

Δ^{18} OLEANE TRITERPENES FROM *SCHAEFFERIA CUNEIFOLIA*

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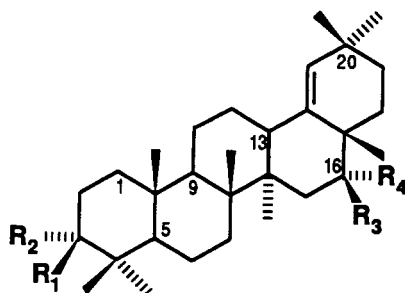
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ABSTRACT.—Four new natural products, olean-18-ene-3 β ,16 β -diol [**1**], 3 β ,16 β -diacetoxyolean-18-ene [**2**], 16 β -hydroxyolean-18-en-3-one [**3**], and 16 α -hydroxyolean-18-en-3-one [**4**], were isolated from *Schaefferia cuneifolia* and identified from their ^1H - and ^{13}C -nmr data, DEPT experiments, chemical correlations, and chemical shift values.

As part of an ongoing study (1–5) of the chemical composition of flora used in Latin American folk medicine, *Schaefferia cuneifolia* A. Gray (Celastraceae) was re-examined (6,7). This species grows in northern Mexico and has shown activity in the treatment of venereal diseases. Four new products, assigned the structures olean-18-ene-3 β ,16 β -diol [**1**], 3 β ,16 β -diacetoxyolean-18-ene [**2**], 16 β -hydroxyolean-18-en-3-one [**3**], and 16 α -hydroxyolean-18-en-3-one [**4**], were isolated.

Hrms of **1** gave the molecular formula $\text{C}_{30}\text{H}_{50}\text{O}_2$. The ir spectrum showed signals for hydroxy groups. In ^1H nmr a vinyl proton appeared as a broad singlet at δ 4.83, two protons geminal to secondary equatorial alcohol groups as double doublets centered at δ 3.20 ($J = 5.8, J = 10.2$) and 3.62 ($J = 6.4, J = 9.8$), and eight singlets for methyls at δ 0.72, 0.76, 0.88, 0.95, 0.96, 1.01, 1.07, and 1.25. These data, taken in conjunction with the ms fragmentation pattern (m/z 220, 206, 205, 175) (8), characterize **1** as a 3 β -hydroxyolean-18-ene with the second hydroxy group at 15 α , 16 β , 21 α , or 22 β .

When **1** was oxidized with pyridine chlorochromate (9), diketone **7** was produced, and its ^{13}C nmr spectrum (Table 1) proved virtually identical to that previously published (10)¹ for olean-18-ene-3,16-dione [**7**]; substitution positions and stereochemis-



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|----------|---|
| 1 | $\text{R}_1 = \text{R}_3 = \text{OH}, \text{R}_2 = \text{R}_4 = \text{H}$ |
| 2 | $\text{R}_1 = \text{R}_3 = \text{OAc}, \text{R}_2 = \text{R}_4 = \text{H}$ |
| 3 | $\text{R}_1\text{R}_2 = \text{O}, \text{R}_3 = \text{OH}, \text{R}_4 = \text{H}$ |
| 4 | $\text{R}_1\text{R}_2 = \text{O}, \text{R}_3 = \text{H}, \text{R}_4 = \text{OH}$ |
| 5 | $\text{R}_1\text{R}_2 = \text{O}, \text{R}_3 = \text{OAc}, \text{R}_4 = \text{H}$ |
| 6 | $\text{R}_1\text{R}_2 = \text{O}, \text{R}_3 = \text{H}, \text{R}_4 = \text{OAc}$ |
| 7 | $\text{R}_1\text{R}_2 = \text{O}, \text{R}_3\text{R}_4 = \text{O}$ |

¹The published nmr spectrum of olean-18-ene-3,16-dione was taken at the University of Sussex on a JEOL PFT-100 at 25.15 MHz.

TABLE 1. ^{13}C -nmr Chemical Shifts (δ) (CDCl_3).

