Cycloarta-16,24-dien-3β-ol: Revised Structure of Cimicifugenol, a Cycloartane Triterpenoid

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The structure of a triterpene alcohol isolated from the nonsaponifiable lipids of both the root and aerial part extracts of *Cimicifuga simplex* (Ranunculaceae) was established to be cycloarta-16,24-dien-3β-ol (1). Spectral identity of the 24,25-dihydro derivative (4) of 1 with 24,25-dihydrocimicifugenol demonstrated that cimicifugenol, previously assigned the erroneous structure of cycloarta-7,24-dien-3β-ol, possesses structure 1.

Key words *Cimicifuga simplex*; Ranunculaceae; cycloartane triterpenoid; cimicifugenol; cycloarta-16,24-dien-3β-ol; 17-isocycloartanol

The roots of *Cimicifuga simplex* WORMSK (Japanese name: sarashina shoma; Ranunculaceae) and other *Cimicifuga* species have been used as the Chinese crude drug Cimicifugae Rhizoma as an anti-inflammatory, analgesic and antipyretic.[1)] A cycloartane triterpenoid, cimicifugenol, isolated from the root extracts of *Cimicifuga* (*C.*) *aerina*, *C. japonica*, and *C. simplex*, has been assigned the structure cycloarta-7,24-dien-3β-ol.[2)] Subsequently, a number of highly oxygenated cycloartane triterpenoids as glycosyl esters[3—5)] have been isolated from some *Cimicifuga* species. In this paper, we report the isolation and structural elucidation of a cycloartane triterpene alcohol as cycloarta-16,24-dien-3β-ol (**1**) isolated from the nonsaponifiable lipids of both the root and aerial part extracts of *C. simplex*. The ^{1}H-NMR and mass spectral data of the 24,25-dihydro derivative of **1**-acetate (**1a**), *i.e.*, cycloart-16-en-3β-yl acetate (**4a**), were essentially the same with those reported for 24,25-dihydrocimicifugenyl acetate,[6)] which demonstrated that cimicifugenol possesses the same structure as **1**, but not the cycloarta-7,24-dien-3β-ol structure previously assigned.[2)]

Preparative thin-layer chromatography (TLC) of the nonsaponifiable lipids of the methylene chloride extract of *C. simplex* on silica gel afforded a triterpene alcohol fraction. Preparative HPLC of the triterpene alcohol fraction from the root extract yielded compound **1** and cycloartenol (cycloart-24-en-3β-ol), whereas the fraction from the aerial part extract gave both compound **1**, cycloartenol, and 24-methylenecycloartanol [24-methylcycloart-24(24^1)-en-3β-ol]. Identification of cycloartenol and 24-methylenecycloartanol was performed by spectral comparison with authentic compounds.

The molecular formula of compound **1** was determined to be $C_{30}H_{48}O$ on the basis of the high-resolution mass spectrum (HR-MS) (M^+, *m/z* 424.3726). Compound **1** has a secondary hydroxyl group (ν_{max} 3320 cm^{-1}) associated with an adjacent methine [δ_H 3.29 (dd, J=4.4, 11.4 Hz)]. The shift and coupling constants of the methine ^{1}H signal suggested that the hydroxyl group is oriented equatorially (β) at C-3.[7)] In addition, compound **1** possesses two trisubstituted double bonds [ν_{max} 831 and 796 cm^{-1}; δ_H 5.11 (1H, tt, J=1.5, 7.3 Hz) and 5.20 (1H, br s)], a cyclopropyl group [ν_{max} 3038 cm^{-1}; δ_H 0.28 and 0.68 (each 1H and d, J=4.3 Hz)], a terminal isopropylidene group [δ_H 1.59 (s) and 1.68 (s)], and one secondary [δ_H 1.01 (d, J=6.7 Hz)] and four tertiary [δ_H 0.82, 0.93, 0.98, and 1.06 (each s)] methyl groups. These data, in combination with MS fragment ions[7)] having *m/z* 313 [$M^+-C_8H_{15}$ (side-chain (s.c.))], 284 [$M^+-C_9H_{16}O$ (ring A)], 255 [$M^+-C_{11}H_{21}O$ (s.c.+ring D (C_3H_4)+H_2O)], and 69 [$CH_2CH=C(Me)_2^+$], suggested that compound **1** has an isooctenyl side-chain and a cycloartan-3β-ol skeleton with a double bond in ring D, most probably at C-16(17). From the foregoing, compound **1** was assigned a cycloarta-16,24-dien-3β-ol structure. Analysis of the ^{13}C distortionless enhancement by polarization transfer (DEPT), ^{1}H–^{1}H correlation spectroscopy (COSY), ^{1}H detected multiple quantum coherence (HMQC), heteronuclear multiple-bond correlation (HMBC), and phase-sensitive nuclear Overhauser and exchange spectroscopy (NOESY) spectra, and the ^{13}C- and ^{1}H-

