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Article

An Efficient Total Synthesis of a Synthetic Equivalent of the Prelog-Djerassi Lactonic Acid

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A síntese de **2a**, precursor da lactona de Prelog-Djerassi, foi alcançada em 5 etapas e 37% de rendimento total a partir de (S)-O-p-toluenossulfonil-3-hidroxi-2-metilpropanal (**3c**). As etapas chaves envolveram a condensação aldólica do enolato de boro da (R)-N-propionil-4-benzil-2-oxazolidinona (**4**) com o aldeído **3c** e alquilação intramolecular do enolato de potássio de O-propionil tosilato, **6f**, seguida de equilibração em meio básico (^{t}BuOK/^{t}BuOH).

(3*R*, 5*S*, 6*S*, 1'*S*)- Tetrahydro- 6- (1'- methyl-2'-tert-butyldimethyl-silyloxyethyl)-3,5-dimethyl-2H-pyran-2-one (**2a**), a known precursor of the Prelog-Djerassi lactonic acid, has been prepared in 5 steps and 37% overall yield from (*S*)-*O*-*p*-toluenesulfonyl-3-hydroxy-2-methylpropanal (**3c**). The key steps involved an aldol condensation of the boron enolate of (*R*)-N-propionyl-4- benzyl-2-oxazolidinone **(4)** and aldehyde **3c** and an intramolecular alkylation of the potassium enolate of O-propionyl tosylate **6f**.

Keywords: *Prelog-Djerassi lactonic acid, intramolecular alkylation, oxazolidinone, boron enolate*

Introduction

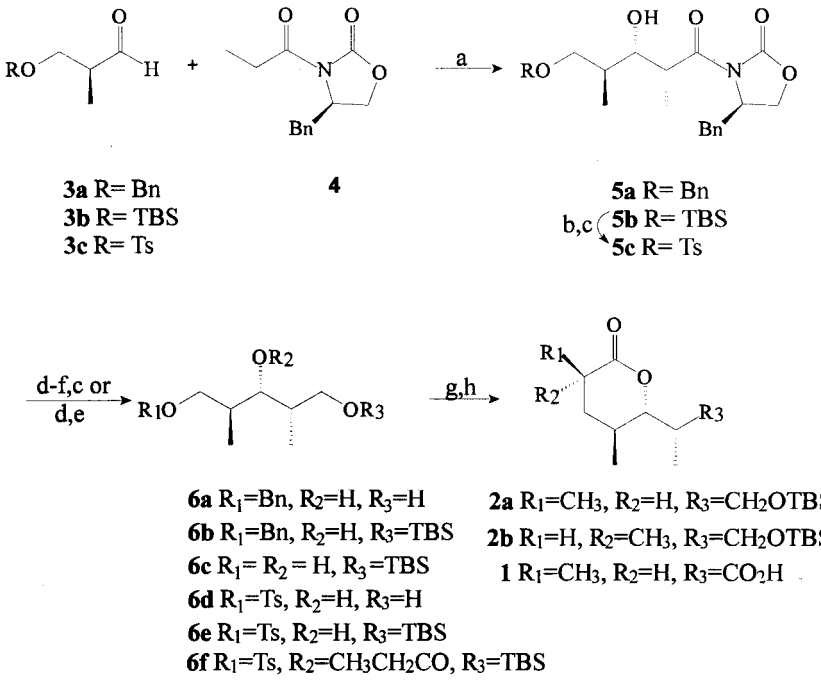
The Prelog-Djerassi lactonic acid (**1**) was first isolated as a degradation product of some macrolide antibiotics providing valuable information for their structural elucidation. Since its stereochemical pattern is also found in many natural products it became a synthetic target against which the efficiency of new synthetic methodologies has been tested[1].

As part of our efforts to prepare macrolides from the methymycin family we developed a concise and efficient preparation of δ-lactone **2a** which relies on an enantioselective aldol condensation of tosyl aldehyde **3c** followed by an intramolecular alkylation of an ester enolate (Scheme 1), an approach previously employed by us in the total synthesis of (+/-)-invictolide[2a].

