Supporting Information
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Taming Silylium Ions for Synthesis:  
N-Heterocycle Synthesis via Stereospecific C–C Bond Formation  
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Supporting Information  
I. General Methods ................................................................. 2  
1. Instrumentation ................................................................. 2  
2. Chemicals ................................................................. 3  
II. Substrate Synthesis and Characterization ................................ 7  
1. Synthesis of N-arylsulfonyl-protected amino alcohols .................. 7  
2. Preparation of allyl bromides ............................................. 11  
3. N-alkylation of N-arylsulfonyl-protected amino alcohols ................. 14  
4. Synthesis of amino aldehydes ............................................. 21  
III. Silylium Ion-Catalyzed Prins Cyclization Employing Various R₃Si–Nu  
(trialkylhydrosilanes, allylsilanes, and silyl azides) as Trapping Nucleophiles .......... 30  
1. General procedures ................................................................. 30  
2. Preparation and characterization ............................................. 31  
IV. Silylium Ion-Catalyzed Prins Cyclization Employing Silyl Enol Ethers  
as Trapping Nucleophiles ................................................................. 42  
1. General procedures ................................................................. 42  
2. Preparation and characterization ............................................. 43  
3. X-ray crystallographic data and structure for 20 ......................... 60  
4. Removal of aryl sulfonamide protecting group .......................... 61  
V. Prins Cyclizations using other Lewis acids ................................. 62  
1. Prins-cyclization promoted by TiCl₄ ............................................. 62  
2. Prins-cyclization catalyzed by HBARF₂₄ (Brookhart’s acid) ............. 64  
3. Silylium-ion catalyzed Prins-cyclization in the absence of trapping nucleophiles .... 65  
4. Prins-cyclization catalyzed by B(C₆F₅)₃ ............................................. 67  
a. X-ray crystallographic data and structure for S19 ......................... 70  
VI. ¹H and ¹³C NMR spectra ................................................................. 71
I. General Methods

All catalytic reactions were set up in a nitrogen-filled glovebox and run outside the glovebox under nitrogen atmosphere in oven-dried (130 °C) 1 dram (4 mL) vials with magnetic stirring unless otherwise specified. All catalytic reactions were run in duplicate on 0.05-0.1 mmol scale unless otherwise specified. Catalytic reactions that were performed at −78 °C were pre-cooled in vacuum dewars containing an acetone/CO\(_2\) mixture that was maintained throughout the course of the reaction. All other reactions were performed at ambient temperature (22 °C, RT) unless otherwise specified. All solvents were subjected to three freeze-pump-thaw cycles and stored over activated molecular sieves in the glovebox prior to use. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Column chromatography was performed using SilaFlash P60 40-63 µm (230-400 mesh). Catalytic reaction products were purified via silica gel column chromatography on a 1.5 cm x 22 cm column using mixtures of n-pentane and ethyl acetate as eluents and gravity as pressure. Thin layer chromatography (TLC) was performed on SiliCycle Silica Gel 60 F254 plates and was visualized with UV light, cerium ammonium molybdate (CAM) stain, or potassium permanganate (KMnO\(_4\)) stain.

**General deprotection procedure:** Where indicated, catalytic reactions were treated with an acidic resin before attempted isolation to remove labile silyl protecting groups. The catalytic reactions were quenched by addition of an excess of Et\(_3\)N (50 µL) or i-PrNH\(_2\) (50 µL) at −78 °C (unless otherwise stated) and allowed to warm to room temperature before concentration in vacuo and placement under high vacuum for at least 1 h to remove excess amine. **Note:** Complete removal of excess amine is necessary for the reproducibility of subsequent acid-catalyzed deprotections; repeated azeotroping with CH\(_2\)Cl\(_2\) and drying under high vacuum facilitates removal of excess base. The resulting residue was taken up in 2 mL of 1:1 CH\(_2\)Cl\(_2\)/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the reaction was stirred at 22 °C for 1 h (or the time indicated). **Note:** Other, less aggressive acidic resins can also afford deprotected product, including pyridinium p-toluene sulfonate polymer-bound resin (PPTS) with extent of labeling 3.5 mmol/g toluene sulfonate loading purchased through Aldrich. The solution was then filtered by gravity through a plug of sand and cotton, rinsed through with excess CH\(_2\)Cl\(_2\) (x2), concentrated in vacuo, and placed under high vacuum for at least 1 h before NMR analysis.

1. **Instrumentation:** All NMR spectra were recorded on a Bruker Avance 600 MHz spectrometer at standard temperature and pressure. All deuterated solvents were used as received from
Cambridge Isotope Laboratories, Inc. The residual solvent protons (\( ^1\text{H} \)) or the solvent carbons (\( ^{13}\text{C} \)) were used as internal references. The following abbreviations are used in reporting NMR data: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sept, septet; dd, doublet of doublets; dt, doublet of triplets; dq, doublet of quartets; td, triplet of doublets; dt, doublet of triplets; tt, triplet of triplets; quint d, quintet of doublets; ddd, doublet of doublet of doublets; and m, multiplet. Where necessary, 2D COSY, 2D HSQC, and \( ^{13}\text{C} \) DEPT135 data were used for peak assignment. All IR spectra were recorded on a Jasco 260 Plus Fourier transform infrared spectrometer with reporting from 4000-1000 cm\(^{-1} \) using the following abbreviations: s, strong; m, medium; w, weak; br, broad. High resolution mass spectra were obtained on a hybrid LTQ FT (ICR 7T) (ThermoFisher, Bremen, Germany) mass spectrometer where samples were introduced via a micro-electrospray source at a flow rate of 3 \( \mu \text{L/min} \). The data were analyzed using Xcalibur (ThermoFisher, Breman, Germany) and theoretical masses were calculated using IsoPro 3.1. Specific rotations were obtained on a Jasco DIP-1000 digital polarimeter equipped with a sodium lamp at STP utilizing a 3.5 x 100 mm cell. X-ray crystallographic data were recorded on a Bruker APEX-II CCD diffractometer. A NesLab cryobath CB-80 was utilized for reduced temperature reactions where temperature was verified by low-temperature thermometer. Sonication was performed in a Fisher Scientific FS60 Ultrasonic Cleaner with a frequency of 42 kHz.

2. **Chemicals:** Me\(_2\)EtSiH, Et\(_3\)SiH, t-BuMe\(_2\)SiH, and i-Pr\(_3\)SiH were purchased from Gelest and stored over pre-activated molecular sieves in a dry, \( \text{N}_2 \)-filled glovebox. Dichloromethane (CH\(_2\)Cl\(_2\)) and tetrahydrofuran (THF) were purchased from Sigma-Aldrich and used as received. Methanol was purchased from Fisher and used as received. Dichloromethane (for air/water free reactions) and toluene were passed through an alumina column in a solvent purification system prior to use. Trityl tetra(pentafluorophenyl)borate ([Ph\(_3\)C][B(C\(_6\)F\(_5\))\(_4\)], trityl BArF\(_{20}\)) was purchased from Strem and used as received. All aldehyde substrates were azeotropically dried three times with either dry toluene (solvent purification system) or benzene (freshly distilled over calcium hydride), followed by placement under high vacuum (~100 mtorr) overnight, before being stored at room temperature in a dry, \( \text{N}_2 \)-filled glovebox. **Note:** Based on periodic checks via \( ^1\text{H} \) NMR, the aldehydes appear to be stable for at least 6-12 months when stored at room temperature and under nitrogen in a glove box. The aldehydes often start to turn yellow \( \rightarrow \text{orange} \rightarrow \text{brown} \) over weeks to months of time, but no decomposition can be detected.
from periodic (homogenous) NMR aliquots. Silyl enol ethers were prepared from their corresponding freshly distilled (over CaH₂) parent ketones using modified literature procedures,¹ purified via aluminum oxide chromatography (Aldrich; activated, neutral, Brockmann activity I slurried with 10% H₂O), and stored in a dry, N₂-filled glovebox.

3-bromo-2-methylpropene (97%) was purchased from Sigma-Aldrich and used as received.
4-bromobenzenesulfonyl chloride (98%, brosyl chloride; Bs—Cl) was obtained from Acros Organics and used as received without recrystallization.
2’-iodoacetophenone (97%) was obtained from Aldrich and used as received.
2-naphthalenesulfonyl chloride (99%) was purchased from Sigma-Aldrich as used as received.
α-methylstyrene (99%) was obtained from Aldrich, stored at 4 °C, and used as received.
Acetone (99.8%, Extra Dry, AcroSeal®) was obtained from Acros Organics and used within one year.
Allyltrimethylsilane was purchased from Sigma-Aldrich, distilled, and stored in a dry, N₂-filled glovebox.
Calcium hydride was purchased from Sigma-Aldrich and used without further purification.
Chloroform-d was purchased from Cambridge Isotope Laboratories and stored over 3Å molecular sieves.
Chlorotrimethylsilane (98%) was purchased from Acros Organics, freshly distilled over calcium hydride into a Schlenk flask shortly before use, and stored under nitrogen in a –30 °C freezer.
Cinnamyl bromide (97%, predominantly trans) was obtained from Acros Organics, distilled in vacuo, and stored in a –20 °C freezer.
Dess-Martin periodinane (DMP) was synthesized in two steps according to literature procedure.²
Dowex® resin “Dowex® resin” refers to Dowex® 50W-X8, a strongly acidic cation exchange resin distributed by Baker Chemical Company. Before use, the orange 20-50 mesh Dowex® resin beads were washed five times with methanol and five times with methylene chloride and then allowed to dry under nitrogen flow.

**L-alaninol** ((S)-2-amino-1-propanol, 99.8% chiral purity) was obtained from Chem-Impex Int’l Inc. and used as received. [CAS Reg. No. 2749-11-3]

**L-phenylalaninol** ((S)-(−)-2-amino-3-phenyl-1-propanol; 99.2% chiral purity) was obtained from Chem-Impex Int’l Inc. and used as received. [CAS Reg. No. 3182-95-4]

**L-valinol** ((S)-2-amino-3-methyl-1-butanol, ≥98% chiral purity) was obtained from Chem-Impex Int’l Inc. and used as received. [CAS Reg. No. 2026-48-4]

**Magnesium** (ReagentPlus) ≥99%, powder, 50 mesh was obtained from Aldrich and used as received.

**Methallyltrimethylsilane** was purchased from Sigma-Aldrich, distilled, and stored in a dry, N₂-filled glovebox.

**Methanol** (99.8%, Extra Dry, AcroSeal®) was obtained from Acros Organics and used within one year.

**Methyltriphenylphosphonium bromide** (98%) was obtained from Aldrich and used as received.

**N-bromosuccinimide** (99%, ReagentPlus®) was obtained from Aldrich and used as received.

**N,N-dimethylformamide** was purchased from Sigma-Aldrich and stored over 3Å molecular sieves.

**p-Toluenesulfonic acid monohydrate** (98.5%, ReagentPlus®) was obtained from Sigma-Aldrich and used as received.

**p-Toluenesulfonyl chloride** (≥98%, reagent grade) was purchased from Sigma Aldrich and recrystallized from chloroform before use.

**Potassium carbonate anhydrous** (certified ACS granular powder) was obtained from Fisher and used as received.

**Potassium tert-butoxide** (95%, reagent grade) was obtained from Aldrich and stored in a nitrogen-filled glove box.

**Silyl enol ethers (R1-R5)** All of the silyl enol ethers utilized in catalytic reactions in this manuscript were synthesized according to the general literature procedure reported by Knochel and coworkers. The silyl enol ethers were extracted from the reaction mixture with n-pentane and purified by column chromatography in n-pentane through neutral aluminum oxide (Brockmann activity I slurried with 10% H₂O). All obtained silyl enol ethers matched previously
reported $^1$H and $^{13}$C{$^1$H} NMR data.\(^3\)

**Sodium bicarbonate** (NaHCO\(_3\); Certified ACS) was obtained from Fisher and used as received.  
**Sodium sulfate anhydrous** (granular, certified ACS) was obtained from Fisher and used as received.  
**Sodium thiosulfate pentahydrate** (Na\(_2\)S\(_2\)O\(_3\)\(\cdot\)5H\(_2\)O; ≥99.5\%) was obtained from Sigma-Aldrich and used as received.  
**Tetrabutylammonium iodide** (98\%, reagent grade) was obtained from Sigma-Aldrich and used as received.  
**Tetrahydrofuran** (99.5\%, Extra Dry over Molecular Sieve, Stabilized, AcroSeal\(^\circledR\)) was obtained from Acros Organics and used within six months.  
**Tetrakis[3,5-bis(trifluoromethyl)phenyl]borate** (HBArF\(_{24}\)) was prepared according to literature procedure and stored at −35 °C in a dry, N\(_2\)-filled glove box.\(^4\)  
**Titanium tetrachloride** (99.9\%) was purchased from Acros Organics and stored and dispensed inside of a dry, N\(_2\)-filled glove box.  
**Triethylamine** (Et\(_3\)N, 99\% reagent grade) was obtained from Fisher and freshly distilled over calcium hydride before each use.  
**Trimethylsilyl azide** was purchased from Sigma-Aldrich, distilled, and stored at −30 °C in a dry, N\(_2\)-filled glovebox.  
**Tris(pentafluorophenyl)borane** (97\%; should be off-white to white) was purchased sealed from Strem Chemical and used as received in a dry, N\(_2\)-filled glovebox.  
**Trityl tetra(pentafluorophenyl)borate** (97\%, trityl BArF\(_{20}\)) was purchased from Strem Chemicals (catalog # 05-5000) and stored at room temperature in a dry, N\(_2\)-filled glove box.

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II. Substrate Synthesis and Characterization

1. Synthesis of N-arylsulfonyl-protected amino alcohols (aryl sulfonamides)

Preparation of aryl sulfonamide 2:

To a flame-dried 250 mL round-bottom flask equipped with a magnetic stir bar was added (S)-phenylalaninol (1, 26.5 mmol, 4.00 g, 1.00 eq.) and tetrabutylammonium iodide (0.530 mmol, 196 mg, 0.02 eq.). The flask was capped with a septum, an N₂ needle was inserted, and the headspace of the flask was purged with anhydrous N₂. CH₂Cl₂ (133 mL) and Et₃N (33.1 mmol, 4.62 mL, 1.25 eq.) were added. The flask was placed in an ice-water bath and cooled to 0 °C. The septum was quickly removed and 4-bromobenzenesulfonyl chloride (brosyl chloride, Bs–Cl; 27.8 mmol, 7.10 g, 1.05 eq.) was added quickly and the flask resealed. The homogeneous solution was warmed to 22 °C and stirred for 24 h. After 24 h, the solution was decanted into a separatory funnel and diluted with excess CH₂Cl₂ and washed with deionized water. The organic phase was separated and the aqueous phase was extracted with CH₂Cl₂ (x4). The combined organics were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (9:1 dichloromethane:methanol; Rf = 0.35 in 1:1 hexanes:ethyl acetate) to yield the desired N-Bs amino alcohol 2 as an off-white, crystalline solid in 92% yield (9.05 g).

Data for 2

\( \text{(S)-4-bromo-N-}(1\text{-hydroxy-3-phenylpropan-2-yl})\text{benzenesulfonamide (2).} \) \( ^1\text{H NMR (CDCl}_3, \) 600 MHz): \( \delta 7.52-7.44 \) (m, 4H), 7.21-7.15 (m, 3H), 6.96 (d, 2H, \( J = 6.5 \) Hz), 4.76 (d, 1H, \( J = 7.2 \) Hz), 3.69 (ddd, 1H, \( J = 11.3, 6.1, 4.0 \) Hz), 3.60 (dt, 1H, \( J = 11.1, 4.8 \) Hz), 3.45 (ddddd, 1H, \( J = 11.0, 8.0 \) Hz), 3.39 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 3.32 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 3.27 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 3.22 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 3.16 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 3.11 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 3.06 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 2.95 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 2.88 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 2.83 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 2.69 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 2.63 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 2.58 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 2.53 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 2.48 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 2.39 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 2.33 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 2.28 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 2.23 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 2.18 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 2.13 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 2.08 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 2.03 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 2.00 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 1.95 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 1.89 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 1.84 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 1.79 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 1.75 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 1.70 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 1.65 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 1.60 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 1.55 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 1.50 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 1.45 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 1.40 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 1.35 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 1.30 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 1.25 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 1.20 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 1.15 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 1.10 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 1.05 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 1.00 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 0.95 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 0.90 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 0.85 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 0.80 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 0.75 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 0.70 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 0.65 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 0.60 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 0.55 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 0.50 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 0.45 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 0.40 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 0.35 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 0.30 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 0.25 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 0.20 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 0.15 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 0.10 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz), 0.05 (ddd, 1H, \( J = 11.0, 8.0 \) Hz), 0.00 (ddddd, 1H, \( J = 11.0, 7.5 \) Hz).
11.4, 8.4, 6.2, 4.3 Hz), 2.83 (dd, 1H, J = 14.0, 6.2 Hz), 2.67 (dd, 1H, J = 13.9, 8.3 Hz), 2.01 (t, 1H, J = 5.6 Hz); $^{13}$C $^{1}$H NMR (CDCl$_3$, 151 MHz): δ 138.8, 136.6, 132.4, 129.2, 128.9, 128.5, 127.7, 127.0, 64.7, 57.0, 38.0.

Preparation of aryl sulfonamide S2:

To a flame-dried 100 mL round-bottom flask equipped with a magnetic stir bar was added (S)-alaninol (S1, 20.0 mmol, 1.56 mL, 1.00 eq.). The flask was capped with a septum, an N$_2$ needle was inserted, and the headspace of the flask was purged with anhydrous N$_2$. CH$_2$Cl$_2$ (40 mL) and Et$_3$N (22.0 mmol, 3.07 mL, 1.10 eq.) were added. The flask was placed in an ice-water bath and cooled to 0 °C. The septum was quickly removed and 4-bromobenzensulfonyl chloride (brosyl chloride, Bs–Cl; 20.0 mmol, 5.11 g, 1.00 eq.) was added quickly and the flask resealed. The solution was warmed to 22 °C and stirred for 24 h. After 24 h, the solution was decanted into a separatory funnel and diluted with excess CH$_2$Cl$_2$ and washed with deionized water. The organic phase was separated and the aqueous phase was extracted with CH$_2$Cl$_2$ (x4). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (9:1 dichloromethane:methanol; R$_f$ = 0.5 in 2:1 ethylacetate:hexanes) to yield the desired N-Bs amino alcohol S2 as a white, crystalline solid in 91% yield (5.32 g).

Data for S2

(S)-4-bromo-N-(1-hydroxypropan-2-yl)benzenesulfonamide (S2). $^1$H NMR (CDCl$_3$, 600 MHz): δ 7.76 (d, 2H, J = 8.6 Hz), 7.66 (d, 2H, J = 8.6 Hz), 4.82 (d, 1H, J = 7.2 Hz), 3.58 (d, 1H, J = 8.6 Hz), 4.82 (d, 1H, J = 7.2 Hz), 3.58 (d, 1H, J = 8.6 Hz).
$J = 10.2 \text{ Hz}$), 3.49-3.39 (m, 2H), 1.88 (br s, 1H), 1.07 (d, 3H, $J = 6.5 \text{ Hz}$); $^{13}\text{C}^{1}\text{H}$ NMR (CDCl$_3$, 151 MHz): δ 139.7, 132.6, 128.8, 127.9, 66.3, 51.6, 18.0.

Preparation of aryl sulfonamide S4:

To a flame-dried 100 mL round-bottom flask equipped with a magnetic stir bar was added (S)-valinol (S3, 19.4 mmol, 2.16 mL, 1.00 eq.). The flask was capped with a septum, an N$_2$ needle was inserted, and the headspace of the flask was purged with anhydrous N$_2$. CH$_2$Cl$_2$ (39 mL) and Et$_3$N (21.3 mmol, 2.97 mL, 1.10 eq.) were added. The septum was quickly removed and 4-bromobenzenesulfonyl chloride (brosyl chloride, Bs–Cl; 19.4 mmol, 4.96 g, 1.00 eq.) was added quickly and the flask resealed. The solution was stirred for 75 h. After this time, the solution was decanted into a separatory funnel and diluted with excess CH$_2$Cl$_2$ and washed with deionized water. The organic phase was separated and the aqueous phase was extracted with CH$_2$Cl$_2$ (x4). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (9:1 dichloromethane:methanol) to yield the desired $N$-Bs amino alcohol S4 as an off-white, crystalline solid in 84% yield (5.24 g).

Data for S4

(S)-4-bromo-$N$-(1-hydroxy-3-methylbutan-2-yl)benzenesulfonamide (S4). $^1\text{H}$ NMR (CDCl$_3$, 600 MHz): δ 7.76 (d, 2H, $J = 8.6 \text{ Hz}$), 7.65 (d, 2H, $J = 8.5 \text{ Hz}$), 4.83 (d, 1H, $J = 8.6 \text{ Hz}$), 3.63-3.54 (m, 2H), 3.09-3.04 (m, 1H), 1.84-1.78 (m, 2H), 0.81 (d, 6H, $J = 6.2 \text{ Hz}$); $^{13}\text{C}^{1}\text{H}$ NMR (CDCl$_3$, 151 MHz): δ 139.9, 132.5, 128.8, 127.8, 63.1, 61.2, 29.7, 19.3, 18.6.
Preparation of aryl sulfonamide S5:

To a flame-dried 100 mL round-bottom flask equipped with a magnetic stir bar was added (S)-phenylalaninol (1, 6.61 mmol, 1.00 g, 1.00 eq.) and tetrabutylammonium iodide (0.13 mmol, 49 mg, 0.02 eq.). The flask was capped with a septum, an N\textsubscript{2} needle was inserted, and the headspace of the flask was purged with anhydrous N\textsubscript{2}. CH\textsubscript{2}Cl\textsubscript{2} (33 mL) and Et\textsubscript{3}N (8.27 mmol, 1.15 mL, 1.25 eq.) were added. The flask was placed in an ice-water bath and cooled to 0 °C. The septum was quickly removed and 2-naphthalenesulfonyl chloride (Naph–Cl; 6.94 mmol, 1.57 g, 1.05 eq.) was added quickly and the flask resealed. The solution was warmed to 22 °C and stirred for 17 h. After 17 h, the solution was decanted into a separatory funnel and diluted with excess CH\textsubscript{2}Cl\textsubscript{2} and washed with deionized water. The organic phase was separated and the aqueous phase was extracted with CH\textsubscript{2}Cl\textsubscript{2} (x4). The combined organics were dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated \textit{in vacuo}. The crude residue was purified by silica gel chromatography (1:1 hexanes:ethyl acetate; R\textsubscript{f} = 0.3) to yield the desired N-arylsulfonyl amino alcohol S5 as a white, crystalline solid in 87% yield (1.97 g).

