Stereoselective Construction of *cis*-2,6-Disubstituted Tetrahydropyrans *via* the Reductive Etherification of δ -Trialkylsilyloxy Substituted Ketones: Total Synthesis of (-)-Centrolobine

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Representative Experimental Procedures and Spectra

General. The chemical shifts of the ^1H -NMR and ^{13}C -NMR spectra were all recorded relative to chloroform, benzene or tetramethylsilane. Multiplicities were determined with the aid of an APT sequence, separating methylene and quaternary carbons = e (even), from methyl and methine = o (odd). GC and HPLC analysis was carried out using an HP 5890 GC Series 2 and HP 1100 HPLC respectively. All compounds were purified using flash chromatography, and gave spectroscopic data consistent with being $\geq 95\%$ the assigned structure. Analytical t.l.c. was carried out on pre-coated 0.2 mm thick Merck 60 F₂₄₅ silica plates. Flash chromatography was carried out using Merck Silica Gel 60 (230-400 mesh).

(5*RS*)-5-(*tert*-Butyldimethylsilyloxy)-1,6-diphenylhexan-1-one (1a). IR (neat) 3086 (m), 3063 (m), 3028 (m), 2929 (s), 2857 (s), 1716 (m), 1689 (s), 1599 (m), 1582 (m), 1496 (m), 1472 (s), 1462 (s), 1449 (s), 1409 (m), 1361 (s), 1256 (s), 1180 (m), 1088 (s), 1059 (s), 1003 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.99-7.97 (m, 2H), 7.58 (t, $J = 7.4$ Hz, 1H), 7.48 (t, $J = 7.6$ Hz, 2H), 7.30 (t, $J = 7.3$ Hz, 2H), 7.24-7.20 (m, 3H), 3.92 (quin, $J = 5.9$ Hz, 1H), 2.98 (ABX₂, $J = 8.1, 1.3$ Hz, 2H), 2.79 (d, $J = 6.3$ Hz, 2H), 1.98-1.75 (m, 2H), 1.63-1.49 (m, 2H), 0.89 (s, 9H), 0.00 (s, 3H), -0.15 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 200.44 (e), 139.49 (e), 137.24 (e), 133.17 (o), 130.03 (o), 128.82 (o), 128.40 (o), 128.30 (o), 126.31 (o), 73.85 (o), 44.09 (e), 39.08 (e), 36.76 (e), 26.17 (o), 20.35 (e), 18.34 (e), -4.45 (o), -4.63 (o); HRMS (EI, $\text{M}^+ - \text{C}_4\text{H}_9$) calcd for $\text{C}_{20}\text{H}_{25}\text{O}_2\text{Si}$ 325.1624, found 325.1616.

(6*RS*)-6-(*tert*-Butyldimethylsilyloxy)-7-phenylheptan-2-one (1b). IR (neat) 3086 (m), 3064 (m), 3029 (m), 2930 (s), 2857 (s), 1718 (s), 1604 (m), 1496 (m), 1472 (s), 1463 (s), 1455 (s), 1409 (m), 1361 (s), 1255 (s), 1161 (m), 1092 (s), 1041 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.28 (t, $J =$

7.2 Hz, 2H), 7.22-7.17 (m, 3H), 3.86 (quin, $J = 5.9$ Hz, 1H), 2.75 (d, $J = 6.3$ Hz, 2H), 2.42 (ABX₂, $J = 7.4$, 0.9 Hz, 2H), 2.13 (s, 3H), 1.78-1.57 (m, 2H), 1.50-1.36 (m, 2H), 0.88 (s, 9H), -0.02 (s, 3H), -0.17 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 208.80 (e), 139.35 (e), 129.93 (o), 128.34 (o), 126.26 (o), 73.68 (o), 44.02 (e), 36.48 (e), 29.92 (o), 26.11 (o), 19.76 (e), 18.25 (e), -4.53 (o), -4.69 (o); HRMS (EI, M⁺-C₄H₉) calcd for C₁₅H₂₃O₂Si 263.1467, found 263.1458.

(7RS)-7-(tert-Butyldimethylsilyloxy)-2-methyl-8-phenyloctan-3-one (1c). IR (neat) 3086 (w), 3064 (m), 3028 (m), 2956 (s), 2930 (s), 2857 (s), 1714 (s), 1603 (m), 1496 (m), 1471 (s), 1463 (s), 1408 (m), 1383 (m), 1362 (m), 1255 (s), 1178 (m), 1087 (s), 1060 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.24 (t, $J = 7.2$ Hz, 2H), 7.18-7.13 (m, 3H), 3.81 (quin, $J = 6.0$ Hz, 1H), 2.70 (d, $J = 6.1$ Hz, 2H), 2.55 (sept, $J = 6.9$ Hz, 1H), 2.39 (ABX₂, $J = 7.3$, 2.1 Hz, 2H), 1.74-1.51 (m, 2H), 1.45-1.32 (m, 2H), 1.05 (d, $J = 6.7$ Hz, 6H), 0.83 (s, 9H), -0.06 (s, 3H), -0.21 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 214.94 (e), 139.42 (e), 129.95 (o), 128.32 (o), 126.23 (o), 73.78 (o), 44.07 (e), 40.93 (o), 40.67 (e), 36.67 (e), 26.10 (o), 19.82 (e), 18.45 (o), 18.27 (e), -4.54 (o), -4.71 (o); HRMS (EI, M⁺-H) calcd for C₂₁H₃₅O₂Si 347.2406, found 347.2404.

