Supporting Information

Alkynyl Prins Carbocyclization Cascades for the Synthesis of Linear-Fused Heterocyclic Ring Systems

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**General Remarks:**

All reactions were carried out under an argon atmosphere in flame-dried glassware with magnetic stirring. Syringe needles used to dispense solvent were not flame-dried. Reagents were used as obtained from commercial suppliers without further purification. Tetrahydrofuran (THF), diethyl ether (Et$_2$O), methylene chloride (DCM), 1,2-dichloroethane (DCE), and toluene (PhMe) were purchased from Fisher and dispensed using the Glass Contour solvent purification system. 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP) was purchased from Oakwood Chemicals and used without further drying (bottle stored in desiccator after opening. Hydrocarbon-stabilized (ChromAR®). 5Å molecular sieves used as desiccants were purchased from Aldrich, stored in an oven, and activated under high vacuum prior to use. Celite 545 was purchased from EMD. ACS grade hexanes, toluene, ethyl acetate, and DCM were used for column chromatography. Thin-layer chromatography (TLC) was performed on pre-coated silica gel 60 F254 glass-supported plates from EMD, and visualization was performed with a UV lamp followed by staining with p-anisaldehyde solution followed by heating. Column chromatography was carried out on EM Science silica gel (60 Å pore size, 230-400 mesh). Preparatory thin-layer chromatography (prep-TLC) was carried out using Analtech Uniplate F254 Prep-20x20 cm TLC plates. High-performance liquid chromatography (HPLC) was performed using Prominence-i LC 2030 Plus with a chiral stationary phase column (Chiralpak AD-H, Daicel Corp, 0.46 cm x 0.15 cm). Deuterated chloroform was purchased from Cambridge Isotope Laboratories.

$^1$H NMR spectra were recorded at room temperature on a 400 MHz Bruker Avance spectrometer or a 500 MHz Bruker Avance spectrometer. Chemical shifts are given in parts per million (ppm) referenced to solvent residual proton resonance (δ = 7.26 for CHCl$_3$). NMR data are reported as: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dq = doublet of quartets, br = broad), coupling constants (J) given in Hz, and integration. In cases where two stereoisomers are present in greater than 2:1 ratio, only chemical shifts from the major stereoisomer are listed. For these cases a characteristic peak from both major and minor stereoisomer is given, with proton integrations, from which the ratio of stereoisomers can be extrapolated. In cases where two stereoisomers are present in less than 2:1 ratio, all peaks are listed. $^1$C NMR spectra were recorded at room temperature unless otherwise stated on a 125 MHz or 101 MHz Bruker Avance spectrometer with proton decoupling. Chemical shifts are given in parts per million (ppm) from referenced to solvent carbon resonance (δ = 77.0 for CHCl$_3$). In cases where two stereoisomers are present in greater than 2:1 ratio, only chemical shifts from the major stereoisomer are listed. For these cases a characteristic peak from both major and minor stereoisomer is given, with proton integrations, from which the ratio of stereoisomers can be extrapolated. In cases where two stereoisomers are present in less than 2:1 ratio, all peaks are listed. For spectra where solvent residue is present, yields were obtained after placing sample under vacuum and bringing to a constant weight. High resolution mass spectra (HRMS) were measured at the University of Rochester Mass
Spectrometry Resource Lab. X-ray crystallography data were collected by Dr. William W. Brennessel at the X-ray Crystallographic Facility of the University of Rochester, Rochester, NY 14627 (USA).

Experimental Details:

**Primary Alcohols:** Alcohols shown in Scheme S1 were prepared according to reported experimental procedures. Sonogashira cross-couplings for 9a, S1a,b, S2, S3, S4, and S9a-c.1-3 Internal alkyne S5 was made following a procedure reported by Sutherland et al.4 Silyl alkyne S6 was made following a procedure by Trost et al.5 Bromo alkyne S7 was prepared using Wang’s procedure.6 Dialkyne S8 was made using Nitz’s conditions.7 Alcohol with a sulfonamide in the tether S10 was made following conditions by Cardenas.8 Characterization data matched the literature reports.

![Scheme S1: Primary Alcohols Synthesized](image)

**Procedures for Preparation of Secondary Alcohols:** Secondary alcohols were prepared by doing a Swern oxidation of the desired primary alcohol to afford an aldehyde to which a Grignard reagent of choice can be added to give products 13a, S11b, S12, and S13.9,10 Alcohol S11a was prepared following the Ito procedure.11 Spectroscopy data matched literature reports.

![Scheme S2: Secondary Alcohols Synthesized](image)  
(a) Made using Bates’s procedure11  
(b) Yield over two-steps.

**Procedure for Preparation of Sulfonamides:** Alpha-primary tosyl amine 15a was prepared following the literature procedure. Spectra for this compound matched what has been reported in the literature.12 Alpha-secondary amine 15b was prepared following the procedure depicted in Scheme S3.13,14
Alpha-Secondary Sulfonamide Preparation:

**Step 1.** A solution of alcohol 9a (3.70 g, 23.3 mmol) and Et$_3$N (14.1 g, 19.5 mL, 140 mmol) in DCM (50 mL) was cooled to 0 °C. Pyridine SO$_3$ (10.9 g, 69.8 mmol) was dissolved in DMSO (50 mL) and added dropwise to the cooled solution over 15 minutes. After addition, the reaction was warmed to room temperature and allowed to stir until full consumption of the alcohol by TLC (using 20% ethyl acetate/hexanes as the mobile phase and p-anisaldehyde to stain the plates). After the reaction was complete, the reaction was diluted with Et$_2$O, washed with 1M HCl until aqueous layer was acidic (pH < 1.0), extracted with Et$_2$O (3 x 100 mL), washed with brine, dried over MgSO$_4$, filtered, and concentrated under vacuum. The crude aldehyde was used in Step 2.

**Step 2.** Crude aldehyde was added to a flask charged with a stir bar and purged with argon, then dissolved in dry THF and cooled to -78 °C. MeMgCl (15.5 mL, 46.6 mmol, 3 M in THF) was added dropwise, then the dry ice/isopropanol bath was removed, and the mixture was allowed to warm up to room temperature. After full consumption of the aldehyde by TLC, the mixture was cooled to 0 °C and saturated ammonium chloride solution was added dropwise to quench the reaction. When the bubbling had subsided, added 1:1 saturated ammonium chloride/water, extracted with Et$_2$O (3 x 100 mL), washed with brine, dried over MgSO$_4$, filtered, and concentrated under vacuum. Crude alcohol was used in the next step.

**Step 3.** The crude alcohol was dissolved in DCM (60 mL) and cooled to 0 °C. MsCl (4.5 mL, 58 mmol) was added in one portion, followed by Et$_3$N (8.1 mL, 58 mmol), which was added dropwise. The reaction was allowed to warm to room temperature slowly overnight. It is important to note that the mesylated alcohol and the starting material are very close in Rf (when 20% ethyl acetate/hexanes is used for the mobile phase). Reaction mixture was poured into a separatory funnel with ice and washed with 1 M HCl. The aqueous layer was washed with Et$_2$O (3 x 50 mL), and the combined organic layers were washed with saturated sodium bicarbonate solution, then with brine, dried over MgSO$_4$, filtered, and concentrated under vacuum. The crude mesylated alcohol was used in the next step.

**Step 4.** The crude mesylated alcohol from Step 3 was dissolved in DMA (60 mL) and sodium azide was added (6.07 g ,93.2 mmol, 4.0 equivalents). The mixture was heated to 60 °C and sonicated for three hours, then moved to an oil bath and heated at 60 °C overnight. After consumption of the starting material by TLC, the reaction was washed with water, extracted with pentane, dried over MgSO$_4$, filtered, and concentrated under vacuum. Crude was used for the next step (3.1 g, 65% crude yield over 4 steps).

**Step 5.** Crude azide from previous step (500 mg, 2.51 mmol) was dissolved in THF (16 mL). PPh$_3$ (1.35 g, 5.02 mmol) was added followed by water (2.05 mL, 120 mmol) and the reaction was allowed to stir at room temperature for an hour before heating to 60 °C overnight. Reaction mixture
was concentrated to remove the THF, diluted with Et₂O, and washed with 1 M HCl (2 x 50 mL). The acidic aqueous layer was washed with EtOAc (3 x 50 mL), then basified with solid NaOH (pH > 12) and extracted with Et₂O (3 x 50 mL), dried over MgSO₄, filtered, and concentrated under vacuum. The crude amine was used in the next step.

**Step 6.** Crude amine from previous step was added to a vial charged with a stir bar, under argon, then dissolved in DCM (10 mL) and cooled to 0 °C. TsCl (484 mg, 2.54 mmol) was added, followed by Et₃N (700 μL, 5.02 mmol). Cold bath was removed, and mixture was allowed to warm to room temperature. After the reaction was complete, water was added, extracted with Et₂O, washed with brine, dried over MgSO₄, filtered, and concentrated under vacuum. Crude was purified by column chromatography, using 10 to 15% EtOAc in hexanes to give sulfonamide 15b (550 mg, 67% over 2 steps) as a yellow, viscous oil.

**Procedures for Preparation of Aldehydes/Ketones:** Aldehydes and ketals were prepared following previously reported procedures. General reaction schemes below show the pathways used for aldehyde/ketal preparation. Spectroscopy data for aldehydes matched literature reports.

**General Procedure for Carbocyclization Cascade:**

**Scheme S5.** General Procedure for Carbocyclization

Oven dried, 5 Å molecular sieves (300 mg/mmol of limiting reagent 4) were transferred to a flask equipped with a stir bar and dried further under vacuum while heating over a Bunsen burner for about 2 minutes. The reaction vessel was allowed to cool under a flow of argon before adding DCM/HFIP (10:1) (0.1 M with respect to the limiting reagent), followed by the alcohol 9/13 (1.2 equivalents) and aldehyde/ketal (1.0 equivalents for aldehydes, 1.5 equivalents for ketals). The reaction mixture was cooled to -40 °C before adding triflic acid (TfOH) (20 mol%) dropwise. Mixture was allowed to stir at -40 °C until all of the limiting reagent was consumed by TLC (using 20% ethyl acetate/hexane mixture as mobile phase and p-anisaldehyde to stain the plates). After completion, the reaction was quenched by adding solid sodium bicarbonate (300 mg/mmol of 10) and diluting with ether (Et₂O). The quenched reaction mixture was filtered through a silica plug, eluted with Et₂O, and concentrated under vacuum. Pure product was isolated after preparatory TLC (using 20% ethyl acetate/hexane as mobile phase) or column chromatography using 5% ethyl acetate/hexane as mobile phase.
Compound 12a was isolated as white solid (30.2 mg, 95%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.33 (t, $J = 7.3$ Hz, 2H), 7.26 (dd, $J = 8.7$, 5.9 Hz, 1H), 7.12 (d, $J = 7.9$ Hz, 2H), 6.72 (s, 1H), 6.25 (s, 1H), 5.87 (s, 1H), 4.02 (dd, $J = 11.1$, 6.9 Hz, 1H), 3.99 $-$ 3.90 (m, 1H), 3.45 (dt, $J = 11.0$, 8.2 Hz, 1H), 2.85 $-$ 2.73 (m, 1H), 2.56 (ddd, $J = 14.0$, 6.7, 2.9 Hz, 1H), 2.53 $-$ 2.45 (m, 2H), 2.42 $-$ 2.32 (m, 1H), 2.32 $-$ 2.23 (m, 1H), 2.05 (dd, $J = 11.8$, 5.6 Hz, 1H), 1.79 $-$ 1.68 (m, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 146.0, 145.7, 141.4, 138.4, 134.7, 134.3, 133.4, 129.9, 128.1, 126.7, 109.6, 108.4, 100.8, 63.3, 39.6, 30.4, 25.0, 22.8; m.p = 95-97°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{21}$H$_{22}$O$_3$: 321.1485, found: 321.1477.

Compound 12b was isolated as white solid (330 mg, 83%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.46 (d, $J = 7.9$ Hz, 2H), 6.99 (d, $J = 7.9$ Hz, 2H), 6.71 (s, 1H), 6.20 (s, 1H), 5.88 (s, 2H), 3.97 (dt, $J = 30.7$, 9.6 Hz, 1H), 3.43 (dd, $J = 18.3$, 9.0 Hz, 1H), 2.73 (dd, $J = 14.9$, 7.6 Hz, 1H), 2.57 $-$ 2.43 (m, 3H), 2.37 (dd, $J = 20.3$, 11.4 Hz, 1H), 2.26 (dd, $J = 19.1$, 11.0 Hz, 1H), 2.05 (s, 1H), 1.71 (s, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 146.2, 145.9, 140.3, 139.2, 134.8, 133.7, 132.3, 131.6, 131.3, 120.8, 109.5, 108.5, 100.9, 77.2, 63.2, 39.6, 30.4, 24.9, 22.9; m.p = 60-63°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{21}$H$_{19}$BrO$_3$: 399.0519, found: 399.0585.

Compound 12c was isolated as viscous oil, as a 1.7:1 of the para-ortho trapped products (57.8 mg, 94%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.37 $-$ 7.30 (m, 4H), 7.30 $-$ 7.24 (m, 5H), 7.19 (dd, $J = 16.1$, 7.9 Hz, 2H), 7.12 (dd, $J = 13.9$, 7.6 Hz, 6H), 6.89 (d, $J = 7.5$ Hz, 1H), 6.79 (s, 2H), 6.74 $-$ 6.67 (m, 3H), 6.64 (d, $J = 8.5$ Hz, 2H), 4.11 (dt, $J = 14.4$, 7.2 Hz, 1H), 4.05 (dt, $J = 16.2$, 8.2 Hz, 2H), 4.00 $-$ 3.89 (m, 3H), 3.80 (s, 6H), 3.57 $-$ 3.43 (m, 3H), 3.32 (s, 4H), 2.93 $-$ 2.75 (m, 4H), 2.58 (dt, $J = 20.6$, 7.0 Hz, 5H), 2.54 $-$ 2.20 (m, 9H), 2.12 $-$ 1.98 (m, 3H), 1.86 $-$ 1.69 (m, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 158.1, 157.0, 142.4, 141.8, 138.5, 137.4, 133.6, 133.3, 130.8, 130.6, 129.9, 129.4, 128.7, 128.31, 128.0, 127.4, 126.6, 125.8, 120.8, 113.6, 111.3, 110.9, 77.4, 76.5, 63.5, 62.9, 55.6, 55.1, 38.8, 38.1, 30.7, 30.5, 25.1, 24.7, 23.1, 21.6; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{21}$H$_{22}$O$_2$: 307.1693, found: 307.1686.

Compound 12d was isolated as a foam (55.1 mg, 89%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.35 (t, $J = 7.4$ Hz, 4H), 7.28 (t, $J = 7.3$ Hz, 2H), 7.24 (d, $J = 7.3$ Hz, 2H), 7.15 (d, $J = 7.6$ Hz, 5H), 7.10 (dd, $J = 14.6$, 7.2 Hz, 3H), 6.78 (d, $J = 7.5$ Hz, 2H), 4.03 (dd, $J = 10.8$, 7.5 Hz, 2H), 3.97 (dd, $J = 11.4$, 8.7, 2.9 Hz, 2H), 3.53 $-$ 3.39 (m, 2H), 2.89 (td, $J = 12.8$, 8.1 Hz, 2H), 2.68 $-$ 2.56 (m, 4H), 2.53
Reaction mixture was allowed to stir at -40 °C for an hour after addition of the acid, then allowed to warm up to room temperature until all of the aldehyde had been consumed. Compound 12e was isolated as a yellow oil (21.1 mg, 31%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.40–7.27 (m, 5H), 7.12 (s, 1H), 7.11 (s, 1H), 7.01 (s, 1H), 3.96 (dd, $J$ = 10.9, 8.2 Hz, 2H), 3.53–3.34 (m, 1H), 2.88 (dd, $J$ = 12.7, 8.2 Hz, 1H), 2.68 (dd, $J$ = 13.0, 6.5 Hz, 1H), 2.64–2.57 (m, 1H), 2.57–2.47 (m, 1H), 2.38 (ddd, $J$ = 28.2, 19.3, 11.4 Hz, 2H), 2.16–2.02 (m, 1H), 1.82–1.68 (m, 1H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 144.6, 141.7, 140.6, 132.9, 129.8, 128.7, 128.4, 127.1, 126.1, 125.3, 123.4, 76.9, 63.4, 39.2, 30.4, 24.8, 23.1; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{21}$H$_{19}$F$_3$O: 345.1461, found: 345.1459.

