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SUPPORTING INFORMATION

Room-Temperature Palladium-Catalyzed Direct 2-Arylation of Benzoxazoles with Aryl and Heteroaryl Bromides

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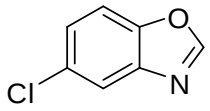
TABLE OF CONTENTS

1. General Methods

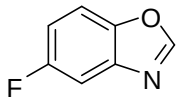
All reactions were conducted under an inert atmosphere of dry nitrogen. Anhydrous dioxane and cyclopentyl methyl ether (CPME) were purchased from Sigma-Aldrich and used without further purification. Dimethoxyethane (DME) tetrahydrofuran (THF) and toluene were dried through activated alumina columns under nitrogen. Unless otherwise stated, Silica gel (Silicaflash, P60, 40-63 μm, Silicycle) was used for air-flashed chromatography. Solvents were commercially available and used as received without further purification. Chemicals were purchased from Sigma-Aldrich, Acros, or Matrix Scientific and solvents were obtained from Fisher Scientific. Thin-layer chromatography was performed on Whatman precoated silica gel 60 F-254 plates and visualized by ultraviolet light. Flash chromatography was performed with Silica gel (Silicaflash, P60, 40-63 μm, Silicycle). NMR spectra were obtained using a Brüker 500 MHz Fourier-transform NMR spectrometer at the University of Pennsylvania NMR facility. The infrared spectra were obtained with KBr plates using a Perkin-Elmer Spectrum 1600 Series spectrometer. High resolution mass spectrometry (HRMS) data were obtained on a Waters LC-TOF mass spectrometer (model LCT-XE Premier) using chemical ionization (CI) or electrospray ionization (ESI) in positive or negative mode, depending on the analyte. Melting points were determined on a Unimelt Thomas-Hoover melting point apparatus and are uncorrected. Benzoxazole (99%) was purchased from Acros (Alfa Aesar) and used as received. Benzoxazole derivatives were synthesized according to known procedures starting from commercially available 2-amino-phenol derivatives.[1]

2. Preparation of benzoxazoles

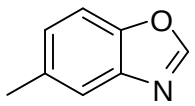
General Procedure A for the synthesis of benzoxazoles: In a 25 mL two-necked flask under N_2 was added the 2-aminophenol derivatives (1.0 g) and triethyl orthoformate (10 mL). The resulting mixture was refluxed for 4–8 h until TLC showed complete consumption of 2-aminophenol derivatives. The excess triethyl orthoformate was then removed under reduced pressure. The residue was purified by flash on silica gel column to obtain desired products.



5-Chlorobenzoxazole (1b): The reaction was performed following General Procedure A with 2-amino-4-chlorophenol (1.0 g, 6.99 mmol) in triethyl orthoformate (10 mL). The crude product was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:40) to give the product (0.90 g, 85% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.72 (s, 1H), 7.45 (d, J = 9.0 Hz, 1H), 7.30 (d, J = 9.0 Hz, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 153.6, 148.4, 141.0, 130.0, 125.9, 120.5, 111.6 ppm. The spectroscopic data match the previously reported data.[2]

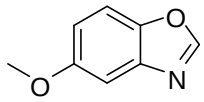


5-Fluorobenzoxazole (1c): The reaction was performed following General procedure A with 2-amino-4-fluorophenol (1.0 g, 7.87 mmol) in triethyl orthoformate (10 mL). The crude product was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:40) to give the product (0.95 g, 88% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.50 (dd, J_1 = 9.0 Hz, J_2 = 4.0 Hz, 1H), 7.45 (dd, J_1 = 8.0 Hz, J_2 = 2.5 Hz, 1H), 6.98 (dt, J_1 = 9.0 Hz, J_2 = 2.5 Hz, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 160.0 (d, J = 239.6 Hz), 153.9, 146.2, 140.8 (d, J = 12.8 Hz), 113.4 (d, J = 26.3 Hz), 111.2 (d, J = 10.0 Hz), 106.8 (d, J = 25.3 Hz), ppm. The spectroscopic data match the previously reported data.[1c]



5-Methylbenzoxazole (1d): The reaction was performed following General Procedure A with 2-amino-4-methylphenol (1.0 g, 8.13 mmol) in triethyl orthoformate (10 mL). The crude product was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:40) to give the product (0.99 g, 92% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.57 (s, 1H), 7.45 (d, J = 11.5 Hz, 1H), 7.19 (d, J = 11.5 Hz, 1H), 2.48 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 152.5, 148.2, 140.2, 134.4, 126.7, 120.4, 110.2, 21.4 ppm. The

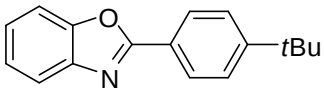
spectroscopic data match the previously reported data.[1c]

 **5-Methoxybenzoxazole (1e):** The reaction was performed following General Procedure A with 2-amino-4-methoxyphenol (1.0 g, 7.19 mmol) in triethyl orthoformate (10 mL). The crude product was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 1:40) to give the product (0.96 g, 90% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.05 (s, 1H), 7.45 (d, J = 12.5 Hz, 1H), 7.25 (d, J = 3.5 Hz, 1H), 6.98 (dd, J_1 = 12.5 Hz, J_2 = 3.5 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 157.4, 153.2, 144.6, 140.9.4, 114.5, 111.0, 103.2, 55.9 ppm. The spectroscopic data match the previously reported data [1c]

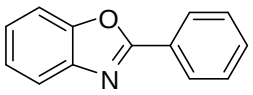
3. Procedure and characterization of Pd-catalyzed arylation of benzoxazoles

General Procedure B for the Pd-catalyzed arylation of benzoxazoles:

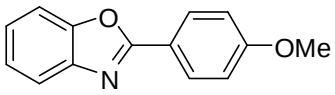
An oven-dried 10 mL reaction vial equipped with a stir bar was charged with benzoxazole (0.12 mmol) and NaO*t*Bu (23.0 mg, 0.24 mmol, 2 equiv) in a dry box under a nitrogen atmosphere. A solution (from a stock solution) of $Pd(OAc)_2$ (1.12 mg, 0.0050 mmol) and NiXantphos (4.14 mg, 0.0075 mmol) in 1 mL of dry DME was taken up by syringe and added to the reaction vial. The vial was then sealed with a septum and removed from the dry box. After stirring for 5 min at 24 ℃, aryl bromide (0.1 mmol, 1.0 equiv) was added to the reaction mixture by syringe. Note that solid aryl bromides were added to the reaction vial prior to addition of NaO*t*Bu. The reaction mixture was stirred for 12 h at room temperature (24 ℃), quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with additional ethyl acetate, and the solution was concentrated *in vacuo*. The crude material was loaded onto a silica gel column and purified by flash chromatography.



2-(4-*tert*-Butylphenyl)benzoxazole (3a): The reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 1-bromo-4-*ter*t-butylbenzene (**2a**, 17.5 μL, 21.3 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 2:98) to give the product (24.5 mg, 98% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (d, *J* = 8.0 Hz, 2H), 7.76–7.78 (m, 1H), 7.54–7.58 (m, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.26–7.34 (m, 2H), 1,38 (s, 9H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 163.2, 155.1, 150.7, 142.2, 127.5, 125.9, 124.8, 124.4, 124.4, 119.9, 110.5, 35.0, 31.1 ppm. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data.[3]

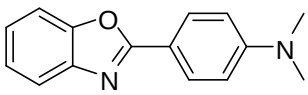


2-Phenylbenzoxazole (3b): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and bromobenzene (**2b**, 10.5 μL, 15.7 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 2:98) to give the product (17.8 mg, 92% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23–8.27 (m, 2H), 7.75–7.77 (m, 1H), 7.55–7.58 (m, 1H), 7.51–7.54 (m, 3H), 7.32–7.36 (m, 2H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 162.9, 150.7, 142.0, 131.4, 128.8, 127.5, 127.1, 125.0, 124.4, 119.9, 110.5 ppm. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data.[4]

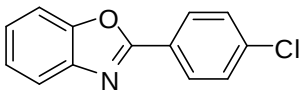


2-(4-Methoxyphenyl)benzoxazole (3c): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 1-bromo-4-methoxybenzene (**2c**, 12.5 μL, 18.7 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 3:97) to give the product (19.8 mg, 88% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18 (d, *J* = 8.0 Hz, 2H), 7.71–7.74 (m,

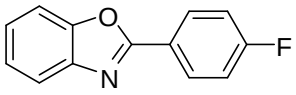
1H), 7.51–7.55 (m, 1H), 7.29–7.33 (m, 2H), 7.00 (d, J = 8.0 Hz, 2H), 3.87 (s, 3H) ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 163.1, 162.2, 150.6, 142.2, 129.3, 124.5, 124.3, 119.6, 119.5, 114.2, 110.2, 55.3 ppm. The ^{1}H and $^{13}C\{^{1}H\}$ NMR data for this compound match the literature data.[5]



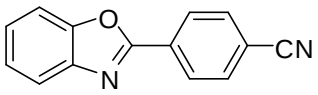
4-(Benzoxazol-2-yl)-*N*,*N*-dimethylaniline (3d): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 4-bromo-*N*,*N*-dimethylaniline (**2d**, 20.0 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 5:95) to give the product (20.4 mg, 86% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (d, J = 9.0 Hz, 2H), 7.68 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 9.0 Hz, 1H), 7.24–7.28 (m, 2H), 6.75 (d, J = 9.0 Hz, 2H), 3.05 (s, 6H) ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 164.1, 152.3, 150.5, 142.5, 129.0, 124.0, 123.7, 119.0, 114.1, 111.5, 110.0, 40.0 ppm. The ^{1}H and $^{13}C\{^{1}H\}$ NMR data for this compound match the literature data. [6]



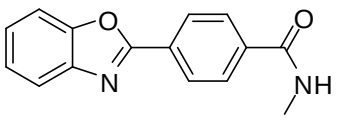
2-(4-Chlorophenyl)benzoxazole (3e): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 1-bromo-4-chlorobenzene (**2e**, 19.1 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 2:98) to give the product (22.7 mg, 99% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (d, J = 8.5 Hz, 2H), 7.73–7.76 (m, 1H), 7.53–7.57 (m, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.32–7.36 (m, 2H) ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 161.9, 150.7, 141.9, 137.6, 129.1, 128.7, 125.6, 125.2, 124.6, 120.0, 110.5 ppm. The ^{1}H and $^{13}C\{^{1}H\}$ NMR data for this compound match the literature data.[7]



2-(4-Fluorophenyl)benzoxazole (3f): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 1-bromo-4-fluorobenzene (**2f**, 13.0 μL, 17.5 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 2:98) to give the product (17.2 mg, 81% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22–8.26 (m, 2H), 7.74–7.76 (m, 1H), 7.55–7.56 (m, 1H), 7.32–7.36 (m, 2H), 7.17–7.22 (m, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 164.7 (d, J = 250.0 Hz), 162.0, 150.7, 142.0, 129.7 (d, J = 9.0 Hz), 125.0, 124.5, 123.4, 119.9, 116.1 (d, J = 22.0 Hz), 110.4 ppm. The 1H and ^{13}C{1H} NMR data for this compound match the literature data.[3]

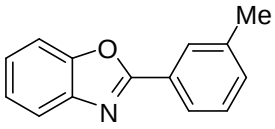


4-(Benzoxazol-2-yl)benzonitrile (3g): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 4-bormobenzonitrile (**2g**, 18.2 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 5:95) to give the product (18.9 mg, 86% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (d, J = 7.5 Hz, 2H), 7.76–7.83 (m, 3H), 7.59 (d, J = 7.5 Hz, 1H), 7.38–7.42 (m, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.8, 150.8, 141.8, 132.6, 131.0, 127.8, 126.0, 125.0, 120.5, 118.0, 114.6, 110.7 ppm. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data.[8]

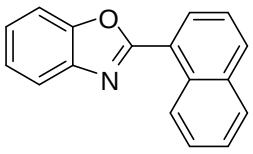


4-(Benzoxazol-2-yl)-*N*-methylbenzamide (3h): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 4-bromo-*N*-methylbenzamide (**2h**, 21.4 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 8:92) to give the product (15.1 mg, 60% yield) as a

yellow solid. R_f = 0.30 (EtOAc:Hexane = 2:1); m.p. = 163–165 ℃; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (d, *J* = 7.5 Hz, 2H), 8.18 (d, *J* = 7.5 Hz, 2H), 7.77–7.80 (m, 1H), 7.57–7.60 (m, 1H), 7.35–7.40 (m, 2H), 3.95 (s, 3H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.2, 161.8, 150.8, 141.9, 132.4, 130.9, 130.0, 127.4, 125.6, 124.8, 120.3, 110.6, 52.3 ppm. IR (thin film): 3434, 3091, 3065, 1612, 1575, 1515, 1448, 1406, 1365, 1277, 1055, 864, 798, 722, 590 cm^{-1}; HRMS calculated for $C_{15}H_{13}N_2O_2$, 253.0977, found 253.0978, $[M+H]^+$.

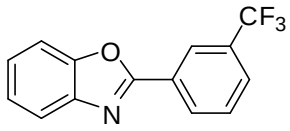


2-*m*-Tolylbenzoxazole (3i): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 1-bromo-3-methylbenzene (**2i**, 12.2 μL, 17.1 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 3:97) to give the product (17.7 mg, 85% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (s, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.74–7.77 (m, 1H), 7.55–7.58 (m, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.32–7.35 (m, 3H), 2.44 (s, 3H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 163.1, 150.6, 142.0, 138.6, 132.2, 128.7, 128.1, 126.9, 124.9, 124.7, 124.4, 119.8, 110.4, 21.1 ppm. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data.[3]

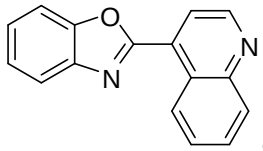


2-(Naphthalen-1-yl)benzoxazole (3j): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 1-bromonaphthalene (**2j**, 14.0 μL, 20.7 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 2:98) to give the product (20.5 mg, 84% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.45 (d, *J* = 7.5 Hz, 1H), 8.42 (d, *J* = 7.5 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.87–7.88 (m, 1H) 7.70–7.72 (m, 1H),

7.62–7.64 (m, 1H), 7.60–7.62 (m, 3H), 7.38–7.40 (m, 2H) ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 162.7, 150.1, 142.2, 133.9, 132.2, 130.6, 129.2, 128.5, 127.8, 126.3, 126.2, 125.2, 124.8, 124.4, 123.5, 120.2, 110.4 ppm. The ^{1}H and $^{13}C\{^{1}H\}$ NMR data for this compound match the literature data. [9]

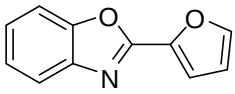


2-(2-(Trifluoromethyl)phenyl)benzoxazole (3k): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 1-bromo-2-(trifluoromethyl)benzene (**2k**, 13.6 μL, 22.5 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 5:95) to give the product (22.3 mg, 85% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.42 (d, *J* = 7.5 Hz, 1H), 7.76–7.79 (m, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.56–7.60 (m, 1H), 7.35–7.39 (m, 2H)ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 161.4, 150.7, 141.8, 131.9, 131.8, 130.5, 129.4 (q, *J* = 32.5 Hz), 128.0, 127.8 (q, *J* = 3.5 Hz), 125.6, 124.8, 124.4 (q, *J* = 280.5 Hz), 120.2, 110.6 ppm. The ^{1}H and $^{13}C\{^{1}H\}$ NMR data for this compound match the literature data. [10]

