Efficient synthesis of oxazoles by dirhodium(II)-catalyzed reactions of styryl diazoacetate with oximes

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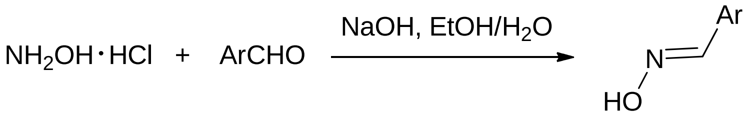
Supporting Information

General Information

All reactions, unless noted, were carried out under an inert atmosphere of dried nitrogen in flame-dried or oven-dried glassware with magnetic stirring. Analytical thin layer chromatography (TLC) was performed on Dynamic Adsorbents precoated (0.25 mm thickness) silica gel plates with F_{254} indicator. Visualization was accomplished by UV light (254 nm). Flash chromatography was performed with silica gel (32-63 μm) supplied by Dynamic Adsorbents. ^{1}H NMR spectra were recorded on a Bruker DRX-400 (400 MHz) spectrometer, and chemical shifts were reported in ppm. The peak information was described as: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite; coupling constant(s) in Hz. ^{13}C NMR spectra were recorded on a Bruker DRX-400 (100 MHz) spectrometer with complete proton decoupling. High-resolution mass spectra (HRMS) were performed on JEOL AccuTOF-CS mass spectrometer using CsI as the standard. Styryl diazoacetate **1**[1] and oximes **2**[2] were prepared according to the literature procedures. Solvents were dried with 3 Å MS before use. All the other chemicals and Lewis acid were obtained from commercial sources and used without further purification.

General Procedure for the Preparation of Oximes 2.[2]



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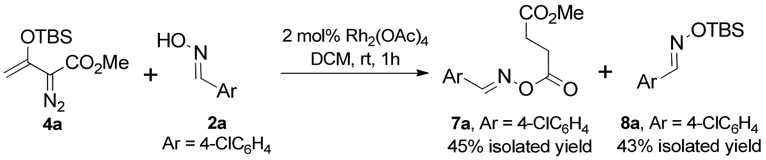
To a 100-mL oven-dried round-bottomed flask containing a magnetic stirring bar, hydroxylamine hydrochloride (0.77 g, 11 mmol), and aldehyde (10 mmol) in ethanol/H_2O (25/25 mL), was added NaOH (11 mmol) at 0 °C. The reaction mixture was stirred for 3-12 hours under these conditions. After complete consumption of aldehyde, monitored by thin layer chromatography (TLC), the reaction mixture was diluted with ether (50 mL), and the organic phase was washed with aqueous sodium bicarbonate (50 mL) and brine (50 mL X 2), and the organic layer was dried ($MgSO_4$). After filtering the salt, the solvent was removed under reduced pressure, and the residue was further purified by recrystallization in ether and hexanes or by column chromatography (eluent: hexanes:EtOAc = 90:10) to give pure oximes.

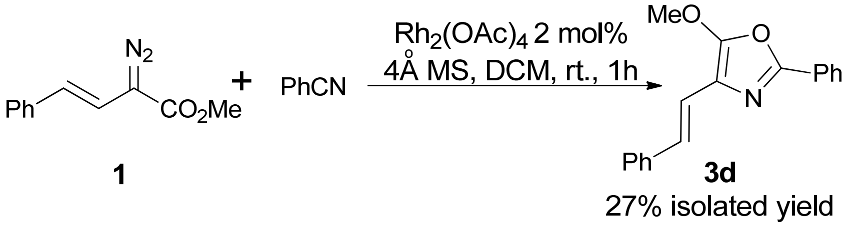
General Procedure for the dirhodium(II) catalyzed reaction of enoldiazoacetates 4a with oxime 2a.



To an oven-dried flask containing a magnetic stirring bar, oxime **2a** (0.5 mmol), and rhodium catalyst (2.0 mol%) in the DCM (1.5 mL), was added enodiazoacetate **4a** (0.6 mmol) in DCM (1.5 mL) over 1 h via a syringe pump at room temperature. The reaction mixture was stirred for another hour under these conditions then purified by column chromatography on silica gel (eluent: hexanes:EtOAc = 100:0 to 90:10) to give the succinate derivative **7a** and TBS-substituted oxime **8a**.[3]

(7a): 45% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.35 (s, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 3.74 (s, 3H), 2.86-2.75 (comp, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): 172.68, 170.29, 155.22, 138.13, 129.80, 129.52, 128.74, 52.24, 28.95, 28.02. HRMS (ESI) calculated for $C_{12}H_{13}ClNO_4$ $[M+H]^+$: 270.0528; found: 270.0526. The pure product was recrystallized in DCM, EtOAc and hexanes, and the generated single-crystal was suitable for X-ray analysis, see S-26.

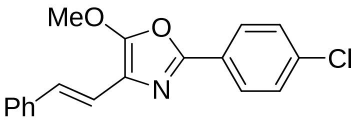
Procedure for oxazole synthesis with styryl diazoacetate 1 and benzonitrile.



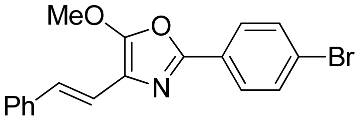
To an oven-dried flask containing a magnetic stirring bar, benzonitrile (1.0 mmol), 4 Å molecular sieves (100 mg) and rhodium catalyst (2.0 mol%) in DCM (2.0 mL), was added styryl diazoacetate **1** (1.2 mmol) in DCM (1.5 mL) over 1 h via a syringe pump at room temperature. The reaction mixture was stirred for another hour under these conditions then purified by column chromatography on silica gel (eluent: hexanes:EtOAc = 100:0 to 90:10) to give oxazole **3d** in 27% yield.

General procedure for the oxazoles synhtesis.

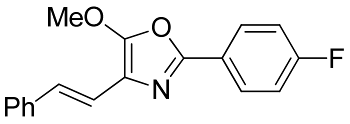
To an oven-dried flask containing a magnetic stirring bar, oximes **2** (0.5 mmol), 4 Å molecular sieves (100 mg) and rhodium catalyst (2.0 mol%) in DCM (1.5 mL) was added styryl diazoacetate **1** (0.6 mmol) in DCM (1.0 mL) over 1 h via a syringe pump at room temperature. The reaction mixture was stirred for another hour under these conditions then purified by column chromatography on silica gel (eluent: hexanes:EtOAc = 100:0 to 90:10) to give oxazoles **3**.



(*E*)-2-(4-Chlorophenyl)-5-methoxy-4-styryloxazole (3a). 82% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.95 (d, *J* = 8.0 Hz, 2H), 7.53-7.25 (comp, 5H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 16.0 Hz, 1H), 6.93 (d, *J* = 16.0 Hz, 1H), 4.15 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 155.44, 151.64, 137.66, 136.07, 129.24, 128.83, 127.90, 127.48, 127.10, 126.45, 126.06, 116.51, 115.95, 60.73. HRMS (ESI) calculated for $C_{18}H_{15}ClNO_2$ [M+H]$^+$: 312.0786; found: 312.0771.

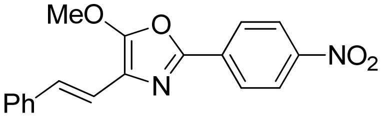


(*E*)-2-(4-Bromophenyl)-5-methoxy-4-styryloxazole (3b). 89% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.88 (d, *J* = 8.7 Hz, 2H), 7.61 (d, *J* = 8.7 Hz, 2H), 7.53 (d, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 16.0 Hz, 1H), 6.93 (d, *J* = 16.0 Hz, 1H), 4.15 (s, 1H).; ^{13}C NMR ($CDCl_3$, 100 MHz): 155.46, 151.69, 137.65, 132.19, 128.84, 127.93, 127.49, 127.30, 126.49, 126.46, 124.40, 116.55, 115.94, 60.7. HRMS (ESI) calculated for $C_{18}H_{15}BrNO_2$ [M+H]$^+$356.0281; found: 356.0273. The pure product was recrystallized in DCM, EtOAc, and hexanes, and the generated single-crystal was suitable for X-ray analysis, see S-27.

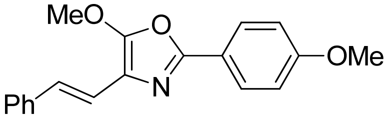


(*E*)-2-(4-Fluorophenyl)-5-methoxy-4-styryloxazole (3c). 71% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.01 (m, 2H), 7.55-7.26 (comp, 5H), 7.23 (d, *J* = 16.0 Hz, 1H), 7.17 (t, *J* = 8.8 Hz, 2H), 6.93 (d, *J* = 16.0 Hz, 1H), 4.13 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 163.95 (d, *J* = 250.0 Hz), 155.38, 151.84, 137.69, 128.82, 127.93 (d, *J* = 8.5

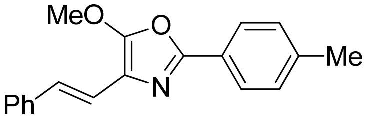
Hz), 127.76, 127.43, 126.43, 123.95 (d, *J* = 3.2 Hz), 116.37, 116.22, 116.01 (d, *J* = 2.1 Hz), 60.76. HRMS (ESI) calculated for $C_{18}H_{15}FNO_2$ $[M+H]^+$: 296.1081; found: 296.1099.



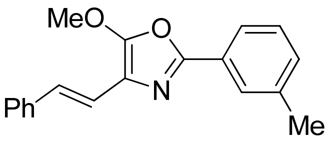
(*E*)-5-Methoxy-2-(4-nitrophenyl)-4-styryloxazole (3d). 91% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.34 (d, *J* = 9.0 Hz, 2H), 8.15 (d, *J* = 9.0 Hz, 2H), 7.54 (d, *J* = 8.0, Hz, 2H), 7.38-7.29 (comp, 3H), 7.25 (d, *J* = 16.0 Hz, 1H), 6.93 (d, *J* = 16.0 Hz, 1H), 4.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 156.20, 150.15, 148.33, 137.44, 132.93, 128.91, 128.69, 127.75, 126.55, 126.27, 124.46, 117.44, 115.58, 60.64. HRMS (ESI) calculated for $C_{18}H_{15}N_2O_4$ $[M+H]^+$: 323.1026; found: 323.1022.

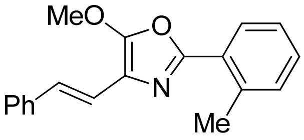


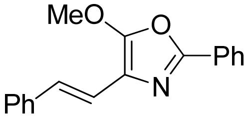
(*E*)-5-Methoxy-2-(4-methoxyphenyl)-4-styryloxazole (3e). 67% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.95 (d, *J* = 9.0 Hz, 2H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.430-7.24 (comp, 3H), 7.21 (d, *J* = 16.0 Hz, 1H), 6.99 (d, *J* = 9.0 Hz, 2H), 6.93 (d, *J* = 16.0 Hz, 1H), 4.13 (s, 3H), 3.89 (s, 3H).); ^{13}C NMR ($CDCl_3$, 100 MHz): 161.27, 155.17, 152.92, 137.86, 128.82, 127.60, 127.46, 127.34, 126.43, 120.44, 116.25, 116.19, 114.39, 60.88, 55.62. HRMS (ESI) calculated for $C_{19}H_{18}NO_3$ $[M+H]^+$: 308.1281; found: 308.1288.

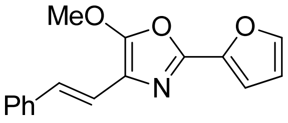


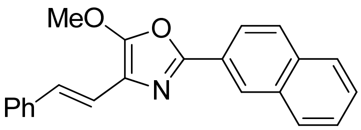
(*E*)-5-Methoxy-4-styryl-2-(*p*-tolyl)oxazole (3f). 77% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.91 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.32-7.24 (comp, 3H), 7.22 (d, *J* = 16.0 Hz, 1H), 6.94 (d, *J* = 16.0 Hz, 1H), 4.15 (s, 3H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 155.20, 152.86, 140.29, 137.80, 129.61, 128.78, 127.47, 127.31, 126.38, 125.83, 124.86, 116.21, 116.12, 60.66, 21.68. HRMS (ESI) calculated for $C_{19}H_{18}NO_2$ $[M+H]^+$: 292.1332; found: 292.1310.


(*E*)-5-Methoxy-4-styryl-2-(*m*-tolyl)oxazole (3g). 71% isolated yield. ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.86 (s, 1H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 7.2 Hz, 2H), 7.43-7.19 (comp, 6H), 6.95 (d, *J* = 16.0 Hz, 1H), 4.15 (s, 3H), 2.45 (s, 4H); ^{13}C NMR (CDCl$_3$, 100 MHz): 155.35, 152.81, 138.72, 137.80, 130.94, 128.85, 128.81, 127.62, 127.46, 127.37, 126.43, 123.05, 116.25, 116.20, 60.70, 21.59. HRMS (ESI) calculated for $C_{19}H_{18}NO_2$ [M+H]$^+$: 292.1332; found: 292.1311.


(*E*)-5-Methoxy-4-styryl-2-(*o*-tolyl)oxazole (3h). 68% isolated yield. ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.99-7.24 (comp, 10H), 6.99 (d, *J* = 16.0 Hz, 1H), 4.15 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz): 155.16, 152.89, 137.85, 137.26, 131.81, 129.69, 128.79, 128.40, 127.45, 127.30, 126.51, 126.40, 126.10, 116.35, 115.78, 60.44, 22.17. HRMS (ESI) calculated for $C_{19}H_{18}NO_2$ [M+H]$^+$: 292.1332; found: 292.1307.

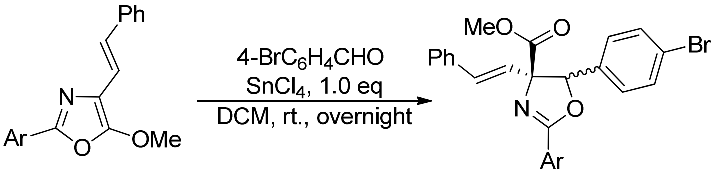

(*E*)-5-Methoxy-2-phenyl-4-styryloxazole (3i). 83% isolated yield. ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 8.04 (d, *J* = 8.0 Hz, 1H), 7.76-7.18 (comp, 9H), 6.96 (d, *J* = 16.0 Hz, 1H), 4.16 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): 155.40, 152.61, 137.78, 130.09, 128.94, 128.82, 127.69, 127.59, 127.39, 126.44, 125.88, 116.32, 116.17, 60.71. HRMS (ESI) calculated for $C_{18}H_{16}NO_2$ [M+H]$^+$: 278.1176; found: 278.1161.


(*E*)-2-(Furan-2-yl)-5-methoxy-4-styryloxazole (3j). 62% isolated yield. ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.69 (d, *J* = 16.0 Hz, 1H), 7.64-7.24 (comp, 7H), 7.06 (d, *J* = 16.0 Hz, 1H), 6.58 (m, 1H), 3.91 (s, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz): 169.43, 162.55, 158.81, 147.26, 145.79, 134.86, 131.15, 129.27, 128.67, 127.33, 120.97, 119.09, 112.61, 53.48. HRMS (ESI) calculated for $C_{16}H_{14}NO_3$ [M+H]$^+$: 268.0968; found: 268.0993.



(*E*)-5-Methoxy-2-(naphthalen-2-yl)-4-styryloxazole (3k). 87% isolated yield. ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 8.49 (s, 1H), 8.25-7.19 (comp, 12H), 6.99 (d, *J* = 16.0 Hz, 1H), 4.21 (s, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz): 155.57, 152.76, 137.80, 134.13, 133.31, 128.85, 128.82, 128.79, 128.11, 127.77, 127.43, 127.26, 126.98, 126.48, 125.49, 124.9, 123.08, 116.55, 116.18, 60.77. HRMS (ESI) calculated for $C_{22}H_{18}NO_2$ [M+H]$^+$: 328.1332; found: 328.1312.

General procedure for the synthesis of 9.

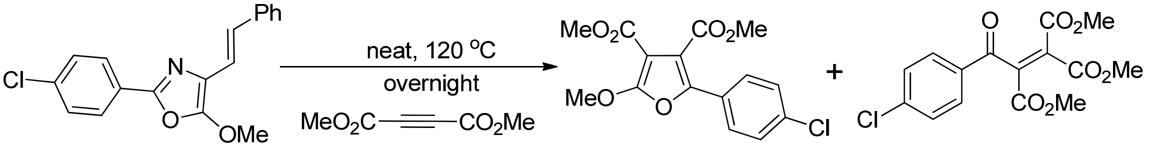


3a, Ar = 4-ClC$_6$H$_4$

9, Ar = 4-ClC$_6$H$_4$
66% isolated yield, *dr* 2:1

To an oven-dried flask containing a magnetic stirring bar, **3a** (0.5 mmol) and 4-bromobenzaldehyde (1.0 mmol) in DCM (2.0 mL), was added SnCl$_4$ (1.0 mL, 1.0 mmol, 1.0 M in DCM) over 30 min at 0 °C. The reaction mixture was warmed to room temperature slowly and stirred overnight under this condition. The reaction was quenched with saturated aqueous NaHCO$_3$ (10 mL) and extracted with DCM (10 mL X 3). The combined organic layer was dried (MgSO$_4$). After filtering the salt, the solvent was removed under reduced pressure, and the residue was subjected to ^{1}H NMR spectroscopic analysis to determine diastereoselectivity. The reaction mixture was purified by column chromatography on silica gel (eluent: hexanes:EtOAc = 90:10 to 80:20) to give pure oxazoline derivative **9** in 66% isolated yield with *dr* 2:1. HRMS (ESI) calculated for $C_{25}H_{20}BrClNO_3$ [M+H]$^+$: 496.0310; found: 496.0307. *cis*-**7**: ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.65 (d, *J* = 8.8 Hz, 2H), 7.56-7.23 (comp, 9H), 7.20 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 16.0 Hz, 1H), 6.83 (d, *J* = 16.0 Hz, 1H), 6.38 (s, 1H), 3.87 (s, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz): 169.63, 168.48, 138.34, 136.26, 135.94, 132.57, 131.92, 130.61, 130.45, 129.36, 129.21, 128.89, 128.66, 127.29, 125.80, 123.84, 109.31, 88.69, 53.41. *trans*-**7**: ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.65 (d, *J* = 8.8 Hz, 2H), 7.58-7.14 (comp, 11H), 6.98 (d, *J* = 16.0 Hz, 1H), 6.69 (d, *J* = 16.0 Hz, 1H), 6.19 (s, 1H), 3.87 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): 169.87, 168.91, 138.33, 136.58, 136.05, 132.66, 132.55, 130.53, 130.41, 129.23, 128.90, 128.65, 128.55, 127.29, 126.05, 123.77, 109.84, 89.21, 53.47.

