

Synthesis of β , β -diaryl propiophenones via palladium-catalyzed domino arylboronation, elimination and enone hydroarylation of enaminones

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Contents

General information.....	S1
General procedure for the synthesis of ketones 3 and 5	S2
Characterization data of all products.....	S2-S9
References.....	S9
¹ H and ¹³ C NMR spectra of all products.....	S10-S27
X-Ray crystal structure of 3a	S28

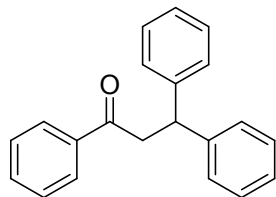
General information

All experiments were carried out under air atmosphere. All enaminones were synthesized following literature process,¹ and other chemicals and solvents used in the experiments were obtained from commercial sources and used directly without further treatment. ¹H and ¹³C NMR spectra were recorded in 400 MHz apparatus. The frequencies for ¹H NMR and ¹³C NMR test are 400 MHz and 100 MHz, respectively. The chemical shifts were reported in ppm with TMS as internal standard. Melting points were tested in X-4A instrument without correcting temperature and the HRMS were obtained under ESI model with TOF analyzer.

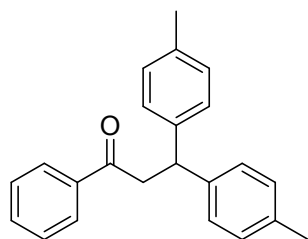
General procedure for the synthesis of ketones 3

To a 25 mL round-bottom flask were added enaminone **1** (0.3 mmol), aryl boronic acid **2** (0.75 mmol), Pd(OAc)₂ (0.015 mol), bpy (0.03 mmol) and DMF/water (0.4 mL/1.6 mL). Then the mixture was heated up to 90 °C, and stirred at the same temperature for 12 h under (TLC). After cooling down to room temperature, 5 mL of water was added, and the resulting mixture was extracted with ethyl acetate (3 × 8 mL). The organic phases were collected and washed with small amount of water for three times. After drying with anhydrous Na₂SO₄, the solid was filtered and the acquired solution was subjected to reduced pressure to remove the solvent. The resulting residue was subjected to flash silica gel column chromatography to provide pure products with the elution of mixed petroleum ether/ethyl acetate (v/v = 20:1).

Characterization data of all products

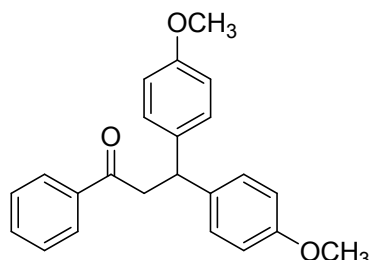


1,3,3-Triphenylpropan-1-one (3a). Yield: 64 mg (75 %); white solid; m.p. 97-99 °C; ¹H NMR (400 MHz, CDCl₃): δ 7.93 (d, 2 H, *J* = 7.6 Hz), 7.53 (t, 1 H, *J* = 7.2 Hz), 7.42 (t, 2 H, *J* = 7.6 Hz), 7.27-7.23 (m, 7 H), 7.18-7.15 (m, 3 H), 4.83 (t, 1 H, *J* = 7.2 Hz), 3.73(d, 2 H, *J* = 7.2 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 198.0, 144.2, 137.1, 133.1, 128.6, 128.5, 128.1, 127.9, 126.4, 46.0, 44.7; ESI-HRMS: Calcd for C₂₁H₁₉O, [M+H]⁺ 287.1430, found 287.1436.

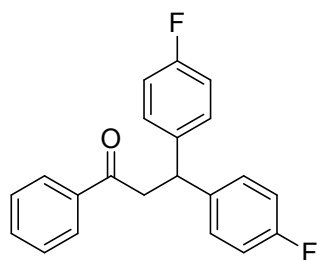


1-Phenyl-3,3-di-*p*-tolylpropan-1-one (3b). Yield: 70 mg (74 %); white solid; m.p. 104-107 °C; ¹H NMR (400 MHz, CDCl₃): δ 7.92 (d, 2 H, *J* = 7.6 Hz), 7.52 (t, 1 H, *J* =

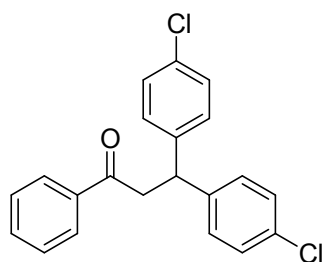
6.8 Hz), 7.41 (t, 2 H, $J = 7.2$ Hz), 7.14 (d, 4 H, $J = 8.0$ Hz), 7.06 (d, 4 H, $J = 7.6$ Hz), 4.74 (t, 1 H, $J = 6.8$ Hz), 3.69 (d, 2 H, $J = 7.2$ Hz), 2.26 (s, 6 H); ^{13}C NMR (100 MHz, CDCl_3): δ 198.2, 141.5, 137.2, 135.8, 133.0, 129.3, 128.6, 128.1, 127.7, 45.2, 44.9, 21.0; ESI-HRMS: Calcd for $\text{C}_{23}\text{H}_{23}\text{O}$ $[\text{M}+\text{H}]^+$ 315.1743, found 315.1728.



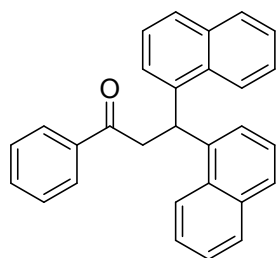
3,3-Bis(4-methoxyphenyl)-1-phenylpropan-1-one (3c). Yield: 75 mg (72 %); white solid; m.p. 109-111 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.91 (d, 2 H, $J = 8.4$ Hz), 7.51 (t, 1 H, $J = 7.2$ Hz), 7.41 (t, 2 H, $J = 7.6$ Hz), 7.15 (d, 4 H, $J = 8.0$ Hz), 6.79 (d, 4 H, $J = 8.4$ Hz), 4.72 (t, 1 H, $J = 7.2$ Hz), 3.72 (s, 6 H), 3.66 (d, 2 H, $J = 8.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 198.3, 158.1, 137.2, 136.7, 133.0, 128.7, 128.6, 128.1, 114.0, 55.2, 45.2, 44.5; ESI-HRMS: Calcd for $\text{C}_{23}\text{H}_{26}\text{NO}_3$ $[\text{M}+\text{NH}_4]^+$ 364.1907, found 364.1906.



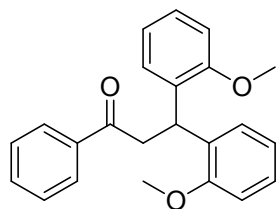
3,3-Bis(4-fluorophenyl)-1-phenylpropan-1-one (3d). Yield: 69 mg (71 %); white solid; m.p. 102-103 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.92 (d, 2 H, $J = 7.6$ Hz), 7.54 (t, 1 H, $J = 7.6$ Hz), 7.42 (t, 2 H, $J = 7.6$ Hz), 7.22-7.17 (m, 4 H), 6.94 (t, 4 H, $J = 8.4$ Hz), 4.79 (t, 1 H, $J = 6.8$ Hz), 3.68 (d, 2 H, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 197.7, 161.5 (d, $J = 242.7$ Hz), 139.8 (d, $J = 3.0$ Hz), 136.9, 133.3, 129.2 (d, $J = 7.7$ Hz), 128.7, 128.1, 115.5 (d, $J = 21.1$ Hz), 44.9, 44.4; ESI-HRMS: Calcd for $\text{C}_{21}\text{H}_{17}\text{F}_2\text{O}$ $[\text{M}+\text{H}]^+$ 323.1242, found 323.1232.



3,3-Bis(4-chlorophenyl)-1-phenylpropan-1-one (3e).⁴ Yield: 74 mg (70 %); white solid; m.p. 123-125 °C; ¹H NMR (400 MHz, CDCl₃): δ 7.92 (d, 2 H, *J* = 8.0 Hz), 7.56 (t, 1 H, *J* = 7.2 Hz), 7.44 (t, 2 H, *J* = 7.6 Hz), 7.24 (d, 4 H, *J* = 8.0 Hz), 7.16 (d, 4 H, *J* = 8.0 Hz), 4.78 (t, 1 H, *J* = 7.2 Hz), 3.86 (d, 2 H, *J* = 7.2 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 197.3, 142.2, 136.8, 133.3, 132.4, 129.1, 128.8, 128.7, 128.0, 44.6, 44.4.

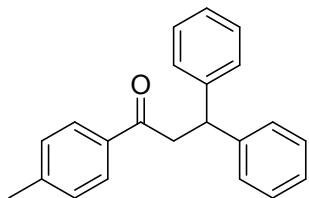


3,3-Di(naphthalen-1-yl)-1-phenylpropan-1-one (3f). Yield: 83 mg (72 %); white solid; m.p. 199-201 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.16 (d, 2 H, *J* = 8.0 Hz), 7.96 (d, 2 H, *J* = 8.0 Hz), 7.86 (d, 2 H, *J* = 8.0 Hz), 7.72 (d, 2 H, *J* = 8.0 Hz), 7.55 (t, 1 H, *J* = 7.2 Hz), 7.48-7.41 (m, 6 H), 7.30 (t, 2 H, *J* = 8.0 Hz), 7.19 (d, 2 H, *J* = 7.2 Hz), 6.46 (t, 1 H, *J* = 7.2 Hz), 3.92 (d, 2 H, *J* = 7.2 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 197.8, 139.6, 137.0, 134.3, 133.3, 131.4, 129.0, 128.7, 128.1, 127.4, 126.5, 125.7, 125.4, 124.7, 123.5, 44.0, 37.1; ESI-HRMS: Calcd for C₂₉H₂₆NO [M+NH₄]⁺ 404.2009, found 404.2017.

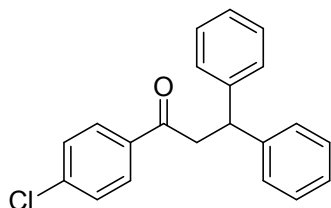


3,3-Bis(2-methoxyphenyl)-1-phenylpropan-1-one (3g). Yield: 65 mg (63 %); white solid; m.p. 119-121 °C; ¹H NMR (400 MHz, CDCl₃): δ 7.96 (d, 2 H, *J* = 7.2 Hz), 7.52 (t, 1 H, *J* = 7.2 Hz), 7.41 (t, 2 H, *J* = 7.6 Hz), 7.19-7.10 (m, 4 H), 6.87-6.82 (m, 4 H),

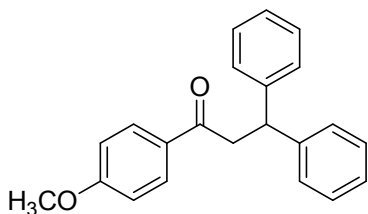
5.43 (t, 1 H, $J = 7.6$ Hz), 3.73 (s, 6 H), 3.68 (d, 2 H, $J = 7.6$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 198.9, 157.2, 137.3, 132.7, 131.9, 128.6, 128.5, 128.2, 127.3, 120.3, 110.9, 55.5, 42.9, 34.6; ESI-HRMS: Calcd for $\text{C}_{23}\text{H}_{23}\text{O}_3$ $[\text{M}+\text{H}]^+$ 347.1642, found 347.1632.



3,3-Diphenyl-1-(p-tolyl)propan-1-one (3h). Yield: 68 mg (75 %); white solid; m.p. 104-107 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.82 (d, 2 H, $J = 7.6$ Hz), 7.26-7.25 (m, 8 H), 7.22-7.20 (m, 2 H), 7.17-7.14 (m, 2 H), 4.82 (t, 1 H, $J = 7.6$ Hz), 3.70 (d, 2 H, $J = 7.2$ Hz), 2.37 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3): δ 197.6, 144.3, 143.9, 134.7, 129.3, 128.6, 128.2, 127.9, 126.4, 46.1, 44.7, 21.6; ESI-HRMS: Calcd for $\text{C}_{22}\text{H}_{21}\text{O}$ $[\text{M}+\text{H}]^+$ 301.1587, found 301.1593.

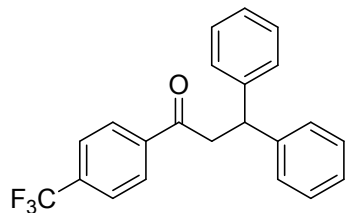


1-(4-Chlorophenyl)-3,3-diphenylpropan-1-one (3i). Yield: 70 mg (73 %); white solid; m.p. 131-135 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.83 (d, 2 H, $J = 8.0$ Hz), 7.38 (d, 2 H, $J = 8.0$ Hz), 7.28-7.22 (m, 8 H), 7.17-7.14 (m, 2 H), 4.79 (t, 1 H, $J = 7.2$ Hz), 3.68 (d, 2 H, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 196.9, 144.0, 139.6, 135.4, 129.6, 129.0, 128.7, 127.9, 126.6, 46.1, 44.7; ESI-HRMS: Calcd for $\text{C}_{21}\text{H}_{18}\text{ClO}$ $[\text{M}+\text{H}]^+$ 321.1041, found 321.1038.

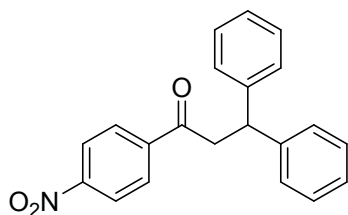


1-(4-Methoxyphenyl)-3,3-diphenylpropan-1-one (3j). Yield: 66 mg (70 %); white solid; m.p. 115-118 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.88 (d, 2 H, $J = 8.4$ Hz), 7.25-7.19 (m, 8 H), 7.11 (t, 2 H, $J = 6.4$ Hz), 6.83 (d, 2 H, $J = 8.8$ Hz), 4.81 (t, 1 H, J

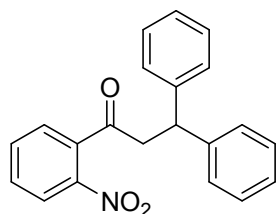
= 7.6 Hz), 3.72 (s, 3 H), 3.64 (d, 2 H, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 196.6, 163.6, 144.5, 130.5, 130.2, 128.7, 128.0, 126.5, 113.9, 55.5, 46.2, 44.4; ESI-HRMS: Calcd for $\text{C}_{22}\text{H}_{21}\text{O}_2$ $[\text{M}+\text{H}]^+$ 317.1536, found 317.1537.



3,3-Diphenyl-1-(4-(trifluoromethyl)phenyl)propan-1-one (3k). Yield: 73 mg (69 %); white solid; m.p. 119-121 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.00 (d, 2 H, $J = 8.4$ Hz), 7.69 (d, 2 H, $J = 8.4$ Hz), 7.30-7.25 (m, 8 H), 7.20-7.16 (m, 2 H), 4.81 (t, 1 H, $J = 7.2$ Hz), 3.75 (d, 2 H, $J = 7.6$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 197.2, 143.8, 139.8, 134.4 (q, $J = 31.9$ Hz), 128.7, 128.4, 127.8, 126.6, 125.7 (q, $J = 3.6$ Hz), 123.7 (d, $J = 271.1$ Hz), 46.1, 45.1; ESI-HRMS: Calcd for $\text{C}_{22}\text{H}_{21}\text{F}_3\text{NO}$ $[\text{M}+\text{NH}_4]^+$ 372.1570, found 372.1575.