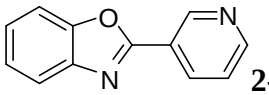


2-(Quinolin-4-yl)benzoxazole (3l): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 4-bromoquinoline (**2l**, 20.8 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 5:95) to give the product (22.6 mg, 92% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.46 (d, *J* = 8.0 Hz, 1H), 9.42 (s, 1H), 9.36 (s, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 7.5 Hz, 1H), 7.86-7.88 (m, 1H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.65–7.68 (m, 1H), 7.40–7.41 (m, 2H) ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 161.0, 155.6, 150.1, 145.2, 142.1, 132.8, 132.2, 128.4, 128.3, 127.9, 125.7, 125.6, 124.7, 120.3, 117.8,

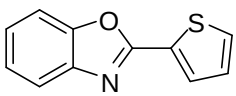
110.7 ppm. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data.[11]



2-(Furan-2-yl)benzoxazole (3m): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 2-bromofuran (**2m**, 9.0 μL, 14.7 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 8:92) to give the product (18.2 mg, 98% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71–7.75 (m, 1H), 7.65 (s, 1H), 7.52–7.55 (m, 1H), 7.31–7.35 (m, 2H), 7.25 (d, J = 3.0 Hz, 1H), 6.59 (d, J = 3.0 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 155.2, 150.0, 145.6, 142.5, 141.5, 125.1, 124.7, 120.0, 114.1, 112.1, 110.4 ppm. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data. [12]

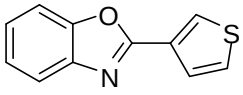


2-(Pyridin-3-yl)benzoxazole (3n): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 3-bromopyridine (**2n**, 9.0 μL, 15.8 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 10:90) to give the product (17.0 mg, 87% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.48 (s, 1H), 8.76 (d, J = 5.0 Hz, 1H), 8.51 (d, J = 8.0 Hz, 1H), 7.78–7.90 (m, 1H), 7.62–7.64 (m, 1H), 7.46 (dd, J_1 = 8.0 Hz, J_2 = 5.0 Hz, 1H), 7.36–7.40 (m, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.7, 152.0, 150.7, 148.8, 141.8, 134.7, 125.7, 124.9, 123.6, 123.5, 120.3, 110.7 ppm. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data. [13]

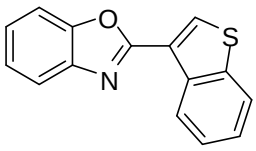


2-(Thiophen-2-yl)benzoxazole (3o): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 2-bromothiophene (**2o**, 10.0 μL, 16.3 mg, 0.1 mmol, 1.0 equiv). The crude

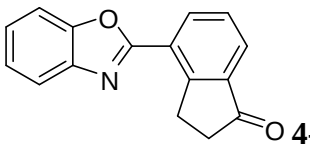
material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 8:92) to give the product (17.9 mg, 89% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, *J* = 4.5 Hz, 1H), 7.72–7.35 (m, 1H), 7.53–7.57 (m, 2H), 7.32–7.36 (m, 2H), 7.18 (t, *J* = 4.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 159.0, 150.4, 142.0, 130.2, 129.9, 129.6, 128.2, 125.0, 124.7, 119.8, 110.4 ppm. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data. [14]



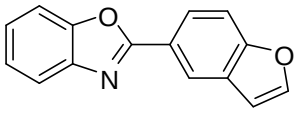
2-(Thiophen-3-yl)benzoxazole (3p): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 3-bromothiophene (**2p**, 9.5 μL, 16.3 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 8:92) to give the product (15.0 mg, 75% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.78 (d, *J* = 4.5 Hz, 1H), 7.72–7.35 (m, 1H), 7.52–7.56 (m, 1H), 7.42–7.45 (m, 1H), 7.31–7.34 (m, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 159.6, 150.3, 141.8, 129.2, 127.9, 126.8, 126.5, 124.9, 124.4, 119.8, 110.3 ppm. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data. [14]



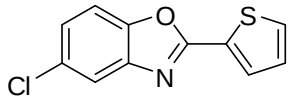
2-(Benzo[b]thiophen-3-yl)benzoxazole (3q): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 3-bromobenzo[b]thiophene (**2q**, 13.0 μL, 21.3 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 8:92) to give the product (23.8 mg, 95% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.02 (d, *J* = 8.0 Hz, 1H), 8.42 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.83 (s, 1H), 7.55–7.59 (m, 2H), 7.47 (t, *J* = 8.0 Hz, 1H), 7.35–7.39 (m, 2) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 159.2, 149.9, 142.0, 140.2, 136.0, 131.3, 125.5, 125.3, 125.1, 124.9, 124.5, 123.6, 122.5, 120.1, 110.3 ppm. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data. [15]



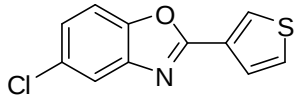
4-(Benzoxazol-2-yl)-2,3-dihydro-1*H*-inden-1-one (3r): This reaction was performed following General Procedure B in with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 4-bromo-2,3-dihydro-1*H*-inden-1-one (**2r**, 21.2 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 10:90) to give the product (18.7 mg, 75% yield) as a yellow solid. R_f = 0.40 (EtOAc:Hexane = 3:1); m.p. = 193–195 ℃; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.79–7.83 (m, 1H), 7.58–7.64 (m, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.36–7.40 (m, 2H), 3.70–3.73 (m, 2H), 2.78–2.81 (m, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 206.4, 161.3, 154.6, 150.2, 141.9, 138.4, 134.0, 127.8, 126.3, 125.5, 125.4, 124.7, 120.3, 110.5, 36.1, 27.5 ppm; IR (thin film): 1710, 1469, 1240, 1152, 7430 cm^{-1}; HRMS calculated for $C_{16}H_{12}NO_2$, 250.0869, found 250.0868, $[M+H]^+$.



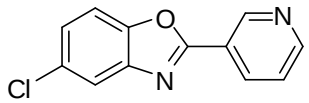
2-(Benzofuran-5-yl)benzoxazole (3s): This reaction was performed following General Procedure B with benzoxazole (**1a**, 14.3 mg, 0.12 mmol, 1.2 equiv) and 5-bromobenzofuran (**2s**, 19.8 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 8:92) to give the product (21.2 mg, 90% yield) as a yellow solid. R_f = 0.30 (EtOAc:hexane = 3:1); m.p. = 145–147 ℃; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (s, 1H), 8.24 (d, *J* = 9.0 Hz, 1H), 7.74–7.78 (m, 1H), 7.70 (s, 1H), 7.63 (d, *J* = 9.0 Hz, 1H), 7.54–7.58 (m, 1H), 7.28–7.31 (m, 2H), 6.87 (s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 163.5, 156.7, 150.8, 146.3, 142.3, 128.0, 124.8, 124.5, 124.2, 122.2, 121.2, 119.8, 112.0, 110.4, 107.0 ppm; IR (thin film): 1614, 1558, 1529, 1454, 1441, 1244, 1261, 1158, 1128, 1108, 1025, 804, 747 cm^{-1}; HRMS calculated for $C_{15}H_{10}NO_2$, 236.0712, found 236.0710, $[M+H]^+$.



5-Chloro-2-(thiophen-2-yl)benzoxazole (3t): This reaction was performed following General Procedure B with 5-chlorobenzoxazole (**1b**, 18.4 mg, 0.12 mmol, 1.2 equiv) and 2-bromothiophene (**2o**, 10.0 μL, 16.3 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 5:95) to give the product (21.6 mg, 92% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88 (d, J = 3.5 Hz, 1H), 7.67 (s, 1H), 7.56 (d, J = 3.5 Hz, 1H), 7.43 (d, J = 8.5 Hz, 1H), 7.28 (d, J = 8.5 Hz, 1H), 7.17 (dd, J_1 = 5.0 Hz, J_2 = 3.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.2, 148.9, 143.1, 130.7, 130.4, 130.1, 129.0, 128.2, 125.2, 119.6, 111.0 ppm. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data. [16]

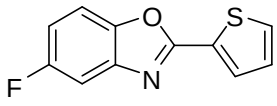


5-Chloro-2-(thiophen-3-yl)benzoxazole (3u): This reaction was performed following General Procedure B with 5-chlorobenzoxazole (**1b**, 18.4 mg, 0.12 mmol, 1.2 equiv) and 2-bromothiophene (**2p**, 9.5 μL, 16.3 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 5:95) to give the product (20.2 mg, 86% yield) as a yellow solid. R_f = 0.40 (EtOAc:Hexane = 4:1); m.p. = 133–135 ℃; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18 (d, J = 3.5 Hz, 1H), 7.75 (d, J = 5.0 Hz, 1H), 7.67–7.70 (m, 1H), 7.42–7.46 (m, 2H), 7.29 (d, J = 8.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.8, 148.8, 143.0, 129.9, 128.7, 128.6, 127.1, 126.5, 125.1, 119.7, 111.0 ppm. IR (thin film): 1721, 1553, 1453, 1409, 1277, 1194, 1108, 1053, 745 cm^{-1}; HRMS calculated for $C_{11}H_7NClNOS$, 235.9937, found 235.9939, $[M+H]^+$.

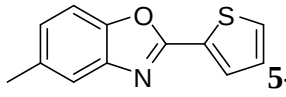


5-Chloro-2-(pyridin-3-yl)benzoxazole (3v): This reaction was performed following General Procedure B with 5-chlorobenzoxazole (**1b**, 18.4 mg, 0.12 mmol, 1.2 equiv) and 3-bromopyridine (**2n**, 9.0 μL, 15.8 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted

with EtOAc:hexanes = 5:95) to give the product (20.1 mg, 88% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.43 (s, 1H), 8.76 (d, *J* = 5.0 Hz, 1H), 8.47 (d, *J* = 7.5 Hz, 1H), 7.75 (s, 1H), 7.51 (d, *J* = 9.0 Hz, 1H), 7.44–7.47 (m, 1H), 7.33 (d, *J* = 9.0 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 161.9, 152.3, 149.2, 148.8, 142.8, 134.7, 130.3, 125.9, 123.6, 123.0, 120.1, 111.4 ppm. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data. [17]

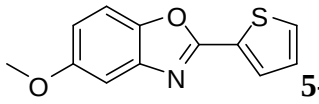


5-Fluoro-2-(thiophen-2-yl)benzoxazole (3w): This reaction was performed following General Procedure B with 5-fluorobenzoxazole (**1c**, 13.8 mg, 0.12 mmol, 1.2 equiv) and 2-bromothiophene (**2o**, 10.0 μL, 16.3 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 10:90) to give the product (19.7 mg, 90% yield) as a yellow solid. R_f = 0.50 (EtOAc:hexane = 3:1); m.p. = 127–129 ℃; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86 (d, *J* = 4.0 Hz, 1H), 7.53 (d, *J* = 5.0 Hz, 1H), 7.42 (dd, J_1 = 9.0 Hz, J_2 = 4.0 Hz, 1H), 7.36 (dd, J_1 = 9.0 Hz, J_2 = 1.0 Hz, 1H), 7.14 (dt, J_1 = 5.0 Hz, J_2 = 1.0 Hz, 1H), 7.01 (t, *J* = 9.0 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 161.1, 159.9 (d, *J* = 180.0 Hz), 146.6, 142.8 (d, *J* = 13.0 Hz), 130.6, 130.1, 129.1, 128.2, 112.4 (d, *J* = 26.0 Hz), 110.5 (d, *J* = 10.0 Hz), 106.1 (d, *J* = 25.0 Hz) ppm; IR (thin film): 1573, 1473, 1419, 1136, 1003, 853, 796, 772, 714, 697 cm^{-1}; HRMS calculated for $C_{11}H_7FNOS$, 220.0232, found 220.0234, $[M+H]^+$.



5-Methyl-2-(thiophen-2-yl)benzoxazole (3x): This reaction was performed following General Procedure B with 5-methylbenzoxazole (**1d**, 16.0 mg, 0.12 mmol, 1.2 equiv) and 2-bromothiophene (**2o**, 10.0 μL, 16.3 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 3:97) to give the product (19.8 mg, 93% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, *J* = 3.0 Hz, 1H), 7.46–7.52 (m, 2H), 7.36 (d, *J* = 8.5 Hz, 1H), 7.13 (t, *J* = 5.0 Hz, 1H), 7.09 (d, *J* = 8.5 Hz, 1H), 2.43 (s, 3H)

ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 159.0, 148.6, 142.1, 134.4, 129.9, 129.7, 129.6, 128.0, 126.0, 119.6, 109.6, 21.4 ppm. The ^1H and $^{13}C\{^1H\}$ NMR data for this compound match the literature data. [18]



5-Methoxy-2-(thiophen-2-yl)benzoxazole (3y): This reaction was performed following General Procedure B with 5-methoxybenzoxazole (**1e**, 17.9 mg, 0.12 mmol, 1.2 equiv) and 2-bromothiophene (**2o**, 10.0 μL, 16.3 mg, 0.1 mmol, 1.0 equiv). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 3:97) to give the product (21.0 mg, 91% yield) as a yellow solid. R_f = 0.45 (EtOAc:Hexane = 3:1); m.p. = 88–90 ℃; ^1H NMR (500 MHz, $CDCl_3$): δ 7.82 (d, J = 3.5 Hz, 1H), 7.49 (d, J = 5.0 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 7.18 (d, J = 2.5 Hz, 1H), 7.12 (t, J = 5.0 Hz, 1H), 6.88 (dd, J_1 = 9.0 Hz, J_1 = 2.5 Hz, 1H), 3.81 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 159.6, 157.4, 144.9, 142.7, 129.9, 129.7, 129.5, 128.1, 113.4, 110.4, 102.7, 55.8 ppm; IR (thin film): 3117, 3005, 1611, 1584, 1481, 1438, 1421, 1339, 1289, 1153, 1006, 827 cm^{-1}; HRMS calculated for $C_{12}H_{10}NOS$, 232.0432, found 232.0432 $[M+H]^+$.

