Novel Polymer-Bound Chiral Selenium-Electrophiles

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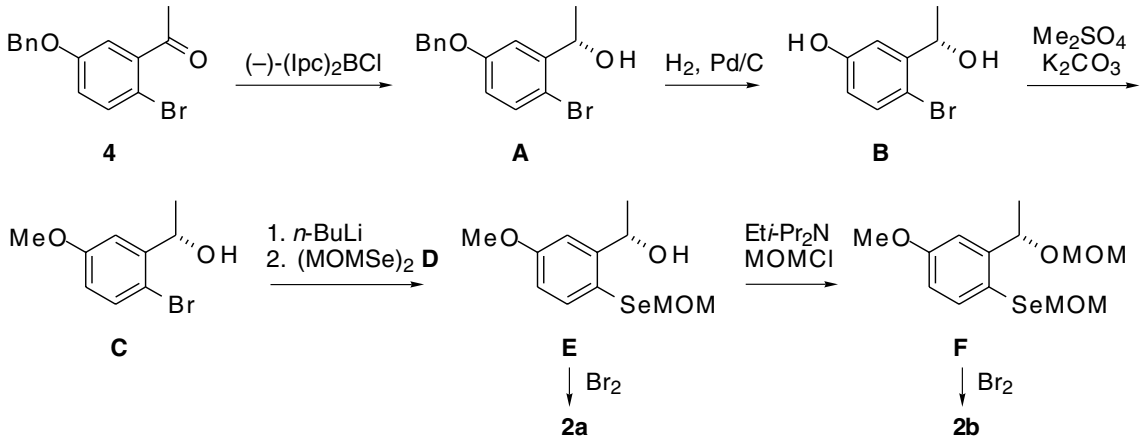
Supporting Information

All reactions were performed under argon with anhydrous solvents. The ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ using TMS as an internal standard. Melting points are uncorrected.

4-Phenyl-4-penten-1-ol (**1**)
Prepared according to literature.[1]



(*S*)-1-(5-Benzyloxy-2-bromophenyl)ethanol (**A**)
A solution of (–)-*B*-chlorodiisopinocampheylborane $[(–)(Ipc)_2BCl]$[2] (4.6 g, 14 mmol) in THF (15 mL) was cooled down to –25 °C and a solution of 4-benzyloxy-2-bromoacetophenone **4** (4.0 g, 13 mmol) in THF (5 mL) was added dropwise. After stirring for 20 h at –25 °C, the solvent was removed under vacuo. The remaining oil was diluted with diethyl ether (100 mL) and diethanolamine (3.1 mL, 32 mmol) was added. The reaction was stirred vigorously for 2 h at room temperature and the solvent removed under vacuo. The residues of pinene were removed by kugelrohr distillation (150 °C, 0.03 mbar) and the remaining oil purified by flash chromatography (silica gel (280 g), CH_2Cl_2:hexane:methanol 15:30:1) to yield **A** (3.3 g, 82%) as a pale yellow oil. 95% *ee* (HPLC, Daicel OD, *n*-hexane:2-propanol 95:5, 0.5 ml/min, $R_f(S)$: 58.06 min, $R_f(R)$: 68.94

(1) Wenkert, E.; Michelotti, E. L.; Swindell, C. S.; Tingoli, M. *J. Org. Chem.* **1984**, *49*, 4894–4899.

(2) (a) Srebnik, M.; Ramachandran, P. V.; Brown, H. C. *J. Org. Chem.* **1988**, *53*, 2916–2920. (b) Brown, H. C.; Chandrasekharan, J.; Ramachandran, P. V. *J. Am. Chem. Soc.* **1988**, *110*, 1539–1546.

min)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 (d, *J* = 6.3 Hz, 3H, C*H*$_3$), 2.17 (s (br), 1H, O*H*), 5.03 (s, 2H,C*H*$_2$), 5.14 (dq, *J* = 3.1 Hz, *J* = 6.2 Hz, 1H, C*H*OH), 6.73 (dd, *J* = 3.1 Hz, *J* = 6.8 Hz, 1H, C4*H*), 7.23 (d, *J* = 3.3 Hz, 1H, C6*H*), 7.30-7.42 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.5 (q, *C*H$_3$), 69.1 (d, *C*HOH), 70.1 (t, *C*H$_2$O), 112.1 (s, *C*2), 113.0 (d, *C*4), 115.4 (d, *C*6), 127.5 (d, 2C, *C*2', *C*6'), 128.0 (d, *C*4'), 128.6 (d, 2C, *C*3', *C*5'), 133.2 (d, *C*3), 136.5 (s, *C*1'), 145.8 (s, *C*1), 158.5 (s, *C*5). IR ($CHCl_3$): 3861, 3356, 3066, 3035, 2974, 1595, 1573, 1469, 1407, 1381, 1294, 1233, 1171, 1131, 1092, 1049, 1014, 932, 882, 806, 737, 698, 658 cm^{-1}. MS (EI, 70eV): *m/z* (%) 308 (62), 306 (61) [M$^+$], 291 (5), 228 (5), 200 (9), 172 (26), 143 (10), 119 (8), 107 (33), 91 (100), 77 (62), 65 (97), 51 (69), 43 (67). HRMS for $C_{15}H_{15}BrO_2$•NH_4: calcd.: 324.0599, found: 324.0589. $[\alpha]_D^{25}$ = –41.1 (c 0.72, $CHCl_3$).

