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Supporting information

Copper-catalysed intramolecular *O*-arylation: a simple and efficient method for benzoxazoles synthesis

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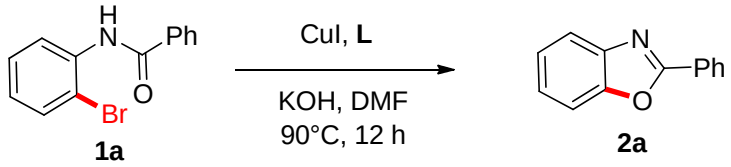
General information

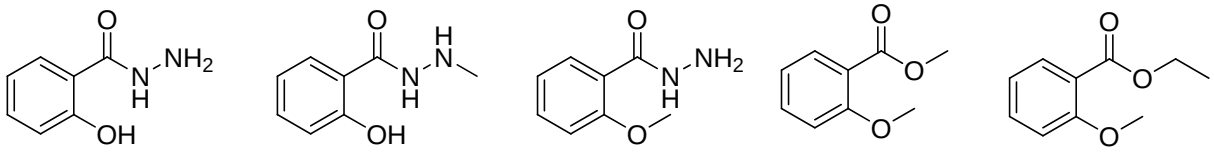
All reagents were purchased from commercial suppliers and used without further purification. Column chromatography was performed with silica gel (200-300 mesh) purchased from Qingdao Haiyang Chemical Co. Ltd. Thin-layer chroma-tography was carried out with Merck silica gel GF254 plates. All 2-substituted benzoxazoles were characterized by ^{1}H NMR, ^{13}C NMR and MS, which were compared with the previously reported data. NMR spectra were recorded at room temperature on a Bruker Avance III HD 400 instrument at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR. Mass spectra were recorded on GC-MS (Agilent 7890A/5975C) instrument under EI model.

Optimization of ligands for intramolecular *O*-arylation of *N*-(2-bromophenyl)benzamide:

Table 1. Optimization of ligands



1a **2a**



L1 **L2** **L3** **L4** **L5**

Entry	Ligand	Yield (%)[b]	Entry	Ligand	Yield (%)[b]
1	**L1**	37	4	**L4**	40
2	**L2**	35	5	**L5**	32
3	**L3**	35			

[a] Reaction conditions: *N*-(2-bromophenyl)benzamide (0.5 mmol), CuI (10 mol%), **L** (20 mol%), KOH (1.0 mmol), DMF (1.0 mL), 90 °C, 12 h. [b] Isolated yield.

General procedure for benzoxazoles synthesis *via* intramolecular *O*-arylation:

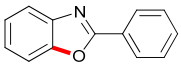
To a 10 mL of tube was added CuI (0.05 mmol), L (0.1 mmol), *N*-(2-halophenyl)benzamide (0.5 mmol), K_3PO_4 (1.0 mmol) and anhydrous DMF (1 mL). The tube was then sealed with a rubber septum without inert atmosphere and heated at 90 °C (for 2-iodoanilides and 2-bromoanilides) or 135 °C (for 2-chloroanilides) in a preheated oil bath for 12 h. The reaction mixture was cooled to room temperature, diluted with 10 mL water and extracted with ethyl acetate (3×20 mL). The combined organic phase was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatograph on silica gel (ethyl acetate/petroleum ether as the eluent) to afford the target products.

General procedure for benzoxazoles synthesis *via* domino C-N/C-O coupling reaction:

To a 10 mL of tube was added CuI (0.05 mmol), L (0.1 mmol), benzamides (0.75 mmol), 1,2-dihalobenzene (0.5 mmol), K_3PO_4 (1.0 mmol) and anhydrous DMF (1 mL). The tube was then sealed with a rubber septum without inert atmosphere and heated at 135 °C in a preheated oil bath for 12 h. The reaction mixture was cooled to room temperature, diluted with 10 mL water and extracted with ethyl acetate (3×20 mL). The combined organic phase was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatograph on silica gel (ethyl acetate/petroleum ether as the eluent) to afford the target products.

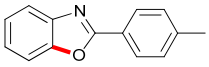
The ^{1}H NMR and ^{13}C NMR spectra datas of the benzoxazoles.

2-Phenylbenzo[d]oxazole[1] (2a)



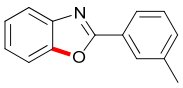
White solid, m.p.: 101-102°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28-8.25 (m, 2H), 7.79-7.77 (m, 1H), 7.60-7.49 (m, 4H), 7.38-7.32 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 150.8, 142.2, 131.6, 129.0, 127.7, 127.3, 125.2, 124.7, 120.1, 110.7. GC-MS (EI): m/z = 195 $[M]^+$.

2-*p*-Tolylbenzo[d]oxazole[2] (2b)



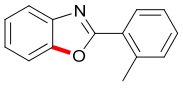
White solid. m.p.: 115-116°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16-8.13 (m, 2H), 7.77-7.75 (m, 1H), 7.59-7.55 (m, 1H), 7.37-7.31 (m, 4H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 150.8, 142.3, 142.1, 129.7, 127.7, 124.9, 124.6, 124.5, 119.9, 110.6, 21.7. GC-MS (EI): m/z = 209 $[M]^+$.

2-*m*-Tolylbenzo[d]oxazole[3] (2c)



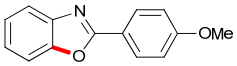
White solid, m.p.: 80-82°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 8.05 (d, *J* = 7.6 Hz, 1H), 7.79-7.77 (m, 1H), 7.58-7.55 (m, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.37-7.32 (m, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.3, 150.8, 142.2, 138.8, 132.4, 128.9, 128.2, 127.1, 125.1, 124.8, 124.6, 120.0, 110.6, 21.4. GC-MS (EI): m/z = 209 $[M]^+$.

2-*o*-Tolylbenzo[d]oxazole[1] (2d)



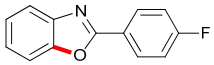
White solid, m.p.: 69-70°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21-8.17 (m, 1H), 7.83-7.81 (m, 1H), 7.62-7.58 (m, 1H), 7.44-7.33 (m, 5H), 2.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5, 150.4, 142.2, 139.0, 131.9, 131.0, 130.0, 126.3, 126.2, 125.1, 124.5, 120.2, 110.6, 22.3. GC-MS (EI): m/z = 209 $[M]^+$.

2-(4-Methoxyphenyl)benzo[d]oxazole[1] (2e)



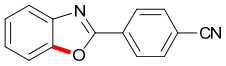
White solid, m.p.:52-54°C. ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.19 (d, *J* = 8.4 Hz, 2H), 7.75-7.72 (m, 1H), 7.56-7.54 (m, 1H), 7.35-7.29 (m, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.3, 162.4, 150.8, 142.4, 129.5, 124.7, 124.5, 119.8, 119.7, 114.5, 110.5, 55.6. GC-MS (EI): m/z = 225 $[M]^+$.

2-(4-Fluorophenyl)benzo[d]oxazole[4] (2f)



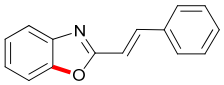
White solid, m.p.: 94-95°C. ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.29-8.24 (m, 2H), 7.79-7.75 (m, 1H), 7.60-7.56 (m, 1H), 7.38-7.34 (m, 2H), 7.24-7.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.2, 163.7, 162.3, 150.9, 142.2, 130.0 (d, *J* = 8.8 Hz), 125.3, 124.8, 123.6 (d, *J* = 3.2 Hz), 120.1, 116.3 (d, *J* = 22.1 Hz), 110.7. GC-MS (EI): m/z = 213 $[M]^+$.

4-(Benzo[d]oxazol-2-yl)benzonitrile[5] (2g)



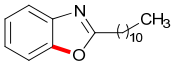
White solid, m.p.: 203-204°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36-8.33 (m, 2H), 7.83-7.77 (m, 3H), 7.62-7.60 (m, 1H), 7.44-7.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0, 151.0, 142.0, 132.8, 131.2, 128.1, 126.3, 125.2, 120.7, 118.3, 114.8, 111.0. GC-MS (EI): m/z = 220 $[M]^+$.

(*E*)-2-styrylbenzo[d]oxazole[5] (2h)



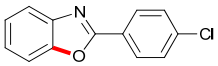
Yellow solid, m.p.: 79-81°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 16.4 Hz, 1H), 7.74-7.71 (m, 1H), 7.62-7.59 (m, 2H), 7.56-7.51 (m, 1H), 7.45-7.31 (m, 5H), 7.09 (d, *J* = 16.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9, 150.5, 142.3, 139.6, 135.3, 129.9, 129.1, 127.7, 125.3, 124.6, 120.0, 114.1, 110.5. GC-MS (EI): m/z = 221 $[M]^+$.

2-Undecylbenzo[d]oxazole[6] (2i)



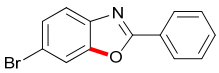
Pale yellow oli. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69-7.64 (m, 1H), 7.50-7.45 (m, 1H), 7.32-7.26 (m, 2H), 2.92 (t, *J* = 7.6 Hz, 2H), 1.89 (apparent quintet, *J* = 7.6 Hz, 2H), 1.46-1.23 (m, 16H), 0.88 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 150.9, 141.5, 124.5, 124.2, 119.7, 110.4, 32.0, 29.7, 29.6, 29.5, 29.4, 29.3, 28.8, 26.9, 22.8, 14.3. GC-MS (EI): m/z = 273 $[M]^+$.

2-(4-Chlorophenyl)benzo[d]oxazole[1] (2j)



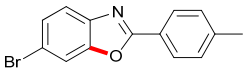
White solid, m.p.: 141-142°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21-8.18 (m, 2H), 7.78-7.76 (m, 1H), 7.59-7.57 (m, 1H), 7.52-7.49 (m, 2H), 7.39-7.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 150.9, 142.2, 137.9, 129.4, 129.0, 125.8, 125.5, 124.9, 120.2, 110.8. GC-MS (EI): m/z = 229 $[M]^+$.

6-Bromo-2-phenylbenzo[d]oxazole[7] (2k)



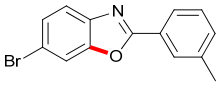
White solid, m.p.: 89-92°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25-8.22 (m, 2H), 7.76 (d, *J* = 1.6 Hz, 1H), 7.63 (d, *J* = 8.4, 1H), 7.57-7.51 (m, 3H), 7.48 (q, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5, 151.2, 141.4, 131.9, 129.0, 128.0, 127.7, 126.7, 121.0, 118.0, 114.1. GC-MS (EI): m/z = 273 $[M]^+$.

6-Bromo-2-*p*-tolylbenzo[d]oxazole[7] (2l)



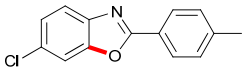
White solid, m.p.: 121-124°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14-8.10 (m, 2H), 7.74 (d, *J* = 2.0 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.45 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.33 (d, *J* = 8.8 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9, 151.3, 142.6, 141.5, 129.8, 128.0, 127.8, 124.0, 120.9, 117.8, 114.1, 21.8. GC-MS (EI): m/z = 287 $[M]^+$.

6-Bromo-2-*m*-tolylbenzo[d]oxazole[7] (2m)



White solid, m.p.: 92-94°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (m, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.74 (dd, *J* = 1.6, 0.4 Hz, 1H), 7.62 (dd, *J* = 8.4, 0.4 Hz, 1H), 7.49-7.46 (m, 1H), 7.42 (t, *J* = 3.6 Hz, 1H), 7.38-7.35 (m, 1H) 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9, 151.3, 141.5, 139.0, 132.9, 129.0, 128.4, 128.1, 126.7, 125.0, 121.0, 118.0, 114.2, 21.5. GC-MS (EI): m/z = 287 $[M]^+$.

