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Stereoselective synthesis of simplactone B via Prins cyclisation

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Abstract—The synthesis of simplactone B has been achieved through a series of nine steps in 85% overall yield using Prins cyclisation as the key step with high stereochemical control.
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1. Introduction

δ-Lactones are of great importance as structural components of a large number of organic natural products and as intermediates in the synthesis of several drugs and natural products. They represent important structural moieties in a large number of bioactive natural products such as mevinolin, compactin, pironetin, phomalactone[1a] and asperlin,[1b] massoialactone,[1c] (3*R*,4*S*,5*S*,9*S*)-3,5,9-trihydroxy-4-methyl-undecanoic acid δ-lactone,[1d] tetrahydro 6-(1-hydroxyundecyl)-2*H*-pyran-2-one[1e] (Fig. 1) and as inhibitors of cholesterol biosynthesis.[1f] Hence, the synthesis of δ-lactones[2–4] is receiving increasing attention.

The δ-lactones, simplactones A **1** and B **2** possessing interesting cytotoxic activities were isolated from the Caribbean sponge, *Plakortis simplex*; their structures were proposed based on spectroscopic analyses and assigned as 4*R*,5*S*-5-ethyl-4-hydroxytetrahydropyran-2-one for the former (**1**) and as 4*R*,5*R*-5-ethyl-4-hydroxytetrahydropyran-2-one for the latter (**2**)[5] (Fig. 1).

Although a number of synthetic procedures for the construction of δ-lactones have been reported,[6] there is an increasing demand for new convenient methods. We report here a new synthetic route to simplactone B **2** utilising the highly stereoselective Prins cyclisation and PCC mediated over oxidation from (*R*)-benzyl glycidyl ether **3**.

2. Results and discussion

Our synthetic approach is described in Scheme 1. Ring opening of epoxide in (*R*)-benzyl glycidyl ether **3** (obtained via Jacobsen's HKR methodology),[7] which on treatment with butynyl lithium in the presence of $BF_3 \cdot OEt_2$, produced homopropargyl alcohol **4** in 90% yield.

Subjection of **4** to Birch reduction (Na in liq NH_3 at −33 °C) for 6 h resulted in diol **5** in 85% yield, which on selective protection of 1° hydroxy group as its benzyl ether in the presence of BnBr (1.1 equiv) and NaH in DMF produced key intermediate **6** in 70% yield with recovery of 18% of the starting material. Protection of the alcohol **6** as its MEM ether by treatment of the compound with MEMCl and DIPEA gave **7** in 99% yield. Compound **7** underwent crucial Prins cyclisation in the presence of TFA[8] to produce alcohol **8** in 59% yield. This Prins cyclisation step proceeds through the formation of oxocarbenium ion generated in situ from the MEM ether **7**, which undergoes intramolecular cyclisation in the presence of TFA giving rise to pyranyl trifluoroacetate, which upon hydrolysis with K_2CO_3 in MeOH[8] and flash chromatography results in **8** as the only product. The stereochemistry of **8** was assumed on the basis of extensive previous studies[8b] and also through further transformation to the known natural product B **2**. Protection of **8** as MOM ether **9** by treatment with MOMCl and DIPEA followed by deprotection of benzylic ether linkage using Na in liquid ammonia yielded tetrahydropyran **10** in 99% yield. Oxidation of **10** using excess of PCC in refluxing conditions[9] in benzene resulted in the lactone **11** in 83% (the only isolable isomer from column chromatography). This oxidation is presumed to proceed as shown in Scheme 2. Deprotection of MOM group of **11** using TFA in DCM furnished the target product simplactone B **2** in 85% yield. The spectroscopic (^{1}H NMR, ^{13}C NMR, IR, mass) and physical data of the simplactone B **2** were in good agreement with the reported data.[6]

3. Conclusion

In summary, we have achieved the stereoselective synthesis of simplactone B via Prins cyclisation as the key step, through a series of nine steps in 85% overall yield. This