Initially the preparation of the required tosyl derivative **6e** was envisaged from **5a** based on the known preference for the syn, anti-Felkin stereochemistry in the aldol adduct obtained from (+)-**3a** and the boron enolate of (R)-4-isopropyl-3-propionyl-2-oxazolidinone(4). Indeed, the reaction of the boron enolate of imide **4**[3] and aldehyde **3a**[4] afforded aldol **5a** in 88% yield after purification by flash chromatography. The syn,anti-stereochemistry of **5a** was established after $LiBH_4$ reduction to afford the known diol **6a**[2a,5] which required careful purification by flash chromatography on silica gel to be separated from (*R*)-4-benzyl-2-oxazolidinone. Preparatively, the crude mixture of **6a** and oxazolidinone was silylated (TBDMSCl, Et_3N, cat. DMAP, CH_2Cl_2) and alcohol **6b** (80% overall yield) was readily separated from the recovered chiral auxiliary (80% yield) by column chromatography.

Alcohol **6b** was transformed into the tosyl derivative **6e** after hydrogenolysis and tosylation (76% overall yield). Most of the reaction conditions previously described for the intramolecular alkylation of ester enolates[2b-d] failed when applied to (-)-**6f**. However, upon treatment of (-)-**6f** with freshly sublimed *t*-BuOK (4 equiv.) in THF (0°C- > rt) afforded a 2:1 mixture of epimeric lactones **2a**/**2b** (68% yield). Under equilibrating conditions (*t*-BuOK/*t*-BuOH, rt) this ratio could be improved to 10:1 in favor of **2a**[6], a known precursor of the Prelog-Djerassi lactonic acid (**1**)[7].

The success of the lactonization step led us to consider a more direct route to **6e** which required the preparation of



3a R= Bn
3b R= TBS
3c R= Ts

4

5a R= Bn
5b R= TBS
5c R= Ts

6a R_1=Bn, R_2=H, R_3=H
6b R_1=Bn, R_2=H, R_3=TBS
6c R_1= R_2 = H, R_3=TBS
6d R_1=Ts, R_2=H, R_3=H
6e R_1=Ts, R_2=H, R_3=TBS
6f R_1=Ts, R_2=CH_3CH_2CO, R_3=TBS

2a R_1=CH_3, R_2=H, R_3=CH_2OTBS
2b R_1=H, R_2=CH_3, R_3=CH_2OTBS
1 R_1=CH_3, R_2=H, R_3=CO_2H

Scheme 1. **a)** i. Bu_2BOTf, CH_2Cl_2, DIPEA, 0 °C; ii. 3a or 3b or 3c, -78 °C; iii. H_2O_2, MeOH, 0 °C; b) HF, CH_3CN, H_2O, rt; c) TsCl, Et_3N, DMAP (cat.), CH_2Cl_2; d) $LiBH_4$, MeOH, THF, 0 °C; e) TBDMSCl, Et_3N, DMAP (cat.), CH_2Cl_2, rt; f) H_2, Pd/C, EtOH; g) $(CH_9CH_2CO)_2O$, Et_3N, DMAP (cat.), CH_2Cl_2; h) i. ^tBuOK, THF, rt; ii. ^tBuOK, tBuOH, rt.

tosyl aldehyde **3c**. Attempts to carry out the reduction of methyl (*S*)-3-*O*-(*p*-toluenesulfonyl)-3-hydroxy-2-methylpropionate[8] with DIBAL in CH_2Cl_2 at -78 °C led to the formation of **3c** in low yields together with the corresponding alcohol[9]. When the reaction was carried out in toluene and the reaction temperature of the cooling bath (liq. N_2/hexanes) carefully controlled below -90 °C overreduction was supressed. Crude aldehyde **3c** was isolated in 86% yield, pure enough by ^{1}H-NMR to be used in the next step without further purification.

The di-n-butyl boron triflate/diisopropylamine reaction conditions were sufficiently mild to allow us to carry out the desired aldol condensation of the base sensitive aldehyde **3c** with the boron enolate of imide **4**. Stereochemically homogeneous aldol (-)-**5c** was isolated in 72% overall yield, as judged by its ^{1}H-NMR spectrum (300 MHz).

The syn,anti-Felkin stereochemistry of (-)-**5c** was assigned after comparison with an authentic sample prepared from (-)-**5b**[10]: desilylation (HF/CH_3CN/H_2O) followed by tosylation of the primary alcohol (TsCl, Et_3N, CH_2Cl_2, DMAP) afforded (-)-**5c** in 81% yield. Reduction of (-)-**5c** with $LiBH_4$ and protection of the primary alcohol with TBDMSCl afforded (-)-**6e** (89% overall yield) and recovered chiral oxazolidinone (86% yield) after purification by column chromatography.[11] Propionylation of (-)-**6e** afforded (-)-**6f** (95% yield) and intramolecular alkylation as described above was followed by equilibration in *t*-BuOK/*t*-BuOH to afford (+)-**2a** in 62% yield.