General procedure for the synthesis of 10.



3a

9

10

72% isolated yield, **9**:**10** = 10:1

5a (0.5 mmol) in dimethyl but-2-ynedioate (2.0 mL) was stirred at 120 °C for 12 h in an oven-dried sealed tube tube containing a magnetic stirring bar; the tube was suited for use under high pressure. Then the reaction mixture was cooled to room temperature, and then purified by column chromatography on silica gel (eluent: hexanes:EtOAc = 90:10 to 70:30) to give furan derivative **9** in 65% yield accompanied by hydrated furan **10** in 7% yield. .

(**9**): 65% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.56 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 4.22 (s, 3H), 3.93 (s, 3H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 165.02, 162.35, 161.04, 141.22, 134.68, 129.20, 127.21, 126.85, 115.65, 92.91, 58.82, 53.02, 51.94. HRMS (ESI) calculated for $C_{15}H_{14}ClO_6$ $[M+H]^+$: 325.0473; found: 325.0459.

(**10**): 7% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.87 (d, *J* = 8.0 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 3.97 (s, 3H), 3.78 (s, 3H), 3.70 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 189.20, 164.08, 162.62, 162.13, 142.17, 140.91, 135.67, 133.87, 130.24, 129.60, 53.89, 53.74, 53.59. HRMS (ESI) calculated for $C_{15}H_{14}ClO_7$ $[M+H]^+$: 341.0423; found: 341.0410.

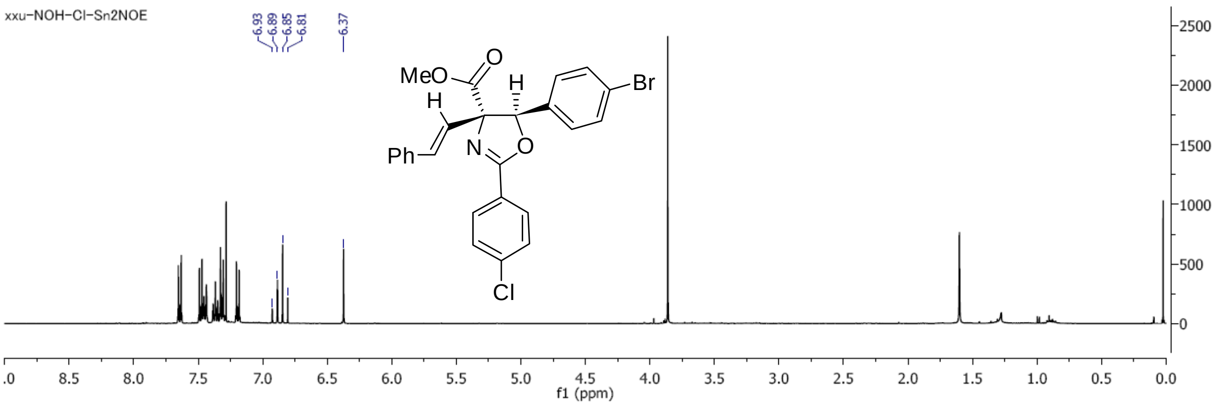
References

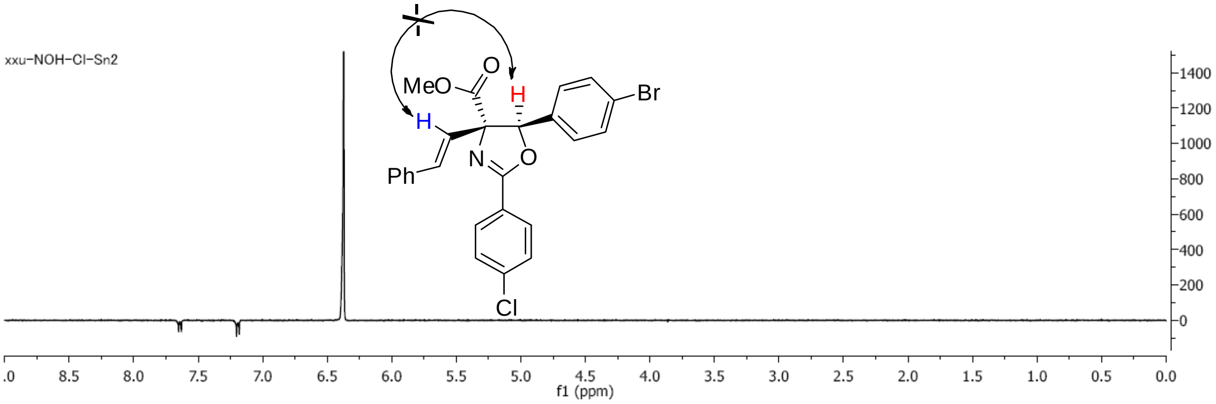
1 a) M. P. Doyle, M. A. McKervey and T. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*, Wiley, New York, NY, 1998; b) J. S. Baum, D. A. Shook, H. M. L. Davies and H. D. Smith, *Synth. Commun.*, 1987, **17**,1709; c) H. M. L. Davies and A. M. Walji, *Angew. Chem. Int. Ed.*, 2005, **44**, 1733; d) M. P. Doyle, M. Yan , W. Hu, L. S. Gronenberg, *J. Am. Chem. Soc.*, 2003, **125**, 4692.

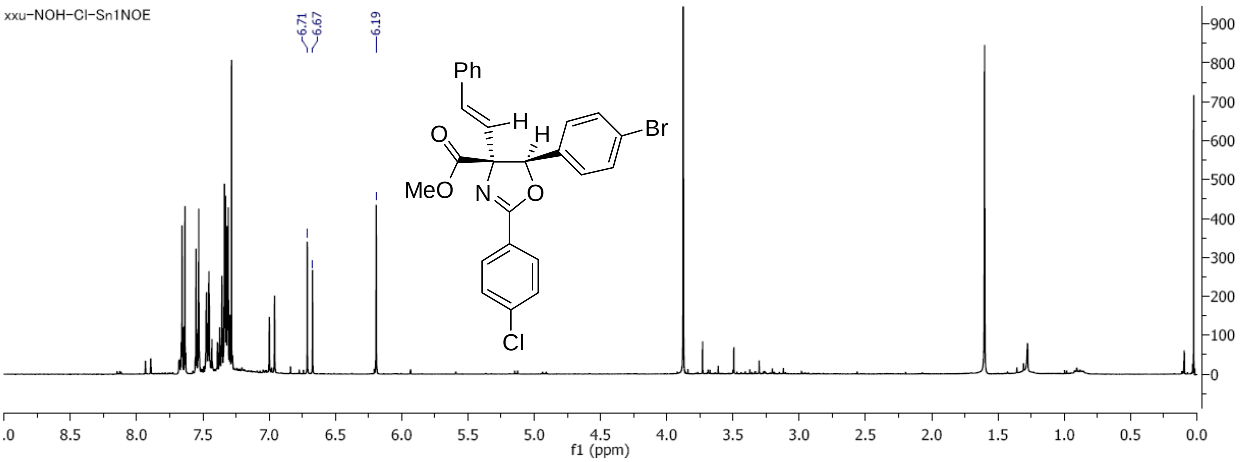
2 a) H. Zheng, R. McDonald and D. G. Hall, *Chem. Eur. J.*, 2010, **16**, 5454; b) G. Zhang, X. Wen, Y. Wang, W. Mo and C. Ding, *J. Org. Chem.*, 2011, **76**, 4665; c) B. C Sanders; F. Friscourt, P. A Ledin, N. E. Mbua, S. Arumugam, J. Guo, T. J. Boltje, V. V. Popik and G. Boons, *J. Am. Chem. Soc.*, 2011, **133**, 949; d) S. H. Yang and S. Chang, *Org. Lett.*, 2001, **3**, 4209; e) A. M. Jawalekar, E. Reubsaet, F. P. J. T. Rutjes and F. L. Delft, *Chem. Commun.*, 2011, **47**, 3198.

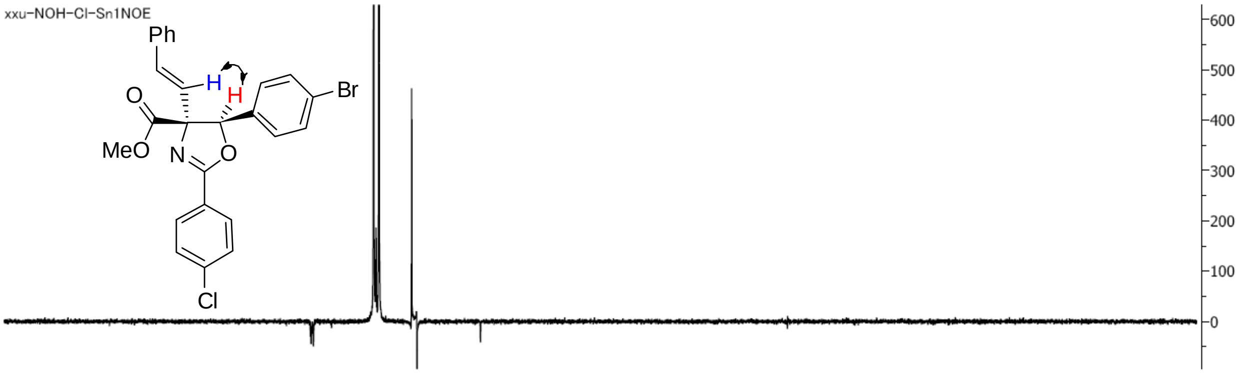
3 For analysis data of **8a** see: X. Xu, D. Shabashov, P. Y. Zavalij and M. P. Doyle, *J. Org. Chem.*, 2012, **77**, 5313.