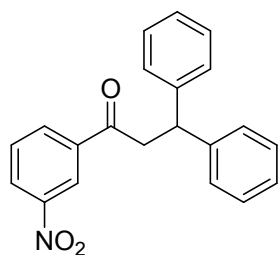


1-(4-Nitrophenyl)-3,3-diphenylpropan-1-one (3l).² Yield: 71 mg (71 %); white solid; m.p. 145-148 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.26 (d, 2 H, $J = 8.8$ Hz), 8.03 (d, 2 H, $J = 8.8$ Hz), 7.30-7.24 (m, 8 H), 7.20-7.17 (m, 2 H), 4.79 (t, 1 H, $J = 7.2$ Hz), 3.76 (d, 2 H, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 196.8, 150.3, 143.5, 141.5, 129.1, 128.7, 127.8, 126.7, 123.9, 46.1, 45.3.

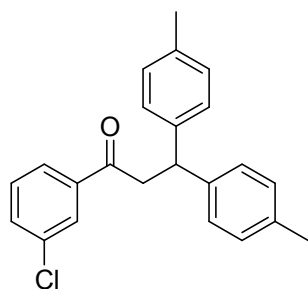


1-(2-Nitrophenyl)-3,3-diphenylpropan-1-one (3m). Yield: 65 mg (65 %); white solid; m.p. 129-131 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.71 (s, 1 H), 8.36 (d, 1 H, $J =$

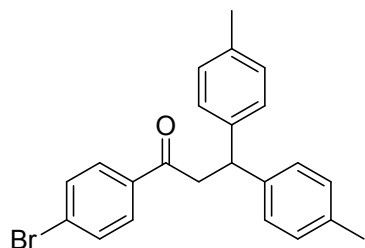
8.0 Hz), 8.21 (d, 1 H, $J = 7.6$ Hz), 7.60 (t, 1 H, $J = 8.0$ Hz), 7.27 (d, 8 H, $J = 4.4$ Hz), 7.20-7.15 (m, 2 H), 4.82 (t, 1 H, $J = 7.2$ Hz), 3.79 (d, 2 H, $J = 7.6$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 196.0, 148.4, 143.6, 138.2, 133.7, 130.0, 128.7, 127.8, 127.4, 126.7, 123.0, 46.0, 45.0; ESI-HRMS: Calcd for $\text{C}_{21}\text{H}_{21}\text{N}_2\text{O}_3$ $[\text{M}+\text{NH}_4]^+$ 349.1547, found 349.1558.



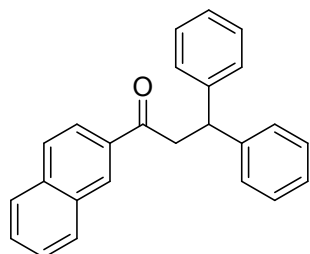
1-(3-Nitrophenyl)-3,3-diphenylpropan-1-one (3n). Yield: 67 mg (68 %); white solid; m.p. 129-131 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.71 (s, 1 H), 8.38 (d, 1 H, $J = 8.4$ Hz), 8.22 (d, 1 H, $J = 7.6$ Hz), 7.62 (t, 1 H, $J = 8.0$ Hz), 7.28 (d, 8 H, $J = 4.4$ Hz), 7.20-7.16 (m, 2 H), 4.82 (t, 1 H, $J = 7.2$ Hz), 3.78 (d, 2 H, $J = 7.6$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 196.0, 148.4, 143.6, 138.2, 133.6, 129.9, 128.7, 127.8, 127.4, 126.7, 123.0, 46.0, 44.9; ESI-HRMS: Calcd for $\text{C}_{21}\text{H}_{21}\text{N}_2\text{O}_3$ $[\text{M}+\text{NH}_4]^+$ 349.1547, found 349.1552.



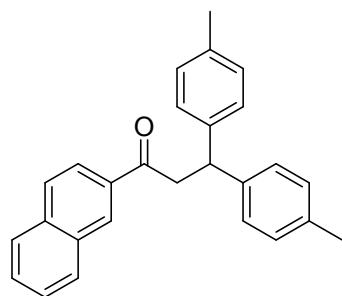
1-(3-Chlorophenyl)-3,3-di-p-tolylpropan-1-one (3o). Yield: 71 mg (68 %); white solid; m.p. 87-89 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.87 (s, 1 H), 7.79 (d, 1 H, $J = 8.0$ Hz), 7.51 (d, 1 H, $J = 7.6$ Hz), 7.37 (t, 1 H, $J = 8.0$ Hz), 7.13 (d, 4 H, $J = 7.6$ Hz), 7.07 (d, 4 H, $J = 7.6$ Hz), 4.72 (t, 1 H, $J = 7.6$ Hz), 3.66 (d, 2 H, $J = 7.2$ Hz), 2.28 (s, 6 H); ^{13}C NMR (100 MHz, CDCl_3): δ 197.0, 141.1, 138.6, 136.0, 134.9, 133.0, 130.0, 129.3, 128.3, 127.6, 126.2, 45.2, 45.0, 21.0; ESI-HRMS: Calcd for $\text{C}_{23}\text{H}_{25}\text{ClNO}$ $[\text{M}+\text{NH}_4]^+$ 366.1619, found 366.1623.



1-(4-Bromophenyl)-3,3-di-p-tolylpropan-1-one (3p). Yield: 81 mg (69 %); white solid; m.p. 110-114 °C; ¹H NMR (400 MHz, CDCl₃): δ 7.78 (d, 2 H, *J* = 8.8 Hz), 7.57 (d, 2 H, *J* = 8.8 Hz), 7.13 (d, 4 H, *J* = 8.0 Hz), 7.06 (d, 4 H, *J* = 8.0 Hz), 4.71 (t, 1 H, *J* = 7.2 Hz), 3.65 (d, 2 H, *J* = 7.2 Hz), 2.28 (s, 6 H); ¹³C NMR (100 MHz, CDCl₃): δ 197.3, 141.2, 136.0, 135.8, 131.9, 129.7, 129.3, 128.3, 127.6, 45.2, 44.8, 21.1; ESI-HRMS: Calcd for C₂₃H₂₅BrNO [M+NH₄]⁺ 410.1114, found 410.1098.



1-(Naphthalen-2-yl)-3,3-diphenylpropan-1-one (3q).³ Yield: 72 mg (71 %); white solid; m.p. 103-105 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.46 (d, 1 H, *J* = 9.6 Hz), 8.00-7.97 (m, 1 H), 7.93 (d, 1 H, *J* = 8.0 Hz), 7.86 (d, 2 H, *J* = 8.4 Hz), 7.60-7.53 (m, 2 H), 7.32-7.25 (m, 8 H), 7.19-7.15 (m, 2 H), 4.89 (t, 1 H, *J* = 7.2 Hz), 3.87 (d, 2 H, *J* = 7.2 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 198.0, 144.3, 135.6, 134.5, 132.6, 129.8, 129.6, 128.7, 128.6, 128.5, 128.0, 127.9, 126.9, 126.5, 124.0, 46.2, 44.9.



1-(Naphthalen-2-yl)-3,3-di-p-tolylpropan-1-one (3r). Yield: 78 mg (71 %); white solid; m.p. 134-137 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.44 (s, 1 H), 7.98 (d, 1 H, *J* = 8.8 Hz), 7.92 (d, 1 H, *J* = 8.0 Hz), 7.85 (d, 2 H, *J* = 8.4 Hz), 7.60-7.51 (m, 2 H), 7.17

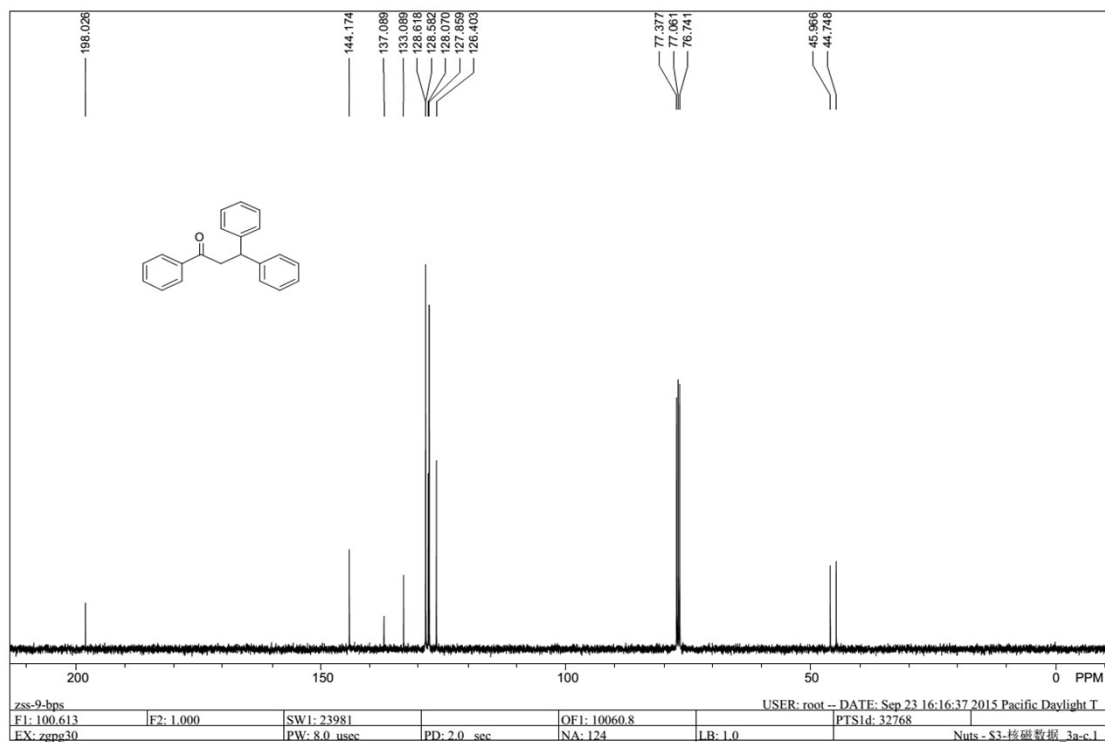
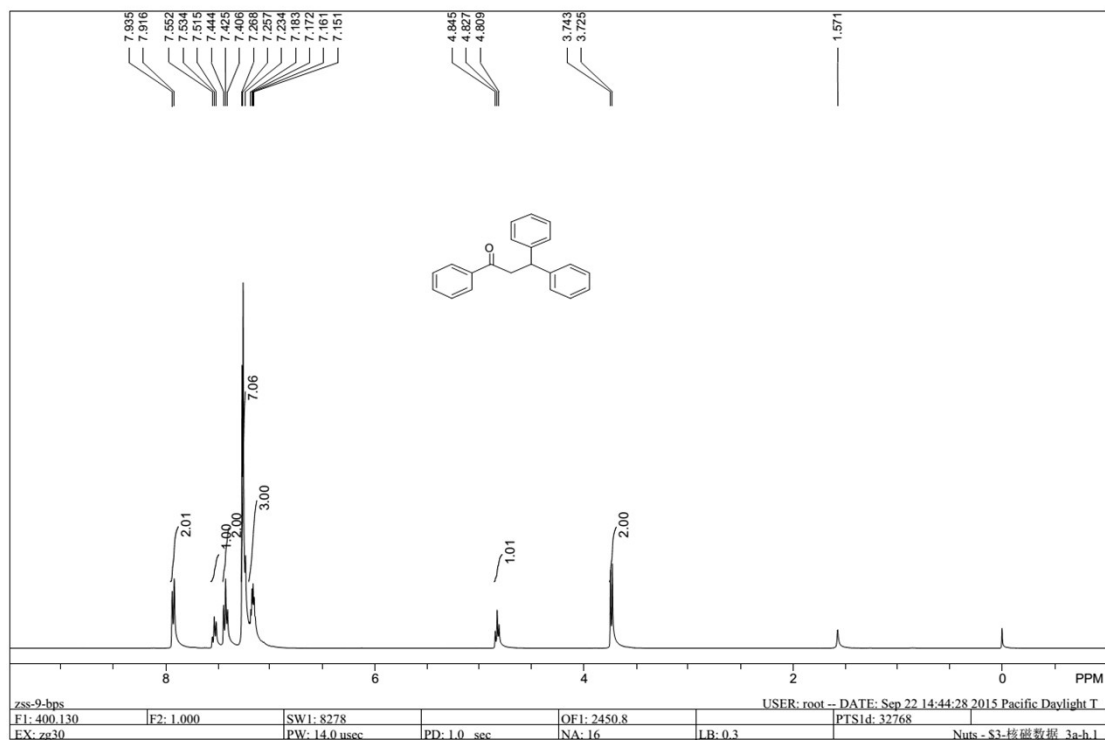
(d, 4 H, $J = 7.6$ Hz), 7.07 (d, 4 H, $J = 7.6$ Hz), 4.80 (t, 1 H, $J = 7.2$ Hz), 3.82 (d, 2 H, $J = 7.2$ Hz), 2.27 (s, 6 H); ^{13}C NMR (100 MHz, CDCl_3): δ 198.2, 141.5, 135.9, 135.6, 134.5, 132.6, 129.8, 129.6, 129.3, 128.5, 127.8, 127.7, 126.8, 124.0, 45.4, 45.0, 21.0; ESI-HRMS: Calcd for $\text{C}_{27}\text{H}_{25}\text{O}$ $[\text{M}+\text{H}]^+$ 365.1900, found 365.1892.

