Taraxastane-Type Triterpenes from the Aerial Roots of *Ficus microcarpa*

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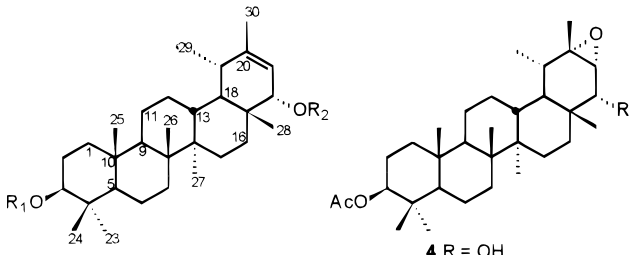
Received December 22, 1999

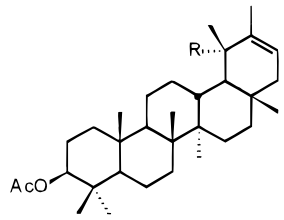
Seven new taraxastane-type triterpenes—20-taraxastene-3β,22α-diol (**1**), 3β-acetoxy-20-taraxasten-22α-ol (**2**), 3β-acetoxy-22α-methoxy-20-taraxastene (**3**), 3β-acetoxy-20α,21α-epoxytaraxastan-22α-ol (**4**), 3β-acetoxy-19α-methoxy-20-taraxastene (**5**), 3β-acetoxy-19α-hydroperoxy-20-taraxastene (**6**), 3β-acetoxy-20α,21α-epoxytaraxastane (**7**)—were isolated from the aerial roots of *Ficus microcarpa*. Their structures were elucidated by spectroscopic and chemical methods.

Ficus microcarpa L. f. (Moraceae) is a popular ornamental plant in Taiwan. Antiplatelet activity, as well as the strong vitality, of this plant prompted us to research the chemical components. Phytochemical studies of this plant have identified six triterpenoids from the leaves.[1] Two isoflavones,[2] 28 known components,[3] and six new compounds were previously isolated from its bark and heartwood.[4,5] Recently, five taraxastane-type triterpenes were isolated from its aerial roots.[6] Reinvestigation of the aerial root extract has yielded seven new taraxastane-type triterpenes, **1**−**7**. This paper describes the structures of **1**−**7**.



1 $R_1 = R_2 = H$
2 R_1 = Ac, R_2 = H
3 R_1 = Ac, R_2 = Me

4 R = OH
7 R = H



5 R = OMe
6 R = OOH

Results and Discussion

Triterpene **1** had HREIMS and ^{13}C NMR data consistent with the molecular formula $C_{30}H_{50}O_2$. The IR spectrum of **1** showed the presence of a hydroxyl group (3425 cm^{-1}) and a trisubstituted double bond (1655 and 840 cm^{-1}). The ^{1}H NMR spectrum of **1** exhibited signals for six singlet methyl groups (δ 0.63, 0.74, 0.83, 0.95, 0.97, 1.02), a doublet methyl group (δ 1.02), an olefinic methyl group (δ 1.66), one carbinol methine proton (δ 3.19), an allylic carbinol methine proton (δ 3.32), and an olefinic proton (δ 5.59). All spectral data suggested that **1** was a pentacyclic triterpene with two hydroxyl groups and a trisubstituted double bond. Comparison of the ^{13}C NMR data (Table 1) of **1** with those of 20-taraxastene-3β,22β-diol[6] suggested they were epimeric at C-22. In compound **1**, H-22 was assigned as β-quasi-equatorial on the basis of the coupling constant (6.6 Hz) with the vicinal olefinic proton H-21 and the NOE with H_3-28. The α-quasi-axial hydroxyl at C-22 also shifted the H-16α signal downfield to δ 1.91. The ^{1}H and ^{13}C NMR assignments were confirmed by DEPT, HMBC, and HMQC experiments. Thus, compound **1** was deduced to be 20-taraxastene-3β,22α-diol.

