Supporting Information

Synthesis of Functionalized Benzoxazines by Copper-Catalyzed C(sp^3)-H Bond Functionalization of Acetonitrile with Olefinic Amides

Xue-Qiang Chu, Xiao-Ping Xu,* Hua Meng and Shun-Jun Ji*

Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science & Collaborative Innovation Center of Suzhou Nano Science and Technology, Soochow University, Suzhou, 215123, China. Fax: (+)86 512o 65880307; Tel: +86-512-65880307; E-mail: xuxp@suda.edu.cn; shunjun@suda.edu.cn

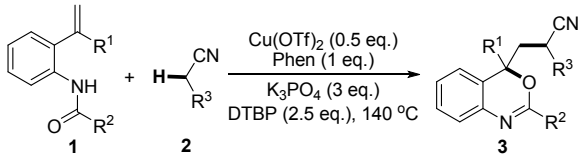
Table of Contents

Experimental Section:

General

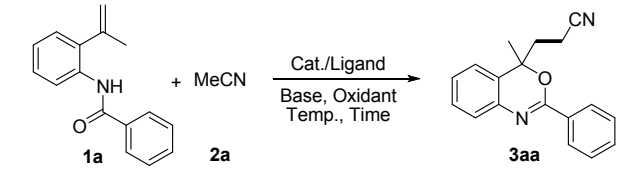
Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All reactions were carried out in air and using undistilled solvent, without need of precautions to exclude air and moisture unless otherwise noted. Melting points were recorded on an Electrothermal digital melting point apparatus. IR spectra were recorded on a FT-IR spectrophotometer using KBr optics. ^{1}H, ^{13}C NMR spectra were recorded in $CDCl_3$ on 400 MHz spectometers. Tetramethylsilane (TMS) served as internal standard for ^{1}H NMR and ^{13}C NMR. High resolution mass spectra were obtained using a commercial apparatus (ESI or EI Source).

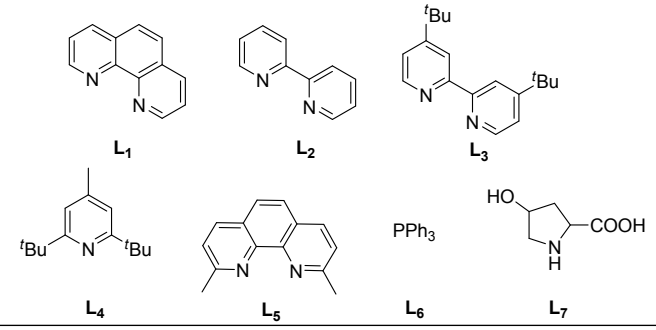
General procedure for oxycyanomethylation of olefinic amides with acetonitrile



Olefinic amide **1** (0.2 mmol), acetonitrile **2** (2 mL), $Cu(OTf)_2$ (0.1 mmol), 1,10-phenanthroline (0.2 mmol), K_3PO_4 (0.6 mmol) and di-*tert*-butyl peroxide (0.5 mmol) was stirred at 140 ^{o}C under air in pressure-tight tube. Upon completion of the reaction (indicated by TLC), solvent was removed in vacuum and the residue was purified by flash silica gel column chromatography purification afforded pure product **3** with petroleum/ethyl acetate as the eluent.

Table S1: Optimization of the reaction conditions[a]



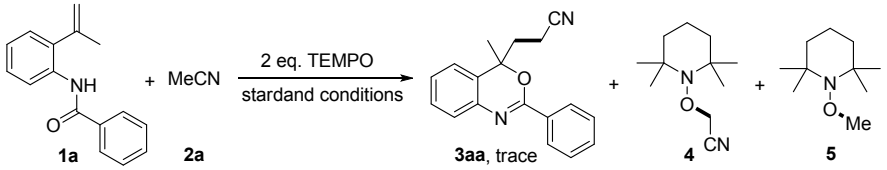


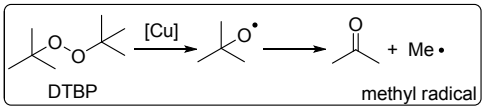
Entry	Catalyst (equiv)	Ligand (equiv)	Oxidant (equiv)	Base (equiv)	Time (h)	Temp. (°C)	GC-Yeild(%)[b]
1	$Cu(OTf)_2$(1)	L_1(1)	DTBP(2.5)	K_2CO_3(3)	14	140	53
2	$Cu(OTf)_2$(1)	L_2(1)	DTBP(2.5)	K_2CO_3(3)	14	140	39
3	$Cu(OTf)_2$(1)	L_3(1)	DTBP(2.5)	K_2CO_3(3)	14	140	45
4	$Cu(OTf)_2$(1)	L_4(1)	DTBP(2.5)	K_2CO_3(3)	14	140	trace
5	$Cu(OTf)_2$(1)	L_5(1)	DTBP(2.5)	K_2CO_3(3)	14	140	0
6	$Cu(OTf)_2$(1)	L_6(1)	DTBP(2.5)	K_2CO_3(3)	14	140	trace
7	$Cu(OTf)_2$(1)	L_7(1)	DTBP(2.5)	K_2CO_3(3)	14	140	trace
8	$Cu(OTf)_2$(1)	L_1(1)	DTBP(2.5)	Cs_2CO_3(3)	14	140	trace
9	$Cu(OTf)_2$(1)	L_1(1)	DTBP(2.5)	CsOAc(3)	14	140	55
10	$Cu(OTf)_2$(1)	L_1(1)	DTBP(2.5)	Na_2CO_3(3)	14	140	31
11	$Cu(OTf)_2$(1)	L_1(1)	DTBP(2.5)	NaOAc(3)	14	140	20
12	$Cu(OTf)_2$(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	67(58)[c]
13	$Cu(OTf)_2$(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	130	66
14	$Cu(OTf)_2$(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	120	50
15	CuCl(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	20
16	$Cu(OCOCF_3)_2$(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	53
17	$Cu(OAc)_2$(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	55
18	CuBr(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	0
19	CuI(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	30
20	Cu_2O(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	59
21	CuOAc(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	53
22	$CuCl_2$(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	0
23	$Cu(acac)_2$(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	0

24	$Cu(NO_3)_2$(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	57
25	$Fe(OAc)_2$(1)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	0
26	$Cu(OTf)_2$(0.5)	L_1(0.5)	DTBP(2.5)	K_3PO_4(3)	14	140	52
27	$Cu(OTf)_2$(2)	L_1(2)	DTBP(2.5)	K_3PO_4(3)	14	140	56
28	$Cu(OTf)_2$(0.5)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	77(64)[c]
29	$Cu(OTf)_2$(0.3)	L_1(0.6)	DTBP(2.5)	K_3PO_4(3)	14	140	40
30	$Cu(OTf)_2$(0.2)	L_1(0.4)	DTBP(2.5)	K_3PO_4(3)	14	140	27
31	$Cu(OTf)_2$(0.5)	L_1(1)	$K_2S_2O_8$(2.5)	K_3PO_4(3)	14	140	0
32	$Cu(OTf)_2$(0.5)	L_1(1)	TBPB(2.5)	K_3PO_4(3)	14	140	46
33	$Cu(OTf)_2$(0.5)	L_1(1)	DCP(2.5)	K_3PO_4(3)	14	140	63
35	$Cu(OTf)_2$(0.5)	L_1(1)	BPO(2.5)	K_3PO_4(3)	14	140	23
36	$Cu(OTf)_2$(0.5)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	24	140	77
37	$Cu(OTf)_2$(0.5)	L_1(1)	DTBP(2.5)	K_3PO_4(3)	14	140	79(66)[c,d]

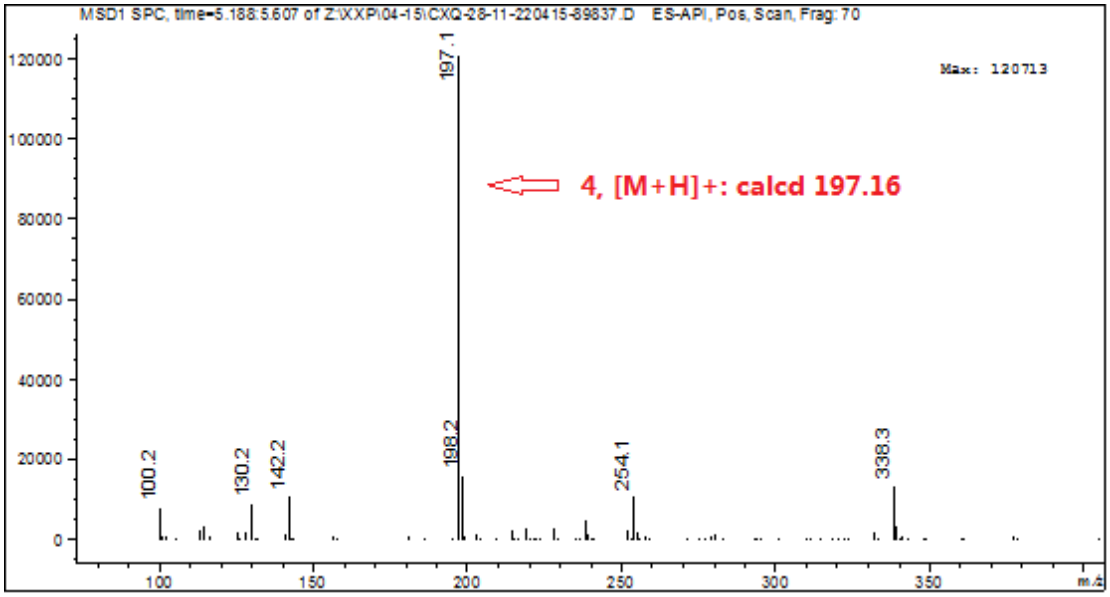
[a]Reaction conditions: **1a** (0.2 mmol), **2a** (2 mL), catalyst (1 equiv), base (3 equiv) and oxidant (2.5 equiv) at 140 °C under air; DTBP = di-*tert*-butyl peroxide; TBPB = *tert*-butylperoxybenzoate; DCP = dicumyl peroxide; BPO = benzoyl peroxide. [b]Yields were determined by GC with an internal standard (biphenyl) as the ratio between the formed products and the initial amount of limiting reactant. [c]Isolated yields. [c]Under air. [d]Under Argon atmosphere.

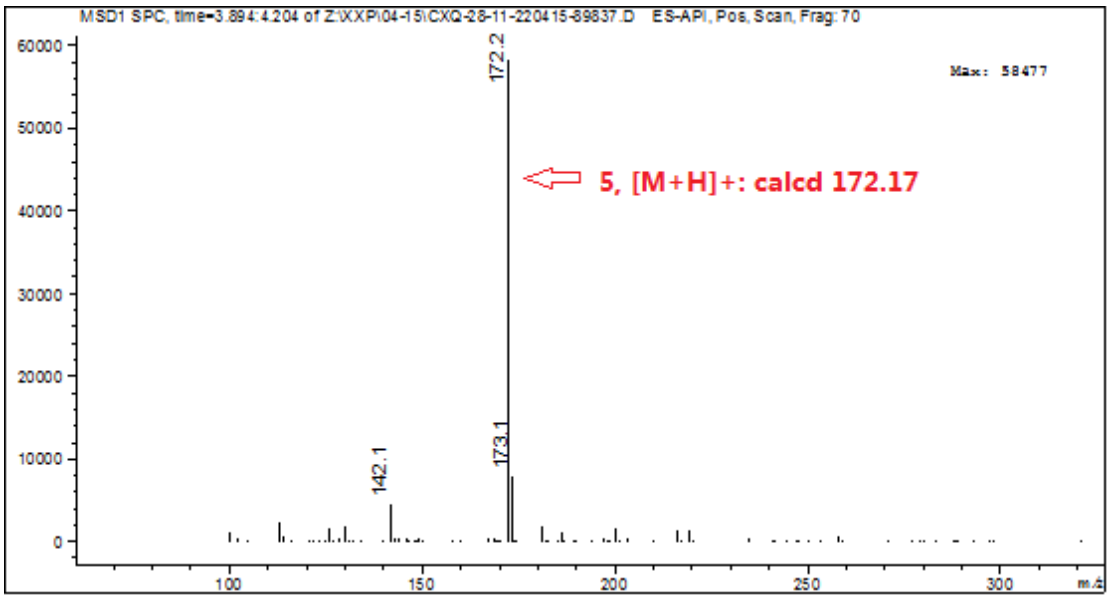
Figure S1: Trapping experiment with 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO).



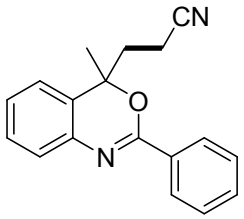


1a, $[M+H]^+$: calcd 238.12
3aa, $[M+H]^+$: calcd 277.13
4, $[M+H]^+$: calcd 197.16
5, $[M+H]^+$: calcd 172.17

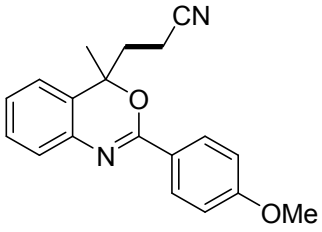




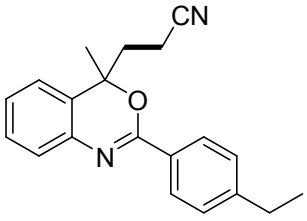
Analytical and spectral data for compounds:



3-(4-methyl-2-phenyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3aa): Yield = 64%. Yellow oil. IR (KBr) ν = 3030, 2927, 2853, 2247, 1624, 1572, 1321, 1262, 1066, 764, 694 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$): δ = 8.16–8.10 (m, 2H), 7.54–7.44 (m, 3H), 7.36–7.31 (m, 2H), 7.25–7.21 (m, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 2.53–2.45 (m, 2H), 2.44–2.31 (m, 2H), 1.70 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 139.1, 132.5, 131.8, 129.5, 128.6, 128.0, 127.4, 127.3, 126.1, 122.5, 119.5, 79.7, 36.9, 28.3, 12.6 ppm. HRMS m/z: calcd for $C_{18}H_{17}N_2O$ $[M+H]^+$ 277.1341, found: 277.1351.

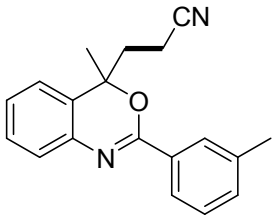


3-(2-(4-methoxyphenyl)-4-methyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3ba): Yield = 58%. Brown oil. IR (KBr) ν = 2959, 2922, 2839, 2247, 1595, 1509, 1247, 1166, 1026, 768 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$): δ = 8.08 (d, *J* = 8.9 Hz, 2H), 7.36–7.27 (m, 2H), 7.23–7.17 (m, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.96 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H), 2.53–2.42 (m, 2H), 2.42–2.31 (m, 2H), 1.68 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.7, 156.0, 139.4, 129.8, 129.4, 127.3, 126.8, 125.7, 124.9, 122.5, 119.5, 113.9, 79.5, 55.6, 36.8, 28.2, 12.6 ppm. HRMS m/z: calcd for $C_{19}H_{19}N_2O_2$ $[M+H]^+$ 307.1447, found: 307.1455.

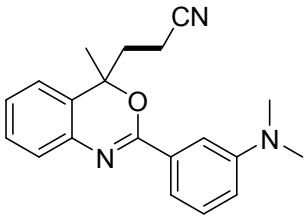


3-(2-(4-ethylphenyl)-4-methyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3ca): Yield = 53%.

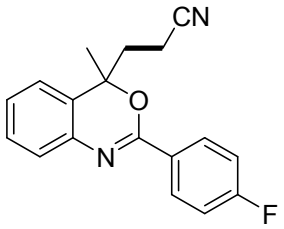
Yellow oil. IR (KBr) ν = 2965, 2929, 2871, 2247, 1621, 1596, 1482, 1321, 1262, 1066, 842, 767 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ = 8.04 (d, J = 8.3 Hz, 2H), 7.34–7.25 (m, 4H), 7.25–7.18 (m, 1H), 7.07 (d, J = 7.5 Hz, 1H), 2.71 (q, J = 7.6 Hz, 2H), 2.52–2.42 (m, 2H), 2.43–2.32 (m, 2H), 1.69 (s, 3H), 1.27 (t, J = 7.6 Hz, 3H) pm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2, 148.6, 139.3, 129.9, 129.4, 128.1, 128.1, 127.4, 127.1, 125.9, 122.5, 119.5, 79.5, 36.9, 29.1, 28.3, 15.6, 12.6 ppm. HRMS m/z: calcd for $C_{20}H_{21}N_2O$ $[M+H]^+$ 305.1654, found: 305.1655.



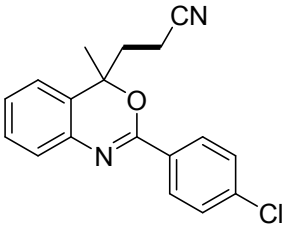
3-(4-methyl-2-m-tolyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3da): Yield = 54%. Yellow oil. IR (KBr) ν = 2958, 2919, 2850, 2247, 1624, 1573, 1482, 1263, 1077, 767, 714 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ = 7.94 (s, 1H), 7.91 (d, J = 6.7 Hz, 1H), 7.37–7.30 (m, 4H), 7.25–7.19 (m, 1H), 7.07 (d, J = 7.5 Hz, 1H), 2.54–2.49 (m, 2H), 2.43 (s, 3H), 2.42–2.31 (m, 2H), 1.70 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.3, 139.1, 138.3, 132.7, 132.4, 129.5, 128.5, 128.5, 127.4, 127.2, 126.0, 125.1, 122.5, 119.5, 79.7, 36.9, 28.3, 21.6, 12.6 ppm. HRMS m/z: calcd for $C_{19}H_{19}N_2O$ $[M+H]^+$ 291.1498, found: 291.1501.



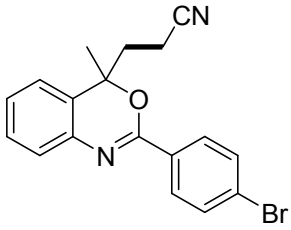
3-(2-(3-(dimethylamino)phenyl)-4-methyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3ea): Yield = 31%. Brown oil. IR (KBr) ν = 2971, 2926, 2901, 2805, 2247, 1592, 1481, 1259, 1076, 994, 868, 767, 720, 683 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ =7.51 (dd, J = 2.5, 1.6 Hz, 1H), 7.43 (d, J = 7.7 Hz, 1H), 7.36–7.28 (m, 3H), 7.24–7.20 (m, 1H), 7.07 (d, J = 7.6 Hz, 1H), 6.89 (dd, J = 8.0, 2.4 Hz, 1H), 3.03 (s, 6H), 2.57–2.44 (m, 2H), 2.43–2.33 (m, 2H), 1.70 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.8, 150.8, 139.3, 133.2, 129.4, 129.2, 127.6, 127.1, 126.1, 122.5, 119.6, 116.3, 116.1, 111.7, 79.5, 40.9, 36.9, 28.2, 12.6 ppm. HRMS m/z: calcd for $C_{20}H_{22}N_3O$ $[M+H]^+$ 320.1763, found: 320.1757.



3-(2-(4-fluorophenyl)-4-methyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3fa): Yield = 57%. Yellow oil. IR (KBr) ν = 2972, 2927, 2901, 2248, 1635, 1598, 1482, 1320, 1152, 1066, 845, 807, 768, 710 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ = 8.17–8.10 (m, 2H), 7.37–7.29 (m, 2H), 7.26–7.21 (m, 1H), 7.17–7.10 (m, 2H), 7.08 (dd, J = 7.6, 0.9 Hz, 1H), 2.51–2.43 (m, 2H), 2.43–2.32 (m, 2H), 1.70 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.2, 139.0, 130.3, 130.2, 129.6, 128.7 (d, J = 2.9 Hz), 127.4, 127.2, 126.1, 122.6, 119.4, 115.7 (d, J = 21.8 Hz), 80.0, 36.9, 28.5, 12.7 ppm. ^{19}F NMR (376MHz, $CDCl_3$): δ = -107.9 ppm. HRMS m/z: calcd for $C_{18}H_{16}FN_2O$ $[M+H]^+$ 295.1247, found: 295.1252.

