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Efficient Total Synthesis of (–)-(3*S*,6*R*)-3,6-Dihydroxy-10-methylundecanoic Acid

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Keywords: Jacobsen's hydrolytic kinetic resolution (HKR) / Grignard reaction / Hydroboration–oxidation / Dihydroxylation / Regioselectivity / Cyclic sulfate

An efficient enantioselective synthesis of (–)-(3*S*,6*R*)-3,6-dihydroxy-10-methylundecanoic acid (**1**) from epichlorohydrin is described. The key steps include Jacobsen's HKR, Sharpless asymmetric dihydroxylation, regioselective opening of epoxide and cyclic sulfate.

Introduction

(–)-(3*S*,6*R*)-3,6-Dihydroxy-10-methylundecanoic acid (**1**) and its trimer **2** were isolated from the aerial parts of *Lafuentea rotundifolia* Lag.[1] The original structure of **1** was assigned on the basis of the spectroscopic methods and absolute configuration of chiral centre by Mosher's analysis (Figure 1).[2]

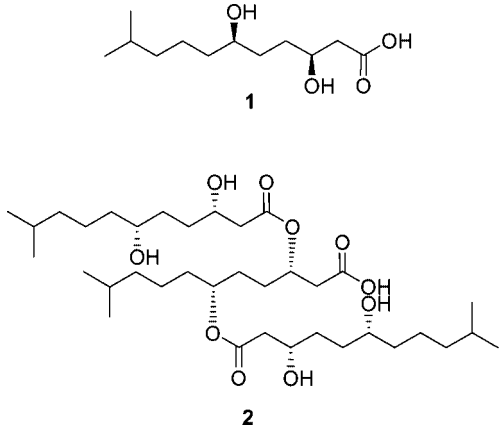
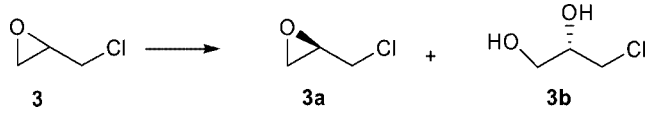


Figure 1. (–)-(3*S*,6*R*)-3,6-dihydroxy-10-methylundecanoic acid (**1**) and its trimer (**2**).

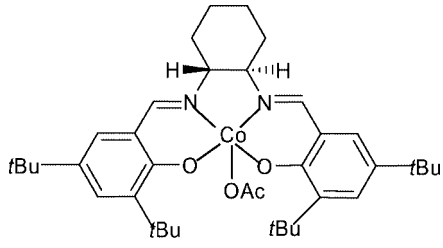
Compound **1** has been a synthetic target of considerable interest due to its β-hydroxy acid skeleton and unique 1,4-dihydroxy structure with an array of functionalities. Very recently, Li et al. reported the first total synthesis of **1** in 11 steps using asymmetric allylboration by *B*-allyldiisopinocampheylborane and hydroboration–oxidation reactions as the key steps.[3] As part of our continuing interest towards asymmetric synthesis of naturally occurring compounds,[4] we have accomplished the total synthesis of (–)-(3*S*,6*R*)-3,6-dihydroxy-10-methylundecanoic acid (**1**) from commercially available epichlorohydrin using Jacobsen's HKR, Sharpless asymmetric dihydroxylation and regioselective opening of epoxide and cyclic sulfate as the key steps.

Results and Discussions

The synthesis of (–)-(3*S*,6*R*)-3,6-dihydroxy-10-methylundecanoic acid (**1**) started from the commercially available epichlorohydrin (**3**) as shown in Scheme 1. Epichlorohydrin (**3**) was subjected to Jacobsen's HKR using the (*R*,*R*)-(salen)Co^{III}·OAc complex (Figure 2) as catalyst to give (*R*)-



Scheme 1. Reagents and conditions: (i) (*R*,*R*)-(salen)Co^{III}·OAc (0.5 mol-%), distd. H_2O (0.55 equiv.), 0 °C, 14 h, (46% for **3a**, 45% for **3b**).



(*R*,*R*)-SalenCo^{III} OAc complex

Figure 2. Jacobsen's hydrolytic kinetic resolution (HKR) catalyst.

