Supporting Information

Dual Catalysis in Enantioselective Oxidopyrylium-Based [5+2] Cycloadditions

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1. General Information

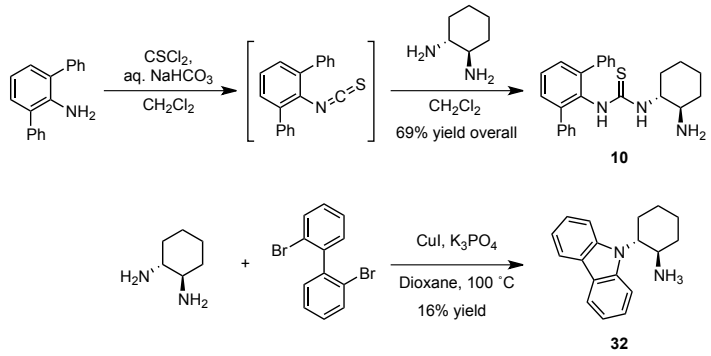
Cycloaddition reactions were performed in oven-dried 0.5-dram vials; all other reactions were performed in oven- or flame-dried round bottom flasks unless otherwise noted. The vials and flasks were fitted with rubber septa and reactions were conducted under air unless noted. Stainless steel syringes were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed using silica gel 60 (230-400 mesh) from EM Science or Davisil® (Grade 643, pore size 150Å, 200-425 mesh) from Sigma-Aldrich. Commercial reagents were purchased from Sigma-Aldrich, Alfa Aesar, or TCI, and used as received with the following exceptions: dichloromethane, toluene, tetrahydrofuran, diethyl ether, 1,4-dioxane, and methanol were dried by passing through columns of activated alumina. Triethylamine and pyridine were distilled from CaH_2 at 760 torr. Furfural was distilled at 20 torr. *n*-Butyllithium was titrated using *N*-benzylbenzamide as an indicator. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Varian-Mercury-400 (400 MHz), Inova-500 (500 MHz), or Inova-600 (600 MHz) spectrometers. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$ = δ 7.27). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$ = δ 77.0). Data are represented as follows: chemical shift, multiplicity (br. = broad, s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet,

m = multiplet), coupling constants in Hertz (Hz), integration. Infrared (IR) spectra were obtained using a Bruker Optics Tensor 27 FTIR spectrometer. Optical rotations were measured using a Jasco DIP 370 digital polarimeter. The mass spectral data were obtained on an Agilent Technologies 6120 quadrupole LC/MS spectrometer (when designated ESI, APCI, or ESI-APCI) or on a Bruker micrOTOF-Q II time-of-flight LC/MS spectrometer (when designated ESI-TOF). Chiral HPLC analysis was performed using an Agilent analytical chromatograph with commercial ChiralPak or ChiralCel columns.

Abbreviations: *ee* – enantiomeric excess, HPLC – high performance liquid chromatography, *n*-BuLi – butyllithium, EDC – 1-(3-(dimethyl-amino)propyl)-3-ethyl-carbodiimide hydrochloride, CH_2Cl_2 – dichloromethane, EtOAc – ethyl acetate, Et_2O – diethyl ether, MeOH – methanol, EtOH – ethanol, *i*PrOH – isopropanol, NEt_3 – triethylamine, AcOH – acetic acid, BzOH – benzoic acid, DMAP – 4-(dimethylamino)pyridine, DBU – 1,8-Diazabicyclo[5.4.0]undec-7-ene, pyr. – pyridine, imid. – imidazole, NMO – *N*-Methylmorpholine-*N*-oxide, TBAF – tetrabutylammonium fluoride, THF – tetrahydrofuran, diast. – diastereomer.

2. Synthesis and Characterization of Catalysts 10 and 32

Scheme S1. Synthesis of catalysts **10** and **32**



1-([1,1':3',1''-terphenyl]-2'-yl)-3-((1*R*,2*R*)-2-aminocyclohexyl)thiourea (10):
2,6-diphenylaniline[1] (150.0 mg, 0.611 mmol) was dissolved in CH_2Cl_2 (3.1 mL) and sat. aq. $NaHCO_3$ (3.1 mL) was added. The resulting biphasic solution was cooled to 0 °C and thiophosgene (0.061 mL, 0.795 mmol, 1.3 equiv) was then carefully added via syringe. The reaction was allowed to warm to room temperature and stirred for 5 h. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The crude product was then redissolved in hexanes and minimal CH_2Cl_2 and filtered through a plug of silica gel, eluting with hexanes, to afford 2,6-diphenylphenylisothiocyanate as a white solid (170.0 mg, 97%) which was used directly in the subsequent reaction.

[1] 2,6-diphenylaniline synthesized according to: Miura, Y.; Oka, H.; Momoki, M.; *Synthesis* **1995**, 1419–1422.

(*R,R*)-1,2-*trans*-diaminocyclohexane[2] (203.0 mg, 1.78 mmol, 3.0 equiv) was dissolved in CH_2Cl_2 (2.0 mL) and the resulting solution was cooled to 0 °C. To this was added dropwise a solution of 2,6-diphenylphenylisothiocyanate (170.0 mg, 0.592 mmol, 1.0 equiv) in CH_2Cl_2 (2 mL). The resulting reaction mixture was allowed to warm to room temperature and stir for 3 h. The solution was then concentrated and loaded directly onto silica gel. Column chromatography (silica gel, 95:5 CH_2Cl_2/MeOH) afforded clean primary aminothiourea as a slightly yellow foam. This was redissolved in minimal benzene and triturated with hexanes. Filtration and further washing of the solid with hexanes afforded **10** as a white solid (170 mg, 71%).

R_f = 0.44 (silica gel, 90:10 CH_2Cl_2/MeOH);

IR (film) ν_{max} 3237, 3054, 2926, 2854, 2360, 2341, 1692, 1522, 755, 700, 613 cm^{-1};

^{1}H NMR (400 MHz, CD_3OD) δ 7.64 - 7.29 (br. m, 13H), 4.03 - 3.83 (br. s, 1H), 2.24 - 2.12 (br. ap. tr, 1H), 1.90 - 1.76 (br. ap. d, 1H), 1.70 - 1.46 (2 br. s, 3H), 1.25 - 1.09 (br. s, 2H), 1.09 - 1.94 (br. m, 2H);

^{13}C NMR[3] (100 MHz, $CDCl_3$) δ 180.3, 140.5, 138.3, 131.1, 129.1 (br. s), 128.9 (br. s), 128.5 (br. s), 62.3, 56.3, 34.8, 32.3, 25.2;

MS (ESI-TOF) calcd. for $C_{25}H_{27}N_3S$ [M + H^+] 402.2004, found 402.1995;

$[\alpha]_D^{22}$ = +38.4 (c = 1.0, $CHCl_3$).

(1*R*,2*R*)-2-(9H-carbazol-9-yl)cyclohexanamine (32):

A flame-dried vial was charged sequentially with 2,2'-dibromobiphenyl (500 mg, 1.60 mmol), (*R,R*)-1,2-*trans*-diaminocyclohexane[2] (220 mg, 1.92 mmol, 1.2 equiv), copper iodide (152 mg, 0.80 mmol, 0.5 equiv), and potassium phosphate (747 mg, 3.52 mmol, 2.2 equiv). The vial was sealed and then evacuated and backfilled with nitrogen three times. 1,4-Dioxane (3.2 mL, 0.5 M) was added and the sealed vessel was placed in a 100 ˚C oil bath and the reaction mixture was stirred vigorously for 24 h. The reaction mixture was allowed to cool to room temperature and then diluted with EtOAc (20 mL), filtered through a pad of celite, and concentrated. Purification by column chromatography (silica gel, 95:5 CH_2Cl_2/MeOH) afforded **32** as an off-white solid (67.2 mg, 16%, unoptimized).

R_f = 0.45 (silica gel, 90:10 CH_2Cl_2/MeOH);

IR (film) ν_{max} 2936, 2858, 1594, 1482, 1453, 1329, 1221, 910, 750, 724 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 7.3, 16.5 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.56 - 7.40 (m, 3H), 7.25 (t, *J* = 7.6 Hz, 2H), 4.23 (ddd, *J* = 3.9, 10.5, 12.6 Hz, 1H), 3.77 (td, *J* = 3.9, 10.6 Hz, 1H), 2.47 - 2.38 (m, 1H), 2.23 - 2.17 (m, 1H), 2.02 - 1.92 (m, 3H), 1.61 - 1.52 (m, 2H), 1.44 (dq, *J* = 3.2, 12.8 Hz, 1H), 1.26 (br. s, 2H);

^{13}C NMR (125 MHz, $CDCl_3$) 126.1, 125.5, 120.8, 120.3, 119.2, 111.9, 109.3, 63.4, 52.2, 35.6, 29.6, 26.4, 25.4;

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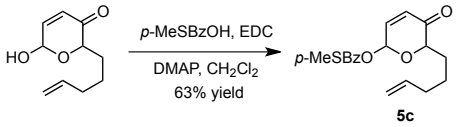
[2] (*R,R*)-1,2-*trans*-diaminocyclohexane was resolved according to: Larrow, J. F.; Jacobsen, E. N.; Gao, Y.; Hong, Y.; Nie, X.; Zepp, C. M. *J. Org. Chem.* **1994**, *59*, 1939–1942.

[3] ^{13}C NMR spectra of **10** in a variety of solvents at room or elevated temperature all showed broad signals preventing the observation of distinct peaks for all carbons. The obtained X-ray crystal structure also exhibits whole molecular disorder.

MS (ESI-TOF) calcd. for $C_{18}H_{20}N_2$ [M + H^+] 265.1699, found 265.1691;
$[\alpha]_D^{25}$ = +66.8 (c = 0.9, $CHCl_3$).

3. Synthesis and Characterization of Substrates

Scheme S2. Synthesis of substrate **5c**



5c

5-oxo-6-(pent-4-en-1-yl)-5,6-dihydro-2*H*-pyran-2-yl 4-(methylthio)benzoate (5c):
6-Hydroxy-2-(pent-4-en-1-yl)-2*H*-pyran-3(6*H*)-one[4] (700 mg, 3.84 mmol) was dissolved in CH_2Cl_2 (15.4 mL, 0.25 M) and the flask was cooled to 0 ˚C. To this solution was added sequentially 4-methylthiobenzoic acid (775 mg, 4.61 mmol, 1.2 equiv), EDC (884 mg, 4.61 mmol, 1.2 equiv), and DMAP (563 mg, 4.61 mmol, 1.2 equiv). The reaction mixture was stirred at 0 ºC for 30 min and then allowed to warm to room temperature and stirred a further 30 min. The reaction mixture was then diluted with Et_2O (60 mL) and quenched with 1N HCl (25 mL). The layers were separated and the organic layer was washed succesively with 1N HCl (25 mL), sat. aq. $NaHCO_3$ (25 mL), water (25 mL), and brine (25 mL). The organic layer was dried over Na_2SO_4, filtered, concentrated and purified by column chromatography (silica gel, 95:5 to 5:1 hexanes, Et_2O) to afford **5c** as a yellow oil as a 3:2 mixture of diastereomers which solidified upon storage at –30 ˚C (798 mg, 63%). [Note- in some instances 4-methylthiobenzoic anhydride was found to coelute with the desired product upon column chromatography. Treatment of this mixture with 1 equiv DMAP (relative to anhydride) in a 1:1 mixture of CH_2Cl_2 and MeOH (0.2 M relative to anhydride) instantaneously converted the anhydride to the methyl ester, which could be separated from the desired product under the same chromatography conditions.]
$\mathbf{R}_f$ = 0.37, 0.44 (silica gel, 5:1 hexanes/EtOAc);
IR (film) ν_{max} 3079, 2924, 2866, 1721, 1693, 1595, 1263, 1095, 1072, 907, 754 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.3 Hz, 2H), 7.27 - 7.23 (m, 2H), 7.02 - 6.95 (m, 1H), 6.78 (minor diast., dd, *J* = 1.0, 2.9, 0.4H), 6.73 (major diast., d, *J* = 3.4 Hz, 0.6H), 6.28 - 6.27 (m, 1H), 5.81 - 5.71 (major diast., m, 0.6H), 5.69 - 5.59 (minor diast., m, 0.4H), 5.00 - 4.84 (m, 2H), 4.57 (major diast., dd, *J* = 3.9, 7.3 Hz, 0.6H), 4.27 (minor diast., dd, *J* = 4.6, 9.5 H, 0.4H), 2.51 (s, 3H), 2.04 (q, *J* = 7.3 Hz, 1H), 2.01 - 1.82 (m, 2H), 1.81 - 1.72 (m, 1H), 1.54 - 1.47 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 195.9, 165.0, 164.9, 147.1, 147.0, 142.8, 142.0, 138.5, 138.2, 130.4, 129.0, 128.4, 125.3, 125.2, 115.2, 115.1, 88.0 ,87.7, 79.8, 76.1, 33.6, 33.5, 33.2, 29.3, 24.9, 24.1, 15.0;
MS (ESI-TOF) calcd. for $C_{18}H_{20}O_4S$ [M + Na^+] 355.0975, found 355.0994.

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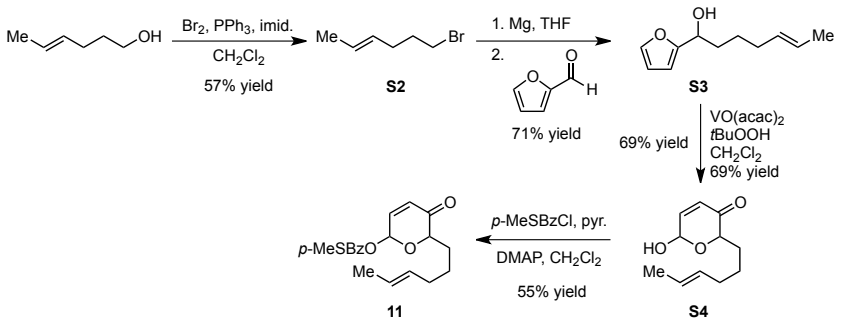
[4] 6-Hydroxy-2-(pent-4-en-1-yl)-2*H*-pyran-3(6*H*)-one synthesized according to: Sammes, P. G.; Street, L. J.; Kirby, P. *J. Chem. Soc. Perkin Trans. 1* **1983**, 2729–2734.

Scheme S3. Synthesis of substrate **11**



(*E*)-6-bromohex-2-ene (S2):

Triphenylphosphine (20.058 g, 76.5 mmol, 1.8 equiv) and imidazole (8.688 g, 128 mmol, 3 equiv) were dissolved in CH_2Cl_2 (150 mL, 0.28 M) and the resulting solution was cooled to 0 °C. To this mixture was slowly added bromine (3.7 mL, 71.8 mmol, 1.7 equiv) by syringe and the resulting solution was stirred for 15 min at 0 °C under an atmosphere of nitrogen. (*E*)-4-hexen-1-ol[5] (5.0 mL, 42.5 mmol) was then added neat by syringe, and the solution was stirred under nitrogen for a further 45 min at 0 °C. The resulting suspension was washed with 3% aq. hydrogen peroxide (25 mL), then 1M $Na_2S_2O_3$ (2 x 50 mL). The thiosulfate layers were extracted with CH_2Cl_2 (70 mL). The pooled organic layers were dried over Na_2SO_4, filtered, and concentrated. The resultant crude white paste was then redissolved in hexanes and minimal CH_2Cl_2 and filtered through a plug of silica gel, eluting with hexanes, to afford **S2** as a pale yellow oil (3.926 g, 57%).

Spectroscopic data agree with previously reported data.[6]

(*E*)-1-(furan-2-yl)hept-5-en-1-ol (S3):

Magnesium turnings (374 mg, 15.4 mmol, 5 equiv) were rigorously flame-dried under vacuum in a round bottom flask attached with a condenser. Once the magnesium had cooled, it was exposed to an atmosphere of nitrogen and suspended in THF (7.7 mL, 0.4 M). To this suspension was added sequentially 1,2-dibromoethane activator (0.01 mL, 0.12 mmol) then **S2** (503 mg, 3.09 mmol). This was stirred and gently heated (approx. 40 °C) until an exotherm was observed. The suspension was then stirred for a further 30 min at room temperature, after which the dark suspension was cannulated into a solution of furfural (0.26 mL, 3.1 mmol, 1 equiv) in THF (7.7 mL 0.4 M), pre-cooled to 0 °C. This reaction mixture was stirred under an atmosphere of nitrogen at 0 °C for 1 h. The resulting solution was then washed with sat. aq. NH_4Cl (2 x 15 mL), and the pooled aqueous layers were extracted with EtOAc (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by flash chromatography (silica gel, 9:1 to 3:2 hexanes/EtOAc) to afford **S3** as a colorless oil (393 mg, 71%).

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[5] (*E*)-4-Hexen-1-ol was purchased from Sigma-Aldrich as a "predominantly *trans*" mixture. A small amount (approx. 4%) of inseparable (*Z*)-4-Hexen-1-ol impurity was carried through the synthesis of substrate **11** and subsequent cycloaddition to **12**.

[6] Oppolzer, W.; Siles, S.; Snowden, R. L.; Bakker, B. H.; Petrzilka, M. *Tetrahedron* **1985**, *41*, 3497–3509.

R_f = 0.37 (silica gel, 2:1 hexanes/EtOAc);
IR (film) ν_{max} 3375 (br), 2938, 1505, 1453, 1149, 1008, 967, 914, 736 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 2.0 Hz, 1H), 6.30 (dd, *J* = 1.7, 3.2 Hz, 1H), 6.20 (d, *J* = 3.4 Hz, 1H), 5.46 - 5.35 (m, 2H), 4.67 - 4.60 (m, 1H), 2.27 (d, *J* = 4.4 Hz, 1H), 2.03 - 1.97 (m, 3H), 1.85 - 1.79 (m, 2H), 1.63 (d, *J* = 4.4 Hz, 2H), 1.52 - 1.42 (m, 1H), 1.40 - 1.29 (m, 1H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 142.0, 131.2, 125.4, 110.3, 106.0, 67.9, 35.2, 32.5, 25.7, 18.1;
MS (ESI-APCI) calcd. for $C_{11}H_{16}O_2$ $[M - OH]^+$ 163.1, found 163.2.

(*E*)-2-(hex-4-en-1-yl)-6-hydroxy-2*H*-pyran-3(6H)-one (S4):
Alcohol **S3** (521 mg, 2.89 mmol) was dissolved in CH_2Cl_2 (10 mL, 0.3 M), and the resulting solution was cooled to 0 °C. To this solution was added solid vanadyl acetylacetonate (77 mg, 0.29 mmol, 0.1 equiv), then *tert*-butyl hydroperoxide (0.79 mL of a 5.5 M solution in dodecane, 4.35 mmol, 1.5 equiv) by syringe. The reaction was stirred at 0 °C for 1 h, before it was quenched with 1M $Na_2S_2O_3$ (20 mL) and stirred for a further 30 min. The aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL) and the pooled organic layers were dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by flash chromatography (silica gel, 9:1 to 3:2 hexanes/EtOAc) to afford **S4** as a colorless oil as a 2:1 mixture of diastereomers (389 mg, 69%).
R_f = 0.31 (silica gel, 2:1 hexanes/EtOAc);
IR (film) ν_{max} 3398 (br), 2929, 1687, 1438, 1375, 1241, 1153, 1089, 1027, 967, 911, 732 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (minor diast., dd, *J* = 1.4, 10.5 Hz, 0.33H), 6.90 (major diast., dd, *J* = 3.7, 10.5 Hz, 0.67H), 6.15 (minor diast., dd *J* = 1.4, 10.5 Hz, 0.33H), 6.10 (major diast., d, *J* = 10.5 Hz, 0.67H), 5.67 - 5.62 (m, 1H), 5.48 - 5.37 (m, 2H), 4.56 (major diast., dd, *J* = 3.9, 8.0 Hz, 0.67H), 4.08 (minor diast., dd, *J* = 3.4, 8.0 Hz, 0.33H), 3.81 (minor diast., dd, *J* = 1.8, 7.3 Hz, 0.33H), 3.54 (major diast., dd, *J* = 1.8, 5.0, 0.67H), 2.05 - 1.88 (m, 3H), 1.82 - 1.42 (m, 6H);
^{13}C NMR (500 MHz, $CDCl_3$) δ 197.1, 196.6, 148.1, 144.8, 131.0, 129.0, 127.8, 125.6, 125.5, 91.1, 87.8, 79.1, 74.4, 32.5, 30.4, 29.4, 25.3, 25.1, 18.1;
MS (ESI-TOF) calcd. for $C_{11}H_{16}O_3$ $[M + Na]^+$ 219.0992, found 219.1005.

(*E*)-6-(hex-4-en-1-yl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl 4-(methylthio)benzoate (11):
Hemiacetal **S4** (1.330 g, 6.78 mmol) was dissolved in CH_2Cl_2 (34 mL, 0.2 M) and the resulting solution was cooled to 0 °C. To this solution was added sequentially, 4-thiomethylbenzoyl chloride (1.464 g, 7.45 mmol, 1.1 equiv), pyridine (0.88 mL, 10.88 mmol, 1.6 equiv), and DMAP (250 mg, 2.05 mmol, 0.3 equiv). The reaction was stirred under nitrogen and allowed to warm to room temperature overnight. The solution was diluted with ethyl acetate (60 mL), then washed with 1N HCl (2 x 50 mL), saturated $NaHCO_3$ (50 mL), and brine (50 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by flash chromatography (silica gel, 9:1 to 3:1 hexanes/Et_2O) to afford **11** as a white powder as a 2:1 mixture of diastereomers (1.286 g, 55%). [Note- in some instances 4-methylthiobenzoic anhydride was found to coelute with the desired product upon column chromatography. Treatment of this mixture with 1 equiv DMAP (relative to anhydride) in a 1:1 mixture of CH_2Cl_2 and MeOH (0.2 M relative to anhydride) instantaneously converted the anhydride to the methyl ester, which could be separated from the

desired product under the same chromatography conditions.]

R_f = 0.15, 0.19 (silica gel, 4:1 hexanes/Et_2O);

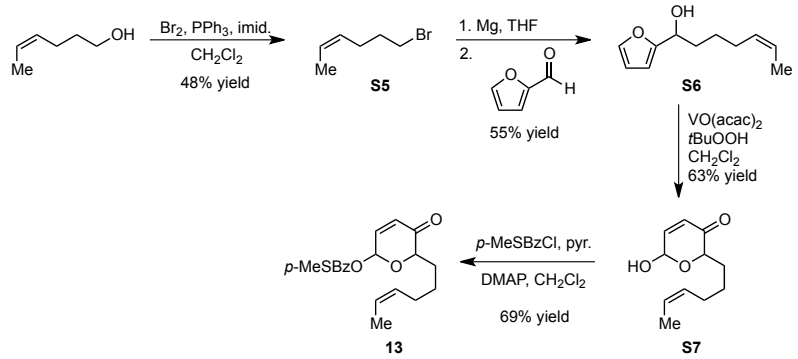
IR (film) ν_{max} 2920, 2361, 1721, 1695, 1593, 1437, 1401, 1327, 1261, 1178, 1094, 1067, 1013, 967, 922, 841, 757, 689 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 - 7.91 (m, 2H), 7.28 - 7.24 (m, 2H), 7.02 - 6.95 (m, 1H), 6.79 (minor diast., dd, *J* = 1.5, 2.9 Hz, 0.33H), 6.74 (major diast., d, *J* = 3.9 Hz, 0.67H), 6.28 - 6.24 (m, 1H), 5.40 - 5.26 (m, 2H), 4.56 (major diast., dd, *J* = 3.9, 7.8 Hz, 0.67H), 4.27 (minor diast., dd, *J* = 4.9, 9.8 Hz, 0.33H), 2.53 - 2.51 (m, 3H), 2.00 - 1.41 (m, 9H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 196.0, 165.0, 147.1, 147.0, 142.7, 142.0, 131.0, 130.7, 130.4, 129.1, 128.4, 125.6, 125.5, 125.2, 88.0, 87.7, 79.9, 76.2, 33.3, 32.5, 32.3, 29.4, 25.5, 24.8, 18.1, 15.0;

MS (ESI-TOF) calcd. for $C_{19}H_{22}O_4S$ $[M + Na]^+$ 369.1131, found 369.1127.

Scheme S4. Synthesis of substrate **13**



(*Z*)-6-bromohex-2-ene (S5):

Reaction of triphenylphosphine (20.204 g, 77.0 mmol, 1.8 equiv), imidazole (8.745 g, 128 mmol, 3 equiv), and bromine (3.8 mL, 73.8 mmol, 1.7 equiv) in CH_2Cl_2 (160 mL, 0.27 M) followed by (Z)-4-hexen-1-ol (5.0 mL, 42.8 mmol) according to **S2** above afforded **S5** as a pale yellow oil (3.341 g, 48%).

R_f = 0.87 (silica gel, hexanes);

IR (film) ν_{max} 3014, 2928, 2855, 1436, 1245, 700, 565 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) 5.56 - 5.47 (m, 1H), 5.37 - 5.29 (m, 1H), 3.40 (t, *J* = 6.6 Hz, 2H), 2.20 (q, *J* = 7.3 Hz, 2H), 1.91 (quin, *J* = 7.0 Hz, 2H), 1.63 (d, *J* = 6.8 Hz, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 126.6, 125.7, 33.6, 32.7, 25.5, 13.1;

(*Z*)-1-(furan-2-yl)hept-5-en-1-ol (S6):

Grignard formation between magnesium turnings (2.498 g, 103 mmol, 5 equiv) and **S5** (3.341 g, 20.5 mmol) with 1,2-dibromoethane (0.05 mL, 0.58 mmol) was carried out in THF (50 mL, 0.41 M) according to **S3** above. Addition of this Grignard reagent to furfural (1.70 mL, 20.5 mmol, 1 equiv) in THF (50 mL) according to **S3** above afforded **S6** as a colorless oil after column chromatography (silica gel, 9:1 to 3:2 hexanes/EtOAc) (2.031 g, 55%).

R_f = 0.37 (silica gel, 2:1 hexanes/EtOAC);

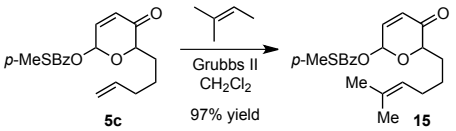
IR (film) ν_{max} 3375 (br), 3013, 2936, 2862, 2360, 2341, 1505, 1443, 1404, 1231, 1148, 1006 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 - 7.34 (m, 1H), 6.31 (dd, *J* = 2.1, 3.0 Hz, 1H), 6.21 (d, *J* = 3.2 Hz, 1H), 5.52 - 5.42 (m, 1H), 5.42 - 5.34 (m, 1H), 4.67 - 4.60 (m, 1H), 2.56 (br. s., 1H), 2.07 (q, *J* = 7.3 Hz, 2H), 1.92 - 1.78 (m, 2H), 1.60 (dd, *J* = 0.9, 7.3 Hz, 3H), 1.54 - 1.44 (m, 1H), 1.43 - 1.33 (m, 1H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 157.2, 142.0, 130.4, 124.4, 110.3, 106.0, 67.9, 35.3, 26.7, 25.7, 13.0;
MS (ESI-APCI) calcd. for $C_{11}H_{16}O_2$ $[M - OH]^+$ 163.1, found 163.1.

(*Z*)-2-(hex-4-en-1-yl)-6-hydroxy-2*H*-pyran-3(6H)-one (S7):
Reacion of **S6** (2.031 g, 11.3 mmol), vanadyl acetylacetonate (300 mg, 1.13 mmol, 0.1 equiv), and *tert*-butyl hydroperoxide (3.1 mL of a 5.5 M solution in dodecane, 17.1 mmol, 1.5 equiv) in CH_2Cl_2 (38 mL, 0.3 M) according to **S4** above afforded **S7** as a colorless oil after column chromatography (silica gel, 9:1 to 3:2 hexanes/EtOAc) as a 2:1 mixture of diastereomers (1.402 g, 63%).
R_f = 0.37 (silica gel, 2:1 hexanes/EtoAc);
IR (film) ν_{max} 3401 (br), 2929, 1694, 1438, 1373, 1241, 1143, 1091, 1033, 964, 913, 737 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (minor diast., dd, *J* = 1.4, 10.1 Hz, 0.33H), 6.91 (major diast., dd, *J* = 3.2, 10.3 Hz, 0.67H), 6.18 (minor diast., dd, *J* = 1.6, 10.3 Hz, 0.33H), 6.13 (major diast., d, *J* = 10.1 Hz, 0.67H), 5.70 - 5.65 (m, 1H), 5.52 - 5.45 (m, 1H), 5.43 - 5.37 (m, 1H), 4.59 (major diast., dd, *J* = 4.1, 8.4 Hz, 0.67H), 4.11 (minor diast., dd, *J* = 4.1, 8.2 Hz, 0.33H), 3.10 (minor diast., d, *J* = 7.3 Hz, 0.33H), 2.89 (major diast., d, *J* = 5.0 Hz, 0.67H), 2.10 (q, *J* = 7.0 Hz, 2H), 2.02 - 1.94 (m, 1H), 1.86 - 1.78 (minor diast., m, 0.33H), 1.78 - 1.69 (major diast., m, 0.67H), 1.62 (d, *J* = 6.4 Hz, 3H), 1.56 - 1.47 (m, 2H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 198.5, 147.7, 144.3, 130.3, 130.2, 129.06, 128.0, 124.6, 91.1, 87.9, 79.1, 74.4, 30.5, 29.5, 26.38, 25.3, 25.2, 13.0;
MS (ESI-TOF) calcd. for $C_{11}H_{16}O_3$ $[M + Na]^+$ 219.0992, found 219.1004.

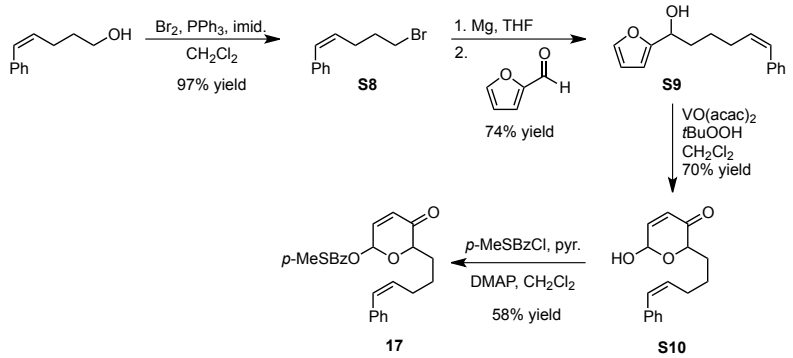
(*Z*)-6-(hex-4-en-1-yl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl 4-(methylthio)benzoate (13):
Reaction of **S7** (687 mg, 3.50 mmol), 4-thiomethylbenzoyl chloride (756 mg, 3.85 mmol, 1.1 equiv), pyridine (0.45 mL, 5.56 mmol, 1.59 equiv), and DMAP (130 mg, 1.06 mmol, 0.3 equiv) in CH_2Cl_2 (18 mL, 0.19 M) according to **11** above afforded **13** as a white gel after column chromatography (silica gel, 9:1 to 3:1 hexanes/Et_2O) as a 2:1 mixture of diastereomers (835 mg, 69%).
R_f = 0.15, 0.19 (silica gel, 4:1 hexanes/Et_2O);
IR (film) ν_{max} 2924, 1720, 1695, 1593, 1491, 1437, 1402, 1327, 1262, 1177, 1094, 1067, 1013, 922, 840, 756, 689 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 - 7.89 (m, 2H), 7.27 - 7.24 (m, 2H), 7.03 - 6.94 (m, 1H), 6.78 (minor diast., d, *J* = 2.4 Hz, 0.33H), 6.73 (major diast., d, *J* = 3.4 Hz, 0.67H), 6.28 - 6.24 (m, 1H), 5.46 - 5.17 (m, 2H), 4.56 (major diast., dd, *J* = 3.7, 7.6 Hz, 0.67H), 4.27 (minor diast., dd, *J* = 4.4, 9.8 Hz, 0.33H), 2.50 (s, 3H), 2.08 - 1.80 (m, 4H), 1.76 (dq, *J* = 7.5, 14.7 Hz, 1H), 1.54 (d, *J* = 6.3 Hz, 2H), 1.51 - 1.43 (m, 2H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 196.1, 196.0, 165.0, 164.9, 147.1, 147.0, 142.8, 142.0, 130.4, 130.2, 129.9, 129.1, 128.4, 125.2, 124.6, 124.5, 88.0, 87.7, 79.9, 76.1, 33.4, 29.5, 26.7, 26.5, 25.5, 24.7, 15.0, 13.0;
MS (ESI-TOF) calcd. for $C_{19}H_{22}O_4S$ $[M + Na]^+$ 369.1131, found 369.1133.

