

Dolabellane Diterpenoids from the Higher Plant *Aglaia odorata*

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Two new dolabellane diterpenoids, (1*R*,3*R*,7*E*,11*S*,12*R*)-dolabella-4(16),7-diene-3,18-diol (**1**) and (1*R*,3*E*,7*R*,11*S*,12*R*)-dolabella-3,8(17)-diene-7,18-diol (**2**), and the known (1*R*,3*E*,7*E*,11*S*,12*R*)-dolabella-3,7-dien-18-ol (**3**) were isolated from *Aglaia odorata*, along with twelve other known compounds. Their structures were elucidated on the basis of spectroscopic data. This is the first time that dolabellane-type diterpenoids were detected in higher plants.

Introduction. – Dolabellane-type diterpenoids have not been found in higher plants, but in marine algae, herbivorous molluscs, and liverworts [1][2]. Because the genus *Aglaia* of the family Meliaceae has attracted considerable interest as a possible new source of unique natural products for integrated pest management, many chemical compounds have been isolated from this genus [3]. Nevertheless, we continued our search for novel constituents in the Meliaceae family [4]. *A. odorata* is naturally occurring in India, Malaysia, and Oceania, and is cultivated as ornamental plant [5]. From *A. odorata*, cultivated in Kunming, Yunnan province, two new compounds, (1*R*,3*R*,7*E*,11*S*,12*R*)-dolabella-4(16),7-diene-3,18-diol (**1**) and (1*R*,3*E*,7*R*,11*S*,12*R*)-dolabella-3,8(17)-diene-7,18-diol (**2**), along with thirteen known compounds, (1*R*,3*E*,7*E*,11*S*,12*R*)-dolabella-3,7-dien-18-ol (**3**) [2][6], aglaxiflorin D (**4**) [7], (±)-odorinol (**5** and **6**) and (±)-odorine (**7** and **8**) [3][8], β-sitosterol palmitate (**9**) [9], sitoindoside I (**10**) [10], β-sitosterol (**11**), (3β,5α,8α)-5,8-epidioxyergosta-6,22-dien-3-ol (**12**) [11], 2,3-dihydro-5-hydroxy-4',7-dimethoxyflavone (**13**) [12], glycerol 1-hexadecanoate (**14**) [13], and 4-methoxybenzoic acid (**15**) were isolated (*Fig.*). Compounds **1**–**3**, dolabellane-type diterpenoids, were isolated from higher plants for the first time. The present paper describes the isolation and identification of the new compounds **1** and **2**.

Results and Discussion. – Air-dried whole plants (7 kg) were crushed and extracted with MeOH at room temperature. The viscous MeOH extract was partitioned between H₂O and AcOEt, and the AcOEt fraction was subjected to column chromatography (silica gel) to give **1** (25 mg) and **2** (22 mg).

Judging from its HR-ESI-MS, compound **1** has the molecular formula C₂₀H₃₄O₂. Its IR spectrum showed absorption bands for OH groups (3396 cm⁻¹) and C=C bonds (1638 cm⁻¹). A comparison of the ¹H- and ¹³C-NMR data of **1** (*Table*) with those of the known compound **3** [2][6] suggested that **1** is a dolabelladien-18-ol deriva-

