Supporting Information for

Sulfoxide-Directed Intramolecular [4+2] Cycloadditions between 2-Sulfinyl Butadienes and Unactivated Alkynes

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Materials and methods.

Reagents and solvents were handled by using standard syringe techniques. Anhydrous solvents were prepared according to standard methods by distillation over drying agents or via elution through a Pure Solv™ column drying system[1]. Acetone was distilled over $KMnO_4$ and stirred for one night with anhydrous $CaSO_4$, filtered, distilled again and collected over molecular sieves (4 Å). Crude products were purified by flash chromatography on 230-400 mesh silica gel with distilled solvents. Analytical TLC was carried out on silica gel plates with detection by UV light, iodine, acidic vanillin solution, 10% phosphomolybdic acid solution in ethanol. Through this section, the volume of solvents is reported in mL/mmol of starting material. ^{1}H and ^{13}C NMR spectra were recorded at 200, 300, 400 or 500 MHz (^{1}H) using $CDCl_3$ as solvent unless otherwise noted and with the residual solvent signal as internal reference ($CDCl_3$, 7.24 and 77.0 ppm). The atom connectivities were established by gCOSY experiments and spatial relationships were determined by NOESY-1D and NOESY-2D experiments. The following abbreviations are used to describe peak patterns when appropriate: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). Melting points are uncorrected. Optical rotations were measured at 20 ºC using a sodium lamp and in $CHCl_3$ solution. Low resolution mass spectra were recorded using the electrospray (ES) chemical ionization technique in its positive or negative modes. High resolution mass spectra were recorded using electrospray (ES) in its positive or negative modes.

2-Methoxynaphthalen-1-yl disulfide,[2] *tert*-butyl(pent-4-ynyloxy)diphenylsilane,[3] ethylaminopyridine,[4] stannanes **SI-26**,[5] **SI-29**,[6] **SI-31**,[7] **SI-32**,[8] alkynes **SI-37**,[9] **SI-38**, **7**,[10] and allene **8**[11] were prepared as described in the literature.

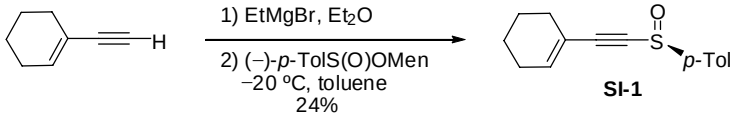
1. Synthesis of sulfenyl and sulfinyl stannanes.

1.1. General procedure for the synthesis of alkynyl sulfoxides.

A dry two-necked round-bottomed flask fitted with reflux condenser, septum and magnetic stirrer was charged with dry Mg turnings (1.6-2 equiv) under argon and anhydrous Et_2O was added (0.1 mL/mmol Mg) and 5-10 drops of EtBr. The mixture was heated slowly until the formation of the Grignard reagent was initiated. Then a solution of EtBr (1.7-2.2 equiv) in Et_2O (0.4 mL/mmol Mg) was added dropwise, maintaining a moderate reflux. After the addition was complete, the mixture was heated to reflux until complete disappearance of Mg was observed. To the solution of EtMgBr at rt the alkyne (1.6-2.2 equiv) was added and the mixture was heated to reflux for 2 h. The alkynyl Grignard was added (via syringe) to a cold solution (−20 ºC) of (−)-menthyl *p*-toluenesulfinate (1 equiv) in

anhydrous toluene (5 mL/mmol sulfoxide) and the reaction was stirred at low temperature until disappearance of starting material was observed (TLC). The mixture was quenched by addition of a saturated NH_4Cl solution (4 mL/mmol sulfoxide) and H_2O (4 mL/mmol sulfoxide) and diluted with EtOAc. The layers were separated, the aqueous layer was extracted with EtOAc (2 x 4 mL/mmol) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (5-30% EtOAc-hexane) with the appropriate combination of solvents.

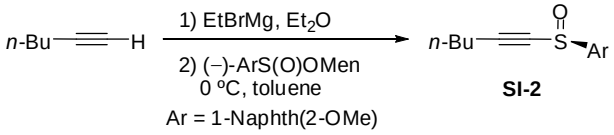
1.2. Synthesis of (–)-(*S*)-1-Cyclohexenylethynyl *p*-tolyl sulfoxide, SI-1.



From 1-ethynylcyclohex-1-ene (0.70 mL, 6.0 mmol), Mg (0) (136 mg, 5.6 mmol), EtBr (0.42 mL, 5.6 mmol) and (–)-menthyl *p*-toluenesulfinate (1.17 g, 4.0 mmol), following the general procedure, compound **SI-1** was obtained. In this example, the reaction mixture was warmed up to room temperature after the alkynyl Grignard addition and stirred for 15 h. Purification by column chromatography afforded **SI-1** (231 mg, 0.94 mmol, 24%) as a yellow oil and 435 mg (1.47 mmol, 37%) of starting material.

Data for **SI-1**: $\boldsymbol{R_f}$ = 0.28 (20% EtOAc-hexane); $\boldsymbol{[\alpha]_D^{20}}$ = –1.0 (*c* = 0.59); **^{1}H NMR** (300 MHz) δ = 1.55 (m, 5 H), 2.08-2.15 (m, 3 H), 2.40 (s, 3 H, Me-*p*-Tol), 6.34 (quint, 1 H, *J* = 1.9 Hz), 7.31 (d, 2 H, *J* = 8.1 Hz), 7.81 (d, 2 H, *J* = 8.3 Hz); **^{13}C NMR** (50 MHz) δ = 21.0, 21.5, 21.8, 25.9, 28.0, 55.7, 104.6, 118.7, 125.2 (2 C), 130.1 (2 C), 141.2, 141.3, 142.2; **IR** (film): 2934, 2861, 1716, 1594, 1491, 1447, 1328, 1143, 1080, 1042, 809 cm^{-1}; **MS** (ES) m/z (%): 245 $[M+H]^+$; **Anal. calcd for** $C_{15}H_{16}OS$: C 73.73, H 6.60, S 13.12; **found**: C 73.81, H 6.67, S 13.23.

1.3. Synthesis of (–)-(*R*)-1-Hexynyl 2-methoxynaphthalen-1-yl sulfoxide, SI-2.

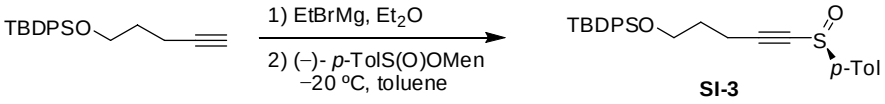


From 1-hexyne (0.59 mL, 5.10 mmol), Mg (0) (117 mg, 4.80 mmol), EtBr (0.38 mL, 5.10 mmol) and (–)-menthyl 2-methoxynaphthalenesulfinate (1.08 g, 3.00 mmol) following the general procedure, compound **SI-2** was obtained. In this example the Grignard reagent was added at 0 ºC due to

poor solubility of the sulfinate in toluene at –20 ºC. Purification by chromatography (5-50% EtOAc-hexane) afforded **SI-2** (645 mg, 2.25 mmol, 75%) as a yellow oil.

Data for **SI-2**: R_f = 0.25 (30% EtOAc-hexane); $[\alpha]^{20}_D$ = –8.5 (*c* = 1.61); **^{1}H NMR** (300 MHz) δ = 0.82 (t, *J* = 7.0 Hz, 3 H, Me-*n*-Bu), 1.28-1.67 (m, 4 H, *n*-Bu), 2.35 (t, *J* = 6.8 Hz, 2 H,), 4.02 (s, 3 H, OMe), 7.25 (d, *J* = 9.1 Hz, 1 H, H-3'), 7.42 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1 H, H-6'), 7.60 (ddd, *J* = 8.6, 7.0, 1.5 Hz, 1 H, H-7'), 7.80 (d, *J* = 8.1 Hz, 1 H, H-5'), 7.96 (d, *J* = 9.1 Hz, 1 H, H-4'), 8.92 (d, *J* = 8.8 Hz, 1 H, H-8'); **^{13}C NMR** (50 MHz) δ = 13.4 (Me-*n*-Bu), 19.6, 21.8, 29.6, 57.1, 77.7, 105.9, 112.9, 123.7, 123.9, 124.7, 128.2, 128.7, 129.6, 130.6, 135.0, 156.1; **IR** (film): 3051, 2957, 2932, 2871, 2176, 1621, 1594, 1562, 1506, 1468, 1430, 1356, 1337, 1273, 1252, 1217, 1182, 1151, 1136, 1055, 1025, 980, 952, 898, 859, 812, 773, 750, 708 cm^{-1}; **MS** (ES) m/z (%): 287 (100) $[M+H]^+$; **Anal. calcd for** $C_{17}H_{18}O_2S$: C 71.30, H 6.34, S 11.20; **found**: C 71.48, H 6.23, S 11.41.

1.4. Synthesis of (+)-(*S*)-*tert*-Butyldiphenyl-[5-(*p*-tolylsulfinyl)pent-4-ynyloxy]silane, SI-3.



SI-3

From *tert*-butyl(pent-4-ynyloxy)diphenylsilane (7.01 g, 21.72 mmol, 1.70 equiv), EtBr (1.61 mL, 21.72 mmol, 1.70 equiv), Mg (0) (497 mg, 20.44 mmol, 1.60 equiv) and (–)-menthyl *p*-toluenesulfinate (3.76 g, 12.77 mmol, 1.00 equiv), following the general procedure, alkynyl sulfoxide **SI-3** was obtained. Purification by chromatography (2-100% EtOAc-hexane) afforded **SI-3** (4.77 g, 10.34 mmol, 81%) as a yellow oil.

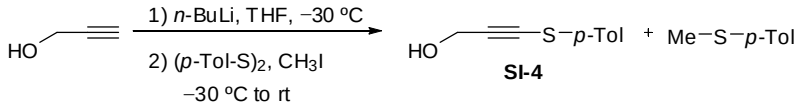
Data for **SI-3**: R_f = 0.24 (20% EtOAc-hexane); $[\alpha]^{20}_D$ = +28.6 (*c* = 0.95); **^{1}H NMR** (300 MHz) δ = 1.01 (s, 9 H, *t*-Bu), 1.77 (m, 2 H, H-2), 2.40 (s, 3 H, Me-*p*-Tol), 2.57 (t, *J* = 7.1 Hz, 2 H, H-3), 3.67 (t, *J* = 5.8 Hz, 2 H, H-1), 7.27-7.43 (m, 8 H), 7.59-7.65 (m, 6 H); **^{13}C NMR** (75 MHz) δ = 16.4, 19.2, 21.4, 26.8, 30.4, 61.9, 78.3, 105.3, 125.1 (2 C), 127.7 (4 C), 129.7 (2 C), 130.1 (2 C), 133.5 (4 C), 135.4, 141.2, 142.1; **IR** (film): 3070, 3049, 2956, 2930, 2857, 2182, 1589, 1427, 1390, 1186, 1111, 1089, 1061, 998, 959, 823, 809, 740, 703 cm^{-1}; **MS** (ES) m/z (%): 484 $[M+Na]^+$, 461 $[M+H]^+$, 383 (100) $[M-77]^+$; **Anal. calcd for** $C_{28}H_{32}O_2SSi$: C 73.00, H 7.00, S 6.96, Si 6.10; **found**: C 72.85, H 7.13, S 6.71, Si 5.97.

1.5. General procedure for the synthesis of alkynyl sulfides.[12]

To a cold solution (–30 ºC) of the alkyne in anhydrous THF (2 mL/mmol), under argon atmosphere, a solution of *n*-BuLi (1-2 equiv) was added dropwise. The mixture was stirred for 30

minutes at this temperature and then a solution of the disulfide and CH_3I in THF (2 mL/mmol), previously stirred for 1 hour at room temperature, was added. The reaction mixture was allowed to reach room temperature and was stirred until starting material disappearance (TLC). The reaction mixture was quenched with a saturated solution of NH_4Cl (2 mL/mmol of disulfide) and water (4 mL/mmol of disulfide). Phases were separated and the aqueous layer was extracted with EtOAc (twice). The resulting organic extract was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by column chromatography using the appropriate mixture of solvents.

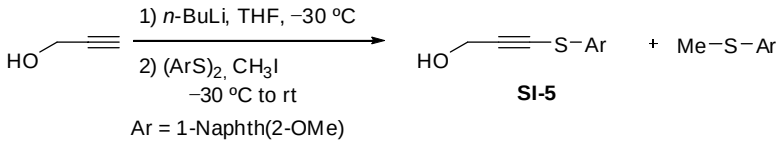
1.6. Synthesis of 3-(*p*-Tolylsulfenyl)prop-2-yn-1-ol, SI-4.



From *p*-tolyl disulfide (1.27 g, 5.15 mmol, 1.03 equiv), CH_3I (0.37 mL, 6.00 mmol, 1.2 equiv), propargyl alcohol (0.3 mL, 5.0 mmol, 1.0 equiv) and *n*-BuLi (8.23 mL, 10.27 mmol, 1.3 M, 2.14 equiv), following the general procedure, compound **SI-4** was obtained. Purification by chromatography afforded 446 mg (2.5 mmol, 50%) of **SI-4** as a white solid that was recrystallized from Et_2O-hexane.

Data for **SI-4**: $\boldsymbol{R_f}$ = 0.28 (30% EtOAc-hexane); **^{1}H NMR** (200 MHz) δ = 1.64 (t, *J* = 6.0 Hz, 1 H, OH), 2.32 (s, 3 H, Me-*p*-Tol), 4.46 (d, *J* = 6.0 Hz, 2 H), 7.13 (d, *J* = 8.1 Hz 2 H, *p*-Tol), 7.31 (d, *J* = 8.4 Hz, 2 H, *p*-Tol); **Anal. calcd for** $C_{10}H_{10}OS$: C 67.30, H 5.65, S 17.99; **found**: C 67.56, H 5.40, S 18.05.

1.7. Synthesis of 3-(2-Methoxynaphthalen-1-ylsulfenyl)prop-2-yn-1-ol, SI-5.



From 2-methoxynaphthalen-1-yl disulfide (1.38 g, 3.65 mmol, 1.03 equiv), CH_3I (0.24 mL, 3.82 mmol, 1.08 equiv), propargyl alcohol (0.21 mL, 3.54 mmol, 1.00 equiv) and *n*-BuLi (4.73 mL, 7.57 mmol, 1.6 M, 2.14 equiv) following the general procedure, compound **SI-5** was obtained. Purification by chromatography afforded 393 mg (1.61 mmol, 44%) of **SI-5** as a white solid that was recrystallized from Et_2O-hexane.

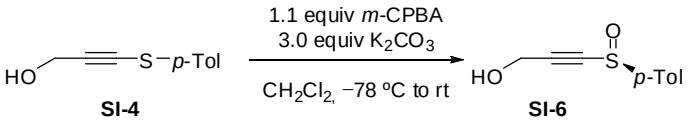
Data for **SI-5**: $\boldsymbol{R_f}$ = 0.15 (30% EtOAc-hexane); **mp** 80-81 ºC; **^{1}H NMR** (300 MHz) δ = 1.44 (t, *J* = 6.1 Hz, 1 H, OH), 4.05 (s, 3 H, OMe), 4.24 (d, *J* = 6.1 Hz, 2 H, H-1), 7.29 (d, *J* = 9.0 Hz, 1 H, H-3'), 7.40 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1 H, H-6'), 7.60 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1 H, H-7'), 7.79 (d, *J* =

8.3 Hz, 1 H, H-5'), 7.90 (d, *J* = 9.0 Hz, 1 H, H-4'), 8.47 (dd, *J* = 8.5, 0.7 Hz, 1 H, H-8'); **^{13}C NMR** (75 MHz) δ = 52.0 (OMe), 57.0, 76.4, 89.0, 111.4, 113.4, 124.2, 125.0, 127.8, 128.4, 129.5, 132.1, 134.6, 157.8; **IR** (KBr): 3428, 3292, 2972, 2891, 2844, 2175, 2109, 1621, 1590, 1503, 1466, 1438, 1428, 1350, 1330, 1271, 1249, 1179, 1147, 1135, 1064, 1023, 987, 807, 771, 745, 710 cm^{-1}; **MS** (ES) m/z (%): 267 $[M+Na]^+$, 245 (100) $[M+H]^+$; **Anal. calcd for** $C_{14}H_{12}O_2S$: C 68.83, H 4.95, S 13.12; **found**: C 68.66, H 4.91, S 13.43.

1.8. General procedure for oxidation of sulfides and sulfoxides with *m*-CPBA.

To a solution of the sulfide or sulfoxide in CH_2Cl_2 (8 mL/mmol) at room temperature, under an argon atmosphere, 3.0 equiv of K_2CO_3 were added. The reaction mixture was cooled (–78 ºC for sulfide oxidation to sulfoxides and 0 ºC for the oxidation of sulfoxides to sulfones) and then *m*-CPBA (1-2 equiv, 70%) was added. The reaction mixture was allowed to warm up until starting material disappearance. The reaction mixture was quenched with a 1.0 M aqueous solution of $Na_2S_2O_4$ (3 mL/mmol *m*-CPBA), a saturated solution of $NaHCO_3$ (2 mL/mmol *m*-CPBA) and water (3 mL/mmol *m*-CPBA). The aqueous phase was extracted with EtOAc (twice) and the organic extracts were washed with a saturated solution of $NaHCO_3$ and brine. The resulting organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by chromatography using the appropriate mixture of solvents.

1.9. Synthesis of (±)-3-(*p*-Tolylsulfinyl)prop-2-yn-1-ol, SI-6.



SI-4 **SI-6**

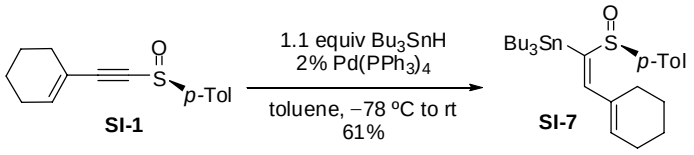
From sulfide **SI-4** (420 mg, 2.35 mmol), *m*-CPBA (638 mg, 2.59 mmol, 1.1 equiv) and K_2CO_3 (932 mg, 7.05 mmol, 3.0 equiv) following the general procedure (3 h), sulfoxide **SI-6** was obtained. Purification by chromatography (30-80% EtOAc-hexane) afforded **SI-4** (30 mg, 0.17 mmol, 7%) and **SI-6** (203 mg, 1.04 mmol, 44%) as a white solid that was recrystallized from Et_2O-hexane.

Data for **SI-6**: R_f = 0.20 (50% EtOAc-hexane); **^{1}H NMR** (200 MHz) δ = 2.23 (t, *J* = 6.6 Hz, 1 H, OH), 2.41 (s, 3 H, Me-*p*-Tol), 4.42 (d, *J* = 6.6 Hz, 2 H, H-1), 7.39 (d, *J* = 8.4 Hz, 2 H, *p*-Tol), 7.73 (d, *J* = 8.4 Hz, 2 H, Me-*p*-Tol); **Anal. calcd for** $C_{10}H_{10}O_2S$: C 61.83, H 5.19, S 16.51; **found**: C 62.01, H 5.25, S 16.31.

1.10. General procedure for the synthesis of 1-sulfinyl alkenyl tributylstannanes.

To a solution of alkynyl sulfoxide in anhydrous toluene (6 mL/mmol sulfoxide) at rt under argon, $Pd(Ph_3P)_4$ (0.02 equiv) was added. The mixture was cooled to −78 ºC and a solution of 1.1 equiv of freshly distilled Bu_3SnH in toluene (1 mL/mmol sulfoxide) was added. The mixture was stirred and warmed up to room temperature until disappearance of starting material was observed (TLC). Solvent was removed and the crude product was purified by column chromatography on silica gel with the appropriate mixture of solvents.

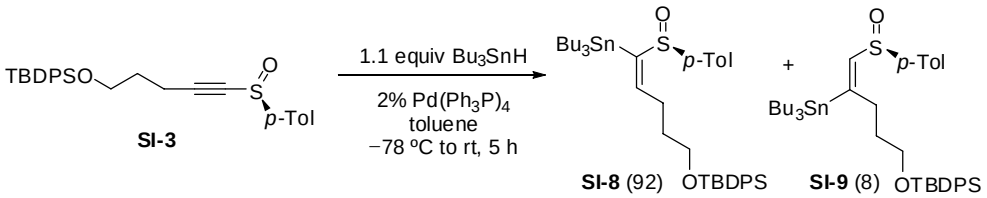
1.11. Synthesis of (–)-(*S*)-(*E*)-[2-Cyclohex-1-enyl-1-(*p*-tolylsulfinyl)vinyl]tributyl stannane, SI-7.



From alkyne **SI-1** (205 mg, 0.84 mmol), Bu_3SnH (0.25 mL, 0.92 mmol) and $Pd(PPh_3)_4$ (20 mg, 0.017 mmol), following the general procedure (3 h), compound **SI-7** was obtained. Purification by chromatography (1-50% EtOAc-hexane) afforded **SI-7** (189 mg, 0.51 mmol, 61%) as a yellow oil.

Data for **SI-7**: R_f = 0.66 (20% EtOAc-hexane); $[\alpha]_D^{20}$ = –127.2 (*c* = 0.82). **^{1}H NMR (300 MHz)** δ = 0.73-0.97 (m, 15 H), 1.11-1.42 (m, 14 H), 1.48-1.72 (m 3 H), 2.17-2.26 (m, 3 H), 2.35 (s, 3 H, Me-*p*-Tol), 5.93-5.96 (m, 1 H), 6.59 (s, 1 H), 7.21 (d, 2 H, *J* = 8.8 Hz), 7.38 (d, 2 H, *J* = 8.5 Hz); **^{13}C NMR (75 MHz)** δ = 11.8, 13.6 (3 C), 17.5, 26.2, 26.8, 27.3, 27.8, 28.7, 29.7, 124.9 (2 C), 129.4 (2 C), 129.9, 135.6, 136.4, 139.7, 142.9, 148.3; **IR** (film): 2954, 2924, 2870, 1616, 1553, 1490, 1456, 1375, 1178, 1076, 1034, 1015, 807 cm^{-1}; **MS** (ES) m/z (%): 1071 $[2M+H]^+$; **Anal. calcd for** $C_{27}H_{44}O_SSn$: C 60.57, H 8.28, S 5.99, Sn 22.17; **found**: C 60.43, H 8.39, S 6.24, Sn 22.31.

1.12. Synthesis of (–)-(*S*)-(*E*)-*tert*-Butyldiphenyl-[5-(*p*-tolylsulfinyl)-5-(tributylstannyl)pent-4-enyloxy]silane, SI-8.

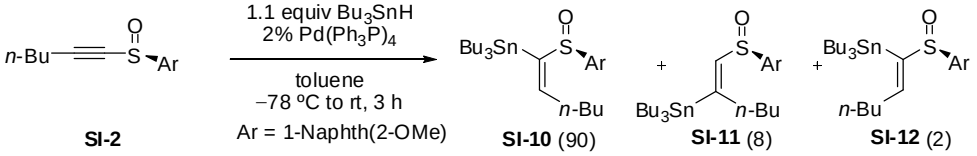


From alkynyl sulfoxide **SI-3** (4.77 g, 10.34 mmol, 1.00 equiv), Bu_3SnH (2 mL, 12.41 mmol, 1.20 equiv) and $Pd(PPh_3)_4$ (239 mg, 0.27 mmol, 0.02 equiv), following the general procedure, a 92:8 mixture of **SI-8** and **SI-9** was obtained. Purification by chromatography (1-20% EtOAc-hexane) afforded **SI-8** (6.14 g, 8.18 mmol, 79%) and **SI-9** (908 mg, 1.20 mmol, 11%), both as colorless oils.

Data for **SI-8**: R_f = 0.62 (20% EtOAc-hexane); **[α]$^{20}_{D}$** = –41.9 (*c* = 0.83); **^{1}H NMR** (300 MHz) δ = 0.83 (t, *J* = 7.1 Hz, 9 H, Me-*n*-Bu), 0.76-0.91 (m, 5 H), 1.06 (s, 9 H, *t*-Bu), 1.13-1.43 (m, 13 H), 1.74 (m, 2 H, H-2), 2.37 (s, 3 H, Me-*p*-Tol), 2.44-2.58 (m, 1 H, H-3), 2.69-2.84 (m, 1 H, H-3), 3.72 (m, 2 H, H-1), 6.16 (dd, *J* = 8.3, 6.0 Hz, 1 H, H-4), 7.23 (d, *J* = 7.9 Hz, 2 H), 7.35-7.45 (m, 8 H), 7.65-7.68 (m, 4 H); **^{13}C NMR** (75 MHz) δ = 11.3, 13.6, 19.2, 21.2, 26.8, 27.2, 28.7, 29.5, 32.2, 63.0, 124.4 (2 C), 127.6 (4 C), 129.5 (2 C), 129.6 (2 C), 133.8, 135.5 (4 C), 139.9, 142.5, 148.2, 156.8; **IR** (film): 3071, 2955, 2928, 2856, 1589, 1491, 1463, 1427, 1376, 1111, 1038, 1016, 823, 804, 701, 687 cm^{-1}; **MS** (ES) m/z (%): 774 [M+Na]$^{+}$, 752 [M+H]$^{+}$; **Anal. calcd for** $C_{40}H_{60}O_2SSiSn$: C 63.91, H 8.04, S 4.27, Si 3.74, Sn 15.79; **found**: C 63.76, H 8.16, S 4.07, Si 3.63, Sn 15.87.

Data for **SI-9**: ***R*$_f$** = 0.42 (20% EtOAc-hexane); **[α]$^{20}_{D}$** = –71.4 (*c* = 0.58); **^{1}H NMR** (300 MHz) δ = 0.81 (t, *J* = 7.2 Hz, 9 H, Me-*n*-Bu), 0.88-0.93 (m, 6 H), 1.05 (s, 9 H, *t*-Bu), 1.22 (sext, *J* = 7.2 Hz, 6 H), 1.34-1.42 (m, 6 H), 1.57-1.77 (m, 2 H, H-3), 2.37 (s, 3 H, Me-*p*-Tol), 2.74-2.94 (m, 2 H, H-2), 3.70 (t, *J* = 6.3 Hz, 2 H, H-1), 6.15 (s, 1 H, H-5), 7.23-7.26 (m, 2 H), 7.34-7.46 (m, 8 H), 7.64-7.67 (m, 4 H); **^{13}C NMR** (75 MHz) δ = 10.2, 13.6, 19.2, 21.3, 26.8, 27.2, 28.9, 32.6, 33.2, 63.4, 124.2 (2 C), 127.7 (4 C), 129.6 (2 C), 129.8 (2 C), 133.7, 135.5 (4 C), 140.6, 142.0, 143.6, 160.4; **IR** (film): 2950, 2928, 2855, 1456, 1427, 1111, 1042, 808, 701 cm^{-1}; **MS** (ES) m/z (%): 775 (100) [M+Na+1]$^{+}$, 774 [M+Na]$^{+}$; **Anal. calcd for** $C_{40}H_{60}O_2SSiSn$: C 63.91, H 8.04, S 4.27, Si 3.74, Sn 15.79; **found**: C 63.79, H 7.89, S 4.43, Si 3.56, Sn 15.87.

1.13. Synthesis of (+)-(*S*)-(*E*)-[1-(2-Methoxynaphthalen-1-ylsulfinyl)hex-1-enyl]tributylstannane, SI-10.



SI-2 → **SI-10** (90) + **SI-11** (8) + **SI-12** (2)

From alkyne **SI-2** (576 mg, 2.09 mmol), Bu_3SnH (0.59 mL, 2.21 mmol) and $Pd(Ph_3P)_4$ (46 mg, 0.04 mmol) following the general procedure (3 h), a 90:8:2 mixture of compounds **SI-10**, **SI-11** and **SI-12** was obtained. Purification by chromatography (10-50% EtOAc-hexane) afforded **SI-10** (969 mg, 1.68 mmol, 80%), **SI-11** (80 mg, 0.14 mmol, 7%) and **SI-12** (28 mg, 0.05 mmol, 2%), all of them as colorless oils.

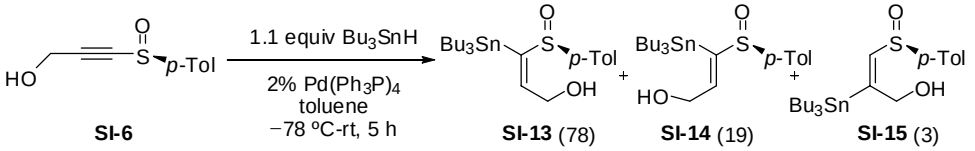
Data for **SI-10**: ***R*$_f$** = 0.35 (30% EtOAc-hexane); **[α]$^{20}_{D}$** = +142.6 (*c* = 1.99); **^{1}H NMR** (300 MHz) δ = 0.68 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 0.86 (t, *J* = 7.1 Hz, 9 H, 3 Me-*n*-Bu), 0.88-1.08 (m, 10 H), 1.21-1.34 (m, 6 H), 1.38-1.52 (m, 6 H), 1.92 (m, 1 H), 2.18 (m, 1 H), 3.97 (s, 3 H, OMe), 5.89 (t, *J*

= 7.1 Hz, 1 H, H-2), 7.22 (d, *J* = 9.0 Hz, 1 H, H-3'), 7.36 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1 H, H-6'), 7.50 (ddd, *J* = 8.3, 6.8, 1.5 Hz, 1 H, H-7'), 7.76 (dd, *J* = 8.1, 1.2 Hz, 1 H, H-5'), 7.90 (d, *J* = 9.0 Hz, 1 H, H-4'), 8.85 (dd, *J* = 8.5, 1.0 Hz, 1 H, H-8'); **^{13}C NMR** (75 MHz) δ = 11.8 (3 C), 13.7 (4 C), 22.1, 27.3, 28.9, 30.9, 31.9, 56.6, 113.0, 123.8, 124.3, 125.0, 127.6, 128.5, 129.4, 132.1, 133.9, 145.5, 155.7, 156.1; **IR** (film): 2955, 2925, 2870, 2854, 1621, 1594, 1507, 1465, 1430, 1333, 1271, 1250, 1150, 1136, 1066, 1024, 981, 811, 773, 748 cm^{-1}; **MS** (ES) m/z (%): 1155 $[2M+H]^+$, 521 (100) $[(M–Bu)+H]^+$; **Anal. calcd for** $C_{29}H_{46}O_2SSn$: C 60.32, H 8.03, S 5.55, Sn 20.56; **found**: C 60.56, H 8.25, S 5.34, Sn 20.71.

Data for **SI-11**: R_f = 0.14 (30% EtOAc-hexane); **$[\alpha]^{20}_D$** = –5.2 (*c* = 2.89); **^{1}H NMR** (300 MHz) δ = 0.67-0.95 (m, 19 H), 1.06-1.37 (m, 15 H), 2.46 (m, 2 H), 3.92 (s, 3 H, OMe), 6.97 (s, 1 H, H-1), 7.14 (d, *J* = 9.3 Hz, 1 H, H-3'), 7.28 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1 H, H-6'), 7.44 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1 H, H-7'), 7.68 (dd, *J* = 8.1, 0.7 Hz, 1 H, H-5'), 7.81 (d, *J* = 9.0 Hz, 1 H, H-4'), 8.74 (dd, *J* = 8.8, 0.7 Hz, 1 H, H-8'); **IR** (film): 2927, 2853, 1621, 1593, 1561, 1506, 1465, 1430, 1376, 1335, 1272, 1250, 1181, 1150, 1024, 865, 810, 774, 750 cm^{-1}; **Anal. calcd for** $C_{29}H_{46}O_2SSn$: C 60.32, H 8.03, S 5.55, Sn 20.56; **found**: C 60.22, H 7.86, S 5.35, Sn 20.68.

Data for **SI-12**: R_f = 0.19 (30% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 0.71 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 0.79 (t, *J* = 7.1 Hz, 9 H, 3 Me-*n*-Bu), 1.02-1.46 (m, 20 H), 1.87 (m, 2 H), 2.44 (m, 2 H), 4.00 (s, 3 H, OMe), 5.47 (t, *J* = 7.0 Hz, 1 H, H-2), 7.22 (d, *J* = 9.3 Hz, 1 H, H-3'), 7.37 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1 H, H-6'), 7.52 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1 H, H-7'), 7.77 (d, *J* = 8.1 Hz, 1 H, H-5'), 7.89 (d, *J* = 9.3 Hz, 1 H, H-4'), 8.94 (d, *J* = 8.5 Hz, 1 H, H-8'); **IR** (film): 2956, 2920, 2847, 1617, 1593, 1506, 1465, 1371, 1331, 1270, 1250, 1149, 1064, 1036, 810, 750 cm^{-1}; **Anal. calcd for** $C_{29}H_{46}O_2SSn$: C 60.32, H 8.03, S 5.55, Sn 20.56; **found**: C 60.15, H 8.18, S 5.76, Sn 20.65.

1.14. Synthesis of (±)-(*E*)-3-(Tributylstannyl)-3-(*p*-tolylsulfinyl)prop-2-en-1-ol, SI-13.



SI-6 **SI-13** (78) **SI-14** (19) **SI-15** (3)

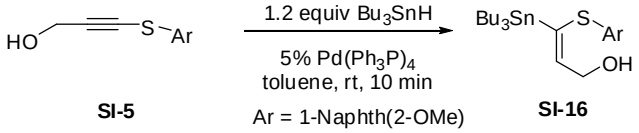
From alkyne **SI-6** (200 mg, 1.02 mmol), Bu_3SnH (0.36 mL, 1.12 mmol) and $Pd(PPh_3)_4$ (24 mg, 0.02 mmol) following the general procedure (5 h) a 78:19:3 mixture of stannanes **SI-13**, **SI-14** and **SI-15** was obtained. Purification by chromatography (10-40% EtOAc-hexane) afforded **SI-13** (237 mg, 0.49 mmol, 48%), 59 mg of a 32:68 mixture of **SI-13** and **SI-14**, and **SI-15** (10 mg, 0.02 mmol, 2%), all of them as colorless oils.

Data for **SI-13**: R_f = 0.38 (50% EtOAc-hexane); **^{1}H NMR** (200 MHz) δ = 0.80 (t, *J* = 7.1 Hz, 9 H, Me-*n*-Bu), 0.81 (m, 6 H), 1.13-1.39 (m, 12 H), 2.36 (s, 3 H, Me-*p*-Tol), 4.09 (dd, *J* = 7.0, 5.0 Hz, 1 H, OH), 4.33 (ddd, *J* = 14.5, 7.1, 4.4 Hz, 1 H, H-1), 4.71 (ddd, *J* = 14.6, 6.6, 4.8 Hz, 1 H, H-1), 6.38 (dd, *J* = 6.6, 4.4 Hz, 1 H, H-2), 7.24 (d, *J* = 8.2 Hz, 2 H, *p*-Tol), 7.44 (d, *J* = 8.2 Hz, 2 H, *p*-Tol); **Anal. calcd for** $C_{22}H_{38}O_2SSn$: C 54.45, H 7.89, S 6.61, Sn 24.46; **found**: C 54.23, H 7.75, S 6.34, Sn 24.65.

Data for **SI-14**: **^{1}H NMR** (200 MHz) δ = 0.60-0.95 (m, 3 H), 0.79 (t, *J* = 6.9 Hz, 9 H, Me-*n*-Bu), 1.07-1.36 (m, 15 H), 2.35 (s, 3 H, *p*-Tol), 2.93 (t, *J* = 5.5 Hz, 1 H, OH), 4.35 (ap t, *J* = 5.3 Hz, 2 H, H-1), 7.22 (d, *J* = 8.4 Hz, 2 H, *p*-Tol), 7.27 (t, *J* = 5.3 Hz, 1 H, H-2), 7.46 (d, *J* = 8.2 Hz, 2 H, *p*-Tol).

Partial data for **SI-15**: R_f = 0.10 (30% EtOAc-hexane); **^{1}H NMR** (200 MHz) δ = 2.38 (s, 3 H, Me-*p*-Tol), 2.87 (br s, 1 H, OH), 4.51 (ddd, *J* = 15.0, 6.0, 2.0 Hz, 1 H, H-1), 4.89 (ddd, *J* = 15.0, 4.9, 2.0 Hz, 1 H, H-1), 6.14 (t, *J* = 2.0 Hz, 1 H, H-3), 7.27 (d, *J* = 8.4 Hz, 2 H, *p*-Tol), 7.48 (d, *J* = 8.4 Hz, 2 H, *p*-Tol).