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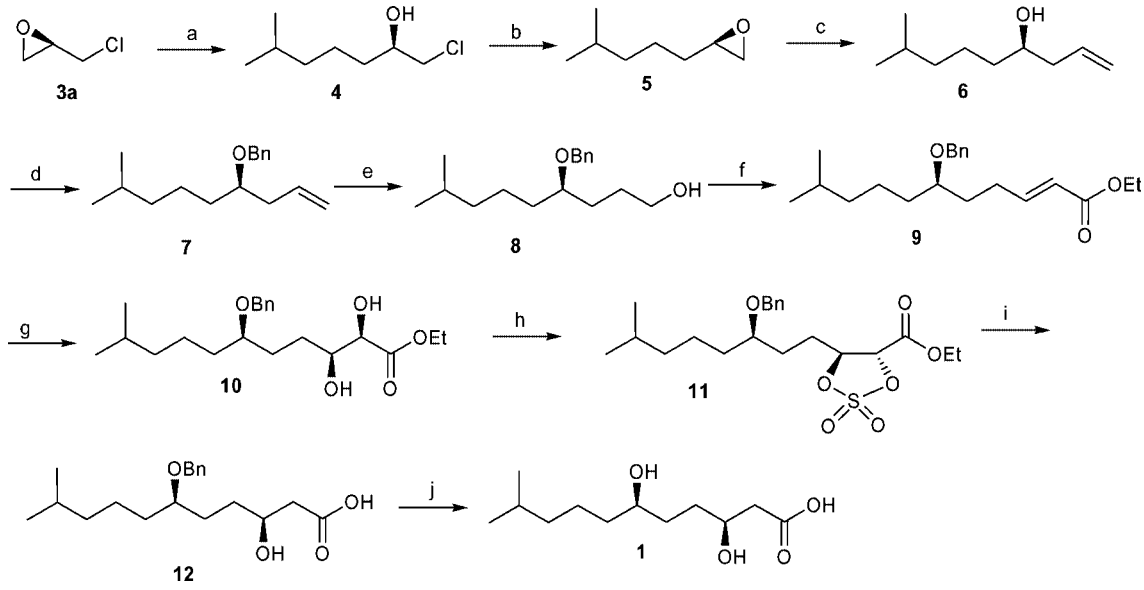

Scheme 2. Reagents and conditions: (a) $Me_2CH(CH_2)_2MgBr$, CuI, dry Et_2O, –78 °C, 12 h, 98%; (b) KOH, Et_2O, 0 °C to room temp., 6 h, 96%; (c) C_2H_3MgBr, CuI, THF, –78 °C to room temp., 12 h, 95%; (d) BnBr, TBAI, NaH, DMF, 0 °C to room temp., 1.5 h, 97%; (e) (i) $BH_3.SMe_2$, THF, 0 °C to room temp., 4 h; (ii) 3 N NaOH, H_2O_2, 0 °C to room temp., 6 h, 88%; (f) $(COCl)_2$, DMSO, CH_2Cl_2, –78 °C, 1.5 h, Et_3N, –60 °C, 1 h (ii) $Ph_3P{=}CHCO_2Et$, THF, room temp., 24 h, 93%; (g) $(DHQ)_2PHAL$ (1 mol-%), 0.1 M OsO_4 (0.5 mol-%), K_2CO_3, $K_3Fe(CN)_6$, $MeSO_2NH_2$, *t*BuOH/H_2O, 1:1, 0 °C, 24 h, 96%; (h) (i) $SOCl_2$, Et_3N, CH_2Cl_2, 0 °C, 30 min; (ii) $RuCl_3$, $NaIO_4$, CCl_4/MeCN/H_2O; 2:2:3, 0 °C, 1 h, 98%; (i) $NaBH_4$, DMAC, 25 °C, 30 min, then 20% aq. H_2SO_4, overnight, 86%; (j) 20% $Pd(OH)_2$/C, H_2, EtOAc, room temp., 10 h, 81%.

epichlorohydrin (**3a**) as a single isomer $[\alpha]_D^{25}$ = –32.5 (*c* = 1.25, MeOH); {ref.[5] $[\alpha]_D^{26}$ = –32.8 (*c* = 1.27, MeOH)}, which was easily isolated from the more polar diol **3b** by distillation (Scheme 1).[5]

With enantiomerically pure epichlorohydrin (**3a**) in hand, we then subjected it to copper-catalysed (CuI) regioselective ring-opening with isoamylmagnesium bromide (**3a**→**4**) followed by treatment with base to give the epoxide **5** (Scheme 2). Subsequent reaction with vinylmagnesium bromide furnished **6** in overall 89% yield. The hydoxyl protection of **6** with benzyl bromide in the presence of NaH gave **7** in 97% yield, which was then subjected to hydroboration–oxidation reaction to afford the alcohol **8** in 88% yield.

