Electronic Supplementary Information (ESI)

2-Lithiated-2-Phenyloxetane: A New Attractive Synthon for the Preparation of Oxetane Derivatives

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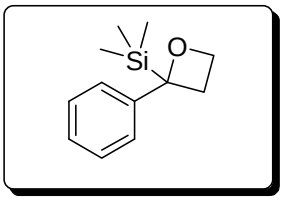
1. General Methods

Tetrahydrofuran (THF), toluene and hexane were freshly distilled under a nitrogen atmosphere: THF over sodium/benzophenone ketyl, toluene and hexane over calcium hydride. For the ^{1}H and ^{13}C NMR spectra (^{1}H NMR 400 or 600 MHz; ^{13}C NMR 100 or 150 MHz), $CDCl_3$ was used as the solvent. GC-MS spectrometry analyses were performed on a gas chromatograph (dimethylsilicon capillary column, 30 m, 0.25 mm i.d.) equipped with a mass selective detector operating at 70 eV (EI). Elemental analyses were performed by using a Carlo Erba CHNS-O EA1108-Elemental Analyzer. Analytical thin layer chromatography (TLC) was carried out on precoated 0.25 mm thick plates of Kieselgel 60 F254; visualization was accomplished by UV light (254 nm) or by spraying with a solution of 5 % (w/v) ammonium molybdate and 0.2 % (w/v) cerium(III) sulfate in 100 ml 17.6 % (w/v) aq. sulphuric acid and heating to 473 K for some time until blue spots appear. All reactions involving air-sensitive reagents were performed under nitrogen in oven-dried glassware using syringe-septum cap technique. Lithiation-deuteration (electrophilic trapping) reactions were performed in an ethanol/liquid N_2 (–116 °C) or acetone/dry ice (–78 °C) cold bath. Racemic or (*R*)-2-phenyloxetane (**2**) were prepared starting from racemic or (*R*)-3-chloro-1-phenylpropan-1-ol (**1**), respectively, as similarly reported for other cases.[1] The enantiomeric ratios were determined as follows: 2-phenyloxetane (**2**) by GC analysis employing a Chirasil-DEX CB column (250 × 0.25 mm), column head pressure 18 psi, He flow 1.5 mL/min, oven temperature 90 °C, retention times 27.9 min [(*S*)-**2**] and 29.8 min [(*R*)-**2**]; 2-trimethylsilyl-2-phenyloxetane (**2c**) by HPLC analysis employing a Cellulose Lux-2 column (250 × 4.6 mm), eluent hex/*i*-PrOH 99.8/0.2, 1.0 mL/min, retention times 4.93 min and 5.88 min. Spectroscopic data of oxetanes **2a,b** have been reported.[2]

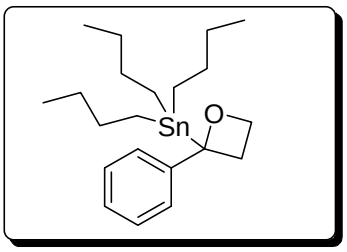
[1] F. Bertolini, S. Crotti, V. Di Bussolo, F. Macchia, and M. Pineschi, *J. Org. Chem.* 2008, **73**, 8998.
[2] E. D. Butova, A. V. Barabash, A. A. Petrova, C. M. Kleiner, P. R. Schreiner, and A. A. Fokin, *J. Org. Chem.* 2010, **75**, 6229.

2. Experimental Procedures and characterization data

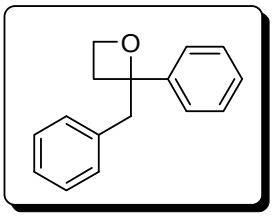
Preparation of 2-deuterated [D]-2 or 2-substituted-2-phenyloxetanes 2a–l, 4 – General procedure: A solution of **2** (134 mg, 1.0 mmol) in 5 mL of dry THF was cooled to • 78 °C (or to – 116 °C, when required) and treated with *s*-BuLi (1.08 mL, 1.4 mmol, 1.3 M solution in cyclohexane) under N_2. After stirring the resulting mixture for 5 min at the above temperature, MeOD (10 mmol) or the electrophile (2.0 mmol) (as pure liquid or as a solution in 1 mL of THF if solid) was added all at once. The cooling bath was removed and the reaction mixture was allowed to warm to room temperature, then diluted with brine (5 mL), and extracted with Et_2O (3 × 10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. The crude product so obtained was purified by flash-chromatography (silica gel; hexane/Et_2O 9/1–95/5).



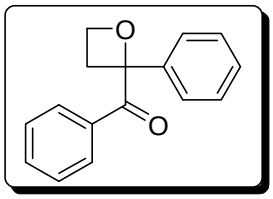
2-Trimethylsilyl-2-phenyloxetane (2c): Colorless oil, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.02 (s, 9 H), 2.66 • 2.73 (m, 1 H), 3.06 • 3.12 (m, 1 H), 4.67 • 4.71 (m, 2 H), 7.06 • 7.33 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ, • 5.1, 31.6, 68.8, 86.8, 123.2, 125.1, 127.7, 147.8; GC-MS (70 eV) *m/z* (%) 205 (72, M^+ • 1), 105 (53), 73 (100); FT-IR (film, cm^{-1}) 2955, 2919, 2850, 1467, 839. Anal. Calcd. For $C_{12}H_{18}OSi$: C, 69.84; H, 8.79. Found: C, 70.12; H, 9.02.



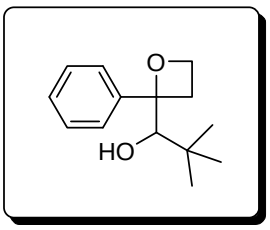
2-Tributylstannyl-2-phenyloxetane (2d): Colorless oil, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 • 0.90 (m, 15 H), 1.23 • 1.26 (m, 6 H), 1.38 • 1.41 (m, 6 H), 2.86 • 2.91 (m, 1 H), 3.20 • 3.29 (m, 1 H), 4.65 • 4.71 (m, 1 H), 4.82 • 4.88 (m, 1 H), 7.02 • 7.08 (m, 3H), 7.27 • 7.31 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.1, 13.6, 27.4, 28.9, 35.6, 69.5, 92.8, 121.1, 124.2, 128.1, 151.3; GC-MS (70 eV) *m/z* (%) 337 (100), 281 (50), 223 (70), 77 (4); FT-IR (film, cm^{-1}) 2956, 2924, 1376, 1068, 699.



2-Benzyl-2-phenyloxetane (2e): Colorless oil, 60% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.71 • 2.76 (m, 1 H), 2.88 • 2.93 (m, 1 H), 3.19 (s, 2 H), 4.27 • 4.31 (m, 1 H), 4.43 • 4.47 (m, 1 H), 7.19 • 7.43 (m, 10 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 32.6, 49.4, 64.7, 88.5, 124.2, 126.4, 126.6, 127.8, 127.9, 130.6, 136.6, 147.1; GC-MS (70 eV) *m/z* (%) 224 (M^+, 9), 194 (17), 179 (15), 133 (100), 105 (79), 77 (31); FT-IR (film, cm^{-1}) 3061, 3000, 2882, 1602, 1495, 1447, 1231, 979, 766, 700.

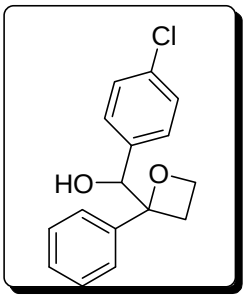


Phenyl 2-phenyloxetan-2-yl ketone (2f): Colorless oil, 70 % yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.73 • 2.78 (m, 1 H), 3.68 • 3.73 (m, 1 H), 4.63 • 4.75 (m, 2 H), 7.29 • 7.47 (m, 6 H), 7.61 • 7.63 (m, 2 H), 7.97 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 34.3, 66.4, 92.5, 123.7, 127.8, 128.9, 130.2, 133.0, 133.2, 141.9, 199.0; GC-MS (70 eV) *m/z* (%) 238 (M^+, 1), 208 (16), 133 (96), 105 (100), 77 (61), 51 (18); FT-IR (film, cm^{-1}) 3060, 2972, 2890, 1681, 1598, 1447, 1269, 952, 755, 700.

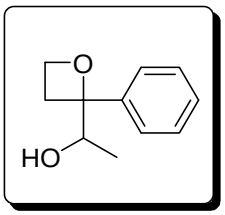


2,2-Dimethyl-1-(2-phenyloxetan-2-yl)propan-1-ol (2g): Inseparable mixture of diastereoisomers (dr = 2/1), 73% overall yield, yellow solid, mp 96 • 97 °C (Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.61 (s, 3 H minor), 0.64 (s, 3 H major), 2.52 • 2.59 (m, 1 H minor), 2.72 • 2.78 (m, 1 H major), 2.98 (d, *J* = 8.4 Hz, 1 H minor, exchanges with D_2O), 3.22 (d, *J* = 2.8 Hz, 1 H major, exchanges with D_2O), 3.29 • 3.43 (m, 1 H minor + 1 H major), 3.52 (d, *J* = 2.8 Hz, 1 H major, s after exchange with D_2O), 3.61 (d, *J* = 8.4 Hz, 1 H minor, s after exchange with D_2O), 4.39 • 4.52 (m, 2 H minor + 2 H major), 7.27 • 7.43 (m, 5 H minor + 5 H major); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2 (minor), 27.4 (major), 28.6 (major), 31.6 (minor), 33.9 (minor), 34.6 (major), 66.0 (minor), 66.3 (major), 83.0 (minor), 83.7 (major), 91.5 (minor), 91.9 (major), 125.3 (minor), 126.0 (major), 126.9

(minor), 127.5 (major), 127.9 (minor), 127.9 (major), 143.9 (major), 144.5 (minor); GC-MS (70 eV) *m/z* (%) minor (t_R = 8.82 min): 220 (M^+, 1), 134 (65), 133 (100), 105 (85), 77 (31), 57 (15); major (t_R = 8.90 min) 220 (M^+, 1), 190 (3), 134 (88), 133 (100), 105 (82), 77 (33) 57 (20); FT-IR (film, cm^{-1}) 3368, 2963, 2885, 1489, 1446, 1085, 702. Anal. Calcd. For $C_{16}H_{15}ClO_2$: C, 69.95; H, 5.50. Found: C, 69.75; H, 5.84.

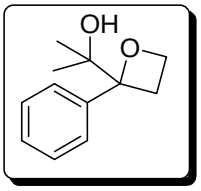


(4-Chlorophenyl)(2-phenyloxetan-2-yl)methanol (2h): Inseparable mixture of diastereoisomers (dr = 2/1), yellow solid, mp 96 • 97 °C (Et_2O), 80% overall yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 • 2.50 (m, 1 H major), 2.63 • 2.69 (m, 1 H minor), 3.05 (d, *J* = 6.1 Hz, 1 H minor, exchanges with D_2O), 3.23 • 3.33 (m, 1 H major + 1 H minor), 3.66 (s, 1 H, exchanges with D_2O), 4.45 • 4.60 (m, 2 H major + 2 H minor), 4.60 (s, 1 H major), 4.78 (d, *J* = 6.1 Hz, 1 H minor, s after exchange with D_2O), 6.85 • 7.01 and 6.93 • 7.02 and 7.10 • 7.27 (3 × m, 9 H major + 9 H minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8 (major), 30.6 (minor), 66.0 (minor), 66.2 (major), 78.6 (minor), 78.9 (major), 90.2 (minor), 91.4 (major), 124.9 (minor), 125.7 (major), 127.0 (minor), 127.4 (major), 127.6_2 (major), 127.6_7 (minor), 127.6_8 (major), 127.7_1 (minor), 128.7_0 (minor), 128.7_3 (major), 133.3 (minor), 133.5 (major), 135.4 (major), 137.2 (minor), 142.4 (minor), 143.0 (major); GC-MS (70 eV) *m/z* (%) minor (t_R = 11.69 min): 274 (M^+, 1), 133 (100), 105 (85), 77 (70); major (t_R = 11.73 min) 274 (M^+, 1), 133 (100), 105 (82), 77 (73); FT-IR (film, cm^{-1}) 3368, 2963, 2885, 1489, 1446, 1085, 702. Anal. Calcd. For $C_{16}H_{15}ClO_2$: C, 69.95; H, 5.50. Found: C, 69.75; H, 5.84.