(2RS)-12-Bromo-2-(tert-butyldimethylsilyloxy)-1-phenyldodecan-6-one (1d). IR (neat) 3085 (w), 3063 (w), 3028 (m), 2931 (s), 2856 (s), 1715 (s), 1604 (w), 1496 (m), 1472 (m), 1462 (m), 1454 (m), 1409 (m), 1362 (m), 1255 (s), 1088 (s), 1057 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.24 (t, $J = 7.2$ Hz, 2H), 7.18-7.12 (m, 3H), 3.80 (quin, $J = 6.0$ Hz, 1H), 3.38 (t, $J = 6.9$ Hz, 2H), 2.70 (d, $J = 6.1$ Hz, 2H), 2.38-2.30 (m, 4H), 1.82 (quin, $J = 7.2$ Hz, 2H), 1.76-1.50 (m, 4H), 1.45-1.32 (m, 4H), 1.30-1.23 (m, 2H), 0.82 (s, 9H), -0.07 (s, 3H), -0.22 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 211.23 (e), 139.38 (e), 129.93 (o), 128.34 (o), 126.26 (o), 73.70 (o), 44.05 (e), 43.16 (e), 42.67 (e), 36.55 (e), 34.09 (e), 32.72 (e), 28.51 (e), 28.13 (e), 26.10 (o), 23.71 (e), 19.86 (e), 18.28 (e), -4.53 (o), -4.69 (o); HRMS (EI, M⁺-H) calcd for C₂₄H₄₀O₂Si⁷⁹Br 467.1981, found 467.1954.

(8RS)-8-(tert-Butyldimethylsilyloxy)-9-phenylnon-1-en-4-one (1e). IR (neat) 3084 (w), 3064 (w), 3028 (m), 2953 (s), 2929 (s), 2887 (s), 2857 (s), 1717 (s), 1638 (w), 1496 (m), 1472 (m), 1462 (m), 1455 (m), 1407 (m), 1361 (m), 1255 (s), 1088 (m), 1005 (m) cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 7.09 (t, $J = 7.2$ Hz, 2H), 7.04-6.99 (m, 3H), 5.78 (ddt, $J = 14.0$, 10.4, 7.0 Hz, 1H), 4.92 (dq, $J = 10.4$, 1.7, 1H), 4.85 (dq, $J = 17.9$, 1.5 Hz, 1H), 3.69 (quin, $J = 6.0$ Hz, 1H), 2.66 (d, $J = 7.0$ Hz, 2H), 2.61 (ABX, $J = 13.4$, 6.4 Hz, 1H), 2.56 (ABX, $J = 13.1$, 6.1 Hz, 1H), 1.87 (t, $J = 7.3$ Hz, 2H), 1.64-1.53

(m, 1H), 1.50-1.39 (m, 1H), 1.31-1.23 (m, 2H), 0.87 (s, 9H), -0.07 (s, 3H), -0.25 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 205.99 (e), 139.44 (e), 131.52 (o), 130.02 (o), 128.37 (o), 126.34 (o), 117.90 (e), 73.84 (o), 47.45 (e), 44.14 (e), 42.01 (e), 36.59 (e), 26.08 (o), 19.51 (e), 18.19 (e), -4.59 (o), -4.83 (o); HRMS (EI, $\text{M}^+-\text{C}_4\text{H}_9$) calcd for $\text{C}_{18}\text{H}_{29}\text{O}_2\text{Si}$ 305.1937, found 305.1934.

(7*RS*)-Ethyl 7-(*tert*-Butyldimethylsilyloxy)-3-oxo-8-phenyloctanoate (1f). IR (neat) 3086 (w), 3064 (w), 3029 (m), 2930 (s), 2857 (s), 1747 (s), 1717 (s), 1652 (m), 1605 (w), 1496 (m), 1472 (m), 1463 (m), 1455 (m), 1410 (m), 1367 (m), 1312 (m), 1256 (s), 1155 (m), 1090 (s), 1032 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.28 (t, $J = 7.2$ Hz, 2H), 7.22-7.17 (m, 3H), 4.20 (q, $J = 7.1$ Hz, 2H), 3.86 (quin, $J = 5.9$ Hz, 1H), 3.42 (s, 2H), 2.74 (d, $J = 6.4$ Hz, 2H), 2.56-2.52 (m, 2H), 1.81-1.59 (m, 2H), 1.51-1.37 (m, 2H), 1.29 (t, $J = 7.1$ Hz, 3H), 0.87 (s, 9H), -0.02 (s, 3H), -0.16 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 202.84 (e), 167.42 (e), 139.29 (e), 129.92 (o), 128.35 (o), 126.28 (o), 73.61 (o), 61.54 (e), 49.45 (e), 44.02 (e), 43.34 (e), 36.27 (e), 26.08 (o), 19.41 (e), 18.25 (e), 14.31 (o), -4.54 (o), -4.71 (o); HRMS (EI, $\text{M}^+-\text{C}_4\text{H}_9$) calcd for $\text{C}_{18}\text{H}_{27}\text{O}_4\text{Si}$ 335.1679, found 335.1662.

