SUPPORTING INFORMATION

SYN-ANTI ISOMERIZATION OF ALDOLS BY ENOLIZATION

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Preparation of 5a and 5s

MgBr₂·OEt₂ (3.43g, 13.3 mmol) was added to a stirred solution of **4** (500mg, 2.66 mmol) in CH₂Cl₂ (18 mL). After 5 min, the resulting suspension was placed in a dry-ice/acetone cooling bath and a solution of **12** (1.0 g, 5.32 mmol) in CH₂Cl₂ (5 mL) was added via syringe. After 15 min, the reaction mixture was allowed to warm to 0 °C and was maintained at that temperature for 12 h. The mixture was diluted with water and extracted with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄, concentrated, and fractionated by medium pressure chromatography (MPC) (SiO₂, 5-50% ethyl acetate in hexane) to give **5a** (350 mg, 21%) and **5s** (1.15 g, 65%).

(1'*R**, 3*S**, 6''*R**)-3-[(1,4-Dioxo-8-thiaspiro[4.5]dec-6-yl)hydroxymethyl]tetrahydro-4*H*-thiopyran-4-one: **IR** (DRIFT)

max: 3496, 2916, 1702, 1415, 1259, 1092, 1093 cm⁻¹; **¹H NMR** (300 MHz, CDCl₃) : 4.24 (1H, ddd, *J* = 3.5, 3.5, 7.5 Hz, HC-1'), 4.12-3.95 (4H, m, H₂CO), 3.93 (1H, d, *J* = 3.5 Hz, HO), 3.25 (1H, dd, *J* = 11.5, 14.5 Hz, HC-2), 3.02 (1H, ddd, *J* = 4, 10, 13.5 Hz, HC-6), 2.95-2.56 (9H, m, HC-2, HC-3, H₂C-5, HC-6, H₂C-7'', H₂C-9''), 2.41 (1H, ddd, *J* = 3, 7.5, 7.5 Hz, HC-6''), 2.15 (1H, ddd, *J* = 4, 9, 13.5 Hz, HC-10''), 1.79 (1H, ddd, *J* = 3.5, 7, 13.5 Hz, HC-10''); **¹³C NMR** (75 MHz, CDCl₃) : 210.1 (s), 110.5 (s), 72.9 (d), 64.7 (t), 64.2 (t), 54.7 (d), 46.4 (d), 44.2 (t), 34.5 (t), 33.2 (t), 30.0 (t), 29.4 (t), 26.8 (t); **LRMS** (EI), *m/z* (relative intensity): 304 ([M]⁺, 12), 286 (10), 159 (20), 132 (86), 115 (12), 99 (100), 86 (20), 55 (17); **HRMS** *m/z* calcd. for C₁₃H₂₀O₄S₂: 304.0803; found: 304.0801.

(1'*R**, 3*R**, 6''*R**)-3-[(1,4-Dioxo-8-thiaspiro[4.5]dec-6-yl)hydroxymethyl]tetrahydro-4*H*-thiopyran-4-one: **IR** (DRIFT)

max: 3497, 2917, 1706, 1426, 1274, 1151, 1102, 1040 cm⁻¹; **¹H NMR** (300 MHz, CDCl₃) : 4.57 (1H, ddd, *J* = 2.5, 3.5, 7.5 Hz, HC-1'), 4.10-3.89 (4H, m, H₂CO), 3.85 (1H, d, *J* = 2.5 Hz, OH), 3.13 (1H, dd, *J* = 11, 13.5 Hz, HC-2), 3.0 (1H, ddd, *J* = 4, 10.5, 13.5 Hz, HC-6), 2.91-2.57 (9H, m, HC-2, HC-3, HC-6, H₂C-5, H₂C-7'', H₂C-9''), 2.22-2.13 (1H, m, HC-10''), 2.07 (1H, ddd, *J* = 3.5, 7.5, 8 Hz, HC-6''), 1.82-1.71 (1H, m, HC-10''); **¹³C NMR** (75 MHz, CDCl₃) : 209.1 (s), 110.8 (s), 69.7 (d), 64.8 (t), 64.1 (t), 55.3 (d), 46.2 (d), 44.1 (t), 34.9 (t), 29.7 (t), 29.4 (t), 29.3 (t), 26.7 (t); **LRMS** (EI), *m/z* (relative intensity): 304 ([M]⁺, 12), 286 (8), 159 (12), 132 (90), 115 (11), 99 (100), 86 (18), 55 (12); **HRMS** *m/z* calcd. for C₁₃H₂₀O₄S₂: 304.0803; found: 304.0807.

