Supporting Information

Nickel-Catalyzed C–H/C–O Coupling of Azoles with Phenol Derivatives

Kei Muto, Junichiro Yamaguchi, and Kenichiro Itami*

Department of Chemistry, Graduate School of Science, Nagoya University, Chikusa, Nagoya 464-8602, Japan

E-mail: itami.kenichiro@a.mbox.nagoya-u.ac.jp

Table of Contents

1. General

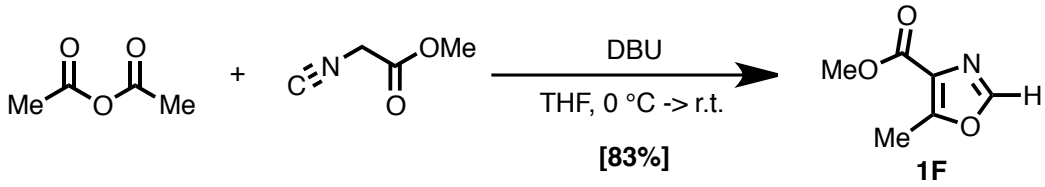
Unless otherwise noted, all reactants or reagents including dry solvents were obtained from commercial suppliers and used as received. $Ni(cod)_2$ and Cs_2CO_3 were obtained from Wako Chemicals. 1,2-Bis(dicyclohexylphosphino)ethane was obtained from Sigma-Aldrich. 1,4-Dioxane was freshly distilled by calcium hydride before coupling reaction. Unless otherwise noted, all reactions were performed with dry solvents under an atmosphere of argon in flame-dried glassware using standard vacuum-line techniques. All C–H bond arylation reactions were performed in 20-mL glass vessel tubes equipped with J. Young® O-ring tap and heated in an 8-well reaction block (heater + magnetic stirrer). All work-up and purification procedures were carried out with reagent-grade solvents in air.

Analytical thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F_{254} precoated plates (0.25 mm). The developed chromatogram was analyzed by UV lamp (254 nm). Flash column chromatography was performed with E. Merck silica gel 60 (230–400 mesh). Preparative thin-layer chromatography (PTLC) was performed using Wakogel B5-F silica coated plates (0.75 mm) prepared in our laboratory. Preparative high performance liquid chromatography (preparative HPLC) was performed with a Biotage Isolera One equipped with Biotage® SNAP Cartridge KP-C18-HS columns using acetonitrile/water as an eluent. Gas chromatography (GC) analysis was conducted on a Shimadzu GC-2010 instrument equipped with a HP-5 column (30 m × 0.25 mm, Hewlett-Packard) with decane as an internal standard. GCMS analysis was conducted on a Shimadzu GCMS-QP2010 instrument equipped with a HP-5 column (30 m × 0.25 mm, Hewlett-Packard). High-resolution mass spectra (HRMS) was obtained from a JEOL JMS-T100TD instrument (DART). Nuclear magnetic resonance (NMR) spectra was recorded on a JEOL JNM-ECA-400 (^{1}H 400 MHz, ^{13}C 100 MHz) spectrometer. Chemical shifts for ^{1}H NMR are expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.00 ppm). Chemical shifts for ^{13}C NMR are expressed in ppm relative to $CDCl_3$ (δ 77.0 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet, br = broad signal), integration, and coupling constant (Hz).

2. Synthesis of Azoles for C–H/C–O Coupling

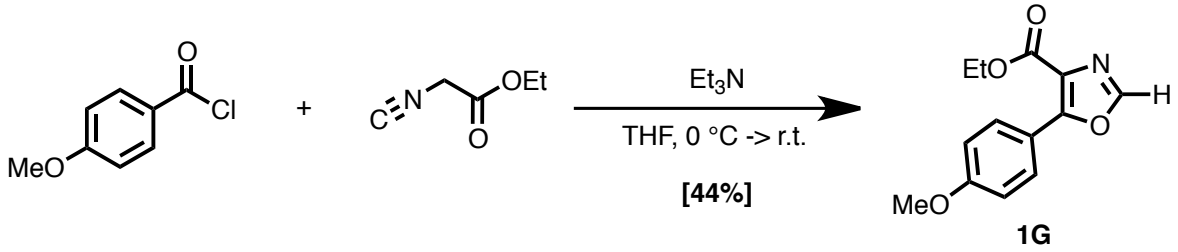
Note: 6-Methylbenzo[*d*]oxazole (**1B**),[1] 5-phenyloxazole (**1C**),[2] 5-(benzo[*d*][1,3]dioxol-5-yl)oxazole (**1D**),[2] 5-(4-methoxyphenyl)oxazole (**1E**),[2] and 5-phenylthiazole (**1I**)[3] were synthesized according to procedures reported in the literature.

Methyl 5-methyloxazole-4-carboxylate (1F)[4]



To a solution of methyl 2-isocyanoacetate (1.98 g, 20 mmol) in THF (24 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU: 3.39 g, 22 mmol, 1.1 equiv). After cooling the reaction mixture to 0 °C, a solution of acetic anhydride (2.25 g, 22 mmol, 1.1 equiv) in THF (6 mL) was added slowly. The resultant mixture was stirred at room temperature and the reaction progress was monitored by TLC. On completion of reaction, the reaction mixture was concentrated in vacuo. To this vessel was added 30 mL of EtOAc and 20 mL of water. The aqueous layer was extracted with EtOAc (20 mL x 3) and the combined organic layer was dried over Na_2SO_4 and then filtered. Following evaporation of the solvent under reduced pressure, the crude residue was purified by flash column chromatography (hexane/EtOAc = 3:1) to afford **1F** as a white solid (2.35 g, 83% yield). R_f 0.43 (hexane/EtOAc = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 1H), 3.92 (s 3H), 2.65 (s, 3H).

Ethyl 5-(4-methoxyphenyl)oxazole-4-carboxylate (1G)[5]



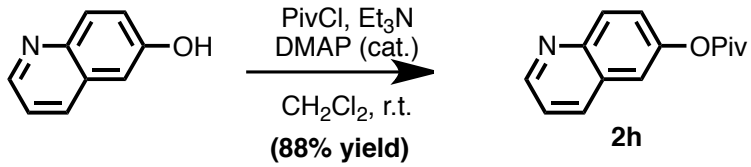
To a solution of ethyl 2-isocyanoacetate (903 mg, 8.0 mmol) and triethylamine (3.34 mL, 24 mmol, 3.0 equiv) in THF (15 mL) was added a solution of *p*-methoxybenzoyl chloride (1.61 g, 9.5 mmol) in THF (4 mL) slowly at 0 °C. After stirring for 40 minutes under 0 °C, the reaction mixture was warmed to room temperature. After stirring for 12 h, the reaction mixture was concentrated in vacuo, then to this vessel was added 30 mL of EtOAc and 20 mL of water. The aqueous layer was extracted with EtOAc (20 mL x 2) and the combined organic layer was dried over Na_2SO_4 and then filtered. Following evaporation of the solvent under reduced pressure, the crude residue was purified by flash column chromatography (hexane/EtOAc = 5:1) to afford **1G** as a yellow solid (865 mg, 44% yield). R_f

0.07 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, 2H, *J* = 9.3 Hz), 7.86 (s, 1H), 6.99 (d, 2H, *J* = 9.0 Hz), 4.42 (q, 2H, *J* = 7.1 Hz), 3.87 (s, 3H), 1.42 (t, 3H, *J* = 7.1 Hz).

3. Synthesis of Phenol Derivatives for C–H/C–O Coupling

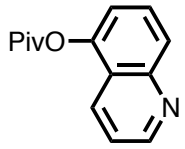
Note: Aryl pivalates **2a**,[6] **2b**,[6] **2g**,[6] **2j**,[6] *N,N*-dimethyl-2-naphtalenylcarbamate,[7] *N,N*-dimethyl-2-naphthalenylsulfamate,[8] *tert*-butyl-2-naphthalenylcarbonate,[9] 2-naphthalenyltosylate,[10] 2-naphthalenylmesylate[11] were synthesized according to procedures reported in the literature.

3-1. Procedure for Synthesis of Aryl Pivalates



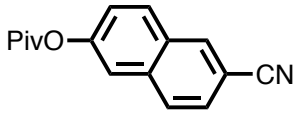
Representative procedure: 6-Quinolinyl pivalate (**2h**)

To a solution of 2-quinolinol (1.60 g, 11 mmol) and a piece of 4,4-dimethylaminopyridine (DMAP) in CH_2Cl_2 (20 mL) was added triethylamine (1.84 mL, 13.2 mmol, 1.2 equiv) at room temperature. Then pivaloyl chloride (1.62 mL, 13.2 mmol, 1.2 equiv) was added dropwise over 3 min at 0 °C. After stirring for 15 min, the reaction mixture was quenched with sat. $NaHCO_3$ aq. (10 mL), then the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (25 mL × 3) and the combined organic layer was dried over Na_2SO_4 and then filtrated. Following evaporation of the solvent under reduced pressure, the crude residue was purified by flash column chromatography (hexane/EtOAc = 5:1) to afford **2h** as a yellow solid (2.21 g, 88% yield). R_f 0.49 (hexane/EtOAc = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.90 (dd, 1H, *J* = 4.0, 1.2 Hz), 8.14–8.07 (m, 2H), 7.53 (d, 1H, *J* = 2.4 Hz), 7.43 (dd, 1H, *J* = 8.8, 2.4 Hz), 7.40 (dd, 1H, *J* = 8.4, 4.0 Hz), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 150.1, 148.9, 146.2, 135.7, 130.9, 128.5, 124.7, 121.5, 118.2, 39.1, 27.1; HRMS (DART) *m*/*z* calcd for $C_{14}H_{15}NO_2$ $[MH]^+$: 230.1181 found 230.1181.



2i

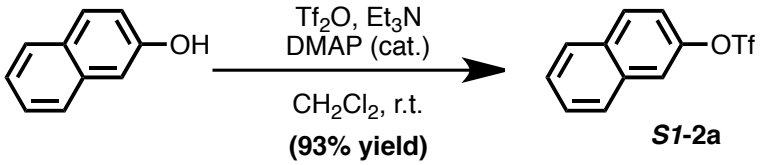
5-Quinolinyl pivalate (2i): Purification by flash column chromatography (hexane/EtOAc = 3:1) afforded **2i** as a white solid (95 % yield). R_f 0.50 (hexane/EtOAc = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.94 (dd, 1H, *J* = 4.1, 1.4 Hz), 8.18 (dq, 1H, *J* = 8.7, 0.9 Hz), 8.01 (d, 1H, *J* = 8.7 Hz), 7.71 (t, 1H, *J* =7.8 Hz), 7.42 (dd, 1H, *J* = 8.0, 4.1 Hz), 7.29 (dd, 1H, *J* = 0.9, 7.8 Hz), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 150.8, 148.9, 146.3, 129.7, 128.8, 127.3, 122.4, 121.3, 118.5, 39.5, 27.3; HRMS (DART) *m*/*z* calcd for $C_{14}H_{15}NO_2$ $[MH]^+$: 230.1181 found 230.1181.



2k

6-Cyanonaphthalen-2-yl pivalate (2k): Purification by flash column chromatography (hexane/$CHCl_3$ = 5:1) afforded **2k** as a white solid (85 % yield). R_f 0.08 (hexane/$CHCl_3$ = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (s, 1H), 7.90 (d, 1H, *J* = 9.2 Hz), 7.86 (d, 1H, *J* = 8.4 Hz), 7.86 (d, 2H), 7.66–7.58 (m, 2H), 7.33 (dd, 1H, *J* = 8.8, 2.4 Hz), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 151.2, 135.3, 133.9, 130.1, 129.9, 128.8, 127.1, 123.2, 119.1, 118.8, 109.1, 39.2, 27.1; HRMS (DART) *m*/*z* calcd for $C_{16}H_{16}NO_2$ $[MH]^+$: 254.1181 found 254.1181.

3-2. Procedure for Synthesis of Aryl Triflates

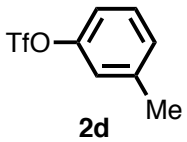


***S1*-2a**

Representative procedure: Naphthalen-2-yl triflate (**S1-2a**)[12]

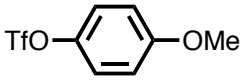
To a solution of 2-naphthalene (1.59 g, 11 mmol) and a piece of 4,4-dimethylaminopyridine (DMAP) in CH_2Cl_2 (20 mL) was added triethylamine (1.84 mL, 13.2 mmol, 1.2 equiv) at room temperature. Then trifluoromethanesulfonic anhydride (1.99 mL, 13.2 mmol, 1.2 equiv) was added dropwise over 3 min at 0 °C. After stirring for 2 h, the reaction mixture was quenched with water (10 mL), then the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (25 mL × 3) and

the combined organic layer was dried over Na_2SO_4 and then filtrated. Following evaporation of the solvent under reduced pressure, the crude residue was purified by flash column chromatography (hexane/EtOAc = 10:1) to afford **S1-2a** as a colorless oil (2.82 g, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, 1H, *J* = 9.0 Hz), 7.91–7.86 (m, 2H), 7.77 (d, 1H, *J* = 2.5 Hz), 7.60–7.57 (m, 2H), 7.38 (dd, 1H, *J* = 9.0, 2.5 Hz).



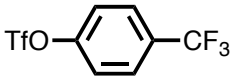
2d

3-Methylphenyl trifluoromethanesulfonate (2d):[13] Purification by flash column chromatography (hexane/EtOAc = 8:1) afforded **2d** as a yellow oil (86 % yield). R_f 0.54 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (t, 1H, *J* = 7.6 Hz), 7.18 (d, 1H, *J* = 7.6 Hz), 7.12–7.05 (m, 2H), 2.40 (s, 3H).



2e

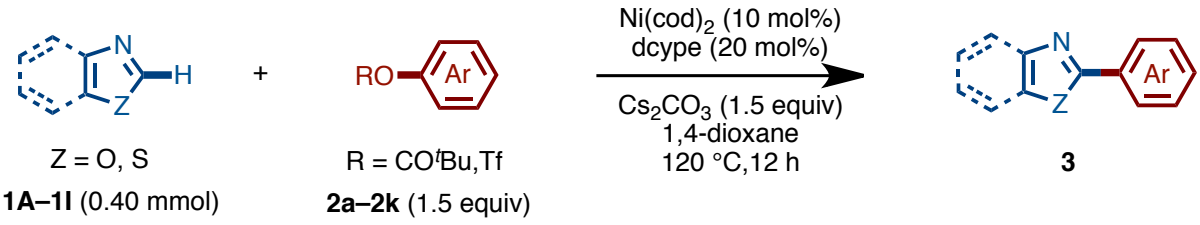
4-Methoxyphenyl trifluoromethanesulfonate (2e):[14] Purification by flash column chromatography (hexane/EtOAc = 9:1) afforded **2e** as a colorless oil (70 % yield). R_f 0.57 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (d, 2H, *J* = 9.6 Hz), 6.92 (d, 2H, *J* = 9.2 Hz), 3.82 (s, 3H).



2f

4-(Trifluoromethyl)phenyl trifluoromethanesulfonate (2f):[15] Purification by flash column chromatography (hexane/EtOAc = 3:1) afforded **2d** as a colorless oil (64 % yield). R_f 0.57 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, 2H, *J* = 8.8 Hz), 7.43 (d, 2H, *J* = 8.8 Hz).

4. Nickel-Catalyzed C–H/C–O Coupling of Azoles with Phenol Derivatives

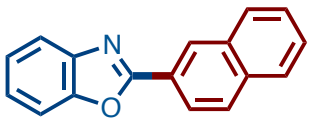


Z = O, S
1A–1l (0.40 mmol)

R = CO^{t}Bu,Tf
2a–2k (1.5 equiv)

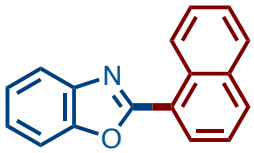
3

General Procedure: A 20-mL glass vessel equipped with J. Young® O-ring tap containing a magnetic stirring bar and Cs_2CO_3 (195.5 mg, 0.60 mmol, 1.5 equiv) was dried with a heatgun under reduced pressure and filled with argon after cooling to room temperature. To this vessel was added a phenol derivative **2** (0.60 mmol, 1.5 equiv) then introduced into an argon-atmosphere glovebox. To the reaction vessel was added $Ni(cod)_2$ (11.2 mg, 0.04 mmol, 10 mol%) and 1,2-bis(dicyclohexylphosphino)ethane (dcype) (33.8 mg, 0.08 mmol, 20 mol%). The vessel was taken out of the glovebox, then to it was added an azole **1** (0.40 mmol) and dry 1,4-dioxane (1.6 mL) under a stream of argon. The vessel was sealed with O-ring tap and then heated at 120 °C for 12 h in an 8-well reaction block with stirring. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad with EtOAc. The filtrate was concentrated and the residue was subjected to preparative thin-layer chromatography to afford a 2-arylated azole **3** (C–H/C–O coupling product).



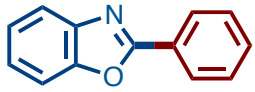
3Aa: 95% (R = CO^{t}Bu)

2-(Naphthalen-2-yl)benzoxazole (3Aa):[16] Purification by preparative thin-layer chromatography (hexane/EtOAc = 10:1) afforded **3Aa** (93.2 mg, 95%) as a white solid. R_f = 0.48 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.79 (s, 1H), 8.33 (dd, 1H, *J* = 8.7, 1.4 Hz), 8.03–7.96 (m, 2H), 7.93–7.87 (m, 1H), 7.82 (dd, 1H, *J* = 6.0, 3.6 Hz), 7.63 (dd, 1H, *J* = 6.4, 2.8 Hz), 7.60–7.52 (m, 2H), 7.41–7.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.2, 150.9, 142.2, 134.7, 133.0, 128.9, 128.8, 128.1, 127.9, 127.8, 126.9, 125.2, 124.6, 124.4, 124.0, 120.0, 110.6; HRMS (DART) *m*/*z* calcd for $C_{17}H_{12}NO$ $[MH]^+$: 246.0919 found 246.0919.



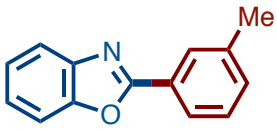
3Ab: 90% (R = CO^{t}Bu)

2-(Naphthalen-1-yl)benzoxazole (3Ab):[17] Purification by preparative thin-layer chromatography (hexane/EtOAc = 10:1) afforded **3Ab** (88.2 mg, 90%) as a white solid. R_f = 0.61 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.47 (d, 1H, *J* = 8.4 Hz), 8.38 (d, 1H, *J* = 7.2 Hz), 7.97 (d, 1H, *J* = 8.0 Hz), 7.91–7.82 (m, 2H), 7.68 (t, 1H, *J* = 8.0 Hz), 7.62–7.57 (m, 1H), 7.54 (t, 2H, *J* = 8.4 Hz), 7.40–7.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.7, 150.1, 142.3, 133.9, 132.2, 130.6, 129.2, 128.6, 127.8, 126.4, 126.2, 125.2, 124.8, 124.4, 123.5, 120.2, 110.4; HRMS (DART) *m/z* calcd for $C_{17}H_{12}NO$ $[MH]^+$: 246.0919 found 246.0918.



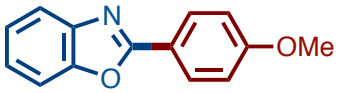
3Ac: 11% (R = CO^{t}Bu)
75% (R = Tf)

2-Phenylbenzoxazole (3Ac):[18] Purification by preparative thin-layer chromatography (hexane/EtOAc = 10:1) afforded **3Ac** (8.6 mg, 11%, R = CO^{t}Bu) (58.6 mg, 75%, R = Tf) as a white solid. R_f = 0.40 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30–8.24 (m, 2H), 7.78 (dd, 1H, *J* = 5.6, 3.2 Hz), 7.59 (dd, 1H, *J* = 6.4, 3.2 Hz), 7.56–7.49 (m, 3H) 7.38–7.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 150.7, 142.1, 131.4, 128.8, 127.6, 127.1, 125.0, 124.5, 120.0, 110.5; HRMS (DART) *m/z* calcd for $C_{13}H_{10}NO$ $[MH]^+$: 196.0762 found 196.0762.



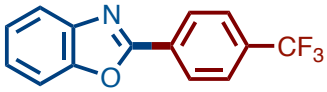
3Ad: 85% (R = Tf)

2-(3-Methylphenyl)benzoxazole (3Ad):[19] Purification by preparative thin-layer chromatography (hexane/EtOAc = 10:1) afforded **3Ad** (71.4 mg, 85%) as a white solid. R_f = 0.56 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (s, 1H), 8.02 (d, 1H, *J* = 7.6 Hz), 7.79–7.71 (m, 1H), 7.58–7.49 (m, 1H), 7.41–7.27 (m, 4H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 150.6, 142.1, 138.6, 132.2, 128.7, 128.1, 126.9, 124.9, 124.6, 124.4, 119.8, 110.4, 21.2; HRMS (DART) *m/z* calcd for $C_{14}H_{12}NO$ $[MH]^+$: 210.0919 found 210.0919.



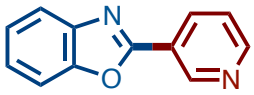
3Ae: 55% (R = Tf)

2-(4-Methoxyphenyl)benzoxazole (3Ae):[18] Purification by preparative thin-layer chromatography (hexane/EtOAc = 10:1) afforded **3Ae** (49.6 mg, 55%) as a white solid. R_f = 0.32 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (dd, 2H, *J* = 9.2, 1.4 Hz), 7.72 (dd, 1H, *J* = 6.9, 2.3 Hz), 7.53 (dd, 1H, *J* = 6.0, 2.3 Hz), 7.37–7.27 (m, 2H) 7.00 (dd, 2H, *J* = 8.9, 1.4 Hz) 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 162.2, 150.6, 142.2, 129.3, 124.5, 124.3, 119.6, 119.5, 114.3, 110.3, 55.4; HRMS (DART) *m/z* calcd for $C_{14}H_{12}NO_2$ $[MH]^+$: 226.0868 found 226.0868.



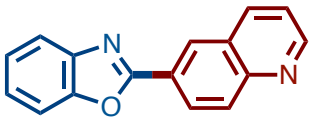
3Af: 52% (R = Tf)

2-(4-Trifluoromethylphenyl)benzoxazole (3Af):[18] Purification by preparative thin-layer chromatography (hexane/EtOAc = 10:1) afforded **3Af** (54.4 mg, 52%) as a white solid. R_f = 0.61 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, 2H, *J* = 7.8 Hz), 7.82–7.73 (m, 3H), 7.62–7.55 (m, 1H), 7.41–7.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4, 150.8, 141.9, 132.9 ($J_{C–F}$ = 33.5 Hz), 130.4, 127.8, 125.9 ($J_{C–F}$ = 3.8 Hz), 125.8, 124.9, 123.7 ($J_{C–F}$ = 274.0 Hz), 120.4, 110.8; HRMS (DART) *m/z* calcd for $C_{14}H_9F_3NO$ $[MH]^+$: 264.0636 found 264.0635.



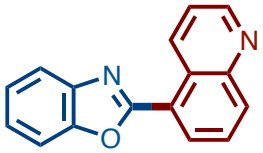
3Ag: 81% (R = CO^{t}Bu)

2-(Pyridin-3-yl)benzoxazole (3Ag):[20] Purification by preparative thin-layer chromatography (hexane/EtOAc = 3:1) afforded **3Ag** (63.2 mg, 81%) as a tan solid. R_f = 0.23 (hexane/EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.46 (s, 1H), 8.74 (dd, 1H, *J* = 3.4, 1.8 Hz), 8.47 (d, 1H, *J* = 8.2 Hz), 7.84–7.76 (m, 1H), 7.65–7.58 (m, 1H), 7.50–7.43 (m, 1H), 7.43–7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5, 151.9, 150.6, 148.6, 141.6, 134.5, 125.6, 124.8, 123.5, 123.4, 120.1, 110.6; HRMS (DART) *m/z* calcd for $C_{12}H_9N_2O$ $[MH]^+$: 197.0715 found 197.0715.



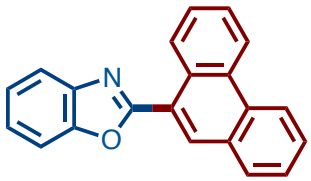
3Ah: 99% (R = CO*t*Bu)

2-(Quinolin-6-yl)benzoxazole (3Ah):[21] Purification by preparative thin-layer chromatography (hexane/EtOAc = 5:1) afforded **3Ah** (98.0 mg, 99%) as a white solid. R_f = 0.17 (hexane/EtOAc = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.04–8.97 (m, 1H), 8.76 (s, 1H), 8.56 (dt, 1H, *J* = 7.3, 1.8 Hz), 8.29 (d, 1H, *J* = 8.2 Hz), 8.24 (d, 1H, *J* = 8.7 Hz), 7.86–7.79 (m, 1H), 7.68–7.59 (m, 1H), 7.53–7.46 (m, 1H), 7.44–7.36 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4, 152.0, 150.9, 149.5, 142.1, 136.8, 130.4, 128.0, 127.9, 127.7, 125.5, 125.2, 124.8, 122.1, 120.2, 110.7; HRMS (DART) *m*/*z* calcd for $C_{16}H_{11}N_2O$ $[MH]^+$: 247.0871 found 247.0871.