Compound **2** had the molecular formula $C_{32}H_{52}O_3$ on the basis of HREIMS and ^{13}C NMR data. Its IR spectrum showed the presence of an ester group, a hydroxyl group, and a trisubstituted double bond. Its ^{1}H NMR data were similar to those of compound **1**, except for the presence of an acetoxyl group (δ 2.02) instead of a hydroxyl group in **1**. H-3 exhibited a downfield shift (δ 4.46) compared with the corresponding proton in **1**. Comparison of ^{1}H and ^{13}C NMR data with those of **1** indicated that **2** is 3β-acetoxy-20-taraxasten-22α-ol.

HREIMS and ^{13}C NMR data of **3** indicated the molecular formula $C_{33}H_{54}O_3$. The IR spectrum of **3** showed bands attributable to an acetoxyl group (1729, 1247 cm^{-1}). The ^{1}H NMR spectrum of **3** exhibited signals for six singlet methyl groups (δ 0.63, 0.82, 0.83, 0.85, 0.96, 1.01), a doublet methyl group (δ 0.99), an olefinic methyl group (δ 1.67), an allylic proton associated with a methoxyl group (δ 2.88 and 3.28), a methine proton associated with an acetoxyl group (δ 4.46 and 2.02), and an olefinic proton (δ 5.57). Comparison of ^{13}C NMR data of **3** with those of **2** suggested that **3** was a taraxastene triterpene with an acetoxyl group at C-3 and a methoxyl group at C-22. In compound **3**, H-22 showed almost the same coupling constant (6.0 Hz) as the corresponding proton in **2**. The configuration of H-22 was assigned as β-equatorial based on the coupling constant (6.0 Hz) and NOE correlation with H_3-28. HMBC correlation of H-22 with the methoxyl carbon also caused a shift of H-16α downfield to δ 1.98. Therefore, compound **3** was assigned as 3β-acetoxy-22α-methoxy-20-taraxastene.

Compound **4** showed a molecular ion at *m*/*z* 500, and HREIMS indicated a molecular formula of $C_{32}H_{52}O_4$. IR absorption bands at 3489, 1722, and 1248 cm^{-1} indicated hydroxyl and acetoxyl groups. ^{1}H NMR signals at δ 0.69, 0.81, 0.82, 0.85, 0.86, 1.00, 1.33, 2.02 (each 3H, s), and 1.07 (3H, d, J = 5.2 Hz) were attributed to nine methyl groups. Comparison of ^{1}H and ^{13}C NMR data of **4** with those of **2** suggested that **4** was a taraxastane derivative. The ^{13}C NMR signal at δ 80.9 and corresponding proton signal at δ 4.45 were assigned as C-3 and H-3α, respectively. No olefinic signals were observed. Allowing for one acetoxyl

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10.1021/np990630i CCC: $19.00
Published on Web 06/27/2000

Table 1. ^{13}C NMR Data (δ) for **1**−**7** (100 MHz in $CDCl_3$)