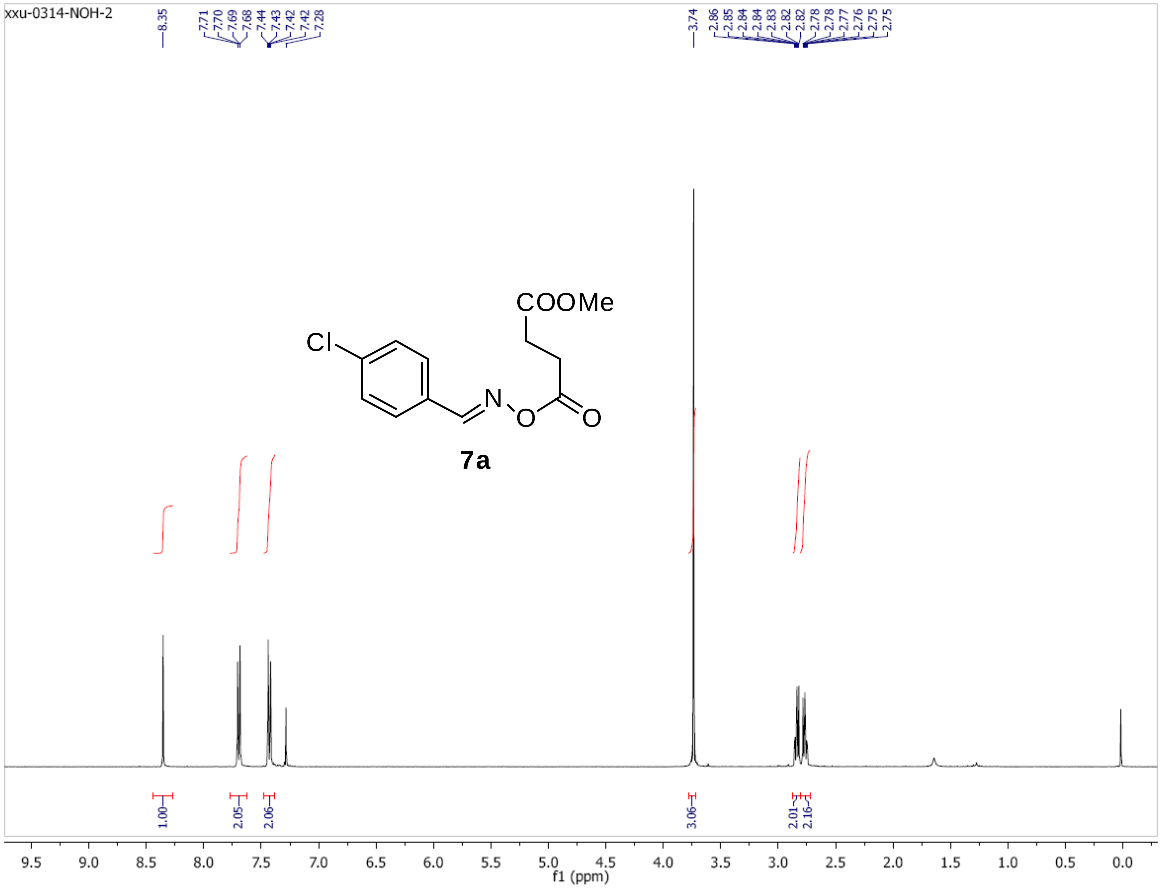
1D-Noe study of 9

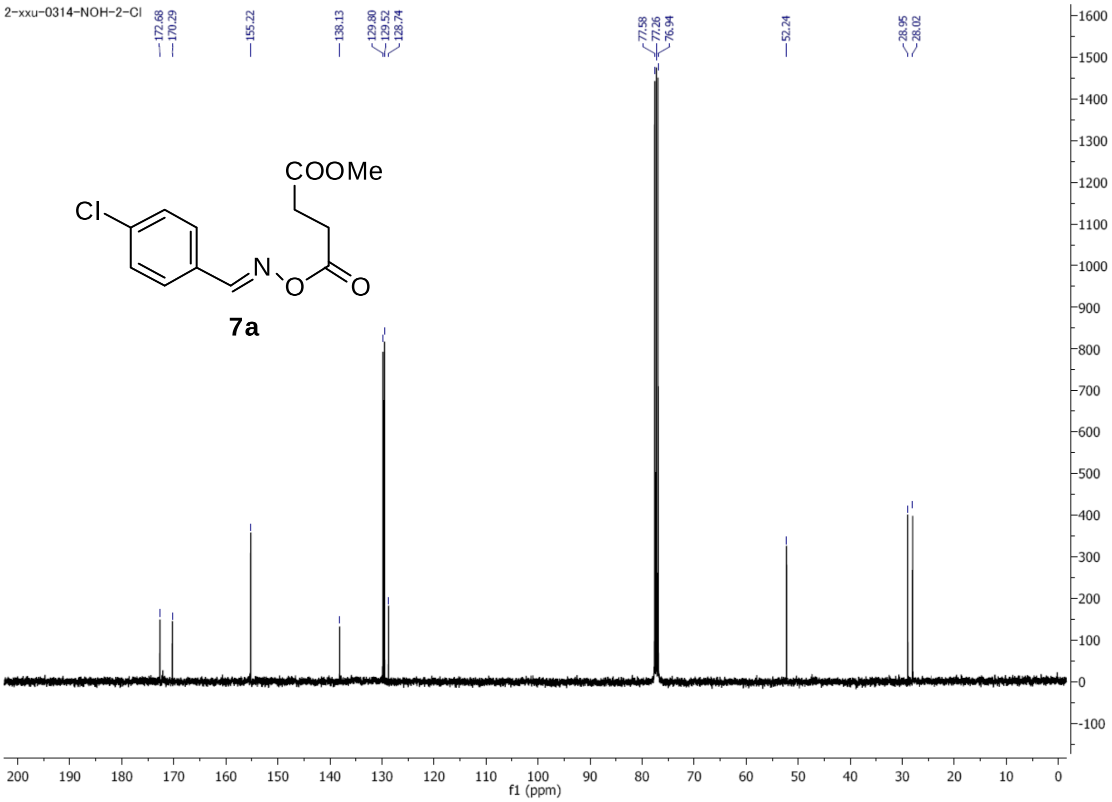


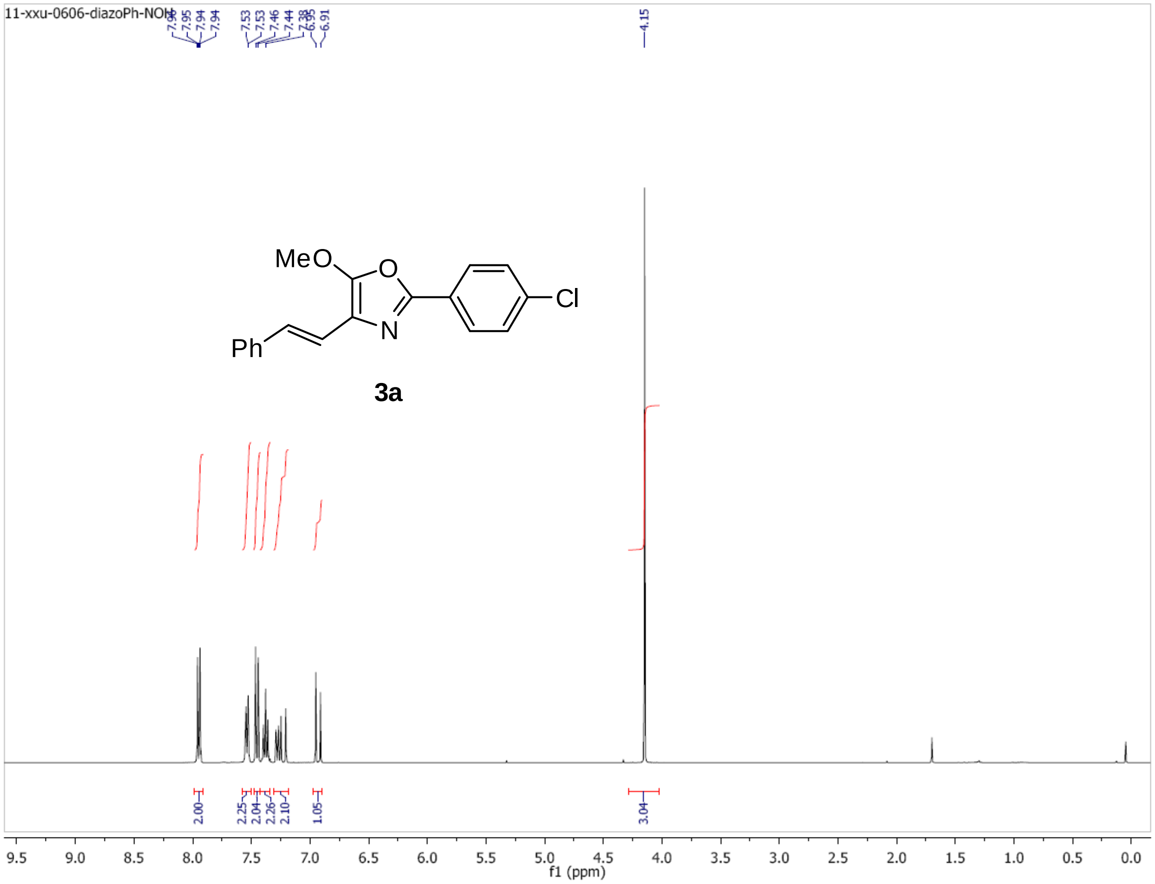


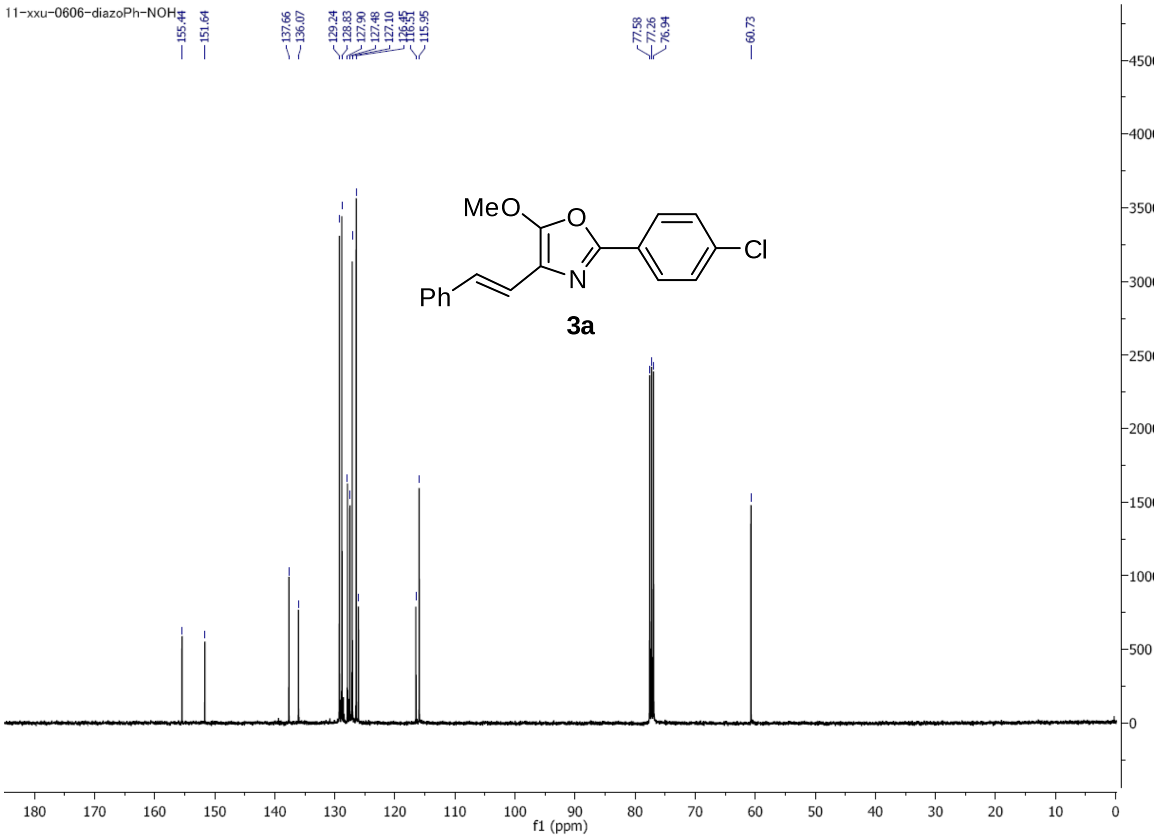


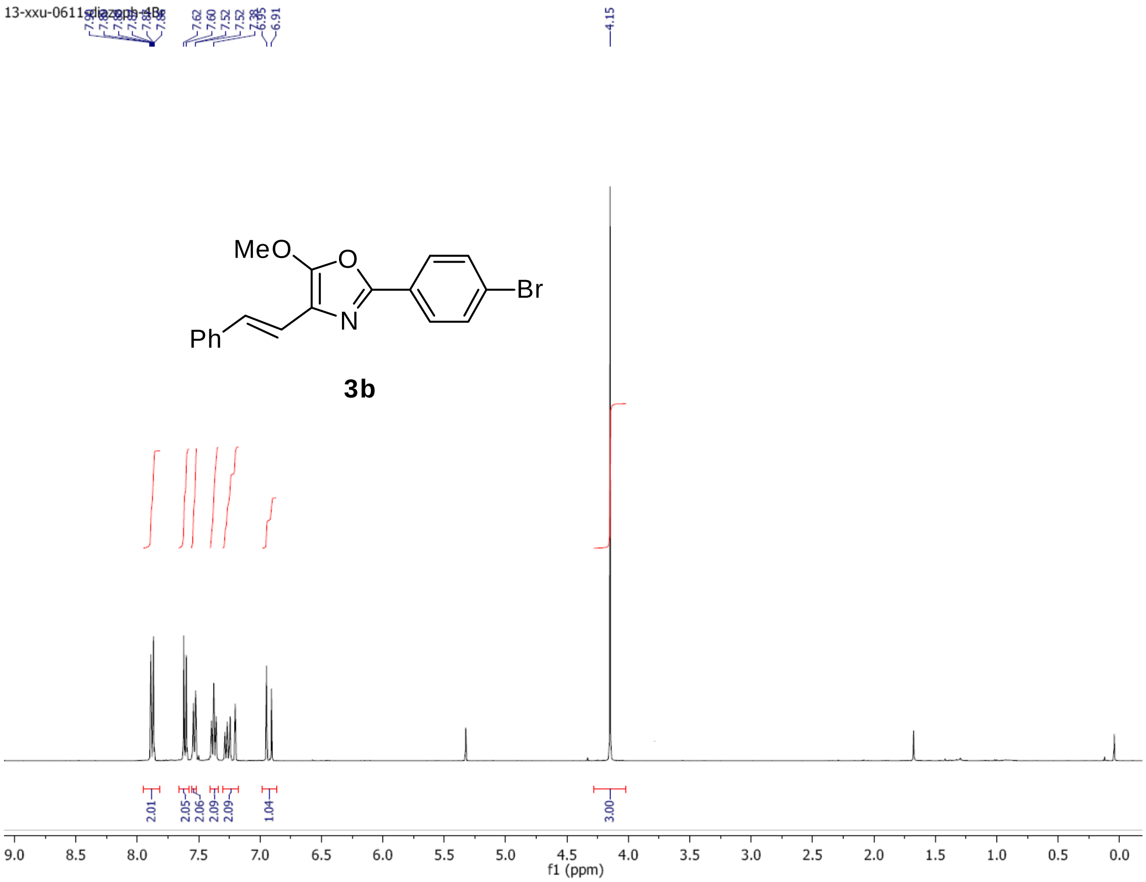


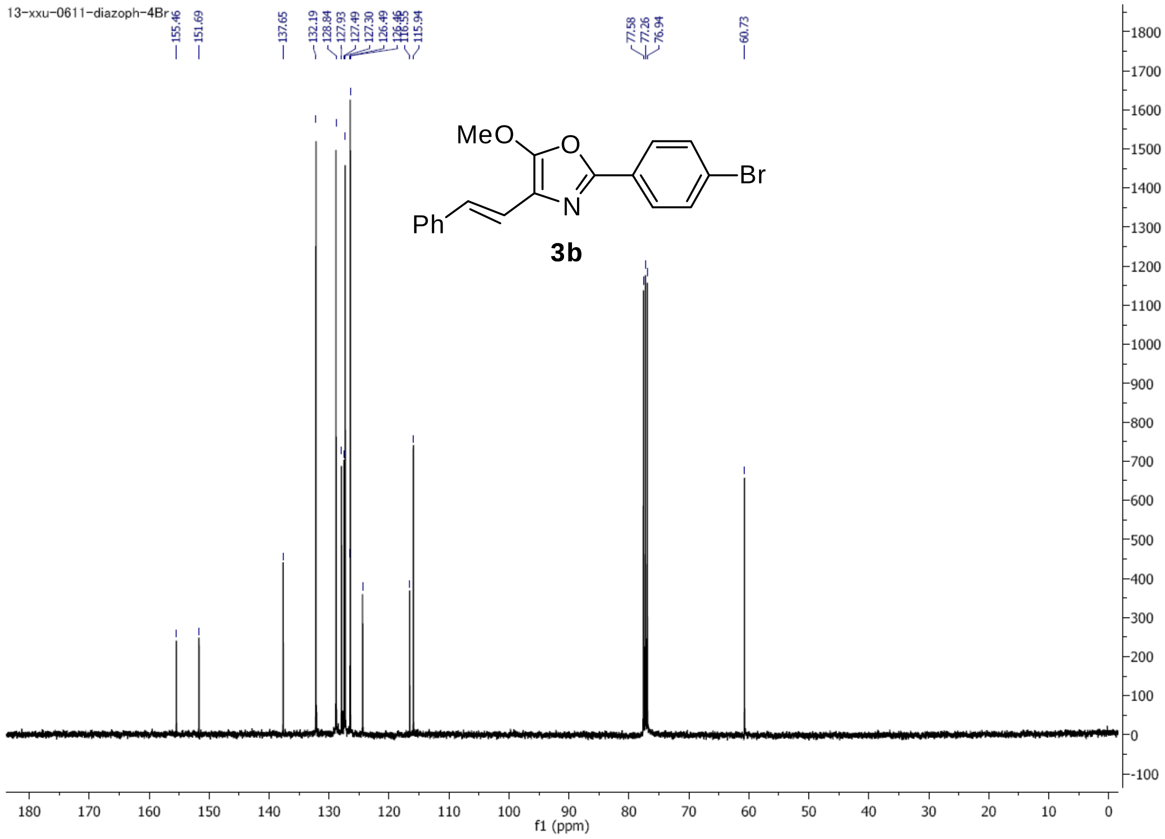

xxu-0314-NOH-2
8.35
7.71
7.70
7.69
7.68
7.44
7.43
7.42
7.42
7.28
3.74
2.86
2.85
2.84
2.84
2.83
2.82
2.82
2.78
2.78
2.77
2.76
2.75
2.75
COOMe
Cl
N
O
O
7a
1.00
2.05
2.06
3.06
2.01
2.16
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

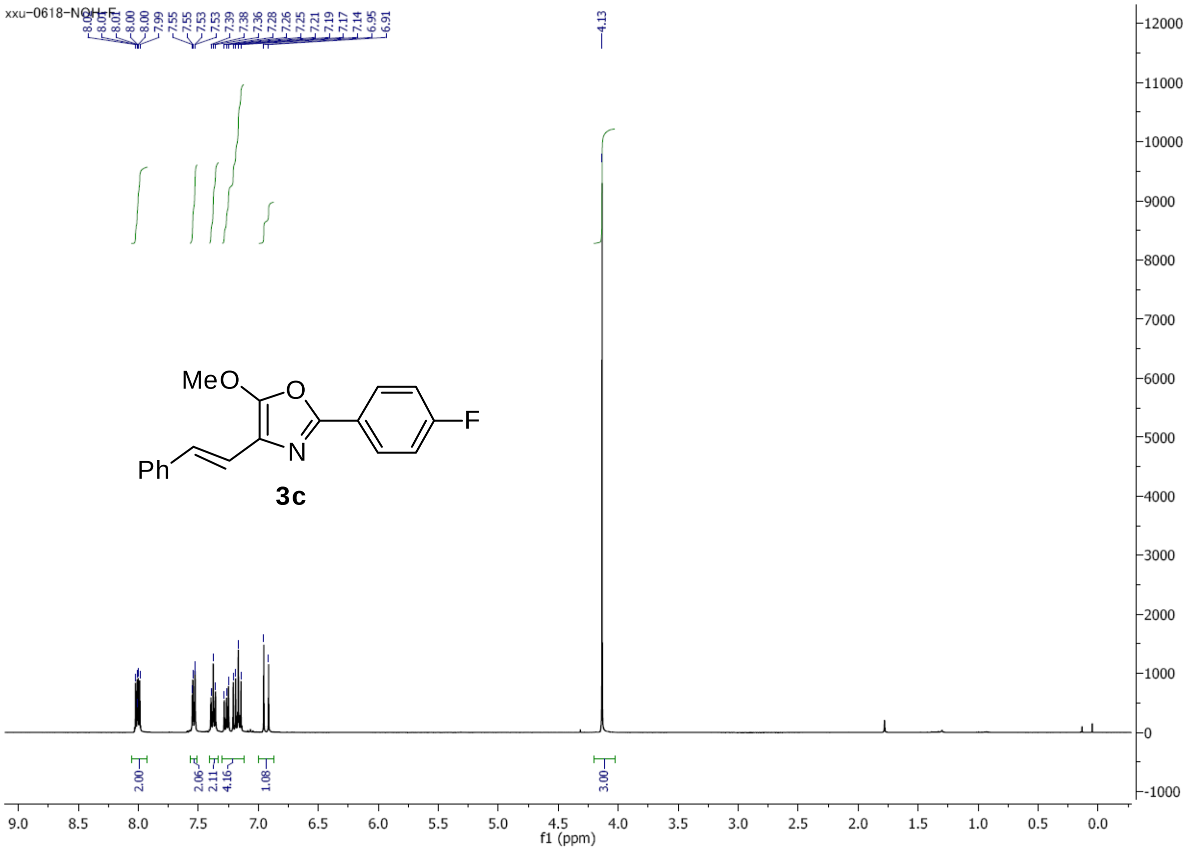

2-xxu-0314-NOH-2-Cl
172.68
170.29
155.22
138.13
129.80
129.52
128.74
77.58
77.26
76.94
52.24
28.95
28.02
COOMe
Cl
N
O
O
7a
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

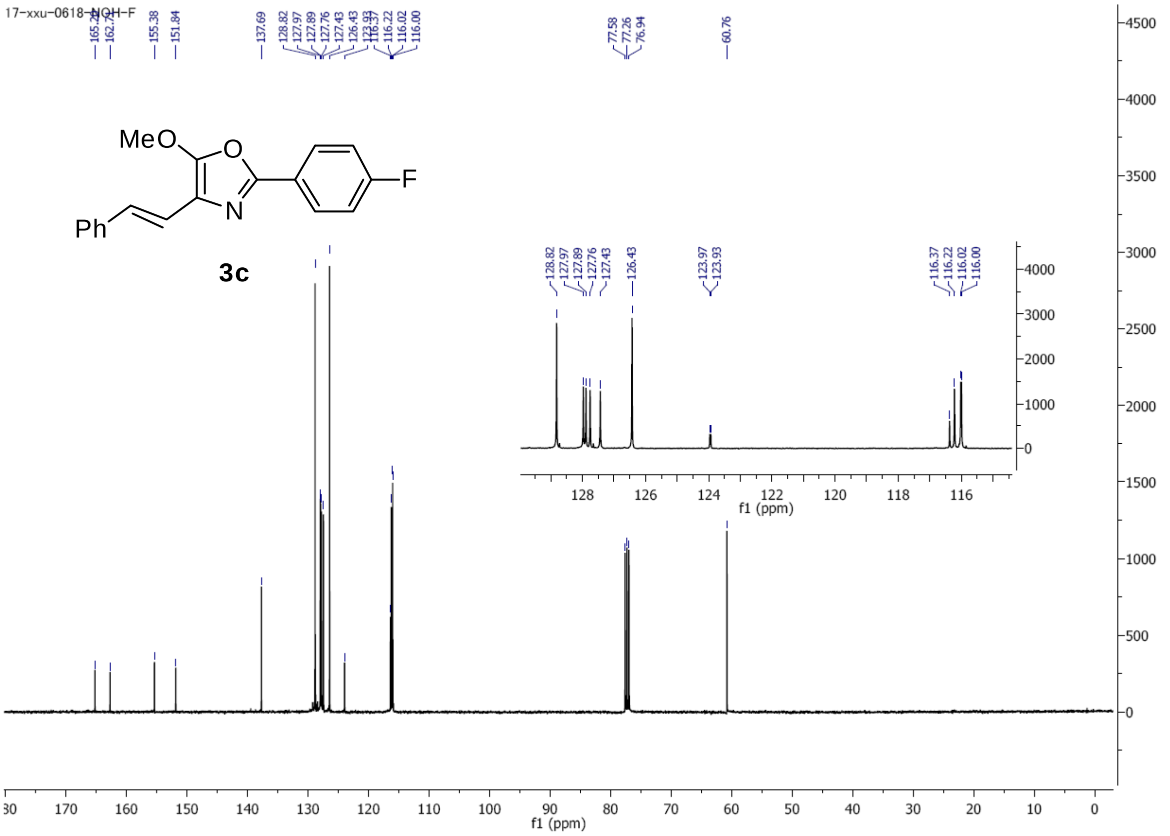

11-xxu-0606-diazoPh-NOH
7.96
7.95
7.94
7.94
7.53
7.53
7.46
7.44
7.38
6.95
6.91
4.15
MeO
O
N
Ph
Cl
3a
2.00
2.25
2.04
2.26
2.10
1.05
3.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

