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SESQUITERPENE LACTONES FROM *ONOPORDON LACONICUM* AND *O. SIBTHORPIANUM*

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Key Word Index—*Onopordon laconicum*; *O. sibthorpianum*; Compositae; sesquiterpene lactones; elemanolides; elemane derivatives; eudesmanolides; germacranolides; guaianolides.

Abstract—The investigation of two *Onopordon* species afforded, in addition to known sesquiterpene lactones and other constituents, six new germacranolides and a new eudesmanolide. The structures were elucidated by spectroscopic methods. © 1997 Elsevier Science Ltd. All rights reserved

INTRODUCTION

In continuation of our work on *Onopordon* sp. (Compositae, tribe Cynareae, subtribe Carduinae) [1–6] we have now investigated specimens of two Greek plants, *Onopordon laconicum* Heldr. and Sart. ex Rouy [7] and *O. sibthorpianum* Boiss. and Heldr. [8]. Phytochemical studies of this genus have led to the isolation of flavonoids [1, 3, 6, 9], sesquiterpene lactones [5, 6, 10–14] and several unusual hydroxyester sesquiterpene derivatives [2, 6, 14, 15].

We now report the isolation of the germacranolides **1–2** and **13–27**, the guaianolides **3–7**, the elemanolides **8–10**, the elemanolide derivatives **11–12** and the eudesmanolides **28–31** as well as coniferaldehyde, arctigenin [16] and pinoresinol [17]. Compounds **16**, **18**, **23**, **25–27** and **31** are described for the first time in this paper, and their structures were elucidated by extensive highfield NMR studies.

RESULTS AND DISCUSSION

The aerial parts of *O. laconicum* afforded the costunolide derivatives 15-hydroxycostunolide (**1**) [18, 19] and 11β,13-dihydro-15-hydroxycostunolide (**2**) [18]; the guaianolides 4β,15-dihydrodehydrozaluzanin C (**3**) [20], tetrahydrodehydrozaluzanin C (**4**) [20], isoamberboin (**5**) [21, 22], zaluzanin C (**6**) [23, 24] and 11β,13-dihydrozaluzanin C (**7**) [25]; the elemanolides melitensin (**8**) [2, 26, 27], **9** [2, 11, 13] and **10** [6]; the germacranolides onopordopicrin (**13**) [2, 10, 12, 28], **14** [29, 30], **15** [29], **17** [12, 30] **19** [6], **20** [31], **22** [29] and **24** [29]; the eudesmanolides **28** [14] and **30** [6] and the new germacranolides **16**, **18**, **23**, **25** and **26**. Though guaianolides are common metabolites of other Compositae [32, 33], this is the first time that its presence is reported in *Onopordon* sp.

In the aerial parts of *O. sibthorpianum* onopordopicrin (**13**) was the main sesquiterpene lactone. Minor components isolated from this plant were the known elemanolide **10** and the elemane derivatives **11** [2, 15] and **12** [6]; the known germacranolides **14**, **15**, **20**, 11α,13-dihydrosalonitenolide (**2**) [31], **22**, **24**; the known eudesmanolides **28**, **29** [14] and **30** [6] and four new compounds, the germacranolides **16**, **23**, **27** and the eudesmanolide **31**. The new compounds **16** and **23** were isolated from both plants.

We also report in this paper spectroscopic data for several known compounds, as the high resolution (400 MHz) ^{1}H NMR spectra of **1**, **2**, **17** and **22** and the ^{13}C NMR of compounds **1**, **10**, **22** and **28**. ^{1}H NMR spectra of compounds **1** and **2** have previously been reported [18, 19] but not in chloroform-*d*, the usual solvent for this type of compound. On the other hand, the ^{1}H NMR data reported in the literature for compounds **17** [12] and **22** [29] are not complete as they were isolated as mixtures with other compounds. ^{13}C NMR data of compounds **1**, **10**, **22** and **28** have not been previously reported in the literature.

