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Ceriopsins F and G, diterpenoids from *Ceriops decandra*☆

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Abstract

Chemical examination of the ethyl acetate solubles of the CH_3OH:CH_2Cl_2 (1:1) extract of the roots of *Ceriops decandra* collected from Kauvery estuary resulted in the isolation of two more diterpenoids, ceriopsins F and G (**1**–**2**) and five known compounds, *ent*-13-hydroxy-16-kauren-19-oic acid (steviol, **3**), methyl *ent*-16β,17-dihydroxy-9(11)-kauren-19-oate (**4**), *ent*-16β,17-dihydroxy-9(11)-kauren-19-oic acid (**5**), *ent*-16-oxobeyeran-19-oic acid (isosteviol, **6**), 8,15*R*-epoxypimaran-16-ol (**7**). The structures of the new diterpenoids were elucidated by a study of their physical and spectral data as methyl *ent*-13,17-epoxy-16-hydroxykauran-19-oate (**1**) and *ent*-16-oxobeyeran-19-al (**2**).

Keywords: Indian mangrove; *Ceriops decandra*; Rhizophoraceae; Diterpenoids; Ceriopsins F and G

1. Introduction

In our continuing interest on the chemical constituents of Indian mangrove plants (Anjaneyulu and Lakshmana Rao, 2000, 2001; Anjaneyulu et al., 2000, 2002a,b,d) we have examined the roots of *Ceriops decandra* (Rhizophoraceae) collected from Kauvery estuary (Parangipettai coast) and reported the isolation of four new diterpenoids (Anjaneyulu and Lakshmana Rao, 2002), methyl 17-hydroxy-16-oxobeyeran-18-oate (ceriopsin A), methyl 16(*R*)-16,17-dihydroxybeyeran-18-oate (ceriopsin B), 1β,15(*S*)-isopimar-7-ene-1,15,16-triol (ceriopsin C), and 8,15(*R*)-epoxypimarane-1β,16-diol (ceriopsin D). A new epoxy-*ent*-kaurene diterpenoid methyl *ent*-12,17-epoxy-16β-hydroxy-9(11)-kauren-19-oate (ceriopsin E), has been recently reported (Anjaneyulu et al., 2002c) from the same extract. After a thorough examination of the various chromatographic fractions of the same extract we report herein the isolation of seven more diterpenoids, two of which, ceriopsin F (**1**), a kaurenoid and ceriopsin G (**2**), a beyeranoid happened to be new members. The structures of ceriopsin F and ceriopsin G were established as methyl *ent*-13,17-epoxy-16-hydroxykauran-19-oate (**1**) and *ent*-16-oxobeyeran-19-al (**2**) respectively by a study of their spectral data. The remaining five were identified as known members, *ent*-13-hydroxy-16-kauren-19-oic acid (steviol, **3**), methyl *ent*-16β,17-dihydroxy-9(11)-kauren-19-oate (**4**), *ent*-16β,17-dihydroxy-9(11)-kauren-19-oic acid (**5**), *ent*-16-oxobeyeran-19-oic acid (isosteviol, **6**), and 8,15*R*-epoxypimaran-16-ol (**7**) respectively. This formed the first report of natural occurrence of compound **7** while it was reported earlier as a derivative by synthesis (Herz and Kulanthaivel, 1983). Similarly, compound **4** has now been reported for the first time from nature, while it was known earlier as methyl ester of **5** (Bohlmann et al., 1982).

2. Results and discussion

Ceriopsin F (**1**) was isolated as colorless needles from MeOH, mp 130–133 °C, $[\alpha]_D^{25}$ + 40.2° (*c* 0.4, $CHCl_3$) and its molecular formula was established as $C_{21}H_{32}O_4$ from elemental analysis and EIMS, $[M]^+$ at *m*/*z* 348. It exhibited hydroxyl (3460 cm^{-1}), carbonyl (1710 cm^{-1}) and ether absorptions (1140, 1085 cm^{-1}) in the IR spectrum. A preliminary study of its ^1H and ^{13}C NMR spectral data (Table 1) revealed that it might be a new pentacyclic epoxykaurenoid, very close in structure to ceriopsin E (**8**) (Anjaneyulu et al., 2002c). Like ceriopsin

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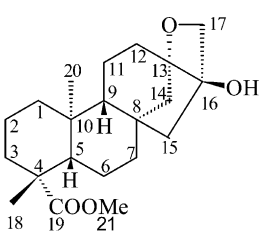

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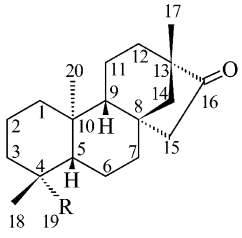