References

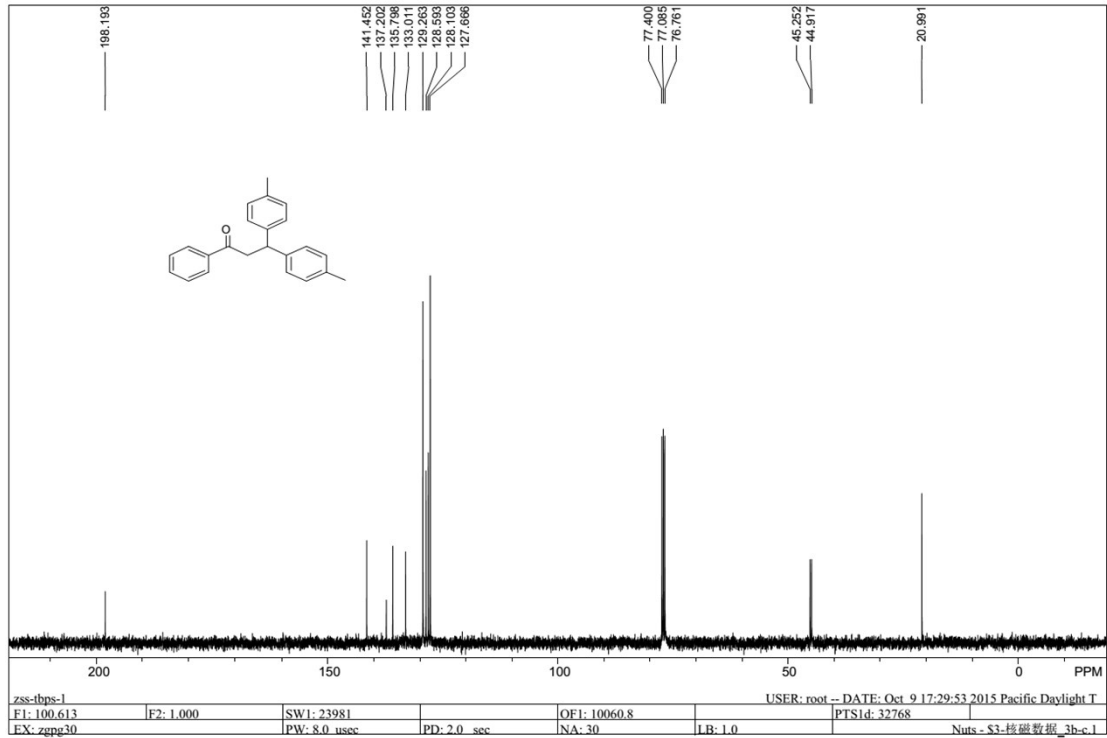
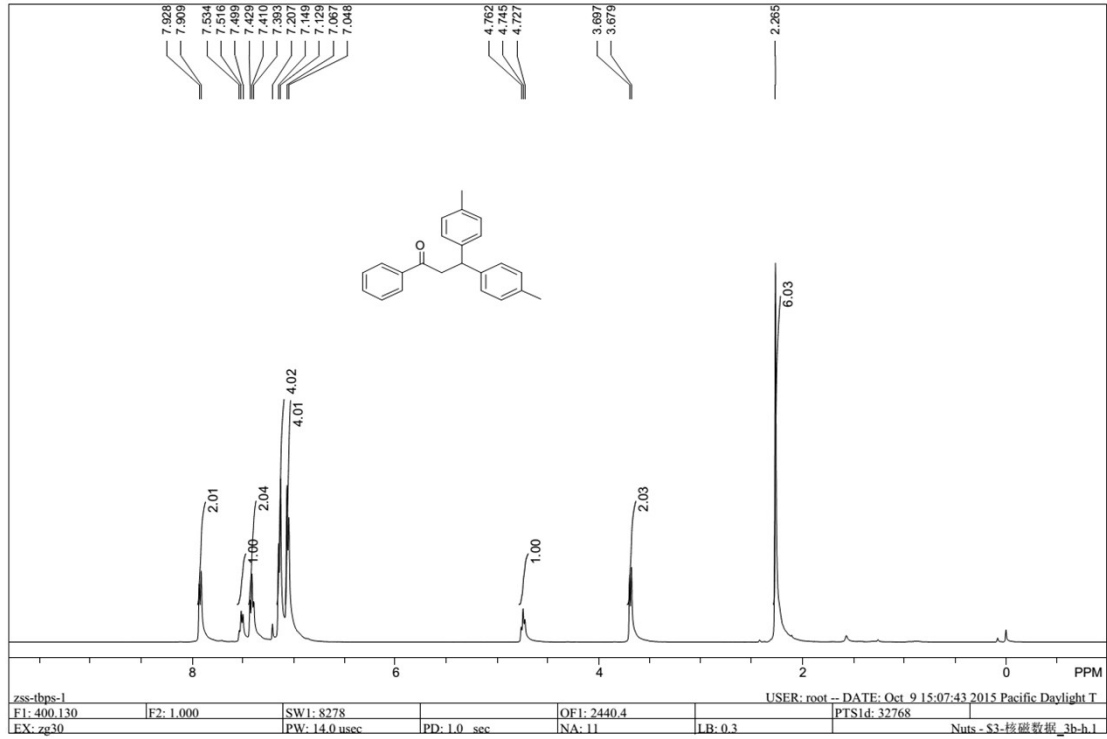
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^1H and ^{13}C NMR spectra of all products

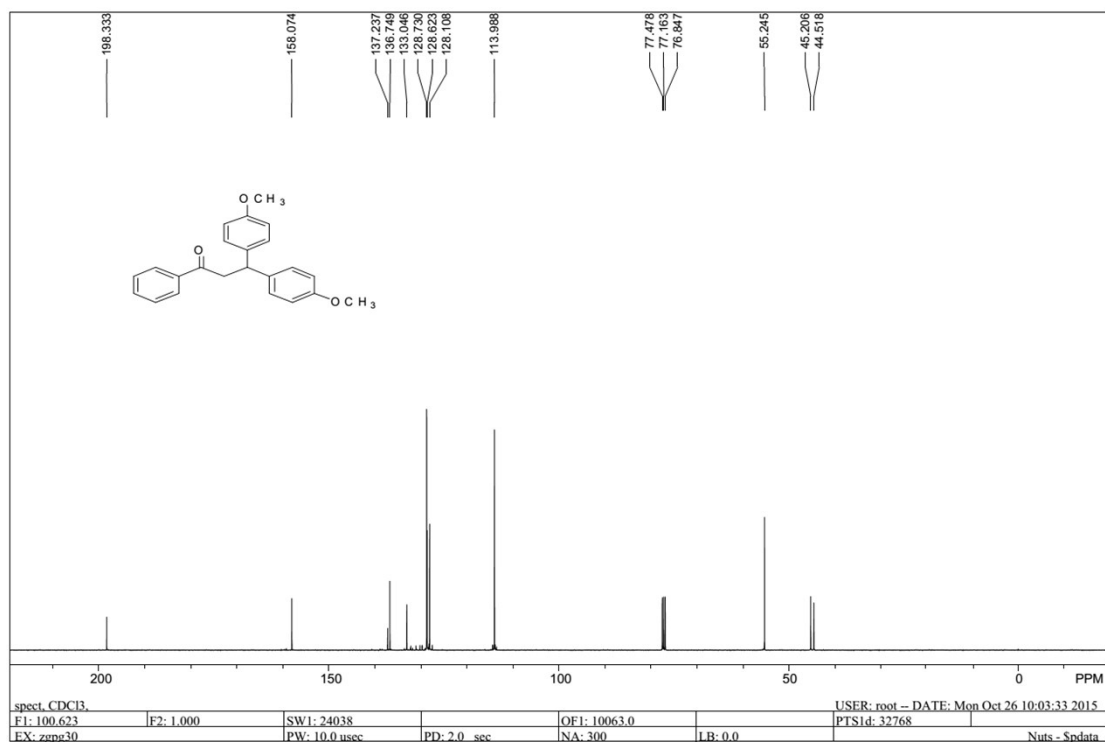
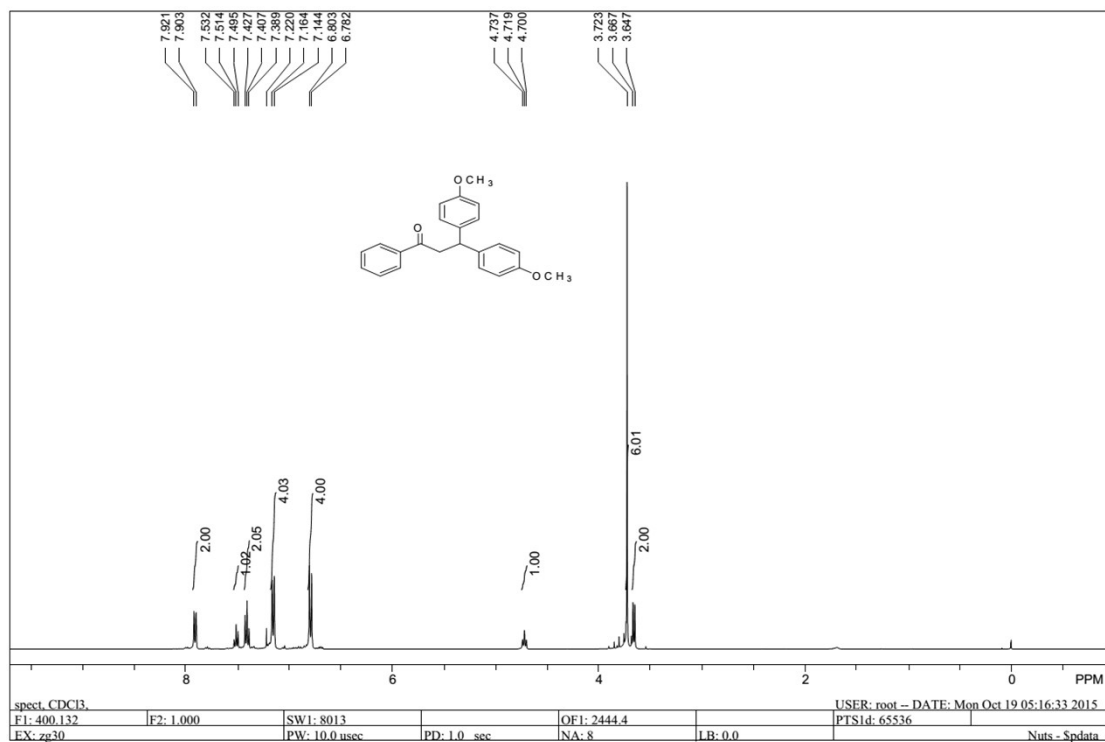
3a