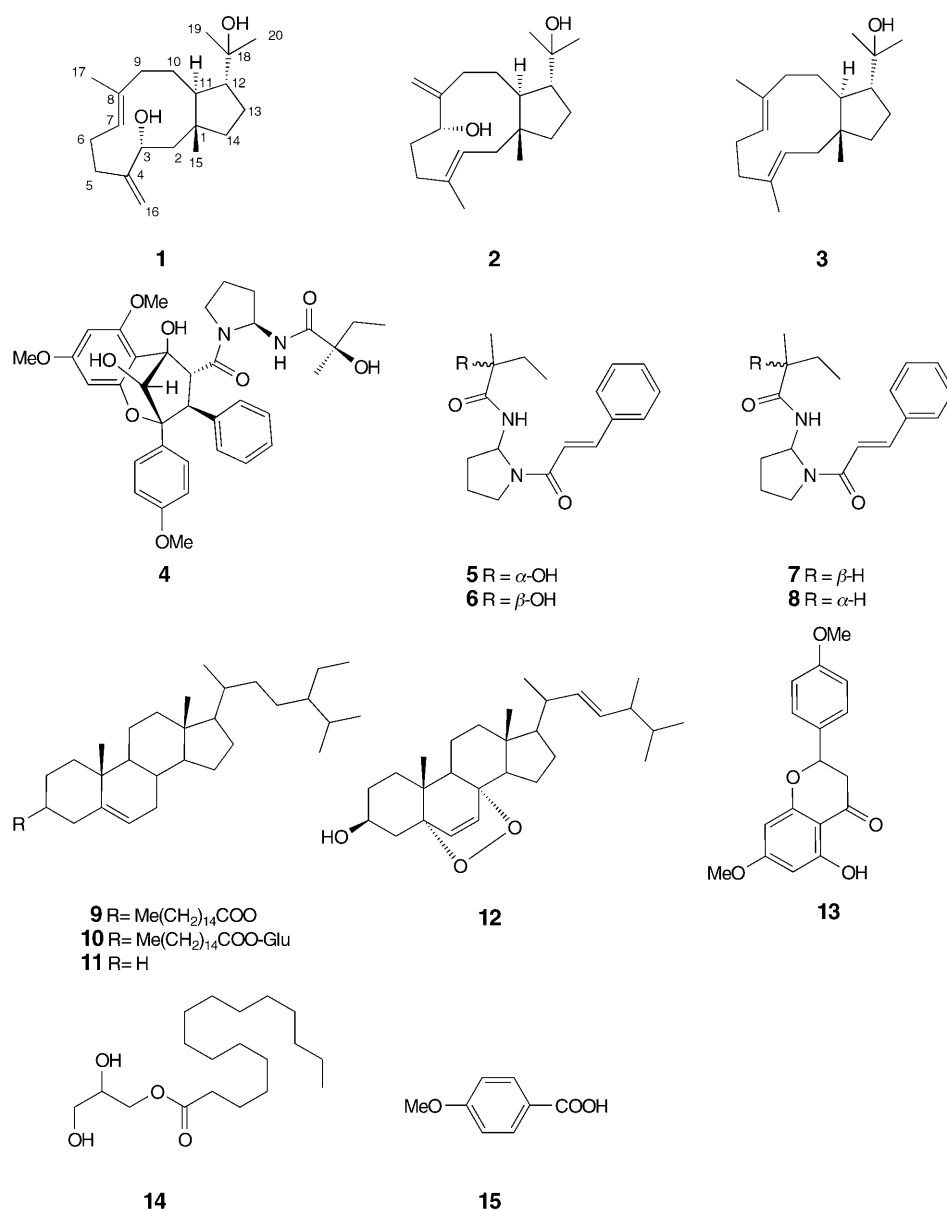


Figure. Compounds **1–15** isolated from *Aglaia odorata*. Trivial atom numbering.

tive. HMBC, ROESY and HMQC data established the structure of **1** as (1*R*,3*R*,7*E*,11*S*,12*R*)-dolabella-4(16),7-diene-3,18-diol.

The ¹H-NMR of **1** showed 4 tertiary Me groups at δ (H) 1.67, 1.27, 1.24, and 1.02 (4*s*). ¹³C-NMR and DEPT spectra displayed signals for 20 C-atoms, namely 4 tertiary Me groups (δ (C) 29.3, 24.8, 20.5, and 16.1 (4*q*)), 8 CH₂

Table. ^1H - and ^{13}C -NMR and ^1H , ^{13}C -HMBC Data (CDCl_3) of Compounds **1** and **2**. δ in ppm, J in Hz.