The reaction sequence described herein for the preparation of (+)-**2a** (7 steps, 26% overall yield from **3a** and 5 steps, 34% overall yield from **3c**) compares favorably with other approaches to the Prelog-Djerassi lactonic acid and provides a short entry into other non-racemic trisubstituted δ-lactones.

Experimental

For general information see Ref. 2a. n-Bu_2BOTf was prepared according to Ref. 3b and distilled immediately prior to use.

*(4R)-N-[(2'R,3'S,4'S)-5'-O-Benzyl-2',4'-dimethyl-3',5'-dihydroxy-1'-oxopentyl]-4-benzyl-2-oxazolidinone (**5a**)*

To a 0.5 M soln. of imide **4**[3] (1.6 g, 6.9 mmol) in CH_2Cl_2, under an argon atmosphere at 0°C, was added di-n-butylboron triflate (2.1 mL, 8.3 mmol) followed by diisopropylethylamine (1.6 mL, 9.0 mmol). After allowing 30 min. for complete enolization, the reaction mixture was cooled to -78°C and aldehyde **3a**[4] (0.98 g, 5.5 mmol, 0.5 M soln. in CH_2Cl_2) was added dropwise. Stirring was continued for 30 min at -78 °C, followed by 2.0 h at 0 °C. The reaction mixture was quenched with pH 7.0 phosphate buffer (6.0 mL) and methanol (18 mL). A solution of hydrogen peroxide (30% v/v, 6.0 mL) in methanol (12 mL) was added and the mixture allowed to stir for 1.0 h at 0 °C. The reaction mixture was diluted with Et_2O (50 mL) and successively washed with 5% aq. $NaHCO_3$ (40 mL), 10%

HCl (40 mL) and brine (40 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. Purification by column flash chromatography on silica gel (20% EtOAc in hexanes, v/v) afforded **5a** (2.0 g, 4.9 mmol), in 88% yield : $[\alpha]_D^{25}$ = -37.8 (c 0.9, $CHCl_3$); IR(film) 3490, 1779, 1697 cm^{-1}; ^{1}H-NMR: δ 0.96 (d, 3H, *J* = 7.0), 1.26 (d, 3H, *J* = 6.7), 1.92-2.06 (m, 1H), 2.76 (dd, 1H, *J* = 9.9 and 13.3), 3.31 (dd, 1H, *J* = 3.0 and 13.3), 3.50-3.65 (m, 2H), 3.85-4.00 (m, 2H), 4.16 (d, 2H, *J* = 5.4 Hz), 4.51 (s, 2H), 4.61-4.70 (m, 1H), 7.2-7.4 (m, 10H); ^{13}C-NMR: δ 9.5, 13.4, 35.9, 37.6, 40.5,55.5, 66.1, 73.4, 74.8, 75.25, 127.4, 127.7, 127.8, 128.5, 129.0, 129.5, 135.4, 137.8, 153.2, 176.3. Anal. calcd. for $C_{24}H_{29}NO_5$: C, 70.05; H, 7.10; N, 3.40. Found: C, 70.37; H, 7,01; N, 3.26.

(4R)-N-[(2'R,3'S,4'S)-5'-O-tert-butyldimethylsilyl-3',5'-dihydroxy -2',4'-dimethyl-1'-oxopentyl]-4-benzyl-2-oxazolidinone (5b)

The same procedure described above afforded **5b** (0.754 g, 1.73 mmol), in 78% yield from imide **4** (0.65 g, 2.8 mmol) and aldehyde **3b**[12] (0.45 g, 2.2. mmol), after purification by flash chromatography on silica gel (20% ethyl acetate/hexanes). $[\alpha]_D^{25}$ = -27.5 (c 1.1, $CHCl_3$); IR (film): 3516, 3440, 1769, 1671 cm^{-1}; ^{1}H-NMR: δ 0.072 (s, 3H), 0.079 (s, 3H), 0.89 (s, 9H), 0.90 (d, 3H, *J* = 6.9), 1.26 (d, 3H, *J* = 6.9), 1.75-1.85 (m, 1H), 2.76 (dd, 1H, *J* = 13.2 and 9.7), 3.33 (dd, 1H, *J* = 13.2 and 3.1), 3.71 (AB of an ABX system, 2H, J_{AB} = 9.9, J_{AX} = 3.1, J_{BX} = 9.7, $\Delta\nu_{AB}$= 37.4), 3.87-3.97 (m, 2H), 4.11-4.25 (m, 3H), 4.66-4.73 (m, 1H), 7.20-7.32 (m, 5H); ^{13}C-NMR : δ -5.6, 9.27,12.9, 18.1, 25.8, 37.3, 37.6, 40.8, 55.6, 66.1, 68.2, 75.8, 127.2, 128.8, 129.4, 135.3, 153.1,176.0.