Carbon	Compound				
	1	2	5	7	8
1	38.5 (t)	38.8 (t)	39.9 (t)	40.0 (t)	38.5 (t)
2	27.4 (t)	23.8 (t)	34.2 (t)	34.2 (t)	27.4 (t)
3	79.1 (d)	81.1 (d)	218.3 (s)	218.3 (s)	79.0 (s)
4	39.0 (s)	38.8 (s)	47.4 (s)	47.4 (s)	39.0 (s)
5	55.7 (d)	55.7 (d)	54.9 (d)	55.0 (d)	55.7 (d)
6	18.4 (t)	18.3 (t)	19.8 (t)	19.8 (t)	18.3 (t)
7	34.5 ^a (t)	34.6 ^a (t)	33.8 (t)	33.9 (t)	34.7 (t)
8	40.8 (s)	40.8 (s)	40.7 (s)	40.1 (s)	40.8 (s)
9	51.3 (d)	51.2 (d)	50.6 (d)	50.6 (d)	51.3 (d)
10	37.4 (s)	37.8 (s)	37.1 (s)	38.3 (s)	37.3 (s)
11	21.3 (t)	21.3 (t)	21.8 (t)	21.7 (t)	21.2 (t)
12	26.7 (t)	26.6 (t)	26.7 (t)	26.9 (t)	26.2 (t)
13	39.1 (d)	38.4 (d)	38.4 (d)	38.3 (d)	39.0 (d)
14	42.8 (s)	42.8 (s)	42.8 (s)	50.3 (s)	43.4 (s)
15	34.7 (t)	34.2 (t)	34.2 (t)	47.2 (t)	27.6 (t)
16	76.7 (d)	78.9 (d)	78.9 (d)	216.0 (s)	37.4 (t)
17	39.6 (s)	38.6 (s)	38.6 (s)	47.4 (s)	34.4 (s)
18	141.7 (s)	141.3 (s)	141.2 (s)	142.3 (s)	142.8 (s)
19	129.4 (d)	129.6 (d)	129.7 (d)	129.8 (d)	129.8 (d)
20	31.9 (s)	29.8 (s)	29.8 (s)	34.2 (s)	32.3 (s)
21	33.7 ^a (t)	33.8 ^a (t)	33.8 (t)	33.9 (t)	33.4 (t)
22	37.4 (t)	38.0 (t)	37.9 (t)	29.8 (t)	37.7 (t)
23	28.1 (q)	28.0 (q)	27.1 (q)	27.0 (q)	28.0 (q)
24	15.5 (q)	16.2 (q)	21.0 (q)	21.1 (q)	15.4 (q)
25	16.3 ^b (q)	16.6 ^b (q)	16.0 ^a (q)	16.1 ^a (q)	16.1 (q)
26	16.9 ^b (q)	16.9 ^b (q)	16.7 ^a (q)	16.7 ^a (q)	16.7 (q)
27	14.8 (q)	14.8 (q)	14.8 (q)	14.3 (q)	14.6 (q)
28	27.4 (q)	28.0 (q)	29.7 (q)	27.1 (q)	25.3 (q)
29	31.9 (q)	31.7 (q)	31.7 (q)	30.7 (q)	31.3 (q)
30	30.0 (q)	29.7 (q)	29.7 (q)	30.0 (q)	29.2 (q)

^{a,b}Chemical shifts with the same letter can be interchanged.

try were thus determined. Because the two alcohol groups are equatorial in **1**, the ^1H - and ^{13}C -nmr data of its diacetate **2** are in accordance with the data given above, and assignments were based on DEPT experiments (11), correlation with other data (9), Beierback and Saunders' methods for calculating shifts (12, 13), and Iida's (14) observations on the effect of hydroxy groups on shifts. The acetylation product of **1** proved identical to the natural substance **2**, and its structure was established accordingly. A mixture of **3** and **4** proved inseparable although the major product was clearly **3**. This mixture was acetylated and the acetates **5** and **6** separated.

The data of product **5** showed it to be a keto-acetate, formula $\text{C}_{32}\text{H}_{50}\text{O}_3$, and the ^1H - and ^{13}C -nmr data (Table 1) and ms (15, 16) indicated a 16β -acetoxylean-18-en-3-one structure.

Compound **6**, formula $\text{C}_{32}\text{H}_{50}\text{O}_3$, differed from **5** most notably in the signal for the acetate group geminal proton, which in **5** appeared as a double doublet superimposed on the vinyl proton with the same characteristics as the proton geminal to the acetate at 16β in **2**. In **6**, however, the chemical shift and the form of the signal (a doublet) were not the same as in **2**: compound **6** therefore had to be an epimer of product **5** at C-16 and its structure was determined as 16α -acetoxylean-18-en-3-one, which was confirmed when the mixture of **3** and **4** oxidized under the same conditions as **1** gave di-

ketone **7** as sole product. For comparison purposes, the data of germanicol [**8**] are included in Table 1.

While 16-substituted triterpenes with fully documented stereochemistry (17–20) abound in the Δ^{12} -oleane series, these triterpenes, **1**, **2**, **3**, and **4**, are, together with the previously described **7**, the only known 16-substituted products in the Δ^{18} -oleane series.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mp's were determined on a Kofler-type apparatus and are uncorrected. ^1H (200 MHz) and ^{13}C nmr (50 MHz) were determined on a Bruker WP-200SY spectrometer with CDCl_3 as solvent. High and low resolution mass spectra were obtained on a VG-Micromass ZAB-2F at 15 or 70 eV. Optical activities were measured on a Perkin-Elmer 241 polarimeter. The ir spectra were taken on a Perkin-Elmer 681 spectrophotometer with NaCl cells (0.1 mm) and CHCl_3 as solvent.