(*S*)-4-Bromo-3-(1-hydroxyethyl)phenol (B)
1.0 g Pd/C (10%) (1.0 g) suspended in dry ethanol (50 mL) was degassed and saturated with hydrogen. Then **A** (3.0 g, 14 mmol) was added and the mixture was shaken until the consumption of hydrogen had stopped. The solvent was removed in vacuo and the remaining oil purified by flash chromatography (silica gel (110 g), ethyl acetate:pentane 1:4) to yield **B** (1.56 g, 75%) as a colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (d, *J* = 6.3 Hz, 3H, C*H*$_3$), 2.77 (s (br), 1H, O*H*), 5.25 (q, *J* = 6.4 Hz, 1H, C*H*), 6.71 (dd, *J* = 3.0 Hz, *J* = 8.6 Hz, 1H, C4*H*), 7.21 (d, *J* = 3.0 Hz, 1H, C6*H*), 7.38 (d, *J* = 8.8 Hz, 1H, C5*H*), 7.81 (s (br), 1H, ArO*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.2 (q, CH_3), 70.6 (d, *C*H), 112.3 (s, *C*4), 114.5 (d, *C*6), 117.4 (d, *C*2), 134.6 (d, *C*5), 146.1 (s, *C*3), 156.1 (s, *C*1). IR ($CHCl_3$): 3872, 3339, 2976, 2926, 1596, 1443, 1370, 1288, 1237, 1168, 1130, 1087, 1030, 944, 879, 813, 739, 629 cm^{-1}. MS (EI, 70eV): *m/z* (%) 218 (22) [M$^+$], 201 (39), 173 (7), 145 (5), 121 (10), 94 (100), 77 (11), 63 (32), 51 (9), 43 (30). HRMS for $C_8H_9BrO_2$•NH_4: calcd.: 234.0130, found: 234.0131. $[\alpha]_D^{25}$ = –29.4 (c 1.09, $CHCl_3$).

(*S*)-1-(2-Bromo-5-methoxyphenyl)ethanol (C)[3]
B (250 mg, 1.15 mmol) in acetone (1 mL) was added to a suspension of potassium carbonate (175 mg, 1.26 mmol) in acetone (7 mL). The mixture was stirred for 30 minutes, then dimethylsulfate (189 mg, 1.5 mmol) was added and the reaction heated to reflux for 6 h, before it was quenched with a 5% aqueous ammonia solution. The aqueous layer was extracted twice with *t*-butyl methyl ether, the combined organic layers were washed with water and the solvent evaporated in vacuo. Chromatographic purification (silica gel (17 g), *t*-butyl methyl ether:pentane 1:2) yielded **C** (240 mg, 91%) as a colorless oil.
^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.44 (d, *J* = 6.3 Hz, 3H, C*H*$_3$), 2.08 (s (br), 1H, O*H*), 3.80 (s, 3H, OC*H*$_3$), 5.17 (q, *J* = 6.5 Hz, 1H, C*H*OH), 6.73 (dd, *J* = 3.1 Hz, *J* = 8.8 Hz, 1H, C4*H*), 7.15 (d, *J* = 3.3 Hz, 1H, C6*H*), 7.38 (d, *J* = 8.8 Hz, C3*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.6 (q, CH_3), 55.5 (q, O*C*H$_3$), 68.6 (d, *C*HOH), 113.8 (d, *C*6), 117.6 (d, *C*4), 121.9 (s, *C*2), 127.2 (d, 2C, *C*2', *C*6'), 136.5 (s, *C*1), 159.0 (s, *C*5). IR ($CHCl_3$): 3772, 3379, 2973, 2934, 2837, 1597, 1574,

(3) Racemate: Fleming, I.; Woolias, M. *J. Chem. Soc., Perkin Trans. 1* **1979**, 829–837.

1471, 1416, 1368, 1293, 1235, 1192, 1167, 1130, 1092, 1057, 1018, 926, 874, 808, 715, 619, 571 cm^{-1}. MS (EI, 70eV): *m/z* (%) 230 (14) [M^+], 215 (100), 135 (9), 108 (53), 91 (53), 77 (14), 63 (13), 51 (6), 43 (24). HRMS for $C_9H_{11}BrO_2$: calcd.: 229.9942, found: 229.9944. $[\alpha]_D^{25}$ = –59.8 (c 0.66, $CHCl_3$).

Dimethoxymethyl diselenide (**D**)

Sodium (230 mg, 10 mmol), selenium powder (790 mg, 10 mmol), and naphthalene (128 mg, 1 mmol) were refluxed in dry THF (10 mL) under nitrogen for 7 h. After cooling to 0 °C, chloromethyl methylether (845 mg, 10.5 mmol) was added and the mixture treated in an ultrasonic bath for 12 h. The reaction mixture was quenched with sat. aq. NH_4Cl (2 mL), and the aqueous phase extracted with *t*-butyl methyl ether (3 × 50 mL). The solvent of the combined organic phases was removed in vacuo and subsequent flash chromatography (*t*-butyl methyl ether:pentane 1:4) yielded 0.75–1.00 g (60–80%) dimethoxymethyl diselenide as a yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.31 (s, 4H), 3.40 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 76.7, 57.3. ^{77}Se NMR (95 MHz, $CDCl_3$): δ = 365.5. IR (NaCl): 2989, 2926, 2817, 2002, 1445, 1416, 1260, 1179, 1083, 926, 868, 800 cm^{-1}. HRMS for $C_4H_{10}O_2Se_2$: calcd.: 249.9011, found 249.9015.

