Supporting Information

for

Determination of the relative configuration of tropinone and granatanone aldols by using TBDMS ethers

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Experimental procedures for the preparation and characterization of the remaining compounds

**exo,anti-2-[Hydroxy(phenyl)methyl]-9-methyl-9-azabicyclo[3.3.1]nonan-3-one (exo,anti-4)** [¹] Mp 103–106 °C; Rf 0.38 (10% MeOH/DCM); ¹H NMR δ 7.72 (br s, 1H), 7.36-7.30 (m, 5H), 5.27 (d, J = 3.6 Hz, 1H), 3.38 (d, J = 4.1 Hz, 1H), 3.35-3.28 (m, 1H), 2.98 (dd, J = 16.2 Hz, 7.0 Hz, 1H), 2.74 (s, 3H), 2.57 (d, J = 3.8 Hz, 1H), 2.45 (d, J = 16.2 Hz, 1H), 2.20-2.05 (m, 2H), 1.61-1.52 (m, 2H), 1.38-1.29 (m, 2H).
Typical procedure for preparation exo, syn aldols:

**exo,syn-2-[Hydroxy(phenyl)methyl]-9-methyl-9-azabicyclo[3.3.1]nonan-3-one**

(exo,syn-4) [1] Benzaldehyde (0.102 mL, 1 mmol) was added to a mixture of granatanone (0.306 g, 2 mmol) and water (0.011 mL, 0.61 mmol). The reaction mixture was then stirred at room temperature until NMR monitoring showed satisfactory conversion (33 d – conversion 30%). The mixture was taken up in toluene and evaporated under vacuum (repeated 3 times). The residue was crystallized from cyclohexane or diethyl ether to give exo,syn-4 (0.047 g, 18%). Mp 117–118 °C (decomp.); Rf 0.46 (7% MeOH/DCM); $^1$H NMR δ 7.62 (br s, 1H), 7.44–7.22 (m, 5H), 5.08 (d, J = 2.0 Hz, 1H), 3.34–3.28 (m, 1H), 3.17 (dd, J = 17.1 Hz, 7.2 Hz, 1H), 3.05 (d, J = 4.2 Hz, 1H), 2.64 (s, 3H), 2.54 (d, J = 17.1 Hz, 1H), 2.48 (s, 1H), 2.12–2.01 (m, 1H), 1.97–1.88 (m, 1H), 1.55–1.42 (m, 2H), 1.36–1.29 (m, 1H), 1.01–0.91 (m, 1H); $^{13}$C NMR δ 211.6, 143.7, 128.2, 126.8, 125.4, 76.1, 60.0, 53.6, 53.5, 46.9, 39.6, 22.6, 22.3, 16.4; HRMS (ESI): 282.1465 [M+ H] calcd for C16H21NO2Na, 282.1470.

**exo,anti-2-[(tert-Butyldimethylsilyloxy)(phenyl)methyl]-9-methyl-9-azabicyclo[3.3.1]nonan-3-one**

(exo,anti-6) The aldol exo,anti-4 (0.259 g, 1 mmol) was dissolved in dry DCM (3 mL). DMAP (0.013 g, 0.11 mmol) and dry Et$_3$N (1.4 mL) were added, followed by the addition of TBDMSCl (0.300 g, 2 mmol). The resulting solution was allowed to stand at rt for 16 h. The reaction mixture was then diluted with DCM, shaken with 20% aq. K$_2$CO$_3$ and extracted with DCM (3 × 10 mL). The combined organic extracts were dried (Na$_2$SO$_4$), the solvent was removed under vacuum, and the residue was subjected to flash chromatography in hexanes/AcOEt (1:9), which gave the pure product as a white solid (0.306 g, 82%). Mp 59–60°C (decomp.); Rf 0.57
exo, syn-2-[(tert-Butyldimethylsilyloxy)(phenyl)methyl]-9-methyl-9-azabicyclo[3.3.1]nonan-3-one (exo,syn-6) Product exo,syn-6 was obtained as a white solid (0.243 g, 65%) in the same way as exo,anti-6 by using exo,syn-4 (0.259 g, 1 mmol), dry DCM (3 mL), DMAP (0.013 g, 0.11 mmol), Et₃N (1.4 mL) and TBDMSCl (0.300 g, 2 mmol). Mp 77–78 °C (decomp.); Rᵣ 0.57 (7% MeOH/DCM); ¹H NMR δ 7.45-7.18 (m, 5H), 5.16 (d, J = 8.6 Hz, 1H), 3.44 (d, J = 4.0 Hz 1H), 3.27-2.20 (m, 1H), 2.68 (s, 3H), 2.64 (d, J = 6.9 Hz,1H), 2.54 (s, 1H, eq-H at C-2), 2.20 (dt, J = 16.9 Hz,1.3 Hz, 1H), 2.14-1.95 (m, 2H), 1.60-1.42 (m, 2H), 1.30-1.12 (m, 2H), 0.85 (s, 9H), 0.05 (s, 3H), -0.28 (s, 3H); ¹³C NMR δ 211.0, 142.5, 128.0, 127.6, 126.6, 106.6, 74.8, 66.2, 55.2, 47.3, 40.8, 25.8, 23.1, 22.9, 18.1, 17.0, -4.6, -5.0; HRMS (ESI): 396.2354 [M⁺ + Na] calcd for C₂₂H₃₅NO₂SiNa, 396.2335.