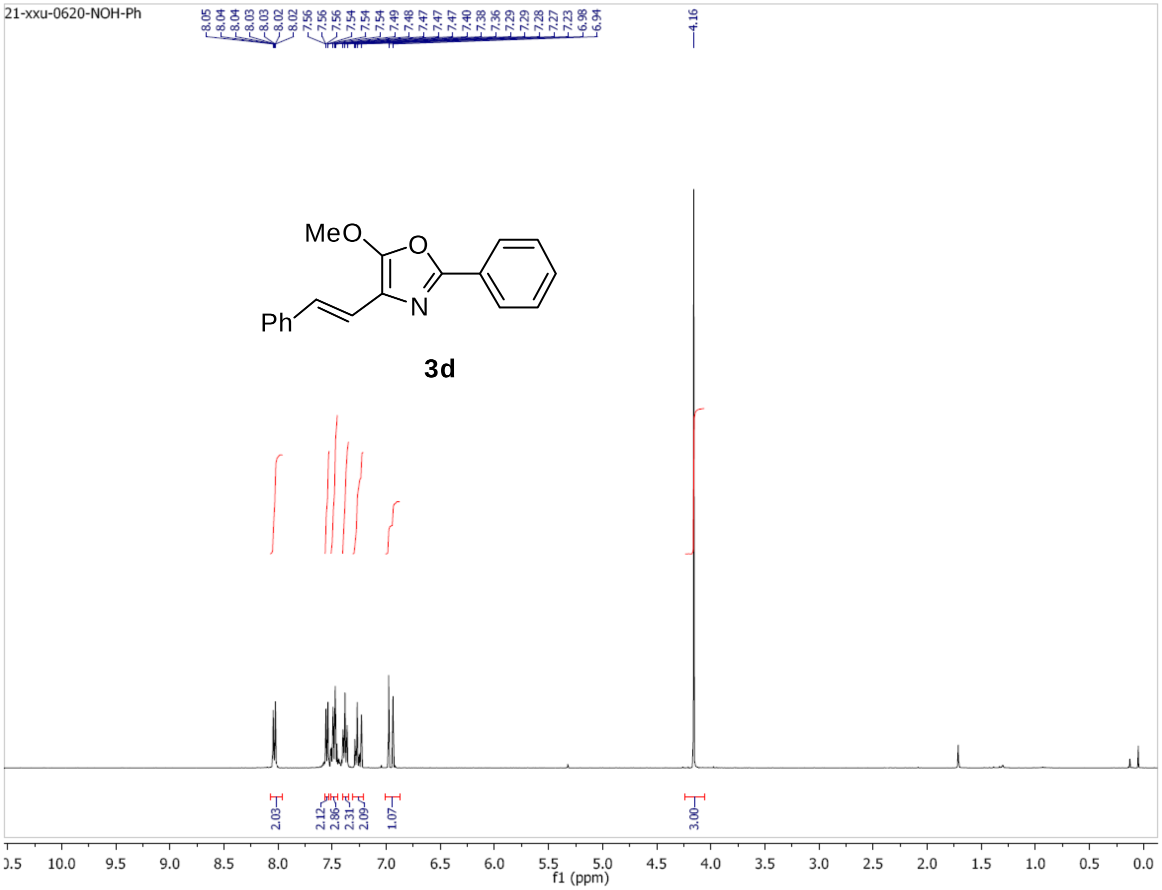

11-xxu-0606-diazoPh-NOH
155.44
151.64
137.66
136.07
129.24
128.83
127.90
127.48
127.10
126.45
116.51
115.95
77.58
77.26
76.94
60.73
MeO
O
N
Ph
Cl
3a
4500
4000
3500
3000
2500
2000
1500
1000
500
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

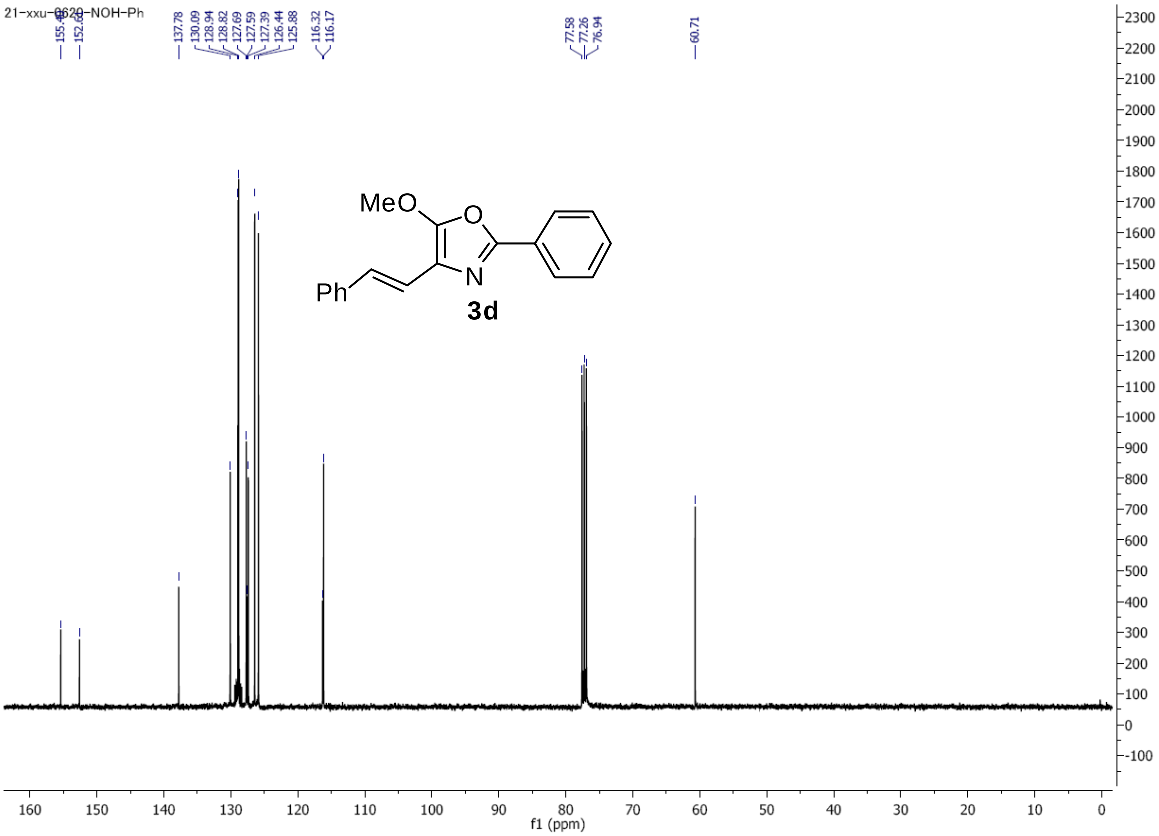

13-xxu-0611-diazoph-4Br
7.62
7.60
7.52
7.52
7.38
6.95
6.91
4.15
MeO
O
N
Br
Ph
3b
2.01
2.05
2.06
2.09
2.09
1.04
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

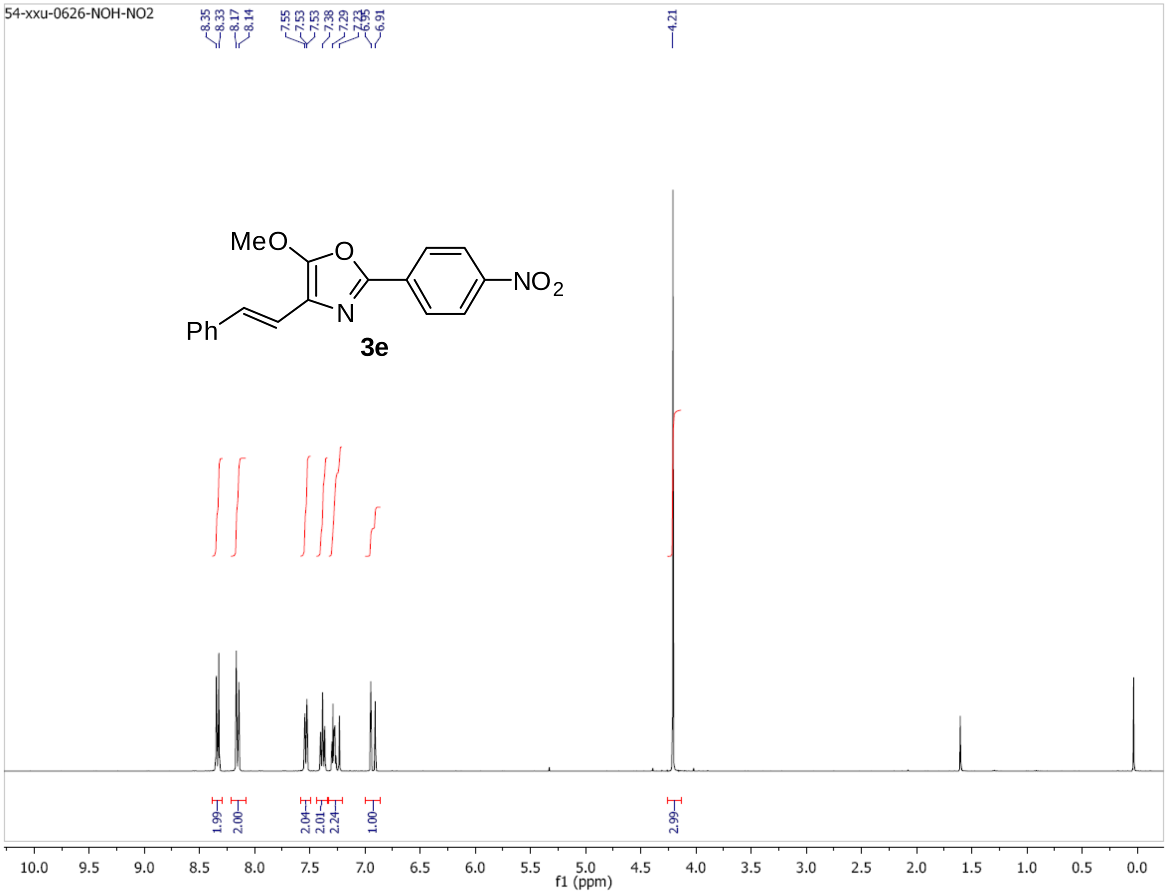

13-xxu-0611-diazoph-4Br
155.46
151.69
137.65
132.19
128.84
127.93
127.49
127.30
126.49
126.46
116.55
115.94
77.58
77.26
76.94
60.73
MeO
O
N
Br
Ph
3b
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

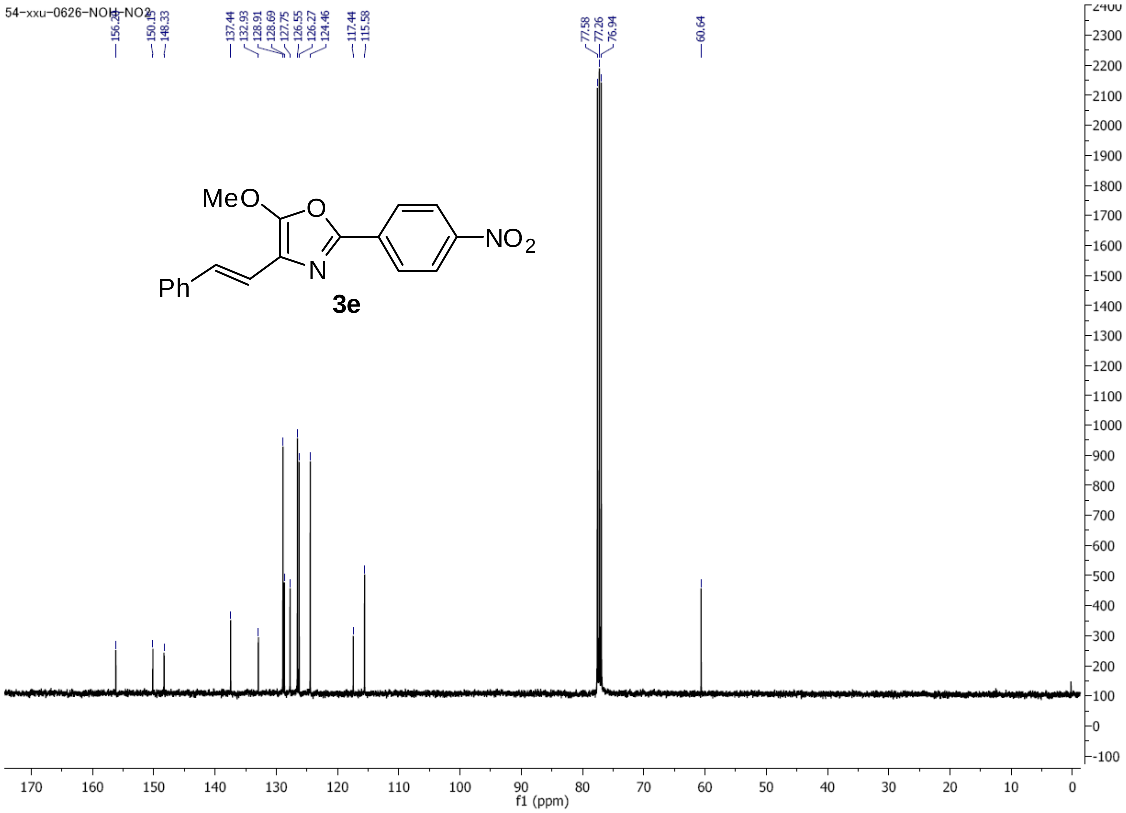

xxu-0618-NOH-F
8.01
8.01
8.00
8.00
7.99
7.55
7.55
7.53
7.53
7.39
7.38
7.36
7.28
7.26
7.25
7.21
7.19
7.17
7.14
6.95
6.91
4.13
MeO
O
N
F
Ph
3c
2.00
2.06
2.11
4.16
1.08
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000

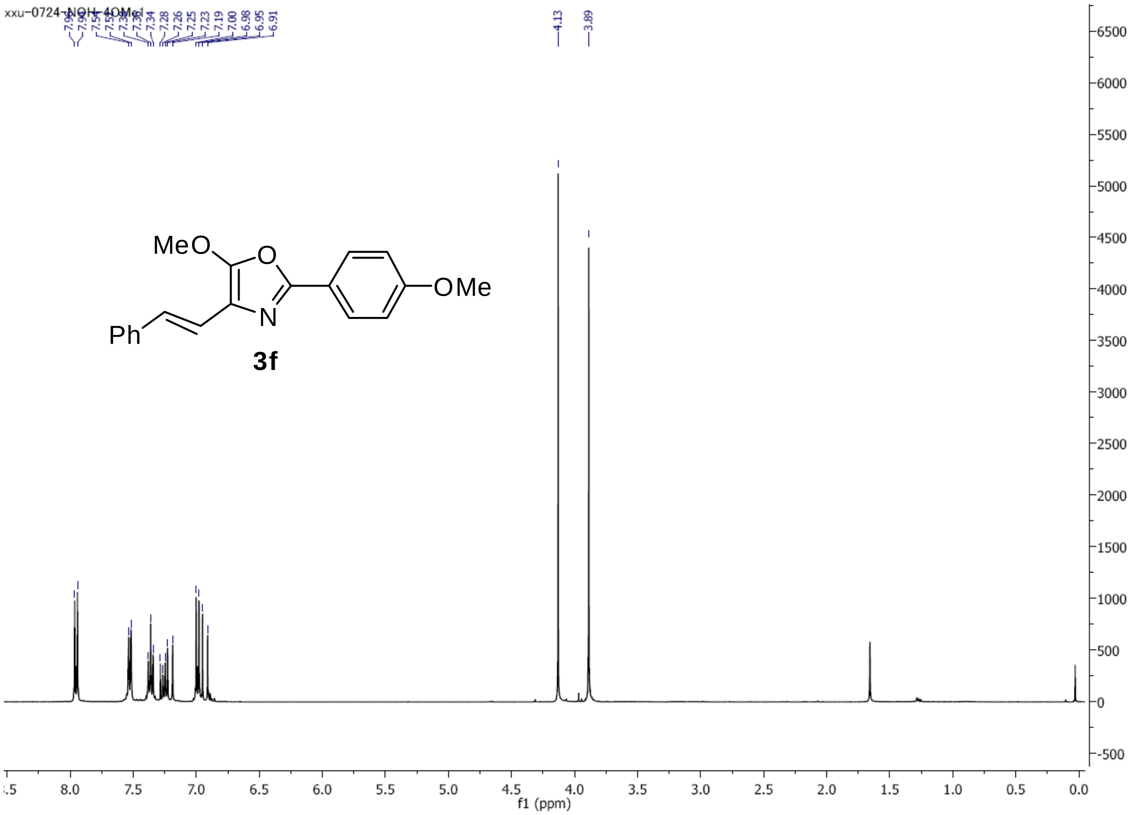

17-xxu-0618-NOH-F
165.2
162.7
155.38
151.84
137.69
128.82
127.97
127.89
127.76
127.43
126.43
123.97
123.93
116.37
116.22
116.02
116.00
77.58
77.26
76.94
60.76
MeO
O
N
F
Ph
3c
128
126
124
122
120
118
116
f1 (ppm)
4000
3000
2000
1000
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
4500
4000
3500
3000
2500
2000
1500
1000
500
0