(*S*)-1-(5-Methoxy-2-methoxymethylselenylphenyl)ethanol (**E**)

C (80 mg, 0.35 mmol) were dissolved in diethyl ether (5 mL), the solution cooled to –78 °C and *n*-butyl lithium (0.55 ml, 0.875 mmol, 1.6M in hexane) added dropwise. The reaction was stirred for 20 min and dimethoxymethyl diselenide **D** (130 mg, 0.53 mmol) was added. After warming up to room temperature, the solution was stirred another 2 h, then quenched with 1M hydrochloric acid, the organic solvent removed in vacuo and the remaining aqueous layer extracted with *t*-butyl methyl ether. Chromatographic purification (silica gel (8 g), *t*-butyl methyl ether:pentane 1:2) yielded **E** (62 mg, 69%) as a pale yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.48 (d, *J* = 6.3 Hz, 3H, C*H*$_3$), 2.76 (s (br), 1H, O*H*), 3.39 (s, 3H, OC*H*$_3$*),* 3.81 (s, 3H, OC*H*$_3$*),* 5.04 (d, J = 1.6 Hz, 2H, C*H*$_2$), 5.33 (q, *J* = 6.5 Hz, 1H, C*H*OH), 6.75 (dd, *J* = 3.1 Hz, *J* = 8.8 Hz, 1H, C4*H*), 7.11 (d, *J* = 3.3 Hz, 1H, C6*H*), 7.59 (d, *J* = 8.5 Hz, C3*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.5 (q, *C*H$_3$), 55.3 (q, O*C*H3), 57.2 (q, O*C*H3), 69.1 (d, *C*HOH), 75.6 (t, *C*H$_2$), 113.2 (d, *C*4), 114.0 (d, *C*6), 119.2 (d, *C*2), 137.2 (s, *C*3), 149.7 (s, *C*1), 160.3 (s, *C*5). IR ($CHCl_3$): 3420, 2929, 1594, 1472, 1289, 1230, 1180, 1084, 1019, 925, 872, 814 cm^{-1}. MS (EI, 70eV): *m/z* (%) 276 (14) [M^+], 244 (5), 214 (93), 199 (18), 183 (8), 152 (15), 134 (36), 109 (26), 91 (8), 77 (14), 63 (7), 45 (100). HRMS for $C_{11}H_{16}O_3Se$: calcd.: 276.0265, found: 276.0261. $[\alpha]_D^{25}$ = –45.65 (c 0.62, $CHCl_3$).

(*S*)-4-Methoxy-2-(1-methoxymethoxyethyl)-1-methoxymethylselenylbenzene (**F**)

E (70 mg, 0.25 mmol) was dissolved in diisopropylethylamine (2.5 mL), cooled to 0 °C and chloromethyl methylether (0.3 mL, 3.5 mmol) was added. The mixture was allowed to warm up slowly to room temperature and stirred for 24 h. The reaction was quenched with 5% aqueous ammonia solution, stirred 15 min and carefully acidified with 1M hydrochloric acid. After extraction with *t*-butyl methyl ether, the solvent was removed in vacuo and the remaining oil

purified by flash chromatography (silica (5 g), *t*-butyl methyl ether:pentane 1:10) yielding **F** (45 mg, 56 %) as a colorless oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 (d, *J* = 6.5 Hz, 3H, C*H*$_3$), 3.37 (s, 3H, OC*H*$_3$), 3.40 (s, 3H, OC*H*$_3$) 3.81 (s, 3H, OC*H*$_3$), 4.56 (q, *J* = 6.6 Hz, 2H, OC*H*$_2$O), 5.06 (d, *J* = 8.6 Hz, 1H, SeCH*H*O), 5.13 (d, *J* = Ar, 8.6 Hz, 1H, SeC*H*HO), 5.29 (q, *J* = 6.4 Hz, 1H, C*H*), 6.75 (dd, *J* = 2.9 Hz, *J* = 8.6 Hz, 1H, C5*H*), 7.07 (d, *J* = 3.0 Hz, 1H, C3*H*), 7.57 (d, *J* = 8.5 Hz, C6*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.6 (q, CH_3), 55.3 (q, O*C*H$_3$), 55.4 (q, O*C*H$_3$), 57.1 (q, O*C*H$_3$), 73.3 (d, *C*H), 75.5 (t, Se*C*H$_2$), 94.4 (t, O*C*H$_2$O), 111.6 (d, *C*5), 113.4 (d, *C*3), 119.4 (s, *C*1), 136.9 (s, *C*6), 147.8 (s, *C*2), 160.1 (s, *C*4). IR ($CHCl_3$): 2930, 1594, 1566, 1472, 1371, 1288, 1230, 1180, 1084, 1034, 921, 874, 816 cm^{-1}. MS (EI, 70eV): *m/z* (%) 320 (9) [M$^+$], 244 (8), 214 (83), 199 (14), 183 (5), 134 (30), 91 (8), 45 (100). HRMS for $C_{13}H_{20}O_4Se$: calcd.: 320.0527, found: 320.0532. $[\alpha]_D^{25}$ = –140.5 (c 0.97, $CHCl_3$).