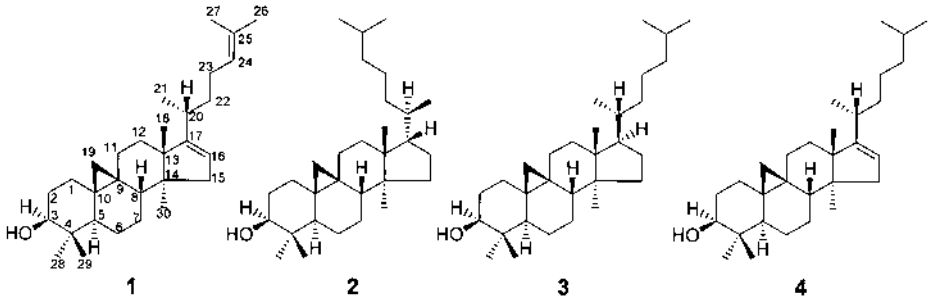

Chart 1

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Table 1. ^{13}C-NMR (125 MHz) and ^{1}H-NMR (500 MHz) Spectral Data (δ Values, $CDCl_3$) and ^{1}H–^{13}C Long-Range Correlations of Cycloarta-16,24-dien-3β-ol (**1**) Obtained by DEPT, ^{1}H–^{1}H COSY, HMQC, and HMBC

C No.		δ_C	δ_H [a)]	Cross peaks (δ_C) in HMBC spectrum
1	CH_2	32.0	1.57 (α), 1.26 (β)	
2	CH_2	30.4	1.76 (α), 1.56 (β)	
3	CH	78.8	3.29 (dd, 4.9, 10.1)	14.0 (C-29), 25.5 (C-28), 30.4 (C-2), 40.5 (C-4)
4	C	40.5		
5	CH	47.3	1.30 (dd, 4.0, 10.4)	14.0 (C-29), 20.9 (C-6), 25.5 (C-28), 27.0 (C-10), 40.5 (C-4), 78.8 (C-3)
6	CH_2	20.9	1.60 (α), 0.84 (β, dq, 2.3, 12.8)	
7	CH_2	26.6	1.10 (α), 1.37 (β)	
8	CH	46.2	1.74 (dd,4.9, 12.8)	20.1 (C-9), 20.6 (C-30), 26.6 (C-7), 42.1 (C-15), 48.3 (C-14), 51.6 (C-13)
9	C	20.1		
10	C	27.0		
11	CH_2	26.3	2.04 (α), 1.16 (β)	
12	CH_2	26.0	1.83 (α), 1.44 (β)	
13	C	51.6		
14	C	48.3		
15	CH_2	42.1	2.05 (α), 1.77 (β)	
16	CH	119.1	5.20 (br s)	31.7 (C-20), 42.1 (C-15), 48.3 (C-14), 51.6 (C-13), 156.9 (C-17)
17	C	156.9		
18	Me	22.4	1.06 (s)	26.0 (C-12), 48.3 (C-14), 51.6 (C-13), 156.9 (C-17)
19	CH_2	31.5	0.28 (*exo*, d, 4.3), 0.68 (*endo*, br d, 4.3)	
20	CH	31.7	2.02	
21	Me	21.8	1.01 (d, 6.7)	31.7 (C-20), 37.0 (C-22), 156.9 (C-17)
22	CH_2	37.0	1.41, 1.53	
23	CH_2	26.3	1.95 (2H)	
24	CH	125.0	5.11 (tt, 1.5, 7.3)	17.7 (C-27), 25.7 (C-26), 26.3 (C-23), 37.0 (C-22)
25	C	131.1		
26	Me	25.7	1.68 (s)	17.7 (C-27), 125.0 (C-24), 131.1 (C-25)
27	Me	17.7	1.59 (s)	25.7 (C-26), 125.0 (C-24), 131.1 (C-25)
28	Me	25.5	0.98 (s)	14.0 (C-29), 40.5 (C-4), 47.3 (C-5), 78.8 (C-3)
29	Me	14.0	0.82 (s)	25.5 (C-28), 40.5 (C-4), 47.3 (C-5), 78.8 (C-3)
30	Me	20.6	0.93 (s)	42.1 (C-15), 46.2 (C-8), 48.3 (C-14), 51.6 (C-13)

