苯酚衍生物的电化学选择性 C-H 唑胺化反应研究

一．搭建电化学反应可选用的器材：

本实验所涉及的电化学反应可以用多种反应容器搭建，如三口瓶，单电解槽，试管等，取材方便，价格低廉，便于推广。本项目中报道的产率为使用三口瓶为反应容器得到。初步探索的结果显示，反应可以相当的效率在其他两种容器内进行。

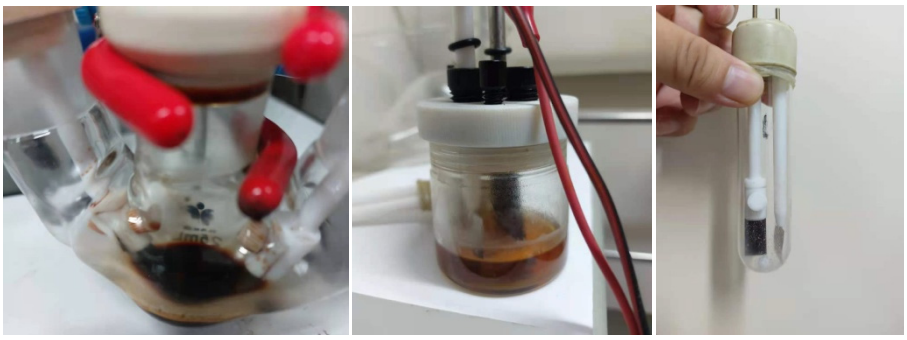


图 搭建电化学反应可选择的反应容器

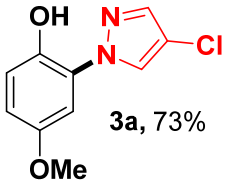
该电化学反应适用不同材质的电极，目前探索了铂电极，石墨及玻碳电极，电极展示如下图。从实验结果看，反应使用铂电极为正负极，会给出最高的反应收率，若换为石墨或玻碳为正负极材料，反应产率会稍有下降（下降幅度小于 10%）。

图 反应电极展示

二．反应的特殊说明：

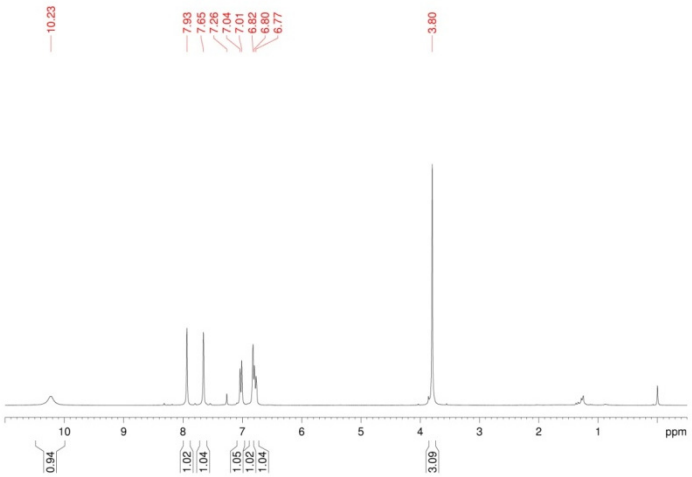
该电化学反应有特殊的底物限制，苯酚对位必须与氧原子相连，可以为各类烷氧基，若没有次特殊结构，则反应不能发生。目前其内在原因还未知，有待继续探索。另外反应所用的溶解均为挥发性比较强的溶剂，反应不能敞口进行，但无需惰性气体保护。

三．产物表征：

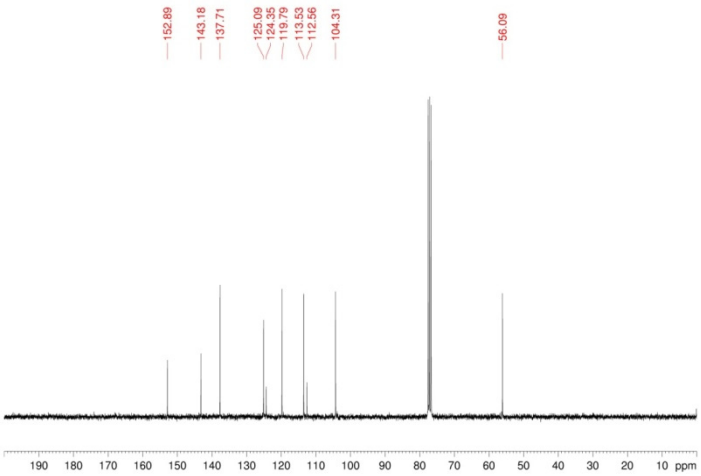


3a, 73%

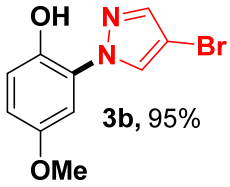
淡黄色固体 (82 mg, 73% yield), R_f = 0.75 (PE:EtOAc = 5:1). R_f = 0.75 (PE:EtOAc = 5:1). Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 10.23 (s, 1H), 7.93 (s, 1H), 7.65 (s, 1H), 7.02 (d, J = 8.82 Hz, 1H), 6.82 (s, 1H), 6.78 (d, J = 8.94 Hz, 1H), 3.80 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 152.89, 143.18, 137.71, 125.09, 124.35, 119.79, 113.53, 112.56, 104.31, 56.09. Mass Spectrometry: HRMS (ESI-TOF) (m/z): HRMS (ESI-TOF) (m/z): calcd for $C_{10}H_8ClN_2O_2^-$ ([M - H])$^-$, 223.0280 found, 223.0286.