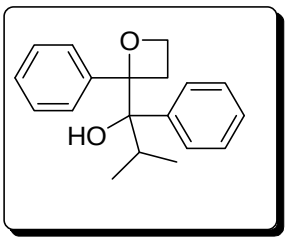


1-(2-Phenyloxetan-2-yl)-1-ethanol (2i): Inseparable mixture of diastereoisomers (dr = 1.2/1), colorless oil, 80% overall yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.89 (d, *J* = 6.5 Hz, 3 H major), 0.96 (d, *J* = 6.4 Hz, 3 H minor), 2.52 • 2.56 (m, 1 H minor), 2.58 (br s, exchanges with D_2O, 1 H minor), 2.64 • 2.68 (m, 1 H major), 3.17 • 3.22 (m, 1 H major), 3.24 • 3.29 (m, 1 H minor), 3.30 (br s, exchanges with D_2O, 1 H major), 3.73 (q, *J* = 6.5 Hz, 1 H major), 3.92 (br s, 1 H minor),

4.50 • 4.57 (m, 2 H minor + 2 H major), 7.25 • 7.37 (m, 5 H minor + 5 H major); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7 (major), 16.1 (minor), 26.3 (major), 30.6 (minor), 65.9 (major), 72.6 (minor), 72.8 (major), 90.9 (minor), 91.8 (major), 124.4 (minor), 125.2 (major), 126. (minor), 127.2 (major), 127.9 (major), 128.0 (minor), 143.4 (major), 144.0 (minor); GC-MS (70 eV) *m/z* (%) minor (t_R = 7.32 min): 178 (M^+, 1), 160 (3), 133 (100), 105 (96), 77 (40); major (t_R = 7.46 min) 178 (M^+, 1), 160 (4), 133 (100), 105 (94), 77 (38); FT-IR (film, cm^{-1}) 3430, 2972, 2886, 1447, 968, 757, 702.

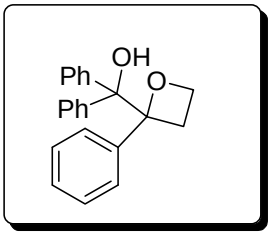


2-(2-Phenyloxetan-2-yl)propan-2-ol (2j): Colorless oil, 75% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.97 (s, 3 H), 1.15 (s, 3 H), 2.53 • 2.57 (m, 1 H), 3.40 • 3.45 (m, 1 H), 4.43 • 4.47 (m, 1 H), 4.50 • 4.54 (m, 1 H), 7.34 • 7.38 (m, 5 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.8, 23.1, 29.5, 65.6, 73.8, 93.3, 125.9, 126.8, 127.4, 144.0; GC-MS (70 eV) *m/z* (%) 147 (4), 134 (81), 105 (100), 77 (40); FT-IR (film, cm^{-1}) 3436, 2971, 2884, 1447, 961, 703.

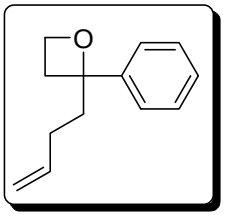


2-Methyl-1-phenyl-1-(2-phenyloxetan-2-yl)propan-1-ol (2k): Separable mixture of diastereomers, (dr = 2/1), 82% overall yield. Major diastereoisomer: colorless oil, 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.52 (d, *J* = 6.6 Hz, 3 H), 1.17 (d, *J* = 6.6 Hz, 3 H), 1.94 (hept, *J* = 6.6 Hz, 1 H), 1.99 • 2.05 (m, 1 H), 3.38 • 3.44 (m, 1 H), 3.77 (s, 1 H, exchanges with D_2O), 4.35 • 4.43 (m, 2 H), 7.08 • 7.11 (m, 2 H) 7.20 • 7.31 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6, 19.0, 31.5, 32.1, 66.2, 80.7, 95.7, 126.8_0, 126.8_2, 126.8_5, 127.1, 127.6, 128.5, 139.3, 142.2; GC-MS (70 eV) *m/z* (%) 282 (M^+, 1) 264 (9), 209 (18), 149 (54), 133 (100), 105 (63), 77 (36), 43 (20); FT-IR (film, cm^{-1}) 3542, 2965, 2884, 1446, 961, 703. Minor diastereoisomer: colorless oil, 32% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.68 (d, *J* = 6.6 Hz, 3 H), 1.20 (d, *J* = 6.6 Hz, 3 H), 2.20 (hept, *J* = 6.6 Hz, 1 H), 2.44 • 2.50 (m, 1 H), 3.31 (s, 1 H, exchanges with D_2O), 3.64 • 3.71 (m, 1 H), 4.27 • 4.38 (m, 2 H), 6.83 • 6.87 (m, 2 H), 7.07 • 7.14 (m, 4 H), 7.23 • 7.30 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.1, 18.4, 32.7, 33.2, 66.2, 81.2, 94.1, 126.4, 126.6, 126.7, 127.0, 127.2; 127.4, 140.5, 143.0; GC-MS (70

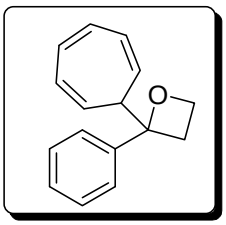
eV) *m*/*z* (%) 282 (M^+, 1) 264 (9), 209 (18), 149 (54), 133 (100), 105 (63), 77 (36), 43 (20); FT-IR (film, cm^{-1}) 3542 , 2969, 2882, 1446, 1003, 701.



Diphenyl(2-phenyloxetan-2-yl)methanol (2l): White solid, mp 98 ^oC (Et_2O), 70% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 2.56 • 2.63 (m, 1 H), 3.20 • 3.27 (m, 1 H), 4.06 • 4.12 (m, 1 H), 4.38 • 4.43 (m, 1 H), 7.15 • 7.31 (m, 11 H), 7.58 • 7.61 (m 2 H), 7.75 • 7.77 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 32.4, 66.1, 80.5, 93.1, 126.9, 127.0, 127.1, 127.2, 127.3, 127.4_7, 127.5_0, 127.8, 142.9, 143.0, 143.6; GC-MS (70 eV) *m*/*z* (%) 316 (M^+, 2), 270 (5), 183 (47), 133 (100), 105 (90), 77 (47); FT-IR (KBr, cm^{-1}) 3564, 2968, 2886, 1493, 1446, 909, 885. Anal. Calcd. For $C_{22}H_{20}O_2$: C, 83.51; H, 6.37. Found: C, 83.32; H, 6.51.



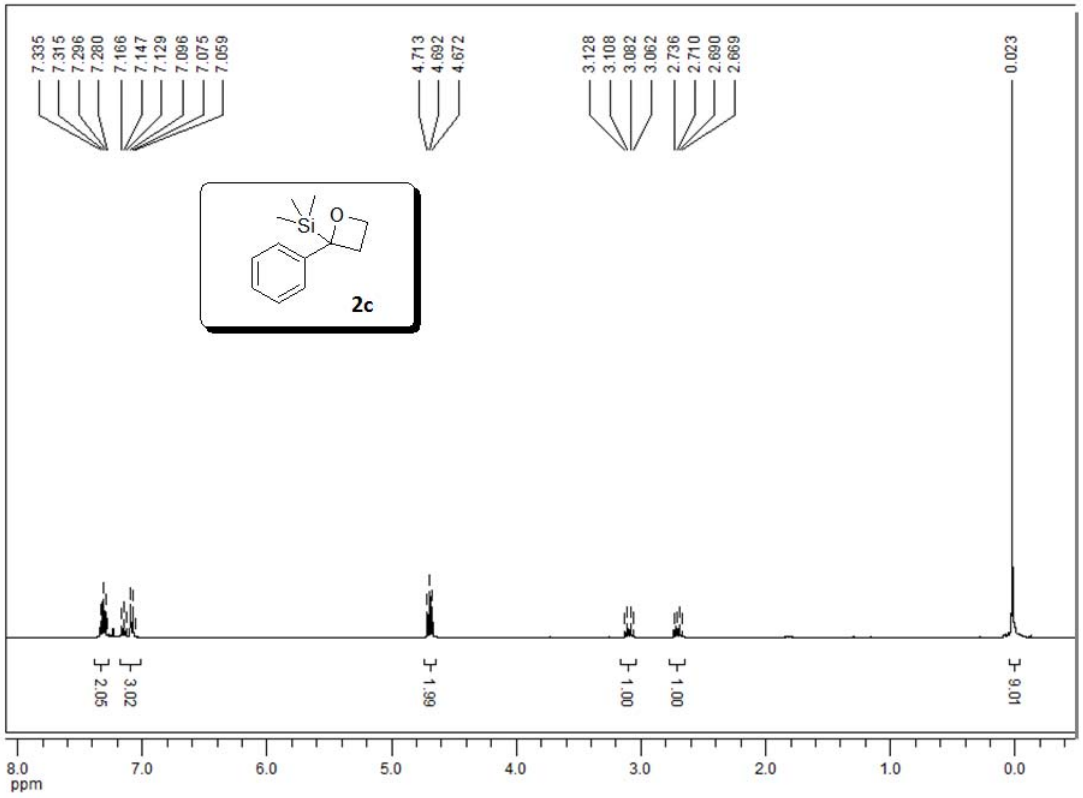
2-(But-3-enyl)-2-phenyloxetane (4): Colorless oil, 40% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 1.81 • 2.17 (m, 4 H), 2.64 • 2.71 (m, 1 H), 2.80 • 2.87 (m, 1 H), 4.47 • 4.59 (m, 2 H), 4.89 (d, *J* = 9.2 Hz, 1 H), 4.95 (d, *J* = 17.4 Hz, 1 H), 5.72 • 5.82 (m, 1 H), 7.21 • 7.37 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.5, 34.0, 42.4, 65.0, 88.6, 114.3, 124.0, 126.6, 128.1, 138.3, 146.6; GC-MS (70 eV) *m*/*z* (%) 188 (M^+, 2), 187 (5), 159 (17), 133 (77), 105 (100), 77 (41); FT-IR (film, cm^{-1}) 2933, 2882, 1641, 1447, 963, 760, 702.



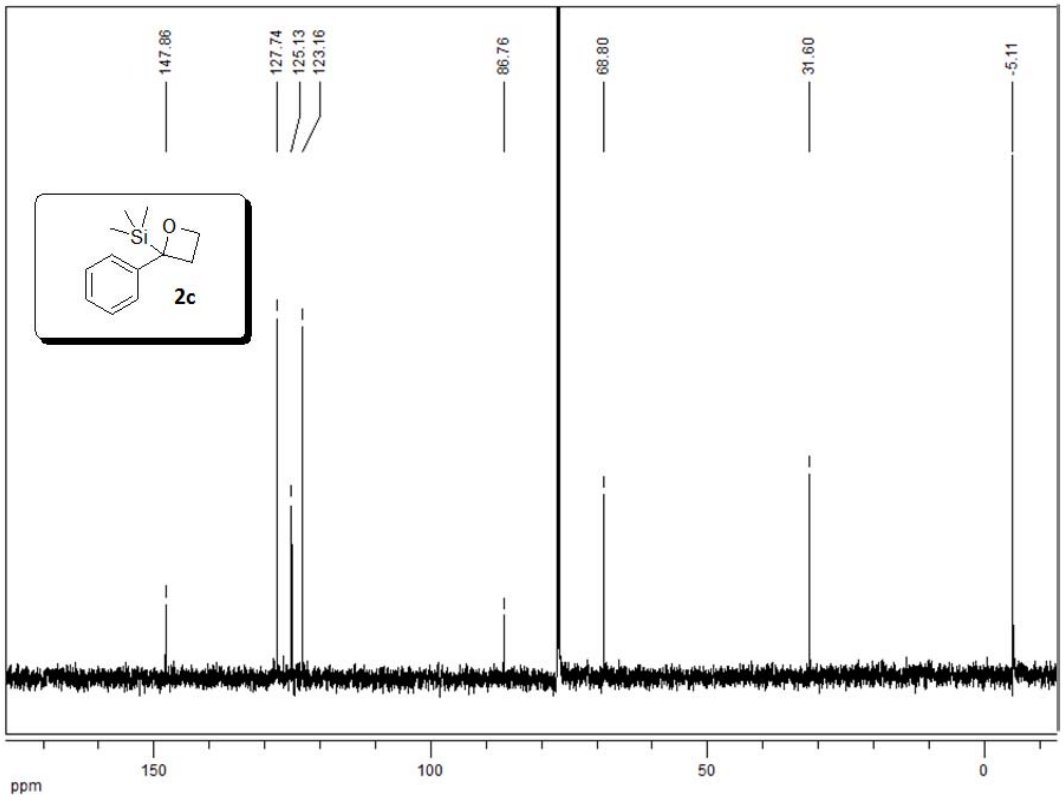
Preparation of 2-(2,4,6-cycloheptatrien-1-yl)-2-phenyloxetane (6): A solution of **2** (134 mg, 1.0 mmol) in 5 mL of dry THF was cooled to ・78 °C and treated with *s*-BuLi (1.08 mL, 1.4 mmol, 1.3 M solution in cyclohexane) under Ar. After 5 min stirring at the above temperature, the addition of 1.8 mmol (320 mg) of powdered tropylium tetrafluoroborate in limited amounts produced a color change of the solution, first, from a dark red to a deep green one and finally, with the time, to a pale yellow one. The reaction mixture was stirred for additional 60 min at –78 °C, then slowly allowed to warm up to room temperature, diluted with brine (5 mL), and extracted with Et_2O (3 × 10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash-chromatography (silica gel; hexane/Et_2O 9/1) to give **6** as a colorless oil (46 mg, 20 %). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.93 (t, *J* = 5.6 Hz, 1 H), 2.67・2.72 (m, 1 H), 3.24・3.28 (m, 1 H), 4.68・4.75 (m, 2 H), 5.19・5.22 (m, 1 H), 5.82・5.84 (m, 1 H), 6.12・6.14 (m, 1 H), 6.36・6.39 (m, 1 H), 6.65・6.72 (m, 2 H), 7.35・7.43 (m, 5 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 32.3, 49.4, 65.9, 88.3, 121.3, 121.4, 124.6, 125.0, 125.6, 126.9, 128.2, 130.6, 130.9, 146.0; ESI-MS: 247 [M^+ + 23 (Na)]; FT-IR (film, cm^{-1}) 3022, 2929, 2880, 1682, 1446, 962, 747.