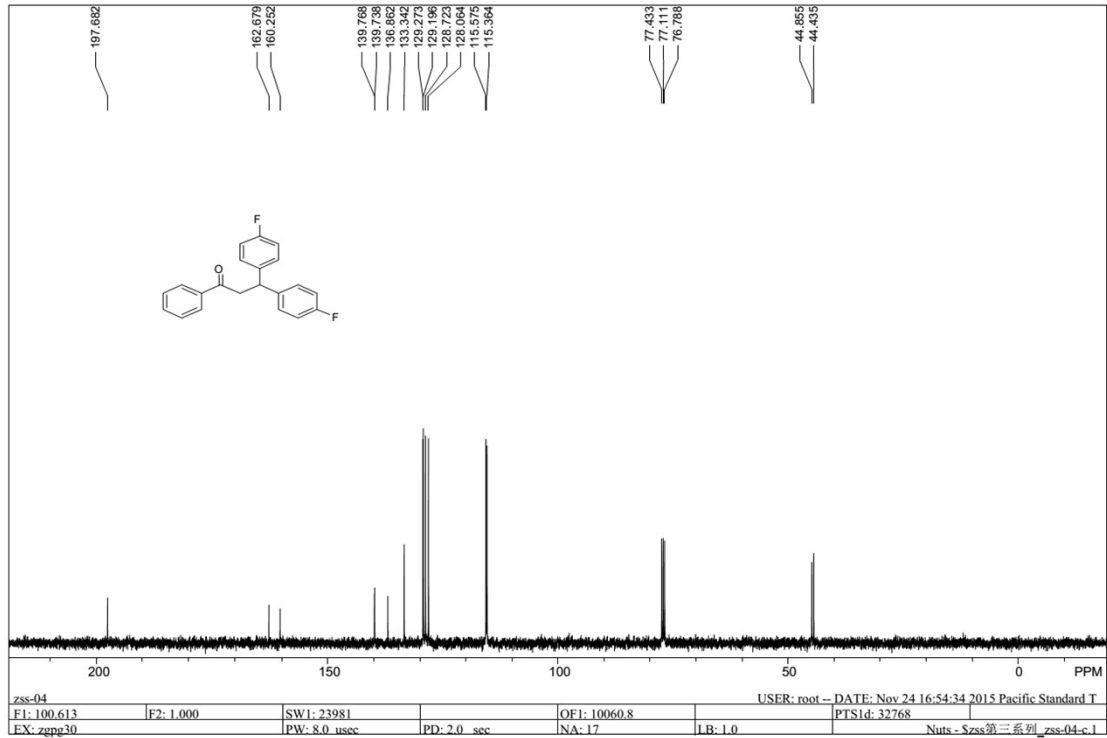
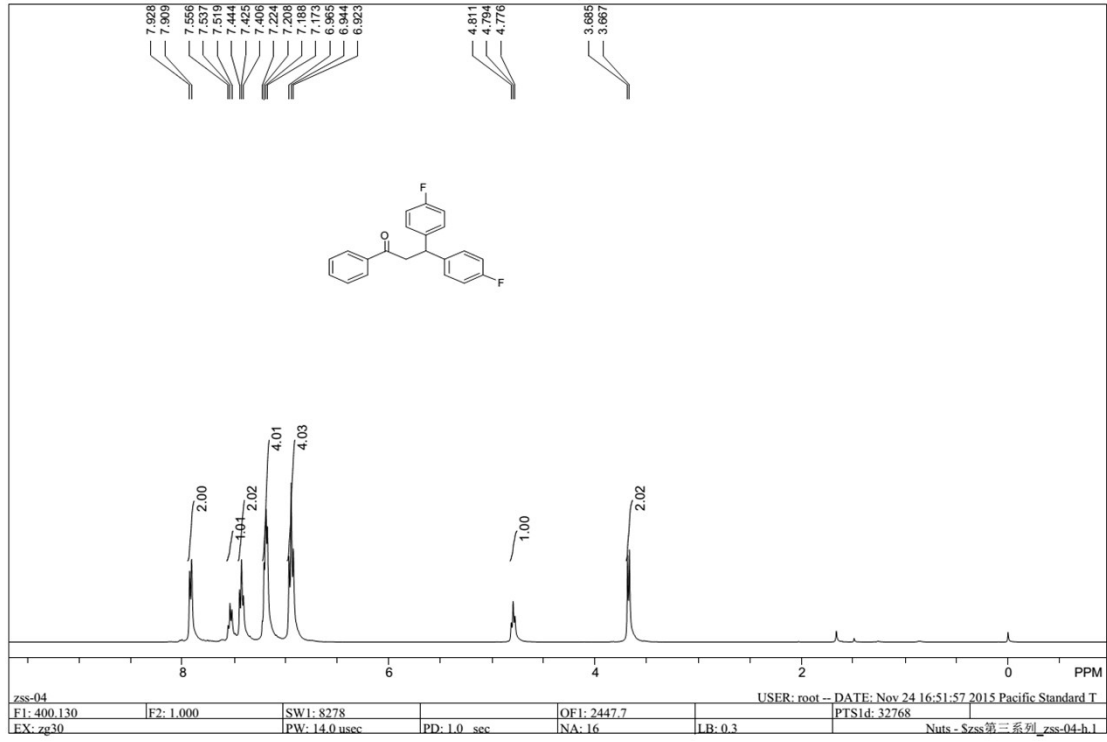
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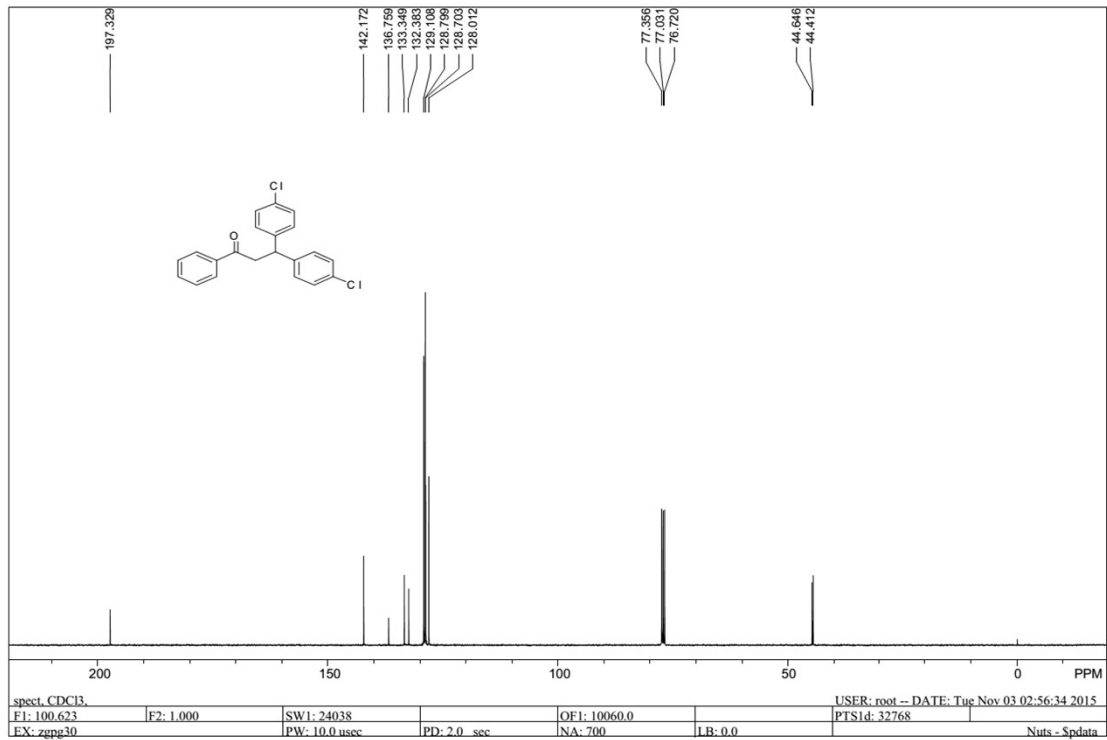
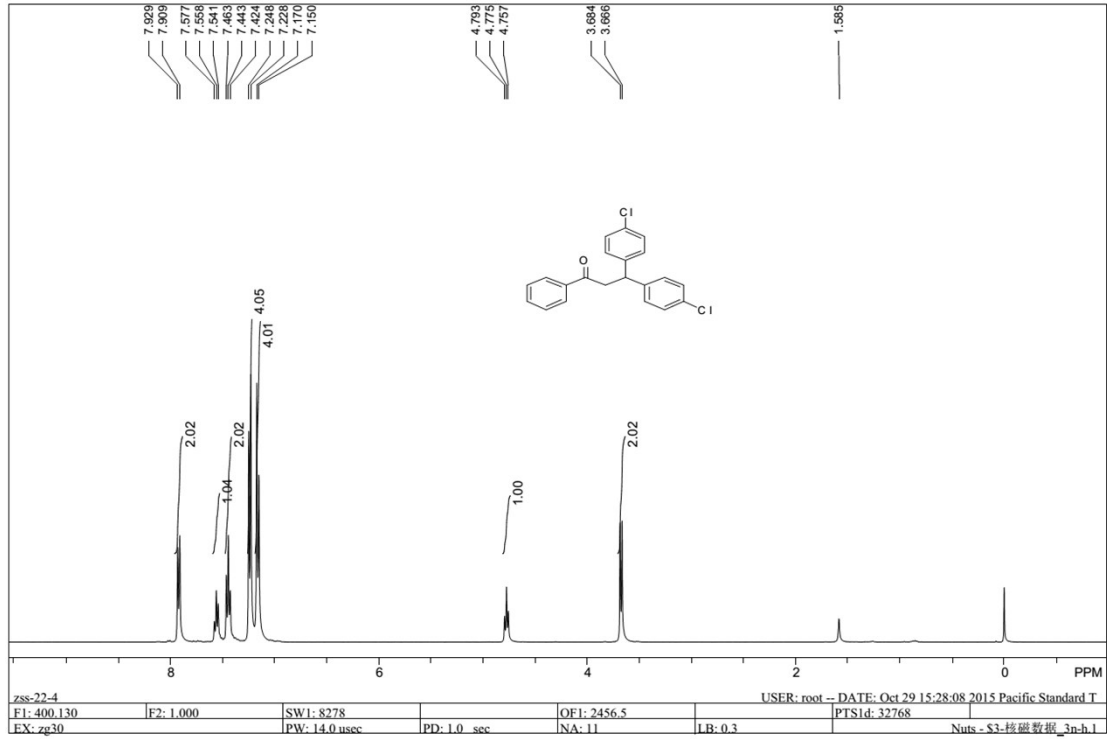
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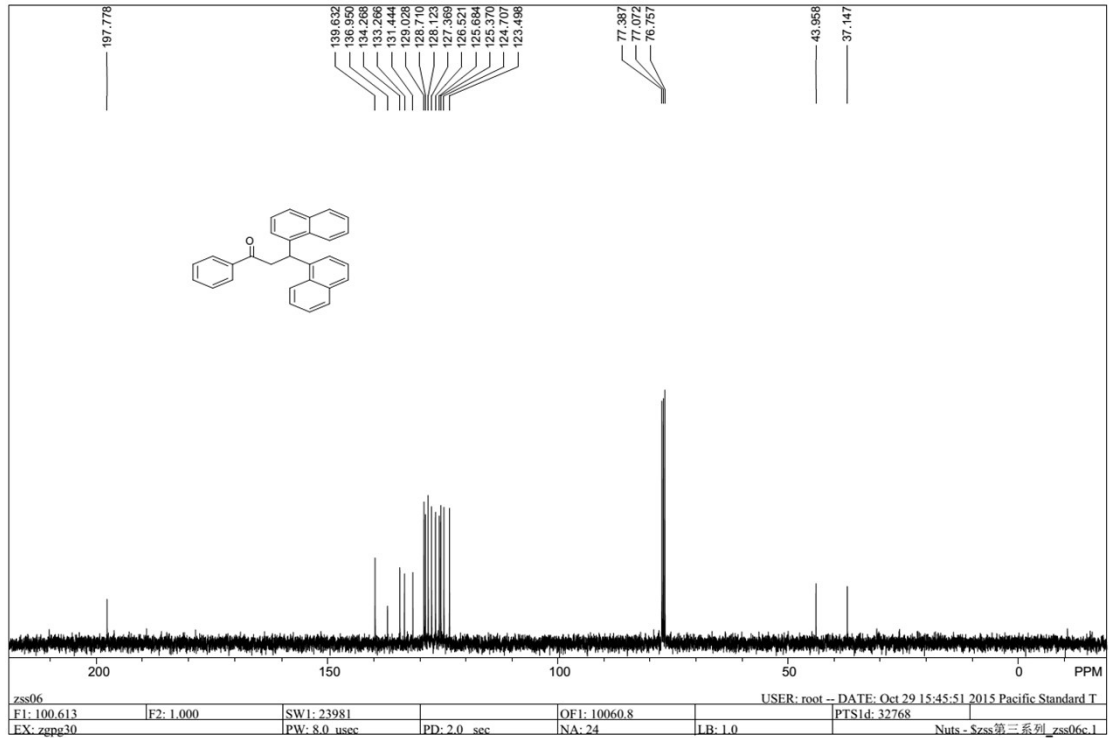
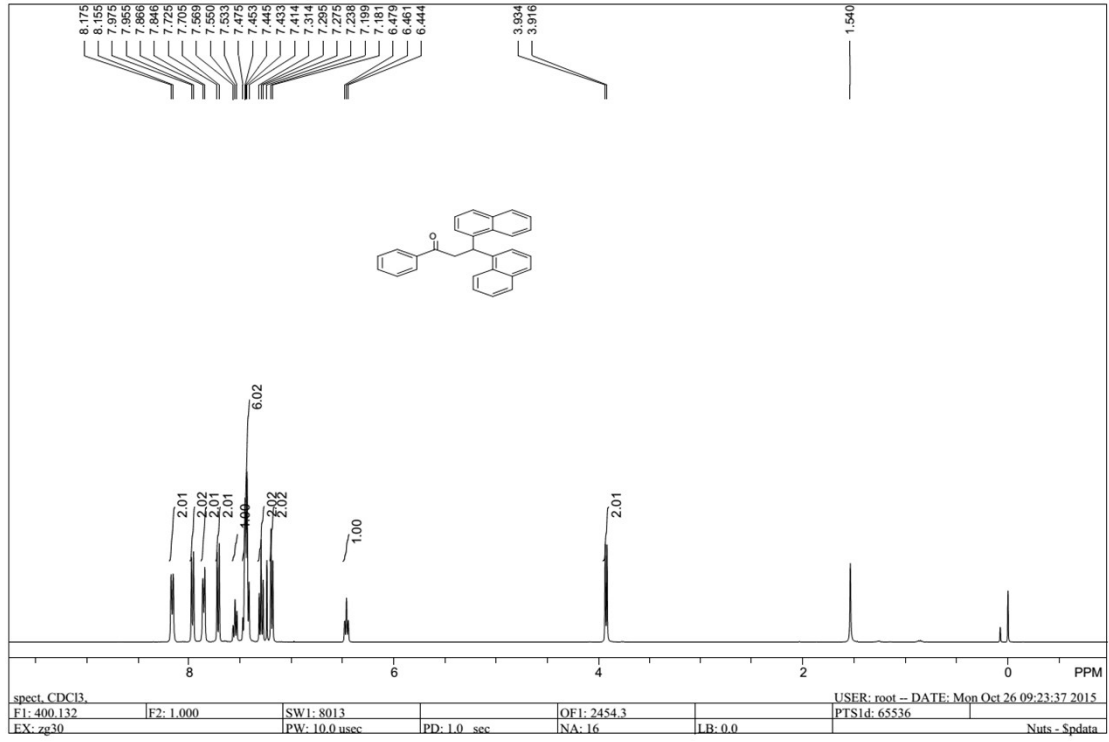
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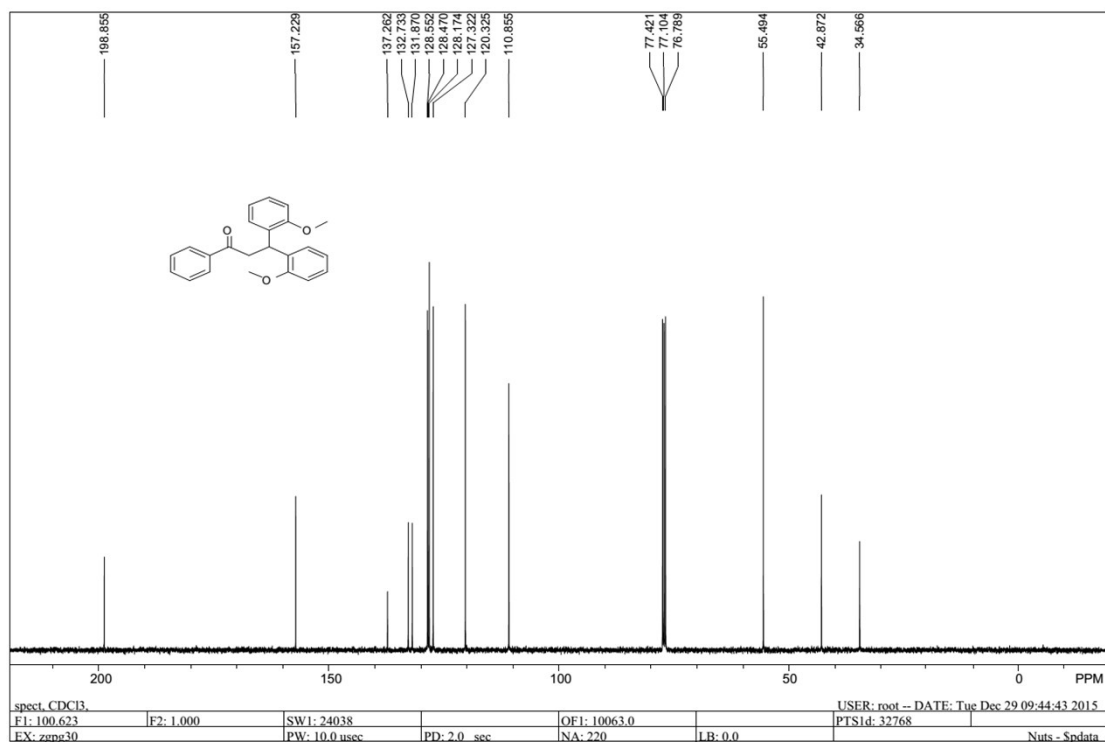
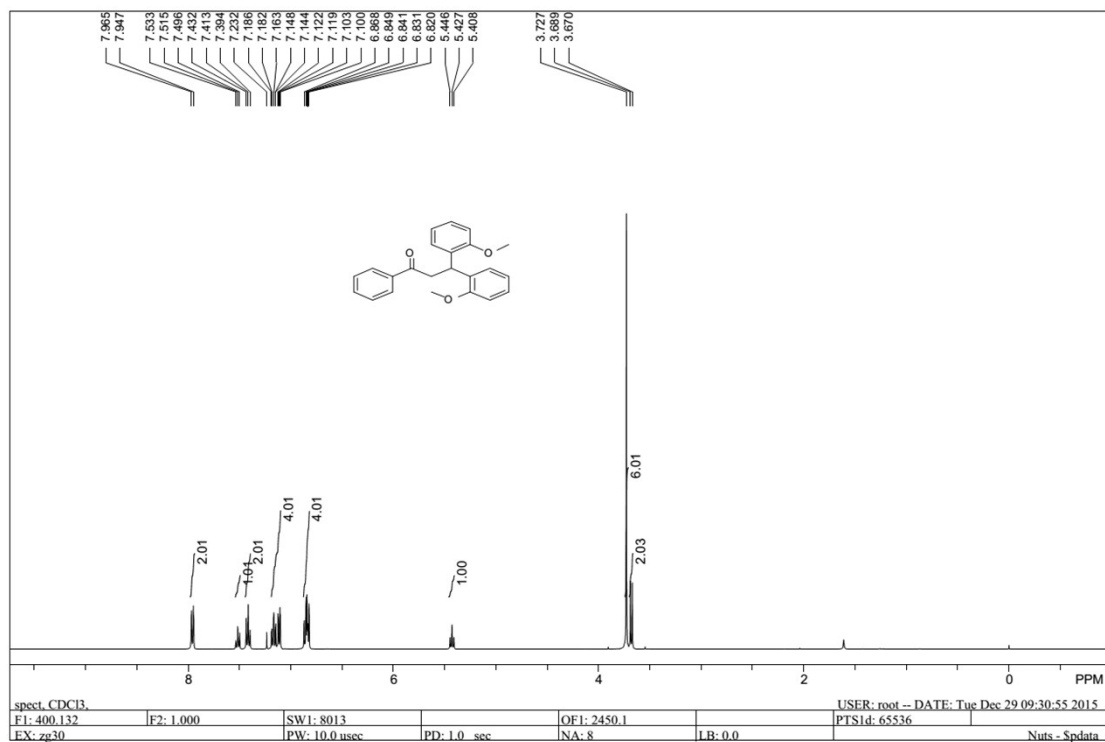
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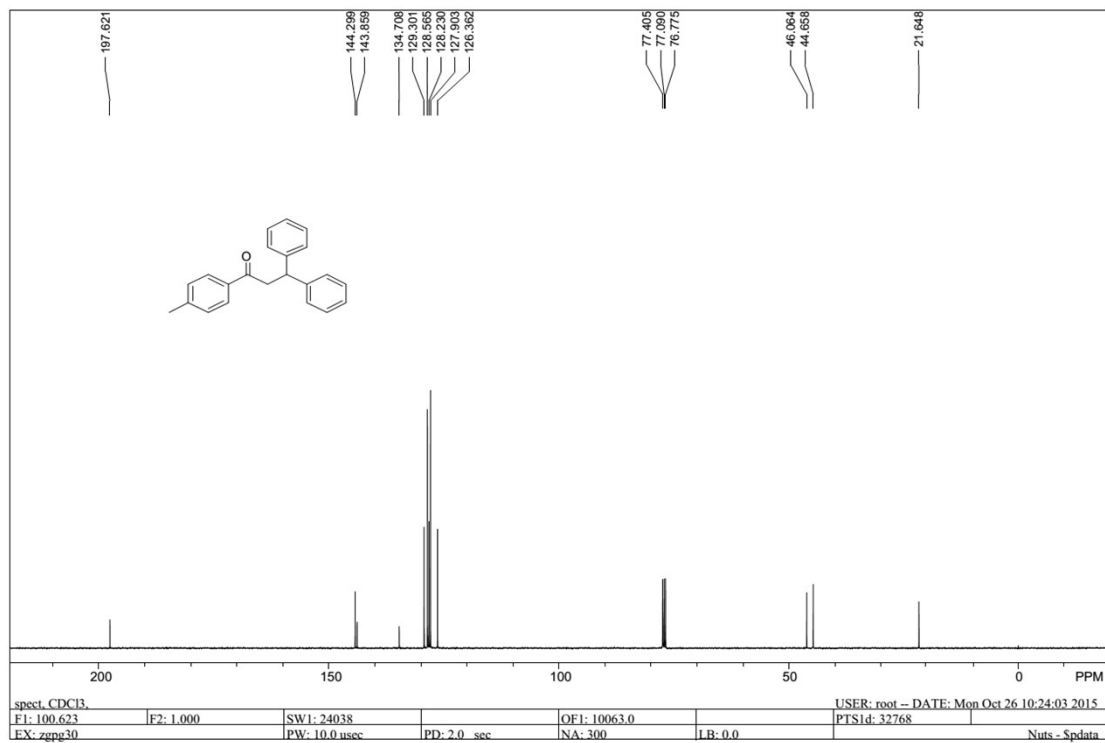
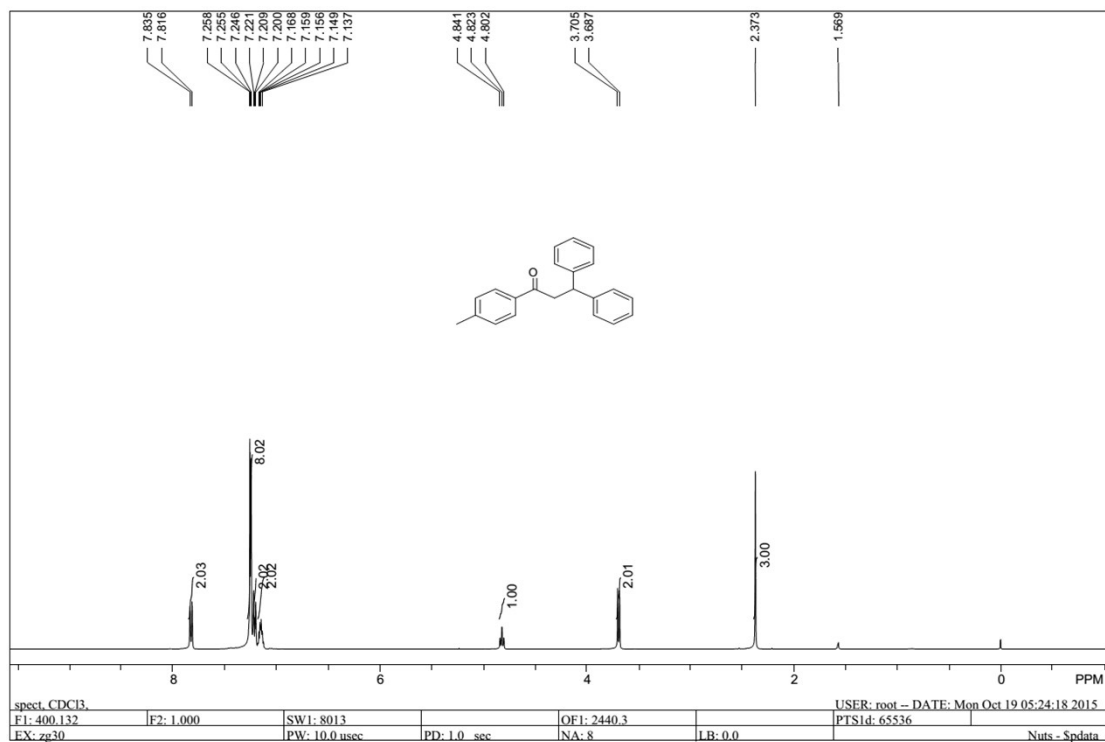