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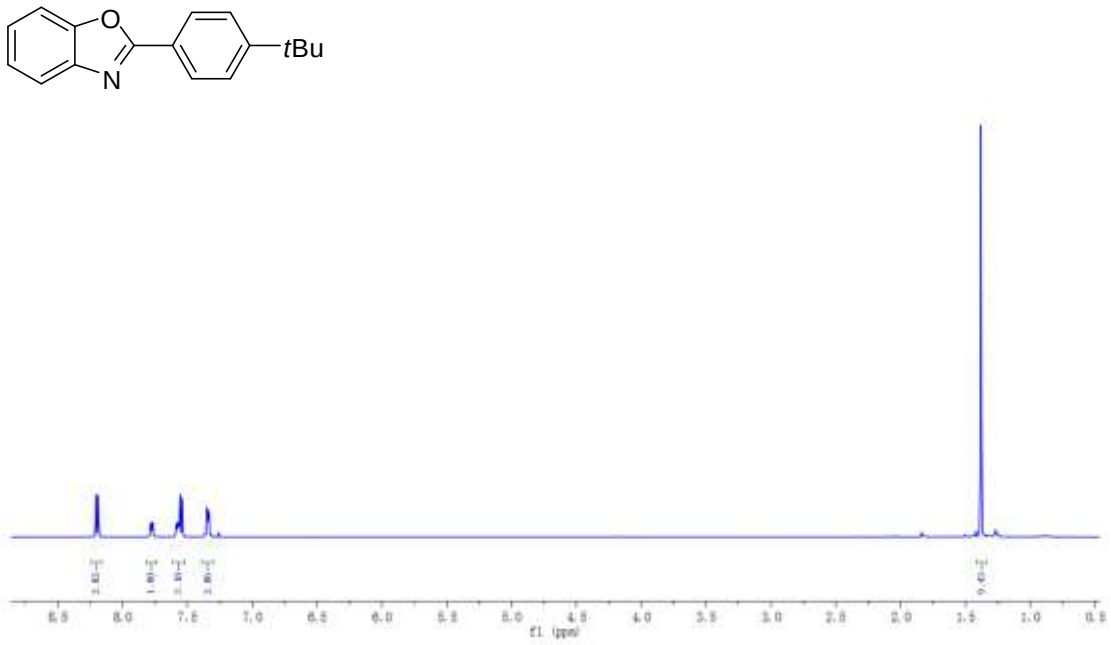
2-(4-Tert-butylphenyl)benzoxazole (3a)



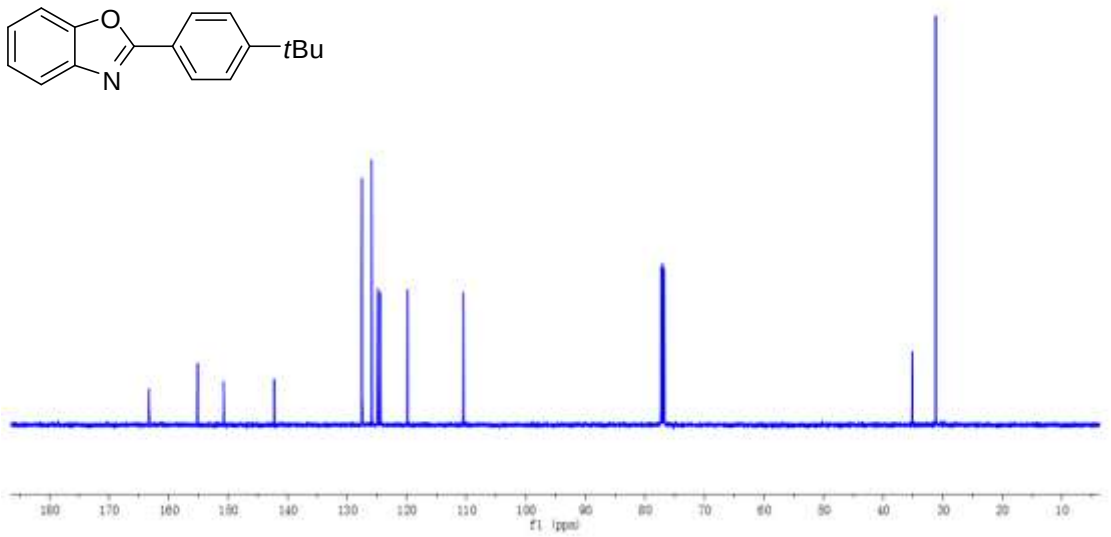
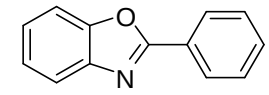
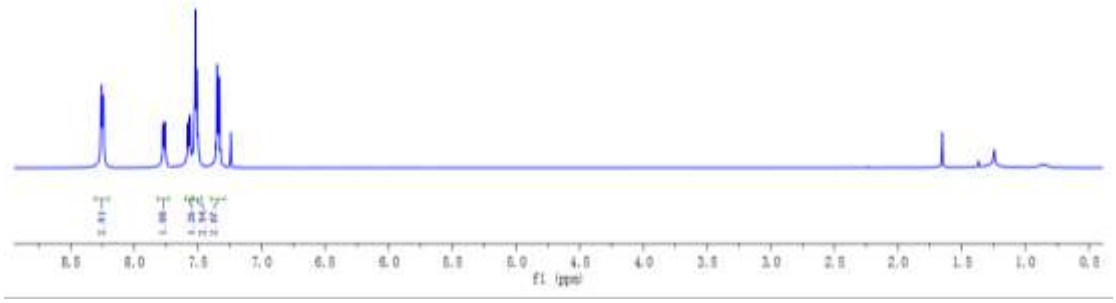
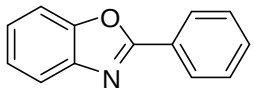


Fig. S1 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3a** in $CDCl_3$

2-Phenylbenzoxazole (3b)







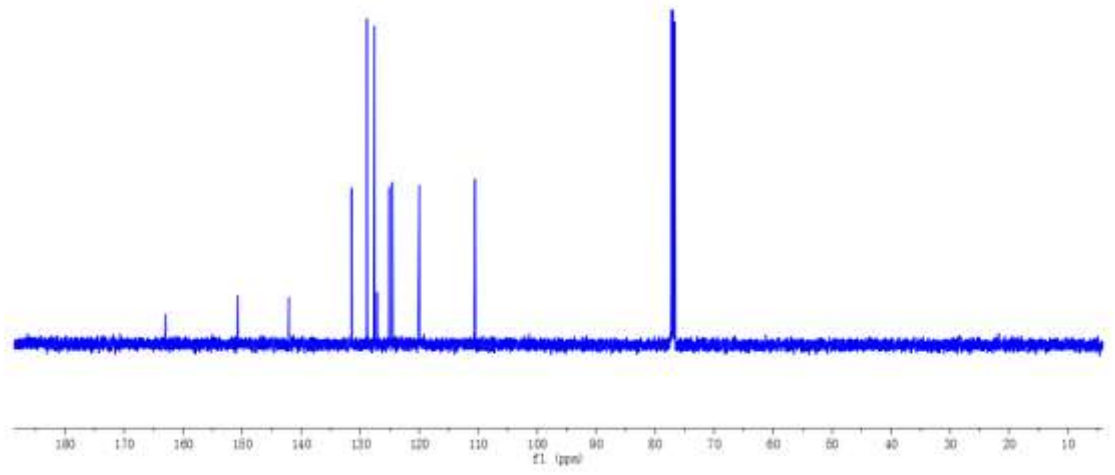
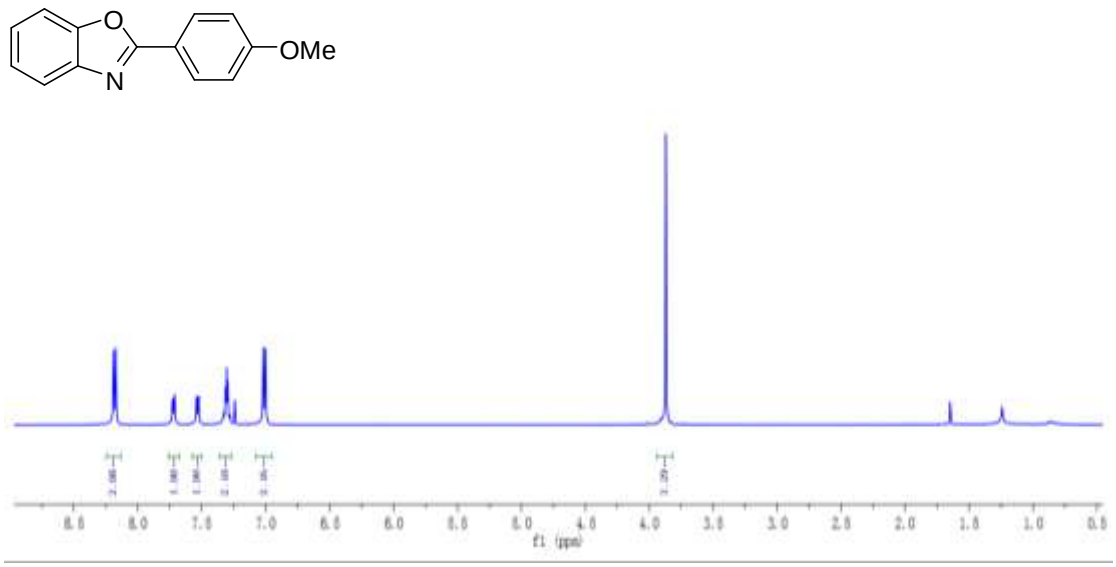


Fig. S2 ^{1}H (500 MHz) and ^{13}C{^{1}H} NMR (125 MHz) NMR spectra of **3b** in $CDCl_3$

2-(4-Methoxyphenyl)benzoxazole (3c)



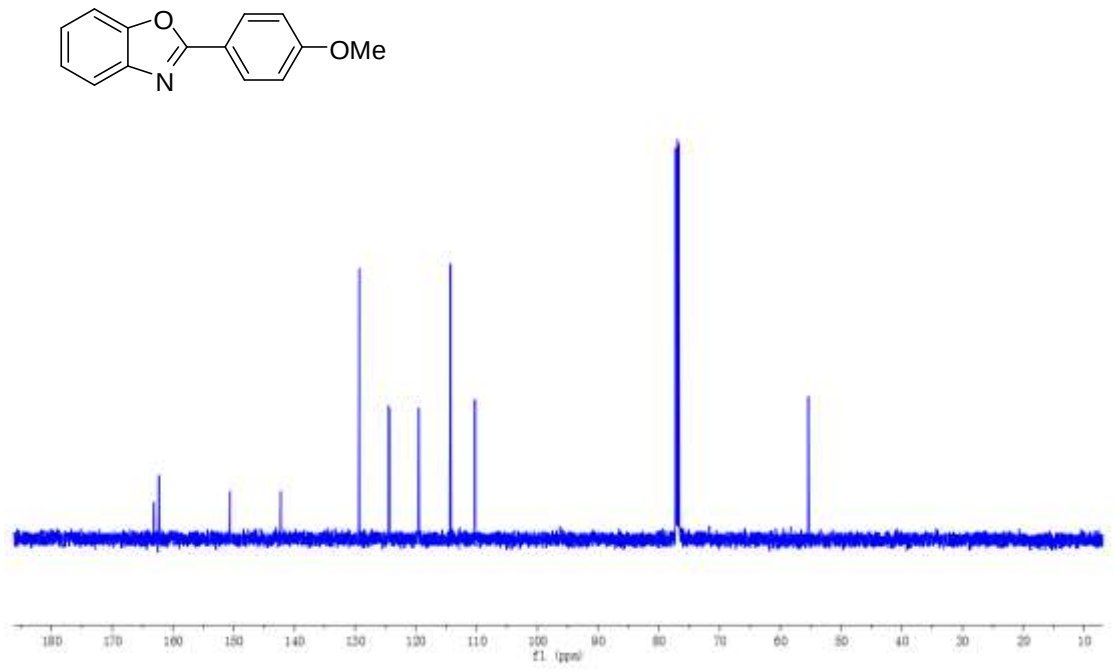


Fig. S3 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3c** in $CDCl_3$

2-(4-*N*,*N*-Dimethylanilinephenyl)benzoxazole (3d)

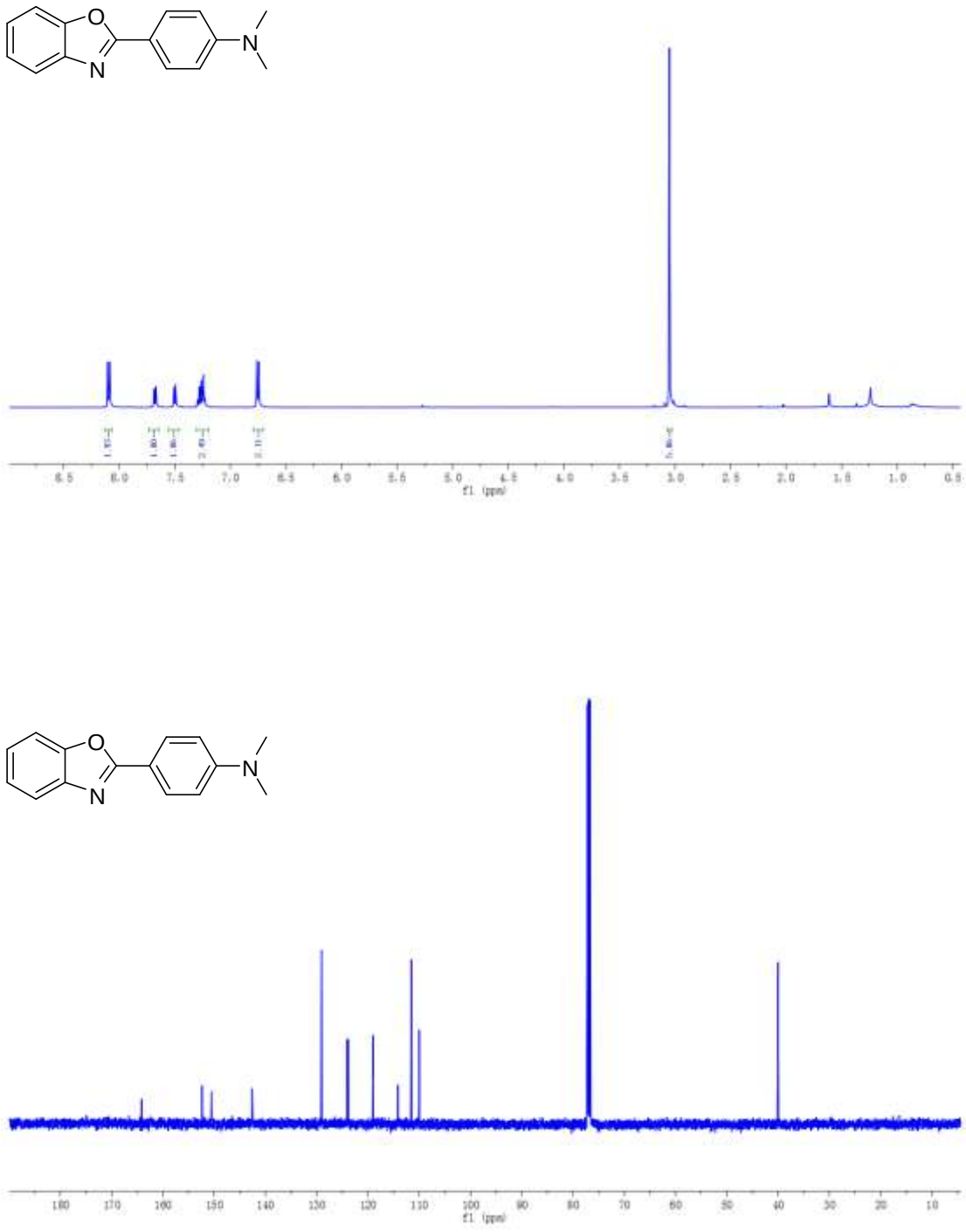
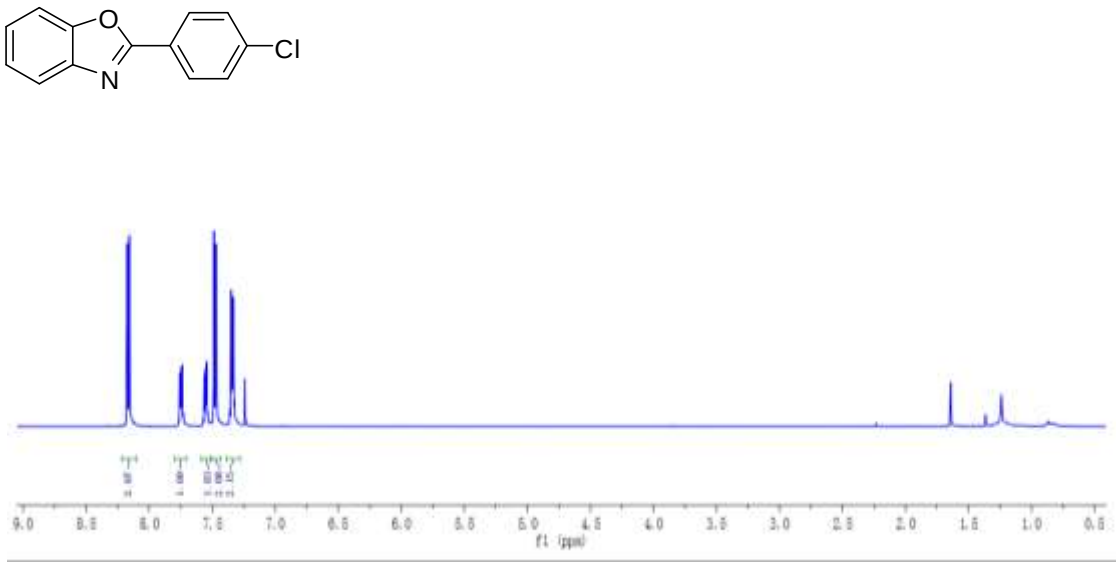


