K_2CO_3-mediated, direct C–H bond selenation and thiolation of 1,3,4-oxadiazoles in the absence of metal catalyst: An eco-friendly approach

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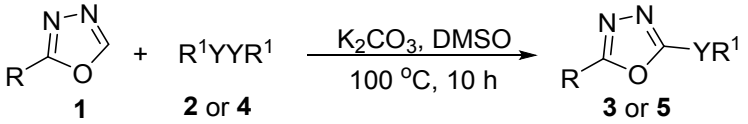
I. Materials and Methods

Proton nuclear magnetic resonance spectra (^{1}H NMR) were obtained at 200 MHz on a Bruker AC-200 NMR spectrometer or at 400 MHz on a Varian AS-400 NMR spectrometer. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$ or tetramethylsilane (TMS) as the external reference. Data are reported as follows: chemical shift (δ), multiplicity, coupling constant (J) in Hertz and integrated intensity. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained either at 50 MHz on a Bruker AC-200 NMR spectrometer or at 100 MHz on a Varian AS-400 NMR spectrometer. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$. Abbreviations to denote the multiplicity of a particular signal are: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet) and m (multiplet). Selenium-77 nuclear magnetic resonance spectra (^{77}Se NMR) at 38.14 MHz on a Bruker AC-200 NMR spectrometer. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to diphenyl diselenide as the external reference (463.15 ppm). High resolution mass spectra were recorded on a Bruker micrOTOF-Q II ESI mass spectrometer equipped with an automatic syringe pump for sample injection. Infrared spectra were recorded on a Bruker Optics Alpha benchtop FT-IR spectrometer and are reported in frequency of absorption (cm^{-1}). The melting points were determined in a Microquimica MQRPF-301 digital model equipment with heating plate. Column chromatography was performed using Silica Gel (230-400 mesh) following the methods described by Still.[1] Thin layer chromatography (TLC) was performed using Merck Silica Gel GF_{254}, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or stained with iodine vapor and acidic vanillin. Most reactions were monitored by TLC for disappearance of starting material.

Unless otherwise stated, all reactions were carried out in open atmosphere; all reagents and solvents were obtained from commercial sources and used without any further purification. Oxadiazoles **1a-m**,[2,3] diselenides **2a-m**[4] and disulfides **4a-b**[5] were prepared according to the reported methods. Potassium carbonate (99.997%) for controlled reaction was purchased from Sigma-Aldrich. Reactions under inert atmosphere were conducted in flame-dried or oven dried glassware equipped with tightly fitted rubber septa and under a positive atmosphere of dry argon. Reagents and solvents were handled using standard syringe techniques. Temperatures above room temperature were maintained by use of a mineral oil bath with an electrically heated coil connected to a Variac speed controller.

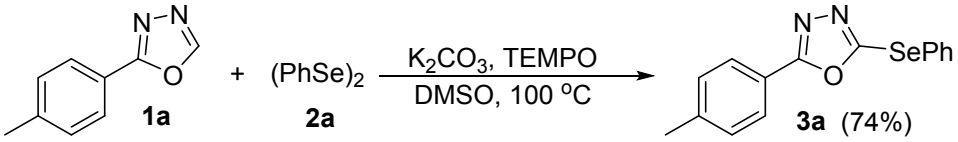
II. General Procedure for the synthesis of chalcogenated oxdiazoles



In a Schlenck tube, containing DMSO (1 mL), the appropriate oxadiazole **1** (0.5 mmol), diorganyl dichalcogenide **2** or **4** (0.26 mmol), was added K_2CO_3 (0.5 mmol). The reaction was heated to 100 ºC in an oil bath for 10 h. After this, the mixture was diluted with ethyl acetate (20 mL) and washed with a saturated solution of NaCl (20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by crystallization using hexane/methanol system or by flash chromatography eluted with mixture of hexane/acetate (95:5).

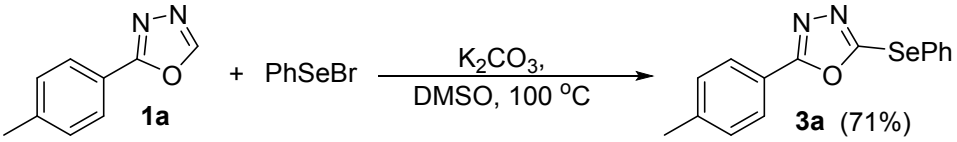
III. Control Experiments for the Study of Mechanism

a) Radical trapping study



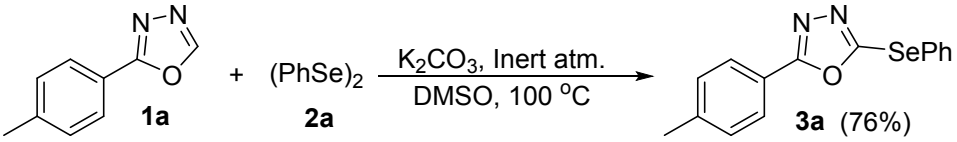
In a Schlenck tube, containing DMSO (1 mL), the oxadiazole **1a** (0.5 mmol), diphenyl diselenide **2a** (0.26 mmol), was added K_2CO_3 (0.5 mmol) and TEMPO (0.5 mmol). The reaction was heated to 100 ºC in an oil bath for 10 h. After this, the mixture was diluted with ethyl acetate (20 mL) and washed with a saturated solution of NaCl (20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with mixture of hexane/acetate (95:5). Yield: 74%.

b) Reaction between oxadiazole 1a and phenylselenium bromide



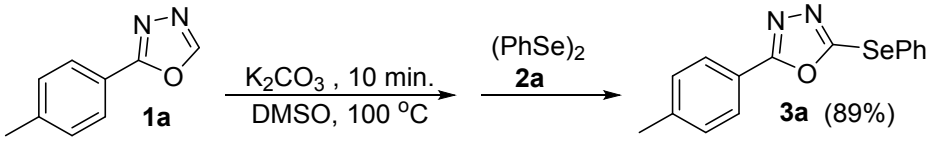
In a Schlenck tube, containing DMSO (1 mL), the oxadiazole **1a** (0.5 mmol), phenylselenium bromide (0.5 mmol), was added K_2CO_3 (0.5 mmol). The reaction was heated to 100 ºC in an oil bath for 10 h. After this, the mixture was diluted with ethyl acetate (20 mL) and washed with a saturated solution of NaCl (20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with mixture of hexane/acetate (95:5). Yield: 71%.

c) Reaction between oxadiazole 1a and diselenide 2a under inert atmosphare



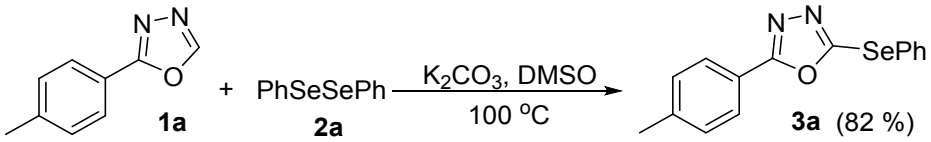
In a Schlenck tube, under argon,, containing DMSO (1 mL), the oxadiazole **1a** (0.5 mmol), diphenyl diselenide **2a** (0.26 mmol), was added K_2CO_3 (0.5 mmol). The reaction was heated to 100 ºC in an oil bath for 10 h. After this, the mixture was diluted with ethyl acetate (20 mL) and washed with a saturated solution of NaCl (20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with mixture of hexane/acetate (95:5). Yield: 76%.

d) Control addition for diphenyl diselenide 2a



In a Schlenck tube, containing DMSO (1 mL), the oxadiazole **1a** (0.5 mmol), was added K_2CO_3 (0.5 mmol).The reaction was heated to 100 ºC in an oil bath. After 10 minutes diphenyl diselenide **2a** (0.26 mmol) was added and the reaction mixture was allowed for 10 h. After this, the mixture was diluted with ethyl acetate (20 mL) and washed with a saturated solution of NaCl (20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with mixture of hexane/acetate (95:5). Yield: 89%.

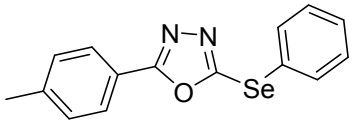
IV. Procedure for the synthesis of selenated oxadiazole in 10 mmole scale



In a Schlenck tube, containing DMSO (25 mL), the oxadiazole **1** (10 mmol), diselenide **2a** (5.05 mmol), was added K_2CO_3 (10 mmol). The reaction was heated to 100 ºC in an oil bath for 12 h. After this, the mixture was diluted with ethyl acetate (100 mL) and washed with a saturated solution of NaCl (30 mL x 3). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with mixture of hexane/acetate (95:5). Yield 82 %.

V. Characterization data of compounds 3a-3y and 5a-5b

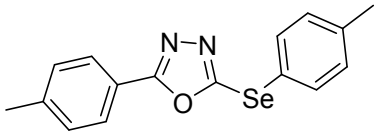
2-(4-methylphenyl)-5-(phenylselanyl)-1,3,4-oxadiazole (3a).



3a

Yield: 86%; Yellow solid; mp: 84 – 85 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.82 (d, J = 8.2 Hz, 2H), 7.78 – 7.70 (m, 2H), 7.42 – 7.34 (m, 3H), 7.24 (d, J = 8.2 Hz, 2H), 2.38 (s, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.3, 155.7, 142.4, 134.9, 129.8, 129.7, 129.6, 126.7, 124.4, 120.7, 21.7.; ^{77}Se NMR (38.14 MHz, $CDCl_3$) δ = 365.34.; IR (KBr): 3050, 2881, 2761, 1614, 1482, 1356, 1256, 1142, 1085, 1025, 964, 835, 734, 642 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{15}H_{13}N_2OSe$ $[M + H]^+$ 317.0188, found: 317.0193.

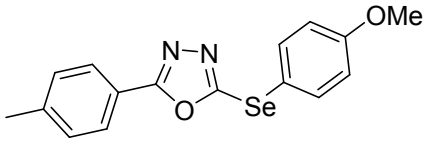
2-(4-methylphenyl)-5-((4-methylphenyl)selanyl)-1,3,4-oxadiazole (3b).



3b

Yield: 88%; Yellow solid; mp: 82 – 84 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.76 (d, J = 8.2 Hz, 2H), 7.57 (d, J = 8.1 Hz, 2H), 7.20 – 7.09 (m, 4H), 2.32 (s, 3H), 2.29 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.4, 156.2, 142.4, 140.1, 135.4, 130.7, 129.8, 126.9, 120.9, 120.7, 21.8, 21.4.; IR (KBr): 3056, 2922, 2853, 1652, 1558, 1478, 1362, 1209, 136, 1066, 1022, 950, 836, 805, 730, 668 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{15}H$ $C_{16}H_{15}N_2OSe$ $[M + H]^+$ 331.0348, found: 331.0352.

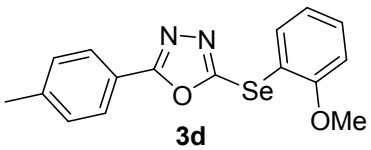
2-(4-methylphenyl)-5-((4-methoxyphenyl)selanyl)-1,3,4-oxadiazole (3c).



3c

Yield: 96%; Yellow solid; mp: 74 – 75 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.74 (d, J = 8.1 Hz, 2H), 7.62 (d, J = 8.7 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 3.74 (s, 3H), 2.31 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.2, 161.0, 156.5, 142.3, 137.6, 137.4, 129.7, 126.7, 120.8, 115.8, 115.5, 114.0, 55.4, 21.6.; IR (KBr): 3098, 3065, 2994, 2925, 2842, 1658 1610, 1575, 1478, 1297, 1268, 1184, 1156, 1036, 954, 830, 740, 662 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{16}H_{15}N_2O_2Se$ $[M + H]^+$ 347.0294, found: 347.0291.

2-(4-methylphenyl)-5-((2-methoxyphenyl)selanyl)-1,3,4-oxadiazole (3d).

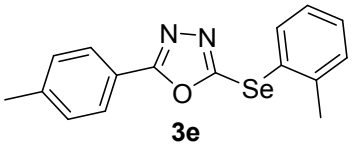


3d

Yield: 88%; Yellow solid; mp: 69 – 71 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.88 (d, J = 8.3 Hz, 2H), 7.57 (dd, J = 8.0, 1.6 Hz, 1H), 7.40 – 7.33 (m, 1H), 7.28 (d, J = 8.4 Hz, 2H), 6.98 – 6.90 (m, 2H), 3.87 (s, 3H), 2.41 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.5, 157.6, 155.2, 142.5, 133.7, 130.4, 129.8, 126.9, 122.1, 120.9, 115.2, 111.3, 56.2, 21.7.; IR (KBr): 3104, 3038, 2990,

2861, 1610, 1594, 1484, 1439, 1344, 1258, 1193, 1127, 1063, 964, 835, 840, 803, 766, 738, 662, 605 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{16}H_{15}N_2O_2Se$ $[M + H]^+$ 347.0294, found: 347.0297.

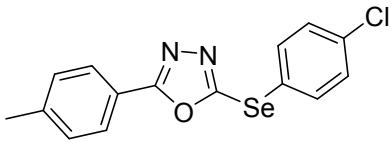
2-(4-methylphenyl 5-((2-methylphenyl)selanyl)-1,3,4-oxadiazole (3e).



3e

Yield: 88%; Yellow solid; mp: 58 – 59 °C. ^1H NMR (200 MHz, $CDCl_3$) δ = 7.83 (d, *J* = 8.0 Hz, 2H), 7.39 – 7.16 (m, 5H), 2.55 (s, 3H), 2.39 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.3, 155.7, 142.4, 141.8, 136.5, 130.9, 130.3, 129.8, 127.2, 126.8, 125.5, 120.8, 23.0, 21.7.; IR (KBr): 3062, 3032, 2955, 2924, 2868, 1698, 1652, 1558, 1457, 1435, 1337, 1260, 1156, 1064, 950, 848, 821, 728, 688 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{16}H_{15}N_2OSe$ $[M + H]^+$ 331.0345, found: 331.0346.

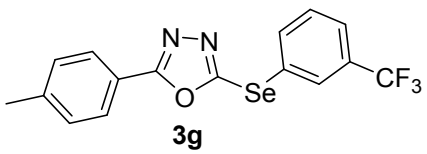
2-(4-methylphenyl)-5-((4-chlorophenyl)selanyl)-1,3,4-oxadiazole (3f).



3f

Yield: 82%; Yellow solid; mp: 82 – 83 °C. ^1H NMR (200 MHz, $CDCl_3$) δ = 7.77 (d, *J* = 8.2 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 2.33 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.6, 155.4, 142.6, 136.4, 136.3, 130.1, 129.8, 126.9, 122.4, 120.7, 21.7.; IR (KBr): 3076, 3045, 2914, 2850, 1629, 1566, 1482, 1344, 1303, 1292, 1272, 1189, 1163, 1115, 1101, 1078, 1015, 993, 964, 838, 738, 677, 630 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{15}H_{12}ClN_2OSe$ $[M + H]^+$ 350.9796, found: 350.9790.

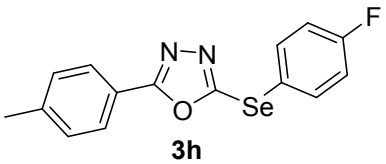
2-(4-methylphenyl)-5-((3-(trifluoromethyl)phenyl)selanyl) -1,3,4-oxadiazole (3g).



3g

Yield: 70%; Yellow solid; mp: 60 – 61 °C. ^1H NMR (200 MHz, $CDCl_3$) δ = 7.97 (s, 1H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 2.34 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.7, 154.8, 142.2, 138.2, 132.26 (d, $J_{C\text{-}F}$ = 32.9 Hz), 131.59 (q, $J_{C\text{-}F}$ = 3.8 Hz),130.3, 129.9, 126.9, 126.53 (q, $J_{C\text{-}F}$ = 3.7 Hz),125.5, 123.49 (q, $J_{C\text{-}F}$ = 272.9 Hz), 120.68, 21.7.; IR (KBr): 3100, 3052, 2992, 2915, 2881, 1629, 1564, 1478, 1431, 1322, 1223, 1152, 1110, 803, 713, 679, 662 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{16}H_{12}F_3N_2OSe$ $[M + H]^+$ 385.0062, found: 385.0066.

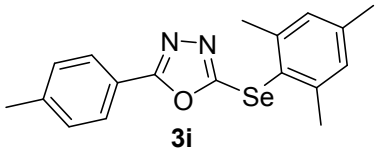
2-(4-methylphenyl)-5-((4-fluorophenyl)selanyl)-1,3,4-oxadiazole (3h).



3h

Yield: 65%; Yellow solid; mp: 85 – 87 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.83 (d, J = 8.2 Hz, 2H), 7.80 – 7.72 (m, 2H), 7.26 (d, J = 8.2 Hz, 2H), 7.14 – 7.04 (m, 2H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.4, 163.76 (d, $J_{C\text{-}F}$ = 250.7 Hz), 155.76, 142.52, 137.66 (d, $J_{C\text{-}F}$ = 8.4 Hz), 129.79, 126.79, 120.72, 118.84, 117.20 (d, $J_{C\text{-}F}$ = 22.0 Hz), 21.69.; IR (KBr): 3106, 3165, 2979, 2885, 1692, 1629, 1594, 1492, 1460, 1441, 1322, 1299, 1254, 1152, 1170, 1080, 962, 832, 742, 603 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{15}H_{12}FN_2OSe$ $[M + H]^+$ 335.0092, found: 335.0098.

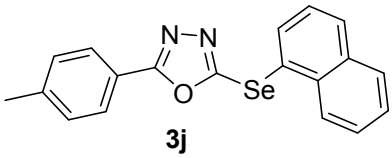
2-(4-methylphenyl)-5-(mesitylselanyl)-1,3,4-oxadiazole (3i).



3i

Yield: 62%; Yellow solid; mp: 62 – 64 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.80 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 7.01 (s, 2H), 2.56 (s, 6H), 2.39 (s, 3H), 2.30 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.0, 156.2, 143.6, 142.2, 140.6, 129.7, 129.3, 126.7, 122.8, 121.0, 24.5, 21.7, 21.1.; IR (KBr): 3083, 3000, 2952, 2923, 2846, 2831, 1601, 1564, 1513, 1480, 1441, 1333, 1291, 1176, 1127, 1083, 991, 864, 832, 740, 675, 630 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{18}H_{19}N_2OSe$ $[M + H]^+$ 359.0658, found: 359.0656.

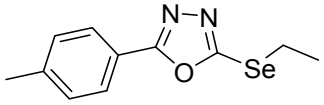
2-(4-methylphenyl)-5-(naphthalen-1-ylselanyl)-1,3,4-oxadiazole (3j).



3j

Yield: 63%; Yellow solid; mp: 122 – 124 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 8.42 (d, J = 7.8 Hz, 1H), 8.09 (dd, J = 7.2, 1.0 Hz, 1H), 7.95 (d, J = 8.3 Hz, 1H), 7.86 (dd, J = 7.1, 2.0 Hz, 1H), 7.69 (d, J = 8.2 Hz, 2H), 7.63 – 7.52 (m, 2H), 7.49 – 7.40 (m, 1H), 7.17 (d, J = 8.2 Hz, 2H), 2.34 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.3, 155.6, 142.3, 136.3, 134.4, 131.4, 129.7, 129.6, 128.8, 127.7, 127.6, 126.8, 126.7, 126.7, 126.0, 125.9, 123.4, 120.7, 21.6.; IR (KBr): 3089, 3052, 3023, 2954, 2918, 1629, 1594 1548, 1513, 1480, 1348, 1266, 1174, 1083, 1038, 964, 834, 807, 781, 662 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{19}H_{15}N_2OSe$ $[M + H]^+$ 367.0345, found: 367.0346.

