# 169. A Formal Total Synthesis of (+)-Methyl Trachyloban-18-oate and (+)-Methyl 16-Oxo-17-norkauran-18-oate: Regio- and Diastereoselective Preparation of Methyl (13*S*)-13-Hydroxyisoatisiren-18-oate from (−)-Abietic Acid

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Dedicated to Prof. *Alessandro Ballio* on the occasion of his 75th birthday

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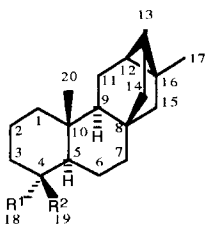
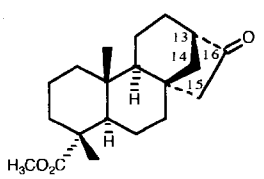
A novel preparation of methyl (13*S*)-13-hydroxyisoatisiren-18-oate (**4**), a key-intermediate in a synthesis of (+)-methyl trachyloban-18-oate ((+)-**1**), from (−)-abietic acid, is described. Since (−)-**1** has been previously converted into (−)-methyl 16-oxo-17-norkauran-18-oate ((−)-**16**), our preparation of **4** constitutes also a formal total synthesis, from (−)-abietic acid, of (+)-**16**. Key steps in this approach were the allene photoaddition to podocarp-8(14)-en-13-one (**5**) and the conversion of the *endo*-toluene-4-sulfonate **11** into the *exo*-benzoate **12b**.

**Introduction.** – Trachylobane diterpenes were first isolated in 1963 by *Ourisson* and coworkers [1] from *Trachylobium verrucosum* (Cesalpinaceae), an ornamental tree, present in Madagascar and other areas of Africa, used for the preparation of copal. The interest in trachylobane diterpenes is due not only to their unique pentacyclic structure, containing a cyclopropane ring, but also to their biogenetic relevance [2].

A synthesis of (+)-methyl trachyloban-18-oate (**1**) was described in 1968 by *Herz et al.* [3]. Syntheses of (±)-trachylobane (**2**) and (+)-trachyloban-19-oic acid (**3**) were reported by *Kelly et al.* [4] and *Cory et al.* [5], respectively.




**1** $R^1 = CO_2CH_3$, $R^2 = CH_3$
**2** $R^1 = CH_3$, $R^2 = CH_3$
**3** $R^1 = CH_3$, $R^2 = CO_2H$




**16**

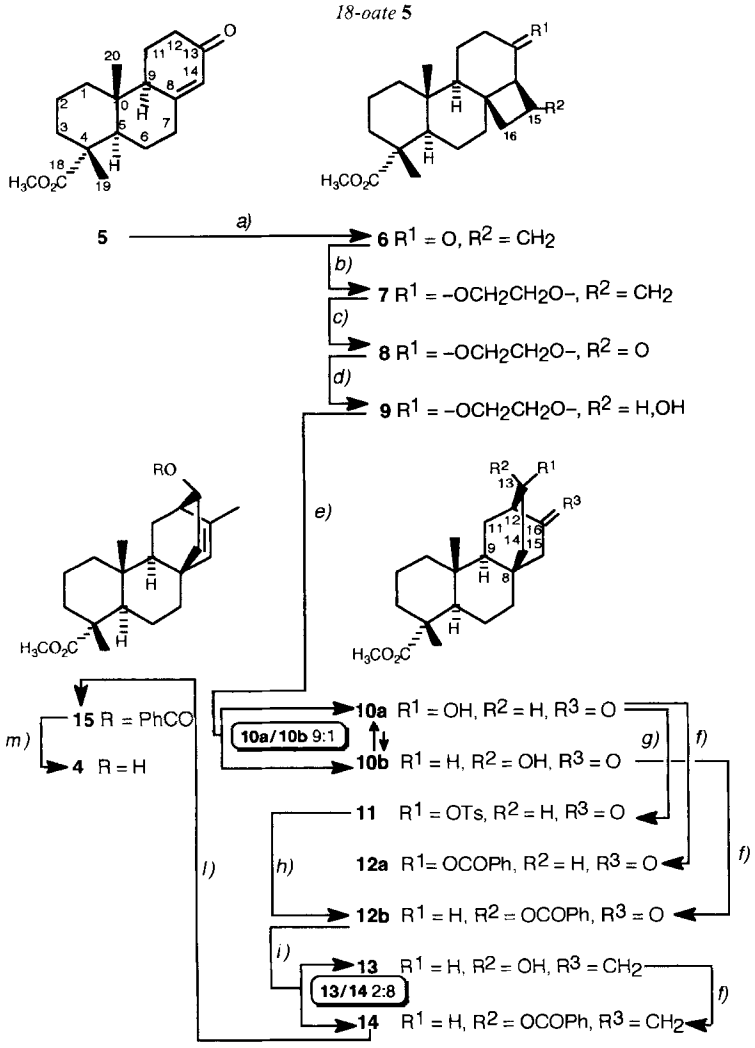
In the present paper, we wish to describe a novel preparation of the key intermediate **4** in the synthesis of *Herz et al.* for the conversion of 6-*endo*-hydroxybicyclo[2.2.2]octan-2-ones into the benzoyl derivatives of their *exo*-epimers[1]), based on a combined applica-