position	1	2	3	4	5	6	7
1	38.7 t	38.4 t	38.4 t	38.4 t	38.4 t	38.4 t	38.2 t
2	27.3 t	23.7 t	23.7 t	23.6 t	23.7 t	23.7 t	23.5 t
3	79.0 d	80.9 d	81.0 d	80.9 d	81.0 d	81.0 d	80.7 d
4	38.8 s	37.8 s	37.8 s	37.8 s	37.8 s	37.8 s	37.6 s
5	55.2 d	55.3 d	55.4 d	55.3 d	55.5 d	55.4 d	55.2 d
6	18.3 t	18.1 t	18.2 t	18.1 t	18.2 t	18.2 t	18.0 t
7	34.2 t	34.1 t	34.2 t	34.2 t	33.9 t	33.9 t	34.0 t
8	41.0 s	41.0 s	41.0 s	41.0 s	41.2 s	41.2 s	40.8 s
9	50.4 d	50.3 d	50.3 d	49.9 d	50.7 d	50.5 d	49.8 d
10	37.1 s	37.0 s	37.0 s	37.0 s	37.0 s	37.0 s	36.8 s
11	21.6 t	21.6 t	21.6 t	21.5 t	21.2 t	21.1 t	21.4 t
12	27.6 t	27.5 t	27.4 t	27.8 t	25.5 t	26.4 t	27.8 t
13	38.6 d	38.6 d	38.7 d	39.0 d	35.4 d	35.2 d	39.3 d
14	42.2 s	42.2 s	42.2 s	42.3 s	42.8 s	42.7 s	42.3 s
15	26.7 t	26.7 t	26.9 t	25.9 t	26.8 t	26.7 t	26.3 t
16	29.8 t	29.8 t	30.0 t	29.8 t	39.1 t	38.8 t	36.2 t
17	38.2 s	38.2 s	38.3 s	38.8 s	34.6 s	34.7 s	33.8 s
18	40.9 d	40.9 d	41.5 d	37.7 d	40.9 d	41.6 d	45.6 d
19	36.4 d	36.4 d	36.7 d	34.0 d	80.3 s	87.5 s	34.0 d
20	145.7 s	145.7 s	145.7 s	64.8 s	136.3 s	135.6 s	61.0 s
21	121.7 d	121.7 d	119.6 d	62.5 d	125.3 d	125.8 d	60.3 d
22	74.0 d	74.0 d	82.7 d	71.1 d	42.7 t	42.5 t	42.4 t
23	28.0 q	27.9 q	27.9 q	27.9 q	27.9 q	27.9 q	27.6 q
24	15.4 q	16.5 q	16.5 q	16.5 q	16.5 q	16.5 q	16.4 q
25	16.3 q	16.4 q	16.3 q	16.3 q	16.4 q	16.4 q	16.2 q
26	16.0 q	16.0 q	16.0 q	16.0 q	15.8 q	15.8 q	15.9 q
27	14.7 q	14.6 q	14.8 q	14.3 q	15.8 q	15.7 q	14.3 q
28	18.1 q	18.1 q	18.5 q	18.9 q	20.6 q	20.8 q	18.2 q
29	22.9 q	22.9 q	22.4 q	16.2 q	20.8 q	17.6 q	18.9 q
30	21.8 q	21.8 q	22.0 q	22.9 q	17.5 q	17.4 q	23.0 q
CH_3CO		171.0 s	171.0 s	171.0 s	171.0 s	171.0 s	170.7 s
CH_3CO		21.3 q	21.3 q	21.3 q	21.3 q	21.3 q	21.2 q
OCH_3			56.6 q		48.9 q		

group (δ 171.0), the calculated number of rings for **4** was six, including a pentacyclic skeleton. However, the remaining three oxygenated carbons at δ 71.1 (corresponding ^1H signal at δ 3.37), 64.8, and 62.5 (corresponding ^1H signal at δ 3.30) were predicted to involve epoxide and hydroxyl functionalities (C-22, C-20, and C-21, respectively). An ABX system, with signals at δ 3.37 (1H, dd, J = 8.0, 6.4 Hz, H-22), 3.30 (1H, d, J = 6.4 Hz, H-21), and 2.24 (1H, d, J = 8.0 Hz, OH, exchangeable with D_2O) coincided with the assigned partial structure. NOE correlation of H_3-28 with H-21 and H-22 indicated that H-21 and H-22 all were β oriented. HMBC supported the assigned structure. Thus, **4** was deduced to be 3β-acetoxy-20α,21α-epoxytaraxastan-22α-ol.

