SUPPORTING INFORMATION

Exploiting the Ring Strain in Bicyclo[2.2.1]heptane Systems for the Stereoselective Preparation of Highly Functionalized Cyclopentene, Dihydrofuran, Pyrroline and Pyrrolidine Scaffolds

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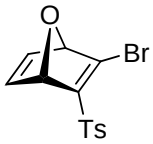
General Procedures.

Optical rotations were measured in a 1.0 cm or 1 dm tube with a Jasco P-2000 spectropolarimeter. ^{1}H and ^{13}C NMR spectra were obtained for solutions in $CDCl_3$, [d_6]DMSO and CD_3OD. All the assignments were confirmed by two-dimensional NMR experiments. The FAB mass spectra were obtained using glycerol or 3-nitrobenzyl alcohol as the matrix. TLC was performed on silica gel HF_{254} (Merck), with detection by UV light charring with H_2SO_4 or with Pancaldi reagent [$(NH_4)_6MoO_4$, $Ce(SO_4)_2$, H_2SO_4, H_2O]. Silica gel 60 (Merck, 230 mesh) was used for preparative chromatography.

General strategy for the synthesis of 7-aza/oxa/carbabicyclo[2.2.1]hepta-2,5-diene derivatives 4,5 and 6.

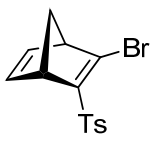
To a stirred solution of *p*-tolyl-2-bromoethynyl sulfone **3**[1] (1 mmol) in anhydrous toluene (3 mL) the corresponding diene (12 eq) was added. For X = CH_2, the diene was distilled over a solution of alkyne **3** in dry toluene. The mixture was heated (90 ºC (for X = NBoc), 45 ºC (for X = O) and 25 ºC (for X = CH_2)) until the reaction was completed. The solvent was removed and the residue purified by chromatography column on silica gel.

(±)-2-Bromo-3-(*p*-toluenesulfonyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (5)



The cycloaddition of **3** with furan following the general procedure afforded, after chromatographic purification (AcOEt/petroleum ether, 1:6), compound **5** (91% yield). ^{1}H RMN (300 MHz, $CDCl_3$, 298 K, δ ppm, *J* Hz) δ 7.78 (m, 2H, H-Ts), 7.36 (m, 2H, H-Ts), 7.10-7.04 (m, 2H, H-5, H-6), 5.57 (m, 1H, H-1 or H-4), 5.34 (m, 1H, H-1 or H-4), 2.45 (s, 3H, C*H*$_3$ of Ts). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 150.7, 146.2, 145.5, 136.3 (C-Ar, C-2, C-3), 143.9, 140.4 (C-5, C-6), 130.2, 127.9 (C-Ar), 90.6, 85.4 (C-1, C-4), 21.9 (*C*H$_3$ of Ts). CIMS *m/z* 329 [5%, $(M+H)^+$], 326 [5%, $(M+H)^+$].CIHRMS *m/z* found 328.9692, calcd. for $C_{13}H_{12}O_3SBr(81)$ $(M+H)^+$: 328.9670 and *m/z* found 326.9692, calcd. for $C_{13}H_{12}O_3SBr(79)$ $(M+H)^+$: 326.9691

(±)-2-Bromo-3-(*p*-toluenesulfonyl)bicyclo[2.2.1]hepta-2,5-diene (6)

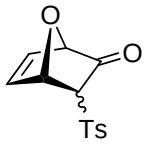


The cycloaddition of **3** with cyclopentadiene following the general procedure afforded, after chromatographic purification (ether/petroleum ether, 1:3), compound **6** (97% yield).

[1] Zhang, C.; Ballay II, C. J.; Trudell, M. L. *J. Chem. Soc., Perkin Trans. 1* **1999**, 675.

^{1}H RMN (300 MHz, $CDCl_3$, 298 K, δ ppm, *J* Hz) δ 7.75 (m, 2H, H-Ts), 7.31 (m, 2H, H-Ts), 6.68 (br. dd, 1H, *J* = 4.8, *J* = 3.1, H-5 or H-6), 6.61 (br. dd, 1H, *J* = 4.8, *J* = 2.9, H-5 or H-6), 3.93 (m, 1H, H-1 or H-4), 3.72 (m, 1H, H-1 or H-4), 2.43 (s, 3H, C*H*$_3$ of Ts), 2.34 (dt, 1H, J = 6.8, J = 1.6, H-7a), 2.34 (dt, 1H, J = 6.8, J = 1.7, H-7b). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 149.5, 145.4, 144.7, 136.8 (C-Ar, C-2, C-3), 142.3, 139.4 (C-5, C-6), 129.9, 127.8 (C-Ar), 71.7 (c-7), 62.4, 53.6 (C-1, C-4), 21.8 (*C*H_3 of Ts). CIMS *m/z* 325 [50%, $(M+H)^+$], 327 [50%, $(M+H)^+$]. CIHRMS *m/z* found 324.9898, calcd. for $C_{14}H_{14}O_2SBr(79)$ $(M+H)^+$: 324.9898 and *m/z* found 326.9863, calcd. for $C_{14}H_{14}O_2SBr(81)$ $(M+H)^+$: 324.9877.

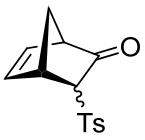
(±)-3-*endo* and 3-*exo*-(*p*-Toluenesulfonyl)-7-oxabicyclo[2.2.1]hept-5-en-2-one (7)



To a solution of **5** (1.62 g, 4.95 mmoles) in anhydrous CH_3CN (22 mL) was added Et_3N (3.62 mL) followed by a slowly addition of a solution of Et_2NH (580 μL) in anhydrous CH_3CN (12 mL). The reaction was stirred for 1.5 h. at room temperature. An aqueous solution of HCl (10 %, 18 mL) was added and the mixture was stirred for 3.5 h. at r.t. The solution was diluted with CH_2Cl_2 and washed with water. The aqueous phase was extracted with CH_2Cl_2 and dried over Na_2SO_4, concentrated and purified by chromatography column on silica gel (CH_2Cl_2, acetone, 50:1) to give **7** (1.26 g, 4.77 mmoles, 97%) as a mixture of isomers (*endo*/*exo* = 1).

^{1}H RMN (300 MHz, $CDCl_3$, 298 K, δ ppm, *J* Hz, mixture of isomers a/b: 1/1) δ 7.82-7.78 (m, 4H, H-Ts(a), H-Ts(b)), 7.39-7.34 (m, 4H, H-Ts(a), H-Ts(b)), 7.02 (dd, 1H, $J_{5,6}$ = 5.7, $J_{5,4}$ = 1.6, H-5a), 6.76 (dd, 1H, $J_{5,6}$ = 5.7 , $J_{5,4}$ = 1.7, H-5b), 6.59 (br. dd, 1H, $J_{6,1}$ = 1.8, H-6b), 6.55 (m, 1H, H-6a), 5.81 (m, 1H, H-4b), 5.49 (m H-4a), 4.77 (dd, 1H, $J_{1,6}$ = 2.1, $J_{1,4}$ = 0.9, H-1a), 4.56 (m, 1H, H-1b), 4.04 (br. d, 1H, $J_{3,4}$ = 4.2, H-3a), 3.49 (s, 1H, H-3b), 2.46, 2.45 (2s, 6H, C*H*$_3$ of Ts (a), C*H*$_3$ of Ts (b)). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 195.3, 194.3 (CO(a), CO(b)), 145.7 (C-Ar), 141.2 (C-5b), 139.9 (C-5a), 136.0, 135.5 (C-Ar), 134.1 (C-6b), 130.45 (C-6a), 130.1, 130.0, 129.3, 128.7 (C-Ar), 83.7 (C-1a), 81.9 (C-1b), 81.0 (C-4b), 79.6 (C-4a), 65.1 (C-3a), 64.3 (C-3b), 21.9 (*C*H_3 of Ts (a), *C*H_3 of Ts (b)). CIMS *m/z* 265 [4%, $(M+H)^+$]. CIHRMS *m/z* found 265.0534, calcd. for $C_{13}H_{13}O_4S$ $(M+H)^+$: 265.0535

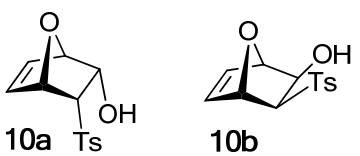
(±)-3-*endo*- and 3-*exo*-(*p*-Toluenesulfonyl)bicyclo[2.2.1]hept-5-en-2-one (8)



To a solution of **6** (304 mg, 0.938 mmoles) in anhydrous CH_3CN (4.2 mL) was added Et_3N (0.7 mL) followed by a slowly addition of a solution of Et_2NH (107 μL) in anhydrous CH_3CN (2.3 mL). The reaction was stirred for 7 h. at 50 ºC. An aqueous solution of HCl (10 %, 3.5 mL) was added and the mixture was stirred for 3.5 h. at r.t. The solution was diluted with CH_2Cl_2 and washed with water. The aqueous phase was extracted with CH_2Cl_2 and dried over Na_2SO_4, concentrated and purified by chromatography column on silica gel (AcOEt/petroleum ether, 1:4) to give **8** (203 mg, 83%) as a mixture of isomers (*endo*/*exo* = 2.6) as a white solid.

^{1}H RMN (300 MHz, $CDCl_3$, 298 K, δ ppm, *J* Hz, mixture of isomers a and b, a/b = 2.6/1) δ 7.79-7.74 (m, 4H, H-Ts(a), H-Ts(b)), 7.35-7.30 (m, 4H, H-Ts(a), H-Ts(b)), 6.70 (dd, 1H, $J_{6,5}$ = 5.4, $J_{6,1}$ = 2.6, H-6b), 6.55 (dd, 1H, $J_{6.5}$ = 5.4, $J_{6,1}$ = 3.0, H-6a), 6.24 (dd, 1H, $J_{5,4}$ = 3.3, H-5a), 6.07 (m, 1H, H-5b), 3.82 (d, 1H, $J_{3,4}$ = 3.0, H-3b), 3.69 (br. s, 1H, H-1a), 3.44 (m, 1H, H-1b), 3.40 (d, 1H, H-4a), 3.15 (m, 1H, H-4b), 3.10 (m, 1H, H-3a), 2.86 (br. d, 1H, $J_{H,H}$ = 10.0, H-7(a)), 2.43, 2.41 (2s, 6H, C*H*$_3$ of Ts(a), C*H*$_3$ of Ts(b)), 2.18-10 (m, 2H, H-7(a), H-7(b)), 1.86 (d, 1H, $J_{H,H}$ = 9.8, H-7(b)). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 201.9, 200.1 (CO(a), CO(b)), 145.2, 145.0 (C-Ar), 142.5 (C-6a), 139.9 (C-6b), 136.4 (C-Ar), 136.3, 135.3, 129.9, 129.7, 129.2, 128.8, 128.7 (C-Ar, C-5b), 69.0 (C-3b), 66.0 (C-4[a]), 56.7 (C-4b), 55.2 (C-3a), 48.1 (C-7b), 46.9 (C-7a), 43.6 (C-1a), 43.0 (C-1b), 21.7 (*C*H$_3$ of Ts (a), *C*H$_3$ of Ts (b)). CIMS *m/z* 263 [100%, $(M+H)^+$]. CIHRMS *m/z* found 263.0737, calcd. for $C_{14}H_{15}O_3S$ $(M+H)^+$: 263.0742

(±)-3-*endo*-(*p*-Toluenesulfonyl)-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (10a) and (±)-3-*exo*-(*p*-Toluenesulfonyl)-7-oxabicyclo[2.2.1]hept-5-en-2-*exo*-ol (10b).



To a solution of **7** (294.8 mg, 1.14 mmoles) in anhydrous THF (7 mL) at -78 ºC was added a solution of $LiBH_4$ in THF (2 M, 680 μL). The mixture was stirred for 30 min at -78 ºC, then a saturated aqueous solution of NH_4Cl was added and the mixture allowed to warm to r.t. under stirring. The solution was diluted with AcOEt, washed with water and brine, and concentrated. The resulting residue was purified by column chromatography (AcOEt/petroleum ether, 1:2→1:1) to give first **(±)-10a** (142 mg, 53%) and second **(±)-10b** (42 mg, 14%).

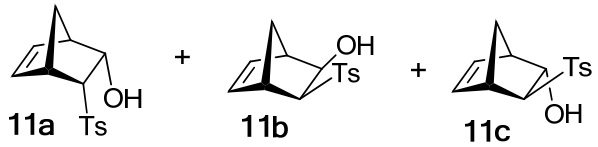
Data for **(±)-10a**:

^{1}H RMN (300 MHz, $CDCl_3$, 298 K, δ ppm, *J* Hz) δ 7.83 (d, 2H, *J* = 8.3, H-Ts), 7.38 (d, 2H, H-Ts), 6.90 (br. dd, 1H, $J_{5,6}$ = 5.9, $J_{5,4}$ = 1.7, H-5), 6.68 (br. dd, 1H, $J_{6.1}$ = 1.7, H-6), 5.17 (m, 1H, H-4), 5.03 (m, 1H, H-1), 4.57 (ddd, 1H, $J_{2,OH}$ = 11.2, $J_{2,3}$ = 7.8, $J_{2,1}$ = 4.4, H-6), 3.76 (dd, 1H, $J_{3,4}$ = 4.3, H-5), 3.23 (d, 1H, OH), 2.46 (s, 3H, C*H*$_3$ of Ts). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 145.4, 137.4 (C-Ar), 136.6 (C-5), 134.9 (C-6), 130.2. 128.1 (C-Ar), 81.5 (C-1), 79.9 (C-4), 70.6 (C-2), 65.3 (C-3), 21.8 (*C*H$_3$ of Ts). CIMS *m/z* 267 [4%, $(M+H)^+$]. CIHRMS *m/z* found 267.0688, calcd. for $C_{13}H_{15}O_4S$ $(M+H)^+$: 267.0691

Data for **(±)-10b**:

^{1}H RMN (300 MHz, $CDCl_3$, 298 K, δ ppm, *J* Hz) δ 7.87 (d, 2H, *J* = 8.3. H-Ts), 7.36 (d, 2H, H-Ts), 6.46 (dd, 1H, *J* = 5.8, *J* = 1.5, H-5 or H-6), 6.41 (dd, 1H, *J* = 5.8, *J* = 1.6, H-5 or H-6), 5.49 (m, 1H, H-1 or H-4), 4.87 (m, 1H, H-1 or H-4), 4.11 (dd, 1H, $J_{2,OH}$ = 11.0, $J_{2,3}$ = 6.1, H-2), 3.60 (d, 1H, OH), 3.26 (d, 1H, H-3), 2.45 (s, 3H, C*H*$_3$ of Ts). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 145.2 (C-Ar), 138.3 (C-5 or C-6), 136.7 (C-Ar), 135.5 (C-5 or C-6), 130.0, 128.8 (C-Ar), 86.1 (C-1 or C-4), 78.8 (C-1 or C-4), 71.2 (C-2), 65.5 (C-3), 21.8 (*C*H$_3$ of Ts). CIMS *m/z* 267 [5%, $(M+H)^+$], 249 [23%, $(M-OH)^+$]. CIHRMS *m/z* found 267.0699, calcd. for $C_{13}H_{15}O_4S$ $(M+H)^+$: 267.0691.

