Enantio- and Diastereoselective Tandem Zn-promoted Brook Rearrengement/Ene-Allene Carbocyclization Reaction

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Supporting Information

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General comments

All reactions involving air- and moisture- sensitive compounds were carried out under argon atmosphere, using flamed flask and dry, oxygen-free solvents. Diethyl ether, tetrahydrofuran and toluene were distilled under argon from sodium benzophenone ketyl. All Grignard reagents were prepared and titrated under argon atmosphere by 1M solution of 2-isobutanol in toluene, using 2,2'-biquinoline as indicator. Unless otherwise noted, commercially available materials were used without further purification. Flash chromatography (FC) was performed using silica gel 60 (230-400 mesh). Thin layer chromatography was performed using precoated plates (silica gel 60, 0.25mm). All NMR spectra were recorded at room temperature with a Bruker-Avance-300, and Bruker-Avance-500 MHz instruments at operating frequencies 300/500 MHz (^{1}H) or 75/125 MHz (^{13}C) respectively. Chemical shifts are referenced to the residual proton or carbon resonance of the deuteriated solvent (chloroform δ = 7.24 for ^{1}H NMR or δ = 77.00 for proton decoupled ^{13}C NMR, and (*J*) in Hz). Optical rotation was measured at 25 ^{o}C on a Optical Activity LTD polarimeter. The enantiomeric ratios, expressed at er, were determined by HPLC (Chiral column Chiralcel AD-H), analysis as specified in the individual experimental description and verified using the appropriate racemic mixtures. The absolute configurations of the **4a** and **5a** were determined by comparison of experimentally measured and calculated CD. All other absolute configurations were assigned by analogy.

Acylsilanes were prepared from literature procedures[1].

1-(Dimethyl(phenyl)silyl)-hex-5-en-1-one **2a**, ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.52 (s, 6H), 1.60 (dquint, J_1 =7.2 Hz, J_2 =1.2 Hz, 2H), 1.97 (dq, J_1 =7.4 Hz, J_2 = 0.9 Hz, 2H), 2.61 (dt, J_1 =0.9 Hz, J_2 = 7.2 Hz, 2H), 4.91-4.97 (m, 2H), 5.65-5.75 (m, 1H), 7.35-7.42 (m, 3H), 7.57-7.59 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm): -4.9, 21.0, 32.9, 47.7, 114.8, 128.0, 129.7, 132.8, 133.8, 137.9, 245.8; FTIR (thin film): 912, 998, 1026, 1062, 1114, 1253, 1428, 1642, 2939, 2958, 3071 cm^{-1}.

1-Trimethylsilyl-hex-5-en-1-one **2d**, ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm): 0.16 (s, 9H), 1.59 (quint, J =7.5 Hz, 2H), 1.99 (q, J =7.0 Hz, 2H), 2.57 (t, J =7.2 Hz, 2H), 4.91-4.98 (m, 2H), 5.69-5.74 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm): -3.2, 21.1, 33.2, 47.5, 115.0, 138.1, 248.3; FTIR (thin film): 912, 997, 1079, 1091, 1162, 1249, 1351, 1411, 1443, 1642, 2856, 2927, 2956 cm^{-1}.

3-(tert-Butyl(dimethyl)silyl)-1-phenyloct-(7-en)-1-yn-3-ol **2c**, ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm): 0.09 (s, 9H), 0.84 (s, 9H), 1.52 (quint, J = 7.5 Hz, 2H), 1.93 (q, J = 5.1 Hz, 2H), 2.51 (t, 2H), 4.84-4.91 (m, 2H), 5.62-5.68 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): -7.2, 16.3, 20.7, 26.2, 33.0, 49., 114.8, 138.0, 246.7; FTIR (thin film) : 912, 998, 1251, 1363, 1405, 1467, 1641, 2859, 2887, 2898, 2931, 2952 cm^{-1}.

1-(Methyl(diphenyl)silyl)-hex-5-en-1-one **2b**, ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.69 (s, 3H), 1.52 (quint, J = 7.2 Hz, 2H), 1.84 (q, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 2H), 2.60 (dt, J_1 =3.4 Hz, J_2 = 7.1 Hz, 2H), 4.78-4.84 (m, 2H), 5.52-5.57 (m, 1H), 7.26-7.29 (m, 6H), 7.51-7.54 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm):-5.6, 20.9, 32.7, 48.5, 114.7, 127.9, 129.8, 129.8, 134.7, 137.7, 243.6; FTIR (thin film): 913, 997, 1112, 1253, 1429, 1642, 2931, 3050, 3071 cm^{-1}.

1-Trimethylsilyl-hex-(6-trimethylsilyl)-5-yn-1-one **10**, ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.03 (s, 9H), 0.09 (s, 9H), 1.60 (quint, J = 6 Hz, 2H), 2.11 (t, J = 6 Hz, 2H), 2.64 (t, J = 6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): -3.4, -3.3, 0.0, 19.0, 20.7, 46.4, 85.0, 106.4, 247.2; (thin film) : 911, 1044, 1248, 1351, 1407, 1430, 1645, 2173, 2900, 2957 cm^{-1}.

General procedure for the preparation of enantiomerically enriched α-hydroxypropargylsilane derivatives 4 (Table 1 and Scheme 4).

To a flame-dried round bottom flask charged with alkyne (1 mmol) in toluene (2 mL) was added diethylzinc (1 mmol, 1.5 M in toluene). The solution was first stirred at room temperature for 1 h, and then ligand **3** (0.1 mmol) was added in toluene (1 mL). After stirring for additional 1 h, acylsilane (0.5 mmol) dissolved in toluene (1 mL) was added at room temperature. The yellow solution was stirred until complete consumption of acylsilane (8 to 12 h, followed by TLC analysis with a 10% EtOAc/hexane eluent) at room temperature. The reaction was then quenched at room temperature with a saturated aqueous solution of NH_4Cl and extracted with Et_2O (3x10 mL). The organic solution was washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered and concentrated to give the unpurified propargyl silane. The product was purified by flash chromatography (5% EtOAc/hexanes).