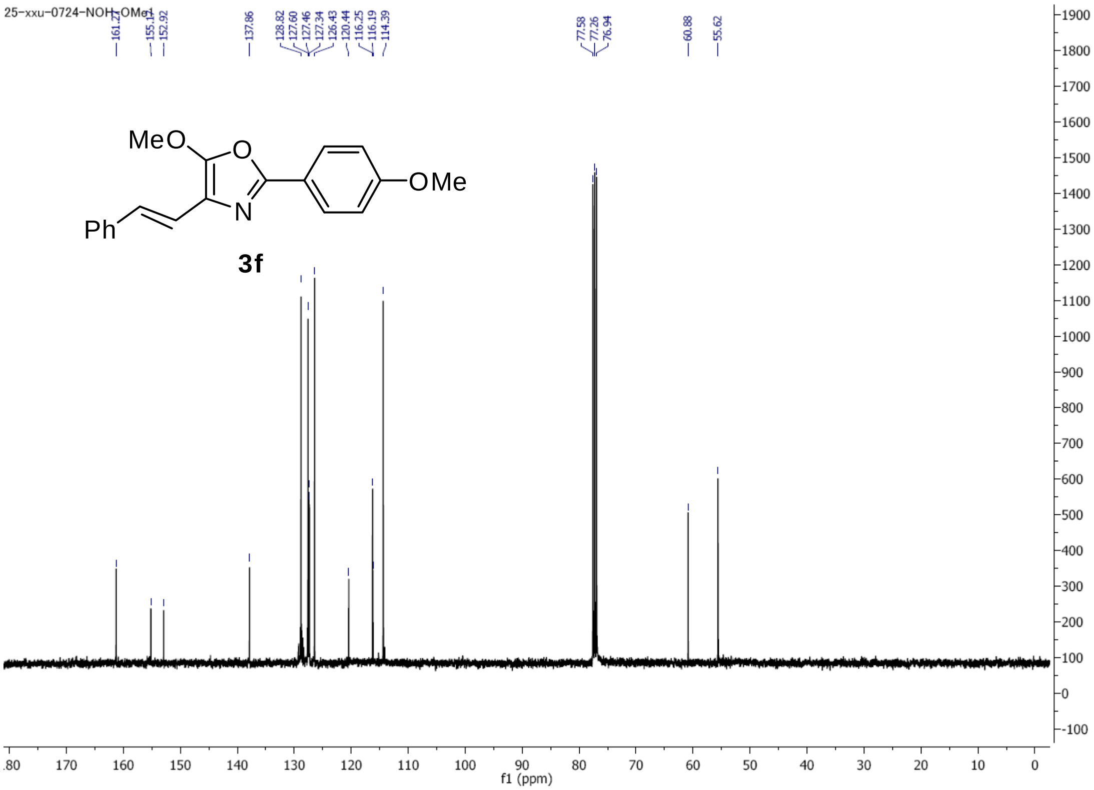

21-xxu-0620-NOH-Ph
8.05
8.04
8.04
8.03
8.03
8.02
8.02
7.56
7.56
7.56
7.54
7.54
7.54
7.49
7.48
7.47
7.47
7.47
7.40
7.38
7.36
7.29
7.29
7.28
7.27
7.23
6.98
6.94
4.16
MeO
O
N
Ph
3d
2.03
2.12
2.86
2.31
2.09
1.07
3.00
0.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

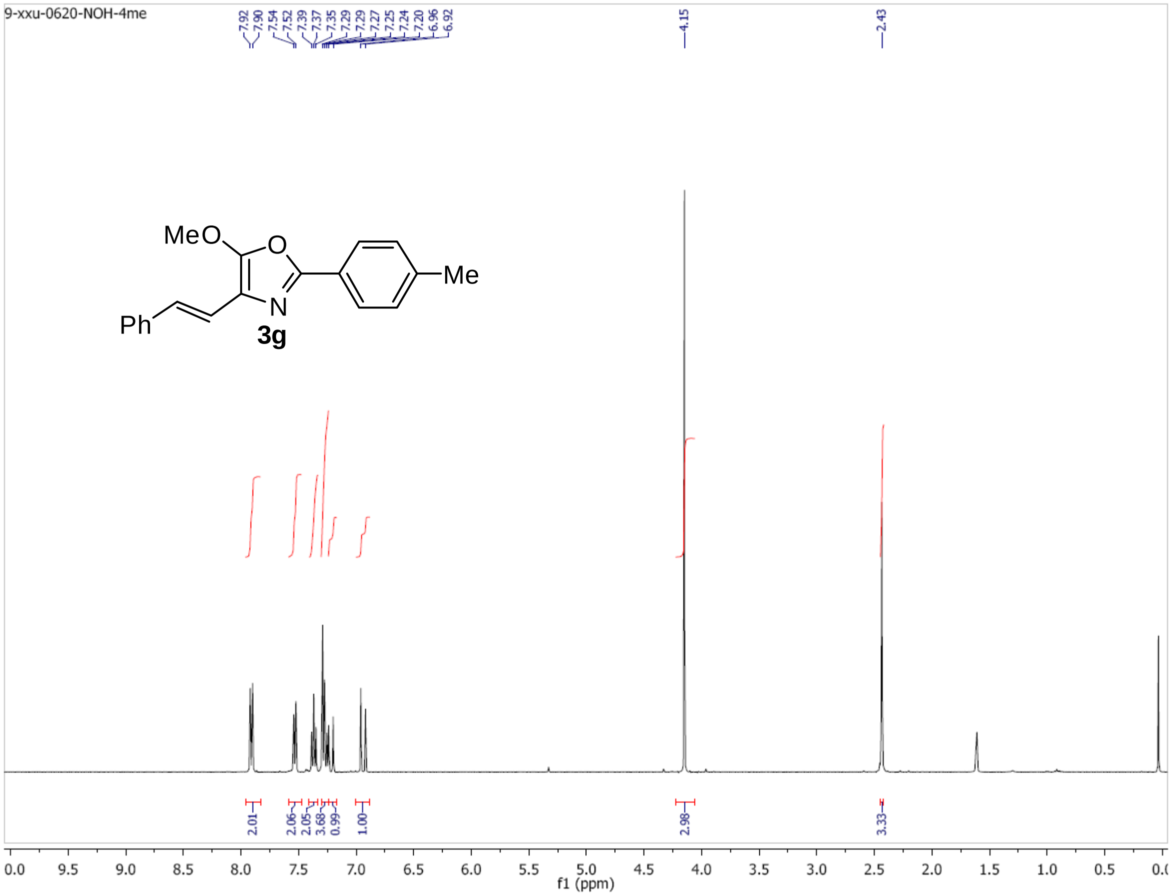

21-xxu-0620-NOH-Ph
155.4
152.6
137.78
130.09
128.94
128.82
127.69
127.59
127.39
126.44
125.88
116.32
116.17
77.58
77.26
76.94
60.71
MeO
O
N
Ph
3d
2300
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

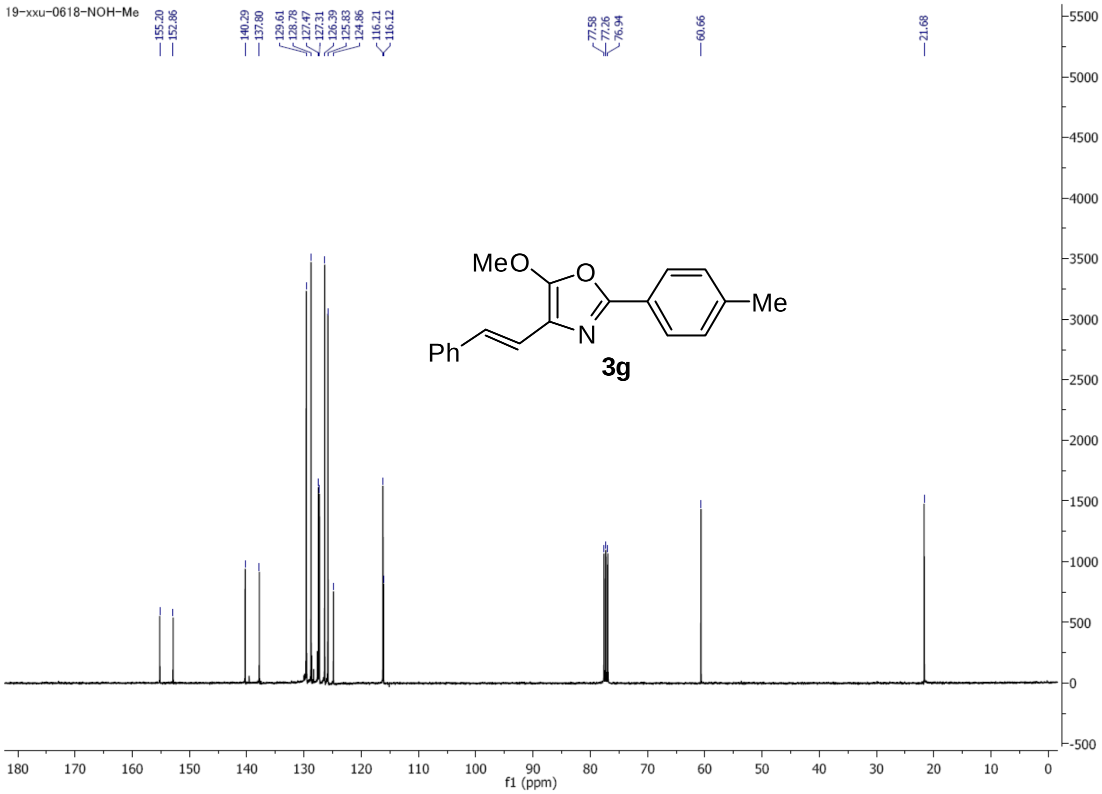

54-xxu-0626-NOH-NO2
8.35
8.33
8.17
8.14
7.55
7.53
7.53
7.38
7.29
7.23
6.95
6.91
4.21
MeO
O
N
NO2
Ph
3e
1.99
2.00
2.04
2.01
2.24
1.00
2.99
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

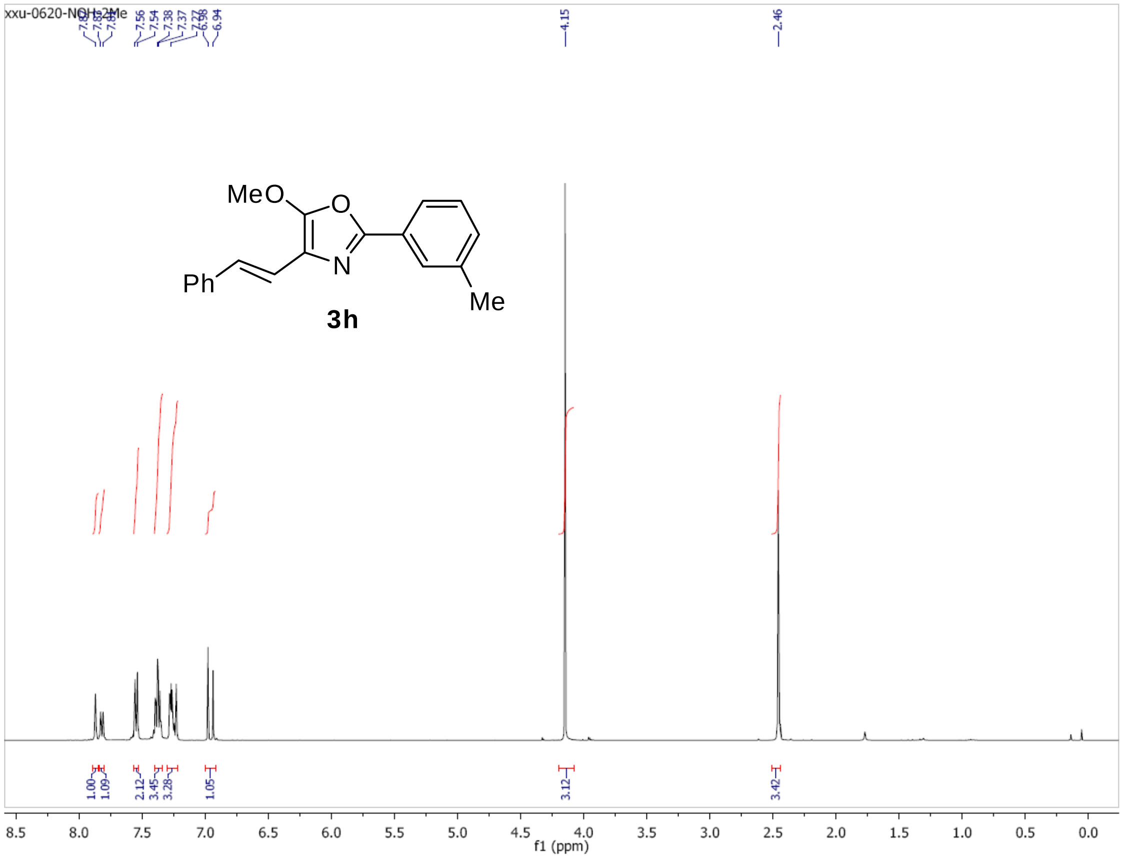

54-xxu-0626-NOH-NO2
156.24
150.19
148.33
137.44
132.93
128.91
128.69
127.75
126.55
126.27
124.46
117.44
115.58
77.58
77.26
76.94
60.64
MeO
O
N
NO2
Ph
3e
2400 2300 2200 2100 2000 1900 1800 1700 1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 -100
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

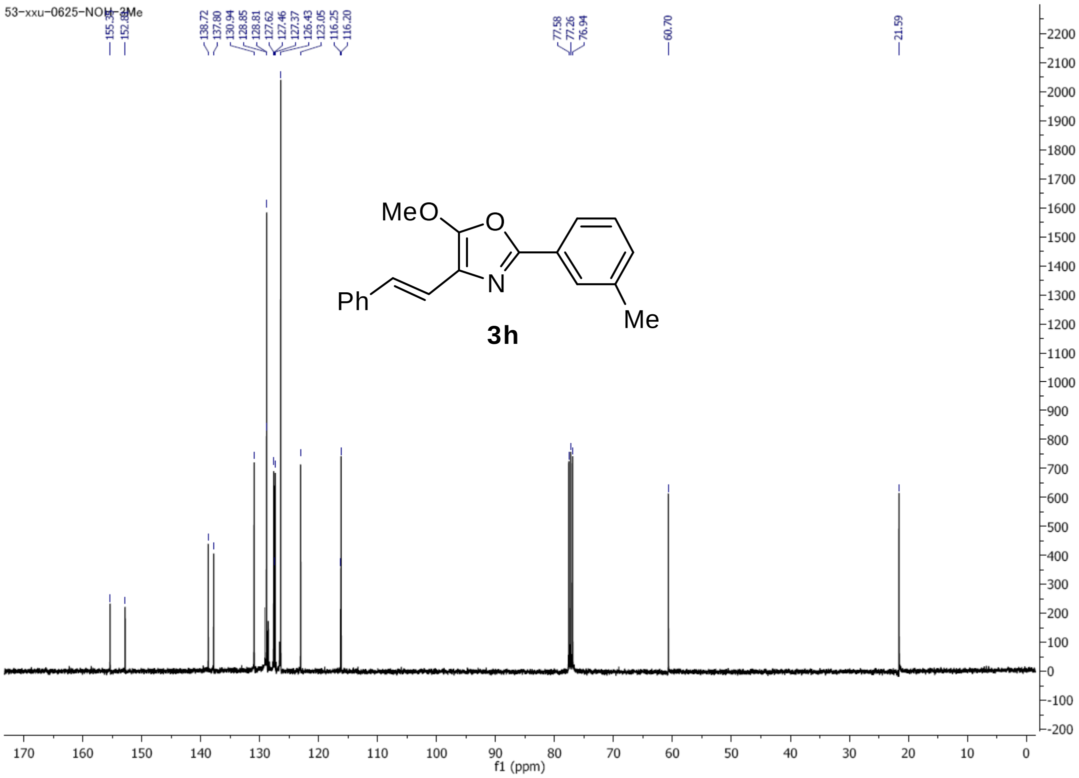

xxu−0724−NOH−4OMe1
7.34
7.28
7.26
7.25
7.23
7.19
7.00
6.98
6.95
6.91
4.13
3.89
MeO
O
N
OMe
Ph
3f
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500