3Ai: 86% (R = CO*t*Bu)

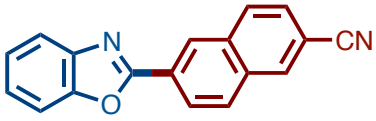
2-(Quinolin-5-yl)benzoxazole (3Ai): Purification by preparative thin-layer chromatography (hexane/EtOAc = 3:1) afforded **3Ai** (84.4 mg, 86%) as a white solid. R_f = 0.23 (hexane/EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (d, 1H, *J* = 8.2 Hz), 9.00 (dd, 1H, *J* = 4.1, 1.4 Hz), 8.49 (dd, 1H, *J* = 7.3, 0.9 Hz), 8.29 (d, 1H, *J* = 8.2 Hz), 7.90–7.78 (m, 2H), 7.67–7.63 (m, 1H), 7.60 (dd, 1H, *J* = 8.4, 4.0 Hz), 7.45–7.36 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6, 150.8, 150.0, 148.4, 142.1, 135.0, 133.6, 129.3, 128.5, 126.3, 125.6, 124.7, 123.7, 122.5, 120.3, 110.6; HRMS (DART) *m*/*z* calcd for $C_{16}H_{11}N_2O$ $[MH]^+$: 247.0871 found 247.0872.



3Aj: 55% (R = CO*t*Bu)

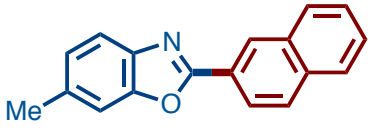
2-(Phenanthren-9-yl)benzoxazole (3Aj):[22] Purification by preparative thin-layer chromatography (hexane/EtOAc = 10:1) afforded **3Aj** (65.2 mg, 55%) as a white solid. R_f = 0.61 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.54 (dd, 1H, *J* = 8.2, 2.0 Hz), 8.80 (dd, 1H, *J* = 7.5, 2.1 Hz) 8.78–8.72 (m, 2H), 8.04, (d, 1H, *J* = 8.0 Hz), 7.95–7.88 (m, 1H), 7.84–7.74 (m, 3H), 7.73–7.63 (m, 2H), 7.46–7.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.6, 150.1, 142.2, 131.6, 131.5, 130.7, 130.4,

129.7, 128.6, 127.6, 127.0, 125.3, 124.5, 122.9, 122.6, 122.4, 120.3, 110.4; HRMS (DART) *m*/*z* calcd for $C_{21}H_{14}NO$ $[MH]^+$: 296.1075 found 296.1075.



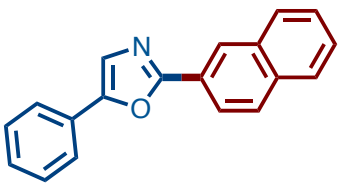
3Ak: 79% (R = CO*t*Bu)

2-(6-Cyanonaphthalen-2-yl)benzoxazole (3Ak): Purification by preparative thin-layer chromatography (hexane/$CHCl_3$ = 1:1) afforded **3Ak** (85.6 mg, 79%) as a white solid. R_f = 0.27 (hexane/$CHCl_3$ = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (s, 1H), 8.38 (dd, 1H, *J* = 8.7, 1.4 Hz), 8.22 (s, 1H), 8.00 (t, 2H, *J* = 9.9 Hz), 7.84–7.76 (m, 1H), 7.64 (dd, 1H, *J* = 8.7, 0.9 Hz), 7.63–7.57 (m, 1H), 7.45–7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 150.8, 142.0, 134.2, 133.8, 133.3, 130.0, 129.2, 127.6, 127.34, 127.28, 125.8, 125.6, 124.9, 120.3, 118.7, 111.0, 110.7; HRMS (DART) *m*/*z* calcd for $C_{18}H_{11}N_2O$ $[MH]^+$: 271.0871 found 271.0872.



3Ba: 96% (R = CO*t*Bu)

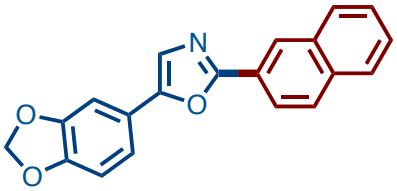
6-Methyl-2-(naphthalen-2-yl)benzoxazole (3Ba):[23] Purification by preparative thin-layer chromatography (hexane/EtOAc = 10:1) afforded **3Ba** (99.7 mg, 96%) as a white solid. R_f = 0.44 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67 (s, 1H), 8.24 (dd, 1H, *J* = 8.7, 1.4 Hz), 7.95–7.86 (m, 2H), 7.85–7.77 (m, 1H), 7.63 (d, 1H, *J* = 8.2 Hz), 7.54–7.46 (m, 2H), 7.33 (s, 1H), 7.12 (d, 1H, *J* = 8.2 Hz), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6, 151.0, 139.9, 135.5, 134.5, 132.9, 128.8, 128.6, 127.8, 127.7, 127.5, 126.7, 125.7, 124.5, 123.8, 119.2, 110.7, 21.7; HRMS (DART) *m*/*z* calcd for $C_{18}H_{14}NO$ $[MH]^+$: 260.1075 found 260.1075.



3Ca: 82% (R = CO*t*Bu)

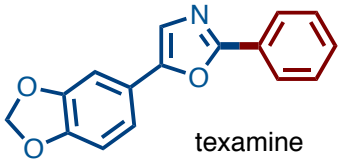
2-(Naphthalen-1-yl)-5-phenyloxazole (3Ca):[2] Purification by preparative thin-layer chromatography

(hexane/EtOAc = 5:1) afforded **3Ca** (88.6 mg, 82%) as a white solid. R_f = 0.36 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (s, 1H), 8.16 (dd, 1H, *J* = 8.2, 1.8 Hz), 7.95–7.86 (m, 2H), 7.86–7.77 (m, 1H), 7.72 (d, 2H, *J* = 7.8 Hz), 7.53–7.47 (m, 2H), 7.47–7.38 (m, 3H), 7.32 (t, 1H, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 151.3, 134.1, 133.0, 128.9, 128.62, 128.58, 128.4, 127.9, 127.8, 127.1, 126.7, 126.0, 124.6, 124.2, 123.6, 123.2; HRMS (DART) *m*/*z* calcd for $C_{19}H_{14}NO$ $[MH]^+$: 272.1075 found 272.1075.



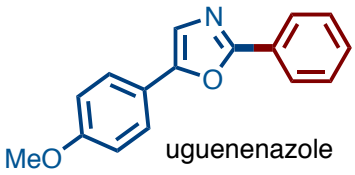
3Da: 72% (R = CO^{t}Bu)

5-(Benzo[*d*][1,3]dioxol-5-yl)-2-(naphthalen-2-yl)oxazole (3Da): Purification by preparative thin-layer chromatography (hexane/EtOAc = 3:1) afforded **3Da** (90.2 mg, 72%) as a white solid. R_f = 0.55 (hexane/EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (s, 1H), 8.16 (dd, 1H, *J* = 8.8, 2.0 Hz), 7.97–7.89 (m, 2H), 7.88–7.83 (m, 1H), 7.56–7.50 (m, 2H), 7.35 (s, 1H), 7.28 (dd, 1H, *J* = 8.4, 2.0 Hz), 7.21 (d, 1H, *J* = 1.2 Hz), 6.90 (d, 1H, *J* = 8.4 Hz), 6.02 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8, 151.3, 148.2, 147.9, 134.0, 133.1, 128.6, 128.5, 127.9, 127.2, 126.7, 125.9, 124.7, 123.2, 122.5, 122.2, 118.4, 108.9, 104.9, 101.4; HRMS (DART) *m*/*z* calcd for $C_{20}H_{14}NO_3$ $[MH]^+$: 316.0974 found 316.0973.



3Dc: 62% (R = Tf)

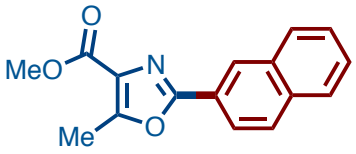
Texamine (3Dc):[2] Purification by preparative thin-layer chromatography (hexane/EtOAc = 4:1) afforded texamine (**3Dc**; 65.8 mg, 62%) as a white solid. R_f = 0.46 (hexane/EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (dd, 2H, *J* = 8.4, 1.6 Hz), 7.50–7.39 (m, 3H), 7.28 (s, 1H), 7.20 (dd, 1H, *J* = 8.0, 1.6 Hz), 7.14 (s, 1H), 6.84 (d, 1H, *J* = 8.0 Hz), 5.97 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5, 151.0, 148.1, 147.8, 130.1, 128.7, 127.4, 126.1, 122.3, 122.1, 118.2, 108.7, 104.7, 101.3; HRMS (DART) *m*/*z* calcd for $C_{16}H_{12}NO_3$ $[MH]^+$: 266.0817 found 266.0817.



uguenenazole

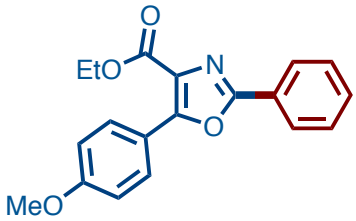
3Ec: 73% (R = Tf)

Uguenenazole (3Ec):[24] Purification by preparative thin-layer chromatography (hexane/EtOAc = 4:1) afforded uguenenazole (**3Ec**; 73.8 mg, 73%) as a white solid. R_f = 0.46 (hexane/EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (dd, 2H, *J* = 8.0, 1.8 Hz), 7.62 (dd, 2H, *J* = 9.2, 2.3 Hz), 7.50–7.39 (m, 3H), 7.31 (s, 1H), 6.95 (dd, 2H, *J* = 9.2, 2.3 Hz), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5, 159.7, 151.2, 130.0, 128.7, 127.5, 126.1, 125.7, 121.9, 120.8, 114.3, 55.3; HRMS (DART) *m*/*z* calcd for $C_{16}H_{14}NO_2$ $[MH]^+$: 252.1025 found 252.1025.



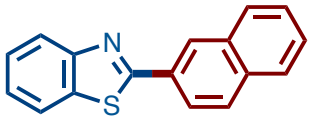
3Fa: 72% (R = CO^{t}Bu)

Methyl 5-methyl-2-(naphthalen-2-yl)oxazole-4-carboxylate (3Fa): Purification by preparative thin-layer chromatography (hexane/EtOAc = 3:1) afforded **3Fa** (76.7 mg, 72%) as a white solid. R_f = 0.29 (hexane/EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (s, 1H), 8.11 (dd, 1H, *J* = 8.7, 1.8 Hz), 7.92–7.85 (m, 2H), 7.84–7.79 (m, 1H), 7.78 (m, 3H), 7.53–7.47 (m, 2H), 3.95 (s, 3H), 2.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.7, 159.7, 156.4, 134.1, 132.8, 128.6, 128.53, 128.48, 127.7, 127.3, 126.7, 126.5, 123.7, 123.1, 51.9, 12.1; HRMS (DART) *m*/*z* calcd for $C_{16}H_{14}NO_3$ $[MH]^+$: 268.0974 found 268.0974.



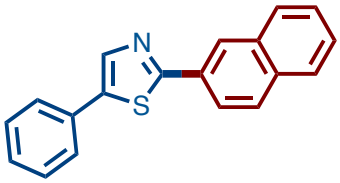
3Gc: 73% (R = Tf)

Ethyl 5-(4-methoxyphenyl)-2-phenyloxazole-4-carboxylate (3Gc): Purification by preparative thin-layer chromatography ($CHCl_3$) afforded **3Gc** (94.3 mg, 73%) as a white solid. R_f = 0.47 (hexane/EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17–8.06 (m, 4H), 7.49–7.43 (m, 3H), 7.00 (dd, 2H, *J* = 9.2, 2.4 Hz), 4.45 (q, 2H, *J* = 7.2 Hz), 3.86 (s, 3H), 1.43 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4, 161.0, 159.0, 155.3, 130.7, 130.1, 128.6, 126.9, 126.6, 126.4, 119.5, 113.7, 61.2, 55.3, 14.2; HRMS (DART) *m*/*z* calcd for $C_{19}H_{18}NO_4$ $[MH]^+$: 324.1236 found 324.1236.



3Ha: 65% (R = CO^{t}Bu)

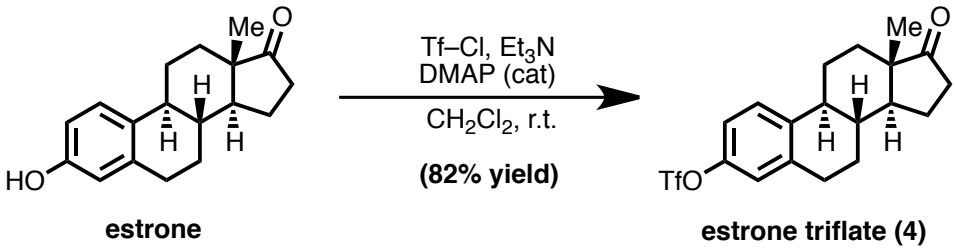
2-(Naphthalen-2-yl)benzothiazole (3Ha):[25] Purification by preparative thin-layer chromatography (hexane/EtOAc = 5:1) afforded **3Ha** (71.6 mg, 65%) as a white solid. R_f = 0.48 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (s, 1H), 8.21 (dd, 1H, *J* = 8.8, 2.0 Hz), 8.12 (d, 1H, *J* = 8.4 Hz), 8.01–7.92 (m, 3H), 7.91–7.84 (m, 1H), 7.60–7.49 (m, 3H), 7.41 (t, 1H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.0, 154.2, 135.0, 134.5, 133.1, 130.1, 128.7, 127.8, 127.5, 127.4, 126.8, 126.3, 125.1, 124.3, 123.1, 121.6; HRMS (DART) *m/z* calcd for $C_{17}H_{12}NS$ $[MH]^+$: 262.0690 found 262.0690.



3Ia: 64% (R = CO^{t}Bu)

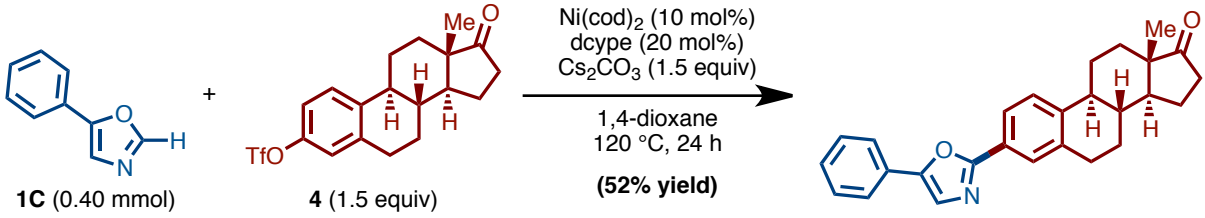
2-(Naphthalen-2-yl)-5-phenylthiazole (3Ia): Purification by preparative thin-layer chromatography (hexane/CH_2Cl_2 = 1:1) afforded **3Ia** (73.7 mg, 64%) as a pale yellow solid. R_f = 0.44 (hexane/CH_2Cl_2 = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H), 8.09–8.00 (m, 2H), 7.93–7.78 (m, 3H), 7.60 (d, 2H, *J* = 7.8 Hz), 7.52–7.48 (m, 2H), 7.40 (t, 2H, *J* = 7.8 Hz), 7.32 (t, 1H, *J* = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 139.4, 139.3, 134.1, 133.2, 131.4, 131.0, 129.1, 128.7, 128.6, 128.3, 127.8, 127.0, 126.8, 126.6, 125.7, 123.7; HRMS (DART) *m/z* calcd for $C_{19}H_{14}NS$ $[MH]^+$: 288.0847 found 288.0846.

5. Nickel-Catalyzed Arylation of Complex Steroid and Alkaloid Scaffolds.



estrone **estrone triflate (4)**

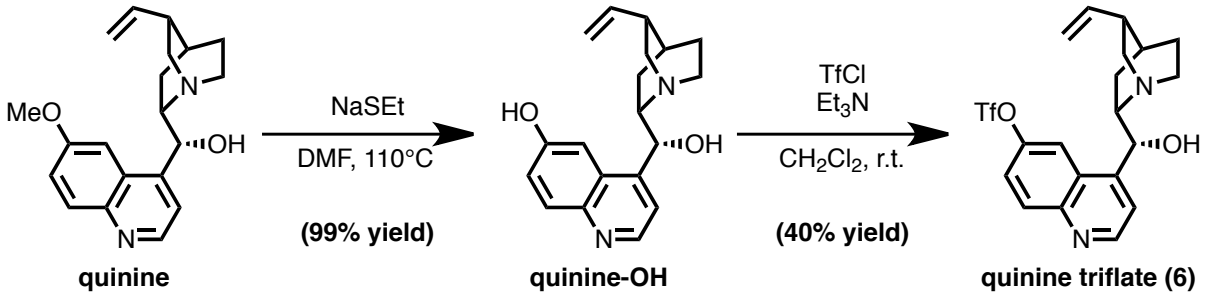
To a solution of estrone (1.62 g, 6.0 mmol) in CH_2Cl_2 (10 mL) was added triethylamine (1.0 mL, 7.2 mmol, 1.2 equiv) at room temperature. Then trifluoromethanesulfonyl chloride (760 μL, 7.2 mmol, 1.2 equiv) was added dropwise over 3 min at 0 °C. After stirring for 6 h, the reaction mixture was quenched with sat. $NaHCO_3$ aq. (10 mL), then the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (20 mL × 3) and the combined organic layer was dried over Na_2SO_4 and then filtrated. Following evaporation of the solvent under reduced pressure, the crude residue was purified by flash column chromatography (hexane/EtOAc = 5:1) to afford estrone triflate **4**[26] as a white solid (1.98 g, 82% yield). R_f = 0.36 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, 1H, *J* = 9.2 Hz), 7.03 (d, 1H, *J* = 8.7 Hz), 6.99 (s, 1H), 3.00–2.90 (m, 2H), 2.52 (ddd, 1H, *J* = 18.8, 9.2, 2.8 Hz), 2.50–2.36 (m, 1H), 2.36–2.25 (m, 1H), 2.24–2.01 (m, 3H), 1.98 (dd, 1H, *J* = 9.6, 2.3 Hz), 1.69–1.44 (m, 6H), 0.92 (s, 3H).



1C (0.40 mmol) **4** (1.5 equiv) **5**

A 20-mL glass vessel equipped with J. Young® O-ring tap containing a magnetic stirring bar and Cs_2CO_3 (195.5 mg, 0.60 mmol, 1.5 equiv) was dried with a heatgun under reduced pressure and filled with argon after cooling to room temperature. To this vessel was added 5-phenyloxazole (**1C**: 58.0 mg, 0.40 mmol) and estrone triflate **4** (241.5 mg, 0.60 mmol, 1.5 equiv) then introduced into an argon-atmosphere glovebox. To the reaction vessel was added $Ni(cod)_2$ (11.2 mg, 0.04 mmol, 10 mol%) and 1.2-bis(dicyclohexylphosphino)ethane (dcype) (33.8 mg, 0.08 mmol, 20 mol%). The vessel was taken out of the glovebox, then to it was added 1,4-dioxane (1.6 mL) under a stream of argon. The vessel was sealed with O-ring tap and then heated at 120 °C for 24 h in an 8-well reaction block with stirring.

After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad with EtOAc. The filtrate was concentrated and the residue was subjected to preparative thin-layer chromatography ($CHCl_3$) to afford 5-phenyloxazol-2-yl estrone (**5**: 83.3 mg, 52%) as a white solid. R_f = 0.50 (hexane/EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87–7.79 (m, 2H), 7.70 (d, 2H, *J* = 7.6 Hz), 7.46–7.39 (m, 3H), 7.38–7.29 (m, 2H), 3.01–2.92 (m, 2H), 2.50 (d, 1H, *J* = 18.8, 8.8 Hz), 2.44–2.38 (m, 1H), 2.33–2.25 (m, 1H), 2.18–1.94 (m, 4H), 1.68–1.39 (m, 6H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 220.5, 161.2, 150.8, 142.3, 137.0, 128.8, 128.2, 127.9, 126.6, 125.7, 124.8, 124.0, 123.5, 123.2, 50.3, 47.8, 44.4, 37.7, 35.7, 31.4, 29.2, 26.2, 25.5, 21.4, 13.7; HRMS (DART) *m*/*z* calcd for $C_{27}H_{28}NO_2$ $[MH]^+$: 398.2120 found 398.2119.

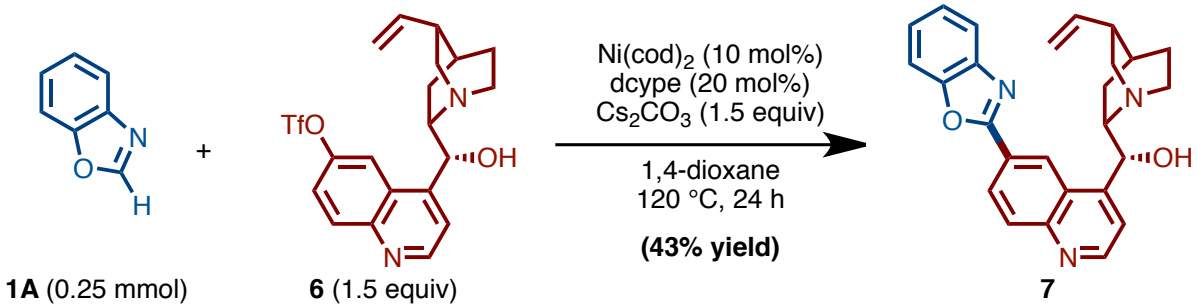


quinine **quinine-OH** **quinine triflate (6)**

A 100-mL two necked round flask containing a magnetic stirring bar was dried with a heatgun under reduced pressure and filled with argon after cooling to room temperature. To this vessel was added quinine (1.33 g, 4.1 mmol), sodium ethane sulfide (1.38 g, 16.4 mmol, 4.0 equiv), and then DMF (30 mL). This vessel was heated at 120 °C in an oil bath overnight. After cooling the reaction vessel to room temperature, the reaction mixture was quenched with sat. NH_4Cl (30 mL), then the layers were separated. The aqueous layer was extracted with EtOAc (25 mL × 5), then the combined organic layer was washed with brine (25 ml × 3). The organic layer was dried over Na_2SO_4 and then filtrated. Following evaporation of the solvent under reduced pressure, the crude mixture was washed with 10% CH_2Cl_2 in hexane to afford demethylated quinine (quinine–OH: 1.27 g, 99% yield) as a white solid.[26] ^{1}H NMR (400 MHz, CD_3OD): δ 8.60 (d, 1H, *J* = 4.8 Hz), 7.91 (d, 1H, *J* = 9.2 Hz), 7.63 (d, 1H, *J* = 4.4 Hz), 7,34 (dd, 1H, *J* = 9.2, 2.8 Hz), 7.29 (d, 1H, *J* = 2.4 Hz), 5.81–5.69 (m, 1H), 5.57 (d, 1H, *J* = 2.8 Hz), 5.03–4.89 (m, 1H), 4.88–4.83 (m, 1H), 3.78 (br, 1H), 3.24–3.12 (m, 2H), 2.86–2.72 (m, 2H), 2.43 (br, 1H), 1.97–1.86 (m, 2H), 1.84 (br, 1H), 1.65 (br, 1H), 1.51–1.41 (m, 1H).

Without further purification, quinine–OH (465.6 mg, 1.5 mmol) was added to a dry 30 mL two necked round flask containing a magnetic stirring bar. To this vessel was added triethylamine (238 μL, 1.1 equiv), CH_2Cl_2 (3.0 mL) then trifluromethanesulfonyl chloride (166 μL, 1.05 equiv) at 0 °C. After stirring for 8 h at room temperature, the reaction mixture was quenched with sat. $NaHCO_3$ (5 mL). The

aqueous layer was extracted with CH_2Cl_2 (15 mL × 5) and the combined organic layer was dried over Na_2SO_4 and then filtrated. Following evaporation of the solvent under reduced pressure, the crude residue was purified by flash column chromatography ($CHCl_3$/MeOH = 9:1) then reversed phase HPLC (H_2O/MeCN gradient) afforded 265.9 mg of quinine triflate **6**[26] as a white solid (40% yield). R_f = 0.26 ($CHCl_3$/MeOH = 10:1); ^{1}H NMR (400 MHz, CD_3OD): δ 8.91 (d, 1H, *J* = 4.4 Hz), 8.36 (d, 1H, *J* = 2.4 Hz), 8.20 (d, 1H, *J* = 9.6 Hz), 7.77–7.71 (m, 2H), 5.82–5.71 (m, 1H), 5.45 (d, 1H, *J* = 4.8 Hz), 5.01–4.85 (m, 2H), 3.58–3.46 (br, 1H), 3.20–3.12 (br, 1H), 3.05 (dd, 1H, *J* = 14.0, 10.8 Hz), 2.71–2.60 (m, 2H), 2.39–2.29 (br, 1H), 1.89–1.78 (m, 3H), 1.68–1.52 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ 153.9, 149.9, 149.3, 144.0, 134.5, 128.8, 125.5, 123.0, 121.6 (q, J_{C-F} = 322.0 Hz), 119.2, 116.3, 74.6, 63.2, 58.6, 45.0, 42.1, 30.4, 29.5, 24.5.