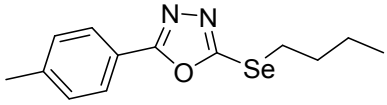
2-(4-methylphenyl)-5-(ethylselanyl)-1,3,4-oxadiazole (3k).



3k

Yield: 80%; Yellow solid; mp: 41 – 42 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.90 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 3.33 (q, J = 7.4 Hz, 2H), 2.41 (s, 3H), 1.65 (t, J = 7.4 Hz, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.0, 156.2, 142.2, 129.7, 126.7, 121.0, 32.2, 22.2, 21.6, 16.0.; IR (KBr): 3055, 3046, 2977, 2959, 2916,2870, 2863, 1684, 1615, 1558, 1464, 1331, 1238, 1184, 1062, 954, 834, 795, 672, 668, 613 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{11}H_{13}N_2OSe$ $[M + H]^+$ 269.0188, found: 269.0197.

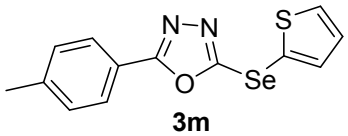
2-(4-methylphenyl)-5-(butylselanyl)-1,3,4-oxadiazole (3l).



3l

Yield: 81%; Yellow solid; mp: 58 – 60 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 8.05 – 7.79 (m, 2H), 7.35 – 7.22 (m, 2H),), 3.33 (t, J = 7.5 Hz, 2H), 2.40 (s, 3H), 1.99 – 1.80 (m, 2H), 1.58 – 1.39 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 166.8, 156.2, 142.0, 129.6, 126.5, 120.8, 32.2, 28.0, 22.7, 21.5, 13.4.; IR (KBr): 3049, 3002, 2972, 2948, 2883, 2861,1658, 1629, 1572, 1513, 1480, 1321, 1225, 1176, 1085, 991, 834, 818, 736, 701, 660 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{13}H_{17}N_2OSe$ $[M + H]^+$ 297.0501, found: 297.0501.

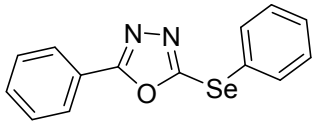
2-(4-chlorophenyl)-5-(thiophen-2-ylselanyl)-1,3,4-oxadiazole (3m).



3m

Yield: 79%; Yellow solid; mp: 68 – 69 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.81 (d, J = 8.3 Hz, 2H), 7.57 – 7.46 (m, 1H), 7.30 – 7.21 (m, 3H), 7.13 – 6.98 (m, 1H), 2.37 (s, 3H).; ^{13}C (100 MHz, $CDCl_3$) δ = 167.2, 155.5, 142.2, 138.6, 133.7, 131.9, 129.7, 128.4, 126.7, 120.6, 21.68.; IR (KBr): 3055, 2998, 2921, 2846, 1612, 1566, 1460, 1403, 1304, 1299, 1176, 1091, 1025, 972, 928, 836, 813, 722, 709 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{13}H_{11}SN_2OSe$ $[M + H]^+$ 322.9751, found: 322.9755.

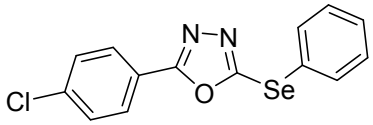
2-phenyl-5-(phenylselanyl)-1,3,4-oxadiazole (3n).



3n

Yield: 84%; Yellow solid; mp: 51 – 52 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.96 – 7.91 (m, 2H), 7.81 – 7.70 (m, 2H), 7.49 – 7.37 (m, 6H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.2, 156.2, 135.0, 131.8, 129.8, 129.6, 129.0, 126.8, 124.2, 123.4.; IR (KBr): 3094, 3055, 2977, 2920, 1546, 1484, 1463, 1335, 1280, 1158, 1111, 1061, 1022, 982, 782, 741, 688 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{14}H_{11}N_2OSe$ $[M + H]^+$ 303.0031, found: 303.0028.

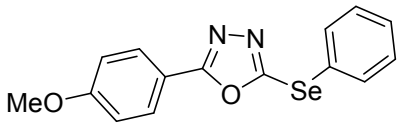
2-(4-chlorophenyl)-5-(phenylselanyl)-1,3,4-oxadiazole (3o).



3o

Yield: 79%; Yellow solid; mp: 85 – 87 °C. ^{1}H NMR (400 MHz, $CDCl_3$)δ = 7.82 (d, J = 8.2 Hz, 2H), 7.70 (d, J = 7.7 Hz, 2H), 7.40 – 7.31 (m, 5H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.3, 162.5, 156.5, 138.0, 135.1, 129.8, 129.7, 129.4, 128.0, 121.9.; IR (KBr): 3064, 3044, 2917, 1655, 1613, 1553, 1482, 1464, 1384, 1293, 1189, 1084, 1067, 953, 817, 725, 669, 623 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{14}H_{10}ClN_2OSe$ $[M + H]^+$ 336.9639, found: 336.9638.

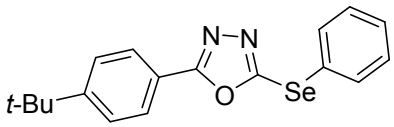
2-(4-methoxyphenyl)-5-(phenylselanyl)-1,3,4-oxadiazole (3p).



3p

Yield: 95%; Yellow solid; mp: 93 – 95 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 8.01 – 7.63 (m, 4H), 7.43 – 7.36 (m, 2H), 7.03 – 6.87 (m, 2H), 3.85 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.3, 162.5, 155.3, 134.9, 129.9, 129.6, 128.7, 124.6, 116.1, 114.5, 55.5.; IR (KBr): 3059, 3034, 2985, 2952, 1652, 1609, 1553, 1541, 1498, 1464, 1337, 1306, 1255, 1178, 1150, 1062, 1017, 958, 835, 738, 687 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{15}H_{13}N_2O_2Se$ $[M + H]^+$ 333.0137, found: 317.0133.

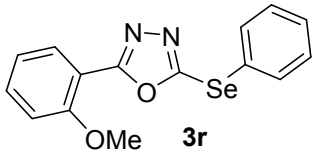
2-(4-(tert-butyl)phenyl)-5-(phenylselanyl)-1,3,4-oxadiazole (3q).



3q

Yield: 96%; Yellow solid; mp: 59 – 60 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.88 (dt, J = 8.7, 1.3 Hz, 2H), 7.82 – 7.66 (m, 2H), 7.51 – 7.35 (m, 5H), 1.33 (s, 9H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.3, 155.8, 155.5, 135.0, 129.9, 129.6, 126.7, 126.1, 124.4, 120.7, 35.1, 31.1.; IR (KBr): 3089, 3008, 2949, 2923, 2916, 2903, 2860, 1614, 1581, 1565, 1546, 1495, 1463, 1378, 1333, 1265, 1150, 1122, 1107, 1061, 1012, 984, 951, 847, 838, 739, 704, 685 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{18}H_{19}N_2OSe$ $[M + H]^+$ 359.0658, found: 359.0659.

2-(2-methoxyphenyl)-5-(phenylselanyl)-1,3,4-oxadiazole (3r).

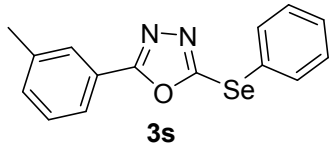


3r

Yield: 83%; Yellow solid; mp: 63 – 64 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.90 – 7.64 (m, 3H), 7.51 – 7.32 (m, 4H), 7.07 – 6.92 (m, 2H), 3.86 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 165.9,

157.7, 155.8, 135.0, 133.2, 130.2, 129.7, 129.4, 124.5, 120.7, 112.6, 111.9, 55.9.; IR (KBr): 3057, 3020, 2971, 2936, 2836, 1652, 1558, 1495, 1455, 1435, 1413, 1354, 1240, 1178, 1125, 1006, 1004, 915, 842, 770, 738, 689, 666 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{15}H_{13}N_2O_2Se$ $[M + H]^+$ 333.0137, found: 317.0135.

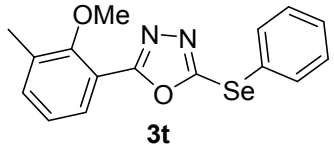
2-(3-methylphenyl)-5-(phenylselanyl)-1,3,4-oxadiazole (3s).



3s

Yield: 85%; Yellow viscous liquid. ^1H NMR (200 MHz, $CDCl_3$) δ = 7.84 – 7.65 (m, 4H), 7.44 – 7.28 (m, 5H), 2.38 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.3, 156.0, 138.9, 134.9, 132.6, 129.8, 129.5, 128.9, 127.3, 124.3, 123.9, 123.3, 21.3.; IR (KBr): 3020, 2911, 2861, 1610, 1411, 1331, 1278, 1155, 1091, 1020, 968, 832, 735, 642 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{15}H_{13}N_2OSe$ $[M + H]^+$ 317.0185, found: 317.0185.

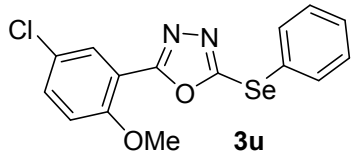
2-(2-methoxy-3-methylphenyl)-5-(phenylselanyl)-1,3,4-oxadiazole (3t).



3t

Yield: 88%; Yellow solid; mp: 59 – 60 °C. ^1H NMR (200 MHz, $CDCl_3$) δ = 7.83 – 7.62 (m, 3H), 7.41 – 7.26 (m, 4H), 7.08 (t, *J* = 7.7 Hz, 1H), 3.61 (s, 3H), 2.32 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 165.7, 156.8, 156.3, 135.3, 134.9, 132.9, 129.8, 129.6, 127.7, 124.2, 124.1, 117.4, 60.9, 15.9.; IR (KBr): 3042, 3021, 2975, 2937, 2861, 2853, 1612, 1604, 1547, 1512, 1488, 1454, 1328, 1310, 1257, 1173, 1155, 1052, 1007, 957, 829, 738, 686 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{16}H_{15}N_2O_2Se$ $[M + H]^+$ 347.0294, found: 347.0291.

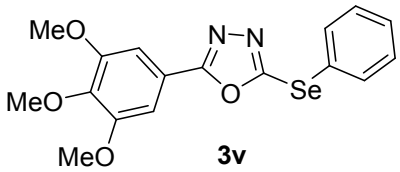
2-(5-chloro-2-methoxyphenyl)-5-phenylselanyl-1,3,4-oxadiazole (3u).



3u

Yield: 89%; Yellow solid; mp: 56 – 58 °C. ^1H NMR (200 MHz, $CDCl_3$) δ = 7.83 – 7.66 (m, 3H), 7.45 – 7.35 (m, 4H), 6.93 (d, *J* = 8.9 Hz, 1H), 3.83 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 166.2, 164.7, 156.2, 135.0, 134.9, 132.6, 129.6, 129.5, 125.5, 124.1, 113.8, 113.3, 56.2.; IR (KBr): 3060, 3040, 2960, 2928, 2861, 2847, 1652, 1617, 1576, 1558, 1539, 1507, 1497, 1486, 1470, 1456, 1439, 1337, 1272, 1180, 1027, 989, 874, 823, 740, 668 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{15}H_{12}ClN_2O_2Se$ $[M + H]^+$ 366.9745, found: 366.9744.

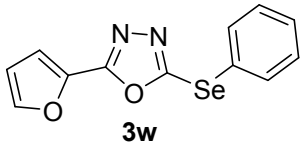
2-(3,4,5-trimethoxyphenyl)-5-phenylselanyl-1,3,4-oxadiazole (3v).



3v

Yield: 92%; Yellow solid; mp: 122 – 125 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.88 – 7.67 (m, 2H), 7.46 – 7.34 (m, 3H), 7.19 (s, 2H), 3.90 (s, 9H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 167.1, 155.9, 153.6, 141.1, 134.9, 129.8, 129.6, 124.4, 118.5, 104.1, 61.0, 56.3.; IR (KBr): 3057, 3020, 2971, 2936, 2864, 2830, 1652, 1594, 1558, 1541, 1497, 1456, 1435, 1411, 1354, 1240, 1125, 1005, 862, 842, 742, 666 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{17}H_{17}N_2O_4Se$ $[M + H]^+$ 393.0327, found: 393.0321.

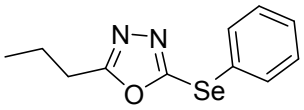
2-(furan-2-yl)-5-phenylselanyl-1,3,4-oxadiazole (3w).



3w

Yield: 82%; Yellow solid; mp: 60 – 61 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.83 – 7.69 (m, 2H), 7.61 (bd, *J* = 1.8 Hz, 1H), 7.45 – 7.35 (m, 3H), 7.09 (d, *J* = 3.5 Hz, 1H), 6.56 (dd, *J* = 3.5, 1.8 Hz, 1H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 160.0, 155.7, 145.8, 139.1, 135.1, 129.9, 129.7, 124.0, 114.4, 112.2.; IR (KBr): 3133, 3061, 2985, 2928, 1698, 1932, 1560, 1513, 1460, 1448, 1348, 1132, 1081, 949, 900, 826, 748, 689, 675 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{12}H_9N_2OSe$ $[M + H]^+$ 292.9824, found: 292.9834.

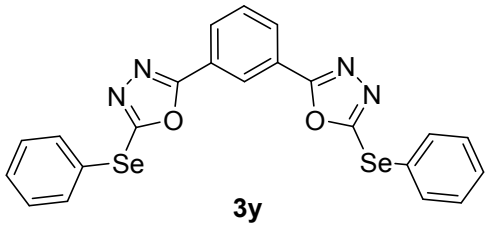
2-(*n*-propyl)-5-phenylselanyl-1,3,4-oxadiazole (3x).



3x

Yield: 84%; Yellow viscous liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.82 – 7.61 (m, 2H), 7.46 – 7.30 (m, 3H), 2.78 (t, *J* = 7.4 Hz, 2H), 1.82 – 1.69 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 169.5, 155.8, 134.8, 129.7, 129.4, 124.2, 27.1, 19.8, 13.4.; IR (KBr): 3053, 2977, 2959, 2916, 2863, 1661, 1615, 1558, 1505, 1464, 1158, 1062, 1017, 954, 834, 726, 668, 636 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{11}H_{13}N_2OSe$ $[M + H]^+$ 269.0188, found: 269.0195.

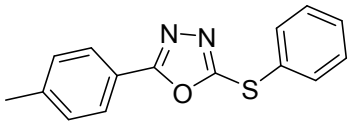
(1,3-bis(5-phenylselanyl)-1,3,4-oxadiazol-2-yl)benzene (3y).



3y

Yield: 61%; yellow solid; mp: 122 - 124 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 8.53 (t, J = 1.7 Hz, 1H), 8.12 (dd, J = 7.9 Hz, 1.7 Hz, 2H), 7.82 – 7.75 (m, 4H), 7.64 – 7.56 (m, 1H), 7.46 – 7.38 (m, 6H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 166.2, 157.1, 135.3, 130.0, 129.9, 129.8, 125.0, 124.7, 124.0.; IR (KBr): 3074, 3045, 2979, 2937, 1648, 1567, 1492, 1465, 1327, 1282, 1159, 1163, 1051, 1028, 981, 788, 734, 668 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{22}H_{15}N_4O_2Se_2$ $[M + H]^+$ 526.9522, found: 596.9519.

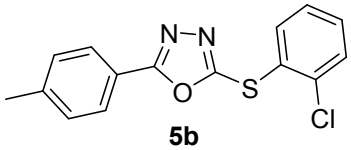
2-(4-Methylphenyl)-5-(phenylthio)-1,3,4-oxadiazole (5a).



5a

Yield: 55%; white solid; mp: 68 – 69 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.69 (d, J = 8.1 Hz, 2H), 7.59 – 7.44 (m, 2H), 7.39 – 7.15 (m, 3H), 7.11 (d, J = 8.1 Hz, 2H), 2.24 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 166.4, 162.2, 142.3, 133.3, 129.6, 127.1, 126.5, 120.5, 21.5.; IR (KBr): 3075, 3021, 2938, 1612, 1558, 1478, 1460, 1304, 1285, 1254, 1176, 1117, 1065, 1163, 1067, 1022, 955, 835, 803, 752, 733, 697 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{15}H_{13}N_2OS$ $[M + H]^+$ 269.0743, found: 269.0738.

2-(4-Methylphenyl)-5-(2-chlorophenylthio)-1,3,4-oxadiazole (5b).



5b

Yield: 49%; white solid; mp: 87 - 89 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.78 (d, J = 8.2 Hz, 2H), 7.61 – 7.55 (m, 1H), 7.43 (dd, J = 7.7 Hz, 1.7 Hz, 1H), 7.33 – 7.22 (m, 2H), 7.19 (d, J = 8.2 Hz, 2H), 2.32 (s, 3H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 166.8, 161.1, 142.6, 136.9, 134.7, 130.9, 130.6, 129.8, 127.9, 127.3, 126.9, 120.7, 21.7.; IR (KBr): 3098, 3016, 1652, 1594, 1548, 1492, 1462, 1268, 1142, 1021, 962, 832, 728, 707, 669 cm^{-1}.; ESI-HRMS *m/z*: calcd. for $C_{15}H_{12}ClN_2OS$ $[M + H]^+$ 303.0353, found: 303.0357.

