

Supporting Information

Regulation of Stereoselectivity Using Lewis Acid in the Cyclization of Allenic Aldehydes Catalyzed by Palladium Complex

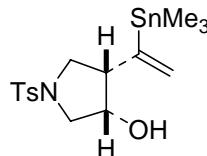
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Department of Chemistry and Institute of Basic sciences

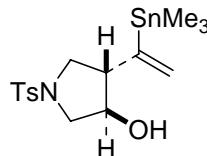
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General: All reactions were run in flame dried glassware under an atmosphere of nitrogen or argon. Tetrahydrofuran (THF) was dried by refluxing over sodium/benzophenone ketyl until a permanent purple coloration was presented, and distilled prior to use. Dichloromethane (CH_2Cl_2) was distilled from CaH_2 prior to use. All liquid reagents purchased from the Aldrich were distilled properly prior to use, unless otherwise indicated. Purification was conducted by flash column chromatography on silica gel (230-400 mesh), eluting with a mixture of hexane and ethyl acetate, unless otherwise stated. All reactions were monitored by thin layer chromatography carried out on Merck silica gel plate (60 F₂₅₄) using UV light as visualizing agent and ethanolic anisaldehyde solution and heat as developing agent. Silica gel 60 (TA792685, 230-400 mesh) from Merck was used for column chromatography. The reported yields are for chromatographically pure isolated products. FT-IR spectra were recorded on a Nicolet 320. ^1H NMR spectra were recorded on a Varian Unity Inova at 500 MHz in CDCl_3 as a solvent with TMS or residual chloroform as the internal standard. ^{13}C NMR spectra were measured on a Varian Unity Inova at 125 MHz in CDCl_3 as a solvent. All x-ray data were collected with a Siemens P4 diffractometer equipped with a Mo X-ray tube at our departmental X-ray facility.

General Procedure for Condition A, (3*S,4*S**)-1-(*p*-Toluenesulfonyl)-4-{1-(trimethylstannylyl)vinyl}pyrrolidin-3-ol (2a).** A flame-dried Schlenk flask containing allene-aldehyde **1a** (50 mg, 0.188 mmol) was charged with dry CH₂Cl₂ (1 mL) followed by (π -allyl)₂PdCl₂ (0.7 mg, 0.7 mL, 1.9 x 10⁻³ mmol, freshly prepared 1 mg/mL solution in CH₂Cl₂). The resulting mixture was cooled to -20 °C. To this mixture was added dropwise hexamethyldistannane (75 mg, 0.23 mmol) in CH₂Cl₂ (1 mL) over 10 min along the wall of the flask while keeping the temperature below -20 °C. After stirring for 30 min at -20 °C, aqueous NaHCO₃ (5 mL) was added to the reaction mixture, and then diluted with CH₂Cl₂ (10 mL). The aqueous layer was extracted with CH₂Cl₂ (ca 20 mL). After drying the combined organic solution over anhydrous Na₂SO₄, the solvents were removed under reduced pressure. Fresh column chromatography (3:1, hexanes:EtOAc) afforded **2a** (73.6 mg, 0.17 mmol, 91%) as a colorless liquid. R_f 0.53 (hexane:EtOAc = 2:1). IR (neat) 3481, 3025, 2954, 1453, 728 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 0.11 (s, 9H), 1.42 (d, 1H, J = 2.8 Hz), 2.43 (s, 3H), 2.93 (dddt, 1H, J = 1.7, 3.4, 9.4, 10.7 Hz), 3.28 (dd, 1H, J = 9.6, 8.7 Hz), 3.40 (d, 1H, J = 11.2 Hz), 3.49 (dd, 1H, J = 9.6, 8.7 Hz), 3.54 (dd, 1H, J = 3.4, 11.2 Hz), 4.17 (ddd, 1H, J = 3.4, 3.4, 3.4 Hz), 5.44 (dd, 1H, J = 1.7, 1.7 Hz), 5.74 (dd, 1H, J = 1.7, 1.7 Hz), 7.34 (d, 2H, J = 8.4 Hz), 7.75 (d, 2H, J = 8.4 Hz). ¹³C NMR (125 MHz, CDCl₃): δ -8.3, 21.8, 49.0, 53.5, 56.5, 72.1, 127.8, 129.0, 129.3, 134.3, 143.7, 149.9. Anal. Calcd for C₁₆H₂₅NO₃SSn: C, 44.68; H, 5.86; N, 3.26; S, 7.45. Found: C, 44.31; H, 5.92; N, 3.11; S, 7.41.

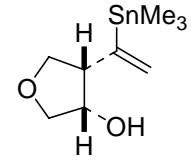


General Procedure for Condition B, (3*R,4*S**)-1-(*p*-Toluenesulfonyl)-4-{1-(trimethylstannylyl)vinyl}pyrrolidin-3-ol (3a).** A flame-dried Schlenk flask containing tris(pentafluorophenyl)borane, B(C₆F₅)₃ (19.4 mg, 0.038 mmol) was charged with dry CH₂Cl₂ (1 mL) followed by (π -allyl)₂PdCl₂ (1.4 mg, 1.4 mL, 3.8 x 10⁻³ mmol, freshly prepared 1 mg/mL solution in CH₂Cl₂). The resulting mixture was cooled to -78 °C in a dry ice-acetone bath. To this mixture was added dropwise a mixture of **1a** (50 mg, 0.188 mmol) and hexamethyldistannane (75 mg, 0.23 mmol) in CH₂Cl₂ (1.5 mL) with gas-tight syringe via a syringe pump over 40 min along the wall of the flask while keeping the temperature below -78 °C. After stirring for 20 min at -78 °C, aqueous NaHCO₃ (5 mL) was added to the reaction mixture, and then diluted with CH₂Cl₂ (10 mL). The aqueous layer was extracted with CH₂Cl₂ (ca 10 mL). After drying the combined organic solution dried over anhydrous Na₂SO₄, the solvents were removed under reduced pressure. Fresh column

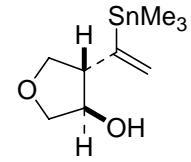


chromatography (3:1, hexanes:EtOAc) afforded **3a** (65.5 mg, 0.152 mmol, 81%) as a colorless liquid. R_f 0.45 (hexane:EtOAc = 2:1). IR (neat) 3493, 3022, 2955, 1453, 1267, 737 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 0.12 (s, 9H), 1.82 (d, 1H, J = 4.5 Hz), 2.43 (s, 3H), 2.75 (q, 1H, J = 7.9), 3.09 (dd, 1H, J = 1.1, 10.1 Hz), 3.10 (d, 1H, J = 10.5 Hz), 3.52 (dd, 1H, J = 7.9, 10.2 Hz), 3.62 (dd, 1H, J = 6.7, 10.9 Hz), 3.92 (ddd, 1H, J = 6.6, 6.6, 10.9 Hz), 5.28 (dd, 1H, J = 1.7, 1.7 Hz), 5.70 (dd, 1H, J = 1.7, 1.7 Hz), 7.34 (d, 2H, J = 7.9 Hz), 7.72 (d, 2H, J = 7.9 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ -8.4, 21.8, 51.1, 53.9, 56.8, 74.5, 127.9, 127.9, 130.0, 133.7, 143.9, 152.0. Anal. Calcd for $\text{C}_{16}\text{H}_{25}\text{NO}_3\text{SSn}$: C, 44.68; H, 5.86; N, 3.26; S, 7.45. Found: C, 44.43; H, 5.74; N, 3.31; S, 7.37.

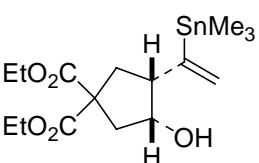
(3*S,4*S**)-4-{1-(Trimethylstannylyl)vinyl}-tetrahydrofuran-3-ol (2b).** R_f 0.53 (hexanes : EtOAc, 2 : 1). IR (neat) 3501, 3032, 2967, 1367, 1107 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 0.19 (s, 9H), 1.63 (d, 1H, J = 3.9 Hz), 3.09 (m, 1H), 3.89 (m, 3H), 4.00 (dd, 1H, J = 3.7, 9.8 Hz), 4.28 (ddd, 1H, J = 4.2, 4.2, 4.2 Hz), 5.51 (dd, 1H, J = 1.7, 1.7 Hz), 5.84 (dd, 1H, J = 1.7, 1.7 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ -8.3, 54.5, 69.7, 73.2, 76.2, 129.2, 150.4. Anal. Calcd for $\text{C}_9\text{H}_{18}\text{O}_2\text{Sn}$: C, 39.03; H, 6.55. Found: C, 38.91; H, 6.35.



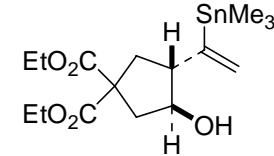
(3*R,4*S**)-4-{1-(Trimethylstannylyl)vinyl}-tetrahydrofuran-3-ol (3b).** R_f 0.44 (hexanes : EtOAc = 2 : 1). IR (neat) 3510, 3022, 2943, 1456, 1258, 1123 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 0.19 (s, 9H), 1.77 (d, 1H, J = 5.1 Hz), 2.97 (dd, 1H, J = 6.7, 11.2 Hz), 3.68 (d, 1H, J = 11.2), 3.69 (d, 1H, J = 8.7 Hz), 4.02 (dd, 1H, J = 5.2, 8.7 Hz), 4.10 (dd, 1H, J = 6.7, 8.4 Hz), 4.21 (ddd, 1H, J = 5.2, 5.2, 10.1 Hz), 5.32 (dd, 1H, J = 1.7, 1.7 Hz), 5.82 (dd, 1H, J = 1.7, 1.7 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ -8.5, 59.3, 72.1, 74.6, 77.0, 126.7, 153.2. Anal. Calcd for $\text{C}_9\text{H}_{18}\text{O}_2\text{Sn}$: C, 39.03; H, 6.55. Found: C, 39.11; H, 6.44.



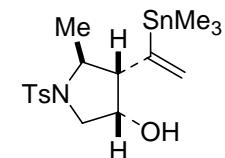
(3*R,4*S**)-Diethyl-3-hydroxyl-4-{1-(trimethylstannylyl)vinyl}cyclopentane-1,1-dicarboxylate(2c).** R_f 0.66 (hexanes : EtOAc = 3 : 1). IR (neat) 3477, 3025, 2953, 1731, 1459, 1249, 727 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 0.15 (s, 9H), 1.26 (dd, 6H, J = 11.8, 7.3 Hz), 1.98 (d, 1H, J = 3.9 Hz), 2.44 (m, 4H), 2.86 (m, 1H), 4.15 (ddd, 1H, J = 3.4, 3.4, 3.4 Hz), 4.20 (m, 4H), 5.42 (dd, 1H, J = 1.7, 1.7 Hz), 5.85 (dd, 1H, J = 1.7, 1.7 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ -8.1, 14.2, 36.2, 42.8, 55.5, 58.6, 61.9, 74.8, 127.5, 153.1, 172.7, 173.1. Anal. Calcd for $\text{C}_{16}\text{H}_{28}\text{O}_5\text{Sn}$: C, 45.85; H, 6.73. Found: C, 46.01; H, 6.67.



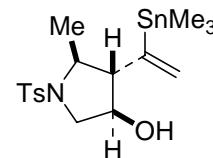
(3*S,4*S**)-Diethyl-3-hydroxyl-4-{1-(trimethylstannyl)vinyl}cyclopentane-1,1-dicarboxylate (3c).** R_f 0.54 (hexanes : EtOAc = 3 : 1). IR (neat) 3470, 3022, 29613, 1734, 1455, 1381, 1245, 733 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 0.18 (s, 9H), 1.26 (dd, 6H, J = 5.6, 14.1 Hz), 1.91 (d, 1H, J = 5.6 Hz), 2.02 (dd, 1H, J = 11.8, 13.5 Hz), 2.15 (dd, 1H, J = 7.9, 14.1 Hz), 2.56 (dd, 1H, J = 7.9, 13.5 Hz), 2.65 (dd, 2H, J = 7.3, 14.1 Hz), 3.93 (ddt, 1H, J = 7.9, 7.9, 6.5 Hz), 4.20 (m, 4H), 5.29 (dd, 1H, J = 1.7, 1.7 Hz), 5.79 (dd, 1H, J = 1.7, 1.7 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ -8.3, 14.3, 37.8, 41.3, 56.7, 58.4, 61.9, 76.3, 126.7, 155.0, 172.2, 172.7. Anal. Calcd for $\text{C}_{16}\text{H}_{28}\text{O}_5\text{Sn}$: C, 45.85; H, 6.73. Found: C, 46.01; H, 6.67.



(3*S,4*S**,5*S**)-5-Methyl-1-(*p*-toluenesulfonyl)-4-{1-(trimethylstannyl)vinyl}pyrrolidin-3-ol (2d).** R_f 0.26 (hexanes : EtOAc = 3 : 1). IR (neat) 3511, 3018, 2965, 1598, 1446, 1163, 737 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 0.05 (s, 9H), 1.37 (d, 3H, J = 8.6), 1.58 (bs, 1H), 2.42 (s, 3H), 2.60 (dd, 1H, J = 3.9, 9.8 Hz), 3.56 (m, 3H), 3.96 (m, 1H), 5.44 (dd, 1H, J = 1.7, 1.7 Hz), 5.73 (dd, 1H, J = 1.7, 1.7 Hz), 7.30 (d, 2H, J = 8.3 Hz), 7.74 (d, 2H, J = 8.3 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ -7.9, 20.4, 21.8, 53.6, 57.0, 63.2, 71.7, 128.1, 129.8, 129.8, 135.0, 143.7, 150.1. Anal. Calcd for $\text{C}_{17}\text{H}_{27}\text{NO}_3\text{SSn}$: C, 45.97; H, 6.13; N, 3.15; S, 7.22. Found: C, 45.91; H, 6.013; N, 3.33; S, 7.12.