化合物 3a 的 ^{1}H NMR 谱图

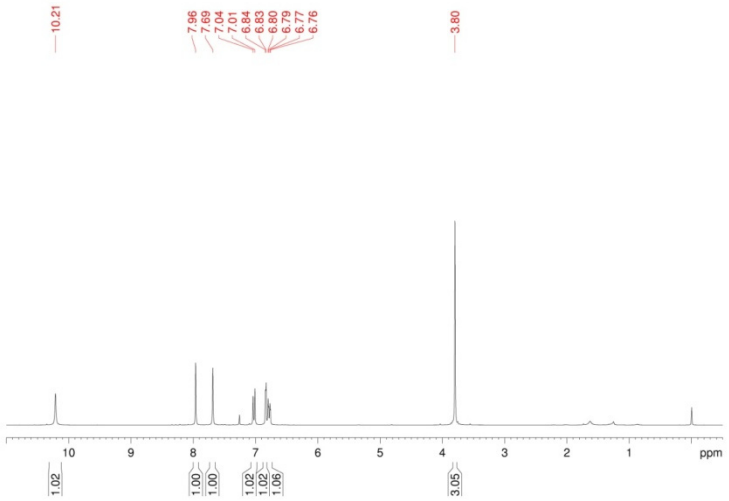


化合物 3a 的 ^{13}C NMR 谱图

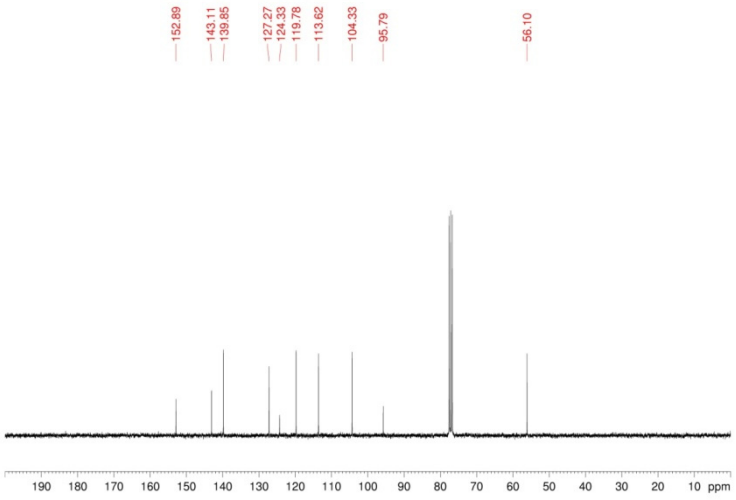


3b, 95%

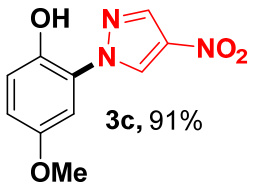
黄色固体 (128 mg, 95% yield), R_f = 0.7 (PE:EtOAc=5:1), Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 10.21 (s, 1H), 7.96 (s, 1H), 7.69 (s, 1H), 7.02 (d, *J* = 8.91 Hz, 1H), 6.84 (d, *J* = 2.46 Hz, 1H), 6.78 (dd, *J* = 8.88 Hz, 2.7 Hz, 1H), 3.80 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 152.89, 143.11, 139.85, 127.27, 124.33, 119.78, 113.62, 104.33, 95.79, 56.10. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{10}H_{10}BrN_2O_2^+$ ($[M + H]$)$^+$, 268.9920, found, 268.9938.



化合物 3b 的 ^{1}H NMR 谱图

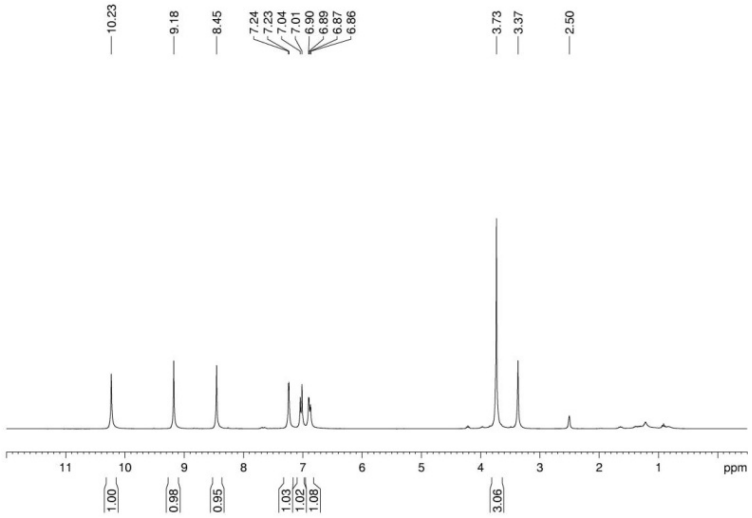


化合物 3b 的 ^{13}C NMR 谱图

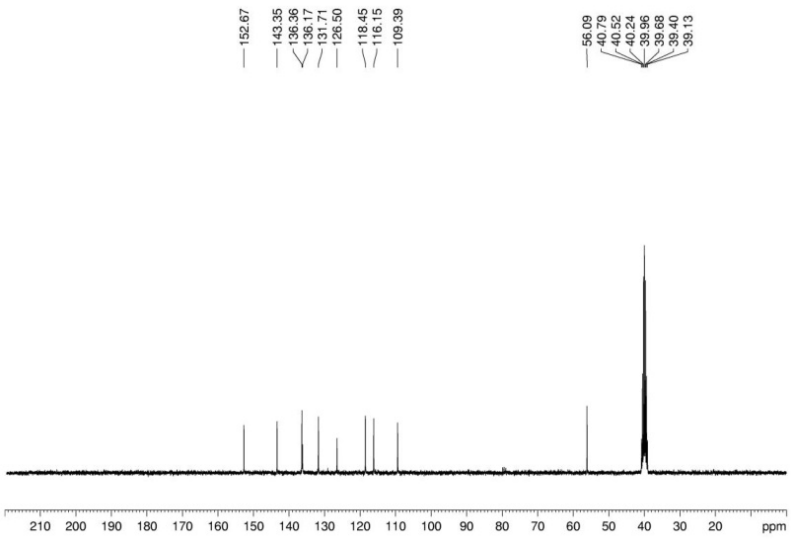


3c, 91%

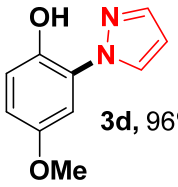
白色固体 (107 mg，91 % yield, R_f = 0.26 (PE/EtOAc = 5 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $(CD_3)_2SO$, 25 ºC, δ): 10.23 (s, 1H), 9.18 (s, 1H), 8.45 (s, 1H), 7.24 (d, *J* = 2.8 Hz, 1H), 7.03 (d, *J* = 8.9 Hz, 1H), 6.88 (dd, *J* = 8.9, 2.9 Hz, 1H), 3.73 (s, 3H). ^{13}C NMR (75 MHz, $(CD_3)_2SO$, 25 ºC, δ): 152.7, 143.4, 136.4, 136.2, 131.8, 126.5, 118.5, 116.1, 109.4, 56.1. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{10}H_8N_3O_4^-$ ([M-H]$^-$), 234.0520, found, 234.0510.



