A Concise Total Synthesis of (+)-(6*S*,9*R*,10*R*)-Bovidic Acid

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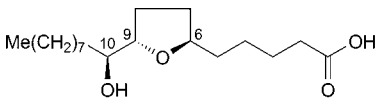
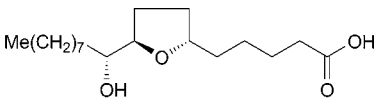
A straightforward strategy for the stereoselective synthesis of (+)-bovidic acid has been developed in eleven steps with an overall yield of 8.85%. The synthesis started from commercially available nonanal, and the key reactions involved were *Sharpless* asymmetric dihydroxylation, *Grignard* reaction, and *Corey–Bakshi–Shibata* reduction.

Introduction. – Worldwide threat of biting arthropods transmitted diseases, with their associated morbidity and mortality, underscores the need for effective insect repellents to protect people. Repellents have been isolated from many naturally occurring plants and animals [1]. Integument of some animals is used for a comparative study with secretary components of macroscopic glands [2]. This outer tough protective part of animals is a source of natural products such as fatty acids, alcohols, and triacylglycerols [3]. These natural products inhibit potential pathogens and repel insects [4].

Oliver et al. reported the C_{18} natural compound (−)-gaur acid (=10-hydroxy-6,9-oxidooctadecanoic acid; **1**), with an absolute configuration of (6*R*,9*S*,10*S*) [5]. Recently, *Ishii et al.* isolated a C_{18} hydroxy-furanoid acid from pelage extracts of *B. frontalis*, called (+)-bovidic acid (**2**), with the absolute configuration (6*S*,9*R*,10*R*), *i.e.*, the enantiomer of **1** [6]. It exhibits insect repellent activity, which is effective to provide protection against *Aedes aegypti* (L) mosquitoes. The configuration of the tetrahydrofuran moiety of (+)-bovidic acid was confirmed by the comparison of its ^{1}H- and ^{13}C-NMR data with those of synthetic compounds. The configuration at C(10) bearing a secondary OH group was determined by NOE, *Mosher* ester analysis method, and circular dichroism (CD) *Tweezer* methods [6]. So far, only one synthesis of (+)-bovidic acid has been published [7].



(–)-(6*R*,9*S*,10*S*)-Gaur acid (**1**)

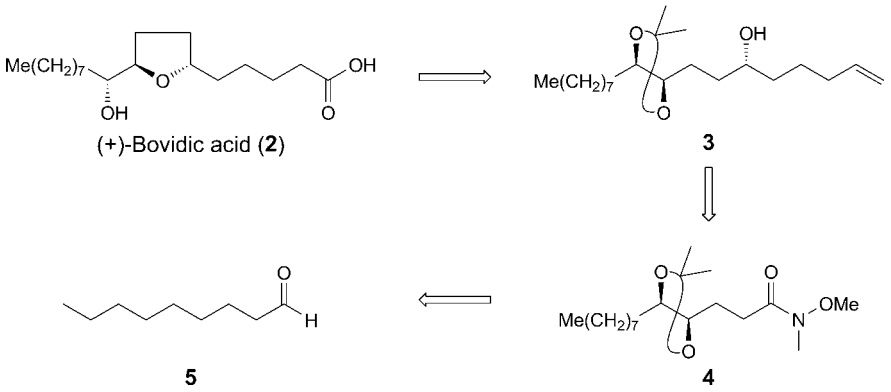


(+)-(6*S*,9*R*,10*R*)-Bovidic acid (**2**)

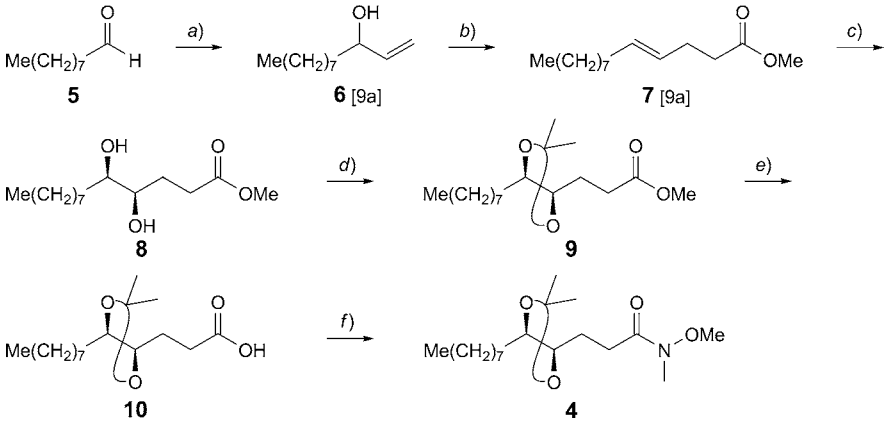
Results and Discussion. – As part of our ongoing research on the synthesis of biologically active natural and synthetic compounds [8], herein we report the stereoselective synthesis of (+)-bovidic acid (**2**) by applying *Sharpless* asymmetric dihydroxylation (*AD-mix*) and *Corey–Bakshi–Shibata* (*CBS*) reduction.

