Copper-Catalyzed Tandem Aryl-Halogen Hydroxylation and CH_2Cl_2-Based *N,O*-acetalization Toward the Synthesis of 2,3-Dihydrobenzoxazinones

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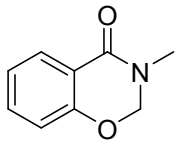
Contents

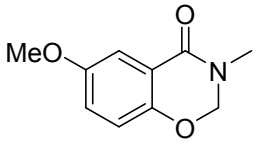
General experimental information

All *o*-haloamides were prepared via *N*-alkylation or *N*-arylation reactions following literature procedure,[1] all other chemicals were obtained from commercial sources and used as obtained. Solvents used in the experiment have been treated following standard procedure before use. The ^{1}H and ^{13}C NMR were recorded in 400 MHz apparatus in $CDCl_3$. The frequencies for measuring ^{1}H and ^{13}C NMR were 400 MHz and 100 MHz, respectively. Chemical shifts were recorded in ppm using TMS (for ^{1}H NMR) or the solvent peak of $CDCl_3$ (77.0 ppm, for ^{13}C NMR) as internal standard. HRMS data were obtained under ESI model in apparatus equipped with TOF analyzer. Melting points were recorded in X-4A apparatus without correcting temperature.

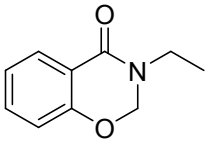
Characterization data of all products



3-Methyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (**3a**)**.** Yield 57% (28 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1 H), 7.43 (t, J = 7.8 Hz, 1 H), 7.11 (t, J = 8.0 Hz, 1 H), 6.96 (d, J = 8.4 Hz, 1 H), 5.17 (s, 2 H), 3.11 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.5, 157.8, 133.9, 128.3, 122.6, 118.8, 116.3, 79.5, 31.4; ESI-HRMS Calcd for $C_9H_{10}NO_2$ $[M + H]^+$ 164.0706, found 164.0703.

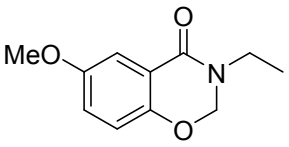


6-Methoxy-3-methyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (**3b**)**.** Yield 52% (30 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, J = 3.2 Hz, 1 H), 7.02-6.99 (m, 1 H), 6.88 (d, J = 8.8 Hz, 1 H), 5.12 (s, 2 H), 3.82 (s, 3 H), 3.11 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.5, 155.1, 151.9, 121.8, 119.1, 117.4, 110.2, 79.5, 55.9, 31.4; ESI-HRMS Calcd for $C_{10}H_{12}NO_3$ $[M + H]^+$ 194.0812, found 194.0801.

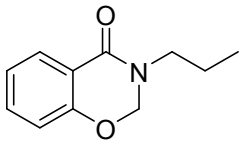


3-Ethyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (**3c**)**.** Yield 64% (34 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 7.6 Hz, 1 H), 7.43 (t, J = 7.8 Hz, 1 H), 7.11 (t, J = 7.6 Hz, 1 H), 6.96 (d, J = 8.0 Hz, 1 H), 5.19 (s, 2 H), 3.63-3.57 (m, 2 H), 1.24 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.9, 157.8,

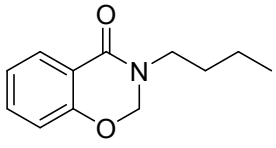
133.8, 128.3, 122.6, 119.2, 116.2, 77.8, 39.3, 13.5; ESI-HRMS Calcd for $C_{10}H_{12}NO_2$ $[M + H]^+$ 178.0863, found 178.0863.



3-Ethyl-6-methoxy-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (3d). Yield 56% (35 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, J = 3.2 Hz, 1 H), 7.01 (dd, J_1 = 9.0 Hz, J_2 = 3.0 Hz, 1 H), 6.89 (d, J = 8.8 Hz, 1 H), 5.15 (s, 2 H), 3.82 (s, 3 H), 3.63-3.57 (m, 2 H), 1.24 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.9, 155.0, 151.9, 121.8, 119.4, 117.3, 110.2, 77.9, 55.9, 39.4, 13.5; ESI-HRMS Calcd for $C_{11}H_{14}NO_3$ $[M + H]^+$ 208.0968, found 208.0960.

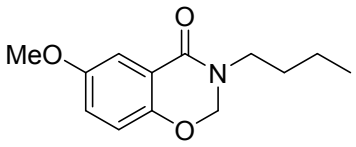


3-Propyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (3e). Yield 70% (40 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1 H), 7.43 (t, J = 7.6 Hz, 1 H), 7.11 (t, J = 7.6 Hz, 1 H), 6.96 (d, J = 8.4 Hz, 1 H), 5.18 (s, 2 H), 3.51 (t, J = 7.2 Hz, 2 H), 1.71-1.62 (m, 2 H), 0.97 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.1, 157.8, 133.8, 128.4, 122.6, 119.2, 116.2, 78.3, 46.3, 21.6, 11.4; ESI-HRMS Calcd for $C_{11}H_{14}NO_2$ $[M + H]^+$ 192.1019, found 192.1022.

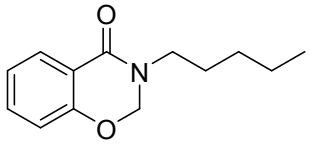


3-Butyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (3f). Yield 72% (44 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1 H),

7.35 (td, J_1 = 7.8 Hz, J_2 = 1.6 Hz, 1 H), 7.03 (td, J_1 = 7.6 Hz, J_2 = 0.8 Hz, 1 H), 6.88 (d, J = 8.0 Hz, 1 H), 5.09 (s, 2 H), 3.46 (t, J = 7.2 Hz, 2 H), 1.57-1.49 (m, 2 H), 1.36-1.26 (m, 2 H), 0.87 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.1, 157.8, 133.8, 128.4, 122.6, 119.2, 116.2, 78.2, 44.4, 30.4, 20.1, 13.8; ESI-HRMS Calcd for $C_{12}H_{16}NO_2$ $[M + H]^+$ 206.1176, found 206.1172.

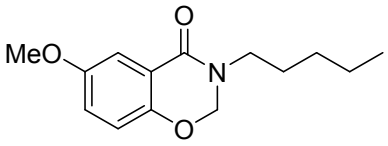


3-Butyl-6-methoxy-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (3g). Yield 65% (46 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, J = 3.2 Hz, 1 H), 7.01 (dd, J_1 = 8.8 Hz, J_2 = 3.2 Hz, 1 H), 6.88 (d, J = 9.2 Hz, 1 H), 5.13 (s, 2 H), 3.81 (s, 3 H), 3.54 (t, J = 7.2 Hz, 2 H), 1.65-1.57 (m, 2 H), 1.44-1.34 (m, 2 H), 0.95 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.0, 155.0, 151.9, 121.8, 119.4, 117.3, 110.3, 78.3, 55.9, 44.5, 30.5, 20.1, 13.8; ESI-HRMS Calcd for $C_{13}H_{18}NO_3$ $[M + H]^+$ 236.1281, found 236.1285.

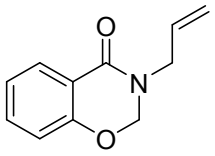


3-Pentyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (3h). Yield 81% (53 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1 H), 7.43 (td, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1 H), 7.11 (t, J = 7.2 Hz, 1 H), 6.96 (d, J = 7.6 Hz, 1 H), 5.18 (s, 2 H), 3.53 (t, J = 7.4 Hz, 2 H), 1.67-1.59 (m, 2 H), 1.39-1.33 (m, 4 H), 0.90 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.0, 157.8, 133.8, 128.4, 122.6, 119.2, 116.2, 78.3, 44.7, 29.1, 28.1, 22.4, 14.0; ESI-HRMS Calcd for

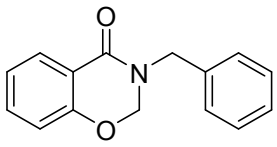
$C_{13}H_{18}NO_2$ $[M + H]^+$ 220.1332, found 220.1335.



6-Methoxy-3-pentyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (**3i**)**.** Yield 88% (66 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, J = 3.2 Hz, 1 H), 7.01 (dd, J_1 = 9.0 Hz, J_2 = 2.6 Hz, 1 H), 6.89 (d, J = 8.8 Hz, 1 H), 5.13 (s, 2 H), 3.82 (s, 3 H), 3.53 (t, J = 7.2 Hz, 2 H), 1.66-1.59 (m, 2 H), 1.39-1.34 (m, 4 H), 0.91 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.0, 155.0, 151.9, 121.8, 119.4, 117.3, 110.3, 78.3, 55.9, 44.8, 29.0, 28.0, 22.4, 14.0; ESI-HRMS Calcd for $C_{14}H_{20}NO_3$ $[M + H]^+$ 250.1438, found 250.1446.

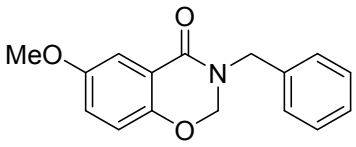


3-Allyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (**3j**)**.** Yield 63% (36 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 7.6 Hz, 1 H), 7.44 (td, J_1 = 7.7 Hz, J_2 = 0.8 Hz, 1 H), 7.12 (td, J_1 = 7.6 Hz, J_2 = 0.8 Hz, 1 H), 6.97 (d, J = 8.4 Hz, 1 H), 5.90-5.81 (m, 1 H), 5.33-5.24 (m, 2 H), 5.15 (s, 2 H), 4.19 (d, J = 6.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.9, 157.9, 134.0, 132.3, 128.5, 122.7, 118.9, 118.1, 116.3, 77.5, 46.4; ESI-HRMS Calcd for $C_{11}H_{12}NO_2$ $[M + H]^+$ 190.0863, found 190.0864.

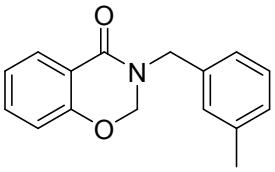


3-Benzyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (**3k**)**.** Yield 61% (44 mg);

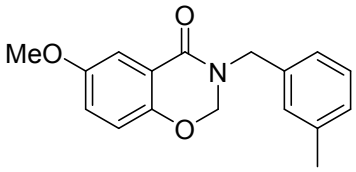
yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1 H), 7.43 (td, J_1 = 7.7 Hz, J_2 = 1.5 Hz, 1 H), 7.33-7.25 (m, 6 H), 7.11 (t, J = 7.6 Hz, 1 H), 6.94 (d, J = 8.4 Hz, 1 H), 5.10 (s, 2 H), 4.75 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.2, 157.8, 136.3, 134.1, 128.9, 128.6, 127.9, 122.7, 118.9, 116.4, 77.6, 47.6; ESI-HRMS Calcd for $C_{15}H_{14}NO_2$ $[M + H]^+$ 240.1019, found 240.1013.



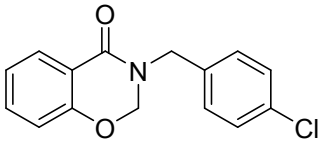
3-Benzyl-6-methoxy-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (3l). Yield 86% (69 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 3.2 Hz, 1 H), 7.37-7.30 (m, 5 H), 7.02 (dd, J_1 = 8.8 Hz, J_2 = 3.2 Hz, 1 H), 6.88 (d, J = 8.8 Hz, 1 H), 5.08 (s, 2 H), 4.77 (s, 2 H), 3.83 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.3, 155.1, 152.0, 136.3, 128.9, 127.8, 122.2, 119.1, 117.5, 110.4, 77.7, 55.9, 47.7; ESI-HRMS Calcd for $C_{16}H_{16}NO_3$ $[M + H]^+$ 270.1125, found 270.1134.



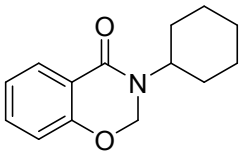
3-(3-Methylbenzyl)-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (3m). Yield 65% (49 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1 H), 7.43 (td, J_1 = 7.8 Hz, J_2 = 0.8 Hz, 1 H), 7.23 (t, J = 7.4 Hz, 1 H), 7.14-7.09 (m, 4 H), 6.94 (d, J = 8.0 Hz, 1 H), 5.11 (s, 2 H), 4.73 (s, 2 H), 2.33 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.2, 157.8, 138.7, 136.2, 134.1, 128.8, 128.61, 128.59, 125.0, 122.7, 118.9, 116.4, 77.6, 47.5, 21.4; ESI-HRMS Calcd for $C_{16}H_{16}NO_2$ $[M + H]^+$ 254.1176, found 254.1170.



6-Methoxy-3-(3-methylbenzyl)-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (3n). Yield 62% (53 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 3.2 Hz, 1 H), 7.23 (t, J = 7.4 Hz, 1 H), 7.14-7.09 (m, 3 H), 7.02 (dd, J_1 = 9.0 Hz, J_2 = 3.0 Hz, 1 H), 6.88 (d, J = 9.2 Hz, 1 H), 5.07 (s, 2 H), 4.73 (s, 2 H), 3.83 (s, 3 H), 2.34 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.2, 155.1, 152.0, 138.6, 136.2, 128.8, 128.6, 128.5, 124.9, 122.1, 119.2, 117.5, 110.4, 77.7, 55.9, 47.6, 21.4; ESI-HRMS Calcd for $C_{16}H_{16}NO_2$ $[M + H]^+$ 284.1281, found 284.1292.

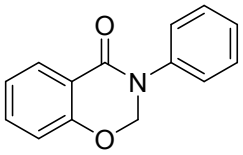


3-(4-Chlorobenzyl)-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (3o). Yield 60% (49 mg); yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1 H), 7.47 (td, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1 H), 7.33-7.29 (m, 4 H), 7.14 (t, J = 7.6 Hz, 1 H), 6.96 (dd, J_1 = 8.0 Hz, J_2 = 0.4 Hz, 1 H), 5.11 (s, 2 H), 4.72 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.3, 157.8, 134.9, 134.2, 133.8, 129.2, 129.1, 128.6, 122.8, 118.7, 116.4, 77.6, 47.0; ESI-HRMS Calcd for $C_{15}H_{13}ClNO_2$ $[M + H]^+$ 274.0629, found 274.0638.