1.15. Synthesis of (*E*)-3-(2-Methoxynaphthalen-1-sulfenyl)-3-(tributylstannyl)prop-2-en-1-ol, SI-16.



SI-5 **SI-16**

From alkyne **SI-5** (456 mg, 1.87 mmol), Bu_3SnH (0.60 mL, 2.21 mmol) and $Pd(PPh_3)_4$ (108 mg, 0.09 mmol) following the general procedure (10 minutes) compound **SI-16** was obtained. Purification by chromatography (10-30% EtOAc-hexane) afforded **SI-16** (966 mg, 1.80 mmol, 96%) as a colorless oil.

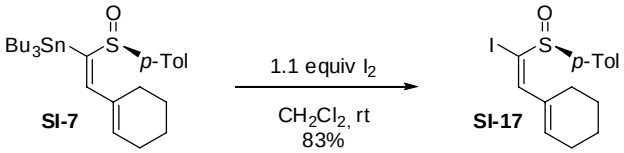
Data for **SI-16**: R_f = 0.38 (30% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 0.75 (t, *J* = 7.0 Hz, 9 H, Me-*n*-Bu), 1.00-1.30 (m, 18 H), 1.90-1.97 (m, 1 H, OH), 3.98 (s, 3 H, OMe), 4.55 (t, *J* = 5.7 Hz, 2 H, H-1), 6.01 (t, *J* = 5.7 Hz, 1 H, H-2), 7.25 (d, *J* = 9.1 Hz, 1 H, H-3'), 7.35 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1 H, H-6'), 7.50 (ddd, *J* = 8.5, 6.8, 1.3 Hz, 1 H, H-7'), 7.77 (d, *J* = 8.1 Hz, 1 H, H-5'), 7.86 (d, *J* = 9.1 Hz, 1 H, H-4'), 8.36 (d, *J* = 8.6 Hz, 1 H, H-8'); **^{13}C NMR** (75 MHz) δ = 10.3 (3 C), 13.5 (3 C), 27.2 (3 C), 28.5 (3 C), 56.4 (OMe), 60.0, 112.7, 115.9, 124.0, 125.7, 127.3, 127.9, 129.5, 131.2, 136.4, 139.6, 142.9, 158.4; **IR** (film): 3369, 2955, 2923, 2870, 2852, 1621, 1591, 1505, 1463, 1428, 1375, 1350, 1327, 1267, 1245, 1179, 1147, 1136, 1070, 1023, 960, 894, 863, 806, 771, 747 cm^{-1}; **MS** (ES) m/z (%): 559 $[M+Na]^+$, 519 (100) $[(M-18)+H]^+$; **Anal. calcd for** $C_{26}H_{40}O_2SSn$: C 58.33, H 7.53, S 5.99, Sn 22.17; **found**: C 58.54, H 7.29, S 6.18, Sn 21.97.

2. Synthesis of iodo vinyl sulfoxides.

2.1. General procedure for the synthesis of 1-iodo-1-sulfinyl alkenes.

To a solution of sulfinyl vinyl stannane in CH_2Cl_2 (5 mL/mmol sulfoxide) at rt under argon, a solution of I_2 (1.2 equiv) in CH_2Cl_2 (6 mL/mmol sulfoxide) was added. The mixture was stirred at rt until starting material disappearance (TLC), and then it was quenched with a $Na_2S_2O_4$ solution (2 mL/mmol, 1 M) and diluted with EtOAc. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 4 mL/mmol sulfoxide). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by column chromatography on silica gel.

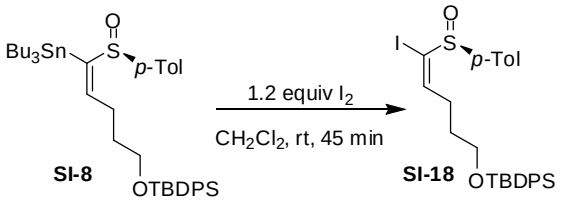
2.2. Synthesis of (–)-(*S*)-(*E*)-2-(Cyclohexen-1-yl)-1-(*p*-tolylsulfinyl)-1-iodoethene, SI-17.



From **SI-7** (253 mg, 0.47 mmol) and iodine (132 mg, 0.47 mmol), following the general procedure (45 min), iodide **SI-17** was obtained. Purification by chromatography (1-50% EtOAc-hexane) afforded **SI-17** (161 mg, 0.39 mmol, 83%) as a yellow oil.

Data for **SI-17**: $\boldsymbol{R_f}$ = 0.31 (20% EtOAc-hexane); $\boldsymbol{[\alpha]_D^{20}}$ = –27.2 (*c* = 1.68); **^{1}H NMR** (200 MHz) δ = 1.52-1.75 (m, 5 H), 2.17-2.34 (m, 2 H), 2.37 (s, 3 H, Me-*p*-Tol), 2.40-2.42 (m, 1 H), 6.07 (m, 1 H), 7.27 (m, 3 H, *J* = 8.5 Hz), 7.40 (d, 2 H, *J* = 8.3 Hz); **^{13}C NMR** (75 MHz) δ = 21.1, 21.2, 22.1, 26.1, 29.1, 112.5, 124.4 (2 C), 125.5, 129.4 (2 C), 135.9, 138.6, 141.0, 153.0; **IR** (film): 2928, 2859, 1711, 1611, 1595, 1561, 1491, 1447, 1430, 1302, 1262, 1177, 1083, 1057, 806 cm^{-1}; **MS** (ES) m/z (%): 745 $[2M+H]^+$, 373 $[M+H]^+$; **Anal. calcd for** $C_{15}H_{17}IOS$: C 48.40, H 4.60, I 34.0, S 8.61; **found**: C 48.14, H 4.35, I 33.86, S 8.47.

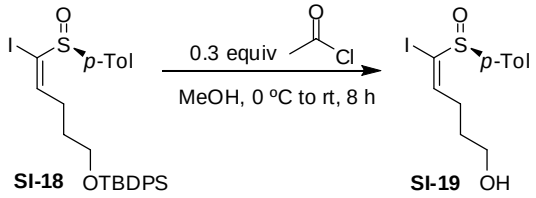
2.3. Synthesis of (–)-(*S*)-(*E*)-*tert*-Butyl-[5-iodo-5-(*p*-tolylsulfinyl)pent-4-enyloxy]diphenylsilane, SI-18.



From stannane **SI-8** (6.14 g, 8.12 mmol, 1.0 equiv), and iodine (2.49 g, 9.82 mmol, 1.2 equiv), following the general procedure (45 min) iodide **SI-18** was obtained. Purification by chromatography (5-30% EtOAc-hexane) afforded **SI-18** (4.20 g, 7.14 mmol, 88%) as a white solid that was recrystallized from EtOAc-hexane.

Data for **SI-18**: $\boldsymbol{R_f}$ = 0.31 (20% EtOAc-hexane); **mp** 77-79 ºC; $\boldsymbol{[\alpha]^{20}_D}$ = –62.4 (*c* = 2.12); **^{1}H NMR** (300 MHz) δ = 1.07 (s, 9 H, *t*-Bu),1.69-1.80 (m, 2 H, H-2), 2.39 (s, 3 H, Me-*p*-Tol), 2.70-2.92 (m, 2 H, H-3), 3.75 (td, *J* = 5.9, 1.6 Hz, 2 H, H-1), 6.85 (t, *J* = 7.9 Hz, 1 H, H-4), 7.27 (d, *J* = 7.9 Hz, 2 H), 7.36-7.46 (m, 8 H), 7.66-7.69 (m, 4 H); **^{13}C NMR** (75 MHz) δ = 19.1, 21.5, 26.8, 30.4, 31.6, 62.6, 114.8, 124.3 (2 C), 127.7 (4 C), 129.7 (2 C), 129.8 (2 C), 133.5, 135.5 (4 C), 139.9, 141.6, 151.3; **IR** (KBr): 3065, 2890, 2930, 2858, 1631, 1428, 1111, 1058, 808, 704, 615, 508 cm^{-1}; **MS** (ES) m/z (%): 611 (100) $[M+Na]^+$; **Anal. calcd for** $C_{28}H_{33}IO_2SSi$: C 57.13, H 5.65, S 5.45, I 21.56, Si 4.77; **found**: C 57.32, H 5.71, S 5.36, I 21.67.

2.4. Synthesis of (–)-(*S*)-[(*E*)-5-Iodo-5-(*p*-tolylsulfinyl)]pent-4-en-1-ol, SI-19.

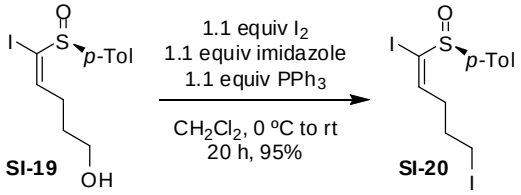


To a cold solution (0 ºC) of **SI-18** (4.203 g, 7.14 mmol, 1.0 equiv) in anhydrous MeOH (43 mL), acetyl chloride (0.15 mL, 2.14 mmol, 0.3 equiv) was slowly added. The reaction was allowed to reach room temperature and was stirred until starting material disappearance (TLC, 20 h). Then, the reaction mixture was diluted with CH_2Cl_2 and a saturated solution of $NaHCO_3$ was added. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 times). The organic layer was washed with water and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by chromatography (30-80% EtOAc-hexane) to afford **SI-19** (2.06 g, 5.89 mmol, 83%) as a colorless oil.

Data for **SI-19**: $\boldsymbol{R_f}$ = 0.24 (80% EtOAc-hexane); $\boldsymbol{[\alpha]^{20}_D}$ = –55.0 (*c* = 1.20); **^{1}H NMR** (300 MHz) δ = 1.78 (m, 2 H, H-2), 2.38 (s, 3 H, Me-*p*-Tol), 2.62-2.74 (m, 1 H, 1 H-3), 2.89-3.02 (m, 1 H, 1 H-3), 3.70 (br s, 1 H, OH), 3.73 (t, *J* = 5.9 Hz, 2 H, H-1), 6.86 (dd, *J* = 8.9, 7.1 Hz, 1 H, H-4), 7.28 (d, *J* = 8.1 Hz, 2 H), 7.43 (d, *J* = 8.1 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 21.5, 30.1, 31.4, 61.2, 114.2, 124.4 (2 C), 129.8 (2 C), 139.6, 141.8, 151.4; **IR** (film): 3401, 2920, 2868, 1594, 1489, 1444, 1084, 1053, 810 cm^{-1};

MS (ES) m/z (%): 723 $[2M+Na]^+$, 373 $[M+Na]^+$, 351 (100) $[M+H]^+$; **Anal. calcd for** $C_{12}H_{15}IO_2S$: C 41,15, H 4.32, S 9.16, I 36.24; **found**: C 41.06, H 4.24, S 9.27, I 36.48.

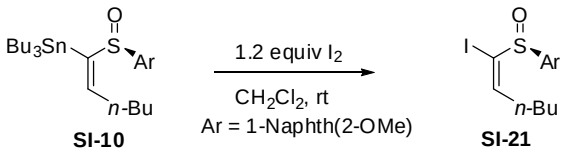
2.5. Synthesis of (–)-(*S*)-(*E*)-[1,5-Diiodo-1-(*p*-tolylsulfinyl)]pent-1-ene, SI-20.



To a cold solution (0 ºC) of PPh_3 (1.44 g, 5.50 mmol, 1.10 equiv) and imidazole (374 mg, 5.50 mmol, 1.10 equiv) in CH_2Cl_2 (15 mL), a solution of I_2 (1.39 g, 5.50 mmol, 1.10 equiv) in CH_2Cl_2 (10 mL) was added dropwise. The mixture was stirred at 0 ºC for 15 minutes and then, a solution of **SI-19** (1.74 g, 4.96 mmol, 1.00 equiv) in CH_2Cl_2 (25 mL) was added dropwise. The reaction was allowed to reach room temperature and stirred until starting material disappearance (TLC, 20 h). The crude product was filtered through a pad of celite and concentrated under reduced pressure. Purification by chromatography (5-50% EtOAc-hexane) afforded **SI-20** (2.17 g, 4.71 mmol, 95%) as a white solid that was recrystallized from EtOAc-hexane.

Data for **SI-20**: $\boldsymbol{R_f}$ = 0.25 (20% EtOAc-hexane); **mp** 65-67 ºC; $\boldsymbol{[\alpha]^{20}_D}$ = –90.6 (*c* = 0.57); **^{1}H NMR** (300 MHz) δ = 1.99-2.09 (m, 2 H, H-2), 2.38 (s, 3 H, Me-*p*-Tol), 2.68 (m, 1 H, 1 H-3), 2.87-2.99 (m, 1 H, 1 H-3), 3.16-3.30 (m, 2 H, H-1), 6.78 (dd, *J* = 8.8, 7.0 Hz, 1 H, H-4), 7.29 (d, *J* = 8.1 Hz, 2 H), 7.43 (d, *J* = 8.1 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 4.5 (C-1), 21.5, 32.1, 34.2, 116.3, 124.4 (2 C), 129.9 (2 C), 139.7, 141.9, 148.9; **IR** (KBr): 2019, 2846, 1593, 1427, 1219, 1086, 1058, 807 cm^{-1}; **MS** (ES) m/z (%): 943 $[2M+Na]^+$, 483 $[M+Na]^+$, 461 (100) $[M+H]^+$; **Anal. calcd for** $C_{12}H_{14}I_2OS$: C 31.32, H 3.07, S 6.97, I 55.16; **found**: C 31.25, H 3.34, S 6.76, I 55.27.

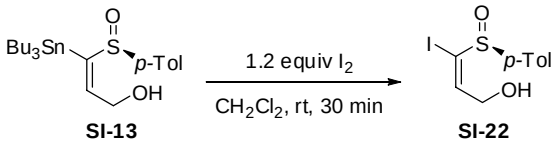
2.6. Synthesis of (–)-(*S*)-(*E*)-(2-Methoxynaphthalen-1-ylsulfinyl)-1-iodohex-1-ene, SI-21.



From stannane **SI-10** (900 mg, 1.56 mmol) and iodine (457 mg, 1.87 mmol) following the general procedure (30 minutes), compound **SI-21** was obtained. Purification by chromatography (2-50% EtOAc-hexane) afforded **SI-21** (577 mg, 1.39 mmol, 89%) as a colorless oil.

Data for **SI-21**: R_f = 0.16 (30% EtOAc-hexane); $[\alpha]^{20}_D$ = –66.6 (*c* = 1.02); **^{1}H NMR** (300 MHz) δ = 0.88 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 1.22-1.50 (m, 4 H, *n*-Bu), 2.44 (m, 1 H, H-3), 2.69 (m, 1 H, H-3), 3.95 (s, 3 H, OMe), 6.74 (dd, *J* = 8.3, 7.2 Hz, 1 H, H-2), 7.18 (d, *J* = 9.0 Hz, 1 H, H-3'), 7.37 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1 H, H-6'), 7.52 (ddd, *J* = 8.3, 6.8, 1.5 Hz, 1 H, H-7'), 7.75 (d, *J* = 8.3 Hz, 1 H, H-5'), 7.92 (d, *J* = 9.0 Hz, 1 H, H-4'), 9.43 (ddd, *J* = 8.8, 1.8, 0.8 Hz, 1 H, H-8'); **^{13}C NMR** (50 MHz) δ = 13.8 (Me-*n*-Bu), 22.2, 30.8, 32.8, 56.7 (OMe), 107.0, 112.1, 121.7, 123.9, 124.4, 127.5, 128.3, 129.5, 133.1, 134.4, 150.9, 155.8; **IR** (film): 3047, 3004, 2956, 2927, 2857, 1620, 1593, 1560, 1507, 1465, 1430, 1377, 1352, 1333, 1272, 1251, 1216, 1181, 1151, 1134, 1061, 1024, 977, 898, 863, 811, 770, 750, 710 cm^{-1}; **MS** (ES) m/z (%): 851 $[2M+Na]^+$, 437 $[M+Na]^+$, 415 (100) $[M+H]^+$; **Anal. calcd for** $C_{17}H_{19}IO_2S$: C 49.28, H 4.62, S 7.74, I 30.63; **found**: C 49.36, H 4.75, S 7.58, I 30.47.

2.7. Synthesis of (±)-(*E*)-3-(*p*-Tolylsulfinyl)-3-iodoprop-2-en-1-ol, SI-22.

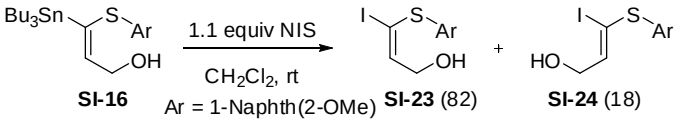


SI-13 **SI-22**

From stannane **SI-13** (137 mg, 0.49 mmol) and iodine (150 mg, 0.29 mmol) following the general procedure (30 minutes), compound **SI-22** was obtained. Purification by chromatography (10-50% EtOAc-hexane) afforded **SI-22** (73 mg, 0.23 mmol, 47%) as a white solid that was recrystallized from EtOAc-hexane.

Data for **SI-22**: R_f = 0.31 (50% EtOAc-hexane); **^{1}H NMR** (200 MHz) δ = 2.38 (s, 3 H, Me-*p*-Tol), 3.93 (dd, *J* = 7.3, 4.8 Hz, 1 H, OH), 4.41 (ddd, *J* = 14.3, 7.3, 5.3 Hz, 1 H, H-1), 4.80 (ddd, *J* = 14.3, 7.7, 4.2 Hz, 1 H, H-1), 7.06 (dd, *J* = 7.7, 5.3 Hz, 1 H, H-2), 7.28 (d, *J* = 8.4 Hz, 2 H, *p*-Tol), 7.47 (d, *J* = 8.2 Hz, 2 H, *p*-Tol); **Anal. calcd for** $C_{10}H_{11}IO_2S$: C 37.28, H 3.44, S 9.95, I 39.39; **found**: C 37.40, H 3.54, S 9.83, I 39.41.

2.8. Synthesis of (*E*)-3-(2-Methoxynaphthalen-1-ylsulfenyl)-3-iodoprop-2-en-1-ol, SI-23.



SI-16 **SI-23** (82) **SI-24** (18)

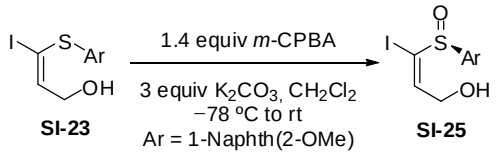
From stannane **SI-16** (966 mg, 1.08 mmol, 1.0 equiv) and *N*-iodosuccinimide (445 mg, 1.98 mmol, 1.1 equiv), following the general procedure (10 min), an 82:18 mixture of **SI-23** and **SI-24** was obtained. Purification by chromatography (10-50% EtOAc-hexane) afforded **SI-16** (112 mg, 0.21

mmol, 12%), **SI-23** (100 mg, 0.27 mmol, 15%), 390 mg (1.05 mmol, 58%) of a mixture of **SI-23** and **SI-24** and pure **SI-24** (70 mg, 0.19 mmol, 10%), all of them as colorless oils.

Data for **SI-23**: R_f = 0.12 (30% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 2.09 (br s, 1 H, OH), 4.01 (s, 3 H, OMe), 4.46 (m, 2 H, H-1), 6.84 (t, *J* = 6.6 Hz, 1 H, H-2), 7.29 (d, *J* = 9.0 Hz, 1 H, H-3'), 7.39 (ddd, *J* = 8.1, 6.8, 1.0 Hz, 1 H, H-6'), 7.56 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1 H, H-7'), 7.81 (d, *J* = 8.1 Hz, 1 H, H-5'), 8.00 (d, *J* = 9.0 Hz, 1 H, H-4'), 8.33 (dd, *J* = 8.5, 1.0 Hz, 1 H, H-8'); **^{13}C NMR** (75 MHz) δ = 56.9 (OMe), 62.0 (C-1), 92.8 (C-3), 113.2, 115.5, 124.2, 124.9, 127.6, 128.3, 129.4, 132.4, 135.5, 144.6, 158.8; **IR** (film): 3436, 2928, 1622, 1505, 1464, 1269, 1148, 1066, 808, 747 cm^{-1}; **MS** (ES) m/z (%): 395 $[M+Na]^+$, 373 (100) $[M+H]^+$; **Anal. calcd for** $C_{14}H_{13}IO_2S$: C 45.17, H 3.52, S 8.61, I 34.09; **found**: C 45.34, H 3.62, S 8.71, I 33.87.

Data for **SI-24**: R_f = 0.11 (30% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 1.26 (br s, 1 H, OH), 4.00 (s, 3 H, OMe), 4.09 (m, 2 H, H-1), 5.64 (t, *J* = 6.2 Hz, 1 H, H-2), 7.32 (d, *J* = 9.0 Hz, 1 H, H-3'), 7.38 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1 H, H-6'), 7.55 (ddd, *J* = 8.3, 6.8, 1.2 Hz, 1 H, H-7'), 7.80 (d, *J* = 8.1 Hz, 1 H, H-5'), 7.98 (d, *J* = 9.0 Hz, 1 H, H-4'), 8.34 (d, *J* = 8.5 Hz, 1 H, H-8'); **IR** (film): 3435, 2925, 1622, 1505, 1464, 1268, 1147, 1065, 808, 747 cm^{-1}; **MS** (ES) m/z (%): 355 (100) $[(M-18)+1]^+$; **Anal. calcd for** $C_{14}H_{13}IO_2S$: C 45.17, H 3.52, I 34.09, S 8.61; **found**: C 45.06, H 3.63, I 33.86, S 8.87.

2.9. Synthesis of (±)-(*E*)-3-(2-Methoxynaphthalen-1-ylsulfinyl)-3-iodoprop-2-en-1-ol, SI-25.

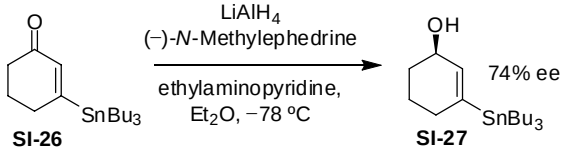


From iodide **SI-23** (259 mg, 0.07 mmol), *m*-CPBA (242 mg, 0.98 mmol) and K_2CO_3 (278 mg, 2.1 mmol), following the general procedure, compound **SI-25** was obtained along with a complex mixture of byproducts. Purification by chromatography (10-30% EtOAc-CH_2Cl_2) afforded **SI-25** (100 mg, 0.26 mmol, 37%) as a white solid that was recrystallized from EtOAc-hexane.

Data for **SI-25**: R_f = 0.12 (20% EtOAc-CH_2Cl_2); **mp** 177-178 ºC; **^{1}H NMR** (300 MHz) δ = 3.02 (t, *J* = 6.5 Hz, 1 H, OH), 4.04 (s, 3 H, OMe), 4.49 (dt, *J* = 13.9, 6.8 Hz, 1 H, H-1), 4.64 (dt, *J* = 13.9, 6.6 Hz, 1 H, H-1), 7.10 (t, *J* = 6.8 Hz, 1 H, H-2), 7.26 (d, *J* = 9.3 Hz, 1 H, H-3'), 7.42 (ddd, *J* = 8.3, 6.8, 1.2 Hz, 1 H, H-6'), 7.58 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1 H, H-7'), 7.80 (d, *J* = 8.1 Hz, 1 H, H-5'), 8.00 (d, *J* = 9.0 Hz, 1 H, H-4'), 8.96 (dd, *J* = 8.8, 1.0 Hz, 1 H, H-8'); **^{13}C NMR** (75 MHz) δ = 56.9 (OMe), 60.9 (C-1), 104.1 (C-3), 112.9, 121.4, 123.5, 124.7, 128.2, 128.6, 129.2, 133.1, 135.3, 148.8, 156.9; **IR** (KBr): 3399, 1618, 1592, 1507, 1467, 1429, 1278, 1253, 1211, 1152, 1133, 1044, 1024, 821, 768, 750

cm^{-1}; **MS** (ES) m/z (%): 799 $[2M+Na]^+$, 427 (100) $[M+K]^+$, 389 $[M+H]^+$; **Anal. calcd for** $C_{14}H_{13}IO_3S$: C 43.31, H 3.38, I 32.69, S 8.26; **found**: C 43.46, H 3.05, I 32.44, S 8.51.

3. Synthesis of (+)-(*R*)-3-(Tributylstannyl)cyclohex-2-enol, SI-27.



SI-26 **SI-27**

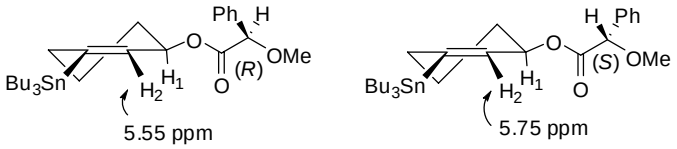
To an argon filled flask containing Et_2O (5 mL/mmol enone), $LiAlH_4$ (76 mg, 2.01 mmol, 3.3 equiv) was slowly added to generate a suspension. Then a solution of (−)-*N*-methylephedrine (393 mg, 2.2 mmol, 3.6 equiv) in Et_2O (3 mL/mmol enone) was added. The mixture was then heated to reflux for 1 h before a solution of ethylaminopyridine (537 mg, 4.40 mmol, 7.2 equiv) in Et_2O (3 mL/mmol) was added. The reflux was maintained for 1 h and then the reaction mixture was cooled to −78 ºC. At this temperature, a solution of enone **SI-26** (220 mg, 0.61 mmol, 1.0 equiv) in Et_2O (1 mL/mmol) was added dropwise. The resulting mixture was stirred at −78 ºC until starting material disappearance (TLC) and then quenched at low temperature with MeOH. The mixture was allowed to warm up to room temperature, diluted with EtOAc and stirred 45 minutes with a 1.0 M solution of Rochelle's salt. The phases were separated, the aqueous layer was extracted twice with Et_2O and the combined organic extracts were washed with 10% aqueous HCl solution, a saturated solution of $NaHCO_3$ and brine. Then organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give a crude product that was purified by chromatography (2-50% EtOAc-hexane) to give **SI-27** (130 mg, 0.33 mmol, 55%) as a colorless oil.

Data for **SI-27**: R_f = 0.26 (10% EtOAc-hexane); $[\alpha]^{20}_D$ = +31.1 (*c* = 0.55); **^{1}H NMR** (300 MHz): δ = 0.73-0.95 (m, 6 H), 0.85 (t, *J* = 7.1 Hz, 9 H), 1.26 (sext, *J* = 7.2 Hz, 6 H), 1.39-1.47 (m, 6 H), 1.50-1.60 (m, 2 H), 1.63-1.72 (m, 1 H), 1.82-1.90 (m, 1 H), 2.01-2.19 (m, 2 H), 4.10 (br s, 1 H, H-1), 5.71-5.93 (m, J_{Sn-H} = 64.6 Hz, 1 H, H-2); **^{13}C NMR** (75 MHz) δ = 8.8, 13.6, 20.3, 27.3, 29.1, 31.8, 32.1, 66.5, 139.4, 145.1; **IR** (film): 3307, 2956, 2926, 2871, 2855, 1464, 1418, 1376, 1341, 1291, 1180, 1156, 1068, 1012, 963, 941, 906, 863, 688, 661 cm^{-1}; **HRMS** (ES) calcd for $C_{18}H_{36}NaOSn$ $[M+Na]^+$: 411.1686; **found**: 411.1679.

3.1. Absolute stereochemistry determination of SI-27.

To determine the absolute configuration of **SI-27**, we synthesized the methoxyphenyl acetates. To a cold (0 ºC) solution of **SI-27** (7 mg, 0.019 mmol) in CH_2Cl_2 (10 mL/mmol), (+)-2-methoxy-2-phenylacetic acid (3.5 mg, 0.021 mmol, 1.1 equiv), DMAP (1 mg, 0.009 mmol, 0.5 equiv) and DCC

(4.3 mg, 0.021 mmol, 1.1 equiv) were added. The mixture was allowed to warm up to room temperature until starting material disappearance (TLC). Then the reaction mixture was filtered and H_2O was added. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (twice). The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by column chromatography (1-5% EtOAc-hexane) afforded (+)-(*R*)-3-(tributylstannyl)cyclohex-2-enyl-(*S*)-2-methoxy-2-phenylacetate (5 mg, 0.0009 mmol, 49%) as a colorless oil with 74% ee. In an identical experiment with (±)-2-methoxy-2-phenyl acetic acid a mixture of (*R*)-3-(tributylstannyl)cyclohex-2-enyl-(*S*)-2-methoxy-2-phenylacetate and (*R*)-3-(tributylstannyl)cyclohex-2-enyl-(*R*)-2-methoxy-2-phenylacetate was obtained. Previous studies have shown that in the L_2L_1CH-CO-CHPh-OMe fragment the preferred conformer is that where the C-OMe bond, the C=O and the C1-H_1 bond are nearly eclipsed.[13] In the (*R*)-2-methoxy-2-phenylacetate H_2 is upfield due to the shielding effect of the phenyl group.



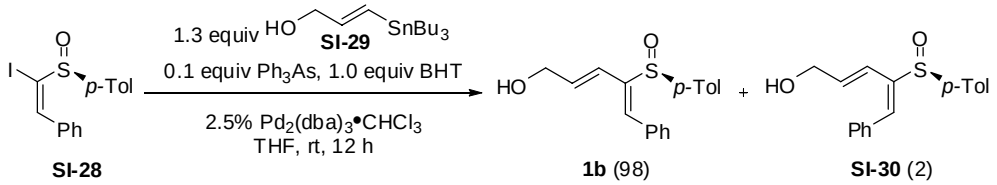
Data for (+)-(*R*)-3-(tributylstannyl)cyclohex-2-enyl-(*S*)-2-methoxy-2-phenylacetate (74% ee): $\boldsymbol{R_f}$ = 0.48 (10% EtOAc-hexane); $\boldsymbol{[\alpha]^{20}_D}$ = +6.14 (*c* = 0.72); **^{1}H NMR** (300 MHz) δ = 0.74-0.97 (m, 6 H), 0.87 (t, *J* = 7.2 Hz, 9 H), 1.28 (sext, *J* = 7.1 Hz, 6 H), 1.40-1.54 (m, 9 H), 1.66-1.75 (m, 1 H), 2.01-2.22 (m, 2 H), 3.41 (s, 3 H, MeO), 4.75 (s, 1 H), 5.25 (m, 1 H, H-1), 5.75 (m, $J_{Sn\text{-}H}$ = 61.2 Hz, 1 H), 7.29-7.37 (m), 7.41-7.45 (m); **^{13}C NMR** (100 MHz) δ = 9.0, 13.7, 19.9, 27.3, 28.1, 29.1, 31.6, 57.3, 69.7, 82.7, 127.2, 128.5, 128.6, 134.1, 136.5, 148.6, 170.5; **IR** (film): 2927, 1746, 1455, 1249, 1174, 1115, 1018, 913, 696 cm^{-1}; **HRMS** (ES) calcd for $C_{27}H_{44}NaO_3Sn$ $[M+Na]^+$: 559.2210; **found**: 559.2229.

4. Synthesis of hydroxy 4-sulfinyl butadienes.

4.1. General procedure for the synthesis of hydroxy 4-sulfinyl butadienes.

To a solution of sulfinyl vinyl iodide in THF (10 mL/mmol sulfoxide) at room temperature, 1.0 equiv of 2,6-di-*tert*-butyl-4-methyphenol (BHT), 0.2 equiv of Ph_3As and 1.2-1.5 equiv of the corresponding hydroxy vinyl stannane were added. Argon was bubbled through the solution for 10 min and 0.05-0.10 equiv of $Pd_2(dba)_3{\cdot}CHCl_3$ was added. The mixture was stirred at room temperature until starting material disappearance. The solvent was then evaporated and the crude was purified by column chromatography on silica gel. Treatment of SiO_2 with 1-2% of Et_3N afforded less-colored products.

4.2. Synthesis of (–)-(*S*)-2-(*E*)-4-(*Z*)-5-Phenyl-4-(*p*-tolylsulfinyl)penta-2,4-dien-1-ol, 1b.

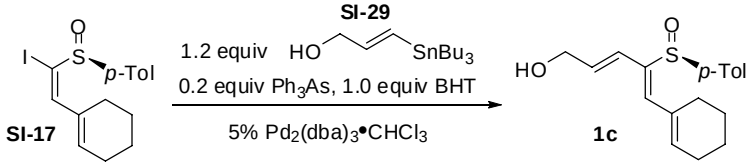


From iodide **SI-28** (5.06 g, 13.74 mmol, 1.00 equiv), stannane **SI-29** (6.20 g, 17.86 mmol, 1.30 equiv), BHT (3.03 g, 13.74 mmol, 1.00 equiv), Ph_3As (421 mg, 1.37 mmol, 0.10 equiv) and $Pd_2(dba)_3{\cdot}CHCl_3$ (356 mg, 0.34 mmol, 0.025 equiv) following the general procedure (12 h), a 98:2 mixture of **1b** and isomerized diene **SI-30** was obtained. Purification by chromatography (5-80% EtOAc-hexane) afforded **1b** (3.10 g, 10.39 mmol, 76%) and **SI-30** (57 mg, 0.19 mmol, 1%), both as pale brown solids that were recrystallized from EtOAc-hexane.

Data for **1b**: $\boldsymbol{R_f}$ = 0.30 (80% EtOAc-hexane); **mp** 123-125 ºC; $\boldsymbol{[\alpha]^{20}_D}$ = –377.1 (*c* = 0.55); **^{1}H NMR** (300 MHz) δ = 1.64 (br s, 1 H, OH), 2.37 (s, 3 H, Me-*p*-Tol), 4.14 (tm, *J* = 4.9 Hz, 2 H, H-1), 6.25 (ddd, *J* = 15.6, 2.1, 1.3 Hz, 1 H, H-3), 6.35 (dt, *J* = 15.6, 4.8 Hz, 1 H, H-2), 7.26 (m, 3 H), 7.34-7.43 (m, 5 H), 7.51 (m, 2 H); **^{13}C NMR** (50 MHz) δ = 21.3 (Me-*p*-Tol), 63.1 (C-1), 121.9, 124.5 (2 C), 128.6 (2 C), 129.0, 129.9 (2 C), 130.0 (2 C), 134.0, 135.1, 135.3, 140.8, 143.1, 153.7; **IR** (KBr): 3357, 3051, 2897, 2833, 1638, 1489, 1445, 1422, 1353, 1285, 1204, 1176, 1106, 1076, 1026, 1013, 959, 928, 910, 890, 810, 774, 758 cm^{-1}; **MS** (ES) m/z (%): 619 $[2M+Na]^+$, 597 $[2M+H]^+$, 321 $[M+Na]^+$, 299 (100) $[M+H]^+$; **Anal. calcd for** $C_{18}H_{18}O_2S$: C 72.45, H 6.08, S 10.75; **found**: C 72.75, H 6.17, S 10.46.

Data for **SI-30**: $\boldsymbol{R_f}$ = 0.23 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 1.60 (br s, 1 H, OH), 2.34 (s, 3 H, Me-*p*-Tol), 4.13 (dd, *J* = 5.1, 1.7 Hz, 2 H, H-1), 6.15 (dt, *J* = 16.3, 5.1 Hz, 1 H, H-2), 6.41 (ddd, *J* = 16.3, 2.9, 1.5 Hz, 1 H, H-3), 7.21 (d, *J* = 8.1 Hz, 2 H), 7.26-7.38 (m, 4 H), 7.42 (m, 2 H), 7.53 (d, *J* = 8.3 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 21.4 (Me-*p*-Tol), 63.0 (C-1), 121.2, 125.9 (2 C), 128.6 (2 C), 128.7, 129.6 (2 C), 129.9 (2 C), 130.3, 134.6, 135.5, 140.3, 140.7, 141.9; **MS** (ES) m/z (%): 597 $[2M+H]^+$, 299 (100) $[M+H]^+$; **Anal. calcd for** $C_{18}H_{18}O_2S$: C 72.45, H 6.08, S 10.75; **found**: C 72.53, H 6.25, S 10.67.

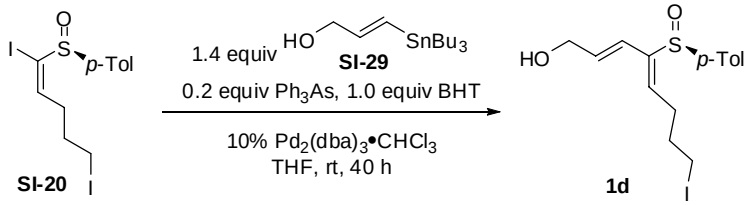
4.3. Synthesis of (–)-(*S*)-2-(*E*)-4-(*Z*)-5-(Cyclohex-1-enyl)-4-(*p*-tolylsulfinyl)penta-2,4-dien-1-ol, 1c.



