Hydrogen-Bonding Catalysis and Inhibition by Simple Solvents in the Stereoselective Kinetic Epoxide-Opening Spirocyclization of Glycal Epoxides to Form Spiroketals

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Supporting Information

A. MATERIALS AND METHODS

Reagents were obtained from Aldrich Chemical (www.sigma-aldrich.com), Strem (www.strem.com), or Acros Organics (www.fishersci.com) and used without further purification unless otherwise indicated. Solvents (Optima or HPLC grade) were obtained from Fisher Scientific (www.fishersci.com), degassed with Ar, and purified on a solvent drying system as described[1] unless otherwise indicated. Reactions were performed in flame-dried glassware under positive Ar pressure with magnetic stirring. Cold baths were generated as follows: 0 °C, wet ice/water; –20 °C, dry ice/ CCl_4; –44 °C, dry ice/CH_3CN; –63 °C, dry ice/chloroform; –78 °C, dry ice/acetone.

TLC was performed on 0.25 mm E. Merck silica gel 60 F254 plates and visualized under UV light (254 nm) or by staining with potassium permanganate ($KMnO_4$), cerium ammonium molybdenate (CAM). Silica flash chromatography was performed on E. Merck 230–400 mesh silica gel 60. Optical rotations were recorded on a JASCO model PTC-103T digital polarimeter. IR spectra were recorded on a Bruker Optics Tensor 27 FTIR spectrometer with peaks reported in cm^{-1}. NMR spectra were recorded on Bruker UltraShield Plus 500 MHz instruments at 24 °C in $CDCl_3$ unless otherwise indicated. Chemical shifts are expressed in ppm relative to TMS (^1H, 0 ppm) or solvent signals: $CDCl_3$ (^{13}C, 77.0 ppm), C_6D_6 (^1H, 7.16 ppm; ^{13}C, 128.0 ppm), CD_2Cl_2 (^1H, 5.31 ppm; ^{13}C, 53.5 ppm), CD_3OD (^1H, 3.31 ppm; ^{13}C, 63.1 ppm) or acetone-d_6 (^{13}C, 206.2 ppm); coupling constants are expressed in Hz. Mass spectra were obtained at the MSKCC Analytical Core Facility on a Waters Acquity TM mass spectrometer by electrospray (ESI) ionization or atmospheric pressure chemical ionization (AP-CI). Curve fits were carried out using GraphPad Prism version 5.0a (GraphPad Software, Inc, La Jolla, CA).

N.B.: Atom numbering in IUPAC compound names herein does not correspond to conventional carbohydrate nomenclature and is used for naming purposes only. Atom numbering in the text and paper corresponds to conventional carbohydrate nomenclature. Compounds not cited in the paper are numbered herein **S1–S30**.

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[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.

B. General procedure for epoxidation and spontaneous spirocyclization (Table 1 of manuscript)

Glycal alcohols **5–7** (1.0 equiv) were dissolved in CH_2Cl_2 (final ratio 6:1 CH_2Cl_2/acetone) and cooled to –78 °C. DMDO (0.073 M in acetone, 1.2 equiv) was added via syringe and the mixture was stirred at –78 °C for 10 min. The reaction was warmed to rt and concentrated by rotary evaporation. The crude reaction mixtures were analyzed by ^{1}H-NMR to determine the ratios listed in Table 1 of the manuscript. Spiroketal retention products **11–13** were purified from product mixtures by silica flash chromatography (20:1–10:1 hexanes/EtOAc with 0.5% Et_3N).

C. General procedure for epoxidation and MeOH-induced spirocyclization (Table 2 of manuscript)

The glycal alcohol **5–7** (1.0 equiv) was dissolved in 5:1 MeOH/CH_2Cl_2 (final ratio after DMDO addition = 5:1:1 MeOH/CH_2Cl_2/acetone) and cooled to –63 °C. DMDO (0.073 M in acetone, 1.2 equiv) was added via syringe, and the reaction mixture was stirred at –63 °C for 3 h. The reaction was warmed to rt and concentrated by rotary evaporation. The crude reaction mixtures were analyzed by ^{1}H-NMR to determine the ratios listed in Table 2 of the manuscript. Silica flash chromatography (20:1–10:1 hexanes/EtOAc with 0.5% Et_3N) of product mixtures provided contrathermodynamic spiroketals **8–10**.

D. General procedure for temperature dependent spirocyclization (Table 3 of manuscript)

The glycal substrate (1.0 equiv) was added as a solution in $CDCl_3$ to an oven-dried, Ar-flushed 5 mm NMR tube. The tube was capped with a rubber septum. The appropriate amount of additional deuterated solvent (CD_3OD, $CDCl_3$) was added, followed by brief mixing and cooling to –78 °C. DMDO (0.073 M in acetone, 1.2 equiv), removed from a –80 °C freezer and used immediately, was added and the tube was shaken vigorously for 3 s, then warmed to –44 °C (except for entry 1, where the epoxide was kept at –78 °C). The tube was transferred quickly to the NMR instrument which was precooled to –40 °C (or –63 °C for entry 1). The sample was locked and shimmed and the NMR was tuned (3 min), then the sample was warmed to the temperature indicated in the table to initiate the spirocyclization reaction. Reactions were run to completion over 2 h and crude ^{1}H-NMR spectra were analyzed. Integration of the C2 proton of spiroketal **18** (δ 3.22) and methyl glycoside **20** (δ 3.33) gave the ratio shown in entry 2. Integration of the benzylic protons of spiroketal **9c** (δ 2.90, 2H) and spiroketal **12c** (δ 2.52, 3.12, 2H) gave the ratio shown in entry 6. Integration of a benzylic proton of spiroketal **13c** (δ 2.44) and methyl glycoside **16c** (δ 2.66) gave the ratio shown in entry 7.

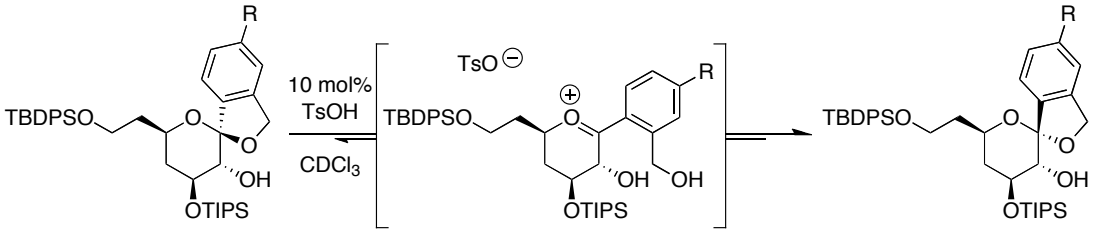
E. KINETIC STUDIES

1. NMR ANALYSIS OF TOSIC ACID EPIMERIZATION OF CONTRATHERMODYNAMIC SPIROKETALS

Contrathermodynamic spiroketals **8b–f** (1.0 equiv) were added as a solution in $CDCl_3$ (0.011 M) to an oven-dried, Ar-flushed 5 mm NMR tube. To each of the $CDCl_3$ solutions was added tosic acid monohydrate (0.1 equiv) as a stock solution in THF-d_8 (0.026 M) for a final tosic acid concentration of 0.0012 M. The tubes were shaken vigorously for 5 s and a timer was started. Conversion of **8b–f** to **11b–f** was recorded over time by NMR integration of the benzylic proton signals (5.00–5.30 ppm) (Table S1, Figure S1). The observed rates of epimerization were calculated based on the method of initial rates (Table S2).[2] For spiroketal **8f** (R = NO_2), no equilibration to spiroketal **11f** was observed under these conditions over >72 h.

Following the above procedure, contrathermodynamic spiroketal **8a** (1.0 equiv) was prepared as a solution in $CDCl_3$ (0.011 M), except in a flame-dried 4 mL vial. To the $CDCl_3$ solution was added tosic acid monohydrate (0.1 equiv) as a stock solution in THF-d_8 (0.026 M) for a final tosic acid concentration of 0.0012 M. At the indicated times in Table S1, the reaction was quenched by the immediate addition of 5 vol. satd aq $NaHCO_3$ and extracted with EtOAc. The organic layer was dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. The product ratio of **8a** to **11a** was determined by NMR as described above.

Table S1. Sample of kinetic data for tosic acid equilibration at room temperature using NMR for each substituted spiroketal **8a–f** (Figure 3b of manuscript).[a]



contrathermodynamic (C1-inversion) **8a–f** | *oxocarbenium intermediate* **21a–f** | *thermodynamic (C1-retention)* **11a–f**

R = OMe		R = Me		R = H		R = Cl		R = CF_3	
time (min)	% 11a	time (min)	% 11b	time (min)	% 11c	time (min)	% 11d	time (min)	% 11e
0	0	0	0	0	0	0	0	0	0
0.083	31	3.25	21.8	6.25	7.4	6.0	1.5	1440	4.0
0.33	57	5.25	35.4	9.0	9.9	15.75	4.3	3413	8.0
0.58	69	7.0	42.8	12.0	12.2	26.0	5.7		
		8.75	51.6	15.0	13.7	36.25	7.4		
		10.5	57.6	18.0	16.6	46.5	9.1		
		12.0	62.5	21.5	19.3	56.75	9.9		

[a] Spiroketal **8f** did not convert to spiroketal **11f** at this concentration of TsOH over >72 h.

[2] Ansyln, E. V.; Dougherty, D. A. *Modern Physical Organic Chemistry*; University Science Books: Sausalito, California, 2006; Chapter 7; p 389.

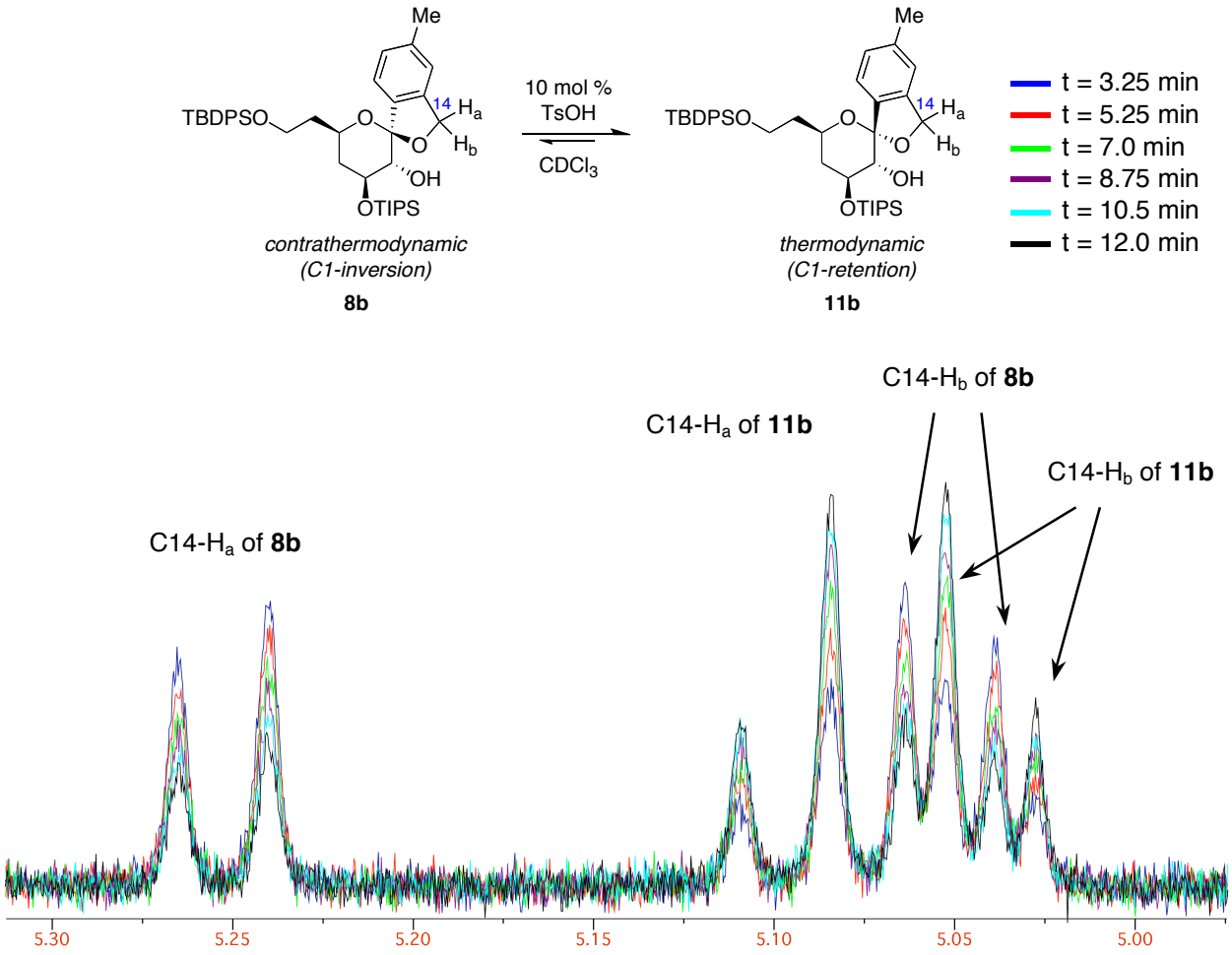


Figure S1. Example of kinetic measurements made by NMR. Contrathermodynamic spiroketal **8b** epimerizes to thermodynamic spiroketal **11b** with 10 mol % TsOH (Figure 3b of manuscript).

Table S2. Observed initial rates from two tosic acid equilibration experiments for each substituent (Figure 3c of manuscript).

k_{obs} (min^{-1})	R = OMe	R = Me	R = H	R = Cl	R = CF_3
experiment 1	157	6.0	0.93	0.13	0.013
experiment 2	161	6.7	0.91	0.18	0.0028

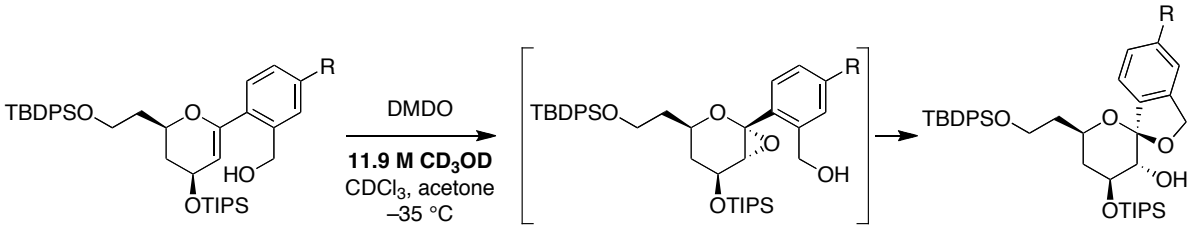
2. General procedure for NMR analysis of glycal epoxide spirocyclizations

Each glycal substrate (1.0 equiv) was added as a solution in $CDCl_3$ to an oven-dried, Ar-flushed 5 mm NMR tube. The tube was capped with a rubber septum. The appropriate amount of additional deuterated solvent (CD_3OD, $CDCl_3$, and C_3D_6O) was added, followed by brief mixing and cooling to –78 °C. Dimethyldioxirane (DMDO) solution (1.2 equiv, 0.073 M in acetone), taken from a –80 °C freezer and used immediately, was added and the tube was shaken vigorously for 3 s and then warmed to –44 °C. The tube was transferred quickly to the NMR instrument which was precooled to –40 °C. The sample was locked and shimmed and the NMR was tuned (3 min), then the sample was warmed to –35 °C to initiate the spirocyclization reaction. When the probe temperature remained constant (2–3 min), conversion of the glycal epoxide intermediate to the spiroketal inversion product was measured by integration of the C3 proton signals at various time intervals (respective ^{1}H-NMR shifts noted below). Reactions were run to ≥10–20% conversion and the method of initial rates was used.[2] Conversion at t = 0 was extrapolated from the linear fits derived from the initial rates data.

3. Methanol-induced glycal epoxide spirocyclization with varying substituents

Following the general procedure above, the appropriate glycal **5a–f** (1.0 equiv, 0.008 mmol) was dissolved in $CDCl_3$ (300 μL) and CD_3OD (400 μL, 11.9 M final concentration), then cooled to –78 °C and epoxidized with DMDO (1.2 equiv, 130 μL, 0.073 M in acetone). Conversion was measured by integration of the C3 protons of glycal epoxide intermediates **22a–e** (4.30–4.40 ppm) and spiroketal inversion products **8a–e** (4.50–4.60 ppm) (Table S3, Figure S2). In the case of glycal epoxide **22f** (R = NO_2), no reaction occurred under these conditions and epoxide persisted for the duration of the experiment (approx. 1 h).

Table S3. Sample of kinetic data collected using NMR for inversion product formation in the presence of 11.9 M CD_3OD at –35 °C for substituted glycals **5a–e** (Figure 4b of manuscript).



5a–e **22a–e** **8a–e**

R = OMe		R = Me		R = H		R = Cl		R = CF_3	
time (min)	% 8a	time (min)	% 8b	time (min)	% 8c	time (min)	% 8d	time (min)	% 8e
0	0	0	0	0	0	0	0	0	0
2.25	4.6	4.25	6.3	6.25	7.4	7.0	3.6	14.75	4.0
4.5	11.1	6.5	10.3	9.5	11.0	13.5	6.3	27.25	6.1
9.0	23.9	8.75	14.1	12.75	14.8	16.75	7.5	33.5	8.8
13.5	32.3	11.0	15.7	16.0	18.2	20.0	10.1	39.75	10.9
15.75	38.5	13.25	19.5	19.25	22.5	23.25	12.8	46.0	12.0
18.0	43.9	17.75	25.8	22.5	25.7	29.75	13.4	52.25	13.6

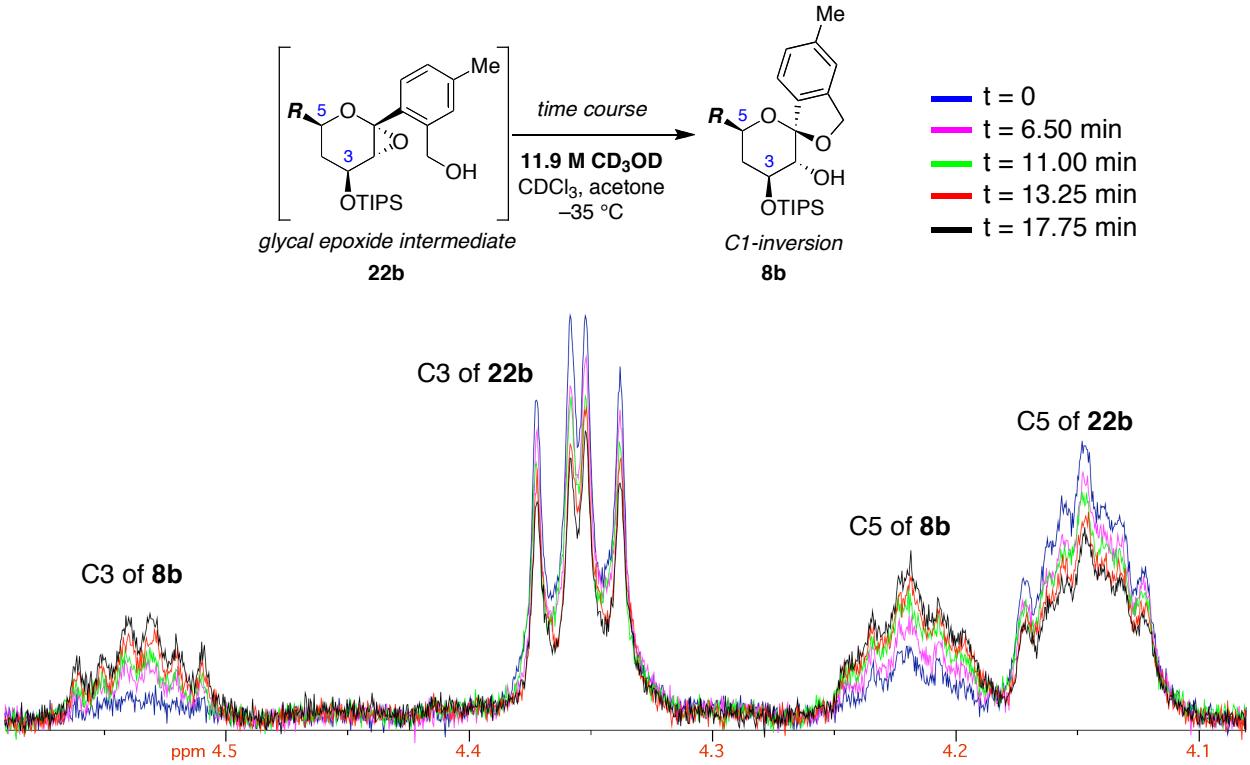


Figure S2. Example of kinetic measurements made by NMR. Glycal epoxide **22b** spirocyclizes to spiroketal inversion product **8b** in 11.9 M CD_3OD at –35 °C (Figure 4b of manuscript).

Table S4. Observed initial rates for three spirocyclization experiments (Figure 4c of manuscript).

k_{obs} (min^{-1})	R = OMe	R = Me	R = H	R = Cl	R = CF_3
experiment 1	0.0248	0.0141	0.0116	0.0058	0.0027
experiment 2	0.0260	0.0163	0.0112	0.0066	0.0013
experiment 3	0.0154	0.0124	0.0110	0.0031	0.0016

4. HAMMETT ANALYSES OF EPIMERIZATION AND SPIROCYCLIZATION REACTIONS

Observed rates for both the tosic acid epimerization (Table S2) and methanol-induced spirocyclization with inversion of configuration (Table S4) gave access to two distinct Hammett plots as a means to compare the same substrates under two different reaction conditions (Figure 3c vs. 4c of manuscript). For the tosic acid epimerization data, the logarithm of the ratio of observed rates of isomerization for each spiroketal **8a–e** (k_{obs} [min^{-1}]) divided by the observed rate of isomerization for **8c** (R = H; k_0 [min^{-1}]) was plotted against known sigma values (Figure 3c of manuscript).[3] For the methanol-induced epoxide opening spirocyclization, the logarithm of the ratio of observed spirocyclization rate for each glycal epoxide **22a–e** (k_{obs} [min^{-1}]) divided by the observed rate of spirocyclization for **22c** (R = H; k_0 [min^{-1}]) was plotted against known sigma values (Figure 4c of manuscript).

[3] Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165–195.

Table S5. Data for Hammett plot analysis of TsOH epimerization, where k_0 is observed rate for isomerization to spiroketal **11c** (R = H) (Figure 3c of manuscript).

	$(\sigma)^3$	k_{obs} [a]		log (k_{obs}/k_0)	
		expt 1	expt 2	expt 1	expt 2
R = OMe	–0.28	157	161	2.23	2.24
R = Me	–0.14	6.0	6.7	0.81	0.87
R = H	0.00	0.93	0.91	0.0	0.0
R = Cl	0.24	0.13	0.18	–0.86	–0.70
R = CF_3	0.53	0.013	0.0028	–1.9	–2.5

[a] Values obtained from Table S2.

Table S6. Data for Hammett plot analysis of methanol-induced spirocyclization, where k_0 is observed rate for the formation of **8c** (R = H) (Figure 4c of manuscript).

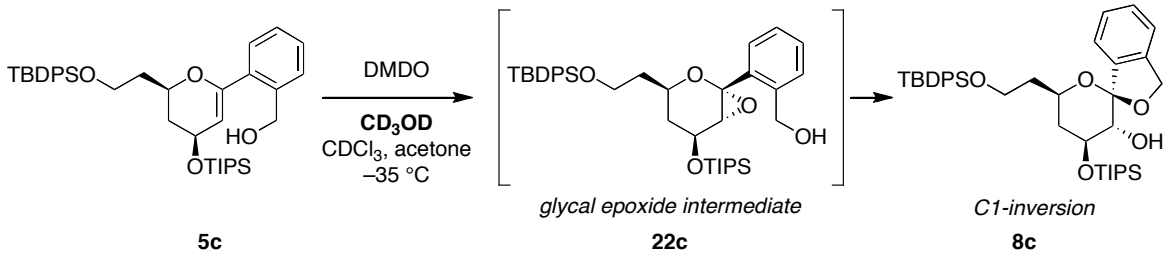
	$(\sigma)^3$	k_{obs} [a]			log (k_{obs}/k_0)		
		expt 1	expt 2	expt 3	expt 1	expt 2	expt 3
R = OMe	–0.28	0.025	0.026	0.015	0.33	0.24	0.14
R = Me	–0.14	0.014	0.016	0.012	0.085	0.042	0.044
R = H	0.00	0.012	0.011	0.011	0.0	0.0	0.0
R = Cl	0.24	0.0058	0.0066	0.0031	–0.30	–0.35	–0.56
R = CF_3	0.53	0.0027	0.0013	0.0016	–0.63	–1.1	–0.85

[a] Values obtained from Table S4.

5. Determination of Kinetic Order of Methanol in Glycal Epoxide Spiro-cyclization

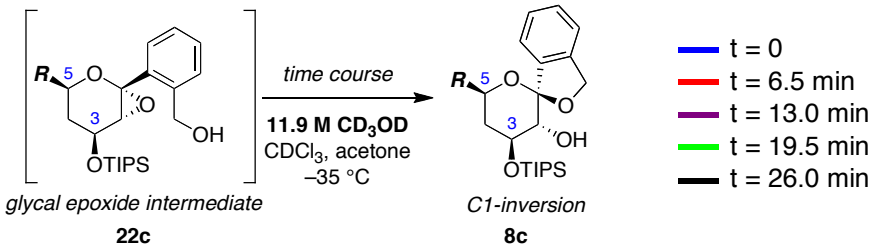
Following the general procedure above, glycal **5c** (1.0 equiv, 0.008 mmol) was dissolved in varying amounts of $CDCl_3$ (100–500 μL) and CD_3OD (200–600 μL, 5.9–17.8 M final concentrations), then cooled to –78 °C and epoxidized with DMDO (1.2 equiv, 130 μL, 0.073 M in acetone). Percent conversion at – 35 °C was measured by integration of the C3 proton of glycal epoxide intermediate **22c** (4.35–4.40 ppm) and spiroketal inversion product **8c** (4.55–4.60 ppm) (Table S7, Figure S3–S4). Initial rates were then calculated for the varying concentrations of CD_3OD (Table S8) and these observed rates were plotted against their respective concentrations of CD_3OD yielding a polynomial curve (Figure 5a of manuscript). In the absence of CD_3OD, no spirocyclization was observed at – 35 °C and the epoxide intermediate persisted for the duration of the experiment (approx. 1 h). The initial rates data in Table S8 was then subjected to a non-linear least squares fit to the equation $f(x) = c[CD_3OD]^n$, yielding $c = 6.1\times10^{-5}$ and $n = 2.1$, which is consistent with two molecules of MeOH in the transition state leading to epoxide opening spirocyclization with inversion of configuration. To confirm this fit, a plot of observed rate as a function of $[CD_3OD]^2$ gave a linear fit with $r^2 = 0.95$ (Figure 5b of manuscript).

Table S7. Sample of kinetic data collected using NMR for spirocyclization in the presence of varying concentrations of CD_3OD at –35 °C (Figure 5a of manuscript).



