Supporting Information

Oxone-mediated oxidative carbon-heteroatom bond cleavage: synthesis of benzoxazinones from benzoxazoles with α-oxocarboxylic acids

Hua Wang[a], Hua Yang[a], Yiping Li[b] and Xin-Hua Duan*[a]

[a]*Department of Chemistry, School of Science and MOE Key Laboratory for Nonequilibrium Synthesis and Modulation of Condensed Matter, Xi'an Jiaotong University, Xi'an 710049, China*

[b]*Department of Pharmacy, College of Medicine, Xi'an Jiaotong University, Xi'an 710061, China.*

duanxh@mail.xjtu.edu.cn

Table of Contents

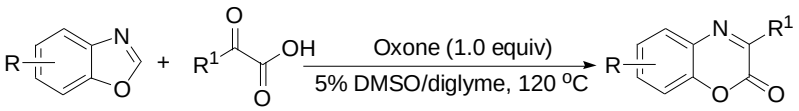
General information:

All Reactions were carried out under an atmosphere of nitrogen with the strict exclusion of moisture. The dry DMSO were distilled from CaH_2 under nitrogen and stored over molecular sieves under nitrogen. Diglyme was purchased from commercial sources and stored under nitrogen. Column chromatography was carried out on silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz in solvents as indicate. Chemical shift are reported in ppm from $CDCl_3$ using TMS as internal standard. IR spectra were recorded on an FT-IR spectrometer and only major peaks are reported in cm^{-1}. HRMS were obtained on a Q-TOF micro spectrometer. Melting points were determined on a microscopic apparatus and were uncorrected.

Starting materials:

Phenylglyoxylic acid **2a** and pyruvic acids were purchased from Sigma-Aldrich and TCI. Other α-oxocarboxylic acids were prepared from the corresponding methyl ketones according to the reported procedure.[1]

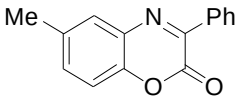
General procedure for the oxidative cleavage/coupling of benzoxazoles with α-oxocarboxylic acids



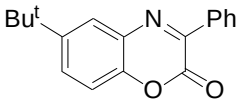
1 **2** **3** or **4**

A 10 mL oven-dried Schlenk-tube was charged with oxone (123 mg, 0.2 mmol, 1.0 equiv). The tube was evacuated and backfilled with nitrogen (three times). Benzoxazoles (**1**, 0.2 mmol) and α-oxocarboxylic acids (**2**, 0.3 mmol, 1.5 equiv) in 5% DMSO/diglyme (1.0 mL) were added by syringe under nitrogen. The tube was then sealed and the mixture was stirred for 10-12h at 120 ^{o}C. Upon completion of the reaction (monitored by TLC), the mixture was diluted with EtOAc, filtered through a pad of Celite, and the filtrate was washed with water, dried over Na_2SO_4. After the solvent was removed, the residue was purified with chromatography column on silica gel (gradient eluent of EtOAc/petroleum ether = 1/50 to 1/20) to give the corresponding products **3** or **4** in yields listed in Table 2 and Table 3.

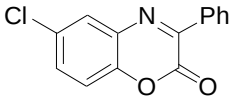
Characterization of products 3



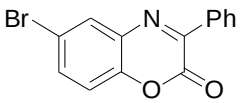
6-Methyl-3-phenyl-benzo[1,4]oxazin-2-one (**3a**). Known compound,[2] R_f 0.3 (EtOAc/petroleum ether = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34-8.31 (dd, *J* = 1.6, 7.6 Hz, 2H), δ = 7.65 (s, 1H), δ = 7.55-7.47 (m, 3H), δ = 7.34-7.31 (dd, *J* = 1.6, 8.4 Hz, 1H), δ = 7.24-7.22 (d, *J* = 8.4 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.5, 150.7, 144.4, 135.5, 134.3, 132.1, 131.4, 131.3, 129.4, 129.3, 128.4, 115.7, 20.9.



6-*tert*-Butyl-3-phenyl-benzo[1,4]oxazin-2-one (**3b**). Known compound,[2] R_f 0.3 (EtOAc/petroleum ether = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34-8.32 (dd, *J* = 1.6, 8.0 Hz, 2H), δ = 7.87-7.86 (d, *J* = 2.0 Hz, 1H), δ = 7.58-7.49 (m, 4H), δ = 7.28-7.26 (d, *J* = 8.4 Hz, 1H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.6, 150.7, 149.0, 144.2, 134.3, 131.3, 131.2, 129.4, 128.7, 128.4, 126.0, 115.5, 34.7, 31.3.

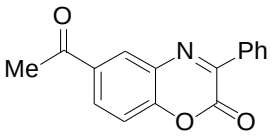


6-Chloro-3-phenyl-benzo[1,4]oxazin-2-one (**3c**). Known compound,[2] R_f 0.4 (EtOAc/petroleum ether = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34-8.33 (d, *J* = 7.2 Hz, 2H), δ = 7.85-7.84 (d, *J* = 2.0 Hz, 1H), δ = 7.58-7.45 (m, 4H), δ = 7.28-7.26 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.7, 151.6, 145.0, 133.7, 132.1, 131.9, 130.9, 130.7, 129.6, 128.8, 128.4, 117.3.

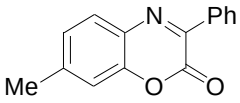


6-Bromo-3-phenyl-benzo[1,4]oxazin-2-one (**3d**). A yellow solid, R_f 0.35 (EtOAc/petroleum ether = 20:1), mp: 148-150 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ =

8.35-8.33 (d, *J* = 7.6 Hz, 2H), δ = 8.01 (s, 1H), δ = 7.62-7.60 (d, *J* = 8.8 Hz, 1H), δ = 7.56-7.49 (m, 3H), δ = 7.24-7.22 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.7, 151.6, 145.5, 133.8, 133.7, 132.5, 131.9, 129.6, 128.5, 117.9, 117.6; IR (KBr): υ_{max} 3437, 2925, 1743, 1384, 1124, 810 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_8BrNNaO_2$ $[M+Na]^+$ 323.9631, found 323.9637.

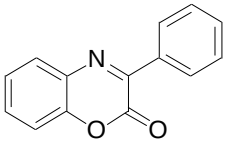


6-Acetyl-3-phenyl-benzo[1,4]oxazin-2-one (**3e**). A yellow solid, R_f 0.2 (EtOAc/petroleum ether = 2:1), mp: 159-161 ^oC; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.44 (s, 1H), δ = 8.36-8.34 (d, *J* = 7.2 Hz, 2H), δ = 8.17-8.14 (d, *J* = 8.8 Hz, 1H), δ = 7.58-7.51 (m, 3H), δ = 7.43-7.41 (d, *J* = 8.8 Hz, 1H), 2.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.0, 151.7, 151.5, 149.5, 134.6, 133.6, 131.9, 131.1, 130.6, 130.2, 129.5, 128.5, 116.7, 26.7; IR (KBr): υ_{max} 3430, 2923, 1742, 1602, 1118, 812 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{11}NNaO_3$ $[M+Na]^+$ 288.0631, found 288.0621.

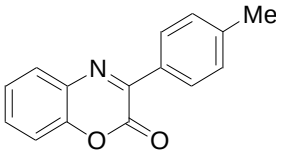


7-Methyl-3-phenyl-benzo[1,4]oxazin-2-one (**3f**). Known compound,[2] R_f 0.3 (EtOAc/petroleum ether = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32-8.30 (d, *J* = 7.6 Hz, 2H), δ = 7.73-7.71 (d, *J* = 8.4 Hz, 1H), δ = 7.51-7.48 (m, 3H), δ = 7.21-7.19 (d, *J* = 8.0 Hz, 1H), 7.13 (s, 1H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.5, 149.6, 146.4, 142.6, 134.3, 131.1, 129.7, 129.3, 129.0, 128.3, 126.7, 116.2, 21.8.

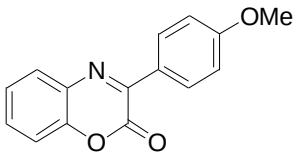
Characterization of Products 4



3-Phenyl-benzo[1,4]oxazin-2-one (**4a**). Known compound,[2] R_f 0.35 (EtOAc/petroleum ether = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.35-8.33 (d, *J* = 7.6 Hz, 2H), δ = 7.87-7.85 (d, *J* = 7.6 Hz, 1H), δ = 7.54-7.49 (m, 4H), δ = 7.42-7.38 (t, *J* = 7.6 Hz, 1H), δ = 7.35-7.33 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.3, 150.9, 146.5, 134.1, 131.7, 131.4, 131.1, 129.4, 128.4, 125.5, 116.2.

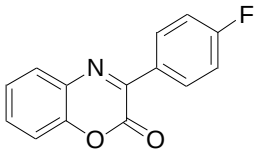


3-*p*-Tolyl-benzo[1,4]oxazin-2-one (**4b**). Known compound,[2] R_f 0.35 (EtOAc/petroleum ether = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28-8.25 (d, *J* = 8.4 Hz, 2H), δ = 7.85-7.82 (dd, *J* = 1.2, 8.0 Hz, 1H), δ = 7.52-7.47 (dt, *J* = 1.2, 8.4 Hz, 1H), δ = 7.40-7.36 (dt, *J* = 0.8, 7.6 Hz, 1H), δ = 7.33-7.30 (m, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.3, 150.6, 146.4, 142.0, 131.7, 131.4, 130.8, 129.4, 129.3, 129.1, 125.5, 116.1, 21.6.

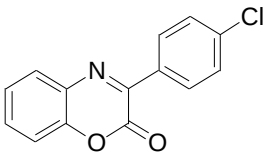


3-(4-Methoxy-phenyl)-benzo[1,4]oxazin-2-one (**4c**). A yellow solid, R_f 0.2 (EtOAc/petroleum ether = 15:1), mp: 133-135 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.41-8.39 (d, *J* = 8.8 Hz, 2H), δ = 7.82-7.80 (d, *J* = 8.0 Hz, 1H), δ = 7.49-7.46 (t, *J* = 8.4 Hz, 1H), δ = 7.39-7.35 (t, *J* = 7.6 Hz, 1H), δ = 7.32-7.30 (d, *J* = 8.0 Hz, 1H),

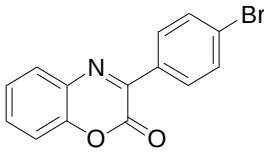
7.01-6.99 (d, *J* = 8.8 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.4, 152.5, 149.8, 146.3, 131.7, 131.4, 130.4, 129.1, 126.8, 125.4, 116.0, 113.8, 55.4; IR (KBr): υ_{max} 3434, 2930, 1730, 1603, 1133, 759 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{11}NNaO_3$ $[M+Na]^+$ 276.0631, found 276.0623.



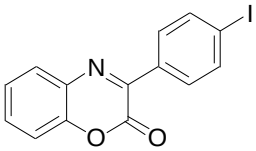
3-(4-Fluoro-phenyl)-benzo[1,4]oxazin-2-one (**4d**). Known compound,[2] R_f 0.4 (EtOAc/petroleum ether = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.43-8.40 (m, 2H), δ = 7.85-7.83 (d, *J* = 8.0 Hz, 1H), δ = 7.54-7.50 (dt, *J* = 0.8, 8.0 Hz, 1H), δ = 7.42-7.38 (t, *J* = 7.6 Hz, 1H), δ = 7.35-7.33 (d, *J* = 8.0 Hz, 1H), 7.20-7.16 (t, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.8 (d, $J_{C,F}$ = 252.0 Hz), 152.2, 149.5, 146.4, 131.9, 131.8, 131.5, 131.2, 130.3, 129.4, 125.6, 116.2, 115.6, 115.4.



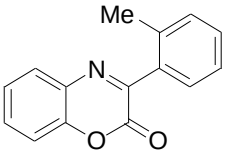
3-(4-Chloro-phenyl)-benzo[1,4]oxazin-2-one (**4e**). Known compound,[2] R_f 0.4 (EtOAc/petroleum ether = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36-8.34 (d, *J* = 8.8 Hz, 2H), δ = 7.85-7.83 (dd, *J* = 1.2, 8.0 Hz, 1H), δ = 7.55-7.51 (dt, *J* = 1.2, 8.4 Hz, 1H), δ = 7.48-7.46 (d, *J* = 8.8 Hz, 2H), δ = 7.42-7.38 (t, *J* = 7.6 Hz, 1H), 7.35-7.33 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.1, 149.5, 146.5, 137.8, 132.5, 131.5, 131.4, 130.8, 129.5, 128.7, 125.7, 116.2.