The mass spectrum of compound **16** showed a molecular peak at *m/z* 365.1970 $[M]^+$ which agreed with the molecular formula $C_{20}H_{28}O_6$. The features of the ^{1}H and ^{13}C NMR spectra suggested a germacrane ring with two double bonds at $\Delta^{1(10)}$ and Δ^4. The broadened doublet of doublets at δ 4.97 (J = 7.2 and 9.6

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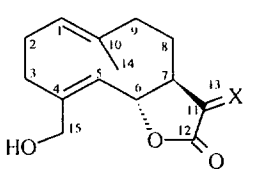

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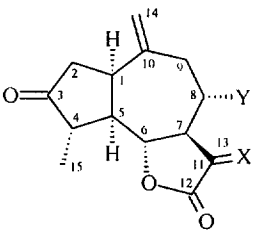
2 X = βH,αMe



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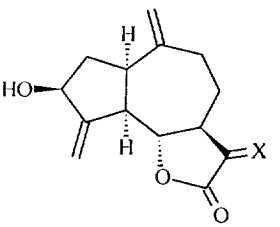

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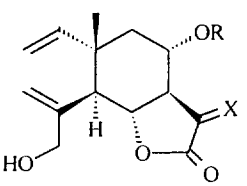
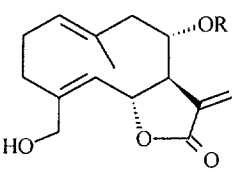


8 R = H X = βH,αCH_3

9 R = A X = CH_2

10 R = B X = CH_2



13 R = A

14 R = B

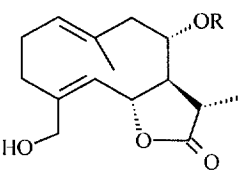
15 R = C

16 R = D

17 R = E

18 R = F

19 R = G



20 R = H, 11βH

21 R = H, 11αH

22 R = A, 11βH

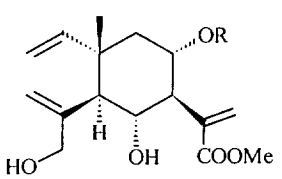
23 R = B, 11βH

24 R = C, 11βH

25 R = D, 11βH

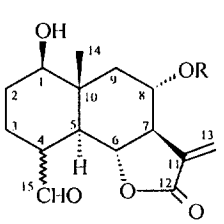
26 R = E, 11βH

27 R = I, 11βH



11 R = A

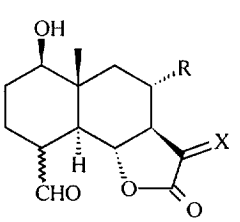
12 R = B



28 R = A, 4αH

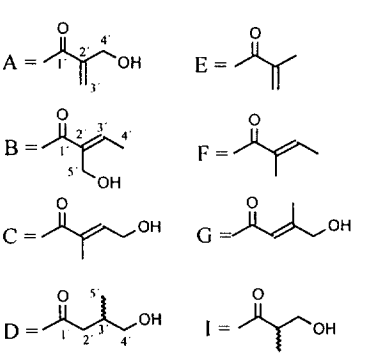
29 R = A, 4βH

30 R = B, 4αH



31 4αH, X = βH,αMe, R = OH

32 4βH, X = CH_2, R = H



Hz) and the broadened doublet at δ 4.80 (J = 10.0 Hz) were assigned to H-1 and H-5, respectively. In the ^{13}C NMR spectrum the signals at δ 129.5, 143.8, 128.7 and 132.6 were assigned to C-1, C-4, C-5 and C-10, respectively. From a pair of doublets at δ 4.29 and 4.08 (J = 14.2 Hz) a hydroxymethyl group (at δ 61.4 in the ^{13}C NMR spectrum) as substituent at C-4 was evident. The presence of an oxygenated group at C-6α (δ 76.6) was inferred from the double doublet at δ 5.06 (J = 9.2 and 10.0 Hz) which showed coupling with the signals at δ 4.80 (H-5) and δ 3.01 (H-7). An α-methylene-γ-lactone (δ 169.7 in the ^{13}C NMR spectrum, and 1760 cm^{-1} in the IR spectrum) and a methylene at δ 135.3 (C-11) and 125.8 (C-13) and at δ 6.34 and 5.87 (H-13) were also evident.

An ester moiety was located at C-8α (δ 72.5) as was deduced from the position and pattern of the signal at δ 5.08 (*br dd*, J = 10.0 and 11.6 Hz). The identity of the ester side chain was inferred from the presence of a multiplet at δ 2.24-2.14 (1H) which was coupled with two double doublets of a methylene group [δ 2.47 (J = 6.8 and 15.6 Hz); δ 2.25 (J = 6.8 and 15.6 Hz)], a methyl doublet (δ 1.97, J = 6.8 Hz) and a hydroxymethyl moiety [δ 3.58 (*dd*, J = 4.8 and 10.4 Hz); δ 3.46 (*dd*, J = 6.4 and 10.4 Hz)]. The chemical shifts and the pattern of these signals strongly suggested the presence of a 4-hydroxy-3-methylbutanoyl group. This was confirmed by the signals at δ 172.1 (C), 67.1 (CH_2), 38.4 (CH_2), 32.7 (CH) and 16.7 (CH_3) in the ^{13}C NMR spectrum and the presence in the mass spectrum of peaks at 246 $[M\text{-}RCOOH]^+$, 119 $[RCOOH_2]^+$, 101 $[RCO]^+$ and a base peak at 99 $[RCOO\text{-}H_2O]^+$. Full analysis of the NMR spectrum by decoupling experiments led to structure **16**, a new 8α-(4-hydroxy-3-methylbutanoyl) derivative of salonitenolide (**16**, R = H).

