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Spectral Data of Two New Asymmetric Sesquiterpene Alcohols: (14*R*)-*β*-Oplopenol and (14*S*)-*β*-Oplopenol

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Abstract: The epimeric sesquiterpene alcohols (14*R*)-*β*-oplopenol and (14*S*)-*β*-oplopenol were obtained by $LiAlH_4$ reduction of *β*-oplopenone. The complete ^{1}H- and ^{13}C-NMR assignments of these two new sesquiterpene alcohols have been made using 1D and 2D NMR techniques, including COSY, NOESY, HSQC, HMBC experiments.

Keywords: β-Oplopenone; (14*R*)-*β*-oplopenol, (14*S*)-*β*-oplopenol, NMR, sesquiterpene alcohols

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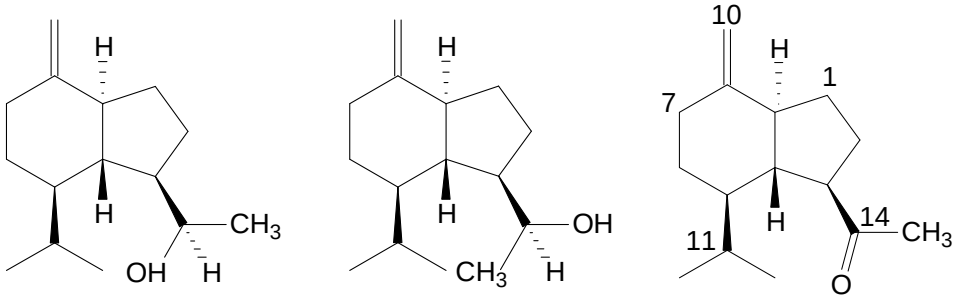
Introduction

The oplopane derivatives were well represented from plants of the Senecioneae family [1-8]. The sesquiterpenic ketone *β*-oplopenone was identified as a major component of the essential oil of *Adenostyles briquetii*, an endemic species from the island of Corsica [9]. To our knowledge, the spectral data of these asymmetric alcohols: (14*R*)-*β*-oplopenol (**1**) and (14*S*)-*β*-oplopenol (**2**), have never been reported. The aim of this study was to establish the spectral assignments and the relative configuration of these two new epimers using extensive NMR assignments data along with EI-mass spectra and IR spectrum.

Results and Discussion

The $LiAlH_4$ reduction of β-oplopenone (**3**), a sesquiterpene isolated from the aerial parts of *Adenostyles briquetii* [9], yielded two new stereoisomers (Figure 1). Their structures were identified as (14*R*)-*β*-oplopenol (**1**) and (14*S*)-*β*-oplopenol (**2**). The retention indice (I_{Rtx-1}), EI-mass spectra, ^{1}H- and ^{13}C-NMR spectral data of *β*-oplopenone (**3**) were in agreement with those reported in the literature [10-16]. Those of compounds **1** and **2** are compiled in Tables 1 and 2.

Figure 1. Structures of (14*R*)-*β*-oplopenol **1**, (14*S*)-*β*-oplopenol **2** and *β*-oplopenone **3**.



(14*R*)-*β*-oplopenol (**1**) (14*S*)-*β*-oplopenol (**2**) *β*-oplopenone (**3**)

The EI-mass spectra of alcohols **1** and **2** showed a molecular ion ($M^{\cdot+}$) at *m/z* 222, while that of ketone **3** appears at *m/z* 220. The EI-mass spectra of components **1** and **2** were similar, except for the relative abundance of several signals. Both epimers exhibited a $[M-18]^{+\cdot}$ signal at *m/z* 204 corresponding to the loss of a hydroxyl group after hydrogen rearrangement. Their IR spectra showed a strong hydroxyl group band (3300-3500 cm^{-1}) and the absence of the carboxyl group one (1710 cm^{-1}) observed for compound **3**. The ^{1}H-NMR spectra of the both epimers showed a methyl-15 signal at significantly smaller chemical shift [δ = 1.18 ppm (d) in **1** and δ = 1.13 ppm (d) in **2**] while in **3** it appeared at δ = 1.97 ppm (s). The C-14 signal appears in the ^{13}C-NMR spectra at δ = 211.71 ppm (s) in **3**, and at δ = 68.71 ppm in **1** and at δ = 69.56 ppm in **2**. In the HMBC spectrum, this signal was correlated with the proton signals of C-15, C-4, C-3 and C-2, proving that C-14 was bonded to the hydroxyl group obtained by reduction of the carbonyl group of **3**. Finally, the stereochemistry of H-3α, H-4β, H-5α and H-9α in agreement with the structure of **3** was confirmed by 1D and 2D NMR spectrum.