VI. References

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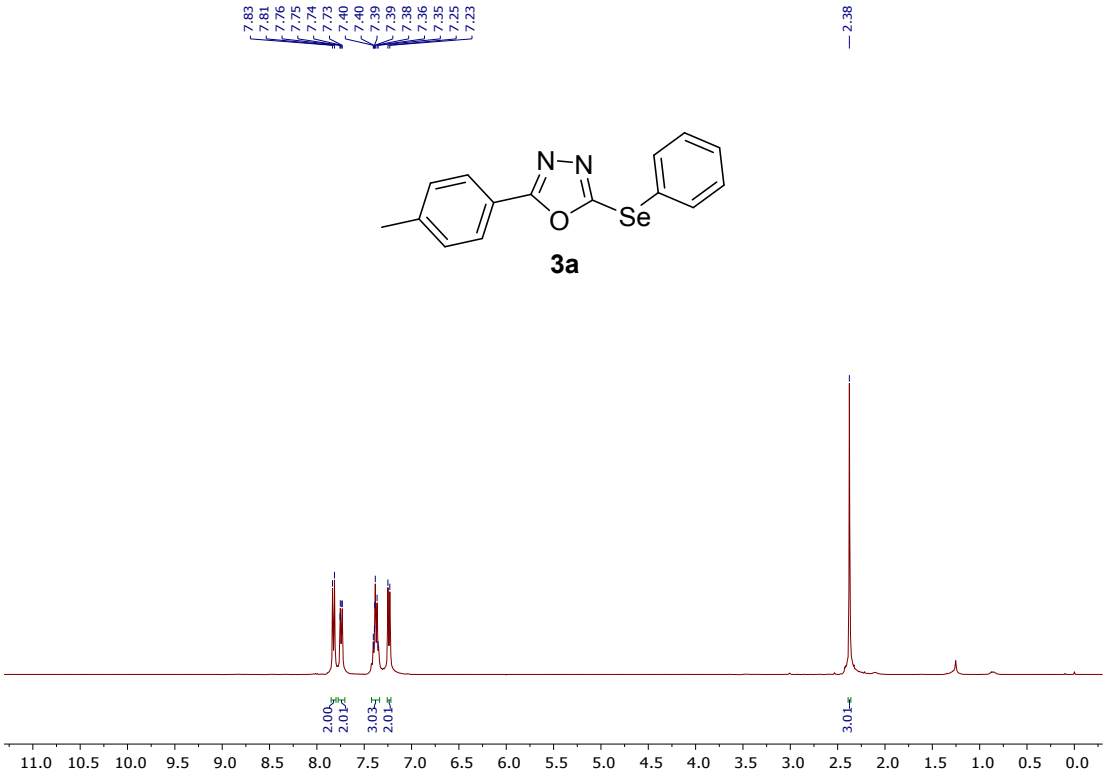
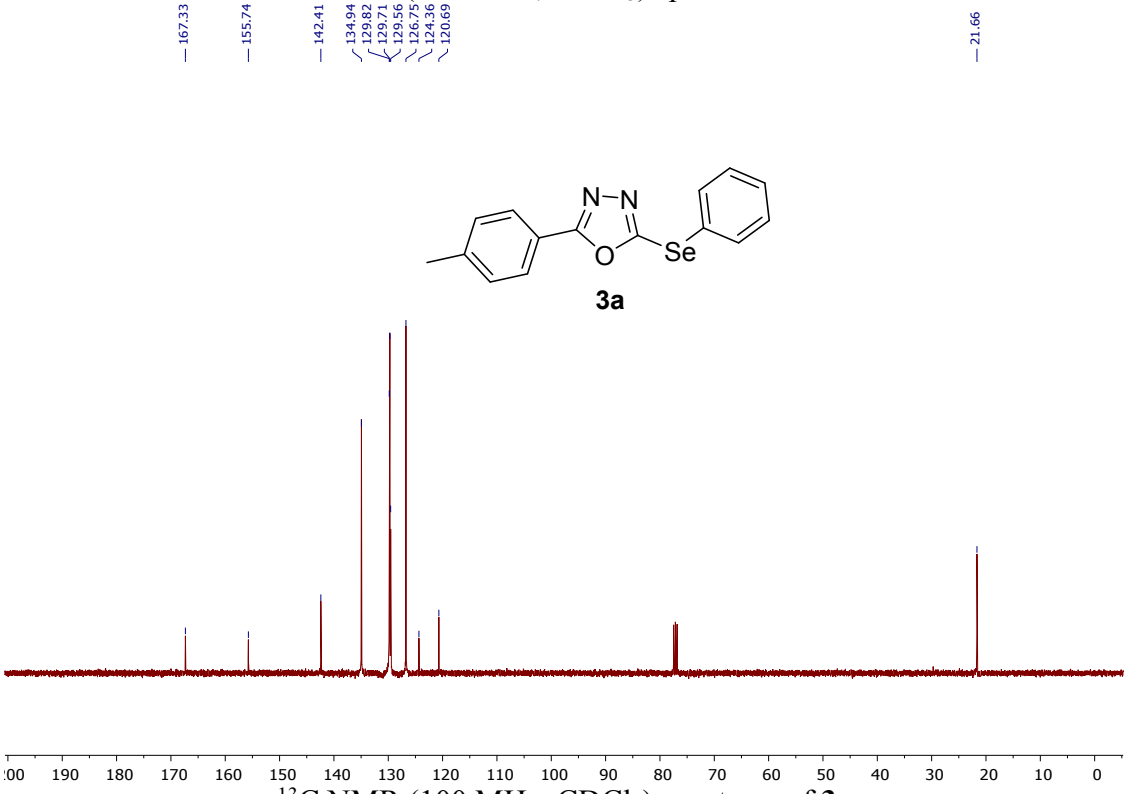
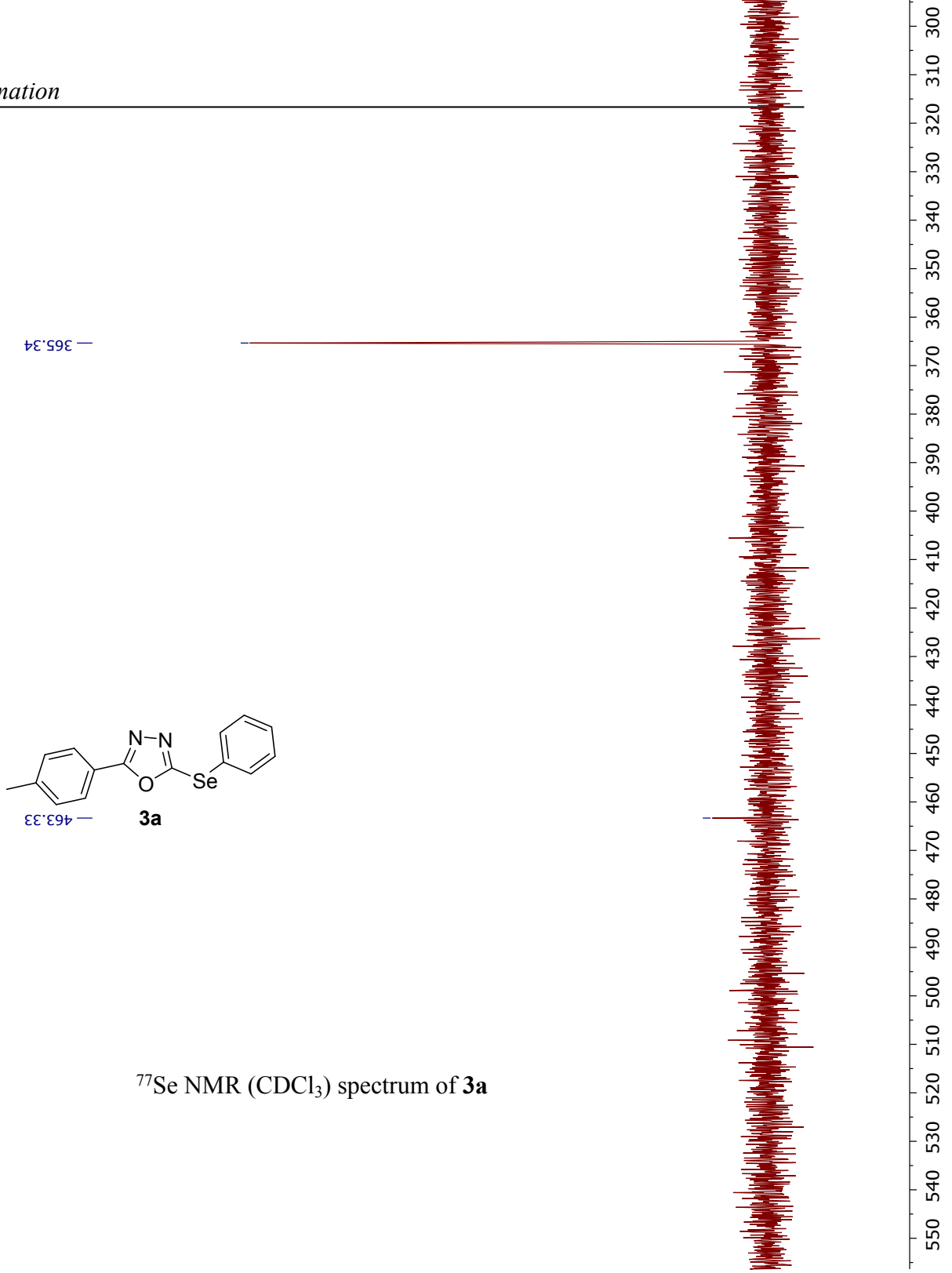
VII. NMR Spectra



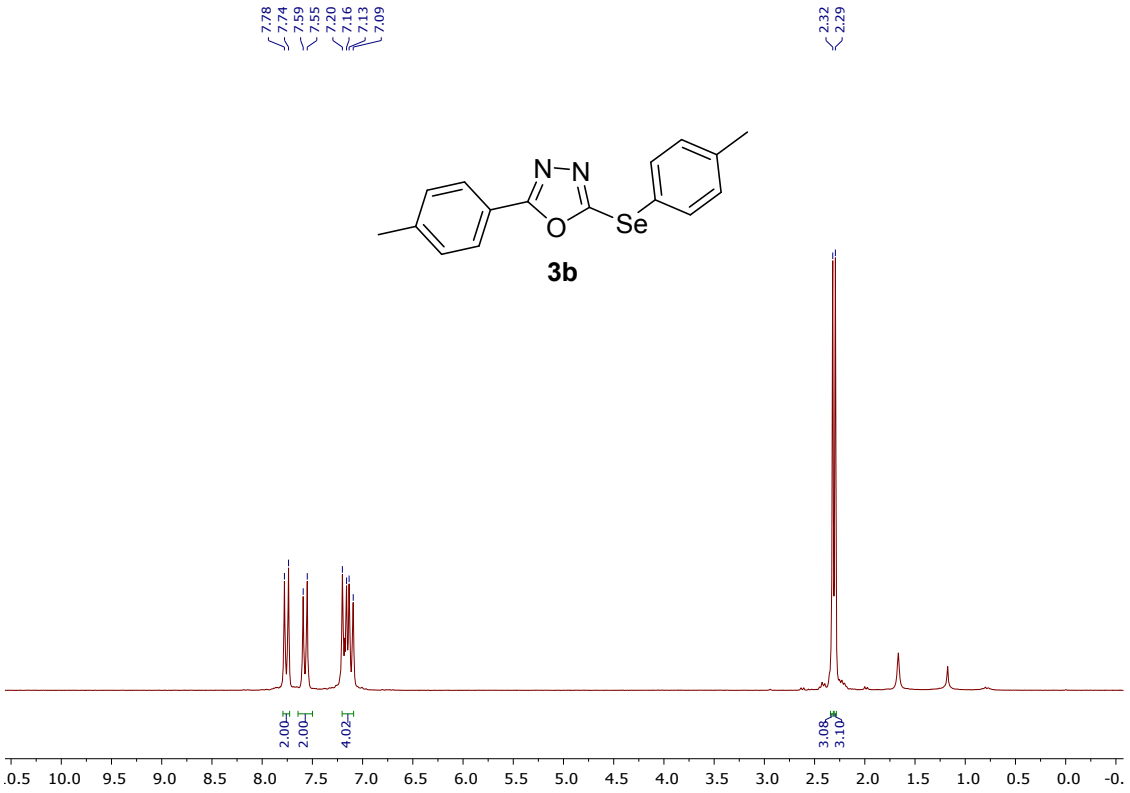
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3a**



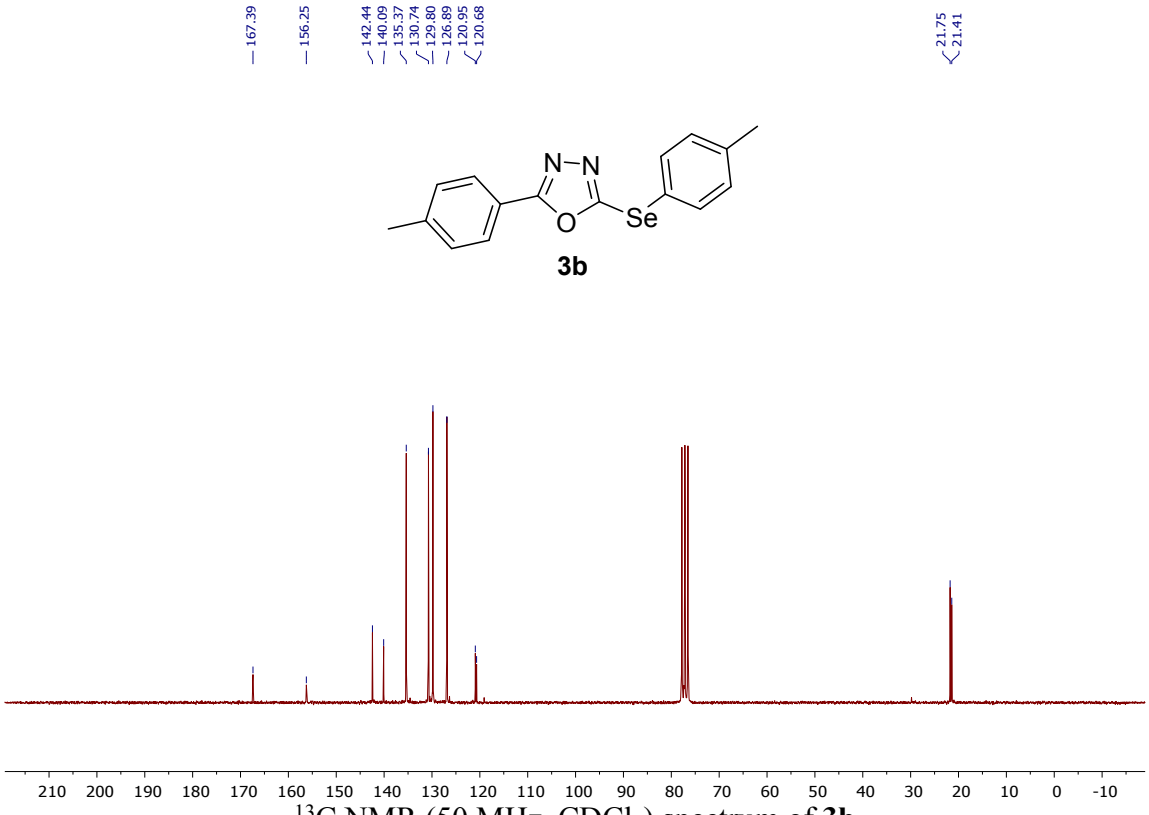
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3a**



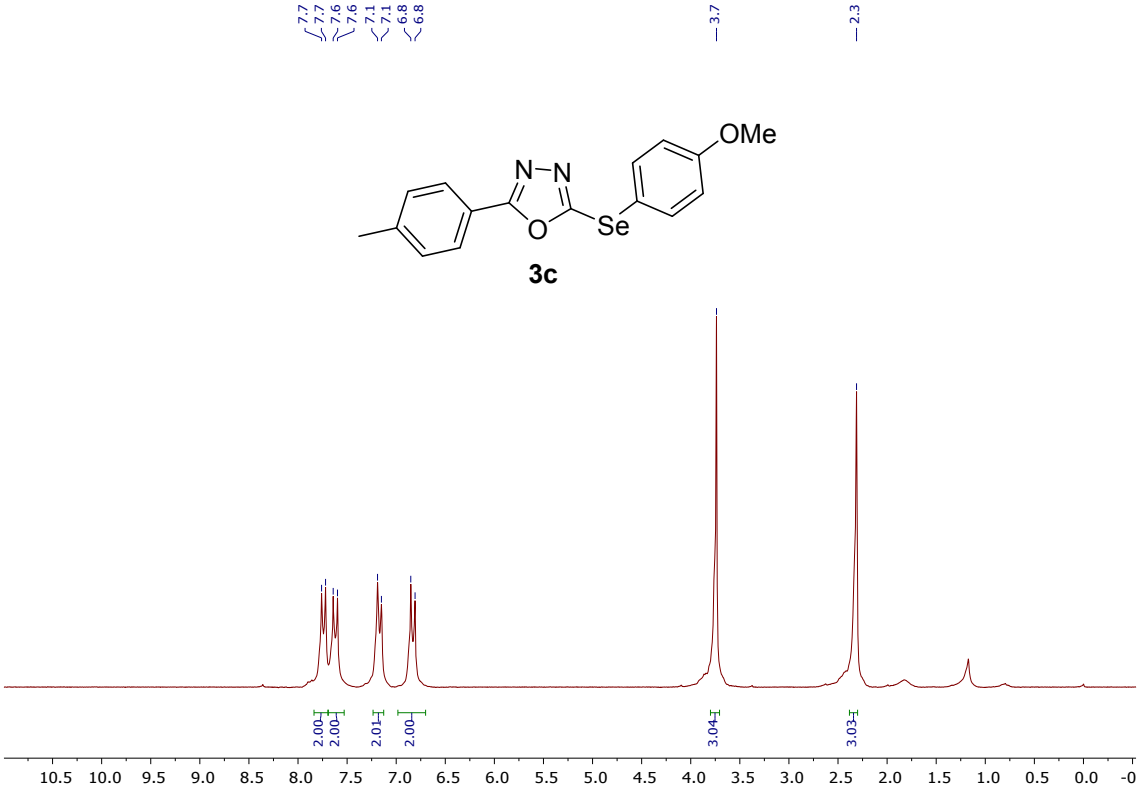
^{77}Se NMR ($CDCl_3$) spectrum of **3a**



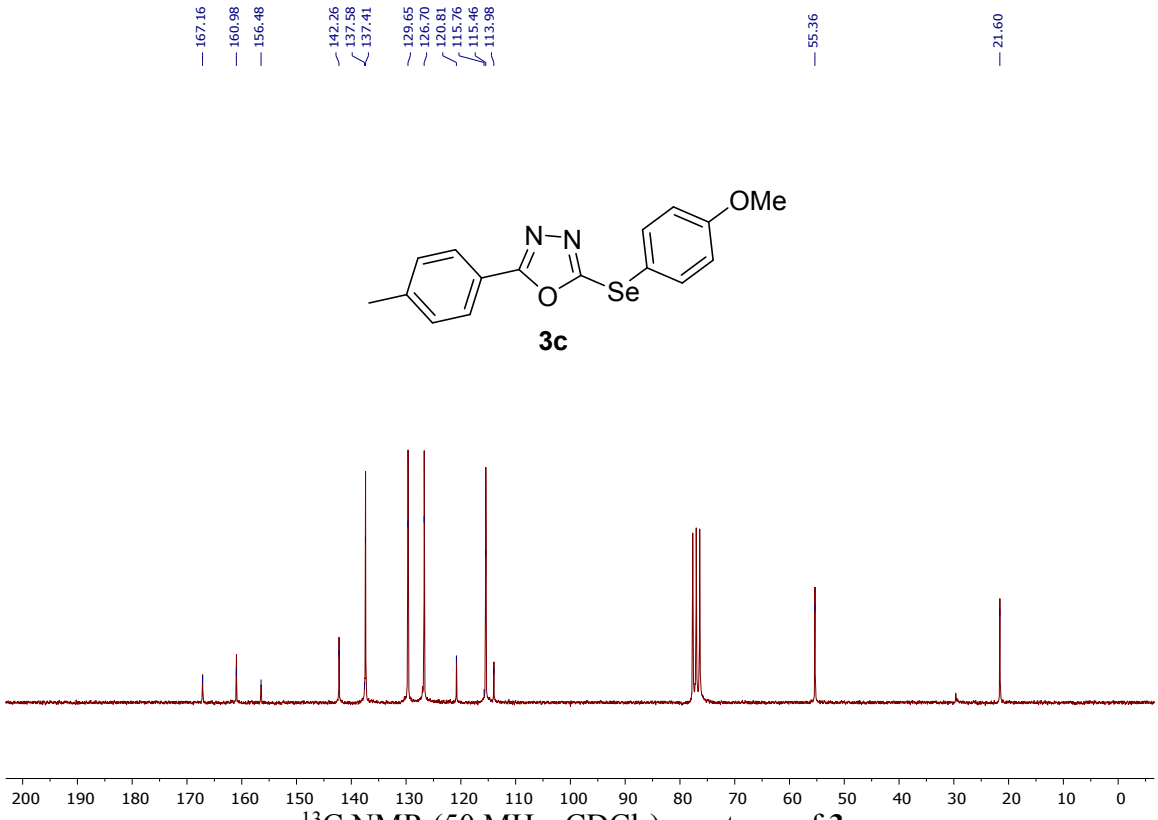
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3b**



