Synthesis of Natural Atisane-Type Diterpenoids by *retro*-Biomimetic Transformations

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An efficient one step, *retro*-biomimetic procedure for the synthesis of natural products having the atisane structure is described (*Scheme 2*), natural products which are components of medicinal plants and possess relevant biological activity. Their structures were confirmed by chemical transformations and spectral data. The starting materials were the known *ent*-kaur-16-en-19-oic acid (**1**) and *ent*-trachyloban-19-oic acid (**2**), diterpenoids readily available from the waste of sunflower.

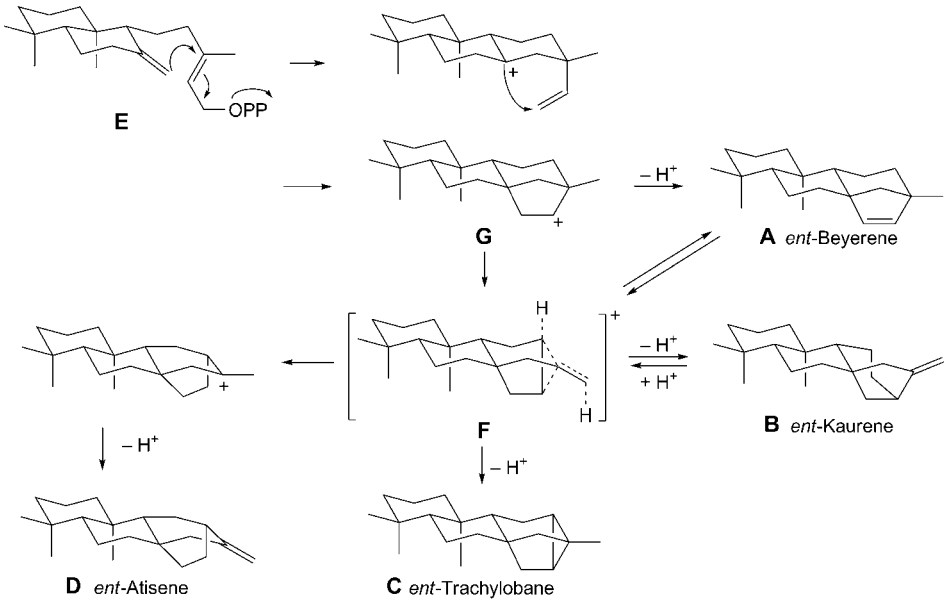
Introduction. – Tetracyclic atisanes, beyeranes, kauranes, and pentacyclic trachylobanes represent an important group of biosynthetically closely related polycyclic diterpenes, many of which display a wide range of biological activities [1–7]. According to the hypothesis of diterpene biogenesis [8], diterpenes belonging to the families of *ent*-beyerene (**A**), *ent*-kaurene (**B**), *ent*-trachylobane (**C**), and *ent*-atisene (**D**) might all arise from (−)-copalyl pyrophosphate **E** *via* nonclassical carbocations such as **F** as common intermediates (*Scheme 1*). This hypothesis [8] has been formulated on the basis of the known isoprene rule and, to the best of our knowledge, has not been turned down yet. *Scheme 1* provides a general overview of this biogenetic scheme, and our primary intention was to perform the *retro*-biomimetic transformation of *ent*-kaurene (**B**) to *ent*-beyerene (**A**) or *ent*-atisene (**D**) (path **B** → **F** → **A** or **D**).

The rearrangements of *ent*-kaurane- and *ent*-trachylobane-type diterpenes have been reported under the action of different reagents [9]. Most of the examples relate on the reactions involving the formation of the nonclassical carbocation of type **F** (*Scheme 1*). It is well-known from the work of *Olah* and co-workers [10] that superacids are very convenient generators of these species, and our own experience on the use of fluorosulfuric acid (= 'fluorosulfonic acid'; FSO_3H) as an efficient promoter of terpenoid cyclizations [11–15] and rearrangements [16–18] provided a motivation to investigate the behavior of *ent*-kaur-16-en-19-oic acid (**1**) [19] and *ent*-trachyloban-19-oic acid (**2**) under superacid treatment (*Scheme 2*).