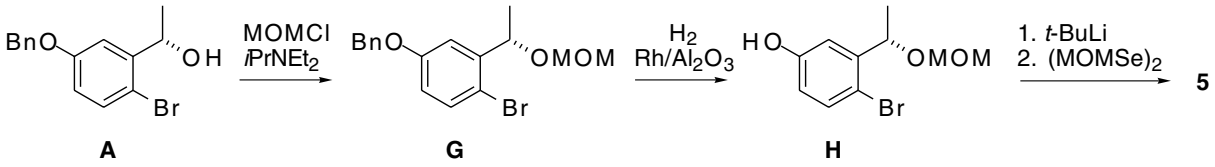
(*S*)-2-(1-Hydroxyethyl)-4-methoxyphenylselenenyl bromide (**2a**)
Generated *in situ* from **E**.

(*S*)-2-(1-Methoxymethoxyethyl)-4-methoxyphenylselenenyl bromide (**2b**)
Generated *in situ* from **F**.

(1*S*,2*R*)-1-[5-Methoxy-2-(2-phenyltetrahydrofuran-2-yl-ethylselenyl)phenyl] ethanol (**3a**)
E (38 mg, 0.14 mmol) was dissolved in diethyl ether (5 mL). The solution was cooled to 0 °C, Br_2 (150 μL, 1M in CCl_4) was added and stirring continued for 10 min. The deep red solution was cooled to –78 °C, and 4-phenyl-4-penten-1-ol **1** (30 mg, 0.19 mmol) was added. The reaction was stirred overnight at –78 °C and subsequently quenched with *sym*-collidine (40 μL, 0.3 mmol) and water (5 mL). After warming up to room temperature, the mixture was acidified with 7% aqueous citric acid and extracted with *t*-butyl methyl ether. The solvent was evaporated in vacuo and the residue purified by flash chromatography (silica (8 g), acetone:chloroforme 1:5) yielding **3a** (14 mg, 26 %) as a colorless oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.48 (d, *J* = 6.3 Hz, 3H, C*H*$_3$), 1.76-2.09 (m, 2H, C*H*$_2$), 2.20-2.35 (m, 2H, C*H*$_3$), 2.41 (d, *J* = 3.2 Hz, 1H, O*H*), 3.24 (d, *J* = 12.0 Hz, 1H, CH*H*Se), 3.37 (d, *J* = 12.0 Hz, 1H, C*H*HSe), 3.79 (s, 3H, OC*H*3), 3.93 (q, *J* = 5.6 Hz, 1H, C*H*HO), 4.05 (q, *J* = 7.1 Hz, 1H, CH*H*O), 5.14 (q, *J* = 6.5 Hz, 1H, C*H*OH), 6.67 (dd, *J* = 3.1 Hz, *J* = 8.8 Hz, 1H, C4*H*), 6.99 (d, *J* = 3.3 Hz, 1H, C6*H*), 7.19-7.42 (m, 6H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.4 (q, *C*H$_3$), 26.3 (t, *C*H$_2$), 38.6 (t, *C*H$_2$), 44.0 (t, *C*H$_2$Se), 55.7 (q, O*C*H$_3$), 68.7 (t, O*C*H$_2$), 69.7 (d, *C*HOH), 86.7 (s, *C*1''), 111.4 (d, *C*4), 114.3 (d, *C*6), 119.2 (s, *C*2), 125.7 (d, 2C, *C*2', *C*6'), 127.8 (d, *C*4'), 128.4 (d, 2C, *C*3', *C5*'), 137.8 (d, *C*3), 146.7 (s, *C*1'), 149.1 (s, *C*1), 159.4 (s, *C*5). IR ($CHCl_3$): 3408, 2970, 2927, 1594, 1567, 1471, 12881230, 1166, 1124, 1088, 1048, 1020, 971, 923, 873, 812, 764, 703, 669 cm^{-1}. MS (FAB): *m/z* (%) 392 (12) [M$^+$], 375(10), 229 (10), 213 (21), 161 (25), 147 (100), 135 (17), 123 (16), 105 (32). HRMS for $C_{20}H_{24}O_3Se$: calcd.: 392.0891, found: 392.0900. $[\alpha]_D^{25}$ = –15.3 (c 0.96, $CHCl_3$).