Scheme S5. Synthesis of substrate **15**



6-(5-methylhex-4-en-1-yl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl 4-(methylthio)benzoate (15):
Grubbs' Catalyst, 2nd Generation (29 mg, 0.034 mmol, 0.03 equiv) was dissolved in CH_2Cl_2 (2.0 mL) in a sealed tube. To the solution was added by syringe **5c** (378 mg, 1.14 mmol), dissolved in CH_2Cl_2 (2.0 mL) then 2-methyl-2-butene (3.3 mL, 31.1 mmol, 27 equiv). The reaction was stirred at 39 °C overnight. The crude mixture was concentrated and purified by flash chromatography (silica gel, 9:1 to 3:2 hexanes/Et_2O) to afford **15** as a colorless oil as a 2:1 mixture of diastereomers (397 mg, 97%).
R_f = 0.13, 0.17 (silica gel, 4:1 hexanes/Et_2O);
IR (film) ν_{max} 2925, 1725, 1698, 1594, 1438, 1402, 1328, 1235, 1177, 1095, 10711013, 930, 841, 758, 690 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 - 7.92 (m, 2H), 7.29 - 7.24 (m, 2H), 7.02 - 6.95 (m, 1H), 6.79 (minor disast., dd, *J* = 1.5, 2.9 Hz, 0.33H), 6.74 (major diast., d, *J* = 3.9 Hz, 0.67H), 6.29 - 6.25 (m, 1H), 5.12 - 5.05 (major diast., m, 0.67H), 5.01 - 4.95 (minor diast., m, 0.33H), 4.56 (major diast., dd, *J* = 3.9, 7.8 Hz, 0.67H), 4.30 (minor diast., dd, *J* = 4.6, 9.5 Hz, 0.33H), 2.54 - 2.51 (m, 3H), 2.02 - 1.81 (m, 3H), 1.80 - 1.71 (m, 1H), 1.69 - 1.60 (m, 3H), 1.58 - 1.53 (m, 2H), 1.52 - 1.41 (m, 3H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 196.0, 165.0, 147.0, 142.8, 141.9, 132.0, 130.4, 129.1, 128.5, 125.2, 124.3, 124.0, 88.0, 87.7, 80.0, 79.2, 33.4, 29.5, 27.9, 27.7, 25.9, 25.8, 25.1, 17.9, 17.8, 15.0;
MS (ESI-TOF) calcd. for $C_{20}H_{24}O_4S$ $[M + Na]^+$ 383.1293, found 383.1276.

Scheme S6. Synthesis of substrate **17**



(*Z*)-(5-bromopent-1-en-1-yl)benzene (S8):
Reaction of triphenylphosphine (10.006 g, 38.1 mmol, 1.8 equiv), imidazole (4.319 g, 63.4 mmol, 3 equiv), and bromine (1.9 mL, 36.9 mmol, 1.7 equiv) in CH_2Cl_2 (71 mL, 0.30 M) followed by (*Z*)-5-phenylpent-4-en-1-ol[7] (3.435 g, 21.2 mmol) according to **S2** above afforded **S8** as a pale yellow

[7] (*Z*)-5-phenylpent-4-en-1-ol synthesized according to: Liu, G.; Stahl, S. S. *J. Am. Chem. Soc.* **2007**, *129*, 6328–6335.

oil (4.646 g, 97%).
Spectroscopic data agree with previously reported data.[8]

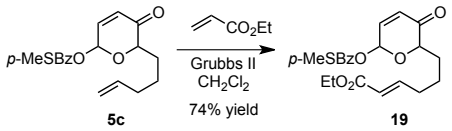
(*Z*)-1-(furan-2-yl)-6-phenylhex-5-en-1-ol (S9):
Grignard formation between magnesium turnings (2.514 g, 103 mmol, 8 equiv) and **S8** (2.910 g, 12.9 mmol) with 1,2-dibromoethane (0.05 mL, 0.58 mmol) was carried out in THF (32 mL, 0.40 M) according to **S3** above. Addition of this Grignard reagent to furfural (1.07 mL, 12.9 mmol, 1 equiv) in THF (32 mL) according to **S3** above afforded **S9** as a yellow oil after column chromatography (silica gel, 9:1 to 3:2 hexanes/Et_2O) (2.307 g, 74%).
$\mathbf{R_f}$ = 0.43 (silica gel, 2:1 hexanes/EtOAc);
IR (film) ν_{max} 3355 (br), 3009, 2939, 2862, 1599, 1494, 1447, 1151, 1170, 1070, 1008, 915, 807, 767, 737, 699 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 - 7.26 (m, 6H), 6.47 (d, *J* = 11.7 Hz, 1H), 6.35 (dd, *J* = 2.0, 3.4 Hz, 1H), 6.24 (d, *J* = 2.9 Hz, 1H), 5.68 (dt, *J* = 7.3, 11.7 Hz, 1H), 4.71 - 4.65 (m, 1H), 2.41 (qd, *J* = 1.7, 7.4 Hz, 2H), 1.95 - 1.88 (m, 2H), 1.69 - 1.59 (m, 1H), 1.56 - 1.46 (m, 1H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 142.2, 137.9, 132.7, 129.5, 129.0, 128.4, 126.8, 110.4, 106.1, 67.8, 35.4, 28.5, 26.1;
MS (ESI-APCI) calcd. for $C_{16}H_{18}O_2$ $[M - OH]^+$ 225.1, found 225.2.

(*Z*)-6-hydroxy-2-(5-phenylpent-4-en-1-yl)-2*H*-pyran-3(6H)-one (S10):
Reacion of **S9** (325 mg, 1.34 mmol), vanadyl acetylacetonate (37 mg, 0.13 mmol, 0.1 equiv), and *tert*-butyl hydroperoxide (0.37 mL of a 5.5 M solution in dodecane, 2.04 mmol, 1.5 equiv) in CH_2Cl_2 (4.5 mL, 0.3 M) according to **S4** above afforded **S10** as a colorless oil after column chromatography (silica gel, 9:1 to 3:2 hexanes/EtOAc) as a 9:1 mixture of diastereomers (245 mg, 70%).
$\mathbf{R_f}$ = 0.26 (silica gel, 2:1 hexanes/EtOAc);
IR (film) ν_{max} 3400 (br), 3009, 2927, 2862, 1687, 1494, 1446, 1371, 1237, 1150, 1092, 1027, 917, 801, 769, 699 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 - 7.31 (m, 2H), 7.27 (d, *J* = 21.5 Hz, 2H), 7.22 (t, *J* = 7.32 Hz, 1H), 6.89 (minor diast., dd, *J* = 1.5, 10.4 Hz, 0.11H), 6.85 (major diast., dd, *J* = 3.4, 10.3 Hz, 0.89H), 6.44 (major diast., d, *J* = 11.2 Hz, 0.89H), 6.40 (minor diast., d, *J* = 15.6 Hz, 0.11H), 6.12 (minor diast., dd, *J* = 1.5, 10.3 Hz, 0.11H), 6.08 (major diast., d, *J* = 10.3 Hz, 0.89H), 5.66 (dt, *J* = 7.2, 11.5 Hz, 1H), 5.57 (dd, *J* = 3.7, 4.6 Hz, 1H), 4.60 (minor diast., dd, *J* = 3.9, 7.8 Hz, 0.11H), 4.54 (major diast., dd, *J* = 3.9, 8.3 Hz, 0.89H), 2.44 - 2.30 (m, 2H), 2.03 - 1.92 (m, 1H), 1.85 - 1.70 (m, 1H), 1.65 - 1.55 (m, 2H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 197.1, 196.7, 148.3, 144.9, 137.9, 137.8, 132.6, 132.5, 129.6, 129.5, 129.0, 128.9, 128.8, 128.4, 127.7, 126.8, 126.2, 91.1, 87.8, 78.8, 74.1, 33.0, 30.3, 29.4, 28.4, 25.6;

[8] Feltenberger, J. B.; Hayashi, R.; Tang, Y.; Babiash, E. S. C; Hsung, R. P. *Org. Lett.* **2009**, *11*, 3666–3669.

(*Z*)-5-oxo-6-(5-phenylpent-4-en-1-yl)-5,6-dihydro-2*H*-pyran-2-yl 4-(methylthio)benzoate (17):
Reaction of **S10** (1.107 g, 4.29 mmol), 4-thiomethylbenzoyl chloride (926 mg, 4.71 mmol, 1.1 equiv), pyridine (0.56 mL, 6.92 mmol, 1.62 equiv), and DMAP (157 mg, 1.29 mmol, 0.3 equiv) in CH_2Cl_2 (21 mL, 0.2 M) according to **11** above afforded **17** as a yellow oil after column chromatography (silica gel, 9:1 to 3:1 hexanes/Et_2O) as a 9:1 mixture of diastereomers (1.010 g, 58%).
$\mathbf{R_f}$ = 0.15, 0.20 (silica gel, 4:1 hexanes/Et_2O);
IR (film) ν_{max} 2924, 1721, 1698, 1593, 1492, 1402, 1328, 1264, 1177, 1094, 1069, 1013, 928, 915, 841, 757, 700, 631 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 - 7.94 (m, 2H), 7.38 - 7.17 (m, 7H), 7.15 (major diast., dd, *J* = 3.3, 10.6 Hz, 0.89H), 7.00 (minor diast., dd, *J* = 3.9, 10.4 Hz, 0.11H), 6.76 (major diast., d, *J* = 3.9 Hz, 0.89H), 6.74 (minor, diast., d, *J* = 3.9 Hz, 0.11H), 6.41 (minor diast., d, *J* = 11.2 Hz, 0.11H), 6.35 (major diast., d, *J* = 15.6 Hz, 0.89H), 6.33 (major diast., m, 0.89H), 6.26 (d, *J* = 10.3 Hz, 0.11H), 5.64 (dt, *J* = 7.1, 11.6 Hz, 1H), 4.61 (major diast., dd, *J* = 3.9, 7.4 Hz, 0.89H), 4.57 (minor, diast., dd, *J* = 3.9, 7.3 Hz, 0.11H), 2.51 (s, 3H), 2.41 - 2.31 (m, 2H), 2.06 - 1.77 (m, 2H), 1.77 - 1.60 (m, 2H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 195.9, 195.8, 164.9, 147.1, 147.0, 142.9, 142.0, 137.8, 132.5, 132.2, 130.4, 130.3, 129.6, 129.5, 129.0, 128.9, 128.5, 128.4, 126.8, 126.7, 126.2, 125.3, 125.2, 88.1, 87.7, 79.7, 76.1, 33.2, 29.6, 28.5, 28.2, 25.9, 25.1, 15.0;
MS (ESI-TOF) calcd. for $C_{24}H_{24}O_4S$ $[M + Na]^+$ 431.1288, found 431.1289.

Scheme S7. Synthesis of substrate **19**

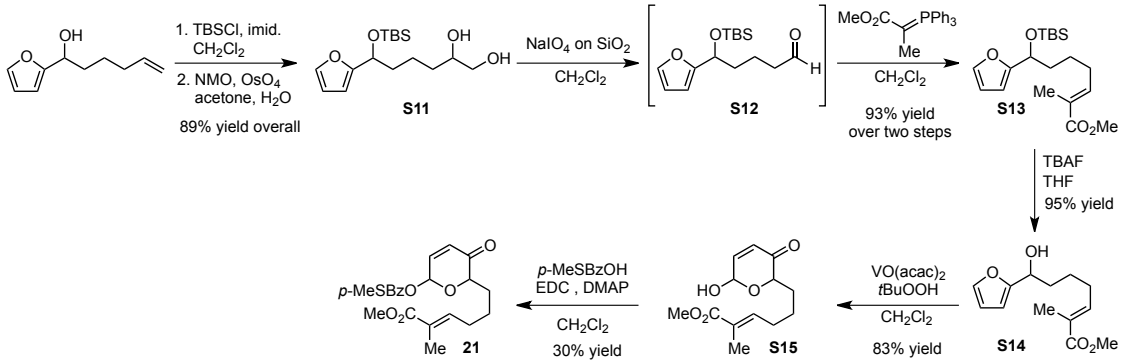


(*E*)-6-(6-ethoxy-6-oxohex-4-en-1-yl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl 4-(methylthio)benzoate (19):
A microwave vial was charged with **5c** (199.0 mg, 0.599 mmol) and Grubbs' Catalyst, 2nd Generation (25.0 mg, 0.03 mmol, 0.05 equiv). The vial was capped and then purged with nitrogen before the addition of CH_2Cl_2 (3.0 mL, 0.2 M). Ethyl acrylate (0.260 mL, 2.40 mmol, 4.0 equiv) was introduced via syringe and the vial was then placed in a 40 ˚C oil bath and stirred for 22 h. The reaction mixture was then concentrated and chromatographed on silica gel to afford **19** as a slightly dark oil as a 3:2 mixture of diastereomers (180.0 mg, 74%).
$\mathbf{R_f}$ = 0.11, 0.17 (silica gel, 5:1 hexanes/EtOAc);
IR (film) ν_{max} 2926, 2867, 1714, 1593, 1262, 1176, 1094, 1067, 924, 757 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 - 7.89 (m, 2H), 7.28 - 7.22 (m, 2H), 7.02 - 6.96 (m, 1H), 6.90 (major diast., dt, *J* = 6.8, 15.6 Hz, 0.6H), 6.81 (minor diast., dt, *J* = 6.8, 15.6 Hz, 0.4H), 6.79 - 6.71 (m, 1H), 6.28 - 6.24 (m, 1H), 5.77 (major diast., dt, *J* = 1.5, 15.6 Hz, 0.6H), 5.71 - 5.66 (minor diast., m, 0.4H), 4.55 (major diast., dd, *J* = 3.9, 7.8 Hz, 0.6H), 4.26 (minor diast., dd, *J* = 5.1, 9.0 Hz, 0.4H), 4.17 - 4.11 (m, 2H), 2.51 (s, 3H), 2.21 - 2.16 (m, 1H), 2.14 - 1.73 (m, 3H), 1.61 - 1.54 (m, 2H), 1.25 (dt, *J* = 2.0, 6.8 Hz, 3H);
^{13}C NMR (100 MHz, $CDCl_3$) δ 195.6, 166.8, 166.7, 165.0, 164.8, 148.6, 148.2, 147.3, 147.1, 143.1,

142.1, 130.4, 129.0, 128.6, 125.2, 122.1, 122.0, 88.1, 87.6, 79.5, 75.9, 60.4, 32.9, 32.0, 31.9, 29.3, 24.1, 23.4, 14.9, 14.5;

MS (ESI-TOF) calcd. for $C_{21}H_{24}O_6S$ [M + Na^+] 427.1186, found 427.1190.

Scheme S8. Synthesis of substrate **21**



6-((*tert*-butyldimethylsilyl)oxy)-6-(furan-2-yl)hexane-1,2-diol (S11):

1-(furan-2-yl)hex-5-en-1-ol[9] (2.096 g, 12.6 mmol) was dissolved in CH_2Cl_2 (63 mL, 0.2 M) under a nitrogen atmosphere and cooled to 0 ˚C. Imidazole (2.06g, 30.3 mmol, 2.4 equiv) was added to the reaction mixture follwed by *tert*-butyldimethylsilyl chloride (2.28 g, 15.1 mmol, 1.2 equiv). The reaction mixture was allowed to warm to room temperature and stirred for 30 min. Sat. aq. NH_4Cl (50 mL) and Et_2O (100 mL) were added and the layers were separated. The organic layer was washed sequentially with water (50 mL) and brine (50 mL) and the organic layer was then dried over Na_2SO_4, filtered, and concentrated to afford the silyl ether as a slightly yellow oil (3.398 g, 96%). This material was dissolved in acetone/H_2O (9:1, 61 mL total volume, 0.2 M) and cooled to 0 ˚C. *N*-Methylmorpholine-*N*-oxide (2.129 g, 18.2 mmol, 1.5 equiv) was added followed by osmium tetroxide (1.52 mL of a 2.5 wt.% solution in *tert*-butanol, 0.121 mmol, 0.01 equiv). The reaction mixture was kept at 0 ˚C for 30 min then allowed to warm to room temperature. After stirring for 3 h, 1M $Na_2S_2O_3$ (30 mL) was added and the mixture was stirred overnight. Sat. aq. $NaHCO_3$ (30 mL) and EtOAc (150 mL) were added and the layers were separated. The aqueous layer was further extracted with EtOAc (3 x 100 mL), and the combined organics were dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (silica gel, 2:1 to 1:1 hexanes/EtOAc) then afforded **S11** as a clear oil (3.55 g, 89% overall).

R_f = 0.08 (silica gel, 2:1 hexanes/EtOAc);

IR (film) ν_{max} 3368 (br), 2930, 2858, 2360, 1462, 1361, 1344, 1254, 1075, 1006, 835, 776, 734 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 - 7.31 (m, 1H), 6.31 - 6.28 (m, 1H), 6.15 (d, *J* = 2.9 Hz, 1H), 4.68 (td, *J* = 1.5, 7.1 Hz, 1H), 3.73 - 3.66 (m, 1H), 3.65 - 3.59 (m, 1H), 3.44 - 3.37 (m, 1H), 1.89 - 1.73 (m, 3H), 1.57 - 1.47 (m, 1H), 1.47 - 1.37 (m, 3H), 1.37 - 1.28 (m, 1H), 0.87 (s, 9H), 0.04 (s, 3H), –0.08 (s, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 157.4, 141.5, 110.2, 106.0, 72.4, 68.6, 67.0, 37.0, 33.1, 26.0, 21.6,

[9] 1-(furan-2-yl)hex-5-en-1-ol was synthesized according to: Sammes, P. G.; Street, L. J.; Kirby, P. *J. Chem. Soc. Perkin Trans. 1* **1983**, 2729–2734.

18.4, –4.7;
MS (ESI-TOF) calcd. for $C_{16}H_{30}O_4Si$ [M + Na^+] 337.1806, found 337.1820.

5-((*tert*-butyldimethylsilyl)oxy)-5-(furan-2-yl)pentanal (S12):
Diol **S11** (1.003 g, 3.19 mmol) was dissolved in CH_2Cl_2 (32 mL, 0.1 M) and to this solution was added sodium periodate immobilized on silica gel[10] (6.36 g, 2 g per mmol substrate). The reaction was vigorously stirred under nitrogen for 30 minutes. The resulting suspension was filtered through a sintered glass funnel, and the silica gel was washed with CH_2Cl_2 (3 x 25 mL). The filtrate was concentrated to afford **S12** as a colorless oil which was used immediately in the subsequent Wittig olefination (848 mg, 94%).
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.74 (t, *J* = 1.4 Hz, 1H), 7.33 (dd, *J* = 0.9, 1.8 Hz, 1H), 6.30 (dd, *J* = 1.6, 3.0 Hz, 1H), 6.17 (d, *J* = 3.2 Hz, 1H), 4.71 (dd, *J* = 5.3, 7.1 Hz, 1H), 2.42 (td, *J* = 1.6, 7.2 Hz, 2H), 1.91 - 1.57 (m, 4H), 0.87 (s, 9H), 0.05 (s, 3H), –0.08 (s, 3H).

(*E*)-methyl 7-((*tert*-butyldimethylsilyl)oxy)-7-(furan-2-yl)-2-methylhept-2-enoate (S13):
Aldehyde **S12** (848 mg, 3.00 mmol) was dissolved in CH_2Cl_2 (11.5 mL, 0.26 M) and the resulting solution was cooled to 0 °C. To this solution was added known ylide methyl 2-(triphenylphosphoranylidene)propanoate[11] (1.361 g, 3.91 mmol, 1.3 equiv) and the solution was allowed to warm to room temperature. The reaction was stirred under nitrogen for 4 h until TLC indicated complete disappearance of **S12**. The resulting solution was concentrated and purified by flash chromatography (silica gel, 9:1 to 3:1 hexanes/EtOAc) to afford **S13** as a colorless oil (1.048 g, 99%).
$\mathbf{R}_f$ = 0.15 (silica gel, hexanes);
IR (film) ν_{max} 2930, 2361, 1715, 1256, 1089, 1006, 835, 776, 734 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (t, *J* = 0.92, 1H), 6.75 (td, *J* = 1.4, 7.5 Hz, 1H), 6.30 (dd, *J* = 2.1, 3.0 Hz, 1H), 6.16 (d, *J* = 3.2 Hz, 1H), 4.69 (dd, *J* = 5.7, 7.1 Hz, 1H), 3.73 (s, 3H), 2.18 (q, *J* = 7.8 Hz, 2H), 1.91 - 1.74 (m, 5H), 1.60 - 1.50 (m, 1H), 1.49 - 1.39 (m, 1H), 0.88 (s, 9H), 0.06 (s, 3H), –0.07 (s, 3H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 157.4, 142.5, 141.5, 127.9, 110.2, 105.9, 68.5, 51.9, 36.8, 28.7, 26.0, 24.6, 18.4, 12.6, –4.7, –4.9;
MS (ESI) calcd. for $C_{19}H_{32}O_4Si$ [M + Na]$^+$ 375.2, found 375.2.

(*E*)-methyl 7-(furan-2-yl)-7-hydroxy-2-methylhept-2-enoate (S14):
Ester **S13** (1.096 g, 3.11 mmol) was dissolved in THF (21 mL, 0.15 M) and the resulting solution was cooled to 0 °C. To this solution was added by syringe TBAF (1.0 M in THF, 4.7 mL, 4.7 mmol, 1.5 equiv). The reaction was stirred under nitrogen for 2 h, until TLC indicated complete disappearance of

[10] Silica gel-supported sodium periodate prepared and used according to: Zhong, Y.-L.; Shing, T. K. M. *J. Org. Chem*. **1997**, *62*, 2622–2624.

[11] Methyl 2-(triphenylphosphoranylidene)propanoate synthesized according to: Eey, S. T.-C.; Lear, M. J. *Org. Lett.* **2010**, *12*, 5510–5513.

S13. The solution was diluted with ethyl acetate (40 mL), then washed with sat. aq. NH_4Cl (40 mL). The aqueous layer was then extracted with ethyl acetate (2 x 30 mL), and the pooled organic layers were washed with brine (40 mL), dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by flash chromatography (silica gel, 9:1 to 3:2 hexanes/EtOAc) to afford **S14** as a colorless oil (707 mg, 95%).

R_f = 0.11 (silica gel, 4:1 hexanes/EtOAc);

IR (film) ν_{max} 3435 (br), 2949, 1709, 1648, 1436, 1259, 1090, 1008, 737 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 1.0, 2.0, 1H), 6.72 (td, *J* = 1.2, 7.4 Hz, 1H), 6.29 (dd, *J* = 2.0, 2.9 Hz, 1H), 6.19 (d, *J* = 3.4 Hz, 1H), 4.64 (t, *J* = 6.8 Hz, 1H), 3.69 (s, 3H), 2.44 (br. s, 1H), 2.18 (q, *J* = 7.3 Hz, 2H), 1.84 (q, *J* = 7.4 Hz, 2H), 1.79 (s, 3H), 1.62 - 1.52 (m, 1H), 1.49 - 1.39 (m, 1H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 159.9, 142.3, 142.1, 128.0, 110.3, 106.1, 67.7, 51.9, 35.3, 28.5, 24.8, 12.5;

MS (APCI) calcd. for $C_{13}H_{18}O_4$ $[M - OH]^+$ 221.1, found 221.1.

(*E*)-methyl 6-(6-hydroxy-3-oxo-3,6-dihydro-2*H*-pyran-2-yl)-2-methylhex-2-enoate (S15):

Reacion of **S14** (707 mg, 2.97 mmol), vanadyl acetylacetonate (80 mg, 0.30 mmol, 0.1 equiv), and *tert*-butyl hydroperoxide (0.81 mL of a 5.5 M solution in dodecane, 1.50 mmol, 1.5 equiv) in CH_2Cl_2 (10 mL, 0.3 M) according to **S4** above afforded **S15** as a colorless oil after column chromatography (silica gel, 4:1 to 1:1 hexanes/EtOAc) as a 2:1 mixture of diastereomers (623 mg, 83%).

R_f = 0.37 (silica gel, 1:1 hexanes/EtOAc);

IR (film) ν_{max} 3412 (br), 2952, 1690, 1648, 1437, 1370, 1264, 1090, 1029, 746 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.93 (minor diast., dd, *J* = 0.9, 9.8 Hz, 0.33H), 6.90 (major diast., dd, *J* = 3.2, 10.1 Hz, 0.67H), 6.78 - 6.71 (m, 1H), 6.11 (minor diast., dd, *J* = 1.1, 10.3 Hz, 0.33H), 6.06 (major diast., d, *J* = 10.5 Hz, 0.67H), 5.65 - 5.59 (m, 1H), 4.56 (dd, *J* = 3.9, 8.0 Hz, 1H), 4.34 (br. s, 1H), 3.71 (s, 3H), 2.19 (q, *J* = 7.3 Hz, 2H), 1.99 - 1.90 (m, 1H), 1.80 (s, 3H), 1.75 - 1.66 (m, 1H), 1.61 - 1.53 (m, 2H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 197.0, 196.5, 169.3, 148.7, 145.2, 142.8, 142.6, 128.8, 127.9, 127.5, 91.1, 87.8, 78.7, 73.8, 52.1, 30.4, 29.5, 28.6, 24.4, 24.2, 12.6;

MS (ESI-TOF) calcd. for $C_{13}H_{18}O_5$ $[M + Na^+]$ 277.1046, found 277.1073.

(*E*)-6-(6-methoxy-5-methyl-6-oxohex-4-en-1-yl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl 4-(methylthio)benzoate (21):

Reaction of **S15** (623 mg, 2.45 mmol), 4-methylthiobenzoic acid (536 mg, 3.19 mmol, 1.3 equiv), EDC (661 mg, 3.45 mmol, 1.4 equiv), and DMAP (391 mg, 3.20 mmol, 1.3 equiv) in CH_2Cl_2 (12 mL, 0.2 M) according to **5c** above afforded **21** as a colorless oil after column chromatography (silica gel, 9:1 to 3:2 hexanes/EtOAc) as a 2:1 mixture of diastereomers (293 mg, 30%).

R_f = 0.22 (silica gel, 4:1 hexanes/EtOAc);

IR (film) ν_{max} 2951, 2360, 1709, 1650, 1593, 1436, 1260, 1178, 1094, 1069, 924, 758 cm^{-1};

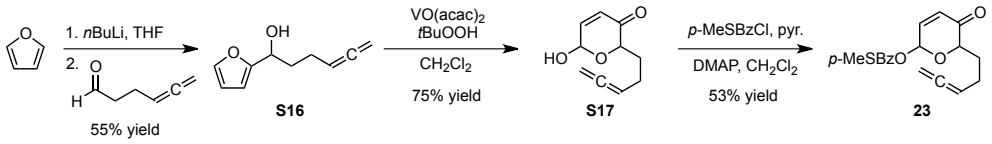
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 0.9, 8.7 Hz, 2H), 7.29 - 7.25 (m, 2H), 7.01 (major diast., td, *J* = 3.2, 10.6 Hz, 0.67H), 6.89 (minor diast., dd, *J* = 3.7, 10.2 Hz, 0.33H), 6.81 (major diast., dd, *J* = 1.4, 2.7 Hz, 0.67H), 6.76 - 6.70 (minor diast. x 2, m, 0.66H), 6.65 (major diast., td, *J* = 1.4, 7.3 Hz,

0.67H), 6.31 - 6.26 (m, 1H), 4.57 (minor diast., dd, J = 3.9, 7.6 Hz, 0.33H), 4.29 (major diast., dd, J = 5.0, 9.2 Hz, 0.67H), 3.72 (major diast., s, 2H), 3.71 (minor diast., s, 1H), 2.53 (d, J = 2.3 Hz, 3H), 2.22 - 1.54 (m, 9H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 201.9, 195.7, 174.9, 171.8, 168.7, 164.9, 147.3, 147.1, 143.1, 142.1, 141.9, 141.6, 130.3, 129.0, 128.6, 128.2, 125.2, 88.1, 87.6, 87.3, 79.6, 76.0, 53.3, 51.9, 47.3, 47.2, 45.8, 35.4, 33.1, 29.5, 28.5, 28.4, 24.6, 24.0, 21.3, 14.9, 12.5;

MS (ESI-TOF) calcd. for $C_{21}H_{24}O_6S$ [M + Na^+] 427.1186, found 427.1184.

Scheme S9. Synthesis of substrate **23**



1-(furan-2-yl)hexa-4,5-dien-1-ol (S16):

Freshly distilled furan (0.952 mL, 13.0 mmol, 1.3 equiv) was dissolved in THF (15 mL, 0.87 M relative to furan) under an atmosphere of nitrogen and the resulting mixture was cooled to –78 ˚C. *n*-BuLi (5.71 mL of a 2.1 M solution in hexanes, 12.0 mmol, 1.2 equiv) was introduced dropwise via syringe. After addition, the reaction mixture was allowed to warm to 0 ˚C and stirred at that temperature for 30 min. A separate flask was charged with a solution of 4,5-hexadien-1-al[12] (0.961 g, 10.0 mmol) in THF (15 mL, 0.67 M in aldehyde) and this mixture was cooled to 0 ˚C. The furan-2-yllithium solution was then added via cannula. An additional amount of THF (3 mL) was used in order to ensure a quantitative transfer. The solution was stirred at 0 ˚C for 30 min before the careful addition of sat. aq. NH_4Cl (20 mL). EtOAc (50 mL) was added and the layers were separated. The organic layer was washed with brine (20 mL), and the combined aqueous layers were extracted with EtOAc (2 x 50 mL). The combined organic layers were then dried over $MgSO_4$, filtered, and concentrated. Purification by column chromatography (silica gel, 95:5 hexanes/EtOAc) afforded **S16** as a clear oil (910 mg, 55%).

R_f = 0.37 (silica gel, 4:1 hexanes/EtOAc);

IR (film) ν_{max} 3468 (br), 2931, 2859, 1955, 1760, 1698, 1010, 842, 787, 738 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 1.5 Hz, 1H), 6.35 (dd, J = 1.7, 3.2 Hz, 1H), 6.26 (d, J = 3.4 Hz, 1H), 5.16 (quin, J = 6.7 Hz, 1H), 4.79 - 4.74 (m, 1H), 4.72 (quin, J = 3.4 Hz, 2H), 2.20 - 2.06 (m, 2H), 2.00 (q, J = 7.3 Hz, 2H), 1.93 - 1.87 (m, 1H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 208.8, 156.7, 142.2, 110.4, 106.2, 89.5, 75.6, 67.4, 34.9, 24.4;

6-hydroxy-2-(penta-3,4-dien-1-yl)-2*H*-pyran-3(6*H*)-one (S17):

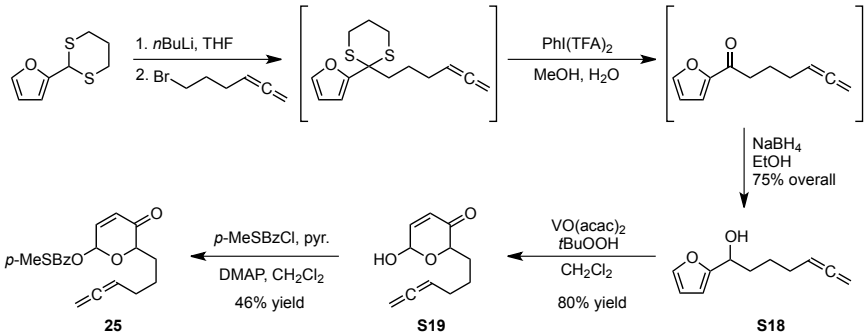
Reaction of **S16** (900 mg, 5.48 mmol), vanadyl acetylacetonate (145 mg, 0.548 mmol, 0.1 equiv), and *tert*-butyl hydroperoxide (1.5 mL of a 5.5 M solution in dodecane, 8.22 mmol, 1.5 equiv) in CH_2Cl_2 (27 mL, 0.2 M) according to **S4** above afforded **S17** as a colorless oil after column chromatography

[12] 4,5-Hexadien-1-al synthesized according to: Tsukamoto, H.; Matsumoto, T.; Kondo, Y. *J. Am. Chem. Soc.* **2008**, *130*, 388–389.

