Supporting Information for

Transition-Metal Free 2-Arylbenzoxazole Formation from Aryl Amides and Cyclohexanones

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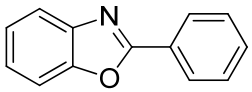
General information:

All experiments were carried out under an atmosphere of oxygen. Flash column chromatography was performed over silica gel 48-75 μm. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker-AV (400 and 100 MHz, respectively) instrument internally referenced to $SiMe_4$ or chloroform signals. MS analyses were performed on an Agilent 5975 GC-MS instrument (EI). High-resolution mass spectra were recorded at Institute of Chemistry, Chinese Academy of Sciences. The structures of known compounds were further corroborated by comparing their NMR data and MS data with those of literature. The structures of unknown compounds were further characterized by HRMS. Reagents were used as received from commercial sources without further purification.

General procedure: (3a):

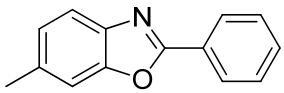
A 25 mL oven-dried reaction vessel was charged with benzamide (**1a**, 36.3 mg, 0.3 mmol), cyclohexanone (**2a**, 21 μL, 0.2 mmol), KI (39.8 mg, 0.24 mmol) and *p*-toluenesulfonic acid (34.2 mg, 0.2 mmol), DMSO (15μL, 0.2 mmol). The reaction vessel was flushed with oxygen three times and then sealed. Toluene / *o*-dichlorobenzene (4:1, 1 mL) were added by syringe and the resulting solution was stirred at 160 ^{o}C for 30 h. After cooling to room temperature, the volatiles were removed under vacuum and the residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3a** as white solid; yield: 71% (27.8 mg), mp 104-105 ^{o}C. R_f = 0.40 (100:2 petroleum ether/ethyl acetate).

2-Phenylbenzoxazole (3a, CAS: 833-50-1) [1]



^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.28-8.26 (m, 2H), 7.80-7.78 (m, 1H), 7.61-7.54 (m, 4H), 7.38-7.35 (m, 2H)； ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 163.1, 150.8, 142.2, 131.5, 128.9, 127.7, 127.3, 125.1, 124.6, 120.1, 110.6; MS (EI) m/z (%): 195 (100), 167, 92, 77, 63, 51.

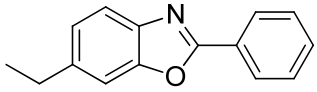
6-Methyl-2-phenylbenzoxazole (3b, CAS: 14016-00-3) [1]



The reaction was conducted with benzamide (**1a**, 36.3 mg, 0.3 mmol) and 4-methylcyclohexanone (**2b**, 25 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3b** as white solid; yield: 73% (30.5 mg), mp 84-86 ^{o}C. R_f = 0.41 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.24 (m, 2H), 7.65 (d, J = 8.0 Hz, 1H), 7.54 (m, 3H), 7.40 (s, 1H), 7.18 (d, J = 8.0 Hz, 1H), 2.52 (s, 3H)；^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 162.6, 151.1, 140.0, 135.5, 131.2, 128.8, 127.5, 127.4, 125.8, 119.4, 110.7, 21.8; MS (EI) m/z (%): 209 (100), 180, 105, 78, 51.

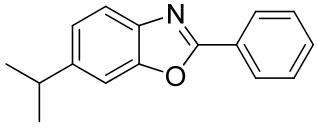
6-Ethyl-2-phenylbenzoxazole (3c)



The reaction was conducted with benzamide (**1a**, 36.3 mg, 0.3 mmol) and 4-ethylcyclohexanone (**2c**, 29 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3c** as yellow solid; yield: 62% (27.7 mg), mp 42-44 ^{o}C. R_f = 0.42 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.24 (m, 2H), 7.67 (d, J = 8.0 Hz, 1H), 7.53 (m, 3H), 7.43 (s, 1H), 7.21 (d, J = 8.0 Hz, 1H), 2.84-2.78 (q, J = 7.3 Hz, 2H), 1.32 (t, J = 7.5 Hz, 3H)；^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 162.7, 151.2, 142.2, 140.2, 131.2, 128.8, 127.6, 127.5, 124.8, 119.5, 109.5, 29.2, 15.9; MS (EI) m/z (%): 223, 208 (100), 180, 77, 51; HRMS (ESI) calcd. for: $C_{15}H_{14}ON$ $[M+H]^+$ 224.1069, found 224.1070.

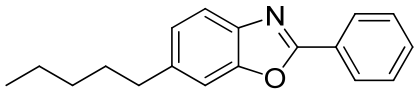
6-Isopropyl-2-phenylbenzoxazole (3d)



The reaction was conducted with benzamide (**1a**, 36.3 mg, 0.3 mmol) and 4-isopropylcyclohexanone (**2d**, 31 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3d** as yellow liquid; yield: 64% (30.3 mg). R_f = 0.41 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.25-8.24 (m, 2H), 7.68 (d, J = 8.0 Hz, 1H), 7.53 (m, 3H), 7.46 (s, 1H), 7.24 (s, 1H), 3.11-3.04 (m, 1H), 1.33 (d, J = 6.9 Hz, 6H)；^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 162.8, 151.2, 145.0, 140.3, 131.2, 128.9, 127.6, 127.5, 123.5, 119.5, 108.0, 34.5, 24.3; MS (EI) m/z (%): 237, 222 (100), 119, 91, 77, 65; HRMS (ESI) calcd. for: $C_{16}H_{16}ON$ $[M+H]^+$ 238.1225, found 238.1226.

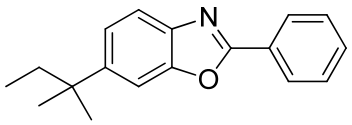
6-Pentyl-2-phenylbenzoxazole (3e)



The reaction was conducted with benzamide (**1a**, 36.3 mg, 0.3 mmol) and 4-pentylcyclohexanone (**2e**, 38 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3e** as yellow liquid; yield: 74% (39.2 mg). R_f = 0.41 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.27-8.26 (m, 2H), 7.68 (d, J = 8.1 Hz, 1H), 7.54-7.53 (m, 3H), 7.41 (s, 1H), 7.20 (d, J = 7.9 Hz, 1H), 2.76 (t, J = 7.7 Hz, 2H), 1.70-1.68 (m, 2H), 1.35 (m, 4H), 0.91 (t, J = 2.4 Hz, 3H)；^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 162.6, 151.2, 140.8, 140.2, 131.2, 128.8, 127.7, 127.5, 125.2, 119.4, 110.1, 36.2, 31.4, 29.7, 22.5, 13.9; MS (EI) m/z (%): 265, 208 (100), 180, 77, 51; HRMS (ESI) calcd. for: $C_{18}H_{20}ON$ $[M+H]^+$ 266.1538, found 266.1539.

6-*tert*-pentyl-2-phenylbenzoxazole (3f)

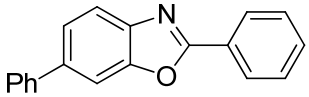


The reaction was conducted with benzamide (**1a**, 36.3 mg, 0.3 mmol) and 4-*tert*-pentylcyclohexanone (**2f**, 38 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3f** as yellow liquid; yield: 76% (40.2 mg). R_f = 0.43 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.27-8.26 (m, 2H), 7.71 (d, J = 8.4Hz, 1H), 7.57-7.53 (m, 4H), 7.37 (d, J = 8.4 Hz, 1H), 1.75-1.70 (q, J = 7.3 Hz, 2H), 1.37 (s, 6H), 0.70 (t, J = 7.4 Hz, 3H)；^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 162.9, 151.2, 147.7, 139.8, 131.2, 128.9, 127.5, 122.8, 119.4, 119.1, 108.1, 38.5, 37.2, 28.9, 9.1; MS (EI) m/z (%): 265, 250, 236 (100), 208, 105, 77; HRMS

(ESI) calcd. for: $C_{18}H_{20}ON$ $[M+H]^+$ 266.1539, found 266.1539.

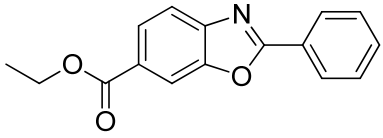
2,6-Diphenylbenzoxazole (3g, CAS: 59005-65-1) [1]



The reaction was conducted with benzamide (**1a**, 36.3 mg, 0.3 mmol) and 4-phenylcyclohexanone (**2g**, 34.8 mg, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3g** as white solid; yield: 82% (44.4 mg), mp 108-110 ^oC. R_f = 0.37 (100:2 petroleum ether/ethyl acetate).

^1H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.33-8.31 (m, 2H), 7.86-7.82 (m, 2H), 7.67-7.65(m, 2H),7.62 (m, 1H), 7.57-7.56 (m, 3H), 7.51-7.48 (m, 2H), 7.42-7.38 (m, 1H)；^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 163.5, 151.5, 141.6, 140.9, 139.1, 131.5, 129.0, 128.9, 127.7, 127.5, 127.4, 127.3, 124.2, 120.0, 109.1; MS (EI) m/z (%): 271(100), 243, 189, 139, 121, 77.

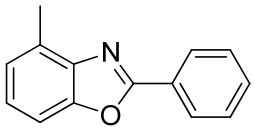
Ethyl 2-phenylbenzoxazole-6-carboxylate (3h, CAS: 1094201-00-9) [2]



The reaction was conducted with benzamide (**1a**, 36.3 mg, 0.3 mmol) and ethyl 4-oxocyclohexanecarboxylate (**2h**, 32 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 60:2) to give **3h** as white solid; yield: 68% (36.3 mg), mp 79-81 ^oC. R_f = 0.26 (60:2 petroleum ether/ethyl acetate).

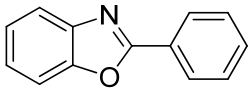
^1H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.30 (m, 3H), 8.12 (d, J = 8.1 Hz, 1H), 7.80 (d, J = 8.3 Hz, 1H), 7.58-7.56 (m, 3H), 4.46-4.41 (q, J = 6.9 Hz, 2H), 1.45 (t, J = 7.1 Hz, 3H)；^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 166.1, 165.5, 150.5, 146.0, 140.9, 132.1, 129.0, 128.0, 127.8, 126.4, 119.5, 112.2, 61.3, 14.4; MS (EI) m/z (%): 267, 239, 222 (100), 166, 139, 63.

8-Methyl-2-Phenylbenzoxazole (3i)



The reaction was conducted with benzamide (**1a**, 36.3 mg, 0.3 mmol) and 2-methylcyclohexanone (**2i**, 25 μL, 0.2 mmol). The residue was purified by GC, yield: 5%.

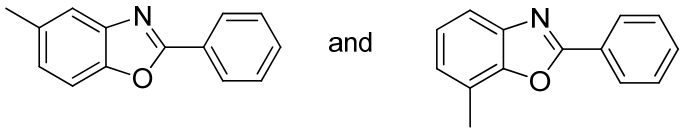
2-Phenylbenzoxazole (3a, CAS: 833-50-1) [1]



^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.28-8.26 (m, 2H), 7.80-7.78 (m, 1H), 7.61-7.54 (m, 4H), 7.38-7.35 (m, 2H)； ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 163.1, 150.8, 142.2, 131.5, 128.9, 127.7, 127.3, 125.1, 124.6, 120.1, 110.6; MS (EI) m/z (%): 95 (100), 167, 92, 77, 63, 51.

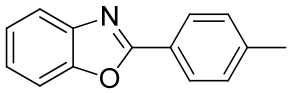
The reaction was conducted with benzamide (**1a**, 36.3 mg, 0.3 mmol) and 2-chlorocyclohexanone (**2j**, 23 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3a** as white solid; yield: 52% (20.3 mg), mp 104-105 ^{o}C. R_f = 0.40 (100:2 petroleum ether/ethyl acetate).

7-Methyl-2-Phenylbenzoxazole (3k) and 5-Methyl-2-Phenylbenzoxazole (3k')



The reaction was conducted with benzamide (**1a**, 36.3 mg, 0.3 mmol) and 3-methylcyclohexanone (**2k**, 25 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3k** and **3k'** (2 : 1)as yellow solid; yield: 80% (33.4 mg). R_f = 0.46 (100:2 petroleum ether/ethyl acetate).

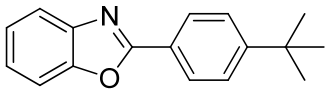
2-(4-Methylphenyl)benzoxazole (3l, CAS: 835-71-2) [3]



The reaction was conducted with 4-methylbenzamide (**1b**, 40.5 mg, 0.3 mmol) and cyclohexanone (**2a**, 21 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3l** as white solid; yield: 75% (31.4 mg), mp 112-114 ^{o}C. R_f = 0.47 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.18 (d, J = 8.0 Hz, 2H), 7.80-7.78 (m, 1H), 7.60-7.58 (m, 1H), 7.38-7.34 (m, 4H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 163.3, 150.7, 142.2, 142.1, 129.7, 127.6, 124.9, 124.5, 124.4, 119.9, 110.5, 21.7; MS (EI) m/z (%): 209 (100), 180, 116, 91, 63.

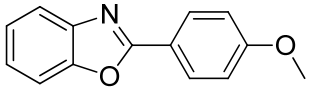
2-(4-*tert*-Butylphenyl)benzoxazole (3m, CAS: 5998-50-5) [4]



The reaction was conducted with 4-(*tert*-butyl)benzamide (**1c**, 53.1 mg, 0.3 mmol) and cyclohexanone (**2a**, 21 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3m** as white solid; yield: 77% (38.7 mg), mp 102-104 ^{o}C. R_f = 0.42 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.22 (d, J = 8.3 Hz, 2H), 7.81-7.79 (m, 1H), 7.61-7.55 (m, 4H), 7.38-7.36 (m, 1H), 1.38 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 163.3, 155.1, 150.8, 142.3, 127.5, 125.9, 124.9, 124.5, 124.4, 119.9, 110.5, 35.1, 31.2; MS (EI) m/z (%): 251, 236 (100), 208, 104, 63.

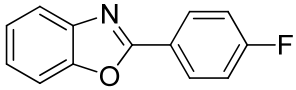
2-(4-Methoxylphenyl)benzoxazole (3n, CAS: 838-34-6) [4]



The reaction was conducted with 4-methoxybenzamide (**1d**, 45.3 mg, 0.3 mmol) and cyclohexanone (**2a**, 21 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3n** as white solid; yield: 71% (32.0 mg), mp 97-99 ^{o}C. R_f = 0.20 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.21 (d, J = 7.8 Hz, 2H), 7.75-7.74 (m, 1H), 7.56 (m, 1H), 7.34-7.33 (m, 2H), 7.04 (d, J = 7.7 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 163.2, 162.4, 150.7, 142.4, 129.4, 124.6, 124.4, 119.8, 119.7, 114.4, 110.4, 55.4; MS (EI) m/z (%): 225 (100), 210, 182, 113, 63.

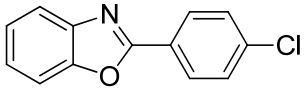
2-(4-Fluorophenyl)benzoxazole (3o, CAS: 397-54-6) [3]



The reaction was conducted with 4-fluorobenzamide (**1e**, 41.7 mg, 0.3 mmol) and cyclohexanone (**2a**, 21 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3o** as white solid; yield: 82% (34.9 mg), mp 101-103 ^{o}C. R_f = 0.41 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.31-8.28 (m, 2H), 7.80-7.78 (m, 1H), 7.61-7.58 (m, 1H), 7.39-7.37 (m, 2H), 7.25-7.21 (m, 2H)；^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 164.8 (d, $J_{C\text{-}F}$ = 251.3 Hz), 162.2, 150.8, 142.1, 129.8 (d, $J_{C\text{-}F}$ = 8.8 Hz), 125.1, 124.6, 123.6 (d, $J_{C\text{-}F}$ = 3.2 Hz), 120.0, 116.2 (d, $J_{C\text{-}F}$ = 22.1 Hz), 110.5; MS (EI) m/z (%): 213 (100), 185, 121, 92, 63.

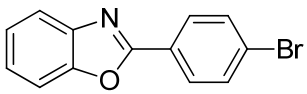
2-(4-Chlorophenyl)benzoxazole (3p, CAS: 1141-35-1) [3]



The reaction was conducted with 4-chlorobenzamide (**1f**, 46.7 mg, 0.3 mmol) and cyclohexanone (**2a**, 21 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3p** as white solid; yield: 83% (38.0 mg), mp 150-152 ^{o}C. R_f = 0.47 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.20 (d, J = 8.4 Hz, 2H), 7.79-7.77 (m, 1H), 7.60-7.58 (m, 1H), 7.51 (d, J = 8.3 Hz, 2H) 7.39-7.36 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 162.1, 150.8, 142.1, 137.8, 129.3, 128.9, 125.7, 125.3, 124.7, 120.1, 110.6; MS (EI) m/z (%): 229 (100), 201, 166, 92, 63.

2-(4-Bromophenyl)benzoxazole (3q, CAS: 3164-13-4) [5]

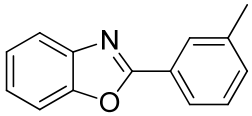


The reaction was conducted with 4-bromobenzamide (**1g**, 59.7 mg, 0.3 mmol) and cyclohexanone (**2a**, 21 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3q** as white solid; yield: 76% (41.6 mg), mp 160-162 ^{o}C. R_f =

0.47 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.12 (d, J = 8.3 Hz, 2H), 7.79-7.77 (m, 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.60-7.58 (m, 1H) 7.39-7.36 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 162.1, 150.8, 142.1, 138.1, 132.2, 129.0, 126.2, 125.4, 124.7, 120.1, 110.6; MS (EI) m/z (%): 273 (100), 245, 194, 92, 63.