a) Figures in parentheses in the ^{1}H chemical shift column denote *J* values (Hz).

NMR spectral comparison of **1** (Table 1) with cycloartanol (**3**, cycloartan-3β-ol; see the Experimental section) supported the above assumption. Compound **1** showed significant NOE correlations between [H-29 (4β-Me)–H-19 (9β,19-cyclopropyl methylene)–H-18 (13β-Me)–H-20] on the β-face, and [H-3α–H-28 (4α-Me)–H-5α–H-7α–H-30 (14α-Me)] on the α-face of the molecule (Fig. 1).[8] Similar correlations were also observed for **3**, indicating that **1** possesses the same stereochemistry as **3** in terms of rings A—C and the C/D-ring junction.

Confirmation of a double bond at C-16(17) and a 20*R*-stereochemistry of **1** was achieved by preparing its tetrahydro derivative. Compound **1**, on hydrogenation in acetic acid–acetic anhydride (1 : 1) over platinum oxide,[2] yielded two tetrahydro derivatives as the acetates **2a** and **3a**, which on alkaline hydrolysis gave free alcohols, **2** and **3**, respectively. Compound **3** was identified as cycloartanol (20*R*) by spectroscopic comparison with an authentic compound. The structure of compound **2** (M^+, *m/z* 428.4009, $C_{30}H_{52}O$) was determined to be (17α,20*R*)-cycloartan-3β-ol (17-isocycloartanol) based on ^{13}C DEPT, ^{1}H–^{1}H COSY, HMQC, HMBC, and phase-sensitive NOESY spectroscopy. Whereas **2** exhibited diagnostic nuclear Overhauser effect (NOE) correlation between [H-17(β)–H-18 (13β-Me)], compound **3** showed the correlation between [H-17(α)–H-30 (14α-Me)] (Fig. 1),[8] which demonstrated that **2** and **3** are the stereoisomers at C-17. We concluded that **1** possesses the structure (20*R*)-cycloarta-16,24-dien-3β-ol.

Compound **1a**, on partial hydrogenation in ethanol over platinum oxide, yielded cycloart-16-en-3β-yl acetate (**4a**). The ^{1}H-NMR and mass spectral data (see the Experimental section) were essentially the same with those reported for 24,25-dihydrocimicifugenyl acetate,[6] thus demonstrating that cimifugenol, which was erroneously assigned the cycloarta-7,24-dien-3β-ol structure,[2] possesses the structure cycloarta-16,24-dien-3β-ol (**1**). This was supported by the close similarity of the melting points and optical rotations of **1** and **1a** (see the Experimental section) with those reported for cimicifugenol and its acetate,[2] respectively.

Experimental

Crystallizations were performed from acetone–MeOH. Melting points measured were uncorrected. TLC plates (silica gel) were developed with *n*-hexane–EtOAc (4 : 1, v/v). Reverse-phase HPLC was carried out on an octadecyl silica column (Superiorex ODS S-5 μm column, 10 mm i.d.×25 cm; Shiseido Co., Ltd., Tokyo) at 25 °C with MeOH (4 ml/min) as the mobile phase. Gas-liquid chromatography (GLC) was performed using a DB-17 fused-silica capillary column (30 m×0.3 mm i.d.; column temp., 275 °C). For both HPLC and GLC, cholesterol (cholest-5-en-3β-ol) was the standard for the determination of Rt_R(I) for hydroxy triterpenes; cholesteryl acetate was the standard for the determination of Rt_R(II) for the acetoxy triterpenes. Electron-impact (EI) MS and HR-MS were recorded at 70 eV. NMR spectra were recorded by JEOL JNM LA-500 and A-500 spectrometers at 500 MHz (^{1}H-NMR) and 125 MHz (^{13}C-NMR) in $CDCl_3$ with tetramethylsilane (TMS) (^{1}H-NMR) and $CDCl_3$ at δ 77.0 (^{13}C-NMR) as internal standards. Chemical shifts were recorded in δ values. IR spectra were recorded in KBr. Optical rotations were measured on a JASCO DIP-370 polarimeter at 25 °C in $CHCl_3$. Other instrumental details were the same as described previously.[10] Hydrolysis of acetates (5% KOH in MeOH) was performed at room