3. ^{1}H and ^{13}C NMR spectra

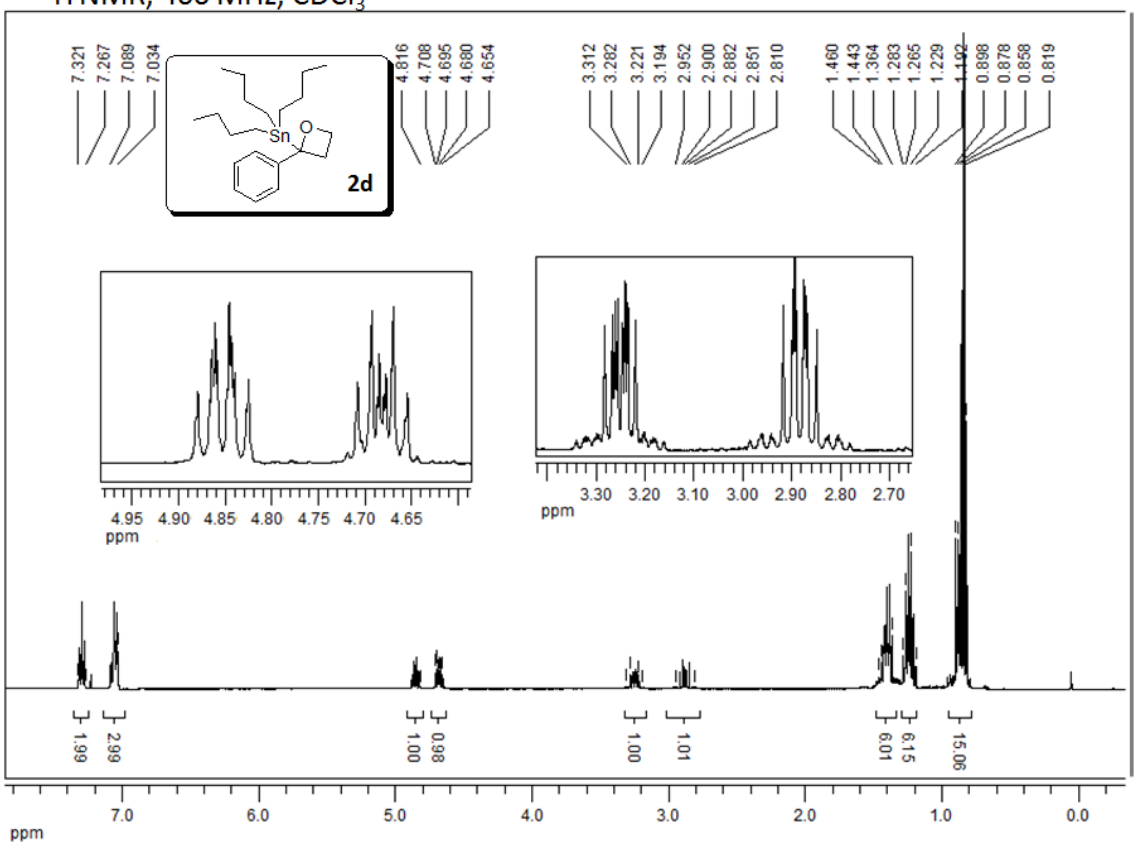
^{1}H NMR, 400 MHz, $CDCl_3$



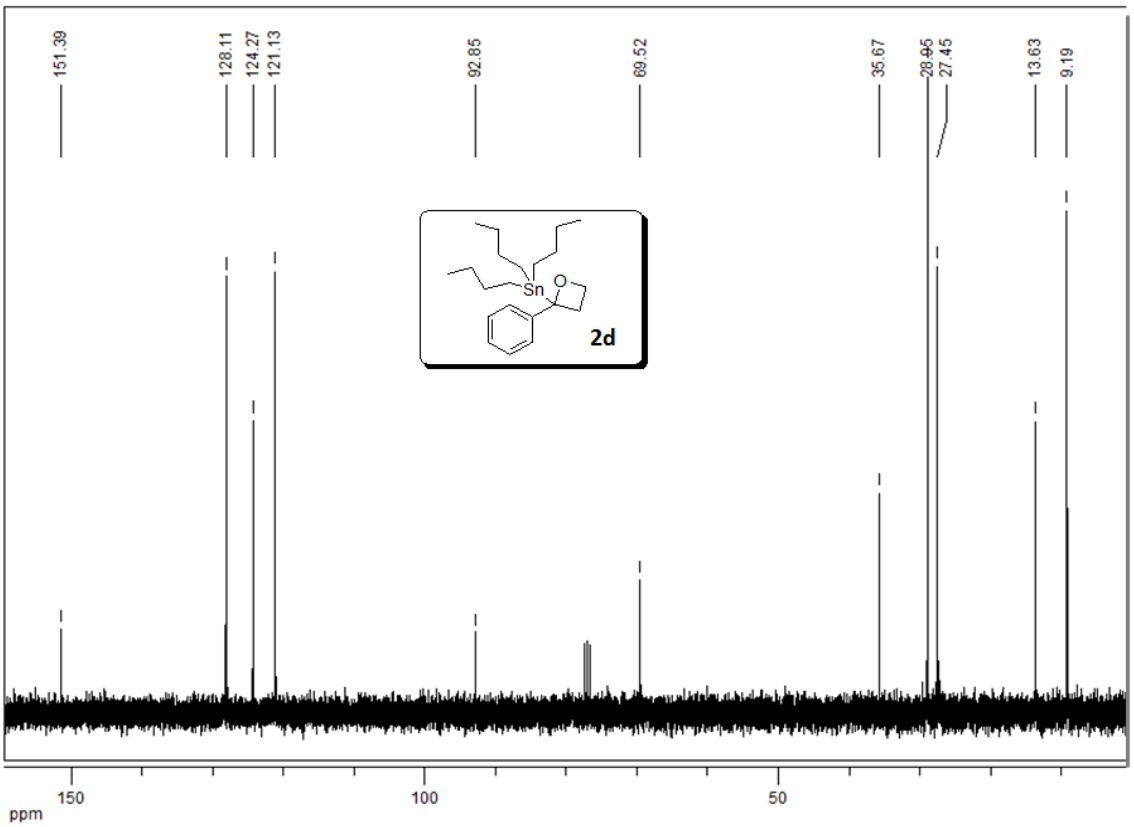
^{13}C NMR, 100 MHz, $CDCl_3$



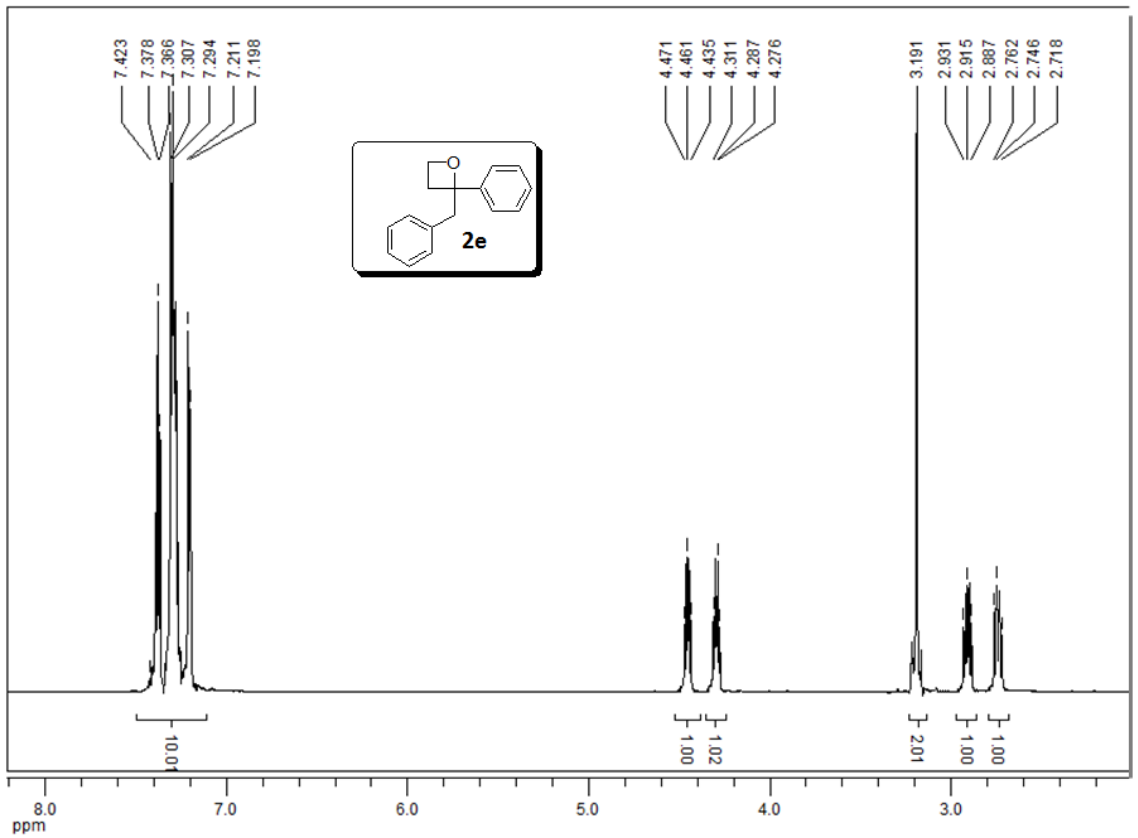
^{1}H NMR, 400 MHz, $CDCl_3$



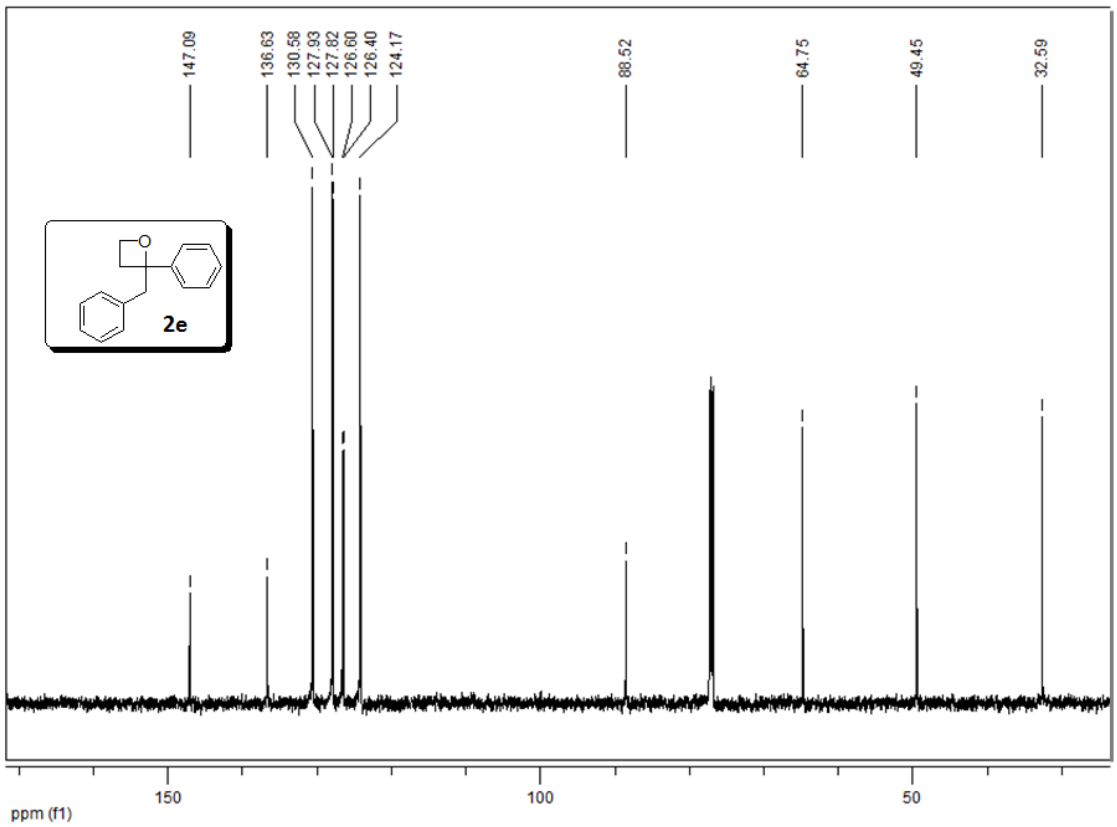
