

Supporting information

Highly Stereoselective Synthesis of Aryl/Heteroaryl-C-Nucleosides via the Merger of Photoredox and Nickel Catalysis

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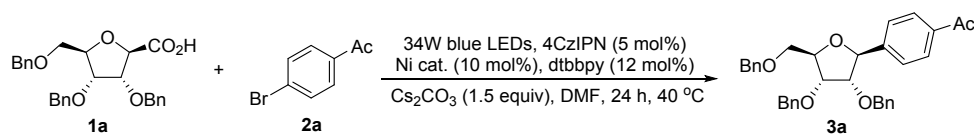
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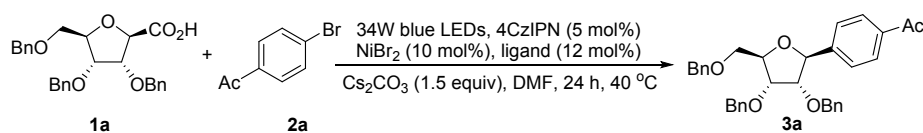
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Table S1 The optimization of nickel catalysts. ^a

entry	Ni cat.	yield ^b
1	NiCl ₂ ·6H ₂ O	32%
2	NiCl ₂ ·glyme	36%
3	NiBr ₂	47%
4	Ni(OAc) ₂ ·4H ₂ O	45%
5	Ni(NO ₃) ₂ ·6H ₂ O	43%
6	Ni(acac) ₂	5%

^a Conditions employed 34 W blue LEDs, **1a** (0.2 mmol), **2a** (0.3 mmol), 4CzIPN (0.01 mmol), Ni cat. (0.02 mmol), dtbbpy (0.024 mmol), Cs₂CO₃ (0.3 mmol), DMF (10 mL), N₂, 40 °C, 24 h, unless otherwise noted; ^b Isolated yields were reported.

Table S2 The optimization of ligands. ^{a,b}

ligand 1 (dtbbpy) 47% yield	ligand 2 51% yield	ligand 3 trace	ligand 4 43% yield
ligand 5 13% yield	ligand 6 (bpy) 51% yield; 38% yield ^c	ligand 7 trace	ligand 8 21% yield

^a Conditions employed 34 W blue LEDs, **1a** (0.2 mmol), **2a** (0.3 mmol), 4CzIPN (0.01 mmol), NiBr₂ (0.02 mmol), ligand (0.024 mmol), Cs₂CO₃ (0.3 mmol), DMF (10 mL), N₂, 40 °C, 24 h, unless otherwise noted; ^b Isolated yields were reported; ^c NiBr₂ (5 mol%) and bpy (6 mol%) were used in the reaction.

Table S3 The optimization of bases. ^a

entry	base	yield ^b
1	CS ₂ CO ₃ (1.5 equiv)	51%
2	K ₂ CO ₃ (1.5 equiv)	66%
3	Na ₂ CO ₃ (1.5 equiv)	10%
4	K ₃ PO ₄ (1.5 equiv)	36%
5	K ₂ HPO ₄ (1.5 equiv)	25%
6	CH ₃ COONa (1.5 equiv)	50%
7	KOH (1.5 equiv)	20%
8	K ₂ CO ₃ (1.0 equiv)	54%
9	K ₂ CO ₃ (2.0 equiv)	68%
10	K ₂ CO ₃ (3.0 equiv)	56%
11	K ₂ CO ₃ (2.0 equiv)	70% ^c
12	K ₂ CO ₃ (2.0 equiv)	66% ^d

^a Conditions employed 34 W blue LEDs, **1a** (0.2 mmol), **2a** (0.3 mmol), 4CzIPN (0.01 mmol), NiBr₂ (0.02 mmol), bpy (0.024 mmol), base, DMF (10 mL), N₂, 40 °C, 24 h, unless otherwise noted; ^b Isolated yields were reported; ^c 0.4 mmol of **2a** was used; ^d 0.6 mmol of **2a** was used.

Table S4 The optimization of solvents. ^a

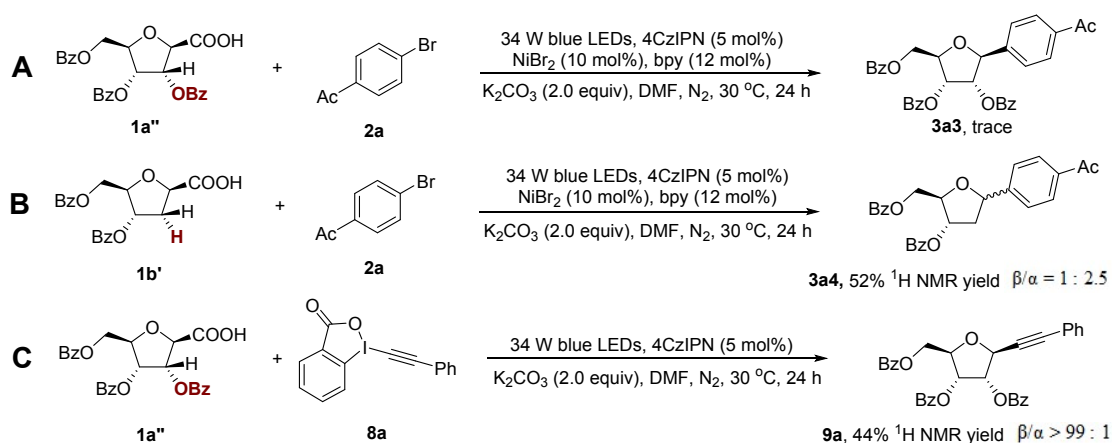
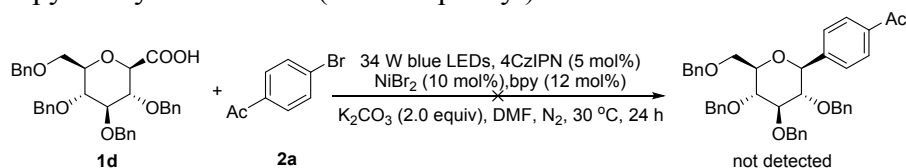
entry	solvent	yield ^b
1	DMF	70%
2	DMA	21%
3	NMP	43%
4	DMSO	7%
5	MeCN	10%
6	DCE	n.d
7	1,4-dioxane	n.d
8	DMF	48% ^c
9	DMF	46% ^d

^a Conditions employed 34 W blue LEDs, **1a** (0.2 mmol), **2a** (0.4 mmol), 4CzIPN (0.01 mmol), NiBr₂ (0.02 mmol), bpy (0.024 mmol), K₂CO₃ (0.4 mmol), solvent (10 mL), N₂, 40 °C, 24 h, unless otherwise noted; ^b Isolated yields were reported; ^c 5 mL of solvent was employed as the reaction solvent; ^d 20 mL of solvent was employed as the reaction solvent.

Table S5 The optimization of reaction temperature and reaction time. ^a

entry	temperature	time	yield ^b
1	40 °C	24h	70%
2	50 °C	24h	57%
3	30 °C	24h	82%
4	30 °C	48h	83%
5	30 °C	12h	63%

^a Conditions employed 34 W blue LEDs, **1a** (0.2 mmol), **2a** (0.4 mmol), 4CzIPN (0.01 mmol), NiBr₂ (0.02 mmol), bpy (0.024 mmol), K₂CO₃ (0.4 mmol), DMF (10 mL), N₂, temperature and time were noted in table; ^b Isolated yields were reported.

Scheme S1 Photocatalytic decarboxylative cross-coupling reactions of *O*-benzoyl protected anomeric ribosyl/deoxyribosyl acids.**Scheme S2** Photoredox/Ni dual-catalyzed decarboxylative cross-coupling reactions of *O*-benzyl protected β -glucopyranosyl acid with 1-(4-bromophenyl)ethan-1-one.

The family of aryl *C*-pyranosides represents another class of saccharides that display high metabolic stability and includes many bioactive natural products and commercial drugs.¹⁻³ However, the coupling reaction of *O*-benzyl protected β -glucopyranosyl acid **1d** with **2a** failed to give the desired product. We reasoned that the failure of this reaction might be associated with the difficulty of promoting SET oxidation of **1d** because of its relatively higher oxidation potential (Figure S2). Further investigation is still ongoing in our laboratory.

Scheme S3 The synthetic application in the synthesis of tiazofurin.

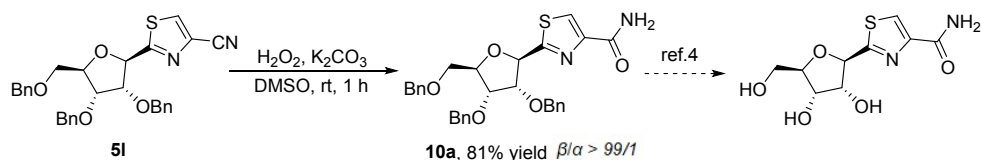
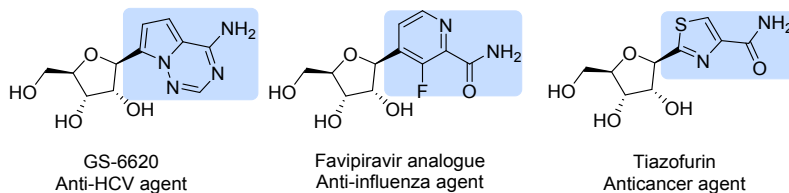


Figure S1 The representative aryl/heteroaryl-*C*-nucleosides employed in drug discovery and chemical biology

a. the representative *C*-nucleosides with antiviral and anticancer biological activities



b. the representative *C*-nucleosides capable of extending the genetic alphabet

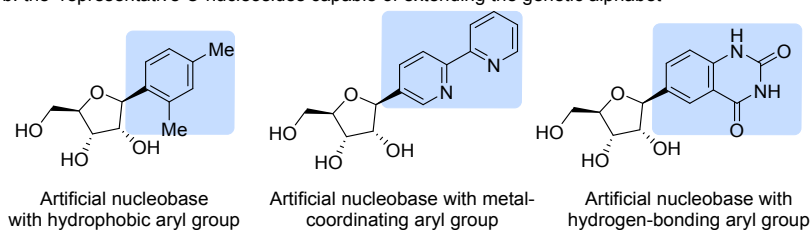
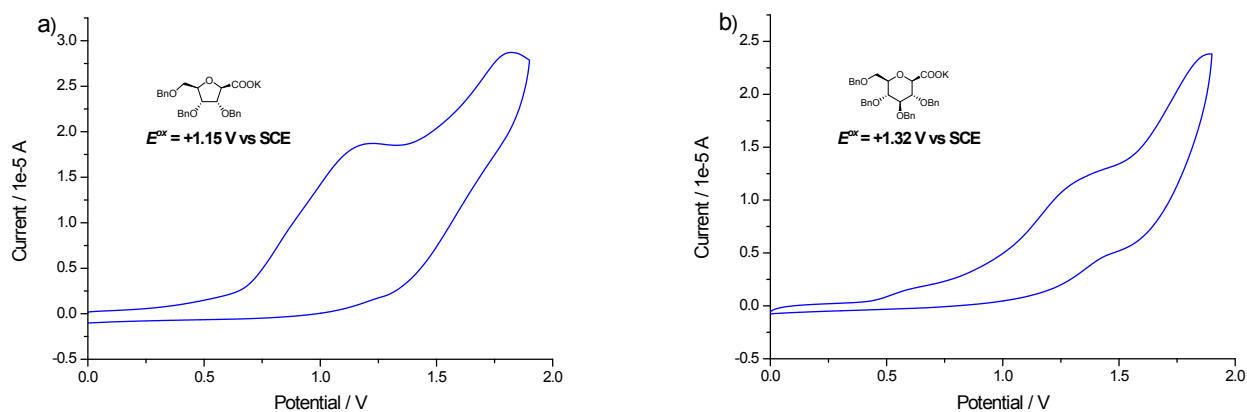


Figure S2 Cyclic voltammogram of *O*-benzyl protected β -ribosyl acid and β -glucopyranosyl acid potassium salts.

