Stereoselective Total Synthesis of Mangiferaelactone using D-Mannose as a Chiral Pool

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A convergent total synthesis of mangiferaelactone has been accomplished in a highly stereoselective manner from readily available D-mannose. The following methods like organocatalytic enantioselective epoxidation, ring-closing metathesis, and *Steglich* esterification have been employed as key steps, which make this approach more attractive.

Introduction. – The polyketide natural products were isolated from fungal sources and are known to possess potent biological activities such as antibacterial, antifungal, cytotoxic, and phytotoxic behavior, which make them attractive synthetic targets. In particular, 10-membered macrolides such as cytospolides [1], decarestrictines [2][3], seimatopolides [3], and stagonolides [4] have received significant attention due to their interesting biological properties.

Mangiferaelactone (**1**) (*Fig.*), a 10-membered macrolide, was isolated from the solid culture of the endophytic fungus, *Pestatotriopsis mangiferae*. The structure of **1** was established by 1D- and 2D-NMR spectroscopy, and the absolute configuration was determined by vibrational circular dichroism (VCD). The minimum inhibitory concentration (*MIC*) of mangiferaelactone against *Listeria monocytogenes* and *Bacillus cereus* was 1.68 mg/ml and 0.55 mg/ml, respectively [5]. Due to inherent biological properties, mangiferaelactone has become an important synthetic target for medicinal chemistry, and to date, only two approaches have been reported for its synthesis [6].

As part of our interest in the total synthesis of biologically active natural products [7], we herein report a novel strategy for the synthesis of mangiferaelactone (**1**) employing D-mannose (**2**) as a cost-effective and readily available precursor.

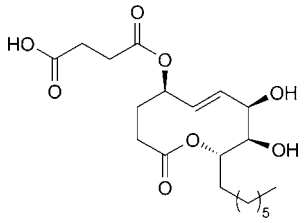

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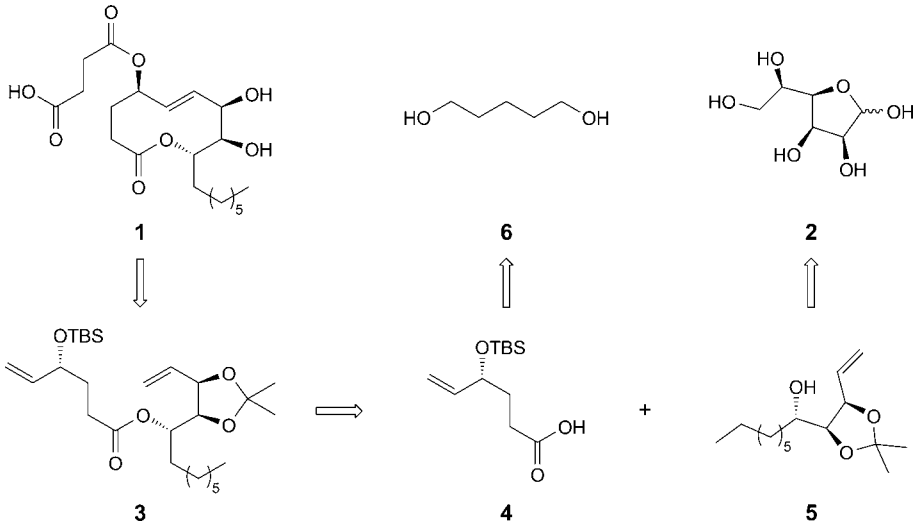
Figure. *Structure of mangiferaelactone*

Results and Discussion. – Our retrosynthetic analysis of mangiferaelactone (**1**) reveals that it could be synthesized through a ring-closing metathesis of **3** [6], which in turn could be prepared by the esterification of acid **4** with alcohol **5**. The intermediates **4** and **5** could easily be accessed from commercially available pentane-1,5-diol **6** and D-mannose **2**, respectively (*Scheme 1*).