[1]) Previously [7], we had defined this stereochemical arrangement as '*syn*' and '*anti*'.

tion of the photochemical method of *Wiesner et al.* [6a] and the methodology we disclosed some time ago [7].

**Results and Discussion.** – The known α,β-unsaturated ketone (+)-**5** [8], available in five steps and in large quantities from commercially available (−)-abietic acid following the procedure of *Arno* and coworkers [8f] and containing several structural features arranged as in the final product, was chosen as starting material. Photoaddition of allene to **5** at −78° proceeded from the β-face and gave the expected [6b,c] cyclophotoadduct **6** (*Scheme*). The latter was then transformed into the acetal **7** by standard methods. Acetal

Scheme. *Preparation of Methyl (13S)-13-Hydroxyisoatisiren-18-oate* **4** *from Methyl 13-Oxopodocarp-8(14)-en-18-oate* **5**




*a*) Allene, THF, *hv*, −78°. *b*) Ethyleneglycol, TsOH, benzene. *c*) $OsO_4$, THF/$NaIO_4$ (aq.). *d*) $NaBH_4$, MeOH/$Et_2O$. *e*) 2:1 THF/2N HCl, reflux. *f*) PhCOCl, Py, r.t. *g*) TsCl, Py, r.t. *h*) $Et_4N$(PhCOO)/THF. *i*) $(Ph)_3PCH_2$, benzene. *l*) $(PhCN)_2PdCl_2$. *m*) MeONa/MeOH.

**7** was converted into the cyclobutanone **8** by the action of $OsO_4$ and $NaIO_4$. $NaBH_4$ Reduction of **8** afforded the hydroxy compound **9**, which was used in the next step without purification. Treatment of **9** with a 2:1 mixture THF/2N HCl under reflux for 24 h gave the hydroxy ketones **10a** and **10b** in a *ca.* 9:1 ratio.

In accordance with precedent cases [4a] [7] [9], the major epimer was attributed the structure **10a**, in which the HO–C(13) is *endo*-configurated. This assignment was confirmed by comparing the $^{13}C$ chemical shifts of the HO–C(13) of **10a** (69.1 ppm) and **10b** (65.5 ppm): as we pointed out before [7], these values are diagnostic in that the signal of the HO–C(13) in the *exo*-epimer appears at higher field. The same $\Delta\delta$ is displayed by the C(11)-atom in **10a** and **10b**. The C(11)- and C(13)-atoms in **10b** seem, therefore, to be in sterically more crowded environment [10] than the corresponding C-atoms in **10a**. This trend is general and could explain why, under equilibration conditions, 6-*endo*-hydroxybicyclo[2.2.2]octan-2-ones, in which no H-bonding exists between the C=O and the OH groups [11], are the major products of the intramolecular aldol condensation of 3-(formylmethyl)cyclohexan-1-ones.

The configuration at C(13) in **10a** is opposite to that required. Hydroxy ketone **10a** was, therefore, converted into the corresponding toluene-4-sulfonate **11** by the action of TsCl in pyridine. The resulting toluene-4-sulfonate was then refluxed in THF in the presence of $Et_4N$ (PhCOO) to give the benzoate **12b**. The inversion of configuration at C(13) was proved as follows: **12b** was identical to the product prepared from **10b** by the action of PhCOCl in pyridine and different from **12a**, obtained from **10a** in the same manner.

Benzoate **12b** was then submitted to a *Wittig* methylenation according to the procedure of *Smith* and *Jerris* [12] to give the methylidene derivatives **13** and **14**, in high yield and in a 2:8 ratio. Benzoylation of **13** with PhCOCl in pyridine gave an additional crop of **14**.

The required atisirene → isoatisirene isomerization was achieved by refluxing a benzene solution of **14** in the presence of bis(benzonitrile)palladium(II) chloride [13]. The reaction proceeded cleanly, though **15** was obtained, after isolation, in a not very satisfactory yield. Shortage of material did not allow us to optimize this step. The enoate **15** was finally treated with MeONa in MeOH to give **4**, whose data were in very good agreement with those reported by *Herz et al.* [3].