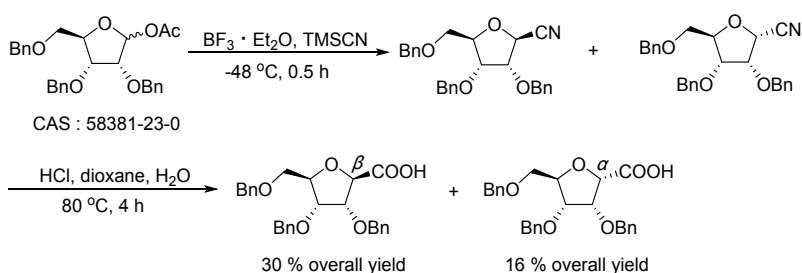
Voltammetric measurements were recorded on a CH Instruments: Model 760E Series Electrochemical Analyzer using a standard three electrodes setup in dry MeCN (10 mL) and Bu_4NClO_4 as the electrolyte (0.1 M). Cyclic voltammograms were recorded at a scan rate of 0.1 V/s.



Experiment Procedures and Product Characterization

Commercial reagents and solvents were used as received, unless otherwise stated. Organic solution was concentrated under reduced pressure on a Büchi rotary evaporator using an isopropyl alcohol-dry ice bath. Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel plates (Qingdao Haiyang Chemical China), and the compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with iodine. Flash chromatography was performed on silica gel 200–300 mesh (purchased from Qingdao Haiyang Chemical China) with commercial solvents (purchased from Adamas-beta®). The ^1H and ^{13}C NMR spectra were recorded on a Bruker AM 400 or 500 Spectrometer (400/500 and 100/125 MHz for ^1H and ^{13}C NMR, respectively) and are internally referenced to residual solvent signals (note: CDCl_3 referenced at 7.26 and 77.00 ppm in ^1H and ^{13}C NMR, respectively). Multiplicities were given as s (singlet), d (doublet), t (triplet), dd (doublet of doublet), and m (multiplets). Coupling constants were reported in Hertz (Hz). Data for ^{13}C NMR are reported in terms of chemical shift. High-resolution mass spectrometry (HRMS) was recorded on Waters LCT Premier XE spectrometer.

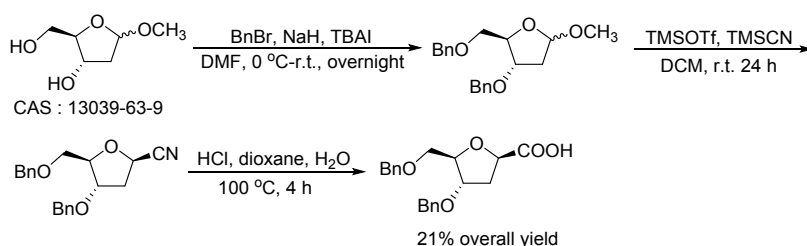
Synthesis of *O*-benzyl protected anomeric ribosyl acid ⁵⁻⁸



***O*-benzyl protected anomeric β -ribosyl acid (1a):** ^1H NMR (400 MHz, CDCl_3) δ 7.42 – 7.19(m, 15H), 4.79 (d, J = 12.0 Hz, 1H), 4.67 (s, 1H), 4.60 (d, J = 3.1 Hz, 1H), 4.57 (d, J = 3.0 Hz, 1H), 4.49 – 4.44 (m, 2H), 4.32 (dd, J = 9.4, 2.5 Hz, 1H), 4.21 (dd, J = 11.7 Hz, 1H), 4.14 (d, J = 4.5 Hz, 1H), 3.97 (dd, J = 9.3, 4.5 Hz, 1H), 3.87 (dd, J = 10.4, 2.9 Hz, 1H), 3.54 (d, J = 10.4, 1H). Spectroscopic data in accordance with literature.⁵

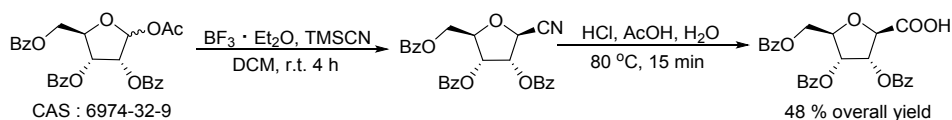
***O*-benzyl protected anomeric α -ribosyl acid (1a’):** ^1H NMR (400 MHz, CDCl_3) δ 7.50 – 7.10(m, 15H), 4.76 (d, J = 11.1 Hz, 1H), 4.64 (d, J = 11.3 Hz, 1H), 4.55 (d, J = 4.6 Hz, 1H), 4.53 (d, J = 4.7 Hz, 1H), 4.46 (s, 1H), 4.44 (d, J = 11.7 Hz, 1H), 4.31 (dd, J = 8.4, 3.0 Hz, 1H), 4.20 (d, J = 11.7 Hz, 1H), 4.14 (d, J = 4.7 Hz, 1H), 3.96 (dd, J = 8.9, 4.7 Hz, 1H), 3.82 (dd, J = 10.0, 2.9 Hz, 1H), 3.52 (d, J = 10.0, 1H). Spectroscopic data in accordance with literature.⁵

Synthesis of *O*-benzyl protected anomeric β -deoxyribosyl acid **1b** ⁸⁻⁹



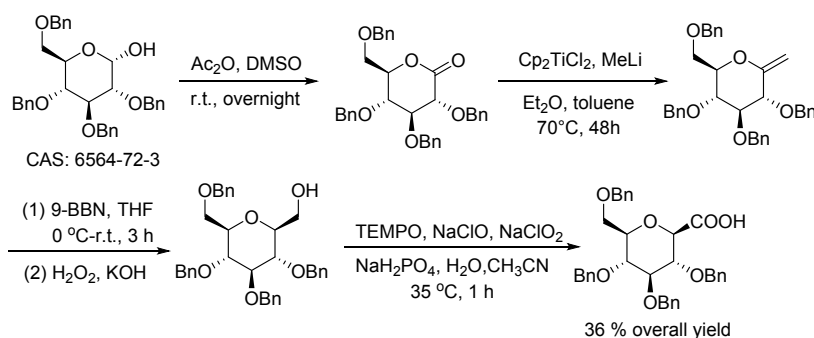
***O*-benzyl protected β -anomeric deoxyribosyl acid (1b):** ^1H NMR (400 MHz, CDCl_3) δ 7.38 – 7.25 (m, 10 H), 4.70 – 4.67 (m, 1 H), 4.61 (d, J = 12.0 Hz, 1 H), 4.54 – 4.50 (m, 2 H), 4.41 (d, J = 12.0 Hz, 1 H), 4.20 – 4.18 (m, 1 H), 4.15 – 4.12 (m, 1 H), 3.73 – 3.69 (m, 1 H), 3.54 – 3.52 (m, 1 H), 2.46 – 2.40 (m, 1 H), 2.39 – 2.30 (m, 1 H). Spectroscopic data in accordance with literature.⁹

Synthesis of *O*-benzoyl protected anomeric β -ribosyl acid 1a''¹⁰⁻¹¹



***O*-benzoyl protected anomeric β -ribosyl acid (1a'')** ^1H NMR (400 MHz, CDCl_3) δ 8.09 – 7.86 (m, 6 H), 7.61 – 7.31 (m, 9 H), 5.99 (dd, J = 5.2, 3.9 Hz, 1 H), 5.75 (dd, J = 6.3, 5.1 Hz, 1 H), 4.86 (d, J = 3.9 Hz, 1 H), 4.80 – 4.69 (m, 3 H). Spectroscopic data in accordance with literature.¹⁰

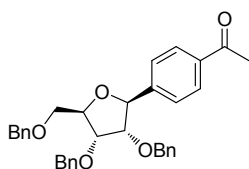
Synthesis of *O*-benzyl protected anomeric β -glucopyranosyl acid 1d¹²⁻¹⁴



***O*-benzyl protected anomeric β -glucopyranosyl acid (1d):** ^1H NMR (400 MHz, CDCl_3) δ 7.36 – 7.24 (m, 18H), 7.16 – 7.14 (m, 2H), 4.89 – 4.70 (m, 5H), 4.57 – 4.48 (m, 3H), 4.00 (d, J = 8.8 Hz, 1H), 3.81 – 3.63 (m, 5H), 3.59 – 3.55 (m, 1H). Spectroscopic data in accordance with literature.¹⁴

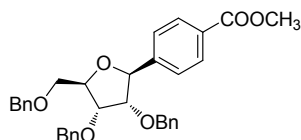
General Procedure of Photoredox/Ni dual-catalyzed Decarboxylative Cross-Coupling Reaction

To an oven-dried 25 mL-Schlenk tube equipped with a stir bar, was added NiBr_2 (4.4 mg, 0.02 mmol), bpy (3.8 mg, 0.024 mmol), K_2CO_3 (55 mg, 0.4 mmol), 4CzIPN (7.9 mg, 0.01 mmol), aromatic bromides (0.4 mmol), anomeric ribosyl/deoxyribosyl acids (0.2 mmol). Then, DMF (10 mL) was injected into the tube by syringe under a N_2 atmosphere. The mixture was degassed for 15 min by bubbling N_2 stream, then sealed with parafilm. The solution was then stirred at room temperature under the irradiation of a blue LED strip for 24 h. After completion of the reaction, the mixture was quenched by addition of 30 mL of H_2O , then extracted with ethyl acetate (3×10 mL). The combined organic layer was washed with brine and then dried over anhydrous Na_2SO_4 and evaporated in vacuum. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.



