# Synthesis of (−)-Pinellic Acid and Its (9*R*,12*S*,13*S*)-Diastereoisomer

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The total synthesis of (−)-pinellic acid with (9*S*,12*S*,13*S*)-configuration and its (9*R*,12*S*,13*S*)-diastereoisomer was achieved in high overall yields from a common intermediate derived from (+)-L-diethyl tartrate.

**Introduction.** – Kampo medicine, 'Sho-seiryu-to', was found to possess potent adjuvant activity by oral administration on nasal influenza infection and nasal influenza vaccination [1]. (−)-Pinellic acid (**1**) was responsible for its adjuvant activity, isolated from pinelliae tuber, one of the component herbs of the Kampo formula, 'Sho-seiryu-to' (SST) [2]. The absolute configuration of (−)-**1** was determined as (9*S*,12*S*,13*S*) (*Fig.*) by its total synthesis [3].

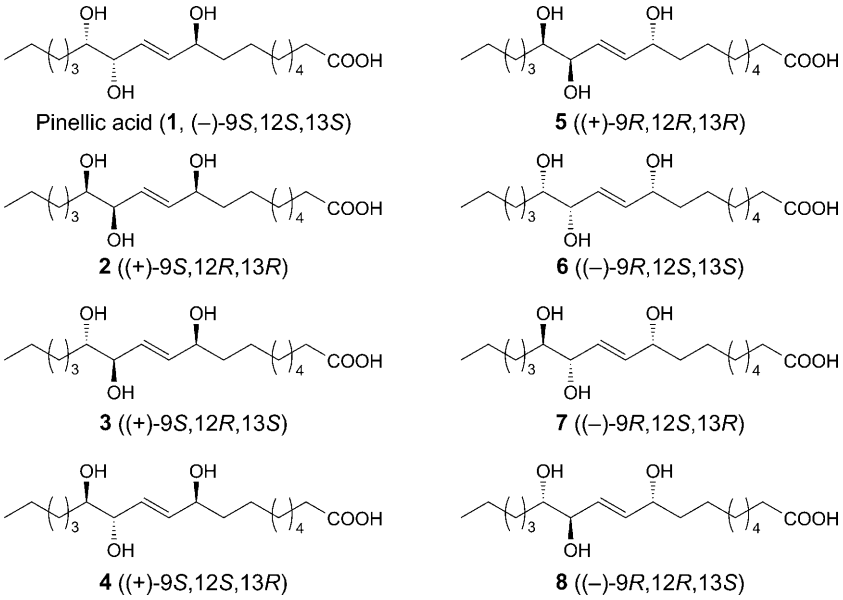


Figure. *All stereoisomers of pinellic acid* (**1**)

Influenza is an infectious respiratory disease caused by specific influenza viruses (RNA virus of the orthomyxoviridae family) leading to both worldwide pandemics and local outbreaks. Influenza virus infection is critical for patients having respiratory

diseases such as asthma, AIDS, or cardiopulmonary disease. The characteristic symptoms of influenza in humans are fever, severe headache, coughing, and malaise. Influenza vaccine is useful as prophylaxis of influenza virus infection [4]. Pinellic acid (**1**) is a novel and potentially useful oral adjuvant when used in conjunction with intranasal inoculation of influenza HA vaccines [2a]. Among the series of pinellic acid isomers, the (9*S*,12*S*,13*S*)-compound, *i.e.*, the natural pinellic acid (**1**), exhibited the most potent adjuvant activity [5].

Recently, we reported the synthesis of the (9*S*,12*R*,13*S*)-isomer **3** [6]. Now, we herein disclose our reports on the synthesis of pinellic acid (**1**, (9*S*,12*S*,13*S*)-configuration) and its (9*R*,12*S*,13*S*)-diastereoisomer **6** starting from a single chiral building block derived from L-(+)-diethyl tartrate ((+)-DET). Only few syntheses of these acids have been reported in the literature [3][6–8].