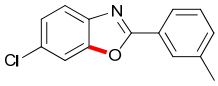
6-Chloro-2-*p*-tolylbenzo[d]oxazole[3] (2n)



White solid, m.p.: 126-128°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13-8.10 (m, 2H), 7.65 (dd, *J* = 8.4, 0.4 Hz, 1H), 7.58 (dd, *J* = 1.6, 0.4 Hz, 1H), 7.35-7.31 (m, 3H), 2.45 (s, 3H); ^{13}C NMR

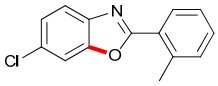
(100 MHz, $CDCl_3$): δ 164.0, 150.9, 142.5, 141.1, 130.5, 129.8, 127.7, 125.2, 124.0, 120.3, 111.2, 21.8. GC-MS (EI): m/z = 243 $[M]^+$.

6-Chloro-2-*m*-tolylbenzo[d]oxazole[3] (2o)



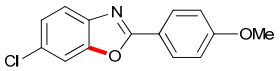
White solid, m.p.: 98-99°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.99 (d, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 1.6 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.34-7.29 (m, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.0, 151.1, 141.1, 138.9, 132.7, 130.7, 129.0, 128.3, 126.6, 125.3, 124.9, 120.4, 111.3, 21.5. GC-MS (EI): m/z = 243 $[M]^+$.

6-Chloro-2-*o*-tolylbenzo[d]oxazole[3] (2p)



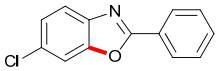
White solid, m.p.: 85-86°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16-8.14 (m, 1H), 7.70 (dd, *J* = 4.4, 0.4 Hz, 1H), 7.60 (dd, *J* = 2.0, 0.4 Hz, 1H), 7.45-7.41 (m, 1H), 7.36-7.33 (m, 3H), 2.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.1, 150.5, 141.1, 139.1, 132.0, 131.3, 130.7, 130.0, 126.2, 125.8, 125.2, 120.7, 111.2, 22.4. GC-MS (EI): m/z = 243 $[M]^+$.

6-Chloro-2-(4-methoxyphenyl)benzo[d]oxazole[8] (2q)



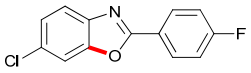
White solid, m.p.: 140-142°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18-8.15 (m, 2H), 7.63 (dd, *J* = 8.4, 0.4 Hz, 1H), 7.56 (dd, *J* = 6.0, 0.4 Hz, 1H), 7.31 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.04-7.02 (m, 2H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.0, 162.7, 151.0, 141.2, 130.2, 129.6, 125.2, 120.2, 119.3, 114.6, 111.2, 55.6. GC-MS (EI): m/z = 259 $[M]^+$.

6-Chloro-2-phenylbenzo[d]oxazole[3] (2r)



Pale pink solid, m.p.: 140-142°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25-8.22 (m, 2H), 7.68 (dd, *J* = 8.4, 0.4 Hz, 1H), 7.60 (dd, *J* = 2.0, 0.4 Hz, 1H), 7.58-7.51 (m, 3H), 7.34 (dd, *J* = 8.8, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8, 151.1, 141.0, 131.9, 130.8, 129.1, 127.8, 126.8, 125.4, 120.6, 111.4. GC-MS (EI): m/z = 229 $[M]^+$.

6-Chloro-2-(4-fluorophenyl)benzo[d]oxazole[3] (2s)



White solid, m.p.: 130-132°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26-8.21 (m, 2H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.59 (dd, *J* = 2.0, 0.4 Hz, 1H), 7.35 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.25-7.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.1 (d, *J* = 251.8 Hz), 162.9 (d, *J* = 1.0 Hz), 151.0, 141.0, 130.8, 130.0 (d, *J* = 8.8 Hz), 125.5, 123.1 (d, *J* = 3.3 Hz), 120.5, 116.4 (d, *J* = 22.1 Hz), 111.3. GC-MS (EI): m/z = 247 $[M]^+$.

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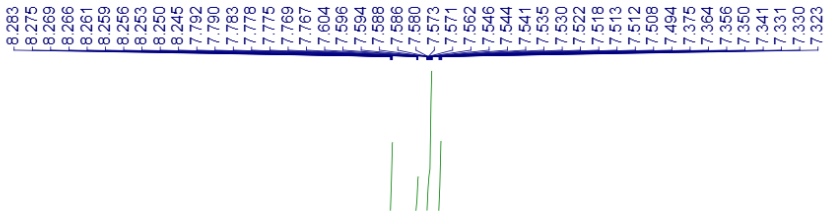
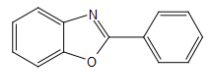
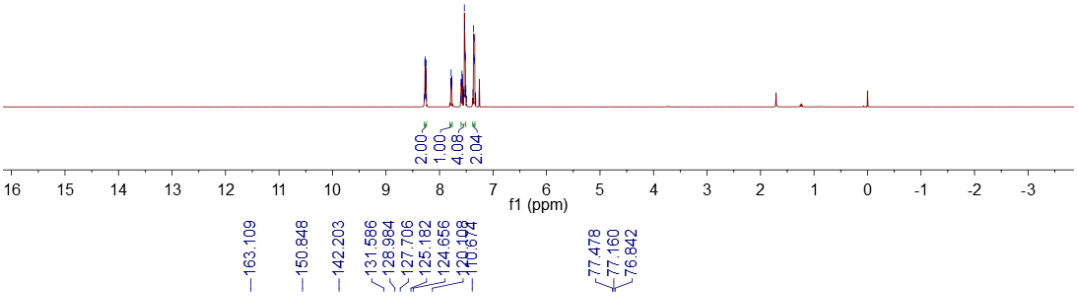
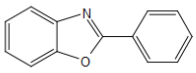
Copies of ^{1}H NMR and ^{13}C NMR spectra of the benzoxazoles.

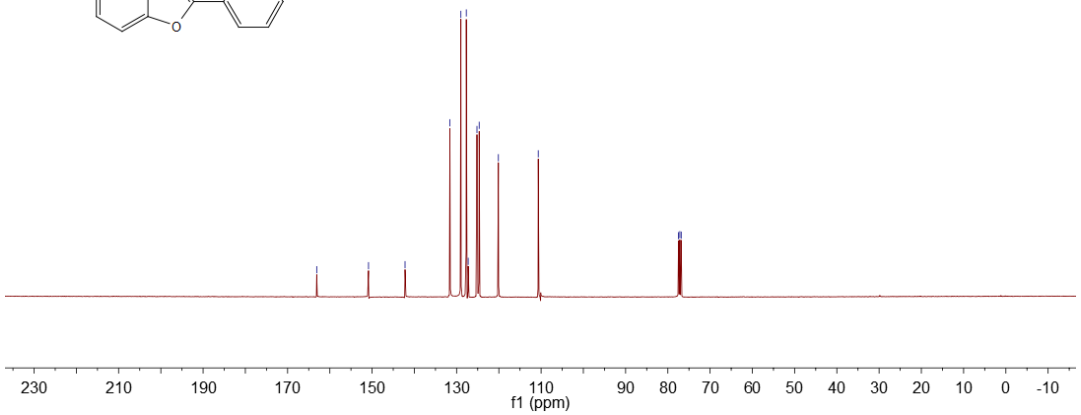
2-Phenylbenzo[d]oxazole (2a)