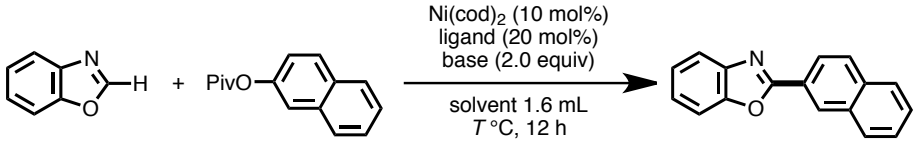
A 20-mL glass vessel equipped with J. Young® O-ring tap containing a magnetic stirring bar and Cs_2CO_3 (122.2 mg, 0.375 mmol, 1.5 equiv) was dried with a heatgun under reduced pressure and filled with argon after cooling to room temperature. To this vessel was added quinine triflate **6** (165.9 mg, 0.375 mmol, 1.5 equiv) then introduced into an argon-atmosphere glovebox. To the reaction vessel was added $Ni(cod)_2$ (7.0 mg, 0.025 mmol, 10 mol%) and 1,2-bis(dicyclohexylphosphino)ethane (dcype) (20.8 mg, 0.05 mmol, 20 mol%). The vessel was taken out of the glovebox, then to it was added benzoxazole (**1A**: 29.8 mg, 0.25 mmol, 1.0 equiv) and 1,4-dioxane (1.0 mL) under a stream of argon. The vessel was sealed with O-ring tap and then heated at 120 °C for 24 h in an 8-well reaction block with stirring. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad with EtOAc. The filtrate was concentrated and the residue was subjected to preparative thin-layer chromatography ($CHCl_3$/MeOH = 10:1), then reversed phase HPLC (H_2O/MeCN gradient) afforded benzoxazol-2-yl quinine (**7**: 43.9 mg, 43%) as a white solid. R_f = 0.17 ($CHCl_3$/MeOH = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (s, 1H), 8.28 (d, 1H, *J* = 4.4 Hz), 8.08 (dd, 1H, *J* = 8.8, 1.2 Hz), 7.93 (d, 1H, *J* = 8.8 Hz), 7.72–7.65 (m, 1H), 7.64–7.57 (m, 1H), 7.44 (d, 1H, *J* = 4.4 Hz), 7.42–7.35 (m, 2H), 5.82 (d, 1H, *J* = 2.8 Hz), 5.72–5.61 (m, 1H), 4.96–4.82 (m, 2H), 3.73–3.58 (m, 1H), 3.13 (dd, 1H, *J* = 14.0, 10.4 Hz), 3.04–2.94 (m, 1H), 2.82–2.68 (m, 1H), 2.60 (dd, 1H, *J*

= 14.0, 3.2 Hz), 2.30 (br, 1H), 2.00–1.85 (m, 2H), 1.85–1.79 (m, 1H), 1.62–1.49 (m, 1H), 1.48–1.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 151.3, 150.7, 150.6, 148.7, 141.4, 141.3, 130.7, 126.4, 125.5, 124.9, 124.8, 123.9, 122.8, 119.8, 118.8, 114.4, 110.9, 70.5, 60.7, 56.4, 42.9, 39.6, 27.9, 27.1, 20.4; HRMS (DART) *m*/*z* calcd for $C_{26}H_{26}N_3O_2$ $[MH]^+$: 412.2025 found 412.2025.

6. Effect of Reaction Parameters

Effect of reaction parameters in the Ni-catalyzed C–H/C–O biaryl coupling was investigated. Representative results using the coupling of benzoxazole (**1A**) and naphthalene-2-yl pivalate (**2a**) as a model reaction are shown in Table S1.

Table S1. Effect of Reaction Parameters.



1A (0.40 mmol) **2a** (1.5 equiv) **3Aa**

entry	ligand	base	solvent	*T* (°C)	yield[a] of **3Aa**	**1A**	**2a**
1	bipy	Cs_2CO_3	dioxane	120	0	50	2
2	dmpe	Cs_2CO_3	dioxane	120	0	39	0
3	depe	Cs_2CO_3	dioxane	120	2	35	0
4	PCy_3	Cs_2CO_3	dioxane	120	0	17	0
5	dppe	Cs_2CO_3	dioxane	120	0	35	1
6	IPr•HCl	Cs_2CO_3	dioxane	120	0	30	0
7	SIPr•HCl	Cs_2CO_3	dioxane	120	0	25	0
8[b]	dcype	Cs_2CO_3	dioxane	120	0	34	0
9[c]	dcype	Cs_2CO_3	dioxane	120	16	42	0
10	dcype	Cs_2CO_3	toluene	120	92	0	27
11	dcype	Cs_2CO_3	DMF	120	92	0	0
12	dcype	Cs_2CO_3	DMAc	120	67	0	0
13[d]	dcype	Cs_2CO_3	dioxane	120	>99	0	8
14	dcype	K_2CO_3	dioxane	120	9	45	86
15	dcype	K_3PO_4	dioxane	120	79	0	43
16	dcype	LiO^{t}Bu	dioxane	120	59	2	9
17	dcype	Cs_2CO_3	dioxane	90	80	11	31
18	dcype	Cs_2CO_3	dioxane	100	99	0	10
19	dcype	Cs_2CO_3	dioxane	120	96	0	4
20	dcype	Cs_2CO_3	dioxane	140	96	0	3
21	dcype	Cs_2CO_3	dioxane	150	93	0	2

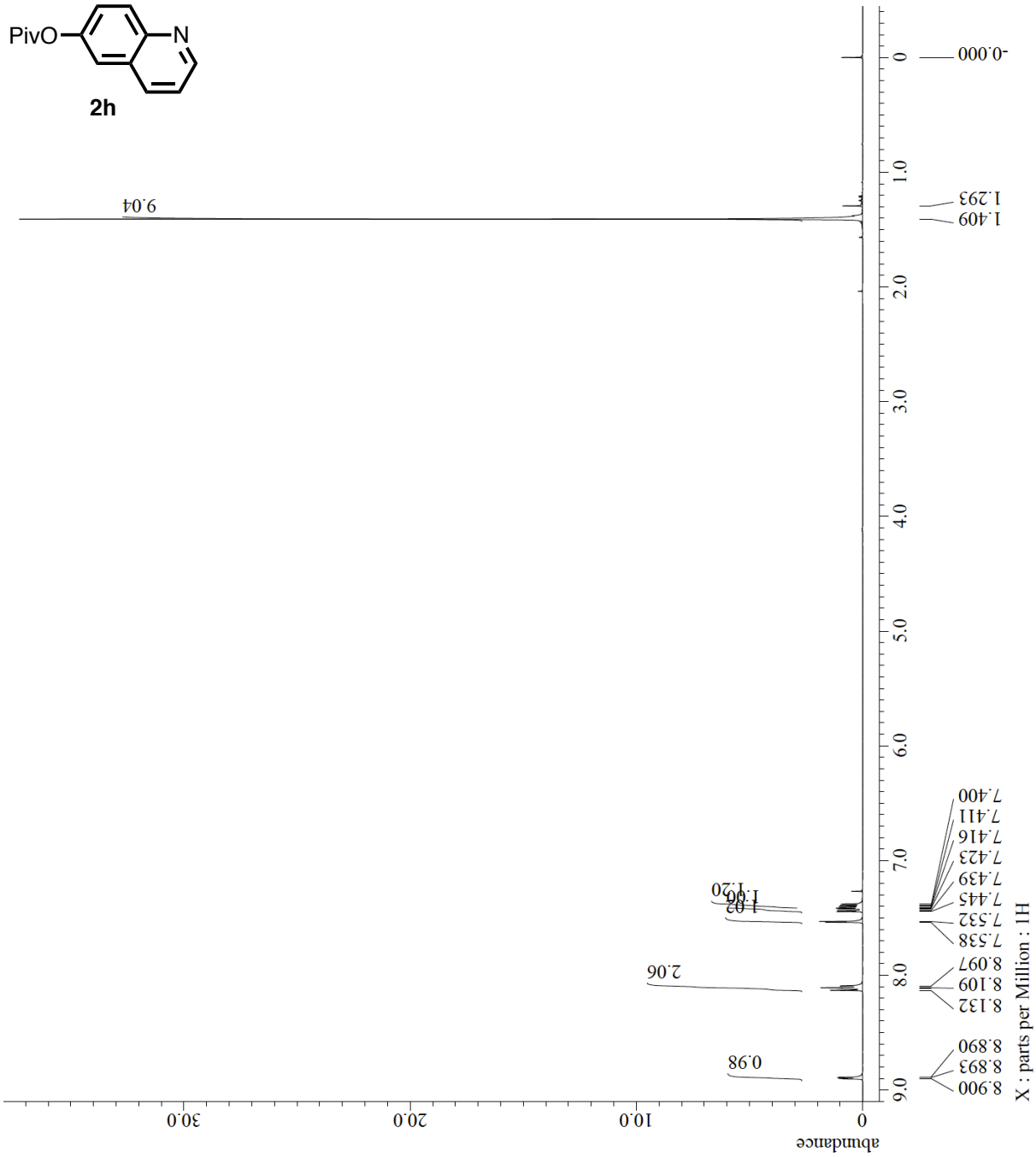
[a] Yields were determined by GC analysis using decane as an internal standard.
[b] 10 mol% $Pd(OAc)_2$ was used instead of $Ni(cod)_2$. [c] 10 mol% $NiBr_2$ was used instead of $Ni(cod)_2$.
[d] 1.5 equiv Cs_2CO_3 was used.
dmpe = 1,2-bis(dimethylphosphino)ethane, depe = 1,2-bis(diethylphosphino)ethane,
dcype = 1,2-bis(dicyclohexylphosphino)ethane

7. Reference

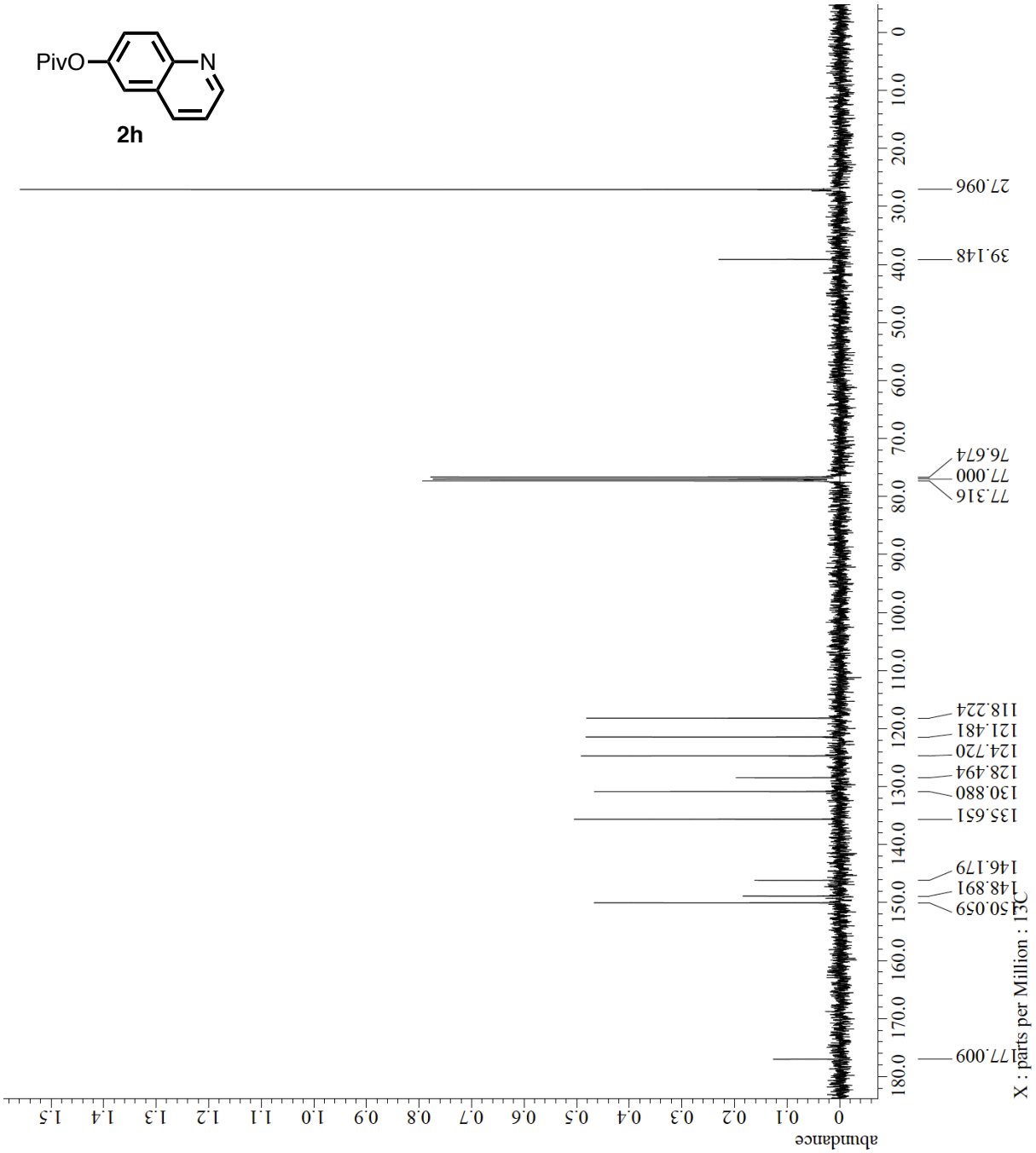
1. Cho, S. H.; Kim, J. Y.; Lee, S. Y.; Chang, S. *Angew. Chem., Int. Ed.* **2009***, 48*, 9127.
2. Besselièvre, F.; Mahuteau-Betzer, F.; Grierson, D. S.; Piguel, S. *J. Org. Chem.* **2008***, 73*, 3278.
3. Parisien, M.; Valette, D.; Fagnou, K. *J. Org. Chem.* **2005**, *70*, 7578.
4. Suzuki, M.; Iwasaki, T.; Miyoshi, M.; Okumura, K.; Matsumoto, K. *J. Org. Chem.* **1973**, *38*, 3571.
5. Reader, J. C.; Ellard, J. M.; Boffey, H.; Taylor, S.; Carr, A. D.; Cherry, M.; Wilson, M.; Owoare, R. B. PCT. Int. Appl. WO2008/139161
6. Quasdorf, K. W.; Tian, X.; Garg, N. K. *J. Am. Chem. Soc.* **2008**, *30,* 14422.
7. Li, B. -J.; Xu, L.; Wu, Z. -H.; Guan, B. –T.; Sun, C. -L.; Wang, B. -Q.; Shi, Z. J. *J. Am. Chem. Soc.* **2009***, 131*, 14656.
8. Ramgren, S. D.; Silberstein, A. L.; Yang, Y.; Garg, N. K. *J. Am. Chem. Soc.* **2011**, *50*, 2171.
9. Quasdorf, K. W.; Riener, M.; Petrova, K. V.; Garg, N. K. *J. Am. Chem. Soc.* **2009**, *131,* 17748.
10. Ogata, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 13848.
11. Wilson, D. A.; Wilson, C. J.; Moldoveanu, C.; Resmerita, A. -M.; Corcoran, P.; Hoang, L. M.; Rosen, B. M.; Percec, V. *J. Am. Chem. Soc.* **2010**, *132*, 1800.
12. Neuville, L.; Bigot, A.; Dau, M. E. T. H.; Zhu, J. *J. Org. Chem.* **1999**, *64*, 7638.
13. Lee, D. -Y.; Hartwig, J. F. *Org. Lett.* **2005**, *7*, 1169.
14. Echavarren, A. M.; Stille*,* J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478.
15. Gill, D.; Hester, A. J.; Lloyd-Jones, G. C. *Org. Biomol. Chem.* **2004***, 2*, 2547.
16. Ackermann, L.; Barfüßer, S.; Pospech, J. *Org. Lett.* **2010**, *12,* 724.
17. Do, H. -Q.; Daugulis, O. *J. Am. Chem. Soc.* **2007**, *129*, 12404.
18. Kawashita, Y.; Nakamichi, N.; Kawabata, H.; Hayashi, M. *Org. Lett.* **2003**, *5,* 3713.
19. Johnson, S. M.; Connelly, S.; Wilson, I. A.; Kelly, J. W. *J. Med. Chem.* **2008**, *51,* 260.
20. Evindar, G.; Batey, R. A. *J. Org. Chem.* **2006**, *71*, 1802.
21. So, C. M.; Lau, C. P.; Kwong, F. Y. *Chem. Eur. J.* **2011**, *17*, 761.
22. Hachiya, H.; Hirano, K.; Satoh, T.; Miura*,* M. *Org. Lett.* **2009**, *11*, 1737.
23. Barbero, N.; Carril, M.; SanMartin, R.; Domínguez, E. *Tetrahedron* **2007**, *63,* 10425.
24. Besselievre, F.; Lebrequier, S.; Mahuteau-Betzer, F.; Piguel, S. *Synthesis* **2009**, *20*, 3511.
25. Yamamoto, T.; Muto, K.; Komiyama, M.; Canivet, J.; Yamaguchi, J.; Itami, K. *Chem. Eur. J.* **2011***, 17*, 10113.
26. Furuya, T.; Storm, A. E.; Ritter, T. *J. Am. Chem. Soc.* **2009***, 131,* 1662.

8. ^{1}H and ^{13}C NMR Spectra of Products

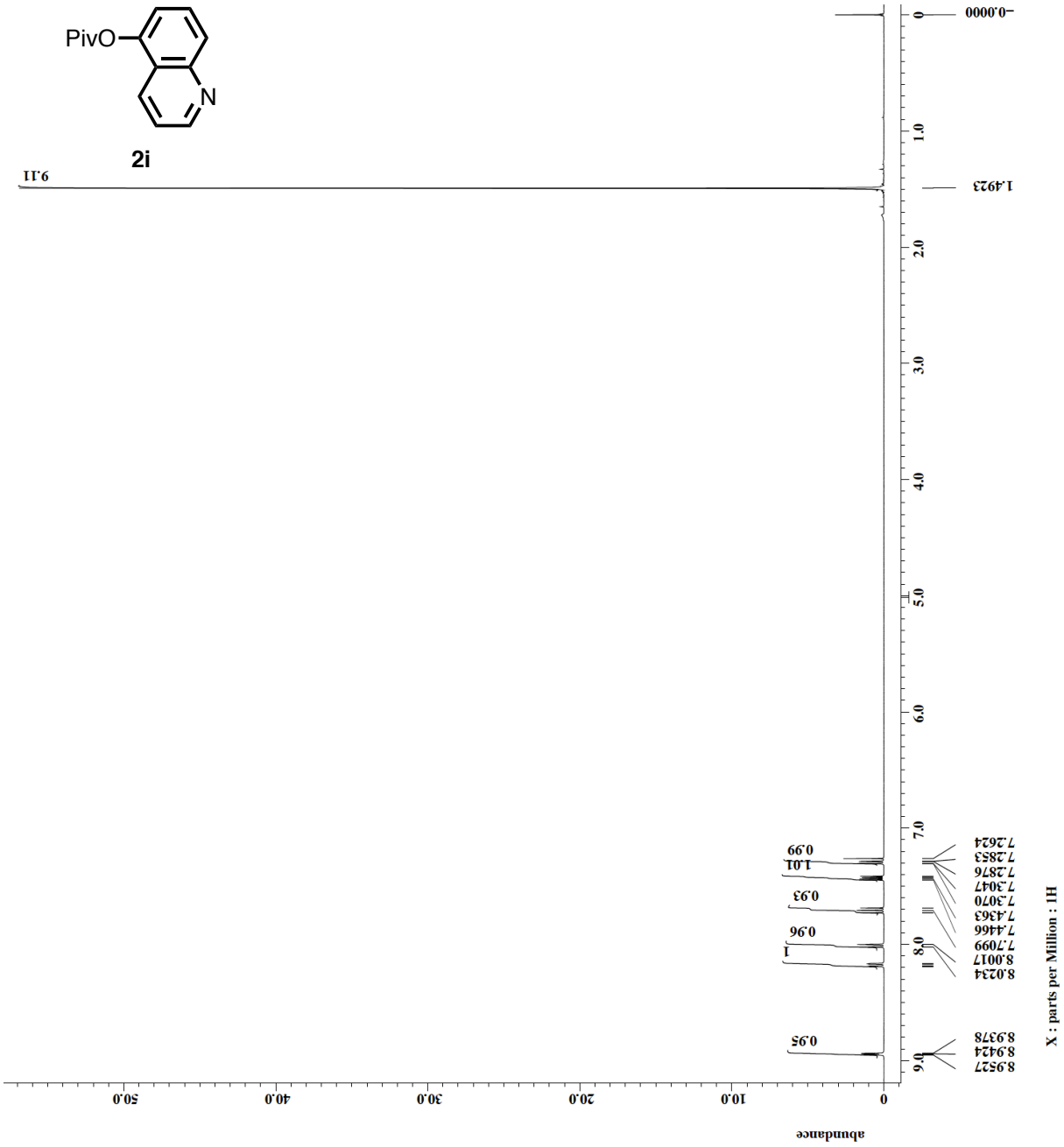
^{1}H NMR (400 MHz, $CDCl_3$)



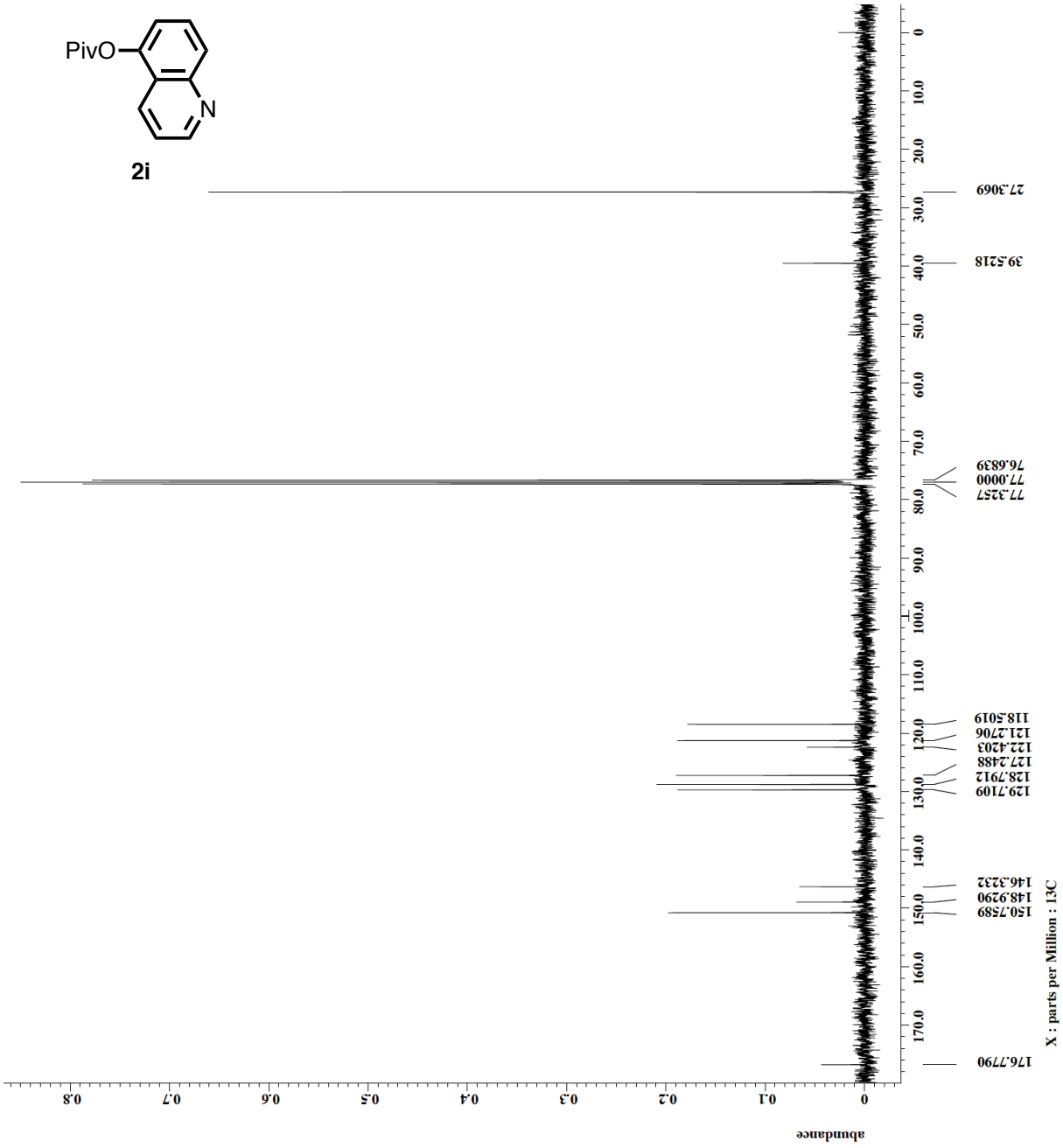
^{13}C NMR (100 MHz, $CDCl_3$)