5c **22c** **8c**

17. 8 M		14.8 M		11.9 M		8.9 M		5.9 M	
time (min)	% 8c	time (min)	% 8c	time (min)	% 8c	time (min)	% 8c	time (min)	% 8c
0	0	0	0	0	0	0	0	0	0
3.75	10.1	4.0	7.2	6.5	7.4	22.5	11.5	29.5	5.3
7.0	20.2	7.5	15.1	9.75	11.0	26.75	13.2	34.75	6.2
10.25	28.4	10.75	20.2	13.0	14.8	31.0	14.6	40.0	6.6
13.5	36.8	14.0	25.4	16.25	18.2	35.25	17.7	50.5	7.3
16.75	44.4	17.25	32.8	19.5	22.5	39.5	19.5	61.0	9.7
20.0	50.3	20.5	36.5	22.75	25.7	43.75	21.9	71.5	12.6



glycal epoxide intermediate *C1-inversion*

22c **8c**

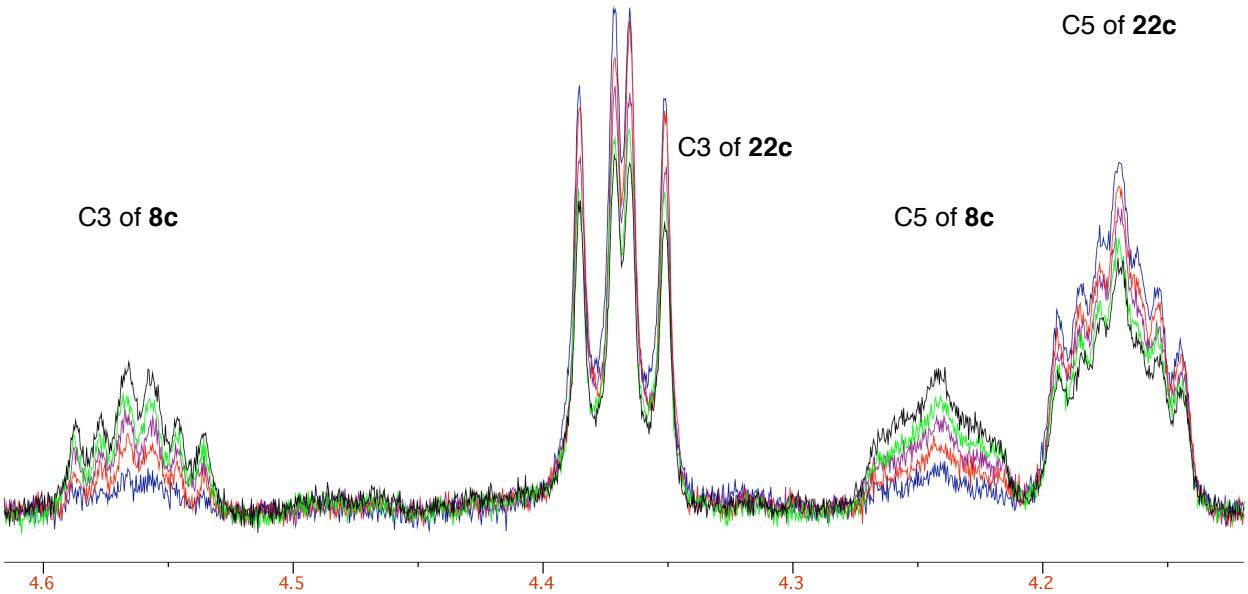


Figure S3. Example of kinetic measurements taken by NMR. Glycal epoxide **22c** spirocyclizes to spiroketal inversion product **8c** in 11.9 M CD_3OD at –35 °C (Figure 5a of manuscript).

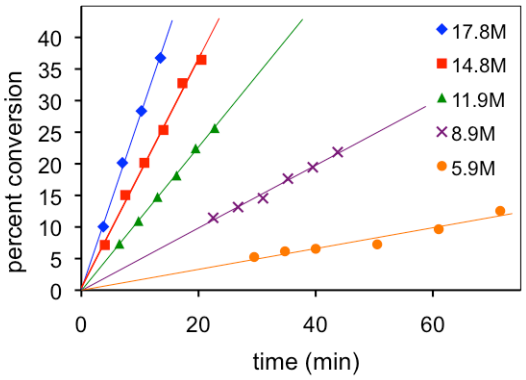


Figure S4. Plot of raw data in Table S7.

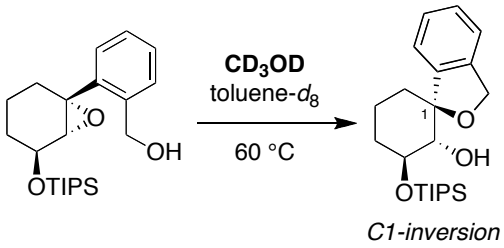
Table S8. Observed initial rates for each concentration CD_3OD for two spirocyclization experiments (Figure 5a of manuscript).

k_{obs} (min^{-1})	17.8 M [CD_3OD]	14.8 M [CD_3OD]	11.9 M [CD_3OD]	8.9 M [CD_3OD]	5.9 M [CD_3OD]
experiment 1	0.0272	0.0178	0.0115	0.0051	0.0018
experiment 2	0.0198	0.0177	0.0105	0.0047	0.0022

6. Determination of Kinetic Order of Methanol in Cyclohexene Oxide Spirocyclization

Epoxide **27** (2 mg, 0.005 mmol) as a solution in toluene-d_8 (100 μL) was added to an oven-dried Ar-flushed 5 mm NMR tube and the tube was capped with a rubber septum. Varying amounts of additional toluene-d_8 (0–300 μL) and CD_3OD (300–700 μL, 10.5–24.6 M final concentrations) were added, followed by shaking for 5 s. (For experiments run in neat CD_3OD (24.6 M), the substrate was loaded in toluene-d_8 as described above then concentrated *in vacuo* before the addition of 700 μL CD_3OD.) The tubes were inserted into a foam tube holder to the depth of the solvent volume, then floated in a 60 °C oil bath for 30 min intervals. At each time point, the tubes were removed from the bath and washed in a hexanes bath at rt to cool the reactions quickly and halt spirocyclization. Although no reaction occurred at rt, the NMR spectra were taken within 15 min before heating was resumed at 60 °C. Percent conversion was measured by integration of the C3 protons of epoxide **27** (4.10 ppm) and the C2 protons of spiroether **28** (3.50 ppm) (Table S9, Figure S5–S6) and initial rates were determined (Table S10). In the absence of CD_3OD (neat toluene-d_8), there was no conversion of epoxide **27** to spirocycle **28** over 24 h at 60 °C.

Table S9. Sample of kinetic data collected using NMR for spiroether formation in the presence of varying concentrations of CD_3OD at 60 °C (Figure 8b of manuscript).



27 **28**

24.6 M		21.1 M		17.6 M		14.1 M		10.5 M	
time (min)	**% 28**	**time (min)**	**% 28**	**time (min)**	**% 28**	**time (min)**	**% 28**	**time (min)**	**% 28**
0	0	0	0	0	0	0	0	0	0
30	5.6	30	4.2	30	4.1	30	2.9	30	3.5
60	7.8	60	8.3	60	6.3	60	6.6	60	5.4
90	12.0	90	10.9	90	9.7	90	7.5	90	7.8
120	14.0	120	14.0	120	11.9	120	10.5	120	9.8
150	20.2	150	17.5	150	15.8	150	12.8	150	12.4
180	21.4	180	20.3	180	18.0	180	15.4	180	13.4

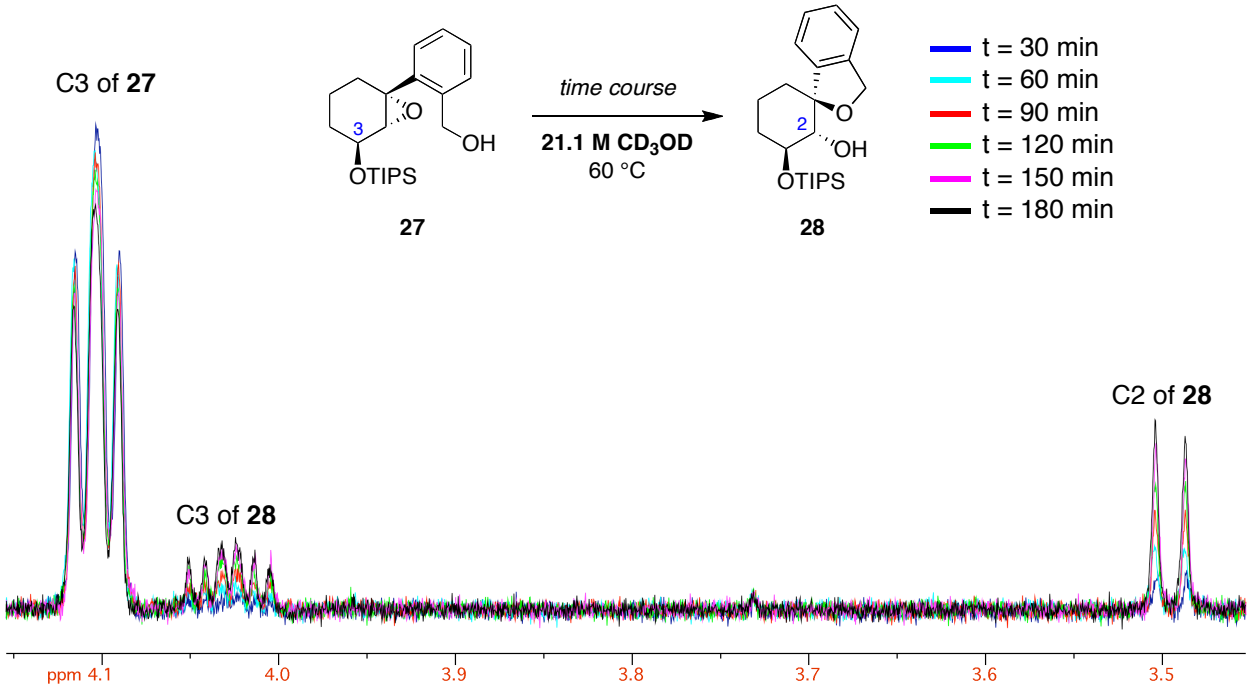


Figure S5. Example of kinetic measurements taken by NMR. Epoxide **27** spirocyclizes to **28** in 21.1 M CD_3OD at 60 °C (Figure 8b of manuscript).

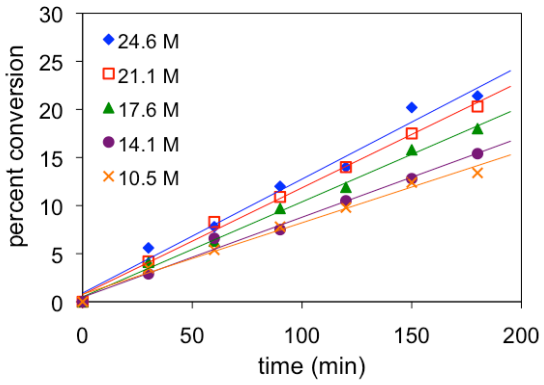


Figure S6. Plot of raw data in Table S9.

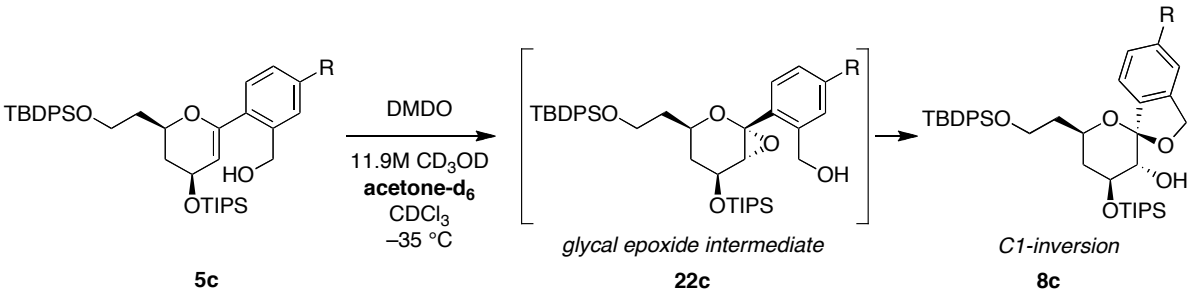
Table S10. Observed initial rates for two experiments at each concentration of CD_3OD (Figure 8b of manuscript).

k_{obs} (min^{-1})	24.6 M [CD_3OD]	21.1 M [CD_3OD]	17.6 M [CD_3OD]	14.1 M [CD_3OD]	10.5 M [CD_3OD]
experiment 1	0.1186	0.1110	0.0988	0.0832	0.0743
experiment 2	0.1161	0.1042	0.0965	0.0815	0.0706

7. Determination of Kinetic Order of Acetone in Glycal Epoxide Spirocyclization

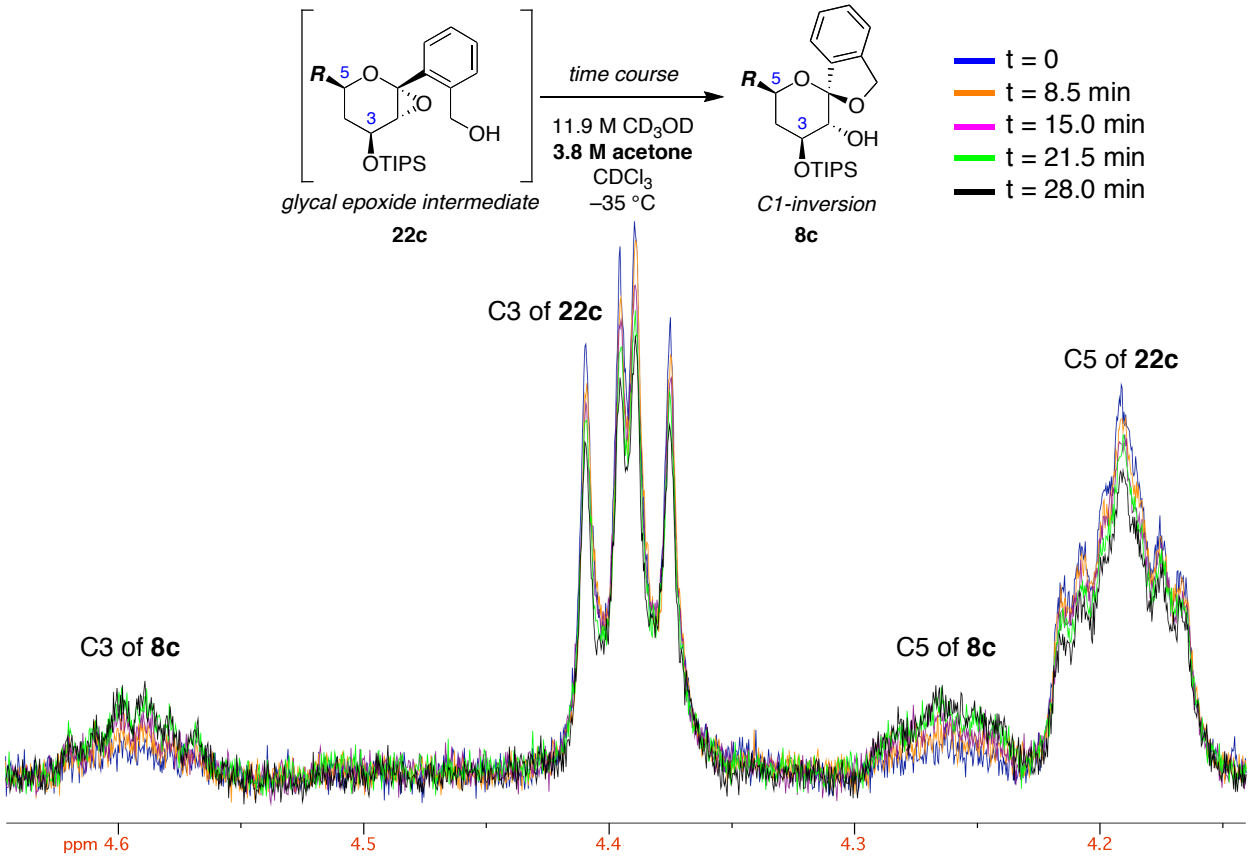
Following the general procedure above, glycal **5c** (1.0 equiv, 0.008 mmol) was dissolved in varying amounts of $CDCl_3$ (0–300 μL), acetone-d_6 (0–300 μL, 2.1–7.0 M final concentration acetone including acetone added from DMDO stock), and CD_3OD (400 μL, 11.9 M) before a brief mixing and cooling to –78 °C and epoxidizing with DMDO (1.2 equiv, 130 μL, 0.073 M in acetone). Percent conversion at –35 °C was measured by integration of the C3 proton of glycal epoxide intermediate **22c** (4.40–4.45 ppm) and inversion spiroketal product **8c** (4.60–4.65 ppm) (Table S11, Figure S7–S8). Initial rates were then calculated for the varying concentrations of acetone (Table S12) and these observed rates were plotted against their respective concentrations of acetone yielding an inhibition curve (Figure 9a of manuscript). This data was then subjected to a non-linear least squares fit to the equation $f(x) = c[\text{acetone}]^n$, yielding $c = 2.2\times10^{-2}$ and $n = -1.0$, which is consistent with first-order inhibition. To confirm this fit, a plot of observed rate as a function of $[\text{acetone}]^{-1}$ gave a linear fit with $r^2 = 0.98$ (Figure 9b of manuscript).

Table S11. Sample of kinetic data collected using NMR for spirocyclization in the presence of varying concentrations of acetone (acetone-d_6 + acetone from DMDO) at –35 °C (Figure 9a of manuscript).



5c **22c** **8c**

2.1 M		3.8 M		5.4 M		7.0 M	
time (min)	% 8c	time (min)	% 8c	time (min)	% 8c	time (min)	% 8c
0	0	0	0	0	0	0	0
6.0	6.7	8.5	4.6	12.5	5.0	15.25	4.9
9.25	8.6	11.75	7.4	16.75	6.2	21.5	6.4
12.5	11.6	15.0	8.2	21.0	7.9	27.75	7.3
15.75	17.3	18.25	8.7	25.25	8.6	34.0	9.7
19.0	20.2	21.5	11.7	29.50	10.5	40.25	12.5
22.25	24.0	24.75	13.6	38.0	13.9	46.5	14.2



22c **8c**

Figure S7. Example of kinetic measurements taken by NMR. Glycal epoxide **22c** opens to spiroketal inversion product **8c** in 3.8 M acetone at –35 °C (Figure 9a of manuscript).

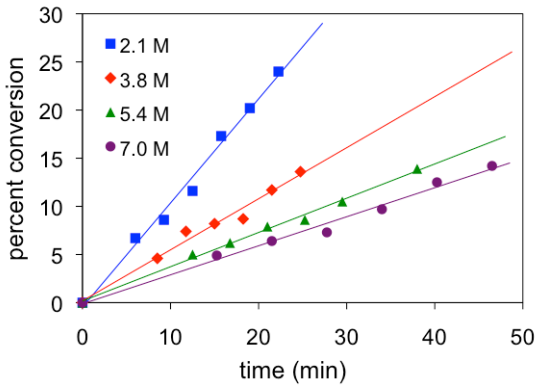


Figure S8. Plot of raw data in Table S11.

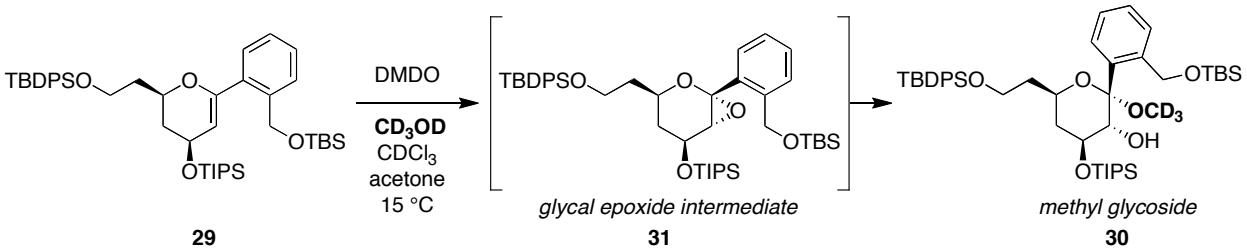
Table S12. Observed initial rates for two spirocyclization experiments at different concentrations of acetone (Figure 9a of manuscript).

k_{obs} (min^{-1})	2.1 M [acetone]	3.8 M [acetone]	5.4 M [acetone]	7.0 M [acetone]
experiment 1	0.0112	0.0054	0.0040	0.0032
experiment 2	0.0105	0.0059	0.0045	0.0038

8. Determination of Kinetic Order of Methanol in Methyl Glycoside Formation

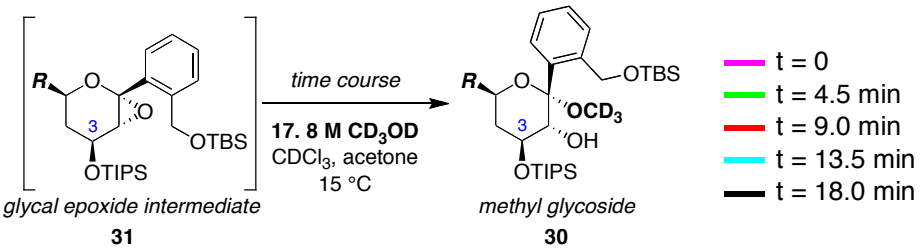
TBS-protected glycal **29** (1.0 equiv, 0.008 mmol) as a solution in $CDCl_3$ (100 μL) was added to an oven-dried, Ar-flushed 5 mm NMR tube. The tube was capped with a rubber septum. Varying amounts of additional $CDCl_3$ (0–400 μL) and CD_3OD (200–600 μL, 5.9–17.8 M final concentrations) were added, followed by brief mixing and cooling to –78 °C. DMDO solution (1.2 equiv, 130 μL, 0.073 M in acetone), taken from a –80 °C freezer and used immediately, was added and the tube was shaken vigorously for 3 s then warmed to 0 °C. The tube was transferred quickly into the NMR instrument which was precooled to 15 °C. The sample was locked and shimmed and the NMR was tuned (3 min). When the probe temperature remained constant (2–3 min), conversion of epoxide **31** to methyl glycoside **30** was measured by integration of the C3 protons of glycal epoxide intermediate **31** (4.30–4.40 ppm) and methyl glycoside product **30** (4.15–4.25 ppm) (Table S13, Figure S9–S10). Reactions were run to at least 20% conversion and initial rates were determined (Table S14).[2] Conversion at t = 0 was extrapolated from the linear fits derived from the initial rates data. These observed rates were plotted against their respective concentrations of methanol, yielding a linear fit with $r^2 = 0.98$ (Figure 10b of manuscript).

Table S13. Sample of kinetic data collected using NMR for methyl glycoside formation in the presence of varying concentrations of CD_3OD at 15 °C (Figure 10b of manuscript).



29 **31** **30**

17. 8 M		14.8 M		11.9 M		8.9 M		5.9 M	
time (min)	**% 30**	**time (min)**	**% 30**	**time (min)**	**% 30**	**time (min)**	**% 30**	**time (min)**	**% 30**
0	0	0	0	0	0	0	0	0	0
4.5	11.0	4.5	8.9	5.75	8.8	7.75	9.3	18.5	10.2
6.75	17.3	6.75	14.3	7.0	13.5	10.0	13.6	20.75	11.5
9.0	23.6	9.0	18.4	9.25	16.2	12.25	14.6	25.25	12.9
11.25	27.2	11.25	23.5	11.5	19.0	14.5	17.4	27.50	14.1
13.5	32.9	13.5	27.0	13.75	22.3	16.75	21.3	29.75	16.7
15.75	37.6	15.75	30.8	16.0	26.0	19.0	23.1	35.25	19.8



31 **30**

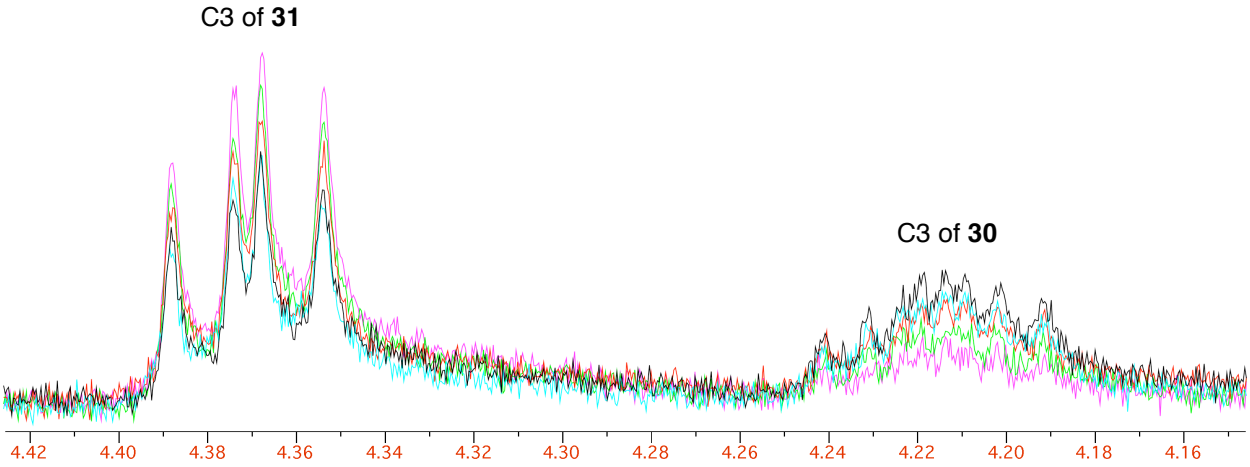


Figure S9. Example of kinetic measurements taken by NMR. Intermediate epoxide **31** forms methyl glycoside **30** in 17.8 M CD_3OD at 15 °C (Figure 10b of manuscript).

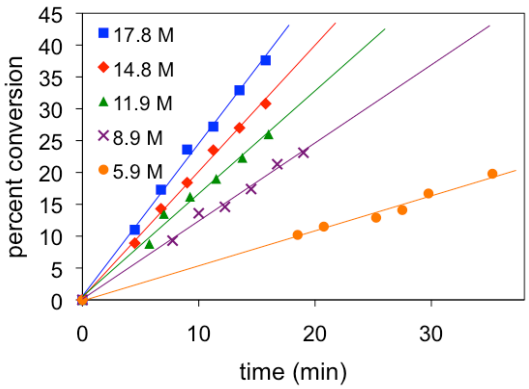


Figure S10. Plot of raw data in Table S13.

Table S14. Observed initial rates for two experiments at each concentration of CD_3OD (Figure 10b of manuscript).

k_{obs} (min^{-1})	**17.8 M [CD_3OD]**	**14.8 M [CD_3OD]**	**11.9 M [CD_3OD]**	**8.9 M [CD_3OD]**	**5.9 M [CD_3OD]**
experiment 1	0.0244	0.0193	0.0154	0.0118	0.0055
experiment 2	0.0201	0.0190	0.0148	0.0128	0.0078

F. SYNTHESIS OF SIDECHAIN PRECURSORS (S1–S25)

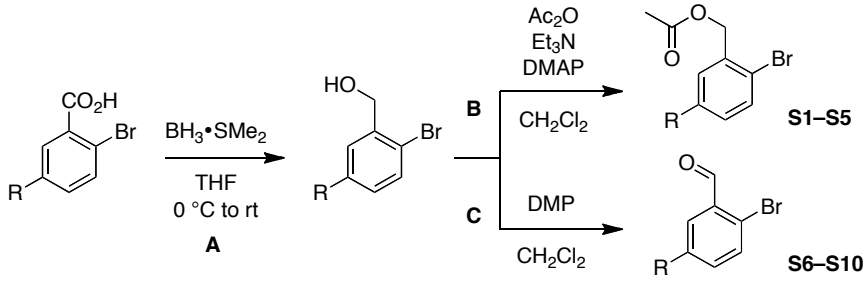


Figure S11. Synthesis of aryl side-chains for 5-membered ring spiroketals and substituted benzaldehydes used for the synthesis of aryl side-chains for 6- and 7-membered ring spiroketals.