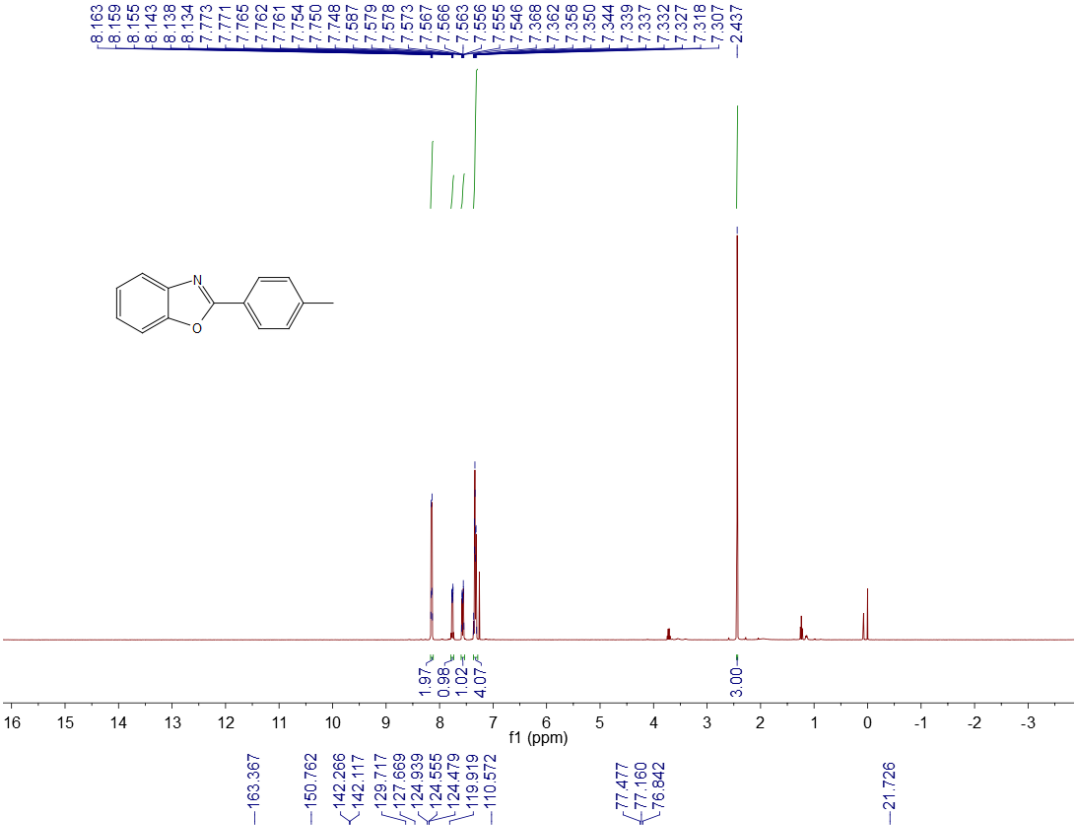


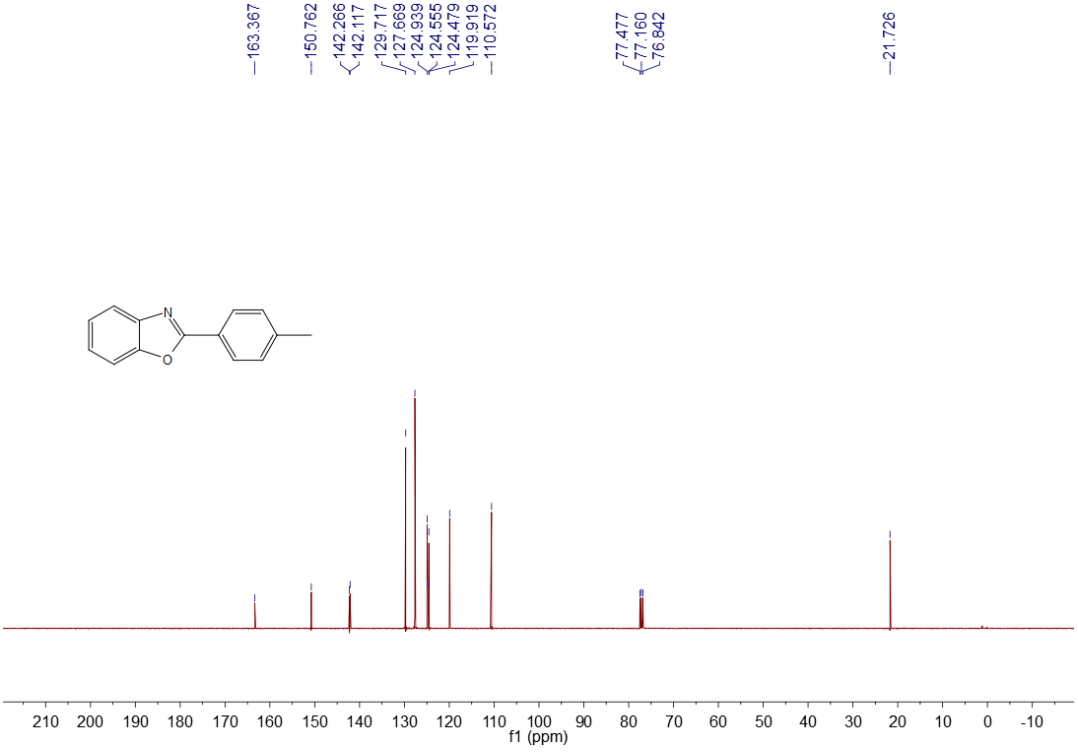




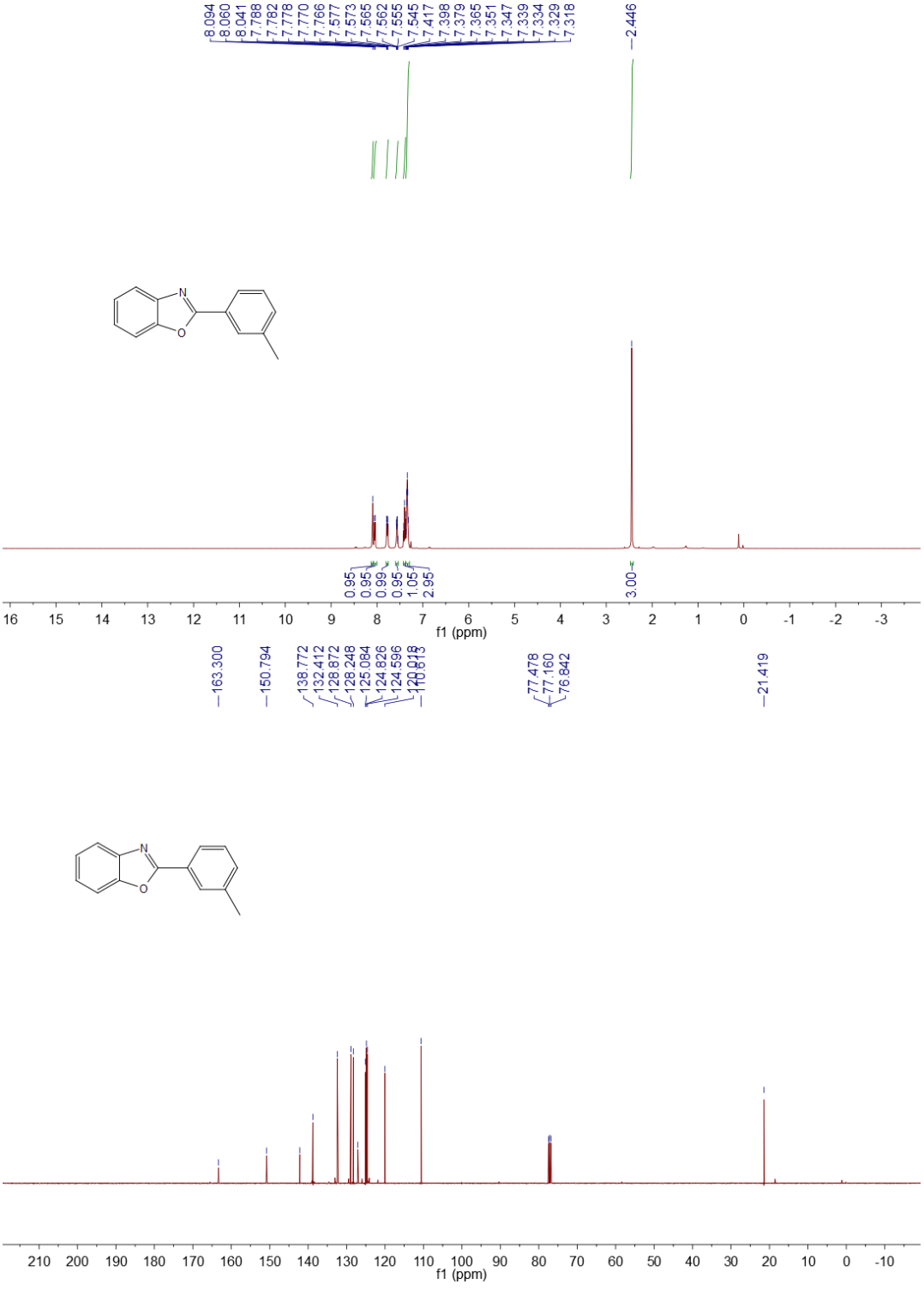


2-*p*-Tolylbenzo[d]oxazole (2b)

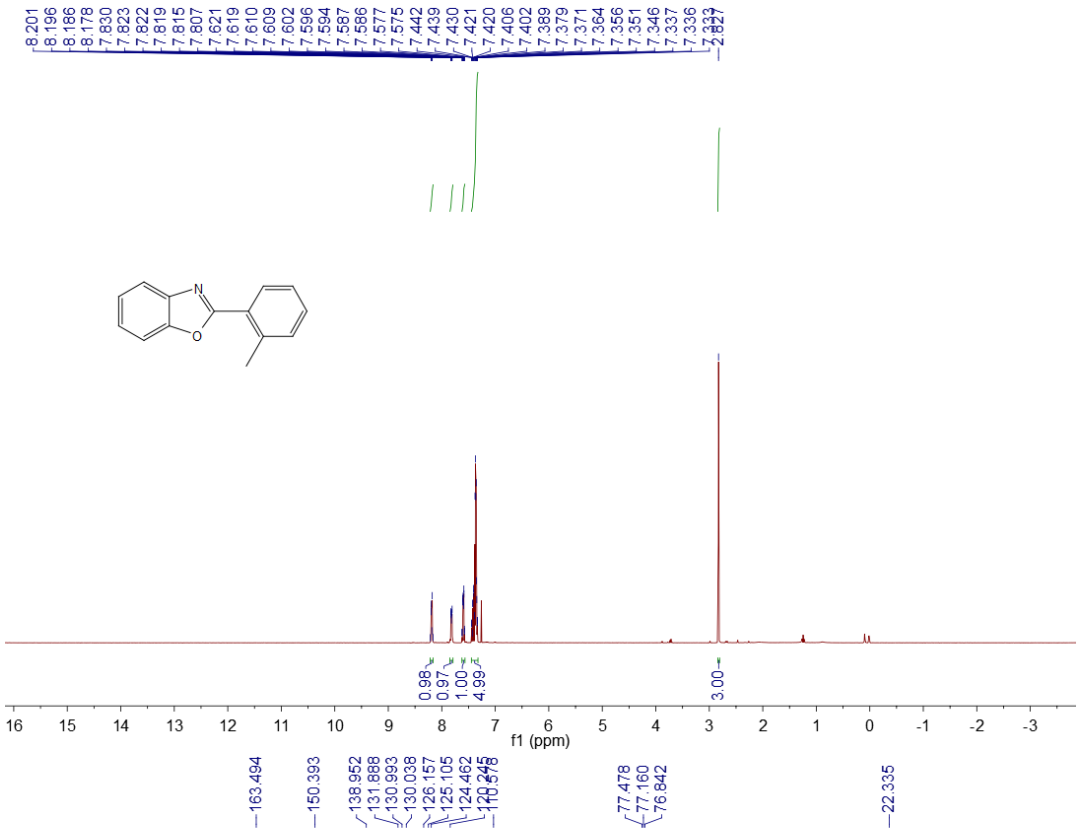


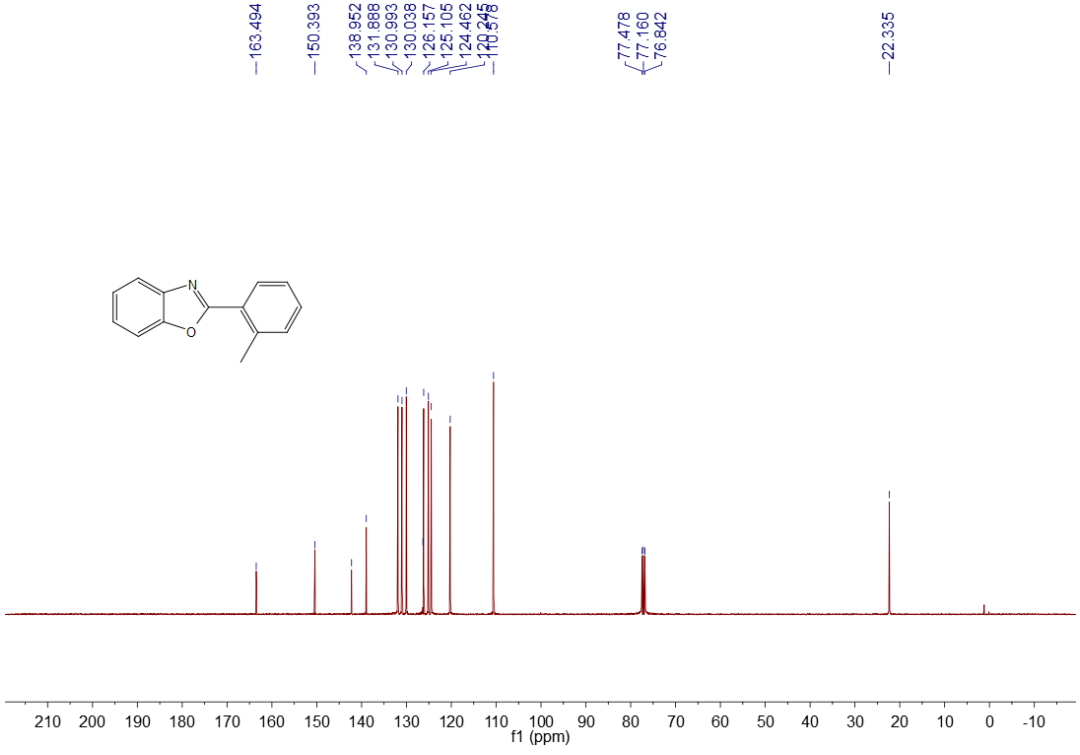


2-*m*-Tolylbenzo[d]oxazole (2c)