	1			2		
	$\delta(\text{H})^{\text{a}}$	$\delta(\text{C})^{\text{b}}$	^1H , ^{13}C -HMBC	$\delta(\text{H})^{\text{c}}$	$\delta(\text{C})^{\text{d}}$	^1H , ^{13}C -HMBC
C(1)		43.7 (s)			47.4 (s)	
CH ₂ (2)	2.58 (<i>dd</i> , $J=13.0, 8.0$), 1.45 (<i>dd</i> , $J=13.0, 0.9$)	47.7 (<i>t</i>)	C(3), C(11), C(14), C(15)	2.10 (<i>dd</i> , $J=13.0, 9.6$), 1.70 (<i>dd</i> , $J=13.0, 2.4$)	43.0 (<i>t</i>)	C(3), C(11), C(14), C(15)
H–C(3)	4.44 (<i>dd</i> , $J=8.0, 0.9$)	69.3 (<i>d</i>)	C(2), C(5), C(16)	5.36 (<i>dd</i> , $J=9.6, 2.4$)	124.0 (<i>d</i>)	C(2), C(5), C(16)
C(4)		155.5 (s)			135.6 (s)	
CH ₂ (5)	2.37–2.29 (<i>m</i>)	34.0 (<i>t</i>)	C(3), C(6), C(7), C(16)	2.09–2.02 (<i>m</i>)	37.4 (<i>t</i>)	C(3), C(6), C(7), C(16)
CH ₂ (6)	2.24–2.21 (<i>m</i>)	28.5 (<i>t</i>)	C(5), C(7)	2.27–2.22 (<i>m</i>), 2.05–1.99 (<i>m</i>)	34.4 (<i>t</i>)	C(5), C(7)
H–C(7)	5.39 (<i>dd</i> , $J=8.5, 6.5$)	126.5 (<i>d</i>)	C(5), C(6), C(9), C(17)	3.85 (<i>br. d</i> , $J=6.4$)	74.7 (<i>d</i>)	C(5), C(6), C(9), C(17)
C(8)		134.4 (s)			153.6 (s)	
CH ₂ (9)	2.21–2.18 (<i>m</i>), 2.11–2.07 (<i>m</i>)	37.8 (<i>t</i>)	C(7), C(10), C(11), C(17)	1.82–1.78 (<i>m</i>)	35.5 (<i>t</i>)	C(7), C(10), C(11), C(17)
CH ₂ (10)	1.84–1.80 (<i>m</i>), 1.59–1.54 (<i>m</i>)	29.8 (<i>t</i>)	C(9), C(11), C(12)	2.03–1.98 (<i>m</i>), 1.44–1.40 (<i>m</i>)	29.7 (<i>t</i>)	C(9), C(11), C(12)
H–C(11)	1.71–1.67 (<i>m</i>)	48.4 (<i>d</i>)	C(2), C(9), C(10), C(11), C(12), C(14)	1.63–1.57 (<i>m</i>)	44.5 (<i>d</i>)	C(2), C(9), C(10), C(11), C(12), C(14)
H–C(12)	1.87–1.83 (<i>m</i>)	59.7 (<i>d</i>)	C(10), C(11), C(13), C(14)	1.67–1.62 (<i>m</i>)	59.9 (<i>d</i>)	C(10), C(11), C(13), C(14)
CH ₂ (13)	1.39–1.34 (<i>m</i>), 1.69–1.64 (<i>m</i>)	25.0 (<i>t</i>)	C(11), C(12), C(14)	1.33–1.28 (<i>m</i>), 1.66–1.61 (<i>m</i>)	27.4 (<i>t</i>)	C(11), C(12), C(14)
CH ₂ (14)	1.52–1.48 (<i>m</i>), 1.46–1.41 (<i>m</i>)	42.0 (<i>t</i>)	C(12), C(13), C(14), C(15)	1.45–1.40 (<i>m</i>), 1.35–1.29 (<i>m</i>)	44.7 (<i>t</i>)	C(12), C(13), C(14), C(15)
Me(15)	1.02 (s)	20.5 (<i>q</i>)	C(2), C(11), C(14)	1.05 (s)	22.1 (<i>q</i>)	C(2), C(11), C(14)
CH ₂ (16) or Me(16)	4.99 (s), 4.87 (s)	108.3 (<i>t</i>)	C(3), C(5)	1.64 (s)	15.8 (<i>q</i>)	C(3), C(5)
Me(17) or CH ₂ (17)	1.67 (s)	16.1 (<i>q</i>)	C(7), C(9)	5.18 (s), 5.16 (s)	108.2 (<i>t</i>)	C(7), C(9)
C(18)		71.8 (s)	C(11), C(12), C(13), C(19), C(20)		73.1 (s)	C(11), C(12), C(13), C(19), C(20)
Me(19)	1.24 (s)	24.8 (<i>q</i>)	C(12), C(20)	1.18 (s)	25.2 (<i>q</i>)	C(12), C(20)
Me(20)	1.27 (s)	29.3 (<i>q</i>)	C(12), C(19)	1.23 (s)	31.9 (<i>q</i>)	C(12), C(19)

^a) 500 MHz. ^b) 125 MHz. ^c) 400 MHz. ^d) 100 MHz.