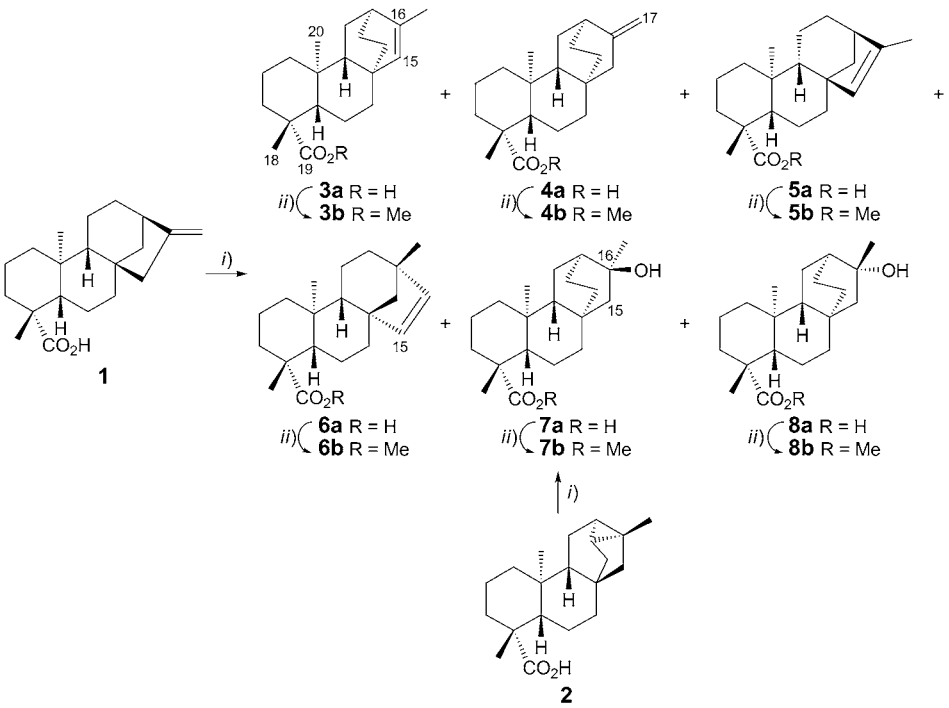
Results and Discussion. – *ent*-Kaur-16-en-19-oic acid (**1**) and *ent*-trachyloban-19-oic acid (**2**) are accessible compounds and have been isolated from the dry waste of sun flower *Helianthus annuus* L. (*Scheme 2*) [20].

Treatment of *ent*-kaur-16-en-19-oic acid (**1**) with an excess (5 equiv.) of fluorosulfuric acid under mild reaction conditions (−60°) allowed carbonium ion generation and skeletal rearrangement to occur. The crude reaction product was first separated by column chromatography (CC) (SiO_2) in an unpolar-compounds fraction

Scheme 1. Wenkert's *Hypothesis of Diterpene Biogenesis*



Scheme 2



i) FSO_3H (5 equiv.), i-$PrNO_2/CH_2Cl_2$, $-60°$, 15 min, then Et_3N. *ii*) CH_2N_2/Et_2O, r.t., 30 min.

A and a polar-compounds fraction *B*. The unpolar compounds (*Fr. A*) were separated by another CC (silver nitrate-impregnated SiO_2, gradient elution) to afford, in the order of increasing polarity, *ent*-atis-15-en-19-oic acid (**3a**; 8%), *ent*-atis-16-en-19-oic acid (**4a**; 22%) [21], recovered starting material **1** (18%), *ent*-kaur-15-en-19-oic acid (**5a**; 17%), and finally *ent*-beyer-15-en-19-oic acid (**6a**; 7%) [21] (*Scheme 2*). The structures of the isolated products were established on the basis of spectral data; *i.e.*, their ^{1}H- and ^{13}C-NMR spectra, assisted by DEPT and two-dimensional experiments (COSY, HSQC, HMBC) for signal assignment. Treatment of the individual acids **3a**, **4a**, **5a**, and **6a** with an Et_2O solution of diazomethane led to the corresponding esters, *i.e.*, methyl *ent*-atis-15-en-19-oate (**3b**) [22], methyl *ent*-atis-16-en-19-oate (**4b**) [21–24], methyl *ent*-kaur-15-en-19-oate (**5b**) [25], methyl *ent*-beyer-15-en-19-oate (**6b**) [21][26]. Their spectral properties matched the available literature data.

The polar compounds (*Fr. B*) were re-submitted to CC (SiO_2) to afford, in the order of increasing polarity; (16α)-16-hydroxy-*ent*-atisan-19-oic acid (**7a**; 5%) [27] and (16β)-16-hydroxy-*ent*-atisan-19-oic acid (**8a**; 4%) [27]. Their physicochemical and spectral properties matched the published data, and diazomethane methylation led to the corresponding methyl esters **7b** and **8b**, with physicochemical and spectral data matching those published earlier [28][29].

Thus, the superacid-promoted rearrangement of *ent*-kaurenoic acid **1** led predominantly to tetracyclic *ent*-atisane diterpenoids (see **3a**, **4a**, **7a**, and **8a**), with an overall yield of 39%. Taking into account the recovered starting material **1**, the combined yield of compounds **3a**, **4a**, **7a** and **8** amounted to *ca.* 62%.

