Two Novel 14-Nor-13,14-secopodocarpanes from the Bark of *Taiwania cryptomeriodes*

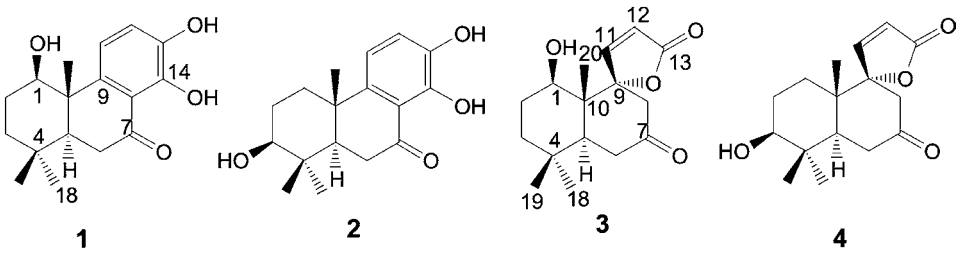
by **Shih-Chang Chien** and **Yueh-Hsiung Kuo***

Department of Chemistry, National Taiwan University, Taipei, Taiwan, ROC

The two novel compounds cryptomelactones A (**3**) and B (**4**) were isolated from the bark of *Taiwania cryptomeriodes*, besides the two known podocarpane derivatives 1β,13,14-trihydroxypodocarpa-8,11,13-trien-7-one (**1**) and 3β,13,14-trihydroxypodocarpa-8,11,13-trien-7-one (**2**), and were characterized by spectroscopic means including 2D-NMR techniques. Compounds **3** and **4** are novel-14-nor-13,14-seco-podocarpanes. The absolute configurations of **3** and **4** were determined by the modified *Mosher* method. The biotransformation mechanism of **3** and **4** is proposed.

1. Introduction. – The plant of *Taiwania cryptomeriodes* HAYATA (Taxodiaceae) is an endemic plant in Taiwan with one genus and one species. It is a decay-resistant and economical building material. In earlier days, we have investigated the phytochemical principles of its heartwood [1–3] and barks [4–5], and found various sesquiterpenes, lignans, and abietane-type diterpenes. *Kamil et al.* [6] have described the bis-flavones found in its leaves. Recently, many other compounds have been obtained from its leaves, including several novel structural skeletons as described by *Lin et al.* [7–10]. Podocarpane-diterpene derivatives are not very common. The genus *Azadirachta* [11–15], *Humirianther* [16], *Micrandropsis* [17], and *Podocarpus* [18] contain plenty of podocarpane derivatives. Podocarpane derivatives have not been discovered in *T. cryptomeriodes* previously. The 1β,13,14-trihydroxypodocarpa-8,11,13-trien-7-one (**1**) [10] was isolated for the first time from its leaves. Because the mother fraction of nimbionone and nimbionol (podocarpane diterpenes) showed significant antibacterial activity [13] and because of the many novel skeletons [7–10] isolated from the leaves of *T. cryptomeriodes*, we were encouraged to study the chemical constituents of its bark again, and we found twenty-three new podocarpane derivatives [19–23]. Among them, four components, including 3β,13,14-trihydroxypodocarpa-8,11,13-trien-7-one (**2**), exhibited significant antioxidative properties [23]. Further detailed reinvestigation of the same extract from the bark of this plant now yielded two novel compounds, namely cryptomelactone A (**3**) and B (**4**) besides the two known podocarpatrienones **1** and **2**. These two novel compounds have a 14-nor-13,14-secopodocarpane skeleton.

2. Results and Discussion. – Cryptomelactone A (**3**) was isolated as colorless crystals. Its molecular formula $C_{16}H_{22}O_4$ was established by ^{13}C-NMR and HR-EI-MS data and corresponded to six indices of hydrogen deficiency. Further spectral data (IR, UV, ^{1}H-NMR, COSY, HMQC, HMBC, and NOESY) established the structure of cryptomelactone A to be 1β-hydroxy-7-oxo-14-nor-13,14-secopodocarp-11-en-13,9α-olactone (**3**). The absolute configuration of **3** was determined by the modified *Mosher*



method [24]. Treatment of **3** with (αR)- and (αS)-α-methoxy-α-(trifluoromethyl)benzeneacetyl chloride (MTPACl) afforded the (αS)- and (αR)-MTPA esters of **3**. The $\Delta\delta$ values ($\delta(S)$-$\delta(R)$) of Me(18) (−4.2), Me(19) (−11.9), and Me(20) (−3.8) showed negative values, thus indicating (1*R*,5*S*)-configuration of **3** (see *Fig. 1*).