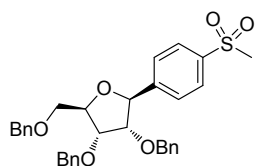
1-((2*S*,3*S*,4*R*,5*R*)-3,4-*bis*(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)phenyl

ethanone (3a): ^1H NMR (400 MHz, CDCl_3) δ 7.87 (d, $J = 8.3$ Hz, 2H), 7.49 (d, $J = 8.2$ Hz, 2H), 7.37 – 7.23 (m, 13H), 7.20 – 7.16 (m, 2H), 5.06 (d, $J = 6.9$ Hz, 1H), 4.63 – 4.53 (m, 4H), 4.52 – 4.41 (m, 2H), 4.38 – 4.35 (m, 1H), 4.01 (dd, $J = 5.1, 3.7$ Hz, 1H), 3.78 (dd, $J = 6.9, 5.2$ Hz, 1H), 3.68 (dd, $J = 10.4, 4.0$ Hz, 1H), 3.62 (dd, $J = 10.4, 3.7$ Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 197.93, 145.92, 137.95, 137.70, 137.46, 136.44, 128.37, 128.33, 128.29, 128.07, 127.82, 127.77, 127.67, 127.58, 126.25, 83.75, 81.98, 81.86, 73.43, 72.35, 71.91, 70.26, 26.60; HRMS (ESI) Calcd. for $\text{C}_{34}\text{H}_{34}\text{NaO}_5^+$ [(M+Na) $^+$] 545.2298, found 545.2305.



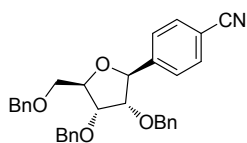
Methyl 4-((2*S*,3*S*,4*R*,5*R*)-3,4-*bis*(benzyloxy)-5-((benzyloxy)methyl) tetrahydro- furan-2-yl)

benzoate (3b): ^1H NMR (400 MHz, CDCl_3) δ 7.96 (d, $J = 8.3$ Hz, 2H), 7.47 (d, $J = 8.2$ Hz, 2H), 7.38 – 7.21 (m, 13H), 7.20 – 7.12 (m, 2H), 5.06 (d, $J = 6.9$ Hz, 1H), 4.64 – 4.52 (m, 4H), 4.50 – 4.40 (m, 2H), 4.38 – 4.35 (m, 1H), 4.01 (dd, $J = 5.0, 3.8$ Hz, 1H), 3.91 (s, 3H), 3.78 (dd, $J = 6.9, 5.2$ Hz, 1H), 3.67 (dd, $J = 10.4, 4.1$ Hz, 1H), 3.62 (dd, $J = 10.4, 3.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 166.97, 145.69, 137.94, 137.73, 137.46, 129.55, 129.39, 128.37, 128.29, 128.07, 127.80, 127.75, 127.66, 127.57, 126.09, 83.75, 81.97, 81.92, 73.42, 72.33, 71.90, 70.27, 52.03; HRMS (ESI) Calcd. for $\text{C}_{34}\text{H}_{34}\text{NaO}_6^+$ [(M+Na) $^+$] 561.2248, found 561.2254.



(2*R*,3*R*,4*S*,5*S*)-3,4-*bis*(benzyloxy)-2-((benzyloxy)methyl)-5-(4-(methylsulfonyl)phenyl)

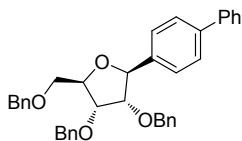
tetrahydrofuran (3c): ^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, $J = 8.4$ Hz, 2H), 7.58 (d, $J = 8.3$ Hz, 2H), 7.39 – 7.23 (m, 13H), 7.18 – 7.15 (m, 2H), 5.06 (d, $J = 7.2$ Hz, 1H), 4.60 – 4.58 (m, 2H), 4.56 – 4.51 (m, 3H), 4.41 – 4.35 (m, 2H), 4.03 (dd, $J = 5.0, 3.4$ Hz, 1H), 3.77 (dd, $J = 7.2, 5.1$ Hz, 1H), 3.68 (dd, $J = 10.3, 3.9$ Hz, 1H), 3.61 (dd, $J = 10.3, 3.5$ Hz, 1H), 3.02 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 146.94, 139.52, 137.81, 137.62, 137.27, 128.40, 128.32, 128.06, 127.87, 127.83, 127.76, 127.58, 127.24, 126.96, 83.80, 82.24, 81.35, 73.46, 72.45, 71.96, 70.25, 44.46; HRMS (ESI) Calcd. for $\text{C}_{33}\text{H}_{34}\text{NaO}_6\text{S}^+$ [(M+Na) $^+$] 581.1968, found 581.1973.



4-((2*S*,3*S*,4*R*,5*R*)-3,4-*bis*(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)benzonitrile

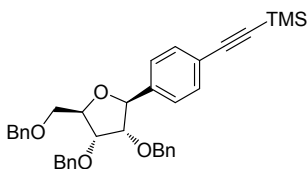
(3d): ^1H NMR (400 MHz, CDCl_3) δ 7.52 (d, $J = 8.4$ Hz, 2H), 7.47 (d, $J = 8.3$ Hz, 2H), 7.38 – 7.22 (m, 13H), 7.17 – 7.13 (m, 2H), 5.01 (d, $J = 7.2$ Hz, 1H), 4.61 – 4.50 (m, 5H), 4.39 – 4.33 (m, 2H), 4.01 (dd, $J = 5.0, 3.3$ Hz, 1H), 3.74 (dd, $J = 7.2, 5.1$ Hz, 1H), 3.67 (dd, $J = 10.3, 3.9$ Hz, 1H), 3.60 (dd, $J = 10.4, 3.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 145.95, 137.79, 137.58, 137.25, 131.97, 128.39, 128.37,

128.30, 128.07, 127.88, 127.83, 127.77, 127.74, 127.56, 126.75, 118.91, 111.21, 83.74, 82.20, 81.38, 73.44, 72.37, 71.91, 70.24; HRMS (ESI) Calcd. for $C_{33}H_{31}NNaO_4^+$ $[(M+Na)^+]$ 528.2145, found 528.2150.



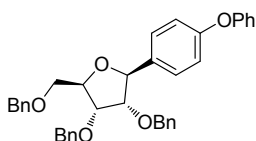
(2*S*,3*S*,4*R*,5*R*)-2-([1,1'-biphenyl]-4-yl)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)

tetrahydrofuran (3e): 1H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.57 (m, 2H), 7.53 – 7.51 (m, 2H), 7.48 – 7.40 (m, 4H), 7.38 – 7.28 (m, 11H), 7.26 – 7.22 (m, 3H), 7.21 – 7.18 (m, 2H), 5.08 (d, J = 6.7 Hz, 1H), 4.66 – 4.54 (m, 4H), 4.54 – 4.46 (m, 2H), 4.39 – 4.36 (m, 1H), 4.04 (dd, J = 4.9, 4.2 Hz, 1H), 3.86 (dd, J = 6.7, 5.2 Hz, 1H), 3.69 (dd, J = 10.4, 4.2 Hz, 1H), 3.65 (dd, J = 10.4, 3.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.94, 140.54, 139.43, 138.12, 137.90, 137.74, 128.71, 128.34, 128.25, 128.05, 127.73, 127.62, 127.57, 127.18, 127.02, 127.00, 126.70, 83.65, 82.34, 81.73, 73.43, 72.19, 71.90, 70.42; HRMS (ESI) Calcd. for $C_{38}H_{36}NaO_4^+$ $[(M+Na)^+]$ 579.2506, found 579.2510.



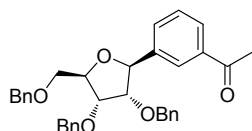
((4-((2*S*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)phenyl)

ethynyl)trimethylsilane (3f): 1H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.2 Hz, 2H), 7.37 – 7.22 (m, 15H), 7.17 – 7.15 (m, 2H), 4.99 (d, J = 6.9 Hz, 1H), 4.61 – 4.49 (m, 4H), 4.48 – 4.38 (m, 2H), 4.35 – 4.32 (m, 1H), 3.98 (dd, J = 5.2, 3.8 Hz, 1H), 3.74 (dd, J = 6.8, 5.3 Hz, 1H), 3.66 (dd, J = 10.4, 4.1 Hz, 1H), 3.60 (dd, J = 10.4, 3.9 Hz, 1H), 0.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.90, 138.01, 137.80, 137.57, 131.90, 128.37, 128.36, 128.30, 128.07, 127.78, 127.76, 127.71, 127.64, 127.56, 126.07, 122.35, 105.07, 94.02, 83.76, 82.13, 81.87, 73.41, 72.31, 71.90, 70.32, -0.03; HRMS (ESI) Calcd. for $C_{37}H_{40}NaO_4Si^+$ $[(M+Na)^+]$ 599.2588, found 599.2595.

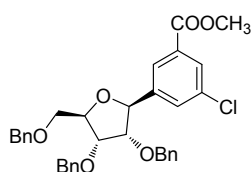


(2*R*,3*R*,4*S*,5*S*)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-5-(4-phenoxyphenyl)tetrahydrofuran

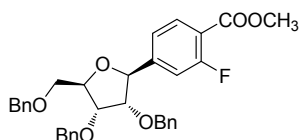
(3g): 1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.22 (m, 17H), 7.19 – 7.17 (m, 2H), 7.10 (t, J = 7.4 Hz, 1H), 7.03 – 6.97 (m, 2H), 6.96 – 6.90 (m, 2H), 5.00 (d, J = 6.9 Hz, 1H), 4.61 – 4.50 (m, 5H), 4.47 – 4.44 (m, 1H), 4.35 – 4.32 (m, 1H), 4.02 (dd, J = 5.1, 3.9 Hz, 1H), 3.81 (dd, J = 6.9, 5.3 Hz, 1H), 3.66 (dd, J = 10.4, 4.1 Hz, 1H), 3.61 (dd, J = 10.4, 3.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.30, 156.71, 138.06, 137.89, 137.74, 129.68, 128.36, 128.28, 128.09, 127.86, 127.78, 127.72, 127.67, 127.63, 127.59, 123.13, 118.78, 118.72, 82.14, 81.77, 73.45, 72.16; HRMS (ESI) Calcd. for $C_{38}H_{36}NaO_5^+$ $[(M+Na)^+]$ 595.2455, found 595.2459.



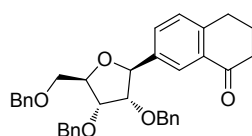
1-(3-((2*S*,3*S*,4*R*,5*R*)-3,4-*bis*(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)phenyl)ethanone (3h): ^1H NMR (400 MHz, CDCl_3) δ 7.97 (s, 1H), 7.87 (dt, $J = 7.8, 1.5$ Hz, 1H), 7.60 (dt, $J = 7.7, 1.4$ Hz, 1H), 7.41 – 7.21 (m, 14H), 7.19 – 7.13 (m, 2H), 5.07 (d, $J = 7.0$ Hz, 1H), 4.63 – 4.54 (m, 4H), 4.53 – 4.41 (m, 2H), 4.39 – 4.36 (m, 1H), 4.04 (dd, $J = 5.0, 3.8$ Hz, 1H), 3.82 (dd, $J = 6.9, 5.2$ Hz, 1H), 3.70 (dd, $J = 10.4, 4.0$ Hz, 1H), 3.63 (dd, $J = 10.4, 3.6$ Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 198.11, 140.94, 137.94, 137.72, 137.46, 137.10, 131.04, 128.54, 128.38, 128.28, 128.08, 127.82, 127.76, 127.74, 127.66, 127.51, 127.47, 126.26, 83.66, 82.00, 81.85, 73.45, 72.26, 71.88, 70.29, 26.56; HRMS (ESI) Calcd. for $\text{C}_{34}\text{H}_{34}\text{NaO}_5^+$ [(M+Na) $^+$] 545.2298, found 545.2304.