**Results and Discussion.** – The known chiral aldehyde **9** derived from (+)-DET [9] was subjected to the *Wittig* olefination reaction with butyltriphenylphosphonium bromide in the presence of potassium *tert*-butoxide in THF to provide the corresponding olefinic compound **10** in a 9:1 (*E*)/(*Z*) ratio in 70% yield. Removal of the Bn protecting group with concomitant hydrogenation of the C=C bond was easily performed at atmospheric pressure, in AcOEt in the presence of 10% Pd/C as the catalyst to afford the saturated alcohol **11** in 94% yield. Oxidation of the primary OH group and subsequent *Wittig* reaction with the stable ylide $Ph_3PCHCO_2Et$ furnished the unsaturated ester **12** (80% yield over two steps). Reduction of the ester group with DIBAL-H in $CH_2Cl_2$ afforded an unstable enal, which, without isolation, was subjected to a *Grignard* reaction with THP protected bromo derivative **13**. The reaction yielded a diastereoisomeric mixture of secondary alcohols **14a** and **14b** in a 1.5:1 ratio. These two isomers were separated by column chromatography and their configurational assignments were confirmed on a later stage. Compound **14b** was converted into **14a** by inversion of the configuration of the alcohol under standard *Mitsunobu* conditions (diisopropyl azodicarboxylate, $Ph_3P$, and *p*-nitrobenzoic acid) (*Scheme 1*). On the other hand, **14b** was also used for the synthesis of the isomer **6** as shown in *Scheme 2*.

The secondary OH group in **14a** was protected as a methoxymethyl (MOM) ether, and subsequent removal of the THP group with catalytic pyridinium *p*-toluene sulphonate (PPTS) in MeOH at room temperature led to the formation of **16a**. This alcohol was oxidized with iodoxybenzoic acid (IBX) reagent in DMSO and dry $CH_2Cl_2$ to afford aldehyde **17a**, which, on subsequent oxidation with $NaClO_2$, $NaH_2PO_4$ in DMSO and $H_2O$, afforded the corresponding acid **18a** in 75% yield. Finally, the acetonide and MOM groups were removed under acidic conditions (HCl in MeOH) to afford the target molecule **1** in 66% yield. The physical and spectroscopic data of **1** were identical with those reported [3][6].

Similarly, compound **14b** was submitted to all steps described above leading to the formation of **6** (*Scheme 2*). The structure of **6** was confirmed by spectral and analytical data.

In summary, a facile, practical, and efficient synthesis was accomplished in high overall yields from a common chiral building block derived from L-(+)-diethyl tartrate.

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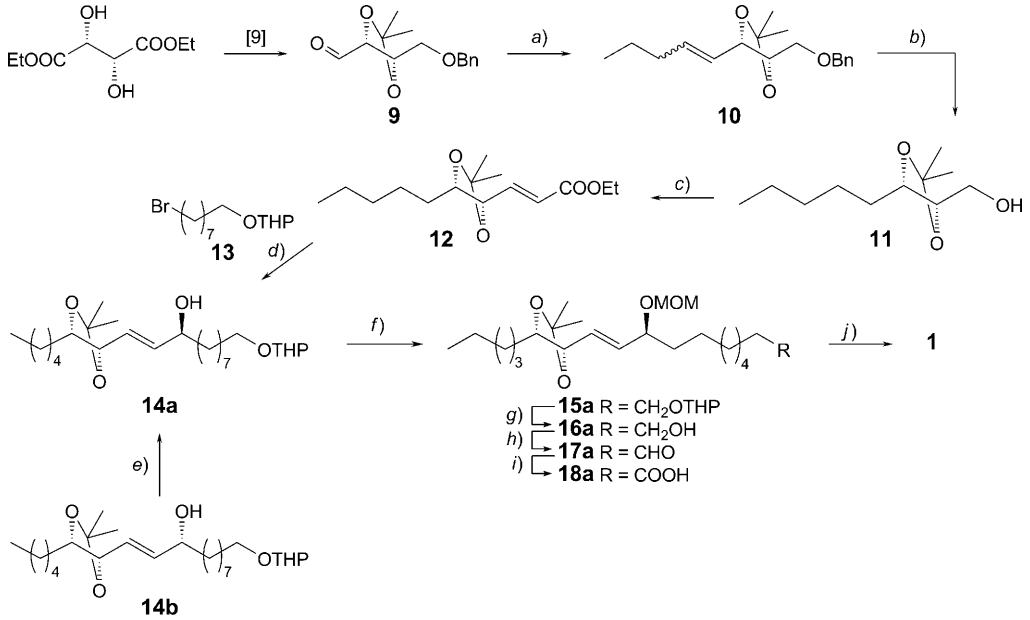
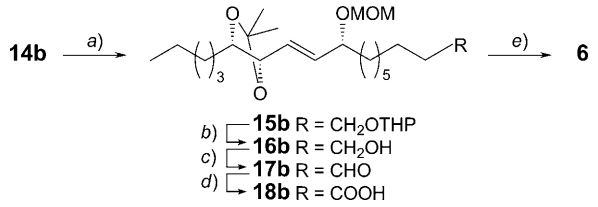
*Scheme 1*