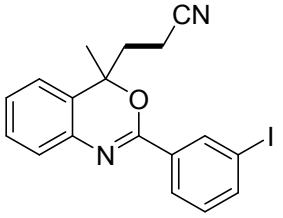


3-(2-(4-chlorophenyl)-4-methyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3ga): Yield = 64%. Yellow oil. IR (KBr) ν = 3034, 2973, 2928, 2853, 2248, 1921, 1623, 1595, 1485, 1401, 1320, 1262, 1169, 1088, 838, 767 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ = 8.10–8.03 (m, 2H), 7.46–7.40 (m, 2H), 7.37–7.29 (m, 2H), 7.24 (dd, J = 6.9, 1.9 Hz, 1H), 7.10–7.05 (m, 1H), 2.53–2.42 (m, 2H), 2.42–2.31 (m, 2H), 1.70 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.1, 138.9, 138.1, 131.0, 129.6, 129.3, 128.9, 127.6, 127.3, 126.1, 122.6, 119.4, 80.0, 36.9, 28.5, 12.7 ppm. HRMS m/z: calcd for $C_{18}H_{16}ClN_2O$ $[M+H]^+$ 311.0952, found: 311.0949.

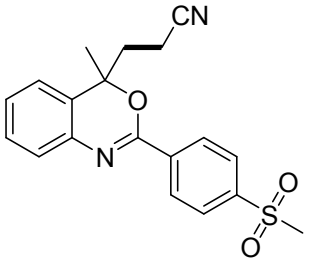


3-(2-(4-bromophenyl)-4-methyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3ha): Yield = 55%. Yellow oil. IR (KBr) ν = 2967, 2926, 2852, 2247, 1622, 1483, 1320, 1261, 1068, 1009, 835,

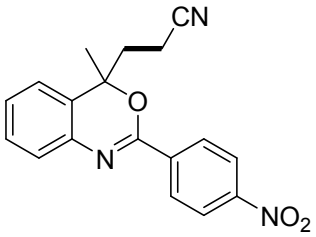
767 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ = 7.99 (d, J = 8.6 Hz, 2H), 7.59 (d, J = 8.6 Hz, 2H), 7.34 (td, J = 7.9, 3.6 Hz, 2H), 7.24 (dd, J = 10.4, 3.5 Hz, 1H), 7.07 (d, J = 7.7 Hz, 1H), 2.54 – 2.42 (m, 2H), 2.43 – 2.31 (m, 2H), 1.69 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.2, 138.9, 131.8, 131.5, 129.6, 129.5, 127.6, 127.3, 126.6, 126.1, 122.6, 119.4, 80.1, 36.8, 28.5, 12.6 ppm. HRMS m/z: calcd for $C_{18}H_{16}BrN_2O$ $[M+H]^+$ 355.0447, found: 355.0457.



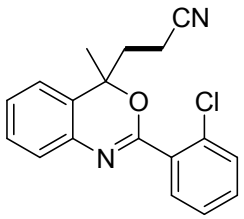
3-(2-(3-iodophenyl)-4-methyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3ia): Yield = 49%. Yellow oil. IR (KBr) ν = 3061, 2972, 2901, 2247, 1622,1597, 1417,1316, 1076, 870,766, 710 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ = 8.45 (t, J = 1.6 Hz, 1H), 8.13–8.05 (m, 1H), 7.85–7.82 (m, 1H), 7.38–7.30 (m, 2H), 7.27–7.23 (m, 1H), 7.19 (t, J = 7.9 Hz, 1H), 7.10–7.04 (m, 1H), 2.52–2.31 (m, 4H), 1.70 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.4, 140.6, 138.7, 136.7, 134.5, 130.2, 129.6, 127.7, 127.3, 127.1, 126.2, 122.6, 119.3, 94.2, 80.2, 36.8, 28.5, 12.7 ppm. HRMS m/z: calcd for $C_{18}H_{16}IN_2O$ $[M+H]^+$ 403.0308, found: 403.0308.



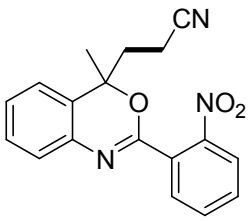
3-(4-methyl-2-(4-(methylsulfonyl)phenyl)-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3ja): Yield = 58%. White solid. M.p. 137.7–138.6 °C. IR (KBr) ν = 2925, 2852, 2251, 1623, 1597, 1297, 1261, 1150, 1066, 957, 770 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ = 8.39–8.32 (m, 2H), 8.08–8.02 (m, 2H), 7.42–7.36 (m, 2H), 7.34–7.29 (m, 1H), 7.11 (d, J = 7.3 Hz, 1H), 3.11 (s, 3H), 2.55–2.47 (m, 2H), 2.46–2.36 (m, 2H), 1.75 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.1, 143.0, 138.5, 137.6, 129.8, 128.8, 128.3, 127.6, 127.3, 126.6, 122.7, 119.2, 80.6, 44.7, 36.9, 28.7, 12.7 ppm. HRMS m/z: calcd for $C_{19}H_{19}N_2O_3S$ $[M+H]^+$ 355.1117, found: 355.1117.



3-(4-methyl-2-(4-nitrophenyl)-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3ka): Yield = 54%. Yellow solid. M.p. 84.5–85.6 °C. (KBr) ν = 2927, 2852, 2247, 1625, 1519, 1344, 1317, 1264, 1067, 862, 760, 703 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ = 8.35–8.27 (m, 4H), 7.41–7.35 (m, 2H), 7.33–7.27 (m, 1H), 7.10 (d, J = 7.7 Hz, 1H), 2.53–2.45 (m, 2H), 2.45–2.34 (m, 2H), 1.73 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9, 149.8, 138.4, 138.3, 129.8, 128.9, 128.4, 127.2, 126.6, 123.7, 122.7, 119.2, 80.7, 77.6, 77.2, 76.9, 36.9, 28.7, 12.7 ppm. HRMS m/z: calcd for $C_{18}H_{16}N_3O_3$ $[M+H]^+$ 322.1192, found: 322.1192.

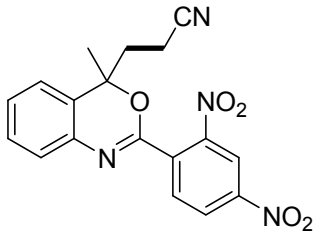


3-(2-(2-chlorophenyl)-4-methyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3la): Yield = 25%. Yellow oil. IR (KBr) ν = 3058, 2926, 2855, 2248, 1600, 1565, 1485, 1461, 1345, 1245, 1155, 1066, 822, 758 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ = 7.80 (dd, J = 8.0, 1.7 Hz, 1H), 7.44–7.39 (m, 1H), 7.37–7.33 (m, 1H), 7.28–7.25 (m, 2H), 7.09 (dd, J = 7.9, 1.3 Hz, 1H), 7.01 (dd, J = 8.3, 0.9 Hz, 1H), 6.93–6.88 (m, 1H), 2.54–2.47 (m, 2H), 2.46–2.37 (m, 2H), 1.74 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.5, 158.5, 136.6, 134.2, 129.8, 127.7, 126.9, 124.9, 122.9, 119.2, 118.9, 117.8, 113.8, 80.6, 36.8, 28.3, 12.6 ppm. HRMS m/z: calcd for $C_{18}H_{16}ClN_2O$ $[M+H]^+$ 311.0952, found: 311.0953.

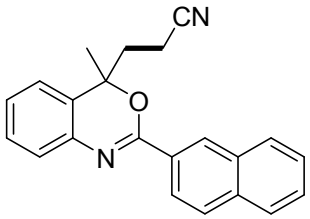


3-(4-methyl-2-(2-nitrophenyl)-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3ma): Yield = 42%. Yellow oil. IR (KBr) ν = 3070, 2977, 2854, 2248, 2227, 1634, 1529, 1484, 1445, 1350,

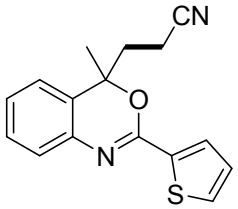
1322, 1118, 862, 769 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$): δ = 7.98 (dd, J = 7.6, 1.5 Hz, 1H), 7.81 (dd, J = 7.9, 1.3 Hz, 1H), 7.69–7.61 (m, 2H), 7.36–7.32 (m, 1H), 7.30–7.26 (m, 2H), 7.05 (dd, J = 7.8, 1.4 Hz, 1H), 2.53–2.39 (m, 2H), 2.39–2.26 (m, 2H), 1.69 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.4 149.3, 138.1 132.5, 131.5, 131.2 129.6, 128.3, 127.8, 126.9, 126.4, 124.0, 122.8, 119.4, 81.6, 37.2, 28.9, 12.6 ppm. HRMS m/z: calcd for $C_{18}H_{16}N_3O_3$ $[M+H]^+$ 322.1192, found: 322.1194.



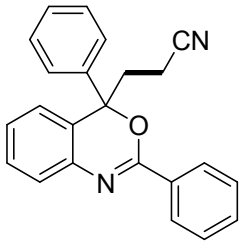
3-(2-(2,4-dinitrophenyl)-4-methyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3na): Yield = 18%. Yellow solid. M.p. 127.2–128.9 ^{o}C. IR (KBr) ν = 2920, 2850, 2247, 1592, 1346, 1052, 832, 767, 738 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$): δ = 8.61 (d, J = 2.1 Hz, 1H), 8.49 (dd, J = 8.6, 2.2 Hz, 1H), 8.28 (d, J = 8.6 Hz, 1H), 7.40–7.28 (m, 3H), 7.10–7.02 (m, 1H), 2.49–2.40 (m, 2H), 2.39–2.30 (m, 2H), 1.71 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.2, 149.5, 148.8, 137.5, 132.7, 132.6, 129.9, 129.1, 126.9, 126.8, 126.5, 122.9, 119.5, 119.1, 82.5, 77.6, 77.2, 76.9, 37.1, 29.1, 12.6 ppm. HRMS m/z: calcd for $C_{18}H_{15}N_4O_5$ $[M+H]^+$ 367.1043, found: 367.1034.



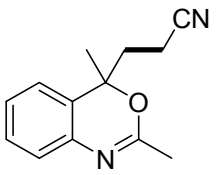
3-(4-methyl-2-(naphthalen-2-yl)-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3oa): Yield = 55%. Yellow oil. IR (KBr) ν =3057, 2968, 2927, 2247, 1619, 1593, 1570, 1482, 1318, 1264, 1064, 957, 864, 769, 749 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$): δ = 8.59 (s, 1H), 8.25 (dd, J = 8.7, 1.7 Hz, 1H), 8.00–7.96 (m, 1H), 7.89 (t, J = 8.8 Hz, 2H), 7.60–7.51 (m, 2H), 7.41–7.33 (m, 2H), 7.26 (q, J = 2.0 Hz, 1H), 7.13–7.09 (m, 1H), 2.60–2.49 (m, 2H), 2.50–2.35 (m, 2H), 1.76 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1, 139.2, 135.2, 132.9, 129.8, 129.6, 129.3, 128.5, 128.3, 128.0, 127.9, 127.5, 127.4, 126.8, 126.1, 124.6, 122.6, 119.5, 79.9, 36.9, 28.4, 12.7 ppm. HRMS m/z: calcd for $C_{22}H_{19}N_2O$ $[M+H]^+$ 327.1498, found: 327.1494.



3-(4-methyl-2-(thiophen-2-yl)-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3pa): Yield = 47%. Yellow oil. IR (KBr) ν =3100, 2072, 2970, 2926, 2852, 2247, 1619, 1592, 1481, 1424, 1262, 1059, 1032, 850, 767, 715 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ = 7.73 (dd, J = 3.7, 1.2 Hz, 1H), 7.51 (dd, J = 5.0, 1.2 Hz, 1H), 7.35–7.27 (m, 2H), 7.24–7.18 (m, 1H), 7.12 (dd, J = 5.0, 3.7 Hz, 1H), 7.06 (dd, J = 7.6, 1.0 Hz, 1H), 2.56–2.43 (m, 2H), 2.42–2.33 (m, 2H), 1.70 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.7, 139.0, 136.9, 130.8, 130.1, 129.5, 128.0, 127.5, 127.1, 126.9, 125.8, 122.6, 119.4, 80.1, 36.7, 28.0, 12.5 ppm. HRMS m/z: calcd for $C_{16}H_{15}N_2OS$ $[M+Na]^+$ 283.0906, found: 283.0908.

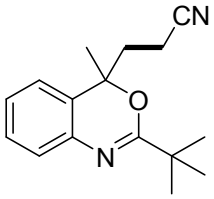


3-(2,4-diphenyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3qa): Yield = 36%. Yellow solid. M.p. 98.2–99.8 °C. IR (KBr) ν = 3059, 2927, 2246, 1517, 1445, 1318, 1248, 1024, 766, 696 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ = 8.22 (d, J = 7.2 Hz, 2H), 7.54–7.45 (m, 3H), 7.38 (dd, J = 12.0, 7.0 Hz, 2H), 7.28 (dd, J = 9.8, 6.7 Hz, 8H), 2.86–2.77 (m, 2H), 2.63–2.51 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1, 142.1, 139.8, 132.2, 132.0, 129.9, 128.9, 128.7, 128.7, 128.1, 127.1, 126.3, 126.0, 125.6, 124.1, 119.5, 82.8, 77.6, 77.2, 76.9, 36.5, 13.2 ppm. HRMS m/z: calcd for $C_{23}H_{19}N_2O$ $[M+H]^+$ 339.1498, found: 339.1497.

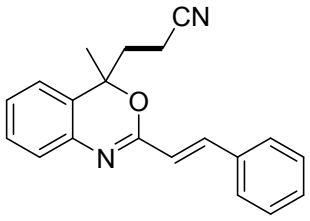


3-(2,4-dimethyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3ra): Yield = 26%. Yellow oil. IR (KBr) ν = 3064, 2973, 2855, 2247, 1640, 1522, 1484, 1376, 1263, 1082, 754 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ = 7.32–7.28 (m, 1H), 7.23–7.14 (m, 2H), 7.01 (dd, J = 7.6, 1.3 Hz, 1H),

2.48–2.34 (m, 2H), 2.34–2.20 (m, 2H), 2.15 (s, 3H), 1.64 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.6, 138.5, 129.5, 127.1, 126.6, 125.1, 122.6, 119.4, 79.5, 37.2, 28.8, 22.0, 12.5 ppm. HRMS m/z: calcd for $C_{13}H_{15}N_2O$ $[M+H]^+$ 215.1185, found: 215.1178.

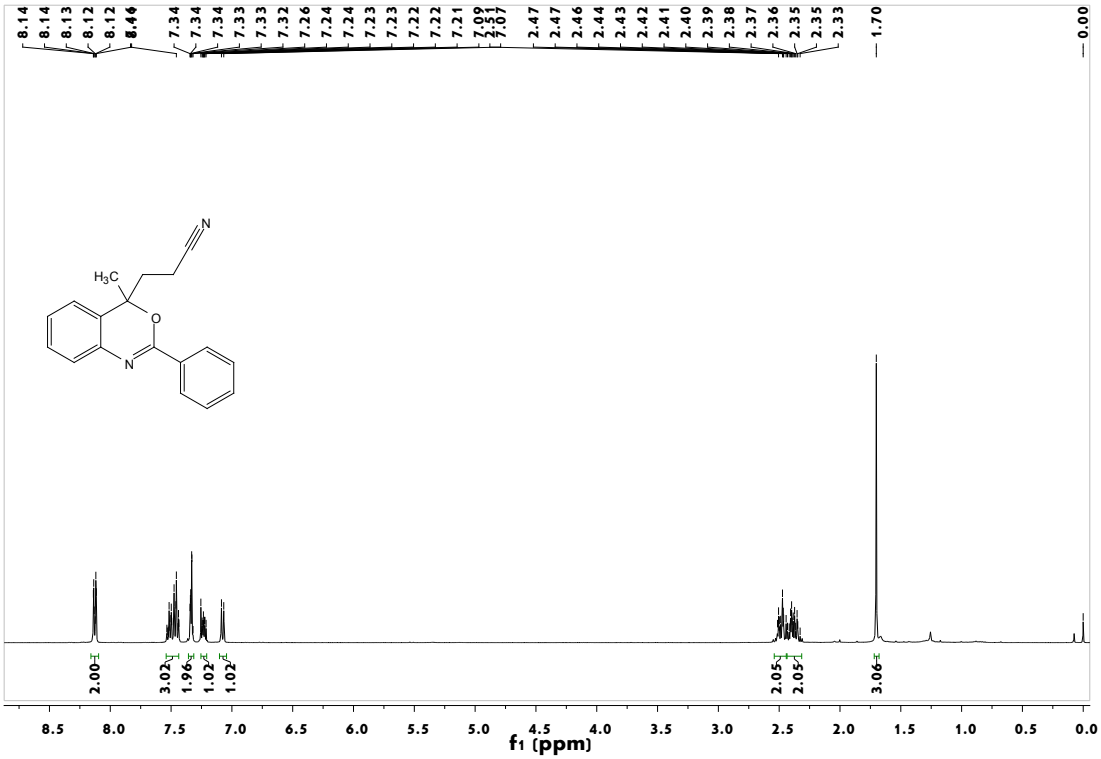


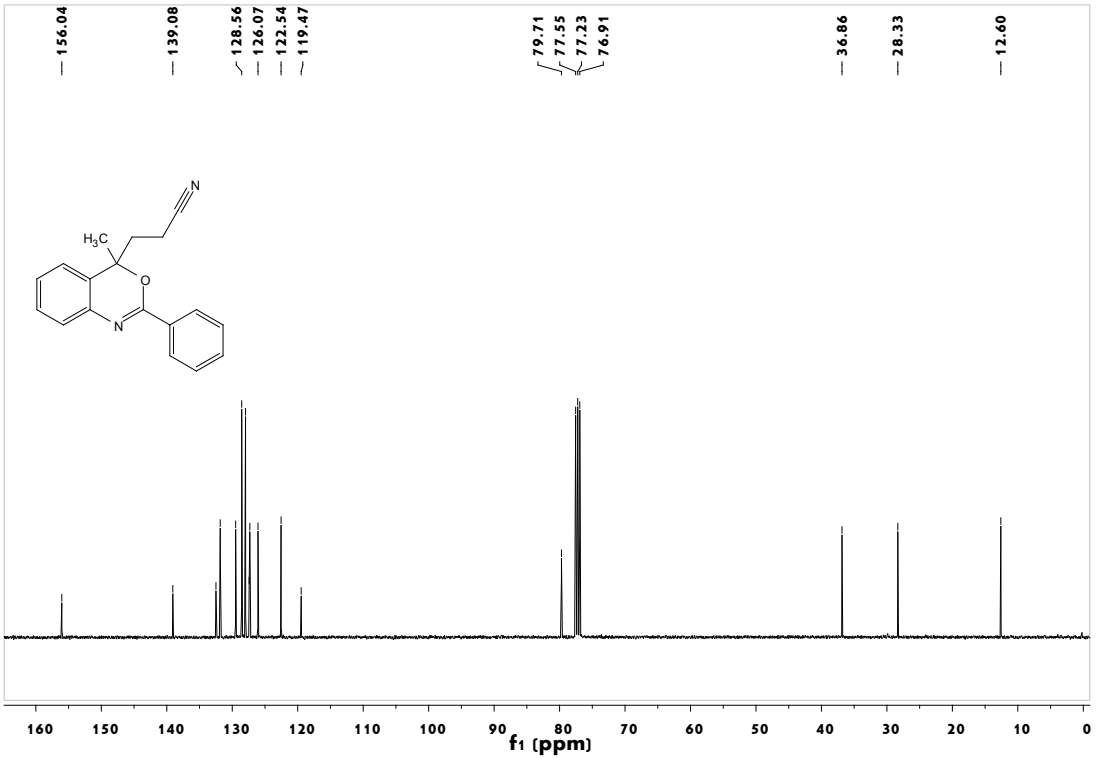
3-(2-*tert*-butyl-4-methyl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3sa): Yield = 26%. Yellow solid. M.p. 57.2–58.4 °C. IR (KBr) ν = 2976, 2929, 2866, 2250, 1633, 1487, 1448, 1374, 1267, 1144, 1080, 955, 870, 777, 709 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$): δ = 7.28 (dd, J = 7.2, 1.5 Hz, 1H), 7.22–7.15 (m, 2H), 7.01–6.96 (m, 1H), 2.44–2.35 (m, 2H), 2.35–2.26 (m, 2H), 1.54 (s, 3H), 1.26 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.2, 139.1, 129.3, 127.0, 126.9, 125.8, 122.3, 119.6, 78.7, 37.5, 36.4, 28.3, 27.6, 12.6 ppm. HRMS m/z: calcd for $C_{16}H_{21}N_2O$ $[M+H]^+$ 257.1654, found: 257.1656.