^{13}C NMR, 100 MHz, $CDCl_3$



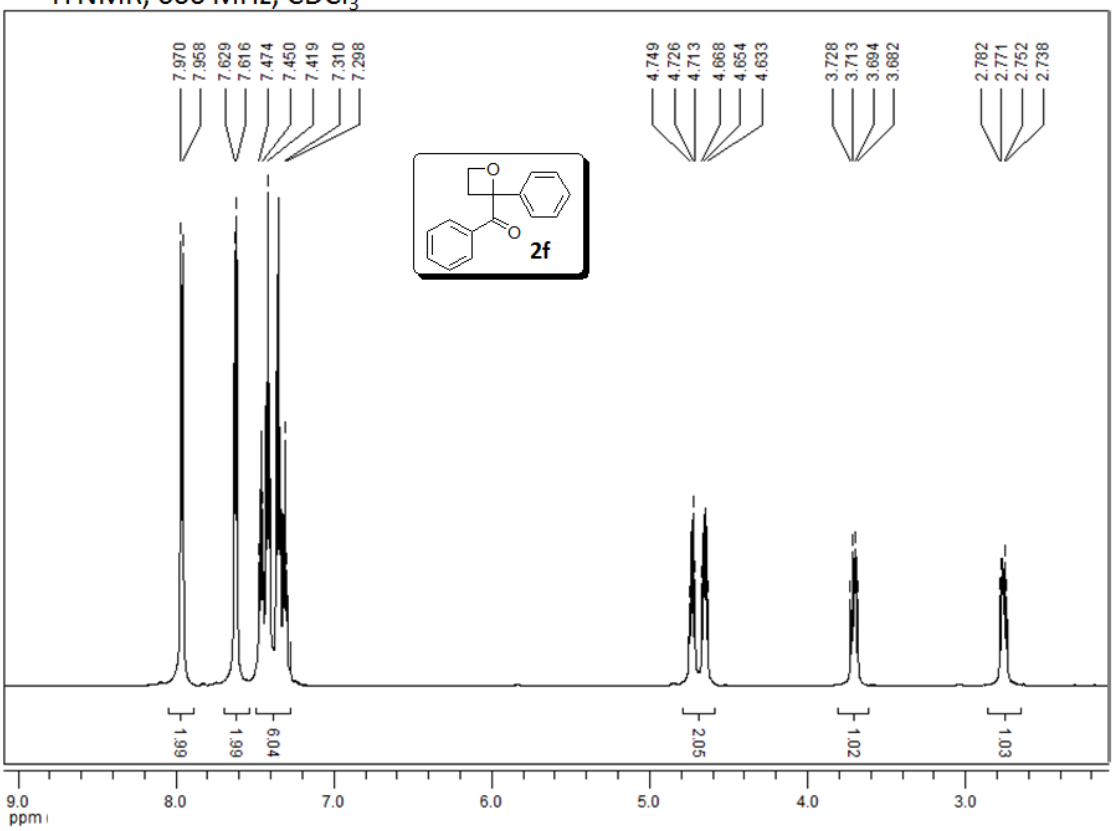
^{1}H NMR, 600 MHz, $CDCl_3$



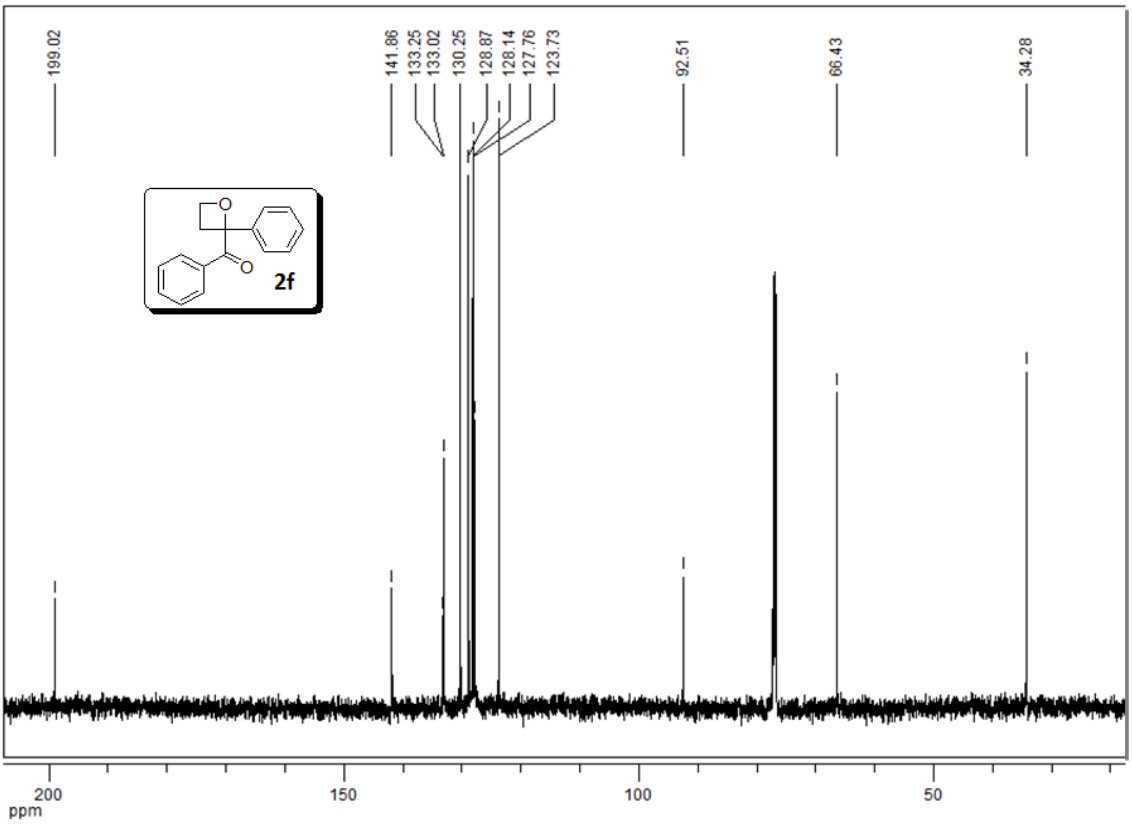
^{13}C NMR, 150 MHz, $CDCl_3$



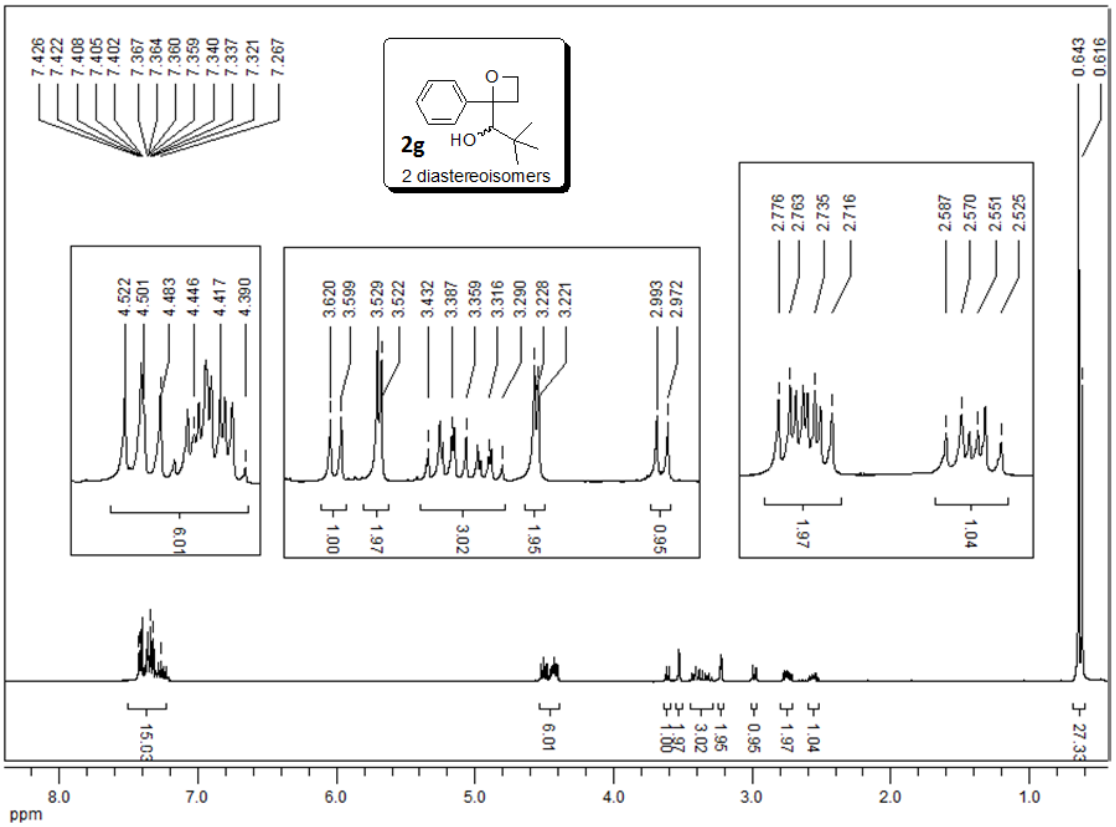
^{1}H NMR, 600 MHz, $CDCl_3$



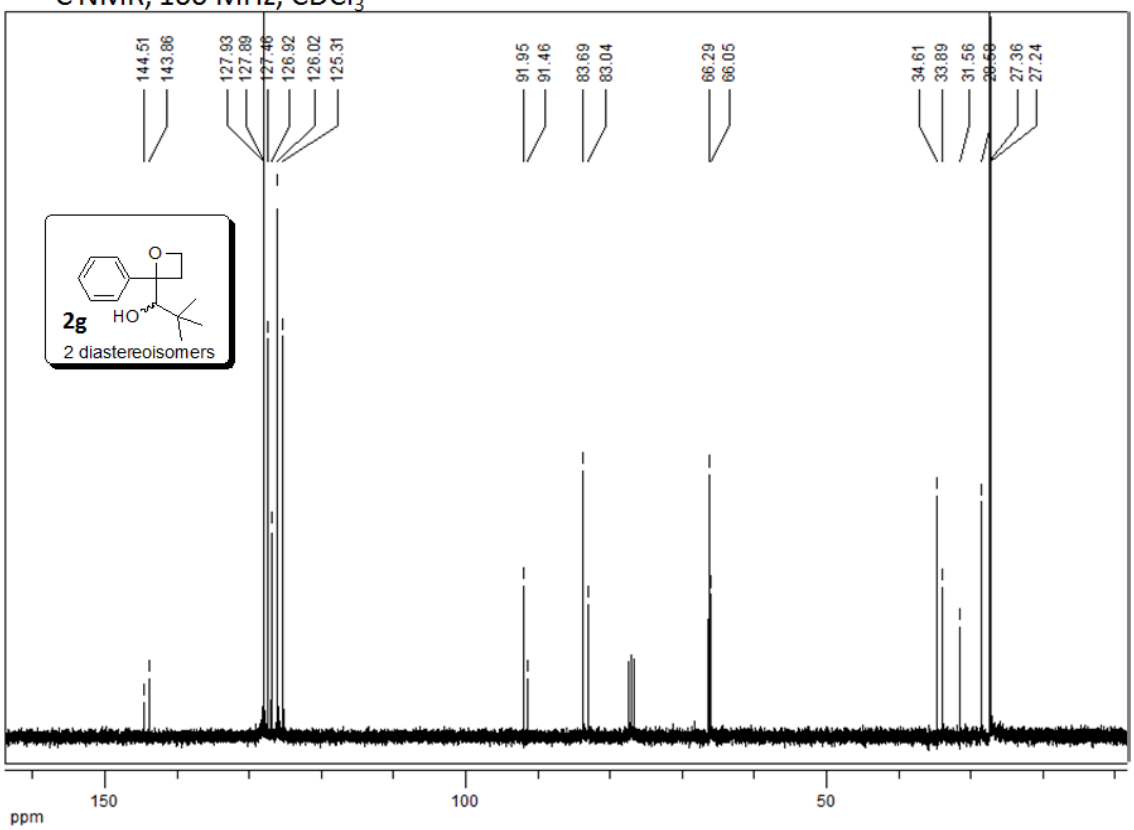