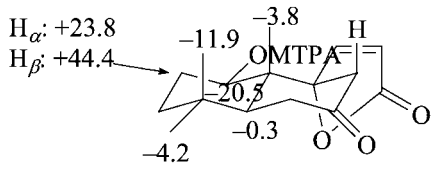


Fig. 1. $\Delta\delta$ *Values* ($\Delta\delta$ [Hz] = $\delta_S - \delta_R$) *obtained for the* (αS)*- and* (αR)*-MTPA esters of* **3**

The IR spectrum of compound **3** indicated the presence of a cyclohexanone (1715 cm^{-1}) and conjugated γ-lactone moiety (1749 cm^{-1}) as well as of an OH group (3330 cm^{-1}). The UV absorption band in MeCN at 217.5 nm confirmed the conjugated γ-lactone. The ^{1}H-NMR spectrum (*Table*) exhibited signals for three Me groups (*s* at δ 0.87 (Me(18)), 0.89 (Me(19)), and 1.26 (Me(20))), a CH proton (δ 3.50 (*t*, H−C(1))), two olefinic protons with mutual coupling (δ 5.93 and 7.67 (2*d*, each J = 5.6 Hz, H−C(12) and H−C(11))). Two geminal protons were assigned as neighboring a ketone group due to their chemical shifts and coupling constants (δ 2.86 (*d*, J = 16.2 Hz, H_β−C(8)) and 2.06 (*dd*, J = 16.2, 1.2 Hz, H_α−C(8))). Also, the signals at δ 2.51 (*ddd*, J = 15.0, 4.0, 1.2 Hz, H_α−C(6)) and 2.38 (*dd*, J = 15.0, 13.8 Hz, H_β−C(6)) arose from geminal protons vicinal to a ketone group. The signals at δ 2.51 and 2.06 exhibited a W-form coupling (J = 1.2 Hz) suggesting that **3** contains a cyclohexanone moiety. The COSY data allowed to assign H−C(5) to a methine proton at δ 2.10 (*dd*, J = 13.8, 4.0 Hz). Two ^{13}C-NMR signals at δ 172.0 and 205.9 (*Table*) were attributed to the γ-lactone and cyclohexanone C=O group, respectively. Only two oxygenated C-atoms appeared at δ 70.1 (CH(1)) and 93.5 (C(9)). The quaternary C-atom at δ 93.5 as well as the *d* of H−C(11) (coupling only with H−C(12)) indicated that the γ-lactone is a spiro γ-lactone. The COSY experiment established the consecutive proton signals of H−C(1) and H−C(2) (δ 1.64, *m*, 2 H), and CH_2(3) (δ 1.32 and 1.43). By the aid of HMQC and DEPT techniques, the correlation of C- and H-atoms was recognized. Further analysis of the HMBC correlations (*Fig. 2*) confirmed the proposed structure of **3**. As to its relative configuration, the NOESY correlations H−C(5)/Me(18), H_α−C(3), and H_α−C(1) as well as Me(20)/Me(19) and H_β−C(8) (*Fig. 2*) confirmed the *trans*-fused *A*–*B* ring system. The NOESY correlations H−C(11)/Me(20) and H_β−C(8) established the β-equatorial orientation of the olefinic function.

Cryptomelactone B (**4**) was given the molecular formula $C_{16}H_{22}O_4$ as deduced from the HR-EI-MS and ^{13}C-NMR data (*Table*). Similarly to **3**, the structure of cryptomelactone B (**4**) was elucidated as 3β-hydroxy-7-oxo-14-nor-13,14-secopodocarp-11-en-13,9α-olactone and its absolute configuration (3*S*,5*S*) determined ($\Delta\delta$ positive for Me(18) (+24.8) and Me(19) (+3.5) and negative for Me(20) (−12.4); *Fig. 3*.