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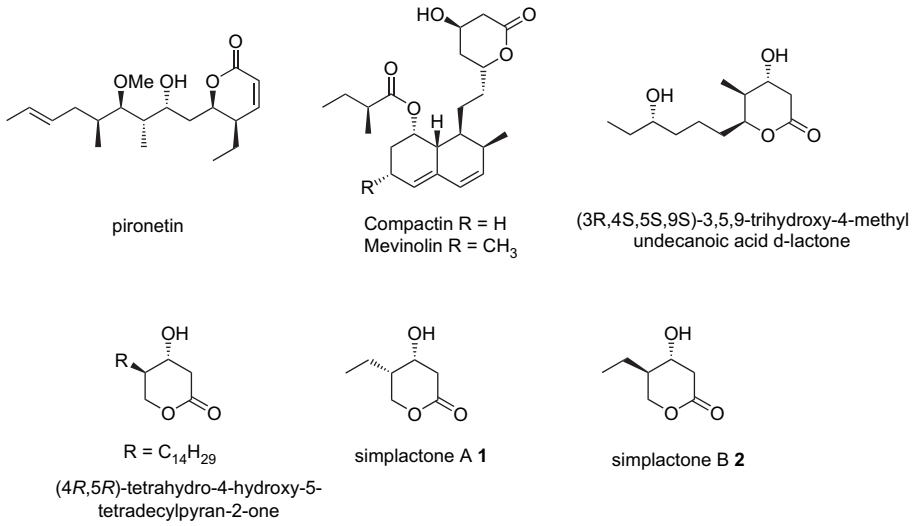
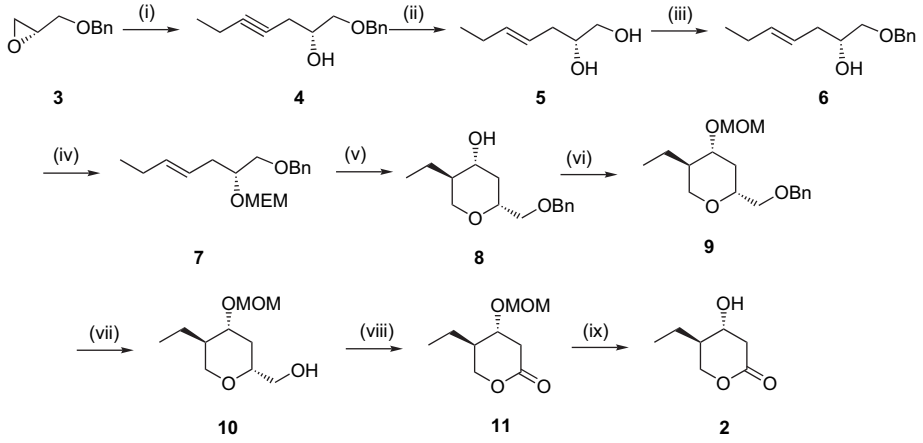
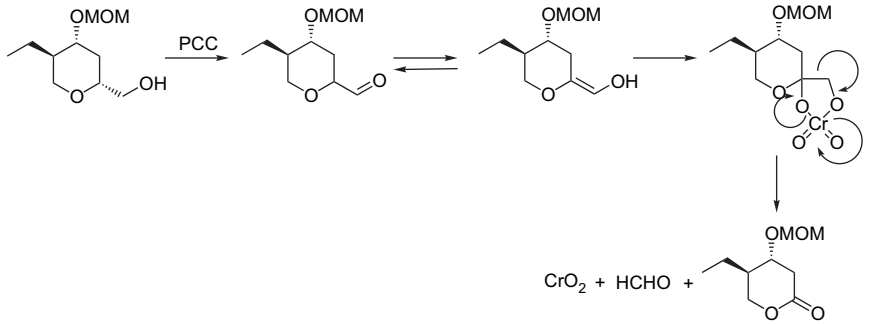


Figure 1.