Fig. S4 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3d** in $CDCl_3$

2-(4-Chlorophenyl)benzoxazole (3e)



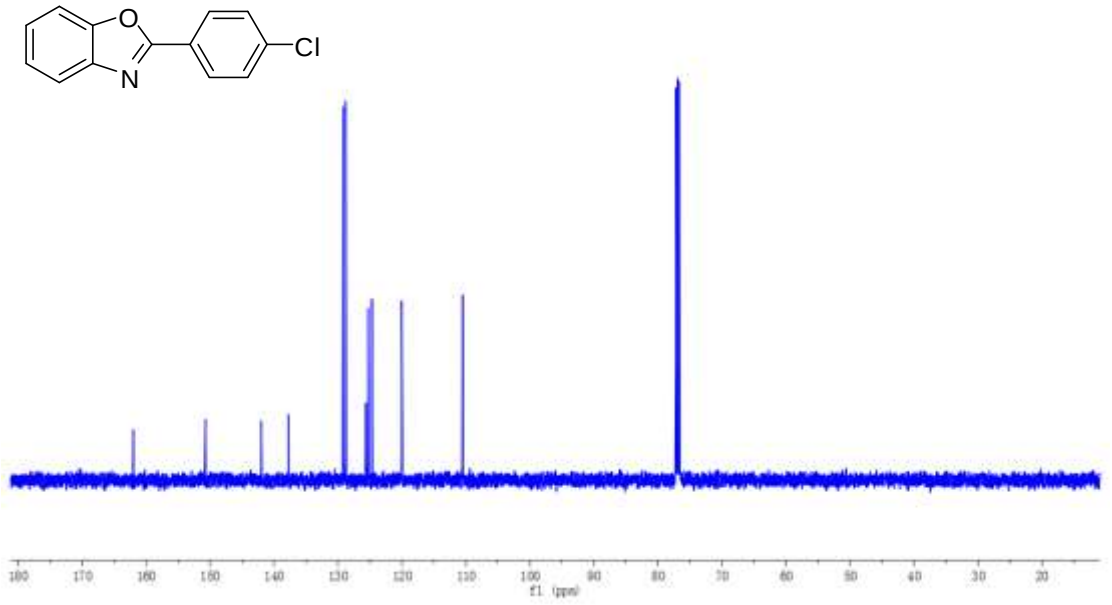
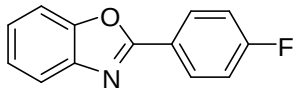
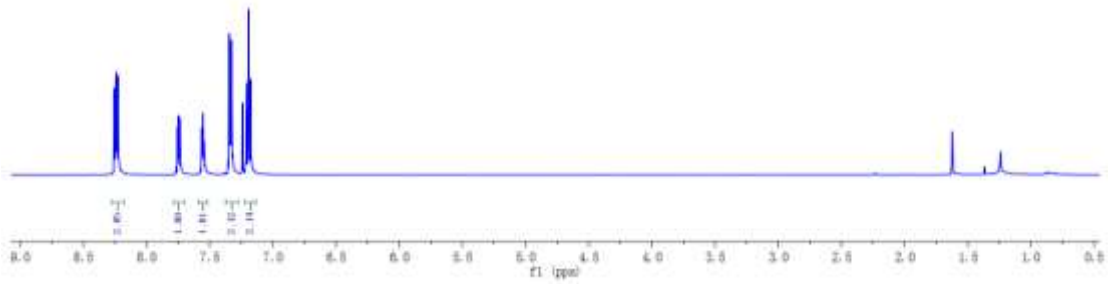


Fig. S5 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3e** in $CDCl_3$

2-(4-Fluorophenyl)benzoxazole (3f)





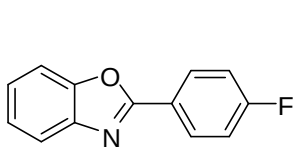
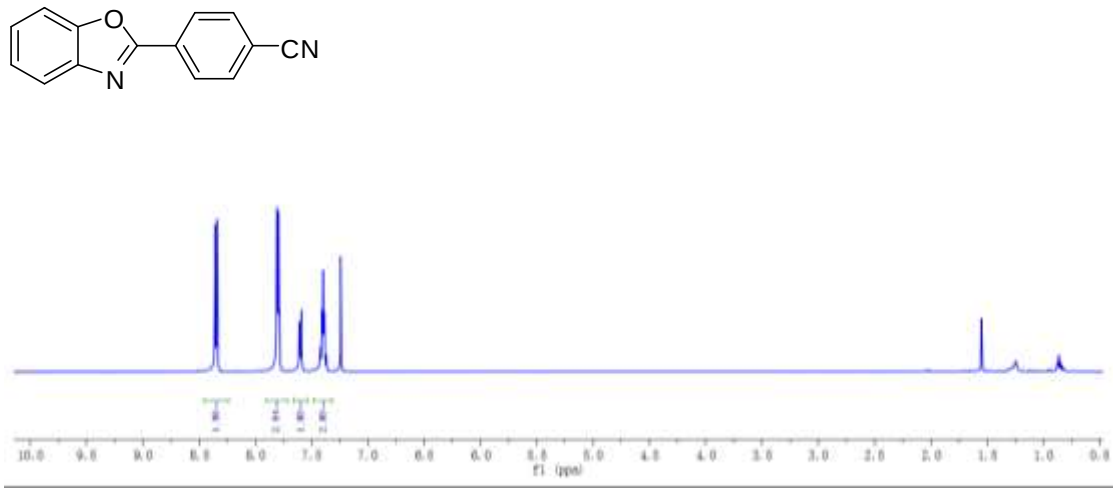


Fig. S6 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3f** in $CDCl_3$

4-(Benzoxazol-2-yl)benzonitrile (3g)



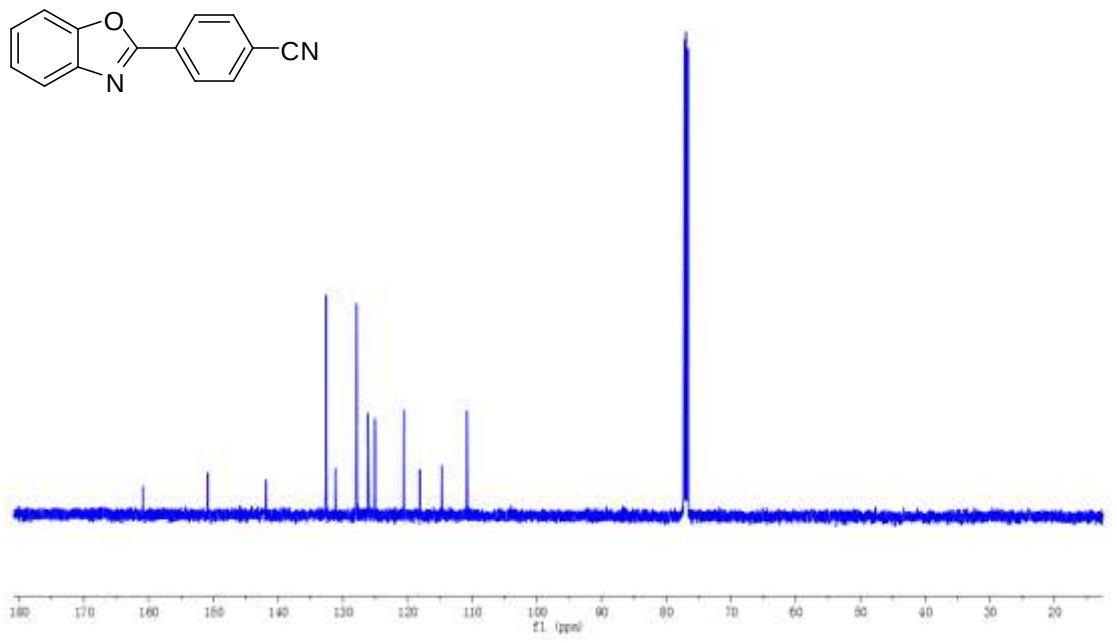
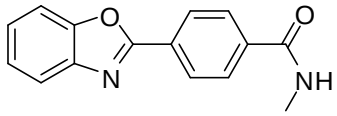
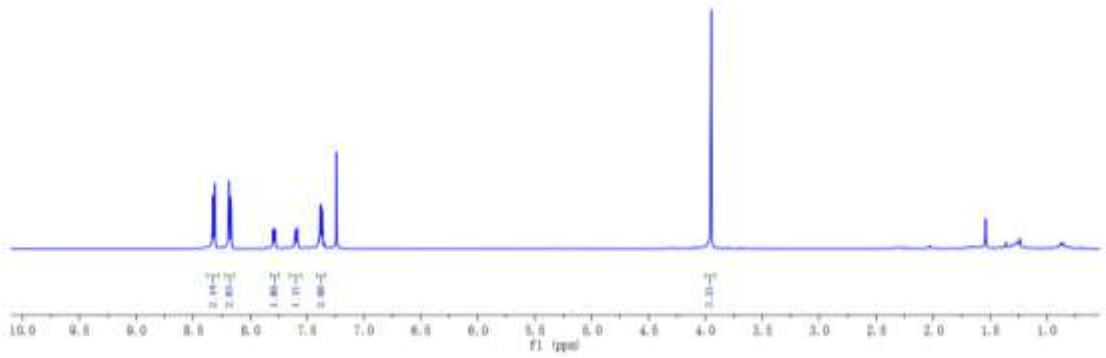


Fig. S7 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3g** in $CDCl_3$

4-(Benzoxazol-2-yl)-N-methylbenzamide (3h)





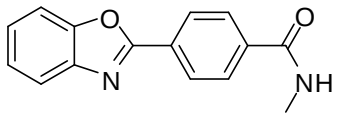
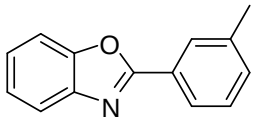
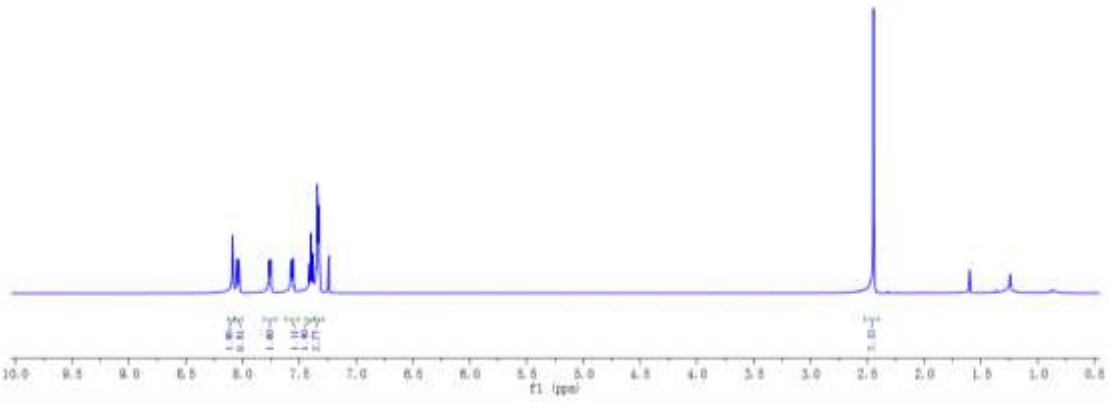
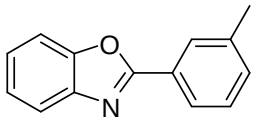


Fig. S8 ^{1}H (500 MHz) and ^{13}C{^{1}H} NMR (125 MHz) NMR spectra of **3h** in $CDCl_3$

2-*o*-Tolylbenzoxazole (3i)







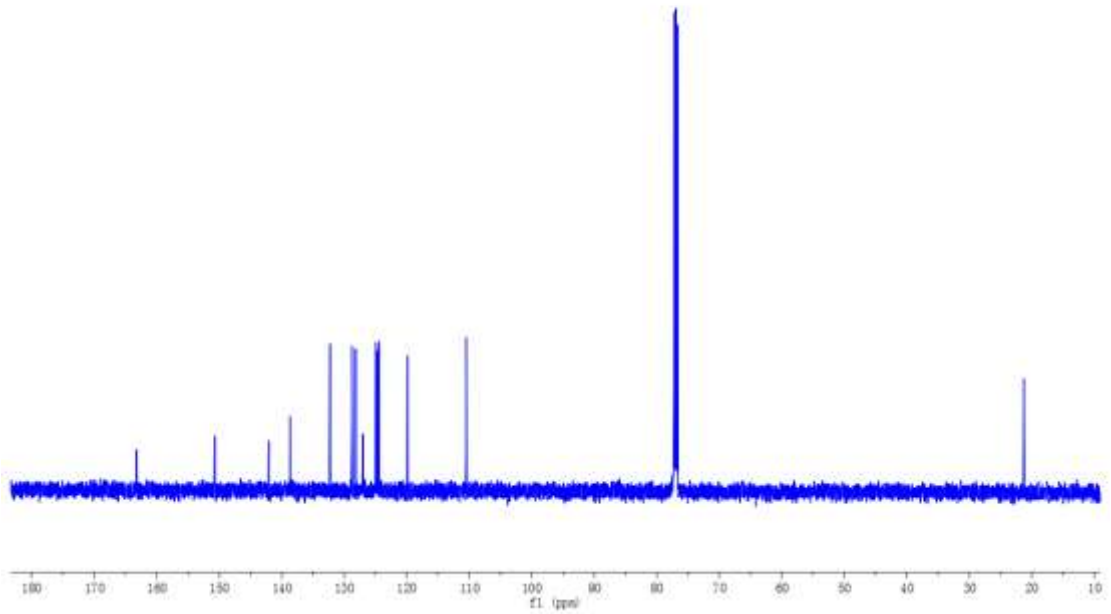


Fig. S9 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3i** in $CDCl_3$

2-(Naphthalen-1-yl)benzoxazole (3j)