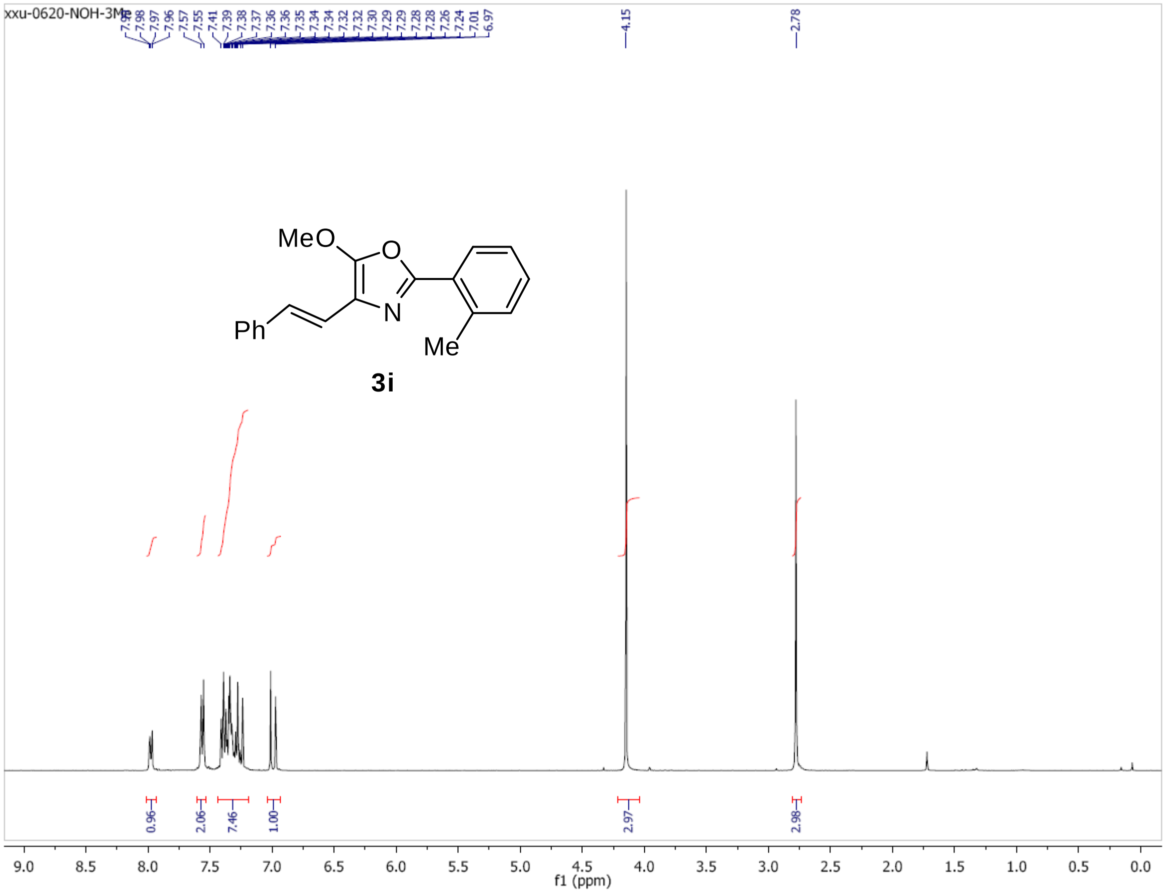

25−xxu−0724−NOH−OMe1
161.27
155.17
152.92
137.86
128.82
127.60
127.46
127.34
126.43
120.44
116.25
116.19
114.39
77.58
77.26
76.94
60.88
55.62
MeO
O
N
OMe
Ph
3f
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

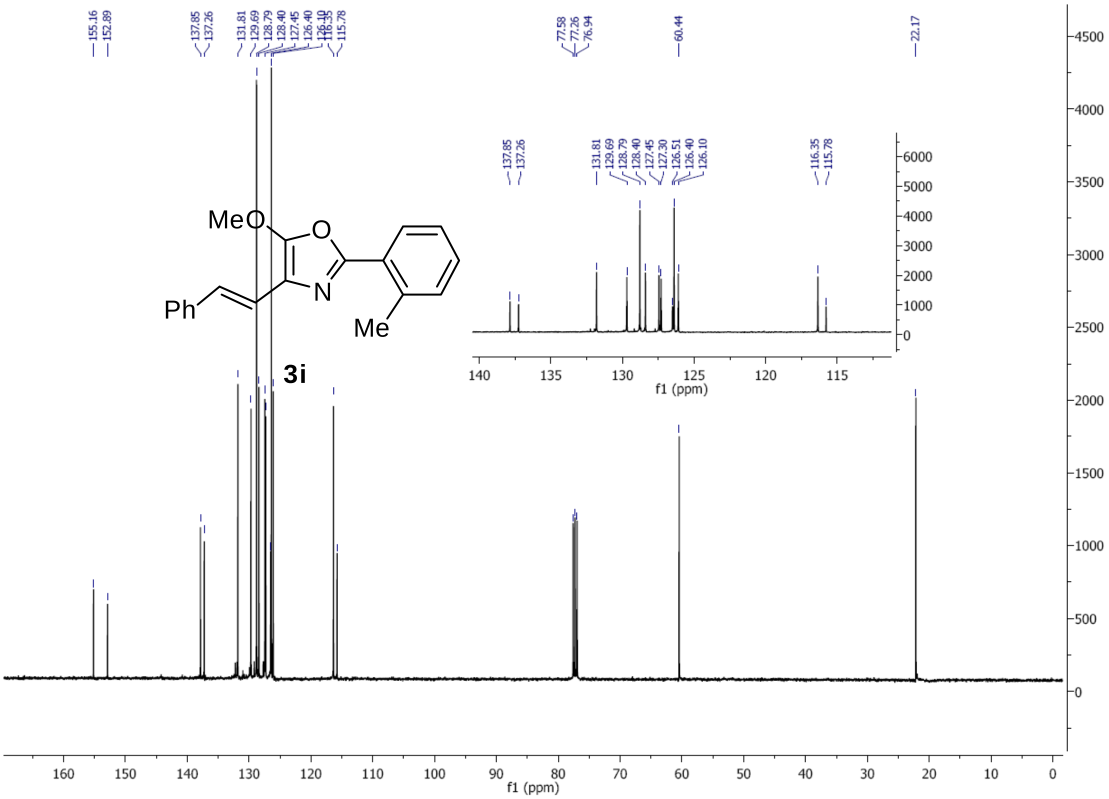

9-xxu-0620-NOH-4me
7.92
7.90
7.54
7.52
7.39
7.37
7.35
7.29
7.29
7.27
7.25
7.24
7.20
6.96
6.92
4.15
2.43
MeO
O
N
Me
Ph
3g
2.01
2.06
2.05
3.68
0.99
1.00
2.98
3.33
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

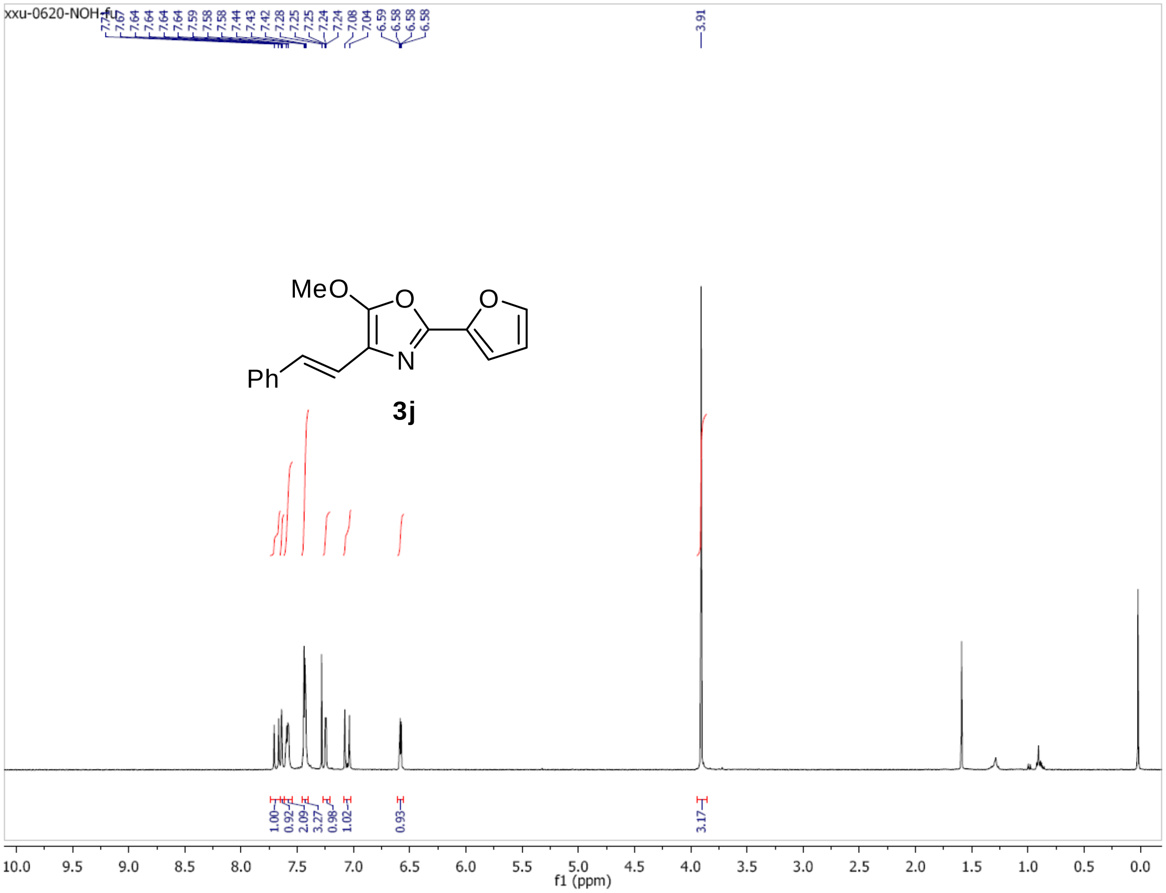

19-xxu-0618-NOH-Me
155.20
152.86
140.29
137.80
129.61
128.78
127.47
127.31
126.39
125.83
124.86
116.21
116.12
77.58
77.26
76.94
60.66
21.68
MeO
O
N
Me
Ph
3g
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

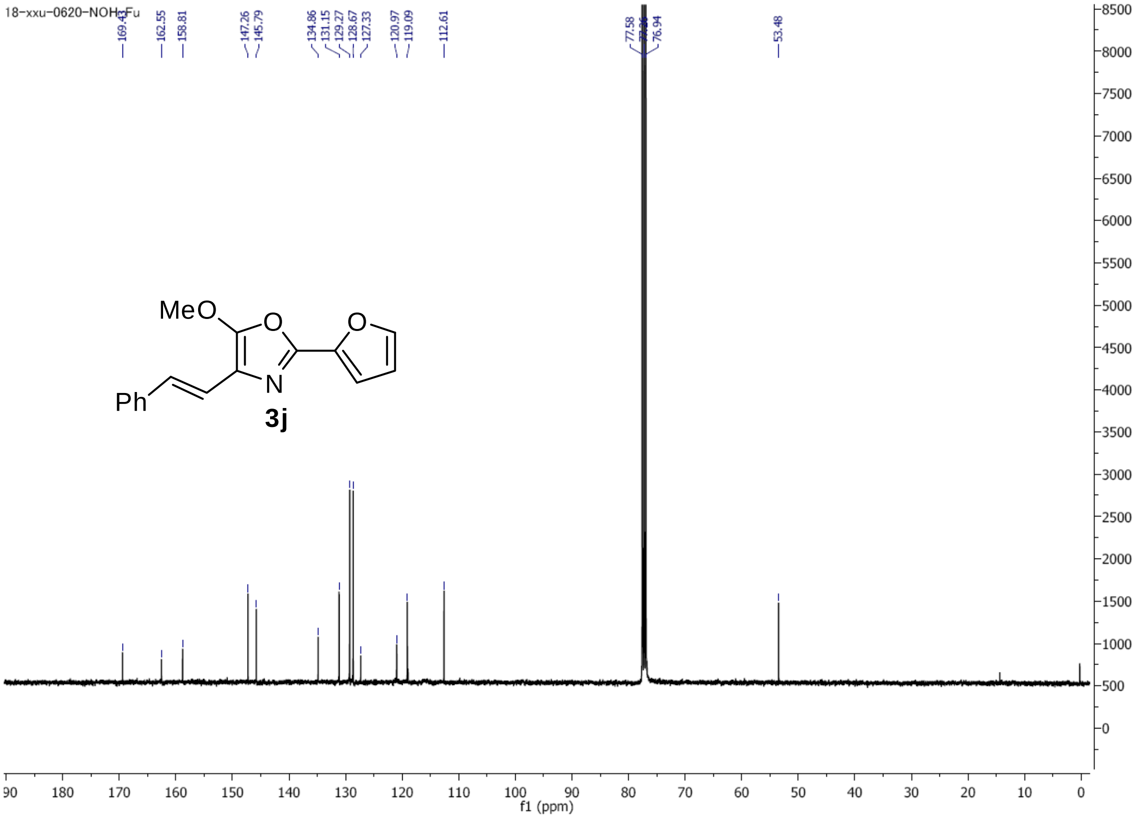

3h
xxu-0620-NOH-2Me
7.56
7.54
7.38
7.37
7.27
6.98
6.94
4.15
2.46
MeO
O
N
Ph
Me
1.00
1.09
2.12
3.45
3.28
1.05
3.12
3.42
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

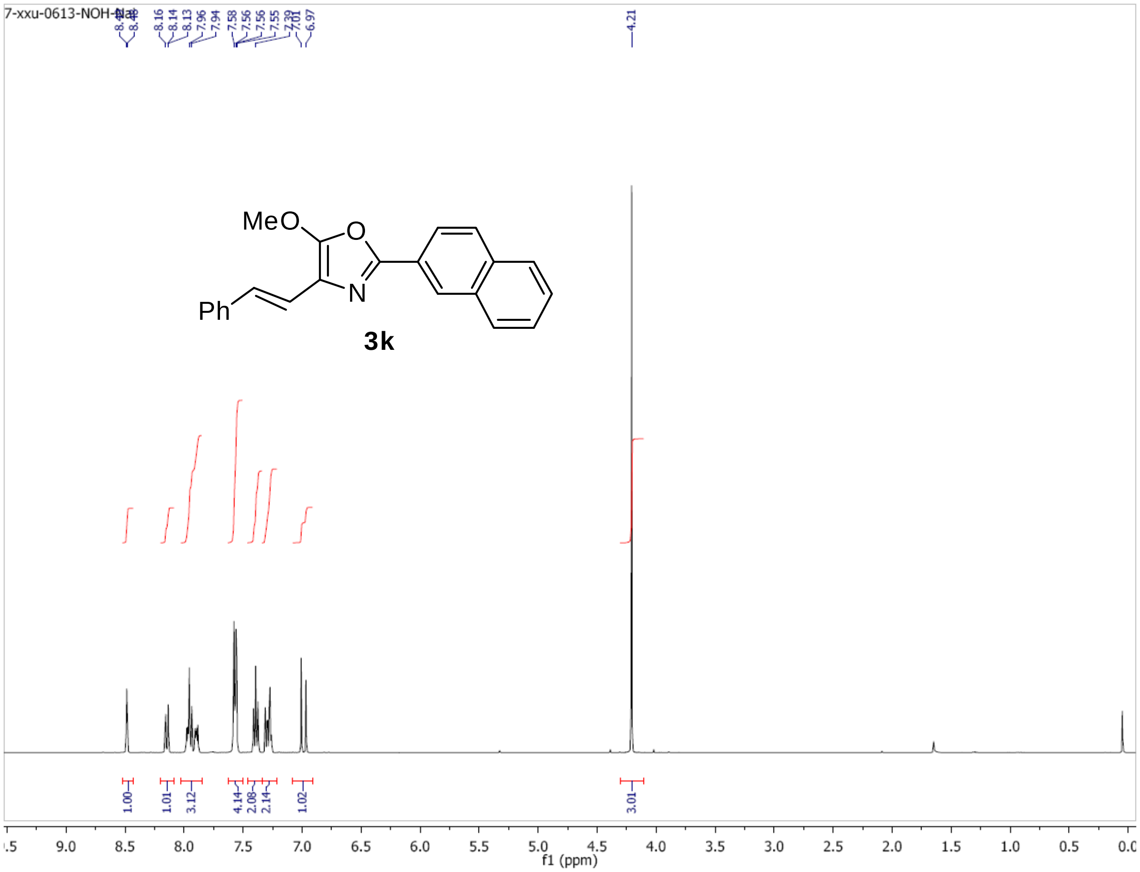

3h
53−xxu−0625−NOH−2Me
155.39
152.88
138.72
137.80
130.94
128.85
128.81
127.62
127.46
127.37
126.43
123.05
116.25
116.20
77.58
77.26
76.94
60.70
21.59
MeO
O
N
Ph
Me
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