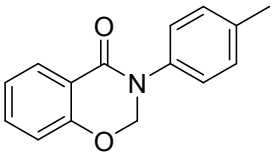


3-Cyclohexyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (3p). Yield 42% (29 mg); white solid; mp 65-67 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (dd, J_1 = 7.6 Hz, J_2 =

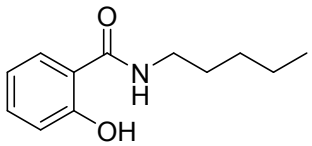
2.4 Hz, 1 H), 7.42 (td, J_1 = 7.8 Hz, J_2 = 1.6 Hz, 1 H), 7.11 (t, J = 7.6 Hz, 1 H), 6.95 (d, J = 8.4 Hz, 1 H), 5.16 (s, 2 H), 4.50-4.45 (m, 1 H), 1.86-1.83 (d, J = 10.8 Hz, 4 H), 1.72-1.68 (m, 2 H), 1.46-1.38 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.7, 157.7, 133.7, 128.7, 122.5, 119.5, 116.1, 74.1, 51.4, 30.7, 25.7, 25.4; ESI-HRMS Calcd for $C_{14}H_{18}NO_2$ $[M + H]^+$ 232.1332, found 232.1336.



3-Phenyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (**3q**)**.** Yield 30% (20 mg); white soild; mp 93-95 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1 H), 7.50 (td, J_1 = 7.9 Hz, J_2 = 1.5 Hz, 1 H), 7.44 (t, J = 7.8 Hz, 2 H), 7.36 (d, J = 7.6 Hz, 2 H), 7.30 (t, J = 7.4 Hz, 1 H), 7.17 (t, J = 7.4 Hz, 1 H), 7.05 (d, J = 8.0 Hz, 1 H), 5.56 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.6, 158.0, 139.3, 134.5, 129.3, 129.0, 127.0, 125.2, 122.9, 119.2, 116.5, 80.3; ESI-HRMS Calcd for $C_{14}H_{12}NO_2$ $[M + H]^+$ 226.0863, found 226.0856.



3-(*p*-Tolyl)-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (**3r**)**.** Yield 35% (25 mg); white soild; mp 121-123 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 8.0 Hz, 1 H), 7.49 (t, J = 8.6 Hz, 1 H), 7.23 (s, 4 H), 7.16 (t, J = 7.4 Hz, 1 H), 7.03 (d, J = 8.0 Hz, 1 H), 5.52 (s, 2 H), 2.37 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.7, 158.0, 136.9, 136.7, 134.4, 129.9, 129.0, 125.2, 122.9, 119.2, 116.4, 80.4, 21.1; ESI-HRMS Calcd for $C_{15}H_{14}NO_2$ $[M + H]^+$ 240.1019, found 240.1021.



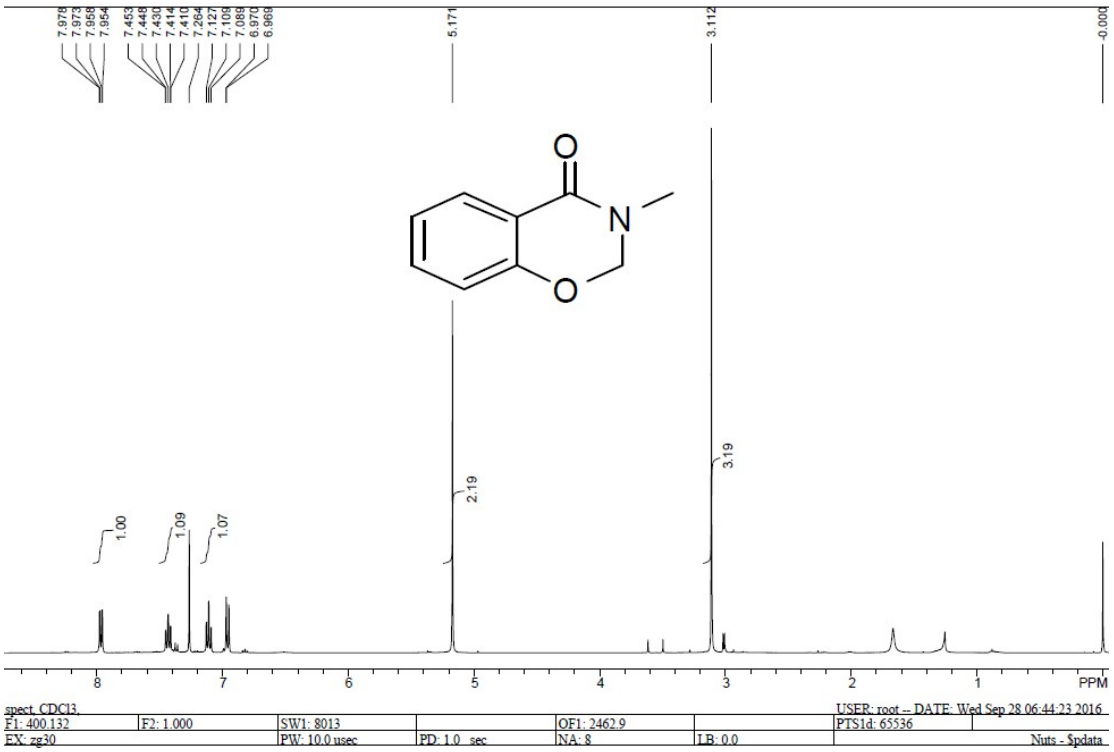
2-Hydroxy-N-pentylbenzamide (**4a**). Yield 82% (51 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.45 (s, 1 H), 7.44 (dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1 H), 7.36 (td, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1 H), 6.96 (dd, J_1 = 8.4 Hz, J_2 = 0.8 Hz, 1 H), 6.83-6.78 (m, 2 H), 3.43-3.38 (m, 2 H), 1.63-1.56 (m, 2 H), 1.35-1.30 (m, 4 H), 0.89 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 170.0, 161.3, 134.0, 125.6, 118.7, 118.4, 114.6, 39.8, 29.2, 29.1, 22.4, 14.0; ESI-HRMS Calcd for $C_{12}H_{18}NO_2$ $[M + H]^+$ 208.1332, found 208.1330.

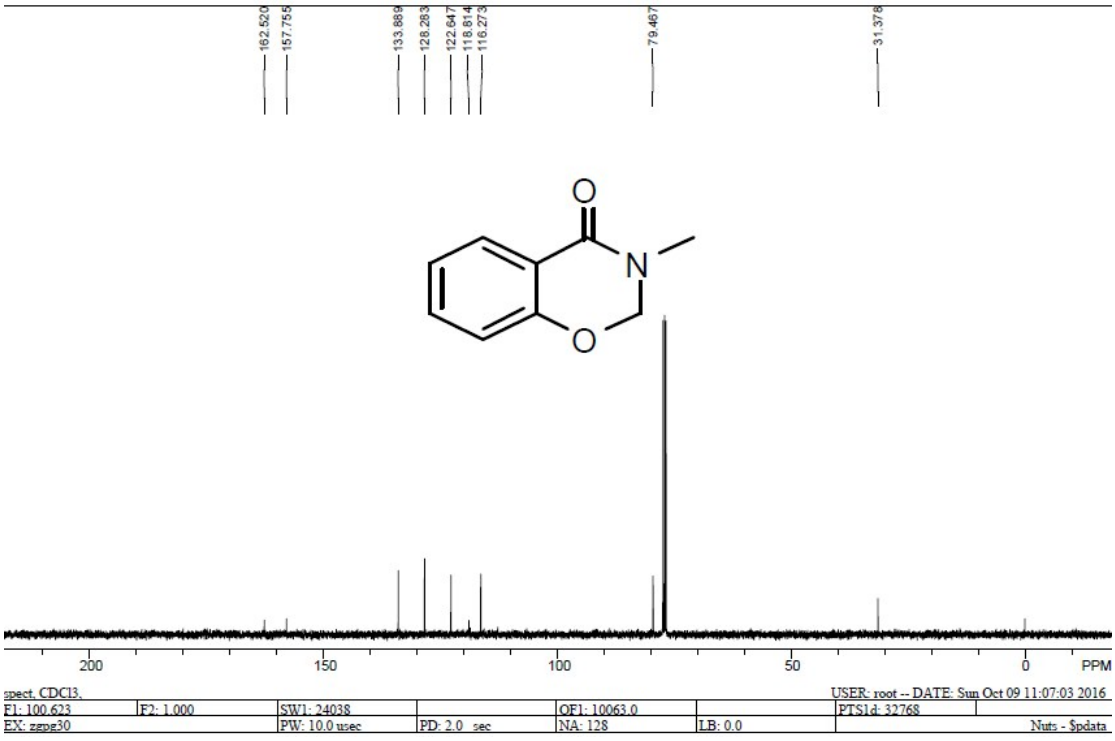
Reference

1. Sukata, K. *Bull. Chem. Soc. Jpn.,* **1985**, *58*, 838.

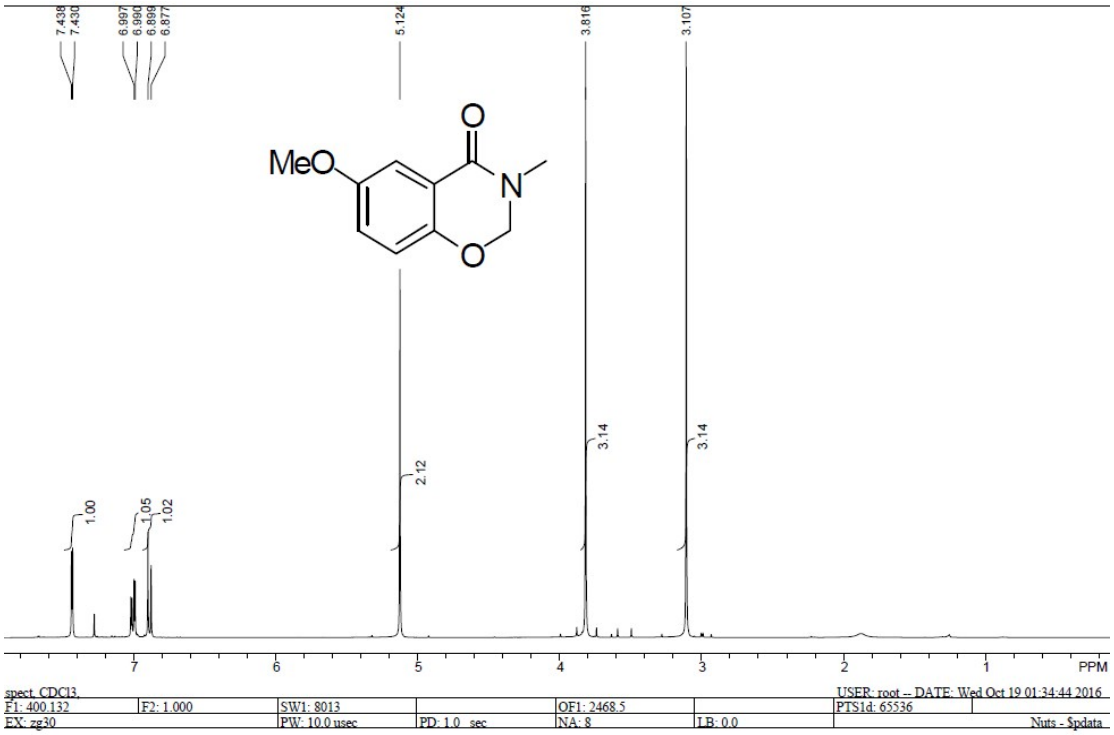
2. K. Dev, R. Maurya, *RSC Adv.,* **2015**, *5*, 13102.