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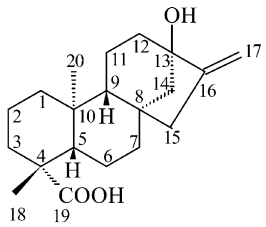
6 R = COOH



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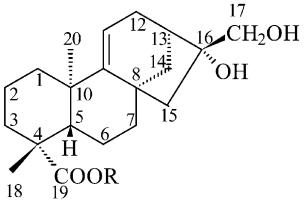
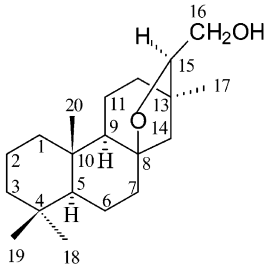


4 R = Me
5 R = H



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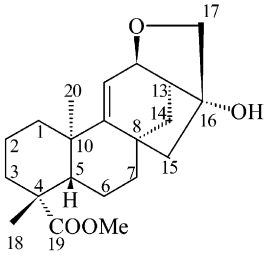

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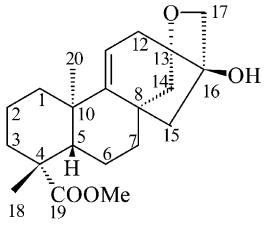

9

E, it contained a carbomethoxyl [δ_H 3.63, 3H, *s*; δ_C 177.6 (*s*), 50.7 (*q*)] and two oxymethylene protons at δ 3.76 (1H, *d*, $J = 11.4$ Hz) and 3.60 (1H, *d*, $J = 11.4$ Hz). But the oxymethine proton 12-H noticed at δ 4.76 and the trisubstituted olefinic proton 11-H noticed at δ 5.18 in ceriopsin E (**8**) were absent in ceriopsin F (**1**) to distinguish them. Ceriopsin F might thus be a saturated kaurenoid with ether bridge possibly between C-17 and C-13. The three oxygenated carbons noticed in ceriopsin F at δ 65.1 (*t*, C-17), 77.9 (*s*, C-16) and 80.4 (*s*, C-13) significantly differed, understandably, from the corresponding values in ceriopsin E (δ 79.4, C-17; 89.7, C-16; 53.1, C-13 and 80.1, C-12) with tetrahydrofuran ring in support of its structure with an oxetane ring between C-17 and C-13.

The important HMBC correlations (Table 1) noticed between C-19 (δ 177.6) and 21-H_3, 18-H_3, 5-H and 3-H_2; between C-13 (δ 80.4) and 17-H_2, 15-H_2, 11-H_2 and 14-H_2; between C-16 (δ 77.9) and 17-H_2, 14-H_2 and 15-H_2 and between C-17 (δ 65.1) and 15-H_2 further supported the structure. The important NOESY correlations (Table 1) noticed between 20-H_3 and 14-H supported *cis* fused B, C rings and the correlations between 15-H and 17-H on one side and 15-H and 11-H on the other side were in support of the stereochemical disposition of the five member ring D and the four member oxetane ring E on the same side. A 13,17-epoxykaurenoid *ent*-kaur-9(11)-ene-13,17-epoxy-16-hydroxy-19-oate (**9**) has been recently reported from *Bruguiera gymnrohiza* (Subrahmanyam et al., 1999) and a comparison of its ^{13}C NMR data with those of ceriopsin F established their structural closeness to consider ceriopsin F as a 9(11)-dihydro derivative of the literature compound. The absolute configuration of ceriopsin F was regarded as an *ent*-derivative in view of the configuration given to the literature compound as well as the occurrence of ceriopsin E, another *ent*-kaurenoid in the same species. The structure of ceriopsin F could thus be derived as methyl *ent*-13,17-epoxy-16-hydroxykauran-19-oate (**1**).

Ceriopsin G (**2**) was isolated as colourless oil, $[\alpha]_D^{25}$ -49.0° (*c* 0.25, $CHCl_3$) and its molecular formula was established as $C_{20}H_{30}O_2$ from elemental analysis and EIMS, $[M\text{-}H]^+$ at *m*/*z* 301 and $[M\text{-}29]^+$ at *m*/*z* 273. Its IR spectrum exhibited five membered keto carbonyl (1737 cm^{-1}) and aldehyde (1695, 2865 cm^{-1}) absorptions. Its ^1H and ^{13}C NMR spectral data, reminiscent of a beyerane diterpenoid, were found to be very close to the data of *ent*-16-oxobeyeran-19-oic acid (isosteviol, **6**)