Since (+)-**1** has already been obtained from **4**, and since (–)-**1** has been previously converted into (–)-methyl 16-oxo-17-norkauran-18-oate ((–)-**16**) [1a,c,d], our route to **4** constitutes a formal total synthesis, from (–)-abietic acid, of both (+)-**1** and (+)-**16**.

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## Experimental Part

*General.* All solns. were evaporated to dryness under vacuum. All solvents were of anal. grade. TLC: *Merck* silica gel *60* $F_{254}$. CC: silica gel *60*, 70–230 mesh ASTM. M.p.: *Mettler-FP-61* apparatus (uncorrected). IR Spectra: *Perkin-Elmer-298* and *Shimadzu*-470 scanning IR spectrophotometer; in $cm^{-1}$. $^1H$- and $^{13}C$-NMR Spectra: *Varian-Gemini-200*, at 200 and 50 MHz respectively; $\delta$ in ppm rel. to internal $Me_4Si$ ( = 0 ppm), $J$ in Hz. MS: Electron ionization (EI) on *VG-4* at 70 eV. The FT-ICR experiments were performed with a *Bruker Spectrospin APEX* 47e spectrometer equipped with an external ion source. Typical operating conditions of the EI source were as follows: source temp. 180°, emission current 10 mA, electron energy 70 eV.

*Methyl 15-Methylidene-13-oxo-8β,14β-ethanopodocarpan-18-oate* (**6**). A soln. of **5**[2]) (320 mg, 1.10 mmol) in freshly distilled THF (50 ml) was poured in a *Pyrex* gas-washing bottle. After cooling to −78°, by means of a dry ice/acetone bath, an excess of allene was condensed into the soln. The mixture was then irradiated, while stirring under $N_2$, with a Hg vapor *Helios Italquartz 1000*-W lamp, placed on a side in a water-cooled *Pyrex* jacket. The irradiation was interrupted when TLC (petroleum ether (40–70°)/$Et_2O$ 1:1, $R_f$(**6**) > $R_f$(**5**)) indicated the disappearance of the starting material. The reaction vessel was then removed from the cooling bath and kept for some h at r.t. under the fumehood to allow the unreacted allene to evolve. Evaporation of the org. solvent gave a residue which was purified by CC ($SiO_2$; petroleum ether (40–70°)/$Et_2O$ 7:3): **6** in 67% yield. M.p. (petroleum ether (40–70°)/$Et_2O$) 97.7–98.8°. IR ($CCl_4$): 1715. $^1H$-NMR ($CDCl_3$): 0.77 (*s*, 3 H); 1.09 (*s*, 3 H); 3.59 (*s*, 3 H); 4.84 (*m*, 1 H); 4.92 (*m*, 1 H). $^{13}C$-NMR ($CDCl_3$): 14.9, 16.2 (C(19), C(20)); 17.2, 18.2, 21.6 (C(2), C(6), C(11)); 36.6, 37.5, 37.6, 37.9, 39.5, 39.9, 40.4 (C(1), C(3), C(7), C(8), C(10), C(12), C(16)); 47.4 (C(4)); 50.2, 51.8, 53.7 (C(5), C(9), (MeO)); 62.9 (C(14)); 110.0 (=$CH_2$); 142.1 (C(15)); 179.2 (C(18)); 210.5 (C(13)). EI-MS: 330 (23, $M^+$). Anal. calc. for $C_{21}H_{30}O_3$ (330.47): C 76.33, H 9.15; found: C 76.22, H 9.17.

*Methyl 13,13-Ethylenedioxy-15-methylidene-8β,14β-ethanopodocarpan-18-oate* (**7**). To a soln. of **6** (200 mg, 0.61 mmol) in anh. benzene (60 ml), an excess of ethyleneglycol and a catal. amount of TsOH were added, and the mixture was refluxed under $N_2$ with azeotropic removal of $H_2O$ (*Dean-Stark* trap), until TLC (petroleum ether (40–70°)/$Et_2O$ 7:3, $R_f$(**7**) > $R_f$(**6**)) indicated the complete disappearance of the starting material. The mixture was then cooled to r.t., diluted with $Et_2O$, washed with $NaHCO_3$ soln., $H_2O$ (till neutral), brine, dried ($Na_2SO_4$), and evaporated. The residue was purified by CC ($SiO_2$; petroleum ether (40–70°)/$Et_2O$ 9:1): **7** in 95% yield. M.p. (petroleum ether (40–70°)/$Et_2O$) 81.2–83.2°. IR ($CCl_4$): 1718. $^1H$-NMR ($CDCl_3$): 0.75 (*s*, 3 H); 1.10 (*s*, 3 H); 3.60 (*s*, 3 H); 3.80–4.00 (*m*, 4 H); 4.83 (*m*, 1 H); 4.94 (*m*, 1 H). $^{13}C$-NMR ($CDCl_3$): 14.1, 16.4 (C(19), C(20)); 17.3, 17.5, 21.9 (C(2), C(6), C(11)); 28.6 (C(12)); 36.7, 37.3, 37.5, 38.0, 38.9, 41.0 (C(1), C(3), C(7), C(8), C(10), C(16)); 47.4 (C(4)); 48.0, 50.2, 51.7 (C(5), C(9), (MeO)); 57.1 (C(14)); 64.1, 64.3 (O*C*$H_2$*C*$H_2$O); 109.8, 110.4 (C(13), (=$CH_2$)); 145.9 (C(15)); 179.5 (C(18)). EI-MS: 374 (100, $M^+$). Anal. calc. for $C_{23}H_{34}O_4$ (374.52): C 73.76, H 9.15; found: C 73.59, H 9.20.