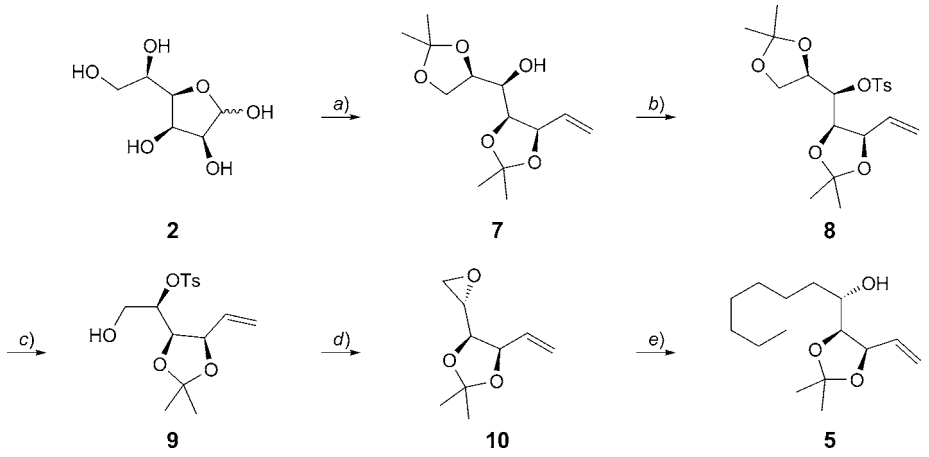
Scheme 1. *Retrosynthetic Analysis of Mangiferaelactone* (**1**)



Accordingly, the synthesis of mangiferaelactone (**1**) began from D-mannose (**2**). Treatment of **2** with I_2 in dry acetone at room temperature over 24 h furnished the corresponding diisopropylidene derivative, which was then subjected to a one-carbon *Wittig* homologation with $MePh_3P^+Br^-$ in the presence of BuLi to give the alkenol **7** in 82% yield [8]. Protection of **7** as its tosylate **8** using TsCl and DABCO in CH_2Cl_2 [9], followed by the selective hydrolysis of **8** using I_2 in MeOH at 0° to 40° afforded the diol in 75% yield [10]. The diol was then subjected to oxidative cleavage using $NaIO_4$ to generate an aldehyde [11], which was subsequently reduced with $NaBH_4$ to provide the alcohol **9** in 80% yield. The alcohol **9** was further treated with K_2CO_3 in MeOH to furnish the epoxide **10** in 75% yield. Regioselective ring-opening of epoxide **10** with *Grignard* reagent $C_6H_{13}MgBr$ in the presence of a catalytic amount of copper cyanide gave the corresponding alkenol **5** in quantitative yield [12] (*Scheme 2*).

Next, we focused on the synthesis of the other key intermediate **4**, which was started from pentane-1,5-diol **6**. Mono-protection of the diol **6** with BnBr in the presence of NaH in THF afforded the benzyl ether in 88% yield, which was then subjected to IBX oxidation to give the aldehyde **11** in 87% yield. The crude aldehyde **11** was further subjected to organo-catalyzed asymmetric epoxidation with catalyst **A** to give the terminal epoxide **12** (90% ee; by HPLC analysis) in 86% yield [13]. Ring opening of **12** with trimethylsulfonium iodide in the presence of BuLi in THF at $-20°$ gave the allylic alcohol in 88% yield [14], which was then protected as its TBS ether **13** using TBSCl

Scheme 2. *Synthesis of the Alcohol Fragment from* D-*Mannose*

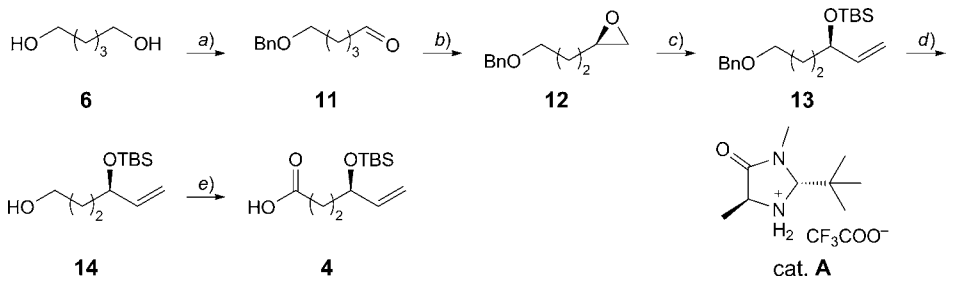


a) 1. I_2, acetone, r.t., 24 h. 2. $MePh_3P^+Br^-$, BuLi, THF, −25° – r.t.; 82%. *b*) TsCl, DABCO, CH_2Cl_2, 15 h; 80%. *c*) 1. I_2, MeOH, 40°, 5 h; 75%. 2. $NaIO_4$, THF/H_2O 4:1, r.t., 2 h. 3. $NaBH_4$, MeOH, 0.5 h; 80%. *d*) K_2CO_3, MeOH, 0° – r.t., 2 h; 75%. *e*) $C_6H_{13}MgBr$, CuCN, THF, −40° – r.t., 1 h; 90%.

and imidazole. Compound **13** was further treated with Li/naphthalene to afford the alcohol **14** in 90% yield. Oxidation of the alcohol **14** with TEMPO-BAIB followed by *Pinnick* oxidation afforded the acid **4** in 82% yield (*Scheme 3*).