*a*) BuPPh$_3$Br, *t*-BuOK, THF, 0° – r.t., 3 h, 70%. *b*) H$_2$/Pd-C, AcOEt, 8 h, 94%. *c*) 1. oxalyl chloride, DMSO, $CH_2Cl_2$, −78°, 45 min; 2. $Ph_3PCHCO_2Et$, $C_6H_6$, r.t., 3 h (80% two steps). *d*) 1. DIBAL-H, $CH_2Cl_2$, −78°, 30 min; 2. Mg, **13**, THF, 66%. *e*) 1. diisopropyl azodicarboxylate, $Ph_3P$, 4-nitrobenzoic acid; 2. $K_2CO_3$, MeOH, 0°, 1 h, 66%. *f*) MOM-Cl, DIPEA, 0° – r.t., 2 h, 90%. *g*) Pyridinium *p*-toluenesulfonate (PPTS), MeOH, r.t., 6 h, 80%. *h*) Iodoxybenzoic acid, DMSO, $CH_2Cl_2$, 3 h. *i*) $NaClO_2$, $NaH_2PO_4$, DMSO, $H_2O$, 6 h, 75%. *j*) HCl (cat.), MeOH, r.t., 10 h, 66%.

*Scheme 2*




*a*) MOM-Cl, DIPEA, 0° – r.t., 2 h, 90%. *b*) PPTS, MeOH, r.t., 6 h, 78%. *c*) IBX, DMSO, $CH_2Cl_2$, 3 h. *d*) $NaClO_2$, $NaH_2PO_4$, DMSO, $H_2O$, 6 h, 75%. *e*) HCl (cat.), MeOH, r.t., 10 h, 66%.

## Experimental Part

*General.* Reactions were conducted under $N_2$ using anh. solvents such as $CH_2Cl_2$ and THF. All reactions were monitored by thin layer chromatography (TLC) using silica-coated plates (*Merck 60 F-254* silica gel plates) and visualizing under UV light. Light petroleum ether (60–80°; PE) was used. Column chromatography (CC): silica gel ($SiO_2$; 60–120 mesh) supplied by *Acme Chemical Co.*, India. Yields refer to chromatographically and spectroscopically ($^1$H, $^{13}$C) homogeneous material. Air sensitive reagents were transferred by syringe or with a double-ended needle. Evaporation of solvents was

performed at reduced pressure, using a *Büchi* rotary evaporator. Optical rotations: *Jasco DIP-370* polarimeter at 20°. $^1$H-NMR Spectra: *Varian FT-200* MHz (*Gemini*) and *Bruker UXNMR FT-300* MHz (*Avance*) spectrometers in $CDCl_3$; chemical shift values were reported in ppm rel. to TMS ($\delta = 0.0$) as an internal standard. EI-MS: at 70 eV on *LC-MSD* (*Agilent Technologies*).