1. GENERAL PROCEDURE A FOR REDUCTION OF ARYL ACIDS[4]

A solution of the commercially available aryl acid (1.0 equiv) was dissolved in THF (0.15 M) and cooled to 0 °C. Borane dimethyl sulfide (1.0 M CH_2Cl_2, 3.0 equiv) was added dropwise at a rate of 0.5 mL/min. After stirring for 3 h at 0 °C, the mixture was warmed to rt for 12 h, then quenched slowly with 1 N aq HCl. The aqueous layer was separated and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. The crude products were acetylated according General Procedure B or oxidized according to General Procedure C below.

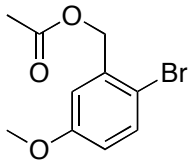
2. GENERAL PROCEDURE B FOR ACETYLATION OF ALCOHOLS (S1–S5, S11–S15, S21–S25)

To a solution of alcohol (1.0 equiv) in CH_2Cl_2 (0.1 M) was added triethylamine (2.0 equiv), 4-dimethylaminopyridine (0.2 equiv), and acetic anhydride (2.0 equiv). After stirring for 2 h at rt, the mixture was washed with satd aq NH_4Cl and the aqueous layer was separated and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (95:5–90:10 hexanes/EtOAc with 0.5% Et_3N) provided **S1–S5**.

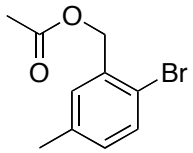
3. GENERAL PROCEDURE C FOR OXIDATION OF BENZYL ALCOHOLS (S6–S10)

To a solution of alcohol (1.0 equiv) in CH_2Cl_2 (0.2 M) was added Dess–Martin periodinane (1.1 equiv) and the mixture was stirred for 1 h at rt. The reaction was washed with 10% aq $Na_2S_2O_3$ and the aqueous layer was separated and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (9:1 hexanes/EtOAc with 0.5% Et_3N) provided **S6–S10**.

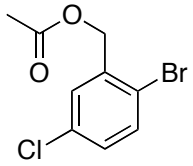
[4] Lane, C. F.; Myatt, H. L.; Daniels, J.; Hopps, H. B. *J. Org. Chem.* **2002**, *39*, 3052–3054.



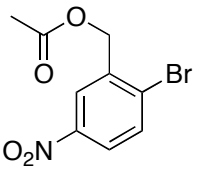
2-Bromo-5-methoxybenzyl acetate (S1). White solid (46 mg, 81%, 2 steps). **TLC**: R_f 0.50 (4:1 hexanes/EtOAc). **mp**: 34.2–34.7°C. **IR** (NaCl, film): 1740 (C=O st), 1699, 1653, 1575, 1540, 1521, 1507, 1473, 1248 (C–O st), 1165, 1048, 1023, 868, 807. **^{1}H-NMR** (500 MHz): δ 7.45 (d, 1H, J = 8.8 Hz), 6.96 (d, 1H, J = 3.0 Hz), 6.74 (dd, 1H, J = 8.8, 3.1 Hz), 5.15 (s, 2H), 3.80 (s, 3H), 2.14 (s, 3H). **^{13}C-NMR** (125 MHz): δ 170.6, 159.1, 136.2, 133.5, 115.7, 115.0, 113.5, 65.8, 55.4, 20.8. **ESI-MS** *m/z* (rel int): (pos) 280.8 ([M+Na]$^+$, 95).



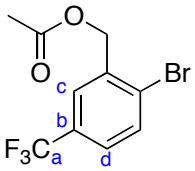
2-Bromo-5-methylbenzyl acetate (S2). White solid (42 mg, 75%, 2 steps). **TLC**: R_f 0.60 (4:1 hexanes/EtOAc). **mp**: 51.3–51.8 °C. **IR** (NaCl, film): 1741 (C=O st), 1699, 1635, 1558, 1473, 1457, 1376, 1240 (C–O st), 1024, 810. **^{1}H-NMR** (500 MHz): δ 7.44 (d, 1H, J = 8.0 Hz), 7.21 (d, 1H, J = 1.8 Hz), 7.00 (dd, 1H, J = 8.1, 2.1 Hz), 5.15 (s, 2H), 2.31 (s, 3H), 2.14 (s, 3H). **^{13}C-NMR** (125 MHz): δ 170.7, 137.5, 134.8, 132.6, 130.8, 130.6, 120.2, 65.9, 21.0 (2). **ESI-MS** *m/z* (rel int): (pos) 264.8 ([M+Na]$^+$, 100).



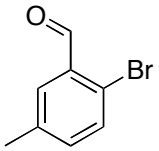
2-Bromo-5-chlorobenzyl acetate (S3). White solid (41 mg, 74%, 2 steps). **TLC**: R_f 0.68 (4:1 hexanes/EtOAc). **mp**: 65.4–66.4 °C. **IR** (NaCl, film): 1740 (C=O st), 1461, 1378, 1361, 1248 (C–O st), 1052, 876, 821. **^{1}H-NMR** (500 MHz): δ 7.49 (d, 1H, J = 8.5 Hz), 7.39 (d, 1H, J = 2.5 Hz), 7.17 (dd, 1H, J = 8.5, 2.6 Hz), 5.14 (s, 2H), 2.17 (s, 3H). **^{13}C-NMR** (125 MHz): δ 170.4, 137.1, 134.0, 133.7, 129.7, 129.2, 120.7, 65.1, 21.0. **ESI-MS** *m/z* (rel int): (pos) 286.8 ([M+Na]$^+$, 40).



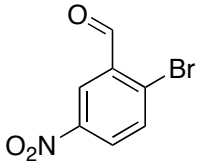
2-Bromo-5-nitrobenzyl acetate (S4). White solid (43 mg, 78%, 2 steps). **TLC**: R_f 0.38 (4:1 hexanes/EtOAc). **mp**: 106.9–107.9 °C. **IR** (NaCl, film): 1730 (C=O st), 1559, 1527, 1340 (N–O st), 1232 (C–O st), 1053, 921, 824, 811, 740. **^{1}H-NMR** (500 MHz): δ 8.27 (d, 1H, J = 2.7 Hz), 8.05 (dd, 1H, J = 8.7, 2.7 Hz), 7.77 (d, 1H, J = 8.7 Hz), 5.24 (s, 2H), 2.21 (s, 3H). **^{13}C-NMR** (125 MHz): δ 170.3, 147.3, 137.6, 133.9, 129.8, 124.1, 123.7, 64.8, 20.9. **ESI-MS** *m/z* (rel int): (pos) 296.0 ([M+Na]$^+$, 100).



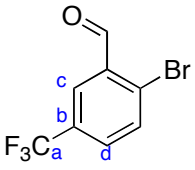
2-Bromo-5-(trifluoromethyl)benzyl acetate (S5). White solid (1.16 g, 99%, 1 step from commercially available benzyl OH). **TLC**: R_f 0.75 (4:1 hexanes/EtOAc). **mp**: 42.0–43.0 °C. **IR** (NaCl, film): 1749 (C=O st), 1653, 1558, 1507, 1418, 1329, 1224 (C–O st), 1169, 1127, 1082, 1027, 827. **^{1}H-NMR** (500 MHz): δ 7.71 (d, 1H, J = 8.3 Hz), 7.66 (d, 1H, J = 1.2 Hz), 7.45 (dd, 1H, J = 8.5, 1.3 Hz), 5.22 (s, 2H), 2.18 (s, 3H). **^{13}C-NMR** (125 MHz): δ 170.1, 136.6, 133.3, 129.9 (1C$_b$, q, J = 33.1 Hz), 126.7, 126.0 (1C$_c$, q, J = 3.7 Hz), 125.8 (1C$_d$, q, J = 3.7 Hz), 123.7 (1C$_a$, q, J = 272.1 Hz), 64.9, 20.5. **ESI-MS** *m/z* (rel int): (pos) 319.1 ([M+Na]$^+$, 30).



2-Bromo-5-methylbenzaldehyde (S6). White solid (81 mg, 98%, 2 steps). **TLC**: R_f 0.67 (4:1 hexanes/EtOAc). **mp**: 42.5–43.0 °C. **IR** (NaCl, film): 1697 (C=O st), 1593, 1466, 1386, 1271, 1225, 1153, 1026, 936, 816, 743, 657. **^{1}H-NMR** (500 MHz): δ 10.25 (s, 1H), 7.63–7.63 (m, 1H), 7.44 (d, 1H, J = 8.2 Hz), 7.21–7.19 (ddt, 1H, J = 8.2, 2.3, 0.6 Hz), 2.31 (s, 3H). **^{13}C-NMR** (125 MHz): δ 191.6, 138.0, 136.2, 133.5, 133.0, 130.0, 123.8, 20.7. **ESI-MS** *m/z* (rel int): (neg) 196.9 ([M–H]$^-$, 20).

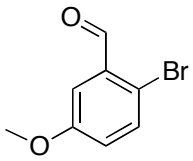


2-Bromo-5-nitrobenzaldehyde (S7). White solid (169 mg, 91%, 2 steps). **TLC**: R_f 0.45 (4:1 hexanes/EtOAc). **mp**: 103.5–104.5 °C. **IR** (NaCl, film): 1685 (C=O st), 1604, 1573, 1524, 1451, 1350 (N–O st), 1185, 1036, 930, 845, 816, 735. **^{1}H-NMR** (500 MHz): δ 10.35 (s, 1H), 8.66 (d, 1H, J = 2.6 Hz), 8.27 (dd, 1H, J = 8.7, 2.7 Hz), 7.88 (d, 1H, J = 8.7 Hz). **^{13}C-NMR** (125 MHz): δ 189.4, 147.7, 135.4, 134.4, 133.0, 128.8, 124.6. **ESI-MS** *m/z* (rel int): (neg) 227.9 ([M–H]$^-$, 60).

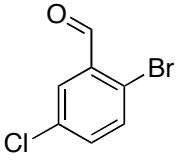


2-Bromo-5-(trifluoromethyl)benzaldehyde (S8). Light yellow oil (986 mg, 99%, 1 step from commercially available benzyl OH). **TLC**: R_f 0.67 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 1700 (C=O st), 1653, 1606, 1558, 1327, 1253, 1176, 1131, 1078, 1031, 913, 834. **^{1}H-NMR** (500 MHz): δ 10.38 (s, 1H), 8.17 (d, 1H, J = 1.8 Hz), 7.82 (d, 1H, J = 8.4 Hz), 7.70 (dd, 1H, J = 8.4, 2.0 Hz). **^{13}C-NMR** (125 MHz): δ 190.2, 134.7, 133.9, 131.4 (1C$_c$, q, J = 3.7 Hz), 130.8

($1C_b$, q, J = 33.8 Hz), 130.4, 126.8 ($1C_d$, q, J = 3.7 Hz), 123.2 ($1C_a$, q, J = 272.2 Hz). **ESI-MS** *m/z* (rel int): (pos) 253.1 ($[M+H]^+$, 60).



2-Bromo-5-methoxybenzaldehyde (S9). Previously reported.[5]



2-Bromo-5-chlorobenzaldehyde (S10). Previously reported.[5]

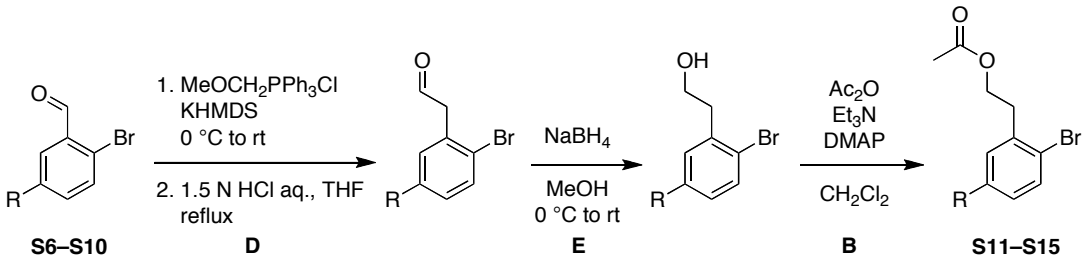


Figure S12. Synthesis of aryl side-chains for 6-membered ring spiroketals from substituted benzaldehydes **S6–S10**.

4. General Procedure D for one carbon homologation of substituted benzaldehydes

To a solution of methoxymethyl triphenyl phosphonium chloride (1.6 equiv) in toluene (0.25 M), cooled to 0 °C was added potassium bis(trimethylsilyl) amide (0.5 M in toluene, 2.0 equiv) dropwise at a rate of 0.5 mL/min. The solution was allowed to warm to rt over 1 h, then cooled back to 0 °C for the addition of benzaldehyde (**S6–S10**) (0.3 M in toluene, 1.0 equiv) at a rate of 0.5 mL/min. The solution was warmed to rt over 7 h, then quenched with satd aq NH_4Cl. The aqueous layer was separated and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude enol ether product, which was used without further purification.

The crude enol ether was redissolved in THF (0.1 M), and 1.5 N aq HCl (3 vol) was added. The solution was refluxed for 12 h. The reaction was washed with sat aq $NaHCO_3$ and the aqueous layer was separated and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude aryl acetaldehyde product, which was used without further purification below.

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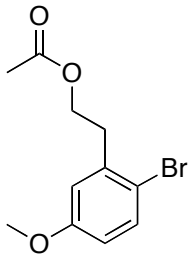
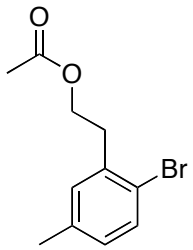
[5] Spring, D. R.; Krishnan, S.; Blackwell, H. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1354–1363.

5. General Procedure E for reduction of aryl acetaldehydes

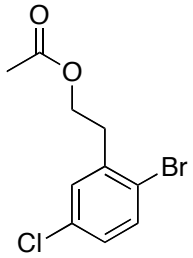
To a solution of aryl acetaldehyde (1.0 equiv) in methanol (0.1 M) cooled to 0 °C was added sodium borohydride (10.0 equiv) in several portions over 10 min. After an additional 15 min, the reaction was warmed to rt. Upon complete conversion as judged by TLC analysis (90 min), the reaction was cooled back to 0 °C and quenched with satd aq NH_4Cl. The aqueous layer was separated and extracted with Et_2O. The combined organic extracts were washed with brine, dried with ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude alcohol product, which was acetylated without further purification according to the General Procedure B above.



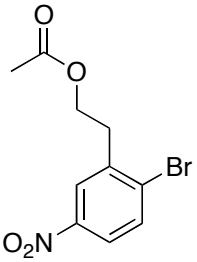
2-Bromo-5-methoxyphenethyl acetate (S11). Yellow oil (641 mg, 66%, 3 steps from **S9**). **TLC**: R_f 0.44 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 1738 (C=O st), 1595, 1572, 1473, 1363, 1239 (C–O st), 1163, 1036, 852, 809. **^{1}H-NMR** (500 MHz): δ 7.41 (d, 1H, *J* = 8.8 Hz), 6.79 (d, 1H, *J* = 3.0 Hz), 6.66 (dd, 1H, *J* = 8.8, 3.0 Hz), 4.29 (t, 2H, *J* = 7.0 Hz), 3.76 (s, 3H), 3.03 (t, 2H, *J* = 7.0 Hz), 2.03 (d, 3H, *J* = 6.1 Hz). **^{13}C-NMR** (125 MHz): δ 170.9, 159.0, 138.1, 133.4, 116.7, 115.0, 113.9, 63.3, 55.4, 35.5, 20.9. **ESI-MS** *m/z* (rel int): (pos) 294.9 ($[M+Na]^+$, 100).



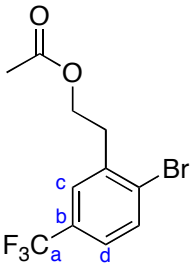
2-Bromo-5-methylphenethyl acetate (S12). Light yellow oil (492 mg, 89%, 3 steps from **S6**). **TLC**: R_f 0.64 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 1740 (C=O st), 1473, 1383, 1363, 1239 (C–O st), 1035, 808. **^{1}H-NMR** (500 MHz): δ 7.41 (d, 1H, *J* = 8.1 Hz), 7.07 (s, 1H), 6.90 (d, 1H, *J* = 8.1 Hz), 4.31 (t, 2H, *J* = 7.1 Hz), 3.06 (t, 2H, *J* = 7.1 Hz), 2.29 (s, 3H), 2.04 (s, 3H). **^{13}C-NMR** (125 MHz): δ 170.8, 137.4, 136.8, 132.6, 131.8, 129.3, 128.4, 121.3, 63.5, 35.2, 20.9. **ESI-MS** *m/z* (rel int): (pos) 278.9 ($[M+Na]^+$, 100).



2-Bromo-5-chlorophenethyl acetate (S13). Yellow oil (437 mg, 66%, 3 steps from **S10**). **TLC**: R_f 0.51 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 1740 (C=O st), 1558, 1462, 1363, 1234 (C–O st), 1098, 1037, 810. **^{1}H-NMR** (500 MHz): δ 7.47 (d, 1H, J = 8.5 Hz), 7.24 (d, 1H, J = 2.5 Hz), 7.09 (dd, 1H, J = 8.5, 2.6 Hz), 4.30 (t, 2H, J = 6.8 Hz), 3.05 (t, 2H, J = 6.8 Hz), 2.05 (s, 3H). **^{13}C-NMR** (125 MHz): δ 170.9, 139.1, 133.9, 133.4, 130.9, 128.5, 122.5, 62.9, 35.2, 21.0. **ESI-MS** *m/z* (rel int): (pos) 298.9 ($[M+Na]^+$, 70).



2-Bromo-5-nitrophenethyl acetate (S14). Orange solid (62 mg, 50%, 3 steps from **S7**). **TLC**: R_f 0.58 (4:1 hexanes/EtOAc). **mp**: 47.5–48.5 °C. **IR** (NaCl, film): 1735 (C=O st), 1653, 1558, 1522, 1457, 1345 (N–O st), 1232 (C–O st), 1037, 740. **^{1}H-NMR** (500 MHz): δ 8.10 (d, 1H, J = 2.7 Hz), 7.94 (dd, 1H, J = 8.7, 2.7 Hz), 7.72 (d, 1H, J = 8.7 Hz), 4.33 (t, 2H, J = 6.6 Hz), 3.17 (t, 2H, J = 6.6 Hz), 2.01 (s, 3H). **^{13}C-NMR** (125 MHz): δ 170.8, 147.2, 139.5, 133.9, 131.9, 125.6, 123.0, 62.4, 35.3, 20.8. **ESI-MS** *m/z* (rel int): (pos) 309.9 ($[M+Na]^+$, 60).



2-Bromo-5-(trifluoromethyl)phenethyl acetate (S15). Yellow oil (880 mg, 57%, 3 steps from **S8**). **TLC**: R_f 0.62 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 1743 (C=O st), 1605, 1365, 1327, 1236, 1169, 1128 (C–O st), 1084, 1040, 896. **^{1}H-NMR** (500 MHz): δ 7.69 (dd, 1H, J = 8.3, 3.6 Hz), 7.50 (s, 1H), 7.38–7.36 (m, 1H), 4.33 (td, 2H, J = 6.7, 4.4 Hz), 3.15 (td, 2H, J = 6.7, 4.1 Hz), 2.04–2.03 (m, 3H). **^{13}C-NMR** (125 MHz): δ 170.9, 138.5, 133.5, 130.0 (1C_b, q, J = 33.0 H), 128.5, 127.8 (1C_c, q, J = 3.7 Hz), 125.1 (1C_d, q, J = 3.7 Hz), 123.8 (1C_a, q, J = 272.2 Hz), 62.7, 35.3, 20.9. **ESI-MS** *m/z* (rel int): (neg) 333.0 ($[M+Na]^+$, 60).

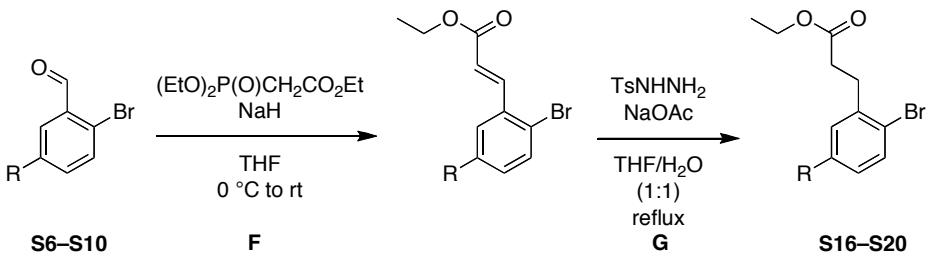


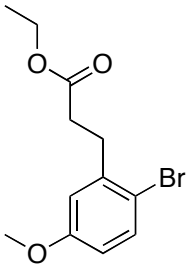
Figure S13. Synthesis of ester precurors of aryl side-chains for 7-membered ring spiroketals from substituted benzaldehydes **S6–S10**.

6. General Procedure F for Horner–Wadsworth–Emmons olefination of substituted benzaldehydes

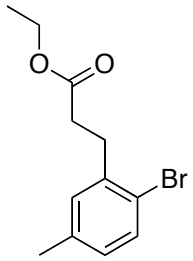
To a solution of NaH (1.1 equiv) in THF (0.2 M) cooled to 0 °C was added triethyl phosphonoacetate (1.2 equiv) dropwise at a rate of 0.25 mL/min. After addition the solution was warmed to rt over 25 min. The reaction was cooled back to 0 °C and benzaldehyde (**S6–10**) (0.2 M, 1.0 equiv) was added. The reaction was warmed to rt and stirred for 30 min. The mixture was washed with satd aq NH_4Cl and the aqueous layer was separated and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude ethyl enoate, which was used without further purification below.

7. General Procedure G for tosyl hydrazide reduction (S16–S20)

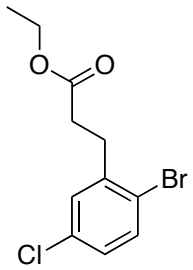
To a solution of ethyl enoate (1.0 equiv) in mixture of THF/H_2O (1:1, final concentration 0.15 M) was added tosyl hydrazide (2.0 equiv) and NaOAc (3.0 equiv). The reaction was refluxed over 20 h. The solution was washed with H_2O and aqueous layer was separated and extracted with EtOAc. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (9:1 hexanes/EtOAc with 0.5% Et_3N) provided **S16–S20**.



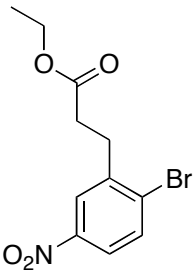
Ethyl 3-(2-bromo-5-methoxyphenyl)propanoate (S16). Light yellow oil (277 mg, 96%, 2 steps from **S9**). **TLC**: R_f 0.54 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 2981, 1733 (C=O st), 1596, 1574, 1474, 1374, 1279, 1243, 1164 (C–O st), 1058, 1022, 857, 806. **^{1}H-NMR** (500 MHz): δ 7.35 (d, 1H, J = 8.7 Hz), 6.78 (d, 1H, J = 2.9 Hz), 6.60 (dd, 1H, J = 8.7, 3.0 Hz), 4.11 (q, 2H, J = 7.1 Hz), 3.72 (s, 3H), 2.99 (t, 2H, J = 7.8 Hz), 2.60 (t, 2H, J = 7.8 Hz), 1.22 (t, 3H, J = 7.1 Hz). **^{13}C-NMR** (125 MHz): δ 172.4, 159.0, 140.8, 133.3, 116.1, 114.6, 113.6, 60.4, 55.3, 34.1, 31.6, 14.2. **ESI-MS** *m/z* (rel int): (pos) 308.9 ($[M+Na]^+$, 100).



Ethyl 3-(2-bromo-5-methylphenyl)propanoate (S17). Yellow oil (201 mg, 74%, 2 steps from **S6**). **TLC**: R_f 0.42 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 2926, 1735 (C=O st), 1474, 1372, 1300, 1181 (C–O st), 1127, 1026, 879, 807. **^{1}H-NMR** (500 MHz): δ 7.28 (d, 1H, J = 8.1 Hz), 6.96 (d, 1H, J = 1.6 Hz), 6.78 (dd, 1H, J = 8.1, 1.6 Hz), 4.04 (q, 2H, J = 7.1 Hz), 2.92 (t, 2H, J = 7.8 Hz), 2.52 (t, 2H, J = 7.7 Hz), 2.17 (s, 3H), 1.15 (t, 3H, J = 7.1 Hz). **^{13}C-NMR** (125 MHz): δ 172.7, 139.4, 137.4, 132.6, 131.3, 128.9, 120.9, 60.5, 34.3, 31.4, 20.8, 14.2. **ESI-MS** *m/z* (rel int): (pos) 293.1 ([M+Na]$^+$, 100).

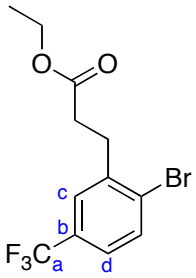


Ethyl 3-(2-bromo-5-chlorophenyl)propanoate (S18). Yellow oil (215 mg, 74%, 2 steps from **S10**). **TLC**: R_f 0.46 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 2981, 1734 (C=O st), 1462, 1373, 1349, 1184 (C–O st), 1097, 1030, 873, 809. **^{1}H-NMR** (500 MHz): δ 7.36 (d, 1H, J = 8.5 Hz), 7.16 (d, 1H, J = 2.5 Hz), 6.97 (dd, 1H, J = 8.5, 2.5 Hz), 4.06 (q, 2H, J = 7.1 Hz), 2.94 (t, 2H, J = 7.7 Hz), 2.54 (t, 2H, J = 7.7 Hz), 1.16 (t, 3H, J = 7.1 Hz). **^{13}C-NMR** (125 MHz): δ 172.3, 141.6, 133.9, 130.4, 129.9, 128.1, 122.2, 60.7, 33.8, 31.3, 14.2. **ESI-MS** *m/z* (rel int): (pos) 313.1 ([M+Na]$^+$, 80); (neg) 325.3 ([M+Cl]$^-$, 100).



Ethyl 3-(2-bromo-5-nitrophenyl)propanoate (S19). Yellow–orange oil (128 mg, 83%, 2 steps from **S7**). **TLC**: R_f 0.50 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 2981, 1732 (C=O st), 1569, 1526, 1346 (N–O st), 1295, 1268, 1187 (C–O st), 1032, 893, 826, 793, 740. **^{1}H-NMR** (500 MHz): δ 8.07 (d, 1H, J = 2.5 Hz), 7.86 (dd, 1H, J = 8.7, 2.6 Hz), 7.65 (d, 1H, J = 8.7 Hz), 4.08 (q, 2H, J = 7.1 Hz), 3.09 (t, 2H, J = 7.6 Hz), 2.63 (t, 2H, J = 7.6 Hz), 1.18 (t, 3H, J = 7.1

Hz). **^{13}C-NMR** (125 MHz): δ 171.9, 141.8, 133.8, 131.7, 129.9, 125.0, 122.7, 60.9, 33.4, 31.4, 14.2. **ESI-MS** *m/z* (rel int): (pos) 324.0 ([M+Na]$^+$, 100).