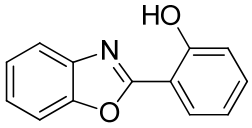
2-(3-Methylphenyl)benzoxazole (3r, CAS: 14625-58-2) [5]



The reaction was conducted with 3-methylbenzamide (**1h**, 40.5 mg, 0.3 mmol) and cyclohexanone (**2a**, 21 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3r** as white solid; yield: 64% (26.8 mg), mp 75-77 ^{o}C. R_f = 0.53 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.12 (s, 1H), 8.07 (d, J = 7.2 Hz, 1H), 7.80-7.79 (m, 1H), 7.60-7.59 (m, 1H), 7.45-7.43 (m, 1H) 7.38-7.36 (m, 3H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 163.3, 150.8, 142.2, 138.7, 132.3, 128.8, 128.2, 127.1, 125.0, 124.8, 124.4, 120.0, 110.6, 21.3; MS (EI) m/z (%): 209 (100), 180, 116, 91, 63.

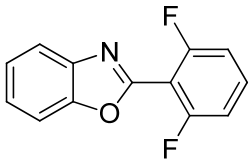
2-(2-Hydroxyphenyl)benzoxazole (3s, CAS: 835-64-3) [4]



The reaction was conducted with 2-hydroxybenzamide (**1i**, 41.1 mg, 0.3 mmol) and cyclohexanone (**2a**, 21 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3s** as white solid; yield: 67% (28.3 mg), mp 122-124 ^{o}C. R_f = 0.26 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 11.5 (s, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.75-7.73 (m, 1H), 7.63-7.61 (m, 1H), 7.47-7.38 (m, 3H), 7.13 (d, J = 8.3 Hz, 1H), 7.02 (t, J = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 163.0, 158.8, 149.2, 140.1, 133.5, 127.1, 125.5, 125.4, 125.0, 119.5, 119.3, 117.5, 110.6; MS (EI) m/z (%): 211 (100), 183, 154, 91, 63.

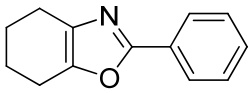
2-(2,6-Difluorophenyl)benzoxazole (3t)



The reaction was conducted with 2,6-difluorobenzamide (**1j**, 47.1 mg, 0.3 mmol) and cyclohexanone (**2a**, 21 μL, 0.2 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **3t** as white solid; yield: 51% (23.6 mg), mp 74-76 ^{o}C. R_f = 0.50 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.90-7.88 (m, 1H), 7.66-7.64 (m, 1H), 7.55-7.48 (m, 1H), 7.43-7.39 (m, 2H), 7.11(t, J = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 161.2 (dd, $J_{1\ C\text{-}F}$ = 257.2, J_2 = 5.4 Hz), 154.8, 150.5, 141.4, 132.9 (t, $J_{\ C\text{-}F}$ = 10.6 Hz), 125.8, 124.7, 120.6, 112.5-112.3 (m), 110.9, 106.5 (t, $J_{\ C\text{-}F}$ = 15.7 Hz); MS (EI) m/z (%): 231 (100), 203, 139, 92, 63; HRMS (ESI) calcd. for: $C_{13}H_8ONF_2$ $[M+H]^+$ 232.0566, found 232.0569.

2-Phenyl-4,5,6,7-tetrahydrobenzoxazole (4a, CAS: 61766-91-4) [6]



A 25 mL oven-dried reaction vessel was charged with benzamide (**1a**, 36.3 mg, 0.3 mmol), cyclohexanone (**2a**, 21 μL, 0.2 mmol), KI (39.8 mg, 0.24 mmol) and *p*-TsOH (34.2 mg, 0.2 mmol), DMSO (15μL, 0.2 mmol). The reaction vessel was flushed with oxygen three times and then sealed. Toluene/*o*-dichlorobenzene (0.8 mL / 0.2 mL) were added by syringe and the resulting solution was stirred at 160 ^{o}C for 2 h. After cooling to room temperature, the volatiles were removed under vacuum and the residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 100:2) to give **4a** as white solid; mp 73-75 ^{o}C. R_f = 0.43 (100:2 petroleum ether/ethyl acetate).

^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.01-7.99 (m, 2H), 7.43-7.41 (m, 3H), 2.70-2.61 (m, 4H), 1.91-1.85 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 159.8, 146.9, 135.2, 129.6, 128.6, 128.2, 125.9, 23.2, 23.0, 23.0, 22.0; MS (EI) m/z (%): 199 (100), 171, 103, 77, 51.

References:

[1] S. Ueda, H, Nagasawa, *Angew. Chem*. *Int. Ed*. **2008**, *47*, 6411.

[2] Mitsubishi Tanabe Pharma Corporation, Patent; EP2172450 A1 English, **2010**.

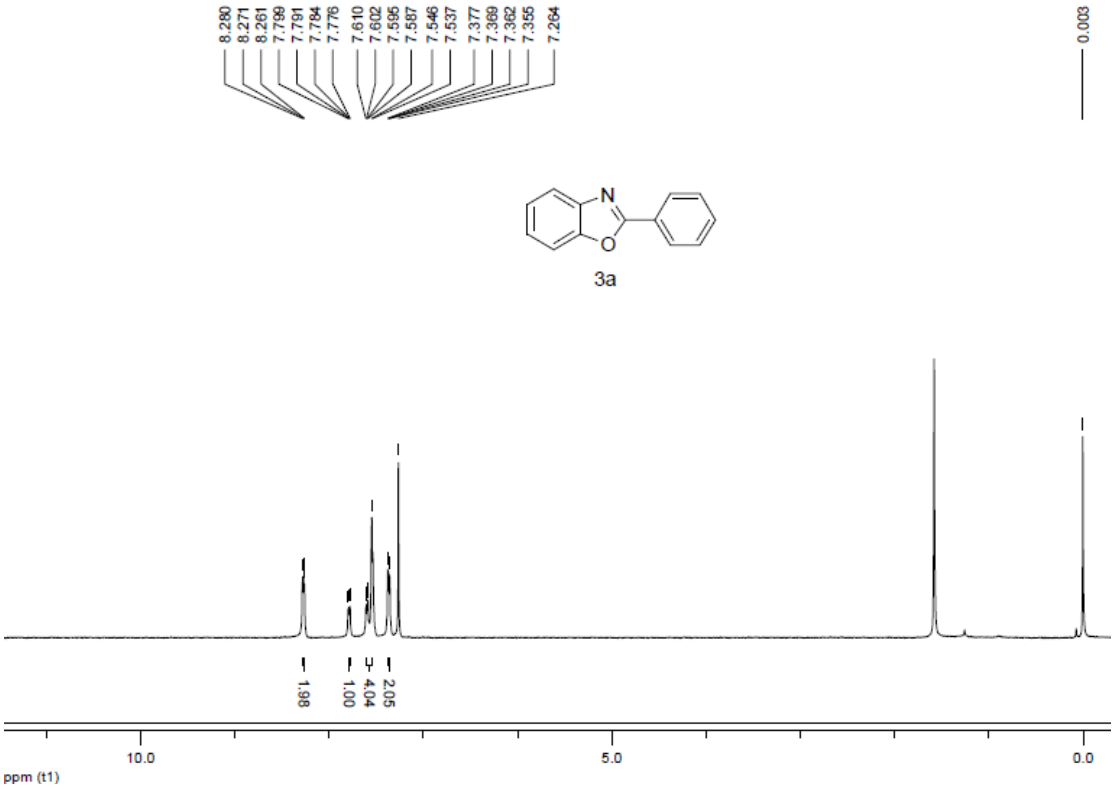
[3] L. Wang, X. Ren, J. Yu, Y. Jiang, J. Cheng, *J. Org. Chem*. **2013**, *78*, 12076.

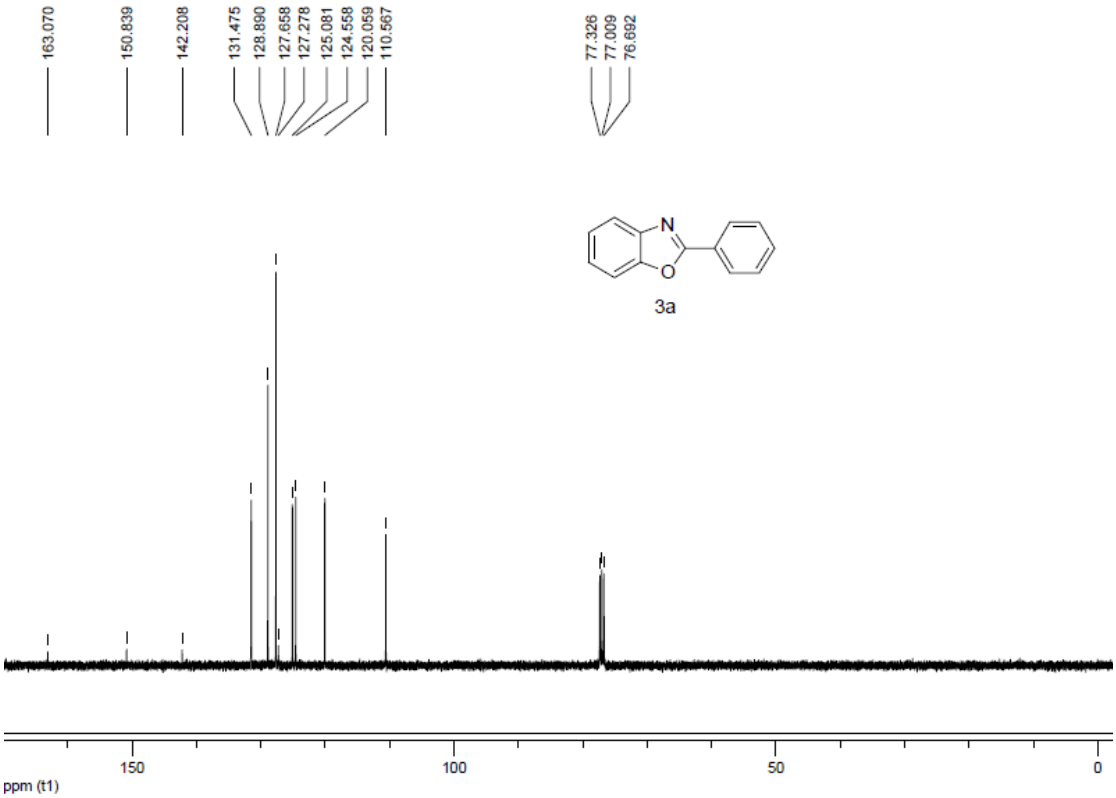
[4] Y. Cho, C. Y. Lee, D. C. Ha, C. H. Cheon, *Adv. Synth. Catal*. **2012**, *354*, 2992.

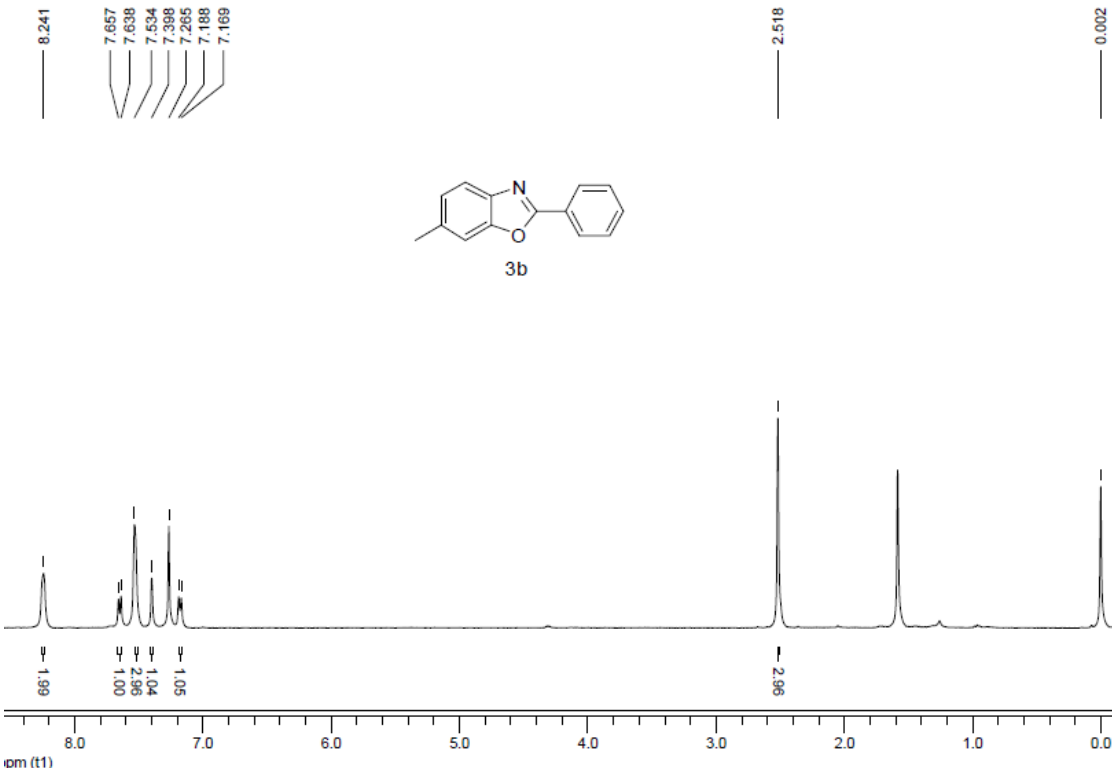
[5] X. W. Li, B. S. Wan, X. Z. Yu, *Org. Biomol. Chem*. **2012**, *10*, 7479.

[6] A. O'Brate, W. Brenzovich, D. Chen, P. Giannakakou, N. Giuseppone, J. Hao, X. Huang, P. Rao, G. Rassias, M. Reddy, S. Snyder, *J. Am. Chem. Soc.* **2004**, *126,* 12897.