Compound **5** was an isomer of **3** ($C_{33}H_{54}O_3$) based on HREIMS and ^{13}C NMR (Table 1) data. IR indicated the presence of an acetoxyl group. The ^1H NMR spectrum of **5** exhibited signals for seven singlet methyl groups, an olefinic methyl group, an acetoxyl group, a methoxyl group, a methine proton associated with an acetoxyl group, and an olefinic proton. The olefinic proton (br, d) was typical of a taraxastene-type triterpene.[6] Comparison of the ^{13}C NMR data with those of 3β-acetoxy-20-taraxastene[7] suggested that **5** had the same ring system with an additional methoxyl group attached to C-19, which had long-range correlations (HMBC) with H-18, H-21, H_3-29, H_3-30, and OCH_3. The methoxyl group caused shifting of H_3-29 downfield to δ 1.22. NOE correlation between H_3-29 and H_3-28 indicated that C-29 was β oriented. The α-quasi-equatorial-oriented methoxy group at C-29 caused a downfield shift of H-12β from δ 1.62 (pseudo-taraxasterol[8]) to δ 2.25 (br d, J = 14.8 Hz). HMQC, HMBC, and NOESY methods confirmed the assigned structure. Thus, compound **5** was elucidated as 3β-acetoxy-19α-methoxy-20-taraxastene.

The molecular formula of **6**, $C_{32}H_{52}O_4$, was established from HREIMS and ^{13}C NMR data. Its IR spectrum exhibited absorption bands, suggesting the presence of hydroxyl (or hydroperoxyl) and acetoxyl moieties. ^1H NMR data showed seven singlet methyl groups, an olefinic methyl group, an acetoxyl group, a methine proton, a methine proton associated with an acetoxyl group (δ 4.46), and an olefinic proton (δ 5.55). Only two oxygenated carbons (δ_C 81.0 and 87.5) were observed in **6**, one of these bearing the acetoxy group. The other, at δ_c 87.5 (C-19), was considered to bear a hydroperoxide group. This was supported by the presence of a lower field signal at δ 6.79 (s) exchangeable with D_2O.[9] The ^1H NMR data for **6** were similar to those of **5**, the only difference being a hydroperoxyl group in **6** instead of the methoxyl group in **5**. ^{13}C NMR and DEPT spectra of **6** indicated nine CH_3, nine CH_2, six CH, and eight C, including one olefinic carbon (C-20, C-21), two oxygen-bearing carbons (C-3, C-19), and one carbonyl carbon. Comparison of ^{13}C NMR data with those of **5** showed that the only difference was C-19 (δ_C 87.5 in **6**) shifted downfield from the corresponding carbon (δ 80.3) in **5**. The hydroperoxyl group was assigned the α orientation on the basis of the NOE correlation between H_3-29 and H_3-28, as well as the downfield shift of H-12β to δ 2.08. Thus, **6** was established as 3β-acetoxy-19α-hydroperoxy-20-taraxastene.

Compound **7** had the molecular formula $C_{32}H_{52}O_3$ on the basis of HREIMS and ^{13}C NMR data. Its IR spectrum indicated the presence of an acetoxyl group (1734, 1247 cm^{-1}). ^1H NMR data of **7** were similar to those of 3β-hydroxy-21α,22α-epoxytaraxastane (isolated from same source),[6] except for the presence of an acetoxyl group (δ 2.02) instead of a hydroxyl group. H-3 exhibited a downfield shift (δ 4.45) from the corresponding proton in 3β-hydroxy-21α,22α-epoxytaraxastane. ^1H and ^{13}C NMR data suggested that **7** was 3β-acetoxy-21α,22α-epoxytaraxastane, not previously isolated from natural sources, though it had

been prepared from 3β-acetoxy-20-taraxastene by epoxidation.[10]

Chemical correlations of compounds **1**−**4** were as follows: hydrolysis of **2** gave compound **1**, methylation of **2** by sodium hydride and methyl iodide gave compound **3**, and oxidation of **2** by *m*-chloroperbenzoic acid (*m*-CPBA) provided **4** in good yield. Epoxidation from the α face was attributed to the inductive effect of the α-allylic axial hydroxyl group (C-22, OH).