General Procedure for the preparation of racemic α-hydroxypropargylsilane derivatives.

To a cold (0°C) stirred solution of terminal alkyne (1 mmol) in THF was added dropwise a solution of EtMgBr in Et_2O (1 equiv., 1N solution in Et_2O). After stirring at room temperature for 1 h, the resulting solution was cooled to –78 °C and acylsilane (0.8 mmol) in THF was added slowly over a period of 30 minutes. This solution was allowed to slowly warm to room temperature. After reaction is completed as determined by TLC analysis (eluent: 10% EtOAc/hexane), the reaction mixture was cooled to 0 °C, then quenched with an aqueous saturated solution of NH_4Cl. The mixture was diluted with Et_2O and the resulting layers were separated. The aqueous layer was extracted with Et_2O (3x10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. Purification was performed by column chromatography on silica gel using EtOAc/hexane (10/1) as eluent.

(R)-3-(Dimethyl(phenyl)silyl)-1-phenyl-oct-7-en-1-yn-3-ol, **4a** is prepared according to the general procedure using 1-(dimethyl(phenyl)silyl)-hex-5-en-1-one (116 mg, 0.5 mmol), phenylacetylene (0.11 mL, 1 mmol), $ZnEt_2$ (0.7 mL, 1 mmol), and ligand **3a** (36.5 mg, 0.1 mmol) to afford 157.8 mg (94%) of **4a** as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.52 (s, 6H), 1.67-1.75 (m, 4H), 1.99 (br s, 1H), 2.08-2.10 (m, 2H), 4.93-5.05 (m, 2H), 5.81-5.83 (m, 1H), 7.30-7.32 (m, 3H), 7.38-7.41 (m,

5H), 7.69-7.71 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm):-5.9, -5.6, 23.1, 33.8, 36.9, 64.8, 88.1, 91.8, 114.5, 123.3, 127.7, 127.9, 128.2, 129.6, 131.4, 134.7, 135.2, 138.6; $[\alpha]_D^{25}$ = +23.1 (CH_2Cl_2, c = 0.9, er = 86:14). Enantiomeric ratio was measured by chiral HPLC (Chiralcel AD-H, 5% IPA/Hexanes, Rt_1 = 5.70, Rt_2 = 14.40).

Racemic 3-(dimethyl(phenyl)silyl)-1-phenyl-oct-7-en-1-yn-3-ol, **4a** is prepared according to the general procedure using 1-(dimethyl(phenyl)silyl)-hex-5-en-1-one (116 mg, 0.5 mmol), phenylacetylene (0.06 mL, 0.55 mmol), EtMgBr (0.55 mL, 0.55 mmol) to afford 107.4mg (64%) of expected product as a colorless oil.

(R)-3-(methyl(diphenyl)silyl)-1-phenyl-oct-7-en-1-yn-3-ol, **4b** is prepared according to the general procedure using 1-(methyl(diphenyl)silyl)-hex-5-en-1-one (146 mg, 0.5 mmol), phenylacetylene (0.11 mL, 1 mmol), $ZnEt_2$ (0.7 mL, 1 mmol), and ligand **3a** (36.5 mg, 0.1 mmol) to afford 154.5 mg (78%) of **4b** as a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.75 (s, 3H), 1.54 (br s, 1H), 1.71-1.82 (m, 4H), 2.00-2.05 (m, 2H), 4.88-4.99 (m, 2H), 5.72-5.81 (m, 1H), 7.28-7.40 (m, 11H), 7.76-7.77 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm): -6.2, 23.0, 33.8, 37.3, 64.9, 88.9, 92.0, 114.5, 123.2, 127.8, 127.8, 128.1, 128.2, 129.7, 129.8, 131.4, 133.6, 133.9, 135.6, 135.6, 138.6; $[\alpha]_D^{25}$ = +28.0 (CH_2Cl_2, c = 1, er = 88:12). Enantiomeric ratio was measured by chiral HPLC (Chiralcel AD-H, 5% IPA/Hexanes, Rt_1 = 7.78, Rt_2 = 28.41).

(R)-3-(tert-Butyl(dimethyl)silyl)-1-phenyloct-7-en-1-yn-3-ol, **4c** is prepared according to the general procedure using 1-(*tert*-butyl (dimethyl)silyl)-hex-5-en-1-one (106 mg, 0.5 mmol), phenylacetylene (0.11 mL, 1 mmol), $ZnEt_2$ (0.7 mL, 1 mmol), and ligand **3a** (36.5 mg, 0.1 mmol) to afford 86.4 mg (55%) of **4c** as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.13 (s, 3H), 0.14 (s, 3H), 1.05 (s, 9H), 1.63 (s, 1H), 1.71-1.81 (m, 4H), 2.11-2.14 (m, 2H), 4.94-5.06 (m, 2H), 5.79-5.88 (m, 1H), 7.27-7.29 (m, 3H), 7.36-7.37 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) : -7.6, -7.3, 1.0, 22.7, 27.8, 33.9, 38.0, 65.4, 87.9, 92.7, 114.6, 123.5, 127.9, 128.3, 131.3, 138.7; $[\alpha]_D^{25}$ = 0.0 (CH_2Cl_2, c = 1.1, er = 53:47). Enantiomeric ratio was measured by chiral HPLC (Chiralcel AD-H, 5% IPA/Hexanes, Rt_1 = 6.64, Rt_2 = 8.81).