(silica gel, 9:1 to 7:3 hexanes/EtOAc) as a 7:3 mixture of diastereomers (745 mg, 75%).
R_f = 0.13 (silica gel, 4:1 hexanes/EtOAc);
IR (film) ν_{max} 3431 (br), 2926, 1726, 1065, 995, 913, 848, 731 cm^{-1};
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.00 (minor diast., dd, *J* = 1.8, 10.3 Hz, 0.3H), 6.95 (major diast., dd, *J* = 3.5, 10.3 Hz, 0.7H), 6.21 (minor diast., dd, *J* = 1.5, 10.3 Hz, 0.3H), 6.17 (major diast., dd, *J* = 0.6, 10.3 Hz, 0.7H), 5.73 - 5.69 (m, 1H), 5.20 - 5.15 (m, 1H), 4.77 - 4.72 (m, 2H), 4.69 (major diast., dd, *J* = 3.7, 8.3 Hz, 0.7H), 4.20 (minor diast., ddd, *J* = 1.2, 3.7, 8.6 Hz, 0.3H), 3.36 (minor diast., br. s, 0.3H), 3.10 (major diast., br. s, 0.7H), 2.31 - 2.18 (m, 2H), 2.17 - 2.10 (m, 1H), 2.01 - 1.92 (minor diast., m, 0.3H), 1.88 (dtd, *J* = 5.7, 8.1, 13.9 Hz, 0.7H), ;
^{13}C NMR (125 MHz, $CDCl_3$) δ 208.9, 196.6, 196.2, 147.8, 144.4, 129.0, 127.9, 91.1, 89.3, 87.9, 78.2, 75.5, 73.5, 30.2, 29.2, 23.8;

5-oxo-6-(penta-3,4-dien-1-yl)-5,6-dihydro-2*H*-pyran-2-yl 4-(methylthio)benzoate (23):
Reaction of **S17** (656 mg, 3.64 mmol), 4-thiomethylbenzoyl chloride (1.019 g, 5.46 mmol, 1.5 equiv), pyridine (294 μL, 3.64 mmol, 1.0 equiv), and DMAP (222 mg, 1.82 mmol, 0.5 equiv) in CH_2Cl_2 (18 mL, 0.2 M) according to **11** above afforded **23** as a slightly yellow oil after purification by column chromatography (silica gel, 95:5 to 5:1 hexanes/EtOAc) as a 2:1 mixture of diastereomers (637 mg, 53%).
R_f = 0.33, 0.38 (silica gel, 4:1 hexanes/EtOAc);
IR (film) ν_{max} 2924, 2857, 1954, 1720, 1693, 1593, 1261, 1179, 1094, 1066, 1012, 921, 839, 756, 688 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 - 7.91 (m, 2H), 7.25 (d, *J* = 8.3 Hz, 2H), 7.02 - 6.97 (m, 1H), 6.80 (minor diast., dd, *J* = 1.0, 2.9 Hz, 0.33H), 6.74 (major diast., d, *J* = 3.4 Hz, 0.67H), 6.29 - 6.25 (m, 1H), 5.09 - 5.01 (m, 1H), 4.64 - 4.55 (m, 2H), 4.54 - 4.48 (major diast., m, 0.67H), 4.34 (minor diast., dd, *J* = 4.4, 9.3 Hz, 0.33H), 2.52 (s, 3H), 2.21 - 2.04 (m, 3H), 2.03 - 1.94 (minor diast., m, 0.33H), 1.91 - 1.82 (major diast., m, 0.67H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 195.9, 165.0, 164.9, 147.1, 147.0, 142.8, 141.9, 130.4, 129.0, 128.6, 128.4, 125.2, 89.1, 89.0, 88.1, 87.6, 79.1, 75.8, 75.4, 75.2, 32.9, 29.2, 24.0, 23.6, 15.0;
MS (ESI-TOF) calcd. for $C_{18}H_{18}O_4S$ [M + Na^+] 353.0818, found 353.0809.

Scheme S10. Synthesis of substrate **25**



1-(furan-2-yl)hepta-5,6-dien-1-ol (S18):

2-(2-(hexa-4,5-dien-1-yl)-1,3-dithian-2-yl)furan[13] (1.437 g, 7.71 mmol) was placed in a round bottom flask and azeotroped with benzene (10 mL). Under an atmosphere of nitrogen, THF (19.3 mL, 0.4 M) was added and the solution was cooled to –78 ˚C. *n*-BuLi (3.84 mL of a 2.01 M solution in hexanes, 7.71 mmol, 1.0 equiv) was introduced dropwise via syringe and the resulting mixture was stirred at –78 ˚C for 1 h. A solution of 6-bromohexa-1,2-diene[14] (1.366 g, 8.48 mmol) in THF (10 mL) at 0 ˚C was then added via cannula to the lithiated dithiane at –78 ˚C. An additional amount of THF (5 mL) was used to ensure quantitative transfer. The reaction mixture was then allowed to warm to room temperature and stir for 30 min. The reaction mixture was then cooled to 0 ˚C and quenched with the careful addition of sat. aq. NH_4Cl (20 mL). Et_2O (50 mL) was added and the layers were separated. The organic layer was washed with brine (20 mL), and the combined aqueous layers were extracted again with Et_2O (50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Purification by column chromatography (silica gel, 1:0 to 95:5 hexanes/Et_2O) afforded the allenyldithiane (1.68 g, 82%). A portion of this dithiane (1.62 g, 6.08 mmol) was then dethioacetalized according to the method of Stork and Zhao[15] with bis(trifluoracetoxy)iodobenzene (3.92 g, 9.12 mmol, 1.5 equiv) to give the ketone (~quant.) which was immediatedly dissolved in EtOH (20 mL, 0.3 M) under nitrogen and cooled to 0 ˚C. Sodium borohydride (230 mg, 6.08 mmol, 1.0 equiv) was added portionwise and the resultant mixture was allowed to warm to room temperature. Stirring was continued for 2 h before the careful addition of sat. aq. $NaHCO_3$ (15 mL). EtOAc (50 mL) and water (30 mL) were added and the layers were then separated. The aqueous layer was further extracted with EtOAc (2 x 50 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (silica gel, 95:5 to 5:1 hexanes/EtOAc) then afforded **S18** as a clear oil (989 mg, 91%).

$\mathbf{R}_f$ = 0.40 (silica gel, 4:1 hexanes/EtOAc);

IR (film) ν_{max} 3414 (br), 2934, 2861, 1955, 1718, 1150, 1073, 1010, 883, 842, 789, 739 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 1.0, 2.0 Hz, 1H), 6.35 (dd, *J* = 2.0, 2.9 Hz, 1H), 6.25 (d, *J* = 2.9 Hz, 1H), 5.11 (quin, *J* = 6.8 Hz, 1H), 4.73 - 4.66 (m, 3H), 2.10 - 2.03 (m, 2H), 1.95 - 1.88 (m, 2H), 1.86 (d, *J* = 5.4 Hz, 1H), 1.65 - 1.55 (m, 1H), 1.52 - 1.42 (m, 1H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 208.8, 157.0 , 142.2, 110.4, 106.1, 89.9, 75.1, 67.9, 35.2, 28.2, 25.2;

2-(hexa-4,5-dien-1-yl)-6-hydroxy-2*H*-pyran-3(6*H*)-one (S19):

Reaction of **S18** (983 mg, 5.52 mmol), vanadyl acetylacetonate (146 mg, 0.552 mmol, 0.1 equiv), and *tert*-butyl hydroperoxide (1.5 mL of a 5.5 M solution in dodecane, 8.25 mmol, 1.5 equiv) in CH_2Cl_2 (18 mL, 0.3 M) according to **S4** above afforded **S19** as a yellow oil after column chromatography (silica gel, 9:1 to 7:3 hexanes/EtOAc) as a 17:3 mixture of diastereomers (858 mg, 80%).

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[13] 2-(2-(hexa-4,5-dien-1-yl)-1,3-dithian-2-yl)furan synthesized according to: De, S. K. *Tetrahedron Lett.*, **2004**, *45*, 2339–2341.

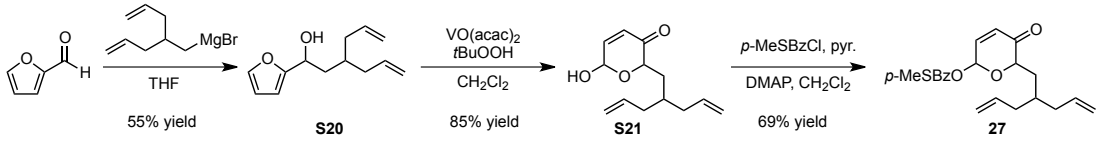
[14] 6-Bromohexa-1,2-diene synthesized occording to: Molander, G. A.; Cormier, E. P. *J. Org. Chem.* **2005**, *70*, 2622–2626.

[15] Stork, G.; Zhao, K. *Tetrahedron Lett.*, **1989**, *30*, 287–290.

R_f = 0.17 (silica gel, 4:1 hexanes/EtOAc);
IR (film) ν_{max} 3393 (br), 2932, 2863, 2361, 2341, 1955, 1686, 1092, 1028, 846 cm^{-1};
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (minor diast., dd, *J* = 1.5, 10.2 Hz, 0.15H), 6.89 (major diast., dd, *J* = 3.7, 10.3 Hz, 0.85H), 6.14 (minor diast., dd, *J* = 1.5, 10.2 Hz, 0.15H), 6.09 (major diast., d, *J* = 10.3 Hz, 0.85H), 5.64 (d, *J* = 3.3 Hz, 1H), 5.08 (quin, *J* = 6.8 Hz, 1H), 4.65 (dt, *J* = 3.3, 6.6 Hz, 2H), 4.56 (major diast., dd, *J* = 4.0, 8.1 Hz, 0.85H), 4.10 - 4.05 (minor diast., m, 0.15H), 3.41 (br. s, 1H), 2.08 - 1.92 (m, 3H), 1.80 - 1.68 (m, 1H), 1.61 - 1.49 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$) δ 208.8, 196.8, 196.4, 148.0, 144.7, 129.0, 127.8, 91.1, 89.8, 87.8, 79.0, 75.1, 74.2, 30.3, 29.3, 28.3, 24.9, 24.7;

6-(hexa-4,5-dien-1-yl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl 4-(methylthio)benzoate (25):
Reaction of **S19** (823 mg, 4.24 mmol), 4-thiomethylbenzoyl chloride (1.028 g, 5.51 mmol, 1.3 equiv), pyridine (480 µL, 5.93 mmol, 1.4 equiv), and DMAP (518 mg, 4.24 mmol, 1.0 equiv) in CH_2Cl_2 (14 mL, 0.3 M) according to **11** above afforded **25** as a slightly yellow oil after purification by column chromatography (silica gel, 95:5 to 5:1 hexanes/EtOAc) as a 3:1 mixture of diastereomers (665 mg, 46%).
R_f = 0.34, 0.42 (silica gel, 4:1 hexanes/EtOAc);
IR (film) ν_{max} 2924, 2861, 1955, 1720, 1695, 1592, 1262, 1177, 1094, 1067, 1012, 923, 840, 756 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 - 7.90 (m, 2H), 7.25 (dt, *J* = 1.6, 8.5 Hz, 2H), 7.02 - 6.95 (m 1H), 6.80 - 6.78 (minor diast., m, 0.25H), 6.74 (major diast., d, *J* = 3.4 Hz, 0.75H), 6.29 - 6.24 (m, 1H), 5.05 (major diast., quin, *J* = 6.8 Hz, 0.75H), 4.94 (minor diast., quin, *J* = 6.8 Hz, 0.25H), 4.64 - 4.55 (m, 2.75H), 4.28 (minor diast., dd, *J* = 4.9, 9.8 Hz, 0.25H), 2.51 (s, 3H), 2.04 - 1.88 (m, 3H), 1.83 - 1.74 (m, 1H), 1.54 (quin, *J* = 7.7 Hz, 1H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 196.0, 195.9, 165.0, 147.1, 147.0, 142.8, 142.0, 130.4, 130.3, 129.0, 128.4, 125.3, 125.2, 89.7, 89.5, 88.1, 87.7, 79.7, 76.0, 75.1, 33.1, 29.3, 28.2, 28.1, 25.1, 24.4, 15.0 ;
MS (ESI-TOF) calcd. for $C_{19}H_{20}O_4S$ [M + Na^+] 367.0975, found 367.0967.

Scheme S11. Synthesis of substrate **27**



3-allyl-1-(furan-2-yl)hex-5-en-1-ol (S20):
Freshly distilled furfural (704 mg, 7.33 mmol, 1.1 equiv) was dissolved in THF (24.4 mL, 0.3 M in furfural) under an atmosphere of nitrogen and cooled to 0 °C. A solution of (2-allylpent-4-en-1-yl)magnesium bromide[16] (13.3 mL of a 0.5 M solution in THF, 6.66 mmol) was added dropwise and the resulting reaction mixture was stirred for 20 min. Sat. aq. NH_4Cl (20 mL) was

[16] (2-Allylpent-4-en-1-yl)magnesium bromide synthesized according to: Krech, F.; Issleib, K. *Z. Anorg. Allg. Chem.* **1988**, *557*, 143–152.

careully added followed by Et_2O (50 mL). The organic layer was washed with brine (20 mL), and the combined aqueous layers were extracted with Et_2O (2 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Purification by column chromatography (silica gel, 95:5 to 9:1 hexanes/Et_2O) afforded **S20** as a clear oil (755 mg, 55%).

$\mathbf{R_f}$ = 0.39 (silica gel, 5:1 hexanes/EtOAc);

IR (film) ν_{max} 3390 (br), 3075, 2976, 2919, 1697, 1639, 1505, 1442, 1150, 995, 910, 734 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 - 7.38 (m, 1H), 6.35 (dd, *J* = 2.0, 3.4 Hz, 1H), 6.25 (d, *J* = 2.9 Hz, 1H), 5.84 - 5.73 (m, 2H), 5.09 - 5.02 (m, 4H), 4.82 (dt, *J* = 5.6, 8.3 Hz, 1H), 2.18 - 2.04 (m, 4H), 1.90 - 1.70 (m, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 142.2, 136.9, 136.7, 116.8, 110.4, 106.1, 66.0, 39.3, 38.4, 37.8, 33.9;

2-(2-allylpent-4-en-1-yl)-6-hydroxy-2*H*-pyran-3(6*H*)-one (S21):

Reaction of **S20** (745 mg, 3.61 mmol), vanadyl acetylacetonate (96 mg, 0.36 mmol, 0.1 equiv), and *tert*-butyl hydroperoxide (1.5 mL of a 5.5 M solution in dodecane, 5.42 mmol, 1.5 equiv) in CH_2Cl_2 (18.1 mL, 0.2 M) according to **S4** above afforded **S21** as a yellow oil after column chromatography (silica gel, 9:1 to 7:3 hexanes/EtOAc) as a 7:3 mixture of diastereomers (680 mg, 85%).

$\mathbf{R_f}$ = 0.28 (silica gel, 5:1 hexanes/EtOAc);

IR (film) ν_{max} 3408 (br), 3076, 2976, 2919, 1686, 1638, 1087, 1028, 995, 911 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (minor diast., dd, *J* = 1.5, 10.3, 0.3H), 6.90 (major diast., dd, *J* = 3.4, 10.3Hz, 0.7H), 6.12 (minor diast., dd, *J* = 2.0, 10.3 Hz, 0.3H), 6.11 (major diast., dd, *J* = 1.0, 10.3 Hz, 0.7H), 5.84 - 5.72 (m, 2H), 5.65 (d, *J* = 2.9 Hz, 1H), 5.08 - 5.01 (m, 4H), 4.67 (major diast., dd, *J* = 3.4, 4.8 Hz, 0.7H), 4.22 - 4.18 (minor diast., m, 0.3H), 3.72 (minor diast., br. s, 0.3H), 3.48 (major diast., br. s, 0.7H), 2.21 - 2.12 (m, 2H), 2.11 - 1.98 (m, 2H), 1.95 - 1.88 (m, 1H), 1.87 - 1.78 (m, 1H), 1.65 (ddd, *J* = 4.2, 10.0, 14.2, 1H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 197.2, 196.8, 147.9, 144.6, 136.9, 136.8, 136.6, 136.5, 128.9, 127.8, 116.9, 116.8, 91.0, 87.8, 72.6, 38.6, 38.5, 37.2, 37.1, 34.5, 33.4, 33.3, 33.2;

6-(2-allylpent-4-en-1-yl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl 4-(methylthio)benzoate (27):

Reaction of **S21** (600 mg, 2.70 mmol), 4-thiomethylbenzoyl chloride (756 mg, 4.05 mmol, 1.5 equiv), pyridine (218 μL, 2.70 mmol, 1.0 equiv), and DMAP (518 mg, 4.24 mmol, 1.0 equiv) in CH_2Cl_2 (14 mL, 0.3 M) according to **11** above afforded **27** as a slightly yellow oil after purification by column chromatography (silica gel, 95:5 to 5:1 hexanes/EtOAc) as a 3:1 mixture of diastereomers (690 mg, 69%).

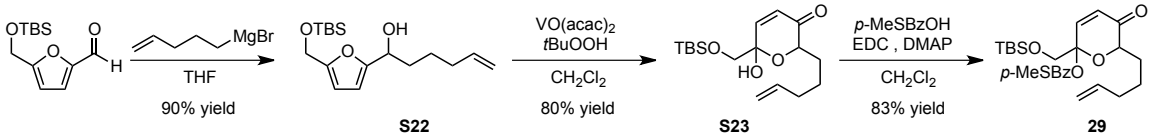
$\mathbf{R_f}$ = 0.37, 0.43 (silica gel, 4:1 hexanes/EtOAc);

IR (film) ν_{max} 3074, 2975, 2920, 1721, 1697, 1593, 1261, 1175, 1094, 1066, 1013, 913, 840, 756 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 - 7.92 (m, 2H), 7.29 - 7.25 (m, 2H), 7.02 - 6.96 (m, 1H), 6.79 (minor diast., dd, *J* = 1.2, 2.7 Hz, 0.25H), 6.73 (major diast., d, *J* = 3.4 Hz, 0.75H), 6.30 - 6.24 (m, 1H), 5.79 - 5.66 (m, 1.75H), 5.59 - 5.49 (minor diast., m, 0.25H), 5.06 - 4.85 (m, 4H), 4.69 (major diast. dd, *J* = 3.4, 9.8 Hz, 0.75H), 4.44 (minor diast., dd, *J* = 3.9, 10.3 Hz, 0.25H), 2.53 (s, 3H), 2.15 - 2.04 (m,

2H), 2.04 - 1.93 (m, 2H), 1.90 - 1.78 (m, 2H), 1.69 (ddd, *J* = 3.9, 10.0, 14.4 Hz, 1H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 196.2, 196.1, 165.0, 147.1, 142.9, 141.7, 136.8, 136.6, 136.5, 136.2, 130.5, 130.3, 129.0, 128.6, 125.3, 125.2, 117.1, 116.8, 88.0, 87.8, 74.3, 38.8, 38.4, 37.3, 37.2, 36.5, 33.2, 33.1, 15.0;
MS (ESI-TOF) calcd. for $C_{21}H_{24}O_4S$ [M + Na^+] 395.1288, found 395.1290.

Scheme S12. Synthesis of substrate **29**



1-(5-(((*tert*-butyldimethylsilyl)oxy)methyl)furan-2-yl)hex-5-en-1-ol (S22):
5-(((*tert*-Butyldimethylsilyl)oxy)methyl)furan-2-carbaldehyde[17] (1.0 g, 4.16 mmol) was dissolved in THF (21 mL, 0.2 M) under an atmosphere of nitrogen and cooled to 0 ˚C. A solution of pent-4-en-1-ylmagnesium bromide (10.0 mL of a 0.5 M solution in THF, 5.0 mmol, 1.2 equiv) was added dropwise and the resulting reaction mixture was stirred for 20 min. Sat. aq. NH_4Cl (20 mL) was then careully added followed by Et_2O (50 mL). The organic layer was washed with brine (20 mL), and the combined aqueous layers were extracted with Et_2O (2 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Purification by column chromatography (silica gel, 95:5 to 9:1 hexanes/EtOAc) afforded **S22** as a clear oil (1.16 g, 90%).
R_f = 0.25 (silica gel, 9:1 hexanes/EtOAc);
IR (film) ν_{max} 3374, 2930, 2858, 1255, 1075, 834, 776 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.18 - 6.16 (m, 2H), 5.85 - 5.76 (m, 1H), 5.02 (dq, *J* = 5.0, 17.1 Hz, 1H), 4.99 - 4.95 (m, 1H), 4.67 (dd, *J* = 5.4, 4.8, 1H), 4.63 (s, 2H), 2.11 (q, *J* = 7.2 Hz, 2H), 1.91 - 1.84 (m, 3H), 1.61 - 1.51 (m, 1H), 1.48 - 1.39 (m, 1H), 0.92 (s, 9H), 0.10 - 0.08 (m, 6H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 156.6, 153.9, 138.7, 115.0, 108.1, 106.7, 68.0, 58.4, 35.2, 33.7, 26.1, 25.0, 18.6, –5.0;
MS (ESI-TOF) calcd. for $C_{17}H_{30}O_3Si$ [M + Na^+] 333.1856, found 333.1866.

6-(((*tert*-butyldimethylsilyl)oxy)methyl)-6-hydroxy-2-(pent-4-en-1-yl)-2*H*-pyran-3(6*H*)-one (S23):
Reaction of **S22** (608 mg, 1.96 mmol), vanadyl acetylacetonate (52 mg, 0.20 mmol, 0.1 equiv), and *tert*-butyl hydroperoxide (534 µL of a 5.5 M solution in dodecane, 2.94 mmol, 1.5 equiv) in CH_2Cl_2 (9.8 mL, 0.2 M) according to **S4** above afforded **S23** as a yellow oil after column chromatography (silica gel, 95:5 to 9:1 hexanes/EtOAc) (512 mg, 80%).
R_f = 0.50 (silica gel, 5:1 hexanes/EtOAc);
IR (film) ν_{max} 3466 (br), 2954, 2930, 2858, 1694, 1254, 1101, 1059, 912, 836, 779 cm^{-1};
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73 (d, *J* = 10.2 Hz, 1H), 6.08 (d, *J* = 10.2 Hz, 1H), 5.85 - 5.73 (m,

[17] 5-(((*tert*-Butyldimethylsilyl)oxy)methyl)furan-2-carbaldehyde prepared according to: Celanire, S.; Marlin, F.; Baldwin, J. E.; Adlington, R. M. *Tetrahedron* **2005**, *61*, 3025–3032.

1H), 4.99 (dq, *J* = 1.8, 16.8 Hz, 1H), 4.96 - 4.92 (m, 1H), 4.53 (dd, *J* = 3.8, 7.9 Hz, 1H), 3.76 - 3.64 (m, 3H), 2.10 - 2.02 (m, 2H), 2.00 - 1.90 (m, 1H), 1.72 - 1.61 (m, 1H), 1.56 - 1.46 (m, 2H), 0.92 (s, 9H), 0.11 (d, *J* = 2.6 Hz, 6H);
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 145.2, 138.7, 128.8, 114.8, 92.8, 74.5, 68.5, 33.7, 29.3, 26.0, 24.4, 18.6, –5.0, –5.2;

2-(((*tert*-butyldimethylsilyl)oxy)methyl)-5-oxo-6-(pent-4-en-1-yl)-5,6-dihydro-2*H*-pyran-2-yl 4-(methylthio)benzoate (29):
Reaction of **S23** (355 mg, 1.09 mmol), EDC (417 mg, 2.18 mmol, 2.0 equiv), 4-methylthiobenzoic acid (366 mg, 2.18 mmol, 2.0 equiv), and DMAP (266 mg, 2.18 mmol, 2.0 equiv) in CH_2Cl_2 (5.4 mL, 0.2 M) according to **5c** above afforded **29** as a clear oil after column chromatography (Davisil®, 1:0 to 99:1 toluene/EtOAc) as a single diastereomer (431 mg, 83%). Decomposition and conversion to **30** was observd to occur upon prolonged exposure of **29** to silica gel; this occurs to a lesser degree with Davisil®.
R_f = 0.60 (silica gel, 5:1 hexanes/EtOAc);
IR (film) ν_{max} 2928, 2857, 1716, 1594, 1272, 1109, 911, 836, 778, 757, 732 cm^{-1};
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 - 7.85 (m, 2H), 7.37 (d, *J* = 10.2 Hz, 1H), 7.25 - 7.21 (m, 2H), 6.19 (d, *J* = 10.2 Hz, 1H), 5.86 - 5.74 (m, 1H), 5.01 (dd, *J* = 2.0, 17.0 Hz, 1H), 4.95 (dt, *J* = 1.1, 10.2 Hz, 1H), 4.61 (dd, *J* = 3.7, 7.7 Hz, 1H), 4.27 (d, *J* = 10.6 Hz, 1H), 3.92 (d, *J* = 10.6 Hz, 1H), 2.50 (s, 3H), 2.09 (q, *J* = 6.6 Hz, 2H), 2.03 - 1.95 (m, 1H), 1.83 - 1.71 (m, 1H), 1.57 (quin, *J* = 7.7 Hz, 2H), 0.85 (s, 9H), 0.07 - 0.04 (m, 6H);
^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 164.8, 146.5, 144.7, 138.6, 130.3, 127.6, 126.1, 125.1, 115.0, 100.1, 77.6, 66.5, 33.7, 29.7, 25.9, 24.2, 18.4, 15.0, –5.2;
MS (ESI-TOF) calcd. for $C_{25}H_{36}O_5SSi$ [M + Na^+] 499.1945, found 499.1938.

4. Procedures for Cycloadditions and Characterization of Products

General Procedure for Thiourea-Catalyzed Cycloadditions (Optimization and Structure-Activity Relationship Studies):

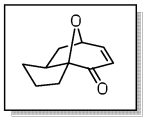
An oven-dried 0.5-dram vial was charged with the specified urea, thiourea, or carbazole catalyst(s) (0.10 or 0.15 equiv as indicated). To these catalysts was added a stock solution of substrate **5** (0.05 mmol) and AcOH (0 or 0.15 equiv as indicated) in toluene (0.2 M or 0.4 M in **5** as indicated). No special precautions were taken to exclude air or moisture. The vial was sealed, placed in a 40 °C bath, and allowed to stir for the designated length of time. The reaction was then removed from heating and quenched with 1N HCl (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL), which was added to a flask containing 1,3,5-trimethoxybenzene (0.0119 M in benzene, 0.10 equiv relative to substrate). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. A yield was then determined by ^1H NMR of this crude reaction mixture in $CDCl_3$. Enantiomeric excess was determined by chiral HPLC after chromatographic purification on silica gel.

General Procedure A for Thiourea-Catalyzed Cycloadditions (Substrate Scope):

An oven-dried 0.5-dram vial was charged with *para*-thiomethylbenzoyl substrate ($\geq$ 50.0 mg). To this vial was then added a stock solution of AcOH (0.15 eq) in toluene such that the final substrate concentration was 0.4 M. To this solution was added chiral primary aminothiourea catalyst **10** (0.10, 0.15, or 0.20 equiv as indicated) and achiral thiourea catalyst **8** (0.10, 0.15, or 0.20 equiv as indicated). No special precautions were taken to exclude air or moisture. The vial was sealed, placed in a 40 °C oil bath, and allowed to stir for the designated length of time. The reaction was then removed from the bath and transferred with CH_2Cl_2 to a separatory funnel containing 1N HCl (15 mL). The aqueous layer was then extracted with CH_2Cl_2 (4 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by silica gel flash chromatography. Some products required a second purification by silica gel flash chromatography eluting with a toluene/EtOAc in order to remove unreacted starting material. A byproduct was observed arrising from presumed decompostion of catalyst **8** and conjugate addition of 3,5-bis(trifluoromethyl)aniline to the enone of the product. The yield of this byproduct was $\leq$ 4% in all cases. An X-ray crystal structure of this byproduct was obtained from the reaction with substrate **27**.

General Procedure for Preparation of Racemic Products:

An oven-dried 2.0-dram vial was charged with substrate ($\geq$ 0.5 mmol) and dissolved in CH_2Cl_2 (0.05 M). To this solution was added DBU (1.5 equiv) via syringe. The vial was sealed and allowed to stir overnight at room temperature. The reaction mixture was then concentrated and the racemic product purified by silica gel flash chromatography.



(3a*S*,7*R*,8a*S*)-2,3,8,8a-tetrahydro-1*H*-3a,7-epoxyazulen-4(7*H*)-one (6):

According to general procedure A, **5c** (102.4 mg, 0.308 mmol), **10** (12.4 mg, 0.031 mmol, 0.10 equiv), and **8** (15.4 mg, 0.031 mmol, 0.10 equiv) were allowed to react in a toluene solution (770 μL, 0.4 M) containing AcOH (2.7 μL, 0.046 mmol, 0.15 equiv) for 48 h to afford **6** (37.3 mg, 74%) as a colorless oil after column chromatography (silica gel, 9:1 to 3:2 hexanes/Et_2O) followed by subsequent column chromatography (silica gel, 98:2 toluene/EtOAc). This material was determined to be 91% *ee* by chiral HPLC analysis (ChiralPak AS-H, 2% *i*PrOH in hexanes, 1 mL/min, 218 nm).

$\mathbf{R}_f$ = 0.24 (silica gel, 95:5 toluene/EtOAc);

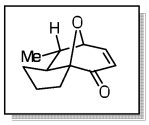
IR (film) ν_{max} 2954, 2868, 1689, 1165, 1038, 789 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 4.4, 9.8 Hz, 1H), 5.95 (d, *J* = 9.8 Hz, 1H), 4.87 (dd, *J* = 4.6, 6.6 Hz, 1H), 2.44 - 2.36 (m, 1H), 2.23 - 2.26 (m, 1H), 2.15 (dd, *J* = 8.8, 11.7 Hz, 1H), 1.95 - 1.75 (m, 4H), 1.73 - 1.67 (m, 1H), 1.61 - 1.55 (m, 1H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 152.2, 126.4, 98.3, 76.3, 44.8, 36.9, 32.6, 30.3, 26.3;

MS (ESI-TOF) calcd. for $C_{10}H_{12}O_2$ [M + H^+] 165.0916, found 165.0794;

$[\alpha]_D^{23}$ = –155.4 (c = 1.4, $CHCl_3$).



(3a*S*,7*S*,8*S*,8a*S*)-8-methyl-2,3,8,8a-tetrahydro-1*H*-3a,7-epoxyazulen-4(7*H*)-one (12):

According to general procedure A, **11** (100.0 mg, 0.29 mmol), **10** (17.4 mg, 0.043 mmol, 0.15 equiv), and **8** (21.7 mg, 0.043 mmol, 0.15 equiv) were allowed to react in a toluene solution (722 μL, 0.4 M) containing AcOH (2.5 μL, 0.043 mmol, 0.15 equiv) for 72 h to afford **12** (35.9 mg, 70%) as a colorless oil after column chromatography (silica gel, 9:1 to 3:2 hexanes/Et_2O) followed by subsequent column chromatography (silica gel, 98:2 toluene/EtOAc). This material was determined to be 90% *ee* by chiral HPLC analysis (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 218 nm).

$\mathbf{R}_f$ = 0.52 (silica gel, 4:1 hexanes/EtOAc);

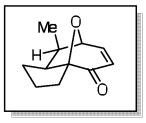
IR (film) ν_{max} 2959, 2871, 1694, 1457, 1380, 1265, 1160, 1050, 929, 669 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (dd, *J* = 4.4, 9.8 Hz, 1H), 6.09 (d, *J* = 9.8 Hz, 1H), 4.67 (dd, *J* = 4.4, 5.9 Hz, 1H), 2.25 - 2.14 (m, 2H), 1.96 - 1.90 (m, 1H), 1.88 - 1.77 (m, 3H), 1.72 - 1.61 (m, 2H), 1.07 (d, *J* = 6.8 Hz, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 150.7, 128.1, 98.3, 79.4, 52.7, 45.8, 30.8, 30.3, 25.7, 15.8;

MS (ESI-TOF) calcd. for $C_{11}H_{14}O_2$ [M + Na^+] 201.0886, found 201.0887;

$[\alpha]_D^{23}$ = –143.5 (c = 2.0, $CHCl_3$).