Data for S5

\textit{(S)-N-(1-hydroxy-3-phenylpropan-2-yl)naphthalene-2-sulfonamide (S5).} \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 600 MHz): \(\delta\) 8.29 (d, 1H, \(J = 1.8\) Hz), 7.90 (t, 2H, \(J = 8.3\) Hz), 7.83 (d, 1H, \(J = 8.6\) Hz), 7.66 (td, 1H, \(J = 6.9, 1.3\) Hz), 7.62 (td, 1H, \(J = 6.8, 1.4\) Hz), 7.59 (dd, 1H, \(J = 8.6, 1.9\) Hz), 7.06-7.01 (m, 3H), 6.90 (dd, 2H, \(J = 8.0, 1.9\) Hz), 4.83 (d, 1H, \(J = 7.0\) Hz), 3.67 (ddd, 1H, \(J = 10.6, 6.3, 3.9\) Hz), 3.57 (dt, 1H, \(J = 11.1, 5.0\) Hz), 3.51 (qd, 1H, \(J = 7.1, 3.4\) Hz), 2.79 (dd, 1H, \(J = 13.9, 6.6\) Hz), 2.68 (dd, 1H, \(J = 13.9, 7.7\) Hz), 1.06 (t, 1H, \(J = 6.6\) Hz); \textsuperscript{13}C\{\textsuperscript{1}H\} NMR (CDCl\textsubscript{3}, 151 MHz): \(\delta\)
2-Phenylallyl bromide was synthesized according to modified literature procedure.\textsuperscript{5} A flame-dried round-bottom flask equipped with a magnetic stir bar was charged with α-methylstyrene (100 mmol, 13.0 mL, 1.00 eq.), N-bromosuccinimide (105 mmol, 18.7 g, 1.05 eq.), tosic acid monohydrate (TsOH·H\textsubscript{2}O; 1.00 mmol, 190 mg, 0.0100 eq.) and anhydrous THF (300 mL). The homogeneous solution was brought to reflux and vigorously stirred for 20 h. The reaction was allowed to cool to room temperature. The solution was decanted into a separatory funnel, diluted with hexanes and deionized water, and the organic layer was separated. The aqueous layer was then washed with three portions of hexanes. The combined organic layers were dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated \textit{in vacuo} to afford a yellow oil. The crude residue was purified by silica gel column chromatography (hexanes; R\textsubscript{f} = 0.5) to provide the desired 2-phenylallyl bromide as a clear, light yellow oil in 58% yield (11.4 g). The spectral data of the bromide matched those previously reported.

\textbf{Data for 2-phenylallyl bromide}

\begin{align*}
\text{1H NMR (CDCl}_3\text{, 600 MHz): } & \delta 7.52-7.49 (m, 2H), 7.41-7.32 (m, 3H), 5.57 (s, 1H), 5.50 (s, 1H), 4.40 (s, 2H). \\
\text{13C\{1H\} NMR (CDCl}_3\text{, 151 MHz): } & \delta 144.3, 137.7, 128.6, 128.4, 126.2, 117.4, 34.4.
\end{align*}

\textsuperscript{5}Tripathi, C. B.; Mukherjee, S. \textit{Angew. Chem. Int. Ed.} \textbf{2013}, \textit{52}, 8450-8453.
Preparation of 1-iodo-2-(prop-1-en-2-yl)benzene (S6):

The title compound (S6) was synthesized via modification to a general literature procedure. A flame-dried Schlenk flask equipped with a magnetic stir bar was charged with anhydrous potassium tert-butoxide (14.6 mmol, 1.64 g, 1.20 eq.) and methyltriphenylphosphonium bromide (14.6 mmol, 5.23 g, 1.20 eq.). The flask was placed under vacuum, backfilled with nitrogen, and then placed in a 0°C ice-water bath. Anhydrous THF (16 mL) was added down the side of the flask and the bright yellow mixture was stirred at 0°C for 45 minutes. Then a solution of 2'-iodoacetophenone (12.2 mmol, 1.74 mL, 1.00 eq.) in anhydrous THF (8 mL) was added dropwise. The solution was gradually warmed to room temperature with stirring for 16 h. The solution was filtered, the filtrand washed with diethyl ether, and the resulting filtrate concentrated in vacuo. The crude residue was purified by silica gel column chromatography (hexanes; Rf = 0.65) to provide the desired 1-iodo-2-(prop-1-en-2-yl)benzene (S6) as a clear, colorless oil in 89% yield (2.64 g).

Data for S6

1-iodo-2-(prop-1-en-2-yl)benzene (S6) 1H NMR (CDCl3, 600 MHz): δ 7.83 (d, 1H, J = 7.9 Hz), 7.30 (t, 1H, J = 7.5 Hz), 7.18 (d, 1H, J = 7.6 Hz), 6.94 (t, 1H, J = 7.7 Hz), 5.22 (s, 1H), 4.89 (s, 1H), 2.07 (s, 1H); 13C{1H} NMR (CDCl3, 151 MHz): δ 148.9, 148.6, 139.3, 128.6, 128.5, 128.2, 116.2, 97.1, 24.1.

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Preparation of 2-(o-iodophenyl)allyl bromide S7:

The title compound (S7) was synthesized according to modified literature procedure. A flame-dried round-bottom flask equipped with a magnetic stir bar was charged with 1-iodo-2-(prop-1-en-2-yl)benzene (S6) (10.6 mmol, 2.57 g, 1.00 eq.), N-bromosuccinimide (11.1 mmol, 1.97 g, 1.05 eq.), tosic acid monohydrate (TsOH·H₂O; 0.11 mmol, 20 mg, 0.010 eq.) and anhydrous THF (32 mL). The homogeneous solution was brought to reflux and vigorously stirred for 4 h. The reaction was then cooled to room temperature. The solution was decanted into a separatory funnel, diluted with hexanes and deionized water, and the organic layer was separated. The aqueous layer was then washed with three portions of hexanes. The combined organic layers were dried over Na₂SO₄, filtered, and concentrated in vacuo to afford a yellow oil. The crude residue was purified by silica gel column chromatography (hexanes; Rₐ = 0.5) to provide the desired 1-(3-bromoprop-1-en-2-yl)-2-iodobenzene (S7) as a clear, colorless oil in 10% yield (347 mg). Note: 63% (1.62 g) of the starting material was able to be cleanly recovered (27% yield BORSM).

Data for S7

1-(3-bromoprop-1-en-2-yl)-2-iodobenzene (S7) \(^1\)H NMR (CDCl₃, 600 MHz): δ 7.86 (dd, 1H, J = 7.9, 1.2 Hz), 7.36 (td, 1H, J = 7.5, 1.2 Hz), 7.27 (dd, 1H, J = 7.6, 1.8 Hz), 7.02 (td, 1H, J = 7.7, 1.8 Hz), 5.65 (s, 1H), 5.19 (s, 1H), 4.31 (s, 2H); \(^{13}\)C\(^{1}\)H NMR (CDCl₃, 151 MHz): δ 148.0, 144.3, 139.3, 130.7, 129.6, 128.1, 121.1, 97.5, 35.9.

\(^7\)Tripathi, C. B.; Mukherjee, S. *Angew. Chem. Int. Ed.* 2013, 52, 8450-8453.
3. N-alkylation of N-arylsulfonyl-protected amino alcohols

Preparation of N-alkylated amino alcohol S8:

To a flame-dried 50 mL round-bottom flask equipped with a magnetic stir bar was added aryl sulfonamide 2 (2.97 mmol, 1.10 g, 1.00 eq.) and powdered, anhydrous potassium carbonate (8.91 mmol, 1.23 g, 3.00 eq.). The flask was capped with a septum, an N2 needle was inserted, and the headspace of the flask was purged with anhydrous N2. Anhydrous acetone (22 mL) was added to dissolve the substrate, followed by cinnamyl bromide (2.97 mmol, 440 µL, 1.00 eq.). The flask was equipped with a reflux condenser, placed in an oil bath, and heated to reflux (approximately 60-65 °C oil bath temperature). The heterogeneous mixture was vigorously stirred for 5 h and then cooled to room temperature. The mixture was filtered through a cotton plug to remove potassium salts and then concentrated in vacuo. The crude residue was purified by silica gel chromatography (3:1 hexanes:ethyl acetate; Rf = 0.3) to yield the N-alkylated amino alcohol product S8 as a clear, colorless, glassy solid in 89% yield (1.29 g).

Data for S8

(S)-4-bromo-N-cinnamyl-N-(1-hydroxy-3-phenylpropan-2-yl)benzenesulfonamide (S8). 1H NMR (CDCl3, 600 MHz): δ 7.50-7.44 (m, 4H), 7.35-7.31 (m, 2H), 7.31-7.27 (m, 3H), 7.24-7.21 (m, 3H), 7.08-7.04 (m, 2H), 6.56 (d, 1H, J = 16.0 Hz), 6.10 (ddd, 1H, J = 16.0, 7.4, 6.0 Hz), 4.21 (qd, 1H, J = 7.8, 4.6 Hz), 4.13 (ddd, 1H, J = 16.0, 6.0, 1.6 Hz), 4.06 (ddd, 1H, J = 16.0, 7.4, 1.3 Hz), 3.75 (ddt, 1H, J = 11.6, 8.3, 4.8 Hz), 3.68 (dt, 1H, J = 11.3, 5.1 Hz), 2.85 (dd, 1H, J = 13.9, 7.6 Hz), 2.78 (dd, 1H, J = 13.9, 7.4 Hz), 1.85 (br s, 1H, J = 4.8 Hz); 13C{1H} NMR (CDCl3, 151
1H NMR (CDCl₃, 600 MHz): δ 139.9, 137.6, 136.1, 133.5, 132.3, 129.1, 128.9, 128.8, 128.4, 127.5, 126.9, 126.6, 126.2, 63.1, 62.2, 46.9, 36.5.

Preparation of N-alkylated amino alcohol S9:

To a flame-dried 250 mL round-bottom flask equipped with a magnetic stir bar was added aryl sulfonamide 2 (10.0 mmol, 3.70 g, 1.00 eq.), tetrabutylammonium iodide (0.20 mmol, 75 mg, 0.02 eq.), and powdered, anhydrous potassium carbonate (40.0 mmol, 5.53 g, 4.00 eq.). The flask was capped with a septum, an N₂ needle was inserted, and the headspace of the flask was purged with anhydrous N₂. Anhydrous acetone (75 mL) was added to dissolve the substrate, followed by 2-phenylallyl bromide (10.5 mmol, 1.51 mL, 1.05 eq.). The flask was equipped with a reflux condenser, placed in an oil bath, and heated to reflux (approximately 60-65 °C oil bath temperature). The heterogeneous mixture was vigorously stirred for 26 h and then cooled to room temperature. The mixture was filtered through a cotton plug to remove potassium salts and then concentrated in vacuo. The crude residue was purified by silica gel chromatography (3:1 hexanes:ethyl acetate; Rₜ = 0.3) to yield the N-alkylated amino alcohol product S9 as a crystalline white solid in 91% yield (4.41 g).

Data for S9

(S)-4-bromo-N-(1-hydroxy-3-phenylpropan-2-yl)-N-(2-phenylallyl)benzenesulfonamide (S9). 1H NMR (CDCl₃, 600 MHz): δ 7.62 (d, 2H, J = 8.6 Hz), 7.58 (d, 2H, J = 8.6 Hz), 7.42-7.39 (m, 2H), 7.38-7.33 (m, 3H), 7.24-7.18 (m, 3H), 6.95 (dd, 2H, J = 7.7, 1.7 Hz), 5.49 (s, 1H), 5.44 (s, 1H), 4.54 (d, 1H, J = 16.3 Hz), 4.35 (d, 1H, J = 15.8 Hz), 3.95 (tdd, 1H, J = 9.1, 5.0, 4.1 Hz), 3.61 (ddd, 1H, J = 12.1, 8.5, 5.5 Hz), 3.49 (ddd, 1H, J = 12.1, 7.2, 4.0 Hz), 2.77 (dd, 1H, J =
13.5, 9.8 Hz), 2.62 (dd, 1H, J = 13.5, 5.0 Hz), 1.51 (dd, 1H, J = 7.2, 5.6 Hz); $^{13}$C{$_{^{1}}$H} NMR (CDCl$_3$, 151 MHz): δ 145.1, 139.4, 138.4, 137.7, 132.5, 129.1, 129.1, 129.0, 128.8, 128.5, 127.9, 126.9, 126.8, 116.8, 62.5, 62.3, 49.4, 36.1.

**Preparation of N-alkylated amino alcohol S10:**

![Chemical Reaction](image)

To a flame-dried 100 mL round-bottom flask equipped with a magnetic stir bar was added aryl sulfonamide S2 (5.10 mmol, 1.50 g, 1.00 eq.), tetrabutylammonium iodide (0.10 mmol, 38 mg, 0.02 eq.), and powdered, anhydrous potassium carbonate (20.4 mmol, 2.82 g, 4.00 eq.). The flask was capped with a septum, an N$_2$ needle was inserted, and the headspace of the flask was purged with anhydrous N$_2$. Anhydrous acetone (38 mL) was added to dissolve the substrate, followed by 2-phenylallyl bromide (5.35 mmol, 770 µL, 1.05 eq.). The flask was equipped with a reflux condenser, placed in an oil bath, and heated to reflux (approximately 60-65 °C oil bath temperature). The heterogeneous mixture was vigorously stirred for 24 h and then cooled to room temperature. The mixture was filtered through a cotton plug to remove potassium salts and then concentrated in vacuo. The crude residue was purified by silica gel chromatography (25:1 dichloromethane:methanol; R$_f$ = 0.25 in 2:1 hexanes:ethyl acetate) to yield the N-alkylated amino alcohol product S10 as a white, crystalline solid in 97% yield (2.03 g).

**Data for S10**

![Chemical Structure](image)

(S)-4-bromo-N-(1-hydroxypropan-2-yl)-N-(2-phenylallyl)benzenesulfonamide (S10). $^{1}$H NMR (CDCl$_3$, 600 MHz): δ 7.66-7.62 (m, 4H), 7.44 (d, 2H, J = 6.9 Hz), 7.36 (t, 2H, J = 7.7 Hz), 7.34 (t, 1H, J = 7.1 Hz), 5.45 (s, 1H), 5.38 (s, 1H), 4.60 (d, 1H, J = 16.1 Hz), 4.08 (d, 1H, J = 16.1 Hz), 3.94 (dqd, 1H, J = 8.8, 7.0, 4.6 Hz), 3.49 (ddd, 1H, J = 11.7, 8.8, 4.6 Hz), 3.38 (ddd,
$^{1}$H, $J = 11.7, 8.2, 4.8$ Hz), 1.51 (dd, $1^H, J = 8.3, 4.7$ Hz), 0.91 (d, $3^H, J = 7.0$ Hz); $^{13}$C($^1$H) NMR (CDCl$_3$, 151 MHz): $\delta$ 145.0, 139.3, 138.3, 132.5, 129.0, 128.8, 128.5, 127.8, 126.8, 116.2, 64.7, 56.3, 48.3, 13.7.

**Preparation of N-alkylated amino alcohol S11:**

To a flame-dried 100 mL round-bottom flask equipped with a magnetic stir bar was added aryl sulfonamide S4 (4.66 mmol, 1.50 g, 1.00 eq.), tetrabutylammonium iodide (0.093 mmol, 34 mg, 0.02 eq.), and powdered, anhydrous potassium carbonate (18.6 mmol, 2.57 g, 4.00 eq.). The flask was capped with a septum, an N$_2$ needle was inserted, and the headspace of the flask was purged with anhydrous N$_2$. Anhydrous acetone (35 mL) was added to dissolve the substrate, followed by 2-phenylallyl bromide (4.89 mmol, 703 $\mu$L, 1.05 eq.). The flask was equipped with a reflux condenser, placed in an oil bath, and heated to reflux (approximately 60-65 °C oil bath temperature). The heterogeneous mixture was vigorously stirred for 24 h and then cooled to room temperature. The mixture was filtered through a cotton plug to remove potassium salts and then concentrated in vacuo. The crude residue was purified by silica gel chromatography (3:1 hexanes:ethyl acetate; $R_f = 0.5$ in 2:1 hexanes:ethyl acetate) to yield the N-alkylated amino alcohol product S11 as a clear, colorless, viscous oil in 86% yield (1.76 g).

**Data for S11**

(S)-4-bromo-$N$-(1-hydroxy-3-methylbutan-2-yl)-$N$-(2-phenylallyl)benzenesulfonamide (S11). $^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ 7.66 (d, 2H, $J = 8.6$ Hz), 7.59 (d, 2H, $J = 8.6$ Hz), 7.32-7.29 (m, 3H), 7.26-7.24 (m, 2H), 5.42 (s, 1H), 5.39 (s, 1H), 4.40 (d, 1H, $J = 16.0$ Hz), 4.28 (d,
1H, J = 16.2 Hz), 3.70 (dt, 1H, J = 12.6, 3.9 Hz), 3.59 (ddd, 1H, J = 12.3, 6.1, 2.8 Hz), 3.47 (ddd, 1H, J = 10.3, 8.5, 3.6 Hz), 1.89 (dsept, 1H, J = 10.3, 6.6 Hz), 0.88 (d, 3H, J = 6.5 Hz), 0.58 (d, 3H, J = 6.6 Hz); 13C{1H} NMR (CDCl₃, 151 MHz): δ 145.0, 140.0, 139.0, 132.2, 129.4, 128.7, 128.4, 127.6, 126.7, 117.5, 67.3, 62.4, 49.4, 28.2, 20.9, 20.4.

Preparation of N-alkylated amino alcohol S12:

\[
\begin{align*}
\text{Br} & \quad \text{Ph} & \quad \text{NH} \\
\text{O} & \quad \text{OH} \\
2 (1.00 \text{ eq.}) & \quad & + \\
TBAI (5 \text{ mol \%}), & \quad \text{K}_2\text{CO}_3 (4.00 \text{ eq.}) & \quad \text{acetone, 22 °C to 65 °C, 13 h} \\
\rightarrow & \quad \text{S7 (1.00 eq.)} & \quad \text{S12}
\end{align*}
\]

To a flame-dried 20 mL scintillation vial equipped with a magnetic stir bar was added aryl sulfonamide 2 (1.07 mmol, 398 mg, 1.00 eq.), tetrabutylammonium iodide (0.054 mmol, 20 mg, 0.05 eq.), and powdered, anhydrous potassium carbonate (4.30 mmol, 594 mg, 4.00 eq.). The vial was capped with a septum, an N₂ needle was inserted, and the headspace of the vial was purged with anhydrous N₂. Anhydrous acetone (8.1 mL) was added to dissolve the substrate, followed by 1-(3-bromoprop-1-en-2-yl)-2-iodobenzene (S7, 1.07 mmol, 347 mg, 1.00 eq.). The vial was capped, placed in an oil bath, and heated to 65 °C. The heterogeneous mixture was vigorously stirred for 13 h and then cooled to room temperature. The mixture was filtered through a cotton plug to remove potassium salts and then concentrated in vacuo. The crude residue was purified by silica gel chromatography (3:1 hexanes:ethyl acetate; R_f = 0.3) to yield the N-alkylated amino alcohol product S12 as a white, sticky solid in 77% yield (507 mg).

Data for S12

\[
\begin{align*}
\text{(S)-4-bromo-N-(1-hydroxy-3-phenylpropan-2-yl)-N-(2-(2iodophenyl)allyl)benzenesulfonamide (S12).} & \quad \text{H} \text{ NMR (CDCl}_3, 600 \text{ MHz): δ 7.85 (d, 1H, J = 7.9 Hz), 7.63 (d, 2H, J = 8.7 Hz), 7.55 (d, 2H, J = 8.5 Hz), 7.33 (t, 1H, J = 7.4 Hz), 7.28-7.21 (m,}
\end{align*}
\]
3H), 7.12 (d, 1H, J = 7.6 Hz), 7.08 (d, 2H, J = 8.1 Hz), 7.04 (t, 1H, J = 7.7 Hz), 5.62 (s, 1H), 5.20 (s, 1H), 4.22 (d, 1H, J = 17.3 Hz, 1H), 4.17 (d, 1H, J = 17.2 Hz, 1H), 4.09-4.03 (m, 1H), 3.73 (ddd, 1H, J = 13.3, 7.9, 5.8 Hz), 3.67 (ddd, 1H, J = 11.6, 6.3, 4.1 Hz), 2.90 (dd, 1H, J = 13.7, 9.2 Hz), 2.78 (dd, 1H, J = 13.7, 5.6 Hz), 1.89 (t, 1H, J = 6.1 Hz); \textsuperscript{13}C{\textsuperscript{1}H} NMR (CDCl\textsubscript{3}, 151 MHz): δ 148.0, 144.8, 139.5, 139.2, 137.7, 132.4, 130.1, 129.5, 129.1, 129.0, 128.8, 128.4, 127.8, 126.9, 118.7, 97.7, 63.2, 63.0.