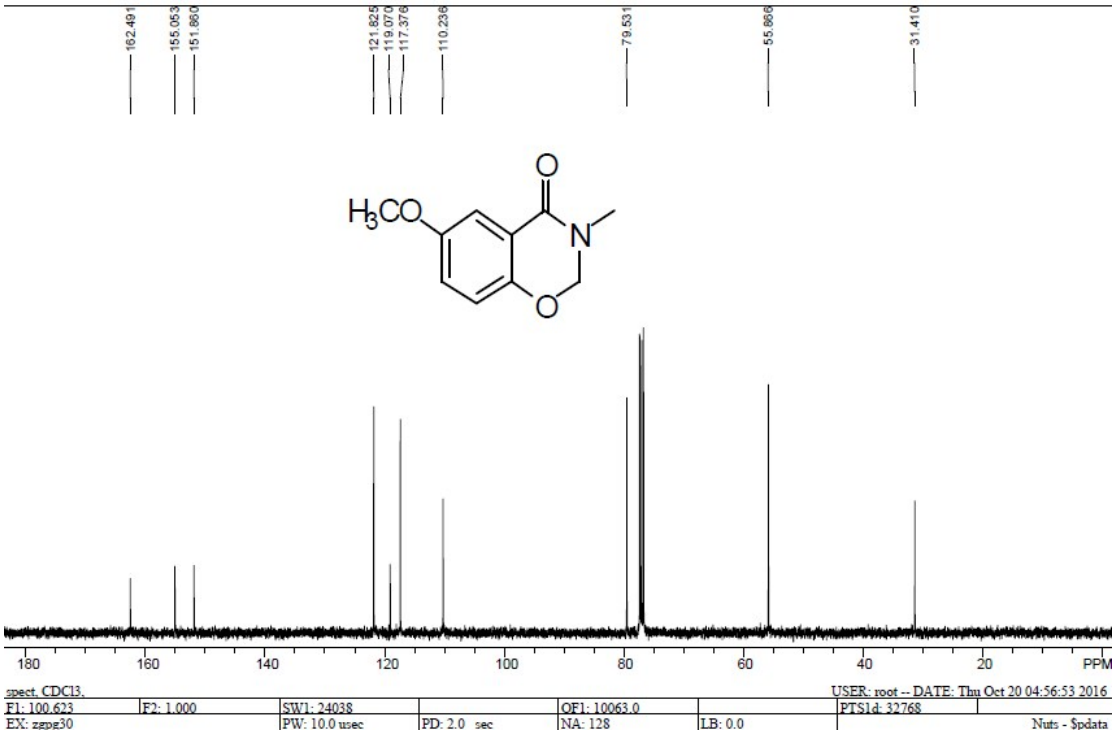
^{1}H and ^{13}C NMR spectra of 3a



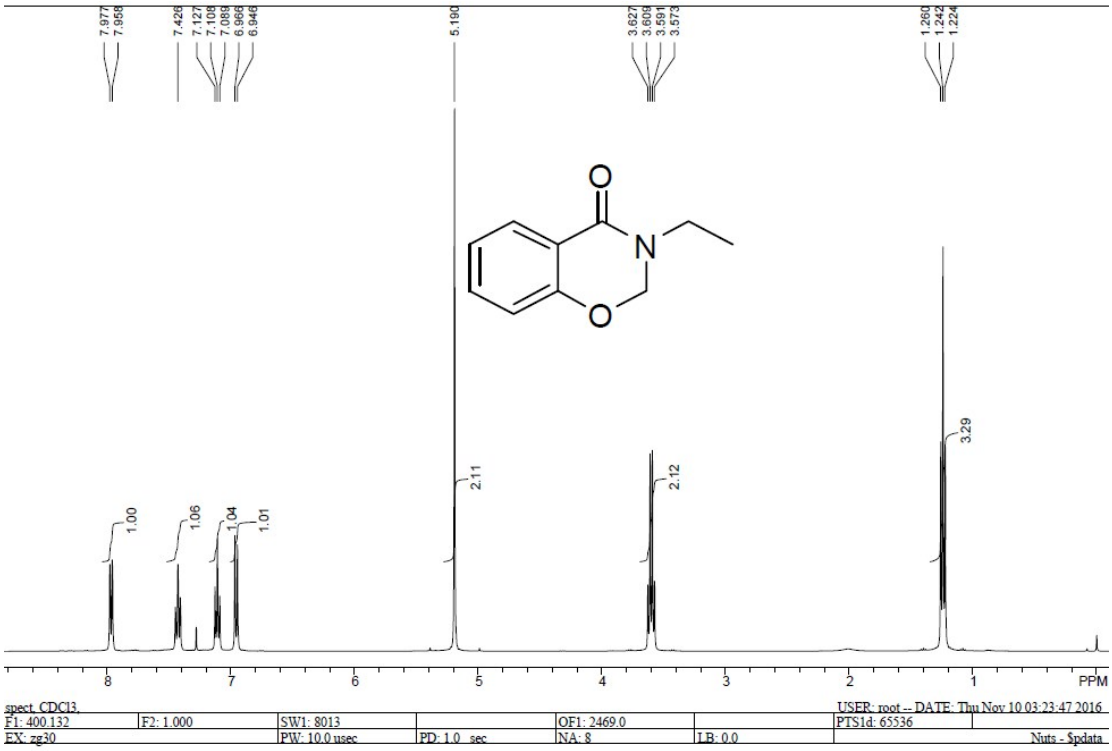


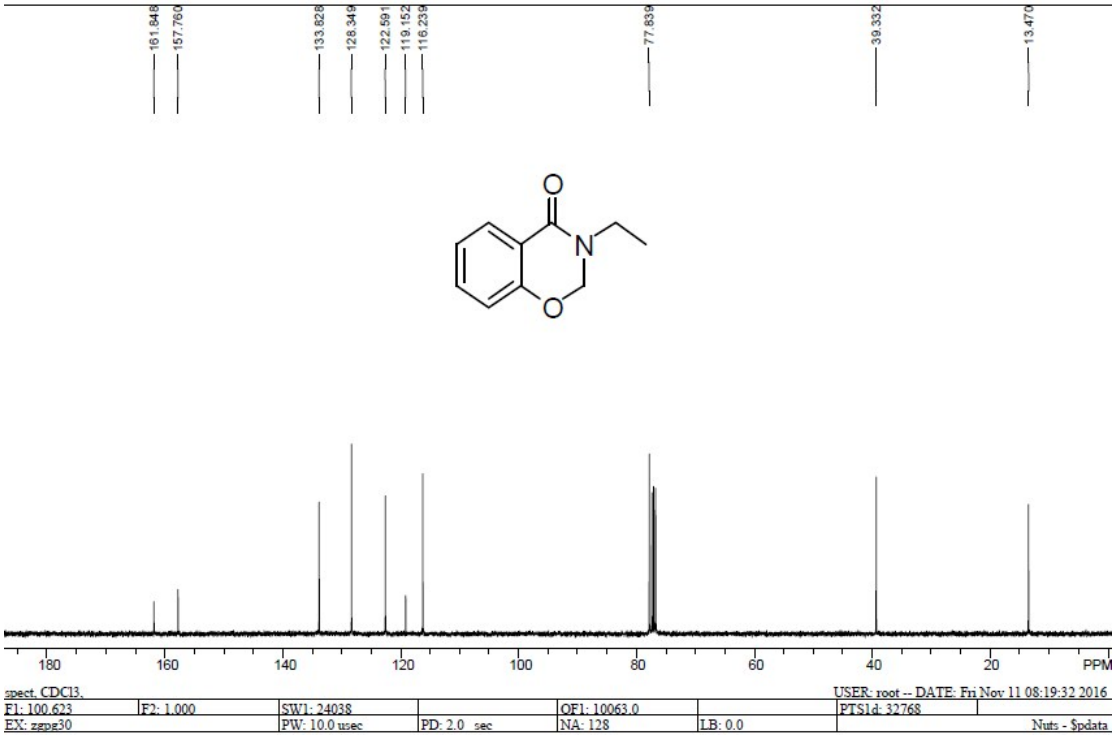
^{1}H and ^{13}C NMR spectra of 3b



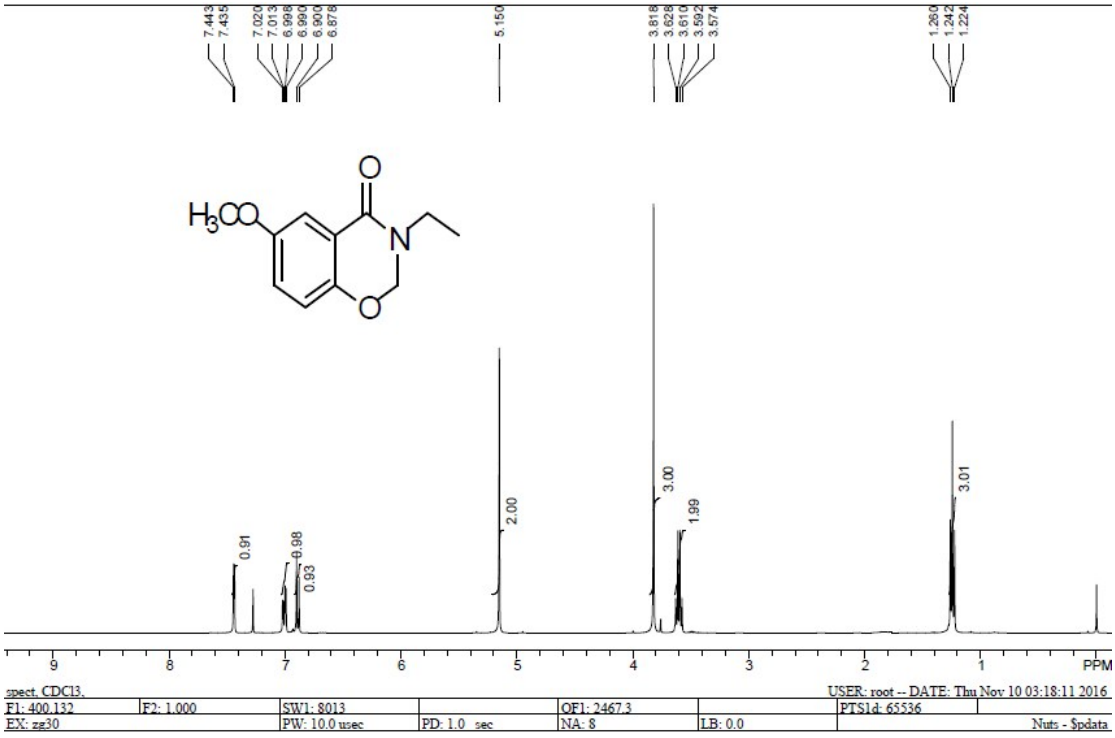


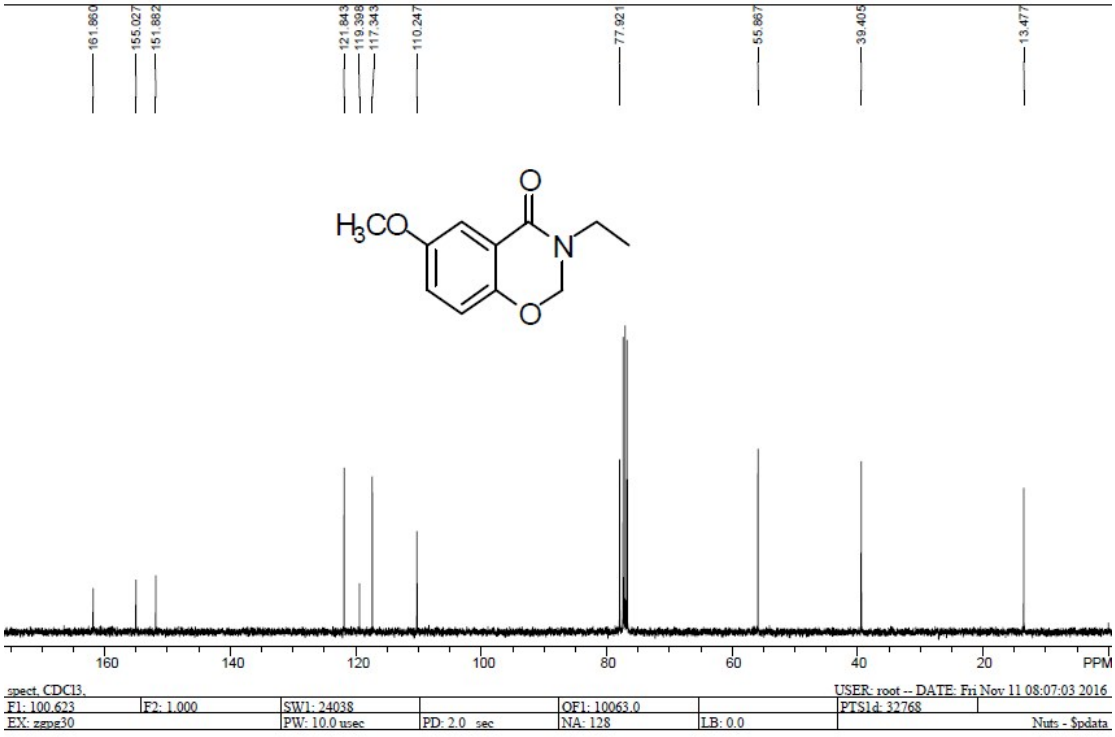
^{1}H and ^{13}C NMR spectra of 3c



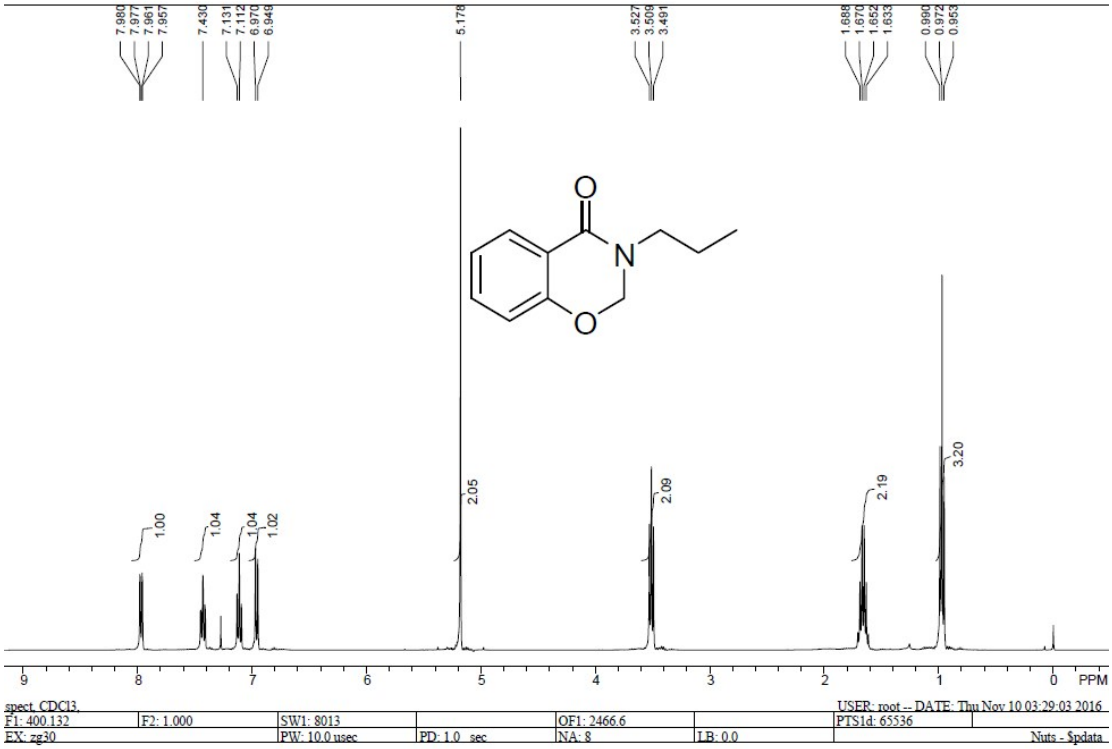