(S)-O-p-Toluenesulfonyl-3-hydroxy-2-methylpropanal (3c)

To a soln. of methyl (*S*)-*O*-*p*-toluenesulfonyl-3-hydroxy-2-methylpropionate[11] (0.65 g, 2.4 mmol) in toluene at -94 °C (liq. N_2/hexanes bath) was added dropwise (ca. 0.8 mL.min^{-1}) a 1.0 M soln. of DIBAL toluene (3.1 mL, 3.1 mmol) . The reaction mixture was stirred 1.5 h at -94 °C, quenched with ethyl acetate (3.0 mL), followed by addition of Et_2O (20 mL) and satd. sodium tartrate (1.5 mL). The reaction mixture was allowed to warm up to rt and stirring was continued until phase separation. The organic phase was separated, the aqueous phase was further extracted with Et_2O (2 x 20 mL), the combined organic phase was concentrated under reduced pressure and the residue filtered through celite. Evaporation under reduced pressure afforded crude **3c** (0.500 g) which was used in the next step without further purification. IR (film): 2979, 1735 cm^{-1}; ^{1}H-NMR: 1.16 (d, 3H, *J* = 7.3), 2.46 (s, 3H), 2.70-2.80 (m, 1H), 4.20 (AB of an ABX system, 2H, J_{AB} = 9.9, J_{AX} = 6.2, J_{BX} = 5.5, $\Delta\nu\delta_{AB}$ = 27.9),7.36 (d, 2H, *J* = 8.1), 7.78 (d, 2H, *J* = 8.1), 9.60 (s, 1H); ^{13}C-NMR: δ 10.5, 21.6, 45.5, 68.9, 127.9, 129.8, 129.9, 145.1, 200.7.

(4R)-N-[(2'R,3'S,4'S)-2',4'-Dimethyl-3'-hydroxy-5'-O-p-toluenesulfonyl-1'-oxopentyl]-4-benzyl-2-oxazolidinone (5c)

a) From **3c**

The same procedure described above for **5a** afforded **5c** (0.883 g, 1.85 mmol, 72% yield) as a colorless oil from imide **4** (0.72 g, 3.1 mmol) and aldehyde **3c** (0.62 g, 2.6 mmol) after purification by flash chromatography on silica gel (35% ethyl acetate/hexanes). $[\alpha]_D^{25}$ = -27.7 (c 2.5, $CHCl_3$); IR (film) : 3524, 1779, 1688 cm^{-1}; ^{1}H-NMR: δ 0.94 (d, 3H, *J* = 6.9), 1.21 (d, 3H, *J* = 6.9), 1.9-2.0 (m, 1H), 2.44 (s, 3H), 2.79 (dd, br, 2H, *J* = 13.3 and 9.3), 3.22 (dd, 1H, *J* = 13.3 and 3.3), 3.78 (dd,1H, *J* = 8.6 and 2.9), 3.85 (dq,1H, *J* = 6.9 and 2.9), 4.10-4.31 (m, 4H), 4.67-4.73 (m, 1H), 7.20-7.35 (m, 7H), 7.78 (d, 2H, *J* = 8.3); ^{13}C-NMR: δ 10.2, 13.3, 21.6, 35.6, 37.7, 39.2, 54.9, 66.2, 71.4,72.4, 127.4, 127.9, 128.9, 129.4, 129.8, 132.8, 134.9, 144.6, 152.8, 177.4. Anal. calcd. for $C_{24}H_{29}NO_7S$: C, 60.61, H, 6.14, N, 2.94. Found: C, 60.15, H, 5.94, N, 2.75.