(6*RS*)-6-(*tert*-Butyldimethylsilyloxy)-1-hydroxy-7-phenylheptan-2-one (1g). IR (neat) 3473 (bm), 3064 (w), 3029 (m), 2953 (s), 2929 (s), 2857 (s), 1721 (s), 1604 (w), 1496 (m), 1472 (m), 1463 (m), 1455 (m), 1407 (m), 1361 (m), 1256 (s), 1090 (s), 1065 (s), 1005 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.25 (t, $J = 7.3$ Hz, 2H), 7.19-7.12 (m, 3H), 4.19 (d, $J = 4.6$ Hz, 2H), 3.82 (quin, $J = 5.9$ Hz, 1H), 3.09 (t, $J = 4.7$ Hz, OH), 2.73 (ABX, $J = 13.4, 6.4$ Hz, 1H), 2.68 (ABX, $J = 13.4, 6.4$ Hz, 1H), 2.36 (t, $J = 7.5$ Hz, 2H), 1.81-1.70 (m, 1H), 1.69-1.58 (m, 1H), 1.46-1.33 (m, 2H), 0.89 (s, 9H), -0.05 (s, 3H), -0.19 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 209.74 (e), 139.14 (e), 129.88 (o), 128.41 (o), 126.37 (o), 73.49 (o), 68.24 (e), 44.08 (e), 38.73 (e), 36.33 (e), 26.08 (o), 19.62 (e), 18.27 (e), -4.53 (o), -4.65 (o); HRMS (EI, M^++H) calcd for $\text{C}_{19}\text{H}_{33}\text{O}_3\text{Si}$ 337.2199, found 337.2204.

(6*RS*)-Benzoic acid 6-(*tert*-butyldimethylsilyloxy)-2-oxo-7-phenylheptyl ester (1h). IR (neat) 3064 (m), 3029 (m), 2929 (s), 2857 (s), 1732 (s), 1602 (m), 1585 (m), 1495 (m), 1472 (m), 1454 (m), 1416 (m), 1373 (m), 1272 (s), 1177 (m), 1096 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.15-8.13 (m, 2H), 7.63 (t, $J = 7.5$ Hz, 1H), 7.50 (t, $J = 7.7$ Hz, 2H), 7.30 (t, $J = 7.2$ Hz, 2H), 7.24-7.20 (m, 3H), 4.89 (s, 2H), 3.90 (quin, $J = 5.9$ Hz, 1H), 2.78 (d, $J = 6.2$ Hz, 2H), 2.52 (t, $J = 7.3$ Hz, 2H), 1.89-1.78 (m, 1H), 1.77-1.66 (m, 1H), 1.56-1.42 (m, 2H), 0.90 (s, 9H), 0.02 (s, 3H), -0.13 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 204.15 (e), 166.12 (e), 139.34 (e), 133.70 (o), 130.17 (o), 130.00 (o),

129.52 (e), 128.76 (o), 128.61 (o), 128.45 (o), 126.37 (o), 73.68 (o), 68.64 (e), 44.12 (e), 39.29 (e), 36.47 (e), 26.17 (o), 19.28 (e), 18.34 (e), -4.44 (o), -4.61 (o); HRMS (EI, $M^+ - C_4H_9$) calcd for $C_{22}H_{27}O_4Si$ 383.1679, found 383.1679.

(6*RS*)-1-Benzoyloxy-6-(*tert*-butyldimethylsilyloxy)-7-phenylheptan-2-one (1i). IR (neat) 3087 (w), 3064 (m), 3029 (m), 2952 (s), 2929 (s), 2886 (s), 2857 (s), 1722 (s), 1604 (w), 1586 (w), 1496 (m), 1472 (m), 1462 (m), 1455 (m), 1361 (m), 1255 (s), 1209 (m), 1098 (s), 1052 (s), 1006 (m) cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.13 (m, 10H), 4.56 (s, 2H), 4.02 (s, 2H), 3.81 (quin, $J = 6.0$ Hz, 1H), 2.70 (d, $J = 6.4$ Hz, 2H), 2.42 (t, $J = 7.5$ Hz, 2H), 1.76-1.65 (m, 1H), 1.66-1.54 (m, 1H), 1.46-1.33 (m, 2H), 0.83 (s, 9H), -0.06 (s, 3H), -0.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.77 (e), 139.35 (e), 137.45 (e), 129.92 (o), 128.72 (o), 128.34 (o), 128.20 (o), 128.08 (o), 126.26 (o), 75.21 (e), 73.64 (o), 73.57 (e), 44.02 (e), 39.34 (e), 36.53 (e), 26.08 (o), 19.27 (e), 18.25 (e), -4.53 (o), -4.68 (o); HRMS (CI, $M^+ + H$) calcd for $C_{26}H_{39}O_3Si$ 427.2668, found 427.2657.

(2*R,6*S**)-2-Benzyl-6-phenyltetrahydro-2*H*-pyran (2a).** A 10-mL round bottom flask equipped with a magnetic stir-bar was charged with (5*RS*)-5-(*tert*-butyldimethylsilyloxy)-1,6-diphenyl-hexan-1-one **1a** (80 mg, 0.20 mmol) and dissolved in acetonitrile (2 mL). At room temperature, triethylsilane (39 μ L, 0.24 mmol) and bismuth tribromide (4.6 mg, 0.01 mmol, prepared as a solution in acetonitrile at 1 mg/10 μ L) were added simultaneously via syringes. The reaction mixture was then stirred for one hour. The solvent was removed under reduced pressure to afford the crude reaction mixture, which was purified by flash chromatography (eluting with 5% ethyl acetate/hexanes) to furnish the *tetrahydropyran* **2a** (50 mg, 97%) as a colorless oil: GC analysis of the crude reaction mixture (HP-1 Methyl Siloxane capillary column) *cis:trans* $\geq 99:1$; IR (neat) 3086 (m), 3062 (m), 3028 (s), 2936 (s), 2857 (s), 1947 (w), 1874 (w), 1806 (w), 1605 (m), 1495 (s), 1454 (s), 1439 (m), 1379 (m), 1368 (m), 1336 (m), 1307 (m), 1211 (m), 1189 (m), 1079 (s), 1052 (s) cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.17 (m, 5H), 4.37 (dd, $J = 11.1, 2.0$ Hz, 1H), 3.17 (ddt, $J = 11.1, 7.6, 1.8$ Hz, 1H), 3.01 (ABX, $J = 13.6, 6.0$ Hz, 1H), 2.74 (ABX, $J = 13.6, 6.9$ Hz, 1H), 1.92-1.80 (m, 2H), 1.66-1.24 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.75 (e), 139.08 (e), 129.84 (o), 128.43 (o), 128.35 (o), 127.29 (o), 126.26 (o), 125.97 (o), 79.89 (o), 79.33 (o), 43.36 (e), 33.86 (e), 30.72 (e), 24.14 (e); HRMS (EI, $M^+ - H$) calcd for $C_{18}H_{19}O$ 251.1436, found 251.1426.