3-(4-Bromo-phenyl)-benzo[1,4]oxazin-2-one (**4f**). Known compound,[2] R_f 0.4 (EtOAc/petroleum ether = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27-8.25 (d, *J* = 8.4 Hz, 2H), δ = 7.85-7.83 (dd, *J* = 0.8, 8.0 Hz, 1H), δ = 7.63-7.61 (d, *J* = 8.8 Hz, 2H), δ = 7.55-7.51 (dt, *J* = 0.8, 8.4 Hz, 1H), δ = 7.42-7.38 (t, *J* = 7.6 Hz, 1H), 7.34-7.32 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.1, 149.5, 146.4, 132.9, 131.6, 131.5, 131.4, 131.0, 129.5, 126.4, 125.7, 116.2.

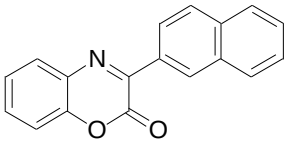


3-(4-Iodo-phenyl)-benzo[1,4]oxazin-2-one (**4g**). A yellow solid, R_f 0.4 (EtOAc/petroleum ether = 20:1), mp: 126-128 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11-8.09 (d, *J* = 8.4 Hz, 2H), δ = 7.84-7.82 (m, 3H), δ = 7.55-7.51 (dt, *J* = 1.2, 8.4 Hz, 1H), δ = 7.41-7.37 (t, *J* = 8.0 Hz, 1H), δ = 7.33-7.31 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.0, 149.7, 146.4, 137.6, 133.4, 131.5, 131.4, 130.9, 129.5, 125.7, 116.2, 98.9; IR (KBr): υ_{max} 3436, 2924, 1731, 1585, 1111, 750 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_8INNaO_2$ $[M+Na]^+$ 371.9492, found 371.9504.

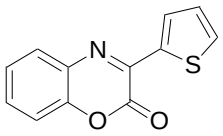


3-*o*-Tolyl-benzo[1,4]oxazin-2-one (**4h**). A yellow solid, R_f 0.4 (EtOAc/petroleum ether = 20:1), mp: 124-126 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85-7.83 (dd, *J* = 1.2, 8.0 Hz, 1H), δ = 7.58-7.52 (m, 2H), δ = 7.43-7.36 (m, 3H), δ = 7.33-7.30 (m, 2H), δ = 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.0, 152.4, 146.7, 137.2, 134.0, 131.4, 130.9, 130.2, 129.5, 125.8, 125.6, 116.4, 20.1; IR (KBr): υ_{max} 3436, 2929, 1730,

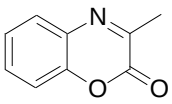
1456, 1133, 761 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{11}NNaO_2$ $[M+Na]^+$ 260.0682, found 260.0680.



3-Naphthalen-2-yl-benzo[1,4]oxazin-2-one (**4j**). A yellow solid, R_f 0.2 (EtOAc/petroleum ether = 20:1), mp: 173-175 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 9.07 (s, 1H), δ = 8.42-8.39 (dd, *J* = 1.2, 8.4 Hz, 1H), δ = 8.02-8.00 (d, *J* = 8.0 Hz, 1H), δ = 7.95-7.87 (m, 3H), δ = 7.60-7.51 (m, 3H), δ = 7.43-7.40 (t, *J* = 7.2 Hz, 1H), δ = 7.37-7.35 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.4, 150.2, 146.4, 134.7, 132.8, 131.7, 131.4, 131.1, 129.6, 129.4, 128.0, 127.9, 127.6, 126.5, 125.6, 125.3, 116.1; IR (KBr): υ_{max} 3462, 2925, 1744, 1605, 1108, 751 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{11}NNaO_2$ $[M+Na]^+$ 296.0682, found 296.0677.



3-Thiophen-2-yl-benzo[1,4]oxazin-2-one (**4k**). Known compound,[2] R_f 0.4 (EtOAc/petroleum ether = 20:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.43-8.42 (m, 1H), δ = 7.80-7.78 (dd, *J* = 1.2, 7.6 Hz, 1H), δ = 7.62-7.61 (d, *J* = 4.8 Hz, 1H), δ = 7.50-7.46 (dt, *J* = 1.2, 8.0 Hz, 1H), δ = 7.40-7.36 (m, 1H), δ = 7.33-7.31 (d, *J* = 8.4 Hz, 1H), δ = 7.20-7.18 (t, *J* = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.5, 146.0, 145.6, 138.5, 133.3, 132.5, 131.5, 130.5, 128.9, 128.6, 125.7, 116.2.



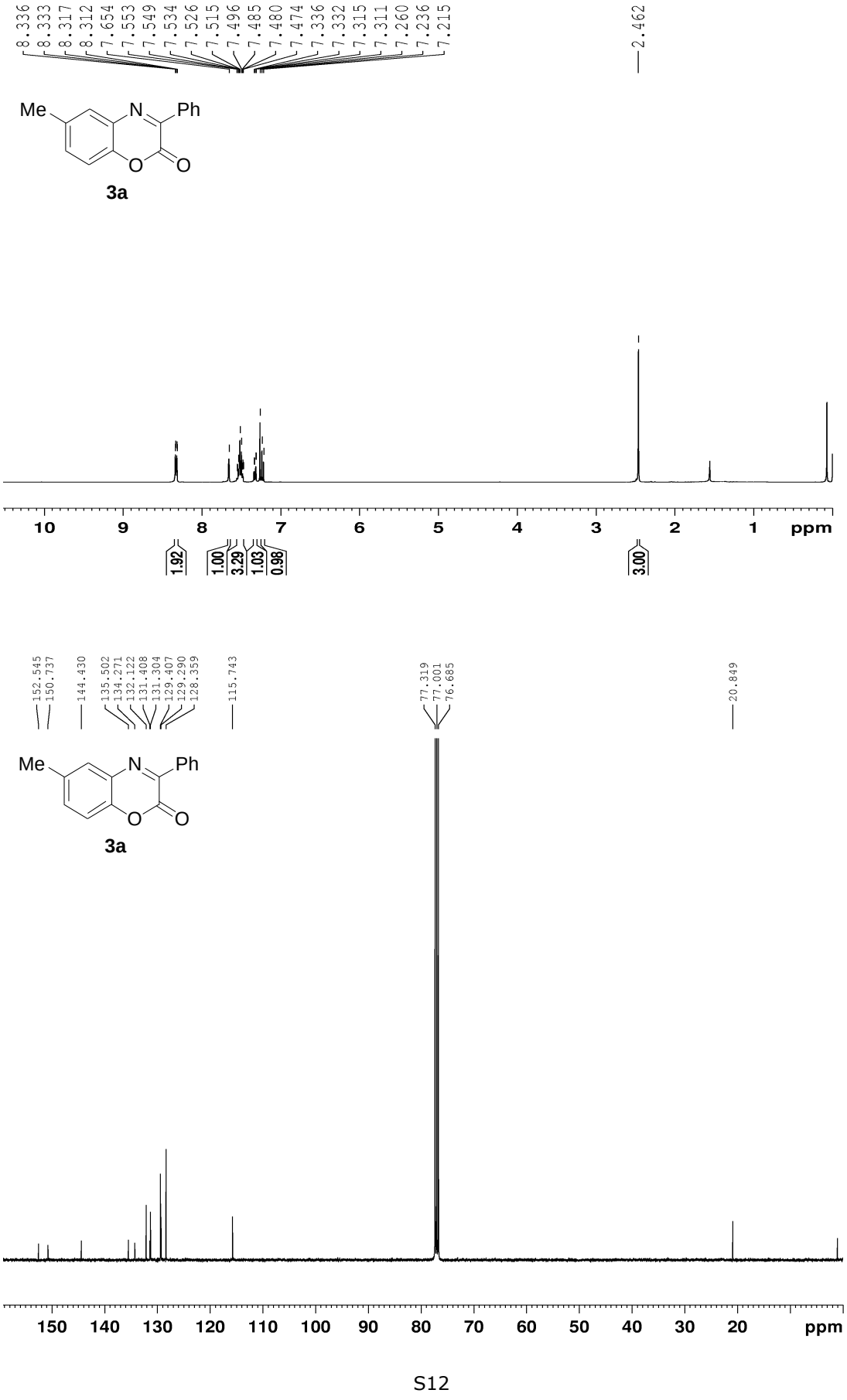
3-Methyl-benzo[1,4]oxazin-2-one (**4l**). Known compound,[2] R_f 0.2 (EtOAc/petroleum ether = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72-7.70 (dd, *J* = 1.2, 8.0 Hz, 1H), δ = 7.49-7.45 (dt, *J* = 1.2, 8.0 Hz, 1H), δ = 7.37-7.33 (dt, *J* = 1.2, 8.0 Hz, 1H), δ = 7.30-7.28 (d, *J* = 8.4 Hz, 1H), δ = 2.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.2, 153.3, 146.6, 131.2, 130.5, 128.6, 125.4, 116.4, 21.3.