Scheme 1. Reagents, conditions and yields: (i) *n*-butyne, BuLi, $BF_3 \cdot OEt_2$, THF, −78 °C, 2 h, 90%; (ii) Na, liq NH_3, THF, 6 h, 85%; (iii) BnBr, NaH, DMF, 0 °C–rt, 6 h, 70%; (iv) $(^iPr)_2$ NEt, MEMCl, DMAP, DCM, 0 °C–rt, 20 h, 99%; (v) TFA, DCM, rt, 5–6 h, then K_2CO_3, MeOH, rt, 1 h, 59%; (vi) $(^iPr)_2$ NEt, MOMCl, DMAP, DCM, 0 °C–rt, 15 h, 99%; (vii) Li, liq NH_3, 5 min, 99%; (viii) PCC, benzene, reflux, 6 h, 83%; (ix) TFA, DCM, rt, 2 h, 85%.



Scheme 2.

synthesis is a propagating proof for the utilisation of Prins cyclisation in the natural product synthesis.

4. Experimental

4.1. General

Commercial reagents were used without further purification. All solvents were purified by standard techniques. Infrared (IR) spectra were recorded on a Perkin–Elmer 683 spectrometer. Optical rotations were obtained on a Jasco Dip 360 digital polarimeter. Melting points are uncorrected. NMR spectra were recorded in $CDCl_3$ on Varian Gemini 200, Bruker 300 or Varian Unity 400 NMR spectrometer. Chemical shifts (δ) are quoted in parts per million and are referenced to tetramethylsilane (TMS) as internal standard. Coupling constants (J) are quoted in hertz. Column chromatographic separations were carried out on silica gel (60–120 mesh). Mass spectra were obtained on Finnegan MAT

1020B or micromass VG 70-70H spectrometer operating at 70 eV using a direct inlet system.

4.2. (*R*)-1-(Benzyloxy)-4-heptyn-2-ol (4)

Under nitrogen atmosphere, a solution of *n*-butyl lithium in hexane (71 mL, 115.2 mmol, 2.6 M solution in hexane) was added to a solution of butyne (8.2 g, 153.6 mmol) in THF (110 mL) at −78 °C and the mixture was stirred for 15 min. Then, $BF_3 \cdot OEt_2$ (14.0 g, 99.8 mmol) was added to the solution and stirring was continued for 15 min at −78 °C. Finally a solution of epoxide **3** (12.6 g, 76.8 mmol) in dry THF (40 mL) was added and after stirring the reaction mixture for 2 h at −78 °C, the reaction was quenched by adding saturated aqueous NH_4Cl solution (70 mL). The reaction mixture was extracted with ethyl acetate (2×150 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent resulted in crude alcohol, which was purified by column chromatography (SiO_2, 15% EtOAc in hexane as eluent) to afford pure alcohol **4** (15.0 g, 90%) as a colourless oil, R_f=0.45.

$[\alpha]_D^{25}$ −10.8 (*c* 0.51, $CHCl_3$); IR (Neat): 3447.1, 2920.8, 2856.7, 1635.0, 1113.0 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.34–7.25 (m, 5H), 4.55 (s, 2H), 3.91–3.81 (m, 1H), 3.55 (dd, 1H, *J*=9.8, 4.5 Hz), 3.44 (dd, 1H, *J*=9.8, 6.7 Hz), 2.39–2.35 (m, 2H), 2.18–2.07 (m, 2H), 1.10 (t, 3H, *J*=7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 137.9, 128.4, 127.7, 127.6, 77.1, 74.7, 73.3, 72.9, 69.1, 23.8, 14.1, 12.3; MS (ESIMS): *m/z* 241 $[M+Na]^+$; HRMS (ESI) calcd for $C_{14}H_{18}O_2Na$ $[M+Na]^+$: 241.1204, found: 241.1197.