On the basis of a strategy represented in the *retro*-synthetic analysis outlined in *Scheme 1*, the synthesis of fragment **4** started from easily available nonanal (**5**) which was subjected to vinyl *Grignard* reagent in dry THF at 0° to furnish the secondary allyl alcohol **6** in 90% yield (*Scheme 2*). The orthoester *Johnson–Claisen* rearrangement [9] of **6** with $MeC(OMe)_3$ in the presence of a catalytic amount of propanoic acid at reflux afforded the γ,δ-unsaturated ester **7** in 85% yield. Compound **7** was subjected to *Sharpless* asymmetric dihydroxylation [10] with OsO_4 and $K_3Fe(CN)_6$ as co-oxidant in the presence of $MeSO_2NH_2$ and $(DHQD)_2PHAL$ as the chiral ligand in ^{t}BuOH/H_2O (1:1) as solvent at 0° to give diol **8** in 80% yield with 94% de ($[\alpha]_D^{27} = -44.1$ ($c = 0.5$, $CHCl_3$)). Treatment of **8** with a catalytic amount of camphorsulfonic acid (CSA) and

Scheme 1. retro-*Synthetic Strategy of (+)-Bovidic Acid*



Scheme 2

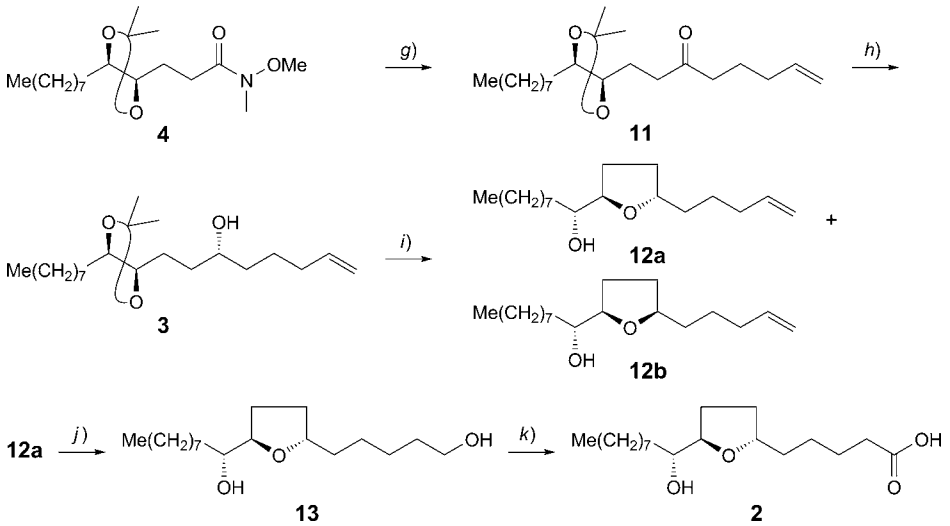


a) CH_2=CHMgBr, $MgBr_2 \cdot Et_2O$, THF, 0°, 1 h; 90%. *b*) $MeC(OMe)_3$, propanoic acid, 142°, 12 h; 85%. *c*) OsO_4, Hydroquinidine phtalizine-1,4-diyl diether ($(DHQD)_2PHAL$), $K_3Fe(CN)_6$, K_2CO_3, $MeSO_2NH_2$, ^{t}BuOH/H_2O 1:1, 0°, 24 h; 80%. *d*) 2,2-Dimethoxypropane (2,2-DMP), camphorsulfonic acid (CSA), CH_2Cl_2, 0°, 2 h; 95%. *e*) $LiOH \cdot H_2O$, THF/H_2O 1:1, r.t., 10 h; 85%. *f*) $Me(NH)OMe \cdot HCl$, ClCOOEt, Et_3N, 0°, 1 h; 80%.