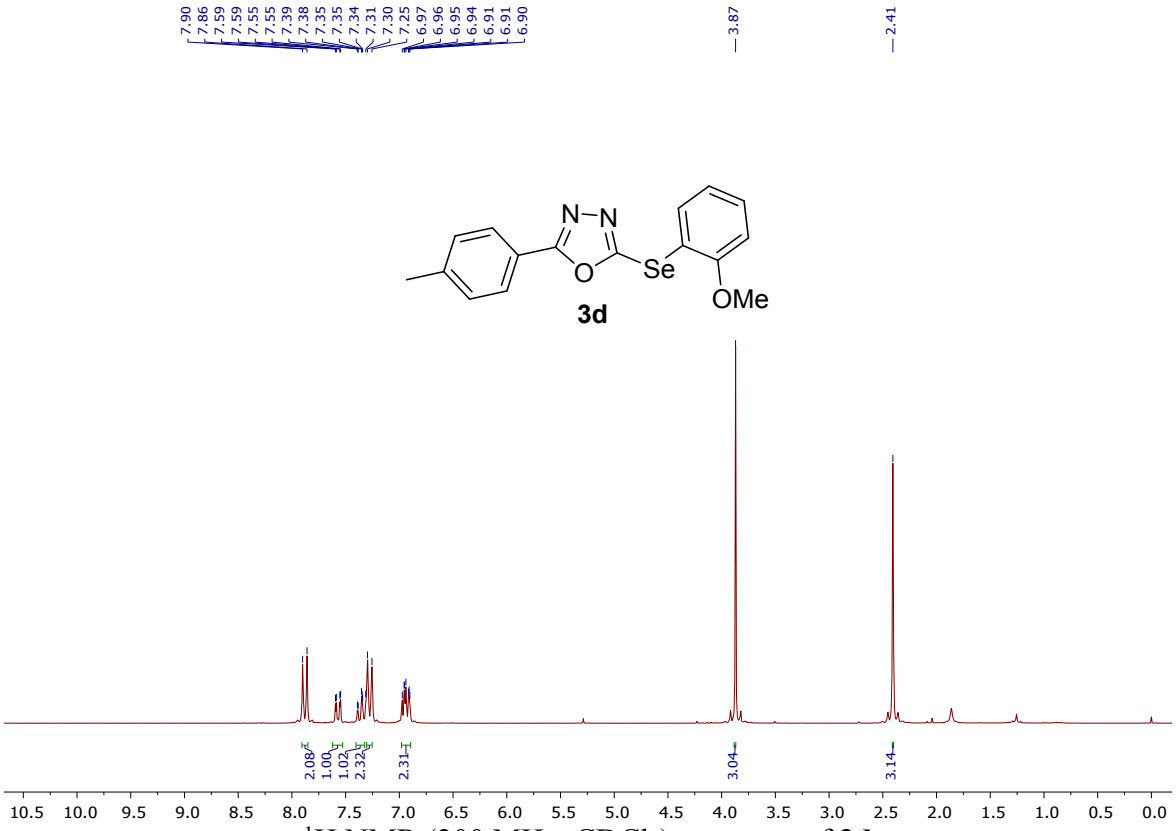
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3b**



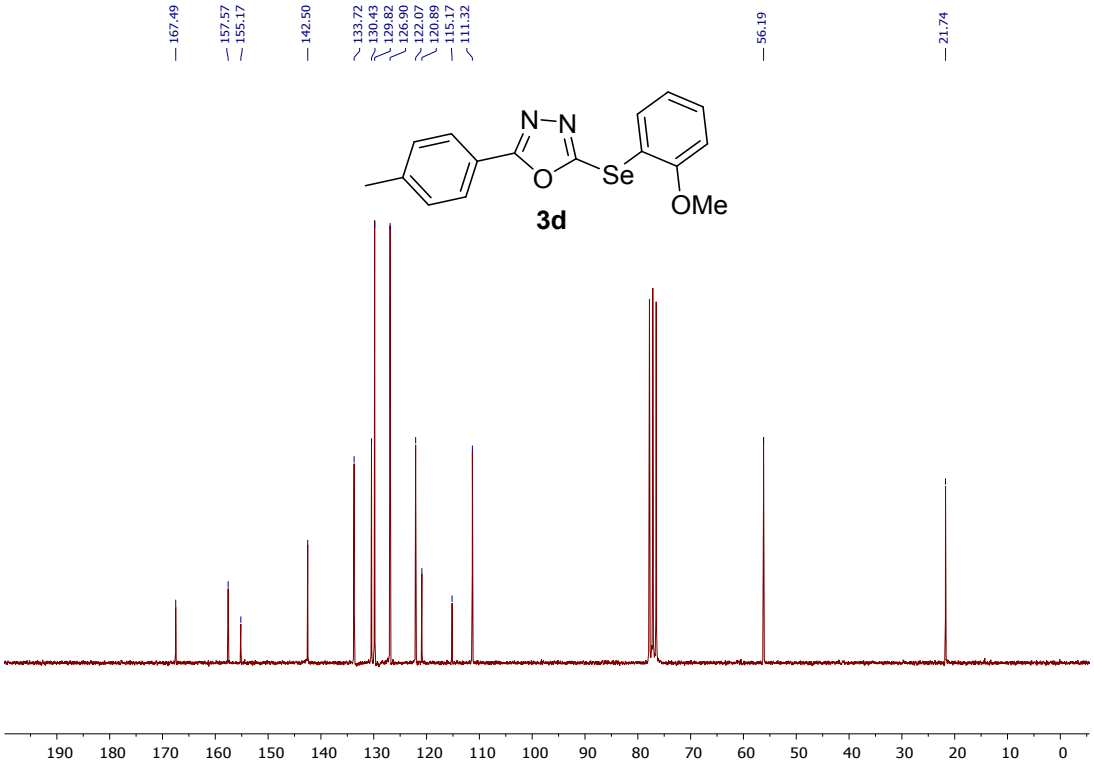
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3c**



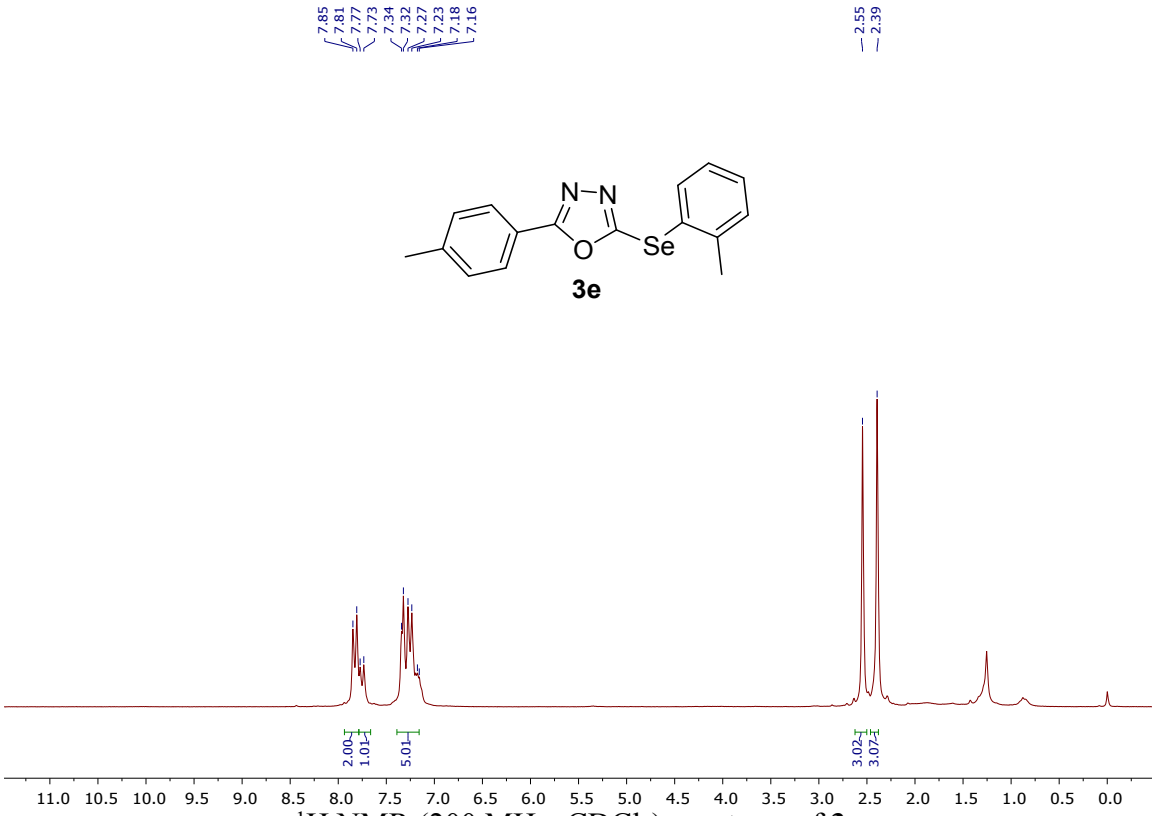
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3c**



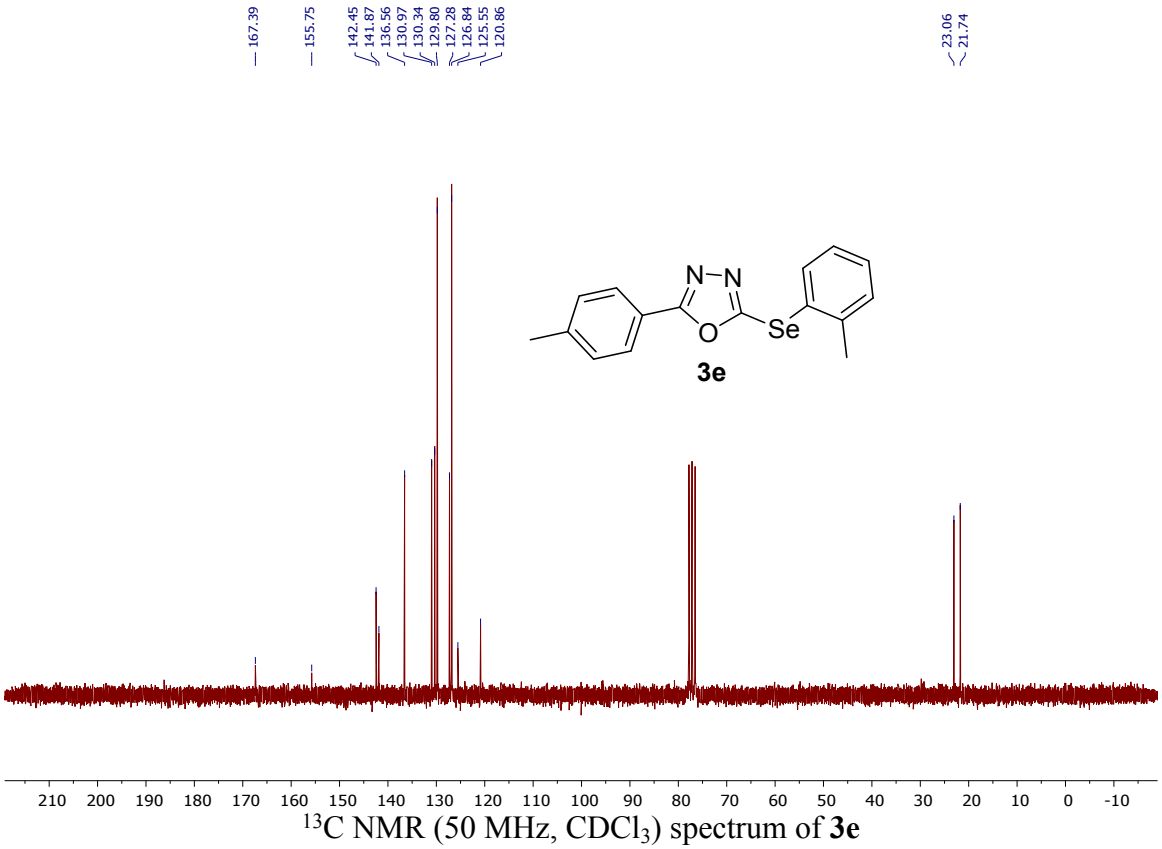
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3d**



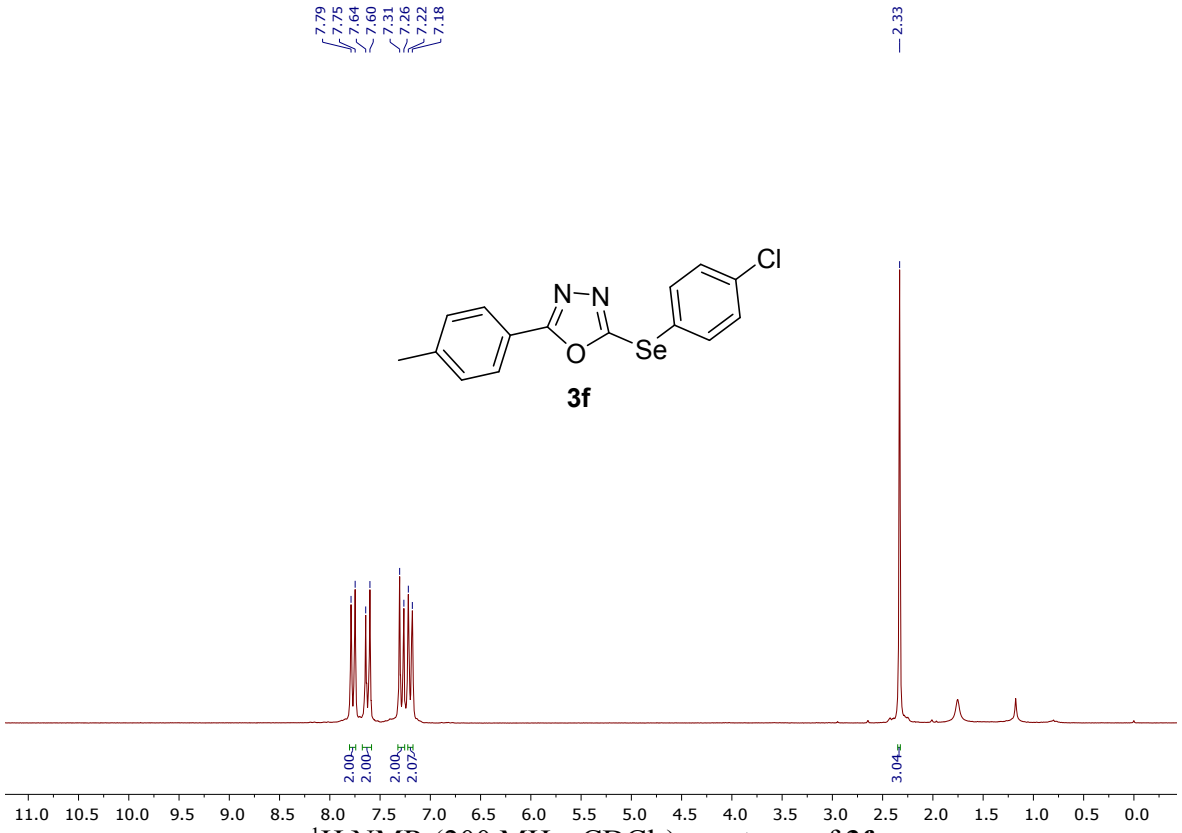
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3d**



