1** (0.05 g) was refluxed with 20% KOH in MeOH (40 ml) and C_6H_6 (10 ml) for 24 hr. The product (0.045 g), mp 383–385°, was identified to be unchanged **1**. (b) Compound **1** (0.1 g), was refluxed with 40% KOH in diethylene glycol (30 ml) for 2 days. The product on repeated recrystallization from MeOH gave needles (0.035 g), mp 287–289°, $[\alpha]_D$ + 69.0°, MS: *m/e* 456 (M^+), IR ν_{max} cm^{-1}: 3470 (OH), 3500–2500, 1725 (COOH), 1650, 830 (C=CH), identical with ursolic acid (**7**). It formed an acetate, mp 298–299° (from $CHCl_3$), $[\alpha]_D$ + 75.0°, IR ν_{max} cm^{-1}: 3500–2600, 1720 (COOH), 1740, 1270 (OAc), 1655, 810 (C=CH), and a methyl ester, mp 171–172°, (from petrol), $[\alpha]_D$ + 57.0°, IR ν_{max} cm^{-1}. 3350 (OH), 1740, 1200 (COOMe), 1640, 820 (C=CH), identical with acetyl ursolic acid and methyl ursolate respectively.

Reduction of **2**. (a) Compound **2** (0.05 g) was refluxed with $NaBH_4$ (0.1 g) in $(Me)_2CHOH$ (25 ml) for 12 hr. The product, mp 340–342°, was identified to be unreacted **2**. (b) Compound **2**, (0.05 g) was refluxed with $LiAlH_4$ (0.1 g) in dry $(C_2H_5)_2O$ or THF (25 ml) for 18 hr. Needles of **1** (0.04 g), mp 385–387°, were obtained. (c) **2** (0.05 g) was refluxed with $LiAlH_4$ (0.3 g) in dry dioxan (25 ml) for 6 days to give an amorphous solid product (**8**) (0.03 g), mp 267–272° (from MeOH), (Found: M^+ 460. $C_{30}H_{52}O_3$ requires M^+ 460), IR ν_{max} cm^{-1}: 3300 (OH). This was acetylated to give an oily product, which on purification by PLC yielded fine needles (0.015 g), mp 152–154° (from aq. MeCOMe), $[\alpha]_D$ + 49.0°, MS. *m/e* 526 (M^+), IR ν_{max} cm^{-1}: 1745, 1250 (OAc), 1645, 820 (C=CH), identical with uvaol diacetate (**9**).

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