Reaction was allowed to stir at -40 °C for an hour after addition of TfOH, then warmed up to room temperature until full consumption of starting material was observed by TLC. Compound 12f was isolated as a viscous, colorless oil (33.3 mg, 70%). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.56 (d, $J$ = 7.7 Hz, 1H), 7.48 (t, $J$ = 7.7 Hz, 1H), 7.41 (s, 1H), 7.34 (d, $J$ = 7.6 Hz, 1H), 7.27 (d, $J$ = 6.9 Hz, 1H), 7.15 (dt, $J$ = 21.8, 7.4 Hz, 2H), 6.73 (d, $J$ = 7.6 Hz, 1H), 4.09–3.93 (m, 2H), 3.47 (dd, $J$ = 18.3, 9.6 Hz, 1H), 2.89 (td, $J$ = 12.8, 8.1 Hz, 1H), 2.66 (dd, $J$ = 13.0, 6.5 Hz, 1H), 2.61–2.48 (m, 2H), 2.48–2.28 (m, 2H), 2.17–2.04 (m, 1H), 1.76 (ddd, $J$ = 12.6, 8.3, 5.2 Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 142.3, 140.9, 140.5, 140.2, 133.3, 132.3, 129.4, 128.6, 128.4, 127.1, 126.1, 125.2, 126.2, 77.3, 77.2, 63.3, 39.2, 30.4, 24.9, 23.1. $^{19}$F NMR (250 MHz) δ -62.7. HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{21}$H$_{19}$F$_3$O: 345.1461, found: 345.1459.

Reaction was allowed to stir at -40 °C for an hour after addition of TfOH, then warmed up to room temperature until full consumption of starting material was observed by TLC. Compound 12g was isolated as a viscous oil (22.1 mg, 69%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.15 (d, $J$ = 8.1 Hz, 1H), 8.00 (s, 1H), 7.52 (t, $J$ = 7.8 Hz, 1H), 7.47 (d, $J$ = 7.6 Hz, 1H), 7.28 (dd, $J$ = 12.0, 6.2 Hz, 1H), 7.18 (dd, $J$ = 16.7, 9.2 Hz, 1H), 7.10 (t, $J$ = 7.4 Hz, 1H), 6.68 (d, $J$ = 7.6 Hz, 1H), 4.03 (dd, $J$ = 10.9, 7.5 Hz, 1H), 3.97 (ddd, $J$ = 11.5, 8.6, 2.9 Hz, 1H), 3.49–3.42 (m, 1H), 2.87 (td, $J$ = 12.9, 8.0 Hz, 1H), 2.65 (dd, $J$ = 13.2, 6.4 Hz, 1H), 2.59–2.48 (m, 2H), 2.48–2.38 (m, 1H), 2.33 (dd, $J$ = 19.5, 11.6 Hz, 1H), 2.16–2.05 (m, 1H), 1.78 (ddd, $J$ = 10.1, 6.7, 3.0 Hz, 1H). $^{13}$C NMR (126
Compound 12h was isolated as a foamy viscous oil, as a 6.3:1 mixture of E/Z isomers (22.4 mg, 70%). ^1H NMR (500 MHz, CDCl3) δ 6.72 (s, 1H), 6.67 (s, 1H), 5.93 (d, J = 10 Hz, 1H), 5.51 (dq, J = 15.2, 7.0 Hz, 1H), 3.86 – 3.76 (m, 3H), 3.36 (dt, J = 14.2, 7.2 Hz, 1H), 2.88 (dd, J = 14.7, 6.3 Hz, 1H), 2.54-2.47 (m, 1H), 2.45 – 2.10 (m, 5H), 1.99 (dt, J = 14.8, 7.3 Hz, 1H), 1.78 (d, J = 6.7 Hz, 3H), 1.67 (dt, J = 11.7, 6.3 Hz, 1H); ^13C NMR (126 MHz, CDCl3) δ 146.0, 145.4, 135.4, 134.5, 131.5, 130.0, 128.3, 128.1, 109.7, 108.2, 100.7, 76.5, 62.8, 38.3, 29.8, 24.1, 20.8, 18.6; HRMS (ESI) m/z: [M+H]^+ Calculated for C20H19NO3: 322.1438, found: 322.1437.

Compound 12i was isolated as a white solid, as a 7.9:1 mixture of E/Z isomers (22.4 mg, 75%). ^1H NMR (500 MHz, CDCl3) δ 7.35 (s, 1H), 7.27 (d, J = 8.4 Hz, 1H), 7.04 (d, J = 7.8 Hz, 1H), 6.52 (d, J = 15.5 Hz, 1H), 5.49 (dd, J = 14.9, 7.0 Hz, 1H), 3.88 – 3.76 (m, 2H), 3.38 – 3.29 (m, 1H), 2.79 – 2.68 (m, 1H), 2.59 – 2.47 (m, 1H), 2.47 – 2.36 (m, 2H), 2.21 – 2.12 (m, 1H), 2.05 – 1.94 (m, 1H), 1.80 (d, J = 6.1 Hz, 3H), 1.70-1.60 (m, 1H); ^13C NMR (126 MHz, CDCl3) δ 141.6, 140.0, 131.8, 132.0, 129.7, 129.6, 129.0, 128.6, 127.7, 119.3, 76.2, 62.8, 37.8, 29.3, 23.9, 20.8, 18.6; m.p = 105-107°C; HRMS (ESI) m/z: [M+H]^+ Calculated for C17H19BrO: 319.0692, found: 319.0687.

Compound 12j was isolated as a foamy viscous oil (255 mg, 78%). ^1H NMR (500 MHz, CDCl3) δ 6.67 (s, 1H), 6.60 (s, 1H), 5.99 – 5.81 (m, 2H), 5.61 (s, 1H), 3.89 (t, J = 9.1 Hz, 2H), 3.35 (dd, J = 18.4, 9.0 Hz, 1H), 2.79 – 2.68 (m, 1H), 2.59 (dd, J = 14.3, 7.4 Hz, 1H), 2.51 – 2.34 (m, 6H), 2.34 – 2.24 (m, 1H), 2.16 (dd, J = 18.2, 10.5 Hz, 2H), 2.08 – 1.97 (m, 1H), 1.94 – 1.84 (m, 2H), 1.63 (s, 1H); ^13C NMR (126 MHz, CDCl3) δ 145.8 (2C), 142.6, 137.1, 134.4, 132.5, 130.1, 129.1, 108.6, 108.2, 100.7, 77.1, 63.2, 39.1, 36.0, 32.8, 30.1, 24.9, 23.8, 22.7; HRMS (ESI) m/z: [M+H]^+ Calculated for C20H22O5: 311.1642, found: 311.1636.

Added 40 mol% of TfOH at -40°C, allowed to stir at this temperature for an hour and then warmed to room temperature until all of the aldehyde was consumed. Compound 12k was isolated as a light-yellow oil, as a 3.9:1 inseparable mixture of para/ortho-trapped adduct (33.0 mg, 64%). ^1H NMR (500 MHz, CDCl3) δ 6.74 (d, J = 7.9 Hz, 1H), 6.70 (s, 1H), 6.66 (d, J = 6.8 Hz, 1H), 5.92
(s, 2H), 4.39 – 4.30 (m, 1H), 3.78 (td, J = 11.4, 3.8 Hz, 1H), 3.67 (d, J = 11.4 Hz, 1H), 2.80 (d, J = 14.3 Hz, 1H), 2.70 – 2.60 (m, 1H), 2.55 (dt, J = 13.4, 6.9 Hz, 1H), 2.29-2.13 (m, 3H), 1.92 (s, 3H), 1.77 – 1.67 (m, 4H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 147.7, 145.8, 139.4, 134.9, 129.9, 121.2, 108.9, 108.2, 100.8, 100.7, 72.3, 60.3, 32.7, 31.2, 25.6, 21.4, 16.2; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{16}$H$_{18}$O$_3$: 259.1329, found: 259.1329.

Compound 12l was isolated as white solid (84.3 mg, 92%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.35 (t, J = 6.9 Hz, 2H), 7.28 (d, J = 7.7 Hz, 1H), 7.24 (t, J = 10.3 Hz, 2H), 6.75 (s, 1H), 6.32 (d, J = 1.7 Hz, 1H), 5.88 (d, J = 2.0 Hz, 1H), 4.35 (t, J = 8.6 Hz, 1H), 4.01 (dd, J = 10.0, 6.1 Hz, 1H), 3.98 – 3.88 (m, 1H), 2.99 (dd, J = 16.2, 8.0 Hz, 1H), 2.87 – 2.75 (m, 1H), 2.65 – 2.47 (m, 3H), 2.14 (dd, J = 18.9, 8.7 Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 145.9, 145.8, 141.9, 141.0, 135.0, 134.6, 130.8, 129.3, 128.2, 127.9, 126.8, 109.0, 108.6, 100.8, 78.5, 67.0, 40.3, 32.2, 30.8; m.p = 39-40°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{20}$H$_{18}$O$_3$: 307.1334, found: 307.1323.

Compound 12m was isolated as white solid (82.9 mg, 82%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.31 (t, J = 7.0 Hz, 2H), 7.25 (dd, J = 9.1, 4.6 Hz, 1H), 7.13 (s, 2H), 6.71 (s, 1H), 6.26 (d, J = 1.7 Hz, 1H), 5.89 – 5.82 (m, 2H), 4.05 (d, J = 12.0 Hz, 1H), 4.00 (dd, J = 10.6, 6.0 Hz, 1H), 3.32 – 3.22 (m, 1H), 2.83 – 2.71 (m, 1H), 2.53 – 2.41 (m, 2H), 2.41 – 2.31 (m, 2H), 2.14 – 2.04 (m, 1H), 2.01 (d, J = 11.0 Hz, 1H), 1.72 (s, 2H), 1.53 (d, J = 6.9 Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 146.0, 145.7, 143.2, 141.9, 134.7, 134.6, 134.5, 129.6, 127.9, 126.6, 109.6, 108.1, 100.7, 80.7, 71.7, 40.6, 30.7, 30.4, 29.9, 28.7; m.p = 47-49°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{22}$H$_{22}$O$_3$: 335.1647, found: 335.1634.

Added 40 mol% of TfOH at -40 °C, allowed to stir at this temperature for an hour and then warmed to 0 °C until all of the aldehyde was consumed. Compound 12n was isolated as a white foam (20 mg, 34%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.31 (t, J = 7.4 Hz, 2H), 7.26 – 7.19 (m, 1H), 7.09 (d, J = 7.1 Hz, 2H), 6.67 (s, 1H), 6.34 (s, 1H), 5.89 – 5.82 (m, 2H), 4.02 (d, J = 10.9 Hz, 1H), 3.79 (dd, J = 14.1, 6.8 Hz, 1H), 3.66 (d, J = 11.3 Hz, 1H), 2.77 (dd, J = 12.9, 7.9 Hz, 1H), 2.64 (d, J = 15.0 Hz, 1H), 2.43 (t, J = 12.6 Hz, 1H), 2.35 – 2.23 (m, 1H), 2.17 – 2.06 (m, 1H), 1.99 (dd, J = 16.6, 12.8, 5.4 Hz, 1H), 1.93 – 1.72 (m, 3H), 1.53 (dt, J = 12.0, 7.5 Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 147.1, 145.3, 141.9, 136.8, 135.5, 132.9, 129.2, 128.1, 126.7, 108.9, 108.6, 100.8, 76.3, 61.3, 32.8, 29.7, 27.8, 27.7, 23.7; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{22}$H$_{22}$O$_3$: 335.1642, found: 335.1634.
Added 1.5 equivalents of dimethyl ketal and 1.0 equivalents of alcohol 9a. Stir at -40 °C until all of the alcohol was consumed. Compound 12o was isolated as white solid (38.7 mg, 48%). Recrystallized by dissolving in hot methanol and allowing to cool to room temperature in an uncapped vial. ¹H NMR (500 MHz, CDCl₃) δ 7.32 (t, J = 7.2 Hz, 2H), 7.28 – 7.22 (m, 1H), 7.08 (d, J = 5.5 Hz, 2H), 6.67 (s, 1H), 6.17 (s, 1H), 5.85 (s, 2H), 3.94 – 3.84 (m, 1H), 3.81 (t, J = 9.4 Hz, 1H), 2.95 (dd, J = 19.6, 11.4, 6.4 Hz, 2H), 2.17 – 2.04 (m, 1H), 1.81 – 1.59 (m, 2H), 1.06 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 145.9, 145.7, 143.7, 143.1, 135.0, 134.6, 133.0, 130.1, 128.1, 126.5, 110.0, 108.0, 100.7, 78.1, 58.6, 47.4, 31.5, 25.7, 24.0; m.p = 115-117°C; HRMS (ESI) m/z: [M+H]⁺ Calculated for C₂₂H₂₂O₃: 335.1642, found: 335.1634.

Compound 12p was isolated as white solid (196 mg, 84%). ¹H NMR (500 MHz, CDCl₃) δ 8.20 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 7.1 Hz, 2H), 7.30 (d, J = 5.9 Hz, 3H), 7.26 (s, 1H), 7.23 (d, J = 7.5 Hz, 2H), 7.16 (t, J = 7.7 Hz, 1H), 7.10 (d, J = 6.2 Hz, 2H), 6.89 (t, J = 7.0 Hz, 1H), 6.33 (d, J = 8.0 Hz, 1H), 3.97 (t, J = 9.7 Hz, 2H), 3.68 (dd, J = 14.7, 6.5 Hz, 1H), 3.42 (q, J = 8.9 Hz, 1H), 2.82 (dd, J = 21.5, 13.6 Hz, 1H), 2.73 – 2.62 (m, 1H), 2.53 – 2.39 (m, 3H), 2.37 (s, 3H), 2.07 (d, J = 24.1 Hz, 1H), 1.77 (s, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 144.9, 142.1, 140.5, 139.1, 136.8, 135.8, 129.8, 129.5, 128.8, 128.5, 128.3, 127.1, 126.4, 123.7, 123.2, 121.8, 120.3, 114.9, 78.3, 63.6, 40.9, 25.3, 22.7, 21.8, 21.6; m.p = 78-80°C; HRMS (ESI) m/z: [M+H]⁺ Calculated for C₂₉H₂₇NO₃S: 470.1785, found: 470.1776.

