Triterpenoids from the Leaves of *Eucalyptus camaldulensis* var. *obtusa*

Sabira Begum,* Farhat, and Bina S. Siddiqui

H.E.J. Research Institute of Chemistry, University of Karachi, Karachi-75270, Pakistan

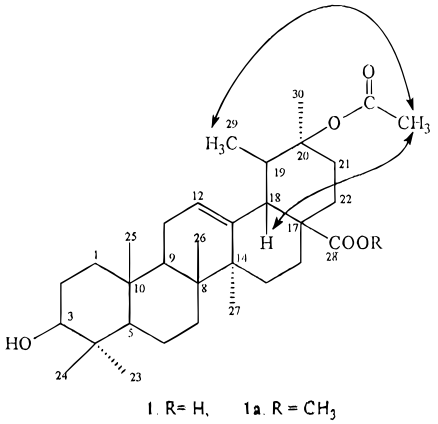
Received October 25, 1995[⊗]

An investigation on the constituents of the fresh, uncrushed leaves of *Eucalyptus camaldulensis* var. *obtusa* has led to the isolation of three new and one known triterpenoids. The new products were characterized by chemical and spectroscopic studies as camaldulic acid (20β-acetoxy-3β-hydroxyurs-12-en-28-oic acid) (**1**), camaldulensic acid (3β,30-dihydroxy-11α-methoxyurs-12-en-28-oic acid) (**2**) and camaldulenic acid (2α,3β-dihydroxyolean-11,13(18)-dien-28-oic acid) (**3**), whereas the known compound was identified as ursolic acid lactone (3β-hydroxyurs-11-en-13β(28)-olide).

Eucalyptus belonging to the family Myrtaceae is a large genus of aromatic trees comprising more than 500 species indigenous to Australia, Tasmania, and the neighboring islands. Various species of *Eucalyptus* are famous for their medicinal values. Different parts of the plant *Eucalyptus camaldulensis* Dehnk. var *obtusa* are used in the indigenous system of medicine to cure various human ailments such as diarrhea, chronic dysentery, malaria, infection of the upper respiratory tract, and certain skin diseases.[1] Oil and some flavonoids of the plant are found to possess antifungal and antibacterial activity.[2,3] Phytochemical investigations by different groups of workers on different parts of the plant have led to the isolation and identification of various known terpenoids and flavonoids.[2−7] In the literature only two known triterpenoids, oleanolic and maslinic acids, are reported from this source.[5] The present chemical investigation on the fresh and uncrushed leaves of the plant led to the isolation and structure elucidation of three new pentacyclic triterpenoids, namely, camaldulic acid (**1**), camaldulensic acid (**2**), and camaldulenic acid (**3**), and the known triterpenoid ursolic acid lactone.[8] This is the first report of the isolation of the latter compound from this plant.

The ethanolic extract of the leaves of *Eucalyptus camaldulensis* var. *obtusa* on careful separation afforded **1**−**3** and ursolic acid lactone.

The molecular formula of compund **1** was established as $C_{32}H_{50}O_5$ by CIMS measurement. It formed methyl derivative **1a** on reaction with diazomethane. The ^{1}H- and ^{13}C-NMR data (Tables 1 and 2) are comparable with the reported data of ursolic acid[9,10] with an additional acetoxy group [δ_H 1.90 (3H, s); δ C 22.9 (CH_3, DEPT and HETCOR), 170.9 broad band spectrum] that could be placed at C-20 in view of the fact that its ^{1}H-NMR spectrum showed only one methyl doublet instead of two doublets in ursolic acid and a one-proton doublet due to H-18[11] at δ 2.21. The ^{13}C-NMR data of ring E confirmed this assignment. The β orientation of the acetoxy group was confirmed by NOESY interaction of OAc with H-18 and Me-29 (Figure 1). In light of these observations, the structure of camaldulic acid (**1**) was elucidated as 20β-acetoxy-3β-hydroxyurs-12-en-28-oic acid. This is the first report of an ursane derivative having an acetoxy function at C-20 from natural sources.



1, R= H, 1a, R = CH_3

Figure 1. Significant NOESY interactions of **1**.