3-(*p*-Toluenesulfonyl)bicyclo[2.2.1]hept-5-en-2-ols (±)-11a, (±)-11b and (±)-11c.



To a solution of **8** (286 mg, 1.09 mmoles) in anhydrous THF (5 mL) at -78 ºC was added a solution of $LiBH_4$ in THF (2 M, 0.54 mL). The mixture was stirred for 15 min at -78 ºC, then a saturated aqueous solution of NH_4Cl was added and the mixture allowed to warm to r.t. under stirring. The solution was diluted with AcOEt, washed with water and brine, and concentrated. The resulting residue was purified by column chromatography (CH_2Cl_2→CH_2Cl_2:Acetone (20:1)) to give first a mixture of **(±)-11a** and **(±)-11b** (164 mg, 57%, **11a**/**11b** = 1.4) and second **(±)-11c** (76 mg, 27%).

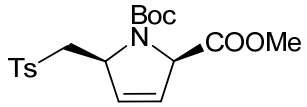
Data for **11a** + **11b**:

^{1}H RMN (300 MHz, $CDCl_3$, 298 K, δ ppm, *J* Hz, mixture of isomers a+b) δ 7.77 (d, 2H, *J* = 8.3. H-Ts(b)), 7.75 (d, 2H, *J* = 8.3. H-Ts(a)), 7.27 (d, 2H, *J* = 8.3. H-Ts(a+b)), 6.53 (dd, 1H, $J_{5,6}$ = 5.7, $J_{1,6}$ = 2.9, H-6(a)), 6.24 (dd, 1H, $J_{5,6}$ = 5.7, $J_{4,5}$ = 3.1, H-5(a)), 6.1 (m, 2H, H-5(b) and H-6(b)), 4.56 (ddd, 1H, $J_{2,OH}$ = 11.0, $J_{2,3}$ = 7.8, $J_{1,2}$ = 3.8, H-2), 4.10 (br t, 1H, $J_{2,OH}$ = $J_{2,3}$ = 6.1, H-2(b)), 3.52 (dd, 1H, $J_{3,4}$ = 3.0, $J_{2,3}$ = 7.8, H-3(a)), 3.38 (d, 1H, $J_{2,OH}$ = 6.3, OH(b)), 3.16 (br s, 1H, H-4(a)), 3.10 (br s, 2H, H-1(a) and H-4(b)), 3.03 (dd, 1H, $J_{2,3}$ = 6.3, $J_{3,7b}$ = 1.5, H-3(b)), 2.95 (d, 1H, $J_{2,OH}$ = 11.0, OH(a)), 2.80 (br s, 1H, H-1(b)), 2.37 (s, 6H, CH_3 of Ts(a) and CH_3 of Ts(b)), 2.22 (br d, 1H, $J_{7a,7b}$ = 9.5, H-7a(b)), 1.57 (dt, 1H, $J_{7a,7b}$ = 9.5, $J_{7b,2}$ = $J_{7b,3}$ = 1.5, H-7b(b)), 1.50 (br d, 1H, $J_{7a,7b}$ = 9.4, H-7a(a)), 1.16 (d, 1H, $J_{7a,7b}$ = 9.4, H-7b(a)). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 144.6 (C-1 of Ts(b)), 144.5 (C-1 of Ts(a)), 138.9 (C-5(b)), 137.7 (C-4 of Ts(b)), 137.2 (C-6(b)), 136.9 (C-6(a)), 133.5 (C-5(a)), 129.8, 128.5, 128.2 (C-2, C-3, C-5, C-6 of Ts(a+b), C-4 of Ts(a)), 73.7 (C-2(a)), 73.0 (C-2(b)), 68.0 (C-3(a)), 66.8 (C-3(b)), 49.6 (C-1(b)), 49.5 (C-1(a)), 46.4 (C-7(a)), 45.8 (C-4(a)), 44.1 (C-7(b)), 44.0 (C-4(b)), 21.6 (CH_3 of Ts(a+b)). FABMS *m/z* 287 [100%, $(M+Na)^+$]. FABHRMS *m/z* found 287.0718, calcd. for $C_{14}H_{16}O_3SNa$ $(M+Na)^+$: 287.0718.

Data for **11c**:

^{1}H RMN (300 MHz, $CDCl_3$, 298 K, δ ppm, *J* Hz) δ 7.73 (d, 2H, *J* = 8.3. H-2 and H-6 of Ts), 7.29 (d, 2H, *J* = 8.3. H-3 and H-5 of Ts), 6.29 (dd, 1H, $J_{5,6}$ = 5.7, $J_{4,5}$ = 3.2, H-5), 6.21 (dd, 1H, $J_{5,6}$ = 5.7, $J_{1,6}$ = 2.9, H-6), 4.77 (dt, 1H, $J_{2,OH}$ = 6.2, $J_{1,2}$ = $J_{2,3}$ = 3.6, H-2), 3.02 (br s, 1H, H-4), 2.99 (br s, 1H, H-1), 2.57 (dd, 1H, $J_{2,3}$ = 3.6 $J_{3,7b}$ = 2.4, H-3), 2.38 (s, 3H, CH_3 of Ts), 1.99 (br d, 1H, $J_{7a,7b}$ = 9.5, H-7a), 1.89 (d, 1H, $J_{2,OH}$ = 6.2, OH), 1.48 (dq, 1H, $J_{7a,7b}$ = 9.5, $J_{7b,1}$ = $J_{7b,4}$ = $J_{7b,3}$ = 2.4, H-7b). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 144.7 (C-1 of Ts), 138.1 (C-5), 136.4 (C-4 of Ts), 136.2 (C-6), 74.0 (C-2), 73.4 (C-3), 47.9 (C-1), 45.2 (C-4), 45.1 (C-7), 21.6 (CH_3 of Ts). FABMS *m/z* 287 [100%, $(M+Na)^+$]. FABHRMS *m/z* found 287.0724, calcd. for $C_{14}H_{16}O_3SNa$ $(M+Na)^+$: 287.0718.

(±)-(2*RS*,5*SR*)-*N*-*tert*-Butoxycarbonyl-2-methoxycarbonyl-5-(*p*-toluene-sulphonyl)methyl-3-pyrroline (2).

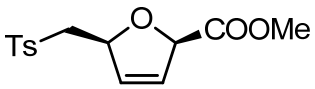


Basic catalysis-Method a: To a solution of the racemic 7-azanorbornenone **1** (100 mg, 0.275 mmol) in MeOH (3 mL), NaOMe (1.5 mg, 0.028 mmol) was added and the mixture was stirred for 45 min. at room temperature. Then, acidic resin IR-120 H^+ was added till pH 7, the resin was filtered and the solution evaporated to give pure **2** (87 mg, 82% yield) as a yellowish powder. Characterization data for this compound were in agreement with those reported previously.[2]

Acid catalysis-Method b: To a solution of the racemic 7-azanorbornenone **1** (100 mg, 0.275 mmol) in MeOH (3 mL), a solution of 10% AcOH (glacial) in MeOH (16 μl) was added and the mixture was stirred for 45 min. at room temperature. Then, the solution was evaporated to give pure **2** (107 mg, quant. yield) as a yellowish oil.

[2] Moreno-Vargas, A. J.; Schütz, C.; Scopelliti, R.; Vogel, P. *J. Org. Chem.* **2003**, *68*, 5632.

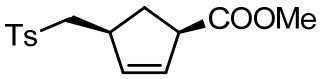
(±)-(2*RS*,5*SR*)-2-Methoxycarbonyl-5-(*p*-toluenesulphonyl)methyl-2,5-dihydrofuran (12).



This compound was synthesized using the same protocol (method a or b) that for the synthesis of **2**, except that racemic 7-oxanorbornenone **5** (mixture of epimers 1:1) was used as starting material. Pure **12** (quant. yield) was obtained as a white solid.

^{1}H RMN (300 MHz, $CDCl_3$, 298 K, δ ppm, *J* Hz) δ 7.81 (d, 2H, *J* = 8.3, H-Ts), 7.34 (d, 2H, H-Ts), 6.11 (ddd, 1H, *J* = 6.1, *J* = 2.4, *J* = 1.6, H-3 or H-4), 5.91 (dt, 1H, *J* = 6.0, *J* = 1.9, H-3 or H-4), 5.35 (m, 1H, H-5), 5.16 (m, 1H, H-2), 3.67 (dd, 1H, $J_{H,H}$ = 14.1, $J_{H,5}$ = 5.8, C*H*HTs), 3.66 (s, 3H, COOC*H*$_3$), 3.29 (dd, 1H, $J_{H,5}$ = 6.7, CH*H*Ts), 2.44 (s, 3H, C*H*$_3$ of Ts). ^{13}C NMR (75.4 MHz, $CDCl_3$, δ ppm) δ 171.0 (*C*OOCH$_3$), 144.9, 136.9 (C-Ar), 130.8 (C-3 or C-4), 129.9 (C-Ar), 128.2 (C-Ar), 126.6 (C-3 or C-4), 84.6 (C-2), 81.7 (C-5), 61.9 (*C*H$_2$Ts), 52.4 (COO*C*H$_3$), 21.8 (*C*H$_3$ of Ts). CIMS *m/z* 297 [100%, $(M+H)^+$]. CIHRMS *m/z* found 297.0797, calcd. for $C_{14}H_{17}O_5S$ $(M+H)^+$: 297.0797.

(±)-(1*RS*,4*SR*)-Methyl 4-(*p*-toluenesulphonyl)methylcyclopent-2-enecarboxylate (13).

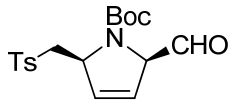


To a solution of compound **8** (53 mg, 0.202 mmol, mixture of epimers) in dry MeOH (2 mL), pyridine (17 μL, 0.21 mmol) was added and the mixture was stirred at room temperature for 24 h. Then the solution was evaporated to give pure **13** (59 mg, quant. yield) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$, 298 K, δ ppm, *J* Hz) 7.72 (d, 2H, $^3J_{2',3'} = {}^3J_{5',6'}$ = 8.2, H-2' and H-6' of Ts), 7.29 (d, 2H, H-3' and H-5'), 5.73 (m, 2H, H-2 and H-3), 3.60 (s, 3 H, COOC*H*$_3$), 3.46 (m, 1H, H-1), 3.12 (m, 3H, C*H*$_2$Ts and H-4), 2.37 (s, 3H, C*H*$_3$ of Ts), 2.30 (dt, 1H, $^2J_{5a,5b}$ = 13.8, $^3J_{5a,1} = {}^3J_{5a,4}$ = 8.5, H-5a), 1.82 (dt, 1H, $^3J_{5b,1} = {}^3J_{5b,4}$ = 5.6, H-5b). ^{13}C-NMR (75.4 MHz, $CDCl_3$, 298 K, δ ppm) 174.3 (COOMe), 144.7 (C-1' of Ts), 136.8 (C-4' of Ts), 134.8, 130.5 (C-2, C-3), 130.0, (C-2' and C-6' of Ts), 128.0 (C-3' and C-5' of Ts), 61.4 (*C*H$_2$Ts), 52.0 (COO*C*H$_3$), 50.1 (C-1), 39.7 (C-4), 32.8 (C-5), 21.6

(CH_3 of Ts). CIMS *m/z* 295 [30%, $(M+H)^+$]. HRCIMS *m/z* found 295.1013, calculated for $C_{15}H_{19}O_4S$ 295.1004.

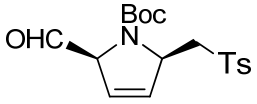
(±)-(2*RS*,5*SR*)-*N*-*tert*-Butoxycarbonyl-2-formyl-5-(*p*-toluenesulphonyl)methyl-3-pyrroline (14).



To a solution of the racemic alcohol **9**[2] (1.17 g, 3.19 mmol) in MeOH, NaOMe (43 mg, 0.8 mmol) was added and the mixture was stirred for 2 h at room temperature. Then, acidic resin IR-120 H^+ was added till pH 7, the resin was filtered and the solution concentrated to give pure **14** (1.20 g, quant.) as a yellowish oil. ^{1}H-NMR (300 MHz, DMSO-d_6, 363 K, δ ppm, *J* Hz) 9.43 (d, 1H, ^3J = 2.0, -C*H*O), 7.81 (d, 2H, $J_{2',3'} = J_{5',6'}$ = 8.2, H-2' and H-6' of Ts), 7.49 (d, 2H, $J_{2',3'} = J_{5',6'}$ = 8.2, H-3' and H-5' of Ts), 6.12 (dt, 1H, $^3J_{3,4}$ = 6.4, $^3J_{4,5} = {}^4J_{2,4}$ = 2.0, H-4*), 5.86 (br. dt, 1H, $^3J_{3,4}$ = 6.4, $^3J_{2,3} = {}^4J_{3,5}$ = 1.6, H-3*), 4.87-4.81 (m, 2H, H-2 and H-5), 3.89 (br d, 1H, ^2J = 13.9, C*H*HTs), 3.40 (dd, ^2J = 13.9, $^3J_{CHTs,5}$ = 9.5, CH*H*Ts), 2.45 (s, 3H, CH_3 of Ts), 1.35 (s, 9H, CH_3 of Bu^t). ^{13}C-NMR (75.4 MHz, DMSO-d_6, 363 K, δ ppm, *J* Hz) 198.0 (CHO), 152.2 (CO of Boc), 144.2 (C-1 of Ts), 136.7 (C-4 of Ts), 131.2 (C-3 or C-4) 129.5 (C-2 and C-6 of Ts), 127.0 (C-3 and C-5 of Ts), 123.4 (C-3 or C-4), 80.2 ($C(CH_3)_3$), 72.2 (C-2), 59.3 (CH_2Ts), 58.6 (C-5), 27.4 (($CH_3)_3$C), 20.4 (CH_3 of Ts). FABMS m/z 388 [10%, $(M+Na)^+$], 266 [60%, $(M - Boc + H)^+$]. CIMS m/z 366 [1%, $(M+H)^+$], 266 [100%, $(M - Boc + H)^+$]. HRCIMS m/z found 366.1374, calculated for $C_{18}H_{24}NO_5S$ 366.1375.

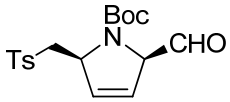
*Exchangable assignment.

(2*S*,5*R*)-*N*-*tert*-Butoxycarbonyl-2-formyl-5-(*p*-toluenesulphonyl)methyl-3-pyrroline ((-)-14).



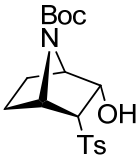
This compound was synthesized in the same manner than **(±)-14**, except that enantiomerically pure alcohol (+)-**9**[2] was used as starting material. $[\alpha]_{26}$ = -41 (0.5, $CHCl_3$).

(2*R*,5*S*)-*N*-*tert*-Butoxycarbonyl-2-formyl-5-(*p*-toluenesulphonyl)methyl-3-pyrroline ((+)-14).