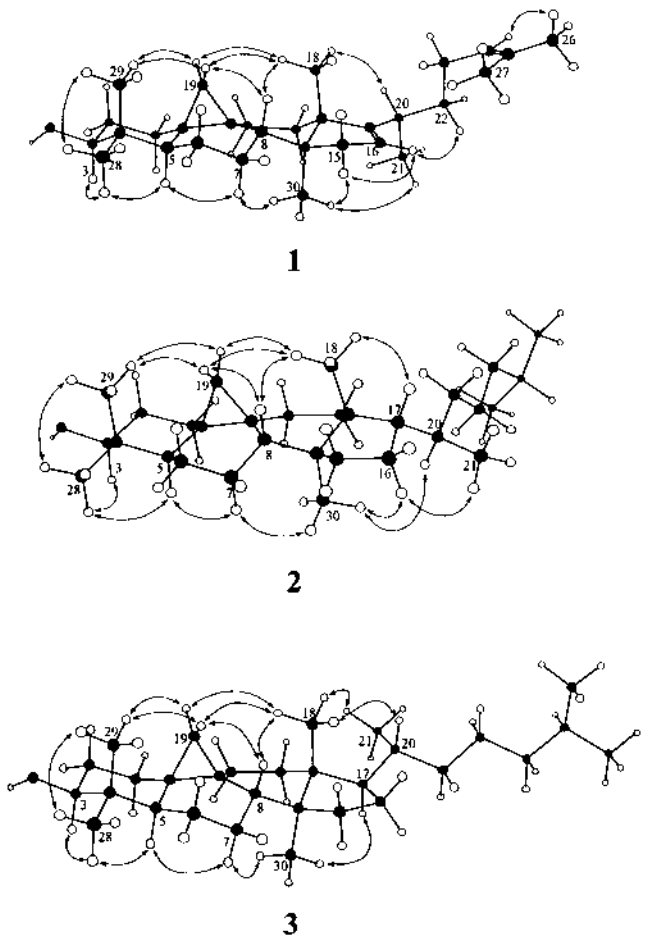

Fig. 1. Major NOE Correlations (↔) for Cycloarta-16,24-dien-3β-ol (**1**), 17-Isocycloartanol (**2**), and Cycloartanol (**3**)

temperature overnight. The roots and aerial parts of *C. simplex* were collected at the Medicinal Plant Garden of the School of Pharmaceutical Sciences, Toho University, and a voucher specimen was deposited at the school herbarium of the university. Cyclartanol (**3**),[11] and cycloartenol and 24-methylenecycloartanol[7,10] were used as reference compounds. Since the fully assigned ^{1}H- and ^{13}C-NMR spectral data for **3** were unavailable in literature, these are also shown below.

Isolation Procedures Fresh plant materials [roots (RT): 1 kg; aerial parts (AP): 560 g] were air dried (RT, 228 g; AP, 173 g), and on extraction with CH_2Cl_2 under reflux yielded the extracts (RT, 4.8 g; AP, 10.9 g). Alkaline hydrolysis (5% KOH in MeOH, reflux, 3 h) of the extracted lipids, followed by diisopropyl ether extraction, yielded neutral nonsaponifiable lipid fractions (RT, 760 mg; AP, 1.3 g) from which were separated triterpene alcohol fractions (RT, 60 mg; AP, 140 mg) by preparative TLC. Reverse-phase HPLC of the triterpene alcohol fraction from the RT material yielded **1** (21 mg) and cycloartenol (10 mg), whereas the fraction from the AP material gave **1** (23 mg), cycloartenol (8 mg), and 24-methylenecycloartanol (1 mg). Acetylation of a portion of **1** in Ac_2O–pyridine at room temperature overnight afforded the acetyl derivative **1a**.