(R)-3-Trimethylsilyl-1-phenyl-oct-7-en-1-yn-3-ol, **4d** is prepared according to the general procedure using 1-trimethysilyl-hex-5-en-1-one (85 mg, 0.5 mmol),

phenylacetylene (0.11 mL, 1 mmol), $ZnEt_2$ (0.7 mL, 1 mmol), and ligand **3a** (36.5 mg, 0.1 mmol) to afford 130.2 mg (96%) of **4d** as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.17 (s, 9H), 1.67-1.75 (m, 4H), 2.12-2.14 (m, 2H), 4.94-5.06 (m, 2H), 5.79-5.88 (m, 1H), 7.27-7.29 (m, 3H), 7.37-7.40 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): -4.2, 23.1, 33.9, 36.8, 64.9, 87.6, 91.8, 114.6, 123.4, 127.9, 128.2, 131.5, 138.6; $[\alpha]_D^{25}$ = +13.6 (CH_2Cl_2, c = 0.9, er = 76:24). Enantiomeric ratio was measured by chiral HPLC (Chiralcel AD-H, 3% IPA/Hexanes, Rt_1 = 8.12, Rt_2 = 14.02).

(R)-3-(Dimethyl(phenyl)silyl)-1-phenyl-oct-7-en-1-yn-3-ol, **4e** is prepared according to the general procedure using 1-(dimethyl(phenyl)silyl)-hex-5-en-1-one (116 mg, 0.5 mmol), 1-octyne (0.13 mL, 1 mmol), $ZnEt_2$ (0.7 mL, 1 mmol), and ligand **3a** (36.5 mg, 0.1 mmol) to afford 136.9 mg (80%) of **4e** as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.40 (s, 6H), 0.88 (t, *J*= Hz, 3H), 1.23-2.23 (m, H), 2.00- (m, 2H), 2.21 (t, *J*=6 Hz, 2H), 4.88-4.99 (m, 2H), 5.70-5.81 (m, 1H), 7.34-7.67 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ(ppm): -5.8, -5.6, 14.1, 19.0, 22.6, 28.6, 28.9, 29.7, 31.4, 33.9, 37.1, 60.1, 82.3, 88.7, 114.4, 127.6, 129.4, 130.9, 134.7, 138.8; $[\alpha]_D^{25}$ = +23.1 (CH_2Cl_2, c = 0.9, er = 86:14). Enantiomeric ratio was measured by chiral HPLC (Chiralcel AD-H, 5% IPA/Hexanes, Rt_1 = 5.70, Rt_2 = 14.40).

(R)-3-(Dimethyl(phenyl)silyl)-1-trimethylsilyl-oct-7-en-1- yn-3-ol, **4f** is prepared according to the general procedure using 1-(dimethyl(phenyl)silyl)-hex-5-en-1-one (116 mg, 0.5 mmol), trimethylsilyl acetylene (0.14 mL, 1 mmol), $ZnEt_2$ (0.7 mL, 1 mmol), and ligand **3a** (36.5 mg, 0.1 mmol) to afford 142 mg (87%) of **4f** as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.16 (s, 9H), 0.42 (s, 6H), 1.52-1.65 (m, 4H), 2.02-2.04 (m, 2H), 4.89-5.01 (m, 2H), 5.72-5.82 (m, 1H), 7.34-7.38 (m, 3H), 7.61-7.64 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): -6.0,-5.8, 0.0, 22.9, 33.8, 36.6, 65.2, 92.6, 108.5, 114.5, 127.7, 129.6, 134.8, 135.2, 138.7; $[\alpha]_D^{25}$ = +21.7 (CH_2Cl_2, c = 1, er = 67:33). Enantiomeric ratio was measured by chiral HPLC (Chiralcel AD-H, 3% IPA/Hexanes, Rt_1 = 5.15, Rt_2 = 7.98).

*(S)-3-Trimethylsilyl-1-phenyl-oct-7-yn-8-trimethylsilyl-1-yn-3-ol***,** **11** is prepared according to general procedure using 1-trimethylsilyl-hex-(6-trimethylsilyl)-5-yn-1-one (120 mg, 0.5 mmol), phenylacetylene (0.11 mL, 1 mmol), $ZnEt_2$ (0.7 mL, 1 mmol), and ligand **3a**[2] (36.5 mg, 0.1 mmol) to afford 161.7 mg (80%) of **11** as a

colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm): 0.13 (s, 9H), 0.14 (s, 9H), 1.66 (br s, 1H), 1.80-1.88 (m, 4H), 2.32 (dt, J_1=6.6 Hz, J_2=1.5 Hz, 2H), 7.27-7.29 (m, 3H), 7.37-7.39 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm): -4.2, 0.1, 20.0, 23.2, 36.4, 64.7, 85.0, 87.7, 91.6, 107.2, 123.3, 127.9, 128.2, 131.5; $[\alpha]_D^{25}$ = -21.0 (CH_2Cl_2, c = 1, er = 23:77). Enantiomeric ratio was measured by chiral HPLC (Chiralcel AD-H, 5% IPA/Hexanes, Rt_1 = 4.49, Rt_2 = 5.21).

General procedure for the enantioselective carbocyclization from chiral α-hydroxypropargylsilane derivatives (Scheme 2).

To a flame-dried round bottom flask charged with α-hydroxypropargylsilane **4d** (1 eq) in tetrahydrofuran (5 mL) was added diethylzinc (1.05 eq, 1M in toluene). The reaction mixture was stirred at +40 ^{o}C for 24 h. The reaction was then quenched with an aqueous saturated solution of NH_4Cl and extracted with Et_2O (3x10 mL). The solution was washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered and concentrated to give the unpurified propargyl silane, which was further desilylated

General procedure for desilylation

To a solution of the corresponding silyl ether (1 mmol) in THF (3 mL) at room temperature was added Bu_4NF (1.05 eq., 1M solution in THF). When the reaction was over, the crude mixture was concentrated under reduced pressure. Then, brine was added and the aqueous phase was extracted 5 times with Et_2O. The combined organic phases were washed once with brine and dried over $MgSO_4$ and purified by column chromatography (5% EtOAc/hexanes) to give cyclic products **5a** as a colorless liquid.