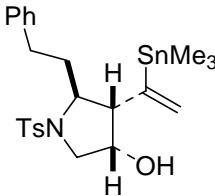


(3*R,4*S**,5*S**)-5-Methyl-1-(*p*-toluenesulfonyl)-4-{1-(trimethylstannyl)vinyl}pyrrolidin-3-ol (3d).** R_f 0.20 (hexanes : EtOAc = 3 : 1). IR (neat) 3478, 3024, 2978, 1600, 1446, 1381, 1143, 741 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 0.01 (s, 9H), 1.38 (d, 3H, J = 6.8 Hz), 1.61 (d, 1H, J = 3.9 Hz), 2.43 (s, 3H), 2.44 (m, 1H), 3.24 (m, 2H), 3.51 (dd, 1H, J = 6.8, 13.7 Hz), 3.77 (dd, 1H, J = 6.8, 10.7 Hz), 5.32 (d, 1H, J = 2.0 Hz), 5.73 (d, 1H, J = 2.0 Hz), 7.33 (d, 2H, J = 7.8 Hz), 7.73 (d, 2H, J = 7.8 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ -8.4, 20.7, 21.7, 53.6, 59.4, 67.4, 72.4, 127.7, 130.1, 130.6, 135.1, 143.9, 151.5. Anal. Calcd for $\text{C}_{17}\text{H}_{27}\text{NO}_3\text{SSn}$: C, 45.97; H, 6.13; N, 3.15; S, 7.22. Found: C, 45.91; H, 6.01; N, 3.33; S, 7.12.

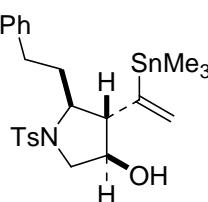


(3*R,4*S**,5*S**)-5-Phenethyl-1-(*p*-toluenesulfonyl)-4-{1-(trimethylstannyl)vinyl}pyrrolidin-3-ol (2e).** R_f 0.45 (hexanes : EtOAc = 2 : 1). IR (neat) 3478, 3028, 2950, 1601, 1446, 1173, 741 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 0.06 (s, 9H), 1.33 (d, 1H, J = 4.0 Hz),

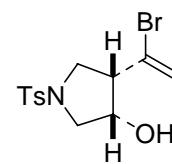
2.01 (m, 1H), 2.20 (m, 1H), 2.42 (s, 3H), 2.57 (ddd, 1H, J = 5.6, 11.2, 11.2 Hz), 2.82 (ddd, 1H, J = 5.6, 11.8, 11.8 Hz), 2.90 (dd, 1H, J = 3.4, 10.1 Hz), 3.53 (dd, 1H, J = 2.8, 12.9 Hz), 3.64 (d, 1H, J = 12.9 Hz), 3.72 (m, 1H), 3.96 (q, 1H, J = 3.4 Hz), 5.45 (dd, 1H, J = 1.4, 1.4 Hz), 5.72 (dd, 1H, J = 1.4, 1.4 Hz), 7.20 (m, 3H), 7.27 (m, 2H), 7.29 (d, 2H, J = 8.4 Hz), 7.74 (d, 2H, J = 8.4 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ –9.3, 21.8, 30.4, 34.4, 57.4, 59.6, 60.1, 71.9, 126.0, 128.1, 128.6, 128.8, 129.8, 130.0, 135.2, 142.2, 143.7, 150.9. Anal. Calcd for $\text{C}_{24}\text{H}_{33}\text{NO}_3\text{SSn}$: C, 53.95; H, 6.23; N, 2.62; O, 8.98; S, 6.00. Found: C, 54.22; H, 6.31; N, 2.51; S, 5.77.



(3*R*^{*,4*S*^{*,5*S*^{*}})-5-Phenethyl-1-(*p*-toluenesulfonyl)-4-{1-(trimethylstannyl)vinyl}pyrrolidin-3-ol (3e).} R_f 0.57 (hexanes : EtOAc = 2 : 1). IR (neat) 3484, 3023, 2965, 1598, 1451, 1171, 733 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 0.03 (s, 9H), 1.67 (d, 1H, J = 3.9 Hz), 2.01 (m, 1H), 2.22 (m, 1H), 2.43 (s, 3H), 2.61 (ddd, 1H, J = 5.9, 13.5, 8.4 Hz), 2.72 (t, 1H, J = 8.4 Hz), 2.85 (m, 1H), 3.22 (dd, 1H, J = 8.4, 11.2 Hz), 3.47 (ddd, 1H, J = 2.8, 9.6, 6.7 Hz), 3.54 (m, 1H), 3.80 (dd, 1H, J = 6.7, 11.2 Hz), 5.29 (d, 1H, J = 1.1 Hz), 5.62 (d, 1H, J = 1.1 Hz), 7.20 (m, 3H), 7.28 (m, 2H), 7.31 (d, 2H, J = 7.9 Hz), 7.70 (d, 2H, J = 7.9 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ –8.4, 21.7, 30.4, 35.1, 54.3, 62.4, 63.3, 72.9, 126.1, 127.8, 128.6, 128.8, 130.0, 130.1, 135.2, 142.1, 144.0, 152.4. Anal. Calcd for $\text{C}_{24}\text{H}_{33}\text{NO}_3\text{SSn}$: C, 53.95; H, 6.23; N, 2.62; O, 8.98; S, 6.00. Found: C, 53.88; H, 6.33; N, 2.72; S, 5.83.

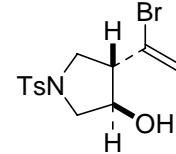


Typical procedure for bromination, (3*S*^{*,4*S*^{*})-4-(1-Bromovinyl)-1-(*p*-toluenesulfonyl)pyrrolidin-3-ol (4a).} To a solution of **2a** (75 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) at –78 °C was added bromine (30.0 mg, 0.187 mmol) in CH_2Cl_2 (1 mL). After 30 min, the mixture was quenched with 10% Na_2CO_3 , and then extracted with CH_2Cl_2 (2 X). The organic layer was dried over anhydrous MgSO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by SiO_2 column chromatography to give a product **4a** (45.9 mg, 0.13 mmol, 78%). R_f 0.16 (hexanes : EtOAc = 1 : 1). IR (neat) 3504, 3031, 2970, 1624, 1598, 1337, 1159, 671 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 1.69 (bs, 1H), 2.43 (s, 3H), 2.99 (m, 1H), 3.38 (dd, 1H, J = 9.2, 7.3 Hz), 3.43 (d, 1H, J = 11.2 Hz), 3.58 (dd, 1H, J = 4.3, 7.3 Hz), 3.61 (dd, 1H, J = 9.2, 11.2 Hz), 4.48 (m, 1H), 5.61 (d, 1H, J = 1.5 Hz), 5.69 (d, 1H, J = 1.5 Hz), 7.33 (d, 2H, J = 8.2 Hz), 7.74 (d, 2H, J = 8.2 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ 21.8, 47.9, 54.2, 55.4,

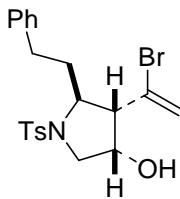


71.7, 120.2, 127.2, 127.5, 130.0, 134.2, 144.0. Anal. Calcd for $C_{13}H_{16}BrNO_3S$: C, 45.10; H, 4.66; N, 4.05; S, 9.26. Found: C, 45.33; H, 4.32; N, 4.11; S, 8.98.

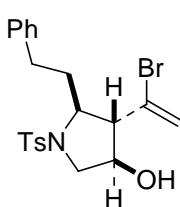
(3*R*^{*},4*S*^{*})-4-(1-Bromovinyl)-1-(*p*-toluenesulfonyl)pyrrolidin-3-ol (5a). R_f 0.20 (hexanes : EtOAc = 1 : 1). IR (neat) 3489, 3028, 2973, 1611, 1599, 1148, 738, 660 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 1.94 (d, 1H, J = 5.0 Hz), 2.45(s, 3H), 2.85 (dd, 1H, J = 8.0, 14.1 Hz), 3.18 (ddd, 1H, J = 6.1, 7.3, 8.0 Hz), 3.36 (ddd, 1H, J = 8.0, 8.0, 14.1 Hz), 3.58 (ddd, 1H, J = 6.1, 8.0, 8.0 Hz), 3.61 (dd, 1H, J = 6.1, 8.0 Hz), 4.24 (m, 1H), 5.54 (dd, 1H, J = 1.7, 1.7 Hz), 5.73 (dd, 1H, J = 1.7, 1.7 Hz), 7.38 (d, 2H, J = 8.2 Hz), 7.68 (d, 2H, J = 8.2 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ 21.8, 50.2, 53.7, 56.4, 73.7, 120.1, 127.9, 130.0, 130.8, 133.6, 144.1. Anal. Calcd for $C_{13}H_{16}BrNO_3S$: C, 45.10; H, 4.66; N, 4.05; S, 9.26. Found: C, 45.13; H, 4.72; N, 3.93; S, 9.11.



(3*S*^{*},4*S*^{*},5*S*^{*})-4-(1-Bromovinyl)-5-phenethyl-1-(*p*-toluenesulfonyl)pyrrolidin-3-ol (4b). R_f 0.33 (hexanes : EtOAc = 1 : 1). IR (neat) 3498, 3028, 2972, 1621, 1601, 1159, 735, 668 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 1.40 (bs, 1H), 2.15 (m, 1H), 2.23 (m, 1H), 2.41 (s, 3H), 2.60 (ddd, 1H, J = 6.18, 13.5, 12.1 Hz), 2.85 (ddd, 1H, J = 5.1, 12.1, 14.1 Hz), 3.03 (dd, 1H, J = 4.2, 9.4 Hz), 3.54 (dd, 1H, J = 3.7, 12.5 Hz), 3.66 (dd, 1H, J = 1.7, 12.5 Hz), 3.82 (ddd, 1H, J = 2.8, 6.7, 9.6 Hz), 4.29 (m, 1H), 5.53 (d, 1H, J = 2.8 Hz), 5.69 (d, 1H, J = 2.8 Hz), 7.20 (m, 3H), 7.27 (m, 2H), 7.29 (d, 2H, J = 7.3 Hz), 7.72 (d, 2H, J = 7.3 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ 21.8, 30.6, 35.5, 56.1, 60.1, 71.1, 76.7, 120.7, 126.2, 127.8, 128.2, 128.7, 128.7, 129.7, 135.0, 141.5, 144.0. Anal. Calcd for $C_{21}H_{24}BrNO_3S$: C, 56.00; H, 5.37; N, 3.11; S, 7.12. Found: C, 56.21; H, 5.55; N, 3.01; S, 6.98.

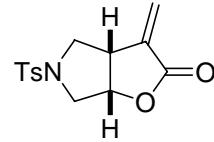


(3*R*^{*},4*S*^{*},5*S*^{*})-4-(1-Bromovinyl)-5-phenethyl-1-(*p*-toluenesulfonyl)pyrrolidin-3-ol (5b). R_f 0.30 (hexanes : EtOAc = 1 : 1). IR (neat) 3502, 3026, 2968, 1624, 1598, 1348, 1148, 733, 663 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 1.83 (d, 1H, J = 4.5 Hz), 2.20 (dt, 2H, J = 5.1, 8.3 Hz), 2.40 (s, 3H), 2.68 (m, 2H), 2.86 (ddd, 1H, J = 6.7, 6.7, 7.3 Hz), 3.26 (dd, 1H, J = 7.3, 10.7 Hz), 3.74 (m, 3H), 5.49 (d, 1H, J = 1.7 Hz), 5.61 (d, 1H, J = 1.7 Hz), 7.21 (m, 3H), 7.30 (m, 4H), 7.68 (d, 2H, J = 8.4 Hz). ^{13}C NMR (125 MHz, CDCl_3): δ 21.8, 31.1, 36.7, 53.8, 61.7, 62.4, 72.1, 121.4, 126.2, 128.0, 128.7, 128.8, 130.0, 131.7, 134.8, 141.6, 144.0. Anal. Calcd for $C_{21}H_{24}BrNO_3S$: C, 56.00; H, 5.37; N, 3.11; S, 7.12. Found: C, 56.11; H, 5.21; N,

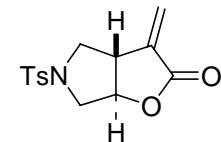


3.23; S, 7.02.

Typical procedure for carbocyclization, (*3aS*,6aS)-3-Methylene-5-(*p*-toluene sulfonyl)-hexahydrofuro[2,3-*c*]pyrrol-2-one (6a).** A schlenk flask equipped with a reflux condenser was charged with bis(triphenylphosphine)dicarbonylnickel (131.5 mg, 0.20 mmol) and 4a (65 mg, 0.187 mmol). The system was alternately evacuated and filled with argon. Freshly distilled tetrahydrofuran (4 mL) was introduced via syringe, the system was alternately evacuated (until the solvent vigorously frothed) and filled with argon two times and then triethylamine (38 mg, 0.375 mmol) was added. The mixture was heated at reflux for 2 h, during which the color changed from yellow to orange to brown and finally to green. The mixture was cooled to 25 °C, poured into ether (20 mL), and washed with two portion of aqueous 1N hydrochloride acid. The combined aqueous layers were extracted with ether (20x2 mL), and then the combined organic layers were washed with saturated aqueous sodium bicarbonate and saturated aqueous sodium chloride. After drying over anhydrous MgSO₄, the organic solution was concentrated under reduced pressure to yield a heterogeneous green residue. Final purification was effected by column chromatography to give **6a** (41.1 mg, 0.14 mmol, 75%) as a white solid. R_f 0.48 (hexane:EtOAc = 1:1). IR (film) 3047, 2991, 2861, 1765, 1661, 1596, 1348, 1265, 1163, 734, 663 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 2.45 (s, 3H), 3.04 (dd, 1H, J = 4.9, 11.7 Hz), 3.19 (dd, 1H, J = 7.8, 9.8 Hz), 3.38 (dd, 1H, J = 2.9, 9.8 Hz), 3.55 (m, 1H), 3.63 (d, 1H, J = 11.7 Hz), 4.96 (m, 1H), 5.76 (d, 1H, J = 2.0 Hz), 6.32 (d, 1H, J = 2.0 Hz), 7.35 (d, 2H, J = 8.8 Hz), 7.66 (d, 2H, J = 8.8 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 21.8, 42.2, 54.2, 55.2, 79.2, 125.2, 128.3, 130.1, 131.7, 137.1, 144.7, 169.2.

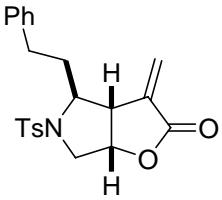


(*3aS*,6aR)-3-Methylene-5-(*p*-toluenesulfonyl)-hexahydrofuro[2,3-*c*]pyrrol-2-one (7a).** R_f 0.48 (hexanes : EtOAc = 1 : 1). IR (film) 3044, 2992, 2865, 1767, 1664, 1596, 1265, 1163, 735 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 2.45 (s, 3H), 3.07 (dd, 1H, J = 5.3, 11.7 Hz), 3.22 (dd, 1H, J = 10.0, 7.6 Hz), 3.37 (dd, 1H, J = 10.0, 2.9 Hz), 3.55 (m, 1H), 3.63 (dd, 1H, J = 0.6, 11.7 Hz), 4.97 (m, 1H), 5.77 (d, 1H, J = 2.4 Hz), 6.35 (d, 1H, J = 2.4 Hz), 7.36 (d, 2H, J = 8.2 Hz), 7.68 (d, 2H, J = 8.2 Hz). ¹³C NMR (125MHz, CDCl₃): δ 22.3, 42.6, 54.7, 55.2, 79.7, 125.8, 128.7, 130.6, 132.1, 137.4, 145.2, 169.6. Anal. Calcd for C₁₄H₁₅NO₄S: C, 57.32; H, 5.15; N, 4.77; S, 10.93. Found: C, 57.28; H, 5.11; N, 4.88; S, 11.10.