^{1}H and ^{13}C NMR spectra of product



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7.265
7.188
7.169
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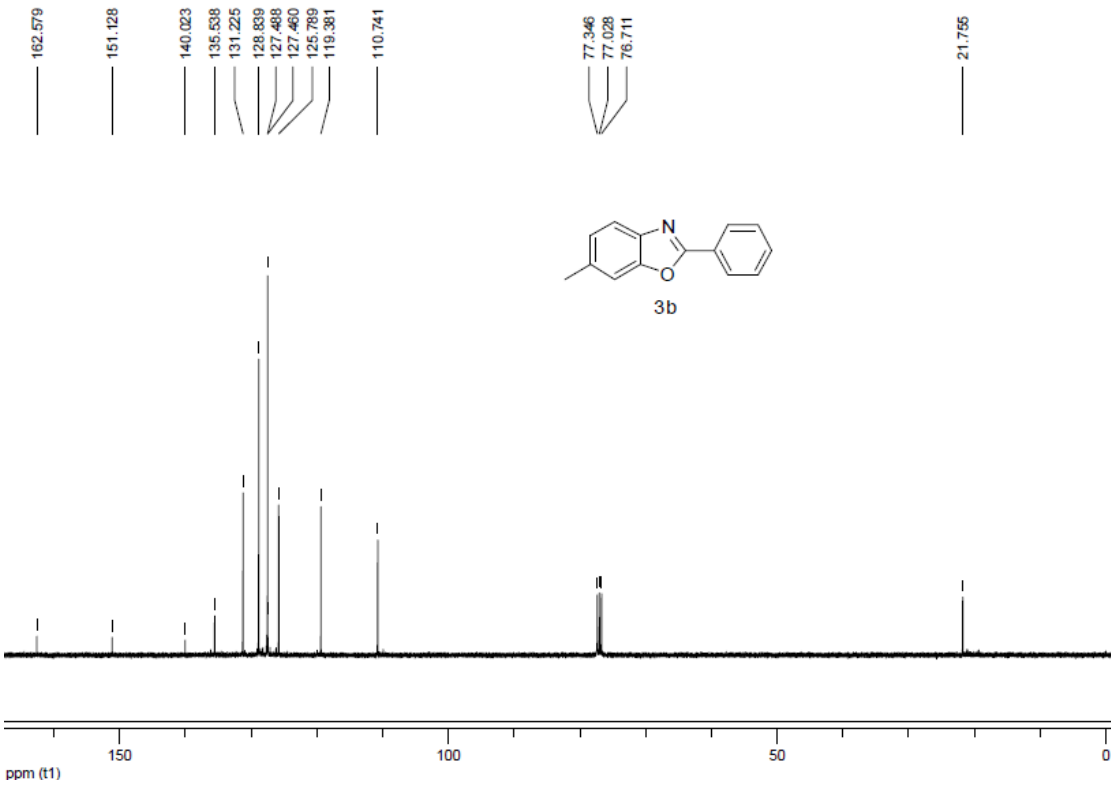
0.002
3b
1.99
1.00
2.96
1.04
1.05
2.96
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)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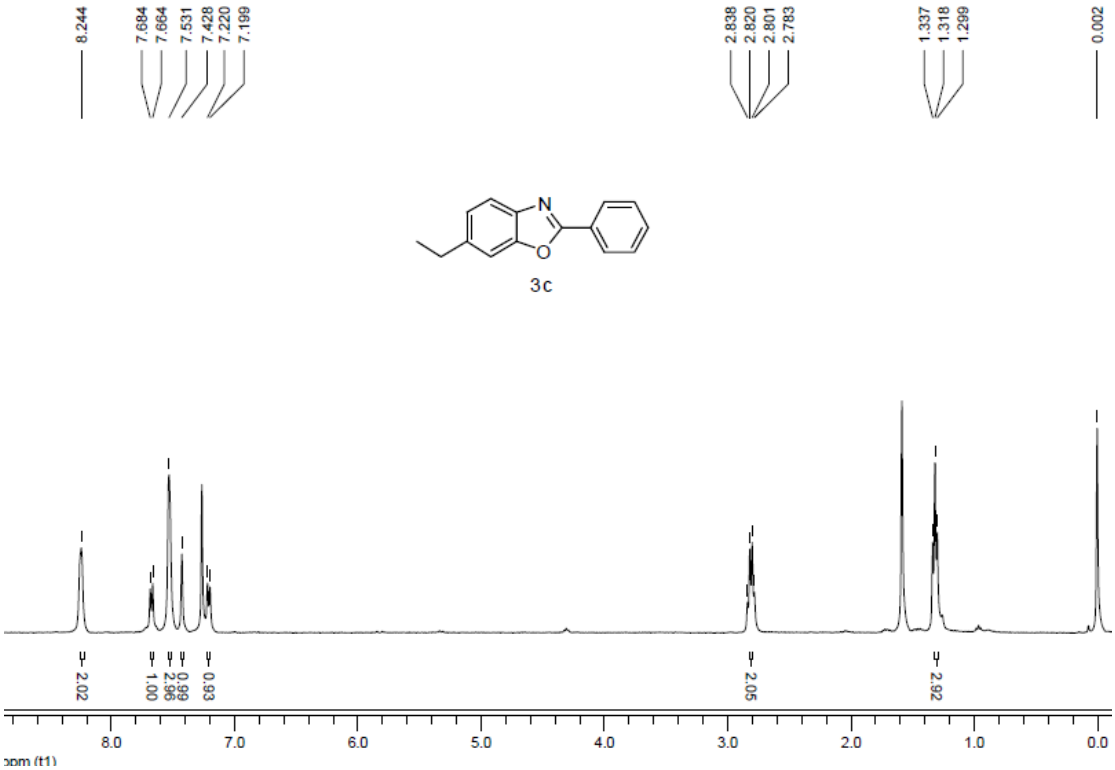
ppm (t1)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1.318
1.299
0.002
3c
2.02
1.00
2.96
0.99
0.93
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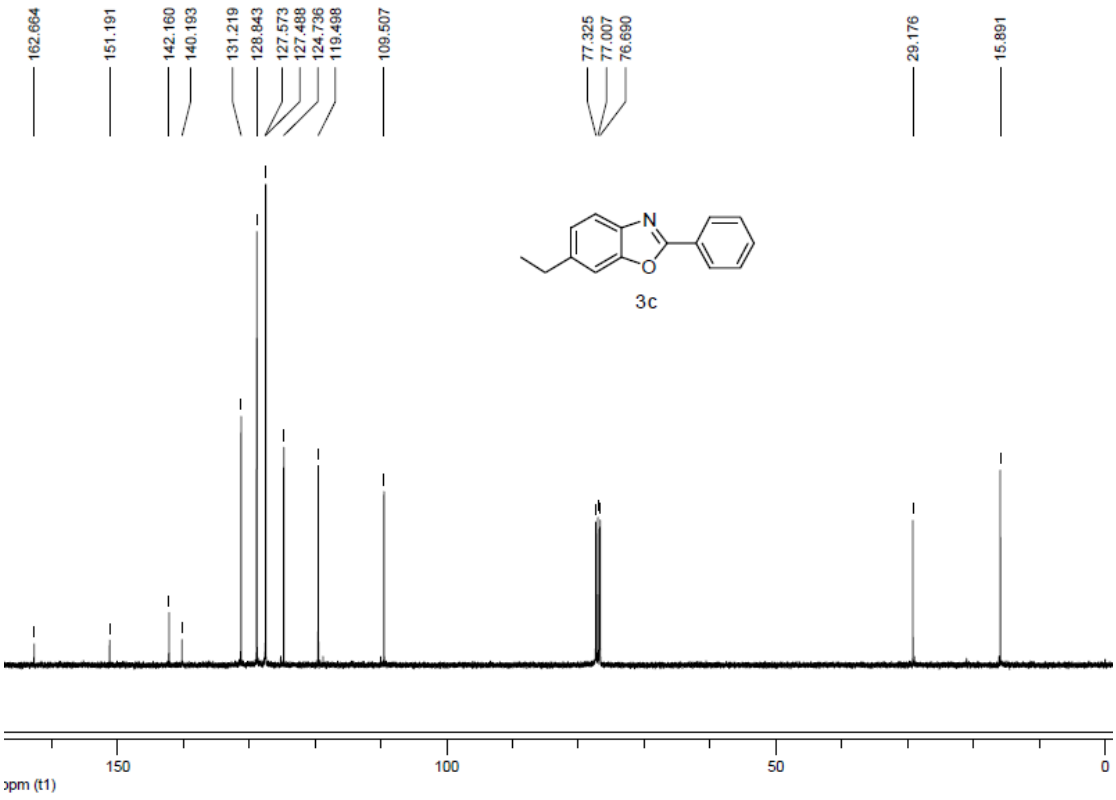
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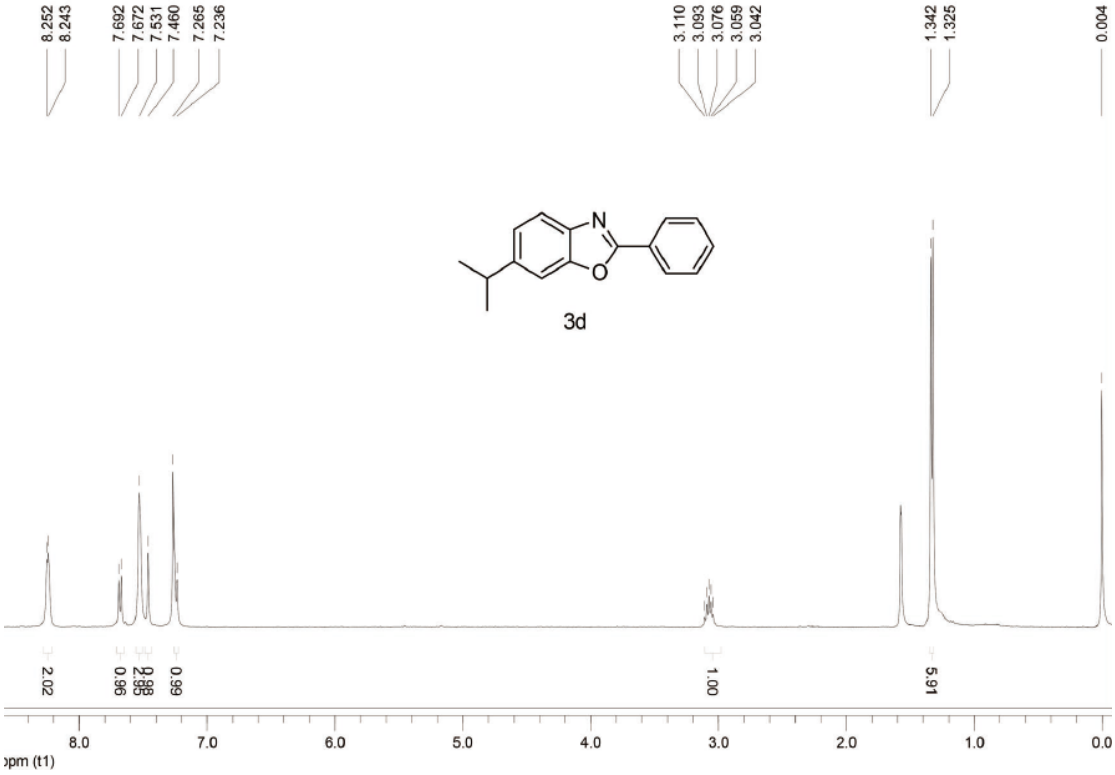
ppm (t1)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1.325
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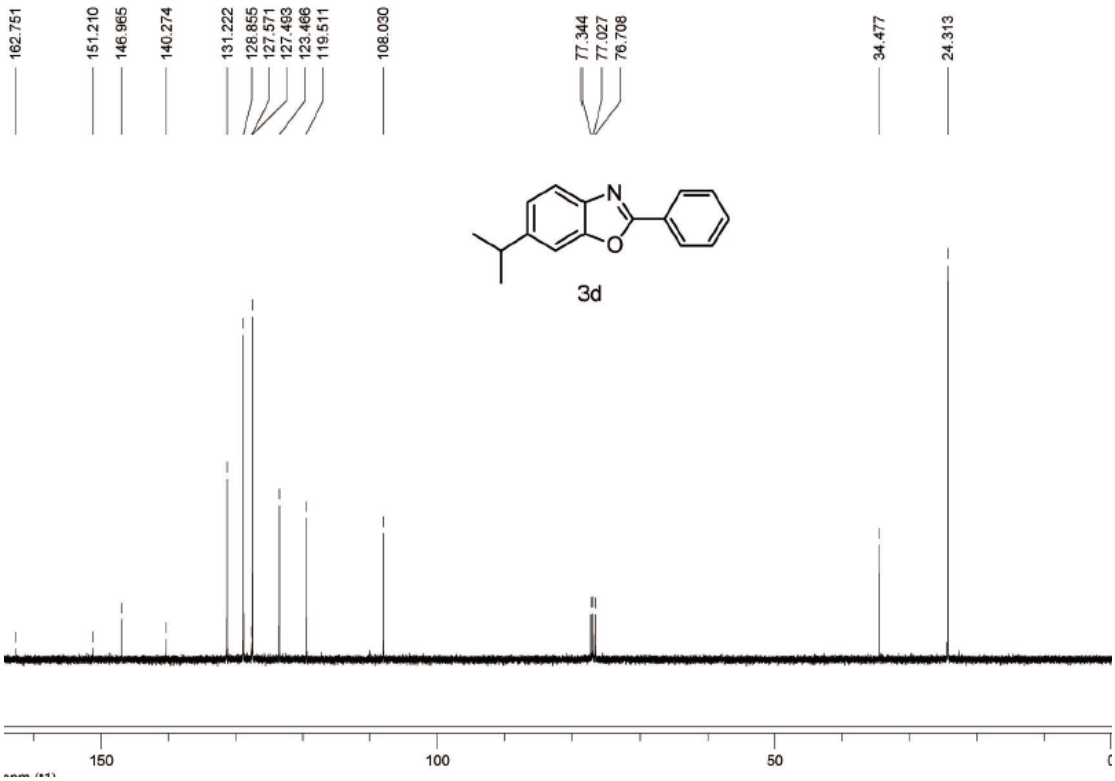
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34.477
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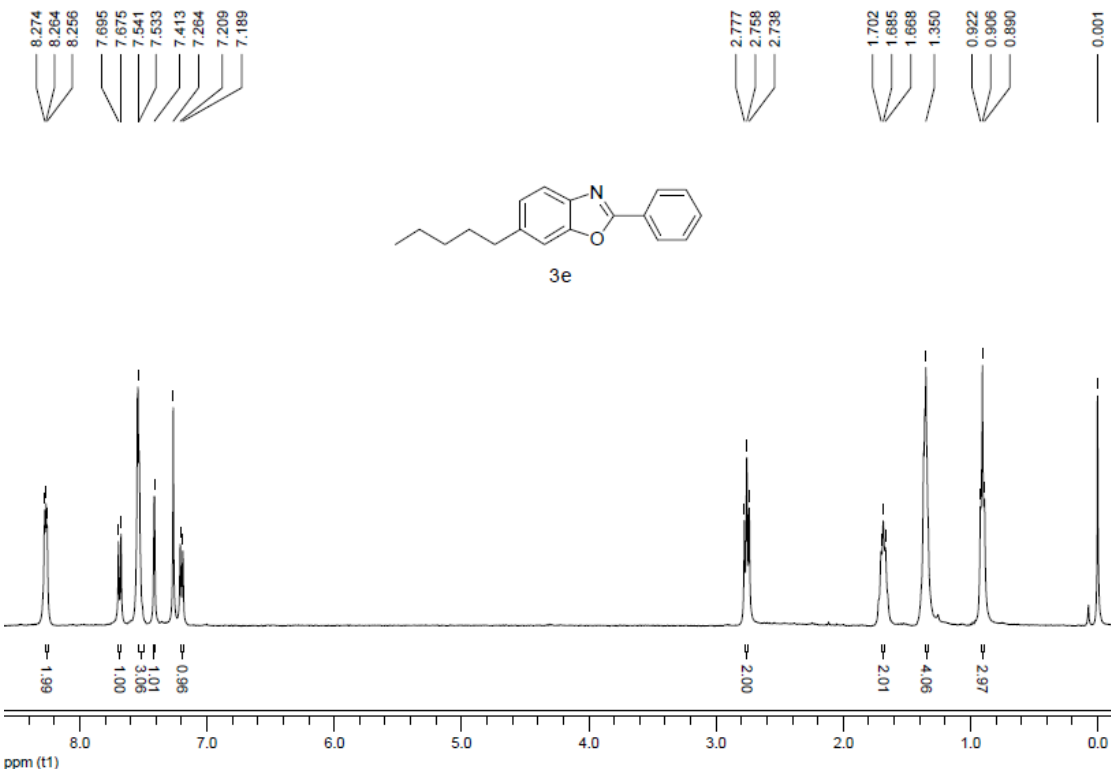
100
50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2.758
2.738
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1.685