Finally, we attempted the coupling of alcohol **5** with carboxylic acid **4** so as to construct a 10-membered ring *via* RCM reaction [6]. Under *Steglich* conditions (DCC/DMAP), the coupling of alcohol **5** with acid **4** gave the corresponding ester **3** in 85% yield [15]. Removal of the TBS ether using pyridine·HF followed by a ring-closing metathesis of **3** using *Grubbs*' second generation catalyst [16] in CH_2Cl_2 under reflux conditions for 6 h gave the 10-membered macrolide **15** in 80% yield. Esterification of

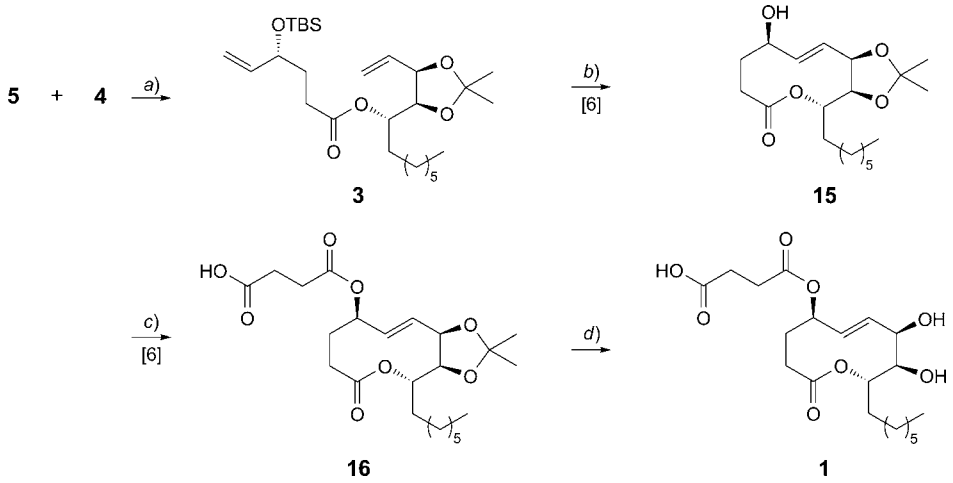
Scheme 3. *Synthesis of the Acid Fragment from Diol*



a) 1. BnBr, NaH, THF, 0° – r.t., 6 h; 88%. 2. IBX, DMSO, CH_2Cl_2, 0° – r.t., 4 h; 87%. *b*) 50 mol-% $(CF_3COO)_2Cu·H_2O$, 20 mol-% cat. **A**, LiCl, $Na_2S_2O_8$, MeCN, $NaBH_4$, 0°, 15 min, KOH, r.t., 30 min; 86% *c*) 1. Me_3SI, BuLi, THF, −20° – r.t., 10 h; 88%. 2. TBSCl, imidazole, CH_2Cl_2, 4 h; 85%. *d*) Li, naphthalene, −20°, 70 min; 90%. *e*) 1. TEMPO-BAIB, CH_2Cl_2, 0° – r.t., 2 h. 2. $NaClO_2$, $NaH_2PO_4·2$ H_2O, 2-methylbut-2-ene, MeCN, 30 min; 82%.

the macrolide **15** with succinic anhydride (75% yield) [17] followed by the removal of acetonide using $CeCl_3 \cdot 7\ H_2O$ under reflux conditions [18] furnished the desired molecule, mangiferaelactone (**1**) in 73% yield. The spectroscopic data (^{1}H- and ^{13}C-NMR, IR, $[\alpha]_D^{25}$) of mangiferaelactone (**1**) were identical in all respects with the data reported in the literature [6] (*Scheme 4*).

Scheme 4. *Synthesis of Mangiferaelactone*



a) DCC, DMAP, CH_2Cl_2, r.t., 6 h; 85%. *b*) 1. Pyridine · HF, THF, 0° – r.t., 8 h; 80%. 2. 5 mol-% *Grubbs*' catalyst-II, CH_2Cl_2, reflux, 6 h; 80%. *c*) $C_4H_4O_3$, DMAP, CH_2Cl_2, r.t., 8 h; 75%. *d*) $CeCl_3 \cdot 7\ H_2O$, MeCN, 80°, 5 h; 73%.