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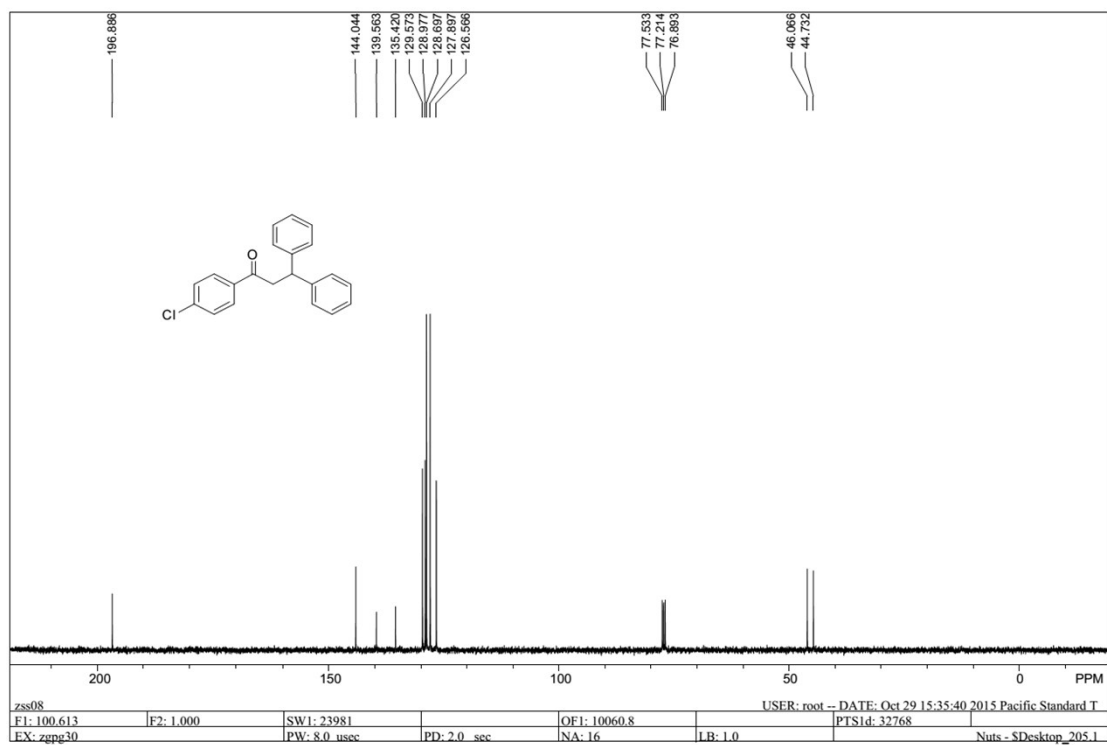
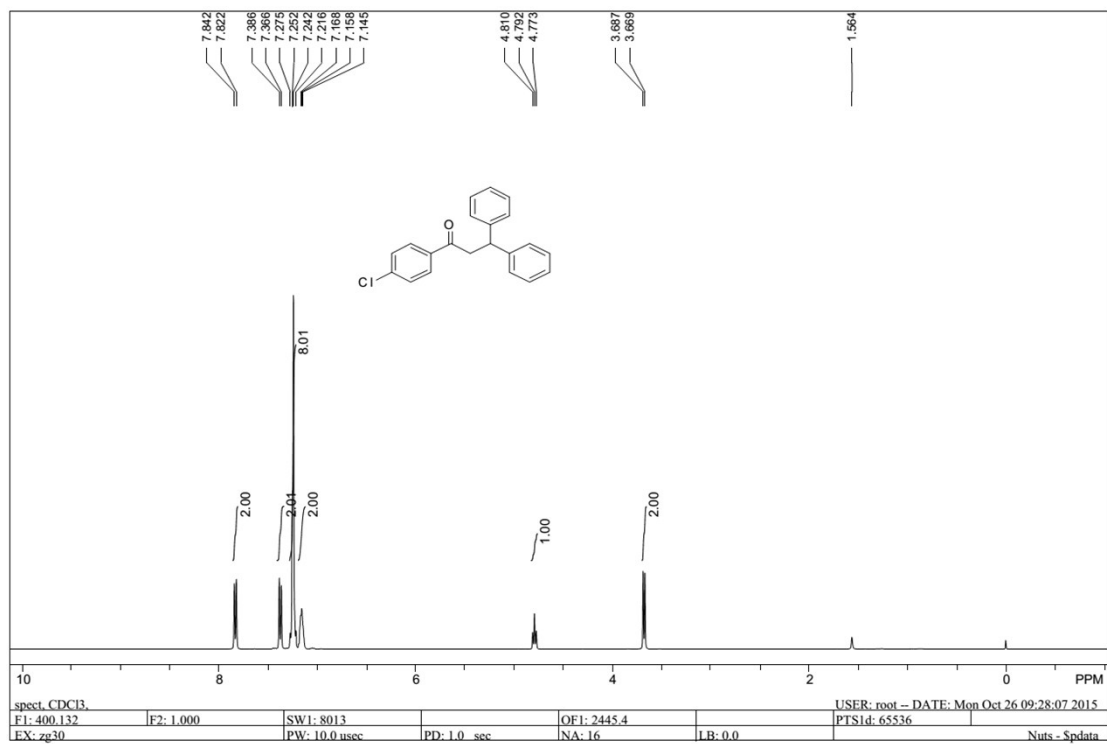
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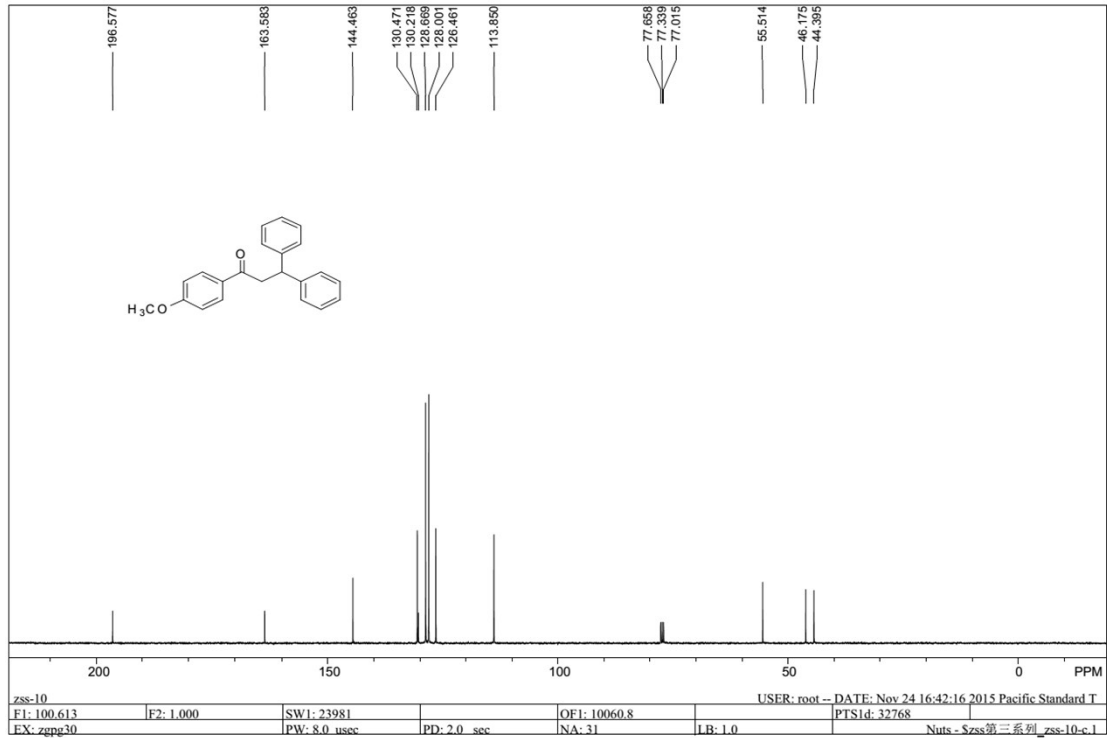
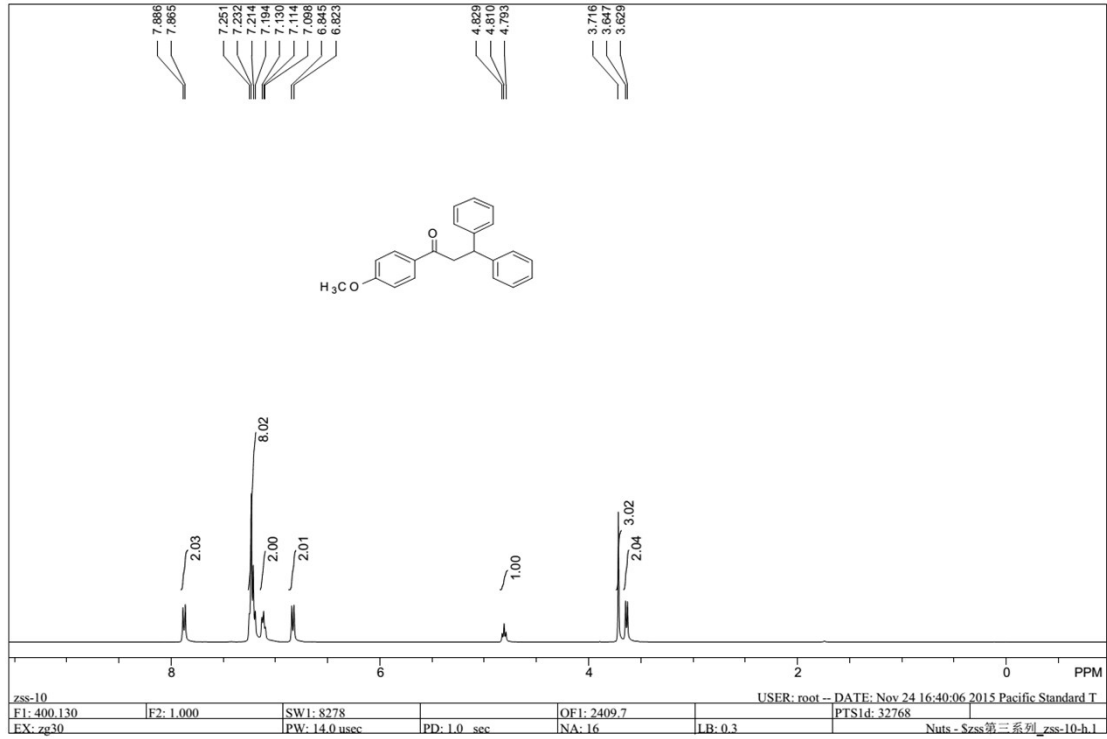
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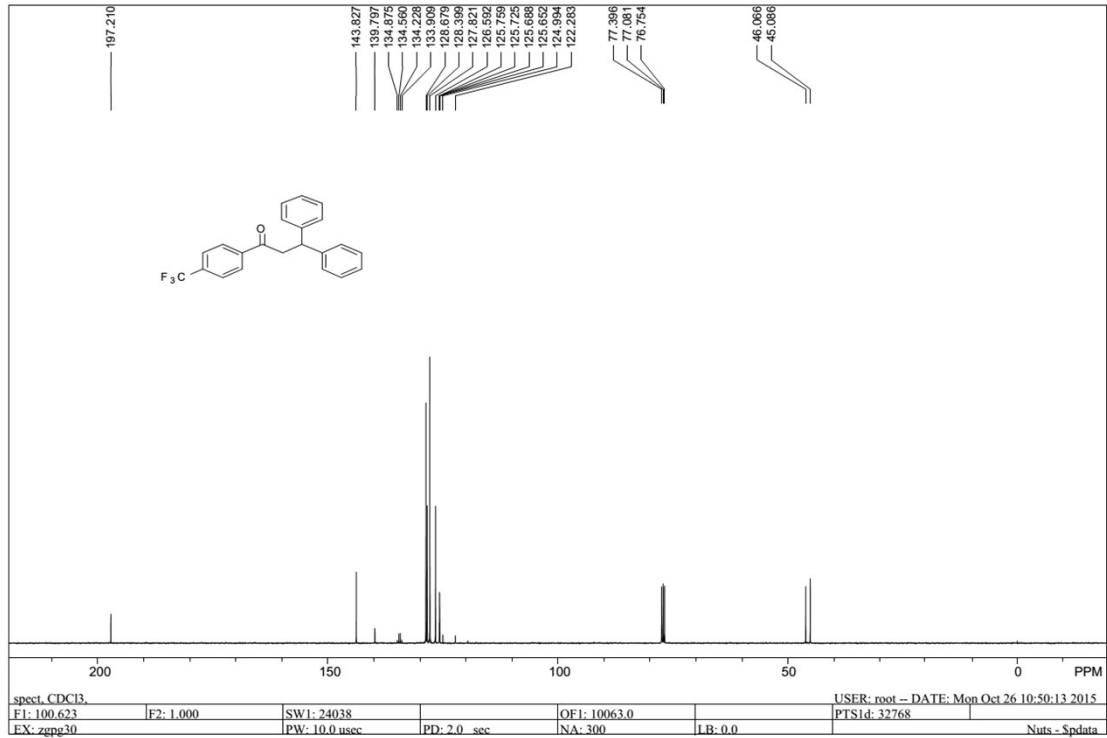
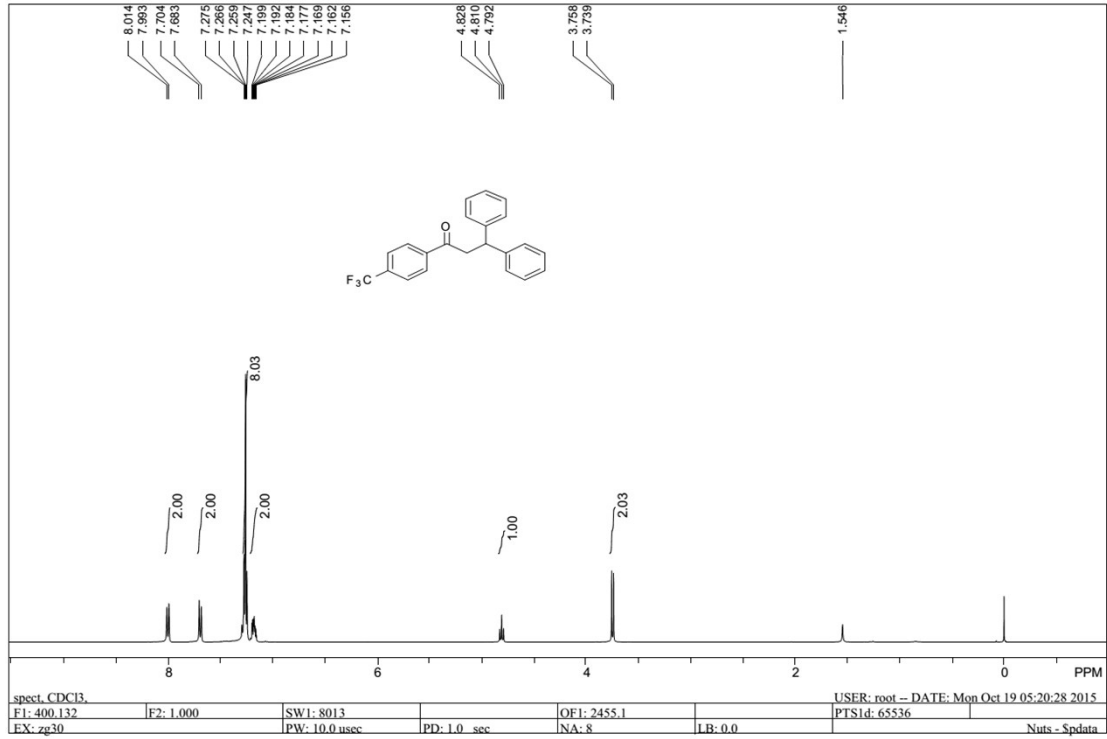
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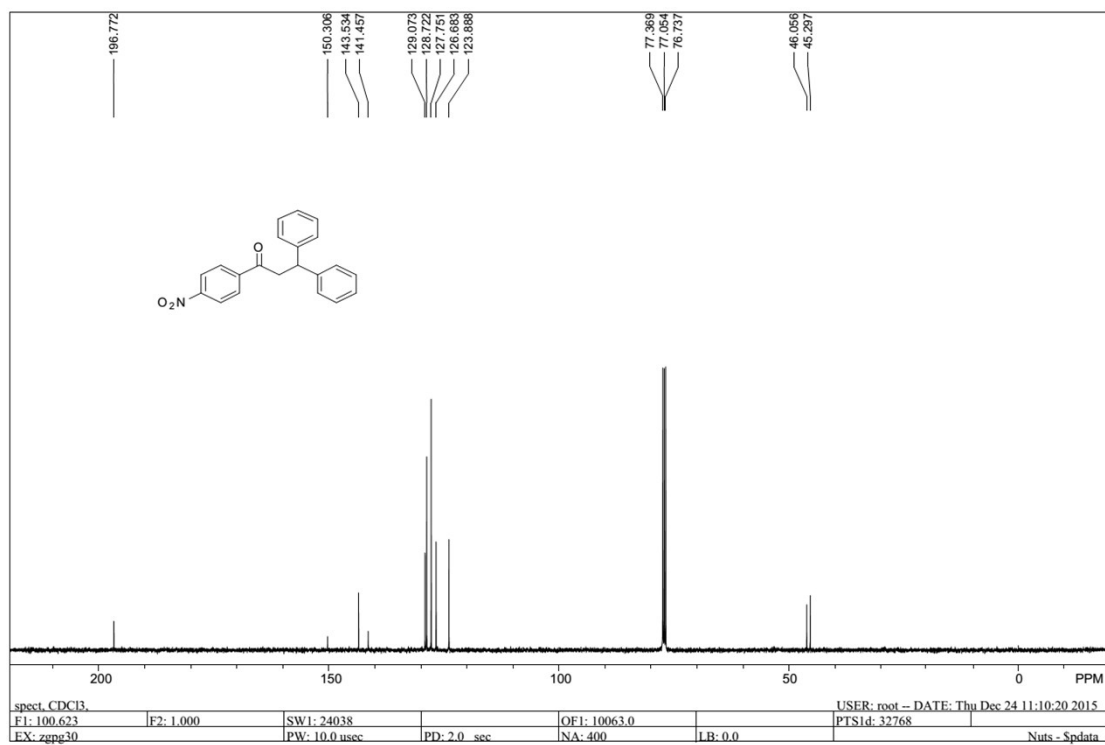
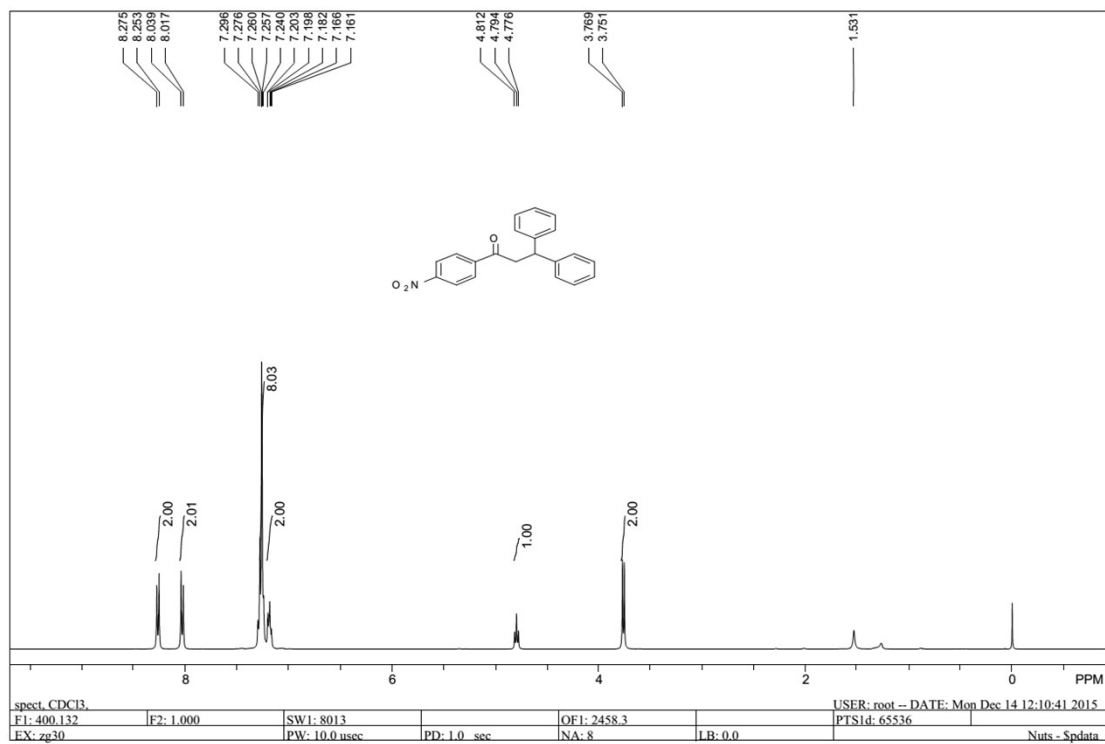
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3k