From iodide **SI-17** (129 mg, 0.35 mmol, 1.0 equiv), stannane **SI-29** (156 mg, 0.45 mmol, 1.3 equiv), BHT (77 mg, 0.35 mmol, 1.0 equiv), Ph_3As (21 mg, 0.07 mmol, 0.20 equiv) and $Pd_2(dba)_3{\cdot}CHCl_3$ (18 mg, 0.017 mmol, 0.05 equiv), following the general procedure (4 h), diene **1c** was obtained. Purification by chromatography (1-50% EtOAc-hexane) afforded **1c** (101 mg, 0.33 mmol, 95%) as a pale brown oil.

Data for **1c**: $\boldsymbol{R_f}$ = 0.11 (60% EtOAc-hexane); $\boldsymbol{[\alpha]_D^{20}}$ = –10.9 (*c* = 1.28); **^{1}H NMR** (300 MHz) δ = 1.53-1.78 (m, 6 H), 2.21-2.26 (m, 2 H), 2.37 (s, 3 H, Me-*p*-Tol), 4.07 (d, 2 H, *J* = 3.8 Hz, H-1), 6.05-6.08 (m, 1 H), 6.13-6.16 (m, 2 H), 6.68 (s, 1 H), 7.26 (d, 2 H, *J* = 8.4 Hz), 7.42 (d, 2 H, *J* = 8.3 Hz); **^{13}C NMR** (75 MHz) δ = 21.3, 21.5, 22.5, 26.4, 29.5, 63.3, 122.9, 124.6 (2 C), 129.8 (2 C), 133.2, 134.1, 137.2, 138.5, 139.1, 140.1, 140.4; **IR** (film): 3436, 2928, 2859, 1638, 1491, 1448, 1178, 1080, 1033, 1013, 809 cm^{-1}. **MS** (ES) m/z (%): 341 $[M+K]^+$, 325 $[M+Na]^+$, 303 $[M+H]^+$; **Anal. calcd for** $C_{18}H_{22}O_2S$: C 71.48, H 7.33, S 10.60; **found**: C 71.26, H 7.57, S 10.48.

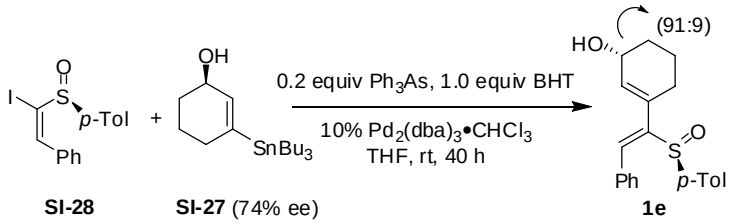
4.4. Synthesis of (–)-(*S*)-2-(*E*)-4-(*Z*)-8-Iodo-4-(*p*-tolylsulfinyl)octa-2,4-dien-1-ol, 1d.



From **SI-20** (1.145 g, 2.48 mmol, 1.0 equiv), stannane **SI-29** (1.207 g, 3.48 mmol, 1.4 equiv), Ph_3As (150 mg, 0.50 mmol, 0.2 equiv), BHT (546 mg, 2.49 mmol, 1.00 equiv) and $Pd_2(dba)_3{\cdot}CHCl_3$ (259 mg, 0.25 mmol, 0.1 equiv), following the general procedure, diene **1d** was obtained. Purification by chromatography (30-90% EtOAc-hexane) afforded **1d** (765 mg, 1.96 mmol, 79%) as a white solid that was recrystallized from EtOAc-hexane.

Data for **1d**: $\boldsymbol{R_f}$ = 0.27 (80% EtOAc-hexane); **mp** 69-71 ºC; $\boldsymbol{[\alpha]^{20}_D}$ = –119.6 (*c* = 1.01); **^{1}H NMR** (300 MHz) δ = 2.03 (ap quint, *J* = 6.9 Hz, 2 H, H-7), 2.37 (s, 3 H, Me-*p*-Tol), 2.62 (m, 1 H, 1 H-6), 2.38 (m, 1 H, 1 H-6), 3.16-3.29 (m, 2 H, H-8), 4.07 (d, *J* = 4.4 Hz, 2 H, H-1), 6.04-6.19 (m, 3 H), 7.27 (d, *J* = 8.2 Hz, 2 H), 7.41 (d, *J* = 8.2 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 5.1 (C-8), 21.3, 29.6, 32.8, 63.0, 121.3, 124.2 (2 C), 129.9 (2 C), 134.2, 135.5, 139.3, 140.9, 143.7; **IR** (KBr): 3391, 2921, 2857, 1595, 1491, 1445, 1222, 1081, 1040, 809 cm^{-1}; **MS** (ES) m/z (%): 803 $[2M+Na]^+$, 781 $[2M+H]^+$, 413 $[M+Na]^+$, 391 (100) $[M+H]^+$; **Anal. calcd for** $C_{15}H_{19}IO_2S$: C 46.16, H 4.91, S 8.22, I 32.52; **found**: C 45.93, H 4.83, S 8.17, I 32.71.

4.5. Synthesis of (–)-(*R*,*S*$_S$)-3-[(*Z*)-2-Phenyl-1-(*p*-tolylsulfinyl)vinyl]cyclohex-2-enol, 1e.

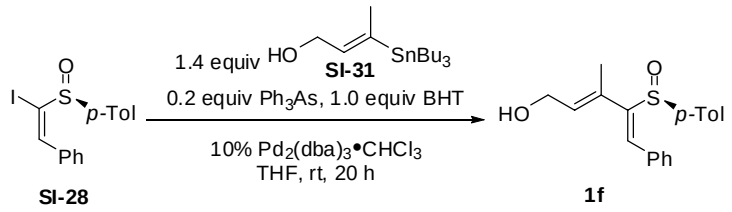


SI-28 **SI-27** (74% ee) **1e**

From **SI-28** (88 mg, 0.24 mmol, 1.0 equiv), stannane **SI-27** (137 mg, 0.35 mmol, 1.5 equiv), Ph_3As (14 mg, 0.048 mmol, 0.2 equiv), BHT (53 mg, 0.24 mmol, 1.0 equiv) and $Pd_2(dba)_3{\cdot}CHCl_3$ (24 mg, 0.024 mmol, 0.1 equiv), following the general procedure (20 h), diene **1e** was obtained. Purification by chromatography (1-80% EtOAc-hexane) afforded **1e** (58 mg, 0.17 mmol, 71%) as a 91:9 mixture of diastereomers, epimers at the allylic stereocenter. This result shows that a partial kinetic resolution is taking place during the Stille coupling.

Data for **1e**: $\boldsymbol{R_f}$ = 0.28 (80% EtOAc-hexane); $\boldsymbol{[\alpha]^{20}_D}$ = –143.0 (*c* = 0.82); **^{1}H NMR** (300 MHz) δ = 1.36-1.61 (m, 4 H), 1.69-1.82 (m, 1 H), 2.04-2.12 (m, 1 H), 2.37 (s, 3 H, Me-*p*-Tol), 4.07-4.11 (m, 1 H, H-1), 5.86-5.87 (m, 1 H, H-2), 7.13 (s, 1 H), 7.22-7.25 (m, 2 H), 7.35-7.40 (m, 5 H), 7.53-7.55 (m, 2 H); **^{13}C NMR** (75 MHz) δ = 19.1, 21.3, 29.6, 30.8, 65.5, 124.5 (2 C), 128.4 (2 C), 128.7, 129.4 (2 C), 129.8 (2 C), 132.6, 133.9, 134.8, 137.8, 139.3, 140.5, 146.6; **IR** (film): 3386, 3053, 2934, 2860, 1595, 1491, 1446, 1341, 1266, 1215, 1179, 1080, 1036, 1014, 984, 961, 915, 809, 751, 735, 696 cm^{-1}; **HRMS** (ES) calcd for $C_{21}H_{22}NaO_2S$ $[M+Na]^+$: 361.1238; **found**: 361.1235 $[M+Na]^+$.

4.6. Synthesis of (–)-(*S*)-2-(*E*)-4-(*Z*)-3-Methyl-5-phenyl-4-(*p*-tolylsulfinyl)penta-2,4-dien-1-ol, 1f.



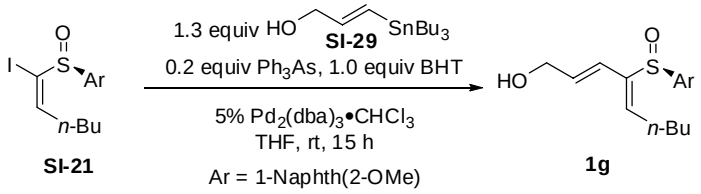
SI-28 **1f**

From **SI-28** (51 mg, 0.14 mmol, 1.0 equiv), stannane **SI-31** (69 mg, 0.19 mmol, 1.4 equiv), Ph_3As (8 mg, 0.028 mmol, 0.1 equiv), BHT (31 mg, 0.14 mmol, 1.0 equiv) and $Pd_2(dba)_3{\cdot}CHCl_3$ (15 mg, 0.014 mmol, 0.1 equiv), following the general procedure (20 h), diene **1f** was obtained. Purification by chromatography (20-80% EtOAc-hexane) afforded **1f** (44 mg, 0.14 mmol, 100%) as a brown oil.

Data for **1f**: $\boldsymbol{R_f}$ = 0.31 (80% EtOAc-hexane); $\boldsymbol{[\alpha]^{20}_D}$ = –218.5 (*c* = 0.82); **^{1}H NMR** (300 MHz) δ = 1.63 (s, 3 H, Me), 2.36 (s, 3 H, Me-*p*-Tol), 4.09 (dm, *J* = 6.5 Hz, 2 H, H-1), 5.73 (tq, *J* = 6.6, 1.3 Hz, 1 H, H-2), 7.13 (s, 1 H, H-5), 7.23 (d, *J* = 7.2 Hz, 2 H), 7.35-7.43 (m, 5 H), 7.2 (d, *J* = 7.2 Hz, 2 H); **^{13}C**

NMR (75 MHz) δ = 17.6 (Me), 21.2 (Me), 58.9 (C-1), 124.4 (2 C), 128.5 (2 C), 128.7, 129.6 (2 C), 129.8 (2 C), 131.9, 132.7, 133.9, 137.7, 139.2, 140.6, 147.9; **IR** (film): 3420, 3016, 2920, 1624, 1491, 1445, 1287, 1081, 1028, 1010, 809, 752, 697, 628, 572, 495 cm^{-1}; **MS** (ES) m/z (%): 313 $[M+H]^+$, 335 $[M+Na]^+$, 625 $[2M+H]^+$, 647 (100) $[2M+Na]^+$; **Anal. calcd for** $C_{19}H_{20}O_2S$: C 73.04, H 6.45, S 10.26; **found**: C 73.12, H 6.52, S 10.45.

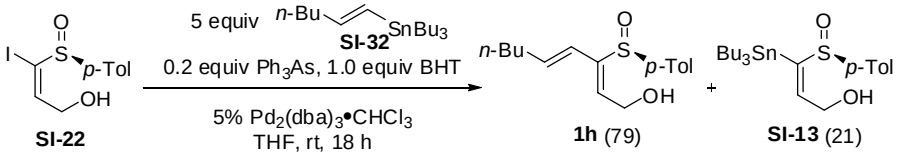
4.7. Synthesis of (–)-(*R*)-2-(*E*)-4-(*Z*)-4-(2-Methoxynaphthalen-1-ylsulfinyl)nona-2,4-dien-1-ol, 1g.



From iodide **SI-21** (339 mg, 0.82 mmol, 1.00 equiv), stannane **SI-29** (379 mg, 1.07 mmol, 1.3 equiv), BHT (181 mg, 0.82 mmol, 1.00 equiv), Ph_3As (50 mg, 0.16 mmol, 0.20 equiv) and $Pd_2(dba)_3{\cdot}CHCl_3$ (42 mg, 0.04 mmol, 0.05 equiv) following the general procedure (15 h), diene **1g** was obtained. Purification by chromatography (5-80% EtOAc-hexane) afforded **1g** (253 mg, 0.73 mmol, 89%) as a yellow oil.

Data for **1g**: R_f = 0.12 (80% EtOAc-hexane); $[\alpha]^{20}_D$ = –26.1 (*c* = 0.64); **^{1}H NMR** (300 MHz) δ = 0.79 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 1.09-1.36 (m, 4 H, *n*-Bu), 1.43 (m, 1 H, OH), 2.16 (m, 1 H, H-6), 2.47 (m, 1 H, H-6), 3.95 (s, 3 H, OMe), 4.07 (m, 2 H, H-1), 6.00 (dt, *J* = 15.6, 5.6 Hz, 1 H, H-2), 6.05 (t, *J* = 7.7 Hz, 1 H, H-5), 6.62 (dd, *J* = 15.6, 1.0 Hz, 1 H, H-3), 7.21 (d, *J* = 9.0 Hz, 1 H, H-3'), 7.37 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1 H, H-6'), 7.52 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1 H, H-7'), 7.76 (dd, *J* = 8.1, 0.7 Hz, 1 H, H-5'), 7.91 (d, *J* = 9.0 Hz, 1 H, H-4'), 9.09 (d, *J* = 8.3 Hz, 1 H, H-8'); **^{13}C NMR** (75 MHz) δ = 13.8 (Me-*n*-Bu), 22.3, 28.5, 31.1, 56.5 (OMe), 63.4, 112.8, 122.3, 123.0, 124.4, 124.7, 127.7, 128.6, 129.2, 131.8, 133.0, 134.0, 134.6, 142.2, 156.0; **IR** (film): 3370, 2956, 2926, 2853, 1621, 1593, 1561, 1507, 1466, 1430, 1352, 1334, 1272, 1251, 1151, 1135, 1096, 1023, 966, 812, 751 cm^{-1}; **MS** (ES) m/z (%): 711 $[2M+Na]^+$, 367 $[M+Na]^+$, 345 (100) $[M+H]^+$; **Anal. calcd for** $C_{20}H_{24}O_3S$: C 69.73, H 7.02, S 9.31; **found**: C 69.87, H 7.13, S 9.35.

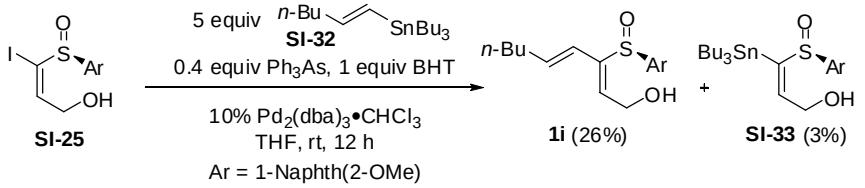
4.8. Synthesis of (±)-2-(*Z*)-4-(*E*)-4-(*p*-Tolylsulfinyl)nona-2,4-dien-1-ol, 1h.



From iodide **SI-22** (43 mg, 0.133 mmol, 1.0 equiv), stannane **SI-32** (248 mg, 0.665 mmol, 5.0 equiv),[14] BHT (29 mg, 0.133 mmol, 1.0 equiv), Ph_3As (8 mg, 0.027 mmol, 0.2 equiv) and $Pd_2(dba)_3{\cdot}CHCl_3$ (7 mg, 0.007 mmol, 0.05 equiv) following the general procedure (18 h), a 79:21 mixture of **1h** and **SI-13** was obtained. Purification by chromatography (CH_2Cl_2-20% EtOAc-CH_2Cl_2) afforded **1h** (20 mg, 0.074 mmol, 56%) and **SI-13** (10 mg, 0.02 mmol, 15%).

Data for **1h**: R_f = 0.16 (50% EtOAc-hexane); **^{1}H NMR** (200 MHz) δ = 0.79 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 1.03-1.32 (m, 4 H), 1.99 (ap q, *J* = 6.6 Hz, 2 H, H-6), 2.36 (s, 3 H, Me-*p*-Tol), 3.20 (m, 1 H, OH), 4.44 (dt, *J* = 13.9, 6.4 Hz, 1 H, H-1), 4.64 (ddd, *J* = 13.9, 7.3, 3.8 Hz, 1 H, H-1), 5.86 (d, *J* = 15.9 Hz, 1 H, H-4), 5.99 (dt, *J* = 15.7, 6.2 Hz, 1 H, H-5), 6.28 (t, *J* = 7.0 Hz, 1 H, H-2), 7.25 (d, *J* = 8.1 Hz, 2 H, *p*-Tol), 7.45 (d, *J* = 8.4 Hz, 2 H, *p*-Tol); **Anal. calcd for** $C_{16}H_{22}O_2S$: C 69.02, H 7.96, S 11.52; **found**: C 69.15, H 8.03, S 11.43.

4.9. Synthesis of (±)-2-(*Z*)-4-(*E*)-4-(2-Methoxynaphthalen-1-sulfinyl)nona-2,4-dien-1-ol, 1i.



From iodide **SI-25** (150 mg, 0.39 mmol, 1.0 equiv), stannane **SI-32** (728 mg, 1.95 mmol, 5.0 equiv),[14] BHT (86 mg, 0.39 mmol, 1.0 equiv), Ph_3As (48 mg, 0.156 mmol, 0.4 equiv) and $Pd_2(dba)_3{\cdot}CHCl_3$ (41 mg, 0.039 mmol, 0.1 equiv) following the general procedure (12 h), a complex mixture of products was obtained. Purification by chromatography (20-80% EtOAc-hexane) afforded **SI-33** (7 mg, 0.013 mmol, 3%) as a colorless oil and diene **1i** (33 mg, 0.10 mmol, 26%) as a white solid that was recrystallized from EtOAc-hexane.

Data for **SI-33**: **^{1}H NMR** (300 MHz) δ = 0.77 (t, *J* = 7.1 Hz, 9 H, 3 Me-*n*-Bu), 1.04-1.40 (m, 18 H, *n*-Bu), 3.83 (dd, *J* = 7.8, 5.9 Hz, 1 H, OH), 4.01 (s, 3 H, OMe), 4.34 (ddd, *J* = 13.7, 7.6, 5.9 Hz, 1 H, H-1), 4.52 (dt, *J* = 14.2, 5.9 Hz, 1 H, H-1), 6.43 (t, *J* = 5.9 Hz, 1 H, H-2), 7.26 (d, *J* = 9.0 Hz, 1 H, H-3'), 7.39 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1 H, H-6'), 7.55 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1 H, H-7'), 7.79 (d, *J* = 8.1 Hz, 1 H, H-5'), 7.97 (d, *J* = 9.0 Hz, 1 H, H-4'), 8.69 (dd, *J* = 8.5, 0.7 Hz, 1 H, H-8'); **Anal. calcd for** $C_{26}H_{40}O_3SSn$: C 56.64, H 7.31, S 5.82, Sn 21.53; **found**: C 56.35, H 7.57, S 5.49, Sn 21.37.

Data for **1i**: R_f = 0.32 (80% EtOAc-hexane); **mp** 80-82 ºC; **^{1}H NMR** (300 MHz) δ = 0.66 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 0.81-1.06 (m, 4 H), 1.81 (m, 2 H, H-6), 2.98 (t, *J* = 6.1 Hz, 1 H, OH), 3.99 (s, 3 H, OMe), 4.44 (dt, *J* = 13.4, 6.7 Hz, 1 H, H-1), 4.64 (m, 1 H, H-1), 5.76 (dt, *J* = 15.6, 6.4 Hz, 1 H, H-5), 5.87 (d, *J* = 16.1 Hz, 1 H, H-4), 6.30 (t, *J* = 7.0 Hz, 1 H, H-2), 7.22 (d, *J* = 9.0 Hz, 1 H, H-3'), 7.39

(ddd, *J* = 8.1, 6.8, 1.2 Hz, 1 H, H-6'), 7.54 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1 H, H-7'), 7.78 (dd, *J* = 8.1, 0.6 Hz, 1 H, H-5'), 7.94 (d, *J* = 9.0 Hz, 1 H, H-4'), 8.91 (dd, *J* = 8.8, 0.7 Hz, 1 H, H-8'); **^{13}C NMR** (75 MHz) δ = 13.7 (Me-*n*-Bu), 21.6, 30.6, 32.3, 56.8 (OMe), 58.2, 112.9, 121.1, 122.9, 123.0, 124.5, 128.0, 128.6, 129.3, 132.4, 132.7, 134.6, 136.1, 144.7, 156.4; **IR** (KBr): 3436, 3010, 2978, 2930, 2848, 1617, 1589, 1509, 1472, 1459, 1442, 1432, 1338, 1272, 1259, 1143, 1121, 1063, 1019, 912, 881, 820, 784, 754, 719 cm^{-1}; **MS** (ES) m/z (%): 711 $[2M+Na]^+$, 367 $[M+Na]^+$, 345 (100) $[M+H]^+$; **Anal. calcd for** $C_{20}H_{24}O_3S$: C 69.73, H 7.02, S 9.31; **found**: C 69.78, H 7.12, S 9.26.

5. Intramolecular Diels-Alder cycloaddition of sulfinyl dienynes.

5.1. General procedure for the synthesis of dienyne ethers

To a solution of the corresponding dienyl sulfoxide in CH_2Cl_2 (10 mL/mmol of sulfoxide), 3 equiv of propargyl bromide (80% wt), 0.2-0.5 equiv of Triton B (40% wt) and 60% aqueous sodium hydroxide (10 mL/mmol of sulfoxide) were added. The mixture was vigorously stirred at room temperature and monitored by TLC until starting material disappearance. Then the reaction mixture was filtered through celite, a saturated solution of NaCl (5 mL/mmol of sulfoxide) was added and the layers were separated. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were dried over anhydrous $MgSO_4$ and filtered to give, after evaporation of the solvents, a crude product that was purified by chromatography on silica gel using the appropriate mixture of solvents.

5.2. General procedure for Mitsunobu-type reaction of hydroxy 4-sulfinyl butadienes.[15a,b]

To a solution of dienyl sulfoxide in THF or benzene (5 mL/mmol sulfoxide), under an argon atmosphere, 1.5 equiv of Ph_3P (recrystallized), 1.1 equiv of a propargylic derivative in anhydrous THF or benzene (10 mL/mmol of sulfoxide) and 1.5 equiv of diisopropyl azodicarboxylate were added. The reaction was monitored by TLC until starting material disappearance. Then the solvent was removed and the crude product was purified by chromatography on silica gel using the appropriate mixture of solvents.

5.3. General procedure for the thermal Diels-Alder reaction of sulfinyl dienynes

A kimble vial equipped with a stirring bar was charged with a solution of the corresponding dienyne and 0.2 equiv of 2,6-di-*tert*-butyl-4-methylphenol (BHT) in anhydrous toluene (10 mL/mmol of dienyne). Argon was bubbled through the solution for 15 min using a needle, and the vial was quickly stoppered. The vial was then immersed in a preheated oil bath (80-90 ºC) if appropriate and the

reaction was monitored by TLC until starting material disappearance. The solvent was removed and the crude product was purified by chromatography using the appropriate mixture of solvents.

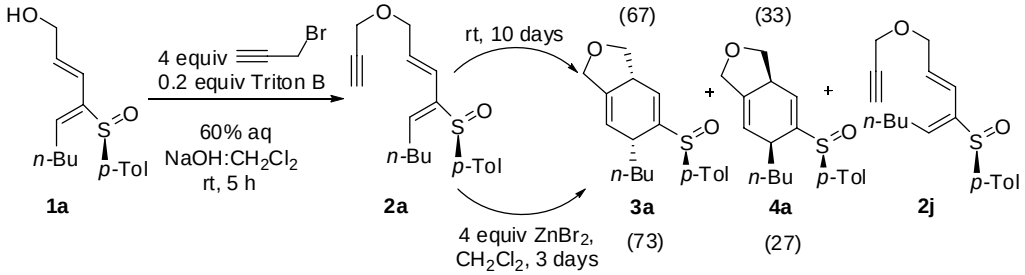
5.4. General procedure for the Diels-Alder reaction of sulfinyl dienynes in presence of $ZnBr_2$.

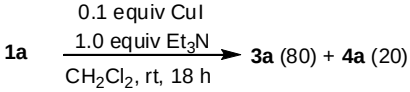
To a solution of sulfinyl dienyne in anhydrous CH_2Cl_2 (10 mL/mmol), under an argon atmosphere, $ZnBr_2$ (4.0 equiv) was added. The reaction mixture was stirred until starting material disappearance (TLC). The reaction was quenched with a 5% solution of $NaHCO_3$, phases were separated and the aqueous layer was extracted with CH_2Cl_2 (twice). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The resulting crude was purified by chromatography using the appropriate mixture of solvents.

5.5. General procedure for the CuI catalyzed Diels-Alder reaction of sulfinyl dienynes.

To a solution of sulfinyl dienyne in CH_2Cl_2 (4 mL/mmol), 0.1 equiv of CuI and 1.0 equiv of Et_3N were added at room temperature. The mixture was stirred until starting material disappearance (TLC). Then the solvent was removed under reduced pressure and the resulting crude product was purified by chromatography using the appropriate mixture of solvents.

5.6. Synthesis of (–)-(*S*)-4-Oxa-8-(*p*-tolylsulfinyl)-6-(*E*)-8-(*Z*)-tridecadien-1-yne, 2a, (+)-(3a*R*,6*R*,S_S)-6-*n*-Butyl-5-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 3a, and (–)-(3a*S*,6*S*,S_S)-6-*n*-Butyl-5-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 4a.





From sulfinyl diene **1a**[16] (835 mg, 3.00 mmol), propargyl bromide (1.29 mL, 1.78 g, 12.00 mmol), Triton B (0.30 mL, 275 mg, 0.60 mmol) and 60% aqueous sodium hydroxide (15 mL) following the general procedure (5 h) compound **2a** was obtained. Purification by chromatography (20-50% EtOAc-hexane) afforded **2a** (518 mg, 1.86 mmol, 62%) as a yellow oil, 92 mg (0.33 mmol, 11%) of a 67:33 mixture of **3a** and **4a** and 84 mg (0.30 mmol, 10%) of starting material.

Data for **2a**: R_f = 0.22 (30% EtOAc-hexane); **[α]$^{20}_{D}$** = –161.1 (*c* = 1.11); **^{1}H NMR** (300 MHz) δ = 0.93 (t, *J* = 7.0 Hz, 3 H, Me-*n*-Bu), 1.33-1.54 (m, 4 H, 2 CH_2-*n*-Bu), 2.35-2.37 (m, 4 H, Me-*p*-Tol, H-1), 2.49 (m, 1 H, H-10), 2.71 (m, 1 H, H-10), 3.90 (dd, *J* = 2.4, 1.4 Hz, 2 H, 2 H-3), 3.98 (m, 2 H, 2 H-5), 5.98 (dt, *J* = 15.9, 5.9 Hz, 1 H, H-6), 6.12 (d, *J* = 15.7 Hz, 1 H, H-7), 6.24 (dd, *J* = 8.3, 7.4 Hz, 1 H, H-9), 7.25 (d, *J* = 8.1 Hz, 2 H, *p*-Tol), 7.39 (d, *J* = 8.3 Hz, 2 H, *p*-Tol); **^{13}C NMR** (50 MHz) δ = 13.8 (Me-*n*-Bu), 21.3 (Me-*p*-Tol), 22.3, 28.6, 31.5, 56.7, 69.6, 74.4, 79.5, 124.2 (2 C), 124.4, 128.3, 129.5, 129.8 (2 C), 139.0, 140.6, 142.1; **IR** (film): 3036, 2955, 2929, 2859, 1595, 1492, 1465, 1399, 1379, 1303, 1178, 1147, 1083, 1049, 1014, 899, 844, 810, 705 cm^{-1}; **MS** (ES) m/z (%): 633 $[2M+H]^+$, 317 (100) $[M+H]^+$; **Anal. calcd for** $C_{19}H_{24}O_2S$: C 72.11, H 7.64, S 10.13; **found**: C 71.97, H 7.35, S 10.36.

From **2a** (492 mg, 1.55 mmol), $ZnBr_2$ (1400 mg, 6.20 mmol) following the general procedure (3 days), a 73:27 mixture of **3a** and **4a** with traces of **2j** was obtained. Purification by chromatography (10-50% EtOAc-hexane) afforded 5 mg of **2j** as a colorless oil, 47 mg (0.15 mmol, 10%) of **4a** as a colorless oil, 168 mg (0.53 mmol, 34%) of a mixture of **4a** and **3a** and 172 mg (0.54 mmol, 35%) of **3a** as a white solid that was recrystallized from Et_2O-hexane.

In a related experiment a solution of **2a** in $CDCl_3$ was kept at room temperature and monitored by ^{1}H NMR until cycloaddition was complete (10 days), affording a 67:33 mixture of **3a** and **4a**.

From **2a** (96 mg, 0.30 mmol), CuI (6 mg, 0.03 mmol) and Et_3N (40 μL, 0.30 mmol) following the general procedure (18 h), an 80:20 mixture of **3a** and **4a** was obtained. Purification by chromatography (10-50% EtOAc-hexane) afforded 48 mg (0.015 mmol, 50%) of an 83:17 mixture of **3a** and **4a** and 28 mg (0.093 mmol, 31%) of pure **3a**.

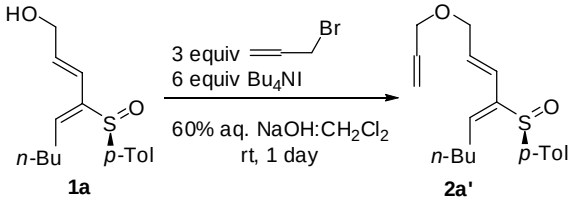
Data for **2j**: R_f = 0.27 (30% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 0.89 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 1.22-1.55 (m, 4 H, 2 CH_2-*n*-Bu), 2.25-2.39 (m, 3 H), 2.35 (s, 3 H, Me-*p*-Tol), 3.94 (d, *J* = 2.4 Hz, 2 H, 2 H-3), 4.00 (d, *J* = 5.6 Hz, 2 H, 2 H-5), 5.89 (dt, *J* = 16.3, 5.6 Hz, 1 H, H-6), 6.20 (d, *J* = 16.3 Hz, 1 H, H-7), 6.50 (t, *J* = 7.6 Hz, 1 H, H-9), 7.22 (d, *J* = 8.1 Hz, 2 H, *p*-Tol), 7.46 (d, *J* = 8.2 Hz, 2 H, *p*-Tol); **Anal. calcd for** $C_{19}H_{24}O_2S$: C 72.11 H 7.64, S 10.13; **found**: C 72.34 H 7.35, S 10.41.

Data for **3a**: R_f = 0.22 (50% EtOAc-hexane); **mp** 83-85 ºC; **[α]$^{20}_{D}$** = +179.2 (*c* = 1.00); **^{1}H NMR** (300 MHz) δ = 0.87 (t, *J* = 7.0 Hz, 3 H, Me-*n*-Bu), 1.08-1.38 (m, 4 H, 2 CH_2-*n*-Bu), 1.57-1.67 (m, 2 H, CH_2-*n*-Bu), 2.39 (s, 3 H, Me-*p*-Tol), 2.58 (m, 1 H, H-6), 3.32-3.34 (m, 2 H, H-3a, 1 H-3), 4.25-4.41 (m, 3 H, 1 H-3, 2 H-1), 5.36 (br s, 1 H, H-7), 6.86 (t, *J* = 2.2 Hz, 1 H, H-4), 7.23 (d, *J* = 8.1 Hz, 2 H, *p*-Tol), 7.53 (d, *J* = 8.1 Hz, 2 H, *p*-Tol); **^{13}C NMR** (50 MHz) δ = 13.9 (Me-*n*-Bu), 21.5 (Me-*p*-Tol), 22.8, 26.4, 31.7, 36.0, 41.0, 69.0, 71.4, 119.1, 123.0, 126.4 (2 C), 130.2 (2 C), 137.9, 139.4, 142.6, 146.6; **IR** (KBr): 2952, 2930, 2859, 1631, 1593, 1493, 1455, 1378, 1306, 1182, 1082, 1044,

1012, 896, 872, 819 cm^{-1}; **MS** (ES) m/z (%): 633 $[2M+H]^+$, 317 (100) $[M+H]^+$; **Anal. calcd for** $C_{19}H_{24}O_2S$: C 72.11, H 7.64, S 10.13; **found**: C 72.30, H 7.93, S 10.41.

Data for **4a**: R_f = 0.27 (50% EtOAc-hexane); $[\alpha]^{20}_D$ = –11.4 (*c* = 1.19); **^{1}H NMR** (300 MHz) δ = 0.80 (t, *J* = 7.0 Hz, 3 H, Me-*n*-Bu), 1.11-1.25 (m, 4 H, 2 CH_2-*n*-Bu), 1.62-1.75 (m, 2 H, CH_2-*n*-Bu), 2.39 (s, 3 H, Me-*p*-Tol), 3.05 (m, 1 H, H-6), 3.28 (m, 1 H, H-3a), 3.33 (dd, *J* = 10.9, 6.6 Hz, 1 H, H-3), 4.21-4.27 (m, 2 H, H-3, H-1), 4.35 (dm, *J* = 12.0 Hz, 1 H, H-1), 5.37 (m, 1 H, H-7), 6.63 (t, *J* = 2.4 Hz, 1 H, H-4), 7.29 (d, *J* = 7.9 Hz, 2 H, *p*-Tol), 7.48 (d, *J* = 8.3 Hz, 2 H, *p*-Tol); **^{13}C NMR** (50 MHz) δ = 13.9 (Me-*n*-Bu), 21.3 (Me-*p*-Tol), 22.6, 27.6, 31.9, 36.6, 41.2, 69.0, 70.8, 120.2, 125.3 (2 C), 129.8 (2 C), 131.5, 136.1, 138.7, 141.2, 148.3; **IR** (film): 2956, 2926, 2857, 1651, 1456, 1260, 1084, 1048, 898, 809 cm^{-1}; **MS** (ES) m/z (%): 633 (100) $[2M+H]^+$, 317 $[M+H]^+$. **Anal. calcd for** $C_{19}H_{24}O_2S$: C 72.11, H 7.64, S 10.13; **found**: C 72.20, H 7.78, S 10.27.

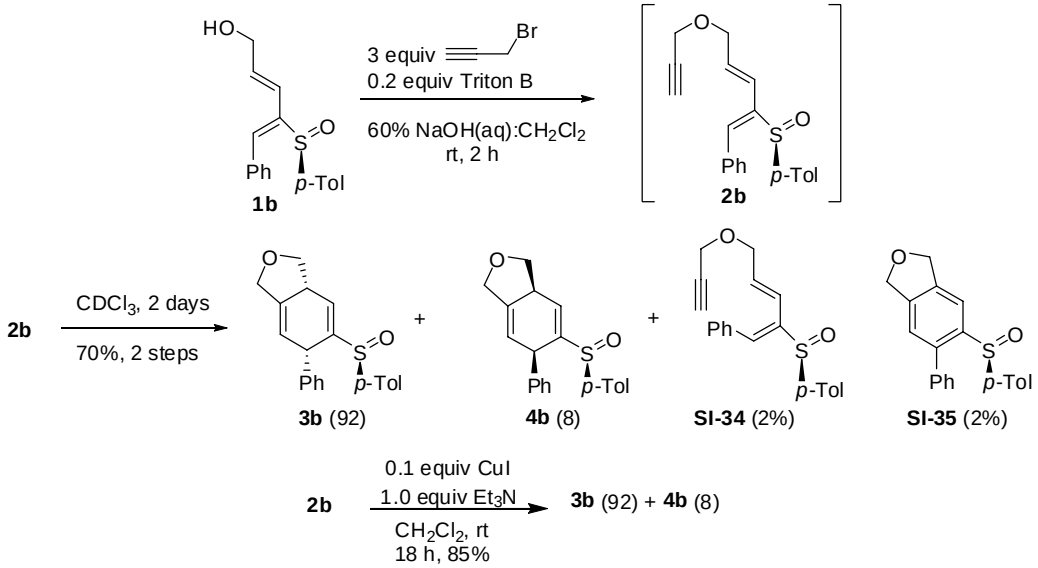
5.7. Synthesis of (*R*)-4-Oxa-8-(*p*-tolylsulfinyl)-1-6-(*E*)-8-(*Z*)-tridecatriene, 2a'.



From dienol **1a** (28 mg, 0.1 mmol), allyl bromide (26 μL, 0.3 mmol, 3.0 equiv), Bu_4NI (80 mg, 0.6 mmol, 6.0 equiv) and NaOH 60% (1 mL) following the general procedure (16 h), compound **2a'** was obtained. Purification by chromatography (20-50% EtOAc-hexane) afforded **2a'** (22 mg, 0.07 mmol, 70%) as a colorless oil.