*(4*S*,5*S*)-4-[(Benzyloxy)methyl]-2,2-dimethyl-5-[(1*E*)-pent-1-en-1-yl]-1,3-dioxolane* (**10**). To the suspension of butyltriphenylphosphonium bromide (13.5 g, 33.8 mmol) in THF was added dropwise a soln. of *tert*-BuOK (3.1 g, 27.6 mmol) in THF at 0° followed by a soln. of aldehyde **9** [9] (3.3 g, 13.2 mmol) in THF. The mixture was stirred for 3 h, then quenched with aq. $NH_4Cl$, extracted with $Et_2O$ ($2 \times 10$ ml), and washed with brine and $H_2O$. The combined org. layer was dried (anh. $Na_2SO_4$), concentrated under reduced pressure to give the crude product, which was purified by flash CC using hexane/AcOEt 95:5 to afford **10** (9:1 (*E*)/(*Z*), 70% yield). Colorless oil. IR (neat): 2928, 2858, 1610, 1420. $^1$H-NMR ($CDCl_3$, 300 MHz): 7.31–7.27 (*m*, 5 H); 5.66–5.56 (*m*, 1 H); 5.40–5.30 (*m*, 1 H); 4.61 (*t*, *J* = 8.3, 1 H); 4.57 (*s*, 2 H); 3.81–3.74 (*m*, 1 H); 3.60–3.46 (*m*, 2 H); 2.16–1.94 (*m*, 2 H); 1.41 (*s*, 3 H); 1.39–1.32 (*m*, 5 H); 0.89 (*t*, *J* = 7.3, 3 H). LC-MS: 313 ($[M + Na]^+$).

*[(4*S*,5*S*)-2,2-Dimethyl-5-pentyl-1,3-dioxolan-4-yl]methanol* (**11**). To a soln. of olefin **10** (2.4 g, 8.3 mmol) in anh. AcOEt was added a cat. amount of Pd/C, and the mixture stirred under $H_2$ atmosphere for 8 h. Then, the mixture was filtered through a *Celite* pad, washed with AcOEt, and the filtrate was concentrated under reduced pressure. The crude product was subjected to flash CC (hexane/AcOEt 70:30) to give pure **11** (94%). Viscous liquid. IR (neat): 3440, 2930, 2858, 1420. $^1$H-NMR ($CDCl_3$, 300 MHz): 3.87–3.80 (*m*, 1 H); 3.79–3.71 (*m*, 1 H); 3.68–3.62 (*m*, 1 H); 3.57–3.48 (*m*, 1 H); 1.71 (*dd*, *J* = 5.2, 2.2, 1 H); 1.57–1.47 (*m*, 2 H); 1.37 (*s*, 6 H); 1.35–1.29 (*m*, 4 H); 0.90 (*t*, *J* = 6.7, 3 H). LC-MS: 225 ($[M + Na]^+$).

*Ethyl (2*E*)-3-[(4*S*,5*S*)-2,2-Dimethyl-5-pentyl-1,3-dioxolan-4-yl]prop-2-enoate* (**12**). To a soln. of DMSO (3.3 ml, 46.5 mmol) in $CH_2Cl_2$ was added dropwise at −78° oxalyl chloride (2.0 ml, 23.3 mmol), followed by a soln. of **11** (2.2 g, 10.9 mmol) in $CH_2Cl_2$. The mixture was stirred for 45 min at −78°, and the reaction was quenched with $Et_3N$ (9.8 ml, 70.3 mmol). To this mixture were added 5 ml of benzene followed by the *Wittig* ylide $Ph_3PCHCO_2Et$ (6.1 g, 17.5 mmol) and stirred at r.t. for 3 h. After completion of the reaction, the mixture was diluted with $CH_2Cl_2$, washed with brine and $H_2O$. The combined org. layer was dried ($Na_2SO_4$) and concentrated under vacuum. The crude compound eluted on CC ($SiO_2$; hexane/AcOEt 95:5) afforded pure **12** (80%). Colorless liquid. IR (neat): 2928, 2858, 1725, 1602, 1453. $^1$H-NMR ($CDCl_3$, 200 MHz): 6.81 (*dd*, *J* = 15.4, 5.1, 1 H); 6.07 (*dd*, *J* = 15.4, 1.5, 1 H); 4.27–4.04 (*m*, 3 H); 3.75–3.62 (*m*, 1 H); 1.60–1.49 (*m*, 2 H); 1.42–1.25 (*m*, 15 H); 0.90 (*t*, *J* = 6.6, 3 H). LC-MS: 293 ($[M + Na]^+$).