Compound 12q was isolated as white solid (38.2 mg, 52%). ¹H NMR (500 MHz, CDCl₃) δ 7.83 (s, 1H), 7.77 (d, J = 8.1 Hz, 2H), 7.41 (d, J = 1.9 Hz, 1H), 7.30 (t, J = 7.2 Hz, 2H), 7.24 (t, J = 9.6 Hz, 4H), 7.10 (d, J = 7.4 Hz, 2H), 6.90 (s, 1H), 6.42 (s, 1H), 3.93 (dd, J = 20.6, 12.4 Hz, 2H), 3.40 (dd, J = 18.4, 8.9 Hz, 1H), 2.94 (dd, J = 20.7, 12.4 Hz, 1H), 2.74 (dd, J = 12.9, 6.4 Hz, 1H), 2.63 – 2.42 (m, 2H), 2.36 (d, J = 17.2 Hz, 4H), 2.32 – 2.26 (m, 1H), 2.03 (s, 1H), 1.71 (s, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 144.9, 141.9, 138.0, 137.1, 135.4, 133.6, 133.3, 130.0, 129.0, 128.1, 126.7, 126.0, 122.3, 112.5, 109.0, 65.8, 63.2, 38.7, 31.1, 25.0, 22.9, 21.6, 15.3; m.p = 92-95°C; HRMS (ESI) m/z: [M+H]⁺ Calculated for C₂₉H₂₇NO₃S: 470.1785, found: 470.1783.
Compound 12r was isolated as an amorphous solid, as a 1:1 mixture of conformers (96.8 mg, 41%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.68 (d, $J$ = 8.1 Hz, 2H), 7.57 (d, $J$ = 8.1 Hz, 2H), 7.40 (d, $J$ = 4.3 Hz, 2H), 7.34 (s, 2H), 7.31 (d, $J$ = 13.6 Hz, 2H), 7.26 (s, 2H), 7.21 (d, $J$ = 2.3 Hz, 2H), 7.19 – 6.96 (m, 2H), 6.80 (q, $J$ = 8.1 Hz, 2H), 6.57 (s, 2H), 6.04 (d, $J$ = 7.1 Hz, 2H), 5.94 (d, $J$ = 7.5 Hz, 2H), 5.84 (s, 2H), 5.44 (s, 1H), 4.21 – 4.10 (m, 1H), 4.01 (d, $J$ = 7.1 Hz, 2H), 3.90 (dd, $J$ = 25.5, 9.3 Hz, 2H), 3.76 (q, $J$ = 4.3 Hz, 2H), 3.67 – 3.49 (m, 2H), 2.63 – 2.50 (m, 2H), 2.46 (dd, $J$ = 16.9, 10.0 Hz, 2H), 2.32 (d, $J$ = 16.8 Hz, 2H), 2.03 (d, $J$ = 12.9 Hz, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 143.3, 141.0, 140.3, 138.0, 137.4, 137.1, 136.4, 135.4, 134.9, 134.8, 131.5, 131.4, 129.8, 129.8, 129.8, 129.6, 129.5, 128.1, 127.8, 127.8, 127.7, 127.6, 127.5, 126.9, 126.8, 126.5, 126.4, 125.0, 124.2, 123.8, 123.7, 122.7, 122.2, 113.0, 112.4, 98.7, 89.3, 89.2, 81.2, 81.0, 75.0, 74.1, 71.4, 70.0, 68.0, 67.7, 53.4, 53.1, 29.2, 28.9, 28.4, 28.0, 27.9, 27.6, 26.6, 26.0, 25.7, 21.4, 21.4, 16.2, 16.2; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{29}$H$_{28}$NO$_3$S: 470.1785, found: 470.1784.

Compound 12s was isolated as light-yellow solid (49.3 mg, 79%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.44 – 7.36 (m, 2H), 7.34 (d, $J$ = 8.2 Hz, 1H), 7.25 (s, 1H), 7.09 (t, $J$ = 7.7 Hz, 1H), 6.57 (d, $J$ = 7.6 Hz, 1H), 5.97 (d, $J$ = 7.9 Hz, 1H), 4.32 (t, $J$ = 5.7 Hz, 1H), 4.05 (dd, $J$ = 14.5, 5.4 Hz, 1H), 3.60 (td, $J$ = 10.6, 6.8 Hz, 1H), 3.27 – 3.11 (m, 2H), 2.52 – 2.42 (m, 1H), 2.42 – 2.27 (m, 3H), 2.04 (dd, $J$ = 13.8, 9.5 Hz, 1H), 1.80 – 1.67 (m, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 157.3, 153.8, 140.5, 139.2, 129.8, 128.6, 128.3, 127.0, 126.0, 123.0, 121.9, 112.2, 114.8, 110.4, 79.1, 64.7, 32.7, 25.4, 24.3; m.p = 86-88°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{22}$H$_{20}$O$_2$: 317.1536, found: 317.1530.

Compound 12t was isolated as white solid (58.4 mg, 70%). Recrystallized by dissolving in hot methanol and allowing to cool to room temperature in an uncapped vial. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.52 (d, $J$ = 7.7 Hz, 2H), 7.35 (d, $J$ = 8.1 Hz, 1H), 7.11 (t, $J$ = 8.4 Hz, 3H), 6.87 (t, $J$ = 7.5 Hz, 1H), 6.06 (d, $J$ = 7.8 Hz, 1H), 4.29 (s, 1H), 4.04 (t, $J$ = 9.9 Hz, 1H), 3.56 (dd, $J$ = 17.6, 10.0 Hz, 1H), 3.25 – 3.08 (m, 2H), 2.48 – 2.39 (m, 1H), 2.33 (dd, $J$ = 24.7, 6.9 Hz, 2H), 2.04 (d, $J$ = 12.0 Hz, 2H), 1.70 (d, $J$ = 3.5 Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 157.5, 153.9, 140.1, 139.3, 131.5 (2C), 128.3, 124.9, 123.2, 122.1, 121.0 (2C), 114.2, 110.5, 79.0, 64.5, 32.7, 25.2, 24.9, 24.2; m.p = 126-128°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{22}$H$_{19}$BrO$_2$: 395.0641, found: 395.0630.
After addition of TfOH, stirred at -40 °C for 30 minutes before warming to 0 °C until all the starting material was consumed. Compound 16a was isolated as a white solid (24 mg, 54%). 1H NMR (500 MHz, CDCl3) δ 7.59 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.23 (s, 2H), 6.77 (d, J = 6.4 Hz, 2H), 6.75 (s, 1H), 6.23 (s, 1H), 5.93 (d, J = 7.0 Hz, 2H), 4.50 (dd, J = 12.1, 7.3 Hz, 1H), 3.76 – 3.62 (m, 1H), 3.40 (dd, J = 11.9, 6.5 Hz, 1H), 2.64 (td, J = 13.1, 7.4 Hz, 1H), 2.53 – 2.49 (m, 1H), 2.47 (s, 3H), 2.42 (dt, J = 19.9, 6.7 Hz, 1H), 2.29 (td, J = 12.2, 7.2 Hz, 1H), 2.17 (dd, d = 15.8, 6.1, 3.4 Hz, 1H), 1.79 – 1.70 (m, 1H), 1.59 (s, 2H), 1.48 (dd, d = 9.5, 4.0 Hz, 1H); 13C NMR (126 MHz, CDCl3) δ 146.6, 146.2, 142.9, 140.5, 137.5, 135.4, 134.2, 134.0, 130.1, 129.5, 127.9, 127.1, 126.9, 109.4, 108.9, 100.9, 54.5, 41.7, 41.2, 30.9, 26.0, 21.9, 21.5; m.p = 155-157°C; HRMS (ESI) m/z: [M+H]+ Calculated for C28H27NO4S : 474.1734, found: 474.1728.

Compound 14a was isolated as white solid, 9:1 dr (61 mg, 91%). Recrystallized by dissolving in hot methanol and allowing to cool to room temperature in an uncapped vial. 1H NMR (500 MHz, CDCl3) δ 7.33 (t, J = 7.4 Hz, 2H), 7.27 (dd, J = 8.8, 5.6 Hz, 1H), 7.12 (d, J = 7.1 Hz, 2H), 6.72 (d, J = 6.9 Hz, 1H), 6.25 (d, J = 6.1 Hz, 1H), 5.86 (s, 2H), 4.01 (dd, d = 10.7, 7.5 Hz, 1H), 3.48 (dt, J = 6.2, 4.1 Hz, 1H), 2.80 (td, J = 12.6, 7.9 Hz, 1H), 2.56 (td, J = 12.3, 6.4 Hz, 1H), 2.49 (dd, J = 12.9, 7.0 Hz, 2H), 2.40 (dd, J = 21.4, 11.4 Hz, 1H), 2.20 (td, J = 11.5, 8.2 Hz, 1H), 1.94 – 1.82 (m, 1H), 1.73 (dd, J = 20.9, 9.8 Hz, 1H), 1.24 (d, J = 4.8 Hz, 3H); 13C NMR (126 MHz, CDCl3) δ 145.9, 145.7, 141.6, 139.2, 134.8, 134.3, 133.0, 129.8, 128.1, 126.7, 109.6, 108.4, 100.7, 77.9, 40.1, 33.5, 30.4, 23.0, 22.3; m.p = 132-135°C; HRMS (ESI) m/z: [M+H]+ Calculated for C22H22O3: 335.1642, found: 335.1642.

Compound 14b isolated as a white solid, 7:1 dr (53.3 mg, 83%). 1H NMR (500 MHz, CDCl3) δ 7.36 (t, J = 7.3 Hz, 4H), 7.27 (dd, J = 14.5, 6.8 Hz, 3H), 7.19 (d, J = 7.0 Hz, 4H), 6.72 (s, 2H), 6.29 (s, 2H), 5.99 – 5.82 (m, 4H), 5.08 (d, J = 10.0, 3.0 Hz, 2H), 5.06 (d, J = 10.0, 5.9 Hz, 2H), 2.98 – 2.84 (m, 4H), 2.74 – 2.61 (m, 2H), 2.51 (dd, J = 12.6, 4.3 Hz, 2H), 2.22 (dd, J = 14.2, 9.4 Hz, 4H), 1.30 (d, J = 5.9 Hz, 7H); 13C NMR (126 MHz, CDCl3) δ 145.8, 142.5, 142.0, 134.9, 134.1, 131.1, 129.4, 128.8, 128.4, 128.0, 126.8, 108.9, 108.7, 100.8, 128.1, 126.7, 109.6, 108.4, 100.7, 77.5, 42.6, 39.6, 30.8, 20.8; m.p = sample decomposed after heating to 100°C; HRMS (ESI) m/z: [M+H]+ Calculated for C21H20O3: 321.1491, found: 321.1481.

Compound 14c isolated as a white amorphous solid, 13:1 (43.7 mg, 63%). 1H NMR (500 MHz, CDCl3) δ 7.31 (t, J = 7.1 Hz, 2H), 7.27 – 7.21 (m, 1H), 7.12 (s, 2H), 6.72 (s, 1H), 6.26 (s, 1H),
5.87 (s, 2H), 4.01 (dd, \( J = 11.3, 6.3 \) Hz, 1H), 3.39 (d, \( J = 6.4 \) Hz, 1H), 2.81 – 2.70 (m, 1H), 2.53 – 2.41 (m, 2H), 2.36 (s, 2H), 2.10 (t, \( J = 11.2 \) Hz, 1H), 1.98 (d, \( J = 7.6 \) Hz, 1H), 1.74 (d, \( J = 11.0 \) Hz, 1H), 1.51 (dd, \( J = 22.8, 14.1 \) Hz, 2H), 1.15 (d, \( J = 6.2 \) Hz, 3H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \( \delta \) 145.9, 145.7, 143.9, 141.9, 134.9, 134.6, 134.1, 129.7, 127.9, 126.6, 109.6, 108.1, 100.7, 79.6, 77.5, 40.7, 37.2, 30.4, 29.6, 28.3, 23.2; HRMS (ESI) m/z: [M+H]+ Calculated for C\(_{23}\)H\(_{24}\)O\(_3\): 349.1804, found: 349.1792.

**Compound 14d** isolated as an amorphous white solid, \( >20:1 \) dr (28 mg, 96%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.34 (t, \( J = 7.2 \) Hz, 5H), 7.31 – 7.25 (m, 3H), 7.23 (d, \( J = 7.1 \) Hz, 2H), 7.14 (d, \( J = 6.7 \) Hz, 6H), 7.09 (dd, \( J = 14.8, 7.2 \) Hz, 3H), 6.77 (d, \( J = 7.4 \) Hz, 2H), 4.01 (dd, \( J = 9.8, 7.4 \) Hz, 2H), 3.55 – 3.43 (m, 2H), 2.88 (t, \( J = 11.4 \) Hz, 2H), 2.60 (dt, \( J = 12.0, 6.5 \) Hz, 4H), 2.55 – 2.48 (m, 2H), 2.43 (dd, \( J = 21.5, 11.1 \) Hz, 2H), 2.31 – 2.20 (m, 2H), 1.94 – 1.83 (m, 2H), 1.74 (dd, \( J = 20.5, 10.0 \) Hz, 2H), 1.24 (d, \( J = 5.0 \) Hz, 3H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \( \delta \) 141.8, 141.1, 140.9, 139.7, 133.2, 129.9, 129.5, 128.2, 128.1, 126.6, 125.9, 77.9, 70.6, 39.7, 33.5, 30.4, 23.3, 22.3; HRMS (ESI) m/z: [M+H]+ Calculated for C\(_{21}\)H\(_{22}\)O: 291.1749, found: 291.1742.

**Compound 14e** isolated as an amorphous solid, \( >20:1 \) dr (55.0 mg, 99%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.35 (t, \( J = 7.2 \) Hz, 2H), 7.27 (t, \( J = 6.8 \) Hz, 1H), 7.13 – 7.03 (m, 2H), 6.80 (d, \( J = 7.2 \) Hz, 1H), 4.32 (t, \( J = 8.2 \) Hz, 1H), 4.09 – 3.99 (m, 1H), 3.04 – 2.88 (m, 2H), 2.74 – 2.65 (m, 1H), 2.62 (d, \( J = 12.6 \) Hz, 1H), 2.24 (dd, \( J = 22.5, 12.7 \) Hz, 2H), 1.30 (d, \( J = 4.9 \) Hz, 3H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \( \delta \) 142.6, 140.8, 140.7, 131.3, 129.5, 128.7, 128.6, 128.4, 126.7, 126.5, 125.9, 78.7, 75.4, 42.2, 39.7, 30.8, 20.8; HRMS (ESI) m/z: [M+H]+ Calculated for C\(_{20}\)H\(_{20}\)O: 277.1592, found: 277.1584.

**Compound 14f** isolated as an amorphous solid, 8:1 dr (50.4 mg, 99%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.31 (t, \( J = 7.0 \) Hz, 108H), 7.24 (dd, \( J = 14.6, 6.8 \) Hz, 125H), 7.16 – 7.07 (m, 203H), 6.77 (d, \( J = 7.3 \) Hz, 46H), 4.00 (dd, \( J = 11.2, 7.0 \) Hz, 46H), 3.38 (d, \( J = 6.4 \) Hz, 43H), 2.90 – 2.78 (m, 48H), 2.60 – 2.53 (m, 55H), 2.53 – 2.44 (m, 44H), 2.38 (d, \( J = 11.5 \) Hz, 101H), 2.20 – 2.08 (m, 48H), 2.00 (d, \( J = 11.0 \) Hz, 48H), 1.74 (d, \( J = 12.4 \) Hz, 52H), 1.63 – 1.45 (m, 101H), 1.14 (d, \( J = 6.0 \) Hz, 150H), 1.06 (t, \( J = 10.1 \) Hz, 8H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \( \delta \) 144.2, 142.1, 141.8, 140.8, 134.2, 129.8, 129.4, 127.9, 127.8, 126.7, 126.5, 126.0, 79.4, 77.5, 40.4, 37.2, 30.5, 29.5, 28.3, 23.2; HRMS (ESI) m/z: [M+H]+ Calculated for C\(_{22}\)H\(_{23}\)O: 305.1905, found: 305.1897.
Compound 14g isolated as a viscous oil, 16:1dr (155 mg, 98%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.37 (t, $J$ = 7.3 Hz, 2H), 7.31 (t, $J$ = 7.0 Hz, 1H), 7.26 (s, 1H), 7.21−7.09 (m, 4H), 6.81 (d, $J$ = 7.4 Hz, 1H), 5.86 (ddt, $J$ = 17.0, 10.3, 6.9 Hz, 1H), 5.13 (d, $J$ = 17.2 Hz, 1H), 5.07 (d, $J$ = 10.3 Hz, 1H), 4.04 (dd, $J$ = 10.9, 6.8 Hz, 1H), 3.43 (dt, $J$ = 9.1, 6.5 Hz, 1H), 2.93 (dt, $J$ = 14.6, 7.4 Hz, 1H), 2.70−2.62 (m, 2H), 2.62−2.54 (m, 1H), 2.51−2.38 (m, 2H), 2.35−2.23 (m, 2H), 1.95−1.80 (m, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 141.7, 141.1, 140.8, 139.7, 134.8, 133.2, 129.9, 129.4, 128.2, 128.1, 126.6, 125.9, 116.6, 78.0, 74.0, 40.9, 39.6, 31.5, 30.4, 23.0; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{23}$H$_{34}$O: 317.1900, found: 317.1898.

