

Sequential Aldol Condensation – Transition Metal-Catalyzed Addition Reactions of Aldehydes, Methyl Ketones and Arylboronic Acids

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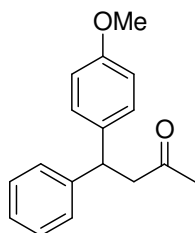
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Supporting Information

General: NMR spectra were recorded on Varian 300MHz or 600MHz spectrometers. Elemental analysis was carried out by Altantic Microanalysis, Inc., Norcross, GA. High resolution mass spectra(HRMS) were acquired by Agilent G6520 Q-TOF mass spectrometer. All yields reported refer to isolated yields unless otherwise indicated, and the product purity was estimated to be greater than 95% as determined by ^1H NMR. Compounds described in the literature were characterized by comparison of their ^1H NMR and ^{13}C NMR spectra to reported data. New compounds were also characterized by element analysis or high resolution mass.

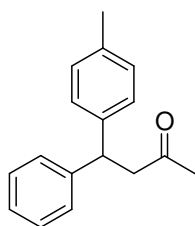
Arylboronic acids were obtained as gifts from Frontier Scientific, Inc. Palladacycle **1** was prepared according to the reported method.¹ Other chemical reagents were purchased from Strem Chemicals, Aldrich or Alpha Aesar and used directly.

General procedure for sequential aldol condensation-transition metal-catalyzed addition reactions of aldehydes, methyl ketones and arylboronic acids: In a glove-box, to a vial containing aldehyde (0.25 mmol) and K_2CO_3 (0.75 mmol) were added ketone (0.2 mL), methanol (0.1 mL) and water (0.1 mL). After the mixture was stirred at 50 - 60 °C for 30 min, arylboronic acid (0.5 mmol), THF (1 mL) and $[\text{Rh}(\text{COD})\text{Cl}]_2$ or palladacycle **1** (0.0025 mmol) (An Ohaus Explorer analytic balance with 0.1 mg accuracy was used for weighing the catalysts) were added into reaction mixture and then stirred at room temperature for another 6 hours. The reaction was quenched by adding 4 N HCl (2 mL) aqueous solution. The mixture was extracted with CH_2Cl_2 (3 x15 mL). The organic layers were combined. After evaporation of the organic solvents, the residue was subjected to column chromatography [silica gel, ethyl acetate/hexane (v/v=1:20) as eluent] to afford the products.



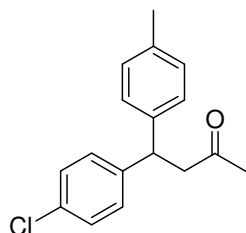
4-(4-Methoxyphenyl)-4-phenylbutan-2-one (**2a**)²

84% yield (53 mg). ^1H NMR (CDCl_3 , 600 MHz): δ 7.26 (t, $J=7.2$ Hz, 4H), 7.21-7.19 (m, 2H), 7.17-7.12 (m, 3H), 6.82-6.79(m, 2H), 4.53 (t, $J=7.2$ Hz, 1H), 3.70 (s, 3H), 3.14 (d, $J=7.8$ Hz, 1H), 2.06 (3H, s) ppm. ^{13}C NMR (CDCl_3 , 150 MHz): δ 207.0, 158.0, 144.2, 135.9, 128.6, 128.5, 127.5, 126.3, 113.9, 55.2, 49.8, 45.2, 30.6 ppm.



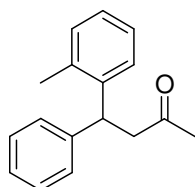
4-Phenyl-4-p-tolylbutan-2-one (2b)²

81% yield (475 mg). ¹H NMR (CDCl₃, 600 MHz): δ 7.27-7.24 (m, 2H), 7.21-7.20 (m, 2H), 7.17-7.14 (m, 1H), 7.11-7.06 (m, 4H), 4.57 (t, *J*=7.2 Hz, 1H), 3.13 (d, *J*=7.2 Hz, 2H), 2.28 (s, 3H), 2.06 (s, 3H) ppm. ¹³C NMR (CDCl₃, 150 MHz): δ 206.9, 144.0, 140.7, 135.9, 129.2, 128.5, 127.6, 127.5, 126.3, 49.7, 45.6, 30.6, 20.9 ppm.



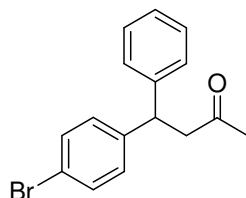
4-(4-Chlorophenyl)-4-p-tolylbutan-2-one (2c)

88% yield (60 mg). White solid, m.p. 70-71°C. ¹H NMR (CDCl₃, 600 MHz): δ 7.24 (d, *J*=8.4 Hz, 2H), 7.15 (d, *J*=8.4 Hz, 2H), 7.08 (m, 4H), 4.53 (t, *J*=7.2 Hz, 1H), 3.14 (d, *J*=7.2 Hz, 2H), 2.30 (s, 3H), 2.09 (s, 3H) ppm. ¹³C NMR (CDCl₃, 150 MHz): 206.5, 142.6, 140.3, 136.2, 132.1, 129.4, 129.0, 128.7, 127.4, 126.3, 49.7, 45.6, 30.6, 20.9 ppm. IR (neat) ν 3030(w), 3001(w), 2920(m), 1704(s), 1490(s), 1349(s), 762(s) cm⁻¹. HR-MS (ESI): calcd. for C₁₇H₁₈ClO [M+H]⁺ 273.1041, found 273.1043.



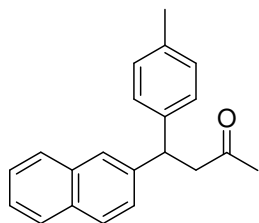
4-Phenyl-4-o-tolylbutan-2-one (2d)²

85% yield (51 mg). ¹H NMR (CDCl₃, 600 MHz): δ 7.25-7.22 (m, 4H), 7.17-7.12 (m, 5H), 4.78 (t, *J*=7.2 Hz, 1H), 3.14 (d, *J*=7.2 Hz, 2H), 2.29 (s, 3H), 2.06 (s, 3H) ppm. ¹³C NMR (CDCl₃, 150 MHz): δ 206.8, 143.5, 141.5, 136.3, 130.8, 128.4, 127.9, 126.40, 126.2 (2C), 126.0, 50.0, 41.9, 30.6, 19.8 ppm.



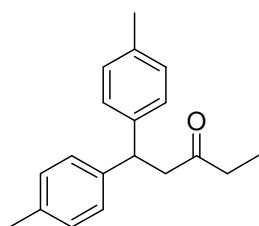
4-(4-Bromophenyl)-4-phenylbutan-2-one (2e)

86% yield (65 mg). Light yellow oil. ¹H NMR (CDCl₃, 600 MHz): δ 7.38 (d, *J*=7.8 Hz, 2H), 7.27 (t, *J*=7.8 Hz, 2H), 7.18-7.17 (m, 3H), 7.09 (d, *J*=8.4 Hz, 2H), 4.55 (t, *J*=7.2 Hz, 1H), 3.15 (d, *J*=7.2 Hz, 1H), 2.07 (3H, s) ppm. ¹³C NMR (CDCl₃, 150 MHz): δ 206.3, 143.2, 142.9, 131.6, 129.4, 128.6, 127.5, 126.6, 120.2, 49.3, 45.3, 30.6 ppm. IR (neat): 3060(w), 3027(w), 2969(w), 2897(w), 1717(s), 1487(s), 699(s) cm⁻¹. HR-MS (ESI): calcd. for C₁₆H₁₉BrNO [M+NH₄]⁺ 322.0626, found 322.0626.



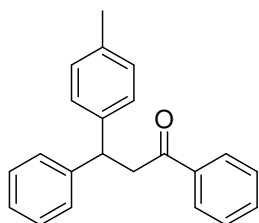
4-(Naphthalen-2-yl)-4-p-tolylbutan-2-one (2f)

84% yield (60 mg). Pale yellow solid, m. p.: 79-80 °C. ^1H NMR (CDCl_3 , 600 MHz): δ 7.77 (t, $J=7.8$ Hz, 2H), 7.73 (d, $J=8.4$ Hz, 1H), 7.67 (m, 4H), 7.45-7.40 (m, 2H), 7.31 (d, $J=8.4$ Hz, 1H), 7.15-7.03 (m, 4H), 4.71 (t, $J=7.2$ Hz, 1H), 3.25 (t, $J=7.8$ Hz, 2H), 2.28 (s, 3H), 2.09 (s, 3H) ppm. ^{13}C NMR (CDCl_3 , 150 MHz): δ 206.9, 141.5, 140.7, 136.0, 133.4, 132.2, 129.3, 128.3, 127.7 (2C), 127.5, 126.5, 126.0, 125.6, 125.5, 49.6, 45.7, 30.7, 20.9 ppm. IR (neat) 3025(w), 2968(m), 1710(s) cm^{-1} . HR-MS (ESI): calcd. for $\text{C}_{21}\text{H}_{24}\text{NO}$ $[\text{M}+\text{NH}_4]^+$ 306.1852, found 306.1854.



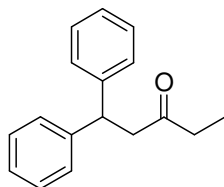
1,1-Dip-tolylpentan-3-one (2g)

86% yield (57 mg). White solid, m. p.: 83-84 °C. ^1H NMR (CDCl_3 , 600 MHz): δ 7.10-7.05 (m, 8H), 4.53 (t, $J=7.8$ Hz, 1H), 3.76 (s, 3H), 3.11 (d, $J=7.2$ Hz, 2H), 2.32 (q, $J=7.2$ Hz, 2H), 2.78 (s, 6H), 0.96 (t, $J=7.2$ Hz, 3H) ppm. ^{13}C NMR (CDCl_3 , 150 MHz): δ 209.7, 141.2, 135.8, 129.2, 127.5, 48.6, 45.3, 36.7, 20.9, 7.5 ppm. IR (neat) 2980(m), 2923(m), 1712(s), 1512(m), 1373(m), 1108(s), 805(s) cm^{-1} . Anal. Calcd for $\text{C}_{19}\text{H}_{22}\text{O}$: C, 85.67; H, 8.32; Found: C, 85.51; H, 8.34.



1,3-Diphenyl-3-p-tolylpropan-1-one (2h) ³

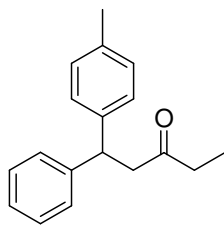
74% yield (56 mg). ^1H NMR (CDCl_3 , 600 MHz): δ 7.93 (d, $J=8.4$ Hz, 2H), 7.54 (t, $J=8.4$ Hz, 2H), 7.43 (t, $J=7.2$ Hz, 4H), 7.26-7.25 (m, 4H), 7.17-7.15 (m, 3H), 7.07 (d, $J=8.4$ Hz, 2H), 4.79 (t, $J=7.2$ Hz, 1H), 3.72 (d, $J=7.2$ Hz, 2H), 2.28 (s, 3H) ppm. ^{13}C NMR (CDCl_3 , 150 MHz): δ 198.7, 144.4, 141.1, 137.1, 135.9, 133.0, 129.2, 128.6, 128.5, 128.0, 127.8, 127.6, 126.3, 45.5, 44.8, 21.0 ppm.



1,1-Diphenylpentan-3-one (2i)

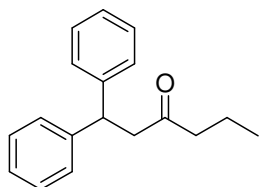
86% yield (57 mg). White solid, m.p.: 26-27 °C. ^1H NMR (CDCl_3 , 600 MHz): δ 7.27-7.25 (m, 4H), 7.22-7.21 (m, 4H), 7.18-7.15 (m, 2H), 4.61 (t, $J=7.2$ Hz, 1H), 3.14 (d, $J=7.2$ Hz, 2H), 2.32 (q, $J=7.2$ Hz, 2H), 0.94 (t, $J=7.2$ Hz, 3H) ppm. ^{13}C NMR (CDCl_3 , 150 MHz): δ 209.5, 143.9, 128.5, 127.7, 126.4, 48.4, 46.0,

36.7, 7.5 ppm. IR (neat) 3028(w), 2940(w), 1710(m), 1494(m), 1452(m), 697(s) cm^{-1} . HR-MS (ESI): calcd. for $\text{C}_{17}\text{H}_{22}\text{NO}$ $[\text{M}+\text{NH}_4]^+$ 256.1696, found 256.1697.



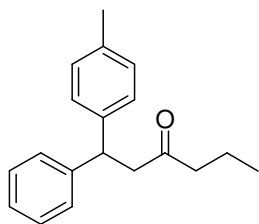
1-Phenyl-1-p-tolylpentan-3-one (2j)

85% yield (54 mg). White solid, m. p.: 28-29 °C. ^1H NMR (CDCl_3 , 600 MHz): δ 7.27-7.24 (m, 2H), 7.20-7.19 (m, 2H), 7.17-7.14 (m, 1H), 7.11-7.07 (m, 4H), 4.54 (t, $J=7.2$ Hz, 1H), 3.15 (d, $J=7.2$ Hz, 2H), 2.33 (q, $J=7.2$ Hz, 2H), 2.28 (s, 3H), 0.95 (t, $J=7.2$ Hz, 3H) ppm. ^{13}C NMR (CDCl_3 , 150 MHz): δ 209.6, 144.2, 141.0, 129.2, 128.5, 127.7, 127.6, 126.3, 48.6, 45.7, 36.7, 21.0, 7.6 ppm. IR (neat) 3025(w), 2921(m), 1711(s), 1514(m), 1454(m), 773(m), 726(s), 699(s) cm^{-1} . HR-MS (ESI): calcd. for $\text{C}_{18}\text{H}_{20}\text{NaO}$ $[\text{M}+\text{Na}]^+$ 275.1406, found 275.1409.



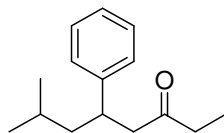
1,1-Diphenylhexan-3-one (2k)

81% yield (51 mg). Light yellow oil. ^1H NMR (CDCl_3 , 600 MHz): δ 7.27-7.14 (m, 10H), 4.61 (t, $J=7.8$ Hz, 1H), 3.13 (d, $J=7.2$ Hz, 2H), 2.30-2.27 (m, 2H), 1.53-1.46 (m, 2H), 0.79 (t, $J=7.2$ Hz, 3H) ppm. ^{13}C NMR (CDCl_3 , 150 MHz): δ 208.9, 143.9, 128.5, 127.7, 126.3, 48.7, 45.9, 45.4, 16.9, 13.5 ppm. IR (neat) 3061(w), 3028(w), 2961(w), 2874(w), 1712(m), 698(s) cm^{-1} . HR-MS (ESI): calcd. for $\text{C}_{18}\text{H}_{20}\text{NaO}$ $[\text{M}+\text{Na}]^+$ 275.1406, found 275.1408.



1-Phenyl-1-p-tolylhexan-3-one (2l)

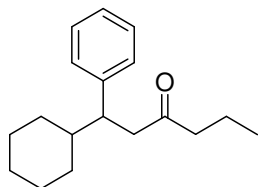
84% yield (53 mg). Light yellow oil. ^1H NMR (CDCl_3 , 600 MHz): δ 7.24 (t, $J=7.8$ Hz, 3H), 7.21-7.19 (m, 2H), 7.14 (t, $J=7.2$ Hz, 3H), 7.10 (d, $J=8.4$ Hz, 2H), 7.06 (d, $J=8.4$ Hz, 2H), 4.57 (t, $J=7.8$ Hz, 1H), 3.11 (d, $J=7.2$ Hz, 2H), 2.29-2.26 (m, 5H), 1.49 (sext, $J=7.2$ Hz, 2H), 0.79 (t, $J=7.2$ Hz, 3H) ppm. ^{13}C NMR (CDCl_3 , 150 MHz): δ 209.0, 144.2, 140.9, 135.8, 129.1, 128.4, 127.6, 127.5, 126.2, 48.8, 45.5, 45.4, 20.9, 16.9, 7.5 ppm. IR (neat) 3085(w), 3027(m), 2962(m), 2874(w), 1714(s), 698(s) cm^{-1} . HR-MS (ESI): calcd. for $\text{C}_{19}\text{H}_{23}\text{O}$ $[\text{M}+\text{H}]^+$ 267.1743, found 267.1744.



7-Methyl-5-phenyloctan-3-one (2m)

65% yield (35 mg). Colorless oil. ^1H NMR (CDCl_3 , 600 MHz) δ 7.29-7.26 (m, 2H), 7.18-7.16 (m, 3H), 3.27-3.22 (m, 1H), 2.70-2.60 (m, 2H), 2.34-2.27 (m, 1H), 2.21-2.15 (m, 1H), 1.59-1.54 (m, 1H), 1.40-

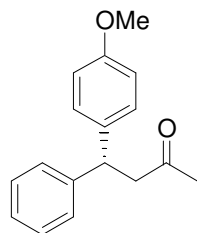
1.35 (m, 1H), 1.34-1.28 (m, 1H), 0.93 (t, $J = 9.0$ Hz, 3H), 0.88 (d, $J = 6.6$ Hz, 3H), 0.81 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 210.6, 144.6, 128.4, 127.5, 126.2, 50.2, 45.5, 39.1, 36.7, 25.3, 23.5, 21.5, 7.5. IR (neat, cm^{-1}) 3062(w), 3028(w), 2954(w), 2904(m), 1714(s), 700(s). HR-MS (ESI): calcd. for $\text{C}_{15}\text{H}_{23}\text{O}$ $[\text{M}+\text{H}]^+$ 219.1743, found 219.1743.