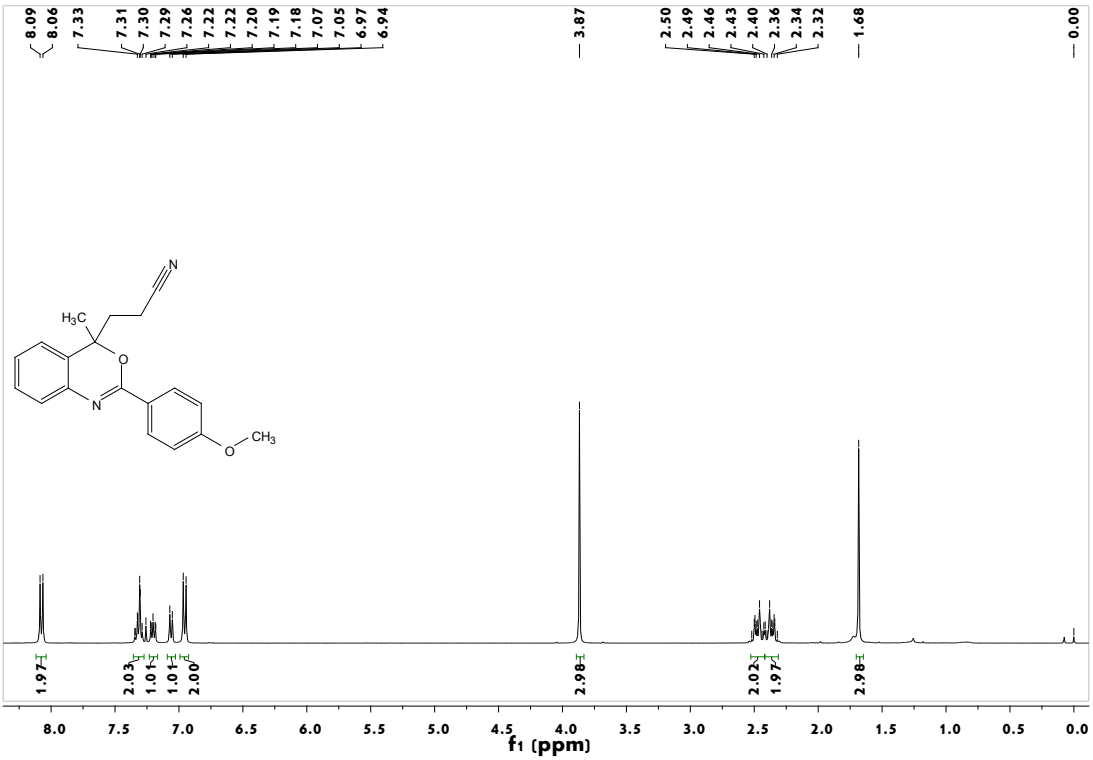


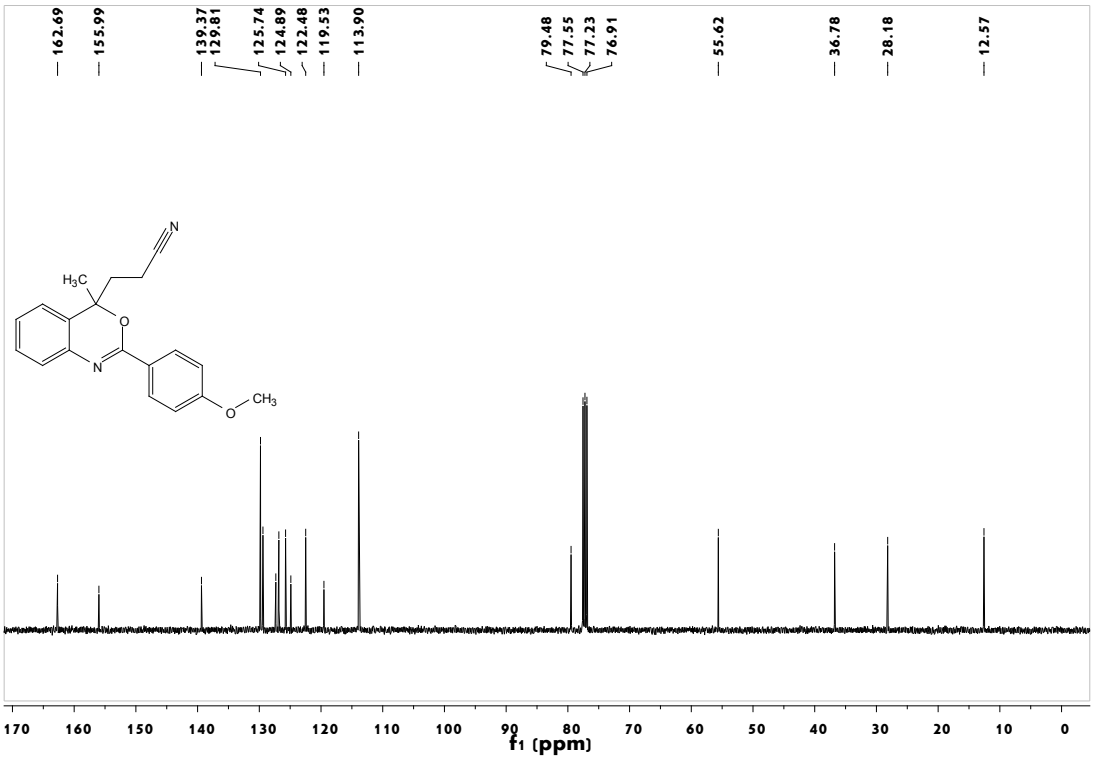
(*E*)-3-(4-methyl-2-styryl-4*H*-benzo[*d*][1,3]oxazin-4-yl)propanenitrile (3ua): Yield = 25%. Yellow oil. IR (KBr) ν = 3060, 3026, 2965, 2852, 2247, 1567, 1481, 1260, 1076, 768, 696 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$): δ = 7.55 (dd, J = 7.9, 1.3 Hz, 2H), 7.50 (d, J = 16.1 Hz, 1H), 7.41–7.31 (m, 4H), 7.26–7.20 (m, 2H), 7.08–7.04 (m, 1H), 6.67 (d, J = 16.1 Hz, 1H), 2.56–2.43 (m, 2H), 2.42–2.33 (m, 2H), 1.68 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.6, 139.3, 135.4, 129.9, 129.6, 129.1, 127.9, 127.6, 127.4, 125.9, 122.6, 122.0, 119.5, 79.4, 36.8, 28.3, 12.6 ppm. HRMS m/z: calcd for $C_{20}H_{19}N_2O$ $[M+H]^+$ 303.1498, found: 303.1505.

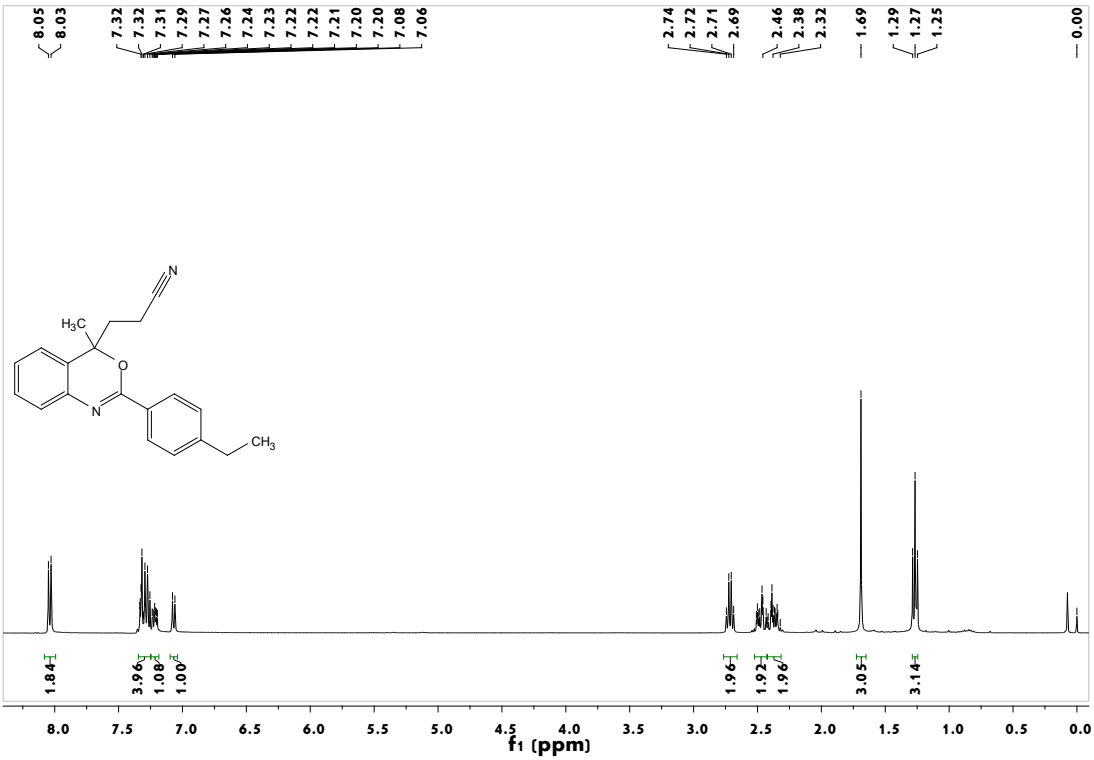
The ^{1}H , ^{13}C spectra of compounds:

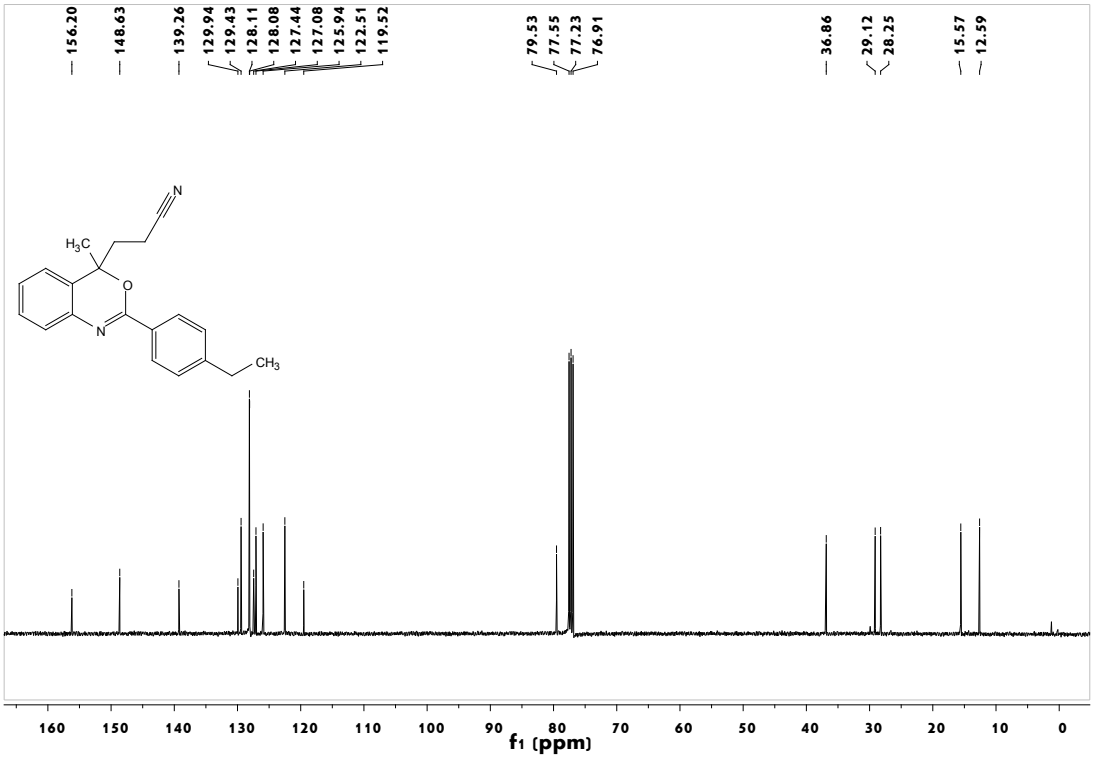


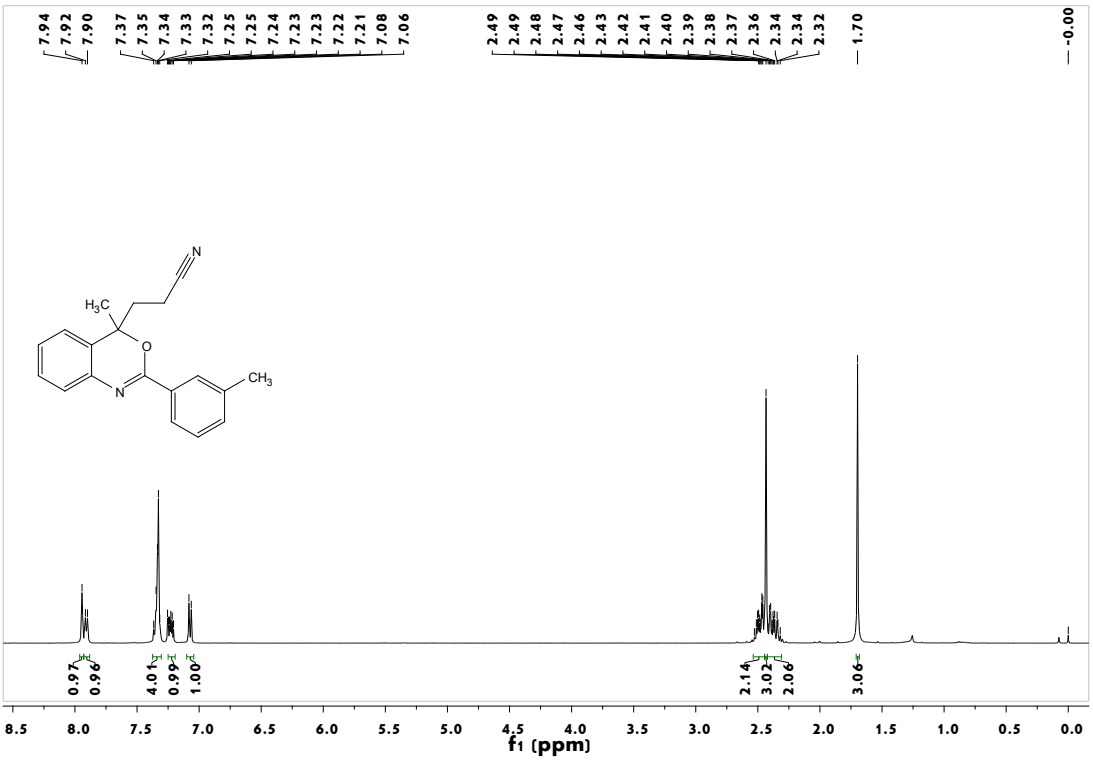


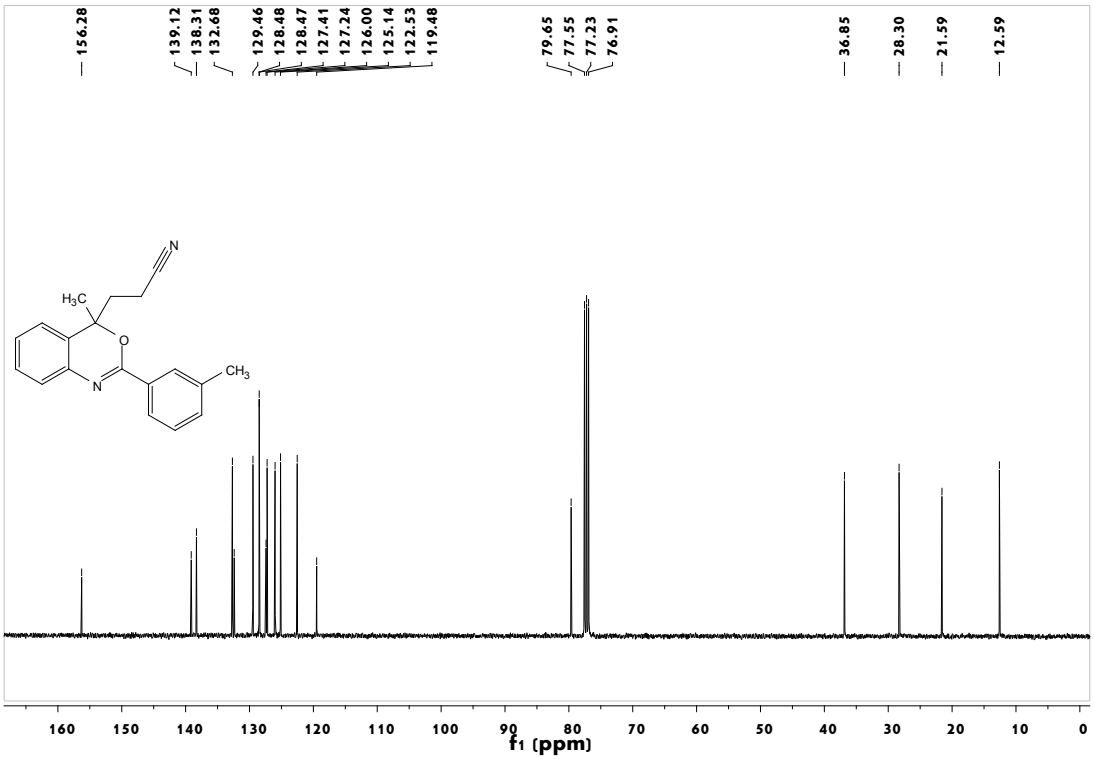

8.09
8.06
7.33
7.31
7.30
7.29
7.26
7.22
7.22
7.20
7.19
7.18
7.07
7.05
6.97
6.94
3.87
2.50
2.49
2.46
2.43
2.40
2.36
2.34
2.32
1.68
0.00
N
H3C
O
N
O
CH3
1.97
2.03
1.01
1.01
2.00
2.98
2.02
1.97
2.98
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

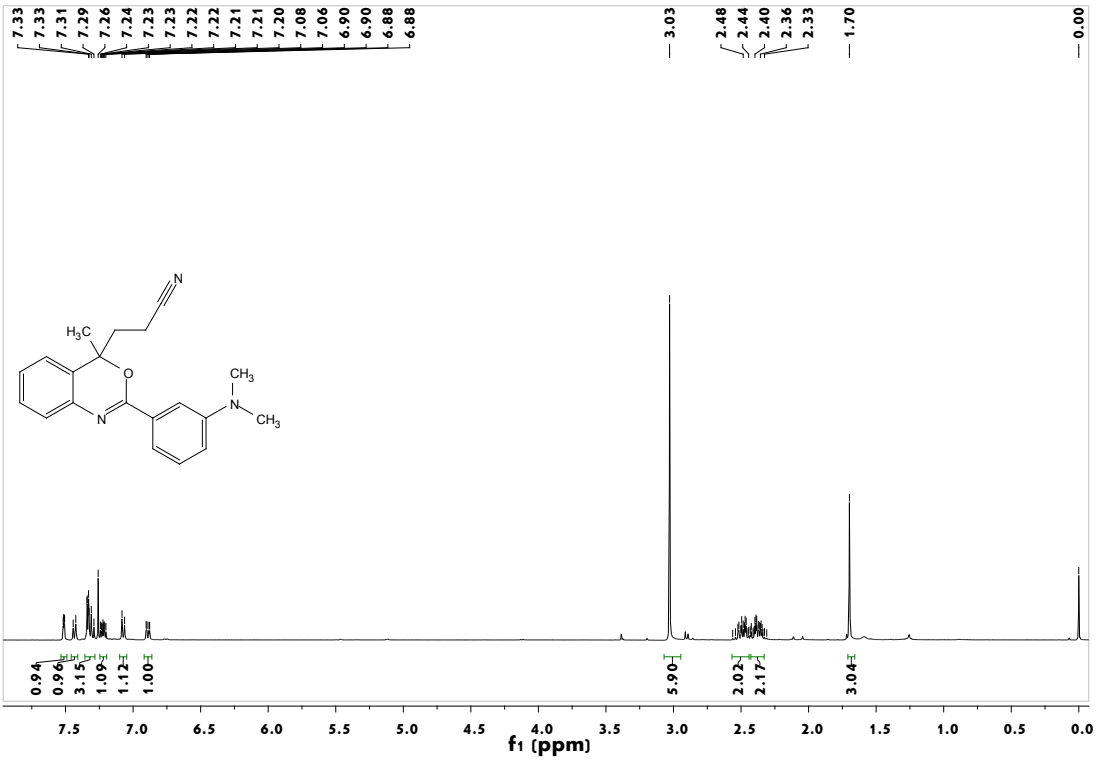

162.69
155.99
139.37
129.81
125.74
124.89
122.48
119.53
113.90
79.48
77.55
77.23
76.91
55.62
36.78
28.18
12.57
N
H3C
O
N
O
CH3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