General procedure for the enantioselective tandem Zn-Brook rearrangement/Zn-ene-allene carbocyclization reaction (Table 2).

To a flame-dried round bottom flask charged with alkyne (1 mmol) in toluene (2 mL) was added diethylzinc (1 mmol, 1.5 M in toluene). The solution was first stirred at room temperature for 1 h, and then ligand **3** (0.1 mmol) was added in toluene (1 mL). After stirring for additional 1 h, acylsilane (0.5 mmol) dissolved in toluene (1 mL) was added at room temperature. The yellow solution was stirred until complete consumption of acylsilane (8 to 12 h, followed by TLC analysis with a 10% EtOAc/hexane eluent) at room temperature. Then, THF (5 times volume of toluene) was added and the reaction mixture was stirred at +40^{o}C for 24 h. The reaction was then quenched with an aqueous saturated solution of NH_4Cl and extracted with Et_2O

(3x10 mL). The solution was washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered and concentrated to give the unpurified cyclic product, which was further desilylated as described below.

General procedure for desilylation

To a solution of the corresponding silyl ether (1 mmol) in THF (3 mL) at room temperature was added Bu_4NF (1.05 eq., 1M solution in THF). When the reaction was over, the crude mixture was concentrated under reduced pressure. Then, brine was added and the aqueous phase was extracted 5 times with Et_2O. The combined organic phases were washed once with brine and dried over $MgSO_4$ and purified by column chromatography (5% EtOAc/hexanes) to give cyclic products **5a,d** as a colorless liquid.

(R,R)-Cyclopentanol, 2-methyl-1-(phenylethynyl)-, trans, **5a** is prepared according to the general procedure using 1-(dimethyl(phenyl)silyl)-hex-5-en-1-one (116 mg, 0.5 mmol), phenyl acetylene (0.11 mL, 1 mmol), $ZnEt_2$ (0.7 mL, 1 mmol), ligand **3a** (36.5 mg, 0.1 mmol). After purification by column chromatography, 92.1 mg (92%) of product **5a** was obtained as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.10 (d, J = 6.6 Hz, 3H), 1.40-1.43 (m, 1H), 1.56 (br s, 1H), 1.73-1.78 (m, 2H), 1.96-2.16 (m, 4H), 7.27–7.43 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm): 16.5, 20.6, 31.2, 40.9, 46.1, 78.9, 85.9, 90.6, 122.9, 128.2, 128.2, 131.6; $[\alpha]_D^{25}$ = +8.4 (CH_2Cl_2, c = 1, er = 81:19). Enantiomeric ratio was measured by chiral HPLC (Chiralcel AD-H, 5% IPA/Hexanes, Rt_1 = 13.35, Rt_2 = 14.04).

(R,R)-Cyclopentanol, 2-iodomethyl-1-(1-octynyl), trans, **5b** is prepared according to the general procedure using 1-(dimethyl(phenyl)silyl)-hex-5-en-1-one (116 mg, 0.5 mmol), 1-octyne (0.15 mL, 1 mmol), $ZnEt_2$ (0.7 mL, 1 mmol), ligand **3a** (36.5 mg, 0.1 mmol). After purification by column chromatography, 94.8 mg (91%) of product **5b** was obtained as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.87 (t, *J* = 6.8 Hz, 3H), 1.01 (d, *J* = 6.6 Hz, 3H), 1.23-1.27 (m, 4H), 1.31-1.39 (m, 2H), 1.41-1.48 (m, 2H), 1.51-1.57 (m, 2H), 1.62-1.70 (m, 2H), 1.82-1.97 (m, 3H), 1.99-2.04 (m, 1H), 2.20 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 14.0, 16.3, 18.7, 20.4, 22.5, 28.4, 28.7, 30.9, 31.3, 40.9, 45.6, 68.1, 78.5, 86.4 ; $[\alpha]_D^{25}$ = + 4.2 (CH_2Cl_2, c = 0.8). Both enantiomers were not separated by chiral HPLC on chiracel AD-H

column. The enantiomeric ratio was deduced from the reaction with iodine (formation of **5c**).

(R,R)-Cyclopentanol, 2-iodomethyl-1-(1-octynyl), trans, **5c** is prepared according to the general procedure using 1-(dimethyl(phenyl)silyl)-hex-5-en-1-one (116 mg, 0.5 mmol), 1-octyne (0.15 mL, 1 mmol), $ZnEt_2$ (0.7 mL, 1 mmol), ligand **3a** (36.5 mg, 0.1 mmol), and I_2 (6 equiv) was added at -30°C in 10 ml of THF. The reaction was warmed to room temperature, stirred for an additional 2 hours before the hydrolysis and further treatment are done as usual to afford 108.6 mg (65%) of **5c** as a yellow liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.88 (t, *J* = 6.8 Hz, 3H), 1.23-1.31 (m, 5H), 1.34-1.40 (m, 3H), 1.47-1.55 (m, 2H), 1.65-1.70 (m, 2H), 1.92-1.96 (m, 1H), 2.08-2.12 (m, 2H), 2.20 (t, *J* = 7.1 Hz, 2H), 2.28-2.30 (m, 1H), 3.08 (t, *J* = 9.3 Hz, 1H) ,3.45 (dd, J_1 = 9.5 Hz, J_2 = 5.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm): 7.6, 14.1, 18.7, 19.7, 22.6, 28.5, 28.6, 31.2, 31.3, 42.5, 53.1, 77.6, 80.0, 87.0; $[\alpha]_D^{25}$ = +8.0 (CH_2Cl_2, c = 0.8, er = 74:26[3]). Enantiomeric ratio was measured by chiral HPLC (Chiralcel AD-H, 4% IPA/Hexanes, Rt_1 = 14.90, Rt_2 = 15.37).