1-Cyclohexyl-1-phenylhexan-3-one (2n)

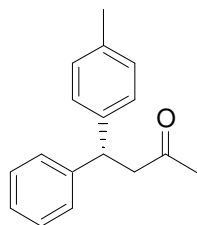
82% yield (53 mg). White solid, m. p.: 33-34 °C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.25 (t, $J=7.2$ Hz, 2H), 7.16 (t, $J=7.2$ Hz, 2H), 2.97-2.94 (m, 1H), 2.81-2.70 (m, 2H), 2.27-2.22 (m, 1H), 2.16-2.11 (m, 1H), 1.79-1.72 (m, 1H), 1.63-1.58 (m, 2H), 1.48-1.41 (m, 4H), 1.27-1.17 (m, 1H), 1.31-1.03 (m, 2H), 0.97-0.90 (m, 1H), 0.81-0.78 (m, 1H), 0.75 (t, $J=7.8$ Hz, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 210.5, 143.6, 128.3, 128.0, 126.1, 47.1, 46.6, 45.4, 42.9, 31.2, 30.7, 26.5, 26.3, 16.9, 13.5. IR (neat, cm^{-1}) 3060(w), 3027(w), 2934(m), 2914(m), 2848(m), 1701(s), 740(s), 699(s). HR-MS (ESI): calcd. for $\text{C}_{18}\text{H}_{27}\text{O}$ $[\text{M}+\text{H}]^+$ 259.2056, found 259.2056.

General procedure for asymmetric sequential Aldol condensation-Rh(I)-catalyzed addition reactions of aldehydes, methyl ketones and arylboronic acids: In a glove-box, to a vial was charged with $[\text{RhCl}(\text{CH}_2\text{CH}_2)_2]_2$ (1 mol %) and ligand (*R*)-**5** (3 equiv to Rh) and THF (0.6 mL), and the mixture was stirred at room temperature for 30 min. To another vial was charged with aldehyde (0.25 mmol), methyl ketone (0.2 mL), K_2CO_3 (0.25 mmol), methanol (0.1 mL) and water (0.1 mL), and the mixture was taken out of the glove-box and stirred at 50 °C for 30 min. Then the yellow mixture was brought into drybox again and mixed with arylboronic acid (0.5 mmol) and prepared catalyst solution. Finally, the mixture was stirred at 0 °C for 4-6 hours. The reaction was quenched by adding 4 N HCl (2 mL) aqueous solution. The mixture was extracted with CH_2Cl_2 (3 x 15 mL). The organic layers were combined. After evaporation of the organic solvents, the residue was subjected to column chromatography [silica gel, ethyl acetate/hexane (v/v=1:20) as eluent] to afford the products. The product was subjected to the analysis of enantiomeric excess by HPLC with Chiralcel OD column. The absolute configuration of which was determined by comparison of its specific rotation and the retention time of the HPLC analysis with the reported one.⁵



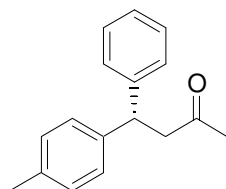
(*R*)-4-(4-Methoxyphenyl)-4-phenylbutan-2-one⁵

80 % yield (51 mg). $[\alpha]_{\text{D}} = 15.42$ (CHCl_3 , $c = 0.088$). 87% ee. [HPLC condition: Chiralcel OD column, *n*-hexane/2-propanol = 92/8, 1.0 ml/min, 230 nm UV detector, $t = 12.05$ min for (*S*)-isomer and $t = 14.08$ min for (*R*)-isomer]. ^1H NMR (CDCl_3 , 600 MHz) δ 7.26 (t, $J=7.2$ Hz, 4H), 7.21-7.19 (m, 2H), 7.17-7.12 (m, 3H), 6.82-6.79(m, 2H), 4.53 (t, $J=7.2$ Hz, 1H), 3.70 (s, 3H), 3.14 (d, $J=7.8$ Hz, 1H), 2.06 (3H, s).



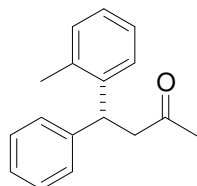
(R)-4-Phenyl-4-p-tolylbutan-2-one⁶

84% yield (50 mg). $[\alpha]_D = 11.39$ (CHCl_3 , $c = 0.154$). 92% e. e. [HPLC condition: Chiralcel OD column, *n*-hexane/2-propanol = 92/8, 1.0 ml/min, 230 nm UV detector, $t = 9.06$ min for (*S*)-isomer and $t = 10.57$ min for (*R*)-isomer]. ¹H NMR (CDCl_3 , 600 MHz) δ 7.27-7.24 (m, 2H), 7.21-7.20 (m, 2H), 7.17-7.14 (m, 1H), 7.11-7.06 (m, 4H), 4.57 (t, $J=7.2$ Hz, 1H), 3.13 (d, $J=7.2$ Hz, 2H), 2.28 (s, 3H), 2.06 (s, 3H).



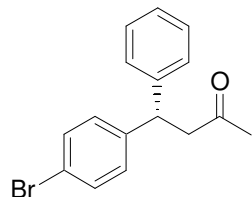
(S)-4-Phenyl-4-p-tolylbutan-2-one⁶

86% yield (51 mg). $[\alpha]_D = -10.98$ (CHCl_3 , $c = 0.108$). 91% e. e. [HPLC condition: Chiralcel OD column, *n*-hexane/2-propanol = 92/8, 1.0 ml/min, 230 nm UV detector, $t = 8.68$ min for (*S*)-isomer and $t = 10.44$ min for (*R*)-isomer]. ¹H NMR (CDCl_3 , 600 MHz) δ 7.27-7.24 (m, 2H), 7.21-7.20 (m, 2H), 7.17-7.14 (m, 1H), 7.11-7.06 (m, 4H), 4.57 (t, $J=7.2$ Hz, 1H), 3.13 (d, $J=7.2$ Hz, 2H), 2.28 (s, 3H), 2.06 (s, 3H).



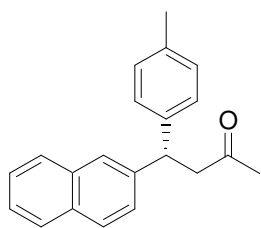
(R)-4-Phenyl-4-o-tolylbutan-2-one²

87% yield (52 mg). $[\alpha]_D = -89.28$ (CHCl_3 , $c = 0.050$). 82% e. e. [HPLC condition: Chiralcel OD column, *n*-hexane/2-propanol = 88/12, 1.0 ml/min, 230 nm UV detector, $t = 10.08$ min for the isomer in a minor amount and $t = 13.52$ min for the isomer in a major amount]. ¹H NMR (CDCl_3 , 600 MHz) δ 7.25-7.22 (m, 4H), 7.17-7.12 (m, 5H), 4.78 (t, $J=7.2$ Hz, 1H), 3.14 (d, $J=7.2$ Hz, 2H), 2.29 (s, 3H), 2.06 (s, 3H).



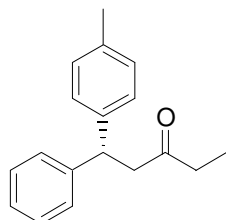
(S)-4-(4-Bromophenyl)-4-phenylbutan-2-one

87% yield (66 mg). $[\alpha]_D = -7.95$ (CHCl_3 , $c = 0.100$). 83% e. e. [HPLC condition: Chiralcel OD column, *n*-hexane/2-propanol = 88/12, 1.0 ml/min, 230 nm UV detector, $t = 10.79$ min for the isomer in a major amount and $t = 14.49$ min for the isomer in a minor amount]. ¹H NMR (CDCl_3 , 600 MHz) δ 7.38 (d, $J=7.8$ Hz, 2H), 7.27 (t, $J=7.8$ Hz, 2H), 7.18-7.17 (m, 3H), 7.09 (d, $J=8.4$ Hz, 2H), 4.55 (t, $J=7.2$ Hz, 1H), 3.15 (d, $J=7.2$ Hz, 1H), 2.07 (3H, s).



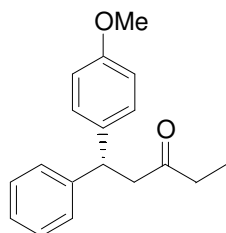
(S)-4-(Naphthalen-2-yl)-4-p-tolylbutan-2-one

85% yield (61 mg). $[\alpha]_D = 32.90$ (CHCl_3 , $c = 0.113$). 86% e. e. [HPLC condition: Chiralcel OD column, *n*-hexane/2-propanol = 94/6, 1.0 ml/min, 230 nm UV detector, $t = 10.08$ min for the isomer in a minor amount and $t = 13.52$ min for the isomer in a major amount]. $^1\text{H NMR}$ (CDCl_3 , 600 MHz) δ 7.77 (t, $J=7.8$ Hz, 2H), 7.73 (d, $J=8.4$ Hz, 1H), 7.67 (m, 4H), 7.45-7.40 (m, 2H), 7.31 (d, $J=8.4$ Hz, 1H), 7.15-7.03 (m, 4H), 4.71 (t, $J=7.2$ Hz, 1H), 3.25 (t, $J=7.8$ Hz, 2H), 2.28 (s, 3H), 2.09 (s, 3H).



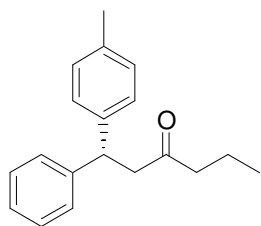
(R)-1-Phenyl-1-p-tolylpentan-3-one

81% yield (51 mg). $[\alpha]_D = -26.57$ (CHCl_3 , $c = 0.066$). 87% e. e. [HPLC condition: Chiralcel OD column, *n*-hexane/2-propanol = 96/4, 1.0 ml/min, 230 nm UV detector, $t = 7.67$ min for the isomer in a minor amount and $t = 8.53$ min for the isomer in a major amount]. $^1\text{H NMR}$ (CDCl_3 , 600 MHz) δ 7.27-7.24 (m, 2H), 7.20-7.19 (m, 2H), 7.17-7.14 (m, 1H), 7.11-7.07 (m, 4H), 4.54 (t, $J=7.2$ Hz, 1H), 3.15 (d, $J=7.2$ Hz, 2H), 2.33 (q, $J=7.2$ Hz, 2H), 2.28 (s, 3H), 0.95 (t, $J=7.2$ Hz, 3H).



(R)-1-(4-Methoxyphenyl)-1-phenylpentan-3-one

80% yield (54 mg). $[\alpha]_D = -15.30$ (CHCl_3 , $c = 0.088$). 82% e. e. [HPLC condition: Chiralcel OD column, *n*-hexane/2-propanol = 94/6, 1.0 ml/min, 230 nm UV detector, $t = 10.37$ min for the isomer in a minor amount and $t = 11.39$ min for the isomer in a major amount]. $^1\text{H NMR}$ (CDCl_3 , 600 MHz) δ 7.27-7.24 (m, 2H), 7.21-7.20 (m, 2H), 7.17-7.12 (3 m, H), 6.81-6.80 (m, 2H), 4.55 (t, $J=7.2$ Hz, 1H), 3.75 (s, 3H), 3.11 (d, $J=7.8$ Hz, 2H), 2.32 (q, $J=7.2$ Hz, 2H), 0.95 (t, $J=7.2$ Hz, 3H).



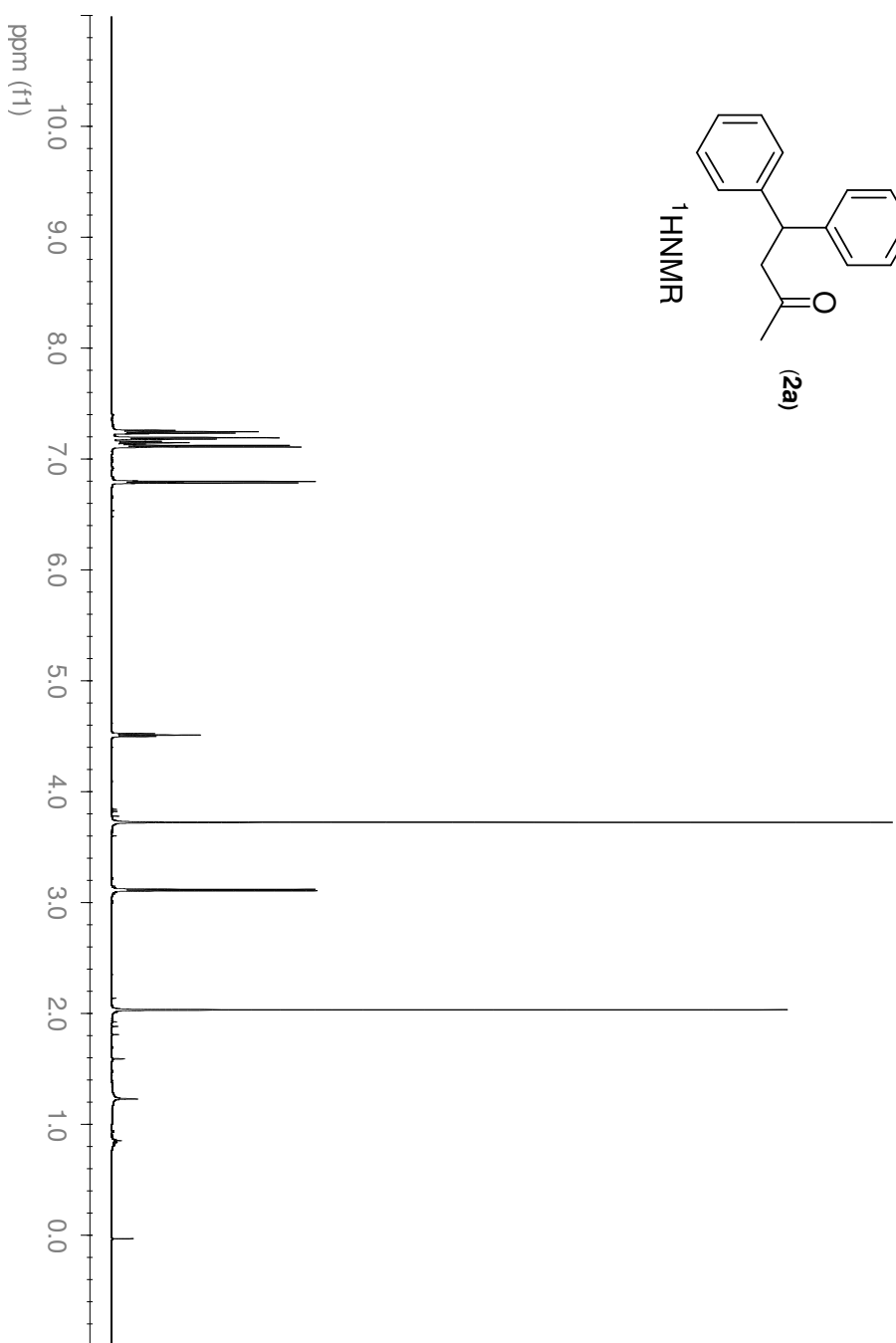
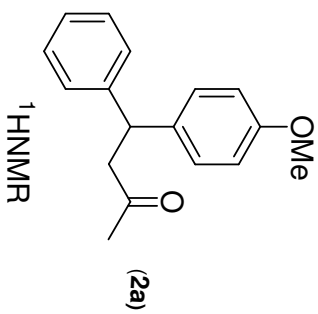
(R)-1-Phenyl-1-p-tolylhexan-3-one

83% yield (55 mg). $[\alpha]_D = -0.55$ (CHCl_3 , $c = 0.150$). 86% e. e. [HPLC condition: Chiralcel OD column, *n*-hexane/2-propanol = 99/1, 1.0 ml/min, 230 nm UV detector, $t = 8.87$ min for the isomer in a minor amount and $t = 9.46$ min for the isomer in a major amount]. $^1\text{H NMR}$ (CDCl_3 , 600 MHz): δ 7.24 (t, $J=7.8$

Hz, 3H), 7.21-7.19 (m, 2H), 7.14 (t, $J=7.2$ Hz, 3H), 7.10 (d, $J=8.4$ Hz, 2H), 7.06 (d, $J=8.4$ Hz, 2H), 4.57 (t, $J=7.8$ Hz, 1H), 3.11 (d, $J=7.2$ Hz, 2H), 2.29-2.26 (m, 5H), 1.49 (m, 2H), 0.79 (t, $J=7.2$ Hz, 3H).

References:

1. Bedford, R. B.; Hazelwood, S. L.; Limmert, M. E.; Albisson, D. A.; Draper, S. M.; Scully, P. N.; Coles, S. J.; Hursthouse, M. B. *Chem. Eur. J.* **2003**, *9*, 3216-3227.
2. He, P.; Lu, Y.; Dong, C.-G., Hu, Q.-S. *Org. Lett.* **2007**, *9*, 343-346.
3. Liao, Y.-X; Xing, C.-H; He, P; Hu, Q.-S. *Org. Lett.* **2008**, *10*, 2509-2512.
4. Duan, H.-F.; Xie, J.-H.; Shi, W.-J.; Zhang, Q.; Zhou, Q.-L. *Org. Lett.* **2006**, *8*, 1479-1481.
5. Chen, Q.; Kuriyama, M.; Hao, X.; Soeta, T.; Yamamoto, Y.; Yamada, K.-I.; Tomioka, K. *Chem. Pharm. Bull.* **2009**, *57*, 1024—1027. HPLC conditions: (OD-H, hexane/*i*-PrOH=50/1, 1.0 ml/min, 254 nm; major 37.4 min, minor 44.7 min).
6. Nishimura T.; Nagaosa, M.; Hayashi, T. *Chem. Lett.* **2008**, *37*, 860-861.