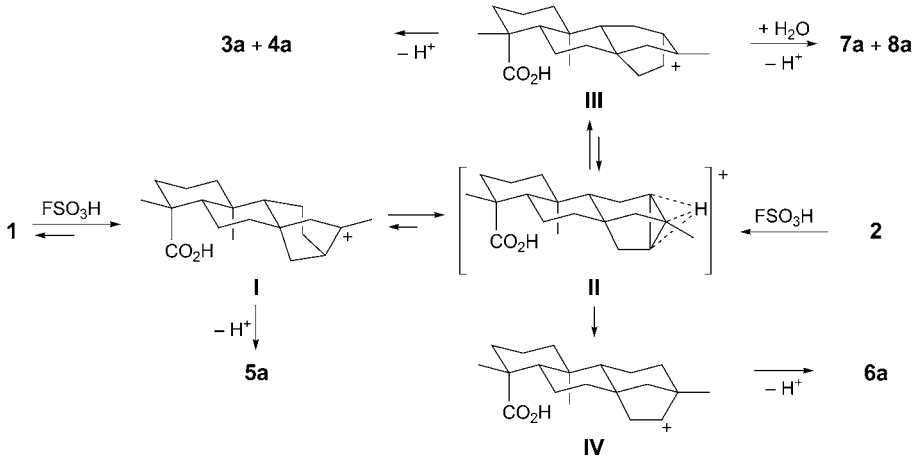
Isomerization of *ent*-trachyloban-19-oic acid (**2**) was performed under conditions identical to those used for *ent*-kaur-16-en-19-oic acid (**1**). Superacid treatment afforded a mixture of rearranged compounds which were separated following the same protocol as described above for **1**. From the unpolar-compounds fraction, *ent*-atis-15-en-19-oic acid (**3a**; 12%), *ent*-atis-16-en-19-oic acid (**4a**; 22%), *ent*-kaur-16-en-19-oic acid (**1**; 3%), *ent*-kaur-15-en-19-oic acid (**5a**; 1%), and finally *ent*-beyer-15-en-19-oic acid (**6a**; 2%) were obtained, identical by their spectral data with those formed from **1**.

The polar-compounds fraction was separated into (16α)-16-hydroxy-*ent*-atisan-19-oic acid (**7a**; 23%) and (16β)-1b-hydroxy-*ent*-atisan-19-oic acid (**8a**; 16%), identical by their spectral data with those formed from **1**.

Thus, the superacid-promoted isomeritzation of *ent*-trachiloban-19-oic acid (**2**), yielded also essentially atisane diterpenoids, the overall yield of compounds **3a**, **4a**, **7a**, and **8a** amounting to *ca*. 73%.

The transformation of *ent*-kaur-16-en-19-oic acid (**1**) into *ent*-atisane-type compounds takes place by the formation of carbonium ion **I**, which rearranges *via* the nonclassical pentacyclic ion **II** to the *ent*-atisane carbonium ion **III** (*Scheme 3*). The latter undergoes a H-atom loss from either C(15) or C(17) to form the C=C bond isomeric *ent*-atisenoic acids **3a** and **4a**. The hydroxylated *ent*-atisanoic acids **7a** and **8a** are formed by quenching of **III** with a water molecule. On loss of one H-atom from C(15) of *ent*-kaurenoic acid carbonium ion **I**, the *ent*-kaur-15-en-19-oic acid (**5a**) is obtained. The *ent*-beyer-15-en-19-oic acid (**6a**) is formed after transformation of the nonclassical carbonium ion **II** to the *ent*-beyeranoic acid cation **IV** and subsequent H-atom loss from C(16).

Scheme 3. *Proposed Reaction Course for Superacid-Promoted Isomerization of* **1** *and* **2**



Conclusions. – A new concept of natural-product synthesis is suggested, namely the *retro*-biomimetic approach. Based on this concept, easily accessible *ent*-kaurene-and *ent*-trachilobane-type diterpenoids were transformed to diterpenoids with an *ent*-atisane-type skeleton.

It is noteworthy mentioning that *ent*-atisane-type diterpenoids possess cytotoxic activity [30–33].

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Experimental Part

1. *General*. Treatment of reaction mixtures in org. solvents included the extraction by Et_2O, washing of the extract with H_2O up to neutral reaction, drying (Na_2SO_4), and solvent removal *in vacuo*. Column flash chromatography (CC): *Merck* silca gel *60* (70–230 mesh; *ASTM*). TLC: *Merck* precoated silica gel plates; detection by spraying with 0.1% cerium(IV) sulfate in 2N H_2SO_4 followed by heating at 80° for 5 min. M.p.: *Boethius* heating stage. Optical rotations: *Jasco-DIP-370* polarimeter; 5-cm cell; in $CHCl_3$. IR Spectra: *Spectrum-100* FT-IR spectrophotometer (*Perkin–Elmer*), with the universal ATR sampling accessory; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Bruker-Avance-III* spectrometer (400.13 and 100.61 MHz); in $CDCl_3$; δ in ppm rel. to $CHCl_3$ as internal standard (δ(H) 7.26 and δ(C) 77.0), *J* in Hz. GC/MS: *Agilent-7890A* chromatograph; quadrupole MS detector *MSD 5975C*; *HP-5ms* capillary column (30 m/0.25 μm). EI-MS: operating at an ionization potential of 70 eV.; in *m/z* (rel. %), Elemental analyses: CHNOS analyzer *Vario EL III*.