**Preparation of N-alkylated amino alcohol S13:**

To a flame-dried 20 mL scintillation vial equipped with a magnetic stir bar was added aryl sulfonamide 2 (2.03 mmol, 750 mg, 1.00 eq.), tetrabutylammonium iodide (0.041 mmol, 15 mg, 0.02 eq.), and powdered, anhydrous potassium carbonate (8.10 mmol, 1.12 g, 4.00 eq.). The vial was capped with a septum, an N\textsubscript{2} needle was inserted, and the headspace of the vial was purged with anhydrous N\textsubscript{2}. Anhydrous acetone (15 mL) was added to dissolve the substrate, followed by 3-bromo-2-methylpropene (2.13 mmol, 221 µL, 1.05 eq.). The vial was capped, placed in an oil bath, and heated to 65 °C. The heterogeneous mixture was vigorously stirred for 4 h and then cooled to room temperature. The mixture was filtered through a cotton plug to remove potassium salts and then concentrated in vacuo. The crude residue was purified by silica gel chromatography (3:1 hexanes:ethyl acetate; R\textsubscript{f} = 0.3) to yield the N-alkylated amino alcohol product S13 as a light yellow, viscous oil in 93% yield (800 mg).

**Data for S13**
(S)-4-bromo-N-(1-hydroxy-3-phenylpropan-2-yl)-N-(2-methylallyl)benzenesulfonamide (S13). \(^1\)H NMR (CDCl\(_3\), 600 MHz): \(\delta\) 7.62 (d, 2H, \(J = 8.6\) Hz), 7.57 (d, 2H, \(J = 8.6\) Hz), 7.24-7.16 (m, 3H), 7.00 (dd, 2H, \(J = 7.2, 2.2\) Hz), 5.06 (s, 1H), 5.00 (s, 1H), 4.01-3.93 (m, 2H), 3.86 (d, 1H, \(J = 15.8\) Hz), 3.70 (ddd, 1H, \(J = 11.8, 8.1, 6.2\) Hz), 3.60 (ddd, 1H, \(J = 11.8, 5.9, 4.2\) Hz), 2.80 (dd, 1H, \(J = 13.6, 9.0\) Hz), 2.71 (dd, 1H, \(J = 13.7, 5.8\) Hz), 1.93 (t, 1H, \(J = 6.1\) Hz), 1.80 (s, 3H); \(^{13}\)C\(^{\text{\texttt{1}}}\)H NMR (CDCl\(_3\), 151 MHz): \(\delta\) 142.7, 139.7, 137.7, 132.4, 129.0, 128.8, 128.8, 127.7, 126.8, 114.5, 62.7, 62.4, 51.6, 36.0, 20.2.

**Preparation of N-alkylated amino alcohol S14:**

To a flame-dried 20 mL scintillation vial equipped with a magnetic stir bar was added aryl sulfonamide S5 (2.20 mmol, 750 mg, 1.00 eq.), tetrabutylammonium iodide (0.044 mmol, 16 mg, 0.02 eq.), and powdered, anhydrous potassium carbonate (8.79 mmol, 1.22 g, 4.00 eq.). The vial was capped with a septum, an \(N_2\) needle was inserted, and the headspace of the vial was purged with anhydrous \(N_2\). Anhydrous acetone (8.8 mL) was added to dissolve the substrate, followed by 2-phenylallyl bromide (2.31 mmol, 332 \(\mu\)L, 1.05 eq.). The vial was capped, placed in an oil bath, and heated to 65 °C. The heterogeneous mixture was vigorously stirred for 18 h and then cooled to room temperature. The mixture was filtered through a cotton plug to remove potassium salts and then concentrated in vacuo. The crude residue was purified by silica gel chromatography (3:1 hexanes:ethyl acetate; \(R_f = 0.25\)) to yield the N-alkylated amino alcohol product S14 as a white, crystalline solid in 93% yield (937 mg).

**Data for S14**
(S)-N-(1-hydroxy-3-phenylpropan-2-yl)-N-(2-phenylallyl)naphthalene-2-sulfonamide (S14).

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ 8.43 (br s, 1H), 7.96 (d, 1H, $J$ = 8.0 Hz), 7.92 (dd, 2H, $J$ = 8.4, 5.0 Hz), 7.75 (dd, 1H, $J$ = 8.8, 1.3 Hz), 7.67 (t, 1H, $J$ = 7.0 Hz), 7.64 (t, 1H, $J$ = 7.1 Hz), 7.43 (dd, 2H, $J$ = 6.6, 2.9 Hz), 7.34-7.31 (m, 3H), 7.20 (d, 1H, $J$ = 16.1 Hz), 3.99 (tt, 1H, $J$ = 8.7, 4.1 Hz), 3.61 (ddd, 1H, $J$ = 12.2, 8.6, 5.4 Hz), 3.48 (ddd, 1H, $J$ = 11.8, 7.6, 3.8 Hz), 2.74 (dd, 1H, $J$ = 13.3, 10.4 Hz), 2.53 (dd, 1H, $J$ = 13.3, 4.4 Hz), 1.60 (dd, 1H, $J$ = 7.6, 5.4 Hz);

$^{13}$C{$^1$H} NMR (CDCl$_3$, 151 MHz): $\delta$ 145.4, 138.4, 137.7, 137.0, 135.0, 132.3, 129.7, 129.4, 129.2, 129.1, 129.0, 128.8, 128.7, 128.5, 128.1, 127.8, 126.8, 126.7, 122.7, 116.5, 62.4, 62.2, 49.4, 36.0.

4. Synthesis of amino aldehydes:

Preparation of amino aldehyde 3:

![Diagram of the reaction](image)

To a flame-dried 20 mL scintillation vial equipped with a magnetic stir bar was added $N$-alkylated amino alcohol S8 (0.905 mmol, 440 mg, 1.00 eq.) and Dess-Martin periodinane (DMP; 1.81 mmol, 767 mg, 2.00 eq.). The vial was capped with a septum, an N$_2$ needle was inserted, the headspace of the vial was purged with anhydrous N$_2$, and the vial was placed in a 0 °C ice-water bath. Anhydrous CH$_2$Cl$_2$ (9.1 mL) was added down the side of the vial with vigorous stirring, resulting in a colorless, homogeneous solution. Deionized water (0.996 mmol, 17.9 μL, 1.10 eq.) was injected via microliter syringe and the ice-water bath was removed, allowing the solution to warm to 22 °C. The solution rapidly became heterogeneous and milky white upon addition of the water. The heterogeneous mixture was vigorously stirred for 1.0 h, at which time thin layer chromatography on SiO$_2$ showed complete conversion. The mixture was again cooled to 0 °C in an ice-water bath and quenched by the drop-wise addition of an equal volume of 1:1 sat. NaHCO$_3$ (aq.): sat. Na$_2$S$_2$O$_3$ (aq.) (sodium thiosulfate). After evolution of CO$_2$ was complete, the solution was warmed to room temperature and stirred for an additional 30 minutes. The resulting homogeneous solution was then decanted into a separatory funnel, diluted with excess CH$_2$Cl$_2$,
and washed with deionized water. The organic phase was separated and the aqueous phase was extracted with CH₂Cl₂ (x4). The combined organics were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude residue was purified first by filtration with dichloromethane through a short plug of neutral aluminum oxide (Brockmann activity I slurried with 10% H₂O), followed by silica gel chromatography (4:1 hexanes:ethyl acetate; Rₜ = 0.4) to yield the amino aldehyde product 3 as an off-white crystalline solid in 84% yield (370 mg).

**Data for 3**

\[
\begin{align*}
\text{(S)-4-bromo-}\text{N-cinnamyl-N-(1-oxo-3-phenylpropan-2-yl)benzenesulfonamide (3).} & \quad \text{\textsuperscript{1}H NMR} \\
& \quad (\text{CDCl₃, 600 MHz}): \delta 9.72 (s, 1H), 7.47 (d, 2H, J = 8.6 Hz), 7.40 (d, 2H, J = 8.6 Hz), 7.35-7.30 (m, 2H), 7.30-7.26 (m, 3H), 7.26-7.20 (m, 3H), 7.06 (d, 2H, J = 6.6 Hz), 6.42 (d, 1H, J = 15.8 Hz), 5.98 (dt, 1H, J = 15.9, 7.0 Hz), 4.59 (dd, 1H, J = 9.5, 5.2 Hz), 4.03-3.92 (m, 2H), 3.45 (dd, 1H, J = 14.7, 9.5 Hz); \quad \text{\textsuperscript{13}C\textsuperscript{1}H NMR} (\text{CDCl₃, 151 MHz}): \delta 198.9, 139.2, 136.9, 135.8, 135.6, 132.4, 129.1, 128.9, 128.9, 128.8, 128.6, 127.9, 127.0, 126.7, 123.7, 67.7, 48.6, 33.3; \quad [\alpha]_D^{26} = -129.0^\circ (c = 1.070, \text{CH}_2\text{Cl}_2, l = 100 \text{ mm}).
\end{align*}
\]

**Preparation of amino aldehyde 4:**

To a flame-dried 250 mL round-bottom flask equipped with a magnetic stir bar was added N-alkylated amino alcohol S9 (4.79 mmol, 2.33 g, 1.00 eq.) and Dess-Martin periodinane (DMP; 9.58 mmol, 4.06 g, 2.00 eq.). \textit{Note: In our hands, 1.75-2.00 eq. of DMP are necessary to attain full conversion.} The flask was capped with a septum, an N₂ needle was inserted, the headspace of the flask was purged with anhydrous N₂, and the flask was placed in a 0 °C ice-water bath. Anhydrous CH₂Cl₂ (48 mL) was added down the side of the flask with vigorous stirring,
resulting in a colorless, homogeneous solution. Deionized water (5.27 mmol, 95 µL, 1.10 eq.) was injected via microliter syringe and the ice-water bath was removed, allowing the solution to warm to 22 °C. The solution rapidly became heterogeneous and milky white upon addition of the water. The heterogeneous mixture was vigorously stirred for 0.75 h, at which time thin layer chromatography on SiO₂ showed complete conversion. The mixture was again cooled to 0 °C in an ice-water bath and quenched by the drop-wise addition of an equal volume of 1:1 sat. NaHCO₃ (aq.): sat. Na₂S₂O₃ (aq.) (sodium thiosulfate). After evolution of CO₂ (g) was complete, the solution was warmed to room temperature and stirred for an additional 30 minutes. The resulting homogeneous solution was then decanted into a separatory funnel, diluted with excess CH₂Cl₂, and washed with deionized water. The organic phase was separated and the aqueous phase was extracted with CH₂Cl₂ (x4). The combined organics were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude residue was purified first by filtration with dichloromethane through a short plug of neutral aluminum oxide (Brockmann activity I slurried with 10% H₂O), followed by silica gel chromatography (4:1 hexanes:ethyl acetate; Rₖ = 0.5) to yield the amino aldehyde product 4 as a beige solid in 85% yield (1.98 g).

**Data for 4**

![Structure of 4](image)

(S)-4-bromo-N-(1-oxo-3-phenylpropan-2-yl)-N-(2-phenylallyl)benzenesulfonamide (4). ¹H NMR (CDCl₃, 600 MHz): ᶦ 9.15 (s, 1H), 7.61-7.55 (m, 4H), 7.32-7.27 (m, 3H), 7.23-7.20 (m, 3H), 7.20-7.18 (m, 2H), 7.00-6.96 (m, 2H), 5.41 (s, 1H), 5.04 (s, 1H), 4.37 (d, 1H, J = 14.8 Hz), 4.10 (dd, 1H, J = 8.3, 5.5 Hz), 3.94 (d, 1H, J = 14.8 Hz), 3.41 (dd, 1H, J = 14.6, 5.5 Hz), 2.82 (dd, 1H, J = 14.6, 8.3 Hz); ¹³C{¹H} NMR (CDCl₃, 151 MHz): ᶦ 197.9, 142.9, 138.8, 137.6, 137.5, 132.6, 129.3, 129.2, 128.8, 128.8, 128.6, 128.4, 127.0, 126.7, 119.3, 67.5, 51.5, 33.6; [α]D²⁵ = −100.7° (c = 1.525, CH₂Cl₂, l = 100 mm).
Preparation of amino aldehyde 10:

To a flame-dried 100 mL round-bottom flask equipped with a magnetic stir bar was added N-alkylated amino alcohol S10 (2.44 mmol, 1.00 g, 1.00 eq.) and Dess-Martin periodinane (DMP; 6.09 mmol, 2.58 g, 2.50 eq.). The flask was capped with a septum, an N₂ needle was inserted, the headspace of the flask was purged with anhydrous N₂, and the flask was placed in a 0 °C ice-water bath. Anhydrous CH₂Cl₂ (24 mL) was added down the side of the flask with vigorous stirring, resulting in a colorless, homogeneous solution. Deionized water (2.68 mmol, 48 µL, 1.10 eq.) was injected via microliter syringe and the ice-water bath was removed, allowing the solution to warm to 22 °C. The solution rapidly became heterogeneous and milky white upon addition of the water. The heterogeneous mixture was vigorously stirred for 1.0 h, at which time thin layer chromatography on SiO₂ showed complete conversion. The mixture was again cooled to 0 °C in an ice-water bath and quenched by the drop-wise addition of an equal volume of 1:1 sat. NaHCO₃ (aq.): sat. Na₂S₂O₃ (aq.) (sodium thiosulfate). After evolution of CO₂ (g) was complete, the solution was warmed to room temperature and stirred for an additional 30 minutes. The resulting homogeneous solution was then decanted into a separatory funnel, diluted with excess CH₂Cl₂, and washed with deionized water. The organic phase was separated and the aqueous phase was extracted with CH₂Cl₂ (x4). The combined organics were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude residue was purified first by filtration with dichloromethane through a short plug of neutral aluminum oxide (Brockmann activity I slurried with 10% H₂O), followed by silica gel chromatography (3:1 hexanes:ethyl acetate; Rf = 0.5) to yield the amino aldehyde product 10 as a white, crystalline solid in 54% yield (524 mg).

Data for 10
(S)-4-bromo-N-(1-oxopropan-2-yl)-N-(2-phenylallyl)benzenesulfonamide (10). \(^1\)H NMR (CDCl\(_3\), 600 MHz): \(\delta\) 9.17 (s, 1H), 7.66 (s, 4H), 7.36-7.32 (m, 5H), 5.49 (s, 1H), 5.29 (s, 1H), 4.47 (d, 1H, \(J = 14.9\) Hz), 4.17 (d, 1H, \(J = 14.9\) Hz), 4.07 (q, 1H, \(J = 7.0\) Hz), 1.18 (d, 3H, \(J = 7.0\) Hz); \(^1\)C\(^1\)H NMR (CDCl\(_3\), 151 MHz): \(\delta\) 199.5, 142.5, 138.6, 137.4, 132.7, 129.1, 128.8, 128.6, 128.4, 126.8, 118.8, 61.5, 50.0, 11.0; \([\alpha]_D^{26} = -3.04^\circ\) (c = 0.540, CH\(_2\)Cl\(_2\), l = 100 mm).

**Preparation of amino aldehyde S15:**

To a flame-dried 50 mL round-bottom flask equipped with a magnetic stir bar was added N-alkylated amino alcohol S11 (1.71 mmol, 750 mg, 1.00 eq.) and Dess-Martin periodinane (DMP; 4.28 mmol, 1.81 g, 2.50 eq.). The flask was capped with a septum, an N\(_2\) needle was inserted, the headspace of the flask was purged with anhydrous N\(_2\), and the flask was placed in a 0 °C ice-water bath. Anhydrous CH\(_2\)Cl\(_2\) (17 mL) was added down the side of the flask with vigorous stirring, resulting in a colorless, homogeneous solution. Deionized water (1.88 mmol, 34 \(\mu\)L, 1.10 eq.) was injected via microliter syringe and the ice-water bath was removed, allowing the solution to warm to 22 °C. The solution rapidly became heterogeneous and milky white upon addition of the water. The heterogeneous mixture was vigorously stirred for 1.0 h, at which time thin layer chromatography on SiO\(_2\) showed complete conversion. The mixture was again cooled to 0 °C in an ice-water bath and quenched by the drop-wise addition of an equal volume of 1:1 sat. NaHCO\(_3\) (aq.) : sat. Na\(_2\)S\(_2\)O\(_3\) (aq.) (sodium thiosulfate). After evolution of CO\(_2\) (g) was complete, the solution was warmed to room temperature and stirred for an additional 30 minutes. The resulting homogeneous solution was then decanted into a separatory funnel, diluted with excess CH\(_2\)Cl\(_2\), and washed with deionized water. The organic phase was separated and the aqueous phase was extracted with CH\(_2\)Cl\(_2\) (x4). The combined organics were dried over Na\(_2\)SO\(_4\), filtered, and concentrated in vacuo. The crude residue was purified first by filtration with dichloromethane through a short plug of neutral aluminum oxide (Brockmann activity I slurried with 10% H\(_2\)O), followed by silica gel chromatography (4:1 hexanes:ethyl acetate) to yield the amino aldehyde product S15 as a clear, colorless, viscous oil in 94% yield (701 mg).
Data for S15

(S)-4-bromo-N-(3-methyl-1-oxobutan-2-yl)-N-(2-phenylallyl)benzenesulfonamide (S15). $^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ 9.36 (s, 1H), 7.61-7.58 (m, 4 H), 7.31-7.26 (m, 3H), 7.25-7.21 (m, 2H), 5.43 (s, 1H), 5.30 (s, 1H), 4.40 (d, 1H, $J$ = 15.7 Hz), 4.28 (d, 1H, $J$ = 15.8), 3.70 (d, 1H, $J$ = 10.1), 2.32 (dsept, 1H, $J$ = 10.1, 6.6 Hz), 1.03 (d, 3H, $J$ = 6.5 Hz), 0.79 (d, 3H, $J$ = 6.7 Hz); $^{13}$C$^1$H NMR (CDCl$_3$, 151 MHz): $\delta$ 198.4, 143.3, 139.1, 138.3, 132.4, 129.3, 128.7, 128.4, 128.4, 126.7, 118.8, 71.5, 51.3, 27.9, 20.5, 20.3; $[\alpha]$$_D$$^{26}$ = −3.13° (c = 0.565, CH$_2$Cl$_2$, l = 100 mm).

Preparation of amino aldehyde 11:

To a flame-dried 20 mL scintillation vial equipped with a magnetic stir bar was added N-alkylated amino alcohol S12 (0.804 mmol, 492 mg, 1.00 eq.) and Dess-Martin periodinane (DMP; 1.61 mmol, 682 mg, 2.00 eq.). The vial was capped with a septum, an N$_2$ needle was inserted, the headspace of the vial was purged with anhydrous N$_2$, and the vial was placed in a 0 °C ice-water bath. Anhydrous CH$_2$Cl$_2$ (8.0 mL) was added down the side of the vial with vigorous stirring, resulting in a colorless, homogeneous solution. Deionized water (0.884 mmol, 15.9 µL, 1.10 eq.) was injected via microliter syringe and the ice-water bath was removed, allowing the solution to warm to 22 °C. The solution rapidly became heterogeneous and milky white upon addition of the water. The heterogeneous mixture was vigorously stirred for 1.0 h, at which time thin layer chromatography on SiO$_2$ showed complete conversion. The mixture was again cooled to 0 °C in an ice-water bath and quenched by the drop-wise addition of an equal volume of 1:1 sat. NaHCO$_3$ (aq): sat. Na$_2$S$_2$O$_3$ (aq) (sodium thiosulfate). After evolution of CO$_2$(g) was complete, the solution was warmed to room temperature and stirred for an additional 30
minutes. The resulting homogeneous solution was then decanted into a separatory funnel, diluted with excess CH$_2$Cl$_2$, and washed with deionized water. The organic phase was separated and the aqueous phase was extracted with CH$_2$Cl$_2$ (x4). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude residue was purified first by filtration with dichloromethane through a short plug of neutral aluminum oxide (Brockmann activity I slurried with 10% H$_2$O), followed by silica gel chromatography (4:1 hexanes:ethyl acetate; $R_f = 0.4$) to yield the amino aldehyde product 11 as a light yellow, waxy solid in 79% yield (386 mg).

**Data for 11**

(S)-4-bromo-N-(2-(2-iodophenyl)allyl)-N-(1-oxo-3-phenylpropan-2-yl)benzenesulfonamide (11). $^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ 9.62 (s, 1H), 7.68 (dd, 1H, $J = 8.0, 1.2$ Hz), 7.47 (d, 2H, $J = 8.7$ Hz), 7.44 (d, 2H, $J = 8.7$ Hz), 7.34-7.30 (m, 2H), 7.28-7.24 (m, 3H), 7.20 (td, 1H, $J = 7.5, 1.2$ Hz), 6.96 (td, 1H, $J = 7.7, 1.7$ Hz), 6.82 (dd, 1H, $J = 7.6, 1.7$ Hz), 5.14 (s, 1H), 5.09 (s, 1H), 4.21 (dd, 1H, $J = 8.7, 5.2$ Hz), 4.15 (d, 1H, $J = 15.7$ Hz), 3.59 (dd, 1H, $J = 14.5, 5.2$ Hz), 3.41 (d, 1H, $J = 15.7$ Hz), 3.08 (dd, 1H, $J = 14.5, 8.7$ Hz); $^{13}$C{$^1$H} NMR (CDCl$_3$, 151 MHz): $\delta$ 197.6, 145.9, 143.4, 139.7, 137.8, 137.7, 132.4, 129.5, 129.5, 129.4, 129.4, 129.0, 128.5, 128.2, 127.2, 121.9, 97.5, 67.9, 52.4, 35.0; $[\alpha]_D^{26} = -58.2^\circ$ (c = 0.645, CH$_2$Cl$_2$, l = 100 mm).