Data for **2a'**: R_f = 0.53 (80% EtOAc-hexane); **^{1}H NMR** (200 MHz) δ = 0.90 (t, *J* = 7.0 Hz, 3 H, Me-*n*-Bu), 1.38-1.62 (m, 4 H, *n*-Bu), 2.34 (s, 3 H, Me-*p*-Tol), 2.48 (m, 1 H, H-10), 2.67 (m, 1 H, H-10), 3.73 (dt, *J* = 5.7, 1.3 Hz, 2 H, H-3), 3.88 (m, 2 H, H-5), 5.11 (m, 2 H, 2 H-1), 5.77 (ddt, *J* = 17.2, 10.3, 5.6 Hz, 1 H, H-2), 6.00 (dd, *J* = 15.7, 4.8 Hz, 1 H, H-6), 6.07 (d, *J* = 15.9 Hz, 1 H, H-7), 6.22 (t, *J* = 7.3 Hz, 1 H, H-9), 7.22 (d, *J* = 8.4 Hz, 2 H, *p*-Tol), 7.37 (d, *J* = 8.4 Hz, 2 H, *p*-Tol); **^{13}C NMR** (50 MHz) δ = 13.8 (Me-*n*-Bu), 21.3 (Me-*p*-Tol), 22.3, 28.6, 31.5, 70.1, 70.7, 117.0, 123.4, 124.2 (2 C), 129.7 (2 C), 130.5, 134.5, 138.7, 139.8, 140.5, 142.2; **Anal. calcd for** $C_{19}H_{26}SO_2$: C 71.66, H 8.23, S 10.07; **found**: C 71.83, H 8.35, S 10.27.

5.8. Synthesis of (*S*)-4-Oxa-9-phenyl-8-(*p*-tolylsulfinyl)-6-(*E*)-8-(*Z*)-nonadien-1-yne, 2b, (+)-(3a*R*,6*S*,S_S)-6-Phenyl-5-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 3b, and (+)-(3a*S*,6*R*,S_S)-6-Phenyl-5-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 4b.



From sulfinyl diene **1b** (298 mg, 1 mmol), propargyl bromide (0.32 mL, 446 mg, 3 mmol), Triton B (0.10 mL, 91 mg, 0.2 mmol) and 60% aqueous sodium hydroxide (10 mL) following the general procedure (2 h) compound **2b** was obtained. The ^{1}H NMR spectra of the crude product run after the work-up procedure showed a 30:65:5 mixture of **2b**, **3b** and **4b** with traces of **SI-34**. After 2 days at room temperature the cycloaddition was complete and a 92:8 mixture of **3b** and **4b** was obtained. Purification by chromatography (20-80% EtOAc-hexane) afforded 14 mg of a 1:1 mixture of **SI-34** (2%) and the aromatized derivative **SI-35** (2%), 218 mg (0.65 mmol, 65%) of **3b** as a white solid that was recrystallized from EtOAc-hexane, 19 mg (0.05 mmol, 5%) of **4b** and 7 mg (0.02 mmol, 2%) of starting material **1b**.

From sulfinyl dienyne **2b** (165 mg, 0.49 mmol), CuI (9 mg, 0.04 mmol) and Et_3N (68 μL, 0.49 mmol) following the general procedure (18 h), a 92:8 mixture of **3b** and **4b** was obtained. Purification by chromatography afforded **3b** (124 mg, 0.34 mmol, 75%) as a white solid that was recrystallized from EtOAc-hexane, and 17 mg (0.05 mmol, 10%) of a mixture of **3b** and **4b**.

Data for **2b**: R_f = 0.37 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 2.36 (s, 3 H, Me-*p*-Tol), 2.37 (m, 1 H, H-1 overlapped), 3.94 (m, 2 H, 2 H-3), 4.04 (m, 2 H, 2 H-5), 6.17 (dt, *J* = 15.7, 5.6 Hz, 1 H, H-6), 6.31 (dd, *J* = 15.7, 1.0 Hz, 1 H, H-7), 7.23-7.29 (m, 4 H), 7.35-7.42 (m, 4 H), 7.48-7.51 (m, 2 H).

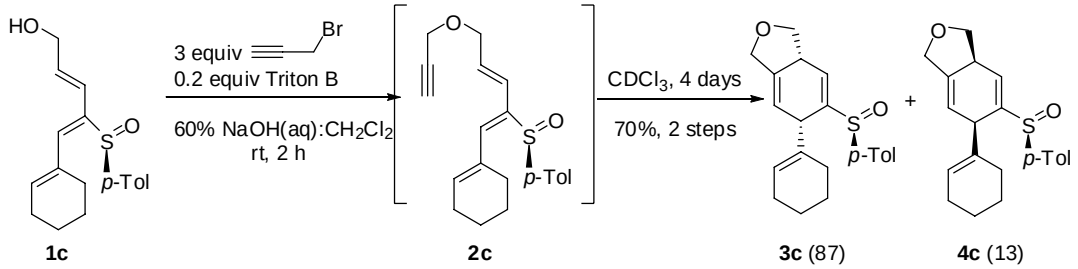
Data for **SI-34**: R_f = 0.37 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 2.36 (s, 3 H, Me-*p*-Tol), 2.89 (t, *J* = 2.4 Hz, 1 H, H-1), 3.87 (d, *J* = 2.4 Hz, 2 H, 2 H-3), 3.96 (d, *J* = 6.0 Hz, 2 H, 2 H-5),

6.07 (dt, *J* =16.3, 5.8 Hz, 1 H, H-6), 6.43 (d, *J* = 16.5 Hz, 1 H, H-7), 7.31-7.47 (m, 8 H), 7.55 (d, *J* = 8.2 Hz, 2 H).

Data for **3b**: R_f = 0.11 (50% EtOAc-hexane); **mp** 164 ºC; $[\alpha]_D^{20}$ = + 243.3 (*c* = 0.55); **^{1}H NMR** (300 MHz) δ = 2.39 (s, 3 H, Me-*p*-Tol), 3.41 (m, 1 H, H-3a), 3.47 (ddd, *J* = 11.0, 7.0, 0.7 Hz, 1 H, H-3), 3.56 (m, 1 H, H-6), 4.26 (dm, *J* = 11.7 Hz, 1 H, H-1), 4.37-4.43 (m, 2 H, H-3, H-1), 5.34 (t, *J* = 2.0 Hz, 1 H, H-7), 6.92-6.96 (m, 2 H), 6.99 (t, *J* = 2.2 Hz, 1 H, H-4), 7.22-7.33 (m, 7 H); **^{13}C NMR** (75 MHz) δ = 21.5 (Me-*p*-Tol), 40.8, 43.4, 68.9, 71.5, 119.6, 122.9, 126.9 (2 C), 127.6, 128.8 (2 C), 129.1 (2 C), 130.0 (2 C), 136.6, 138.9, 140.5, 142.6, 147.4; **IR** (KBr): 3026, 2922, 2859, 1629, 1595, 1493, 1452, 1328, 1306, 1182, 1082, 1047, 1014, 959, 896, 851, 813, 763, 700 cm^{-1}; **MS** (ES) m/z (%): 695 (100) $[2M+Na]^+$, 673 $[2M+H]^+$, 659 $[M+Na]^+$, 337 $[M+H]^+$; **Anal. calcd for** $C_{21}H_{20}O_2S$: C 74.97, H 5.99, S 9.53; **found**: C 74.68, H 6.10, S 9.42.

Data for **4b**: R_f = 0.20 (50% EtOAc-hexane); **mp** 175-177 ºC; $[\alpha]_D^{20}$ = + 3.5 (*c* = 0.35); **^{1}H NMR** (300 MHz) δ = 2.31 (s, 3 H, Me-*p*-Tol), 3.40-3.48 (m, 2 H, H-3a, 1 H-3), 4.26-4.35 (m, 2 H, 1 H-1, 1 H-6), 4.39-4.47 (m, 2 H, 1 H-1, 1 H-3), 5.46 (br s, 1 H, H-7), 6.70 (t, *J* = 2.3 Hz, 1 H, H-4), 6.90-6.94 (m, 2 H), 6.97-7.15 (m, 7 H); **^{13}C NMR** (75 MHz) δ = 21.3 (Me-*p*-Tol), 40.8, 43.9, 69.0, 71.3, 119.5, 125.6 (2 C), 125.9, 127.3, 128.4 (2 C), 129.4 (2 C), 129.5 (2 C), 136.9, 139.6, 139.9, 141.2, 148.6; **IR** (KBr): 3026, 2922, 2859, 1595, 1493, 1452, 1306, 1082, 1047, 1014, 959, 896, 813, 763, 700 cm^{-1}; **MS** (ES) m/z (%): 659 $[M+Na]^+$, 337 (100) $[M+H]^+$; **Anal. calcd for** $C_{21}H_{20}O_2S$: C 74.97, H 5.99, S 9.53; **found**: C 74.80, H 6.04, S 9.42.

5.9. Synthesis of (*S*)-9-(Cyclohex-1-enyl)-4-oxa-8-(*p*-tolylsulfinyl)-6-(*E*)-8-(*Z*)-nonadien-1-yne, 2c, (+)-(3a*R*,6*S*,*S*$_S$)-6-(Cyclohex-1-enyl)-5-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 3c, and (+)-(3a*S*,6*R*,*S*$_S$)-6-(Cyclohex-1-enyl)-5-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 4c.



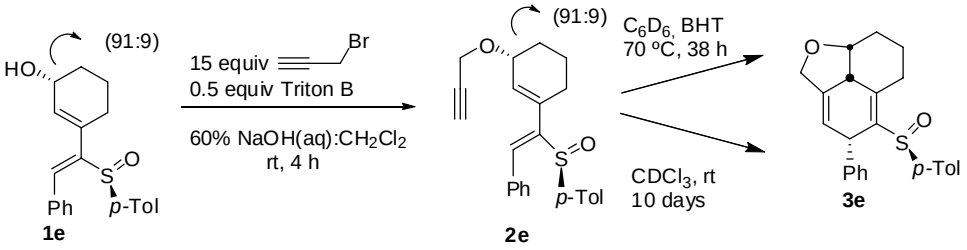
From diene **1c** (70 mg, 0.23 mmol), propargyl bromide (74 μL, 0.69 mmol, 3.0 equiv), Triton B (23 μL, 0.046 mmol, 0.2 equiv) and 60% aqueous NaOH (2.3 mL), following the general procedure (2 h), dienyne **2c** was obtained. Purification by chromatography (20-50% EtOAc-hexane) afforded **2c** (31 mg, 0.09 mmol, 39%) as a colorless oil, 7 mg (0.02 mmol, 9%) of a mixture of **3c** and **4c** and 16 mg

(0.05 mmol, 23%) of starting material **1c**. After 2 days at room temperature, in a $CDCl_3$ solution, the cycloaddition of **2c** (31 mg, 0.09 mmol) was complete and an 87:13 mixture of **3c** and **4c** was obtained. Purification by chromatography (20-80% EtOAc-hexane) afforded 22 mg (0.063 mmol, 70%) of an inseparable mixture of **3c** and **4c** in an identical diastereomeric ratio to that described above.

Data for **2c**: R_f = 0.55 (50% EtOAc-hexane); **^{1}H NMR** (200 MHz) δ = 1.57-1.79 (m, 4 H), 2.26-2.31 (m, 2 H), 2.35-2.53 (m, 3 H), 2.41 (s, 3 H, Me-*p*-Tol), 3.92 (dd, *J* = 2.4, 0.7 Hz, 2 H, H-3), 3.99-4.05 (m, 2 H, H-5), 5.97-6.29 (m, 3 H, H-6, H-7, H-2'-c-hex), 6.72 (s, 1 H, H-9), 7.30 (d, *J* = 8.5 Hz, 2 H), 7.45 (d, *J* = 8.3 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 21.3, 21.5, 22.5, 26.4, 29.5, 56.6, 69.7, 74.4, 79.5, 124.6 (2 C), 125.6, 129.1, 129.7 (2 C), 134.1, 137.3, 138.4, 139.4, 140.3, 140.4; **Anal. calcd for** $C_{21}H_{24}O_2S$: C 74.08, H 7.10, S 9.42; **found**: C 73.87, H 7.31, S 9.23.

Partial data for **3c** and **4c** (from the mixture): R_f = 0.22 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 1.20-2.00 (m, 8 H each), 2.38 (s, 3 H each, Me-*p*-Tol), 2.99-3.03 (m, 1 H each), 3.28-3.38 (m, 2 H each), 4.24-4.41 (m, 3 H each), 5.21-5.25 (m, 2 H each), 6.62 (t, 1 H, *J* = 2.4 Hz, H-4, **4c**), 6.89 (t, 1 H, *J* = 2.3 Hz, H-4, **3c**), 7.25 (d, *J* = 7.6 Hz, 2 H each, *p*-Tol), 7.48 (d, *J* = 8.1 Hz, 2 H each, *p*-Tol).

5.10. Synthesis of (1*R*,*S*$_S$)-(*Z*)-(2-[(3-Prop-2-ynyloxy)cyclohex-1-enyl]-2-(*p*-tolylsulfinyl)vinyl)benzene, 2e, and (–)-(2a*S*,4*S*,8a*R*,*S*$_S$)-4-Phenyl-5-(*p*-tolylsulfinyl)-2a,4,6,7,8,8a-hexahydro-2*H*-naphtho[1,8-bc]furan, 3e.



From diene **1e** (40 mg, 0.12 mmol, 1.0 equiv), propargyl bromide (0.20 mL, 1.77 mmol, 15.0 equiv) and Triton B (27 μL, 0.059 mmol, 0.5 equiv) following the general procedure (6 h), dienyne **2e** was obtained. Purification by flash chromatography afforded dienyne **2e** (7 mg, 0.019 mmol, 16%, 44% based on recovered starting material) as a yellow oil, and 24 mg (0.017 mmol, 60%) of **1e**.

A solution of **2e** in $CDCl_3$ was kept at room temperature and monitored by ^{1}H NMR until cycloaddition was complete (10 days) affording **3e** as a single diastereomer.

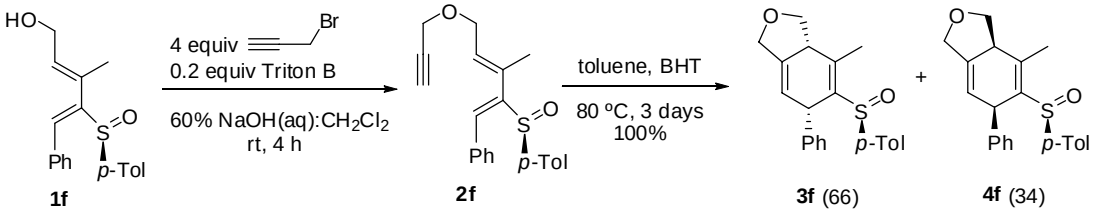
In a related experiment, a solution of **2e** in C_6D_6 was heated at 70 ºC for 38 h affording **3e** as a single diastereomer. To our delight, the minor diastereomer from the 91:9 mixture of dienynes **2e**

cyclizes more slowly. Purification by chromatography (10-50% EtOAc-hexane) gave **3e** (11 mg, 0.029 mmol, 73%) as a colorless oil.

Data for **2e**: R_f = 0.33 (30% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 1.36-1.72 (m, 4 H), 1.83-1.92 (m, 1 H), 2.16-2.27 (m, 1 H), 2.37 (s, 3 H, Me-*p*-Tol), 2.38 (brs, 1 H, H-alkyne), 3.94-3.98 (m, 1 H), 4.05 (d, *J* = 2.4 Hz, 2 H), 5.79-5.80 (m, 1 H), 7.15 (s, 1 H), 7.23 (d, *J* = 7.9 Hz, 2 H), 7.35-7.40 (m, 5 H), 7.52-7.55 (m, 2 H); **MS** (ES) m/z (%): 399 (100) $[M+Na]^+$; **Anal. calcd for** $C_{24}H_{24}O_2S$: C 76.56, H 6.42, S 8.52; **found**: C 76.41, H 6.37, S 8.75.

Data for **3e**: R_f = 0.20 (50% EtOAc-hexane); **$[\alpha]_D^{20}$** = –62.3 (*c* = 0.19); **^{1}H NMR** (300 MHz) δ = 1.29-1.40 (m, 1 H), 1.75-1.89 (m, 2 H), 1.95-2.04 (m, 1 H), 2.20-2.33 (m, 1 H), 2.27 (s, 3 H, Me-*p*-Tol), 3.29 (m, 1 H), 3.26-3.40 (m, 1 H), 4.27 (m, 2 H), 4.31-4.41 (m, 2 H), 5.50 (dd, *J* = 3.0, 1.5 Hz, 1 H), 6.78-6.81 (m, 3 H), 6.90-6.93 (m, 6 H); **^{13}C NMR** (75 MHz) δ = 19.3, 21.1, 26.0, 28.2, 43.9, 45.2, 68.8, 77.5, 123.1 (3 C), 123.2, 126.4, 127.4, 129.2 (2 C), 130.1, 132.1, 134.7, 138.3, 138.7, 140.2 (2 C), 146.4; **IR** (film): 3027, 2925, 2856, 1598, 1492, 1454, 1376, 1081, 1042, 863, 806, 768, 734, 699, 619, cm^{-1}; **HRMS** calcd for $C_{24}H_{25}O_2S$ $[M+H]^+$: 377.1575; **found**: 377.1569.

5.11. Synthesis of (–)-(*S*)-7-Methyl-4-oxa-9-phenyl-8-(*p*-tolylsulfinyl)-6-(*E*)-8-(*Z*)-nonadien-1-yne, 2f, (–)-(3a*S*,6*S*,*S*$_S$)-4-Methyl-6-phenyl-5-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 3f, and (+)-(3a*R*,6*R*,*S*$_S$)-4-Methyl-6-phenyl-5-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 4f.



From diene **1f** (17 mg, 0.054 mmol, 1.0 equiv), propargyl bromide (24 μL, 0.218 mmol, 4.0 equiv), Triton B (5 μL, 0.011 mmol, 0.2 equiv), following the general procedure, dienyne **2f** was obtained. Purification by chromatography (10-30% EtOAc-hexane) afforded **2f** (10 mg, 0.0285 mmol, 53%) as a yellow oil.

Data for **2f**: R_f = 0.27 (30% EtOAc-hexane); **$[\alpha]_D^{20}$** = –247.3 (*c* = 0.68); **^{1}H NMR** (300 MHz) δ = 1.69 (s, 3 H, Me), 2.36 (s, 3 H, Me-*p*-Tol), 2.38 (t, *J* = 2.2 Hz, 1 H, H-1), 3.90 (t, *J* = 2.2 Hz, 2 H), 3.97-4.09 (m, 2 H), 5.60 (tm, *J* = 6.6 Hz, 1 H, H-6), 7.14 (s, 1 H, H-9), 7.23 (d, *J* = 8.5 Hz, 2 H), 7.35-7.43 (m, 5 H), 7.54 (d, *J* = 8.2 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 17.8, 21.3, 56.6, 65.4, 74.3, 79.7, 124.5 (2 C), 128.5 (2 C), 128.7, 128.8, 129.6 (2 C), 129.9 (2 C), 134.0, 135.0, 138.0, 139.6, 140.5, 148.3; **IR** (film): 2918, 2846, 1080, 1042, 807, 751 cm^{-1}; **MS** (ES) m/z (%): 723 $[2M+Na]^+$, 701

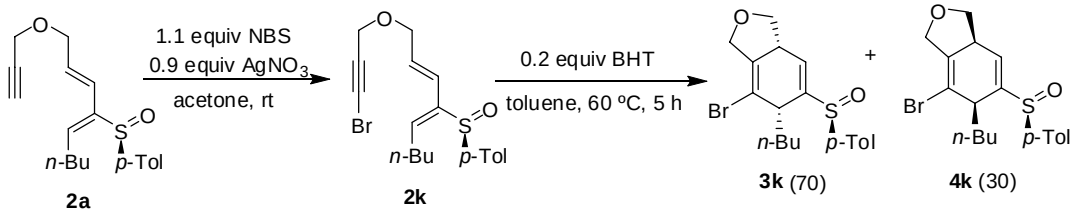
$[2M+H]^+$, 373 $[M+Na]^+$, 351 (100) $[M+H]^+$; **Anal. calcd for** $C_{22}H_{22}SO_2$: C 75.39, H 6.33, S 9.15; **found**: C 75.43, H 6.42, S 9.36.

From dienyne **2f** (10 mg, 0.028 mmol), following the general procedure for the thermal cycloaddition (80 ºC, 3 days), a 66:34 mixture of **3f** and **4f** was obtained. Purification by chromatography (10-50% EtOAc-hexane) afforded **3f** (4 mg, 0.011 mmol, 40%), a mixture of **3f** and **4f** (3 mg, 0.008 mmol, 30%) and **4f** (3 mg, 0.008 mmol, 30%), both as colorless oils.

Data for **3f**: R_f = 0.22 (50% EtOAc-hexane); $[\alpha]_D^{20}$ = –88.9 (*c* = 0.63); **^{1}H NMR** (300 MHz): 2.22 (s, 3 H), 2.27 (s, 3 H), 3.35-3.42 (m, 1 H), 3.47-3.53 (m, 1 H), 4.24 (dm, *J* = 11.8 Hz, 1 H), 4.36-4.43 (m, 2 H), 4.67-4.73 (m, 1 H), 5.35-5.36 (m, 1 H, H-7), 6.72-6.92 (m, 9 H); **^{13}C NMR** (75 MHz) δ = 19.9, 21.0, 41.7, 46.7, 69.3, 71.3, 121.0, 123.0 (2 C), 124.8, 126.3, 127.6 (2 C), 129.0 (2 C), 129.6 (2 C), 132.9, 138.7, 139.0, 139.7, 140.6; **IR** (film): 3054, 3021, 2922, 2851, 1598, 1492, 1452, 1380, 1302, 1144, 1080, 1039, 895, 809 cm^{-1}; **HRMS** (ES) calcd for $C_{22}H_{23}O_2S$ $[M+H]^+$: 351.1419; **found**: 351.1421 $[M+H]^+$.

Data for **4f**: R_f = 0.18 (50% EtOAc-hexane); $[\alpha]_D^{20}$ = +48.5 (*c* = 0.42); **^{1}H NMR** (400 MHz) δ = 2.27 (s, 3 H), 2.38 (s, 3 H), 3.35 (qm, 1 H), 3.52 (m, 1 H), 4.05 (dm, *J* = 8,2 Hz, 1 H), 4.24 (dq, *J* = 11.9, 1.4 Hz, 1 H), 4.34-4.39 (m, 2 H), 5.28-5.29 (m, 1 H, H-7), 6.69-6.98 (m, 2 H), 7.13-7.15 (m, 2 H), 7.19-7.26 (m, 5 H); **^{13}C NMR** (125 MHz) δ = 18.7, 21.3, 44.7, 46.5, 69.4, 71.1, 121.1, 124.8 (2 C), 126.9, 128.2, 128.9 (2 C), 129.5 (2 C), 133.2, 139.6, 139.7, 140.4, 141.4, 142.2; **IR** (film): 2922, 2851, 1630, 1035, 809 cm^{-1}; **HRMS** (ES) calcd for $C_{22}H_{23}O_2S$ $[M+H]^+$: 351.1419; **found**: 351.1412.

5.12. Synthesis of (*R*)-1-Bromo-4-oxa-8-(*p*-tolylsulfinyl)-6-(*E*)-8-(*Z*)-tridecadien-1-yne, 2k, (+)-(3a*R*,6*S*,*S*$_S$)-7-Bromo-6-*n*-butyl-5-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 3k, and (+)-(3a*S*,6*R*,*S*$_S$)-7-Bromo-6-*n*-butyl-5-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 4k.



To a solution of **2a** (81 mg, 0.26 mmol) in anhydrous acetone (1 mL) NBS (51 mg, 0.29 mmol, 1.1 equiv) and $AgNO_3$ (40 mg, 0.23 mmol, 0.9 equiv) were added. The mixture was stirred at room temperature until starting material disappearance (1 h). The reaction was filtered and diluted with CH_2Cl_2. The resulting solution was washed with H_2O and brine, dried over anhydrous $MgSO_4$ and

concentrated under reduced pressure. Purification by chromatography (10-30% EtOAc-hexane) afforded **2k** (65 mg, 0.16 mmol, 63%) as a colorless oil.

Data for **2k**: R_f = 0.27 (30% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 0.86 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 1.27-1.48 (m, 4 H, *n*-Bu), 2.30 (s, 3 H, Me-*p*-Tol), 2.45 (ap sext, *J* = 7.3 Hz, 1 H, *n*-Bu), 2.64 (ap sext, *J* = 7.5 Hz, 1 H, *n*-Bu), 3.85 (s, 2 H, H-3), 3.90 (m, 2 H, H-5), 5.90 (dt, *J* = 15.8, 5.8 Hz, 1 H, H-6), 6.05 (d, *J* = 15.9 Hz, 1 H, H-7), 6.18 (t, *J* = 7.8 Hz, 1 H, H-9), 7.20 (d, *J* = 8.3 Hz, 2 H), 7.33 (d, *J* = 8.3 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 13.8, 21.3, 22.3, 28.6, 31.5, 45.9, 57.6, 69.7, 76.0, 124.1 (2 C), 124.5, 129.3, 129.7 (2 C), 139.0, 139.7, 140.6, 142.0; **MS** (EI) m/z (%): 395 $[M]^+$, 379, 293, 139 (100); **Anal. calcd for** $C_{19}H_{23}BrO_2S$: C 57.72, H 5.86, Br 20.21, S 8.11; **found**: C 57.38, H 5.65, Br 20.53, S 7.95.

From **2k** (16 mg, 0.04 mmol) and $ZnBr_2$ (36 mg, 0.10 mol) following the general procedure (4 days), a 70:30 mixture of **3k** and **4k** was obtained. Purification by chromatography (5-50% EtOAc-hexane) afforded a mixture of **3k** and **4k** (3 mg, 0.007 mmol, 19%) and 3 mg (0.007 mmol, 19%) of **2k**.

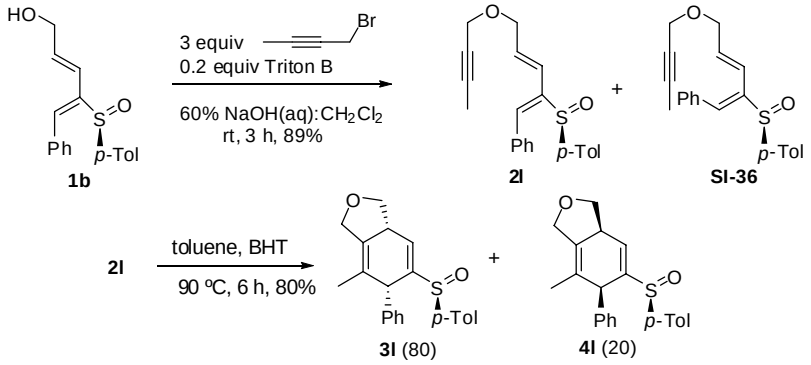
From **2k** (65 mg, 0.16 mmol) following the general procedure described for the thermal cycloaddition (60 ºC, 5 h), a 70:30 mixture of compounds **3k** and **4k** was obtained. Purification by chromatography (10-50% EtOAc-hexane) afforded **3k** (22 mg, 0.055 mmol, 35%), a mixture of **3k** and **4k** (24 mg, 0.061 mmol, 38%), and **4k** (12 mg, 0.030 mmol, 19%), all of them as colorless oils.

Data for **3k**: R_f = 0.38 (50% EtOAc-hexane); **$[\alpha]_D^{20}$** = +11.2 (*c* = 0.65); **^{1}H NMR** (300 MHz) δ = 0.84 (t, *J* = 7.3 Hz, 3 H, Me-*n*-Bu), 0.90-1.03 (m, 2 H, *n*-Bu), 1.16-1.25 (m, 2 H, *n*-Bu), 1.86-1.98 (m, 1 H, *n*-Bu), 2.04-2.16 (m, 1 H, *n*-Bu), 2.42 (s, 3 H, Me-*p*-Tol), 3.24-3.27 (m, 1 H, H-6), 3.36-3.45 (m, 2 H, H-3), 4.27 (m, 1 H, H-3a), 4.31-4.33 (m, 2 H, H-1), 6.67 (t, *J* = 2.7 Hz, 1 H, H-4), 7.33 (d, *J* = 8.2 Hz, 2 H), 7.49 (d, *J* = 8.3 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 13.9, 21.4, 22.4, 25.3, 29.0, 42.4, 44.7, 70.3, 71.1, 117.3, 125.1 (2 C), 130.0 (2 C), 130.3, 137.0, 138.1, 141.5, 147.2; **IR** (film): 2957, 2930, 2859, 1625, 1596, 1492, 1455, 1397, 1302, 1215, 1082, 1051, 899, 810, 754, 614 cm^{-1}; **MS** (EI) m/z (%): 395 $[M]^+$, 379 (100), 349, 293, 140, 123; **Anal. calcd for** $C_{19}H_{23}BrSO_2$: C 57.72, H 5.86, S 8.11; **found**: C 57.63, H 5.89, S 8.20.

Data for **4k**: R_f = 0.28 (50% EtOAc-hexane); **$[\alpha]_D^{20}$** = +40.5 (*c* = 0,21); **^{1}H NMR** (300 MHz) δ = 0.89 (t, *J* = 7.2 Hz, 3 H, Me-*n*-Bu), 1.06-1.19 (m, 2 H), 1.21-1.35 (m, 2 H), 1.59-1.69 (m, 1 H), 1.95-2.07 (m, 1 H), 2.39 (s, 3 H, Me-*p*-Tol), 2.77-2.81 (m, 1 H, H-6), 3.35-3.49 (m, 2 H, H-3), 4.33-4.36 (m, 3 H, H-1, H-3a), 6.87-6.88 (t, *J* = 2.3 Hz, 1 H, H-4), 7.29 (d, *J* = 8.1 Hz, 2 H), 7.52 (d, *J* = 8.1 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 13.8, 21.5, 22.6, 24.6, 29.1, 41.7, 44.4, 70.4, 71.7, 115.7, 121.7, 126.4 (2 C),

130.4 (2 C), 138.7, 138.8, 142.9, 145.8; **MS** (EI) m/z (%): 395 $[M]^+$, 379 (100), 349, 293; **Anal. calcd for** $C_{19}H_{23}BrSO_2$: C 57.72, H 5.86, S 8.11; **found**: C 57.75, H 5.91, S 8.27.

5.13. Synthesis of (±)-5-Oxa-10-phenyl-9-(*p*-tolylsulfinyl)-7-(*E*)-9-(*Z*)-decadien-2-yne, 2l, (±)-(3a*R*,6*S*,*S*$_S$)-7-Methyl-6-phenyl-5-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 3l, and (±)-(3a*S*,6*R*,*S*$_S$)-7-Methyl-6-phenyl-5-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 4l.



From dienol **1b** (90 mg, 0.3 mmol), 4-bromo-but-2-yne (79 μL, 120 mg, 0.9 mmol), Triton B (30 μL, 8 mg, 0.06 mmol) and 60% aqueous sodium hydroxide (3 mL) following the general procedure (3 h) compound **2l** was obtained with traces of **SI-36**. Purification by chromatography (20% EtOAc-hexane) afforded **SI-36** (2 mg, 0.005 mmol, 2%) as a colorless oil and **2l** (91 mg, 0.26 mmol, 87%) as a colorless oil.

Data for **SI-36**: R_f = 0.50 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 1.82 (t, *J* = 2.3 Hz, 3 H, Me-1), 2.36 (s, 3 H, Me-*p*-Tol), 3.93 (q, *J* = 2.3 Hz, 2 H, H-4), 4.04 (dt, *J* = 5.7, 1.5 Hz, 2 H, 2 H-6), 6.08 (dt, *J* = 16.3, 5.7 Hz, 1 H, H-7), 6.31 (dq, *J* = 16.5, 1.4 Hz, 1 H, H-8), 7.23 (d, *J* = 7.9 Hz, 2 H), 7.30-7.48 (m, 6 H), 7.56 (d, *J* = 8.2 Hz, 2 H); **Anal. calcd for** $C_{22}H_{22}O_2S$: C 75.39, H 6.33, S 9.15 **found**: 75.15, H 6.02, S 9.43.

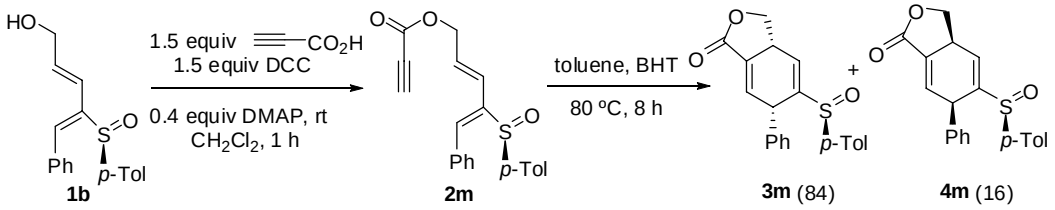
Data for **2l**: R_f = 0.45 (50% EtOAc-hexane); **^{1}H NMR** (200 MHz) δ = 1.81 (t, *J* = 2.3 Hz, 3 H, Me-1), 2.36 (s, 3 H, Me-*p*-Tol), 3.90 (q, *J* = 2.4 Hz, 2 H, H-4), 4.01 (m, 2 H, 2 H-6), 6.18 (dt, *J* = 15.7, 5.1 Hz, 1 H, H-7), 6.31 (d, *J* = 15.7 Hz, 1 H, H-8), 7.22-7.26 (m, 3 H), 7.35-7.46 (m, 5 H), 7.47-7.52 (m, 2 H); **^{13}C NMR** (75 MHz) δ = 3.6 (C-1), 21.3 (Me-*p*-Tol), 57.5, 69.5, 74.8, 82.6, 124.3, 124.5 (2 C), 128.6 (2 C), 129.0, 129.9 (2 C), 130.0 (2 C), 131.2, 134.0, 135.6, 139.6, 140.8, 142.9; **IR** (film): 2922, 2852, 1595, 1491, 1445, 1355, 1261, 1137, 1080, 1045, 966, 924, 877, 808, 753, 695 cm^{-1}; **MS** (ES) m/z (%): 701 (100) $[2M+H]^+$, 351 $[M+H]^+$; **Anal. calcd for** $C_{22}H_{22}SO_2$: C 75.39, H 6.33, S 9.15; **found**: C 75.29, H 6.04, S 9.21.

From dienyne **2l** (90 mg, 0.26 mmol) following the general procedure for the thermal cycloaddition (90 ºC, 6 h) an 80:20 mixture of **3l** and **4l** was obtained. Purification by chromatography (10-80% EtOAc-CH_2Cl_2) afforded **3l** (40 mg, 0.11 mmol, 42%) as a white solid that was recrystallized from Et_2O-hexane, and an inseparable mixture of **4l** and the aromatized derivative (34 mg, 0.10 mmol, 38%).

Data for **3l**: $\boldsymbol{R_f}$ = 0.19 (50% EtOAc-hexane); **mp** 76-78 ºC; **^{1}H NMR** (200 MHz) δ = 1.16 (s, 3 H, Me-7), 2.40 (s, 3 H, Me-*p*-Tol), 3.36-3.50 (m, 3 H, H-3a, 1 H-3, H-6), 4.30-4.40 (m, 3 H, 2 H-1, 1 H-3), 6.86-7.02 (m, 3 H), 7.23-7.36 (m, 7 H); **^{13}C NMR** (50 MHz) δ = 16.8 (Me-7), 21.3 (Me-*p*-Tol), 41.5, 47.2, 67.8, 71.5, 122.0 (2 C), 123.8, 127.0 (2 C), 127.6 (2 C), 128.6, 129.5, 130.0 (2 C), 131.5, 138.9, 139.2, 142.5, 147.5; **IR** (KBr): 2917, 2854, 1632, 1492, 1453, 1302, 1147, 1083, 1048, 899, 809, 771, 703 cm^{-1}; **MS** (ES) m/z (%): 701 $[2M+H]^+$, 351 (100) $[M+H]^+$; **Anal. calcd for** $C_{22}H_{22}O_2S$: C 75.39, H 6.33, S 9.15; **found**: C 75.41, H 6.65, S 9.48.

Partial data for **4l** from the mixture: $\boldsymbol{R_f}$ = 0.19 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 1.25 (s, 3 H, Me-7), 2.32 (s, 3 H, Me-*p*-Tol), 3.34-3.45 (m, 2 H), 4.25-4.39 (m, 4 H), 6.54 (dd, *J* = 2.9, 1.9 Hz, 1 H, H-5).

5.14. Synthesis of (±)-2-(*E*)-4-(*Z*)-5-Phenyl-4-(*p*-tolylsulfinyl)penta-2,4-dienyl propiolate, 2m, (±)-(3a*R*,6*S*,*S*$_S$)-6-Phenyl-5-(*p*-tolylsulfinyl)-3a,6-dihydro-3*H*-isobenzofuran-1-one, 3m, (±)-(3a*S*,6*R*,*S*$_S$)-6-Phenyl-5-(*p*-tolylsulfinyl)-3a,6-dihydro-3*H*-isobenzofuran-1-one, 4m.