Compound 14h isolated as a viscous oil, 3:4:1dr (56.6 mg, 90%) or 2:8:1 dr (282 mg, 90%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.35 (t, $J$ = 7.1 Hz, 1H), 7.29 (dd, $J$ = 13.4, 6.5 Hz, 1H), 7.23 (t, $J$ = 6.8 Hz, 1H), 7.18−7.07 (m, 2H), 6.78 (d, $J$ = 7.4 Hz, 1H), 4.05 (dt, $J$ = 18.3, 9.2 Hz, 1H), 3.61−3.51 (m, 1H), 2.96−2.85 (m, 1H), 2.70−2.34 (m, 3H), 2.28 (dt, $J$ = 19.6, 9.8 Hz, 1H), 2.05−1.85 (m, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 141.6, 140.9, 140.8, 138.9, 133.5, 130.0, 129.9, 129.5, 128.2, 128.1, 126.7, 125.9, 80.9, 78.1, 72.6, 69.5, 39.6, 31.2, 30.3, 26.2, 23.0. HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{23}$H$_{34}$O: 315.1744, found: 315.1741.

![Structure](image_url)

Added 1.5 equivalents of dimethyl ketal and 1.0 equivalent of alcohol 13a. Stir at -40°C until all of the alcohol was consumed. Compound 14i was isolated as an amorphous solid, 1:2:1 dr (70.6 mg, 51%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.43−7.38 (m, 0.8H, minor diastereomer), 7.36−7.29 (m, 4H), 7.29−7.21 (m, 2H), 7.20−7.14 (m, 2H), 7.13−7.04 (m, 4H), 7.01 (dd, $J$ = 13.8, 6.1 Hz, 1H), 6.90 (d, $J$ = 7.2 Hz, 0.8H, minor diastereomer), 6.68 (t, $J$ = 7.6 Hz, 1H), 4.11−4.02 (m, 1H), 3.99−3.92 (m, 0.8H, minor diastereomer), 3.29 (d, $J$ = 7.3 Hz, 0.8H, minor diastereomer), 3.13−2.97 (m, 1H), 2.82 (d, $J$ = 13.9 Hz, 0.8H, minor diastereomer), 2.69−2.56 (m, 1H), 2.49−2.28 (m, 4H), 2.16−2.05 (m, 1.8H), 1.78−1.64 (m, 3H), 1.56−1.41 (m, 2H), 1.22 (dd, $J$ = 9.4, 6.3 Hz, 4H), 1.15 (s, 3H), 1.00 (s, 2.5H, minor diastereomer). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 144.4, 143.3, 143.2, 142.1, 141.8, 141.0, 140.1, 133.4, 133.0, 130.5, 130.4, 129.9, 129.6, 128.6, 128.2, 128.2, 128.2, 127.9, 127.7, 127.5, 127.3, 126.6, 126.5, 126.4, 126.3, 126.0, 125.5, 78.5, 78.4, 71.7, 64.3, 63.3, 49.3, 46.4, 34.4, 33.2, 32.3, 31.1, 30.4, 30.3, 29.9, 26.8, 26.2, 25.8, 24.8, 23.1, 22.8, 20.9, 17.0; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{22}$H$_{24}$O: 305.1900, found: 305.1897.

![Structure](image_url)

Added 1.5 equivalents of dimethyl ketal and 1.0 equivalents of alcohol 13a. Stir at -40°C for an hour, then warmed to 0°C until all of the alcohol was consumed. Compound 14j was obtained as a crystalline solid, 1:6:1 dr (21.6 mg, 28%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.36 (d, $J$ = 6.8 Hz, 2H), 7.31−7.27 (m, 1H), 7.18−7.11 (m, 4H), 7.01−6.96 (m, 1H), 6.82 (d, $J$ = 7.8 Hz, 1H), 5.73 (t, $J$ = 7.0 Hz, 1H), 3.67−3.58 (m, 1H), 3.15 (dd, $J$ = 12.4, 7.9 Hz, 1H), 2.93−2.84 (m, 1H), 2.67−2.57 (m,
1H), 2.54 – 2.38 (m, 2H), 1.52 – 1.40 (m, 3H), 1.32 (d, J = 8.8 Hz, 2H), 1.08 (dd, J = 6.3, 3.7 Hz, 3H), 1.04 (d, J = 6.1 Hz, 3H), 0.98 (d, J = 6.1 Hz, 3H, corresponds to the alpha methyl of the minor diastereomer), 0.81 (d, J = 6.8 Hz, 3H). 13C NMR (126 MHz, CDCl₃) δ 143.8, 143.8, 143.4, 143.2, 141.8, 141.1, 140.9, 140.1, 138.9, 130.6, 130.5, 130.2, 130.0, 128.3, 128.1, 126.9, 126.7, 126.6, 125.5, 124.8, 122.4, 122.4, 68.0, 67.1, 39.4, 39.1, 33.7, 29.9, 29.7, 28.2, 27.9, 23.3, 23.1, 23.0, 22.8, 20.5; m.p = 108–110°C; HRMS (ESI) m/z: [M+H]+ Calculated for C₂₄H₂₈O:

After addition of TfOH, stirred at -40 °C for 30 minutes before warming to 0 °C until all the starting material was consumed. Compound 16b was isolated as an amorphous white solid, >20:1 dr (50 mg, 56%). 1H NMR (400 MHz, CDCl₃) δ 8.04 (d, J = 7.7 Hz, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.43 (d, J = 7.3 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.33 – 7.24 (m, 4H), 7.24 – 7.15 (m, 4H), 7.08 (d, J = 7.5 Hz, 2H), 4.43 (s, 1H), 3.32 (t, J = 4.5 Hz, 1H), 2.40 (dd, J = 14.8, 6.3 Hz, 1H), 2.31 (d, J = 6.5 Hz, 3H), 2.15 (dddd, J = 28.8, 16.9, 14.6, 4.9 Hz, 6H), 1.38 (dd, J = 12.1, 5.8 Hz, 1H), 1.30 – 1.19 (m, 2H), 1.12 (d, J = 6.8 Hz, 3H). 13C NMR (126 MHz, CDCl₃) δ 145.0, 143.7, 142.2, 136.1, 135.2, 133.7, 128.4, 128.2, 128.0, 126.6, 125.8, 124.8, 122.5, 51.5, 48.4, 32.4, 30.6, 23.5, 21.4, 18.7, 17.8. HRMS (ESI) m/z: [M+H]+ Calculated for C₂₈H₁₆NO₂S: 444.1992, found: 444.1984.

Compound 19 was isolated as a white solid (394 mg, 89%). 1H NMR (500 MHz, CDCl₃) δ 7.62 (d, J = 8.1 Hz, 2H), 7.34 (d, J = 6.8 Hz, 3H), 7.30 (d, J = 8.0 Hz, 3H), 7.22 (d, J = 8.5 Hz, 1H), 7.18 (t, J = 7.3 Hz, 1H), 7.13 (t, J = 7.4 Hz, 1H), 6.80 (d, J = 7.7 Hz, 1H), 4.37 (d, J = 11.5 Hz, 1H), 4.01 (dd, J = 11.7, 6.9 Hz, 1H), 3.94 – 3.86 (m, 1H), 3.69 (d, J = 13.4 Hz, 1H), 3.54 (d, J = 11.3 Hz, 2H), 3.00 – 2.92 (m, 1H), 2.83 – 2.73 (m, 1H), 2.56 (dd, J = 13.1, 7.1 Hz, 1H), 2.48 (dd, J = 12.9, 6.8 Hz, 1H), 2.43 (s, 3H), 2.03 (dd, J = 20.4, 11.8 Hz, 1H); 13C NMR (126 MHz, CDCl₃) δ 143.5, 141.8, 140.7, 140.4, 139.6, 134.7, 134.0, 130.5, 129.8, 129.6, 128.0, 127.8, 127.7, 127.7, 126.3, 79.3, 68.8, 49.4, 47.9, 40.1, 30.0, 21.5; m.p = compound turns brown after 95 °C; HRMS (ESI) m/z: [M+H]+ Calculated for C₂₈H₂₇NO₃S: 490.1683, found: 490.1676.

Greater than 1.0 mmol Scale Experiments:

**Scheme S6.** General Procedure for Carbocyclizations (>1.0 mmol scale)
Oven dried, 5 Å molecular sieves (1.5 g) were transferred to a 100 mL flask equipped with a stir bar and dried further under vacuum while heating over a Bunsen burner for about 3 minutes. The reaction vessel was allowed to cool under a flow of argon before adding DCM/HFIP (10:1) (50 mL), followed by the alcohol 9a (961 mg, 6.0 mmol, 1.2 equivalents) and aldehyde 10a (891 mg, 5.0 mmol, 1.0 equivalents). The reaction mixture was cooled to -40 °C before adding triflic acid (TfOH) (88 μL, 20 mol%) dropwise. Mixture was allowed to stir at -40 °C until all of the limiting reagent was consumed by TLC (using 20% ethyl acetate/hexane mixture as mobile phase and p-anisaldehyde to stain the plates). After completion, the reaction was quenched by adding solid sodium bicarbonate (1.5 g) and diluting with ether (Et₂O). The quenched reaction mixture was filtered through a silica plug, eluted with Et₂O, and concentrated under vacuum. Crude was purified by column chromatography, using 5% ethyl acetate/hexane as mobile phase. Pure product 12a was obtained as a pale yellow amorphous solid (1.3 g, 81%).

**Procedure for Deprotection of N-Tosyl Piperidines:**

**Scheme S7. General Procedure for Piperidine Detosylation**

In a flame-dried 25 mL round bottom flask under argon, prepared a 1.0M solution of naphthalene (640 mg, 5.0 mmol) in dry dimethoxyethane (DME, 5.0 mL) and cooled to 0 °C. Na (140 mg, 6.0 mmol) that had been cut into small cubes was added and the mixture was stirred vigorously at 0 °C for about 15 minutes, then warmed up to room temperature and allowed to stir for 1 hour. The deep green solution (162 μL, 0.162 mmol, 4.0 equivalents) was added dropwise to a 0.2 M solution of sulfonamide 16a (19.2 mg, 0.0405 mmol) in DME (0.4 mL). The drops were added slowly, allowing time for the coloration to disappear before the next addition. After 5 minutes, 1M HCl was added to quench the reaction. Acidic mixture was washed with Et₂O (2 x 15 mL) and the ethereal layer was discarded. The aqueous layer was then basified by adding solid NaOH and extracted with Et₂O (3 x 15 mL), dried over MgSO₄, filtered, and concentrated under vacuum to afford amine 17a as a yellow oil, no further purification needed. ¹H NMR (500 MHz, CDCl₃) δ 7.31 (t, J = 7.4 Hz, 2H), 7.24 (s, 1H), 7.10 (d, J = 7.5 Hz, 2H), 6.71 (s, 1H), 6.25 (s, 1H), 5.86 (s, 2H), 3.42 – 3.36 (m, 1H), 3.00 (dt, J = 12.6, 6.2 Hz, 1H), 2.75 (ddd, J = 25.4, 13.2, 7.4 Hz, 2H), 2.60 (dt, J = 14.9, 4.8 Hz, 1H), 2.49 (dd, J = 13.2, 6.1 Hz, 1H), 2.37 – 2.19 (m, 3H), 2.04 (s, 1H), 1.86 – 1.76 (m, 1H), 1.65 (dt, J = 12.0, 5.9 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 145.9, 145.8, 141.7, 138.6, 135.0, 134.8, 134.1, 129.9, 128.1, 126.6, 109.7, 108.5, 100.7, 55.8, 41.2, 40.4, 31.3, 25.4, 24.8. HRMS (ESI) m/z: [M+H]⁺ Calculated for C₂₁H₂₁NO₂: 320.1645, found: 320.1638.
Explanation of Acetal Byproduct (Observed in the absence of HFIP, and for cases 12k and 12n):

In less efficient alkynyl Prins reactions, it is notable that acetal S14 and tricycle 12 are the only products observed in significant quantities. During optimization, the acetal S14a was isolated in 15% yield when HFIP was left out of the reaction mixture. Using the optimized conditions (HFIP present), the acetal was also observed in two other cases, namely 12k and 12n. For alkyne 9k (R=Me; n=1), the reaction produces the corresponding acetal S14b exclusively when left at -40°C. Higher temperatures are required for the alkynyl Prins/carbocyclization to occur. For the extended chain arenyne 9n (R=Ph; n=2) acetal S14c is isolated as the major product when the reaction is left to stir at -40 °C. Once again, warming is required to push the acetal to undergo cyclization (Scheme S8B). The combination of HFIP and the adjacent π-system in R (arene/alkene) helps stabilize 11b-2 (-1.2 kcal/mol relative to the oxocarbenium, Scheme S8C), improving the efficiency of arene capture and disfavoring the reversibility of the Prins, back to 11a-2. The vinyl cation produced from 9k (R = Me), however, has no adjacent π-system, which could account for the reduced efficiency (+6.4 kcal/mol relative to the oxocarbenium, Scheme S8C).21 For the 12n case (m = 2), it seems logical that the longer tether makes capture of the vinyl cation less efficient. This, when 11b is either unstable, or has a poorly aligned arene, oxocarbenium 11a is trapped by a second molecule of alcohol 9. We also note that in these inefficient cases, numerous other undesired byproducts form over the course of the experiment, ultimately compromising the yield of the reaction.

A possible explanation for these observations is shown in Scheme S8. The reversal of the alkyn/oxocarbenium ring closure is similar to the Eshenmoser class of fragmentations,22 which could establish an equilibrium between oxocarbenium 11a and vinyl cation 11b (Scheme S8A). This is supported by DFT calculations, which show that generation of the vinyl cation 11b-1, is endergonic for 9k, and slightly exergonic in the case of 11b-2 for arenyne 9a (Scheme S8C). Either way, the energetic barrier is readily available in both directions. At the vinyl cation stage 11b, it is plausible for the oxacycle to open and regenerate the oxocarbenium 11a, or to undergo carbocyclization after aryl trapping of the vinyl cation, terminating the process.

**Scheme S8.** A. Explanation of Acetal Byproducts Observed. B. Acetals Isolated C. DFT Backing for Plausible Reversibility of Alkynyl Prins Step (Theory level: M062X/Def2TZVP, Solvation: CPCM: Dichloromethane, Energy in kcal/mol).
a) Isolated from the reaction of 9a with aldehyde 10a, in the absence of HFIP (See Table 1, Entry 1) b) Isolated from the reaction of 9k with aldehyde 10a, using 40 mol% TfOH and quenching after stirring at -40 °C c) Isolated from the reaction of 9n with the longer-tether aldehyde, using 40 mol% TfOH and quenching after stirring at -40 °C.

**Compound S14a.** Acetal isolated as a yellow solid after preparatory TLC with 20% ethyl acetate in hexanes as the mobile phase (14 mg, 15%). S14a was observed as the major byproduct of subjecting 9a and 10a to 20 mol% TfOH in dichloromethane (no HFIP), in the presence of molecular sieves. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.37 (s, 3H), 7.26 (s, 9H), 6.72 – 6.58 (m, 3H), 5.90 (d, $J$ = 4.3 Hz, 2H), 4.51 (dd, $J$ = 12.8, 5.0 Hz, 1H), 3.76 (d, $J$ = 5.5 Hz, 1H), 3.64 – 3.55 (m, 1H), 2.62 (s, 2H), 2.58 – 2.50 (m, 3H), 1.98 – 1.81 (m, 5H), 1.58 (s, 1H), 1.22 (t, $J$ = 5.6 Hz, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 147.6, 145.6, 135.6, 135.6, 131.5, 128.2, 127.6, 123.9, 121.1, 108.9, 108.1, 102.4, 102.2, 100.7, 89.4, 81.0, 64.0, 63.8, 61.2, 35.3, 35.2, 30.7, 29.0, 16.3, 15.4. HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{32}$H$_{32}$O$_4$: 481.2374, found: 481.2366.