Experimental Section

General Experimental Procedures. Melting points were determined with a Yanagimoto micromelting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 983G spectrophotometer. ^{1}H and ^{13}C spectra were run on a Varian Unity Plus 400 spectrometer and a Bruker AM-300 spectrometer. EIMS and specific rotations were taken on a JEOL JMS−HX 300 mass spectrometer and a JASCO DIP-1000 digital polarimeter, respectively. Extracts were chromatographed on Si gel (Merck 70−230 mesh, 230−400 mesh, ASTM).

Plant Material. The aerial roots of *F. microcarpa* were collected on the campus of National Taiwan University, Taiwan, in 1996. The plant was identified by Mr. Muh-Tsuen Gun, formerly a technician of the Department of Botany, National Taiwan University. A voucher specimen (no. 038671) has been deposited at the Herbarium of the Department of Botany, National Taiwan University, Taipei, Taiwan.

Extraction and Isolation. The dried, aerial roots of *F. microcarpa* were crushed to give 18 kg of raw material, which was extracted with MeOH (150 L) at room temperature (7 days × 2). The extract was evaporated in vacuo to yield a residue that was suspended in H_2O (1 L), and this was partitioned with ethyl acetate (1 L × 3). The combined ethyl acetate layer afforded a black syrup (250 g) that was subsequently chromatographed over Si gel with a hexane−EtOAc gradient solvent system. Crude compounds **3**, **5**, **7**, **2**, **6**, **4**, and **1** were all eluted with 20% EtOAc in hexane. Further purification by HPLC [Merck LichroCART 250−10 Cat. 1.50179 Lichrosorb Si 60 (7μm)] gave **3** (13 mg), **5** (6 mg), **7** (62 mg), **2** (115 mg), **6** (10 mg), **4** (8 mg), **1** (4 mg) using 5% EtOAc−hexane, 10% EtOAc−hexane, 10% EtOAc−hexane, 20% EtOAc−hexane, 20% EtOAc−hexane, 25% EtOAc−hexane, 30% EtOAc−hexane, respectively.

20-Taraxastene-3β,22α-diol (1): colorless needles (CH_2Cl_2); mp 255−257 °C; $[\alpha]^{25}_D$ +180.7° (*c* 0.2, $CHCl_3$); IR (KBr) ν_{max} 3425, 2938, 1655, 1381, 1028, 840, 739 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.63, 0.74, 0.83, 0.95, 0.97, 1.02 (each 3H, s), 1.02 (3H, d, J = 6.4 Hz, H-29), 1.66 (3H, br s, H-30), 1.91 (1H, td, J = 13.6, 4.4 Hz, H-16α), 3.19 (1H, dd, J = 10.4, 5.1 Hz, H-3), 3.32 (1H, d, J = 6.6 Hz, H-22), 5.59 (1H, d, J = 6.6 Hz, H-21); ^{13}C NMR data, see Table 1; EIMS *m*/*z* 442 [M]$^+$ (5), 424 (5), 406 (22), 187 (40), 133 (44), 84 (100); HREIMS *m*/*z* 442.3823 (calcd for $C_{30}H_{50}O_2$, 442.3813).

3β-Acetoxy-20-taraxasten-22α-ol (2): colorless needles (CH_2Cl_2); mp 236−238 °C; $[\alpha]^{25}_D$ +98.3° (*c* 0.7, $CHCl_3$); IR (KBr) ν_{max} 3504, 2932, 1732, 1680, 1378, 1245, 1030, 890, 820 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.63, 0.82, 0.83, 0.86, 0.96, 1.02, 1.66, 2.02 (each 3H, s), 1.02 (3H, d, J = 6.4 Hz), 1.91 (1H, td, J = 13.2, 4.4 Hz, H-16α), 3.32 (1H, d, J = 6.6 Hz, H-22), 4.46 (1H, dd, J = 11.2, 5.6 Hz, H-3), 5.59 (1H, d, J = 6.6 Hz, H-21); ^{13}C NMR data, see Table 1; EIMS *m*/*z* 484 [M]$^+$ (8), 466 (23), 406 (56), 363 (28), 189 (98), 133 (100); HREIMS *m*/*z* 484.3907 (calcd for $C_{32}H_{52}O_3$, 484.3919).