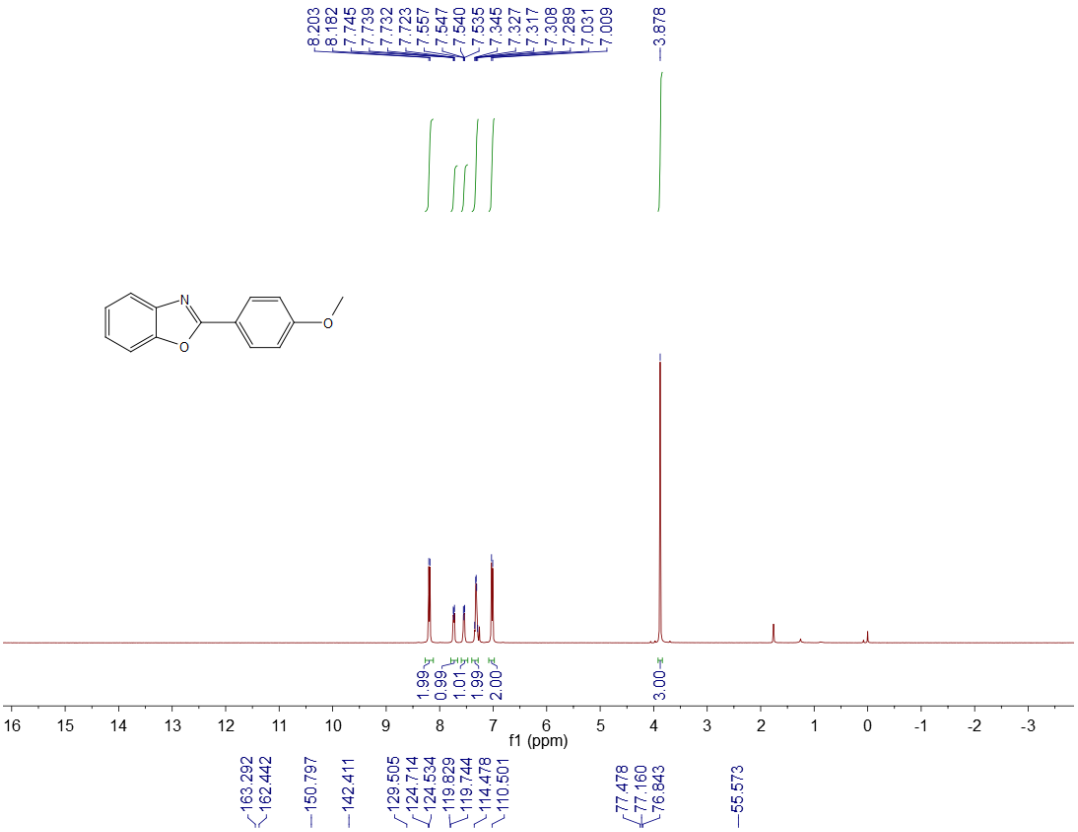


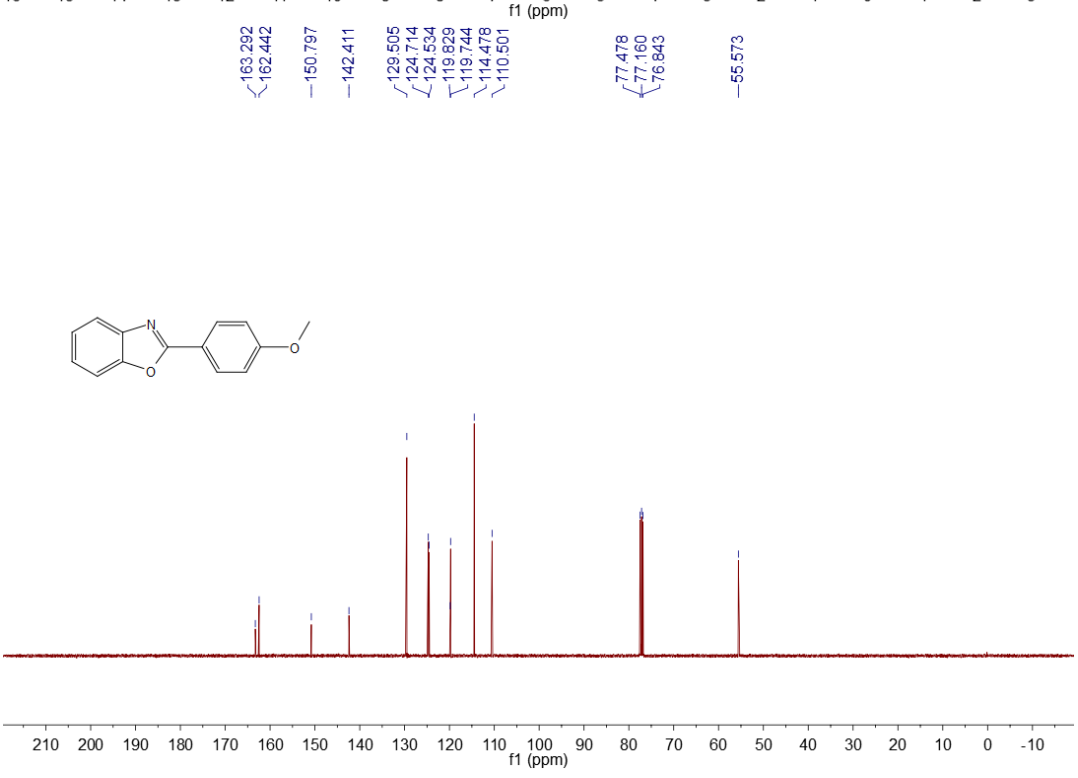
2-*o*-Tolylbenzo[d]oxazole (2d)



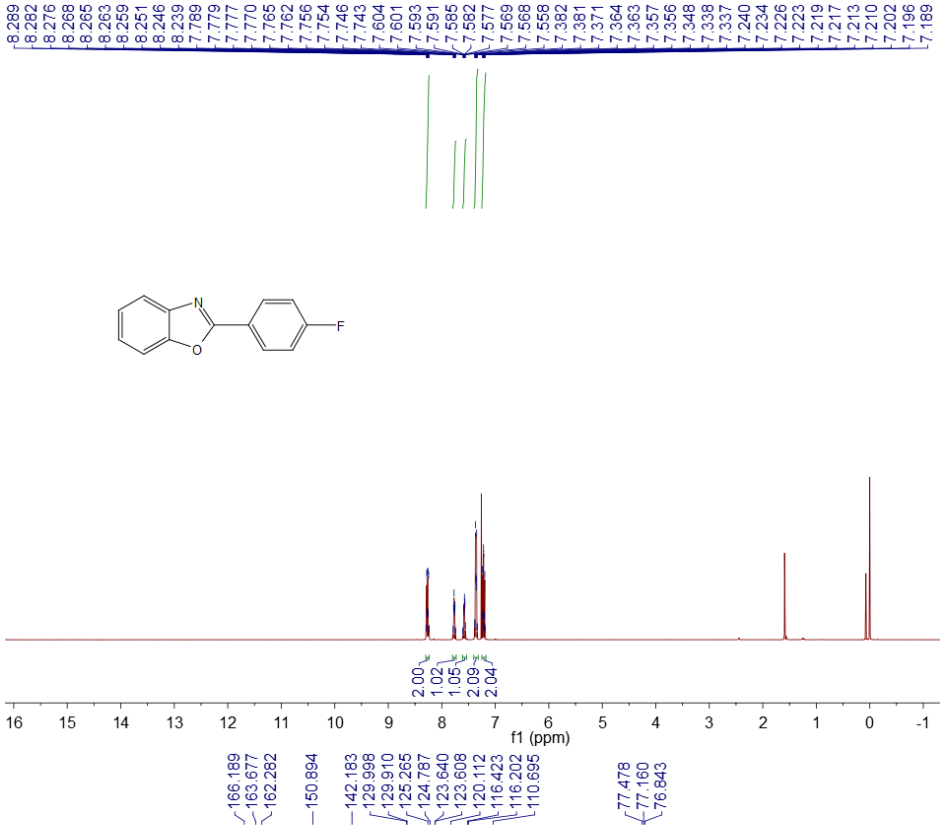


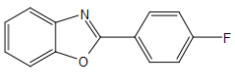
2-(4-Methoxyphenyl)benzo[d]oxazole (2e)

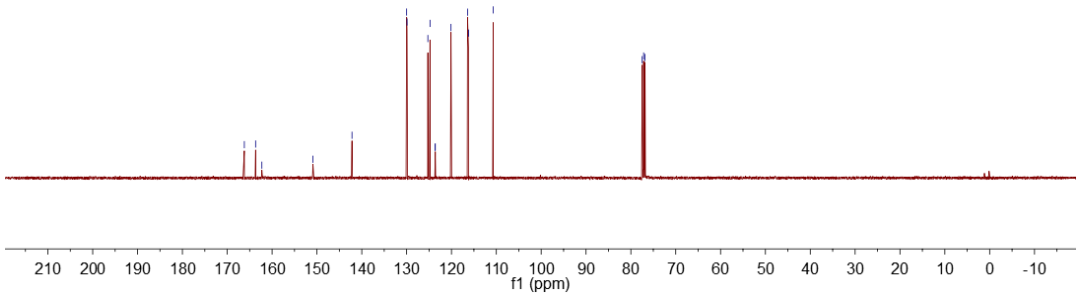




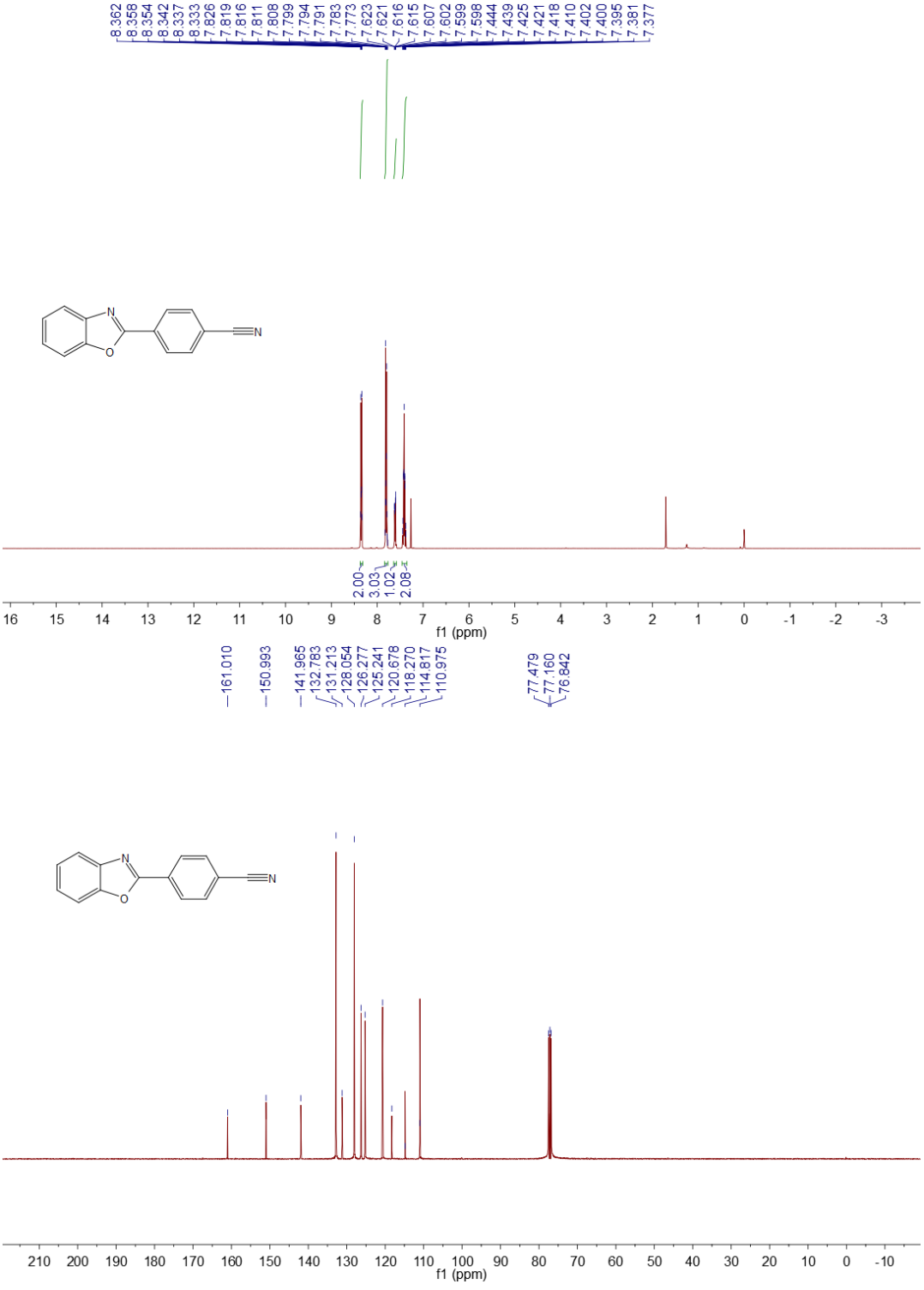
2-(4-Fluorophenyl)benzo[d]oxazole (2f)