(2*R,6*R**)-2-Benzyl-6-methyltetrahydro-2*H*-pyran (2b).** GC analysis *cis:trans* ≥99:1; IR (neat) 3086 (w), 3063 (w), 3028 (m), 2970 (s), 2932 (s), 2844 (s), 1604 (w), 1497 (m), 1454 (m), 1443 (m), 1385 (m), 1369 (m), 1318 (m), 1203 (m), 1078 (s), 1054 (s) cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 7.16-7.10 (m, 4H), 7.05-7.01 (m, 1H), 3.36 (ddt, *J* = 10.7, 6.4, 2.0 Hz, 1H), 3.17 (ddq, *J* = 10.7, 6.2, 1.9 Hz, 1H), 2.92 (ABX, *J* = 13.5, 6.4 Hz, 1H), 2.57 (ABX, *J* = 13.5, 6.4 Hz, 1H), 1.52-1.47 (m, 1H), 1.30-1.26 (m, 1H), 1.24-1.16 (m, 1H), 1.14-0.96 (m, 3H), 1.10 (d, *J* = 6.2 Hz, 3H); ¹³C NMR (100 MHz, C₆D₆) δ 139.53 (e), 129.87 (o), 128.38 (o), 126.26 (o), 78.70 (o), 73.79 (o), 43.66 (e), 33.50 (e), 31.02 (e), 23.94 (e), 22.46 (o); HRMS (EI, M⁺+H) calcd for C₁₃H₁₉O 191.1436, found 191.1440.

(2*R,6*S**)-2-Benzyl-6-isopropyltetrahydro-2*H*-pyran (2c).** GC analysis *cis:trans* ≥99:1; IR (neat) 3087 (w), 3064 (w), 3028 (m), 2938 (s), 2875 (s), 2859 (s), 1605 (w), 1496 (m), 1471 (m), 1455 (m), 1439 (m), 1387 (m), 1377 (m), 1365 (m), 1080 (s), 1054 (s), 1028 (s) cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 7.14-7.09 (m, 4H), 7.03-7.00 (m, 1H), 3.33-3.28 (m, 1H), 2.83 (ABX, *J* = 13.4, 7.0 Hz, 1H), 2.79-2.75 (m, 1H), 2.53 (ABX, *J* = 13.6, 5.6 Hz, 1H), 1.63-1.51 (m, 2H), 1.31-1.24 (m, 2H), 1.18-0.96 (m, 3H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (100 MHz, C₆D₆) δ 139.52 (e), 129.84 (o), 128.23 (o), 126.15 (o), 82.72 (o), 78.71 (o), 43.48 (e), 33.65 (o), 31.48 (e), 28.28 (e), 23.99 (e), 18.78 (o), 18.60 (o); HRMS (EI, M⁺) calcd for C₁₅H₂₂O 218.1671, found 218.1673.

(2*R,6*R**)-2-Benzyl-6-(6-bromohexyl)tetrahydro-2*H*-pyran (2d).** GC analysis *cis:trans* ≥99:1; IR (neat) 3085 (w), 3062 (w), 3026 (m), 2933 (s), 2857 (s), 1604 (w), 1496 (m), 1454 (m), 1439 (m), 1371 (m), 1331 (m), 1263 (m), 1197 (m), 1080 (s), 1052 (s) cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 7.13-7.09 (m, 4H), 7.06-7.01 (m, 1H), 3.36-3.30 (m, 1H), 3.06-2.98 (m, 1H), 2.88 (t, *J* = 7.0 Hz, 2H), 2.86 (ABX, *J* = 13.4, 7.0 Hz, 1H), 2.54 (ABX, *J* = 13.4, 5.6 Hz, 1H), 1.55-0.92 (m, 16H); ¹³C NMR (100 MHz, C₆D₆) δ 139.59 (e), 129.81 (o), 128.29 (o), 126.23 (o), 78.70 (o), 77.59 (o), 43.54 (e), 36.79 (e), 33.66 (e), 32.89 (e), 31.87 (e), 31.50 (e), 28.92 (e), 28.31 (e), 25.58 (e), 23.97 (e); HRMS (CI, M⁺+H) calcd for C₁₈H₂₈O⁸¹Br 341.1303, found 341.1298.