Compound **18** was also identified as an 8α-acyl-derivative of salonitenolide, since its IR, ^1H and ^{13}C NMR spectra were similar to those of compound **16** except for the signals due to the 8-acyl side-chain in the NMR spectra. Compound **18** showed signals of a proton at δ 6.86 (*dq*, J = 1.2 and 7.6 Hz) and two methyl groups at δ 1.83 (*d*, J = 7.6 Hz) and δ 1.84 (*br d*, J = 1.2 Hz) in the ^1H NMR spectrum, which suggested the presence of a tiglate moiety [34, 35]. This was confirmed by the signals at δ 166.7 (C), 128.4 (C), 138.6 (CH), 14.6 and 12.8 (two CH_3) in the ^{13}C NMR spectrum and by a base peak at 83 $[RCO]^+$ in the mass spectrum.

The ^1H NMR spectra of compounds **22–27** suggested structures of 8-acyl derivatives of 11β,13-dihydrosalonitenolide (**20**). Compounds **22** and **24** were identified as the 11β,13-dihydroderivatives of onopordopicrin (**13**) and of compound **15**, respectively, which have been previously reported in *Centaurea glomerata* [29]. Compound **23** presented ^1H and ^{13}C NMR spectra which were similar to those of compound **14** [29, 30] except for the absence of the typical signals of the α-methylene group. Instead it presents in the ^1H NMR spectrum a methyl doublet at δ 1.36 (J = 6.8 Hz) coupled to a new double quadruplet at δ 2.55 (1H, J = 6.8 and 11.2 Hz), assigned to H-13 and H-11, respectively. The stereochemistry at C-11 was deduced to be 11βH by the *trans*-diaxial disposition for H-7 and H-11 (J = 11.2 Hz) and the chemical shifts in the ^{13}C NMR spectrum of C-11 (δ 40.2) and C-13 (δ 17.0) [36, 27]. Full analysis of the ^1H NMR spectrum by decoupling experiments and ^1H-^{13}C correlation (HMQC) as well as the presence of the usual peaks at the mass spectrum confirmed for compound **23** the structure of an 11β,13-dihydroderivative of compound **14**. In a similar way the new compounds **25** and **26** were identified as the 11β,13-dihydroderivatives of compounds **16** and **17**, respectively.

Compound **27** showed the typical signals of an 8α-acyl derivative of 11β,13-dihydrosalonitenolide also, with ^1H and ^{13}C NMR spectra very similar to those of compound **22**. The characteristics of the ester side-chain were inferred from the presence of the signals of a 3-hydroxy-2-methylpropanoyl group in its NMR spectra. It appeared in the ^1H NMR spectrum as a double double quadruplet a δ 2.68 (1H, J = 4.6, 7.2 and 7.6 Hz) which was coupled to a doublet at δ 1.18 (3H, J = 7.2 Hz) and two double doublets at δ 3.76 (1H, J = 7.6 and 10.8 Hz) and δ 3.71 (1H, J = 4.6 and 10.8 Hz). These signals were assigned to H-2′, H-4′, H-3′a and H-3′b, respectively. This was confirmed by the four carbons at δ 174.8 (C), 64.4 (CH_2), 41.9 (CH) and 13.5 (CH_3) in the ^{13}C NMR spectrum which were assigned to C-1′, C-3′, C-2′ and C-4′, respectively. Full analysis for the ^1H NMR spectrum by decoupling experiments led to structure **27**, a dihydroderivative of compound **22**.