2,2-dimethoxypropane (2,2-DMP) resulted in the acetonide protected compound **9** in 95% yield. The latter was treated with LiOH in THF/H_2O (1:1) at room temperature to give acid **10** in 85% yield, which was transformed into the corresponding *Weinreb* amide [11] **4** ($[\alpha]_D^{27} = +43.5$ ($c = 0.5$, $CHCl_3$)) in 80% yield by the mixed anhydride method (*Scheme* 2).

The treatment of the *Weinreb* amide **4** with *Grignard* reagent, freshly prepared from 5-bromopent-1-ene and Mg metal in dry THF at room temperature, gave the desired enone **11** in 82% yield (*Scheme 3*). Stereoselective reduction of **11** in the presence of (*S*)-*CBS* catalyst [12] afforded selectively the (6*R*)-configured alcohol **3** ($[\alpha]_D^{27} = +30.3$ ($c = 0.25$, $CHCl_3$)) in 80% yield. Compound **3** was converted to its methanesulfonate by using $MeSO_2Cl$, Et_3N, and DMAP (4-(dimethylamino)pyridine; catalytic amount) in CH_2Cl_2 followed by deprotection of the acetonide group by using aqueous CF_3COOH in CH_2Cl_2, to afford a diastereoisomeric tetrahydrofuran mixture **12a**/**12b** 7:3, which was separated by column chromatography. The terminal C=C bond of the more stable major isomer **12a** was hydroborated to give the primary alcohol by treating with $BH_3 \cdot Me_2S$ [13] in THF, followed by treatment with NaOH and H_2O_2 to afford the corresponding alcohol **13** ($[\alpha]_D^{27} = +14.5$ ($c = 0.5$, $CHCl_3$)) in 75% yield. Selective oxidation of **13** with TEMPO and BAIB [14] in CH_2Cl_2/H_2O (1:1) gave the target acid **2** in 65% yield as yellowish semi-solid. The analytical and spectral properties of **2** were in good agreement with the data reported in the literature. All the products were characterized by their IR, ^{1}H- and ^{13}C-NMR, and mass spectra, and optical-rotation data were compared with those reported in the literature.

Scheme 3



g) $CH_2{=}CH(CH_2)_3MgBr$, THF, 0°, 2 h; 82%. *h*) (*S*)-*CBS* Catalyst, THF, −40°, $BH_3 \cdot Me_2S$, 3 h; 80%. *i*) 1) MsCl, Et_3N, CH_2Cl_2, 0°, 1 h; 2) CF_3COOH, CH_2Cl_2, 0° – r.t., 2 h; 70% (two steps). *j*) $BH_3 \cdot Me_2S$, THF, 0°, 3 h, then 20% NaOH, 30% H_2O_2, 3 h; 75%. *k*) (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO), [bis(acetyloxy)iodo]benzene (BAIB), CH_2Cl_2/H_2O 2:1, 12 h; 65%.

Conclusions. – The total synthesis of (+)-bovidic acid (**2**) has been accomplished, starting from a commercially available nonanal and completed in eleven steps with an overall yield of 8.85%. Key reactions to generate stereogenic centers include *Sharpless* asymmetric dihydroxylation and *Corey–Bakshi–Shibata* reduction.

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Experimental Part

General. All reagents were purchased from commercial sources and were used without further purification. All reactions were performed under an inert atmosphere unless noted otherwise. THF was freshly distilled over Na-benzophenone ketyl. Petroleum ether refers to the fraction boiling in the 60–80° range. TLC: Pre-coated SiO_2 *60* F_{254} plates (*Merck*); visualization under UV light, in an I_2 chamber, or by spraying with phosphomolybdic acid. Column chromatography (CC): silica gel (SiO_2; *Acme* grade 60–120 mesh). M.p.: *Büchi M-560* melting-point apparatus; uncorrected. Optical rotations: *Rudolph Autopol IV* polarimeter at 27°. IR Spectra: *PerkinElmer FT-IR 240-c* spectrophotometer; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR spectra: *Bruker-300 MHz* spectrometer in $CDCl_3$, at 300 and 75 MHz, resp.; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. MS: *Finnigan MAT 1020* mass spectrometer operating at 70 eV; in *m*/*z*.