**Preparation of amino aldehyde 12:**

To a flame-dried 50 mL round-bottom flask equipped with a magnetic stir bar was added $N$-alkylated amino alcohol S13 (1.91 mmol, 812 mg, 1.00 eq.) and Dess-Martin periodinane (DMP; 3.83 mmol, 1.62 g, 2.00 eq.). The flask was capped with a septum, an N$_2$ needle was inserted, the headspace of the flask was purged with anhydrous N$_2$, and the flask was placed in a 0 °C ice-
water bath. Anhydrous CH$_2$Cl$_2$ (19 mL) was added down the side of the flask with vigorous stirring, resulting in a colorless, homogeneous solution. Deionized water (2.11 mmol, 38 µL, 1.10 eq.) was injected via microliter syringe and the ice-water bath was removed, allowing the solution to warm to 22 °C. The solution rapidly became heterogeneous and milky white upon addition of the water. The heterogeneous mixture was vigorously stirred for 1.0 h, at which time thin layer chromatography on SiO$_2$ showed complete conversion. The mixture was again cooled to 0 °C in an ice-water bath and quenched by the drop-wise addition of an equal volume of 1:1 sat. NaHCO$_3$ (aq.): sat. Na$_2$S$_2$O$_3$ (aq.) (sodium thiosulfate). After evolution of CO$_2$ (g) was complete, the solution was warmed to room temperature and stirred for an additional 30 minutes. The resulting homogeneous solution was then decanted into a separatory funnel, diluted with excess CH$_2$Cl$_2$, and washed with deionized water. The organic phase was separated and the aqueous phase was extracted with CH$_2$Cl$_2$ (x4). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude residue was purified first by filtration with dichloromethane through a short plug of neutral aluminum oxide (Brockmann activity I slurried with 10% H$_2$O), followed by silica gel chromatography (4:1 hexanes:ethyl acetate; R$_f$ = 0.4) to yield the amino aldehyde product 12 as an off-white, crystalline solid in 75% yield (603 mg).

**Data for 12**

\[
(\text{S})-\text{4-bromo-}\text{-N-(2-methylallyl)-N-(1-oxo-3-phenylpropan-2-yl)benzenesulfonamide (12).}\]

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ 9.70 (s, 1H), 7.57 (s, 4H), 7.22-7.17 (m, 3H), 7.01-6.97 (m, 2H), 4.96 (s, 1H), 4.81 (s, 1H), 4.20 (dd, 1H, $J = 8.5$, 5.7 Hz), 3.78 (d, 1H, $J = 14.7$ Hz), 3.52 (d, 1H, $J = 14.7$ Hz), 3.43 (dd, 1H, $J = 14.6$, 5.7 Hz), 2.83 (dd, 1H, $J = 14.6$, 8.5 Hz), 1.66 (s, 3H); $^1$H NMR (CDCl$_3$, 151 MHz): $\delta$ 198.2, 139.6, 139.1, 137.2, 132.5, 129.1, 129.1, 128.9, 128.1, 127.0, 117.7, 67.4, 53.3, 33.3, 19.9. $[\alpha]_D^{25} = -52.3^\circ$ (c = 0.650, CH$_2$Cl$_2$, l = 100 mm).
Preparation of amino aldehyde S16:

To a flame-dried 50 mL round-bottom flask equipped with a magnetic stir bar was added N-alkylated amino alcohol S14 (1.37 mmol, 625 mg, 1.00 eq.) and Dess-Martin periodinane (DMP; 2.73 mmol, 1.16 g, 2.00 eq.). The flask was capped with a septum, an N$_2$ needle was inserted, the headspace of the flask was purged with anhydrous N$_2$, and the flask was placed in a 0 °C ice-water bath. Anhydrous CH$_2$Cl$_2$ (14 mL) was added down the side of the flask with vigorous stirring, resulting in a colorless, homogeneous solution. Deionized water (1.50 mmol, 27 μL, 1.10 eq.) was injected via microliter syringe and the ice-water bath was removed, allowing the solution to warm to 22 °C. The solution rapidly became heterogeneous and milky white upon addition of the water. The heterogeneous mixture was vigorously stirred for 1.0 h, at which time thin layer chromatography on SiO$_2$ showed complete conversion. The mixture was again cooled to 0 °C in an ice-water bath and quenched by the drop-wise addition of an equal volume of 1:1 sat. NaHCO$_3$(aq.): sat. Na$_2$S$_2$O$_3$(aq.) (sodium thiosulfate). After evolution of CO$_2$(g) was complete, the solution was warmed to room temperature and stirred for an additional 30 minutes. The resulting homogeneous solution was then decanted into a separatory funnel, diluted with excess CH$_2$Cl$_2$, and washed with deionized water. The organic phase was separated and the aqueous phase was extracted with CH$_2$Cl$_2$(x4). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude residue was purified first by filtration with dichloromethane through a short plug of neutral aluminum oxide (Brockmann activity I slurried with 10% H$_2$O), followed by silica gel chromatography (4:1 hexanes:ethyl acetate; R$_f$ = 0.4) to yield the amino aldehyde product S16 as an off-white to light yellow crystalline solid in 95% yield (591 mg).
Data for S16

(S)-N-(1-oxo-3-phenylpropan-2-yl)-N-(2-phenylallyl)naphthalene-2-sulfonamide (S16). $^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ 9.19 (s, 1H), 8.39 (d, 1H, $J$ = 1.9 Hz), 7.95 (d, 2H, $J$ = 9.3 Hz), 7.92 (d, 1H, $J$ = 8.7 Hz), 7.75-7.60 (m, 3H), 7.26-7.22 (m, 1H), 7.19-7.13 (m, 4H), 7.15-7.12 (m, 3H), 6.91 (d, 2H, $J$ = 6.4 Hz), 5.39 (s, 1H), 4.99 (s, 1H), 4.46 (d, 1H, $J$ = 14.7 Hz), 4.11 (dd, 1H, $J$ = 8.0, 5.5 Hz), 3.97 (d, 1H, $J$ = 14.7 Hz), 3.42 (dd, 1H, $J$ = 14.5, 5.4 Hz), 2.84 (dd, 1H, $J$ = 14.5, 8.1 Hz); $^{13}$C$^1$H NMR (CDCl$_3$, 151 MHz): $\delta$ 198.1, 142.9, 137.8, 137.4, 136.4, 135.1, 132.2, 129.7, 129.5, 129.5, 129.3, 129.2, 128.6, 128.6, 128.5, 128.0, 127.9, 126.7, 126.7, 122.8, 119.1, 67.3, 51.5, 33.5; [$\alpha$]$_D$$^{26}$ = $-$110.5° (c = 0.515, CH$_2$Cl$_2$, l = 100 mm).

III. Silylium Ion-Catalyzed Prins Cyclization Employing Various R$_3$Si–Nu (trialkyhydrosilanes, allylsilanes, and silyl azides) as Trapping Nucleophiles

1. General procedures:

Prins cyclization and trapping with R$_3$Si–Nu (non-silyl enol ether):

In a dry, N$_2$-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg, 1.00 eq.) and [Ph$_3$C][B(C$_6$F$_5$)$_4$] (trityl BArF$_{20}$, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et$_3$SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) and R$_3$Si–Nu (0.125 mmol, 2.50 eq.) were dissolved in 1.00 mL of CH$_2$Cl$_2$ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N$_2$ atmosphere via piercing of the septa with N$_2$ needles, and the vial containing the aldehyde and trityl BArF$_{20}$ was cooled to $-78$ °C in an acetone/CO$_2(s)$ bath. Using careful inert atmosphere technique, the room temperature solution in CH$_2$Cl$_2$ was...
syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. During the addition, the solution turned clear bright yellow in color, which persisted throughout the course of the reaction. The solution was stirred for an additional 1 h at –78 °C, quenched at the cryogenic temperature with 50 µL i-PrNH2 (resulting in rapid loss of color), and warmed to room temperature. The residue was repeatedly washed with CH2Cl2 and concentrated in vacuo (x3; to remove excess base), and then placed under high vacuum for ≥1 h to remove excess i-PrNH2 (residual base must be removed before the acid-catalyzed deprotection step; this can be facilitated by repetitive azeotroping with CH2Cl2).

**Acid-catalyzed silyl ether cleavage (deprotection):**

The crude residue was taken up in 2 mL of 1:1 CH2Cl2/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added and the reaction was stirred at 22 °C for 1-24 h (–OSiMe3 requires significantly less time (~1 h) compared to –OSiEt3 or larger (~overnight)). Note: for potentially sensitive products, less aggressive acidic resins can also afford deprotected product, including pyridinium p-toluene sulfonate polymer-bound resin (PPTS). The solution was then filtered by gravity through a plug of sand and cotton to remove the Dowex beads, rinsed with 2x1mL CH2Cl2, and concentrated in vacuo. Dimethylformamide (0.050 mmol, 3.9 µL) was added as an internal standard and the residue taken up in CDCl3 for 1H and 13C NMR analyses to determine conversion, product identity, NMR yield, and crude diastereomeric ratios (d.r.). After re-concentration in vacuo, the crude residue was purified by silica gel chromatography (mixtures of n-pentane:ethyl acetate), providing analytically pure heterocycles 6-9 for which isolated yields and post-purification diastereomeric ratios are reported.

**2. Preparation and characterization:**

**Preparation of pyrrolidine 5:**

In a dry, N2-filled glove box, aldehyde 3 (0.100 mmol, 48.4 mg, 1.00 eq.) and [Ph3C][B(C6F5)4] (trityl BArF20, 0.010 mmol, 9.2 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial,
Et₃SiH (0.250 mmol, 40 µL, 2.50 eq.) was dissolved in 2.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 10 minutes. The solution was stirred for an additional 1 h at −78 °C, quenched at the cryogenic temperature with 50 µL i-PrNH₂, and warmed to room temperature. The residue was repeatedly washed with CH₂Cl₂ and concentrated in vacuo (x3), and was then placed under high vacuum for ≥1 h to remove excess i-PrNH₂. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the reaction was stirred at 22 °C for 18 h. The solution was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (3:1 n-pentane:ethyl acetate; Rₛ = 0.3-0.4) to yield pyrrolidine 5 as a white, crystalline solid in 77% yield (37.5 mg average on a 0.1 mmol scale) and as a mixture of three partially separable diastereomers in 76:13:11 d.r. (major diastereomer A separates from co-eluting minor diastereomers B and C).

Data for 5

![Image of compound 5]

(2S)-2,4-dibenzyl-1-((4-bromophenyl)sulfonyl)pyrrolidin-3-ol (5). Major diastereomer (A):

**¹H NMR** (CDCl₃, 600 MHz): δ 7.70-7.64 (m, 4H), 7.32-7.16 (m, 8H), 6.99 (d, 2H, J = 6.8 Hz), 3.78 (q, 1H, J = 3.9 Hz), 3.74 (dt, 1H, J = 11.5, 4.1 Hz), 3.55-3.50 (m, 2H), 3.36 (t, 1H, J = 11.8 Hz), 3.09 (dd, 1H, J = 13.5, 11.4 Hz), 2.69 (dd, 1H, J = 13.8, 7.3 Hz), 2.56 (dd, 1H, J = 13.9, 7.9 Hz), 1.69-1.60 (m, 2H); **¹³C¹H NMR** (CDCl₃, 151 MHz): δ 139.3, 138.4, 137.0, 132.6, 129.0, 128.9, 128.9, 128.8, 128.5, 127.9, 126.8, 126.6, 72.2, 67.8, 52.3, 45.3, 36.0, 32.4; **¹³C NMR DEPT135** (CDCl₃, 151 MHz): δ 132.6 (CH), 129.0 (CH), 128.9 (CH), 128.9 (CH), 128.8 (CH), 128.5 (CH), 126.8 (CH), 72.2 (CH), 67.8 (CH), 52.3 (CH₂), 45.3 (CH), 36.0 (CH₂), 32.4 (CH₃); **IR** (v/cm⁻¹): 3529 (s, br, OH), 3085 (w), 3061 (w), 3027 (w), 3002 (w), 2925 (m),
2856 (w), 1603 (w), 1574 (m), 1495 (m), 1470 (w), 1454 (m), 1389 (m), 1347 (s), 1295 (w), 1275 (w), 1162 (s), 1126 (w), 1088 (m), 1068 (m), 1032 (w), 1009 (m); HRMS-(ESI⁺) [M+H]⁺ calcd for C₄₂H₂₅NO₅SBr⁺ 486.0739, found: 486.0738; [α]D²⁵ = +40.1° (c = 1.13, CH₂Cl₂, l = 100 mm). Minor diastereomers (B, C): ¹H NMR (CDCl₃, 600 MHz; aliphatic resonances only, distinguished by 1D TOCSY): δ 4.02 (ddd, 1H, J = 8.5, 6.8, 3.8 Hz, C), 3.79-3.75 (m, 1H, B), 3.63 (td, 1H, J = 6.8, 4.4 Hz, C), 3.51-3.47 (m, 1H, B), 3.46-3.42 (m, 1H, B), 3.44 (dd, 1H, J = 10.3, 7.0 Hz, C), 3.38 (dd, 1H, J = 11.8, 7.3 Hz, B), 3.18 (dd, 1H, J = 13.8, 4.4 Hz, C), 3.07 (dd, 1H, J = 13.8, 9.0 Hz, C), 2.99-2.91 (m, 2H, B), 2.94 (dd, 1H, J = 10.1, 7.1 Hz, C), 2.78 (dd, 1H, J = 13.8, 5.3 Hz, B), 2.62 (dd, 1H, J = 13.6, 5.2 Hz, C), 2.38 (dd, 1H, J = 13.9, 9.7 Hz, B), 2.34 (dd, 1H, J = 13.9, 8.6 Hz, C), 2.30-2.22 (m, 1H, C), 1.70 (ttd, 1H, J = 9.6, 7.4, 5.3 Hz, B), 1.53 (d, 1H, J = 4.3 Hz, C), 1.07 (d, 1H, J = 3.8 Hz, B); ¹³C¹H NMR (CDCl₃, 151 MHz): δ 138.9, 138.6, 138.5, 137.2, 137.0, 136.2, 132.6, 132.5, 129.8, 129.7, 129.1, 129.1, 129.0, 128.9, 128.9, 128.8, 128.7, 128.5, 128.1, 127.8, 127.1, 126.7, 126.7, 79.4 (B), 75.8 (C), 68.2 (B), 63.8 (C), 51.6 (B), 50.3 (C), 46.6 (B), 44.9 (C), 40.5 (B), 36.6 (C), 36.5 (C), 36.4 (B); IR (ν/cm⁻¹): 3516 (s, br, OH), 3086 (w), 3061 (w), 2927 (w), 2924 (m), 2855 (w), 1603 (w), 1574 (m), 1496 (m), 1471 (w), 1454 (m), 1389 (m), 1346 (s), 1275 (w), 1164 (s), 1088 (m), 1069 (m), 1031 (w), 1008 (m); HRMS-(ESI⁺) [M+H]⁺ calcd for C₄₂H₂₅NO₅SBr⁺ 486.0739, found: 486.0741.

Preparation of piperidine 6 with 1.20 eq. Et₃Si–H:

In a dry, N₂-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg, 1.00 eq.) and [Ph₃C][B(C₆F₅)₄] (trityl BArF₂₀, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et₃SiH (0.060 mmol, 9.6 μL, 1.20 eq.) was dissolved in 1.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂(ℓ) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring
solution over approximately 5 minutes. The solution was stirred for an additional 1 h at
−78 °C, quenched at the cryogenic temperature with 50 µL Et₃N, and warmed to room
temperature. The residue was repeatedly washed with CH₂Cl₂ and concentrated in vacuo (x3),
and was then placed under high vacuum for ≥1 h to remove excess Et₃N. The resulting residue
was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, approximately 10-20 beads of Dowex resin (50W-
X8) were added, and the reaction was stirred at 22 °C for 16 h. The solution was then filtered by
gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo.

Dimethylformamide (0.050 mmol, 3.9 µL) was added as an internal standard and the
residue taken up in CDCl₃ for ¹H and ¹³C NMR analyses to determine crude NMR yield and
diastereomeric ratios; the desired piperidine 6 was produced in 69% yield and in 51:29:20 d.r.

**Preparation of piperidine 6 with 2.50 eq. Et₃Si–H:**

![Reaction Scheme](image)

In a dry, N₂-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg, 1.00 eq.) and [Ph₃C][B(C₆F₅)₄]
(trityl BArF₂₀, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial
equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial,
Et₃SiH (0.125 mmol, 20.0 µL, 2.50 eq.) was dissolved in 1.00 mL of CH₂Cl₂ and the vial sealed
with a septum cap. Both vials were removed from the glove box and placed under a positive N₂
atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and
trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂ bath. The room temperature solution in
CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring
solution over approximately 5 minutes. The solution was stirred for an additional 1 h at −78 °C,
quenched at the cryogenic temperature with 50 µL Et₃N, and warmed to room temperature. The
residue was repeatedly washed with CH₂Cl₂ and concentrated in vacuo (x3), and was then placed
under high vacuum for ≥1 h to remove excess Et₃N. The resulting residue was taken up in 2 mL
of 1:1 CH₂Cl₂/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and
the reaction was stirred at 22 °C for 16 h. The solution was then filtered by gravity through a
plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. The crude
residue was purified by silica gel chromatography (3:1 *n*-pentane:ethyl acetate; *R*$_f$ = 0.2-0.3) to yield piperidine 6 as a white, crystalline solid in 92% yield (22.3 mg average per reaction over two 0.05 mmol scale trials) and as a mixture of three inseparable diastereomers in 60:21:19 d.r. (partial separation of minor diastereomer C and application of 1D TOCSY experiments allowed for full characterization of diastereomers).

**Data for 6**

![Chemical Structure](image)

(2S)-2-benzyl-1-((4-bromophenyl)sulfonyl)-5-phenylpiperidin-3-ol (6). **Major diastereomer A:** $^1$H NMR (CDCl$_3$, 600 MHz): $δ$ 7.38-7.32 (m, 4H), 7.30-7.25 (m, 4H), 7.17 (t, 2H, $J$ = 8.3 Hz), 7.07 (d, 2H, $J$ = 7.1 Hz), 6.99 (d, 2H, $J$ = 8.6 Hz), 4.54 (dq, 1H, $J$ = 11.6, 4.0 Hz), 4.26 (dt, 1H, $J$ = 11.8, 4.9 Hz), 3.63 (dd, 1H, $J$ = 14.1, 4.4 Hz), 3.19 (dd, 1H, $J$ = 14.3, 3.7 Hz), 3.11 (ddt, 1H, $J$ = 12.6, 8.9, 4.6 Hz), 3.00 (dd, 1H, $J$ = 14.1, 12.0 Hz), 2.82 (dd, 1H, $J$ = 14.4, 11.6 Hz), 2.25 (s, br, 1H), 2.13 (dt, 1H, $J$ = 12.9, 4.2 Hz), 2.06 (dd, 1H, $J$ = 12.2, 12.2 Hz); $^{13}$C($^1$H) NMR (CDCl$_3$, 151 MHz): $δ$ 141.0, 139.2, 138.5, 132.0, 129.3, 128.9, 128.8, 128.6, 127.4, 127.2, 127.1, 126.5, 69.4, 59.1, 45.6, 42.1, 34.4, 29.4; **Minor diastereomer B:** $^1$H NMR (CDCl$_3$, 600 MHz): $δ$ 7.44 (d, 2H, $J$ = 8.6 Hz), 7.34 (d, 2H, $J$ = 9.1 Hz), 7.30-7.21 (m, 8H), 7.13 (dd, 2H, $J$ = 6.6, 2.9 Hz), 4.42 (t, 1H, $J$ = 8.0 Hz), 4.02-3.97 (m, 1H), 3.74 (dd, 1H, $J$ = 13.9, 4.4 Hz), 3.35-3.24 (m, 1H), 3.11 (t, 1H, $J$ = 13.1 Hz), 2.89 (d, 2H, $J$ = 7.9 Hz), 2.48 (s, br, 1H), 2.13 (dt, 1H, $J$ = 14.6, 5.8 Hz), 2.09-2.02 (m, 1H); $^{13}$C($^1$H) NMR (CDCl$_3$, 151 MHz): $δ$ 141.8, 139.3, 137.4, 132.2, 129.1, 129.0, 128.9, 127.3, 127.3, 127.0, 126.8, 66.2, 60.5, 46.3, 35.6, 35.6, 33.0; **Minor diastereomer C:** $^1$H NMR (CDCl$_3$, 600 MHz): $δ$ 7.53-7.48 (m, 4H), 7.32-7.26 (m, 4H), 7.26-7.21 (m, 4H), 7.17 (d, 2H, $J$ = 6.7 Hz), 4.02 (dd, 1H, $J$ = 13.4, 4.3 Hz), 3.89 (dt, 1H, $J$ = 6.4, 3.3 Hz), 3.76 (ddd, 1H, $J$ = 9.7, 5.0, 2.9 Hz), 3.36 (dd, 1H, $J$ = 12.8, 7.8 Hz), 3.31 (tt, 1H, $J$ = 8.4, 4.3 Hz), 3.26 (dd, 1H, $J$ = 13.7, 9.7 Hz), 3.01 (dd, 1H, $J$ = 13.7, 5.1 Hz), 2.18-2.13 (m, 1H), 1.87 (ddd, 1H, $J$ = 13.9, 8.9, 3.4 Hz); $^{13}$C($^1$H) NMR (CDCl$_3$, 151 MHz): $δ$ 141.7, 139.9, 138.2, 132.4, 129.4, 128.8, 128.6, 127.6, 127.4, 127.0, 126.8, 65.1, 63.6, 51.8, 37.5, 36.0, 34.0; **IR (v/cm$^{-1}$):** 3512 (s, br, OH), 3087 (w), 3061 (w), 3028 (m), 3004 (w), 2934 (s), 2871 (m), 1603...
Preparation of piperidine 7 with 1.10 eq. allyltrimethylsilane (Me₃Si–allyl):