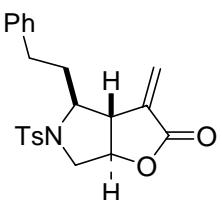
(3a*S*^{*,4*S*^{*,6a*S*^{*}}})-3-Methylene-4-phenethyl-5-(*p*-toluenesulfonyl)-hexahydrofuro[2,3-*c*]pyrrol-2-one (**6b**)

*R*_f 0.67 (hexanes : EtOAc = 1 : 1). IR (film) 3048, 2994, 2860, 1764, 1667, 1601, 1598, 1249, 1177, 734, 662 cm⁻¹. ¹H NMR (500MHz, CDCl₃): δ 1.97 (m, 1H), 2.14 (m, 1H), 2.42 (s, 3H), 2.8 (m, 2H), 3.31 (dd, 1H, *J* = 2.2, 6.7 Hz), 3.70 (dd, 1H, *J* = 4.5, 14.1 Hz), 3.83 (td, 1H, *J* = 2.2, 6.7 Hz), 3.92 (d, 1H, *J* = 14.1 Hz), 4.93 (dd, 1H, *J* = 4.5, 6.7 Hz), 5.48 (d, 1H, *J* = 2.2 Hz), 6.01 (d, 1H, *J* = 2.2 Hz), 7.24 (m, 5H), 7.32 (d, 2H, *J* = 8.4Hz), 7.60 (d, 2H, *J* = 8.4 Hz). ¹³C NMR (125MHz, CDCl₃): δ 21.77, 32.23, 36.85, 48.86, 53.14, 67.96, 80.59, 124.48, 126.58, 127.45, 128.56, 128.87, 130.06, 135.73, 136.81, 140.55, 144.46, 168.23. Anal. Calcd for C₂₂H₂₃NO₄S: C, 66.48; H, 5.83; N, 3.52; S, 8.07. Found: C, 66.55; H, 5.72; N, 3.32; S, 8.21.

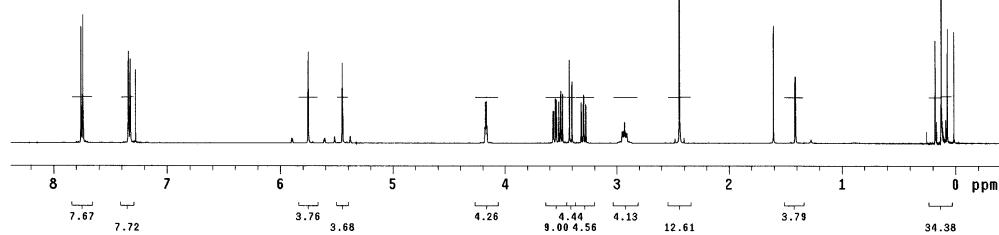
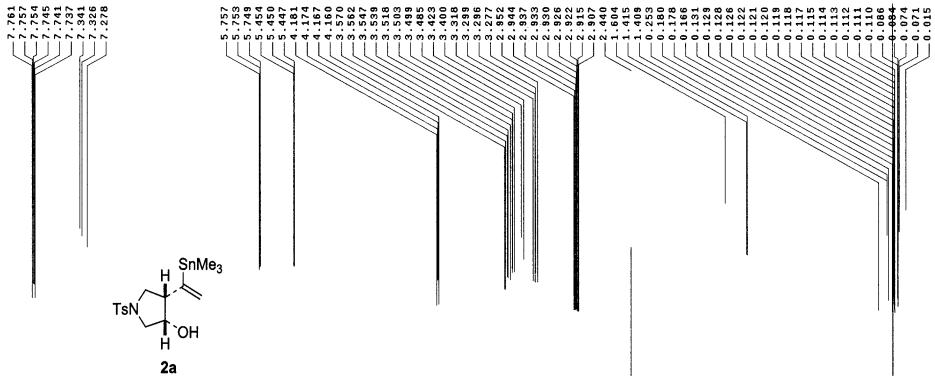


(3a*S*^{*,4*S*^{*,6a*R*^{*}}})-3-Methylene-4-phenethyl-5-(*p*-toluenesulfonyl)-hexahydrofuro[2,3-*c*]pyrrol-2-one (**7b**)

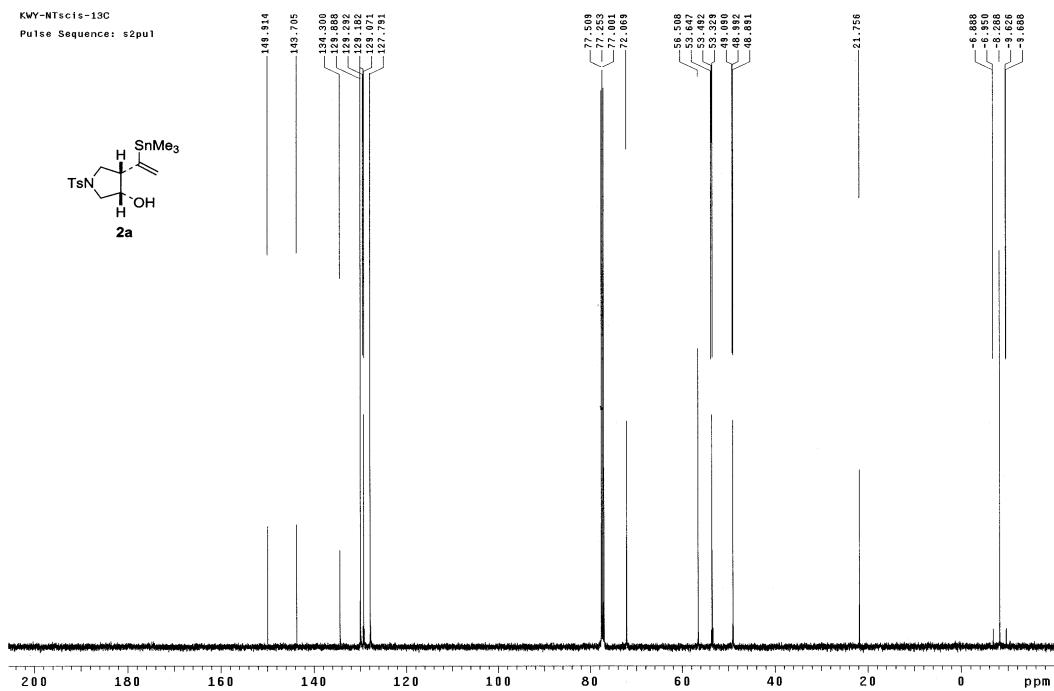
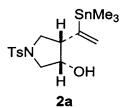
mp 108 °C. *R*_f 0.53 (hexane:EtOAc = 1:1). IR (film) 3049, 2992, 2863, 1767, 1668, 1599, 1249, 1177, 734, 662 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 2.20 (m, 1H), 2.44 (s, 3H), 2.62 (m, 1H), 2.70 (m, 1H), 2.82 (m, 2H), 3.12 (ddd, 1H, *J* = 6.2, 11.8, 11.8 Hz), 3.37 (t, 1H, *J* = 10.7 Hz), 3.73 (ddd, 1H, *J* = 3.4, 11.8, 10.1 Hz), 3.92 (dd, 1H, *J* = 6.2, 10.1 Hz), 5.55 (d, 1H, *J* = 2.8 Hz), 6.11 (d, 1H, *J* = 2.8 Hz), 7.25 (m, 3H), 7.32 (m, 2H), 7.33 (d, 2H, *J* = 8.4 Hz), 7.69 (d, 2H, *J* = 8.4 Hz). ¹³C NMR (125MHz, CDCl₃): δ 21.80, 31.13, 31.82, 36.93, 49.95, 55.66, 58.92, 119.16, 126.57, 127.52, 128.53, 128.87, 130.37, 134.97, 136.02, 140.56, 144.55, 171.17. Anal. Calcd for C₂₂H₂₃NO₄S: C, 66.48; H, 5.83; N, 3.52; S, 8.07. Found: C, 66.33; H, 5.91; N, 3.32; S, 8.13.