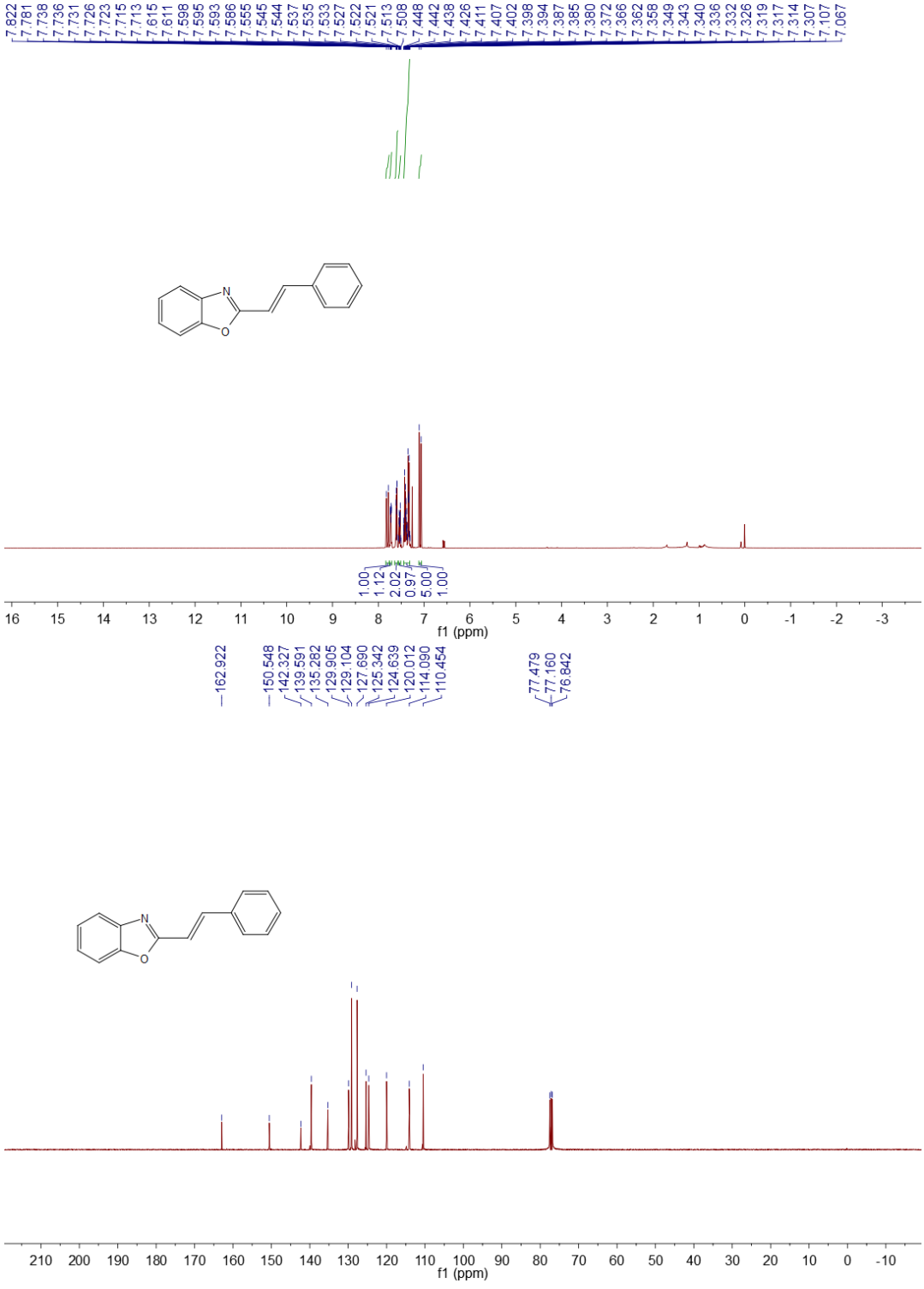




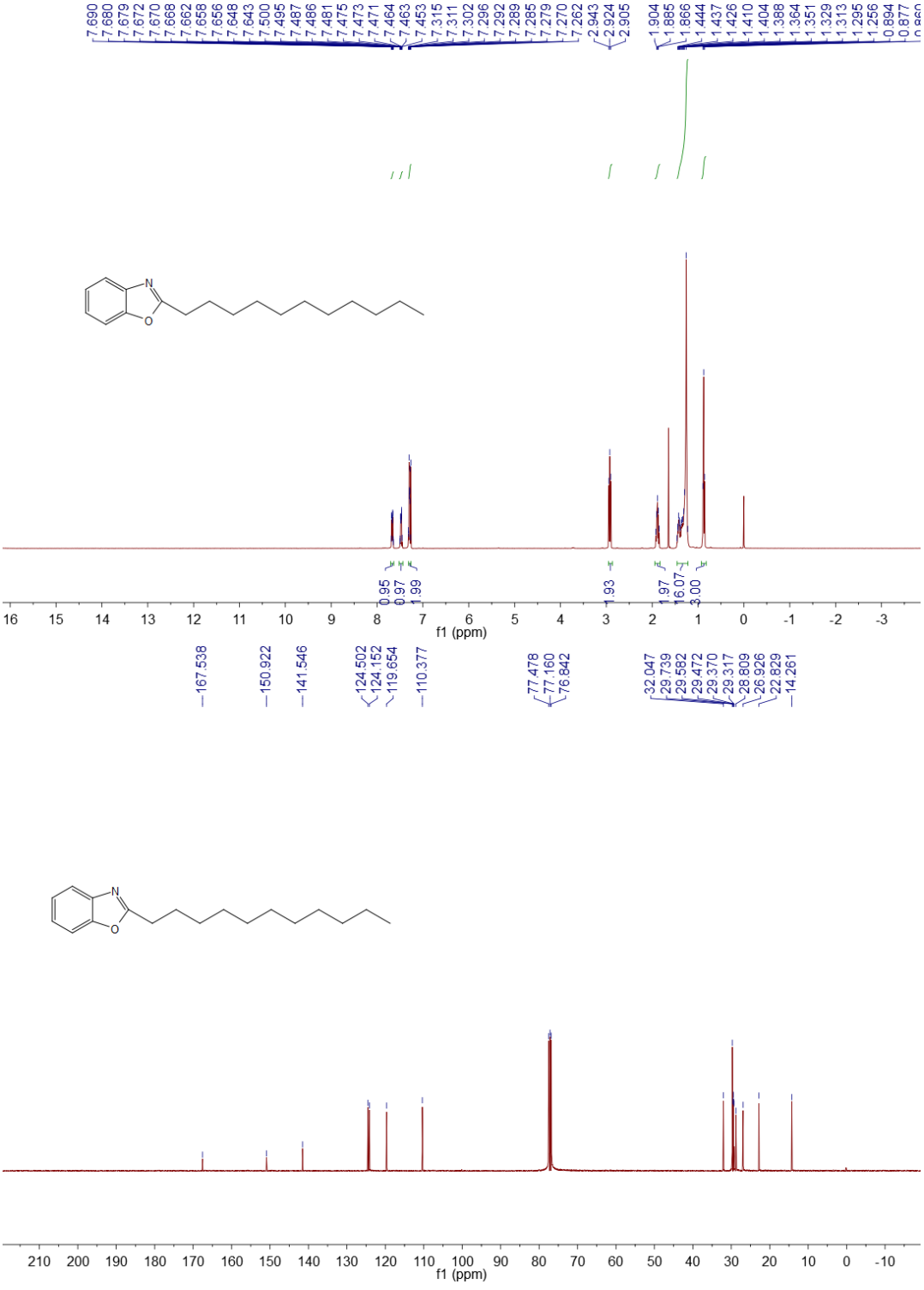
4-(Benzo[d]oxazol-2-yl)benzonitrile (2g)



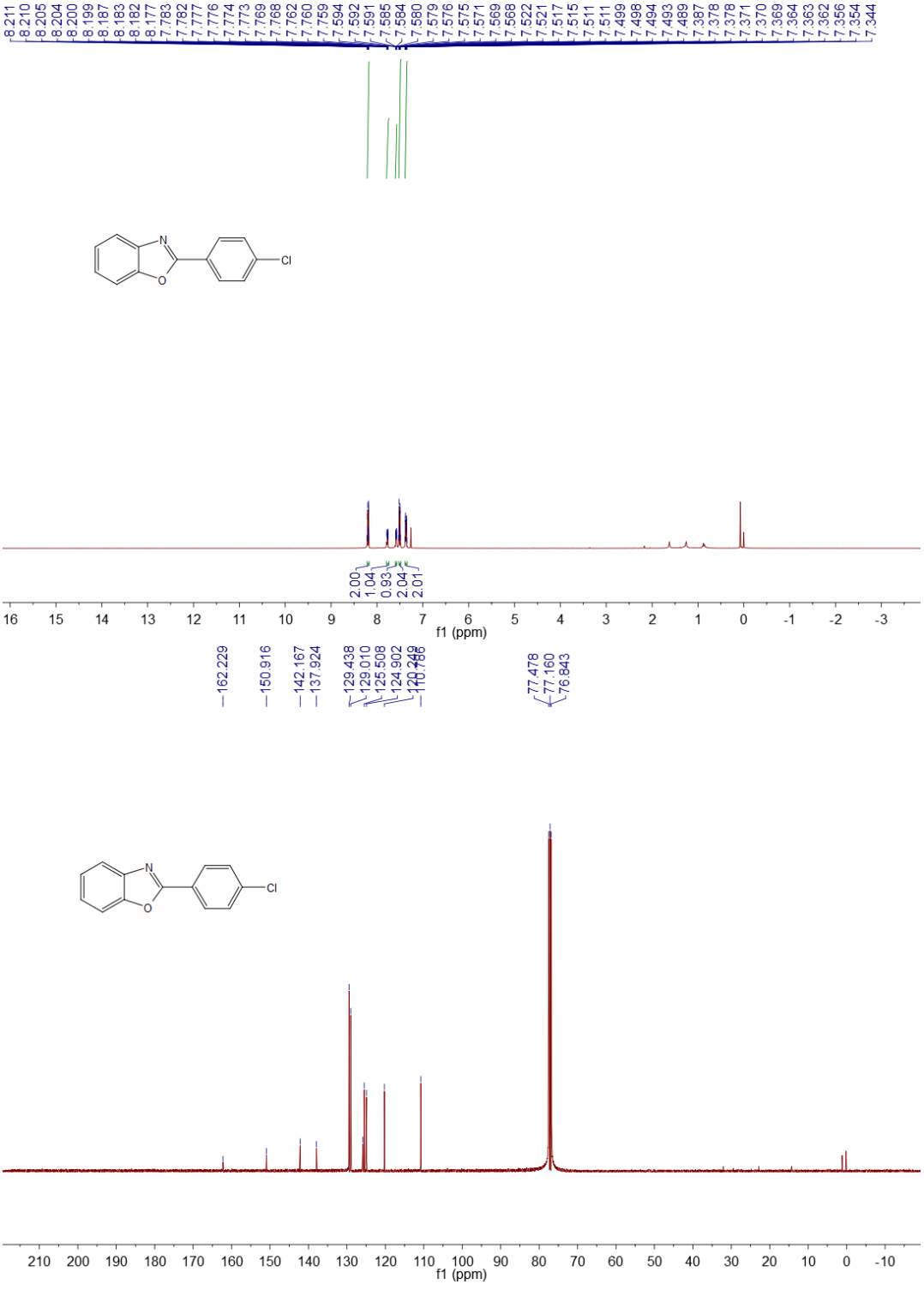
(*E*)-2-styrylbenzo[d]oxazole (2h)