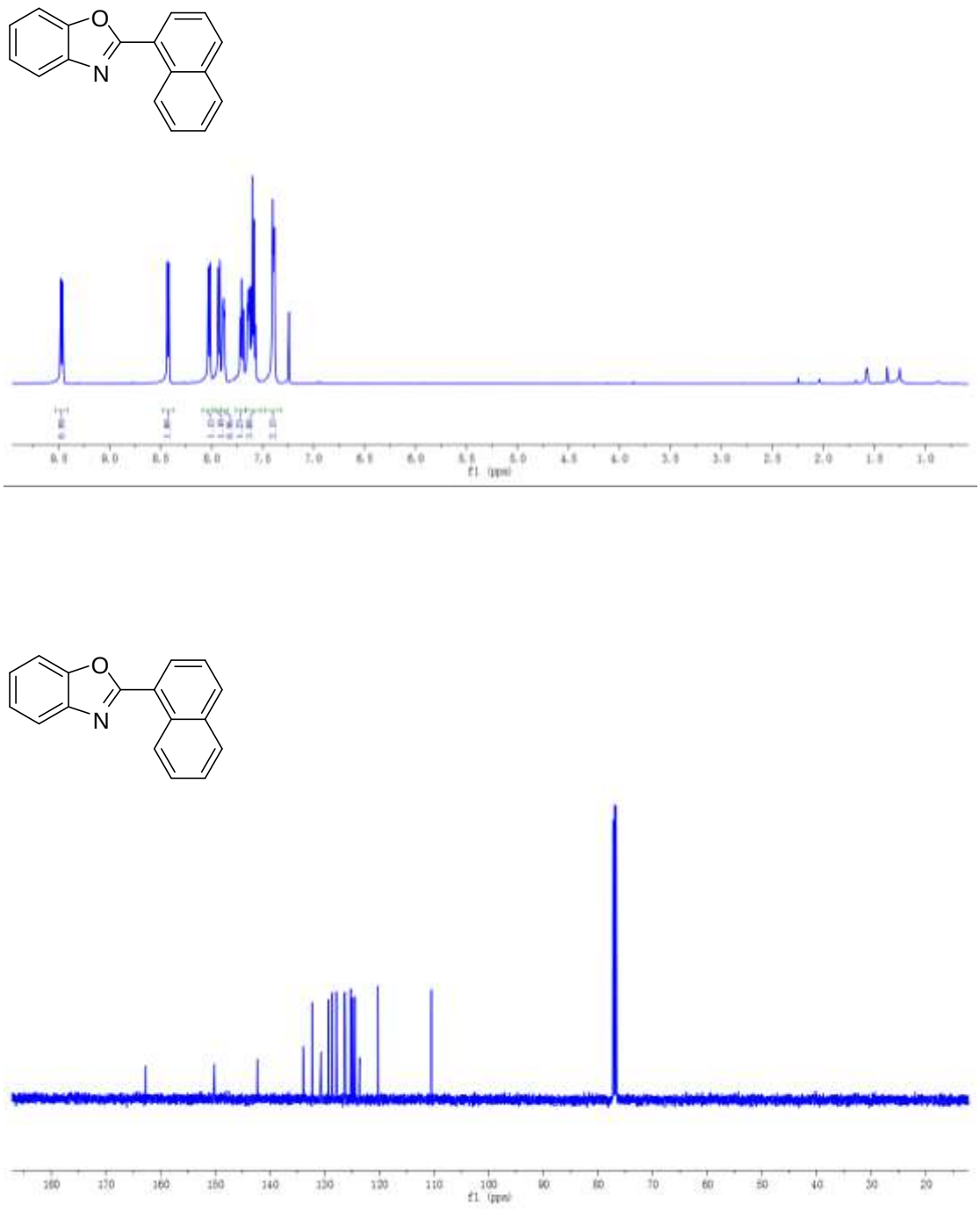
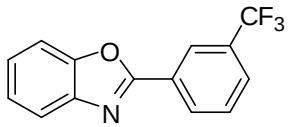
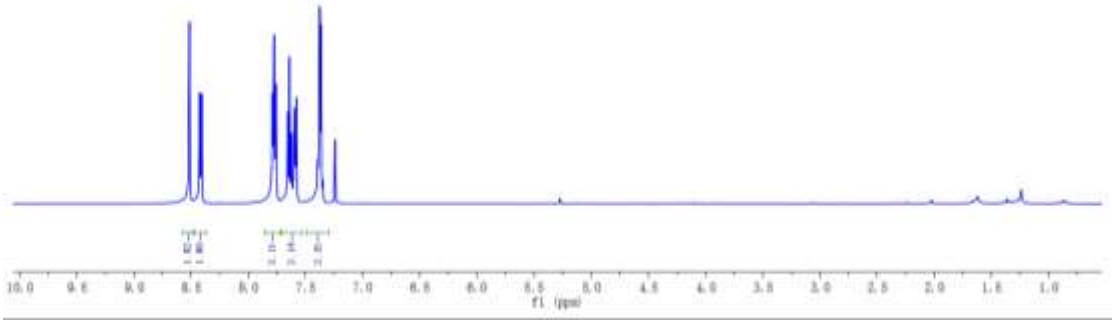
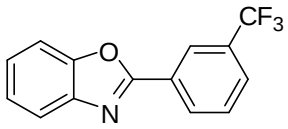


Fig. S10 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3j** in $CDCl_3$

2-(2-(Trifluoromethyl)phenyl)benzoxazole (3k)、







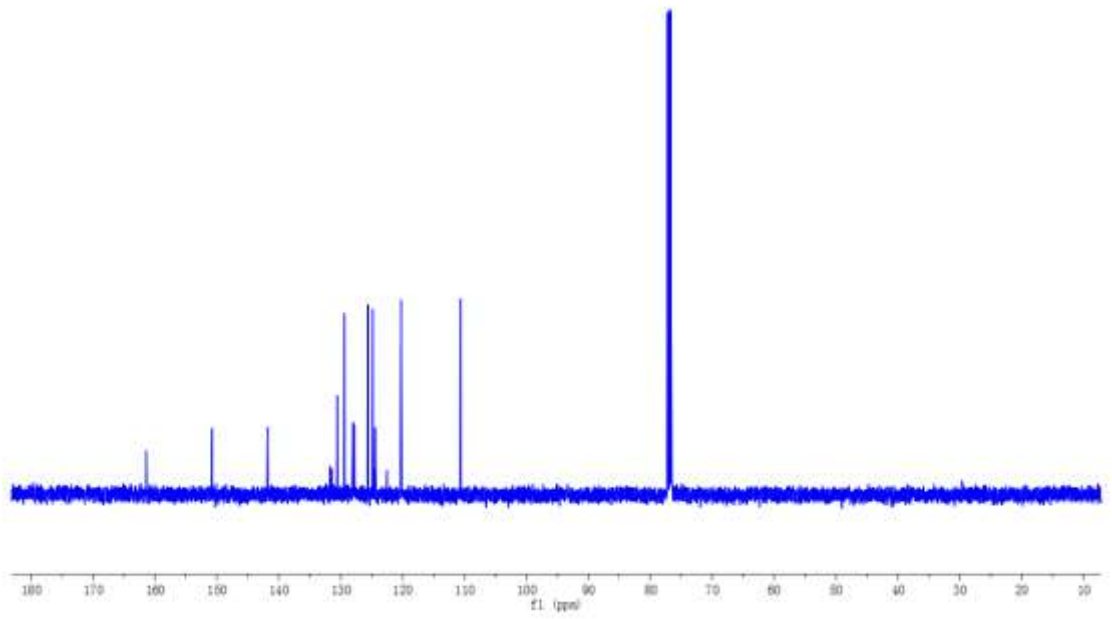


Fig. S11 ^{1}H (500 MHz) and ^{13}C{^{1}H} NMR (125 MHz) NMR spectra of **3k** in $CDCl_3$

2-(Quinolin-4-yl)benzoxazole (3l)

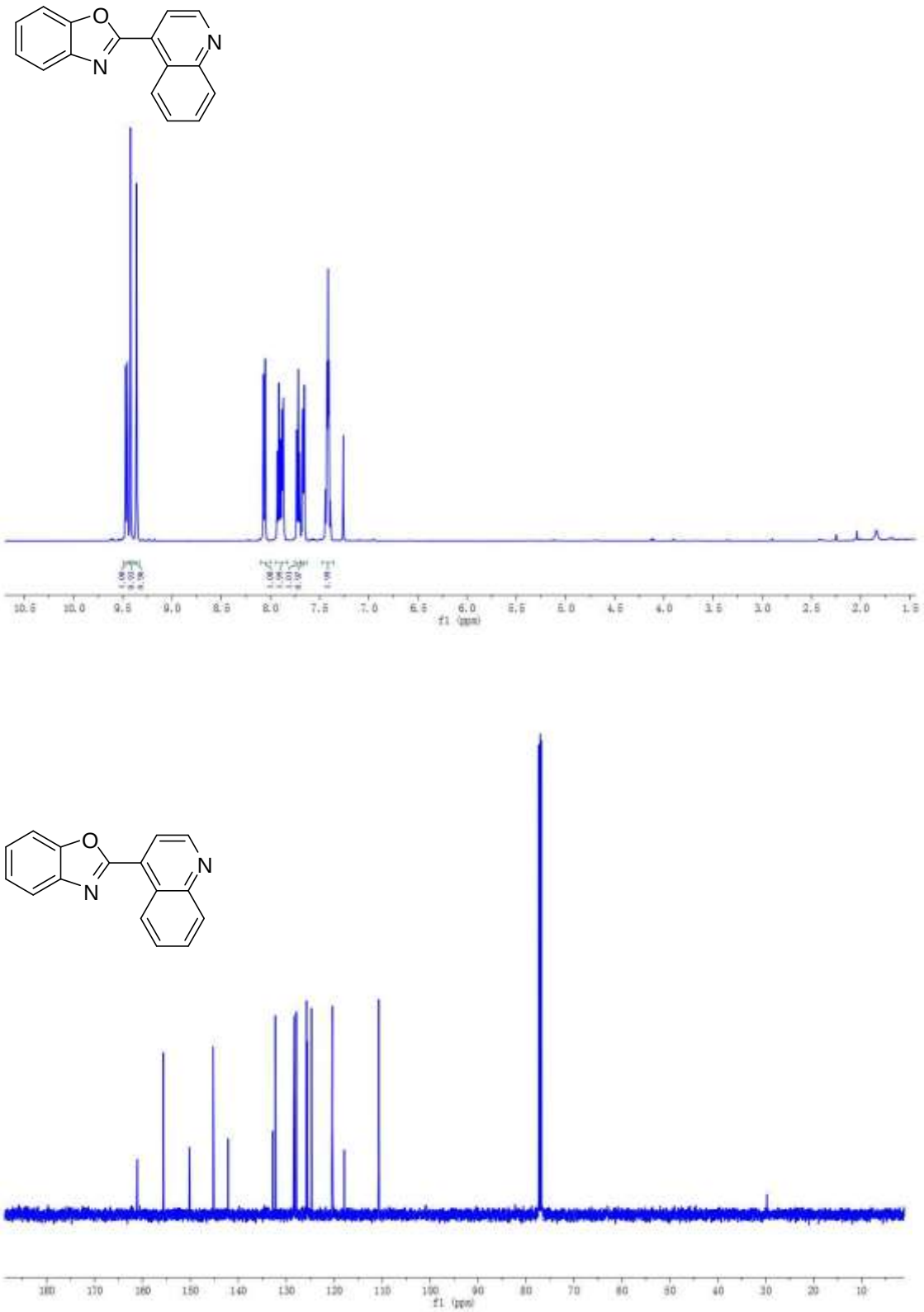
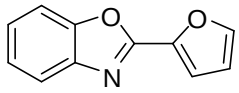
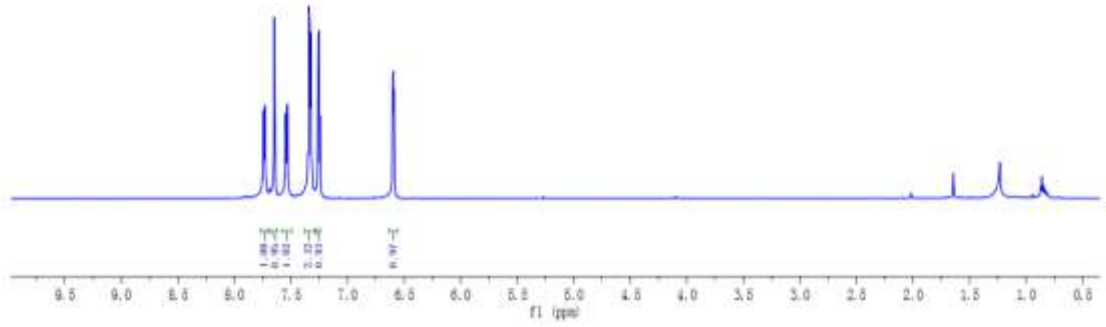
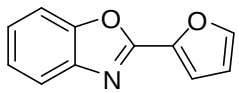


Fig. S12 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3l** in $CDCl_3$

2-(Furan-2-yl)benzoxazole (3m)







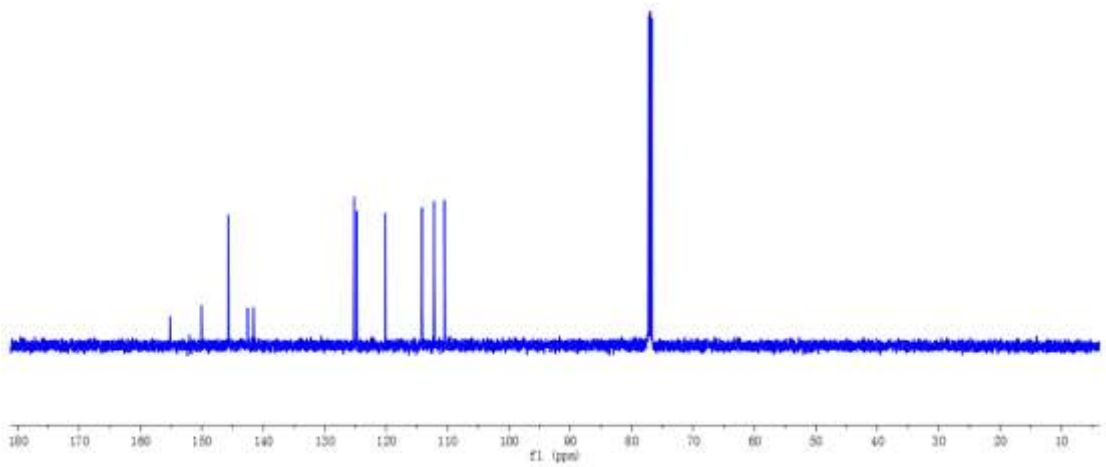


Fig. S13 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3m** in $CDCl_3$

2-(Pyridin-3-yl)benzoxazole (3n)