化合物 3c 的 ^{1}H NMR 谱图

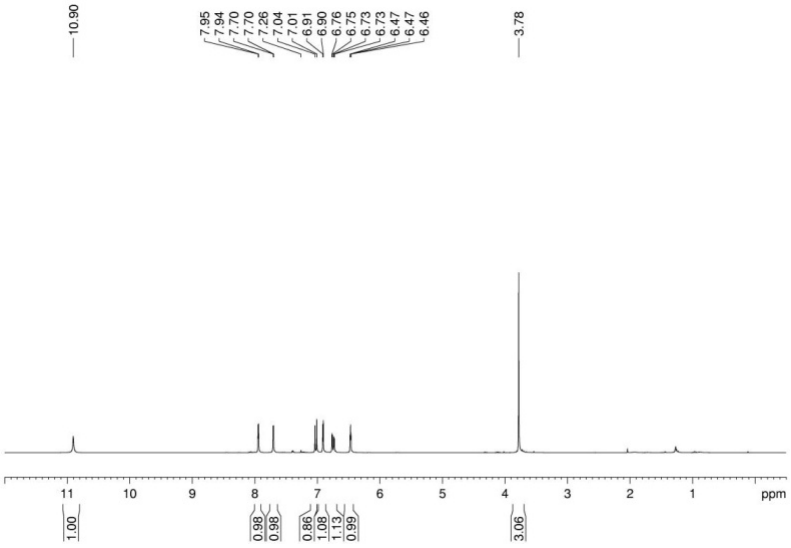


化合物 3c 的 ^{13}C NMR 谱图

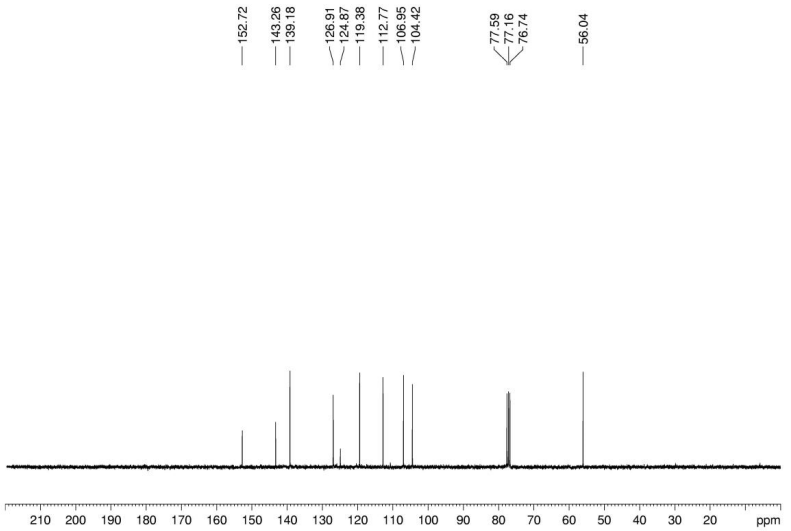


3d, 96%

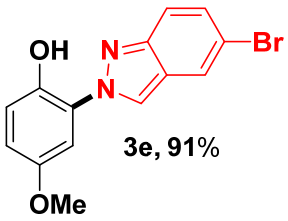
淡黄色固体 (91 mg，96 % yield, R_f = 0.41 (PE/EtOAc = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 10.9 (s, 1H), 7.94 (d, *J* = 2.5 Hz, 1H), 7.70 (d, *J* = 1.8 Hz, 1H), 7.02 (d, *J* = 8.9 Hz, 1H), 6.91 (d, *J* = 2.9 Hz, 1H), 6.75 (dd, *J* = 8.9, 2.9 Hz), 6.47 (t, *J* = 2.2 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 152.7, 143.2, 139.2, 126.9, 124.9, 119.4, 112.78, 106.9, 104.4, 56.0. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{10}H_{11}N_2O_2$ ($[M + H]^+$), 191.0815, found, 191.0816.



化合物 3d 的 ^{1}H NMR 谱图

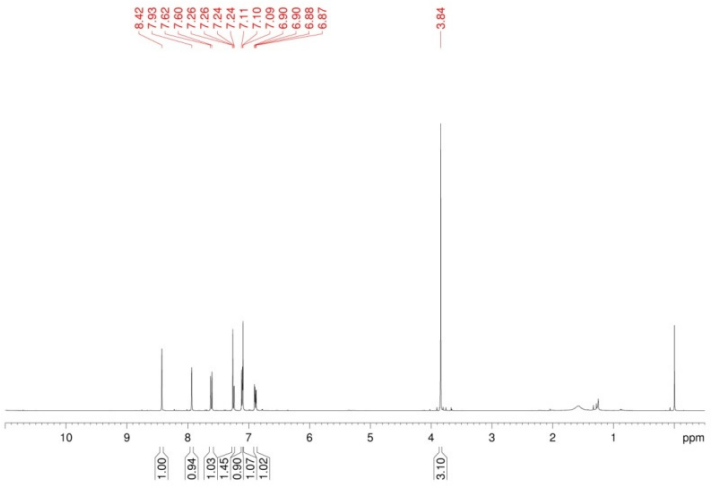


化合物 3d 的 ^{13}C NMR 谱图

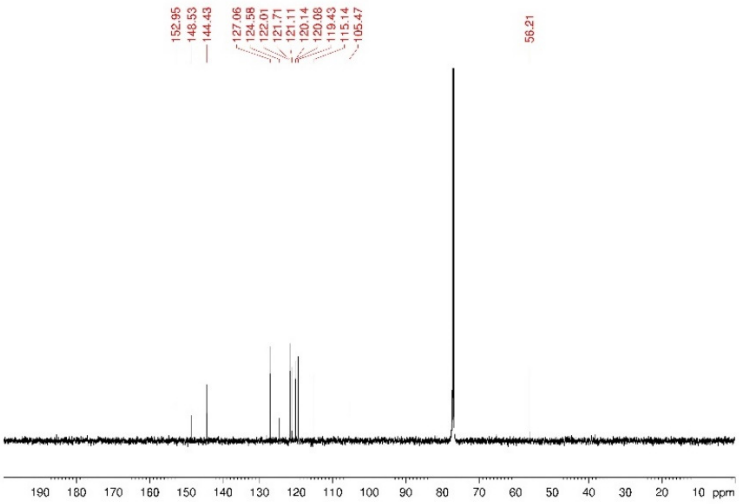


3e, 91%

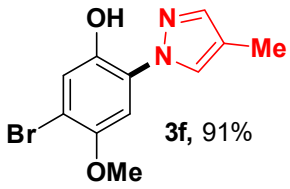
黄色固体 (145 mg, 91% yield), R_f = 0.65 (PE:EtOAc = 5:1). NMR Spectroscopy: ^{1}H NMR (400 MHz, $CDCl_3$, 25 ºC, δ): 8.42 (s, 1H), 7.93 (s, 1H), 7.61 (d, *J* = 8.88 Hz, 1H), 7.25(dd, *J* = 8.76 Hz, 1.52 Hz, 1H), 7.11 (d, *J* = 5.6 Hz, 1H), 7.09 (s, 1H), 6.89 (dd, *J* = 9.04 Hz, 2.76 Hz), 3.84 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 ºC, δ): 152.95, 148.53, 144.43, 127.06, 124.58, 122.01, 121.71, 121.11, 120.14, 120.08, 119.43, 115.14, 105.47, 56.21. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{14}H_{10}BrN_2O_2^-$ ([M - H]), 316.9931, found, 316.9937.