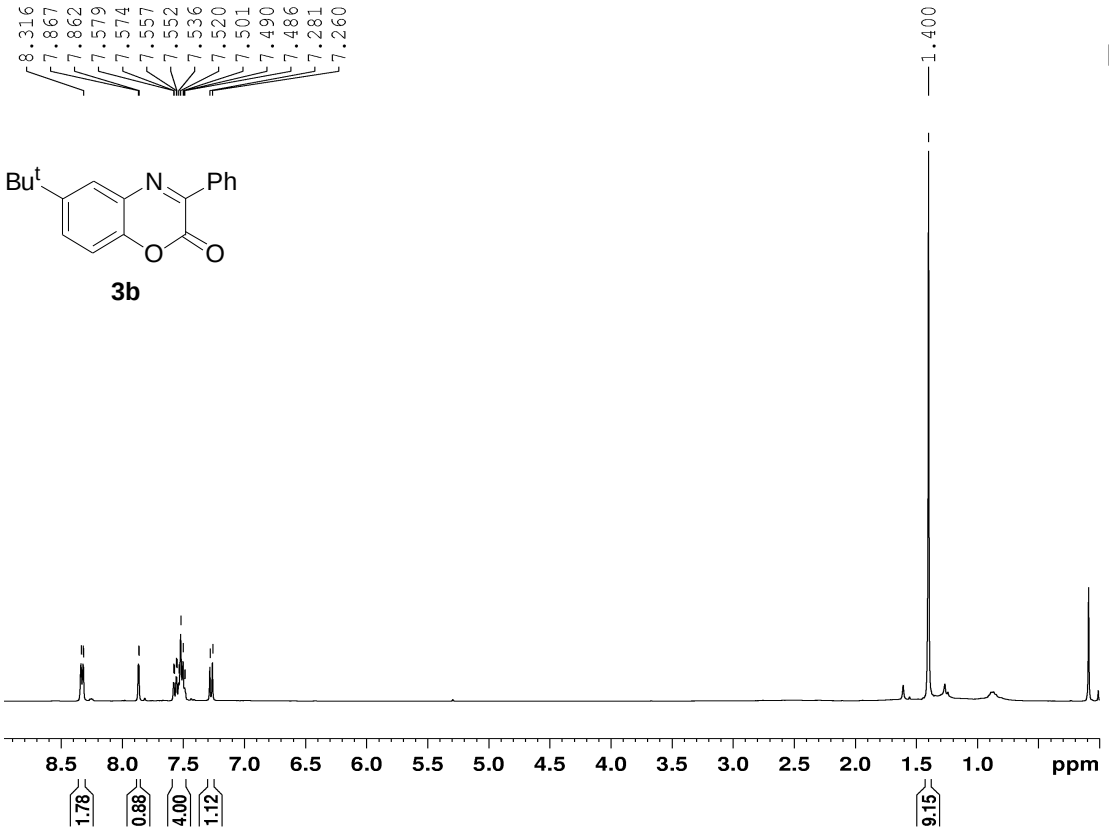
References

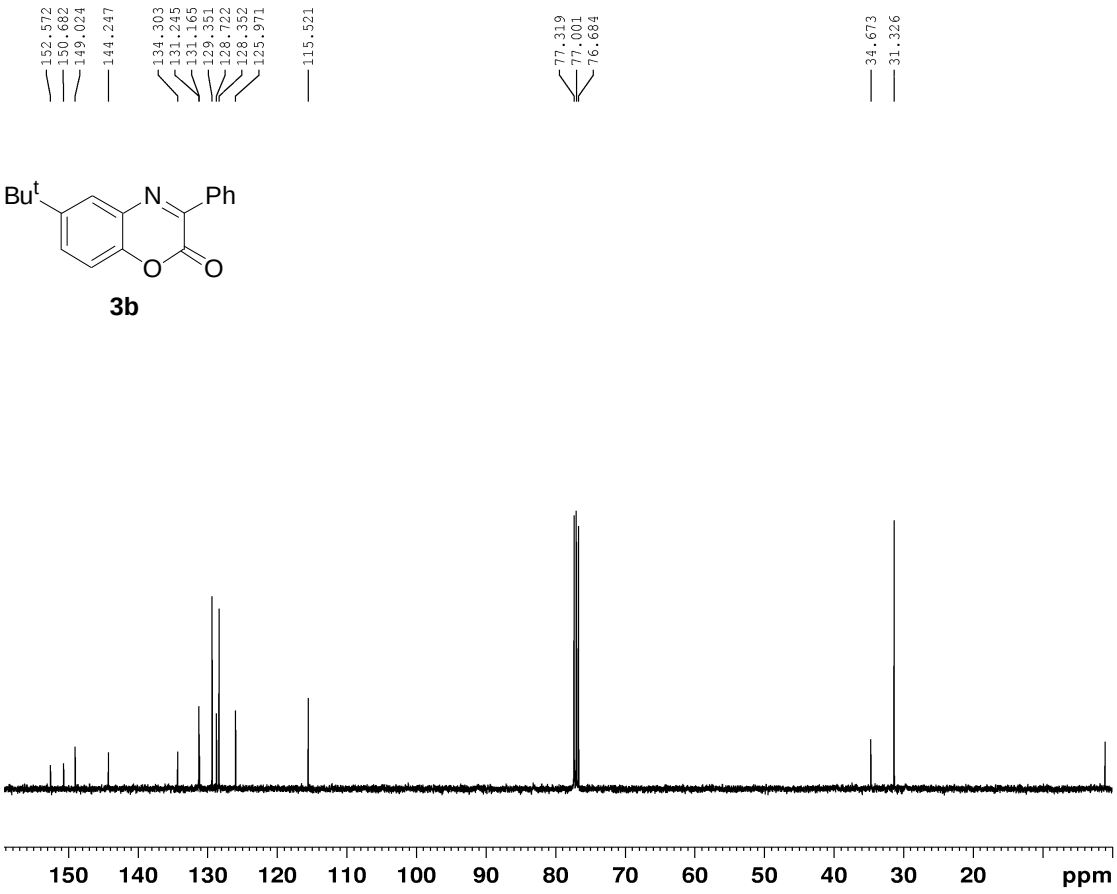
1. Wadhwa, K.; Yang, C.; West, P. R.; Deming, K. C.; Chemburkar, S. R.; Reddy, R. E. *Synth. Commun.* **2008**, *38*, 4434.

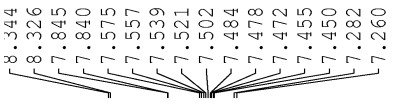
2. (a) Rueping, M.; Antonchick, A. P.; Theissmann, T. *Angew. Chem. Int. Ed.* **2006**, *45*, 6751. (b) Xue, Z.-Y.; Jiang, Y.; Peng, X.-Z.; Yuan, W.-C.; Zhang, X.-M. *Adv. Synth. Catal.* **2010**, *352*, 2132. (c) Chen, Q.-A.; Chen, M.-W.; Yu, C.-B.; Shi, L.; Wang, D.-S.; Yang, Y.; Zhou, Y.-G. *J. Am. Chem. Soc.* **2011**, *133*, 16432. (d) Yavari, I.; Souri, S.; Sirouspour, M.; Djahaniani, H. *Synthesis* **2006**, 3243.

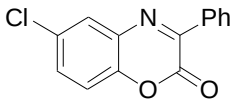
^{1}H NMR and ^{13}C NMR Spectra of the Products