(R,R)-Silane, trimethyl[[(cis-1-(trimethylsilylethynyl)-2-methyl-cyclopentyl]oxy], **5d** is prepared according to the general procedure using 1-(dimethyl(phenyl)silyl)-hex-5-en-1-one (116 mg, 0.5 mmol), trimethylsilyl acetylene (0.14 mL, 1 mmol), $ZnEt_2$ (0.7 mL, 1 mmol), and ligand **3a** (36.5 mg, 0.1 mmol) to afford 85.3 mg (87%) of **5d** as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.15 (s, 9H), 1.11 (d, J = 6.6 Hz, 3H), 1.30-1.32 (m, 1H), 1.67-1.71 (m, 2H), 1.87-2.00 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 0.0, 16.5, 20.6, 31.1, 40.8, 45.8, 78.7, 90.1, 107.3; $[\alpha]_D^{25}$ = +12.4 (CH_2Cl_2, c = 1, er = 61:39). Enantiomeric ratio was measured by chiral HPLC (Chiralcel AD-H, 3% IPA/Hexanes, Rt_1 = 8.91, Rt_2 = 10.09). In this case, the two enantiomers were only partially separated.

(S)-Cyclopentanol, 2(E)-[(phenyl)-methylidene]-1-(phenylethynyl), **12** is prepared according to general procedure using silane, trimethyl(1-oxo-6-trimethylsilyl-5-hexynyl) (120 mg, 0.5 mmol), phenyl acetylene (0.11 mL, 1 mmol), $ZnEt_2$ (0.7 mL, 1 mmol), ligand **3a**[2] (36.5 mg, 0.1 mmol).). After purification by column chromatography, 105.0 mg (79%) of product **12** was obtained as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.13 (s, 9H), 1.84-1.95 (m, 4H), 2.04-2.13 (m,

2H), 2.46-2.49 (m, 1H), 2.56-2.57 (m, 1H), 6.02 (t, J = 2.4 Hz, 1H), 7.28– 7.30 (m, 3H), 7.42-7.43 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): -0.7, 22.0, 29.8, 41.4, 76.7, 84.7, 91.2, 121.6, 122.8, 128.2, 131.7, 163.3; $[\alpha]_D^{25}$ = -24.7 (CH_2Cl_2, c = 1, er = 23:77). Enantiomeric ratio was measured by chiral HPLC (Chiralcel AD-H, 3% IPA/Hexanes, Rt_1 = 12.73, Rt_2 = 14.44).

Computational details

Gaussian 03 suite of programs[3] was used for the computational work. All the systems under study underwent full geometry optimization and analytical frequencies calculations to ensure real minima (N_{imag}=0) at the B3LYP/6-311G* theoretical level. TD-DFT calculations were carried out at B3LYP/AUG-cc-pVDZ level with twenty singlet transitions in CH_2Cl_2 using PCM model. The R (velocity), oscillator strength and λ_{max} derived from the TD-DFT were used to simulate the CD and electronic spectra respectively. The spectra are simulated as a sum of Gaussians assuming 20 nm line-width (equation 1, where L is the line, i=20, R_i is the oscillator strength for the electronic spectra or velocity for the CD spectra of the i'st absorption, $\Delta\lambda$=20 nm and λ_i is the i'st λ_{max}).

$$(1)\ L=\Sigma_i(R_i EXP-(\ (\lambda-\lambda_i)^2/(\Delta\lambda)^2)$$

The simulated electronic spectra were compared to the experimental one, affording the correction for λ (that's it, the wavelength deviation of the computed *vs* the experimental electronic spectra), which was applied in the comparison of the computed *vs* the experimental CD spectra.

In the model structure of **4a** the pentenyl moiety was replaced by the ethyl to save the computational time (Figure S1).

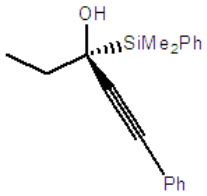

Figure S1. Model structure of the experimentally obtained alkynol **4a**

Three rotamers around the Si-C(OH) bond of the model structure, each representing a minimum on the potential surface, were identified and calculated for the *S* enantiomer. Figure S2 represents their energy differences (ΔH at B3LYP/6-311G*) and percentage equilibrium composition according to Bolzman equation at RT.

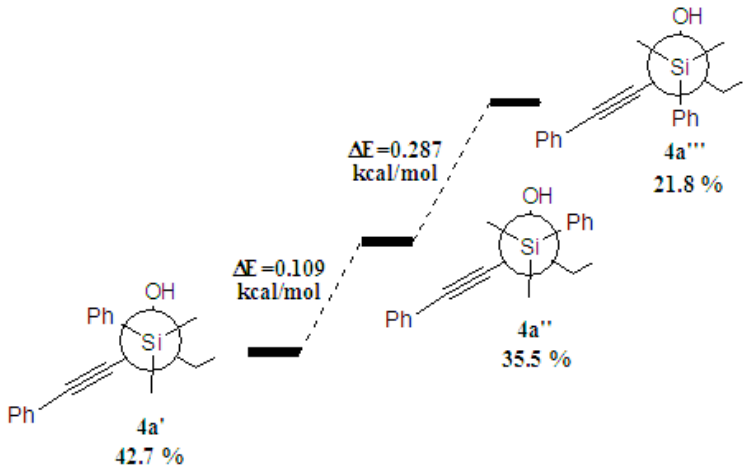

Figure S2. Three rotamers of the model structure of **4a** (***S*** enantiomer), their relative energies and percentage composition

The calculated CD spectra of the three rotamers, shown in Figure S3, look rather different. Hence, the population weighted calculated CD spectrum was built according to percentage contribution of each spectrum and compared to the experimental CD of **4a** (23 nm correction was applied to superimpose both spectra, Figure S4).