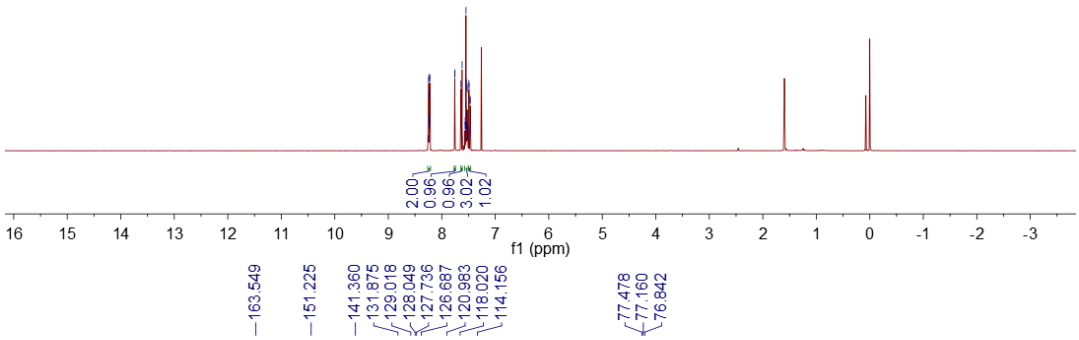
2-Undecylbenzo[d]oxazole (2i)

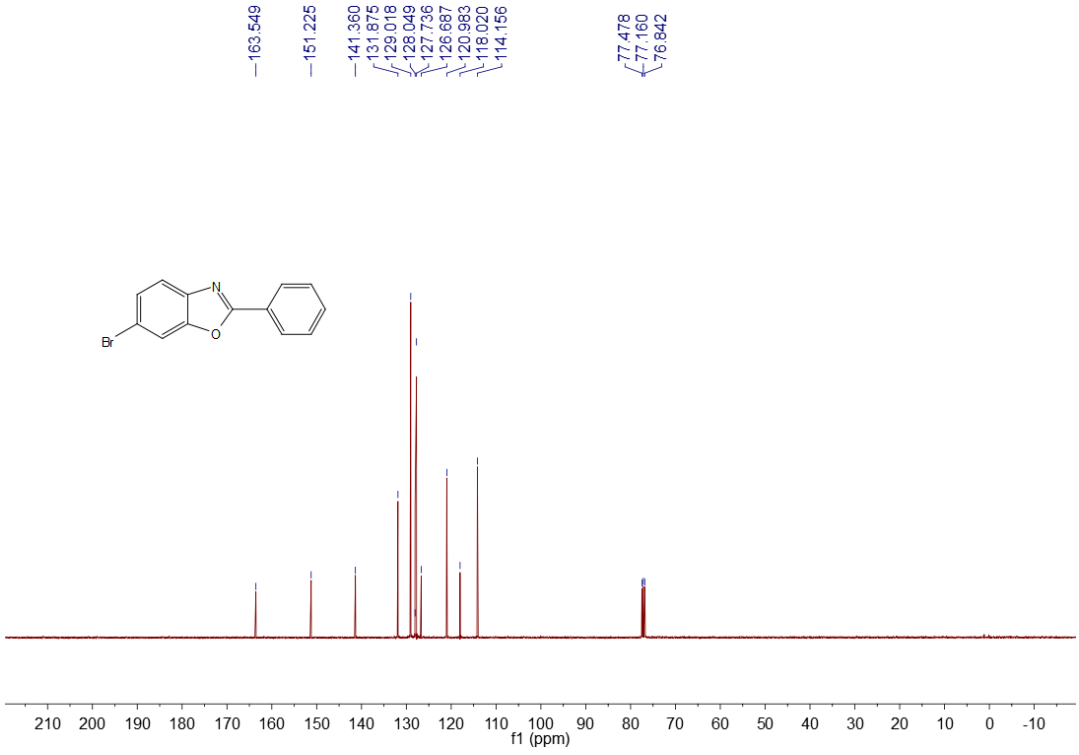


2-(4-Chlorophenyl)benzo[d]oxazole (2j)

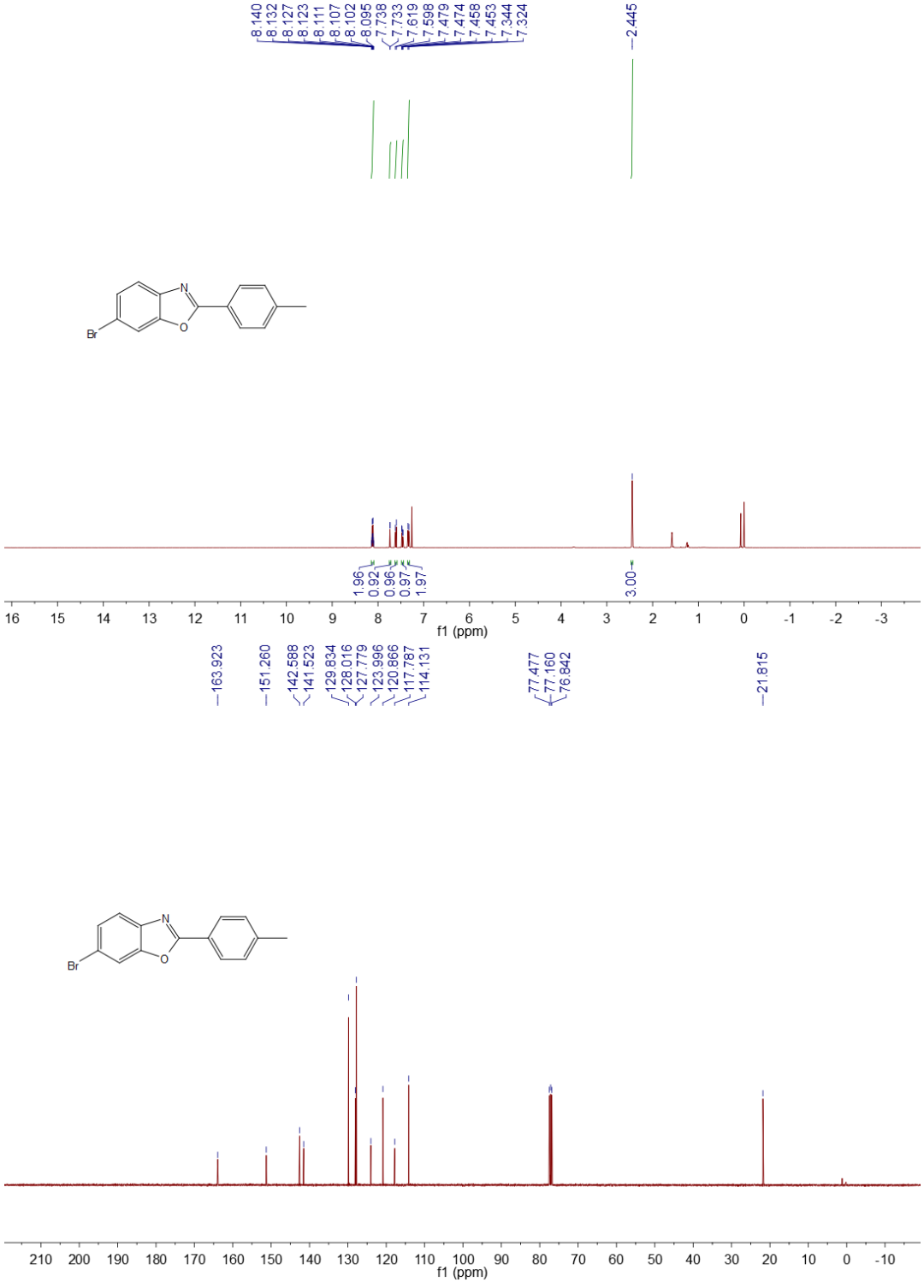


6-Bromo-2-phenylbenzo[d]oxazole (2k)