To solution of **(±)-1b** (120 mg, 0.40 mmol), and propiolic acid (37 μL, 42 mg, 0.60 mmol) in 4 mL of CH_2Cl_2, at 0 ºC, dicyclohexylcarbodiimide (124 mg, 0.6 mmol) and dimethylaminopyridine (20 mg, 0.16 mmol) were added. The mixture was allowed to warm to room temperature and monitored by TLC until starting material disappearance (1 h). The reaction mixture was filtered to remove dicyclohexylurea and the ester was purified by column chromatography (20% EtOAc-hexane) affording **2m** (83 mg, 0.28 mmol, 70%) as a colorless oil that cyclized slowly upon standing in solution.

Data for **2m**: $\boldsymbol{R_f}$ = 0.41 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 2.38 (s, 3 H, Me-*p*-Tol), 2.87 (s, 1 H, H-3'), 4.66 (d, *J* = 5.9 Hz, 2 H, H-1), 6.25 (dt, *J* = 15.9, 6.0 Hz, 1 H, H-2), 6.38 (dm, *J* =

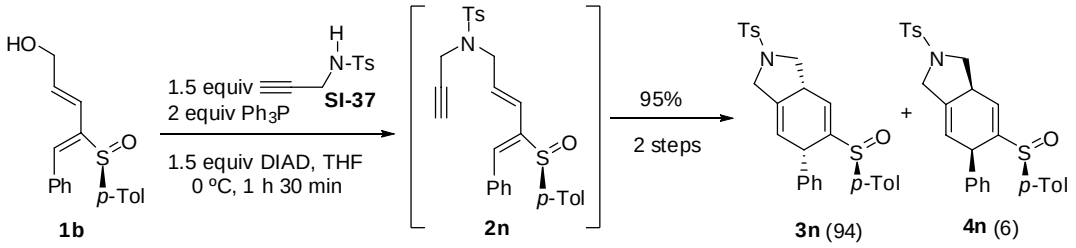
15.6 Hz, 1 H, H-3), 7.25-7.28 (m, 3 H), 7.38-7.44 (m, 5 H), 7.51-7.54 (m, 2 H); **^{13}C NMR** (50 MHz) δ = 21.3 (Me-*p*-Tol), 65.9 (C-1), 74.3, 75.1, 124.4 (2 C), 126.6, 127.2, 128.6 (2 C), 129.3, 129.9 (2 C), 130.0 (2 C), 133.7, 136.6, 139.3, 141.0, 142.2, 152.2 (CO); **Anal. calcd for** $C_{21}H_{18}O_3S$: C 71.98, H 5.18, S 9.15; **found**: C 72.19, H 5.30, S 8.96.

From dienyne **2m** (62 mg, 0.17 mmol) following the general procedure for the thermal cycloaddition (80 ºC, 8 h) an 84:16 mixture of **3m** and **4m** was obtained. Purification by chromatography (5-20% EtOAc-CH_2Cl_2) afforded **3m** (45 mg, 0.12 mmol, 72%) as a white solid that was recrystallized from EtOAc-hexane and **4m** (9 mg, 0.025, 14%) as a white solid that was recrystallized from Et_2O.

Data for **3m**: R_f = 0.26 (80% EtOAc-hexane); **mp** 208-210 ºC; **^{1}H NMR** (300 MHz) δ = 2.41 (s, 3 H, Me-*p*-Tol), 3.71 (dt, *J* = 11.7, 2.2 Hz, 1 H, H-6), 3.84 (m, 1 H, H-3a), 4.06 (dd, *J* = 10.1, 8.2 Hz, 1 H, 1 H-3), 4.84 (t, *J* = 8.4 Hz, 1 H, 1 H-3), 6.55 (t, *J* = 2.4 Hz, 1 H, H-7), 6.91-6.94 (m, 2 H), 7.03 (t, *J* = 2.3 Hz, 1 H, H-4), 7.27 (m, 4 H), 7.32-7.35 (m, 3 H); **^{13}C NMR** (50 MHz) δ = 21.6 (Me-*p*-Tol), 38.4, 43.9, 70.1 (C-3), 122.2, 126.2, 126.8 (2 C), 128.4, 129.1 (2 C), 129.2 (2 C), 130.2 (2 C), 135.7, 137.9, 138.0, 143.1, 148.3, 168.3 (CO); **IR** (KBr): 3027, 2912, 1760, 1693, 1627, 1492, 1454, 1333, 1205, 1182, 1085, 1048, 1021, 974, 897, 809, 757, 739, 701 cm^{-1}; **MS** (ES) m/z (%): 373 $[M+Na]^+$, 351 (100) $[M+H]^+$; **Anal. calcd for** $C_{21}H_{18}O_3S$: C 71.98, H 5.18, S 9.15; **found**: C 72.12, H 5.35, S 9.32.

Data for **4m**: R_f = 0.21 (80% EtOAc-hexane); **mp** 202-204 ºC; **^{1}H NMR** (300 MHz) δ = 2.31 (s, 3 H, Me-*p*-Tol), 3.86 (m, 1 H, H-3a), 3.99 (dd, *J* = 10.3, 8.7 Hz, 1 H, 1 H-3), 4.59 (dt, *J* = 12.1, 2.3 Hz, 1 H, H-6), 4.79 (t, *J* = 8.7 Hz, 1 H, 1 H-3), 6.70 (m, 1 H, H-7), 6.77 (t, *J* = 2.6 Hz, 1 H, H-4), 6.85-6.87 (m, 2 H), 6.93-7.19 (m, 7 H); **^{13}C NMR** (50 MHz) δ = 21.4 (Me-*p*-Tol), 38.3, 44.5, 69.9 (C-3), 124.9, 125.6 (2 C), 127.0, 128.0, 128.7 (2 C), 129.4 (2 C), 129.7 (2 C), 135.8, 137.3, 139.2, 141.8, 149.3, 168.1 (CO); **IR** (KBr): 3038, 2917, 1753, 1626, 1454, 1178, 1080, 1045, 981, 807, 759, 702 cm^{-1}; **MS** (ES) m/z (%): 373 $[M+Na]^+$, 351 (100) $[M+H]^+$; **Anal. calcd for** $C_{21}H_{18}O_3S$: C 71.98, H 5.18, S 9.15; **found**: C 72.18, H 5.26, S 9.32.

5.15. Synthesis of (±)-*N*-[5-Phenyl-4-(*p*-tolylsulfinyl)penta-2-(*E*)-4-(*Z*)-dienyl]-*N*-prop-2-ynyl-*p*-tolylsulfonamide, 2n, (±)-(3a*R*,6*S*,*S*$_S$)-6-Phenyl-5-(*p*-tolylsulfinyl)-2-(*p*-tolylsulfonyl)-2,3,3a,6-tetrahydroisoindole, 3n, and (±)-(3a*S*,6*R*,*S*$_S$)-6-Phenyl-5-(*p*-tolylsulfinyl)-2-(*p*-tolylsulfonyl)-2,3,3a,6-tetrahydroisoindole, 4n.



From dienol **1b** (60 mg, 0.2 mmol), Ph_3P (79 mg, 0.3 mmol), *N*-(prop-2-ynyl)-*p*-tolylsulfonamide **SI-37** (63 mg, 0.3 mmol) and diisopropyl azodicarboxylate (60 μL, 61 mg, 0.3 mmol), following the general procedure for Mitsunobu transformations, (THF, 0 ºC, 1 h 30 min) compound **2n** was obtained. Purification by chromatography (20-50% EtOAc-hexane) afforded a 72:28 mixture of **2n** and **3n** with traces of **4n** (95 mg, 0.19 mmol, 95%).

A solution of this mixture in $CDCl_3$ was cooled at 5 ºC and monitored by ^{1}H NMR until cycloaddition was complete (3 days), affording a 94:6 mixture of **3n** and **4n**. Purification by chromatography (20-50% EtOAc-hexane) afforded **3n** (89 mg, 0.18 mmol, 90%) as white solid that was recrystallized from EtOAc-hexane and **4n** (5 mg, 0.01 mmol, 5%) as a white solid that was recrystallized from EtOAc-hexane.

When the amino-Mitsunobu reaction was carried out at room temperature **2n** was not detected and a mixture of **3n** and **4n** was obtained after chromatography in an identical diastereomeric ratio to that described above.

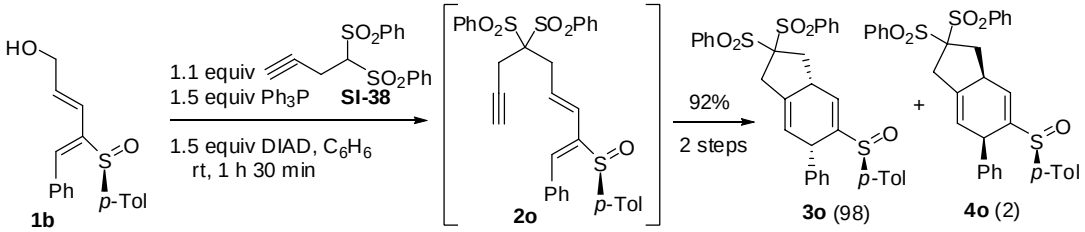
Partial data for **2n**: $\boldsymbol{R_f}$ = 0.12 (30% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 2.35 (s, 3 H, Me-*p*-Tol), 2.37 (m, 1 H, H-1 overlapped), 2.38 (s, 3 H, Me-*p*-Tol), 3.50-3.90 (m, 4 H, 2 H-3, 2 H-5), 5.97 (dt, *J* = 15.6, 6.8 Hz, 1 H, H-6), 6.30 (dd, *J* = 15.7, 0.9 Hz, 1 H, H-7).

Data for **3n**: $\boldsymbol{R_f}$ = 0.19 (50% EtOAc-hexane); **mp** 97-98 ºC; **^{1}H NMR** (300 MHz-COSY) δ = 2.37 (s, 3 H, Me-*p*-Tol), 2.43 (s, 3 H, Me-*p*-Tol), 2.89 (dd, *J* = 11.2, 9.3 Hz, 1 H, H-3), 3.23 (m, 1 H, H-3a), 3.44 (m, 1 H, H-6), 3.76 (dd, *J* = 13.4, 1.2 Hz, 1 H, H-1), 4.00 (m, 1 H, H-1), 4.04 (dd, *J* = 9.0, 8.3 Hz, 1 H, H-3), 5.29 (t, *J* = 1.8 Hz, 1 H, H-7), 6.76-6.82 (m, 2 H), 6.87 (t, *J* = 2.4 Hz, 1 H, H-4), 7.20-7.27 (m, 7 H), 7.32 (m, 2 H), 7.71 (d, *J* = 8.3 Hz, 2 H); **^{13}C NMR** (50 MHz) δ = 21.5 (2 C, 2 Me-*p*-Tol), 39.2 (C-3a), 42.8 (C-6), 50.3 (C-1), 52.2 (C-3), 121.7, 122.5, 126.7 (2 C), 127.5 (2 C), 127.7, 128.7 (2 C), 128.9 (2 C), 129.8 (2 C), 130.0 (2 C), 132.9, 133.7, 138.5, 139.8, 142.7, 143.7, 147.2; **IR**

(KBr): 2923, 2862, 1630, 1492, 1453, 1346, 1163, 1095, 1051, 811, 703 cm^{-1}; **MS** (ES) m/z (%): 979 $[2M+H]^+$, 490 (100) $[M+H]^+$; **Anal. calcd for** $C_{28}H_{27}NO_3S_2$: C 68.68, H 5.56, N 2.86, S 13.10; **found**: C 68.57, H 5.35, N 2.82, S 13.42.

Data for **4n**: R_f = 0.14 (50% EtOAc-hexane); **mp** 140-142 ºC; **^{1}H NMR** (300 MHz) δ = 2.29 (s, 3 H, Me-*p*-Tol), 2.42 (s, 3 H, Me-*p*-Tol), 2.86 (dd, *J* = 11.2, 9.3 Hz, 1 H, H-3), 3.15 (m, 1 H, H-3a), 3.83 (dd, *J* = 14.2, 1.0 Hz, 1 H, H-1), 3.95 (ap t, *J* = 8.5 Hz, 1 H, H-3), 3.97 (m, 1 H, H-1), 4.29 (m, 1 H, H-6), 5.40 (br s, 1 H, H-7), 6.53 (t, *J* = 2.6 Hz, 1 H, H-4), 6.73-6.80 (m, 2 H), 6.93-7.12 (m, 7 H), 7.31 (d, *J* = 8.1 Hz, 2 H), 7.70 (d, *J* = 8.1 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 21.4 (Me-*p*-Tol), 21.6 (Me-*p*-Tol), 39.1 (C-3a), 43.4 (C-6), 50.4 (C-1), 52.1 (C-3), 121.7, 125.5 (2 C), 125.6, 127.4, 127.5 (2 C), 128.4 (2 C), 129.2 (2 C), 129.5 (2 C), 129.9 (2 C), 133.1, 134.0, 139.3, 141.4, 143.8 (2 C), 148.6; **IR** (KBr): 2922, 2851, 1631, 1493, 1453, 1344, 1155, 1091, 1038, 805, 756, 701, 667 cm^{-1}; **MS** (ES) m/z (%): 490 $[M+H]^+$; **Anal. calcd for** $C_{28}H_{27}NO_3S_2$: C 68.68, H 5.56, N 2.86, S 13.10; **found**: C 68.71, H 5.43, N 2.91, S 13.12.

5.16. Synthesis of (±)-(3a*R*,6*S*,S_S)-2,2-Bis-benzenesulfonyl-6-phenyl-5-(*p*-tolylsulfinyl)-2,3,3a,6-tetrahydro-1*H*-indene, 3o, and (±)-(3a*S*,6*R*,S_S)-2,2-Bis-benzenesulfonyl-6-phenyl-5-(*p*-tolylsulfinyl)-2,3,3a,6-tetrahydro-1*H*-indene, 4o.



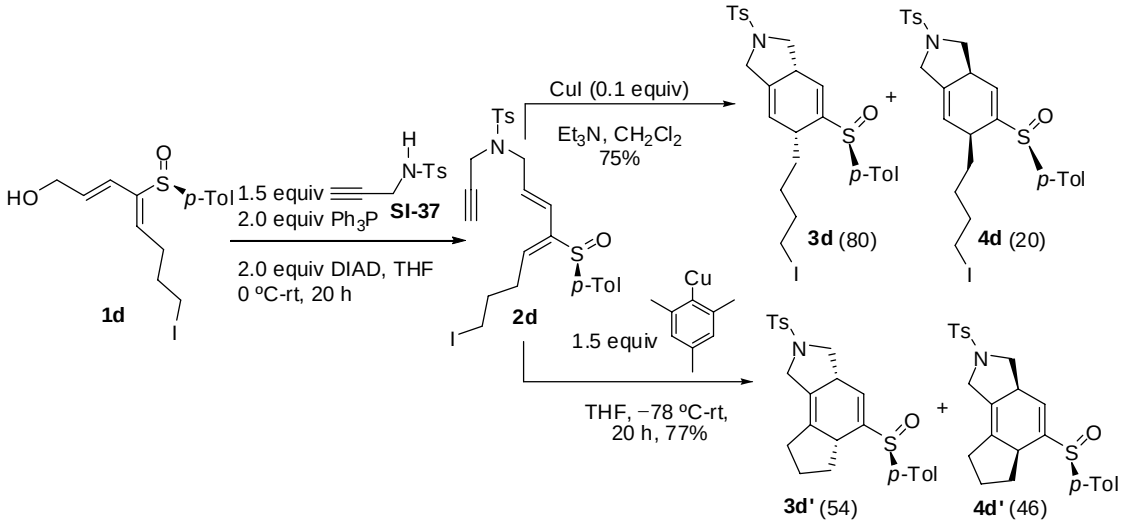
From dienol **1b** (49 mg, 0.16 mmol), Ph_3P (63 mg, 0.24 mmol), 4,4-bis-benzenesulfonylbut-1-yne **SI-38** (60 mg, 0.18 mmol) and diisopropyl azodicarboxylate (50 μL, 49 mg, 0.24 mmol), following the general procedure for Mitsunobu transformations (C_6H_6, rt, 1 h 30 min), a 98:2 mixture of **3o** and **4o** was obtained. Dienyne **2o** was not detected in the ^{1}H NMR spectra of the crude product. Purification by chromatography (20-50% EtOAc-hexane) afforded **3o** (90 mg, 0.146 mmol, 90%) as a white solid that was recrystallized from EtOAc-hexane and **4o** (2 mg, 0.003 mmol, 2%) as a white solid.

Data for **3o**: R_f = 0.45 (80% EtOAc-hexane); **mp** 229-230 ºC; **^{1}H NMR** (300 MHz) δ = 2.37-2.42 (m, 1 H), 2.40 (s, 3 H, Me-*p*-Tol), 3.08 (t, *J* = 7.3 Hz, 1 H), 3.16 (d, *J* = 18.6 Hz, 1 H), 3.37 (m, 1 H), 3.41-3.54 (m, 2 H), 5.23 (br s, 1 H, H-7), 6.78-6.82 (m, 2 H), 6.93 (br s, 1 H, H-4), 7.24-7.35 (m, 6 H), 7.54-7.78 (m, 7 H), 7.99 (m, 2 H), 8.13 (m, 2 H); **^{13}C NMR** (50 MHz) δ = 21.5 (Me-*p*-Tol), 35.7, 37.3, 39.7, 42.9, 89.9, 121.7, 124.2, 126.9 (2 C), 127.6, 128.7 (2 C), 128.8 (2 C), 128.9 (2 C), 129.0 (2

C), 130.0 (2 C), 131.3 (2 C), 131.5 (2 C), 134.1, 134.7, 134.9, 135.8, 135.9, 138.6, 140.0, 142.7, 145.6; **IR** (KBr): 3060, 3021, 2917, 2840, 1631, 1491, 1448, 1323, 1312, 1143, 1077, 1051, 757, 733, 703 cm^{-1}; **MS** (ES) m/z (%): 615 (100) $[M+H]^+$; **Anal. calcd for** $C_{34}H_{30}O_5S_3$: C 66.42, H 4.92, S 15.65; **found**: C 66.33, H 5.08, S 15.43.

Data for **4o**: R_f = 0.41 (80% EtOAc-hexane); **mp** 114-115 ºC; **^{1}H NMR** (300 MHz) δ = 2.32 (s, 3 H, Me-*p*-Tol), 2.36 (m, 1 H), 2.98 (dd, *J* = 14.4, 8.1 Hz, 1 H), 3.14 (d, *J* = 9.4 Hz, 1 H), 3.23-3.47 (m, 2 H), 4.28 (m, 1 H), 5.35 (br s, 1 H, H-7), 6.59 (t, *J* = 2.6 Hz, 1 H, H-4), 6.83 (dd, *J* = 8.1, 1.7 Hz, 1 H), 6.98-7.11 (m, 7 H), 7.50-7.77 (m, 6 H), 8.00 (dd, *J* = 8.5, 1.2 Hz, 2 H), 8.09 (dd, *J* = 8.5, 1.2 Hz, 2 H); **^{13}C NMR** (50 MHz) δ = 21.4 (Me-*p*-Tol), 36.2, 36.8, 39.4, 43.6, 90.0 (C-2), 122.0, 125.5 (2 C), 127.3, 127.8, 128.4 (2 C), 128.9 (2 C), 129.0 (2 C), 129.4 (2 C), 129.5 (2 C), 131.3 (2 C), 131.4 (2 C), 134.2, 134.7, 135.0, 136.1, 139.5, 139.6, 141.3, 147.2, 153.1; **IR** (KBr): 3060, 2924, 2851, 1631, 1492, 1447, 1331, 1312, 1146, 1078, 1042, 809, 757, 730 cm^{-1}; **MS** (ES) m/z (%): 615 (100) $[M+H]^+$; **Anal. calcd for** $C_{34}H_{30}O_5S_3$: C 66.42, H 4.92, S 15.65; **found**: C 66.29, H 5.15, S 15.57.

5.17. Synthesis of (–)-(*S*)-*N*-[8-Iodo-4-[*p*-tolylsulfinyl]octa-2-(*E*)-4-(*Z*)-dienyl]-*N*-prop-2-ynyl-*p*-tolylsulfonamide, 2d, (3a*R*,6*R*,*S*$_S$)-6-(3-Iodopropyl)-5-(*p*-tolylsulfinyl)-2-(*p*-tolylsulfonyl)-2,3,3a,6-tetrahydroisoindole, 3d, (3aS,6S,*S*$_S$)-6-(3-Iodopropyl)-5-(*p*-tolylsulfinyl)-2-(*p*-tolylsulfonyl)-2,3,3a,6-tetrahydroisoindole, 4d, (3a*R*,5a*R*,*S*$_S$)-5-(*p*-Tolylsulfinyl)-2-tosyl-1,2,3,3a,5a,6,7,8-octahydrocyclopenta[*e*]isoindole, 3d´, and (3a*S*,5a*S*,*S*$_S$)-5-(*p*-Tolylsulfinyl)-2-tosyl-1,2,3,3a,5a,6,7,8-octahydrocyclopenta[*e*]isoindole, 4d´.



From diene **1d** (83 mg, 0.21 mmol, 1.0 equiv), *N*-(prop-2-ynyl)-*p*-tolylsulfonamide **SI-37** (65 mg, 0.31 mmol, 1.5 equiv), PPh_3 (110 mg, 0.42 mmol, 2.0 equiv) and diisopropyl azodicarboxylate (83

μL, 0.42 mmol, 2.0 equiv), following the general procedure for Mitsunobu transformations (20 h), dienyne **2d** was obtained. Purification by chromatography (1-4% EtOAc-CH_2Cl_2) afforded **2d** (45 mg, 0.10 mmol, 50%) as a colorless oil.

Data for **2d**: $\boldsymbol{R_f}$ = 0.27 (50% EtOAc-hexane); $\boldsymbol{[\alpha]_D^{20}}$ = –105.7 (*c* = 1.71); **^{1}H NMR** (300 MHz) δ = 1.93 (t, *J* = 2.4 Hz, 1 H, H-alkyne), 2.03 (m, 2 H, H-7), 2.37 (s, 3 H), 2.39 (s, 3 H), 2.63 (ap sext, *J* = 7.4 Hz, 1 H, 1 H-6), 2.85 (ap sext, *J* = 7.4 Hz, 1 H, 1 H-6), 3.17-3.30 (m, 2 H, H-8), 3.51(dd, *J* = 18.3, 2.3 Hz, 1 H), 3.62 (dd, *J* = 14.4, 7.2 Hz, 1 H), 3.80 (dd, *J* = 14.3, 6.2 Hz, 1 H), 3.84 (dd, *J* = 18.4, 1.9 Hz, 1 H), 5.79 (dt, *J* = 15.7, 7.0 Hz, 1 H, H-2), 6.11-6.16 (m, 2 H, H-5 and H-3), 7.26 (d, *J* = 8.1 Hz, 2 H), 7.37 (d, *J* = 8.2 Hz, 2 H), 7.64 (d, *J* = 8.3 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 5.1 (C-8), 21.3, 21.5, 29.6, 32.7, 35.4, 48.1, 73.9, 76.1, 124.1 (2 C), 125.8, 127.6 (2 C), 128.1, 129.4 (2 C), 129.9 (2 C), 135.7, 136.2, 139.4, 140.9, 143.4, 143.6. **Anal. calcd for** $C_{25}H_{28}INO_3S_2$: C 51.63, H 4.85, I 21.82, N 2.41, S 11.03; **found**: C 51.47, H 4.76, I 21.98, N 2.23, S 11.17.

From sulfinyl dienyne **2d** (15 mg, 0.023 mmol), CuI (1 mg, 0.0052 mmol) and Et_3N (3 μL, 0.023 mmol) following the general procedure (20 h), a 80:20 mixture of **3d** and **4d** was obtained. Purification by chromatography (10-40% EtOAc-hexane) affored and inseparable 80:20 mixture of **3d** and **4d** (10 mg, 0.017 mmol, 75%) as a white solid.

Partial data for **3d** (from the mixture): $\boldsymbol{R_f}$ = 0.33 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 1.53-1.63 (m. 4 H), 2.37 (s, 3 H), 2.43 (s, 3 H), 2.49-2.55 (m, 1 H), 2.70 (dd, *J* = 11.3, 9.1 Hz, 1 H), 3.03 (t, *J* = 6.1 Hz, 2 H), 3.09-3.20 (m, 1 H), 3.74-3.79 (m, 1 H), 3.87-4.01 (m, 2H), 5.25 (br s, 1 H), 6.76 (ap t, *J* = 2.4 Hz, 1 H), 7.26 (d, *J* = 7.9 Hz, 2 H), 7.33 (d, *J* = 7.9 Hz, 2 H), 7.49 (d, *J* = 8.2 Hz, 2 H), 7.70 (d, *J* = 8.3 Hz, 2 H); **IR** (KBr): 2922, 2861, 1732, 1596, 1492, 1453, 1399, 1344, 1305, 1219, 1162, 1096, 1045, 1014, 811, 706, 666, 595, 549 cm^{-1}; **HRMS** (ES) calcd for $C_{25}H_{28}INO_3S_2$ $[M+H]^+$: 581.0584; **found**: 582.0664 $[M+H]^+$, 1163.1177 $[2M+H]^+$.

Partial data for **4d** (from the mixture): $\boldsymbol{R_f}$ = 0.33 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 2.39 (s, 3 H), 5.20 (br s, 1 H), 6.63 (dd, *J* = 2.7, 2.1 Hz, 1 H), 7.41 (d, *J* = 8.4 Hz, 2H); **IR** (KBr): 2922, 2861, 1732, 1596, 1492, 1453, 1399, 1344, 1305, 1219, 1162, 1096, 1045, 1014, 811, 706, 666, 595, 549 cm^{-1}; **HRMS** (ES) calcd for $C_{25}H_{28}INO_3S_2$ $[M+H]^+$: 581.0584; **found**: 582.0664 $[M+H]^+$, 1163.1177 $[2M+H]^+$.

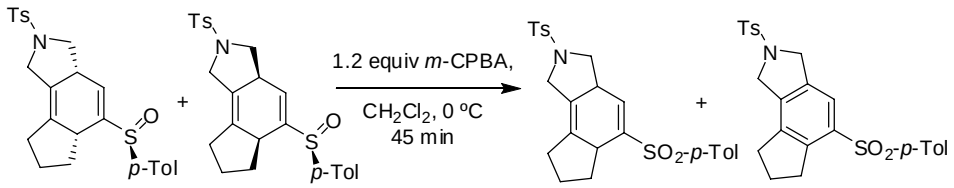
To a cold suspension (–78 ºC) of mesityl copper (6 mg, 0.035 mmol, 1.5 equiv) in anhydrous THF (0.3 mL), a solution of **2d** in THF (0.3 mL) was added dropwise. The mixture was allowed to reach room temperature and was stirred during one night until starting material disappearance (TLC). Water was added, and the aqueous layer was extracted with Et_2O (3 times), dried over anhydrous

$MgSO_4$, filtered and concentrated. The crude product was purified by chromatography (10-40% EtOAc-hexane) to afford an inseparable 54:46 mixture of **3d'** and **4d'** (8 mg, 0.017 mmol, 77%) as a white solid.

Partial data for **3d'** (from the mixture): R_f = 0.27 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 2.37 (s, 3 H), 2.43 (s, 3 H), 6.59 (t, *J* = 2.3 Hz, 1 H, H-4); **IR** (KBr): 2922, 1596, 1492, 1450, 1345, 1162, 1092, 1047, 812, 666, 595, 549 cm^{-1}; **MS** (ES) m/z (%): 929 $[2M+Na]^+$, 907 $[2M+H]^+$, 476 (100) $[M+Na]^+$, 454 $[M+H]^+$.

Partial data for **4d'** (from the mixture): R_f = 0.27 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 2.38 (s, 3 H), 2.42 (s, 3 H), 6.55 (t, *J* = 2.3 Hz, 1 H, H-4).

5.18. Synthesis of 2,5-Ditosyl-1,2,3,3a,5a,6,7,8-octahydrocyclopenta[*e*]isoindole, 5d.

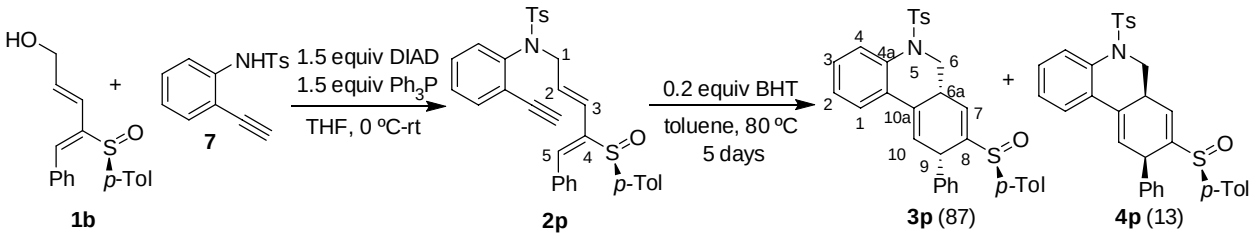


3d (54) **4d** (46) **5d** (86) **6d** (14)

From a 54:46 mixture of **3d** and **4d** (8 mg, 0.017 mmol, 1.0 equiv), *m*-CPBA (5 mg, 0.021 mmol, 1.2 equiv), following the general procedure (45 minutes), an 86:14 mixture of **5d** and **6d** was obtained. Purification by chromatography (5-30% EtOAc-hexane) afforded an inseparable mixture of **5d** and **6d** (6 mg, 0.011 mmol, 64%).

Partial data for **5d** (from the mixture): **^{1}H NMR** (300 MHz) δ = 0.97-1.08 (m, 2 H), 1.68-1.79 (m, 2 H), 2.06-2.17 (m, 2 H), 2.41 (s, 3 H), 2.42 (s, 3 H), 2.62 (dd, *J* = 10.8, 8.9 Hz, 1 H), 2.77-2.94 (m, 1 H), 3.25-3.38 (m, 1 H), 3.58 (dm, *J* = 13.4 Hz, 1 H), 3.86-3.95 (m, 2 H), 6.89 (t, *J* = 2.4 Hz, 1 H, H-4), 7,29 (d, *J* = 7.8 Hz, 2 H), 7.32 (d, *J* = 7.8 Hz, 2 H), 7.67 (d, *J* = 8.0 Hz, 2 H), 7.69 (d, *J* = 7.9 Hz, 2 H); **HRMS** (ES) calcd for $C_{25}H_{28}NO_4S_2$ $[M+H]^+$: 470.1460; **found**: 470.1483 $[M+H]^+$.

5.19. Synthesis of (*S*)-*N*-(2-Ethynylphenyl)-*N*-[(2*E*,4*Z*)-5-phenyl-4-(*p*-tolylsulfinyl)penta-2,4-dienyl]*p*-tolylsulfonamide, 2p, (–)-(6a*R*,9*S*,S_S)-9-Phenyl-8-(*p*-tolylsulfinyl)-5-tosyl-5,6,6a,9-tetrahydrophenanthridine, 3p, and (6a*S*,9*R*,S_S)-9-Phenyl-8-(*p*-tolylsulfinyl)]-5-tosyl-5,6,6a,9-tetrahydrophenanthridine, 4p.



From diene **1b** (61 mg, 0.20 mmol, 1.0 equiv), sulfonamide **7** (60 mg, 0.22 mmol, 1.1 equiv), PPh_3 (79 mg, 0.30 mmol, 1.5 equiv) and DIAD (59 μL, 0.3 mmol, 1.5 equiv), following the general procedure for Mitsunobu transformations (20 h), compound **2p** was obtained. Purification by chromatography (10-50% EtOAc-hexane) afforded **2p** (58 mg, 0.11 mmol, 55%) as a yellow oil.

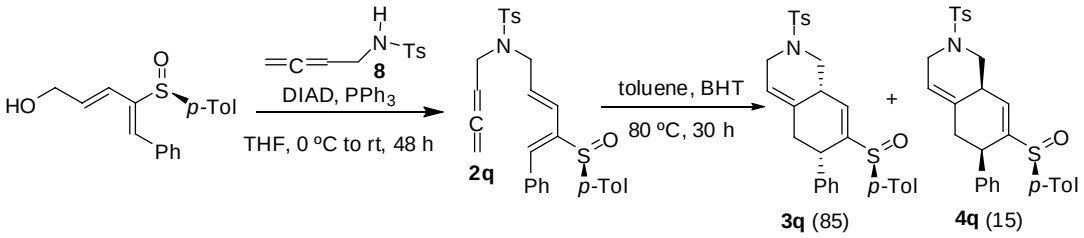
Data for **2p**: R_f = 0.42 (50 % EtOAc-hexane); **^{1}H NMR** (400 MHz-COSY) δ = 2.31 (s, 3 H), 2.33 (s, 3 H), 2.85 (s, 1 H, H-alkyne), 4.16 (d, *J* = 5.9 Hz, 2 H, H-1), 6.01 (d, *J* = 16.0 Hz, 1 H, H-3), 6.10 (dt, *J* =15.6, 6.2 Hz, 1 H, H-2), 6.84-6.86 (m, 1 H), 7.07-7.37 (m, 15 H), 7.47 (d, *J* = 8.3 Hz, 1 H), 7.46-7.49 (m, 1 H); **^{13}C NMR** (100 MHz) (partial data) δ = 21.4, 21.5, 52.9, 80.1, 81.9, 124.5 (2 C), 127.8 (2 C), 128.5 (2 C), 129.4 (2 C), 129.8 (2 C), 129.9 (2 C), 131.3, 134.1, 135.8.

From **2p** (32 mg, 0.06 mmol), BHT (3 mg, 0.012 mmol), following the general procedure for thermal cycloadditions (80 ºC, 5 days), an 87:13 mixture of **3p** and **4p** was obtained. Purification by chromatography (10-50% EtOAc-hexane) afforded **3p** (7 mg, 0.012 mmol, 21%) as a white solid and a mixture of **3p** and **4p** (12 mg, 0.022 mmol, 36%).

Data for **3p**: R_f = 0.44 (50% EtOAc-hexane); **mp** 113-115 ºC; **$[\alpha]_D^{20}$** = –5.6 (*c* = 0.63); **^{1}H NMR** (400 MHz) δ = 2.37 (s, 3 H), 2.40 (s, 3 H), 2.94-3.02 (m, 1 H, H-6a), 3.30 (t, *J* = 12.7 Hz, 1 H, H-6), 3.55 (ddd, *J* = 9.0, 2.9, 1.9 Hz, 1 H, H-9), 4.76 (dd, *J* = 13.2, 3.8 Hz, 1 H, H-6), 5.85 (dd, *J* = 2.8, 2.6 Hz, 1 H, H-10), 6.77 (dd, *J* = 3.0, 1.8 Hz, 1 H, H-7), 6.89-6.92 (m, 2 H), 7.00 (td, *J* = 8.1, 1.2 Hz, 1 H), 7.18-7.28 (m, 8 H), 7.32-7.35 (m, 3 H), 7.58 (d, *J* = 8.3 Hz, 2 H), 7.87 (dd, *J* = 8.4, 1.1 Hz, 1 H); **^{13}C NMR** (100 MHz) δ = 21.5, 21.6, 33.7, 42.7, 51.4, 122.5, 123.9, 124.1, 124.2, 124.8, 126.2, 126.6 (2 C), 127.1 (2 C), 127.7, 128.4, 128.7, 128.8 (2 C), 128.9 (2 C), 129.8 (2 C), 130.1 (2 C), 135.6, 136.4, 138.6, 140.0, 142.7, 144.0, 146.0; **IR** (KBr): 2923, 2851, 1631, 1451, 1354, 1166, 1083, 810, 761, 667, 578 cm^{-1}; **MS** (ES) m/z (%): 574 $[M+Na]^+$, 552 $[M+H]^+$; **Anal. calcd for** $C_{33}H_{29}NO_3S_2$: C 71.84, H 5.30, N 2.54, S 11.62; **found**: C 71.67, H 5.39, N 2.38, S 11.75.

Partial data for **4p** (from the mixture): R_f = 0.40 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 2.27 (s, 3 H), 2.31 (s, 3 H), 2.77-2.87 (m, 1 H, H-6a), 3.20 (t, *J* = 13.1 Hz, 1 H, H-6), 4.33 (ddd, *J* = 8.8, 2.3, 1.9 Hz, 1 H, H-9), 4.62 (dd, *J* = 13.2, 3.8 Hz, 1 H, H-6), 5.90 (t, *J* = 2.5 Hz, 1 H, H-10), 6.37 (dd, *J* = 3.2, 1.9 Hz, 1 H, H-7), 6.77-6.80 (m, 2 H), 6.93-7.02 (m, 1 H), 7.35 (dd, *J* = 8.0, 1.5 Hz, 2 H), 7.45 (d, *J* = 8.3 Hz, 2 H), 7.84 (dd, *J* = 8.4, 0.9 Hz, 1 H).