2. *Superacid-Promoted Isomerization of* ent-*Kaur-16-en-19-oic Acid* (**1**). A soln. of **1** (403 mg, 1.324 mmol) in 2-nitropropane (2 ml) and CH_2Cl_2 (9 ml) was chilled to −60° and treated with a soln. of FSO_3H (662 mg, 6.62 mmol) in 2-nitropropane (1.4 ml), also chilled to −60°. After 15 min stirring at −60°, the mixture was quenched with Et_3N/hexane 1:1 (8 ml). Dilution with H_2O (10 ml) and usual workup gave a crude product (395 mg) which was submitted to CC (SiO_2 (10 g), AcOEt/petroleum ether 1:49, then 1:1): *Fraction A* of nonpolar compounds (298 mg, 74%) and *Fraction B* of polar compounds (74 mg, 18%). *Fr. A* (298 mg) was re-subjected to CC (silver nitrate impregnated SiO_2 (16 g), benzene and AcOEt/benzene): **3a** (33 mg, 8%; with benzene), **4a** (89 mg, 22%) and **1** (74 mg, 18%; with 1% AcOEt/benzene), and **5a** (68 mg, 17%) and **6a** (30 mg, 7%; with 3% AcOEt/benzene). *Fr. B* (74 mg) was

re-subjected to CC (SiO_2 (4 g), gradient AcOEt/benzene 7:93 → 15:85): **7a** (19 mg, 5%) and **8a** (16 mg, 4%).

3. *Superacid-Promoted Isomerization of* ent-*Trachyloban-19-oic Acid* (**2**). As described in *Exper. 2*, with **2** (297 mg, 0.938 mmol) in 2-nitropropane (1.6 ml) and CH_2Cl_2 (7.2 ml) and FSO_3H (692 mg, 6.92 mmol) in 2-nitropropane (1.2 ml). Quenching with Et_3N/hexane 1:1 (10 ml), dilution with H_2O (12 ml), usual workup, and CC (SiO_2 (7g)) of the crude product (290 mg) gave *Fraction A* of nonpolar compounds (123 mg, 41%) and *Fraction B* of polar compounds (150 mg, 51%). *Fr. A* (123 mg) was subjected to CC as described in *Exper. 1:* **3a** (36 mg, 12%), **4a** (66 mg, 22%) and **1** (8.3 mg, 3%), and **5a** (3 mg, 1%) and **6a** (5.5 mg, 2%). *Fr. B* (150 mg) was subjected to CC (SiO_2 (8 g)) as described in *Exper. 1:* **7a** (68 mg, 23%) and **8a** (47 mg, 16%).

ent-*Atis-15-en-19-oic Acid* (**3a**). White crystalline solid. M.p. 184–185° (MeOH). $[\alpha]_D^{20} = -78.6$ ($c = 0.16$, $CHCl_3$). IR (liquid film): 3550–3220, 3050, 1695, 1467, 1440, 1272, 1250. ^{1}H-NMR (400 MHz): 5.58 (br. *t*, $J = 2$, H–C(15)); 1.76 (*s*, Me(17)); 1.25 (*s*, Me(18)); 0.90 (*s*, Me(20)). ^{13}C-NMR (100 MHz): 182.7 (*s*, C(19)); 140.3 (*s*, C(16)); 135.9 (*t*, C(15)); 57.2 (*d*, C(5)); 53.3 (*d*, C(9)); 43.7 (*s*, C(4)); 40.3 (*t*, C(1)); 38.0 (*t*, C(3)); 38.0 (*s*, C(10)); 37.9 (*t*, C(7)); 37.4 (*s*, C(8)); 35.9 (*d*, C(12)); 28.9 (*q*, C(18)); 28.3 (*t*, C(14)); 27.5 (*t*, C(11)); 26.6 (*t*, C(13)); 20.4 (*t*, C(6)); 20.0 (*q*, C(17)); 18.8 (*t*, C(2)); 11.9 (*q*, C(20)). EI-MS: 302 (12, M^+), 287 (10, $[M - Me]^+$), 274 (18), 256 (3), 241 (6), 207 (10), 159 (14), 119 (29), 106 (44), 81 (50), 44 (100). Anal. calc. for $C_{20}H_{30}O_2$: C 79.42, H 10.00; found: C 79.39, H 9.98.