In summary, we have developed a concise and convergent approach for the total synthesis of mangiferaelactone (**1**) in a highly stereoselective manner. Our approach involves *MacMillan* asymmetric epoxidation, *Steglich* esterification, and ring-closing metathesis as the key steps.

P. S. R. and B. P. R. thank *CSIR*, and *K. V. B. thanks UGC New Delhi* for the award of fellowship.

Experimental Part

General. All reagents were reagent grade and used without further purification unless specified otherwise. Solvents were distilled prior to use: THF, toluene, and Et_2O were distilled from Na and benzophenone ketyl; MeOH from Mg and I_2; CH_2Cl_2 from CaH_2. All air- or moisture-sensitive reactions were conducted under N_2 or Ar in flame-dried or oven-dried glassware with magnetic stirring. Column chromatography (CC): silica gel (SiO_2, 60–120 mesh or 100–200 mesh) packed in glass columns. Technical grade AcOEt and petroleum ether used for CC were distilled prior to use. Optical rotations: *JASCO DIP 300* digital polarimeter using a 1 ml cell with a 1 dm path length. IR Spectra: *PerkinElmer IR-683* spectrophotometer; KBr pellets and $CHCl_3$; neat (as mentioned); $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra: *Varian Gemini FT-200*, *Bruker Avance 300*, and *Bruker Avance 500* spectrometers at 200, 300 or 500 MHz, in $CDCl_3$ or C_6D_6; δ in ppm rel. to Me_4Si as internal standard, J in Hz. ESI-MS and HR-ESI-MS: *CEC-21-11013* or *Finnigan Mat 1210* double-focusing mass spectrometers operating at a direct inlet system or LC/MSD Trap SL (*Agilent Technologies*); in *m*/*z*.

*(*R*)-[(4*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl][(4*S,*5*R*)-5-ethenyl-2,2-dimethyl-1,3-dioxolan-4-yl]methanol* (**7**). For synthetic procedure and spectroscopic data, see [8].

*(*R*)-[(4*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl][(4*R,*5*R*)-5-ethenyl-2,2-dimethyl-1,3-dioxolan-4-yl]methyl 4-Methylbenzenesulfonate* (**8**). For synthetic procedure and spectroscopic data, see [9].

*(1*R*)-1-[(4*R,*5*R*)-5-Ethenyl-2,2-dimethyl-1,3-dioxolan-4-yl]-2-hydroxyethyl 4-Methylbenzenesulfonate* (**9**) [10][11]. To a stirred soln. of **8** (10 g, 24.27 mmol) in MeOH (80 ml) at 0°, I_2 was added, the mixture was warmed to 40° and then stirred at the same temp. for 5 h. After completion of the reaction as indicated by TLC, a sat. aq. $Na_2S_2O_3$ soln. (50 ml), was added. The org. phase was separated, and the aq. layer was extracted with AcOEt (3 × 70 ml). Purification by CC over SiO_2 provided the diol. Then, the resulting diol was treated with $NaIO_4$ in the mixture of THF/H_2O 4:1 at r.t. for 2 h. After completion of the reaction as indicated by TLC, filtration of the mixture gave the crude aldehyde (5.6 g, 16.47 mmol). This crude aldehyde was treated with $NaBH_4$ (1.25 g, 32.94 mmol) in MeOH for 30 min, and the mixture was concentrated *in vacuo*. Purification by CC over SiO_2 provided the alcohol **9** (4.5 g, 80%) as a colorless oil. R_f (AcOEt/hexane 1:4) 0.45. $[\alpha]_D^{25} = +34.6$ ($c = 1.0$, $CHCl_3$). IR (KBr): 3234, 2928, 2848, 1545, 1452, 1363, 1258, 926, 768. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.26 (*s*, 3 H); 1.35 (*s*, 3 H); 2.45 (*s*, 3 H); 3.82–3.95 (*m*, 2 H); 4.37 (*t*, $J = 6.5$, 1 H); 4.62–4.68 (*m*, 2 H); 5.22–5.39 (*m*, 2 H); 5.76–5.84 (*m*, 1 H); 7.35 (*d*, $J = 8.0$, 2 H); 7.80 (*d*, $J = 8.3$, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.6; 29.6; 30.9; 61.7; 76.1; 82.9; 86.0; 117.7; 119.8; 127.8; 129.9; 130.1; 131.1; 137.0; 145.5. ESI-MS: 365 ($[M + Na]^+$).