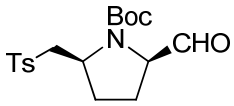
This compound was synthesized in the same manner than **(±)-14**, except that pure camphanoate (-)-**9**[2] was used as starting material. $[\alpha]_{26}$ = +43 (*c* 0.7, $CHCl_3$).

(±)-(1*RS*,2*SR*,3*RS*,4*SR*)-7-*tert*-Butoxycarbonyl-3-*endo*-(*p*-toluenesulfonyl)-7-azabicyclo[2.2.1]heptan-2-*endo*-ol (15).



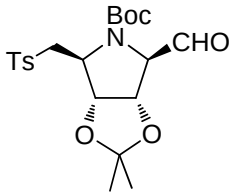
A solution of bicyclic alcohol **9** (206 mg, 0.564 mmol) in MeOH (6 mL) was hydrogenated under atmospheric pressure using Pd on charcoal (10%, 20 mg) as catalyst. The suspension was stirred for 1 h at room temperature. Then, the mixture was filtered (celite) and the filtered solution was evaporated. The resulting crude of the reaction was purified by column chromatography (AcOEt:petroleum ether, 1:3) to give pure **15** (170 mg, 82%) as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$, 298 K, δ ppm, *J* Hz) 7.75 (d, 2H, $^3J_{2',3'} = {}^3J_{5',6'}$ = 8.3, H-2' and H-6' of Ts), 7.29 (d, 2H, H-3' and H-5'), 4.35-4.20 (m, 3H, H-1, H-2 and H-4), 3.93 (d, 1H, $^3J_{2,OH}$ = 9.5, OH), 3.50 (br. dd, 1H, $^3J_{2,3}$ = 9.4, $^3J_{3,4}$ = 4.7, H-3), 2.52 (t, 1H, $^2J_{6a,6b} = {}^3J_{6a,5a}$ = 9.21, H-6a), 2.37 (s, 3H, CH_3 of Ts), 2.11 (t, 1H, $^2J_{5a,5b}$ = 8.4, $^3J_{6a,5a}$ = 9.21, H-5a), 1.72 (m, 2H, H-5b and H-6b), 1.34 (s, 9H, CH_3 of Bu^t). ^{13}C-NMR (75.4 MHz, $CDCl_3$, 298 K, δ ppm, mixture of rotamers) 154.5 (CO of carbamate), 145.2 (C-1' of Ts), 137.3 (C-4' of Ts), 130.1, 130.0 (C-2' and C-6' of Ts), 127.9, 127.8 (C-3' and C-5' of Ts), 80.8 ($C(CH_3)_3$, 70.0, 69.9 (C-2), 64.2, 64.1 (C-3), 61.3, 61.2, 59.0, 58.8 (C-1 and C-4), 28.2 (CH_3 of Ts), 24.7 (br s, C-6), 21.7, 21.6 ($(CH_3)_3C$), 20.3 (C-5). FABMS m/z 390 [100%, $(M+Na)^+$]. HRFABMS m/z found 390.1354, calculated for $C_{18}H_{25}NO_5SNa$ ($M+Na^+$) 390.1351.

(2*SR*,5*RS*)-*N*-*tert*-Butoxycarbonyl-2-formyl-5-(*p*-toluenesulphonyl)methyl-pyrrolidine (16).



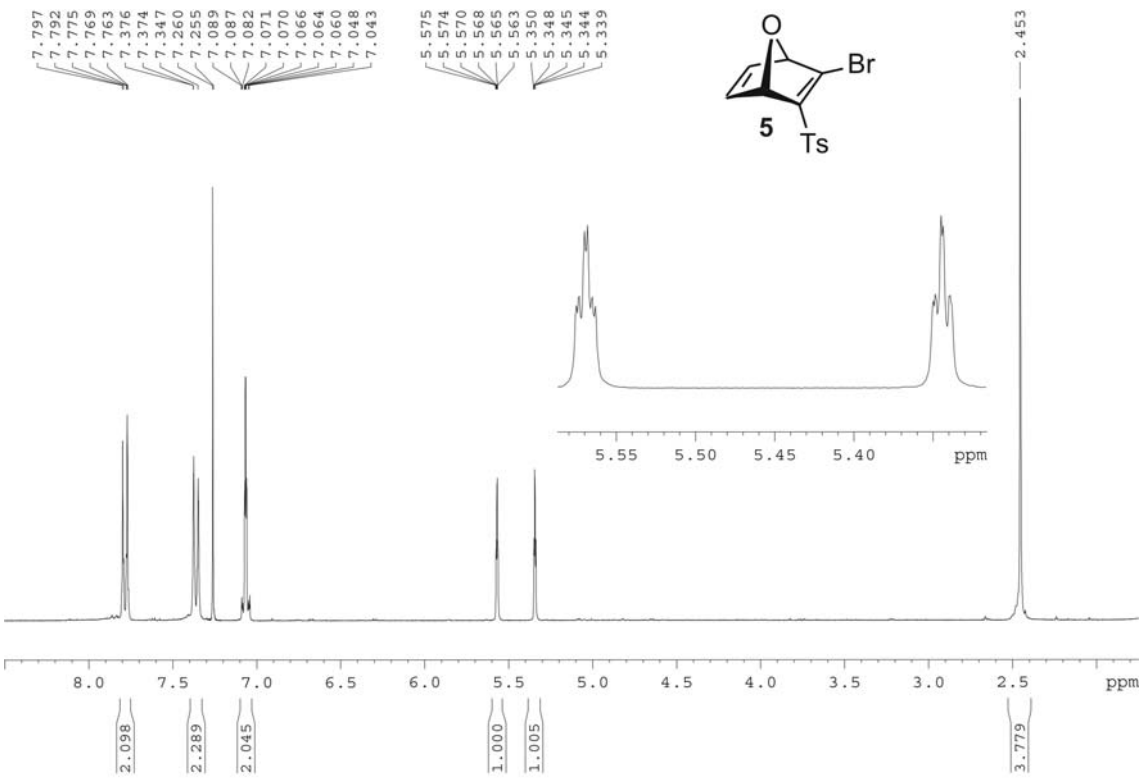
To a solution of the bicyclic alcohol **15** (59 mg, 0.159 mmol) in dry MeOH (2 mL), NaOMe (1.7 mg, 0.032mmol) was added and the mixture was stirred for 10 h at room temperature. Then, acidic resin IR-120 H^+ was added till pH 7, the resin was filtered and the solution evaporated to give pure **16** (56 mg, 96% yield) as a colorless oil. ^{1}H-NMR (300 MHz, DMSO-d_6, 363 K, δ ppm, *J* Hz, mixture of rotamers) 9.46 (d, 1 H, $^3J_{CH,2}$ = 1.92, CHO of minor rotamer), 9.37 (d, 1 H, $^3J_{CH,2}$ = 1.92, CHO of major rotamer), 7.78 (m, 2H, H-2' and H-6' of Ts), 7.47 (m, 2H, H-3' and H-5' of Ts), 4.2-4.05 (m, 2H, H-2 and H-5), 3.60 (br. d, 1H, ^2J = 13.9, C*H*HTs), 3.45 (dd, 1H, ^2J = 13.9, $^3J_{CH,5}$ = 10.2, CH*H*Ts), 244 (s, 3H, CH_3 of Ts), 2.03-1.94 (m, 4H, H-3a, H-3b, H-4a and H-4b), 1.34 (s, 9H, (C*H*$_3$)$_3$C). ^{13}C-NMR (75.4 MHz, DMSO-d_6, 363 K, δ in ppm, major rotamer) 200.0 (CHO), 152.6 (CO of carbamate), 144.0, 136.8 (C-1' and C-4' of Ts), 129.5 (C-2' and C-6'), 127.0 (C-3' and C-5'), 79.8 (C(*C*H$_3$)$_3$), 64.8 (C-2), 57.7 (*C*H$_2$Ts), 52.9 (C-5), 28.4 (C-3 or C-4), 27.4 ((*C*H$_3$)$_3$C), 23.9 (C-3 or C-4), 20.5 (CH_3 of Ts). FABMS m/z 390 [8%, $(M+Na)^+$], m/z 390 [8%, $(M+Na)^+$], m/z 290 [20%, $(M\text{-Boc}+H+Na)^+$], m/z 239 [25%, $(M\text{-Boc}+2H\text{-CHO})^+$]. HRCIMS m/z found 367.1453, calculated for $C_{18}H_{25}NO_5S$ 367.1429.

(2*SR*,3*RS*,4*SR*,5*RS*)-*N*-*tert*-Butoxycarbonyl-3,4-isopropylidenedioxy-2-formyl-5-(*p*-toluenesulphonyl)-methylpyrrolidine (18).

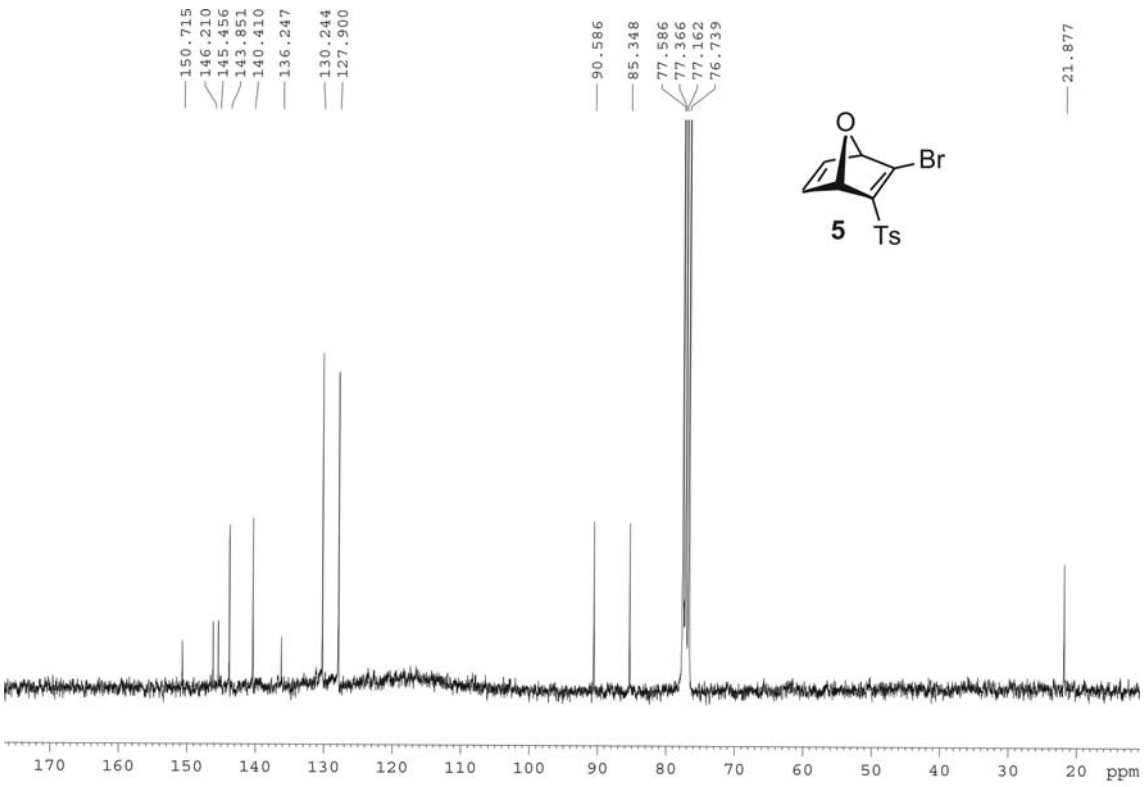


To a solution of the bicyclic alcohol **17**[2] (72 mg, 0.164 mmol) in dry MeOH (2.5 mL), NaOMe (1.8 mg, 0.034 mmol) was added and the mixture was stirred for 10 h at room temperature. Then, acidic resin IR-120 H^+ was added till pH 7, the resin was filtered and the solution evaporated to give pure **18** (68 mg, 95% yield) as a colorless oil. ^{1}H-NMR

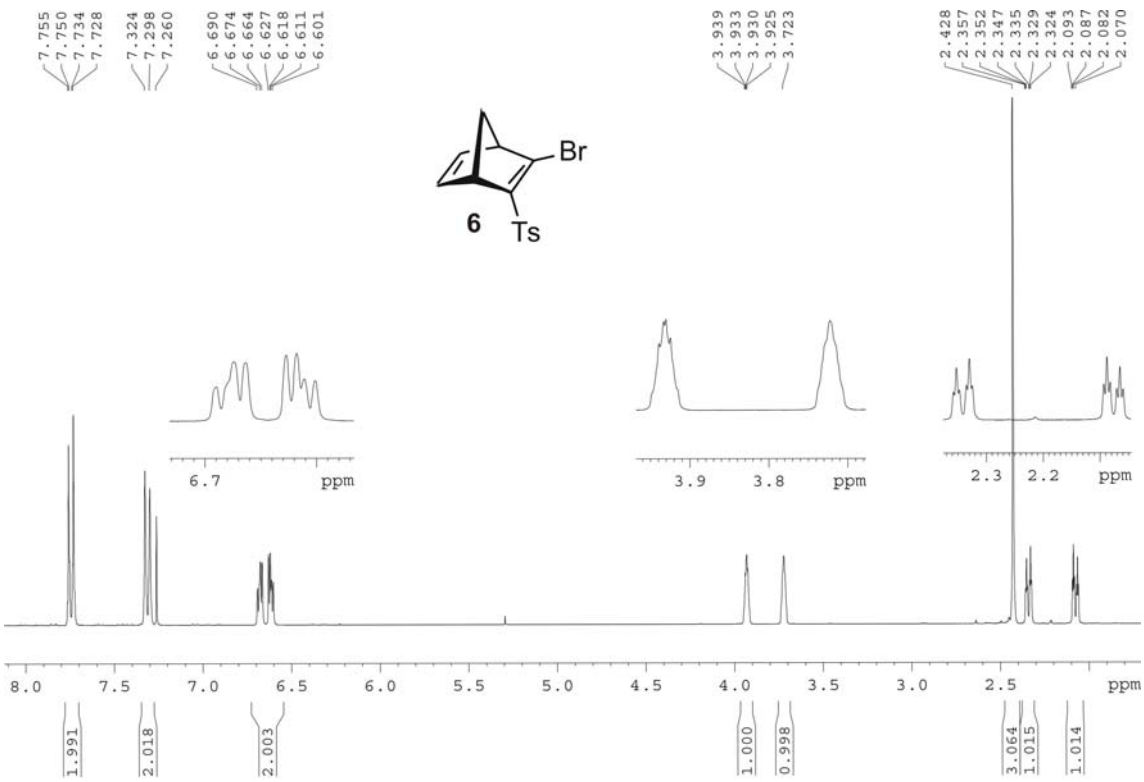
(300 MHz, DMSO-d_6, 363 K, δ ppm, *J* Hz, mixture of rotamers, data for major rotamer) 7.80 (d, 1H, *J* = 8.2, H-2 and H-6 of Ts), 7.50 (d, 1H, *J* = 8.2, H-3 and H-5 of Ts), 5.01 (dd, 1H, $J_{3,4}$ = 5.8, $J_{2,3}$ = 1.8, H-3), 4.76 (d, 1H, $J_{3,4}$ = 5.8, H-4), 4.36 (br s, 1H, H-2), 4.27 (dd, 1H, $J_{5,CHHTs}$ = 10.1, $J_{5,CHHTs}$ = 2.8, H-5), 3.49 (dd, 1H, ^2J = 14.2, $J_{5,CHHTs}$ = 10.1, CH*H*Ts), 3.38 (br d, 1 H, ^{2}J = 14.2, C*H*HTs), 2.44 (s, 3H, CH_3 of Ts), 1.40 (s, 3H, CH_3 of acetonide), 1.33 (s, 9H, CH_3 of Boc), 1.29 (s, 3H, CH_3 of acetonide). ^{13}C-NMR (75.4 MHz, DMSO-d_6, 363 K, δ in ppm, mixture of rotamers, data for major rotamer) 202.4 (CO), 152.4 (CO of carbamate), 144.3 (C-1' of Ts), 136.3 (C-4' of Ts), 129.5 (C-2' and C-6' of Ts), 127.2 (C-3' and C-5' of Ts), 111.2 (C*q* of acetonide), 82.5 (br. s, C-3 or C-4), 80.2 ($(CH_3)_3C$), 78.4 (br. s, C-3 or C-4), 72.0 (C-2), 58.7 (C-5), 55.5 (CH_2Ts), 27.3 ($(CH_3)_3$C), 26.3, 24.5 (2 CH_3 of acetonide), 20.5 (CH_3 of Ts). FABMS m/z 462 (20%, $[M+Na]^+$), 340 [25%, $(M - Boc + 2H)^+$]. HRCIMS m/z found 439.1636, calculated for $C_{21}H_{29}NO_7S$ 439.1665.