^{13}C NMR, 150 MHz, $CDCl_3$



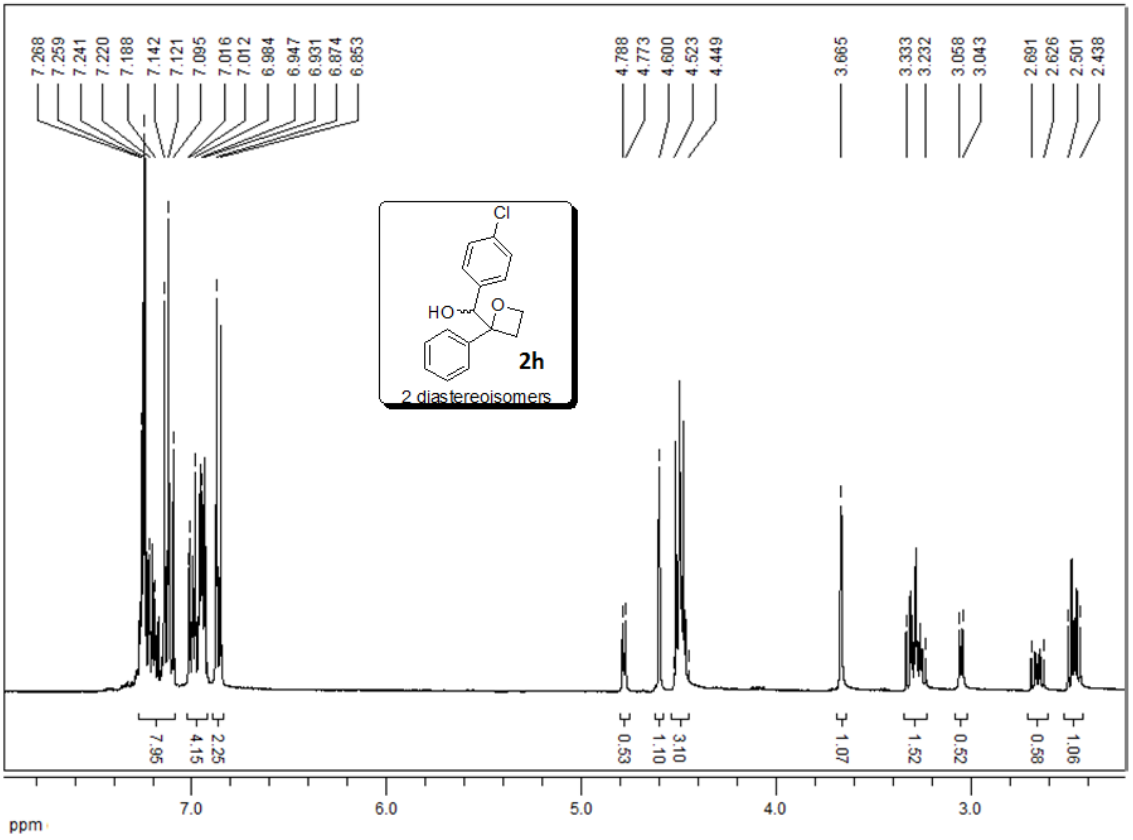
^{1}H NMR, 400 MHz, $CDCl_3$



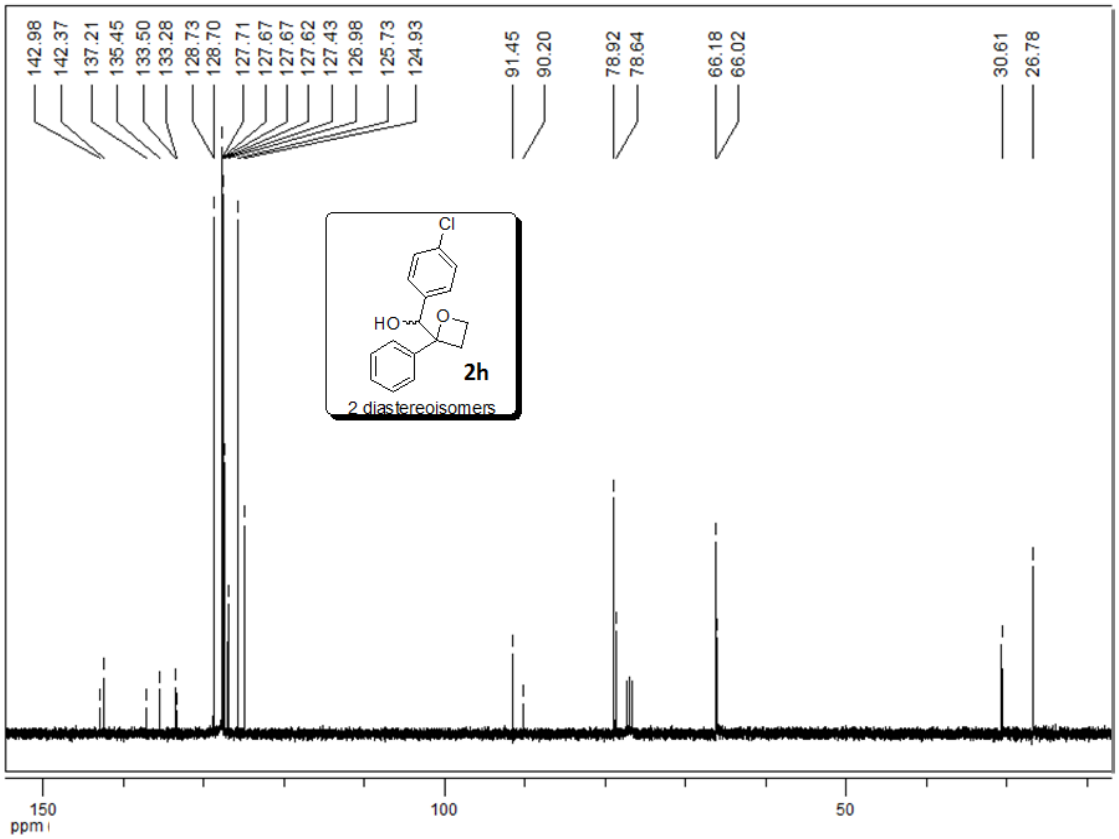
^{13}C NMR, 100 MHz, $CDCl_3$



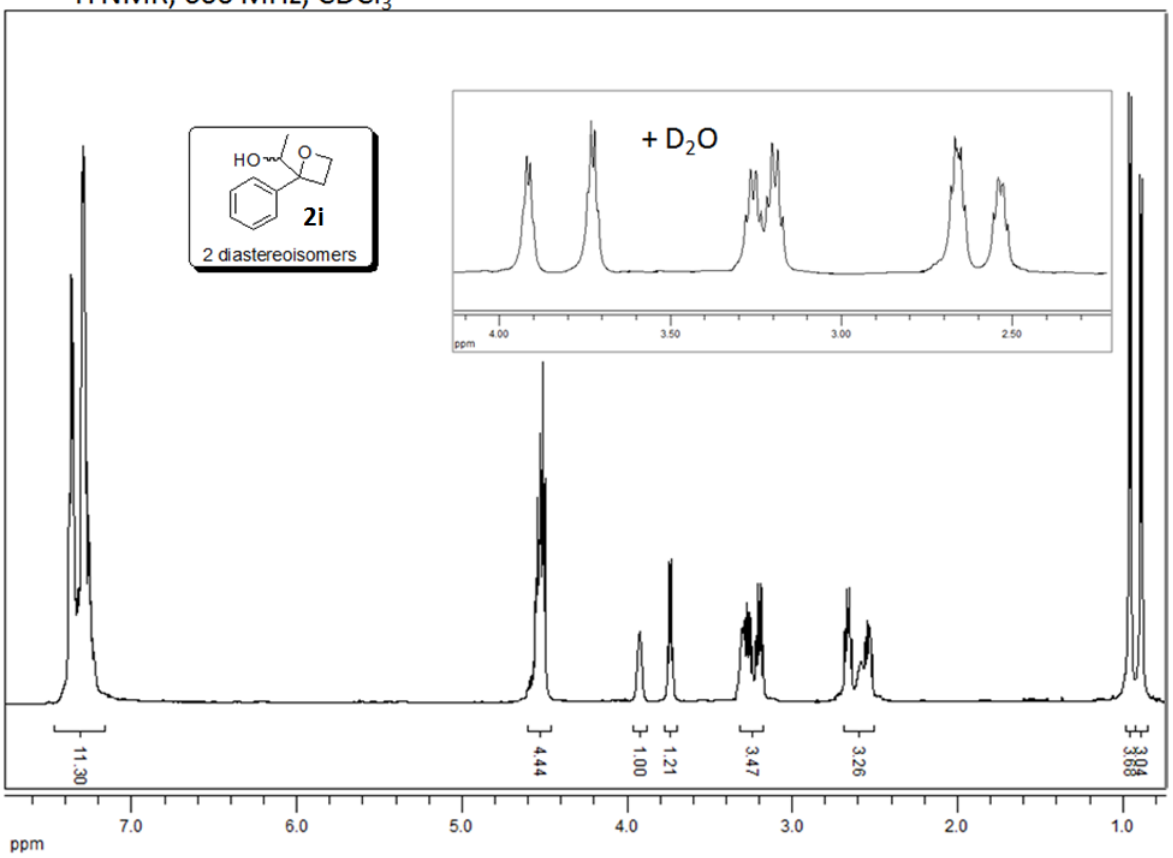
^{1}H NMR, 400 MHz, $CDCl_3$



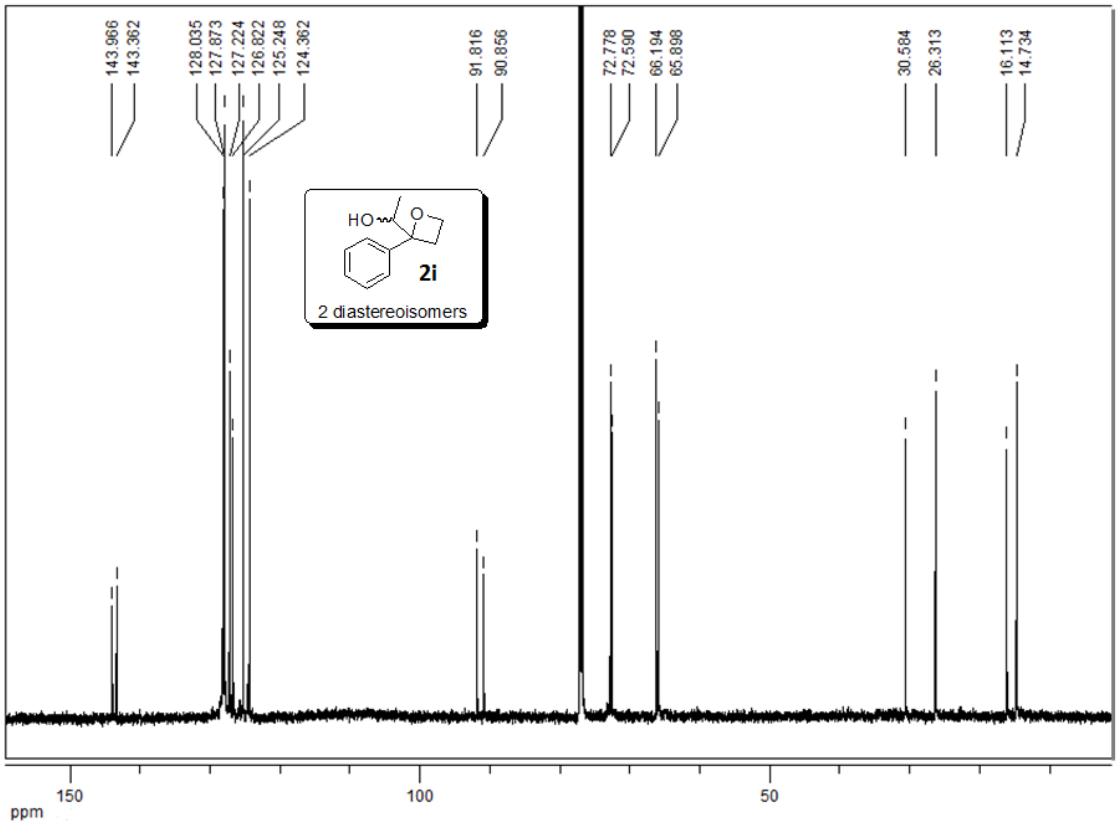
^{13}C NMR, 100 MHz, $CDCl_3$