Spectrum Title:
Jan0710_lyx-4-58-2_1H

Frequency (MHz):

(f1) 599.936

Acquisition Time (sec):

(f1) 2.0486

Spectral Width (ppm):

(f1) 16.027

Pulse Program:

s2pul

Temperature:

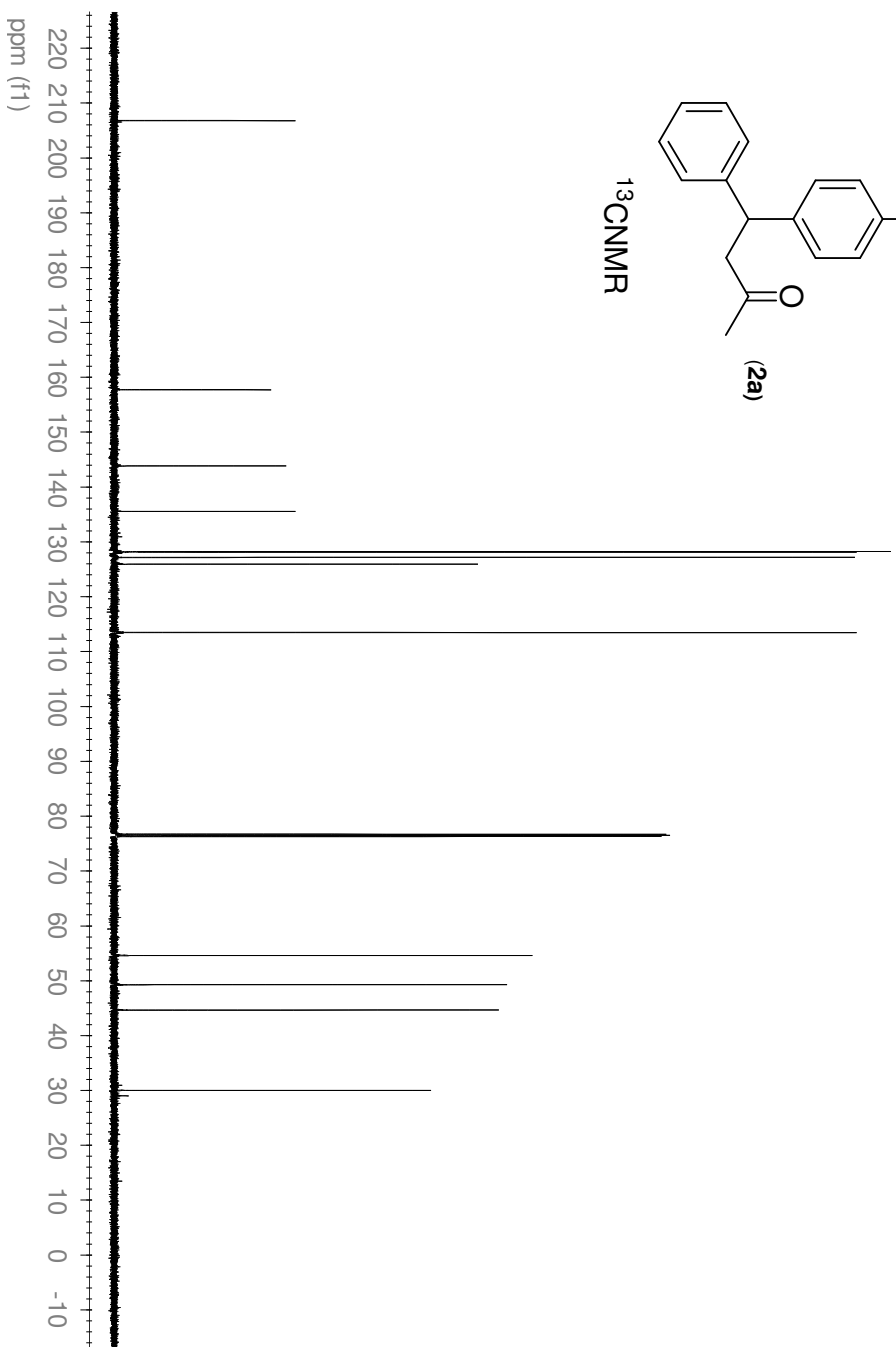
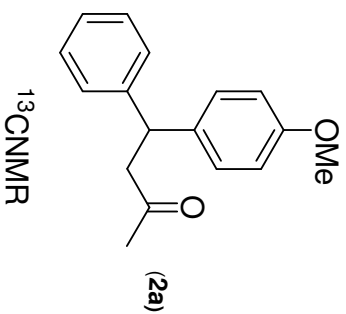
25

Number of Scans:

4

Acq. Date:

Jan 7 2010



Spectrum Title:
Jan0710_lyx-4-88-2_13C

Frequency (MHz):

(f1) 150.889

Acquisition Time (sec):

(f1) 1.3005

Spectral Width (ppm):

(f1) 243.886

Pulse Program:

sQpul

Temperature:

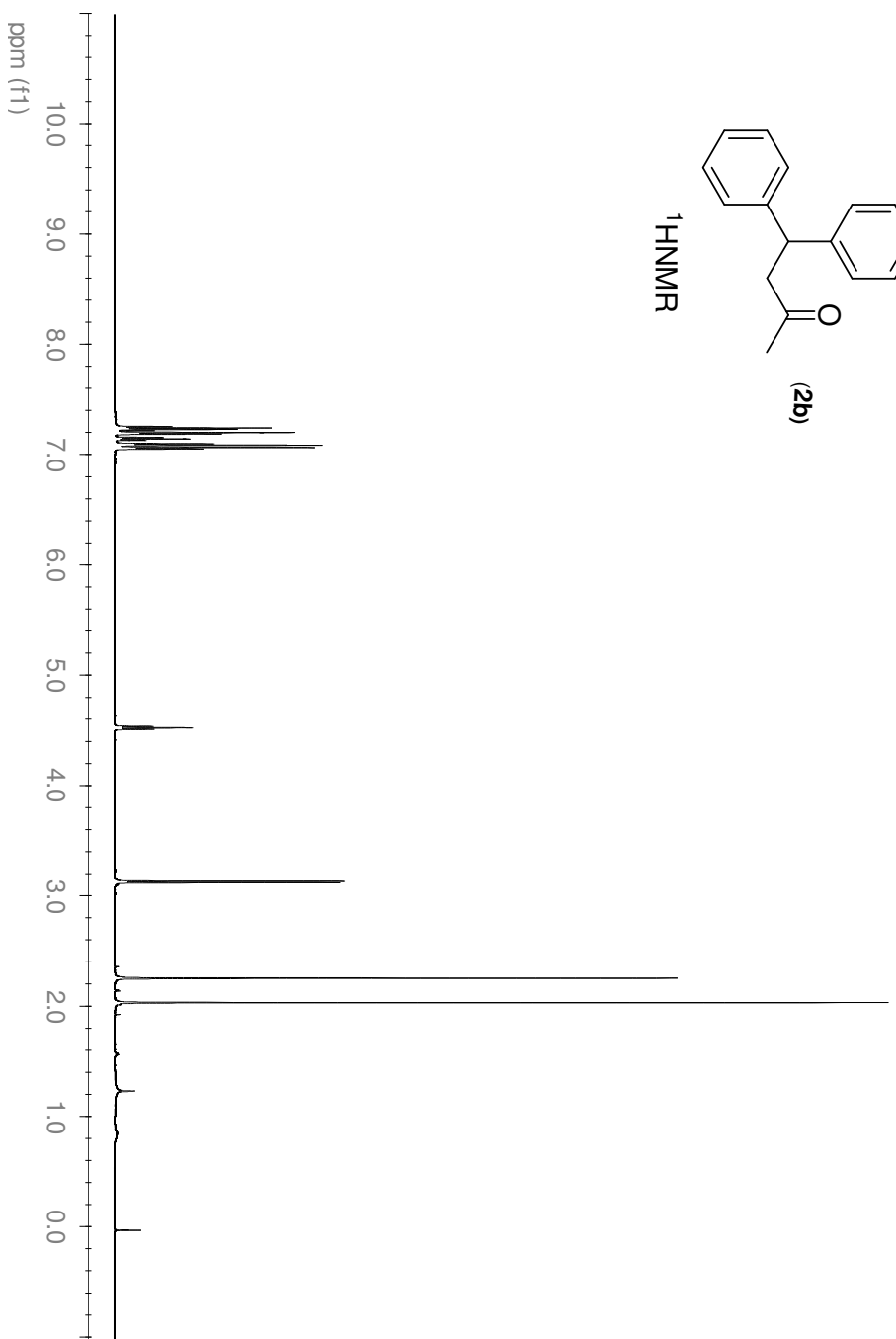
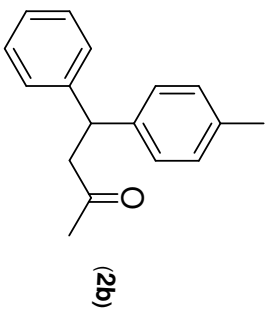
25

Number of Scans:

256

Acq. Date:

Jan 7 2010



Spectrum Title:
Mar1009_lvx-3-87_1H

Frequency (MHz):

(f1) 599.936

Acquisition Time (sec):

(f1) 2.0486

Spectral Width (ppm):

(f1) 16.027

Pulse Program:

s2pu1

Temperature:

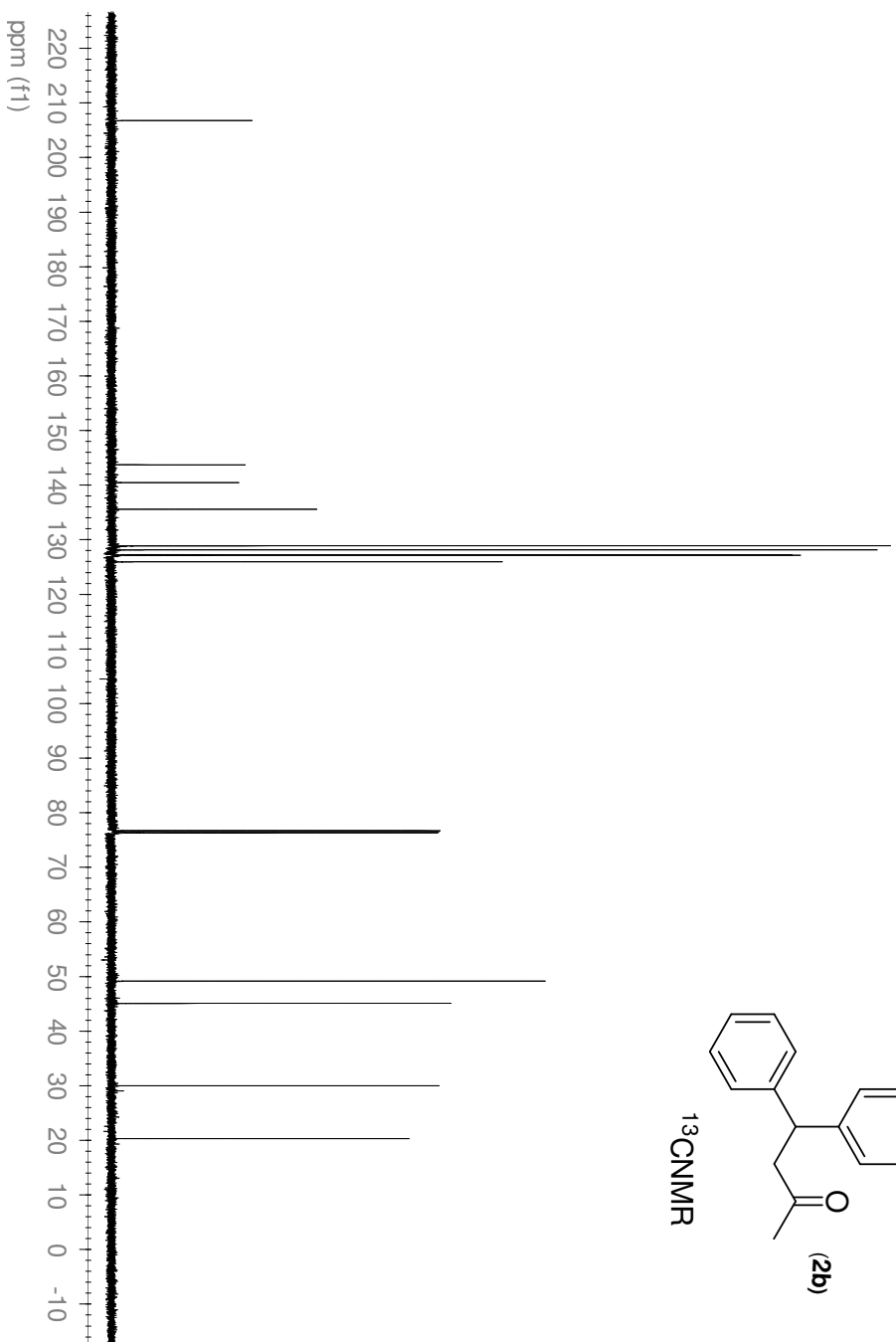
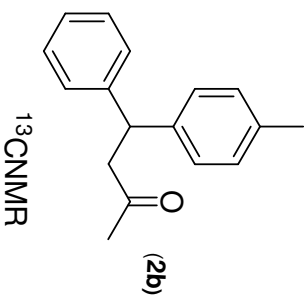
25

Number of Scans:

8

Acq. Date:

Mar 10 2009



Spectrum Title:
Mar1009_lyx-3-87_13C

Frequency (MHz):

(f1) 150.869

Acquisition Time (sec):

(f1) 1.3005

Spectral Width (ppm):

(f1) 243.686

Pulse Program:

s2pul

Temperature:

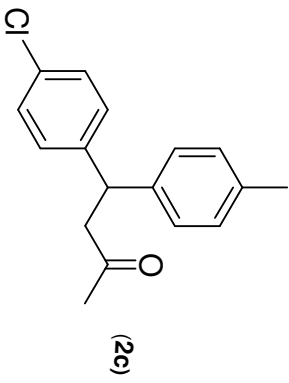
25

Number of Scans:

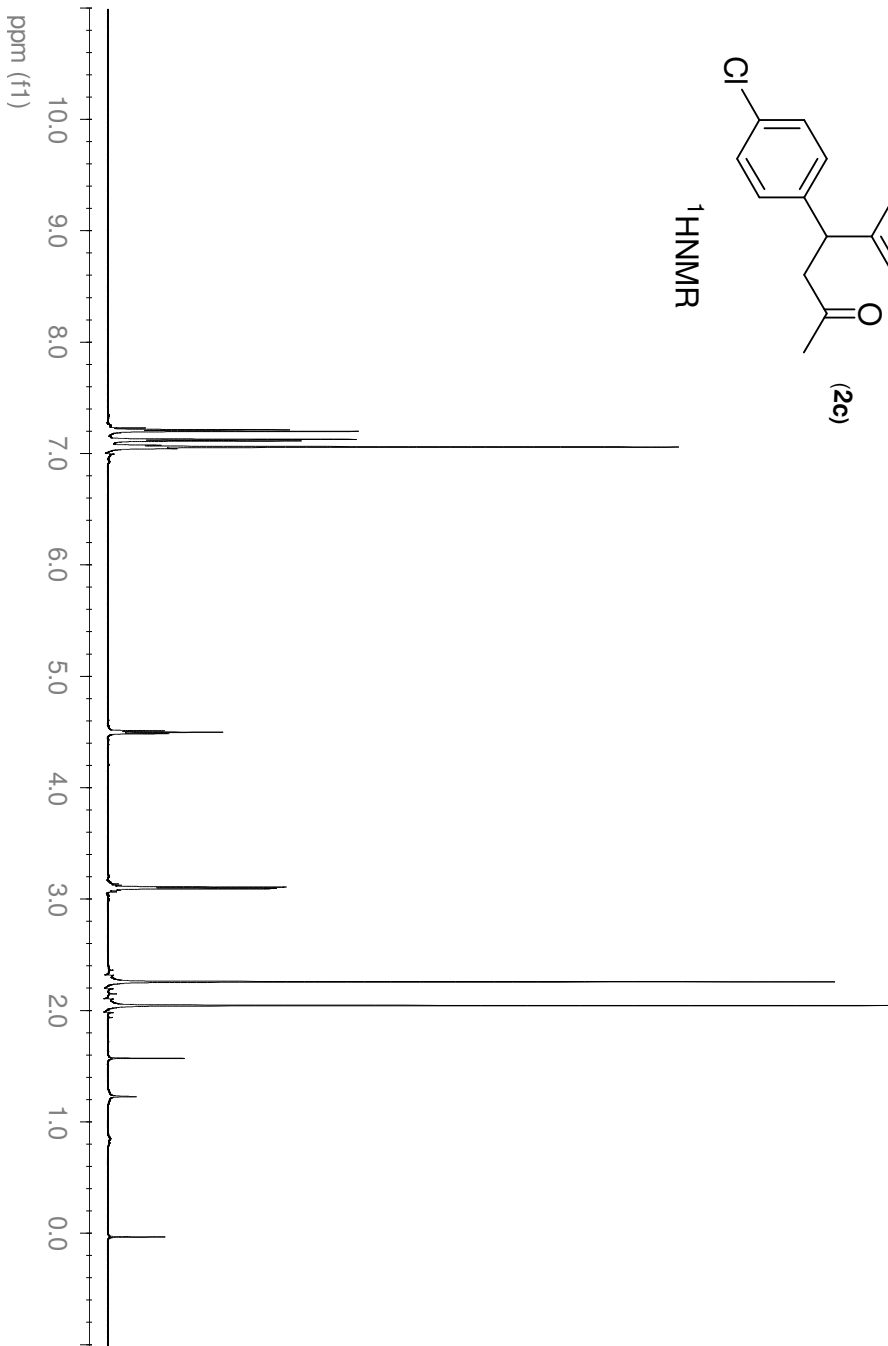
256

Acq. Date:

Mar 10 2009



¹H NMR



Spectrum Title:
Jan2510_ljx-461-1_1H

Frequency (MHz):
(f1) 599.336

Acquisition Time (sec):
(f1) 2.0486

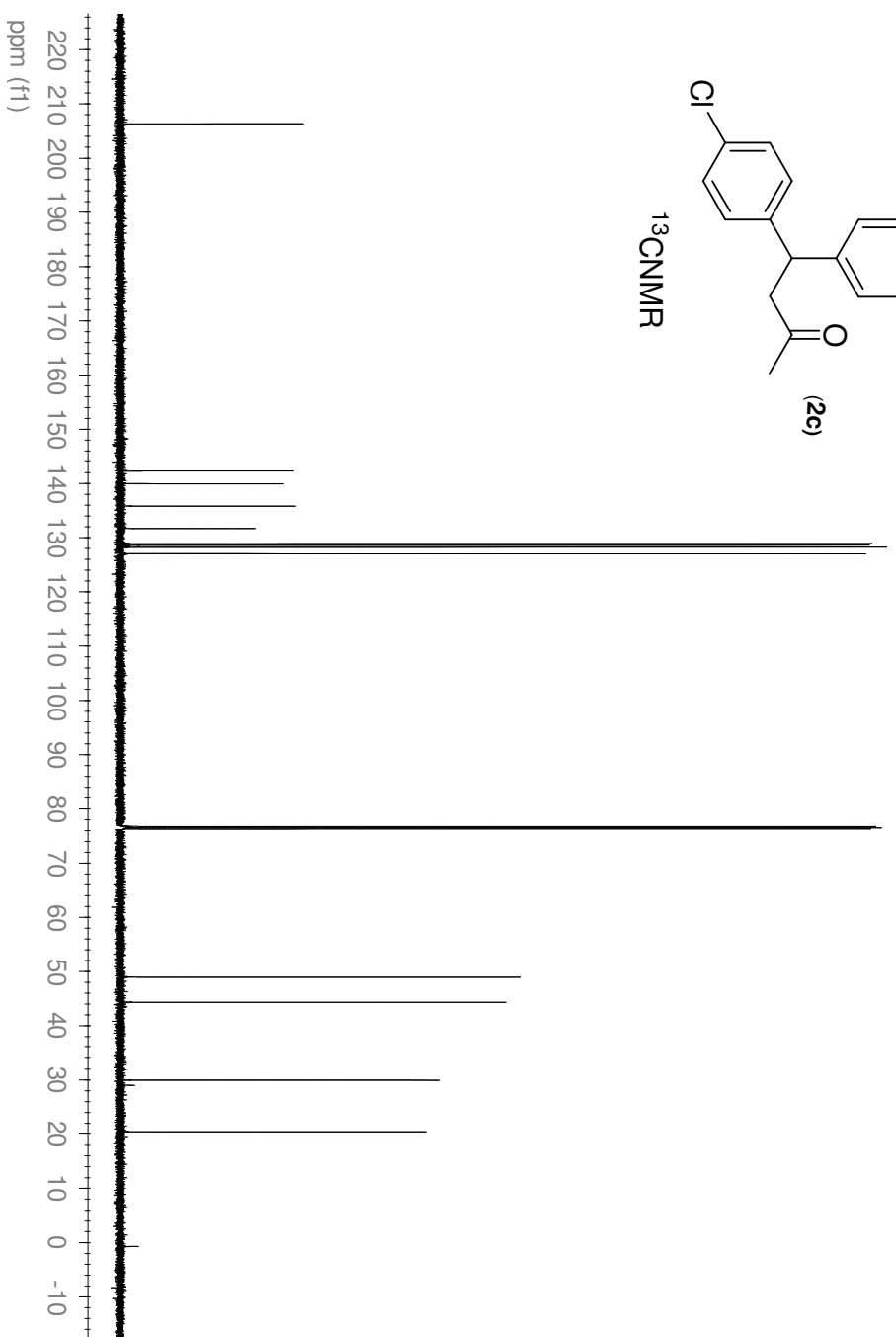
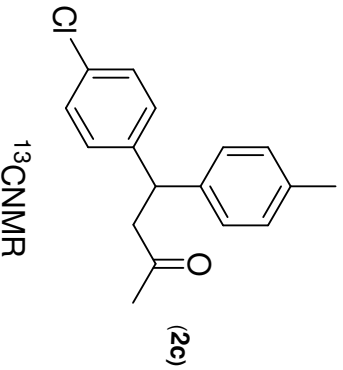
Spectral Width (ppm):
(f1) 16.027

Pulse Program:
s2pul

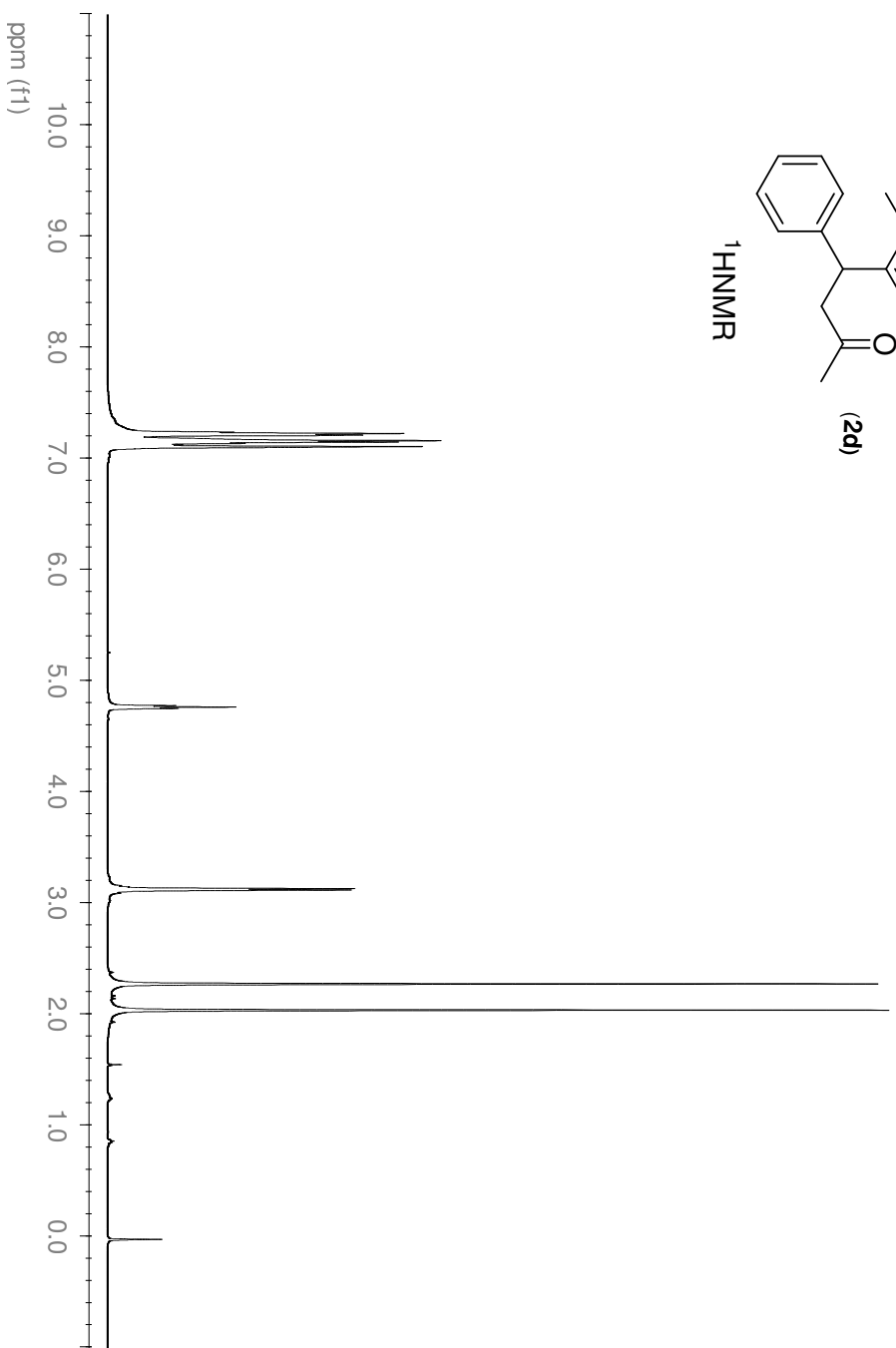
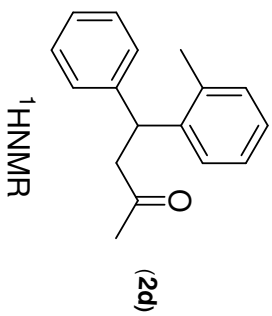
Temperature:
27

Number of Scans:
8

Acq. Date:
Jan 25 2010



Spectrum Title:
 Jan2510_lyx-4-61-1_13C
Frequency (MHz):
 (f1) 150.869
Acquisition Time (sec):
 (f1) 1.3005
Spectral Width (ppm):
 (f1) 243.686
Pulse Program:
 s2pul
Temperature:
 27
Number of Scans:
 256
Acq. Date:
 Jan 25 2010



Spectrum Title:

Jan2910_lyx-4-56-1_1H

Frequency (MHz):

(f1) 599.936

Acquisition Time (sec):

(f1) 2.0486

Spectral Width (ppm):

(f1) 16.027

Pulse Program:

s2pul

Temperature:

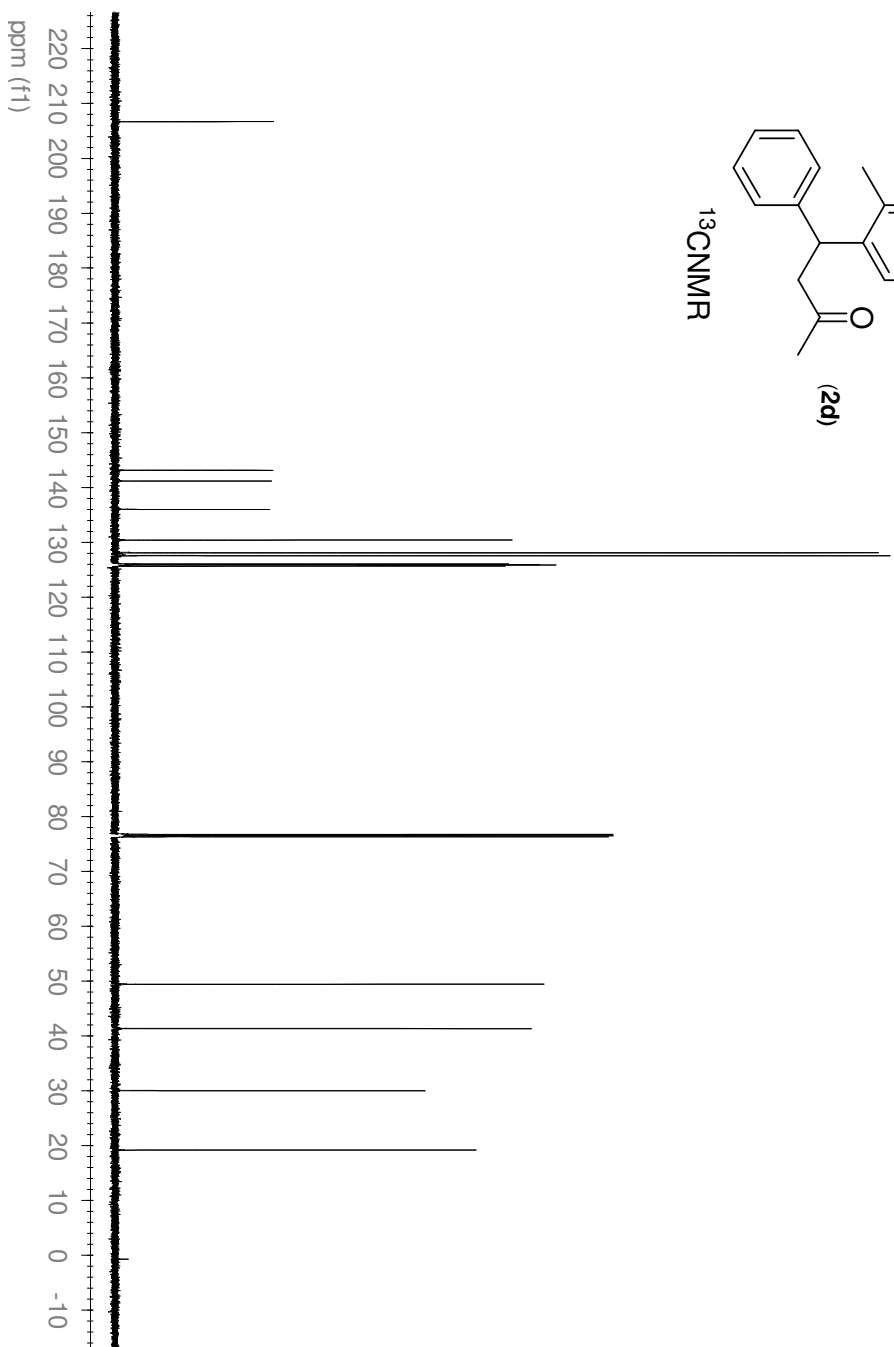
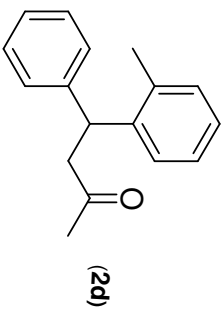
27

Number of Scans:

8

Acq. Date:

Jan 29 2010



Spectrum Title:
Jan2910_lyx-4-56-1_13C

Frequency (MHz):

(f1) 150.889

Acquisition Time (sec):

(f1) 1.3005

Spectral Width (ppm):

(f1) 243.696

Pulse Program:

s2pul

Temperature:

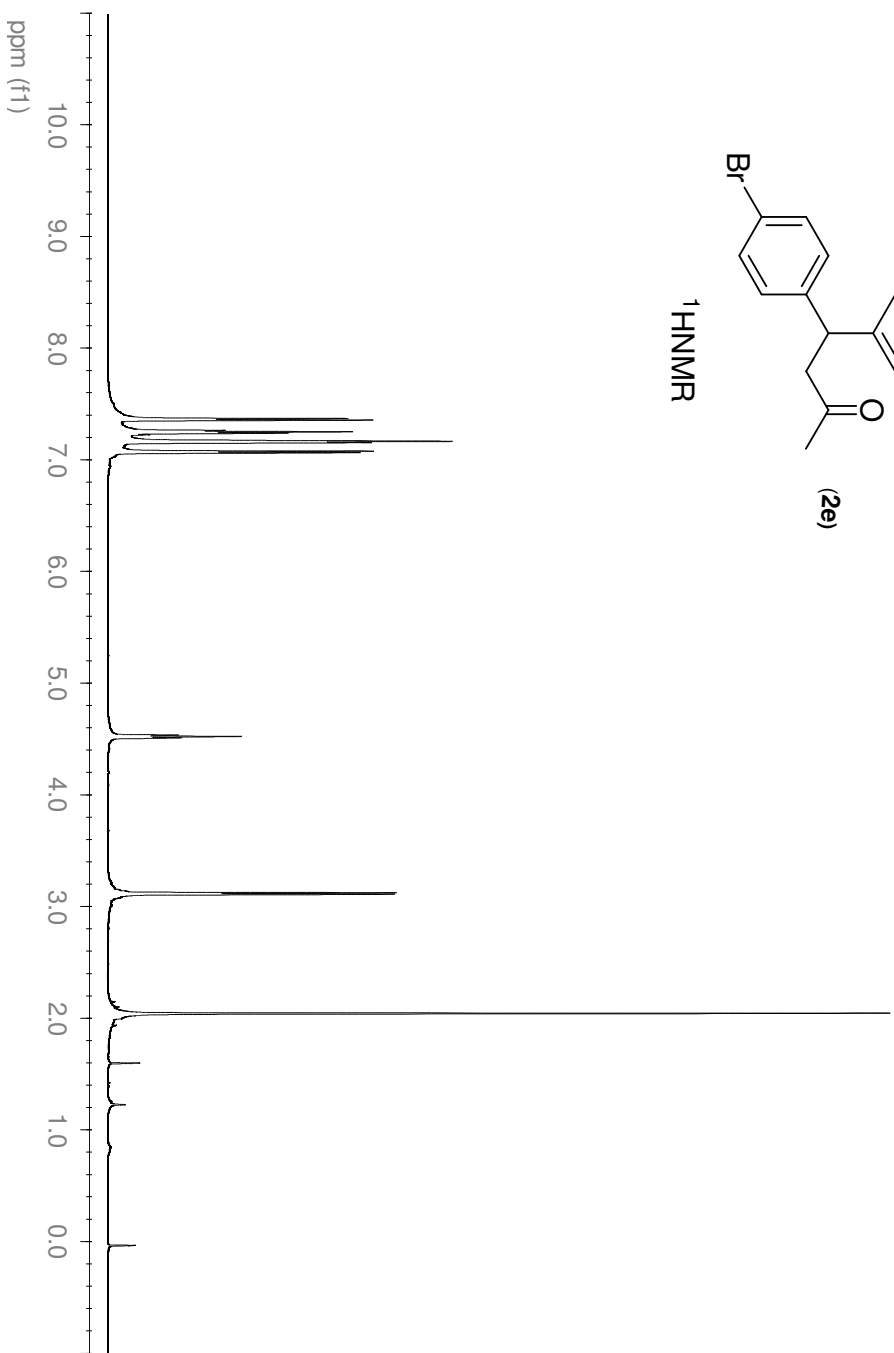
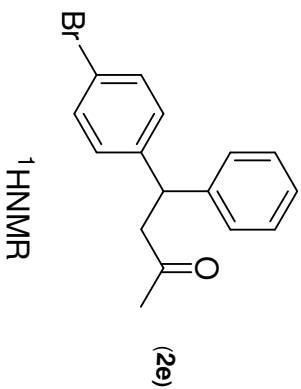
27