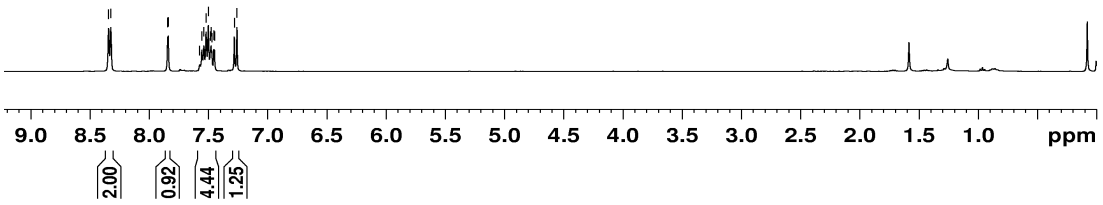


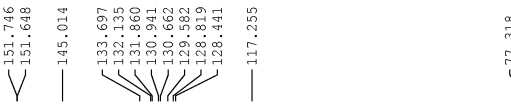


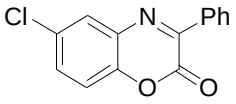




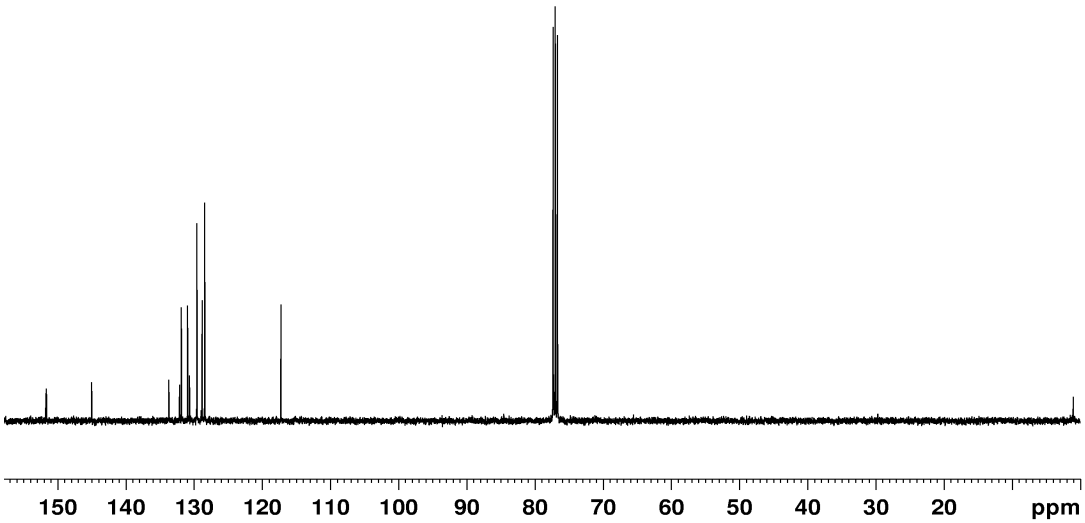
3c

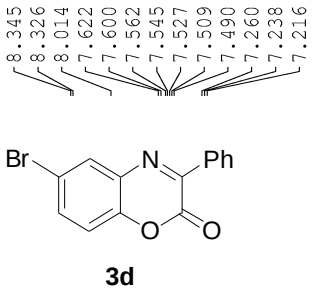




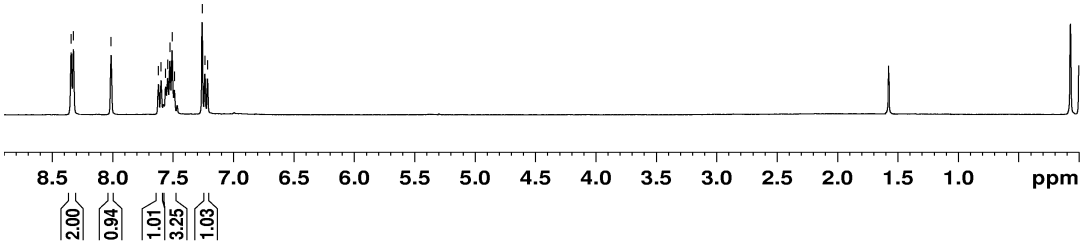


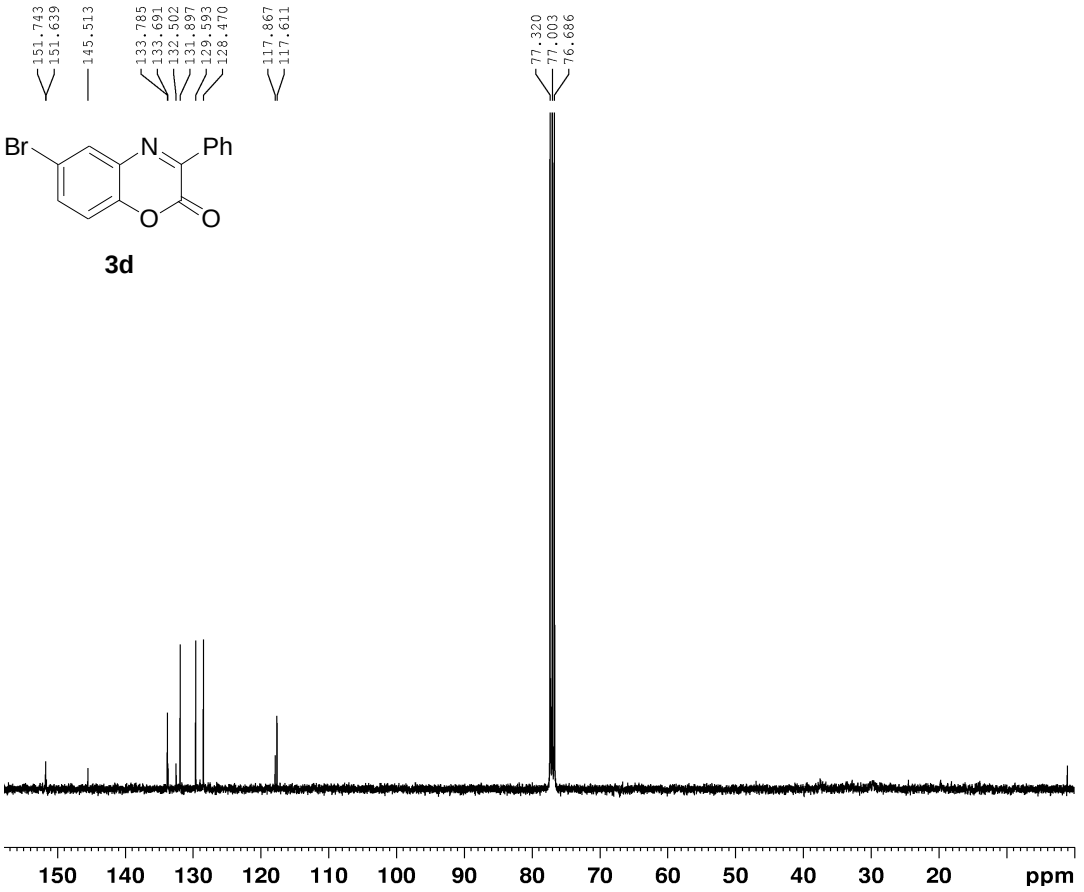
3c



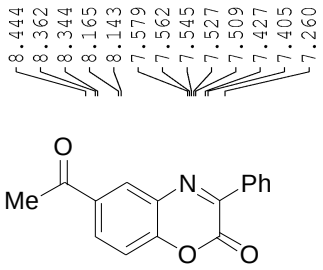


3d

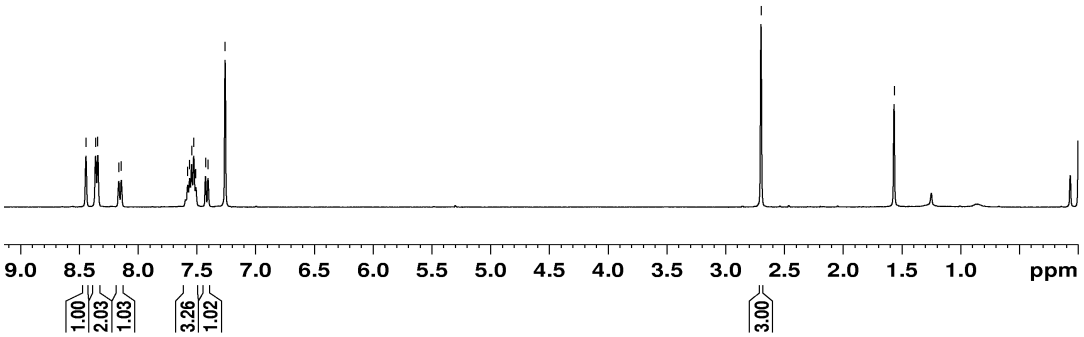


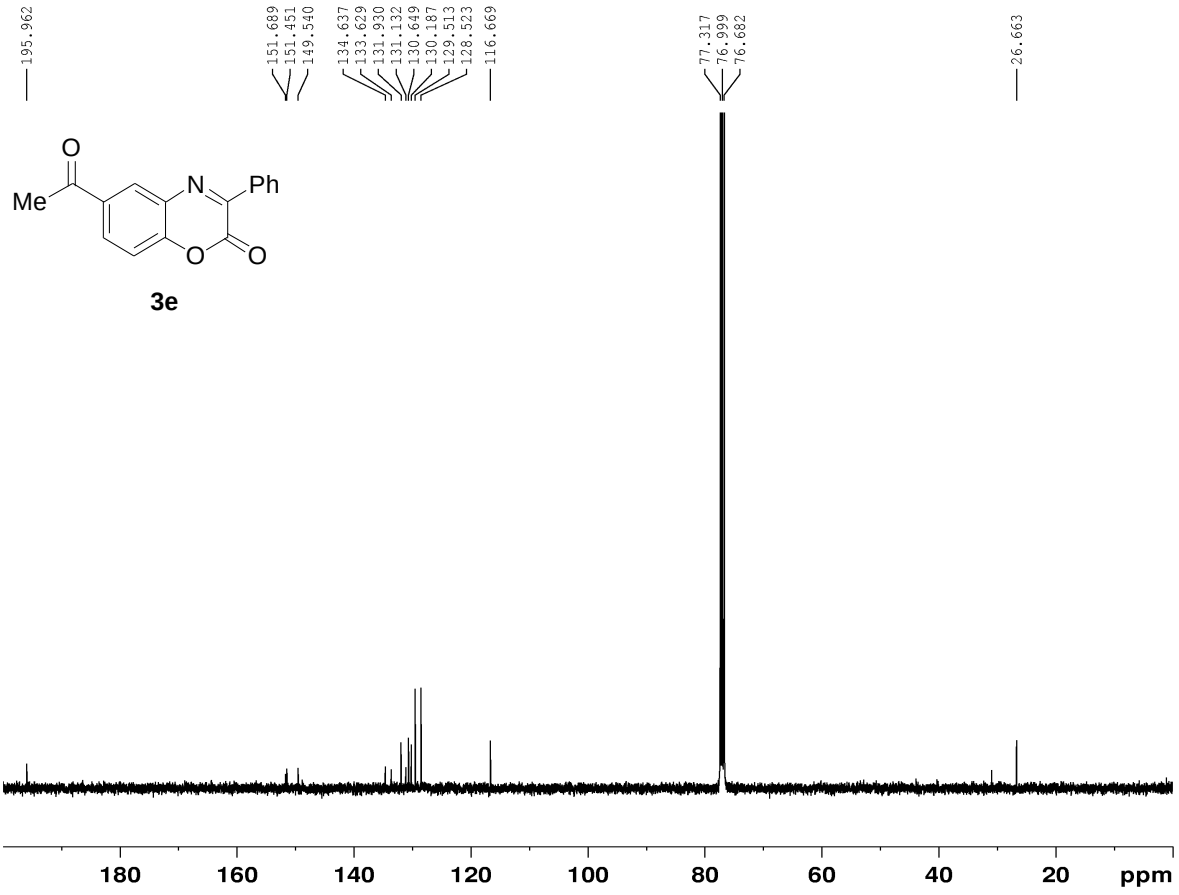


3d

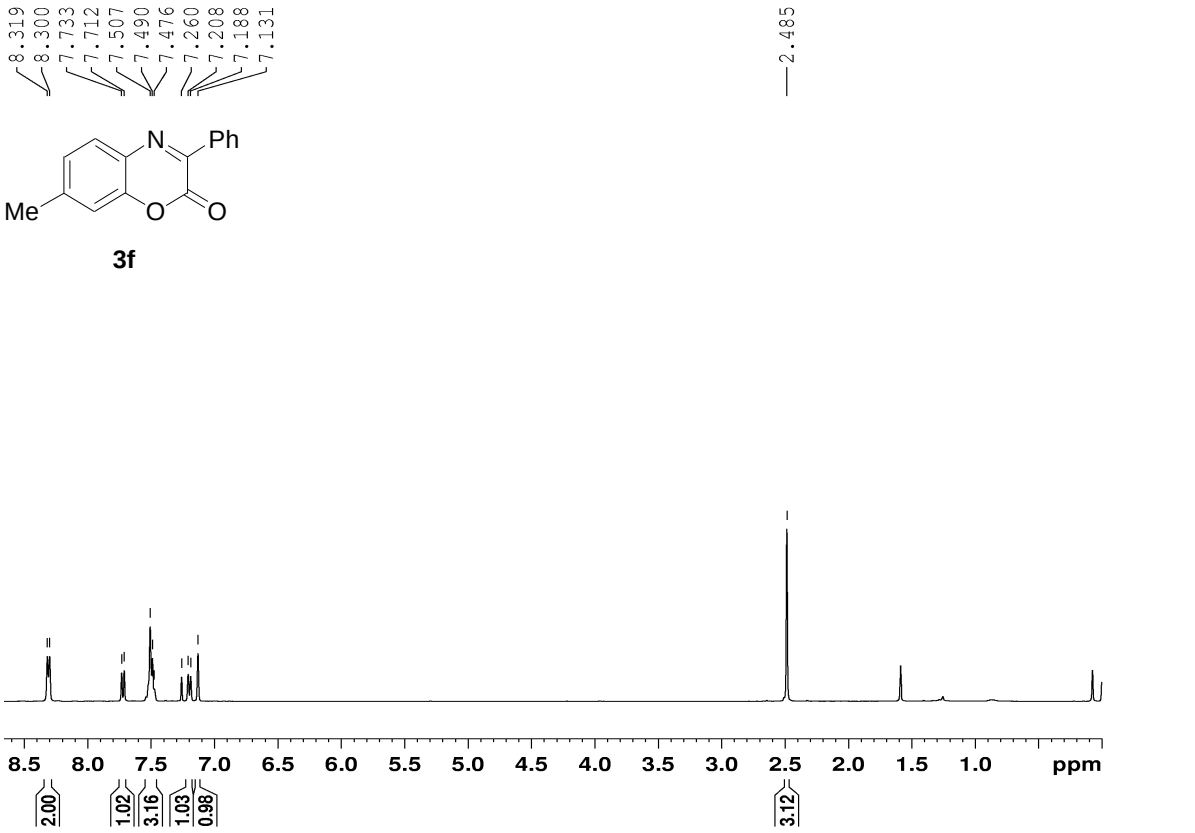


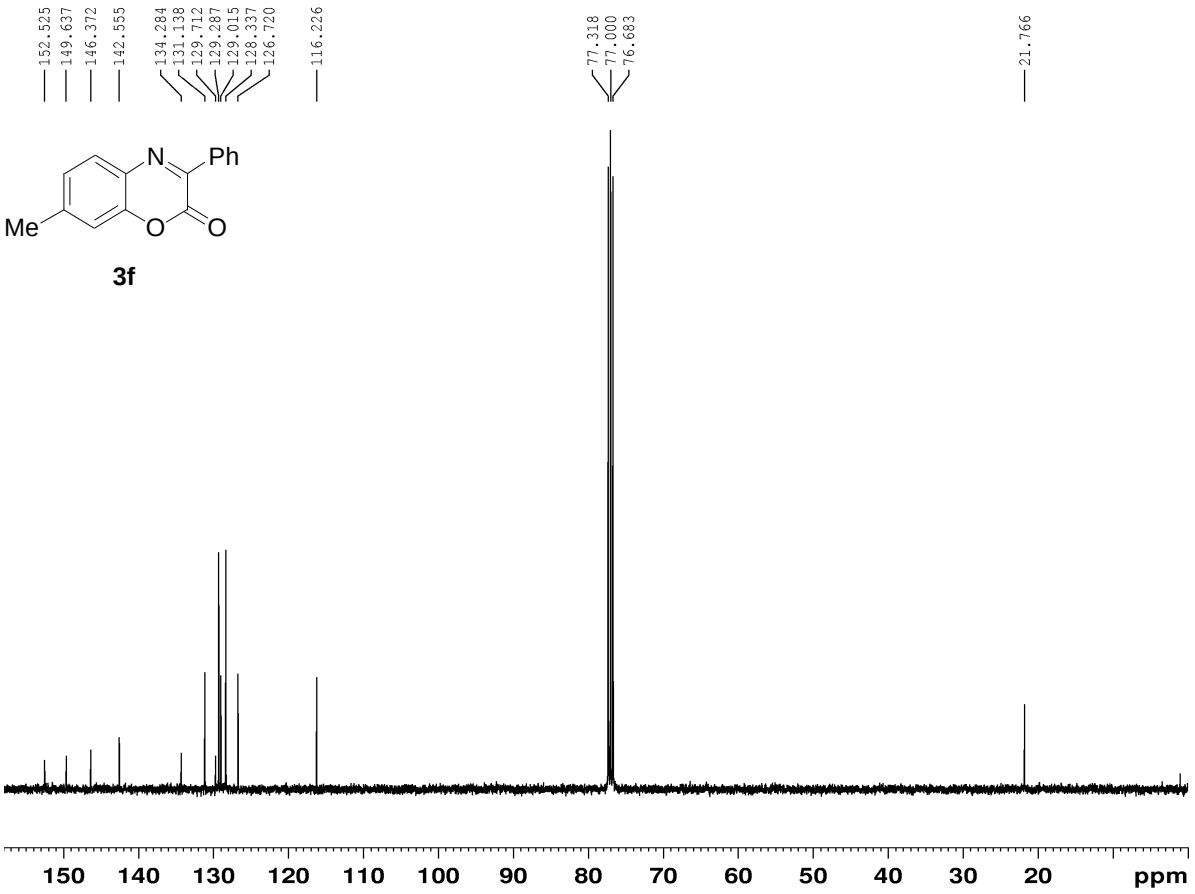
3e

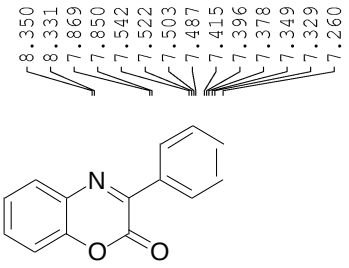