Ethyl 3-(2-bromo-5-(trifluoromethyl)phenyl)propanoate (S20). Clear oil (117 mg, 61%, 2 steps from **S8**). **TLC**: R_f 0.66 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 2983, 1734 (C=O st), 1410, 1374, 1329, 1277, 1168, 1128 (C–O st), 1082, 1030, 902, 824. **^{1}H-NMR** (500 MHz): δ 7.66 (d, 1H, J = 8.3 Hz), 7.51 (d, 1H, J = 1.8 Hz), 7.34 (dd, 1H, J = 8.3, 1.8 Hz), 4.14 (qd, 2H, J = 7.1, 0.9 Hz), 3.12 (t, 2H, J = 7.7 Hz), 2.67 (t, 2H, J = 7.8 Hz), 1.24 (td, 3H, J = 7.1, 0.9 Hz). **^{13}C-NMR** (125 MHz): δ 172.1, 140.9, 133.5, 130.0 (1C$_b$, q, J = 33.0 Hz), 128.3, 127.2 (1C$_c$, q, J = 3.5 Hz), 124.8 (1C$_d$, q, J = 3.7 Hz), 123.8 (1C$_a$, q, J = 272.1 Hz), 60.7, 33.7, 31.4, 14.2. **ESI-MS** *m/z* (rel int): (pos) 346.8 ([M+Na]$^+$, 60); 325.0 ([M+H]$^+$, 10).

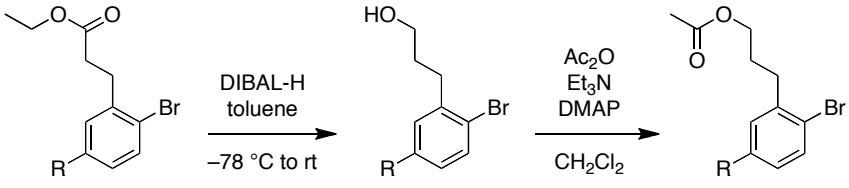
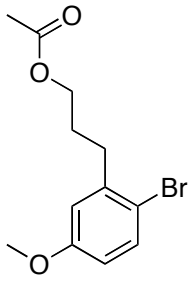


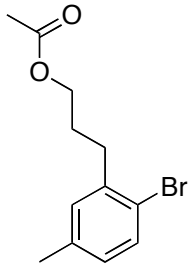
Figure S14. Synthesis of the aryl side-chains **S21–S25** for 7-membered ring spiroketals from substituted ethyl esters **S16–S20**.

8. General Procedure H for DIBAL reduction of ethyl esters

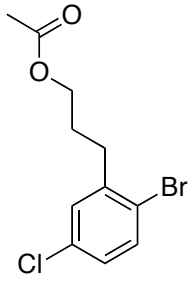
To a solution of ethyl ester (1.0 equiv) in toluene (0.15 M) cooled to –78 °C was added DIBAL (1.2 M in toluene, 3.0 equiv) dropwise at a rate of 0.5 mL/min. The reaction was allowed to warm to rt over 30 min. The reaction was quenched with 1 N HCl and the aqueous layer was separated and extracted with Et_2O. The combined extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. The crude product was used without further purification and was acetylated according to General Procedure B.



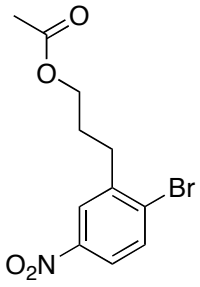
3-(2-Bromo-5-methoxyphenyl)propyl acetate (S21). Yellow oil (145 mg, 97%, 2 steps). **TLC**: R_f 0.48 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 2958, 1737 (C=O st), 1595, 1572, 1472, 1365, 1241 (C–O st), 1162, 1041, 1014, 850, 803. **^{1}H-NMR** (500 MHz): δ 7.39 (d, 1H, J = 8.7 Hz), 6.76 (d, 1H, J = 3.0 Hz), 6.62 (dd, 1H, J = 8.6, 3.1 Hz), 4.10 (t, 2H, J = 6.5 Hz), 3.76 (s, 3H), 2.76 (t, 2H, J = 7.7 Hz), 2.06 (s, 3H), 1.98–1.92 (m, 2H). **^{13}C-NMR** (125 MHz): δ 171.1, 159.0, 141.5, 133.4, 116.1, 114.8, 113.3, 63.7, 55.4, 32.8, 28.7, 21.0. **ESI-MS** *m/z* (rel int): (pos) 309.2 ([M+Na]$^+$, 90).



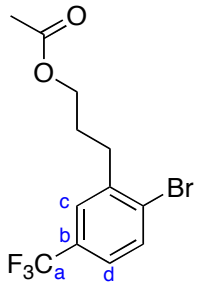
3-(2-Bromo-5-methylphenyl)propyl acetate (S22). Clear oil (152 mg, 76%, 2 steps). **TLC**: R_f 0.58 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 2955, 1738 (C=O st), 1472, 1364, 1237 (C–O st), 1023, 807, 668. **^{1}H-NMR** (500 MHz): δ 7.39 (d, 1H, J = 8.1 Hz), 7.02 (s, 1H), 6.86 (d, 1H, J = 8.0 Hz), 4.11 (t, 2H, J = 6.5 Hz), 2.76 (t, 2H, J = 7.8 Hz), 2.27 (s, 3H), 2.06 (s, 3H), 1.95 (quintet, 2H, J = 7.3 Hz). **^{13}C-NMR** (125 MHz): δ 171.1, 140.2, 137.3, 132.6, 131.2, 128.6, 121.0, 63.8, 32.5, 28.8, 21.0 (2). **ESI-MS** *m/z* (rel int): (pos) 293.1 ([M+Na]$^+$, 100).



3-(2-Bromo-5-chlorophenyl)propyl acetate (S23). Clear oil (190 mg, 88%, 2 steps). **TLC**: R_f 0.61 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 2957, 1740 (C=O st), 1463, 1389, 1367, 1239 (C–O st), 1100, 1029, 888, 811, 670. **^{1}H-NMR** (500 MHz): δ 7.43 (d, 1H, J = 8.5 Hz), 7.20 (d, 1H, J = 2.4 Hz), 7.04 (dd, 1H, J = 8.5, 2.5 Hz), 4.11 (t, 2H, J = 6.4 Hz), 2.77 (t, 2H, J = 7.8 Hz), 2.06 (s, 3H), 1.94 (quintet, 2H, J = 6.5 Hz). **^{13}C-NMR** (125 MHz): δ 171.0, 142.4, 133.9, 133.4, 130.2, 127.9, 122.2, 63.5, 32.6, 28.5, 20.9. **ESI-MS** *m/z* (rel int): (pos) 313.1 ([M+Na]$^+$, 60); (neg) 325.3 ([M+Cl]$^-$, 35).



3-(2-Bromo-5-nitrophenyl)propyl acetate (S24). Orange oil (75 mg, 58%, 2 steps). **TLC**: R_f 0.44 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 2959, 1737 (C=O st), 1569, 1525, 1462, 1345 (N–O st), 1237 (C–O st), 1028, 906, 829, 810, 740. **^{1}H-NMR** (500 MHz): δ 8.10 (d, 1H, J = 2.7 Hz), 7.93 (dd, 1H, J = 8.7, 2.7 Hz), 7.72 (d, 1H, J = 8.7 Hz), 4.14 (t, 2H, J = 6.3 Hz), 2.92 (dd, 2H, J = 8.8, 7.0 Hz), 2.08 (s, 3H), 2.04–1.98 (m, 2H). **^{13}C-NMR** (125 MHz): δ 171.0, 147.3, 142.6, 133.9, 131.7, 124.8, 122.5, 63.3, 32.8, 28.3, 20.9. **ESI-MS** *m/z* (rel int): (pos) 324.1 ($[M+Na]^+$, 100).



3-(2-Bromo-5-(trifluoromethyl)phenyl)propyl acetate (S25). Clear oil (574 mg, 93%, 2 steps). **TLC**: R_f 0.53 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 2960, 1741 (C=O st), 1604, 1410, 1367, 1330, 1240, 1168, 1126 (C–O st), 1084, 1025, 903, 824. **^{1}H-NMR** (500 MHz): δ 7.66 (d, 1H, J = 8.3 Hz), 7.47 (s, 1H), 7.33 (d, 1H, J = 8.2 Hz), 4.13 (td, 2H, J = 6.4, 1.8 Hz), 2.88 (td, 2H, J = 7.8, 1.6 Hz), 2.07 (s, 3H), 2.02–1.96 (m, 2H). **^{13}C-NMR** (125 MHz): δ 171.1, 141.7, 133.5, 130.0 ($1C_b$, q, J = 32.6 Hz), 128.3, 126.9 ($1C_c$, q, J = 3.7 Hz), 124.5 ($1C_d$, q, J = 3.5 Hz), 123.8 ($1C_a$, q, J = 272.0 Hz), 63.6, 32.8, 28.5, 21.0. **ESI-MS** *m/z* (rel int): (pos) 347.1 ($[M+Na]^+$, 100).

G. SYNTHESIS OF SUBSTITUTED C1-ARYL GLYCAL SUBSTRATES (S26, 5–7)

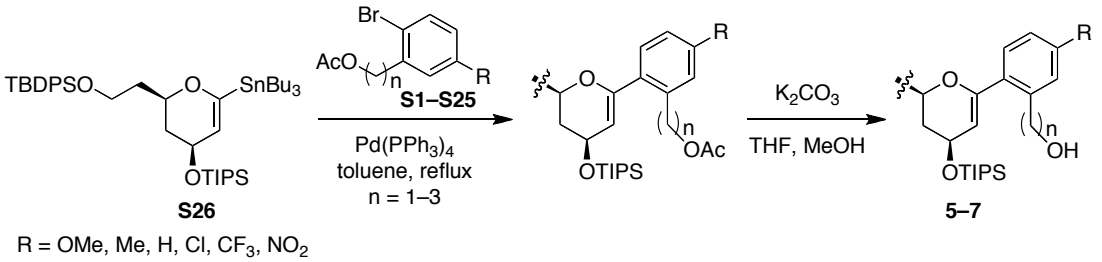
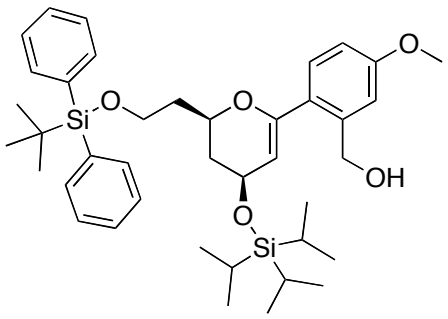


Figure S15. Synthesis of glycals **5–7** from glycal stannane **S26** by Stille cross coupling of aryl bromides, followed by K_2CO_3 deacetylation.

GENERAL PROCEDURE FOR STILLE COUPLING OF ARYL BROMIDES[6]

To a solution of glycal stannane **S26** (1.0 equiv), prepared as previously described,[7] in degassed toluene (0.1 M) was added the appropriate aryl bromide sidechain **S1–S25** (1.2 equiv) and $Pd(PPh_3)_4$ (0.2 equiv). The yellow solution was shielded from light with aluminum foil[8] and heated to reflux for 6–8 h, then cooled to rt and concentrated by rotary evaporation. Passage over a short silica plug yielded the intermediate *O*-acetyl *C*1-aryl glycals. These protected glycals were dissolved in THF/MeOH (1:1, final concentration 0.1 M) and K_2CO_3 (2.0 equiv) was added.[6] After stirring for 3–4 h, the mixture was diluted with Et_2O, filtered through a plug of celite, dried ($MgSO_4$), and concentrated by rotary evaporation. Purification by silica flash chromatography (20:1–10:1 hexanes/EtOAc with 1% Et_3N) afforded **5–7**.



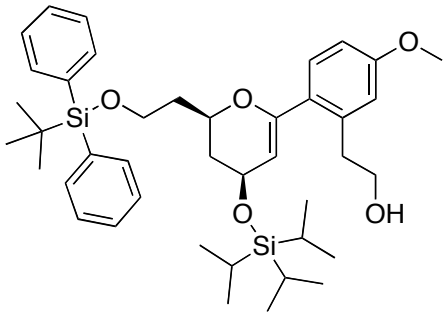
(–)-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-methoxyphenyl)methanol (5a). Clear oil (352 mg, 86%, 2 steps). **TLC**: R_f 0.33 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –4.5° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3446 (O–H st), 3070, 2941, 2864, 1653, 1697, 1572, 1485, 1463, 1427, 1388, 1272, 1095 (C–O st), 882, 822, 737, 702. **^{1}H-NMR** (500 MHz): δ 7.68–7.65 (m, 4H), 7.44–7.32 (m, 6H), 7.31 (d, 1H, *J* = 8.4 Hz), 6.98 (d, 1H, *J* = 2.7 Hz), 6.80 (dd, 1H, *J* = 8.4, 2.7 Hz), 4.93 (t, 1H, *J* = 2.1 Hz), 4.69 (ddd, 1H, *J* = 8.8, 6.6, 2.2 Hz), 4.59 (d, 2H, *J* = 6.1 Hz), 4.43–4.38 (m, 1H), 3.88–3.78 (m, 5H), 2.35 (t, 1H, *J* = 6.5 Hz), 2.21–2.17 (m, 1H), 2.05–1.98 (m, 1H), 1.92–1.87 (m, 1H), 1.85–1.78 (m, 1H),

[6] (a) Friesen, R. W.; Sturino, C. F. *J. Org. Chem.* **1990**, *55*, 2572–2574. (b) Beau, J.; Dubois, E. *Carbohydr. Res.* **1992,** *228*, 103–120. (c) Liu, G.; Wurst, J. M.; Tan, D. S. *Org. Lett.* **2009**, *11*, 3670–3673.

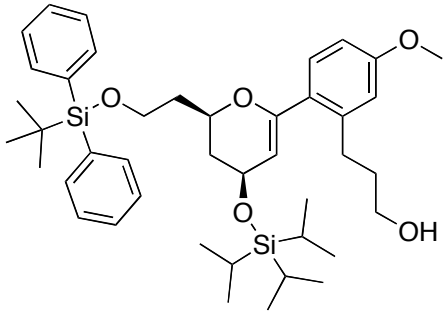
[7] (a) Potuzak, J. S.; Moilanen, S. B.; Tan, D. S. *J. Am. Chem. Soc.* **2005**, *127*, 13796–13797. (b) Moilanen, S. B.; Tan, D. S. *Org. Biomol. Chem.* **2005**, *3*, 798–803.

[8] Crawforth, C. M.; Burling, S.; Fairlamb, I. J. S.; Kapdi, A.; Taylor, R. J. K.; Whitwood, A. C. *Tetrahedron* **2005**, *61*, 9736–9751.

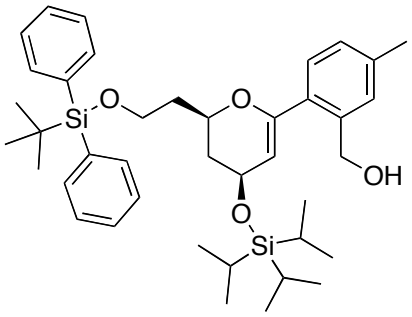
1.12–1.08 (m, 21H), 1.07–1.05 (m, 9H). **^{13}C-NMR** (125 MHz): δ 160.2, 153.5, 140.9, 135.7, 133.8, 130.7, 129.8, 129.7, 127.8, 114.2, 113.1, 106.0, 73.1, 64.4, 64.2, 60.3, 55.5, 37.9, 37.7, 27.0, 19.3, 18.3, 12.5. **ESI-MS** *m/z* (rel int): (pos) 697.4 ([M+Na]$^+$, 100).



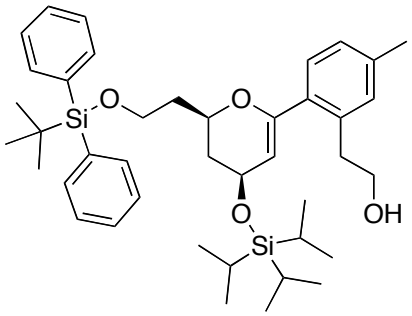
(–)-2-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-methoxyphenyl)ethanol (6a). Clear oil (300 mg, 67%, 2 steps). **TLC**: R_f 0.40 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –5.0° (*c* 1.5, $CHCl_3$). **IR** (NaCl, film): 3413 (O–H st), 3070, 2941, 2864, 1657, 1606, 1499, 1463, 1427, 1389, 1274, 1105 (C–O st), 882, 822, 738, 702. **^{1}H-NMR** (500 MHz): δ 7.67–7.63 (m, 4H), 7.44–7.39 (m, 2H), 7.38–7.33 (m, 4H), 7.27–7.24 (m, 1H), 6.75–6.72 (m, 2H), 4.84 (dd, 1H, *J* = 1.8, 1.6 Hz), 4.67 (ddd, 1H, *J* = 8.8, 6.6, 2.2 Hz), 4.37–4.32 (m, 1H), 3.88–3.81 (m, 1H), 3.81–3.77 (m, 6H), 2.96 (dt, 1H, *J* = 13.4, 6.6 Hz), 2.83 (dt, 1H, *J* = 13.5, 6.7 Hz), 2.15–2.11 (m, 1H), 2.00–1.96 (m, 1H), 1.85–1.77 (m, 2H), 1.74 (t, 1H, *J* = 5.8 Hz), 1.10–1.05 (m, 21H), 1.05–1.02 (m, 9H). **^{13}C-NMR** (125 MHz): δ 159.8, 153.7, 138.8, 135.6, 135.5, 133.8, 133.6, 129.5, 127.8, 115.7, 111.3, 106.0, 72.7, 72.5, 64.4, 63.5, 60.3, 37.8, 37.0, 26.9, 26.8, 19.2, 18.1, 12.4. **ESI-MS** *m/z* (rel int): (pos) 711.5 ([M+Na]$^+$, 100).



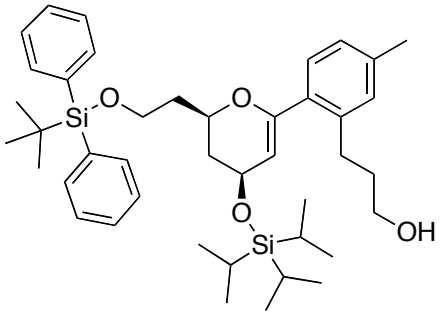
(–)-3-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-methoxyphenyl)propan-1-ol (7a). Clear oil (52 mg, 67%). **TLC**: R_f 0.28 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –7.3° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3421 (O–H st), 2941, 2341, 1654, 1606, 1497, 1463, 1427, 1388, 1362, 1337, 1272, 1239, 1105 (C–O st), 1062, 882, 822, 738, 702. **^{1}H-NMR** (500 MHz): δ 7.71–7.65 (m, 4H), 7.45–7.34 (m, 6H), 7.23 (d, 1H, *J* = 8.4 Hz), 6.76 (d, 1H, *J* = 2.5 Hz), 6.72 (dd, 1H, *J* = 8.4, 2.6 Hz), 4.83 (s, 1H), 4.71 (ddd, 1H, *J* = 8.6, 6.8, 1.9 Hz), 4.39–4.34 (m, 1H), 3.90–3.80 (m, 5H), 3.58 (t, 2H, *J* = 6.0 Hz), 2.84–2.73 (m, 2H), 2.08–2.01 (m, 1H), 1.92–1.80 (m, 4H), 1.71 (brs, 1H), 1.17–1.12 (m, 21H), 1.09–1.06 (m, 9H). **^{13}C-NMR** (125 MHz): δ 159.8, 154.1, 142.3, 135.7, 133.9, 130.9, 129.7, 129.4, 127.8, 115.1, 111.0, 105.6, 72.6, 64.6, 62.1, 60.4, 55.4, 38.1, 34.3, 31.0, 29.7, 27.0, 19.3, 18.2, 12.5. **ESI-MS** *m/z* (rel int): (pos) 725.4 ([M+Na]$^+$, 100).



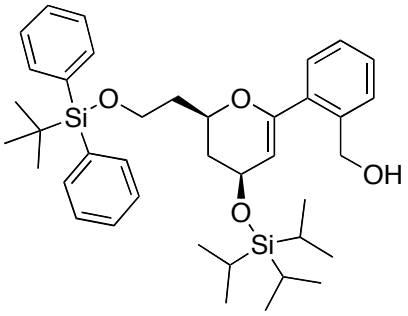
(–)-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-methylphenyl)methanol (5b). Clear oil (133 mg, 67%, 2 steps). **TLC**: R_f 0.48 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –7.5° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3436 (O–H st), 2942, 2864, 1655, 1463, 1427, 1388, 1337, 1275, 1187, 1104 (C–O st), 882, 823, 737, 702. **^{1}H-NMR** (500 MHz): δ 7.68 (ddd, 4H, *J* = 7.1, 5.5, 1.5 Hz), 7.45–7.34 (m, 6H), 7.29 (d, 1H, *J* = 7.7 Hz), 7.25 (s, 1H), 7.10 (d, 1H, *J* = 7.7 Hz), 4.99 (s, 1H), 4.72 (ddd, 1H, *J* = 8.7, 6.6, 2.1 Hz), 4.61 (d, 2H, *J* = 6.2 Hz), 4.45–4.43 (m, 1H), 3.88–3.81 (m, 2H), 2.45 (t, 1H, *J* = 6.4 Hz), 2.37 (s, 3H), 2.22 (dd, 1H, *J* = 13.2, 6.6 Hz), 2.09–2.01 (m, 1H), 1.94–1.84 (m, 2H), 1.14–1.11 (m, 21H), 1.06 (s, 9H). **^{13}C-NMR** (125 MHz): δ 153.7, 139.0, 138.9, 135.6, 133.7, 133.0, 129.9, 129.7, 129.2, 128.3, 127.7, 106.1, 73.1, 64.3, 64.1, 60.2, 37.8, 37.6, 26.9, 21.2, 19.3, 18.2, 12.4. **ESI-MS** *m/z* (rel int): (pos) 681.3 ([M+Na]$^+$, 100).



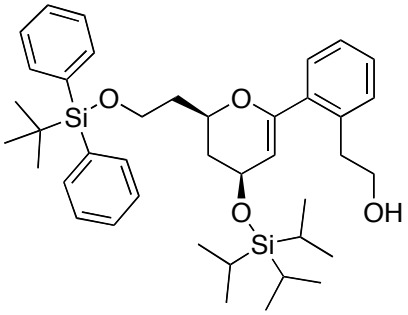
(–)-2-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-methylphenyl)ethanol (6b). Clear oil (120 mg, 59%, 2 steps). **TLC**: R_f 0.41 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –9.6° (*c* 0.6, $CHCl_3$). **IR** (NaCl, film): 3415 (O–H st), 2929, 2864, 1657, 1463, 1427, 1389, 1335, 1274, 1105 (C–O st), 882, 823, 738, 702. **^{1}H-NMR** (500 MHz): δ 7.67–7.63 (m, 4H), 7.43–7.32 (m, 6H), 7.21 (d, 1H, *J* = 7.6 Hz), 7.02–7.00 (m, 2H), 4.86 (t, 1H, *J* = 1.6 Hz), 4.67 (ddd, 1H, *J* = 8.8, 6.6, 2.2 Hz), 4.38–4.33 (m, 1H), 3.88–3.83 (m, 1H), 3.81–3.76 (m, 3H), 2.95 (dt, 1H, *J* = 13.4, 6.6 Hz), 2.83 (dt, 1H, *J* = 13.5, 6.7 Hz), 2.34–2.31 (m, 3H), 2.13 (dd, 1H, *J* = 12.5, 6.5 Hz), 2.03–1.96 (m, 1H), 1.87–1.76 (m, 2H), 1.70 (t, 1H, *J* = 5.7 Hz), 1.10–1.06 (m, 21H), 1.06–1.03 (m, 9H). **^{13}C-NMR** (125 MHz): δ 154.0, 138.5, 137.0, 135.6, 134.0, 133.7, 130.8, 129.8, 129.7, 127.7, 127.1, 106.1, 72.7, 64.4, 63.7, 60.3, 37.9, 37.8, 36.9, 27.0, 21.3, 19.3, 18.2, 12.4. **ESI-MS** *m/z* (rel int): (pos) 695.6 ([M+Na]$^+$, 100).



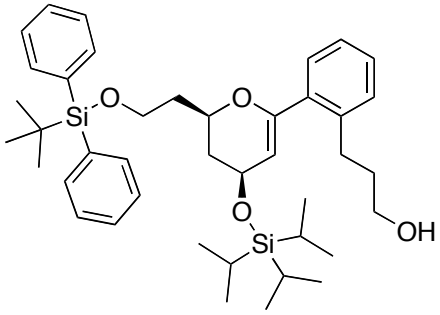
(–)-3-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-methylphenyl)propan-1-ol (7b). Clear oil (120 mg, 69%, 2 steps). **TLC**: R_f 0.41 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –10.4° (*c* 0.9, $CHCl_3$). **IR** (NaCl, film): 3388 (O–H st), 2941, 2864, 1658, 1612, 1462, 1427, 1389, 1360, 1335, 1276, 1104 (C–O st), 1063, 882, 823, 738, 702. **^{1}H-NMR** (500 MHz): δ 7.70–7.68 (m, 4H), 7.46–7.34 (m, 6H), 7.21 (d, 1H, *J* = 7.7 Hz), 7.04 (s, 1H), 7.01 (d, 1H, *J* = 7.6 Hz), 4.86 (s, 1H), 4.73 (td, 1H, *J* = 7.7, 1.8 Hz), 4.42–4.37 (m, 1H), 3.92–3.81 (m, 2H), 3.59 (t, 2H, *J* = 5.9 Hz), 2.79 (td, 2H, *J* = 9.7, 4.7 Hz), 2.36 (s, 3H), 2.21 (dd, 1H, *J* = 13.0, 6.6 Hz), 2.09–2.03 (m, 1H), 1.94–1.82 (m, 4H), 1.75 (brs, 1H), 1.14–1.10 (m, 21H), 1.11 (s, 9H). **^{13}C-NMR** (125 MHz): δ 154.3, 140.4, 138.3, 135.6, 133.9, 133.7, 130.3, 129.7, 129.6, 127.7, 126.5, 105.5, 72.6, 64.5, 62.1, 60.4, 38.0, 37.8, 34.4, 29.3, 26.9, 21.3, 19.3, 18.2, 12.4. **ESI-MS** *m/z* (rel int): (pos) 709.6 ($[M+Na]^+$, 100); (neg) 685.4 ($[M–H]^-$, 75).