*(4*R*,5*R*)-4-Ethenyl-2,2-dimethyl-5-[(2*S*)-oxiran-2-yl]-1,3-dioxolane* (**10**) [19]. To a stirred soln. of **9** (4.5 g, 13.1 mmol) in MeOH (50 ml), K_2CO_3 (3.63 g, 26.2 mmol) was added slowly at 0°portion wise. The resulting mixture was stirred for 2 h at r.t. After completion of the reaction (monitored by TLC), the mixture was diluted with MeOH (20 ml) and filtered through a small pad of *Celite*, evaporated *in vacuo*, and concentrated under reduced pressure. The crude residue was purified by CC over SiO_2 to give **10** (1.67 g, 75%) as colorless oil. R_f (AcOEt/hexane 1:5) 0.3. $[\alpha]_D^{25} = +54.31$ ($c = 1.0$, $CHCl_3$). IR (KBr): 2958, 2856, 1566, 1361, 1253, 1096, 836, 775. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.26 (*s*, 3 H); 1.40 (*s*, 3 H); 2.67–2.70 (*m*, 1 H); 2.84 (*t*, $J = 3.9$, 1 H); 2.94–3.00 (*m*, 1 H); 3.77 (*t*, $J = 6.9$, 1 H); 4.75 (*t*, $J = 6.6$, 1 H); 5.33–5.53 (*m*, 2 H); 5.94–6.06 (*m*, 1 H).^{13}C-NMR (75 MHz, $CDCl_3$): 24.5; 25.6; 46.8; 56.8; 79.2; 82.0; 117.8; 119.8; 130.3. HR-ESI-MS: 193.2051 ($[M + Na]^+$, $C_9H_{14}NaO_3^+$; calc. 193.2057).

*(1*S*)-1-[(4*S,*5*R*)-5-Ethenyl-2,2-dimethyl-1,3-dioxolan-4-yl]octan-1-ol* (**5**) [6a]. To a stirred soln. of epoxide **10** (1.67 g, 9.8 mmol) and CuCN (120 mg, 0.98 mmol) in THF (50 ml) at −40° was added $C_6H_{13}MgBr$ (Mg: 930 mg, 39.20 mmol, $C_6H_{13}Br$: 39.20 mmol); the resulting mixture was stirred at this temp. for 30 min before being allowed to warm to r.t. over a period of 1 h. The reaction was quenched with a sat. aq. NH_4Cl soln. (30 ml). The org. phase was separated, and the aq. layer was extracted with AcOEt (3 × 50 ml). The combined org. phases were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Purification by CC over SiO_2 provided **5** (2.26 g, 90%) as light-yellow oil. R_f (AcOEt/hexane 1:4) 0.50. For spectroscopic data, see [6].

*(2*R*)-2-[3-(Benzyloxy)propyl]oxirane* (**12**) [13]. To a stirred soln. of cat. **A** (20 mol-%, 1.39 g, 5.2 mmol), LiCl (3.28 g, 78.12 mmol), $(CF_3COO)_2Cu \cdot H_2O$ (3.76 mg, 13.02 mmol), $Na_2S_2O_8$ (6.19 g, 26.04 mmol) in MeCN (120 ml) and H_2O (1.03 ml, 57.29 mmol) was added aldehyde **11** (5 g, 26.04 mmol) at 20°, and the mixture was stirred vigorously for 2 h at the same temp. The mixture was then cooled to 0°, before $NaBH_4$ (2.51 g, 66.14 mmol) was added. After 10 min, the mixture was warmed to r.t., and then a freshly prepared aq. soln. of KOH (40 ml) in EtOH (20 ml, 20 g KOH dissolved in 40 ml dist. H_2O) was added. The resulting mixture was stirred vigorously for 30 min. After completion, the reaction was quenched with 50 ml of dist. H_2O. The mixture was extracted with AcOEt (3 × 50 ml), washed with brine (1 × 50 ml), dried (Na_2SO_4), filtered, and concentrated *in vacuo* maintaining the bath temp. at 30°. The resulting oil was purified by CC over SiO_2 to afford the epoxide **12** (4.3 g, 86%) as a colorless oil. R_f (AcOEt/hexane 1:4) 0.70. $[\alpha]_D^{25} = +16.50$ ($c = 1.0$, $CHCl_3$). IR (KBr): 3033, 2860, 1603, 1495, 1258, 1100, 1013, 911. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.55–1.84 (*m*, 4 H); 2.46–2.48 (*m*, 1 H); 2.74 (*t*, $J = 4.8$, 1 H); 2.91–2.96 (*m*, 1 H); 3.48–3.56 (*m*, 2 H); 4.51 (*s*, 2 H); 7.25–7.36 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 26.1; 29.2; 47.0; 52.0; 69.6; 72.8; 127.4; 127.5; 127.6; 128.3; 138.3. HR-ESI-MS: 215.1042 ($[M + Na]^+$, $C_{12}H_{16}NaO_2^+$; calc. 215. 1040).