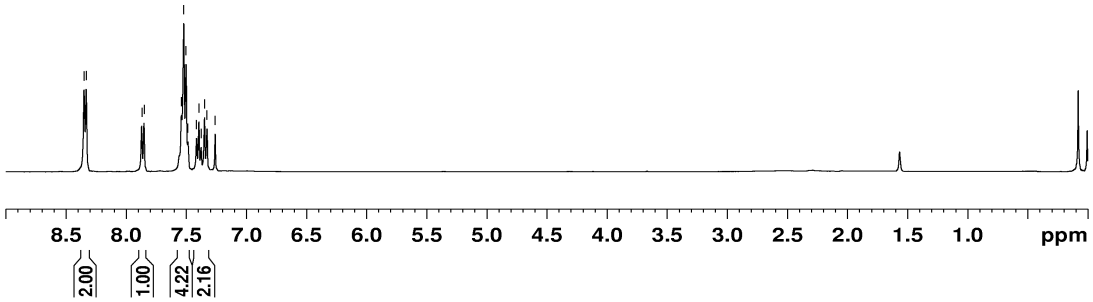
3e

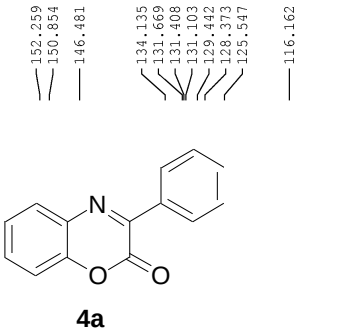




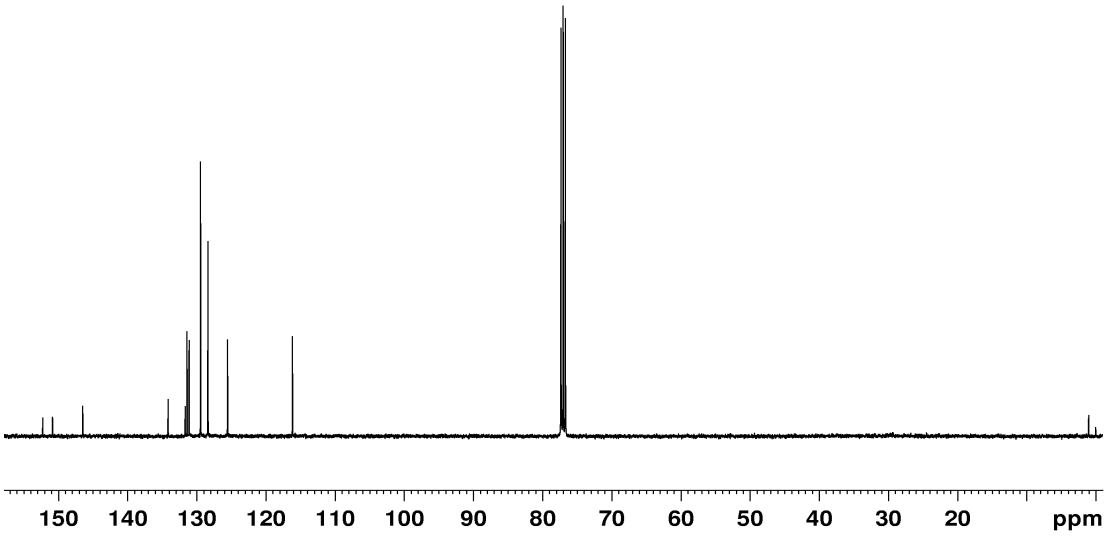


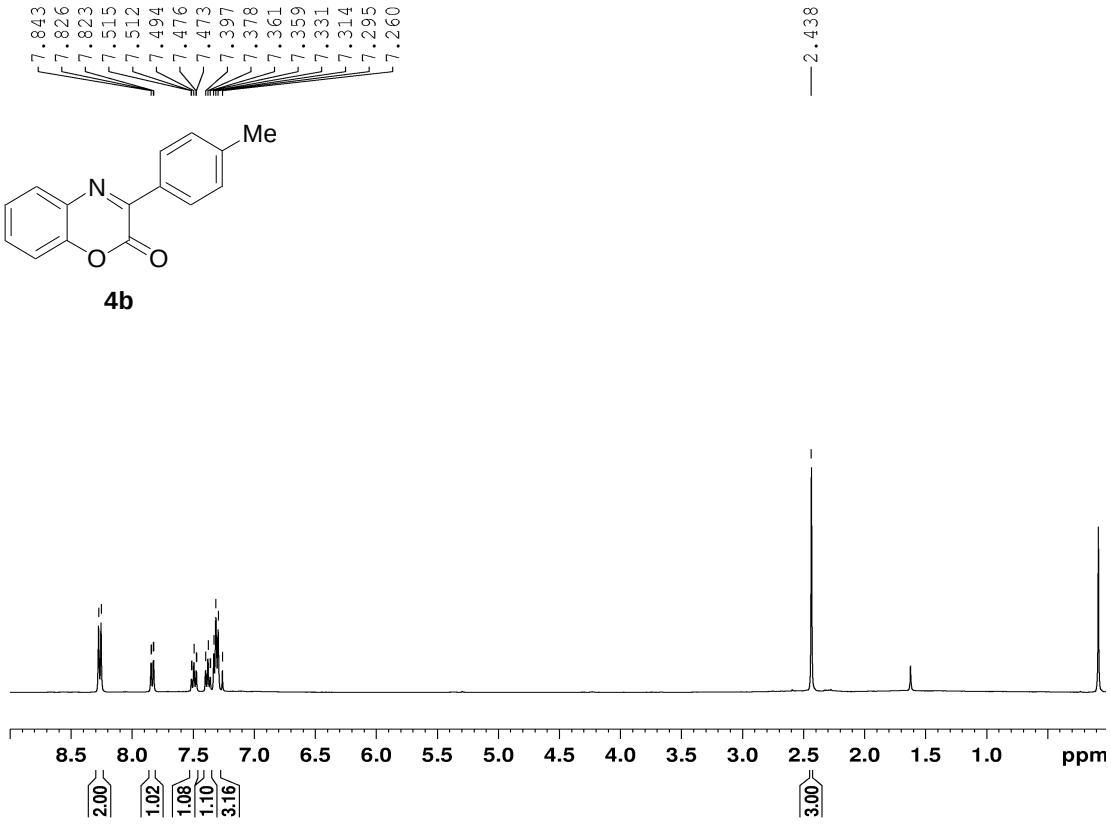
4a



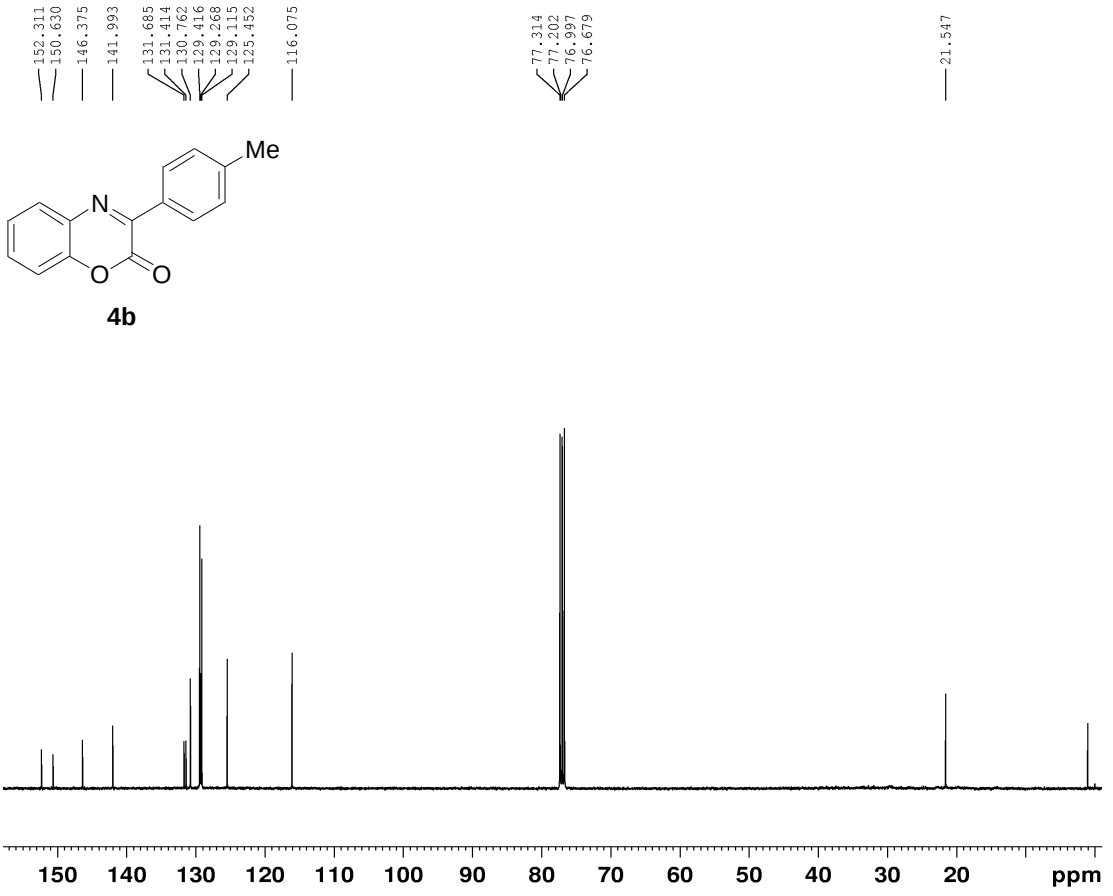


4a



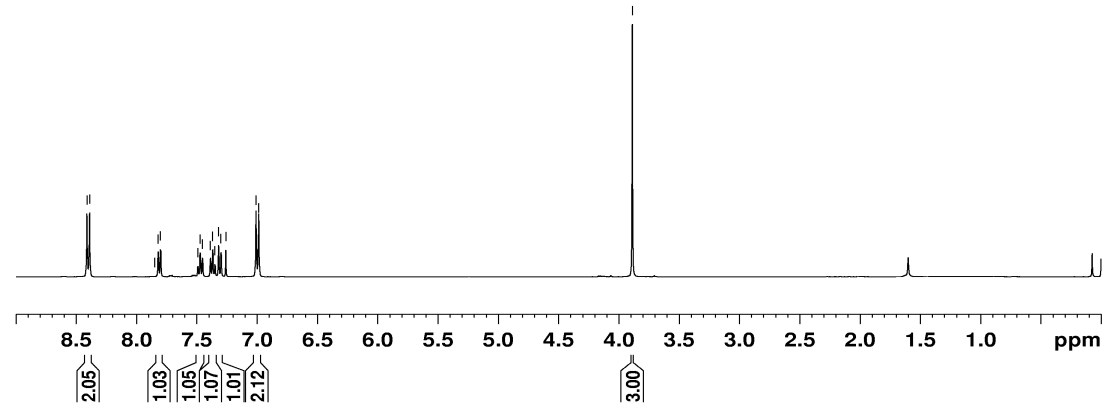


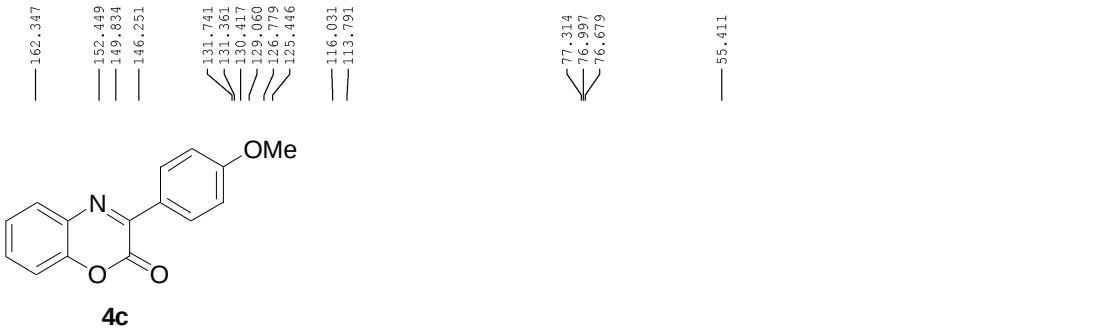
4b



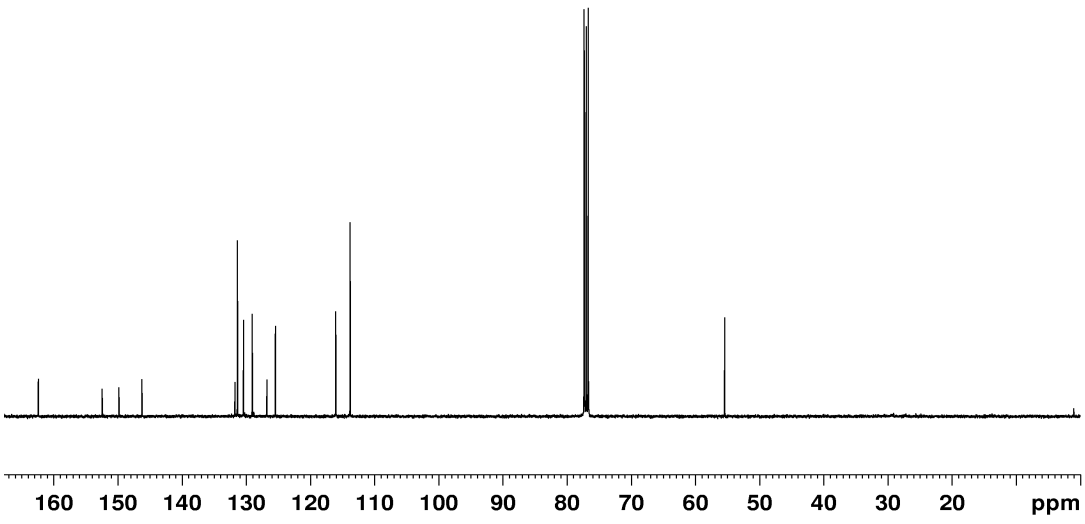
4b

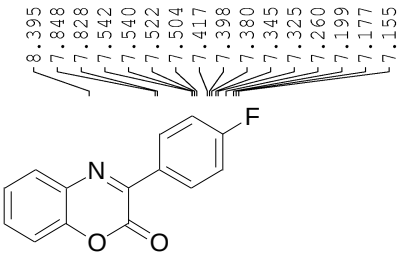
4c



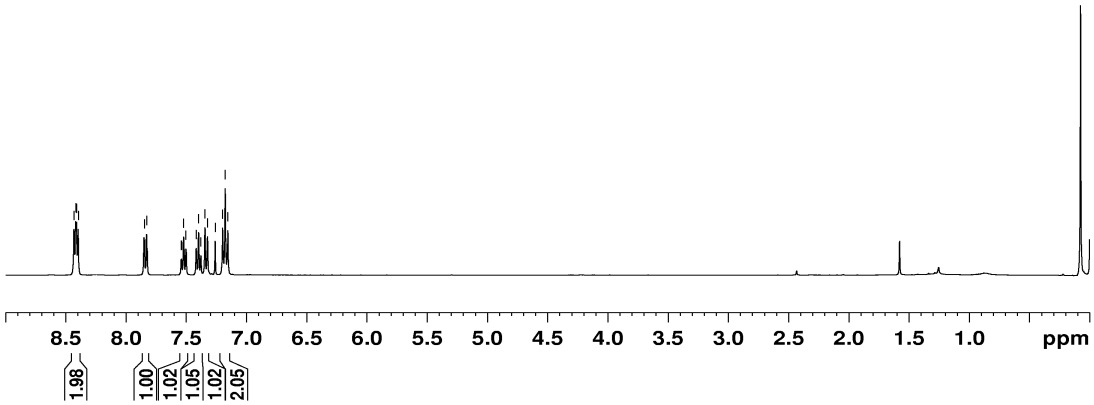


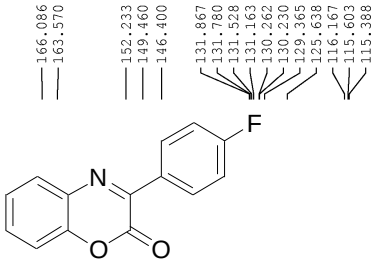
4c



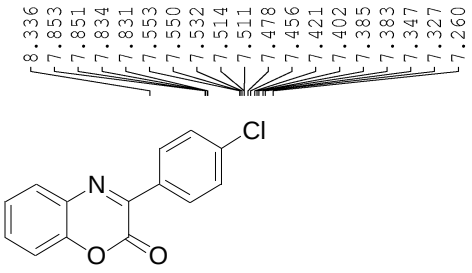