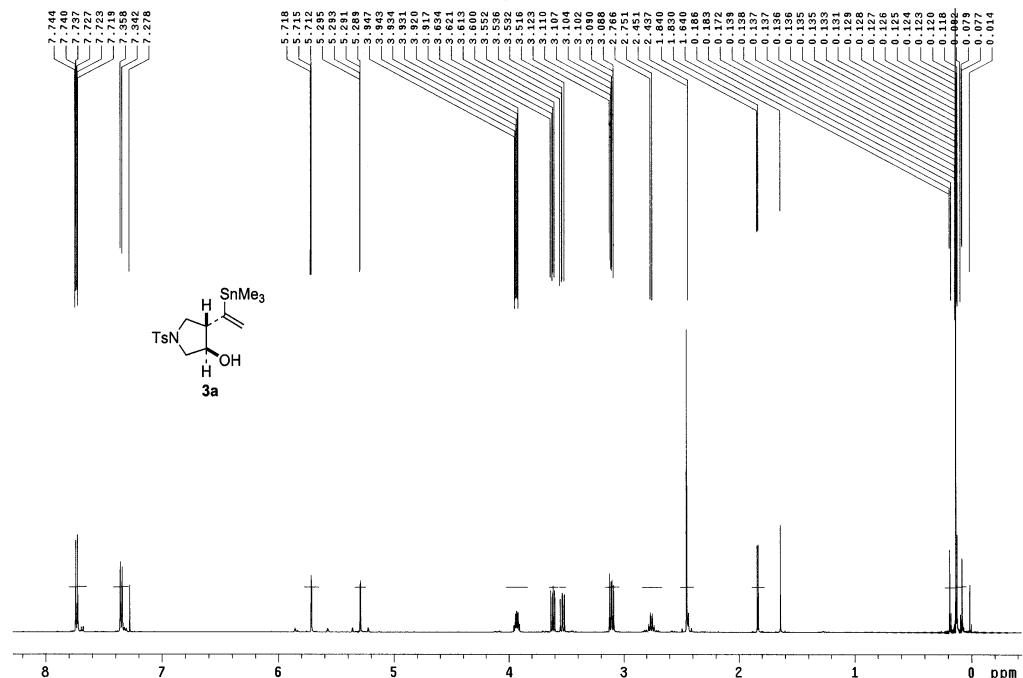
KWY-NTscis
Pulse Sequence: s2pul



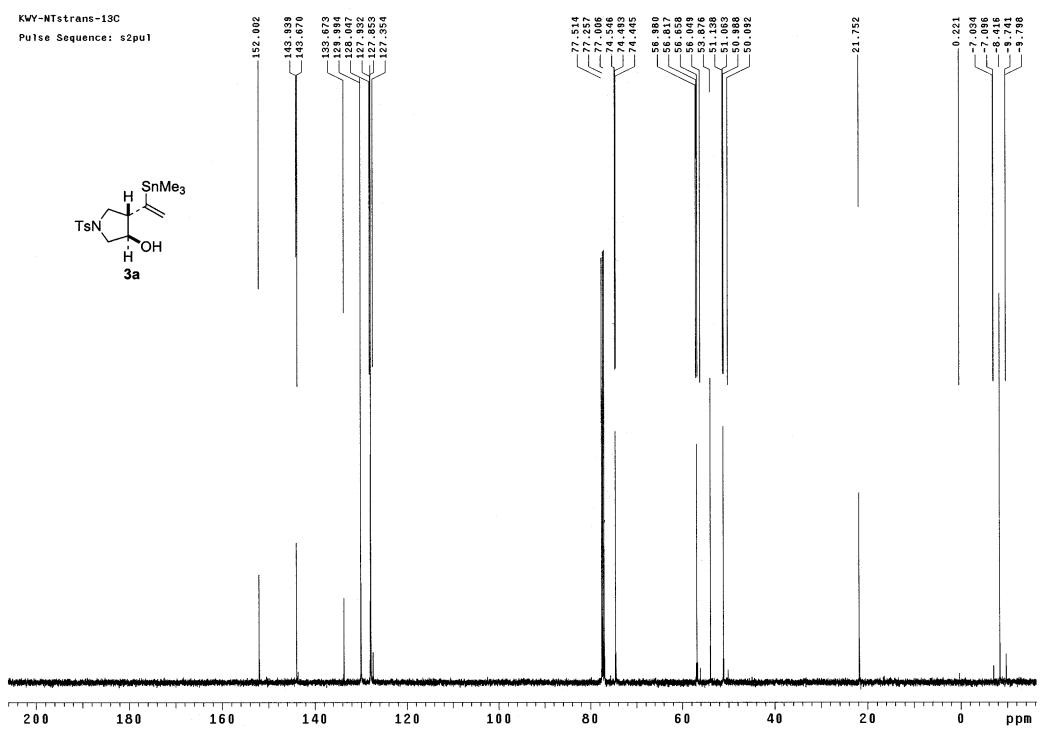
KWY-NTscis-13C
Pulse Sequence: s2pul

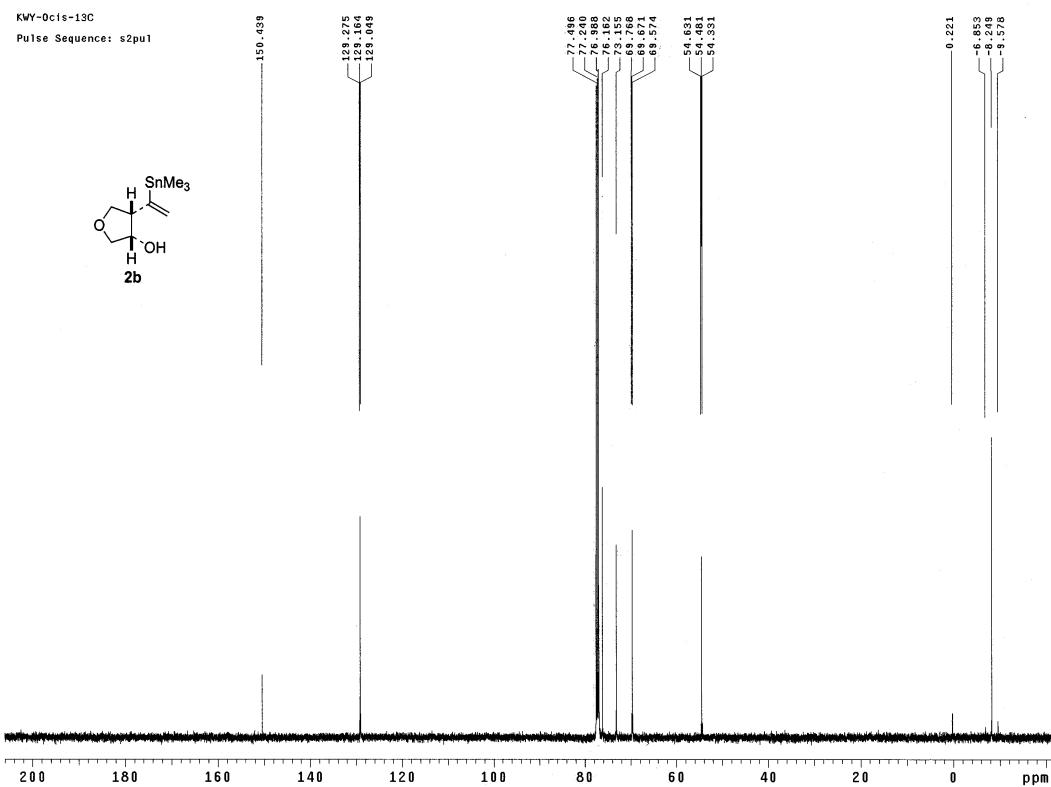
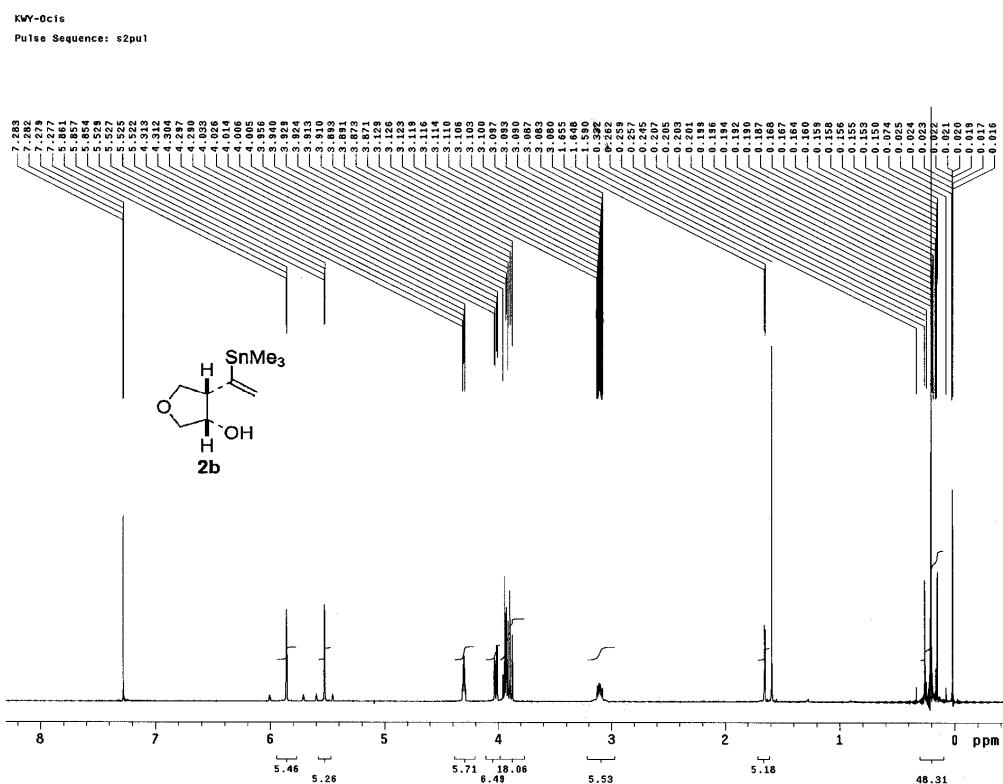