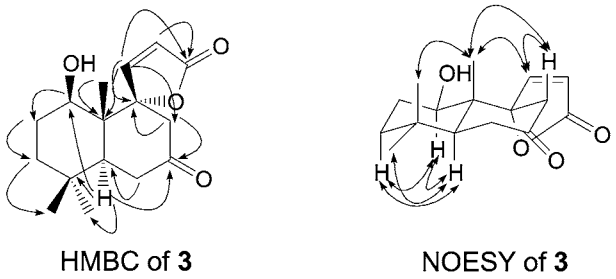


Fig. 2. *Key HMBC and NOESY correlations of* **3**

Table. *NMR Data of* **3** *and* **4**. $CDCl_3$ Solutions; at 500 (^{1}H) and 125 MHz (^{13}C); δ in ppm, J in Hz.

	3		**4**	
	δ(H)	δ(C)	δ(H)	δ(C)
H–C(1) or CH_2(1)	3.50 (t, J = 7.7)	70.1	1.17 (dt, J = 13.5, 3.2), 1.34 (td, J = 13.5, 4.3)	29.5
CH_2(2)	1.64 (m)	28.3	1.63 (m), 1.68 (m)	26.5
CH_2(3) or H–C(3)	1.32 (m), 1.43 (dt, J = 13.2, 3.1)	38.7	3.28 (dd, J = 11.4, 4.6)	77.2
C(4)	–	33.3	–	39.3
H–C(5)	2.10 (dd, J = 13.8, 4.0)	45.3	2.10 (dd, J = 14.0, 3.8)	45.1
CH_2(6)	2.38 (dd, J = 15.0, 13.8), 2.51 (ddd, J = 15.0, 4.0, 1.2)	37.9	2.39 (dd, J = 15.6, 14.0), 2.55 (ddd, J = 15.6, 3.8, 1.4)	38.2
C(7)	–	205.9	–	205.7
CH_2(8)	2.06 (dd, J = 16.2, 1.2), 2.86 (d, J = 16.2)	47.2	2.17 (dd, J = 16.1, 1.4), 2.90 (d, J = 16.1)	46.3
C(9)	–	93.5	–	94.4
C(10)	–	47.2	–	40.4
H–C(11)	7.67 (d, J = 5.6)	159.9	7.42 (d, J = 5.7)	155.5
H–C(12)	5.93 (d, J = 5.6)	118.1	6.13 (d, J = 5.7)	122.9
C(13)	–	172.0	–	171.1
Me(18)	0.87 (s)	31.8	1.00 (s)	27.3
Me(19)	0.89 (s)	20.9	0.88 (s)	15.0
Me(20)	1.26 (s)	12.2	1.29 (s)	17.5

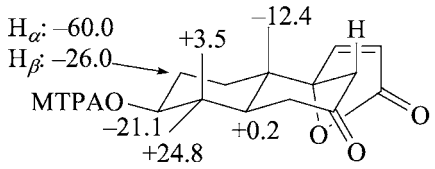


Fig. 3. $\Delta\delta$ *Values* ($\Delta\delta$ [Hz] = $\delta_S - \delta_R$) *obtained for the* (αS)- *and* (αR)-*MTPA esters of* **4**

In the IR spectrum of **4**, OH (3459 cm^{-1}), cyclohexanone (1714 cm^{-1}), and γ-lactone (1768 and 1748 cm^{-1}) absorption bands were present. The UV absorption band at 208.5 nm (MeCN) confirmed the presence of a γ-lactone. The ^{13}C-NMR signals (*Table*) at δ 171.1 and 205.7 arose from the above-mentioned two functionalities. Two mutually coupling olefinic proton signals at δ(H) 6.13 (d, J = 5.7 Hz, H–C(12)) and 7.42 (d, J = 5.7 Hz, H–C(11)) showed HMBC cross-peaks with δ(C) 94.4 (oxygenated quaternary C(9)) and 171.1 (C(13)), establishing the presence of a spiro γ-lactone. The ^{1}H-NMR spectrum (*Table*) showed signals for 3 Me groups (s at δ 1.00 (Me(18)), 0.88 (Me(19)), and 1.29 (Me(20))) and a CH proton (δ 3.28 (dd, J = 11.4, 4.6 Hz, H–C(3))).