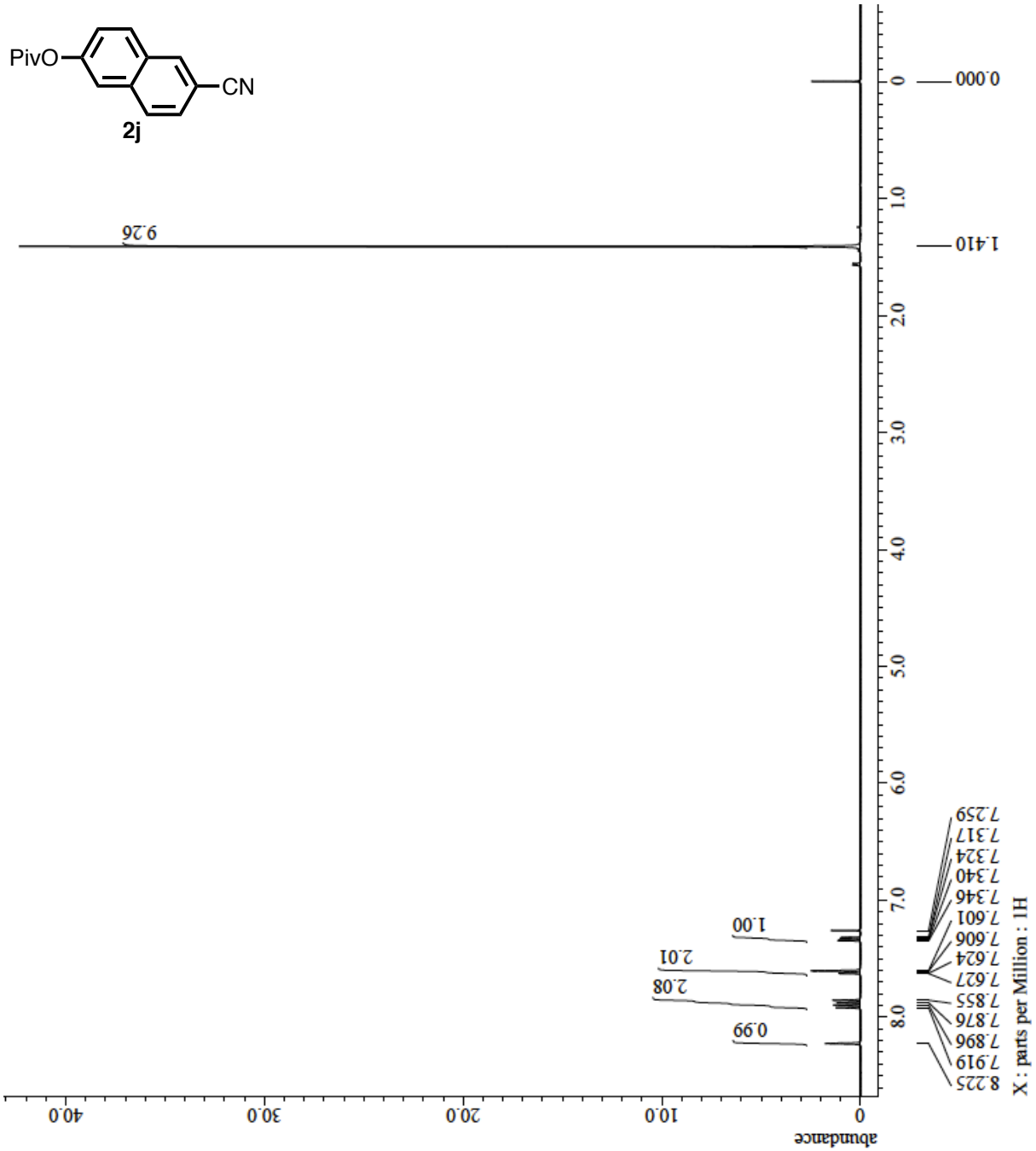
^{1}H NMR (400 MHz, $CDCl_3$)



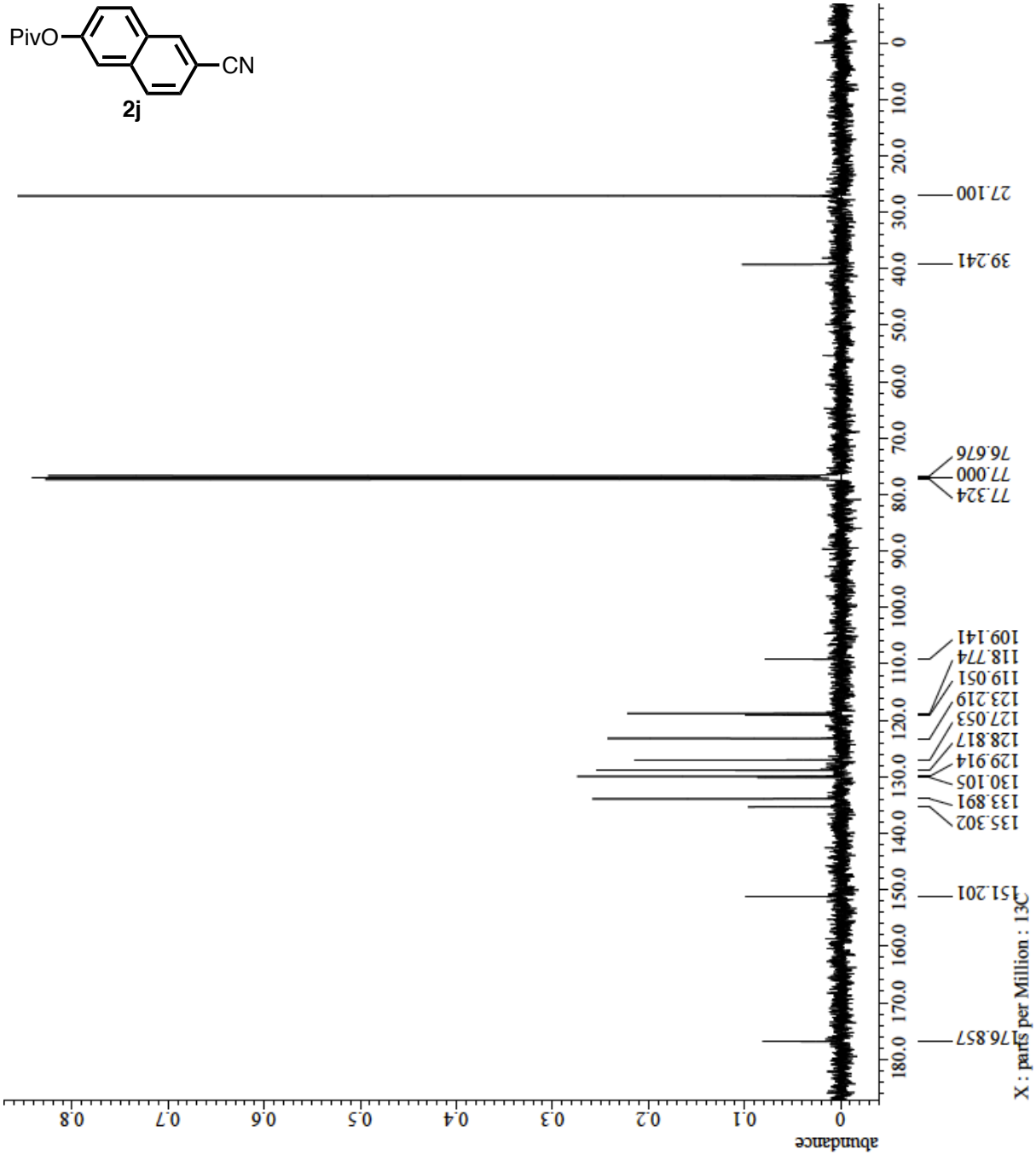
^{13}C NMR (100 MHz, $CDCl_3$)



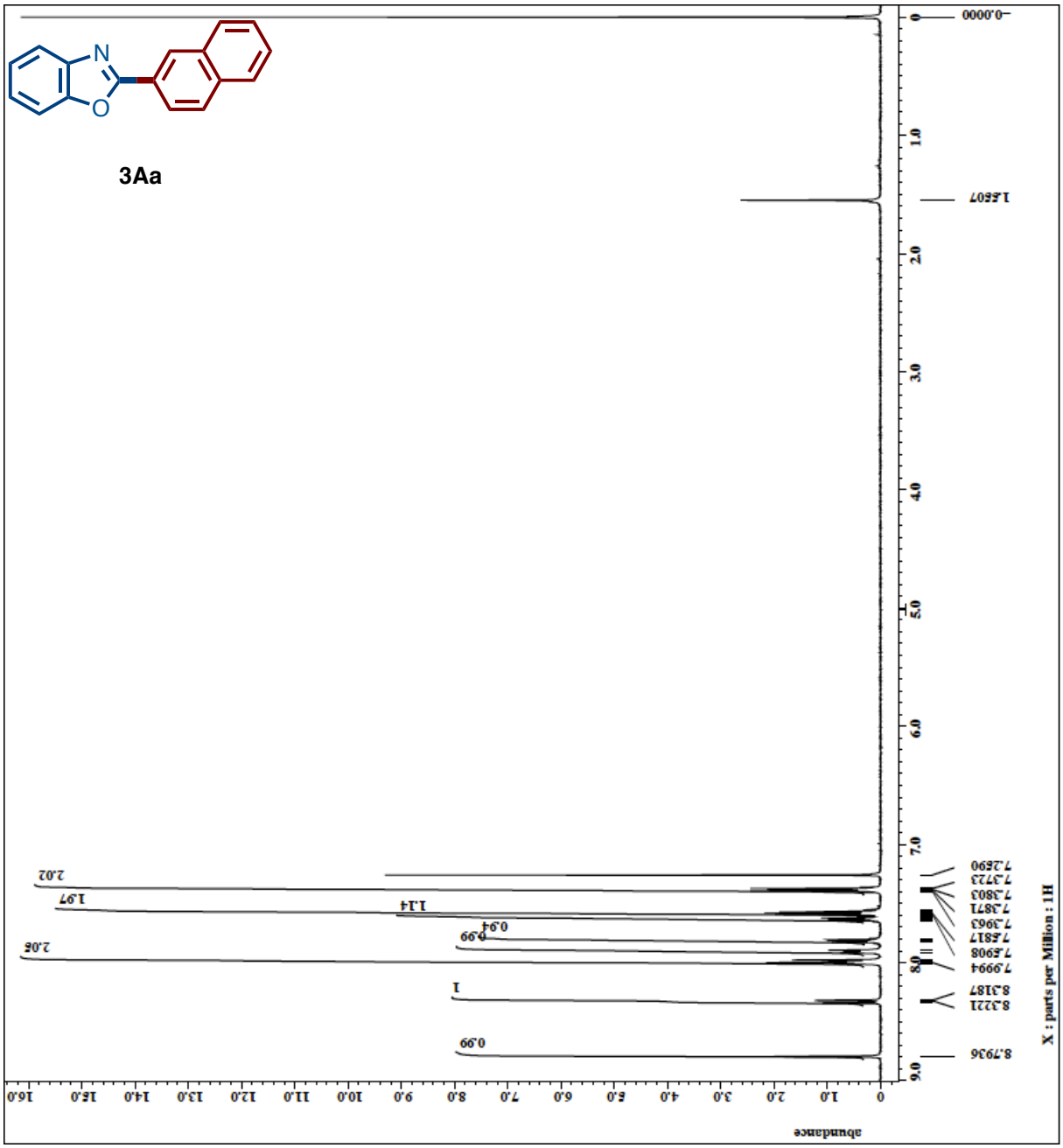
^{1}H NMR (400 MHz, $CDCl_3$)



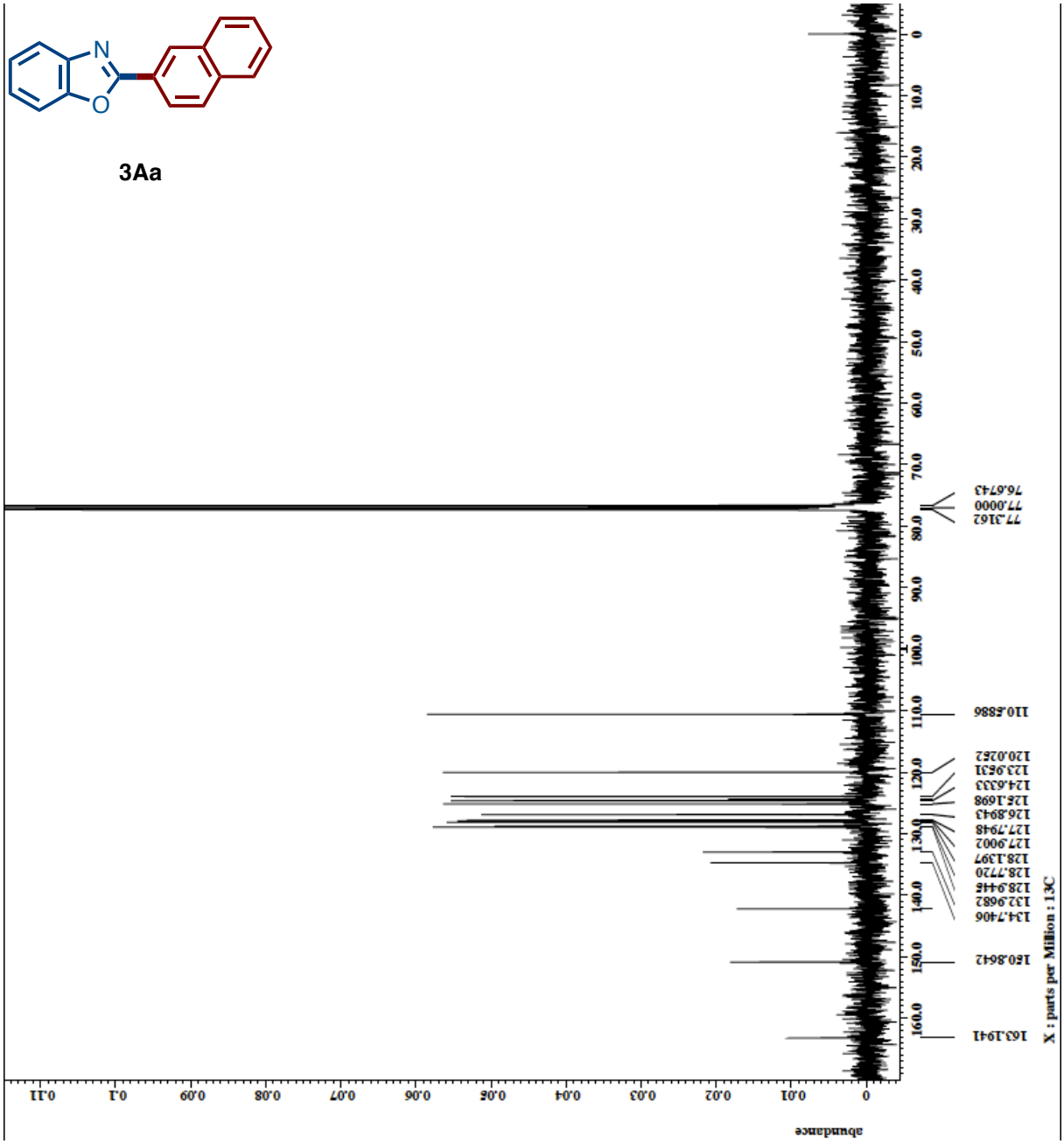
^{13}C NMR (100 MHz, $CDCl_3$)



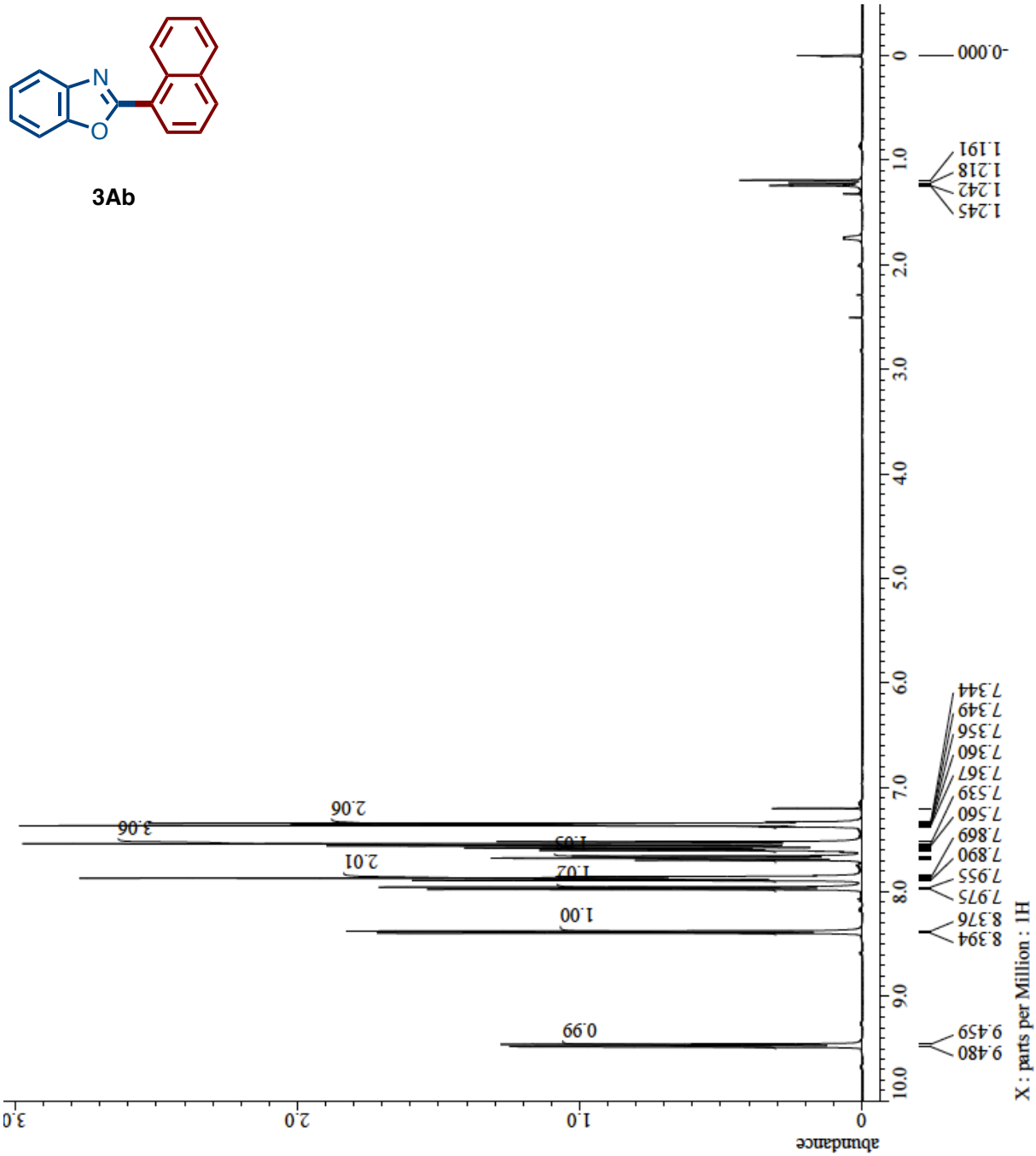
^{1}H NMR (400 MHz, $CDCl_3$)



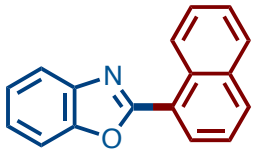
^{13}C NMR (100 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)

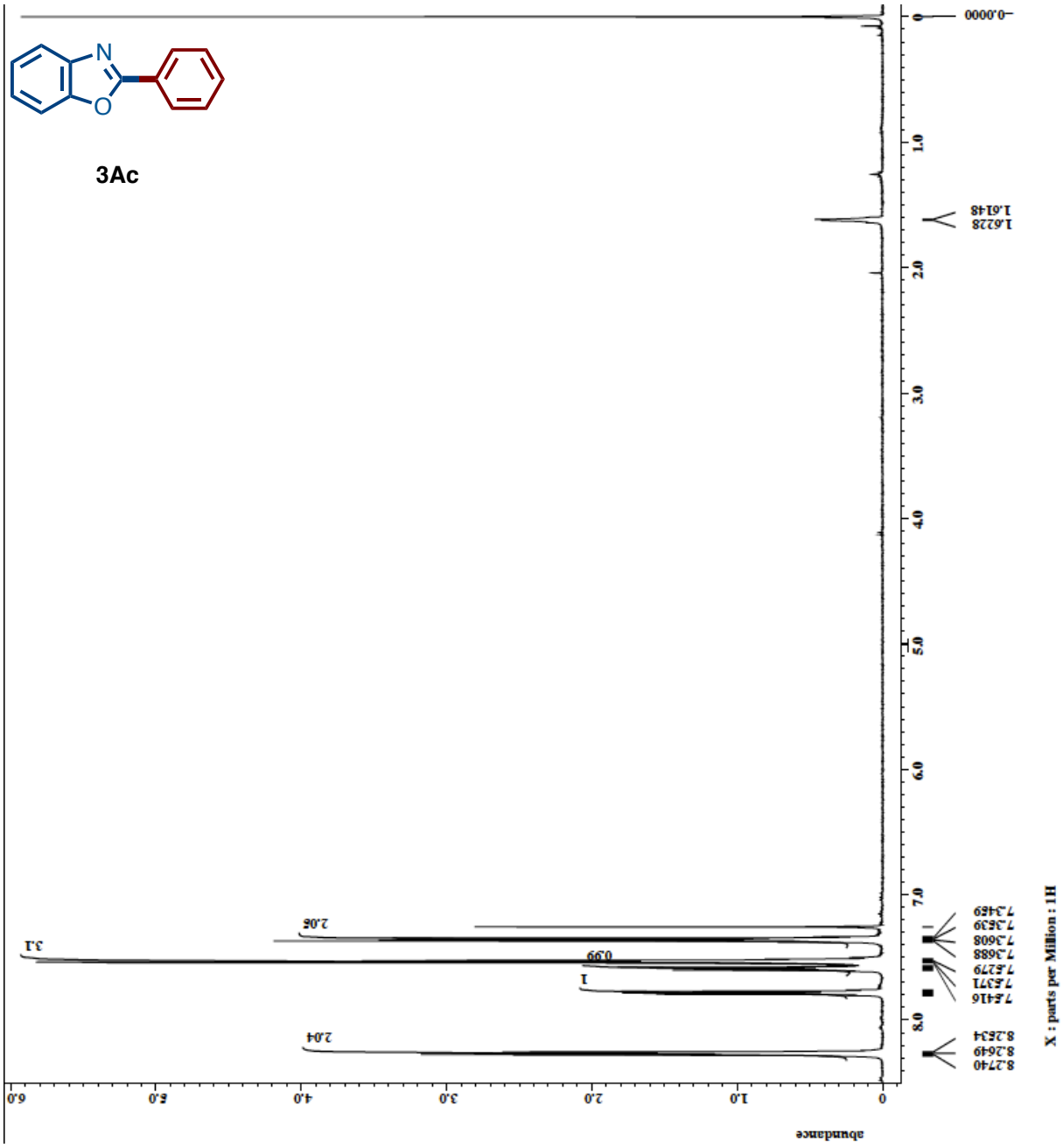


^{13}C NMR (100 MHz, $CDCl_3$)

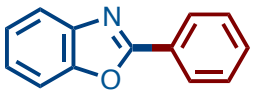


3Ab

^{1}H NMR (400 MHz, $CDCl_3$)

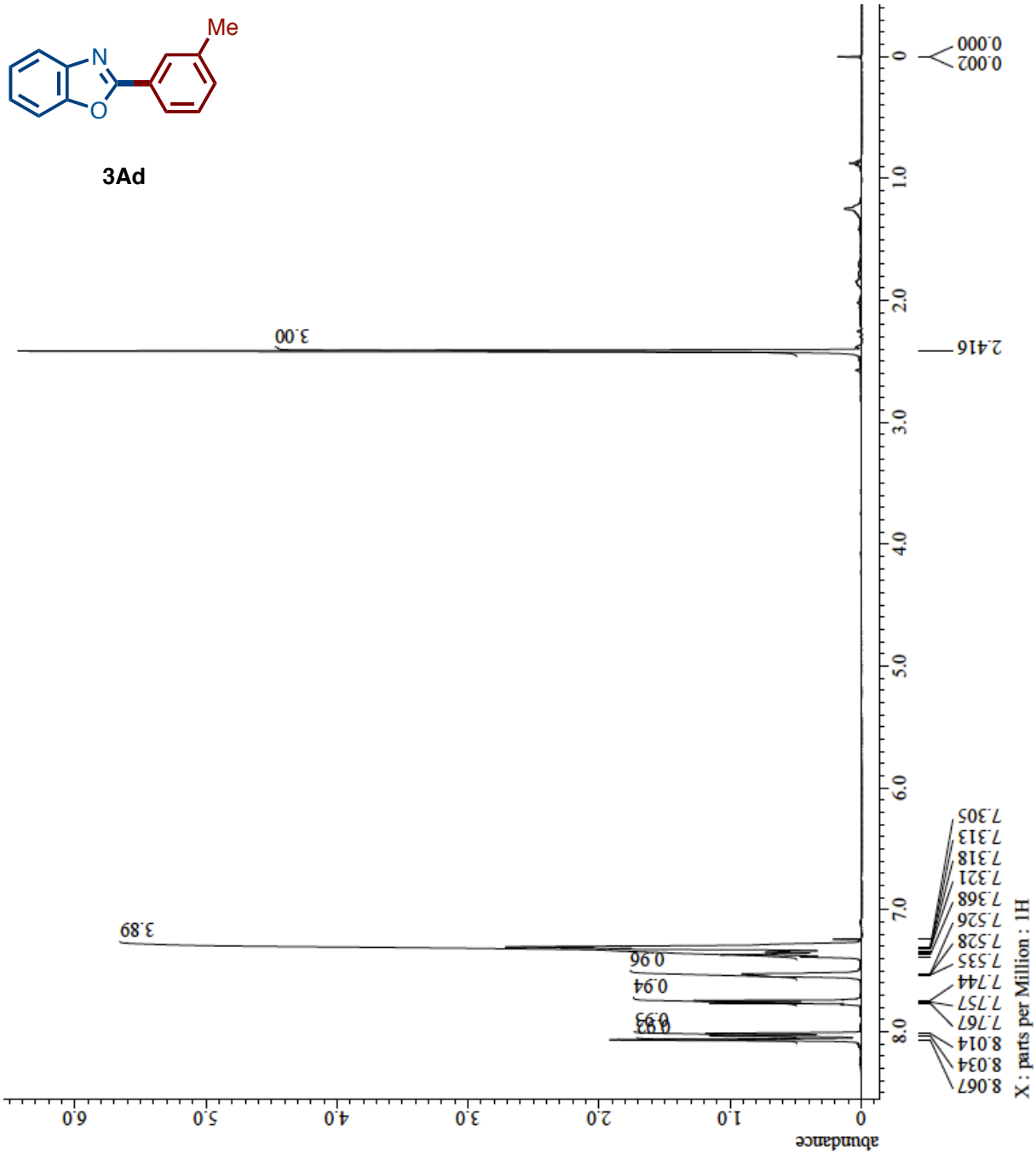


^{13}C NMR (100 MHz, $CDCl_3$)