KWY-NTtrans
Pulse Sequence: s2pu1

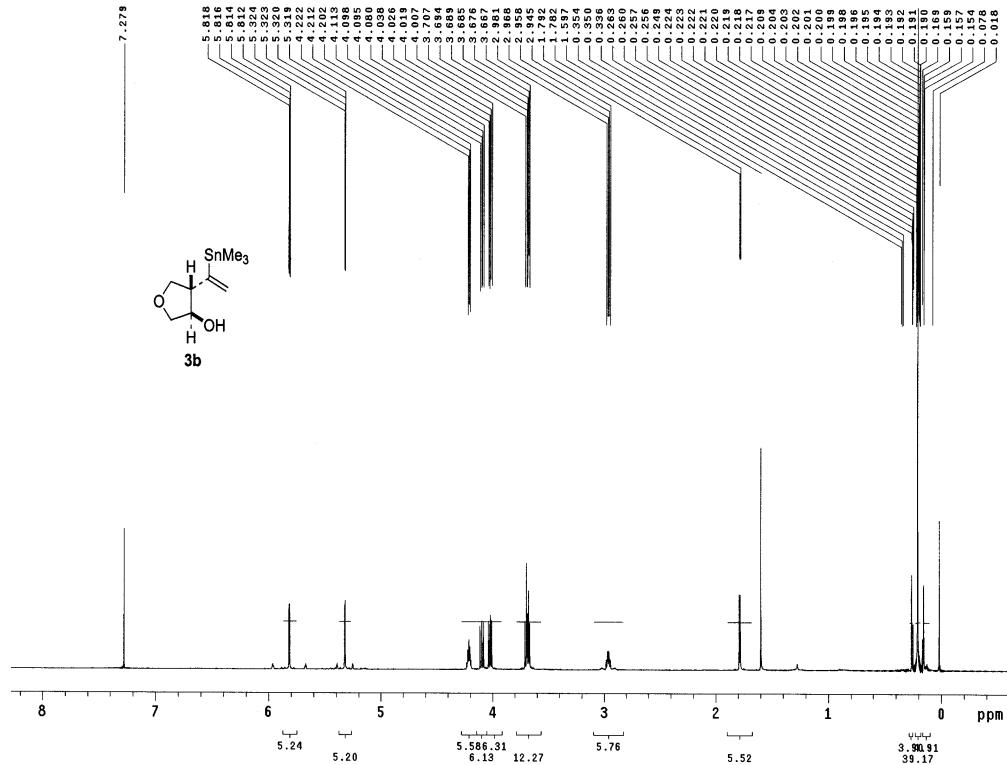


KWY-NTtrans-¹³C
Pulse Sequence: s2pu1

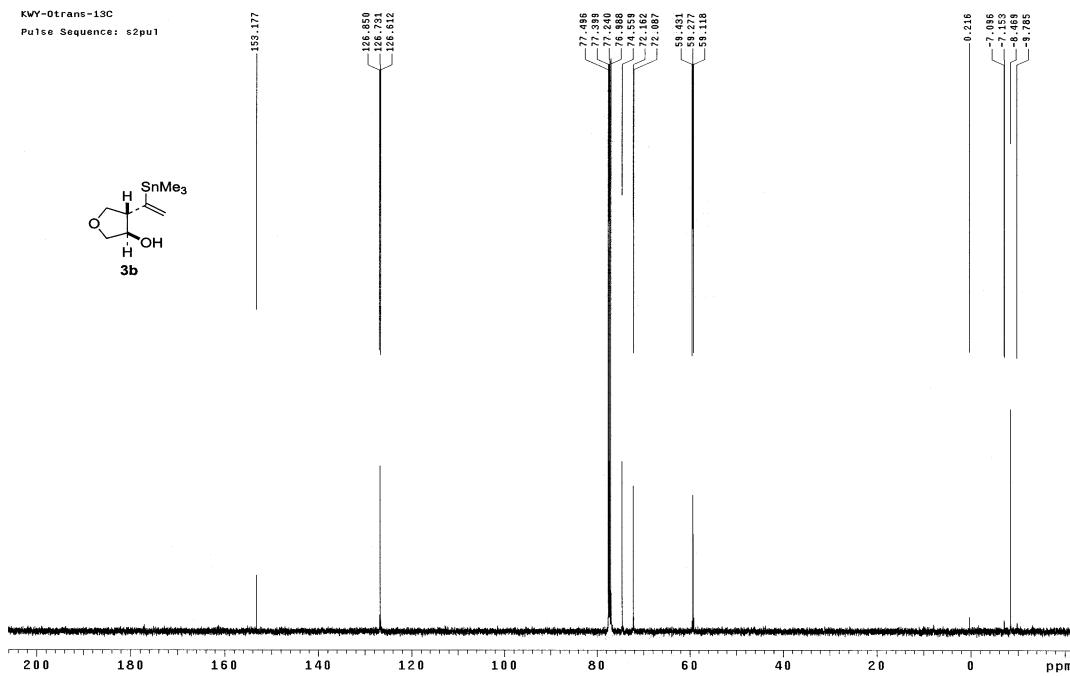




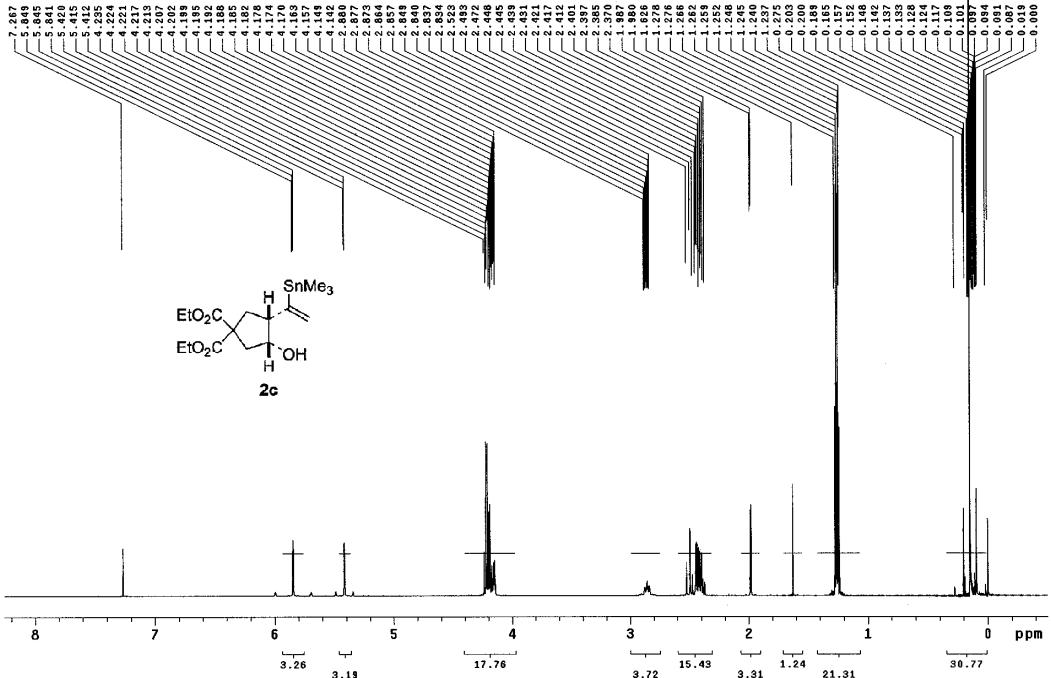
KWY-Otrans
Pulse Sequence: s2pul



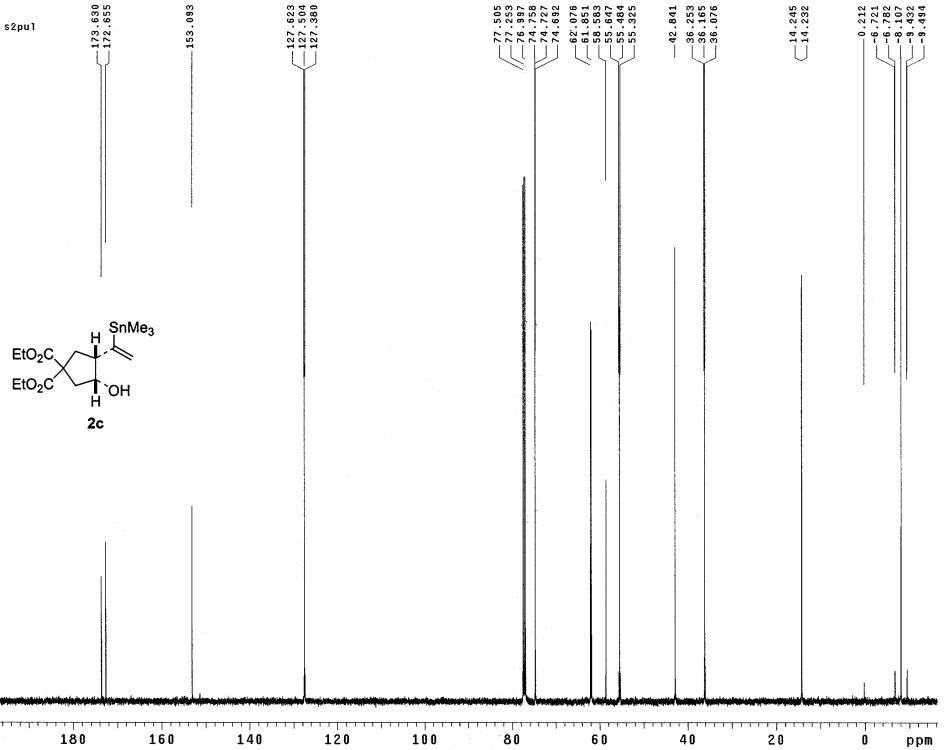
KWY-Otrans-¹³C
Pulse Sequence: s2pul

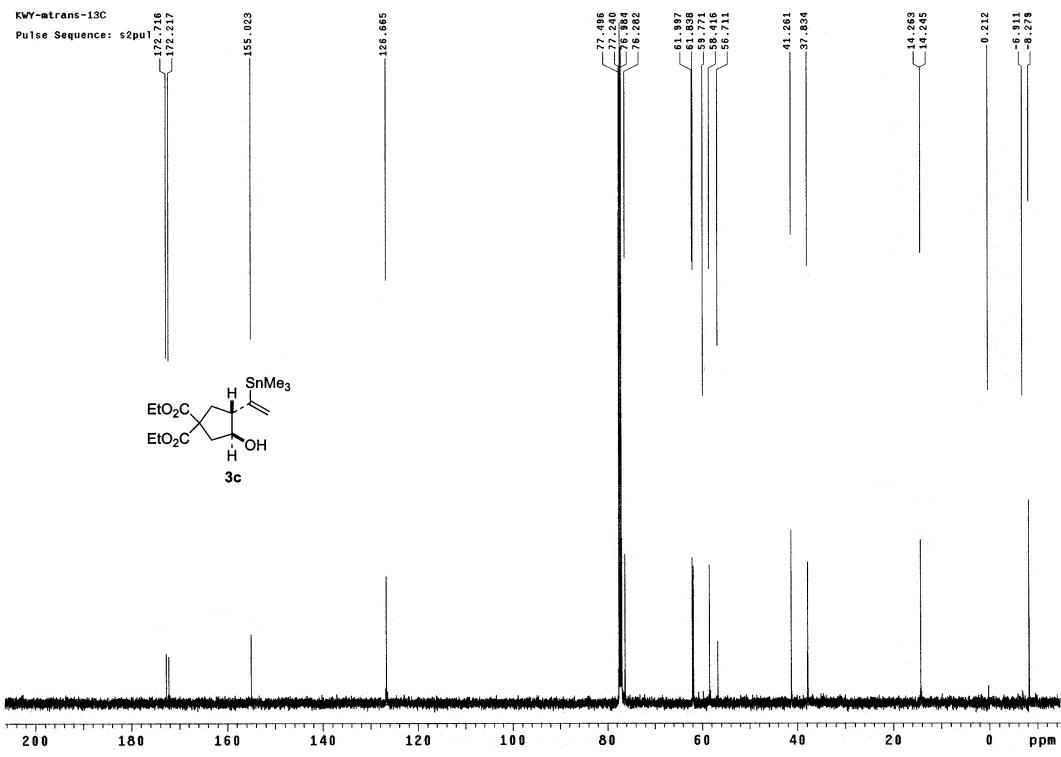
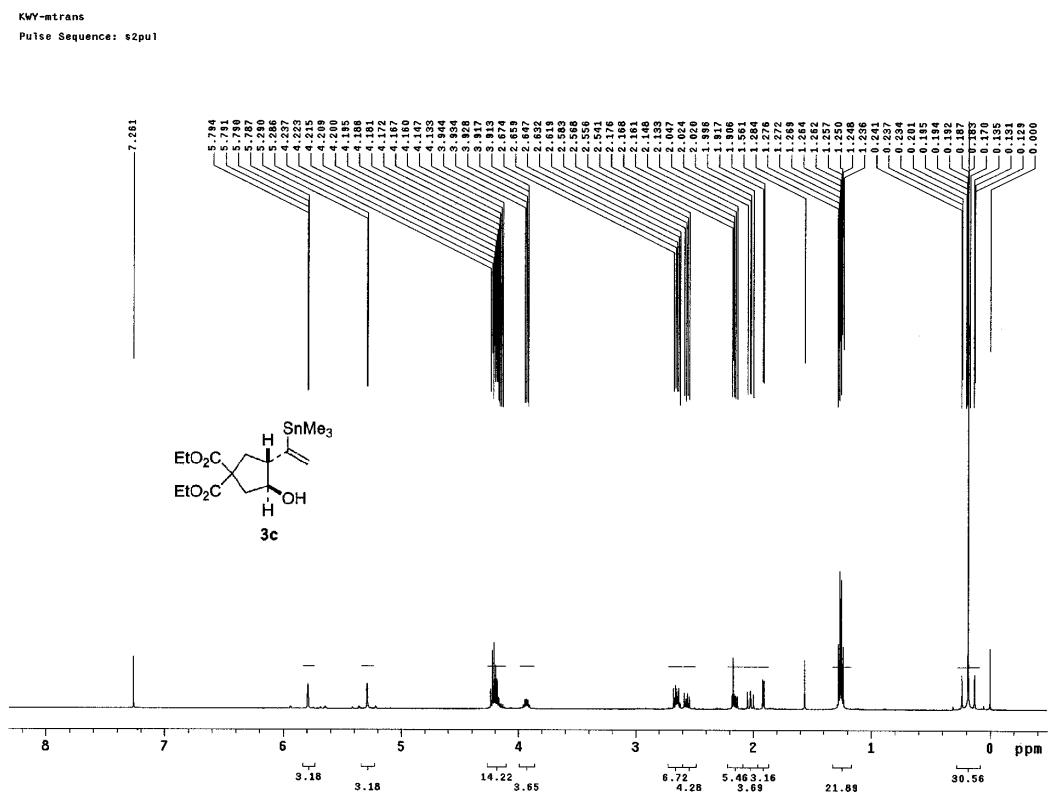


KWY-116

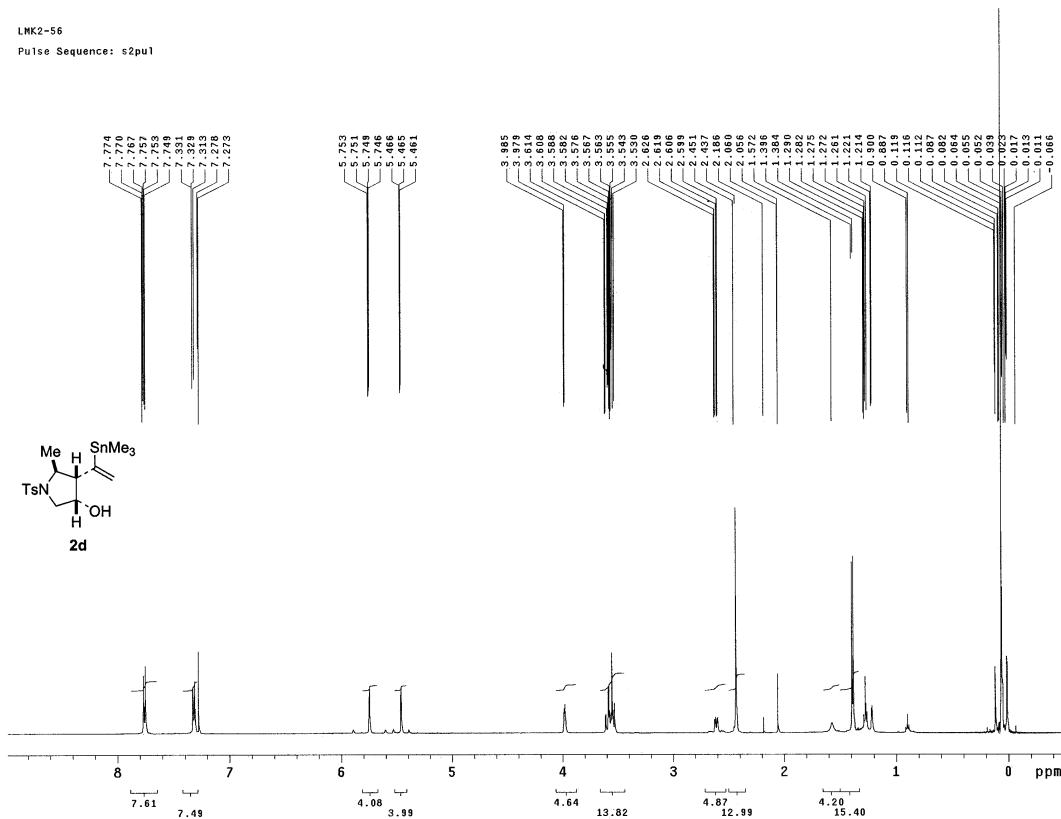
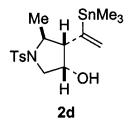
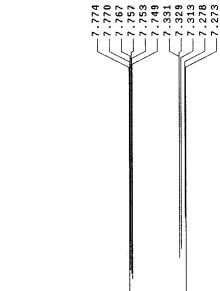


KWY-116-13C
Pulse Sequence: s2pul

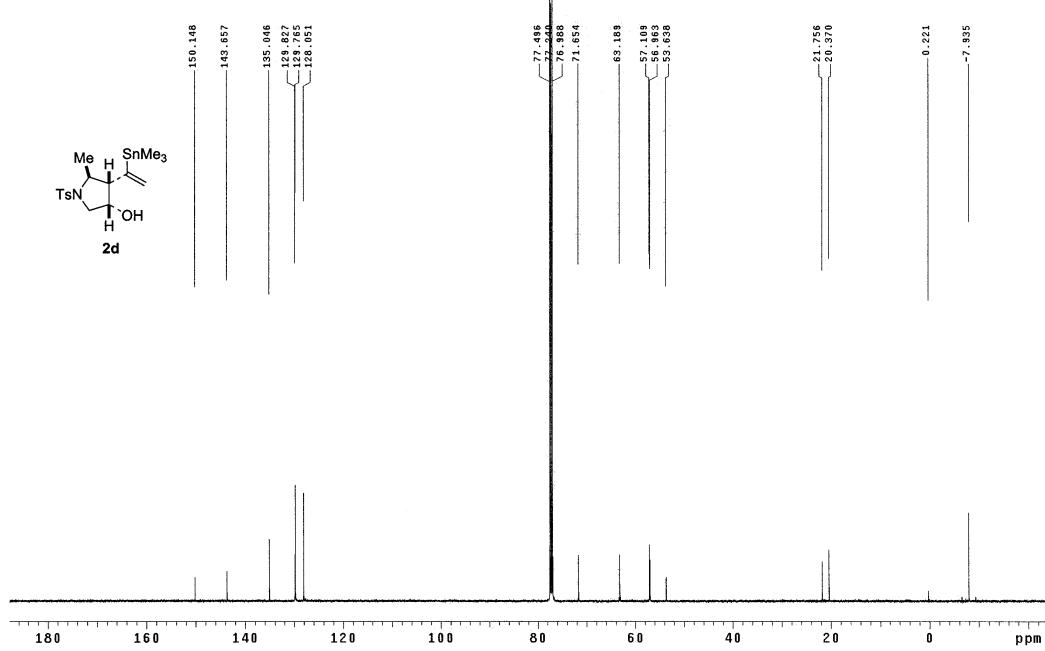
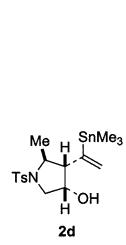