Two geminal protons at δ 2.17 (*dd*, $J = 16.1$, 1.4 Hz, H_α–C(8)) and 2.90 (*d*, $J = 16.1$ Hz, H_β–C(8)) were assigned to those between a carbonyl and a quaternary C-atom due to their chemical shifts, coupling constants, and HMBC correlations to δ 94.4 and 205.7 (*Fig. 4*). A typical *ABX* pattern appeared at δ 2.10 (*dd*, $J = 14.0$, 3.8 Hz, H–C(5)), 2.55 (*ddd*, $J = 15.6$, 3.8, 1.4 Hz, H_α–C(6)), and 2.39 (*dd*, $J = 15.6$, 14.0 Hz, H_β–C(6)) and was assigned by the HMBC data. H_α–C(8) and H_α–C(6) exhibited the W-form coupling, suggesting the presence of a cyclohexanone moiety in **4**. The OH group was assigned to C(3) since C(4) of **4** appeared at lower field than C(4) of **3**, and H–C(3) of **4** exhibited NOESY interactions with Me(18) and H–C(5) (*Fig. 4*). The relative configuration of **4** was revealed by the NOESY correlations (*Fig. 4*).

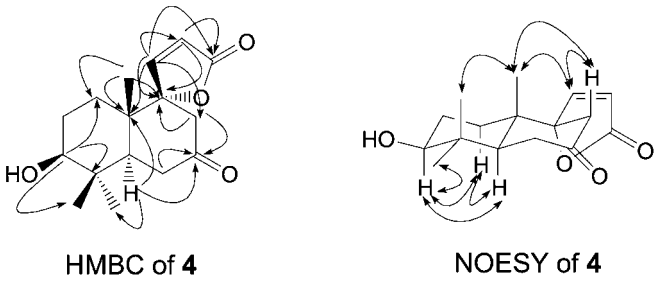
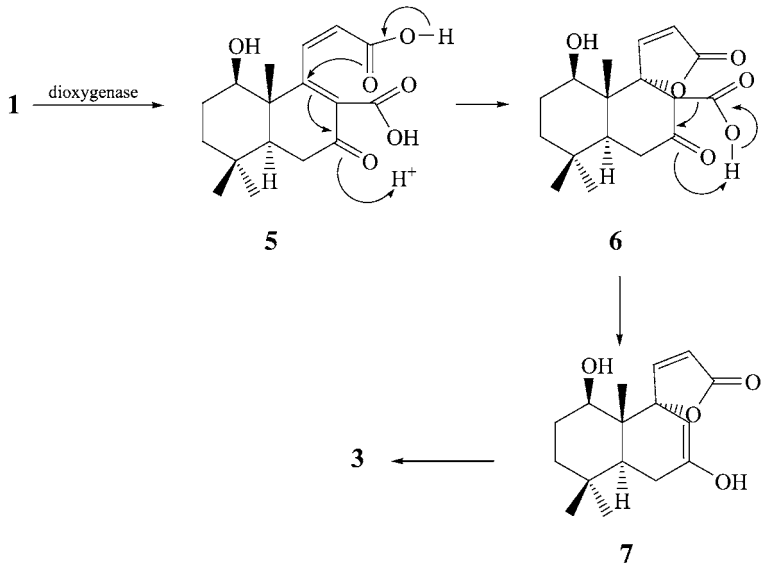


Fig. 4. *Key HMBC and NOESY correlations of* **4**

We propose that the biotransformation to **3** and **4** starts from **1** and **2**, respectively, as shown in the *Scheme*. Oxidation of **1** by dioxygenase would yield **5** which would be converted to spiro γ-lactone **6** under acidic conditions. Compound **6** contains a α-keto acid difunctionality, which can be decarboxylated [25] spontaneously to produce enol **7**. After tautomerization, **3** is formed. Compound **4** is supposed to be formed from **2** *via* the same pathway.

Scheme. *Proposed Biogenetic Pathway for the Formation of* **3**



The authors thank the *National Science Council of the Republic of China* for financial support, and thank Ms *Shou-Ling Huang* for NMR measurement.

Experimental Part

General. Column chromatography (CC): silica gel (*Merck* 70–230 mesh, 230–400 mesh, ASTM). Semi-prep. normal-phase HPLC: 250 × 10 mm column (5 µm, *LiChrosorb Si 60*); *LDC Analytical-III*. M.p.: *Yanagimoto* micro-melting-point apparatus; uncorrected. Optical rotations: *Jasco DIP-180* digital polarimeter. UV Spectra: *Hitachi S-3200* spectrometer; λ_{max} in nm ($\log \varepsilon$). ^{1}H- and ^{13}C-NMR Spectra: *Bruker DMX-500* spectrometer; $CDCl_3$ solns. at 25°; δ values with ref. to the signal of $CDCl_3$, with Me_4Si as internal standard; δ in ppm, *J* in Hz. EI-MS and HR-EI-MS: *Finnigan TSQ-46C* and *Jeol SX-102A* mass spectrometer, respectively; in *m*/*z* (rel. %).