Our next aim was to carry out the two carbon homologation of **8** by means of Wittig reaction. To this end, compound **8** was oxidised to the aldehyde under Swern conditions,[6] the product was subsequently treated with (ethoxycarbonylmethylene)triphenylphosphorane in dry THF at room temperature to furnish the *trans*-Wittig product **9** in 93% yield. The dihydroxylation of olefin **9** with osmium tetroxide and potassium ferricyanide as co-oxidant in the presence of $(DHQ)_2PHAL$ under the Sharpless asymmetric conditions[7] gave the diol **10** in 96% yield with 94% *de*. Treatment of the diol **10** with thionyl chloride and triethylamine in CH_2Cl_2 gave the cyclic sulfite, which was further oxidised using $NaIO_4$ and a catalytic amount of ruthenium trichloride to furnish the corresponding cyclic sulfate **11**[8] in quantitative yield. The synthetic strategy shown in Scheme 2 was based on the presumption that the nucleophilic opening of the cyclic sulfate **11** would occur in a regiospecific manner at the α-carbon.[9] Indeed, the cyclic sulfate **11** reacted with 1 equiv. of $NaBH_4$ with apparent complete selectivity for attack at C-2 position to furnish the intermediate sulfate ester which, without further isolation was subjected to acidic hydrolysis using 4 N H_2SO_4 to give **12** in excellent yield. Finally, benzyl deprotection with 20% $Pd(OH)_2/H_2$ led to **1** as a white powder in 81% yield. The physical and spectroscopic data were in full agreement with the literature.[3]

Conclusions

In conclusion, a practical and enantioselective synthesis of (–)-(3*S*,6*R*)-3,6-dihydroxy-10-methylundecanoic acid has been achieved from epichlorohydrin in 10 steps and 46.5% overall yield, employing Jacobsen's HKR, Sharpless asymmetric dihydroxylation, regioselective opening of epoxide and cyclic sulfate as the key steps. The merits of this synthesis are high diastereoselectivity and high yielding reaction steps. The synthetic strategy described has significant potential for further extension to other analogues of β-hydroxy carboxylic acid with no substituents at C_α.

Experimental Section

Solvents were purified and dried by standard procedures before use. Petroleum ether of boiling range 60–80 °C was used. Optical rotations were measured using sodium D line on JASCO-181 digital polarimeter. Infrared spectra were recorded with a Perkin–Elmer model 683 grating Infrared spectrometer. Mass spectrum was obtained with a TSQ 70, Finningen MAT mass spectrometer. ^1H

NMR (200 MHz) and ^{13}C (50 MHz) NMR spectra were recorded in $CDCl_3$ solution with residual $CHCl_3$ (= 7.27 ppm) and (= 77.00 ppm) respectively as internal standard. Elemental analyses were carried out with a Carlo Erba CHNS-O analyzer. Diastereomeric excess was determined using ^1H and ^{13}C NMR spectroscopy. Column chromatography was performed on silica gel (60–120 and 230–400 mesh) using a mixture of petroleum ether and ethyl acetate as eluent.

(*R*)-1-Chloro-6-methylheptan-2-ol (4): A solution of isoamylmagnesium bromide prepared form isoamyl bromide (9.8 g, 64.85 mmol) and Mg turnings (1.58 g, 64.85 mmol) in dry Et_2O was added dropwise to a stirred solution of (*R*)-epichlorohydrin (**3a**) (>99% *ee*, 3.00 g, 32.43 mmol) and CuI (1.24 g, 6.49 mmol) in dry Et_2O (50 mL) at –78 °C. The mixture was warmed to –20 °C within 12 h and poured into a saturated NH_4Cl solution. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined ethereal extracts were dried with Na_2SO_4. The extracts were concentrated to near dryness and purified on silica gel column chromatography (R_f = 0.40, EtOAc/petroleum ether, 1:9) to give **4** as a colourless oil (5.23 g, 98%). $[\alpha]_D^{25}$ = +6.07 (*c* = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3409, 2955, 1467, 1216 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.6 Hz, 6 H), 1.14–1.64 (m, 7 H), 2.09 (br. s, 1 H), 3.57 (ddd, *J* = 3.3, 8.0, 18.0 Hz, 2 H), 3.76–3.87 (m, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.4, 23.2, 27.8, 34.4, 38.7, 50.3, 71.4 ppm. $C_8H_{17}ClO$ (164.67): calcd. C 58.35, H 10.41; found C 58.40, H 10.39.