ISOLATION OF THE TERPENES.—Aerial parts (1.5 kg) of *S. cuneifolia* collected in northeastern Mexico (voucher specimen 7489 lodged with the Herbarium of the Department of Botany, Instituto Tecnológico y de Estudios Superiores de Monterrey, Monterrey, Mexico) was extracted with MeOH, yielding 20 g of an extract which was chromatographed on Si gel with hexane/EtOAc mixtures of increasing polarity, yielding olean-18-ene-3 β ,16 β -diol [**1**] (27 mg), 3 β ,16 β -diacetoxyolean-18-ene [**2**] (12 mg), and 16 β -hydroxyolean-18-en-3-one [**3**] and 16-hydroxyolean-18-en-3-one [**4**] as an inseparable mixture (25 mg).

OLEAN-18-ENE-3 β ,16 β -DIOL [1**].**—Compound **1** (27 mg): mp 237–238°; $[\alpha]_D^{20} + 8.5$ ($c = 0.07$, CHCl_3); ir λ max 3665, 3020, 1510, 1420, 1210 cm^{-1} ; ^1H nmr (200 MHz) δ 0.72, 0.76, 0.88, 0.95, 0.96, 1.01, 1.07, 1.25 (each 3H, s), 2.30 (1H, d, $J = 13$ Hz), 3.20 (1H, m), 3.62 (1H, dd, $J = 6.4$, 9.8 Hz), 4.83 (1H, s); ms m/z (%) 442 (6), 427 (5), 409 (4), 234 (12), 231 (19), 220 (45), 207 (22), 205 (28), 202 (23), 201 (26), 193 (13), 189 (25), 187 (28), 175 (50), 161 (26), 148 (20), 147 (23), 145 (18), 135 (37), 133 (27), 121 (40), 118 (37), 109 (52), 107 (49), 105 (35), 95 (58), 91 (33), 81 (59), 79 (31), 67 (51), 57 (41), 43 (100); calcd for $\text{C}_{30}\text{H}_{50}\text{O}_2$, 442.3859, found 442.3834; calcd for $\text{C}_{29}\text{H}_{47}\text{O}_2$, 427.3572, found 427.3573; calcd for $\text{C}_{29}\text{H}_{45}\text{O}$, 409.3335, found 409.3402; ^{13}C nmr see Table 1.

3 β ,16 β -DIACETOXYOLEAN-18-ENE [2**].**—Compound **2** (12 mg) was obtained as a natural product by chromatography as a white crystalline solid: mp 230–232° (*n*-hexane/EtOAc); $[\alpha]_D^{20} + 6.35$ ($c = 0.236$, CHCl_3); ir λ max 2950, 1720, 1450, 1370, 1240, 1040, 1020 cm^{-1} ; ^1H nmr (200 MHz) δ 0.72 (3H, s), 0.84 (6H, s), 0.90, 0.96 (each 3H, s), 1.06 (6H, s), 1.08 (3H, s), 2.04 (6H, s), 2.24 (1H, d, $J = 5.4$ Hz), 4.47 (1H, t), 4.86 (1H, s), 4.89 (1H, overlapping signal); ms m/z (%) $[\text{M}]^+$ 526 (6), 466 (12), 423 (6), 406 (4), 391 (22), 279 (2), 262 (33), 247 (4), 235 (4), 231 (12), 216 (10), 204 (20), 203 (40), 202 (49), 189 (50), 187 (68), 175 (68), 161 (30), 159 (23), 145 (21), 135 (32), 133 (30), 121 (33), 119 (64), 109 (26), 107 (31), 93 (28), 81 (31), 79 (15), 69 (36), 67 (18), 57 (16), 55 (33), 43 (100); calcd for $\text{C}_{34}\text{H}_{54}\text{O}_4$, 526.3993, found 526.4006; calcd for $\text{C}_{33}\text{H}_{51}\text{O}_4$, 511.3853, found 511.3819; calcd for $\text{C}_{32}\text{H}_{50}\text{O}_2$, 466.3749, found 466.3779; calcd for $\text{C}_{31}\text{H}_{47}\text{O}_2$, 451.3639, found 451.3607; calcd for $\text{C}_{29}\text{H}_{43}\text{O}_2$, 423.3373, found 423.3317; calcd for $\text{C}_{30}\text{H}_{46}\text{O}$, 406.3598, found 406.3597; calcd for $\text{C}_{29}\text{H}_{43}\text{O}$, 391.3284, found 391.3323; ^{13}C nmr see Table 1.