(2*S,6*R**)-2-Allyl-6-benzyltetrahydro-2*H*-pyran (2e).** GC analysis *cis:trans* ≥99:1; IR (neat) 3064 (m), 3028 (m), 2935 (s), 2858 (s), 1642 (w), 1605 (w), 1497 (m), 1455 (m), 1439 (m), 1373 (m), 1332 (m), 1236 (w), 1196 (m), 1080 (s), 1052 (s), 1016 (m), 1002 (m) cm⁻¹; ¹H NMR (400

MHz, C₆D₆) δ 7.17-7.12 (m, 4H), 7.08-7.02 (m, 1H), 5.92-5.82 (m, 1H), 5.03-5.00 (m, 1H), 4.98 (t, J = 1.3 Hz, 1H), 3.32 (ddt, J = 10.6, 6.4, 2.0 Hz, 1H), 3.11 (ddt, J = 10.6, 6.6, 2.0 Hz, 1H), 2.89 (ABX, J = 13.6, 6.6 Hz, 1H), 2.55 (ABX, J = 13.6, 6.0 Hz, 1H), 2.34-2.26 (m, 1H), 2.13-2.06 (m, 1H), 1.57-1.42 (m, 1H), 1.32-0.94 (m, 5H); ¹³C NMR (100 MHz, C₆D₆) δ 139.44 (e), 135.68 (o), 129.87 (o), 128.29 (o), 126.24 (o), 116.30 (e), 78.70 (o), 77.33 (o), 43.46 (e), 41.44 (e), 31.18 (e), 23.71 (e); HRMS (EI, M⁺-H) calcd for C₁₅H₁₉O 215.1436, found 215.1429.

(2S*,6R*)-Ethyl (6-benzyltetrahydro-2H-pyran-2-yl)acetate (2f). Two equivalents of triethylsilane and 10 mol% bismuth tribromide were necessary for complete consumption of starting material. The reaction mixture was then stirred at room temperature overnight: GC analysis *cis:trans* $\geq$ 99:1; IR (neat) 3086 (w), 3063 (m), 3028 (m), 2980 (s), 2936 (s), 2861 (s), 1738 (s), 1605 (w), 1496 (m), 1455 (m), 1440 (m), 1372 (s), 1343 (s), 1289 (s), 1251 (s), 1186 (s), 1138 (s), 1086 (s), 1053 (s), 1037 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.25-7.14 (m, 5H), 4.04 (ABX₃, J = 7.3, 1.5 Hz, 2H), 3.73 (dddd, J = 10.4, 7.6, 5.5, 2.1 Hz, 1H), 3.51 (ddt, J = 10.7, 7.0, 1.5 Hz, 1H), 2.85 (ABX, J = 13.7, 7.0 Hz, 1H), 2.59 (ABX, J = 13.7, 6.0 Hz, 1H), 2.49 (ABX, J = 14.8, 8.1 Hz, 1H), 2.36 (ABX, J = 14.8, 5.3 Hz, 1H), 1.82-1.76 (m, 1H), 1.62-1.40 (m, 3H), 1.27-1.12 (m, 2H), 1.18 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 171.69 (e), 139.12 (e), 129.60 (o), 128.25 (o), 126.17 (o), 78.98 (o), 74.81 (o), 60.56 (e), 43.02 (e), 42.08 (e), 31.28 (e), 30.92 (e), 23.55 (e), 14.37 (o); HRMS (CI, M⁺+H) calcd for C₁₆H₂₃O₃ 263.1647, found 263.1659.

(2S*,6R*)-(6-Benzyltetrahydro-2H-pyran-2-yl)methanol (2g). Two equivalents of triethylsilane and 20 mol% bismuth tribromide were necessary for complete consumption of starting material. The reaction mixture was then stirred at room temperature for one hour: GC analysis *cis:trans* $\geq$ 99:1; IR (neat) 3436 (bs), 3085 (m), 3062 (m), 3027 (m), 2936 (s), 2859 (s), 1604 (w), 1496 (m), 1454 (m), 1440 (m), 1371 (m), 1338 (m), 1217 (m), 1196 (m), 1085 (s), 1052 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.26 (t, J = 7.5 Hz, 2H), 7.19-7.17 (m, 3H), 3.57-3.39 (m, 4H), 2.88 (ABX, J = 13.7, 7.0 Hz, 1H), 2.55 (ABX, J = 13.6, 6.3 Hz, 1H), 2.04 (dd, J = 8.5, 3.7 Hz, OH), 1.84-1.79 (m, 1H), 1.58-1.56 (m, 1H), 1.51-1.39 (m, 2H), 1.27-1.16 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 138.88 (e), 129.55 (o), 128.41 (o), 126.35 (o), 78.59 (o), 78.18 (o), 66.50 (e), 43.14 (e), 31.24 (e), 27.19 (e), 23.17 (e); HRMS (EI, M⁺+H) calcd for C₁₃H₁₉O₂ 207.1385, found 207.1390.