Hydrogenation of Cycloarta-16,24-dien-3β-ol (1) and Its Acetate (1a) Compound **1** (29 mg) in AcOH–Ac_2O (1 : 1, v/v, 4 ml) over PtO_2 (55 mg) was hydrogenated under atmospheric pressure and temperature overnight. The reaction product was subjected to HPLC, which yielded 17-isocycloartanyl acetate (**2a**, 11 mg) and cycloartanyl acetate (**3a**, 3 mg). Alkaline hydrolysis of **2a** and **3a** yielded **2** and **3**, respectively. On the other hand, hydrogenation of compound **1a** (10 mg) in EtOH (3 ml) over PtO_2 (20 mg) under atmospheric pressure and temperature overnight, followed by HPLC purification, gave **4a** (7 mg).

Cycloarta-16,24-dien-3β-ol (**1**): Colorless needles, mp 112—114°C (cimicifugenol, lit.[2] mp 112—113°C). $[\alpha]_D$ +20.9° (c=1.09) (cimicifugenol, lit.[2] $[\alpha]_D$ +21.4° (c=4.33, $CHCl_3$)). Rt_R(I): 0.79 (HPLC), 1.48 (GLC). IR ν_{max} cm^{-1}: 3320, 3038, 831, 796. MS *m/z*: 424 (M^+, 8), 409 (8), 391 (3), 342 (4), 327 (3), 315 (5), 313 (7), 297 (5), 284 (3), 269 (5), 255 (3), 217 (5), 203 (14), 187 (19), 69 (78), 41 (100). HR-MS *m/z*: 424.3726 [Calcd for $C_{30}H_{48}O$ (M^+): 424.3702], 313.2510 (Calcd for $C_{22}H_{33}O$: 313.2529), 284.2490 (Calcd for $C_{21}H_{32}$: 284.2502), 255.2076 (Calcd for $C_{19}H_{27}$: 255.2101), 69.0703 (Calcd for C_5H_9: 69.0703). See Table 1 for the ^{13}C- and ^{1}H-NMR data.

Cycloarta-16,24-dien-3β-yl Acetate (**1a**): Colorless needles, mp 121—123 °C. (cimicifugenyl acetate, lit.[2] mp 118—119 °C). $[\alpha]_D$+8.0° (c=1.03). Rt_R(II): 0.77 (HPLC), 1.36 (GLC). IR ν_{max} cm^{-1}: 3039, 1730, 1241, 832, 800. MS *m/z*: 466 (M^+, 7), 451 (7), 423 (3), 406 (5), 391 (5), 384 (6), 357 (6), 324 (7), 309 (7), 297 (12), 295 (10), 284 (3), 269 (5), 255 (4), 241 (4), 203 (21), 187 (28), 43 (100). HR-MS *m/z*: 466.3807 [Calcd for $C_{32}H_{50}O_2$ (M^+): 466.3808]. ^{13}C- and ^{1}H-NMR: C-1 [δ_C 31.6; δ_H 1.63 (α), 1.26 (β)], C-2 [26.8; 1.78 (α), 1.64 (β)], C-3 [80.6; 4.57 (dd, J=4.4, 11.4 Hz)], C-4 (39.5), C-5 [47.4; 1.40 (dd, J=4.2, 12.4 Hz)], C-6 [20.7; 1.58 (α), 0.84 (β, dq, J=2.4, 12.4 Hz)], C-7 [26.4; 1.11 (α), 1.37 (β)], C-8 [46.1; 1.75 (dd, J=4.8, 12.5 Hz)], C-9 (20.2), C-10 (26.8), C-11 [26.2; 2.07 (α), 1.18 (β)], C-12 [25.9; 1.82 (α), 1.44 (β)], C-13 (51.6), C-14 (48.3), C-15 [42.1; 2.04 (α), 1.79 (β)], C-16 [119.1; 5.20 (br s)], C-17 (156.8), C-18 [22.4; 1.06 (s)], C-19 [31.5; 0.30 (*exo*, d, J=4.0 Hz), 0.69 (*endo*, br d, J=4.4 Hz)], C-20 (31.6; 2.00), C-21 [21.8; 1.01 (d, J=6.6 Hz)], C-22 (37.0; 1.40, 1.54), C-23 [26.2; 1.94 (2H)], C-24 [125.0; 5.11 (tt, J=1.5, 7.3 Hz)], C-25 (131.1), C-26 [25.7; 1.68 (s)], C-27 [17.7; 1.59 (s)], C-28 [25.4; 0.86 (s)], C-29 [15.2; 0.90 (s)], C-30 [20.6; 0.93 (s)], OCOMe [21.3; 2.06 (s)], OCOMe (171.0).