4.3. (2*R*,4*E*)-4-Heptene-1,2-diol (5)

To a blue solution of sodium metal (6.5 g, 282.7 mmol) in 200 mL of NH_3 was added dropwise a solution of **4** (7.6 g, 34.9 mmol) in THF (40 mL) at −78 °C. During the addition of the compound, the blue colour of the reaction mixture was maintained by the addition of sodium metal. After addition of the whole compound, the reaction mixture was stirred for 6 h at −33 °C. The reaction mixture was quenched with NH_4Cl (6.5 g) and the ammonia was left to completely evaporate. The mixture was then diluted with water (4×30 mL) and extracted with diethyl ether (250 mL). Organic layer was dried (Na_2SO_4) and concentrated. Column chromatography (SiO_2, 40% EtOAc in hexane as eluent) of the crude product gave the compound **5** (3.85 g, 85%) as a viscous liquid, R_f=0.3.

$[\alpha]_D^{25}$ +2.83 (*c* 0.53, $CHCl_3$); IR (Neat): 3421.2, 2926.0, 1644.5, 1074.2 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.60–5.49 (m, 1H), 5.44–5.29 (m, 1H), 3.72–3.58 (m, 2H), 3.39 (dd, 1H, *J*=6.8, 11.3 Hz), 2.82 (br s, 1H, O*H*), 2.19–2.12 (m, 2H), 2.08–1.98 (m, 2H), 0.99 (t, 3H, *J*=7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 135.8, 124.0, 71.7, 66.1, 36.5, 25.5, 13.6; MS (ESIMS): *m/z* 153 $[M+Na]^+$; HRMS (ESI) calcd for $C_7H_{14}O_2Na$ $[M+Na]^+$: 153.0891, found: 153.0899.

4.4. (2*R*,4*E*)-1-(Benzyloxy)-4-hepten-2-ol (6)

To a suspension of NaH (4.2 g, 105.0 mmol) in dry DMF (30 mL) at 0 °C was added diol **5** (3.9 g, 30.0 mmol) in DMF (15 mL) in a dropwise manner. The reaction mixture was stirred at room temperature for 30 min and again the mixture was cooled to 0 °C. After addition of BnBr (3.9 mL, 33.0 mmol), the reaction was brought to room temperature and stirred for 6 h, cooled to 0 °C and quenched with saturated NH_4Cl solution (70 mL) carefully. Then EtOAc (150 mL) was added, organic layer was separated, washed with H_2O (3×30 mL) and brine solution (30 mL) and dried in vacuo. Column chromatography (SiO_2, 15% EtOAc in hexane as eluent) of the crude product afforded **6** (4.62 g, 70%) along with 18% recovered starting material **5**. Compound **6** was a colourless oil, R_f=0.7.

$[\alpha]_D^{25}$ +6.86 (*c* 0.51, $CHCl_3$); IR (Neat): 3445.8, 2924.5, 2860.7, 1454.1, 1102.0 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.34–7.25 (m, 5H), 5.58–5.45 (m, 1H), 5.43–5.29 (m, 1H), 4.53 (s, 2H), 3.84–3.68 (m, 1H), 3.44 (dd, 1H, *J*=10.5, 5.3 Hz), 3.31 (dd, 1H, *J*=10.5, 5.7 Hz), 2.18–2.13 (m, 2H), 2.06–1.97 (m, 2H), 0.97 (t, 3H, *J*=7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.0, 135.6, 128.4, 127.7, 127.5, 124.2, 73.9, 73.3, 70.1, 36.7, 25.6, 13.7; MS (ESIMS): *m/z* 253 $[M+Na]^+$; HRMS (ESI) calcd for $C_{14}H_{20}O_2Na$ $[M+Na]^+$: 243.1360, found: 243.1368.