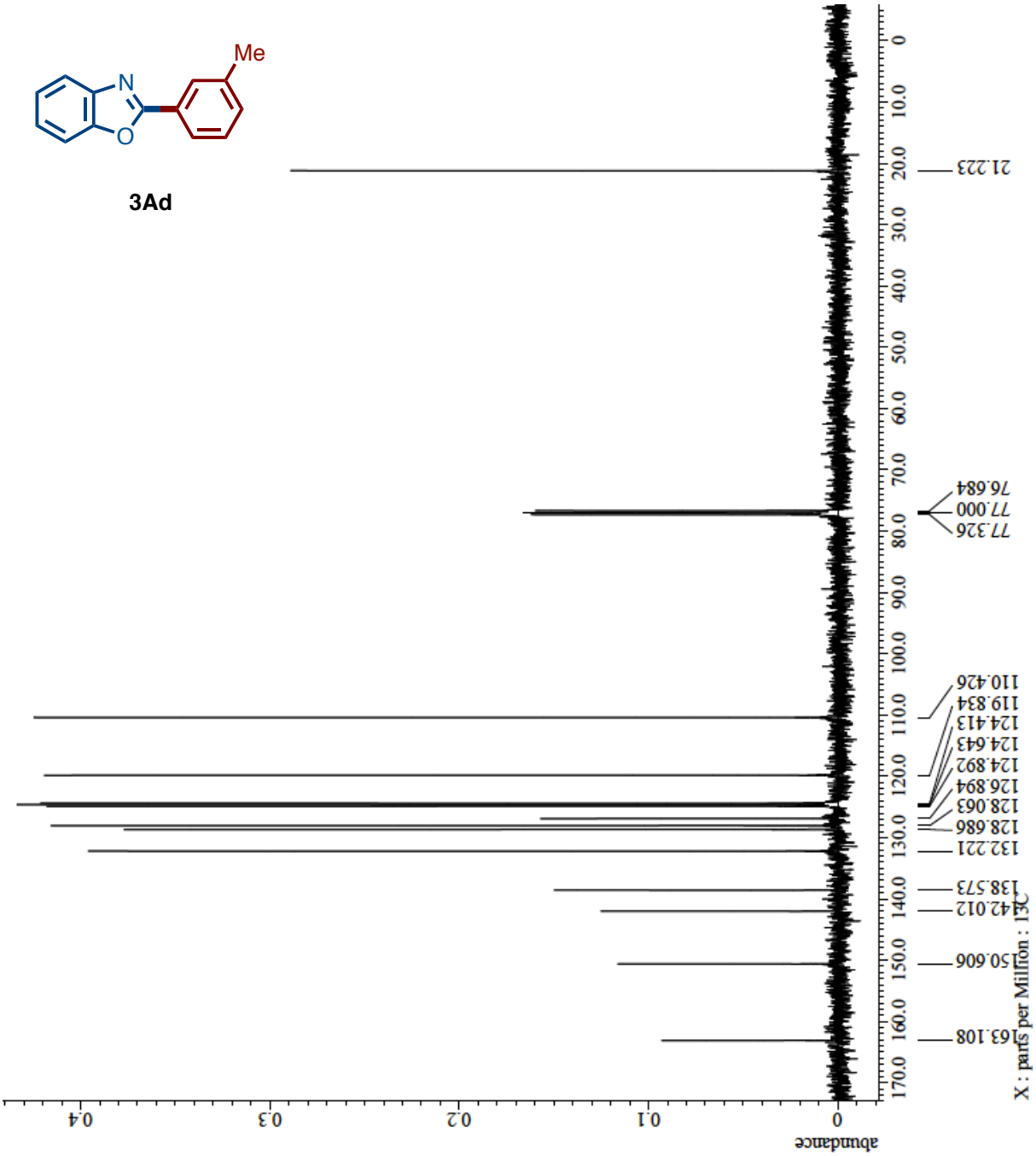


3Ac

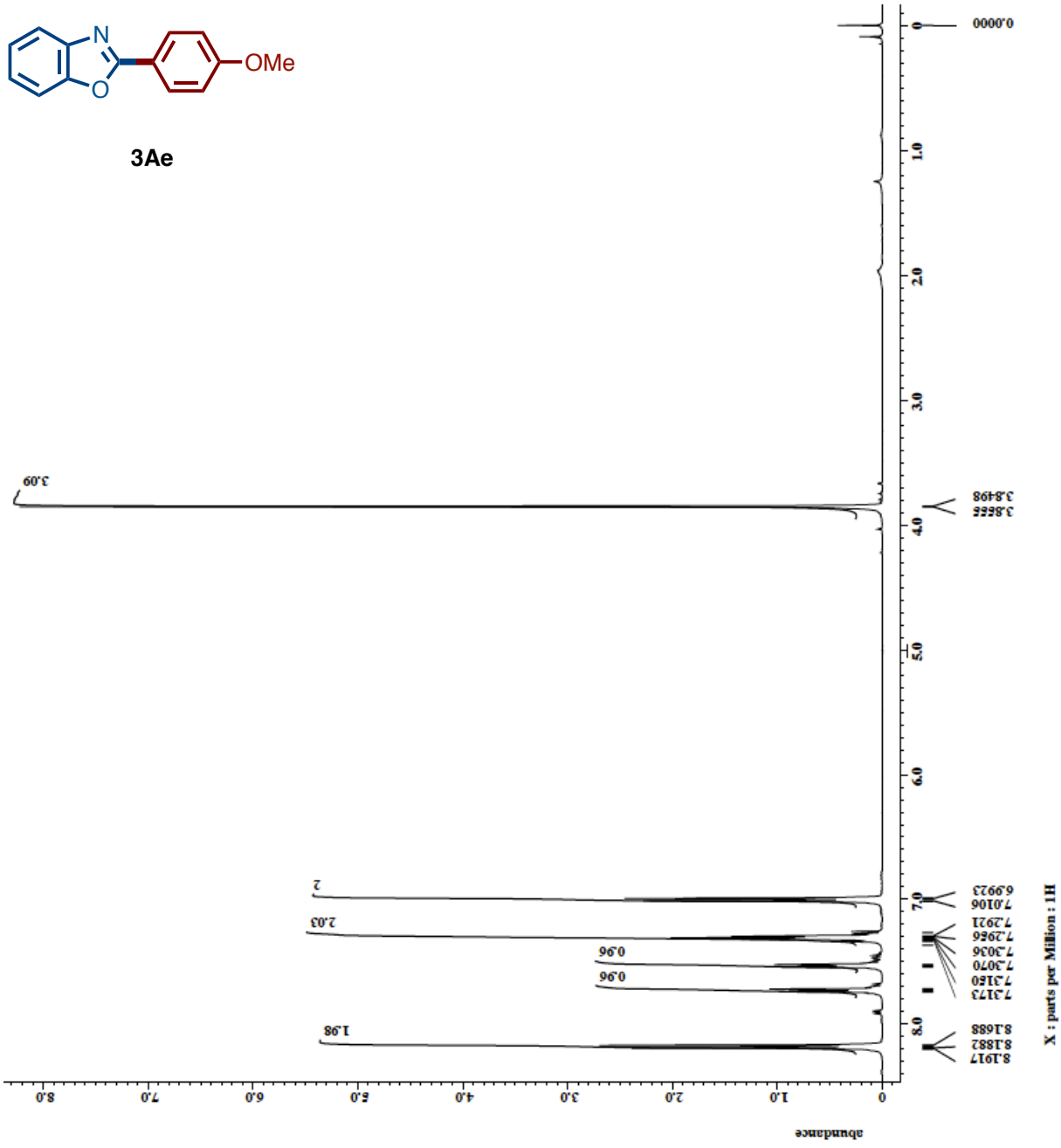
^{1}H NMR (400 MHz, $CDCl_3$)



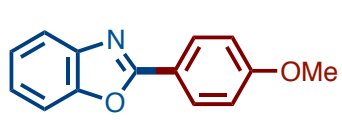
^{13}C NMR (100 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)

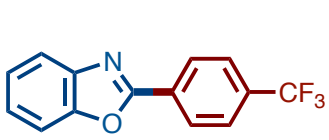


^{13}C NMR (100 MHz, $CDCl_3$)



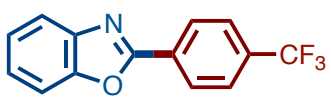
3Ae

^{1}H NMR (400 MHz, $CDCl_3$)



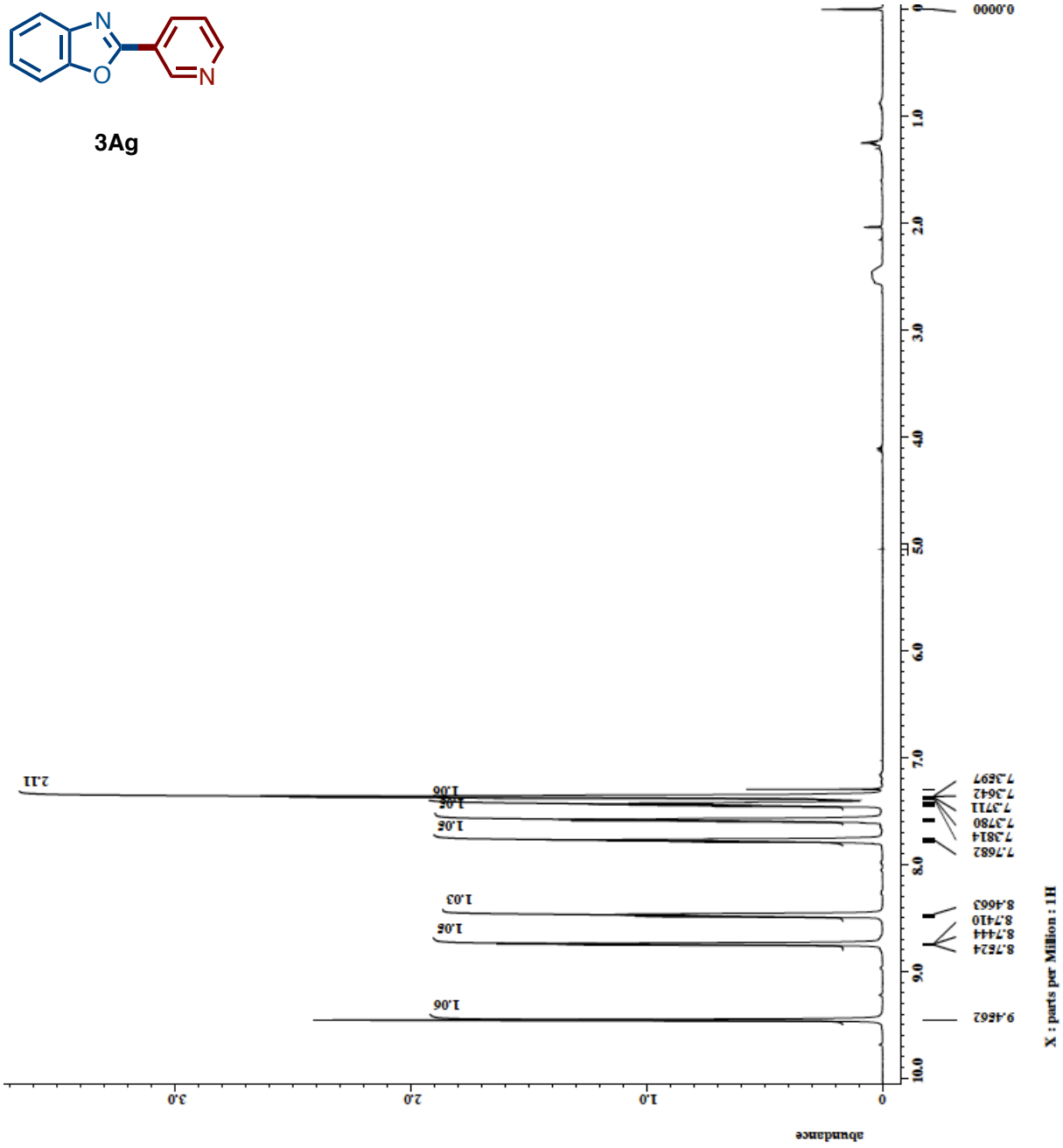
3Af

^{13}C NMR (100 MHz, $CDCl_3$)

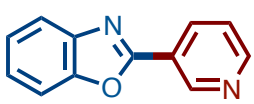


3Af

^{1}H NMR (400 MHz, $CDCl_3$)

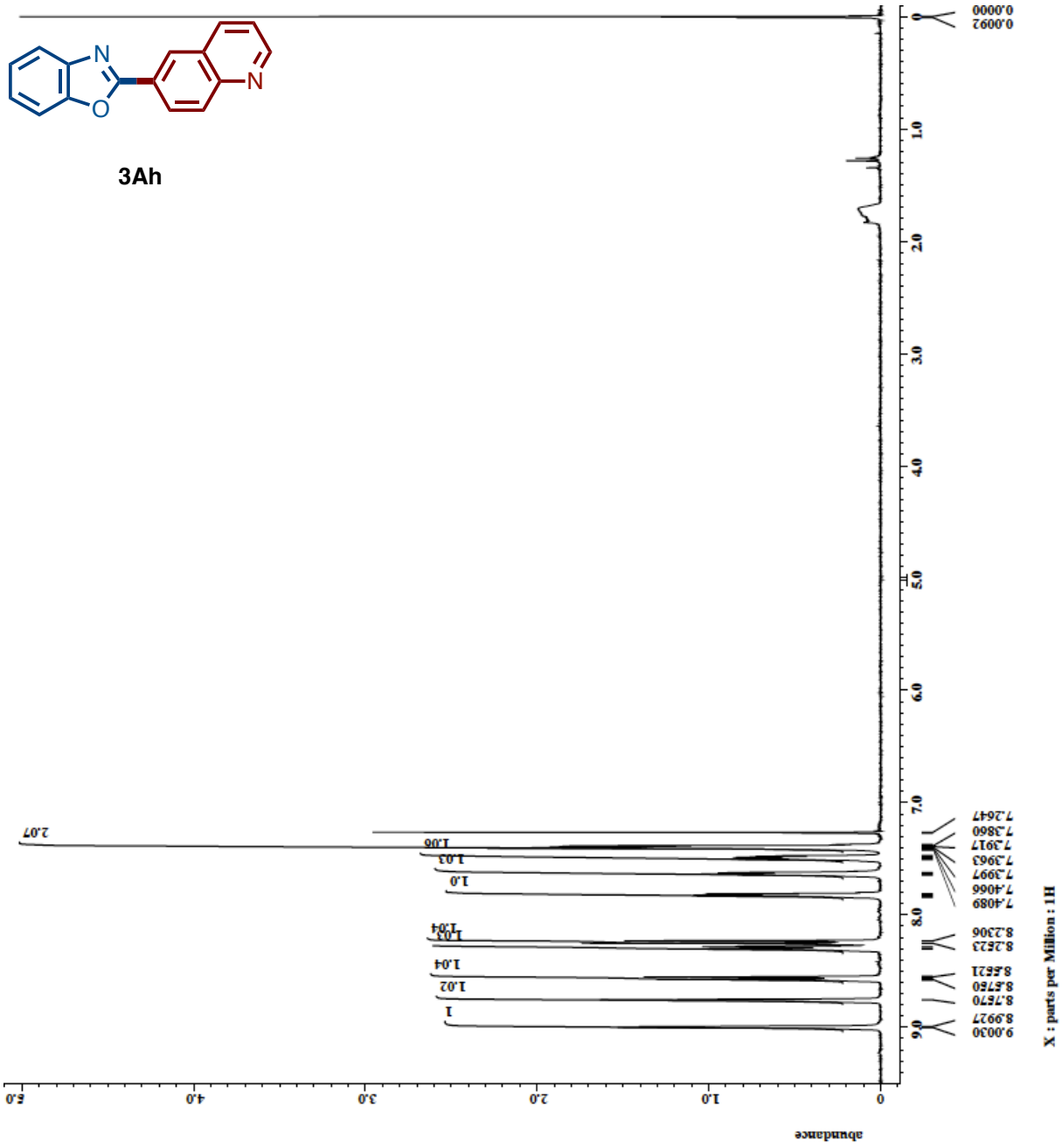


^{13}C NMR (100 MHz, $CDCl_3$)

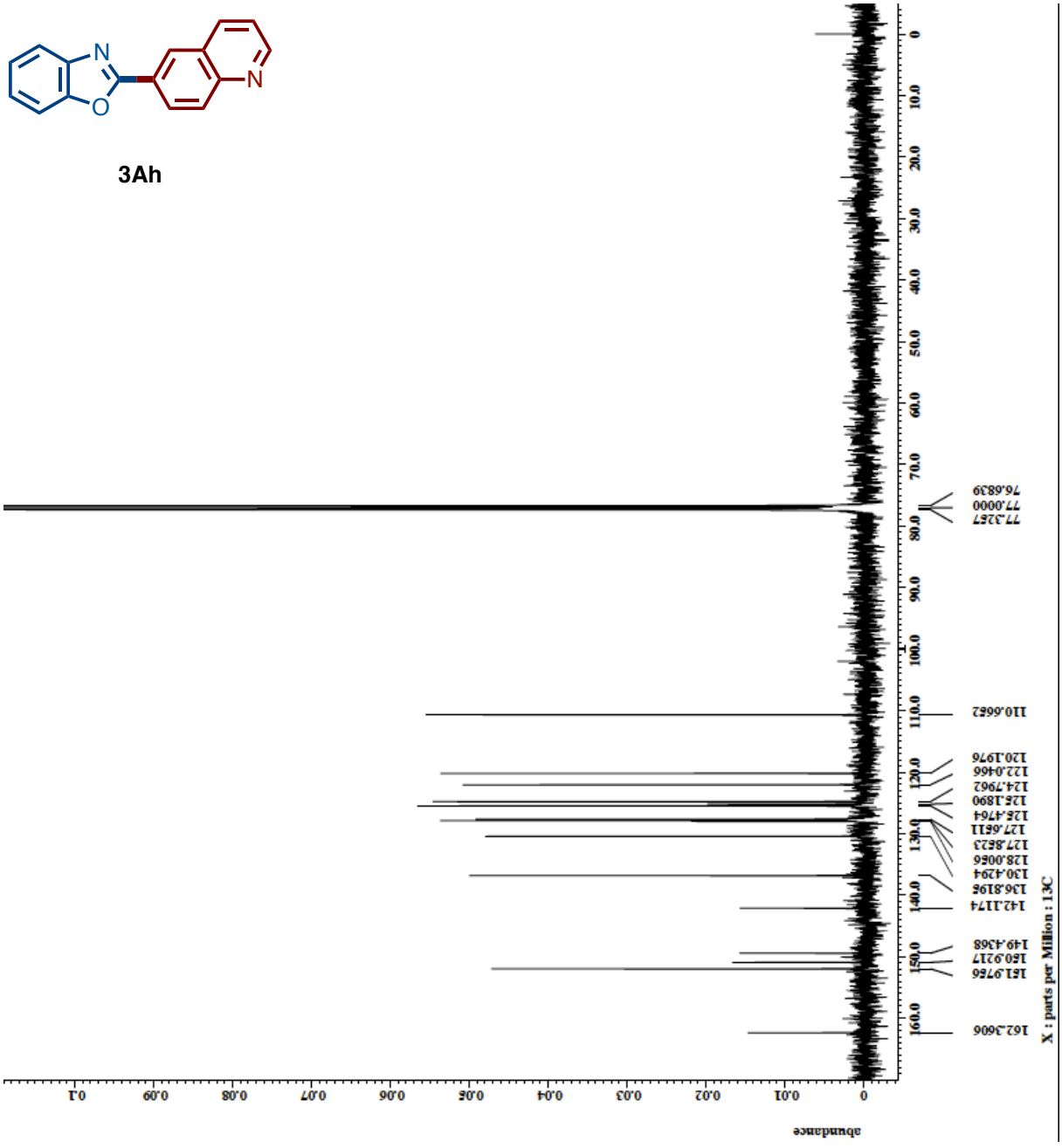


3Ag

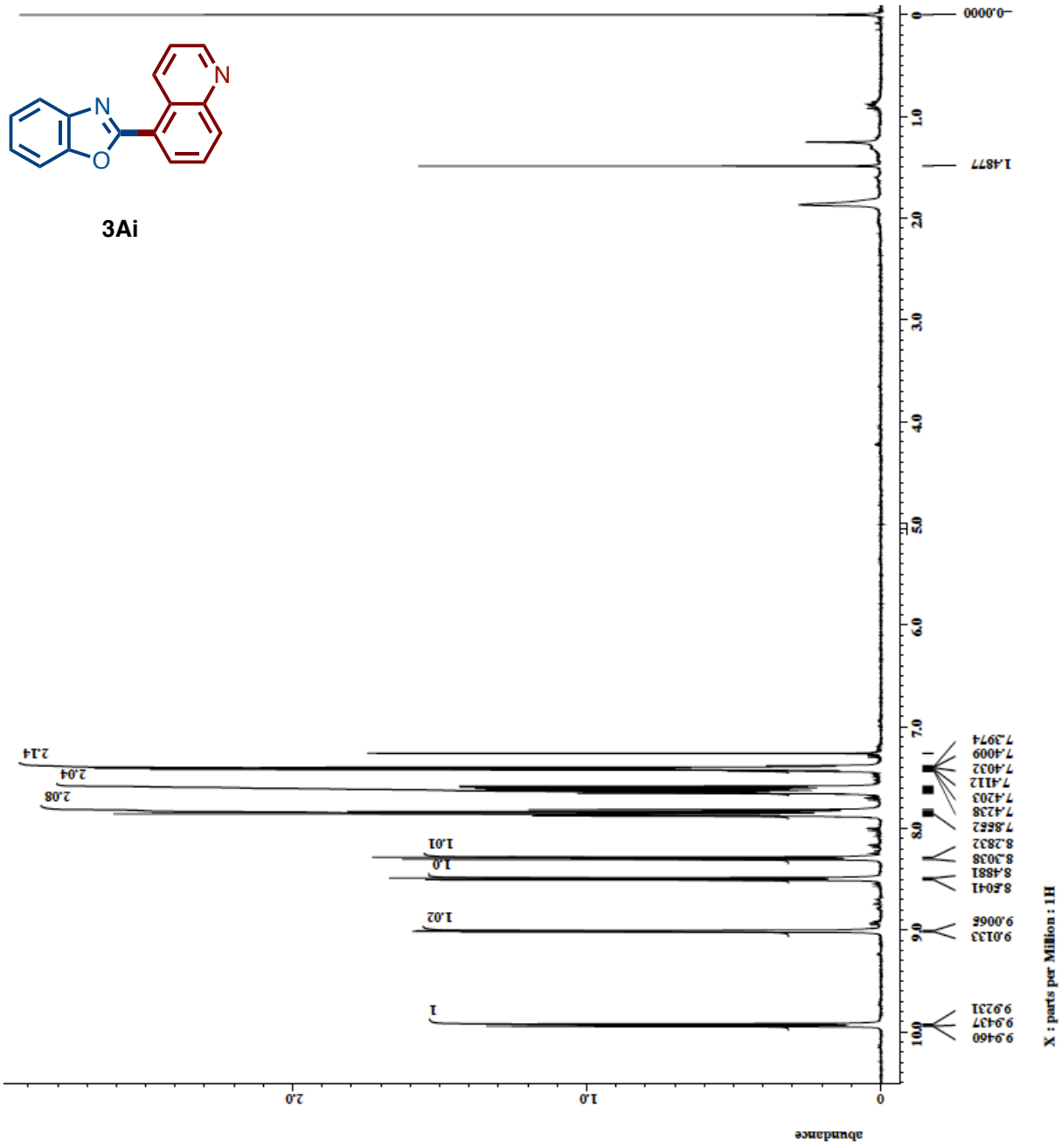
^{1}H NMR (400 MHz, $CDCl_3$)



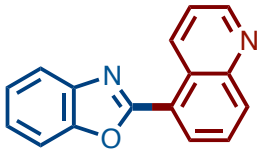
^{13}C NMR (100 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)