2-[4-Methoxy-2-(methoxymethoxyethyl)phenylselenylmethyl]-2-phenyltetrahydrofuran (**3b**)
F (39 mg, 0.12 mmol) was dissolved in diethyl ether (5 mL). The solution was cooled to 0 °C, Br_2 (134 μL, 1M in CCl_4) was added and stirring continued for 10 min. The deep red solution was cooled to –78 °C, and 4-phenyl-4-penten-1-ol **1** (30 mg, 0.19 mmol) was added. The reaction was stirred overnight at –78 °C and subsequently quenched with sym-collidine (40 μL, 0.3 mmol) and water (5 mL). After warming up to room temperature, the mixture was acidified with 7% aqueous citric acid and extracted with *t*-butyl methyl ether. The solvent was evaporated in vacuo and the residue purified by flash chromatography (silica (8 g), *t*-butyl methyl ether:pentane 1:2) yielding **3b** (38 mg, 74 %) as a colorless oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.38 (d, J = 6.4 Hz, 3H, CH_3), 1.74-2.08 (m, 2H, CH_2), 2.21-2-40 (m, 2H, CH_3), 3.21 (d, J = 11.7 Hz, CH*H*Se), 3.34 (s, 3H, OCH_3), 3.35 (d, J = 11.7 Hz, 1H, C*H*HSe), 3.79 (s, 3H, OCH_3), 3.91 (m, 1H, C*H*HO), 4.03 (m, 1H, CH*H*O), 4.56 (q, J = 10.4 Hz, 2H, OCH_2), 5.24 (q, J = 6.4 Hz, 1H, C*H*OH), 6.68 (dd, J = 3.0 Hz, J = 8.5 Hz, 1H, C5*H*), 7.02 (d, J = 3.0 Hz, 1H, C3*H*), 7.20-7.42 (m, 6H, Ar*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.7 (q, *C*H_3), 29.7 (t, *C*H_2), 37.6 (t, *C*H_2), 42.8 (t, *C*H_2Se), 55.2 (q, O*C*H_3), 55.4 (q, O*C*H_3), 68.2 (t, O*C*H_2), 73.4 (d, *C*HOCH_2), 86.2 (s, *C*2''), 94.5 (t, *C*H_2OCH_3), 111.3 (d, *C*5), 113.8 (d, *C*3), 120.1 (s, *C*1), 125.2 (d, 2C, *C*2', *C*6'), 126.8 (d, *C*4'), 128.0 (d, 2C, *C*3', *C*5'), 136.9 (d, *C*6), 145.7 (s, *C*1'), 147.1 (s, *C*2), 159.8 (s, *C*4). IR ($CHCl_3$): 2925, 1594, 1566, 1470, 1439, 1287, 1229, 1155, 1099, 1033, 919, 764, 703 cm^{-1}. MS (EI, 70eV): *m/z* (%) 436 (5) [M$^+$], 147 (100), 105 (20), 91 (13), 77 (6), 45 (15). HRMS for $C_{22}H_{28}O_4Se$: calcd.: 436.1153, found: 436.1158. $[\alpha]_D^{25}$ = –33.6 (c 1.03, $CHCl_3$).

1-[2-Bromo-5-(phenylmethoxy)phenyl]ethanone (**4**)
Prepared according to literature.[4]



A **G** **H**

(*S*)-4-Benzyl-1-bromo-2-(1-methoxymethoxyethyl)benzene (**G**)
A (4.8 g, 16 mmol) was dissolved in diisopropylethylamine (25 mL), cooled to 0 °C and chloromethyl methylether (4 mL, 47 mmol) was added. The mixture was allowed to warm up slowly to room temperature and stirred for 24 h. The reaction was quenched with 5% aqueous ammonia solution, stirred 15 min and carefully acidified with 1M hydrochloric acid. After extraction with *t*-butyl methyl ether, the solvent was removed in vacuo and the remaining oil distilled on the kugelrohr (180 °C, 0.04 mbar) yielding **G** (4.5 g, 82 %) as a colorless oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (d, J = 6.5 Hz, 3H, CH_3), 3.37 (s, 3H, OCH_3), 4.50 (d, J = 6.7 Hz, 1H, OC*H*HO), 4.56 (d, J = 6.7 Hz, 1H, OCH*H*O), 5.05 (s, 2H, PhCH_2), 5.07 (q, J = 6.3 Hz, 1H, C*H*OH), 6.76 (dd, J = 3.0 Hz, J = 8.7 Hz, 1H, C5*H*), 7.14 (d, J = 3.1 Hz, 1H, C3*H*), 7.32-

(4) Bolton, R. E.; Moody, C. J.; Pass, M.; Rees, C. W.; Tojo, G. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2491–2499.

7.45 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.5 (q, *C*H$_3$), 55.6 (q, O*C*H$_3$), 70.2 (t, Ph*C*H$_2$O), 72.9 (d, *C*H), 94.6 (t, *C*H$_2$OCH$_3$), 112.8 (s, *C*1), 113.5 (d, *C*5), 115.7 (d, *C*3), 127.5 (d, 2C, *C*2', *C*6'), 128.0 (d, *C*4'), 128.6 (d, 2C, *C*3', *C*5'), 133.3 (d, *C*6), 136.5 (s, *C*1'), 143.9 (s, *C*2), 158.4 (s, *C*4). IR ($CHCl_3$): 2978, 2933, 2878, 1593, 1573, 1467, 1372, 1290, 1228, 1172, 1151, 1100, 1033, 920, 806, 735, 697 cm^{-1}. MS (EI, 70eV): *m/z* (%) 352 (4) [M$^+$], 291 (4), 197 (5), 91 (100), 65 (8), 45 (16). HRMS for $C_{17}H_{19}BrO_3$: calcd.: 352.0497, found: 352.0497. $[\alpha]_D^{25}$ = –114.0 (c 1.13, $CHCl_3$).