Determination of relative configurations for 5a and 5s

Preparation of 6a, 6s, 7a, and 7s

Using the $\text{MgBr}_2 \cdot \text{OEt}_2$ mediated Mukaiyama aldol procedure described above, the *trans* aldehyde **13** (206 mg, 1.08 mmol) gave a 6:3:1 mixture of **7s**, **6s**, and **7a**, respectively (230 mg, 70%) after fractionation of the crude by MPC (30% ethyl acetate in hexane). Pure samples of **7s** and **6s** and a 1:2.7 mixture of **7a**:**7s** were obtained by preparative TLC (30% ethyl acetate in hexane, multiple development).

A solution of the *trans* aldehyde **13** (525 mg, 2.76 mmol) in THF (1 mL) was added dropwise over 1 min to a solution of the 'amine-free' Li enolate of **2** [prepared by addition of MeLi (1 equiv.) to an ether solution of **12** (1.08 g, 5.73 mmol) at 0°C -rt, 1h] at -78°C . After 5 min, the reaction was quenched by rapid addition of a solution of HOAc (700 mg, 11.6 mmol) in THF (2 mL). Without delay, the mixture was diluted with water and extracted with CH_2Cl_2 ($3 \times 50\text{ mL}$). The combined organic layers were dried over Na_2SO_4 , concentrated, and fractionated MPC (35% ethyl acetate in hexane) to give the aldol **6a** (542 mg, 64%).

(1'R*, 3R*, 3''R*, 4''S*)-3-[Hydroxy(4-(methoxymethoxy)-tetrahydrothiopyran-3-yl)methyl]tetrahydrothiopyran-4-one: **IR** (DRIFT) max: 3516, 2923, 1701, 1427, 1146, 1101, 1053, 1027 cm^{-1} ; **^1H NMR** (500 MHz, CDCl_3) : 4.72 (1H, d, $J = 6.5$ Hz, H_2CO), 4.70 (1H, d, $J = 6.5$ Hz, H_2CO), 4.47 (1H, ddd, $J = 2.5, 4, 9.5$ Hz, HC-1'), 3.61 (1H, ddd, $J = 4, 10, 10.5$ Hz, HC-4''), 3.43 (3H, s, H_3CO), 3.22 (1H, d, $J = 4$ Hz, HO), 3.03-2.93 (2H, m), 2.92-2.83 (2H, m), 2.82-2.65 (5H, m), 2.58 (1H, m, $J = 2.5, 3.5, 4, 13.5$ Hz, HC-6), 2.51 (1H, ddd, $J = 2.5, 3, 13.5$ Hz, HC-2), 2.42 (1H, dddd, $J = 3, 4, 4, 12.5$ Hz, HC-5''), 1.77 (1H, dddd, $J = 3, 3, 9.5, 10$ Hz, HC-3''), 1.74 (1H, dddd, $J = 3, 10.5, 12, 12.5$ Hz, HC-5''); **^{13}C NMR** (125 MHz, CDCl_3) : 212.35 (s), 96.52 (t), 76.18 (d), 67.72 (d), 56.03 (q), 55.45 (d), 45.73 (d), 44.99 (t), 34.90 (t), 32.42 (t), 31.07 (t), 27.75 (t), 26.31 (t); **LRMS** (EI), m/z (relative intensity): 306 ($[\text{M}]^+$, 68), 226 (39), 145 (42), 129 (54), 116 (60), 100 (100), 99 (67), 89 (55); **HRMS** m/z calcd. for $\text{C}_{13}\text{H}_{22}\text{O}_4\text{S}_2$: 306.0960; found: 306.0954 (EI).