1.668
1.350
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0.906
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3e
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1.00
3.06
1.01
0.96
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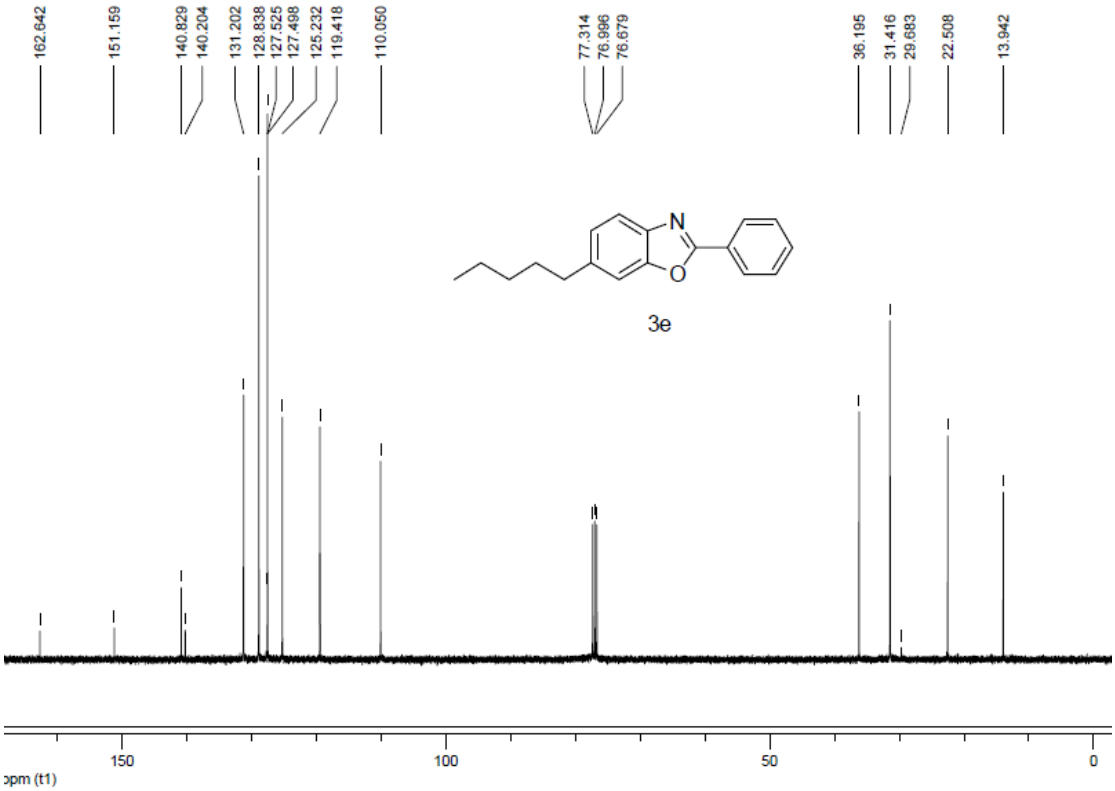
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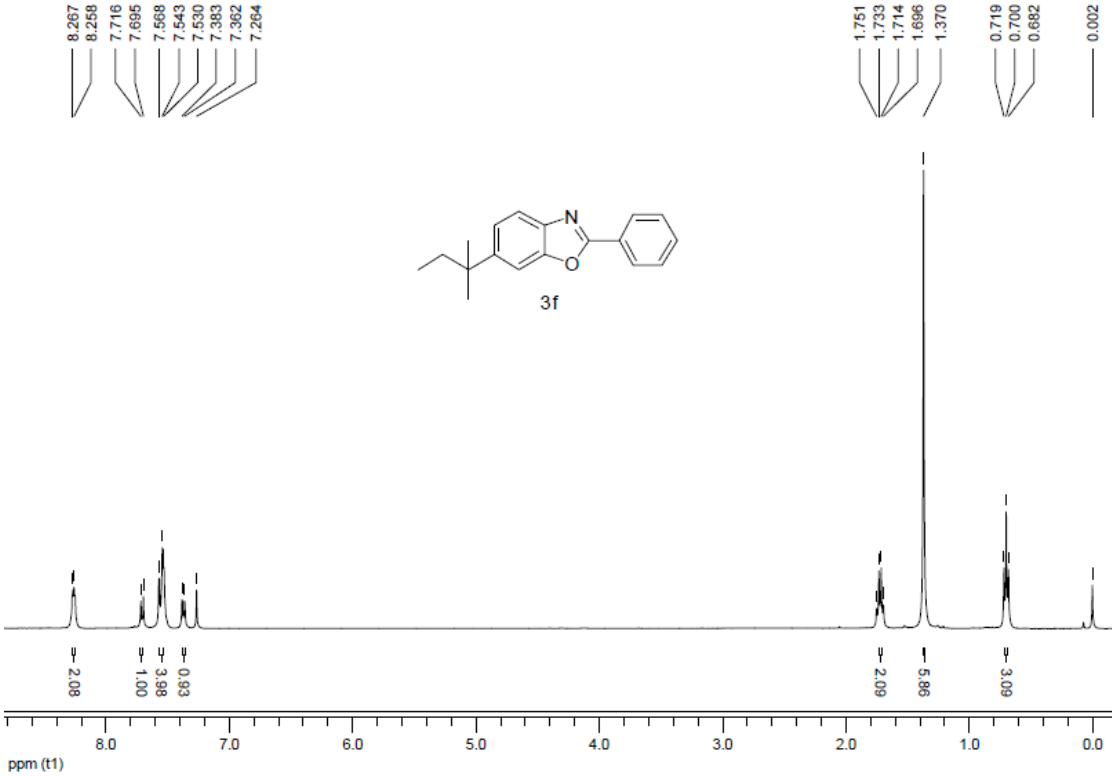
ppm (t1)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1.714
1.696
1.370
0.719
0.700
0.682
0.002
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O
3f
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1.00
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2.09
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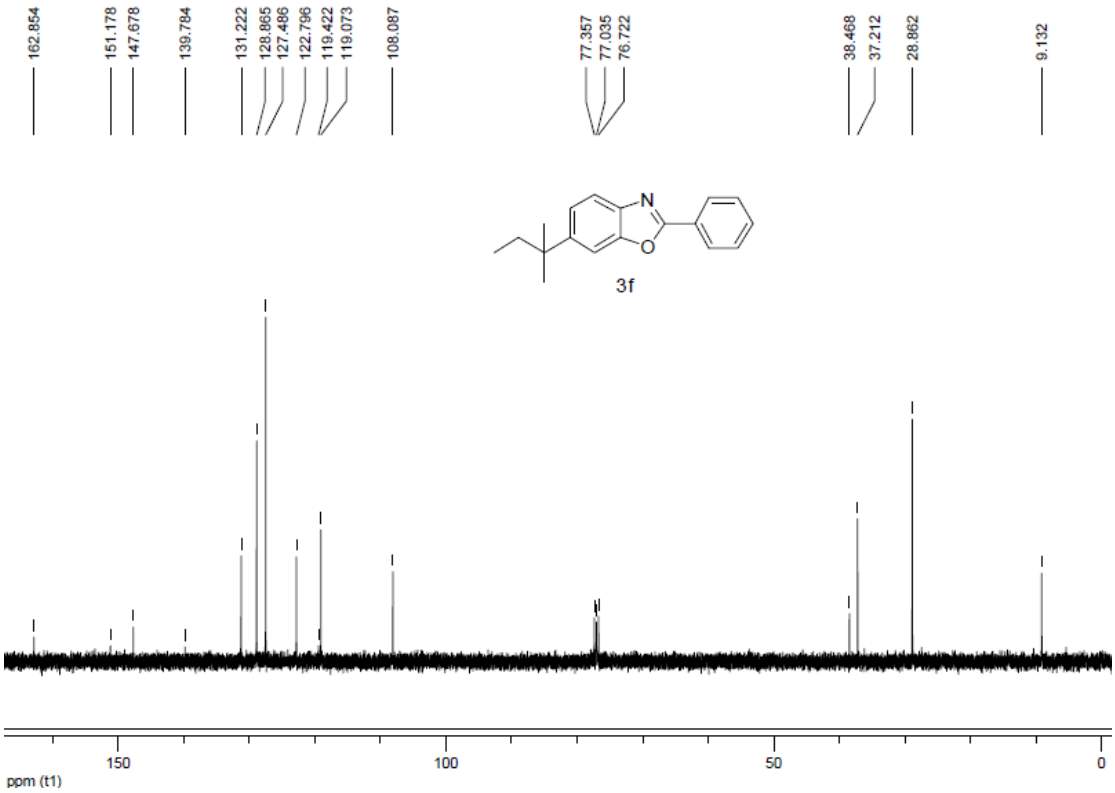
ppm (t1)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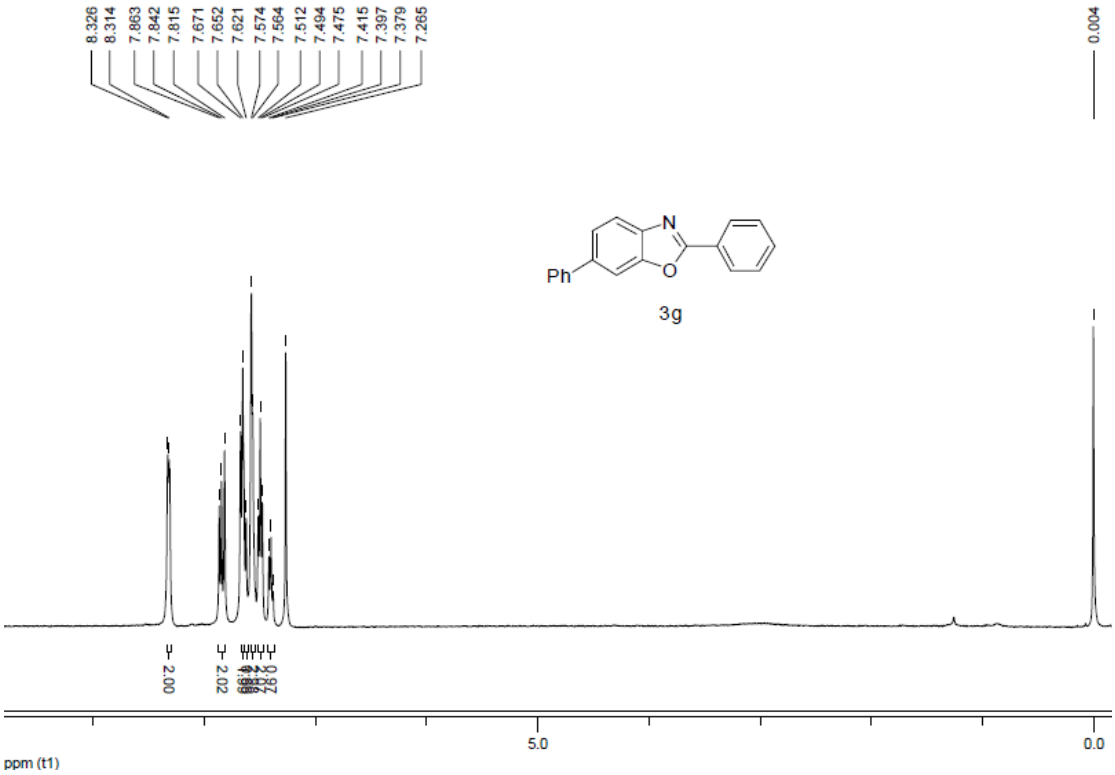
ppm (t1)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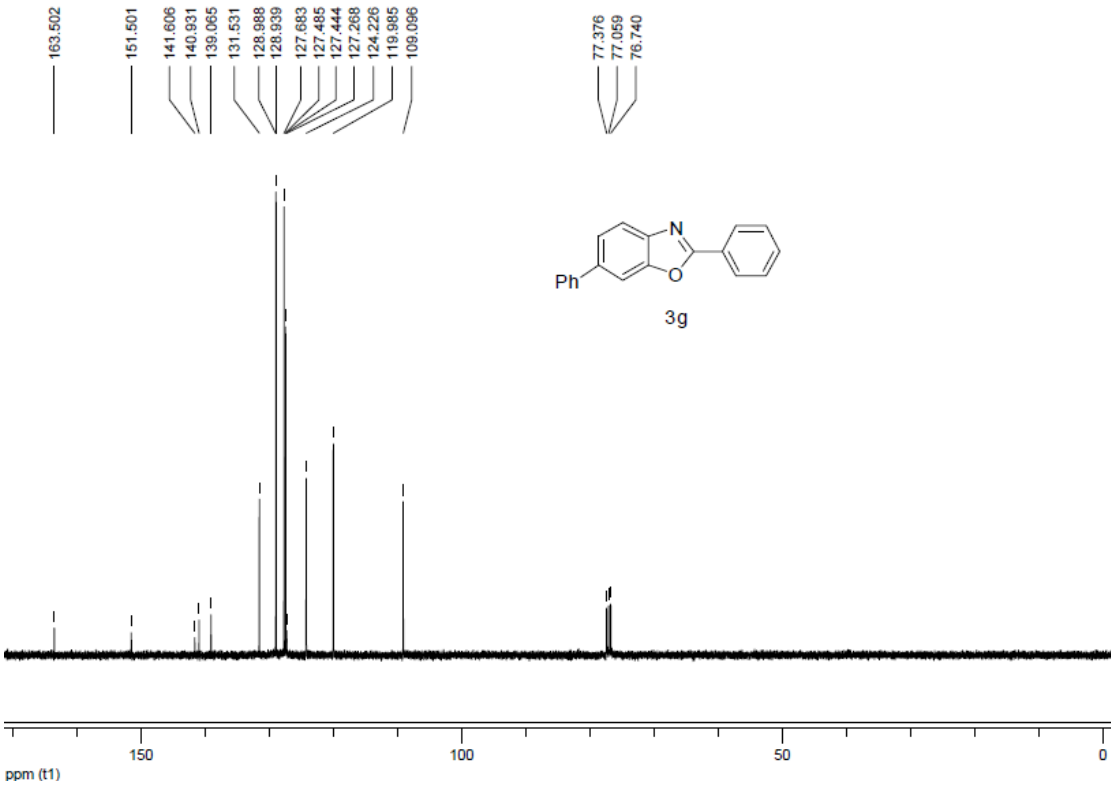
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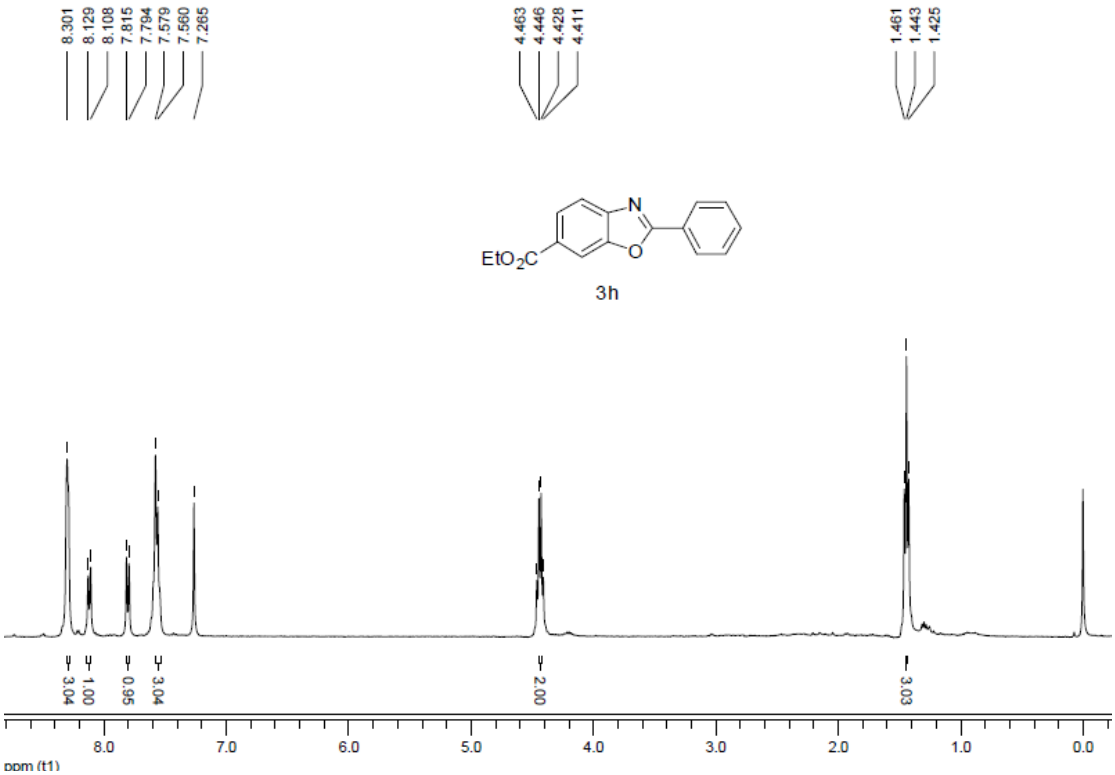