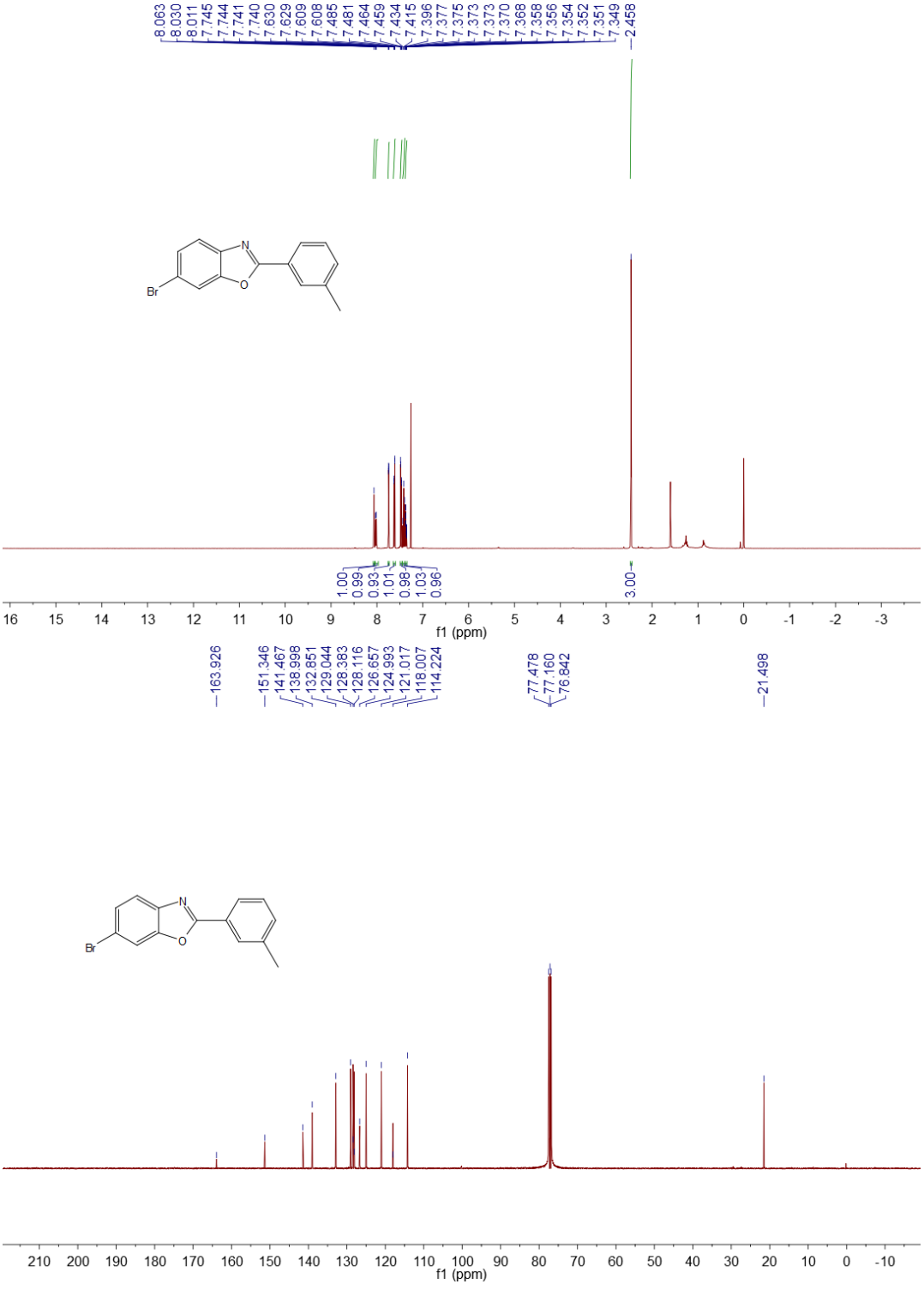




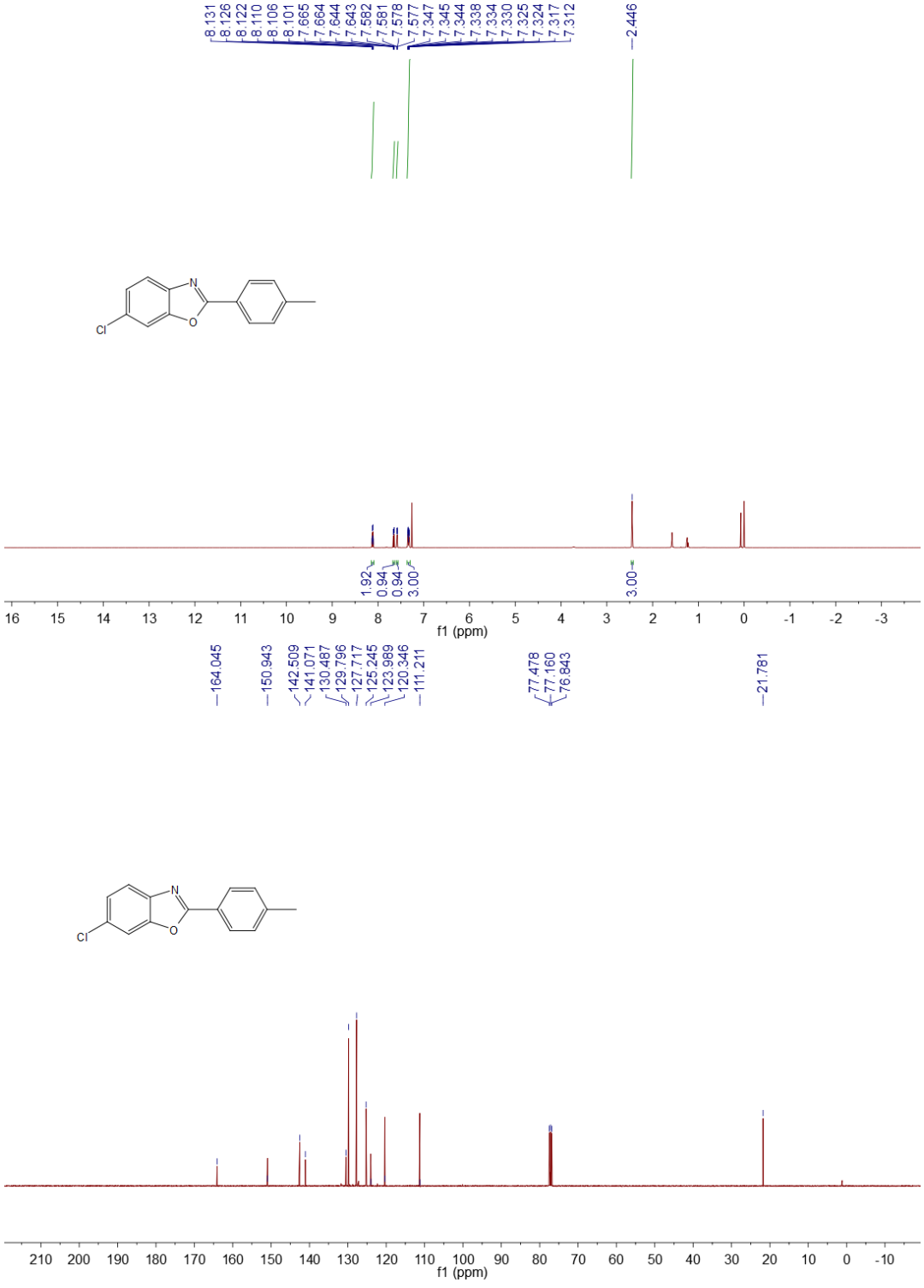
6-Bromo-2-*p*-tolylbenzo[d]oxazole (2l)



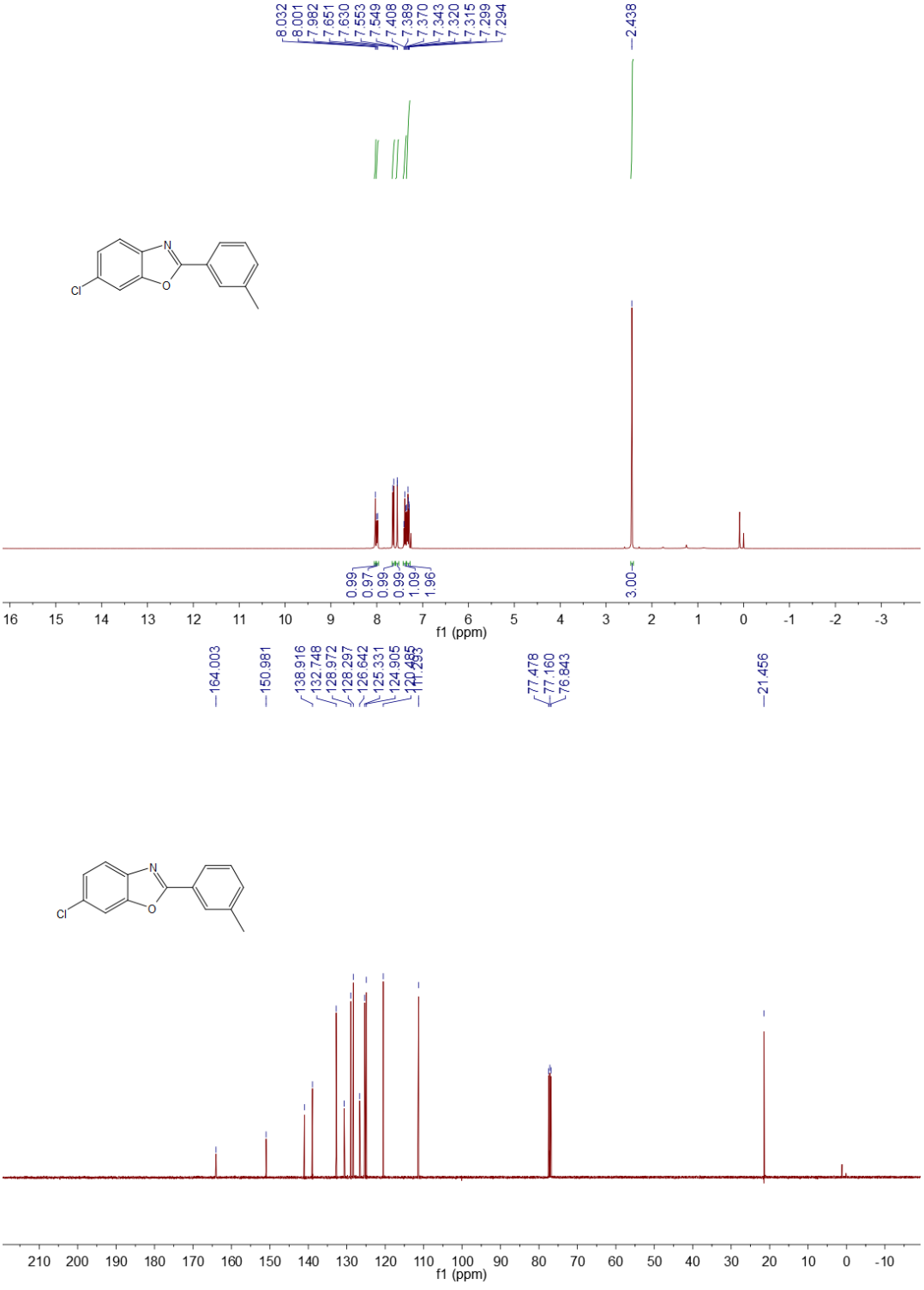
6-Bromo-2-*m*-tolylbenzo[d]oxazole (2m)



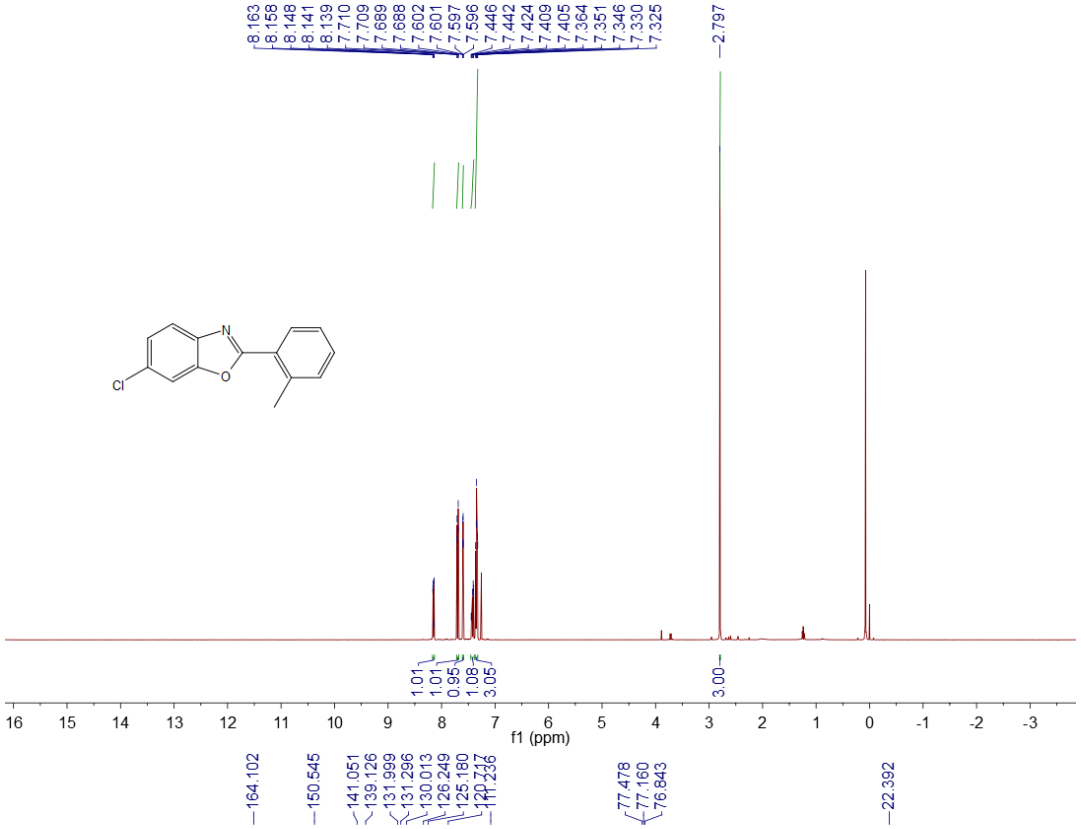
6-Chloro-2-*p*-tolylbenzo[d]oxazole (2n)