b) From **5b**

To a soln. of **5b** (0.52 g, 1.2 mmol) in CH_2Cl_2 (5.0 mL) in CH_3CN (5 mL) was added a soln. of 15% HF (0.7 mL) in CH_3CN (4.3 mL). The reaction mixture was stirred 30 min at rt, diluted with Et_2O (30 mL), washed with brine (10 mL) and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was dissolved in CH_2Cl_2 (5.0 mL) and Et_3N (0.18 mL, 0.128 g, 1.27 mmol), DMAP (0.015 g, 0.13 mmol) and tosyl chloride (0.241 g, 1.27 mmol) were added successively. The mixture was stirred 3 h at rt, diluted with Et_2O (20 mL) and washed with 5% $NaHCO_3$ (10 mL), water (10 mL) and brine (10 mL). The organic phase was dried over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (35% ethyl acetate/hexane) to afford **5c** (0.46 g, 0.97 mmol), in 81% yield.

(2S, 3S, 4S)-5-O-Benzyl-1-O-tert-butyldimethylsilyl-2,4-dimethyl-1,3,5-pentanetriol (6b)

To a soln. of **5a** (0.97 g, 2.4 mmol) in THF (5.0 mL) at 0 °C were added MeOH (0.1 mL) and a 0.5 M soln. of $LiBH_4$ in THF (4.7 mL, 2.4 mmol) was added dropwise. After stirring 40 min. at 0 °C a satd. soln. of sodium and potassium tartrate (15 mL) was added. The reaction mixture was allowed to warm to rt and extracted with CH_2Cl_2 (2 x 20 mL). The combined organic phase was washed with brine (20 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure.

The crude mixture was dissolved in CH_2Cl_2 (14 mL) and Et_3N (0.4 mL, 2.8 mmol,), DMAP (0.030 g, 0.28 mmol) and TBDMSCl (0.42 g, 2.8 mmol) were added. After stirring 1 h ar rt, the reaction mixture was diluted with Et_2O (20 mL), washed with satd. NH_4Cl (20 mL), brine (20 mL) and dried over $MgSO_4$. After filtration the solvent was removed under reduced pressure and the crude product was chromatographed on flash silica gel to afford **6b** (0.665 g, 1.89 mmol, 80% yield, eluted with 5% ethyl acetate/hexanes) and (*R*)-4-benzyl-2-oxazolidinone (0.335 g, 1.89 mmol, 80% yield, eluted with 50% ethyl acetate/hexanes). **6b**: $[\alpha]_D^{25}$ = +18.6 (c 1.6, $CHCl_3$); IR (film): 3506, 1471, 1093 cm^{-1}; ^{1}H-NMR: 0.07 (s, 6H), 0.86 (d, 3H, *J* = 6.9), 0.90 (s, 9H), 0.92 (d, 3H, *J* = 7.0), 1.70-1.80 (m, 1H), 1.90-2.00 (m, 1H), 3.53-3.62 (m, 2H), 3.65-3.70 (m, 4H), 4.53 (s, 2H), 7.20-7.30 (m, 5H); ^{13}C-NMR: δ -5.7, -5.6, 8.8, 13.5, 18.0, 25.8, 36.0, 36.9, 67.1, 73.0, 74.9, 75.2, 127.2, 128.1, 138.0.

*(2S, 3S, 4S)-1-O-tert-butyldimethylsilyl-2,4-dimethyl-1,3,5-pentanetriol (**6c**)*

To a soln. of **6b** (0.70 g, 2.0 mmol) in ethanol (10 mL) was added 10% Pd on charcoal (0.02 g) and the mixture was allowed to stirr under hydrogen pressure (3 atm) for 7.5 h in a Parr apparatus. The reaction mixture was filtered over celite, diluted with ether (30 mL), washed with satd. $NaHCO_3$ (3 x 15 mL) and brine (10 mL). The organic phase was dried over MgSO4, filtered and the solvent was removed under reduced pressure. Purification by silica gel chromatography (20% ethyl acetate/hexanes) afforded **6c** (0.410 g, 1.56 mmol, 78% yield), as a colorless oil. $[\alpha]_D^{25}$ = +9.4 (c 2.4, CH_2Cl_2); IR (filme): 3376, 1471, 1094, 837 cm^{-1}; ^{1}H-NMR: δ -0.11 (s, 6H), 0.56 (d, 3H, *J* = 6.9), 0.70 (s, 9H), 0.79 (d, 3H, *J* = 7.0), 1.50-1.60 (m, 1H), 1.60-1.70 (m 1H), 3.40-3.50 (m, 2H), 3.53 (dd, 1H, *J* = 9.6 and 3.7), 3.59 (dd, 1H, *J* = 9.6 and 1.7), 3.67 (dd, 1H, *J* = 9.6 and 3.2). ^{13}C-NMR: δ -5.8, 8.9, 13.3, 17.9, 25.7, 36.3, 37.1, 68.0, 68.4, 79.3. Elemental analysis calcd. for $C_{13}H_{30}SiO_3$: C, 59.49; H, 11.52. Found: C, 59.35; H, 11.78.