3β-Acetoxy-22α-methoxy-20-taraxastene (3): colorless needles (CH_2Cl_2); mp 255−257 °C; $[\alpha]^{26}_D$ +82.0° (*c* 1.2, $CHCl_3$); IR (KBr) ν_{max} 2937, 1729, 1383, 1247, 1094, 980 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.63, 0.82, 0.83, 0.85, 0.96, 1.01, 1.67 (3H, br s), 2.02, 3.28 (each 3H, s), 0.99 (3H, d, J = 6.4 Hz, H-29), 1.98 (1H, td, J = 13.2, 4.4 Hz, H-16α), 2.88 (1H, d, J = 6.0 Hz, H-22), 4.46 (1H, dd, J = 10.7, 5.6 Hz, H-3), 5.57 (1H, d, J = 6.0 Hz, H-21); ^{13}C NMR data, see Table 1; EIMS *m*/*z* 498 [M]$^+$ (3), 466 (18), 406 (38), 189 (30), 129 (100); HREIMS *m*/*z* 498.4073 (calcd for $C_{33}H_{54}O_3$, 498.4075).

3β-Acetoxy-20α,21α-epoxytaraxastan-22α-ol (4): colorless needles (CH_2Cl_2); mp 259−263 °C; $[\alpha]^{25}_D$ +29.1° (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 3489, 2942, 1722, 1450, 1382, 1248, 1035, 981, 741 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.69, 0.81, 0.82, 0.85, 0.86, 1.00, 1.33, 2.02 (each 3H, s), 1.07 (3H, d, J = 5.2 Hz, H-29), 1.89 (1H, td, J = 13.2, 4.0 Hz, H-16α), 2.24 (1H, d, J = 8.0 Hz, OH, D_2O exchangeable), 3.30 (1H, d, J = 6.4 Hz, H-21), 3.37 (1H, dd, J = 8.0, 6.4 Hz, H-22), 4.45 (1H, dd, J = 10.8, 5.6 Hz, H-3); ^{13}C NMR data, see Table 1; EIMS *m*/*z* 500 [M]$^+$ (8), 482 (8), 466 (12), 451 (11), 440 (10), 422 (15), 407 (17), 391 (20), 379 (17), 297 (15), 189 (100), 121 (68); HREIMS *m*/*z* 500.3868 (calcd for $C_{32}H_{52}O_4$, 500.3868).

3β-Acetoxy-19α-methoxy-20-taraxastene (5): colorless plates (MeOH); mp 216−218 °C; $[\alpha]^{26}_D$ +29.7° (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 2941, 1732, 1380, 1245, 1075, 980 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.82, 0.83, 0.86, 0.86, 0.98, 1.03, 1.22, 1.55 (3H, br s), 2.02, 2.95 (each 3H, s), 2.25 (1H, br d, J = 14.8 Hz, H-12β), 4.47 (1H, dd, J = 10.4, 6.0 Hz, H-3), 5.52 (1H, br d, J = 6.0 Hz, H-21); ^{13}C NMR data, see Table 1; EIMS *m*/*z* 498 [M]$^+$ (4), 466 (100), 406 (44), 391 (24), 363 (14), 255 (15), 189 (60); HREIMS *m*/*z* 498.4073 (calcd for $C_{33}H_{54}O_3$, 498.4075).