Undec-1-en-3-ol (**6**) [9a]. To a stirred soln. of *nonanal* (**5**; 3 g, 2.11 mmol) in dry THF (10 ml) was added slowly CH_2=CHMgBr (42 ml, 1M in THF, 4.22 mmol) at 0°. The mixture was stirred for an additional 1 h, after completion of the reaction (TLC), the reaction was quenched with a sat. NH_4Cl soln., and the mixture was extracted with AcOEt (2 × 25 ml). The combined org. layers were dried (Na_2SO_4) and concentrated. The residue was purified by CC (SiO_2; hexanes/AcOEt 8:2) to give **6** (3.23 g, 90%). Colorless liquid. IR (neat): 3415, 2926, 2855, 1709, 1639, 1461, 990, 920, 768. ^1H-NMR: 5.83–5.92 (*m*, 1 H); 5.22 (*dt*, *J* = 1.5, 15.8, 1 H); 5.10 (*dt*, *J* = 1.5, 9.0, 1 H); 4.09 (*d*, *J* = 5.0, 1 H); 1.46–1.58 (*m*, 2 H); 1.19–1.42 (*m*, 12 H); 0.88 (*t*, *J* = 7.0, 3 H). ^{13}C-NMR: 141.2; 114.5; 73.2; 37.0; 31.8; 29.5 (2C); 29.2; 25.3; 22.6; 14.0. ESI-MS 193 ($[M+Na]^+$).

*Methyl (4*E*)-Tridec-4-enoate* (**7**) [9a]. In a 100-ml *round-bottom flask* dried in oven, $MeC(OMe)_3$ (21 g, 176 mmol) and propanoic acid (0.2 ml) were added to a soln. of **6** (3 g, 17.6 mmol). The mixture was heated at reflux for 1 h in a pre-heated oil bath. After disappearence of starting material (indicated by TLC), the mixture was cooled and concentrated. The residue was purified by CC (SiO_2; hexane/AcOEt 9:1) to afford **7** (3.39 g, 85%). Colorless liquid. IR (neat): 3448, 2995, 2854, 1743, 1438, 1359, 1165, 968, 770. ^1H-NMR: 5.35–5.50 (*m*, 2 H); 3.67 (*s*, 3 H); 2.35–2.39 (*m*, 2 H); 2.28–2.33 (*m*, 2 H); 1.96 (*q*, *J* = 7.0, 13.5, 2 H); 1.22–1.34 (*m*, 12 H); 0.88 (*t*, *J* = 7.1, 3 H). ^{13}C-NMR: 173.3; 131.9; 127.7; 51.4; 34.1; 32.4; 31.8; 29.5; 29.4.; 29.2; 29.1; 27.9; 22.6; 14.0. ESI-MS: 227 ($[M+H]^+$).

*Methyl (4*R*,5*R*)-4,5-Dihydroxytridecanoate* (**8**). Into a 250-ml *round-bottom flask* were added ^{t}BuOH (70 ml) and H_2O (70 ml), followed by OsO_4, $(DHQD)_2PHAL$, $K_3Fe(CN)_6$, K_2CO_3 (19.8 g, 1.4 g/mmol), and $MeSO_2NH_2$ (1.34 g, 0.095 g/mmol). The resulting mixture was stirred at r.t. for *ca.* 15 min and cooled to 0°. To the cooled soln. was added **7** (3.2 g, 14.1 mmol), and the mixture was stirred for 24 h at 0°. The reaction was quenched with solid Na_2SO_3 (20 g) at r.t. The mixture was diluted with AcOEt (100 ml), and, after separation of the layers, the aq. layer was further extracted with AcOEt (2 × 50 ml). The combined org. layers were washed with brine (50 ml) and dried (Na_2SO_4). After evaporation of the solvent, the residue was purified by CC (SiO_2; hexane/AcOEt 5:5) to give **8** (2.9 g, 80%). White solid. M.p. 60–61°. $[\alpha]_D^{27} = -44.1$ ($c = 0.5$, $CHCl_3$). IR (neat): 3453, 3372, 2958, 2923, 2853, 1740, 1464, 1325, 1195, 1082, 987, 817. ^1H-NMR: 4.39–4.46 (*m*, 1 H); 3.70 (*s*, 3 H); 3.53–3.60 (*m*, 1 H); 2.47–2.68 (*m*, 2 H); 2.04–2.30 (*m*, 3 H); 1.62–1.72 (br. *s*, 2 H); 1.46–1.59 (*m*, 3 H); 1.19–1.42 (*m*, 10 H); 0.88 (*t*, *J* = 7.1, 3 H). ^{13}C-NMR: 177.0; 82.8; 76.4; 73.6; 32.9; 31.8; 29.6; 29.4; 29.1; 28.6; 25.4; 24.0; 22.6; 14.0. ESI-MS: 283 ($[M+Na]^+$).