^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3e**

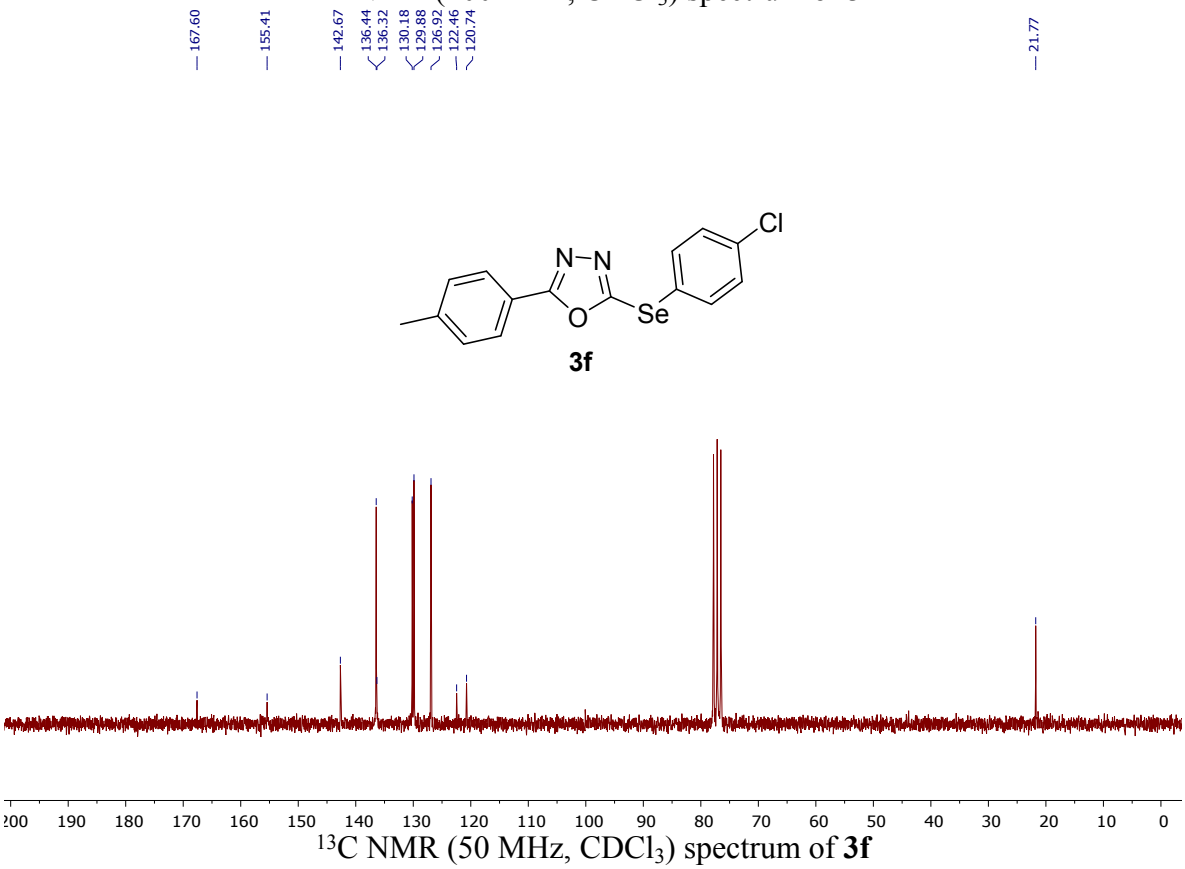


^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3e**



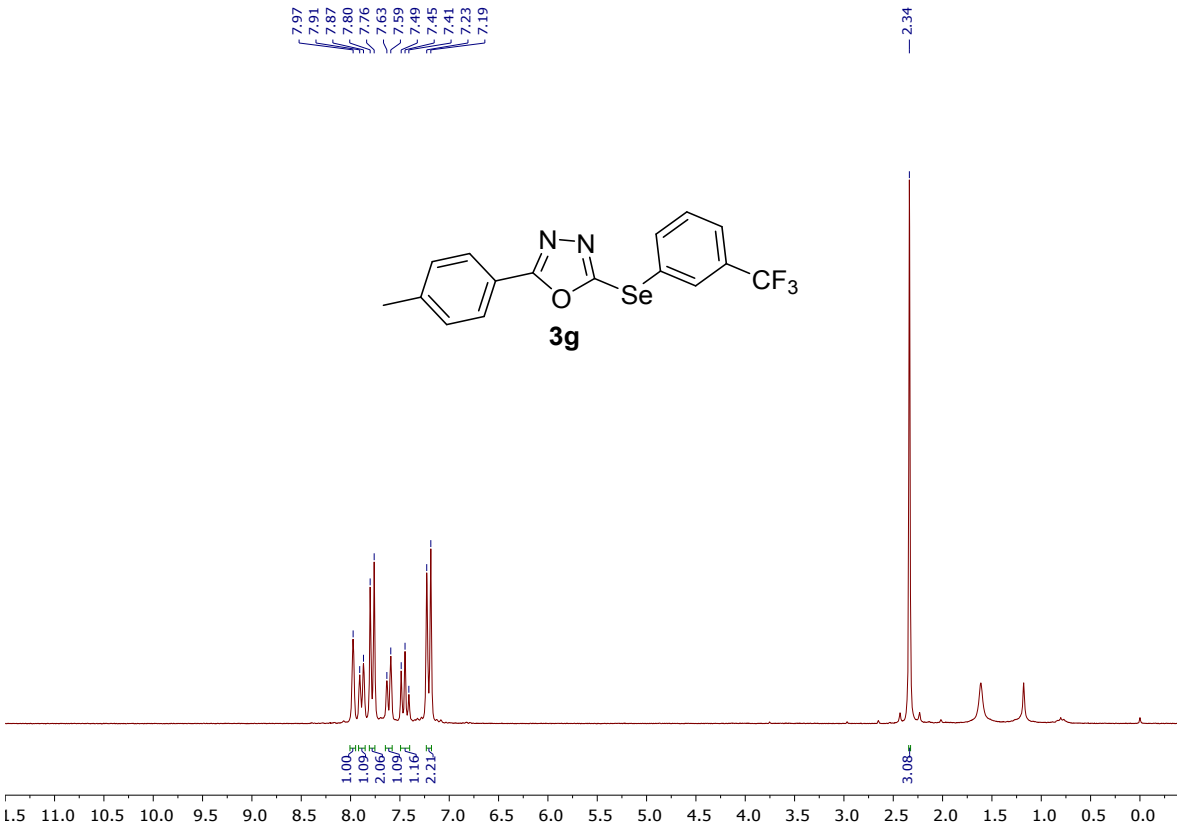
3f

^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3f**

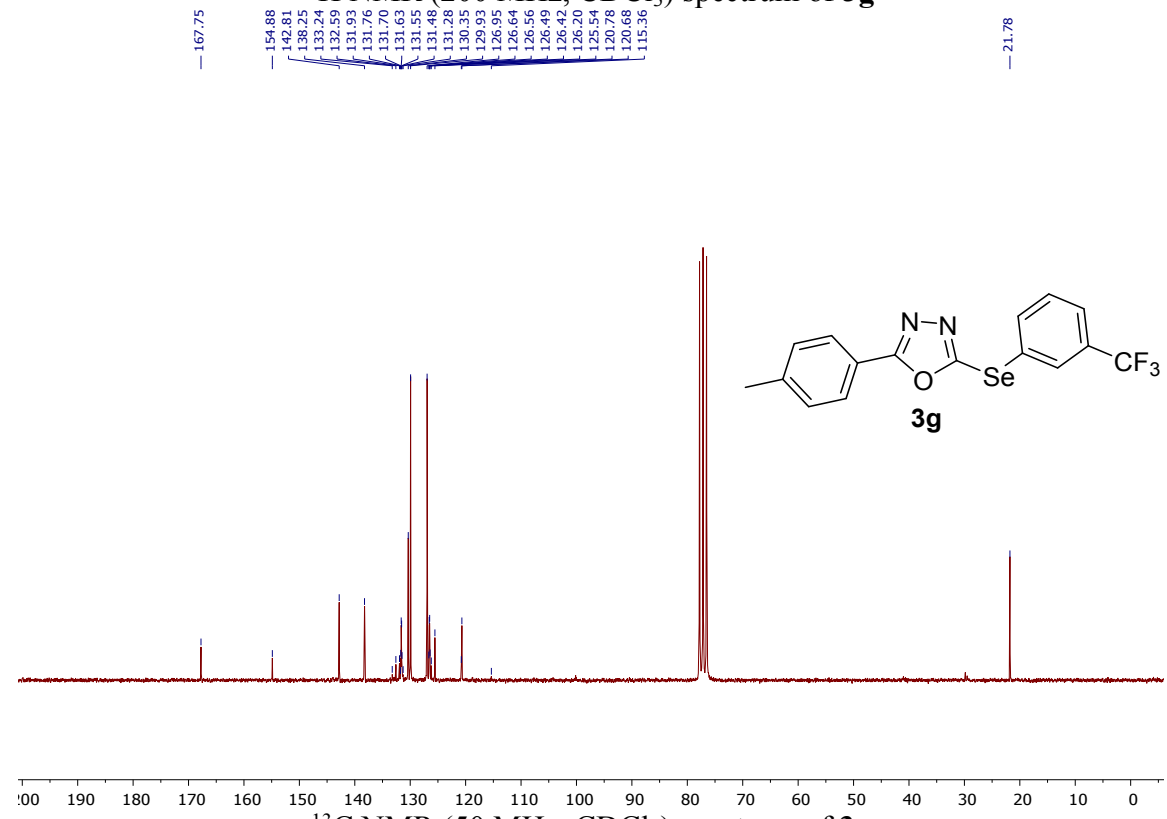


3f

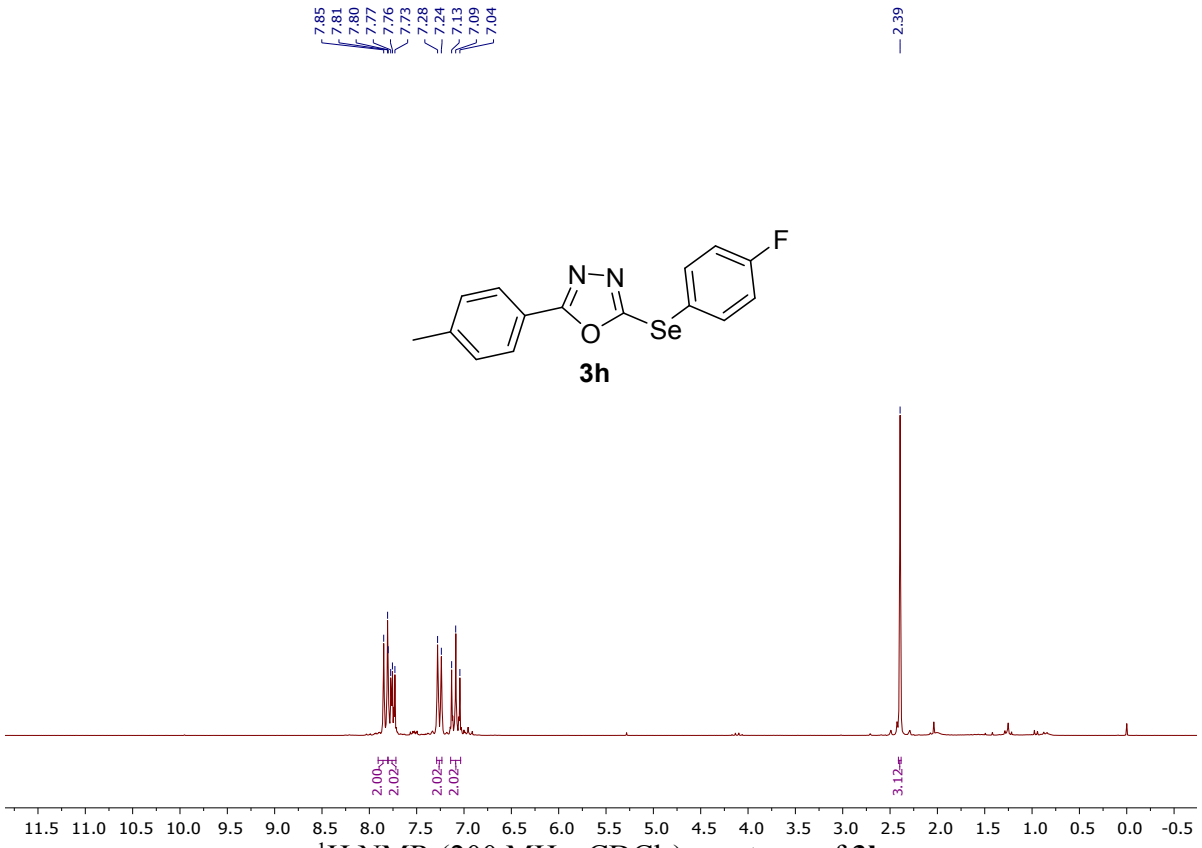
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3f**



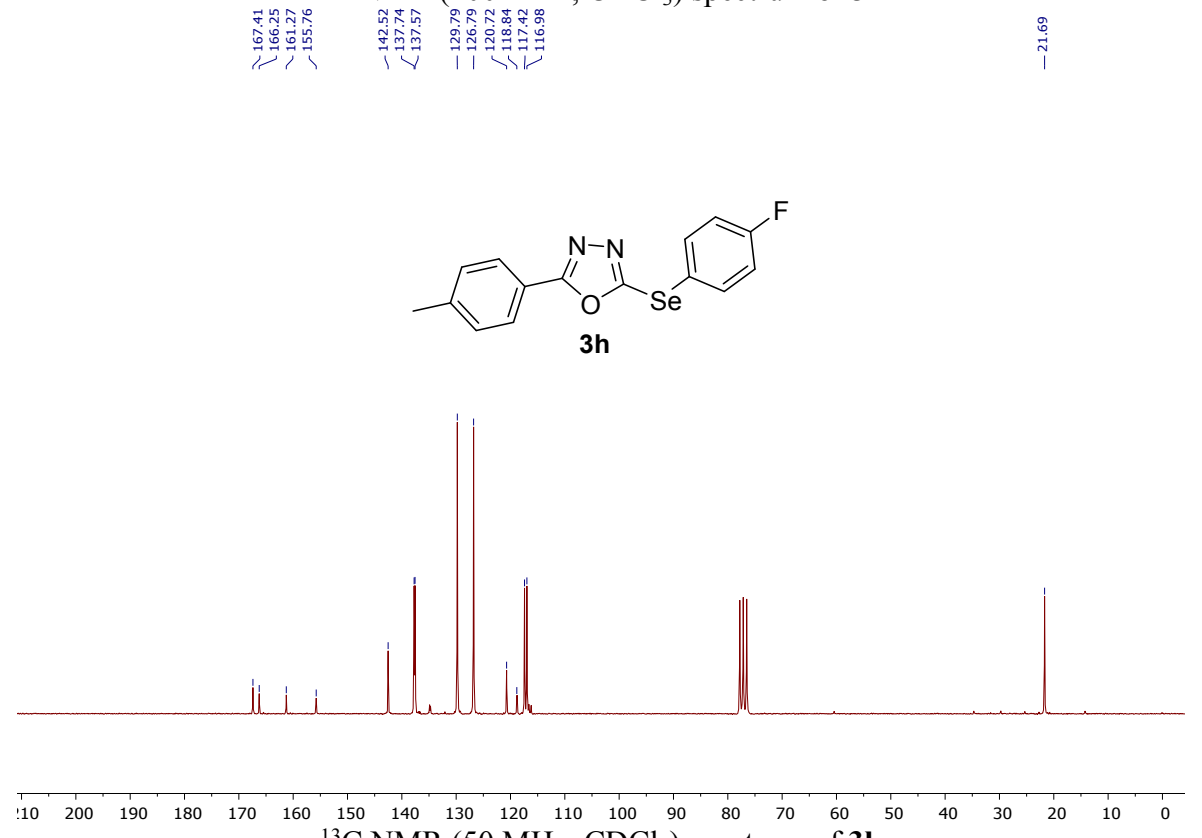
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3g**



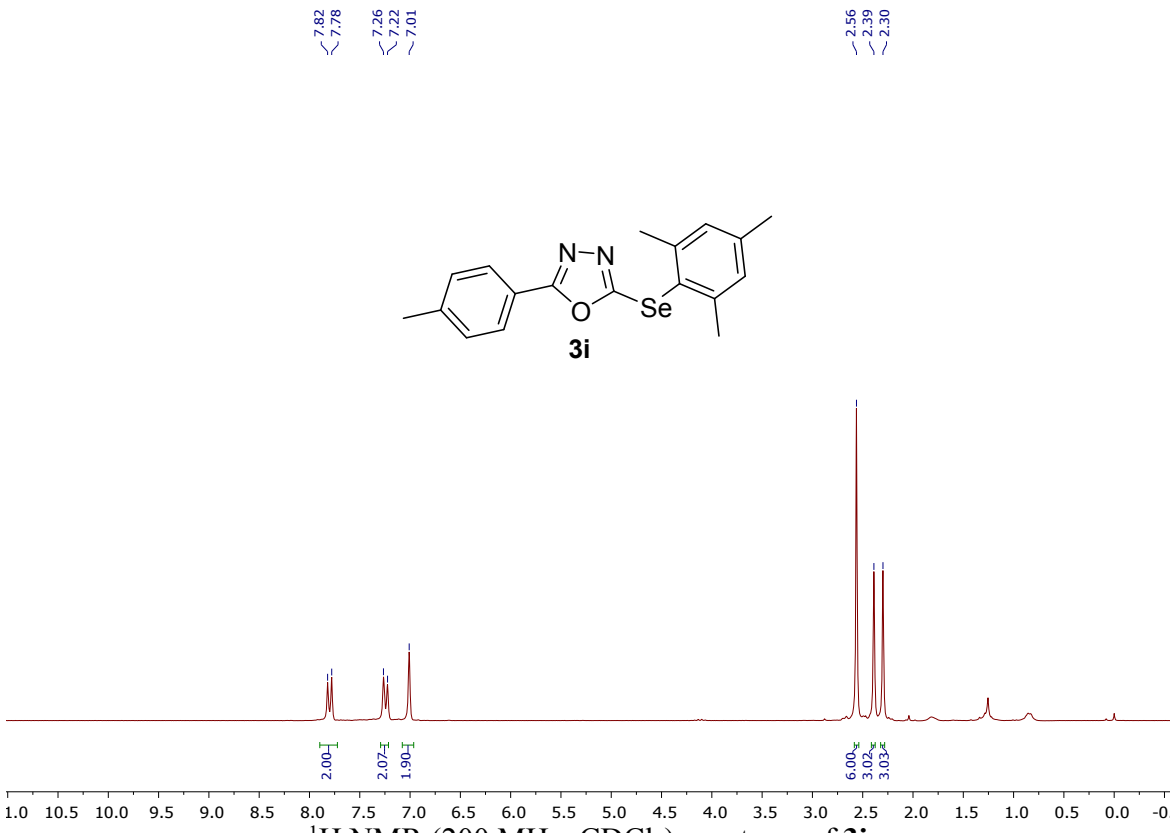
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3g**