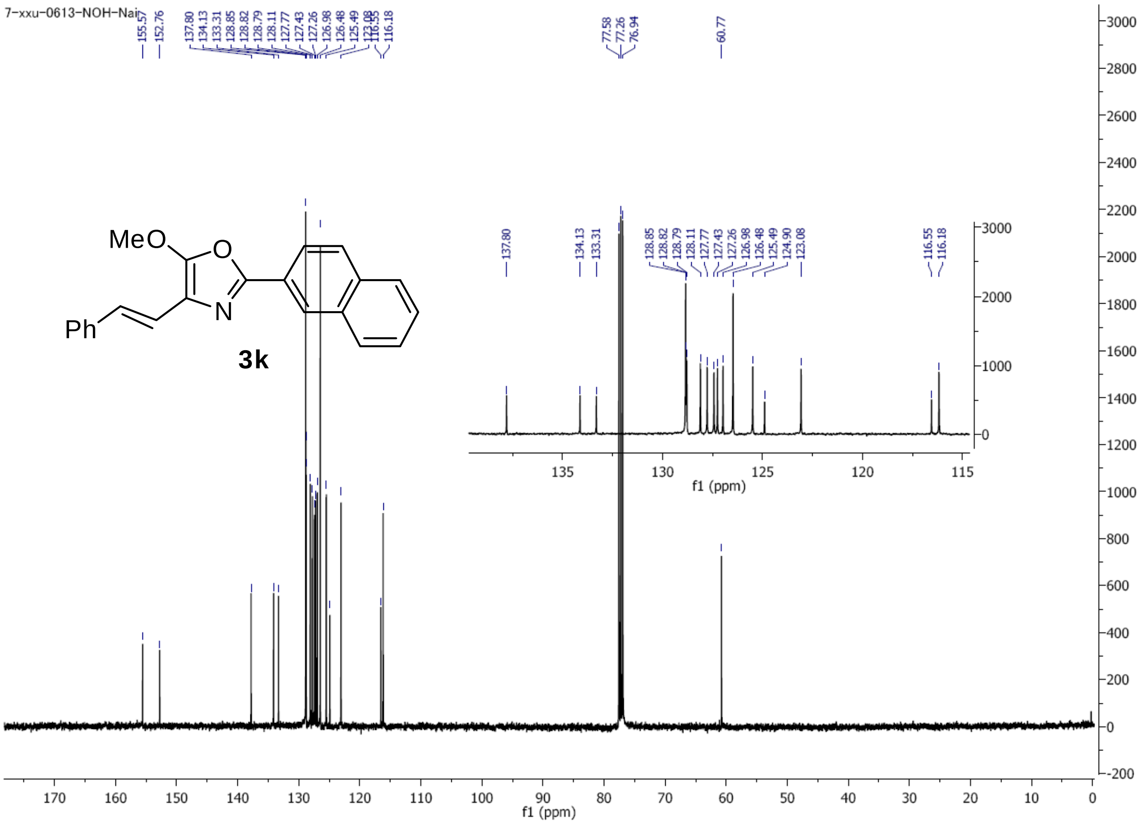

xxu-0620-NOH-3Me
7.99
7.98
7.97
7.96
7.57
7.55
7.41
7.39
7.38
7.37
7.36
7.36
7.35
7.34
7.34
7.32
7.32
7.30
7.29
7.29
7.28
7.28
7.26
7.24
7.01
6.97
4.15
2.78
MeO
O
N
Ph
Me
3i
0.96
2.06
7.46
1.00
2.97
2.98
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

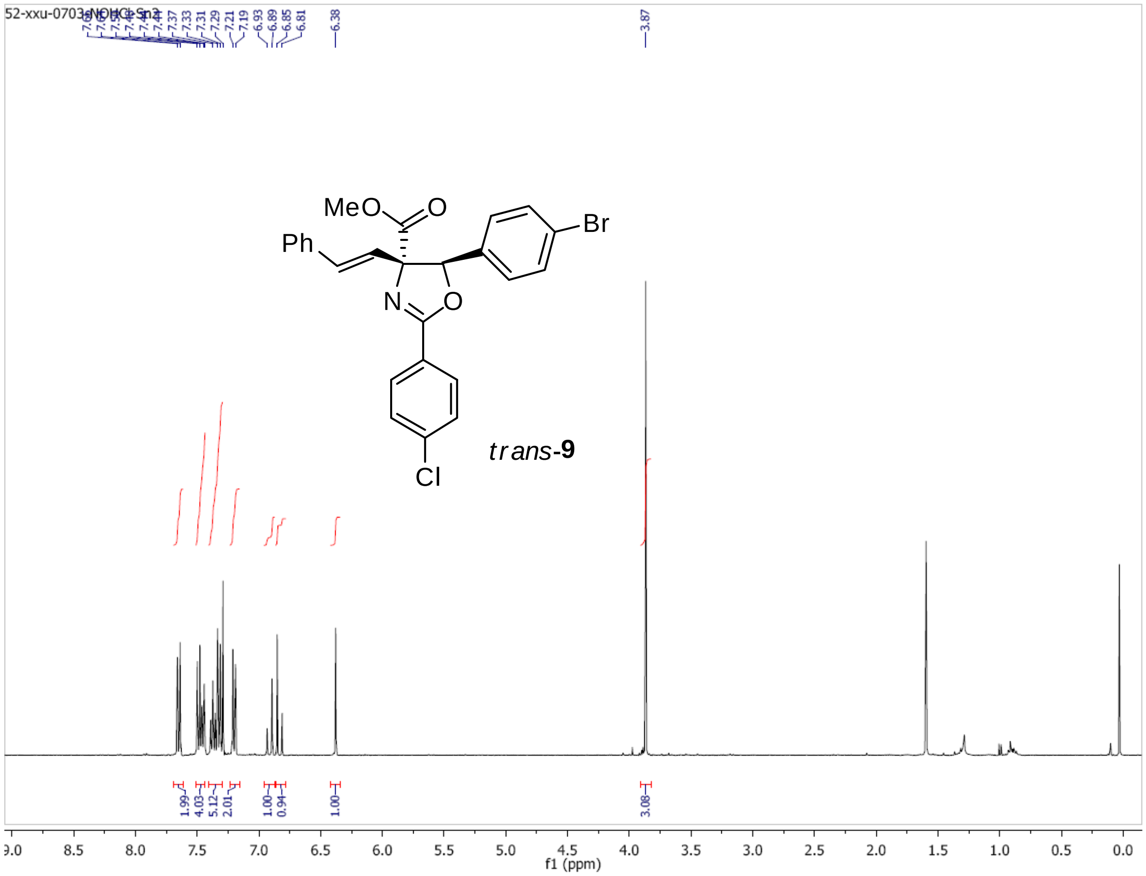

155.16
152.89
137.85
137.26
131.81
129.69
128.79
128.40
127.45
126.40
126.10
116.35
115.78
77.58
77.26
76.94
60.44
22.17
137.85
137.26
131.81
129.69
128.79
128.40
127.45
127.30
126.51
126.40
126.10
116.35
115.78
MeO
O
N
Ph
Me
3i
6000
5000
4000
3000
2000
1000
0
140
135
130
125
120
115
f1 (ppm)
4500
4000
3500
3000
2500
2000
1500
1000
500
0
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

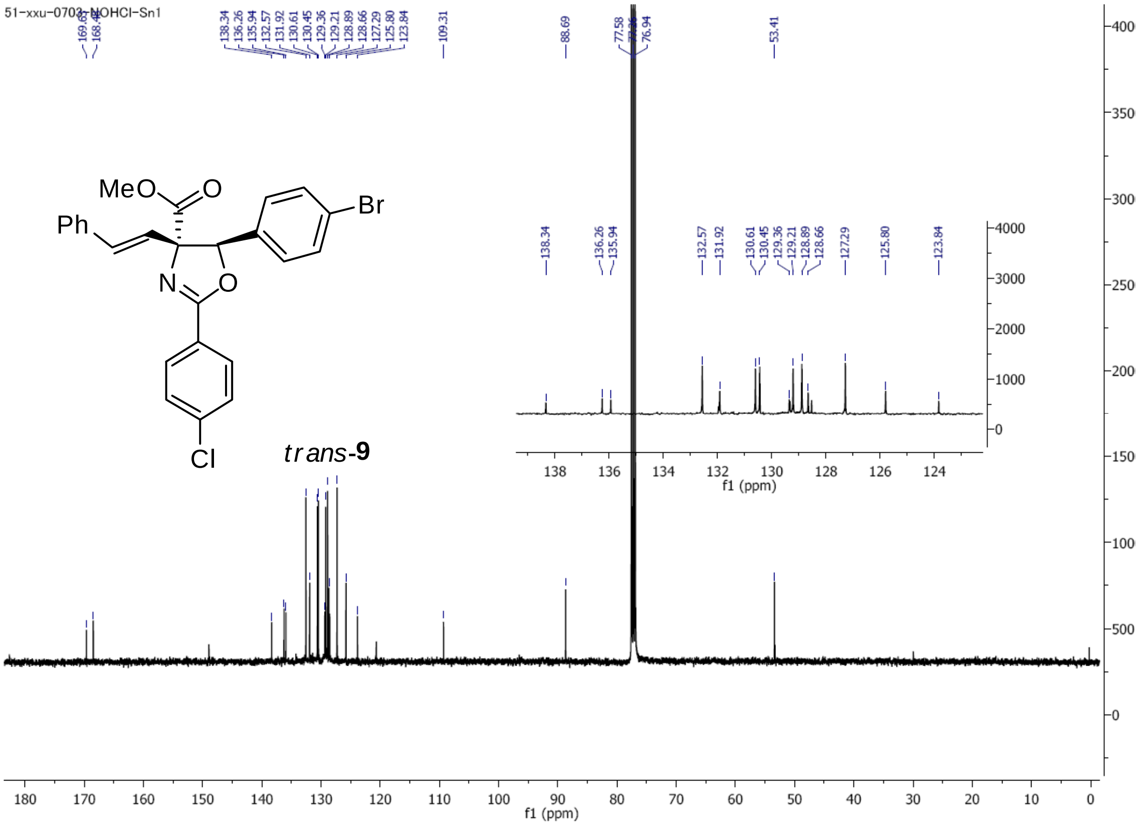

xxu-0620-NOH-fu
7.71
7.67
7.64
7.64
7.64
7.64
7.59
7.58
7.58
7.44
7.43
7.42
7.28
7.25
7.25
7.24
7.24
7.08
7.04
6.59
6.58
6.58
6.58
3.91
MeO
O
O
N
Ph
3j
1.00
0.92
2.09
3.27
0.98
1.02
0.93
3.17
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

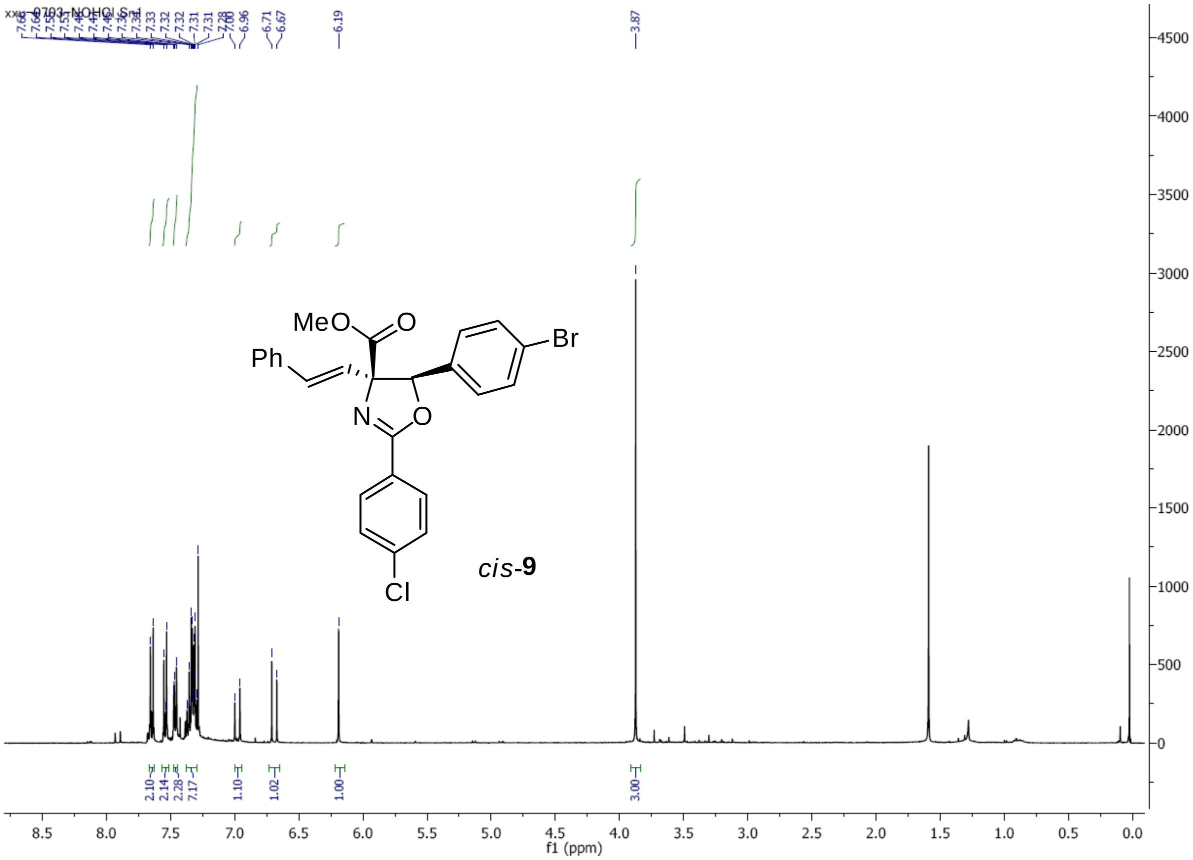

18-xxu-0620-NOH-Fu
169.41
162.55
158.81
147.26
145.79
134.86
131.15
129.27
128.67
127.33
120.97
119.09
112.61
77.58
77.26
76.94
53.48
MeO
O
O
N
Ph
3j
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

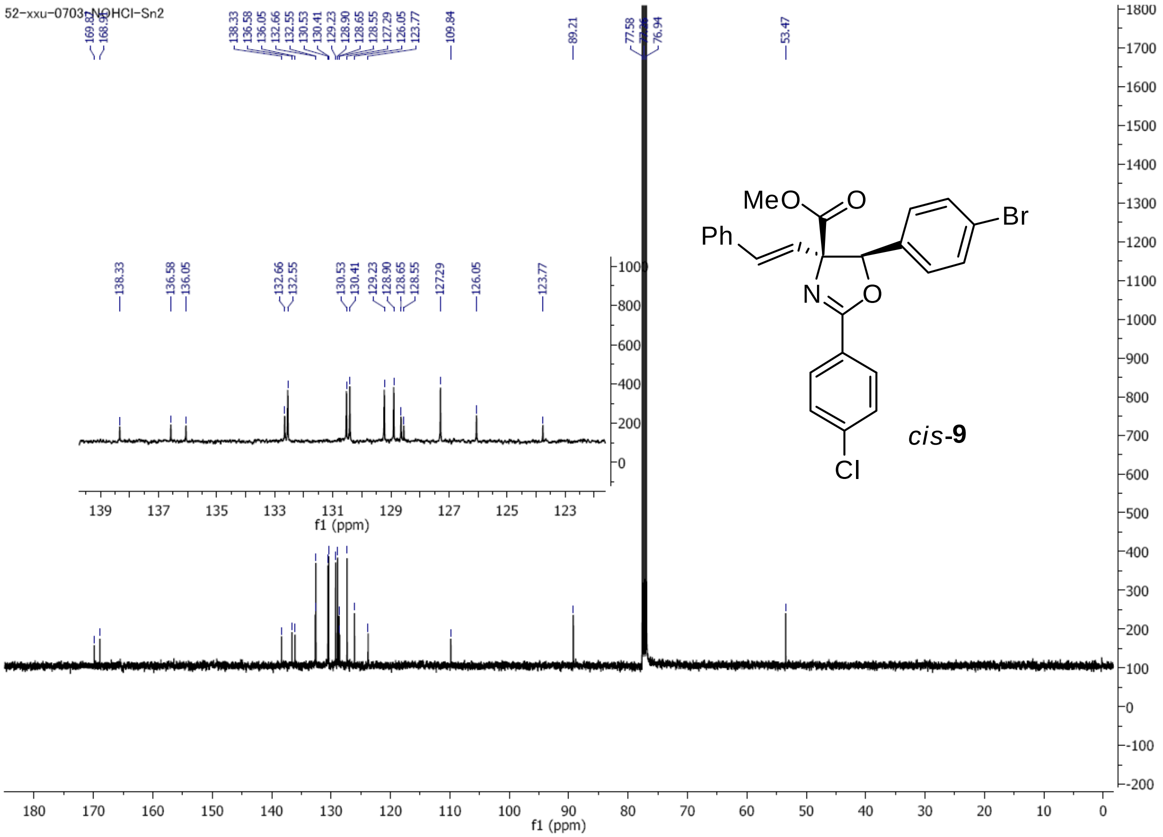

7-xxu-0613-NOH-Nai
8.48
8.16
8.14
8.13
7.96
7.94
7.58
7.56
7.56
7.55
7.39
7.01
6.97
4.21
MeO
O
N
Ph
3k
1.00
1.01
3.12
4.14
2.08
2.14
1.02
3.01
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