Plant Material. The bark of *T. cryptomerioides* was collected in Tai-Chun, Taiwan, in 1996. The plant material was identified by Mr. *Muh-Tsuen Gun*, formerly a technician of the Department of Botany, National Taiwan University. A voucher specimen (No. 013542) has been deposited at the Herbarium of the Department of Botany of the National Taiwan University, Taipei, Taiwan.

Extraction and Isolation. Air-dried pieces of the bark of *T. cryptomerioides* (12 kg) were extracted with acetone (3 × 60 l) at r.t. (7 d for each batch). The acetone extract was evaporated to leave a black residue, which was suspended in H_2O (8 l) and then extracted 3 × with 1 l of AcOEt. The AcOEt extract (360 g) was submitted to CC (silica gel, hexane/AcOEt of increasing polarity) and further purified by HPLC (hexane/AcOEt 2:8): pure 1*β*,13,14-trihydroxypodocarpa-8,11,13-trien-7-one (**1**; 40 mg), 3*β*,13,14-trihydroxypodocarpa-8,11,13-trien-7-one (**2**; 12 mg), cryptomelactone A (**3**; 16 mg), and cryptomelactone B (**4**; 4 mg).

*(1*R*,5*S*,9*S*,10*R*)-1β-Hydroxy-7-oxo-14-nor-13,14-secopodocarp-11-en-13,9α-olactone* (= *Cryptomelactone A* = *(1′*S*,4′a*S*,8′*R*,8′a*R*)-4′a,5′,6′,7′,8′,8′a-Hexahydro-8′-hydroxy-5′,5′,8′a-trimethylspiro[furan-2(5*H*),1′(2′*H*)-naphthalene]-3′,5(4′*H*)-dione*; **3**): White powder. M.p. 189–191°. $[\alpha]_D^{23} = -20.3$ ($c = 0.91$, $CHCl_3$). UV (MeCN): 217.5 (3.76). IR (film): 3330, 1749, 1715, 1013, 825. ^{1}H- and ^{13}C-NMR: *Table*. EI-MS: 278 (60, M^+), 260 (46), 181 (67), 162 (78), 139 (60), 121 (79), 97 (88), 81 (100). HR-EI-MS: 278.1510 ($C_{16}H_{22}O_4^+$; calc. 278.1512).

Mosher *Esters of* **3**. To a CH_2Cl_2 soln. (100 µl) of **3** (1.2 mg) were added *N*,*N*-dimethylpyridin-4-amine (25 µg), Et_3N (10 µl), and (*αR*)-MTPACl (5 µl) at r.t., and stirring was continued for 3 h. After the addition of Et_3N (10 µl) and evaporation the residue was submitted to CC (silica gel, acetone/CH_2Cl_2 1:9): (*αS*)-MTPA ester of **3** (1.2 mg). Amorphous solid. ^{1}H-NMR: 0.87 (*s*, Me(18)); 0.90 (*s*, Me(19)); 1.26 (*s*, Me(20)); 1.30 (*m*, H_α–C(3)); 1.45 (*dt*, *J* = 13.2, 3.1, H_β–C(3)); 1.73 (*m*, H_α–C(2)); 1.93 (*m*, H_β–C(2)); 2.04 (*d*, *J* = 16.2, H_α–C(8)); 2.21 (*dd*, *J* = 13.8, 4.0, H–C(5)); 2.38 (*dd*, *J* = 15.0, 13.8, H_β–C(6)); 2.50 (*dd*, *J* = 15.0, 4.0, H_α–C(6)); 2.85 (*d*, *J* = 16.2, H_β–C(8)); 3.48 (*s*, MeO–C(α)); 4.88 (*t*, *J* = 7.7, H–C(1)); 5.92 (*d*, *J* = 5.6, H–C(12)); 7.40 (*m*, 3 H); 7.47 (*m*, 2 H); 7.67 (*d*, *J* = 5.6, H–C(11)). EI-MS: 494 (4, M^+), 261 (40), 189 (100), 137 (90).