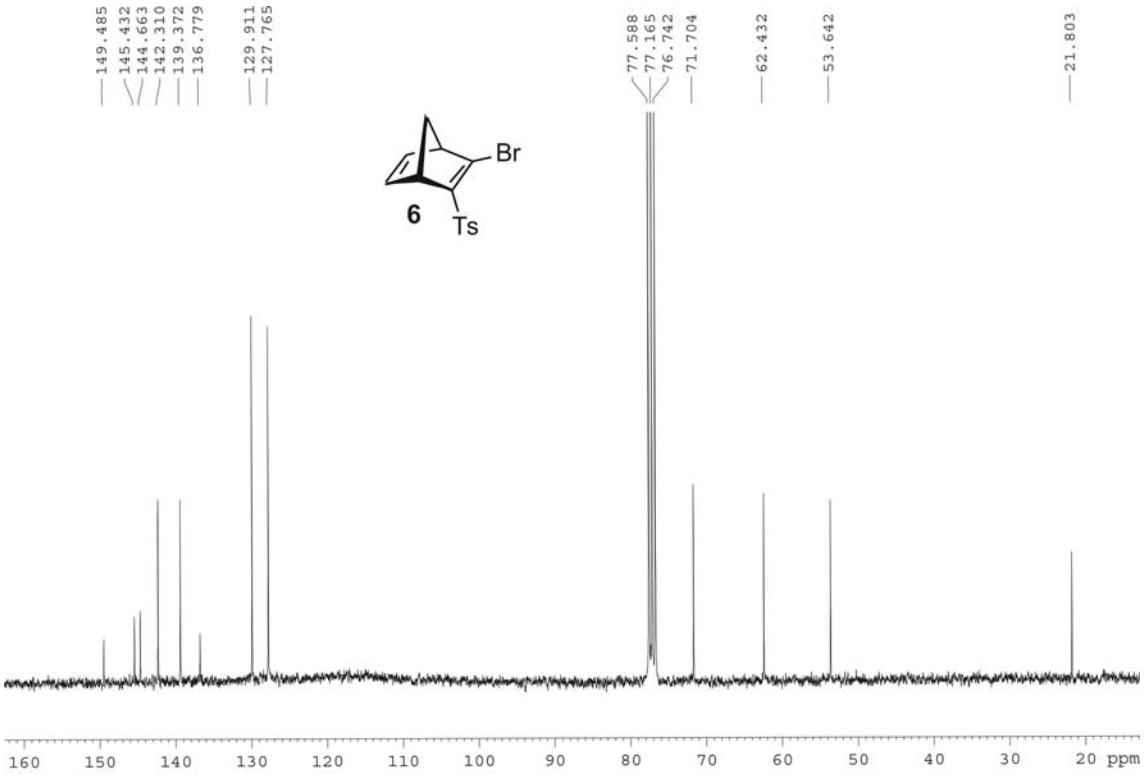
^{1}H-NMR, 300 MHz, $CDCl_3$, 25 ºC



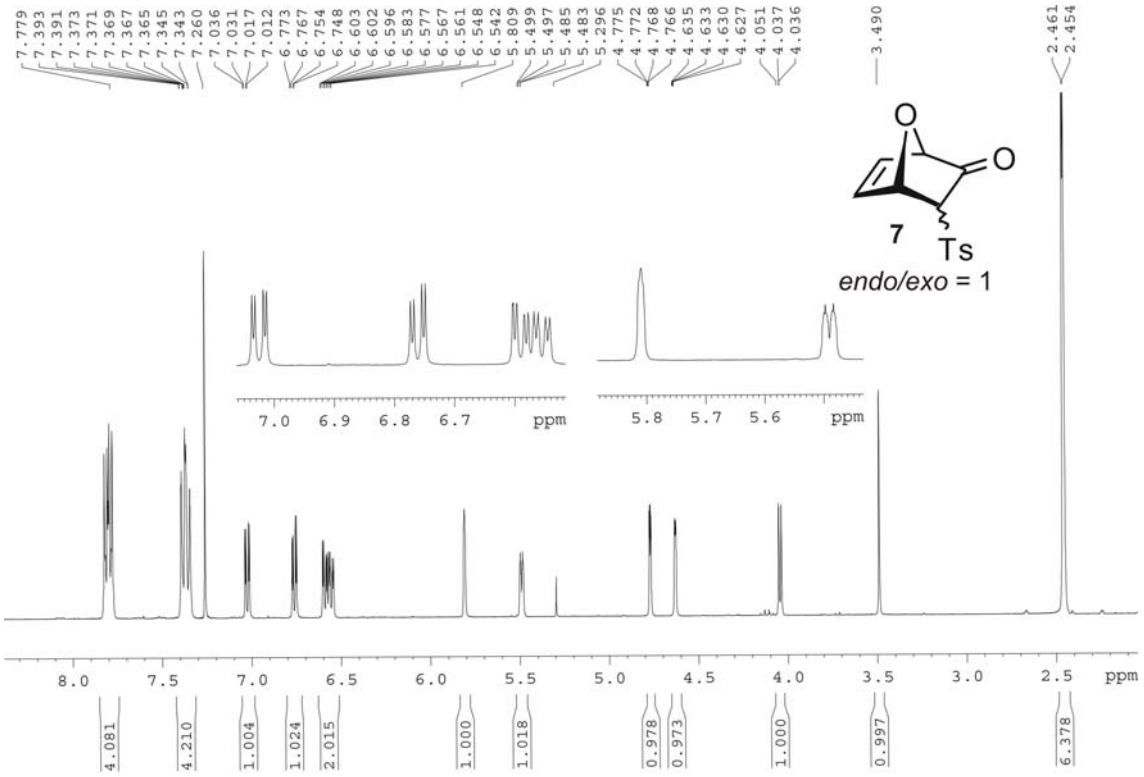
^{13}C-NMR, 75 MHz, $CDCl_3$, 25 ºC



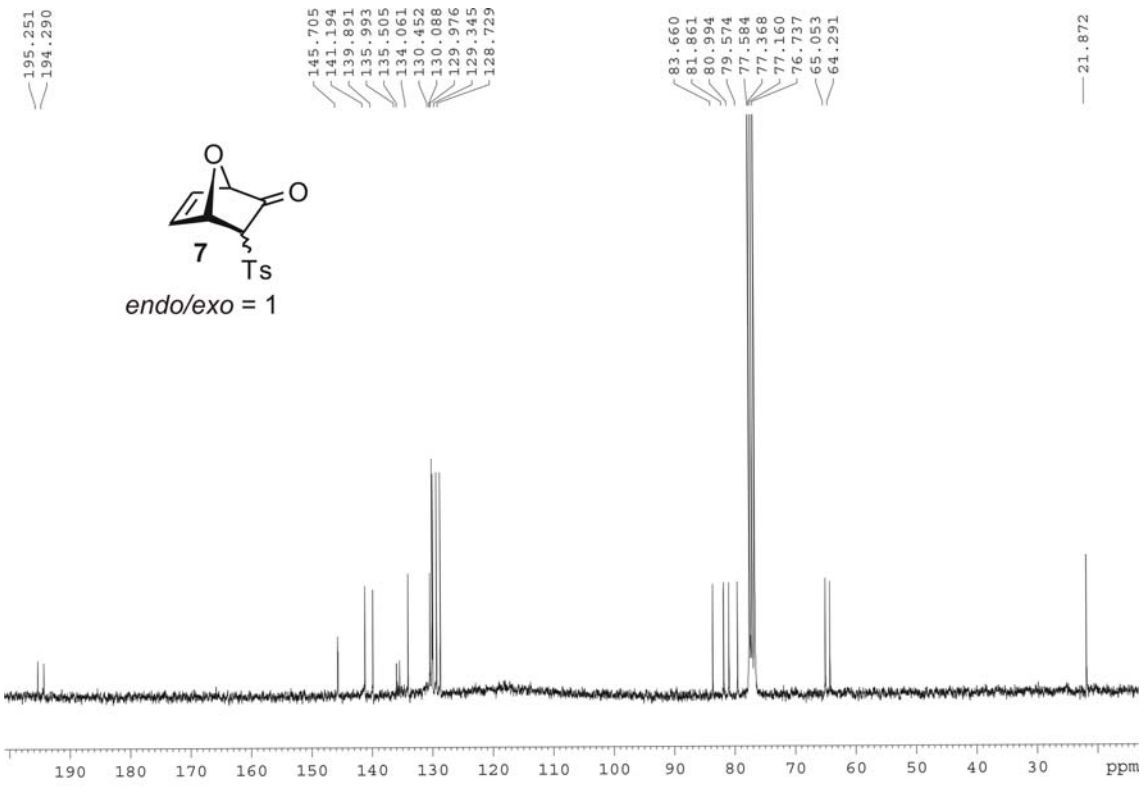
^{1}H-NMR, 300 MHz, $CDCl_3$, 25 ºC



^{13}C-NMR, 75 MHz, $CDCl_3$, 25 ºC



^{1}H-NMR, 300 MHz, $CDCl_3$, 25 ºC



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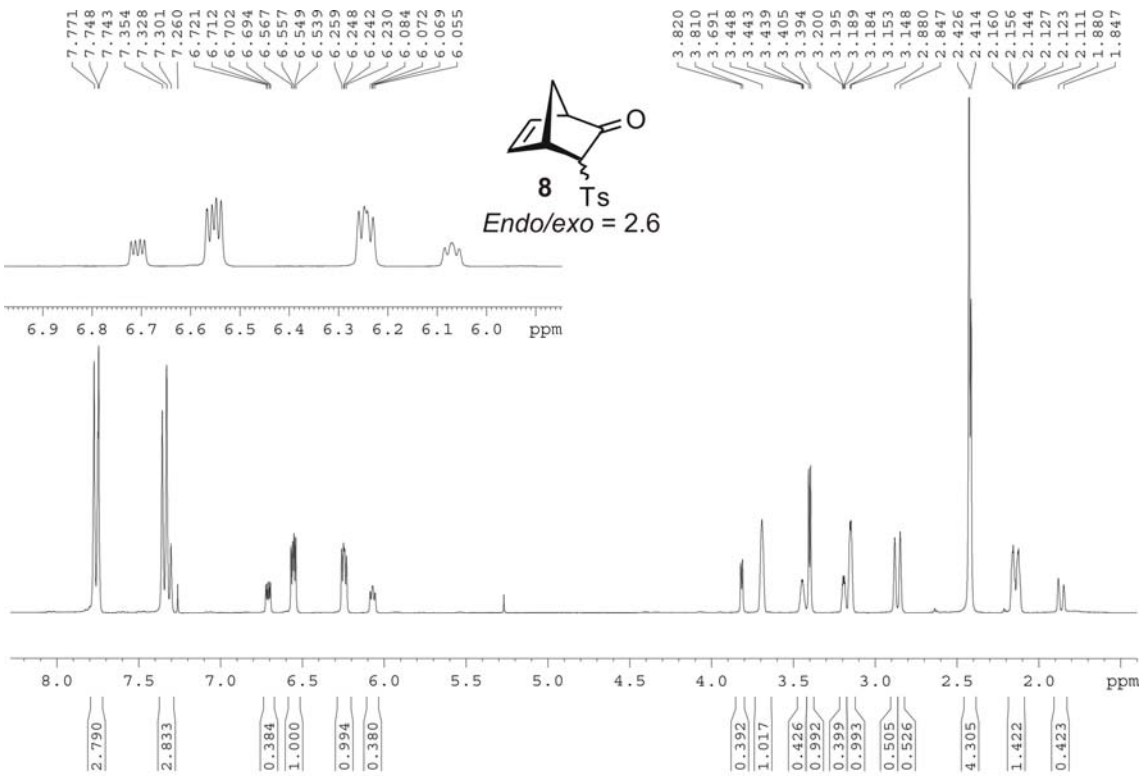
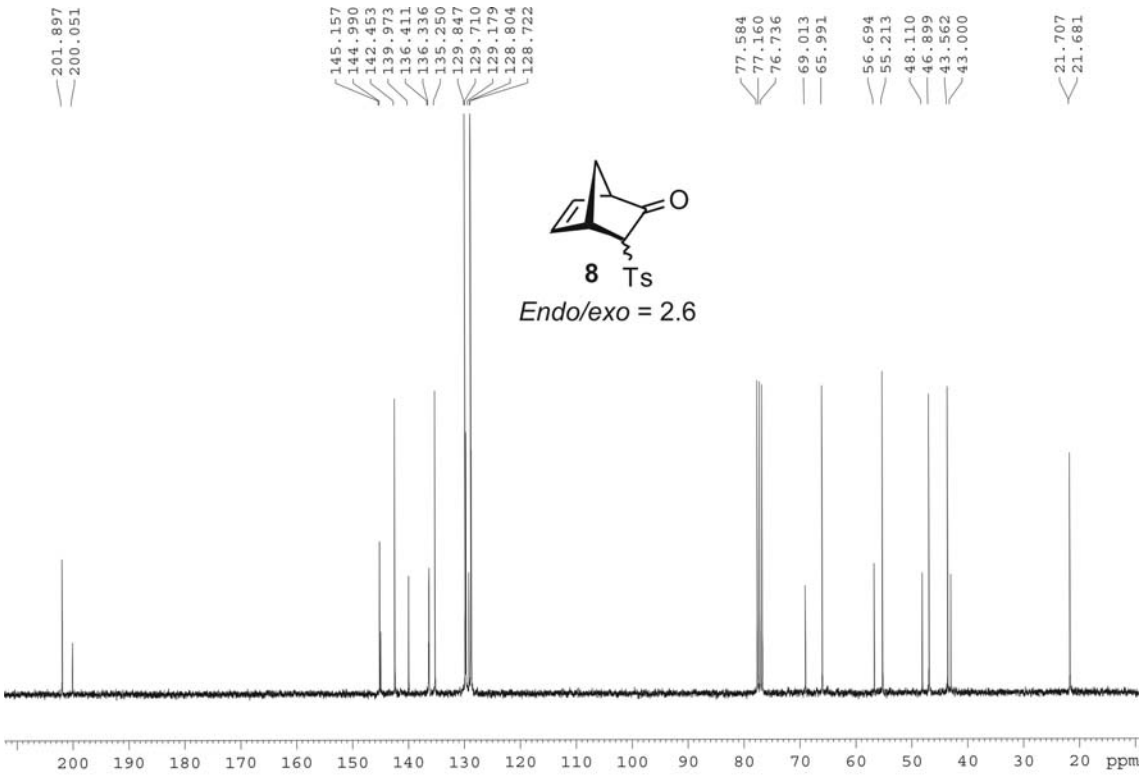