(1'R*, 3S*, 3''R*, 4''S*)-3-[Hydroxy(4-(methoxymethoxy)-tetrahydrothiopyran-3-yl)methyl]tetrahydrothiopyran-4-one: **IR** (DRIFT) max: 3472, 2918, 1702, 1428, 1147, 1097, 1052, 1028 cm^{-1} ; **^1H NMR** (400 MHz, CDCl_3) : 4.84 (1H, ddd, $J = 4, 5, 8.5$ Hz, HC-1'), 4.73 (1H, d, $J = 6.5$ Hz, H_2CO), 4.63 (1H, d, $J = 6.5$ Hz, H_2CO), 3.47 (1H, ddd, $J = 3.5, 9, 9$ Hz, HC-4''), 3.47 (3H, s, H_3CO), 3.17 (1H, d, $J = 5$ Hz, HOC-1'), 3.12 (2H, ap d, $J = 5$ Hz, H_2C -2), 2.99-2.94 (2H, , H_2C -6), 2.86 (1H, ap ddd, $J = 5, 5, 8.5$ Hz, HC-3), 2.79 (1H, ddd, $J = 2, 3, 13.5$ Hz, HC-2''), 2.72-2.65 (3H, , H_2C -5, HC-6''), 2.64 (1H, dd, $J = 9.5, 13.5$ Hz, HC-2''), 2.57 (1H, ddd, $J = 3, 11, 13.5$ Hz, HC-6''), 2.20 (1H, dddd, $J = 3, 3.5, 6, 13$ Hz, HC-5''), 1.79 (1H, dddd, $J = 3.5, 9, 11, 13$ Hz, HC-5''), 1.72 (1H, dddd, $J = 3, 4, 9, 9.5$ Hz, HC-3''); **^{13}C NMR** (100 MHz, CDCl_3) : 210.29, 96.33, 76.79, 66.30, 56.55, 55.26, 45.61, 44.19, 33.32, 33.11, 31.50, 26.85, 26.24; **LRMS** (EI), m/z (relative intensity): 306 ($[\text{M}]^+$, 58), 226 (52), 145 (44), 129 (47), 116 (45), 100 (100), 99 (62), 67 (49); **HRMS** m/z calcd. for $\text{C}_{13}\text{H}_{22}\text{O}_4\text{S}_2$: 306.0960; found: 306.0962 (EI).

(1'S*, 3S*, 3''R*, 4''S*)-3-[Hydroxy(4-(methoxymethoxy)-tetrahydrothiopyran-3-yl)methyl]tetrahydrothiopyran-4-one: This compound was obtained as a 1:2.7 mixture of **7a** and **7s**, respectively, by repeated fractionation of crude aldols obtained as described above. **^1H NMR** (300 MHz, CDCl_3) for **7a**: : 4.66 (2H, ap s, H_2CO), 4.03 (1H, dd, $J = 6, 6.5$ Hz, HC-1'), 3.63 (1H, ddd, $J = 3.5, 7.5, 8$ Hz, HC-4''), 3.40 (3H, s, H_3CO), 3.15-2.68 (8H, m), 2.58-2.47 (2H, m), 2.32-2.25 (1H, m), 2.12-2.03 (1H, m), 1.90-1.78 (2H, m).

(1'S*, 3R*, 3''R*, 4''S*)-3-[Hydroxy(4-(methoxymethoxy)-tetrahydrothiopyran-3-yl)methyl]tetrahydrothiopyran-4-one: **IR** (DRIFT) max: 3483, 2934, 1701, 1430, 1149, 1095, 1070, 1037 cm^{-1} ; **^1H NMR** (MHz,) : 4.70 (1H, d, $J = 6.5$ Hz, H_2CO), 4.67 (1H, d, $J = 6.5$ Hz, H_2CO), 4.52 (1H, ddd, $J = 3, 5, 8$ Hz, HC-1'),

3.95 (1H, ddd, $J = 3, 6, 7$ Hz, HC-4"), 3.40 (3H, s, H₃CO), 3.16 (1H, d, $J = 5$ Hz, HOC-1'), 3.09-2.87 (7H, m), 2.80-2.75 (2H, m), 2.43 (1H, dddd, $J = 1, 3.5, 7, 12.5$ Hz, HC-6"), 2.32 (1H, ddd, $J = 1, 6.5, 13.5$ Hz, HC-2"), 2.20 (1H, dddd, $J = 3, 3.5, 10, 13.5$ Hz, HC-5"), 1.94-1.85 (2H, m, HC-3", HC-5"); ¹³C NMR (100 MHz, CDCl₃) : 211.45, 95.65, 74.40, 69.99, 55.95, 55.66, 45.10, 42.02, 30.86, 30.46, 29.86, 27.44, 24.85; LRMS (EI), m/z (relative intensity): 306 ([M]⁺, 59), 129 (50), 116 (62), 115 (49), 100 (100), 99 (67), 67 (53), 55 (60); HRMS m/z calcd. for C₁₃H₂₂O₄S₂: 306.0960; found: 306.0962 (EI).

Determination of relative configurations for 6a, 6s, 7a, and 7s