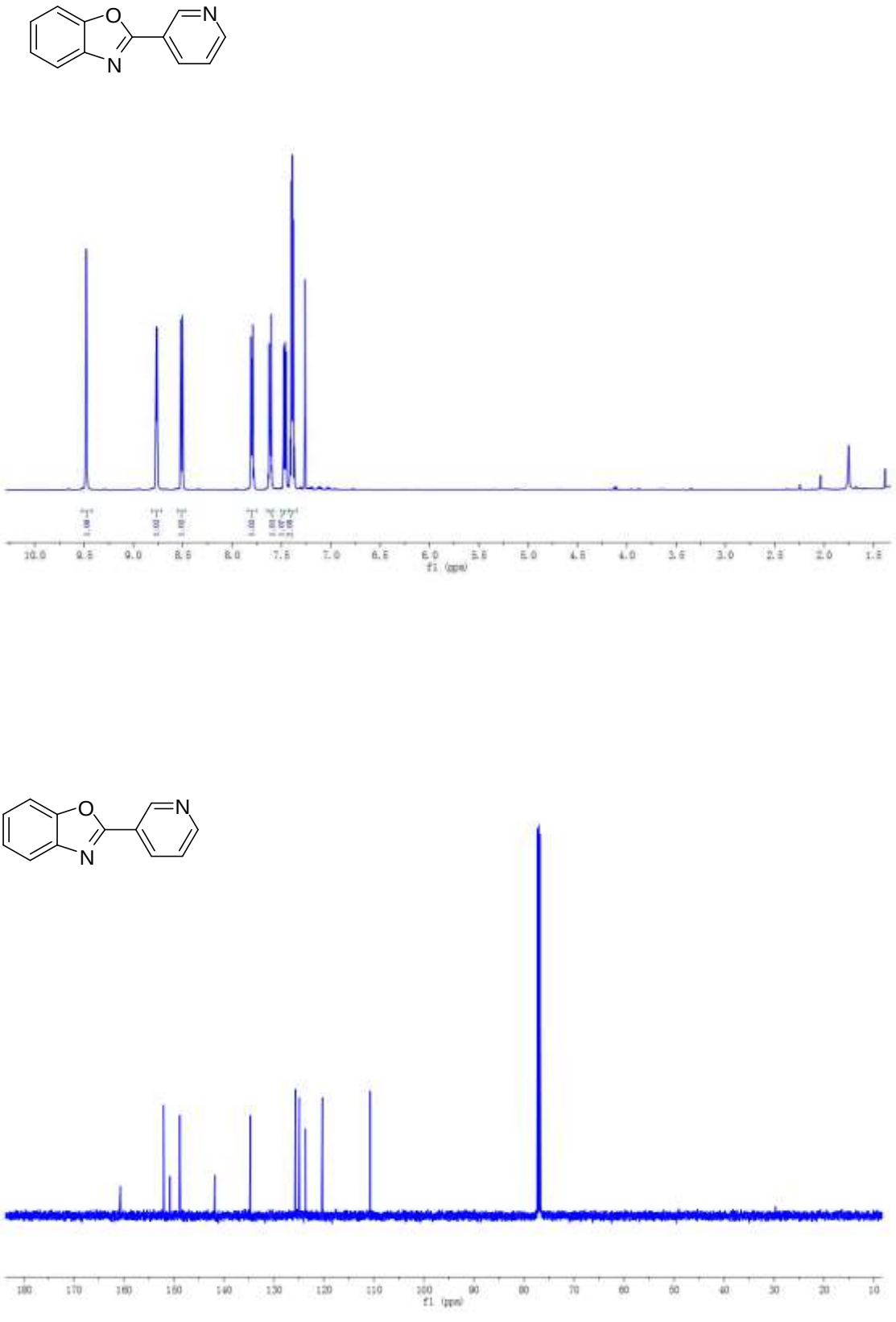
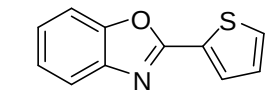
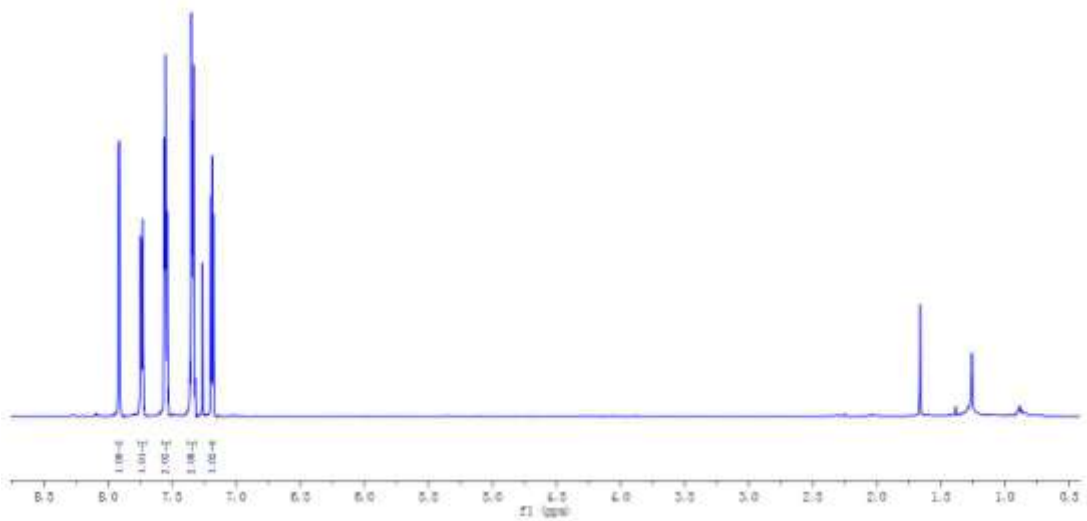
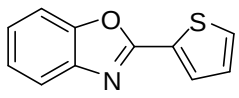


Fig. S14 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3n** in $CDCl_3$

2-(Thiophen-2-yl)benzoxazole (3o)







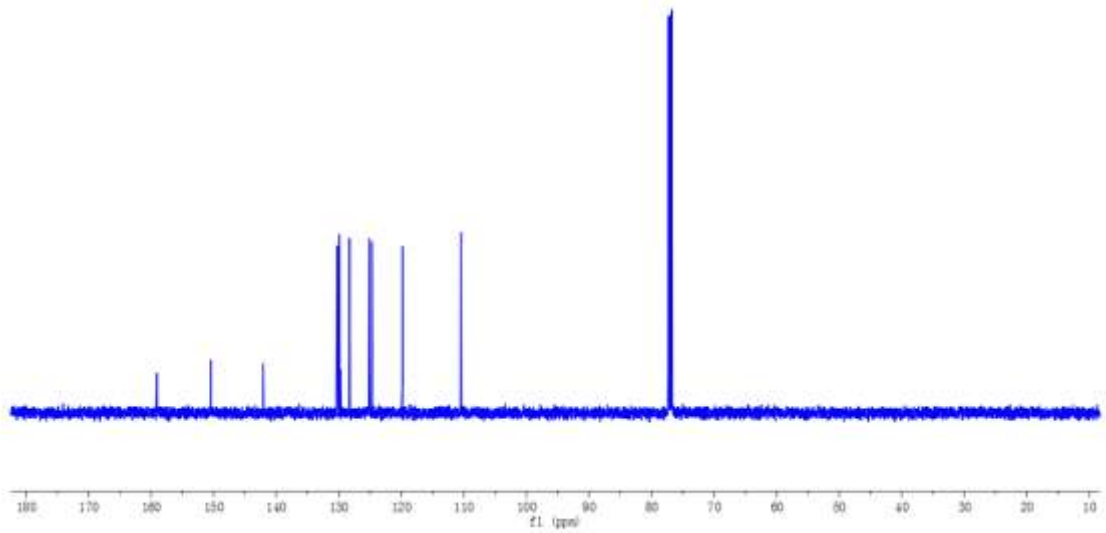


Fig. S15 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3o** in $CDCl_3$

2-(Thiophen-3-yl)benzoxazole (3p)

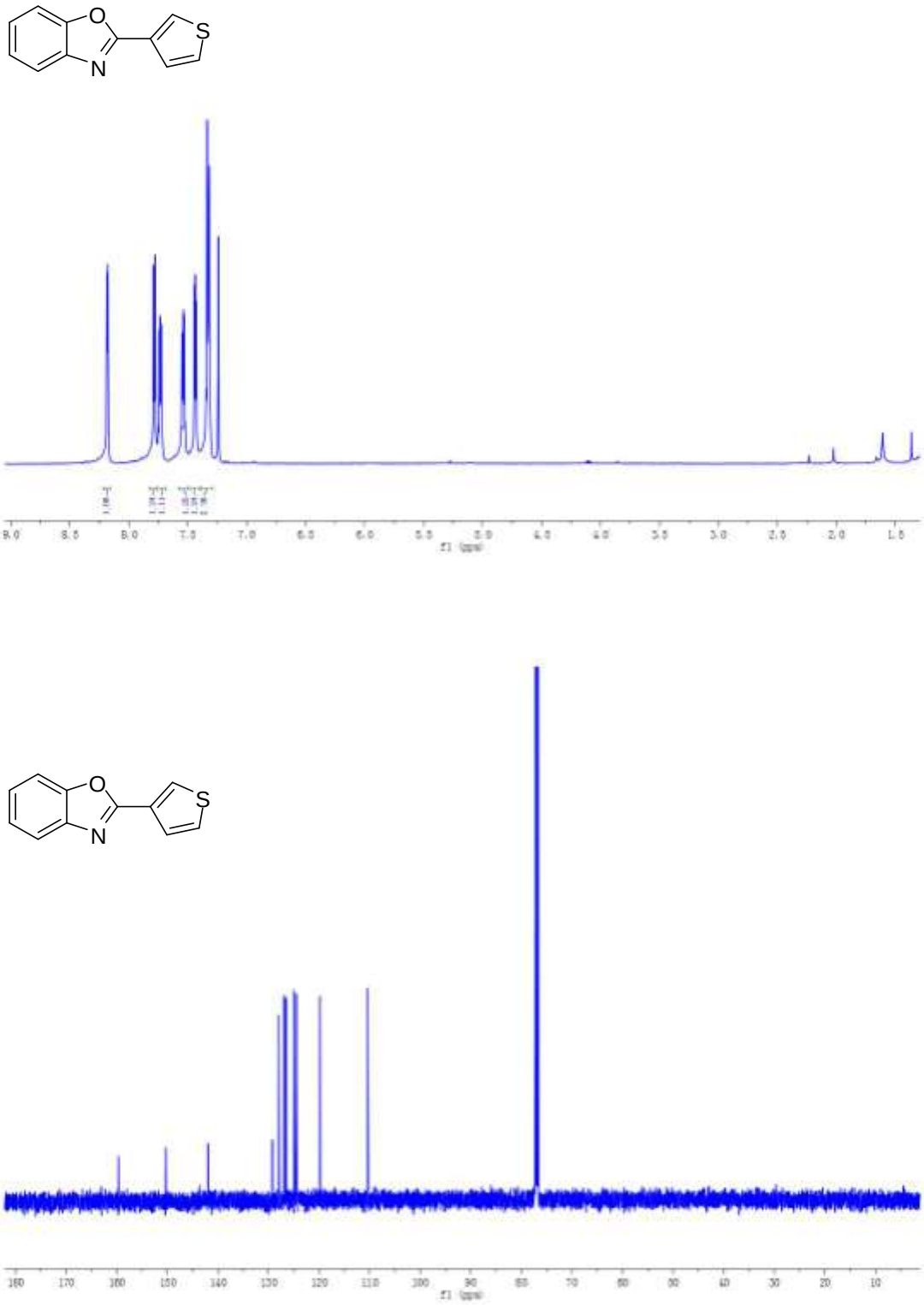
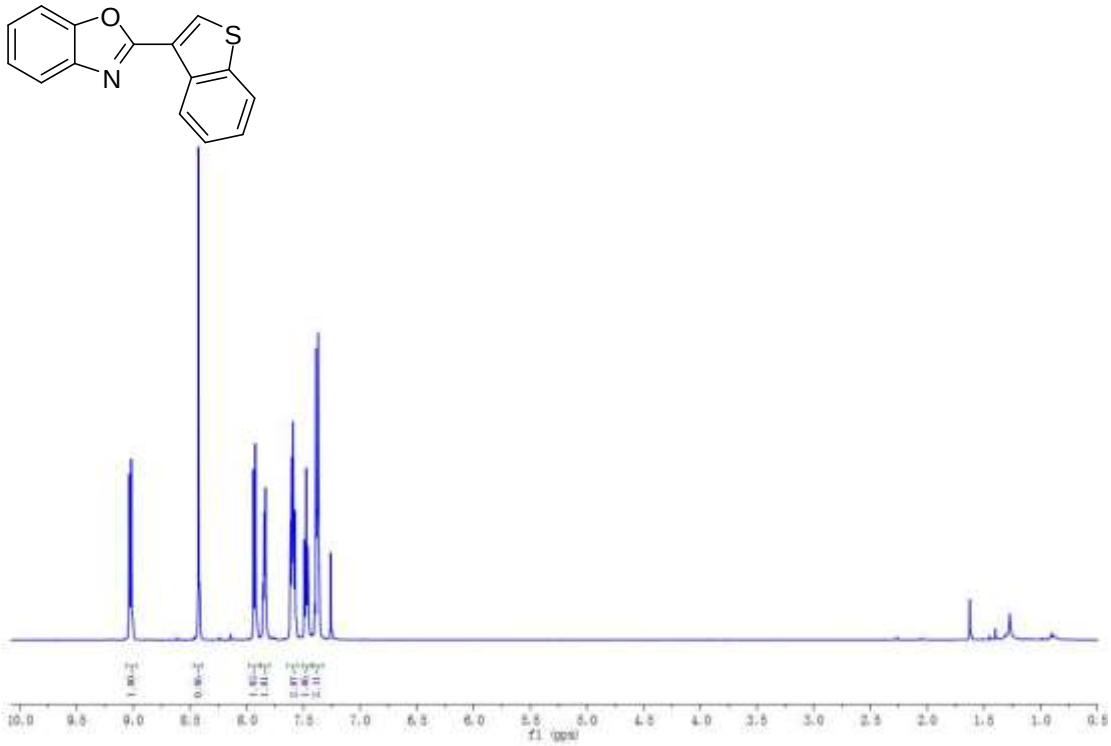


Fig. S16 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3p** in $CDCl_3$

2-(Benzo[b]thiophen-3-yl)benzoxazole (3q)



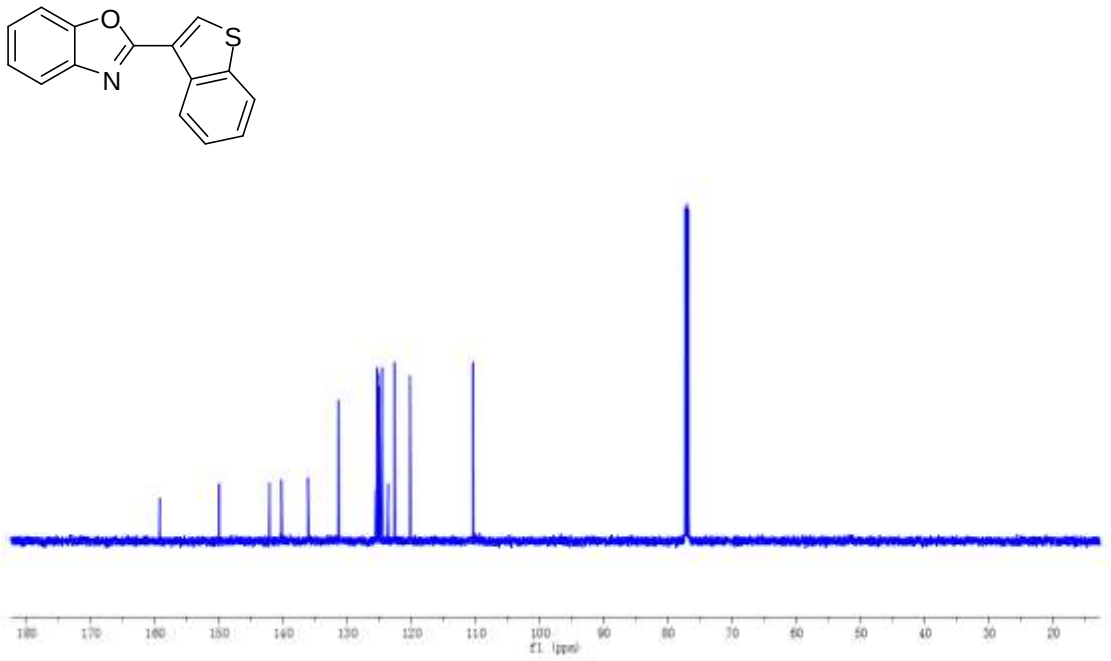


Fig. S17 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3q** in $CDCl_3$

4-(Benzoxazol-2-yl)-2,3-dihydro-1*H*-inden-1-one (3r)