4.5. 1-[((2*R*,4*E*)-2-((2-Methoxyethoxy)methoxy)hept-4-enyloxy)methyl]benzene (7)

To the alcohol **6** (1.76 g, 8.0 mmol) in anhydrous CH_2Cl_2 (20 mL) at 0 °C were added diisopropylethyl amine (6.9 mL, 40 mmol), DMAP (99 mg) and MEMCl (2.73 mL, 24 mmol) successively and the mixture was stirred for 20 h at room temperature and then quenched by adding water (20 mL) and extracted with CH_2Cl_2 (2×25 mL). The organic extracts were washed with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to remove the solvent and the crude oil was purified by column chromatography (SiO_2, 10% EtOAc in hexane eluent) to afford the pure product **7** (2.44 mg, 99%) as a colourless liquid, R_f=0.6.

$[\alpha]_D^{25}$ +1.88 (*c* 0.79, $CHCl_3$); IR (Neat): 2926.0, 2878.2, 1454.2, 1112.6, 1041.7 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.33–7.26 (m, 5H), 5.55–5.42 (m, 1H), 5.39–5.28 (m, 1H), 4.76 (d, 1H, *J*=7.5 Hz), 4.72 (d, 1H, *J*=7.5 Hz), 4.50 (s, 2H), 3.83–3.73 (m, 1H), 3.70–3.60 (m, 2H), 3.49–3.43 (m, 4H), 3.34 (s, 3H), 2.31–2.11 (m, 2H), 2.06–1.94 (m, 2H), 0.95 (t, 3H, *J*=7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.3, 134.9, 128.3, 127.8, 127.5, 124.4, 94.8, 75.8, 73.2, 71.7, 69.3, 66.9, 58.9, 35.0, 25.5, 13.6; MS (ESIMS): *m/z* 331 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{28}O_4Na$ $[M+Na]^+$: 331.1885, found: 331.1897.

4.6. (2*R*,4*R*,5*R*)-2-[(Benzyloxy)methyl]-5-ethyltetrahydro-2*H*-4-pyranol (8)

Trifluoroacetic acid (6.93 mL, 90.0 mmol) was added slowly to a solution of compound **7** (1.85 g, 6.0 mmol) in CH_2Cl_2 (40 mL) at room temperature under nitrogen atmosphere. The reaction mixture was stirred for 5–6 h, and then saturated aqueous sodium hydrogen carbonate solution (60 mL) was added and pH was adjusted to >7 by addition of triethylamine. The layers were separated, the aqueous layer was extracted with CH_2Cl_2 (4×30 mL), the organic layers were

combined, washed with brine (10 mL) and the solvent was removed under reduced pressure. The residue was dissolved in methanol (20 mL) and stirred with potassium carbonate (1.65 g) for 0.5 h. Methanol was then removed under reduced pressure and water (15 mL) was added. The mixture was extracted with dichloromethane (3×20 mL), washed with brine (6 mL) and the combined organic layers were dried (Na_2SO_4) and the solvent was removed under reduced pressure. Column chromatography (SiO_2, 25% EtOAc in hexane as eluent) of the crude afforded **8** (0.89 g, 59%) as a colourless oil, R_f=0.35.

$[\alpha]_D^{25}$ +8.33 (*c* 0.54, $CHCl_3$); IR (Neat): 3442.0, 2923.4, 2856.9, 1455.2, 1373.1, 1102.7, 1065.7 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.31–7.25 (m, 5H), 4.53 (s, 2H), 3.99 (dd, 1H, *J*=4.5, 11.3 Hz), 3.55–3.31 (m, 4H), 3.01 (t, 1H, *J*=11.3 Hz), 1.92 (ddd, 1H, *J*=1.5, 6.0, 12.1 Hz), 1.85–1.71 (m, 1H), 1.46–1.23 (m, 3H, including O*H*), 1.15–0.98 (m, 1H), 0.94 (t, 3H, *J*=7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.1, 128.2, 127.6, 127.4, 75.7, 73.3, 72.9, 72.0, 69.9, 45.7, 37.9, 20.9, 11.4; MS (ESIMS): *m*/*z* 273 $[M+Na]^+$; HRMS (ESI) calcd for $C_{15}H_{22}O_3Na$ $[M+Na]^+$: 273.1466, found: 273.1472.