3β-Acetoxy-19α-hydroperoxy-20-taraxastene (6): colorless gum; $[\alpha]^{27}_D$ +22.1° (*c* 0.3, $CHCl_3$); IR (KBr) ν_{max} 3397, 2942, 1731, 1453, 1381, 1245, 1028, 980 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.82, 0.83, 0.86, 0.88, 1.01, 1.04, 1.15, 1.68 (3H, br s), 2.02 (each 3H, s), 2.08 (1H, m, H-12β, obscured by acetyl group), 2.16 (1H, d, J = 11.2 Hz, H-18), 4.46 (1H, dd, J = 10.8, 6.0 Hz, H-3), 5.55 (1H, d, J = 5.6 Hz, H-21), 6.79 (1H, s, −OOH, exchangeable with D_2O); ^{13}C NMR data, see Table 1; EIMS *m*/*z* 500 [M]$^+$ (1), 482 [M − H_2O]$^+$ (12), 466 (32), 217 (25), 203 (38), 189 (100), 135 (51), 119 (60), 105 (70); HREIMS *m*/*z* 500.3882 (calcd for $C_{32}H_{52}O_4$, 500.3868).

3β-Acetoxy-21α,22α-epoxytaraxastane (7): colorless needles (CH_2Cl_2); mp 258−262 °C; $[\alpha]^{29}_D$ +16.2° (*c* 5.1, $CHCl_3$); IR (KBr) ν_{max} 2946, 1734, 1456, 1384, 1247, 1030, 981, 738 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.77, 0.81, 0.82, 0.84, 0.84, 0.99, 1.29, 2.02 (each 3H, s), 1.09 (3H, d, J = 6.4 Hz) 3.02 (1H, br d, J = 6.8 Hz, H-21), 4.45 (1H, dd, J = 10.8, 6.0 Hz, H-3); ^{13}C NMR data, see Table 1; EIMS *m*/*z* 484 [M]$^+$ (24), 464 (48), 424 (22), 253 (33), 189 (100), 135 (48). HREIMS *m*/*z* 484.3910 (calcd for $C_{32}H_{52}O_3$, 484.3919).

Saponification of 2 in Methanolic NaOH. Compound **2** (8 mg) was dissolved in 1 N NaOH methanolic solution (2 mL) for 5 h under stirring, and the solution was then quenched with 15 mL of H_2O. After removal of MeOH by evaporating in vacuo, the product was extracted with CH_2Cl_2, and dried ($MgSO_4$) to afford **1** (4 mg).

Methylation of 2 with Sodium Hydride and Methyl Iodide. Sodium hydride (250 mg, 80% dispersion in mineral oil) was placed in a 25-mL flask (magnetic stir bar, injection port, condenser with nitrogen inlet). The oil was removed with successive washes of dry hexane (2 × 3 mL). Dry tetrahydrofuran (THF, 2 mL) was added, and the suspension was heated in an oil bath at 45−50 °C. With stirring, methyl iodide (0.1 mL) was added. A solution of compound **2** (30 mg) in dry THF (5 mL) was added dropwise over 30 min, followed by further heating for 2 h. With cooling, the reaction mixture was carefully hydrolyzed by dropwise addition of wet THF (5 mL). After removal of THF, the mixture was extracted with ether (5 mL), and then the ether layer was washed with saturated brine water and dried ($MgSO_4$). The usual purification gave **3** (22 mg).

Oxidation of 2 with *m*-CPBA. Compound **2** (27 mg) and *m*-CPBA (30 mg) were dissolved in CH_2Cl_2 (2 mL), and the mixture was stirred at room temperature for 4 h. The mixture was diluted with CH_2Cl_2 (5 mL) and washed with 1 N NaOH (3 mL) and H_2O (3 mL) and dried ($MgSO_4$). The usual purification gave **4** (19 mg).

Acknowledgment. This research was supported by the National Science Council of the Republic of China.

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NP990630I