(3a*S*,7*S*,8*R*,8a*S*)-8-methyl-2,3,8,8a-tetrahydro-1*H*-3a,7-epoxyazulen-4(7*H*)-one (14):

According to general procedure A, **13** (100.0 mg, 0.29 mmol), **10** (17.4 mg, 0.043 mmol, 0.15 equiv), and **8** (21.7 mg, 0.043 mmol, 0.15 equiv) were allowed to react in a toluene solution (722 μL, 0.4 M) containing AcOH (2.5 μL, 0.043 mmol, 0.15 equiv) for 72 h to afford **14** (33.8 mg, 66%) as a colorless oil after column chromatography (silica gel, 9:1 to 3:2

hexanes/Et_2O) followed by subsequent column chromatography (silica gel, 98:2 toluene/EtOAc). This material was determined to be 89% *ee* by chiral HPLC analysis (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 220 nm).

$\mathbf{R_f}$ = 0.48 (silica gel, 4:1 hexanes/EtOAc);

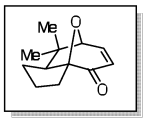
IR (film) ν_{max} 2962, 2873, 1692, 1461, 1377, 1270, 1171, 1009, 912, 794, 669 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 4.3, 9.8 Hz, 1H), 5.98 (d, *J* = 10.1 Hz, 1H), 4.44 (d, *J* = 4.1 Hz, 1H), 2.45 (td, *J* = 3.4, 8.8 Hz, 1H), 2.38 - 2.27 (m, 2H), 1.88 - 1.81 (m, 1H), 1.80 - 1.65 (m, 4H), 1.16 (d, *J* = 7.3 Hz, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 151.7, 125.8, 99.3, 83.0, 47.5, 38.4, 30.1, 27.9, 26.6, 16.7;

MS (ESI-TOF) calcd. for $C_{11}H_{14}O_2$ [M + Na^+] 201.0886, found 201.0876;

$\mathbf{[\alpha]_D^{24}}$ = –43.0 (c = 0.8, $CHCl_3$).



(3a*S*,7*S*,8a*S*)-8,8-dimethyl-2,3,8,8a-tetrahydro-1*H*-3a,7-epoxyazulen-4(7*H*)-one (16):

According to general procedure A, **15** (100.0 mg, 0.28 mmol), **10** (16.7 mg, 0.042 mmol, 0.15 equiv), and **8** (20.8 mg, 0.042 mmol, 0.15 equiv) were allowed to react in a toluene solution (694 µL, 0.4 M) containing AcOH (2.4 µL, 0.042 mmol, 0.15 equiv) for 96 h to afford **16** (27.0 mg, 51%) as a colorless oil after column chromatography (silica gel, 9:1 to 3:2 hexanes/Et_2O) followed by subsequent column chromatography (silica gel, 98:2 toluene/EtOAc). This material was determined to be 89% *ee* by chiral HPLC analysis (ChiralPak AD-H, 5% *i*PrOH in hexanes, 1 mL/min, 220 nm).

$\mathbf{R_f}$ = 0.50 (silica gel, 4:1 hexanes/EtOAc);

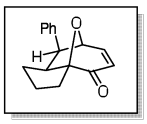
IR (film) ν_{max} 2963, 1696, 1162, 1036, 900, 795, 669 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 4.6, 10.1 Hz, 1H), 6.10 (d, *J* = 9.6 Hz, 1H), 4.31 (d, *J* = 4.6 Hz, 1H), 2.27 (ddd, *J* = 6.9, 1.03, 13.5 Hz, 1H), 2.10 (dd, *J* = 2.5, 9.7 Hz, 1H), 1.88 - 1.73 (m, 3H), 1.71 - 1.62 (m, 2H), 1.23 (s, 3H), 1.09 (s, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 151.4, 127.1, 99.4, 85.4, 54.8, 45.3, 30.1, 27.5, 26.6, 26.5, 25.2;

MS (ESI-TOF) calcd. for $C_{12}H_{16}O_2$ [M + Na^+] 215.1043, found 215.1056;

$\mathbf{[\alpha]_D^{23}}$ = –86.9 (c = 1.4, $CHCl_3$).



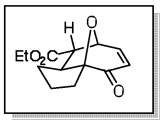
(3a*S*,7*S*,8*S*,8a*S*)-8-phenyl-2,3,8,8a-tetrahydro-1*H*-3a,7-epoxyazulen-4(7*H*)-one (18):

According to general procedure A, **17** (100.0 mg, 0.25 mmol), **10** (14.7 mg, 0.037 mmol, 0.15 equiv), and **8** (18.4 mg, 0.037 mmol, 0.15 equiv) were allowed to react in a toluene solution (612 µL, 0.4 M) containing AcOH (2.1 µL, 0.037 mmol, 0.15 equiv) for 72 h to afford **18** (28.4 mg, 48%) as a colorless oil after column chromatography (silica gel, 9:1 to 3:2 hexanes/Et_2O). This material was determined to be 86% *ee* by chiral HPLC analysis (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 206 nm).

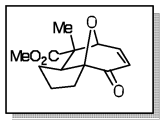
$\mathbf{R_f}$ = 0.50 (silica gel, 4:1 hexanes/EtOAc);

IR (film) ν_{max} 2960, 1695, 1494, 1454, 1267, 1168, 1039, 794, 704 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 - 7.25 (m, 6H), 6.08 (d, *J* = 10.1 Hz, 1H), 5.05 (d, *J* = 4.6 Hz, 1H), 3.47 (d, *J* = 9.6 Hz, 1H), 2.81 (td, *J* = 3.9, 9.7 Hz, 1H), 2.36 (ddd, *J* = 7.3, 10.1, 13.7 Hz, 1H), 1.84 - 1.77 (m, 1H), 1.69 - 1.56 (m, 2H), 1.54 - 1.47 (m, 1H), 1.07 - 1.00 (m, 1H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 198.1, 151.5, 140.9, 128.8, 128.5, 127.0, 126.2, 99.3, 82.2, 50.5, 49.8, 30.2, 27.9, 27.1;
MS (ESI-TOF) calcd. for $C_{16}H_{16}O_2$ [M + H^+] 241.1229, found 241.1247;
$[\alpha]_D^{24}$ = –79.7 (c = 1.4, $CHCl_3$).

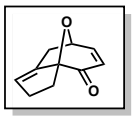


(3a*S*,7*S*,8*S*,8a*S*)- ethyl 4-oxo-2,3,4,7,8,8a-hexahydro-1*H*-3a,7-epoxyazulene-8-carboxylate (20):
According to general procedure A, **19** (100.0 mg, 0.247 mmol), **10** (14.9 mg, 0.037 mmol, 0.15 equiv), and **8** (18.6 mg, 0.037 mmol, 0.15 equiv) were allowed to react in a toluene solution (618 μL, 0.4 M) containing AcOH (2.1 μL, 0.037 mmol, 0.15 equiv) for 72 h to afford **20** (38.8 mg, 66%) as a colorless oil after column chromatography (silica gel, 9:1 to 5:1 hexanes/Et_2O). This material was determined to be 90% *ee* by chiral HPLC analysis (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 220 nm).
R_f = 0.35 (silica gel, 5:1 hexanes/EtOAc);
IR (film) ν_{max} 2961, 2872, 1732, 1694, 1374, 1192, 1166, 1048, 1034, 1019, 929 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 4.4, 9.8 Hz, 1H), 6.06 (d, *J* = 9.8 Hz, 1H), 5.00 (dd, *J* = 4.4, 6.3 Hz, 1H), 4.14 (dq, *J* = 1.5, 7.3 Hz, 2H), 3.11 (t, *J* = 6.6 Hz, 1H), 2.71 (ddd, *J* = 2.9, 6.3, 9.3 Hz, 1H), 2.29 - 2.21 (m, 1H), 2.01 - 1.92 (m, 1H), 1.90 - 1.80 (m, 2H), 1.75 - 1.66 (m, 2H), 1.25 (t, *J* = 7.3 Hz, 3H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 196.6, 170.9, 149.5, 127.9, 98.5, 76.4, 61.4, 56.0, 48.3, 31.7, 30.3, 25.8, 14.4;
MS (ESI-APCI) calcd. for $C_{13}H_{16}O_4$ [M + H^+] 237.1, found 237.1;
$[\alpha]_D^{23}$ = –272.2 (c = 1.21, $CHCl_3$).

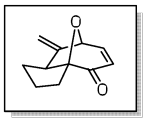


(3a*S*,7*S*,8*S*,8a*S*)-methyl 8-methyl-4-oxo-2,3,4,7,8,8a-hexahydro-1*H*-3a,7-epoxyazulene-8-carboxylate (22):
According to general procedure A, **21** (63.1 mg, 0.16 mmol), **10** (12.5 mg, 0.031 mmol, 0.20 equiv), and **8** (15.6 mg, 0.031 mmol, 0.20 equiv) were allowed to react in a toluene solution (390 μL, 0.4 M) containing AcOH (1.3 μL, 0.023 mmol, 0.15 equiv) for 96 h to afford **22** (13.8 mg, 37%) as a colorless oil after column chromatography (silica gel, 9:1 to 3:2 hexanes/Et_2O). This material was determined to be 80% *ee* by chiral HPLC analysis (ChiralCel OC-H, 5% *i*PrOH in hexanes, 1 mL/min, 218 nm).
R_f = 0.45 (silica gel, 4:1 hexanes/EtOAc);
IR (film) ν_{max} 2958, 1736, 1698, 1277, 1247, 1139, 1122, 1036, 914, 734, 650 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 4.6, 9.7 Hz, 1H), 6.04 (d, *J* = 10.1 Hz, 1H), 4.59 (d, *J* = 4.1 Hz, 1H), 3.70 (s, 3H), 2.88 (dd, *J* = 3.2, 8.7 Hz, 1H), 2.35 - 2.27 (m, 1H), 1.90 - 1.76 (m, 4H), 1.69 (dd, *J* = 4.6, 14.4 Hz, 1H), 1.52 (s, 3H);

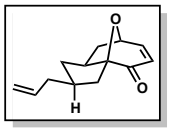
^{13}C NMR (125 MHz, $CDCl_3$) δ 196.9, 175.2, 150.1, 127.1, 99.3, 82.8, 56.6, 52.5, 50.0, 30.1, 27.7, 26.7, 21.8;
MS (ESI-TOF) calcd. for $C_{13}H_{16}O_4$ [M + H^+] 237.1127, found 237.1151;
$[\alpha]_D^{23}$ = –100.7 (c = 0.8, $CHCl_3$).



(3a*S*,7*R*)-7,8-dihydro-2*H*-3a,7-epoxyazulen-4(3*H*)-one (24):
According to general procedure A, **23** (107.4 mg, 0.325 mmol), **10** (19.6 mg, 0.049 mmol, 0.15 equiv), and **8** (24.4 mg, 0.049 mmol, 0.15 equiv) were allowed to react in a toluene solution (813 μL, 0.4 M) containing AcOH (2.8 μL, 0.049 mmol, 0.15 equiv) for 72 h to afford **24** (28.5 mg, 54%) as a white solid after column chromatography (silica gel, 9:1 to 5:1 hexanes/Et_2O) followed by subsequent column chromatography (silica gel, 98:2 toluene/EtOAc). This material was determined to be 95% *ee* by chiral HPLC analysis (ChiralPak AS-H, 3% *i*PrOH in hexanes, 1 mL/min, 218 nm).
$\mathbf{R}_f$ = 0.44 (silica gel, 5:1 hexanes/EtOAc);
IR (film) ν_{max} 2981, 2935, 2855, 1684, 1376, 1167, 1096, 1016, 987, 904, 814, 790, 648 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 4.4, 9.8 Hz, 1H), 6.01 (d, *J* = 9.8 Hz, 1H), 5.76 (dq, *J* = 1.9, 3.7 Hz, 1H), 5.15 - 5.11 (m, 1H), 3.04 - 2.94 (m, 1H), 2.80 - 2.73 (m, 2H), 2.73 - 2.66 (m, 1H), 2.33 - 2.27 (m, 1H), 1.84 (dt, *J* = 9.0, 12.2 Hz, 1H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 195.2, 153.4, 142.5, 127.6, 126.6, 101.0, 79.3, 38.9, 32.5, 30.0;
MS (ESI-TOF) calcd. for $C_{10}H_{10}O_2$ [M + H^+] 163.0759, found 163.0628;
$[\alpha]_D^{23}$ = +56.6 (c = 1.07, $CHCl_3$).



(3a*S*,7*S*,8a*S*)-8-methylene-2,3,8,8a-tetrahydro-1*H*-3a,7-epoxyazulen-4(7*H*)-one (26):
According to general procedure A, **25** (107.4 mg, 0.266 mmol), **10** (16.0 mg, 0.040 mmol, 0.15 equiv), and **8** (20.0 mg, 0.040 mmol, 0.15 equiv) were allowed to react in a toluene solution (665 μL, 0.4 M) containing AcOH (2.3 μL, 0.040 mmol, 0.15 equiv) for 72 h to afford **26** (19.7 mg, 54%) as a clear oil after column chromatography (silica gel, 9:1 to 5:1 hexanes/Et_2O) followed by subsequent column chromatography (silica gel, 98:2 toluene/EtOAc). This material was determined to be 88% *ee* by chiral HPLC analysis (ChiralPak AS-H, 10% *i*PrOH in hexanes, 1 mL/min, 222 nm).
$\mathbf{R}_f$ = 0.45 (silica gel, 4:1 hexanes/EtOAc);
IR (film) ν_{max} 2958, 2870, 1690, 1267, 1163, 1031, 934, 897, 817, 79, 782, 627 cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 4.4, 9.8 Hz, 1H), 6.00 (d, *J* = 9.8 Hz, 1H), 5.17 (d, *J* = 2.4 Hz, 1H), 5.02 - 4.99 (m, 2H), 2.84 - 2.78 (m, 1H), 2.34 (ddd, *J* = 7.6, 9.3, 13.4 Hz, 1H), 2.13 - 2.04 (m, 1H), 1.92 - 1.81 (m, 2H), 1.81 - 1.71 (m, 2H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 196.4, 150.6, 150.5, 126.6, 107.3, 98.9, 79.9, 48.4, 32.2, 30.7, 26.1;
MS (ESI-TOF) calcd. for $C_{11}H_{12}O_2$ [M + Na^+] 199.0735, found 199.0723;
$[\alpha]_D^{23}$ = –526.0 (c = 0.4, $CHCl_3$).



(2*S*,3a*S*,7*R*,8a*S*)-2-allyl-2,3,8,8a-tetrahydro-1*H*-3a,7-epoxyazulen-4(7*H*)-one (28):

According to general procedure A, **27** (111.7 mg, 0.300 mmol), **10** (12.0 mg, 0.030 mmol, 0.10 equiv), and **8** (15.0 mg, 0.049 mmol, 0.10 equiv) were allowed to react in a toluene solution (750 µL, 0.4 M) containing AcOH (2.6 µL, 0.045 mmol, 0.15 equiv) for 72 h to afford **28** (47.0 mg, 77%) as a clear oil after column chromatography (silica gel, 9:1 to 5:1 hexanes/Et_2O) followed by subsequent column chromatography (silica gel, 98:2 toluene/EtOAc). This material was determined to be 90% *ee* by chiral HPLC analysis (ChiralPak AS-H, 4% *i*PrOH in hexanes, 1 mL/min, 230 nm).

R_f = 0.37 (silica gel, 5:1 hexanes/EtOAc);

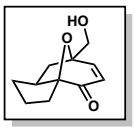
IR (film) ν_{max} 3075, 2971, 2925, 1691, 1166, 1024, 909, 803 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 4.4, 9.8 Hz, 1H), 5.96 (d, *J* = 9.8 Hz, 1H), 5.79 (ddt, *J* = 6.9, 10.1, 17.1 Hz, 1H), 5.02 (dd, *J* = 1.5, 17.1 Hz, 1H), 4.99 - 4.94 (m, 2H), 2.75 (ddd, *J* = 1.5, 7.8, 13.4 Hz, 1H), 2.36 - 2.28 (m, 1H), 2.28 - 2.11 (m, 4H), 2.01 (dd, *J* = 8.3, 11.7 Hz, 1H), 1.95 - 1.89 (m, 1H), 1.31 - 1.18 (m, 2H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 197.8, 152.6, 137.4, 125.8, 115.8, 98.4, 77.7, 46.1, 44.6, 40.6, 39.5, 36.4, 35.6;

MS (ESI-TOF) calcd. for $C_{13}H_{16}O_2$ [M + Na^+] 227.1048, found 227.1069;

$[\alpha]_D^{23}$ = –91.8 (c = 1.2, $CHCl_3$).



(3a*S*,7*R*)-7-(hydroxymethyl)-2,3,8,8a-tetrahydro-1*H*-3a,7-epoxyazulen-4(7*H*)-one (S24):

According to general procedure A, **29** (124.0 mg, 0.260 mmol), **10** (15.7 mg, 0.039 mmol, 0.15 equiv), and **8** (19.5 mg, 0.039 mmol, 0.15 equiv) were allowed to react in a toluene solution (650 µL, 0.4 M) containing AcOH (2.2 µL, 0.039 mmol, 0.15 equiv) for 72 h to afford **30** after column chromatography (silica gel, 98:2 toluene/EtOAc). The silyl ether was then immediately dissolved in THF (1.0 mL) at room temperature. Water (400 µL), AcOH (500 µL), and conc. HCl (100 µL) were then subsequently added, and the reaction mixture was stirred for 2 h at room temperature. Sat. aq. $NaHCO_3$ (10 mL) was then carefully added. The mixture was transferred to a separatory funnel with EtOAc (20 mL). An additional portion of sat. aq. $NaHCO_3$ (10 mL) was then added and the layers were separated. The organic layer was washed with brine (15 mL) and the combined aqueous layers were further extracted with EtOAc (2 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (silica gel, 2:1 hexanes/EtOAc) afforded **S24** as a clear oil (35.7 mg, 70% overall). This material was determined to be 89% *ee* by chiral HPLC analysis (ChiralPak AD-H, 10% *i*PrOH in hexanes, 1 mL/min, 210 nm).

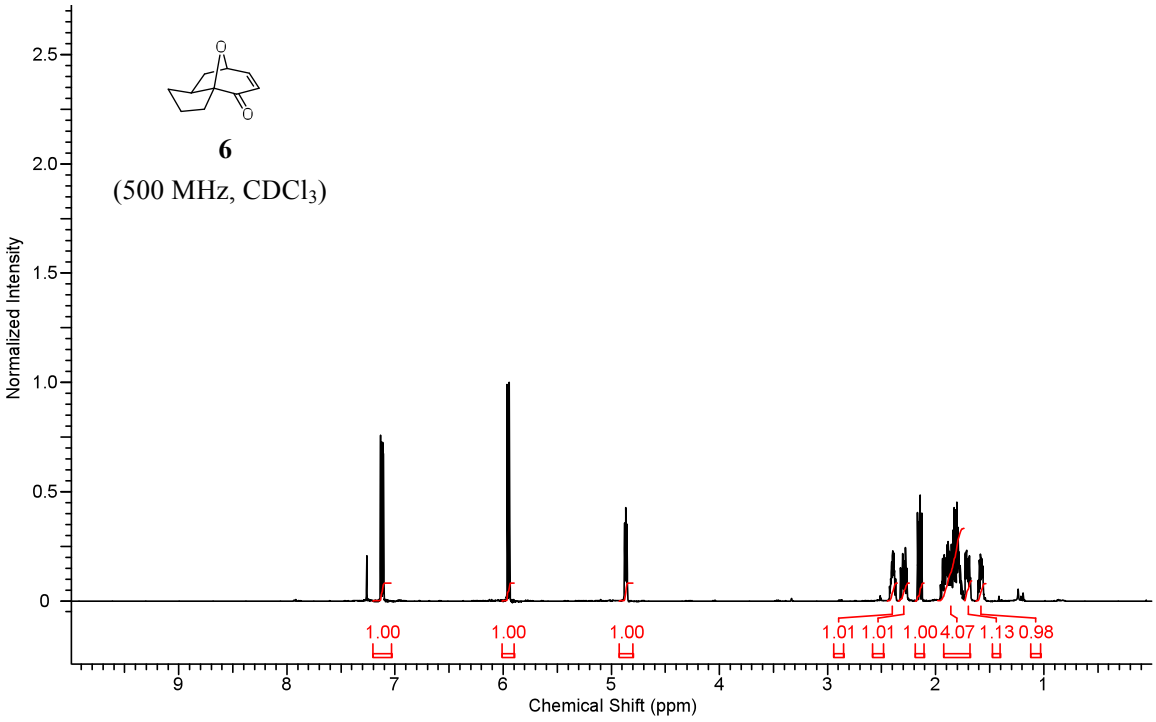
R_f = 0.35 (silica gel, 1:1 hexanes/EtOAc);

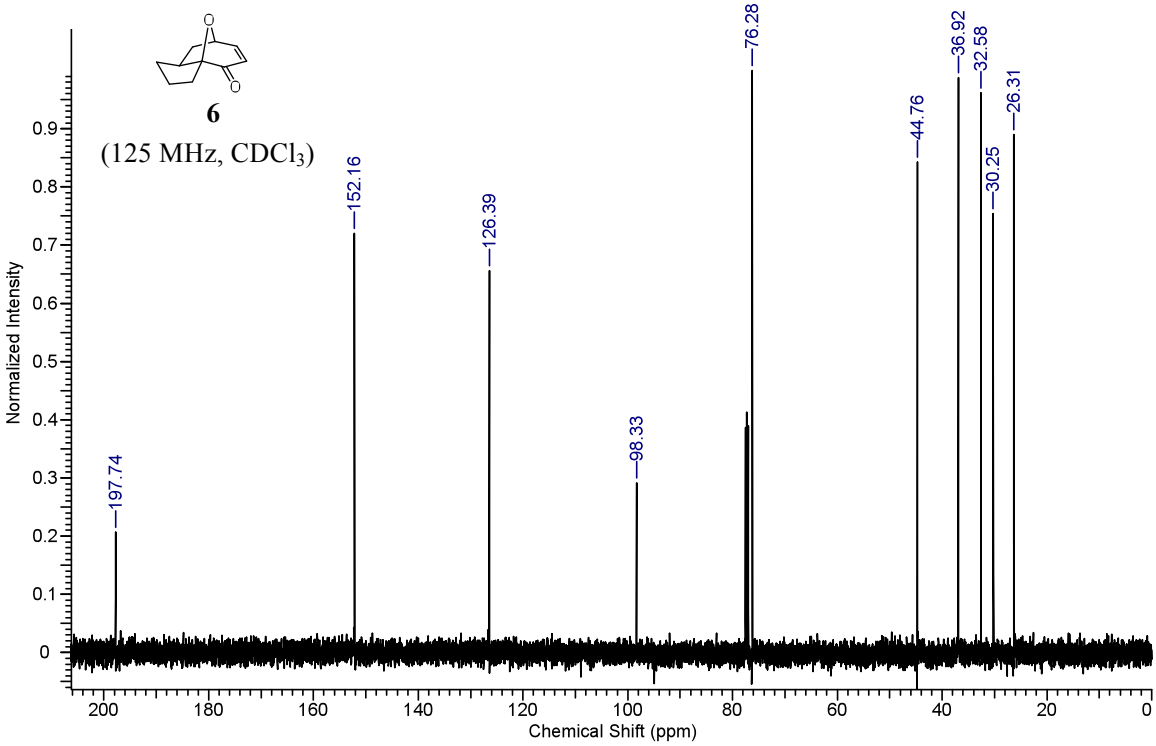
IR (film) ν_{max} 3442, 2952, 2869, 2360, 1688, 1382, 1270, 1169, 1085, 1066, 813 cm^{-1};

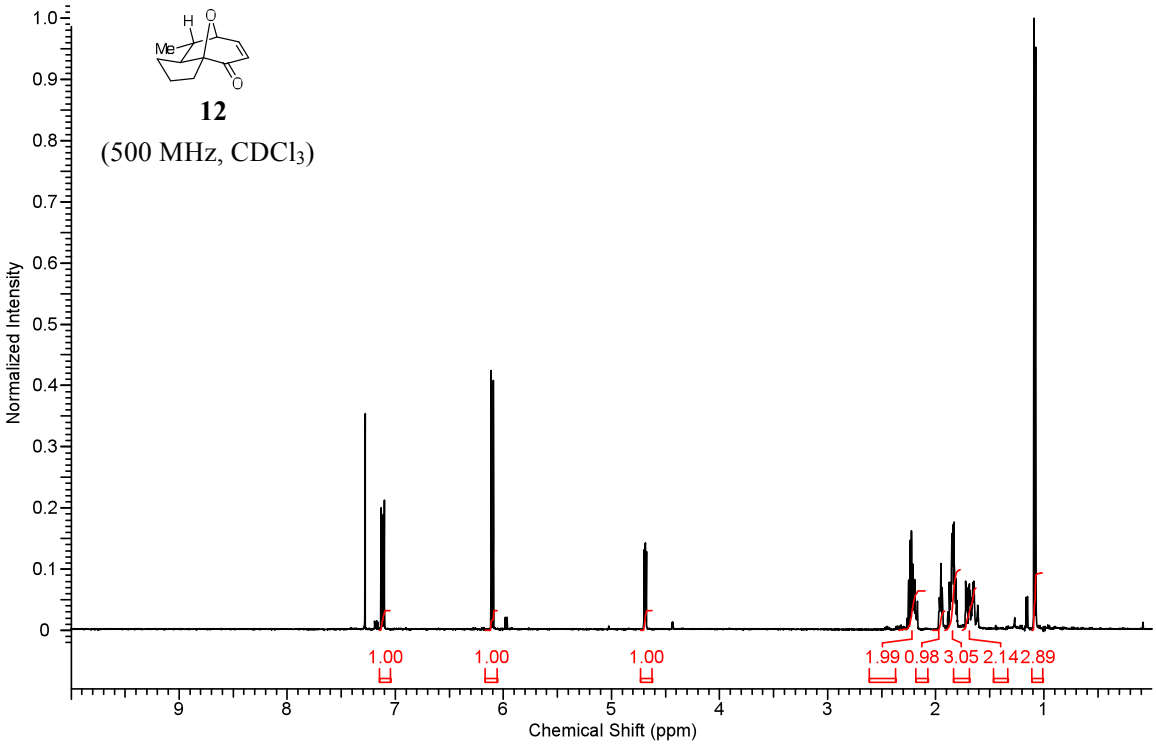
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (d, *J* = 9.8 Hz, 1H), 6.06 (d, *J* = 9.3 Hz, 1H), 3.91 (dd, *J* = 5.4, 11.7 Hz, 1H), 3.80 (dd, *J* = 5.4, 11.7 Hz, 1H), 2.50 - 2.43 (m, 1H), 2.34 - 2.27 (m, 1H), 2.11 (dd, *J* = 8.8, 12.2 Hz, 1H), 1.98 - 1.85 (m, 2H), 1.84 - 1.77 (m, 1H), 1.75 - 1.69 (m, 2H), 1.64 - 1.58 (m, 1H);

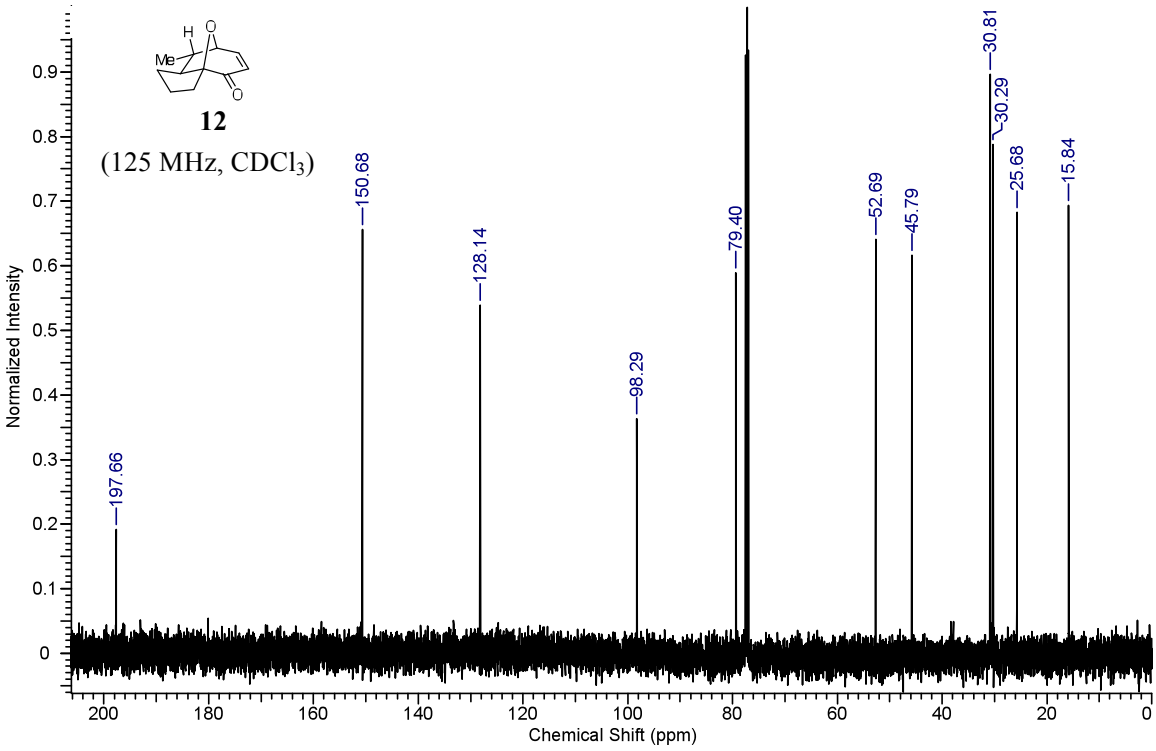
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 152.4, 127.6, 98.5, 86.0, 65.6, 46.1, 38.2, 32.7, 30.4, 26.4;
MS (ESI-TOF) calcd. for $C_{11}H_{14}O_3$ [M + Na^+] 217.0841, found 217.0790;
$[\alpha]_D^{23}$ = –55.2 (c = 0.47, $CHCl_3$).