*(2S, 3R, 4S)-5-O-tert-Butyldimethylsilyl-2,4-dimethyl-1-O-p-toluenesulfonyl-1,3,5-pentanetriol (**6e**)*

a) From **6c**

To a soln. of **6c** (0.27 g, 1.0 mmol) in CH_2Cl_2 (20 mL) at 0 °C were added Et_3N (0.15 mL, 1.1 mmol), DMAP (0.012 g, 0.10 mmol) and p-toluenesulfonyl chloride (0.21 g, 1.1 mmol). After stirring 3 h at 0 °C, the reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with water (5 mL), 1% aq. HCl (5 mL), satd. $NaHCO_3$ (5 mL) and brine (5 mL). The organic phase was dried over $MgSO_4$, evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (10% ethyl acetate/hexanes) to afford **6e** (0.42 g, 1.0 mmol), in 97% yield, as a colorless oil. $[\alpha]_D^{25}$ = -4.0 (c 2.2, $CHCl_3$); IR (film): 2928, 1359, 1177, 839 cm^{-1}; ^{1}H-NMR: δ 0.08 (s, 6H), 0.88 (d, 3H, *J* = 7.0), 0.91 (d, 3H, *J* = 7.0), 0.92 (s, 9H), 1.65-1.75 (m, 1H), 1.75-1.85 (m, 1H), 2.48 (s, 3H), 2.75 (s,br, 1H), 3.57 (d, 1H, *J* = 9.6), 3.66 (dd, 1H, *J* = 8.3 and 4.7), 3.74 (dd, 1H, *J* = 8.3 and 3.7), 4.0-4.1 (m, 2H), 7.32 (d, 2H, *J* = 8.1), 7.77 (d, 2H, *J* = 8.1); ^{13}C-NMR: δ -5.7, -5.6, 8.7, 13.3, 18.0, 21.4, 25.8, 35.5, 36.3, 68.3, 72.2, 73.5, 127.8, 129.2, 134.3, 143.1.

b) From **5c**

To a soln. of **5c** (0.628 g, 1.32 mmol) in THF (10 mL) were added methanol (0.08 mL) followed by $LiBH_4$ (0.043 g, 2.0 mmol). The reaction mixture was stirred 1 h at 0 °C and quenched with 1.0 M sodium and potassium tartrate soln. After stirring 1 h at 0 °C, it was extracted with Et_2O (2 x 20 mL), the organic extract was washed with brine (10 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was dissolved in CH_2Cl_2 (10 mL) followed by addition of Et_3N (0.21 mL, 0.15 g, 1.5 mmol), DMAP (0.018 g, 0.15 mmol) and TBDMSCl (0.23 g, 1.5 mmol). The reaction mixture was stirred 2 h at rt, diluted with Et_2O (40 mL) and washed with water (15 mL), 10% HCl (10 mL) and brine (10 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Purification by column chromatography on silica gel as described above afforded **6e** (0.49 g, 1.2 mmol, 87% yield) and (*R*)-4-benzyl-2-oxazolidinone (0.20 g, 1.1 mmol, 86% yield).