*Methyl 13,13-(Ethylenedioxy)-15-oxo-8β,14β-ethanopodocarpan-18-oate* (**8**). A soln. of $OsO_4$ (20 mg) in THF (2 ml) was added to a soln. of **7** (103 mg, 0.27 mmol) in dioxane (5 ml). After stirring in the dark for 15 min, $H_2O$ (1 ml) and pyridine (1 ml) were added. A soln. of $NaIO_4$ (235 mg, 1.10 mmol) in $H_2O$ (10 ml) was then added dropwise. The mixture was stirred in the dark for 45 h. The mixture was then filtered under reduced pressure through a *Celite* pad, and the filter and the flask were washed with MeOH. The org. solvent was then evaporated and the residue taken up with $H_2O$ and extracted with $Et_2O$. The combined org. extracts were then washed with $NaHCO_3$ soln., $H_2O$ (till neutral), brine, dried ($Na_2SO_4$), and evaporated. The product was then purified by CC ($SiO_2$; petroleum ether (40–70°)/$Et_2O$ 9:1): **8** in 76% yield. TLC: petroleum ether (40–70°)/$Et_2O$ 7:3, $R_f$(**8**) < $R_f$(**7**). M.p. (petroleum ether (40–70°)/$Et_2O$) 155.6–156.1°. IR ($CCl_4$): 1725, 1782. $^1H$-NMR ($CDCl_3$): 0.75 (*s*, 3 H); 1.11 (*s*, 3 H); 2.33 (*dd*, *J* = 6.5, 16.3, 1 H); 2.69 (*dd*, *J* = 2, 6.5, 1 H); 3.34 (*d*, *J* = 16.3, 2 H); 3.61 (*s*, 3 H); 3.70–4.00 (*m*, 4 H). $^{13}C$-NMR ($CDCl_3$): 14.6, 16.1 (C(19), C(20)); 17.4, 17.4, 22.0 (C(2), C(6), C(11)); 34.5, 34.6, 36.7, 37.5, 37.5, 40.6 (C(1), C(3), C(7), C(8), C(10), C(12)); 47.3 (C(4)); 50.3, 51.2, 51.8 (C(5), C(9), (MeO)); 52.2 (C(16)); 64.3, 64.9 (O*C*$H_2$*C*$H_2$O); 73.1 (C(14)); 107.3 (C(13)); 179.3 (C(18)); 205.8 (C(15)). EI-MS: 376 (19, $M^+$). Anal. calc. for $C_{22}H_{32}O_5$ (376.49): C 70.19, H 8.57; found: C 70.23, H 8.59.

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[2]) (+)-**5** (M.p. (hexane/$Et_2O$) 124–126° ([8a,b]: 127–128°; [8c]: 125–127°; [8d]: 126–128°, 126–127°, 125–127°; [8e]: 126–127°; [8f]: 125–127°)) was prepared according to the procedure of *Arno* and coworkers [8f] from technical grade (−)-abietic acid $[\alpha]_D = -65 \pm 10$ ($c$ = 1, EtOH), purchased from *Fluka AG*. $^{13}C$-NMR ($CDCl_3$): 15.3, 16.8 (C(19), C(20)); 17.7, 20.1, 23.9 (C(2), C(6), C(11)); 34.9, 36.5, 36.6, 38.1, 38.2, 47.1 (C(1), C(3), C(4), C(7), C(10), C(12)); 48.0, 51.5, 51.9 (C(5), C(9), (MeO)); 126.3 (C(14)); 165.0 (C(8)); 179.1 (C(18)); 199.9 (C(13)).