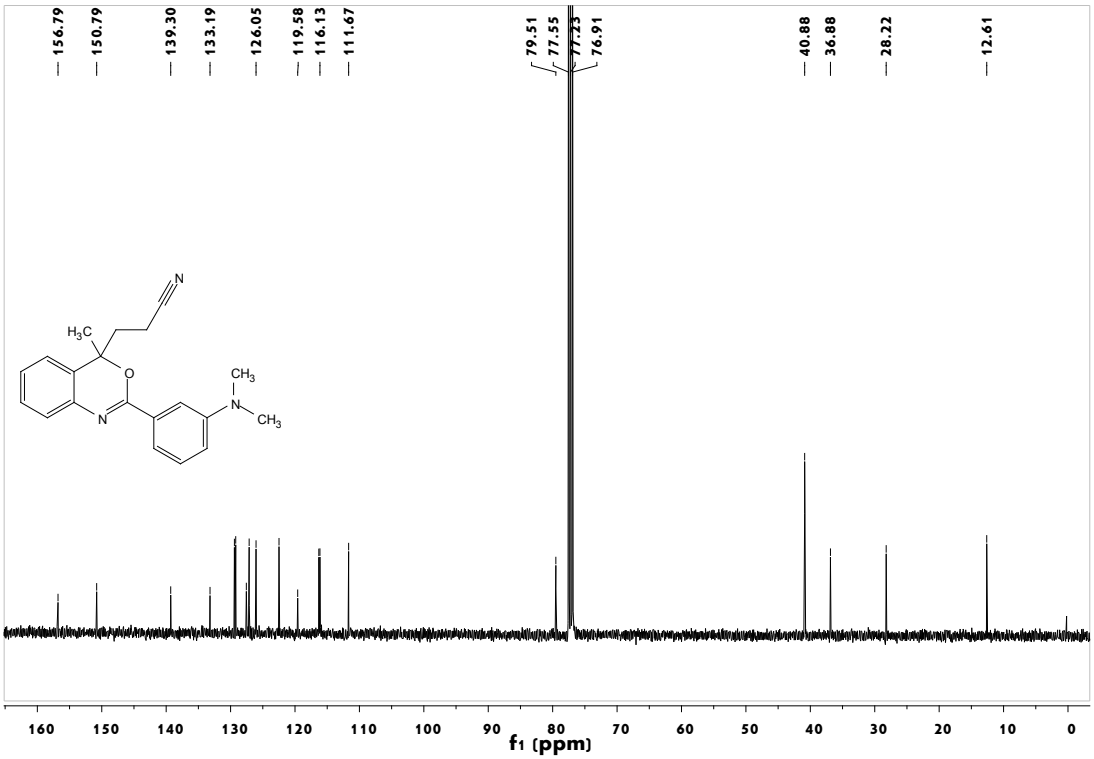

8.05
8.03
7.32
7.32
7.31
7.29
7.27
7.26
7.24
7.23
7.22
7.22
7.21
7.20
7.20
7.08
7.06
2.74
2.72
2.71
2.69
2.46
2.38
2.32
1.69
1.29
1.27
1.25
0.00
N
H3C
O
N
CH3
1.84
3.96
1.08
1.00
1.96
1.92
1.96
3.05
3.14
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

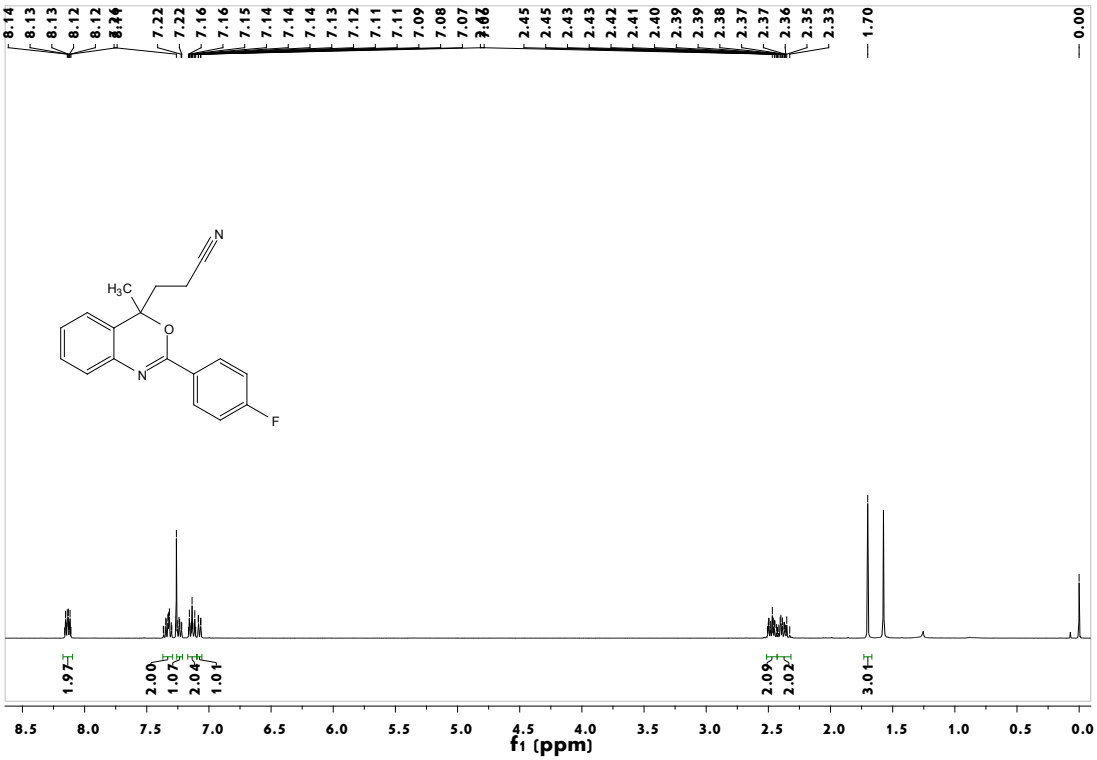

156.20
148.63
139.26
129.94
129.43
128.11
128.08
127.44
127.08
125.94
122.51
119.52
79.53
77.55
77.23
76.91
36.86
29.12
28.25
15.57
12.59
N
H3C
O
N
CH3
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

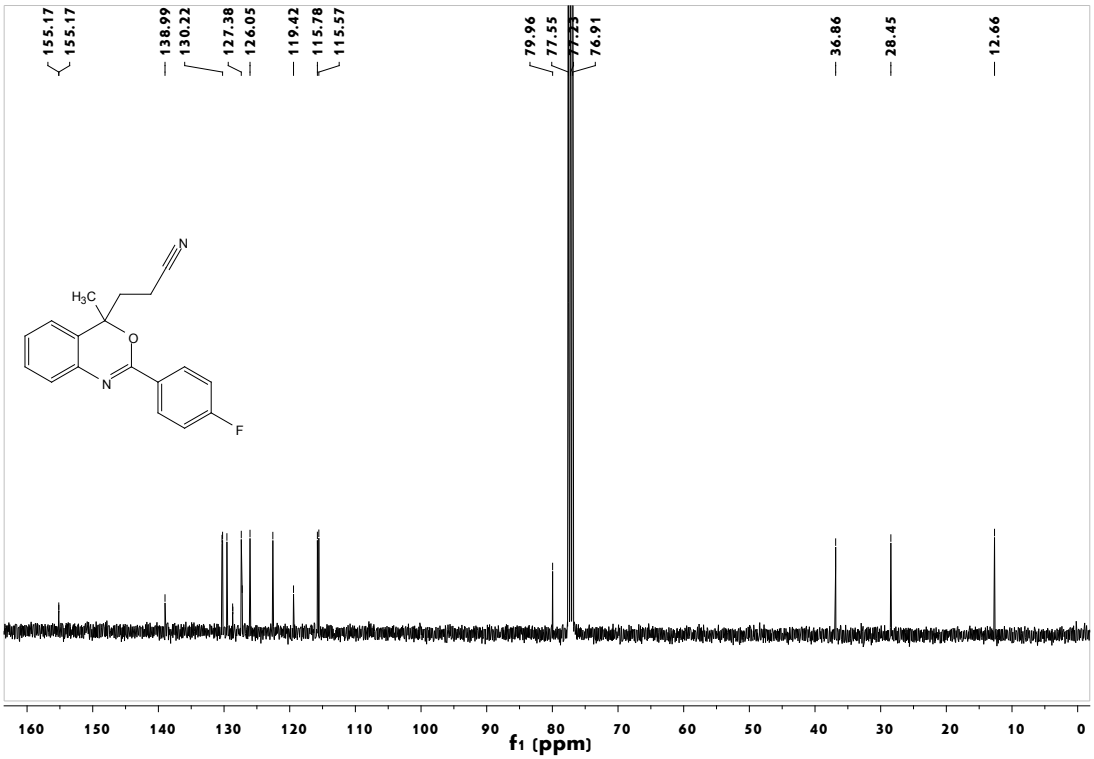

7.94
7.92
7.90
7.37
7.35
7.34
7.33
7.32
7.25
7.25
7.24
7.23
7.23
7.22
7.21
7.08
7.06
2.49
2.49
2.48
2.47
2.46
2.43
2.42
2.41
2.40
2.39
2.38
2.37
2.36
2.34
2.34
2.32
1.70
-0.00
N
H3C
O
N
CH3
0.97
0.96
4.01
0.99
1.00
2.14
3.02
2.06
3.06
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

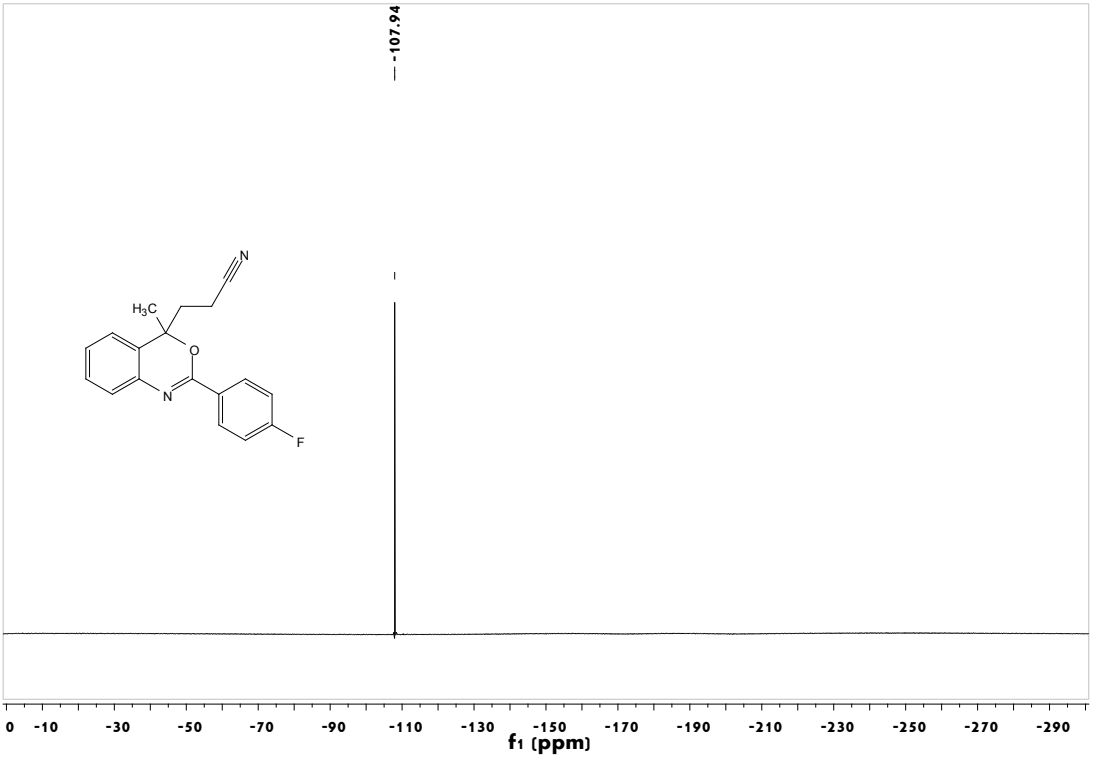

156.28
139.12
138.31
132.68
129.46
128.48
128.47
127.41
127.24
126.00
125.14
122.53
119.48
79.65
77.55
77.23
76.91
36.85
28.30
21.59
12.59
N
H3C
O
N
CH3
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

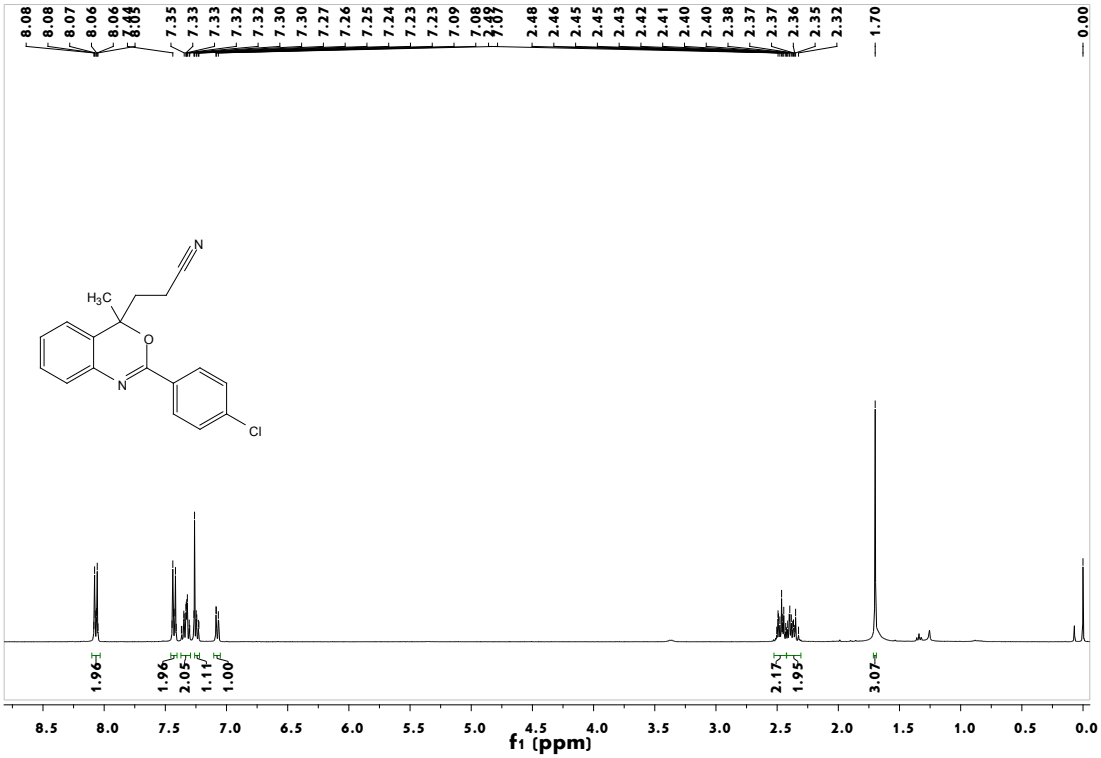

7.33
7.33
7.31
7.29
7.26
7.24
7.23
7.23
7.22
7.22
7.21
7.21
7.20
7.08
7.06
6.90
6.90
6.88
6.88
3.03
2.48
2.44
2.40
2.36
2.33
1.70
0.00
0.94
0.96
3.15
1.09
1.12
1.00
5.90
2.02
2.17
3.04
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
N
H3C
O
N
CH3
N
CH3

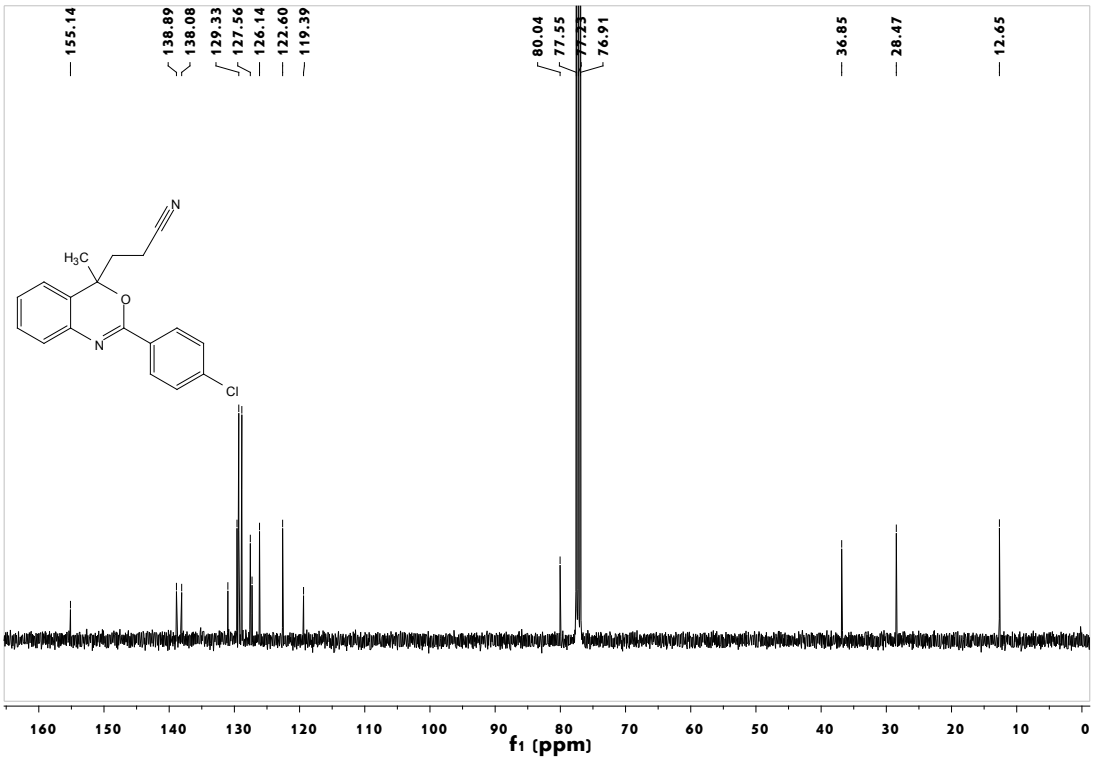

156.79
150.79
139.30
133.19
126.05
119.58
116.13
111.67
79.51
77.55
77.23
76.91
40.88
36.88
28.22
12.61
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
N
H3C
O
N
CH3
N
CH3