The ^1H and ^{13}C NMR spectra of compound **31** ($C_{14}H_{22}O_4$ $[M\text{-}CO]^+$, m/z 254.1506) showed typical signals that suggested an eudesmane framework with features common to those of compound **28** [14] and **30** [6], two previously reported 8-acyl-4-*epi*-derivatives of sonchucarpolide (**32**) [38]. For compound **31** the coupling patterns and the magnitude of the coupling constants of H-1, H-4 and H-5 to H-8 were in full agreement with a H-1α stereochemistry for C-1, a *cis*-disposition of H-4/H-5 and a *trans*-disposition of H-5/H-6, H-6/H-7 and H-7/H-8 as in **28** and **30**. The main differences on the ^1H NMR spectra were the absence of the signals due to the α-methylene-γ-lactone and the 8-acyl side-chain, as well as the high field shift for H-8 (δ 3.97 v δ 5.36 in **28** [14] or δ 5.31 in **30** [6]). The presence of a double quadruplet at δ 2.64 (1H, J = 6.8 and 12.0 Hz) coupled to a methyl doublet at δ 1.40 (J = 6.8 Hz) and to the multiplet of H-7 (δ 1.75–1.65) were assigned to H-11 and H-13, respectively, and indicated the presence of an α-methyl-γ-lactone moiety. The stereochemistry at C-11 was deduced to be 11βH by the *trans*-diaxial coupling for H-7 and H-11 (J = 12.0 Hz) and the chemical shifts in the ^{13}C NMR spectrum of C-11 (δ 41.7) and C-13 (δ 14.3) [36, 37]. We have assigned to compound **31** the structure of an 11β, 13-dihydro-8α-hydroxy-4-*epi* derivative of sonchucarpolide (**32**) [38].

EXPERIMENTAL

General. NMR: 400, 300 MHz (^{1}H) and 75 MHz (^{13}C). Vacuum liquid chromatography (VLC): silica gel (Merck; 43–63 μm); Flash chromatography (FC): silica gel (SDS; 40–63 μm), gradient elution with the solvent mixts indicated in each case; HPLC: Merck Lichrospher 100RP-18 (250 × 10 mm).

Plant material. Aerial parts of *O. laconicum* were collected in Neapolis, Peloponese (Greece), in July 1992 and *O. sibthorpianum* in Atiki (Greece) in May 1994. Both plants were authenticated by Mr Theophanis Constantinidis (Institute of Systematic Botany, University of Patras). Voucher specimens are deposited in the herbarium of the above mentioned Institute (*O. laconicum* no. 4893, *O. sibthorpianum* no. 4894).

Extraction and chromatography. The fresh plant material (*O. laconicum*, 2.25 kg; *O. sibthorpianum*, 4.5 kg) was finely ground and extracted at room temp. with hexane–Et_2O–MeOH (1:1:1). The extract was washed with brine, the aq. layer re-extracted with EtOAc, and the organic layer dried with Na_2SO_4 and concd. under red. pres. The residue (*O. laconicum*, 22 g; *O. sibthorpianum*, 20 g) was prefractionated by VLC [39] on silica gel, using hexane–EtOAc–Me_2CO mixts. of increasing polarity as eluents to give several frs. Frs B (hexane–EtOAc, 1:1), C (hexane–EtOAc, 1:3) and D (EtOAc) were subjected to further chromatographic sepns as described below.

O. laconicum. FC of fr B (hexane–EtOAc, 9:1 to 0:10) followed by HPLC (MeOH–H_2O, 3:2) allowed the isolation of **4** (2 mg), **3** (1.5 mg), arctigenin (4 mg), **6** and **7** (4.5 mg), **1** (12.5 mg), **2** (4 mg), **17** (6.5 mg), **26** (1.5 mg) and **18** (5 mg). FC of fr. C (CH_2Cl_2–MeOH, 10:0 and 9:1) followed when necessary by HPLC (MeOH–H_2O, 3:2 or 4:3) allowed the isolation of pinoresinol (5 mg), arctigenin (17 mg), **5** (1.5 mg), **9** (5 mg), **10** (3 mg), **1** (2 mg), **2** (2 mg), **28** (3 mg), **13** (29 mg), **22** (5.5 mg), **14** (2 mg), **24** (1 mg) and **16** (5 mg).

VLC of fr. D (CH_2Cl_2–MeOH 10:0 to 9:1) allowed the isolation of a mixt. of **14** and **9** (*ca* 320 mg, not sepd), **20** (197 mg) and a complex mixt. which was sepd by further VLC (hexane–EtOAc, 9:1 to 0:10) followed by HPLC (MeOH–H_2O, 4:3) to yield **8** (3 mg), **18** (9 mg), **30** (57 mg), **20** (22 mg), **9** (1 mg), **13** (17 mg), **10** (6 mg), **15** (12 mg), **19** (4 mg), **14** (62 mg), **24** (2.5 mg), **16** (5.5 mg), **23** (33.5 mg) and **15** (2 mg).