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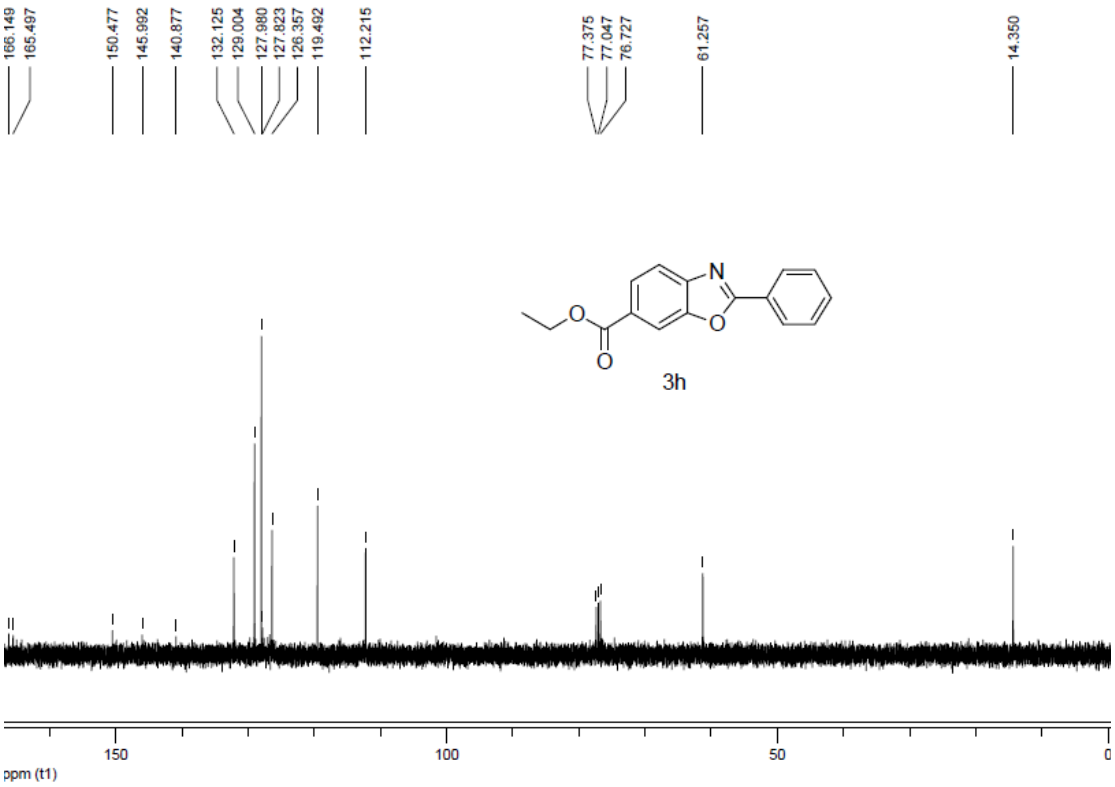
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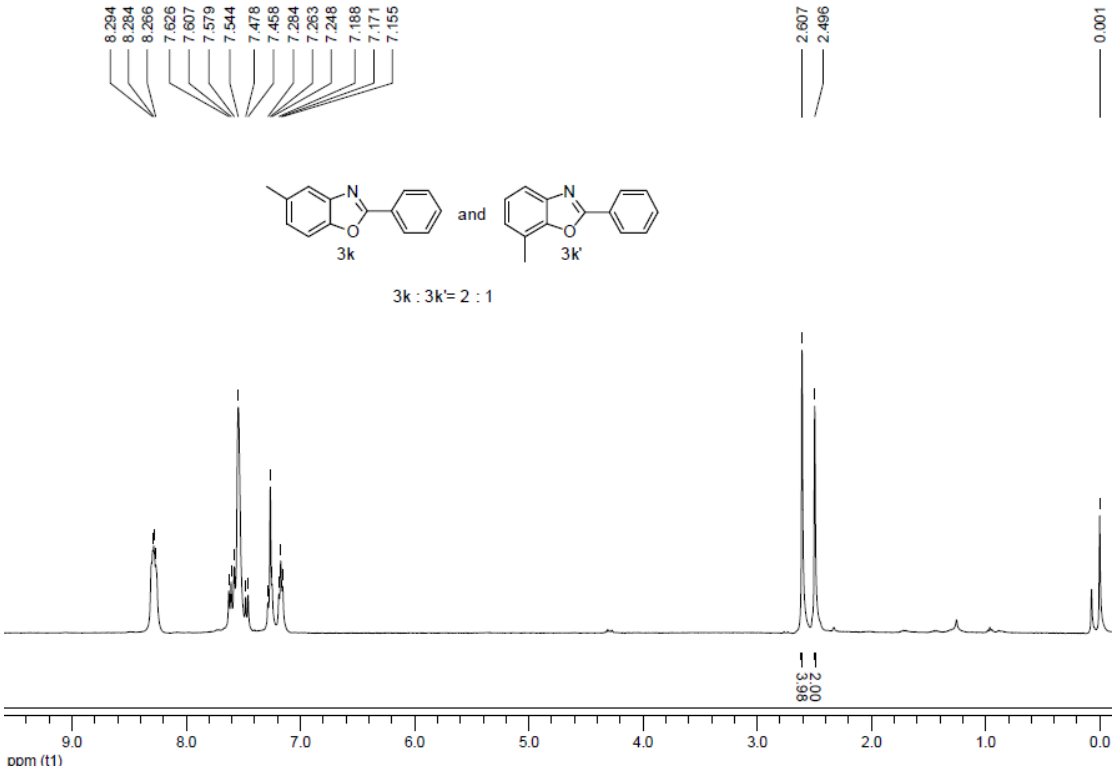
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7.188
7.171
7.155
2.607
2.496
0.001
N
O
3k
and
N
O
3k'
3k : 3k'= 2 : 1
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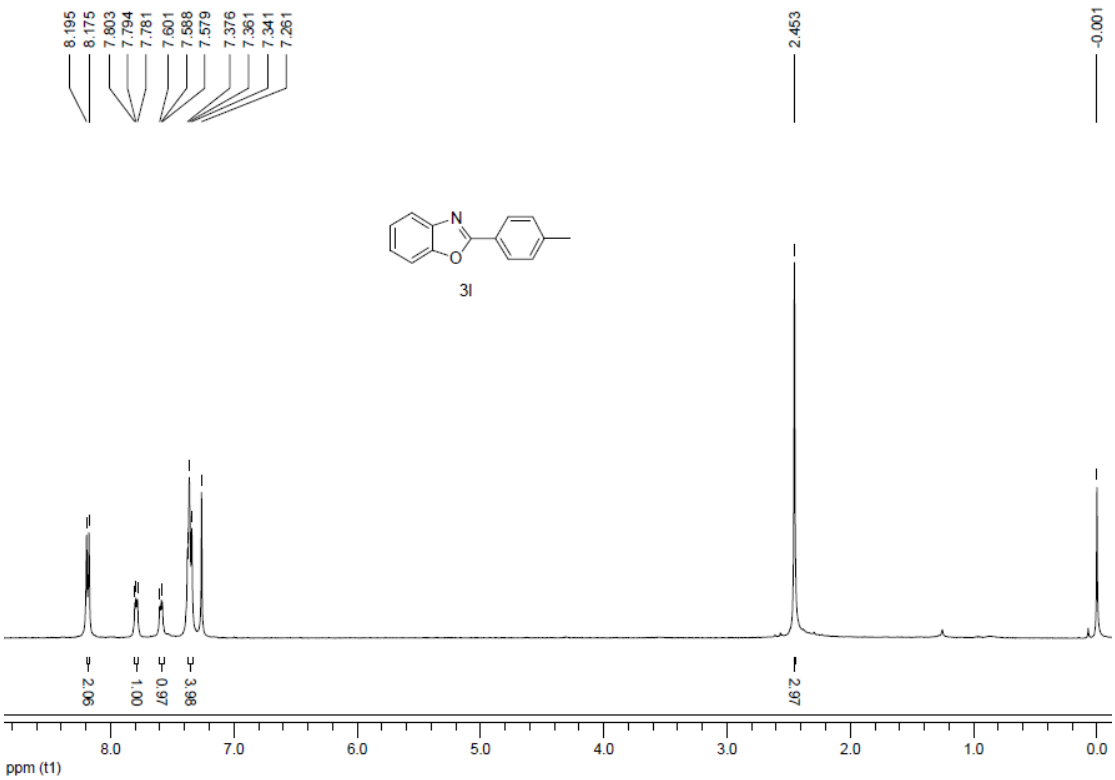
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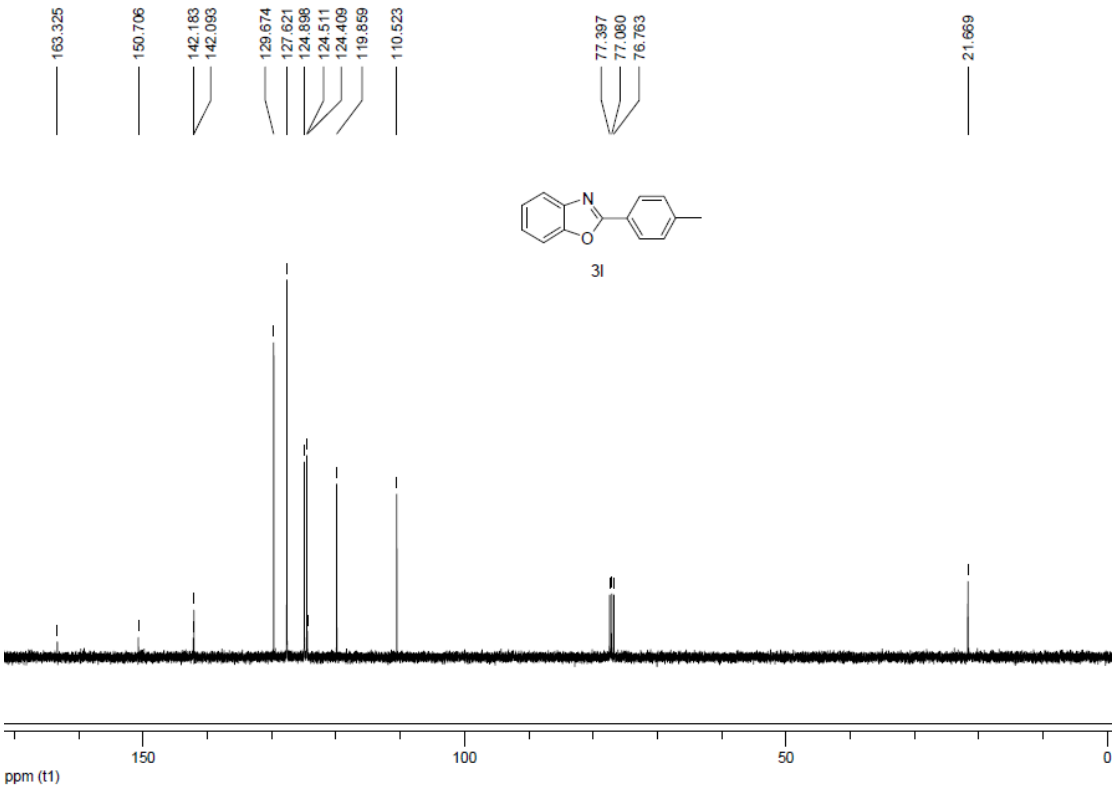
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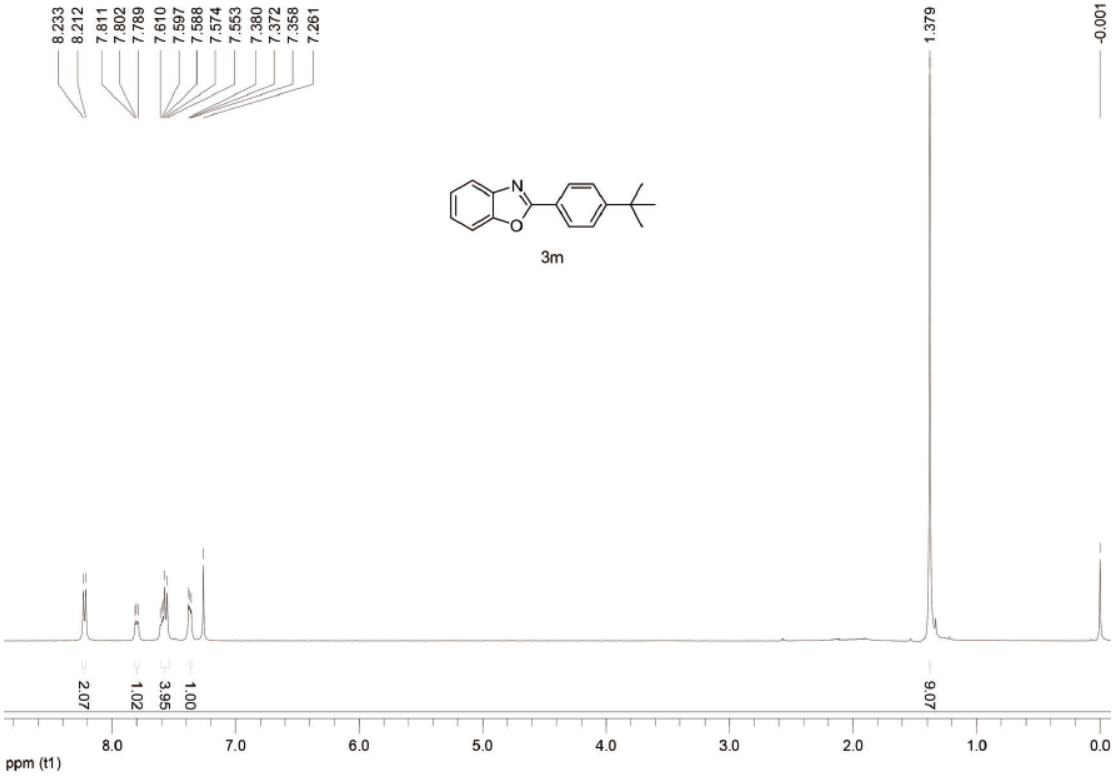
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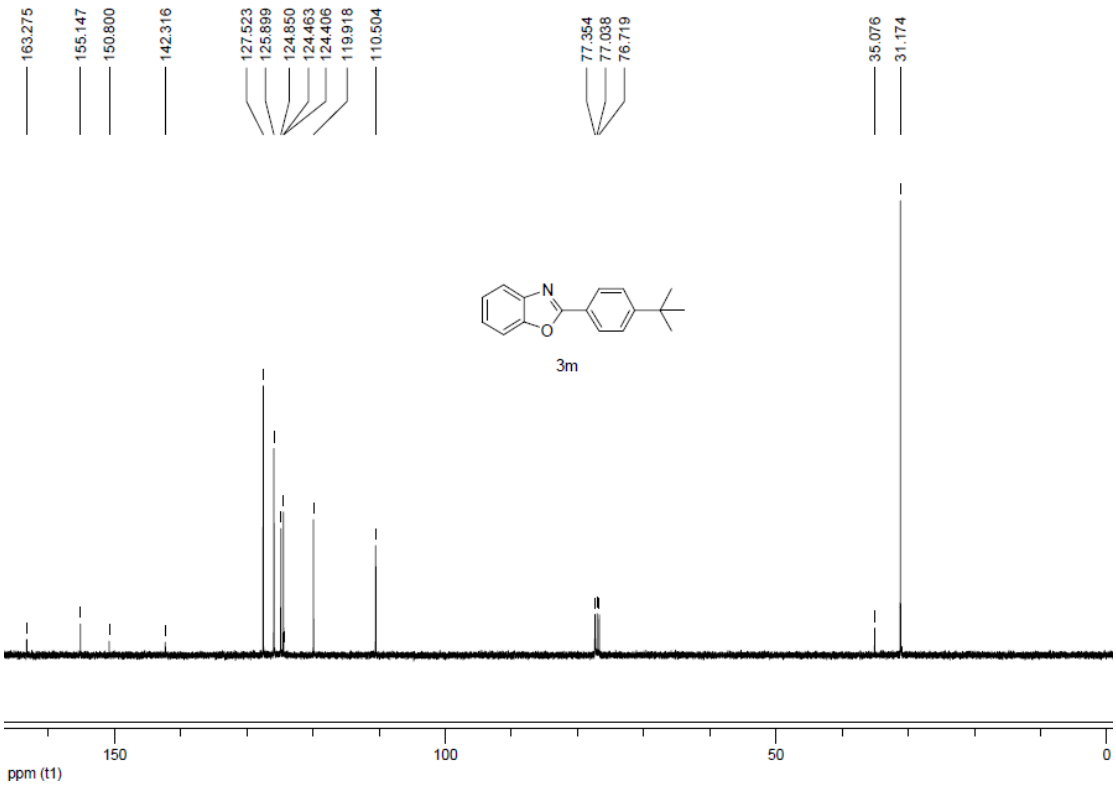
ppm (t1)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150
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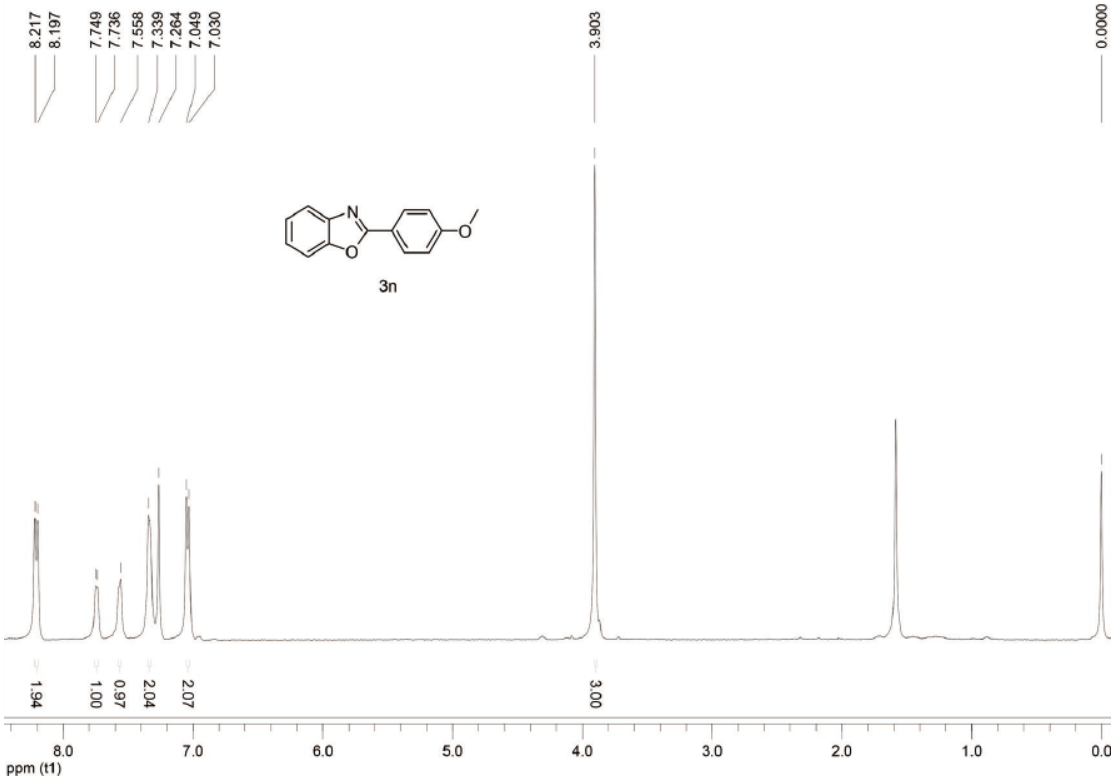
ppm (t1)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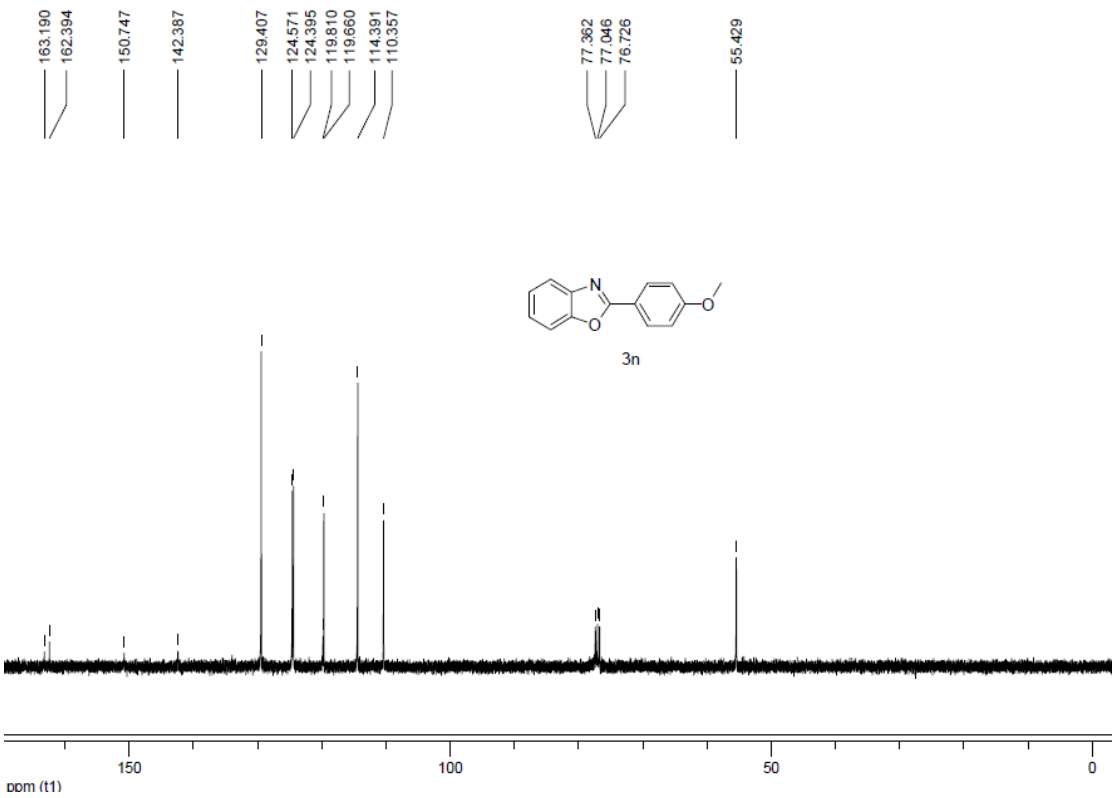
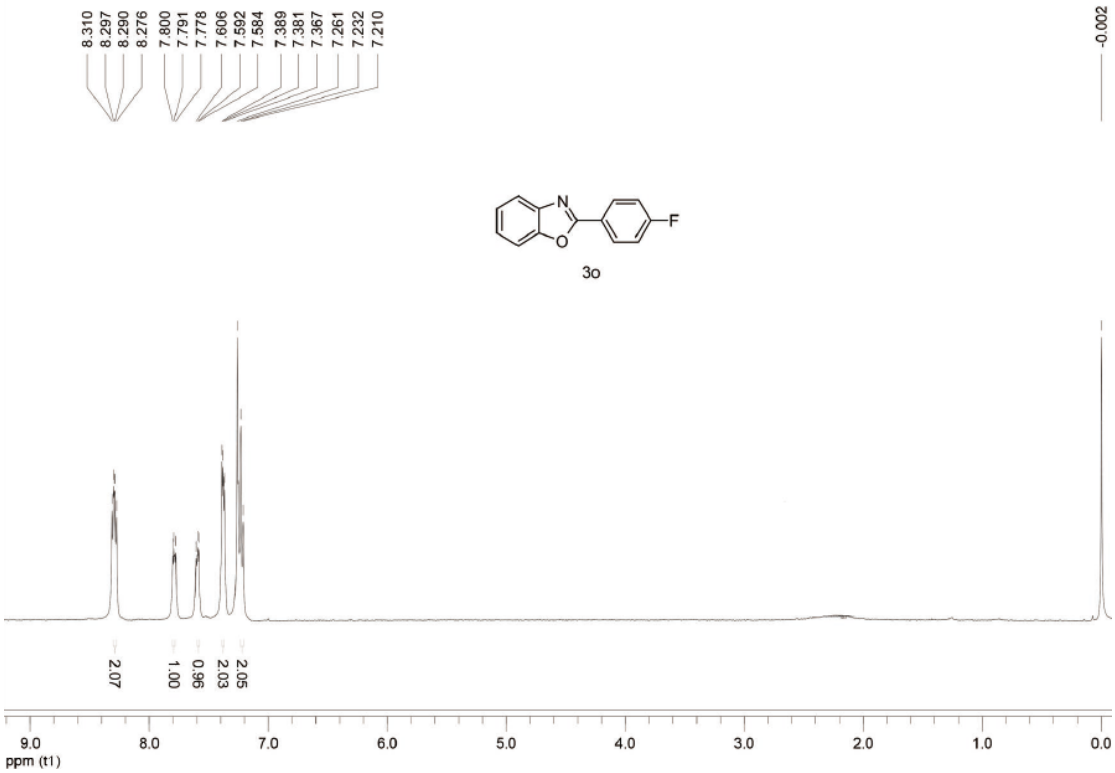
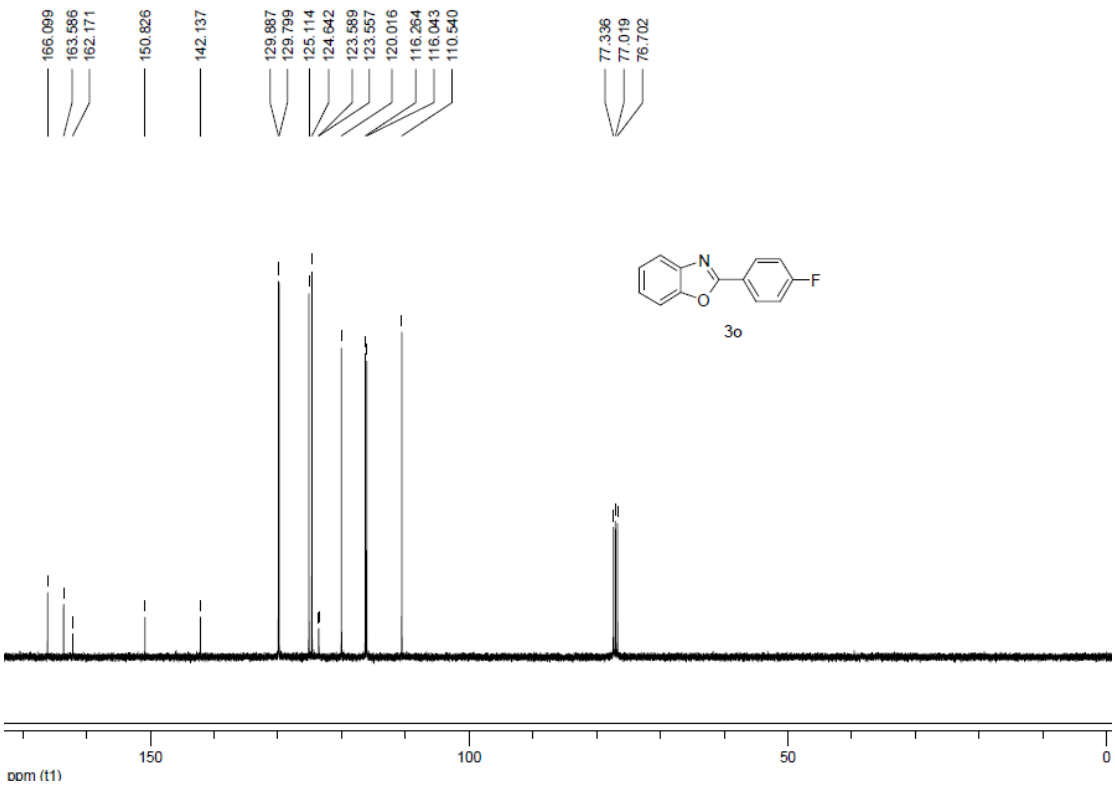
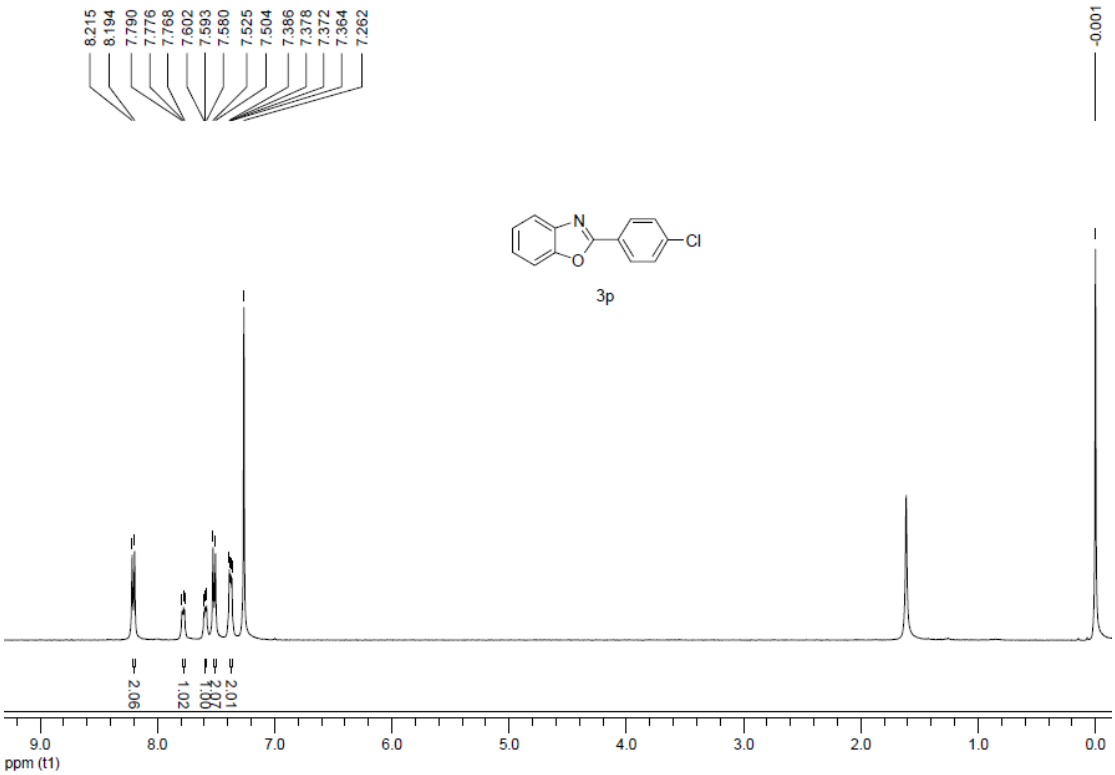
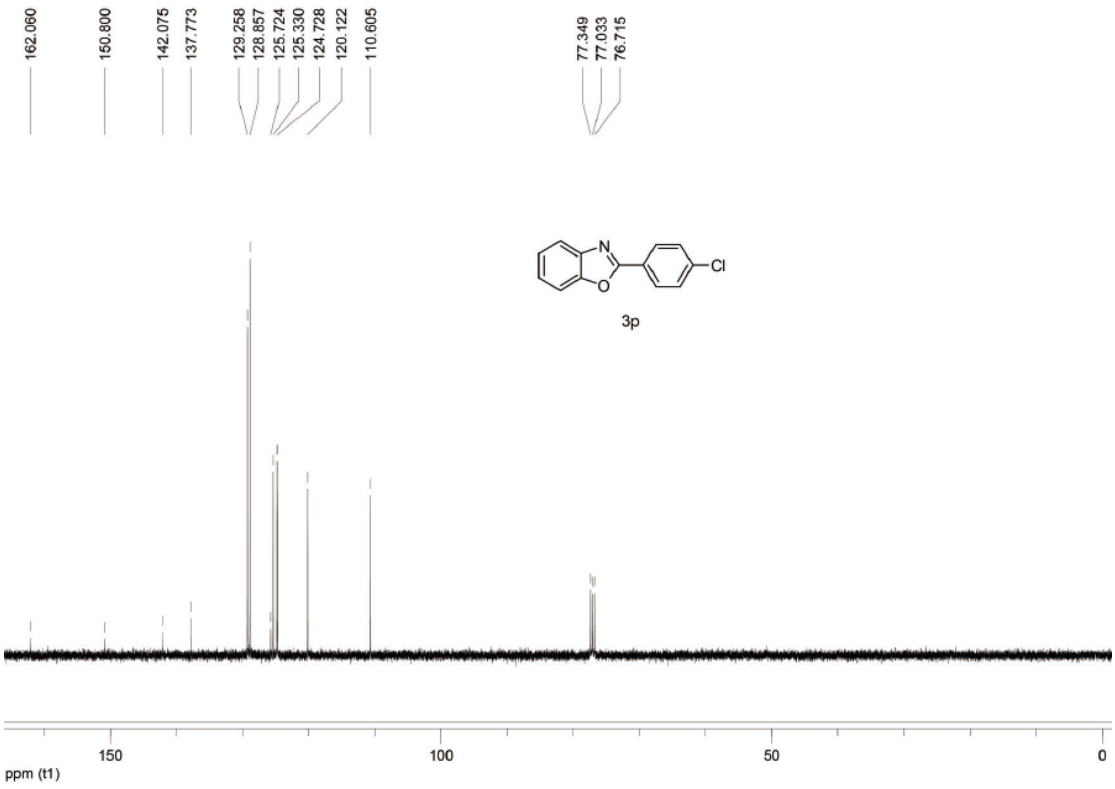
0.0
ppm (t1)