(*R*)-2-(4-Methylpentyl)oxirane (5): Finely powdered KOH (5.21 g, 92.91 mmol) was added to a solution of **4** (5.10 g, 30.97 mmol) in Et_2O (50 mL). The mixture was stirred vigorously for 6 h between 0 °C and room temp. and poured into 20 mL water. After separation of the layers, the aqueous layer was extracted with Et_2O (3 × 50 mL) and the combined organic layers were dried with Na_2SO_4. Evaporation of the solvent and silica gel column chromatographic purification (R_f = 0.70, EtOAc/petroleum ether, 1:49) of the crude product gave **5** as a colourless liquid (3.81 g, 96%). $[\alpha]_D^{25}$ = +5.96 (*c* = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3018, 2869, 1736, 1467, 1216 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.7 Hz, 6 H), 1.16–1.63 (m, 7 H), 2.47 (dd, *J* = 3.1, 5.3 Hz, 1 H), 2.76 (t, *J* = 4.5 Hz, 1 H), 2.87–2.96 (m, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.4, 23.7, 27.9, 32.7, 38.6, 47.0, 52.2 ppm. $C_8H_{16}O$ (128.21): calcd. C 74.94, H 12.58; found C 74.84, H 12.49.

(*R*)-8-Methylnon-1-en-4-ol (6): Vinylmagnesium bromide (3.07 g, 23.40 mmol, 23.40 mL, 1 M solution in THF) was added dropwise to a stirred solution of **5** (2.00 g, 15.60 mmol) and CuI (594 mg, 3.12 mmol) in dry THF (30 mL) over 30 min at –78 °C and stirred for 12 h. The mixture was warmed to 0 °C, before it was quenched with a saturated NH_4Cl solution (20 mL). The layers were separated, the aqueous layer extracted with Et_2O (3 × 30 mL), the combined ethereal extracts were washed with brine (20 mL) and dried (Na_2SO_4). Evaporation of the solvent and purification by silica gel column chromatography (R_f = 0.50, EtOAc/petroleum ether, 1:20) of the crude product gave **6** as a colourless oil (2.32 g, 95%). $[\alpha]_D^{25}$ = +2.80 (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3421, 2955, 1640, 1467, 1216 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.88 (d, *J* = 6.6 Hz, 6 H), 1.13–1.61 (m, 7 H), 2.06–2.38 (m, 2 H), 3.59–3.71 (m, 1 H), 5.08–5.12 (m, 1 H), 5.16–5.20 (m, 1 H), 5.74–5.94 (m, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.5, 23.4, 27.9, 37.0, 38.9, 41.9, 70.6, 117.8, 134.9 ppm. $C_{10}H_{20}O$ (156.27): calcd. C 76.86, H 12.90; found C 76.51, H 12.93.