The molecular formulae of **1** and **2** were confirmed from ^{13}C-NMR, ^{1}H-NMR and DEPT data as $C_{15}H_{26}O$, indicating three degrees of unsaturation. The oplopane sesquiterpene skeleton was directly inferred from its ^{13}C-NMR spectrum with the aid of a DEPT experiment which exhibited fifteen signals comprising three methyl, five methylenes, six methines and one non-protonated carbons atoms. The ^{13}C-NMR assignments of the both epimers **1** and **2** were confirmed from a two dimensional ^{13}C-^{1}H chemical shifts correlation diagram (HSQC) and the assignments of C-3, C-4, C-5 and C-9 were established from a HMBC spectrum and proton-coupled spectrum (COSY). In order to determine the relative configuration of C-14, we have compared the spectral data of both epimers. The H-3 and H-4 proton signals of **1** and **2** differed in the ^{1}H-NMR spectra. The chemical shift at δ = 2.14 ppm (ddt, J = 7.0; 11.0; 3.6 Hz) and δ = 0.87 ppm (q, J = 11.0 Hz) in **2** appears as broadened signals at δ =1.77 ppm (m) and δ = 1.25 ppm (m) in **1**, respectively.

Table 1. ^{1}H- and ^{13}C-NMR spectra data, HSQC and HMBC correlations for (14*R*)-*β*-oplopenol (**1**).

C	δ(^{13}C)	DEPT	δ(^{1}H)	Mutiplicity (*J*, Hz)	HMBC	COSY
1	27.79	CH_2	1.34 1.43	m m	9, 3, 2	2, 3, 9
2	22.62	CH_2	1.62 1.81	dtd (20.0; 7.4; 12.8) m	14, 9, 3, 1	1, 3, 4
3	49.02	CH	1.77	m	14, 15, 6, 4, 2	2, 5, 1
4	50.23	CH	1.25	m	14, 11, 9, 6, 5, 3	3, 9, 1
5	50.09	CH	1.34	m	13, 12, 11, 7, 6, 4	6, 3
6	26.95	CH_2	1.10 1.75	dq (4.4; 13.0) m	11, 7, 5, 4	5, 7
7	35.32	CH_2	1.95 2.35	m ddd (2.4; 4.3; 13.4)	10, 6, 8	10, 6 6,
8	151.98	C	-	-	9, 7, 6, 5, 1	-
9	52.50	CH	1.83	m	10, 7, 5, 4, 3, 2, 1	10, 4
10	102.70	CH_2	4.54 4.62	q (1.7) q (1.7)	9, 7	9 7
11	28.50	CH	1.95	m	13, 12, 6, 5	12, 13
12	21.95	CH_3	0.95	d (6.9)	13, 11, 5	11
13	15.85	CH_3	0.78	d (6.9)	12, 11, 5	11
14	68.71	CH	3.98	q (6.3)	15, 4, 3, 2	15
15	23.01	CH_3	1.18	d (6.3)	14, 4, 3, 2	14

^{1}H directly attached to ^{13}C determined from HSQC experiment

^{1}H-^{13}C long-range correlation (HMBC) corresponding to two or three bond connectivities

Table 2. ^{1}H- and ^{13}C-NMR spectra data, HSQC and HMBC correlations for (14*S*)-*β*-oplopenol (**2**).

C	δ(^{13}C)	DEPT	δ(^{1}H)	Mutiplicity (*J*, Hz)	HMBC	COSY
1	28.12	CH_2	1.33 1.72	m m	9, 2	9, 2 9, 2
2	23.44	CH_2	1.65 1.77	dtd (18.1; 7.0; 11.0) m	14, 1	3, 1
3	48.79	CH	2.14	ddt (7.0; 11.0; 3.6)	15, 4, 2, 1	2,4,14,
4	51.72	CH	0.87	q (11.0)	9, 6, 2, 1	9, 5, 3
5	49.94	CH	1.34	m	13, 12, 6, 4, 7	6, 4
6	26.95	CH_2	1.01 1.73	dq (13.0; 4.5) m	11, 7	7, 5
7	35.18	CH_2	1.96 2.34	m ddd (2.4; 4.5; 13.0)	10, 6	6, 10 6

Table 2. Cont.