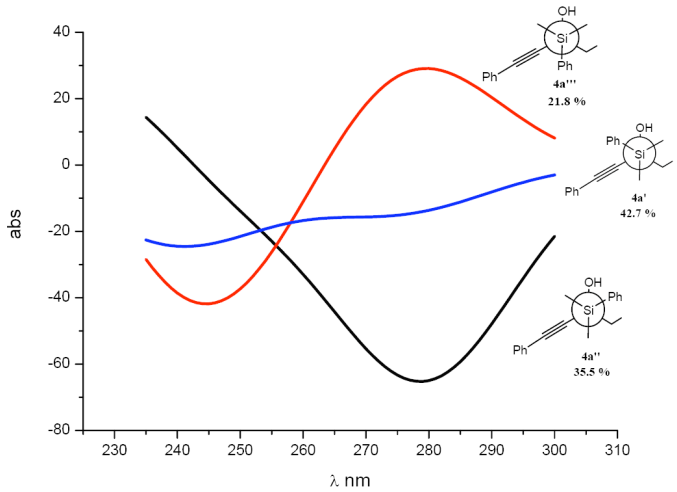

Figure S3. CD spectra of the three rotamers of ***S*** enantiomer of **4a** (model structure)

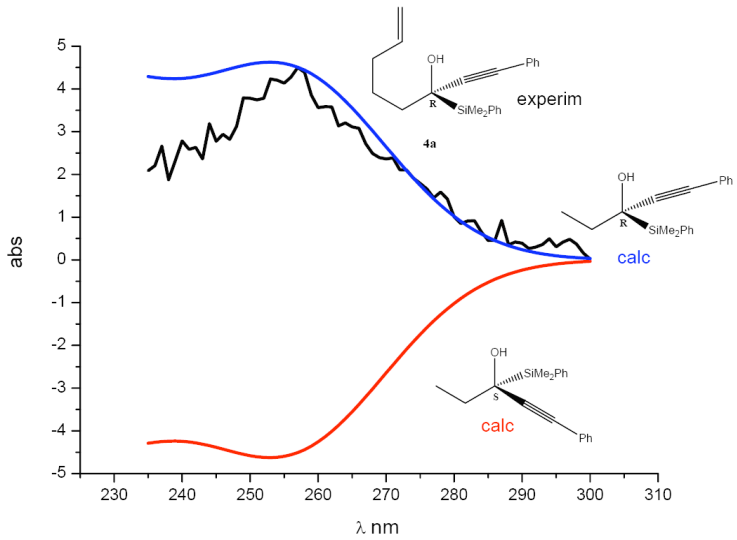

Figure S4. CD spectra of **4a**: black line - experimental; red line - computed ***S*** enantiomer of the model structure (population weighted spectra of three rotamers); blue line - computed ***R*** enantiomer of the model structure (idem)

It can be clearly deduced from the above, that the experimental alkynol **4a** has an ***R*** configuration. Figure S5 represents the computed *vs* the experimental UV spectra of **4a** after applying 23 nm correction.

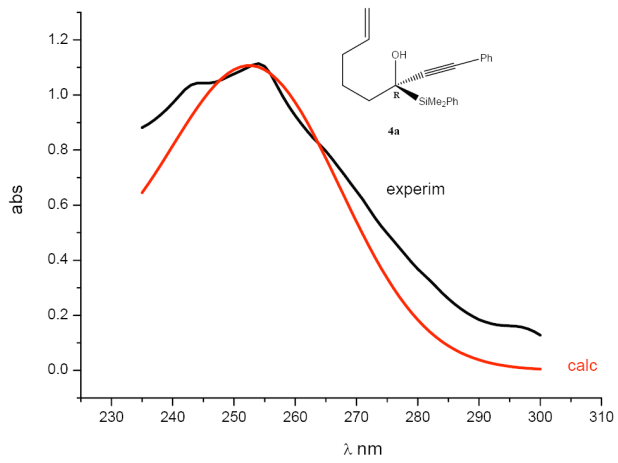

Figure S5. UV spectra of **4a**: black line - experimental; red line - computed (model structure)

The cyclic alkynol **5a** was studied in the similar way. Figure S6 represents the calculated *vs* the experimentally obtained CD spectra of **5a** (15 nm correction was applied to superimpose both spectra). Thus, the absolute configuration of the cyclic alkynol **5a** can be defined as **(1*R*, 2*R*)**. Computed and experimental UV spectra of **5a** after 15 nm correction is shown on Figure S7.