(*R*)-[(8-Methylnon-1-en-4-yloxy)methyl]benzene (7): NaH (60%, 0.85 g, 21.12 mmol) was added to a solution of **6** (2.2 g, 14.07 mmol) in dry DMF (50 mL) at 0 °C. The reaction mixture was then stirred at room temperature for 30 min after which it was again cooled to 0 °C. Benzyl bromide (2.49 g, 15.49 mmol) and tetra-*n*-butylammonium iodide (262 mg, 0.71 mmol) was slowly added thereto with further stirring for 1 h at the same temperature. The reaction mixture was quenched with addition of cold water at 0 °C. The two phases were separated and the aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with water (3 × 20 mL), brine, dried (Na_2SO_4) and concentrated. The residual oil was purified by silica gel column chromatography (R_f = 0.45, EtOAc/petroleum ether, 1:50) to furnish the benzyl-protected alcohol **7** (3.36 g, 97%) as a colourless oil. $[\alpha]_D^{25}$ = +9.44 (*c* = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2867, 1640, 1454, 1095 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.88 (d, *J* = 6.82 Hz, 6 H), 1.11–1.60 (m, 7 H), 2.34 (t, *J* = 6.37 Hz, 2 H), 3.40–3.51 (quint, 1 H), 4.50 (d, *J* = 11.62 Hz, 1 H), 4.59 (d, *J* = 11.62 Hz, 1 H), 5.04–5.06 (m, 1 H) 5.09–5.11 (m, 1 H), 5.14–5.15 (m, 1 H), 7.30–7.41 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.6, 23.1, 27.9, 34.0, 38.3, 39.0, 70.9, 78.5, 116.7, 127.4, 127.7, 128.2, 135.1, 138.9 ppm. $C_{17}H_{26}O$ (246.39): calcd. C 82.87, H 10.64; found C 82.91, H 10.59.

(*R*)-4-(Benzyloxy)-8-methylnonan-1-ol (8): BH_3·DMS (1.09 g, 6.58 mL, 14.29 mmol, 2 M solution in THF) was added to a solution of **7** (3.2 g, 12.99 mmol) in dry THF (35 mL) at 0 °C under argon, and the reaction mixture was warmed to room temperature and stirred for 4 h. The reaction flask was cooled to 0 °C and then a solution of NaOH (1.04 g, 25.98 mmol) in EtOH/H_2O (2:1, 15 mL), followed by H_2O_2 (4.41 mL, 38.96 mmol, 30% w/v solution in water) were added dropwise within 30 min. It was then stirred at room temperature for 6 h. The product was taken up in EtOAc and the aqueous layer extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with brine, water, dried (Na_2SO_4) and concentrated. Purification by silica gel column chromatography (R_f = 0.30, EtOAc/petroleum ether, 2:8) of the crude product gave alcohol **8** as a colourless liquid (3.02 g, 88%). $[\alpha]_D^{25}$ = –6.37 (*c* = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3388, 2867, 1726, 1454, 1063 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.88 (d, *J* = 7.0 Hz, 6 H), 1.11–1.74 (m, 11 H), 1.94 (br. s, 1 H), 3.39–3.50 (quint, 1 H), 3.64 (t, *J* = 6.9 Hz, 2 H), 4.49 (d, *J* = 11.50 Hz, 1 H), 4.57 (d, *J* = 11.50 Hz, 1 H), 7.30–7.37 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.5, 22.9, 27.8, 28.4, 30.1, 33.7, 38.9, 62.7, 70.7, 78.8, 127.4, 127.7, 128.2, 138.6 ppm. $C_{17}H_{28}O_2$ (264.40): calcd. C 77.22, H 10.67; found C 77.15, H 10.70

Ethyl (*R*,*E*)-6-(Benzyloxy)-10-methylundec-2-enoate (9): DMSO (2.56 g, 2.33 mL, 32.83 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a solution of oxalyl chloride (2.02 g, 15.89 mmol) in dry CH_2Cl_2 (30 mL) at –78 °C within 15 min. The reaction mixture was stirred for 30 min and a solution of **8** (2.8 g, 10.59 mmol) in CH_2Cl_2 (20 mL) was added dropwise within 15 min. The reaction mixture was stirred for 30 min at –78 °C and 30 min at –60 °C and then Et_3N (4.72 g, 6.50 mL, 46.60 mmol) in CH_2Cl_2 (5.00 mL) was added dropwise and stirred for 1 h. The reaction mixture was poured into saturated solution of $NaHCO_3$ (50 mL) and the organic layer separated. The aqueous layer was extracted with diethyl ether (3 × 20 mL) and the combined organic layers were washed (brine), dried (Na_2SO_4) and concentrated to give the crude aldehyde. This was used for the next step without further purification.