Compound **2** had the molecular formula $C_{31}H_{50}O_5$ as evidenced by the CIMS and DEPT data. Its IR spectrum displayed hydroxyl (3460 cm^{-1}), carboxyl (3420−2650, 1710 cm^{-1}), olefinic (1630 cm^{-1}), and CO (1150 cm^{-1}) absorption bands, while the UV spectrum showed only a terminal absorption (207 nm). The ^{1}H- and ^{13}C-NMR spectra showed signals for five tertiary methyls (sp^3), one secondary methyl, one methine doublet (δ_H 2.24, J = 11.4 Hz, H-18),[11] and a trisubstituted double bond (δ_H 5.43, d, J = 3.5 Hz, H-12; δ_C 126.3 (C-12), 140.2 (C-13), HETCOR). These data and the molecular formula suggested that **2** belongs to an ursane type of triterpene. A hydroxyl group indicated by its geminal proton in the ^{1}H- and ^{13}C-NMR spectra [δ_H 3.14, dd, J = 11.8, 4.5 Hz, H-3α; δ_C 79.5 (CH, DEPT)] was placed at C-3 considering the biogenesis. Its β-disposition was demonstrated by the δ value and coupling constants of its geminal proton.[12] The peaks observed at m/z 207.1775 and 189.1585 in the HREIMS spectrum (Figure 2) confirmed this assignment.[13] Another oxygenated methine proton (δ_H 3.87, dd, J = 8.6, 3.5 Hz; δ_C 76.6, HETCOR) showing connectivities with H-12 and H-9 in the ^{1}H−^{1}H COSY spectrum was assigned the 11β position having geminal 11α methoxy group, which was confirmed by the ^{13}C-NMR data of ring C (Table 2).[14] The ^{1}H- and ^{13}C-NMR spectra also showed the presence of a hydroxymethylene group (δ_H 3.65 and 3.38, 1H each, dd, J = 8.9, 7.0 Hz; δ_C 63.8, HETCOR) attached to a methine carbon of either C-19 or C-20. Its position at C-20 with α orientation was established by NOESY experiments in which **2** showed a weak interaction between α OMe and H-30b along with a clear interaction

[⊗] Abstract published in *Advance ACS Abstracts,* November 15, 1996.

S0163-3864(96)00535-6 CCC: $14.00

Table 1. ^{1}H-NMR Spectral Data[a] for Compounds **1**−**3a** (CD_3OD)

	compd					
proton	**1**	**1a**	**2**	**2a**	**3**	**3a**
H-1β					2.19 dd (12.6, 4.6)	2.18 dd (12.5, 4.6)
H-1α					1.1 m	1.1 m
H-2β	1.72 m	1.73 m	1.74 m	1.75 m	3.67 ddd (11.4, 9.5, 4.6)	3.68 ddd (11.5, 9.6, 4.6)
H-2α	1.81 m	1.85 m	1.82 m	1.83 m		
H-3α	3.14 dd (11.1, 5.2)	3.16 dd (11.4, 5.1)	3.14 dd (11.8, 4.5)	3.17 dd (11.5, 4.6)	2.92 d (9.5)	2.91 d (9.6)
H-9			1.66 d (8.6)	1.64 d (8.7)	2.01 br s	2.00 br s
H-11β			3.87 dd (8.6, 3.5)	3.88 dd (8.7, 3.4)		
H-11					6.47 dd (10.6, 3.0)	6.46 dd (10.6, 3.2)
H-12	5.21 t (3.2)	5.22 t (3.4)	5.43 d (3.5)	5.44 d (3.4)	5.61 dd (10.6, 1.6)	5.63 dd (10.6, 1.5)
H-18	2.21 d (11.8)	2.22 d (11.6)	2.24 d (11.4)	2.22 d (11.6)		
H-19a					2.50 br d (14.1)	2.51 br d (14.2)
H-19b					1.82 d (14.1)	1.81 d (14.2)
H-20			1.11 m	1.12 m		
CH_3-23	0.97 s	0.96 s	0.97 s	0.97 s	1.0 s	0.99 s
CH_3-24	0.96 s	0.95 s	0.77 s	0.78 s	0.79 s	0.78 s
CH_3-25	0.77 s	0.77 s	1.04 s	1.04 s	0.98 s	0.97 s
CH_3-26	0.86 s	0.86 s	0.85 s	0.86 s	0.79 s	0.78 s
CH_3-27	1.11 s	1.12 s	1.17 s	1.16 s	0.82 s	0.81 s
CH_3-29	0.88 d (6.4)	0.89 d (6.5)	0.94 d (6.3)	0.95 d (6.5)	0.96 s	0.95 s
CH_3-30	0.96 s	0.96 s			0.92 s	0.91 s
H-30a			3.65 dd (8.9, 7.0)	3.66 dd (9.0, 7.0)		
H-30b			3.38 dd (8.9, 7.0)	3.39 dd (9.0, 7.0)		
CO CH_3	1.90 s	1.92 s				
OCH_3			3.26 s	3.25 s		
$COOCH_3$		3.57 s		3.60 s		3.56 s