*(1*E*,3*S*)-1-[(4*S*,5*S*)-2,2-Dimethyl-5-pentyl-1,3-dioxolan-4-yl]-11-(tetrahydro-2*H*-pyran-2-yloxy)undec-1-en-3-ol* (**14a**) *and (1*E*,3*R*)-1-[(4*S*,5*S*)-2,2-Dimethyl-5-pentyl-1,3-dioxolan-4-yl]-11-(tetrahydro-2*H*-pyran-2-yloxy)undec-1-en-3-ol* (**14b**). To a stirred soln. of ester **12** (2.0 g, 7.4 mmol) in $CH_2Cl_2$ was added dropwise at −78° DIBAL-H (7.4 ml, 7.4 mmol), and the mixture was allowed to stir at the same temp. for 30 min. After monitoring with TLC, the reaction was quenched with aq. MeOH at 0°. Then was added sat. soln. of sodium potassium tartrate, and extracted with $CH_2Cl_2$. The org. layer was washed with brine and $H_2O$. The combined org. layer was dried over anh. $Na_2SO_4$, concentrated under vacuum to obtain the aldehyde which was used without further purification. A soln. of bromide **13** (4.3 g, 14.7 mmol) in THF was added to a suspension of Mg (0.35 g, 14.4 mmol) in THF, refluxed for 20 min, then it was cooled to 0° and was added to the soln. of aldehyde in THF. The mixture was stirred for 1 h. After monitoring TLC, the reaction was quenched with aq. $NH_4Cl$, filtered through a *Celite* pad using AcOEt. The filtrate was dried ($Na_2SO_4$), concentrated under vacuum, and purified by CC ($SiO_2$; hexane/AcOEt 80:20), to afford pure **14a** and **14b** in a 1.5:1 ratio (66%).

*Data of* **14a**. Pale yellow oil. IR (neat): 3444, 2930, 2857, 1460. $^1$H-NMR ($CDCl_3$, 300 MHz): 5.81 (*dd*, *J* = 15.1, 6.0, 1 H); 5.61 (*dd*, *J* = 15.1, 7.5, 1 H); 4.59–4.55 (*m*, 1 H); 4.15–4.07 (*m*, 1 H); 3.95 (*t*, *J* = 7.5, 1 H); 3.88–3.80 (*m*, 1 H); 3.75–3.59 (*m*, 2 H); 3.54–3.44 (*m*, 1 H); 3.39–3.31 (*m*, 1 H); 1.91–1.80 (*m*, 1 H); 1.75–1.48 (*m*, 8 H); 1.40 (*s*, 6 H); 1.38–1.28 (*m*, 20 H); 0.93 (*t*, *J* = 6.8, 3 H). LC-MS: 463 ($[M + Na]^+$).

*Data of* **14b**. Pale yellow oil. IR (neat): 3446, 2930, 2857, 1742, 1460. $^1$H-NMR ($CDCl_3$, 300 MHz): 5.82 (*dd*, *J* = 15.8, 5.3, 1 H); 5.62 (*dd*, *J* = 15.8, 6.8, 1 H); 4.57 (*t*, *J* = 3.7, 1 H); 4.20–4.10 (*m*, 1 H); 3.95

($t$, $J$ = 7.5, 1 H); 3.84 ($dt$, $J$ = 8.3, 3.0, 1 H); 3.76–3.59 ($m$, 2 H); 3.54–3.44 ($m$, 1 H); 3.39–3.31 ($m$, 1 H); 1.91–1.27 ($m$, 34 H); 0.93 ($t$, $J$ = 6.0, 3 H). LC-MS: 463 ($[M+Na]^+$).