C	δ(^{13}C)	DEPT	δ(^{1}H)	Mutiplicity (*J*, Hz)	HMBC	COSY
8	152.03	C	-	-	9, 7, 1	
9	52.69	CH	1.86	m	10, 7, 5, 4, 1, 2, 6	10, 4
10	102.55	CH_2	4.54	q (1.7)	11, 7	9
			4.61	q (1.7)		7
11	28.69	CH	1.94	m	13, 12	13, 12, 6
12	21.95	CH_3	0.96	d (6.8)	13, 6	11
13	15.83	CH_3	0.70	d (6.8)	12, 4	11
14	69.56	CH	4.03	dq (3.9; 6.3)	15, 4, 2	3, 15
15	16.89	CH_3	1.13	d (6.3)	12	14

^{1}H directly attached to ^{13}C determined from HSQC experiment

^{1}H-^{13}C long-range correlation (HMBC) corresponding to two or three bond connectivities

Moreover, in **2** the H-14 proton signal was a double quartet at 4.03 ppm (J = 3.6; 6.3 Hz), whereas a quartet was observed at δ = 3.98 ppm (J = 6.32 Hz) in **1**. These results proved the presence of a ^{3}J vicinal coupling between H-3 and H-14 in **2**, not observed in **1**. The $^{3}J_{\text{H-H}}$ coupling constant value measured in **2** (3.6 Hz) and **1** (0 Hz) indicated that the dihedral angle between H-3 and H-14 were close to 110° in **2** and to 90° in **1** (Karplus curve) [17,18]. Furthermore, NOE contacts between H-14, H-11 and H-4 were observed in the NOESY spectra of both epimers, proving that the relative configurations of H-14 and H-11 were β. The variation of the ^{13}C-NMR chemical shifts in **1** and **2**, were quite similar ($\Delta\delta$ always lower than 0.33 ppm) except for the C-2 ($\Delta\delta$ = 0.82 ppm), C-14 ($\Delta\delta$ = 0.85 ppm), C-4 ($\Delta\delta$ = 1.49 ppm) and particularly for the C-15 ($\Delta\delta$ = 6.12 ppm). The strong shielding of the C-15 carbon signal (δ = 16.89 ppm) in **2** may be ascribed to a steric interaction and proved that the hydrogenated carbons C-2 and C-15 were in the γ-gauche position relative to each other. This γ-steric effect was not observed for the C-15 signal in **1** (δ = 23.01 ppm). These results, in combination with the NOE results, allowed us to establish the relative configuration of C-14 as (14*R*)- for **1** and (14*S*)- for **2**. Furthermore the configuration at C-14 was predictable since the isopropyl group causes a marked steric effect on one side of the carbonyl group impeding its easy reduction, favoring formation of alcohol **1**.

Experimental

General

GC analysis were carried out using a Perkin-Elmer (Waltham, MA, USA) Autosystem XL GC apparatus equipped with a dual flame ionization detection (FID) system and two fused-silica capillary columns (60 m × 0.22 mm I.D., film thickness 0.25 μm), Rtx-1 (polydimethylsiloxane) and Rtx-wax (polyethyleneglycol). The oven temperature was programmed from 60 °C to 230 °C at 2 °C/min and then held isothermally at 230 °C for 35 min. Injector and detector temperature was maintained at 280 °C. Samples were injected in the split mode (1/50), using helium as carrier gas (1 mL/min); injection

volume, 0.1 μL of pure component. Retention indices (*I*) of compounds were determined relative to the retention times of series of *n*-alkanes (C_5-C_{30}) with linear interpolation, using Van den Dool and Kratz equation [19] and software from Perkin-Elmer. Components relative concentrations were calculated based on GC peak areas without using correction factors. GC/MS samples were analysed with a Perkin-Elmer Turbo mass detector (quadrupole), coupled to a Perkin-Elmer Autosystem XL, equipped with fused-silica capillary columns Rtx-1 and Rtx-Wax. Carrier gas: helium (1mL/min), ion source temperature: 150°C, oven temperature programmed from 60°C to 230°C at 2°C/min and then held isothermally at 230°C (35 min), injector temperature: 280°C, energy ionization: 70 eV, electron ionization mass spectra were acquired over the mass range 35-350 Da, split: 1/80, injection volume: 0.1 μL of pure component. IR spectra were obtained on a FT-IR spectrometer Perkin-Elmer spectrum RX 1. The components were analysed by ^{13}C-NMR in deuterated chloroform on a Bruker (Wissembourg, France) Avance 400 Fourier Transform spectrometer operating at 100.13 MHz, equipped with a 5 mm probe. All shifts are referred to internal tetramethylsilane (TMS). ^{13}C-NMR spectra were recorded with the following parameters: pulse width = 4 μs (flip angle 45°); acquisition time = 2.7 s for 128 000 data table with a spectral width of 25 000 Hz (250 ppm); CPD mode decoupling; digital resolution = 0.183 Hz/pt. The number of accumulated scans was 5000 for each sample (around 40 mg of pure component in 0.5 mL of $CDCl_3$). Exponential line broadening multiplication (1 Hz) of the free induction decay was applied before Fourier transformation. ^{1}H-NMR spectra were recorded with the following parameters: flip angle 30°; acquisition time = 2.56 s for 32 000 data table with a spectral width of 7000 Hz (17.5 ppm).