[a] ^{1}H-NMR chemical shifts for methyls and various upfield protons were assigned on the basis of 2D *J*-resolved and ^{1}H−^{1}H and ^{13}C−^{1}H COSY experiments.

Table 2. ^{13}C-NMR Spectral Data for Compounds **1**−**3a** (CD_3OD)

	compd					
carbon	**1**	**1a**	**2**	**2a**	**3**	**3a**
C-1	40.1	39.8	41.0	40.9	47.7	47.6
C-2	27.9	27.8	28.1	28.2	69.5	69.4
C-3	79.8	79.7	79.5	79.6	84.5	84.6
C-4	40.8	40.7	39.5	39.4	38.9	38.8
C-5	54.6	54.4	56.8	56.7	56.3	56.4
C-6	19.5	19.6	18.5	18.6	19.5	19.6
C-7	34.4	34.2	34.7	34.6	34.2	34.4
C-8	39.8	39.9	38.3	38.4	40.5	40.5
C-9	*	*	54.0	54.2	55.7	55.7
C-10	38.1	37.9	43.3	43.1	37.2	37.4
C-11	25.5	25.6	76.6	76.7	127.0	127.1
C-12	126.7	126.8	126.3	126.5	126.3	126.2
C-13	139.9	139.7	140.2	140.1	136.6	136.5
C-14	42.7	42.6	43.8	43.9	41.8	41.9
C-15	29.4	29.2	29.6	29.5	26.3	26.4
C-16	24.4	24.5	24.4	24.4	41.5	41.4
C-17	*	*	*	*	*	*
C-18	56.8	56.7	54.3	54.4	135.6	135.5
C-19	40.6	40.5	31.9	31.8	38.3	38.2
C-20	90.5	90.4	40.4	40.3	43.3	43.2
C-21	31.9	32.0	25.5	25.7	33.6	33.5
C-22	38.2	38.1	38.2	38.4	30.7	30.8
C-23	28.8	28.7	28.9	28.8	28.9	28.8
C-24	16.0	16.1	16.3	16.4	17.4	17.3
C-25	16.3	16.4	17.7	17.6	19.6	19.7
C-26	17.6	17.7	19.6	19.7	16.9	16.8
C-27	24.1	24.2	23.4	23.5	24.6	24.6
C-28	179.8	176.9	182.2	177.7	178.9	177.6
C-29	21.6	21.5	17.5	17.6	23.8	23.7
C-30	24.1	24.2	63.8	63.9	32.8	32.6
$OCOCH_3$	170.9	170.8				
$OCOCH_3$	22.9	22.8				
OCH_3			54.0	54.2		
$COOCH_3$		51.9		51.8		51.9

* Superimposed with solvent signals.

between OMe and H-3α indicative of the presence of an α disposition of OMe and a OH at C-30 (α) (Figure 3). This assignment was confirmed by analyzing the ^{13}C-NMR shift values of ring E carbons.[15] Compound **2** formed methyl ester (**2b**) on treatment with diazomethane. The carboxyl group was placed at C-17 due to the appearance of prominent fragments at *m/z* 262.1567 and 218.1672 (*vide* structure **2**).[13] A comparison of ^{13}C-NMR data of **2** with those of the other C-17 carboxyl triterpenoids supported this assignment.[16] Thus, the structure of camaldulensic acid (**2**) was proved as 3β,30-dihydroxy-11α-methoxyurs-12-en-28-oic acid.