ent-*Atis-16-en-19-oic Acid* (**4a**): White crystalline solid. M.p. 218–220° (MeOH). ([21]: m.p. 219°) $[\alpha]_D^{20} = -70.2$ ($c = 1.5$, $CHCl_3$), ([21]: $[\alpha]_D = -69.7$ ($c = 2.0$, $CHCl_3$)). IR (liquid film): 3550–3200, 3040, 2918, 1690, 1464, 1446, 1273, 1260. ^{1}H-NMR (400 MHz): 4.73 (br. *d*, $J = 2$, 1 H); 4.57 (br. *d*, $J = 2$, 1 H); 2.22 (br. *s*, 1 H); 2.15 (br. *d*, $J = 14$, 1 H); 2.04 (br. *d*, $J = 17$, 1 H); 1.29–2.00 (*m*, 19 H); 1.25 (*s*, 3 H); 1.24 (*s*, 3 H); 0.91–1.18 (*m*, 8 H); 0.90 (*s*, 3 H); 0.70–0.88 (*m*, 8 H). ^{13}C-NMR (100 MHz): 182.3 (*s*, C(19)); 152.8 (*s*, C(15)); 104.5 (*t*, C(17)); 57.2 (*d*, C(5)); 52.2 (*d*, C(9)); 48.2 (*t*, C(16)); 43.7 (*s*, C(4)); 39.7 (*t*, C(1)); 39.7 (*t*, C(7)); 38.4 (*s*, C(10)); 38.1 (*t*, C(3)); 36.6 (*d*, C(12)); 33.6 (*s*, C(8)); 28.9 (*q*, C(18)); 28.7 (*t*, C(14)); 28.3 (*t*, C(13)); 27.3 (*t*, C(11)); 20.3 (*t*, C(6)); 18.8 (*t*, C(2)); 12.1 (*q*, C(20)). EI-MS: 302 (23, M^+), 287 (75, $[M - Me]^+$), 274 (4), 257 (21), 241 (27), 213 (15), 159 (21), 107 (58), 91 (100), 44 (86). Anal. calc. for $C_{20}H_{30}O_2$: C 79.42, H 10.00; found: C 79.37, H 9.96.

ent-*Kaur-15-en-19-oic Acid* (**5a**). White crystalline solid. M.p. 172–173° (MeOH). $[\alpha]_D^{20} = -59.2$ ($c = 0.16$, $CHCl_3$). IR (liquid film): 3540–3200, 3030, 1690, 1464, 1442, 1270, 1250. ^{1}H-NMR (400 MHz): 5.07 (br. *t*, $J = 1.8$, H–C(15)); 1.70 (*s*, Me(17)); 1.23 (*s*, Me(18)); 0.97 (*s*, Me(20)). ^{13}C-NMR (100 MHz): 184.0 (*s*, C(19)); 142.5 (*s*, C(16)); 135.2 (*t*, C(15)); 56.9 (*d*, C(5)); 49.2 (*s*, C(8)); 48.2 (*d*, C(9)); 44.8 (*d*, C(13)); 43.9 (*t*, C(14)); 43.8 (*s*, C(4)); 40.8 (*t*, C(1)); 39.9 (*s*, C(10)); 39.5 (*t*, C(7)); 37.9 (*t*, C(3)); 28.9 (*q*, C(18)); 24.9 (*t*, C(12)); 20.8 (*t*, C(6)); 19.1 (*t*, C(11));19.0 (*t*, C(2)); 15.4 (*q*, C(20)); 15.4 (*q*, C(17)). EI-MS: 302 (13, M^+), 287 (9, $[M - Me]^+$), 274 (3), 258 (5), 241 (8), 213 (5), 159 (16), 119 (34), 107 (62), 94 (100). Anal. calc. for $C_{20}H_{30}O_2$: C 79.42, H 10.00; found: C 79.41, H 9.97.

ent-*Beyer-15-en-19-oic Acid* (=*(8β,13β)-13-Methyl-17-nor*-ent-*kaur-15-en-19-oic Acid*; **6a**): White crystalline solid. M.p. 183–185° (MeOH). ([21]: m.p. 184° (MeOH)) $[\alpha]_D^{20} = +8.2$ ($c = 0.33$, $CHCl_3$), ([21]: $[\alpha]_D = +7.0$ ($c = 1.8$, $CHCl_3$)). IR (liquid film): 3025, 2935, 1685, 1445, 1255, 1190. ^{1}H-NMR (400 MHz): 5.76 (*d*, $J = 5.7$, H–C(15)); 5.47 (*d*, $J = 5.7$, H–C(16)); 1.26 (*s*, Me(18)); 1.01 (*s*, Me(17)); 0.69 (*s*, Me(20)). ^{13}C-NMR (100 MHz): 184.3 (*s*, C(19)); 136.5 (*d*, C(16)); 134.8 (*d*, C(15)); 61.1 (*t*, C(14)); 57.2 (*d*, C(5)); 52.4 (*d*, C(9)); 49.2 (*s*, C(8)); 43.9 (*s*, C(4)); 43.7 (*s*, C(13)); 39.6 (*t*, C(1)); 38.0 (*t*, C(3)); 37.7 (*t*, C(7)); 37.7 (*s*, C(10)); 33.2 (*t*, C(12)); 29.1 (*q*, C(18)); 24.9 (*q*, C(17)); 21.6 (*t*, C(6)); 20.5 (*t*, C(11));19.3 (*t*, C(2)); 13.8 (*q*, C(20)). EI-MS: 302 (18, M^+), 287 (8, $[M - Me]^+$, 272 (2), 257 (3), 207 (7), 148 (11), 135 (34), 105 (27), 91 (31), 44 (100). Anal. calc. for $C_{20}H_{30}O_2$: C 79.42, H 10.00; found: C 79.45, H 9.96.