17-Isocycloartanol (**2**): Colorless needles, mp 126—127°C, $[\alpha]_D$ +6.7° (c=0.12). Rt_R(I): 1.22 (HPLC), 1.37 (GLC). IR ν_{max} cm^{-1}: 3419, 3037. MS *m/z*: 428 (M^+, 10), 413 (11), 410 (16), 395 (9), 367 (8), 341 (5), 315 (12), 297 (10), 288 (19), 273 (4), 259 (5), 233 (5), 220 (7), 203 (21), 187 (23), 175 (23), 57 (56), 43 (100). HR-MS *m/z*: 428.4009 [Calcd for $C_{30}H_{52}O_2$ (M^+): 428.4015]. ^{13}C- and ^{1}H-NMR: C-1 [δ_C 32.0; δ_H 1.57 (α), 1.26 (β)], C-2 [30.4; 1.76 (α), 1.55 (β)], C-3 [78.8; 3.28 (dd, J=4.3, 11.0 Hz)], C-4 (40.5), C-5 (47.2; 1.27), C-6 [20.9; 1.56 (α), 0.79 (β, dq, J=2.2, 12.8 Hz)], C-7 [26.3; 1.05 (α), 1.36 (β)], C-8 (48.1; 1.46), C-9 (19.7), C-10 (26.5), C-11 [27.6; 2.09 (α, ddd, J=5.1, 11.4, 15.6 Hz), 1.19 (β)], C-12 [28.3; 1.81 (α), 1.52 (β)], C-13 (46.2), C-14 (47.6), C-15 [36.3; 1.30 (2H)], C-16 [28.4; 1.48 (α), 1.75 (β)], C-17 (55.1; 1.40), C-18 [31.1; 1.13 (s)], C-19 [30.7; 0.31 (*exo*, d, J=4.0 Hz), 0.57 (*endo*, br d, J=4.0 Hz)], C-20 (37.0; 1.37), C-21 [18.3; 0.84 (d, J=5.8 Hz)], C-22 (38.0; 0.95, 1.45), C-23 [25.2; 1.08 (2H)], C-24 (39.5; 1.10, 1.17), C-25 (28.0; 1.49), C-26 [22.6; 0.86 (d, J=6.7 Hz)], C-27 [22.7; 0.86 (d, J=6.7 Hz)], C-28 [25.4; 0.97 (s)], C-29 [14.0; 0.80 (s)], C-30 [19.8; 0.84 (s)].

17-Isocycloartanyl Acetate (**2a**): Colorless needles, mp 88—89°C, $[\alpha]_D$ +4.0° (c=0.10). Rt_R(II): 1.00 (HPLC), 1.28 (GLC). IR ν_{max} cm^{-1}: 3040, 1738, 1246. MS *m/z*: 470 (M^+, 4), 455 (3), 410 (21), 395 (7), 367 (7), 357 (7), 341 (4), 297 (17), 288 (13), 270 (4), 255 (4), 233 (3), 220 (4), 203 (21), 187 (11), 175 (22), 57 (44), 43 (100). HR-MS *m/z*: 470.4108 [Calcd for $C_{32}H_{54}O_2$ (M^+): 470.4120]. ^{13}C- and ^{1}H-NMR: C-1 [δ_C 31.7; δ_H 1.62 (α), 1.26 (β)], C-2 [26.8; 1.77 (α), 1.63 (β)], C-3 [80.7; 4.56 (dd, J=4.6, 11.2 Hz)], C-4 (39.4), C-5 (47.3; 1.38), C-6 [20.7; 1.57 (α), 0.81 (β, dq, J=2.1, 12.8 Hz)], C-7 [26.1; 1.06 (α), 1.38 (β)], C-8 (48.0; 1.48), C-9 (19.8), C-10 (26.3), C-11 [27.6; 2.09 (α), 1.21 (β)], C-12 [28.2; 1.82 (α), 1.51 (β)], C-13 (46.2), C-14 (47.5), C-15 [36.3; 1.31 (2H)], C-16 [28.4; 1.47 (α), 1.74 (β)], C-17 (55.1; 1.40), C-18 [31.1; 1.13 (s)], C-19 [30.7; 0.32 (*exo*, d, J=4.2 Hz), 0.59 (*endo*, br d, J=4.2 Hz)], C-20 (37.0; 1.37), C-21 [18.3; 0.83 (d, J=6.2 Hz)], C-22 (38.0; 0.93, 1.47), C-23 [25.2; 1.08 (2H)], C-24 (39.5; 1.11, 1.17), C-25 (28.0; 1.51), C-26 [22.7; 0.86 (d, J=6.7 Hz)], C-27 [22.7; 0.86 (d, J=6.7 Hz)], C-28 [25.4; 0.85 (s)], C-29 [15.2; 0.88 (s)], C-30 [19.8; 0.84 (s)], OCOMe [21.4; 2.05 (s)], OCOMe (171.0).