groups ($\delta(\text{C})$ 108.3, 47.7, 42.0, 37.8, 34.0, 29.8, 28.5, and 25.0 (*8t*)), 4 CH groups ($\delta(\text{C})$ 126.5, 69.3, 59.7, 48.4 (*4d*)), one of which was an OCH group, 4 quaternary C-atoms ($\delta(\text{C})$ 43.7, 71.8, 134.4, and 155.5), one of which was O-substituted, and 2 C=C ($\delta(\text{C})$ 108.3 (*t*), 126.5 (*d*), 134.4 (*s*), and 155.5 (*s*)), one of them representing an exocyclic CH₂ unit. In the HMBC plot of **1**, cross-peaks between $\delta(\text{H})$ 4.44 (*dd*, $J=8.0, 0.9$ Hz) and $\delta(\text{C})$ 155.5 (*s*), 108.3 (*t*), 47.7 (*t*), 43.8 (*s*, C(1)), and 34.0 (*t*) showed that $\delta(\text{H})$ 4.44 must be assigned to H–C(3), $\delta(\text{C})$ 108.3, 155.5, 47.7, and 34.0 were assigned to C(16), C(4), C(2), and C(5), respectively, and the terminal C=C bond was suggested to be between C(4) and C(16). HMBC Correlations between $\delta(\text{H})$ 5.39 (*dd*, $J=8.5, 6.5$ Hz) and $\delta(\text{C})$ 37.8 (*t*), 34.0 (*t*, C(5)), 28.5 (*t*), and 16.1 (*q*, C(17)) placed the other C=C bond between C(7) and C(8). Interactions between $\delta(\text{H})$ 1.85 (*d*, H–C(12)) and $\delta(\text{H})$ 1.58 (*m*, H–C(10)), 1.02 (*s*, H–C(15)), and 4.44 (H–C(3)) in the ROESY

experiment indicated that OH–C(3) and H–C(11) are α -oriented, and that H–C(12) is β -oriented [6] [14] [15]. The (*E*)-configuration of the C(7)=C(8) bond was substantiated by a ROESY resonance between δ (H) 2.24–2.21 (*m*, CH₂C(6)) and δ (H) 1.67 (*s*, Me(17)).

Compound **2** also possesses a molecular formula C₂₀H₃₄O₂ as determined by the HR-ESI-MS. The ¹H- and ¹³C-NMR (*Table*) and MS data of **2** showed similarities to those of **1**, except for the locations of the second OH group and the C=C bonds. Detailed spectral analyses established the structure of **2** as (1*R*,3*E*,7*R*,11*S*,12*R*)-dolabella-3,8(17)-diene-7,18-diol.

Compound **2** showed ¹³C-NMR signals for 2 olefinic bonds, one at (δ (C) 108.2 (*t*) and 153.6 (*s*)), while the chemical shifts of the other were changed from δ (C) 126.5 (*d*) and 134.4 (*s*) in **1** to δ (C) 124.0 (*d*) and 135.6 (*s*) in **2**, and that of the OCH group was shifted in from δ (C) 69.3 in **1** to 74.7 in **2**. HMBC Cross-peaks between δ (H) 1.05 (*s*, Me(15)) and δ (C) 47.4 (*s*, C(1)), 44.7 (*t*, C(14)), 44.5 (*d*, C(11)), and 43.0 (*t*, C(2)), and between δ (H) 5.36 (*dd*, *J* = 9.6, 2.4 Hz) and δ (C) 43.0 (*t*, C(2)), 37.4 (*t*, C(5)), 15.8 (*q*, C(16)) established that the trisubstituted C=C bond of **2** is positioned between C(3) and C(4). Correlations between δ (H) 3.85 (*br. d*, *J* = 6.4) and δ (C) 153.6 (*s*), 108.2 (*t*), 37.4 (*t*, C(5)), and 35.5 (*t*) suggested that the exocyclic CH₂=C bond is situated at C(8), next to the OH group at C(7). The NOE interactions (δ (H) 1.64 (H–C(12)) with 1.05 (Me(15)), 3.85 (H–C(7)), and 5.36 (H–C(3)), and δ (H) 1.61 (H–C(11)) with 1.18 (Me(19)) and 1.23 (Me(20)) indicated that H–C(11) and OH–C(7) are α -oriented. The (*E*)-configuration of the C(3)=C(4) bond was deduced by a ROESY correlation between δ (H) 5.36 (*dd*, *J* = 9.6, 2.4 Hz, H–C(3)) and δ (H) 2.09–2.02 (*m*, CH₂(5)).