*Methyl 13-Hydroxy-16-oxo-17-noratisan-18-oate* (**10**). To a stirred soln. of **8** (67 mg, 0.18 mmol) in a 1:1 MeOH/$Et_2O$ mixture (5 ml), $NaBH_4$ was added. When TLC (petroleum ether (40–70°)/$Et_2O$ 1:1, $R_f$(**9**) < $R_f$(**8**)) indicated the complete disappearance of **8**, the soln. was evaporated and the residue taken up with $H_2O$ and extracted with $CHCl_3$. The combined org. extracts were then washed with $H_2O$ (till neutral), brine, dried ($Na_2SO_4$), and evaporated. The crude product **9** could be used in the subsequent reaction without purification. A soln. of **9** dissolved in a 2:1 THF/2N HCl (7.5 ml) was refluxed under $N_2$ for 24 h. After neutralization (4N NaOH) and evaporation of the org. solvent, the residue was taken up with $H_2O$ and thoroughly extracted with $Et_2O$. The combined org. extracts were washed with $H_2O$, brine, dried ($Na_2SO_4$), and evaporated. The residue was purified by CC ($SiO_2$, petroleum ether (40–70°)/$Et_2O$ 1:1): **10a** and **10b** in a 76.6% and 8.3% yield (*ca.* 9:1 ratio), respectively. TLC (petroleum ether (40–70°)/EtO 2:8): $R_f$(**10a**) < $R_f$(**10b**).

*Data of* **10a**: M.p. (petroleum ether (40–70°)/$Et_2O$) 221.2–223.2°. IR ($CHCl_3$): 1705, 1720, 3400. $^1$H-NMR ($CDCl_3$): 0.94 (*s*, 3 H); 1.15 (*s*, 3 H); 3.63 (*s*, 3 H); 4.12 (*m*, 1 H). $^{13}$C-NMR ($CDCl_3$): 14.5, 16.3 (C(19), C(20)); 16.9, 21.0, 21.9 (C(2), C(6), C(11)); 36.4, 36.6, 37.0, 37.5, 38.3, 39.1 (C(1), C(3), C(7), C(8), C(10), C(14)); 47.1 (C(4)); 50.2, 50.3, 51.5, 51.9 (C(5), C(9), C(12), (MeO)); 55.1 (C(15)); 69.1 (C(13)); 179.4 (C(18)); 215.3 (C(16)). EI-MS: 334 (25, $M^+$). Anal. calc. for $C_{20}H_{30}O_4$ (334.45): C 71.82, H 9.04; found: C 71.92, H 9.03.

*Data of* **10b**: M.p. (petroleum ether (40–70°)/$Et_2O$) 186.7–187.8°. IR ($CCl_4$): 1710, 1720, 3420. $^1$H-NMR ($CDCl_3$): 1.10 (*s*, 3 H); 1.13 (*s*, 3 H); 3.61 (*s*, 3 H); 4.20 (*m*, 1 H). $^{13}$C-NMR ($CDCl_3$): 15.4, 16.3 (C(19), C(20)); 17.0, 17.5, 21.1 (C(2), C(6), C(11)); 36.3, 36.7, 37.4, 38.1, 38.3, 38.5 (C(1), C(3), C(7), C(8), C(10), C(14)); 47.2 (C(4)); 50.1, 51.8, 51.8, 52.2 (C(5), C(9), C(12), (MeO)); 54.7 (C(15)); 65.8 (C(13)); 179.5 (C(18)); 215.5 (C(16)). EI-MS: 334 (4, $M^+$). Anal. calc. for $C_{20}H_{30}O_4$ (334.45): C 71.82, H 9.04; found: C 71.89, H 9.03.