*Methyl 3-[(4*R*,5*R*)-2,2-Dimethyl-5-octyl-1,3-dioxolan-4-yl]propanoate* (**9**). To a stirred soln. of **8** (2.8 g, 10.7 mmol) in CH_2Cl_2 (30 ml) at 0° was added CSA (0.25 g, 1.07 mmol) followed by 2,2-DMP (1.68 g, 16.1 mmol). The mixture was stirred for 2 h and the reaction was quenched with a sat. aq.

$NaHCO_3$ soln. (10 ml). The org. layer was separated, and the aq. layer further extracted with CH_2Cl_2 (2 × 25 ml). The combined org. layers were washed with brine (25 ml) and dried (Na_2SO_4), and the solvent was evaporated *in vacuo*. The residue obtained was purified by CC (SiO_2; hexane/AcOEt 9:1) to give the **9** (3 g, 95%). Colorless liquid. $[\alpha]_D^{27} = +14.9$ ($c = 0.5$, $CHCl_3$). IR (neat): 3462, 2985, 2927, 2856, 1778, 1741, 1640, 1372, 1242, 1168, 876, 722. ^{1}H-NMR: 3.68 (*s*, 3 H); 3.58–3.62 (*m*, 2 H); 2.38–2.60 (*m*, 2 H); 1.87–2.00 (*m*, 2 H); 1.68–1.83 (*m*, 2 H); 1.43–1.60 (*m*, 4 H); 1.38 (*s*, 6 H); 1.18–1.34 (*m*, 8 H); 0.88 (*t*, $J = 7.1$, 3 H). ^{13}C-NMR: 173.7; 108.0; 80.7; 79.8; 51.5; 32.8; 31.8; 30.5; 29.7; 29.4; 29.2; 27.9; 27.3; 27.2; 26.0; 22.6; 14.0. ESI-MS: 301 ($[M+H]^+$), 323 ($[M+Na]^+$).

*3-[(4*R,5R*)-2,2-Dimethyl-5-octyl-1,3-dioxolan-4-yl]propanoic Acid* (**10**). To a stirred soln. of **9** (2.8 g, 9.3 mmol) in THF/H_2O 50:50 (30 ml) was added LiOH · H_2O (0.45 g, 18.6 mmol). The resulting homogeneous soln. was stirred for 10 h at r.t., and the progress of reaction was monitored by TLC. The org. solvent was removed under reduced pressure, and the aq. residue was extracted with AcOEt (2 × 20 ml). The aq. phase was made acidic (pH 2) with solid $NaHSO_4$ and extracted with AcOEt (2 × 10 ml). The combined org. layers were dried (Na_2SO_4), filtered, and evaporated *in vacuo*. The obtained residue was purified by CC (SiO_2; hexane/AcOEt 7:3) to give **10** (2.2 g, 85%). $[\alpha]_D^{27} = +23.3$ ($c = 0.3$, $CHCl_3$). IR (neat): 3449, 2958, 2927, 2857, 1711, 1163, 1374, 1219, 1069, 771. ^{1}H-NMR: 3.60–3.65 (*m*, 2 H); 2.47–2.63 (*m*, 2 H); 1.90–1.98 (*m*, 1 H); 1.72–1.80 (*m*, 1 H); 1.44–1.56 (*m*, 2 H); 1.38 (*s*, 6 H); 1.20–1.34 (*m*, 12 H); 0.88 (*t*, $J = 7.1$, 3 H). ^{13}C-NMR: 178.9; 108.1; 80.6; 79.6; 46.4; 32.7; 31.7; 30.4; 29.6; 29.4; 29.1; 27.5; 27.2; 27.1; 26.0; 22.6; 14.0. ESI-MS: 287 ($[M+H]^+$), 309 ($[M+Na]^+$).