化合物 3e 的 ^{1}H NMR 谱图

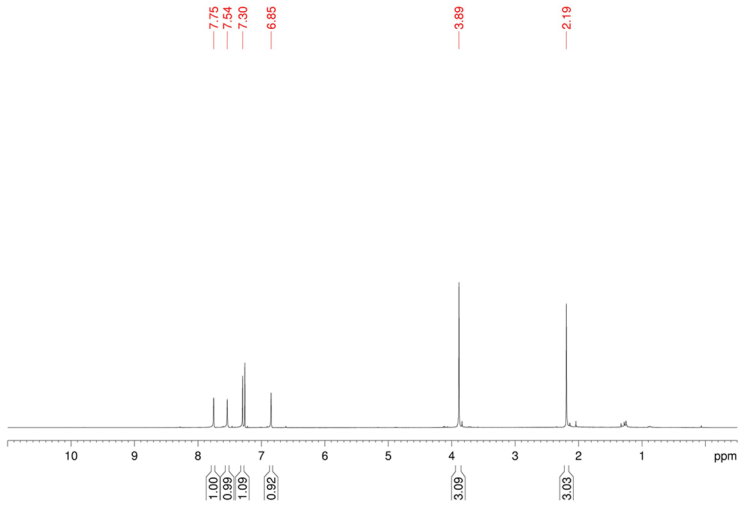


化合物 3e 的 ^{13}C NMR 谱图

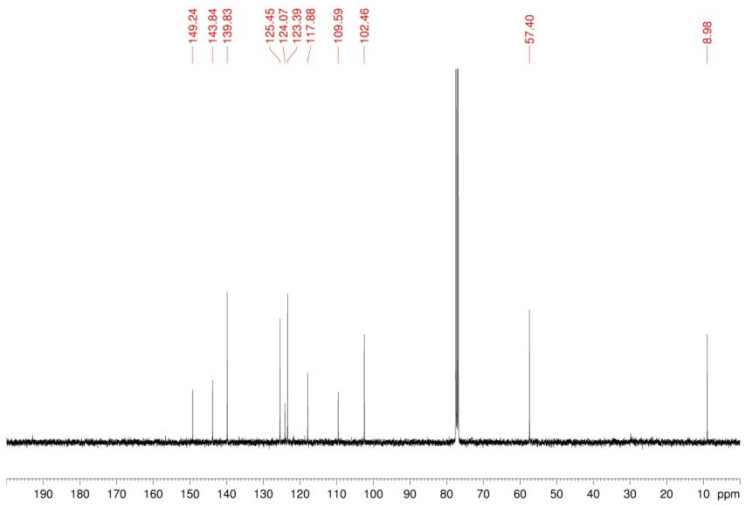


3f, 91%

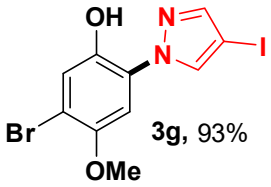
淡棕色固体 (128 mg, 91% yield), R_f = 0.80 (PE:EtOAc = 5:1), Spectroscopy: ^{1}H NMR (400 MHz, $CDCl_3$, 25 ºC, δ): 7.75 (s, 1H), 7.54 (s, 1H), 7.30 (s, 1H), 6.85 (s, 1H), 3.89 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 149.24, 143.84, 139.83, 125.45, 124.07, 123.39, 117.88, 109.59, 102.46, 57.40, 8.98. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{11}H_{12}BrN_2O_2^+$ ([M + H])$^+$, 283.0077, found, 283.0092.



化合物 3f 的 ^{1}H NMR 谱图

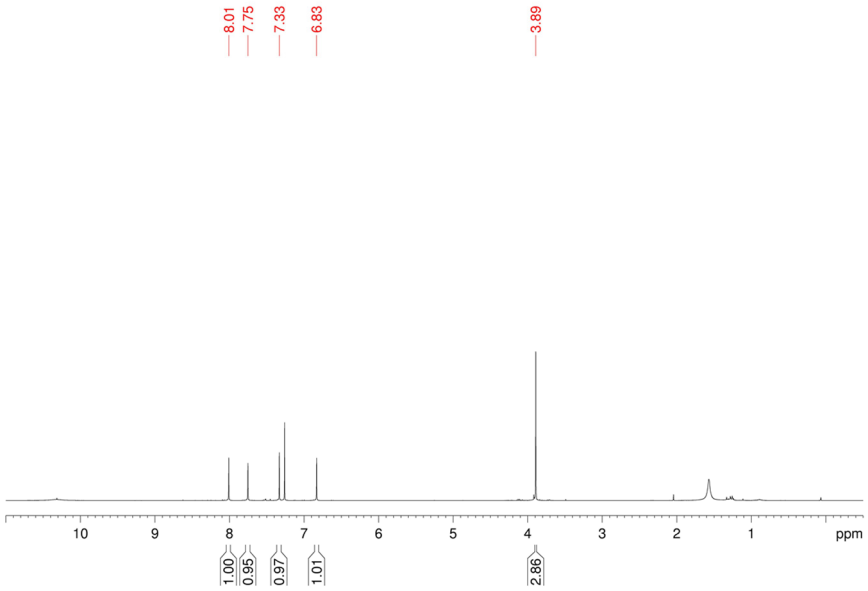


化合物 3f 的 ^{13}C NMR 谱图

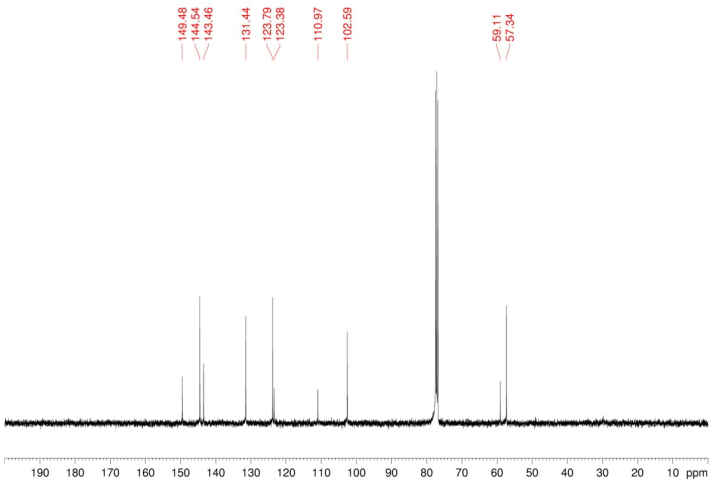


3g, 93%

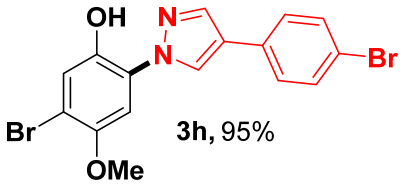
棕色固体 (183 mg, 93% yield), R_f = 0.75 (PE:EtOAc = 5:1), Spectroscopy: ^{1}H NMR (400 MHz, $CDCl_3$, 25 ºC, δ): 8.01 (s, 1H), 7.75 (s, 1H), 7.33 (s,1H), 6.83 (s, 1H), 3.89(s, 3H), ^{13}C NMR (101 MHz, $CDCl_3$, 25 ºC, δ): 149.48, 144.54, 143.46, 131.44, 123.79, 123.38, 110.97, 102.59, 59.11, 57.34. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{10}H_7BrIN_2O_2^-$ ([M - H])$^-$, 394.8721, found, 394.8729.