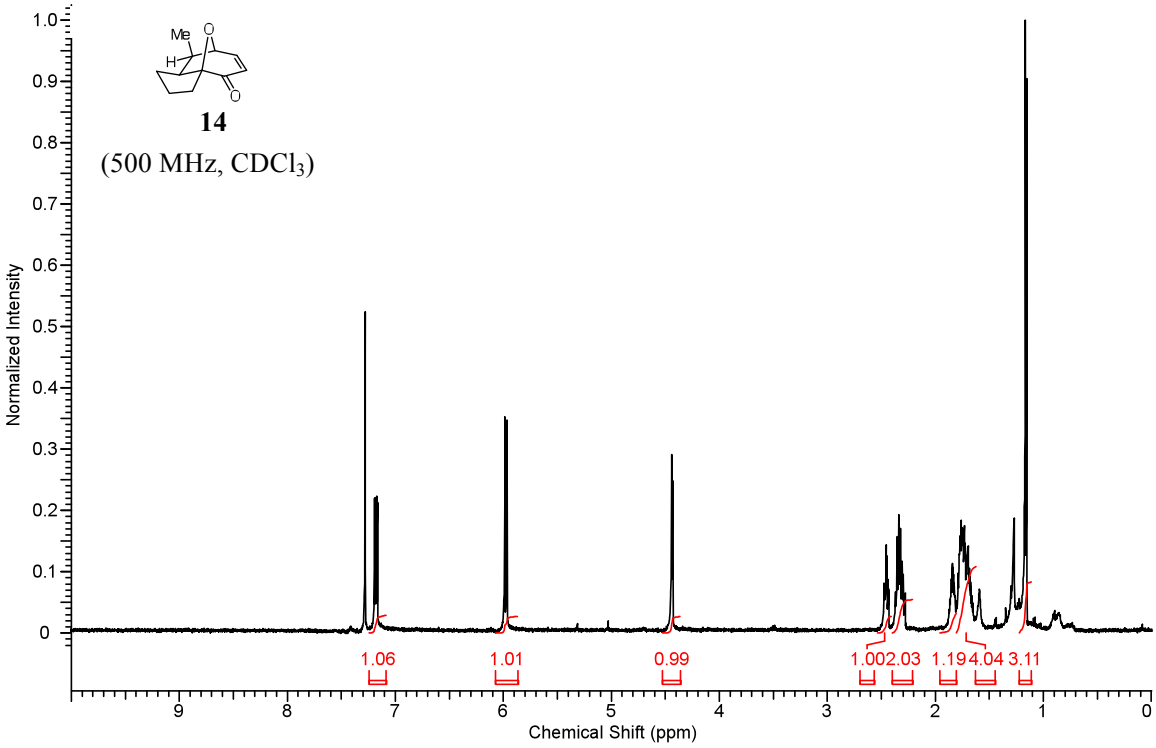
5. ^{1}H and ^{13}C NMR Spectra of Cycloaddition Products

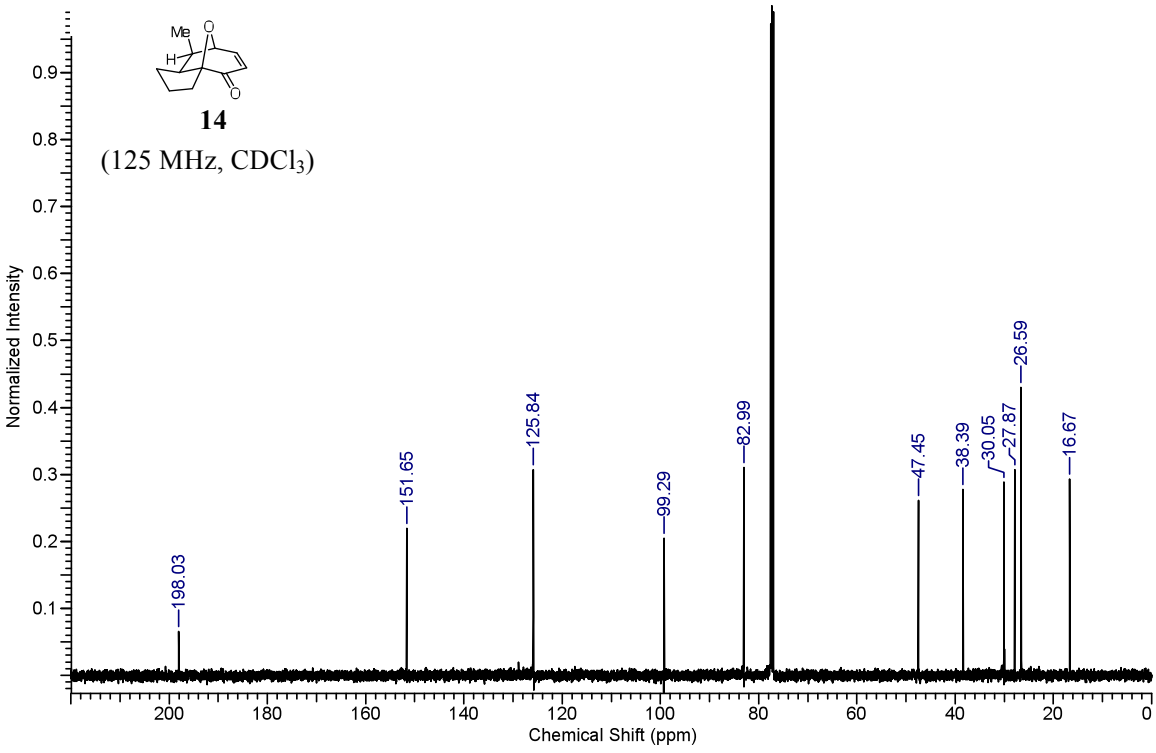





12
(500 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
1.00
1.00
1.00
1.99
0.98
3.05
2.14
2.89


12
(125 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
197.66
150.68
128.14
98.29
79.40
52.69
45.79
30.81
30.29
25.68
15.84


Me
H
O
O
14
(500 MHz, CDCl3)
Normalized Intensity
1.06
1.01
0.99
1.00
2.03
1.19
4.04
3.11
Chemical Shift (ppm)


Me
H
O
O
14
(125 MHz, CDCl3)
Normalized Intensity
198.03
151.65
125.84
99.29
82.99
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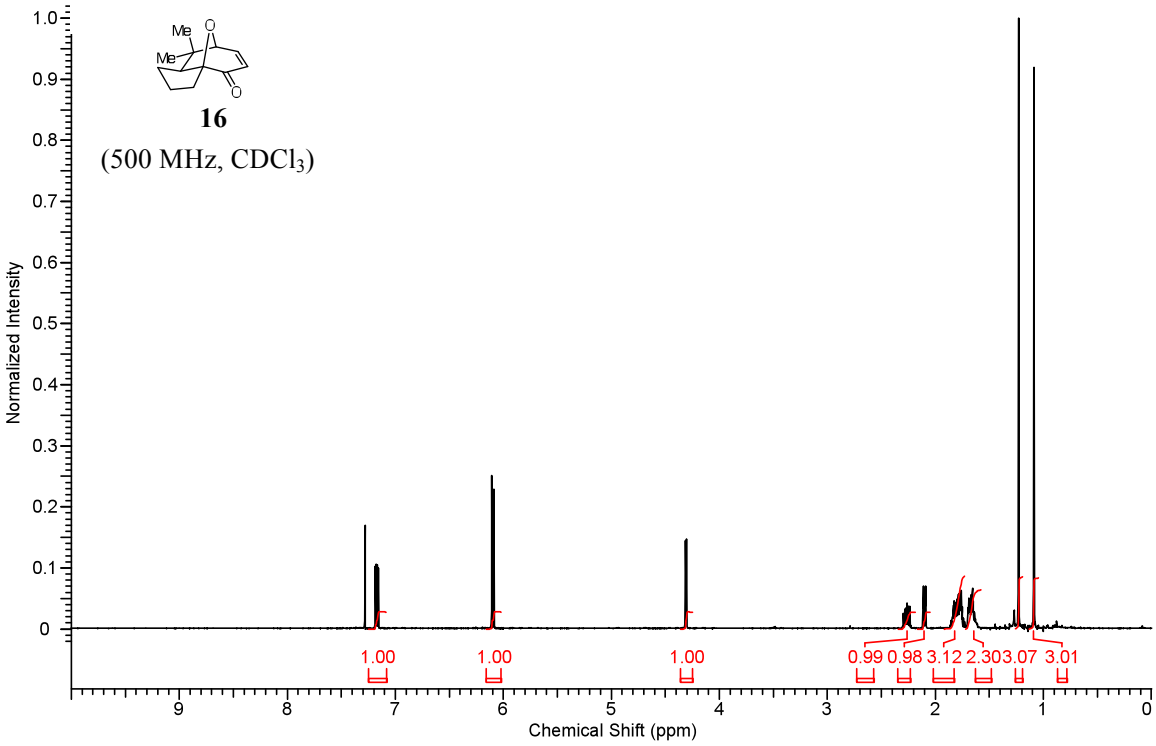
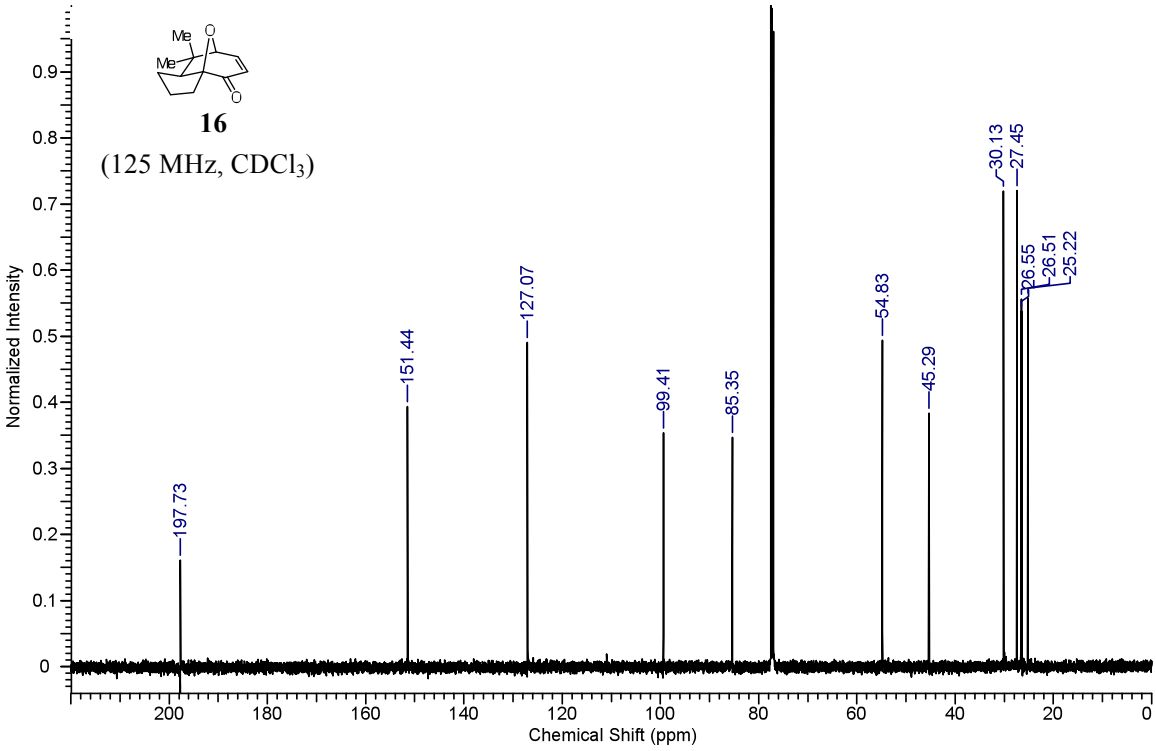
30.05
27.87
26.59
16.67
Chemical Shift (ppm)


Me
Me
O
O
16
(500 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
1.00
1.00
1.00
0.99
0.98
3.12
2.30
3.07
3.01


Me
Me
O
O
16
(125 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
197.73
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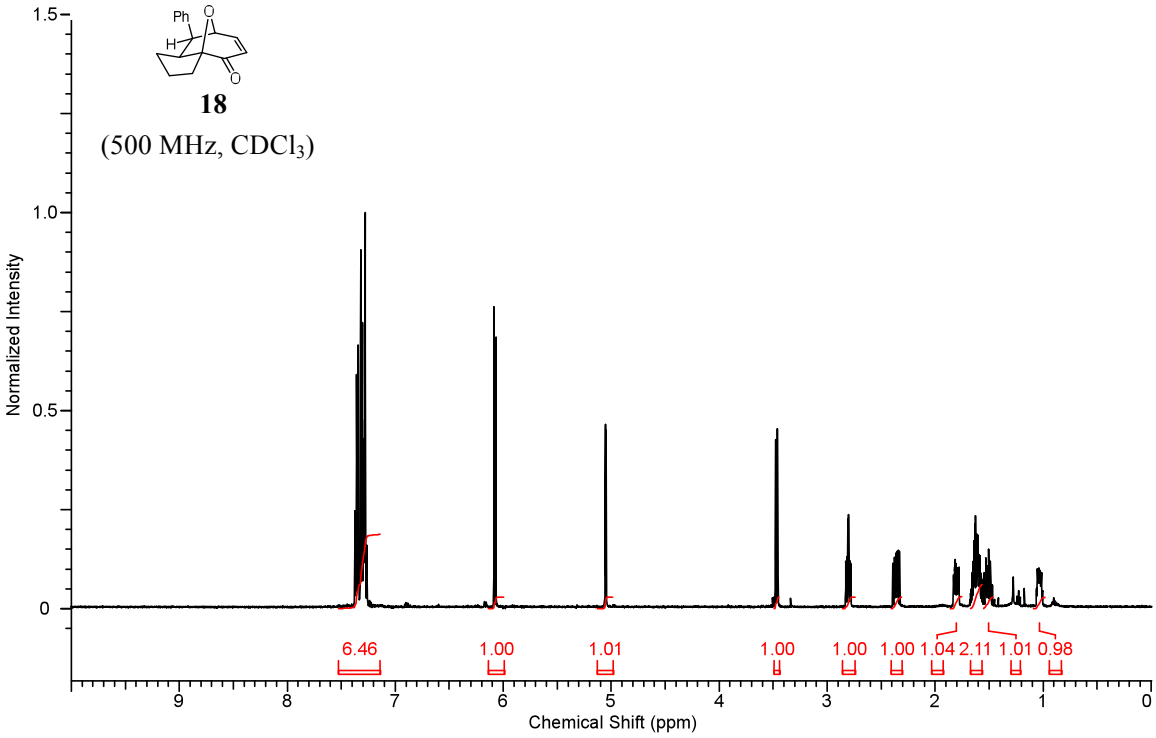
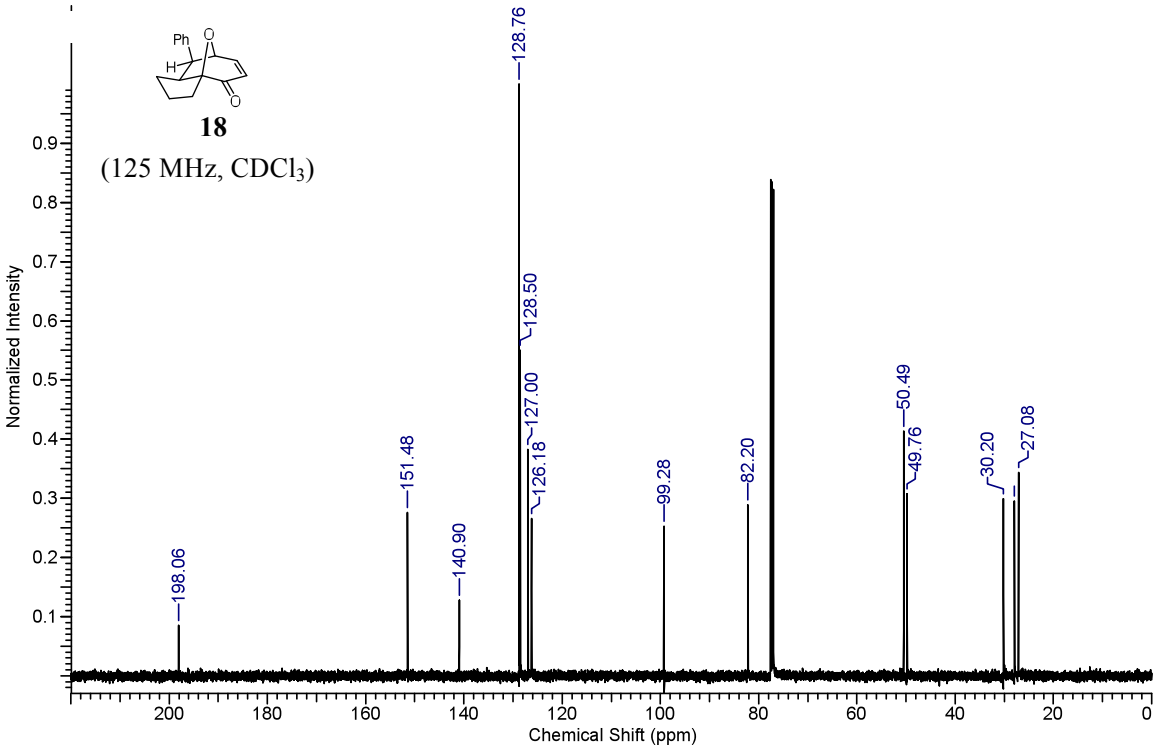
127.07
99.41
85.35
54.83
45.29
30.13
27.45
26.55
26.51
25.22


Ph
O
H
O
18
(500 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
6.46
1.00
1.01
1.00
1.00
1.00
1.04
2.11
1.01
0.98


Ph
O
H
O
18
(125 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
198.06
151.48
140.90
128.76
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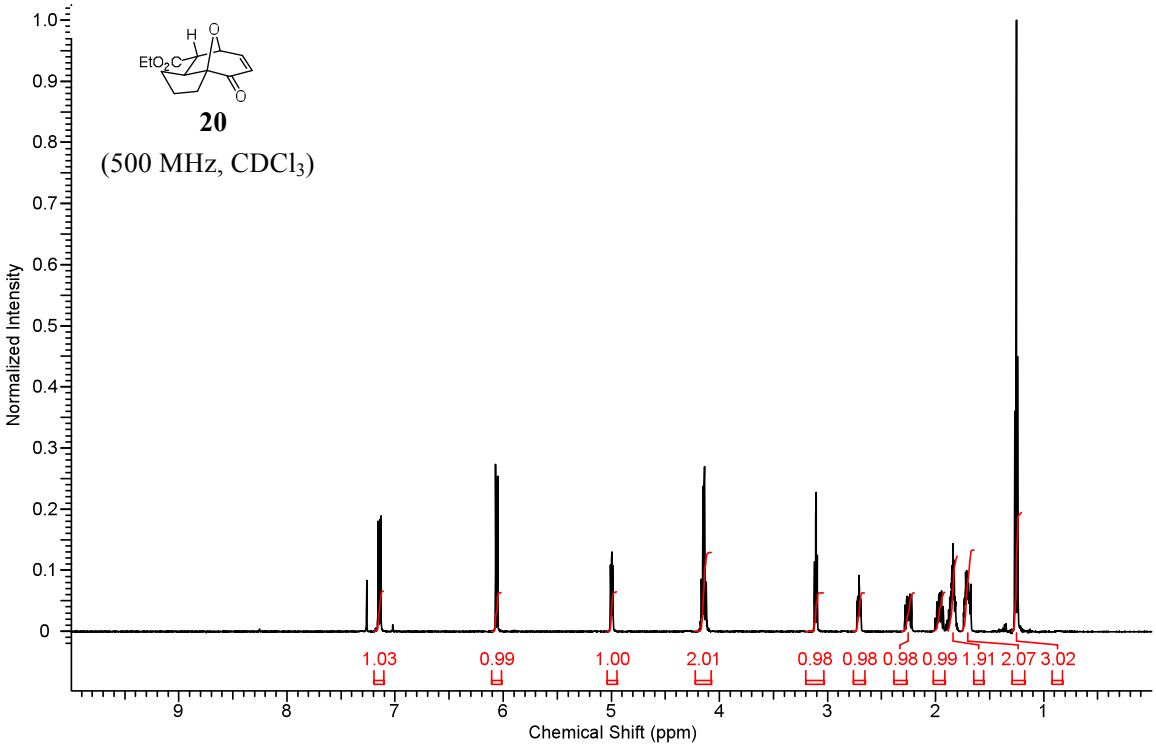
99.28
82.20
50.49
49.76
30.20
27.08


20
(500 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
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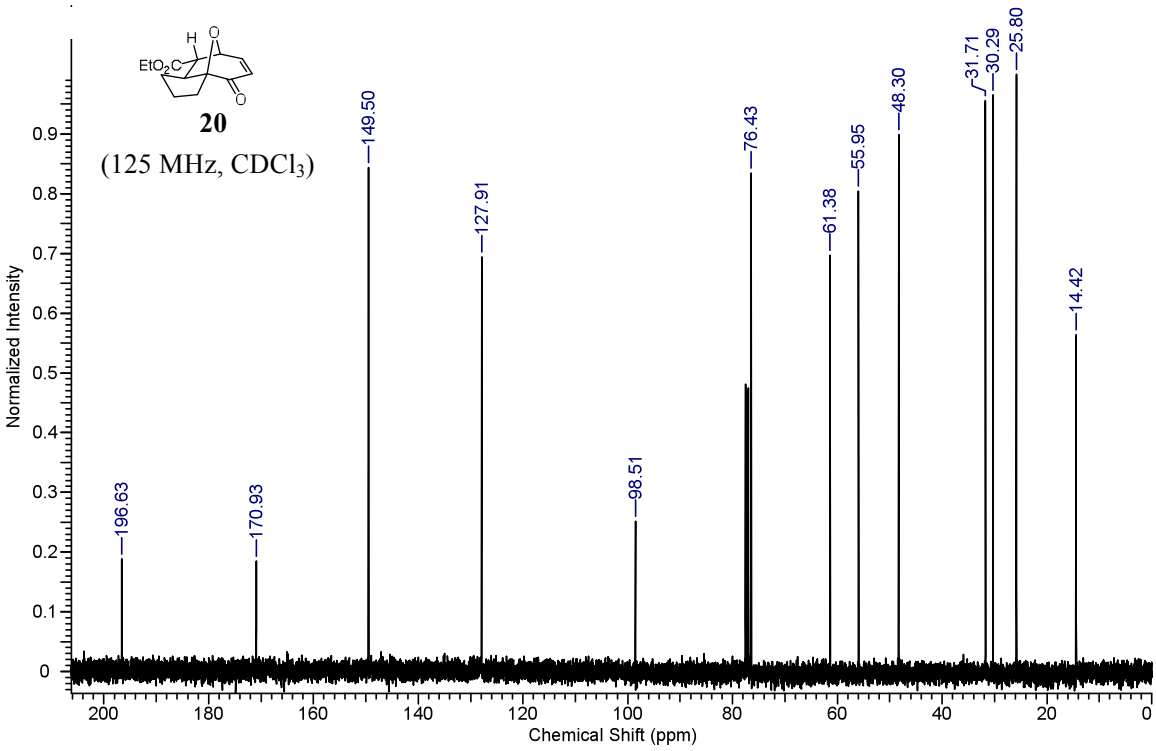
0.99
1.00
2.01
0.98
0.98
0.98
0.99
1.91
2.07
3.02


20
(125 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
196.63
170.93
149.50
127.91
98.51
76.43
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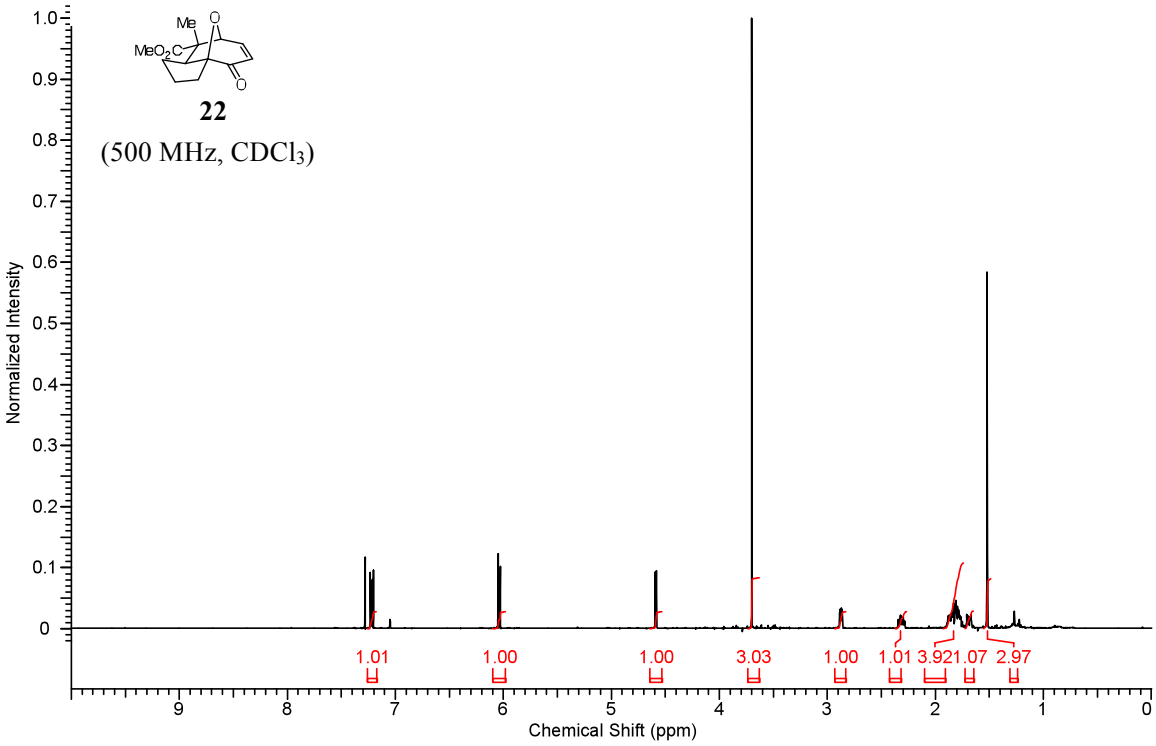
55.95
48.30
31.71
30.29
25.80
14.42


Me
O
MeO2C
O
22
(500 MHz, CDCl3)
Normalized Intensity
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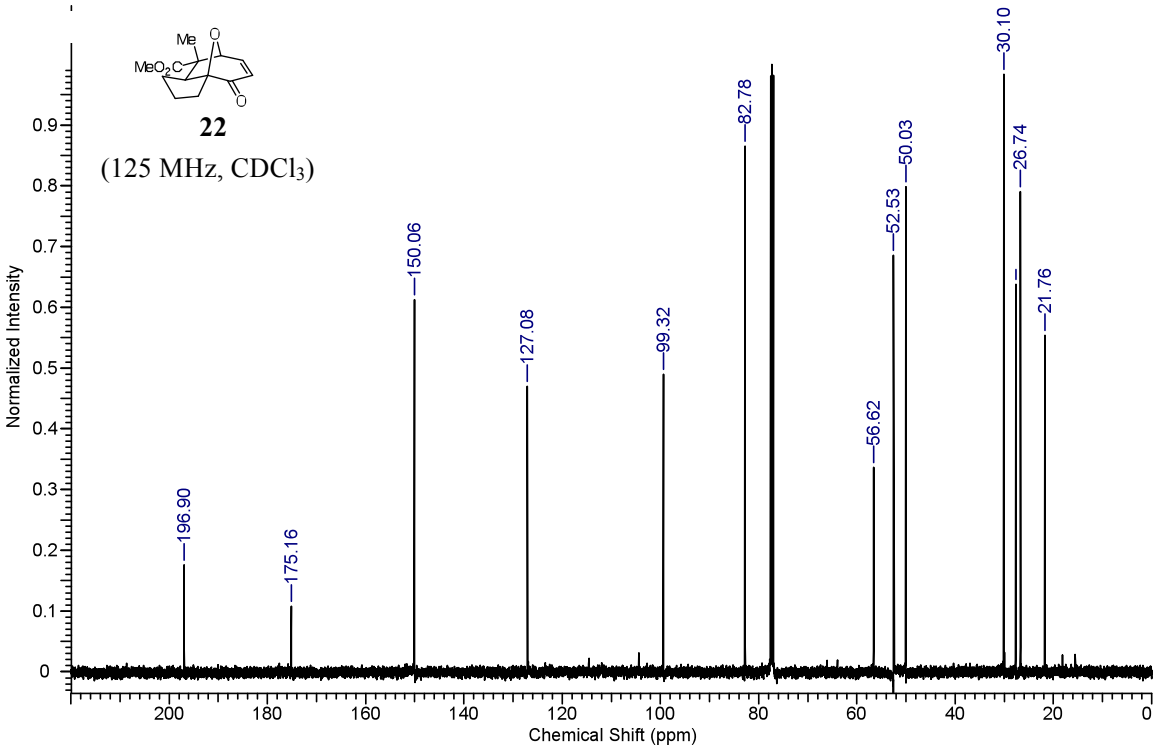
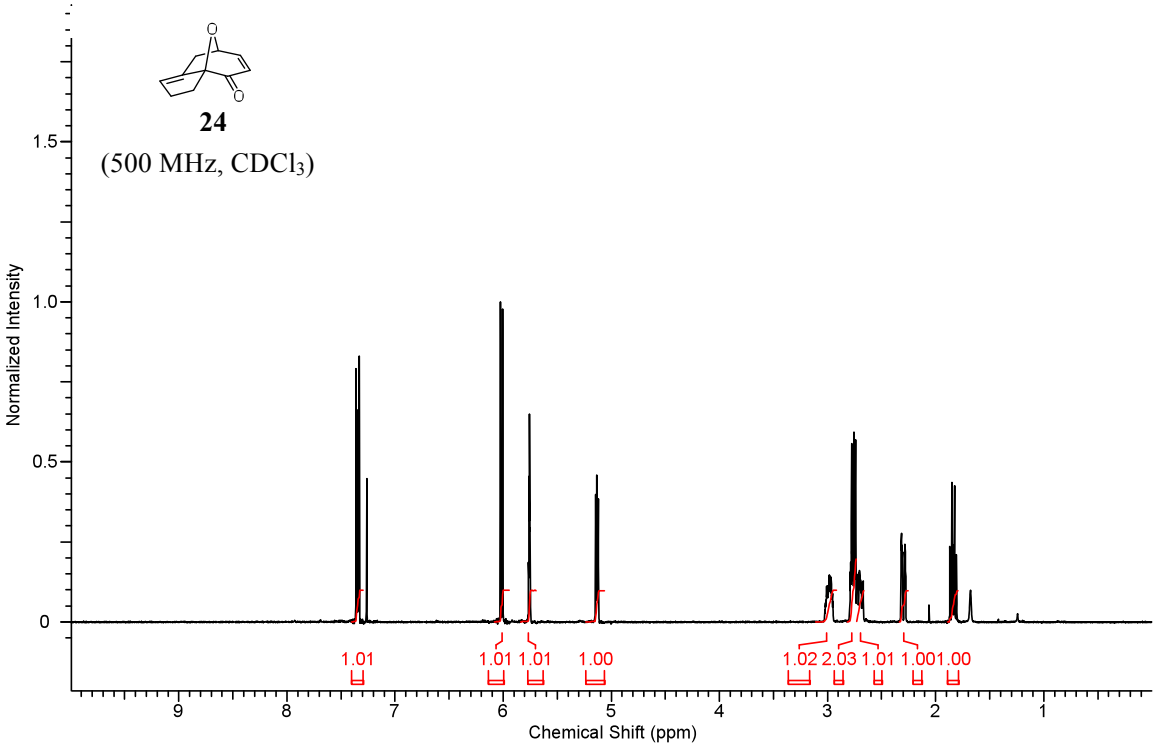
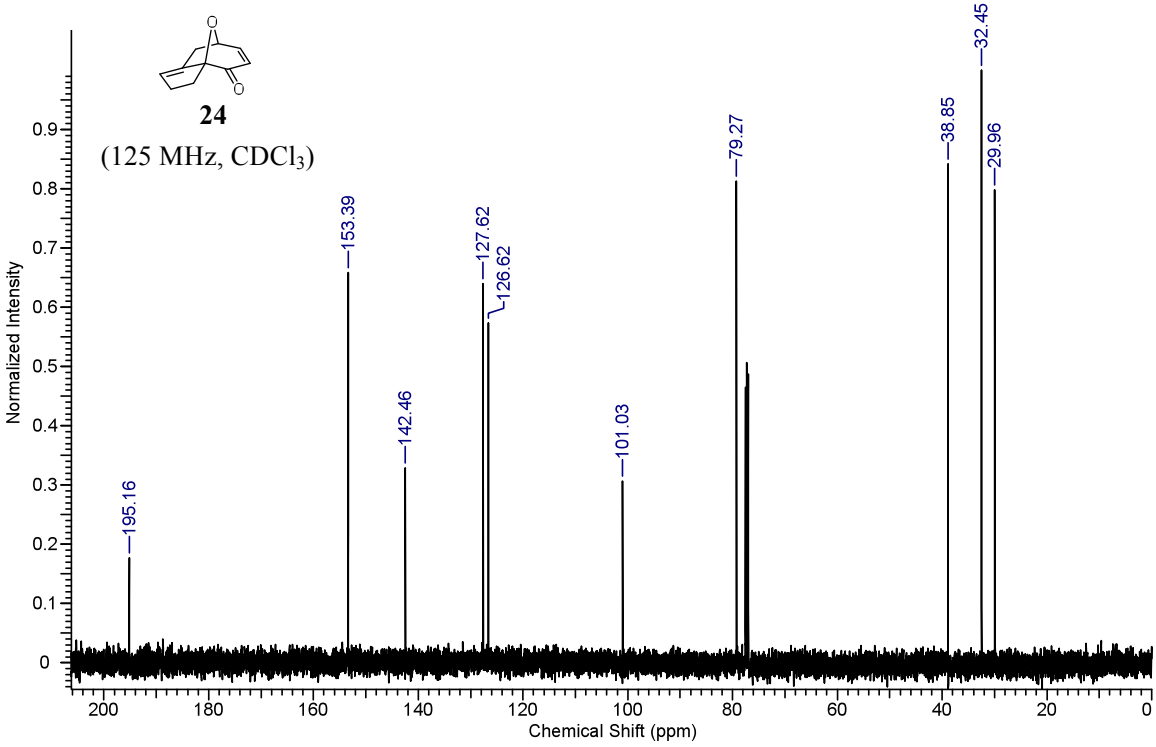
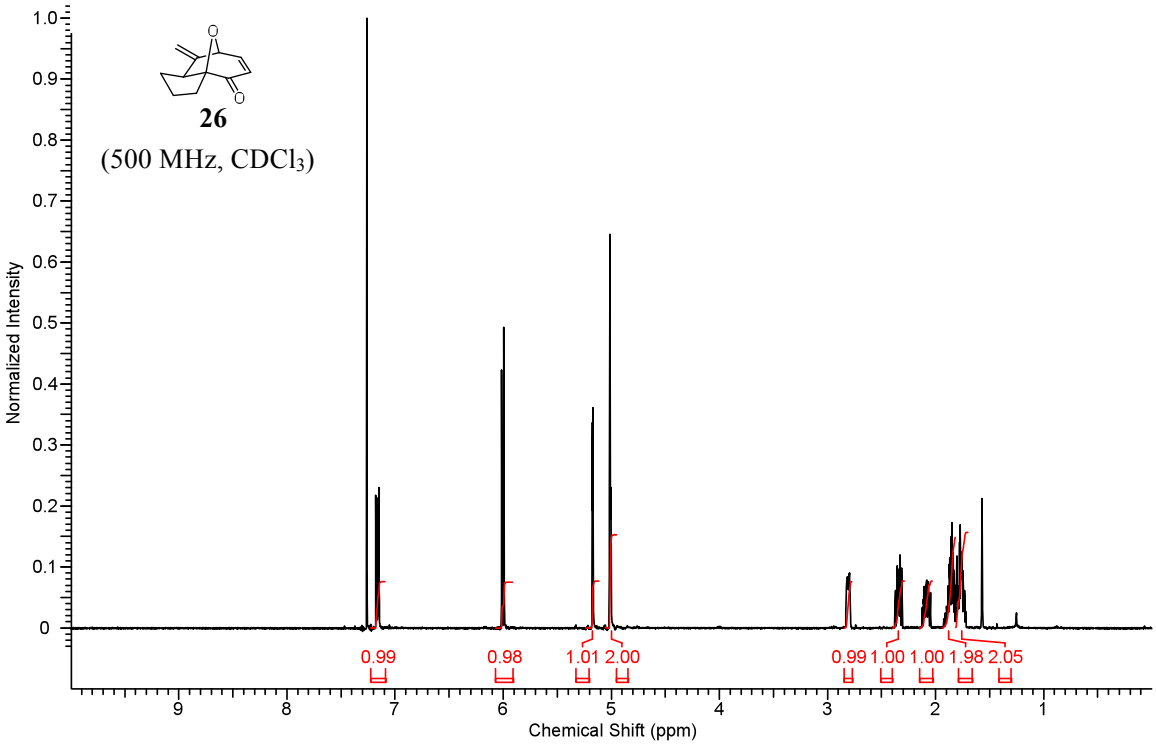
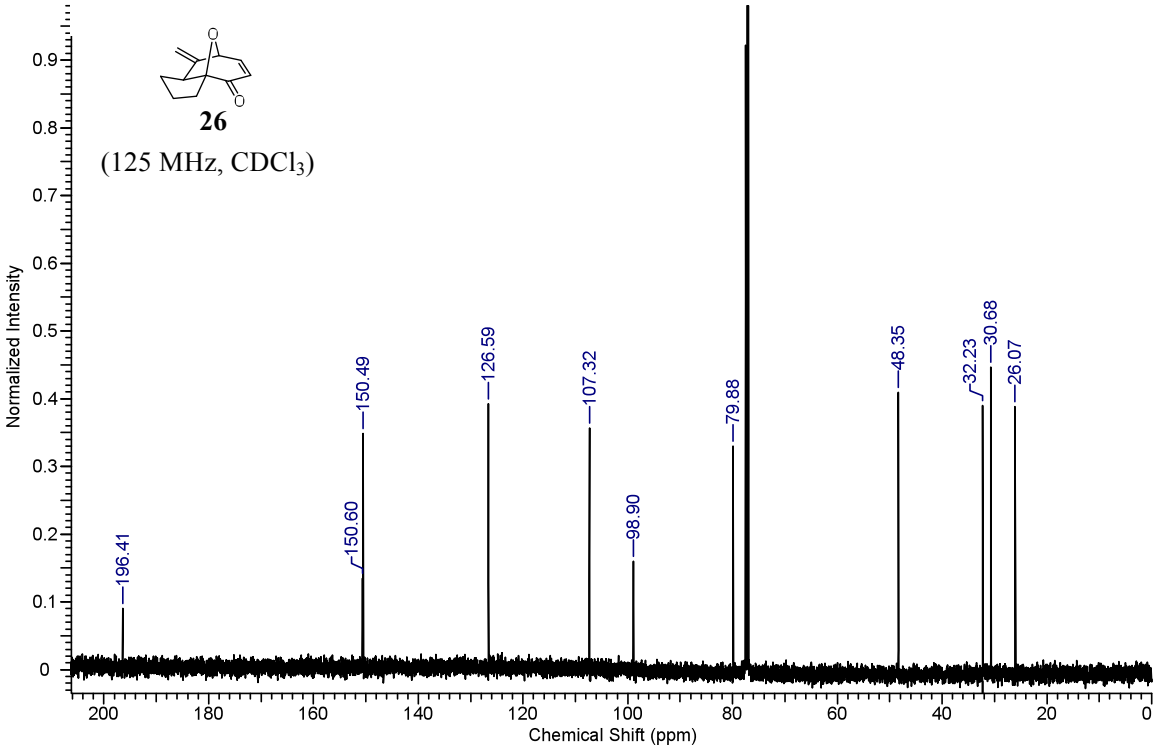
1.00
1.00
3.03
1.00
1.01
3.92
1.07
2.97
Chemical Shift (ppm)