*(2S, 3R, 4S)-5-O-tert-Butyldimethylsilyl-2,4-dimethyl-3-O-propionyl-1-O-p-toluenesulfonyl-1,3,5-pentanetriol (**6f**)*

To a soln. of **6e** (0.40 g, 0.96 mmol) in CH_2Cl_2 (2.0 mL) were added Et_3N (0.15 mL, 1.1 mmol), DMAP (0.012 g, 0.10 mmol) and propionic anhydride (0.20 mL, 1.5 mmol). The reaction mixture was allowed to stir 30 min at rt, it was diluted with CH_2Cl_2 (10 mL) and washed with 1% aq. HCl (5 mL), satd. $NaHCO_3$ (5 mL) and brine (5 mL), successively. The organic phase was dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by column chromatography on silica gel (10% ethyl acetate/hexanes) afforded **6f** (0.43 g, 0.91 mmol), in 95% yield. $[\alpha]_D^{25}$ = -4.4 (c 4.6 CH_2Cl_2); IR (film): 1739, 1178 cm^{-1}; ^{1}H-NMR: δ 0.00 (s, 6H), 0.82 (d, 3H, *J* = 6.9), 0.86 (s, 9H), 0.95 (d, 3H, *J* = 6.9), 1.09 (t, 3H, *J* = 7.6), 1.81-1.85 (m, 1H), 2.0-2.1 (m, 1H), 2.22 (1, 2H, *J* = 7.6), 2.45 (s, 3H), 3.31 (dd, 1H, *J* = 8.2 and 6.2), 3.38 (dd, 1H, *J* = 8.6 and 6.9), 3.74 (dd, 1H, *J* = 9.6 and 6.9), 3.92 (dd, 1H, *J* = 9.6 and 4.4), 4.87 (dd, 1H, *J* = 8.2 and 3.9), 7.30 (d, 2H, *J* = 8.3), 7.72 (d, 2H, *J* = 8.3). ^{13}C-NMR: δ -5.8, 9.0, 10.5, 14.0, 18.0, 21.3, 25.7, 26.9, 34.8, 36.9, 64.9, 70.7, 73.3,

127.9, 129.26, 134.1, 143.4, 172.2. Elemental analysis calcd. for $C_{23}H_{40}SiO_6S$: C, 58.44; H, 8.53. Found: C, 58.55; H, 8.23.

(3R, 5S, 6S, 1'S)-Tetrahydro-6-(1'-methyl-2'-tert-butyldimethyl- silyloxyethyl)-3,5-dimethyl-2H-pyran-2-one (2a)

To a soln. of freshly sublimed ^{t}BuOK (0.095 g, 0.84 mmol) in THF (4.0 mL) at 0 °C was added dropwise a soln. of **6f** (0.10 g, 0.21 mmol) in THF (1.0 mL). The reaction mixture was allowed to stir 30 min at rt and quenched with satd. NH_4Cl (1.0 mL). The aqueous phase was extracted with Et_2O (3 x 5.0 mL), the combined organic phases were washed with brine (10 mL), dried over $MgSO_4$ and the solvent removed under reduced pressure. The residue was purified by colum chromatography on silica gel (20% ethyl acetate/hexanes) to afford a 2:1 molar ratio of **2a/2b** (0.043 g, 0.14 mmol, 68% yield), as determined by ^{1}H-NMR (300 MHz). This mixture was dissolved in ^{t}BuOH (2.0 mL), ^{t}BuOK (0.017 g, 0.15 mmol) was added and the reaction mixture was stirred 70 h at rt. The reaction was quenched with satd. NH_4Cl (1.0 mL), extracted with Et_2O (3 x 5 mL), the combined organic phase was washed with brine (2 x 5 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (10% ethyl acetate/hexanes) to afford **2a** (0.039 g, 0.13 mmol, 62% yield) as a colorless oil. $[\alpha]_D^{25}$ = +55.5 (c 2.7, $CHCl_3$); lit.[8]: $[\alpha]_D^{25}$ = +47.3 (c 2.7, $CHCl_3$). IR (film): 1734, 1096 and 837 cm^{-1}. ^{1}H-NMR: δ 0.02 (s, 6H), 0.81 (d, 3H, J = 6.9), 0.85 (s, 9H), 0.92 (d, 3H, J = 6.4), 1.25 (d, 3H, J = 6.9), 1.34 (q, 1H, J = 13.1), 1.85-1.95 (m, 3H), 2.40-2.50 (m, 1H), 3.46 (dd, 1H, J = 9.8 and 6.1), 3.64 (dd, 1H, J = 9.7 and 8.7), 4.15 (d, 1H, J = 10.3). ^{13}C-NMR: δ -5.4, 8.9, 17.1, 17.3, 18.2, 25.9, 30.6, 36.2, 37.5, 37.7, 64.6, 85.5, 174.6. Elemental analysis calcd. for $C_{16}H_{32}O_3Si$: C, 63.95; H, 10.73. Found: C, 64.21; H, 10.95.

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