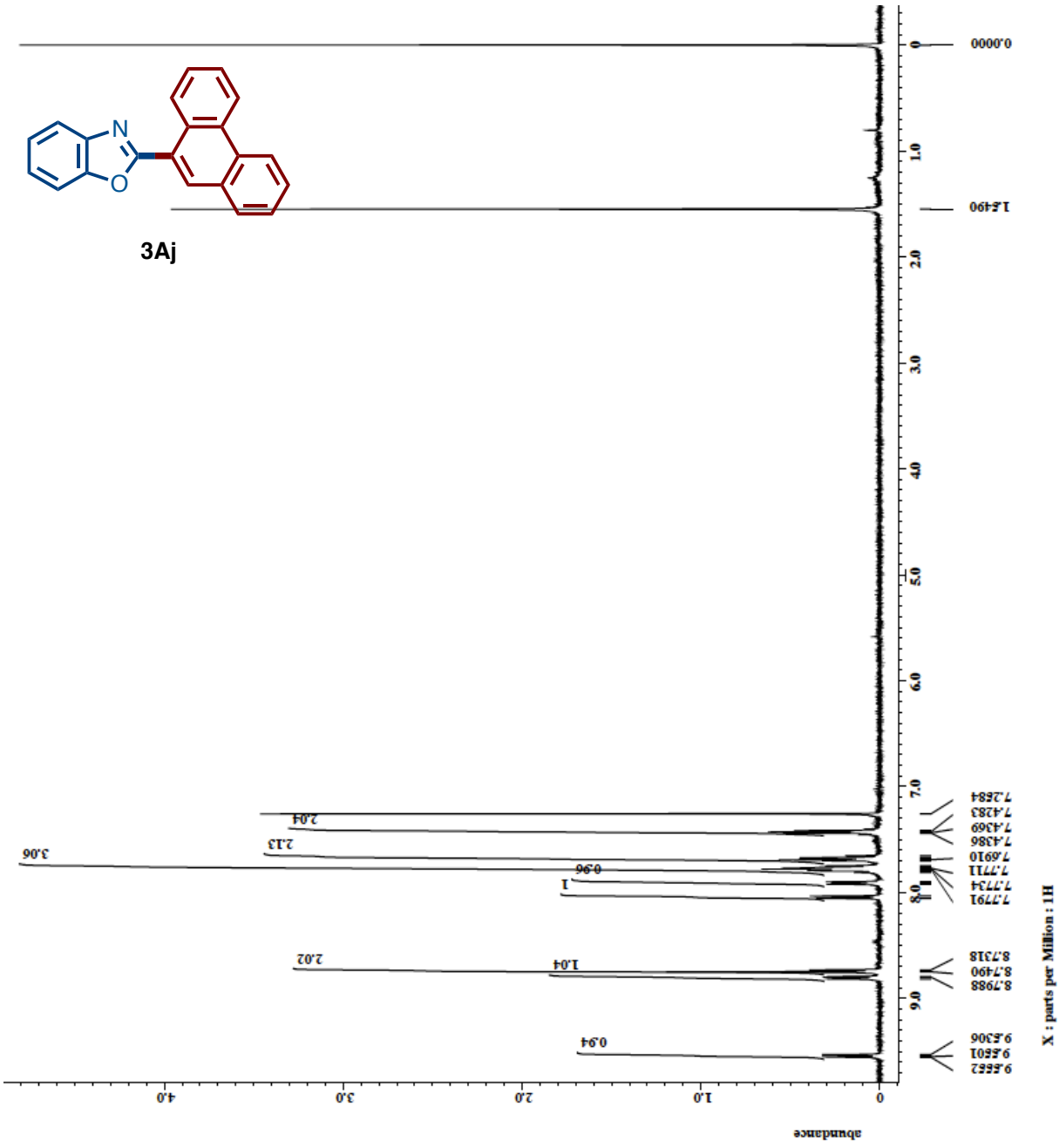


^{13}C NMR (100 MHz, $CDCl_3$)

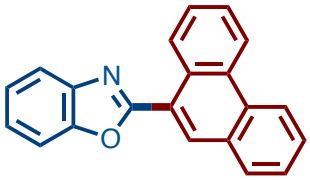


3Ai

^{1}H NMR (400 MHz, $CDCl_3$)

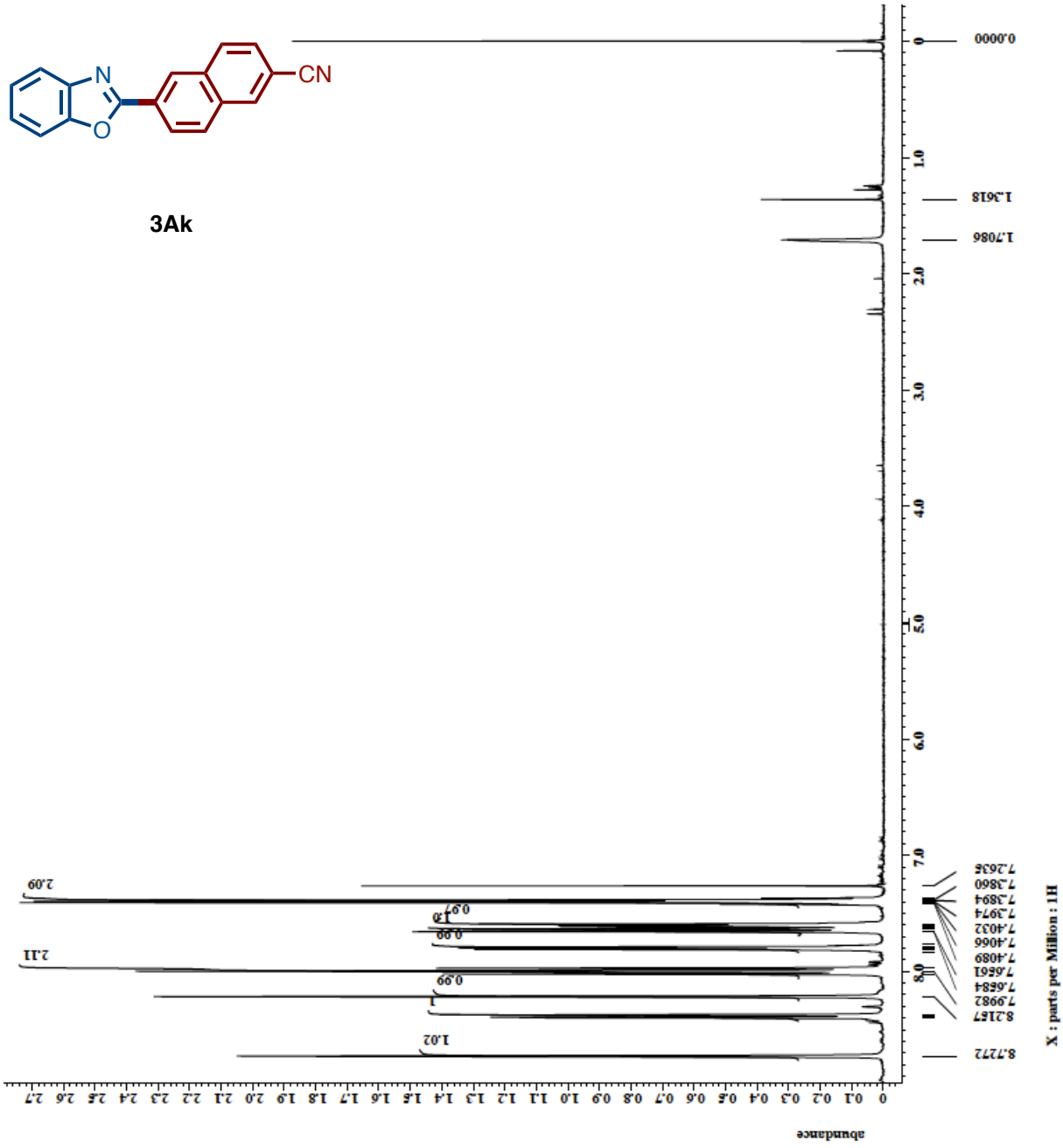


^{13}C NMR (100 MHz, $CDCl_3$)

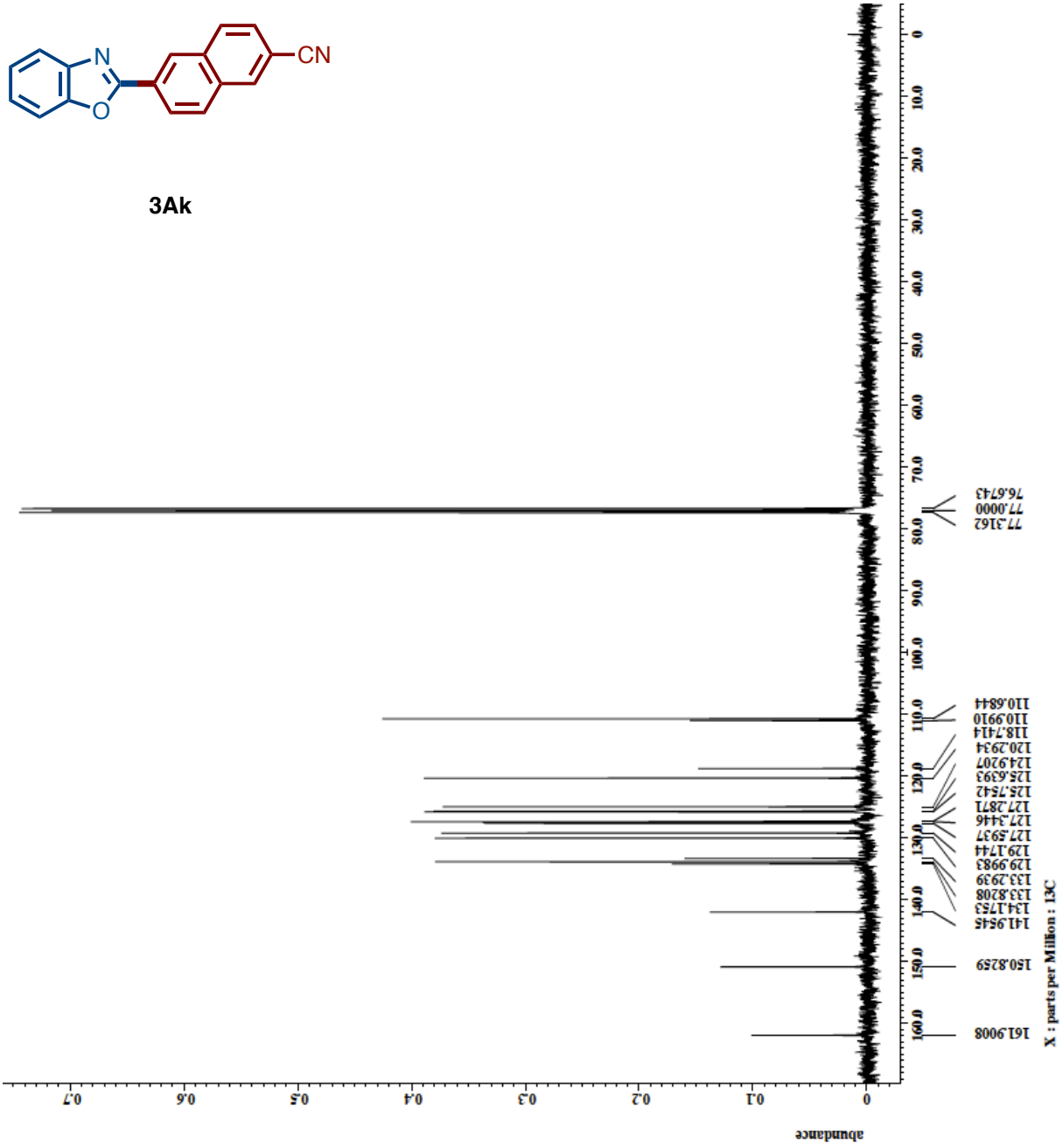


3Aj

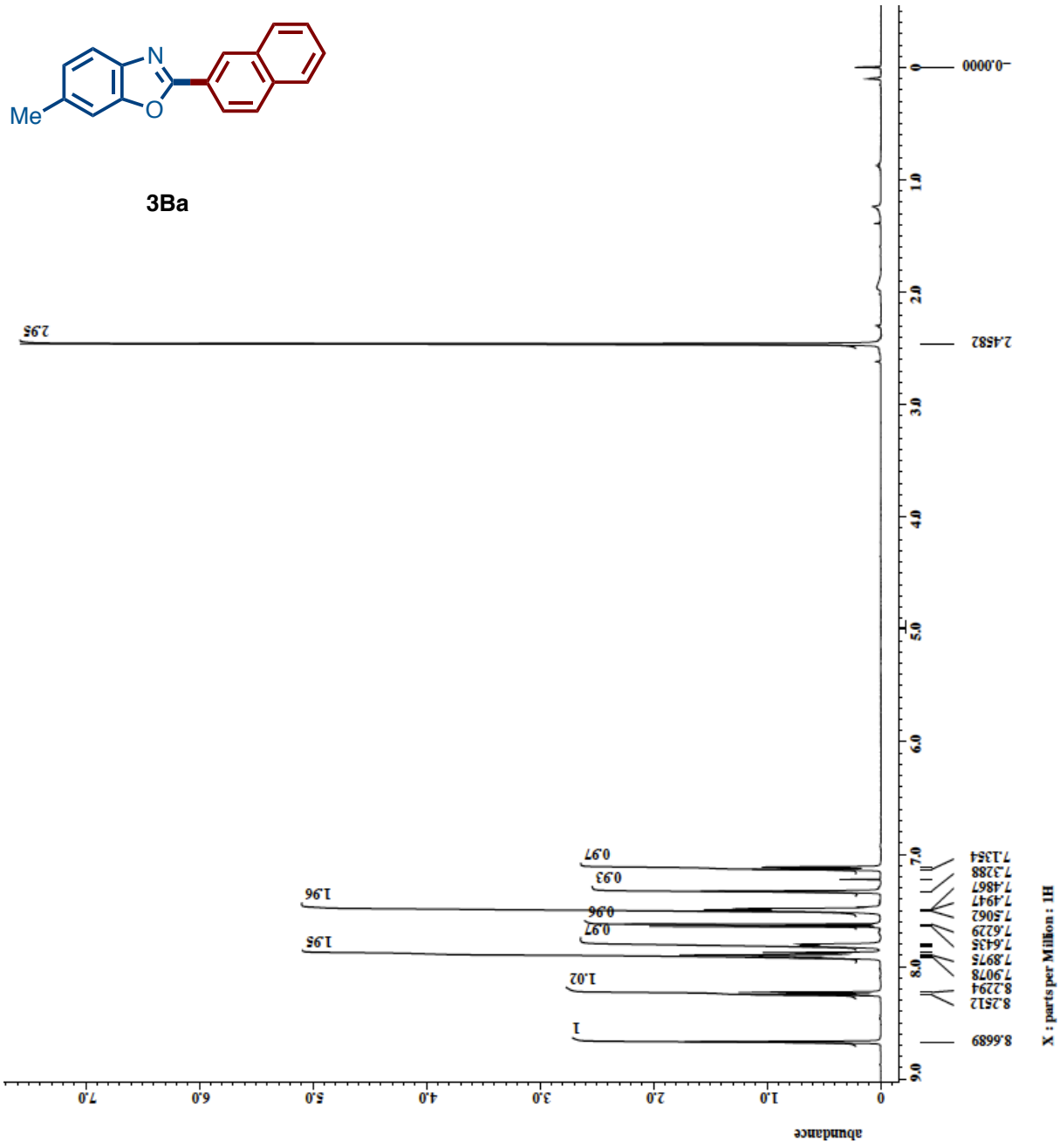
^{1}H NMR (400 MHz, $CDCl_3$)



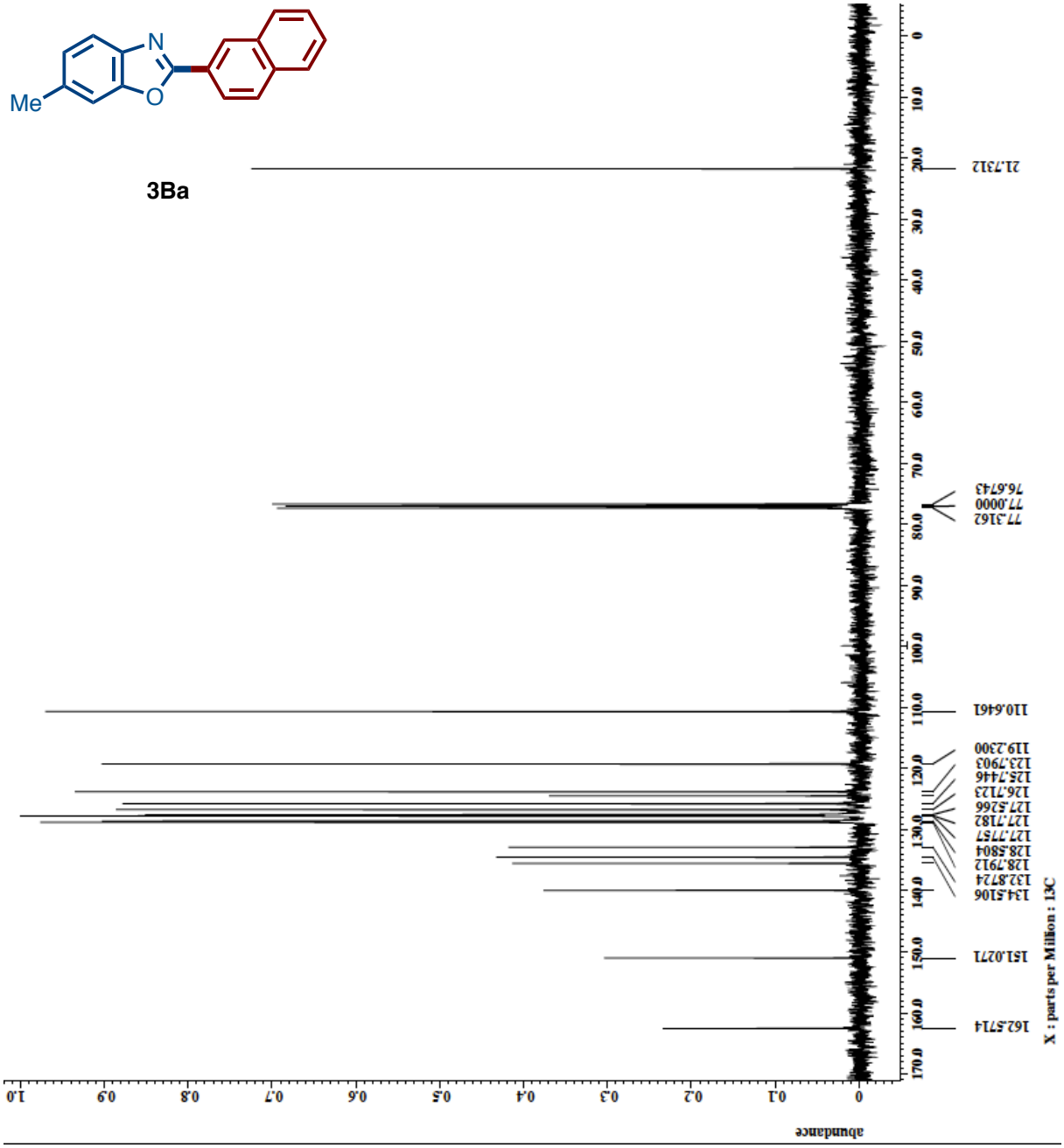
^{13}C NMR (100 MHz, $CDCl_3$)



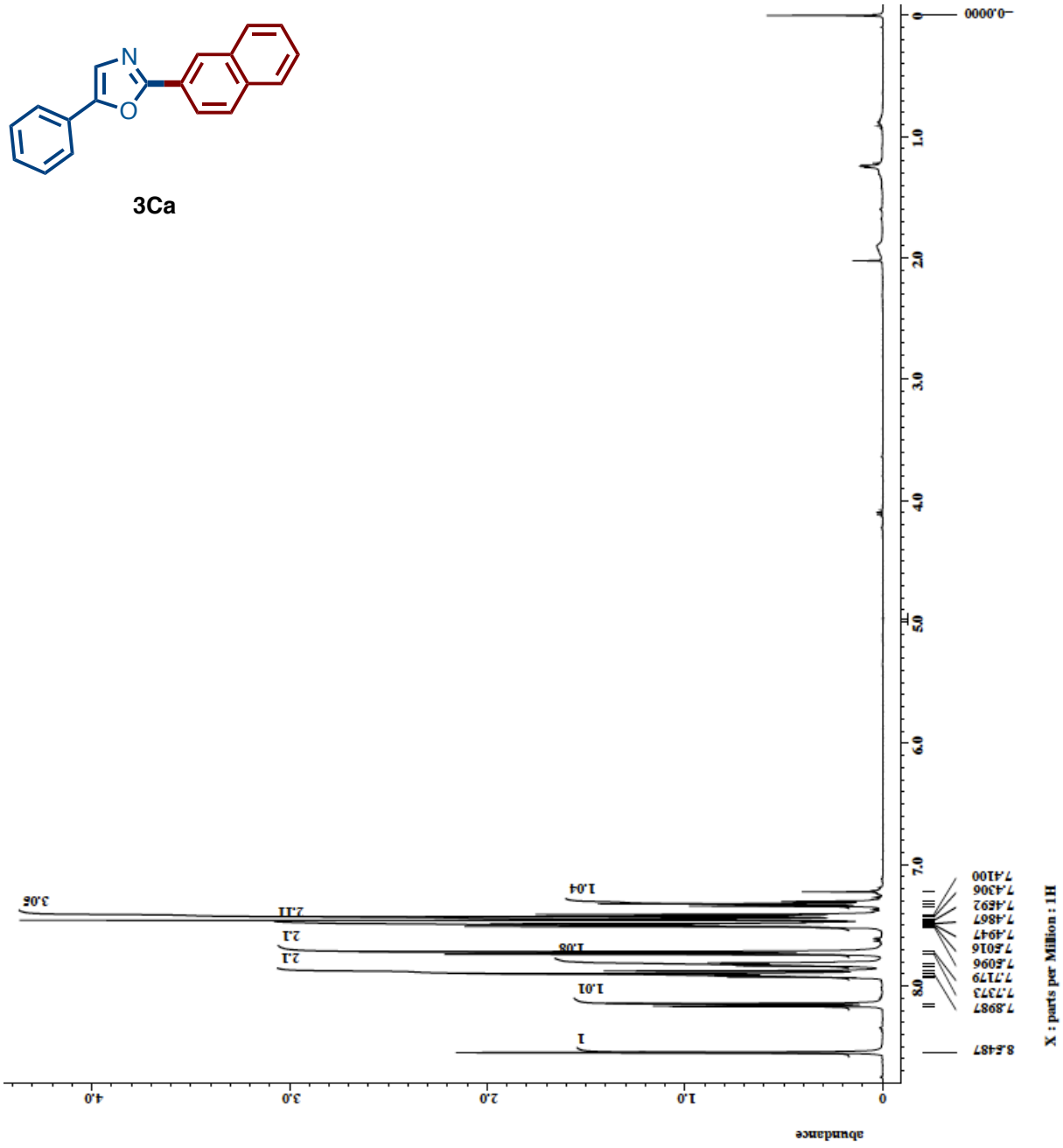
^{1}H NMR (400 MHz, $CDCl_3$)



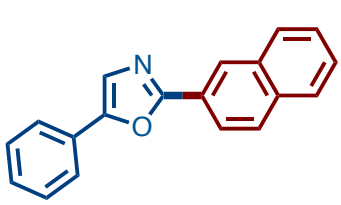
^{13}C NMR (100 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)

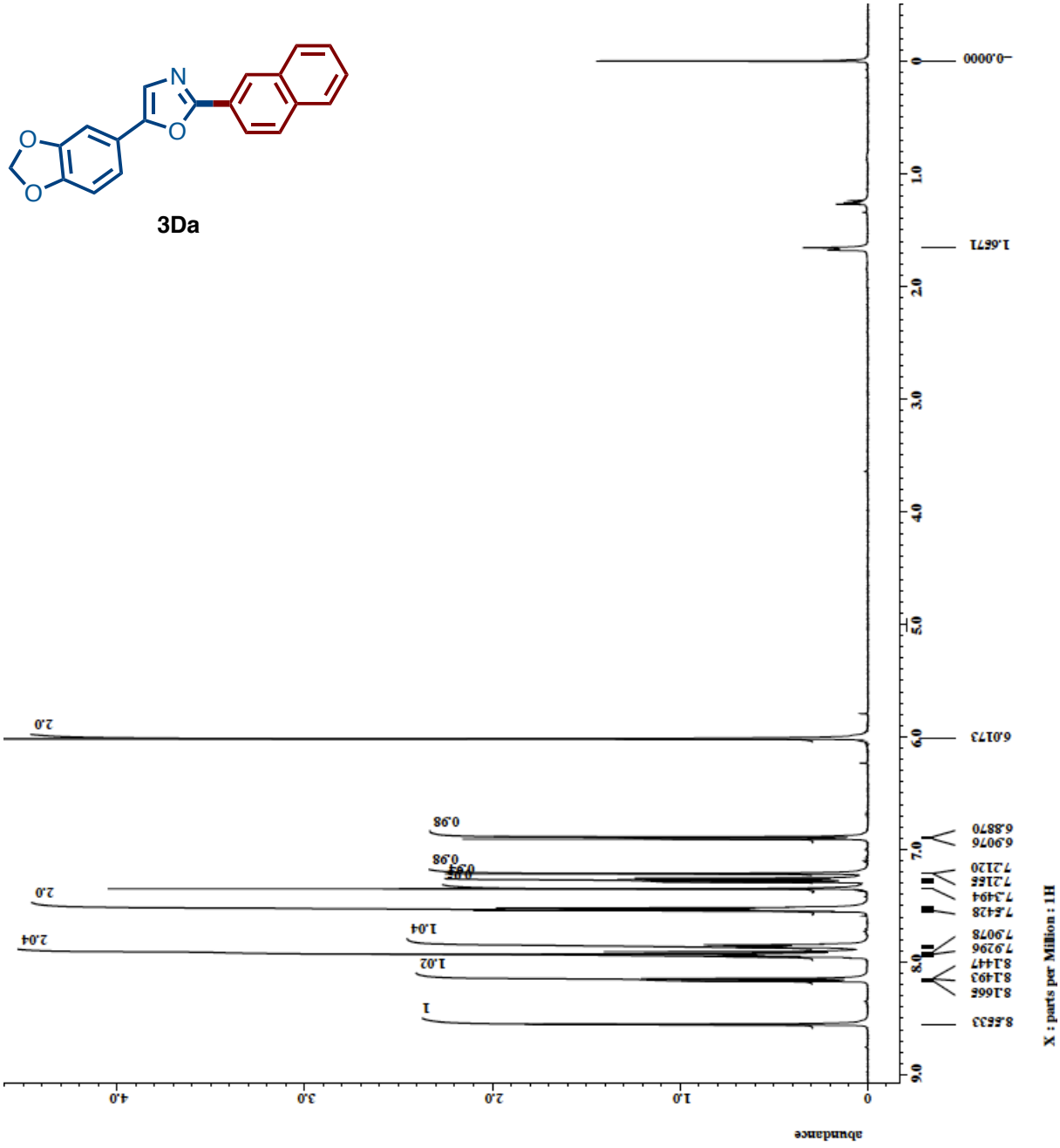


^{13}C NMR (100 MHz, $CDCl_3$)