^{1}H-NMR, 300 MHz, $CDCl_3$, 25 ºC



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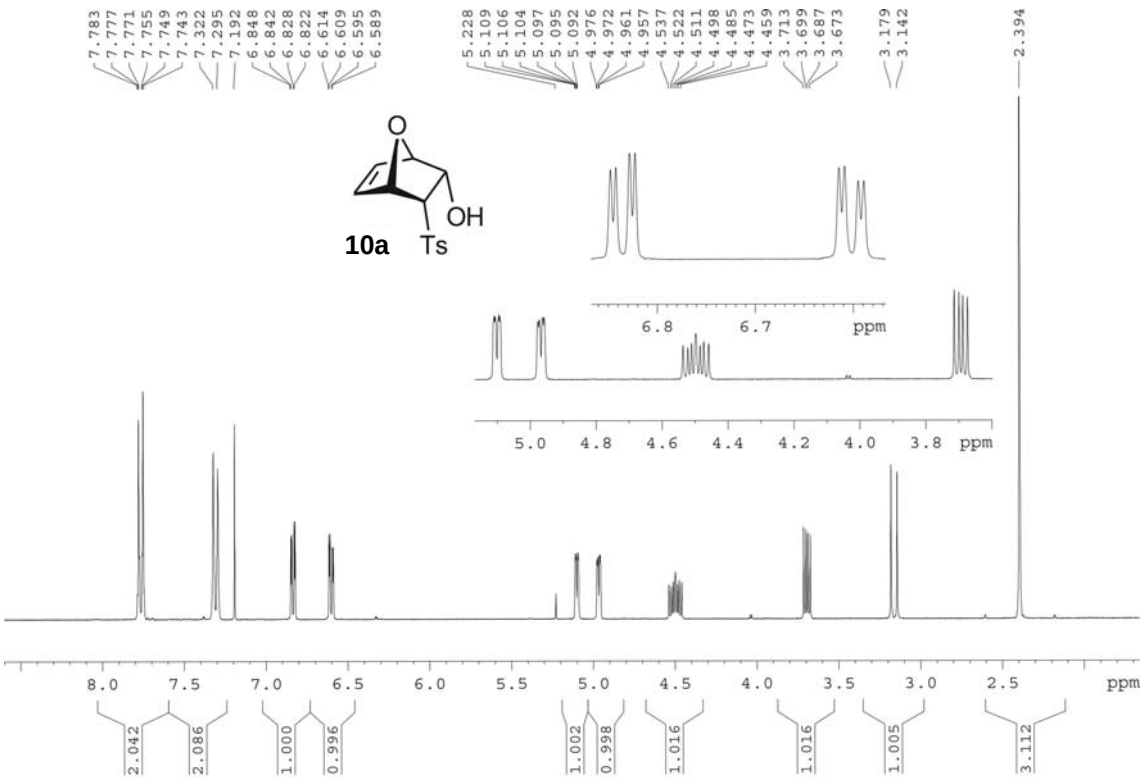
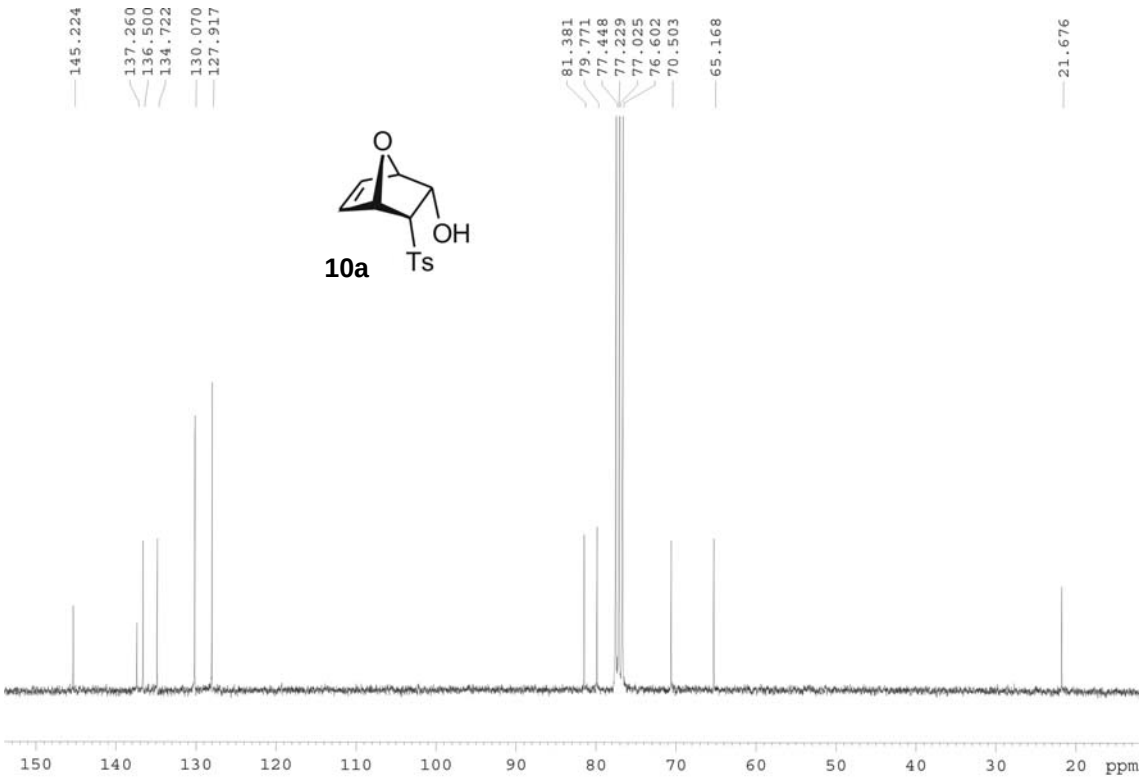
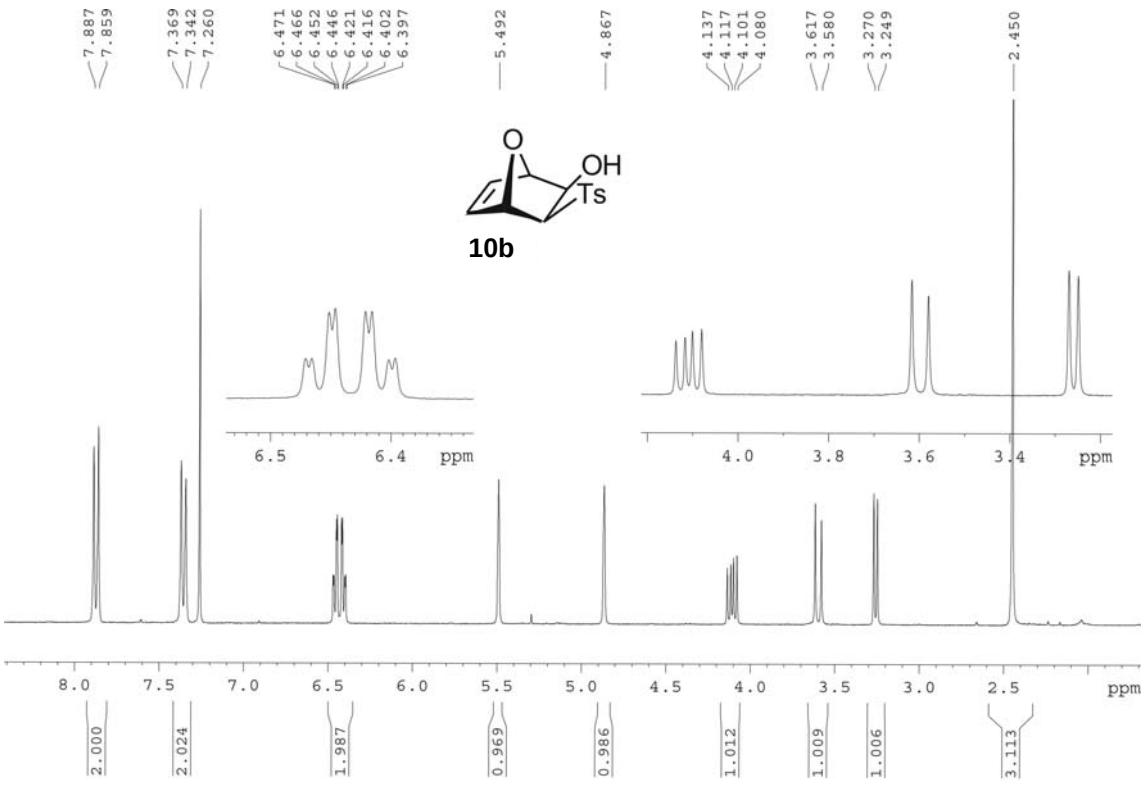