Compounds **1** and **2** were dissolved in CHCl₃, AcOEt, EtOH, or Me₂CO under acid condition, and the solutions were mixed with silica gel and placed in a water bath at 60° for 3 days. There was not any change in all solutions, as established by HPTLC monitoring with **1** as control. So, **1** should be a natural product formed from a plant secondary metabolite. A biosynthesis of compounds **1** and **2** is proposed in the Scheme: Either of the C=C bonds of **3** is oxidized, and the resulting epoxide is opened to form the allylic alcohol **1** or **2**.

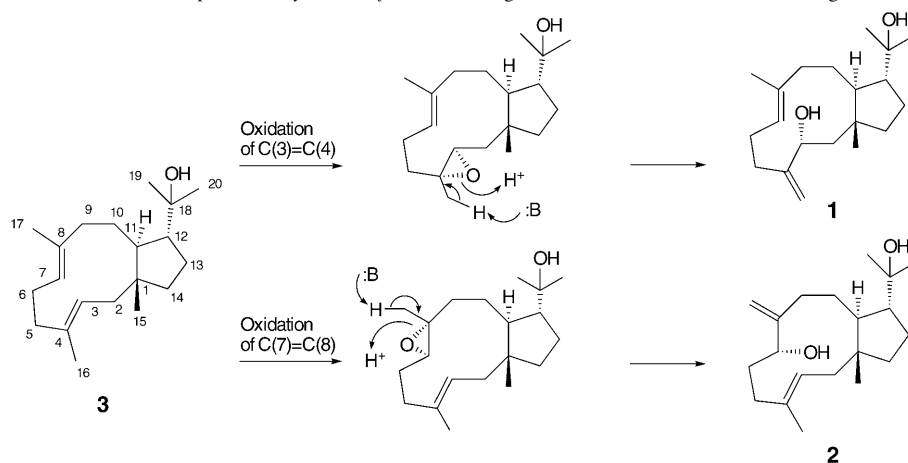
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Experimental Part

General. Column chromatography (CC): silica gel (200–300 mesh) from the Qindao Marine Chemical Factory, Qindao, China. TLC: silica gel GF₂₅₄ from the Qindao Marine Chemical Factory; detection by spraying with 5% H₂SO₄ soln. M.p.: XRC-1 micromelting apparatus; uncorrected. Optical rotations: Horiba SEAP-300 spectropolarimeter. IR Spectra (KBr): Bio-Rad FTS-135 infrared spectrophotometer; in cm⁻¹. ¹H-NMR, ¹³C-NMR, and 2D-NMR Spectra: Bruker AM-400 and DRX-500-MHz NMR spectrometer; SiMe₄ as internal standard δ in ppm, *J* in Hz. MS: VG-Autospec-3000 spectrometer; in *m/z* (rel.%).

Plant Material. The whole plant of *Aglaia odorata* was collected in Kunming city, Yunnan province, People's Republic of China, in September, 2003.

Extraction and Isolation. Air-dried whole plants (7.0 kg) were crushed and extracted with MeOH at r.t. (4 × 48 h). After evaporation of the MeOH, the viscous residue was extracted with AcOEt. The resulting material (310 g) was adsorbed on silica gel and subjected to CC (prepacked Si gel (2.0 kg) column, CHCl₃ → CHCl₃/Me₂CO 1:1); Fractions I–VIII, by TLC (silica gel GF₂₅₄) monitoring. Fr. II (26.0 g) was subjected to CC (silica gel (400 g), petroleum ether/Me₂CO 9:1 and petroleum ether/CHCl₃ 6:1): **3** (100 mg). Fr. III (30.0 g) was subjected to CC (silica gel (600 g), petroleum ether/Me₂CO 3:1): **1** (25 mg), **2** (22 mg), **7** (32 mg), **8** (12 mg), and **11**

Scheme. Proposed Biosynthesis of **1** and **2** in *Aglaia odorata*. Trivial atom numbering.

(1.0 g). *Fr. IV* (25.0 g) was purified by repeated CC (silica gel (280 g), petroleum ether/AcOEt, petroleum ether/CHCl₃); *Fr. IV.a* and *Fr. IV.b*. *Fr. IV.a* (2.5 g) was further purified by CC (*RP*₁₈ gel (80 g), MeOH/H₂O 8:2 → 9:1): **5** (120 mg), **6** (34 mg), and **15** (8 mg). Repeated CC (*RP*₁₈ gel (80 g), MeOH/H₂O 7:3 → 8:2) of *Fr. IV.b* (1.0 g) afforded **4** (15 mg). *Fr. V* (25.5 g) was subjected to CC (silica gel (400 g), petroleum ether/Me₂CO 8:2 → 7:3): **9** (95.6 mg), **10** (76.5 mg), and **12** (12 mg). Compound **13** was crystallized from *Fr. VI* (18.6 g), and the mother liquor was subjected to CC (silica gel (300 g), petroleum ether/Me₂CO (3:1 → 2:1) and CHCl₃/Me₂CO 5:1 → 4:1): **13** (8 mg) and **14** (10 mg), resp.