O. sibthorpianum. FC of fr. B (CH_2Cl_2–MeOH 10:0 to 9:1) followed by HPLC (MeOH–H_2O, 2:1) allowed the isolation of coniferaldehyde (2.5 mg) and arctigenin (29 mg).Onopordopicrin (**13**) was the major component in frs C and D [^{1}H NMR]. In order to isolate the minor components they were subjected to further FC (CH_2Cl_2–MeOH or hexane–EtOAc) and when necessary by HPLC (MeOH–H_2O, 2:1, 4:3 or 1:1). This process allowed the isolation of arctigenin (79 mg), **31** (9.5 mg), **29** (8.5 mg), **28** (39 mg), **30** (6 mg), **20** (6 mg), **9** (1.5 mg), **11** (11 mg), **12** (3.5 mg), **14** (63 mg), **15** (2 mg), **21** (1.5 mg), **22** (8.5 mg), **27** (5 mg), **23** (7 mg), **24** (11 mg), **16** (2 mg), **23** (2.5 mg) and **13** (1.297 g). An aliquot sample (28 mg) of a complex mixt. (*ca* 840 mg) was analysed by HPLC (MeOH–H_2O, 4:3) which allowed the isolation of **28** (2 mg), **9** (1 mg), **13** (8.5 mg), **15** (1.5 mg) and **14** (3 mg).

Compound **16**. Oil; $[\alpha]_D^{22}$ +28.8° ($CHCl_3$, *c* 0.545); IR ν_{max}^{NaCl} cm^{-1}: 3500–3300, 1760, 1710, 1650; EIMS *m/z* (rel. int.): 365.1970 $[M+H]^+$ (4) ($C_{20}H_{29}O_6$ requires 365.1965), 364 $[M]^+$ (2), 248 [365-RCOO]$^+$ (21), 247 [364-RCOO]$^+$ (12), 246 [364-RCOOH]$^+$ (13), 119 $[RCOOH_2]^+$ (51), 117 $[RCOO]^+$ (22), 101 $[RCO]^+$ (28), 99 (100). ^{1}H and ^{13}C NMR spectral data: see Tables 1 and 3, respectively.

Compound **18**. Oil; $[\alpha]_D^{22}$ +123.4° ($CHCl_3$, *c* 0.33); IR ν_{max}^{NaCl} cm^{-1}: 3500–3300, 1760, 1700, 1650; EIMS *m/z* (rel. int.): 246.1261 [M-RCOOH]$^+$ (3) ($C_{15}H_{18}O_3$ requires 246.1256), 228 (3), 83 $[RCO]^+$ (100), 55 (89). ^{1}H and ^{13}C NMR spectral data: see Tables 1 and 3, respectively.

Compound **22**. Oil: $[\alpha]_D^{22}$ +60.6° ($CHCl_3$, *c* 0.35); IR ν_{max}^{NaCl} cm^{-1}: 3500–3300, 1730, 1700, 1650; CIMS *m/z* (rel. int.): 350.1723 $[M]^+$ (100) ($C_{19}H_{26}O_6$ requires 350.1729), 349 $[M-H]^+$ (14), 332 (12), 249 [M-RCOO]$^+$ (17), 246 (17). ^{1}H and ^{13}C NMR spectral data: see Tables 2 and 3, respectively.

Compound **23**. Oil; $[\alpha]_D^{22}$ +18.4° ($CHCl_3$, *c* 0.13); IR ν_{max}^{NaCl} cm^{-1}: 3500–3300, 1770, 1650; CIMS *m/z* (rel. int.): CIMS *m/z* (rel. int.): 364.1850 $[M]^+$ (40) ($C_{20}H_{28}O_6$ requires 364.1885), 363 (71), 362 (54), 346 (28), 262 (41), 248 [M-RCOOH]$^+$ (74), 246 (21), 218 (100). ^{1}H and ^{13}C NMR spectral data: see Tables 2 and 3, respectively.

Compound **25**. Oil; IR ν_{max}^{NaCl} cm^{-1}: 3500–3300, 1750, 1720; CIMS *m/z* (rel. int.): 366.2027 $[M]^+$ (51) ($C_{20}H_{30}O_6$ requires 366.2042), 266 (26), 249 [M-RCOO]$^+$ (18), 248 [M-RCOOH]$^+$ (100), 246 (10), 202 (10). ^{1}H NMR spectral data: see Table 2.