4.7. (2*R*,4*R*,5*R*)-2-[(Benzyloxy)methyl]-5-ethyltetrahydro-4-(methoxymethoxy)-2*H*-pyran (9)

To the alcohol **8** (500 mg, 2.0 mmol) in anhydrous CH_2Cl_2 (10 mL) at 0 °C were added diisopropylethyl amine (1.38 mL, 8.0 mmol), DMAP (20 mg) and MOMCl (0.75 mL, 6.0 mmol) successively and the mixture was stirred for 15 h at room temperature and then quenched by adding water (6 mL) and extracted with CH_2Cl_2 (2×15 mL). The organic extracts were washed with brine (4 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to remove the solvent and the crude was purified by column chromatography (SiO_2, 10% EtOAc in hexane as eluent) to afford the pure product **9** (582 mg, 99%) as a colourless liquid, R_f=0.6.

$[\alpha]_D^{25}$ −36.58 (*c* 0.51, $CHCl_3$); IR (Neat): 2924.7, 2855.9, 1458.0, 1373.5, 1103.3, 1039.4 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.34–7.22 (m, 5H), 4.70 (d, 1H, *J*=7.0 Hz), 4.55 (s, 2H), 4.53 (d, 1H, *J*=7.0 Hz), 4.01 (dd, 1H, *J*=4.7, 11.7 Hz), 3.54–3.25 (m, 7H, including s for O*Me*), 3.04 (t, 1H, *J*=11.4 Hz), 2.04–1.98 (m, 1H), 1.86–1.68 (m, 1H), 1.60–1.39 (m, 1H), 1.36–1.25 (m, 1H), 1.14–0.95 (1H), 0.90 (t, 3H, *J*=7.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.1, 128.3, 127.7, 127.6, 95.1, 75.6, 73.4, 73.2, 70.4, 63.1, 55.5, 32.8, 31.9, 22.6, 14.0; MS (ESIMS): *m*/*z* 317 $[M+Na]^+$; HRMS (ESI) calcd for $C_{17}H_{26}O_4Na$ $[M+Na]^+$: 317.1728, found: 317.1723.

4.8. [(2*R*,4*R*,5*R*)-5-Ethyltetrahydro-4-(methoxymethoxy)-2*H*-2-pyranyl]methanol (10)

To a solution of lithium (52.5 mg, 7.5 mmol) in liq NH_3 (10 mL) was added compound **9** (440 mg, 1.5 mmol) in dry THF (3 mL). The mixture was stirred for 5 min and quenched with solid NH_4Cl (406 mg). Ammonia was allowed to evaporate and the residual mixture was taken in diethyl ether (20 mL) and washed with water (2×4 mL), brine (1×4 mL) and dried (Na_2SO_4). Removal of the solvent and purification by column chromatography (SiO_2, 30% EtOAc in hexane as eluent) of the crude product afforded alcohol **10** (303 mg, 99%) as a colourless liquid, R_f=0.25.

$[\alpha]_D^{25}$ −50.52 (*c* 0.48, $CHCl_3$); IR (Neat): 3448.4, 2926.3, 1038.0 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): 4.70 (d, 1H, *J*=7.0 Hz), 4.53 (d, 1H, *J*=7.0 Hz), 4.01 (dd, 1H, *J*=4.7, 11.5 Hz), 3.61–3.28 (m, 7H, including s for O*Me*), 3.07 (t, 1H, *J*=11.4 Hz), 1.94 (ddd, 1H, *J*=1.9, 6.6, 12.4 Hz), 1.85–1.72 (m, 1H), 1.58–1.43 (m, 1H), 1.39–1.24 (m, 1H), 1.14–0.97 (m, 1H), 0.91 (t, 3H, *J*=7.4 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 95.2, 77.4, 76.7, 70.2, 65.9, 55.5, 43.8, 33.9, 20.8, 11.1; MS (ESIMS): *m*/*z* 227 $[M+Na]^+$; HRMS (ESI) calcd for $C_{10}H_{20}O_4Na$ $[M+Na]^+$: 227.1259, found: 227.1251.