(16β)-16-Hydroxy-ent-*atisan-19-oic Acid* (**7a**): White crystalline solid. M.p. 203–205° (MeOH) ([27]: m.p. 206°) $[\alpha]_D^{20} = -31.2$ ($c = 0.32$, $CHCl_3$), [27]: $[\alpha]_D = -10.81$ ($c = 0.6$, $CHCl_3$)). IR (liquid film): 3420, 2925, 1690, 1455, 1270. ^{1}H-NMR (400 MHz): 1.30 (*s*, Me(17)); 1.26 (*s*, Me(18)); 0.90 (*s*, Me(20)). ^{13}C-NMR (100 MHz): 183.5 (*s*, C(19)); 72.4 (*s*, C(16)); 57.4 (*t*, C(15)); 57.2 (*d*, C(5)); 50.9 (*d*, C(9)); 43.7 (*s*, C(4)); 39.8 (*t*, C(7)); 39.8 (*t*, C(1)); 37.9 (*d*, C(12)); 38.2 (*s*, C(10)); 38.0 (*t*, C(3)); 33.7 (*s*, C(8)); 30.7 (*q*, C(17)); 28.9 (*q*, C(18)); 26.9 (*t*, C(14)); 25.5 (*t*, C(13)); 22.0 (*t*, C(11)); 20.0 (*t*, C(6)); 18.7 (*t*, C(2)); 12.1 (*q*, C(20)). EI-MS: 320 (2, M^+), 302 (40, $[M - H_2O]^+$), 287 (51, $[M - H_2O–Me]^+$), 274 (13), 262 (57),

241 (23), 187 (32), 121 (68), 105 (85), 91 (100). Anal. calc. for $C_{20}H_{32}O_3$: C 74.96, H 10.06; found: C 74.89, H 10.02.

(16α)-16-Hydroxy-ent-*atisan-19-oic Acid* (**8a**): White crystalline solid. M.p. 223–224° (MeOH) ([27]: m.p. 225°) $[\alpha]_D^{20} = +60.9$ ($c = 0.31$, $CHCl_3$)) [27]: $[\alpha]_D = +63.16$ ($c = 0.38$, $CHCl_3$). IR (liquid film): 3350, 1690, 1460, 1440, 1270, 1260. ^{1}H-NMR (400 MHz): 1.31 (*s*, Me(17)); 1.26 (*s*, Me(18)); 0.90 (*s*, Me(20)). ^{13}C-NMR (100 MHz): 183.0 (*s*, C(19)); 72.2 (*s*, C(16)); 57.4 (*t*, C(15)); 57.1 (*d*, C(5)); 50.6 (*d*, C(9)); 43.7 (*s*, C(4)); 39.7 (*t*, C(7)); 39.6 (*t*, C(1)); 38.0 (*d*, C(12)); 38.3 (*s*, C(10)); 38.0 (*t*, C(3)); 33.8 (*s*, C(8)); 30.5 (*q*, C(17)); 28.9 (*q*, C(18)); 26.8 (*t*, C(14)); 26.0 (*t*, C(11)); 23.9 (*t*, C(13)); 20.2 (*t*, C(6)); 18.7 (*t*, C(2)); 12.0 (*q*, C(20)). EI-MS: 302 (41, $[M - H_2O]^+$), 287 (100, $[M - H_2O - Me]^+$), 274 (7), 257 (24), 241 (21), 187 (22), 159 (27), 121 (41), 105 (50), 91 (54). Anal. calc. for $C_{20}H_{32}O_3$: C 74.96, H 10.06; found: C 74.91, H 10.07.