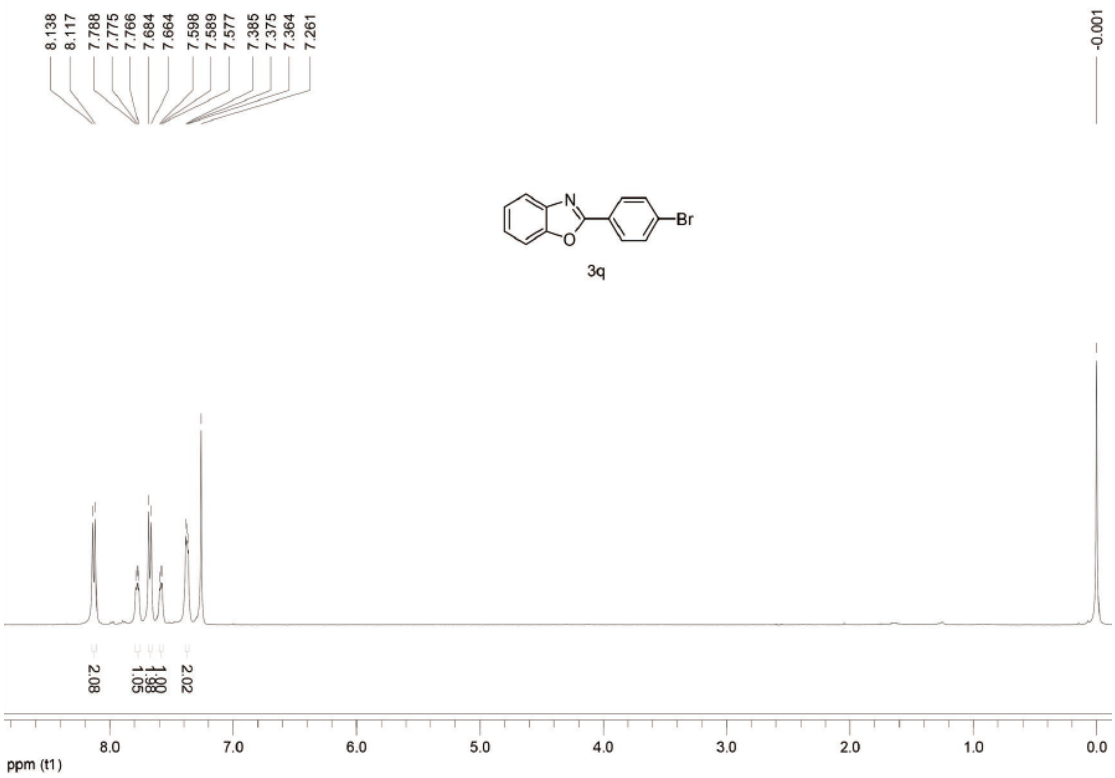

163.190
162.394
150.747
142.387
129.407
124.571
124.395
119.810
119.660
114.391
110.357
77.362
77.046
76.726
55.429
3n
150
100
50
0
ppm (t1)

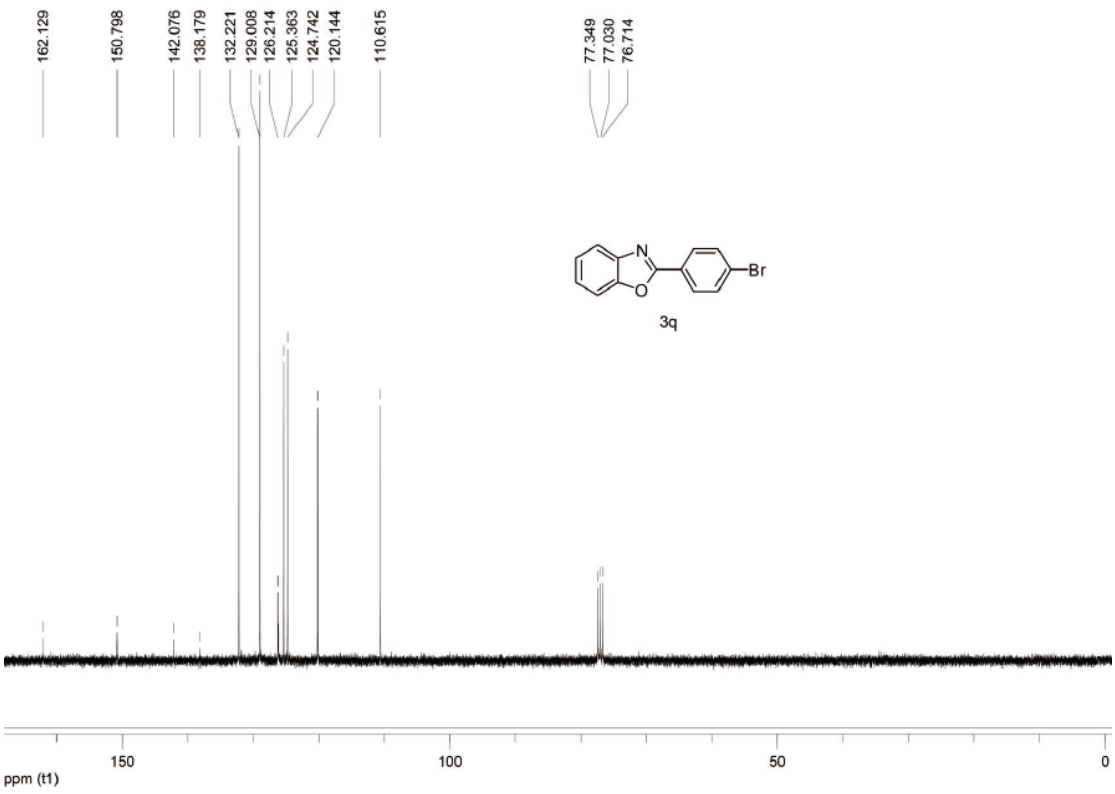

8.310
8.297
8.290
8.276
7.800
7.791
7.778
7.606
7.592
7.584
7.389
7.381
7.367
7.261
7.232
7.210
-0.002
N
O
F
3o
2.07
1.00
0.96
2.03
2.05
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

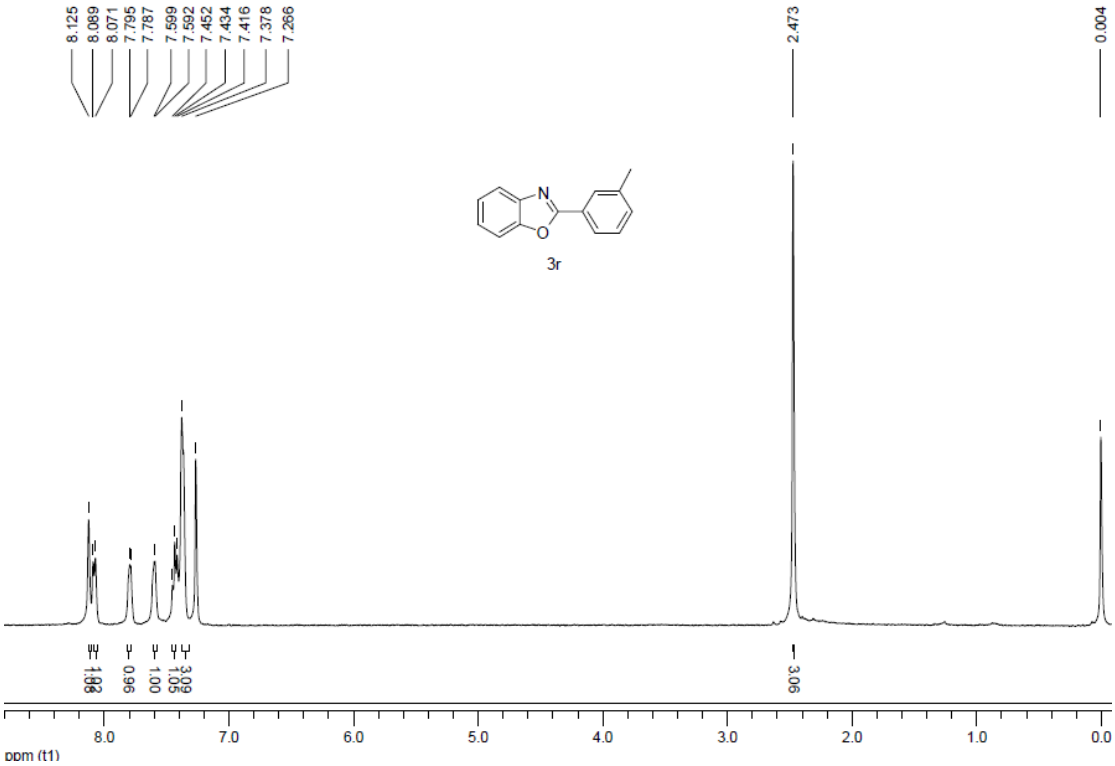

166.099
163.586
162.171
150.826
142.137
129.887
129.799
125.114
124.642
123.589
123.557
120.016
116.264
116.043
110.540
77.336
77.019
76.702
N
O
F
3o
150
100
50
0
ppm (t1)