5.20. Synthesis of (–)-(*S*)-*N*-(Buta-2,3-dienyl)-*N*-[5-phenyl-4-(*p*-tolylsulfinyl)penta-2-(*E*)-4-(*Z*)-dienyl)]-*p*-tolylsulfonamide, 2q, (+)-(6*S*,8a*R*,S_S)-6-Phenyl-7-(*p*-tolylsulfinyl)-2-tosyl-1,2,3,5,6,8a-hexahydroisoquinoline, 3q, and (6*R*,8a*S*,S_S)-6-Phenyl-7-(*p*-tolylsulfinyl)-2-tosyl-1,2,3,5,6,8a-hexahydroisoquinoline, 4q.



From **1b** (58 mg, 0.19 mmol, 1.5 equiv), sulfonamide **8** (38 mg, 0.13 mmol, 1.0 equiv), PPh_3 (68 mg, 0.26 mmol, 2.0 equiv) and diisopropyl azodicarboxylate (51 μL, 0.26 mmol, 2.0 equiv), following the general procedure for Mitsunobu tranformations, compound **2q** was obtained. Purification by chromatography (1-10% EtOAc-hexane) afforded **2q** (60 mg, 0.12 mmol, 92%) as a colorless oil.

Data for **2q**: R_f = 0.46 (70% EtOAc-hexane); **$[\alpha]_D^{20}$** = – 293.9 (*c* = 1.45); **^{1}H NMR** (300 MHz) δ = 2.37 (s, 3 H, Me), 2.40 (s, 3 H, Me), 3.53 (ddt, *J* = 15.1, 7.0, 2.2 Hz, 1 H), 3.65 (ddt, *J* = 15.1, 6.7, 2.4 Hz, 1 H), 3.73 (dd, *J* = 15.4, 7.0 Hz, 1 H), 3.84 (dd, *J* = 15.4, 6.2 Hz, 1 H), 4.62 (m, 2 H), 4.72 (ap quint, *J* = 6.9 Hz, 1 H), 5.99 (dt, *J* =15.7, 6.7 Hz, 1 H), 6.20 (d, *J* = 16.1 Hz, 1 H), 7.18 (s, 1 H), 7.26 (m, 4 H), 7.39 (m, 5 H), 7.50 (m, 2 H), 7.65 (d, *J* = 8.3 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 13.1, 21.3, 21.4, 45.5, 48.5, 76.2, 85.3, 124.5 (2 C), 125.5, 127.1 (2 C), 128.5 (2 C), 129.1, 129.6, 129.7, 129.8, 129.9, 133.8, 135.8, 137.2, 139.6, 140.8, 142.5, 143.3; **IR** (film): 2912, 1953, 1596, 1489, 1445, 1341, 1158, 1044, 811, 752 cm^{-1}; **MS** (ES) m/z (%): 1029 $[2M+Na]^+$, 527 $[M+Na]^+$, 504 (100) $[M+H]^+$; **Anal. calcd for** $C_{29}H_{29}NO_3S_2$: C 69.15, H 5.80, N 2.78, S 12.73; **found**: C 69.23, H 5.63, N 2.82, S 12.91.

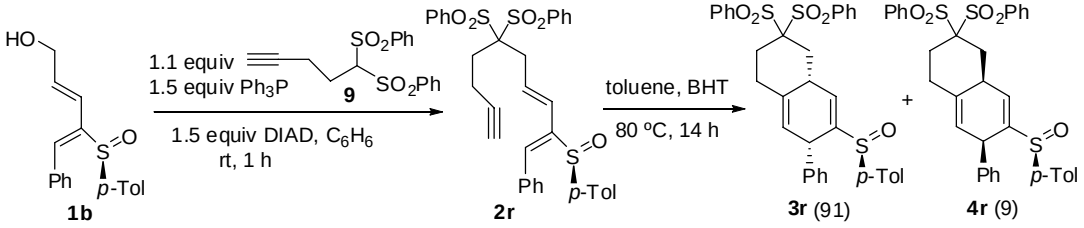
From sulfonamide **2q** (19 mg, 0.037 mmol, 1.0 equiv) following the general procedure for thermal cycloadditions (80 ºC, 30 h), an 85:15 mixture of **3q** and **4q** was obtained. Purification by chromatography (1-10% EtOAc-CH_2Cl_2) afforded an 85:15 mixture of **3q** and **4q** (14 mg, 0.028 mmol,

75%). A second chromatography (10-50% EtOAc-hexane) provided 5 mg of pure **3q** as a white solid that was recrystallized from EtOAc-hexane.

Data for **3q**: R_f = 0.22 (EtOAc-CH_2Cl_2); **mp** 184-186 ºC; $[\alpha]_D^{20}$ = + 9.07 (*c* = 0.52); **^{1}H NMR** (400 MHz) δ = 2.12 (d, *J* = 12.7 Hz, 1 H, H-5), 2.25 (ap t, *J* = 11.2 Hz, 1 H, H-8a), 2.37 (s, 3 H), 2.46 (s, 3 H), 2.49-2.54 (m, 1 H, H-5), 3.08 (dm, *J* = 16.5 Hz, 1 H, H-3), 3.29 (d, *J* = 6.5 Hz, 1 H, H-6), 3.34-3.36 (m, 1 H, H-1), 3.96 (dm, *J* = 16.3 Hz, 1 H, H-3), 4.24 (dd, *J* = 11.4, 5.5 Hz, 1 H, H-1), 5.04 (m, 1 H, H-4), 6.70 (d, *J* = 2.7 Hz, H-8), 6.79-6.82 (m, 2 H), 7.12-7.14 (m, 3 H), 7.21 (d, *J* = 8.4 Hz, 2 H), 7.34-7.39 (m, 4 H), 7.68 (d, *J* = 8.2 Hz, 2 H); **^{13}C NMR** (100 MHz) δ = 21.5, 21.6, 37.1 (C-8a), 39.3 (C-5), 40.4 (C-6), 45.0 (C-3), 47.6 (C-1), 119.4 (C-4a), 125.8 (2 C), 126.8, 127.3, 127.6 (2 C), 127.8 (2 C), 128.3 (2 C), 129.8 (2 C), 130.0 (2 C), 131.4, 133.3, 139.1, 140.9, 142.4, 143.8, 146.8; **IR** (KBr): 3029, 2921, 2850, 1596, 1492, 1455, 1399, 1337, 1158, 1109, 1087, 1049, 961, 811, 753, 702, 678, 551 cm^{-1}; **MS** (ES) m/z (%):1029 $[2M+Na]^+$, 1007 $[2M+H]^+$, 526 $[M+Na]^+$, 504 (100) $[M+H]^+$; **Anal. calcd for** $C_{29}H_{29}NO_3S_2$: C 69.15, H 5.80, N 2.78, S 12.73; **found**: C 68.97, H 5.74, N 2.67, S 12.81.

Partial data for **4q** (from the mixture): R_f = 0.38 (EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 2.25 (s, 3 H), 2.45 (s, 3 H), 3.73 (dm, 1 H, *J* = 6.4 Hz), 4.17 (dd, *J* = 11.5, 5.7 Hz, 1 H), 4.79-4.99 (m, 1 H, H-4), 6.48 (d, *J* = 3.0 Hz, 1 H), 6.75-6.61 (m, 2 H), 6.93-6.99 (m, 5 H), 7.02-7.05 (m, 1 H).

5.21. Synthesis of (±)-5,5-Bis-benzenesulfonyl-10-phenyl-9-(*p*-tolylsulfinyl)-7-(*E*)-9-(*Z*)-decadien-1-yne, 2r, (±)-(4a*R*,7*S*,*S*$_S$)-3,3-Bis-benzenesulfonyl-7-phenyl-6-(*p*-tolylsulfinyl)-1,2,3,4,4a,7-hexahydronaphthalene, 3r, and (±)-(4a*S*,7*R*,*S*$_S$)-3,3-Bis-benzenesulfonyl-7-phenyl-6-(*p*-tolylsulfinyl)-1,2,3,4,4a,7-hexahydronaphthalene, 4r.



From 3-butyn-1-ol (76 μL, 1.0 mmol), PPh_3 (525 mg, 2.0 mmol), 4,4-bis-benzenesulfonylmethane (385 mg, 1.3 mmol) and diisopropyl azodicarboxylate (0.39 mL, 2.0 mmol), following the general procedure for Mitsunobu transformations (C_6H_6, 2 h), compound **9** was obtained. Purification by chromatography (60-100% CH_2Cl_2-hexane) afforded **9** (174 mg, 0.5 mmol, 50%) as a white solid.

From dienol **1b** (39 mg, 0.13 mmol), PPh_3 (52 mg, 0.20 mmol, 1.5 equiv), 5,5-bis-benzenesulfonyl-pent-1-yne **9** (50 mg, 0.14 mmol) and diisopropyl azodicarboxylate (40 μL, 40 mg, 0.20 mmol, 1.5 equiv) following the general procedure (C_6H_6, rt, 1 h) compound **2r** was obtained. Purification by chromatography (10-50% EtOAc-hexane) afforded 70 mg of impure **2r**. A second chromatography (5-50% EtOAc-CH_2Cl_2) afforded pure **2r** (30 mg, 0.05 mmol, 38%).

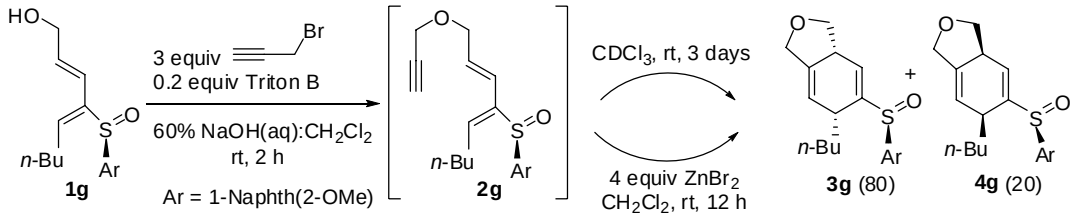
Data for **2r**: $\boldsymbol{R_f}$ = 0.18 (60% Et_2O-hexane); **mp** 84-85 ºC; **^{1}H NMR** (300 MHz) δ = 1.97 (t, *J* = 2.3 Hz, 1 H, H-1), 2.24-2.48 (m, 4 H, 2 H-3, 2 H-4), 2.38 (s, 3 H, Me-*p*-Tol), 2.93 (d, *J* = 6.6 Hz, 2 H, 2 H-6), 6.17 (d, *J* = 16.1 Hz, 1 H, H-8), 6.39 (dt, *J* = 15.7, 6.6 Hz, 1 H, H-7), 7.21-7.75 (m, 15 H), 7.95-7.99 (m, 4 H); **^{13}C NMR** (75 MHz) δ = 13.5, 21.4 (Me-*p*-Tol), 28.8, 33.0, 69.5, 82.3, 89.5, 124.5 (2 C), 126.7, 127.1, 128.6 (2 C), 128.8 (4 C), 130.0 (2 C), 130.1 (2 C), 131.1 (5 C), 133.8, 134.7, 136.1, 136.3, 139.6, 140.9, 142.5; **IR** (KBr): 3060, 2917, 1631, 1447, 1310, 1144, 1079, 724 cm^{-1}; **MS** (ES) m/z (%): 629 (100) $[M+H]^+$; **Anal. calcd for** $C_{35}H_{32}O_5S_3$: C 66.85, H 5.13, S 15.30; **found**: C 66.73, H 5.34, S 15.47.

From dienyne **2r** (30 mg, 0.05 mmol) following the general procedure for thermal cycloadditions (80 ºC, 14 h) a 91:9 mixture of **3r** and **4r** was obtained. Purification by chromatography (2-5% EtOAc-CH_2Cl_2) afforded pure **3r** (18 mg, 0.029 mmol, 58%) as a white solid that was recrystallized from EtOAc-hexane and a mixture of **3r** and **4r** (10 mg, 0.016 mmol, 32%).

Data for **3r**: $\boldsymbol{R_f}$ = 0.23 (10% EtOAc-CH_2Cl_2); **mp** 223-225 ºC; **^{1}H NMR** (300 MHz) δ = 2.00-2.27 (m, 3 H), 2.40 (s, 3 H, Me-*p*-Tol), 2.58 (m, 1 H), 2.88-3.00 (m, 2 H), 3.45 (m, 1 H, H-7), 3.88 (m, 1 H, H-4a), 5.30 (t, *J* = 1.7 Hz, 1 H, H-8), 6.71 (dd, *J* = 3.4, 1.2 Hz, 1 H, H-5), 6.82-6.88 (m, 2 H), 7.20-7.29 (m, 5 H), 7.41 (d, *J* = 8.3 Hz, 2 H), 7.58-7.68 (m, 4 H), 7.71-7.79 (m, 2 H), 7.96 (d, *J* = 8.3 Hz, 2 H), 8.14 (d, *J* = 8.1 Hz, 2 H); **^{13}C NMR** (50 MHz) δ = 21.5 (Me-*p*-Tol), 27.9, 29.7, 33.9, 34.6, 42.3, 87.5 (C-3), 122.7, 126.5, 126.6 (2 C), 127.4, 128.4 (2 C), 128.8 (4 C), 128.9 (2 C), 130.1 (2 C), 131.1 (2 C), 131.5 (2 C), 132.1, 134.6, 134.8, 135.7, 136.6, 138.8, 140.5, 142.7, 144.6; **IR** (KBr): 3060, 2921, 2851, 1633, 1491, 1447, 1376, 1325, 1310, 1146, 1080, 1049, 810, 756, 724, 704, 687 cm^{-1}; **MS** (ES) m/z (%): 629 (100) $[M+H]^+$; **Anal. calcd for** $C_{35}H_{32}O_5S_3$: C 66.85, H 5.13, S 15.30; **found**: C 67.02, H 5.40, S 15.14.

Partial data for **4r** (from the mixture): $\boldsymbol{R_f}$ = 0.21 (10% EtOAc-CH_2Cl_2); **^{1}H NMR** (300 MHz) δ = 2.33 (s, 3 H, Me-*p*-Tol), 3.85 (m, 1 H, H-4a), 4.19 (m, 1 H, H-7), 5.37 (m, 1 H, H-8), 6.46 (d, *J* = 3.8 Hz, 1 H, H-5).

5.22. Synthesis of (+)-(*R*)-4-Oxa-8-(2-methoxynaphthalene-1-ylsulfinyl)-6-(*E*)-8-(*Z*)-tridecadien-1-yne, 2g, (3a*R*,6*R*,R_S)-6-*n*-Butyl-5-(2-methoxynaphthalene-1-ylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 3g, and (3a*S*,6*S*,R_S)-6-*n*-Butyl-5-(2-methoxynaphthalene-1-ylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 4g.



From diene **1g** (69 mg, 0.20 mmol), propargyl bromide (65 μL, 89 mg, 0.60 mmol), Triton B (20 μL, 18 mg, 0.04 mmol) and 60% aqueous sodium hydroxide (2 mL) following the general procedure (2 h) compound **2g** was obtained. Purification by chromatography (20-80% EtOAc-hexane) afforded **2g** (43 mg, 0.11 mmol, 55%) and a mixture of **3g** and **4g** (20 mg, 0.05 mmol, 25%).

Data for **2g**: R_f = 0.54 (80% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 0.78 (t, *J* = 7.0 Hz, 3 H, Me-*n*-Bu), 1.10-1.39 (m, 4 H, 2 CH_2-*n*-Bu), 2.13 (m, 1 H, 1 H-10), 2.33 (t, *J* = 2.4 Hz, 1 H, H-1), 2.45 (m, 1 H, 1 H-10), 3.84 (d, *J* = 2.4 Hz, 2 H, H-3), 3.99 (s, 3 H, OMe), 4.00 (m, 2 H, H-5), 5.89 (dt, *J* = 15.6, 6.3 Hz, 1 H, H-6), 6.08 (t, *J* = 7.8 Hz, 1 H, H-9), 6.68 (dd, *J* = 15.6, 0.8 Hz, 1 H, H-7), 7.20 (d, *J* = 9.0 Hz, 1 H, H-3'), 7.36 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1 H, H-6'), 7.52 (ddd, *J* = 8.6, 6.9, 1.5 Hz, 1 H, H-7'), 7.75 (d, *J* = 8.2 Hz, 1 H, H-5'), 7.90 (d, *J* = 9.0 Hz, 1 H, H-4'), 9.07 (d, *J* = 9.5 Hz, 1 H, H-8'); **Anal. calcd for** $C_{23}H_{26}O_3S$: C 72.22, H 6.85, S 8.38; **found**: C 72.51, H 6.73, S 8.46.

To a solution of **2g** (10 mg, 0.026 mmol) in 0.5 mL of CH_2Cl_2, under an argon atmosphere, $ZnBr_2$ (40 mg, 0.180 mmol) was added and the mixture was stirred at room temperature until starting material disappearance (12 h). Then 5% aqueous $NaHCO_3$ (2 mL), water (2 mL), and CH_2Cl_2 (2 mL) were added, the layers were separated and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic extracts were washed with a saturated solution of NaCl, dried over $MgSO_4$ and filtered to give, after evaporation of the solvents, an 80:20 mixture of **3g** and **4g**. Purification by chromatography (30-80% EtOAc-hexane) afforded 8 mg (0.021 mmol, 80%) of an inseparable mixture of **3g** and **4g** as a colorless oil.

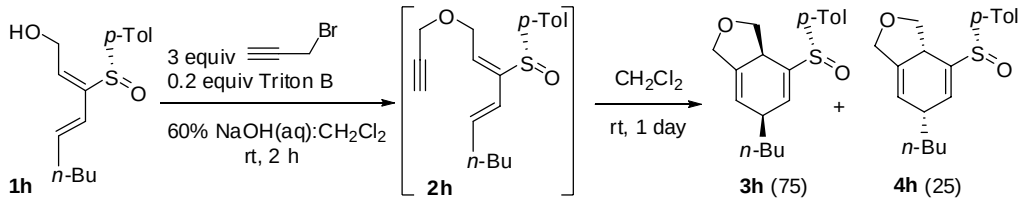
In a related experiment a solution of **2g** in $CDCl_3$ was kept at room temperature and monitored by ^{1}H NMR until cycloaddition was complete (3 days). For an identical sample cooled at 5 ºC the

reaction was complete in 7 days, and using CD_3OD as solvent it took 5 days at room temperature. In all these experiments the diastereomeric ratio measured was identical to that described above.

Partial data for **3g** (from the mixture): R_f = 0.12 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 4.00 (s, 3 H, OMe), 5.29 (br s, 1 H, H-7), 6.98 (t, *J* = 2.2 Hz, 1 H, H-4), 8.63 (d, *J* = 8.8 Hz, 1 H, H-8'); **IR** (film): 2950, 2926, 2855, 1620, 1593, 1560, 1506, 1467, 1430, 1353, 1334, 1272, 1250, 1150, 1135, 1045, 897, 812, 773, 750, 709 cm^{-1}; **MS** (ES): m/z (%): 383 (100) $[M+H]^+$, 381 $[(M-2)+1]^+$.

Partial data for **4g** (from the mixture): R_f = 0.12 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 3.96 (s, 3 H, OMe), 5.47 (br s, 1 H, H-7), 6.62 (t, *J* = 2.2 Hz, 1 H, H-4), 8.71 (d, *J* = 8.5 Hz, 1 H, H-8').

5.23. Synthesis of (±)-4-Oxa-7-(*p*-tolylsulfinyl)-6-(*E*)-8-(*Z*)-tridecadien-1-yne, 2h, (±)-(3a*S*,6*R*,S_S)-6-*n*-Butyl-4-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 3h, and (±)-(3a*R*,6*S*,S_S)-6-*n*-Butyl-4-(*p*-tolylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 4h.



From diene **1h** (20 mg, 0.07 mmol), propargyl bromide (23 μL, 0.21 mmol), Triton B (7 μL, 0.014 mmol) and NaOH 60% (1 mL) following the general procedure (2 h), compound **2h** was obtained. The crude ^{1}H NMR showed 20% of cycloadducts. The cycloaddition was complete after 1 day at room temperature affording a 75:25 mixture of **3h** and **4h**. Purification by chromatography (10-50% EtOAc-hexane) afforded a mixture of **3h** and **4h** (10 mg, 0.032 mmol, 46%) and 10 mg (0.032 mmol, 46%) of pure **3h**, both as colorless oils.

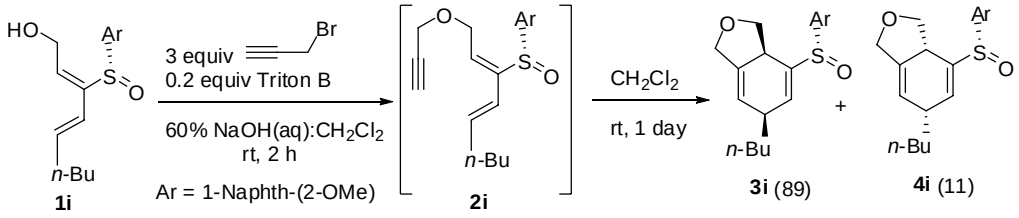
Partial data for **2h**: R_f = 0.44 (10% CH_2Cl_2-EtOAc); **^{1}H NMR** (200 MHz) δ = 0.79 (t, *J* = 7.0 Hz, 3 H, Me-*n*-Bu), 1.06-1.23 (m, 4 H), 2.00 (q, *J* = 6.8 Hz, 2 H, H-10), 2.37 (s, 3 H, Me-*p*-Tol), 2.47 (t, *J* = 2.4 Hz, 1 H, H-1), 4.21 (d, *J* = 2.2 Hz, 2 H, H-3), 4.57 (d, *J* = 6.8 Hz, 2 H, H-5), 5.88 (d, *J* = 15.4 Hz, 1 H, H-8), 6.04 (dt, *J* = 15.7, 6.4 Hz, 1 H, H-9), 6.21 (t, *J* = 6.8 Hz, 1 H, H-6), 7.26 (d, *J* = 8.1 Hz, 2 H, *p*-Tol), 7.45 (d, *J* = 8.4 Hz, 2 H, *p*-Tol).

Data for **3h**: R_f = 0.28 (50% EtOAc-hexane); **^{1}H NMR** (200 MHz) δ = 0.94 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 1.24-1.37 (m, 5 H), 1.59 (m, 1 H), 2.39 (s, 3 H, Me-*p*-Tol), 2.87 (m, 1 H), 3.03 (m, 1 H), 3.04 (dd, *J* = 10.8, 7.7 Hz, 1 H), 3.97 (t, *J* = 7.2 Hz, 1 H), 4.16 (dm, *J* = 10.6 Hz, 1 H), 4.27 (dm, *J* = 12.1 Hz, 1 H), 5.46 (br s, 1 H, H-7), 6.64 (dd, *J* = 3.7, 2.2 Hz, 1 H H-5), 7.28 (d, *J* = 8.1 Hz, 2 H, *p*-

Tol), 7.49 (d, *J* = 8.2 Hz, 2 H, *p*-Tol); **Anal. calcd for** $C_{23}H_{26}O_3S$: C 72.22; H 6.85, S 8.38; **found**: C 72.36; H 6.75, S 8.16.

Partial data for **4h**: R_f = 0.29 (50% EtOAc-hexane); **^{1}H NMR** (200 MHz) δ = 3.37 (dd, *J* = 10.4, 8.8 Hz, 1 H), 5.45 (br s, 1 H, H-7), 6.70 (br s, 1 H, H-5).

5.24. Synthesis of (±)-(3a*S*,6*R*,*R*$_S$)-6-*n*-Butyl-4-(2-methoxynaphthalene-1-ylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 3i, and (±)-(3a*R*,6*S*,*R*$_S$)-6-*n*-Butyl-4-(2-methoxynaphthalene-1-ylsulfinyl)-1,3,3a,6-tetrahydroisobenzofuran, 4i.



From diene **1i** (25 mg, 0.072 mmol), propargyl bromide (39 μL, 54 mg, 0.36 mmol), Triton B (8 μL, 7 mg, 0.04 mmol) and 60% aqueous sodium hydroxide (0.7 mL) following the general procedure (3 h) compound **2i** was obtained. The ^{1}H NMR of the crude product, recorded immediately after work-up showed a 64:32:4 mixture of **2i**, **3i** and **4i**. After 1 day at room temperature the cycloaddition was complete and an 89:11 mixture of **3i** and **4i** was obtained. Purification by chromatography (20-40% EtOAc-hexane) afforded **3i** (18 mg, 0.047 mmol, 65%) as a white solid that was recrystallized in EtOAc-hexane and **4i** (3 mg, 0.008, 11%) as a white solid.

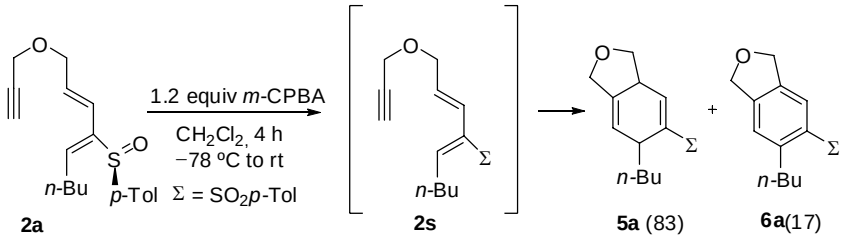
Data for **3i**: R_f = 0.46 (80% EtOAc-hexane); **mp** 155-156 ºC; **^{1}H NMR** (300 MHz) δ = 0.92 (t, *J* = 7.0 Hz, 3 H, Me-*n*-Bu), 1.29-1.44 (m, 4 H, CH_2-*n*-Bu), 1.61-1.68 (m, 2 H, CH_2-*n*-Bu), 2.51 (m, 1 H, H-3a), 3.05 (m, 1 H, H-6), 3.39 (dd, *J* = 10.9, 7.7 Hz, 1 H, H-3), 3.97 (t, *J* = 7.8 Hz, 1 H, H-3), 4.00 (s, 3 H, OMe), 4.17 (br s, 2 H, H-1), 5.47 (br s, 1 H, H-7), 6.78 (m, 1 H, H-5), 7.25 (d, *J* = 9.1 Hz, 1 H, H-3'), 7.37 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1 H, H-6'), 7.49 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1 H, H-7'), 7.78 (d, *J* = 8.1 Hz, 1 H, H-5'), 7.96 (d, *J* = 9.2 Hz, 1 H, H-4'), 8.66 (d, *J* = 8.5 Hz, 1 H, H-8'); **^{13}C NMR** (50 MHz) δ = 14.0 (Me-*n*-Bu), 22.9, 28.6, 34.9, 38.1, 39.3, 56.9, 68.5, 70.7, 112.8, 118.8, 120.0, 122.6, 124.6, 128.2, 128.8, 129.5, 132.2, 132.5, 135.3, 137.7, 138.1, 158.0; **IR** (KBr): 2958, 2932, 2856, 1620, 1592, 1505, 1458, 1432, 1336, 1273, 1250, 1150, 1047, 1027, 904, 879, 829, 777, 753 cm^{-1}; **MS** (ES) m/z (%): 383 (100) $[M+H]^+$; **Anal. calcd for** $C_{23}H_{26}O_3S$: C 72.22, H 6.85, S 8.38; **found**: C 72.68, H 6.72, S 8.45.

Data for **4i**: R_f = 0.43 (80% EtOAc-hexane); **mp** 114-116 ºC; **^{1}H NMR** (300 MHz) δ = 0.91 (t, *J* = 6.8 Hz, 3 H, Me-*n*-Bu), 1.27-1.39 (m, 4 H, CH_2-*n*-Bu), 1.57-1.66 (m, 2 H, CH_2-*n*-Bu), 2.33 (dd, *J* =

10.7, 7.6 Hz, 1 H, H-3), 3.15 (m, 1 H, H-6), 3.36 (m, 1 H, H-3a), 3.49 (t, *J* = 7.5 Hz, 1 H, H-3), 4.00 (s, 3 H, OMe), 4.03 (m, 1 H, H-1), 4.22 (dm, *J* = 12.0 Hz, 1 H, H-1), 5.43 (br s, 1 H, H-7), 6.75 (m, 1 H, H-5), 7.23 (d, *J* = 9.3 Hz, 1 H, H-3'), 7.36 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1 H, H-6'), 7.47 (ddd, *J* = 8.3, 6.8, 1.5 Hz, 1 H, H-7'), 7.76 (dd, *J* = 6.6, 0.7 Hz, 1 H, H-5'), 7.95 (d, *J* = 9.0 Hz, 1 H, H-4'), 8.69 (dd, *J* = 8.5, 1.0 Hz, 1 H, H-8'); **^{13}C NMR** (50 MHz) δ = 14.1 (Me-*n*-Bu), 22.9, 28.5, 35.0, 38.0, 38.9, 56.8, 68.3, 70.0, 112.8, 119.8, 123.1, 124.6, 128.0, 128.3, 128.8, 129.4, 132.5, 133.7, 135.2, 137.4, 138.6, 157.9; **IR** (KBr): 2927, 2856, 1621, 1593, 1506, 1465, 1431, 1335, 1272, 1250, 1151, 1034, 908, 813, 747 cm^{-1}; **MS** (ES) m/z (%): 421, 419 (100), 383 $[M+H]^+$; **Anal. calcd for** $C_{23}H_{26}O_3S$: C 72.22, H 6.85, S 8.38; **found**: C 72.37, H 6.59, S 8.52.

6. Intramolecular Diels-Alder cycloaddition of sulfonyl and sulfoximinoyl dienynes.

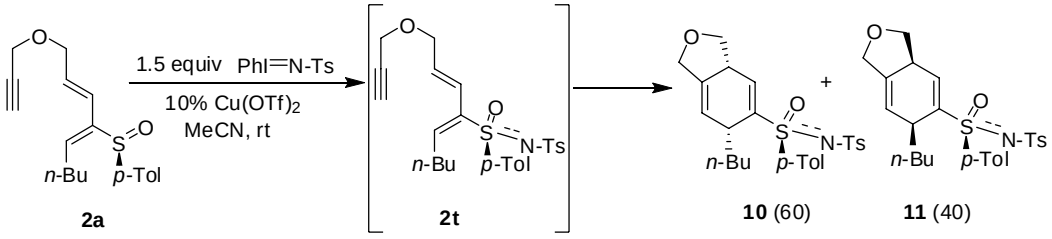
6.1. Oxidation of (–)-(*R*)-4-Oxa-8-(*p*-tolylsulfinyl)-6-(*E*)-8-(*Z*)-tridecadien-1-yne, 2a.



From dienyne **2a** (16 mg, 0.05 mmol) and *m*-CPBA (14 mg, 0.06 mmol, 1.2 equiv, 70%), following the general procedure (4 h), an 83:17 mixture of **5a** and **6a** was obtained. Purification by chromatography (5% EtOAc-CH_2Cl_2) afforded **5a** (10 mg, 0.029 mmol, 58%) and **6a** (2 mg, 0.006 mmol, 12%), both as colorless oils.

Data for **5a**: R_f = 0.20 (30% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 0.72 (t, *J* = 7.0 Hz, 3 H, Me-*n*-Bu), 0.80-1.18 (m, 4 H, 2 CH_2-*n*- Bu), 1.49-1.79 (m, 2 H, CH_2-*n*-Bu), 2.42 (s, 3 H, Me-*p*-Tol), 3.27 (m, 1 H, H-6), 3.32-3.40 (m, 2 H, H-3a, 1 H-3), 4.22-4.27 (m, 2 H, 1 H-3, 1 H-1), 4.35 (m, 1 H, H-1), 5.38 (br s, 1 H, H-7), 7.09 (t, *J* = 2.2 Hz, 1 H, H-4), 7.31 (d, *J* = 7.8 Hz, 2 H, *p*-Tol), 7.73 (d, *J* = 8.3 Hz, 2 H, *p*-Tol); **^{13}C NMR** (50 MHz) δ = 13.9 (Me-*n*-Bu), 21.5 (Me-*p*-Tol), 22.6, 27.0, 32.2, 36.2, 41.3, 68.8, 70.1, 120.1, 128.0 (2 C), 129.7 (2 C), 129.9, 135.1, 135.6, 137.3, 144.3; **IR** (film): 2956, 2928, 2870, 1766, 1597, 1494, 1464, 1402, 1380, 1302, 1151, 1086, 1047, 1017, 902, 845, 814, 709 cm^{-1}; **MS** (ES) m/z (%): 331 (100) $[(M–2)+1]^+$; **Anal. calcd for** $C_{19}H_{24}O_3S$: C 68.64, H 7.28, S 9.64; **found**: C 68.76, H 7.34, S 9.87.

6.2. Synthesis of (3a*R*,6*S*,S_S)-6-*n*-Butyl-5-(*p*-tolyl-*N*-tosylsulfoximinoyl)-1,3,3a,6-tetrahydroisobenzofuran, 10 and (3a*S*,6*R*,S_S)-6-*n*-Butyl-5-(*p*-tolyl-*N*-tosylsulfoximinoyl)-1,3,3a,6-tetrahydroisobenzofuran, 11.



To a solution of **2a** (48 mg, 0.14 mmol, 1.0 equiv) in CH_3CN (1 mL), $Cu(OTf)_2$ (5.8 mg, 0.016 mmol, 0.1 equiv) was added and the mixture was stirred for 5 min. Then, PhI=NTs (78 mg, 0.21 mmol, 1.5 equiv) was added and the mixture was stirred at room temperature (5 h) until starting material disappearance (TLC). The solvent was removed under reduced pressure to give compound **2t**. The cycloaddition rate prevented us to isolate pure **2t**. Purification by chromatography (10-50% EtOAc-hexane) afforded an inseparable mixture of **10** and **11** (0.048 mmol, 34%).

Partial data for **2t**: $\boldsymbol{R_f}$ = 0.42 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 0.83 (t, *J* = 7.1 Hz, 3 H, *n*-Bu), 1.21-1.36 (m, 4 H, *n*-Bu), 2.36 (s, 3 H), 2.41 (s, 3 H), 2.59 (q, *J* = 7.3 Hz, 2 H), 3.99-4.07 (m, 4 H), 5.84 (dt, *J* = 15.4, 5.9 Hz, 1 H), 6.38 (t, *J* = 7.9 Hz, 1 H), 6.44 (d, *J* = 15.4 Hz, 1 H), 7.21-7.35 (m, 4 H), 7.77-7.85 (m, 4 H).

Partial data for **10** (from the mixture): $\boldsymbol{R_f}$ = 0.26 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 0.66 (t, *J* = 7.0 Hz, 3 H, *n*-Bu), 2.37 (s, 3 H), 2.44 (s, 3 H), 5.39 (t, *J* = 1.8 Hz, 1 H, H-7), 7.20-7.25 (m, 2 H), 7.30-7.36 (m, 2 H), 7.78-7.86 (m, 4 H); **MS** (EI) m/z (%): 484 $[M-1]^+$, 139 (100).

Partial data for **11** (from the mixture): $\boldsymbol{R_f}$ = 0.26 (50% EtOAc-hexane); **^{1}H NMR** (300 MHz) δ = 0.66 (t, *J* = 7.0 Hz, 3 H, *n*-Bu), 2.37 (s, 3 H), 2.42 (s, 3 H), 5.37 (t, *J* = 1.8 Hz, 1 H, H-7), 7.20-7.25 (m, 2 H), 7.30-7.36 (m, 2 H), 7.78-7.86 (m, 4 H).

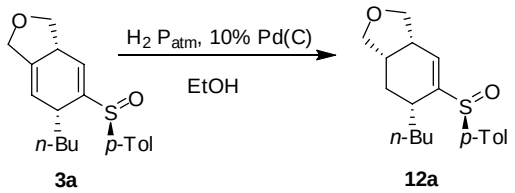
7. Exploratory transformations of cycloadducts.

7.1. General procedure for the catalytic hydrogenation of cycloadducts.

To a solution of the corresponding cycloadduct in EtOH (10 mL/mmol) under an argon atmosphere, a 10% mol of Pd on charcoal was added. A hydrogen atmosphere was achieved using a balloon charged with H_2, and the reaction was stirred until the complete disappearance of the starting material (TLC). The reaction mixture was filtered through a pad of celite and concentrated under

reduced pressure. The crude product was purified by chromatography using the appropriate mixture of solvents.