Table 1
^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) assignments and HMBC, NOESY and COSY correlations of ceriopsin F (**1**)

Carbon No.	^{1}H (δ)	^{13}C (δ)	HMBC	NOESY	COSY
C-1	1.80 *m* 0.80 *m*	40.2	20-H_3, 5-H, 9-H, 3-H_2, 2-H_2	20-H_3	1-H_a
C-2	1.40 *m* 1.80 *m*	18.6	1-H_2, 3-H_2		3-H_a, 1-H_a 2-H_a
C-3	2.18 *m* 0.98 *m*	37.6	2-H_2, 1-H_2, 5-H, 18-H_3		2-H_2, 3-H_e
C-4		43.4	6-H_2, 2-H_2, 3-H_2, 18-H_3, 5-H		
C-5	1.02 *m*	56.3	18-H_3, 20-H_3, 3-H_2, 6-H_2, 7-H_2, 1-H_2, 9-H	9-H	
C-6	0.90 *m* 1.74 *m*	21.7	5-H		5-H
C-7	1.72 *m* 1.72 *m*	33.1	6-H_2, 9-H, 14-H_2	5-H_a	
C-8		41.0	11-H_2, 15-H_2, 7-H_2, 14-H_2, 6-H_2		
C-9	0.92 *m*	54.2	11-H_2, 12-H_2, 15-H_2, 14-H_2, 20-H_3, 5-H		
C-10		38.9	20-H_3, 9-H, 5-H, 2-H_2		
C-11	1.80 *m* 1.80 *m*	19.5	9-H	15-H_e	12-H_e 9-H
C-12	1.60 *m* 1.36 *m*	41.6	9-H, 15-H_2		
C-13		80.4	15-H_2, 14-H_2, 11-H_2, 17-H_2		
C-14	1.70 *m* 1.83 *m*	42.8	15-H_2, 7-H_2, 12-H_2, 9-H	20-H_3 12-H_e	14-H_a
C-15	1.54 *m* 1.40 *m*	50.8	17-H_2, 9-H, 7-H_2, 14-H_2		15-H_a
C-16		77.9	17-H_2, 15-H_2, 14-H_2		
C-17	3.76 (1H, *d*, *J* = 11.4) 3.60 (1H, *d*, *J* = 11.4)	65.1	15-H_2	14-H_a 15-H_e	
C-18	1.15 (3H, *s*)	28.3	5-H, 3-H_2		
C-19		177.6	21-H_3, 5-H, 18-H_3, 3-H_2		
C-20	0.82 (3H, *s*)	14.9	5-H, 9-H, 1-H_2		
C-21	3.63 (3H, *s*)	50.7	–		

Chemical shifts in δ from TMS (multiplicity, *J* in Hz) in $CDCl_3$.

isolated not as such but as a hydrolysis product of stevioside (Mosettig et al., 1963; Oliveira and Starapasson 1996; Oliveira et al., 1999). Isosteviol (**6**) has, in fact, been reported now for the first time from this species. A comparison of the ^{1}H and ^{13}C NMR spectral data of ceriopsin G with those of isosteviol clearly established that isosteviol is 19-oic acid, while ceriopsin G is 19-al. The aldehyde proton in ceriopsin G came at δ 9.78 (1H, s) while the corresponding carbon in ^{13}C NMR at δ 205.3 (d), whereas carboxylic acid carbon in isosteviol was noticed at δ 181.5 as singlet. The structure of ceriopsin G was thus derived as 16-oxobeyeran-19-al (**2**) and its absolute configuration as *ent* derivative in view of the isolation of isosteviol with established *ent*-configuration (Mosettig et al., 1963) from the same species. Similarly the related beyeranoids ceriopsin A and ceriopsin B (Anjaneyulu and Lakshmana Rao, 2002) reported from the same species might be considered as e*n*t-derivatives.

Compound **3**, $C_{20}H_{30}O_3$, EIMS, $[M]^+$ at *m*/*z* 318 was found to be identical in all its physical characteristics including specific rotation and spectral data with *ent*-13-hydroxy-16-kauren-19-oic acid, steviol (**3**). Steviol (**3**) was earlier isolated as an aglycone of the glycosides isolated from *Stevia rebaudiana* (Mosettig and Nes, 1955) and as such only recently from the mangrove

plant *Bruguiera gymnrohiza* (Subrahmanyam et al., 1999). The present isolation forms second report of its natural occurrence.