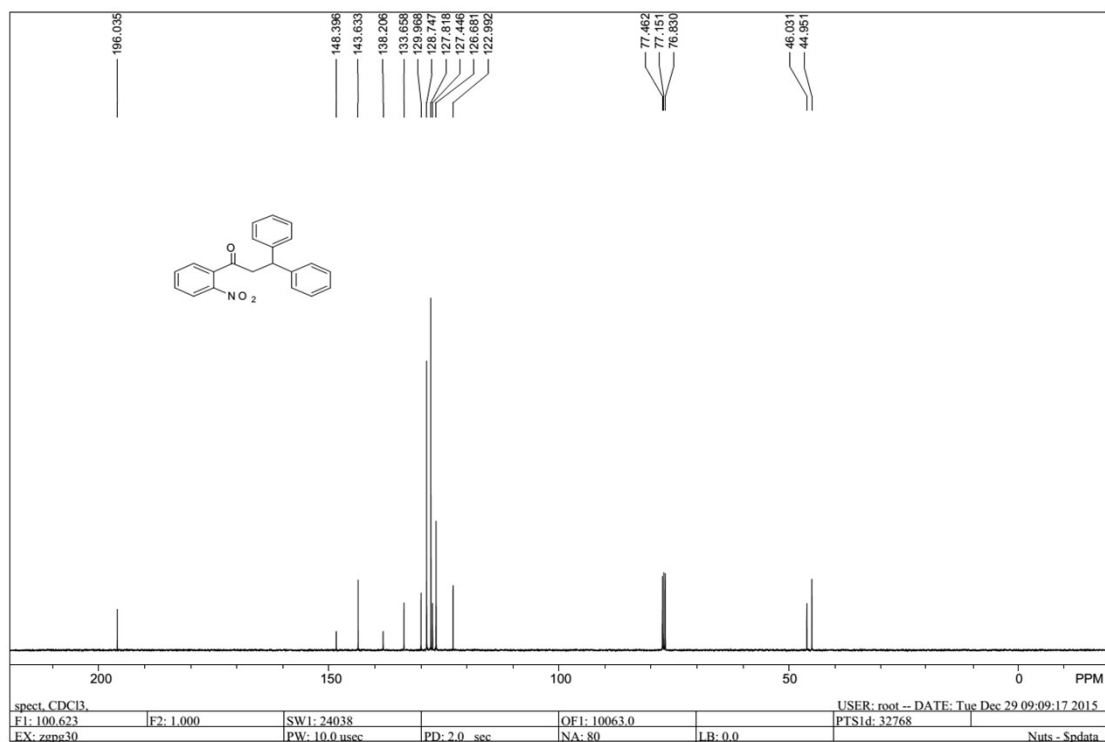
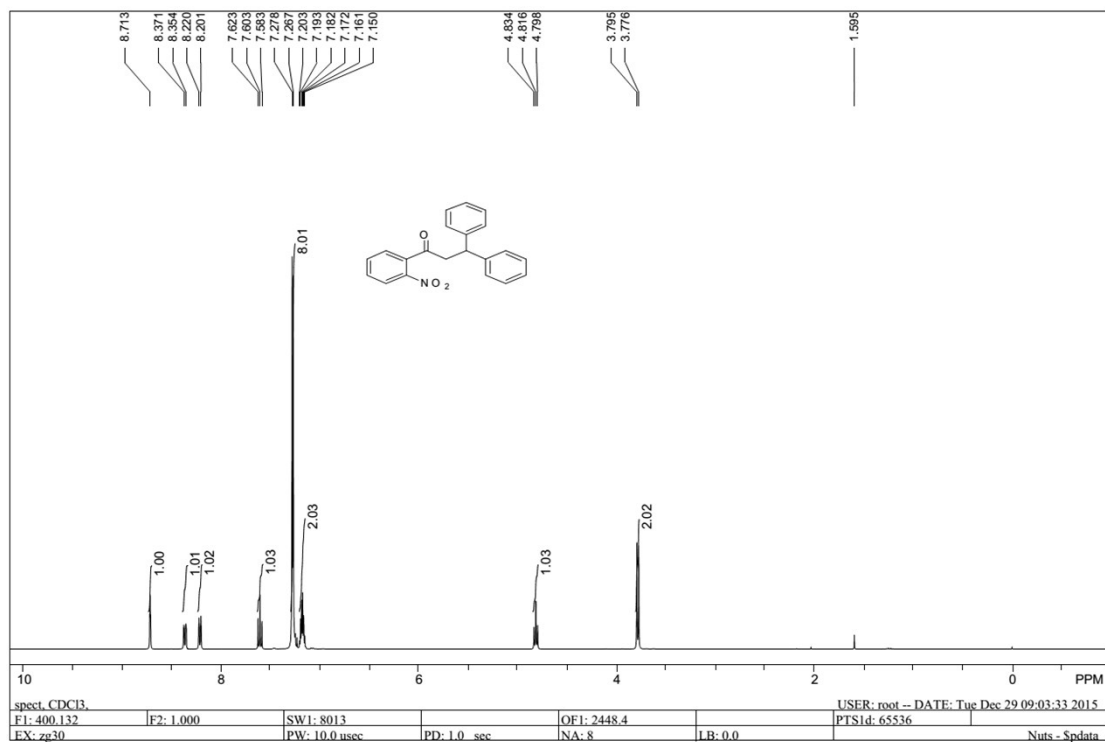