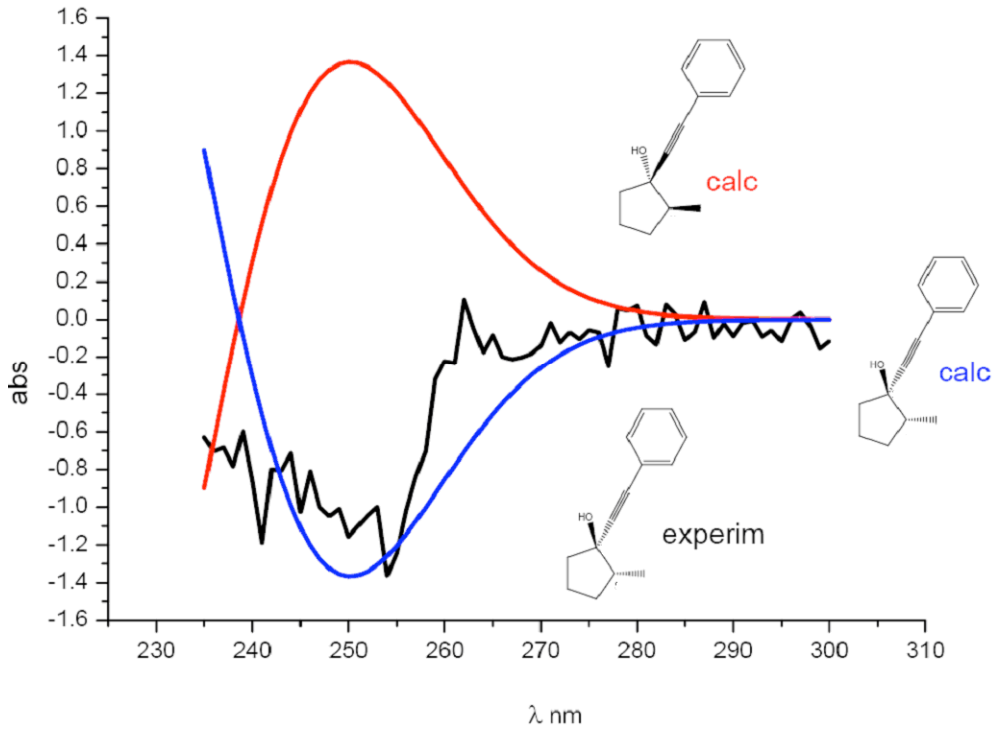

Figure S6. CD spectra of **5a**: black line - experimental; red line - computed **(1*S*, 2*S*)** enantiomer; blue line - computed **(1*R*, 2*R*)** enantiomer

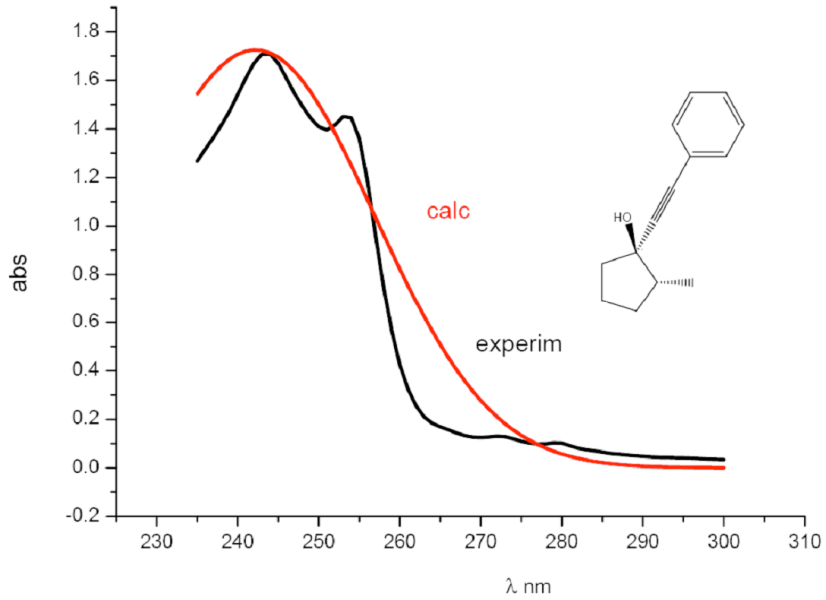

Figure S7. UV spectra of **5a**: black line - experimental; red line - computed

Optimized geometries of the computed molecules (B3LYP/6-311g*, Cartesian coordinates):

Rotamer 4a', S enantiomer

Atom	X	Y	Z
6	0.476528	-0.601192	0.626168
8	0.482057	-0.599224	2.078695
1	1.403533	-0.611086	2.372120
6	1.101140	-1.932427	0.143308
6	1.171840	-2.148670	-1.368838
1	0.538795	-2.742824	0.614033
1	2.117396	-1.975755	0.559976
1	1.733019	-3.059180	-1.594265
1	0.179665	-2.264958	-1.810402
1	1.670753	-1.317291	-1.872776
6	1.218538	0.550872	0.121401
6	1.817611	1.517080	-0.293966
14	-1.426985	-0.358592	0.233672
6	-2.329471	-1.968310	0.649038
6	-3.157451	-2.610139	-0.285975
6	-2.216847	-2.548523	1.926126
6	-3.847527	-3.778462	0.035945
1	-3.272822	-2.195638	-1.283279
6	-2.902520	-3.716410	2.250829
1	-1.572691	-2.087463	2.667919
6	-3.721534	-4.333808	1.306464
1	-4.482909	-4.253702	-0.705448
1	-2.798295	-4.145996	3.242745
1	-4.257675	-5.243219	1.560122
6	-1.697300	0.110856	-1.573459
1	-2.744040	0.381433	-1.744706
1	-1.092402	0.984756	-1.829547
1	-1.441722	-0.681460	-2.280074
6	-2.029183	1.047100	1.330609
1	-3.094102	1.238126	1.166976
1	-1.883242	0.816151	2.387112
1	-1.485165	1.971291	1.115706
6	2.524572	2.660748	-0.770943
6	2.667402	3.801579	0.039017
6	3.090673	2.671168	-2.058133

6	3.356896	4.914894	-0.426977
1	2.232950	3.801950	1.032581
6	3.775628	3.789938	-2.517998
1	2.986768	1.795491	-2.689321
6	3.912561	4.914825	-1.705796
1	3.459446	5.787424	0.210285
1	4.205761	3.783209	-3.514436
1	4.448976	5.786108	-2.067210