*{[(3*R*)-6-(Benzyloxy)hex-1-en-3-yl]oxy}(*tert*-butyl)dimethylsilane* (**13**) [14]. To a stirred soln. of trimethylsulfonium iodide (13.7 g, 67.18 mmol) in dry THF (100 ml) was added BuLi in hexane (2.5M,

26.8 ml, 67.18 mmol) at $-20°$, and the mixture was stirred at r.t. for 3 h. Then, the mixture was cooled to $-20°$ again, and epoxide **12** (4.3 g, 22.39 mmol) in dry THF (40 ml) was slowly added drop wise, and the mixture was stirred at r.t. for 10 h. After completion of the reaction, a sat. aq. NH_4Cl soln. (50 ml) was added. The org. phase was separated, and the aq. layer was extracted with AcOEt (3×60 ml). The combined org. phases were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Purification by CC over SiO_2 provided the alcohol (4.05 g, 88%). To a cooled soln. of the alcohol (4.05 g, 19.66 mmol) and 1*H*-imidazole (2.67 g, 39.32 mmol) in dry CH_2Cl_2 (50 ml) was added TBSCl (3.25 g, 21.62 mmol), and the mixture was stirred at r.t. for 4 h. After completion of the reaction (TLC), the mixture was diluted with H_2O (10 ml) and extracted with CH_2Cl_2 (3×40 ml). The combined extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified by CC to afford the pure product **13** as a colorless liquid (5.34 g, 85%). R_f (AcOEt/hexane 1:9) 0.8. $[\alpha]_D^{25} = -19.56$ ($c = 1.0$, $CHCl_3$). IR (KBr): 2958, 2929, 2856, 1496, 1454, 1275, 1204, 1098, 738. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.03 (*s*, 6 H); 0.90 (*s*, 9 H); 1.52–1.72 (*m*, 4 H); 3.47 (*t*, $J = 6.4$, 2 H); 4.08–4.14 (*m*, 1 H); 4.50 (*s*, 2 H); 5.01–5.16 (*m*, 2 H); 5.75–5.83 (*m*, 1 H); 7.31–7.36 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): -4.9; -4.4; 18.2; 25.4; 25.8; 34.5; 70.4; 72.7; 73.5; 113.6; 127.4; 127.6; 128.2; 138.5; 141.5. HR-ESI-MS: 343.2175 ($[M + Na]^+$, $C_{19}H_{32}NaO_2Si^+$; calc. 343.2172).

*(*R*)-[(6-(Benzyloxy)hex-1-en-3-yl)oxy](*tert*-butyl)dimethylsilane* (**14**) [20]. To a soln. of naphthalene (3.60 g, 37.5 mmol) in THF (40 ml) was added small pieces of Li metal (0.19 g, 37.5 mmol). The mixture was stirred at r.t. under Ar atmosphere, until the Li metal was completely dissolved. The resulting dark green soln. of lithium naphthalenide was cooled to $-20°$ and then, a soln. of compound **13** (3.0 g, 9.3 mmol) in THF (50 ml) was added drop wise over 5 min. The resulting mixture was stirred at $-20°$ for 70 min. Upon completion, the reaction was quenched with a sat. aq. NH_4Cl soln. (20 ml) and H_2O (20 ml), and then, the mixture was extracted with AcOEt (3×50 ml). The combined extracts were washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was then purified by CC over SiO_2 gives the pure product **14** (1.94 g, 90% yield) as a colorless oil. R_f (AcOEt/hexane 3:7) 0.5. $[\alpha]_D^{25} = -19.42$ ($c = 1.0$, $CHCl_3$). IR (KBr): 3234, 2928, 1594, 1365, 1178, 1045, 863, 793. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.03 (*s*, 6 H); 0.89 (*s*, 9 H); 1.53–1.72 (*m*, 4 H); 3.48 (*t*, $J = 6.4$, 2 H); 4.18–4.24 (*m*, 1 H); 5.04–5.18 (*m*, 2 H); 5.78–5.93 (*m*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): -4.9; -4.4; 18.2; 25.4; 25.8; 34.5; 70.4; 72.7; 73.5; 118.6; 138.4. HR-ESI-MS: 231.1769 ($[M + H]^+$, $C_{12}H_{27}SiO_2^+$; calc. 231.1774).