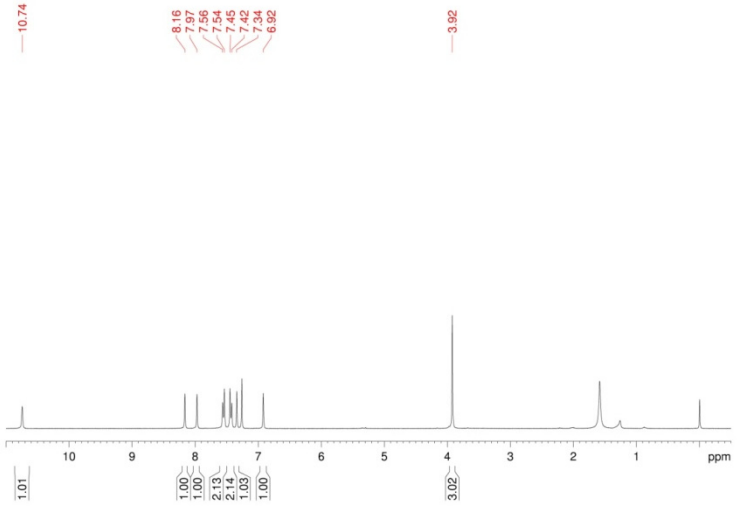
化合物 3g 的 ^{1}H NMR 谱图



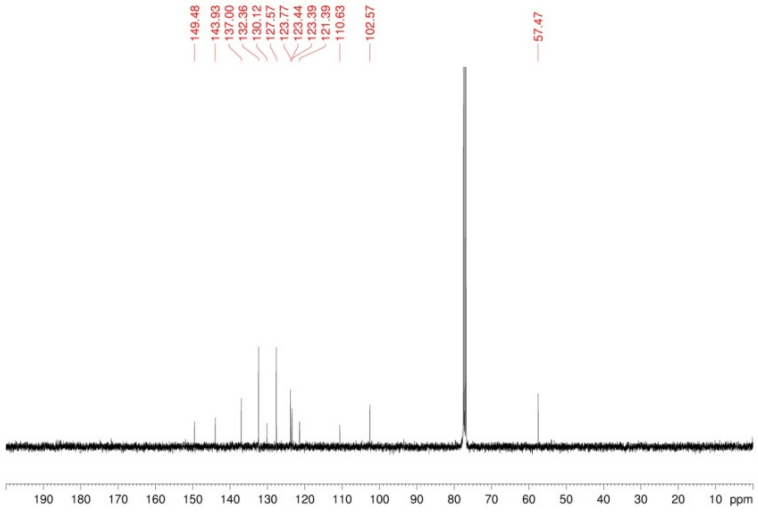
化合物 3g 的 ^{13}C NMR 谱图



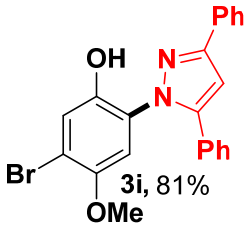
棕色固体 (201 mg, 95% yield), R_f = 0.4 (PE:EtOAc = 5:1), spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 10.74(s, 1H), 8.16 (s,1H), 7.97 (s, 1H), 7.55 (d, *J* = 8.31 Hz, 2H), 7.43 (d, *J* = 8.31 Hz, 2H), 7.34 (s, 1H), 6.92 (s, 1H), 3.92 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 ºC, δ):149.48, 143.93, 137.00, 132.36, 130.12, 127.57, 123.77, 123.44, 123.39, 121.39, 110.63, 102.57, 57.47. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{16}H_{11}Br_2N_2O_2^-$ ($[M - H]^-$, 420.9193, found, 420.9206.



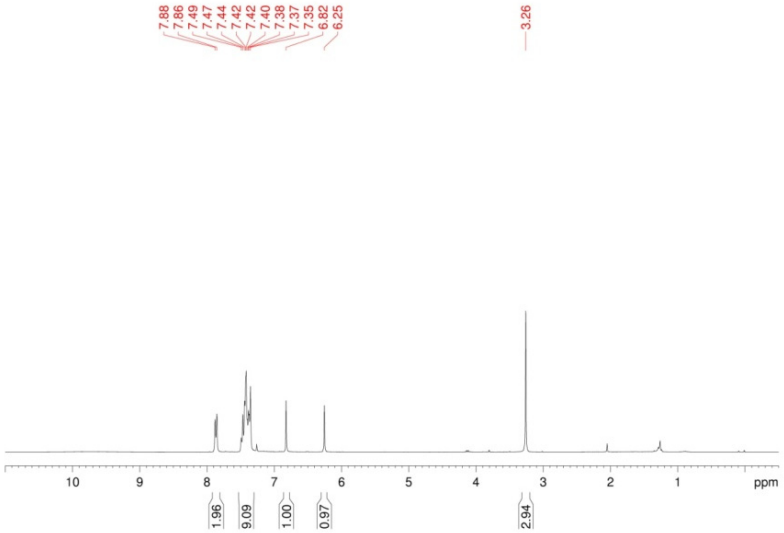
化合物 3h 的 ^{1}H NMR 谱图



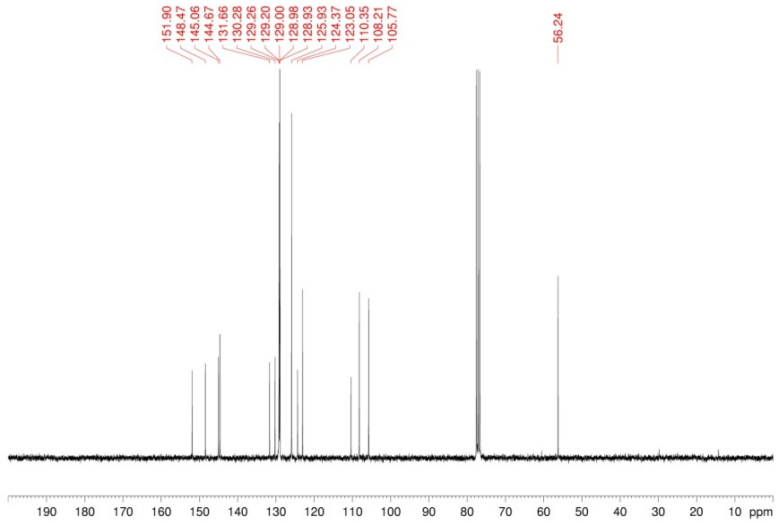
化合物 3h 的 ^{13}C NMR 谱图



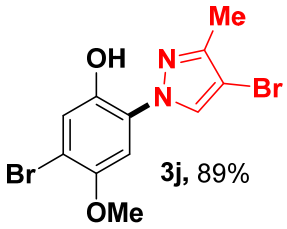
桔黄色固体 (179 mg, 81% yield), R_f =0.8 (PE:EtOAc = 5:1), spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.87 (d, *J* =6.93, 2H), 7.49-7.35 (m, 9H), 6.82 (s, 1H), 6.26 (s, 1H), 3.26 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 151.90, 148.47, 145.06, 144.67, 131.66, 130.28, 129.26, 129.20, 129.00, 128.98, 128.93, 125.93, 124.37, 123.05, 110.35, 108.21, 105.77, 56.24. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{22}H_{18}BrN_2O_2^+$ ([M + H])$^+$, 421.0546, found, 421.0556.