In a dry, N₂-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg, 1.00 eq.) and [Ph₃C][B(C₆F₅)₄] (trityl BArF₂₀, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et₃SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) and allyltrimethylsilane (0.0550 mmol, 8.7 µL, 1.10 eq.) were dissolved in 1.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The solution was stirred for an additional 15 minutes at −78 °C, after which time the reaction was transferred to a −30 °C cryobath and stirred overnight for 20 h (this was necessary for increased yield and reproducibility). The reaction was then quenched at the cryogenic temperature with 50 µL i-PrNH₂ and warmed to room temperature. The residue was repeatedly washed with CH₂Cl₂ and concentrated in vacuo (x3), and was then placed under high vacuum for ≥1 h to remove excess i-PrNH₂. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, a spatula tip of PPTS resin was added, and the reaction was stirred at 22 °C for 24 h. The solution was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. Dimethylformamide (0.050 mmol, 3.9 µL) was added as an internal standard and the residue taken up in CDCl₃ for ¹H and ¹³C NMR analyses to determine crude NMR yield and diastereomeric ratios (d.r.); the desired allyl-piperidine 7 was produced in 57% yield and in 58:42 d.r.
Preparation of piperidine 7 with \textbf{2.50 eq. allyltrimethylsilane (Me}_3\text{Si–allyl)}:

\begin{align*}
\text{Br} & \quad \text{Ph} \\
\text{O} & \quad \text{N} \\
\text{Ph} & \quad \text{Br} \\
\text{O} & \quad \text{N}
\end{align*}

In a dry, N$_2$-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg, 1.00 eq.) and [Ph$_3$C][B(C$_6$F$_5$)$_4$] (trityl BArF$_{20}$, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et$_3$SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) and allyltrimethylsilane (0.125 mmol, 19.9 µL, 2.50 eq.) were dissolved in 1.00 mL of CH$_2$Cl$_2$ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N$_2$ atmosphere \textit{via} piercing of the septa with N$_2$ needles, and the vial containing the aldehyde and trityl BArF$_{20}$ was cooled to –78 °C in an acetone/CO$_2$(s) bath. The room temperature solution in CH$_2$Cl$_2$ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The solution was stirred for an additional 15 minutes at –78 °C, after which time the reaction was transferred to a –30 °C cryobath and stirred overnight for 20 h (this was necessary for increased yield and reproducibility). The reaction was then quenched at the cryogenic temperature with 50 µL i-PrNH$_2$ and warmed to room temperature. The residue was repeatedly washed with CH$_2$Cl$_2$ and concentrated \textit{in vacuo} (x3), and was then placed under high vacuum for \geq1 h to remove excess i-PrNH$_2$. The resulting residue was taken up in 2 mL of 1:1 CH$_2$Cl$_2$/MeOH, a spatula tip of PPTS resin was added, and the reaction was stirred at 22 °C for 24 h. The solution was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH$_2$Cl$_2$, and concentrated \textit{in vacuo}. The crude residue was purified by silica gel chromatography (4:1 n-pentane:ethyl acetate; $R_f = 0.3$) to yield allyl-piperidine 7 as a clear, colorless oil in 84% yield (22.1 mg average per reaction over two 0.05 mmol scale trials) and as a mixture of two inseparable diastereomers in 66:34 d.r..
Data for 7

(2S,3S)-5-allyl-2-benzyl-1-((4-bromophenyl)sulfonyl)-5-phenylpiperidin-3-ol (7). \(^1\)H NMR (CDCl\(_3\), 600 MHz; non-aromatic resonances delineated as major diastereomer A and minor diastereomer B): \(\delta\) 7.41 (t, 1H, \(J = 7.7\) Hz), 7.35 (d, 1H, \(J = 7.2\) Hz), 7.33-7.20 (m, 20H), 7.22-7.16 (m, 1H), 7.15-7.12 (m, 1H), 7.10 (d, 2H, \(J = 8.6\) Hz), 7.01 (t, 1H, \(J = 7.6\) Hz), 6.85 (d, 1H, \(J = 7.2\) Hz), 5.37-5.27 (m, 2H, A, B), 5.03-4.91 (m, 4H, 2A,2B), 4.43-4.34 (m, 3H, A,2B), 4.17 (d, 1H, \(J = 13.9\) Hz, B), 4.08 (q, 1H, \(J = 5.9\) Hz, A), 3.94 (ddd, 1H, \(J = 14.5, 3.8\) Hz, B), 2.85 (dd, 1H, \(J = 14.2, 5.1\) Hz, A), 2.81 (dd, 1H, \(J = 14.5, 9.2\) Hz, B), 2.58-2.52 (m, 2H, 2A, 2B), 2.46 (dt, 1H, \(J = 13.9, 2.9\) Hz, A), 2.35 (dd, 1H, \(J = 13.6, 6.8\) Hz, A), 2.30-2.25 (m, 2H, A,B), 1.94 (t, 1H, \(J = 12.2\) Hz, B), 1.80 (dd, 1H, \(J = 14.0, 12.1\) Hz, A), 1.46 (s, br, 2H, A,B); \(^13\)C\{\(^1\)H\} NMR (CDCl\(_3\), 151 MHz; aliphatic resonances delineated as major diastereomer A and minor diastereomer B): \(\delta\) 144.5, 141.8, 139.7, 139.3, 138.9, 138.4, 133.6, 132.6, 132.1, 132.0, 129.4, 129.1, 128.8, 128.7, 128.6, 128.6, 128.1, 127.3, 127.1, 127.0, 127.0, 126.6, 126.5, 126.3, 125.8, 118.8, 118.4, 66.7 (A), 66.1 (B), 59.6 (B), 59.2 (A), 48.7 (B), 48.6 (A), 48.3 (A), 43.5 (A), 42.7 (B), 41.5 (B), 36.2 (A), 34.2 (B), 31.8 (A), 29.2 (B); \(^13\)C NMR DEPT135 (CDCl\(_3\), 151 MHz): \(\delta\) 133.6 (CH), 132.6 (CH), 132.1 (CH), 132.0 (CH), 129.4 (CH), 129.1 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.6 (CH), 128.1 (CH), 127.1 (CH), 127.0 (CH), 126.6 (CH), 126.5 (CH), 126.3 (CH), 125.8 (CH), 118.8 (CH\(_2\)), 118.4 (CH\(_2\)), 66.7 (CH), 66.1 (CH), 59.6 (CH), 59.2 (CH), 48.7 (CH\(_2\)), 48.6 (CH\(_2\)), 48.3 (CH\(_2\)), 43.5 (A), 42.7 (B), 41.5 (B), 36.2 (CH\(_2\)), 34.2 (CH\(_2\)), 31.8 (CH\(_2\)), 29.2 (CH\(_2\)); IR (\(\nu/cm^-1\)): 3519 (s, br, OH), 3086 (w), 3061 (w), 3027 (w), 3005 (w), 2926 (s), 2870 (w), 1638 (w), 1602 (w), 1576 (m), 1497 (m), 1470 (m), 1454 (m), 1446 (m), 1416 (w), 1389 (m), 1334 (s), 1276 (w), 1266 (w), 1158 (s), 1089 (m), 1069 (m), 1029 (w); HRMS-(ESI\(^+\)) [M+H]\(^+\) calecd for C\(_{27}\)H\(_{29}\)NO\(_3\)SBr\(^+\) 526.1052, found: 526.1055.
Preparation of piperidine 8 with 1.10 eq. Me₃Si–N₃:

In a dry, N₂-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg, 1.00 eq.) and [Ph₃C][B(C₆F₅)₄] (trityl BArF₂₀, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et₃SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) and Me₃Si–N₃ (0.0550 mmol, 7.2 µL, 1.10 eq.) were dissolved in 1.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to –78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The solution was stirred for an additional 2 h at –78 °C, after which time the reaction was quenched at the cryogenic temperature with 50 µL i-PrNH₂ and warmed to room temperature. The residue was repeatedly washed with CH₂Cl₂ and concentrated in vacuo (x3), and was then placed under high vacuum for ≥1 h to remove excess i-PrNH₂. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, a spatula tip of PPTS resin was added, and the reaction was stirred at 22 °C for 16 h. The solution was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (3:1 n-pentane:ethyl acetate; Rₜ = 0.3-0.4) to yield azido-piperidine 8 as a white, crystalline solid in 78% yield (41.0 mg average per reaction over two 0.05 mmol scale trials) and as a mixture of two separable diastereomers in 79:21 d.r..

Preparation of piperidine 8 with 2.50 eq. Me₃Si–N₃:

In a dry, N₂-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg, 1.00 eq.) and [Ph₃C][B(C₆F₅)₄] (trityl BArF₂₀, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et₃SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) and Me₃Si–N₃ (0.0550 mmol, 7.2 µL, 1.10 eq.) were dissolved in 1.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to –78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The solution was stirred for an additional 2 h at –78 °C, after which time the reaction was quenched at the cryogenic temperature with 50 µL i-PrNH₂ and warmed to room temperature. The residue was repeatedly washed with CH₂Cl₂ and concentrated in vacuo (x3), and was then placed under high vacuum for ≥1 h to remove excess i-PrNH₂. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, a spatula tip of PPTS resin was added, and the reaction was stirred at 22 °C for 16 h. The solution was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (3:1 n-pentane:ethyl acetate; Rₜ = 0.3-0.4) to yield azido-piperidine 8 as a white, crystalline solid in 78% yield (41.0 mg average per reaction over two 0.05 mmol scale trials) and as a mixture of two separable diastereomers in 79:21 d.r..
(trityl BArF$_{20}$, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et$_3$SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) and Me$_3$Si–N$_3$ (0.125 mmol, 16.4 µL, 2.50 eq.) were dissolved in 1.00 mL of CH$_2$Cl$_2$ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N$_2$ atmosphere via piercing of the septa with N$_2$ needles, and the vial containing the aldehyde and trityl BArF$_{20}$ was cooled to −78 °C in an acetone/CO$_2$(s) bath. The room temperature solution in CH$_2$Cl$_2$ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The solution was stirred for an additional 2 h at −78 °C, after which time the reaction was quenched at the cryogenic temperature with 50 µL i-PrNH$_2$ and warmed to room temperature. The residue was repeatedly washed with CH$_2$Cl$_2$ and concentrated in vacuo (x3), and was then placed under high vacuum for ≥1 h to remove excess i-PrNH$_2$. The resulting residue was taken up in 2 mL of 1:1 CH$_2$Cl$_2$/MeOH, a spatula tip of PPTS resin was added, and the reaction was stirred at 22 °C for 16 h. The solution was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH$_2$Cl$_2$, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (3:1 n-pentane:ethyl acetate; R$_f$ = 0.3-0.4) to yield azido-piperidine 8 as a white, crystalline solid in 85% yield (45.0 mg average per reaction over two 0.05 mmol scale trials) and as a mixture of two separable diastereomers in 62:38 d.r..

**Data for 8**

(2S,3S)-5-azido-2-benzyl-1-((4-bromophenyl)sulfonyl)-5-phenylpiperidin-3-ol (8). **Major diastereomer A:** $^1$H NMR (CDCl$_3$, 600 MHz): δ 7.52 (d, 2H, $J$ = 7.1 Hz), 7.48 (t, 2H, $J$ = 8.1 Hz), 7.42 (t, 1H, $J$ = 6.3 Hz), 7.29 (s, 4H), 7.14 (t, 1H, $J$ = 7.1 Hz), 7.05 (t, 2H, $J$ = 7.6 Hz), 6.91 (d, 2H, $J$ = 7.2 Hz), 4.50 (dt, 1H, $J$ = 11.3, 4.8 Hz), 4.28-4.26 (m, 1H), 4.24 (dd, 1H, $J$ = 14.0, 2.0 Hz), 3.33 (d, 1H, $J$ = 14.6 Hz), 3.09 (dd, 1H, $J$ = 14.4, 3.9 Hz), 2.65 (dd, 1H, $J$ = 14.4, 10.3 Hz), 2.39 (ddd, 1H, $J$ = 13.7, 4.3, 2.3 Hz), 2.34 (s, br, 1H), 2.26 (dd, 1H, $J$ = 13.7, 11.7 Hz); $^{13}$C($^1$H) NMR (CDCl$_3$, 151 MHz): δ 139.2, 139.1, 137.8, 132.0, 129.4, 129.1, 129.1, 128.6, 128.5, 127.3,
126.4, 125.7, 66.3, 65.6, 59.3, 47.5, 36.2, 29.4; $^{13}$C NMR DEPT135 (CDCl$_3$, 151 MHz): $\delta$ 132.0 (CH), 129.4 (CH), 129.1 (CH), 129.1 (CH), 128.6 (CH), 128.5 (CH), 126.4 (CH), 125.7 (CH), 65.6 (CH), 59.3 (CH), 47.5 (CH$_2$), 36.2 (CH$_2$), 29.4 (CH$_2$); IR (v/cm$^{-1}$): 3514 (s, br, OH), 3078 (w), 3061 (w), 3028 (w), 3004 (w), 2931 (s), 2853 (w), 2105 (s, N$_3$), 1602 (w), 1576 (m), 1496 (m), 1471 (m), 1448 (m), 1389 (m), 1332 (s), 1304 (m), 1264 (m), 1248 (m), 1200 (w), 1154 (s), 1103 (m), 1088 (m), 1069 (m), 1030 (w), 1011 (m); HRMS-(ESI$^+$) [M+Na$^+$] calcd for C$_{24}$H$_{23}$N$_4$O$_3$NaSBr$^+$ 549.0572, found: 549.0579; [α]$_D^{24}$ = –53.9° (c = 1.61, CH$_2$Cl$_2$, l = 100 mm).

Minor diastereomer B: $^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ 7.70-7.48 (m, 2H), 7.25-7.19 (m, 5H), 7.15-7.12 (m, 2H), 4.26 (d, 1H, J = 13.8 Hz), 4.01-3.91 (m, 2H), 3.55 (d, 1H, J = 13.5 Hz), 3.20 (dd, 1H, J = 14.0, 7.3 Hz), 2.87 (dd, 1H, J = 14.0, 5.6 Hz), 2.58 (d, 1H, J = 12.7 Hz), 2.23 (dd, 1H, J = 13.8, 10.1 Hz), 1.99 (s, br, 1H); $^{13}$C $^1$H NMR (CDCl$_3$, 151 MHz): $\delta$ 139.0, 138.3, 137.2, 132.3, 129.3, 129.2, 129.1, 128.8, 128.5, 127.7, 127.0, 126.7, 66.3, 64.5, 60.2, 49.5, 37.3, 31.8; $^{13}$C NMR DEPT135 (CDCl$_3$, 151 MHz): $\delta$ 132.3 (CH), 129.3 (CH), 129.2 (CH), 129.1 (CH), 128.8 (CH), 128.5 (CH), 127.0 (CH), 126.7 (CH), 66.3 (CH), 60.2 (CH), 49.5 (CH$_2$), 37.3 (CH$_2$), 31.8 (CH$_2$); IR (v/cm$^{-1}$): 3517 (s, br, OH), 3087 (w), 3061 (w), 2924 (s), 2851 (m), 2099 (s, N$_3$), 1603 (w), 1575 (m), 1496 (m), 1470 (m), 1454 (m), 1389 (m), 1335 (s), 1312 (m), 1264 (m), 1244 (m), 1160 (s), 1101 (m), 1087 (m), 1069 (m), 1030 (w), 1011 (m); HRMS-(ESI$^+$) [M+Na$^+$] calcd for C$_{24}$H$_{23}$N$_4$O$_3$NaSBr$^+$ 549.0572, found: 549.0578; [α]$_D^{25}$ = –12.1° (c = 0.440, CH$_2$Cl$_2$, l = 100 mm).

**Preparation of piperidine 9:**

In a dry, N$_2$-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg, 1.00 eq.) and [Ph$_3$C][B(C$_6$F$_5$)$_4$] (trityl BArF$_{20}$, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et$_3$SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) was dissolved in 1.00 mL of CH$_2$Cl$_2$ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N$_2$ atmosphere via piercing of the septa with N$_2$ needles. Freshly distilled Me$_3$Si–Cl (0.125 mmol,
15.9 µL, 2.50 eq.) was syringed from a Schlenk flask into the vial containing the solution of Et₃SiH in CH₂Cl₂. The vial containing the aldehyde and trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The stirring solution was allowed to gradually warm from −78 °C to 22 °C in the dewar over the course of 8 h, after which time the reaction was quenched at room temperature with 50 µL i-PrNH₂ and warmed to room temperature. The residue was repeatedly washed with CH₂Cl₂ and concentrated in vacuo (x3), and was then placed under high vacuum for ≥1 h to remove excess i-PrNH₂. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, a spatula tip of PPTS resin was added, and the reaction was stirred at 22 °C for 16 h. The solution was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. Dimethylformamide (0.050 mmol, 3.9 µL) was added as an internal standard and the residue taken up in CDCl₃ for ¹H and ¹³C NMR analyses to determine conversion, product identity, crude NMR yield, and diastereomeric ratios (d.r.): The starting material was completely consumed; <5% of the desired chloride-trapped piperidine 9 was formed. Elimination was instead observed and tetrahydropiperidine diastereomers 22 and 23 were obtained in 54% NMR yield and in 78:22 cis:trans d.r. (vide infra).

IV. Silylium Ion-Catalyzed Prins Cyclization Employing Silyl Enol Ethers as Trapping Nucleophiles

1. General procedures:

Prins cyclization and trapping with silyl enol ether:
In a dry, N₂-filled glove box, aldehyde (0.0500 mmol, 1.00 eq.) and [Ph₃C][B(C₆F₅)₄] (trityl BArF₂₀, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et₃SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) and silyl enol ether (0.125 mmol, 2.50 eq.) were dissolved in 1.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the
glove box and placed under a positive N\textsubscript{2} atmosphere via piercing of the septa with N\textsubscript{2} needles, and the vial containing the aldehyde and trityl BArF\textsubscript{20} was cooled to –78 °C in an acetone/CO\textsubscript{2}(s) bath. Using careful inert atmosphere technique, the room temperature solution in CH\textsubscript{2}Cl\textsubscript{2} was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. During the addition, the reaction turned clear bright yellow in color, which persisted throughout the course of the reaction. The solution was stirred for an additional 1 h at –78 °C, quenched at the cryogenic temperature with 50 µL i-PrNH\textsubscript{2} (resulting in rapid loss of color), and warmed to room temperature. The residue was repeatedly washed with CH\textsubscript{2}Cl\textsubscript{2} and concentrated \textit{in vacuo} (x3; to remove excess base), and was then placed under high vacuum for ≥1 h to remove excess i-PrNH\textsubscript{2} (when issues of reproducibility arise, they are often the result of incomplete removal of residual base; this can be rectified by repetitive washing with CH\textsubscript{2}Cl\textsubscript{2}).

\textit{Acid-catalyzed annulation and elimination:}

The crude residue was taken up in 2 mL of 1:1 CH\textsubscript{2}Cl\textsubscript{2}/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the reaction was stirred at 22 °C for 1 h. The solution was then filtered by gravity through a plug of sand and cotton to remove the Dowex beads, rinsed with 2x1mL CH\textsubscript{2}Cl\textsubscript{2}, and concentrated \textit{in vacuo}. Dimethylformamide (0.050 mmol, 3.9 µL) was added as an internal standard and the residue taken up in CDCl\textsubscript{3} for \textsuperscript{1}H and \textsuperscript{13}C NMR analyses to determine conversion, product identity, NMR yield, and crude diastereomeric ratios (d.r.). After re-concentration \textit{in vacuo}, the crude residue was purified by silica gel chromatography (mixtures of n-pentane:ethyl acetate), providing analytically pure heterocycle for which isolated yields and post-purification diastereomeric ratios are reported.

\textit{2. Preparation and characterization:}

\textbf{Preparation of piperidine 13:}

In a dry, N\textsubscript{2}-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg, 1.00 eq.) and [Ph\textsubscript{3}C][B(C\textsubscript{6}F\textsubscript{5})\textsubscript{4}] (trityl BArF\textsubscript{20}, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial,
Et₃SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) and cyclopentanone-derived silyl enol ether (0.0550 mmol, 9.8 µL, 1.10 eq.) were dissolved in 1.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The solution was stirred and allowed to slowly warm to room temperature in the dewar overnight for 16 h. The reaction was then quenched with 50 µL Et₃N. The solution was diluted with CH₂Cl₂, concentrated in vacuo (x2), and then placed under high vacuum for ≥1 h to remove excess Et₃N. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the mixture was stirred at 22 °C for 16 h. The mixture was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. Dimethylformamide (0.050 mmol, 3.9 µL) was added as an internal standard and the residue taken up in CDCl₃ for ¹H and ¹³C NMR analyses to determine conversion, product identity, NMR yield, and crude diastereomeric ratios (d.r.). Despite full consumption of starting materials, only trace product is visible by ¹³C.

Data for 13

$$\text{(2S,3S,6R)-3-benzyl-4-((4-bromophenyl)sulfonyl)-6-phenyl-2,3,4,5,6,7,8,9-octahydro-2,6-methanocyclopenta[g][1,4]oxazocine (13).}$$ ¹³C{¹H} NMR (CDCl₃, 151 MHz): δ 109.6 (diagnostic vinyl ether peak); HRMS-(ESI⁺) [M+H]⁺ calcd for C₂₉H₂₉NO₃SBr⁺ 550.1052, found: 550.1054.
Preparation of piperidine 14 with 1.10 eq. silyl enol ether:

In a dry, N₂-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg, 1.00 eq.) and [Ph₃C][B(C₆F₅)₄] (trityl BArF₂₀, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et₃SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) and cyclohexanone-derived silyl enol ether (0.0550 mmol, 10.6 µL, 1.10 eq.) were dissolved in 1.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The solution was stirred for an additional 1 h at −78 °C, quenched at the cryogenic temperature with 50 µL Et₃N, and warmed to room temperature. The solution was diluted with CH₂Cl₂, concentrated in vacuo, and then placed under high vacuum for ≥1 h to remove excess Et₃N. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the mixture was stirred at 22 °C for 1 h. The mixture was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (5:1 n-pentane:ethyl acetate; Rᵣ = 0.6) to yield the tricyclic piperidine product 14 as a white, crystalline solid in 52% yield (14.7 mg).