4d

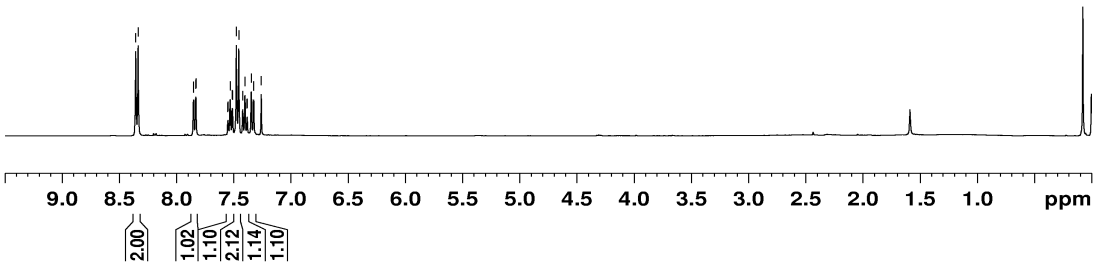


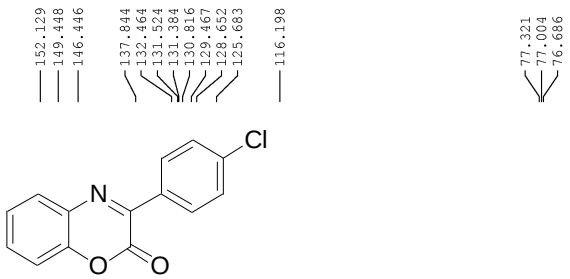


4d

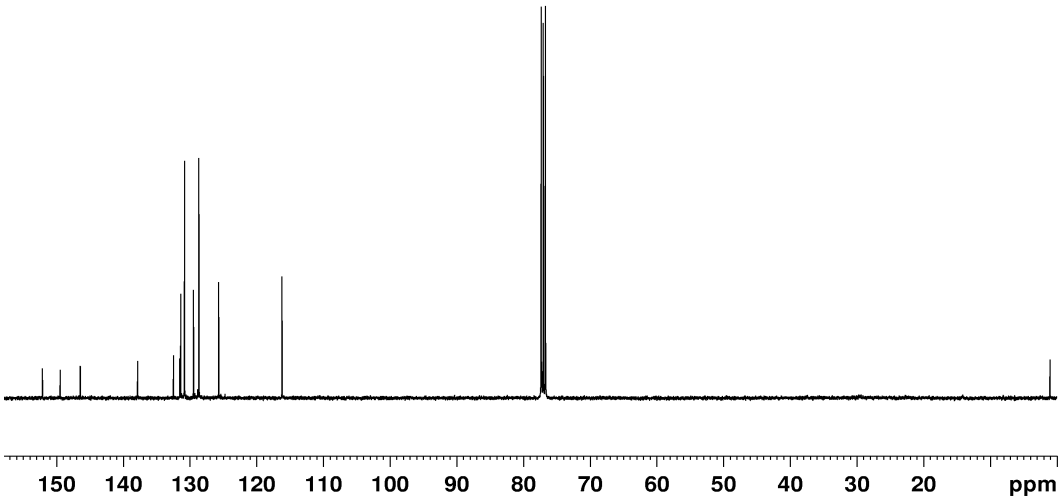

8.336
7.853
7.851
7.834
7.831
7.553
7.550
7.532
7.514
7.511
7.478
7.456
7.421
7.402
7.385
7.383
7.347
7.327
7.260
Cl
N
O
O

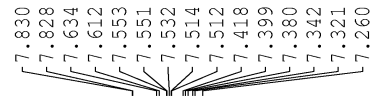
4e

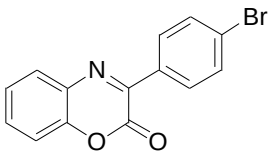

9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.00
1.02
1.10
2.12
1.14
1.10


152.129
149.448
146.446
137.844
132.464
131.524
131.384
130.816
129.467
128.652
125.683
116.198
77.321
77.004
76.686
Cl
N
O
O