*Methyl (13*R*)-16-Oxo-13-[(4-tolylsulfonyl)oxy]-17-noratisan-18-oate* (**11**). To a stirred soln. of **10a** (43 mg, 0.13 mmol) in pyridine (1 ml), TsCl (34 mg, 0.18 mmol) was added. After stirring for 18 h at r.t., $H_2O$ (1 ml) was added, followed, after additional 10 min, by $Et_2O$ (80 ml). The aq. layer was separated and the org. one washed with 2N HCl, $H_2O$, $NaHCO_3$ soln., $H_2O$ (till neutral), brine, dried ($Na_2SO_4$), and evaporated. The residue was purified by CC ($SiO_2$; petroleum ether (40–70°)/$Et_2O$ 1:1): **11** in 79% yield. TLC (petroleum ether (40–70°)/$Et_2O$ 2:8): $R_f$(**11**) > $R_f$(**10a**). M.p. ($CHCl_3$/$Et_2O$) 151.1–152.5°. IR ($CHCl_3$): 1717. $^1$H-NMR ($CDCl_3$): 0.90 (*s*, 3 H); 1.12 (*s*, 3 H); 2.41 (*s*, 3 H); 3.61 (*s*, 3 H); 4.85 (*m*, 1 H); 7.30 (*XX'* of *AA'XX'*, 2 H); 7.71 (*AA'* of *AA'XX'*, 2 H). $^{13}$C-NMR ($CDCl_3$): 14.5, 16.2 (C(19), C(20)); 16.7, 20.8, 22.0 (C(2), C(6), C(11)); 21.4 (Ar*Me*); 36.5, 36.5, 36.8, 37.1, 37.1, 38.1 (C(1), C(3), C(7), C(8), C(10), C(14)); 47.0 (C(4)); 47.9, 49.8, 49.8, 51.8 (C(5), C(9), C(12), (MeO)); 54.9 (C(15)); 78.2 (C(13)); 127.7, 130.0 (2 $C_o$, 2 $C_m$); 134.1, 145.0 ($C_{ipso}$, $C_p$); 179.1 (C(18)); 211.2 (C(16)). EI-MS: 488 (12, $M^+$). Anal. calc. for $C_{27}H_{36}O_6S$ (488.64): C 66.37, H 7.43, S 6.56; found: C 66.33, H 7.27, S 6.52.

*Methyl (13*R*)-13-(Benzoyloxy)-16-oxo-17-noratisan-18-oate* (**12a**). To a soln. of **10a** (25 mg, 0.05 mmol) in pyridine (2.5 ml), PhCOCl (0.1 ml, 0.86 mmol) was added and the mixture stirred at r.t. overnight, $H_2O$ was then added, the mixture diluted with $Et_2O$ and washed with 2N HCl, $H_2O$ (till neutral), brine, dried ($Na_2SO_4$), and evaporated. The residue was purified by CC ($SiO_2$; petroleum ether (40–70°)/$Et_2O$ 7:3): **12a** in 82% yield. TLC (petroleum ether (40–70°)/$Et_2O$ 1:1): $R_f$(**12a**) > $R_f$(**10a**). M.p. ($CHCl_3$/petroleum ether (40–70°)) 156.8–157.5°. IR ($CHCl_3$): 1714. $^1$H-NMR ($CDCl_3$): 1.02 (*s*, 3 H); 1.16 (*s*, 3 H); 3.63 (*s*, 3 H); 5.29 (*m*, 1 H); 7.30–7.60 (*m*, 3 H); 7.85–8.00 (*m*, 2 H). $^{13}$C-NMR ($CDCl_3$): 14.6, 16.3 (C(19), C(20)); 16.8, 20.9, 21.9 (C(2), C(6), C(11)); 36.4, 36.6, 37.0, 37.2, 37.4, 38.3 (C(1), C(3), C(7), C(8), C(10), C(14)); 47.1 (C(4)); 47.5, 50.1, 50.3, 51.8 (C(5), C(9), C(12), (MeO)); 55.1 (C(15)); 71.5 (C(13)); 128.5 (2 $C_m$); 129.7 (2 $C_o$); 129.9 ($C_{ipso}$); 133.3 ($C_p$); 165.9 (*C*OPh); 179.3 (C(18)); 213.5 (C(16)). EI-MS: 438 (29, $M^+$). Anal. calc. for $C_{27}H_{34}O_5$ (438.56): C 73.95, H 7.81; found: C 74.14, H 7.95.

*Methyl (13*S*)-13-(Benzoyloxy)atisiren-18-oate* (**12b**) *from* **11**. To a stirred soln. of **11** (40 mg, 0.08 mmol) in anh. THF (15 ml), $Et_4N$(PhCOO) (55 mg, 0.22 mmol) was added. The soln. was refluxed until TLC (petroleum ether (40–70°)/$Et_2O$ 1:1; $R_f$(**12b**) > $R_f$(**11**)) indicated the complete disappearance of **11**. The mixture was then cooled to r.t., the org. solvent evaporated, and the residue taken up with $Et_2O$, washed with $NaHCO_3$ soln., brine, dried ($Na_2SO_4$), and evaporated. The residue was then purified by CC ($SiO_2$; petroleum ether (40–70°)/$Et_2O$ 8:2): **12b** in 80% yield. M.p. (petroleum ether (40–70°)/$CHCl_3$) 130.0–130.3°. IR ($CCl_4$): 1715. $^1$H-NMR ($CDCl_3$): 1.10 (*s*, 3 H); 1.12 (*s*, 3 H); 2.70 (*m*, 1 H); 3.62 (*s*, 3 H); 5.27 (*m*, 1 H); 7.40–7.65 (*m*, 3 H); 7.95–8.15 (*m*, 2 H). $^{13}$C-NMR ($CDCl_3$): 15.1, 16.3 (C(19), C(20)); 16.9, 18.7, 20.9 (C(2), C(6), C(11)); 36.1, 36.4, 36.6, 37.3, 37.9, 38.4 (C(1), C(3), C(7), C(8), C(10), C(14)); 47.1 (C(4)); 48.3, 50.0, 51.2, 51.8 (C(5), C(9), C(12), (MeO)); 54.9 (C(15)); 68.9 (C(13)); 128.6 (2 $C_m$); 129.7 (2 $C_o$); 130.2 ($C_{ipso}$); 133.3 ($C_p$); 165.8 (*C*OPh); 179.3 (C(18)); 213.5 (C(16)). EI-MS: 438 (1, $M^+$). Anal. calc. for $C_{27}H_{34}O_5$ (438.56): C 73.95, H 7.81; found: C 73.90, H 7.78.