**Compound S14b.** Acetal isolated as a yellow oil after preparatory TLC with 20% ethyl acetate in hexanes as the mobile phase (43 mg, 60%). S14b was observed as the major product when the Prins/carbocyclization with alcohol 9n was quenched after stirring at -40 °C and full consumption of the aldehyde was observed by TLC. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.73 (s, 3H), 7.26 (s, 9H), 6.72 (d, $J$ = 7.9 Hz, 1H), 6.69 (s, 1H), 6.64 (d, $J$ = 7.8 Hz, 1H), 5.91 (s, 2H), 4.46 (t, $J$ = 5.5 Hz, 1H), 3.66 (dt, $J$ = 9.2, 6.2 Hz, 2H), 3.50 (dt, $J$ = 9.2, 6.2 Hz, 2H), 2.66 – 2.56 (m, 2H), 2.24 (dd, $J$ = 9.1, 6.7 Hz, 4H), 1.88 (dd, $J$ = 15.1, 6.2 Hz, 2H), 1.77 (d, $J$ = 1.9 Hz, 6H), 1.73 (dd, $J$ = 13.2, 6.6 Hz, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 147.5, 145.6, 135.6, 121.1, 108.9, 108.1, 102.2, 100.7, 89.4, 81.0, 64.0, 63.8, 61.2, 35.3, 35.2, 30.7, 29.0, 16.3, 15.4. HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{22}$H$_{28}$O$_4$: 357.2061, found: 357.2059.

**Compound S14c.** Acetal isolated as a yellow oil after preparatory TLC with 20% ethyl acetate in hexanes as the mobile phase (19 mg, 27%). S14c was observed as the major product when the
reaction was quenched after stirring at -40 °C and full consumption of the aldehyde was observed by TLC. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.44 – 7.35 (m, 2H), 7.29 – 7.26 (m, 2H), 6.84 (s, 1H), 6.54 (s, 1H), 5.88 (d, $J =$ 6.5 Hz, 2H), 4.31 (t, $J =$ 4.4 Hz, 1H), 3.68 (dt, $J =$ 9.1, 6.2 Hz, 1H), 3.58 – 3.47 (m, 1H), 2.72 (dt, $J =$ 16.3, 5.4 Hz, 1H), 2.61 (dd, $J =$ 14.8, 7.0 Hz, 1H), 2.45 (t, $J =$ 6.8 Hz, 2H), 2.00 – 1.63 (m, 9H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 146.9, 145.7, 131.5, 131.0, 130.2, 128.1, 127.9, 127.5, 124.0, 119.9, 108.9, 108.4, 100.6, 90.0, 80.8, 75.5, 68.0, 29.4, 29.4, 27.9, 25.6, 19.2, 19.0. HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{33}$H$_{34}$O$_4$: 495.2530, found: 495.2522.

Unsuccessful Carbocyclization Substrates:

Alkyne alcohols (highlighted in red) S6-S9 failed to give carbocyclization adducts S15-S18. Complex product mixtures were observed after subjecting these alcohols to the reaction conditions. Terminal alkynes also did not react cleanly and no S18 was isolated.

Carbocyclization adducts S20-S23 did not form under the reaction conditions (aldehyde portion highlighted in red). Aldehyde decomposition was observed in the cases of S20 and S21. In the cases S22 and S23, where the aldehyde had a heteroatom in the tether, recovery of unreacted starting material was observed and decomposition to complex mixtures.

Diversification of Carbocyclization Products:

**Hydrogenations:**

A few different hydrogenation catalysts were explored. Since the olefin at hand was tetrasubstituted, we started with Crabtree catalyst [Ir(cod)(PCy$_3$)(pyr)]PF$_6$, which is known to reduce highly hindered alkenes.$^{23, 24}$ These conditions led to recovery of starting material 12a (Entry 1, Table S1). More recent conditions by Chirk et al. are successful at reducing difficult olefins using a Ni catalyst that is generated in situ after mixing Ni(octanoate)$_2$ with HBPin and an α-diimine ligand (iPrDI) in benzene.$^{25}$ These conditions, however, failed to afford hydrogenated product 21a. To our delight, using 20 mol% of 5% palladium on carbon (Pd/C) with 55 atmospheres of hydrogen. See below.

**Table S1.** Screen of Catalysts for Hydrogenation of 12a
| Entry | Catalyst | Solvent | H$_2$ (atm) | Result |
|-------|----------|---------|------------|--------|
| 1$^{23}$ | [Ir(cod)(PCy$_3$)(pyr)]PF$_6$ | DCM | 1-35 | 100% 12a |
| 2$^{25}$ | Ni(octanoate)$_2$, HBpin, iPrDI | C$_6$H$_6$ | 1-4 | 100% 12a |
| 3$^a$ | Pd/C (20 mol %) | MeOH/DCM | 55 | Quant. 21a |

**General Procedure for hydrogenation:** To a scintillation vial charged with stir bar and compound 12a (32 mg, 0.1 mmol), added DCM (0.3 mL) followed by Pd/C (42 mg, 0.02 mmol Pd, 5% Pd on C). Some additional DCM was added to wash the Pd/C off the sides of the vial. Added MeOH (1.7 mL) and the vial was placed in a bomb reactor, on a stir plate. Pressure was brought up to 55 atm, then purged, refilled back up to 55 atm, and allowed to stir at room temperature for 48 hours. After this time, the hydrogen gas was released and the mixture was carefully filtered through celite, washed with DCM, concentrated, and purified by preparatory TLC using 30% EtOAc in hexanes as the mobile phase. Product was obtained as a 1:1 mixture of separable diastereomers (32 mg, 100% combined yield).

Compound 21a-1 was obtained as a white, crystalline solid (15.4 mg, 48%). Recrystallized after dissolving in hot methanol and allowing to cool to room temperature in an uncapped vial. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.24 (d, $J$ = 7.2 Hz, 2H), 7.19 (s, 3H), 6.62 (s, 1H), 6.49 (s, 1H), 5.88 (d, $J$ = 5.9 Hz, 2H), 4.02 (s, 1H), 3.90 (d, $J$ = 10.2 Hz, 1H), 3.28 (t, $J$ = 10.7 Hz, 2H), 3.00 (d, $J$ = 11.7 Hz, 1H), 2.75 (dd, $J$ = 15.7, 8.8 Hz, 1H), 2.34 – 2.25 (m, 1H), 2.22 (d, $J$ = 10.6 Hz, 1H), 1.92 (d, $J$ = 12.2 Hz, 1H), 1.75 (tt, $J$ = 24.6, 12.3 Hz, 4H), 1.66 – 1.54 (m, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 145.9, 145.7, 142.0, 134.5, 129.7, 127.8, 126.1, 111.5, 110.7, 100.8, 78.7, 67.9, 56.1, 43.7, 34.3, 31.1, 30.7, 30.3, 27.2, 26.6; m.p = 127-130°C; HRMS (ESI) m/z: [M+H]$^+$ Calculated for C$_{21}$H$_{22}$O$_3$: 323.1642, found: 323.1639.

Compound 21a-2 was obtained as an amorphous solid (16.6 mg, 52% yield). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.35 (t, $J$ = 7.3 Hz, 2H), 7.28 (d, $J$ = 7.1 Hz, 2H), 6.67 (s, 1H), 5.98 (s, 1H), 5.84 (d, $J$ = 5.0 Hz, 2H), 4.24 (s, 1H), 4.09 – 4.01 (m, 1H), 3.62 (d, $J$ = 11.2 Hz, 2H), 2.92 (t, $J$ = 13.5 Hz, 1H), 2.81 (d, $J$ = 12.5 Hz, 1H), 2.69 (dd, $J$ = 14.3, 6.5 Hz, 1H), 2.15 – 2.02 (m, 1H), 1.94 – 1.87 (m, 1H), 1.85 – 1.75 (m, 1H), 1.70 (d, $J$ = 13.8 Hz, 1H), 1.51 (d, $J$ = 12.9 Hz, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 145.6, 145.3, 143.7, 135.6, 134.4, 128.6, 128.5, 126.3, 109.4, 108.9, 100.6, 78.3,
60.8, 46.7, 40.9, 30.8, 26.7, 26.1, 22.4; HRMS (ESI) m/z: [M+H]^+ Calculated for C_{21}H_{22}O_3: 323.1642, found: 323.1639.

Compound S23 was isolated as an amorphous solid (as a 5:1 mixture of diastereomers) after subjecting 14a to the hydrogenation conditions (13.7 mg, 78%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.34 (t, $J = 7.5$ Hz, 2H), 7.28 (s, 1H), 7.24 (s, 1H), 6.66 (s, 1H), 5.98 (s, 1H), 5.84 (d, $J = 6.3$ Hz, 2H), 4.27 (s, 1H), 4.08 (dd, $J = 11.2, 5.4$ Hz, 1H), 3.69 (dd, $J = 9.4, 6.0$ Hz, 1H), 2.91 (t, $J = 13.5$ Hz, 1H), 2.75 (d, $J = 13.3$ Hz, 1H), 2.68 (dd, $J = 14.4, 6.5$ Hz, 1H), 2.07 (dd, $J = 25.0, 12.3$ Hz, 1H), 1.95 (dd, $J = 12.5, 6.3$ Hz, 1H), 1.69 (d, $J = 13.6$ Hz, 1H), 1.58 (d, $J = 10.5$ Hz, 1H), 1.41 (dd, $J = 17.0, 5.0$ Hz, 1H), 1.10 (d, $J = 5.8$ Hz, 3H), 0.92 (ddd, $J = 26.9, 13.4, 3.5$ Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 145.6, 145.3, 143.7, 135.7, 134.5, 129.5, 128.7, 128.5, 127.9, 125.7, 125.5, 126.3, 109.4, 108.8, 100.6, 79.0, 65.5, 46.4, 40.5, 34.2, 30.9, 30.8, 26.9, 22.6, 22.3; HRMS (ESI) m/z: [M+H]^+ Calculated for C$_{22}$H$_{24}$O$_3$: 337.1798, found: 337.1794.

Oxidations:

**Scheme S11. General Procedure for m-CPBA Oxidation of 12a**

To a solution of 12a (32 mg, 0.1 mmol) in DCM (0.4 mL) at 0°C, added m-CPBA (26 mg, 0.15 mmol) in one portion. The reaction was allowed to stir at 0°C until all the starting material had been consumed by TLC (using 20% EtOAc in hexanes, and p-anisaldehyde to stain the plates). Reaction was diluted with more DCM (1.0 mL), washed with 10% NaOH (2 x 15 mL), then washed with Brine (20 mL), dried over MgSO$_4$, filtered, and concentrated to afford 22a as a white solid (29.9 mg, 89%). No purification needed. Recrystallized after dissolving in hot methanol and slowly cooling to room temperature in an uncapped vial. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.28 (dd, $J = 13.0, 6.2$ Hz, 5H), 6.70 (s, 1H), 6.65 (s, 1H), 5.89 (d, $J = 9.9$ Hz, 2H), 3.79 (d, $J = 11.8$ Hz, 1H), 3.70 (t, $J = 11.4$ Hz, 1H), 3.50 – 3.41 (m, 1H), 3.04 (td, $J = 13.3, 7.3$ Hz, 1H), 2.70 (dd, $J = 13.8, 6.5$ Hz, 1H), 2.28 (td, $J = 12.2, 7.5$ Hz, 1H), 1.98 (dd, $J = 13.2, 9.3$ Hz, 1H), 1.89 – 1.77 (m, 1H), 1.66 (dt, $J = 19.9, 7.2$ Hz, 2H), 1.41 (d, $J = 14.6$ Hz, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 147.4, 146.9, 137.9, 131.8, 130.4, 129.8, 128.0, 127.4, 127.0, 109.1, 108.5, 101.0, 77.5, 66.0, 65.4, 60.9, 29.4, 24.7, 23.8, 22.8; m.p = 143-146°C; HRMS (ESI) m/z: [M+H]^+ Calculated for C$_{21}$H$_{20}$O$_4$: 337.1435, found: 337.1431.

**Scheme S12. AD-mix α Dihydroxylation of 12i**
A mixture of 12i (32 mg, 0.1 mmol), methanesulfonamide (MeSO₂NH₂) (9.5 mg, 0.1 mmol), and AD-mix α (140 mg, 1.4g/mmol) was placed in a scintillation vial charged with a stir bar. Added tBuOH (0.5 mL) followed by water (0.5 mL), and the reaction mixture was allowed to stir vigorously under air for 4 days (until the starting material had been fully consumed by TLC, using 20% EtOAc in hexanes, and p-anisaldehyde to stain the plates). After this time, added solid sodium sulfite (Na₂SO₃) (140 mg) and vigorously stirred for an hour. Added more water (2 mL) extracted with EtOAc (4 x 15 mL), dry over MgSO₄, filter, and concentrate. The crude was purified by preparatory TLC, using 50% EtOAc in hexanes as the mobile phase to afford 22i as a 1.6:1 mixture of separable diastereomers (70% combined yield).

Compound 22i-1 was isolated as an amorphous solid (9.6 mg, 27%). ¹H NMR (500 MHz, CDCl₃) δ 7.13 (d, J = 8.0 Hz, 1H), 7.10 (s, 1H), 6.90 (d, J = 8.1 Hz, 1H), 4.21 (d, J = 8.4 Hz, 1H), 3.95 – 3.86 (m, 1H), 3.75 – 3.67 (m, 1H), 3.53 (dd, J = 11.1, 7.5 Hz, 1H), 3.10 (dd, J = 19.3, 8.4 Hz, 1H), 2.99 (dd, J = 12.7, 5.9 Hz, 1H), 2.42 – 2.28 (m, 4H), 2.28 – 2.17 (m, 2H), 2.03 (dd, J = 19.5, 11.6 Hz, 1H), 1.92 (dt, J = 17.1, 8.7 Hz, 1H), 1.50 (dd, J = 12.0, 4.1 Hz, 1H), 0.88 (t, J = 9.5 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 143.3, 141.4, 139.4, 130.3, 130.2, 130.1, 129.3, 120.2, 79.6, 76.8, 71.0, 63.0, 38.7, 30.3, 29.7, 24.0, 21.5, 19.2; HRMS (ESI) m/z: [M+H]⁺ Calculated for C₁₇H₂₁BrO₃: 353.0747, found: 353.0783.

Compound 22i-2 was isolated as an amorphous solid (15.2 mg, 43%). ¹H NMR (500 MHz, CDCl₃) δ 7.95 (d, J = 1.4 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.03 (d, J = 8.0 Hz, 1H), 4.57 (d, J = 8.8 Hz, 1H), 3.89 – 3.77 (m, 3H), 3.69 – 3.59 (m, 1H), 3.34 (dt, J = 11.6, 7.8 Hz, 1H), 2.91 (dd, J = 13.8, 6.1 Hz, 1H), 2.84 (s, 1H), 2.44 (dd, J = 16.6, 10.1 Hz, 4H), 2.40 – 2.24 (m, 3H), 2.20 – 1.12 (m, 1H), 2.08 (dd, J = 18.7, 10.5 Hz, 1H), 1.67 (ddd, J = 24.3, 12.2, 5.4 Hz, 2H), 0.92 (d, J = 6.2 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 144.3, 139.4, 138.9, 131.5, 130.1, 129.9, 127.9, 119.8, 76.3, 75.2, 69.6, 62.8, 38.1, 30.3, 29.7, 25.4, 20.9, 18.8; HRMS (ESI) m/z: [M+H]⁺ Calculated for C₁₇H₂₁BrO₃: 353.0747, found: 353.0783.