*2-{[(9*S*,10*E*)-11-[(4*S*,5*S*)-2,2-Dimethyl-5-pentyl-1,3-dioxolan-4-yl]-9-(methoxymethoxy)undec-10-en-1-yl]oxy}tetrahydro-2*H*-pyran* (**15a**). To the soln. of alcohol **14a** (0.7 g, 1.6 mmol) in $CH_2Cl_2$ was added *Hunig*'s base (DIPEA) (1.08 ml, 6.4 mmol) and cooled to 0°, and then MOM-Cl (0.27 ml, 3.6 mmol) was added in dropwise manner, and the mixture was allowed to stir for 2 h. After monitoring TLC, the mixture was diluted with $CH_2Cl_2$, washed with $H_2O$, combined org. layer was dried ($Na_2SO_4$), concentrated under vacuum and purified by CC ($SiO_2$; hexane/AcOEt 85:15) to afford pure **15a** (90%). Pale yellow oil. IR (neat): 2930, 2858, 1460. $^1$H-NMR ($CDCl_3$, 300 MHz): 5.59–5.56 ($m$, 2 H); 4.65–4.47 ($m$, 3 H); 3.96–3.87 ($m$, 2 H); 3.84 ($m$, 1 H); 3.60–3.54 ($m$, 2 H); 3.35–3.30 ($m$, 2 H); 3.34 ($m$, 3 H); 1.67–1.42 ($m$, 10 H); 1.37 ($s$, 6 H); 1.34–1.24 ($m$, 18 H); 0.89 ($t$, $J$ = 7.5, 3 H). LC-MS: 507 ($[M+Na]^+$).

*2-{[(9R,10*E*)-11-[(4*S*,5*S*)-2,2-Dimethyl-5-pentyl-1,3-dioxolan-4-yl]-9-(methoxymethoxy)undec-10-en-1-yl]oxy}tetrahydro-2*H*-pyran* (**15b**). Yield 90%. Pale yellow oil. IR (neat): 2930, 2857, 1460. $^1$H-NMR ($CDCl_3$, 300 MHz): 5.62–5.58 ($m$, 2 H); 4.65–4.47 ($m$, 3 H); 4.04–3.93 ($m$, 2 H); 3.84 ($dt$, $J$ = 11.3, 2.2, 1 H); 3.75–3.59 ($m$, 2 H); 3.53–3.44 ($m$, 1 H); 3.40–3.33 ($m$, 5 H); 2.10–1.79 ($m$, 2 H); 1.75–1.49 ($m$, 8 H); 1.44–1.27 ($m$, 24 H); 0.93 ($t$, $J$ = 6.8, 3 H). LC-MS: 507 ($[M+Na]^+$).

*(9*S*,10*E*)-11-[(4*S*,5*S*)-2,2-Dimethyl-5-pentyl-1,3-dioxolan-4-yl]-9-(methoxymethoxy)undec-10-en-1-ol* (**16a**). Compound **15a** (0.6 g, 1.2 mmol) was dissolved in MeOH, to which was added cat. amount of pyridinium *p*-toluene sulfonate (PPTS) at 0°, the mixture was stirred at r.t. for 6 h. After monitoring TLC, the reaction was quenched with $NaHCO_3$, and MeOH was removed under vacuum, the crude compound was purified through CC ($SiO_2$; hexane/AcOEt 70:30) to afford pure **16a**. Colorless oil (80%). $[\alpha]_D^{25} = +31.7$ ($c$ = 0.5, $CHCl_3$). IR (neat): 3439, 2927, 2857, 1632, 1460. $^1$H-NMR ($CDCl_3$, 200 MHz): 5.61–5.54 ($m$, 2 H); 4.56 ($AB$, $J$ = 6.8, 2 H); 4.05–3.88 ($m$, 2 H); 3.61 ($t$, $J$ = 6.2, 2 H); 3.59–3.54 ($m$, 1 H); 3.33 ($s$, 3 H); 1.62–1.25 ($m$, 28 H); 0.91 ($t$, $J$ = 6.2, 3 H). $^{13}$C-NMR ($CDCl_3$, 75 MHz): 134.6; 130.1; 108.5; 93.8; 81.7; 80.8; 80.7; 76.0; 63.0; 55.4; 35.8; 32.7; 31.9; 31.5; 29.5; 29.4; 29.3; 27.3; 26.9; 25.7; 25.2; 22.5; 14.0. LC-MS: 423 ($[M+Na]^+$).