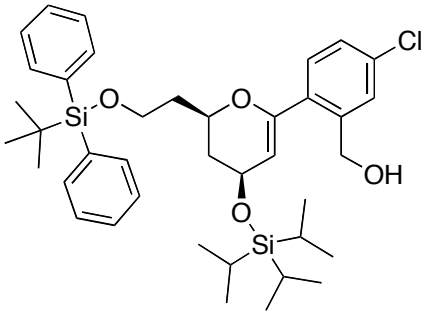
(–)-(2-((2*R*,4*S*)-2-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-4-((triisopropylsilyl)oxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)methanol (5c). Previously reported.[6c]



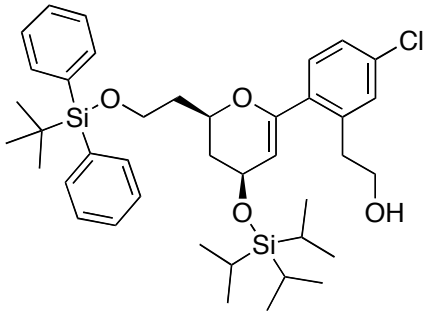
(–)-2-(2-((2*R*,4*S*)-2-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-4-((triisopropylsilyl)oxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)ethanol (6c). Previously reported.[6c]



(–)-3-(2-((2*R*,4*S*)-2-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-4-((triisopropylsilyl)oxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)propan-1-ol (7c). Previously reported.[6c]

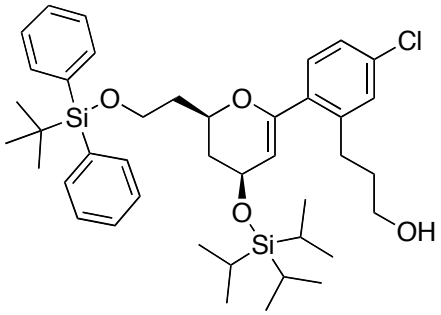


(–)-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-chlorophenyl)methanol (5d). Clear oil (150 mg, 46%, 2 steps). **TLC**: R_f 0.40 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –8.6° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3401 (O–H st), 2942, 2864, 1655, 1594, 1462, 1427, 1361, 1337, 1295, 1091 (C–O st), 882, 823, 738, 701. **^{1}H-NMR** (500 MHz): δ 7.59–7.57 (m, 4H), 7.36–7.25 (m, 7H), 7.21 (d, *J* = 8.2 Hz, 1H), 7.14 (dd, *J* = 7.9, 1.3 Hz, 1H), 4.89 (s, 1H), 4.61 (t, 1H, *J* = 6.8 Hz), 4.51 (s, 2H), 4.36–4.29 (m, 1H), 3.81–3.69 (m, 2H), 2.32 (brs, 1H), 2.12 (dd, 1H, *J* = 13.1, 6.4 Hz), 1.96–1.88 (m, 1H), 1.84–1.70 (m, 2H), 1.06–1.01 (m, 21H), 9.98 (s, 9H). **^{13}C-NMR** (125 MHz): δ 152.7, 141.1, 135.6, 134.7, 133.8, 133.6, 133.4, 130.4, 129.8, 127.7, 127.5, 106.9, 73.1, 64.2, 63.2, 60.2, 37.8, 37.6, 26.9, 19.3, 18.2, 12.4. **ESI-MS** *m/z* (rel int): (pos) 701.3 ($[M+Na]^+$, 100), 696.3 ($[M+NH_4]^+$, 30).

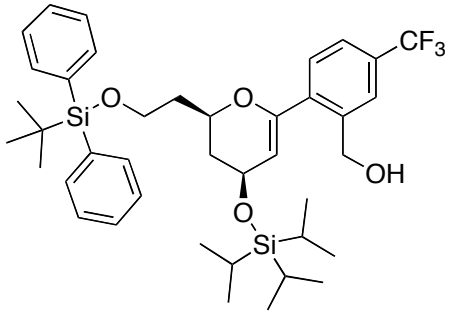


(–)-2-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-chlorophenyl)ethanol (6d). Yellow oil (135 mg, 72%, 2 steps). **TLC**: R_f 0.59 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –8.9° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3360 (O–H st), 2926, 2863, 1660, 1600, 1463, 1427, 1383, 1259, 1112 (C–O st), 1011, 882, 819, 739, 701. **^{1}H-NMR** (500 MHz): δ 7.65 (t, 4H, *J* = 6.1 Hz), 7.42–7.31 (m, 6H), 7.23–7.19 (m, 2H), 7.15 (dd, 1H, *J* = 8.2, 1.9 Hz), 4.87 (s, 1H), 4.67 (t, 1H, *J* = 6.7 Hz), 4.37–4.34 (m, 1H), 3.86–3.74 (m,

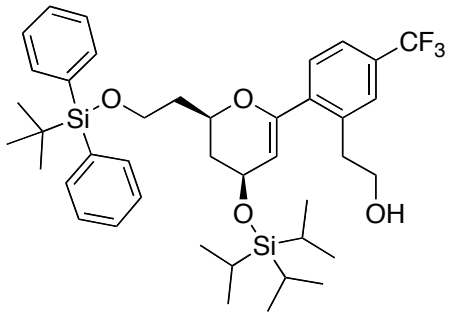
4H), 2.96–2.89 (m, 1H), 2.85–2.78 (m, 1H), 2.15 (dd, 1H, *J* = 13.1, 6.5 Hz), 2.01–1.94 (m, 1H), 1.86–1.76 (m, 2H), 1.69 (t, 1H, *J* = 5.4 Hz), 1.10–1.07 (m, 21H), 1.07 (s, 9H). **^{13}C-NMR** (125 MHz): δ 153.0, 139.3, 135.6, 135.2, 134.4, 133.6, 131.1, 130.0, 129.8, 127.7, 126.5, 106.8, 72.9, 64.3, 63.3, 60.2, 37.8, 37.7, 36.7, 27.0, 19.3, 18.2, 12.4. **ESI-MS** *m/z* (rel int): (pos) 715.6 ([M+Na]$^+$, 100); (neg) 727.6 ([M+Cl]$^-$, 100).



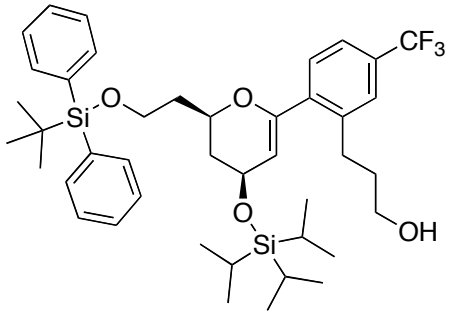
(–)-3-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-chlorophenyl)propan-1-ol (7d). Clear oil (185 mg, 72%, 2 steps). **TLC**: R_f 0.42 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –15.2° (*c* 3.3, $CHCl_3$). **IR** (NaCl, film): 3421 (O–H st), 2942, 2864, 1658, 1592, 1462, 1427, 1361, 1337, 1292, 1092 (C–O st), 882, 823, 738, 701. **^{1}H-NMR** (500 MHz): δ 7.72 (t, *J* = 6.7 Hz, 4H), 7.50–7.38 (m, 6H), 7.30–7.26 (m, 2H), 7.21–7.19 (m, 1H), 4.91 (s, 1H), 4.76 (t, 1H, *J* = 7.1 Hz), 4.46–4.41 (m, 1H), 3.93–3.85 (m, 2H), 3.62 (t, 2H, *J* = 5.9 Hz), 2.83 (t, 2H, *J* = 7.5 Hz), 2.26 (dd, 1H, *J* = 12.9, 6.4 Hz), 2.13–2.04 (m, 1H), 1.97–1.83 (m, 4H), 1.81 (brs, 1H), 1.18–1.15 (m, 21H), 1.13 (s, 9H). **^{13}C-NMR** (125 MHz): δ 153.3, 142.7, 135.6, 134.9, 134.3, 133.7, 130.9, 129.7, 129.5, 127.7, 125.9, 106.2, 72.8, 64.4, 61.8, 60.3, 37.9, 37.7, 34.1, 29.3, 26.9, 19.3, 18.2, 12.4. **ESI-MS** *m/z* (rel int): (pos) 729.5 ([M+Na]$^+$, 100); (neg) 705.3 ([M–H]$^-$, 45).



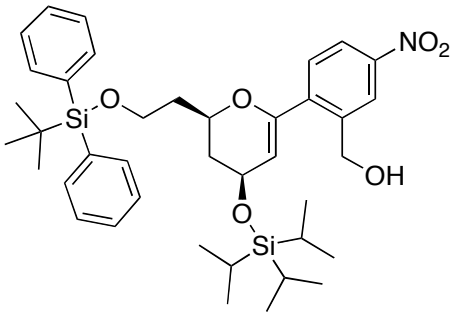
(–)-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-(trifluoromethyl)phenyl)methanol (5e). Clear oil (220 mg, 42%, 2 steps). **TLC**: R_f 0.57 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –6.8° (*c* 4.9, $CDCl_3$). **IR** (NaCl, film): 3433 (O–H st), 2943, 2865, 1654, 1463, 1427, 1329 (C–F st), 1270, 1166, 1127 (C–O st), 1081, 882, 822, 739, 702. **^{1}H-NMR** (500 MHz): δ 7.73 (s, 1H), 7.65–7.62 (m, 4H), 7.52–7.51 (m, 1H), 7.46–7.30 (m, 7H), 5.01 (dd, 1H, *J* = 1.9, 1.4 Hz), 4.71–4.68 (m, 1H), 4.66 (d, 2H, *J* = 6.4 Hz), 4.45–4.38 (m, 1H), 3.83–3.78 (m, 2H), 2.22–2.17 (m, 2H), 2.03–1.95 (m, 1H), 1.92–1.78 (m, 2H), 1.13–1.06 (m, 21H), 1.04 (s, 9H). **^{13}C-NMR** (125 MHz): δ 152.5, 140.1, 138.7, 135.6, 133.6, 133.0, 129.7, 129.4, 127.7, 125.5, 124.3, 123.1, 107.6, 73.2, 64.1, 63.3, 60.1, 37.8, 37.6, 26.9, 19.2, 18.1, 12.3. **ESI-MS** *m/z* (rel int): (pos) 735.7 ([M+Na]$^+$, 100).



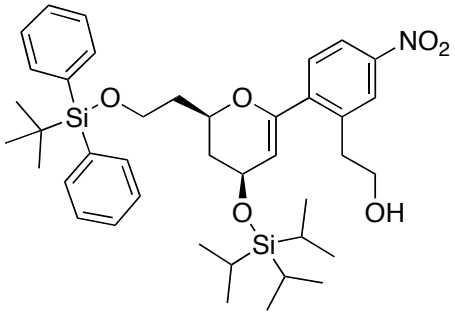
(–)-2-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-(trifluoromethyl)phenyl)ethanol (6e). Clear oil (273 mg, 56%, 2 steps). **TLC**: R_f 0.47 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –6.6° (*c* 6.7, $CDCl_3$). **IR** (NaCl, film): 3460 (O–H st), 2943, 2865, 1655, 1463, 1427, 1324 (C–F st), 1166, 1126 (C–O st), 882, 824, 738, 702. **^{1}H-NMR** (500 MHz): δ 7.66–7.63 (m, 4H), 7.48–7.30 (m, 9H), 4.92 (s, 1H), 4.68 (t, 1H, *J* = 7.6 Hz), 4.40–4.38 (m, 1H), 3.88–3.75 (m, 4H), 3.00 (dd, 1H, *J* = 13.4, 6.6 Hz), 2.92 (dd, 1H, *J* = 13.6, 6.8 Hz), 2.17 (dd, 1H, *J* = 13.2, 6.5 Hz), 2.03–1.94 (m, 1H), 1.90–1.77 (m, 2H), 1.63 (t, 1H, *J* = 5.6 Hz), 1.11–1.08 (m, 21H) 1.05 (s, 9H). **^{13}C-NMR** (125 MHz): δ 152.8, 140.1, 138.3, 135.6, 133.7, 133.6, 130.1, 129.8, 127.7, 126.9, 125.2, 123.2, 107.3, 73.0, 64.2, 63.2, 60.1, 37.8, 37.7, 36.7, 26.9, 19.2, 18.2, 12.4. **ESI-MS** *m/z* (rel int): (pos) 749.7 ([M+Na]$^+$, 100).



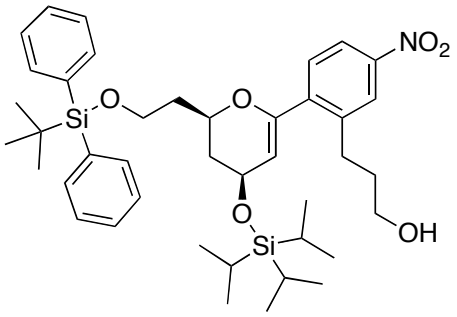
(–)-3-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-(trifluoromethyl)phenyl)propan-1-ol (7e). Clear oil (296 mg, 60%, 2 steps). **TLC**: R_f 0.38 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –8.5° (*c* 6.6, $CDCl_3$). **IR** (NaCl, film): 3369 (O–H st), 2943, 2865, 1658, 1463, 1427, 1329 (C–F st), 1296, 1166, 1126 (C–O st), 1084, 882, 837, 822, 737, 702. **^{1}H-NMR** (500 MHz): δ 7.64 (t, 4H, *J* = 8.1 Hz), 7.49–7.28 (m, 9H), 4.86 (s, 1H), 4.69 (t, 1H, *J* = 8.3 Hz), 4.38–4.36 (m, 1H), 3.85–3.77 (m, 2H), 3.55 (q, 2H, *J* = 5.8 Hz), 2.83 (q, 2H, *J* = 7.0 Hz), 2.19 (dd, 1H, *J* = 13.2, 6.6 Hz), 2.01–1.98 (m, 1H), 1.90–1.79 (m, 4H), 1.64 (t, 1H, *J* = 5.4 Hz), 1.10–1.06 (m, 21H), 1.04 (s, 9H). **^{13}C-NMR** (125 MHz): δ 153.2, 141.7, 139.8, 135.6, 133.7, 133.6, 129.9, 129.7, 127.7, 126.3, 125.2, 122.7, 106.6, 72.9, 64.3, 61.8, 60.2, 37.9, 37.7, 34.2, 29.4, 26.9, 19.3, 18.1, 12.3. **ESI-MS** *m/z* (rel int): (pos) 763.7 ([M+Na]$^+$, 100).



(–)-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-nitrophenyl)methanol (5f). Yellow oil (142 mg, 79%, 2 steps). **TLC**: R_f 0.46 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –0.6° (*c* 4.3, $CHCl_3$). **IR** (NaCl, film): 3432 (O–H st), 2944, 2866, 1657, 1588, 1524, 1465, 1341 (N–O st), 1189, 1107 (C–O st), 884, 805, 740, 704. **^{1}H-NMR** (500 MHz): δ 8.38 (d, 1H, *J* = 2.4 Hz), 8.11 (dd, 1H, *J* = 8.4, 2.4 Hz), 7.68–7.65 (m, 4H), 7.51 (d, 1H, *J* = 8.4 Hz), 7.46–7.35 (m, 6H), 5.08 (dd, 1H, *J* = 2.0, 1.5 Hz), 4.75–4.70 (m, 3H), 4.47–4.40 (m, 1H), 3.90–3.80 (m, 2H), 2.28–2.20 (m, 2H), 2.04–1.98 (m, 1H), 1.95–1.82 (m, 2H), 1.14–1.10 (m, 21H), 1.08 (s, 9H). **^{13}C-NMR** (125 MHz): δ 151.8, 148.0, 141.1, 141.0, 135.5, 133.6, 129.8, 129.7, 127.7, 123.2, 122.3, 108.6, 73.4, 64.1, 62.8, 60.1, 37.7, 37.5, 26.9, 19.2, 18.1, 12.3. **ESI-MS** *m/z* (rel int): (pos) 712.2 ([M+Na]$^+$, 100); (neg) 724.1 ([M+Cl]$^-$, 20).

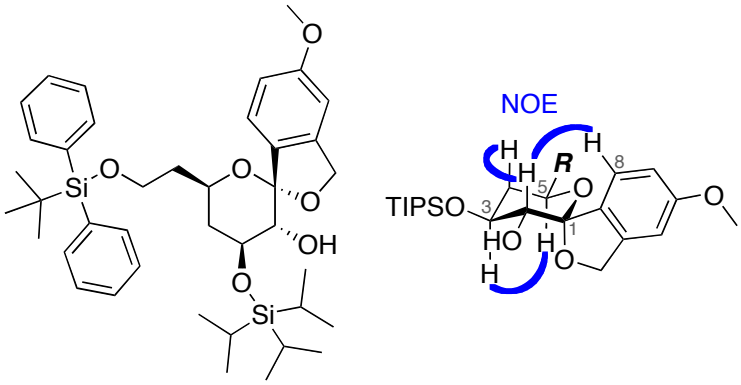


(–)-2-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-nitrophenyl)ethanol (6f). Yellow oil (214 mg, 80%, 2 steps). **TLC**: R_f 0.43 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –0.2° (*c* 5.2, $CHCl_3$). **IR** (NaCl, film): 3438 (O–H st), 2942, 2864, 1656, 1584, 1521, 1463, 1427, 1347 (N–O st), 1292, 1105 (C–O st), 1064, 882, 822, 736, 702. **^{1}H-NMR** (500 MHz): δ 8.12 (d, 1H, *J* = 2.4 Hz), 8.03 (dd, 1H, *J* = 8.4, 2.4 Hz), 7.67–7.63 (m, 4H), 7.47–7.32 (m, 7H), 4.97 (t, 1H, *J* = 1.8 Hz), 4.70 (ddd, 1H, *J* = 8.9, 6.6, 2.3 Hz), 4.42–4.38 (m, 1H), 3.88–3.78 (m, 4H), 3.05 (dt, 1H, *J* = 13.6, 6.7 Hz), 2.96 (dt, 1H, *J* = 13.7, 6.8 Hz), 2.19 (ddt, 1H, *J* = 13.2, 6.6, 1.6 Hz), 2.02–1.96 (m, 1H), 1.90–1.79 (m, 2H), 1.74 (brs, 1H), 1.11–1.08 (m, 21H), 1.06 (s, 9H). **^{13}C-NMR** (125 MHz): δ 152.2, 147.7, 142.7, 139.4, 135.5, 133.7, 130.5, 129.7, 127.7, 125.0, 121.4, 108.2, 73.2, 64.1, 62.8, 60.1, 37.7, 37.5, 36.6, 26.9, 19.2, 18.1, 12.3. **ESI-MS** *m/z* (rel int): (pos) 726.7 ([M+Na]$^+$, 100).

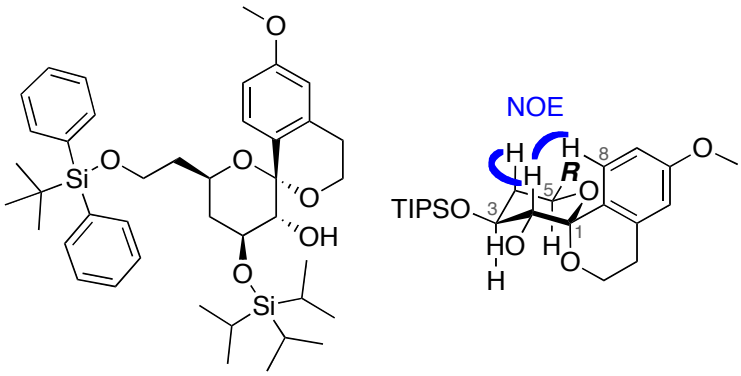


(–)-3-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)-5-nitrophenyl)propan-1-ol (7f). Yellow oil (40 mg, 42%, 2 steps). **TLC**: R_f 0.50 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –5.0° (*c* 3.3, $CHCl_3$). **IR** (NaCl, film): 3410 (O–H st), 2942, 2864, 1658, 1585, 1521, 1462, 1427, 1345 (N–O st), 1293, 1105 (C–O st), 1064, 882, 822, 737, 702. **^{1}H-NMR** (500 MHz): δ 8.10 (d, 1H, *J* = 2.3 Hz), 8.02 (dd, 1H, *J* = 8.4, 2.4 Hz), 7.66 (td, 4H, *J* = 7.1, 1.3 Hz), 7.44–7.33 (m, 7H), 4.94 (s, 1H), 4.75–4.70 (m, 1H), 4.44–4.38 (m, 1H), 3.90–3.79 (m, 2H), 3.62–3.57 (m, 2H), 2.92–2.89 (m, 2H), 2.26–2.19 (m, 1H), 2.08–2.00 (m, 1H), 1.92–1.85 (m, 4H), 1.69 (brs, 1H), 1.11 (m, 21H), 1.07 (s, 9H). **^{13}C-NMR** (125 MHz): δ 152.4, 147.8, 142.7, 142.5, 135.5, 133.7, 130.4, 129.7, 127.7, 124.4, 120.9, 107.4, 73.1, 64.2, 61.7, 60.2, 37.9, 37.6, 33.9, 29.6, 26.9, 19.2, 18.1, 12.3. **ESI-MS** *m/z* (rel int): (pos) 740.6 ($[M+Na]^+$, 80); (neg) 716.6 ($[M–H]^-$, 30).

H. C1-ARYL SPIROKETAL PRODUCTS WITH RETENTION OF CONFIGURATION (11–13)

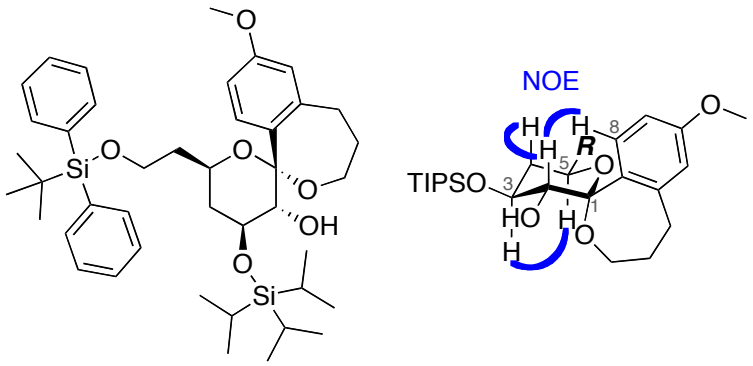


(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-5-methoxy-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (11a). Clear oil (62 mg, 100%). **TLC**: R_f 0.50 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +13.9° (*c* 5.0, $CHCl_3$). **IR** (NaCl, film): 2942, 2864, 1614, 1463, 1428, 1388, 1318, 1272, 1094 (C–O st), 1013, 882, 822, 739, 702. **^{1}H-NMR** (500 MHz): δ 7.66–7.60 (m, 4H), 7.42–7.25 (m, 7H), 6.88 (dd, 1H, *J* = 8.2, 2.1 Hz), 6.75 (d, 1H, *J* = 2.1 Hz), 5.06 (q, 2H, *J* = 14.8 Hz), 4.29–4.25 (m, 1H), 4.18 (ddd, 1H, *J* = 11.1, 9.0, 4.9 Hz), 3.81 (s, 3H), 3.79–3.70 (m, 2H), 3.68–3.64 (m, 1H), 2.07 (ddd, 1H, *J* = 12.9, 4.9, 2.1 Hz), 1.92 (d, 1H, *J* = 6.2 Hz), 1.80–1.68 (m, 2H), 1.62 (q, 1H, *J* = 12.0 Hz), 1.16–1.06 (m, 21H), 0.99 (s, 9H). **^{13}C-NMR** (125 MHz): δ 160.9, 142.0, 135.6, 134.0, 131.4, 129.5, 127.7, 122.9, 114.2, 110.4, 106.2, 72.3, 76.6, 71.6, 67.3, 60.3, 55.6, 40.9, 38.3, 26.9, 19.3, 18.3, 12.7. **ESI-MS** *m/z* (rel int): (neg) 689.7 ([M–H]$^-$, 80).

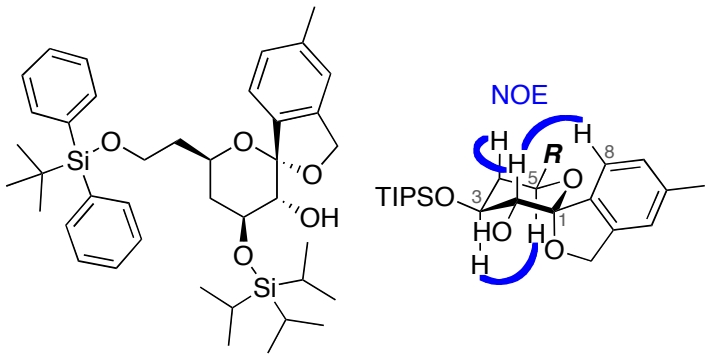


(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-6-methoxy-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (12a). Clear oil (120 mg, 99%). **TLC**: R_f 0.54 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +6.67° (*c* 0.5, $CHCl_3$). **IR** (NaCl, film): 3569 (O–H st), 2941, 2864, 1611, 1583, 1504, 1464, 1427, 1388, 1253, 1109 (C–O st), 1075, 1028, 998, 961, 882, 821, 739, 702. **^{1}H-NMR** (500 MHz): δ 7.64–7.62 (m, 4H), 7.42–7.28 (m, 7H), 6.80 (dd, 1H, *J* = 8.6, 2.6 Hz), 6.62 (d, 1H, *J* = 2.6 Hz), 4.18–4.12 (m, 2H), 4.00–3.95 (m, 1H), 3.92–3.88 (m, 1H), 3.80–3.76 (m, 4H), 3.73–3.69 (m, 2H), 3.09 (dq, 1H, *J* = 15.4, 6.4 Hz), 2.48 (dd, 1H, *J* = 16.5, 2.2 Hz), 2.06–2.02 (m, 1H), 1.95 (d, 1H, *J* = 7.1 Hz), 1.81–1.76 (m, 1H), 1.70–1.66 (m, 1H), 1.58 (q, 1H, *J* = 11.7 Hz), 1.12–1.07 (m, 21H), 1.06–1.04 (m, 9H). **^{13}C-NMR** (125 MHz): δ 159.1, 136.7, 135.6, 134.1, 129.7, 129.6, 127.9, 127.7, 113.2, 113.1,

98.9, 78.4, 71.4, 65.7, 60.6, 58.5, 55.4, 41.0, 38.4, 29.0, 27.0, 19.4, 18.3, 12.7. **ESI-MS** *m/z* (rel int): (pos) 727.5 ([M+Na]$^+$, 100); (neg) 703.5 ([M–H]$^-$, 100).

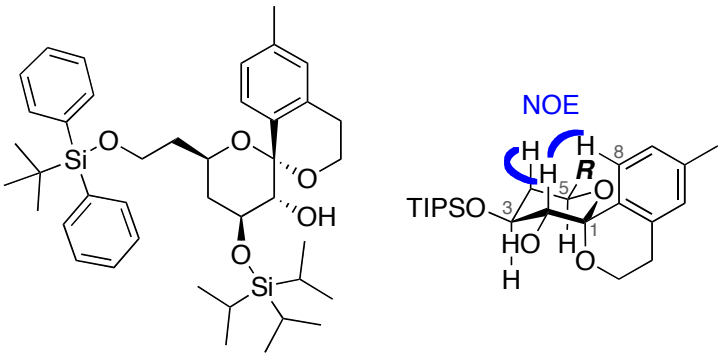


(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-7-methoxy-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*c*]oxepine-1,2′-pyran]-3′-ol (13a). Clear oil (42 mg, 100%). **TLC**: R_f 0.59 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +30.7° (*c* 0.7, $CHCl_3$). **IR** (NaCl, film): 3587 (O–H st), 3070, 2941, 2863, 1608, 1577, 1496, 1463, 1427, 1388, 1252, 1097 (C–O st), 1027, 954, 882, 822, 737, 702. **^{1}H-NMR** (500 MHz): δ 7.67–7.61 (m, 4H), 7.45–7.31 (m, 7H), 6.76 (dd, 1H, *J* = 10.1, 2.0 Hz), 6.60 (d, 1H, *J* = 2.2 Hz), 4.20–4.15 (m, 1H), 4.11–4.06 (m, 1H), 3.82–3.72 (m, 6H), 3.67–3.55 (m, 2H), 3.36 (dd, 1H, *J* = 9.0, 5.5 Hz), 2.39 (dd, 1H, *J* = 13.4, 4.9 Hz), 2.26–2.17 (m, 1H), 2.10 (d, 1H, *J* = 5.5 Hz), 2.03 (dd, 1H, *J* = 12.5, 4.6 Hz), 1.88–1.81 (m, 1H), 1.77–1.64 (m, 2H), 1.55 (q, 1H, *J* = 11.7 Hz), 1.12–1.07 (m, 21H), 1.05–1.01 (m, 9H). **^{13}C-NMR** (125 MHz): δ 159.3, 140.5, 135.6, 134.1, 132.2, 130.0, 129.7, 127.7, 114.8, 112.0, 105.3, 82.3, 71.2, 65.1, 60.8, 58.8, 55.3, 41.0, 38.6, 28.9, 27.0, 19.4, 18.3 (2), 12.7. **ESI-MS** *m/z* (rel int): (pos) 741.5 ([M+Na]$^+$, 100).