Scheme S13. Oxidative Cleavage of 12i

To a solution of 12i (40 mg, 0.13 mmol) in THF/H₂O (3:1, 0.65 mL), added OsO₄ (16 µL, 4% H₂O solution, 2.0 mol%) followed by NaIO₄ (13 mg/0.5 hr for 2 hrs; 88 mg, 0.26 mmol total). The reaction was allowed to stir for 48 hrs, then added saturated Na₂S₂O₃ and stirred for 30 minutes. After this time, added more water (15 mL), extracted with EtOAc (3 x 15 mL), dried over MgSO₄, filtered, and concentrated. The crude material was purified by preparatory TLC using 30% EtOAc in hexanes to afford aldehyde S24 as a foamy solid (14 mg, 38%). ¹H NMR (500 MHz, CDCl₃) δ 10.24 (s, 1H), 7.39 (s, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 4.00 – 3.90 (m, 2H), 3.54 (dd, J = 14.4, 6.5 Hz, 1H), 3.35 (dd, J = 19.7, 8.1 Hz, 1H), 2.70 (dd, J = 23.6, 10.3 Hz, 1H), 2.52 (d, J = 10.6 Hz, 3H), 2.24 (td, J = 15.2, 7.3 Hz, 2H), 1.82 – 1.70 (m, 1H), 0.87 (d, J = 6.4 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 187.7, 164.4, 139.0, 135.1, 132.5, 131.6, 131.0, 129.8, 119.9, 77.1, 62.9, 38.0, 28.9, 23.7, 19.9. HRMS (ESI) m/z: [M+H]⁺ Calculated for C₁₅H₁₅BrO₂: 307.0328, found: 307.0327.

Scheme S14. Wacker Oxidation of 14g

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A solution of 14g (50 mg, 0.158 mmol) in DMF (3.0 mL) was sparged with oxygen for 5 minutes. After this time, added PdCl₂ (6 mg, 32 μmol, 20 mol%), CuCl (16 mg, 0.158 mmol, 1.0 equiv.), and H₂O (128μL, 7.11 mmol, 45 equiv.). The reaction was allowed to stir under an oxygen atmosphere, at room temperature until all of the starting material had been consumed by TLC (using 20% EtOAc in hexanes, and p-anisaldehyde to stain the plates). The reaction mixture was diluted with EtOAc (20 mL), filtered through celite, washed with water (3 x 20 mL), then Brine, dried over MgSO₄, filtered, and concentrated under vacuum to give 25g as a viscous yellow oil (32 mg, 62% yield).

**1H NMR (500 MHz, CDCl₃)** δ 7.33 (t, J = 7.4 Hz, 2H), 7.28 (d, J = 7.3 Hz, 1H), 7.21 (d, J = 7.3 Hz, 1H), 6.76 (d, J = 7.5 Hz, 1H), 4.02 (dd, J = 10.6, 7.2 Hz, 1H), 3.80 (dd, J = 14.5, 6.7 Hz, 1H), 2.93 – 2.82 (m, 1H), 2.77 (dd, J = 16.0, 7.9 Hz, 1H), 2.64 – 2.48 (m, 4H), 2.41 (dd, J = 22.7, 10.0 Hz, 1H), 2.25 – 2.19 (m, 1H), 2.17 (d, J = 6.5 Hz, 3H), 1.95 (dq, J = 10.9, 7.4 Hz, 1H), 1.74 (dd, J = 21.1, 10.0 Hz, 1H); **13C NMR (126 MHz, CDCl₃)** δ 207.0, 141.6, 140.9, 140.7, 138.7, 133.7, 130.0, 129.9, 129.6, 128.2, 128.1, 126.7, 126.7, 126.0, 78.2, 70.7, 50.4, 39.5, 31.6, 30.8, 30.3, 23.0; HRMS (ESI) m/z: [M+H]+ Calculated for C₂₃H₂₄O₂: 333.1849, found: 333.1847.

Cross Coupling and Click Reactions:

**Scheme S15. Ammonia Cross-Coupling with 12i**

A mixture of D-glucosamine (4.4 mg, 0.02 mmol, 0.1 equiv.), NaN₃ (39 mg, 0.6 mmol, 3.0 equiv.), CuI (3.8 mg, 0.02 mmol, 0.1 equiv.), KOH (11.2 mg, 0.2 mmol, 1 equiv.), and KI (33.2 mg, 0.2 mmol, 1 equiv.) in DMF/H₂O (v/v 1:1, 0.6 mL) was added to a sealable tube. The mixture was sparged with argon for about 10 minutes then added 12i (63.8 mg, 0.2 mmol, 1.0 equiv.) and heated to 120°C for 18 hours. After this time, the reaction was cooled to room temperature, diluted with water, extracted with DCM (3 x 15 mL), washed with brine, dried over MgSO₄, filtered, and concentrated under vacuum. The crude material was purified by preparatory TLC using 30% EtOAc in hexanes with 1% Et₃N to give 24i as an orange oil, and 35.8 mg of recovered 12i (25% yield, 58% yield based on recovered starting material). **1H NMR (500 MHz, CDCl₃)** δ 6.96 (t, J = 7.2 Hz, 1H), 6.58 (s, 1H), 6.52 (dd, J = 8.7, 6.9 Hz, 2H), 5.56 (dq, J = 13.5, 6.6 Hz, 1H), 3.94 – 3.86 (m, 1H), 3.86 – 3.78 (m, 1H), 3.53 (bs, 2H), 3.35 (dt, J = 11.4, 7.6 Hz, 1H), 2.82–2.84 (m, 2H), 2.54 – 2.32 (m, 4H), 2.24 (tt, J = 12.9, 6.5 Hz, 1H), 2.10 (dd, J = 19.8, 11.7 Hz, 1H), 2.00 (dd, J = 13.7, 6.7 Hz, 1H), 1.78 (d, J = 6.5 Hz, 3H), 1.72 – 1.58 (m, 2H); **13C NMR (126 MHz, CDCl₃)** δ 143.9, 139.3, 135.6, 131.2, 130.2, 128.7, 128.2, 128.0, 116.4, 114.0, 76.7, 62.8, 37.8, 28.9, 24.2, 20.8, 18.6; HRMS (ESI) m/z: [M+H]+ Calculated for C₁₅H₁₅BrO₂: 307.0328, found: 307.1804.

**Scheme S16. Click Reaction with 14h and Benzyl Azide for Triazole Synthesis**
A mixture of 14h (63 mg, 0.2 mmol), CuSO₄·5H₂O (1 mg, 4 μmol), Cu powder (1 mg, 2 μmol), sodium ascorbate (4 mg, 20 μmol), and benzyl azide (BnN₃) (32 μL, 40 mg, 0.3 mmol), in a 2:1 mixture of H₂O/tBuOH, was stirred at room temperature until all of the starting material 14h was consumed by TLC (using 20% EtOAc in hexanes as the mobile phase, and p-anisaldehyde to stain the plates). Product 26h was obtained as a white solid after purification by preparatory TLC using 45% EtOAc in hexanes (52.3 mg, 58%). 

**Scheme S17. Click Reaction with Imidoyl Chloride for Isoxazole Synthesis**

A mixture of 14h (63 mg, 0.2 mmol), CuSO₄·5H₂O (1 mg, 4 μmol), Cu powder (1 mg, 2 μmol), sodium bicarbonate (72 mg, 0.86 mmol), and S25 (45 mg, 0.24 mmol), in a 1:1 mixture of H₂O/tBuOH, was stirred at room temperature for 24 hours. Product 27h was obtained as a white solid after purification by preparatory TLC using 45% EtOAc in hexanes (52.2 mg, 44%, 52% brsm). Recrystallization was achieved by dissolving in hot hexanes with toluene and slowly allowing to cool to room temperature in an uncapped vial. 

**Procedure for Indole Substrate Deprotection:**

**Scheme S18: General Conditions for Indole Deprotections**
Indole substrates were deprotected following the procedure from Buden et al. To a flame dried vial under argon and charged with a stir bar, added indole adduct followed by DMSO (0.5mL). To this mixture, added KOtBu (15 mg, 0.13 mmol) that was kept in the glovebox. After addition of the base, the black reaction mixture was covered with aluminum foil and allowed to stir at room temperature for 3 hours. After this time, saturated ammonium chloride was added to quench the reaction, extracted with EtOAc (3 x 15mL), dried over MgSO4, filtered, and concentrated. Product was purified by preparatory TLC, using 30% EtOAc in hexane with 2% Et3N to afford deprotected indole as a pale grey amorphous solid (10.5 mg, 74% yield).

Compound 20a was obtained as a grey amorphous solid (10.5 mg, 74%). 1H NMR (500 MHz, CDCl3) δ 8.04 (s, 1H), 7.39 – 7.29 (m, 4H), 7.23 (d, J = 7.2 Hz, 3H), 7.00 (t, J = 7.5 Hz, 1H), 6.72 (t, J = 7.6 Hz, 1H), 6.16 (d, J = 8.1 Hz, 1H), 4.30 (t, J = 6.9 Hz, 1H), 4.06 – 3.97 (m, 1H), 3.57 (td, J = 10.8, 6.1 Hz, 1H), 3.11 (dt, J = 15.6, 7.8 Hz, 1H), 2.87 (dt, J = 15.5, 6.3 Hz, 1H), 2.54 – 2.34 (m, 5H), 2.02 (d, J = 4.9 Hz, 1H), 1.73 (dd, J = 12.6, 6.2 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ 141.6, 139.8, 135.4, 135.0, 129.9, 128.2, 127.9, 126.7, 120.9, 120.4, 119.4, 112.4, 110.2, 79.1, 65.1, 36.2, 30.3, 26.5, 24.8, 23.5; HRMS (ESI) m/z: [M+H]+ Calculated for C22H21NO : 316.1696, found: 316.1687.

Compound 20b was obtained as a grey amorphous solid (6.9 mg, 51%). 1H NMR (500 MHz, CDCl3) δ 8.06 (s, 1H), 7.34 (t, J = 7.3 Hz, 2H), 7.31 – 7.25 (m, 2H), 7.18 (d, J = 7.2 Hz, 2H), 7.10 (s, 1H), 7.05 (s, 1H), 6.36 (s, 1H), 4.08 (dd, J = 10.6, 7.8 Hz, 1H), 3.94 (t, J = 8.4 Hz, 1H), 3.48 – 3.40 (m, 1H), 3.01 (td, J = 12.8, 8.0 Hz, 1H), 2.69 (dd, J = 13.1, 6.5 Hz, 1H), 2.60 (dd, J = 13.9, 4.1 Hz, 1H), 2.55 – 2.44 (m, 1H), 2.40 (dd, J = 20.3, 12.0 Hz, 1H), 2.30 (dd, J = 19.5, 11.5 Hz, 1H), 2.13 – 2.00 (m, 1H), 1.76 (s, 1H). 13C NMR (126 MHz, CDCl3) δ 142.6, 136.4, 135.3, 134.9, 134.3, 133.9, 130.1, 128.0, 126.4, 126.3, 123.9, 122.1, 109.8, 102.7, 77.3, 63.3, 38.5, 31.0, 25.2, 22.8; HRMS (ESI) m/z: [M+H]+ Calculated for C22H21NO : 316.1696, found: 316.1695.

Compound 20c was obtained as a white solid (20.4 mg, 55%). 1H NMR (500 MHz, CDCl3) δ 7.56 (d, J = 6.3 Hz, 1H), 7.45 (dq, J = 14.5, 7.1 Hz, 3H), 7.29 – 7.26 (m, 2H), 7.16 (s, 1H), 7.13-7.05 (m, 3H), 4.31 (dd, J = 7.3, 2.9 Hz, 1H), 4.14 – 4.04 (m, 1H), 3.70 (td, J = 10.8, 5.1 Hz, 1H), 3.20 – 2.99 (m, 2H), 2.44 – 2.14 (m, 4H), 1.97 – 1.83 (m, 1H), 1.66 (dd, J = 11.5, 5.2 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ 139.9, 134.8, 132.7, 129.7, 128.9, 128.3, 127.5, 126.5, 122.0, 119.3,
118.3, 115.7, 110.5, 80.3, 66.5, 33.4, 28.6, 26.9, 20.5; m.p = 140-141°C; HRMS (ESI) m/z: [M+H]⁺ Calculated for C₂₂H₂₁NO : 316.1696, found: 316.1693.

X-Ray Crystal Structures for Compounds 19, 12o, 12t, 14a, 21a-1, 22a, and 27h:

**Compound 19:**

![Image of Compound 19](image-url)

**Table S2.** Crystal data and structure refinement for 19

| Parameter                             | Value                        |
|---------------------------------------|------------------------------|
| Identification code                   | 19                           |
| Empirical formula                     | C₂₇H₂₇NO₃S                   |
| Formula weight                        | 445.55                       |
| Temperature                           | 100.01(10) K                 |
| Wavelength                            | 1.54184 Å                    |
| Crystal system                        | monoclinic                   |
| Space group                           | Pc                           |
| Unit cell dimensions                  | a = 12.17620(10) Å, α = 90°  |
|                                      | b = 11.57040(10) Å, β = 94.5220(10)° |
|                                      | c = 7.98290(10) Å, γ = 90°   |
| Volume                                | 1121.158(19) Å³              |
| Z                                      | 2                            |
| Density (calculated)                  | 1.320 Mg/m³                  |
| Absorption coefficient                | 1.516 mm⁻¹                   |
| F(000)                                | 472                          |
| Crystal color, morphology             | colourless, needle           |
| Crystal size                          | 0.489 x 0.09 x 0.018 mm³     |
| Theta range for data collection       | 3.641 to 80.188°             |
| Index ranges                          | -15 ≤ h ≤ 15, -14 ≤ k ≤ 14, -9 ≤ l ≤ 8 |
| Reflections collected                 | 34948                        |
| Independent reflections               | 4549 [R(int) = 0.0717]        |
Observed reflections 4400
Completeness to theta = 74.504° 100.0%
Absorption correction Multi-scan
Max. and min. transmission 1.00000 and 0.62538
Refinement method Full-matrix least-squares on $F^2$
Data / restraints / parameters 4549 / 2 / 290
Goodness-of-fit on $F^2$ 1.097
Final $R$ indices [$I>2\sigma(I)$] $R1 = 0.0438$, $wr2 = 0.1208$
$R$ indices (all data) $R1 = 0.0450$, $wr2 = 0.1219$
Absolute structure parameter -0.002(16)
Largest diff. peak and hole 0.383 and -0.464 e.Å$^{-3}$

**Compound 12o:**

![Compound 12o](image)

**Table S3.** Crystal data and structure refinement for 12o

| Identification code | 12o |
|---------------------|-----|
| Empirical formula   | C22 H22 O3 |
| Formula weight      | 334.39 |
| Temperature         | 100.00(10) K |
| Wavelength          | 1.54184 Å |
| Crystal system      | monoclinic |
| Space group         | $P2_1/n$ |
| Unit cell dimensions| $a = 17.2159(2)$ Å, $a = 90^\circ$
|                     | $b = 10.13720(10)$ Å, $b = 110.5460(10)^\circ$
|                     | $c = 20.2267(2)$ Å, $g = 90^\circ$ |
| Volume              | 3305.44(6) Å$^3$ |
Z
Density (calculated) 1.344 Mg/m³
Absorption coefficient 0.703 mm⁻¹
F(000) 1424
Crystal color, morphology colourless, block
Crystal size 0.168 x 0.13 x 0.082 mm³
Theta range for data collection 4.179 to 80.392°
Index ranges -22 ≤ h ≤ 16, -12 ≤ k ≤ 12, -25 ≤ l ≤ 25
Reflections collected 35734
Independent reflections 7100 [R(int) = 0.0387]
Observed reflections 6280
Completeness to theta = 74.504° 100.0%
Absorption correction Multi-scan
Max. and min. transmission 1.00000 and 0.87854
Refinement method Full-matrix least-squares on F²
Data / restraints / parameters 7100 / 0 / 453
Goodness-of-fit on F² 1.059
Final R indices [I>2sigma(I)] R1 = 0.0442, wR2 = 0.1209
R indices (all data) R1 = 0.0487, wR2 = 0.1248
Largest diff. peak and hole 0.377 and -0.225 e.Å⁻³