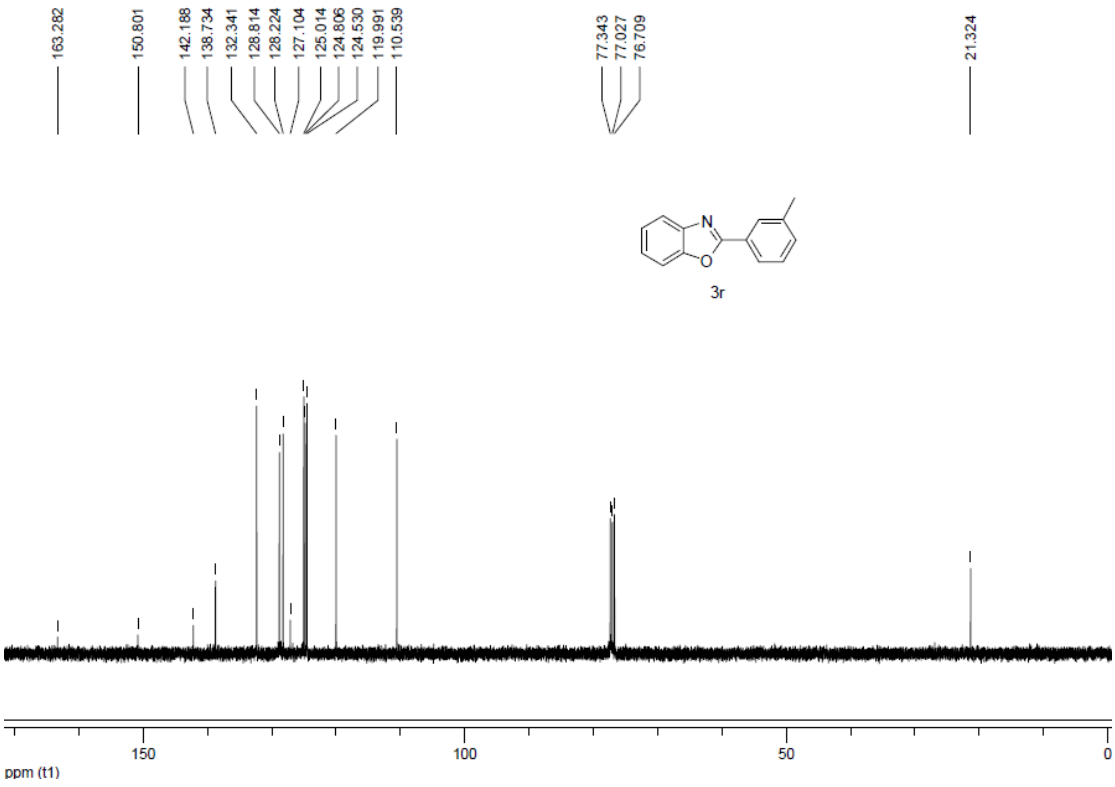

8.215
8.194
7.790
7.776
7.768
7.602
7.593
7.580
7.525
7.504
7.386
7.378
7.372
7.364
7.262
-0.001
N
O
Cl
3p
2.06
1.02
2.00
2.07
2.01
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

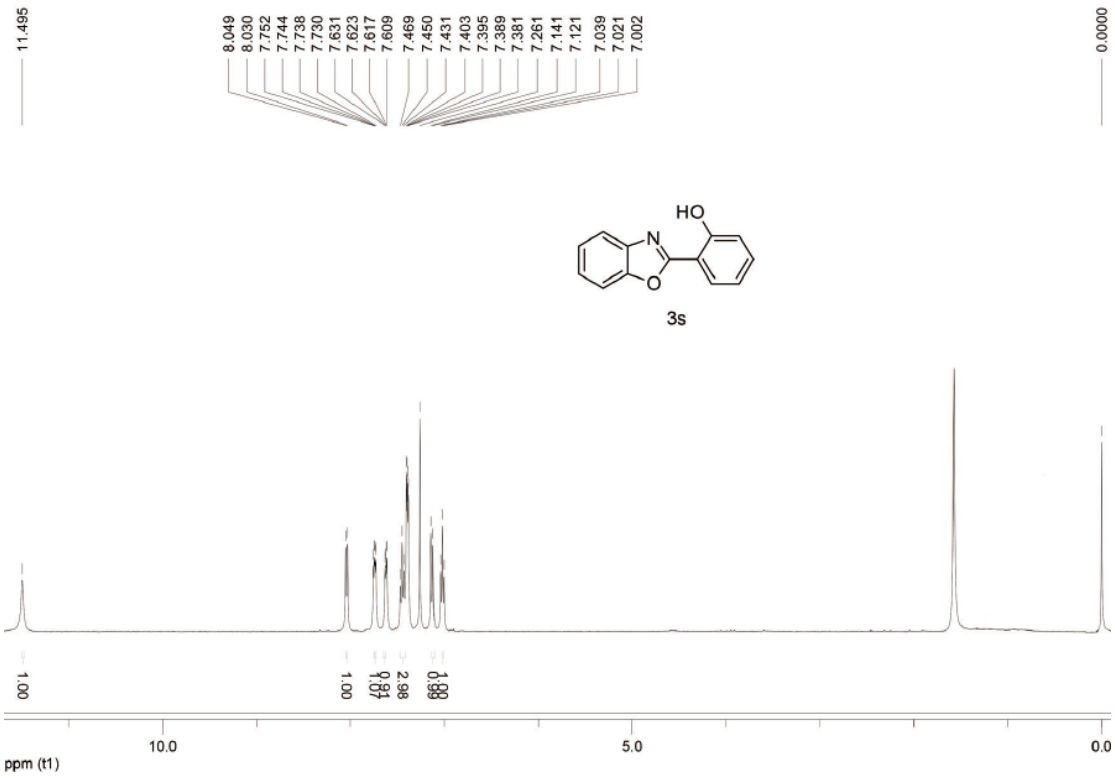

162.060
150.800
142.075
137.773
129.258
128.857
125.724
125.330
124.728
120.122
110.605
77.349
77.033
76.715
N
O
Cl
3p
150
100
50
0
ppm (t1)

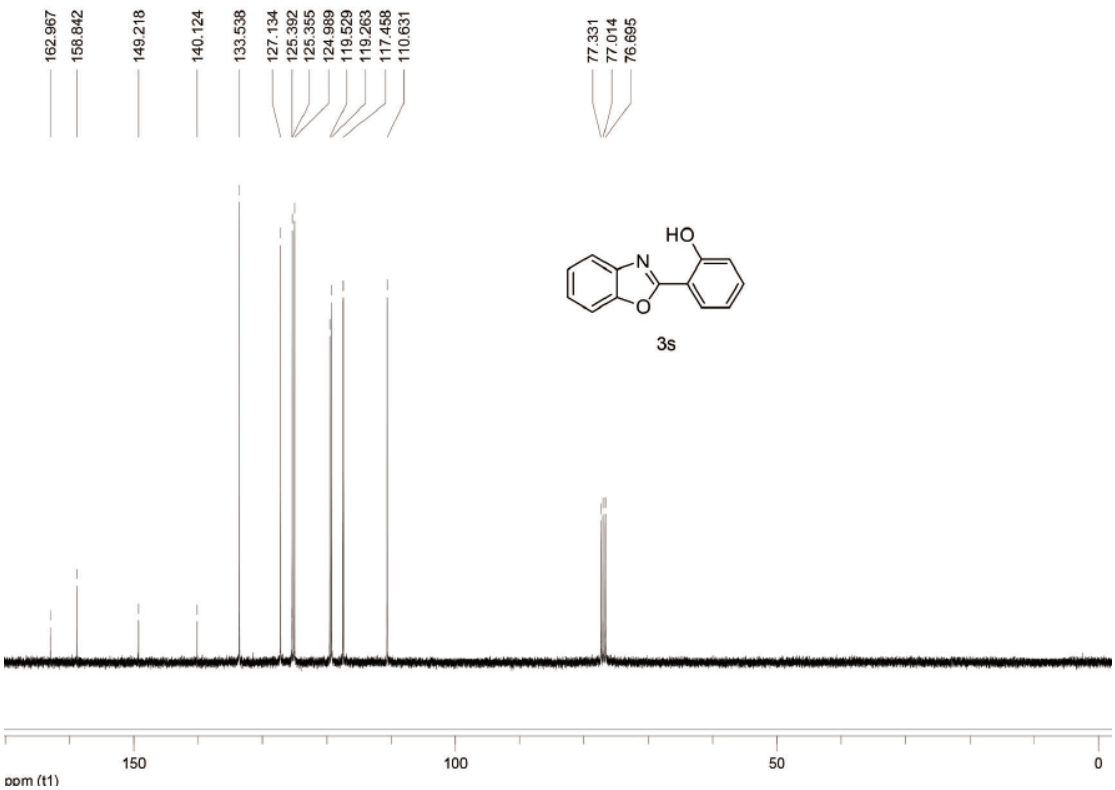

8.138
8.117
7.788
7.775
7.766
7.684
7.664
7.598
7.589
7.577
7.385
7.375
7.364
7.261
-0.001
N
O
Br
3q
2.08
1.05
1.88
1.00
2.02
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

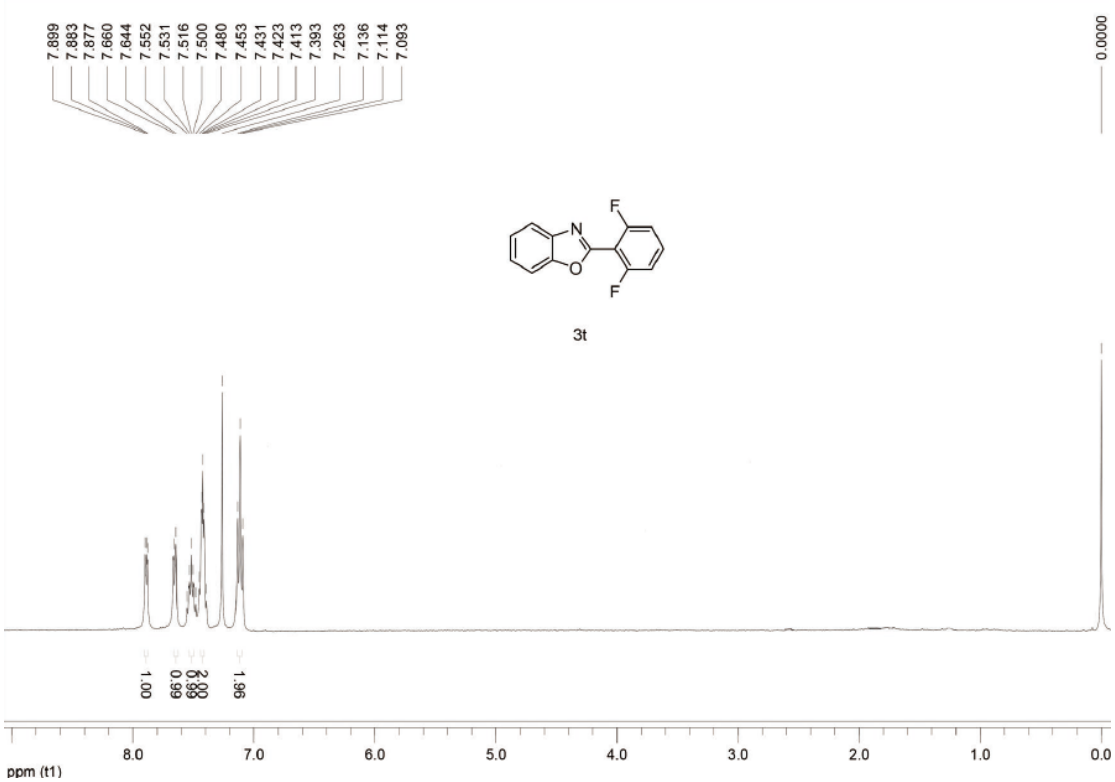

162.129
150.798
142.076
138.179
132.221
129.008
126.214
125.363
124.742
120.144
110.615
77.349
77.030
76.714
N
O
Br
3q
150
100
50
0
ppm (t1)

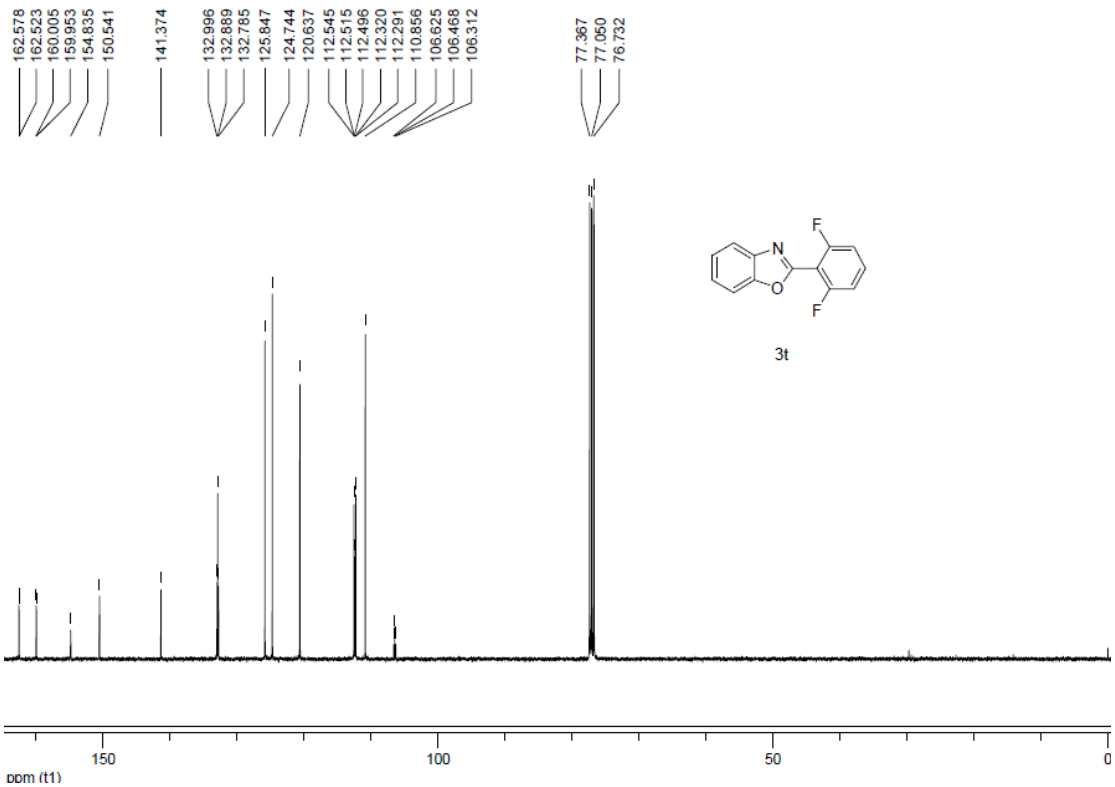

8.125
8.089
8.071
7.795
7.787
7.599
7.592
7.452
7.434
7.416
7.378
7.266
2.473
0.004
3r
1.08
0.96
1.00
3.05
3.09
3.06
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

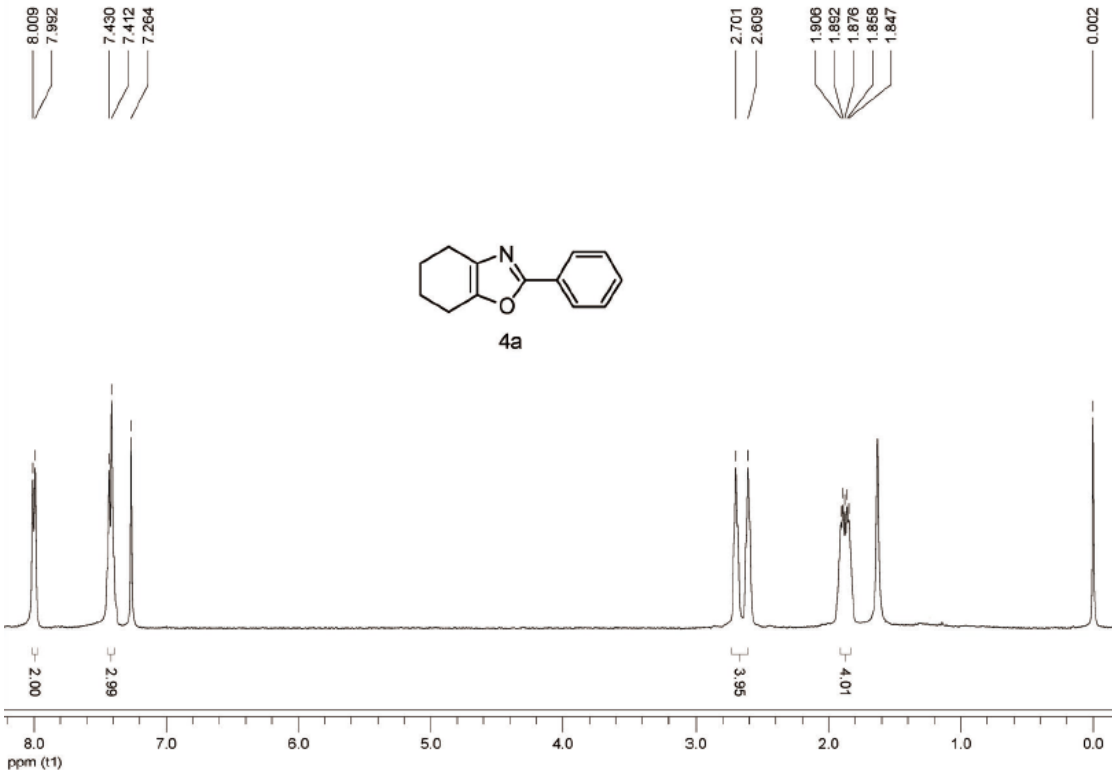

163.282
150.801
142.188
138.734
132.341
128.814
128.224
127.104
125.014
124.806
124.530
119.991
110.539
77.343
77.027
76.709
21.324
3r
150
100
50
0
ppm (t1)