4.9. (4*R*,5*R*)-5-Ethyltetrahydro-4-(methoxymethoxy)-2*H*-2-pyranone (11)

Powdered molecular sieves (3 Å, 600 mg) were heated under N_2 at 320 °C with a Bunsen burner for 1 h. It was allowed to come to room temperature and pyridinium chlorochromate (1.39 g, 7.0 mmol) and dry benzene (10 mL) were added. To this mixture was added a solution of **10** (285 mg, 1.4 mmol) in benzene (4 mL) and stirred under reflux for 6 h. Then, it was cooled to room temperature, diethyl ether (20 mL) was added and the reaction mixture was filtered through a short pad of Celite and silica gel (1:1). The filter cake was washed thoroughly with ether (2×8 mL) and the filtrate was concentrated under vacuo. The residue after flash chromatography (SiO_2, 20% EtOAc in hexane as eluent) afforded the lactone **11** (218 mg, 83%) as a colourless liquid, R_f=0.4.

$[\alpha]_D^{25}$ −18.6 (*c* 0.1, $CHCl_3$); IR (Neat): 2966.0, 2929.0, 1743.0, 1244.0, 1038.0 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 4.65 (d, 1H, *J*=7.1 Hz), 4.63 (d, 1H, *J*=7.1 Hz), 4.45 (dd, 1H, *J*=11.4, 4.3 Hz), 3.96 (dd, 1H, *J*=11.4, 7.2 Hz), 3.84–3.76 (m, 1H), 3.36 (s, 3H), 2.77 (dd, 1H, *J*=5.2, 17.2 Hz), 2.6 (dd, 1H, *J*=5.1, 17.2 Hz), 1.91–1.79 (m, 1H), 1.66–1.51 (m, 1H), 1.45–1.25 (m, 1H), 1.02 (t, 3H, *J*=7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.7, 95.6, 73.5, 69.2, 55.9, 40.7, 35.6, 21.9, 11.5; MS (ESIMS): *m*/*z* 211 $[M+Na]^+$; HRMS (ESI) calcd for $C_9H_{16}O_4Na$ $[M+Na]^+$: 211.0946, found: 211.0954.

4.10. (4*R*,5*R*)-5-Ethyltetrahydro-4-hydroxy-2*H*-2-pyranone (2)

Compound **11** (113 mg, 0.6 mmol) was dissolved in CH_2Cl_2 (2 mL) and then TFA (0.185 mL, 4 mmol) was added dropwise at room temperature. After stirring the mixture at room temperature for 2 h, the reaction mixture was quenched with saturated $NaHCO_3$ solution (6 mL) and extracted with CH_2Cl_2 (2×6 mL). The combined organic extracts were washed with brine (6 mL), concentrated in vacuo and the residue was subjected to column chromatography (SiO_2, 40% EtOAc in hexane as eluent) to afford the alcohol **2** (73 mg, 85% yield) as a semisolid, R_f=0.3.

$[\alpha]_D^{25}$ −23.0 (*c* 0.45, $CHCl_3$) (lit.[6b] $[\alpha]_D^{25}$ −23.1 (*c* 1.0, $CHCl_3$)); IR (Neat): 3474.9, 2968.9, 2924.7, 1717.9,1273.9, 1004.0 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 4.45 (dd, 1H, *J*=4.5, 11.9 Hz), 4.01–3.88 (m, 2H), 2.82

(dd, 1H, J=5.2, 17.1 Hz), 2.53 (dd, 1H, J=5.9, 17.1 Hz), 2.29 (br s, O*H*), 1.86–1.52 (m, 2H), 1.46–1.25 (m, 1H), 1.02 (t, 3H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.7, 69.8, 67.1, 43.2, 39.2, 19.9, 11.5; MS (ESIMS): m/z 145 $[M+H]^+$; HRMS (ESI) calcd for $C_7H_{13}O_3$ $[M+H]^+$: 145.0864, found: 145.0860.

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