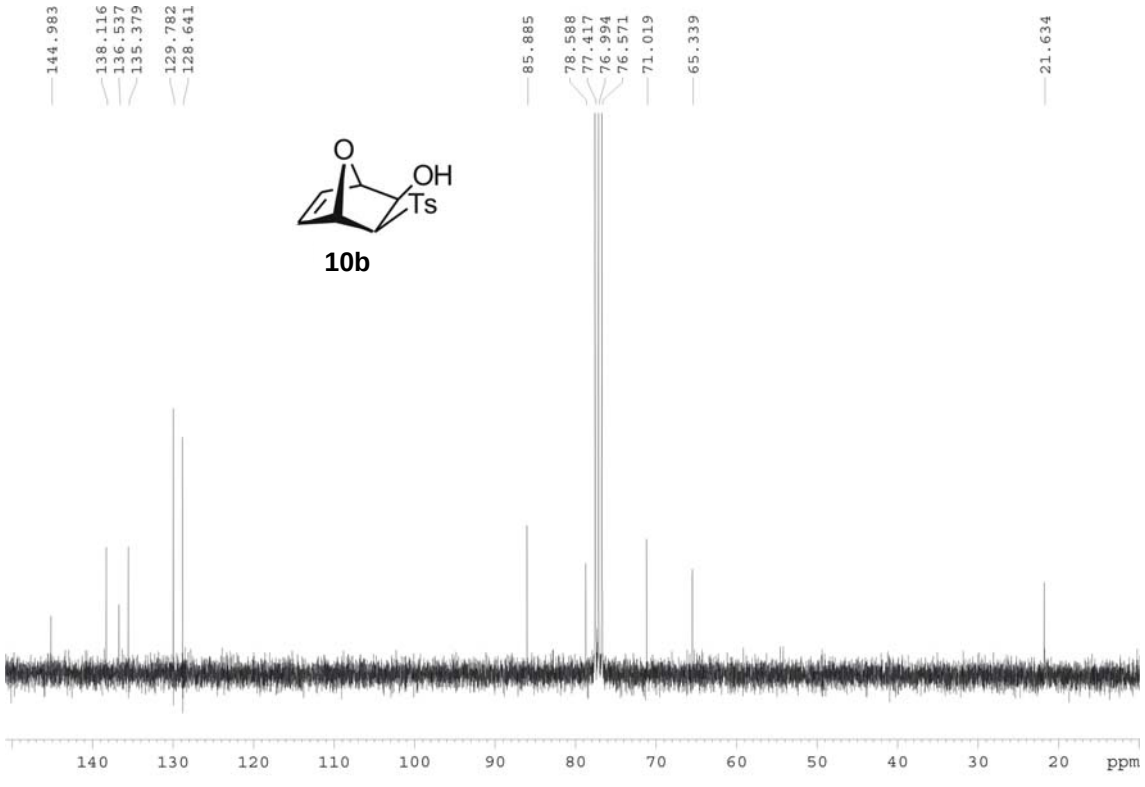
^{1}H-NMR, 300 MHz, $CDCl_3$, 25 ºC



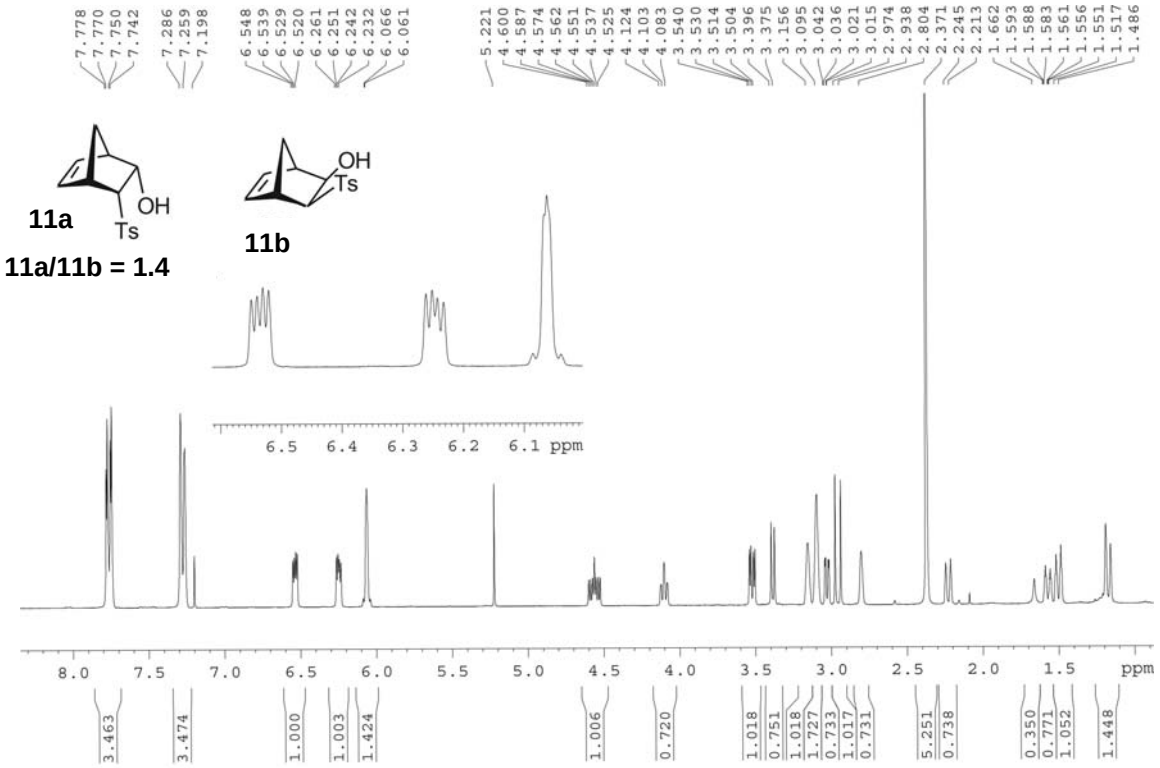
^{13}C-NMR, 75 MHz, $CDCl_3$, 25 ºC



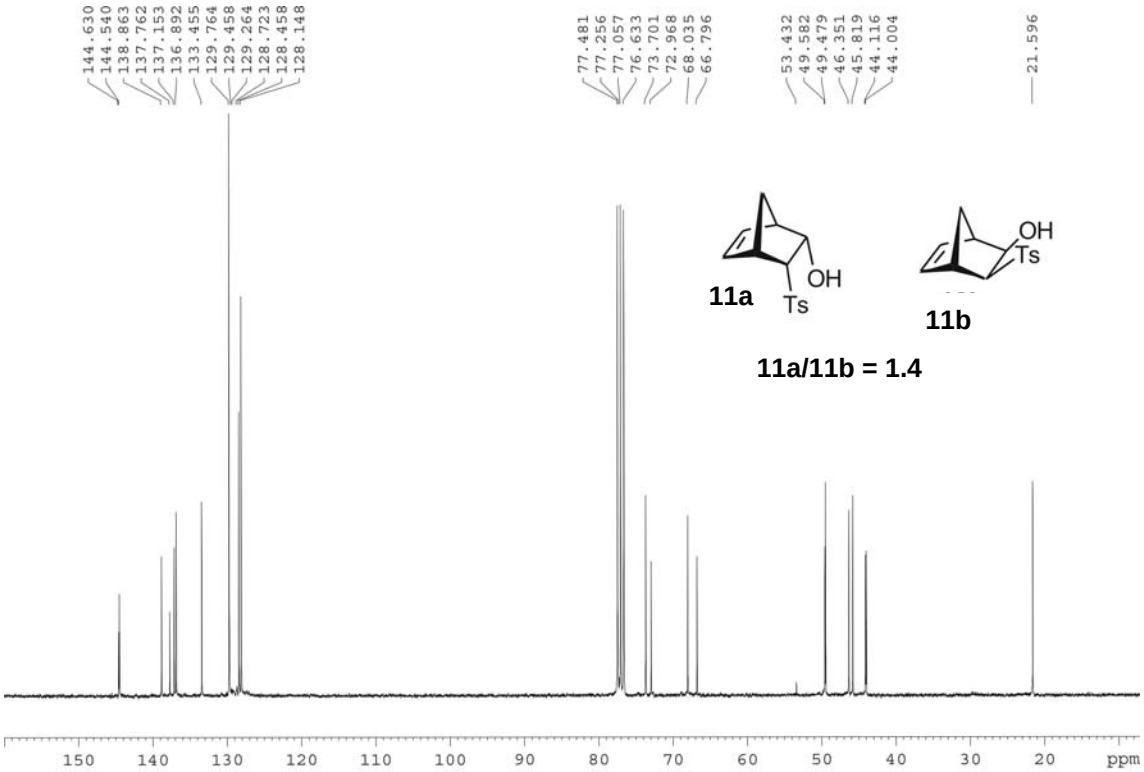
^{1}H-NMR, 300 MHz, $CDCl_3$, 25 ºC



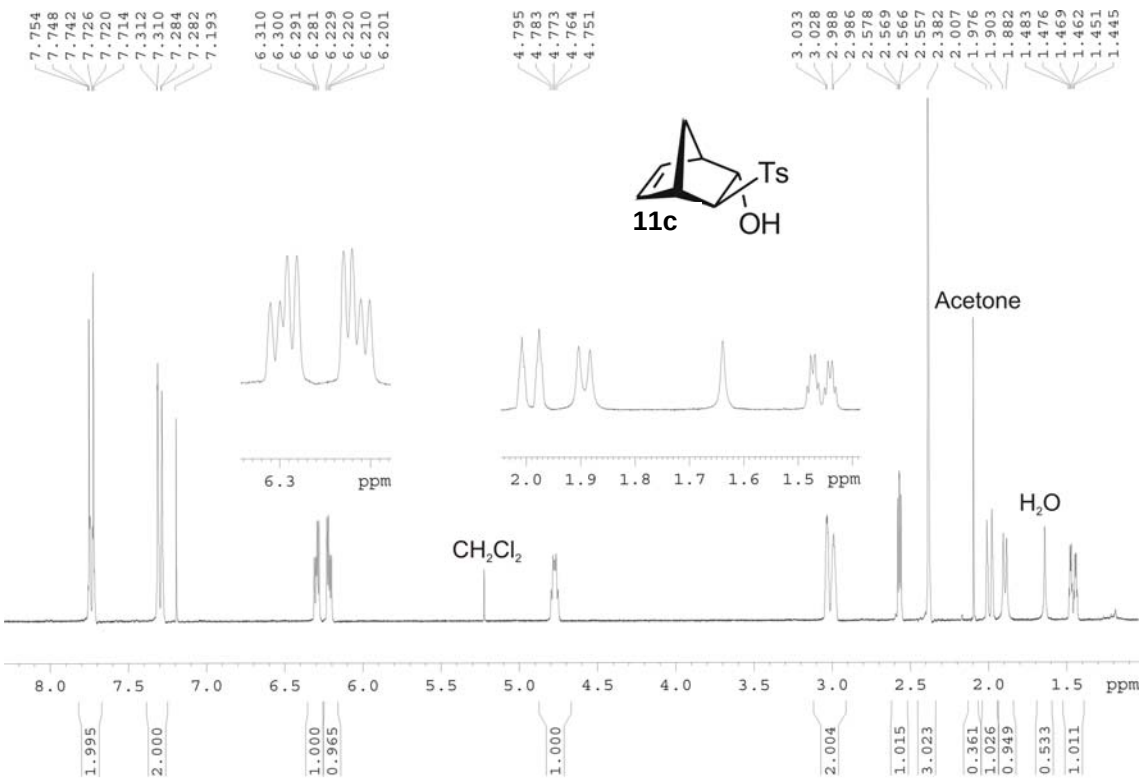
^{13}C-NMR, 75 MHz, $CDCl_3$, 25 ºC



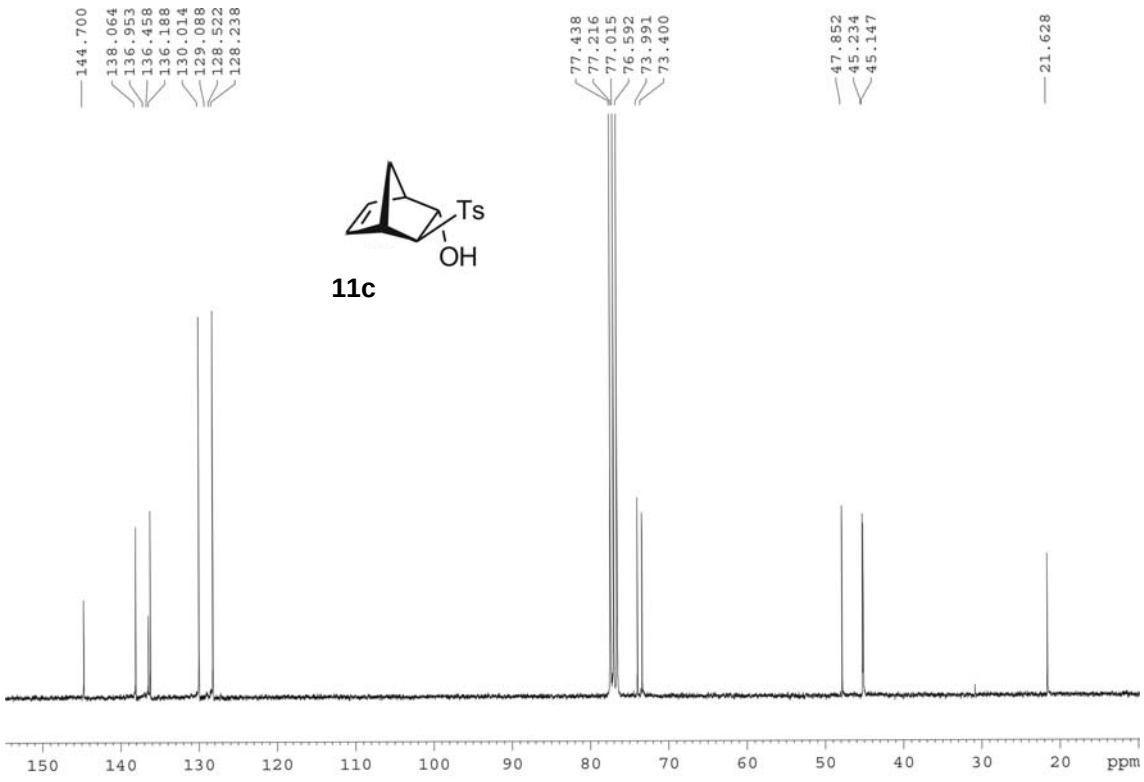
^{1}H-NMR, 300 MHz, $CDCl_3$, 25 ºC



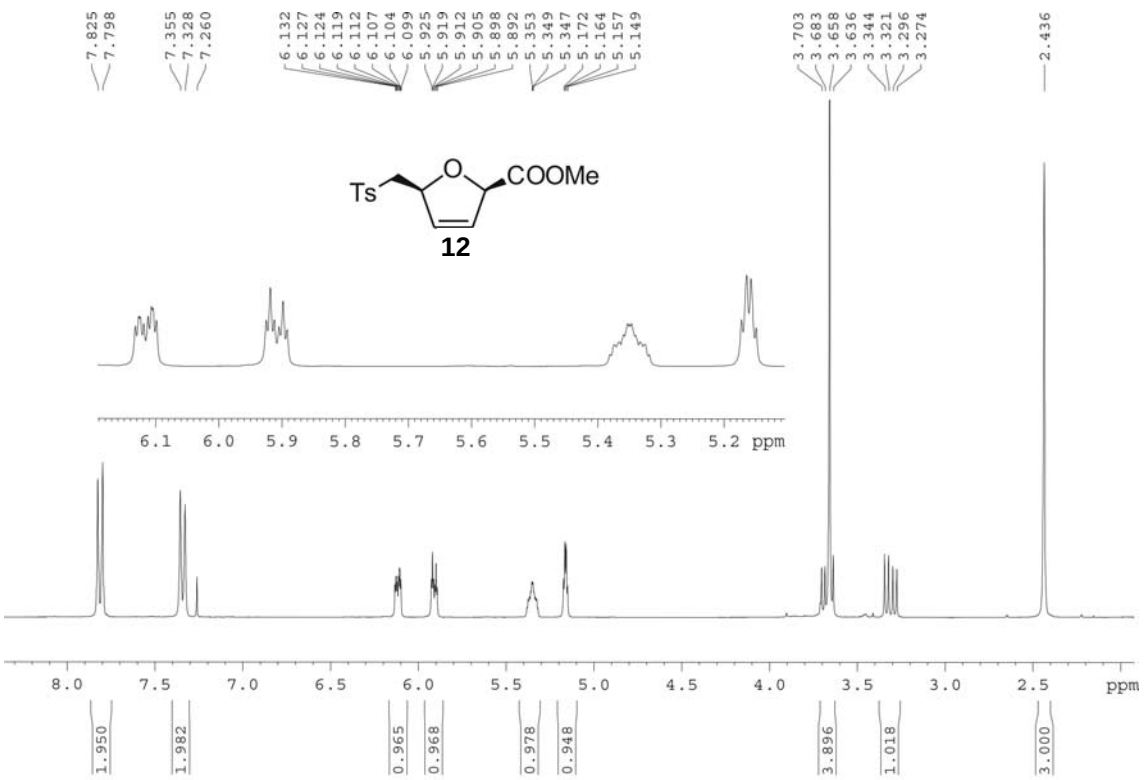
^{13}C-NMR, 75 MHz, $CDCl_3$, 25 ºC



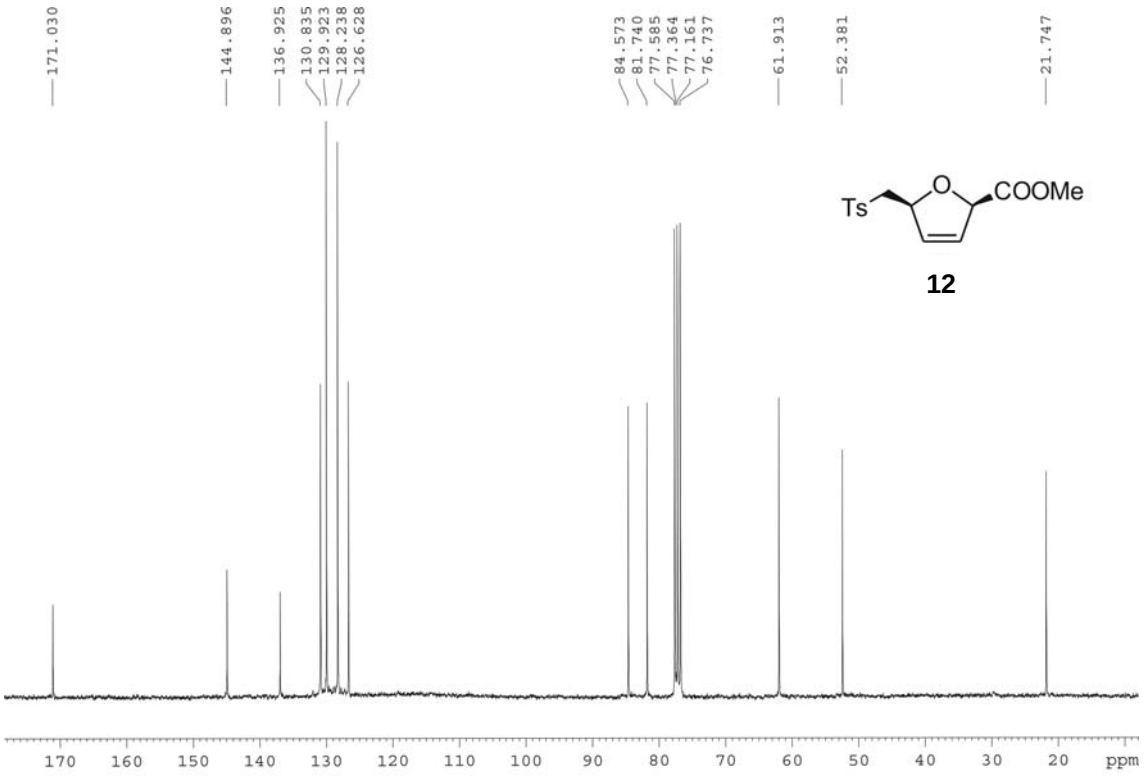