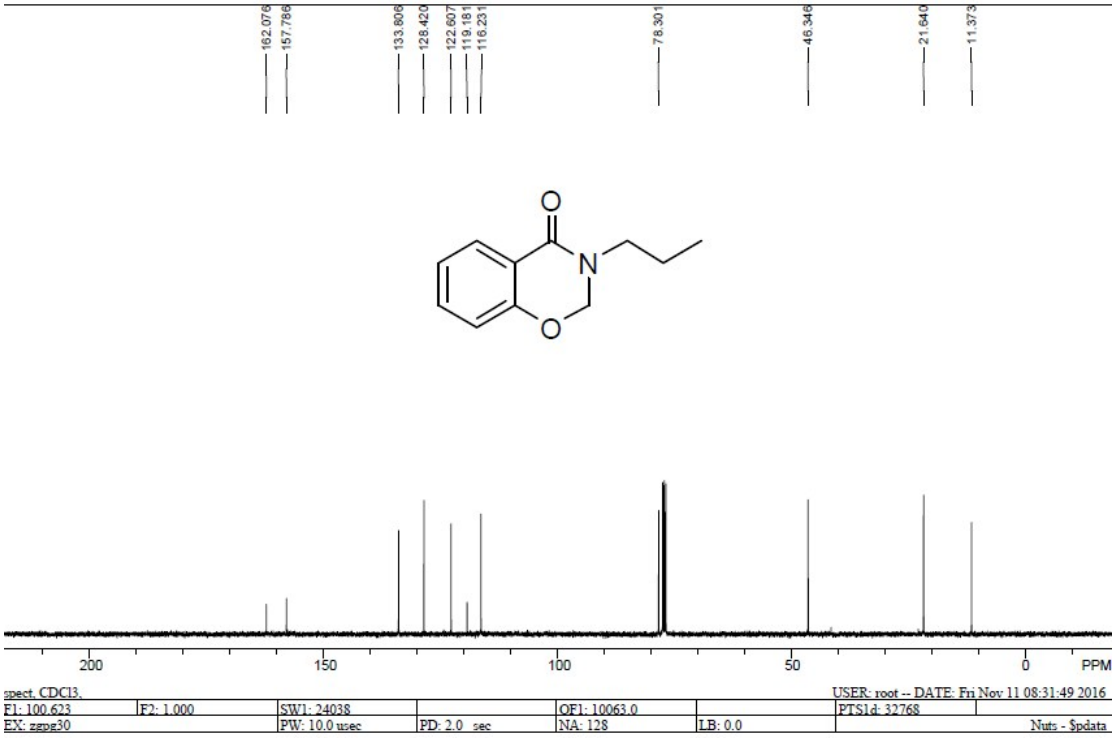
^{1}H and ^{13}C NMR spectra of 3d



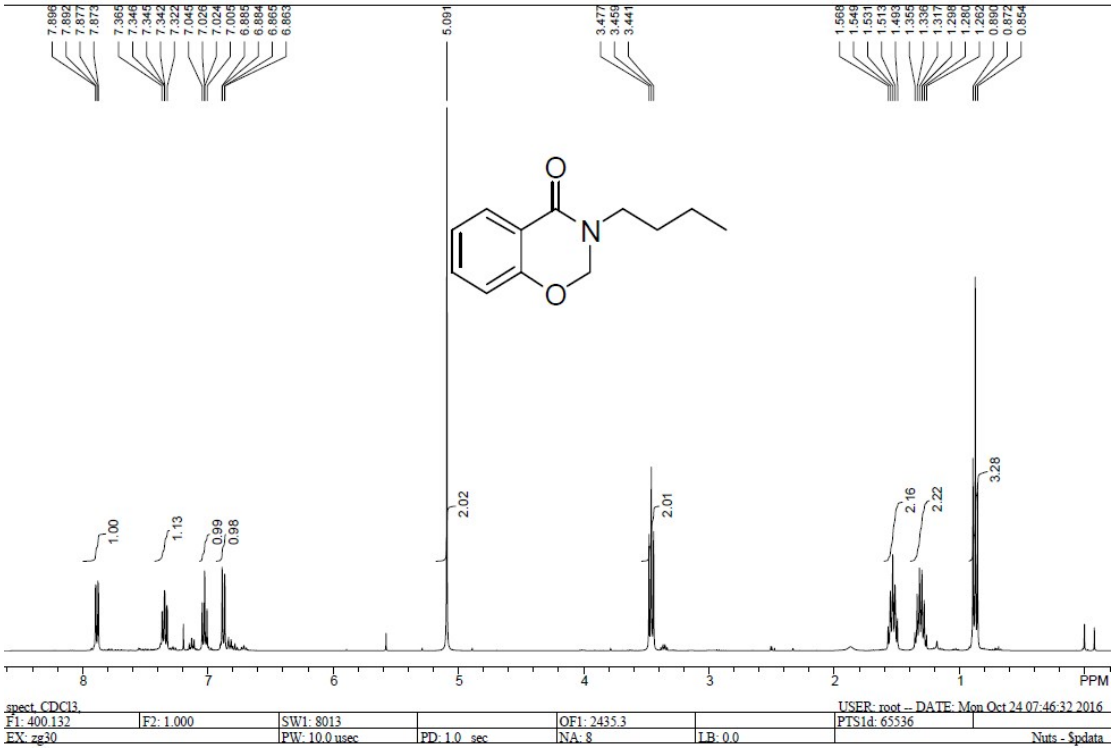


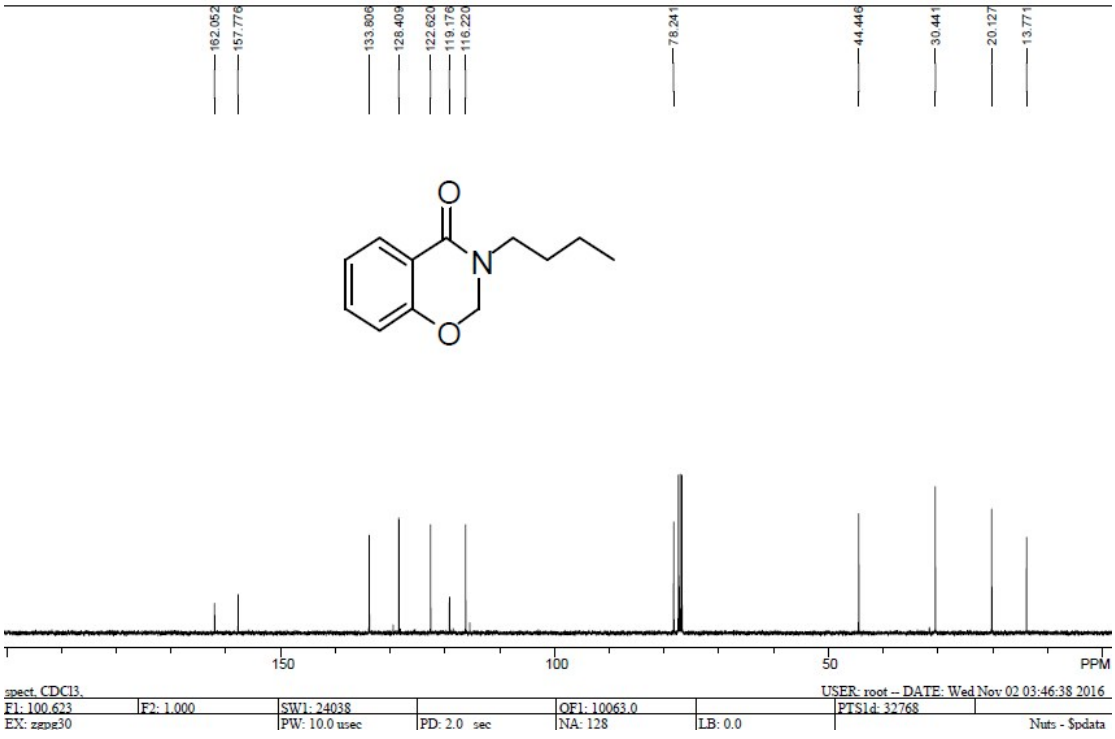
^{1}H and ^{13}C NMR spectra of 3e



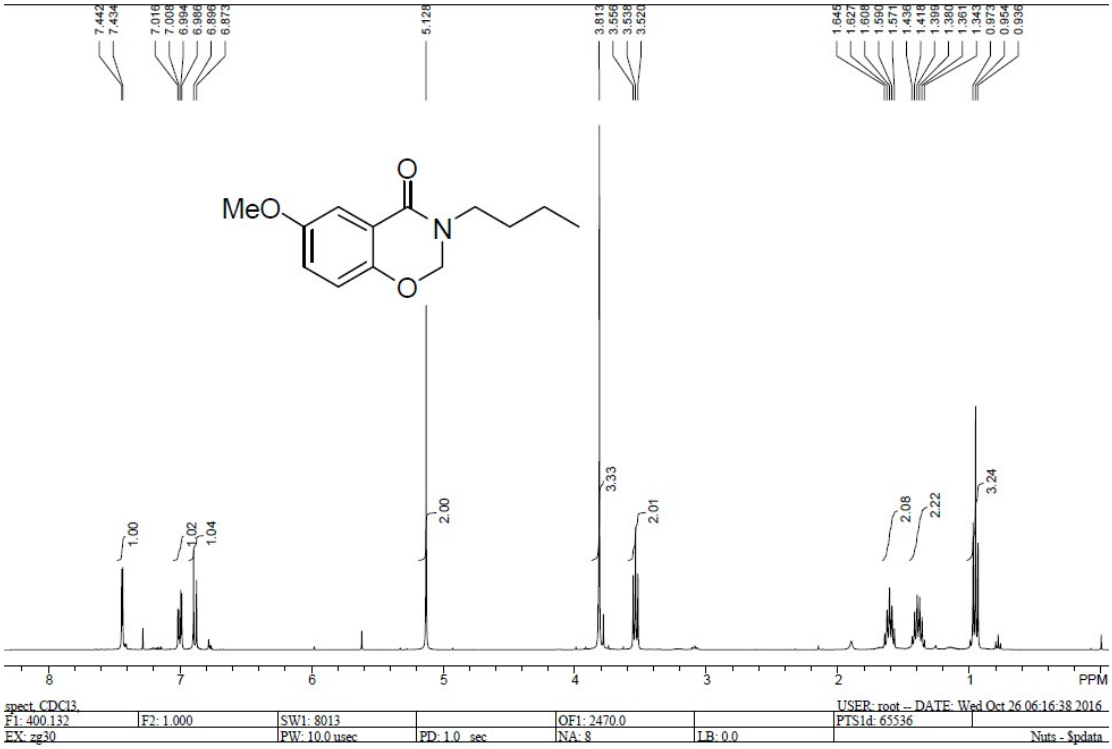


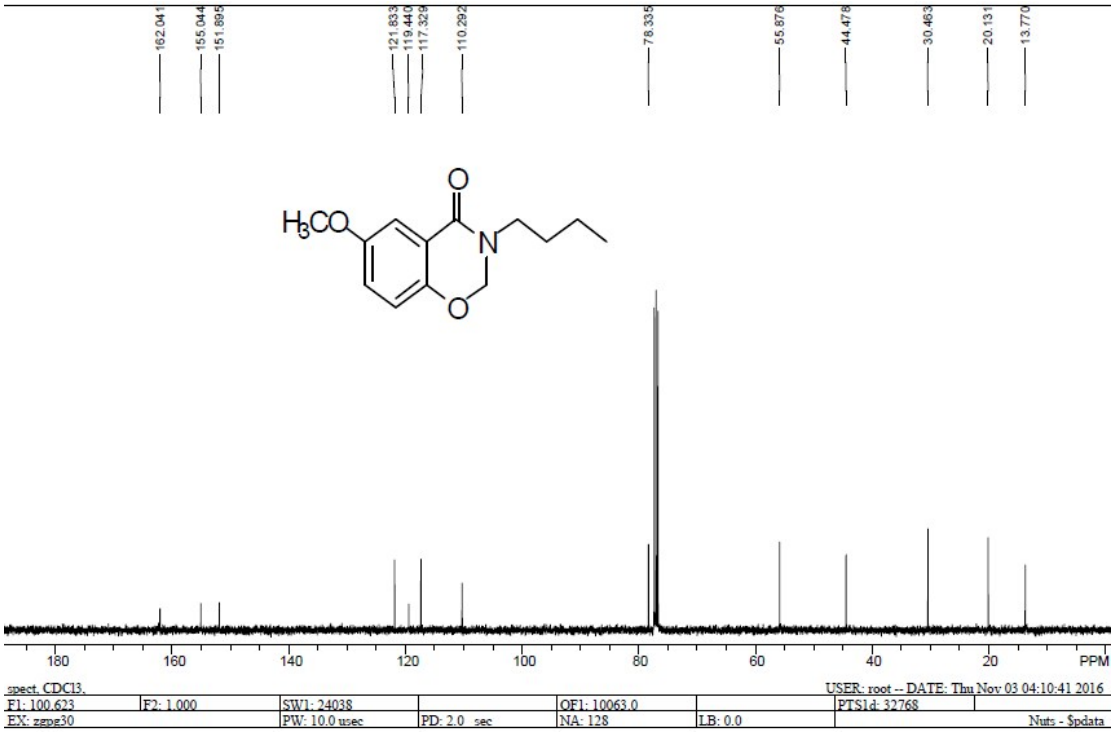
^{1}H and ^{13}C NMR spectra of 3f