Number of Scans:

1000

Acq. Date:

Jan 29 2010



Spectrum Title:
Feb0910_Lyx-467-2_1H

Frequency (MHz):
(f1) 599.996

Acquisition Time (sec):
(f1) 2.0486

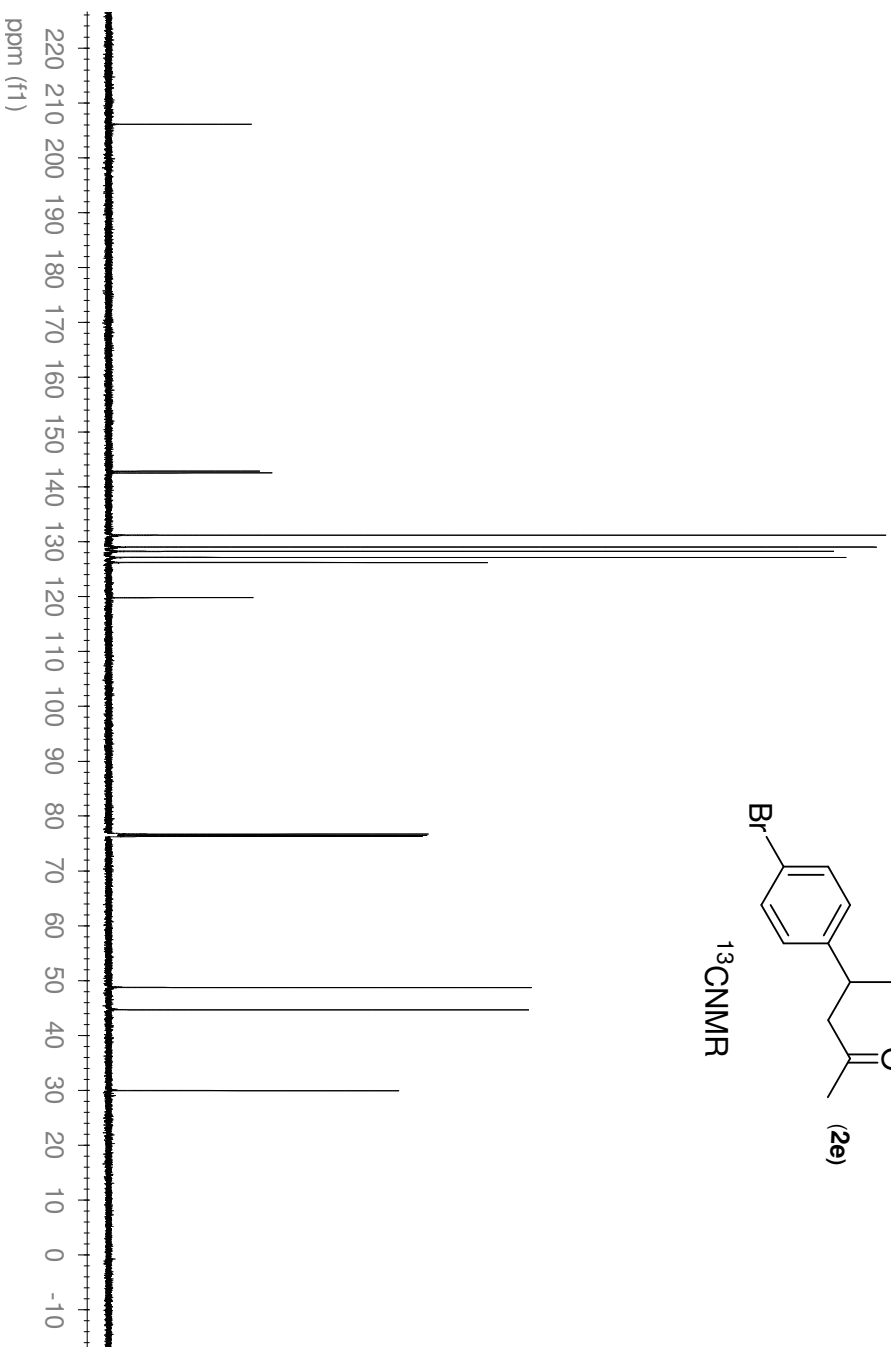
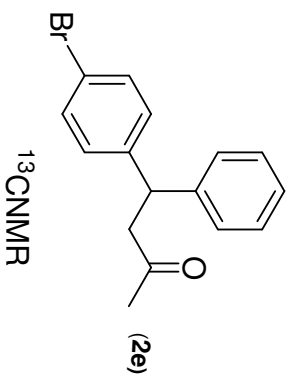
Spectral Width (ppm):
(f1) 16.027

Pulse Program:
s2p1

Temperature:
25

Number of Scans:
512

Acq. Date:
Feb 10 2010



Spectrum Title:
Feb0910_lyx-4-67-2_13C

Frequency (MHz):

(f1) 150.869

Acquisition Time (sec):

(f1) 1.3005

Spectral Width (ppm):

(f1) 243.696

Pulse Program:

s2pul

Temperature:

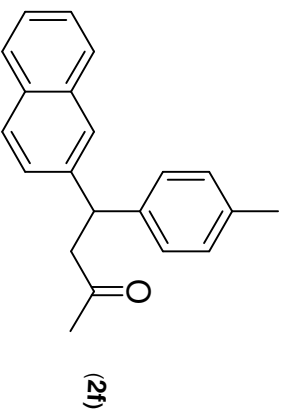
25

Number of Scans:

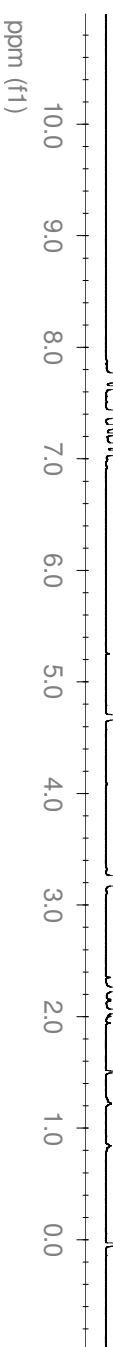
1000

Acq. Date:

Feb 10 2010



¹H NMR



Spectrum Title:
Jan2910_lyx-4-61-2_1H

Frequency (MHz):
(f1) 599.936

Acquisition Time (sec):
(f1) 2.0486

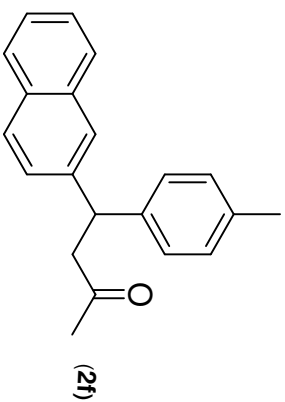
Spectral Width (ppm):
(f1) 16.027

Pulse Program:
s2pul

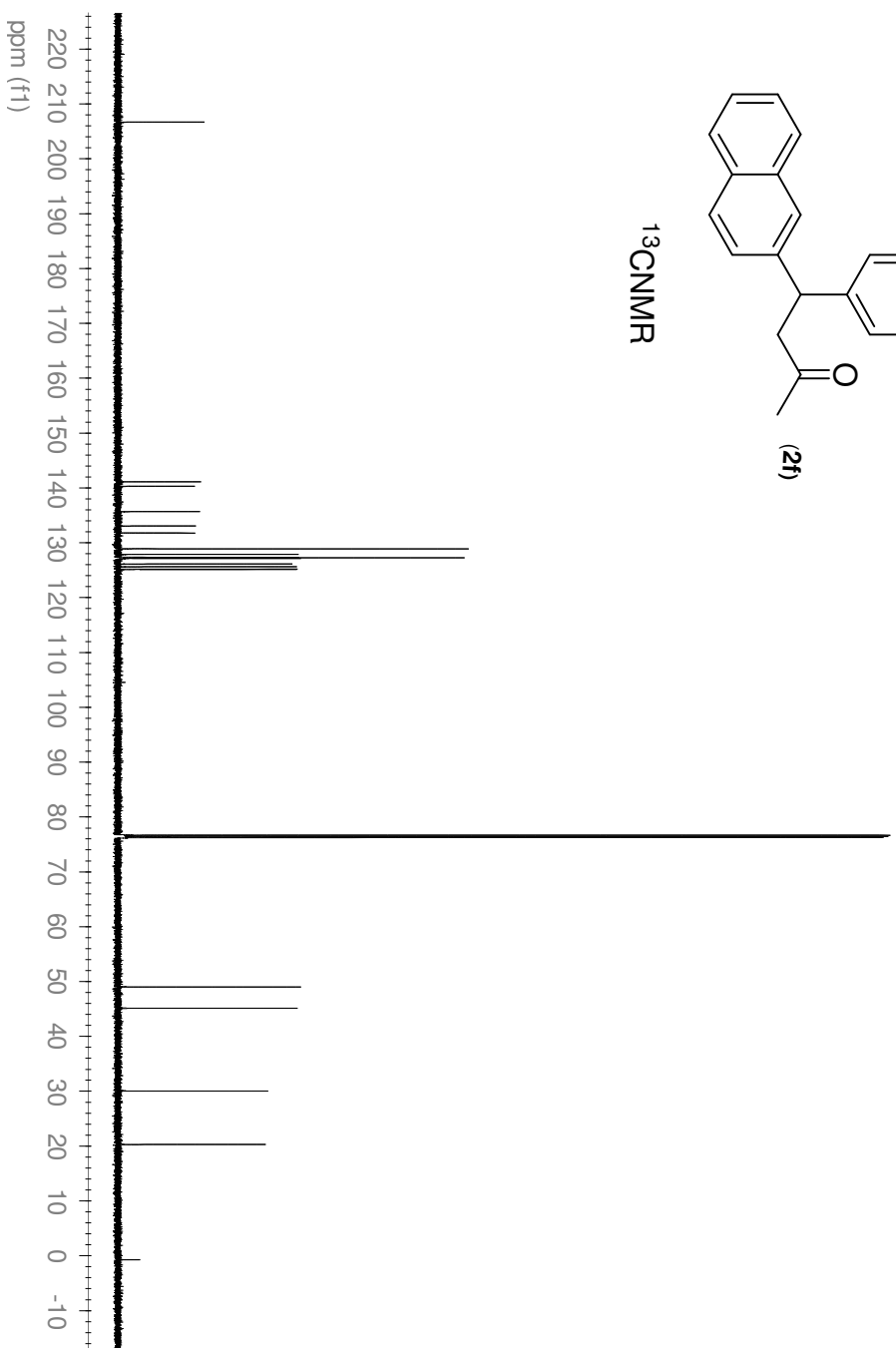
Temperature:
27

Number of Scans:
8

Acq. Date:
Jan 29 2010



¹³CNMR



Spectrum Title:
Jan2910_ljx-4-6f-2_13C

Frequency (MHz):
(f1) 150.889

Acquisition Time (sec):
(f1) 1.3005

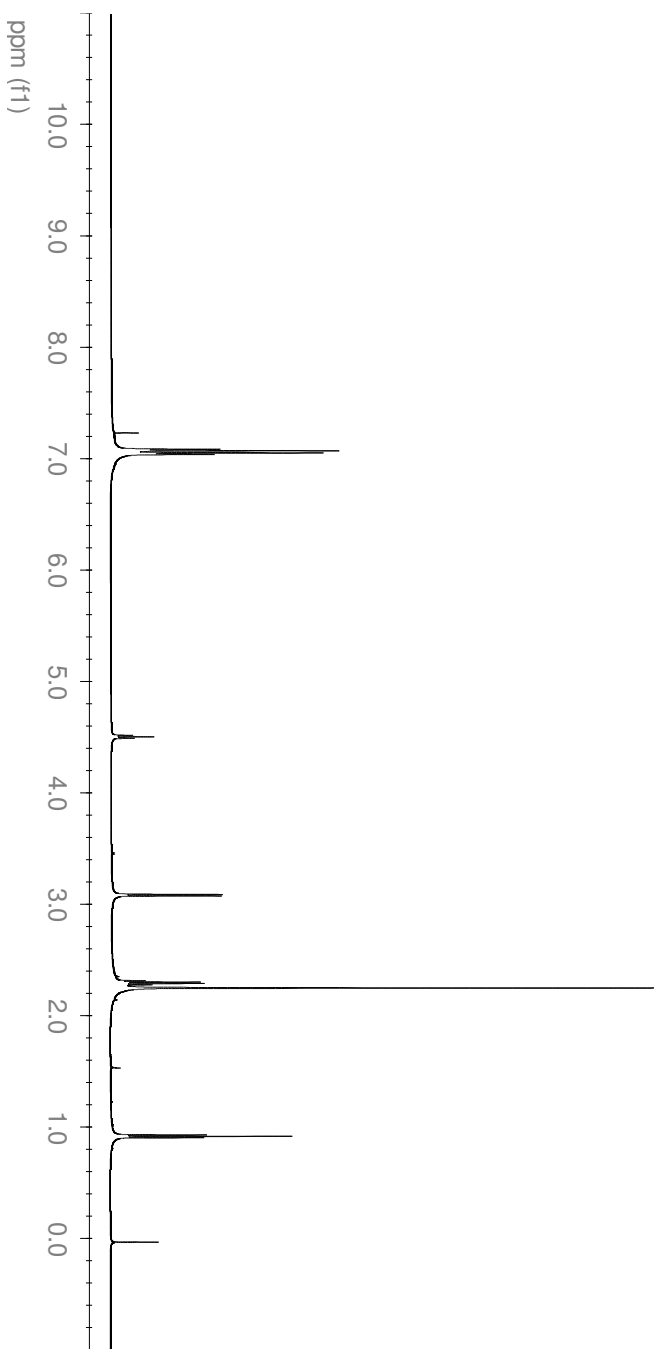
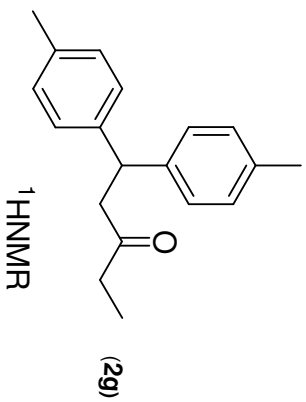
Spectral Width (ppm):
(f1) 243.686

Pulse Program:
s2qa1

Temperature:
27

Number of Scans:
1000

Acq. Date:
Jan 29 2010



Spectrum Title:
Feb0310_lvx-4-64-3_1H

Frequency (MHz):
(f1) 599.936

Acquisition Time (sec):
(f1) 2.0486

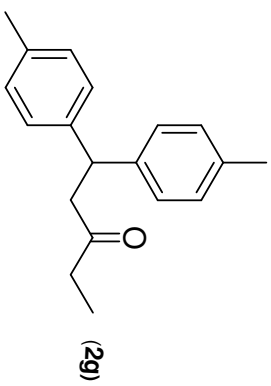
Spectral Width (ppm):
(f1) 16.027

Pulse Program:
s2pul

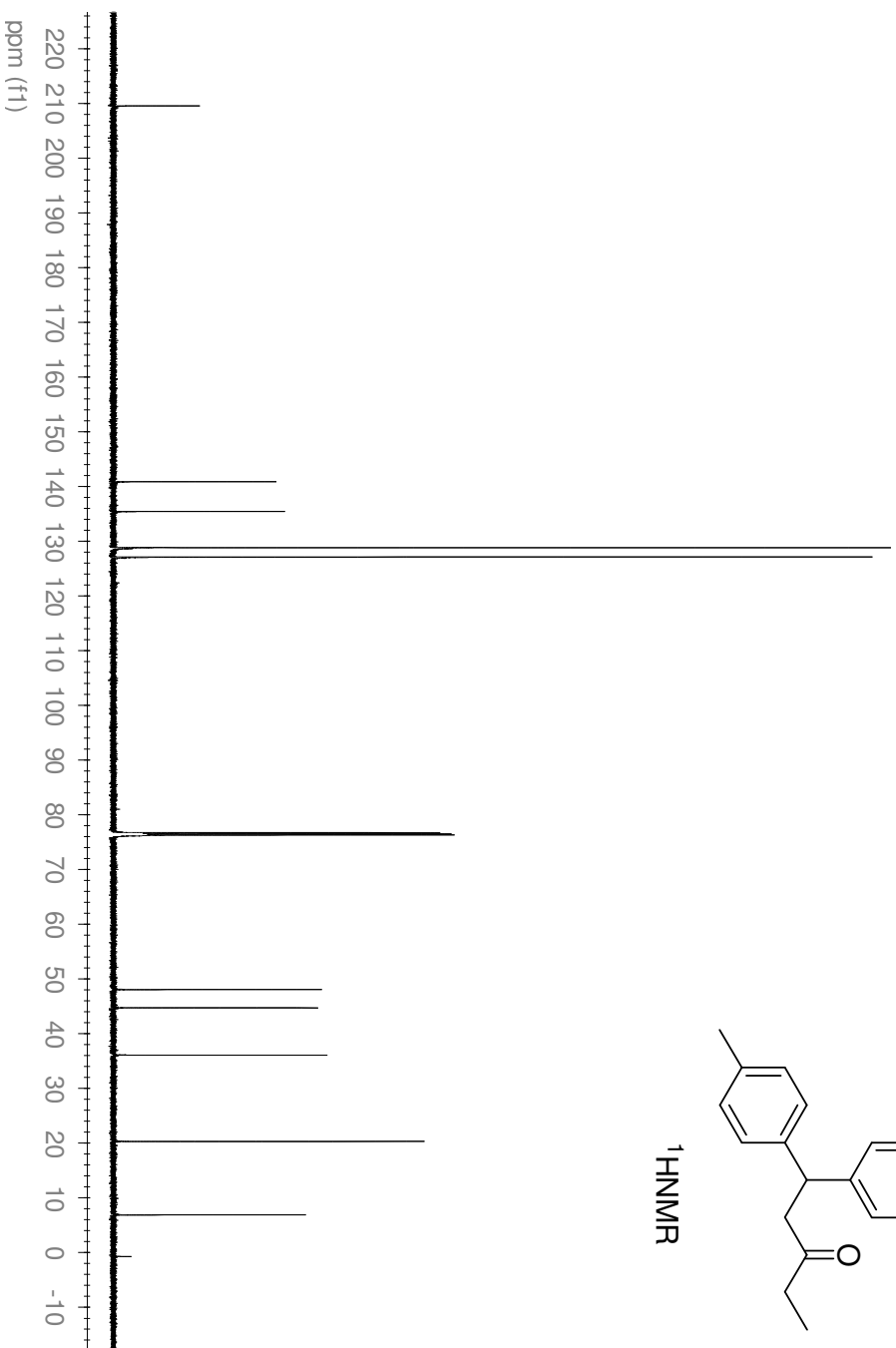
Temperature:
25

Number of Scans:
8

Acq. Date:
Feb 3 2010



¹H NMR



Spectrum Title:

F800310.lv\4-64-3_13C

Frequency (MHz):

(f1) 150.869

Acquisition Time (sec):

(f1) 1.3005

Spectral Width (ppm):

(f1) 243.686

Pulse Program:

s2pul

Temperature:

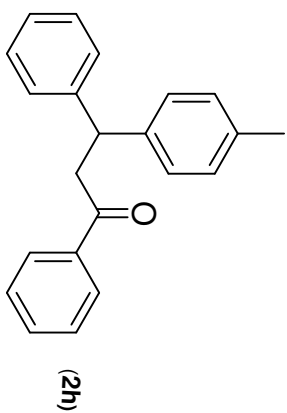
25

Number of Scans:

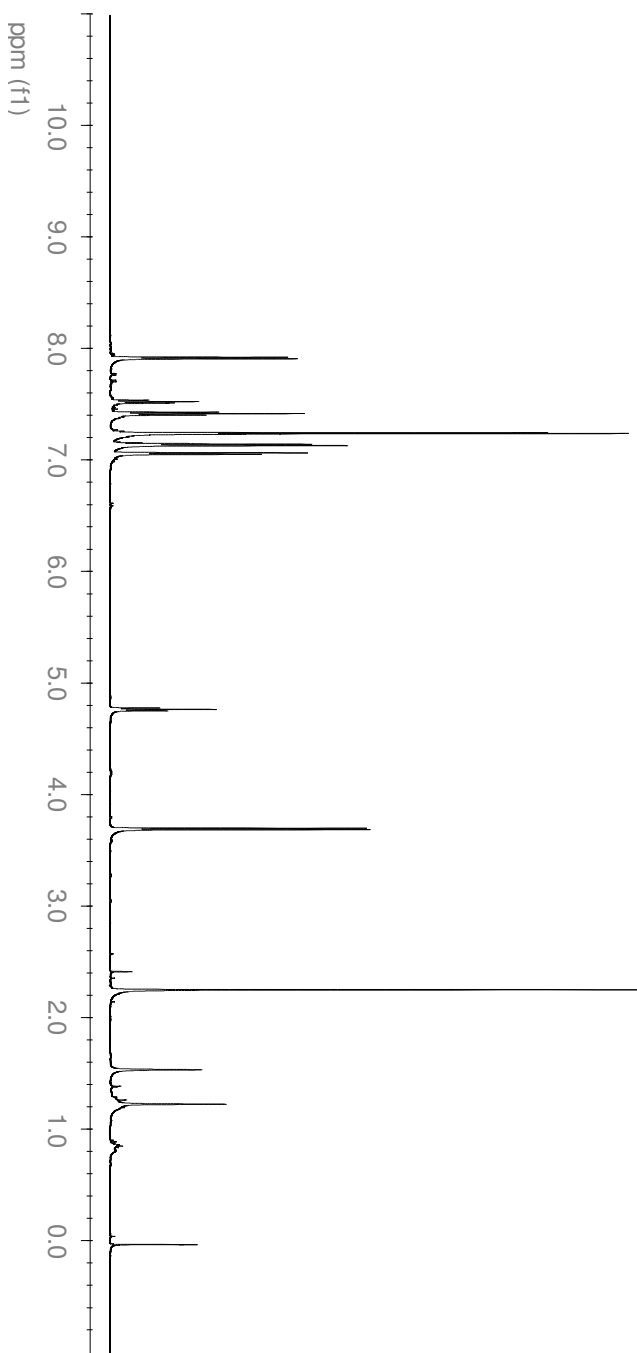
256

Acq. Date:

Feb 3 2010



¹H NMR



Spectrum Title:
 Sep00909_1yx-3-271_1H

Frequency (MHz):
 (f1) 599.996

Acquisition Time (sec):
 (f1) 2.0488

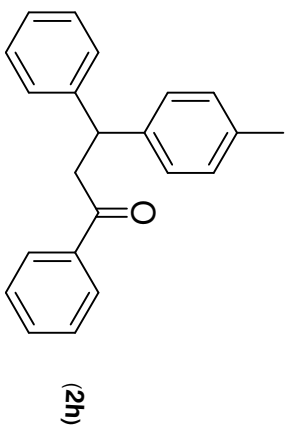
Spectral Width (ppm):
 (f1) 16.027

Pulse Program:
 s2pu1

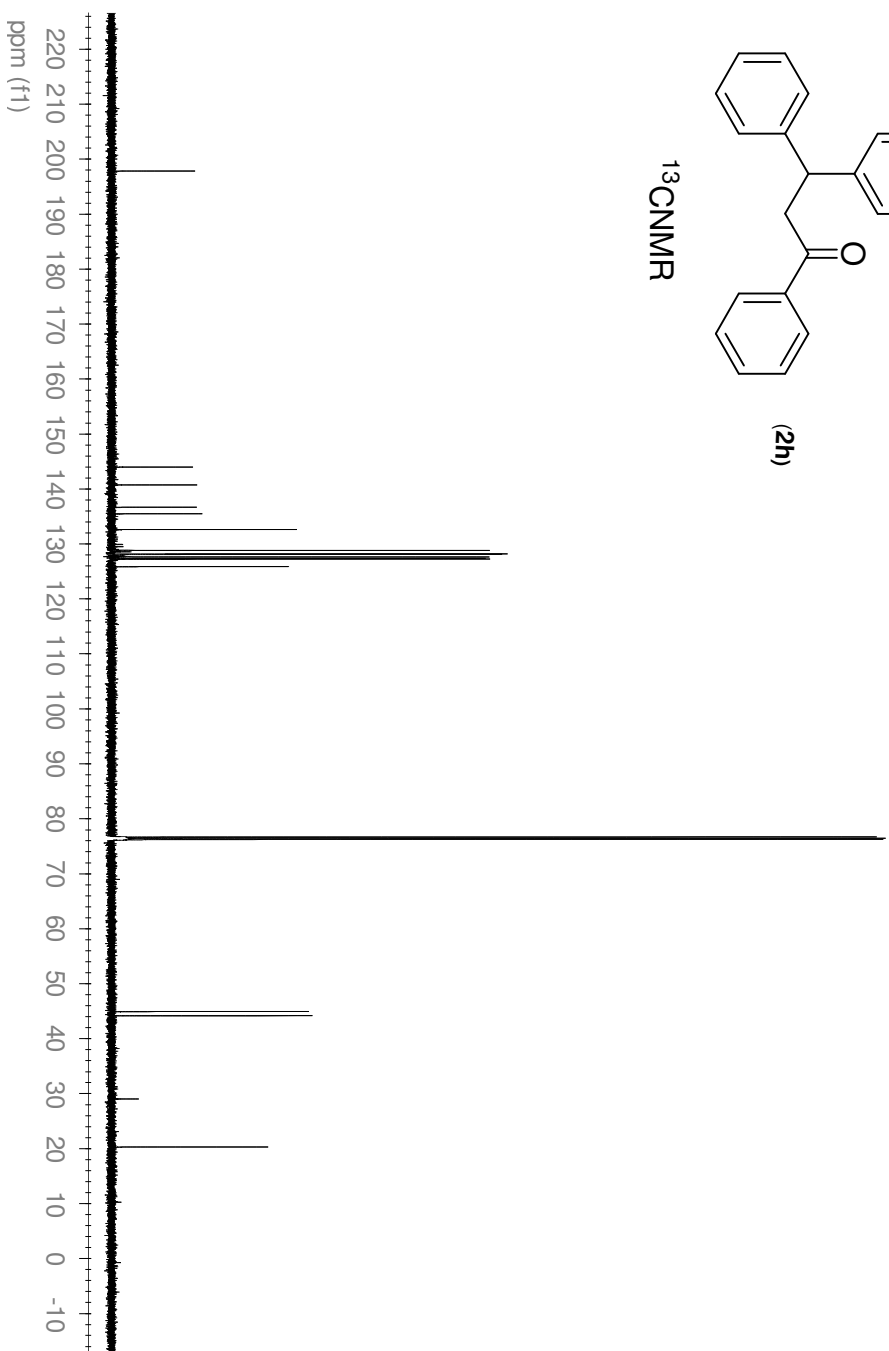
Temperature:
 25

Number of Scans:
 4

Acq. Date:
 Sep 9 2009



¹³CNMR



Spectrum Title:
Sep0909_lvx-3-271_13C

Frequency (MHz):
(f1) 150.889

Acquisition Time (sec):
(f1) 1.3005

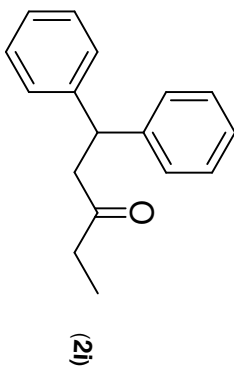
Spectral Width (ppm):
(f1) 243.696

Pulse Program:
s2pul

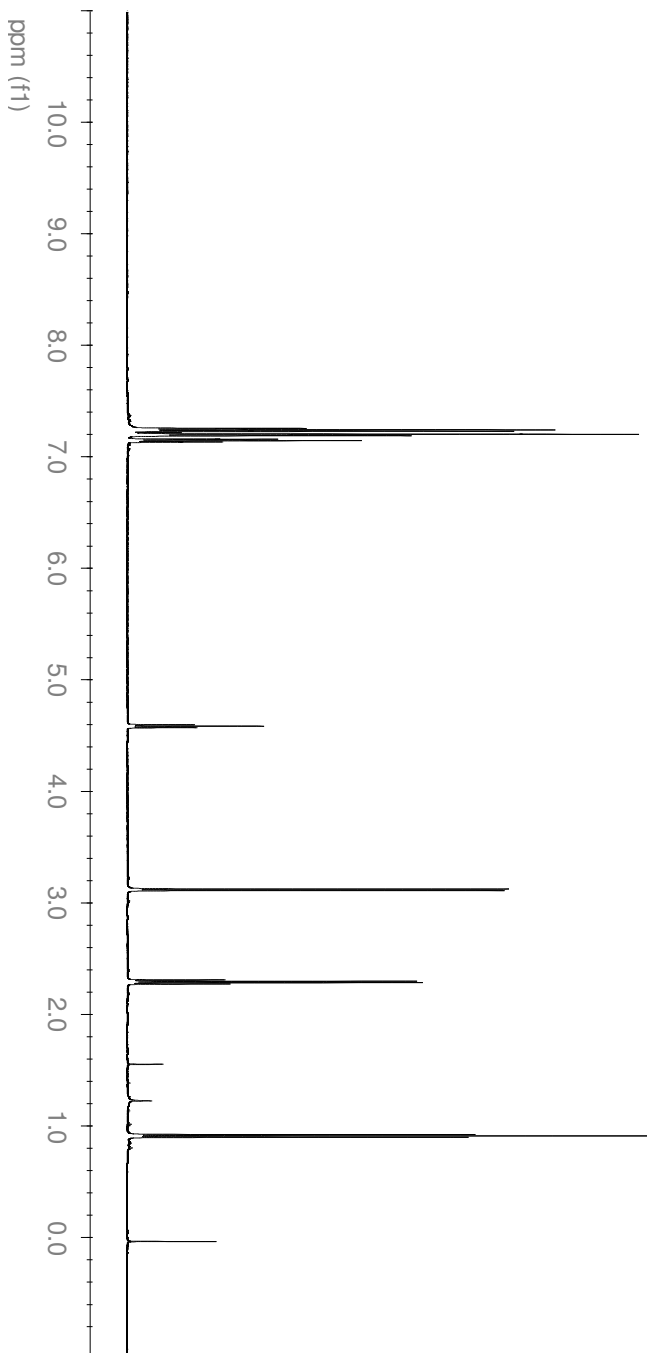
Temperature:
25

Number of Scans:
256

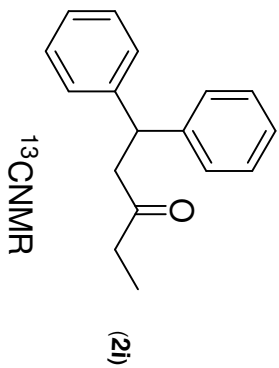
Acq. Date:
Sep 9 2009



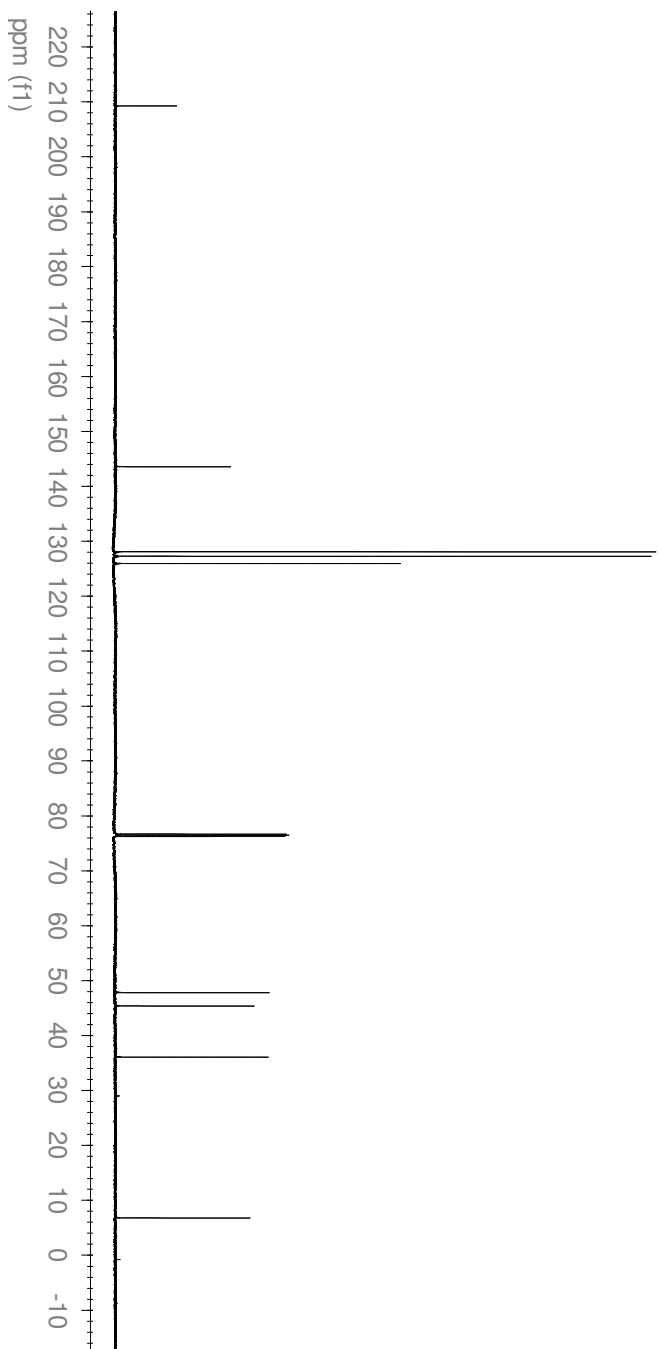
¹H NMR



Spectrum Title:
 JU0909_1yx-3-143_1H
Frequency (MHz):
 (f1) 599.936
Acquisition Time (sec):
 (f1) 2.0486
Spectral Width (ppm):
 (f1) 16.027
Pulse Program:
 sZpu
Temperature:
 25
Number of Scans:
 8
Acq. Date:
 Jul 8 2009



¹³CNMR



Spectrum Title:

JU0909_lyx-3-143_13C

Frequency (MHz):

(f1) 150.889

Acquisition Time (sec):

(f1) 1.3005

Spectral Width (ppm):

(f1) 243.696

Pulse Program:

s2p1

Temperature:

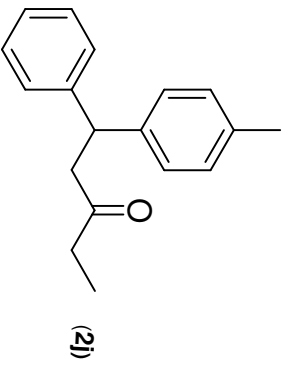
25

Number of Scans:

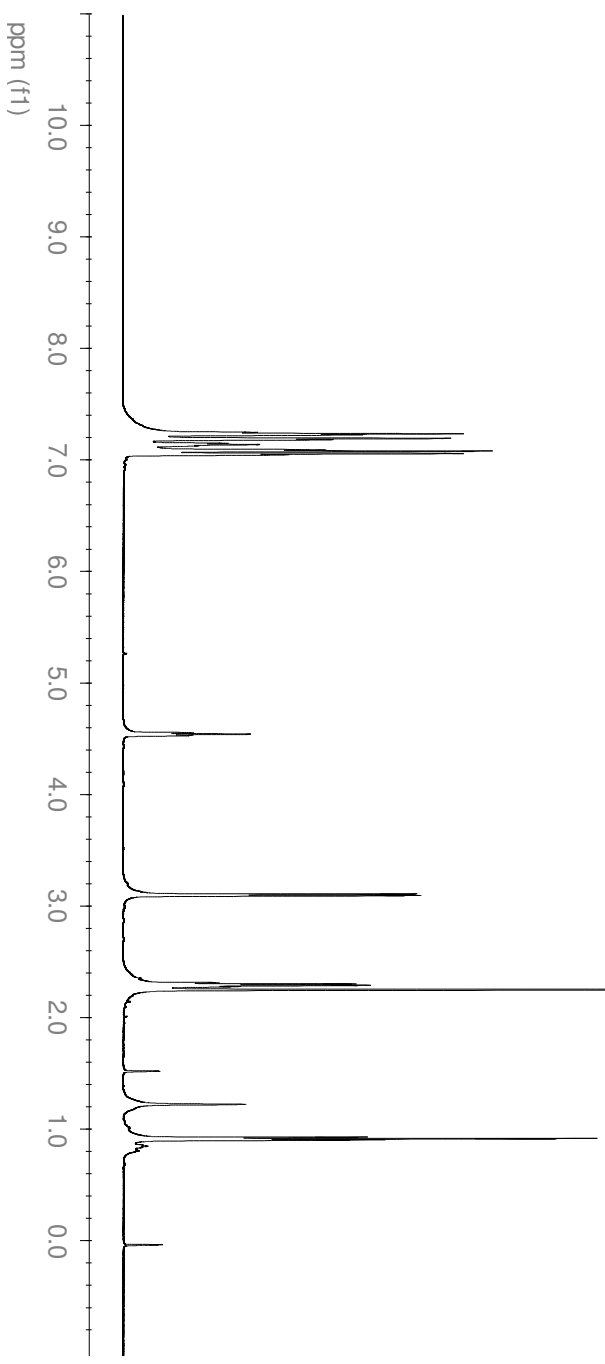
256

Acq. Date:

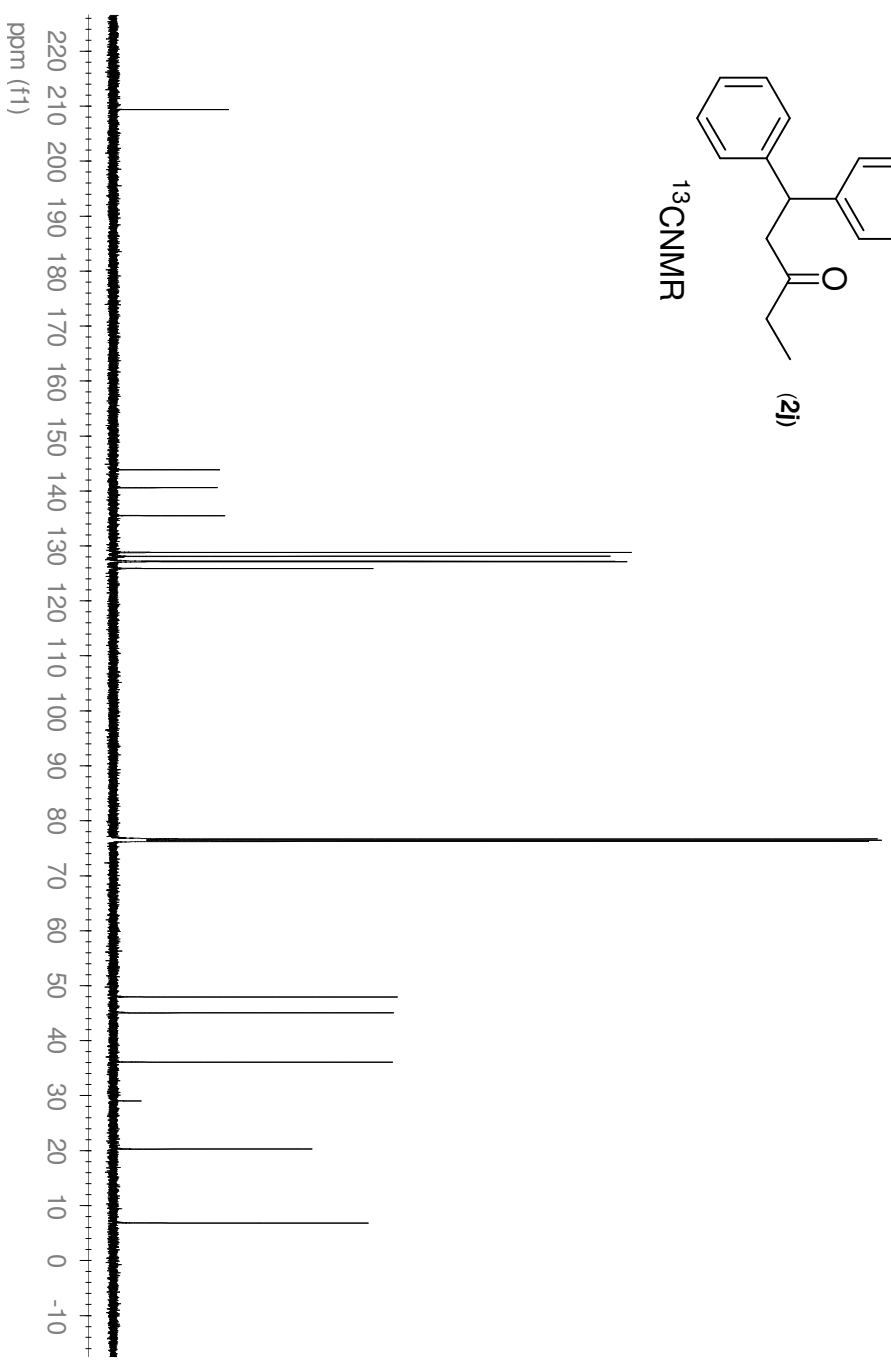
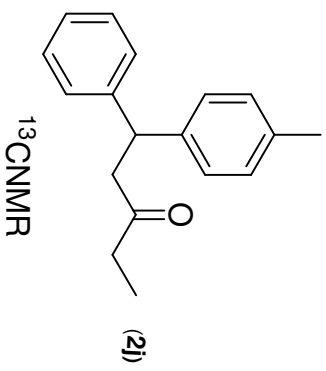
Jul 8 2009



¹H NMR



Spectrum Title:
 Jan1210_lyx4457-1_1H
Frequency (MHz):
 (f1) 599.996
Acquisition Time (sec):
 (f1) 2.0488
Spectral Width (ppm):
 (f1) 16.027
Pulse Program:
 s2x1
Temperature:
 25
Number of Scans:
 8
Acq. Date:
 Jan 12 2010



Spectrum Title:
 Jan1210_lvx-4-57-1_13C

Frequency (MHz):
 (f1) 150.889

Acquisition Time (sec):
 (f1) 1.3005

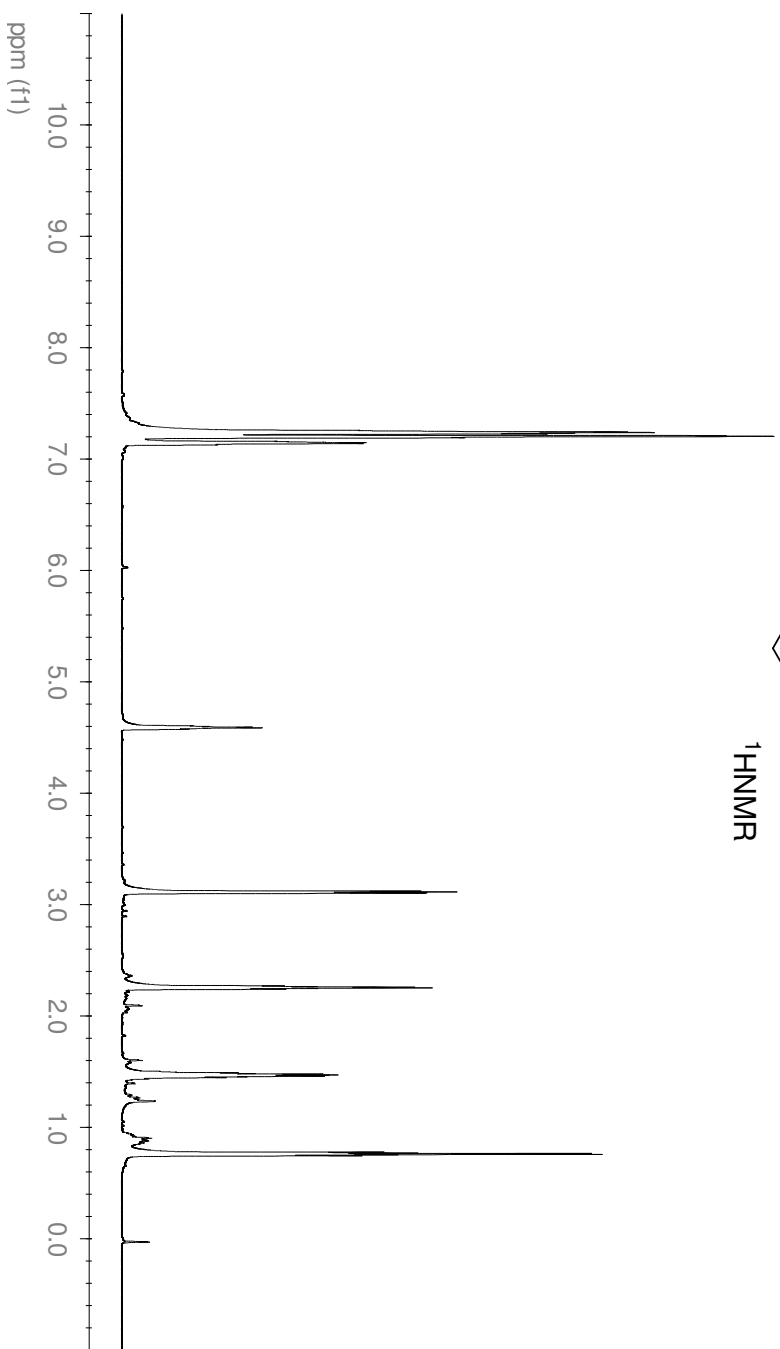
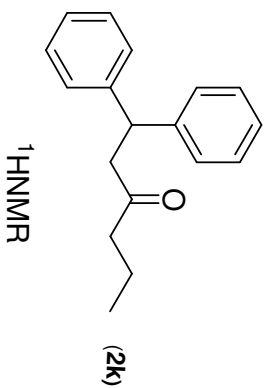
Spectral Width (ppm):
 (f1) 243.696

Pulse Program:
 s2pul

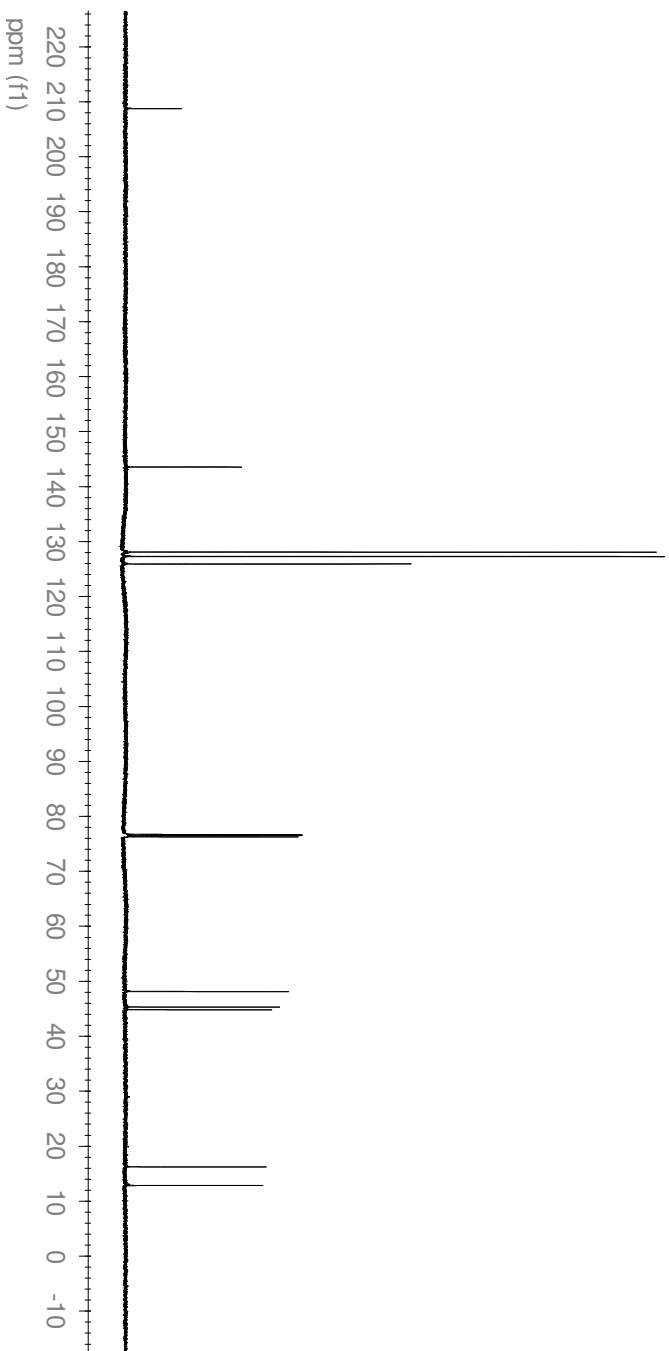
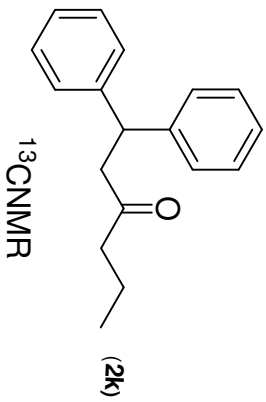
Temperature:
 25

Number of Scans:
 256

Acq. Date:
 Jan 12 2010



Spectrum Title:
 Dec0409_lyx-442-1_1H
Frequency (MHz):
 (f1) 599.936
Acquisition Time (sec):
 (f1) 2.0486
Spectral Width (ppm):
 (f1) 16.027
Pulse Program:
 s2pul
Temperature:
 25
Number of Scans:
 1
Acq. Date:
 Dec 4 2009



Spectrum Title:
Dec0409 jyx-442-1_13C

Frequency (MHz):

(f1) 150.889

Acquisition Time (sec):

(f1) 1.3005

Spectral Width (ppm):

(f1) 243.686

Pulse Program:

s2pkl

Temperature:

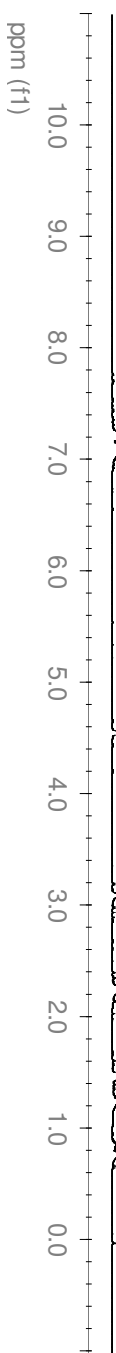
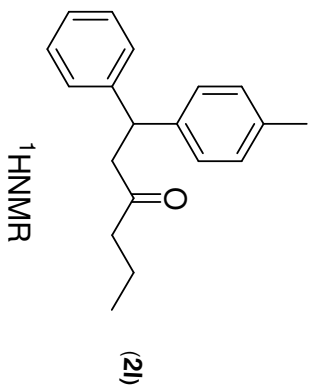
25

Number of Scans:

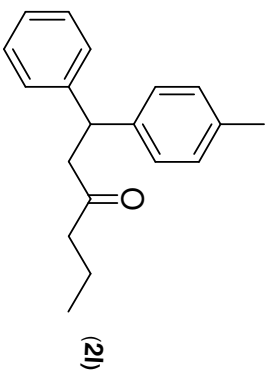
512

Acq. Date:

Dec 4 2009



Spectrum Title:
 Dec0309_lvx-4-45-2_1H
Frequency (MHz):
 (f1) 599.936
Acquisition Time (sec):
 (f1) 2.0486
Spectral Width (ppm):
 (f1) 16.027
Pulse Program:
 s2pul
Temperature:
 25
Number of Scans:
 4
Acq. Date:
 Dec 3 2009



¹³CNMR



Spectrum Title:
Dec0309_lyx-4452_13C

Frequency (MHz):

(f1) 130.869

Acquisition Time (sec):

(f1) 1.3005

Spectral Width (ppm):