^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3h**

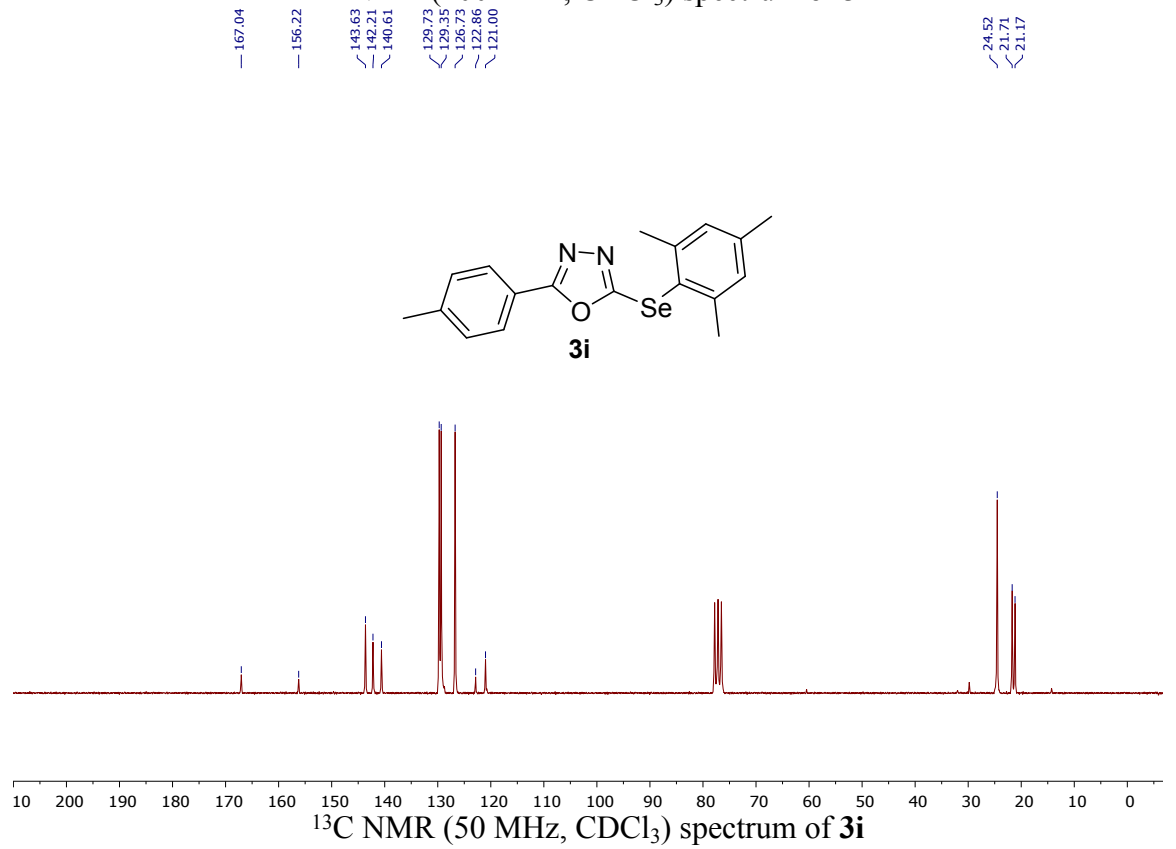


^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3h**



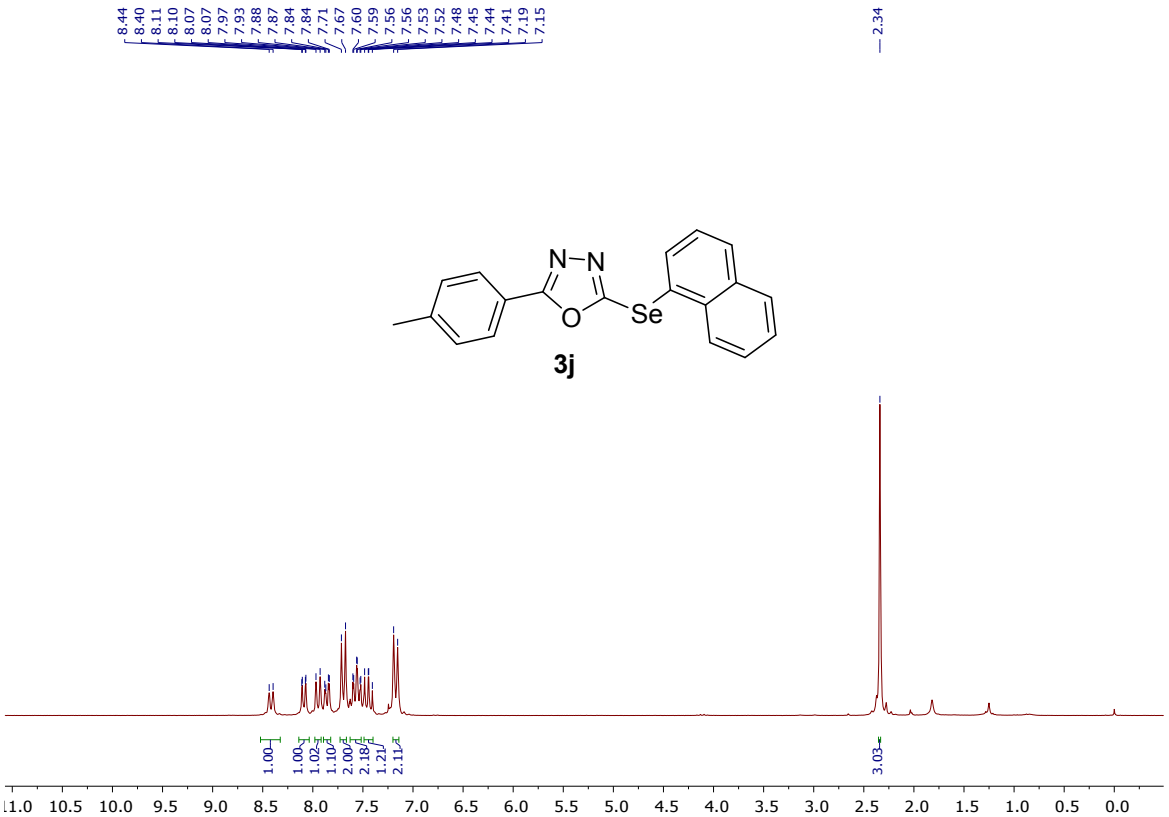
3i

^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3i**

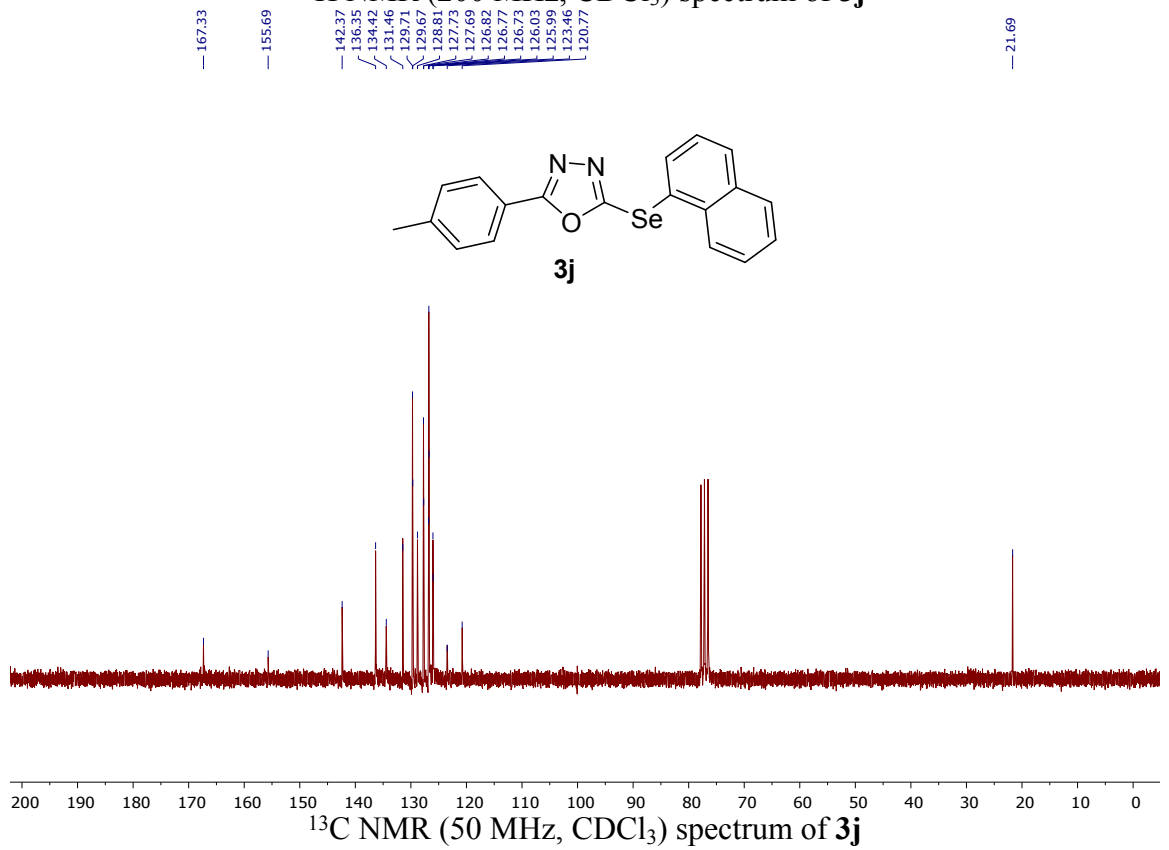


3i

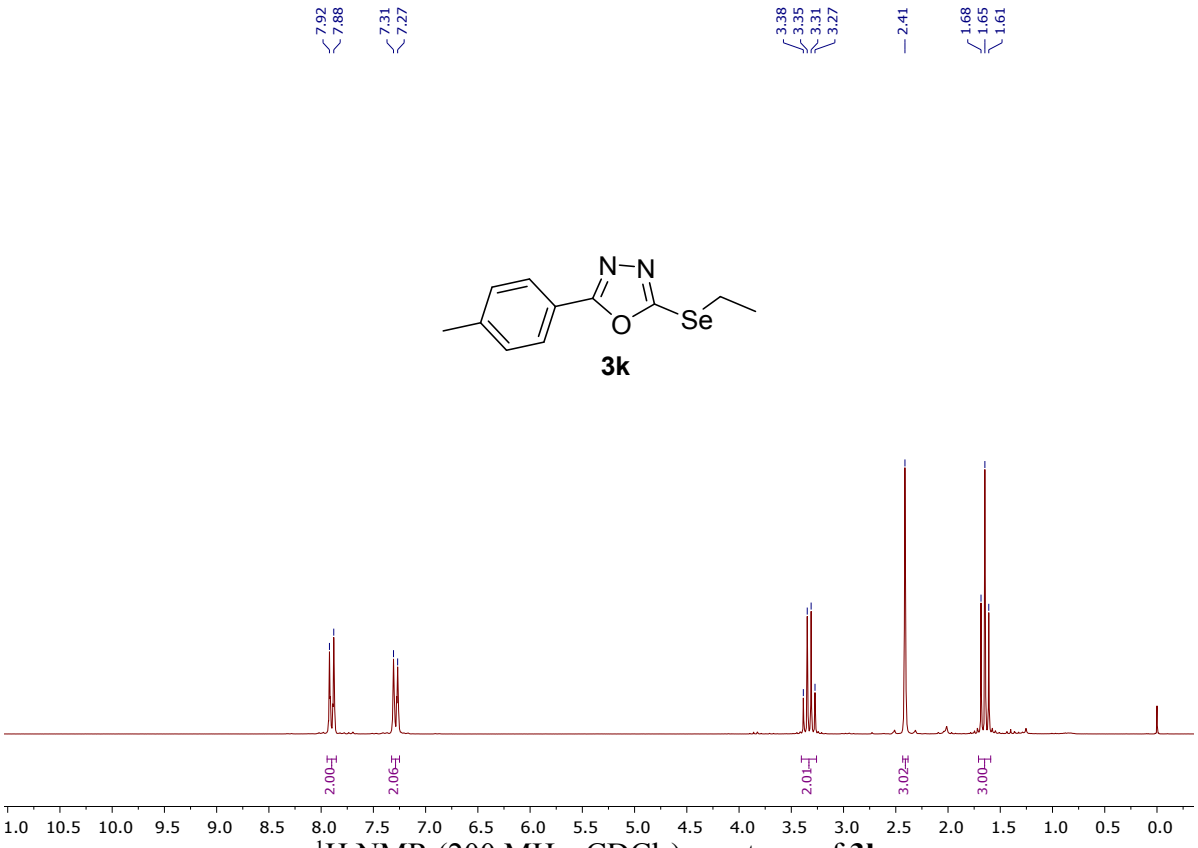
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3i**



^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3j**

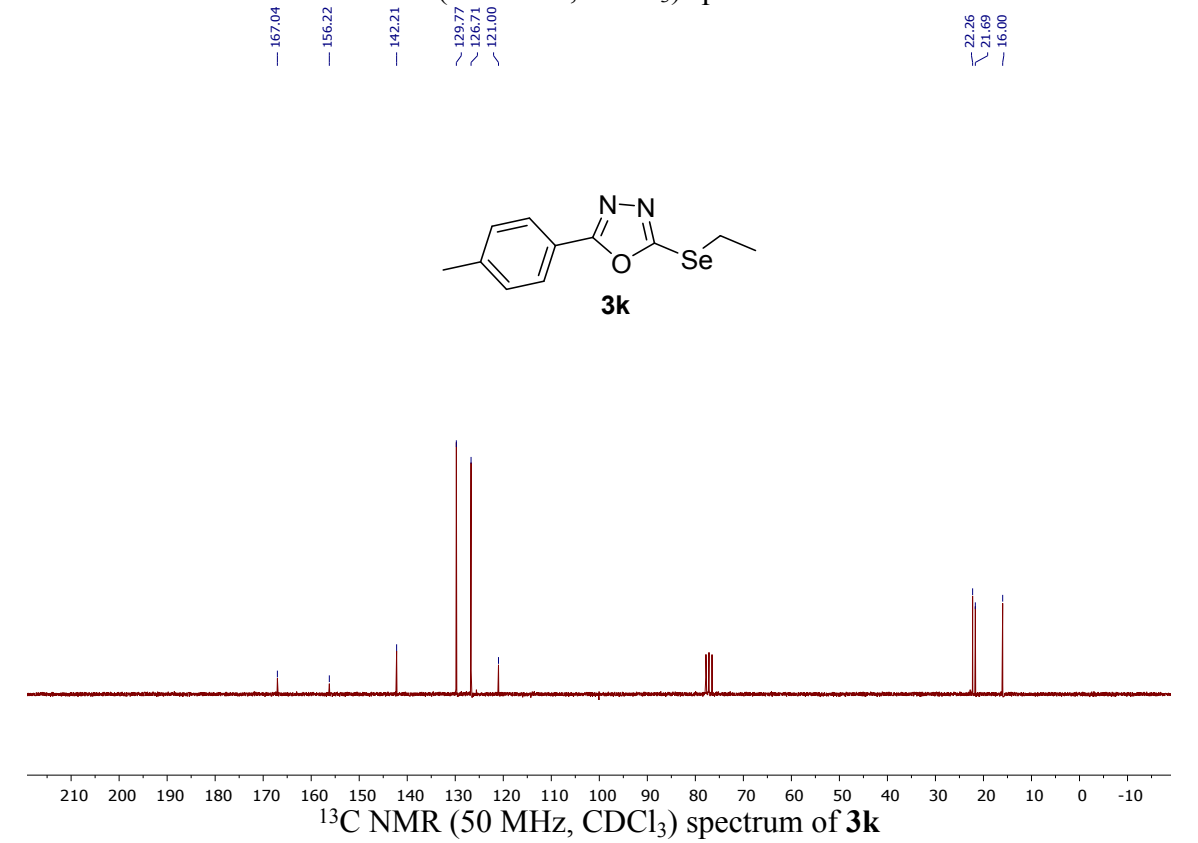


^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3j**



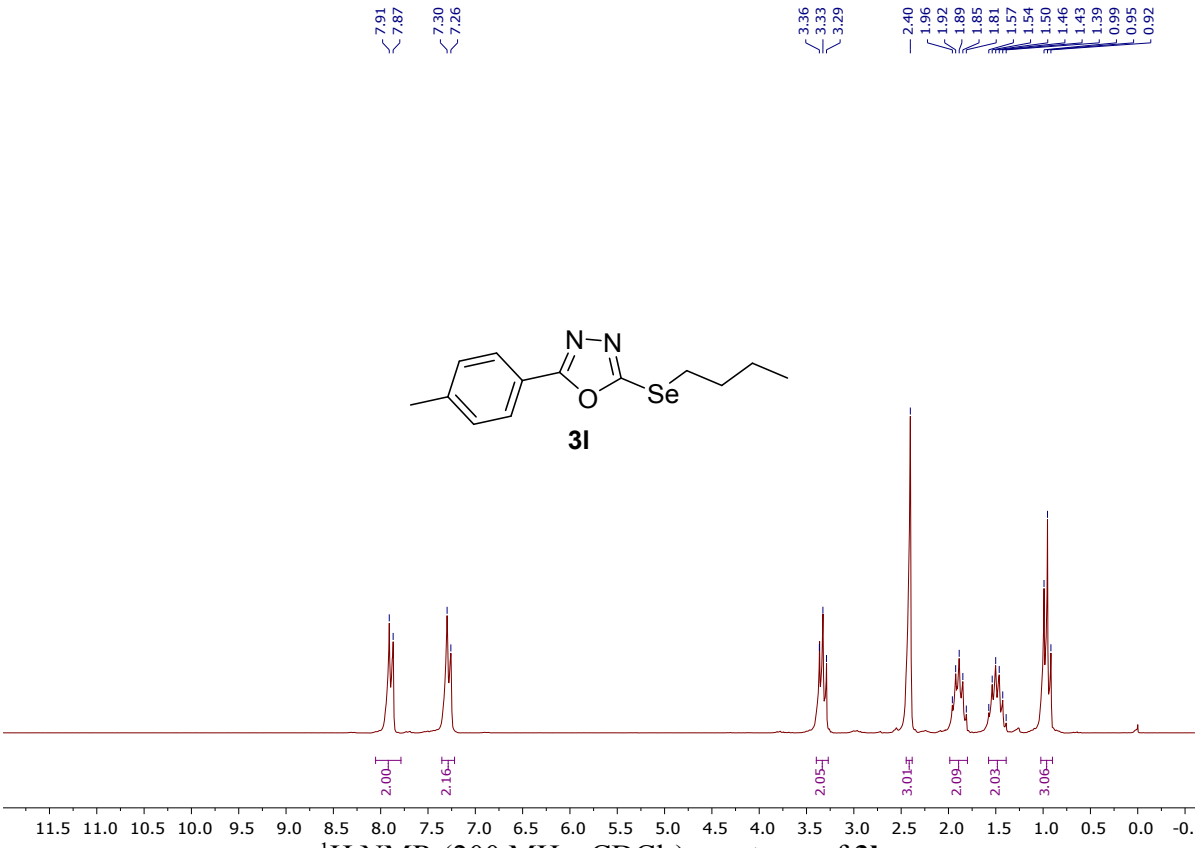
3k

^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3k**

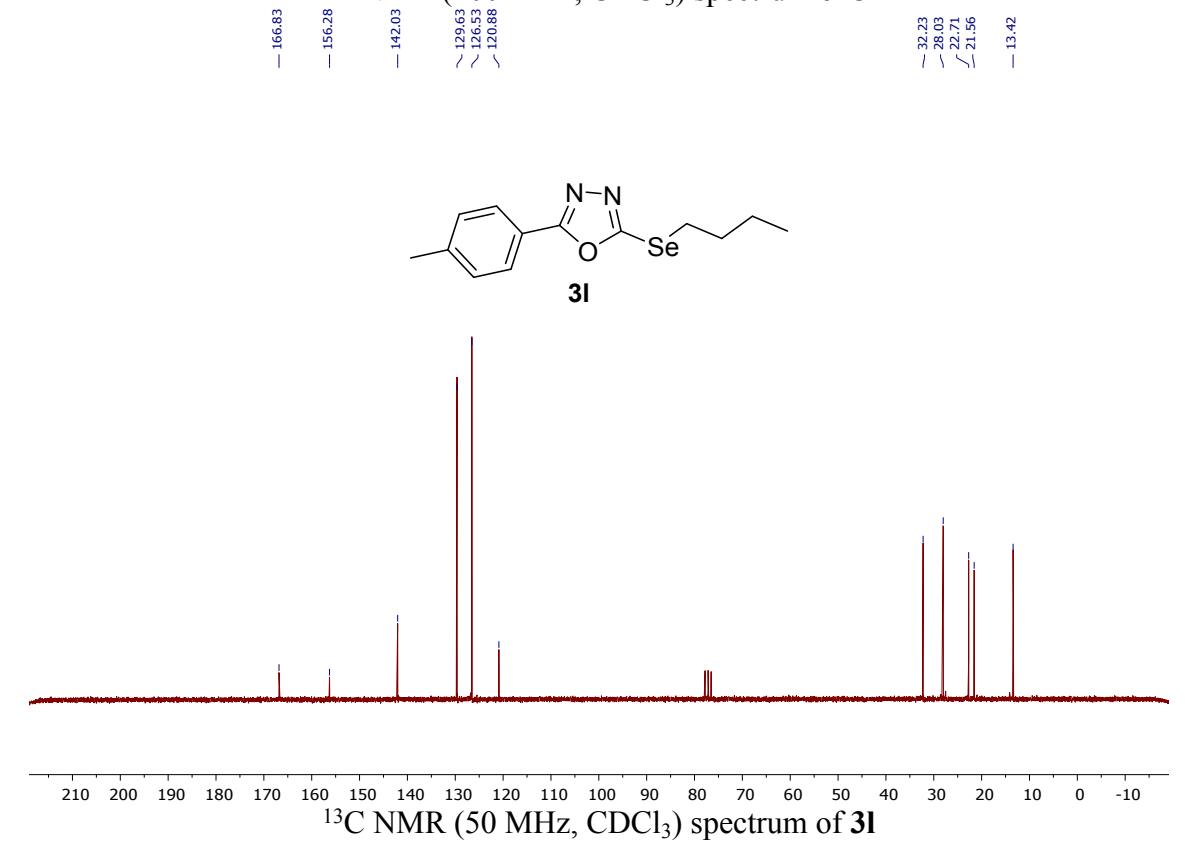


3k

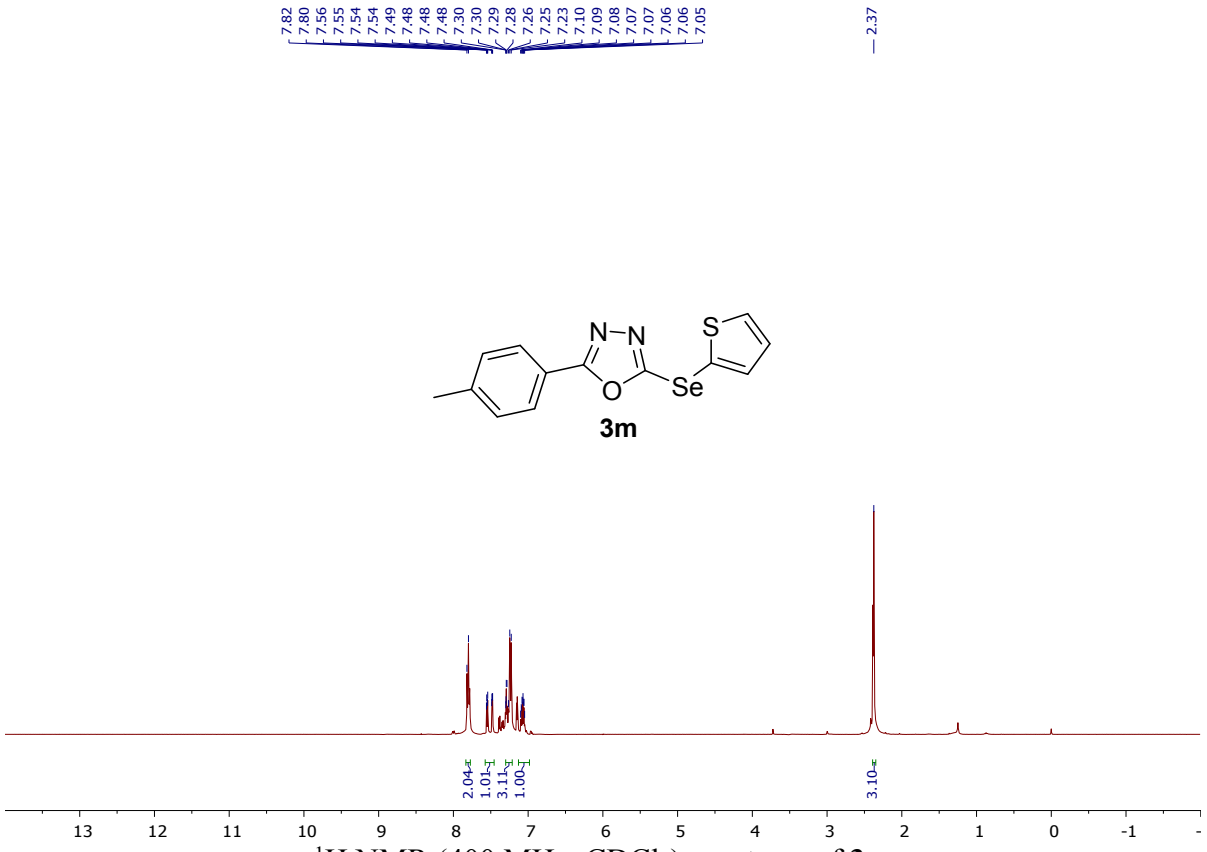
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3k**