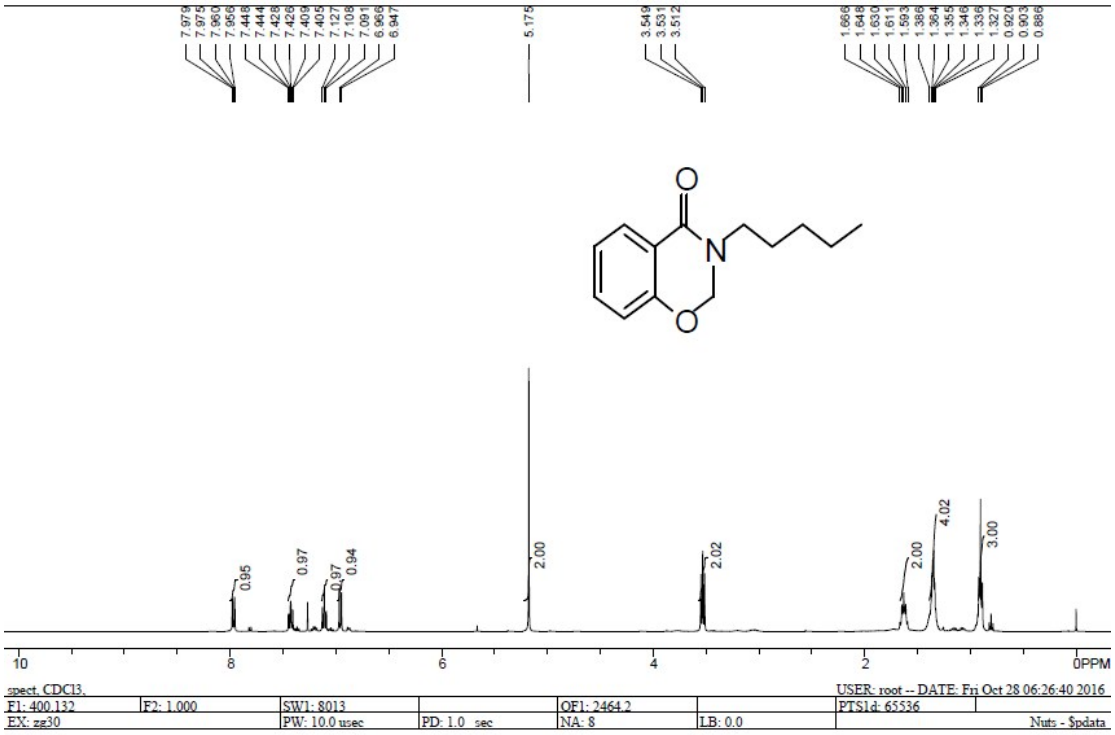


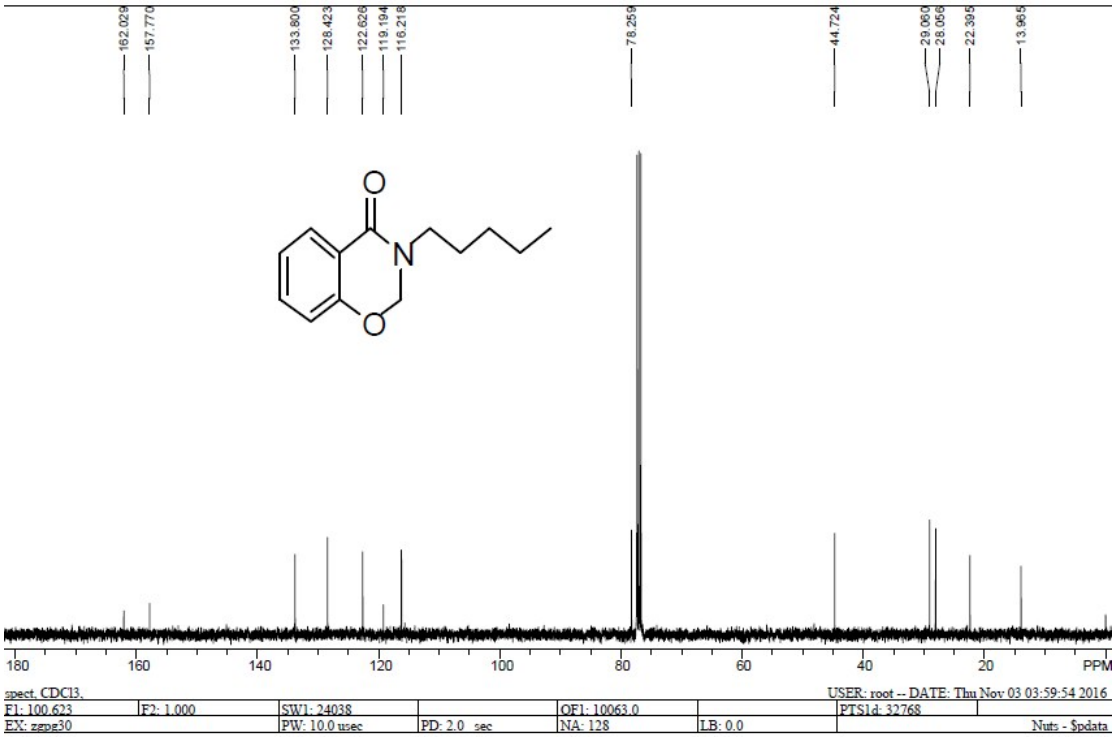
^{1}H and ^{13}C NMR spectra of 3g



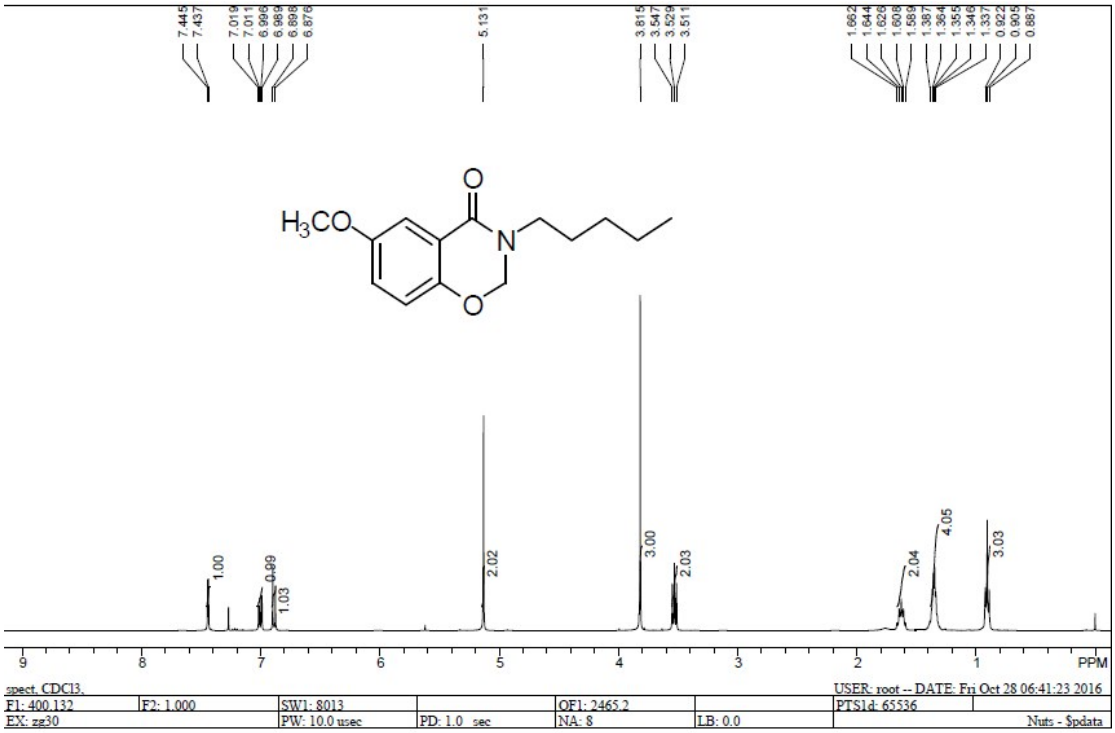


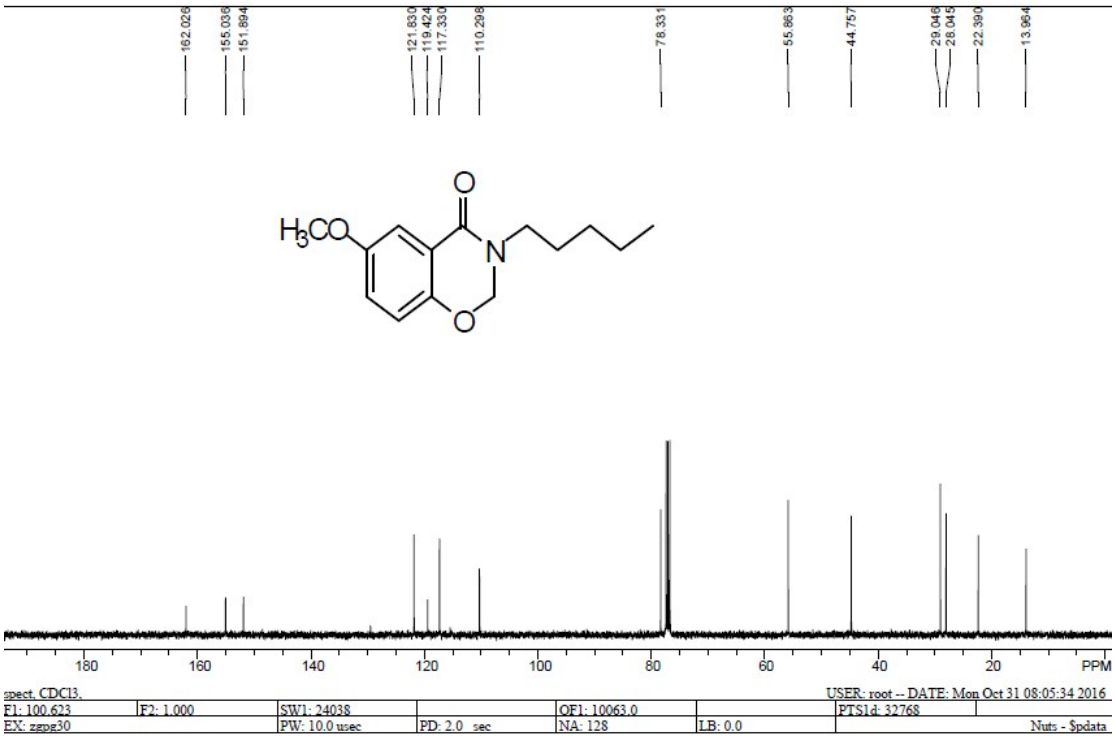
^{1}H and ^{13}C NMR spectra of 3h



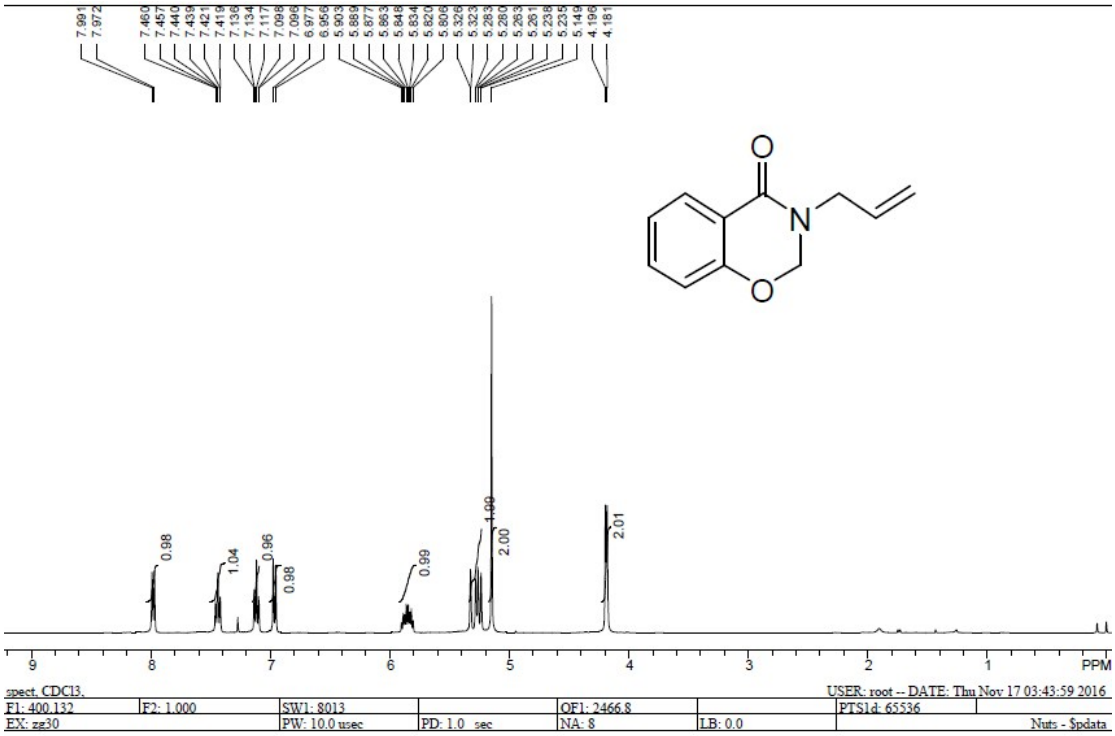


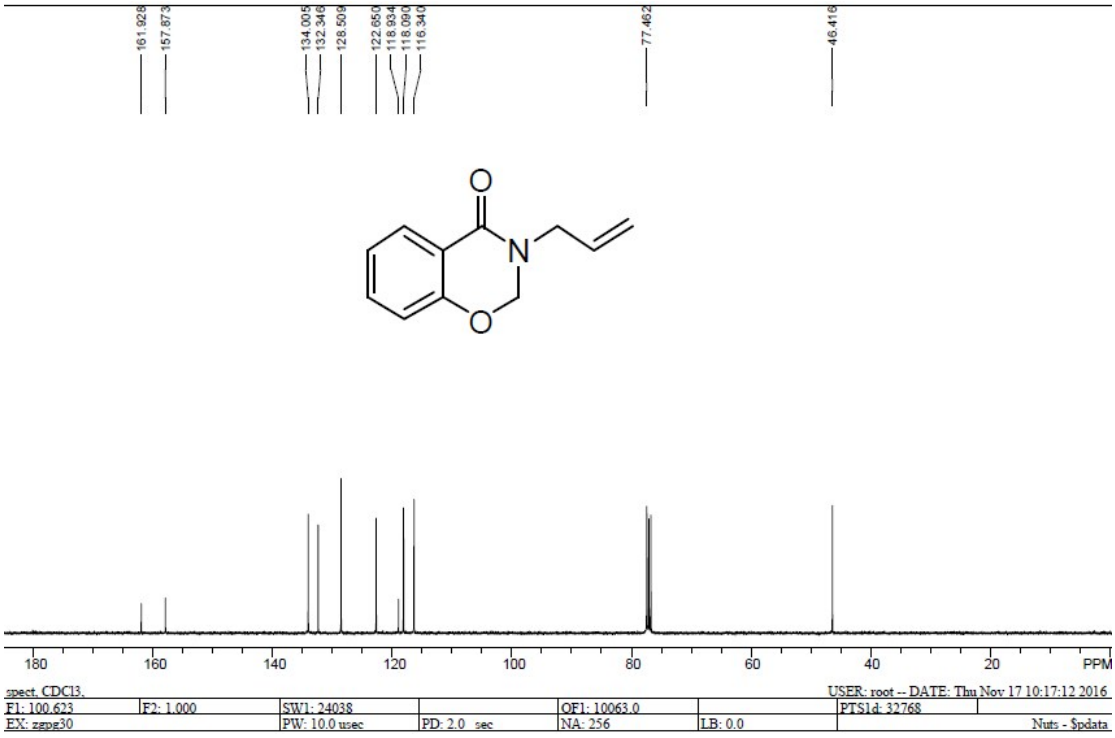
^{1}H and ^{13}C NMR spectra of 3i