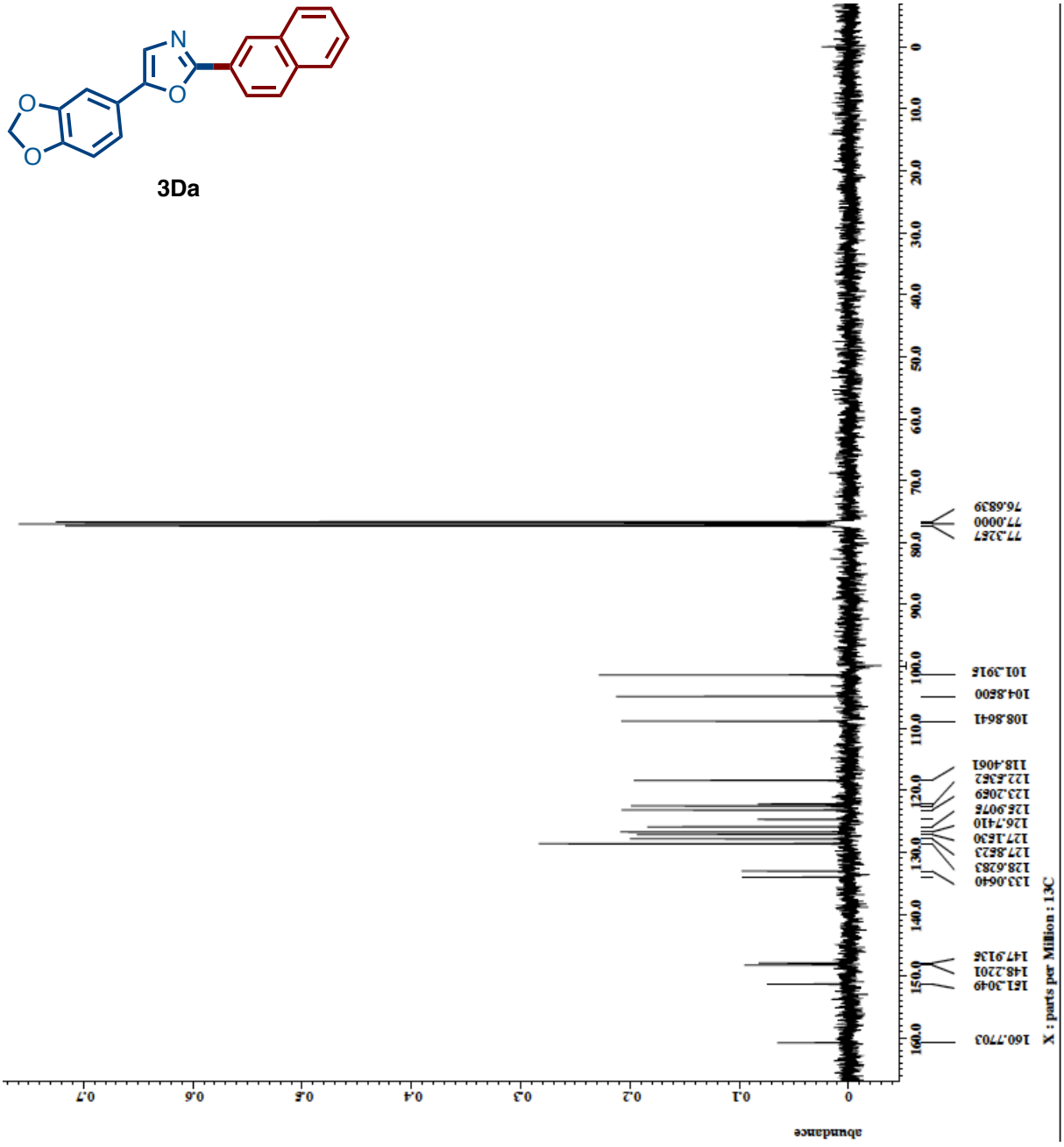


3Ca

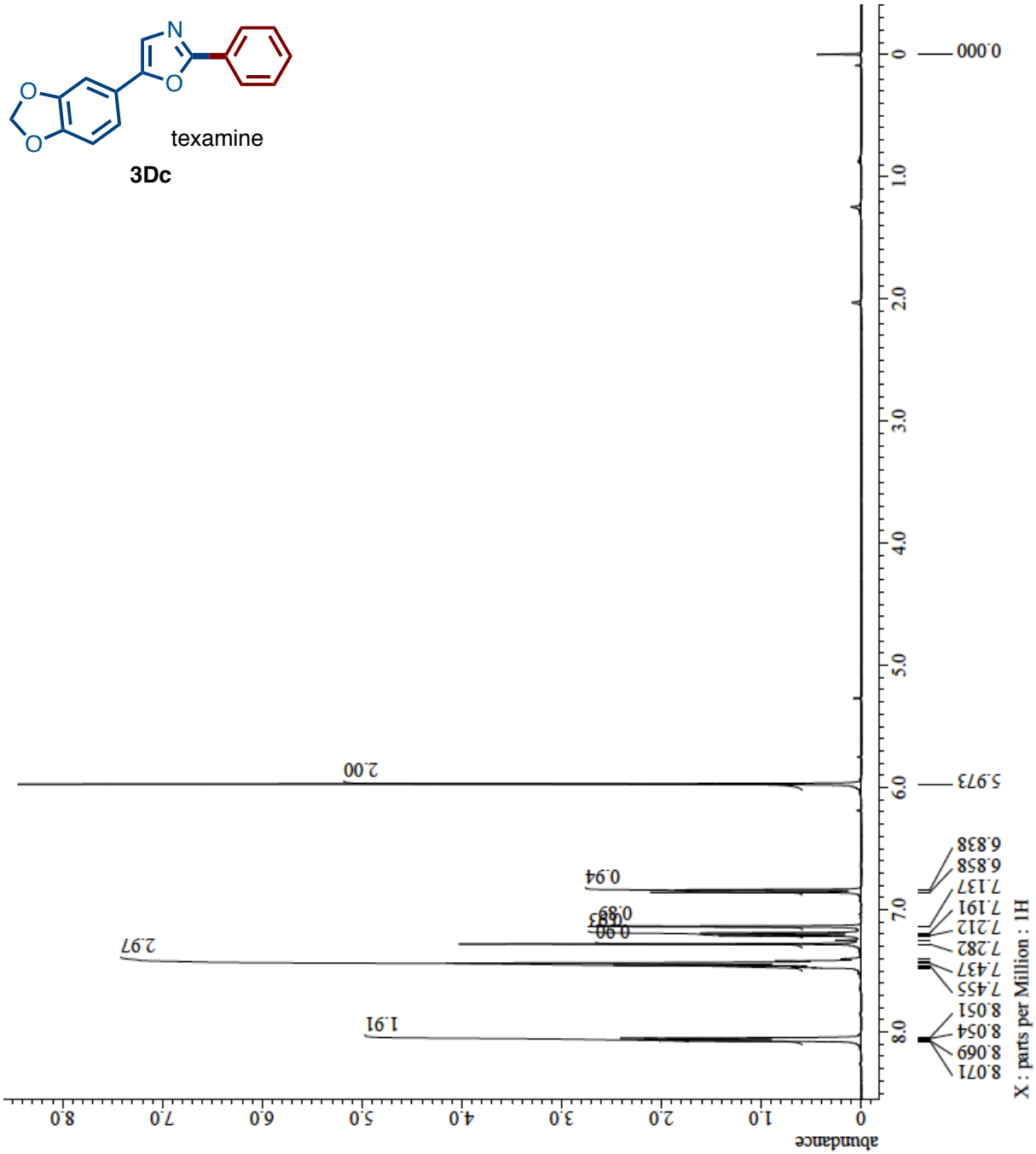
^{1}H NMR (400 MHz, $CDCl_3$)



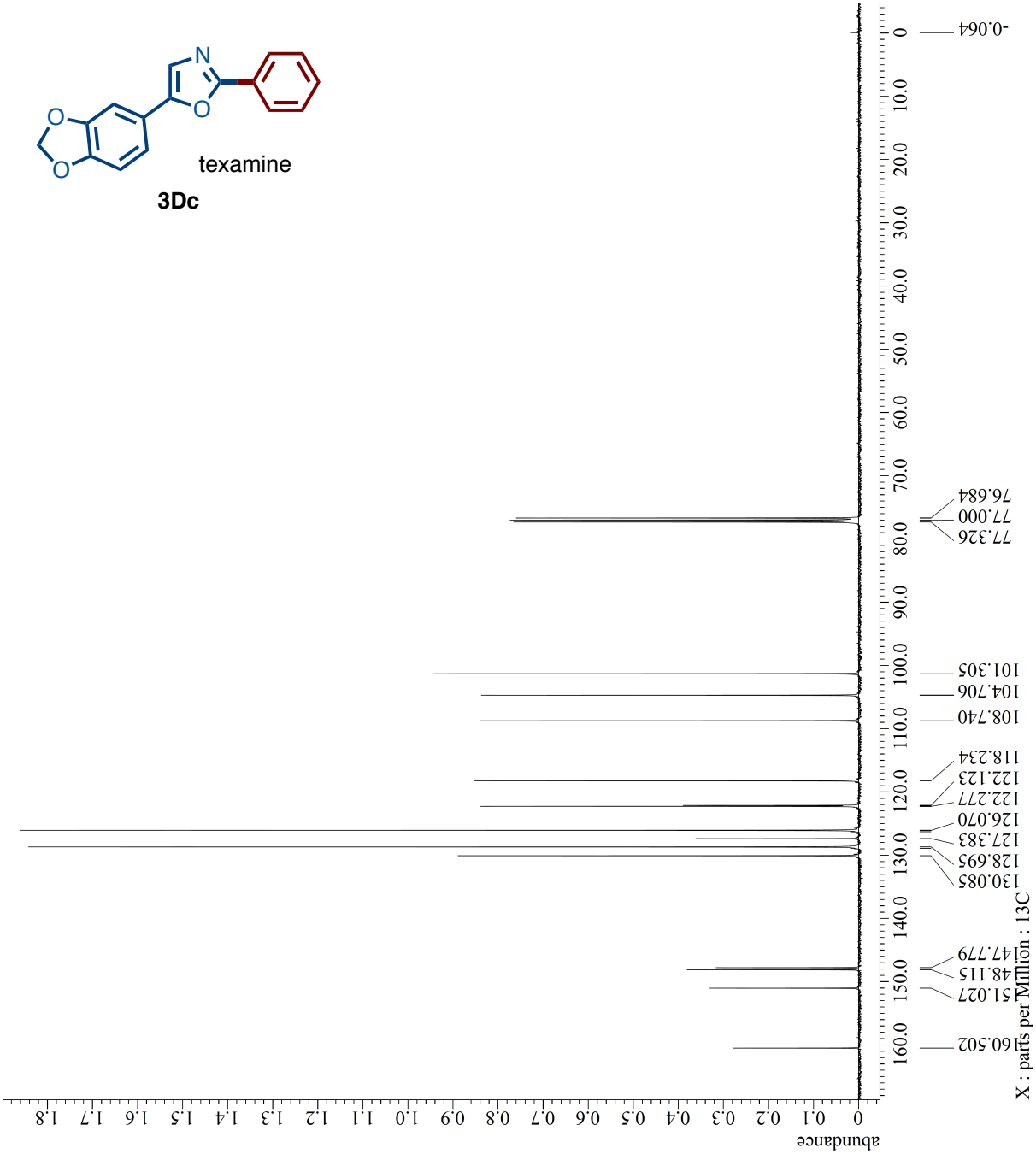
^{13}C NMR (100 MHz, $CDCl_3$)



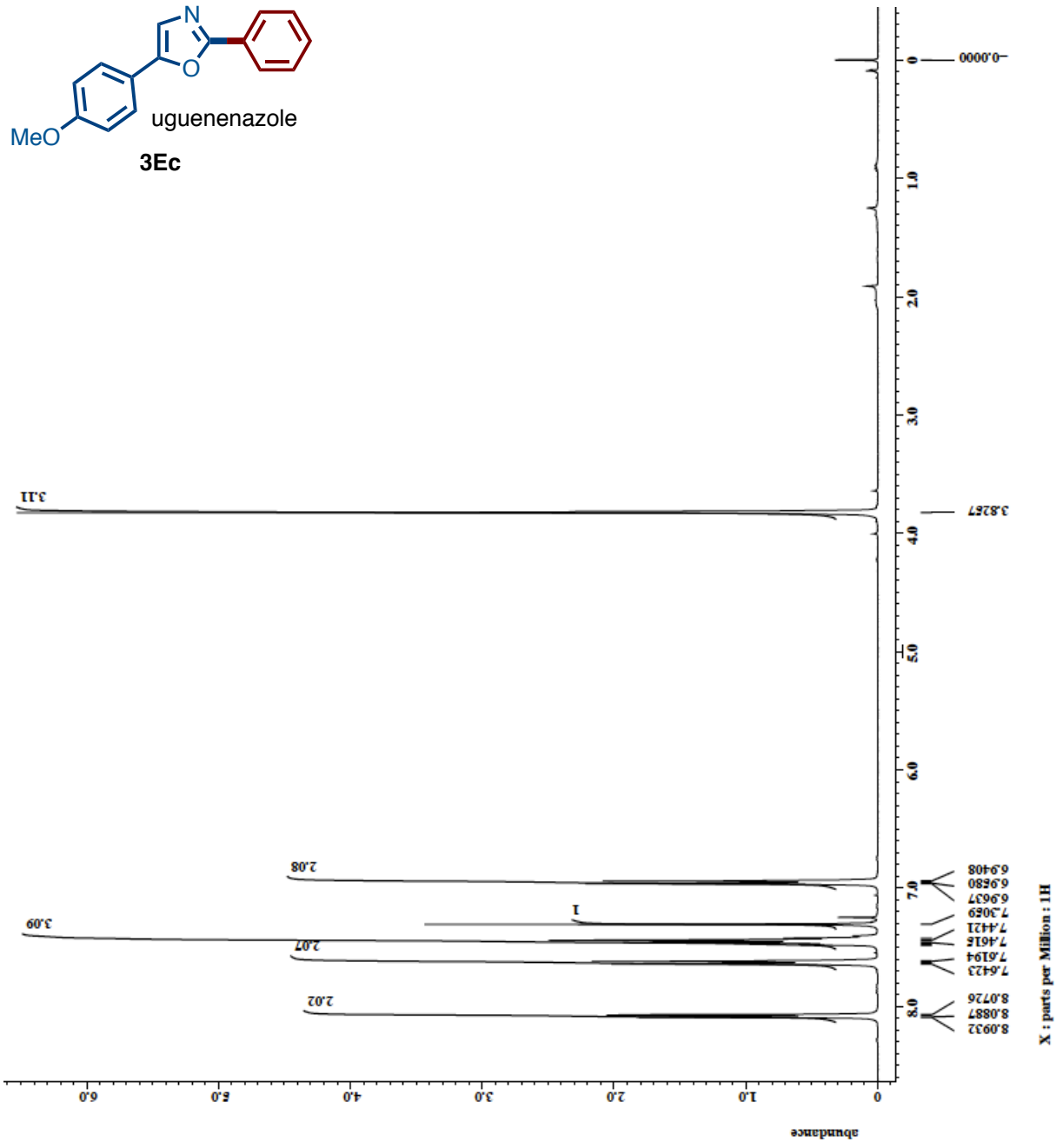
^{1}H NMR (400 MHz, $CDCl_3$)



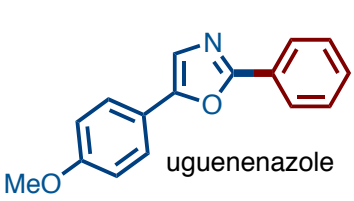
^{13}C NMR (100 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)



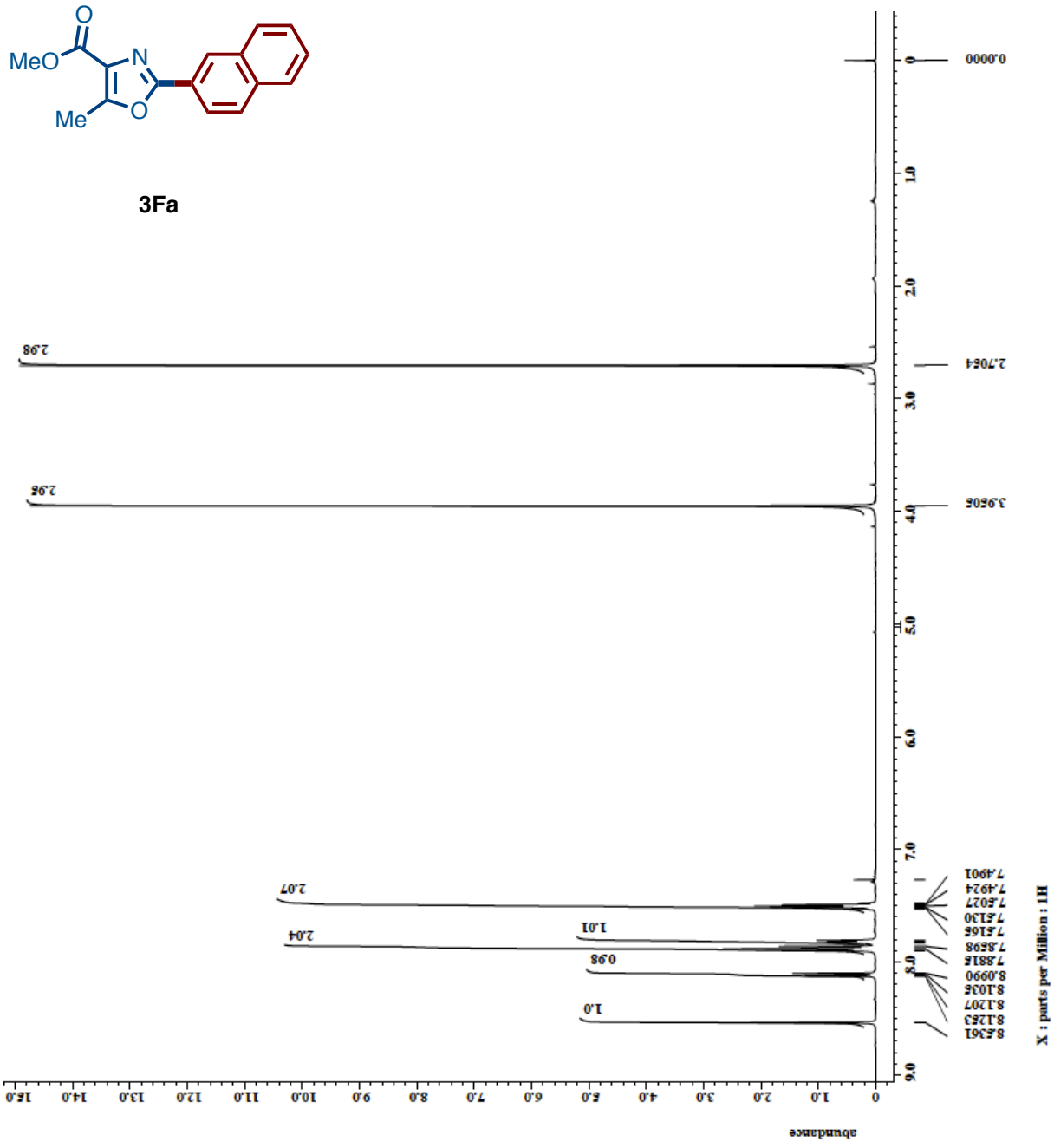
^{13}C NMR (100 MHz, $CDCl_3$)



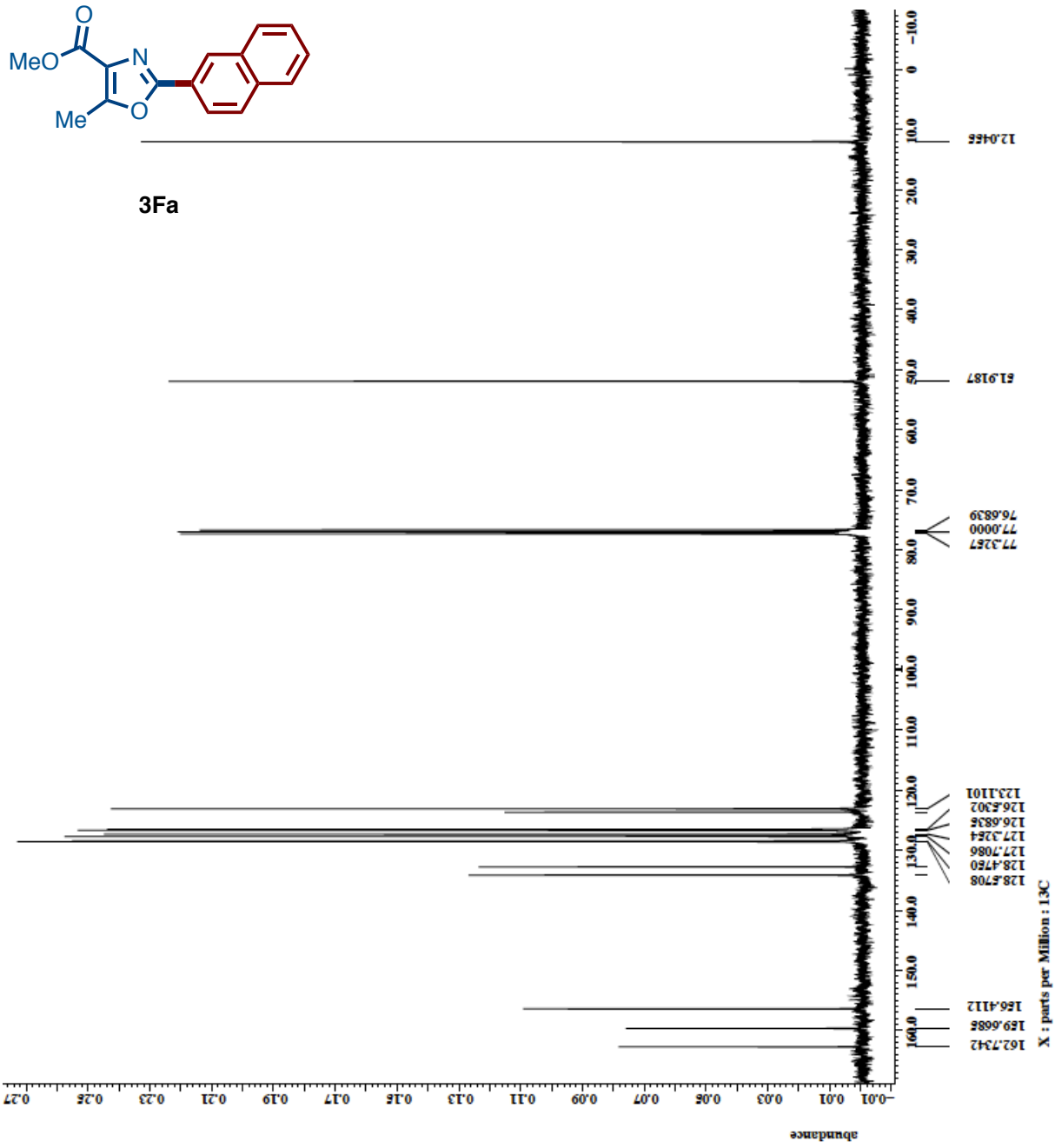
uguenenazole

3Ec

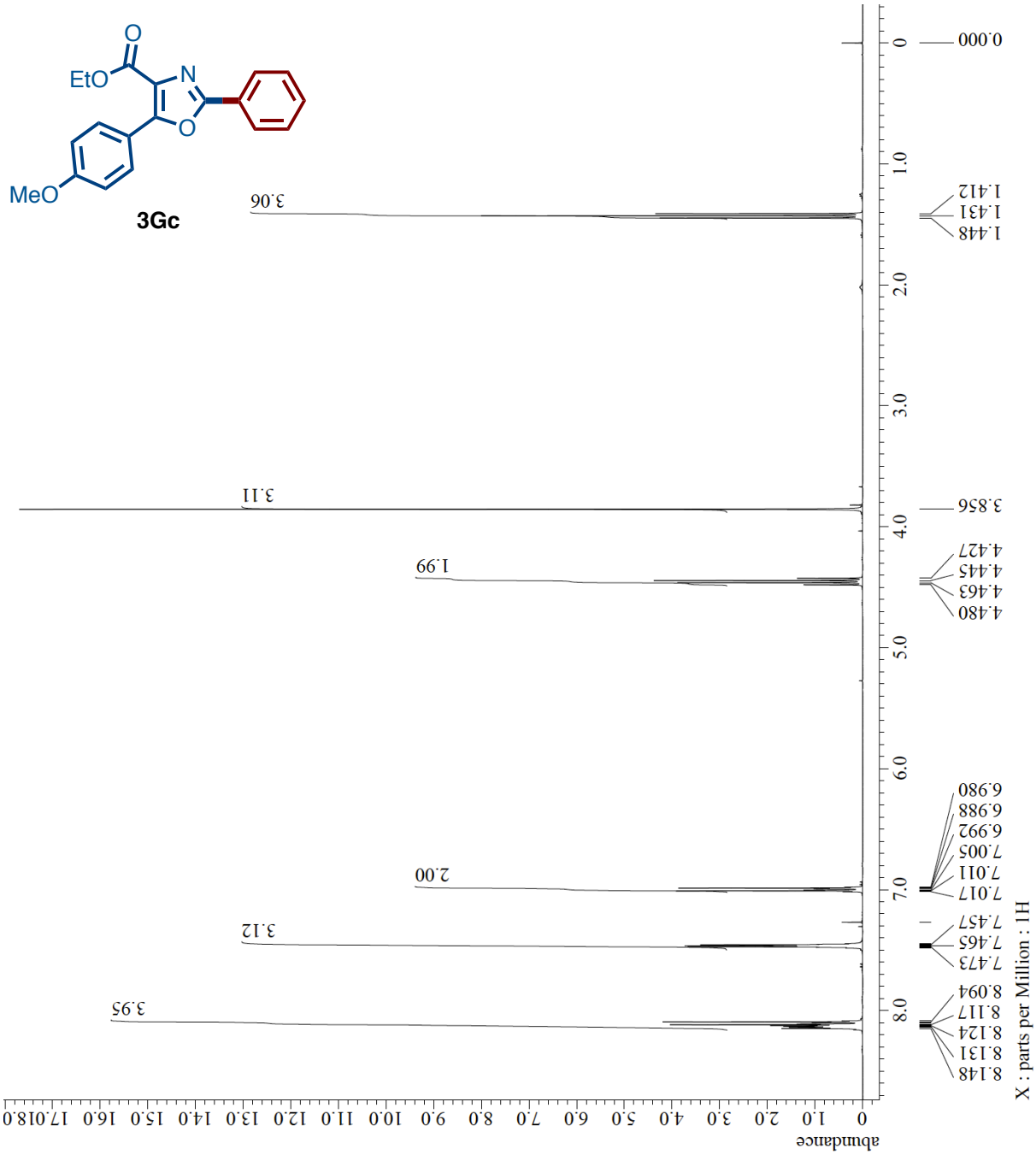
^{1}H NMR (400 MHz, $CDCl_3$)