endo, syn-2-[(tert-Butyldimethylsilyloxy)(phenyl)methyl]-9-methyl-9-azabicyclo[3.3.1]nonan-3-one (endo,syn-6) The TBDMS-ether exo,anti-6 (0.030 g, 0.08 mmol) was applied on a flash silica column in DCM. The column was washed with MeOH/DCM (4:96) to remove the product of isomerization as a colorless oil (0.023 g, 77%). Rᵣ 0.54 (7% MeOH/DCM); ¹H NMR δ 7.40-7.20 (m, 5H), 5.26 (d, J = 6.8 Hz, 1H),
3.43-3.38 (m, 1H), 3.29-3.23 (m, 1H), 3.03-2.91 (m, 1H, ax-H at C-2), 2.70 (dd, J = 15.4 Hz, 6.7 Hz, 1H), 2.58 (s, 3H), 2.18 (d, J = 15.5 Hz, 1H), 2.07-1.89 (m, 2H), 1.87-1.75 (m, 1H), 1.59-1.46 (m, 3H), 0.84 (s, 9H), 0.09 (s, 3H), -0.36 (s, 3H); $^{13}$C NMR δ 209.4, 144.2, 127.9, 127.2, 127.1, 71.4, 58.0, 56.7, 56.2, 43.0, 41.0, 29.4, 25.5, 22.4, 18.1, 16.5, -4.6, -5.3; HRMS (ESI): 396.2344 [M$^{+}$ + Na] calcd for C$_{22}$H$_{35}$NO$_2$SiNa, 396.2335.

**endo,anti-2-[(tert-Butyldimethylsilyloxy)(phenyl)methyl]-9-methyl-9-azabicyclo[3.3.1]nonan-3-one (endo,anti-6)** The TBDMS-ether exo,syn-6 (0.030 g, 0.08 mmol) was applied on a flash silica column in DCM. The column was washed with MeOH/DCM (2:98) to remove the product of isomerization as an oil (0.024 g, 80%). $R_f$ 0.45 (7% MeOH/DCM); $^1$H NMR δ 7.45-7.20 (m, 5H), 5.01 (d, J = 8.7 Hz, 1H), 3.29-3.24 (m, 1H), 3.14 (dd, J = 8.5 Hz, 5.2 Hz, 1H, ax-H at C-2), 2.85 (dd, J = 14.6 Hz, 6.7 Hz, 1H), 2.55 (s, 3H), 2.52 (s, 1H), 2.26 (dd, J = 14.5 Hz, 0.9 Hz, 1H), 2.11 (m, 1H), 1.89-1.78 (m, 1H), 1.65-1.56 (m, 2H), 1.54-1.47 (m, 2H), 0.72 (s, 9H), 0.08 (s, 3H), -0.15 (s, 3H); $^{13}$C NMR δ 210.0, 142.0, 128.2, 127.5, 125.5, 72.1, 59.5, 57.6, 56.0, 47.3, 43.1, 40.8, 30.2, 25.7, 18.1, 16.0, -4.9, -5.1; HRMS (ESI): 396.2315 [M$^{+}$ + Na] calcd for C$_{22}$H$_{35}$NO$_2$SiNa, 396.2335.

**Reference**