Compound **26**. Oil; IR ν_{max}^{NaCl} cm^{-1}: 3500–3300, 1760, 1705, 1640; CIMS *m/z* (rel. int.): 334.1743 $[M]^+$ (11) ($C_{19}H_{26}O_5$ requires 334.1780), 332 (1.4), 331 (5), 248 [M-RCOOH]$^+$ (100), 231 (25), 204 (18). ^{1}H NMR spectral data: see Table 2.

Compound **27**. Oil $[\alpha]_D^{22}$ +36.8° ($CHCl_3$, *c* 0.291); IR ν_{max}^{NaCl} cm^{-1}: 3500–3300, 1750, 1715, 1650; CIMS *m/z* (rel. int.): 352.1862 $[M]^+$ (59) ($C_{19}H_{28}O_6$ requires 352.1885), 351 (9), 350 (26), 278 (36), 262 (57), 250 (34), 248 [M-RCOOH]$^+$ (59), 248 (81), 234 (34) 232 (30), 220 (34), 218 (64), 204 (100). ^{1}H NMR spectral data: see Table 2.

Compound **31**. Oil: $[\alpha]_D^{22}$ +57.3° ($CHCl_3$, *c* 0.225): IR ν_{max}^{NaCl} cm^{-1}: 3500–3300, 2740, 1765, 1705; EIMs *m/z* (rel. int.): 254.1506 [M-CO]$^+$ (46) ($C_{14}H_{22}O_4$ requires 254.1518), 252 (3.5), 237 (16), 236 (100), 218 (12), 192 (22), 191 (15). ^{1}H and ^{13}C NMR spectral data: see Tables 2 and 3, respectively.

Acknowledgements—The authors wish to thank Mr Theophanis Constantinidis (Institute of Systematic Botany, University of Patras) for identification of the plant material.

Table 1. ^{1}H NMR chemical shifts of compounds **1**, **2**, **16**–**18** (400 MHz, $CDCl_3$, δ values)

H	**1**	**2**	**16**	**17**	**18**
1	4.90 *br dd* (5.2,11.2)	4.86 *br dd* (5.2,11.6)	4.97 *br dd* (7.2,9.6)	4.98 *br dd* (6.7,10.0)	4.97 *br dd* (6.2,10.2)
2a	2.24–2.10 *m*	2.20–2.10 *m*	2.24–2.10 *m*	2.30–2.20 *m*	2.30–2.10 *m*
2b					
3a	2.59 *ddd* (2.4,4.8,12.0)	2.58 *ddd* (2.4,4.4,12.0)	2.56 *ddd* (2.8,5.2,11.6)	2.70–2.50 *m*	2.58 *ddd* (2.2,4.4,12.0)
3b	1.94 *ddd* (6.0,11.6,12.0)	1.92 *td* (6.4,12.0)	2.05–1.90 *m*	2.10–1.90 *m*	1.96 *br dddd* (7.2,10.8,12.0)
5	4.80 *br d* (10.2)	4.72 *br d* (10.0)	4.80 *br d* (10.0)	4.82 *br d* (9.5)	4.82 *br d* (9.6)
6	4.78 *t* (10.2)	4.76 *t* (10.0)	5.06 *br dd* (9.2,10.0)	5.06 *dd* (8.5,9.5)	5.06 *dd* (8.6,9.5)
7	2.5–2.6 *m*	1.7–1.5 *m*	3.01 *dddd* (2.4,3.6,9.2,10.0)	3.07 *dddd* (2.8,3.6,8.5,10.0)	3.05 *dddd* (2.8,3.6,8.4,8.6)
8a	2.09 *ddt* (2.0,5.6,15.2)	1.9–1.8 *m*	5.08 *br dd* (10.0,11.6)	5.16 *br dd* (10.0,11.8)	5.17 *br dd* (8.2,11.2)
8b	1.67 *dddd* (2.4,10.0,12.4,15.2)	1.7–1.5 *m*	—	—	—
9a	2.46 *br dd* (5.6,13.2)	2.40 *br dd* (6.0,13.2)	2.57 *br d* (12.8)	2.70–2.50 *m*	2.58 *br d* (12.0)
9b	2.24–2.10 *m*	2.05 *br td* (2.4,13.5)	2.40 *br dd* (11.6,12.8)	2.46 *br dd* (11.8,12.2)	2.44 *br dd* (11.2,12.0)
11	—	2.38 *dq* (6.8,12.0)	—	—	—
13a	6.25 *d* (3.6)		6.34 *d* (3.6)	6.29 *d* (3.6)	6.27 *d* (3.6)
		1.25 *d* (6.8)			
13b	5.52 *d* (3.2)		5.87 *d* (2.4)	5.78 *d* (2.8)	5.75 *d* (2.8)
14	1.34 *br s*	1.34 *br s*	1.49 *br d*	1.49 *br s*	1.48 *br s*
15a	4.29 *br d* (13.6)	4.30 *br d* (13.2)	4.29 *br d* (14.2)	4.30 *br d* (14.0)	4.30 *dd* (1.2,14.0)
15b	4.03 *br d* (13.6)	4.00 *br d* (13.2)	4.08 *br d* (14.2)	4.09 *br d* (14.0)	4.08 *d* (14.0)
2′a	—	—	2.47 *dd* (6.8,15.6)	—	—
2′b	—	—	2.25 *dd* (6.8,15.6)	—	—
3′a	—	—	2.24–2.14 *m*	6.13 *br s*	6.86 *dq* (1.2,7.6)
3′b	—	—	—	5.66 *t* (1.6)	—
4′a	—	—	3.58 *dd* (4.8,10.4)		
				1.95 *br s*	1.83 *d* (7.6)
4′b	—	—	3.46 *dd* (6.4,10.4)		
5′	—	—	1.97 *d* (6.8)	—	1.84 *br d* (1.2)