(*S*)-4-Bromo-3-(1-methoxymethoxyethyl)phenol (H)

Rhodium (5% on alumina, 3.5 g) was suspended in ethanol (50 mL). The mixture was degassed and saturated with hydrogen. Then **G** (3.5 g, 10 mmol) was added and the mixture was shaken until the consumption of hydrogen had stopped. The solvent was removed in vacuo and the remaining oil purified by chromatography (silica gel (110 g), ethyl acetate:pentane 1:4) yielding **H** (1.8 g, 69%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.44 (d, *J* = 6.4 Hz, 3H, C*H*$_3$), 2.76 (s (br), 1H, OH), 3.41 (s, 3H, OC*H*$_3$), 4.60 (q, *J* = 6.6 Hz, 2H, OC*H*$_2$O), 5.05 (s, 2H, PhC*H*$_2$), 5.10 (q, *J* = 6.4 Hz, 1H, C*H*OH), 6.65 (dd, *J* = 3.1 Hz, *J* = 8.5 Hz, 1H, C5*H*), 7.04 (d, *J* = 3.0 Hz, 1H, C2*H*), 7.34 (d, *J* = 8.7 Hz, 1H, C4*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.5 (q, *C*H$_3$), 55.7 (q, O*C*H$_3$), 73.2 (d, *C*H), 94.6 (t, *C*H$_2$), 112.1 (s, *C*4), 113.9 (d, *C*6), 116.3 (d, *C*2), 133.6 (d, *C*5), 143.6 (s, *C*3), 155.8 (s, *C*1). IR ($CHCl_3$): 3355, 2977, 2932, 1595, 1576, 1470, 1434, 1373, 1288, 1171, 1101, 1036, 926, 813 cm^{-1}. MS (EI, 70eV): *m/z* (%) 260 (7) [M$^+$], 201 (83), 151 (5), 138 (7), 107 (5), 94 (54), 77 (8), 65 (19), 43 (100). HRMS for $C_{10}H_{13}BrO_3$: calcd.: 260.0048, found: 260.0044. $[\alpha]_D^{25}$ = –141.0 (c 0.98, $CHCl_3$).

(*S*)-3-(1-Methoxymethoxyethyl)-4-methoxymethylselenylphenol (5)

Compound **H** (1.13 g, 4.3 mmol) was dissolved in diethyl ether (50 mL), the solution cooled to –78 °C and *t*-butyl lithium (10 mL, 16 mmol, 1.6M in hexane) added dropwise. The reaction was allowed to warm up to room temperature, stirred for another 30 min, cooled to 0 °C and dimethoxymethyl diselenide **D** (1.2 g, 4.8 mmol) was added. After warming up to room temperature, the solution was stirred for 2 h, then extracted three times with 1M aqueous sodium hydroxide and washed with *t*-butyl methyl ether. The aqueous layer was acidified with 1M hydrochloric acid and extracted with CH_2Cl_2 and ethyl acetate. Chromatographic purification (silica gel (110 g), ethyl acetate:pentane 1:3) yielded product **5** (1.1 g, 84%) as a pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 (d, *J* = 4.8 Hz, 3H, C*H*$_3$), 3.37 (s, 3H, OC*H*$_3$), 3.39 (s, 3H, OC*H*$_3$), 4.56 (d, *J* = 2.8 Hz, 2H, OC*H*$_2$O), 5.05 (d, *J* = 6.7 Hz, 1H, SeCH*H*O), 5.13 (d, *J* = 6.7 Hz, 1H, SeC*H*HO), 5.32 (q, *J* = 6.4 Hz, 1H, C*H*), 6.65 (dd, *J* = 3.0 Hz, *J* = 8.7 Hz, 1H, C6*H*), 7.04 (d, *J* = 3.1 Hz, 1H, C2*H*), 7.50 (d, *J* = 8.4 Hz, 1H, C5*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.5 (q, *C*H$_3$), 55.5 (q, O*C*H$_3$), 57.0 (q, O*C*H$_3$), 73.5 (d, *C*H), 75.5 (t, Se*C*H$_2$), 94.3 (t, O*C*H$_2$O), 113.0 (d, *C*6), 115.6 (d, *C*2), 118.9 (s, *C*4), 137.4 (d, *C*5), 147.5 (s, *C*3), 156.7 (s, *C*1). IR ($CHCl_3$): 3354, 2974, 2930, 2821, 1594, 1572, 1470, 1447, 1371, 1279, 1217, 1179, 1082, 1026, 927, 873, 816 cm^{-1}. MS (EI, 70eV): *m/z* (%) 306 (4) [M$^+$], 230 (10), 200 (66), 120 (22), 107 (6), 91 (9), 45 (100). HRMS for $C_{12}H_{18}O_4Se$: calcd.: 306.0370, found: 306.0373. $[\alpha]_D^{25}$ = –160.9 (c 1.13, $CHCl_3$).

Mesoporous silica-supported (*S*)-3-(1-Methoxymethoxyethyl)-4-methoxymethylselenylphenol (6)

Mesoporous silica (4.2 g, 10 mL) (Trisoperl, 100 - 200 nm bead diameter, 190 m^2/g, pore size 20 nm) was stirred with 2N HCl (100 mL) at 90 °C for 14 h. After washing with distilled water (1000 mL) and then acetone (1000 mL), the beads were dried at 100 °C in high vacuo. Toluene (20 mL) and of bromopropyl trimethoxysilane (4.2 mmol, 0.8 mL) were added and the mixture was refluxed for 12 h. The mixture was filtered and the beads washed with methanol, acetone, and *t*-butyl methyl ether (200 mL each). Drying was proceeded at 80 °C under high vacuo. Elemental analysis showed a bromine content of 2.30% and a carbon content of 2.46%, which indicates an approximate loading of 0.36 mmol/g.