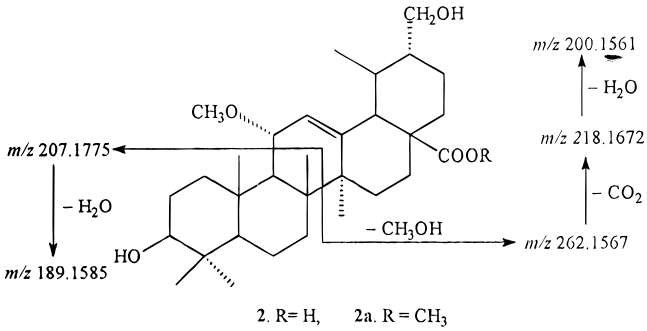


Figure 2. Significant mass fragmentation of **2** in the HRE-IMS.

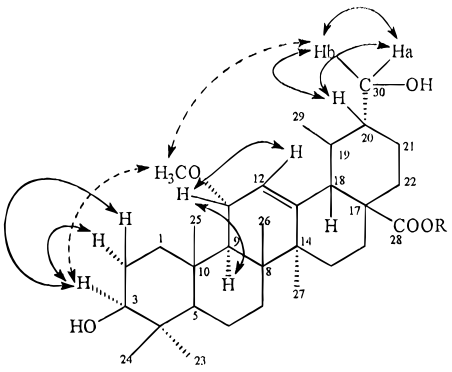
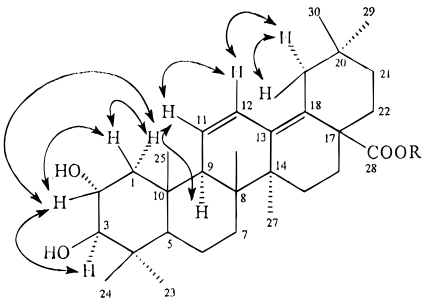


Figure 3. Significant ^{1}H−^{1}H COSY (solid arrow) and NOESY (hashed arrow) correlations for camaldulensic acid (**2**).

The negative-ion FABMS of compound **3** showed a peak at *m/z* 469 [M − 1]$^-$, along with prominent peaks



3, R= H, **3a**, R = CH_3

Figure 4. Significant $^1H-^1H$ COSY correlations for camaldulenic acid (**3**).

at *m/z* 425 $[M - 1 - CO_2]^-$, 407 $[425 - H_2O]^-$, and 389 $[407 - H_2O]^-$, indicating the presence of a carboxyl and two hydroxyl groups in the molecule. Its IR spectrum showed hydroxyl (3450 cm^{-1}), carboxyl (3440−2650, 1710 cm^{-1}), olefinic (1630, 1600 cm^{-1}), and CO (1050 cm^{-1}) absorptions. The molecular formula $C_{30}H_{46}O_4$ was established by ^{13}C-NMR spectral analysis. It formed methyl derivative **3a** on reaction with diazomethane. The ^1H- and ^{13}C-NMR data (Tables 1 and 2) showed seven tertiary methyl groups, suggesting **3** to be an oleanane type of triterpene. The ^1H-NMR (δ 3.67, 1H, ddd, J = 11.4, 9.5, 4.6 Hz, H-2β and δ 2.92, 1H, d, J = 9.5 Hz, H-3α) and ^{13}C-NMR signals (δ 69.5 and 84.5, each CH, DEPT) also showed the presence of two secondary hydroxyl groups. One of these was placed at C-3 on biogenetic grounds and the other at C-2 on the basis of $^1H-^1H$ COSY connectivities (Figure 4). The diequatorial relationship was revealed from the δ values and coupling pattern of their geminal protons.[17] It displayed strong UV absorptions at 248, 256, and 264 nm characteristics of a $\Delta^{11,13(18)}$-diene.[18] This system was confirmed by ^1H- and ^{13}C-NMR data [δ_H 6.47, dd, J = 10.6, 3.0 Hz, H-11 and δ_H 5.61, dd, J = 10.6, 1.6 Hz, H-12; δ_C 127.0 (C-11), 126.3 (C-12), 136.6 (C-13) and 135.6 (C-18)] and [δ_H 2.50, br d, J = 14.1 Hz, H-19a and δ_H 1.82, d, J = 14.1 Hz, H-19b; δ_C 38.3 (C-19)].[19] The carboxyl group was located at C-17 through comparison of the ^{13}C-NMR data with similar compounds.[18,20] All these assignments were substantiated by $^1H-^1H$ (Figure 4) and $^1H-^{13}C$ correlation spectroscopy (COSY) experiments. Thus, camaldulenic acid (**3**) was characterized as 2α,3β-dihydroxy-olean-11,13(18)-dien-28-oic acid.