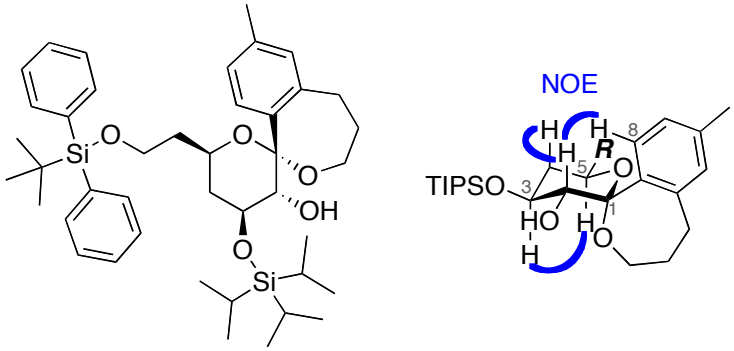


(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-5-methyl-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (11b). Clear oil (40 mg, 78%). **TLC**: R_f 0.59 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +22.0° (*c* 2.0, $CHCl_3$). **IR** (NaCl, film): 3566 (O–H st), 2942, 2864, 1462, 1427, 1388, 1261, 1110 (C–O st), 1046, 976, 941, 882, 821, 739, 702. **^{1}H-NMR** (500 MHz): δ 7.65–7.59 (m, 4H), 7.41–7.31 (m, 4H), 7.29–7.23 (m, 3H), 7.15 (d, 1H, *J* = 7.7 Hz), 7.04 (s, 1H), 5.09 (d, 1H, *J* = 12.5 Hz), 5.04 (d, 1H, *J* = 12.5 Hz), 4.31–4.23 (m, 1H), 4.22–4.16 (m, 1H), 3.78 (dd, 1H, *J* = 9.3, 6.3 Hz), 3.75–3.69 (m, 1H), 3.68–3.64 (m, 1H), 2.38 (s, 3H), 2.07 (ddd, 1H, *J* = 12.7, 5.0, 2.0 Hz), 1.90 (d, 1H, *J* = 6.3 Hz), 1.80–1.74 (m, 1H), 1.73–1.67 (m, 1H), 1.62 (q, 1H, *J* = 12.3 Hz), 1.11–1.06 (m, 21H), 1.03 (s, 9H). **^{13}C-NMR** (125 MHz): δ 140.5, 139.1, 136.3, 135.5, 133.9, 129.5, 128.7, 127.6, 121.6, 121.4, 110.4, 76.5,

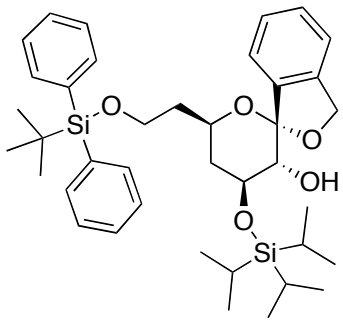
72.3, 71.6, 67.3, 60.3, 40.8, 38.2, 26.8, 21.5, 19.2, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 697.7 ([M+Na]$^+$, 100); (neg) 673.7 ([M–H]$^-$, 100).



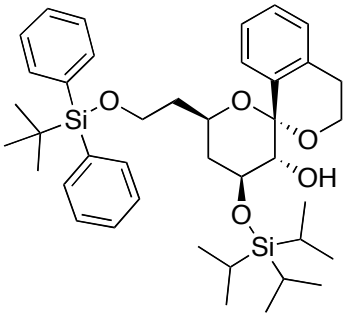
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-6-methyl-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (12b). Clear oil (9 mg, 87%). **TLC**: R_f 0.67 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +4.6° (*c* 1.2, $CHCl_3$). **IR** (NaCl, film): 3573 (O–H st), 2941, 2864, 1618, 1464, 1427, 1390, 1260, 1110 (C–O st), 1075, 1031, 961, 882, 820, 740, 702. **^{1}H-NMR** (500 MHz): δ 7.64–7.62 (m, 4H), 7.42–7.31 (m, 7H), 7.07–7.05 (m, 1H), 6.91 (s, 1H), 4.19–4.13 (m, 2H), 3.98–3.94 (m, 1H), 3.92–3.89 (m, 1H), 3.79–3.75 (m, 1H), 3.74–3.70 (m, 2H), 3.07 (dq, 1H, *J* = 16.5, 6.2 Hz), 2.47 (dd, 1H, *J* = 16.5, 2.1 Hz), 2.30 (s, 3H), 2.05 (ddd, 1H, *J* = 11.8, 4.5, 1.9 Hz), 1.94 (d, 1H, *J* = 7.1 Hz), 1.79–1.76 (m, 1H), 1.70–1.67 (m, 1H), 1.59 (q, 1H, *J* = 12.0 Hz), 1.12–1.05 (m, 21H), 1.05–1.01 (m, 9H). **^{13}C-NMR** (125 MHz): δ 137.7, 135.5, 134.9, 134.0, 132.5, 130.9, 129.6, 129.0, 127.6, 126.1, 98.8, 78.3, 71.2, 65.6, 60.5, 58.5, 40.9, 38.3, 29.7, 28.5, 26.9, 21.1, 19.3, 12.6. **ESI-MS** *m/z* (rel int): (pos) 711.5 ([M+Na]$^+$, 100); (neg) 687.6 ([M–H]$^-$, 100).



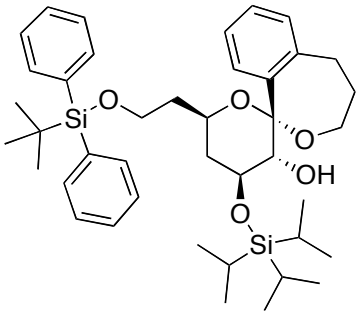
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-7-methyl-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*c*]oxepine-1,2′-pyran]-3′-ol (13b). Clear oil (87 mg, 90%). **TLC**: R_f 0.73 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +22.8° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3586 (O–H st), 2944, 2866, 1615, 1472, 1429, 1392, 1259, 1224, 1112 (C–O st), 1030, 954, 884, 822, 740, 704. **^{1}H-NMR** (500 MHz): δ 7.66–7.60 (m, 4H), 7.43–7.30 (m, 7H), 7.04 (d, 1H, *J* = 8.7 Hz), 6.88 (s, 1H), 4.21–4.14 (m, 1H), 4.12–4.06 (m, 1H), 3.82–3.72 (m, 3H), 3.64 (dd, 1H, *J* = 13.2, 8.5 Hz), 3.56 (dq, 1H, *J* = 13.8, 6.6 Hz), 3.37 (dd, 1H, *J* = 8.3, 5.5 Hz), 2.39 (dd, 1H, *J* = 13.8, 4.5 Hz), 2.30 (s, 3H), 2.25–2.17 (m, 1H), 2.09 (d, 1H, *J* = 5.6 Hz), 2.06–2.00 (m, 1H), 1.90–1.81 (m, 1H), 1.76–1.63 (m, 2H), 1.55 (q, 1H, *J* = 12.1 Hz), 1.09–1.04 (m, 21H), 1.03 (s, 9H). **^{13}C-NMR** (125 MHz): δ 138.6, 138.0, 136.9, 135.6, 135.4, 134.0, 130.2, 129.6, 127.7, 127.6, 105.4, 82.1, 71.1, 65.0, 60.7, 58.8, 40.9, 38.5, 30.3, 28.9, 26.9, 21.0, 19.2, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 725.6 ([M+Na]$^+$, 100); (neg) 701.7 ([M–H]$^-$, 100).



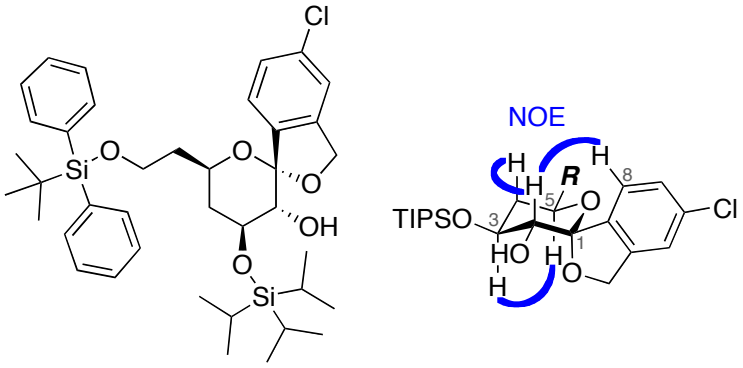
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-4′-((triisopropylsilyl)oxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (11c). Previously reported.[6c]



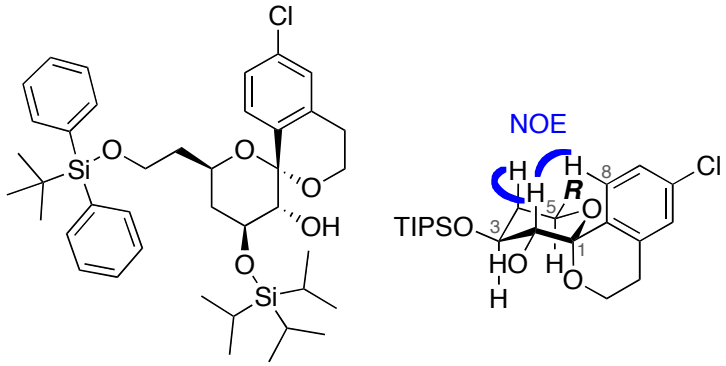
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-4′-((triisopropylsilyl)oxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (12c). Previously reported.[6c]



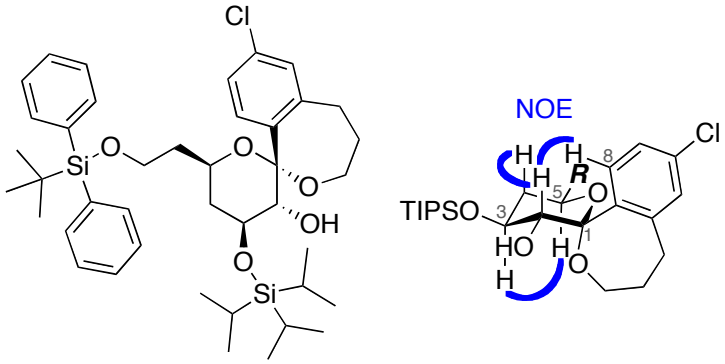
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-4′-((triisopropylsilyl)oxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*c*]oxepine-1,2′-pyran]-3′-ol (13c). Previously reported.[6c]



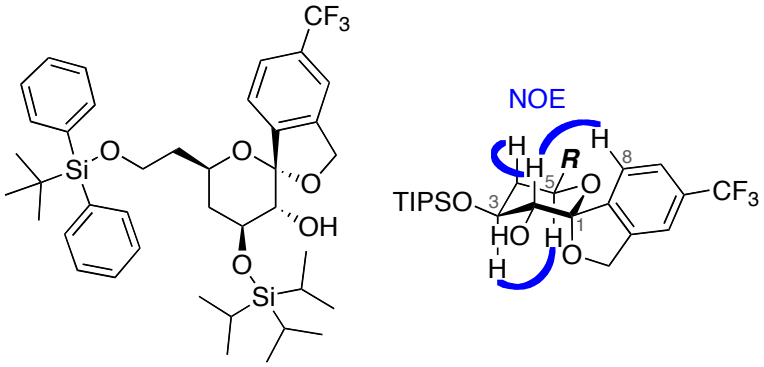
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-5-chloro-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (11d). Clear oil (20 mg, 65%). **TLC**: R_f 0.68 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +17.4° (*c* 1.5, $CHCl_3$). **IR** (NaCl, film): 3572 (O–H st), 2928, 2865, 1610, 1463, 1427, 1388, 1243, 1110 (C–O st), 1072, 1015, 941, 863, 739, 702. **^{1}H-NMR** (500 MHz): δ 7.64–7.60 (m, 4H), 7.41–7.26 (m, 8H), 7.23–7.22 (m, 1H), 5.06 (d, 2H, *J* = 4.3 Hz), 4.29–4.26 (m, 1H), 4.18 (ddd, 1H, *J* = 11.1, 8.9, 4.9 Hz), 3.76 (dd, 1H, *J* = 8.9, 6.2 Hz), 3.73–3.69 (m, 1H), 3.68–3.62 (m, 1H), 2.08 (ddd, 1H, *J* = 12.9, 4.9, 2.1 Hz), 1.95 (d, 1H, *J* = 6.2 Hz), 1.76–1.70 (m, 2H), 1.62 (q, 1H, *J* = 12.0 Hz), 1.11–1.07 (m, 21H), 1.03 (s, 9H). **^{13}C-NMR** (125 MHz): δ 142.2, 137.6, 135.5, 135.1, 133.8, 129.6, 128.2, 127.6, 123.2, 121.4, 110.1, 76.6, 71.9, 71.4, 67.5, 60.1, 40.7, 38.2, 26.8, 19.2, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 717.5 ($[M+Na]^+$, 100); (neg) 693.4 ($[M–H]^-$, 100).



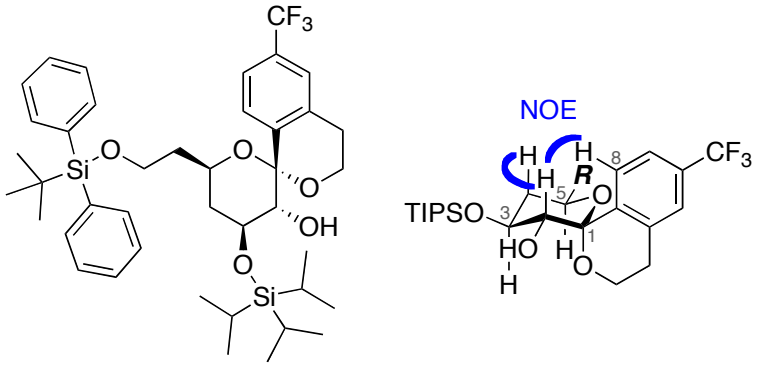
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-6-chloro-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (12d). Clear oil (12 mg, 58%). **TLC**: R_f 0.70 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +3.2° (*c* 2.2, $CHCl_3$). **IR** (NaCl, film): 3574 (O–H st), 2942, 2864, 1601, 1463, 1427, 1389, 1258, 1110 (C–O st), 1074, 1032, 882, 820, 739, 702. **^{1}H-NMR** (500 MHz): δ 7.64–7.62 (m, 4H), 7.42–7.38 (m, 2H), 7.36–7.30 (m, 5H), 7.21 (dd, 1H, *J* = 8.4, 2.0 Hz), 7.10 (d, 1H, *J* = 1.7 Hz), 4.18–4.13 (m, 2H), 3.94–3.91 (m, 2H), 3.80–3.74 (m, 1H), 3.72–3.67 (m, 2H), 3.12–3.03 (m, 1H), 2.50 (d, 1H, *J* = 16.2 Hz), 2.05 (dd, 1H, *J* = 11.1, 4.0 Hz), 1.95 (d, 1H, *J* = 7.4 Hz), 1.81–1.73 (m, 1H), 1.72–1.64 (m, 1H), 1.59 (q, 1H, *J* = 11.9 Hz), 1.11–1.06 (m, 21H), 1.04 (s, 9H). **^{13}C-NMR** (125 MHz): δ 137.0, 135.5, 133.9, 133.8, 133.6, 129.6, 128.2, 127.9, 127.6, 127.0, 98.5, 78.2, 71.0, 65.7, 60.3, 58.1, 40.7, 38.1, 28.3, 26.8, 19.2, 18.2, 12.5. **ESI-MS** *m/z* (rel int): (pos) 731.7 ($[M+Na]^+$, 100); (neg) 707.7 ($[M–H]^-$, 70).



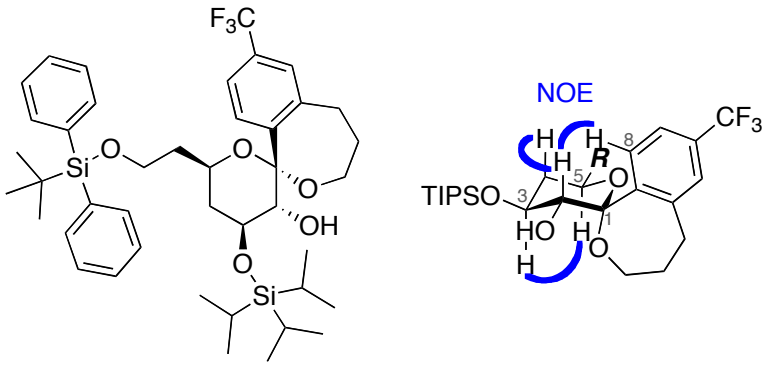
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-7-chloro-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*c*]oxepine-1,2′-pyran]-3′-ol (13d). Clear oil (52 mg, 92%). **TLC**: R_f 0.80 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +27.3° (*c* 3.5, $CHCl_3$). **IR** (NaCl, film): 3590 (O–H st), 2943, 2864, 1594, 1470, 1427, 1389, 1254, 1097 (C–O st), 1027, 997, 952, 881, 822, 737, 702. **^{1}H-NMR** (500 MHz): δ 7.66–7.61 (m, 4H), 7.43–7.31 (m, 7H), 7.18 (dd, 1H, *J* = 8.4, 2.2 Hz), 7.05 (d, 1H, *J* = 2.2 Hz), 4.20–4.14 (m, 1H), 4.11–4.06 (m, 1H), 3.81–3.53 (m, 5H), 3.33 (dd, 1H, *J* = 8.9, 5.5 Hz), 2.40 (dd, 1H, *J* = 13.6, 5.2 Hz), 2.27–2.19 (m, 1H), 2.10 (d, 1H, *J* = 5.4 Hz), 2.03 (ddd, 1H, *J* = 12.8, 4.6, 2.1 Hz), 1.87–1.79 (m, 1H), 1.77–1.62 (m, 2H), 1.54 (q, 1H, *J* = 11.9 Hz), 1.11–1.05 (m, 21H), 1.04 (s, 9H). **^{13}C-NMR** (125 MHz): δ 140.8, 138.4, 135.5, 133.9, 133.7, 130.1, 129.6, 129.1, 127.6, 126.8, 105.1, 82.1, 70.9, 65.2, 60.6, 58.7, 40.8, 38.4, 30.1, 28.6, 26.9, 19.2, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 745.7 ($[M+Na]^+$, 100); (neg) 721.5 ($[M–H]^-$, 100).



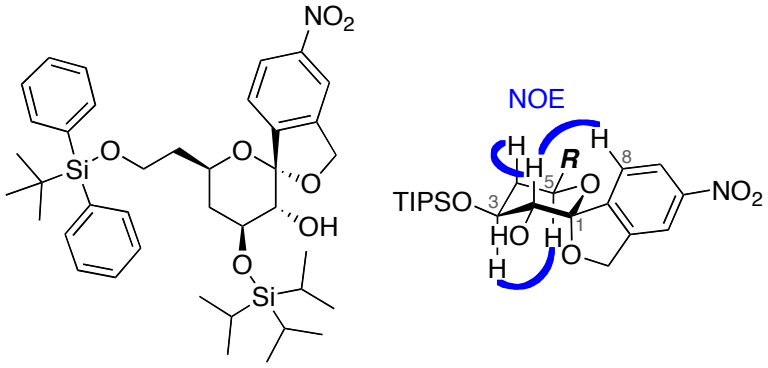
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-5-(trifluoromethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (11e). Clear oil (37 mg, 67%). **TLC**: R_f 0.67 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +19.7° (*c* 2.5, $CHCl_3$). **IR** (NaCl, film): 3576 (O–H st), 2943, 2865, 1464, 1428, 1390, 1326 (C–F st), 1248, 1166, 1127 (C–O st), 1063, 1015, 883, 830, 741, 702. **^{1}H-NMR** (500 MHz): δ 7.63–7.58 (m, 5H), 7.51 (s, 1H), 7.48 (d, 1H, *J* = 7.9 Hz), 7.41–7.31 (m, 4H), 7.25 (q, 2H, *J* = 6.8 Hz), 5.13 (s, 2H), 4.33–4.28 (m, 1H), 4.21 (ddd, 1H, *J* = 11.0, 9.0, 4.9 Hz), 3.82 (dd, 1H, *J* = 11.8, 6.2 Hz), 3.74–3.69 (m, 1H), 3.65 (td, 1H, *J* = 8.7, 4.6 Hz), 2.10 (ddd, 1H, *J* = 12.8, 4.8, 1.8 Hz), 1.98 (d, 1H, *J* = 6.1 Hz), 1.79–1.69 (m, 2H), 1.64 (q, 1H, *J* = 12.0 Hz), 1.15–1.07 (m, 21H), 1.03 (m, 9H). **^{13}C-NMR** (125 MHz): δ 142.7, 141.1, 135.5, 133.9, 131.5, 129.6, 127.6, 127.5, 125.3, 122.6, 118.4, 110.1, 76.6, 72.1, 71.3, 67.6, 60.1, 40.7, 38.1, 26.8, 19.2, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 751.6 ($[M+Na]^+$, 100); (neg) 727.6 ($[M–H]^-$, 100).



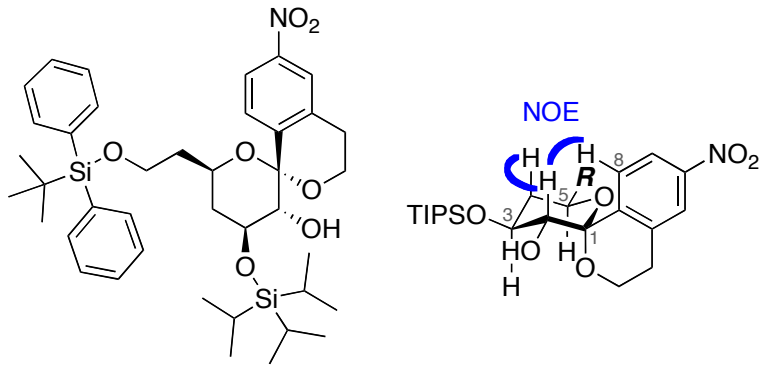
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-6-(trifluoromethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (12e). Clear oil (3 mg, 59%). **TLC**: R_f 0.68 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +5.0° (*c* 1.8, $CDCl_3$). **IR** (NaCl, film): 3575 (O–H st), 2943, 2865, 1464, 1427, 1340, 1323 (C–F st), 1168, 1126 (C–O st), 1072, 1036, 884, 827, 738, 702. **^{1}H-NMR** (500 MHz): δ 7.62 (dd, 4H, *J* = 6.6, 1.4 Hz), 7.49 (s, 2H), 7.41–7.31 (m, 7H), 4.19–4.16 (m, 2H), 3.95 (dd, 2H, *J* = 7.8, 1.6 Hz), 3.76–3.70 (m, 3H), 3.14 (dt, 1H, *J* = 16.6, 9.3 Hz) 2.58 (d, 1H, *J* = 16.4 Hz), 2.07 (ddd, 1H, *J* = 15.9, 6.9, 1.9 Hz), 1.97 (d, 1H, *J* = 7.4 Hz), 1.81–1.66 (m, 2H), 1.61 (q, 1H, *J* = 12.2 Hz), 1.11–1.06 (m, 21H), 1.04 (s, 9H). **^{13}C-NMR** (125 MHz): δ 139.2, 135.9, 135.5, 133.9, 129.9, 129.6, 127.6, 127.1, 125.4, 123.6, 122.9, 98.5, 78.3, 71.0, 66.0, 60.3, 58.3, 40.8, 38.2, 28.5, 26.9, 19.2, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 765.7 ([M+Na]$^+$, 100).



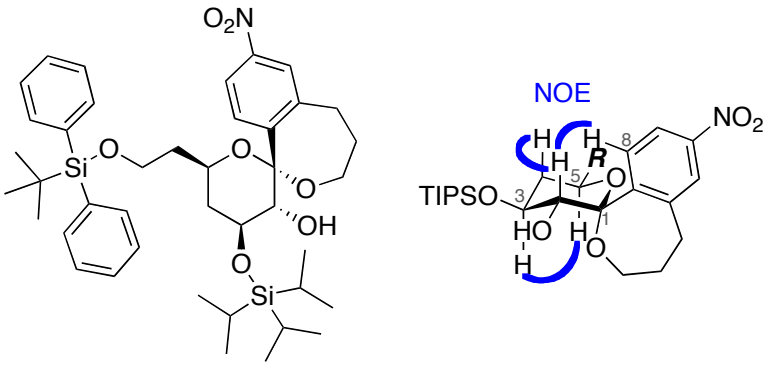
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-7-(trifluoromethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*c*]oxepine-1,2′-pyran]-3′-ol (13e). Clear oil (86 mg, 89%). **TLC**: R_f 0.71 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +27.4° (*c* 4.3, $CDCl_3$). **IR** (NaCl, film): 3587 (O–H st), 2943, 2865, 1558, 1471, 1427, 1329 (C–F st), 1165, 1125 (C–O st), 1079, 953, 882, 833, 736, 702. **^{1}H-NMR** (500 MHz): δ 7.64–7.62 (m, 4H), 7.55 (d, 1H, *J* = 8.3 Hz), 7.46 (d, 1H, *J* = 8.2 Hz), 7.42–7.31 (m, 7H), 4.19 (ddd, 1H, *J* = 10.9, 8.8, 4.9 Hz), 4.13–4.10 (m, 1H), 3.81–3.74 (m, 2H), 3.71–3.64 (m, 3H), 3.36 (dd, 1H, *J* = 8.8, 5.5 Hz), 2.50 (dd, 1H, *J* = 11.6, 4.4 Hz), 2.31–2.21 (m, 1H), 2.13 (d, 1H, *J* = 5.5 Hz), 2.05 (ddd, 1H, *J* = 12.8, 4.9, 1.9 Hz), 1.88–1.81 (m, 1H), 1.78–1.65 (m, 2H), 1.58 (q, 1H, *J* = 12.2 Hz), 1.12–1.05 (m, 21H), 1.03 (s, 9H). **^{13}C-NMR** (125 MHz): δ 143.8, 139.7, 135.6, 135.4, 133.9, 129.8, 129.3, 128.5, 127.8, 126.4, 123.7, 105.1, 82.0, 70.8, 65.3, 60.5, 58.9, 40.8, 38.4, 30.2, 28.6, 26.8, 19.2, 18.1, 12.6. **ESI-MS** *m/z* (rel int): (pos) 779.7 ([M+Na]$^+$, 100); (neg) 755.7 ([M–H]$^-$, 30).