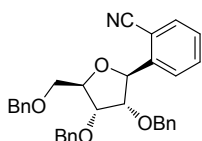
Methyl 3-((2*S*,3*S*,4*R*,5*R*)-3,4-*bis*(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)-5-chlorobenzoate (3i): ^1H NMR (400 MHz, CDCl_3) δ 7.96 (s, 1H), 7.91 (s, 1H), 7.61 (s, 1H), 7.36 – 7.23 (m, 13H), 7.19 – 7.16 (m, 2H), 5.00 (d, $J = 7.1$ Hz, 1H), 4.63 – 4.52 (m, 5H), 4.40 (d, $J = 11.9$ Hz, 1H), 4.37 – 4.34 (m, 1H), 4.02 (dd, $J = 5.1, 3.3$ Hz, 1H), 3.88 (s, 3H), 3.77 (dd, $J = 7.2, 5.0$ Hz, 1H), 3.67 (dd, $J = 10.4, 3.9$ Hz, 1H), 3.60 (dd, $J = 10.4, 3.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.77, 142.97, 137.87, 137.72, 137.28, 134.47, 131.63, 130.56, 128.82, 128.39, 128.29, 128.02, 127.92, 127.83, 127.65, 127.57, 83.74, 82.25, 81.14, 73.46, 72.49, 71.96, 70.22, 52.30; HRMS (ESI) Calcd. for $\text{C}_{34}\text{H}_{33}\text{ClNaO}_6^+$ [(M+Na) $^+$] 595.1858, found 595.1860.



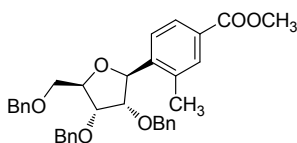
Methyl 4-((2*S*,3*S*,4*R*,5*R*)-3,4-*bis*(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)-2-fluorobenzoate (3j): ^1H NMR (400 MHz, CDCl_3) δ 7.84 (t, $J = 7.8$ Hz, 1H), 7.40 – 7.13 (m, 17H), 5.00 (d, $J = 7.1$ Hz, 1H), 4.59 – 4.53 (m, 4H), 4.51 – 4.39 (m, 2H), 4.36 – 4.34 (m, 1H), 3.99 (dd, $J = 4.9, 3.5$ Hz, 1H), 3.92 (s, 3H), 3.75 (dd, $J = 7.0, 5.1$ Hz, 1H), 3.66 (dd, $J = 10.4, 4.0$ Hz, 1H), 3.59 (dd, $J = 10.4, 3.6$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 164.82, 164.78, 163.21, 160.63, 148.45, 148.36, 137.79, 137.62, 137.28, 131.97, 128.41, 128.39, 128.33, 128.07, 127.86, 127.73, 127.64, 121.57, 121.54, 117.52, 117.42, 114.48, 114.24, 83.70, 82.13, 81.12, 73.46, 72.48, 71.93, 70.15, 52.22; HRMS (ESI) Calcd. for $\text{C}_{34}\text{H}_{33}\text{FNaO}_6^+$ [(M+Na) $^+$] 579.2153, found 579.2159.



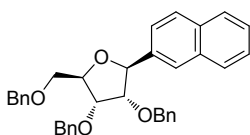
7-((2*S*,3*S*,4*R*,5*R*)-3,4-*bis*(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)-3,4-dihydronaphthalen-1(2*H*)-one (3k): ¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, *J* = 1.9 Hz, 1H), 7.54 (dd, *J* = 7.9, 2.0 Hz, 1H), 7.40 – 7.12 (m, 16H), 5.04 (d, *J* = 6.6 Hz, 1H), 4.69 – 4.54 (m, 4H), 4.52 – 4.44 (m, 2H), 4.36 – 4.33 (m, 1H), 4.01 (dd, *J* = 5.2, 4.0 Hz, 1H), 3.81 (dd, *J* = 6.6, 5.3 Hz, 1H), 3.70 – 3.59 (m, 2H), 2.94 (t, *J* = 6.0 Hz, 2H), 2.70 – 2.58 (m, 2H), 2.19 – 2.07 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 198.17, 143.89, 138.99, 138.08, 137.82, 137.59, 132.47, 131.61, 128.82, 128.34, 128.25, 128.04, 127.83, 127.74, 127.66, 127.58, 124.80, 83.55, 82.00, 81.80, 73.44, 72.25, 71.85, 70.29, 39.15, 29.48, 23.23; HRMS (ESI) Calcd. for C₃₆H₃₆NaO₅⁺ [(M+Na)⁺] 571.2455, found 571.2459.



2-((2*S*,3*S*,4*R*,5*R*)-3,4-*bis*(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)benzonitrile (3l): ¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, *J* = 7.8 Hz, 1H), 7.61 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.40 – 7.20 (m, 17H), 5.40 (d, *J* = 4.6 Hz, 1H), 4.70 – 4.46 (m, 6H), 4.42 – 4.38 (m, 1H), 4.10 (t, *J* = 5.4 Hz, 1H), 3.95 (t, *J* = 4.8 Hz, 1H), 3.85 (dd, *J* = 10.6, 3.4 Hz, 1H), 3.72 (dd, *J* = 10.7, 3.6 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 143.71, 138.00, 137.66, 137.57, 132.99, 132.83, 128.27, 128.18, 128.04, 127.85, 127.79, 127.71, 127.57, 117.51, 110.35, 82.64, 81.63, 81.32, 76.55, 73.33, 72.05, 71.95, 69.33; HRMS (ESI) Calcd. for C₃₃H₃₁NNaO₄⁺ [(M+Na)⁺] 528.2145, found 528.2143.

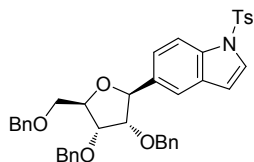


Methyl 4-((2*S*,3*S*,4*R*,5*R*)-3,4-*bis*(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)-3-methylbenzoate (3m): ¹H NMR (400 MHz, CDCl₃) δ 7.80 (s, 1H), 7.78 – 7.76 (m, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.39 – 7.21 (m, 13H), 7.16 – 7.14 (m, 2H), 5.30 (d, *J* = 6.5 Hz, 1H), 4.69 – 4.50 (m, 5H), 4.42 – 4.39 (m, 1H), 4.36 – 4.33 (m, 1H), 4.05 (t, *J* = 4.7 Hz, 1H), 3.90 (s, 3H), 3.84 (dd, *J* = 6.3, 5.2 Hz, 1H), 3.73 (dd, *J* = 10.4, 3.8 Hz, 1H), 3.64 (dd, *J* = 10.4, 3.7 Hz, 1H), 2.40 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.14, 143.78, 137.02, 137.83, 137.67, 136.03, 131.17, 128.99, 128.38, 128.26, 128.01, 127.81, 127.66, 127.59, 127.27, 126.01, 83.94, 81.65, 79.26, 77.59, 73.42, 72.52, 72.20, 70.09, 51.98, 19.43; HRMS (ESI) Calcd. for C₃₅H₃₆NaO₆⁺ [(M+Na)⁺] 575.2404, found 575.2411.

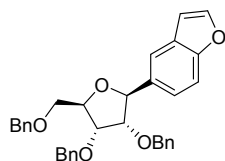


(2*R*,3*R*,4*S*,5*S*)-3,4-*bis*(benzyloxy)-2-((benzyloxy)methyl)-5-(naphthalen-2-yl)tetrahydrofuran (3n): ¹H NMR (400 MHz, CDCl₃) δ 7.88 (s, 1H), 7.83 – 7.78 (m, 1H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.72 – 7.65 (m, 1H), 7.50 – 7.40 (m, 3H), 7.38 – 7.25 (m, 10H), 7.22 – 7.17 (m, 5H), 5.20 (d, *J* = 6.4 Hz, 1H), 4.65 – 4.56 (m, 4H), 4.53 – 4.45 (m, 2H), 4.42 – 4.39 (m, 1H), 4.08 (t, *J* = 4.7 Hz, 1H), 3.91 (dd, *J* = 6.4, 5.1 Hz, 1H), 3.75 (dd, *J* = 10.4, 4.0 Hz, 1H), 3.68 (dd, *J* = 10.4, 3.8 Hz, 1H); ¹³C NMR (100

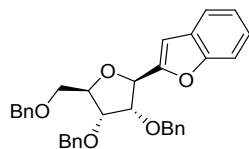
MHz, CDCl₃) δ 138.10, 137.84, 137.76, 137.65, 133.16, 133.01, 128.35, 128.32, 128.21, 128.00, 127.98, 127.76, 127.73, 127.62, 127.56, 127.55, 125.88, 125.67, 125.28, 124.09 83.48 82.77, 81.62, 73.39, 72.22, 71.89, 70.28; HRMS (ESI) Calcd. for C₃₆H₃₄NaO₄⁺ [(M+Na)⁺] 553.2349, found 553.2354.



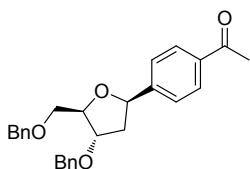
5-((2*S*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)-1-tosyl-1*H*-indole (3o): ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J* = 8.6 Hz, 1H), 7.74 – 7.70 (m, 2H), 7.55 – 7.51 (m, 2H), 7.35 – 7.27 (m, 12H), 7.23 – 7.14 (m, 4H), 7.13 – 7.06 (m, 2H), 6.51 (d, *J* = 3.6 Hz, 1H), 5.06 (d, *J* = 6.7 Hz, 1H), 4.64 – 4.52 (m, 4H), 4.49 – 4.40 (m, 2H), 4.35 – 4.32 (m, 1H), 4.04 (dd, *J* = 5.2, 4.0 Hz, 1H), 3.82 (dd, *J* = 6.7, 5.2 Hz, 1H), 3.69 (dd, *J* = 10.4, 4.0 Hz, 1H), 3.63 (dd, *J* = 10.4, 3.8 Hz, 1H), 2.32 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 144.89, 138.11, 135.49, 130.81, 129.81, 128.55, 128.38, 128.20, 128.05, 127.77, 127.70, 127.62, 127.56, 126.97, 126.75, 126.59, 123.14, 119.36, 113.36, 109.26, 83.63, 82.73, 81.71, 73.43, 72.15, 71.92, 70.37; HRMS (ESI) Calcd. for C₄₁H₃₉NNaO₆S⁺ [(M+Na)⁺] 696.2390, found 696.2397.