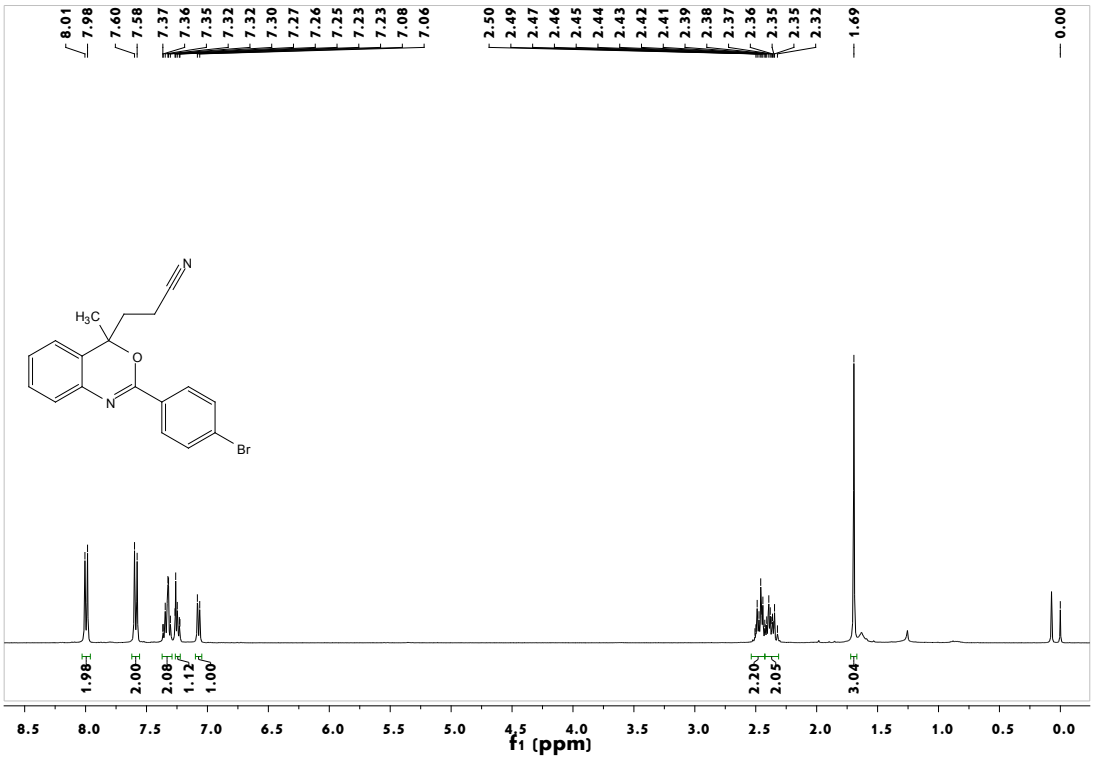

8.14
8.13
8.13
8.12
8.12
7.22
7.22
7.16
7.16
7.15
7.14
7.14
7.14
7.13
7.12
7.11
7.11
7.09
7.08
7.07
2.45
2.45
2.43
2.43
2.42
2.41
2.40
2.39
2.39
2.38
2.37
2.37
2.36
2.35
2.33
1.70
0.00
N
H3C
O
N
F
1.97
2.00
1.07
2.04
1.01
2.09
2.02
3.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

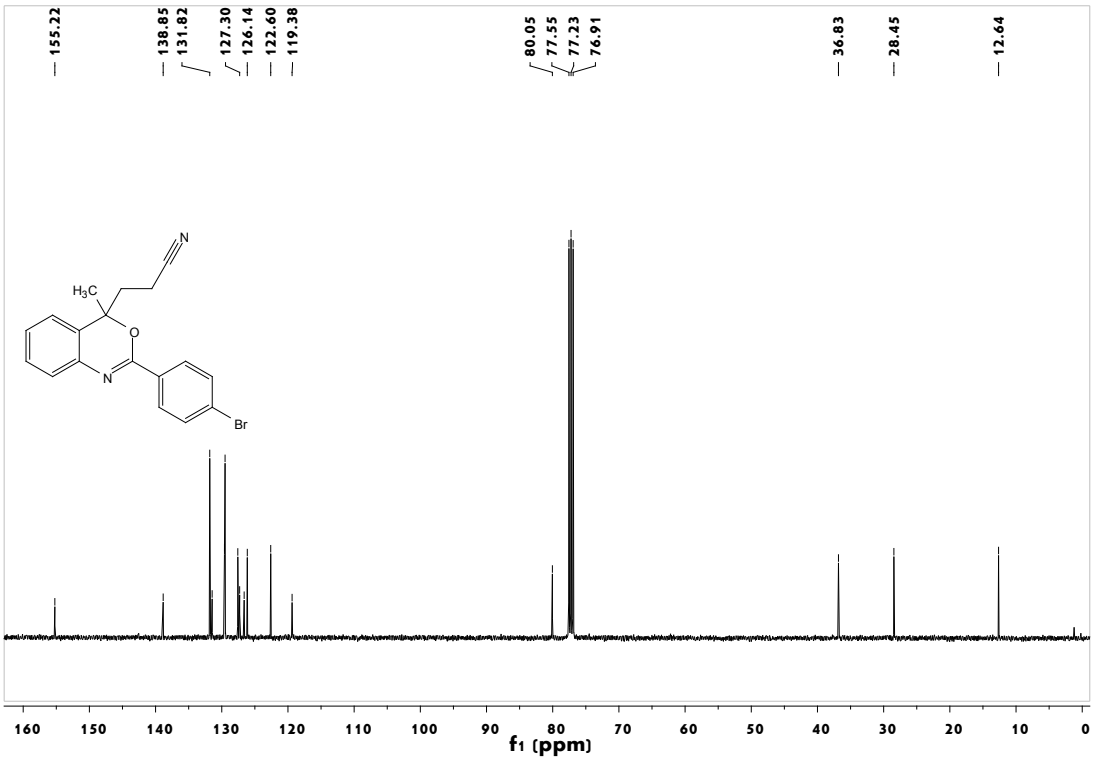

155.17
155.17
138.99
130.22
127.38
126.05
119.42
115.78
115.57
79.96
77.55
77.23
76.91
36.86
28.45
12.66
N
H3C
O
N
F
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

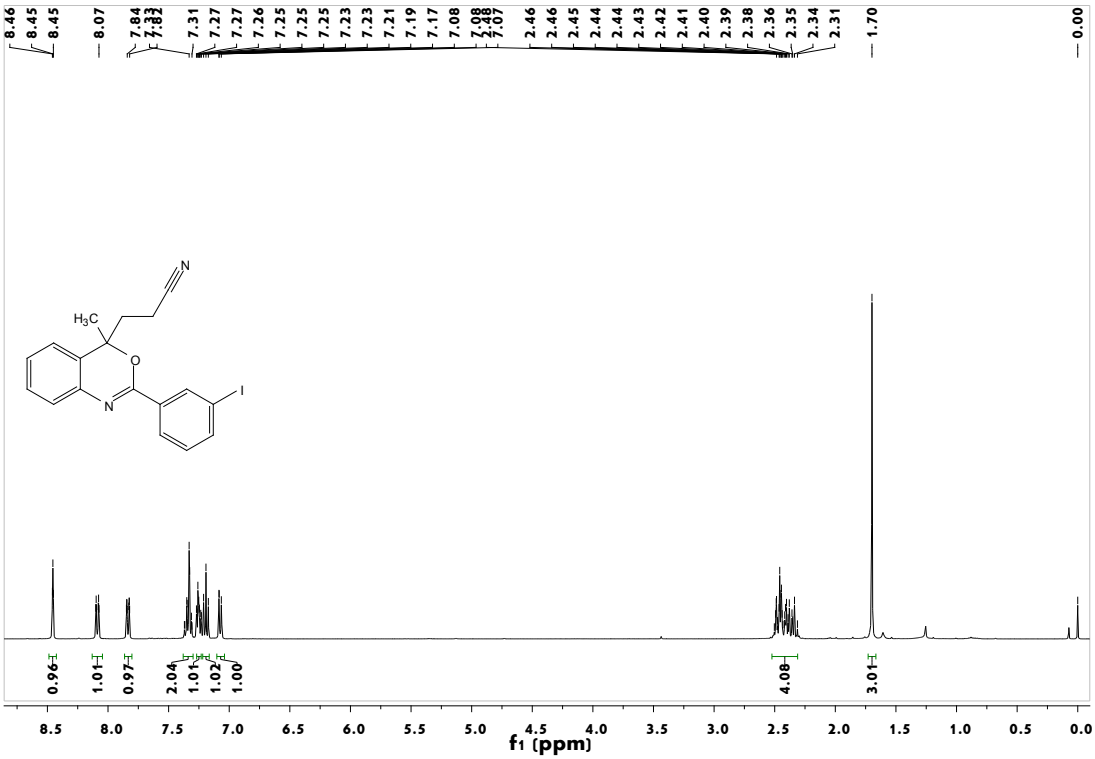

-107.94
N
H3C
O
N
F
0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230 -250 -270 -290
f1 (ppm)

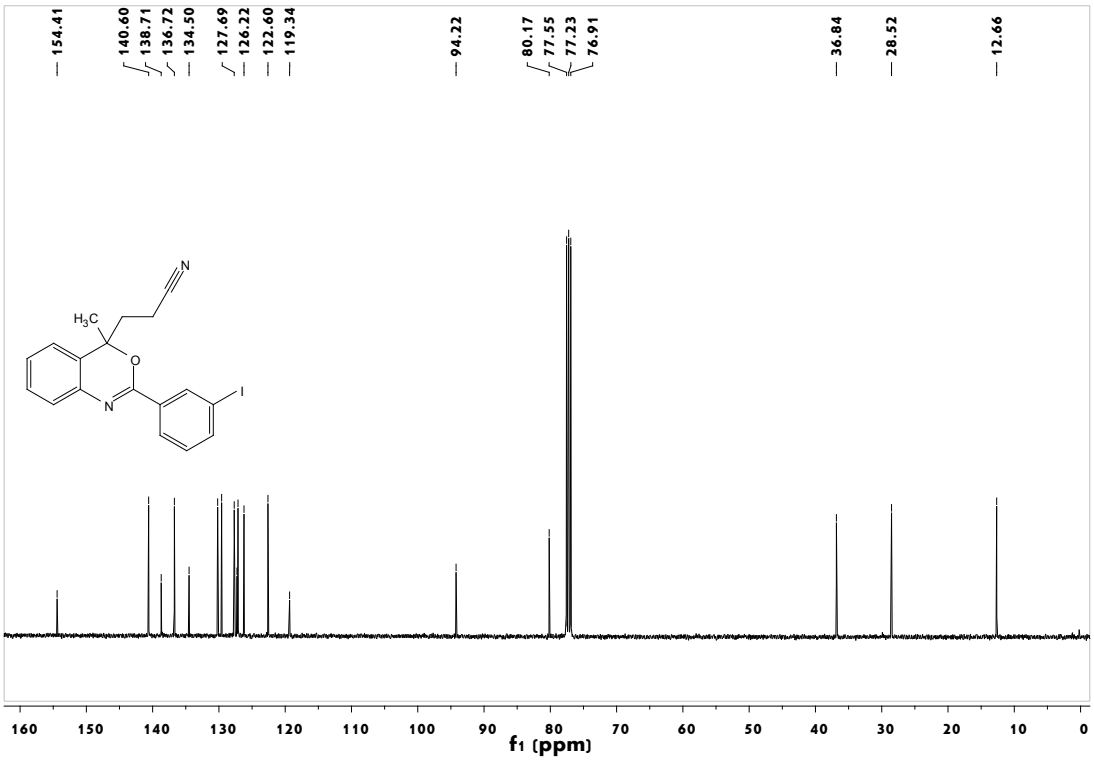

8.08 8.08 8.07 8.06 8.06 7.44 8.05
7.35 7.33 7.33 7.32 7.32 7.30 7.30 7.27 7.26 7.25 7.24 7.23 7.23 7.09 7.08 7.07
2.48 2.46 2.45 2.45 2.43 2.42 2.41 2.40 2.40 2.38 2.37 2.37 2.36 2.35 2.32
1.70
0.00
N
H3C
O
N
Cl
1.96 1.96 2.05 1.11 1.00 2.17 1.95 3.07
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

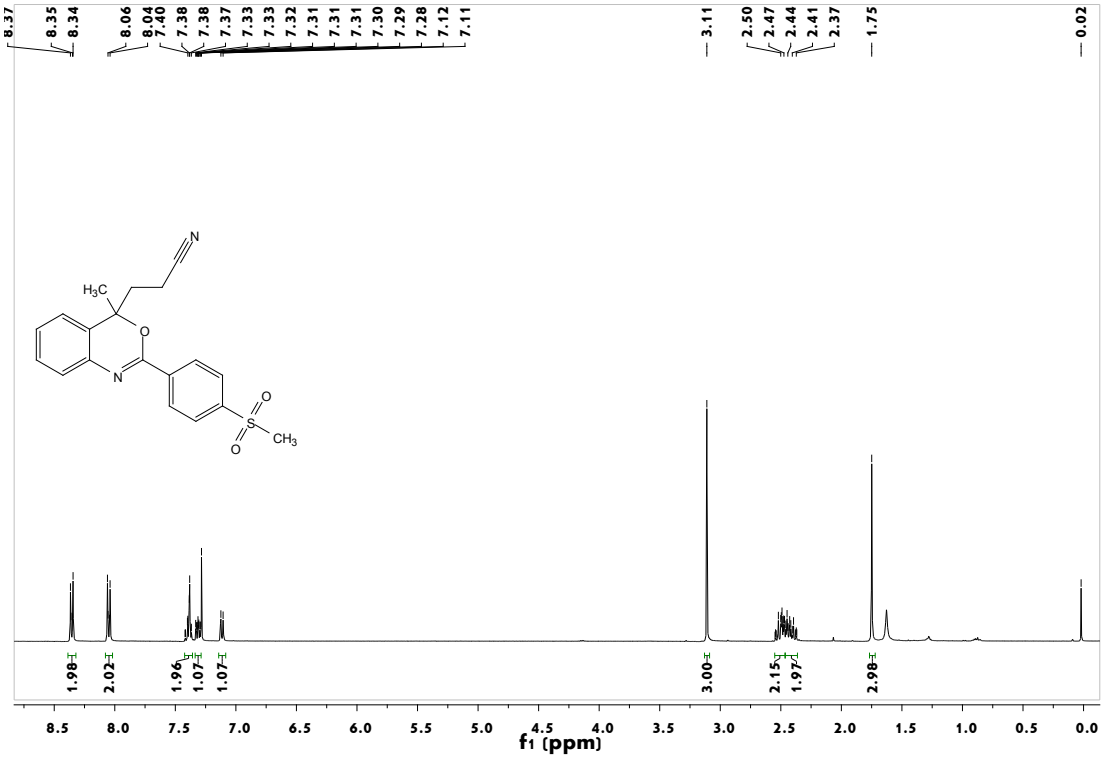

155.14
138.89
138.08
129.33
127.56
126.14
122.60
119.39
80.04
77.55
77.23
76.91
36.85
28.47
12.65
N
H3C
O
N
Cl
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

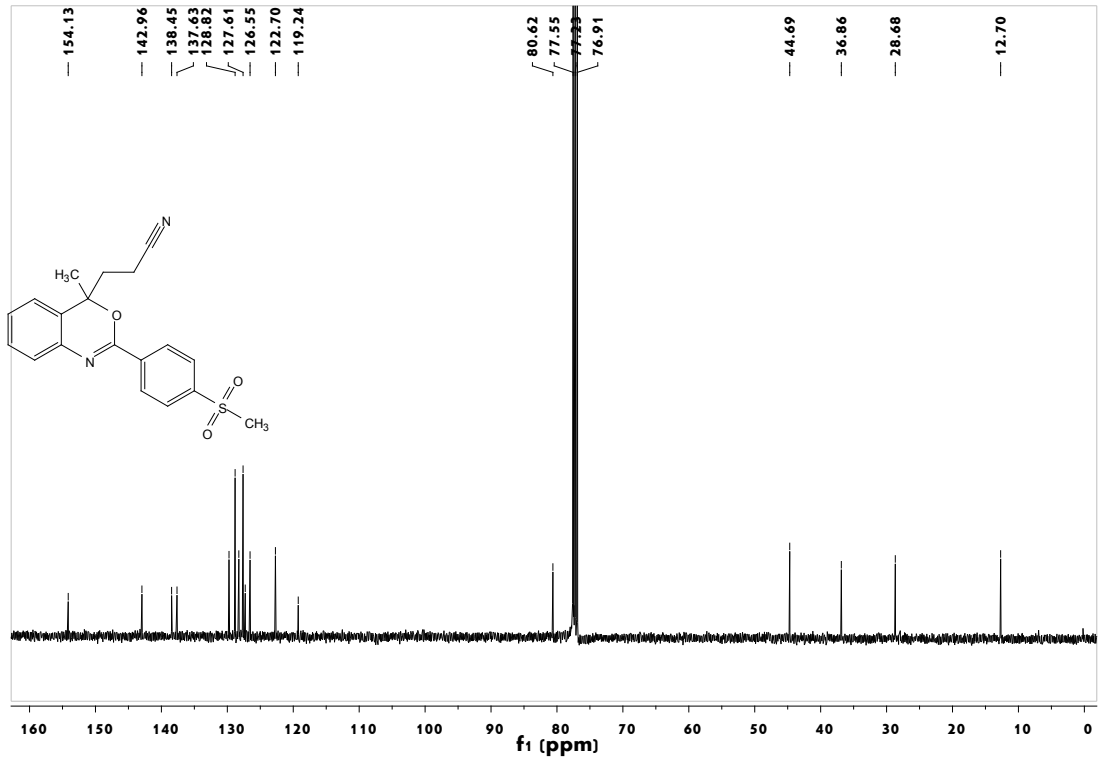

8.01
7.98
7.60
7.58
7.37
7.36
7.35
7.32
7.32
7.30
7.27
7.26
7.25
7.23
7.23
7.08
7.06
2.50
2.49
2.47
2.46
2.45
2.44
2.43
2.42
2.41
2.39
2.38
2.37
2.36
2.35
2.35
2.32
1.69
0.00
N
H3C
O
N
Br
1.98
2.00
2.08
1.12
1.00
2.20
2.05
3.04
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

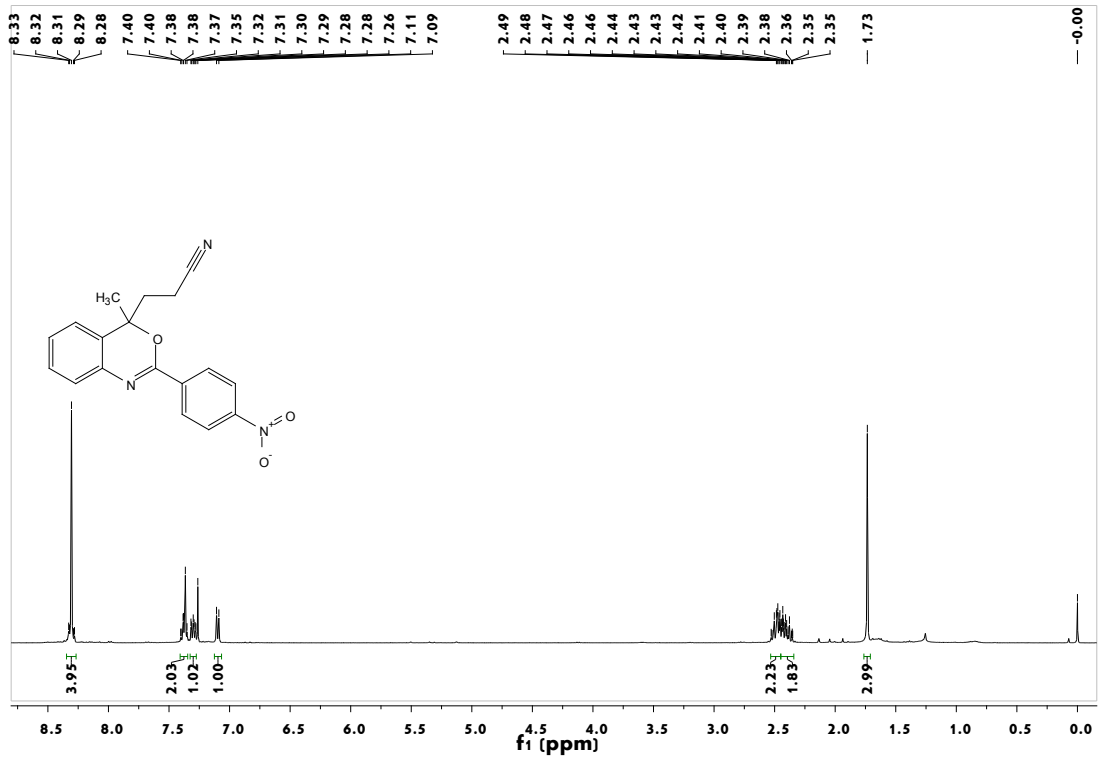

155.22
138.85
131.82
127.30
126.14
122.60
119.38
80.05
77.55
77.23
76.91
36.83
28.45
12.64
N
H3C
O
N
Br
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