(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-5-nitro-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (11f). Clear oil (37 mg, 25%). **TLC**: R_f 0.65 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +17.6° (*c* 2.5, $CHCl_3$). **IR** (NaCl, film): 3565 (O–H st), 2942, 2865, 1528, 1463, 1427, 1389, 1346 (N–O st), 1244, 1110 (C–O st), 1016, 941, 883, 821, 738, 702. **^{1}H-NMR** (500 MHz): δ 8.24 (d, 1H, *J* = 8.3 Hz), 8.11 (s, 1H), 7.63–7.57 (m, 4H), 7.49 (d, 1H, *J* = 8.3 Hz), 7.42–7.26 (m, 6H), 5.15 (d, 2H, *J* = 2.7 Hz), 4.34–4.28 (m, 1H), 4.24–4.18 (m, 1H), 3.81 (dd, 1H, *J* = 8.8, 5.9 Hz), 3.74–3.62 (m, 2H), 2.10 (ddd, 1H, *J* = 14.4, 4.9, 1.8 Hz), 2.01 (d, 1H, *J* = 5.9 Hz), 1.79–1.69 (m, 2H), 1.65 (q, 1H, *J* = 12.0 Hz), 1.12–1.06 (m, 21H), 1.03 (s, 9H). **^{13}C-NMR** (125 MHz): δ 149.1, 145.5, 142.1, 135.5, 133.8, 129.6, 127.7, 123.8, 123.1, 116.8, 109.9, 76.6, 71.8, 71.2, 67.9, 60.1, 40.6, 38.1, 26.8, 19.3, 18.2, 12.6. **ESI-MS** *m*/*z* (rel int): (pos) 728.6 ([M+Na]$^+$, 100); (neg) 704.5 ([M–H]$^-$, 100).

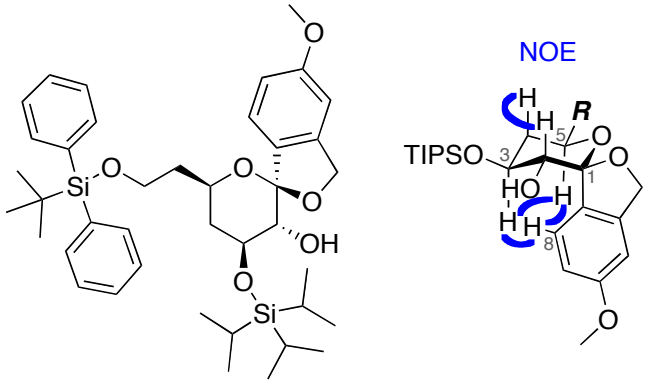


(–)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-6-nitro-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (12f). Clear oil (14 mg, 85%). **TLC**: R_f 0.60 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –3.6° (*c* 2.9, $CHCl_3$). **IR** (NaCl, film): 3567 (O–H st), 2942, 2864, 1732, 1524, 1464, 1427, 1389, 1348 (N–O st), 1259, 1107 (C–O st), 1074, 1037, 884, 822, 738, 702. **^{1}H-NMR** (500 MHz): δ 8.08 (dd, 1H, *J* = 8.5, 2.2 Hz), 7.99 (d, 1H, *J* = 2.2 Hz), 7.63–7.60 (m, 4H), 7.54 (d, 1H, *J* = 8.7 Hz), 7.42–7.38 (m, 2H), 7.35–7.31 (m, 4H), 4.20–4.15 (m, 2H), 3.98–3.91 (m, 2H), 3.78–3.68 (m, 3H), 3.22–3.13 (m, 1H), 2.64 (d, 1H, *J* = 16.4 Hz), 2.07 (ddd, 1H, *J* = 12.9, 5.0, 2.1 Hz), 1.97 (d, 1H, *J* = 7.3 Hz), 1.77–1.68 (m, 2H), 1.61 (q, 1H, *J* = 12.1 Hz), 1.11–1.06 (m, 21H), 1.04 (s, 9H). **^{13}C-NMR** (125 MHz): δ 147.3, 142.3, 137.1, 135.5, 133.8, 129.7, 127.9, 127.6, 123.4, 121.7, 98.4, 78.3, 70.9, 66.2, 60.3, 58.2, 40.8, 38.1, 28.6, 26.9, 19.2, 18.2, 12.6. **ESI-MS** *m*/*z* (rel int): (pos) 742.7 ([M+Na]$^+$, 100); (neg) 718.7 ([M–H]$^-$, 20).

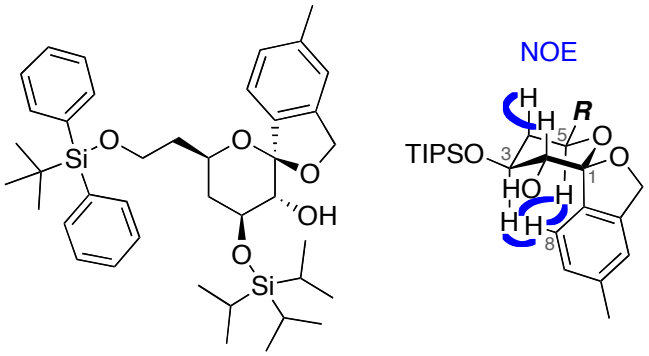


(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-7-nitro-4′-(triisopropylsilyl-oxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*c*]oxepine-1,2′-pyran]-3′-ol (13f). Yellow oil (33 mg, 81%). **TLC**: R_f 0.69 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +27.7° (*c* 2.2, $CHCl_3$). **IR** (NaCl, film): 3599 (O–H st), 2944, 2866, 1590, 1524, 1465, 1429, 1346 (N–O st), 1107 (C–O st), 1032, 956, 884, 825, 738, 704. **^{1}H-NMR** (500 MHz): δ 8.04 (dd, 1H, *J* = 8.6, 2.2 Hz), 7.96 (d, 1H, *J* = 2.1 Hz), 7.64–7.60 (m, 5H), 7.43–7.32 (m, 6H), 4.23–4.18 (m, 1H), 4.14–4.10 (m, 1H), 3.80–3.64 (m, 5H), 3.35 (dd, 1H, *J* = 8.7, 5.2 Hz), 2.57 (dd, 1H, *J* = 13.4, 5.1 Hz), 2.34–2.24 (m, 1H), 2.14 (d, 1H, *J* = 5.2 Hz), 2.06 (dt, 1H, *J* = 12.7, 2.4 Hz), 1.85 (dt, 1H, *J* = 13.7, 6.9 Hz), 1.78–1.68 (m, 2H), 1.58 (q, 1H, *J* = 11.7 Hz), 1.09–1.05 (m, 21H), 1.03 (s, 9H). **^{13}C-NMR** (125 MHz): δ 147.5, 147.1, 140.9, 135.5, 133.8, 129.9, 129.7, 127.6, 124.2, 121.6, 104.9, 81.9, 70.7, 65.6, 60.5, 58.9, 40.7, 38.3, 30.2, 28.4, 26.9, 19.2, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 756.7 ($[M+Na]^+$, 80); (neg) 732.4 ($[M–H]^–$, 60).

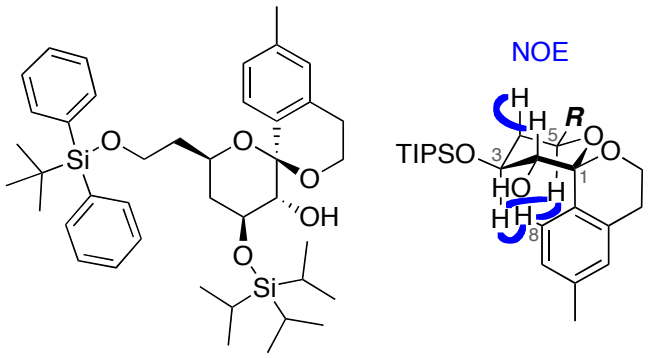
I. C1-ARYL SPIROKETAL PRODUCTS WITH INVERSION OF CONFIGURATION (8–10)



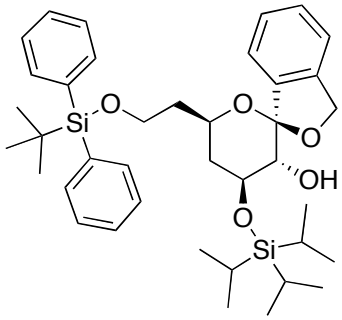
(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-5-methoxy-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (8a). Clear oil (17 mg, 83%). **TLC**: R_f 0.29 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +20.8° (*c* 3.1, $CHCl_3$). **IR** (NaCl, film): 3626 (O–H st), 2925, 2863, 1681, 1613, 1463, 1428, 1273, 1109 (C–O st), 1030, 883, 821, 738, 702. **^{1}H-NMR** (500 MHz): δ 7.53 (d, 2H, *J* = 6.8 Hz), 7.45-7.25 (m, 9H), 6.84 (s, 1H), 6.77 (dd, 1H, *J* = 8.3, 1.9 Hz), 5.25 (d, 1H, *J* = 12.6 Hz), 5.05 (d, 1H, *J* = 12.6 Hz), 4.53-4.44 (m, 1H), 4.13-4.05 (m, 1H), 3.81-3.77 (m, 4H), 3.69-3.63 (m, 1H), 3.60-3.54 (m, 1H), 2.22 (d, 1H, *J* = 2.7 Hz), 2.14 (dd, 1H, *J* = 12.8, 3.6 Hz), 1.77-1.60 (m, 3H), 1.17-1.01 (m, 21H), 0.91 (s, 9H). **^{13}C-NMR** (125 MHz): δ 160.6, 143.7, 135.5, 133.8, 133.6, 129.5, 127.5, 124.0, 113.1, 111.1, 107.1, 78.3, 71.9, 71.0, 65.7, 59.6, 55.5, 40.5, 38.5, 26.8, 19.1, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 691.3 ($[M+H]^+$, 90).



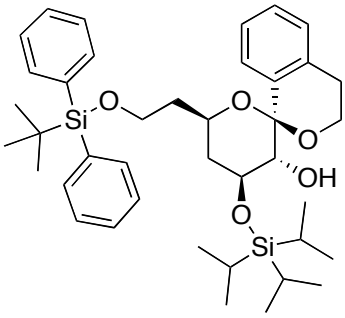
(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-5-methyl-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (8b). Clear oil (54 mg, 95%). **TLC**: R_f 0.48 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +18.5° (*c* 3.3, $CHCl_3$). **IR** (NaCl, film): 3482 (O–H st), 2942, 2864, 1462, 1427, 1388, 1350, 1267, 1109 (C–O st), 1029, 940, 882, 812, 739, 702. **^{1}H-NMR** (500 MHz): δ 7.54–7.51 (m, 2H), 7.43–7.28 (m, 9H), 7.14 (s, 1H), 7.05 (d, 1H, *J* = 7.4 Hz), 5.26 (d, 1H, *J* = 12.6 Hz), 5.06 (d, 1H, *J* = 12.6 Hz), 4.52 (ddd, 1H, *J* = 11.3, 9.5, 5.2 Hz), 4.14–4.08 (m, 1H), 3.80 (dd, 1H, *J* = 9.4, 3.0 Hz), 3.65 (ddd, 1H, *J* = 10.4, 4.4, 1.8 Hz), 3.56 (dt, 1H, *J* = 10.2, 5.1 Hz), 2.35 (s, 3H), 2.21 (d, 1H, *J* = 3.0 Hz), 2.15 (ddd, 1H, *J* = 12.9, 5.1, 1.9 Hz), 1.78–1.68 (m, 2H), 1.64 (q, 1H, *J* = 12.5 Hz), 1.18–1.05 (m, 21H), 0.89–0.87 (m, 9H). **^{13}C-NMR** (125 MHz): δ 142.1, 139.0, 135.4, 134.3, 133.8, 129.5, 128.0, 127.5, 122.9, 122.3, 111.2, 78.4, 71.9, 70.9, 65.7, 59.6, 40.5, 38.5, 26.7, 21.3, 19.1, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 697.7 ($[M+Na]^+$, 50); (neg) 673.6 ($[M–H]^-$, 100).



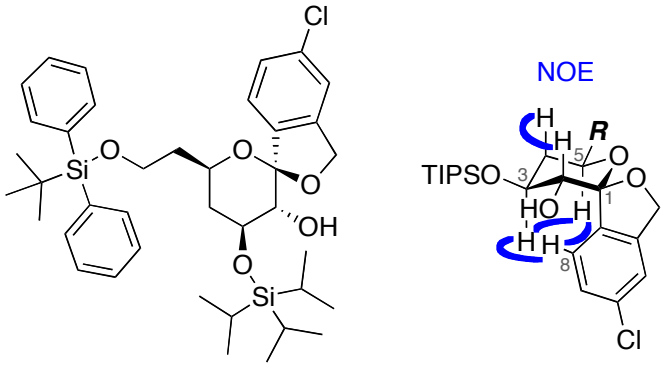
(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-6-methyl-4′-(triisopropylsilyl-oxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (9b). Yellow oil (38 mg, 34%). **TLC**: R_f 0.54 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +19.4° (*c* 2.5, $CHCl_3$). **IR** (NaCl, film): 3468 (O–H st), 1463, 1427, 1383, 1247, 1096 (C–O st), 1019, 939, 882, 813, 737, 701. **^{1}H-NMR** (500 MHz): δ 7.53–7.46 (m, 4H), 7.41–7.29 (m, 7H), 7.00 (d, 2H, *J* = 6.0 Hz), 4.58 (ddd, 1H, *J* = 10.9, 9.0, 5.6 Hz), 4.31–4.26 (m, 1H), 3.87–3.77 (m, 2H), 3.71 (dd, 1H, *J* = 8.9, 3.3 Hz), 3.66–3.55 (m, 2H), 2.86 (t, 2H, *J* = 6.0 Hz), 2.29 (s, 3H), 2.18 (d, 1H, *J* = 3.4 Hz), 2.07 (ddd, 1H, *J* = 12.8, 5.6, 1.9 Hz), 1.77–1.59 (m, 3H), 1.18–1.07 (m, 21H), 0.88 (s, 9H). **^{13}C-NMR** (125 MHz): δ 137.7, 136.3, 135.5, 133.9, 131.0, 129.8, 129.5, 127.6, 127.0, 126.1, 99.8, 81.0, 71.7, 66.2, 60.8, 60.0, 40.2, 38.8, 28.9, 26.7, 21.1, 19.1, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 711.6 ($[M+Na]^+$, 30); (neg) 687.7 ($[M–H]^-$, 100).



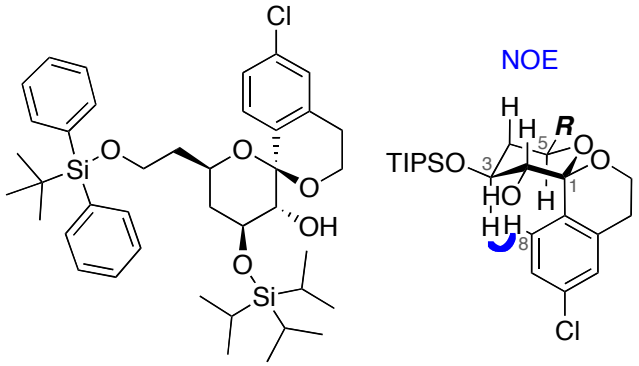
(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-4′-((triisopropylsilyl)oxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (8c). Previously reported.[6c]



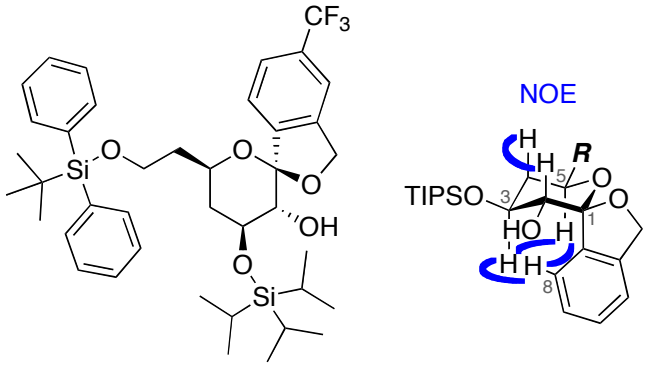
(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-4′-((triisopropylsilyl)oxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (9c). Previously reported.[6c]



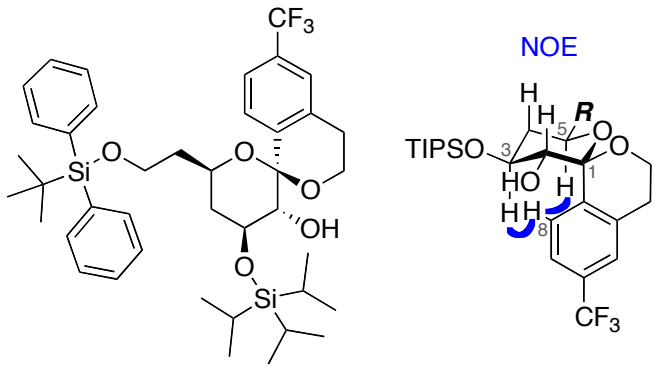
(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-5-chloro-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (8d). Yellow oil (23 mg, 90%). **TLC**: R_f 0.46 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +18.2° (*c* 1.5, $CHCl_3$). **IR** (NaCl, film): 3491 (O–H st), 2941, 2864, 1605, 1470, 1427, 1249, 1110 (C–O st), 1031, 940, 883, 815, 740, 702. **^{1}H-NMR** (500 MHz): δ 7.52–7.50 (m, 2H), 7.45–7.43 (m, 2H), 7.42–7.28 (m, 8H), 7.21 (dd, 1H, *J* = 8.1, 1.2 Hz), 5.23 (d, 1H, *J* = 12.9 Hz), 5.05 (d, 1H, *J* = 12.9 Hz), 4.48–4.42 (m, 1H), 4.05–4.02 (m, 1H), 3.80 (dd, 1H, *J* = 9.3, 2.9 Hz), 3.66–3.62 (m, 1H), 3.60–3.54 (m, 1H), 3.49 (d, 1H, *J* = 5.5 Hz), 2.25 (d, 1H, *J* = 2.9 Hz), 2.15 (ddd, 1H, *J* = 12.9, 4.2, 1.9 Hz), 1.75–1.70 (m, 1H), 1.64 (q, 1H, *J* =12.0 Hz), 1.17–1.05 (m, 21H), 0.92 (s, 9H). **^{13}C-NMR** (125 MHz): δ 143.8, 135.9, 135.6, 135.2, 133.7, 133.6, 129.5, 127.5, 124.0, 122.4, 111.0, 78.3, 71.5, 70.9, 65.8, 59.6, 40.3, 38.5, 26.7, 19.2, 18.1, 12.6. **ESI-MS** *m/z* (rel int): (pos) 717.5 ($[M+Na]^+$, 100).



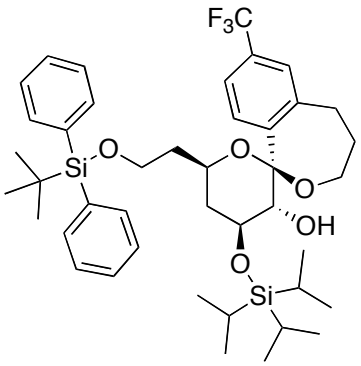
(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-6-chloro-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (9d). Clear oil (43 mg, 48%). **TLC**: R_f 0.61 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +18.7° (*c* 2.8, $CHCl_3$). **IR** (NaCl, film): 3490 (O–H st), 2941, 2864, 1599, 1470, 1427, 1387, 1096 (C–O st), 1013, 882, 849, 814, 738, 701. **^{1}H-NMR** (500 MHz): δ 7.50 (d, 4H, *J* = 7.1 Hz), 7.42–7.31 (m, 7H), 7.18–7.14 (m, 2H), 4.54–4.47 (m, 1H), 4.27–4.23 (m, 1H), 3.83 (dt, 1H, *J* = 10.8, 5.6 Hz), 3.72 (dd, 2H, *J* = 8.9, 3.1 Hz), 3.66–3.55 (m, 2H), 2.91–2.79 (m, 2H), 2.23 (d, 1H, *J* = 3.2 Hz), 2.08–2.05 (m, 1H), 1.73–1.63 (m, 3H), 1.17–1.03 (m, 21H), 0.90 (s, 9H). **^{13}C-NMR** (125 MHz): δ 138.4, 135.5, 133.8, 133.6, 132.6, 129.6, 129.0, 128.5, 127.6, 125.4, 99.5, 80.8, 71.7, 66.5, 60.3, 59.9, 39.9, 38.8, 28.6, 26.7, 19.1, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 731.7 ($[M+Na]^+$, 100); (neg) 743.6 ($[M+Cl]^-$, 100).



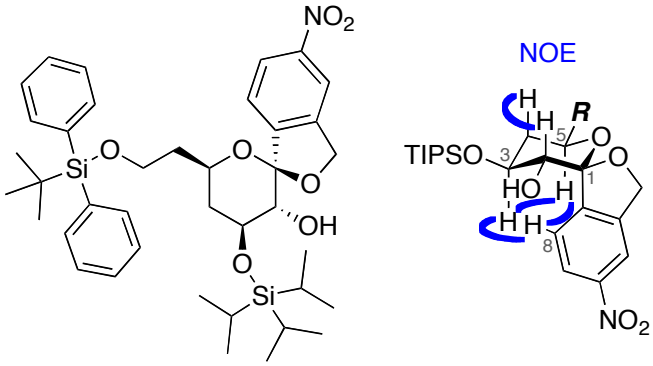
(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-5-(trifluoromethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (8e). Clear oil (19 mg, 93%). **TLC**: R_f 0.45 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +20.0° (*c* 3.1, $CHCl_3$). **IR** (NaCl, film): 3486 (O–H st), 2943, 2865, 1464, 1428, 1388, 1360, 1328 (C–F st), 1255, 1168, 1129 (C–O st), 1091, 1033, 940, 883, 822, 738, 702. **^{1}H-NMR** (500 MHz): δ 7.58 (s, 1H), 7.52–7.48 (m, 4H), 7.42–7.26 (m, 8H), 5.28 (d, 1H, *J* = 13.0 Hz), 5.12 (d, 1H, *J* = 13.0 Hz), 4.51 (td, 1H, *J* = 10.3, 4.4 Hz), 4.09–4.04 (m, 1H), 3.84 (d, 1H, *J* = 9.2 Hz), 3.66–3.61 (m, 1H), 3.56 (dt, 1H, *J* = 10.2, 5.0 Hz), 2.30 (d, *J* = 2.0 Hz, 1H), 2.18 (dd, 1H, *J* = 12.8, 3.7 Hz), 1.73–1.64 (m, 3H), 1.19–1.08 (m, 21H), 0.88 (s, 9H). **^{13}C-NMR** (125 MHz): δ 142.6, 141.1, 135.4, 133.5, 131.5, 129.6, 127.5, 124.4, 123.5, 119.0, 111.0, 78.1, 71.6, 70.9, 66.1, 59.5, 40.3, 38.4, 26.7, 19.1, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 751.6 ($[M+Na]^+$, 100); (neg) 727.5 ($[M–H]^-$, 100).



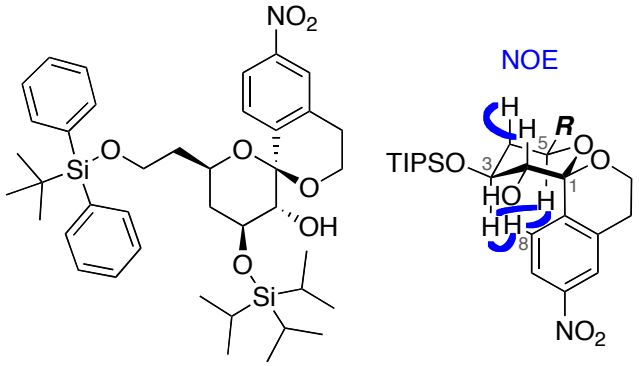
(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-6-(trifluoromethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (9e). Clear oil (18 mg, 64%). **TLC**: R_f 0.58 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +19.7° (*c* 2.2, $CHCl_3$). **IR** (NaCl, film): 3494 (O–H st), 2942, 2865, 1464, 1427, 1389, 1324 (C–F st), 1276, 1168, 1127 (C–O st), 1027, 882, 824, 738, 702. **^{1}H-NMR** (500 MHz): δ 7.58 (d, 1H, *J* = 8.0 Hz), 7.51–7.48 (m, 4H), 7.45–7.38 (m, 4H), 7.32 (q, 4H, *J* = 7.6 Hz), 4.55–4.52 (m, 1H), 4.28 (dt, 1H, *J* = 10.5, 6.2 Hz), 3.86 (dt, 1H, *J* = 10.8, 5.6 Hz), 3.76–3.71 (m, 2H), 3.60 (ddd, 2H, *J* = 13.2, 8.9, 4.6 Hz), 2.93 (t, 2H, *J* = 6.1 Hz), 2.28 (brs, 1H), 2.09 (ddd, 1H, *J* = 9.7, 5.6, 2.2 Hz), 1.74–1.63 (m, 3H), 1.15–1.09 (m, 21H), 0.88 (s, 9H). **^{13}C-NMR** (125 MHz): δ 138.0, 137.2, 135.4, 133.7, 133.5, 130.2, 129.6, 127.6, 125.9, 122.1, 99.4, 80.7, 71.7, 66.8, 60.3, 59.9, 39.8, 38.8, 28.6, 26.6, 19.0, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 765.7 ($[M+Na]^+$, 100); (neg) 741.7 ($[M–H]^-$, 100).



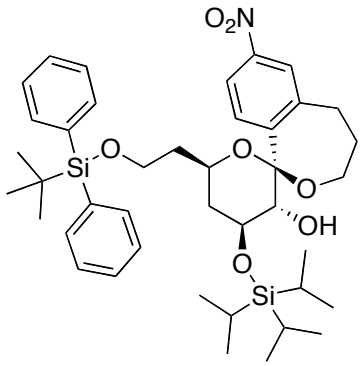
(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-7-(trifluoromethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*c*]oxepine-1,2′-pyran]-3′-ol (10e). Clear oil (8.5 mg, 85%). **IR** (NaCl, film): 3421 (O–H st), 2943, 2866, 1463, 1427, 1330 (C–F st), 1246, 1166, 1127 (C–O st), 1030, 945, 882, 737, 700. **^{1}H-NMR** (500 MHz): δ 7.64–7.60 (m, 4H), 7.56 (d, 1H, *J* = 7.9 Hz), 7.47 (d, 1H, *J* = 7.9 Hz), 7.41–7.29 (m, 7H), 4.36 (dd, 1H, *J* = 10.0, 7.2 Hz), 4.11–4.09 (m, 1H), 3.77–3.65 (m, 3H), 3.60–3.57 (m, 1H), 3.12 (m, 2H), 2.82 (m, 1H), 2.07 (dd, 1H, *J* = 15.9, 7.6 Hz), 1.92–1.76 (m, 4H), 1.60 (q, 1H, *J* = 13.1 Hz), 1.56 (s, 1H), 1.12–1.05 (m, 21H), 1.03 (s, 9H). **^{13}C-NMR** (125 MHz): δ 141.8, 138.3, 135.5, 133.8, 133.6, 129.6, 127.7, 127.6, 126.5, 122.8, 84.8, 66.0, 61.9, 61.2, 60.0, 50.9, 38.0, 36.0, 34.3, 28.5, 26.9, 19.2, 18.0, 12.1. **ESI-MS** *m/z* (rel int): (pos) 779.3 ([M+Na]$^+$, 100); (neg) 755.2 ([M–H]$^-$, 60).