Compound **4**, was characterised as methyl *ent*-16β,17-dihydroxy-9(11)-kauren-19-oate (**5**) by comparing its physical and spectral (UV, IR and ^{1}H NMR) data of the literature compound which was, in fact, not reported as such from a natural source but only as methyl ester of the corresponding 19-oic acid isolated from the plant *Ichthyothere terminallis* (Bohlmann et al., 1982). Thus this formed the first report of its natural occurrence. The ^{13}C NMR data of the compound were obtained now and presented in the experimental.

The physical and spectral (UV, IR and ^{1}H NMR) characteristics of compound **5** were found to be identical with those of *ent*-16β,17-dihydroxy-9(11)-kauren-19-oic acid (**5**), isolated long ago from the roasted coffee seeds *Coffea arabica* (Obermann and Spiteller, 1975). The ^{13}C NMR spectral data of the compound were obtained now and presented in the experimental. As stated above compound **6** was identified as isosteviol.

The physical and spectral characteristics (UV, IR and ^{1}H NMR) of compound **7** agreed with those of *ent*-8,15R-epoxypimaran-16-ol, a compound known by synthesis from *ent*-8,15R-epoxypimarane-3β,12α,16-triol isolated from *Liatris laevigata* (Herz and Kulanthaivel, 1983). Thus this forms the first report of natural occurrence of compound **7**.

3. Experimental

3.1. General

Melting points were determined on a VEB-Analytic Dreader HMK hot plate and are uncorrected. IR spectra were recorded on a Perkin-Elmer-841 IR spectrometer in $CHCl_3$ solution. UV spectra were recorded on a Milton Roy Spectronic 1201 spectrometer in $CHCl_3$. ^{1}H NMR spectra were measured on a Bruker Advance DRX 300 and Jeol JNM EX-90 spectrometers. ^{13}C NMR spectra were measured on a Bruker Advance DRX 300 spectrometer at 75 MHz and Jeol JNM EX-90 spectrometer at 22.5 MHz using $CDCl_3$ as a solvent and tetramethylsilane as an internal reference. Optical rotations were determined on a Rudolph Autopol-III polarimeter. Elemental analyses were determined on a Carlo Erba 1108 instrument. Mass spectra were obtained on a Jeol JMS-300 spectrometer.

3.2. Plant material

The roots of Ceriops decandra were collected from Parangipettai coast (latitude 11° 07′ N and longitude 79° 50′ E), Kauvery estuary of India in March, 1999. The plant material was kindly identified by Professor B. Kondala Rao, Department of Marine Living Sources, Andhra University, Visakhapatnam. Voucher specimens (Code: AU1/182) are deposited at the Marine Museums of the School of Chemistry, Andhra University and the National Institute of Oceanography, Goa.

3.3. Extraction and isolation

The air-dried and powdered plant material (3.0 kg) was exhaustively extracted with CH_2Cl_2:MeOH (1:1). Removal of the solvent from the combined CH_2Cl_2:MeOH extracts gave a residue (60 g) which was extracted with EtOAc (5×600 ml). Removal of the solvent from the EtOAc extract under reduced pressure gave a residue (35 g). This residue was subjected to column chromatography over silica gel (Acme brand, 100–200 mesh, 350 g) using solvents of increasing polarity from n-hexane through EtOAc. In all 240 fractions (800 ml) were collected. The fractions showing similar spots were combined and the residues from therein were subjected to rechromatography over silica gel or silver nitrate (20%) impregnated silica gel columns to yield ceriopsins A-D (Anjaneyulu and Lakshmana Rao, 2002) and ceriopsin E (Anjaneyulu et al., 2002c). Further examination of the fractions 101–125 (*n*-hexane:EtOAc; 9.0:1.0) furnished isosteviol (40 mg, **3**), ceriopsin G (35 mg, **2**) and compound **7** (40 mg), the residue from the column fractions 186–210 (*n*-hexane:EtOAc; 6.0:4.0) furnished ceriopsin F (38 mg, **1**) and compounds **4** (40 mg), **5** (30 mg) and **6** (25 mg).

3.3.1. Ceriopsin F (*1*)

Colorless needles from MeOH, mp 130–133 °C, $[\alpha]_D^{25}$ + 40.2° (*c* 0.4, $CHCl_3$). IR (Nujol) ν_{max} cm^{-1} 3460 (OH), 1710 (ester), 1140, 1085 (ether). Found. C 72.20%, H 9.10%, $C_{21}H_{32}O_4$ requires C 72.41%, H 9.19%. EIMS *m*/*z*: 348 [M]$^+$, 318, 291, 257, 231, 181, 161. ^{1}H NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, $CDCl_3$,): see Table 1.