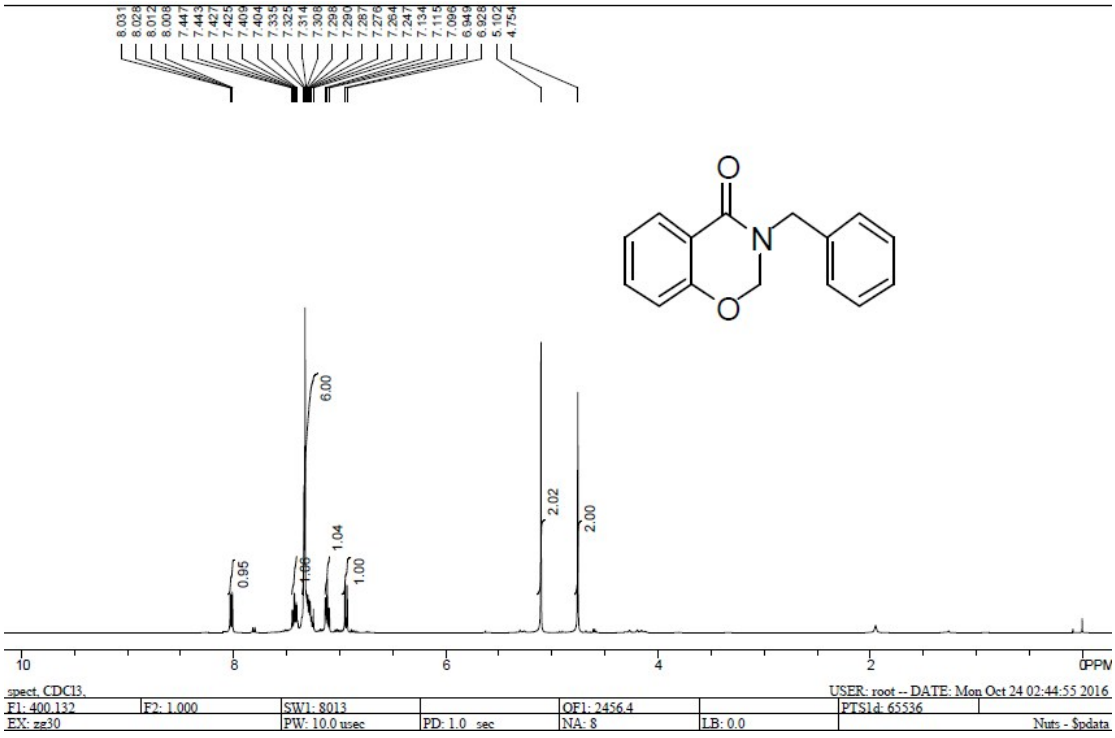


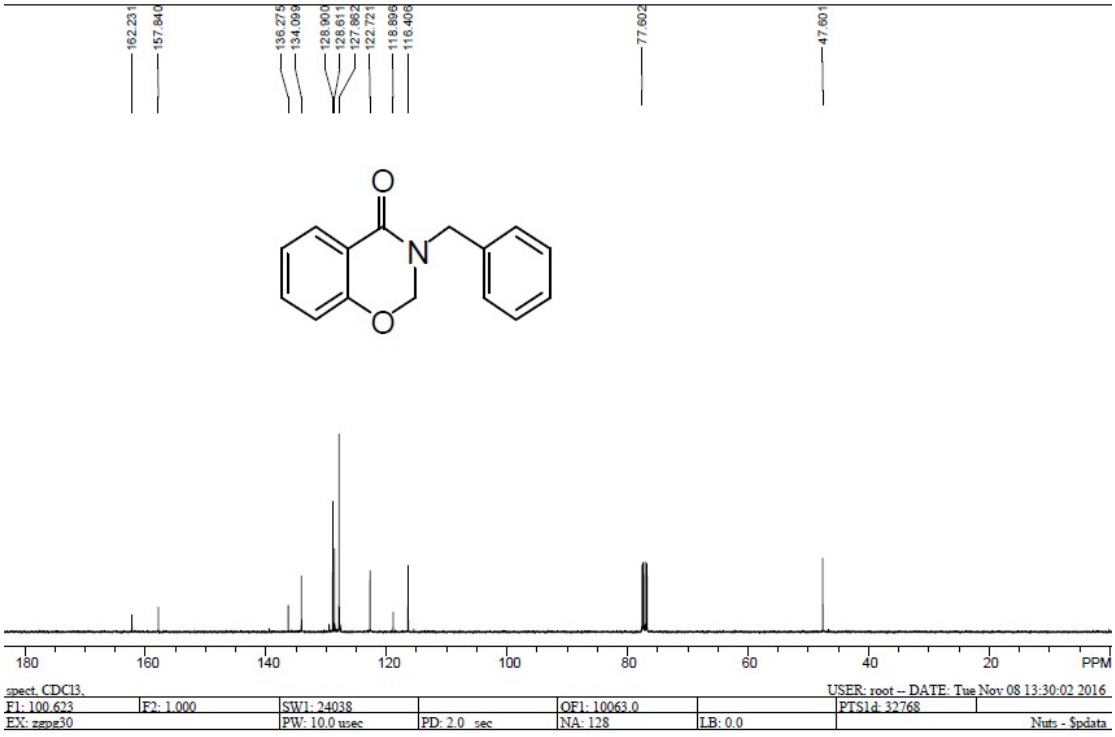
^{1}H and ^{13}C NMR spectra of 3j



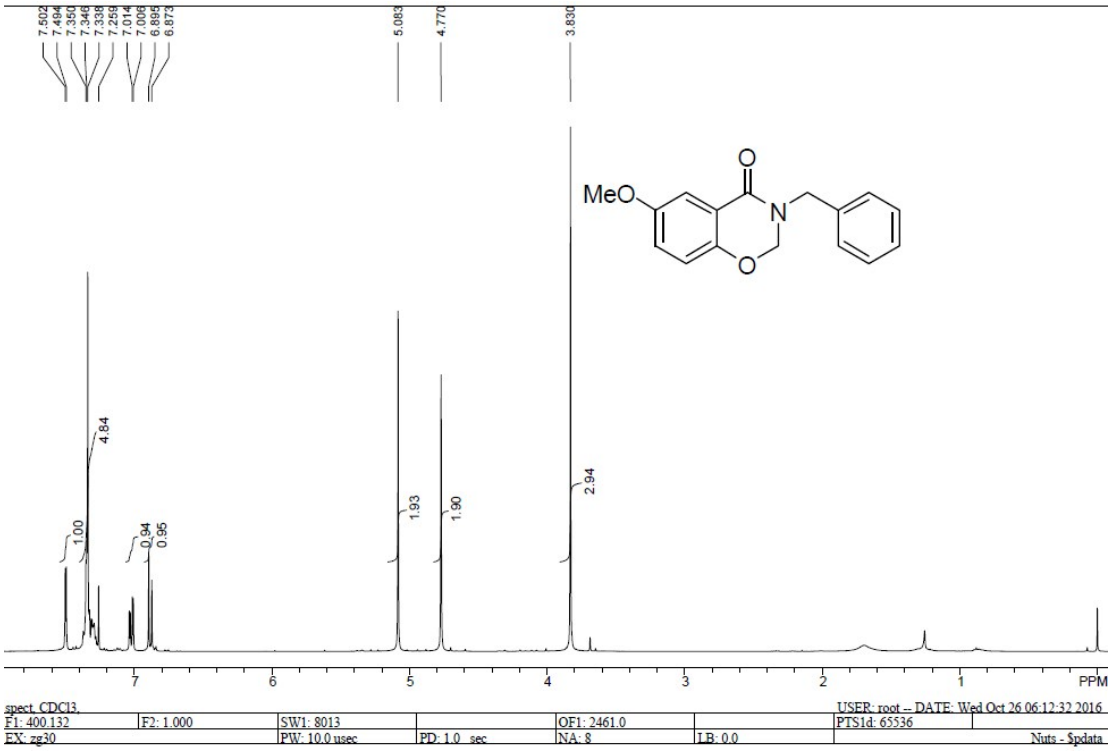


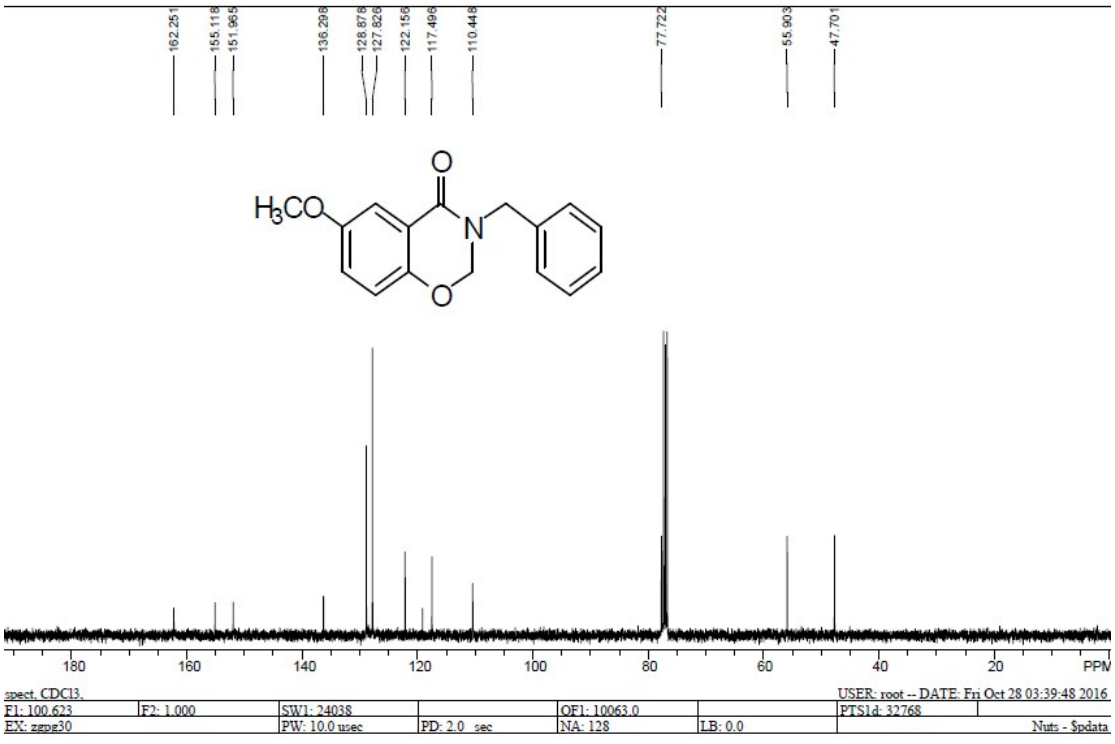
^{1}H and ^{13}C NMR spectra of 3k



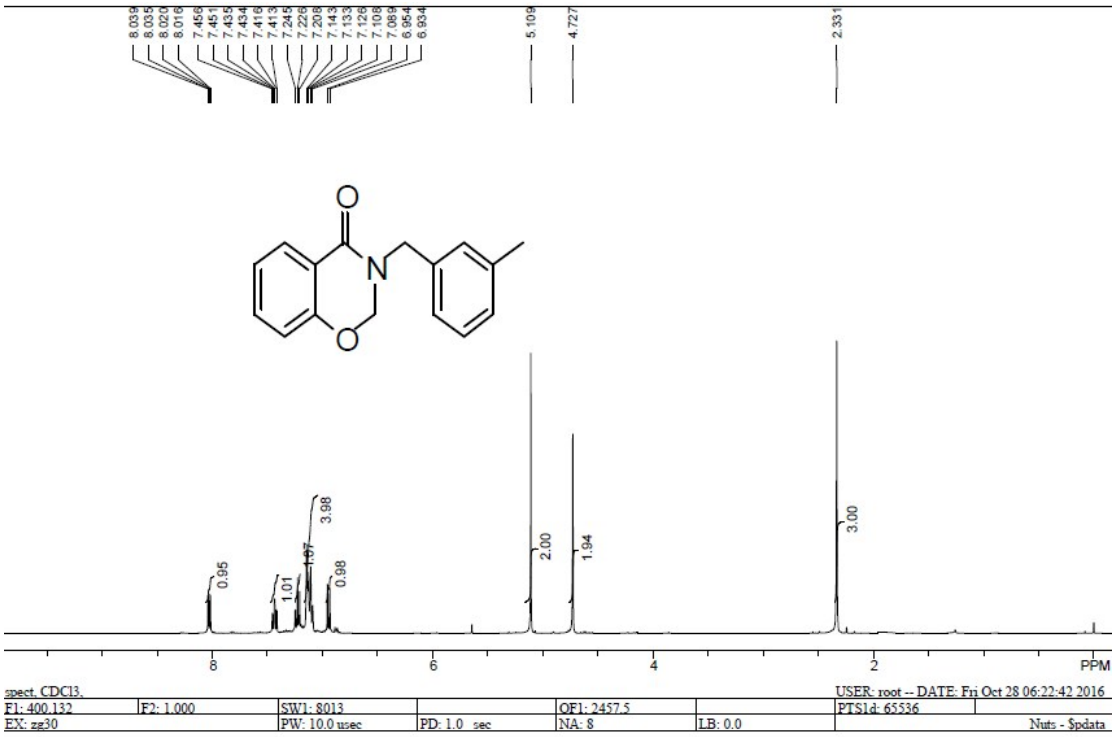


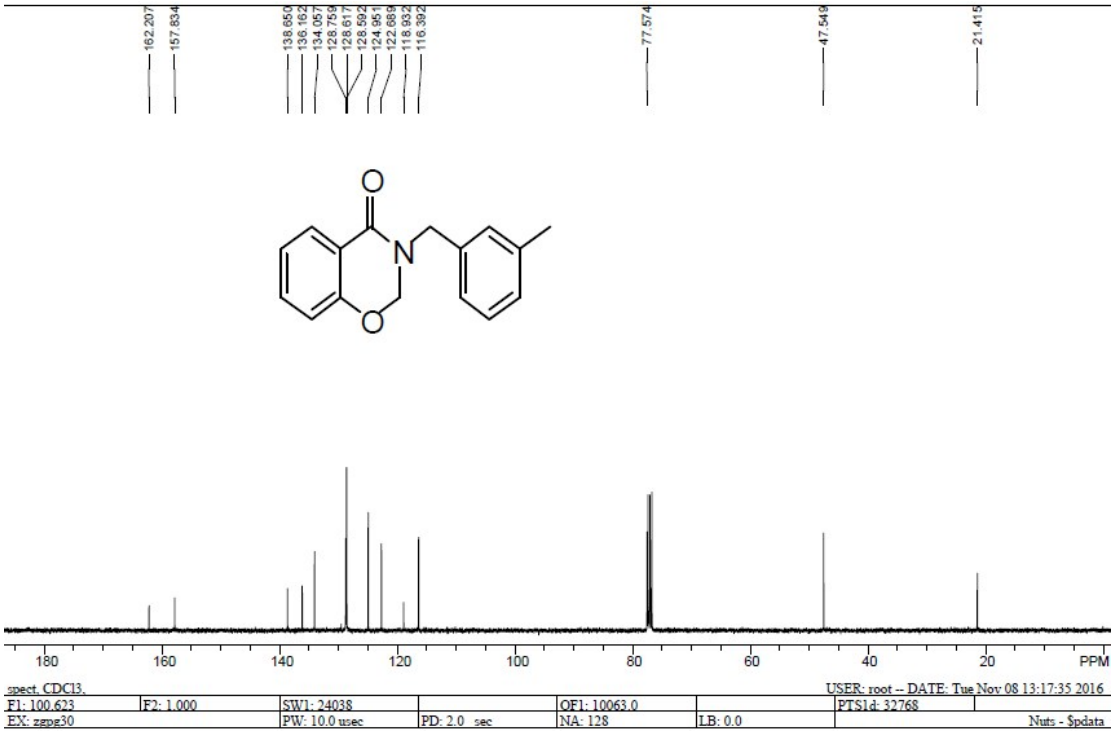
^{1}H and ^{13}C NMR spectra of 3l