*Compound* **12b** *from* **10b**. Compound **12b** was prepared from **10b** as described for **12a** from **10a**. TLC (petroleum ether (40–70°)/$Et_2O$ 1:1): $R_f$(**12b**) > $R_f$(**10b**). This compound displays the same spectral data of **12b** obtained from **11**. Anal. calc. for $C_{27}H_{34}O_5$ (438.56): C 73.95, H 7.81; found: C 73.87, H 7.83.

*Methyl (13S)-13-Hydroxyatisiren-18-oate* (**13**) *and Methyl (13S)-13-(Benzoyloxy)atisiren-18-oate* (**14**). To a soln. of $Ph_3PCH_2Br$ (122 mg, 0.34 mmol) in anh. benzene (2 ml), a 1.55M soln. (0.2 ml) of potassium *tert*-amylate in benzene was added, followed, after refluxing for 1 h under $N_2$, by a soln. of **12b** (18 mg, 0.04 mmol) in the same solvent. The whole was then stirred at 80° for 1 h. The mixture was then cooled, diluted with $Et_2O$, washed with $NaHCO_3$ soln., brine, dried ($Na_2SO_4$), and evaporated. The residue was purified by CC ($SiO_2$, petroleum ether (40–70°)/$Et_2O$ 8:2) to give **13** and **14** in a 16 and 64% yield (8:2 ratio), respectively. TLC (petroleum ether (40–70°)/$Et_2O$ 1:1): $R_f$(**13**) > $R_f$(**12b**) > $R_f$(**14**).

*Data of* **13**: M.p. (petroleum ether 40–70°) 137.2–137.8°. IR ($CHCl_3$): 1646, 1723, 3620. $^1$H-NMR ($CDCl_3$): 1.05 (*s*, 3 H); 1.14 (*s*, 3 H); 2.22 (*m*, 1 H); 3.62 (*s*, 3 H); 3.98 (*m*, 1 H); 4.65 (*m*, 1 H); 4.82 (*m*, 1 H). $^{13}$C-NMR ($CDCl_3$): 15.5, 16.4 (C(19), C(20)); 17.1, 20.5, 21.4 (C(2), C(6), C(11)); 34.5, 36.8, 37.3, 38.5, 38.8, 39.1 (C(1), C(3), C(7), C(8), C(10), C(14)); 47.3 (C(4)); 44.6, 46.6, 50.2, 51.7 (C(5), C(9), C(15), (MeO)); 52.2 (C(12)); 69.2 (C(13)); 107.4 (C(17)); 149.2 (C(16)); 179.8 (C(18)). EI-MS: 332 (61, $M^{+\cdot}$). Anal. calc. for $C_{21}H_{32}O_3$ (332.48): C 75.86, H 9.70; found: C 75.70, H 9.65.

*Data of* **14**: M.p. (petroleum ether 40–70°) 124.9–126.2°. IR ($CHCl_3$): 1708. $^1$H-NMR ($CDCl_3$): 1.07 (*s*, 3 H); 1.12 (*s*, 3 H); 2.58 (*m*, 1 H); 3.63 (*s*, 3 H); 4.75 (*m*, 1 H); 4.92 (*m*, 1 H); 5.10 (*m*, 1 H); 7.40–7.60 (*m*, 3 H); 8.00–8.10 (*m*, 2 H). $^{13}$C-NMR ($CDCl_3$): 15.2, 16.4 (C(19), C(20)); 17.0, 21.3, 21.6 (C(2), C(6), C(11)); 34.3, 36.8, 36.8, 37.3, 38.5, 38.6 (C(1), C(3), C(7), C(8), C(10), C(14)); 47.2 (C(4)); 41.0, 46.6, 50.2, 51.7, 51.8 (C(5), C(9), C(12), C(15), (MeO)); 72.8 (C(13)); 108.8 (C(17)); 128.5 (2 $C_m$); 129.6 (2 $C_o$); 130.9 ($C_{ipso}$); 133.0 ($C_p$); 147.4 (C(16)); 166.3 (*C*OPh); 179.6 (C(18)). EI-MS: 436 (48, $M^{+\cdot}$). HR-MS: 436.2516 ($C_{28}H_{36}O_4$, $M^{+\cdot}$; calc. 436.2613).