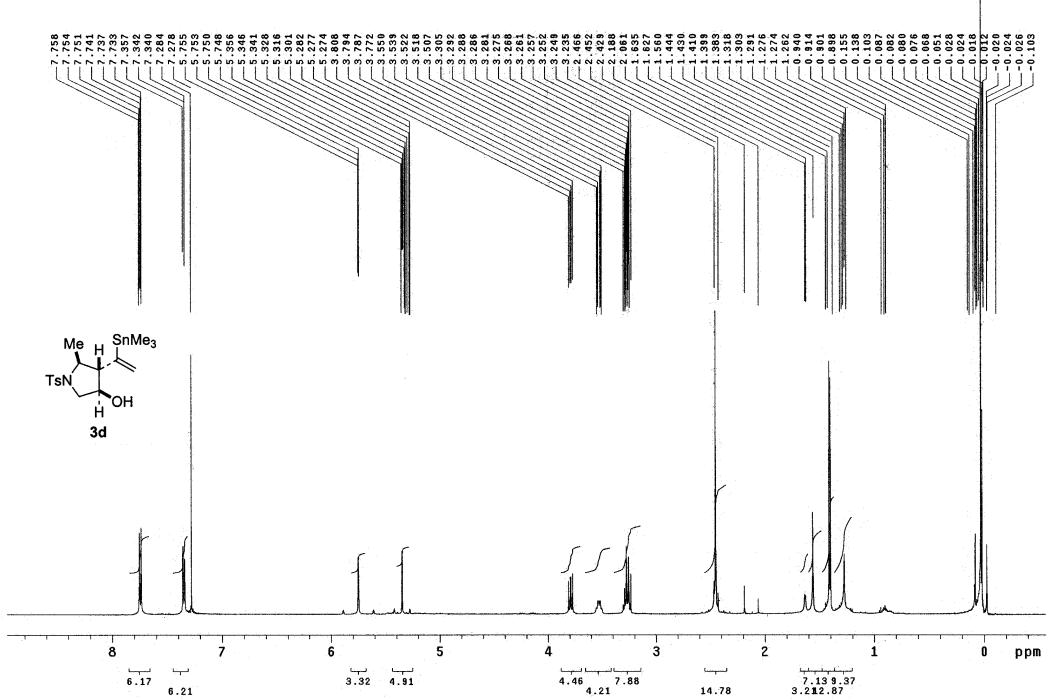
LMK2-56
Pulse Sequence: s2pul



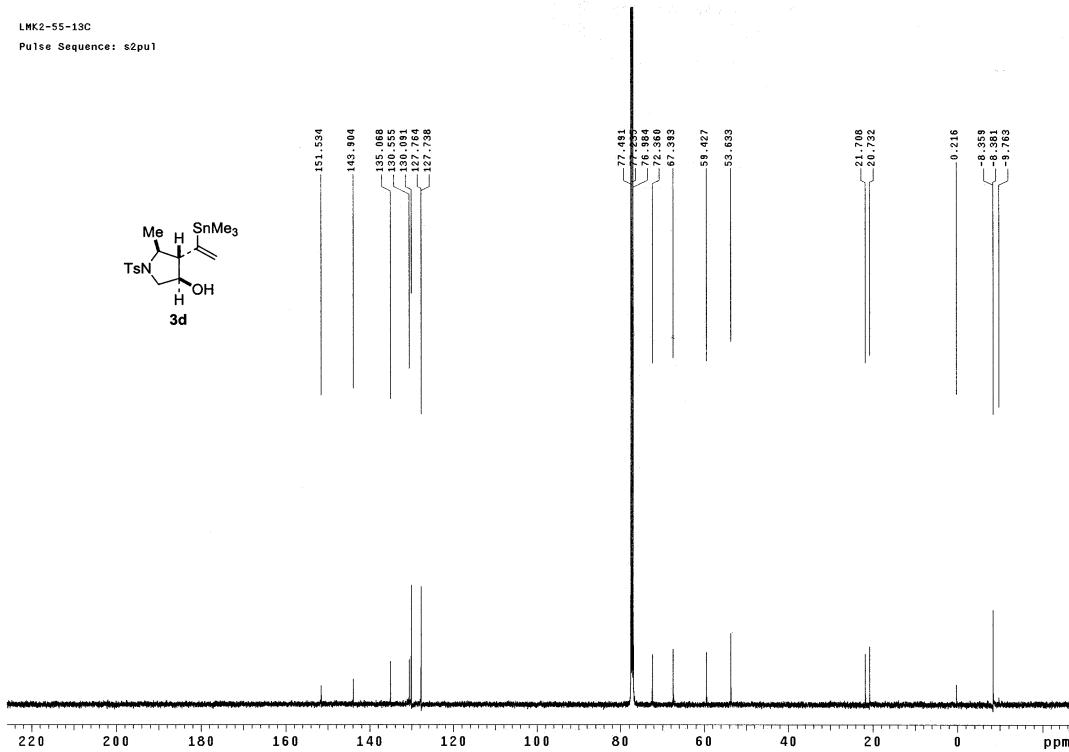
LMK2-56-13C
Pulse Sequence: s2pul



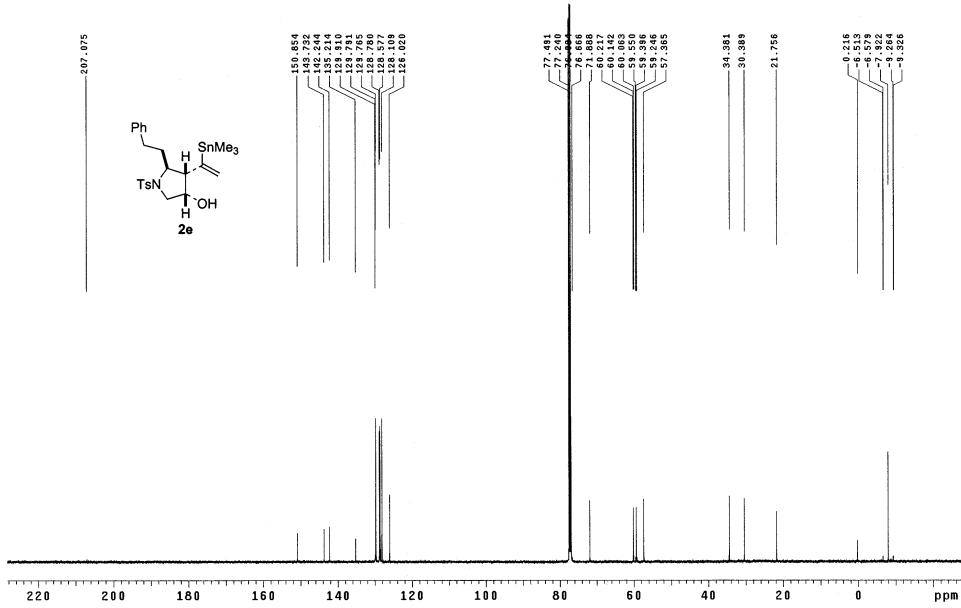
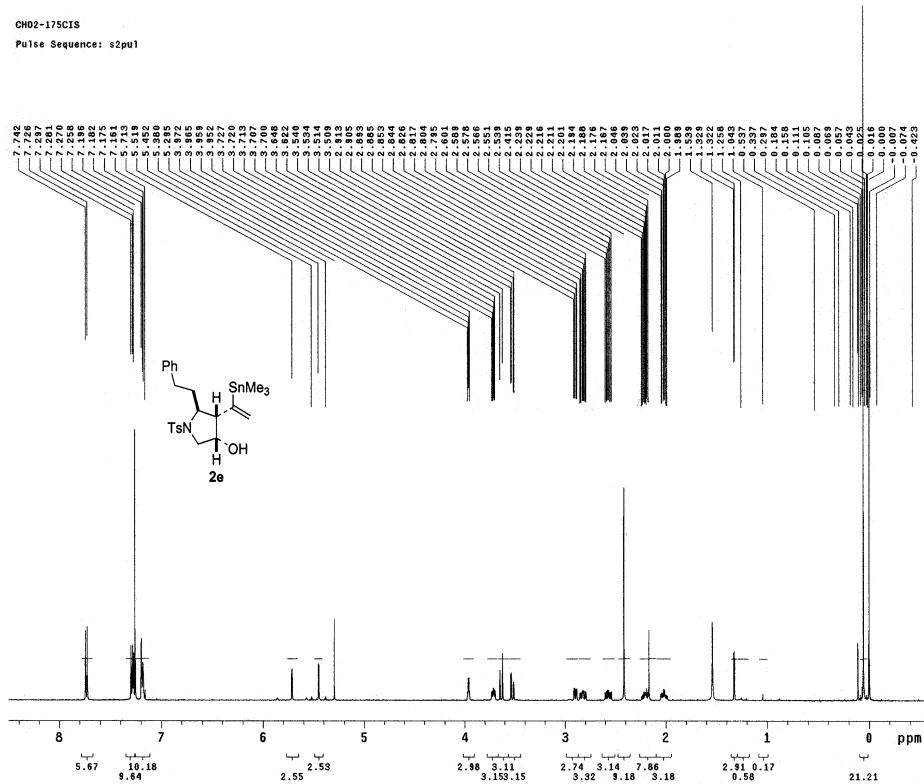
LMK2-55
Pulse Sequence: s2pu1



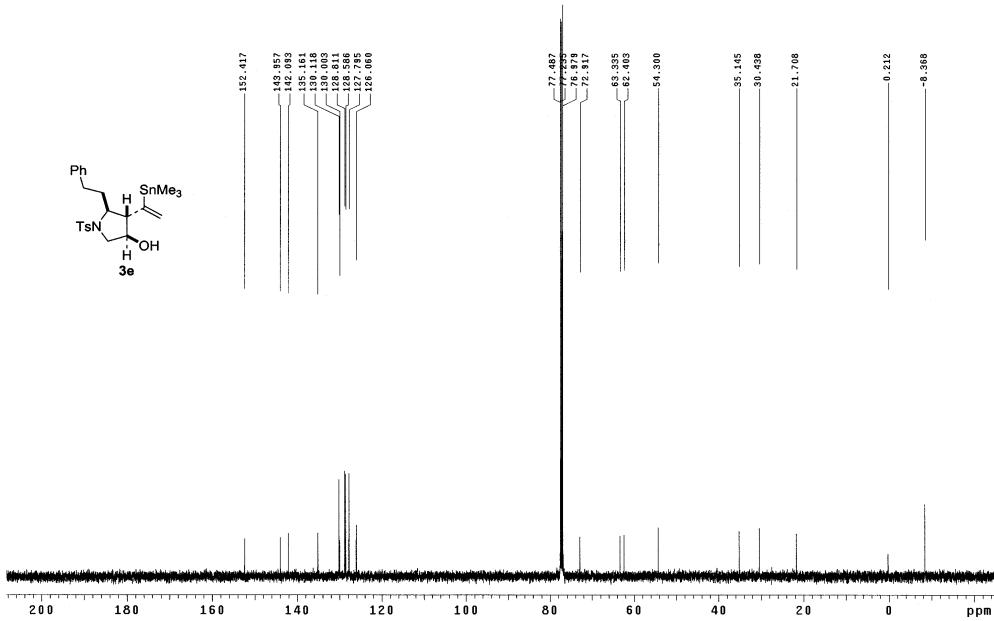
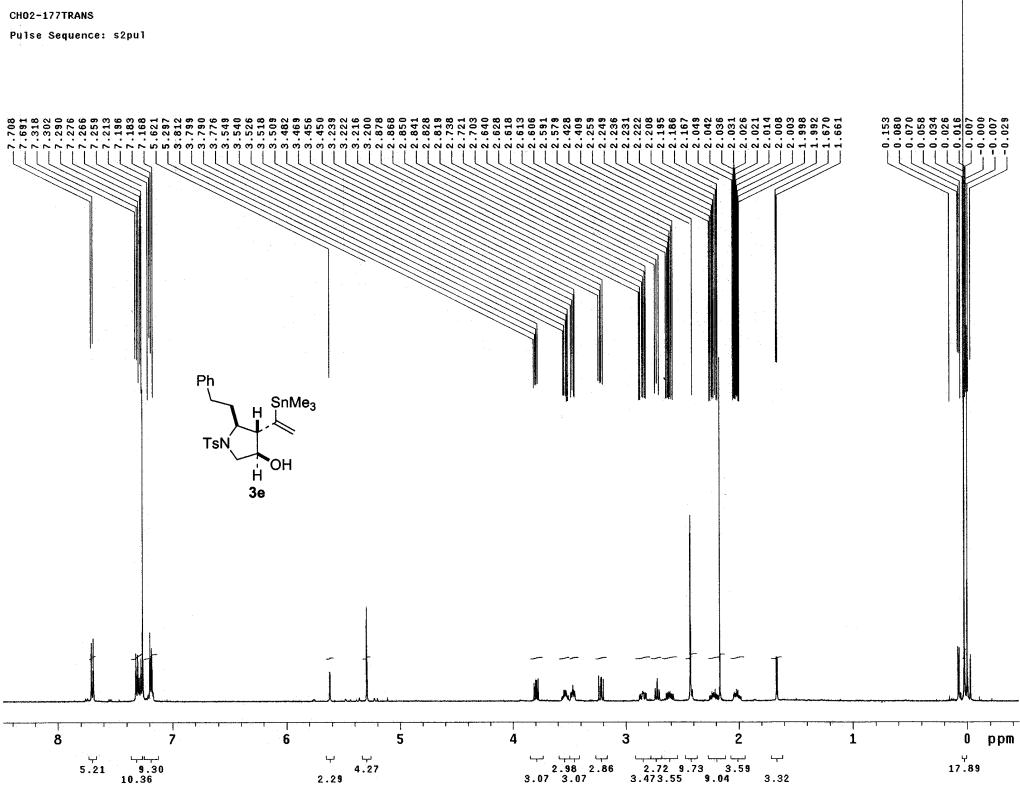
LMK2-55-13C
Pulse Sequence: s2pu1