(2*S,6*R**)-(6-Benzyltetrahydro-2*H*-pyran-2-yl)methyl benzoate (2h).** GC analysis *cis:trans* ≥99:1; IR (neat) 3086 (m), 3062 (m), 3028 (m), 2939 (s), 2859 (s), 1722 (s), 1603 (m), 1585 (m), 1495 (m), 1452 (s), 1377 (m), 1315 (s), 1272 (s), 1201 (m), 1176 (m), 1086 (s), 1053 (s), 1028 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.05-8.03 (m, 2H), 7.59 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.28-7.16 (m, 5H), 4.35 (ABX, *J* = 11.5, 4.2 Hz, 1H), 4.30 (ABX, *J* = 11.4, 6.8 Hz, 1H), 3.72 (dddd, *J* = 11.3, 6.6, 4.2, 2.1 Hz, 1H), 3.58 (dddd, *J* = 10.9, 7.3, 5.8, 1.9 Hz, 1H), 2.95 (ABX, *J* = 13.7, 7.1 Hz, 1H), 2.68 (ABX, *J* = 13.8, 5.8 Hz, 1H), 1.93-1.88 (m, 1H), 1.68-1.48 (m, 3H), 1.41-1.26 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 166.79 (e), 139.24 (e), 133.12 (o), 130.53 (e), 129.98 (o), 129.68 (o), 128.54 (o), 128.32 (o), 126.20 (o), 78.90 (o), 75.77 (o), 67.93 (e), 43.00 (e), 31.15 (e), 27.88 (e), 23.34 (e); HRMS (EI, M⁺+H) calcd for C₂₀H₂₃O₃ 311.1647, found 311.1641.

(2*R,6*S**)-2-Benzyl-6-(benzyloxy)methyl-tetrahydro-2*H*-pyran (2i).** GC analysis *cis:trans* ≥99:1; IR (neat) 3086 (m), 3062 (m), 3028 (m), 2935 (s), 2858 (s), 1604 (w), 1496 (m), 1454 (s), 1440 (m), 1368 (m), 1313 (m), 1198 (m), 1079 (s), 1053 (s), 1029 (m) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.39-7.19 (m, 10H), 4.61 (AB, *J* = 12.2 Hz, 1H), 4.56 (AB, *J* = 12.2 Hz, 1H), 3.64-3.54 (m, 2H), 3.53 (ABX, *J* = 10.1, 6.1 Hz, 1H), 3.46 (ABX, *J* = 10.1, 4.2 Hz, 1H), 3.02 (ABX, *J* = 13.4, 6.0 Hz, 1H), 2.68 (ABX, *J* = 13.4 Hz, 7.2 Hz, 1H), 1.88-1.81 (m, 1H), 1.61-1.41 (m, 3H), 1.34-1.19 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 139.11 (e), 138.78 (e), 129.77 (o), 128.58 (o), 128.41 (o), 127.96 (o), 127.75 (o), 126.29 (o), 78.96 (o), 77.61 (o), 74.01 (e), 73.60 (e), 43.27 (e), 31.00 (e), 28.32 (e), 23.42 (e); HRMS (EI, M⁺) calcd for C₂₀H₂₄O₂ 296.1776, found 296.1779.

(3*S*)-1-(*tert*-Butyldimethylsilyloxy)-4-(3-triethylsilyloxyhex-5-en-1-yl)benzene (6). A 100-mL flame-dried round bottom flask equipped with a magnetic stir-bar and rubber septum was charged with (*R*)-BINOL (360 mg, 1.27 mmol) and anhydrous dichloromethane (13 mL). The suspension was stirred until the binaphthol was completely dissolved and powered 4Å molecular sieves (5.1 g) were added. Titanium tetrakisopropoxide (0.4 mL, 1.27 mmol) was then added by syringe at ambient temperature, and the resulting orange-red suspension was heated at gentle reflux for *ca.* 1 hour. The red-brown mixture was cooled to ambient temperature and a dichloromethane (6 mL) solution of 3-[4-(*tert*-butyldimethylsilyloxy)phenyl]propionaldehyde **5** (3.36 g, 12.7 mmol) was injected via syringe. The resulting mixture was stirred for *ca.* 5 minutes at ambient temperature and cooled to -78 °C. Allyltributyltin (4.7 mL, 15.2 mmol) was then added to the reaction mixture via syringe, and the resulting reaction mixture kept in a freezer at -20 °C for ≥96 hours without stirring.

The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate solution (16 mL), diluted with dichloromethane (16 mL), and stirred at ambient temperature for two hours. The molecular sieves were removed by filtration through a pad of Celite, and the aqueous layer was extracted with dichloromethane. The combined organic extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo* to afford a crude oil. Purification by flash chromatography (eluting with 5%-10% ethyl acetate/hexanes) furnished the *allyl alcohol* (3.04 g, 78%) as a colorless oil: $[\alpha]_{\text{D}}^{23}$ -11.0 ($c = 1.73$, CHCl_3); Chiral HPLC analysis of corresponding ester with (*S*)-(+)-Mosher's acid chloride (Diacel[®] OD column): 95% *ee*; IR (neat) 3361 (bs), 3077 (m), 3029 (m), 3002 (m), 2931 (s), 2859 (s), 1641 (m), 1610 (s), 1511 (s), 1472 (s), 1463 (s), 1415 (m), 1391 (m), 1362 (m), 1259 (s), 1169 (m), 1054 (m), 1006 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.03 (d, $J = 8.5$ Hz, 2H), 6.74 (d, $J = 8.2$ Hz, 2H), 5.85-5.74 (m, 1H), 5.14-5.10 (m, 2H), 3.64 (tt, $J = 7.6, 4.9$ Hz, 1H), 2.75-2.68 (m, 1H), 2.63-2.56 (m, 1H), 2.32-2.26 (m, 1H), 2.19-2.12 (m, 1H), 1.76-1.70 (m, 2H), 1.65 (s, OH), 0.96 (s, 9H), 0.16 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 153.86 (e), 134.90 (o), 134.84 (e), 129.44 (o), 120.12 (o), 118.46 (e), 70.14 (o), 42.26 (e), 38.81 (e), 31.42 (e), 25.90 (o), 18.39 (e), -4.22 (o); HRMS (EI, M^+) calcd for $\text{C}_{18}\text{H}_{30}\text{O}_2\text{Si}$ 306.2015, found 306.2025.