(f1) 243.696

Pulse Program:

s2pul

Temperature:

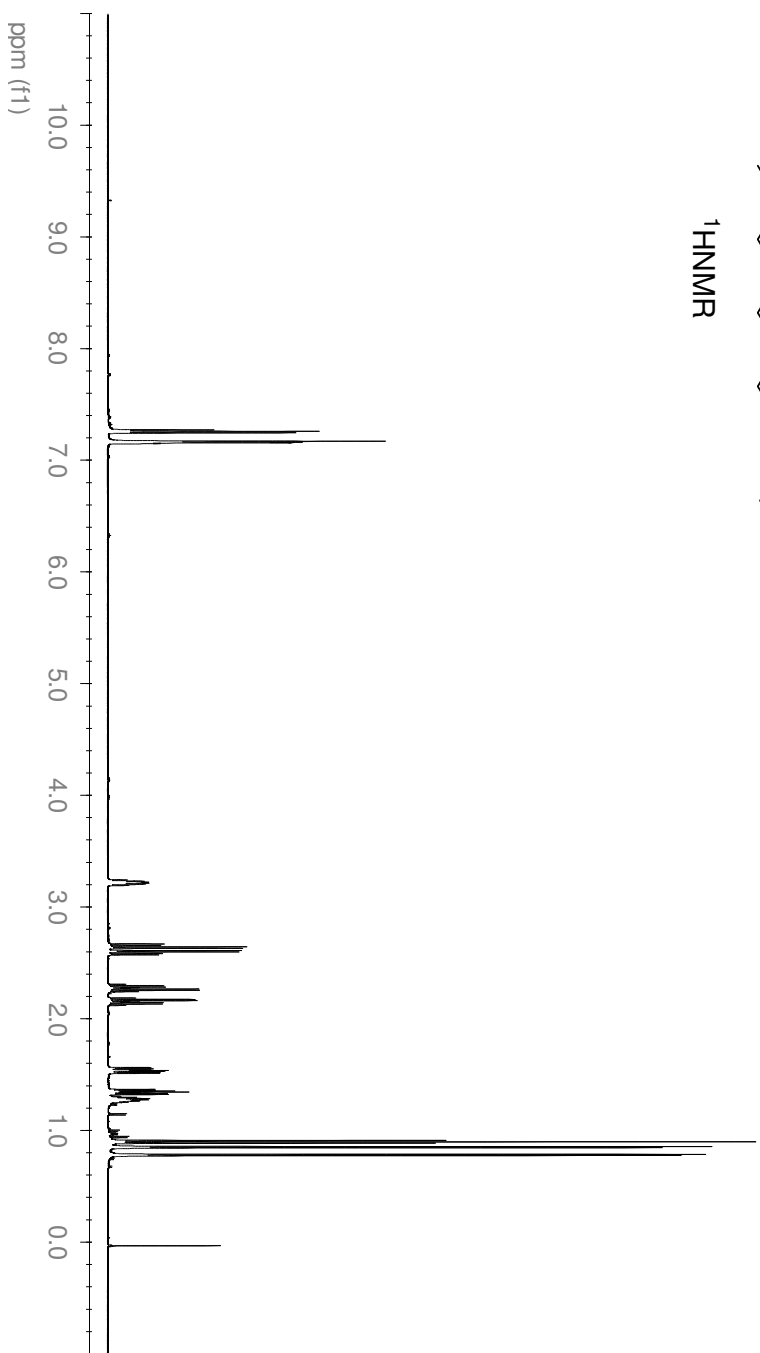
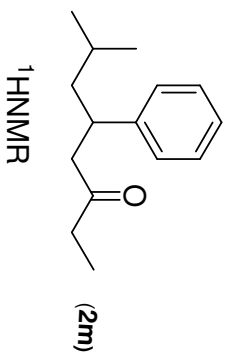
25

Number of Scans:

512

Acq. Date:

Dec 3 2009



Spectrum Title:
Feb0710_lyx-4-64-2_1H

Frequency (MHz):
(f1) 599.936

Acquisition Time (sec):
(f1) 2.0486

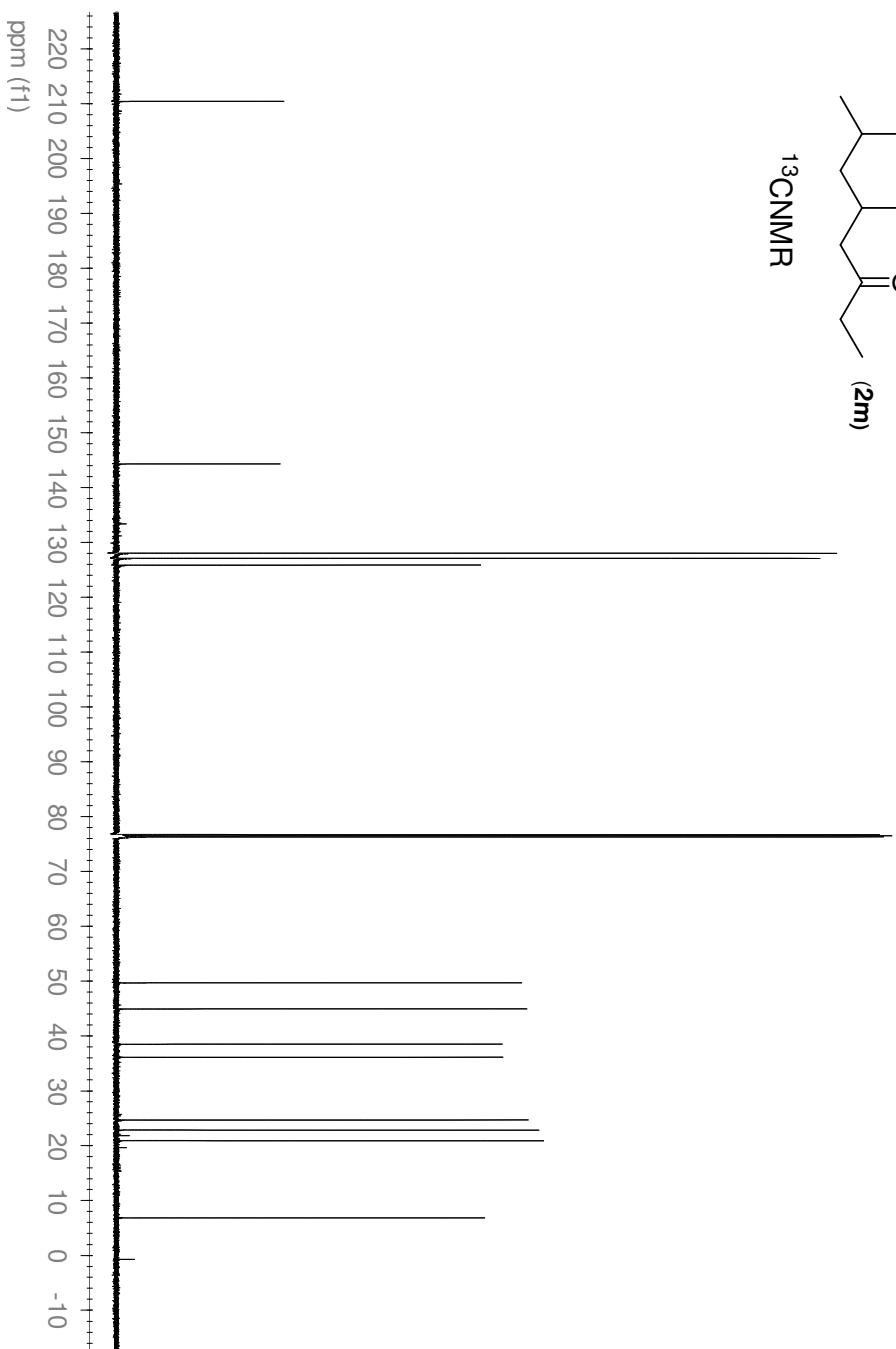
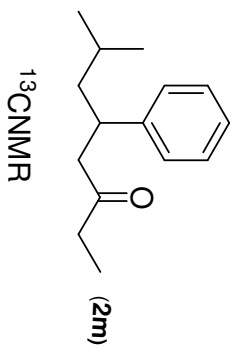
Spectral Width (ppm):
(f1) 16.027

Pulse Program:
s2pul

Temperature:
25

Number of Scans:
8

Acq. Date:
Feb 7 2010



Spectrum Title:
 Feb0710_lyx-4-64-2_13C

Frequency (MHz):
 (f1) 150.889

Acquisition Time (sec):
 (f1) 1.3005

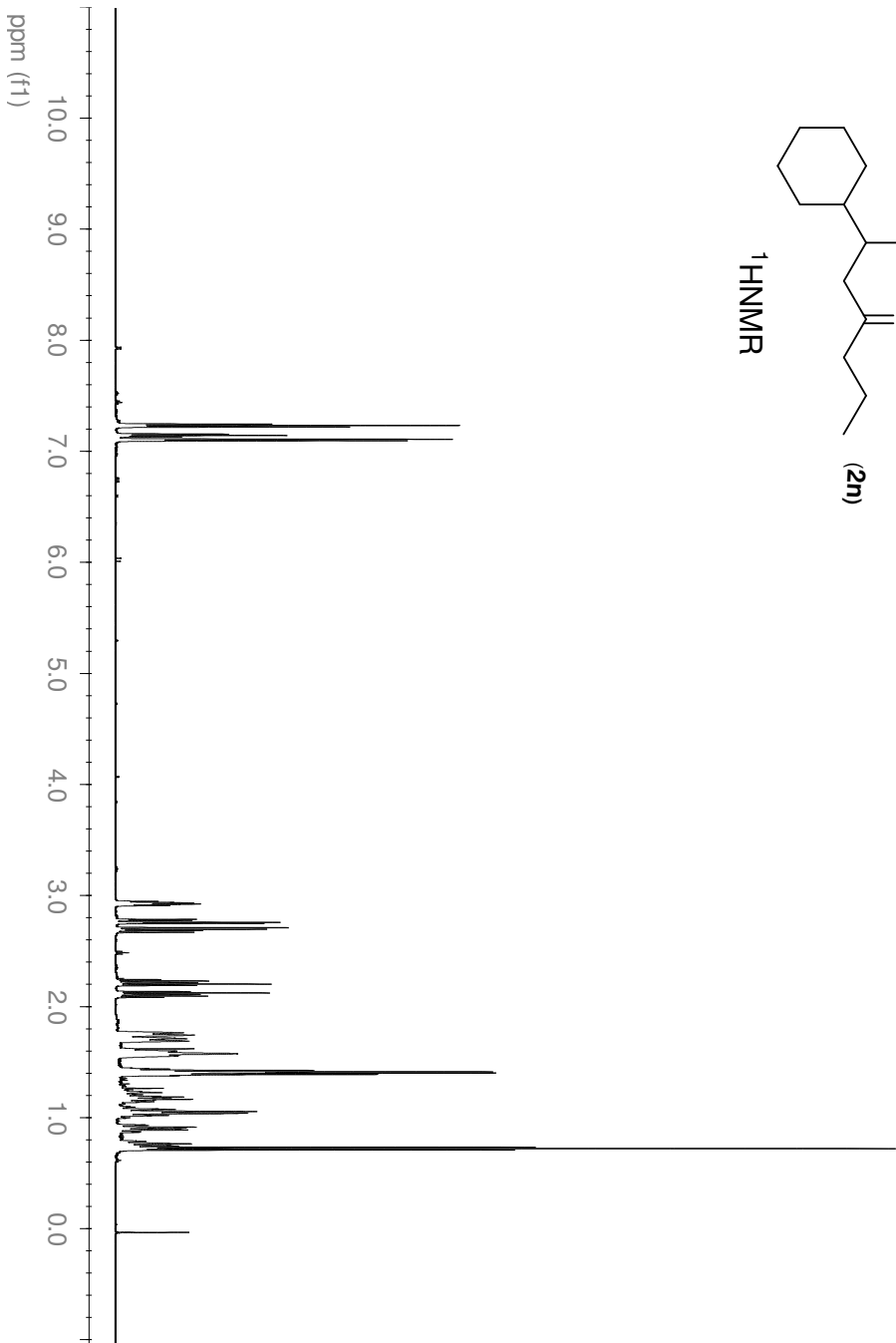
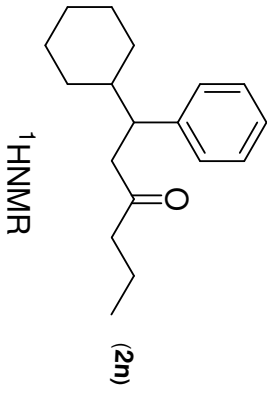
Spectral Width (ppm):
 (f1) 243.696

Pulse Program:
 s2pul

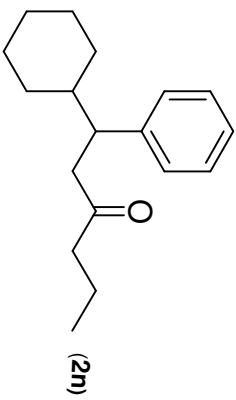
Temperature:
 25

Number of Scans:
 1000

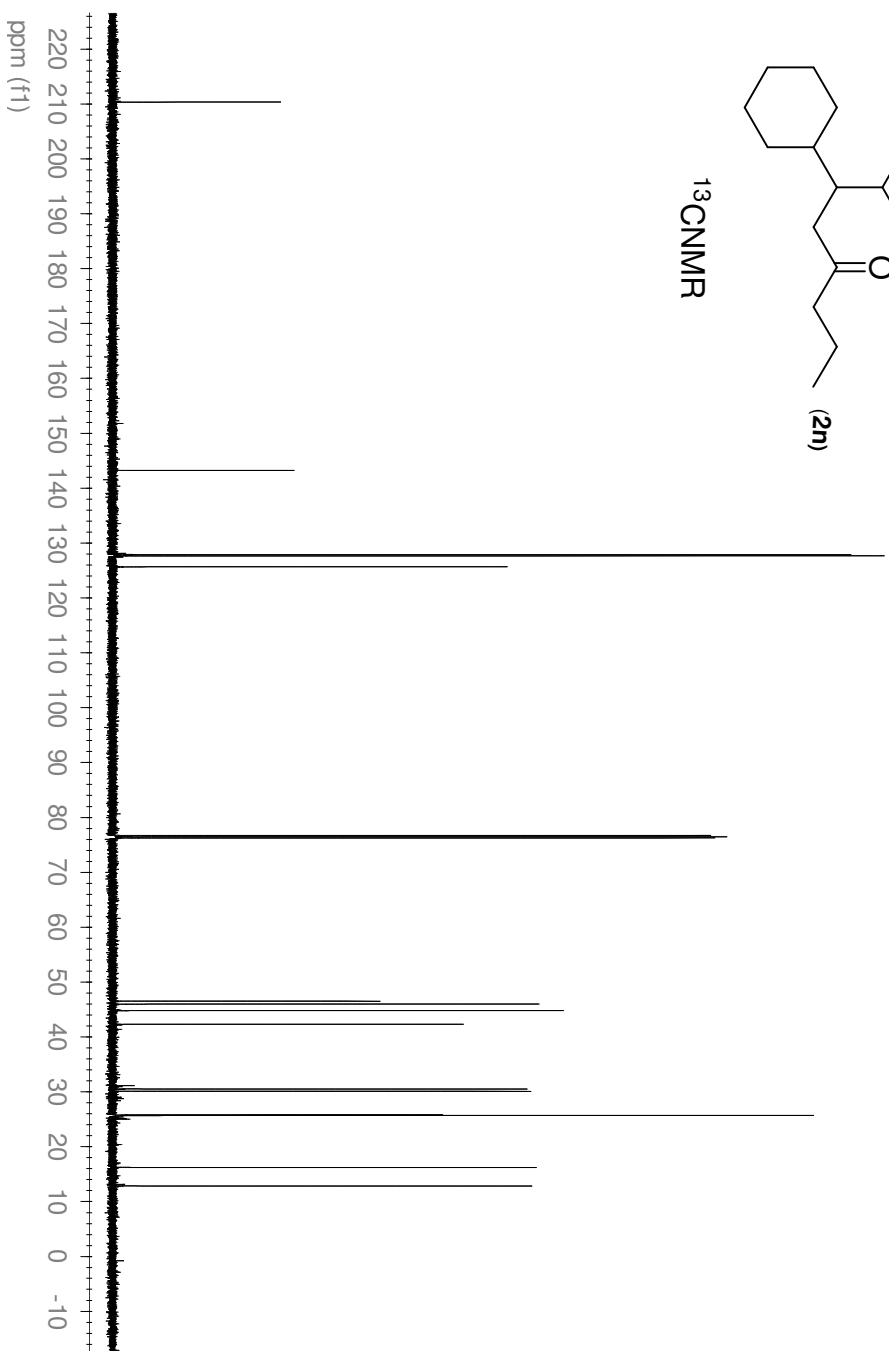
Acq. Date:
 Feb 7 2010



Spectrum Title:
 Dec0909_ljx-4-46-2_1H
Frequency (MHz):
 (f1) 599.396
Acquisition Time (sec):
 (f1) 2.0486
Spectral Width (ppm):
 (f1) 16.027
Pulse Program:
 s2pd
Temperature:
 25
Number of Scans:
 4
Acq. Date:
 Dec 9/2009



¹³CNMR



Spectrum Title:
Dec0909_jyx-4462_13C

Frequency (MHz):

(f1) 150.889

Acquisition Time (sec):

(f1) 1.3005

Spectral Width (ppm):

(f1) 243.696

Pulse Program:

s2pul

Temperature:

25

Number of Scans:

512

Acq. Date:

Dec 9 2009