Rotamer 4a'', S enantiomer

Atom	X	Y	Z
6	0.80497	-1.51109	-0.78558
8	1.37873	-0.99895	-2.02308
1	1.27045	-0.03926	-2.02829
6	0.83901	-3.04184	-0.97638
6	0.27263	-3.87614	0.17175
1	1.87666	-3.32365	-1.17791
1	0.2842	-3.24796	-1.89773
1	0.25921	-4.93407	-0.10254
1	0.86681	-3.78761	1.0849
1	-0.75214	-3.58354	0.41336
6	-0.55634	-1.01792	-0.60454
6	-1.66503	-0.5672	-0.42459
14	1.95018	-0.82345	0.64136
6	2.12509	1.03151	0.29544
6	3.11614	1.5233	-0.57244
6	1.2545	1.96809	0.8794
6	3.23361	2.88561	-0.84469
1	3.81234	0.83551	-1.04311
6	1.36828	3.33107	0.61254
1	0.47354	1.63267	1.55501
6	2.35908	3.79321	-0.2516
1	4.01022	3.23784	-1.51681
1	0.68507	4.03285	1.08135
1	2.45014	4.85469	-0.46003
6	3.63421	-1.66026	0.50677
1	4.36578	-1.16918	1.15529
1	3.58481	-2.71064	0.80775
1	4.02153	-1.63114	-0.51455
6	1.21919	-1.06647	2.36447
1	1.77132	-0.47572	3.1018
1	0.17066	-0.76215	2.41179
1	1.26887	-2.11109	2.68124
6	-2.96965	-0.02607	-0.22281
6	-3.1905	1.35957	-0.32009
6	-4.05825	-0.86379	0.0776
6	-4.46174	1.88634	-0.12346
1	-2.35619	2.0121	-0.55269
6	-5.3255	-0.32863	0.27761
1	-3.89812	-1.93386	0.14992
6	-5.53317	1.04641	0.17736
1	-4.61682	2.95752	-0.20452
1	-6.15559	-0.98823	0.50963
1	-6.52426	1.46064	0.33132

Rotamer 4a''', S enantiomer

Atom	X	Y	Z
6	0.668458	-1.799891	0.525482
8	0.661815	-3.163491	0.023075
1	-0.073988	-3.631398	0.440635
6	1.119209	-1.831825	2.006585
6	1.132613	-0.493955	2.747955
1	2.108103	-2.298765	2.037064
1	0.443095	-2.524738	2.526452
1	1.416649	-0.645075	3.793004
1	1.839235	0.213422	2.310673
1	0.146560	-0.023824	2.736070
6	-0.658113	-1.209118	0.383587
6	-1.760751	-0.727852	0.251370
14	1.919726	-0.972832	-0.731983
6	2.148428	0.878166	-0.407200
6	1.100851	1.790266	-0.626708
6	3.378757	1.398620	0.026943
6	1.271870	3.155780	-0.413011
1	0.132911	1.432271	-0.963719
6	3.557018	2.765021	0.239279
1	4.217495	0.731465	0.202343
6	2.501810	3.647189	0.021285
1	0.444957	3.837489	-0.587783
1	4.519988	3.139842	0.573013
1	2.637164	4.711775	0.185732
6	1.207797	-1.229762	-2.455115
1	1.892024	-0.851437	-3.220352
1	1.035044	-2.291911	-2.641664
1	0.253667	-0.711305	-2.579684
6	3.564565	-1.876239	-0.551724
1	4.283952	-1.541070	-1.305023
1	4.025173	-1.734964	0.429808
1	3.412458	-2.949204	-0.690148
6	-3.059865	-0.162275	0.085003
6	-3.556523	0.779919	1.003353
6	-3.868275	-0.535271	-1.003886
6	-4.821448	1.330783	0.833521
1	-2.940361	1.072968	1.846169
6	-5.133540	0.017418	-1.164288
1	-3.492827	-1.260948	-1.716931
6	-5.615024	0.952097	-0.248535
1	-5.190196	2.057613	1.550259
1	-5.746021	-0.281550	-2.008940
1	-6.602799	1.382500	-0.377195

Cyclic alkynol 5a (1*S*, 2*R*):

Atom	X	Y	Z
6	-3.901406	0.795277	-1.131961
6	-3.963014	1.044080	0.401435
6	-2.505770	0.951429	0.906806
6	-1.910333	-0.130796	-0.033468
6	-2.482215	0.246995	-1.421268
1	-4.670924	0.084186	-1.437756
1	-4.081444	1.712628	-1.697747
1	-4.565105	0.271166	0.880396
1	-4.413408	2.009071	0.648910
1	-1.847963	1.005009	-1.888004

1	-2.478514	-0.621657	-2.085098
6	-0.450919	-0.245937	-0.017890
6	0.751264	-0.366575	-0.015950
6	2.170890	-0.516009	-0.000347
6	2.847733	-0.778388	1.203737
6	2.917885	-0.404339	-1.185940
6	4.229996	-0.924750	1.217363
1	2.277239	-0.866182	2.121678
6	4.300083	-0.551167	-1.164405
1	2.402630	-0.201706	-2.118390
6	4.960819	-0.811794	0.035360
1	4.739029	-1.127556	2.154168
1	4.863982	-0.462156	-2.087426
1	6.039838	-0.926373	0.049162
6	-1.773792	2.294371	0.840817
1	-0.722554	2.197194	1.120530
1	-1.812145	2.736229	-0.159628
1	-2.239599	3.006250	1.527695
1	-2.461831	0.565291	1.928577
8	-2.505667	-1.364286	0.418054
1	-2.131220	-2.081486	-0.107233

References and notes

1 a) Reich, H. J.; Olson, R. E.; Clark, M. C. *J. Am. Chem. Soc.* **1980**, *102*, 1423 b) Hammaecher, C.; Ouzzane, I.; Portella, C.; Bouillon, J-P. *Tetrahedron* **2005**, *61*, 657 c) Janlowski, P.; Plesniak, K.; Wicha, J. *Org. Lett.* **2003**, *5*, 2789 d) Unger, R.; Cohen, T.; Marek, I. *Org. Lett.,* **2005**, **7**, 5313.

2 In this example, the opposite enantiomer of ligand **3a** was used.

3 Gaussian 03, Revision C.02. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Wallingford CT, 2004.