A 100-mL flame-dried round bottom flask equipped with a magnetic stir-bar was charged with (3*S*)-1-[4-(*tert*-butyldimethylsilyloxy)phenyl]hex-5-en-3-ol (666 mg, 2.17 mmol) obtained above and dissolved in anhydrous dichloromethane (20 mL) and cooled with stirring to 0 °C under an atmosphere of argon. 2,6-Lutidine (0.5 mL, 4.34 mmol) was added, followed by the dropwise addition of triethylsilyl trifluoromethanesulfonate (0.73 mL, 3.26 mmol). The reaction mixture was then allowed to warm up to room temperature slowly and stirred overnight. The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate solution, and extracted with dichloromethane. The combined organic extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford a crude oil. Purification by flash chromatography (eluting with 2-5% ethyl acetate/hexanes) furnished the *silyl ether* **6** (910 mg, 99%) as a colorless oil: $[\alpha]_{\text{D}}^{23}$ -3.0 ($c = 1.44$, CHCl_3); IR (neat) 3077 (w), 3028 (w), 2955 (s), 2934 (s), 2878 (s), 2860 (s), 1641 (w), 1610 (m), 1510 (s), 1472 (m), 1463 (m), 1415 (m), 1362 (m), 1255 (s), 1169 (m), 1072 (s), 1006 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.04 (d, $J = 8.5$ Hz, 2H), 6.77 (d, $J = 8.5$ Hz, 2H), 5.85 (ddt, $J = 14.3, 10.4, 7.3$ Hz, 1H), 5.10-5.05 (m, 2H), 3.77 (quin, $J = 5.9$ Hz, 1H), 2.67 (ABXY, $J = 13.7, 10.4, 6.1$ Hz, 1H), 2.56 (ABXY, $J = 13.7, 10.4, 6.1$ Hz, 1H), 2.29 (t, $J = 6.6$ Hz, 2H), 1.83-1.68 (m, 2H), 1.00 (s, 9H), 1.00 (t, $J = 7.9$ Hz, 9H), 0.63 (q, $J = 7.9$ Hz, 6H), 0.20 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3)

δ 153.79 (e), 135.36 (e), 135.32 (o), 129.32 (o), 120.07 (o), 117.01 (e), 71.75 (o), 42.20 (e), 39.02 (e), 31.15 (e), 25.93 (o), 18.41 (e), 7.15 (o), 5.36 (e), -4.24 (o); HRMS (EI, M^+) calcd for $C_{24}H_{44}O_2Si_2$ 420.2880, found 420.2862.

(5*R*)-7-[4-(*tert*-Butyldimethylsilyloxy)phenyl]-1-(4-methoxyphenyl)-5-triethylsilyloxyheptan-1-one (7). A 50-mL flame-dried round bottom flask equipped with a magnetic stir-bar and reflux condenser was charged with (3*S*)-1-(*tert*-butyldimethylsilyloxy)-4-(3-triethylsilyloxyhex-5-en-1-yl)benzene **6** (311 mg, 0.74 mmol), 1-(4-methoxyphenyl)propenone (240 mg, 1.48 mmol) and anhydrous dichloromethane (8 mL) under an atmosphere of argon, and degassed for 5 minutes. Second generation Grubbs' catalyst (63 mg, 0.074 mmol) was added in a single portion resulting in an orange solution, which was heated at 40 °C for *ca.* 12 hours (t.l.c. control). The reaction mixture was then allowed to cool to room temperature, and the mixture concentrated *in vacuo* to afford dark brown oil. Purification by flash chromatography (eluting with 5-10% ethyl acetate/hexanes) furnished the α,β -unsaturated ketone (320 mg, 78%) as a colorless oil: *E/Z* $\geq$ 19:1 (by 1H NMR); $[\alpha]_D^{23} +3.7$ ($c = 1.30$, $CHCl_3$); IR (neat) 3005 (w), 2955 (m), 2935 (m), 2877 (m), 2859 (m), 1667 (m), 1600 (s), 1575 (m), 1510 (s), 1463 (m), 1420 (m), 1308 (m), 1259 (s), 1171 (s), 1111 (m), 1079 (m), 1031 (m), 1013 (m) cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, $J = 8.9$ Hz, 2H), 7.06-6.98 (m, 1H), 6.99 (d, $J = 7.9$ Hz, 2H), 6.92 (d, $J = 8.8$ Hz, 2H), 6.92-6.87 (m, 1H), 6.72 (d, $J = 8.2$ Hz, 2H), 3.87 (quin, $J = 5.8$ Hz, 1H), 3.85 (s, 3H), 2.67-2.60 (m, 1H), 2.57-2.43 (m, 3H), 1.82-1.68 (m, 2H), 0.95 (s, 9H), 0.93 (t, $J = 7.9$ Hz, 9H), 0.58 (q, $J = 7.9$ Hz, 6H), 0.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.92 (e), 163.56 (e), 153.90 (e), 145.25 (o), 134.95 (e), 131.08 (o), 130.97 (e), 129.39 (o), 127.81 (o), 120.20 (o), 114.00 (o), 71.18 (o), 55.70 (o), 41.18 (e), 39.57 (e), 31.20 (e), 25.96 (o), 18.44 (e), 7.21 (o), 5.29 (e), -4.19 (o); HRMS (EI, M^+) calcd for $C_{32}H_{50}O_4Si_2$ 554.3248, found 554.3259.