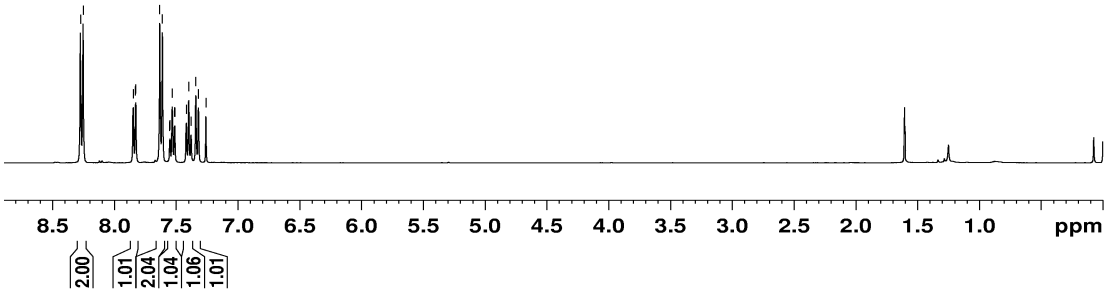
4e

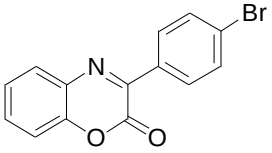

150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm



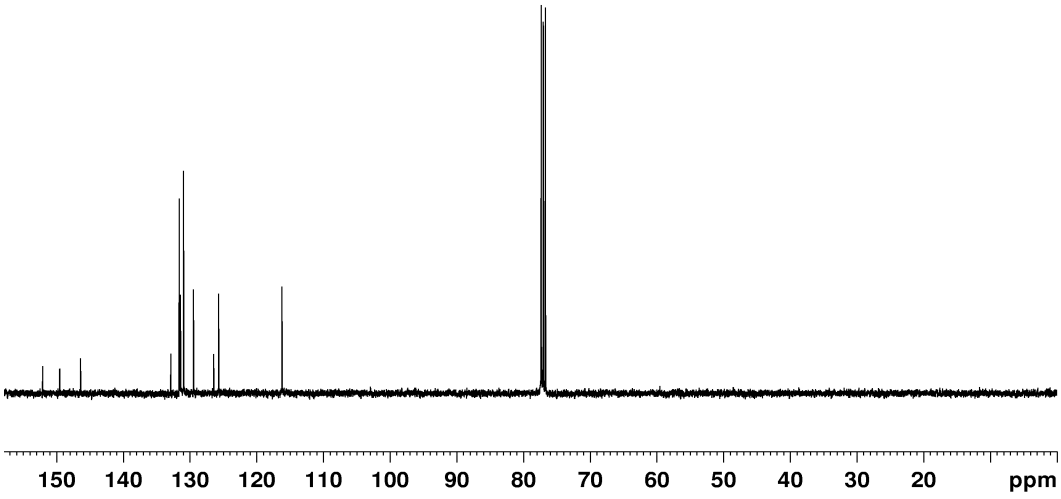


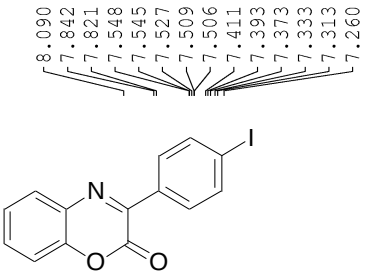
4f



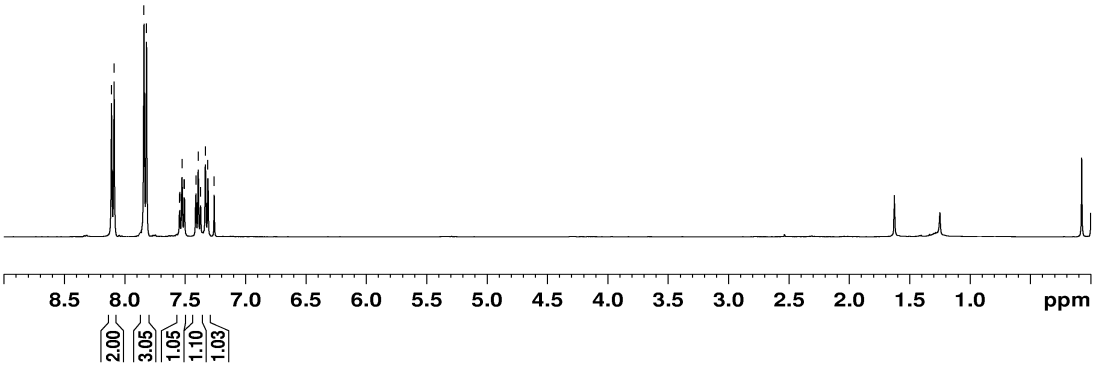


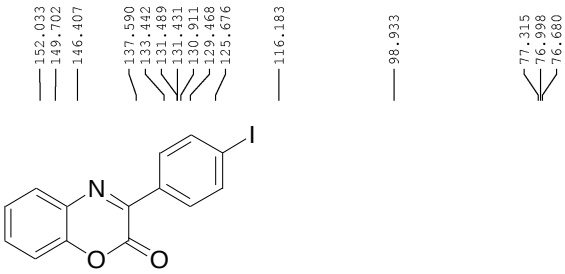
4f



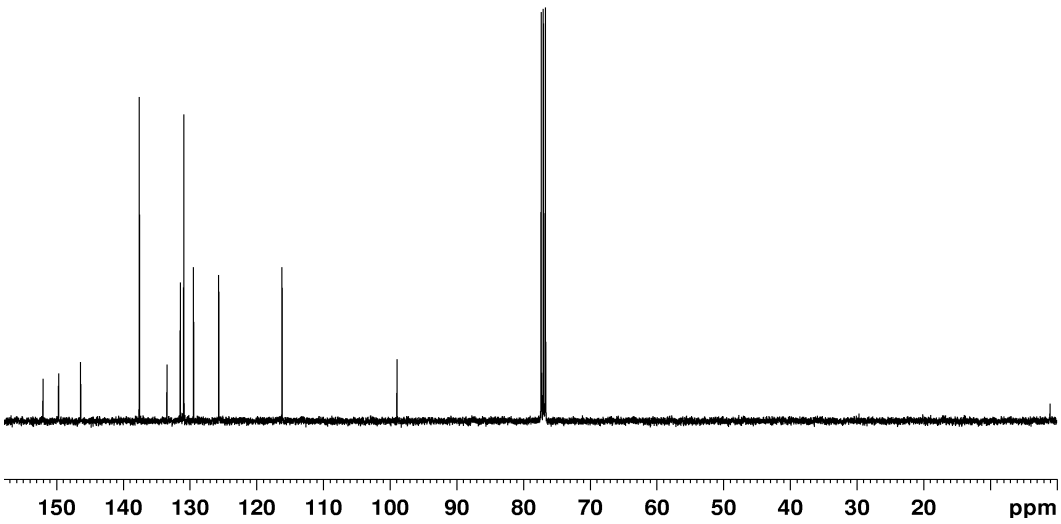


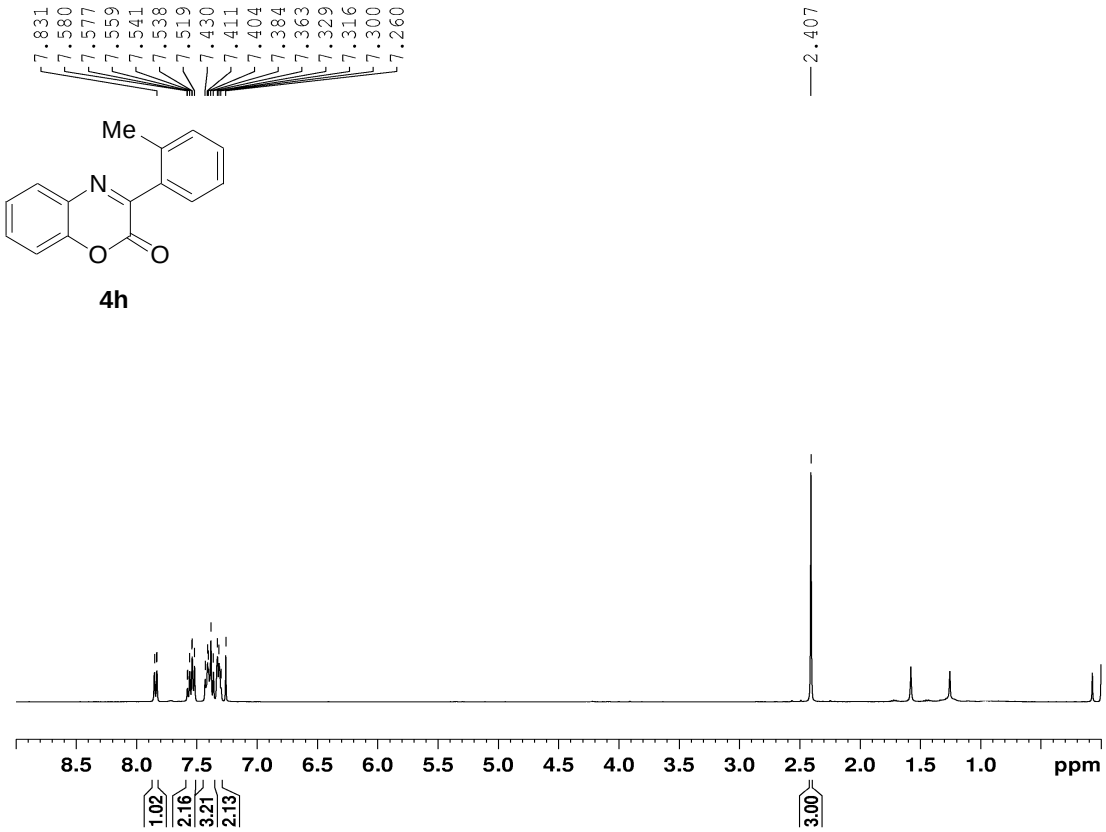
4g

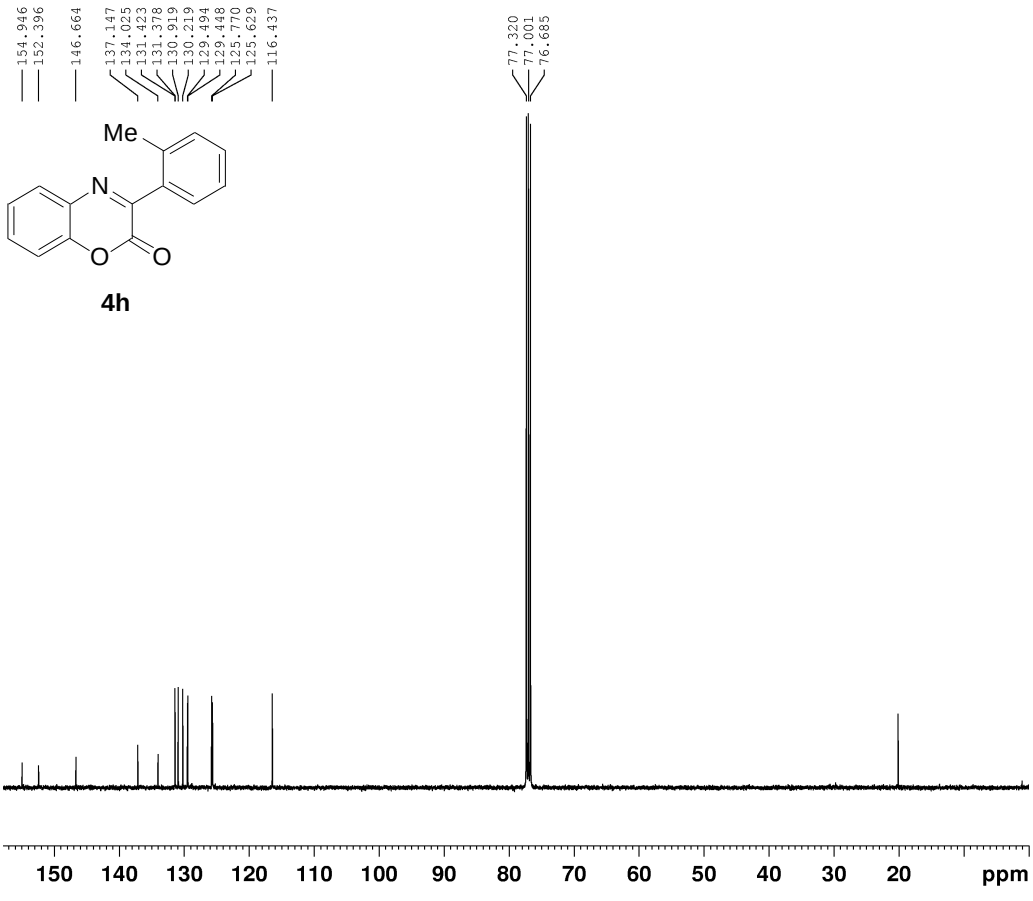


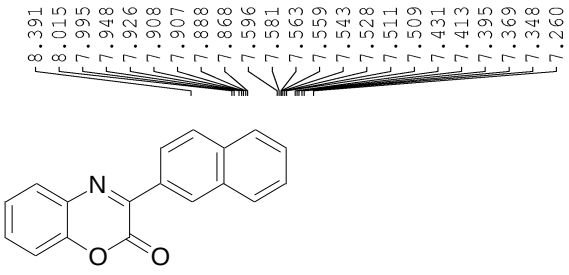


4g

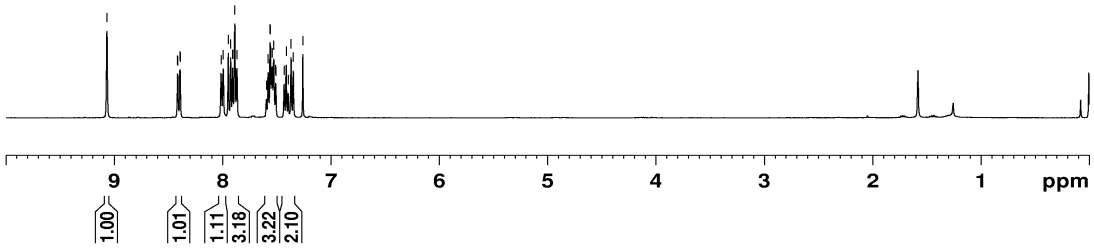


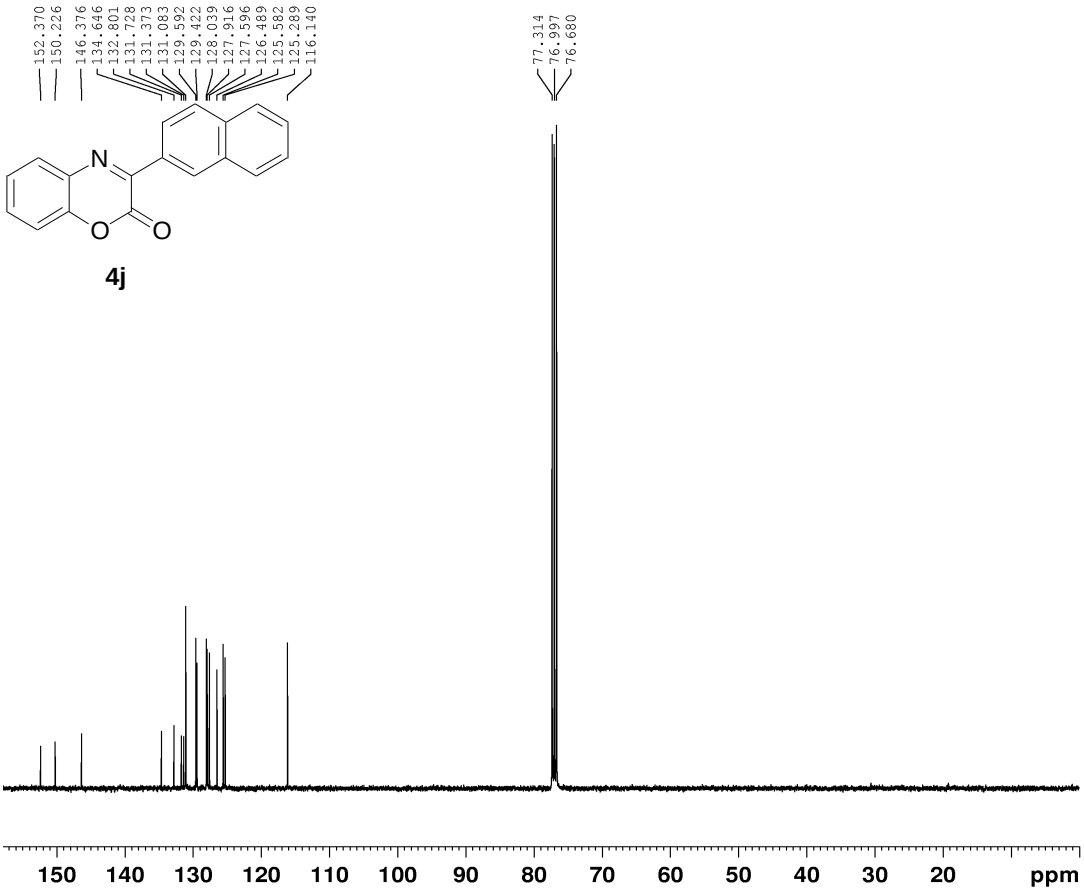

7.831
7.580
7.577
7.559
7.541
7.538
7.519
7.430
7.411
7.404
7.384
7.363
7.329
7.316
7.300
7.260
2.407
Me
N
O
O
4h
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.02
2.16
3.21
2.13
3.00