*(4*R*)-4-{[*tert*-Butyl(dimethyl)silyl]oxy}hex-5-enoic Acid* (**4**). To the soln. of **14** (1.9 g, 8.2 mmol) in CH_2Cl_2 (30 ml) at 0° were added TEMPO (650 mg, 4.1 mmol), and BAIB (5.32 g, 16.52 mmol). After stirring at 0° for 2 h, 20% aq. $Na_2S_2O_3$ soln. was added. The products were extracted with $CHCl_3$, and the org. layer was washed with a 20% aq. $Na_2S_2O_3$ soln. and then dried (Na_2SO_4). Removal of the solvent gave a crude aldehyde. The aldehyde was dissolved in MeCN (25 ml) and H_2O (2.5 ml). To this soln. were added 2-methylbut-2-ene (0.08 ml, 22.36 mmol), $NaH_2PO_4 \cdot 2\ H_2O$ (2.32 g, 14.91 mmol), and $NaClO_2$ (1.34 g, 14.91 mmol), and the mixture was stirred at r.t. for 30 min. To this mixture was added a 1M aq. citric acid soln. at 0°, and the products were extracted with $CHCl_3$, and then dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by CC to afford the pure product **4** as colorless liquid (1.49 g, 82%). R_f (AcOEt/hexane 3:7) 0.4. $[\alpha]_D^{25} = -19.20$ ($c = 1.0$, $CHCl_3$). IR (KBr): 2955, 2928, 1710, 1467, 1179, 1035, 833, 773. ^{1}H-NMR ($CDCl_3$, 300 MHz): 0.03 (*s*, 6 H); 0.89 (*s*, 9 H); 1.76–1.92 (*m*, 2 H); 2.36–2.46 (*m*, 2 H); 4.18–4.25 (*m*, 1 H); 5.05–5.19 (*m*, 2 H); 5.71–5.86 (*m*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): -5.0; -4.6; 25.6; 25.9; 29.4; 32.4; 72.3; 115.6; 140.6; 180.2. HR-ESI-MS: 245.1564 ($[M + H]^+$, $C_{12}H_{25}O_3Si^+$; calc. 245.1567).

*(1*S*)-1-[(4*S*,5*R*)-5-Ethenyl-2,2-dimethyl-1,3-dioxolan-4-yl]octyl (4*R*)-4-{[*tert*-Butyl(dimethyl)silyl]oxy}hex-5-enoate* (**3**) [15].To a stirred soln. of **4** (1.5 g, 6.1 mmol) were added *N,N'*-dicyclohexylcarbodimide (DCC, 2.53 g, 12.2 mmol) and 4-(dimethylamino)pyridine (DMAP, 160 mg, 1.2 mmol) in CH_2Cl_2 (20 ml) at 0°, followed by compound **5** (1.88 g, 7.3 mmol) at 0°. The resulting mixture was stirred for 6 h at r.t.. After completion, the mixture was filtered through a *Celite* pad which was then extracted with CH_2Cl_2. The combined extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified by CC to afford the pure product **3** (2.51 g, 85%) as colorless oil. R_f (AcOEt/hexane 1:9) 0.8. $[\alpha]_D^{25} = +12.58$ ($c = 1.0$, $CHCl_3$). IR (KBr): 2956, 2928, 2857, 1739, 1465, 1375, 1253, 1166, 1074, 837, 777. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.04 (*s*, 6 H); 0.84–0.90 (*m*, 12 H); 1.22–1.34 (*m*,

10 H); 1.38 (*s*, 3 H); 1.48 (*s*, 3 H); 1.57–1.64 (*m*, 2 H); 1.75–1.83 (*m*, 2 H); 2.30 (*t*, *J* = 9.0, 2 H); 4.14–4.20 (*m*, 2 H); 4.58–4.63 (*m*, 1 H); 4.88–4.92 (*m*, 1 H); 5.04–5.08 (*m*, 1 H); 5.14–5.24 (*m*, 2 H); 5.30–5.37 (*m*, 1 H); 5.74–5.85 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −5.0; −4.5; 14.0; 22.6; 24.5; 25.2; 25.7; 25.8; 27.6; 29.2; 29.6; 29.7; 31.1; 31.8; 32.6; 71.8; 72.4; 78.4; 78.8; 108.7; 114.4; 118.4; 128.2; 128.8; 133.2; 140.7; 172.7. HR-ESI-MS: 483.3500 ($[M+H]^+$, $C_{27}H_{51}O_5Si^+$; calc. 483.3486).