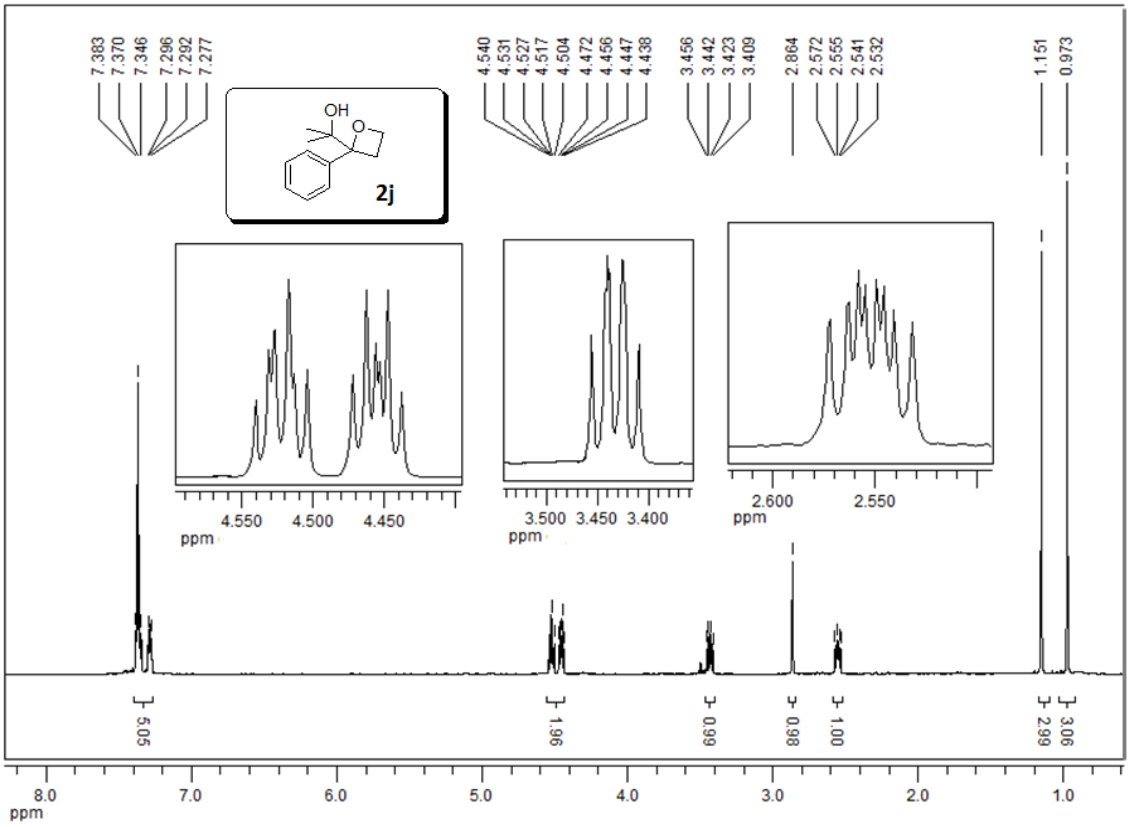
^{1}H NMR, 600 MHz, $CDCl_3$



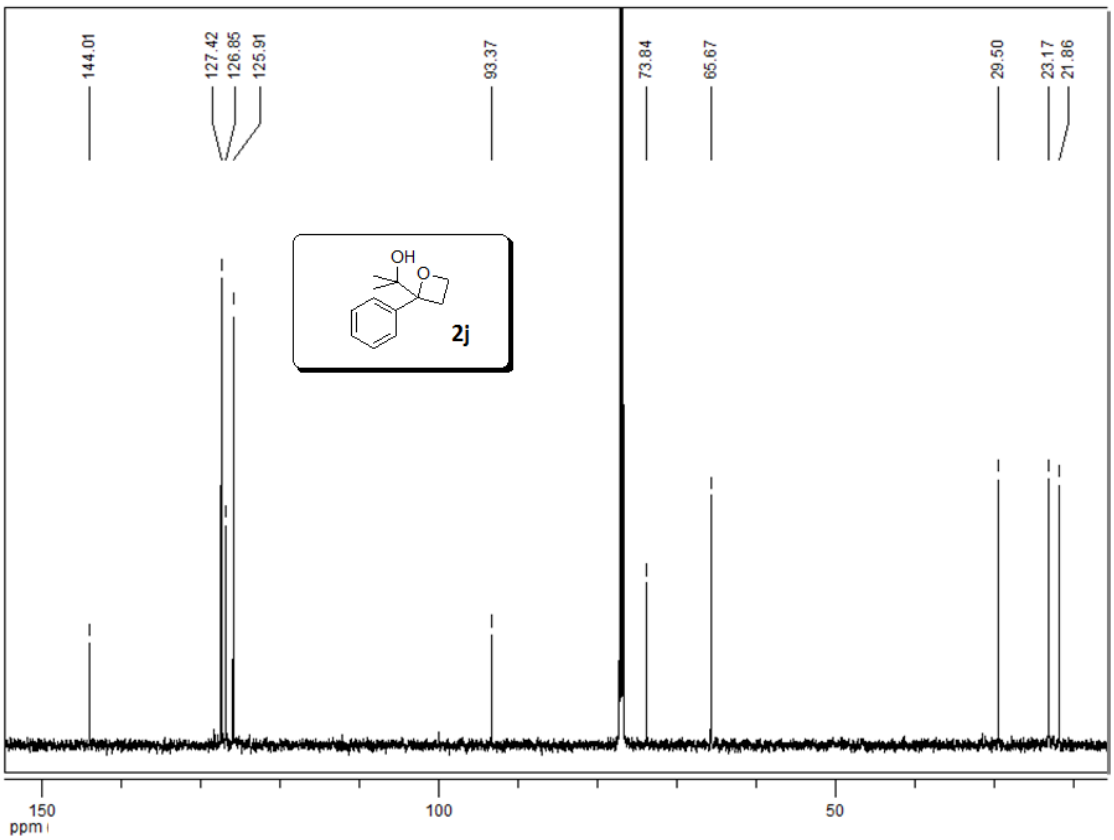
^{13}C NMR, 150 MHz, $CDCl_3$



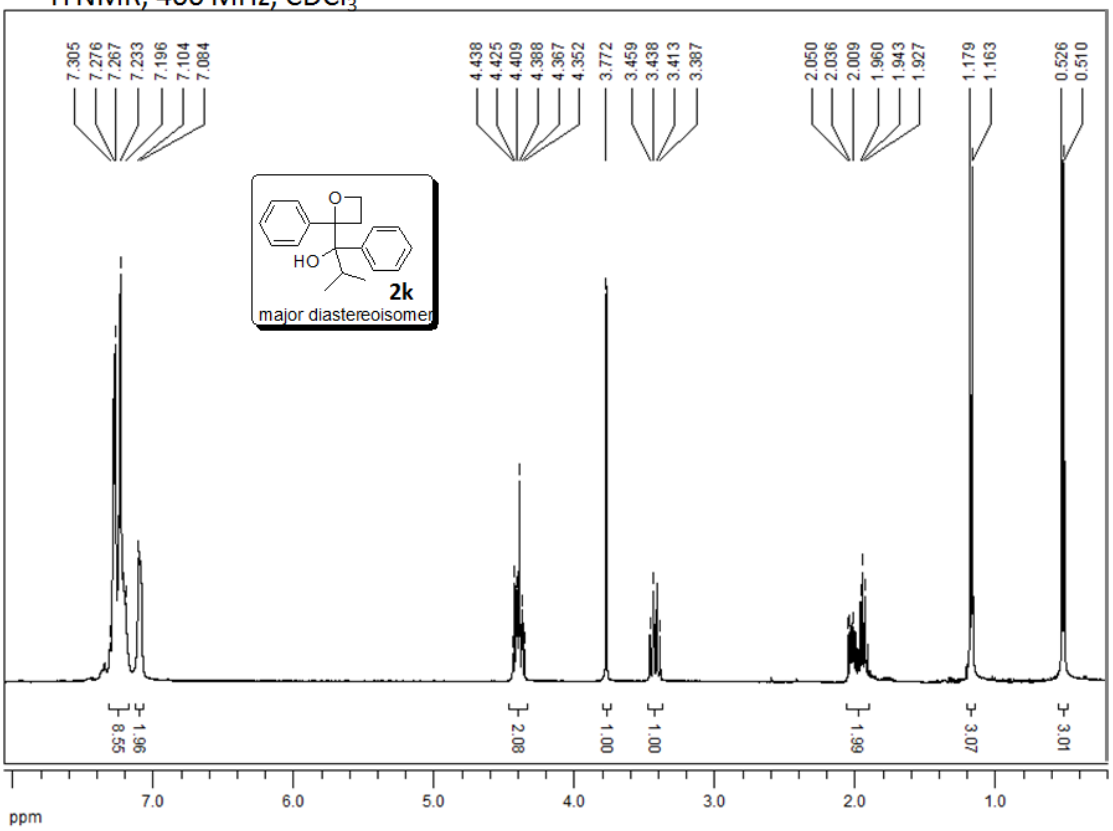
^{1}H NMR, 600 MHz, $CDCl_3$



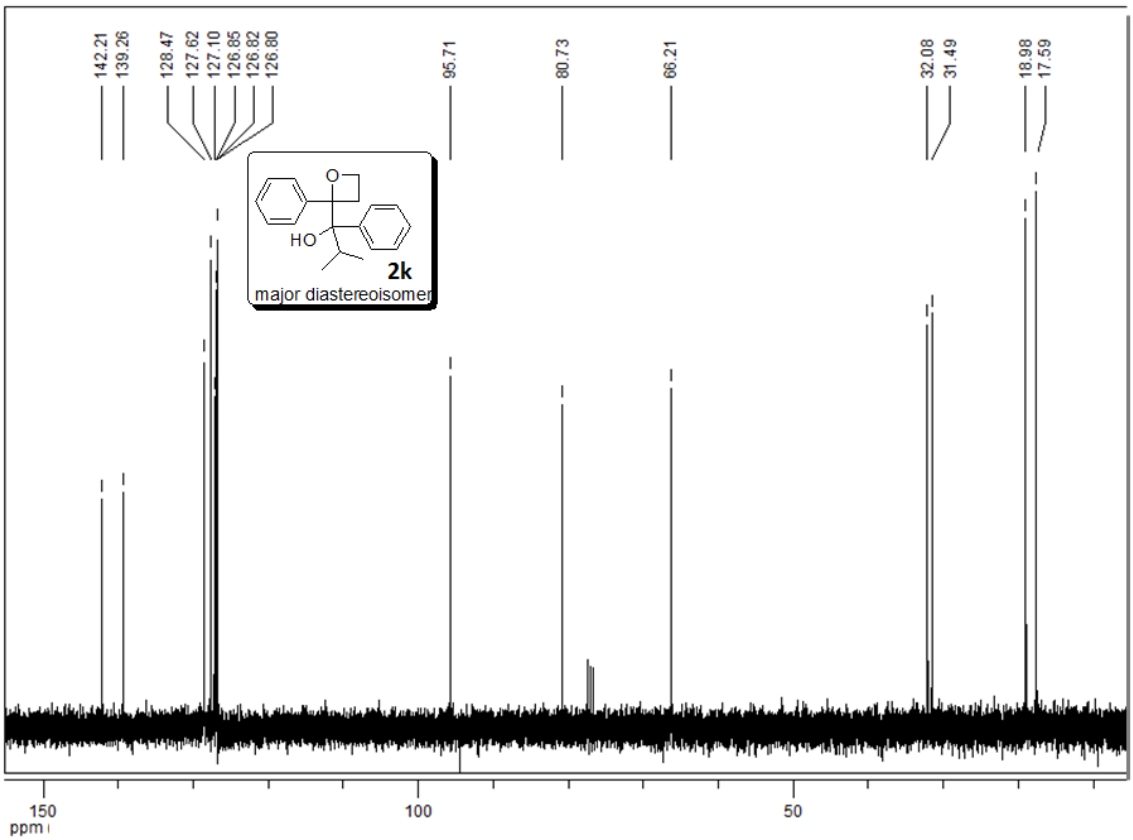
^{13}C NMR, 150 MHz, $CDCl_3$