Compound **14** was prepared from **13** as described for **12a** from **10a**.

*Methyl (13S)-13-(Benzoyloxy)isoatisiren-18-oate* (**15**). A soln. of **14** (15 mg, 0.03 mmol) in anh. benzene (2.5 ml) was refluxed in the presence of bis(benzonitrile)Pd(II) chloride (10 mg, 0.03 mmol) until TLC (petroleum ether (40–70°)/$Et_2O$ 95:5; $R_f$(**13**) < $R_f$(**15**), 4 developments) indicated the disappearance of the starting material. After cooling to r.t., the mixture was filtered through a *Celite* pad and evaporated. The residue was then purified by CC ($SiO_2$; petroleum ether (40–70°)/$Et_2O$ 8:2): **15** in 43% yield. M.p. (petroleum ether (40–70°)) 89.7–91.6°. IR ($CHCl_3$): 1710. $^1$H-NMR ($CDCl_3$): 1.10 (*s*, 3 H); 1.12 (*s*, 3 H); 1.76 (*d*, *J* = 1.6, 3 H); 2.60 (*s*, 1 H); 3.63 (*s*, 3 H); 4.98 (*m*, 1 H); 5.61 (s, 1 H); 7.40–7.60 (*m*, 3 H); 8.00–8.12 (*m*, 2 H). $^{13}$C-NMR ($CDCl_3$): 15.8, 16.3 (C(19), C(20)); 17.1, 19.3, 19.7, 21.5 (C(2), C(6), C(11), C(17)); 35.1, 36.8, 37.2, 37.6, 38.1, 39.2 (C(1), C(3), C(7), C(8), C(10), C(14)); 47.3 (C(4)); 40.4, 50.4, 51.8, 54.0 (C(5), C(9), C(12), (MeO)); 73.7 (C(13)); 128.5 (2 $C_m$); 129.6 (2 $C_o$); 131.0 ($C_{ipso}$); 132.9 ($C_p$); 137.6, 137.9 (C(15), C(16)); 166.7 (–*C*OPh); 179.6 (C(18)). HR-MS: 436.2451 ($C_{28}H_{36}O_4$, $M^{+\cdot}$; calc. 436.2613).

*Methyl (13S)-13-Hydroxyisoatisiren-18-oate* (**4**). A soln. of **15** (57 mg, 0.13 mmol) in anh. MeOH (5 ml) was refluxed in the presence of MeONa until TLC (petroleum ether (40–70°)/$Et_2O$ 1:1; $R_f$(**15**) > $R_f$(**4**)) indicated the disappearance of the starting material. After cooling to r.t., the mixture was neutralized with 2N HCl. The org. solvent was evaporated and the residue taken up with $Et_2O$. The org. layer was separated and washed with $H_2O$, brine, dried ($Na_2SO_4$), and evaporated. The residue was then purified by CC ($SiO_2$; petroleum ether (40–70°)/$Et_2O$ 8:2): **4** in 95% yield. M.p. (MeOH): 172.7–174.1° ([3]: 172–173°). IR ($CCl_4$): 3615, 3500, 1722. $^1$H-NMR ($CDCl_3$): 1.09 (*s*, 3 H); 1.13 (*s*, 3 H); 1.70 (*d*, *J* = 1.6, 3 H); 2.22 (*s*, 1 H); 3.63 (*s*, 3 H); 3.90 (*m*, 1 H); 5.50 (*s*, 1 H). $^{13}$C-NMR ($CDCl_3$): 16.2, 16.3 (C(19), C(20)); 17.1, 18.1, 21.5 (C(2), C(6), C(11)); 19.8 (C(17)); 36.8, 37.5, 37.5, 37.6, 38.3, 39.2 (C(1), C(3), C(7), C(8), C(10), C(14)); 47.3 (C(4)); 44.0, 50.4, 51.7 (C(5), C(9), (MeO)); 54.6 (C(12)); 70.2 (C(13)); 137.0, 138.4 (C(15), C(16)); 179.6 (C(18)). HR-MS: 332.2356 ($C_{21}H_{32}O_3$, $M^{+\cdot}$; calc. 332.2351).

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