^{1}H-NMR, 300 MHz, $CDCl_3$, 25 ºC



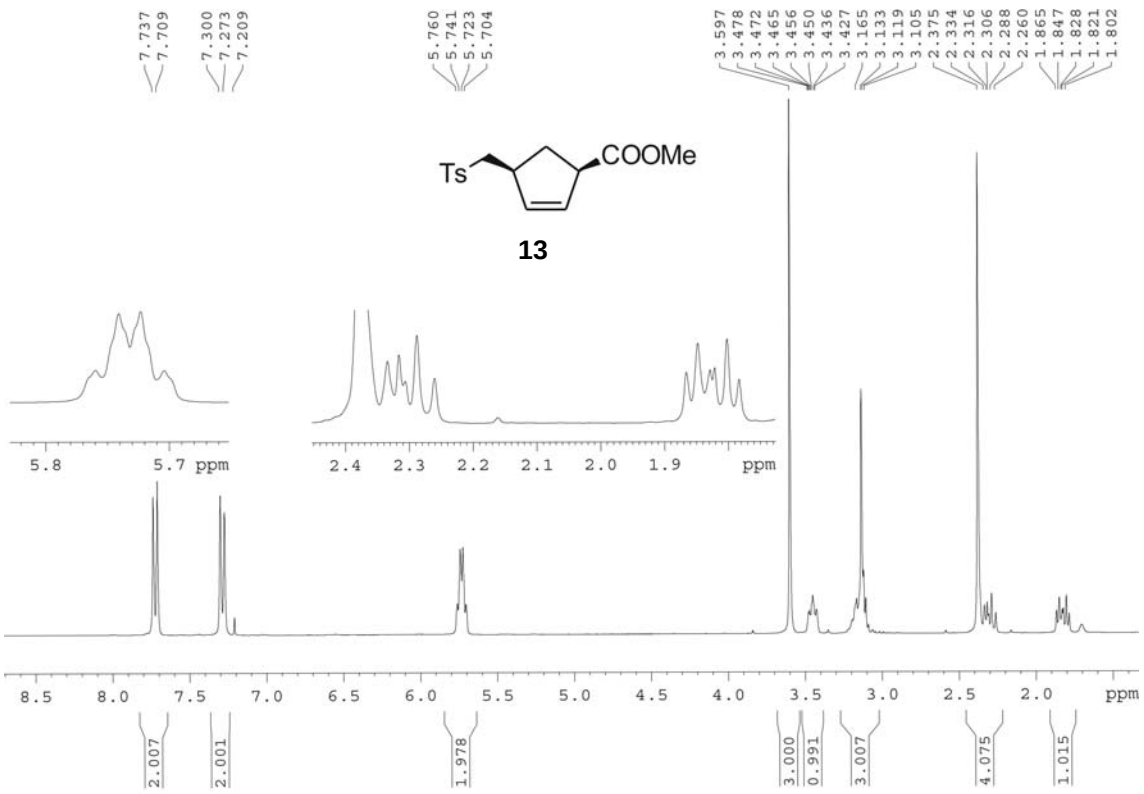
^{13}C-NMR, 75 MHz, $CDCl_3$, 25 ºC



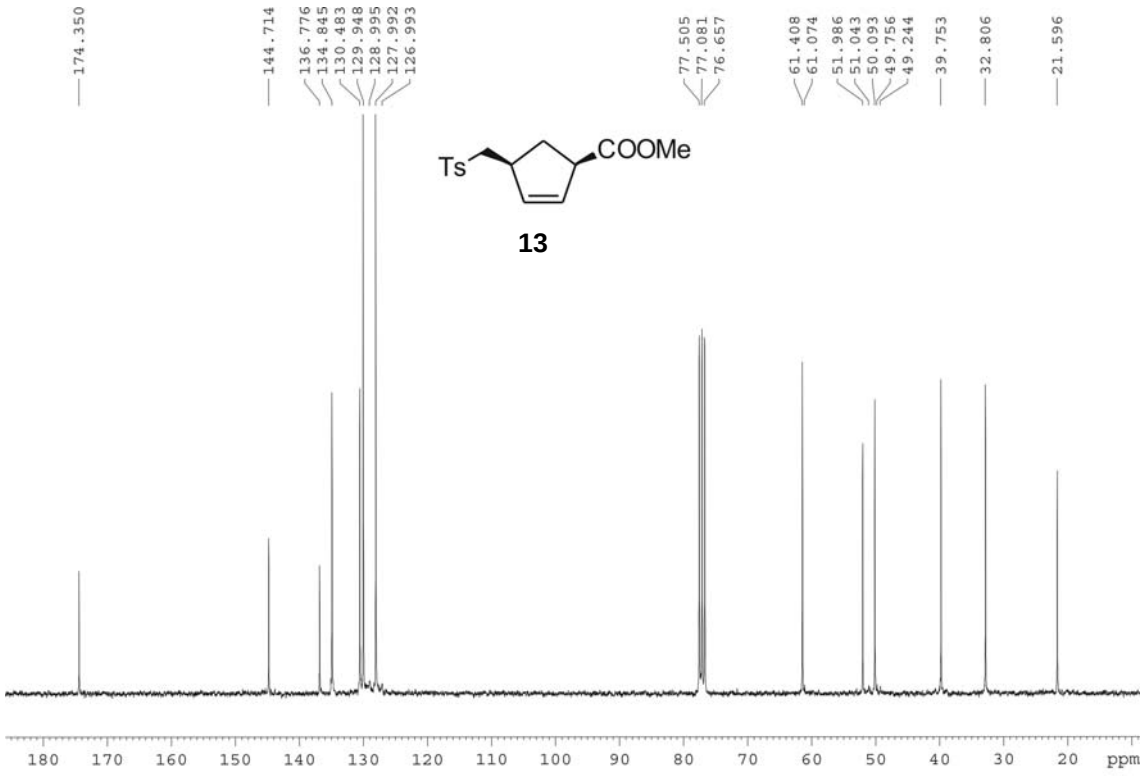
^{1}H-NMR, 300 MHz, $CDCl_3$, 25 ºC



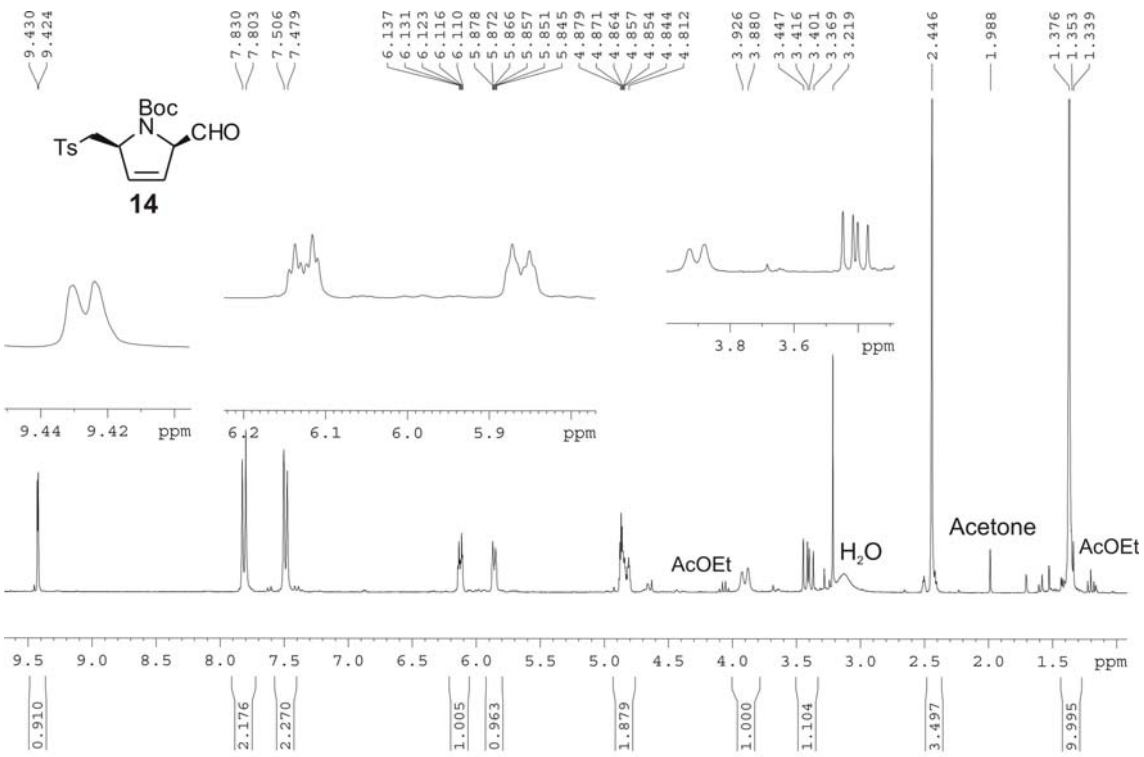
^{13}C-NMR, 75 MHz, $CDCl_3$, 25 ºC



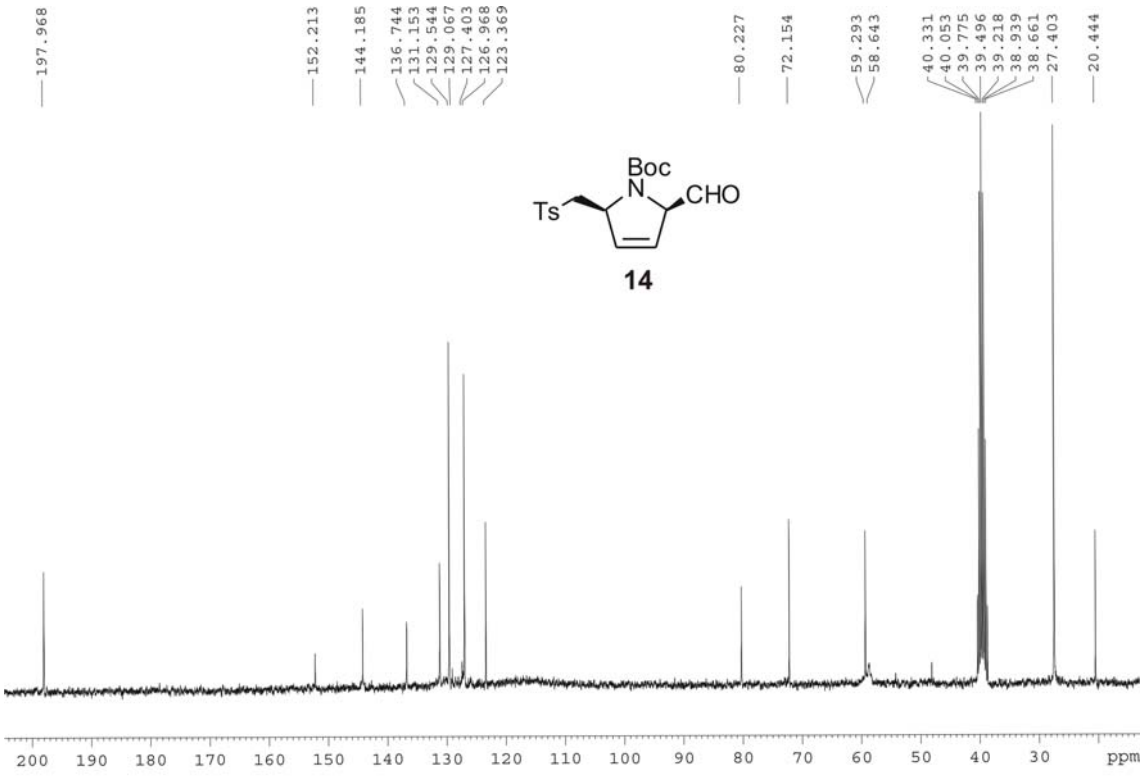
^{1}H-NMR, 300 MHz, $CDCl_3$, 25 ºC



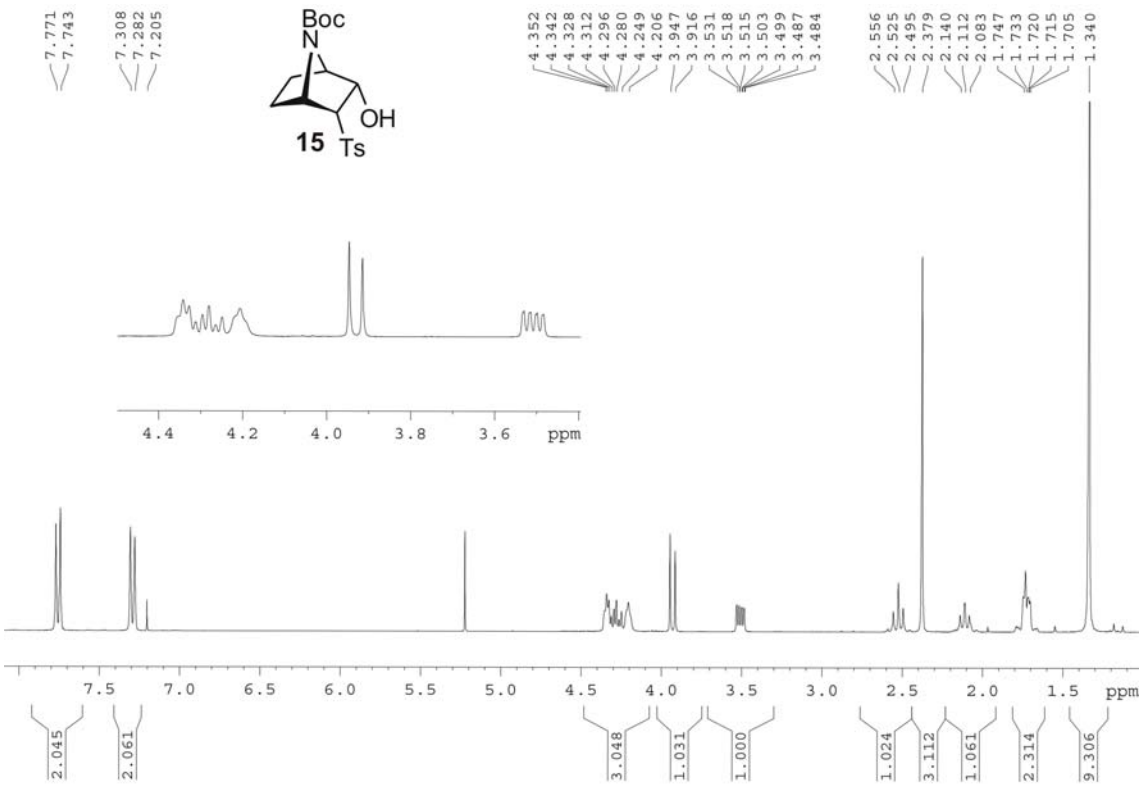
^{13}C-NMR, 75 MHz, $CDCl_3$, 25 ºC



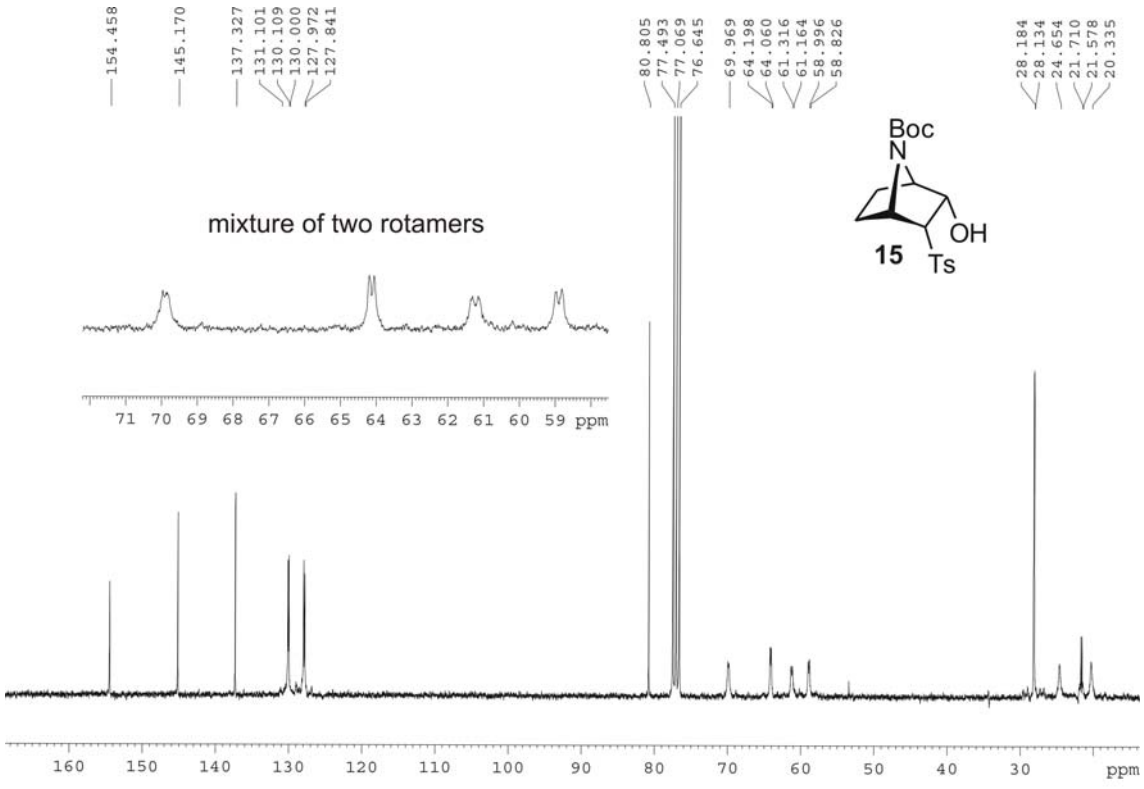