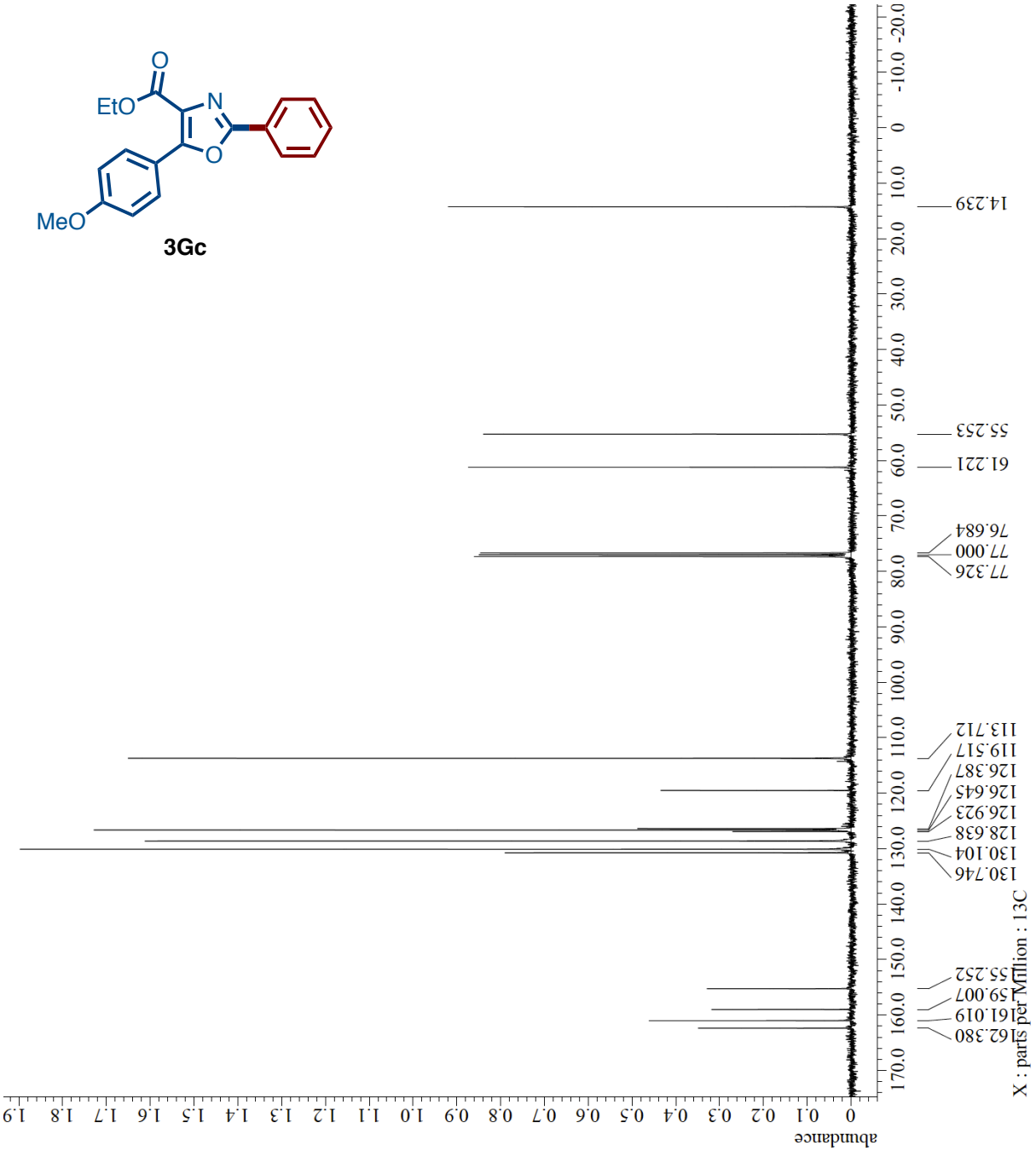
^{13}C NMR (100 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)

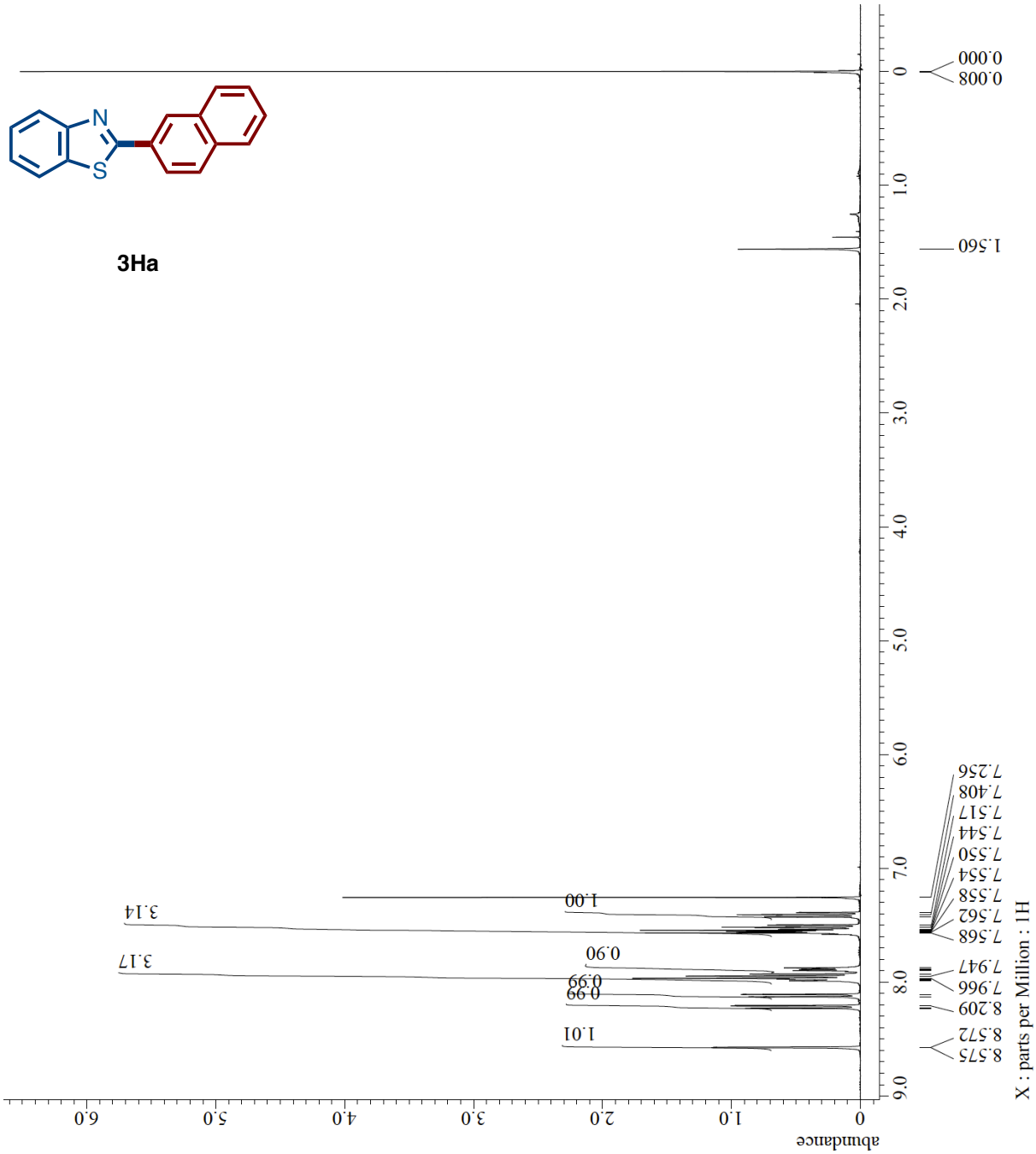


^{13}C NMR (100 MHz, $CDCl_3$)

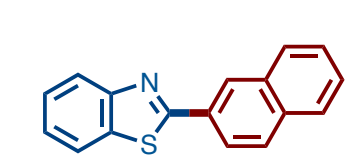


3Gc

^{1}H NMR (400 MHz, $CDCl_3$)

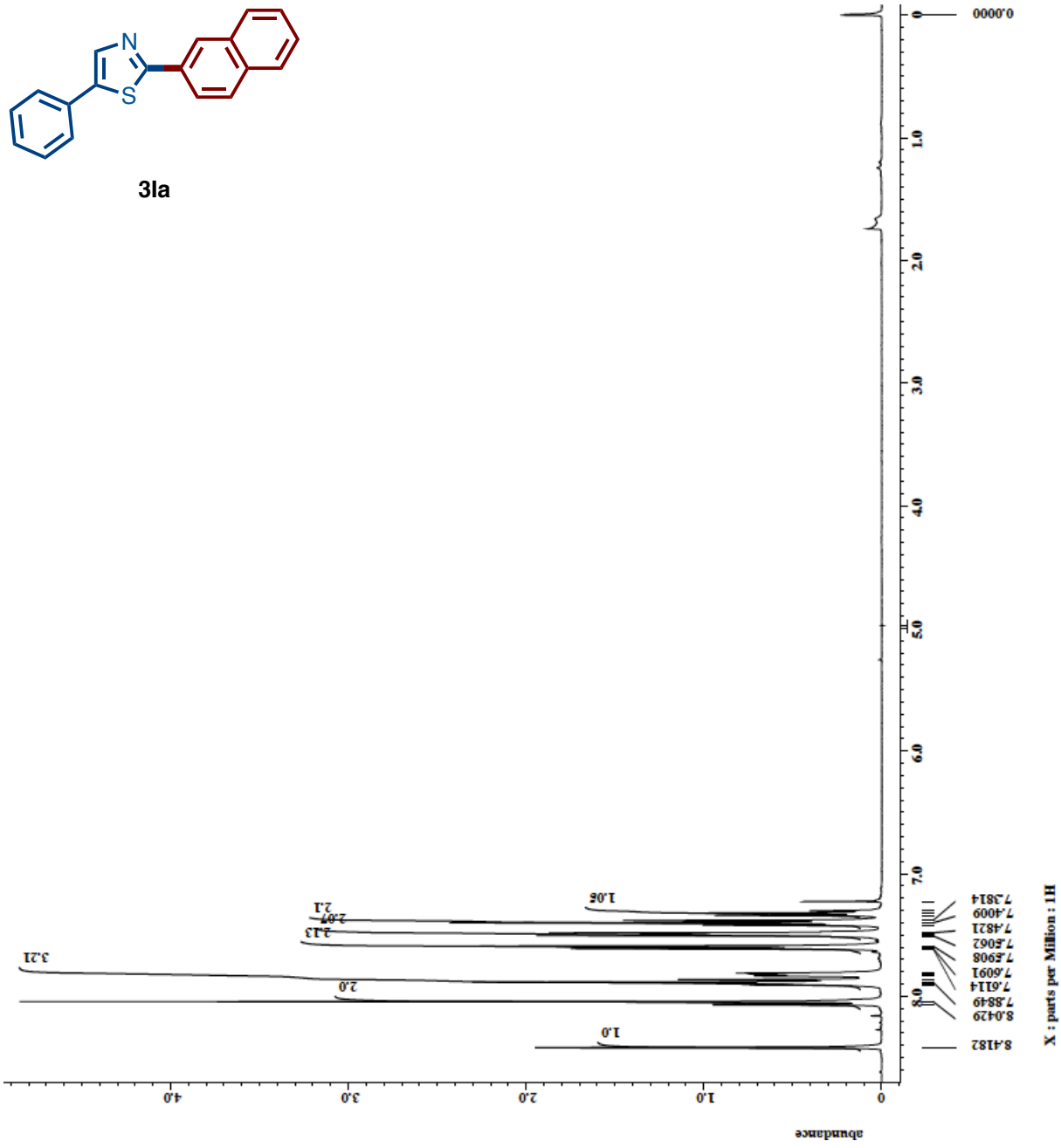


^{13}C NMR (100 MHz, $CDCl_3$)

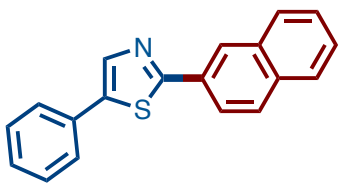


3Ha

^{1}H NMR (400 MHz, $CDCl_3$)

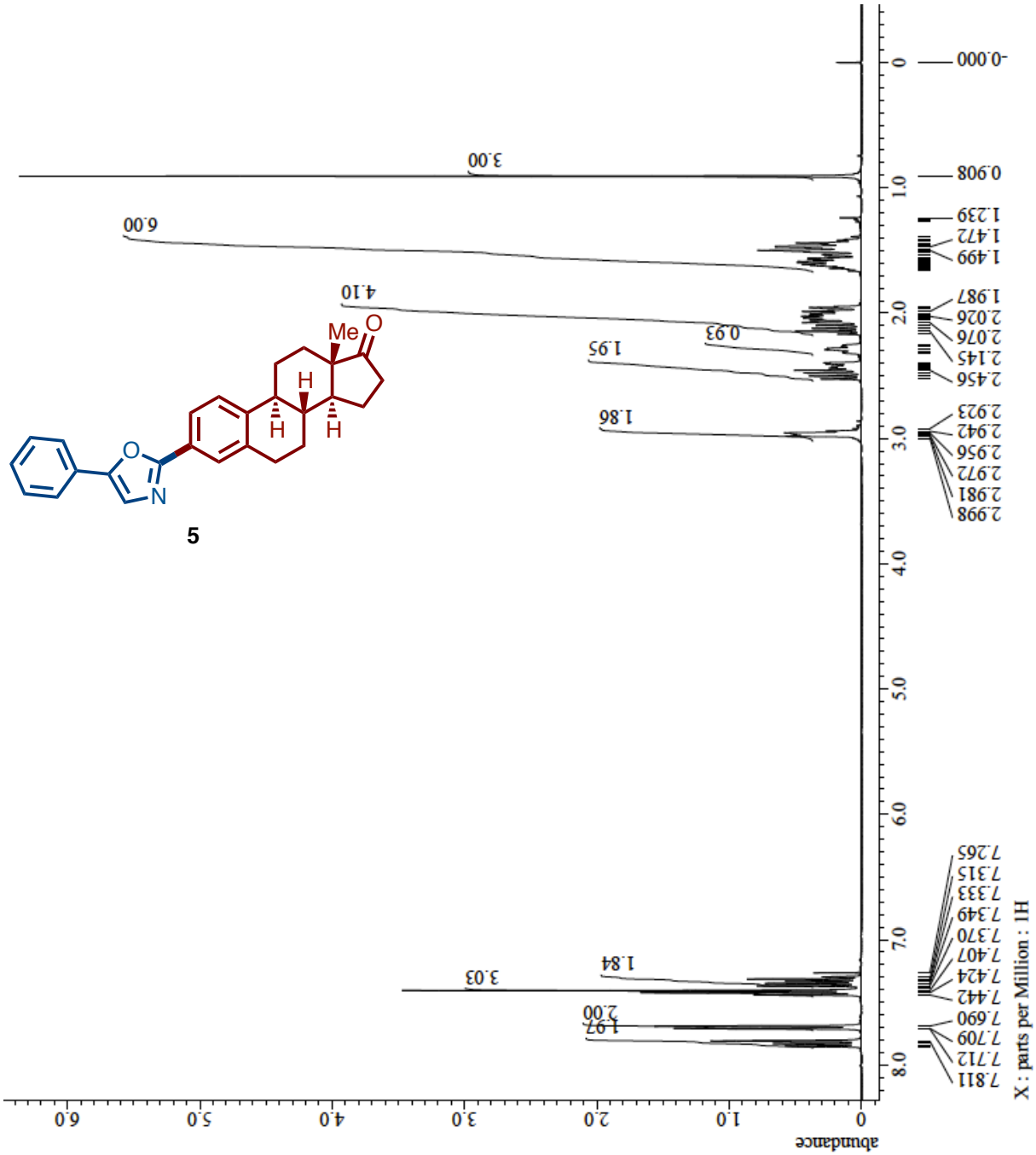


^{13}C NMR (100 MHz, $CDCl_3$)

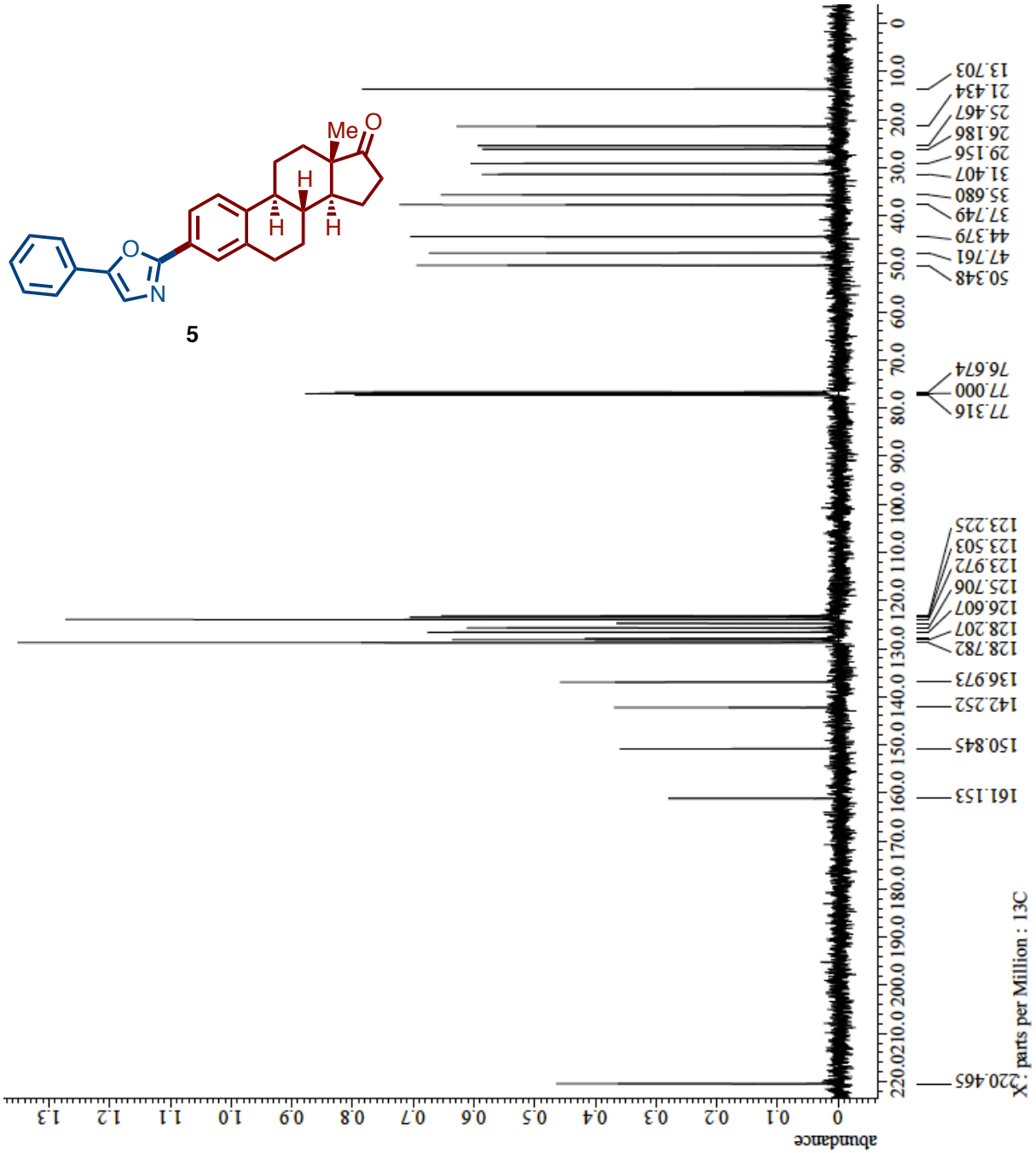


3la

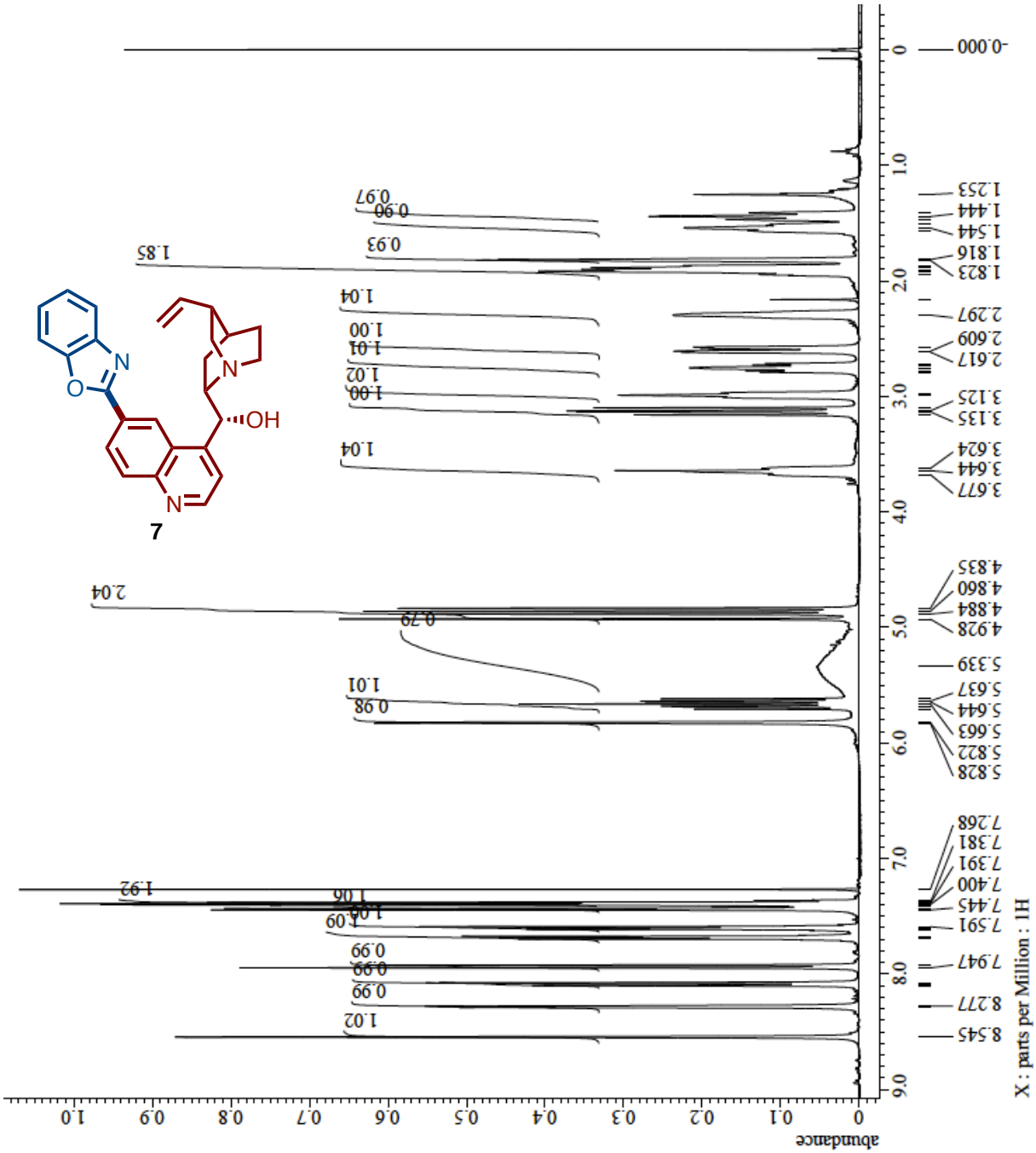
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)