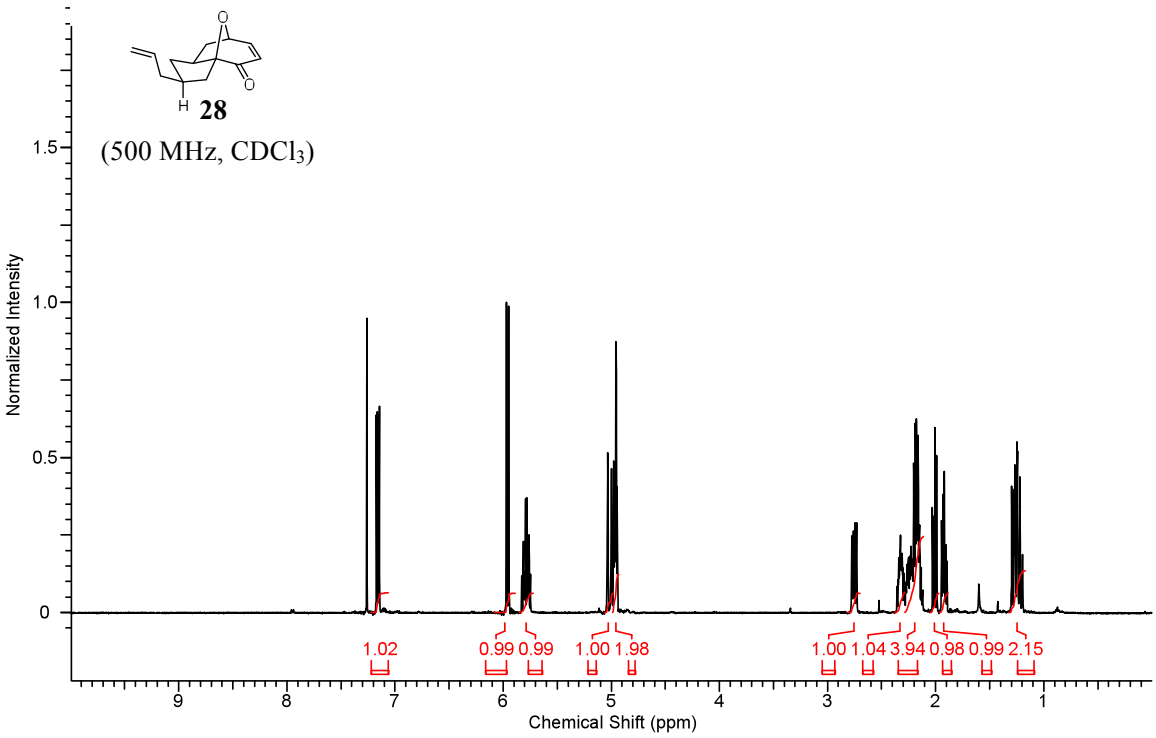

Me
O
MeO2C
O
22
(125 MHz, CDCl3)
Normalized Intensity
196.90
175.16
150.06
127.08
99.32
82.78
56.62
52.53
50.03
30.10
26.74
21.76
Chemical Shift (ppm)

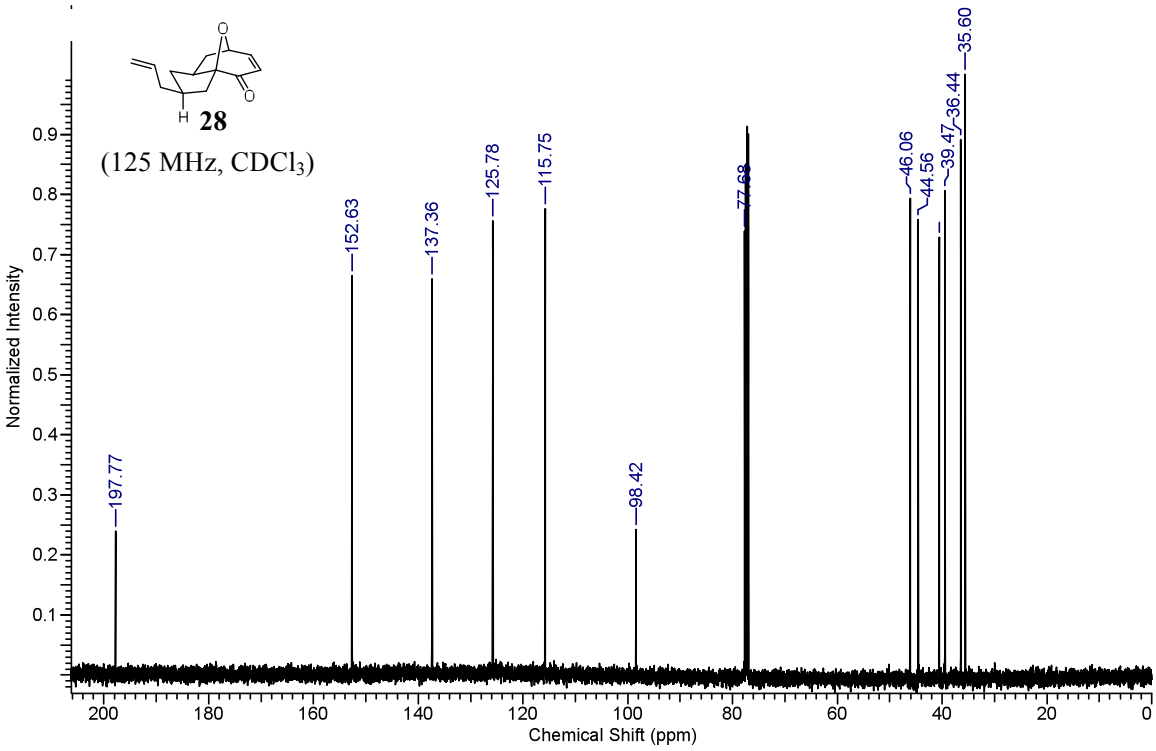

24
(500 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
1.01
1.01
1.01
1.00
1.02
2.03
1.01
1.00
1.00

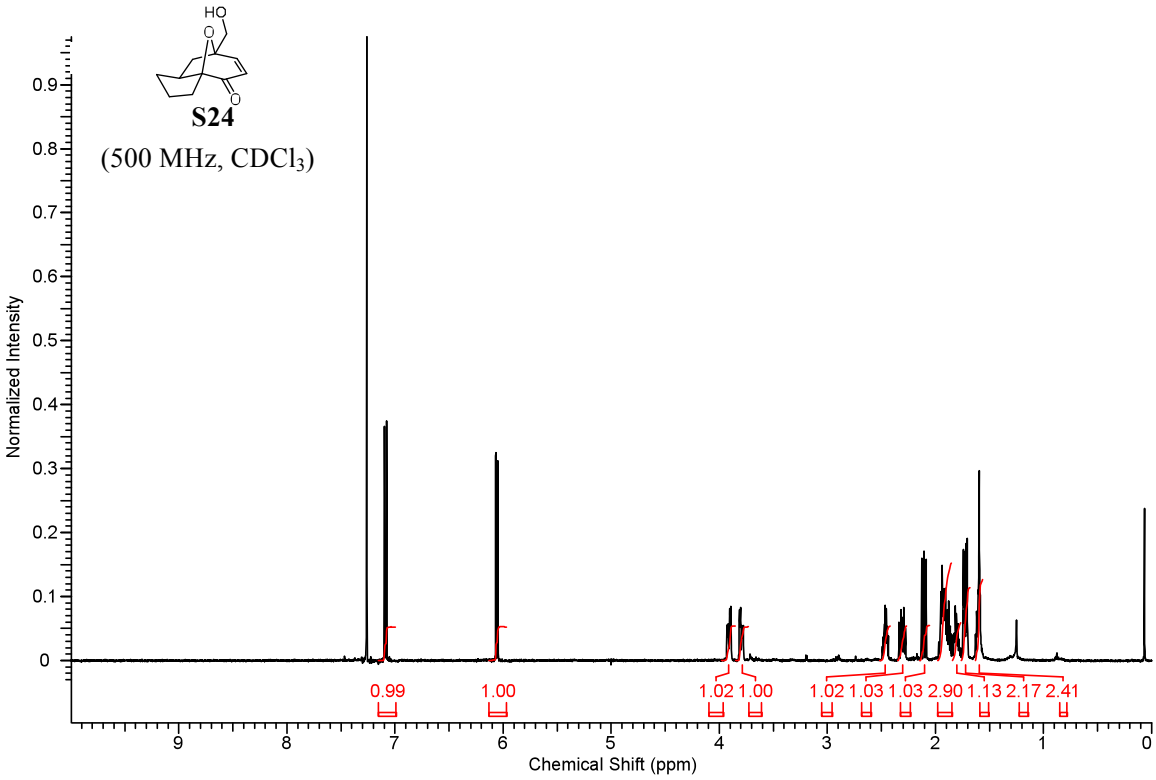

24
(125 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
195.16
153.39
142.46
127.62
126.62
101.03
79.27
38.85
32.45
29.96

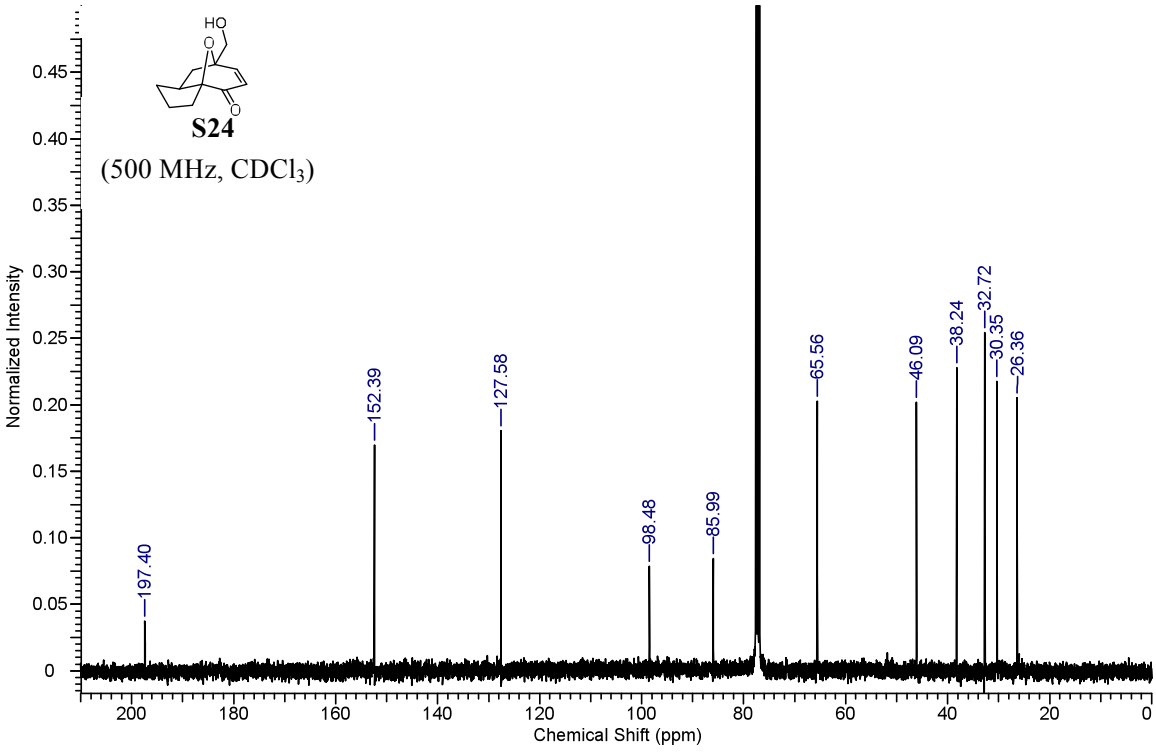

26
(500 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
0.99
0.98
1.01
2.00
0.99
1.00
1.00
1.98
2.05


26
(125 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
196.41
150.60
150.49
126.59
107.32
98.90
79.88
48.35
32.23
30.68
26.07


28
(500 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
1.02
0.99 0.99
1.00 1.98
1.00 1.04 3.94 0.98 0.99 2.15


28
(125 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)
197.77
152.63
137.36
125.78
115.75
98.42
77.68
46.06
44.56
39.47
36.44
35.60

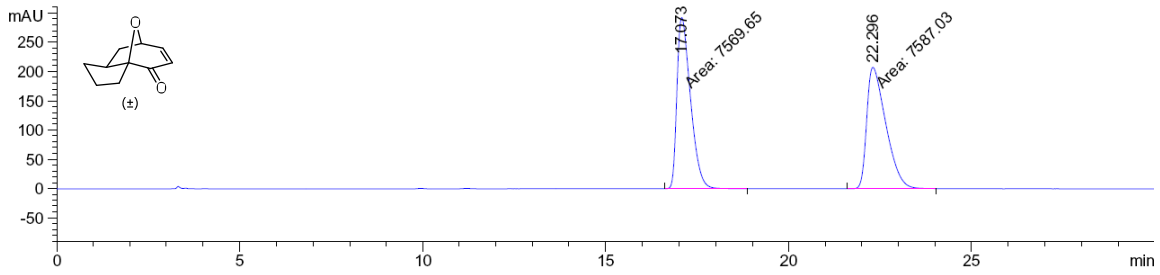

HO
O
O
S24
(500 MHz, CDCl3)
Normalized Intensity
0.99
1.00
1.02 1.00
1.02 1.03 1.03 2.90 1.13 2.17 2.41
Chemical Shift (ppm)


HO
O
O
S24
(500 MHz, CDCl3)
Normalized Intensity
197.40
152.39
127.58
98.48
85.99
65.56
46.09
38.24
32.72
30.35
26.36
Chemical Shift (ppm)

6. Chiral HPLC Traces of Scalemic Cycloaddition Products

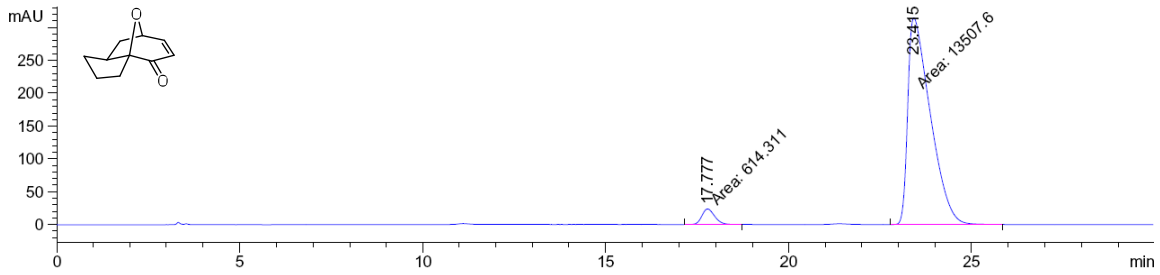
Product 6:

Racemic Sample: HPLC (ChiralPak AS-H, 2% *i*PrOH in hexanes, 1 mL/min, 218 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.073	FM	0.4312	7569.65479	292.55481	49.9427
2	22.296	MM	0.6088	7587.02881	207.70081	50.0573
Totals :				1.51567e4	500.25562	

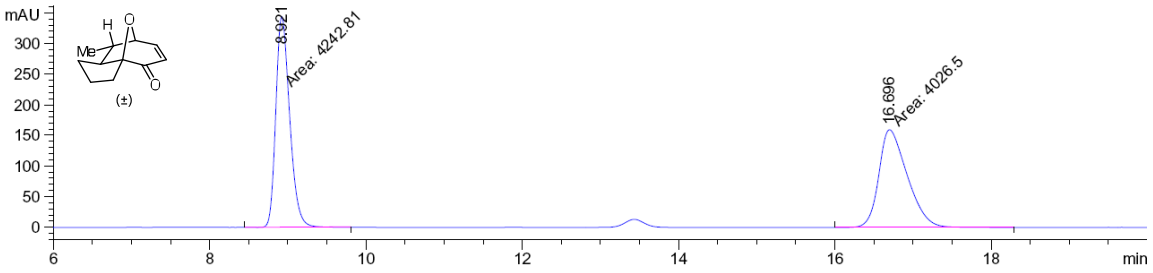
Scalemic Sample: HPLC (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 218 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.777	MF	0.4250	614.31061	24.09299	4.3500
2	23.415	MM	0.7146	1.35076e4	315.05191	95.6500
Totals :				1.41220e4	339.14490	

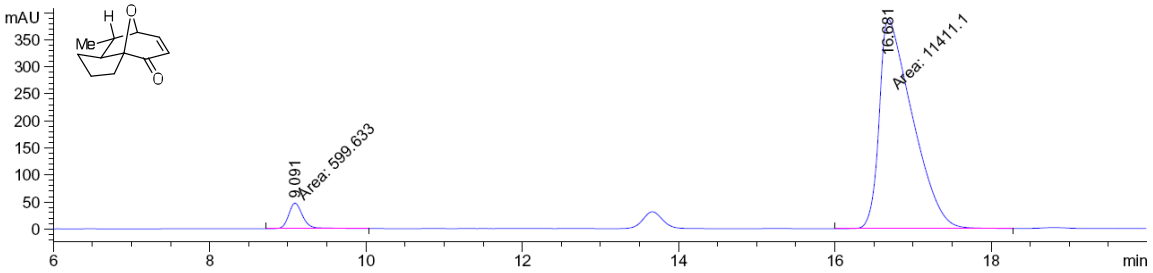
Product 12:

Racemic Sample: HPLC (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 218 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.921	MM	0.2055	4242.81250	344.10196	51.3079
2	16.696	MM	0.4208	4026.49683	159.48712	48.6921
Totals :				8269.30933	503.58908	

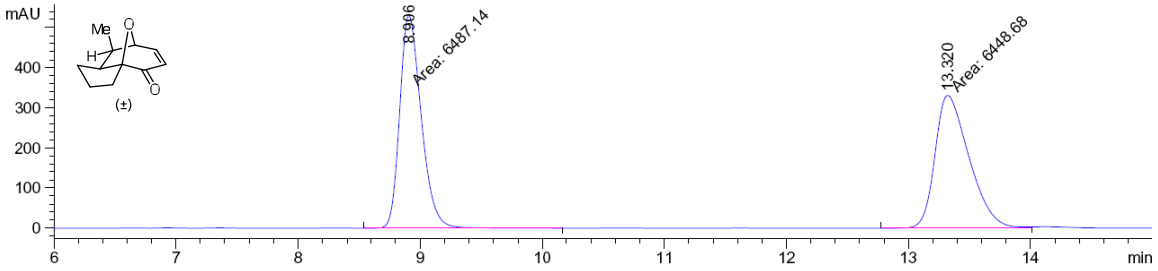
Scalemic Sample: HPLC (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 218 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.091	MM	0.2114	599.63275	47.28025	4.9925
2	16.681	MM	0.4908	1.14111e4	387.47278	95.0075
Totals :				1.20108e4	434.75303	

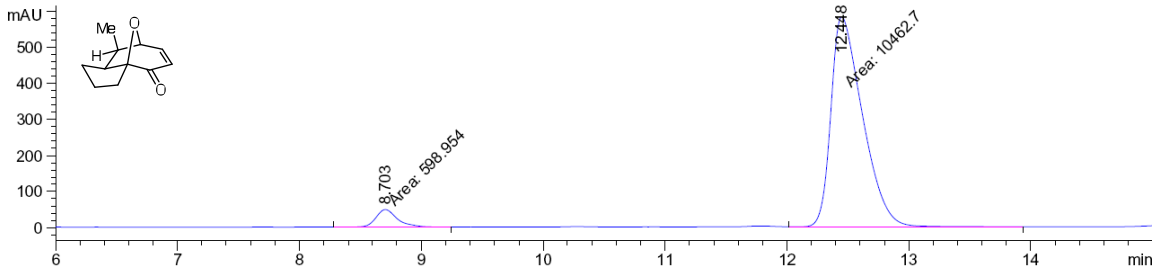
Product 14:

Racemic Sample: HPLC (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 220 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.906	MM	0.2036	6487.13525	531.03607	50.1486
2	13.320	MM	0.3243	6448.67871	331.45233	49.8514
Totals :				1.29358e4	862.48840	

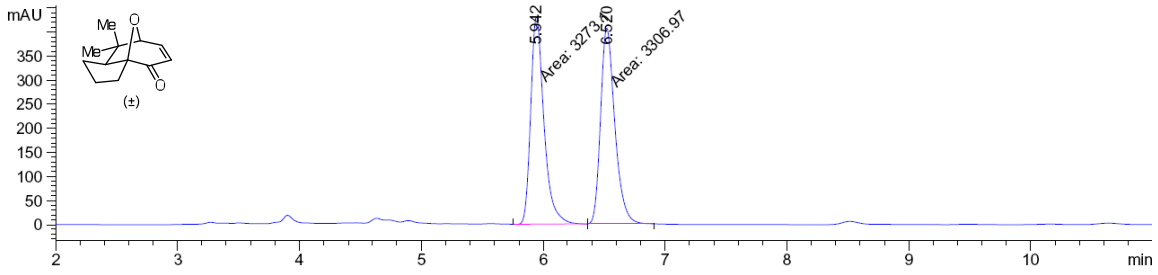
Scalemic Sample: HPLC (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 220 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.703	MM	0.2054	598.95447	48.60786	5.4147
2	12.448	MM	0.2998	1.04627e4	581.72681	94.5853
Totals :				1.10617e4	630.33467	

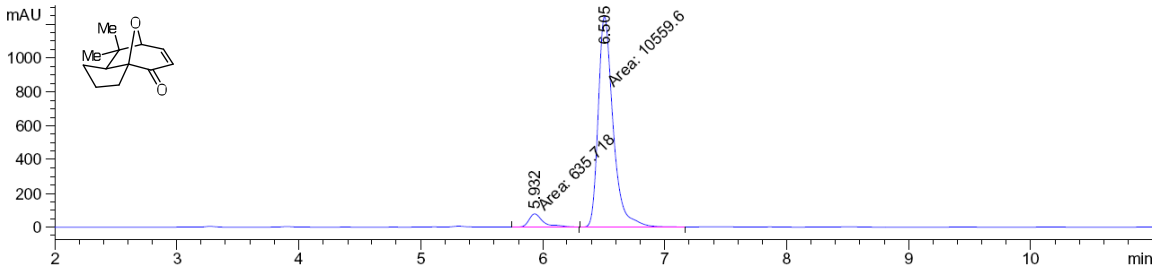
Product 16:

Racemic Sample: HPLC (ChiralPak AD-H, 5% *i*PrOH in hexanes, 1 mL/min, 220 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.942	MM	0.1261	3273.09570	432.44745	49.7426
2	6.520	MM	0.1352	3306.96851	407.52863	50.2574
Totals :				6580.06421	839.97607	

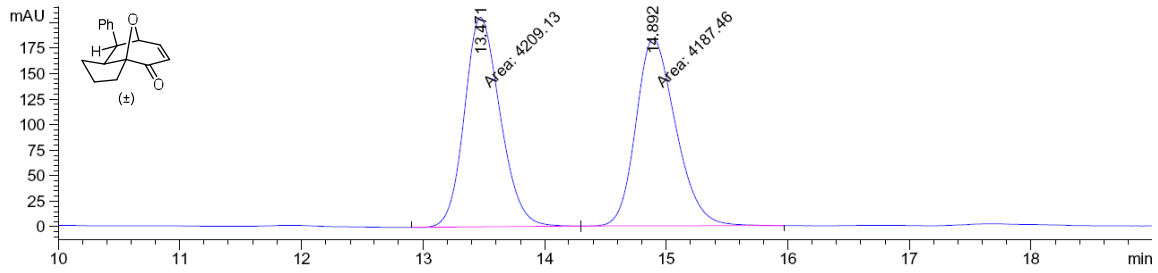
Scalemic Sample: HPLC (ChiralPak AD-H, 5% *i*PrOH in hexanes, 1 mL/min, 220 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.932	MM	0.1354	635.71765	78.24420	5.6784
2	6.505	MM	0.1410	1.05596e4	1247.91870	94.3216
Totals :				1.11953e4	1326.16290	

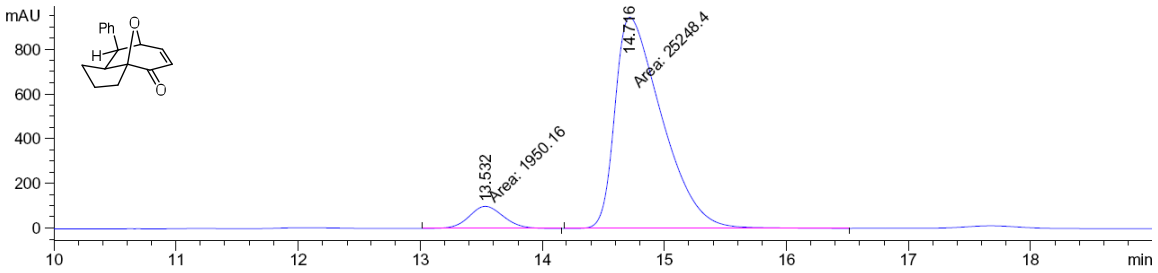
Product 18:

Racemic Sample: HPLC (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 206 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.471	MM	0.3412	4209.13232	205.59442	50.1291
2	14.892	MM	0.3803	4187.45801	183.49408	49.8709
Totals :				8396.59033	389.08850	