The functionalized mesoporous silica (2.0 g, 0.36 mmol/g loading) and dry cesium carbonate (650 mg, 2.0 mmol) were mixed under Ar. Then compound **5** (490 mg, 2.0 mmol), dissolved in dry DMF (8 mL), was added and the mixture stirred at 60 °C for 3 d. The beads were removed by filtration and washed with methanol, acetone, and *t*-butyl methyl ether (50 mL each). Drying was proceeded at 80 °C under high vacuum. The combined washing phases were acidified with 1N HCl (6 mL) and extracted three times with *t*-butyl methyl ether (3 × 50 mL), the organic phase then washed with water (2 × 50 mL). The solvent was removed under vacuo and 270 mg of **5** remained. The loading of the polymer was 0.35 mmol/g. The chemical stability of **5** was tested by stirring it with unfunctionalized mesoporous silica under the same conditions, whereby 99% of **5** was recovered.

Polystyrene-supported (*S*)-3-(1-Methoxymethoxyethyl)-4-methoxymethylselenylphenol (6)

Merrifield resin (250 mg, 2.0 mmol Br/g) was added to toluene (5 mL) and the solvent removed in vacuo to azeotropically remove traces of water from the resin. Dry cesium carbonate (200 mg, 62 mmol) was added under Ar and a solution of of **5** (190 mg, 0.72 mmol) in dry DMF (3 mL). The reaction was stirred at 60 °C for 3 d. The mixture was worked up in the same way described above for the mesoporous silica. 40 mg of **5** was recovered. The loading of the polymer was 1.3 mmol/g.

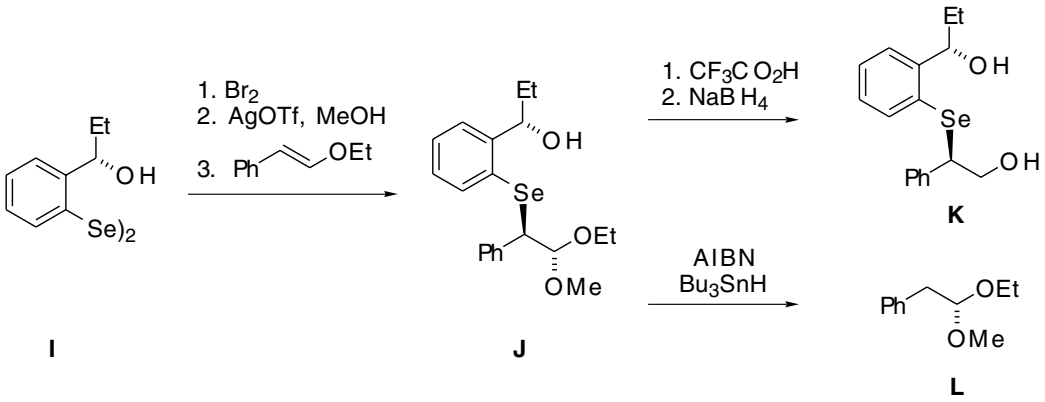
General procedure for the selenenylation of alkenes with polymer-supported selenium reagents of type **6**:

To the carefully dried polymer with a total amount of 0.2 mmol selenium reagent loading was added dry diethyl ether (5 mL); (For the reagent on Merrifield resin THF was used). The mixture was cooled to 0 °C and bromine in carbon tetrachloride (1M solution, 0.22 mL) was added dropwise. The reaction was stirred for 15 min, then the solvent filtered off and the residue washed with the solvent (2 × 5 mL). Then solvent was added (5 mL) and the reaction cooled down to the temperature mentioned in the procedure. The alkene in methanol (0.2 mL) was added and the mixture stirred for 3 d. Quenching with *sym*-collidine (0.1 mL) and water (2 mL) followed by subsequent filtration and washing with water (20 mL), methanol (50 mL), aceton (50 mL) as well as *t*-butyl methyl ether (100 mL) and drying at 50 °C in vacuo finished the work up.

General procedures for the cleavage from the solid support:

a) **Tributyltin hydride**: The dried polymer was added to dry benzene (5 mL), AIBN (10 mg), and tributyl tin hydride (5 eq.). The mixture refluxed for 3 h. 2N Sodium hydroxide solution (3 mL) was added and the reaction stirred for another 3 h at room temperature. The polymer was removed by filtration and the organic layer was separated. The solvent was carefully removed in the kugelrohr due to the volatility of some compounds. Then the remaining oil was purified by column chromatography.
b) **Allyltributyltin**: To the carefully dried polymer (0.25 g) dry benzene (3 mL) and AIBN (0.25 eq.) was added. Then allyl tributyl tin (10 eq.) was added and the mixture was refluxed for 3 h. 2N Sodium hydroxide solution (3 mL) was added and the reaction stirred for another 3 h at room temperature. The polymer was removed by filtration and the organic layer was separated. The solvent was carefully removed in the kugelrohr due to the volatility of some compounds. Then the remaining oil was purified by column chromatography.
c) **Hydrogen peroxide**: To the polymer (0.25 g) THF (3 mL) and hydrogen peroxide (10 eq.) were added and the mixture was stirred at room temperature for 3 h. The polymer was removed by filtration and the organic layer was separated.