化合物 3i 的 ^{1}H NMR 谱图

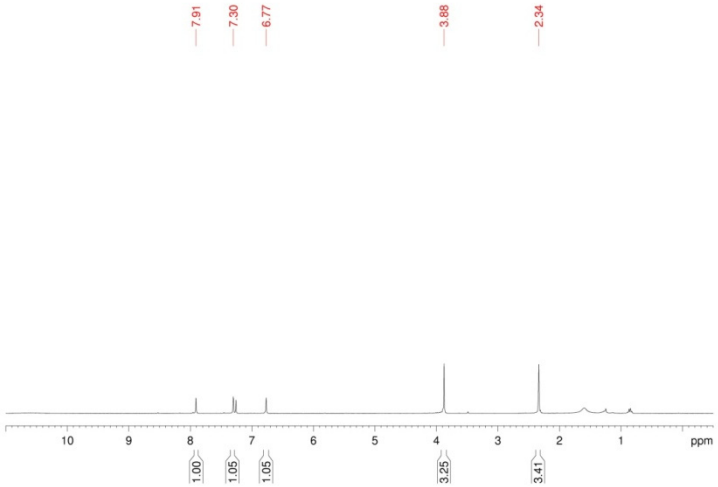


化合物 3i 的 ^{13}C NMR 谱图

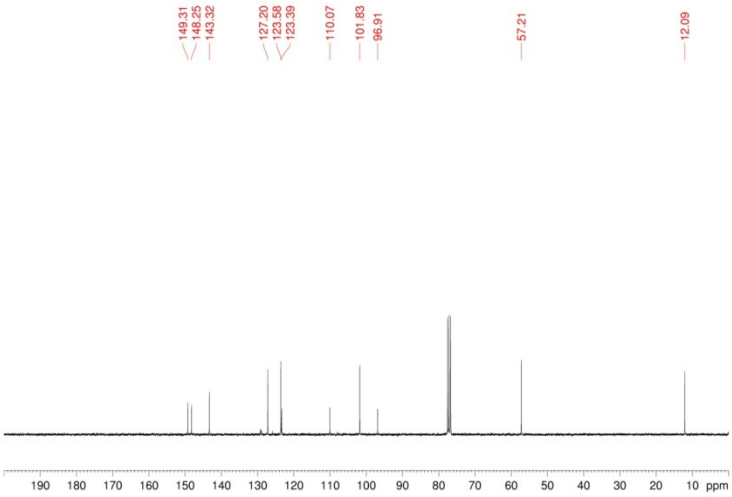


3j, 89%

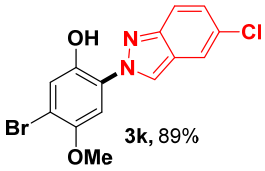
棕色固体 (0161 mg, 89% yield), R_f = 0.75 (PE:EtOAc = 5:1), spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.91 (s, 1H), 7.30 (s, 1H), 6.77 (s, 1H), 3.88 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 149.31, 148.25, 143.32, 127.20, 123.58, 123.39, 110.07, 101.83, 96.91, 57.21, 12.09. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{11}H_{11}Br_2N_2O_2^+$ ([M + H])$^+$, 360.9182, found, 360.9047.



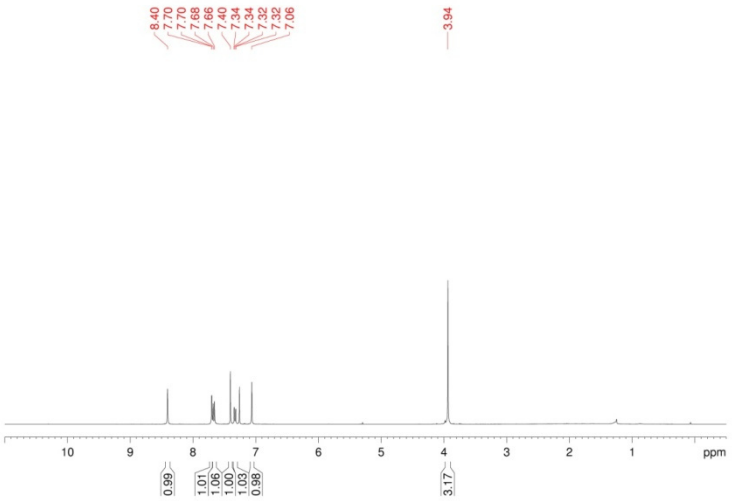
化合物 3j 的 ^{1}H NMR 谱图



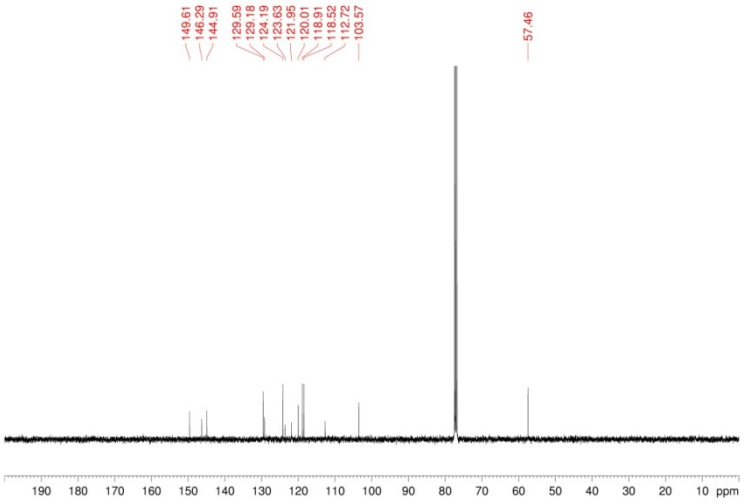
化合物 3j 的 ^{13}C NMR 谱图



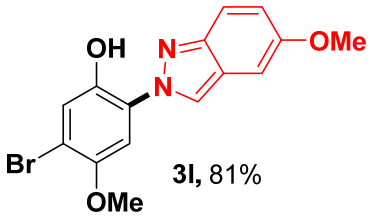
黄色固体 (157 mg, 89% yield), R_f = 0.7 (PE:EtOAc = 5:1), spectroscopy: ^{1}H NMR (400 MHz, $CDCl_3$, 25 ºC, δ): 8.40 (s, 1H), 7.70 (d, *J* = 1.04 Hz, 1H), 7.67 (d, *J* = 9.16 Hz, 1H), 7.40 (s, 1H), 7.33 (dd, *J* = 9.2 Hz, 1.68 Hz, 1H), 7.06 (s, 1H), 3.94 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 ºC, δ): 149.61, 146.29, 144.91, 129.59, 129.18, 124.19, 123.63, 121.95, 120.01, 118.91, 118.52, 112.72, 103.57, 57.46. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{14}H_{11}BrClN_2O_2^+$ $([M + H])^+$, 352.9687, found, 352.9694.