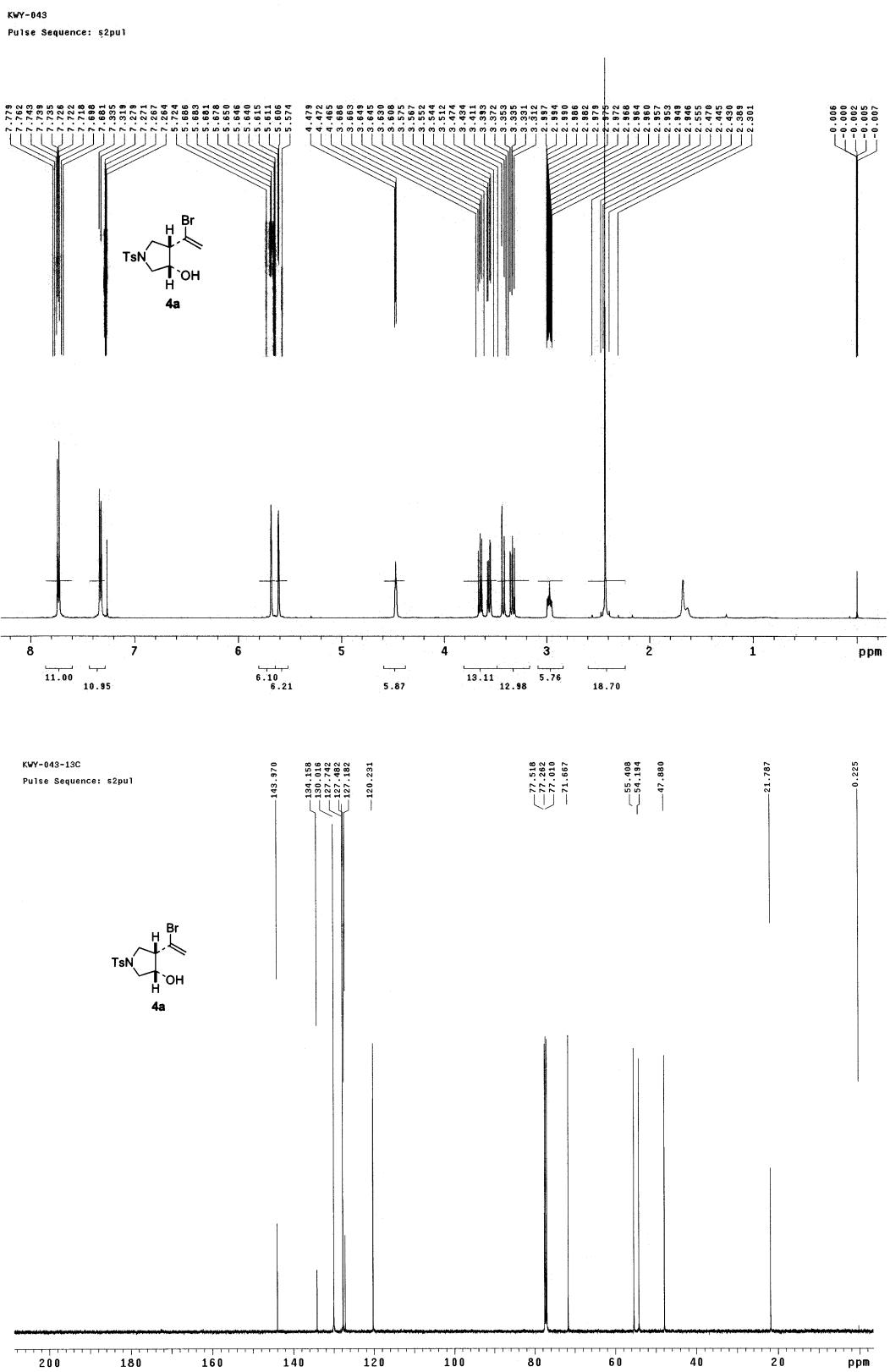


CHO2-175CIS
Pulse Sequence: s2pul

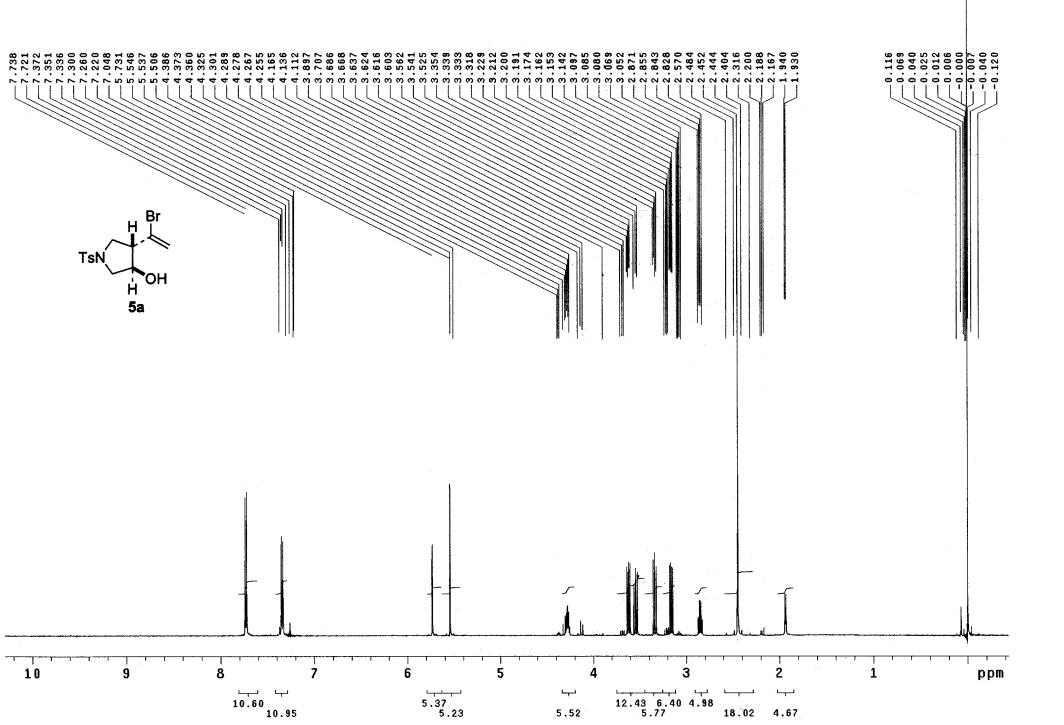


CHO2-177TRANS
Pulse Sequence: s2pul

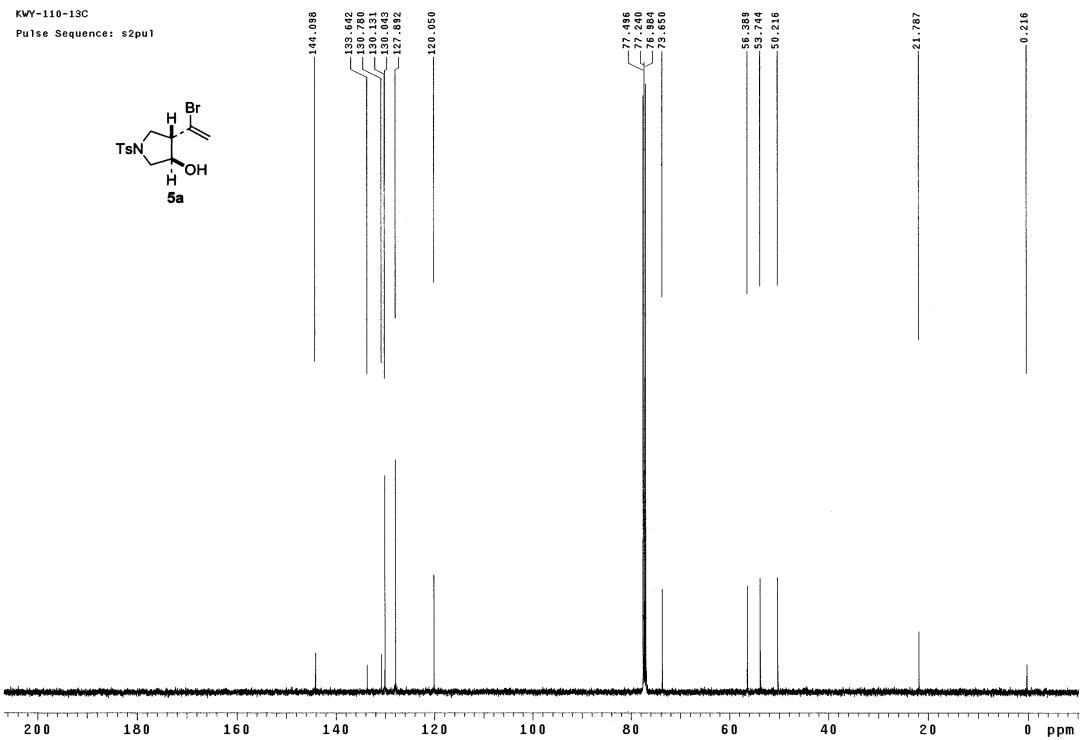




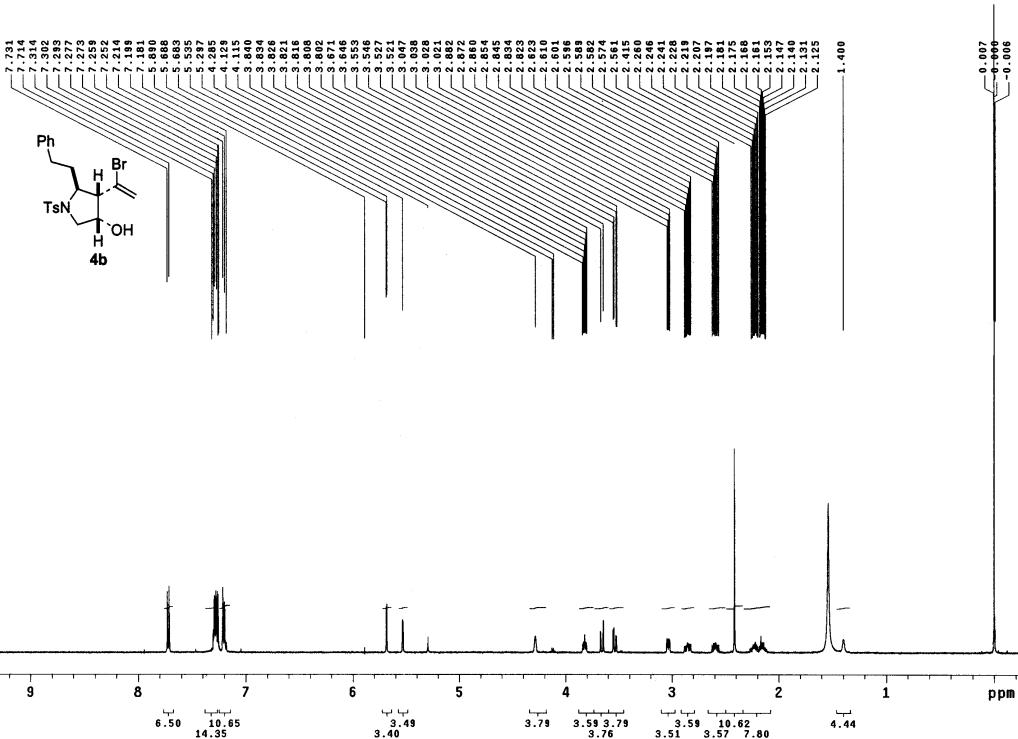
KWY-110
Pulse Sequence: s2pul



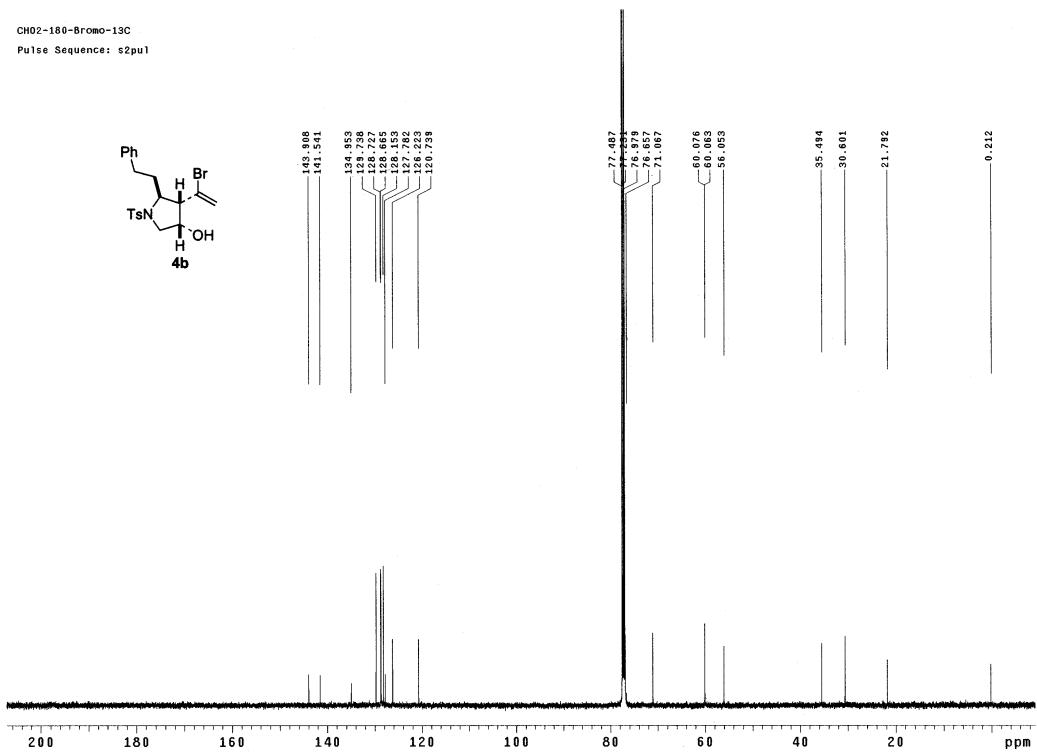
KWY-110-13C
Pulse Sequence: s2pul



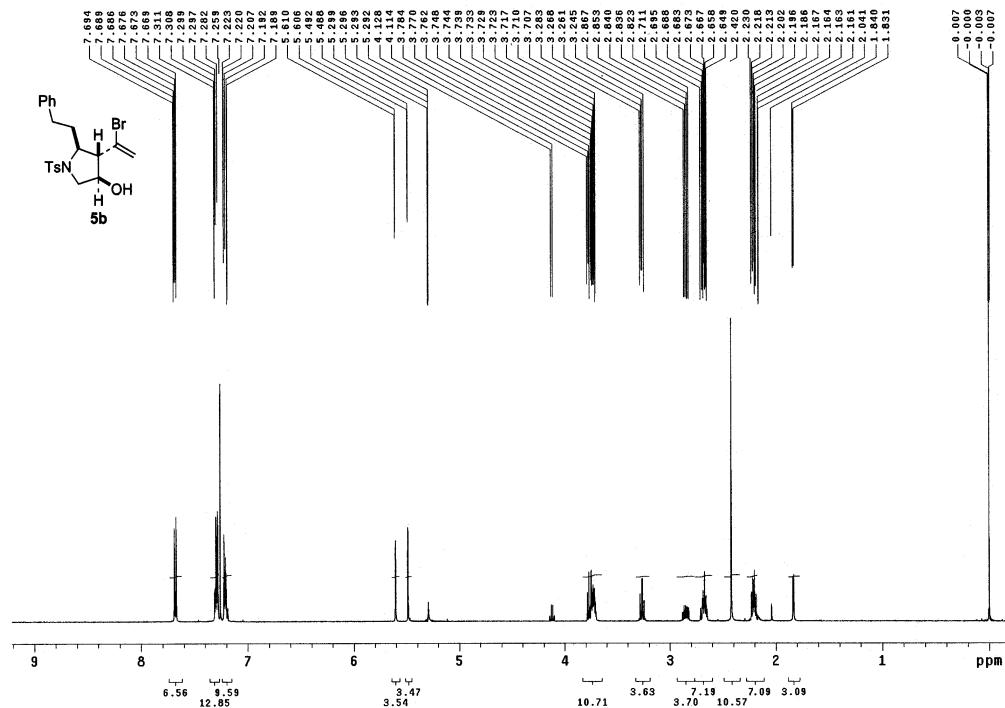
CH02-180-Bromo
Pulse Sequence: s2pu1



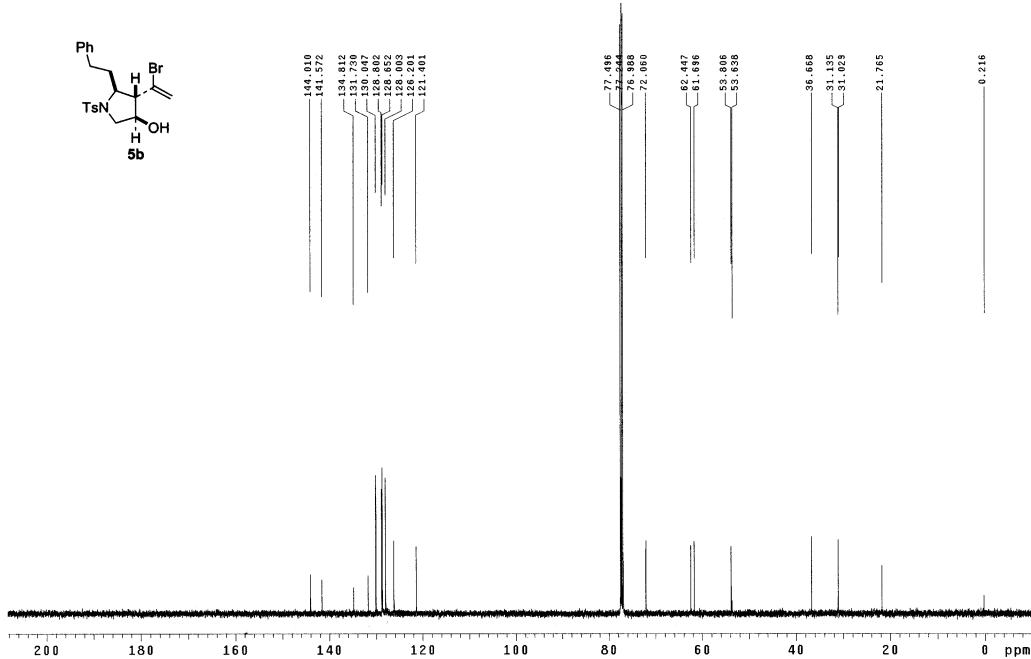
CH02-180-Bromo-13C
Pulse Sequence: s2pul