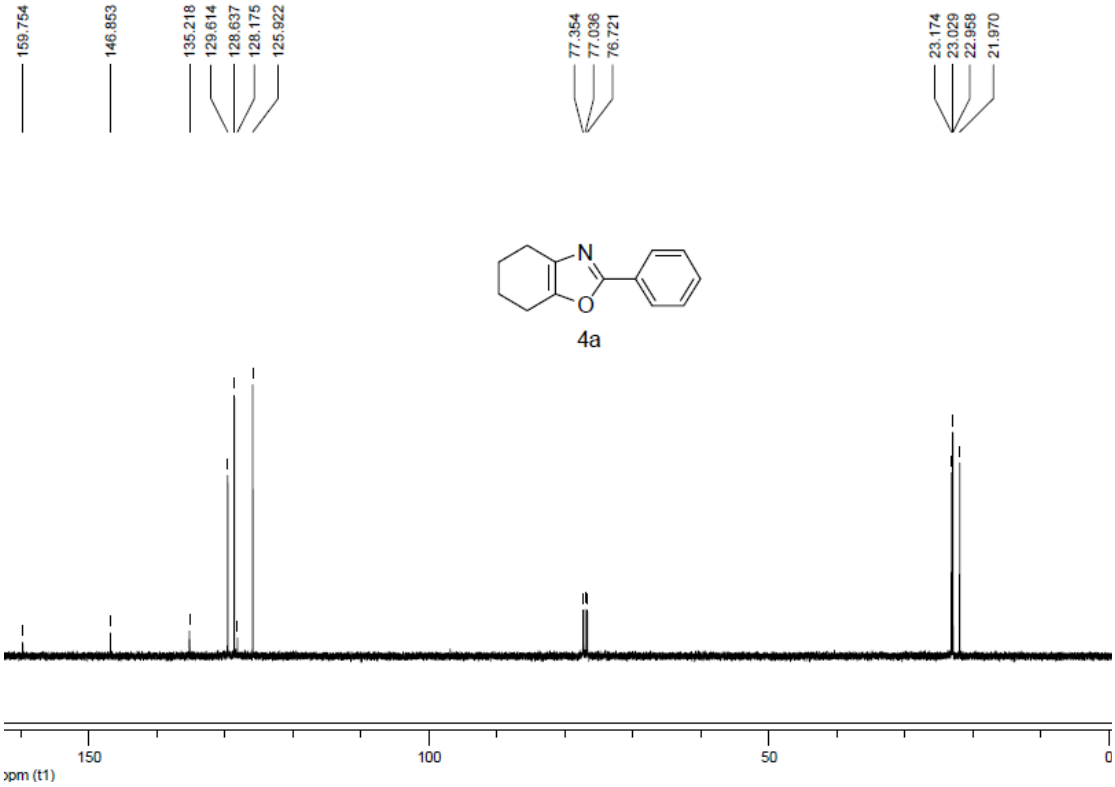

11.495
8.049
8.030
7.752
7.744
7.738
7.730
7.631
7.623
7.617
7.609
7.469
7.450
7.431
7.403
7.395
7.389
7.381
7.261
7.141
7.121
7.039
7.021
7.002
0.0000
HO
N
O
3s
1.00
1.00
1.07
0.81
2.98
0.99
1.00
10.0
5.0
0.0
ppm (t1)


162.967
158.842
149.218
140.124
133.538
127.134
125.392
125.355
124.989
119.529
119.263
117.458
110.631
77.331
77.014
76.695
HO
N
O
3s
150
100
50
0
ppm (t1)

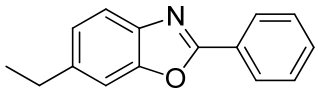

7.899
7.883
7.877
7.660
7.644
7.552
7.531
7.516
7.500
7.480
7.453
7.431
7.423
7.413
7.393
7.263
7.136
7.114
7.093
0.0000
F
N
O
F
3t
1.00
0.99
2.00
0.98
1.96
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


162.578
162.523
160.005
159.953
154.835
150.541
141.374
132.996
132.889
132.785
125.847
124.744
120.637
112.545
112.515
112.496
112.320
112.291
110.856
106.625
106.468
106.312
77.367
77.050
76.732
F
N
O
F
3t
150
100
50
0
ppm (t1)

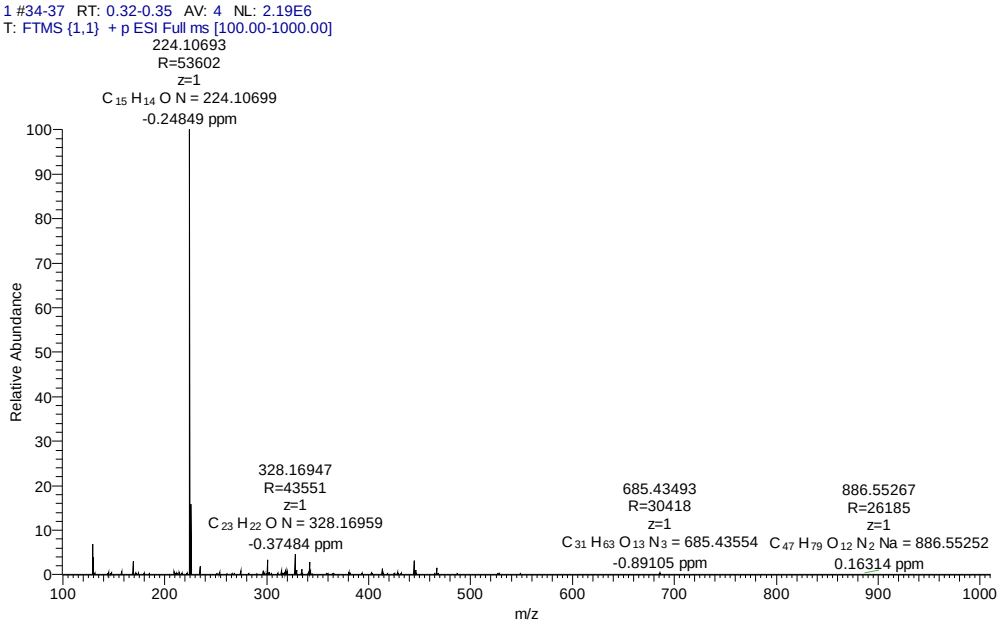

8.009
7.992
7.430
7.412
7.264
2.701
2.609
1.906
1.892
1.876
1.858
1.847
0.002
N
O
4a
2.00
2.99
3.95
4.01
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

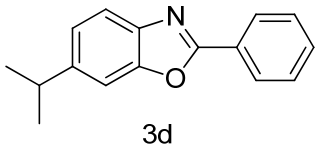

159.754
146.853
135.218
129.614
128.637
128.175
125.922
77.354
77.036
76.721
23.174
23.029
22.958
21.970
N
O
4a
150
100
50
0
ppm (t1)

HRMS (ESI) spectra of new products

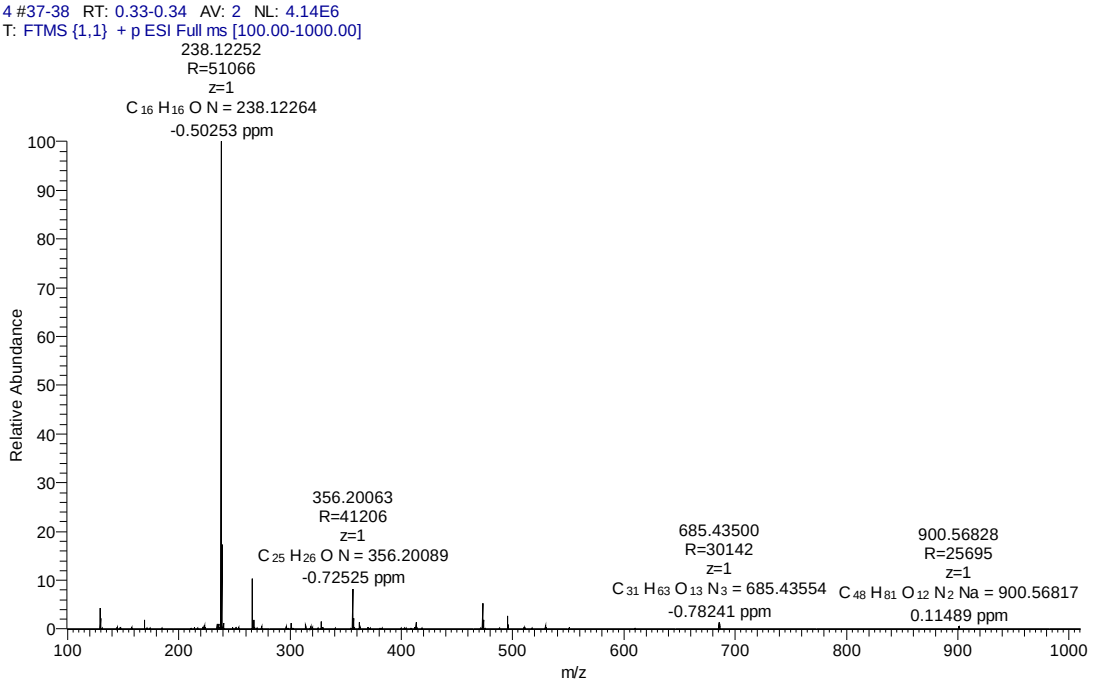


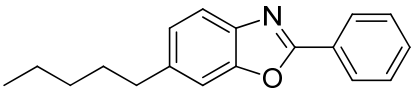
3c





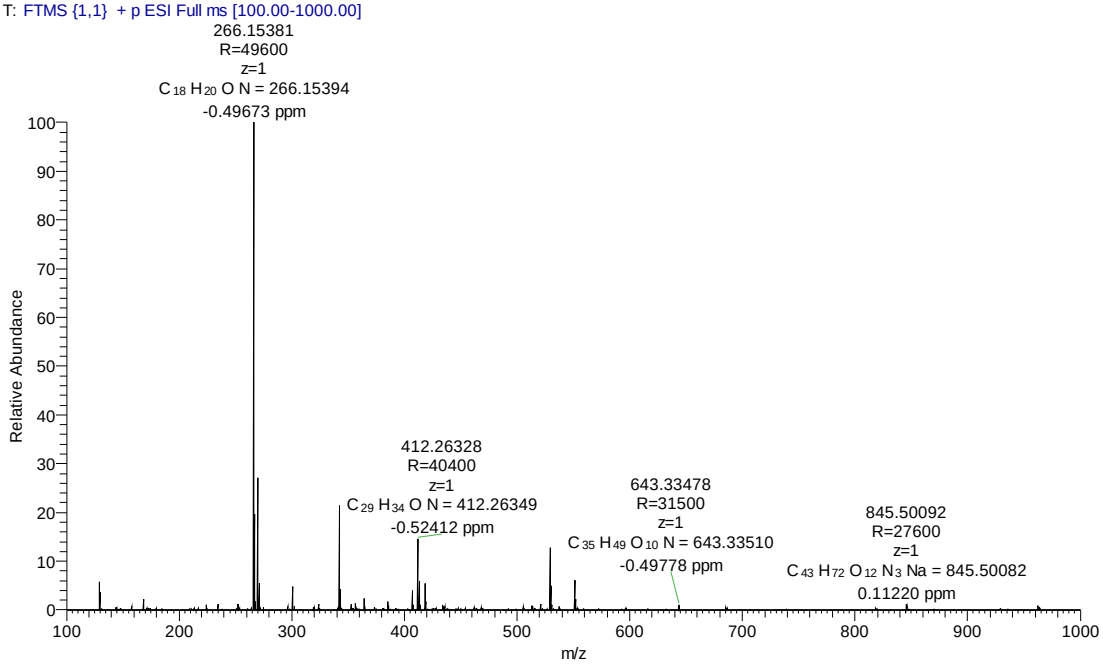
3d

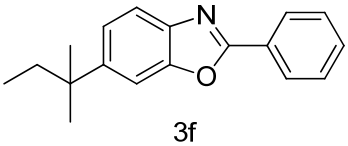




3e

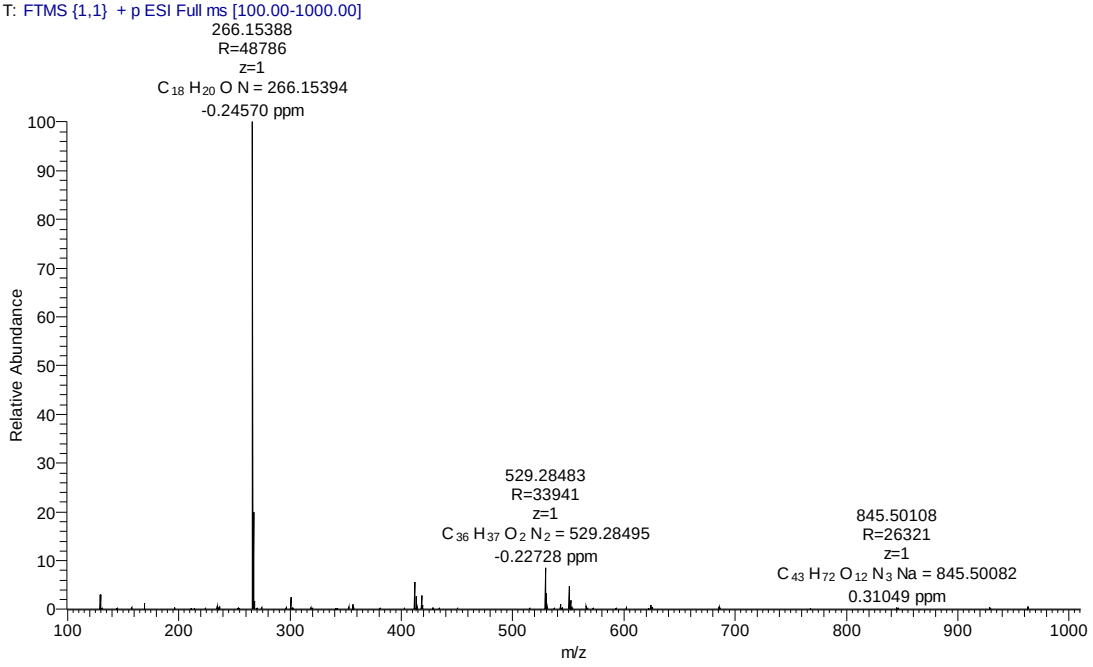
2 #48 RT: 0.41 AV: 1 NL: 1.84E6
T: FTMS {1,1} + p ESI Full ms [100.00-1000.00]

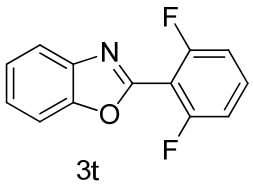




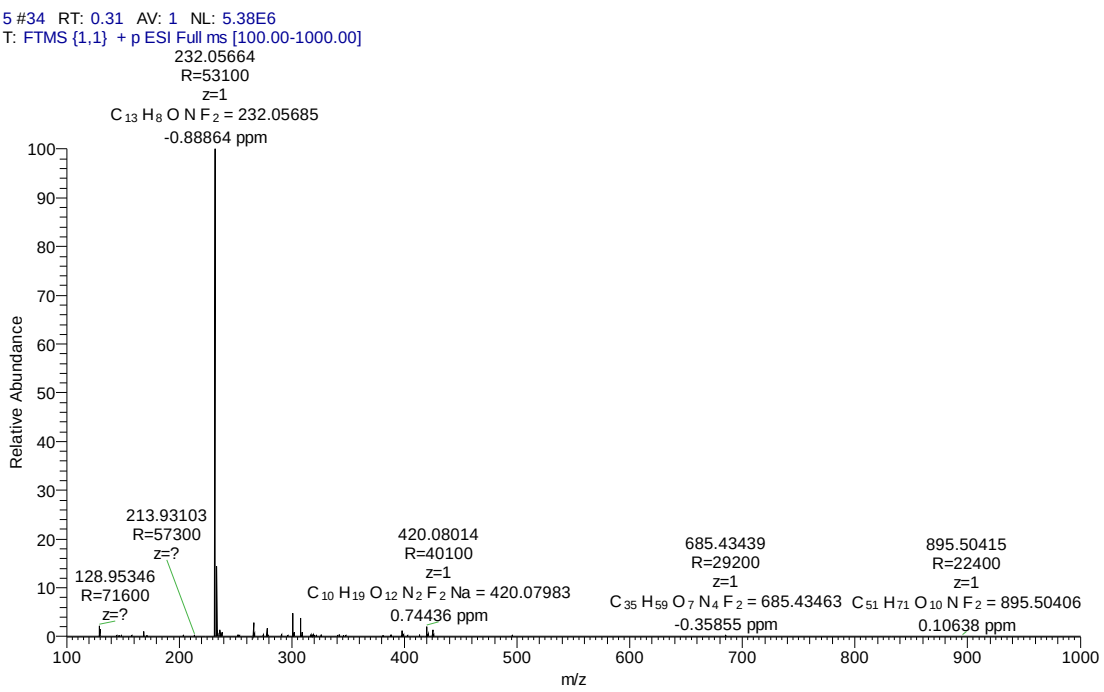
3f

3 #43-51 RT: 0.37-0.44 AV: 9 NL: 4.21E6
T: FTMS {1,1} + p ESI Full ms [100.00-1000.00]




F
N
O
F

3t


5 #34 RT: 0.31 AV: 1 NL: 5.38E6
T: FTMS {1,1} + p ESI Full ms [100.00-1000.00]
232.05664
R=53100
z=1
C13 H8 O N F2 = 232.05685
-0.88864 ppm
213.93103
R=57300
z=?
128.95346
R=71600
z=?
420.08014
R=40100
z=1
C10 H19 O12 N2 F2 Na = 420.07983
0.74436 ppm
685.43439
R=29200
z=1
C35 H59 O7 N4 F2 = 685.43463
-0.35855 ppm
895.50415
R=22400
z=1
C51 H71 O10 N F2 = 895.50406
0.10638 ppm
Relative Abundance
m/z