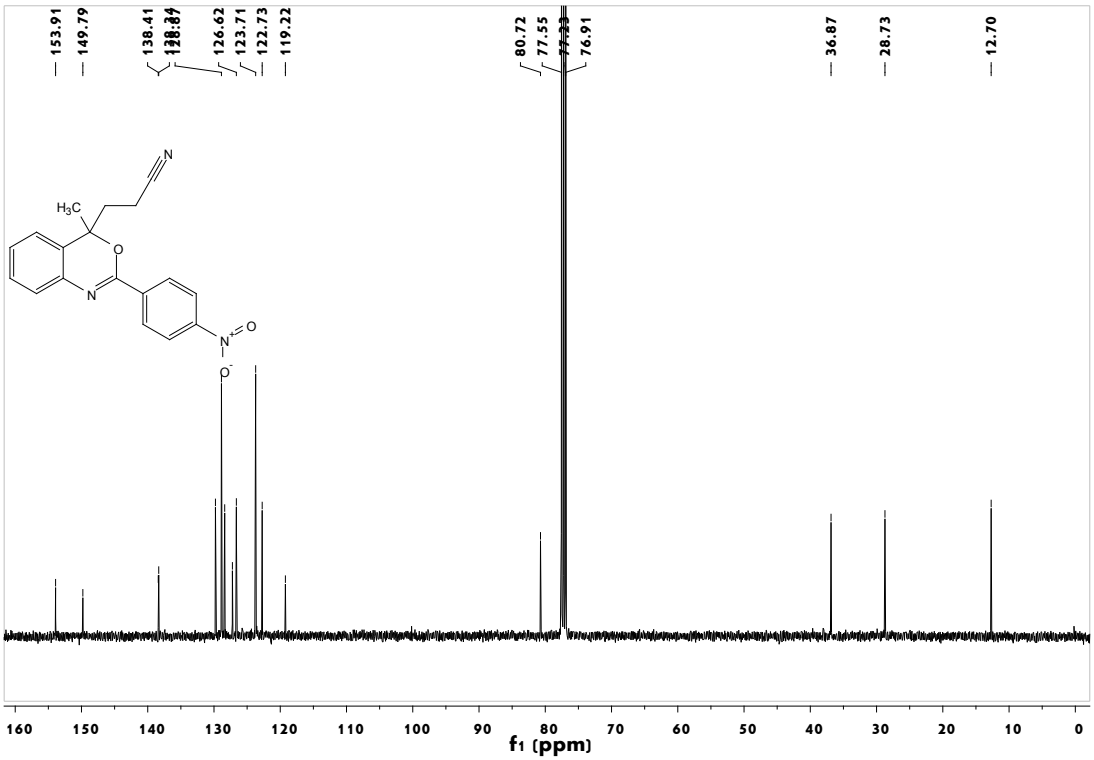

8.46
8.45
8.45
8.07
7.84
7.33
7.32
7.31
7.27
7.27
7.26
7.25
7.25
7.25
7.23
7.23
7.21
7.19
7.17
7.08
7.08
7.08
7.07
2.46
2.46
2.45
2.44
2.44
2.43
2.42
2.41
2.40
2.39
2.38
2.36
2.35
2.34
2.31
1.70
0.00
N
H3C
O
N
I
0.96
1.01
0.97
2.04
1.01
1.02
1.00
4.08
3.01
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

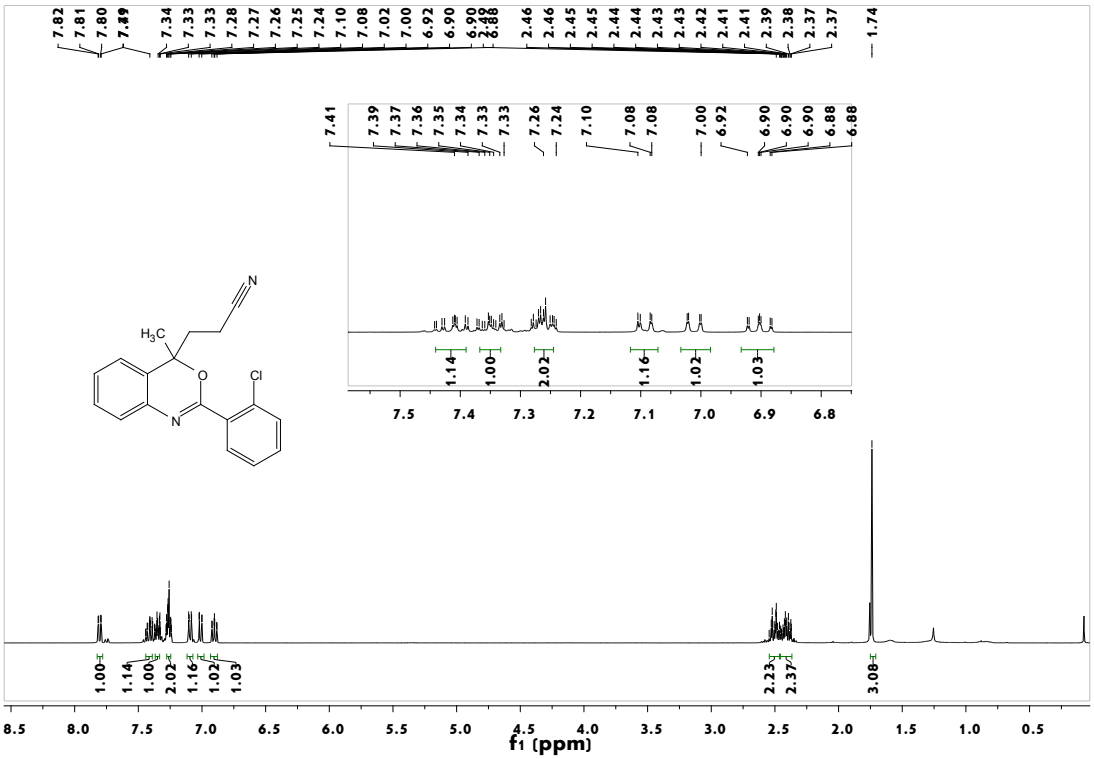

154.41
140.60
138.71
136.72
134.50
127.69
126.22
122.60
119.34
94.22
80.17
77.55
77.23
76.91
36.84
28.52
12.66
N
H3C
O
N
I
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

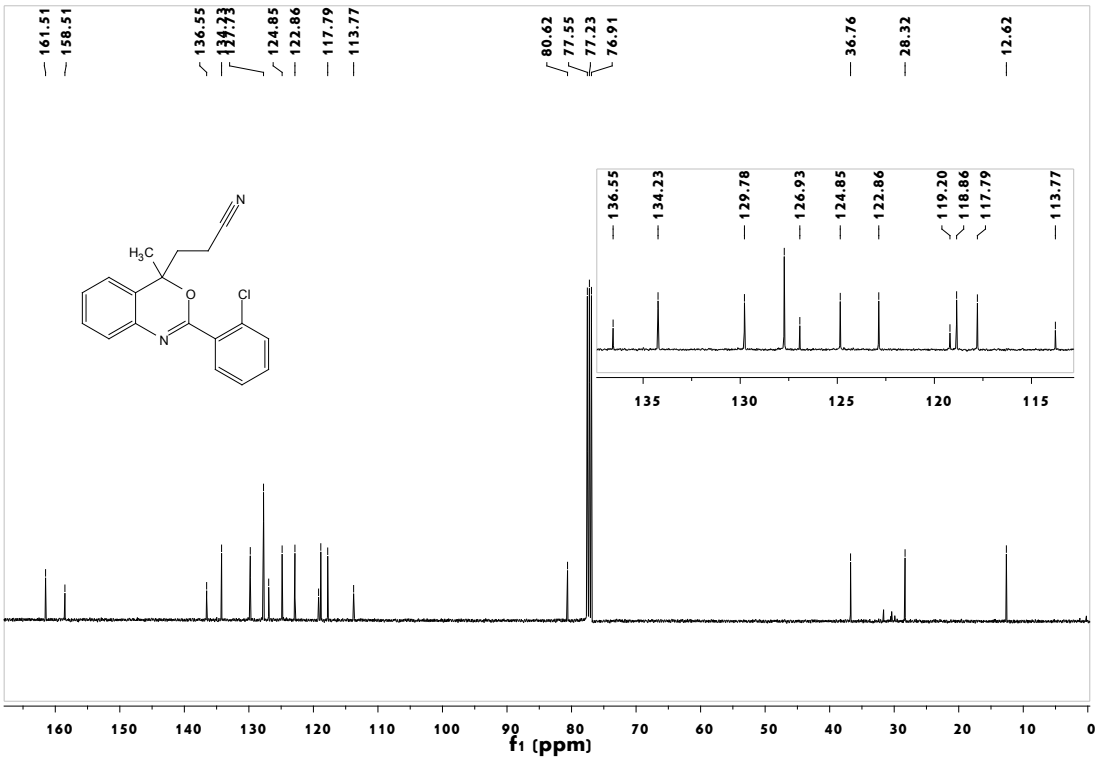

8.37
8.35
8.34
8.06
8.04
7.40
7.38
7.38
7.37
7.33
7.32
7.31
7.31
7.31
7.30
7.29
7.28
7.12
7.11
3.11
2.50
2.47
2.44
2.41
2.37
1.75
0.02
N
H3C
O
N
O
S
O
CH3
1.98
2.02
1.96
1.07
1.07
3.00
2.15
1.97
2.98
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

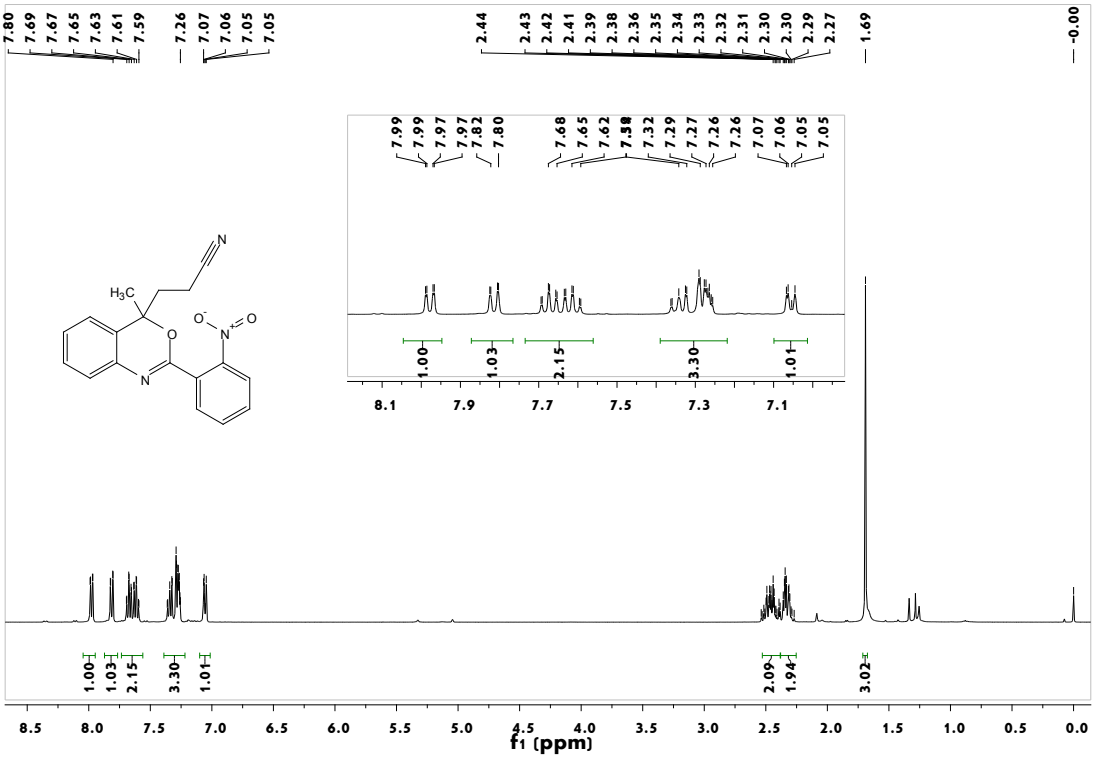

154.13
142.96
138.45
137.63
128.82
127.61
126.55
122.70
119.24
80.62
77.55
76.91
44.69
36.86
28.68
12.70
N
H3C
O
N
O
S
O
CH3
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

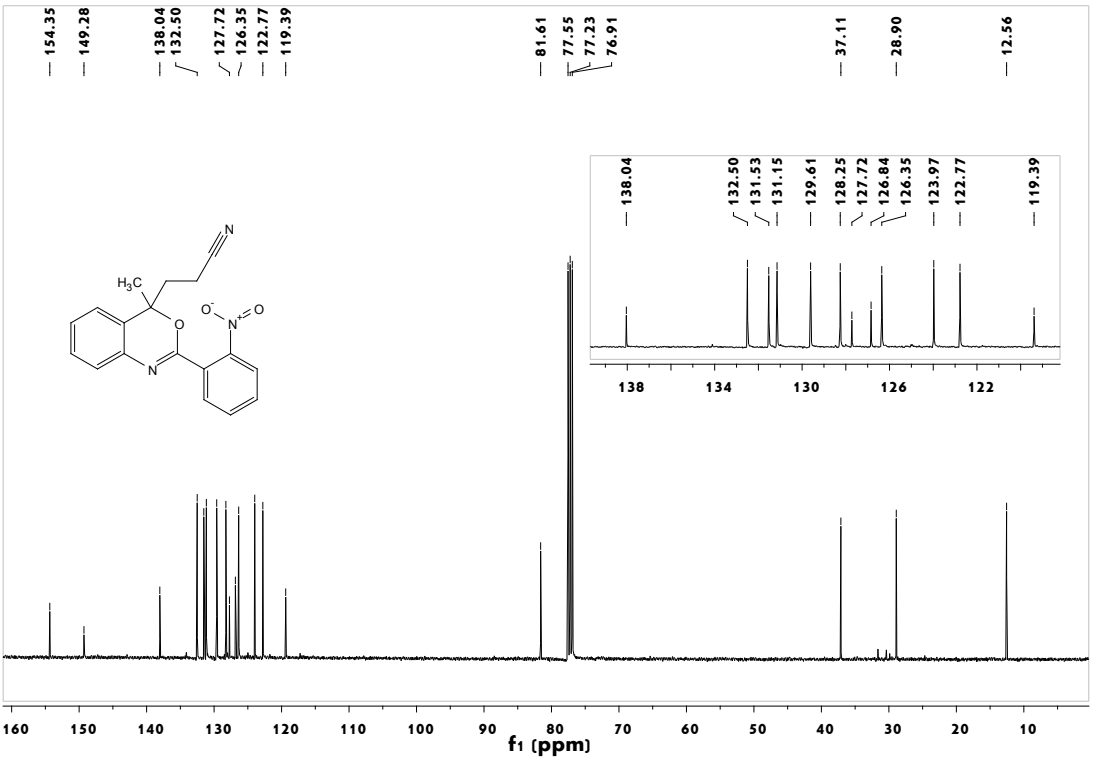

8.33
8.32
8.31
8.29
8.28
7.40
7.40
7.38
7.38
7.37
7.35
7.32
7.31
7.30
7.29
7.28
7.28
7.26
7.11
7.09
2.49
2.48
2.47
2.46
2.46
2.44
2.43
2.43
2.42
2.41
2.40
2.39
2.38
2.36
2.35
2.35
1.73
-0.00
N
H3C
O
N
O
O
3.95
2.03
1.02
1.00
2.23
1.83
2.99
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

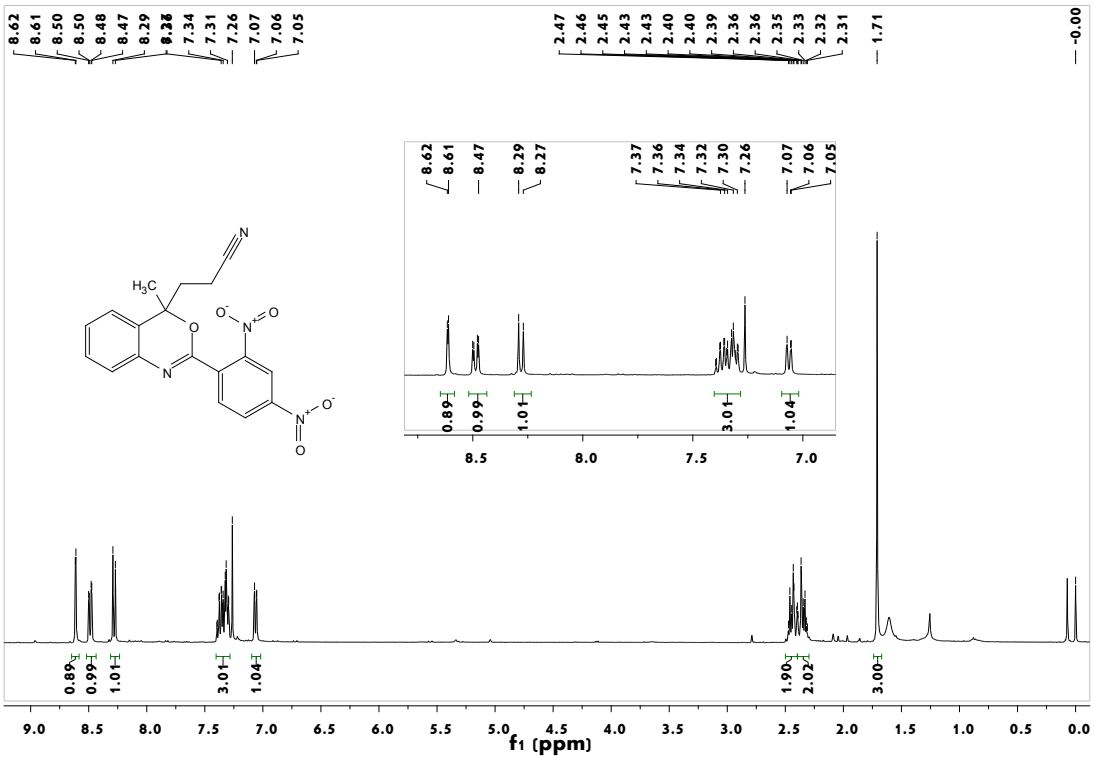

153.91
149.79
138.41
126.62
123.71
122.73
119.22
80.72
77.55
76.91
36.87
28.73
12.70
N
H3C
O
N
N
O
O
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