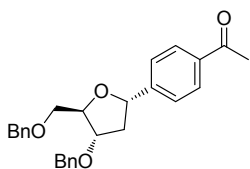
5-((2*S*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)benzofuran (3p): ¹H NMR (400 MHz, CDCl₃) δ 7.63 (d, *J* = 1.6 Hz, 1H), 7.60 (d, *J* = 2.2 Hz, 1H), 7.41, (d, *J* = 8.6 Hz, 1H), 7.36 – 7.14 (m, 16 H), 6.65 (d, *J* = 2.1 Hz, 1H), 5.12 (d, *J* = 6.6 Hz, 1H), 4.65 – 4.50 (m, 5H), 4.48 – 4.45(m, 1H), 4.38 – 4.35(m, 1H), 4.06 (t, *J* = 4.6 Hz, 1H), 3.85 (dd, *J* = 6.7, 5.2 Hz, 1H), 3.72 (dd, *J* = 10.4, 4.0 Hz, 1H), 3.66 (dd, *J* = 10.4, 3.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 154.80, 145.36, 138.34, 138.11, 137.94, 135.08, 128.59, 128.53, 128.52, 128.49, 128.39, 128.32, 128.22, 127.77, 127.74, 127.52, 122.94, 119.32, 111.25, 106.84, 84.04, 83.05, 81.85, 77.36, 73.63, 72.38, 72.10, 70.61; HRMS (ESI) Calcd. for C₃₄H₃₂NaO₅⁺ [(M+Na)⁺] 543.2147, found 543.2148.



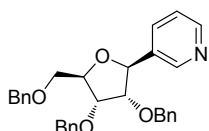
2-((2*R*,3*R*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)benzofuran (3q): ¹H NMR (400 MHz, CDCl₃) δ 7.49 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.33 – 7.18 (m, 17H), 6.70 (s, 1H), 5.18 (d, *J* = 5.3 Hz, 1H), 4.65 – 4.52 (m, 6H), 4.37 – 4.34 (m, 1H), 4.26 (t, *J* = 5.2 Hz, 1H), 4.11 (t, *J* = 5.2 Hz, 1H), 3.71 (dd, *J* = 10.7, 3.9 Hz, 1H), 3.64 (dd, *J* = 10.7, 4.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 155.24, 155.17, 138.35, 137.97, 137.67, 128.51, 128.47, 128.45, 128.25, 128.10, 128.06, 127.93, 127.92, 127.76, 127.70, 124.38, 122.85, 121.24, 111.42, 105.49, 81.66, 79.99, 77.69, 77.37, 73.63, 72.31, 72.29, 70.19; HRMS (ESI) Calcd. for C₃₄H₃₂NaO₅⁺ [(M+Na)⁺] 543.2147, found 543.2148.



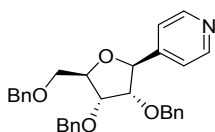
(β)-1-(4-((2R,4S,5R)-4-(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)phenyl)ethanone (β-3a1): ¹H NMR (400 MHz, CDCl₃) δ 7.91 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.38 – 7.28 (m, 10H), 5.20 (dd, *J* = 10.7, 5.3 Hz, 1H), 4.58 (d, *J* = 13.4 Hz, 4H), 4.34 (td, *J* = 4.9, 2.2 Hz, 1H), 4.18 (dt, *J* = 5.9, 1.6 Hz, 1H), 3.68 (dd, *J* = 10.1, 4.5 Hz, 1H), 3.60 (dd, *J* = 10.1, 5.2 Hz, 1H), 2.59 (s, 3H), 2.40 (ddd, *J* = 13.2, 5.3, 1.2 Hz, 1H), 1.88 (ddd, *J* = 13.3, 10.8, 5.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 198.01, 147.53, 138.21, 138.09, 136.48, 128.60, 128.60, 128.54, 127.89, 127.84, 127.82, 127.75, 126.17, 84.18, 81.54, 80.05, 73.62, 71.23, 71.14, 41.45, 26.76; HRMS (ESI) Calcd. for C₂₇H₂₈NaO₄⁺ [(M+Na)⁺] 439.1880, found 439.1886.



(α)-1-(4-((2S,4S,5R)-4-(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)phenyl)ethanone (α-3a1): ¹H NMR (400 MHz, CDCl₃) δ 7.92 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.12 (m, 10H), 5.17 (t, *J* = 7.3 Hz, 1H), 4.63 – 4.55 (m, 2H), 4.49 – 4.43 (m, 2H), 4.40 (q, *J* = 4.3 Hz, 1H), 4.26 (ddd, *J* = 6.6, 5.5, 4.1 Hz, 1H), 3.63 (dd, *J* = 4.5, 2.9 Hz, 2H), 2.66 (dt, *J* = 13.4, 6.9 Hz, 1H), 2.59 (s, 3H), 2.04 (ddd, *J* = 12.1, 7.6, 5.5 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 198.04, 148.72, 138.24, 137.99, 136.25, 128.59, 128.53, 128.49, 127.82, 127.80, 127.77, 127.71, 126.00, 83.41, 80.72, 79.86, 73.63, 71.71, 70.93, 40.96, 26.77; HRMS (ESI) Calcd. for C₂₇H₂₈NaO₄⁺ [(M+Na)⁺] 439.1880, found 439.1884.

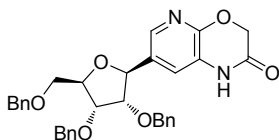


3-((2S,3S,4R,5R)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)pyridine (5a): ¹H NMR (500 MHz, CDCl₃) δ 8.62 (d, *J* = 2.1 Hz, 1H), 8.51 (dd, *J* = 4.3, 1.7 Hz, 1H), 7.71 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.37 – 7.24 (m, 14H), 7.20 – 7.14 (m, 2H), 5.02 (d, *J* = 7.4 Hz, 1H), 4.60 – 4.50 (m, 5H), 4.41 – 4.38 (m, 1H), 4.37 – 4.35 (m, 1H), 4.02 (dd, *J* = 5.1, 3.2 Hz, 1H), 3.79 (dd, *J* = 7.3, 5.1 Hz, 1H), 3.65 (dd, *J* = 10.4, 4.1 Hz, 1H), 3.59 (dd, *J* = 10.4, 3.7 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 147.14, 146.09, 137.78, 137.58, 137.19, 136.96, 135.56, 128.41, 128.35, 128.10, 127.88, 127.74, 127.66, 123.77, 83.60, 82.41, 79.73, 73.49, 72.44, 71.92, 70.27; HRMS (ESI) Calcd. for C₁₆H₂₁O₅⁺ [(M+H)⁺] 293.1389, found 293.1390.



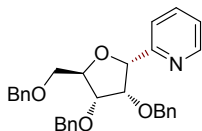
4-((2*S*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)pyridine (5b):

¹H NMR (400 MHz, CDCl₃) δ 8.49 (d, *J* = 1.6 Hz, 1H), 8.48 (d, *J* = 1.7 Hz, 1H), 7.36 – 7.25 (m, 15H), 7.20 – 7.18 (m, 2H), 4.98 (d, *J* = 6.9 Hz, 1H), 4.62 – 4.51 (m, 5H), 4.44 – 4.41 (m, 1H), 4.38 – 4.35 (m, 1H), 4.00 (dd, *J* = 5.0, 3.6 Hz, 1H), 3.75 (dd, *J* = 7.0, 5.0 Hz, 1H), 3.67 (dd, *J* = 10.4, 4.0 Hz, 1H), 3.60 (dd, *J* = 10.4, 3.7 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 149.74, 137.98, 137.73, 137.42, 128.52, 128.48, 128.22, 128.02, 127.96, 127.86, 127.73, 121.07, 83.66, 82.22, 80.93, 77.36, 77.27, 73.60, 72.55, 72.08, 70.32; HRMS (ESI) Calcd. for C₃₁H₃₂N₂O₄⁺ [(M+H)⁺] 482.2331, found 482.2332.



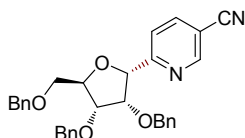
7-((2*S*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)-1*H*-pyrido

[2,3-*b*][1,4]oxazin-2(3*H*)-one (5c): ¹H NMR (400 MHz, CDCl₃) δ 7.80 (d, *J* = 2.0 Hz, 1H), 7.47 (s, 1H), 7.40 – 7.33 (m, 8H), 7.31 – 7.22 (m, 4H), 7.20 – 7.17 (m, 2H), 7.07 (d, *J* = 2.0 Hz, 1H), 4.96 (d, *J* = 6.7 Hz, 1H), 4.71 (s, 2H), 4.66 (d, *J* = 12.1 Hz, 1H), 4.60 (d, *J* = 4.2 Hz, 1H), 4.57 (d, *J* = 4.2 Hz, 1H), 4.56 – 4.49 (m, 2H), 4.43 (d, *J* = 12.0 Hz, 1H), 4.35 – 4.32 (m, 1H), 4.07 (dd, *J* = 4.9, 3.6 Hz, 1H), 3.81 (dd, *J* = 6.8, 4.9 Hz, 1H), 3.74 (dd, *J* = 10.4, 3.4 Hz, 1H), 3.64 (dd, *J* = 10.5, 2.7 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 164.07, 150.34, 140.14, 138.03, 137.67, 137.31, 131.92, 128.64, 128.47, 128.35, 128.31, 128.01, 127.95, 127.90, 127.78, 121.84, 120.62, 83.34, 82.02, 79.69, 73.57, 72.38, 72.04, 70.37, 67.17; HRMS (ESI) Calcd. for C₃₃H₃₂N₂NaO₆⁺ [(M+Na)⁺] 575.2153, found 575.2158.



2-((2*R*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)pyridine (5d):

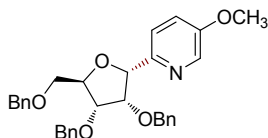
¹H NMR (400 MHz, CDCl₃) δ 8.58 (d, *J* = 4.8 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.37 – 7.21 (m, 14H), 7.16 – 7.13 (m, 2H), 5.24 (d, *J* = 3.0 Hz, 1H), 4.78 (d, *J* = 12.0 Hz, 1H), 4.67 (d, *J* = 12.0 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.57 (d, *J* = 4.9 Hz, 1H), 4.54 (d, *J* = 5.1 Hz, 1H), 4.45 – 4.39 (m, 2H), 4.16 (dd, *J* = 4.9, 3.5 Hz, 1H), 3.99 (dd, *J* = 7.2, 5.1 Hz, 1H), 3.84 (dd, *J* = 10.7, 3.1 Hz, 1H), 3.69 (dd, *J* = 10.7, 4.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 159.70, 148.87, 138.21, 137.89, 137.84, 136.69, 128.27, 128.26, 128.21, 127.75, 127.64, 127.59, 127.50, 122.45, 121.36, 84.70, 81.31, 80.79, 73.30, 71.95, 71.46, 69.60; HRMS (ESI) Calcd. For C₃₁H₃₂NO₄⁺ [(M+H)⁺] 482.2326, found 482.2332.