*(9*R*,10*E*)-11-[(4*S*,5*S*)-2,2-Dimethyl-5-pentyl-1,3-dioxolan-4-yl]-9-(methoxymethoxy)undec-10-en-1-ol* (**16b**). Yield 78%. Colorless oil. $[\alpha]_D^{25} = -75.8$ ($c$ = 1.0, $CHCl_3$). IR (neat): 3444, 2930, 2859, 1640, 1461. $^1$H-NMR ($CDCl_3$, 300 MHz): 5.63–5.58 ($m$, 2 H); 4.56 ($AB$, $J$ = 6.2, 2 H); 4.05–3.92 ($m$, 2 H); 3.67–3.59 ($m$, 3 H); 3.36 ($s$, 3 H); 1.62–1.28 ($m$, 28 H); 0.93 ($t$, $J$ = 6.8, 3 H). $^{13}$C-NMR ($CDCl_3$, 75 MHz): 134.9; 130.0; 108.5; 93.7; 81.9; 80.8; 76.0; 63.0; 55.4; 35.5; 32.7; 31.9; 29.5; 29.4; 29.3; 27.3; 26.9; 25.7; 25.2; 22.5; 14.0. LC-MS: 423 ($[M+Na]^+$).

*(9*S*,10*E*)-11-[(4*S*,5*S*)-2,2-Dimethyl-5-pentyl-1,3-dioxolan-4-yl]-9-(methoxymethoxy)undec-10-enoic Acid* (**18a**). To an ice-cold soln. of iodoxybenzoic acid (0.33 g, 1.18 mmol) in DMSO (1 ml) was added a soln. of alcohol **16a** (0.3 g, 0.75 mmol) in $CH_2Cl_2$ and stirred for 3 h at r.t. The mixture was filtered through a *Celite* pad, washed with $CH_2Cl_2$, the filtrate was washed with $H_2O$, and the combined org. layer was dried ($Na_2SO_4$) and concentrated under reduced pressure. The crude aldehyde was dissolved in DMSO, at 0°, aq. solns of $NaH_2PO_4$ (0.07 g, 0.58 mmol) and $NaClO_2$ (0.12 g, 1.33 mmol) were added dropwise and stirred for 6 h at r.t. The mixture was extracted with $Et_2O$, washed with brine and $H_2O$. The combined org. layer was dried ($Na_2SO_4$), concentrated, and purified to afford **18a** (70%). Pale yellow oil. $[\alpha]_D^{25} = +22.8$ ($c$ = 0.5, $CHCl_3$). IR (neat): 3439, 2930, 2858, 1711, 1461. $^1$H-NMR ($CDCl_3$, 300 MHz): 5.62–5.58 ($m$, 2 H); 4.56 ($AB$, $J$ = 6.8, 2 H); 4.03–3.92 ($m$, 2 H); 3.65–3.56 ($m$, 1 H); 3.36 ($s$, 3 H); 2.34 ($t$, $J$ = 7.5, 2 H); 1.71–1.27 ($m$, 26 H); 0.91 ($t$, $J$ = 6.8, 3 H). $^{13}$C-NMR ($CDCl_3$, 75 MHz): 134.5; 130.0; 108.5; 93.7; 81.7; 80.8; 80.7; 75.9; 63.0; 55.4; 35.4; 33.9; 31.9; 31.8; 29.2; 29.0; 28.9; 27.2; 26.9; 25.7; 25.2; 22.5; 14.0. LC-MS: 437 ($[M+Na]^+$).