Compound 12t:

Table S4. Crystal data and structure refinement for 12t
Empirical formula
C22 H19 Br O2
Formula weight
395.28
Temperature
100.00(10) K
Wavelength
1.54184 Å
Crystal system
triclinic
Space group
P-1
Unit cell dimensions
\(a = 7.14240(10) \text{ Å}\)
\(b = 9.29770(10) \text{ Å}\)
\(c = 13.9152(2) \text{ Å}\)
\(a = 93.7290(10)°\)
\(b = 99.1970(10)°\)
\(c = 107.703(2)°\)
Volume
862.63(2) Å³
\(Z\)
2
Density (calculated)
1.522 Mg/m³
Absorption coefficient
3.338 mm⁻¹
\(F(000)\)
404
Crystal color, morphology
colourless, block
Crystal size
0.155 x 0.113 x 0.078 mm³
Theta range for data collection
3.241 to 80.002°
Index ranges
\(-9 \leq h \leq 9, -11 \leq k \leq 10, -17 \leq l \leq 17\)
Reflections collected
28144
Independent reflections
3680 [R(int) = 0.0421]
Observed reflections
3503
Completeness to theta = 74.504°
99.7%
Absorption correction
Multi-scan
Max. and min. transmission
1.00000 and 0.88565
Refinement method
Full-matrix least-squares on \(F^2\)
Data / restraints / parameters
3680 / 0 / 226
Goodness-of-fit on \(F^2\)
1.081
Final \(R\) indices \([I>2\sigma(I)]\)
\(R1 = 0.0325, wR2 = 0.0764\)
\(R\) indices (all data)
\(R1 = 0.0340, wR2 = 0.0772\)
Largest diff. peak and hole
0.371 and -0.694 e.Å⁻³

**Compound 14a:**
Table S5. Crystal data and structure refinement for 14a

| Property                                      | Value                              |
|-----------------------------------------------|------------------------------------|
| Identification code                           | 14a                                |
| Empirical formula                            | C22 H22 O3                         |
| Formula weight                                | 334.39                             |
| Temperature                                   | 100.00(10) K                       |
| Wavelength                                    | 1.54184 Å                          |
| Crystal system                                | monoclinic                         |
| Space group                                   | $P2_1/c$                           |
| Unit cell dimensions                          | $a = 11.11210(10)$ Å, $a = 90^\circ$ |
|                                               | $b = 14.44820(10)$ Å, $b = 100.5810(10)^\circ$ |
|                                               | $c = 11.06860(10)$ Å, $g = 90^\circ$ |
| Volume                                        | 1746.85(3) Å$^3$                   |
| $Z$                                           | 4                                  |
| Density (calculated)                          | 1.271 Mg/m$^3$                     |
| Absorption coefficient                        | 0.665 mm$^{-1}$                    |
| $F(000)$                                      | 712                                |
| Crystal color, morphology                     | colourless, block                  |
| Crystal size                                  | 0.234 x 0.139 x 0.108 mm$^3$       |
| Theta range for data collection               | 4.047 to 80.156°                   |
| Index ranges                                  | -14 ≤ $h$ ≤ 14, -18 ≤ $k$ ≤ 18, -12 ≤ $l$ ≤ 13 |
| Reflections collected                         | 20536                              |
| Independent reflections                       | 3744 [$R$(int) = 0.0366]            |
| Observed reflections                          | 3460                               |
| Completeness to theta                         | 74.504°                           |
| Absorption correction                         | Multi-scan                         |
Max. and min. transmission 1.00000 and 0.89800
Refinement method Full-matrix least-squares on $F^2$
Data / restraints / parameters 3744 / 106 / 256
Goodness-of-fit on $F^2$ 1.052
Final $R$ indices [$I>2\sigma(I)$] $R1 = 0.0417$, $wR2 = 0.1039$
$R$ indices (all data) $R1 = 0.0442$, $wR2 = 0.1057$
Largest diff. peak and hole 0.228 and -0.249 e.Å$^{-3}$

Compound 21a-1:

![Compound 21a-1](image)

Table S6. Crystal data and structure refinement for 21a-1

| Identification code    | 21a -1 |
|------------------------|--------|
| Empirical formula      | C21 H22 O3 |
| Formula weight         | 322.38 |
| Temperature            | 99.97(10) K |
| Wavelength             | 1.54184 Å |
| Crystal system         | orthorhombic |
| Space group            | $Pna2_1$ |
| Unit cell dimensions   | $a = 14.11320(10)$ Å, $a = 90^\circ$
|                        | $b = 19.7985(2)$ Å, $b = 90^\circ$
|                        | $c = 5.92430(10)$ Å, $g = 90^\circ$
| Volume                 | 1655.37(3) Å$^3$ |
| $Z$                    | 4 |
| Density (calculated)   | 1.294 Mg/m$^3$ |
| Absorption coefficient | 0.680 mm$^{-1}$ |
| $F(000)$               | 688 |
Crystal color, morphology: colourless, block
Crystal size: 0.284 x 0.227 x 0.1 mm³
Theta range for data collection: 3.846 to 80.166°
Index ranges: -17 ≤ h ≤ 17, -24 ≤ k ≤ 25, -6 ≤ l ≤ 7
Reflections collected: 19326
Independent reflections: 3305 [R(int) = 0.0399]
Observed reflections: 3221
Completeness to theta = 67.684°: 100.0%
Absorption correction: Multi-scan
Max. and min. transmission: 1.00000 and 0.87289
Refinement method: Full-matrix least-squares on F²
Data / restraints / parameters: 3305 / 1 / 217
Goodness-of-fit on F²: 1.048
Final R indices [l>2sigma(I)]: R1 = 0.0312, wR2 = 0.0777
R indices (all data): R1 = 0.0319, wR2 = 0.0783
Absolute structure parameter: -0.06(10)
Largest diff. peak and hole: 0.138 and -0.196 e.Å⁻³

**Compound 22a:**

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**Table S7.** Crystal data and structure refinement for 22a

| Identification code | 22a |
|---------------------|-----|
| Empirical formula   | C21 H20 O4 |
| Formula weight      | 336.37 |
| Temperature         | 100.00(10) K |
| Wavelength          | 1.54184 Å |
Crystal system: monoclinic
Space group: \(P2_1/n\)
Unit cell dimensions:
- \(a = 11.33020(10) \text{ Å}\)
- \(b = 9.30400(10) \text{ Å}\)
- \(c = 15.25110(10) \text{ Å}\)
Theta range for data collection: 4.782 to 80.320°
Index ranges:
- \(-14 \leq h \leq 14\)
- \(-9 \leq k \leq 11\)
- \(-19 \leq l \leq 19\)
Reflections collected: 28132
Independent reflections: 3482 \( [R(\text{int}) = 0.0354] \)
Observed reflections: 3218
Completeness to theta = 74.504°: 100.0%
Absorption correction: Multi-scan
Max. and min. transmission: 1.00000 and 0.94365
Refinement method: Full-matrix least-squares on \(F^2\)
Data / restraints / parameters: 3482 / 0 / 226
Goodness-of-fit on \(F^2\): 1.061
Final \(R\) indices \([>2\sigma(I)]\): \(R1 = 0.0358\), \(wR2 = 0.0917\)
\(R\) indices (all data): \(R1 = 0.0384\), \(wR2 = 0.0935\)
Largest diff. peak and hole: 0.234 and -0.208 e.Å\(^{-3}\)

**Compound 27h:**

![Chemical structure of Compound 27h]
| Identification code | 27h |
|---------------------|-----|
| Empirical formula   | C31 H29 N O3 |
| Formula weight      | 463.55 |
| Temperature         | 99.99(10) K |
| Wavelength          | 1.54184 Å |
| Crystal system      | monoclinic |
| Space group         | P2₁/n |
| Unit cell dimensions| \(a = 15.9276(3) \text{ Å} \quad a = 90° \) |
|                      | \(b = 5.55609(9) \text{ Å} \quad b = 98.7546(18)° \) |
|                      | \(c = 27.3254(5) \text{ Å} \quad g = 90° \) |
| Volume              | 2389.99(7) Å³ |
| Z                   | 4 |
| Density (calculated)| 1.288 Mg/m³ |
| Absorption coefficient | 0.651 mm⁻¹ |
| \(F(000)\)          | 984 |
| Crystal color, morphology | colourless, needle |
| Crystal size        | 0.2 x 0.104 x 0.077 mm³ |
| Theta range for data collection | 3.273 to 80.341° |
| Index ranges        | -20 \(\leq h \leq 20\), -7 \(\leq k \leq 7\), -34 \(\leq l \leq 34\) |
| Reflections collected | 47366 |
| Independent reflections | 9452 \([R(int) = 0.044]\) |
| Observed reflections | 8533 |
| Completeness to theta = 74.504° | 99.5% |
| Absorption correction | Multi-scan |
| Max. and min. transmission | 1.000000 and 0.63440 |
| Refinement method   | Full-matrix least-squares on \(F^2\) |
| Data / restraints / parameters | 9452 / 36 / 355 |
| Goodness-of-fit on \(F^2\) | 1.099 |
| Final \(R\) indices [\(I > 2\sigma(I)\)] | \(R1 = 0.0706\), \(wR2 = 0.1831\) |
| \(R\) indices (all data) | \(R1 = 0.0762\), \(wR2 = 0.1865\) |
| Largest diff. peak and hole | 0.617 and -0.408 e.Å⁻³ |
NMR Spectra:

**500 MHz**

![500 MHz NMR Spectrum]

**126 MHz**

![126 MHz NMR Spectrum]
500MHz

12c (1.7:1 p/o-trapped)

126MHz

12c (1.7:1 p/o-trapped)
12f (70%)
This space was left blank intentionally
12k (3.9:1 p/o-trapped)

500 MHz

Me

126 MHz

Me

12k (3.9:1 p/o-trapped)
500MHz

121

126MHz

121
500MHz

12r (1:1 mix of conformers)

126MHz

12r (1:1 mix of conformers)
500 MHz

14c (13.3:1 dr)

126 MHz

14c (13.3:1 dr)
14d (31.5:1 dr)
14e (35.8:1 dr)

500 MHz

126 MHz

3H-877-IA_213
Avance 800
Carbon (13C) 121.3 test
Updated: 24 October 2018
2H(13) 126.8 MHz, 300°c
500 MHz

14f (7.9:1 dr)

126 MHz

14f (7.9:1 dr)
400 MHz

16a (>20:1 dr)

100 MHz

16b (>20:1 dr)
500 MHz

22a (crude)

126 MHz

22a (crude)
500 MHz

$S_{24}$

126 MHz

$S_{24}$
500 MHz

26h (2.8:1 dr)

126 MHz

26h (2.8:1 dr)
500 MHz

27h (2.8:1 dr)

126 MHz

27h (2.8:1 dr)
500 MHz

126 MHz
Computational Methods:

Input files for ground state or transition state intermediates of a given reaction were prepared locally using GaussView 6.0 and transferred to the University of Rochester Blue Hive Linux cluster where DFT calculations were carried out in the Gaussian 16 suite of programs. Optimization calculations (either to a ground state or a transition state) were first carried out at the M06-2x functional and Def2TZVP basis set level of theory,\textsuperscript{30,31} with implicit solvation using the Polarizable Continuum Model (PCM = dichloromethane).\textsuperscript{32} Intrinsic reaction coordinate (IRC)\textsuperscript{iv} calculations were carried out on the transition state structures to verify that they connected to the associated reactant and product structures. Thereafter, frequency DFT calculations at the M06-2x/Def2TZVP level (PCM = dichloromethane), of the obtained optimized structures were carried out to confirm that ground state structures had zero imaginary frequencies and that transition states had a single imaginary frequency. All shown free energies are ZPE and thermally corrected (reported in Hartree units, at 298.15 K and 1 atm) and were obtained from the frequency calculations.

![DFT Optimized Structures](image)

DFT Optimized Structures

11a-1
Imaginary Frequencies: 0

ZPE and thermally corrected free energy: -657.679999 Ha

| Center Number | Atomic Number | Forces (Hartrees/Bohr) |          |          |          |
|---------------|---------------|------------------------|----------|----------|----------|
|               |               | X                      | Y        | Z        |
| 1             | 6             | -0.033778506           | -0.023072397 | -0.026009855 |
| 2             | 1             | 0.001406698            | -0.001659511 | 0.013578900  |
| 3             | 1             | 0.012515378            | -0.001945708 | -0.003722202 |
| 4             | 6             | -0.012274634           | -0.027203809 | 0.015798334  |
| 5             | 1             | 0.002616691            | 0.012184343 | 0.004740189  |
| 6             | 1             | 0.001268686            | 0.001443613 | -0.015793244 |
| 7             | 6             | 0.036677908            | 0.032561971 | 0.019031334  |
| 8             | 6             | -0.015930393           | -0.051451601 | -0.031740989 |
| 9             | 6             | -0.011130619           | 0.059638130 | 0.080600156  |
| 10            | 1             | -0.010469710           | 0.005858830 | -0.025360129 |
| 11            | 1             | 0.017108042            | -0.009269989 | -0.030087377 |
| 12            | 1             | 0.020445405            | -0.020550836 | -0.001647008 |
| 13            | 6             | 0.029734389            | 0.023631618 | -0.006333732 |
| 14            | 1             | -0.006209053           | -0.009285478 | 0.011874592  |
| 15            | 1             | -0.007949863           | 0.006398891 | 0.004085740  |
| 16            | 8             | -0.033402757           | -0.013127737 | -0.018190281 |
| 17            | 6             | 0.015900952            | 0.062734729 | 0.006326405  |
| 18            | 1             | -0.004300629           | -0.013896594 | 0.006236565  |
| 19            | 6             | 0.004431825            | -0.041608670 | -0.014194430 |
| 20            | 1             | -0.013815710           | 0.005904664 | 0.010695588  |
| 21            | 1             | 0.006897949            | 0.007219079 | -0.00042150  |
| 22            | 6             | 0.028199153            | -0.014913520 | 0.008593356  |
| 23            | 1             | -0.011941710           | -0.006198985 | -0.004177735 |
| 24            | 1             | -0.003474219           | 0.011105178 | -0.004671257 |
| 25            | 6             | -0.015449116           | -0.010871535 | 0.008631716  |
| 26            | 6             | -0.016667191           | 0.007928171 | 0.005722941  |
| 27            | 6             | 0.002118518            | 0.018605551 | -0.000127838 |
| 28            | 6             | 0.020096129            | 0.011220562 | -0.005655882 |
| 29            | 6             | -0.009242774           | 0.005551181 | -0.000865474 |
| 30            | 6             | 0.002861905            | -0.021715584 | 0.000884717  |
| 31            | 1             | 0.007156067            | 0.004846961 | -0.003101196 |
| 32            | 1             | 0.007071283            | -0.004495433 | -0.003003921 |
| 33            | 1             | 0.000505680            | -0.009173036 | 0.000070205  |
| 34            | 1             | -0.009552347           | -0.006286357 | -0.00797693  |
| 35            | 1             | -0.001422973           | 0.009893309 | -0.00966346  |