Values in parentheses are coupling constants in Hz.

Table 2. ^{1}H NMR chemical shifts of compounds **22**, **23**, **25–27**, **31** (400 MHz, $CDCl_3$, δ values)

H	**22**	**23**	**25**	**26**	**27**	**31**
1	4.97 *br dd* (5.2,11.2)	4.96 *br dd* (4.8,11.2)	4.95 *br dd* (5.2,11.0)	4.96 *br dd* (5.2,10.8)	4.95 *br dd* (5.2,11.2)	3.37 *dd* (4.0,11.6)
2a	2.30–2.10 *m*	2.30–2.10 *m*	2.22–2.10 *m*	2.24–2.10 *m*	2.40–2.24 *m*	1.75–1.65 *m*
2b						1.59 *tdd* (4.0,11.6,13.2)
3a	2.54 *ddd* (2.4,4.4,11.2)	2.6–2.5 *m*	2.54 *br ddd* (1.8,4.8,11.3)	2.6–2.5 *m*	2.54 *ddd* (2.4,4.8,11.8)	2.41 *br ddd* (3.2,4.0,13.6)
3b	1.95 *ddd* (6.4,11.6,12.0)	2.00–1.90 *m*	1.93 *ddd* (6.2,11.3,12.6)	1.94 *td* (6.8,12.0)	1.94 *td* (6.4,11.8)	1.42 *br ddd* (4.8,5.6,11.6,13.6)
4	—	—	—	—	—	2.74 *br t* (5.6)
5	4.74 *br d* (9.6)	4.73 *br d* (10.0)	4.73 *br d* (10.0)	4.74 *br d* (9.6)	4.73 *br d* (9.6)	1.87 *dd* (5.6,12.0)
6	5.01 *dd* (8.8,9.6)	5.01 *dd* (9.6,10.0)	4.96 *dd* (9.2,10.0)	4.99 *dd* (9.2,9.6)	4.99 *dd* (8.8,10.0)	4.42 *dd* (11.2,13.0)
7	2.30–2.10 *m*	2.30–2.10 *m*	2.20–2.10 *m*	2.24–2.10 *m*	2.40–2.24 *m*	1.75–1.65 *m*
8	5.26 *br ddd* (2.4,9.2,10.4)	5.26 *ddd* (2.0,8.0,10.4)	5.11 *td* (2.4,10.0)	5.21 *ddd* (2.4,8.0,9.8)	5.13 *br td* (2.2,9.2,10.4)	3.97 *ddd* (4.0,10.8,14.0)
9a	2.52 *br dd* (10.4,12.8)	2.54 *br dd* (2.0,12.8)	2.55 *br dd* (2.4,12.4)	2.60–2.50 *m*	2.46 *br dd* (2.2,13.0)	2.27 *dd* (4.0,12.8)
9b	2.43 *br dd* (10.4,12.8)	2.42 *br dd* (10.4,12.8)	2.35 *br dd* (10.0,12.4)	2.41 *br dd* (10.4,12.4)	2.37 *br dd* (10.4,13.0)	1.24 *dd* (10.8,12.8)
11	2.54 *dq* (7.2,11.6)	2.55 *dq* (6.8,11.2)	2.54 *dq* (6.8,11.2)	2.54 *dq* (7.2,11.4)	2.54 *dq* (6.8,11.2)	2.64 *dq* (6.8,12.0)
13	1.37 *d* (7.2)	1.36 *d* (6.8)	1.40 *d* (6.8)	1.38 *d* (7.2)	1.40 *d* (6.8)	1.40 *d* (6.8)
14	1.49 *br s*	1.48 *br s*	1.47 *br s*	1.49 *br s*	1.48 *br s*	0.84 *s*
15a	4.29 *br d* (14.0)	4.29 *br d* (14.0)	4.28 *br d* (14.0)	4.29 *br dd* (1.2,13.9)	4.28 *br d* (14.0)	9.92 *s*
15b	4.08 *br d* (14.0)	4.07 *br d* (14.0)	4.07 *d* (14.0)	4.07 *d* (13.9)	4.06 *d* (14.0)	—
2′a	—	—	2.45 *dd* (6.4,15.2)	—	2.68 *ddq* (4.6,7.2,7.6)	—
2′b	—	—	2.25 *dd* (6.8,15.2)	—	—	—
3′a	6.26 *s*	6.98 *q* (7.2)	2.24–1.90 *m*	6.12 *br s*	3.76 *dd* (7.6,10.8)	—
3′b	5.94 *s*	—	—	5.64 *br t* (1.4)	3.71 *dd* (4.6,10.8)	—
4′a	4.36 *br s*	1.94 *d* (7.2)	3.62 *dd* (4.8,10.4)	1.97 *br t* (1.1)	1.18 *d* (7.2)	—
4′b			3.45 *dd* (6.8,10.4)			—
5′	—	4.38 *br s*	0.98 *d* (6.8)	—	—	—