154.946
152.396
146.664
137.147
134.025
131.423
131.378
130.919
130.219
129.494
129.448
125.770
125.629
116.437
77.320
77.001
76.685
Me
N
O
O
4h
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

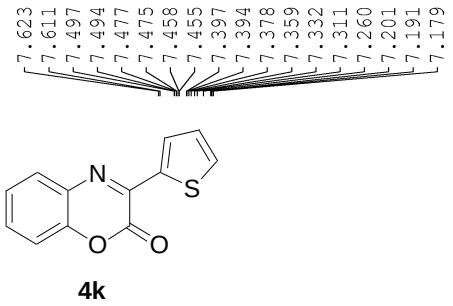


4j

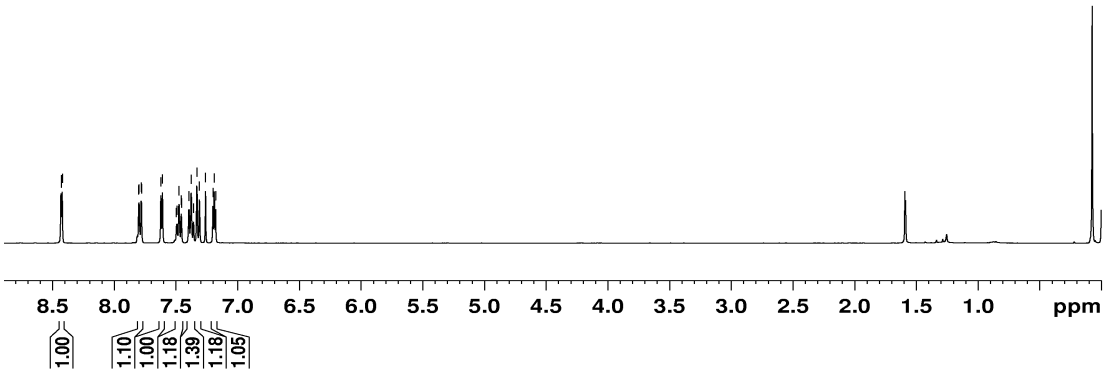


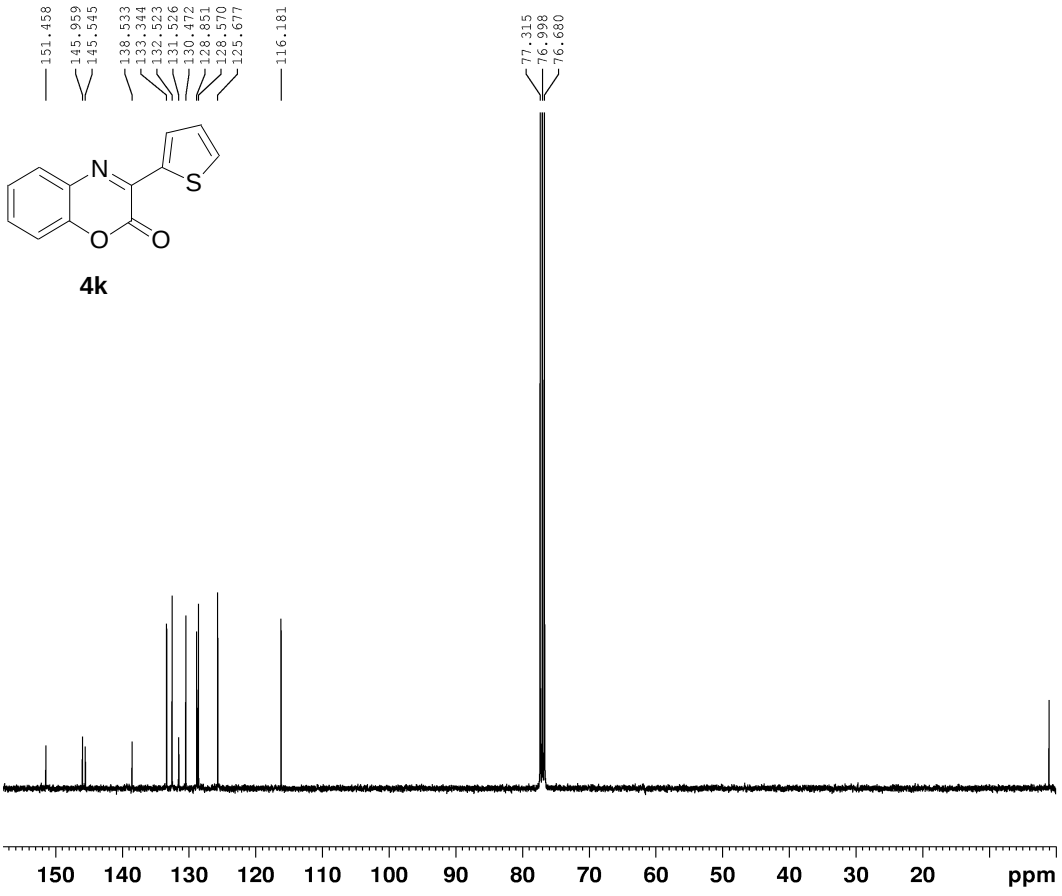


4j

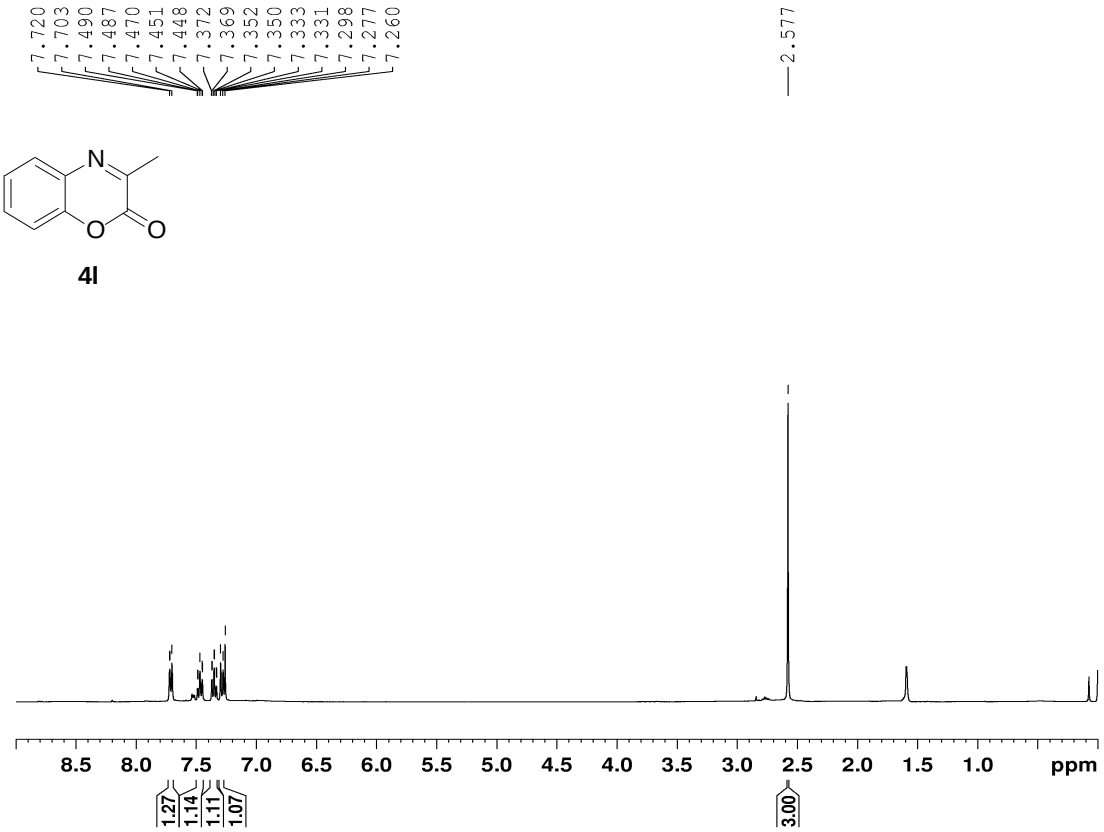

7.623
7.611
7.497
7.494
7.477
7.475
7.458
7.455
7.397
7.394
7.378
7.359
7.332
7.311
7.260
7.201
7.191
7.179
N
S
O
O

4k

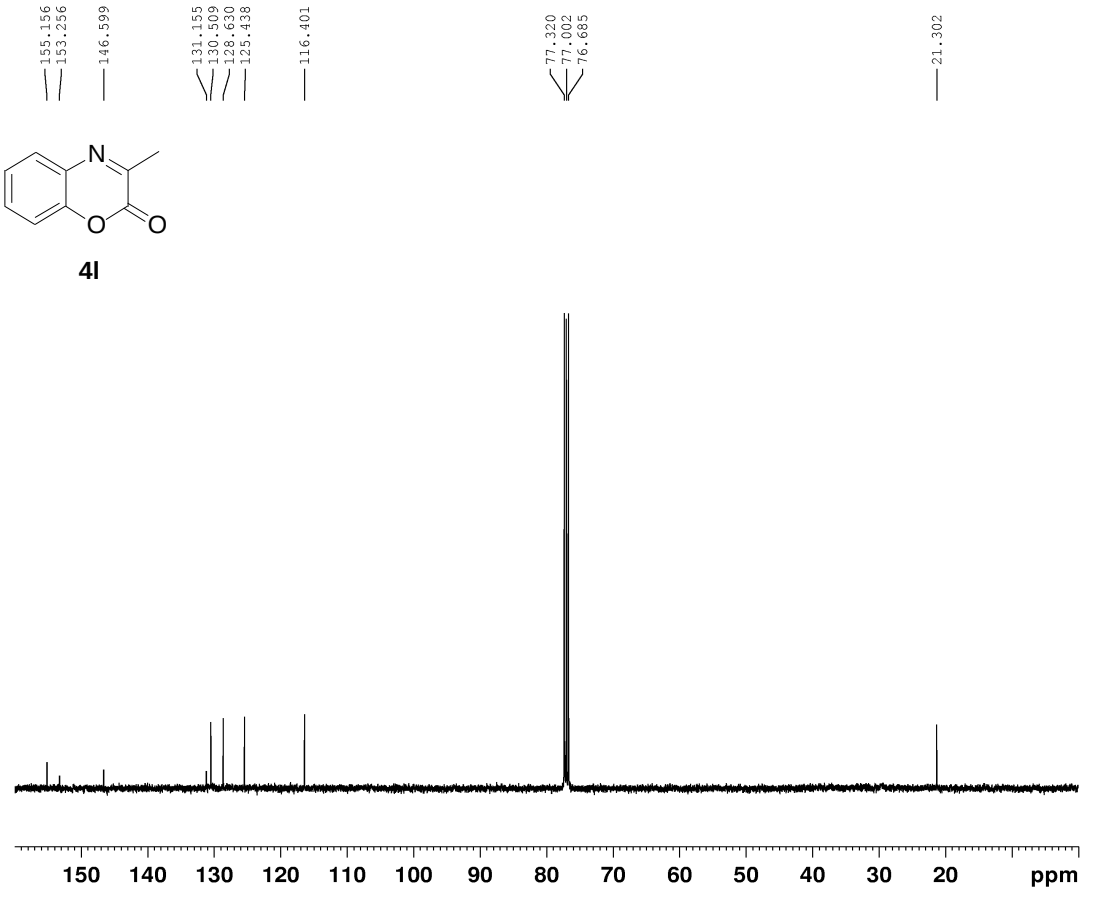

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
1.10
1.00
1.18
1.39
1.18
1.05


151.458
145.959
145.545
138.533
133.344
132.523
131.526
130.472
128.851
128.570
125.677
116.181
77.315
76.998
76.680
N
S
O
O
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

4k



4l



4l