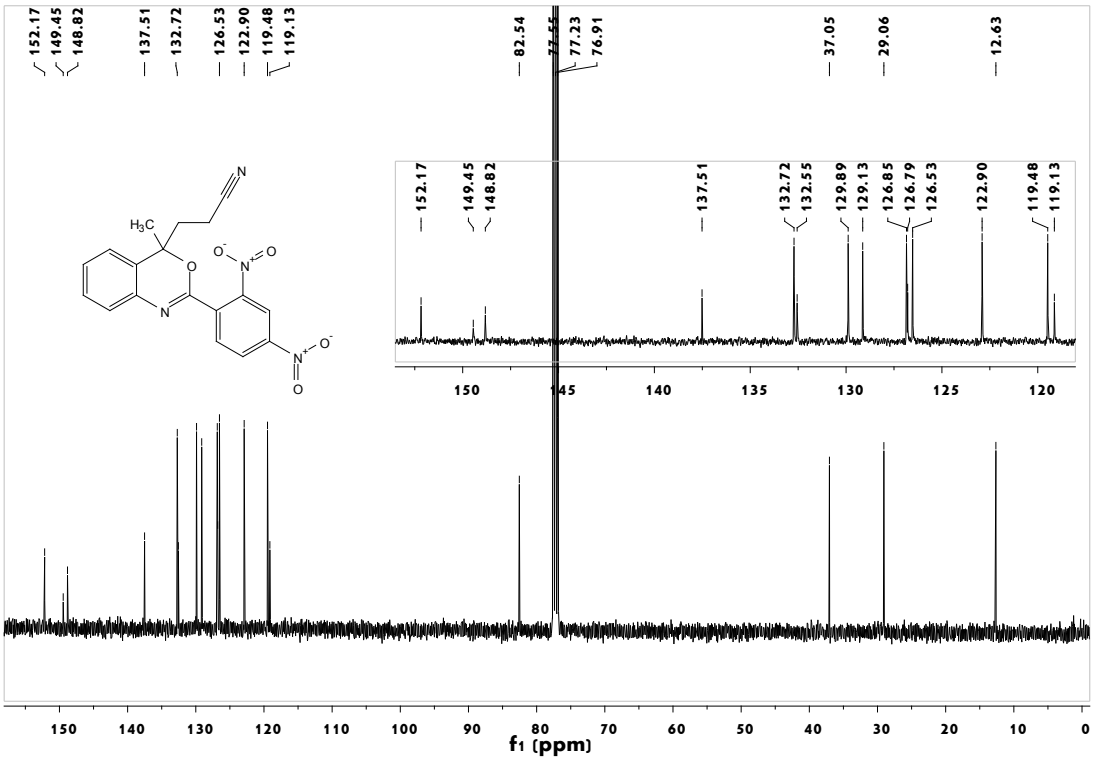

7.82
7.81
7.80
7.34
7.33
7.33
7.28
7.27
7.26
7.25
7.24
7.10
7.08
7.02
7.00
6.92
6.90
2.46
2.45
2.44
2.43
2.42
2.41
2.39
2.38
2.37
1.74
7.41
7.39
7.37
7.36
7.35
7.34
7.33
7.26
7.24
7.10
7.08
7.00
6.92
6.90
6.88
1.14
1.00
2.02
1.16
1.02
1.03
7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8
N
H3C
O
N
Cl
1.00
1.14
1.00
2.02
1.16
1.02
1.03
2.23
2.37
3.08
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 0.5
f1 (ppm)

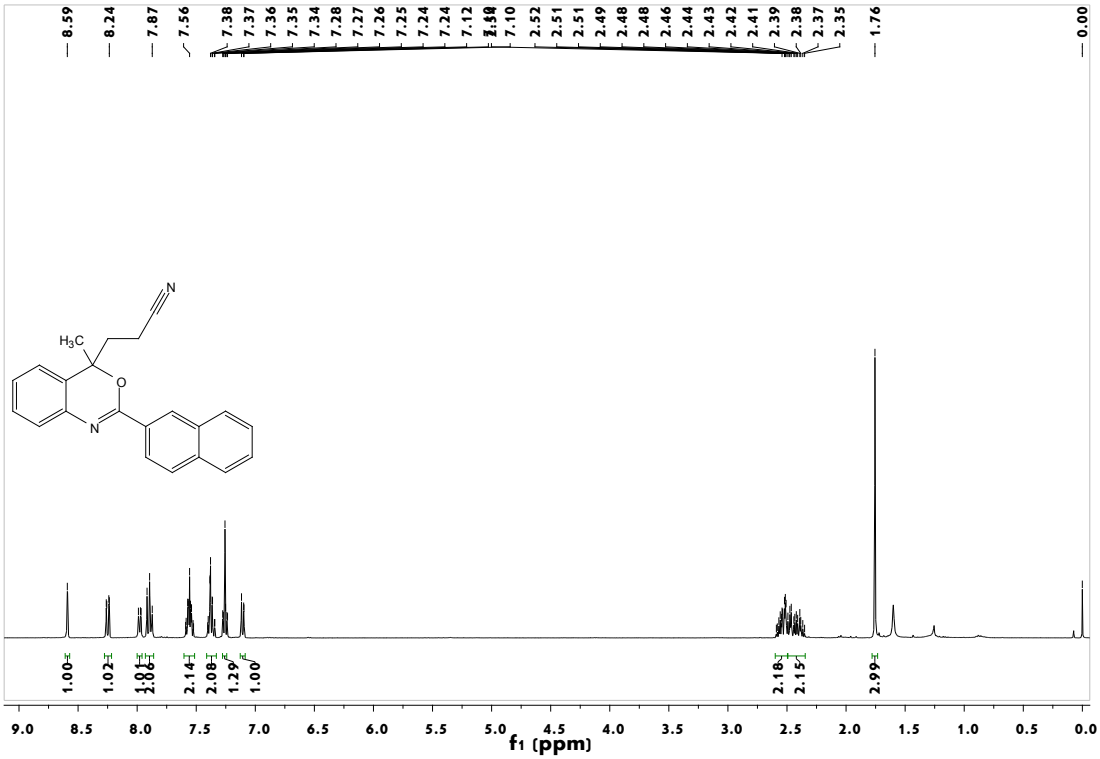

161.51
158.51
136.55
134.23
129.78
126.93
124.85
122.86
119.20
118.86
117.79
113.77
80.62
77.55
77.23
76.91
36.76
28.32
12.62
N
H3C
O
Cl
N
f1 (ppm)

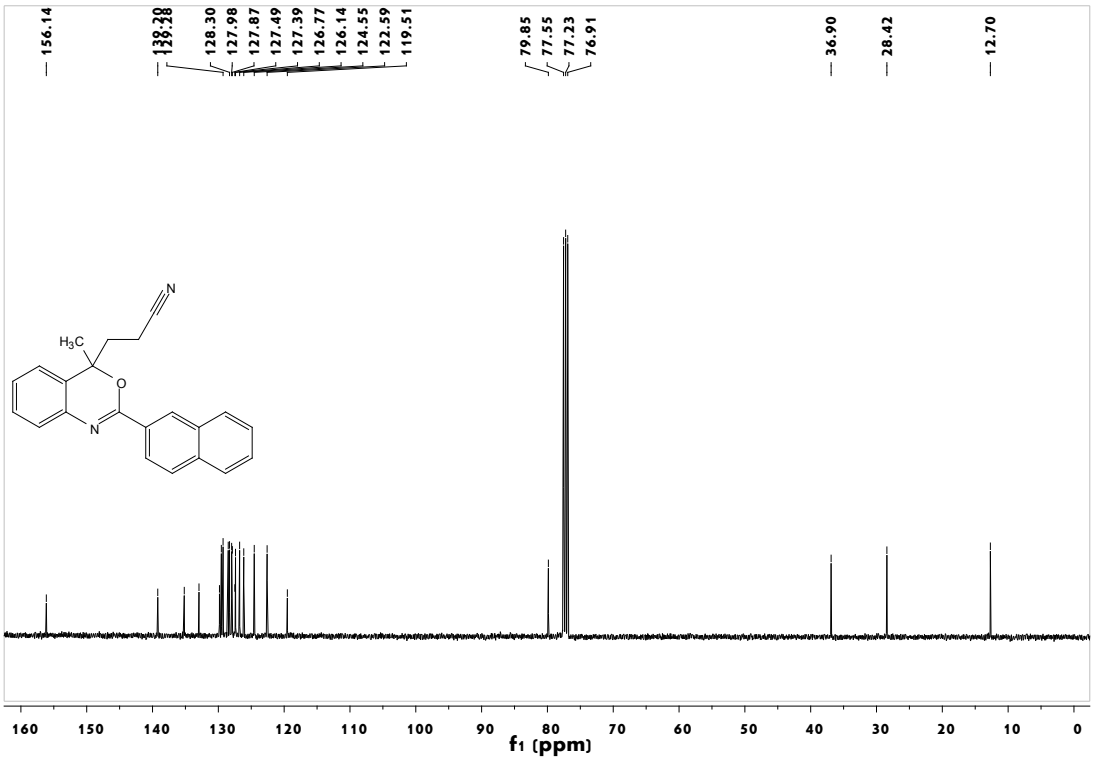

7.80
7.69
7.67
7.65
7.63
7.61
7.59
7.26
7.07
7.06
7.05
7.05
2.44
2.43
2.42
2.41
2.39
2.38
2.36
2.35
2.34
2.33
2.32
2.31
2.30
2.30
2.29
2.27
1.69
-0.00
1.00
1.03
2.15
3.30
1.01
2.09
1.94
3.02
N
H3C
O
O
N
O
f1 (ppm)

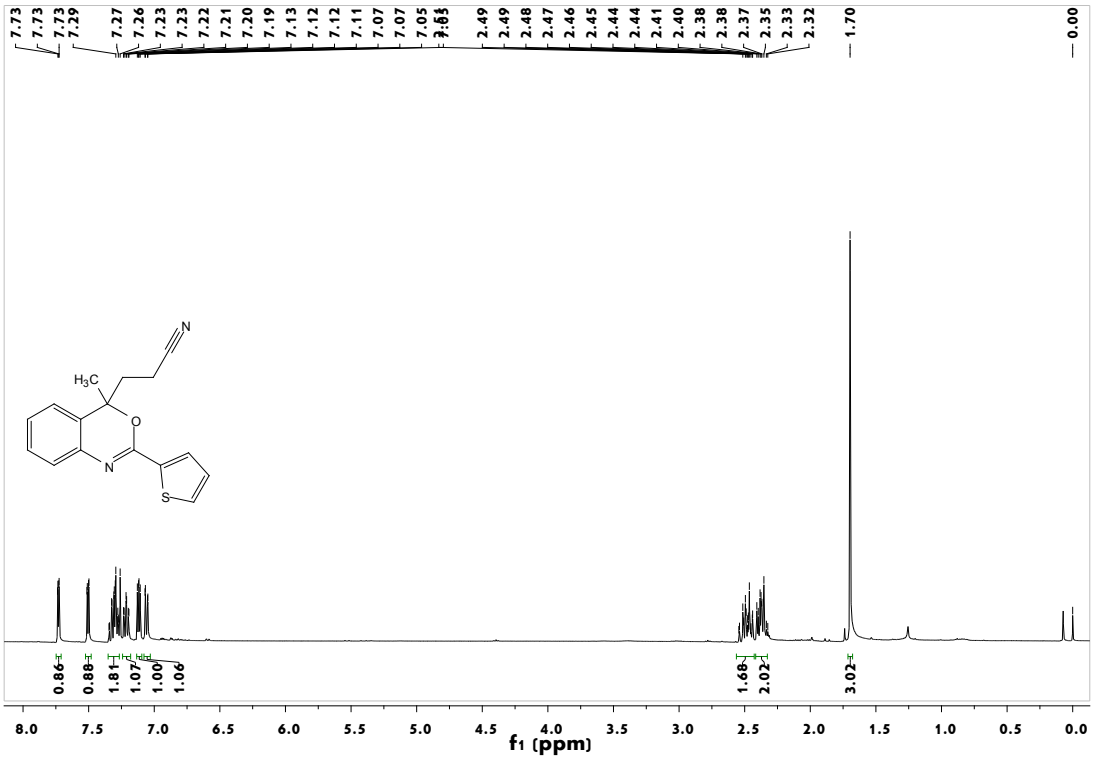

154.35
149.28
138.04
132.50
127.72
126.35
122.77
119.39
81.61
77.55
77.23
76.91
37.11
28.90
12.56
138.04
132.50
131.53
131.15
129.61
128.25
127.72
126.84
126.35
123.97
122.77
119.39
138
134
130
126
122
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

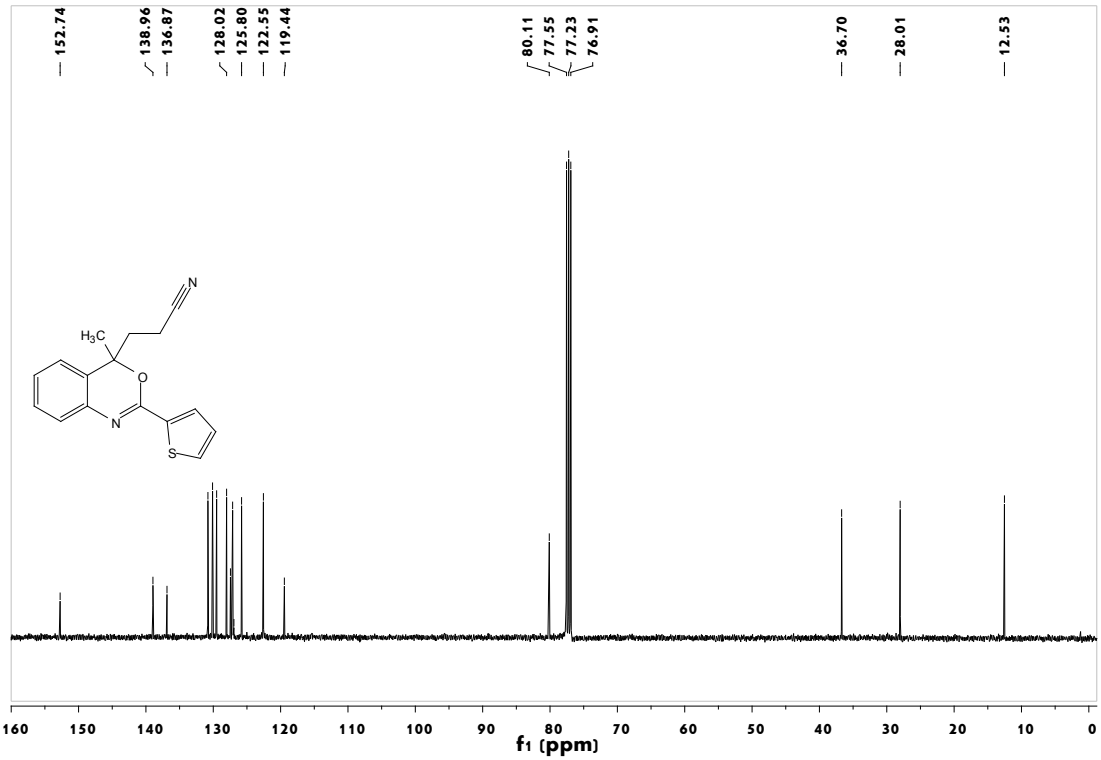

8.62
8.61
8.50
8.50
8.48
8.47
8.29
7.34
7.31
7.26
7.07
7.06
7.05
2.47
2.46
2.45
2.43
2.43
2.40
2.40
2.39
2.36
2.36
2.35
2.33
2.32
2.31
1.71
-0.00
8.62
8.61
8.47
8.29
8.27
7.37
7.36
7.34
7.32
7.30
7.26
7.07
7.06
7.05
0.89
0.99
1.01
3.01
1.04
8.5
8.0
7.5
7.0
0.89
0.99
1.01
3.01
1.04
1.90
2.02
3.00
9.0
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
0.5
0.0
f1 (ppm)

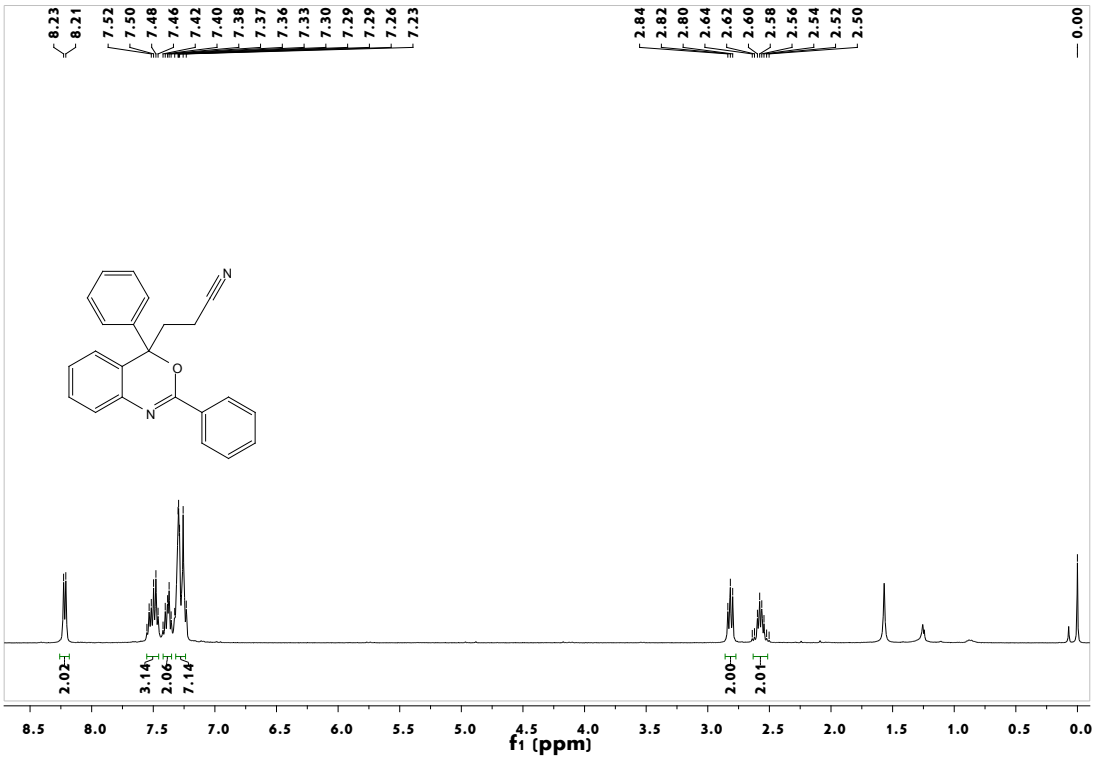

152.17
149.45
148.82
137.51
132.72
126.53
122.90
119.48
119.13
82.54
77.23
76.91
37.05
29.06
12.63
f1 (ppm)

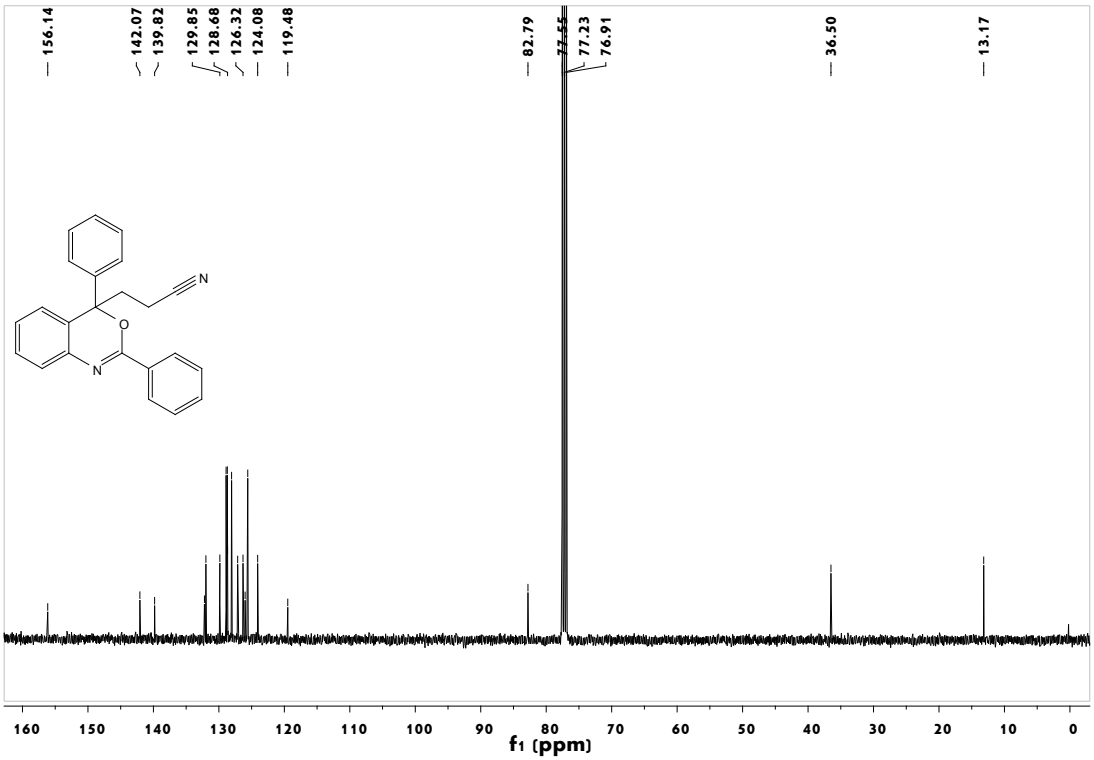

8.59
8.24
7.87
7.56
1.76
0.00
f1 (ppm)