4. *Esterfications with Diazomethane: General Procedure (G.P.) Exemplified for Methyl* ent-*Atis-16-en-19-oate* (**4b**). Acid **4a** (10.5 mg) was treated with a sat. soln. of CH_2N_2 in Et_2O (1.0 ml). After 20 min, the solvent was evaporated and the residue purified by CC (SiO_2 (0.5 g), light petroleum ether): 9.1 mg of **4b**. White crystalline solid. M.p. 124–125° (MeOH) ([21]: m.p. 125–126° (MeOH); [22]: m.p. 126–127° (MeOH); [23]: m.p. 125–128° (MeOH); [24]: (±) **4b**: m.p. 102.5–105°). $[\alpha]_D^{20} = -67.3$ ($c = 0.35$, $CHCl_3$) [21]: $[\alpha]_D = -68.7$ ($c = 1.5$, $CHCl_3$)). IR (liquid film): 3045, 1725, 1460, 1443, 1230. ^{1}H-NMR (400 MHz): 4.74 (br. *d*, $J = 2$, H_A–C(17)); 4.58 (br. *d*, $J = 2$, H_B–C(17)); 3.66 (*s*, MeO); 1.17 (*s*, Me(18)); 0.81 (*s*, Me(20)). ^{13}C-NMR (100 MHz): 177.9 (*s*, C(19)); 152.8 (*s*, C(15)); 104.5 (*t*, C(17)); 57.3 (*d*, C(5)); 52.2 (*d*, C(9)); 51.0 (*q*, MeO); 48.2 (*t*, C(16)); 43.9 (*s*, C(4)); 39.7 (*t*, C(1)); 39.7 (*t*, C(7)); 38.2 (*s*, C(10)); 38.3 (*t*, C(3)); 36.6 (*d*, C(12)); 33.5 (*s*, C(8)); 28.7 (*q*, C(18)); 28.7 (*t*, C(14)); 28.3 (*t*, C(13)); 27.3 (*t*, C(11)); 20.3 (*t*, C(6)); 18.8 (*t*, C(2)); 11.9 (*q*, C(20)).

Methyl ent-*Atis-15-en-19-oate* (**3b**): Accorfing to the *G.P.*, with **3a** (9 mg): 7.7 mg of **3b**. White crystalline solid. M.p. 89–90° (MeOH) ([22]: m.p. 90–91°). $[\alpha]_D^{20} = -81.6$ ($c = 0.16$, $CHCl_3$). IR (liquid film): 2920, 1690, 1465, 1443, 1275, 1258. ^{1}H-NMR (400 MHz): 5.58 (br. *t*, $J = 1.8$, H–C(15)); 3.64 (*s*, MeO); 1.73 (*s*, Me(17)); 1.17 (*s*, Me(18)); 0.77 (*s*, Me(20)). ^{13}C-NMR (100 MHz): 178.1 (*s*, C(19)); 140.3 (*s*, C(16)); 135.8 (*t*, C(15)); 57.2 (*d*, C(5)); 53.3 (*d*, C(9)); 51.1 (*q*, MeO); 43.7 (*s*, C(4)); 40.3 (*t*, C(1)); 38.2 (*t*, C(3)); 37.9 (*s*, C(10)); 37.8 (*t*, C(7)); 37.3 (*s*, C(8)); 35.8 (*d*, C(12)); 28.8 (*q*, C(18)); 28.3 (*t*, C(14)); 27.5 (*t*, C(11)); 26.4 (*t*, C(13)); 20.4 (*t*, C(6)); 20.1 (*q*, C(17)); 18.7 (*t*, C(2)); 11.6 (*q*, C(20)).

Methyl ent-*Kaur-15-en-19-oate* (**5b**). According to the *G.P.*, with **5a** (5 mg): 4.3 mg of **5b**. White crystalline solid. M.p. 78–79.5° (MeOH) ([26]: m.p. 79–80°). $[\alpha]_D^{20} = -61.6$ ($c = 0.18$, $CHCl_3$), [26]: $[\alpha]_D = -54.0$ ($c = 4.1$, $CHCl_3$)). IR (liquid film): 2915, 1686, 1460, 1445, 1271, 1256. ^{1}H-NMR (400 MHz): 5.06 (br. *t*, $J = 2$, H–C(15)); 3.63 (*s*, MeO); 1.69 (*s*, Me(17)); 1.15 (*s*, Me(18)); 0.84 (*s*, Me(20)). ^{13}C-NMR (100 MHz): 178.1 (*s*, C(19)); 142.5 (*s*, C(16)); 135.1 (*t*, C(15)); 56.8 (*d*, C(5)); 51.1 (*q*, MeO); 49.1 (*s*, C(8)); 48.0 (*d*, C(9)); 44.7 (*d*, C(13)); 43.8 (*s*, C(4)); 43.8 (*t*, C(14)); 40.8 (*t*, C(1)); 39.7 (*t*, C(7)); 39.6 (*s*, C(10)); 38.3 (*t*, C(3)); 28.7 (*q*, C(18)); 24.9 (*t*, C(12)); 20.9 (*t*, C(6)); 19.1 (*t*, C(11)); 18.9 (*t*, C(2)); 15.5 (*q*, C(20)), 15.4 (*q*, C(17)).