*(3a*S*,4*S*,9*R*,10*E*,11a*R*)-4-Heptyl-3a,4,7,8,9,11a-hexahydro-9-hydroxy-2,2-dimethyl-6*H*-[1,3]dioxolo[4,5-*c*]oxecin-6-one* (**15**) [6]. To a stirred soln. of **3** (2.5 g, 5.1 mmol) in THF (20 ml) was added pyridine · HF (3.8 ml, 7.5 mmol) at 0°. After stirring the mixture for 8 h at ambient temp., the reaction was quenched with a sat. aq. $NaHCO_3$ soln. (20 ml). The aq. layer was extracted with AcOEt (2 × 20 ml). The combined org. phases were dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified by CC over SiO_2 to afford the alcohol (1.52 g, 80%) as colorless liquid. To a stirred soln. of alcohol (1.5 g, 4.0 mmol) in dry CH_2Cl_2 (150 ml) under N_2, *Grubbs*' 2nd generation catalyst (172 mg, 0.2 mmol) was added. The resulting mixture was heated to reflux for 6 h. After completion of the reaction, the solvent was evaporated, and the crude residue was purified by CC to afford pure product **15** as a colorless oil (1.1 g, 80%). R_f (AcOEt/hexane 2:8) 0.6. $[\alpha]_D^{25} = -7.65$ (*c* = 1.2, $CHCl_3$). IR (KBr): 3447, 2926, 2858, 1728, 1376, 1232, 1144, 1045, 974, 784. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.87 (*t*, *J* = 7.0, 3 H); 1.21–1.34 (*m*, 10 H); 1.38 (*s*, 3 H); 1.54 (*s*, 3 H); 1.74–1.85 (*m*, 2 H); 2.08–2.00 (*m*, 2 H); 2.37–2.31 (*m*, 2 H); 3.98 (*dd*, *J* = 10.0, 5.0, 1 H); 4.22–4.13 (*m*, 1 H); 4.70–4.67 (*m*, 1 H); 4.96–4.90 (*m*, 1 H); 5.66 (*dd*, *J* = 9.0, 1.9, 1 H); 5.82 (*dd*, *J* = 16.0, 3.3, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 14.1; 22.8; 24.6; 26.2; 28.4; 29.2; 29.5; 31.3; 31.8; 31.9; 33.6; 70.2; 75.5; 75.7; 78.6; 109.4; 126.7; 128.2; 175.0. HR-ESI-MS: 363.2143 ($[M+Na]^+$, $C_{19}H_{32}NaO_5^+$; calc. 363.2145).

*4-{[(3a*S*,4*S*,9*R*,10*E*,11a*R*)-4-Heptyl-3a,6,7,8,9,11a-hexahydro-2,2-dimethyl-6-oxo-4*H*-[1,3]dioxolo[4,5-*c*]oxecin-9-yl]oxy}-4-oxobutanoic Acid* (**16**) [17]. To a stirred soln. of **15** (0.5 g, 1.47 mmol), succinic anhydride (294 mg, 2.94 mmol) and DMAP (179 mg, 1.47 mmol) in CH_2Cl_2 (20 ml) were added. The resulting mixture was stirred for 8 h at r.t. and diluted with a sat. aq. $NaHCO_3$ soln., and then extracted with CH_2Cl_2. The org. layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The crude residue was purified by CC over SiO_2 to give the **16** (485 mg, 75%) as yellowish oil. R_f (AcOEt/hexane 1:4) 0.7. Spectroscopic data: see [6].

Mangiferaelactone (=*4-{[(5*R*,6*E*,8*R*,9*R*,10*S*)-10-Heptyl-3,4,5,8,9,10-hexahydro-8,9-dihydroxy-2-oxo-2*H*-oxecin-5-yl]oxy}-4-oxobutanoic Acid*; **1**) [18]. A mixture of compound **16** (100 mg, 0.22 mmol) and $CeCl_3 \cdot 7\,H_2O$ (170 mg, 0.45 mmol) in MeCN (5 ml) was stirred at 80° for 5 h as required to complete the reaction. After completion of the reaction as indicated by TLC, the mixture was extracted with AcOEt, and the combined org. layers were washed with H_2O and brine, dried (Na_2SO_4), and concentrated under reduced pressure to remove the solvent. The crude product was purified by CC to afford the pure product **1** as yellowish-cream solid. (70 mg, 73%). R_f (AcOEt/hexane 4:6) 0.5. Spectroscopic data: see [6].

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