*3-[(4*R,5R*)-2,2-Dimethyl-5-octyl-1,3-dioxolan-4-yl]*-N-*methoxy*-N-*methylpropanamide* (**4**). To a stirred soln. of **10** (2.1g, 7.3 mmol) in dry CH_2Cl_2 (20 ml) were added Et_3N (0.96 g, 9.5 mmol) and ClCOOEt (0.5 g, 8.8 mmol) at 0°, and the mixture was stirred at the same temp. for 30 min. To this mixture, *N*,*O*-dimethylhydroxylamine hydrochloride (0.78 g, 8 mmol) was introduced in one lot, followed by dropwise addition of Et_3N (1.5 ml, 14.6 mmol). The mixture was then stirred for 1 h (until the disappearance of anhydride (TLC)). After completion of the reaction, the mixture was poured into H_2O (20 ml) and diluted with AcOEt (20 ml). The org. layer was separated, and the aq. layer was extracted with AcOEt (2 × 15 ml). The combined org. layers were washed with a sat. NH_4Cl soln. (15 ml), followed by brine (15 ml), and dried (Na_2SO_4). After evaporation of the solvent, the residue was separated by CC (SiO_2; hexane/AcOEt 7:3) to afford **4** (1.9 g, 80%). Viscous oil. $[\alpha]_D^{27} = +43.5$ ($c = 0.5$, $CHCl_3$). IR (neat): 3449, 2958, 2927, 2857, 1711, 1163, 1374, 1219, 1069, 771. ^{1}H-NMR: 3.69 (*m*, 3 H); 3.60–3.65 (*m*, 2 H); 3.19 (*s*, 3 H); 2.50–2.72 (*m*, 2 H); 1.90–2.0 (*m*, 1 H); 1.68–1.80 (*m*, 1 H); 1.49–1.57 (*m*, 2 H); 1.37 (*s*, 6 H); 1.21–1.35 (*m*, 12 H); 0.88 (*t*, $J = 7.1$, 3 H). ^{13}C-NMR: 173.9; 107.9; 80.9; 80.2; 61.1; 32.7; 32.1; 31.8; 29.7; 29.4; 29.2; 28.4; 27.6; 27.3; 27.2; 26.0; 22.6; 22.6; 14.0. ESI-MS: 330 ($[M+H]^+$), 352 ($[M+Na]^+$).

*1-[(4*R,5R*)-2,2-Dimethyl-5-octyl-1,3-dioxolan-4-yl]oct-7-en-3-one* (**11**). To a stirred soln. of **4** (1.8 g, 5.47 mmol) in THF (20 ml) was dropwise added *Grignard* reagent (prepared by adding 5-bromopent-1-ene (1.2 g, 8.20 mmol) in dry THF (5 ml) to a suspension of Mg (0.39 g, 12.3 mmol) in THF (15 ml) at r.t. and stirring for 30 min) at 0°, and stirring was continued for 1 h. After completion (TLC), the reaction was quenched with a sat. aq. NH_4Cl soln. (15 ml), and the mixture was extracted with AcOEt (2 × 15 ml). The combined org. layers were washed with H_2O (20 ml) and brine (20 ml), dried (Na_2SO_4), and evaporated *in vacuo*. The crude product **11** (1.5 g, 82%) was obtained as pale yellow liquid. $[\alpha]_D^{27} = +36.8$ ($c = 0.25$, $CHCl_3$). IR (neat): 3449, 2958, 2927, 2857, 1711, 1163, 1374, 1219, 1069, 771. ^{1}H-NMR: 5.71–5.84 (*m*, 1 H); 4.96–5.05 (*m*, 2 H); 3.52–3.65 (*m*, 2 H); 2.49–2.69 (*m*, 4 H); 2.40–2.47 (*m*, 2 H); 1.87–2.12 (*m*, 2 H); 1.60–1.72 (*m*, 2 H); 1.43–1.57 (*m*, 4 H); 1.36 (*s*, 6 H); 1.21–1.34 (*m*, 10 H); 0.88 (*t*, $J = 7.1$, 3 H). ^{13}C-NMR: 193.0; 152.6; 132.6; 109.7; 80.6; 80.1; 32.1; 31.8; 29.6; 29.4; 29.2; 27.2; 26.5; 25.9; 22.6; 14.1. ESI-MS: 361 ($[M+Na]^+$).