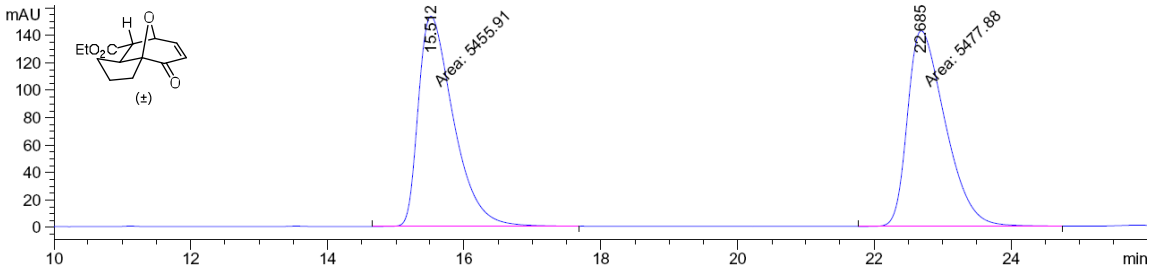
Scalemic Sample: HPLC (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 206 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.532	MM	0.3277	1950.16394	99.17918	7.1701
2	14.716	MM	0.4454	2.52484e4	944.82117	92.8299
Totals :				2.71986e4	1044.00034	

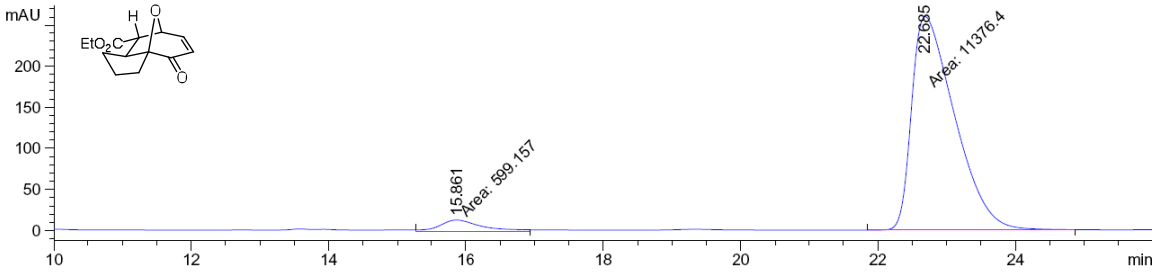
Product 20:

Racemic Sample: HPLC (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 220 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.512	MM	0.5941	5455.90674	153.05791	49.8995
2	22.685	MM	0.6407	5477.88477	142.50661	50.1005
Totals :				1.09338e4	295.56451	

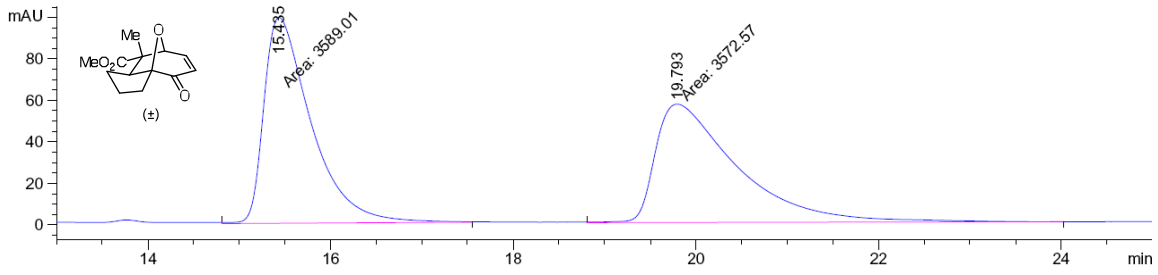
Scalemic Sample: HPLC (ChiralPak AS-H, 5% *i*PrOH in hexanes, 1 mL/min, 220 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.861	MM	0.7236	599.15741	13.79980	5.0032
2	22.685	MF	0.7292	1.13764e4	260.01758	94.9968
Totals :				1.19756e4	273.81738	

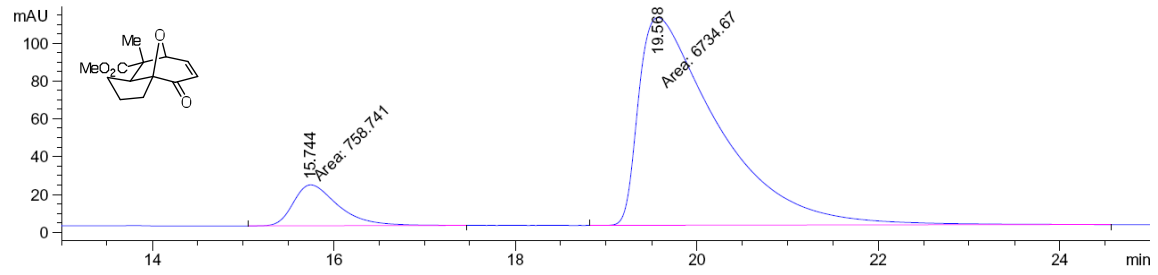
Product 22:

Racemic Sample: HPLC (ChiralCel OC-H, 5% *i*PrOH in hexanes, 1 mL/min, 218 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.435	MM	0.6012	3589.01318	99.49255	50.1148
2	19.793	MM	1.0417	3572.57397	57.16205	49.8852
Totals :				7161.58716	156.65461	

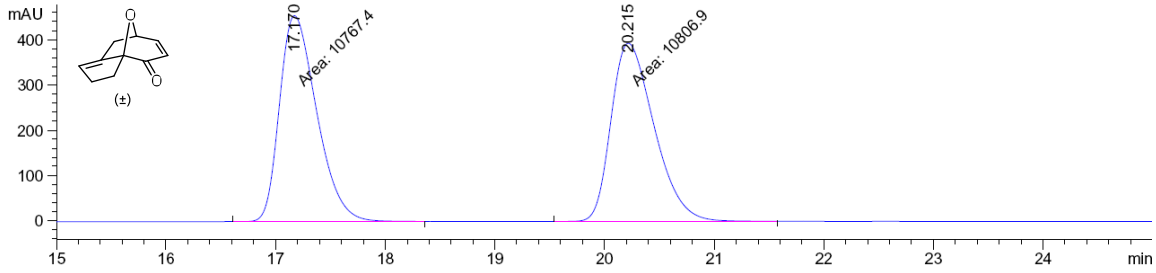
Scalemic Sample: HPLC (ChiralCel OC-H, 5% *i*PrOH in hexanes, 1 mL/min, 218 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.744	MM	0.5826	758.74078	21.70474	10.1254
2	19.568	MM	1.0214	6734.67383	109.89091	89.8746
Totals :				7493.41461	131.59565	

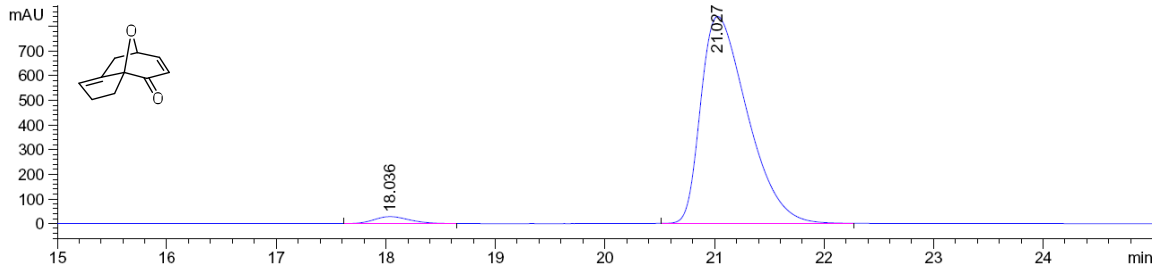
Product 24:

Racemic Sample: HPLC (ChiralPak AS-H, 3% *i*PrOH in hexanes, 1 mL/min, 218 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.170	MM	0.3940	1.07674e4	455.45624	49.9084
2	20.215	MM	0.4568	1.08069e4	394.27094	50.0916
Totals :				2.15743e4	849.72717	

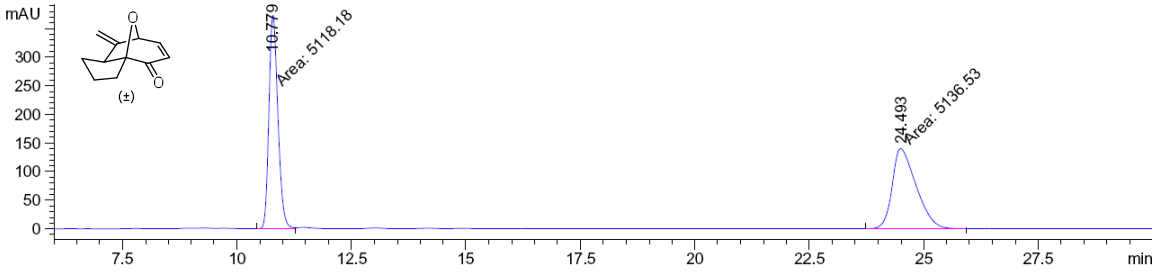
Scalemic Sample: HPLC (ChiralPak AS-H, 3% *i*PrOH in hexanes, 1 mL/min, 218 nm)



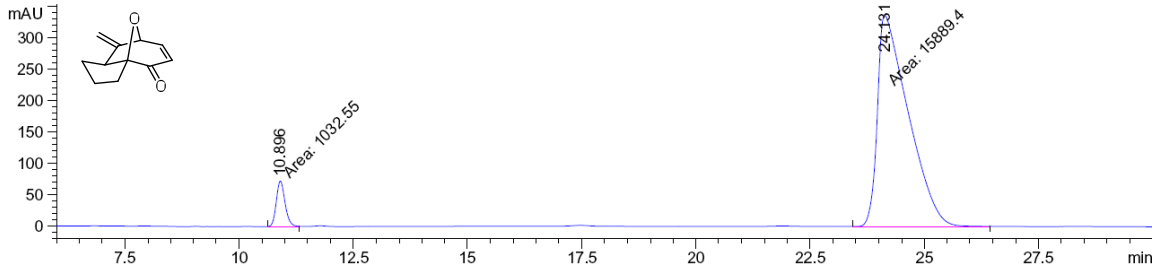
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.036	BB	0.3499	639.62170	28.27456	2.5116
2	21.027	BB	0.4565	2.48274e4	840.79065	97.4884
Totals :				2.54670e4	869.06521	

Product 26:

Racemic Sample: HPLC (ChiralPak AS-H, 10% *i*PrOH in hexanes, 1 mL/min, 222 nm)



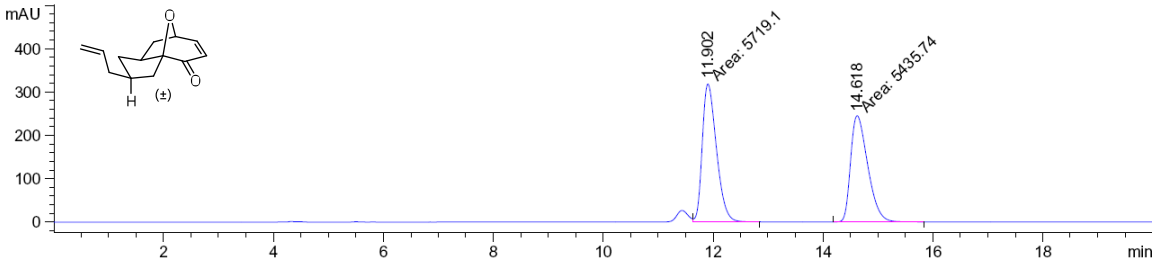
Scalemic Sample: HPLC (ChiralPak AS-H, 10% *i*PrOH in hexanes, 1 mL/min, 222 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.896	MM	0.2320	1032.54687	74.16464	6.1018
2	24.131	MM	0.7856	1.58894e4	337.10806	93.8982
Totals :				1.69219e4	411.27271	

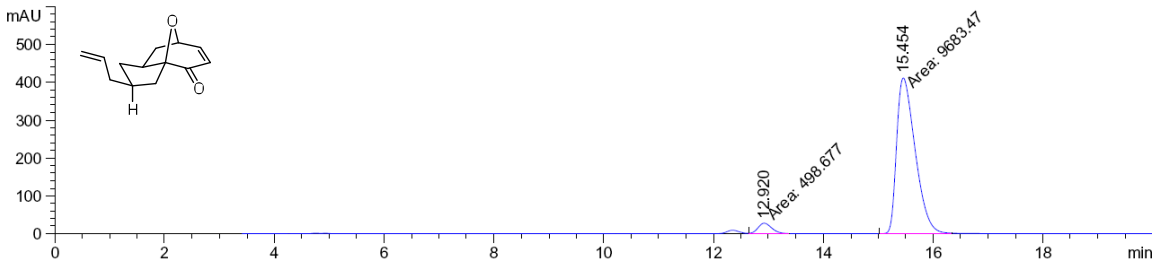
Product 28:

Racemic Sample: HPLC (ChiralPak AS-H, 4% *i*PrOH in hexanes, 1 mL/min, 230 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.902	FM	0.2993	5719.10449	318.44421	51.2702
2	14.618	MM	0.3676	5435.73584	246.45261	48.7298
Totals :				1.11548e4	564.89682	

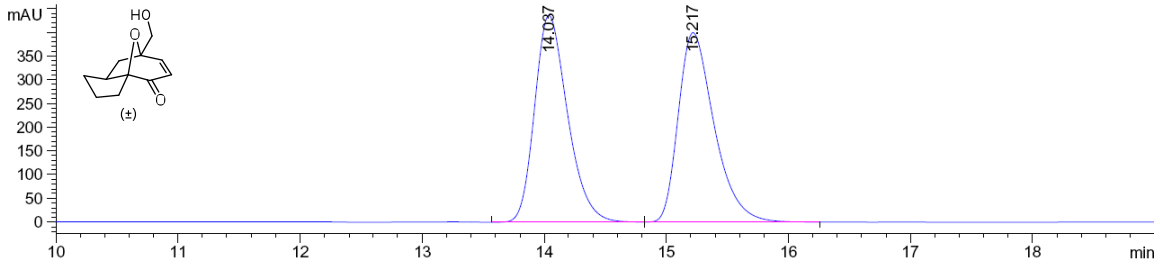
Scalemic Sample: HPLC (ChiralPak AS-H, 4% *i*PrOH in hexanes, 1 mL/min, 230 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.920	MF	0.2964	498.67682	28.03735	4.8976
2	15.454	MF	0.3918	9683.47363	411.96115	95.1024
Totals :				1.01822e4	439.99850	

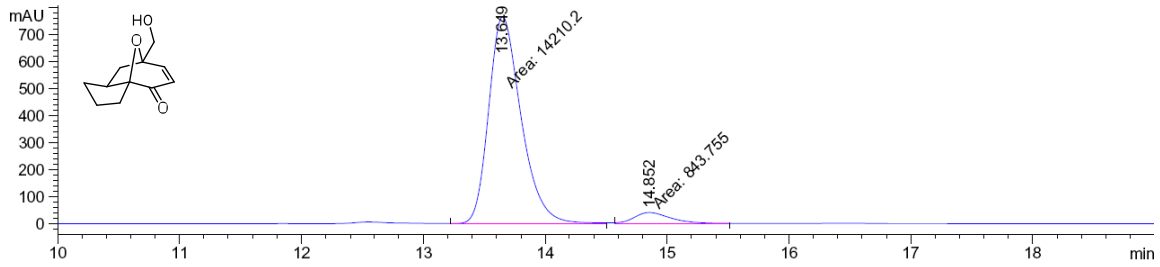
Free alcohol of 30 (S24):

Racemic Sample: HPLC (ChiralPak AD-H, 10% *i*PrOH in hexanes, 1 mL/min, 210 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.037	VV	0.2867	8164.34863	435.62924	49.9921
2	15.217	VB	0.3126	8166.91992	399.32007	50.0079
Totals :				1.63313e4	834.94931	

Scalemic Sample: HPLC (ChiralPak AD-H, 10% *i*PrOH in hexanes, 1 mL/min, 210 nm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.649	MM	0.3085	1.42102e4	767.58899	94.3951
2	14.852	MF	0.3448	843.75458	40.78906	5.6049
Totals :				1.50540e4	808.37805	

7. Computational Procedures and Results

Calculations were performed at Harvard University using Gaussian 09[18] at the B3LYP[19] level of density functional theory with the 6-31G(d)[20] basis set. Transition structures were fully optimized and verified to be first-order saddle points by frequency calculations showing the existence of a single imaginary frequency. Relative energies between diastereomeric transition structures are for uncorrected electronic energy differences. Figures were generated using CYLview.[21]

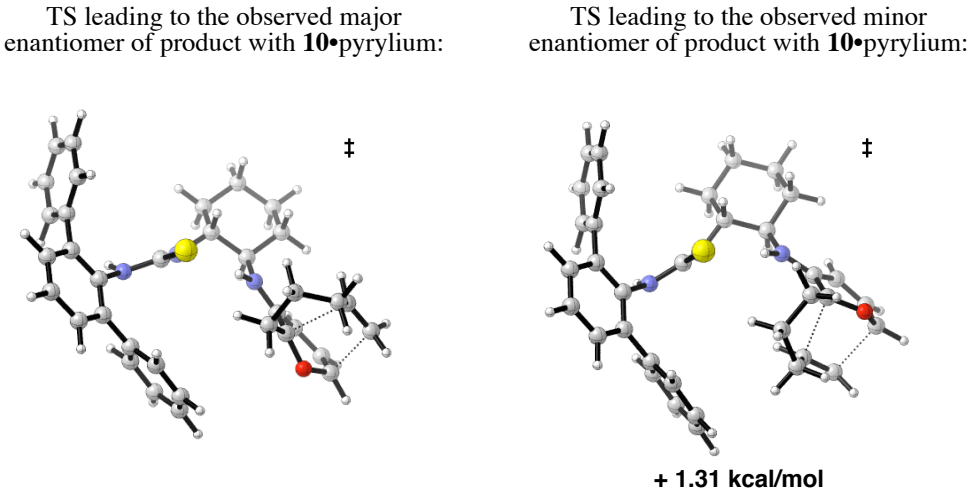


Figure S1. Two lowest-energy diastereomeric transition structures for **10**•pyrylium.

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[18] Gaussian 09, Revision A.1, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

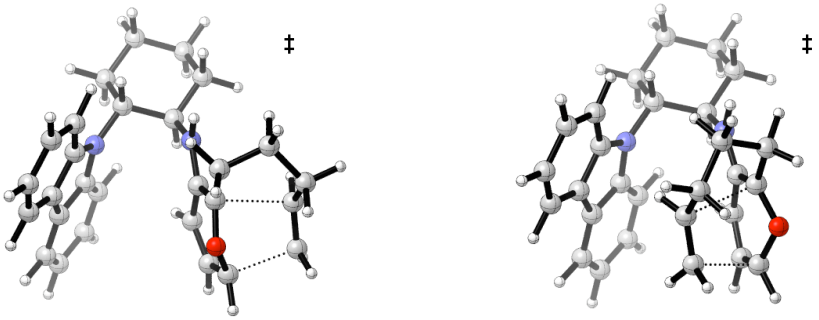
[19] B3LYP = Becke-3-Lee-Yang-Parr density functional theor: (a) Becke, A. D. *J. Chem. Phys.* **1993***, 98*, 1372–1377. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785–789.

[20] (a) Ditchfield, R.; Hehre, W. J.; Pople, J. A. *J. Chem. Phys.* **1971***, 54*, 724–728. (b) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys*. **1972,** *56*, 2257–2261. (c) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta.* **1973***, 28*, 213–223.

[21] CYLview, 1.0b; Legault, C. Y., Université de Sherbrooke, 2009; http://www.cylview.org.

TS leading to the observed minor enantiomer of product with **32**•pyrylium:

TS leading to the observed major enantiomer of product with **32**•pyrylium:



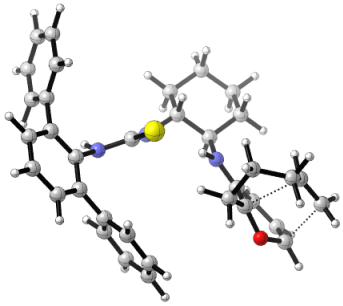
+ 1.33 kcal/mol

Figure S2. Two lowest-energy diastereomeric transition structures for **32**•pyrylium.

While the origin of selectivity for each catalyst is not yet fully understood some speculation is possible based on the structures shown in Figures S1 and S2. The two lowest energy transition structures of **10**•pyrylium both contain an interaction between the N–H of the pyrylium and the sulfur of the thiourea (H–S distance = 2.34 Å and 2.39 Å for the structures leading to the major and minor enantiomers, respectively). This may serve to rigidify the structure and control the orientation of the aminopyrylium with respect to the cyclohexyl unit. The tethered alkene may then approach the pyrylium on the more exposed outer face as in the structure leading to the major enantiomer or on the inner face as in the structure leading to the minor enantiomer. It is possible that the *ortho*-phenyl substituent on the *S*-phenyl of the thiourea serves to block this inner face of the pyrylium and thus raises the energy of cycloaddition on this face due to destabilizing steric interactions.

In each of the two lowest energy transition structures for **32**•pyrylium the carbazole and the pyrylium are both essentially perpendicular to the cyclohexane plane. In contrast to the case with **10**•pyrylium, approach of the alkene to the more exposed outer face now leads to the observed minor enantiomer of product, and it is a structure wherein cycloaddition occurs onto the inner face which is lower in energy and leads to the observed major enantiomer of product. This inner face is in closer proximity to the carbazole and it is possible that this heterocycle engages in a stabilizing cation-π interaction with alkene dipolarophile as it becomes more positively charged in the transition state. Such an interaction is absent from the transition structure leading to the minor enantiomer of product.

Transition structure leading to the observed major enantiomer of product with **10**•pyrylium:



E(RB+HF–LYP): –1994.03711612
Zero-point correction= 0.661700 (Hartree/Particle)
Thermal correction to Energy= 0.696396
Thermal correction to Enthalpy= 0.697340
Thermal correction to Gibbs Free Energy= 0.591999

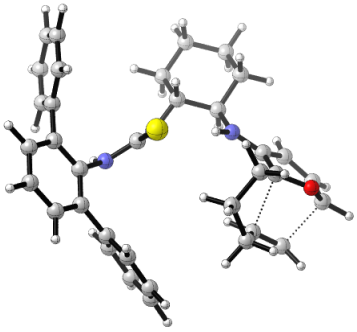
Cartesian coordinates:

C	2.42811600	3.51378200	-0.12486000
C	1.61112100	2.32480800	-0.67184800
C	0.10634300	2.53168400	-0.37176500
C	-0.37782100	3.86957800	-0.95937400
C	0.45222100	5.05848000	-0.45474100
C	1.94855300	4.84665500	-0.71740600
H	1.72586600	2.27421400	-1.76445700
H	2.32110000	3.53012100	0.96829800
H	3.49421600	3.36268700	-0.33367400
H	-0.31813200	3.82350700	-2.05813900
H	-1.43480700	4.00014200	-0.70229300
H	0.10538000	5.97929700	-0.93617000
H	0.28409600	5.18632600	0.62327000
H	2.13860700	4.85732000	-1.80038200
H	2.53217700	5.67012400	-0.29140800
H	-0.02583000	2.54383400	0.71522200
N	-0.72363200	1.44013700	-0.87942100
C	-1.27302400	0.43976300	-0.12818900
N	-2.29805700	-0.20979800	-0.74459900
C	-3.04072900	-1.30163900	-0.17605300
C	-4.30264500	-1.02756900	0.38418800
C	-2.50463600	-2.60410400	-0.18642100
C	-5.01415700	-2.07459500	0.98192600

C	-3.24697500	-3.62181800	0.43174100
C	-4.48395000	-3.36208000	1.01529100
H	-5.98928000	-1.86965200	1.41351600
H	-2.85506800	-4.63433500	0.42180900
H	-5.04471100	-4.16890700	1.47805000
H	-1.08714800	1.56566700	-1.81812400
H	-2.78717100	0.31552900	-1.46152900
N	2.05236700	1.04438200	-0.09750800
C	3.18365600	0.39689200	-0.41378300
C	4.07124100	0.84130600	-1.44526200
C	3.58053100	-0.77799000	0.31115600
H	3.79901800	1.67907700	-2.07481200
C	5.62621900	-0.85485000	-0.74495000
H	6.45469900	-1.51334500	-0.97892400
C	5.29883200	0.24969400	-1.57239800
H	6.04486300	0.63428200	-2.26057500
O	4.59253400	-1.52633000	-0.18467700
S	-0.70899400	0.03920000	1.41773500
H	1.38646100	0.60810400	0.55581600
C	-4.88329300	0.34858400	0.35151900
C	-5.32321600	0.91079700	-0.85811500
C	-5.02352200	1.09248700	1.53148000
C	-5.88368100	2.18875700	-0.88824200
H	-5.26448800	0.32502300	-1.77399700
C	-5.58454300	2.37043800	1.50102700
H	-4.68365600	0.66725600	2.47145900
C	-6.01337900	2.92259400	0.29265300
H	-6.23411400	2.60319100	-1.82973000
H	-5.68881500	2.93384100	2.42421800
H	-6.45575900	3.91462300	0.27239200
C	-1.20521900	-2.94809000	-0.82800600
C	-0.92200600	-2.58791500	-2.15571700
C	-0.25974900	-3.71820000	-0.13127800
C	0.26868100	-2.98154100	-2.76547000
H	-1.65475100	-2.02304100	-2.72391700
C	0.93098700	-4.11481200	-0.74160700
H	-0.46272000	-4.00286100	0.89728700
C	1.20127800	-3.74589000	-2.06069000
H	0.45822500	-2.70951200	-3.80061000
H	1.64167000	-4.72403900	-0.18883600
H	2.12163400	-4.06612400	-2.54163100

C	2.76982300	-1.48332700	1.35245100
H	1.69732500	-1.45312200	1.13387900
H	3.08021000	-2.53242800	1.34727500
C	3.06985000	-0.85029900	2.73690400
H	2.51979200	0.09371400	2.83440700
H	2.71317300	-1.50762000	3.53612400
C	4.57794800	-0.58861600	2.84486800
H	4.80390800	-0.12012900	3.81371700
H	5.13346200	-1.53463800	2.81785300
C	5.06441300	0.32414900	1.74445700
C	6.25837300	0.13551900	1.04783100
H	6.76713300	0.98903800	0.61138200
H	6.91002300	-0.68514000	1.34156200
H	4.60844100	1.31257900	1.71813400

Transition structure leading to the observed minor enantiomer of product with **10**•pyrylium:



E(RB+HF–LYP): –1994.03502204

Zero-point correction= 0.662040 (Hartree/Particle)

Thermal correction to Energy= 0.696602

Thermal correction to Enthalpy= 0.697546

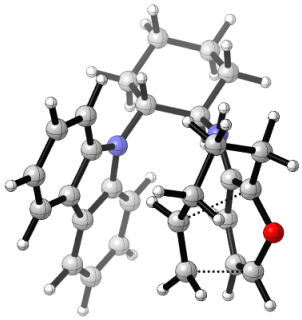
Thermal correction to Gibbs Free Energy= 0.593406

Cartesian coordinates:

C	-1.93555900	4.09210000	-0.18219800
C	-1.52336800	2.71653900	0.38743400
C	0.01822800	2.60495400	0.39617700
C	0.63849000	3.75597200	1.20948200
C	0.19799000	5.13256000	0.69232800
C	-1.33044200	5.24355300	0.63288100
H	-1.87624800	2.62385200	1.42510100
H	-1.59025100	4.14722400	-1.22346400
H	-3.02741000	4.17809100	-0.21589500
H	0.34331500	3.65093900	2.26554600
H	1.72967700	3.65989600	1.16849200
H	0.61550000	5.91683200	1.33326800
H	0.61585700	5.29229700	-0.31083200
H	-1.74208600	5.22930300	1.65262300
H	-1.62727700	6.20134900	0.19170300
H	0.36609700	2.67146500	-0.64005600
N	0.49988700	1.32165100	0.91925800
C	1.07280700	0.34949400	0.14080100
N	1.92120700	-0.47570200	0.81035100
C	2.80424400	-1.42121100	0.17267200
C	4.01720100	-0.94084700	-0.36144400
C	2.44483200	-2.77927800	0.08589900
C	4.85517600	-1.83858500	-1.03346700
C	3.31804900	-3.64494200	-0.59327200
C	4.50336100	-3.18086100	-1.15451500
H	5.79308800	-1.47740500	-1.44443500
H	3.06755900	-4.69949700	-0.65377500
H	5.16548500	-3.87142600	-1.66866700
H	0.80848000	1.36021700	1.88566300
H	2.21756000	-0.15760700	1.72638700
N	-2.09853400	1.61006000	-0.39386400
C	-3.38413500	1.22890500	-0.35815300
C	-4.34107200	1.83320600	0.51825000
C	-3.86225800	0.15106900	-1.18178000
H	-4.05852100	2.67256100	1.13998700
C	-5.94918500	0.19717600	-0.20217100
H	-6.98250400	-0.09511200	-0.34811000
C	-5.58815600	1.27989200	0.63501300
H	-6.29386800	1.62787000	1.38252900
O	-5.20604100	0.00416300	-1.31299300

S	0.71423700	0.17337600	-1.50373500
H	-1.43143700	1.10491600	-0.99136300
C	4.42019000	0.49035000	-0.23103800
C	4.65242200	1.06467400	1.02944500
C	4.60869300	1.28123400	-1.37382000
C	5.04990000	2.39713000	1.14600200
H	4.56561200	0.45021400	1.92381000
C	5.00578400	2.61433900	-1.25845200
H	4.42684400	0.84963000	-2.35369900
C	5.22367800	3.17754500	0.00010300
H	5.24567400	2.81875400	2.12841100
H	5.14706300	3.21235700	-2.15449200
H	5.54149800	4.21272700	0.08797400
C	1.20095600	-3.34188700	0.68058700
C	0.84192100	-3.09878900	2.01672100
C	0.39966200	-4.21562100	-0.07312100
C	-0.27831100	-3.70799900	2.58097400
H	1.46835500	-2.46117600	2.63311000
C	-0.71703500	-4.83293300	0.49245900
H	0.65833200	-4.41222600	-1.10967100
C	-1.06171000	-4.58053200	1.82216400
H	-0.52401000	-3.52245700	3.62325500
H	-1.30837100	-5.52348000	-0.10348700
H	-1.92120400	-5.07294000	2.26883700
C	-3.09602400	-0.53722200	-2.27075800
H	-3.80661400	-0.74586600	-3.07699800
H	-2.30750500	0.10234400	-2.68100000
C	-2.49636500	-1.86681100	-1.73383800
H	-1.54405600	-1.65955000	-1.23439200
H	-2.27444700	-2.54022500	-2.56781400
C	-3.47863700	-2.49747100	-0.74229700
H	-3.02413900	-3.39844400	-0.30785900
H	-4.40051600	-2.81358400	-1.24716900
C	-3.81304200	-1.54547200	0.38052500
C	-5.08929800	-1.43993400	0.93220600
H	-5.21414500	-1.06927700	1.94452400
H	-5.86540600	-2.12328300	0.59366700
H	-2.96728000	-1.18046400	0.96098200

Transition structure leading to the observed major enantiomer of product with **32**•pyrylium:



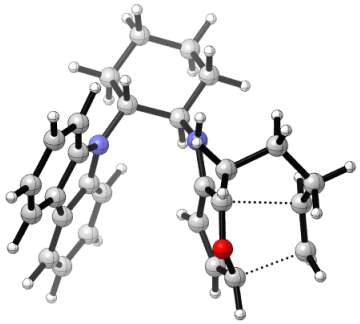
E(RB+HF–LYP): –1270.12693678
Zero-point correction= 0.535358 (Hartree/Particle)
Thermal correction to Energy= 0.560440
Thermal correction to Enthalpy= 0.561384
Thermal correction to Gibbs Free Energy= 0.481163

Cartesian coordinates:

C	2.25419200	-3.15363000	0.07750200
C	1.58970400	-1.78859600	-0.18746700
C	2.13488500	-0.70631800	0.78838500
C	3.67759900	-0.64611200	0.78361600
C	4.29766500	-2.02307400	1.05647700
C	3.78696300	-3.06735300	0.05599000
H	1.80622800	-1.49001500	-1.21490700
H	1.92985300	-3.51725200	1.06527900
H	1.89093400	-3.87758100	-0.66087100
H	4.03918300	-0.26741900	-0.17858200
H	3.98998800	0.08248500	1.53949100
H	5.38950800	-1.95057900	1.00844800
H	4.05210700	-2.34456900	2.07885500
H	4.12563900	-2.80723600	-0.95683300
H	4.20700200	-4.05408400	0.27915800
H	1.83369200	-1.02206900	1.79283300
N	0.13117800	-1.94094000	-0.05994300
C	-0.84640900	-1.55972800	-0.91000000
C	-0.60370000	-0.83917900	-2.11925000
C	-2.21081200	-1.85957900	-0.60219200
H	0.40376100	-0.58702900	-2.42244600
C	-2.99010400	-0.66167700	-2.40291800
H	-3.83950100	-0.54322400	-3.06575600