Experimental Section

General Experimental Procedures. Melting points are uncorrected. MS were recorded on a Finnigan MAT 312 double focusing mass spectrometer connected to a PDP 11/34 computer system. Optical rotations were measured on a JASCO DIP-360 polarimeter. NMR spectra (CD_3OD, 500 MHz for ^1H and 125 MHz for ^{13}C) were recorded on a Bruker AMX 500 NMR spectrometer. The chemical shifts are reported in δ (ppm), and the coupling constants are in Hz. The ^{13}C-NMR spectral assignments (Table 2) have been made partly through a comparison of the chemical shifts with the published data for similar compounds[14,16,19−22] and partly through the appearance of signals in the DEPT and hetero-COSY spectra. Precoated thin-layer cards (E. Merck, DC-karten SiF) were used for TLC. The petroleum ether used was of the boiling range 60−70 °C.

Plant Material. The leaves of the plant were collected from the Karachi region in December 1990. The plant was identified by Mr. MIH Brooker, Eucalyptus botanist, Centre for Plant Biodiversity Research, Australian National Herbarium (CANB), Canberra, Australia, and a voucher specimen has been deposited in the Herbarium.

Extraction and Isolation. Fresh and uncrushed leaves (20 kg) of *E. camaldulensis* var. *obtusa* were repeatedly extracted with EtOH at room temperature. The concentrated syrupy residue, obtained by removal of the solvent from the ethanolic extract in vacuo, was partitioned between EtOAc and water. The former layer was then dried (Na_2SO_4), treated with charcoal, filtered, and washed with EtOAc. The charcoal bed was further washed with MeOH−C_6H_6 (1:1). The residue left on removal of the solvent from the EtOAc filtrate and washings was divided into petroleum ether-soluble and petroleum ether-insoluble fractions. The petroleum ether-insoluble fraction (90 g) was subjected to VLC (silica gel GF_{254}, $CHCl_3$, $CHCl_3$−MeOH, in order of increasing polarity). Various fractions were obtained on combining the eluates on the basis of TLC. The major fraction (17 g) eluted with $CHCl_3$−MeOH (9.9:0.1) was rechromatographed (VLC, petroleum ether, petroleum ether−EtOAc, in order of increasing polarity). The eluates were combined on the basis of TLC, furnishing total 10 fractions. Fraction no. 8 (1.4 g) obtained on combining the eluates with petroleum ether−EtOAc (7.5:2.5, 7:3 and 6.5:3.5) was subjected to flash column chromatography (silica gel E. Merck, 9385; petroleum ether−EtOAc in order of polarity). The petroleum ether−EtOAc eluate (8.25:1.75) of this fraction afforded ursolic acid lactone (50 mg), while the more polar eluate (7.75:2.25), showed three spots on TLC, which were separated on precoated thin-layer cards ($CHCl_3$−MeOH, 7.75:2.25). As a result, pure **1** (7 mg), **2** (7 mg), and **3** (8 mg) were obtained in order of polarity.