*(3*R*)-1-[(4*R,5R*)-2,2-Dimethyl-5-octyl-1,3-dioxolan-4-yl]oct-7-en-3-ol* (**3**). To a stirred soln. of **11** (1.4 g, 4.14 mmol) in THF (15 ml) was added (−)-(*S*)-methyl-*CBS*-oxazaborolidine (1.2 ml, 1M toluene, 1.24 mmol) at −40° and stirred for 30 min. To this mixture was added $BH_3 \cdot Me_2S$ (0.35 ml, 4.55 mmol) slowly, and stirring at same temp. was continued for 1 h. After completion (TLC), the reaction was quenched with MeOH (0.1 ml), followed by an aq. $NaHCO_3$ soln. (10 ml). The mixture was extracted with CH_2Cl_2 (2 × 20 ml), and the combined org. layers were dried (Na_2SO_4) and concentrated on rotary evaporator. The crude product was purified by CC (SiO_2; hexane/AcOEt 7:3) to give **3** (1.12 g, 80%).

Colorless liquid. $[\alpha]_D^{27} = +30.3$ ($c = 0.25$, $CHCl_3$). IR (neat): 3449, 2958, 2927, 2857, 1711, 1163, 1374, 1219, 1069, 771. ^{1}H-NMR: 5.71–5.88 (*m*, 1 H); 4.92–5.05 (*m*, 2 H); 4.09–4.05 (*m*, 1 H); 3.99 (*t*, *J* = 7.9, 1 H); 3.62–3.70 (*m*, 1 H); 2.02–2.12 (*m*, 2 H); 1.45–1.65 (*m*, 8 H); 1.41 (*s*, 6 H); 1.18–1.37 (*m*, 14 H); 0.88 (*t*, *J* = 7.1, 3 H). ^{13}C-NMR: 193.0; 152.6; 132.6; 109.7; 80.6; 80.1; 32.1; 31.8; 29.6; 29.4; 29.2; 27.2; 26.5; 25.9; 22.6; 14.1. ESI-MS: 341 ($[M+H]^+$).

*(1*R*)-1-[(2*R*,5*S*)-2,3,4,5-Tetrahydro-5-(pent-4-en-1-yl)furan-2-yl]nonan-1-ol* (**12a**). To a stirred soln. of **3** (1 g, 2.94 mmol) and Et_3N (0.89 g, 8.82 mmol) in CH_2Cl_2 (10 ml) at 0° was added MsCl (0.43 g, 3.82 mmol), and stirring was continued for 30 min. After total consumption of starting material (TLC), a sat. aq. $NaHCO_3$ soln. was added to this mixture, and the org. layer was separated. The aq. layer was re-extracted with CH_2Cl_2, and the combined org. layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The residue was used for further reaction without purification.

To a cooled stirred soln. of the above obtained compound (1 g, 2.39 mmol) in CH_2Cl_2 (30 ml) was added 50% aq. CF_3COOH soln. (2 ml). The mixture was stirred for 1 h at 0° and the completion of reaction confirmed (TLC). Solid $NaHCO_3$ (2 g) was then added to decompose the excess CF_3COOH, followed by the addition of H_2O. The mixture was extracted with $CHCl_3$ (3 × 15 ml), and the combined org. extracts were washed with brine and dried (Na_2SO_4). After evaporation of the solvent, the residue was separated by CC (SiO_2; hexane/AcOEt 7:3) to give **12a** (0.43 g, 70%). Colorless oil. $[\alpha]_D^{27} = +18.5$ ($c = 0.34$, $CHCl_3$). IR (neat): 3419, 2926, 2856, 1743, 1461, 1375, 1056, 769. ^{1}H-NMR: 5.76–5.86 (*m*, 1 H); 4.98–5.04 (*m*, 1 H); 4.93–4.97 (*m*, 1 H); 3.84–3.91 (*m*, 1 H); 3.68–3.80 (*m*, 1 H); 3.32–3.38 (*m*, 1 H); 2.29–2.42 (*m*, 2 H); 1.85–2.10 (*m*, 4 H); 1.36–1.68 (*m*, 8 H); 1.20–1.35 (*m*, 10 H); 0.88 (*t*, *J* = 7.1, 3 H). ^{13}C-NMR: 138.6; 114.6; 114.5; 82.2; 79.6; 74.4; 35.4; 35.0; 33.9; 33.7; 33.3; 32.4; 31.8; 31.3; 29.7; 29.5; 29.2; 28.3; 27.7; 25.7; 25.6; 25.5; 14.0. ESI-MS: 283 ($[M+H]^+$), 305 ($[M+Na]^+$).