Preparation of piperidine 14 with 2.50 eq. silyl enol ether:

In a dry, N₂-filled glove box, aldehyde 4 (0.100 mmol, 48.4 mg, 1.00 eq.) and [Ph₃C][B(C₆F₅)₄] (trityl BArF₂₀, 0.010 mmol, 9.2 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial
equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et₃SiH (0.012 mmol, 1.9 µL, 0.12 eq.) and cyclohexanone-derived silyl enol ether (0.250 mmol, 48 µL, 2.50 eq.) were dissolved in 2.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 10 minutes. The solution was stirred for an additional 2 h at −78 °C, quenched at the cryogenic temperature with 50 µL Et₃N, and warmed to room temperature. The residue was repeatedly washed with CH₂Cl₂ and concentrated in vacuo (x3), and was then placed under high vacuum for ≥1 h to remove excess Et₃N. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the mixture was stirred at 22 °C for 3 h. The mixture was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (5:1 n-pentane:ethyl acetate; Rₜ = 0.6) to yield the tricyclic piperidine product 14 as a white, crystalline solid in 64% yield (36.4 mg average per reaction over two 0.1 mmol scale trials).

**Data for 14**

(2R,3S,6S)-3-benzyl-4-((4-bromophenyl)sulfonyl)-6-phenyl-3,4,5,6,7,8,9,10-octahydro-2H-2,6-methanobenz[ḡ][1,4]oxazocine (14). ¹H NMR (CDCl₃, 600 MHz): δ 7.77 (d, 2H, J = 8.6 Hz), 7.67 (d, 2H, J = 8.6 Hz), 7.35 (t, 2H, J = 7.9 Hz), 7.30-7.27 (m, 3H), 7.25-7.24 (m, 2H), 7.21 (t, 1H, J = 7.4 Hz), 7.18 (d, 2H, J = 6.6 Hz), 4.57 (dd, 1H, J = 11.6, 2.7 Hz), 3.89 (dt, 1H, J = 4.0, 1.9 Hz), 3.41 (dd, 1H, J = 12.7, 3.6 Hz), 3.32 (d, 1H, J = 11.5 Hz), 3.27 (ddd, 1H, J = 11.6, 3.6, 1.8 Hz), 2.83 (t, 1H, J = 11.6 Hz), 2.36 (dt, 1H, J = 13.2, 4.2 Hz), 2.32-2.25 (m, 1H), 2.23-2.18 (m, 1H), 1.87-1.82 (m, 1H), 1.67-1.56 (m, 4H), 1.55-1.45 (m, 2H); ¹³C{¹H} NMR (CDCl₃, 151 MHz): δ 150.1, 143.3, 141.9, 138.0, 132.4, 129.8, 128.7, 128.6, 128.4, 127.5, 126.8, 126.7,
126.4, 106.3, 67.3, 65.4, 54.1, 39.1, 39.0, 35.8, 27.8, 24.7, 23.3, 23.1; $^{13}$C NMR DEPT135 (CDCl$_3$, 151 MHz): $\delta$ 132.4 (CH), 129.8 (CH), 128.7 (CH), 128.6 (CH), 128.4 (CH), 126.8 (CH), 126.7 (CH), 126.4 (CH), 67.3 (CH), 65.4 (CH), 54.1 (CH$_2$), 39.0 (CH$_2$), 35.8 (CH$_2$), 27.8 (CH$_2$), 24.7 (CH$_2$), 23.3 (CH$_2$), 23.1 (CH$_2$); IR (v/cm$^{-1}$): 3086 (w), 3060 (w), 3027 (w), 2931 (s), 2885 (m), 2857 (m), 2840 (m), 1679 (m), 1602 (w), 1575 (m), 1496 (m), 1471 (w), 1452 (w), 1446 (m), 1389 (w), 1373 (m), 1331 (s), 1266 (w), 1236 (m), 1215 (w), 1166 (s), 1153 (s), 1138 (m), 1126 (m), 1089 (m), 1067 (m), 1023 (w), 1009 (m); HRMS-(ESI$^+$) [M+H]$^+$ calcd for C$_{30}$H$_{31}$NO$_3$SBr$^+$ 564.1208, found: 564.1207; $[\alpha]_D^{26} = +28.9^\circ$ (c = 3.640, CH$_2$Cl$_2$, l = 100 mm).

Preparation of piperidine 15:

In a dry, N$_2$-filled glove box, aldehyde 4 (0.100 mmol, 48.4 mg, 1.00 eq.) and [Ph$_3$C][B(C$_6$F$_5$)$_4$] (trityl BArF$_{20}$, 0.010 mmol, 9.2 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et$_3$SiH (0.012 mmol, 1.9 $\mu$L, 0.12 eq.) and cycloheptanone-derived silyl enol ether (0.250 mmol, 53 $\mu$L, 2.50 eq.) were dissolved in 2.00 mL of CH$_2$Cl$_2$ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N$_2$ atmosphere via piercing of the septa with N$_2$ needles, and the vial containing the aldehyde and trityl BArF$_{20}$ was cooled to $-78^\circ$C in an acetone/CO$_2$(s) bath. The room temperature solution in CH$_2$Cl$_2$ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 10 minutes. The solution was stirred for an additional 2 h at $-78^\circ$C, quenched at the cryogenic temperature with 50 $\mu$L Et$_3$N, and warmed to room temperature. The residue was repeatedly washed with CH$_2$Cl$_2$ and concentrated in vacuo (x3), and was then placed under high vacuum for $\geq$1 h to remove excess Et$_3$N. The resulting residue was taken up in 2 mL of 1:1 CH$_2$Cl$_2$/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the mixture was stirred at 22 $^\circ$C for 3 h. The mixture was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH$_2$Cl$_2$, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (5:1 n-pentane:ethyl acetate; R$_f$ = 0.65) to yield the
tricyclic piperidine product 15 as a white, crystalline solid in 22% yield (12.9 mg average per reaction over two 0.1 mmol scale trials).

**Data for 15**

![Chemical Structure](https://example.com/structure.png)

(2R,3S,6S)-3-benzyl-4-((4-bromophenyl)sulfonyl)-6-phenyl-2,3,4,5,6,7,8,9,10,11-decahydro-2,6-methanocyclohepta[g][1,4]oxazocine (15). \( ^1\)H NMR (CDCl\(_3\), 600 MHz): \( \delta \) 7.80 (d, 2H, \( J = 8.6 \) Hz), 7.73 (d, 2H, \( J = 8.6 \) Hz), 7.34 (t, 2H, \( J = 8.7 \) Hz), 7.29-7.19 (m, 6H), 7.15 (d, 2H, \( J = 6.9 \) Hz), 4.44 (dd, 1H, \( J = 11.2, 2.7 \) Hz), 3.80 (dt, 1H, \( J = 4.1, 2.0 \) Hz), 3.54 (dd, 1H, \( J = 12.8, 3.6 \) Hz), 3.28 (d, 1H, \( J = 11.1 \) Hz), 3.06 (ddd, 1H, \( J = 11.6, 3.6, 1.9 \) Hz), 2.94 (t, 1H, \( J = 12.2 \) Hz), 2.44 (t, 2H, \( J = 5.4 \) Hz), 2.21 (dt, 1H, \( J = 13.4, 4.0 \) Hz), 1.79-1.62 (m, 6H), 1.48 (dd, 1H, \( J = 13.3, 2.2 \) Hz), 1.48-1.43 (m, 1H), 1.38-1.30 (m, 1H); \( ^{13}\)C\( ^1\)H NMR (CDCl\(_3\), 151 MHz): 155.5, 144.2, 140.0, 138.0, 132.6, 129.7, 128.7, 128.7, 128.6, 127.7, 126.8, 126.7, 126.2, 110.1, 67.3, 64.8, 55.0, 40.8, 39.1, 36.2, 33.9, 32.2, 28.8, 27.2, 25.8; \( ^{13}\)C NMR DEPT135 (CDCl\(_3\), 151 MHz): \( \delta \) 132.6, 129.7, 128.7, 128.7, 128.6, 126.7, 126.2, 126.3 (CH), 64.8 (CH), 55.0 (CH\(_2\)), 39.1 (CH\(_2\)), 36.2 (CH\(_2\)), 33.9 (CH\(_2\)), 32.2 (CH\(_2\)), 28.8 (CH\(_2\)), 27.2 (CH\(_2\)), 25.8 (CH\(_2\)); \( \text{IR} \) (v/cm\(^{-1}\)): 3086 (w), 3060 (w), 3027 (w), 2924 (s), 2849 (m), 1669 (m), 1602 (w), 1575 (m), 1496 (m), 1471 (w), 1445 (m), 1389 (w), 1373 (w), 1337 (s), 1265 (w), 1237 (m), 1168 (s), 1125 (m), 1090 (m), 1068 (m), 1030 (w), 1008 (m); \( \text{HRMS} \) - (ESI\(^+\)) [M+H]\(^+\) calcd for C\(_{31}\)H\(_{33}\)NO\(_3\)SBr\(^+\) 578.1365, found: 578.1382; \( [\alpha]_D^{25} = +32.9^\circ \) (c = 0.405, CH\(_2\)Cl\(_2\), l = 100 mm).

**Preparation of piperidine 16:**

In a dry, N\(_2\)-filled glove box, aldehyde 10 (0.100 mmol, 40.8 mg, 1.00 eq.) and [Ph\(_3\)C][B(C\(_6\)F\(_5\))\(_4\)] (trityl BArF\(_{20}\), 0.010 mmol, 9.2 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial
equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et₃SiH (0.012 mmol, 1.9 µL, 0.12 eq.) and cyclohexanone-derived silyl enol ether (0.250 mmol, 48 µL, 2.50 eq.) were dissolved in 2.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 10 minutes. The solution was stirred for an additional 2 h at −78 °C, quenched at the cryogenic temperature with 50 µL Et₃N, and warmed to room temperature. The residue was repeatedly washed with CH₂Cl₂ and concentrated in vacuo (x3), and was then placed under high vacuum for ≥1 h to remove excess Et₃N. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the mixture was stirred at 22 °C for 3 h. The mixture was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (5:1 n-pentane:ethyl acetate; R_f = 0.5) to yield the tricyclic piperidine product 16 as a white, crystalline solid in 38% yield (18.7 mg average per reaction over two 0.1 mmol scale trials).

**Data for 16**

(2R,3S,6S)-4-((4-bromophenyl)sulfonyl)-3-methyl-6-phenyl-3,4,5,6,7,8,9,10-octahydro-2H-2,6-methanobenzo[g][1,4]oxazocine (16). ¹H NMR (CDCl₃, 600 MHz): δ 7.71 (d, 2H, J = 8.5 Hz), 7.65 (d, 2H, J = 8.5 Hz), 7.35 (t, 2H, J = 7.7 Hz), 7.26-7.24 (m, 3H), 4.49 (dd, 1H, J = 11.3, 2.6 Hz), 3.97 (dt, 1H, J = 3.8, 1.9 Hz), 3.17 (d, 1H, J = 11.3 Hz), 3.12 (qd, 1H, J = 6.7, 1.8 Hz), 2.46 (dt, 1H, J = 13.1, 3.3 Hz), 2.21-2.12 (m, 1H), 2.10 (dt, 1H, J = 17.4, 4.9 Hz), 1.83-1.79 (m, 1H), 1.78 (dd, 1H, J = 13.0, 2.1 Hz), 1.65-1.43 (m, 5H), 1.42 (d, 3H, J = 6.6 Hz); ¹³C {¹H} NMR (CDCl₃, 151 MHz): δ 150.0, 143.3, 140.7, 132.3, 128.7, 128.6, 127.4, 126.7, 126.4, 106.5, 73.7, 59.1, 53.9, 39.4, 39.1, 27.6, 24.7, 23.2, 23.0, 18.4; ¹³C NMR DEPT135 (CDCl₃, 151 MHz): δ
132.3, 128.7, 128.6, 126.7, 126.4, 73.7 (CH), 59.1 (CH), 53.9 (CH); IR (v/cm⁻¹): 3087 (w), 3059 (w), 3024 (w), 2982 (w), 2931 (s), 2886 (w), 2855 (m), 2841 (m), 1678 (m), 1603 (w), 1575 (m), 1496 (w), 1471 (m), 1446 (m), 1389 (m), 1372 (m), 1325 (s), 1286 (w), 1270 (w), 1248 (w), 1235 (w), 1217 (w), 1174 (s), 1154 (s), 1136 (m), 1089 (m), 1068 (m), 1037 (m), 1010 (m); HRMS-(ESI⁺) [M+H]⁺ calcd for C₂₄H₂₇NO₃SBr⁺ 488.0895, found: 488.0895; [α]D²⁶ = +2.02° (c = 1.865, CH₂Cl₂, l = 100 mm).

**Preparation of piperidine S17:**

In a dry, N₂-filled glove box, aldehyde S15 (0.0500 mmol, 21.8 mg, 1.00 eq.) and [Ph₃C][B(C₆F₅)₄] (trityl BArF₂₀, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et₃SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) and cyclohexanone-derived silyl enol ether (0.0550 mmol, 10.6 µL, 1.10 eq.) were dissolved in 1.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The solution was stirred for an additional 5 minutes at −78 °C, after which time the reaction was transferred to a −30 °C cryobath and stirred overnight for 24 h. The reaction was then quenched at the cryogenic temperature with 50 µL Et₃N and warmed to room temperature. The solution was diluted with CH₂Cl₂, concentrated in vacuo (x2), and then placed under high vacuum for ≥1 h to remove excess Et₃N. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the mixture was stirred at 22 °C for 1 h. The solution was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. Dimethylformamide (0.050 mmol, 3.9 µL) was added as an internal standard and the
residue taken up in CDCl$_3$ for $^1$H and $^{13}$C NMR analyses to determine conversion, product identity, NMR yield, and crude diastereomeric ratios (d.r.). Despite full consumption of starting materials, no trace of product is visible by $^1$H or $^{13}$C NMR.

**Data for S17**

\[
\begin{align*}
| & \text{Br} & | & \text{O} & | & \text{N} & | & \text{Ph} \\
| & \text{Me} & | & \text{O} & | & \text{N} & | & \text{Ph} \\
\end{align*}
\]

(2S,3S,6R)-4-((4-bromophenyl)sulfonyl)-3-isopropyl-6-phenyl-3,4,5,6,7,8,9,10-octahydro-2H-2,6-methanobenzog][1,4]oxazocine (S17). The starting material was consumed with no generation of desired product detectable by $^1$H and $^{13}$C $^1$H NMR or HRMS-(ESI+).

**Preparation of piperidine 17:**

In a dry, N$_2$-filled glove box, aldehyde 4 (0.100 mmol, 48.4 mg, 1.00 eq.) and [Ph$_3$C][B(C$_6$F$_5$)$_4$] (trityl BArF$_{20}$, 0.010 mmol, 9.2 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et$_3$SiH (0.012 mmol, 1.9 µL, 0.12 eq.) and α-tetralone-derived silyl enol ether (0.250 mmol, 54.6 mg, 2.50 eq.) were dissolved in 2.00 mL of CH$_2$Cl$_2$ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N$_2$ atmosphere via piercing of the septa with N$_2$ needles, and the vial containing the aldehyde and trityl BArF$_{20}$ was cooled to $-78$ °C in an acetone/CO$_2(\text{s})$ bath. The room temperature solution in CH$_2$Cl$_2$ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 10 minutes. The solution was stirred for an additional 2 h at $-78$ °C, quenched at the cryogenic temperature with 50 µL Et$_3$N, and warmed to room temperature. The residue was repeatedly washed with CH$_2$Cl$_2$ and concentrated in vacuo (x3), and was then placed under high vacuum for ≥1 h to remove excess Et$_3$N. The resulting residue was taken up in 2 mL of 1:1
CH₂Cl₂/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the mixture was stirred at 22 °C for 3 h. The mixture was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (10:1 n-pentane:ethyl acetate; Rf = 0.3), followed by washing with n-pentane to remove co-eluting α-tetralone, to yield the tetracyclic piperidine product 17 as a white, crystalline solid in 11% yield (6.8 mg average per reaction over two 0.1 mmol scale trials).

**Data for 17**

(2R,3S,6S)-3-benzyl-4-((4-bromophenyl)sulfonyl)-6-phenyl-3,4,5,6,7,8-hexahydro-2H-2,6-methanonaphtho[2,1-g][1,4]oxazocine (17). ¹H NMR (CDCl₃, 600 MHz): δ 7.57 (d, 3H, J = 8.6 Hz), 7.39 (t, 2H, J = 7.7 Hz), 7.35-7.31 (m, 5H), 7.31-7.27 (m, 4H), 7.26 (t, 1H, J = 5.9 Hz), 7.19 (d, 1H, J = 6.3 Hz), 7.15 (d, 2H, J = 8.6 Hz), 4.61 (dd, 1H, J = 11.7, 2.7 Hz), 4.16 (dt, 1H, J = 3.9, 1.8 Hz), 3.54 (dd, 1H, J = 12.5, 3.5 Hz), 3.46 (d, 1H, J = 11.7 Hz), 3.39 (ddd, 1H, J = 11.9, 3.6, 1.7 Hz), 2.85-2.70 (m, 2H), 2.66 (t, 1H, J = 12.1 Hz), 2.48 (dt, 1H, J = 13.5, 4.1 Hz), 2.04 (ddd, 1H, J = 15.8, 11.7, 6.5 Hz), 1.88 (dt, 1H, J = 15.9, 6.6 Hz), 1.73 (dd, 1H, J = 13.4, 2.1 Hz); ¹³C{¹H} NMR (CDCl₃, 151 MHz): δ 147.5, 143.7, 141.5, 137.8, 136.2, 132.2, 131.0, 129.9, 128.9, 128.8, 128.6, 127.9, 127.5, 127.4, 127.1, 127.0, 126.7, 126.2, 121.5, 110.2, 68.0, 65.5, 53.3, 40.3, 38.9, 35.7, 28.2, 23.8; ¹³C NMR DEPT135 (CDCl₃, 151 MHz): δ 132.2, 129.9, 128.9, 128.8, 128.6, 127.9, 127.5, 127.1, 127.0, 126.7, 126.2, 121.5, 68.0 (CH), 65.5 (CH), 53.3 (CH₂), 38.9 (CH₂), 35.7 (CH₂), 28.2 (CH₂), 23.8 (CH₂); IR (ν/cm⁻¹): 3086 (w), 3060 (w), 3027 (w), 3002 (w), 2952 (m), 2930 (m), 2854 (w), 1645 (m), 1601 (w), 1574 (m), 1496 (w), 1470 (w), 1446 (w), 1427 (w), 1389 (w), 1371 (w), 1329 (m), 1314 (s), 1266 (w), 1243 (w), 1232 (w), 1154 (s), 1121 (w), 1088 (m), 1069 (m), 1025 (w), 1011 (w); HRMS-(ESI⁺) [M+H]⁺ calcd for C₃₄H₃₁NO₅SBr⁺ 612.1208, found: 612.1212; [α]D²⁵ = +2.53° (c = 0.675, CH₂Cl₂, l = 100 mm).
Preparation of piperidine S18:

![Chemical Structure](image)

In a dry, N₂-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg, 1.00 eq.) and [Ph₃C][B(C₆F₅)₄] (trityl BArF₂₀, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et₃SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) and acetophenone-derived silyl enol ether (0.0550 mmol, 11.3 µL, 1.10 eq.) were dissolved in 1.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The solution was allowed to stir for an additional 15 minutes at −78 °C, after which time the reaction was transferred to a −30 °C cryobath and stirred overnight for 21 h. The reaction was then quenched at the cryogenic temperature with 50 µL Et₃N and warmed to room temperature. The solution was diluted with CH₂Cl₂, concentrated in vacuo (x2), and then placed under high vacuum for ≥1 h to remove excess Et₃N. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/Methanol, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the mixture was stirred at 22 °C for 16 h. The mixture was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. Dimethylformamide (0.050 mmol, 3.9 µL) was added as an internal standard and the residue taken up in CDCl₃ for ¹H and ¹³C NMR analyses to determine conversion, product identity, NMR yield, and crude diastereomeric ratios (d.r.). Despite full consumption of starting materials, only trace product is visible by ¹³C.
Data for S18

\(\text{S18} \quad \delta 101.9 \text{ ppm}\)

\((15,5S,8S)-8\text{-benzyl-7-}((4\text{-bromophenyl})\text{ sulfonyl})\text{-3,5-diphenyl-2-oxa-7-azabicyclo[3.3.1]non-3-ene (S18)}\). \(^{13}\text{C}\{\text{H}\} \text{ NMR (CDCl}_3, 151 \text{ MHz})\): \(\delta 101.9\) (diagnostic vinyl ether peak); \text{HRMS-(ESI\(^+\)) \([M+H]^+\) calcd for C\(_{32}\)H\(_{29}\)NO\(_3\)SBr\(^+\) 586.1052, found: 586.1054.}

Preparation of piperidine 18:

In a dry, N\(_2\)-filled glove box, aldehyde 11 (0.0500 mmol, 30.5 mg, 1.00 eq.) and [Ph\(_3\)C][B(C\(_6\)F\(_5\)_4)] (trityl BArF\(_{20}\), 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et\(_3\)SiH (0.0060 mmol, 1.0 \(\mu\)L, 0.12 eq.) and cyclohexanone-derived silyl enol ether (0.125 mmol, 24.1 \(\mu\)L, 2.50 eq.) were dissolved in 1.00 mL of CH\(_2\)Cl\(_2\) and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N\(_2\) atmosphere via piercing of the septa with N\(_2\) needles, and the vial containing the aldehyde and trityl BArF\(_{20}\) was cooled to \(-78 \text{ °C}\) in an acetone/CO\(_2\) bath. The room temperature solution in CH\(_2\)Cl\(_2\) was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The solution was allowed to stir for an additional 15 minutes at \(-78 \text{ °C}\), after which time the reaction was transferred to a \(-30 \text{ °C}\) cryobath and stirred overnight for 22 h (this was necessary for increased yield and reproducibility). The reaction was then quenched at the cryogenic temperature with 50 \(\mu\)L i-PrNH\(_2\) and warmed to room temperature. The residue was repeatedly washed with CH\(_2\)Cl\(_2\) and concentrated \textit{in vacuo} (x3), and was then placed under high vacuum for \(\geq 1 \text{ h}\) to remove excess i-PrNH\(_2\). The resulting residue was taken up in 2 mL of 1:1 CH\(_2\)Cl\(_2\)/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the mixture was stirred at 22 °C for 22 h. The mixture was then
filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH$_2$Cl$_2$, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (5:1 n-pentane:ethyl acetate; R$_f$ = 0.5) to yield the tricyclic piperidine product 18 as a light yellow oil in 24% yield (8.2 mg average per reaction over two 0.05 mmol scale trials).