Values in parentheses are coupling constants in Hz.

Table 3. ^{13}C NMR chemical shifts of compounds **1**, **10**, **16**, **18**, **22**, **23**, **27**, **28** and **31** (75 MHz, $CDCl_3$, δ values)

C	1*	10	16	18	22	23*	27	28*	31
1	126.5	145.6	129.5[a]	129.5[a]	129.4[a]	129.4	129.4[a]	78.0	78.2
2	26.8	113.1	26.3	26.3	26.1	26.1	26.1	27.2	27.3
3	35.4	115.1	34.7	34.7	34.7	34.7	34.7	22.4	22.4
4	143.3	143.6	143.8	143.7	142.9	142.8	142.8	44.9	45.1
5	128.8	50.6	128.7[a]	128.7[a]	129.0[a]	129.1	129.1[a]	48.9	48.6
6	80.1	78.7	76.6	76.5	76.1	76.1	76.1	76.1	76.0
7	50.5	52.4	52.7	53.1	58.3	58.4	58.1	53.8	59.8
8	27.7	69.4	72.5	72.5	73.8	73.4	73.3	69.9	68.9
9	40.8	45.1	49.0	48.8	49.0	49.1	49.0	43.9	48.3
10	137.7[a]	41.9	132.6[b]	132.9[b]	132.6	132.8[a]	132.7	41.5	41.2
11	139.5[a]	136.6	135.3[b]	135.5[b]	40.2	40.2	40.3[b]	136.3[a]	41.7
12	170.2	169.3	169.7	169.9	178.0	178.0	178.1	169.2	178.5
13	120.0	120.3	125.8	125.2	17.0	17.0	17.2	120.5	14.3[a]
14	15.9	18.7	16.7†	16.8	16.6	16.6	16.6	13.9	14.2[a]
15	61.2	67.3	61.4	61.5	61.5[b]	61.5	61.5	201.8	202.1
1′	—	166.4	172.1	166.7	165.3	166.4	174.8	165.2	—
2′	—	131.6	38.4	128.4	139.3	131.9[a]	41.9[b]	139.0[a]	—
3′	—	141.9	32.7	138.6	62.4[b]	141.4	64.4	126.7	—
4′	—	14.4	67.1	14.6	126.3	14.4	13.5	62.3	—
5′	—	56.8	16.7†	12.8	—	56.9	—	—	—

* HMQC.

[a,b,c] The signals with the same superscript may be interchanged within each column.

† Overlapped signals.

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