11-1 (TS)
Imaginary Frequencies: 1

ZPE and thermally corrected free energy: \(-657.666073\) Ha (\(\Delta G^i = 8.7\) kcal/mol for this transition state)

| Center Number | Atomic Number | Forces (Hartrees/Bohr) |
|---------------|---------------|------------------------|
| X             | Y             | Z                      |
| 1             | 6             | 0.000000120 -0.000005403 -0.000001616 |
| 2             | 1             | 0.000001965 0.000001738 -0.000001930 |
| 3             | 1             | 0.000001040 0.000000564 -0.000001605 |
| 4             | 6             | -0.000002986 0.000001650 -0.000002029 |
| 5             | 1             | 0.000001644 0.000001914 -0.000001638 |
| 6             | 1             | 0.000000335 -0.000000424 -0.000002412 |
| 7             | 6             | -0.000217714 0.000028284 -0.000082695 |
| 8             | 6             | -0.000001496 0.000000517 -0.000002922 |
| 9             | 6             | -0.000006039 0.000002592 -0.000000500 |
| 10            | 1             | 0.000001274 0.000000432 0.000003852 |
| 11            | 1             | 0.000001453 -0.000000013 0.000000894 |
| 12            | 1             | 0.000000527 0.000002831 0.000002291 |
| 13            | 6             | 0.000002582 0.000004411 -0.000003697 |
| 14            | 1             | 0.000000494 0.000000476 -0.000001156 |
| 15            | 1             | 0.000000896 -0.000000238 -0.000001661 |
| 16            | 8             | 0.000000807 0.000001841 -0.000000960 |
| 17            | 6             | 0.000221624 -0.000017745 0.000084756 |
| 18            | 1             | 0.000000524 -0.000001707 0.000001156 |
| 19            | 6             | -0.000000126 0.000001733 0.000002200 |
| 20            | 1             | -0.000000127 -0.000000494 0.000000028 |
| 21            | 1             | 0.000001104 -0.000000815 0.000000314 |
| 22            | 6             | -0.000005456 -0.000002181 -0.000002330 |
| 23            | 1             | 0.000000433 -0.000001566 0.0000002196 |
| 24            | 1             | 0.000001181 -0.000001410 0.000001185 |
| 25            | 6             | 0.000004357 -0.000005913 -0.000000103 |
| Center | Atomic Number | Forces (Hartrees/Bohr) | X       | Y       | Z       |
|--------|---------------|------------------------|---------|---------|---------|
| 26     | 6             | 0.000000163            | 0.000004516 | 0.00000374 |
| 27     | 6             | -0.000007261           | -0.000004719 | 0.00000798 |
| 28     | 6             | 0.000007272            | -0.000006457 | 0.000001989 |
| 29     | 6             | -0.000000142           | 0.000006040 | -0.00000300 |
| 30     | 6             | -0.000005157           | -0.000003407 | -0.00001035 |
| 31     | 1             | -0.000000591           | -0.000001286 | -0.00001651 |
| 32     | 1             | -0.000000512           | -0.000002283 | -0.00000155 |
| 33     | 1             | -0.000001009           | -0.000001768 | 0.000002148 |
| 34     | 1             | -0.000001969           | -0.000000801 | 0.00000059 |
| 35     | 1             | 0.000000788            | -0.00000908  | -0.00000284 |

11b-1

Imaginary Frequencies: 0

ZPE and thermally corrected free energy: -657.669757 Ha (6.4 kcal/mol vs 11a-1)
| Number | Atomic Number | X Force (Hartrees/Bohr) | Y Force (Hartrees/Bohr) | Z Force (Hartrees/Bohr) |
|--------|---------------|------------------------|------------------------|------------------------|
| 15     | 1             | 0.003438413            | -0.016269657           | -0.001886373           |
| 16     | 8             | -0.010154658           | 0.001051233            | -0.002989670           |
| 17     | 6             | 0.033747146            | -0.005475536           | 0.018348257            |
| 18     | 1             | 0.004352294            | -0.0002111356          | -0.012745627           |
| 19     | 6             | -0.022078742           | 0.014480031            | -0.013346422           |
| 20     | 1             | 0.010364800            | -0.008317500           | -0.008503908           |
| 21     | 1             | -0.003280429           | -0.014930565           | -0.002295862           |
| 22     | 6             | 0.007104047            | 0.013605311            | 0.032753271            |
| 23     | 1             | -0.004089309           | 0.003407264            | -0.014924465           |
| 24     | 1             | -0.007065911           | -0.010178585           | -0.002536586           |
| 25     | 6             | 0.008089404            | 0.011500432            | -0.014909333           |
| 26     | 6             | 0.008365222            | -0.010476281           | -0.012100029           |
| 27     | 6             | 0.000186660            | -0.019915839           | 0.001172420            |
| 28     | 6             | -0.054787753           | -0.020915834           | 0.064251151            |
| 29     | 6             | 0.001582783            | -0.007891993           | -0.011235608           |
| 30     | 6             | 0.000361728            | 0.024866322            | -0.000276187           |
| 31     | 1             | -0.003435745           | -0.003999709           | 0.006660603            |
| 32     | 1             | -0.003301252           | 0.004581443            | 0.006321227            |
| 33     | 1             | -0.001356714           | 0.009941461            | -0.000017051           |
| 34     | 1             | -0.067143924           | -0.039855427           | 0.049641435            |
| 35     | 1             | -0.000319481           | -0.009534206           | -0.001061200           |

Imaginary Frequencies: 0
ZPE and thermally corrected free energy: -849.364613 Ha

| Center Number | Atomic Number | Forces (Hartrees/Bohr) |
|---------------|---------------|-----------------------|
| 1             | 6             | 0.000074051 0.00034380 0.000019754 |
| 2             | 1             | -0.000187887 0.000195494 -0.000334373 |
| 3             | 1             | -0.000347788 0.000250583 -0.000479096 |
|   |   |   |   |   |
|---|---|---|---|---|
| 4 | 6 | -0.000221724 | -0.000664105 | -0.000440037 |
| 5 | 1 | -0.000112575 | 0.000297270 | -0.000065871 |
| 6 | 1 | -0.000081377 | -0.000105463 | 0.000053352 |
| 7 | 6 | 0.001571325 | -0.000411093 | 0.002328520 |
| 8 | 6 | -0.033455342 | 0.015246665 | -0.045982752 |
| 9 | 6 | 0.000291942 | -0.000118509 | -0.000136902 |
|10 | 1 | -0.000001088 | -0.000054578 | 0.000136902 |
|11 | 1 | -0.000160165 | 0.000000862 | 0.000009635 |
|12 | 8 | 0.000193782 | 0.000419536 | 0.000153693 |
|13 | 6 | -0.000567651 | -0.000452193 | 0.000277300 |
|14 | 1 | -0.000000788 | -0.000054578 | 0.000136902 |
|15 | 6 | 0.000112238 | -0.00040806 | -0.00050367 |
|16 | 1 | 0.000114055 | -0.00043123 | 0.000154074 |
|17 | 1 | -0.000109904 | -0.00005719 | 0.00039285 |
|18 | 6 | 0.000296633 | 0.000072675 | -0.000062552 |
|19 | 1 | 0.000068824 | -0.00048652 | -0.00002415 |
|20 | 6 | 0.000231722 | 0.00063279 | 0.00057525 |
|21 | 6 | 0.00005215 | -0.000122775 | -0.00085442 |
|22 | 6 | -0.000764818 | -0.000273210 | -0.00018911 |
|23 | 6 | -0.000016235 | -0.000106553 | -0.000174439 |
|24 | 6 | 0.000019469 | 0.000245840 | -0.000115315 |
|25 | 6 | 0.000169232 | -0.000067207 | 0.000235245 |
|26 | 1 | 0.000000882 | -0.00031660 | 0.000047285 |
|27 | 1 | -0.000072911 | 0.00083774 | 0.00030416 |
|28 | 1 | 0.000369076 | -0.000102983 | -0.00051158 |
|29 | 1 | 0.000129715 | 0.000340598 | 0.00009364 |
|30 | 1 | -0.000027241 | -0.00002162 | -0.00033812 |
|31 | 6 | 0.028564481 | -0.012748768 | 0.039440740 |
|32 | 6 | -0.004782598 | 0.005779384 | 0.006461551 |
|33 | 6 | 0.005671760 | -0.005681632 | -0.004594782 |
|34 | 6 | -0.002675974 | 0.002239062 | 0.001041491 |
|35 | 6 | 0.003065017 | -0.004634352 | -0.010249645 |
|36 | 6 | 0.001114326 | -0.001991327 | -0.003613265 |
|37 | 6 | -0.008674721 | 0.007771932 | 0.001767314 |
|38 | 6 | -0.003726890 | 0.001462372 | -0.004782786 |
|39 | 1 | 0.009447128 | -0.007073723 | -0.000976208 |
|40 | 1 | -0.002143644 | 0.003876310 | 0.011027552 |
|41 | 1 | 0.006711404 | -0.003008550 | 0.009065465 |

11-2 (TS)
Imaginary Frequencies: 1

ZPE and thermally corrected free energy: $-849.350748$ Ha ($\Delta G^i = 8.7$ kcal/mol for this transition state)

| Center Number | Atomic Number | Forces (Hartrees/Bohr) | X         | Y         | Z         |
|---------------|---------------|------------------------|-----------|-----------|-----------|
| 1             | 6             | -0.001356407           | 0.000710171 | 0.000735663 |           |
| 2             | 1             | -0.000166144           | 0.000026885 | -0.000309697 |           |
| 3             | 1             | 0.000370374            | 0.000291529 | 0.000183803 |           |
| 4             | 6             | 0.000149202            | -0.000126488 | -0.000048005 |           |
| 5             | 1             | -0.000033509           | 0.000135617 | 0.000007677 |           |
| 6             | 1             | -0.000022705           | 0.000040227 | -0.00053537 |           |
| 7             | 6             | 0.000202679            | -0.06783279 | -0.004213658 |           |
| 8             | 6             | -0.005529553           | -0.08157009 | 0.000140949 |           |
| 9             | 6             | -0.000424824           | -0.00642014 | -0.000313562 |           |
| 10            | 1             | 0.000063254            | 0.000105991 | 0.000023948 |           |
| 11            | 1             | 0.0002153478           | 0.000227393 | 0.000027891 |           |
| 12            | 8             | 0.003563091            | 0.00905545 | -0.000791349 |           |
| 13            | 6             | -0.003927382           | 0.000540465 | 0.004233962 |           |
| 14            | 1             | -0.002934389           | -0.03912506 | -0.000380122 |           |
| 15            | 6             | 0.001193147            | -0.00770402 | -0.00015499 |           |
| 16            | 1             | 0.000268191            | 0.000236311 | -0.000235996 |           |
| 17            | 1             | -0.000016354           | 0.000190415 | -0.000134410 |           |
| 18            | 6             | 0.000096621            | 0.000219870 | -0.000115960 |           |
| 19            | 1             | 0.0000519338           | -0.000220970 | -0.000182232 |           |
| 20            | 1             | -0.000197968           | 0.00029635 | 0.000043225 |           |
| 21            | 6             | 0.000007347            | -0.000207695 | -0.000096855 |           |
| 22            | 6             | -0.000072415           | 0.000024240 | 0.000034036 |           |
| 23            | 6             | -0.000146671           | -0.000150202 | 0.000268818 |           |
| 24            | 6             | 0.000034252            | 0.000237778 | 0.000206996 |           |
| 25            | 6             | 0.000226518            | 0.000136457 | -0.000315768 |           |
26   6   -0.000153423  -0.000024371  -0.000097922
27   1   0.000002238   -0.000028525   0.000002878
28   1   0.000017096  -0.000038323  -0.000044726
29   1  -0.000075806   0.000100476  -0.000019340
30   1  -0.000538757   0.000399380  -0.000523255
31   1   0.00007750  -0.000102036  -0.000000713
32   6   0.005748093   0.013272561   0.001868112
33   6  0.010898742  -0.002820310  -0.014018863
34   6  -0.004950443   0.010324857   0.012344838
35   6  0.00582755  -0.001269999  -0.002510665
36   1  -0.001898224   0.007820327   0.008866218
37   6  -0.001796900   0.007042626   0.003757778
38   1   0.010730498   0.007057508  -0.008953293
39   6   0.002785327   0.00455758   0.000001163
40   1  -0.008381915  -0.003410056   0.008567424
41   1   0.001203885  -0.009143054  -0.008368086
42   1  -0.005993706  -0.010404622   0.000356135

11b-2

Imaginary Frequencies: 0

ZPE and thermally corrected free energy: -849.366505 Ha (-1.2 kcal/mol vs 11a-2)

| Center Number | Atomic Number | Forces (Hartrees/Bohr) | X       | Y       | Z       |
|---------------|---------------|------------------------|---------|---------|---------|
| 1             | 6             |                        | -0.003178310 | 0.001313664 | 0.006652844 |
| 2             | 1             |                        | -0.001277528 | -0.000881186 | -0.001410797 |
| 3             | 1             |                        | 0.000210115  | 0.000205687  | 0.000062185  |
| 4             | 6             |                        | 0.000505260  | 0.000072365  | 0.000495412  |
| 5             | 1             |                        | 0.000021331  | 0.000112663  | -0.000043206 |
| 6             | 1             |                        | 0.000200993  | -0.000007869 | 0.00000502   |
| 7             | 6             |                        | -0.0001065710| -0.012859666 | 0.000127445  |
|   |   | 0.002047379 | 0.024734608 | -0.001012505 |
|---|---|-------------|-------------|--------------|
| 9 | 6 | 0.000085739 | 0.000397657 | 0.000534073  |
| 10| 1 | -0.000056544 | -0.00066560 | -0.00006775  |
| 11| 1 | 0.000110375 | -0.000037802| -0.000023727 |
| 12| 8 | -0.000757328 | -0.001918582| -0.000279913 |
| 13| 6 | 0.002370859 | 0.003607000 | -0.006376094 |
| 14| 1 | -0.000280643 | 0.000481614 | -0.000110518 |
| 15| 6 | 0.000265143 | -0.001831999| 0.001249925  |
| 16| 1 | 0.000589902 | -0.000201870| -0.000193722 |
| 17| 1 | -0.000181325 | -0.000002282| 0.000046148  |
| 18| 6 | 0.000361861 | 0.01239164  | -0.000514229 |
| 19| 1 | 0.000307709 | -0.000549649| 0.00038020   |
| 20| 6 | 0.000029316 | -0.00017878 | 0.000042884  |
| 21| 6 | 0.000061064 | 0.00040343  | -0.000053428 |
| 22| 6 | -0.000000743 | 0.00001198  | 0.000023113  |
| 23| 6 | 0.000101240 | 0.00001279  | -0.00064180  |
| 24| 6 | -0.000300988 | 0.000325253 | 0.000482698  |
| 25| 6 | 0.000205037 | 0.00009587  | -0.000217062 |
| 26| 1 | 0.000030398 | -0.00016711 | 0.00001165   |
| 27| 1 | 0.00016479  | -0.00003924 | -0.00028183  |
| 28| 1 | 0.00025633  | -0.00005862 | -0.00030966  |
| 29| 1 | -0.00055630 | 0.00004225  | 0.000044267  |
| 30| 1 | -0.00031026 | 0.00025049  | 0.00009429   |
| 31| 6 | -0.001868082 | -0.018294377| 0.000590152  |
| 32| 6 | -0.005214486 | 0.014392338 | 0.026350973  |
| 33| 6 | 0.010998822 | 0.012362299 | -0.026133627 |
| 34| 6 | 0.000878542 | -0.005721700| 0.008964540  |
| 35| 1 | 0.001211847 | 0.005580706 | -0.010537532 |
| 36| 6 | -0.003373706 | -0.004808465| -0.009449733 |
| 37| 8 | 0.001157871 | 0.005045454 | 0.010756113  |
| 38| 6 | 0.000757405 | 0.003903013 | 0.000448723  |
| 39| 1 | -0.000644016 | -0.00709675 | -0.01055118  |
| 40| 1 | -0.002186409 | -0.007155809| 0.010302010  |
| 41| 1 | -0.002162171 | -0.011668957| -0.000272747 |
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