Data for 18

\[
\begin{align*}
(2S,3S,6S)-3\text{-benzyl}-4-(4\text{-bromophenyl})\text{suflonyl)}-6-(2\text{-iodophenyl})-3,4,5,6,7,8,9,10\text{-octahydro-2H}-2,6\text{-methanobenzo[g][1,4]oxazocine (18).} \quad \text{H NMR (CDCl$_3$, 600 MHz): \(\delta\) 7.99 (dd, 1H, \(J = 7.9, 1.4\) Hz), 7.79 (d, 2H, \(J = 8.6\) Hz), 7.68 (d, 2H, \(J = 8.6\) Hz), 7.35 (td, 1H, \(J = 7.7, 1.4\) Hz), 7.26 (t, 2H, \(J = 3.8\) Hz), 7.22-7.15 (m, 4H), 6.92 (td, 1H, \(J = 7.6, 1.5\) Hz), 4.55 (dd, 1H, \(J = 11.1, 3.0\) Hz), 3.90 (dt, 1H, \(J = 4.2, 1.8\) Hz), 3.40-3.33 (m, 2H), 3.30-3.23 (m, 2H), 2.83 (t, 1H, \(J = 12.1\) Hz), 2.33-2.25 (m, 1H), 2.21 (dt, 1H, \(J = 16.8, 5.5\) Hz), 1.86-1.80 (m, 2H), 1.81-1.75 (m, 1H), 1.65-1.50 (m, 3H), 1.31 (dd, 1H, \(J = 13.3, 1.9\) Hz); \quad \text{C NMR DEPT135 (CDCl$_3$, 151 MHz): \(\delta\) 151.7, 143.7, 142.8, 141.9, 137.8, 132.5, 129.8, 128.7, 128.6, 128.4, 128.4, 127.6, 127.5, 126.9, 103.4, 96.3, 67.1, 65.7, 55.4, 40.9, 35.9, 34.1, 27.8, 24.8, 23.3, 22.4;} \quad \text{C NMR DEPT135 (CDCl$_3$, 151 MHz): \(\delta\) 143.7 (CH), 132.5 (CH), 129.8 (CH), 128.7 (CH), 128.6 (CH), 128.4 (CH), 128.4 (CH), 127.5 (CH), 126.9 (CH), 67.1 (CH), 65.7 (CH), 55.4 (CH$_2$), 35.9 (CH$_2$), 34.1 (CH$_3$), 27.8 (CH$_2$), 24.8 (CH$_2$), 23.3 (CH$_2$), 22.4 (CH$_2$);} \quad \text{IR (v/cm$^{-1}$): 3084 (w), 3060 (w), 3027 (w), 3002 (w), 2929 (s), 2857 (m), 2836 (m), 1684 (m), 1602 (w), 1575 (m), 1496 (w), 1470 (w), 1457 (m), 1388 (m), 1374 (m), 1352 (m), 1333 (s), 1265 (w), 1232 (m), 1209 (w), 1164 (s), 1154 (s), 1128 (w), 1112 (w), 1089 (m), 1067 (m), 1053 (w), 1009 (m);} \quad \text{HRMS-(ESI$^+$) [M+H]$^+$ calcd for C$_{30}$H$_{30}$NO$_3$SBr$^+$ 690.0175, found: 690.0185; \(\alpha\)D$^\circ$ = +21.6° (c = 0.820, CH$_2$Cl$_2$, l = 100 mm).} \end{align*}
\]
Preparation of piperidine 19:

In a dry, N₂-filled glove box, aldehyde 12 (0.0500 mmol, 21.1 mg, 1.00 eq.) and [Ph₃C][B(C₆F₅)₄] (trityl BArF₂₀, 0.0050 mmol, 4.6 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et₃SiH (0.0060 mmol, 1.0 µL, 0.12 eq.) and cyclohexanone-derived silyl enol ether (0.125 mmol, 24.1 µL, 2.50 eq.) were dissolved in 1.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The solution was allowed to stir for an additional 15 minutes at −78 °C, after which time the reaction was transferred to a −30 °C cryobath and stirred overnight for 20 h (this was necessary for increased yield and reproducibility). The reaction was then quenched at the cryogenic temperature with 50 µL i-PrNH₂ and warmed to room temperature. The residue was repeatedly washed with CH₂Cl₂, concentrated in vacuo (x3), and was then placed under high vacuum for ≥1 h to remove excess i-PrNH₂. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the mixture was stirred at 22 °C for 24 h. The mixture was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (10:1 n-pentane:ethyl acetate; Rᵣ = 0.4) to yield the tricyclic piperidine product 19 as a white solid in 22% yield (5.5 mg average per reaction over three 0.05 mmol scale trials).
Data for 19

(2S,3S,6S)-3-benzyl-4-((4-bromophenyl)sulfonyl)-6-methyl-3,4,5,6,7,8,9,10-octahydro-2H-2,6-methanobenzo[g][1,4]oxazocine (19). \(^1H\) NMR (CDCl\(_3\), 600 MHz): \(\delta\) 7.69 (d, 2H, \(J = 8.5\) Hz), 7.63 (d, 2H, \(J = 8.5\) Hz), 7.25 (t, 2H, \(J = 7.4\) Hz), 7.19 (t, 1H, \(J = 7.3\) Hz), 7.15 (d, 2H, \(J = 7.0\) Hz), 3.91 (dd, 1H, \(J = 11.9, 2.4\) Hz), 3.84 (dt, 1H, \(J = 4.0, 2.0\) Hz), 3.36 (dd, 1H, \(J = 12.6, 3.7\) Hz), 3.24 (ddd, 1H, \(J = 11.5, 3.7, 2.0\) Hz), 2.70 (t, 1H, \(J = 12.0\) Hz), 2.68 (d, 1H, \(J = 11.9\) Hz), 2.23-2.14 (m, 1H), 2.09 (dt, 1H, \(J = 16.9, 4.9\) Hz), 2.05-2.00 (m, 2H), 1.84 (dt, 1H, \(J = 12.9, 2.8\) Hz), 1.83-1.75 (m, 1H), 1.67-1.47 (m, 2H), 1.33 (dd, 1H, \(J = 13.0, 2.0\) Hz), 1.02 (s, 3H); \(^{13}C\) \(^1H\) NMR (CDCl\(_3\), 151 MHz): \(\delta\) 148.1, 141.9, 138.2, 132.3, 129.8, 128.6, 128.4, 126.7, 106.7, 67.3, 65.1, 56.7, 37.2, 35.7, 31.1, 27.5, 23.4, 22.9, 22.9, 22.0; \(^{13}C\) NMR DEPT135 (CDCl\(_3\), 151 MHz): \(\delta\) 132.3 (CH), 129.8 (CH), 128.6 (CH), 128.4 (CH), 126.7 (CH), 67.3 (CH), 65.1 (CH), 56.7 (CH\(_2\)), 37.2 (CH\(_2\)), 35.7 (CH\(_2\)), 27.5 (CH\(_2\)), 23.4 (CH\(_2\)), 22.9 (CH\(_2\)), 22.9 (CH\(_2\)), 22.0 (CH\(_3\)); IR (\(\nu/\text{cm}^{-1}\)): 3086 (w), 3061 (w), 3028 (w), 2929 (s), 2875 (m), 2855 (m), 2840 (m), 1679 (m), 1603 (w), 1575 (m), 1495 (w), 1471 (w), 1455 (m), 1387 (m), 1357 (m), 1331 (s), 1315 (m), 1267 (w), 1244 (w), 1189 (m), 1156 (s), 1142 (m), 1130 (m), 1114 (w), 1091 (m), 1068 (m), 1052 (w), 1036 (w), 1008 (m); HRMS-(ESI\(^+\)) [M+H]\(^+\) calcd for C\(_{25}\)H\(_{29}\)NO\(_3\)SBr\(^+\) 502.1052, found: 502.1054; \([\alpha]\)\(_D\)\(^{25}\) = +0.699° (c = 0.830, CH\(_2\)Cl\(_2\), l = 100 mm).

Preparation of piperidine 20:

In a dry, N\(_2\)-filled glove box, aldehyde \(\text{S16}\) (0.150 mmol, 68.3 mg, 1.00 eq.) and [\(\text{Ph}_3\text{C}\)[B(C\(_6\)F\(_3\))\(_4\)]] (trityl BArF\(_{20}\), 0.015 mmol, 13.8 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et\(_3\)SiH (0.018 mmol, 2.9 \(\mu\)L, 0.12 eq.) and cyclohexanone-derived silyl enol ether
(0.375 mmol, 72 µL, 2.50 eq.) were dissolved in 3.00 mL of CH₂Cl₂ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N₂ atmosphere via piercing of the septa with N₂ needles, and the vial containing the aldehyde and trityl BArF₂₀ was cooled to −78 °C in an acetone/CO₂(s) bath. The room temperature solution in CH₂Cl₂ was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 10 minutes. The solution was stirred for an additional 2 h at −78 °C, quenched at the cryogenic temperature with 50 µL Et₃N, and warmed to room temperature. The residue was repeatedly washed with CH₂Cl₂ and concentrated in vacuo (x3), and was then placed under high vacuum for ≥1 h to remove excess Et₃N. The resulting residue was taken up in 2 mL of 1:1 CH₂Cl₂/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the mixture was stirred at 22 °C for 3 h. The mixture was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH₂Cl₂, and concentrated in vacuo. The crude residue was purified by silica gel chromatography (5:1 n-pentane:ethyl acetate; Rᵣ = 0.5) to yield the tricyclic piperidine product 20 as a white, crystalline solid in 55% yield (44.3 mg).

Data for 20 (piperidine resonances assigned in red)

(2R,3S,6S)-3-benzyl-4-(naphthalen-2-ylsulfonyl)-6-phenyl-3,4,5,6,7,8,9,10-octahydro-2H-2,6-methanobenzol[g][1,4]oxazocine (20). The crude residue was purified by silica gel chromatography (5:1 n-pentane:ethyl acetate; Rᵣ = 0.5) to yield the tricyclic piperidine product 20 as a white, crystalline solid in 55% yield (44.3 mg). ¹H NMR (CDCl₃, 600 MHz; piperidine ring protons assigned in red): δ 8.50 (d, 1H, J = 1.9 Hz), 8.01 (d, 1H, J = 8.7 Hz), 7.99 (d, 1H, J = 8.2 Hz), 7.95 (d, 1H, J = 8.0 Hz), 7.90 (dd, 1H, J = 8.7, 1.9 Hz), 7.67 (ddd, 1H, J = 8.2, 6.9, 1.4 Hz), 7.63 (ddd, 1H, J = 8.2, 6.8, 1.4 Hz), 7.37 (t, 2H, J = 7.7 Hz), 7.29 (dd, 2H, J = 8.2, 1.3 Hz), 7.27-7.22 (m, 3H), 7.18 (d, 1H, J = 7.4 Hz), 7.16 (dd, 2H, J = 7.1, 1.6 Hz), 4.69 (dd, 1H, J = 11.4, 2.7 Hz, 1), 3.89 (dt, 1H, J = 4.0, 1.9 Hz, 4), 3.57 (dd, 1H, J = 12.7, 3.5 Hz, 6), 3.40 (d, 1H, J = 11.5 Hz, 1), 3.30 (ddd, 1H, J = 11.6, 3.6, 1.8 Hz, 5), 2.85 (t, 1H, J = 12.8, 11.6 Hz, 6), 2.39-2.32 (m, 2H, 3), 2.24-2.19 (m, 1H), 1.94-1.90 (m, 1H), 1.72-1.53 (m, 6H, 3); ¹³C{¹H} NMR
(CDCl₃, 151 MHz; piperidine ring carbons assigned in red): δ 150.1, 143.5, 139.6, 138.2, 134.8, 132.4, 129.8, 129.4, 129.3, 128.9, 128.6, 128.1, 127.8, 127.7, 126.7, 126.6, 126.4, 122.5, 106.3, 67.4 (4), 65.5 (5), 54.1 (1), 39.1 (2), 39.0 (3), 35.8 (6), 27.8, 24.8, 23.4, 23.1; ¹³C NMR DEPT135 (CDCl₃, 151 MHz): δ 129.8 (CH), 129.4 (CH), 129.3 (CH), 128.9 (CH), 128.6 (CH), 128.6 (CH), 128.1 (CH), 127.8 (CH), 127.7 (CH), 126.7 (CH), 126.6 (CH), 126.4 (CH), 122.5 (CH), 67.4 (CH), 65.5 (CH), 54.1 (CH₂), 39.0 (CH₂), 35.8 (CH₂), 27.8 (CH₂), 24.8 (CH₂), 23.4 (CH₂), 23.1 (CH₂); IR (ν/cm⁻¹): 3059 (w), 3027 (w), 2928 (s), 2855 (m), 1679 (m), 1602 (w), 1496 (m), 1445 (m), 1373 (m), 1327 (s), 1267 (w), 1236 (w), 1166 (s), 1151 (s), 1130 (m), 1074 (m), 1063 (w), 1021 (w); HRMS-(ESI⁺) [M+H]⁺ calcd for C₃₄H₃₄NO₃S⁺ 536.2260, found: 536.2259; [α]D²₆ = +11.7° (c = 1.70, CH₂Cl₂, l = 100 mm). A single crystal X-ray structure was obtained from this compound via recrystallization (solvent vapor) from a mixture of C₆H₆/n-pentane. The data indicate a surprising cis-(axial-equatorial) configuration of the C–O bond and the amino R-group, respectively.
3. X-ray crystallographic data and structure for 20:

ORTEP representation of the solid state molecular structure of 20; ellipsoids drawn at 50% probability, the majority of hydrogen atoms are omitted for clarity. There is disorder in the orientation of the 2-naphthalenesulfonyl group; only one of two adopted conformations of the naphthyl group is shown for clarity.

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⁸ CCDC 1548662 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/structures](http://www.ccdc.cam.ac.uk/structures). (submission is pending)
4. Removal of aryl sulfonamide protecting group (deprotection of piperidine 20):

![Chemical Structure](image)

2-naphthalenesulfonyl-protected piperidine 20 (0.0609 mmol, 32.6 mg, 1.00 eq.) and elemental magnesium (50 mesh; 0.609 mmol, 14.8 mg, 10.0 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. The vial was purged with a stream of dry N₂ for 5 minutes, at which time anhydrous methanol (1.82 mL) was added *via* syringe. The milky white suspension was sonicated for 1 h, during which time the substrate and magnesium dissolved to produce a homogeneous gray solution; TLC (25:1 CH₂Cl₂:MeOH; product R_f = 0.4) showed spot-to-spot conversion. The reaction was quenched with saturated aqueous NH₄Cl, diluted with excess CH₂Cl₂ and rinsed into a separatory funnel, basified with excess aqueous 1M NaOH (until pH ≥ 10), diluted with saturated aqueous NaCl, and then extracted with CH₂Cl₂ (x5). The combined organic washes were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (25:1 dichloromethane:methanol with trace triethylamine; R_f = 0.4) to yield the free amine product 21 as a clear, colorless oil in 91% yield (19.1 mg).

**Data for 21**

![Chemical Structure](image)

(2R,3S,6S)-3-benzyl-6-phenyl-3,4,5,6,7,8,9,10-octahydro-2H-2,6-methanobenzo[g][1,4]oxazocine (21). ¹H NMR (CDCl₃, 600 MHz): δ 7.34-7.29 (m, 6H), 7.24-7.19 (m, 4H), 3.88 (d, 1H, J = 4.1 Hz), 3.19-3.10 (m, 2H), 2.91-2.81 (m, 3H), 2.37-2.29 (m, 2H), 2.27-2.21 (m, 1H), 1.90 (br s, 1H, NH), 1.82-1.77 (m, 1H), 1.74 (dd, J = 13.1, 1.8 Hz, 1H), 1.63-1.58 (m, 2H), 1.54-1.47 (m, 1H), 1.37-1.33 (m, 2H); ¹³C{¹H} NMR (CDCl₃, 151 MHz): δ 151.0, 144.9, 139.1, 129.6, 128.5, 128.4, 126.8, 126.3, 126.2, 106.3, 69.1, 63.8, 51.7, 39.4, 39.1, 39.0, 27.8, 24.9, 23.6, 23.3; ¹³C NMR DEPT135 (CDCl₃, 151 MHz): δ 129.6 (CH), 128.5 (CH), 128.4 (CH), 126.8 (CH), 126.3 (CH), 126.2 (CH), 69.1 (CH), 63.8 (CH), 51.7 (CH₂), 39.4 (CH₂), 39.1
(CH₂), 27.8 (CH₂), 24.9 (CH₂), 23.6 (CH₂), 23.3 (CH₂); IR (ν/cm⁻¹): 3084 (w), 3059 (w), 3026 (w), 2927 (s), 2854 (s), 1669 (m), 1603 (w), 1495 (m), 1446 (m), 1372 (w), 1348 (w), 1266 (w), 1232 (m), 1215 (w), 1150 (m), 1108 (w), 1058 (w), 1032 (w));

HRMS-(ESI⁺) [M+H]⁺ calcd for C₂₄H₂₈NO⁺ 346.2171, found: 346.2164; [α]D²⁵ = +117° (c = 0.955, CH₂Cl₂, l = 100 mm).