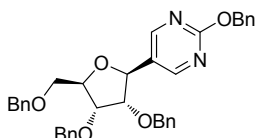
6-((2*R*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)nicotinonitrile

(5e): ¹H NMR (400 MHz, CDCl₃) δ 8.79 (dd, *J* = 2.2, 0.9 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.65 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.38 – 7.23 (m, 15H), 5.25 (d, *J* = 2.9 Hz, 1H), 4.78 (d, *J* = 12.1 Hz, 1H), 4.68 (d, *J* = 12.1 Hz, 1H), 4.59 – 4.50 (m, 3H), 4.44 – 4.41 (m, 1H), 4.36 (d, *J* = 11.9 Hz, 1H), 4.09 (dd, *J*

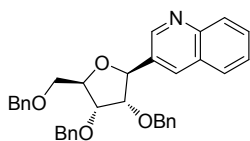
= 4.9, 3.0 Hz, 1H), 3.95 (dd, J = 7.5, 4.9 Hz, 1H), 3.87 (dd, J = 10.8, 2.8 Hz, 1H), 3.67 (dd, J = 10.8, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 164.58, 151.57, 139.70, 137.98, 137.60, 137.47, 128.36, 128.32, 128.26, 127.83, 127.80, 127.75, 127.73, 127.76, 121.19, 116.80, 108.26, 76.16, 73.38, 72.03, 71.55, 69.03; HRMS (ESI) Calcd. for $\text{C}_{32}\text{H}_{30}\text{N}_2\text{NaO}_4^+$ [(M+Na) $^+$] 529.2098, found 529.2301.



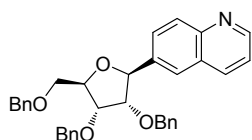
2-((2*R*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)-5-methoxypyridine (5f): ^1H NMR (400 MHz, CDCl_3) δ 8.27 (d, J = 2.9 Hz, 1H), 7.47 (d, J = 8.6 Hz, 1H), 7.35 – 7.23 (m, 15H), 7.03 (dd, J = 8.6, 2.9 Hz, 1H), 5.17 (d, J = 3.7 Hz, 1H), 4.72 (d, J = 12.1 Hz, 1H), 4.64 – 4.53 (m, 4H), 4.44 – 4.37 (m, 2H), 4.16 – 4.13 (m, 1H), 3.99 (dd, J = 6.8, 5.2 Hz, 1H), 3.83 (s, 3H), 3.80 (dd, J = 10.7, 3.3 Hz, 1H), 3.67 (dd, J = 10.7, 4.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 154.83, 151.48, 138.25, 137.95, 137.91, 136.75, 128.27, 128.20, 128.05, 127.79, 127.62, 127.56, 127.50, 121.98, 120.72, 84.22, 81.23, 80.86, 73.30, 71.93, 71.54, 69.75; HRMS (ESI) Calcd. for $\text{C}_{32}\text{H}_{33}\text{NNaO}_5^+$ [(M+Na) $^+$] 534.2251, found 534.2257.



2-(benzyloxy)-5-((2*S*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)pyrimidine (5g): ^1H NMR (400 MHz, CDCl_3) δ 8.48 (s, 2H), 7.49 (d, J = 7.2 Hz, 2H), 7.39 – 7.19 (m, 16H), 7.15 – 7.13 (m, 2H), 5.44 (s, 2H), 4.92 (d, J = 8.0 Hz, 1H), 4.61 – 4.48 (m, 5H), 4.36 – 4.31 (m, 2H), 4.01 (dd, J = 5.0, 2.5 Hz, 1H), 3.78 (dd, J = 8.0, 5.1 Hz, 1H), 3.59 (dd, J = 10.3, 4.0 Hz, 1H), 3.53 (dd, J = 10.3, 3.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 164.90, 157.67, 137.72, 137.61, 137.12, 136.53, 128.46, 128.44, 128.37, 128.15, 127.96, 127.93, 127.90, 127.79, 127.67, 126.90, 83.44, 82.60, 77.91, 73.54, 72.56, 71.93, 70.38, 69.02; HRMS (ESI) Calcd. for $\text{C}_{37}\text{H}_{37}\text{N}_2\text{O}_5^+$ [(M+H) $^+$] 589.2697, found 589.2703.

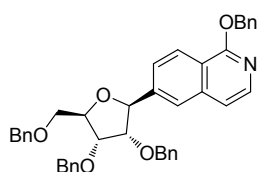


3-((2*S*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)quinoline (5h): ^1H NMR (400 MHz, CDCl_3) δ 8.91 (d, J = 2.2 Hz, 1H), 8.17 (d, J = 1.8 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.71 – 7.67 (m, 1H), 7.60 – 7.58 (m, 1H), 7.51 – 7.47 (m, 1H), 7.36 – 7.27 (m, 10H), 7.22 – 7.16 (m, 5H), 5.22 (d, J = 6.9 Hz, 1H), 4.65 – 4.54 (m, 5H), 4.46 – 4.42 (m, 2H), 4.10 – 4.08 (m, 1H), 3.91 (dd, J = 6.9, 5.1 Hz, 1H), 3.74 (dd, J = 10.4, 3.9 Hz, 1H), 3.66 (dd, J = 10.4, 3.5 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 149.22, 147.72, 137.92, 137.68, 137.27, 133.24, 133.19, 129.22, 129.01, 128.41, 128.38, 128.29, 128.05, 127.88, 127.84, 127.81, 127.75, 127.67, 127.60, 126.56, 83.58, 82.12, 80.46, 73.48, 72.49, 71.96, 70.22; HRMS (ESI) Calcd. for $\text{C}_{35}\text{H}_{34}\text{NO}_4^+$ [(M+H) $^+$] 532.2482, found 532.2489.



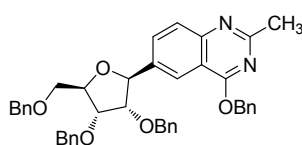
6-((2*S*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)quinoline

(5i): ^1H NMR (400 MHz, CDCl_3) δ 8.88 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.02 (d, $J = 8.7$ Hz, 1H), 7.92 (d, $J = 7.4$ Hz, 1H), 7.85 (d, $J = 1.4$ Hz, 1H), 7.70 (dd, $J = 8.8, 1.8$ Hz, 1H), 7.36 – 7.29 (m, 11H), 7.22 – 7.15 (m, 5H), 5.21 (d, $J = 6.5$ Hz, 1H), 4.66 – 4.58 (m, 4H), 4.54 (d, $J = 12.3$ Hz, 2H), 4.46 (d, $J = 12.0$ Hz, 1H), 4.43 – 4.41 (m, 1H), 4.09 (t, $J = 4.6$ Hz, 1H), 3.90 (dd, $J = 6.5, 5.2$ Hz, 1H), 3.77 (dd, $J = 10.4, 3.9$ Hz, 1H), 3.69 (dd, $J = 10.4, 3.5$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 150.15, 147.92, 138.75, 138.04, 137.80, 137.52, 136.18, 129.35, 128.39, 128.36, 128.24, 128.01, 127.96, 127.78, 127.74, 127.70, 127.65, 127.60, 125.14, 121.08, 83.57, 82.30, 81.86, 73.47, 72.34, 71.98, 70.28; HRMS (ESI) Calcd. for $\text{C}_{35}\text{H}_{34}\text{NO}_4^+$ $[(\text{M}+\text{H})^+]$ 532.2482, found 532.2487.



1-(benzyloxy)-6-((2*S*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)isoquinoline (5j):

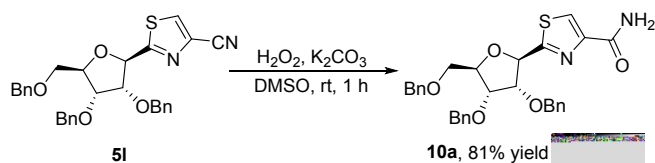
^1H NMR (400 MHz, CDCl_3) δ 8.22 (d, $J = 8.6$ Hz, 1H), 7.97 (d, $J = 5.9$ Hz, 1H), 7.78 (s, 1H), 7.56 – 7.52 (m, 3H), 7.43 – 7.39 (m, 2H), 7.37 – 7.25 (m, 11H), 7.24 – 7.15 (m, 5H), 7.06 (d, $J = 5.8$ Hz, 1H), 5.58 (s, 2H), 5.18 (d, $J = 6.5$ Hz, 1H), 4.64 – 4.39 (m, 7H), 4.06 (t, $J = 4.6$ Hz, 1H), 3.86 (dd, $J = 6.5, 5.1$ Hz, 1H), 3.75 (dd, $J = 10.4, 3.9$ Hz, 1H), 3.67 (dd, $J = 10.4, 3.7$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.22, 143.07, 139.70, 138.03, 137.93, 137.78, 137.51, 137.38, 128.42, 128.40, 128.37, 128.28, 128.03, 127.83, 127.80, 127.76, 127.65, 127.58, 124.86, 124.29, 123.23, 119.24, 115.33, 83.69, 82.32, 81.86, 73.46, 72.40, 71.99, 70.23, 67.72; HRMS (ESI) Calcd. for $\text{C}_{42}\text{H}_{40}\text{NO}_5^+$ $[(\text{M}+\text{H})^+]$ 638.2901, found 638.2907.



4-(benzyloxy)-6-((2*S*,3*S*,4*R*,5*R*)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)-2-methylquinazoline (5k):

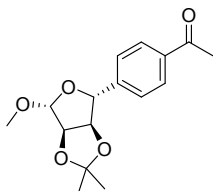
^1H NMR (400 MHz, CDCl_3) δ 8.36 (d, $J = 1.9$ Hz, 1H), 7.79 (dd, $J = 8.5, 2.0$ Hz, 1H), 7.55 (d, $J = 8.4$ Hz, 1H), 7.35 – 7.16 (m, 20H), 5.43 – 5.35 (m, 2H), 5.14 (d, $J = 6.9$ Hz, 1H), 4.64 – 4.37 (m, 7H), 4.04 (dd, $J = 5.2, 3.7$ Hz, 1H), 3.86 (dd, $J = 7.0, 5.2$ Hz, 1H), 3.71 – 3.63 (m, 2H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.16, 154.54, 146.85, 139.13, 137.98, 137.78, 137.50, 135.81, 132.78, 128.88, 128.33, 128.23, 128.06, 127.76, 127.68, 127.64, 127.59, 126.69, 126.46, 124.61, 120.08, 83.83, 82.01, 81.96, 73.47, 72.33, 71.88, 70.37, 47.08, 23.30; HRMS (ESI) Calcd. for $\text{C}_{42}\text{H}_{40}\text{N}_2\text{NaO}_5^+$ $[(\text{M}+\text{Na})^+]$ 675.2829, found 675.2839.