Compound **3** (1.2 mg) was treated with (*αS*)-MTPACl (5 µl) as described above: (*αR*)-MTPA ester of **3** (1.2 mg). Amorphous solid. ^{1}H-NMR: 0.88 (*s*, Me(18)); 0.93 (*s*, Me(19)); 1.27 (*s*, Me(20)); 1.29 (*m*, H_α–C(3)); 1.43 (*dt*, *J* = 13.2, 3.1, H_β–C(3)); 1.62 (*m*, H_α–C(2)); 1.87 (*m*, H_β–C(2)); 2.03 (*d*, *J* = 16.2, H_α–C(8)); 2.21 (*dd*, *J* = 13.8, 4.0, H–C(5)); 2.39 (*dd*, *J* = 15.0, 13.8, H_β–C(6)); 2.50 (*dd*, *J* = 15.0, 4.0, H_α–C(6)); 2.89 (*d*, *J* = 16.2, H_β–C(8)); 3.52 (*s*, MeO–C(α)); 4.93 (*t*, *J* = 7.7, H–C(1)); 5.90 (*d*, *J* = 5.6, H–C(12)); 7.39 (*m*, 3 H); 7.49 (*m*, 2 H); 7.67 (*d*, *J* = 5.6, H–C(11)). EI-MS: 494 (2, M^+), 261 (32), 189 (100), 137 (78).

*(3*S*,5*S*,9*S*,10*S*)-3β-Hydroxy-7-oxo-14-nor-13,14-secopodocarp-11-en-13,9α-olactone* (= *Cryptomelactone B* = *(1′*S*,4′a*S*,6′*S*,8′a*S*)-4′a,5′,6′,7′,8′,8′a-Hexahydro-6′-hydroxy-5′,5′,8′a-trimethylspiro[furan-2(5*H*),1′(2′*H*)-naphthalene]-3′,5(4′*H*)-dione*; **4**). Amorphous solid. $[\alpha]_D^{23} = -3.7$ ($c = 0.22$, $CHCl_3$). UV (MeCN): 208.5 (3.87). IR (film): 3459, 1768, 1748, 1714. ^{1}H- and ^{13}C-NMR: *Table*. EI-MS: 278 (40, M^+), 260 (37), 140 (57), 121 (100). HR-EI-MS: 278.1519 ($C_{16}H_{22}O_4^+$; calc. 278.1512).

Mosher *Esters of* **4**. As described for the *Mosher* esters of **3**, with CH_2Cl_2 (100 µl) **4** (1.0 mg), *N*,*N*-dimethylpyridin-4-amine (25 µg), Et_3N (10 µl), (*αR*)-MTPACl (5 µl), and Et_3N (10 µl): (*αS*)-MTPA ester of **4** (1.2 mg). Amorphous solid. ^{1}H-NMR: 0.88 (*s*, Me(19)); 0.90 (*s*, Me(18)); 1.29 (*s*, Me(20)); 1.19 (*m*, H_β–C(1)); 1.49 (*m*, H_α–C(1)); 1.65 (*m*, H_α–C(2)); 1.86 (*m*, H_β–C(2)); 2.19 (*dd*, *J* = 16.2, 1.8, H_α–C(8)); 2.22 (*dd*, *J* = 13.6, 3.8, H–C(5)); 2.37 (*dd*, *J* = 15.7, 13.6, H_β–C(6)); 2.54 (*ddd*, *J* = 15.7, 3.8, 1.8, H_α–C(6)); 2.89 (*d*, *J* = 16.2, H_β–C(8)); 3.47 (*s*, MeO–C(α)); 4.67 (*dd*, *J* = 11.7, 4.3, H–C(3)); 6.16 (*d*, *J* = 5.7, H–C(12)); 7.40 (*m*, 3 H); 7.42 (*d*, *J* = 5.7, H–C(11)); 7.48 (*m*, 2 H). EI-MS: 494 (3, M^+), 261 (36), 189 (100), 137 (87).