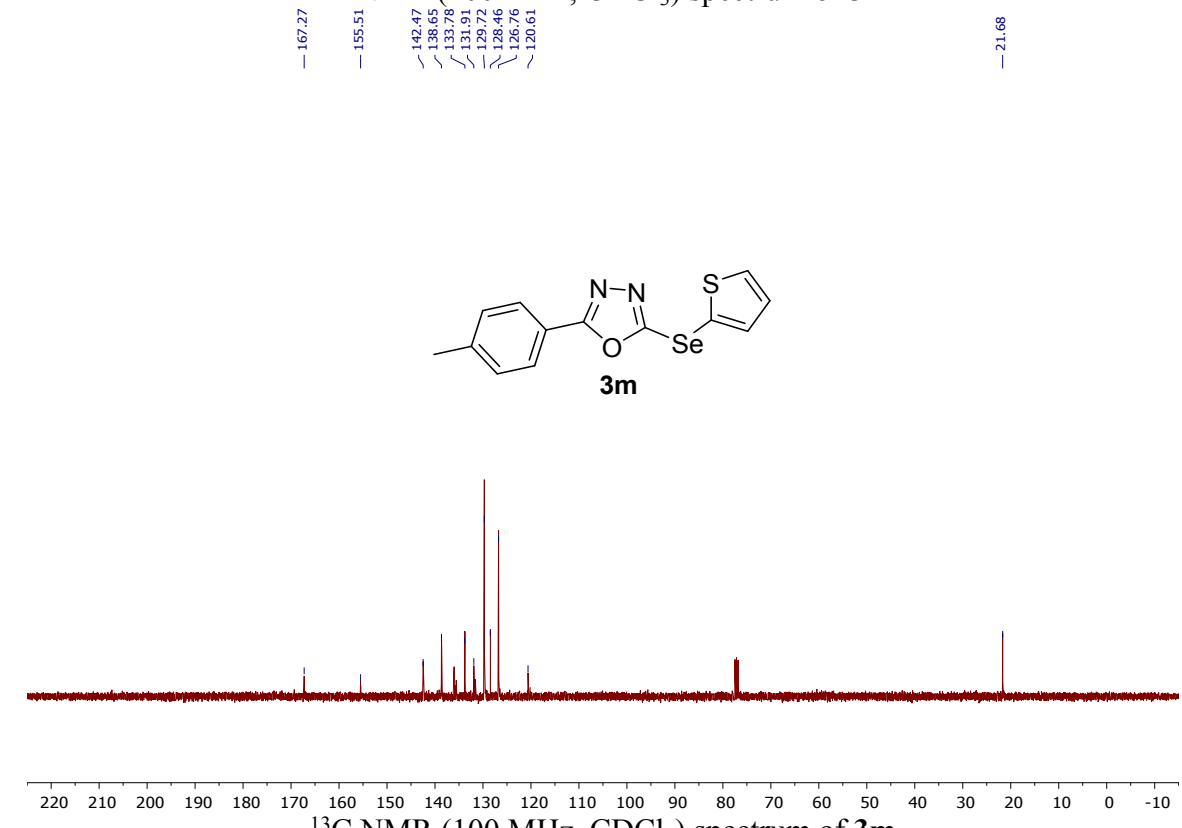
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3l**



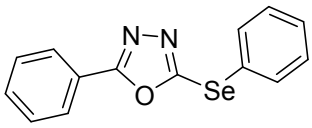
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3l**



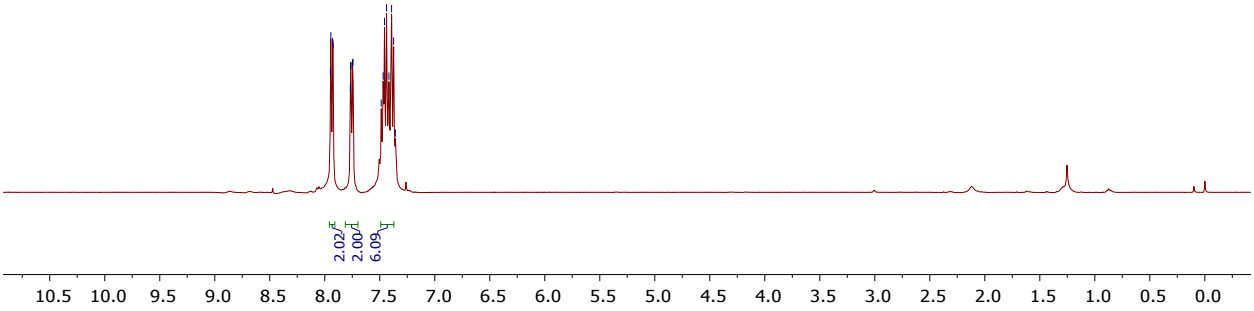
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3m**



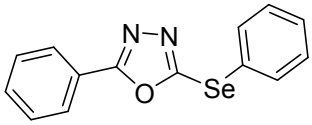
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3m**



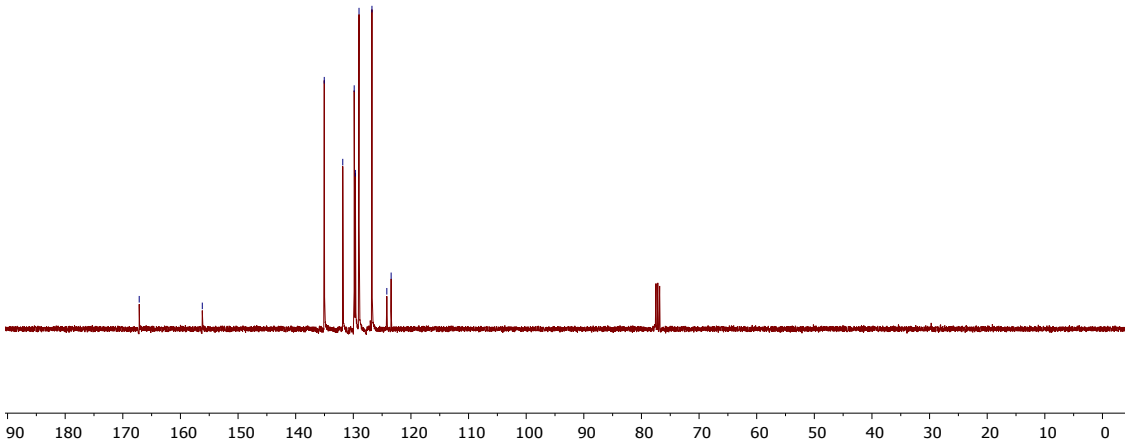
3n



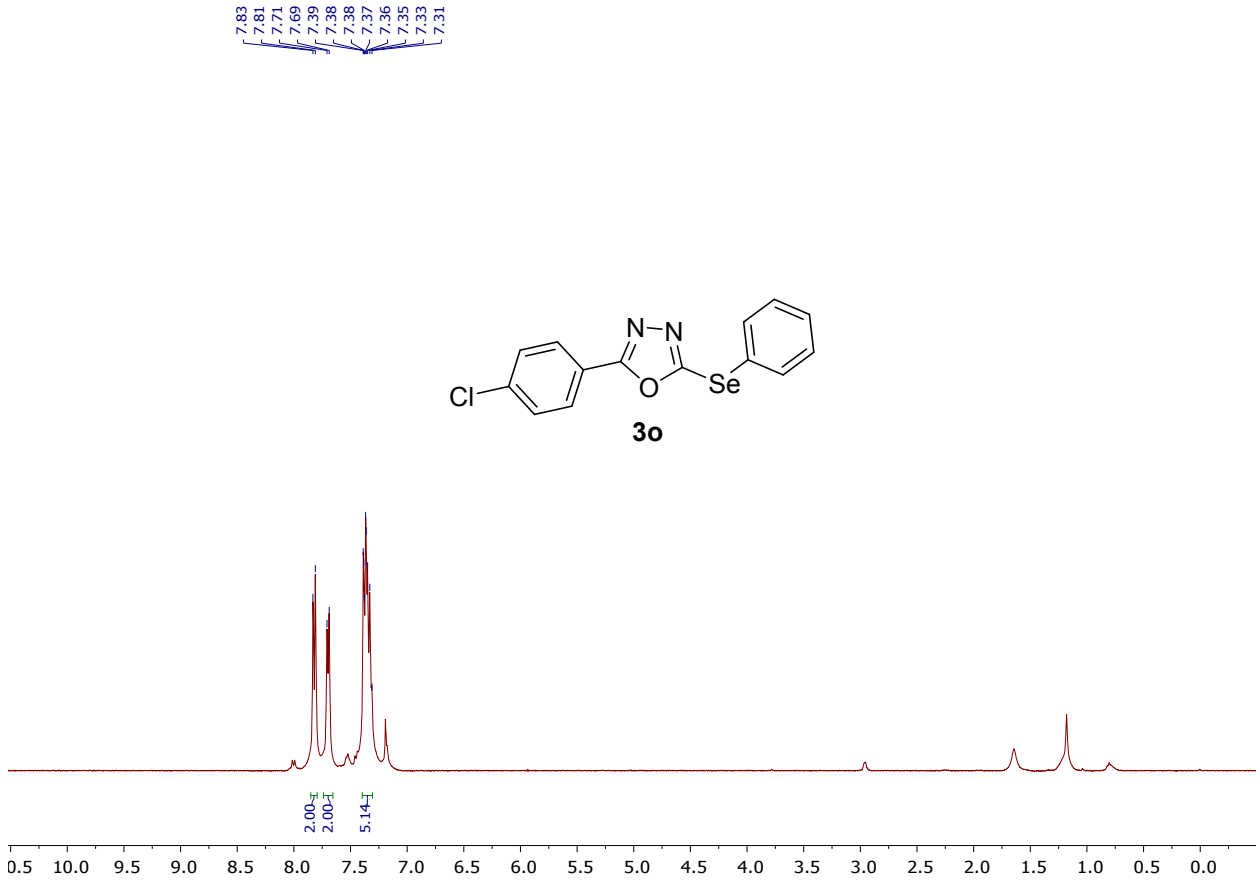
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3n**



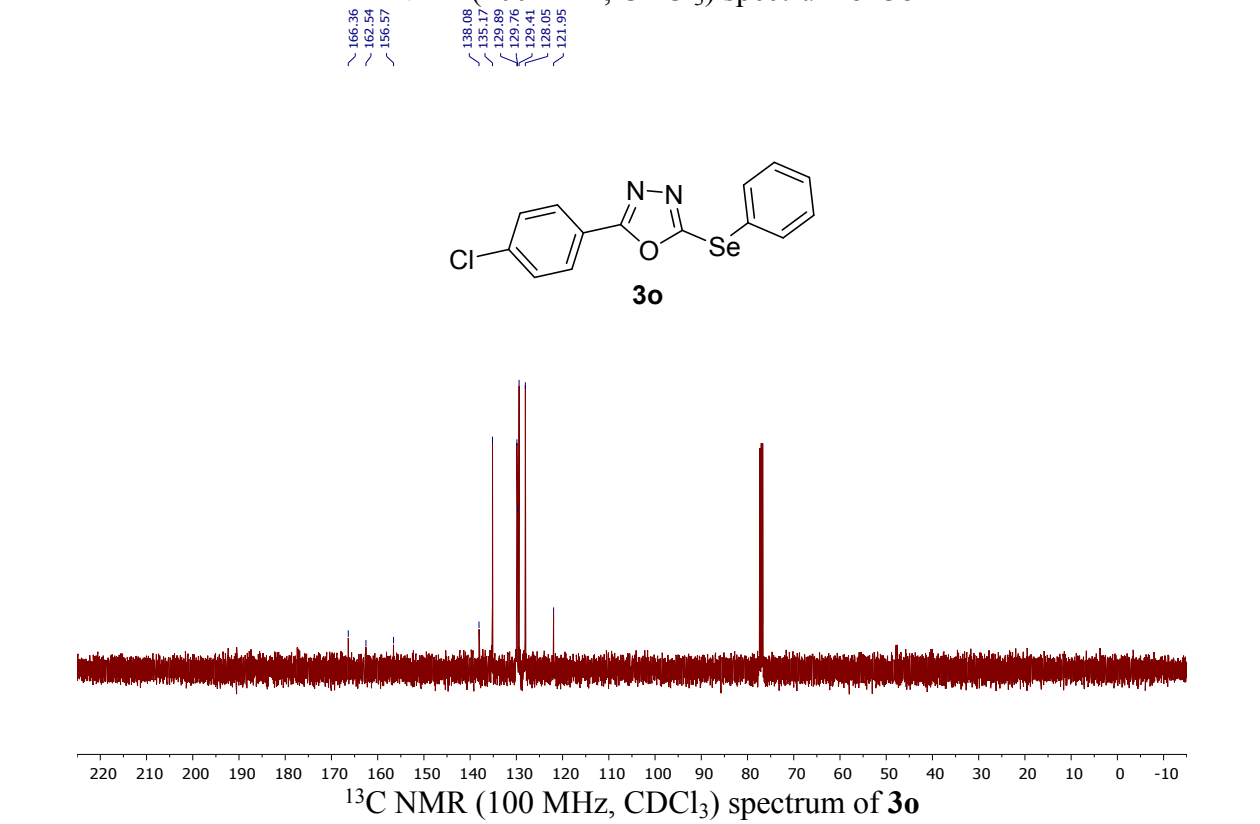
3n



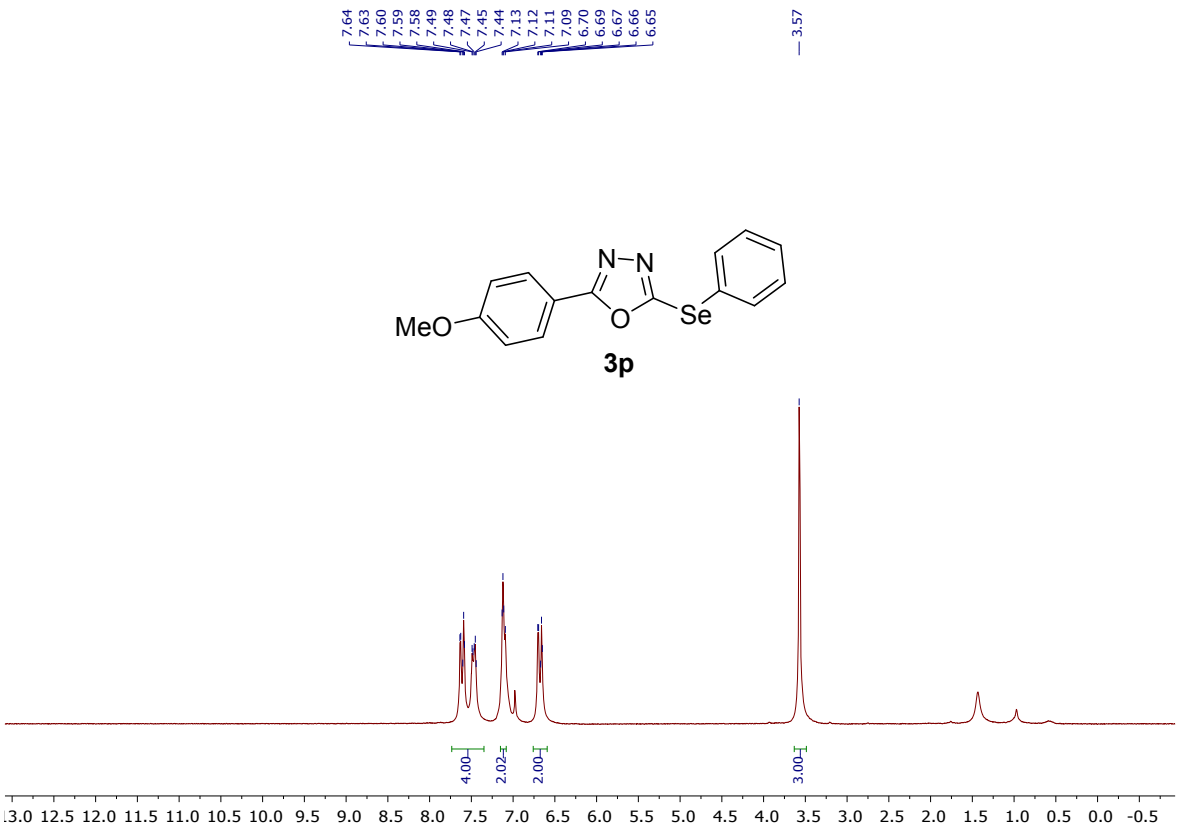
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3n**