The synthesis of O-benzyl protected tiazofurin 10a¹⁵

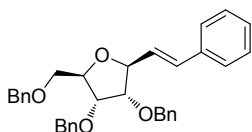


To a stirred solution of **5I** (0.1 mmol) in DMSO (3 mL) was added K_2CO_3 (55 mg, 0.4 mmol) and H_2O_2 (30 %, 1.8 mL) at 0 °C. The resulting mixture was stirred for 1 h at room temperature, then quenched with Na_2SO_3 at 0 °C. The product was extracted with ethyl acetate (3×10 mL), washed with saturated NaCl and dried with Na_2SO_4 . The solvent was evaporated in vacuum, and the product was purified by column chromatography (petroleum ether/ethyl acetate = 1:1, v/v) on silica gel to give the desired product.

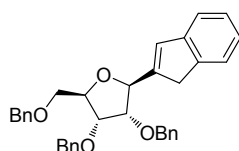
2-((2R,3R,4R,5R)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)thiazole-4-carboxamide (10a): 1H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.34 – 7.25 (m, 15H), 7.05 (brs, 1H), 5.68 (brs, 1H), 5.32 (d, J = 4.6 Hz, 1H), 4.68 – 4.49 (m, 6H), 4.42 – 4.39 (m, 1H), 4.17 (t, J = 4.8 Hz, 1H), 4.00 (t, J = 5.3 Hz, 1H), 3.71 (dd, J = 10.5, 2.8 Hz, 1H), 3.61 (dd, J = 10.8, 4.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.64, 163.13, 149.54, 138.09, 137.74, 137.47, 128.56, 128.55, 128.52, 128.23, 128.13, 128.03, 128.02, 127.81, 127.69, 124.85, 82.21, 82.17, 81.24, 77.36, 73.60, 72.46, 72.41, 69.91; HRMS (ESI) Calcd. for $C_{30}H_{30}N_2NaO_5S^+$ [(M+Na) $^+$] 553.1773, found 553.1774.



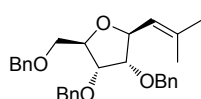
1-(4-((3aR,4R,6R,6aR)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)phenyl)ethan-1-one (3a2): 1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.2 Hz, 2H), 5.28 (d, J = 1.5 Hz, 1H), 5.16 (s, 1H), 4.86 (dd, J = 6.0, 2.1 Hz, 1H), 4.66 (d, J = 6.0 Hz, 1H), 3.39 (s, 3H), 2.60 (s, 3H), 1.59 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.87, 145.98, 136.46, 128.59, 126.40, 113.22, 110.30, 88.72, 85.77, 55.72, 26.94, 26.76, 25.33; HRMS (ESI) Calcd. for $C_{31}H_{32}NO_4^+$ [(M+H) $^+$] 482.2326, found 482.2330.



(2R,3R,4S,5S)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-5-((E)-styryl)tetrahydrofuran (7a): 1H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.20 (m, 20H), 6.69 (dd, J = 15.9, 1.1 Hz, 1H), 6.11 (dd, J = 15.9, 7.1 Hz, 1H), 4.65 – 4.50 (m, 7H), 4.28 – 4.25 (m, 1H), 3.99 (t, J = 4.8 Hz, 1H), 3.77 (dd, J = 6.3, 5.3 Hz, 1H), 3.62 – 3.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.13, 137.92, 137.81, 136.59, 132.49, 128.44, 128.33, 128.00, 127.88, 127.73, 127.65, 127.58, 127.56, 126.57, 81.90, 81.62, 81.46, 77.57, 73.43, 72.21, 71.97, 70.29; HRMS (ESI) Calcd. for $C_{34}H_{34}NaO_4^+$ [(M+Na) $^+$] 529.2349, found 529.2354.



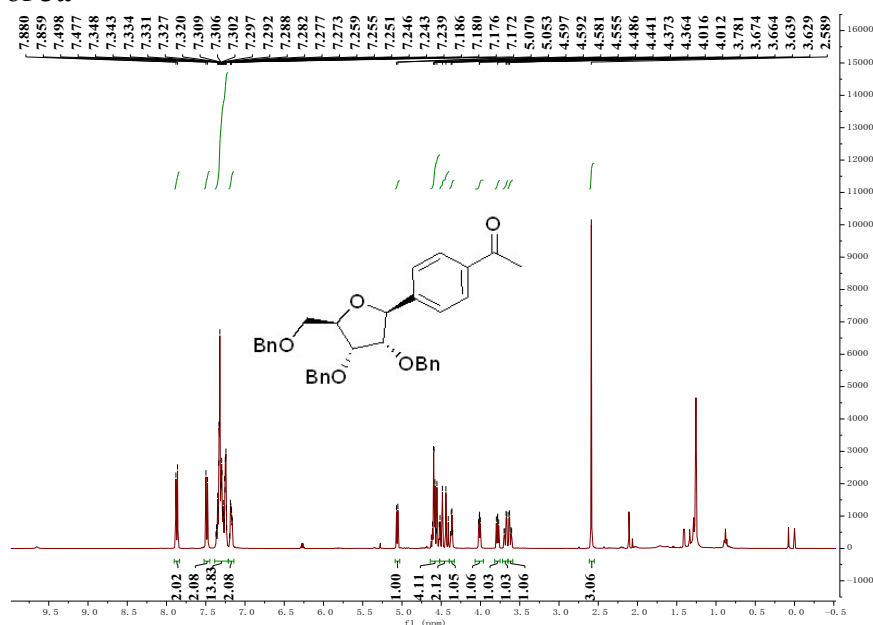
(2R,3R,4S,5S)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-5-(1H-inden-2-yl)tetrahydrofuran (7b): ^1H NMR (400 MHz, CDCl_3) δ 7.35 – 7.21 (m, 18H), 7.13 (td, $J = 7.4, 1.3$ Hz, 1H), 6.81 (s, 1H), 4.98 (d, $J = 6.2$ Hz, 1H), 4.62 – 4.50 (m, 6H), 4.32 – 4.29 (m, 1H), 4.01 (t, $J = 4.7$ Hz, 1H), 3.85 (dd, $J = 6.3, 5.1$ Hz, 1H), 3.64 – 3.57 (m, 2H), 3.36 (d, $J = 22.7$ Hz, 1H), 3.16 (d, $J = 22.7$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 147.35, 144.41, 143.25, 138.11, 137.83, 137.64, 128.79, 128.33, 128.31, 128.03, 127.85, 127.75, 127.73, 127.57, 126.23, 124.40, 123.60, 120.82, 81.36, 81.27, 79.86, 77.52, 73.41, 72.10, 71.90, 70.38, 37.90; HRMS (ESI) Calcd. for $\text{C}_{35}\text{H}_{34}\text{NaO}_4^+$ $[(\text{M}+\text{Na})^+]$ 541.2349, found 541.2354.

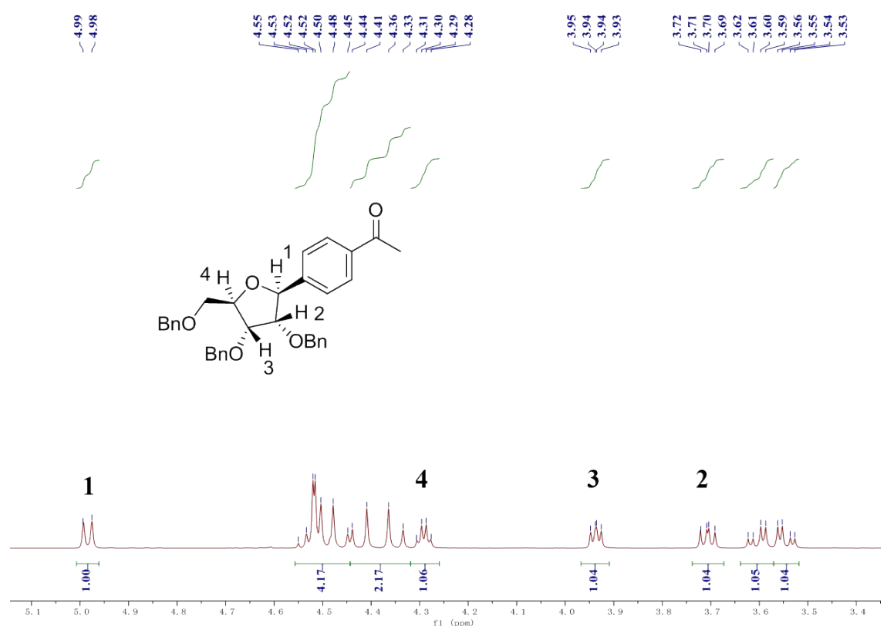


(2R,3R,4S,5S)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-5-(2-methylprop-1-en-1-yl)tetrahydrofuran (7c): ^1H NMR (400 MHz, CDCl_3) δ 7.36 – 7.23 (m, 15H), 5.11 (dt, $J = 9.1, 1.5$ Hz, 1H), 4.72 (dd, $J = 9.1, 6.7$ Hz, 1H), 4.63 – 4.47 (m, 6H), 4.16 (dd, $J = 8.4, 4.4$ Hz, 1H), 3.91 (dd, $J = 5.5, 4.1$ Hz, 1H), 3.63 (dd, $J = 6.7, 5.5$ Hz, 1H), 3.50 (d, $J = 4.3$ Hz, 2H), 1.75 – 1.73 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 138.36, 138.16, 138.09, 137.99, 128.26, 128.22, 128.04, 127.64, 127.55, 127.48, 123.58, 82.03, 81.29, 77.73, 73.36, 72.01, 71.85, 70.43, 29.63, 25.93, 18.47; HRMS (ESI) Calcd. for $\text{C}_{30}\text{H}_{34}\text{NaO}_4^+$ $[(\text{M}+\text{Na})^+]$ 481.2349, found 481.2356.