(1*R*,3*R*,7*E*,11*S*,12*R*)-Dolabella-4(16),7-diene-3,18-diol (= (1*R*,3*aR*,5*R*,9*E*,12*aS*)-1,2,3,3*a*,4,5,6,7,8,11,12,12*a*-Dodecahydro-5-hydroxy- α , α ,3*a*,10-tetramethyl-6-methylenecyclopentacycloundecene-1-methanol; **1**). Colorless prisms from Me₂CO. M.p. 133–134°. [α]_D²⁵ = –80.6 (*c* = 0.60, MeOH). IR (KBr): 3396, 2943, 1638, 1449. ¹H- and ¹³C-NMR: Table. EI-MS: 306 (1, *M*⁺), 288 (10), 273 (8), 255 (7), 245 (18), 227 (17), 161 (38), 149 (45), 135 (52), 121 (75), 107 (70), 95 (100). HR-EI-MS: 329.2465 ([*M* + Na]⁺, C₂₀H₃₄O₂Na⁺, calc. 329.2456).

(1*R*,3*E*,7*R*,11*S*,12*R*)-Dolabella-3,8(17)-diene-7,18-diol (= (1*R*,3*aR*,5*E*,9*R*,12*aS*)-1,2,3,3*a*-4,7,8,9,10,11,12,12*a*-Dodecahydro-9-hydroxy- α , α ,3*a*,6-tetramethyl-10-methylenecyclopentacycloundecene-1-methanol; **2**). Colorless prisms from Me₂CO. M.p. 78–80°. [α]_D²⁵ = –38.5 (*c* = 0.63, MeOH). IR (KBr): 3424, 2944, 1646, 1450. ¹H- and ¹³C-NMR: Table. EI-MS: 306 (48, *M*⁺), 288 (55), 273 (47), 255 (35), 245 (68), 227 (89), 201 (48), 147 (75), 135 (72), 107 (90), 95 (100). HR-EI-MS 329.2462 ([*M* + Na]⁺, C₂₀H₃₄O₂Na⁺; calc. 329.2456).

(1*R*,3*E*,7*E*,11*S*,12*R*)-Dolabella-3,7-diene-18-ol (= (1*R*,3*aR*,5*E*,9*E*)-1,2,3,3*a*,4,7,8,11,12,12*a*-Decahydro- α , α ,3*a*,6,10-pentamethylcyclopentacycloundecene-1-methanol; **3**). Colorless oil. ¹H-NMR (CDCl₃): 4.98 (*t*, *J* = 6.8, H–C(3)); 4.86 (*t*, *J* = 6.8, H–C(7)); 2.14–2.08 (*m*, CH₂(2), CH₂(5), CH₂(6), CH₂(9)); 1.69 (*m*, H–C(12), H–C(11), CH₂(10)); 1.52 (*s*, Me(16), Me(17)); 1.35–1.33 (*m*, CH₂(13), CH₂(14)); 1.21, 1.23 (2*s*, Me(19), Me(20)); 0.97 (*s*, Me(15)). ¹³C-NMR (CDCl₃): 135.4 (*s*, C(8)); 132.9 (*s*, C(4)); 126.5 (*d*, C(7)); 124.6 (*d*, C(3)); 73.2 (*s*, C(18)); 60.3 (*d*, C(12)); 46.6 (*s*, C(1)); 41.8 (*d*, C(11)); 41.1 (*t*, C(14)); 39.5 (*t*, C(2)); 39.3 (*t*, C(5)); 38.7 (*t*, C(9)); 31.5 (*t*, C(10)); 30.7, 26.4 (2*q*, C(19), C(20)); 26.5 (*t*, C(13)); 24.9 (*t*, C(6)); 23.2 (*q*, C(15)); 16.4 (*q*, C(17)); 16.3 (*q*, C(16)). EI-MS: 290 (10, *M*⁺).

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