31

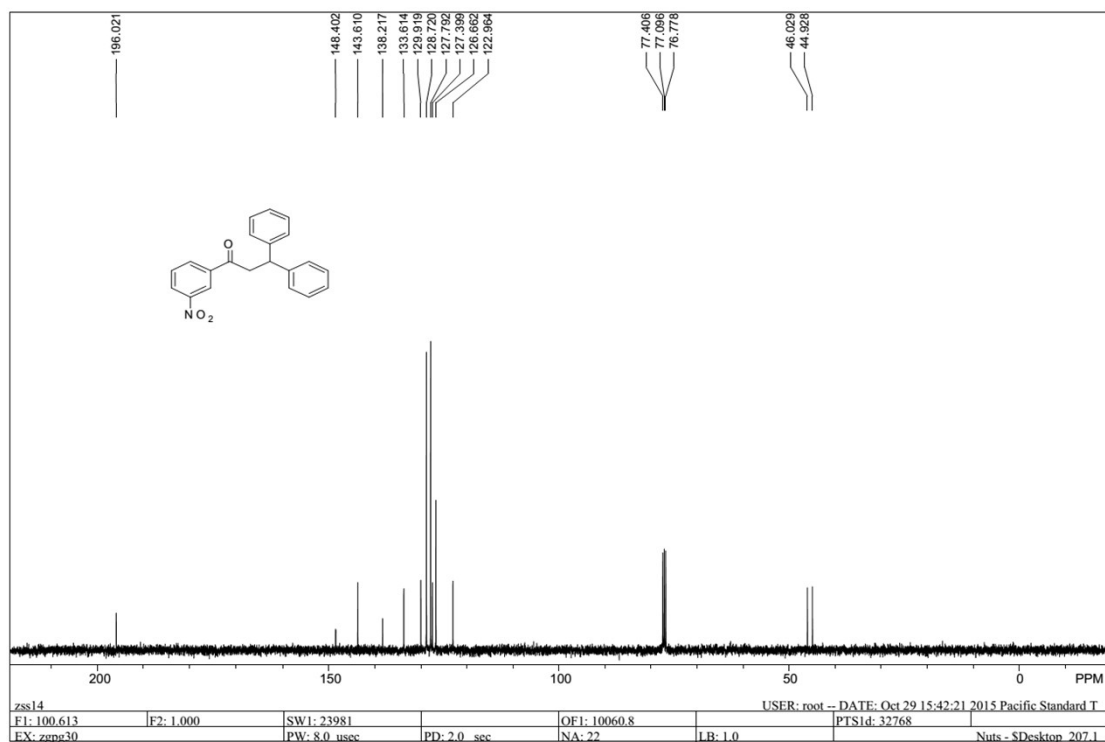
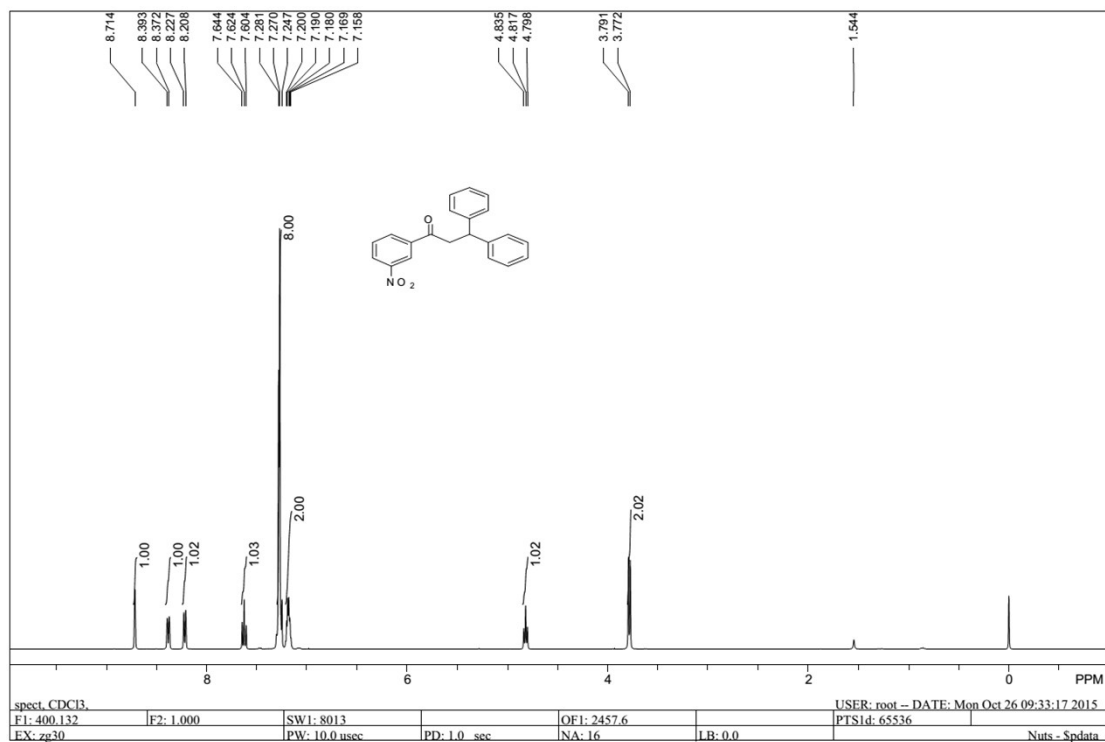


S21

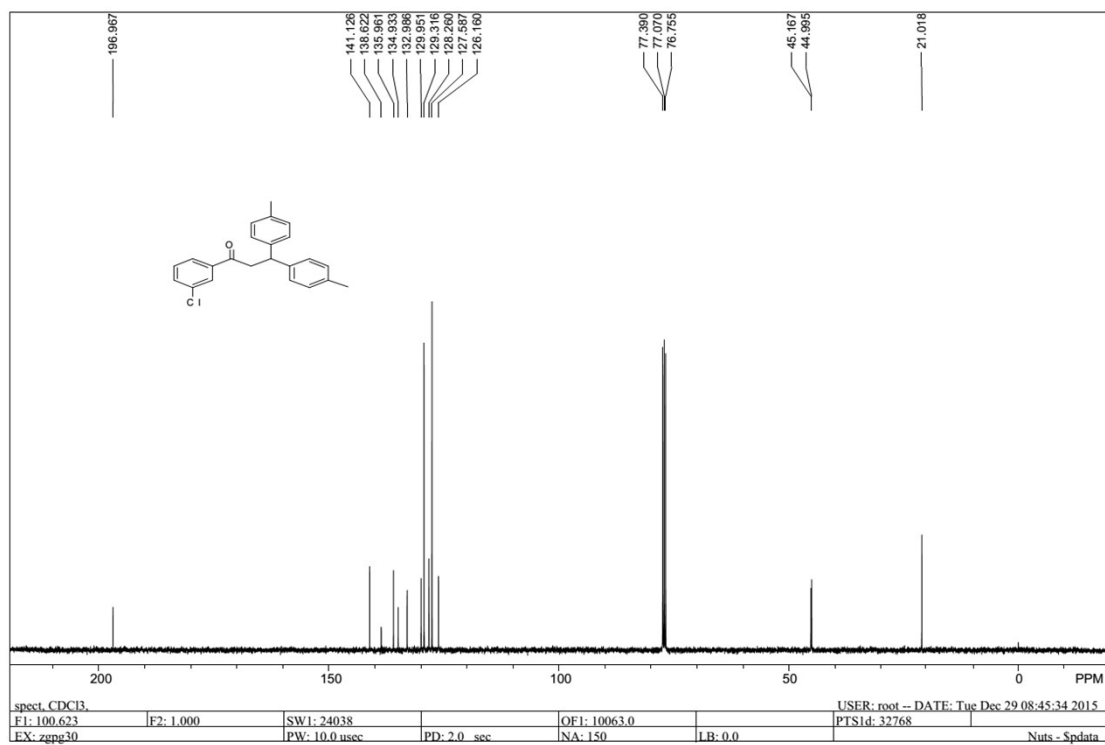
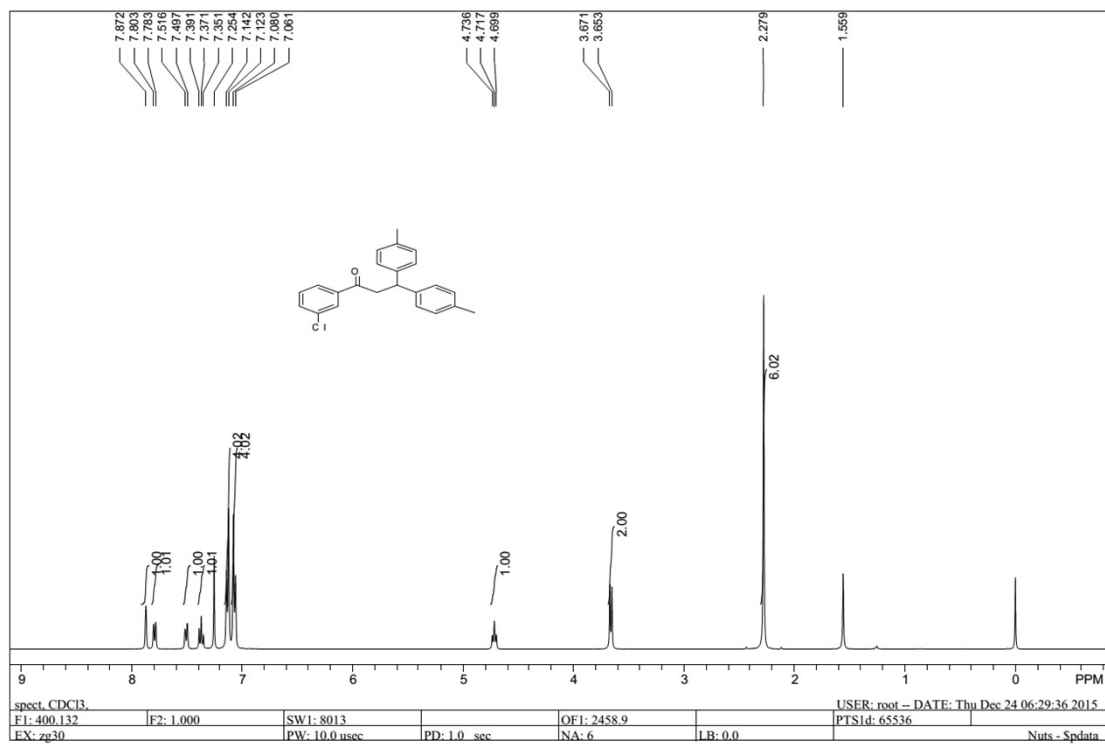
3m