A solution of the above aldehyde in dry THF (10 mL) was added to a solution of (ethoxycarbonylmethylene)triphenylphosphorane (4.06 g, 11.65 mmol) in dry THF (20 mL). The reaction mixture was stirred at room temperature for 24 h. It was then concentrated and purified by silica gel column chromatography (R_f = 0.60, EtOAc/petroleum ether, 1:9) to give olefin **9** as a pale yellow oil

(3.27 g, 93%). $[\alpha]_D^{25}$ = –11.45 (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 2953, 1721, 1654, 1268, 1046 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.88 (d, *J* = 6.4 Hz, 6 H), 1.15–1.74 (m, 12 H), 2.20–2.41 (m, 2 H), 3.36–3.47 (quint, 1 H), 4.19 (q, *J* = 7.6, 14.5 Hz, 2 H), 4.46 (d, *J* = 11.50 Hz, 1 H), 4.55 (d, *J* = 11.50 Hz, 1 H) 5.82 (dt, *J* = 1.70, 15.7 Hz, 1 H) 6.86–7.05 (m, 1 H), 7.29–7.37 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.2, 22.5, 27.8, 28.0, 32.1, 33.8, 39.0, 60.0, 70.8, 77.9, 121.3, 127.4, 127.7, 128.2, 138.7, 149.0, 166.5. $C_{21}H_{32}O_3$ (332.48): calcd. C 75.86, H 9.70; found C 75.88, H 9.69.

Ethyl (2*R*,3*S*,6*R*)-6-(Benzyloxy)-2,3-dihydroxy-10-methylundecanoate (10): Osmium tetroxide (0.22 mL, 0.1 M solution in toluene, 0.5 mol-%) was added to a mixture of $K_3Fe(CN)_6$ (4.46 g, 13.53 mmol), K_2CO_3 (1.87 g, 13.53 mmol), $(DHQ)_2PHAL$ (35 mg, 1 mol-%) in *t*BuOH/H_2O (1:1, 20 mL) at 0 °C, followed by methanesulfonamide (428 mg, 4.50 mmol). After stirring for 2 min at 0 °C, the olefin **9** (1.5 g, 4.51 mmol) was added in one portion. The reaction mixture was stirred at 0 °C for 24 h and then quenched with solid sodium sulfite (3 g). The stirring was continued for additional 15 min and then the solution was extracted with EtOAc (3 × 20 mL). The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. Purification by silica gel column chromatography (R_f = 0.30, EtOAc/petroleum ether, 1:4) of the crude product gave **10** as a colourless syrupy liquid (1.59 g, 96%, 94% *de*). $[\alpha]_D^{25}$ = –15.08 (*c* = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3444, 2867, 1737, 1454, 1275, 1206 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.86 (d, *J* = 6.5 Hz, 6 H), 1.14–1.79 (m, 14 H), 2.40 (br. s, 2 H), 3.38–3.50 (m, 1 H), 3.86–3.91 (m, 1 H), 4.06 (dd, *J* = 2.0, 4.1 Hz, 1 H), 4.30 (q, *J* = 7.1 Hz, 2 H), 4.49 (d, *J* = 11.75 Hz, 1 H), 4.56 (d, *J* = 11.75 Hz, 1 H), 7.30–7.36 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.0, 22.5, 22.9, 27.8, 29.3, 29.7, 33.7, 38.9, 61.7, 70.6, 72.5, 73.3, 78.6, 127.4, 127.7, 128.2, 138.6, 173.4 ppm. $C_{21}H_{34}O_5$ (366.24): calcd. C 68.82, H 9.35; found C 68.64, H 9.43.