化合物 3k 的 ^{1}H NMR 谱图

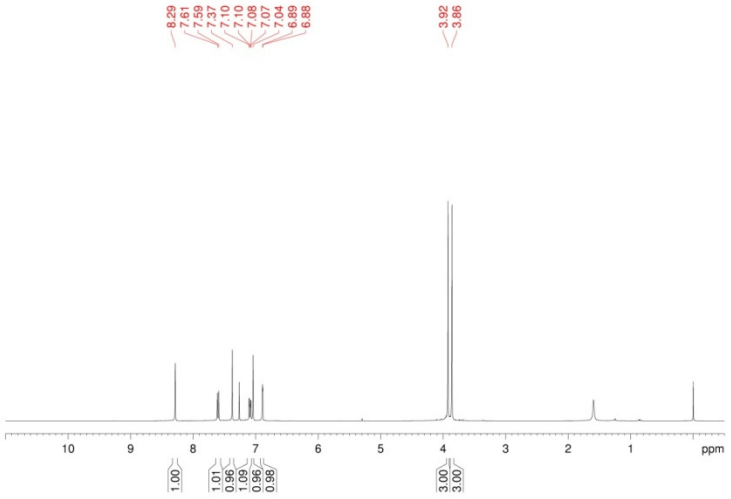


化合物 3k 的 ^{13}C NMR 谱图

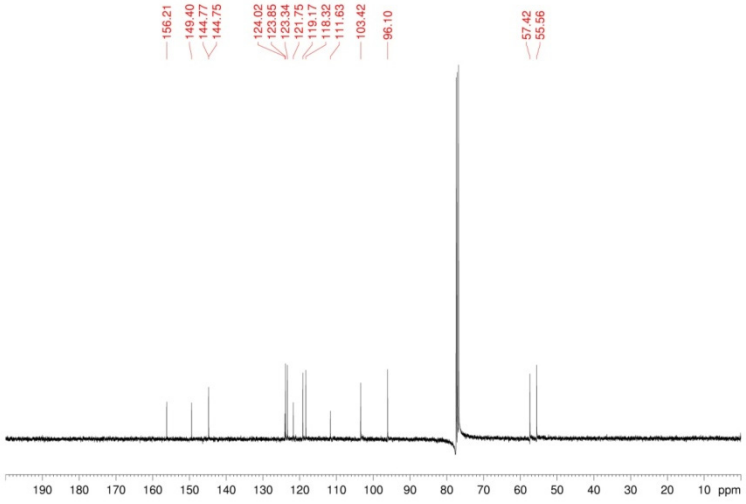


3l, 81%

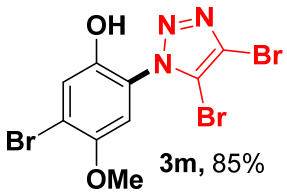
棕色固体 (141 mg, 81% yield), R_f = 0.5 (PE:EtOAc = 5:1), spectroscopy: ^{1}H NMR (400 MHz, $CDCl_3$, 25 ºC, δ): 11.66 (s, 1H), 7.60 (d, *J* = 9.32 Hz, 1H), 7.37 (s, 1H), 7.09 (dd, *J* =9.32 Hz, 2.28 Hz, 1H), 7.04 (s, 1H), 6.89 (d, *J* = 2.08 Hz, 1H), 3.92 (s, 3H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 ºC, δ):156.21, 149.40, 144.77, 144.75, 124.02, 123.85, 123.34, 121.75, 119.17, 118.32, 111.63, 103.42, 96.10, 57.42, 55.56. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{15}H_{14}BrN_2O_3^+$ ([M + H])$^+$, 349.0182, found, 349.0191.



化合物 3l 的 ^{1}H NMR 谱图

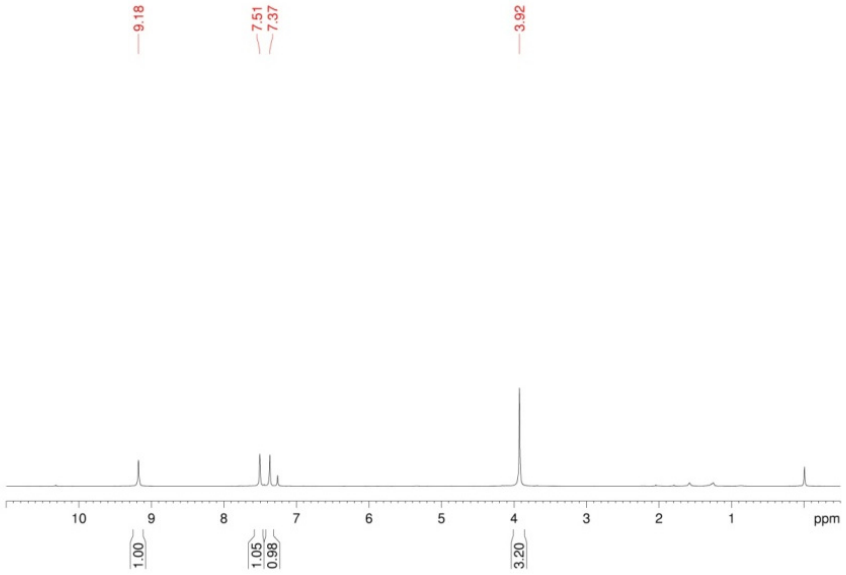


化合物 3l 的 ^{13}C NMR 谱图

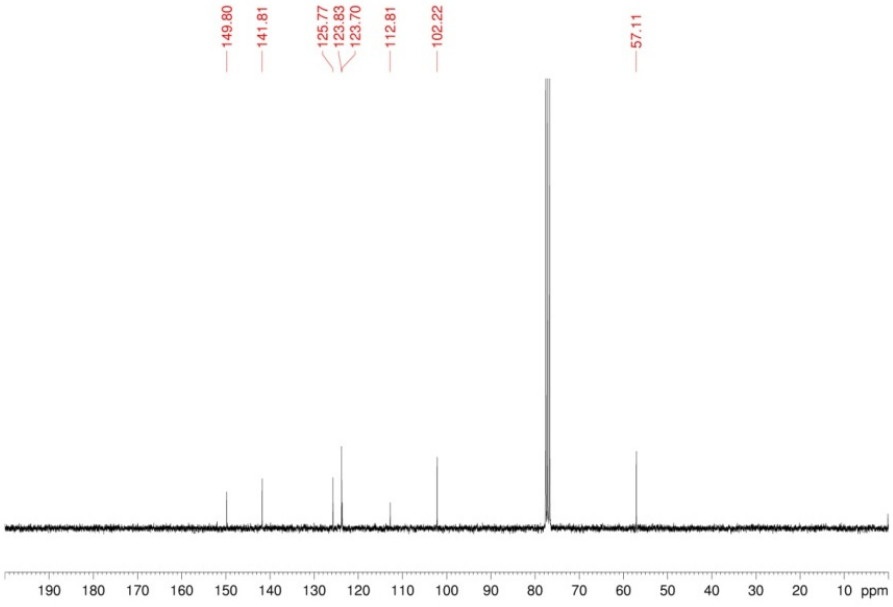


3m, 85%

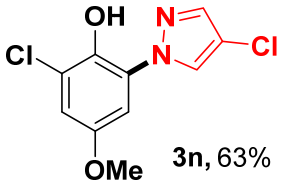
黄色固体 (181 mg, 85% yield), R_f = 0.6 (PE:EtOAc = 5:1), Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 9.18 (s, 1H), 7.51 (s, 1H), 7.37 (s, 1H), 3.92 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 149.80, 141.81, 125.77, 123.83, 123.70, 112.81, 102.22, 57.11. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_9H_7Br_3N_3O_2^+$ ([M + H])$^+$, 425.8083, found, 425.7944.