The determination of the anomeric configuration of 3a and 5d

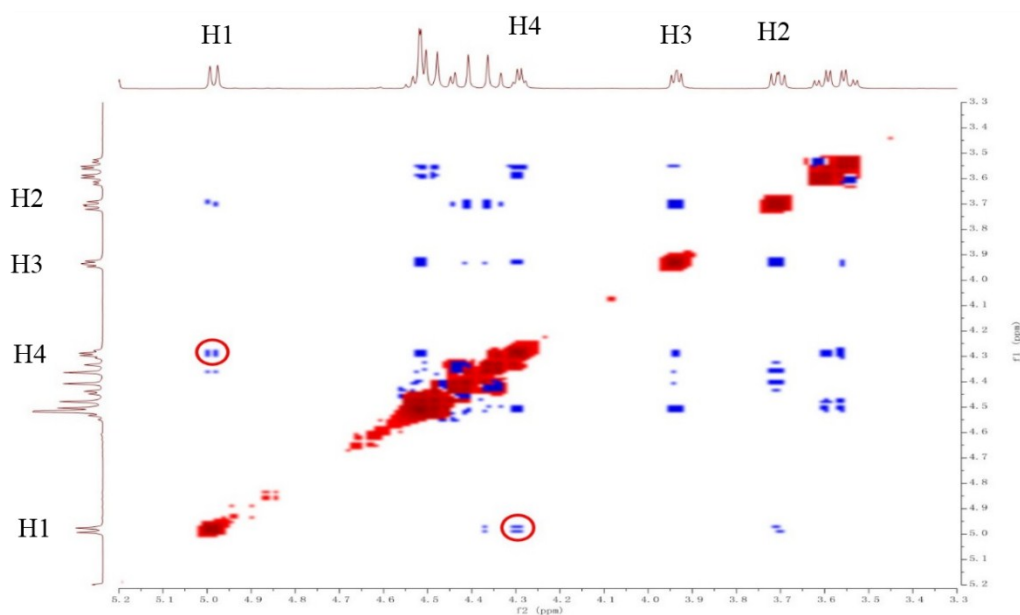
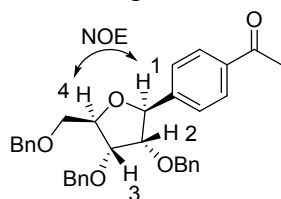
^1H NMR spectra of 3a



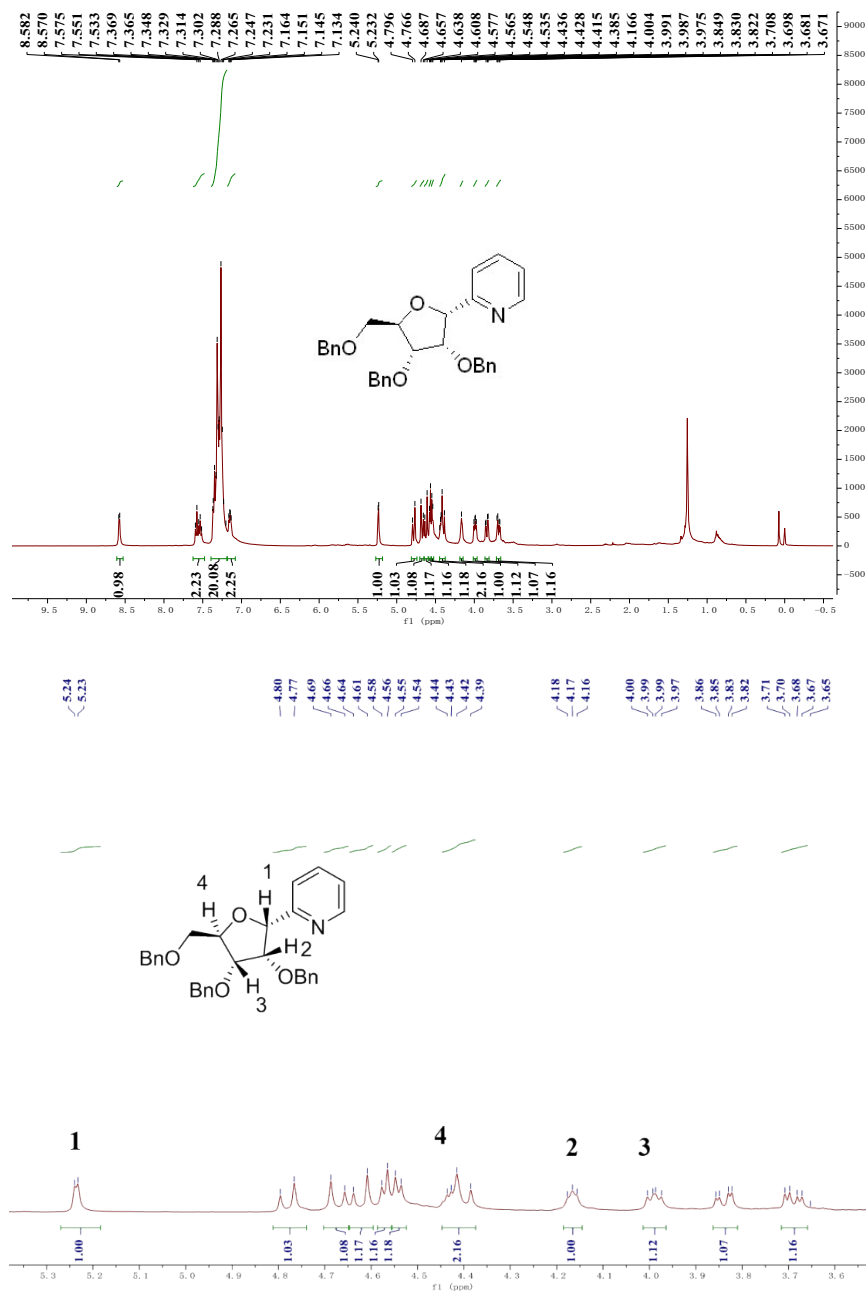


S.No	1H-position	Chemical shift (δ ppm)	Multiplicity	Number of 1Hs
1	1	5.06	d ($J = 6.9$ Hz)	1
2	4	4.38 – 4.35	m	1
3	3	4.01	dd ($J = 5.1, 3.7$ Hz)	1
4	2	3.78	dd ($J = 6.9, 5.2$ Hz)	1

NOESY spectra of **3a**

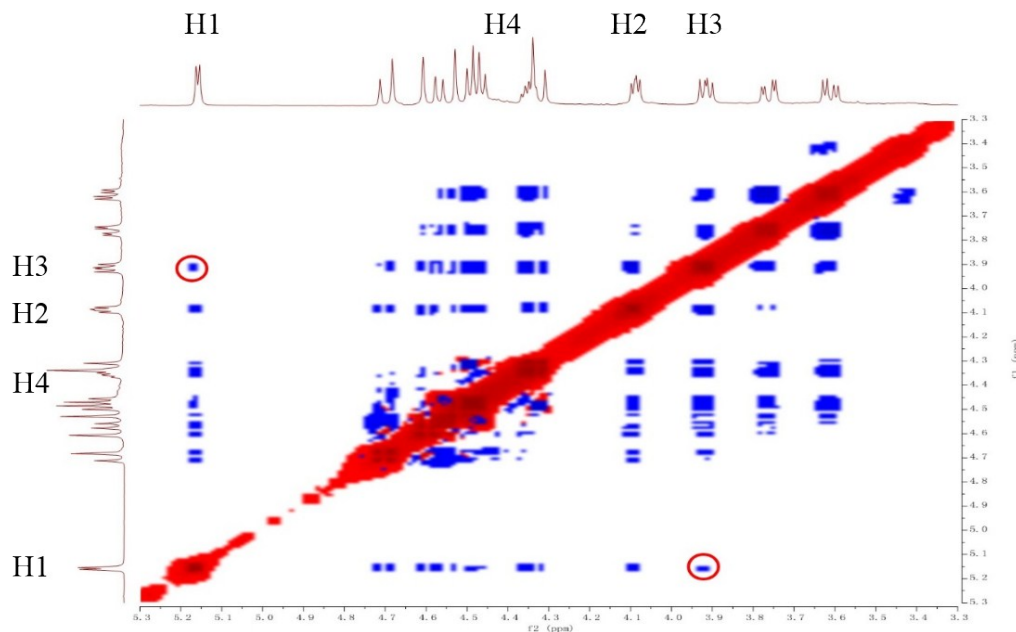
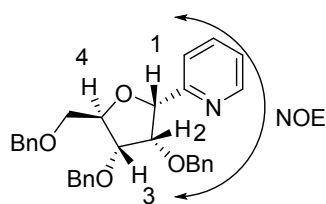


HNMR spectra of **5d**



S.No	1H-position	Chemical shift (δ ppm)	Multiplicity	Number of 1Hs
1	1	5.24	d ($J = 3.0$ Hz)	1
2	4	4.45 – 4.41	m	1
3	2	4.16	dd ($J = 4.9, 3.5$ Hz)	1
4	3	3.99	dd ($J = 7.2, 5.1$ Hz)	1

NOESY spectra of **5d**



Reference

1. É. Bokor, S. Kun, D. Goyard, M. Tóth, J. P. Praly, S. Vidal, L. Somsák, *Chem. Rev.* **2017**, *117*, 1687-1764.
2. K. Kitamura, Y. Ando, T. Matsumoto, K. Suzuki, *Chem. Rev.* **2018**, *118*, 1495-1598.
3. Y. Yang, B. Yu, *Chem. Rev.* **2017**, *117*, 12281-12356.
4. A. Tokarenko, L. P. Slavětínská, B. Klepetářová, M. Hocek, *Eur. J. Org. Chem.* **2015**, 7962-7983.
5. H. Togo, S. Ishigami, M. Fujii, T. Ikuma, M. Yokoyama, *J. Chem. Soc. Perkin Trans. 1* **1994**, 2931-2942.
6. E. R. van Rijssel, P. van Delft, G. Lodder, H. S. Overkleeft, G. A. van der Marel, D. V. Filippov, J. D. C. Codée, *Angew. Chem. Int. Ed.* **2014**, *53*, 10381-10385.
7. L. Araki, K. Morita, M. Yamaguchi, Z.-Y. Zhao, T. J. Wilson, D. M. J. Lilley, S. Harusawa, *J. Org. Chem.* **2009**, *74*, 2350-2356.
8. R. M. Adlington, J. E. Baldwin, G. J. Pritchard, K. C. Spencer, *Tetrahedron Lett.* **2000**, *41*, 575-578.
9. M. Takase, T. Morikawa, H. Abe, M. Inouye, *Org. Lett.* **2003**, *5*, 625-628.
10. P. J. Dudfield, V.-D. Le, S. D. Lindell, C. W. Rees, *J. Chem. Soc. Perkin Trans. 1* **1999**, 2937-2942.
11. Y. Kitamura, K. Edayoshi, Y. Kitade, *Tetrahedron Lett.* **2012**, *53*, 6987-6989.
12. L.-T. Li, L.-F. Zhou, Y.-J. Li, J. Huang, R.-H. Liu, B. Wang, P. Wang, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 642-644.
13. T. V. RajanBabu, G. S. Reddy, *J. Org. Chem.* **1986**, *51*, 5458-5461.
14. D. Sawada, S. Sasayama, H. Takahashi, S. Ikegami, *Tetrahedron* **2008**, *64*, 8780-8788.

15. G.-Y. Wang, J.-Q. Wan, Y.-J. Hu, X.-Y. Wu, M. Prhavc, N. Dyatkina, V. K. Rajwanshi, D. B. Smith, A. Jekle, A. Kinkade, J. A. Symons, Z.-N. Jin, J. Deval, Q.-L. Zhang, Y. Tam, S. Chanda, L. Blatt, L. Beigelman, *J. Med. Chem.* **2016**, *59*, 4611-4624.

Spectral Data for Products