The yields of these reactions have been determined by GC with naphthalene used as an internal standard. The GC was calibrated with the racemates of the corresponding compounds.



I **J** **K** **L**

Determination of the absolute stereochemistry of (*S*)-(2-Ethoxy-2-methoxy-ethyl)-benzene (**L**).
E-*β*-Ethoxystyrene was methoxyselenenylated with the selenium electrophile generated from diselenide **I** using the general procedure descibed in reference 5. The acetal moiety in the addition product **J** was cleaved by trifluoroacetic acid and directly reduced to the corresponding alcohol **K**. Comparison of the optical rotation and of the spectral data of **K** with a reference compound prepared previously[6] confirmed the absolute configuration of **K** and because of the unambiguous stereochemical pathway of the selenenylation reaction the absolute configuration of **L**, obtained by radical cleavage of **J**, was assigned to be (*S*).

(5) Wirth, T.; Fragale, G. *Chem. Eur. J.* **1997**, *3*, 1894–1902.
(6) Wirth, T.; Fragale, G.; Spichty, M. *J. Am. Chem. Soc.* **1998**, *120*, 3376–3381.

(*S*)-1-{[(*S*)-2-Ethoxy-2-methoxy-(*R*)-1-phenyl-ethylselenyl]-phenyl}-propanol (**J**)

^{1}H NMR (300 MHz, $CDCl_3$): δ =0.77 (t, J = 7.4 Hz, 3H, CH_2CH_3), 1.16 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.46 (s, 1H, O*H*), 1.62 (m, 2H, CH_2CH_3), 3.21 (s, 3H, OCH_3), 3.52 (dq, J = 9.3 Hz, J = 7.1 Hz, 1H, $OCHHCH_3$), 3.74 (dq, J = 9.3 Hz, J = 7.1 Hz, 1H, $OCHHCH_3$), 4.34 (d, J = 5.8 Hz, 1H, C*H*Se), 4.73 (t, J = 5.1 Hz, 1H, C*H*OH), 4.88 (d, J = 5.9 Hz, 1H, OC*H*O), 7.00-7.28 (m, 6H), 7.19 (dt, J = 6.5 Hz, J = 1.0 Hz, 1H), 7.25 (dd, J = 7.8 Hz, J = 2.4 Hz, 1H), 7.49 (dd, J = 7.0 Hz, J = 1.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.3 (q, *C*H_3), 15,0 (q, *C*H_3), 30.9 (t, *C*H_2), 52.4 (t, O*C*H_2), 54.1 (q, O*C*H_3), 63.0 (d, *C*HSe), 74.5 (d, Ar*C*HOH), 105.4 (d, O*C*HO), 126.4 (d), 127.1 (d), 127.6 (d), 128.0 (d, 2C), 128.6 (s), 128.7 (d, 2C), 128.8 (d), 137,5 (d), 139.1 (s), 148.2 (s). IR ($CHCl_3$): 3059, 3029, 2934, 2888, 1586, 1496, 1458, 1374, 1259, 1195, 1158, 1107, 1032, 919, 832, 757, 702 cm^{-1}. $[\alpha]_D^{25}$ = 99.1° (c = 1.1, $CHCl_3$).

(*S*)-1-({[(*R*)-(2-Hydroxy-1-phenyl)ethyl]seleno}phenyl)propanol (**K**)

J (20 mg, 0.05 mmol) was dissolved in chloroforme (5 mL), trifluoroacetic acid (1 mL) and water (1 mL) was added and the mixture stirred for 2 h. The aqueous layer was separated and the chloroforme removed in vacuo. The remaining oil was dissolved in dry ethanol (5 mL) and sodium borohydride (2 mg, 0.05 mmol) added at 0 °C. The mixture was allowed to warm up to room temperature and was stirred for 1 h. The solvent was removed in vacuo and the remaining oil purified by preparative TLC (silica, *t*-butyl methyl ether:petroleumether 1:2).

Yield: 5 mg (29 %); $[\alpha]_D^{25}$ = –15.2 (c 0.25, $CHCl_3$); other spectroscopic data see reference 6. From the optical rotation for **K** an diastereomeric ratio of 77:23 (*S*,*R*):(*S*,*S*) (54% *de*) was calculated. (Values for the enantiomerically pure compounds (*S*,*R*)-**K**: $[\alpha]_D^{25}$ = – 64.6; (*S*,*S*)-**K**: $[\alpha]_D^{25}$ = +150.8)[6]

(*S*)-(2-Ethoxy-2-methoxy-ethyl)-benzene (**L**)

After the radical cleavage (for the general reaction procedure see reference 5) the two enantiomers of **L** were separated by GC. Column: Macherey-Nagel, Hydrodex-β-3P, 50 m • 0.25 mm, 20 psi, 115 °C, 60 min, then heating 10 °C/min to 200 °C. R_f*(S)*: 65.7 min, R_f*(R)*: 66.1 min. Other spectroscopic data see reference 7.

(7) Kirmse, W.; Plath, P.; Schaffrodt, H. *Chem. Ber.* **1971**, *108*, 79–87.