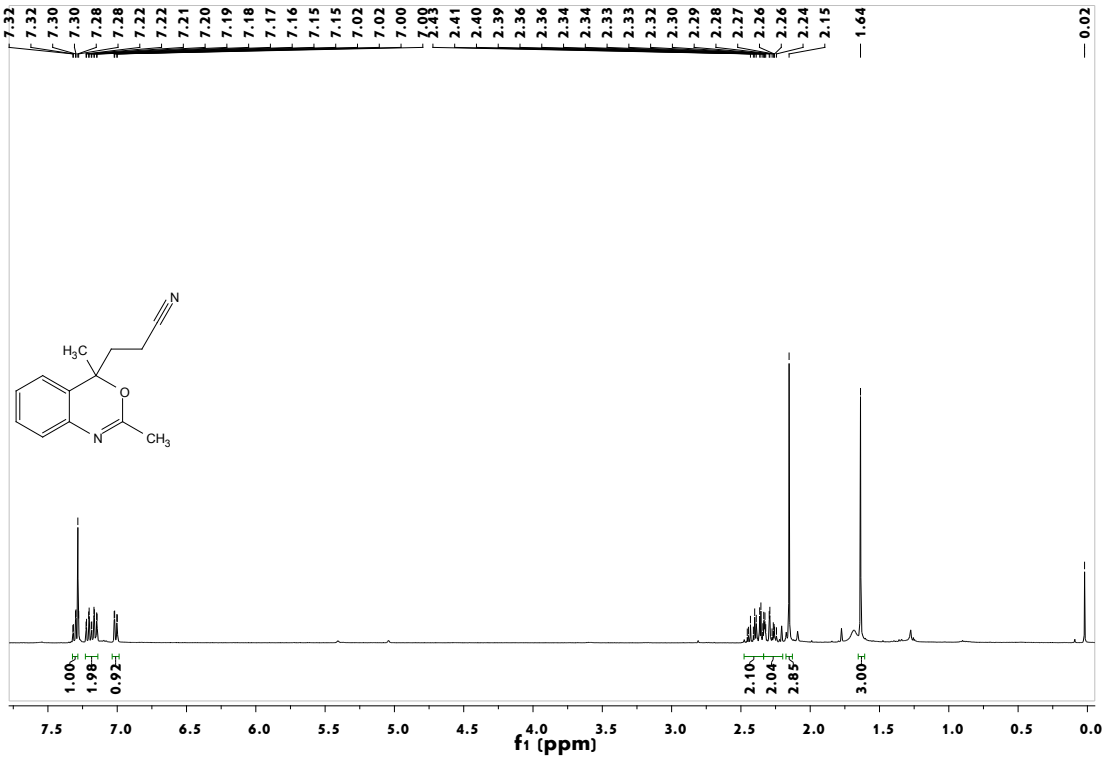

156.14
139.20
138.28
128.30
127.98
127.87
127.49
127.39
126.77
126.14
124.55
122.59
119.51
79.85
77.55
77.23
76.91
36.90
28.42
12.70
N
H3C
O
N
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

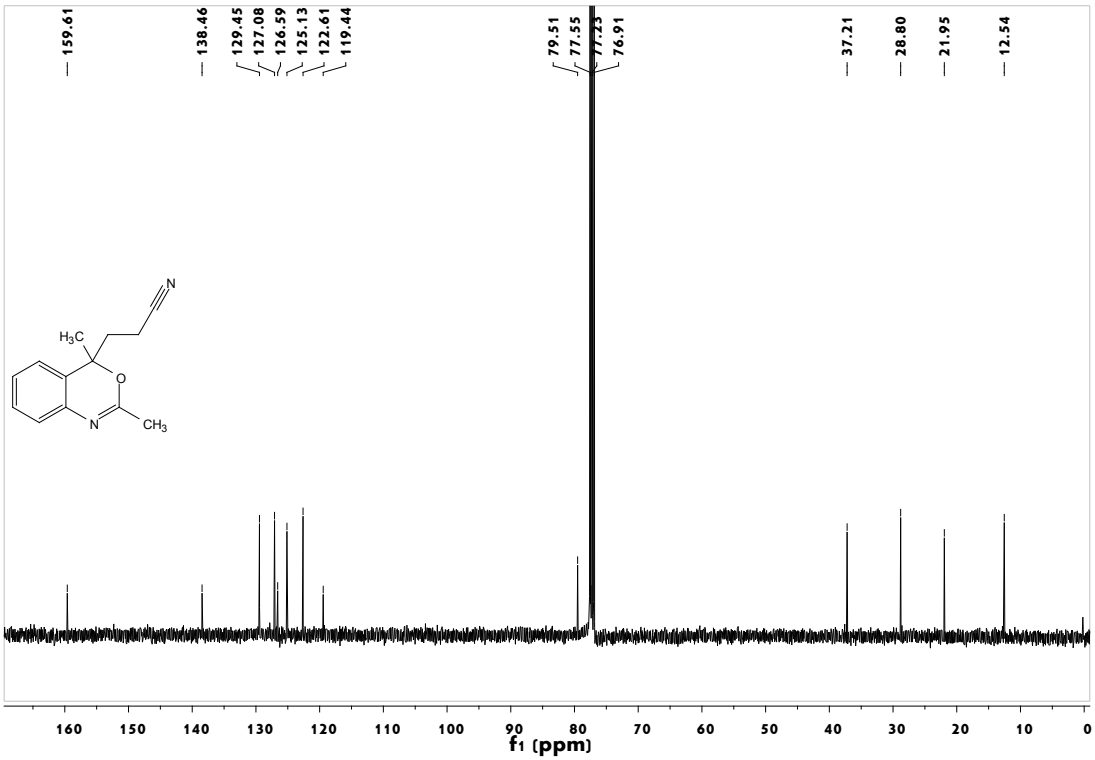

7.73
7.73
7.73
7.29
7.27
7.26
7.23
7.23
7.22
7.21
7.20
7.19
7.13
7.12
7.12
7.11
7.07
7.07
7.05
2.49
2.49
2.48
2.47
2.46
2.45
2.44
2.44
2.41
2.40
2.38
2.38
2.37
2.35
2.33
2.32
1.70
0.00
N
H3C
O
N
S
0.86
0.88
1.81
1.07
1.00
1.06
1.68
2.02
3.02
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

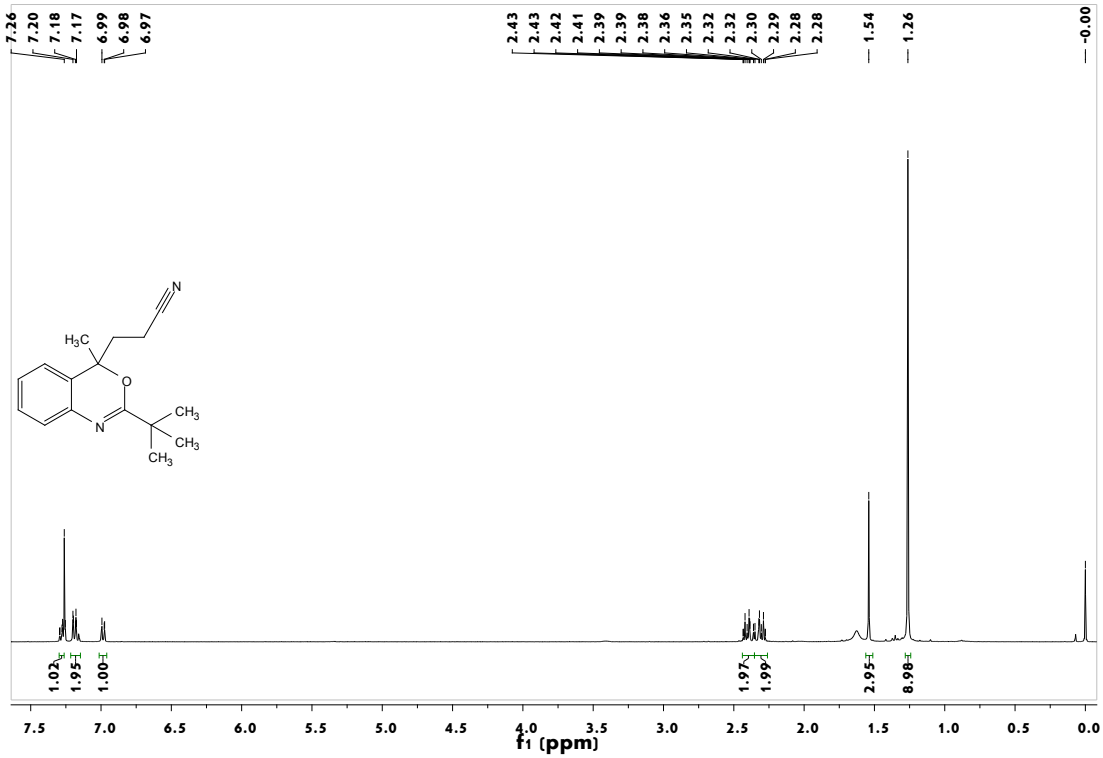

152.74
138.96
136.87
128.02
125.80
122.55
119.44
80.11
77.55
77.23
76.91
36.70
28.01
12.53
N
H3C
O
N
S
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

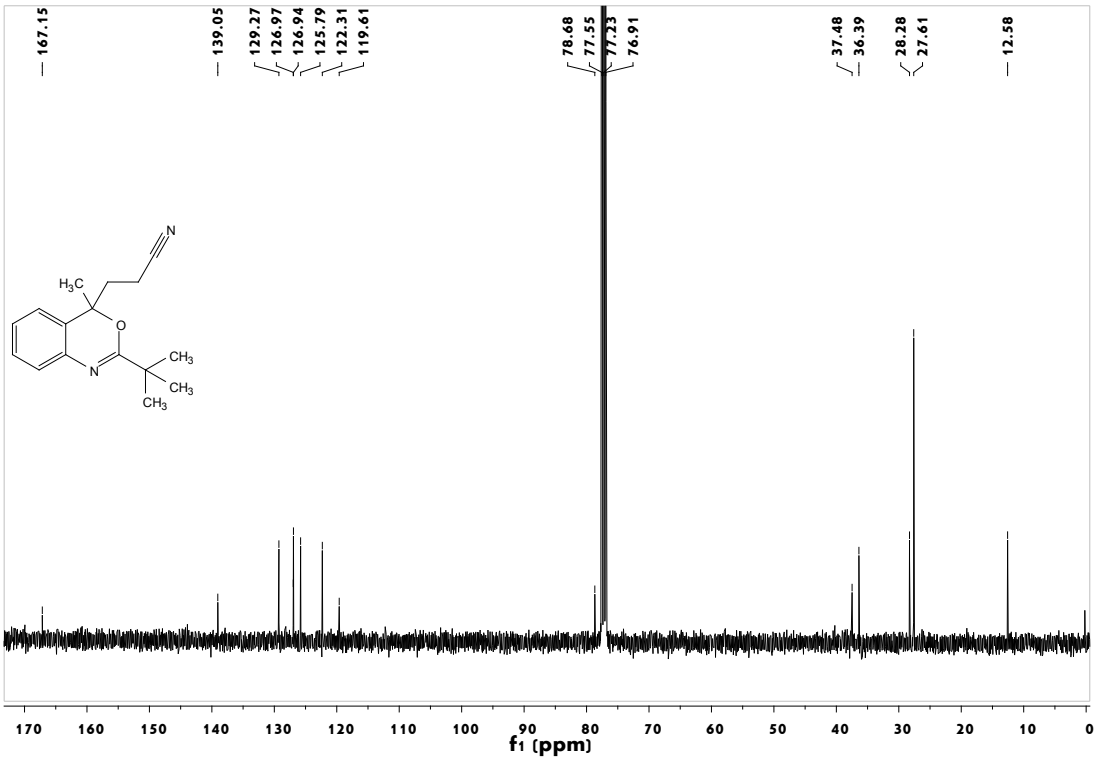

8.23
8.21
7.52
7.50
7.48
7.46
7.42
7.40
7.38
7.37
7.36
7.33
7.30
7.29
7.29
7.26
7.23
2.84
2.82
2.80
2.64
2.62
2.60
2.58
2.56
2.54
2.52
2.50
0.00
N
O
N
2.02
3.14
2.06
7.14
2.00
2.01
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

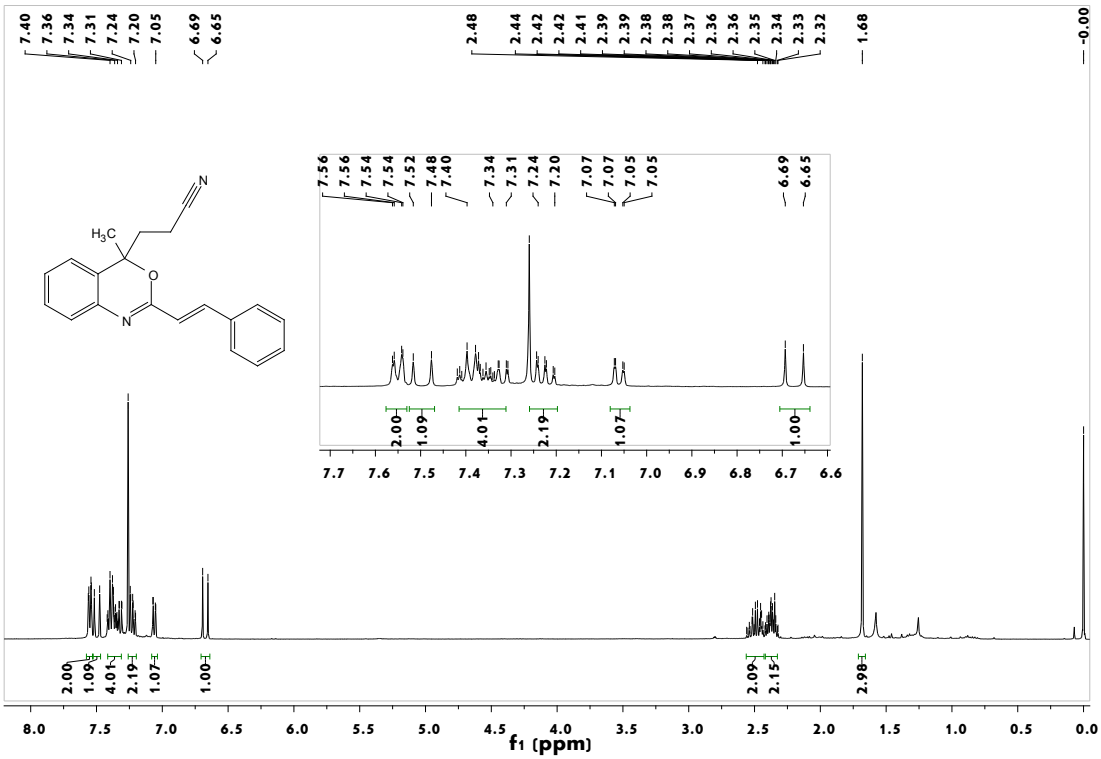

156.14
142.07
139.82
129.85
128.68
126.32
124.08
119.48
82.79
77.55
77.23
76.91
36.50
13.17
N
O
N
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

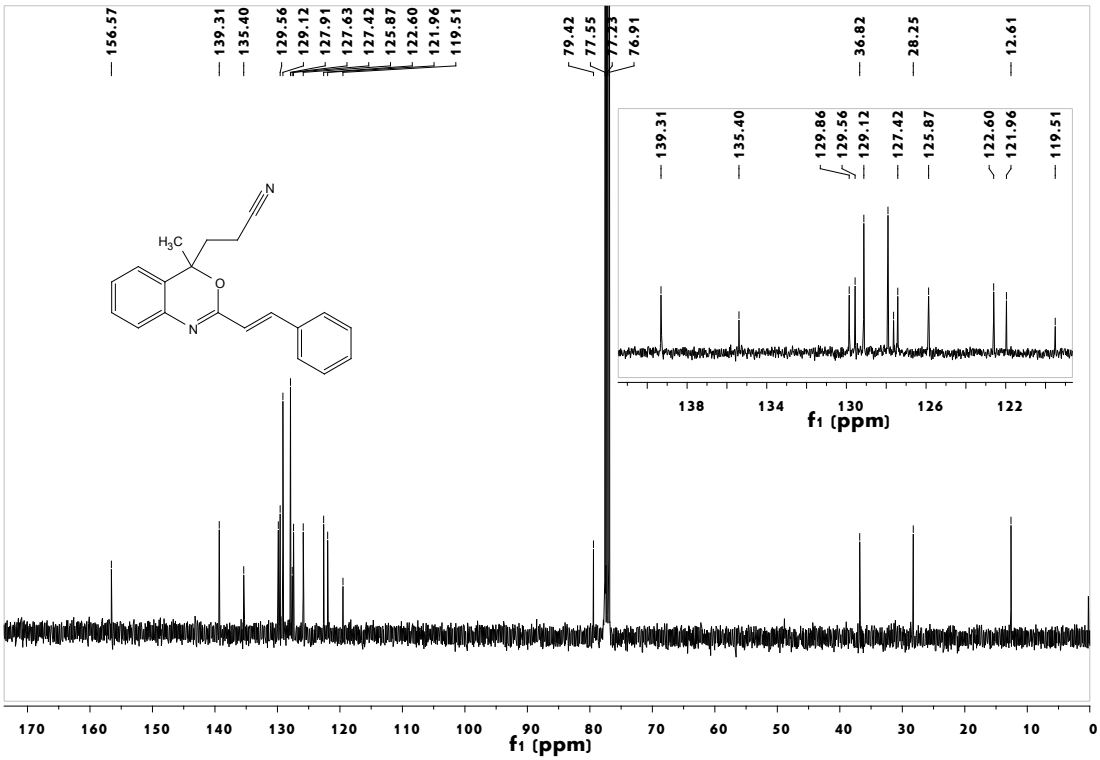

7.32 7.32 7.30 7.30 7.28 7.28 7.22 7.22 7.21 7.20 7.19 7.18 7.17 7.16 7.15 7.15 7.02 7.02 7.00 7.00
2.43 2.41 2.40 2.39 2.36 2.36 2.34 2.34 2.33 2.33 2.32 2.30 2.29 2.28 2.27 2.26 2.26 2.24 2.15
1.64
0.02
N
H3C
O
N
CH3
1.00 1.98 0.92 2.10 2.04 2.85 3.00
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


159.61
138.46
129.45
127.08
126.59
125.13
122.61
119.44
79.51
77.55
77.23
76.91
37.21
28.80
21.95
12.54
N
H3C
O
N
CH3
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.26
7.20
7.18
7.17
6.99
6.98
6.97
2.43
2.43
2.42
2.41
2.39
2.39
2.38
2.36
2.35
2.32
2.32
2.30
2.29
2.28
2.28
1.54
1.26
-0.00
N
H3C
O
N
CH3
CH3
CH3
1.02
1.95
1.00
1.97
1.99
2.95
8.98
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 0.5 0.0
f1 (ppm)


167.15
139.05
129.27
126.97
126.94
125.79
122.31
119.61
78.68
77.55
77.23
76.91
37.48
36.39
28.28
27.61
12.58
f1 (ppm)


7.40
7.36
7.34
7.31
7.24
7.20
7.05
6.69
6.65
2.48
2.44
2.42
2.42
2.41
2.39
2.39
2.38
2.38
2.37
2.36
2.36
2.35
2.34
2.33
2.32
1.68
-0.00
f1 (ppm)


156.57
139.31
135.40
129.56
129.12
127.91
127.63
127.42
125.87
122.60
121.96
119.51
79.42
77.55
77.23
76.91
36.82
28.25
12.61
N
H3C
O
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
139.31
135.40
129.86
129.56
129.12
127.42
125.87
122.60
121.96
119.51
138 134 130 126 122
f1 (ppm)