(2*R*,3*S*,6*R*)-5-(3-Benzyloxy-7-methyloctyl)-4-ethoxycarbonyl-1,3,2-dioxathiolane 2,2-Dioxide (11): Et_3N (290 mg, 0.4 mL, 2.87 mmol) was added to a solution of diol **10** (500 mg, 13.65 mmol) in dry CH_2Cl_2 (15 mL). The mixture was cooled in an ice bath and thionyl chloride (180 g, 0.11 mL, 15.02 mmol) was added dropwise at 0 °C. The reaction mixture was stirred for 30 min and then quenched by adding water (10 mL). The phases were separated and aqueous phase extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried with Na_2SO_4 and concentrated. Then the solution was cooled with an ice-water bath and diluted with CH_3CN (10 mL) and CCl_4 (10 mL). $RuCl_3 \cdot H_2O$ (15 mg, 0.07 mmol) and $NaIO_4$ (518 mg, 2.43 mmol) were added, followed by water (15 mL). The resulting orange mixture was stirred at room temperature for 1 h. The mixture was then diluted with diethyl ether (20 mL), and the two phases separated. The organic layer was washed with water (20 mL), saturated with aq. $NaHCO_3$ (20 mL), brine, dried with Na_2SO_4, and concentrated. Purification by silica gel column chromatography (R_f = 0.60, EtOAc/petroleum ether, 1:5) of the crude product gave the sulfate **11** as a colourless liquid (573 mg, 98%). $[\alpha]_D^{25}$ = –1.27 (*c* = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2954, 1765, 1739, 1454, 1217 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.3 Hz, 6 H), 1.16–1.23 (m, 14 H), 3.40–3.51 (quint, 1 H), 4.30 (q, *J* = 7.6, 11.4 Hz, 2 H), 4.47 (d, *J* = 11.74 Hz, 1 H), 4.56 (d, *J* = 11.74 Hz, 1 H), 4.59–4.73 (m, 1 H), 5.00–5.20 (m, 1 H), 7.30–7.36 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.9, 22.5, 27.8, 29.5, 30.2, 33.7, 38.9, 62.4, 70.8, 81.3, 82.5, 86.64, 127.5, 127.7, 128.3, 138.6, 166.8 ppm. $C_{21}H_{32}O_7S$ (428.54): calcd. C 58.86, H 7.53; found C 58.79, H 7.55.

(3*S*,6*R*)-6-(Benzyloxy)-3-hydroxy-10-methylundecanoic Acid (12): $NaBH_4$ (26 mg, 0.70 mmol) was added under argon to a solution of the cyclic sulfate **11** (300 mg, 0.70 mmol) in dry DMAC (8 mL). The reaction mixture was stirred under argon at room temperature for 30 min. The solvent was removed under reduced pressure and the reaction mixture was acidified with 4 N H_2SO_4 (6 mL) and stirred at room temperature overnight. The solvent was stripped off under reduced pressure and the residue was purified by silica gel column chromatography (R_f = 0.50, EtOAc/petroleum ether, 1:1.5) to give **12** as a colourless syrup (190 mg, 86%). $[\alpha]_D^{25}$ = +4.01 (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3425, 2916, 1651, 1265 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.86 (d, *J* = 6.6 Hz, 6 H), 1.18–1.85 (m, 11 H), 2.33–2.56 (m, 3 H), 3.99–4.09 (m, 1 H), 4.12 (d, *J* = 11.40 Hz, 1 H), 4.20 (d, *J* = 11.40 Hz, 1 H), 5.12–5.24 (quint, 1 H), 7.33–7.61 (m, 3 H), 8.05 (d, *J* = 7.0 Hz, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.7, 19.2, 19.7, 22.5, 22.6, 27.9, 30.5, 38.0, 65.5, 71.7, 72.5, 128.3, 128.8, 130.9, 132.3, 167.7 ppm. $C_{19}H_{30}O_4$ (322.44): calcd. C 70.77, H 9.38; found C 70.84, H 9.41.

(3*S*,6*R*)-3,6-Dihydroxy-10-methylundecanoic Acid (1): A catalytic amount of 20% $Pd(OH)_2$/C was added to a solution of **12** (51 mg, 0.16 mmol) in EtOAc (8 mL). The reaction mixture was hydrogenated using a H_2 balloon for 10 h at room temperature. After this time the reaction mixture was filtered through a pad of celite and the pad was washed with additional EtOAc (30 mL). Purification by silica gel column chromatography (R_f = 0.25, EtOAc/petroleum ether, 8:2) of the crude product gave **1** as a white powder (30 mg, 81%). m.p. 150–151 °C {ref.[3] 149–151 °C}, $[\alpha]_D^{25}$ = –9.66 (*c* = 0.9 $CHCl_3$), {ref.[3] $[\alpha]_D^{25}$ = –7.00 (*c* = 0.9, $CHCl_3$)}. IR ($CHCl_3$): $\tilde{\nu}$ = 3386, 2957, 1685 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.88 (d, *J* = 6.8 Hz, 6 H), 1.16–1.67 (m, 11 H), 1.84 (br. s, 2 H), 2.47–2.50 (m, 2 H), 3.60–3.69 (m, 1 H), 4.01–4.10 (m, 1 H) ppm. MS (ESI): *m*/*z* = 232 $[M]^+$.

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