*(9*R*,10*E*)-11-[(4*S*,5*S*)-2,2-Dimethyl-5-pentyl-1,3-dioxolan-4-yl]-9-(methoxymethoxy)undec-10-enoic Acid* (**18b**). Yield 75% over two steps. Colorless oil. IR (neat): 2930, 2857, 1739, 1710, 1461. $^1$H-NMR ($CDCl_3$, 300 MHz): 5.62–5.58 ($m$, 2 H); 4.56 ($AB$, $J$ = 6.8, 2 H); 4.04–3.93 ($m$, 2 H); 3.68–3.58 ($m$, 1 H); 3.36 ($s$, 3 H); 2.35 ($t$, $J$ = 7.5, 2 H); 1.70–1.27 ($m$, 26 H); 0.93 ($t$, $J$ = 6.8, 3 H). LC-MS: 437 ($[M+Na]^+$).

(−)-*Pinellic Acid* (=*(9*S*,10*E*,12*S*,13*S*)-9,12,13-Trihydroxyoctadec-10-enoic Acid*; **1**). To a soln. of acid **18a** (0.25 g, 0.6 mmol) in MeOH was added a cat. amount of HCl and stirred for 10 h at r.t. The reaction was quenched with $NaHCO_3$, MeOH was removed under vacuum, and the crude product was purified to afford **1** (66%). White powder. M.p. 102–104° ([3]: 104–106°). $[\alpha]_D^{25} = -9.2$ ($c$ = 0.5, MeOH)

([3]: $[\alpha]_D^{22} = -8.0$ ($c = 0.3$, MeOH)). IR (KBr): 3440, 2930, 2858, 1710, 1620. $^1$H-NMR ($CDCl_3$/DMSO, 200 MHz): 5.76–5.56 ($m$, 2 H); 4.45–4.27 ($m$, 1 H); 4.17–3.90 ($m$, 1 H); 3.56–3.22 ($m$, 4 H); 2.21 ($t$, $J$ = 7.0, 2 H); 1.63–1.23 ($m$, 20 H); 0.90 ($t$, $J$ = 7.0, 3 H). $^{13}$C-NMR ($CDCl_3$/DMSO, 75 MHz): 178.2; 134.5; 130.0; 76.8; 75.9; 72.9; 37.6; 33.9; 32.8; 29.8; 29.2; 29.0; 28.8; 26.2; 26.1; 25.8; 23.9; 14.0. LC-MS: 453 ($[M + Na]^+$).

*(9*R*,10*E*,12*S*,13*S*)-9,12,13-Trihydroxyoctadec-10-enoic Acid* (**6**). Yield 66%. White powder. M.p. 66–70° ([5]: 69–74°). $[\alpha]_D^{25} = -24.2$ ($c = 0.5$, MeOH) ([5]: $[\alpha]_D^{22} = -24.0$ ($c = 0.3$, MeOH)). IR (KBr): 3362, 2928, 2850, 1695. $^1$H-NMR ($CDCl_3$/DMSO, 200 MHz): 5.64–5.56 ($m$, 2 H); 3.99–3.90 ($m$, 1 H); 3.78–3.71 ($m$, 1 H); 3.36–3.21 ($m$, 4 H); 2.18 ($t$, $J$ = 7.4, 2 H); 1.63–1.23 ($m$, 20 H); 0.90 ($t$, $J$ = 6.6, 3 H). $^{13}$C-NMR ($CDCl_3$/DMSO, 75 MHz): 180.4; 133.8; 128.8; 75.0; 74.0; 70.0; 36.2; 33.0; 31.6; 31.0; 28.2; 28.0; 27.7; 24.4; 24.2; 23.9; 21.5; 13.2. LC-MS: 453 ($[M + Na]^+$).

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