Reduction

β-Oplopenone (**3**, 140 mg, 99% purity by GC) dissolved in dry Et_2O (10 mL) was carefully added to a suspension of $LiAlH_4$ (40 mg) in dry Et_2O (15 mL) at 0°C. The mixture was stirred at room temperature and then refluxed for 3 h. The reaction mixture was hydrolysed by addition of a solution of 15% NaOH (1 mL) and cold water (1 mL). The organic layer was separated, washed with water to neutrality, dried over Na_2SO_4 and conc. in vacuum. The mixture (120 mg) contained as major components *β*-oplopenone (**3**, GC: 31%) and two alcohols: (14*R*)-*β*-oplopenol (**1**, GC: 55%, characterized after isolation), and (14*S*)-*β*-oplopenol (**2**, GC: 12%, characterized after isolation). The two epimers **1** and **2** and the startuing material **3** were isolated by column chromatography (CC: SiO_2, 63-200 μm). *β*-Oplopenone (**3**, 40 mg, 99% purity by GC) was eluted with a mixture *n*-C_5H_{12}/Et_2O = 95/5, (14*R*)-*β*-oplopenol (**1**, 60 mg, 98% purity by GC) with *n*-C_5H_{12}/Et_2O = 90/10 and (14*S*)-*β*-oplopenol (**2**, 15 mg, 95% purity on GC) with *n*-C_5H_{12}/Et_2O = 85/15.

(14R)-β-oplopenol (**1**). GC: 98%; $I_{\text{Rtx-1}}$ = 1644; $I_{\text{Rtx-Wax}}$ = 2216; EIMS (70 e/v): 222 (3), 204 (17), 177 (18), 161 (83), 135 (58), 119 (38), 105 (57), 91 (82), 79 (69), 67 (48), 55 (39), 45 (71), 43 (93), 41 (100); IR (KBr) υ_{max} cm^{-1}: 3427, 3076, 2932, 1651, 1460, 1375, 886; ^{1}H- and ^{13}C-NMR: see Table 1.

(14S)-β-oplopenol (**2**). GC: 95%; $I_{\text{Rtx-1}}$ = 1670; $I_{\text{Rtx-Wax}}$ = 2296; EIMS (70 e/v): 222 (2), 204 (14), 177 (12), 161 (69), 135 (51), 119 (34), 105 (52), 91 (80), 79 (71), 67 (47), 55 (39), 45 (98), 43 (97), 41 (100); IR (KBr) υ_{max} cm^{-1}: 3349, 3076, 2932, 1652, 1461, 1378, 886; ^{1}H- and ^{13}C-NMR: see Table 2.

β-oplopenone (**3**) [4]. GC: 99%; $I_{\text{Rtx-1}}$ = 1596; $I_{\text{Rtx-Wax}}$ = 2050; EIMS (70 e/v): 220 (4), 177 (31.6), 107 (16), 91 (20), 79 (17), 67 (14), 55 (12), 43 (100), 41 (34); IR (KBr) υ_{max} cm^{-1} (CCl_4): 3070, 2955, 2874, 1710, 1652, 1462, 1358, 887; ^{1}H-NMR: δ 0.65, 0.90 (3H, 2d, *J*= 6.8 Hz, Me-12 and Me-13), 1.97 (3H, s, Me-15), 2.34 (1H, ddd, *J*= 13.4 Hz; 2.6 Hz; 4.3 Hz, H-7*β*), 2.70 (1H, ddd, *J*= 5.1 Hz; 12.0 Hz; 10.5 Hz, H-3), 4.66 (1H, q, *J*= 1.6 Hz, H-10), 4.55 (1H, q, *J*= 1.6 Hz, H-10') and 1.10 (1H, dq, 13.8 Hz; *J*= 4.3 Hz, H-6*β*); ^{13}C-NMR: 27.34 (C-1), 28.48 (C-2), 56.06 (C-3), 52.08 (C-4), 49.26 (C-5), 26.55 (C-6), 35.27 (C-7), 150.86 (C-8), 51.80 (C-9), 103.52 (C-10), 29.58 (C-11), 21.93 (C-12), 15.66 (C-13), 211.71 (C-14), 28.87 (C-15).

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