Supporting Information

Synthesis of Novel Polyhydroxylated Pyrrolidine-Triazole/-Isoxazole Hybrid Molecules

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Section A. Experimental

**Compound S1.** AllylMgBr (1.7M in THF, 4.6 mL, 3 equiv) was slowly added to a solution of compound 1 (1.1 g, 2.63 mmol) in dry THF (10 mL) at 0 °C under argon atmosphere. The reaction was allowed to warm up to room temperature and stirred for 3 h. The reaction was quenched by sat. NH₄Cl(aq) and extracted with CH₂Cl₂. The combined organic layers were dried over anh. MgSO₄, concentrated and purified by column chromatography to give compound S1 as colorless oil (1.16 g, 96 %); TLC (Hexanes/EtOAc = 3/1, v/v) Rₓ = 0.3.

**Compound S2.** A suspension of compound S1 (1.16 g, 2.52 mmol), zinc dust (1.65 g, 10 equiv) and HOAc (2.5 mL) in CH₂Cl₂ (3.9 mL) was stirred at room temperature for 8 h. The excess of zinc dust was filtrated through a pad of Celite. The filtrate was neutralized with NaHCO₃(aq) and extracted with CH₂Cl₂. The combined organic layers were dried over anh. MgSO₄ and concentrated to give the pyrrolidine. TLC (Hexanes/EtOAc = 1/1, v/v) Rₓ = 0.6. The pyrrolidine in dry CH₂Cl₂ (10 mL) was treated with (Boc)₂O (720 μL, 1.25 equiv) and triethylamine (770 μL, 2 equiv). The reaction was stirred at room temperature for 3 h. The reaction was concentrated and purified by column chromatography to give compound S2 (1.02 g, 75 %) as colorless oil. TLC (Hexanes/EtOAc = 5/1, v/v) Rₓ = 0.4.

**Compound 26.** Compound S2 (100 mg, 0.18 mmol) in CH₂Cl₂ (3 mL) at −78 °C was formed to aldehyde by ozonolysis. To a solution of the crude aldehyde and 4-chloroaniline (23 mg, 1 equiv) in CH₂Cl₂ (3 mL) was added acetic acid (32 μL, 0.56 mmol) and NaBH(OAc)₃ (117 mg, 3 equiv). The reaction mixture was stirred at room temperature for 12 h, and the reaction was quenched by sat. NaHCO₃(aq) and extracted with CH₂Cl₂. The combined organic layers were dried over anh. MgSO₄, concentrated and purified by column chromatography to give the protected pyrrolidine as colorless oil (57 mg, 47 %); TLC (Hexane/EtOAc = 5/1, v/v) Rₓ = 0.5. To a solution of the protected pyrrolidine (57 mg, 0.085 mmol) in dry CH₂Cl₂ (5 mL) at 0 °C was added BBr₃ (1M in dichloromethane, 852 μL, 10 equiv). The reaction was warm up to room temperature and kept
stirring for 12 h. After the reaction was complete, the reaction mixture was quenched with MeOH, concentrated and purified by column chromatography to give compound 26 as white solid (11 mg, 44 %); TLC (MeOH/CH₂Cl₂ = 1/4, v/v) Rf = 0.1. [α]D²⁰ +28.86 (c 0.2 in MOH); ¹H NMR (600 MHz, D₂O) δ 7.25 (d, J = 8.8 Hz, 2H), 6.80 (d, J = 8.8 Hz, 2H), 3.88 (t, J = 7.0 Hz, 1H), 3.78 (t, J = 7.4 Hz, 1H), 3.74 (dd, J = 11.8, 4.3 Hz, 1H), 3.68 (dd, J = 11.8, 6.2 Hz, 1H), 3.25–3.09 (m, 4H), 2.03–1.98 (m, 1H), 1.83–1.78 (m, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 146.7, 129.0, 123.0, 115.9, 80.7, 76.9, 61.7, 61.2, 58.4, 41.3, 31.8; HRMS (ESI-TOF) calcd for C₁₃H₁₉ClN₂O₃+H⁺ [M+H⁺] 287.1157, found: 287.1160.