^{1}H-NMR, 300 MHz, DMSO-d_6, 90 ºC



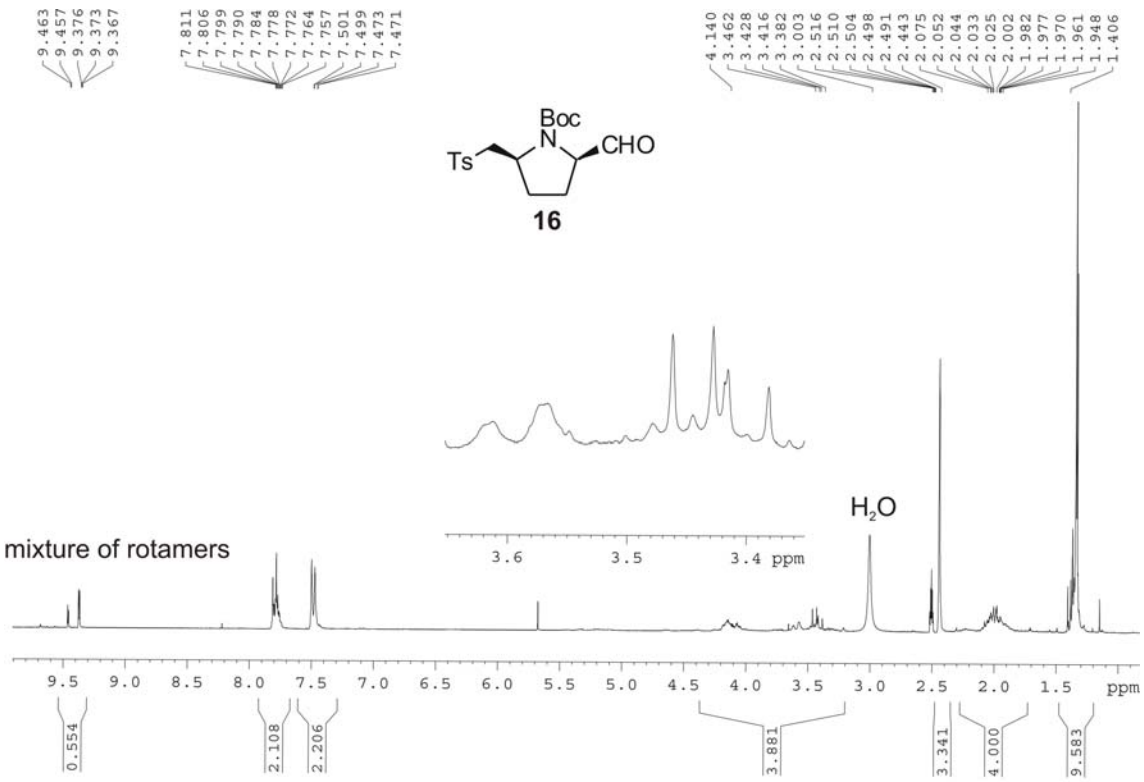
^{13}C-NMR, 75 MHz, DMSO-d_6, 90 ºC



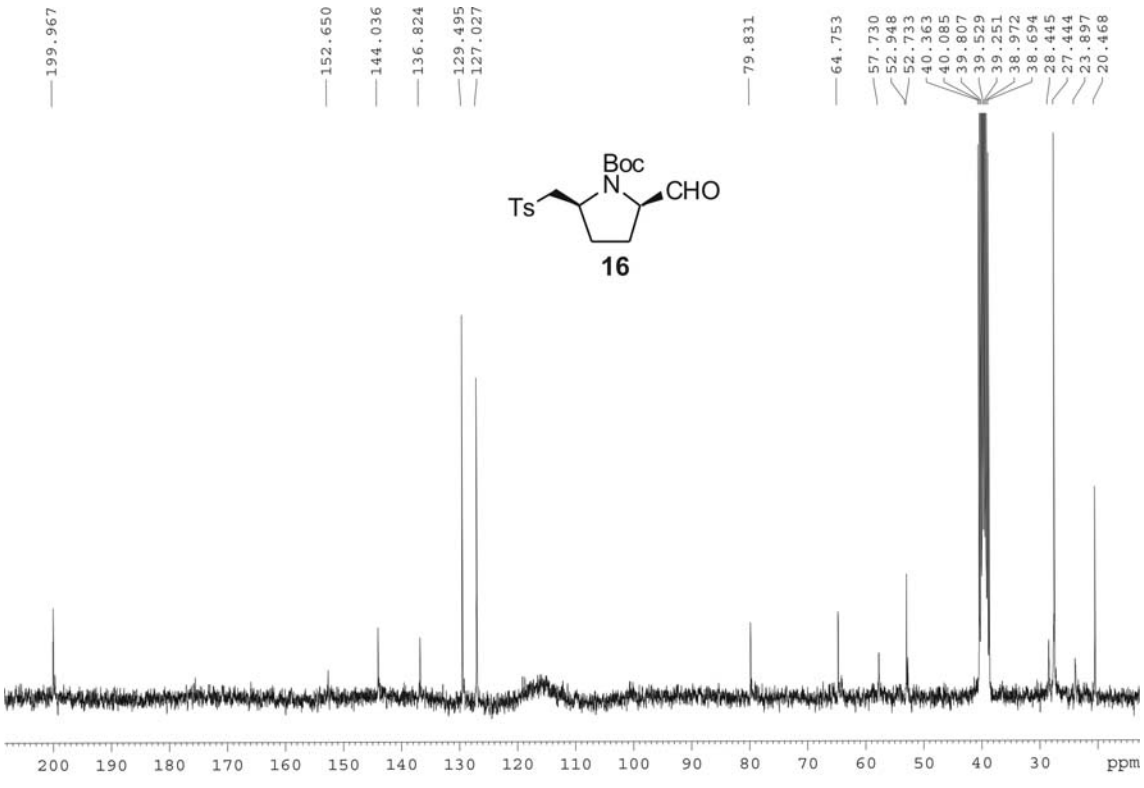
^{1}H-NMR, 300 MHz, $CDCl_3$, 25 ºC



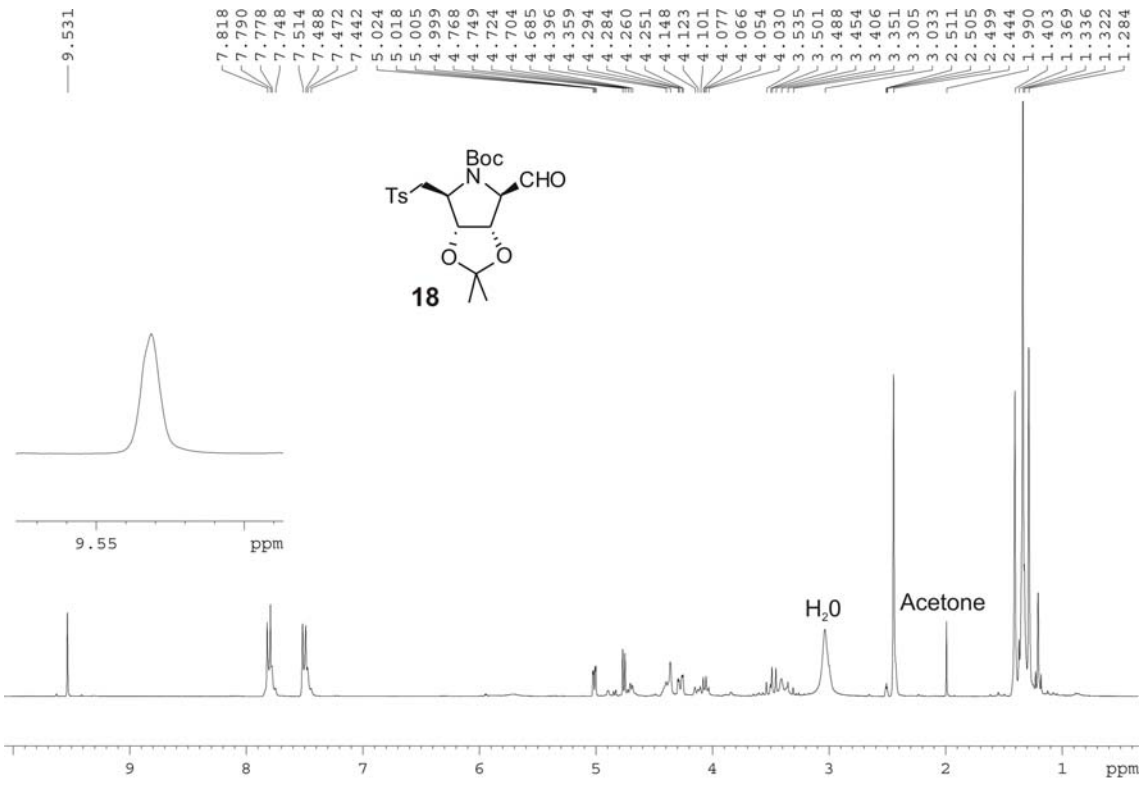
^{13}C-NMR, 75 MHz, $CDCl_3$, 25 ºC



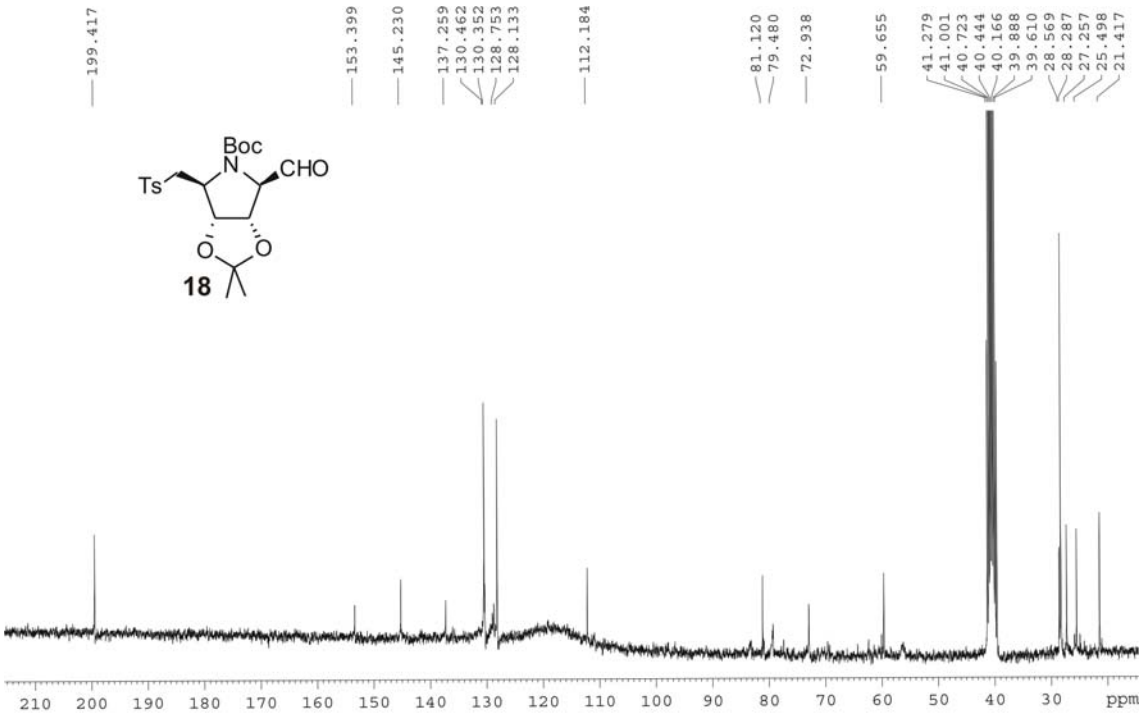
^{1}H-NMR, 300 MHz, DMSO-d_6, 90 ºC



^{13}C-NMR, 75 MHz, DMSO-d_6, 90 ºC (mixture of rotamers)



^{1}H-NMR, 300 MHz, DMSO-d_6, 90 ºC (broad signals, rotamers)



^{13}C-NMR, 75 MHz, DMSO-d_6, 90 ºC