3n

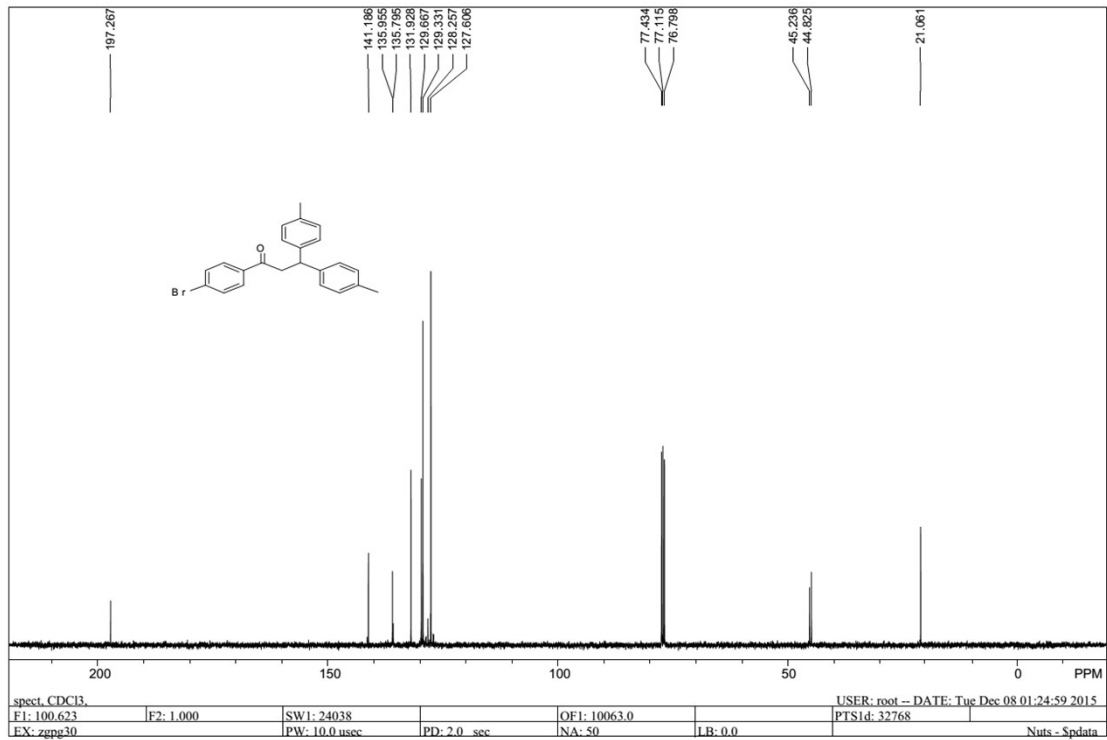
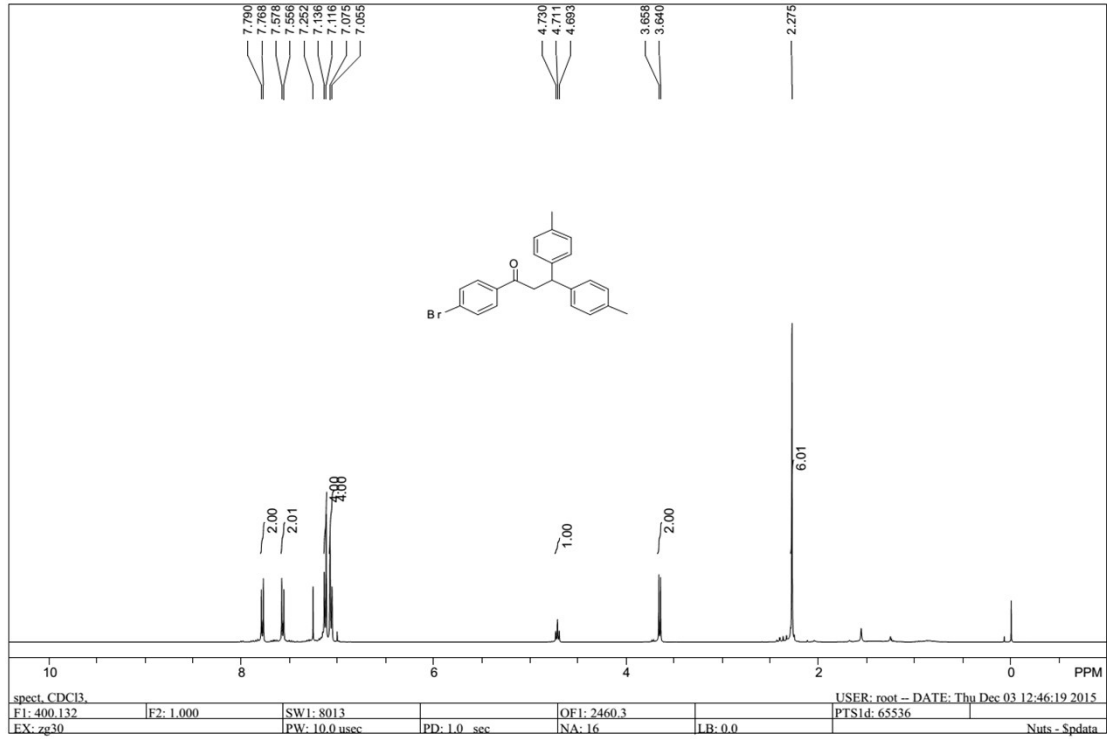


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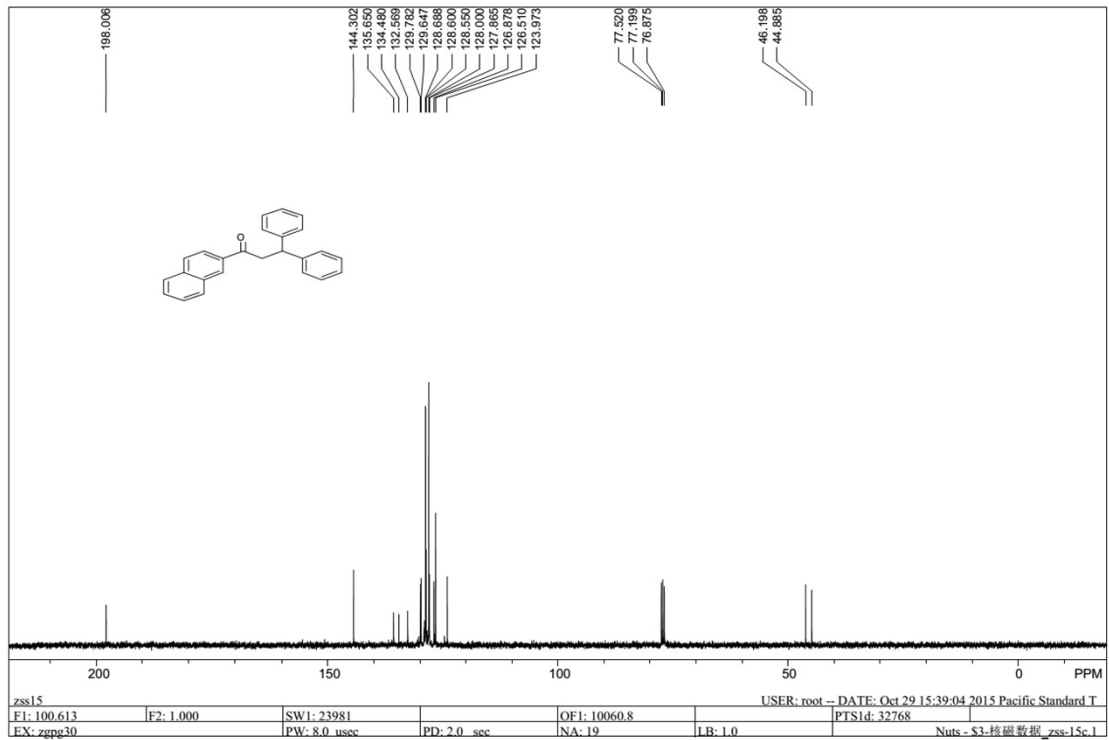
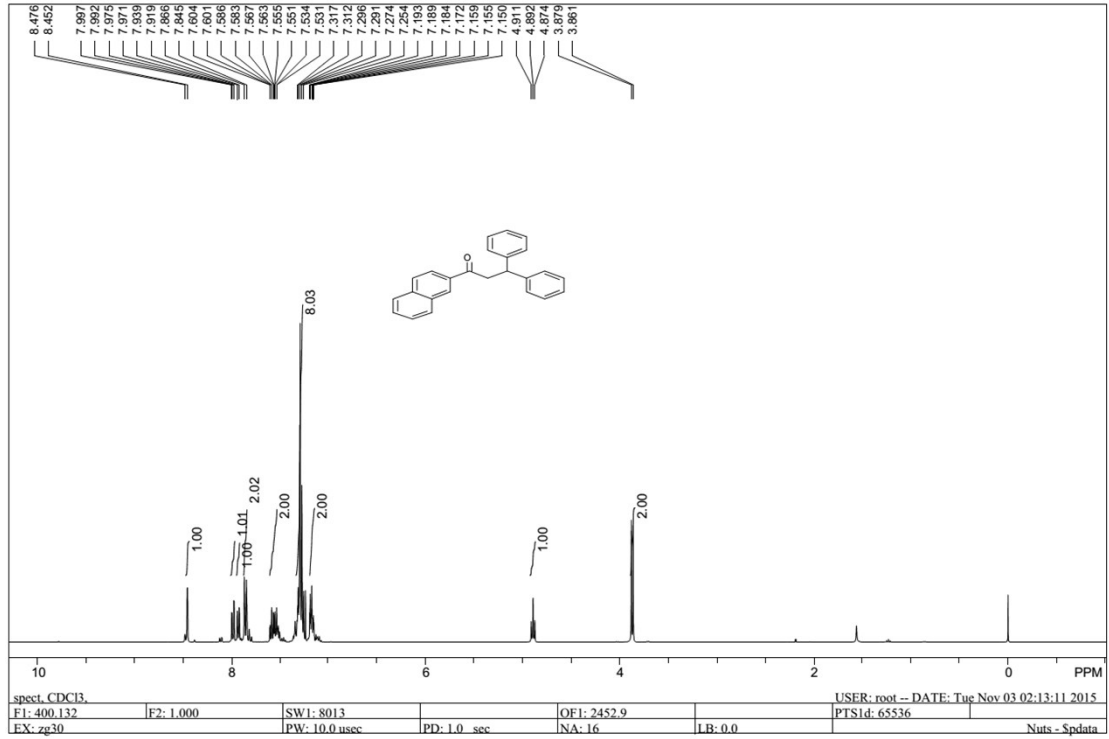


S24

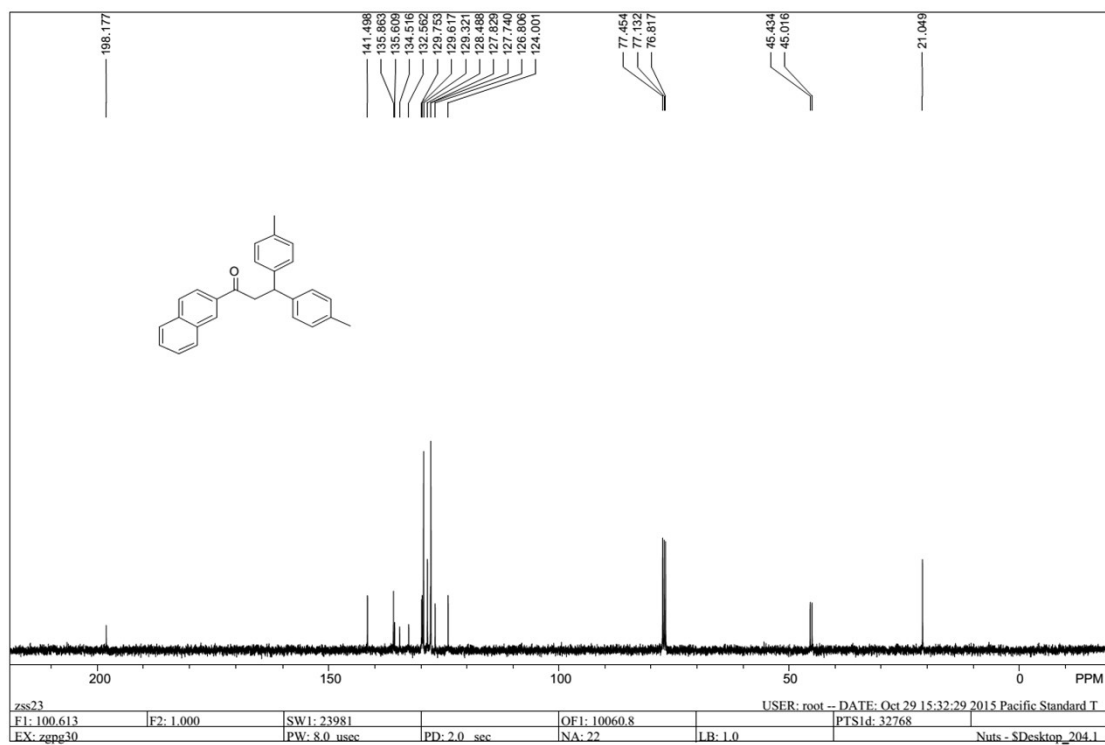
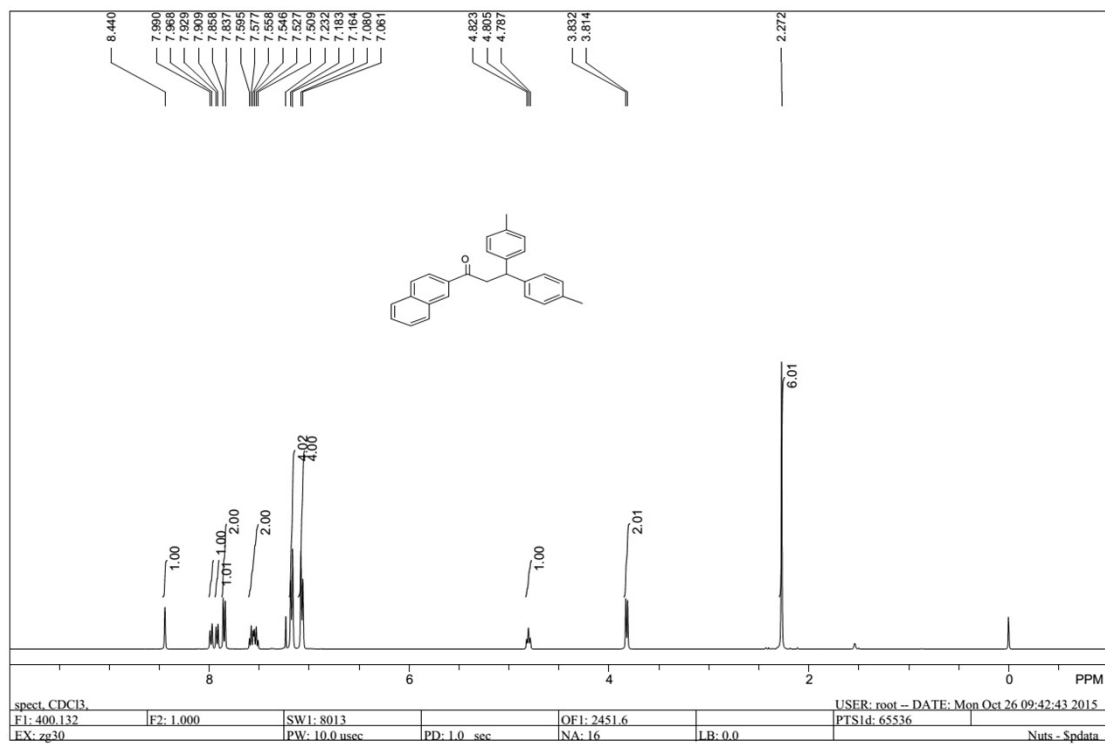
3p



3q



3r



X-Ray crystal structure of 3a