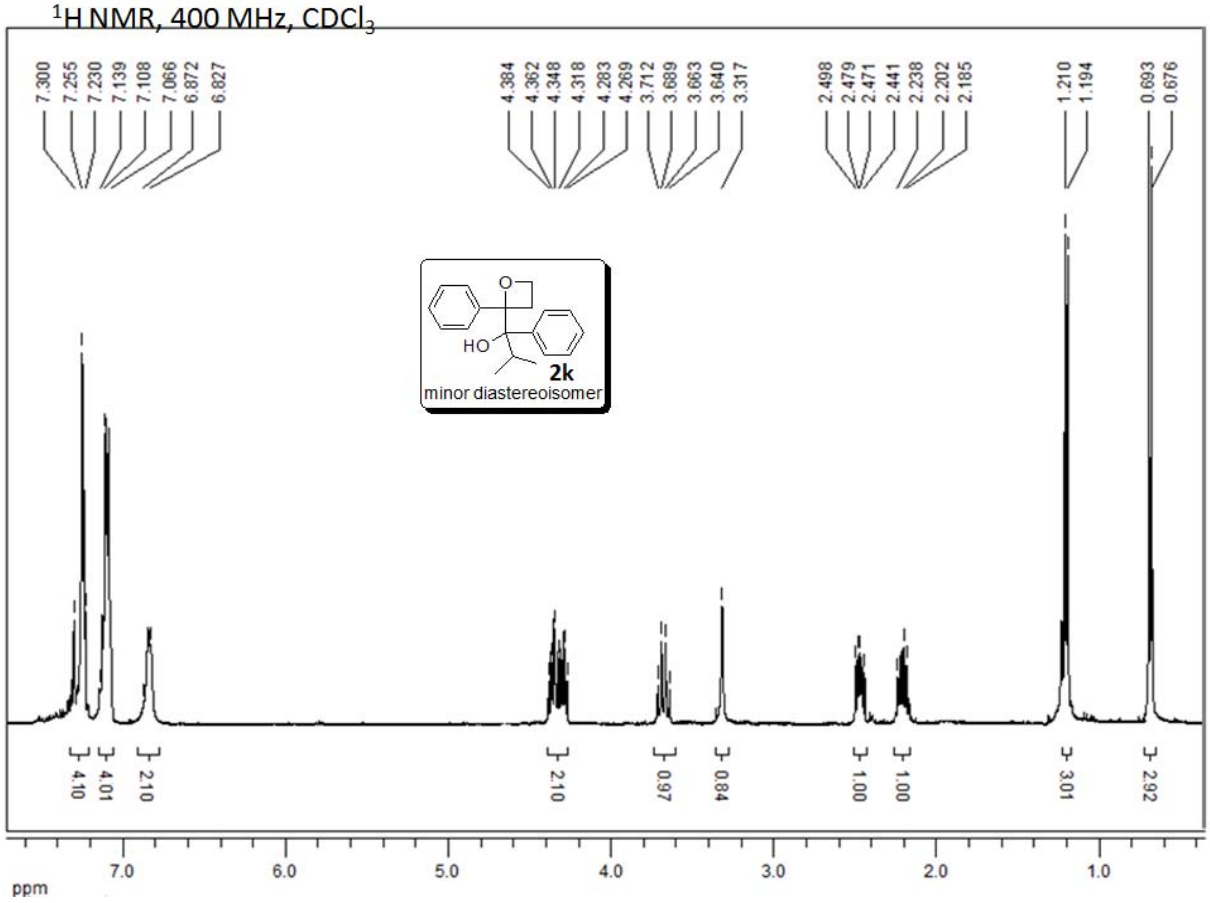
^{1}H NMR, 400 MHz, $CDCl_3$



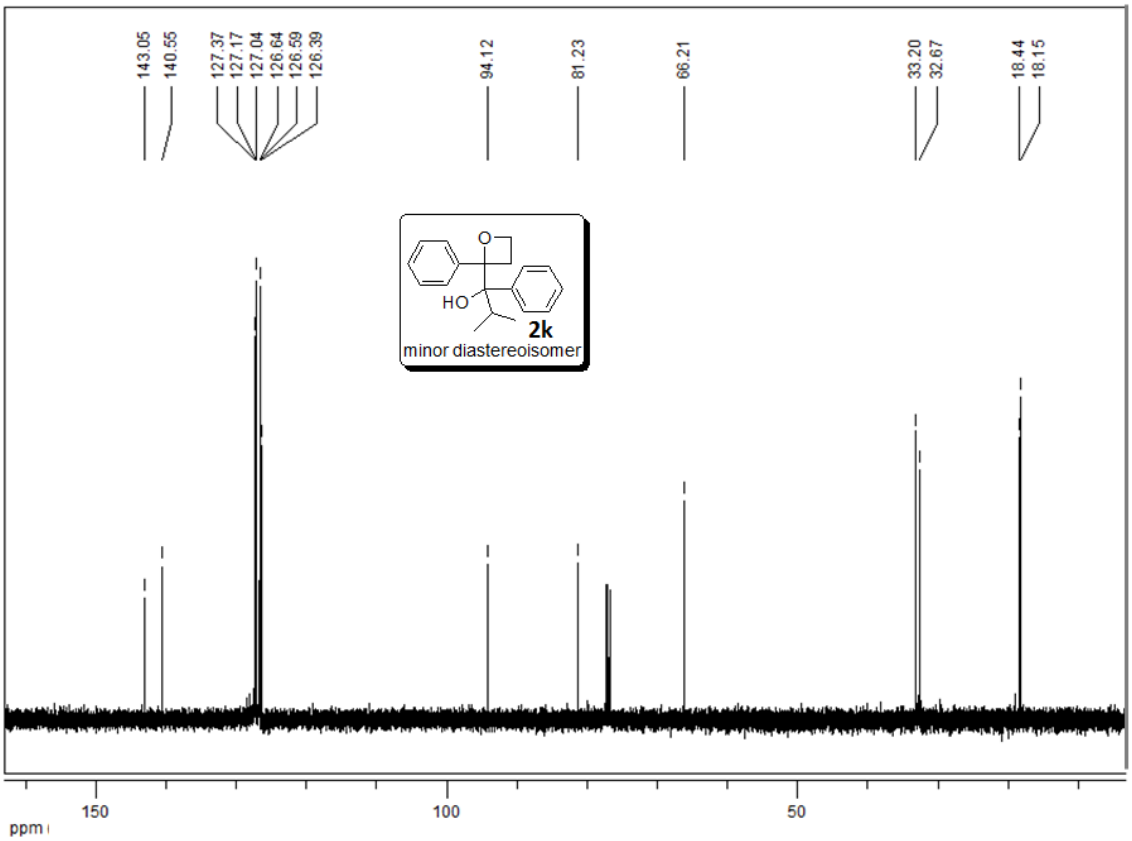
^{13}C NMR, 100 MHz, $CDCl_3$



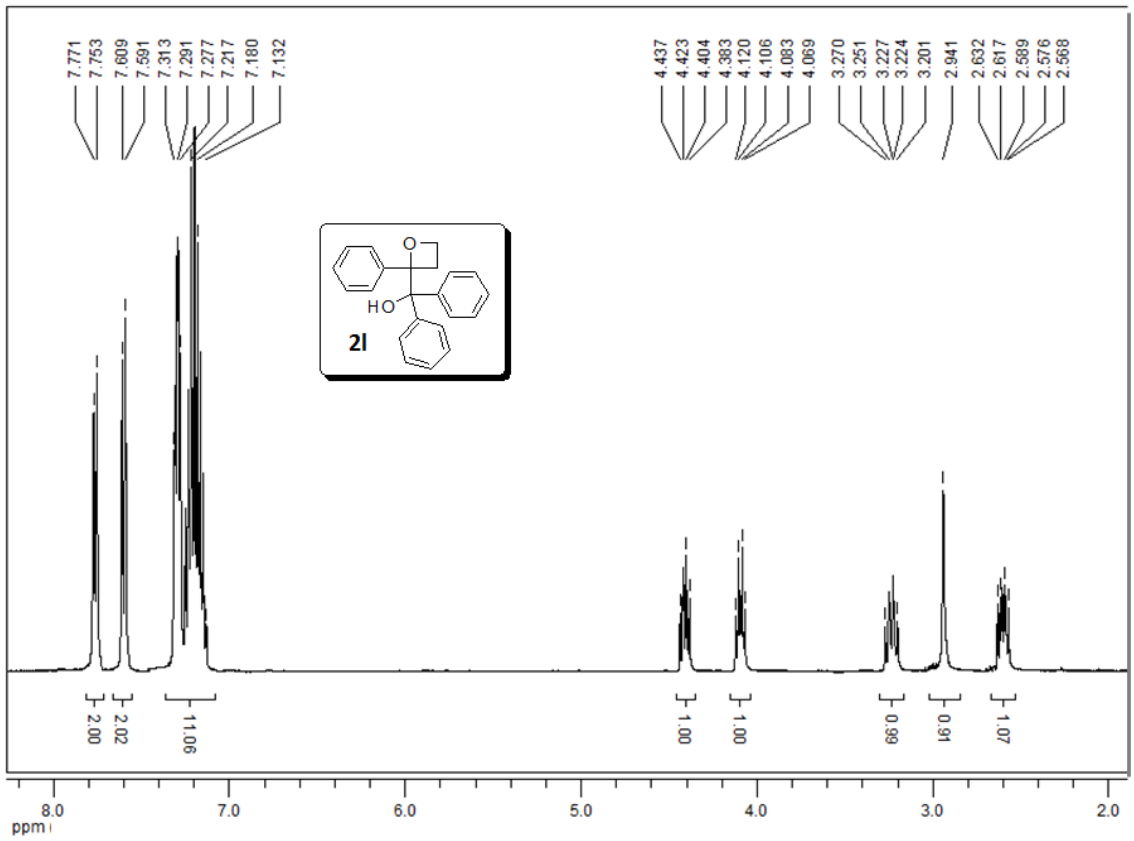
^{1}H NMR, 400 MHz, $CDCl_3$



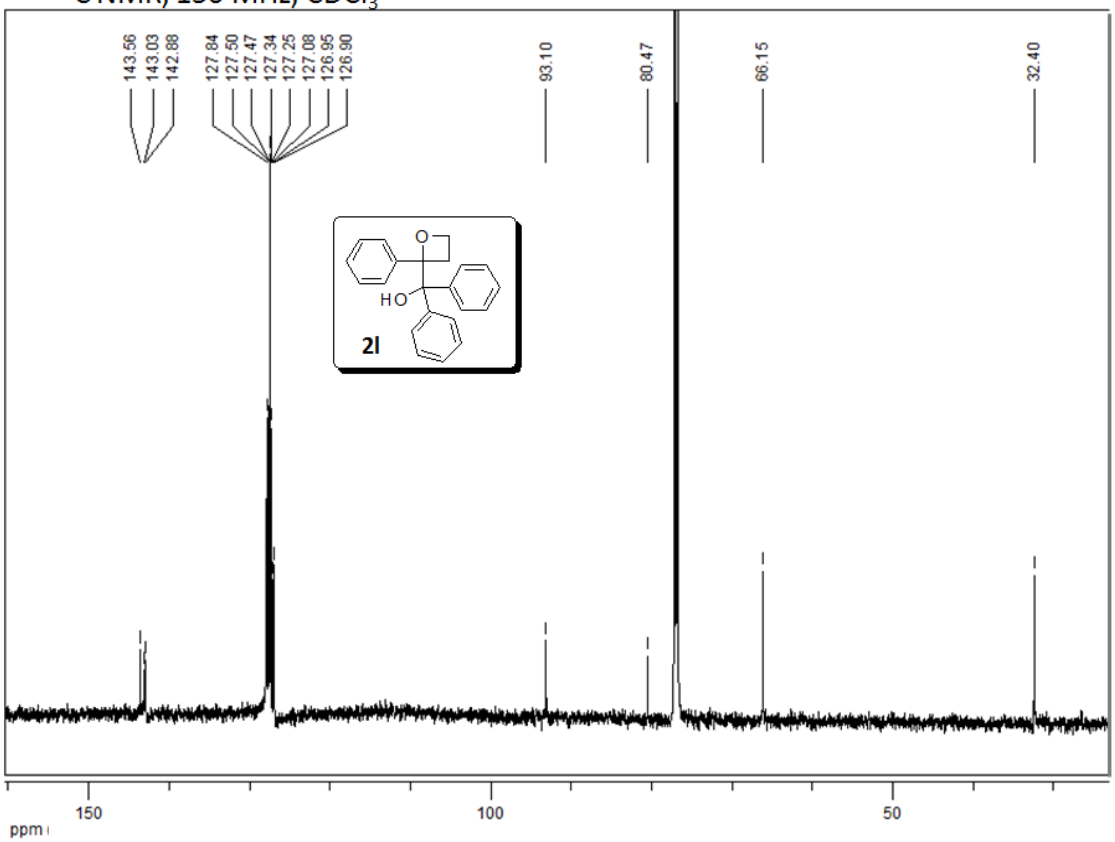
^{13}C NMR, 100 MHz, $CDCl_3$