7.2. Synthesis of (+)-(3a*S*,5*R*,7a*S*,S_S)-5-*n*-Butyl-6-(*p*-tolylsulfinyl)-1,3,3a,4,5,7a-hexahydroisobenzofuran, 12a.

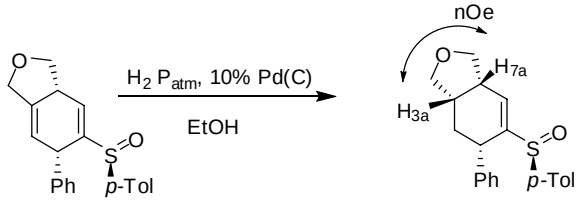


3a **12a**

From **3a** (10 mg, 0.03 mmol) and Pd (C) (3 mg, 0.003 mmol) following the general procedure (2 days), compound **12a** was obtained. Purification by chromatography (10-70% EtOAc-hexane) afforded **12a** (5 mg, 0.015 mmol, 52%) as a colorless oil.

Data for **12a**: R_f = 0.13 (50 % EtOAc-hexane); $[\alpha]_D^{20}$ = +26.7 (*c* = 0.46); **^{1}H NMR** (400 MHz) δ = 0.83 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 1.05-1.44 (m, 6 H), 1.55-1.63 (m, 1 H), 1.74 (dt, *J* = 13.1, 4.8 Hz, 1 H, H-4), 1.84-1.90 (m, 1 H, H-3a), 2.18-2.30 (m, 1 H, H-5), 2.39 (s, 3 H, Me-*p*-Tol), 2.92-3.00 (m, 1 H, H-7a), 3.48 (dd, *J* = 9.2, 8.2 Hz, 1 H, H-3), 3.64 (dd, *J* = 8.7, 1.9 Hz, 1 H, H-1), 3.95 (dd, *J* = 8.7, 5.9 Hz, 1 H, H-1), 4.10 (t, *J* = 8.4 Hz, 1 H, H-3), 6.76 (dd, *J* = 4.8, 2.1 Hz, 1 H, H-7), 7.27 (d, *J* = 7.9 Hz, 2 H), 7.52 (d, *J* = 8.1 Hz, 2 H); **^{13}C NMR** (100 MHz) δ = 13.9, 21.5, 22.6, 27.7, 31.2, 31.9, 34.6, 36.5, 39.9, 71.7, 74.1, 126.1, 126.6 (2 C), 130.1 (2 C), 139.8, 142.3, 147.0; **IR** (film): 2927, 2857, 1732, 1596, 1492, 1456, 1378, 1261, 1082, 1050, 1015, 809 cm^{-1}; **MS** (EI) m/z (%): 318 $[M]^+$, 301 (100); **Anal. calcd for** $C_{19}H_{26}O_2S$: C 71.66, H 8.23, S 10.07; **found**: C 71.42, H 8.15, S 10.13.

7.3. Synthesis of (+)-(3a*S*,5*S*,7a*S*,S_S)-5-Phenyl-6-(*p*-tolylsulfinyl)-1,3,3a,4,5,7a-hexahydroisobenzofuran, 12b.



3b **12b**

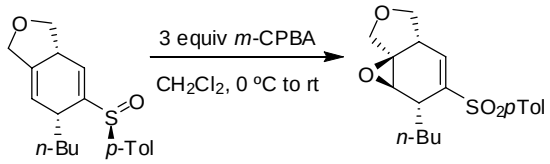
From **3b** (60 mg, 0.18 mmol) and Pd (C) (20 mg, 0.018 mmol), following the general procedure (20 h), compound **12b** was obtained. Purification by chromatography (20-70% EtOAc-hexane) afforded **12b** (43 mg, 0.13 mmol, 71%) as a white solid.

Data for **12b**: R_f = 0.28 (70% EtOAc-hexane); **mp** 145-147 ºC; $[\alpha]_D^{20}$ = +14.8 (*c* = 1.22); **^{1}H NMR** (400 MHz-COSY) δ = 1.65 (ap q, *J* = 13.0 Hz, 1 H, H-4), 1.82 (dt, *J* = 13.3, 4.8 Hz, 1 H, H-4), 2.30 (s, 3 H, Me-*p*-Tol), 2.25-2.35 (m, 1 H, H-3a), 2.85 (dquint, *J* = 11.1, 2.5 Hz, 1 H, H-5), 2.95-3.03 (m, 1 H, H-7a), 3.51 (dd, *J* = 8.8, 1.8 Hz, 1 H, H-3), 3.56 (t, *J* = 8.4 Hz, 1 H, H-1), 3.88 (dd, *J* = 8.8, 5.9 Hz, 1 H, H-3), 4.12 (t, *J* = 8.4 Hz, 1 H, H-1), 6.86-6.88 (m, 3 H), 7.06 (d, *J* = 8.3 Hz, 2 H), 7.10 (d, *J* = 8.1 Hz, 2 H), 7.17-7.21 (m, 3 H); **^{13}C NMR** (75 MHz) δ = 21.5, 36.9, 37.2, 39.8, 42.2, 71.8, 73.8, 126.7 (2 C), 127.0, 127.3, 128.5 (2 C), 128.9 (2 C), 129.8 (2 C), 139.2, 140.5, 142.3, 146.8. NOESY-2D (400 MHz): a correlation peak between H-3a and H-7a was observed; **IR** (KBr): 2924, 2849, 1631, 1595, 1493, 1455, 1084, 1043, 1014, 816, 759, 700, 516 cm^{-1}; **MS** (ES) m/z (%): 361 $[M+Na]^+$, 339 $[M+H]^+$; **Anal. calcd for** $C_{21}H_{22}O_2S$: C 74.52, H 6.55, S 9.47; **found**: C 74.67, H 6.46, S 9.51.

7.4. General procedure for the oxidation-epoxidation of cycloadducts.

To a cold (0 ºC) solution of the corresponding cycloadduct (1.0 equiv) in CH_2Cl_2 (10 mL/mmol), *m*-CPBA (3.0 equiv) was added. The mixture was allowed to reach room temperature and was stirred until starting material disappearance (TLC). Then the reaction mixture was quenched with a 1 M solution of $Na_2S_2O_4$ (2 mL/mmol peracid) and a saturated solution of $NaHCO_3$ (2 mL/mmol peracid) and diluted with CH_2Cl_2. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (twice), the organic extract was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography using the appropriate mixture of solvents.

7.5. Synthesis of (+)-(3a*R*,4*R*,5*R*,7a*S*)-5-*n*-Butyl-3a,4-epoxy-6-tosyl-1,3,3a,4,5,7a-hexahydroisobenzofuran, 13a.



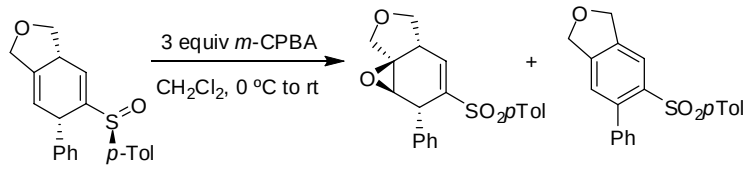
3a **13a**

From **3a** (28 mg, 0.09 mmol) and *m*-CPBA (67 mg, 0.27 mmol) following the general procedure (3 days), compound **13a** was obtained. Purification by chromatography (50% CH_2Cl_2-hexane/10% EtOAc-CH_2Cl_2) afforded **13a** (27 mg, 0.072 mmol, 80%) as a white solid that was recrystallized from Et_2O/hexanes.

Data for **13a**: R_f = 0.40 (50% EtOAc-hexane); **mp** 138-140 ºC; $[\alpha]_D^{20}$ = +61.8 (c = 1.07); **^{1}H NMR** (400 MHz-COSY) δ = 0.81 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 1.09-1.26 (m, 4 H), 1.72-1.90 (m, 2

H), 2.41 (s, 3 H, Me-*p*-Tol), 2.92 (ap quint, *J* = 3.1 Hz, 1 H, H-5) 3.09 (s, 1 H, H-4), 3.22-3.29 (m, 1 H, H-7a), 3.55 (dd, *J* = 11.2, 8.4 Hz, 1 H, H-1), 3.80 (d, *J* = 9.9 Hz, 1 H, H-3), 3.94 (d, *J* = 9.9 Hz, 1 H, H-3), 4.34 (t, *J* = 8.3 Hz, 1 H, H-1), 6.84 (dd, *J* = 5.1, 0.9 Hz, 1 H, H-7), 7.31 (d, *J* = 7.9 Hz, 2 H), 7.69 (d, *J* = 8.3 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 12.3, 21.6, 22.6, 27.9, 30.6, 35.1, 39.8, 62.1, 64.1, 67.3, 70.6, 128.1 (2 C), 129.8 (2 C), 132.1, 136.1, 142.1, 144.6; **IR** (KBr): 2955, 2927, 2872, 1642, 1596, 1465, 1303, 1143, 1092, 1083, 1044, 1008, 902, 686, 544 cm^{-1}; **MS** (ES) m/z (%): 371 [M+Na]$^+$; **Anal. calcd for** $C_{19}H_{24}O_3S$: C 68.64, H 7.28, S 9.64; **found**: C 68.36, H 7.09, S 9.55.

7.6. Synthesis of (+)-(3a*R*,4*R*,5*R*,7a*S*)-3a,4-Epoxy-5-phenyl-6-tosyl-1,3,3a,4,5,7a-hexahydroisobenzofuran, 13b.



3b **13b** **6b**

From **3b** (82 mg, 0.24 mmol) and *m*-CPBA (124 mg, 0.72 mmol), following the general procedure (3 days), compound **13b** was obtained along with **6b**. Purification by chromatography (10-50% EtOAc-hexane) afforded **13b** (53 mg, 0.14 mmol, 60%) and **6b** (4 mg, 0.012 mmol, 5%) both as white solids that were recrystallized from Et_2O-hexane.

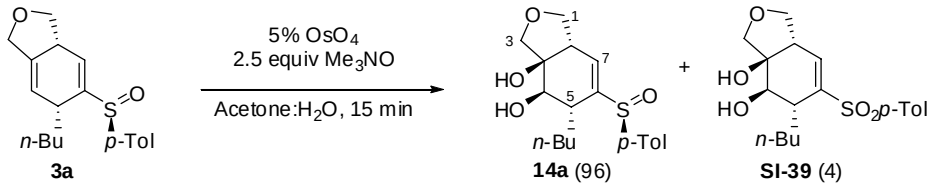
Data for **13b**: R_f = 0.48 (50% EtOAc-hexane); **mp** 179-182ºC; **$[\alpha]_D^{20}$** = +59.8 (*c* = 0.93); **^{1}H NMR** (400 MHz-COSY) δ = 2.23 (s, 3 H, Me-*p*-Tol), 3.09 (s, 1 H, H-4), 3.38 (m, 1 H, H-7a), 3.64 (d, *J* = 8.7 Hz, 1 H), 3.67 (d, *J* = 8.4 Hz, 1 H), 3.88 (d, *J* = 10.0 Hz, 1 H, H-3), 4.23 (d, *J* = 3.4 Hz, 1 H, H-5), 4.43 (ap t, *J* = 8.3 Hz, 1 H, H-1), 6.86 (m, 2 H), 6.91 (d, *J* = 8.3 Hz, 2 H), 7.00-7.09 (m, 4 H), 7.18 (d, *J* = 8.3 Hz, 2 H); **^{13}C NMR** (100 MHz) δ = 21.4, 40.0, 42.5, 61.9, 64.0, 67.5, 71.1, 127.6, 127.8 (2 C), 128.6 (2 C), 128.9 (2 C), 129.3 (2 C), 132.3, 136.6, 136.7, 142.3, 143.7; **IR** (KBr): 3027, 2923, 1644, 1598, 1492, 1457, 1305, 1147, 1089, 1040, 702, 684, 538 cm^{-1}; **MS** (ES) m/z (%): 391 [M+Na]$^+$, 369 [M+H]$^+$; **Anal. calcd for** $C_{21}H_{20}O_3S$: C 71.56, H 5.72, S 9.10; **found**: C 71.67, H 5.68, S 9.23.

Data for **6b**: R_f = 0.60 (70% EtOAc-hexane); **mp** 161-165 ºC; **^{1}H NMR** (400 MHz) δ = 2.31 (s, 3 H, Me-*p*-Tol), 5.12 (s, 2 H), 5.22 (s, 2 H), 6.92-6.97 (m, 4 H), 7.04-7.07 (m, 3 H), 7.15-7.19 (m, 2 H), 7.26-7.30 (m, 1 H), 8.29 (s, 1 H); **^{13}C NMR** (100 MHz) δ = 21.5, 73.2, 73.3, 121.4, 125.2, 127.2 (2 C), 127.6, 127.7 (2 C), 128.9 (2 C), 130.1 (2 C), 137.8, 138.0, 138.9, 139.5, 141.8, 143.4, 144.4; **IR** (KBr): 2921, 1631, 1460, 1306, 1162, 1138, 1088, 710, 555 cm^{-1}; **MS** (ES) m/z (%): 373 [M+Na]$^+$, 351 [M+H]$^+$; **Anal. calcd for** $C_{21}H_{18}O_3S$: C 71.98, H 5.18, S 9.15; **found**: C 72.14, H 5.34, S 9.28.

7.7. General procedure for osmium-catalyzed dihydroxylation.

To a solution of the sulfoxide in a 9:1 mixture of acetone and H_2O (0.1 M), at rt, 2.5 equiv of Me_3NO and 0.05 equiv of OsO_4 were added. The solution was stirred until starting material disappearance and then quenched with a solution of aqueous $Na_2S_2O_4$ (1 M, 5 mL/mmol). The solvent was evaporated and the crude product was filtered through a short pad of silica gel.

7.8. Synthesis of (+)-(3a*S*,4*R*,5*R*,7a*S*,S_S)-5-*n*-Butyl-6-(*p*-tolylsulfinyl)-1,3,3a,4,5,7a-hexahydroisobenzofuran-3a,4-diol, 14a.

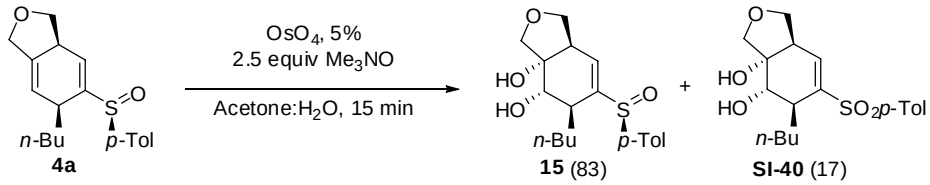


From sulfoxide **3a** (32 mg, 0.100 mmol), Me_3NO (28 mg, 0.250 mmol) and OsO_4 (65 μL, 52 mg (2.5% wt), 0.005 mmol) following the general procedure (15 min) a 96:4 mixture of sulfoxide **14a** and sulfone **SI-39** was obtained. Purification by chromatography (20-50% EtOAc-hexane) afforded 1 mg (0.003 mmol, 3%) of sulfone **SI-39** as a colorless oil and sulfoxide **14a** (25 mg, 0.072 mmol, 72%) as a white solid that was recrystallized from EtOAc-hexane.

Data for **14a**: $\boldsymbol{R_f}$ = 0.27 (100% EtOAc); **mp** 148-150 ºC; $\boldsymbol{[\alpha]^{20}_D}$ = +108.2 (*c* = 0.65); **^{1}H NMR** (300 MHz) δ = 0.88 (t, *J* = 7.0 Hz, 3 H, Me-*n*-Bu), 1.31-1.38 (m, 4 H, 2 CH_2-*n*-Bu), 1.42 (m, 1 H, *n*-Bu), 1.62 (m, 1 H, *n*-Bu), 2.13 (m, 1 H, H-5), 2.38 (s, 3 H, Me-*p*-Tol), 2.39 (m, 1 H, OH), 2.79 (s, 1 H, OH), 3.03 (m, 1 H, H-7a), 3.60 (d, *J* = 9.3 Hz, 1 H, H-3), 3.61 (dd, *J* = 8.8, 7.0 Hz, 1 H, H-1), 3.78 (ap t, *J* = 6.9 Hz, 1 H, H-4), 3.99 (d, *J* = 9.3 Hz, 1 H, H-3), 4.25 (t, *J* = 8.7 Hz, 1 H, H-1), 6.65 (dd, *J* = 4.6, 1.7 Hz, 1 H, H-7), 7.28 (d, *J* = 7.8 Hz, 2 H, *p*-Tol), 7.53 (d, *J* = 8.3 Hz, 2 H, *p*-Tol); DNOE between H-5/OH-4: 1.9%; between H-5/OH-3: 1.6%; between H-5/H-4: 2.1%; between H-5/H-*p*-Tol: 1.8%; between H-7a/H-1 (3.61 ppm): 4.6%; between H-7a/H-1 (4.25 ppm): 1.8%; between H-7a/H-7: 4.4%; between H-4/Me-*n*-Bu: 3.1%; between H-4/CH_2-*n*-Bu: 6.8%; between H-4/H-5: 3.9%; between H-4/CH_3-*p*-Tol: 4.5%; between H-3 (3.99 ppm)/H-3 (3.60 ppm): 19.0%; between H-1 (4.25 ppm)/H-7a: 5.7%; between H-1 (4.25 ppm)/H-7a: 5.7%; between H-1 (4.25 ppm)/H-1 (3.61 ppm): 20.7%; **^{13}C NMR** (50 MHz) δ = 13.9 (Me-*n*-Bu), 21.5 (Me-*p*-Tol), 22.9, 27.1, 27.9, 38.9 (C-5), 47.0 (C-7a), 70.4 (C-4), 72.2 (C-1), 75.4 (C-3), 79.1 (C-3a), 126.4 (C-7), 126.8 (2 C), 130.3 (2 C), 139.0, 142.9, 143.3; **IR** (KBr): 3436, 2959, 2873, 1637, 1454, 1350, 1277, 1082, 1033, 917, 808 cm^{-1}; **MS** (ES) m/z (%): 351 (100) $[M+H]^+$; **Anal. calcd for** $C_{19}H_{26}O_4S$: C 65.11, H 7.48, S 9.15; **found**: C 64.78, H 7.36, S 9.40.

Data for **SI-39**: R_f = 0.18 (50% EtOAc-hexane); **[α]$^{20}_{D}$** = +43.4 (*c* = 0.58); **^{1}H NMR** (300 MHz) δ = 0.83 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 1.17-1.45 (m, 5 H, *n*-Bu), 1.78 (m, 1 H, *n*-Bu), 1.90 (d, *J* = 5.1 Hz, 1 H, OH), 2.42 (s, 3 H, Me-*p*-Tol), 2.62 (dt, *J* = 10.3, 3.4 Hz, 1 H, H-5), 2.88 (m, 1 H, H-7a), 3.01 (s, 1 H, OH), 3.63 (d, *J* = 10.2 Hz, 1 H, H-3), 3.76 (dd, *J* = 9.0, 2.9 Hz, 1 H, H-1), 3.91 (d, *J* = 10 Hz, 1 H, H-3), 3.98 (dd, *J* = 4.9, 3.4 Hz, 1 H, H-4), 4.15 (dd, *J* = 8.8, 7.3 Hz, 1 H, H-1), 6.93 (d, *J* = 4.6 Hz, 1 H, H-7), 7.31 (d, *J* = 8.5 Hz, 2 H, *p*-Tol), 7.72 (d, *J* = 8.5 Hz, 2 H, *p*-Tol); DNOE between H-5/H-4: 2.0%; between H-7a/H-1 (4.15 ppm): 4.2%; between H-7a/H-7: 3.4%; between H-3 (3.63 ppm)/H-3 (3.91 ppm): 13.9%; between H-1 (3.76 ppm)/H-1 (4.15 ppm): 17.4; between H-1 (3.76 ppm)/H-7: 2.2%; between H-3 (3.91 ppm)/H-3 (3.63 ppm): 73.2%; between H-4/H-3 (3.91 ppm): 5.5%; between H-1 (4.15 ppm)/H-7a: 3.2%; H-1 (4.15 ppm)/H-1 (3.76 ppm): 12.4%; **^{13}C NMR** (50 MHz) δ = 13.8 (Me-*n*-Bu), 21.6 (Me-*p*-Tol), 22.4, 29.2, 30.3, 42.5 (C-5), 47.5 (C-7a), 69.7 (C-4), 71.6 (C-1), 76.1 (C-3), 80.0 (C-3a), 128.0 (2 C), 129.9 (2 C), 136.4, 138.3, 141.3, 144.5; **IR** (film): 3435, 2962, 2925, 2862, 1642, 1597, 1261, 1147, 1088, 1020, 803, 671 cm^{-1}; **MS** (ES) m/z (%): 349 (100) $[(M–18)+1]^+$; **Anal. calcd for** $C_{19}H_{26}O_5S$: C 62.27, H 7.15, S 8.75; **found**: C 62.53, H 7.29, S 8.54.

7.9. Synthesis of (–)-(3a*R*,4*S*,5*S*,7a*R*,*S*$_S$)-5-*n*-Butyl-6-(*p*-tolylsulfinyl)-1,3,3a,4,5,7a-hexahydroisobenzofuran-3a,4-diol, 15.



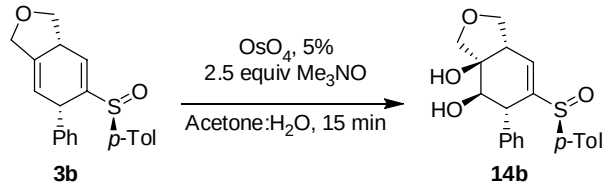
From sulfoxide **4a** (23 mg, 0.073 mmol), Me_3NO (20 mg, 0.180 mmol) and OsO_4 (51 μL, 41 mg (2.5% wt), 0.004 mmol) following the general procedure (15 min) an 83:17 mixture of sulfoxide **15** and sulfone **SI-40** was obtained. Purification by chromatography (20-50% EtOAc-hexane) afforded sulfone **SI-40 (**4 mg, 0.011 mmol, 15%) and sulfoxide **15** (16 mg, 0.046 mmol, 63%) as a white solid that was recrystallized from EtOAc-hexane.

Data for **15**: ***R$_f$*** = 0.21 (100% EtOAc); **mp** 137-138 ºC; **[α]$^{20}_{D}$** = –19.1 (*c* = 0.71); **^{1}H NMR** (300 MHz-COSY) δ = 0.83 (t, *J* = 7.0 Hz, 3 H, Me-*n*-Bu), 1.18-1.32 (m, 4 H, 2 CH_2-*n*-Bu), 1.48-1.61 (m, 1 H, *n*-Bu), 1.73-1.83 (m, 1 H, *n*-Bu), 2.15 (br s, 1 H, OH), 2.39 (s, 3 H, Me-*p*-Tol), 2.52 (ap quint, *J* = 4.4 Hz, 1 H, H-5), 2.86 (m, 1 H, H-7a), 3.17 (br s, 1 H, OH), 3.62 (d, *J* = 9.8 Hz, 1 H, H-3), 3.70 (dd, *J* = 8.8, 4.4 Hz, 1 H, H-1), 3.84 (t, *J* = 4.9 Hz, 1 H, H-4), 3.98 (d, *J* = 9.8 Hz, 1 H, H-3), 4.17 (dd, *J* = 8.8, 7.8 Hz, 1 H, H-1), 6.37 (dd, *J* = 4.6, 1.0 Hz, 1 H, H-7), 7.30 (d, *J* = 8.5 Hz, 2 H, *p*-Tol), 7.46 (d, *J* = 8.3 Hz, 2 H, *p*-Tol); **^{13}C NMR** (50 MHz-HMQC) δ 13.9 (Me-*n*-Bu), 21.4 (Me-*p*-Tol), 22.6, 28.9,

30.2, 41.0 (C-5), 47.6 (C-7a), 70.0 (C-4), 71.9 (C-1), 75.8 (C-3), 79.7 (C-3a), 125.2 (2 C), 130.0 (2 C), 133.8 (C-7), 138.7, 141.6, 145.6; **IR** (KBr): 3466, 2955, 2870, 1630, 1413, 1309, 1082, 1022, 1004, 928, 819, 705 cm^{-1}; **MS** (ES) m/z (%): 701 (100) $[2M+H]^+$, 351 $[M+H]^+$; **Anal. calcd for** $C_{19}H_{26}O_4S$: C 65.11, H 7.48, S 9.15; **found**: C 64.88, H 7.19, S 8.98.

Data for **SI-40** is identical to that described above for **SI-39** except for optical rotation $[\alpha]^{20}_D$ = –56.4 (*c* = 0.54).

7.10. Synthesis of (+)-(3a*R*,4*R*,5*R*,7a*S*,*S*$_S$)-5-Phenyl-6-(*p*-tolylsulfinyl)-1,3,3a,4,5,7a-hexahydroisobenzofuran-3a,4-diol, 14b.



3b **14b**

From **3b** (45 mg, 0.13 mmol, 1.0 equiv), Me_3NO (37 mg, 0.33 mmol, 2.5 equiv) and OsO_4 (2.5% in *t*-butanol, 88 μL, 0.007 mmol, 0.05 equiv), following the general procedure (20 h), compound **14b** was obtained. Purification by chromatography (0-80% EtOAc-hexane) afforded diol **14b** (31 mg, 0.083 mmol, 64%) as a white solid that was recrystallized from EtOAc-hexane.

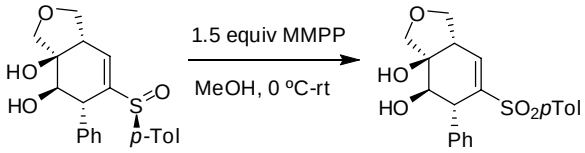
Data for **14b**: R_f = 0.15 (EtOAc); **mp** 191-194 ºC; $[\alpha]_D^{20}$ = +5.8 (*c* = 1.01); **^{1}H NMR** (400 MHz-COSY) δ = 2.07 (d, *J* = 3.8 Hz, 1 H, OH), 2.36 (s, 3 H, Me-*p*-Tol), 2.75 (s, 1 H, OH), 3.06 (dt, *J* = 9.1, 2.2 Hz, 1 H, H-5), 3.17-3.23 (m, 1 H, H-7a), 3.61 (d, *J* = 9.1 Hz, 1 H, H-3), 3.66 (t, *J* = 8.6 Hz, 1 H, H-1), 3.84 (dd, *J* = 9.1, 3.8 Hz, 1 H, H-4), 3.96 (d, *J* = 9.1 Hz, 1 H, H-3), 4.34 (t, *J* = 9.1 Hz, 1 H, H-1), 6.78 (dd, *J* = 4.2, 2.4 Hz, 1 H, H-7), 6.94-6.96 (m, 2 H), 7.06-7.09 (m, 2 H), 7.15 (d, *J* = 8.4 Hz, 2 H), 7.28-7.31 (m, 3 H); **^{13}C NMR** (100 MHz) δ = 21.5, 46.0, 46.8, 72.2, 75.7, 75.8, 78.5, 126.2, 127.1 (2 C), 128.2, 128.8 (2 C), 129.9 (2 C), 130.1 (2 C), 136.2, 138.3, 142.7, 142.9; **IR** (KBr): 3412, 2922, 1638, 1493, 1452, 1320, 1082, 1041, 913, 811, 749, 702, 646, 515 cm^{-1}; **MS** (ES) m/z (%): 393 $[M+Na]^+$, 371 $[M+H]^+$; **Anal. calcd for** $C_{21}H_{22}O_4S$: C 68.08, H 5.99, S 8.66; **found**: C 68.13, H 6.09, S 8.93.

7.11. General procedure for oxidation of sulfoxides with MMPP.

To a cold (0 ºC) solution of the sulfoxide in MeOH (10 mL/mmol) 1.5 equiv of magnesium monoperoxyphthalate hexahydrate (MMPP) was added. The mixture was allowed to warm to rt, monitored by TLC until completion and then quenched with a saturated solution of $NaHCO_3$ (4 mL/mmol). After removal of MeOH under reduced pressure, the mixture was diluted with EtOAc (5

mL/mmol), the layers were separated and the aqueous phase was extracted with EtOAc (3 times, 4 mL/mmol). The combined organic layers were washed with a saturated solution of NaCl (1 mL/mmol), dried over $MgSO_4$, filtered and concentrated under reduced pressure to give a crude product that was purified by chromatography on silica gel using the appropriate mixture of solvents.

7.12. Synthesis of (+)-(3a*R*,4*R*,5*R*,7a*S*)-5-Phenyl-6-tosyl-1,3,3a,4,5,7a-hexahydroisobenzofuran-3a,4-diol, 16.

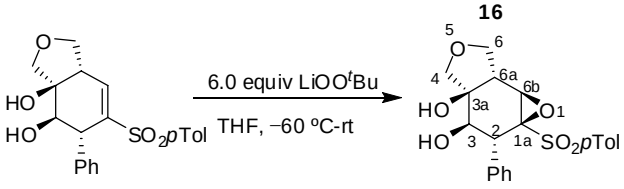


14b **16**

From **14b** (31 mg, 0.082 mmol) and MMPP (61 mg, 0.123 mmol) following the general procedure (20 h), compound **16** was obtained. Purification by chromatography (30-100% EtOAc-hexane) afforded sulfone **16** (24 mg, 0.062 mmol, 76%) as a white solid that was recrystallized from EtOAc-hexane.

Data for **16**: $\boldsymbol{R_f}$ = 0.40 (EtOAc); **mp** 200-207 ºC; $\boldsymbol{[\alpha]_D^{20}}$ = +35.7 (*c* = 0.30); **^{1}H NMR** (300 MHz, CD_3OD-COSY) δ = 2.35 (s, 3 H, Me-*p*-Tol), 3.13 (m, 1 H, H-7a), 3.39 (d, *J* = 9.3 Hz, 1 H, H-3), 3.68 (d, *J* = 9.3 Hz, 1 H, H-3), 3.79 (dd, *J* = 8.8, 6.3 Hz, 1 H, H-1), 3.86 (d, *J* = 6.6 Hz, 1 H, H-5), 3.99 (dm, *J* = 6.6 Hz, 1 H, H-4), 4.26 (t, *J* = 8.5 Hz, 1 H, H-1), 6.92-7.12 (m, 7 H), 7.22-7.29 (m, 3 H); **^{13}C NMR** (75 MHz, CD_3OD) δ = 21.4, 48.8, 49.2, 72.4, 75.6, 76.1, 79.8, 127.8, 128.8 (2 C), 128.9 (2 C), 130.5 (2 C), 130.8 (2 C), 138.7, 139.1, 140.5, 142.4, 145.1; **IR** (KBr): 3448, 2920, 2868, 1632, 1452, 1298, 1146, 1059, 918, 810, 700, 678, 557 cm^{-1}; **MS** (ES) m/z (%): 795 $[2M+Na]^+$, 409 $[M+Na]^+$, 387 $[M+H]^+$; **Anal. calcd for** $C_{21}H_{22}O_5S$: C 65.27, H 5.74, S 8.30; **found**: C 65.36, H 5.99, S 8.21.

7.13. Synthesis of (–)-(3a*R*,4*R*,5*R*,6*R*,7*R*,7a*R*)-6,7-Epoxy-5-phenyl-6-tosyl-1,3,3a,4,5,6,7,7a-octahydroisobenzofuran-3a,4-diol, 17.



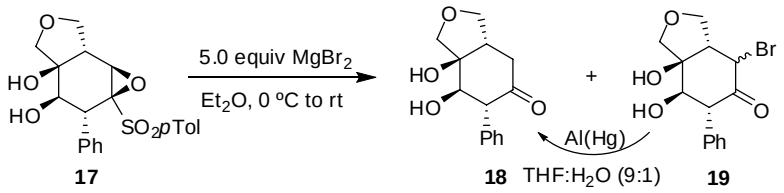
16 **17**

In a two-necked round-bottomed flask, using polyethylene stoppers, anhydrous THF (10 mL/mmol) was charged and it was cooled to 0 ºC. Then *n*-BuLi (1.6 M in hexane, 0.31 mL, 0.50 mmol, 6.0 equiv) and HOO-*t*-Bu (80% wt in *t*-BuOO-*t*-Bu, 54 μL, 0.54 mmol, 6.5 equiv) were added. The

mixture was stirred for 30 minutes and cooled to −60 ºC. Then a solution of **16** (32 mg, 0.083 mmol, 1.0 equiv) in THF (10 mL/mmol) was slowly added. The mixture was allowed to reach room temperature and stirred until starting material disappearance (TLC, 2 days). Then the reaction mixture was quenched with a 1 M solution of $Na_2S_2O_4$, extracted with EtOAc (3 times), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification by chromatography (20-100% EtOAc-CH_2Cl_2) afforded **17** (18 mg, 0.045 mmol, 55%) as a white solid that was recrystallized from Et_2O-hexane.

Data for **17**: $\boldsymbol{R_f}$ = 0.22 (40% EtOAc-hexane); **mp** 227-229 ºC; $\boldsymbol{[\alpha]_D^{20}}$ = –46.4 (*c* = 0.11); **^{1}H NMR** (400 MHz-COSY) δ = 2.40 (s, 3 H, Me-*p*-Tol), 2.62 (d, *J* = 8.6 Hz, 1 H, OH), 2.91 (qd, *J* = 4.6, 1.2 Hz, 1 H, H-7a), 3.16 (s, 1 H, OH), 3.41 (d, *J* = 9.8 Hz, 1 H, H-3), 3.50 (d, *J* = 9.8 Hz, 1 H, H-3), 3.60 (d, *J* = 6.0 Hz, 1 H, H-5), 3.85 (dd, *J* = 8.4, 5.8 Hz, 1 H, H-4), 4.06 (s, 1 H, H-7), 4.08 (dd, *J* = 9.5, 4.6 Hz, 1 H, H-1), 4.24 (dd, *J* = 9.5, 7.9 Hz, 1 H, H-1), 7.17 (d, *J* = 8.5 Hz, 2 H), 7.18-7.31 (m, 5 H), 7.32 (d, *J* = 8.3 Hz, 2 H); **^{13}C NMR** (75 MHz) δ = 21.7, 45.8, 47.1, 59.0, 69.9, 74.1, 74.6, 76.7, 78.1, 128.1 (2 C), 128.2 (2 C), 129.0 (2 C), 129.6 (2 C), 130.6, 132.9, 133.2, 145.4; **IR** (KBr): 3435, 2923, 2851, 1631, 1321, 1148, 1085, 934, 809, 702, 536 cm^{-1}; **MS** (ES) m/z (%): 425 $[M+Na]^+$; **Anal. calcd for** $C_{21}H_{22}O_6S$: C 62.67, H 5.51, S 7.97; **found**: C 62.89, H 5.89, S 8.05.

7.14. Synthesis of (–)-(3a*S*,6*R*,7*R*,7a*R*)-4-7,7a-dihydroxy-6-phenylhexahydroisobenzofuran-5-(1*H*)-one, 18.



A two-necked round-bottomed flask equipped with a reflux condenser was charged with Mg (0) (39 mg, 1.6 mmol, 1.0 equiv) and Et_2O (5 mL/mmol). Then 1,2-dibromoethane (0.16 mL, 1.9 mmol, 1.2 equiv) was added dropwise. The mixture was stirred at room temperature until consumption of Mg (0) affording a $MgBr_2$ solution that was used immediately.

To a cold solution (0 ºC) of **17** (10 mg, 0.025 mmol) in a 50:50 mixture of Et_2O:CH_2Cl_2 (0.5 mL) and under an argon atmosphere, 0.63 mL of a freshly prepared $MgBr_2$ solution (0.2 M, 0.125 mmol, 5.0 equiv) were slowly added. The mixture was allowed to reach room temperature and stirred until starting material disappearance (TLC, 20 h). The reaction was quenched with a 5% solution of $NaHCO_3$ (1 mL) and a 1 M solution of $Na_2S_2O_4$ (1 mL). The phases were separated, the aqueous layer was extracted with EtOAc (3 times), dried over anhydrous $MgSO_4$, filtered and concentrated under

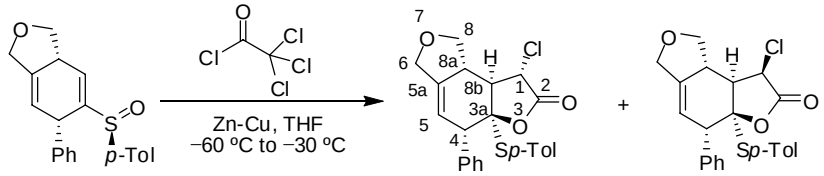
reduced pressure. Purification by chromatography (30-100% EtOAc-hexane) afforded **19** (5 mg, 0.017 mmol, 69%) as a colorless oil and **18** (2 mg, 0.008 mmol, 30%) as a white solid.