Compound **4** (1.0 mg) was treated with (αS)-MTPACl (5 µl) as described above: (αR)-MTPA ester of **4** (1.2 mg). Amorphous solid. ^{1}H-NMR: 0.83 (*s*, Me(19)); 0.89 (*s*, Me(18)); 1.32 (*s*, Me(20)); 1.20 (*m*, H_β–C(1)); 1.50 (*m*, H_α–C(1)); 1.76 (*m*, H_α–C(2)); 1.92 (*m*, H_β–C(2)); 2.19 (*dd*, $J = 16.2, 1.7$, H_α–C(8)); 2.22 (*dd*, $J = 13.8, 3.8$, H–C(5)); 2.37 (*dd*, $J = 15.7, 13.8$, H_β–C(6)); 2.54 (*ddd*, $J = 15.7, 3.8, 1.7$, H_α–C(6)); 2.89 (*d*, $J = 16.2$, H_β–C(8)); 3.53 (*s*, MeO–C(α)); 4.71 (*dd*, $J = 11.9, 4.3$, H–C(3)); 6.16 (*d*, $J = 5.7$, H–C(12)); 7.38 (*m*, 3 H); 7.41 (*d*, $J = 5.7$, H–C(11)); 7.50 (*m*, 2 H). EI-MS: 494 (2, M^+), 261 (30), 189 (100), 137 (90).

REFERENCES

[1] Y. S. Cheng, Y. H. Kuo, Y. T. Lin, *J. Chem. Soc., Chem. Commun*. **1967**, 565.
[2] Y. T. Lin, Y. S. Cheng, Y. H. Kuo, *Tetrahedron Lett*. **1968**, 3881.
[3] Y. H. Kuo, Y. S. Cheng, Y. T. Lin, *Tetrahedron Lett*. **1969**, 2375.
[4] Y. H. Kuo, J. S. Shih, Y. T. Lin, Y. T. Lin, *J. Chin. Chem. Soc*. **1979**, *26*, 71.
[5] Y. H. Kuo, Y. T. Lin, Y. T. Lin, *J. Chin. Chem. Soc*. **1985**, *32*, 381.
[6] M. Kamil, M. Ilyas, W. Rahman, N. Hasaka, M. Okigawa, N. Kawano, *J. Chem. Soc., Perkin Trans. 1* **1981**, 553.
[7] W. H. Lin, J. M. Fang, Y. S. Cheng, *Phytochemistry* **1995**, *40*, 871.
[8] W. H. Lin, J. M. Fang, Y. S. Cheng, *Phytochemistry* **1996**, *42*, 1657.
[9] W. H. Lin, J. M. Fang, Y. S. Cheng, *Phytochemistry* **1997**, *46*, 169.
[10] W. H. Lin, J. M. Fang, Y. S. Cheng, *Phytochemistry* **1998**, *48*, 1391.
[11] P. L. Majumder, D. C. Maiti, W. Kraus, M. Bokel, *Phytochemistry* **1987**, *26*, 3021.
[12] I. Ara, B. S. Siddiqui, S. Faigi, S. Siddiqui, *Phytochemistry* **1988**, *27*, 1801.
[13] S. Siddiqui, I. Ara, S. Faigi, T. Mahmood, B. S. Siddiqui, *Phytochemistry* **1988**, *27*, 3903.
[14] I. Ara, B. S. Siddiqui, S. Faigi, S. Siddiqui, *J. Nat. Prod*. **1988**, *51*, 1054.
[15] I. Ara, B. S. Siddiqui, S. Faigi, S. Siddiqui, *J. Nat. Prod*. **1990**, *53*, 816.
[16] M. D. G. B. Zoghbl, N. F. Roque, H. F. Gottlieb, *Phytochemistry* **1981**, *20*, 1669.
[17] M. A. D. Alvarenga, J. D. Silva, H. E. Gottlieb, O. R. Gottlieb, *Phytochemistry* **1981**, *20*, 1159.
[18] R. C. Cambie, L. M. Mander, *Tetrahedron* **1962**, *18*, 465.
[19] Y. H. Kuo, C. I. Chang, C. K. Lee, *Chem. Pharm. Bull*. **2000**, *48*, 597.
[20] Y. H. Kuo, C. I. Chang, *J. Nat. Prod*. **2000**, *63*, 650.
[21] Y. H. Kuo, S. C. Chien, *Chem. Pharm. Bull*. **2001**, *49*, 1033.
[22] Y. H. Kuo, S. C. Chien, S. L. Huang, *Chem. Pharm. Bull*. **2002**, *50*, 544.
[23] Y. H. Kuo, S. C. Chien, C. C. Kuo, *Planta Med*. **2002**, *68*, 1020.
[24] I. Ohtani, T. Kusumi, Y. Kashman, H. Kakisawa, *J. Am. Chem. Soc*. **1991**, *113*, 4092.
[25] P. M. Dewick, 'Medicinal Natural Product; A Biosynthetic Approach', John Wiley & Sons, Chichester, New York, 1997, p. 20.

Received August 11, 2003