Methyl ent-*Beyer-15-en-19-oate* (= *Methyl (8b,13b)-13-Methyl-17-nor*-ent-*kaur-15-en-19-oate*; **6b**). According to the *G.P.*, with **6a** (7 mg): 6.4 mg of **6b**. White crystalline solid. M.p. 116–117° (MeOH) ([21]: m.p. 118° (MeOH)). $[\alpha]_D^{20} = +6.3$ ($c = 0.18$, $CHCl_3$) ([21]: $[\alpha]_D = +5.0$ ($c = 1.5$, $CHCl_3$)). IR (liquid film): 3050, 3015, 2935, 1715, 1440, 1240, 1150. ^{1}H-NMR (400 MHz): 5.72 (*d*, $J = 5.7$, H–C(15)); 5.44 (*d*, $J = 5.7$, H–C(16)); 3.66 (*s*, MeO); 1.20 (*s*, Me(18)); 1.17 (*s*, Me(17)); 0.55 (*s*, Me(20)). ^{13}C-NMR (100 MHz): 178.1 (*s*, C(19)); 134.5 (*d*, C(16)); 134.7 (*d*, C(15)); 61.1 (*t*, C(14)); 57.0 (*d*, C(5)); 52.2 (d, C(9)); 51.1 (*q*, MeO); 49.1 (*s*, C(8)); 43.6 (*s*, C(4)); 43.8 (*s*, C(13)); 39.5 (*t*, C(1)); 38.2 (*t*, C(3)); 37.6 (*t*, C(7)); 37.7 (*s*, C(10)); 32.9 (*t*, C(12)); 28.9 (*q*, C(18)); 24.9 (*q*, C(17)); 21.6 (*t*, C(6)); 20.4 (*t*, C(11)); 19.3 (*t*, C(2)); 13.6 (*q*, C(20)).

Methyl (16β)-16-Hydroxy-ent-*atisan-19-oate* (**7b**). According to the *G.P.*, with **7a** (10 mg): 9.3 mg of **7b**. White crystalline solid. M.p. 146–148° (hexane) ([28]: m.p. 148–150°; [29]: m.p. 149.5–151.5° (hexane)). $[\alpha]_D^{20} = -34.3$ ($c = 0.35$, $CHCl_3$). ([28]: $[\alpha]_D^{26} = -36.73$ ($c = 0.802$, $CHCl_3$)). IR (liquid film): 3385, 2916, 1690, 1464, 1272, 1257. ^{1}H-NMR (400 MHz): 3.64 (*s*, MeO); 1.31 (*s*, Me(17)); 1.18 (*s*, Me(18)); 0.77 (*s*, Me(20)). ^{13}C-NMR (100 MHz): 178.0 (*s*, C(19)); 72.3 (*s*, C(16)); 57.4 (*t*, C(15)); 57.2 (*d*, C(5)); 51.1 (*q*, MeO); 50.8 (*d*, C(9)); 43.8 (*s*, C(4)); 39.8 (*t*, C(7)); 39.8 (*t*, C(1)); 37.9 (*d*, C(12)); 38.2 (*s*, C(10)); 37.9

(*t*, C(3)); 33.7 (*s*, C(8)); 30.7 (*q*, C(17)); 28.7 (*q*, C(18)); 26.9 (*t*, C(14)); 25.4 (*t*, C(13)); 21.9 (*t*, C(11)); 20.0 (*t*, C(6)); 18.8 (*t*, C(2)); 11.9 (*q*, C(20)).

Methyl (16α)-16-Hydroxy-ent-*Atisan 19-oate* (**8b**). According to the *G.P.*, with **8a** (8 mg): 7.2 mg of **8b**. White crystalline solid. M.p. 135–138° (hexane) ([28]: m.p. 139–141°; [29]: m.p. 134.5–137° (hexane)). $[\alpha]_D^{20} = -48.2$ ($c = 0.36$, $CHCl_3$) [28]: $[\alpha]_D^{26} = -51.76$ ($c = 0.701$, $CHCl_3$)). IR (liquid film): 3388, 2918, 1687, 1465, 1446, 1271, 1255. ^{1}H-NMR (400 MHz): 3.64 (*s*, MeO); 1.28 (*s*, Me(17)); 1.16 (*s*, Me(18)); 0.77 (*s*, Me(20)). ^{13}C-NMR (100 MHz): 178.0 (*s*, C(19)); 72.1 (*s*, C(16)); 57.5 (*t*, C(15)); 57.2 (*d*, C(5)); 51.1 (*q*, MeO); 50.6 (*d*, C(9)); 43.9 (*s*, C(4)); 39.7 (*t*, C(7)); 39.7 (*t*, C(1)); 38.2 (*s*, C(10)); 38.1 (*d*, C(12)); 38.1 (*t*, C(3)); 33.8 (*s*, C(8)); 30.5 (*q*, C(17)); 28.7 (*q*, C(18)); 26.8 (*t*, C(14)); 23.9 (*t*, C(13)); 23.4 (*t*, C(11)); 20.2 (*t*, C(6)); 18.8 (*t*, C(2)); 11.9 (*q*, C(20)).

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