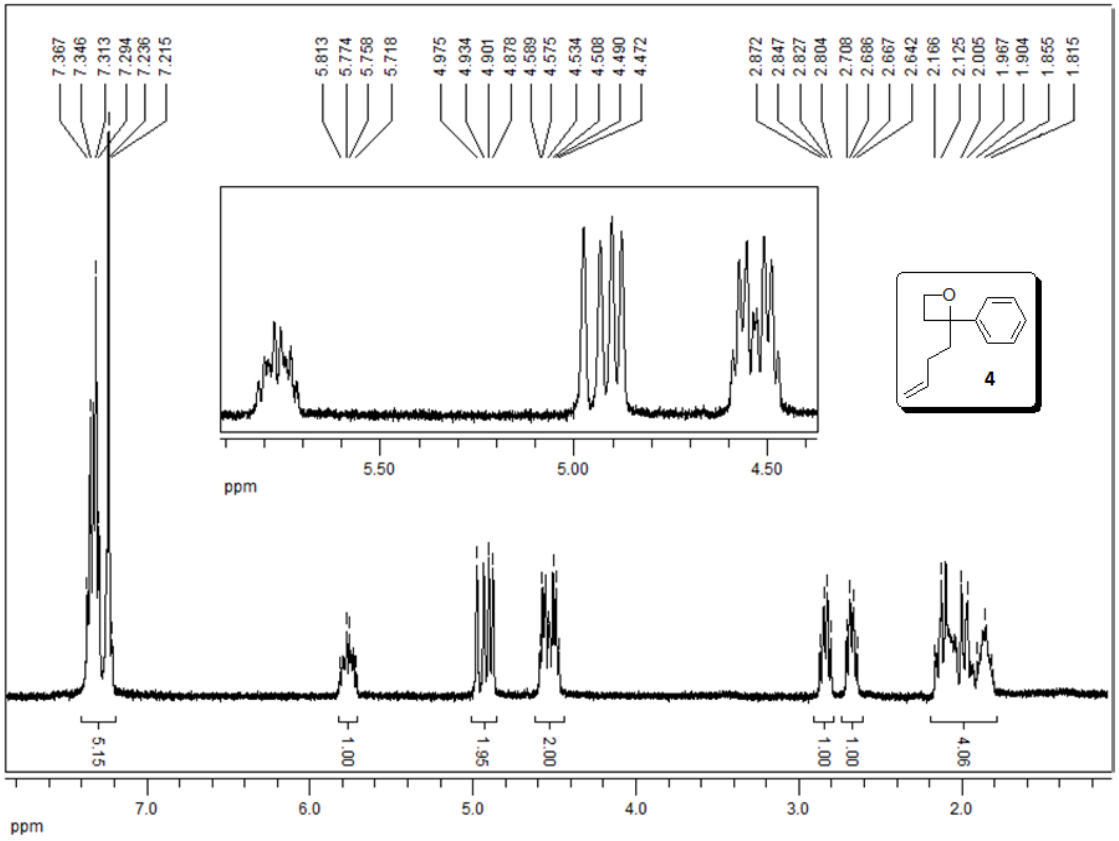
^{1}H NMR, 400 MHz, $CDCl_3$



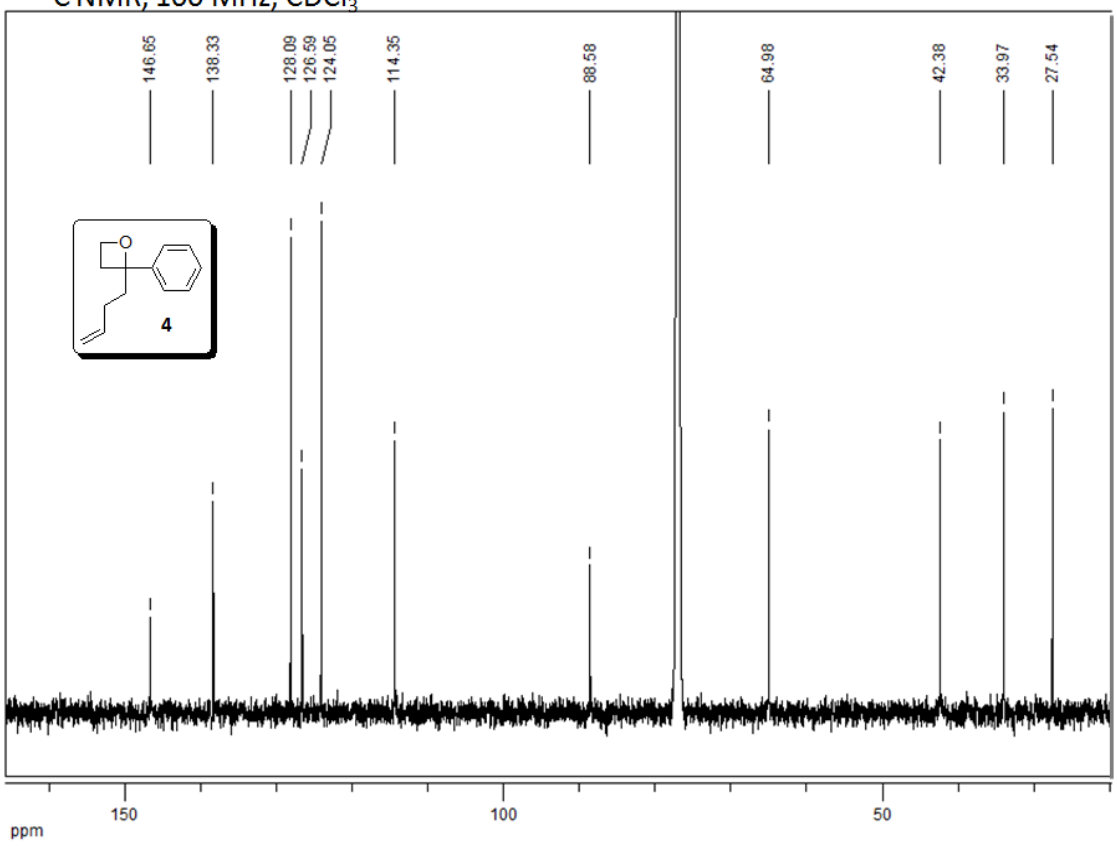
^{13}C NMR, 150 MHz, $CDCl_3$



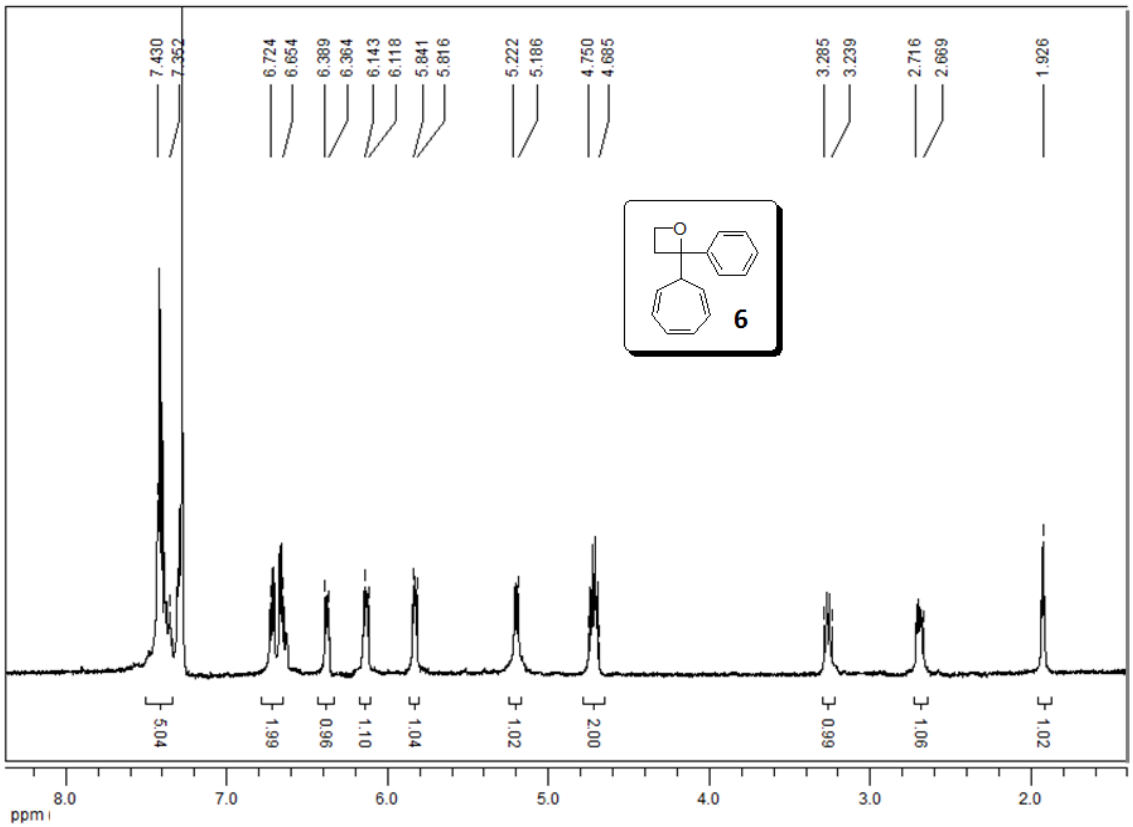
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$



^{1}H NMR, 600 MHz, $CDCl_3$



^{13}C NMR, 150 MHz, $CDCl_3$