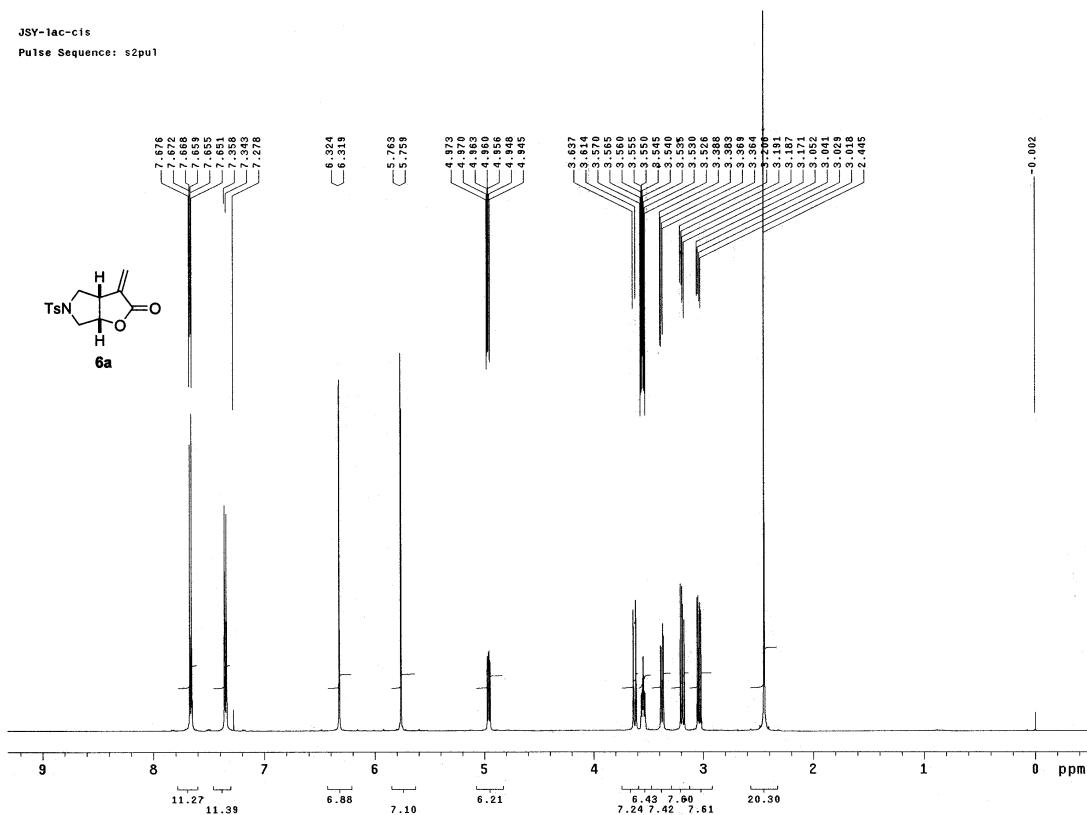
CHO2-194-Bromo
Pulse Sequence: s2pul



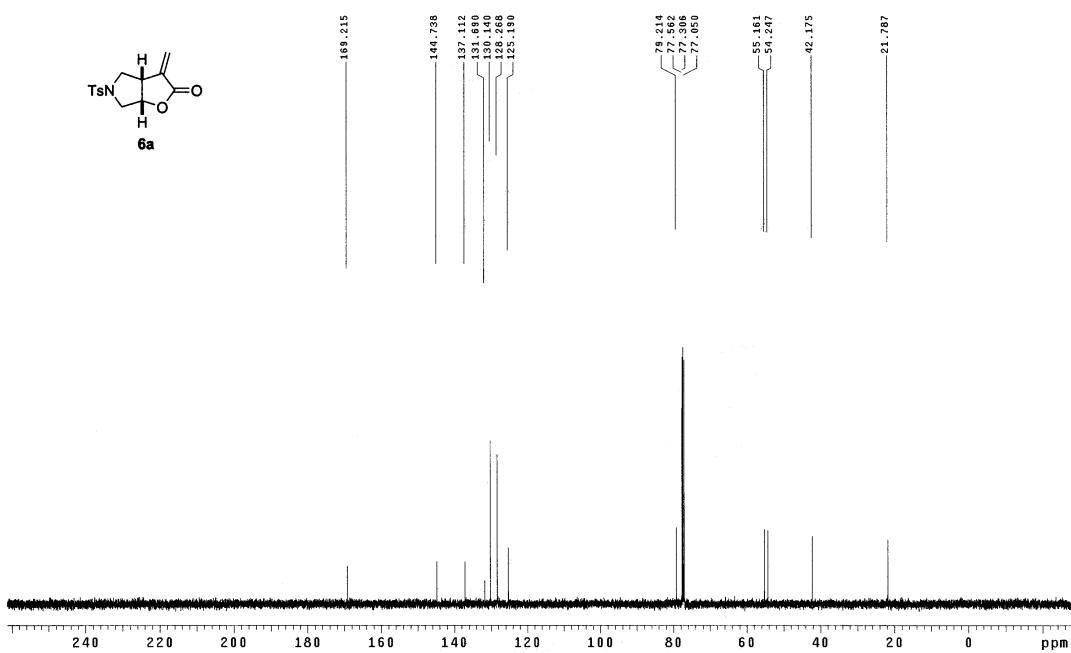
CHO2-194-Bromo-13C
Pulse Sequence: s2pul



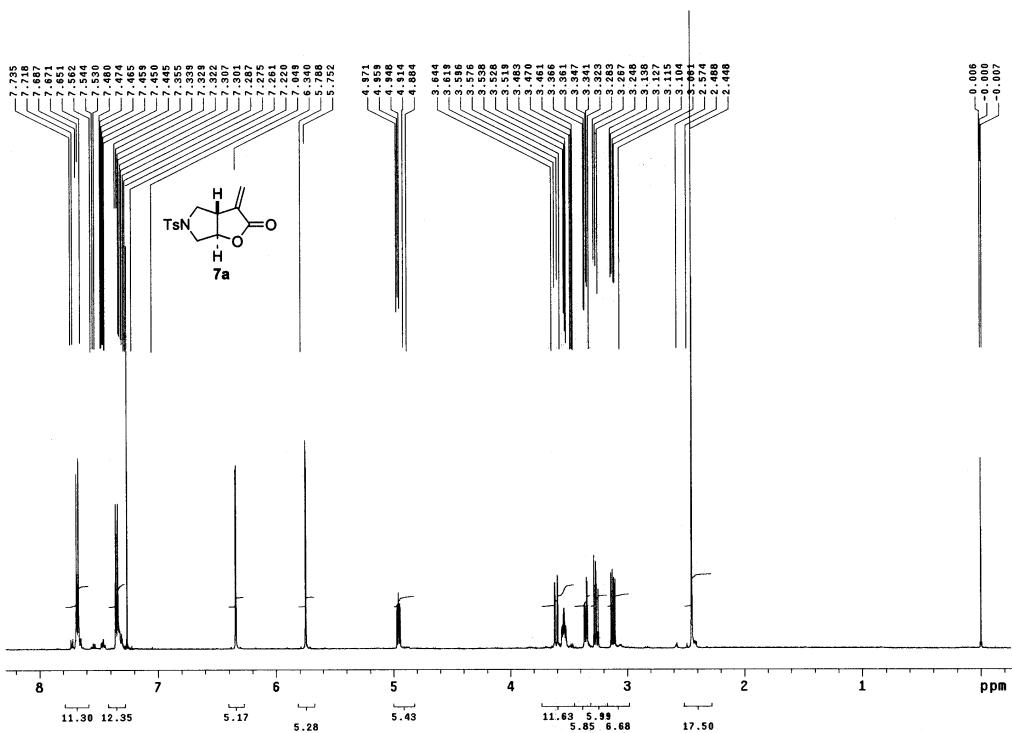
JSY-lac-cis
Pulse Sequence: s2pul



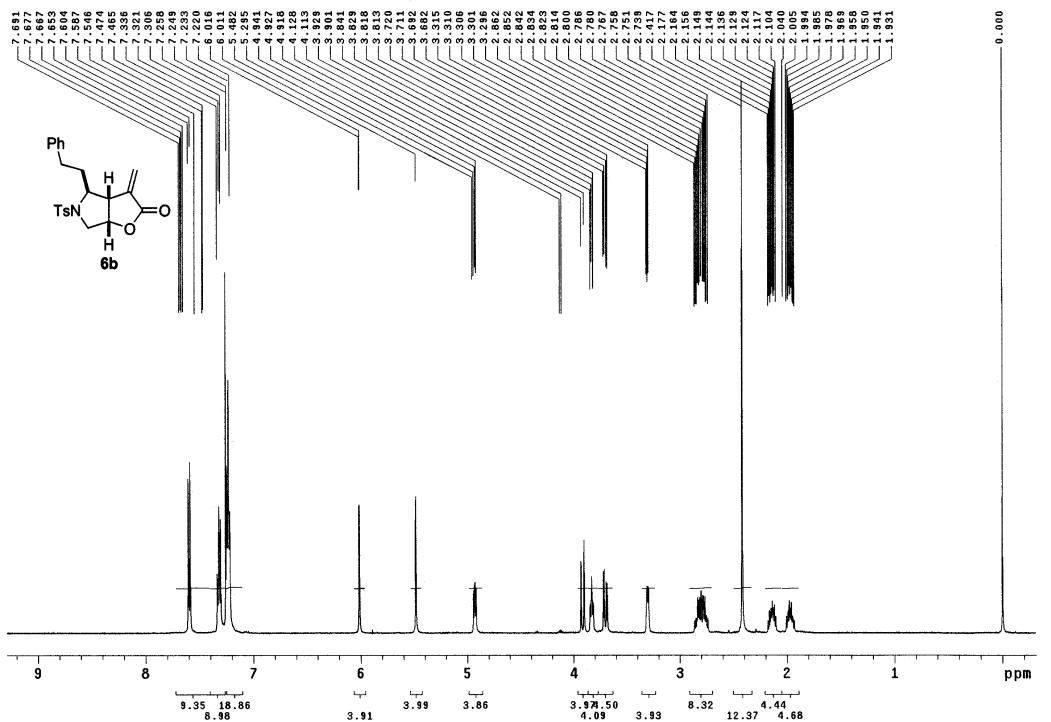
JSY-lac-cis-¹³C
Pulse Sequence: s2pul



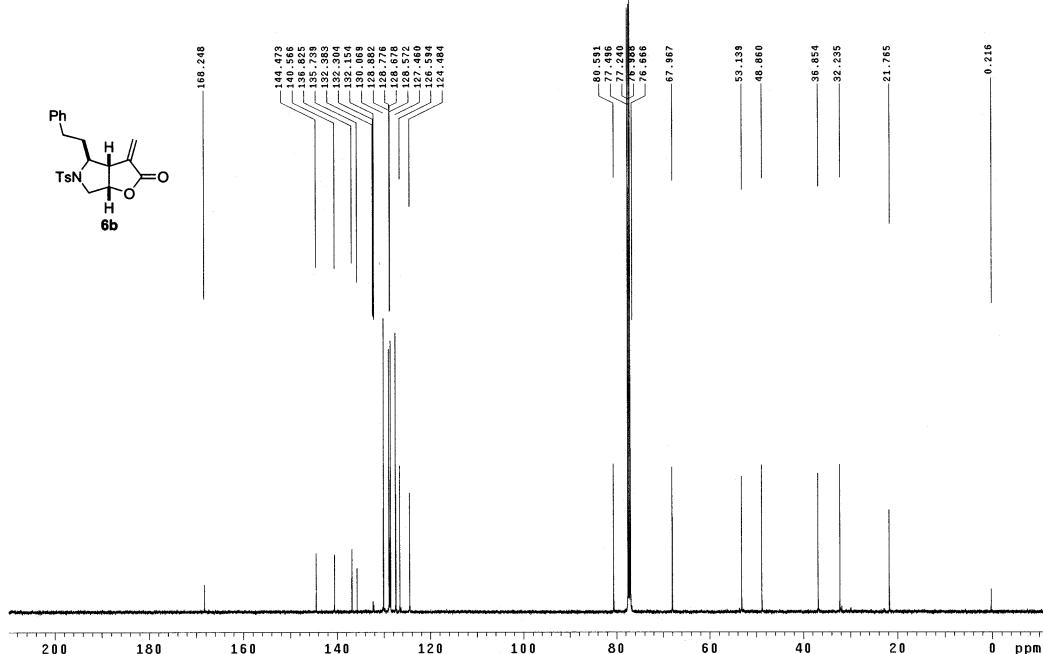
Pulse Sequence: s2pul



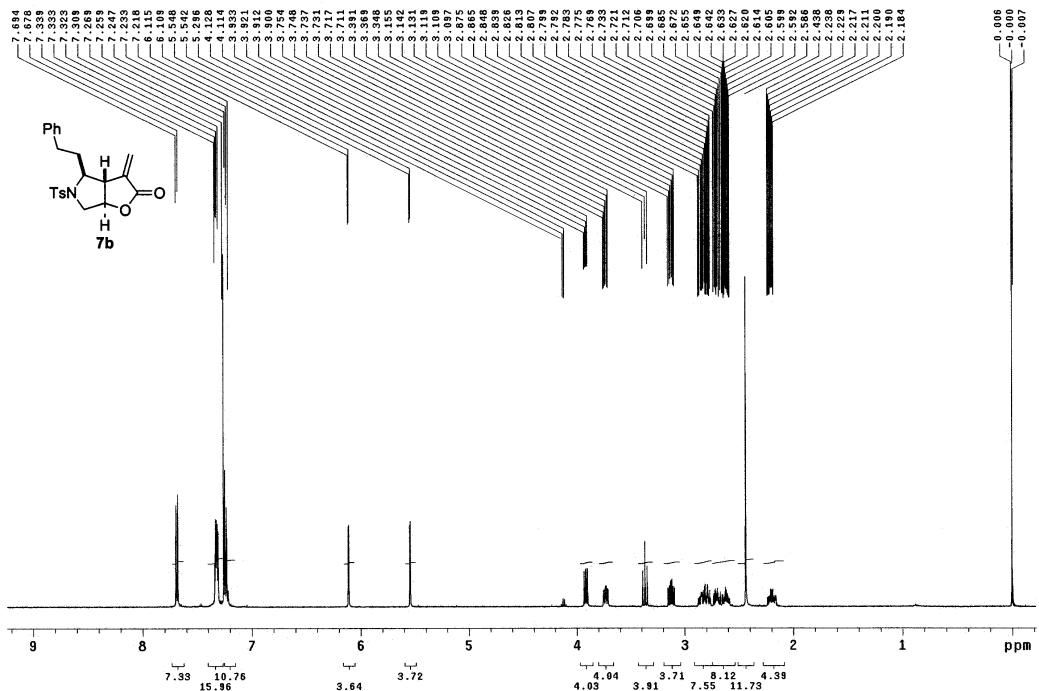
CH02-190-Lactone
Pulse Sequence: s2pul



CH02-190-Lactone-¹³C
Pulse Sequence: s2pul



CH02-195-Lactone
Pulse Sequence: s2pul



CH02-195-Lactone-13C