Partial data for **19** (from a mixture of epimers in C-4): R_{f1} = 0.44; R_{f2} = 0.38 (EtOAc); **^{1}H NMR** (300 MHz) δ = 4.96 (d, *J* = 6.4 Hz, 1 H, H-4), 5.04 (d, *J* = 5.1 Hz, 1 H, H-4), 7.17-7.44 (m); **MS** (ES) m/z (%): 351 $[M(Br^{81})+Na]^+$, 349 $[M(Br^{79})+Na]^+$.

To a solution of **19** (10 mg, 0.031 mmol, 1.0 equiv) in a 9:1 mixture of THF:H_2O (30 mL/mmol), amalgamated Al was added (5 mg, 0.186 mmol, 6.0 equiv) (Al was introduced for a few seconds in a 10% solution of $HgCl_2$, then in EtOH and finally in Et_2O). The reaction was stirred at room temperature until starting material disappearance (TLC, 20 h). Then the solution was filtered through a pad of celite and the solvent was removed under reduced pressure. The crude product was purified by chromatography (0-100% EtOAc-CH_2Cl_2) to afford **18** (4 mg, 0.016 mmol, 53%) as a white solid that was recrystallized from EtOAc-hexane.

Data for **18**: R_f = 0.38 (EtOAc); **mp** 138-142 ºC; **$[\alpha]_D^{20}$** = –59.3 (*c* = 0.26); **^{1}H NMR** (400 MHz-COSY) δ = 2.40 (dd, *J* = 17.4, 10.7 Hz, 1 H, H-4), 2.75 (d, *J* = 10.7 Hz, 1 H, H-4), 2.72-2.80 (m, 1 H, H-3a), 3.56 (dd, *J* = 9.2, 6.6 Hz, 1 H, H-3), 3.77 (d, *J* = 9.1 Hz, 1 H, H-1), 3.82 (d, *J* = 11.6 Hz, 1 H, H-6), 4.06 (d, *J* = 9.1 Hz, 1 H, H-1), 4.19 (d, *J* = 11.6 Hz, 1 H, H-7), 4.21 (dd, *J* = 9.1, 7.7 Hz, 1 H, H-3), 7.14-7.18 (m, 2 H), 7.30-7.42 (m, 3 H); **^{13}C NMR** (100 MHz) δ = 40.0, 42.7, 58.5, 72.6, 73.6, 77.6, 78.9, 128.2, 129.2 (2 C), 129.5 (2 C), 134.7, 207.0 (C=O); **IR** (KBr): 3440, 2924, 2851, 1713, 1630, 1071, 1029 cm^{-1}; **MS** (ES) m/z (%): 271 $[M+Na]^+$; **Anal. calcd for** $C_{14}H_{16}O_4$: C 67.73, H 6.50; found: C 67.92, H 6.76.

7.15. Sulfoxide directed lactonization of cycloadducts.



3b **20a** (65) **20b** (35)

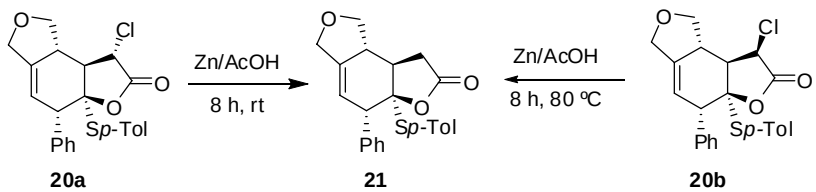
To a solution of **3b** (28 mg, 0.083 mmol, 1.0 equiv) in anhydrous THF (20 mL/mmol), Zn-Cu[17] (84 mg, 1.3 mmol, 20 equiv) was added and the mixture was cooled to –60 ºC. Then, a solution of freshly distilled trichloroacetyl chloride (36 µL, 0.325 mmol, 5.0 equiv) in anhydrous THF (30 mL/mmol) was added dropwise. The reaction mixture was stirred and allowed to warm up slowly. After 2 h (–30 ºC), the reaction mixture was filtered through a pad of celite, and poured into a saturated solution of $NaHCO_3$. The biphasic mixture was stirred for 30 minutes and then extracted with Et_2O (3

times), washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by chromatography (10-30% EtOAc-hexane) to afford a 65:35 mixture of two diastereomeric monochlorolactones (22 mg, 0.053 mmol, 64%) and 10 mg (0.029 mmol, 35%) of starting material. A second chromatography (10-30% EtOAc-hexane) afforded 14 mg (0.047 mmol) of **20a** and 7 mg (0.024 mmol) of **20b**.

Data for major lactone **20a**: R_f = 0.42 (30% EtOAc-hexane); $[\alpha]_D^{20}$ = +11.1 (*c* = 0.52); **^{1}H NMR** (400 MHz) δ = 2.30 (s, 3 H, Me-*p*Tol), 2.56 (dd, *J* = 9.6, 5.3 Hz, 1 H, H-8b), 2.83-2.90 (m, 1 H, H-8a), 3.47 (dd, *J* = 9.6, 8.3 Hz, 1 H, H-8), 3.85 (m, 1 H, H-4), 4.27 (t, *J* = 8.2 Hz, 1 H, H-8), 4.35 (d, *J* = 9.6 Hz, 1 H, H-1), 4.46-4.57 (m, 2 H, H-6), 6.03-6.05 (m, 1 H, H-5), 7.12 (d, *J* = 7.9 Hz, 2 H), 7.20 (d, *J* = 8.0 Hz, 2 H), 7.35-7.42 (m, 5 H); **^{13}C NMR** (100 MHz) δ = 21.2, 44.7, 48.6, 50.9, 57.5, 69.4, 72.5, 99.5, 117.5, 124.4, 128.1, 128.2 (2 C), 130.2 (2 C), 130.4 (2 C), 136.2, 137.0 (2 C), 140.6, 142.1, 169.0 (C=O); **IR** (film): 3033, 2925, 2856, 1791, 1688, 1597, 1492, 1454, 1265, 1188, 1105, 1038, 944, 813, 758, 737, 701, 612, 500 cm^{-1}; **HRMS** (ES) calcd for $C_{23}H_{22}ClO_3SNa$ $[M+Na]^+$: 435.0794; **found**: 435.0793 $[M+H]^+$.

Data for minor lactone **20b**: R_f = 0.33 (30% EtOAc-hexane); $[\alpha]_D^{20}$ = –281.1 (*c* = 0.91); **^{1}H NMR** (300 MHz, C_6D_6) δ = 1.98 (s, 3 H, Me-*p*Tol), 2.43 (t, *J* = 11.2 Hz, 1 H, H-8b), 2.73-2.83 (m, 1 H, H-8a), 3.33 (dd, *J* = 10.2, 8.3 Hz, 1 H, H-8), 4.06-4.10 (m, 2 H, H-4 and H-6), 4.19 (t, *J* = 7.9 Hz, 1 H, H-8), 4.28 (d, *J* = 11.8 Hz, 1 H, H-1), 4.34-4.38 (m, 1 H, H-6), 5.14-5.15 (m, 1 H, H-5), 6.85-6.89 (m, 4 H), 6.92-6.99 (m, 3 H), 7.53 (d, *J* = 7.9 Hz, 2 H); **^{13}C NMR** (75 MHz, C_6D_6) δ = 21.0, 41.9, 49.0, 51.1, 55.0, 68.9, 71.5, 94.8, 117.6, 124.9, 127.8, 128.1 (2 C), 130.0 (2 C), 130.4 (2 C), 135.9, 137.4 (2 C), 140.5, 143.5, 169.6 (C=O); **IR** (film): 3027, 2925, 2856, 1809, 1596, 1492, 1452, 1400, 1364, 1302, 1264, 1236, 1211, 1172, 1129, 1048, 938, 871, 812, 733, 700, 594 cm^{-1}; **HRMS** (ES) calcd for $C_{23}H_{22}ClO_3S$ $[M+H]^+$: 413.0978; **found**: 413.0976 $[M+H]^+$.

7.16. Dechlorination of α-chlorolactones 20.



20a **21** **20b**

To a solution of the major lactone **20a** (15 mg, 0.036 mmol, 1.0 equiv) in AcOH (10 mL/mmol), Zn powder (23 mg, 0.36 mmol, 10 equiv) was added. The reaction mixture was stirred at ambient temperature until starting material disappearance (8 h) (TLC). Then it was filtered by celite, treated with saturated solution of $NaHCO_3$ and extracted with EtOAC (3 times). The combined organic

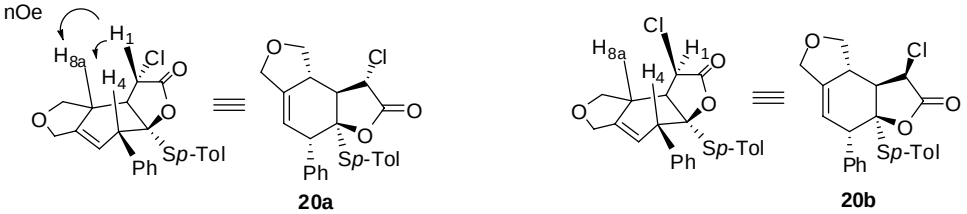
layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting crude was then purified by flash chromatography (20-50% EtOAc-hexane) to afford **21** (10 mg, 0.026 mmol, 73%) as a colorless oil.

When the minor lactone **20b** (14 mg, 0.034 mmol, 1 equiv) was treated with Zn/AcOH under the same reaction conditions, it was necessary to heat the reaction at 80 ºC. After 8 h lactone **21** was obtained (3 mg, 0.0079 mmol, 23%) along with recovered starting material 5 mg (0.012 mmol, 35%).

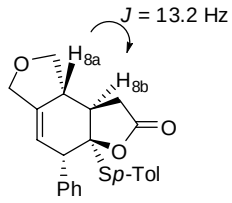
Data for **21**: $\boldsymbol{R_f}$ = 0.29 (50% EtOAc-hexane); $\boldsymbol{[\alpha]_D^{20}}$ = –110.5 (*c* = 0.62); **^{1}H NMR** (500 MHz-COSY) δ = 1.46 (dd, 1 H, *J* = 18.3, 10.6 Hz, 1 H, H-1), 1.94 (dd, *J* = 18.3, 2.9 Hz, 1 H , H-1), 2.30 (s, 3 H, Me-*p*Tol), 2.46, (ddd, *J* = 13.2, 10.2, 2.9 Hz, 1 H, H-8b), 2.55-2.61 (m, 1 H, H-8a), 3.51 (dd, 1 H, *J* = 8.9, 6.3 Hz, H-8), 3.86-3.88 (m, 1 H, H-4), 4.16 (dd, 1 H, *J* = 8.8, 7.5 Hz, H-8), 4.42-4.53 (m, 2 H, H-6), 6.06-6.08 (m, 1 H, H-5), 7.16 (d, 2 H, *J* = 7.8 Hz), 7.28 (d, 2 H, *J* = 8.0 Hz), 7.34-7.42 (m, 3 H), 7.49-7.51 (m, 2 H); **^{13}C NMR** (125 MHz) δ = 21.2, 29.7, 34.8, 45.8, 46.2, 52.9, 70.0, 72.5, 102.1, 117.3, 125.6, 127.8, 128.2 (2 C), 130.1 (2 C), 130.3 (2 C), 137.1 (2 C), 140.2, 144.4, 175.1 (C=O); **IR** (film): 2920, 2850, 1786, 1597, 1493, 1413, 1189, 1094, 1032, 933, 814, 736, 700, 606 cm^{-1}; **HRMS** (ES) calcd for $C_{23}H_{23}O_3S$ $[M+H]^+$: 379.1360; **found**: 379.1359 $[M+H]^+$.

7.17. Structural assignment for lactones 20a, 20b and 21.

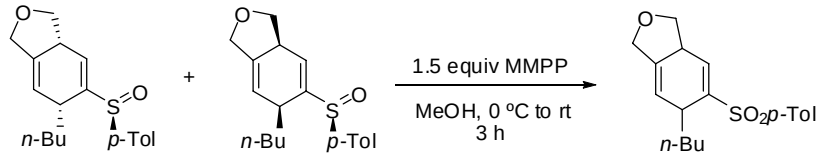
Dechlorination of monochlorolactones **20a** and **20b** afforded a single lactone **21**, revealing that the lactonization was diastereoselective. For the sulfoxide configuration of cycloadduct **3b**, the lactonization is expected to occur on the convex face of the bicycle as shown in compounds **20a** and **20b**, which is also the less hindered face. Compound **20b** showed a nOe effect between H-1 and H-8a and between H-1 and H-4, which supports (*S*) configuration on the chlorinated carbon. Consequently, compound **20b** should have the opposite stereochemistry on this stereocenter. The absence of nOe effect between H-1 and H-8a and between H-1 and H-4 in **20b** is in agreement with the proposed structure. This stereochemistry could explain the difficulties encountered in the dechlorination of compound **20b**, since the chlorine atom is more sterically hindered than in **20a**.



Additionally, the coupling constant (*J* = 13.2 Hz) between H-8a and H-8b in **21** and the absence of nOe effect between H-8b and H-8a or H-4 is consistent with the proposed structure.

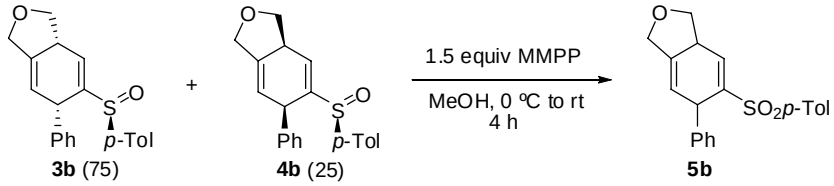


7.18. Synthesis of (3a*R,6*R**)-6-*n*-Butyl-5-(*p*-tolylsulfonyl)-1,3,3a,6-tetrahydroisobenzofuran, 5a.**



From a 67:33 mixture of **3a** and **4a** (13 mg, 0.041 mmol) and MMPP (38 mg (80%), 0.061 mmol) following the general procedure (3 h) a scalemic sulfone **5a** was obtained. Purification by chromatography (10-30% EtOAc-hexane) gave **5a** (13 mg, 0.039 mmol, 95%) as a colorless oil.

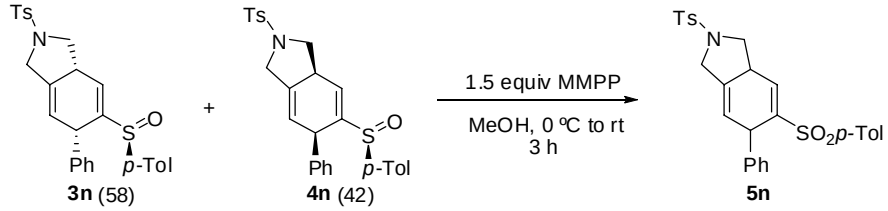
7.19. Synthesis of (3a*R,6*S**)-6-Phenyl-5-(*p*-tolylsulfonyl)-1,3,3a,6-tetrahydroisobenzofuran, 5b.**



From a 75:25 mixture of **3b** and **4b** (19 mg, 0.056 mmol) and MMPP (52 mg (80%), 0.084 mmol) following the general procedure (4 h) scalemic sulfone **5b** was obtained. Purification by chromatography (10-30% EtOAc-hexane) afforded **5b** (16 mg, 0.045 mmol, 80%) as a white solid that was recrystallized from EtOAc-hexane.

Data for **5b**: R_f = 0.41 (50% EtOAc-hexane); **mp** 145-147 ºC; **^{1}H NMR** (300 MHz) δ = 2.28 (s, 3 H, Me-*p*-Tol), 3.41-3.57 (m, 2 H, H-3a, 1 H-3), 4.24 (d, *J* = 11.5 Hz, 1 H, 1 H-1), 4.36-4.43 (m, 2 H, 1 H-3, 1 H-1), 4.50 (m, 1 H, H-6), 5.38 (t, *J* = 1.9 Hz, 1 H, H-7), 6.83-7.14 (m, 9 H), 7.34 (t, *J* = 2.4 Hz, 1 H, H-4); **^{13}C NMR** (75 MHz) δ = 21.4 (Me-*p*-Tol), 41.2, 43.3, 68.8, 70.8, 120.1, 126.9, 127.3 (2 C), 128.1 (2 C), 129.0 (2 C), 129.5 (2 C), 134.2, 134.6, 137.6, 139.9, 142.9, 144.6; **IR** (KBr): 3060, 3027, 2857, 1626, 1492, 1453, 1310, 1153, 1076, 1043, 1016, 812, 766, 700 cm^{-1}; **MS** (ES) m/z (%): 370 (100) $[M+NH_4]^+$, 353 $[M+H]^+$; **Anal. calcd for** $C_{21}H_{20}O_3S$: C 71.56, H 5.72, S 9.10; **found**: C 71.32, H 5.34, S 9.07.

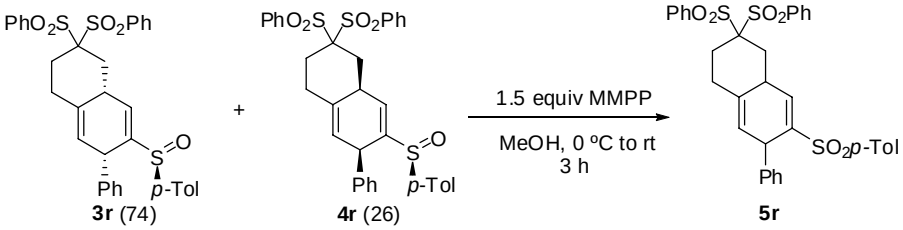
7.20. Synthesis of (3a*R,6*S**)-6-Phenyl-2,5-bis-(*p*-tolylsulfonyl)-2,3,3a,6-tetrahydroisoindole, 5n.**



From a 58:42 mixture of **3n** and **4n** (10 mg, 0.020 mmol) and MMPP (18 mg (80%), 0.03 mmol) following the general procedure scalemic sulfone **5n** was obtained. Purification by chromatography (20-30% EtOAc-hexane) afforded **5n** (8 mg, 0.016 mmol, 79%) as a white solid that was recrystallized from EtOAc-hexane.

Data for **5n**: R_f = 0.43 (50% EtOAc-hexane); **mp** 183-185 ºC; **^{1}H NMR** (300 MHz) δ = 2.28 (s, 3 H, Me-*p*-Tol), 2.42 (s, 3 H, Me-*p*-Tol), 2.25 (dd, *J* = 11.2, 9.3 Hz, 1 H, H-3), 3.23 (m, 1 H, H-3a), 3.80 (dd, *J* = 13.2, 1.2 Hz, 1 H, H-1), 3.95 (m, 1 H, H-1), 4.00 (dd, *J* = 9.0, 8.1 Hz, 1 H, H-3), 4.39 (dm, *J* = 13.2 Hz, 1 H, H-6), 5.35 (t, *J* = 1.7 Hz, 1 H, H-7), 6.69 (m, 2 H), 6.88-6.94 (m, 4 H), 6.98-7.06 (m, 3 H), 7.21 (dd, *J* = 3.3, 1.8 Hz, 1 H, H-4), 7.32 (m, 2 H), 7.71 (d, *J* = 8.1 Hz, 2 H); **^{13}C NMR** (50 MHz) δ = 21.4 (Me-*p*-Tol), 21.6 (Me-*p*-Tol), 39.5 (C-3a), 42.8 (C-6), 50.2 (C-1), 51.8 (C-3), 122.2, 127.0, 127.3 (2 C), 127.4 (2 C), 128.2 (2 C), 129.1 (2 C), 129.3 (2 C), 129.9 (2 C), 130.7, 134.1 (2 C), 137.2, 139.2, 143.2, 143.9, 144.6; **IR** (KBr): 3054, 2923, 2862, 1629, 1599, 1492, 1454, 1349, 1303, 1157, 1092, 1042, 984, 809, 763, 702, 683, 667 cm^{-1}; **MS** (ES) m/z (%): 506 (100) $[M+H]^+$; **Anal. calcd for** $C_{28}H_{27}NO_4S_2$: C 66.51, H 5.38, N 2.77, S 12.68; **found**: C 66.80, H 5.35, N 2.39, S 12.57.

7.21. Synthesis of (4a*R,7*S**)-3,3-Bis-benzenesulfonyl-7-phenyl-6-(*p*-tolylsulfonyl)-1,2,3,4,4a,7-hexahydronaphthalene, 5r.**

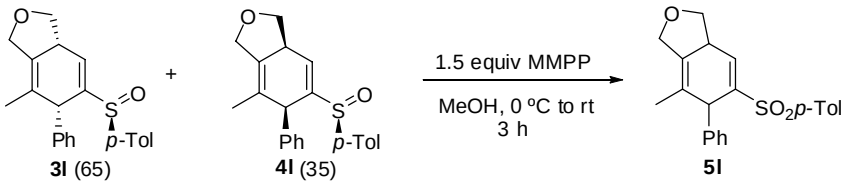


From a 74:26 mixture of **3r** and **4r** (10 mg, 0.016 mmol) and MMPP (15 mg (80%), 0.024 mmol) following the general procedure (3 h) scalemic sulfone **5r** was obtained. Purification by chromatography (20-30% EtOAc-hexane) afforded **5r** (8 mg, 0.012 mmol, 75%) as white solid that was recrystallized from EtOAc-hexane.

Data for **5r**: R_f = 0.14 (30% EtOAc-hexane); **mp** 239-241 ºC; **^{1}H NMR** (300 MHz) δ = 2.22 (m, 3 H), 2.31 (s, 3 H, Me-*p*-Tol), 2.52 (dm, *J* = 14.0 Hz, 1 H), 2.77 (ddd, *J* = 14.5, 4.2, 2.1 Hz, 1 H),

2.95 (m, 1 H), 3.90 (m, 1 H, H-4a), 4.35 (m, 1 H), 5.39 (m, 1 H), 6.76-6.79 (m, 2 H), 6.95-7.07 (m, 6 H), 7.19 (d, *J* = 8.4 Hz, 2 H), 7.58 (m, 2 H), 7.65-7.82 (m, 4 H), 7.94 (m, 2 H), 8.14 (m, 2 H); **^{13}C NMR** (75 MHz) δ = 21.4 (Me-*p*-Tol), 28.1, 29.5, 33.3, 34.2, 42.4, 87.3 (C-3), 123.5, 126.8, 127.6 (2 C), 128.4 (2 C), 128.7 (2 C), 128.8 (2 C), 128.9 (2 C), 129.2 (2 C), 130.2, 131.1 (2 C), 131.5 (2 C), 134.7, 135.0, 135.6, 136.2, 137.1, 138.0, 139.6, 142.4, 143.4, 146.2; **IR** (KBr): 3071, 3021, 2925, 2851, 1638, 1447, 1312, 1148, 1080, 993, 812, 755, 725 cm^{-1}; **MS** (ES) m/z (%): 667 $[M+Na]^+$, 662 (100) $[M+NH_4]^+$, 645 $[M+H]^+$; **Anal. calcd for** $C_{35}H_{32}O_6S_3$: C 65.19, H 5.00, S 14.92; **found**: C 65.23, H 5.18, S 14.84.

7.22. Synthesis of (3a*R**,6*S**)-7-Methyl-6-phenyl-5-(*p*-tolylsulfonyl)-1,3,3a,6-tetrahydroisobenzofuran, 5l.



3l (65) **4l** (35) **5l**

From a 65:35 mixture of **3l** and **4l** (53 mg, 0.15 mmol) and MMPP (139 mg (80%), 0.22 mmol) following the general procedure (3 h) scalemic sulfone **5l** was obtained. Purification by chromatography (10-30% EtOAc-hexane) afforded **5l** (40 mg, 0.11 mmol, 73%) as a white solid that was recrystallized from EtOAc-hexane.

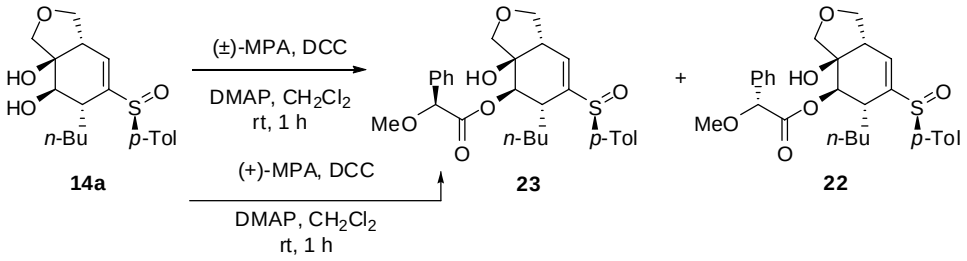
Data for **5l**: R_f = 0.19 (50% EtOAc-hexane); **mp** 179-181 ºC; **^{1}H NMR** (300 MHz) δ = 1.20 (s, 3 H, Me-7), 2.27 (s, 3 H, Me-*p*-Tol), 3.41 (dd, *J* = 11.2, 6.6 Hz, 1 H, H-3), 3.49 (m, 1 H, H-3a), 4.31-4.40 (m, 4 H, 2 H-1, 1 H-3, H-6), 6.88-7.04 (m, 7 H), 7.07 (d, *J* = 8.3 Hz, 2 H), 7.30 (dd, *J* = 3.0, 1.6 Hz, 1 H, H-4); **^{13}C NMR** (75 MHz) δ = 17.0 (Me-7), 21.4 (Me-*p*-Tol), 42.2, 47.3, 67.5, 70.9, 124.8, 126.9, 127.2 (2 C), 128.1, 129.0 (2 C), 129.4, 133.8, 137.9, 138.5, 142.8, 144.9; **IR** (KBr): 3067, 3025, 2919, 2867, 1594, 1444, 1312, 1299, 1193, 1143, 1112, 1084, 1056, 909, 900, 807 cm^{-1}; **MS** (ES) m/z (%): 367 (100) $[M+H]^+$; **Anal. calcd for** $C_{22}H_{22}O_3S$: C 72.10, H 6.05, S 8.75; **found**: C 72.23, H 6.15, S 8.87.

7.23. General procedure for the synthesis of 2-methoxy-2-phenyl acetates.

To a solution of the corresponding alcohol in CH_2Cl_2 (10 mL/mmol of sulfoxide), at 0 ºC, 1 equiv 2-methoxy-2-phenylacetic acid, 1.2 equiv of dicyclohexylcarbodiimide and 0.4 equiv of dimethylaminopyridine were added. The mixture was allowed to warm to room temperature and monitored by TLC until starting material disappearance (1 h). The reaction mixture was filtered to

remove dicyclohexylurea and the ester was purified by chromatography using the appropriate mixture of solvents.

7.24. Synthesis of (+)-(3a*S*,4*R*,5*R*,7a*S*,S_S)-5-*n*-Butyl-3a-hydroxy-6-(*p*-tolylsulfinyl)-1,3,3a,4,5,7a-hexahydroisobenzofuran-4-yl-(*S*)-2-methoxy-2-phenyl acetate, 23, and (3a*S*,4*R*,5*R*,7a*S*,S_S)-5-*n*-Butyl-3a-hydroxy-6-(*p*-tolylsulfinyl)-1,3,3a,4,5,7a-hexahydroisobenzofuran-4-yl-(*R*)-2-methoxy-2-phenyl acetate, 22.



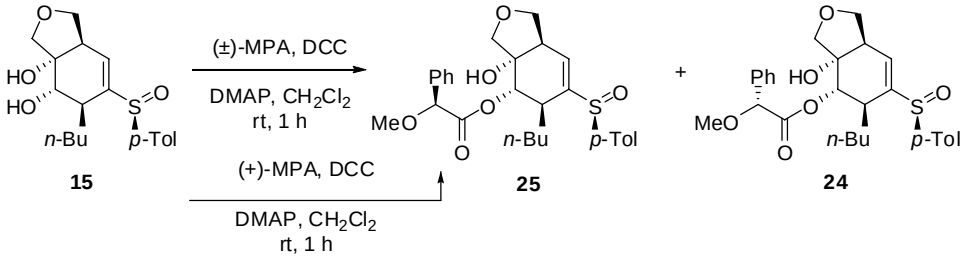
From diol **14a** (10 mg, 0.028 mmol), (±)-2-methoxy-2-phenylacetic acid (4 mg, 0.028 mmol), DCC (7 mg, 0.034 mmol) and DMAP (1 crystal), following the general procedure a 50:50 mixture of **22** and **23** was obtained. Purification by chromatography afforded 12 mg (0.023 mmol, 83%) of **22** and **23**.

In an identical experiment with (+)-2-methoxy-2-phenylacetic acid, **23** (14 mg, 0.027 mmol, 96%) was obtained as a white solid that was recrystallized from EtOAc-hexane. The ^{1}H NMR of the crude product did not show any signal of compound **22** and thus the optical purity of **14a** was established.

Data for **23**: R_f = 0.33 (100% EtOAc); **mp** 60-61 ºC; **[α]$^{20}_D$** = +51.0 (*c* = 1.23); **^{1}H NMR** (300 MHz) δ = 0.79 (t, *J* = 7.3 Hz, 3 H, Me-*n*-Bu), 0.99-1.27 (m, 6 H, *n*-Bu), 2.21 (m, 2 H, H-5, OH), 2.39 (s, 3 H, Me-*p*-Tol), 3.03 (m, 1 H, H-7a), 3.32 (s, 3 H, OMe), 3.48 (d, *J* = 9.3 Hz, 1 H, H-3), 3.62 (d, *J* = 9.5 Hz, 1 H, H-3), 3.64 (t, *J* = 8.1 Hz, 1 H, H-1), 4.24 (t, *J* = 8.7 Hz, 1 H, H-1), 4.70 (s, 1 H, H_α), 5.21 (d, *J* = 7.8 Hz, 1 H, H-4), 6.66 (dd, *J* = 4.4, 1.9 Hz, 1 H, H-7), 7.26 (d, *J* = 8.1 Hz, 2 H, *p*-Tol), 7.34 (m, 5 H, Ph), 7.48 (d, *J* = 8.1 Hz, 2 H, *p*-Tol); **^{13}C NMR** (50 MHz) δ = 13.7 (Me-*n*-Bu), 21.5 (Me-*p*-Tol), 22.6, 26.5, 27.1, 37.0 (C-5), 47.7 (C-7a), 57.4 (OMe), 71.9 (C-4), 73.4 (C-1), 75.2 (C-3), 78.8 (C-3a), 82.8 (C_α), 125.8, 126.7 (2 C), 126.8 (2 C), 128.8 (2 C), 129.1, 130.3 (2 C), 135.8, 139.3, 142.8, 143.2, 170.0; **IR** (KBr): 3436, 2956, 2930, 2868, 1750, 1638, 1456, 1174, 1108, 1039, 811, 733, 698 cm^{-1}; **MS** (ES) m/z (%): 499 (100) $[M+H]^+$; **Anal. calcd for** $C_{28}H_{34}O_6S$: C 67.44, H 6.87, S 6.43; **found**: C 67.57, H 7.02, S 6.70.

Data for **22** (from a mixture of **22** and **23**): R_f = 0.27 (100% EtOAc); **^{1}H NMR** (300 MHz) δ = 0.85 (t, *J* = 7.3 Hz, 3 H, Me-*n*-Bu), 2.10-2.24 (m, 2 H, H-5, OH), 2.40 (s, 3 H, Me-*p*-Tol), 2.75 (m, 1 H, H-7a), 3.30 (s, 3 H, OMe), 3.52 (d, *J* = 9.8 Hz, 1 H, H-3), 3.62 (m, 2 H, 1 H-1, H-3), 4.10 (dd, *J* = 8.7, 7.7 Hz, 1 H, H-1), 4.48 (s, 1 H, H_α), 5.11 (d, *J* = 5.6 Hz, 1 H, H-4), 6.62 (dd, *J* = 4.4, 1.5 Hz, 1 H, H-7), 7.30-7.36 (m, 7 H), 7.52 (d, *J* = 8.1 Hz, 2 H).

7.25. Synthesis of (+)-(3a*R*,4*S*,5*S*,7a*R*,*S*$_S$)-5-*n*-Butyl-3a-hydroxy-6-(*p*-tolylsulfinyl)-1,3,3a,4,5,7a-hexahydroisobenzofuran-4-yl-(*S*)-2-methoxy-2-phenyl acetate, 25, and (3a*R*,4*S*,5*S*,7a*R*,*S*$_S$)-5-*n*-Butyl-3a-hydroxy-6-(*p*-tolylsulfinyl)-1,3,3a,4,5,7a-hexahydroisobenzofuran-4-yl-(*R*)-2-methoxy-2-phenyl acetate, 24.



From diol **15** (8 mg, 0.023 mmol), (±)-2-methoxy-2-phenylacetic acid (4 mg, 0.023 mmol), DCC (7 mg, 0.034 mmol) and DMAP (1 crystal), following the general procedure a 50:50 mixture of **24** and **25** was obtained. Purification by chromatography afforded **25** (5 mg, 0.020 mmol, 45%) and **24** (5 mg, 0.020 mmol, 45%) as white solids.

In an identical experiment with (+)-2-methoxy-2-phenylacetic acid **25** was obtained (10 mg, 0.020 mmol, 90%) as a white solid that was recrystallized from EtOAc-hexane. The ^{1}H NMR of the crude product showed **25** as a single diastereomer.

Data for **25**: R_f = 0.30 (100% EtOAc); **mp** 57 ºC; **$[\alpha]^{20}_D$** = +49.2 (*c* = 0.65); **^{1}H NMR** (300 MHz) δ = 0.82 (t, *J* = 7.2 Hz, 3 H, Me-*n*-Bu), 1.14-1.47 (m, 5 H, *n*-Bu), 1.74 (m, 1 H), 2.41 (s, 3 H, Me-*p*-Tol), 2.49-2.57 (m, 2 H, H-5, H-7a), 3.29 (s, 3 H, OMe), 3.43 (d, *J* = 10.2 Hz, 1 H, H-3), 3.76 (dd, *J* = 8.8, 2.7 Hz, 1 H, H-1), 3.78 (d, *J* = 10.7 Hz, 1 H, H-3), 4.01 (dd, *J* = 8.7, 6.7 Hz, 1 H, H-1), 4.31 (s, 1 H, H_α), 5.11 (d, *J* = 3.2 Hz, 1 H, H-4), 6.44 (d, *J* = 4.1 Hz, 1 H, H-7), 7.27-7.39 (m, 7 H), 7.47 (d, *J* = 8.3 Hz, 2 H, *p*-Tol); **^{13}C NMR** (75 MHz) δ = 13.8 (Me-*n*-Bu), 21.4 (Me-*p*-Tol), 22.2, 28.8, 31.1, 39.1 (C-5), 48.3 (C-7a), 57.2 (OMe), 71.8 (C-4), 73.0 (C-1), 76.0 (C-3), 79.3 (C-3a), 81.7 (C_α), 125.0 (2 C), 126.9 (2 C), 129.1 (2 C), 129.4, 129.9 (2 C), 133.2, 136.3, 139.5, 141.4, 145.5, 169.1 (CO); **IR** (KBr): 3434, 2959, 2926, 2870, 1749, 1631, 1493, 1455, 1261, 1172, 1102, 1082, 1029, 808,

729, 697 cm^{-1}; **MS** (ES) m/z (%): 499 (100) $[M+H]^+$; **Anal. calcd for** $C_{28}H_{34}O_6S$: C 67.44, H 6.87, S 6.43; **found**: C 67.76, H 6.96, S 6.62.

Data for **24**: R_f = 0.25 (100% EtOAc); **^{1}H NMR** (300 MHz) δ = 0.73 (t, *J* = 7.1 Hz, 3 H, Me-*n*-Bu), 1.00-1.36 (m, 6 H), 2.24 (br s, 1 H, OH), 2.40 (s, 3 H, Me-*p*-Tol), 2.50 (m, 1 H, H-5), 2.88 (dtd, *J* = 7.3, 4.1, 1.5 Hz, 1 H, H-7a), 3.34 (s, 3 H, OMe), 3.57 (d, *J* = 9.8 Hz, 1 H, H-3), 3.76 (dd, *J* = 8.8, 4.4 Hz, 1 H, H-1), 3.82 (d, *J* = 9.8 Hz, 1 H, H-3), 4.17 (dd, *J* = 8.6, 7.4 Hz, 1 H, H-1), 4.66 (s, 1 H, H_α), 5.17 (d, *J* = 4.4 Hz, 1 H, H-4), 6.43 (dd, *J* = 4.1, 1.2 Hz, 1 H, H-7), 7.27 (d, *J* = 8.1 Hz, 2 H, *p*-Tol), 7.34 (m, 5 H), 7.42 (d, *J* = 8.3 Hz, 2 H, *p*-Tol); **Anal. calcd for** $C_{28}H_{34}O_6S$: C 67.44, H 6.87, S 6.43; **found**: C 67.17, H 6.95, S 6.28.

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