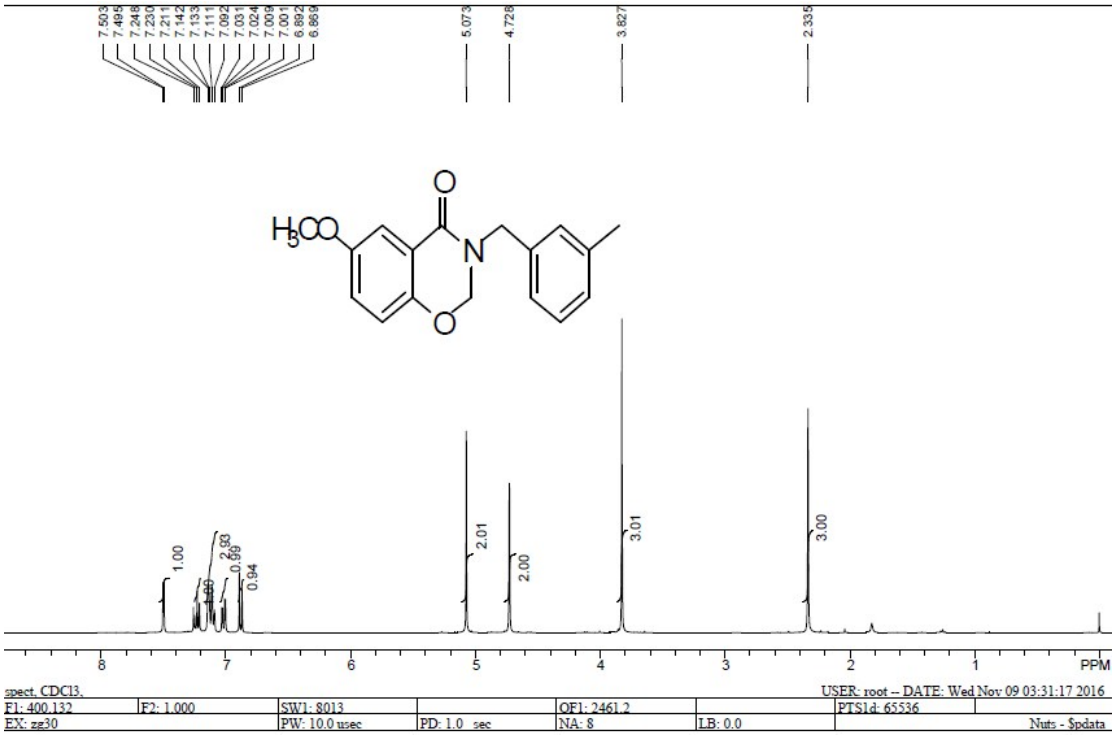


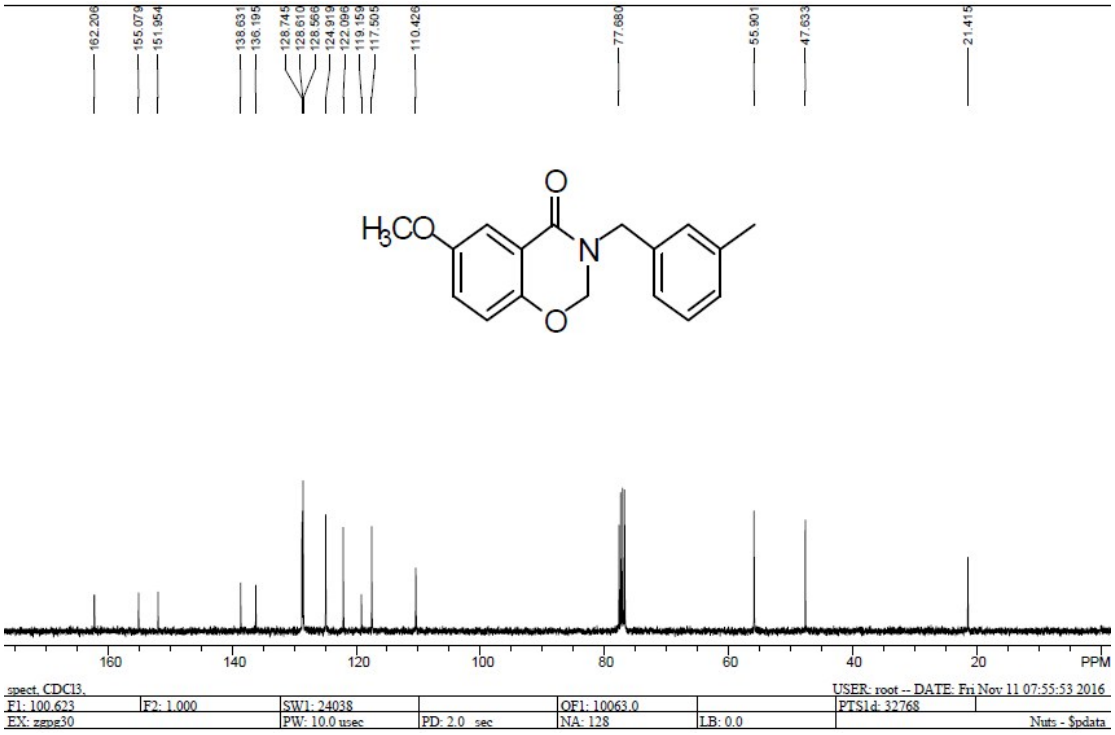
^{1}H and ^{13}C NMR spectra of 3m



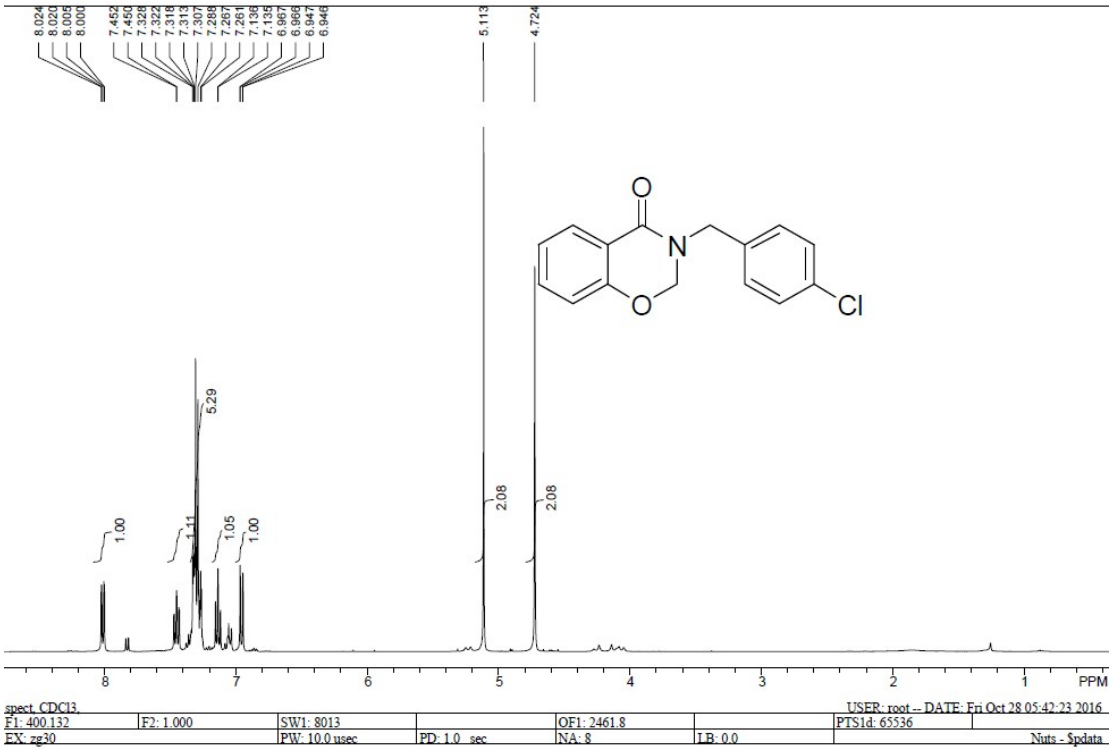


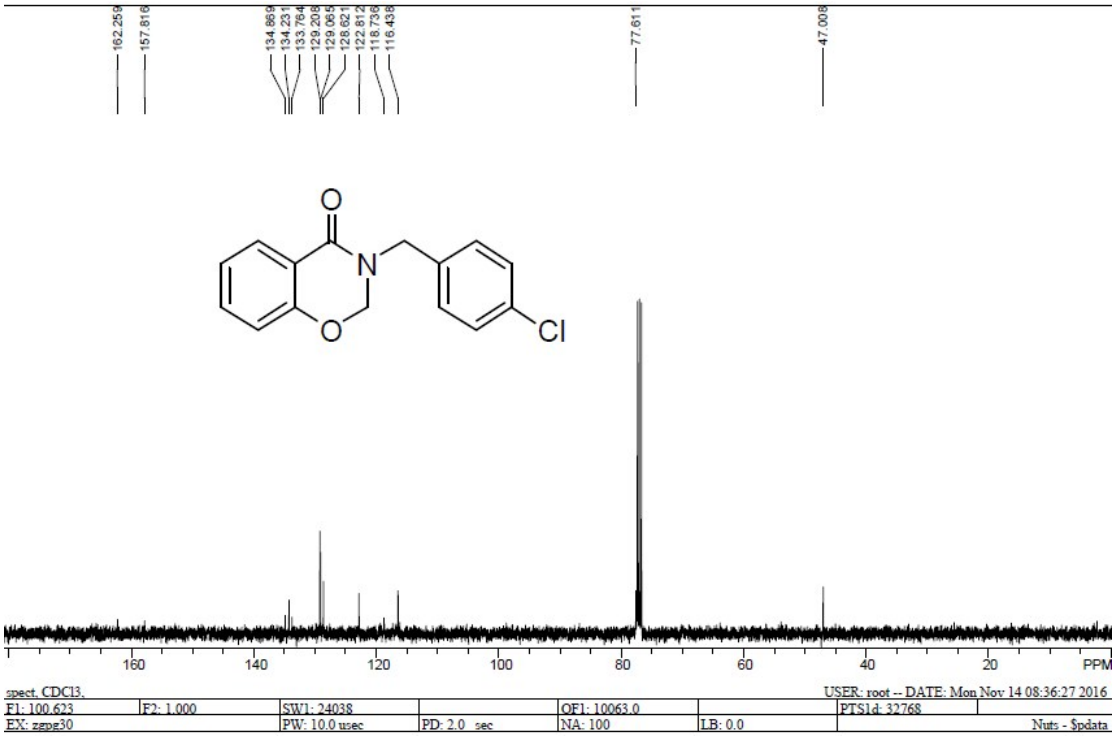
^{1}H and ^{13}C NMR spectra of 3n



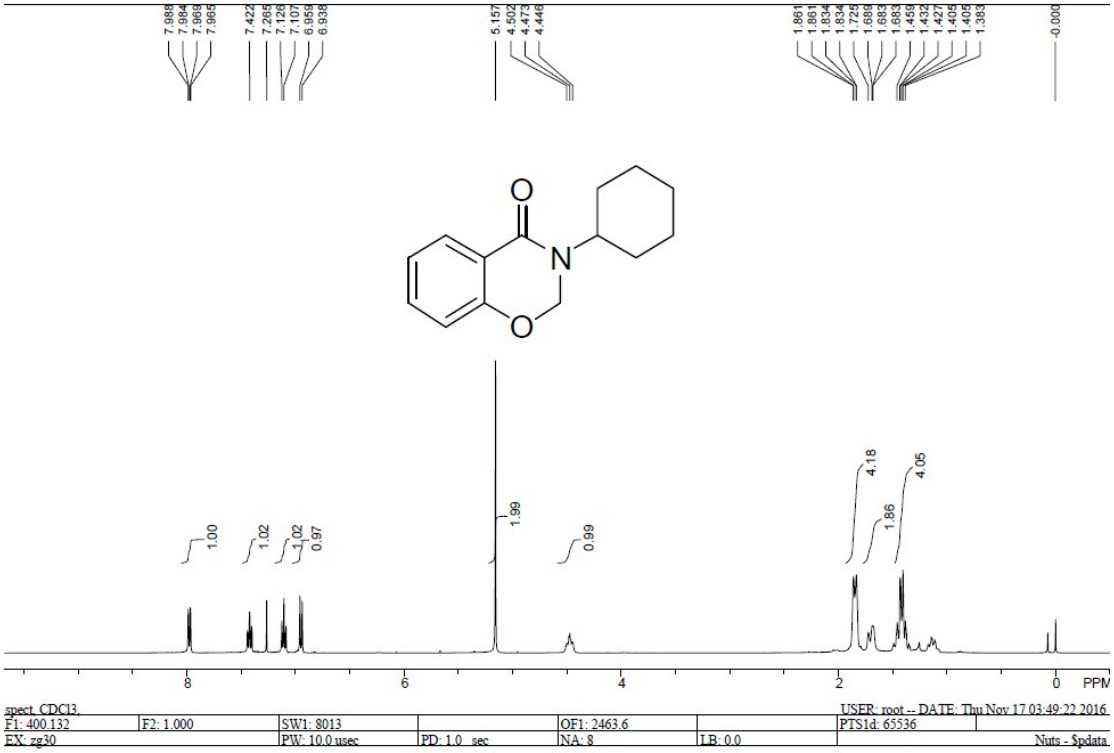


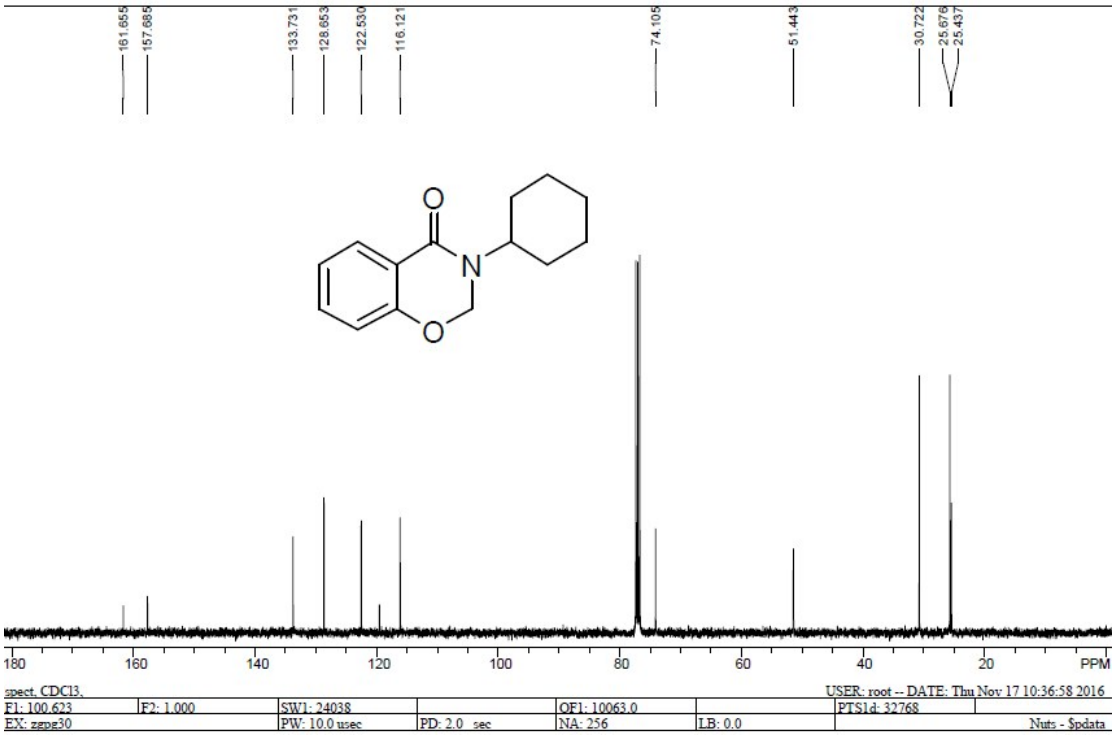