A 50-mL flame-dried round bottom flask equipped with a magnetic stir-bar was charged with (2*E*, 5*S*)-7-[4-(*tert*-butyldimethylsilyloxy)phenyl]-1-(4-methoxyphenyl)-5-triethylsilyloxyhept-2-en-1-one (264 mg, 0.48 mmol) obtained above and dissolved in anhydrous benzene (18 mL) under an atmosphere of argon, and degassed for 5 minutes. Wilkinson's catalyst (88 mg, 0.095 mmol) was added in a single portion. The reaction mixture was stirred at ambient temperature under an atmosphere of hydrogen for *ca.* 4 hours, then concentrated *in vacuo* to afford dark oil. Purification by flash chromatography (eluting with 5% ethyl acetate/hexanes) furnished the *aryl ketone* **7** (252

mg, 95%) as a colorless oil: $[\alpha]_D^{23} +9.5$ ($c = 1.05$, CHCl_3); IR (neat) 3057 (m), 3028 (m), 3003 (m), 2955 (s), 1682 (s), 1602 (s), 1577 (m), 1511 (s), 1463 (m), 1417 (m), 1362 (m), 1308 (m), 1258 (s), 1170 (s), 1084 (m), 1034 (m), 1008 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.94 (d, $J = 8.9$ Hz, 2H), 7.02 (d, $J = 8.3$ Hz, 2H), 6.93 (d, $J = 8.9$ Hz, 2H), 6.74 (d, $J = 8.3$ Hz, 2H), 3.87 (s, 3H), 3.74 (quin, $J = 5.7$ Hz, 1H), 2.92 (t, $J = 7.3$ Hz, 2H), 2.62 (ABXY, $J = 13.8, 10.1, 6.6$ Hz, 1H), 2.54 (ABXY, $J = 13.8, 10.1, 5.9$ Hz, 1H), 1.87-1.68 (m, 4H), 1.64-1.50 (m, 2H), 0.98 (s, 9H), 0.96 (t, $J = 7.9$ Hz, 9H), 0.60 (q, $J = 7.9$ Hz, 6H), 0.18 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 199.06 (e), 163.54 (e), 153.73 (e), 135.36 (e), 130.51 (o), 130.34 (e), 129.32 (o), 120.07 (o), 113.87 (o), 71.93 (o), 55.64 (o), 39.31 (e), 38.58 (e), 36.90 (e), 31.10 (e), 25.91 (o), 20.67 (e), 18.39 (e), 7.21 (o), 5.32 (e), -4.24 (o); HRMS (EI, $\text{M}^+ - \text{C}_2\text{H}_5$) calcd for $\text{C}_{30}\text{H}_{47}\text{O}_4\text{Si}_2$ 527.3013, found 527.3011.

(-)-Centrolobine (4). A 10-mL round bottom flask equipped with a magnetic stir-bar was charged with (5*R*)-7-[4-(*tert*-butyldimethylsilyloxy)phenyl]-1-(4-methoxyphenyl)-5-triethylsilyloxyheptan-1-one **7** (78.7 mg, 0.141 mmol) and dissolved in acetonitrile (1.4 mL) at room temperature. Triethylsilane (32 μL , 0.197 mmol) and bismuth tribromide (6.3 mg, 0.0141 mmol, prepared as a solution in acetonitrile at 1 mg/10 μL) were added simultaneously via syringes, and the resulting reaction mixture stirred at ambient temperature for *ca.* 1 hour. Tetrabutylammonium fluoride (*ca.* 100 μL , 1M in THF) was added, and after *ca.* 10 minutes the solvent was removed under reduced pressure to afford the crude reaction mixture. Purification by flash chromatography (eluting with 10-20% ethyl acetate/hexanes) furnished (-)-*centrolobine* **4** (41.0 mg, 93%) as a colorless solid: $[\alpha]_D^{23} -90.3$ ($c = 0.88$, CHCl_3); Chiral HPLC analysis (Diacel[®] AD column): 93% *ee*; IR (neat) 3391 (bs), 3012 (m), 2935 (s), 2857 (s), 1614 (s), 1515 (s), 1455 (s), 1442 (s), 1367 (m), 1304 (m), 1247 (s), 1176 (s), 1078 (s), 1036 (s) cm^{-1} ; ^1H NMR (400 MHz, acetone- d_6) δ 8.07 (s, OH), 7.31 (d, $J = 8.6$ Hz, 2H), 7.02 (d, $J = 8.5$ Hz, 2H), 6.88 (d, $J = 8.7$ Hz, 2H), 6.74 (d, $J = 8.5$ Hz, 2H), 4.30 (dd, $J = 11.2, 1.8$ Hz, 1H), 3.78 (s, 3H), 3.46-3.40 (m, 1H), 2.72-2.57 (m, 2H), 1.92-1.60 (m, 6H), 1.46-1.36 (m, 1H), 1.34-1.23 (m, 1H); ^{13}C NMR (100 MHz, acetone- d_6) δ 160.42 (e), 156.99 (e), 137.86 (e), 134.72 (e), 130.88 (o), 128.52 (o), 116.66 (o), 114.93 (o), 80.53 (o), 78.42 (o), 56.19 (o), 40.25 (e), 35.42 (e), 32.84 (e), 32.21 (e), 25.50 (e); HRMS (CI, M^+) calcd for $\text{C}_{20}\text{H}_{24}\text{O}_3$ 312.1725, found 312.1733.

H_bH_a