Camaldulic acid (1): needles (1:1 $CHCl_3$−MeOH); mp 218−219 °C; $[\alpha]_D$ +71° (*c* 0.10, $CHCl_3$); UV (MeOH) λ_{max} 205 nm; IR ($CHCl_3$) ν_{max} 3450 (OH), 3430−2600 (COOH), 1730 (ester C=O), 1710 (acid C=O), 1620 (C=C) cm^{-1}; CIMS (+ve) *m/z* (rel intensity) $[M + 1]^+$ 515 (2), $[M + 1 - OH]^+$ 498 (3), $[M + 1 - COCH_2]^+$ 473 (12) $[M + 1 - CH_3COOH]^+$ 455 (20), $[455 - CH_3 - H]^+$ 439 (35), $[439 - CO]^+$ 411 (18), $[411 - H_2O]^+$ 393 (10), [retro-Diels−Alder fragment + 1]$^+$ 307 (4), $[307 - CH_3COOH]^+$ 247 (8), [retro-Diels−Alder fragment]$^+$ 207 (48), $[207 - H_2O]^+$ 189 (42); ^1H NMR (Table 1); ^{13}C NMR (Table 2).

Methyl Ester of 1. Methylation of **1** (2 mg) with a freshly prepared ethereal solution of diazomethane afforded **1a** (1.9 mg): needles (1:1 $CHCl_3$−MeOH); mp 215−216 °C; $[\alpha]_D$ +66° (*c* 0.10, $CHCl_3$); UV (MeOH) λ_{max} 207 nm; IR ($CHCl_3$) ν_{max} 3450 br (OH), 1730 br (ester C=O), 1620 (C=C) cm^{-1}; CIMS (+ve) *m/z* (rel intensity) $[M + 1]^+$ 529 (4); ^1H NMR (Table 1); ^{13}C NMR (Table 2).

Camaldulensic acid (2): needles (1:1 $CHCl_3$−MeOH); mp 295−296 °C; $[\alpha]_D$ +85° (*c* 0.12, $CHCl_3$); UV (MeOH) λ_{max} 207 nm; IR ($CHCl_3$) ν_{max} 3460 (OH), 3420−2650 (COOH), 1710 (acid C=O), 1630 (C=C), 1150 (CO) cm^{-1}; CIMS (+ve) *m/z* (rel intensity) $[M + 1]^+$ 503 (5), $[M + 1 - H_2O]^+$ 485 (4), $[M + 1 - MeOH - OH]^+$ 454 (20), $[454 - CO_2]^+$ 410 (20), $[410 - OH]^+$ 393 (5);

HREIMS *m/z* (rel intensity) $[M - MeOH - OH]^+$ 453.3425 (13), $[453 - COOH]^+$ 408.3368 (31), [r.D.A fragment $- MeOH]^+$ 262.1567 (12), $[262 - H_2O]^+$ 244.1461 (6), $[262 - CO_2]^+$ 218.1672 (8), $[218 - H_2O]^+$ 200.1561 (14), [r.D.A fragment]$^+$ 207.1775 (47), $[207 - H_2O]^+$ 189.1585 (45); ^{1}H NMR (Table 1); ^{13}C NMR (Table 2).

Methyl Ester of 2. Treatment of **2** (2.5 mg) with a freshly prepared ethereal solution of diazomethane gave **2a** (2.4 mg): needles ($CHCl_3$); mp 275−276 °C; $[\alpha]_D$ +77° (*c* 0.10, $CHCl_3$); UV (MeOH) λ_{max} 206 nm; IR ($CHCl_3$) ν_{max} 3445 (OH), 1725 (ester C═O), 1630 (C═C), 1160 (CO) cm^{-1}; CIMS (+ve) *m/z* (rel intensity) $[M + 1]^+$ 517 (5); ^{1}H NMR (Table 1); ^{13}C NMR (Table 2).

Camaldulenic acid (3): needles (1:1 $CHCl_3$−MeOH); mp 236−237 °C; $[\alpha]_D$ −68° (*c* 0.14, $CHCl_3$); UV (MeOH) λ_{max} 248, 256, and 264 nm; IR ($CHCl_3$) ν_{max} 3450 (OH), 3440−2650 (COOH), 1710 (acid C═O), 1630, 1600 (C═C), 1050 (CO) cm^{-1}; FABMS (−ve) *m/z* (rel intensity) $[M - 1]^-$ 469 (4), $[M - 1 - CO_2]^-$ 425 (18), $[425 - H_2O]^-$ 407 (3), $[407 - H_2O]^-$ 389 (3), [ring A and B $- 1 - H_2O]^-$ 205 (14), $[205 - H_2O]^-$ 187 (12); ^{1}H NMR (Table 1); ^{13}C NMR (Table 2).