^{1}H and ^{13}C NMR spectra of 3o



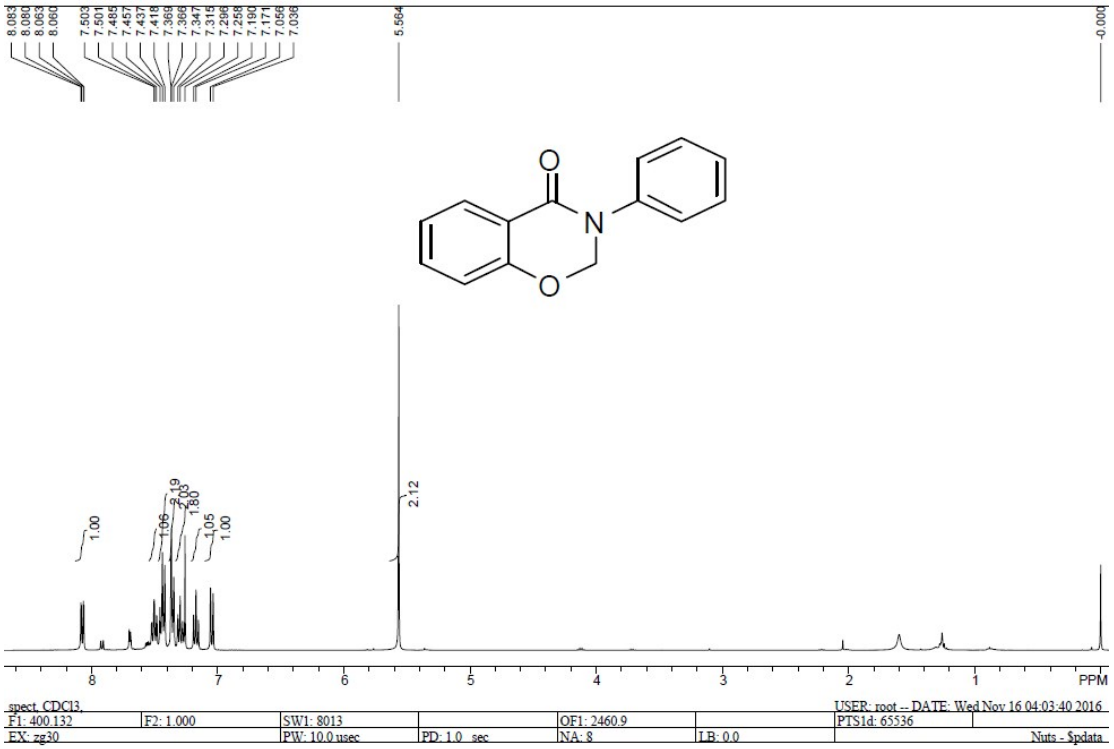


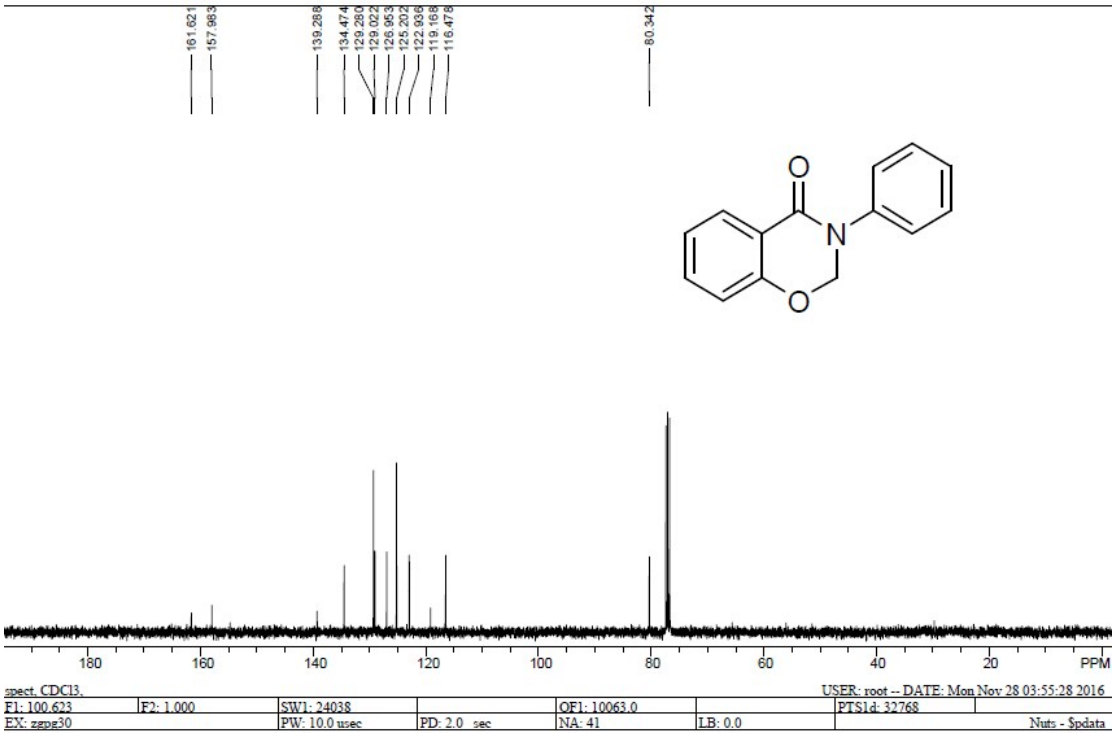
^{1}H and ^{13}C NMR spectra of 3p



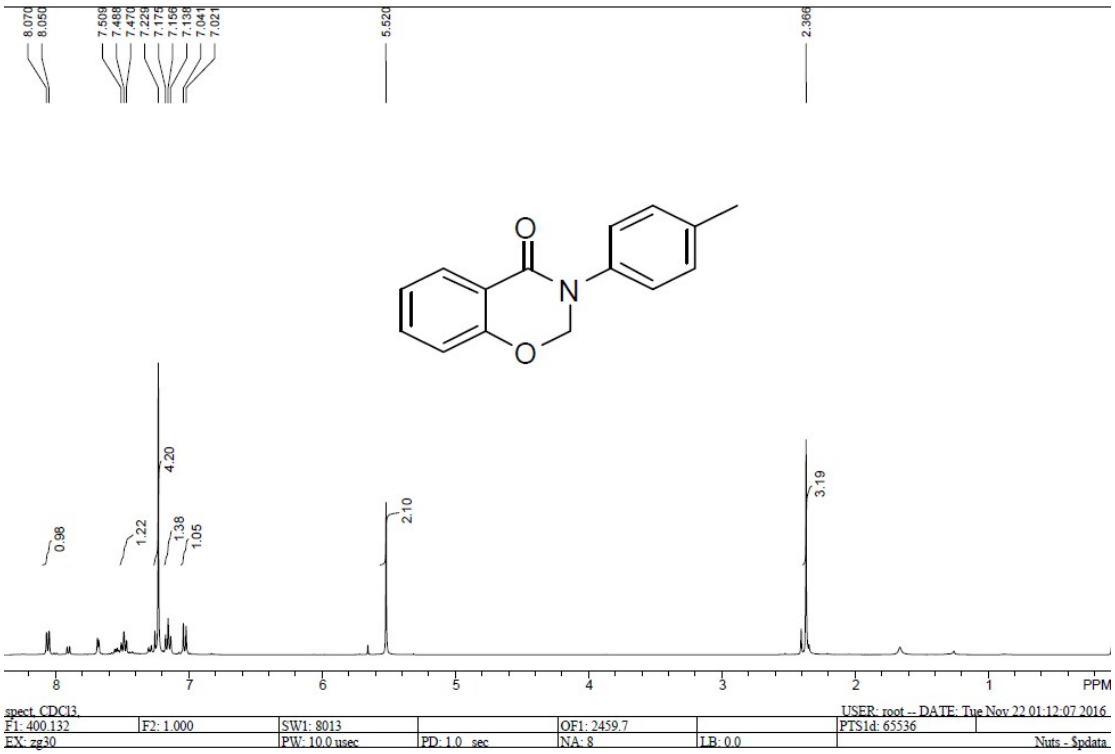


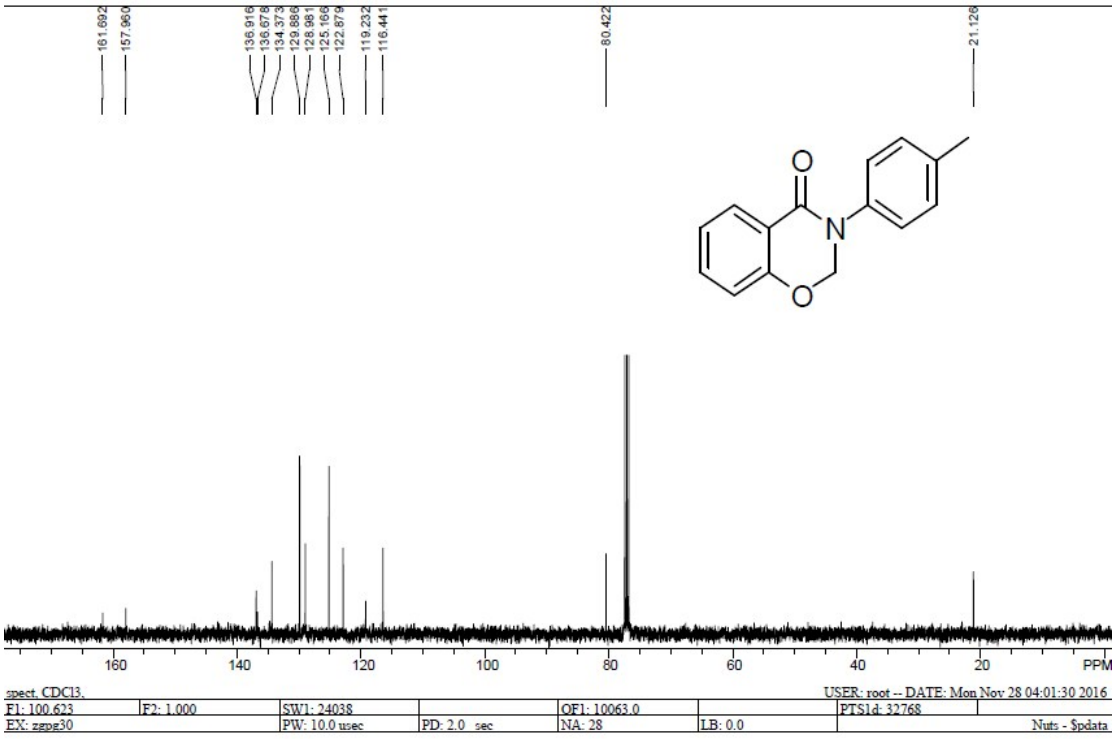
^{1}H and ^{13}C NMR spectra of 3q





^{1}H and ^{13}C NMR spectra of 3r





^{1}H and ^{13}C NMR spectra of 4a