*(1*R*)-1-[(2*R*,5*S*)-2,3,4,5-Tetrahydro-5-(5-hydroxypentyl)furan-2-yl]nonan-1-ol* (**13**). To a stirred soln. of **12a** (0.4 g, 1.41 mmol) in dry THF (5 ml) was slowly added $BH_3 \cdot Me_2S$ (0.8 ml, 8.51 mmol) at 0°, then the mixture was warmed to r.t. and stirred further for 1.5 h. To this mixture, MeOH (0.5 ml, 17 mmol) was added slowly at 0°, followed by 3N NaOH (4.2 ml, 12.7 mmol) and 30% H_2O_2 (3.3 ml, 29.7 mmol), and stirring was continued for 1 h at r.t. The mixture was extracted with AcOEt (2 × 20 ml), and the combined org. layers were washed with brine (25 ml), dried (Na_2SO_4), concentrated, and purified by CC (SiO_2; hexane/AcOEt 7:3) to obtain **13** (0.3 g, 75%). Colorless liquid. $[\alpha]_D^{27} = +14.5$ ($c = 0.5$, $CHCl_3$). IR (neat): 3424, 2926, 2856, 1731, 1629, 1460, 1054, 771. ^{1}H-NMR: 3.84–3.91 (*m*, 1 H); 3.69–3.73 (*m*, 1 H); 3.65 (*t*, *J* = 6.5, 2 H); 3.34–3.39 (*m*, 1 H); 1.86–2.06 (*m*, 4 H); 1.55–1.68 (*m*, 4 H); 1.36–1.54 (*m*, 4 H); 1.22–1.33 (*m*, 14 H); 0.88 (*t*, *J* = 7.1, 3 H). ^{13}C-NMR: 82.2; 79.7; 74.5; 62.8; 35.9; 35.5; 33.8; 33.2; 32.6.32.4; 31.8; 31.3; 29.7; 29.5; 29.2; 27.7; 26.0; 25.7; 25.6; 22.6; 14.1. ESI-MS: 301 ($[M+H]^+$), 323 ($[M+Na]^+$).

(+)-Bovidic Acid (*=5-{(2*S*,5*R*)-2,3,4,5-Tetrahydro-5-[(1*R*)-1-hydroxynonyl]furan-2-yl}pentanoic Acid*; **2**) [6]. To a vigorously stirred soln. of **13** (0.3 g, 1 mmol) in CH_2Cl_2 (6 ml) and H_2O (3 ml) was added TEMPO (35 mg, 0.2 mmol) and [bis(acetyloxy)iodo]benzene (BAIB; 0.7 g, 2.4 mmol). Stirring was continued until TLC indicated complete conversion of the starting material. The reaction was quenched by addition of a sat. $Na_2S_2O_3$ soln (20 ml). The mixture was extracted with CH_2Cl_2 (2 × 10 ml), and the combined org. layers were dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the crude acid by CC (SiO_2; hexane/AcOEt 4:6) afforded pure **2** (0.2 g, 65%). Yellowish semisolid. $[\alpha]_D^{27} = +7.5$ ($c = 0.2$, $CHCl_3$) (+7.3 ($c = 0.2$, $CHCl_3$) [7]). IR (neat): 3449, 2825, 2856, 1711, 1633, 1461, 1218, 1082, 770. ^{1}H-NMR: 3.84–3.92 (*m*, 1 H); 3.71 (*q*, *J* = 6.7, 1 H); 3.34–3.39 (*m*, 1 H); 2.37 (*t*, *J* = 7.6, 2 H); 1.86–2.06 (*m*, 2 H); 1.56–1.71 (*m*, 2 H); 1.44–1.53 (*m*, 5 H); 1.35–1.43 (*m*, 5 H); 1.20–1.32 (*m*, 12 H); 0.88 (*t*, *J* = 7.1, 3 H). ^{13}C-NMR: 179.0; 81.7; 80.8; 72.0; 37.6; 33.8; 31.8; 29.7; 29.4; 29.2; 27.2; 26.8; 26.0; 25.8 (2C); 24.6; 22.6; 14.1. ESI-MS: 337 ($[M+Na]^+$).

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