Methyl Ester of 3. Treatment of **3** (5 mg) with a freshly prepared ethereal solution of diazomethane furnished **3a** (4.8 mg): needles ($CHCl_3$); mp 214−215 °C; $[\alpha]_D$ −81° (*c* 0.12, $CHCl_3$); UV (MeOH) λ_{max} 246, 254, and 264 nm; IR ($CHCl_3$) ν_{max} 3420 (OH), 1725 (ester C═O), 1630, 1600 (C═C), 1050 (CO) cm^{-1}; FABMS (−ve) *m/z* (rel intensity) $[M - 1]^-$ 483 (5); ^{1}H NMR (Table 1); ^{13}C NMR (Table 2).

References and Notes

(1) Sastri, B. N., Ed. *The Wealth of India*; Council of Scientific and Industrial Research: New Delhi, 1952; Vol. VIII, p 210.
(2) Chaudhari, D. C.; Suri, R. K. *Indian Perfum*. **1991**, *35*, 30−34.
(3) El-Gammal, A. A.; Mansour, R. M. A. *Zentralbl. Mikrobial*. **1986**, *141*, 561−565.
(4) Abd-Alla, M. F.; El-Negoumy, S. I.; El-Lakany, M. H.; Saleh, N. A. M. *Phytochemistry* **1980**, *19*, 2629−2632.
(5) Movsumov, I. S.; Aliev, A. M. *Khim. prir. Soedin* **1985**, 271−272.
(6) Dayal, R.; Maheshwari, M. L. *Indian For*. **1985**, *111*, 1077−1080.
(7) Erazo, S.; Bustos, C.; Erazo, A. M.; Rivas, J.; Zollner, O.; Cruzat, C.; Gonzalez, J. *Plant Med. Phytother*. **1990**, *24*, 248−257.
(8) Dayal, R. *Curr. Sci*. **1987**, *56*, 670−671.
(9) Yamaguchi, K. *Spectral Data of Natural Products*; Elsevier: Amsterdam, 1970; p 142.
(10) Seo, S.; Tomita, Y.; Tori, K. *J. Chem. Soc., Chem. Commun*. **1975**, 954−955.
(11) Kojima, H.; Ogura, H. *Phytochemistry* **1986**, *25*, 729−733.
(12) Siddiqui, S.; Siddiqui, B. S.; Naeed, A.; Begum, S. *Phytochemistry* **1989**, *28*, 3143−3147.
(13) Budzikiewicz, H.; Wilson, J. M.; Djerassi, C. *J. Am. Chem. Soc*. **1963**, *85*, 3688−3699.
(14) Amagaya, S.; Takeda, T.; Ogihara, Y.; Yamasaki, K. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2044−2047.
(15) Talapatra, S. K.; Sarkar, A. C.; Talapatra, B. *Phytochemistry* **1981**, *20*, 1923−1927.
(16) Shashi, B. M.; Asish, P. K. *Phytochemistry* **1994**, *37*, 1517−1575.
(17) Kojima, H.; Ogura, H. *Phytochemistry* **1989**, *28*, 1703−1710.
(18) Breton, J. L.; Gonzalez, A. G. *J. Chem. Soc*. **1963**, 1401−1406.
(19) Ohtari, K.; Ogawa, K.; Kasai, R.; Yang, C-R.; Yamasaki, K.; Zhou, J.; Tanaka, O. *Phytochemistry* **1992**, *31*, 1747−1752.
(20) Shimizu, K.; Amagaya, S.; Ogihara, Y. *Chem. Pharm. Bull*. **1985**, *33*, 3349−3355.
(21) Doddrell, D. M.; Khong, P. W.; Lewis, K. G. *Tetrahedron Lett*. **1974**, 2381−2384.
(22) Hartleb, I.; Seifert, K. *Phytochemistry* **1995**, *38*, 221−224.

NP960535Z