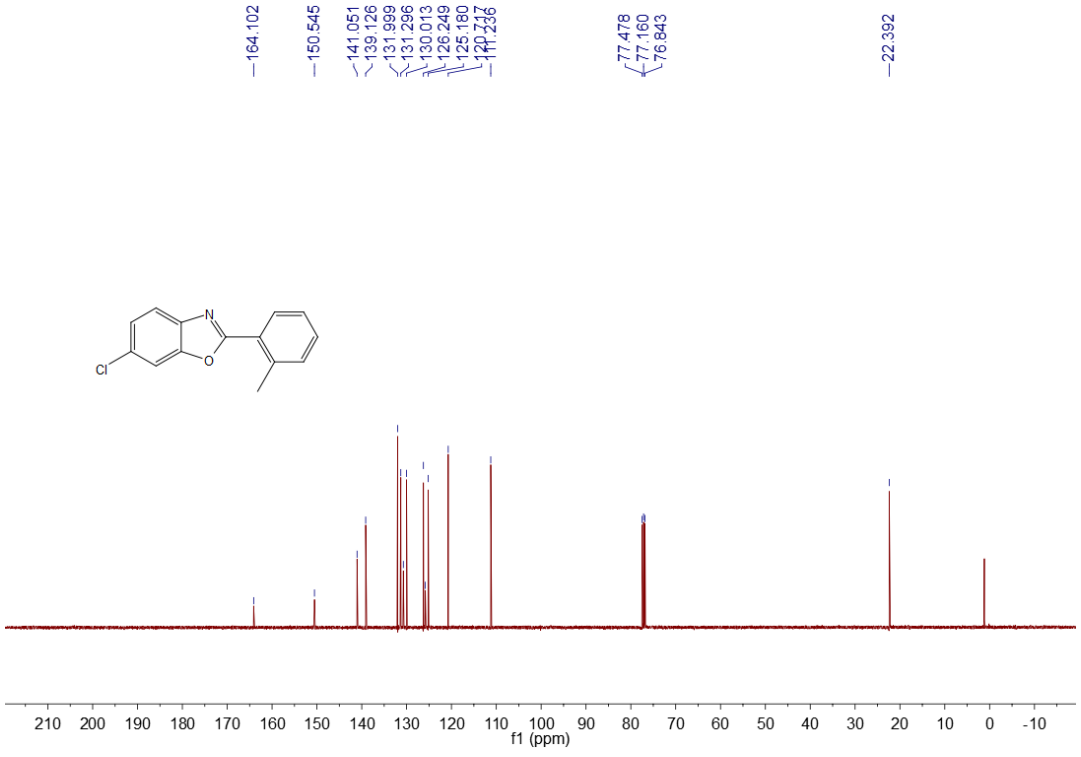


6-Chloro-2-*m*-tolylbenzo[d]oxazole (2o)

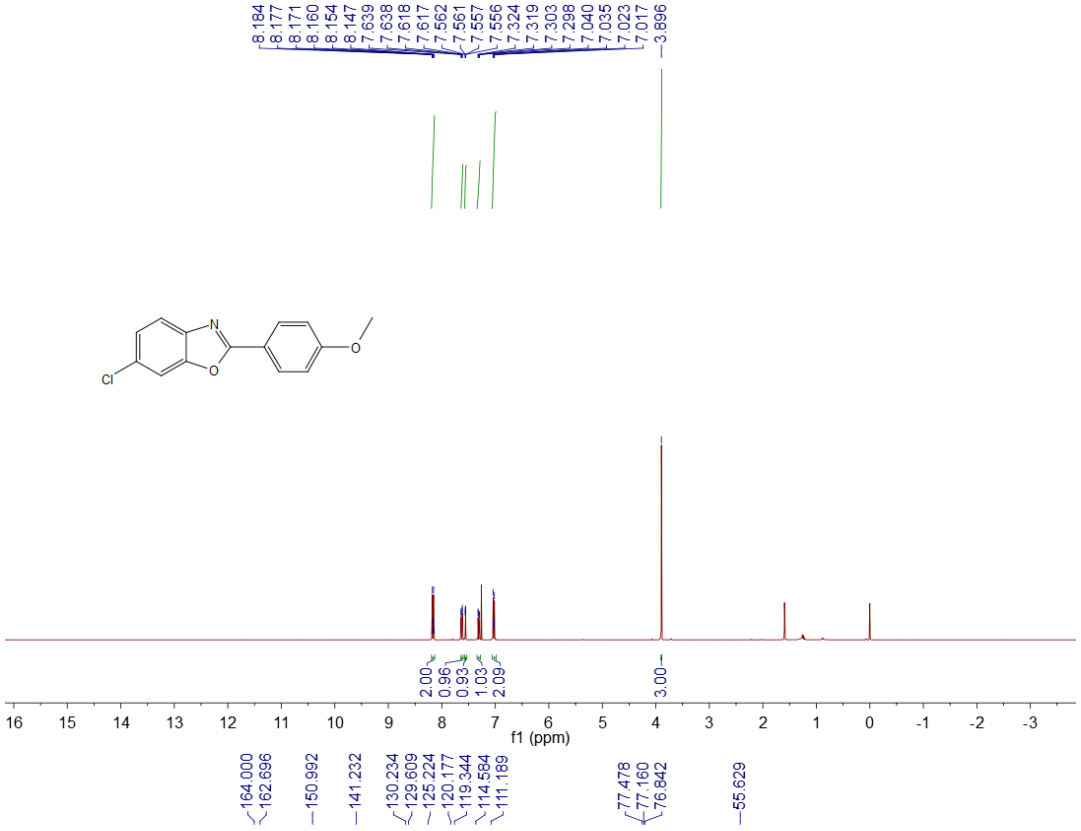


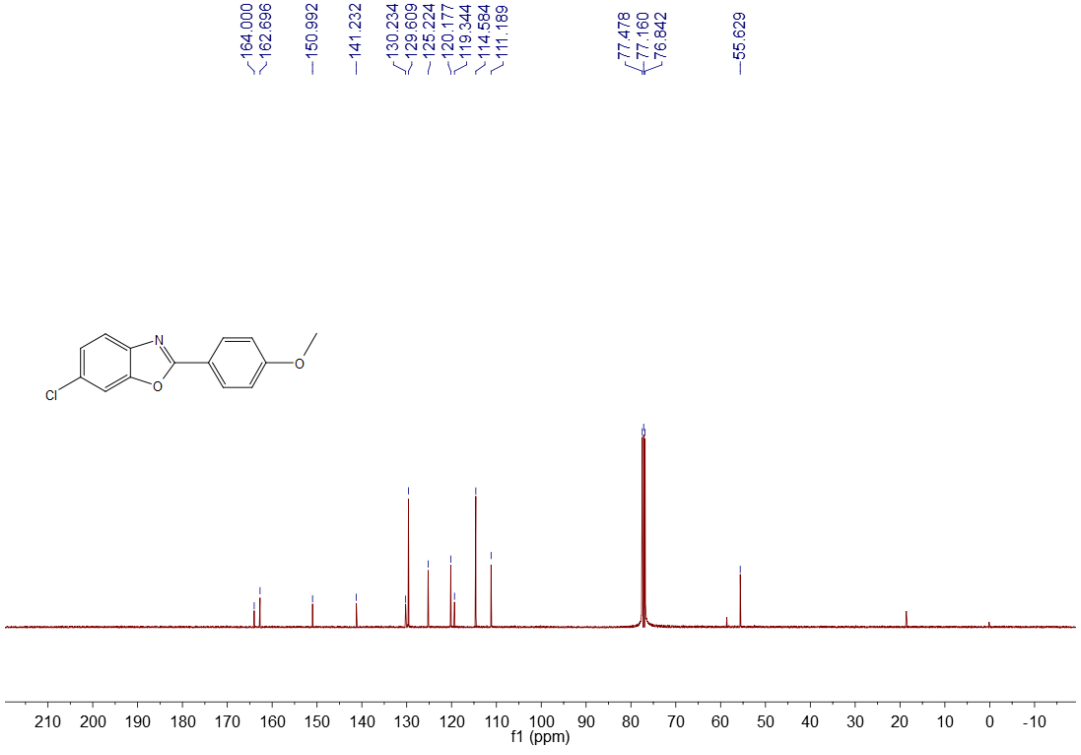
6-Chloro-2-*o*-tolylbenzo[d]oxazole (2p)



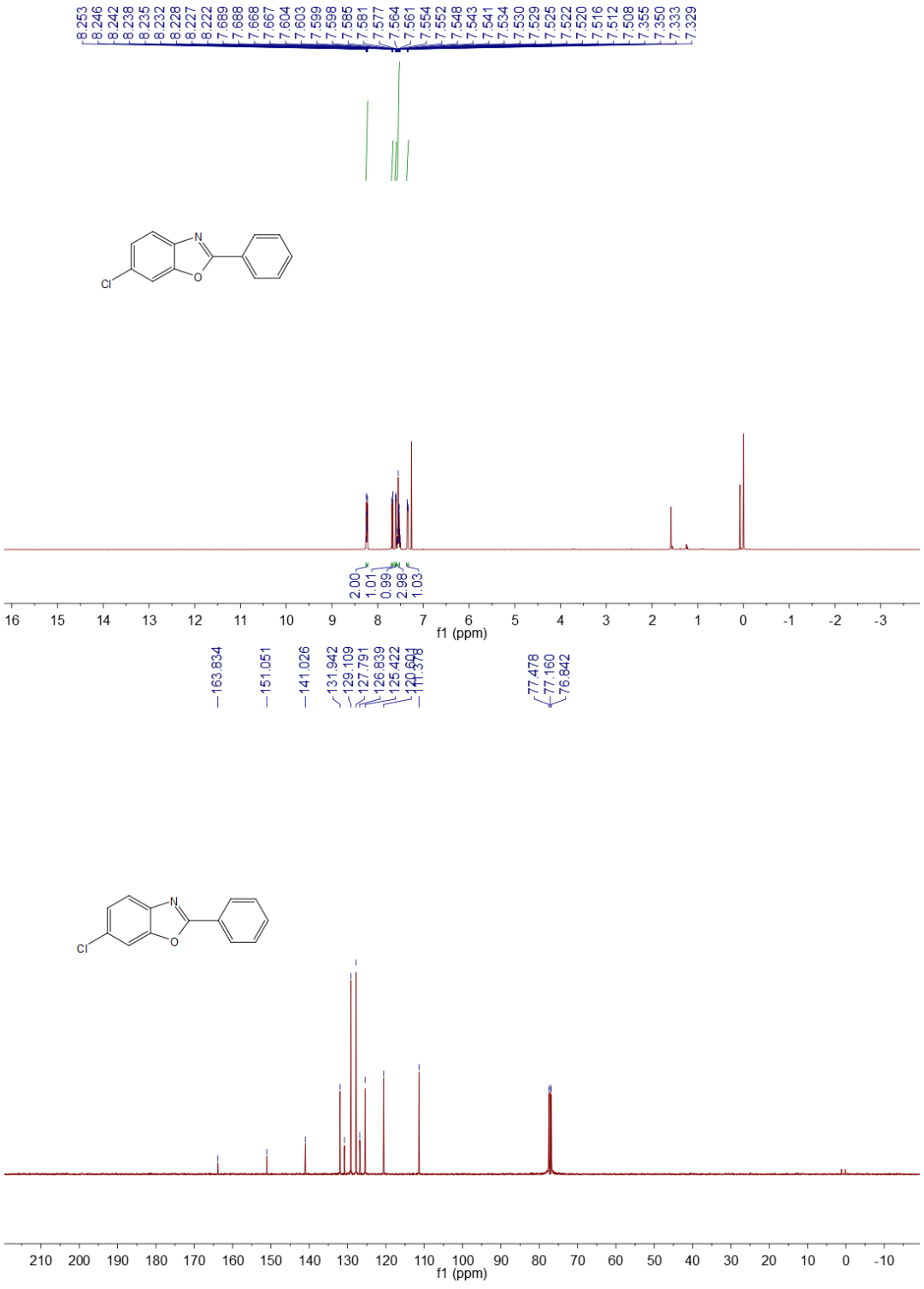


6-Chloro-2-(4-ethoxyphenyl)benzo[d]oxazole (2q)





6-Chloro-2-phenylbenzo[d]oxazole (2r)



6-Chloro-2-(4-fluorophenyl)benzo[d]oxazole (2s)