3.3.2. Ceriopsin G (*2*)

Colorless oil, $[\alpha]_D^{25}$ −49.0° (*c* 0.25, $CHCl_3$). IR (Nujol) ν_{max} cm^{-1} 1737 (five membered ketone), 2865, 1695 (aldehyde). Found C 79.3%, H 9.62%, $C_{21}H_{34}O_4$ requires C 79.47%, H 9.93%. EIMS *m*/*z*: 301 [M-H]$^+$,273, 258, 248, 230, 206, 162, 136. ^{1}H NMR (90 MHz, $CDCl_3$): δ 9.78 (1H, *s*, 19-H), 2.78 (1H, *d*, *J* = 6.0 Hz, 15-H), 2.58 (1H, *d*, *J* = 6.0 Hz, 15-H), 1.04 (3H, *s*, 18-H_3), 1.02 (3H, *s*, 17-H_3), 0.78 (3H, *s*, 20-H_3) and ^{13}C NMR (22.4 MHz, $CDCl_3$): δ 38.9, 19.7, 37.8, 48.2, 56.7, 20.4, 41.3, 48.2, 54.3, 37.2, 18.1, 37.8, 39.3, 54.3, 48.6, 221.7, 19.8, 24.4, 205.3, 14.1 (C-1–C-20).

3.3.3. Ent-13-hydroxy-16-kauren-19-oic acid (steviol, *3*)

Colorless needles from MeOH, mp 190–192 °C, $[\alpha]_D^{25}$ −55.2° (*c* 0.2, $CHCl_3$). IR (Nujol) ν_{max} cm^{-1} 3460 (OH), 1680 (carboxylic acid), 880 (unsaturation). EIMS *m*/*z*:

318 $[M]^+$, 300, 285, 245, 185, 121. ^1H NMR and ^{13}C NMR: see Subrahmanyam et al., 1999.

3.3.4. Methyl ent-16β,17-dihydroxy-9(11)-kauren-19-oate (4)

Colorless needles from MeOH, mp 120–122 °C, $[\alpha]_D^{25}$ −25.2° (*c* 0.2, $CHCl_3$). IR (Nujol) ν_{max} cm^{-1} 3450 (OH), 1710 (ester), 890 (unsaturation). EIMS *m*/*z*: 348 $[M]^+$, 331, 316, 300, 274, 255. ^1H NMR: see Bohlmann et al., 1982 and ^{13}C NMR (22.4 MHz, $CDCl_3$): δ 42.6, 20.9, 40.8, 42.8, 46.5, 19.1, 29.4, 38.1, 157.0, 38.4, 113.5, 29.9, 44.7, 43.8, 54.6, 84.5, 68.0, 27.8, 177.7, 23.1 (C-1–C-20) and 51.0 ($OCOCH_3$).

3.3.5. Ent-16β,17-dihydroxy-9(11)-kauren-19-oic acid (5)

Colorless needles from MeOH, mp 180–182 °C, $[\alpha]_D^{25}$ + 30.2° (*c* 0.3, $CHCl_3$). IR (Nujol) ν_{max} cm^{-1} 3380 (OH), 1670 (carboxyl), 800 (unsaturation). EIMS *m*/*z*: 334 $[M]^+$, 316, 301, 284, 260, 255, 199. ^1H NMR: See Obermann and Spiteller, 1975 and ^{13}C NMR (75.0 MHz, d_5-pyridine): δ 41.6, 20.9, 39.2, 43.3, 46.8, 19.1, 30.9, 39.0, 158.2, 39.0, 114.2, 30.8, 44.8, 43.8, 55.8, 84.7, 68.8, 28.7, 180.1, 24.0 (C-1–C-20).

3.3.6. Ent-16-oxobeyeran-19-oic acid (isosteviol, 6)

Colorless needles from MeOH, mp 115–118 °C, $[\alpha]_D^{25}$ −72.0° (*c* 0.3, $CHCl_3$). IR (Nujol) ν_{max} cm^{-1} 3400, 1690 (COOH), 1737 (keto carbonyl). EIMS *m*/*z*: 318 $[M]^+$, 300, 273, 205, 177, 161. ^1H NMR and ^{13}C NMR: see Oliveira and Starapasson 1996.

3.3.7. 8,15R-Epoxypimaran-16-ol (7)

Colorless needles from MeOH, mp 95–98 °C, $[\alpha]_D^{25}$ + 46.2° (*c* 0.6, $CHCl_3$). IR (Nujol) ν_{max} cm^{-1} 3480 (OH) and 1050 (ether). (+) ve FAB *m*/*z*: 307 $[M+H]^+$, 289, 275, 257, 147. ^1H NMR and ^{13}C NMR: see Herz and Kulanthaivel, 1983.

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