16 β -ACETOXYOLEAN-18-EN-3-ONE [5**].**—Compound **5** (14 mg) was obtained as a white crystalline solid from acetylated fractions which were then chromatographed: mp 208–210° (CHCl_3); $[\alpha]_D^{20} + 31.5$ ($c = 0.14$, CHCl_3); ir λ max 2940, 1710, 1680, 1500, 1450, 1420, 1270, 1240, 1020, 1000, 920 cm^{-1} ; ^1H nmr (200 MHz) δ 0.73, 0.95, 0.96, 1.02 (each 3H, s), 1.07 (9H, s), 1.08, 2.04 (each 3H, s), 2.31 (1H, d, $J = 12$ Hz), 2.48 (2H, m), 4.85 (1H, s), 4.90 (1H, dd, $J = 6$, 10.5 Hz); ms m/z (%) $[\text{M}]^+$ 482 (53), 467 (13), 422 (34), 407 (58), 389 (5), 309 (1), 275 (2), 262 (28), 248 (3), 245 (2), 235 (11), 216 (17), 202 (56), 187 (82), 175 (100), 173 (31), 161 (26), 149 (7), 133 (40), 119 (65), 107 (34), 95 (94), 93 (29), 81 (39), 69 (51), 55 (66), 42 (11); calcd for $\text{C}_{32}\text{H}_{50}\text{O}_3$, 482.3748, found 482.3753; calcd for $\text{C}_{31}\text{H}_{47}\text{O}_3$, 468.3573, found 468.3587; calcd for $\text{C}_{30}\text{H}_{47}\text{O}$, 424.3800, found 424.3751; calcd for $\text{C}_{29}\text{H}_{43}\text{O}$, 407.3314, found 407.3313; ^{13}C nmr see Table 1.

16 β -ACETOXYOLEAN-18-EN-3-ONE [6**].**—Compound **6** (5 mg) crystallized as white needles in CHCl_3 from acetylated fractions which were then chromatographed: mp 210–212° (CHCl_3); $[\alpha]_D^{20} + 37$ ($c = 0.13$, CHCl_3); ir λ max 2930, 1710, 1680, 1500, 1450, 1420, 1360, 1240, 1150, 1020, 930 cm^{-1} ; ^1H nmr (200 MHz) δ 0.76 (3H, s), 0.96 (6H, s), 0.97, 1.02, 1.07, 1.08, 1.12, 2.04 (each 3H, s), 2.45 (2H, m), 4.79 (1H, dd, $J = 4.0$, 6.0 Hz), 4.82 (1H, s); ms m/z (%) $[\text{M}]^+$ 482 (5), 467 (1), 422 (4), 407 (3), 276 (5), 262 (11), 235 (4), 216 (12), 203 (21), 202 (11), 187 (14), 175 (14), 173 (9), 161 (8), 149 (7),

147 (9), 133 (17), 119 (22), 107 (17), 105 (16), 95 (21), 93 (17), 81 (24), 69 (29), 67 (23), 55 (45), 43 (100); calcd for $C_{32}H_{50}O_3$, 482.3778, found 482.3768; calcd for $C_{31}H_{47}O_3$, 467.3514, found 467.3519; calcd for $C_{30}H_{46}O$, 422.3491, found 422.3518; calcd for $C_{29}H_{43}O$, 407.3293, found 407.3302.

OLEAN-18-EN-3,16-ONE [7].—Compound **7** (6 mg, 0.014 mmol, 76%), was obtained as a white, crystalline solid when **1** (8 mg, 0.018 mmol) was dissolved in Me_2CO , oxidized with Jones' reagent, extracted, and purified: mp 210–212°; $[\alpha]^{20} - 7.8$ ($c = 0.14$, $CHCl_3$); ir λ max 2950, 1700, 1460, 1380, 1230, 1100 cm^{-1} ; 1H nmr (200 MHz) δ 0.76, 0.96, 1.00 (each 3H, s), 1.03 (6H, s), 1.07, 1.12, 1.24 (each 3H, s), 2.25–2.58 (5H, m), 5.16 (1H, s); ms m/z (%) $[M]^+$ 438 (13), 423 (14), 232 (40), 220 (23), 219 (83), 218 (100), 205 (37), 203 (60), 189 (26), 187 (11), 177 (16), 175 (38), 163 (43), 161 (46), 149 (29), 147 (34), 135 (25), 133 (26), 121 (30), 119 (36), 109 (27), 107 (36), 105 (30), 93 (30), 79 (23), 77 (12), 69 (45), 67 (34), 57 (20), 55 (58), 43 (42); calcd for $C_{30}H_{43}O_2$, 438.3492, found 438.3493; calcd for $C_{29}H_{43}O_2$, 423.3784, found 423.3272; ^{13}C nmr see Table 1.

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