V. Cyclizations using other Lewis Acids

I. Prins-cyclization promoted by TiCl₄: Preparation of chloride-trapped piperidine 9

\[
\text{Br} \quad \text{SO} \quad \text{N} \quad \text{Ph} \\
\text{Ph} \quad \text{O} \quad \text{O} \\
\text{Br} \quad \text{TiCl₄} \quad \text{CH₂Cl₂} \quad -78 °C, 5 min. \\
\text{Cl} \quad \text{Ph} \quad \text{OH} \quad \text{Ph}
\]

In a dry, N₂-filled glove box, aldehyde 4 (0.100 mmol, 48.4 mg) was weighed into a screw cap 1 dram vial equipped with a stir bar. CH₂Cl₂ (1.00 mL, 0.1 M) was added and the vial was sealed with a septum cap. Simultaneously, a 1.0 M solution of TiCl₄ in CH₂Cl₂ was prepared in a 1 dram vial and the vial was sealed with a septum cap. Both vials were removed from the glove box. The vial containing the substrate was equipped with a nitrogen line and cooled to −78 °C in an acetone/CO₂(s) bath. The 1.0 M TiCl₄ solution in CH₂Cl₂ (0.110 mmol, 110 µL) was taken up by syringe and added drop-wise to the rapidly stirring solution of substrate at −78 °C over 30 seconds. The color was observed to change from light yellow to deep reddish-orange. After 5 minutes, the solution was quenched (resulting in rapid loss of color) by drop-wise addition of a CH₂Cl₂ solution (800 µL) containing NEt₃ (80 µL) and MeOH (30 µL). The solution was stirred at −78 °C for 10 minutes, and was then allowed to warm to room temperature over 10 minutes. The reaction was worked up by dilution with CH₂Cl₂, followed by sequential washes with saturated aqueous NH₄Cl, NaHCO₃, and NaCl, followed by drying over anhydrous MgSO₄ and concentration in vacuo. The crude residue was purified by silica gel chromatography (3:1 n-pentane:ethyl acetate; Rf = 0.3-0.4) to yield chloro-piperidine 9 as a white, crystalline solid in 99% yield (51.5 mg) and as a mixture of three partially separable diastereomers in 85:9:6 d.r..
Data for 9

(2S)-2-benzyl-1-((4-bromophenyl)sulfonyl)-5-chloro-5-phenylpiperidin-3-ol (9). Major
diastereomer A (co-eluted with minor diastereomer B): $^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ 7.59-
7.55 (m, 2H), 7.36-7.33 (m, 3H), 7.27 (d, 2H, $J$ = 8.4 Hz), 7.24-7.18 (m, 3H), 7.16-7.13 (m, 2H),
7.09 (d, 2H, $J$ = 8.2 Hz), 4.80 (d, 1H, $J$ = 13.9 Hz), 4.11 (q, 1H, $J$ = 6.1 Hz), 3.99 (dt, 1H, $J$
= 10.6, 4.6 Hz), 3.74 (d, 1H, $J$ = 13.9 Hz), 3.20 (dd, 1H, $J$ = 14.3, 6.4 Hz), 3.06 (dt, 1H, $J$ = 13.9,
3.1 Hz), 2.86 (dd, 1H, $J$ = 14.3, 6.4 Hz), 2.50 (dd, 1H, $J$ = 13.8, 11.9 Hz), 1.91 (s, br, 1H);
$^{13}$C{$^1$H} NMR (CDCl$_3$, 151 MHz): $\delta$ 139.5, 138.4, 138.4, 132.2, 129.3, 128.8, 128.8,
128.7, 128.5, 127.6, 127.1, 126.6, 66.9, 66.1, 58.9, 50.8, 41.5, 31.0; $^{13}$C NMR DEPT135
(CDCl$_3$, 151 MHz): $\delta$ 132.2 (CH), 129.3 (CH), 128.8 (CH), 128.8 (CH), 128.7 (CH), 128.5 (CH),
127.1 (CH), 126.6 (CH), 66.9 (CH), 58.9 (CH), 50.8 (CH$_2$), 41.5 (CH$_2$), 31.0 (CH$_2$); IR (v/cm$^{-1}$):
3520 (s, br, OH), 3087 (w), 3061 (w), 3028 (w), 2953 (w), 2926 (w), 2853 (w), 1603 (w), 1575 (m),
1496 (m), 1470 (m), 1449 (m), 1335 (s), 1311 (m), 1277 (m), 1266 (m), 1231 (w), 1159 (s),
1098 (m), 1086 (m), 1069 (s), 1031 (w); HRMS-(ESI$^+$) [M–Cl$^+$] calcd for C$_{24}$H$_{23}$NO$_3$SBr$^+$
484.0582, found: 484.0588; [$\alpha$]$_D^{25}$ = –22.2° (c = 2.35, CH$_2$Cl$_2$, l = 100 mm). Minor
diastereomer B (co-eluted with major diastereomer A; aliphatic peaks reported where visible): $^1$H NMR
(CDCl$_3$, 600 MHz; aliphatic only): $\delta$ 4.62 (dt, 1H, $J$ = 10.6, 4.7 Hz), 4.50 (dd, 1H, $J$ = 14.9, 2.3
Hz), 4.33 (dt, 1H, $J$ = 9.7, 4.9 Hz), 3.47 (d, 1H, $J$ = 14.9 Hz), 3.10-3.08 (m, 1H), 2.67-2.60 (m, 1H),
2.57 (dt, 1H, $J$ = 13.7, 3.4 Hz), 2.45 (dd, 1H, $J$ = 14.0, 11.4 Hz); $^{13}$C{$^1$H} NMR (CDCl$_3$, 151
MHz; aliphatic only): $\delta$ 70.6, 66.2, 59.3, 51.1, 40.3, 30.0; $^{13}$C NMR DEPT135 (CDCl$_3$, 151
MHz; aliphatic only): $\delta$ 66.2 (CH), 59.3 (CH), 51.1 (CH$_2$), 40.3 (CH$_2$), 30.0 (CH$_2$). Minor
diastereomer C: $^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ $^1$H NMR 7.81 (d, 2H, $J$ = 8.6 Hz), 7.62 (d, 2H,
$J$ = 8.6 Hz), 7.55 (d, 2H, $J$ = 7.8 Hz), 7.45 (t, 2H, $J$ = 7.7 Hz), 7.41-7.22 (m, 4H), 7.14 (d, 2H, $J$
= 6.9 Hz), 4.56 (dd, 1H, $J$ = 15.2, 2.5 Hz), 4.34 (dd, 1H, $J$ = 11.0, 4.7 Hz), 3.86 (ddt, 1H, $J$
= 11.4, 4.1, 2.0 Hz), 3.67 (d, 1H, $J$ = 14.8 Hz), 3.30 (d, 1H, $J$ = 11.4 Hz), 2.93 (dd, 1H, $J$ = 13.6, 4.6 Hz),
2.74 (dd, 1H, $J$ = 13.6, 10.9 Hz), 2.70 (d, 1H, $J$ = 14.9 Hz), 2.53 (dd, 1H, $J$ = 15.6, 4.0 Hz);
$^{13}$C{$^1$H} NMR (CDCl$_3$, 151 MHz): $\delta$ 141.8, 139.5, 136.8, 132.4, 129.2, 129.2, 129.1, 128.8,
128.0, 127.3, 127.2, 125.3, 68.6, 65.5, 61.5, 51.6, 37.6, 36.3; \(^{13}\text{C NMR DEPT135}\) (CDCl\(_3\), 151 MHz): \(\delta\) 132.4 (CH), 129.2 (CH), 129.2 (CH), 129.1 (CH), 128.8 (CH), 127.3 (CH), 127.2 (CH), 125.3 (CH), 65.5 (CH), 61.5 (CH), 51.6 (CH\(_2\)), 37.6 (CH\(_2\)), 36.3 (CH\(_2\)); IR (ν/cm\(^{-1}\)): 3566 (m, br, OH), 3086 (w), 3061 (w), 3028 (w), 2921 (s), 2850 (m), 1733 (w), 1716 (w), 1698 (w), 1684 (w), 1647 (w), 1575 (m), 1558 (w), 1541 (w), 1521 (w), 1507 (w), 1496 (m), 1472 (w), 1456 (m), 1448 (w), 1419 (w), 1389 (m), 1340 (s), 1266 (m), 1214 (w), 1163 (s), 1090 (m), 1068 (m), 1030 (m), 1010 (m); HRMS-(ESI\(^+\)) \([\text{M–Cl}]^+\) calcd for C\(_{24}\)H\(_{23}\)NO\(_3\)SBr\(^+\) 484.0582, found: 484.0589.

2. **Prins-cyclization catalyzed by the Brønsted acid HBArF\(_{24}\) (Brookhart’s acid)**

In a dry, N\(_2\)-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg, 1.00 eq.) and \([\text{H(OEt}_2\text{)}][\text{B(C}_6\text{H}_3(\text{CF}_3)_2]\text{]}\) (HBArF\(_{24}\) (Brookhart’s acid), 0.0050 mmol, 5.1 mg, 0.10 eq.) were weighed into a screw cap 1 dram vial equipped with a stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et\(_3\)SiH (0.0600 mmol, 9.6 \(\mu\)L, 1.20 eq.) was dissolved in 1.00 mL of CH\(_2\)Cl\(_2\) and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N\(_2\) atmosphere via piercing of the septa with N\(_2\) needles, and the vial containing the aldehyde and HBArF\(_{24}\) was cooled to –78 °C in an acetone/CO\(_2\)(s) bath. The room temperature solution in CH\(_2\)Cl\(_2\) was syringed drop-wise and slowly down the side of the vial into the vigorously stirring solution over approximately 5 minutes. The solution was stirred for an additional 15 minutes at –78 °C, after which time the reaction was transferred to a –30 °C cryobath and stirred overnight for 18 h. The reaction was then quenched at the cryogenic temperature with 50 \(\mu\)L Et\(_3\)N and warmed to room temperature. The residue was repeatedly washed with CH\(_2\)Cl\(_2\) and concentrated \textit{in vacuo} (x3), and was then placed under high vacuum for \(\geq\)1 h to remove excess Et\(_3\)N. The resulting residue was taken up in 2 mL of 1:1 CH\(_2\)Cl\(_2\)/MeOH, approximately 10-20 beads of Dowex resin (50W-X8) were added, and the mixture was stirred at 22 °C for 18 h. The mixture was then filtered by gravity through a plug of sand and cotton, rinsed with 2x1mL CH\(_2\)Cl\(_2\), and concentrated \textit{in vacuo}. Dimethylformamide
(0.050 mmol, 3.9 µL) was added as an internal standard and the residue taken up in CDCl$_3$ for $^1$H and $^{13}$C NMR analyses to determine crude NMR yield and diastereomeric ratios (d.r.); the desired piperidine 6 was produced in 47% yield and in 45:36:19 d.r. favoring the same diastereomers as those resulting from the putative silylium ion catalysis (vide supra).

3. Silylium-ion catalyzed Prins-cyclization in the absence of trapping nucleophiles:

In a dry, N$_2$-filled glove box, aldehyde 4 (0.100 mmol, 48.4 mg) and [Ph$_3$C][B(C$_6$F$_5$)$_4$] (trityl BArF$_{20}$, 0.0100 mmol, 9.2 mg) were weighed into a screw cap 1 dram vial equipped with a magnetic stir bar and sealed with a septum cap. In a separate screw cap 1 dram vial, Et$_3$SiH (0.0120 mmol, 1.9 µL) was dissolved in 2.00 mL of CH$_2$Cl$_2$ and the vial sealed with a septum cap. Both vials were removed from the glove box and placed under a positive N$_2$ atmosphere via piercing of the septa with N$_2$ needles, and the vial containing the aldehyde and trityl BArF$_{20}$ was cooled to $-78$ °C in an acetone/CO$_2$(s) bath. The room temperature solution in CH$_2$Cl$_2$ was syringed drop-wise and slowly down the side of the vial over 5 minutes with magnetic stirring. During addition, the reaction turned clear bright yellow in color, which persisted throughout the course of the reaction. The reaction was allowed to freely and slowly (in the dewar) warm to 22 °C with stirring over the course of 8 hours, after which time the reaction was quenched with 100 µL of i-PrNH$_2$ and concentrated in vacuo. The crude residue was purified by silica gel chromatography (gradient of 5:1 to 3:1 n-pentane:ethyl acetate; $R_f = 0.2$-0.3) to yield cis-tetrahydropyridine 22 and trans-tetrahydropyridine 23 as clear, colorless oils in 58% yield (28.0 mg on a 0.1 mmol scale) and as a mixture of two chromatographically separable diastereomers in 83:17 cis:trans diastereomeric ratio.
Data for 22

(2S,3S)-2-benzyl-1-((4-bromophenyl)sulfonyl)-5-phenyl-1,2,3,4-tetrahydropyridin-3-ol (22).

**Cis-diastereomer:** $^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ 7.54 (d, 2H, $J = 8.6$ Hz), 7.50 (d, 2H, $J = 8.6$ Hz), 7.42 (d, 2H, $J = 7.3$ Hz), 7.40 (d, 2H, $J = 8.6$ Hz), 7.38 (t, 3H, $J = 7.1$ Hz), 7.26 (t, 1H, $J = 3.6$ Hz), 7.20 (d, 2H, $J = 6.7$ Hz), 7.04 (s, 1H), 4.27 (dt, 1H, $J = 9.2$, 4.3 Hz), 3.62 (dt, 1H, $J = 10.5$, 5.4 Hz), 3.02 (dd, 1H, $J = 13.9$, 4.2 Hz), 2.70 (ddd, 1H, $J = 17.1$, 6.0, 1.6 Hz), 2.65 (dd, 1H, $J = 13.9$, 9.5 Hz), 2.40 (ddd, 1H, $J = 17.2$, 10.4, 1.9 Hz), 1.78 (s, br, 1H); $^{13}$C\{\textsuperscript{1}H\} NMR (CDCl$_3$, 151 MHz): $\delta$ 137.9, 137.8, 137.8, 132.6, 129.7, 128.8, 128.6, 128.5, 128.1, 127.6, 126.8, 125.0, 120.3, 119.3, 66.6, 59.1, 32.1, 30.2; $^{13}$C NMR DEPT135 (CDCl$_3$, 151 MHz): $\delta$ 132.6 (CH), 129.7 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 127.6 (CH), 126.8 (CH), 125.0 (CH), 119.3 (CH), 66.6 (CH), 59.1 (CH), 32.1 (CH$_2$), 30.2 (CH$_2$); IR (v/cm$^{-1}$): 3532 (s, br, OH), 3086 (w), 3061 (w), 3028 (w), 2925 (m), 2849 (w), 1632 (m), 1601 (w), 1574 (m), 1496 (m), 1471 (w), 1455 (w), 1445 (w), 1389 (w), 1349 (s), 1265 (w), 1220 (w), 1166 (s), 1093 (m), 1070 (m), 1053 (w), 1018 (w), 1006 (m); HRMS-(ESI)$^+$ [M+H]$^+$ calcd for C$_{24}$H$_{23}$NO$_3$SBr$^+$ 484.0582, found: 484.0590; [$\alpha$]$^2$$_D$ = –41.4° (c = 1.150, CH$_2$Cl$_2$, l = 100 mm).

Data for 23

(2S,3R)-2-benzyl-1-((4-bromophenyl)sulfonyl)-5-phenyl-1,2,3,4-tetrahydropyridin-3-ol (23).

**Trans-diastereomer:** $^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ 7.70 (d, 2H, $J = 8.4$ Hz), 7.59 (d, 2H, $J = 8.3$ Hz), 7.41-7.35 (m, 4H), 7.33 (t, 2H, $J = 7.4$ Hz), 7.30-7.26 (m, 2H), 7.25-7.22 (m, 3H), 4.23 (ddd, 1H, $J = 9.5$, 5.7, 2.6 Hz), 3.94 (dd, 1H, $J = 4.3$, 2.3 Hz), 3.11 (dd, 1H, $J = 13.8$, 5.6 Hz), 2.70 (ddd, 1H, $J = 18.0$, 4.4, 2.0 Hz), 2.64 (dd, 1H, $J = 13.8$, 10.1 Hz), 2.49 (d, 1H, $J = 18.1$ Hz), 1.03 (s, br, 1H); $^{13}$C\{\textsuperscript{1}H\} NMR (CDCl$_3$, 151 MHz): $\delta$ 138.7, 138.4, 136.6, 132.5, 129.3, 128.9,
128.8, 128.7, 127.3, 127.1, 124.8, 119.6, 115.1, 63.3, 60.4, 39.1, 28.5; $^{13}$C NMR DEPT135 (CDCl$_3$, 151 MHz): $\delta$ 132.5, 129.3, 128.9, 128.8, 128.7, 128.1, 127.3, 127.1, 124.8, 119.6, 63.3 (CH), 60.4 (CH), 39.1 (CH$_2$), 28.5 (CH$_2$); IR ($\nu$/cm$^{-1}$): 3542 (s, br, OH), 3085 (w), 3060 (w), 3028 (w), 2923 (m), 2850 (w), 1639 (m), 1599 (w), 1574 (m), 1495 (m), 1471 (w), 1454 (w), 1446 (w), 1389 (m), 1352 (s), 1266 (w), 1215 (w), 1198 (w), 1164 (s), 1092 (s), 1067 (m), 1058 (m), 1032 (w), 1009 (w); HRMS-(ESI$^+$) [M+H]$^+$ calcd for C$_{24}$H$_{23}$NO$_3$SBr$^-$ 484.0582, found: 484.0591; $[\alpha]_D^{25} = -21.4^\circ$ (c = 1.20, CH$_2$Cl$_2$, l = 100 mm).

4. Prins-cyclization catalyzed by B(C$_6$F$_5$)$_3$:

**Independent preparation of trans-tetrahydropyridine 23**

![Prins-cyclization reaction](image-url)

In a dry, N$_2$-filled glove box, aldehyde 4 (0.0500 mmol, 24.2 mg) and B(C$_6$F$_5$)$_3$ (BCF, 0.0050 mmol, 2.6 mg) were weighed into a screw cap 1 dram vial equipped with a magnetic stir bar. CH$_2$Cl$_2$ (1.00 mL, 0.05 M) was added and the vial was sealed with a septum cap and removed from the glove box. The solution was stirred at 22 °C for 1 h, after which time the catalyst was quenched with 50 µL of Et$_3$N and the solvent was removed in vacuo. The crude residue was purified by silica gel chromatography (5:1 $n$-pentane:ethyl acetate; $R_f = 0.3$) to yield the tetrahydropyridine product 23 as a clear, colorless oil in 99% yield (24.0 mg on a 0.05 mmol scale) and as a single diastereomer (>98:2). Analytical data match that of trans-tetrahydropyridine 23 obtained as the minor product of silylium-catalyzed Prins-cyclization in the absence of trapping nucleophiles (*vide supra*). Absolute configuration was assigned by analogy between the $^1$H NMR spectra of trans-tetrahydropyridine products 23 and S19 (*vide infra*).
Preparation of trans-tetrahydropyridine S19 via B(C₆F₅)₃-catalyzed Prins-cyclization:

In a dry, N₂-filled glove box, aldehyde S16 (0.0500 mmol, 22.8 mg) and B(C₆F₅)₃ (BCF, 0.0050 mmol, 2.6 mg) were weighed into a screw cap 1 dram vial equipped with a stir bar. CH₂Cl₂ (1.00 mL, 0.05 M) was added and the vial was sealed with a septum cap and removed from the glove box. The solution was stirred at 22 °C for 1 h, after which time the catalyst was quenched with 50 µL of Et₃N and the solvent was removed in vacuo. The crude residue was purified by silica gel chromatography (5:1 n-pentane:ethyl acetate; Rf = 0.3) to yield the tetrahydropyridine product S19 as a white, crystalline solid in 99% yield (22.6 mg on a 0.05 mmol scale) and as a single diastereomer (>98:2).

Data for S19

(2S,3R)-2-benzyl-1-(naphthalen-2-ylsulfonyl)-5-phenyl-1,2,3,4-tetrahydropyridin-3-ol (S19). ¹H NMR (CDCl₃, 600 MHz): δ 8.47 (d, 1H, J = 2.0 Hz), 7.96 (dd, 1H, J = 8.0, 1.5 Hz), 7.92 (d, 1H, J = 8.7 Hz), 7.87 (d, 1H, J = 7.3 Hz), 7.80 (dd, 1H, J = 8.7, 1.9 Hz), 7.64-7.57 (m, 2H), 7.41 (dd, 2H, J = 8.2, 1.4 Hz), 7.39-7.35 (m, 3H), 7.34-7.30 (m, 2H), 7.29-7.23 (m, 4H), 4.35-4.29 (m, 1H), 3.92-3.87 (m, 1H), 3.16 (dd, 1H, J = 13.7, 5.4 Hz), 2.72-2.62 (m, 2H), 2.47 (dd, 1H, J = 18.1, 1.6 Hz), 0.94 (d, 1H, J = 7.8 Hz); ¹³C {¹H} NMR (CDCl₃, 151 MHz): δ 138.9, 136.7, 136.2, 135.0, 132.2, 129.7, 129.5, 129.3, 129.1, 128.9, 128.8, 128.5, 128.1, 127.8, 127.1, 127.1, 124.8, 122.2, 120.0, 114.4, 63.3, 60.3, 39.2, 28.4; ¹³C NMR DEPT135 (CDCl₃, 151 MHz): δ 129.7 (CH), 129.5 (CH), 129.3 (CH), 129.1 (CH), 128.9 (CH), 128.8 (CH), 128.5 (CH), 128.1 (CH), 127.8 (CH), 127.1 (CH), 127.1 (CH), 124.8 (CH), 122.2 (CH), 120.0 (CH), 63.3 (CH), 60.3 (CH), 39.2 (CH₂), 28.4 (CH₂); IR (v/cm⁻¹): 3540 (m, br, OH), 3058 (w), 3028 (w), 2925 (m), 2853 (w), 1639 (m), 1596 (w), 1496 (w), 1454 (w), 1447 (w), 1348 (s), 1267 (w), 68
1216 (w), 1198 (w), 1161 (s), 1132 (m), 1076 (m), 1056 (m), 1032 (w); **HRMS-(ESI^+)** [M+H]^+ calcd for C_{28}H_{26}NO_{3}S^+ 456.1634, found: 456.1644; [\alpha]_D^{25} = -74.1^\circ (c = 1.06, CH_2Cl_2, l = 100 mm). A single crystal X-ray structure was obtained from this compound via recrystallization (solvent vapor) from a mixture of CDCl_3/n-pentane. The data indicate a *trans*-di-pseudoequatorial configuration between the amino alcohol R-group and the hydroxyl group.
4a. X-ray crystallographic data and structure for S19:

ORTEP representation of the solid state molecular structure of S19; ellipsoids drawn at 50% probability, the majority of hydrogen atoms are omitted for clarity.

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9 CCDC 1548661 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures. (submission is pending)
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### Parameters

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(major diastereomer A)

Parameter | Value
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(minor diastereomers B/C)
(diastereomers A-C)
Ph
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\]
\[\text{O}
\]
\[\text{O}
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\[\text{Ph}
\]
\[\text{Br}
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\[\text{N}_3
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(major diastereomer A)

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(major diastereomer A)
Ph
O

Ph

Ph

Br

N

S

O

Ph

8 (major diastereomer A)

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### Diagram

**Diastereomers A/B**

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\*\OH
Ph
Cl
```

**Diastereomers A/B**

```
Ph
\P\N\S\O\O\Ph
\*\OH
Ph
Cl
```

**Diastereomers A/B**

```
Ph
\P\N\S\O\O\Ph
\*\OH
Ph
Cl
```
Parameter | Value
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2 Experiment | DEPT-135
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6 Nucleus | 13C
7 Acquired Size | 32768
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(diastereomers A/B)
contains trace 22

contains trace 22

(minor diastereomer C)
(minor diastereomer C)
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Crude spectrum indicating presence of trace desired product 13

![Chemical structure of compound 13](image)
Parameter | Value
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4 Spectral Width | 24038.5
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crude spectrum indicating presence of trace desired product S18

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![Chemical Structure](image1)

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<tr>
<td>4 Nucleus</td>
<td>(1H, 1H)</td>
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<tr>
<td>Parameter</td>
<td>Value</td>
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<td>CDCl3</td>
</tr>
<tr>
<td>2 Experiment</td>
<td>DEPT-135</td>
</tr>
<tr>
<td>3 Spectrometer Frequency</td>
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</tr>
<tr>
<td>4 Spectral Width</td>
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</tr>
<tr>
<td>5 Lowest Frequency</td>
<td>52.5</td>
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<tr>
<td>6 Nucleus</td>
<td>13C</td>
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<tr>
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<tr>
<td>8 Spectral Size</td>
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![Chemical structure image]
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Parameter | Value
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2. Spectrometer Frequency | 600.13
3. Spectral Width | 12019.2
4. Lowest Frequency | -2319.4
5. Nucleus | 1H
6. Acquired Size | 32768
7. Spectral Size | 65536
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