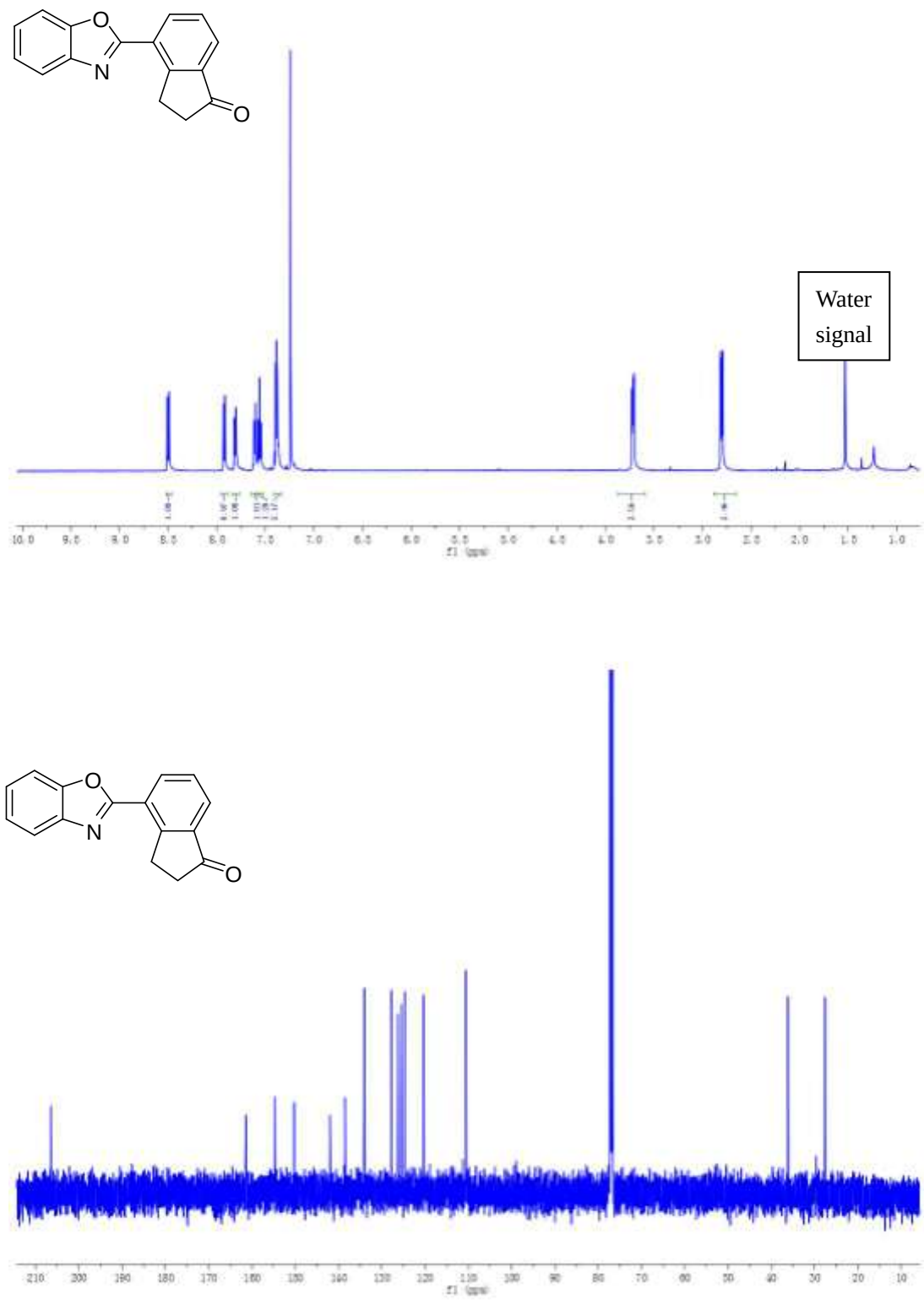


Fig. S18 ^{1}H (500 MHz) and ^{13}C{^{1}H} NMR (125 MHz) NMR spectra of **3r** in $CDCl_3$

2-(Benzofuran-5-yl)benzoxazole (3s)

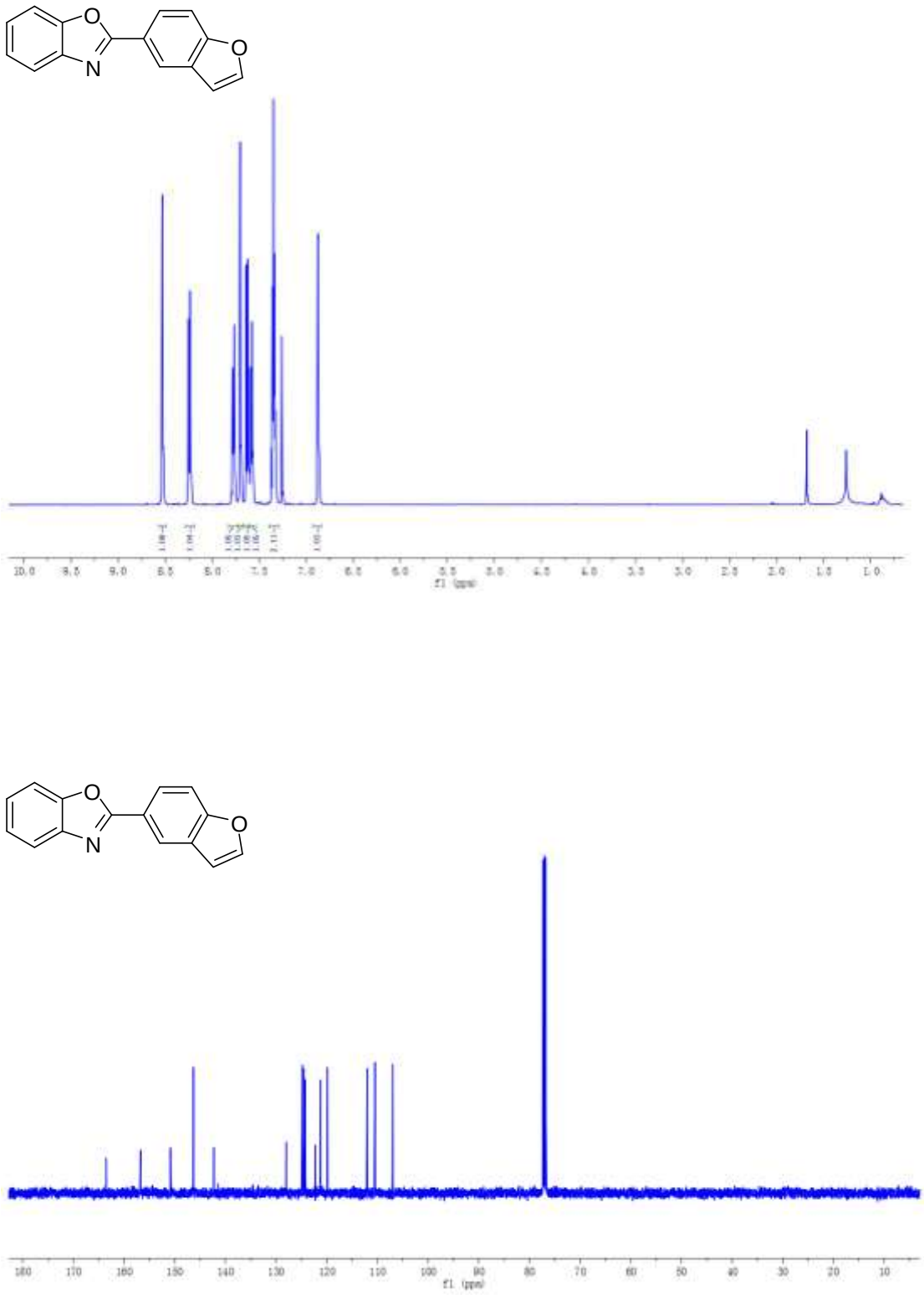
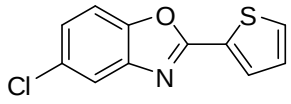
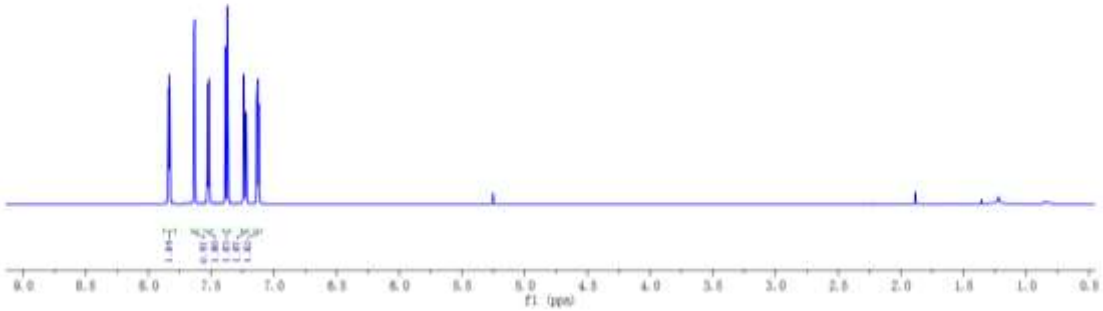


Fig. S19 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3s** in $CDCl_3$

5-Chloro-2-(thiophen-2-yl)benzoxazole (3t)





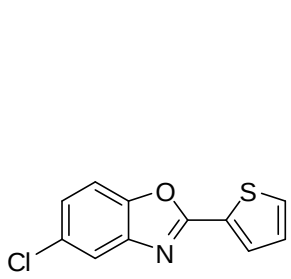


Fig. S20 ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ NMR (125 MHz) NMR spectra of **3t** in $CDCl_3$

5-Chloro-2-(thiophen-3-yl)benzoxazole (3u):

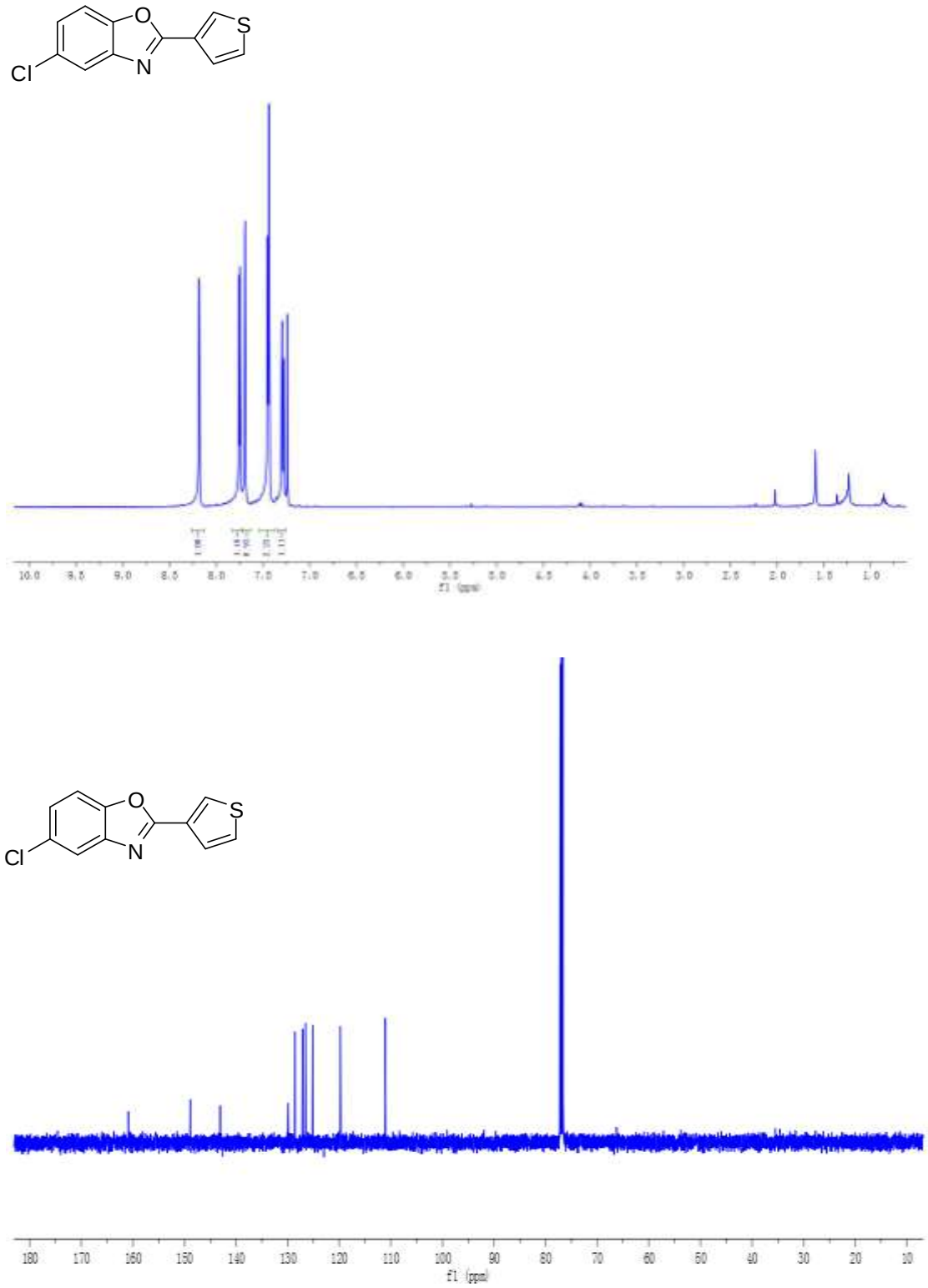


Fig. S21 ^{1}H (500 MHz) and ^{13}C{^{1}H} NMR (125 MHz) NMR spectra of **3u** in $CDCl_3$

5-Chloro-2-(pyridin-3-yl)benzoxazole (3v)