H	-0.16012000	-2.48210400	0.74441700
C	-1.67127600	-0.34944900	-2.82257000
H	-1.52822600	0.31690600	-3.66690700
O	-3.13578400	-1.72858600	-1.58364800
N	1.50885900	0.59398100	0.57667000
C	0.65779900	1.21814900	1.49548800
C	1.59800100	1.40462600	-0.56148700
C	0.18805800	2.43729300	0.94117000
C	0.78374800	2.55394800	-0.37226800
C	2.31550000	1.22639100	-1.75376200
C	0.69074700	3.52089000	-1.38041100
C	1.39846900	3.34013400	-2.56493200
H	1.34168300	4.08742300	-3.35039400
C	2.20297300	2.20309000	-2.74361800
H	2.76399400	2.08379000	-3.66616100
C	-0.68854900	3.24591100	1.67578900
C	0.26147700	0.80693000	2.77445000
C	-1.08906000	2.83564100	2.94392000
H	-1.76104900	3.45758300	3.52723900
C	-0.61386500	1.62858400	3.48470300
H	-0.92050700	1.33298600	4.48402700
H	0.63308300	-0.10621700	3.22965500
H	-1.04497700	4.18594600	1.26338100
H	0.07882300	4.40709200	-1.23480100
H	2.96802800	0.37511700	-1.91417400
C	-2.69172600	-2.67687200	0.55852600
H	-3.62281200	-3.16199700	0.24989300
H	-1.98985100	-3.47852700	0.82130300
C	-2.96322000	-1.74238600	1.76886600
H	-3.56347600	-2.26437500	2.52099200
H	-2.01648800	-1.46307000	2.24835700
C	-3.65880100	-0.47207700	1.26168600
H	-4.64183700	-0.71367100	0.83808000
H	-3.83516800	0.20798200	2.10715200
C	-2.81137500	0.25251400	0.24493800
H	-1.83314400	0.57641600	0.59170100
C	-3.31762800	0.83471800	-0.91716100
H	-2.78388500	1.66538900	-1.36784100
H	-4.39399300	0.83257000	-1.07931100

Transition structure leading to the observed minor enantiomer of product with **32**•pyrylium:



E(RB+HF–LYP): –1270.12481009

Zero-point correction= 0.534791 (Hartree/Particle)

Thermal correction to Energy= 0.560053

Thermal correction to Enthalpy= 0.560998

Thermal correction to Gibbs Free Energy= 0.478788

Cartesian coordinates:

C	0.24084100	3.53137800	0.03668700
C	-0.18428800	2.06924200	-0.19149500
C	-1.50872200	1.74821700	0.56271500
C	-2.62580000	2.75828600	0.22743000
C	-2.16415400	4.20206900	0.47210800
C	-0.88415800	4.51712000	-0.31283600
H	-0.32785100	1.90507500	-1.26201700
H	0.51436100	3.65879500	1.09567400
H	1.14303900	3.74090200	-0.54976800
H	-2.94163900	2.64951200	-0.81510000
H	-3.49895800	2.51557500	0.84247400
H	-2.96332500	4.89608500	0.19037900
H	-1.98273200	4.35631300	1.54544600
H	-1.09066100	4.46965600	-1.39146200
H	-0.54686000	5.53869500	-0.10660200
H	-1.28937100	1.87343400	1.62878000
N	0.88949900	1.17124000	0.26112100
C	1.38929200	0.07240000	-0.33960500
C	0.99164200	-0.37245400	-1.63709700
C	2.42319100	-0.67630700	0.30965900
H	0.13741400	0.06479200	-2.13745600
C	2.81324900	-1.94860300	-1.56139700

H	3.25038000	-2.88039000	-1.90134000
H	1.19294200	1.33767600	1.21289700
C	1.74204900	-1.33335200	-2.26002300
H	1.55276000	-1.61412400	-3.29107200
O	2.78304000	-1.87046400	-0.21038400
N	-1.90239800	0.35551400	0.40216800
C	-1.81368600	-0.60798400	1.41632700
C	-2.32637200	-0.27974200	-0.77241800
C	-2.18994800	-1.87000500	0.89192900
C	-2.51499500	-1.66219500	-0.50258800
C	-2.53983500	0.23324300	-2.06051500
C	-2.93328800	-2.52334800	-1.52333200
C	-3.14918700	-2.01328100	-2.80006400
H	-3.48036900	-2.67087100	-3.59792000
C	-2.95125700	-0.64823000	-3.06127300
H	-3.13300900	-0.26188300	-4.06022600
C	-2.18397000	-2.99867000	1.72010100
C	-1.43291900	-0.46580900	2.75589300
C	-1.80280400	-2.86132800	3.05118200
H	-1.79928100	-3.72755800	3.70559000
C	-1.43330000	-1.60526300	3.56009300
H	-1.15309600	-1.51339200	4.60565000
H	-1.17063400	0.49721700	3.18468600
H	-2.47829800	-3.96873800	1.32903100
H	-3.08972500	-3.57905500	-1.31907600
H	-2.41523300	1.28536200	-2.29189900
C	2.89122700	-0.47547700	1.71926000
H	3.26752600	-1.43908800	2.07541200
H	2.06909800	-0.19099300	2.38792800
C	4.03779600	0.57155300	1.72955200
H	4.58377200	0.52706100	2.67709100
H	3.62277700	1.58482500	1.64953400
C	4.95546100	0.30099900	0.52873600
H	5.76230300	1.04726000	0.50520700
H	5.43811600	-0.67885400	0.63182600
C	4.19726000	0.36596700	-0.77720500
H	3.71461000	1.31792700	-0.99375200
C	4.38957200	-0.52453100	-1.83428400
H	5.16636200	-1.28158300	-1.74586200
H	4.17417600	-0.20657100	-2.84925000

8. Frontier Molecular Orbital Analysis and Intermolecular Reaction Results

Frontier molecular orbital energies were calculated according to the DFT-based method of Musgrave[22] wherein the excitation energy of the first singlet excited state is used as an approximation of the HOMO–LUMO energy gap; the authors also provide linear correction factors to improve the accuracy of computed values. Structures were first fully optimized at the B3LYP/6-311+G(d,p) level of density functional theory and verified to be local minima by the existence of no imaginary frequencies. HOMO energy values were then linearly corrected. A time-dependent DFT (TD–DFT) calculation was then performed on each optimized structure in order to determine the excitation energy of the first singlet excited state, and this value was then linearly corrected and added to the corrected HOMO energy to give a LUMO energy value. This was done for 3-oxidopyrylium, 3-amidopyrylium, 3-aminopyrylium, and the following dipolarophiles: acrylonitrile, methyl acrylate, ethyl vinyl ether, norbornene, styrene, and 4-methoxystyrene (Figure S3).

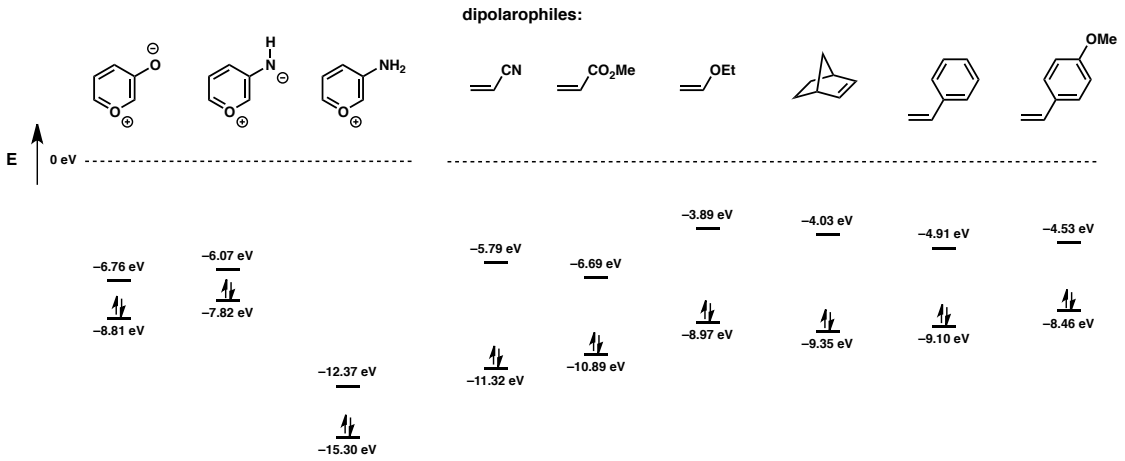
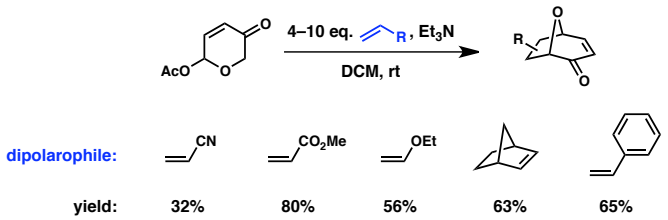


Figure S3. FMO analysis of pyryliums and dipolarophiles.

3-Oxidopyryliums are known to react with both electron-rich and electron-deficient alkenes (Scheme S13).[23] In line with these observations is our FMO analysis showing that either the HOMO or the LUMO of the 3-oxidopyrylium is predicted to interact with either the LUMO or the HOMO of the dipolarophile, respectively, depending on its electronic nature.

Scheme S13. Reported intermolecular 3-oxidopyrylium [5+2] cycloaddition reactions.[23]



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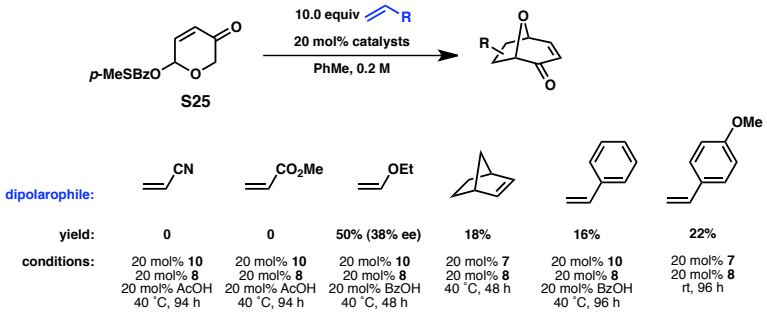
[22] Zhang, G.; Musgrave, C. B. *J. Phys. Chem. A* **2007**, *111*, 1554–1561.

[23] Results from: (a) Ali, M. A.; Bhogal, N.; Findlay, J. B. C.; Fishwick, C. W. G. *J. Med. Chem.* **2005**, *48*, 5655–5658. (b) Sammes, P. G.; Street, L. J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1261–1265. (c) Sammes, P. G.; Street, L. J. *J. Chem. Res., Synop.* **1984**, 196–197.

In an attempt to extend the developed thiourea-catalyzed [5+2] cycloaddition to an intermolecular variant a variety of dipolarophiles were tested under catalytic conditions with pyranone **S25** (Scheme S14). In no cases was a reaction found to occur with electron-deficient alkenes (acrylonitrile or methyl acrylate). On the other hand ethyl vinyl ether, norbornene, styrene, and *para*-methoxystyrene all provided product under these non-basic conditions, albeit with low reactivity. If the catalytic reaction under investigation were proceeding via an oxidopyrylium intermediate, similar trends to reported triethylamine-promoted reactions (Scheme S13) would be expected. This is not the case allowing us to infer that an oxidopyrylium is not the species undergoing cycloaddition.

Scheme S14. Intermolecular results under thiourea-catalyzed conditions.



Computed FMO energy values of a hypothetical amidopyrylium predict this species to have similar reactivity to an oxidopyrylium: either the HOMO or the LUMO of an amidopyrylium can be more relevant to cycloaddition with different dipolarophiles. In addition, the higher HOMO energy value of the amidopyrylium predicts it to be more reactive with electron-deficient dipolarophiles. Again, since the reactivity trends in Scheme S14 are not similar to those in Scheme S13 we conclude that an amidopyrylium is not the species undergoing cycloaddition.

The computed FMO energy values of an aminopyrylium are such that with all examined dipolarophiles it should be the LUMO of this species that is most relevant to cycloaddition. This is consistent with the results in Scheme S14 where only dipolarophiles with high-lying HOMOs react. These results in conjunction with the structure-activity relationship studies have led us to propose that it is an aminopyrylium that is the active species undergoing cycloaddition in the present catalytic reaction. The oxygen-analogue of this species, a protonated oxidopyrylium or 3-hydroxypyrylium, has similar calculated HOMO and LUMO values (–16.7 eV and –12.9 eV, respectively), but this species was eliminated from the list of possible intermediates undergoing cycloaddition because of its expected high acidity (estimated to be similar to that of a protonated carbonyl) and because tertiary aminothiourea **33** is not an active catalyst.

In order to examine the effect of a counteranion an FMO analysis of ion-pair **S26** was also performed (Figure S4). Here a TD–DFT calculation was not possible owing to the fact that the Kohn-Sham orbitals taken into consideration in such a calculation with **S26** are not those relevant to cycloaddition. This was determined through visualization of the HOMO and LUMO surfaces. Visualization of other MO surfaces allowed for the identification of a "HOMO" and "LUMO" that would be involved in cycloaddition of **S26** through analogy to visualized HOMO and LUMO surfaces of the other pyryliums. The identified "HOMO" was linearly corrected as before. Musgrave also provides linear corrections for LUMO values from DFT calculations and shows these to give

comparable yet slightly less accurate results than with TD-DFT calculations. This was used to determine an energy value for the "LUMO" of **S26**. Although both the "HOMO" and the "LUMO" of **S26** are higher in energy than the HOMO and LUMO of the free aminopyrylium, their values are such that the predicted interaction should still be the same with examined dipolarophiles. This is thus still consistent with an aminopyrylium undergoing cycloaddition. Since an overall cationic species such as an aminopyrylium would be expected to have lower-lying frontier MO's as compared to a similar neutral species, it is not surprising that the introduction of a counteranion to give an ion pair should then raise the energy values of these orbitals. That the charge separation in **S26** is greater than in an oxido- or amidopyrylium may be the reason for **S26** still having lower FMO energy values than the zwitterions.

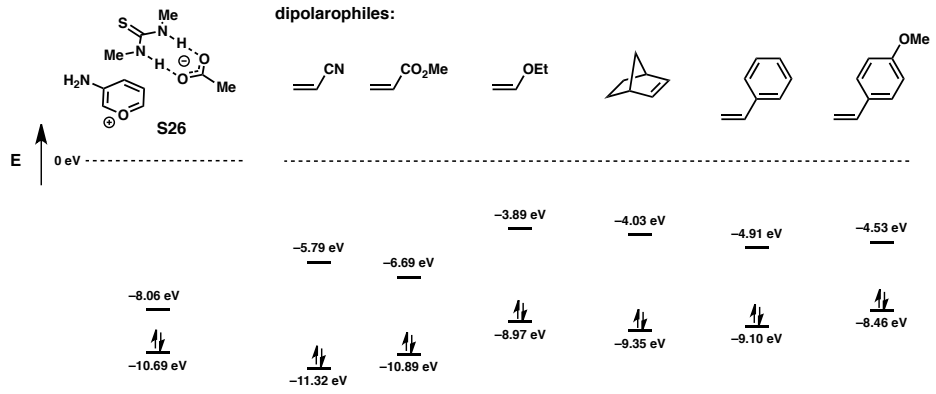
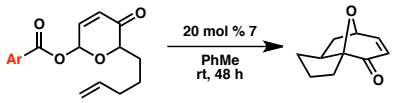


Figure S4. FMO analysis of ion-pair **S26**.

9. Additional Optimization Studies

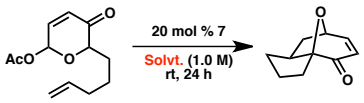
Results with different benzoyl leaving groups:



Entry	Ar	yield (%)[a]	ee (%)
1	Ph	36	58
2	*p*-Me_2NPh	15	55
3	*p*-MeOPh	40	61
4	*o*-MeOPh	13	75
5	*p*-*t*-BuPh	26	58
6	*p*-NO_2Ph	12	43
7	2-napth	36	46

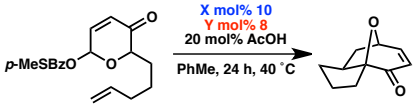
[a] Based on ^1H NMR

Enantioselectivity in different solvents:



Solvent	ee (%)
CH_2Cl_2	46
TBME	20
hexanes	30
Et_2O	22
THF	–
H_2O	6
CH_3CN	18
MeOH	–
PhMe	54
–	28

Catalyst loading studies:

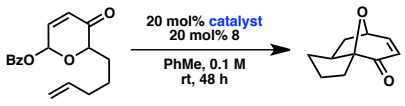


Entry	mol% 10	mol% 8	yield (%)[a]	ee (%)
1	20	20	69	91
2	20	15	68	92
3	20	10	71	90
4	20	5	70	90
5	20	2.5	66	90
6	20	~1	63	87
7	15	20	59	92
8	10	20	43	91

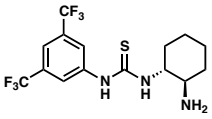
[a] based on ^1H NMR

The above table shows that while the loading of achiral thiourea **8** may be decreased without a compromise in results with the parent substrate (Entries 1–6) any reduction in the loading of catalyst **10** results in lower reactivity (compare Entries 1, 7, and 8).

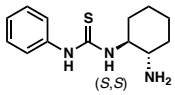
10. Results with Different Aryl Primary Aminothiourea Catalysts



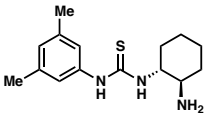
catalysts:



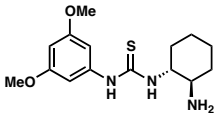
37%, 71%ee



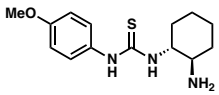
39%, –72%ee



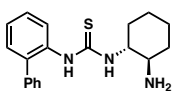
43%, 71%ee



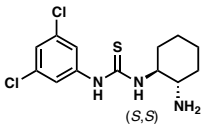
43%, 70%ee



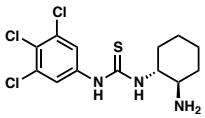
36%, 69% ee



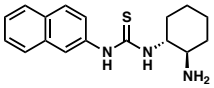
43%, 67%ee



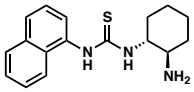
39%, –75%ee



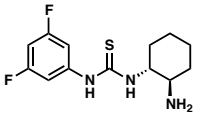
41%, 77%ee



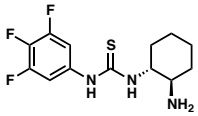
43%, 72%ee



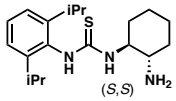
53%, 61%ee



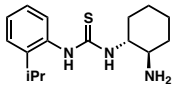
41%, 70%ee



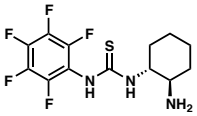
45%, 73%ee



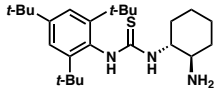
59%, –73%ee



55%, 63%ee



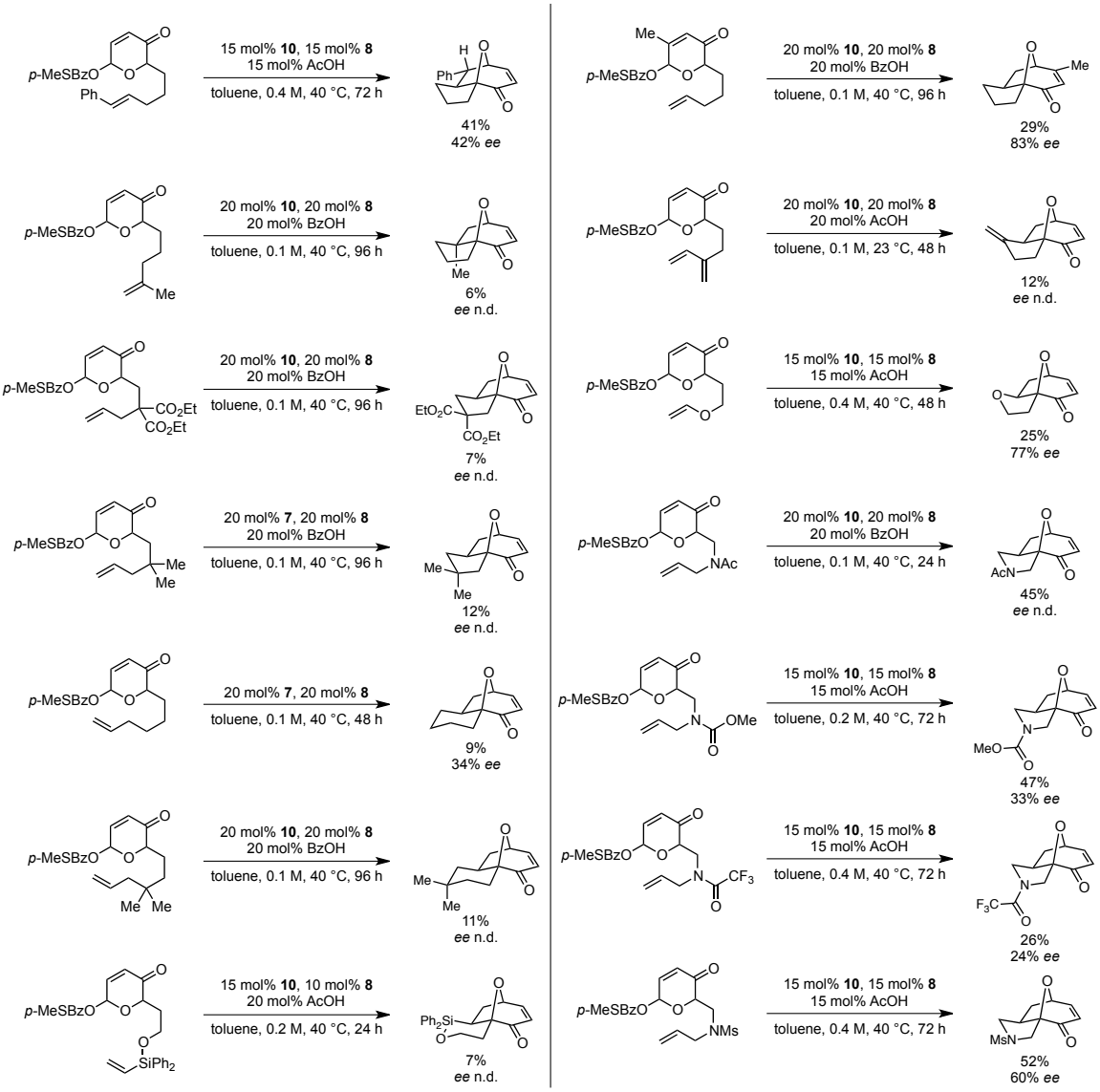
42%, 54%ee



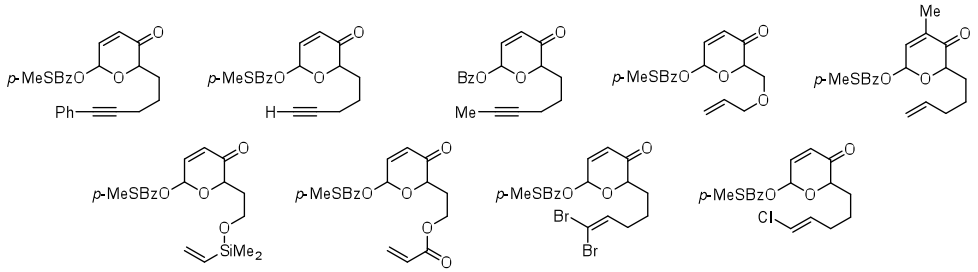
10%, 88% ee

11. Results with Sub-Optimal and Unreactive Substrates

Sub-optimal substrates:

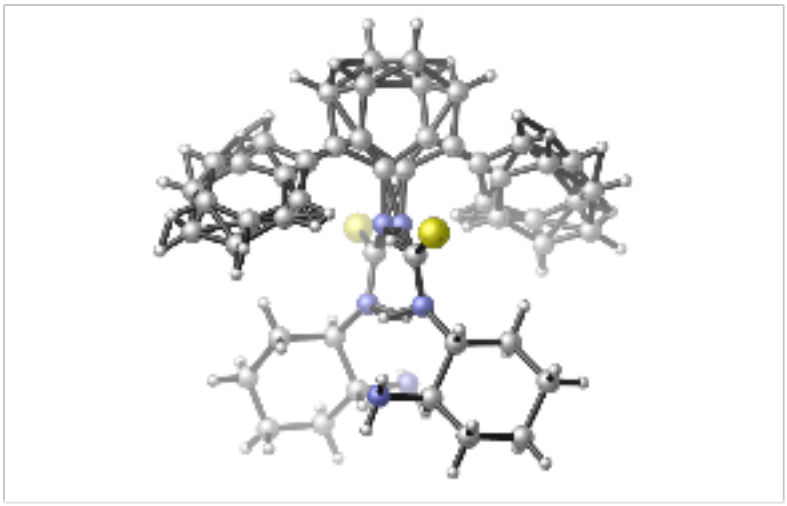


Unreactive substrates:



12. X-Ray Crystallographic Information

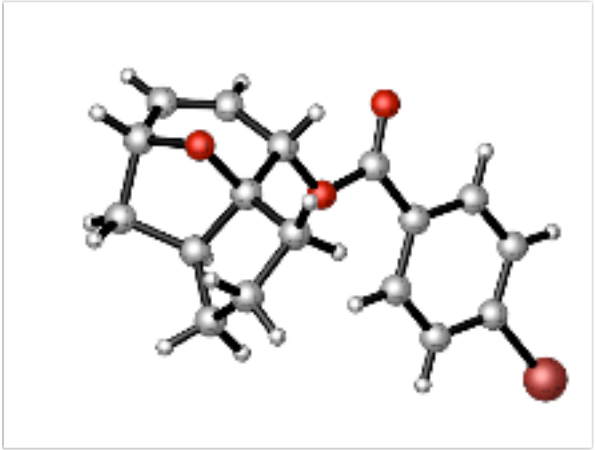
Catalyst **10**:



Crystal data	
Chemical formula	$C_{25}H_{27}N_3S$
M_r	401.56
Crystal system, space group	Trigona, $P3_1$
Temperature (K)	100
a, *b*, *c* (Å)	11.4229 (4), 11.4229 (4), 14.1312 (5)
α, β, γ (°)	90, 90, 120
V (Å^3)	1596.84 (10)
Z	3
Radiation type	Cu *K*α
μ (mm^{-1})	1.46
Crystal size (mm)	0.26 × 0.14 × 0.12
Data collection	
Diffractometer	CCD area detector diffractometer
Absorption correction	Multi-scan *SADABS*
T_{min}, T_{max}	0.703, 0.845
No. of measured, independent and observed [$I > 2\sigma(I)$]	32886, 3653, 3637

reflections	
R_{int}	0.048
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.090, 0.178, 1.02
No. of reflections	3653
No. of parameters	249
No. of restraints	6
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.41, -0.33
Absolute structure	Flack H D (1983), Acta Cryst. A39, 876-881
Flack parameter	-10 (10)

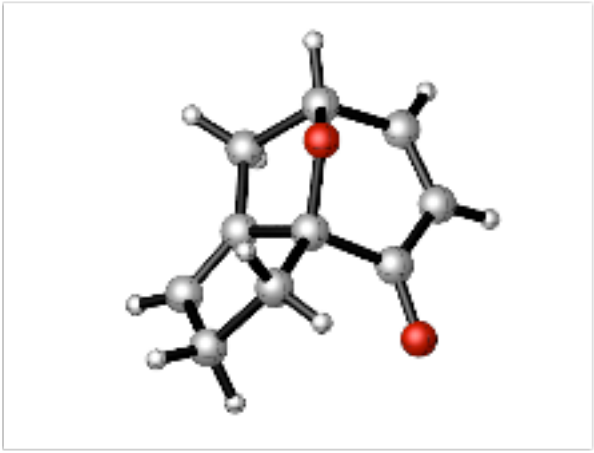
p-Bromobenzoate of reduced product **6**:



Crystal data	
Chemical formula	$C_{17}H_{17}BrO_3$
M_r	349.22
Crystal system, space group	Monoclinic, $P2_1$
Temperature (K)	100
a, b, c (Å)	6.9456 (3), 6.6693 (3), 16.2697 (7)
β (°)	95.464 (2)
V (Å^3)	750.23 (6)

Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	2.75
Crystal size (mm)	0.24 × 0.18 × 0.16
Data collection	
Diffractometer	Bruker D8 goniometer with CCD area detector diffractometer
Absorption correction	Multi-scan *SADABS*
T_{min}, T_{max}	0.559, 0.668
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	20486, 3847, 3623
R_{int}	0.030
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.020, 0.046, 1.08
No. of reflections	3847
No. of parameters	190
No. of restraints	1
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e $Å^{-3}$)	0.31, -0.28
Absolute structure	Flack H D (1983), Acta Cryst. A39, 876-881
Flack parameter	-0.004 (5)

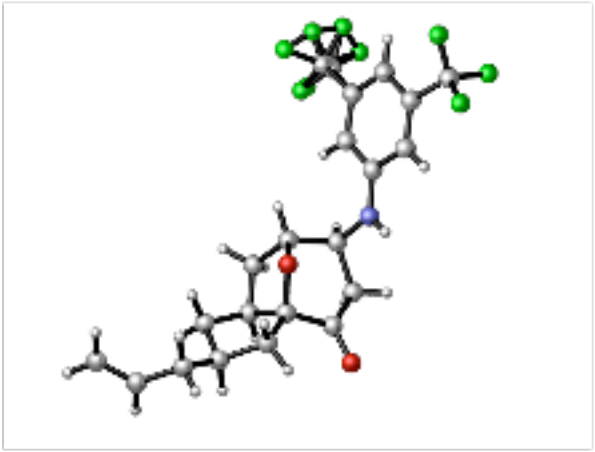
Product **24**:



Crystal data	
Chemical formula	$C_{10}H_{10}O_2$
M_r	162.18
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	100
a, b, c (Å)	7.2085 (1), 7.8988 (1), 13.8528 (2)
V (Å^3)	788.76 (2)
Z	4
Radiation type	Cu $K\alpha$
μ (mm^{-1})	0.77
Crystal size (mm)	0.28 × 0.16 × 0.12
Data collection	
Diffractometer	Bruker D8 goniometer with CCD area detector diffractometer
Absorption correction	Multi-scan *SADABS*
T_{min}, T_{max}	0.814, 0.914
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	13604, 1387, 1378
R_{int}	0.031
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.029, 0.073, 1.15

No. of reflections	1387
No. of parameters	109
No. of restraints	0
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.12, -0.21
Absolute structure	Flack H D (1983), Acta Cryst. A39, 876-881
Flack parameter	0.1 (2)

Derivative of **28** (byproduct in the reaction with substrate **27** – see general procedure A for details):



Crystal data	
Chemical formula	$C_{21}H_{21}F_6NO_2$
M_r	433.39
Crystal system, space group	Monoclinic, *C*2
Temperature (K)	100
a, *b*, *c* (Å)	29.9461 (7), 5.0733 (1), 15.3388 (4)
β (°)	90.381 (2)
V (Å^3)	2330.30 (9)
Z	4
Radiation type	Cu *K*α
μ (mm^{-1})	0.97
Crystal size (mm)	0.22 × 0.18 × 0.08

Data collection	
Diffractometer	Bruker D8 goniometer with CCD area detector diffractometer
Absorption correction	Multi-scan *SADABS*
T_{min}, T_{max}	0.814, 0.926
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	3818, 3818, 3728
R_{int}	0.0000
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.035, 0.094, 1.09
No. of reflections	3818
No. of parameters	288
No. of restraints	26
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.20, -0.19
Absolute structure	Flack H D (1983), Acta Cryst. A39, 876-881
Flack parameter	0.11 (13)