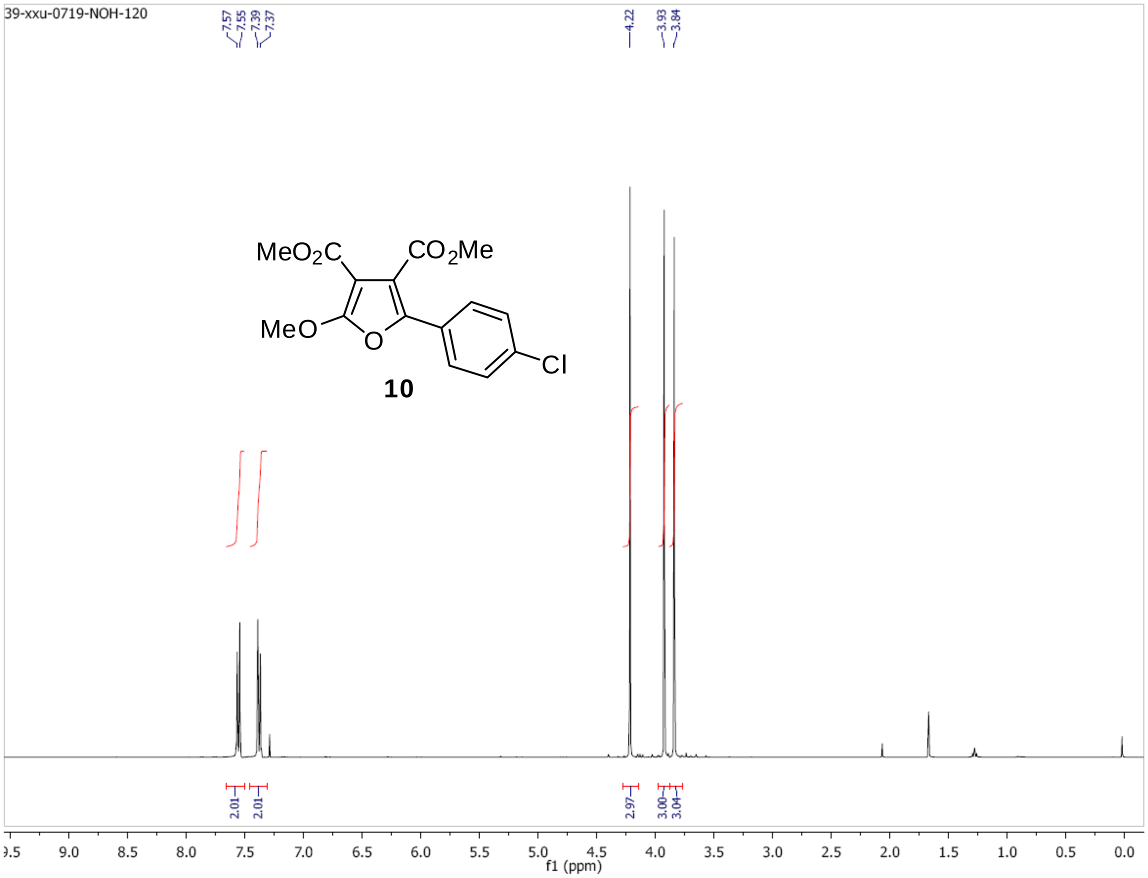

7-xxu-0613-NOH-Nai
155.57
152.76
137.80
134.13
133.31
128.85
128.82
128.79
128.11
127.77
127.43
127.26
126.98
126.48
125.49
124.90
123.08
116.55
116.18
77.58
77.26
76.94
60.77
MeO
O
N
Ph
3k
3000
2000
1000
0
135
130
125
120
115
f1 (ppm)
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

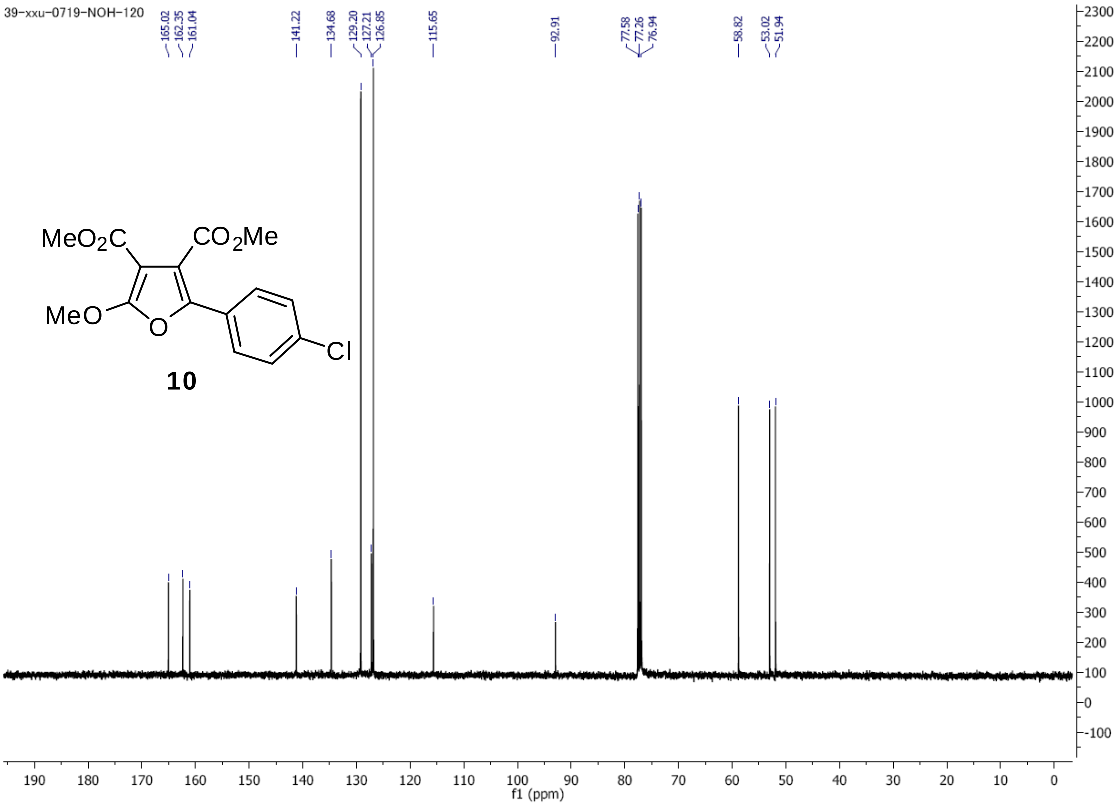

52-xxu-0703-NOHCl-Sn2
7.37
7.33
7.31
7.29
7.21
7.19
6.93
6.89
6.85
6.81
6.38
3.87
MeO
O
Ph
Br
N
O
Cl
trans-9
1.99
4.03
5.12
2.01
1.00
0.94
1.00
3.08
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

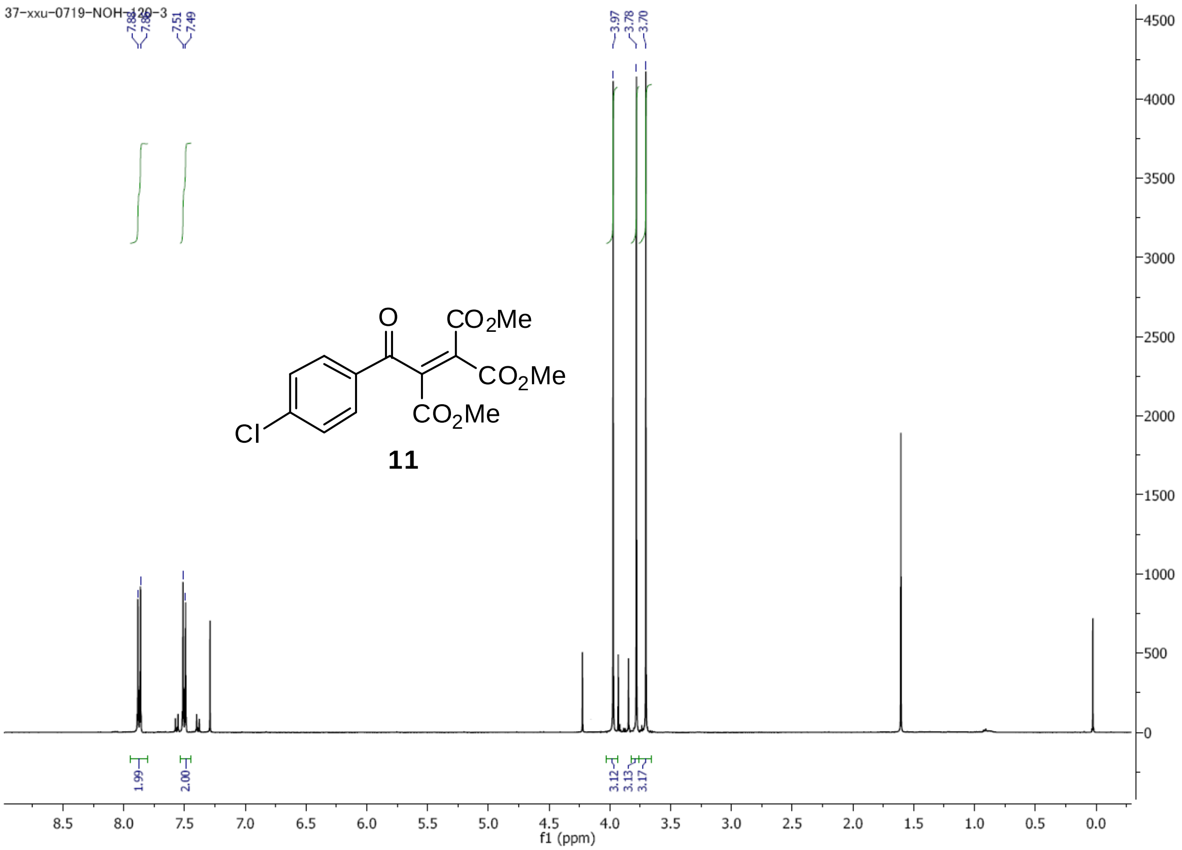

51-xxu-0703-NOHCl-Sn1
169.61
168.44
138.34
136.26
135.94
132.57
131.92
130.61
130.45
129.36
129.21
128.89
128.66
127.29
125.80
123.84
109.31
88.69
77.58
77.26
76.94
53.41
MeO
O
Ph
Br
N
O
Cl
trans-9
138
136
134
132
130
128
126
124
f1 (ppm)
4000
3000
2000
1000
0
400
350
300
250
200
150
100
500
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


xxu-0703-NOHCl-Sn1
7.66
7.64
7.55
7.53
7.33
7.32
7.32
7.31
7.31
7.28
7.00
6.96
6.71
6.67
6.19
3.87
MeO
O
Ph
Br
N
O
Cl
cis-9
2.10
2.14
2.28
7.17
1.10
1.02
1.00
3.00
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)
4500
4000
3500
3000
2500
2000
1500
1000
500
0

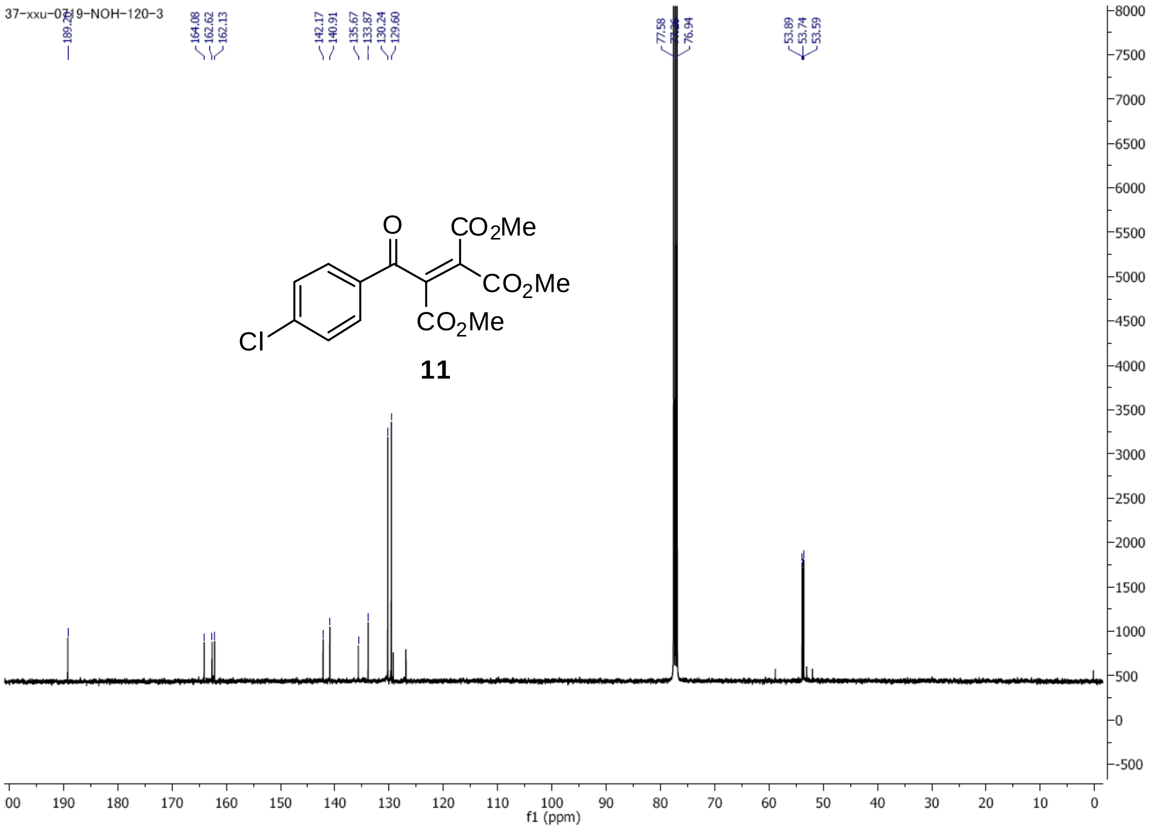

52-xxu-0703-NOHCl-Sn2
169.87
168.95
138.33
136.58
136.05
132.66
132.55
130.53
130.41
129.23
128.90
128.65
128.55
127.29
126.05
123.77
109.84
89.21
77.58
77.26
76.94
53.47
MeO
O
Ph
Br
N
O
Cl
cis-9
139
137
135
133
131
129
127
125
123
f1 (ppm)
1000
800
600
400
200
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200


39-xxu-0719-NOH-120
7.57
7.55
7.39
7.37
4.22
3.93
3.84
MeO2C
CO2Me
MeO
O
Cl
10
2.01
2.01
2.97
3.00
3.04
9.5
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)


39-xxu-0719-NOH-120
165.02
162.35
161.04
141.22
134.68
129.20
127.21
126.85
115.65
92.91
77.58
77.26
76.94
58.82
53.02
51.94
MeO2C
CO2Me
MeO
O
Cl
10
2300
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

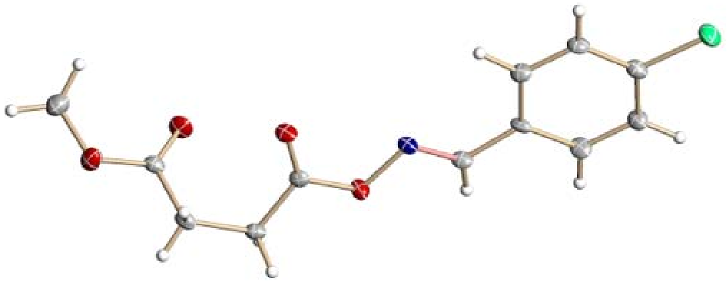

37-xxu-0719-NOH-120-3
7.88
7.86
7.51
7.49
3.97
3.78
3.70
O
CO2Me
CO2Me
CO2Me
Cl
1.99
2.00
3.12
3.13
3.17
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
4500
4000
3500
3000
2500
2000
1500
1000
500
0

11


37-xxu-0719-NOH-120-3
189.20
164.08
162.62
162.13
142.17
140.91
135.67
133.87
130.24
129.60
77.58
77.26
76.94
53.89
53.74
53.59
O
CO2Me
CO2Me
CO2Me
Cl
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500

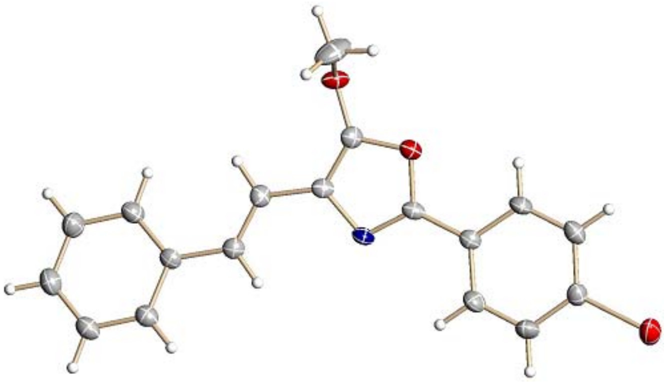
11

Crystallographic data for compound 7a (UM-2280, CCDC 895783)



```
Bond precision:     C-C = 0.0076 A              Wavelength=0.71073
Cell:         a=16.029(5)    b=5.2953(17)   c=29.392(10)
              alpha=90       beta=92.478(4) gamma=90
Temperature:150 K
                   Calculated                      Reported
Volume             2492.4(14)                      2492.4(14)
Space group        C 2/c                           C2/c
Hall group         -C 2yc                          ?
Moiety formula     C12 H12 Cl N O4                 ?
Sum formula        C12 H12 Cl N O4                 C12 H12 Cl N O4
Mr                 269.68                          269.68
Dx,g cm-3          1.437                           1.437
Z                  8                               8
Mu (mm-1)          0.312                           0.312
F000               1120.0                          1120.0
F000'              1121.75
h,k,lmax           18,6,34                         18,6,34
Nref               2195                            2138
Tmin,Tmax          0.845,0.988                     0.850,0.988
Tmin'              0.845
Correction method= ?
Data completeness= 0.974       Theta(max)= 25.000
R(reflections)= 0.0896( 1989)     wR2(reflections)= 0.2234( 2138)
S = 1.175             Npar= 176
```

Crystallographic data for compound 3b (UM 2301, CCDC 895782)



```
Bond precision:     C-C = 0.0030 A              Wavelength=0.71073
Cell:        a=7.0327(5)       b=9.2545(7)      c=12.4679(9)
             alpha=82.8208(11) beta=77.3755(11) gamma=73.6561(12)
Temperature: 150 K
                   Calculated                      Reported
Volume             758.10(10)                      758.10(10)
Space group        P -1                            P-1
Hall group         -P 1                            -P 1
Moiety formula     C18 H14 Br N O2                 C18 H14 Br N O2
Sum formula        C18 H14 Br N O2                 C18 H14 Br N O2
Mr                 356.20                          356.21
Dx,g cm-3          1.561                           1.560
Z                  2                               2
Mu (mm-1)          2.717                           2.717
F000               360.0                           360.0
F000'              359.57
h,k,lmax           9,12,16                         9,12,16
Nref               3475                            3467
Tmin,Tmax          0.433,0.762                     0.432,0.762
Tmin'              0.362
Correction method= MULTI-SCAN
Data completeness= 0.998       Theta(max)= 27.500
R(reflections)= 0.0300( 3246)     wR2(reflections)= 0.0657( 3467)
S = 1.000             Npar= 253
```