Cycloartanol (**3**): Rt_R(I): 1.41 (HPLC), 1.62 (GLC). MS *m/z*: 428 (M^+). ^{13}C- and ^{1}H-NMR: C-1 [δ_C 32.0; δ_H 1.56 (α), 1.24 (β)], C-2 [30.4; 1.75 (α), 1.55 (β)], C-3 [78.9; 3.28 (dd, J=4.3, 11.0 Hz)], C-4 (40.5), C-5 (47.1; 1.30), C-6 [21.1; 1.58 (α), 0.79 (β, dq, J=2.4, 12.8 Hz)], C-7 [26.0; 1.07 (α), 1.33 (β)], C-8 [48.0; 1.50 (dd, J=6.4, 13.1 Hz)], C-9 (20.0), C-10 (26.1), C-11 [26.5; 1.98 (α, ddd, J=7.3, 9.8, 14.9 Hz), 1.10 (β)], C-12 [32.9; 1.62 (2H)], C-13 (45.3), C-14 (48.8), C-15 [35.6; 1.29 (2H)], C-16 [28.2; 1.88 (α), 1.28 (β)], C-17 (52.4; 1.57), C-18 [18.0; 0.96 (s)], C-19 [29.9; 0.33 (*exo*, d, J=4.0 Hz), 0.55 (*endo*, br d, J=4.0 Hz)], C-20 (36.1; 1.34), C-21 [18.3; 0.86 (d, J=6.4 Hz)], C-22 (36.5; 0.99, 1.36), C-23 (24.1; 1.13, 1.35), C-24 [39.5; 1.12 (2H)], C-25 (28.0; 1.53), C-26 [22.6; 0.87 (d, J=6.7 Hz)], C-27 [22.8; 0.86 (d, J=6.4 Hz)], C-28 [25.4; 0.97 (s)], C-29 [14.0; 0.81 (s)], C-30 [19.3; 0.89 (s)].

Cycloart-16-en-3β-yl Acetate (**4a**): Colorless needles, mp 115—117°C (24,25-dihydrocimicifugenyl acetate, lit.[2] mp 116.5—117.5°C). Rt_R(II): 0.97 (HPLC), 1.10 (GLC). MS *m/z*: 468 (M^+, 27), 453 (54), 408 (63), 393 (75),

384 (7), 383 (3), 365 (25), 355 (55), 339 (16), 323 (7), 313 (7), 295 (90), 286 (31), 281 (9), 271 (77), 259 (13), 231 (17), 205 (63), 197 (100). ^{1}H-NMR δ: 0.30 (1H, d, J=4.2 Hz, H-19 *exo*), 0.69 (1H, d, J=4.2 Hz, H-19 *endo*), 0.86 (3H, s, H-28), 0.86 (6H, d, J=6.5 Hz, H-26, H-27), 0.90 (3H, s, H-29), 0.93 (3H, s, H-30), 0.99 (3H, d, J=6.7 Hz, H-21), 1.05 (3H, s, H-18), 2.06 (3H, s, OAc-3), 4.57 (1H, dd like, J=4.2, 11.3 Hz), 5.18 (1H, br s, H-16).

References and Notes

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