**Compound 27.** The title compound 27 was synthesized by the procedure as described for the preparation of compound 26 except for using 2-bromoaniline in the step of reductive amination as write solid. [α]D²⁰ +27.16 (c 0.16 in MOH); ¹H NMR (600 MHz, D₂O) δ 7.54 (d, J = 7.5 Hz, 1H), 7.30 (t, J = 7.5 Hz, 1H), 6.90 (d, J = 7.5 Hz, 1H), 6.74 (d, J = 7.5 Hz, 1H), 3.83 (t, J = 7.0 Hz, 1H), 3.73 (t, J = 7.4 Hz, 1H), 3.69 (dd, J = 11.5, 4.3 Hz, 1H), 3.64 (dd, J = 11.5, 6.4 Hz, 1H), 3.35–3.24 (m, 2H), 3.05–2.98 (m, 2H), 2.01–1.99 (m, 1H), 1.78–1.75 (m, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 144.7, 132.7, 119.5, 113.4, 110.4, 81.4, 77.7, 62.0, 61.5, 58.1, 41.1, 32.2; HRMS (ESI-TOF) calcd for C₁₃H₁₉BrN₂O₃+H⁺ [M+H⁺] 331.0652, found: 331.0652.
Section B

$^1$H NMR spectrum of compound 1 (600 MHz, CDCl$_3$).

$^{13}$C NMR spectrum of compound 1 (150 MHz, CDCl$_3$).
$^1$H NMR spectrum of compound 7 (600 MHz, CDCl$_3$).

$^{13}$C NMR spectrum of compound 7 (150 MHz, CDCl$_3$).
$^1$H NMR spectrum of compound 8 (600 MHz, CDCl$_3$).

$^{13}$C NMR spectrum of compound 8 (150 MHz, CDCl$_3$).
$^1$H NMR spectrum of compound 9 (600 MHz, CDCl$_3$).

$^{13}$C NMR spectrum of compound 9 (150 MHz, CDCl$_3$).
$^1$H NMR spectrum of compound 10 (600 MHz, CD$_3$OD).

$^{13}$C NMR spectrum of compound 10 (150 MHz, CD$_3$OD).
\(^1\)H NMR spectrum of compound 13 (600 MHz, CD\(_3\)OD).

\(^{13}\)C NMR spectrum of compound 13 (150 MHz, CD\(_3\)OD).
$^1$H NMR spectrum of compound 16 (600 MHz, CDCl₃).

$^{13}$C NMR spectrum of compound 16 (150 MHz, CDCl₃).
$^1$H NMR spectrum of compound 18 (600 MHz, CD$_3$OD).

$^{13}$C NMR spectrum of compound 18 (150 MHz, CD$_3$OD).
\(^1\)H NMR spectrum of compound 19 (600 MHz, CD\(_3\)OD).

\(^{13}\)C NMR spectrum of compound 19 (150 MHz, CD\(_3\)OD).
$^1$H NMR spectrum of compound 20 (600 MHz, CD$_3$OD).

$^{13}$C NMR spectrum of compound 20 (150 MHz, CD$_3$OD).
$^1$H NMR spectrum of compound 21 (600 MHz, CD$_3$OD).

$^{13}$C NMR spectrum of compound 21 (150 MHz, CD$_3$OD).
$^1$H NMR spectrum of compound 22 (600 MHz, CD$_3$OD).

$^{13}$C NMR spectrum of compound 22 (150 MHz, CD$_3$OD).
$^1$H NMR spectrum of compound 23 (600 MHz, D$_2$O).

$^{13}$C NMR spectrum of compound 23 (150 MHz, D$_2$O).
$^1$H NMR spectrum of compound 24 (600 MHz, CD$_3$OD).

$^{13}$C NMR spectrum of compound 24 (150 MHz, CD$_3$OD).
$^1$H NMR spectrum of compound 25 (600 MHz, CD$_3$OD).

$^{13}$C NMR spectrum of compound 25 (150 MHz, CD$_3$OD).
$^1$H NMR spectrum of compound 26 (600 MHz, D$_2$O).

$^{13}$C NMR spectrum of compound 26 (150 MHz, D$_2$O).
$^1$H NMR spectrum of compound 27 (600 MHz, D$_2$O).

$^{13}$C NMR spectrum of compound 27 (150 MHz, D$_2$O).