(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-5-nitro-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (8f). Yellow oil (9 mg, 75%). **TLC**: R_f 0.37 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +18.4° (*c* 2.5, $CHCl_3$). **IR** (NaCl, film): 3493 (O–H st), 2942, 2865, 1526, 1463, 1427, 1388, 1347 (N–O st), 1249, 1155 (C–O st), 1036, 883, 815, 737, 702. **^{1}H-NMR** (500 MHz): δ 8.16 (s, 1H), 8.09 (dd, 1H, *J* = 8.5, 1.8 Hz), 7.51 (d, 1H, *J* = 8.4 Hz), 7.48–7.46 (m, 2H), 7.42–7.26 (m, 8H), 5.29 (d, 1H, *J* = 13.1 Hz), 5.15 (d, 1H, *J* = 13.2 Hz), 4.47 (ddd, 1H, *J* = 11.3, 9.5, 5.1 Hz), 4.06–3.99 (m, 1H), 3.84 (dd, 1H, *J* = 13.2, 5.9, 1.8 Hz), 3.67–3.62 (m, 1H), 3.60–3.56 (m, 1H), 2.31 (d, 1H, *J* = 2.9 Hz), 2.17 (ddd, 1H, *J* = 2.9 Hz), 1.76–1.64 (m, 3H), 1.15–1.06 (m, 21H), 0.89 (s, 9H). **^{13}C-NMR** (125 MHz): δ 148.6, 144.0, 143.6, 135.4, 133.5, 129.7, 127.7, 123.7, 122.9, 117.3, 110.8, 77.8, 71.3, 70.9, 66.4, 59.5, 40.2, 38.3, 26.7, 19.2, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 728.3 ([M+Na]$^+$, 100); (neg) 704.3 ([M–H]$^-$, 35).



(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-6-nitro-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (9f). Clear oil (103 mg, 72%). **TLC**: R_f 0.49 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +17.8° (*c* 3.3, $CHCl_3$). **IR** (NaCl, film): 3497 (O–H st), 2942, 2864, 1524, 1463, 1427, 1348 (N–O st), 1249, 1096 (C–O st), 1028, 882, 822, 737, 702. **^{1}H-NMR** (500 MHz): δ 7.62 (d, 1H, *J* = 8.5 Hz), 7.51–7.45 (m, 4H), 7.41–7.29 (m, 8H), 4.51 (ddd, 1H, *J* = 10.9, 9.0, 5.5 Hz), 4.27 (ddd, 1H, *J* = 10.6, 7.3, 5.7 Hz), 3.86 (td, 1H, *J* = 9.1, 5.1 Hz), 3.77 (dd, 1H, *J* = 8.9, 3.0 Hz), 3.75–3.68 (m, 1H), 3.65–3.57 (m, 2H), 3.00–2.89 (m, 2H), 2.32 (d, 1H, *J* = 3.2 Hz), 2.08 (ddd, 1H, *J* = 12.9, 5.4, 2.1 Hz), 1.77–1.63 (m, 3H), 1.20–1.07 (m, 21H), 0.86 (s, 9H). **^{13}C-NMR** (125 MHz): δ 147.0, 141.2, 138.3, 135.4, 133.6, 129.7, 128.2, 127.6, 123.7, 120.2, 99.3, 80.6, 71.7, 67.1, 60.1, 59.8, 39.7, 38.7, 28.6, 26.6, 19.0, 18.2, 12.6. **ESI-MS** *m/z* (rel int): (pos) 742.7 ($[M+Na]^+$, 100); (neg) 718.7 ($[M–H]^-$, 60).



(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-7-nitro-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*c*]oxepine-1,2′-pyran]-3′-ol (10f). Yellow oil (9 mg, 90%). **IR** (NaCl, film): 3450 (O–H st), 2942, 2865, 1524, 1463, 1427, 1347 (N–O st), 1246, 1109 (C–O st), 1030, 947, 881, 822, 739, 702. **^{1}H-NMR** (500 MHz): δ 8.10 (d, 1H, *J* =1.5 Hz), 8.05 (dd, 1H, *J* = 8.4, 1.8 Hz), 7.63–7.59 (m, 5H), 7.42–7.29 (m, 6H), 4.36 (dd, 1H, *J* = 10.8, 7.3 Hz), 4.14–4.08 (m, 1H), 3.79–3.65 (m, 3H), 3.63–3.57 (m, 1H), 3.21–3.15 (m, 1H), 3.10 (s, 1H), 2.90–2.83 (m, 1H), 2.08 (dd, 1H, *J* = 13.4, 7.8 Hz), 1.97–1.90 (m, 1H), 1.88–1.73 (m, 4H), 1.61 (q, 1H, *J* = 11.5 Hz), 1.11–1.06 (m, 21H), 1.03 (s, 9H). **^{13}C-NMR** (125 MHz): δ 148.3, 143.0, 141.1, 135.5, 133.8, 129.6, 128.4, 127.7, 124.6, 121.0, 84.5, 66.1, 65.9, 61.8, 61.2, 59.9, 50.9, 37.9, 35.9, 34.1, 28.6, 26.9, 18.0, 12.1. **ESI-MS** *m/z* (rel int): (pos) 756.7 ($[M+Na]^+$, 100); (neg) 732.6 ($[M–H]^-$, 60). *NOE analysis was not conclusive for this compound; therefore the structure was confirmed by converting this spiroketal to thermodynamic retention spiroketal using tosic acid (1 equiv. TsOH, $CDCl_3$, 1 h, rt).*

J. MeOH-INDUCED SPIROCYCLIZATION OF C1-ARYL CYCLOHEXENE OXIDE (S27–S30, 26–28)

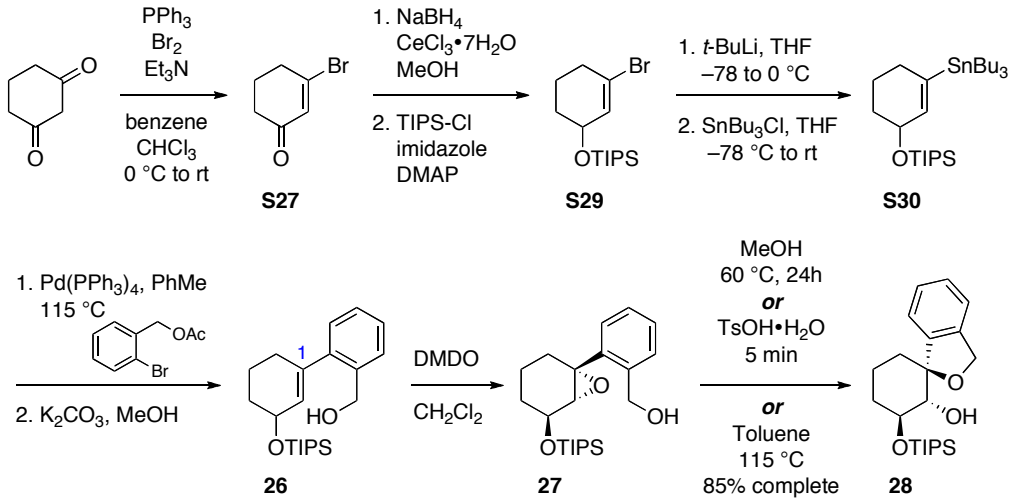
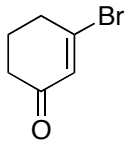
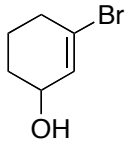


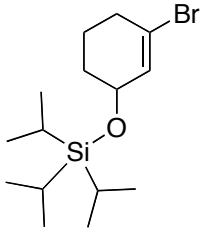
Figure S16. Synthesis of spiroether **28** from commercially available 1,3-cyclohexanedione.



3-Bromocyclohex-2-enone (S27). Previously reported.[9]



3-Bromocyclohex-2-enol (S28). Previously reported.[10]

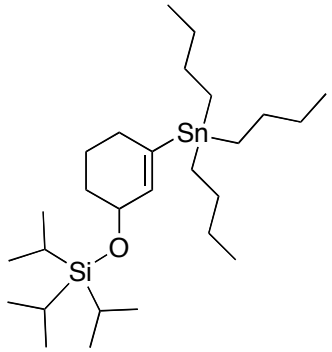


((3-Bromocyclohex-2-en-1-yl)oxy)triisopropylsilane (S29). To enol **S28** (1.58 g, 8.93 mmol) dissolved in 90 mL (0.1 M) CH_2Cl_2 was added imidazole (2.73 g, 40.2 mmol, 4.5 equiv), DMAP (217 mg, 1.79 mmol, 0.2 equiv), and triisopropylsilyl chloride (3.78 mL, 17.9 mmol, 2.0 equiv). After 18 h at rt, additional DMAP (544 mg, 4.47 mmol, 0.5 equiv) was added and the reaction

[9] Marcus, A. P.; Lee, A. S.; Davis, R. L.; Tantillo, D. J.; Sarpong, R. *Angew. Chem. Int. Ed.* **2008**, *47*, 6379–6383.
[10] Attolini, M.; Bouguir, F.; Iacazio, G.; Peiffer, G.; Maffei, M. *Tetrahedron* **2001**, *57*, 537–543.

was heated at 35 °C for 8 h under a reflux condenser. The solution was washed with satd aq NH_4Cl and aqueous layer was separated and extracted with Et_2O. The combined extracts were washed with brine, dried with $MgSO_4$, filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (95:5 hexanes/CH_2Cl_2 with 0.5% Et_3N) provided cyclohexene **S29** as a yellow oil (2.34 g, 79%).

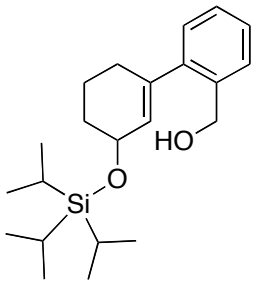
TLC: R_f 0.59 (9:1 hexanes/CH_2Cl_2). **IR** (NaCl, film): 2943, 2866, 1646, 1463, 1359, 1322, 1244, 1160, 1094 (C–O st), 1025, 994, 973, 912, 882, 845, 781. **^{1}H-NMR** (500 MHz): δ 6.09 (dt, 1H, J = 3.5, 1.7 Hz), 4.32 (quintet, 1H, J = 3.8 Hz), 2.48–2.42 (m, 1H), 2.38–2.31 (m, 1H), 1.93–1.87 (m, 1H), 1.85–1.80 (m, 1H), 1.66–1.58 (m, 2H), 1.08–1.04 (m, 21H). **^{13}C-NMR** (125 MHz): δ 132.7, 125.5, 67.9, 35.2, 31.4, 20.9, 18.1, 12.4. **ESI-MS** *m/z* (rel int): (neg) 330.6 ($[M–H]^-$, 40).



Triisopropyl((3-(tributylstannyl)cyclohex-2-en-1-yl)oxy)silane (S30). Following a stannylation procedure by Corey,[11] bromocyclohexene **S29** (720 mg, 2.16 mmol) was dissolved in 11 mL (0.2 M) Et_2O and cooled to –78 °C. *t*-BuLi (1.7 M in pentanes, 2.54 mL, 4.32 mmol, 2.0 equiv) was added dropwise over 25 min down the side of the flask. After 30 min at –78 °C, the solution was warmed to –40 °C over 1.5 h. Tributyltin chloride (1.17 mL, 4.32 mmol, 2.0 equiv) was added dropwise over 10 min and the mixture was stirred for 1.5 h. The reaction was quenched at –40 °C with satd aq $NaHCO_3$ and diluted with water. The aqueous layer was separated and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (hexanes with 0.5% Et_3N) provided tributyltin cyclohexene **S30** as a clear oil (1.08 g, 91%).

TLC: R_f 0.50 (100% hexanes). **IR** (NaCl, film): 2926, 2866, 1463, 1322, 1248, 1158, 1069 (C–O st), 1025, 944, 881, 843, 784. **^{1}H-NMR** (500 MHz): δ 5.82 (d, 1H, J = 2.0 Hz), 4.26 (td, 1H, J = 4.7, 2.4 Hz), 2.16–2.05 (m, 2H), 1.89–1.85 (m, 1H), 1.76 (ddd, 1H, J = 12.5, 4.9, 2.3 Hz), 1.60–1.42 (m, 9H), 1.30 (sextet, 6H, J = 7.4 Hz), 1.11–1.04 (m, 21H), 0.90–0.85 (m, 14H). **^{13}C-NMR** (125 MHz): δ 142.6, 141.2, 67.7, 32.8, 31.8, 29.2, 27.5, 21.2, 18.2, 13.8, 12.5, 9.0. **ESI-MS** *m/z* (rel int): (pos) 567.3 ($[M+Na]^+$, 100).

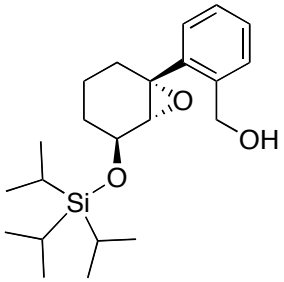
[11] Han, X.; Stoltz, B. M.; Corey, E. J. *J. Am. Chem. Soc.* **1999**, *121*, 7600–7605.



(5´-((Triisopropylsilyl)oxy)-2´,3´,4´,5´-tetrahydro-[1,1´-biphenyl]-2-yl)methanol (26). Following a modified Stille coupling procedure by Corey,[11] a solution of tributyltin cyclohexene **S30** (60 mg, 0.110 mmol, 1.2 equiv) in degassed toluene (3 mL, 0.05 M) was added 2-bromobenzyl acetate (21 mg, 0.092 mmol), LiCl (23 mg, 0.552 mmol, 6.0 equiv), CuCl (46 mg, 0.460 mmol, 5.0 equiv), and $Pd(PPh_3)_4$ (19 mg, 0.018 mmol, 0.2 equiv). The dark brown solution was shielded from light with aluminum foil[8] and heated to 80 °C for 24 h, then to 100 °C for an additional 24 h. The solution was cooled to rt and concentrated by rotary evaporation. Passage over a silica plug yielded the partially purified *O*-acetyl *C*1-aryl cyclohexene.

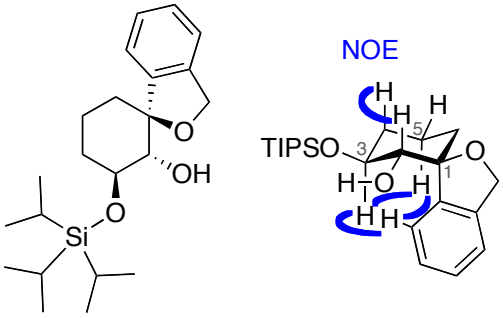
The crude aryl cyclohexene (51 mg, 0.127 mmol) was dissolved in MeOH (3 mL, 0.05 M) and K_2CO_3 (35 mg, 0.254 mmol, 2.0 equiv) was added. After stirring for 3 h, the mixture was diluted with Et_2O, filtered through a plug of celite, dried with $MgSO_4$, and concentrated by rotary evaporation. Purification by silica flash chromatography (9:1 hexanes/ether with 0.5% Et_3N) afforded the free alcohol **26** as a light yellow oil (20 mg, 60%, 2 steps from **S30**).

TLC: R_f 0.43 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 3309 (O–H st), 2943, 1464, 1333, 1161, 1089 (C–O st), 1029, 920, 884, 760. **^{1}H-NMR** (600 MHz): δ 7.44 (dd, 1H, J = 7.1, 1.7 Hz), 7.30–7.24 (m, 2H), 7.13 (dd, 1H, J = 7.1, 1.8 Hz), 5.66–5.64 (m, 1H), 4.68 (d, 2H, J = 6.2 Hz), 4.45–4.44 (m, 1H), 2.29–2.24 (m, 1H), 2.20–2.15 (m, 1H), 1.98–1.90 (m, 2H), 1.75–1.66 (m, 3H), 1.13–1.03 (m, 21H). **^{13}C-NMR** (150 MHz): δ 142.7, 139.7, 137.8, 130.4, 128.2, 128.1, 127.5, 127.2, 66.4, 63.3, 32.2, 30.9, 19.8, 18.1, 12.4. **ESI-MS** *m/z* (rel int): (pos) 383.2 ($[M+Na]^+$, 100).



(2-((1*R*,5*S*,6*R*)-5-(Triisopropylsilyloxy)-7-oxabicyclo[4.1.0]heptan-1-yl)phenyl)methanol (27). To cyclohexene **26** (10 mg, 0.028 mmol) dissolved in CH_2Cl_2 (2.75 mL) was added DMDO (1.2 equiv, 0.073 M in acetone) to give a final solvent ratio of 6:1 CH_2Cl_2:acetone. The mixture was stirred at rt for 1 h. Upon complete conversion as judged by TLC analysis (60 min), concentration by rotary evaporation to afforded epoxide **27** as a clear oil (11 mg, 100%). This epoxide was analytically pure and used without further purification.

TLC: R_f 0.43 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 3446 (O–H st), 2942, 2865, 1653, 1540, 1457, 1418, 1260, 1096 (C–O st), 1026, 918, 881, 843, 798, 758. **^{1}H-NMR** (600 MHz): δ 7.38–7.34 (m, 2H), 7.29 (tt, 2H, *J* = 6.3, 3.1 Hz), 4.88 (dd, 1H, *J* = 12.7, 5.5 Hz), 4.68 (dd, 1H, *J* = 12.5, 7.6 Hz), 4.28 (t, 1H, *J* = 5.7 Hz), 3.19 (s, 1H), 2.77 (t, 1H, *J* = 6.4 Hz), 2.18–2.14 (m, 1H), 2.00–1.95 (m, 1H), 1.91–1.87 (m, 1H), 1.71–1.67 (m, 1H), 1.50–1.44 (m, 1H), 1.42–1.37 (m, 1H), 1.17–1.04 (m, 21H). **^{13}C-NMR** (150 MHz): δ 140.4, 138.2, 129.0, 127.9, 127.8, 127.2, 66.8, 63.2, 62.7, 62.6, 30.7, 29.4, 18.0, 15.4, 12.2. **ESI-MS** *m/z* (rel int): (pos) 399.2 ([M+Na]$^+$, 100). *NOE analysis was not conclusive for this compound; therefore the compound stereochemistry was assigned after spiroetherification (below).*



(1*S*,2*R*,3*S*)-3-(Triisopropylsilyloxy)-3´*H*-spiro[cyclohexane-1,1´-isobenzofuran]-2-ol (28). Cyclohexyl epoxide **27** (5.2 mg, 0.014 mmol) was dissolved in MeOH (1.00 mL) and heated to 60 °C for 24 h. Concentration by rotary evaporation afforded spiroether **28** as a clear oil (5 mg, 96%).

Alternatively, to epoxide **27** (2 mg, 0.005 mmol) dissolved in $CDCl_3$ (0.5 mL) was added TsOH (1 mg, 0.005 mmol, 1.0 equiv). After stirring for 5 min, the reaction was washed with satd aq $NaHCO_3$, extracted with EtOAc, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to yield spiroether **28** as a clear oil (1.9 mg, 95%).

Alternatively, epoxide **27** (3 mg, 0.008 mmol) was dissolved in toluene-d_8 (1.00 mL) and heated to 110 °C for 72 h to yield 85% spiroether **28** and 15% remaining epoxide **27**. Heating epoxide **27** at 60 °C for 24 h in toluene alone did not yield any spiroether product.

TLC: R_f 0.52 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 3463 (O–H st), 2942, 2864, 1673, 1461, 1365, 1128, 1107, 1049 (C–O st), 997, 958, 973, 883, 849, 794, 757, 728. **^{1}H-NMR** (600 MHz): δ 7.32 (t, 2H, *J* = 7.6 Hz), 7.25 (q, 2H, *J* = 8.4 Hz), 5.20 (d, 1H, *J* = 11.9 Hz), 5.10 (d, 1H, *J* = 11.9 Hz), 4.13–4.09 (m, 1H), 3.70 (dd, 1H, *J* = 9.3, 1.7 Hz), 2.36 (d, 1H, *J* = 2.0 Hz), 2.12–2.10 (m, 1H), 1.96–1.94 (m, 1H), 1.84–1.79 (m, 1H), 1.75–1.70 (m, 1H), 1.58–1.52 (m, 2H), 1.10–1.05 (m, 21H). **^{13}C-NMR** (150 MHz): δ 141.6, 141.1, 127.9, 126.8, 122.3, 121.4, 90.8, 82.2, 73.1, 72.2, 36.8, 33.4, 19.2, 18.1, 12.6. **ESI-MS** *m/z* (rel int): (pos) 399.2 ([M+Na]$^+$, 100); (neg) 375.2 ([M–H]$^-$, 100).

K. SYNTHESIS OF TBS-PROTECTED METHYL GLYCOSIDE (29–30)

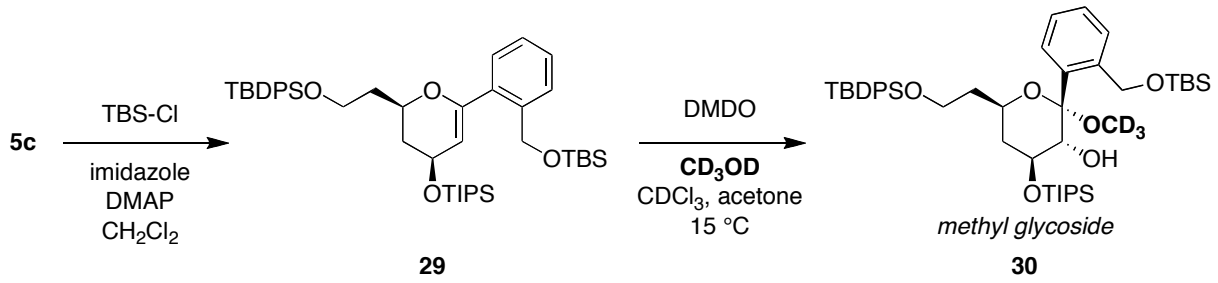
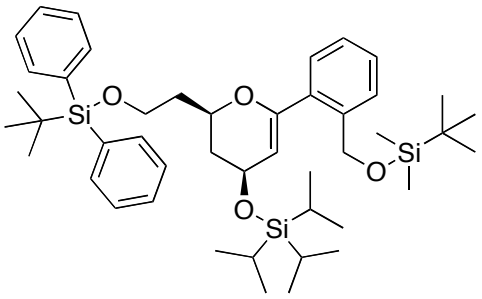
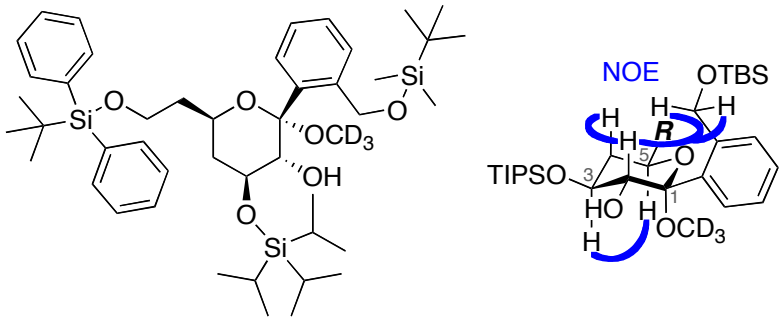


Figure S17. Synthetic route to methyl glycoside **30** from TBS-protected glycal **29**.



(–)-*tert*-Butyl(2-((2*R*,4*S*)-6-(2-((*tert*-butyldimethylsilyloxy)methyl)phenyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-2-yl)ethoxy)diphenylsilane (29). To glycal **5c** (100 mg, 0.16 mmol) dissolved in CH_2Cl_2 (5 mL, 0.03 M) was added imidazole (23 mg, 0.34 mmol, 2.2 equiv), DMAP (4 mg, 0.03 mmol, 0.2 equiv), and *t*-butyldimethylsilyl chloride (26 mg, 0.17 mmol, 1.1 equiv). After 12 h at rt, the solution was washed with satd aq NH_4Cl and aqueous layer was separated and extracted with Et_2O. The combined extracts were washed with brine, dried with $MgSO_4$, filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (95:5 hexanes/EtOAc with 1% Et_3N) provided protected glycal **29** as a clear oil (105 mg, 89%).

TLC: R_f 0.87 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –5.3° (*c* 3.1, $CDCl_3$). **IR** (NaCl, film): 2929, 2862, 1653, 1471, 1254, 1081 (C–O st), 837, 776, 701. **^{1}H-NMR** (500 MHz): δ 7.66–7.63 (m, 4H), 7.58 (d, 1H, *J* = 7.8 Hz), 7.42–7.17 (m, 9H), 4.85–4.76 (m, 3H), 4.69–4.66 (m, 1H), 4.34–4.32 (m, 1H), 3.85–3.79 (m, 2H), 2.18–2.13 (m, 1H), 2.04–1.99 (m, 1H), 1.89–1.85 (m, 1H), 1.81–1.75 (m, 1H), 1.09–1.05 (m, 21H), 1.03 (s, 9H), 0.90 (s, 9H), 0.03 (s, 6H). **^{13}C-NMR** (125 MHz): δ 153.0, 139.8, 135.6, 134.0, 133.8, 133.7, 129.6, 128.4, 127.7, 126.4, 126.2, 105.9, 72.4, 64.3, 62.7, 60.3, 38.0, 37.7, 26.9, 26.0, 19.2, 18.4, 18.2, 12.4, -5.3. **ESI-MS** *m/z* (rel int): (pos) 781.8 ($[M+Na]^+$, 100).



(+)-(2*S*,3*R*,4*S*,6*R*)-2-(2-((*tert*-butyldimethylsilyloxy)methyl)phenyl)-6-(2-(*tert*-butyldiphenylsilyloxy)ethyl)-2-methoxy-4-(triisopropylsilyloxy)tetrahydro-2*H*-pyran-3-ol-d_3 (30). Methyl glycoside **30** was synthesized as described in Kinetics section **B** above (p *S11*). Purification by silica flash chromatography (9:1 hexanes/EtOAc with 0.5% Et_3N) provided protected glycal **29** as a clear oil (6 mg, 94%).

TLC: R_f 0.67 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +16.1° (*c* 4.0, $CDCl_3$). **IR** (NaCl, film): 2930, 2862, 1470, 1428, 1389, 1254, 1107, 1073 (C–O st), 1047, 997, 939, 882, 836, 775, 736, 701. **^{1}H-NMR** (500 MHz): δ 7.65 (d, 1H, *J* = 7.7 Hz), 7.56-7.53 (m, 4H), 7.37-7.23 (m, 8H), 7.16 (t, 1H, *J* = 7.4 Hz), 4.89 (s, 2H), 4.11 (ddd, 1H, *J* = 11.1, 8.6, 4.9 Hz,), 4.01-3.95 (m, 1H), 3.78 (ddd, 1H, *J* = 10.3, 8.1, 5.1 Hz), 3.68 (dt, 1H, *J* = 10.5, 5.4 Hz), 3.33 (dd, 1H, *J* = 8.6, 5.4 Hz), 2.07 (brs, 1H), 1.99 (ddd, 1H, *J* = 12.8, 4.9, 1.9 Hz), 1.77 (ddt, 1H, *J* = 13.8, 8.5, 5.2 Hz), 1.68 (tdd, 1H, *J* = 8.7, 9.3, 4.5 Hz), 1.48 (q, 1H, *J* = 12.0 Hz), 1.02-0.97 (m, 21H), 0.93 (s, 9H), 0.87 (s, 9H), –0.01 (s, 6H). **^{13}C-NMR** (125 MHz): δ 140.3, 135.5, 135.4, 133.8, 133.7, 129.7, 128.2, 127.7, 127.4, 125.9, 103.2, 78.2, 70.9, 65.6, 63.1, 60.3, 40.8, 38.7, 29.7, 26.9, 26.1, 19.2, 18.5, 18.1, 12.6, -5.2. **ESI-MS** *m/z* (rel int): (pos) 832.9 ($[M+Na]^+$, 100); (neg) 808.9 ($[M–H]^-$, 40).