化合物 3m 的 ^{1}H NMR 谱图

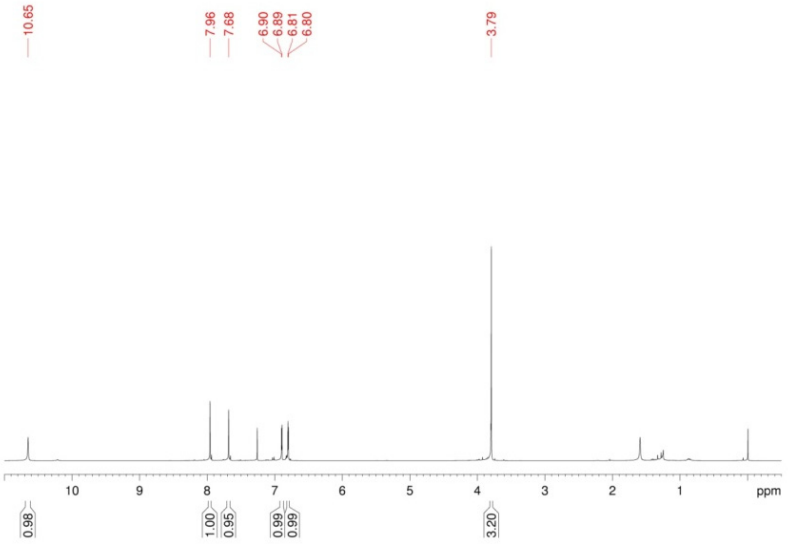


化合物 3m 的 ^{13}C NMR 谱图

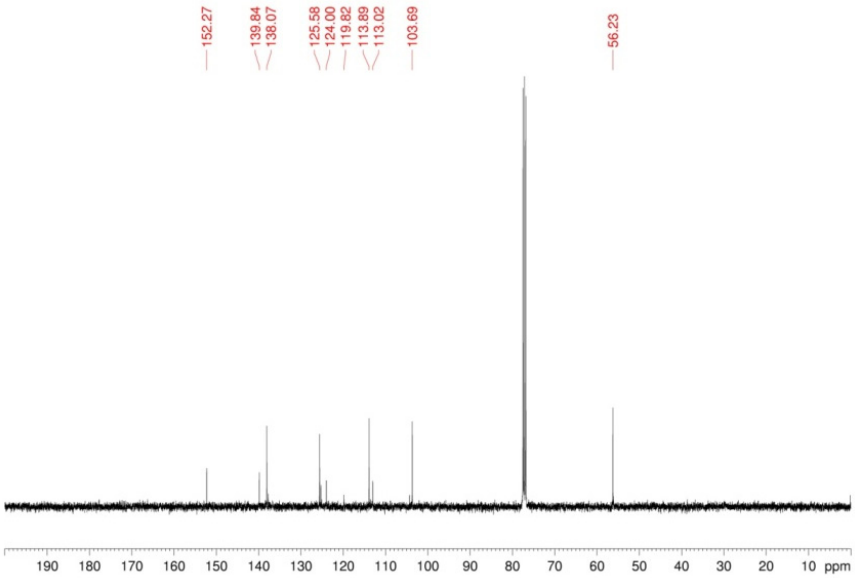


3n, 63%

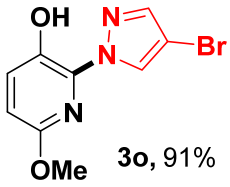
淡黄色固体 (81 mg, 63% yield), R_f = 0.75 (PE:EtOAc = 5:1), spectroscopy: ^{1}H NMR (400 MHz, $CDCl_3$, 25 ºC, δ): 10.65 (s ,1H), 7.96 (s, 1H), 7.68 (s, 1H), 6.90 (d, J = 2.84 Hz, 1H), 6.80 (d, J =2.88 Hz, 1H), 3.79 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 ºC, δ): 152.27, 139.84, 138.07, 125.58, 124.00, 119.82, 113.89, 113.02， 103.69, 56.23. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{10}H_9Cl_2N_2O_2^+$ ($[M + H]$)$^+$, 259.0036, found, 258.9874.



化合物 3n 的 ^{1}H NMR 谱图

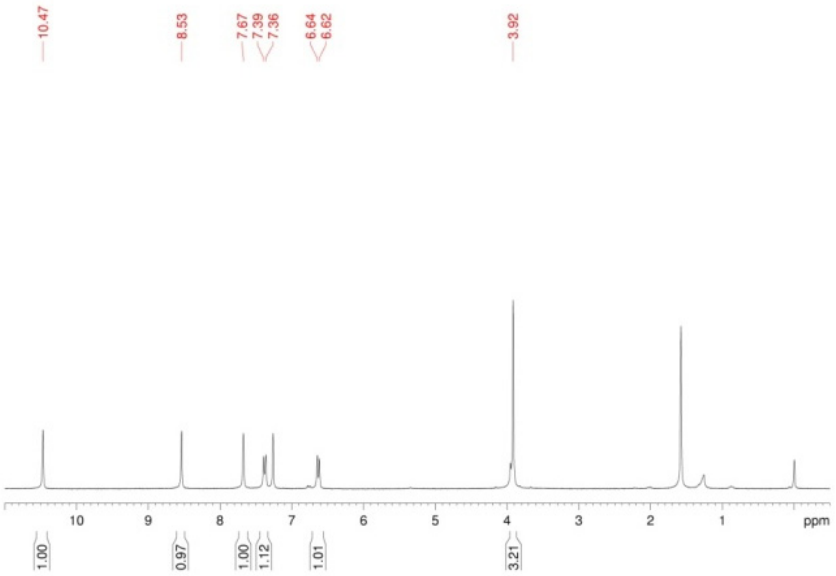


化合物 3n 的 ^{13}C NMR 谱图

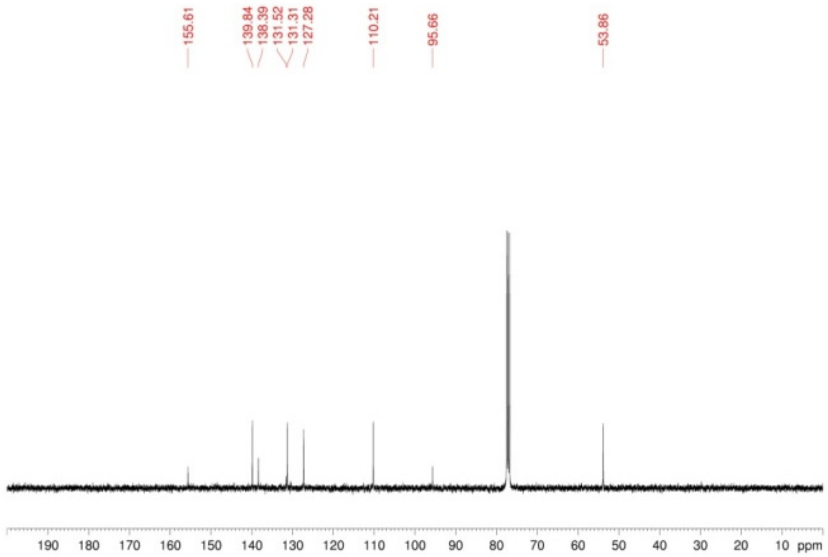


3o, 91%

淡黄色固体 (123 mg, 91% yield), R_f = 0.8 (PE:EA = 5:1), spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 10.47 (s, 1H), 8.53 (s, 1H), 7.67 (s, 1H), 7.38 (d, *J* = 8.61 Hz, 1H), 6.63 (d, *J* = 8.55 Hz, 1H), 3.92 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25ºC, δ): 155. 1, 139.84, 138.39, 131.52, 131.31, 127.28, 110.21, 95.66, 53.86. Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_9H_8BrN_3O_2^-$ ([M - H])$^-$, 267.9727, found, 267.9731.



化合物 3o 的 ^{1}H NMR 谱图



化合物 3o 的 ^{13}C NMR 谱图