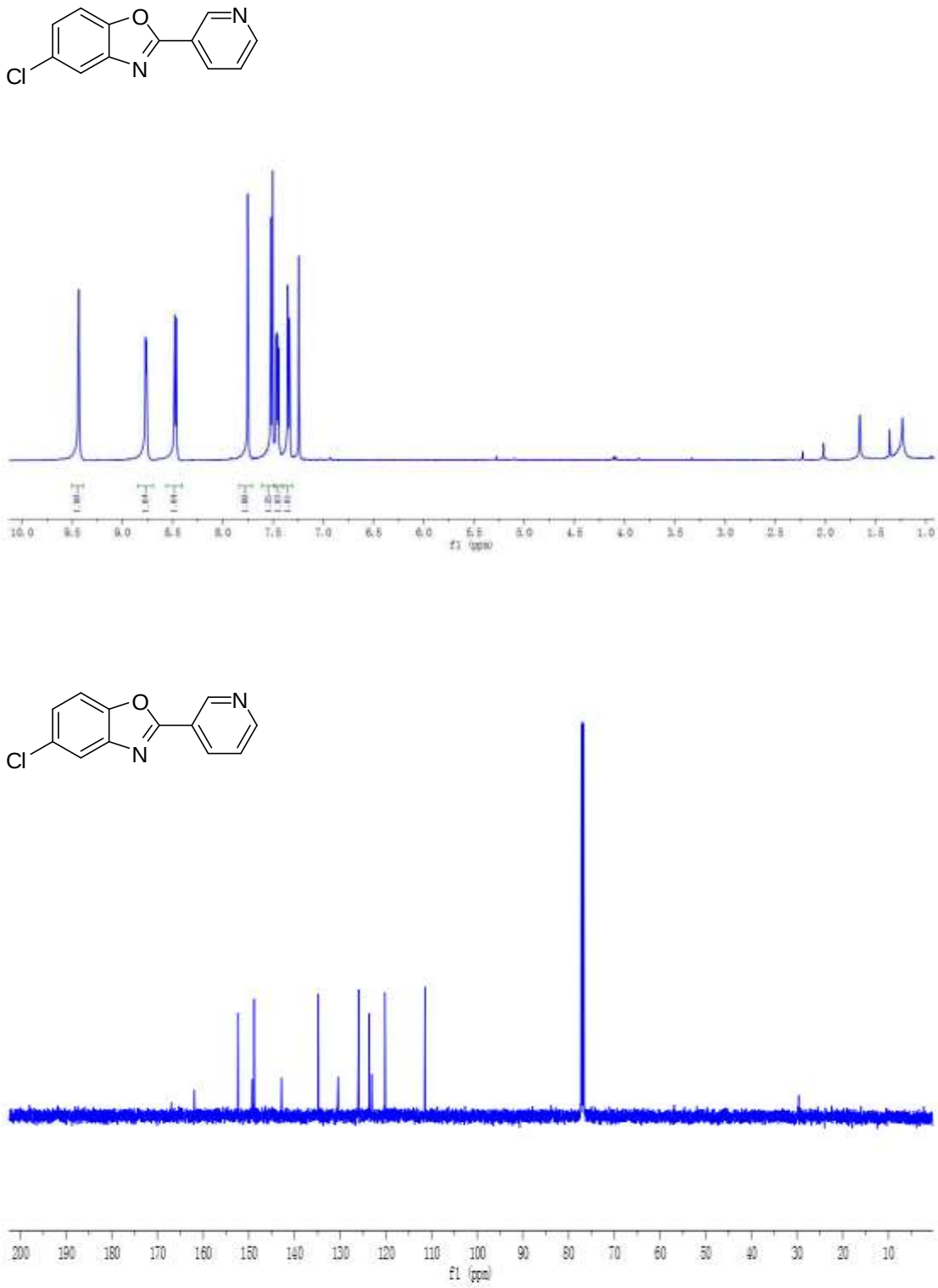
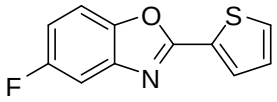
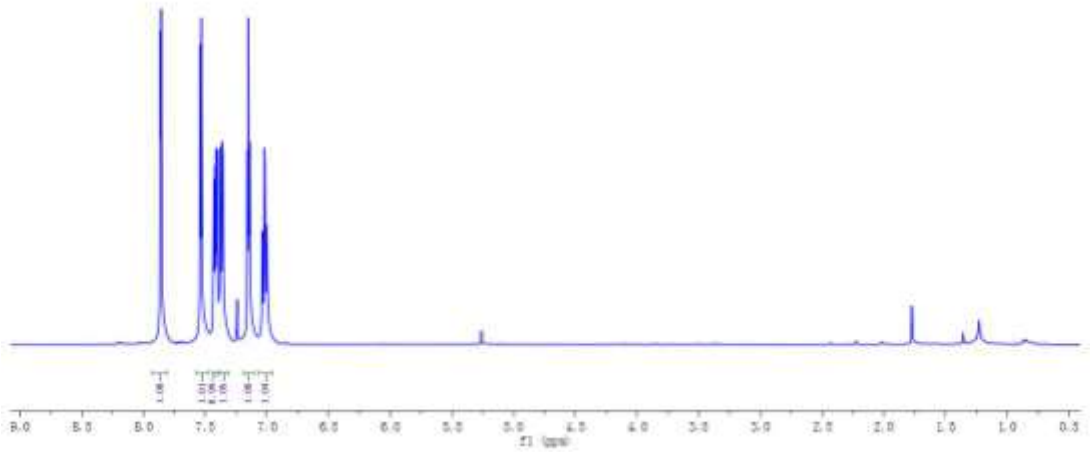
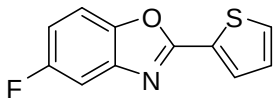


Fig. S22 ^{1}H (500 MHz) and ^{13}C{^{1}H} NMR (125 MHz) NMR spectra of **3v** in $CDCl_3$

5-Fluoro-2-(thiophen-2-yl)benzoxazole (3w)







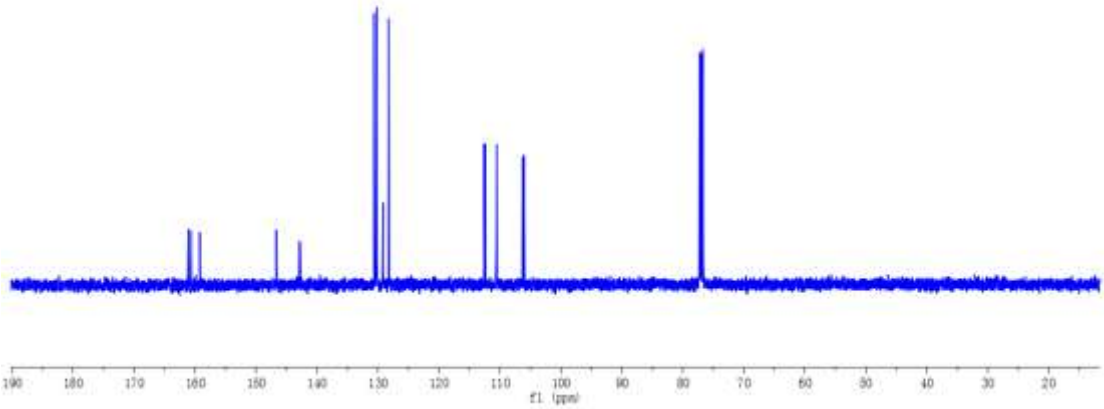
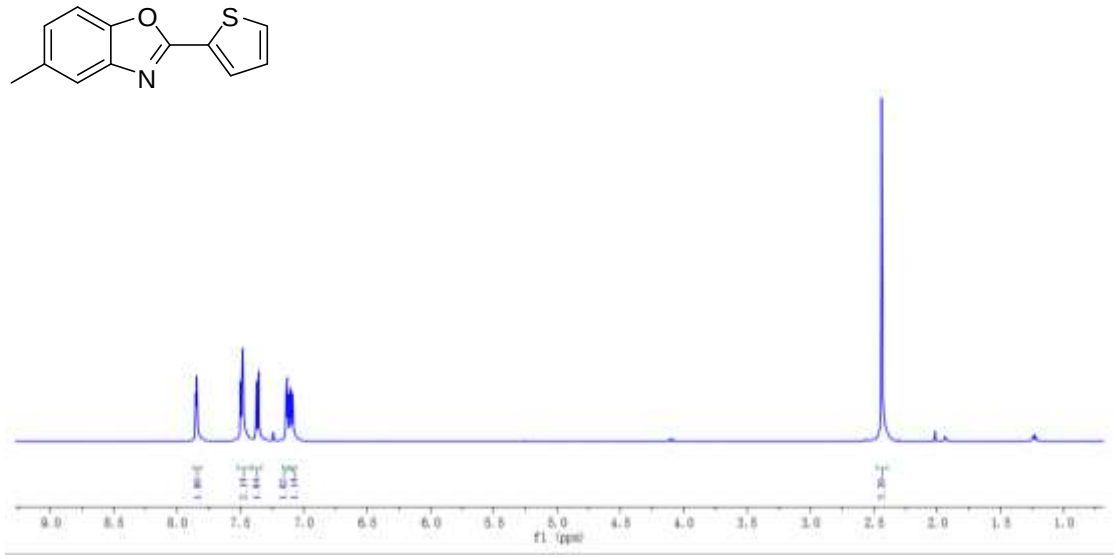


Fig. S23 ^{1}H (500 MHz) and ^{13}C{^{1}H} NMR (125 MHz) NMR spectra of **3w** in $CDCl_3$

5-Methyl-2-(thiophen-2-yl)benzoxazole (3x)



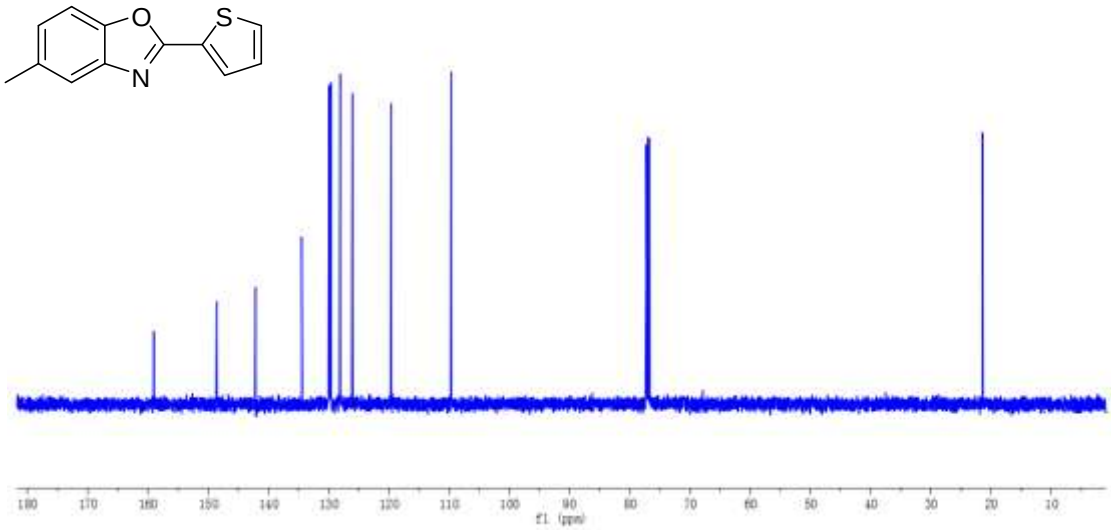
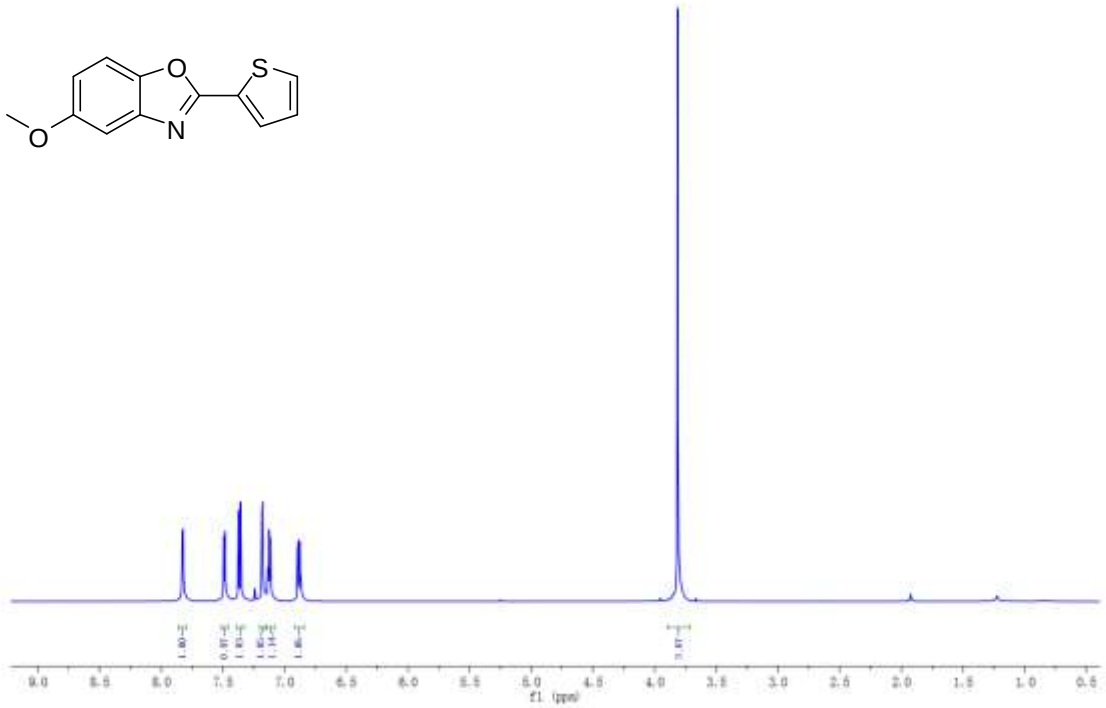


Fig. S24 ^{1}H (500 MHz) and ^{13}C{^{1}H} NMR (125 MHz) NMR spectra of **3x** in $CDCl_3$

5-Methoxy-2-(thiophen-2-yl)benzoxazole (3y)



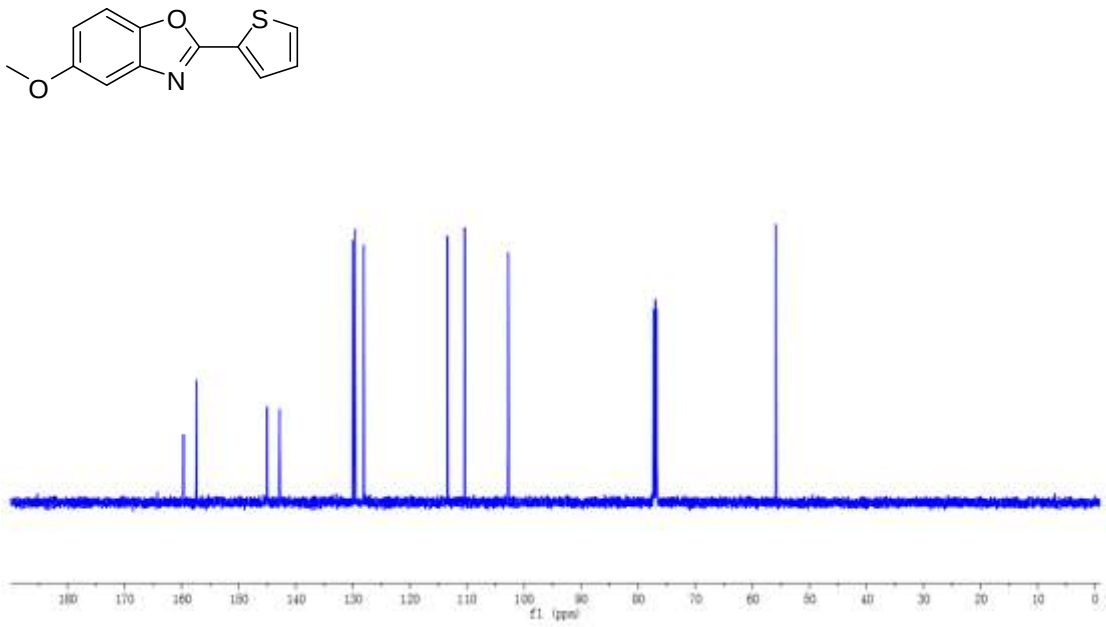


Fig. S25 ^{1}H (500 MHz) and ^{13}C{^{1}H} NMR (125 MHz) NMR spectra of **3y** in $CDCl_3$