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3o**

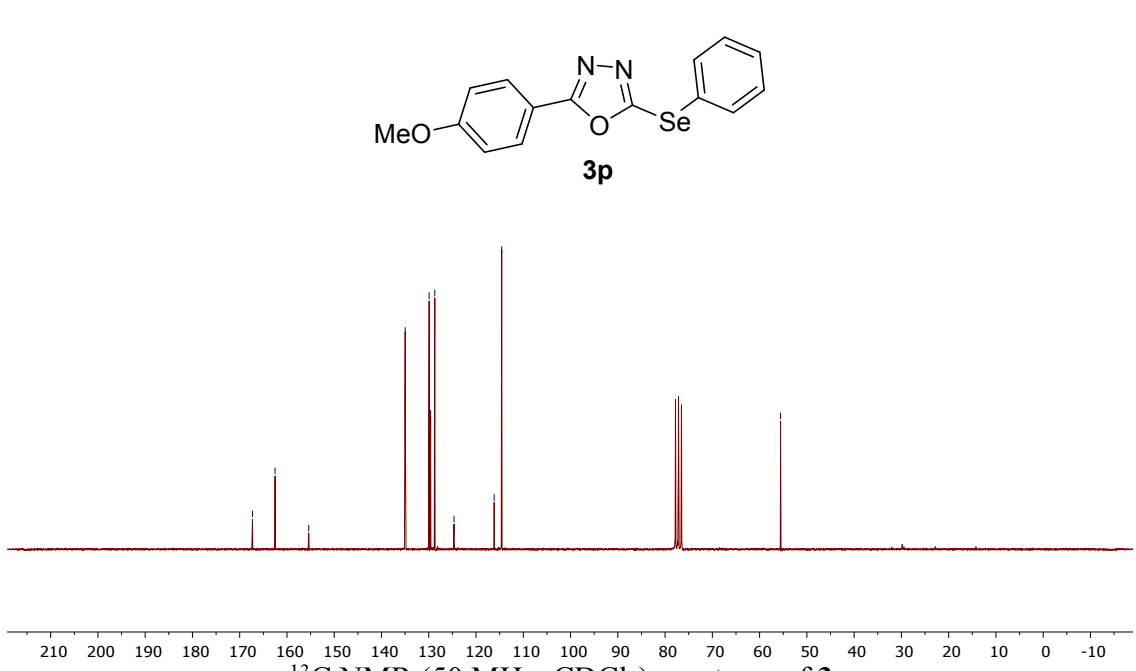


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3o**



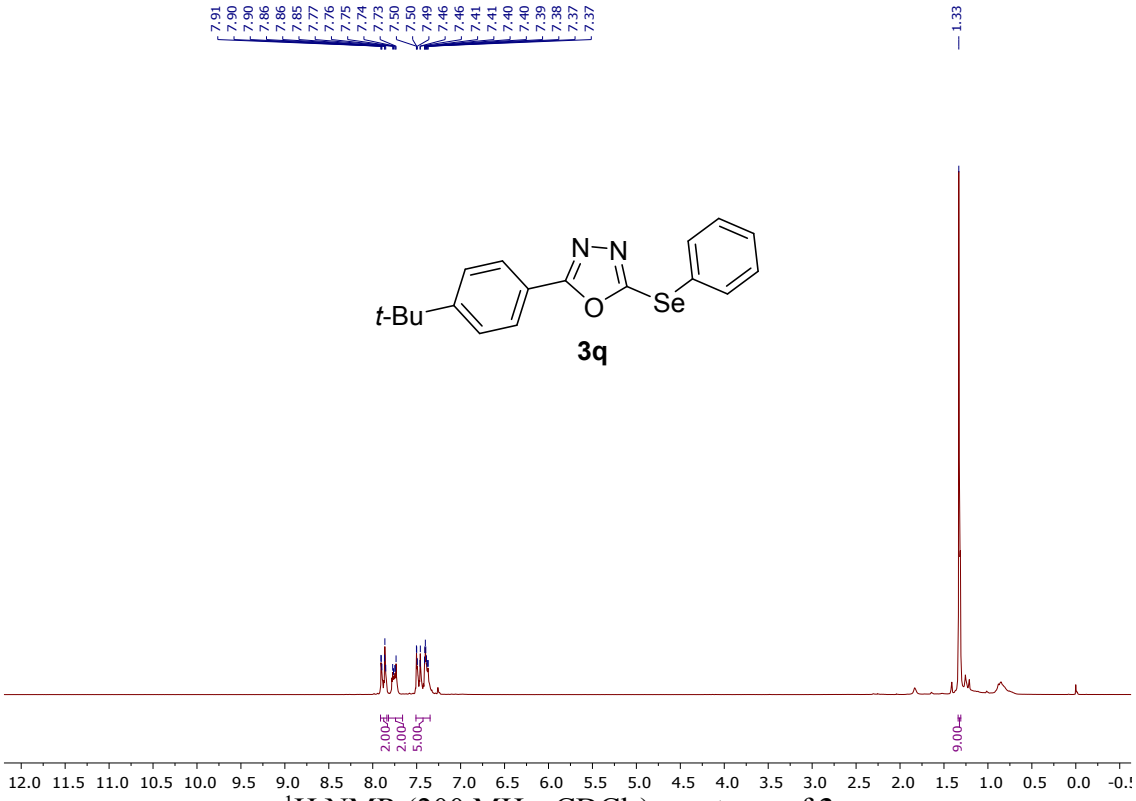
3p

^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3p**

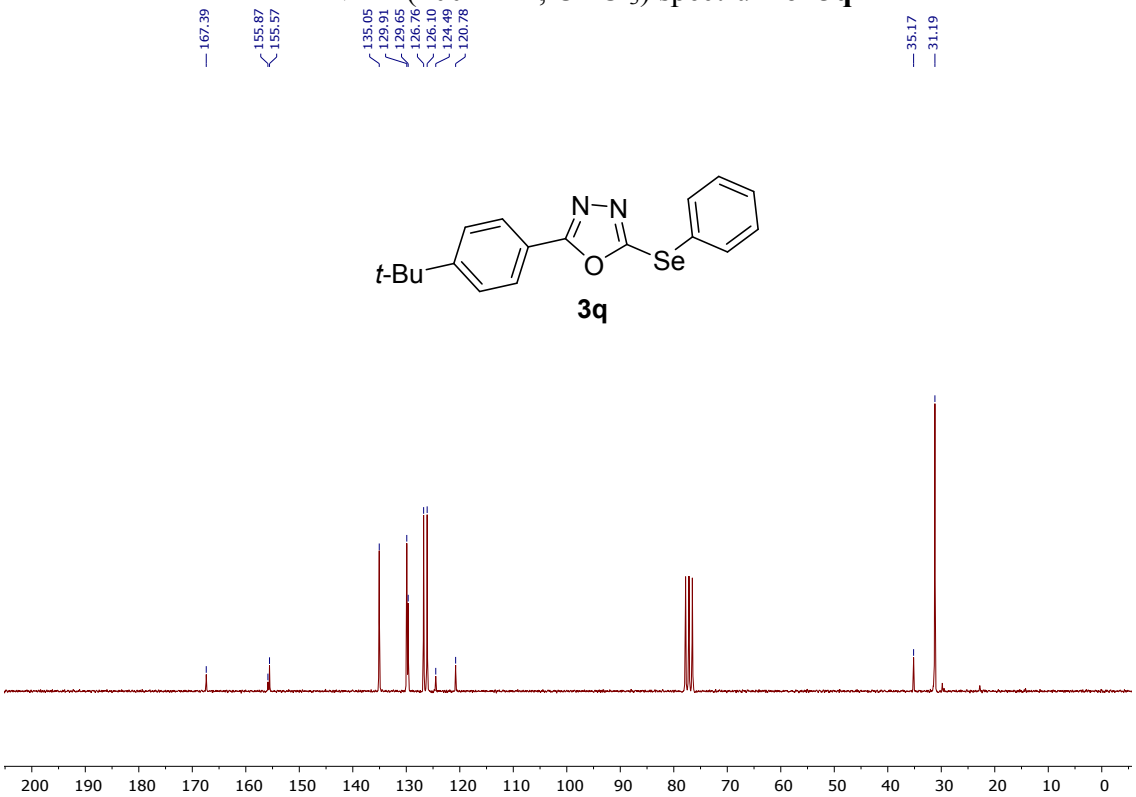


3p

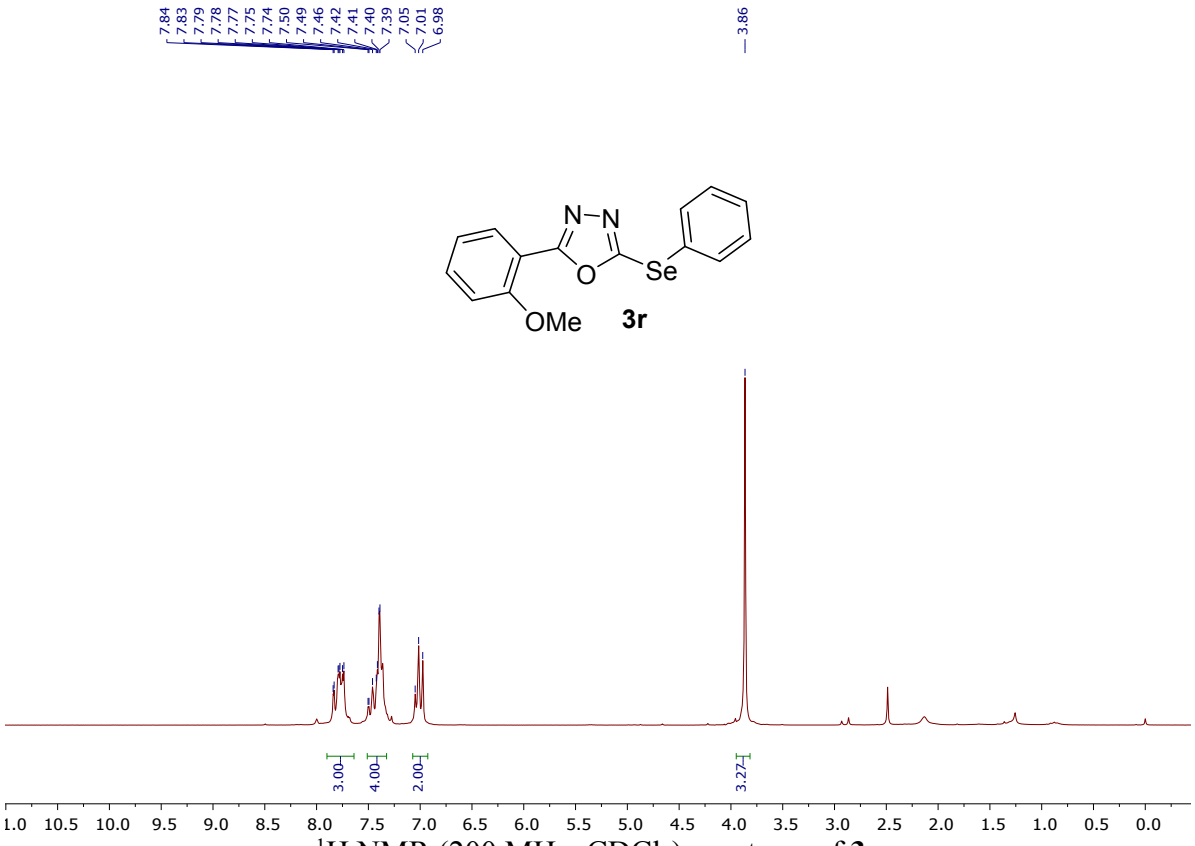
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3p**



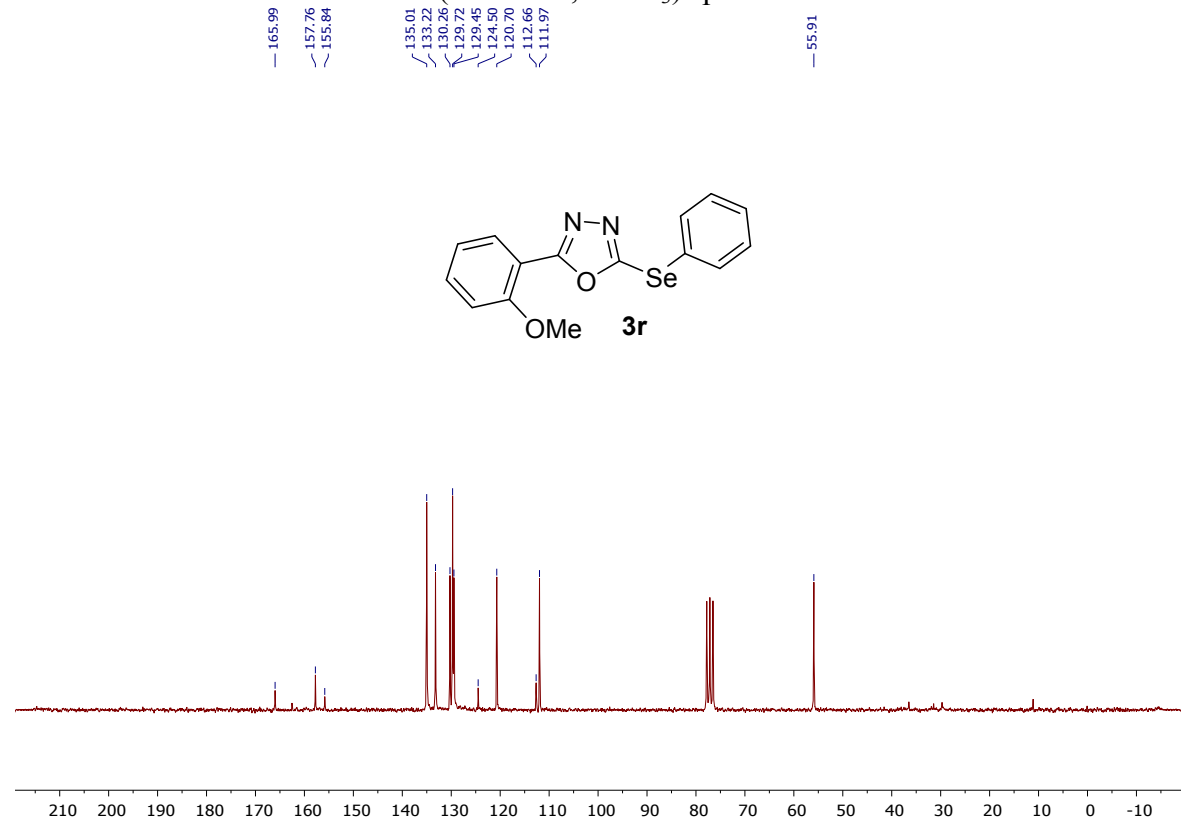
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3q**



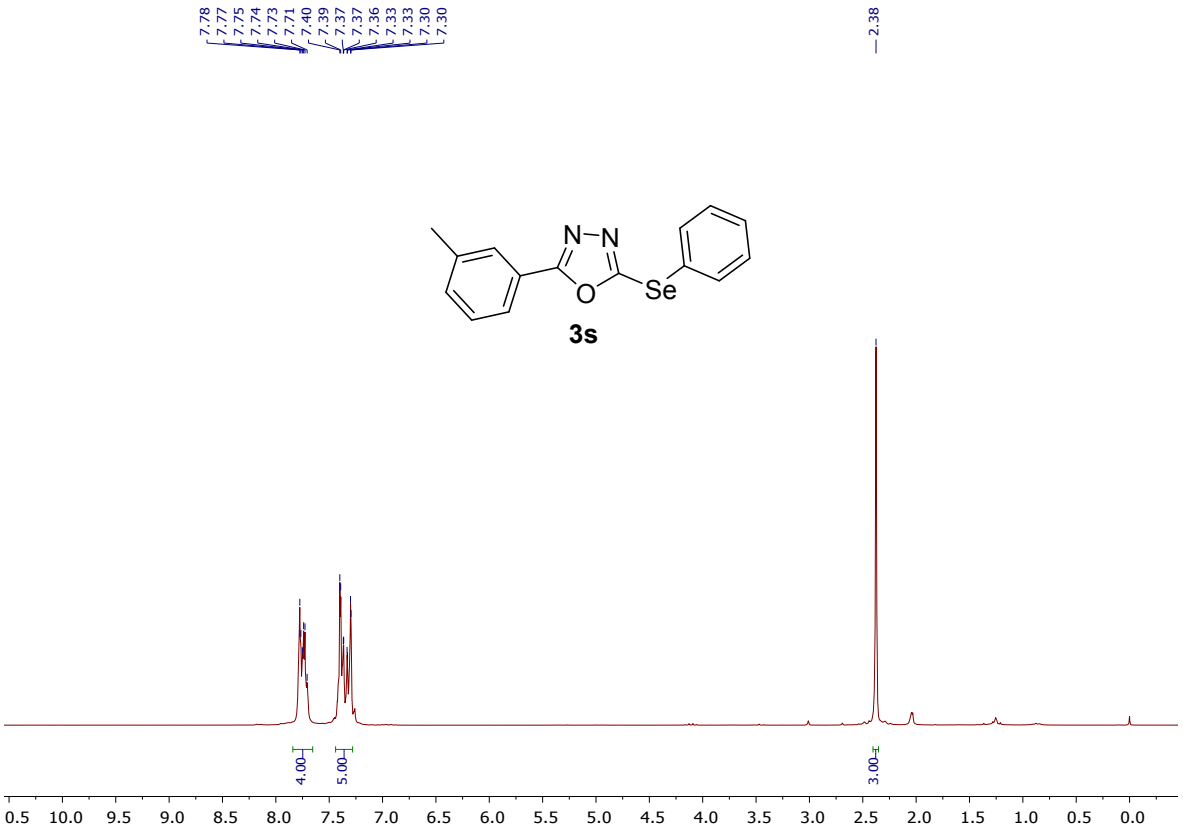
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3q**



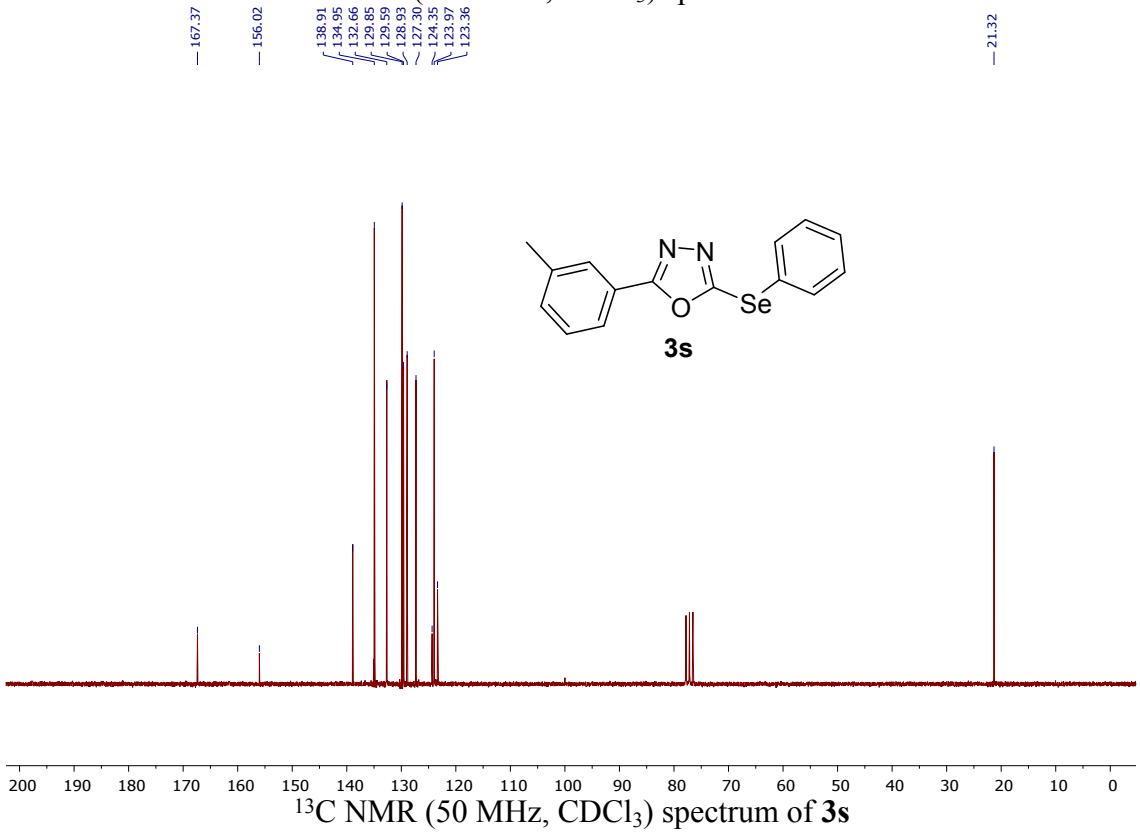
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3r**



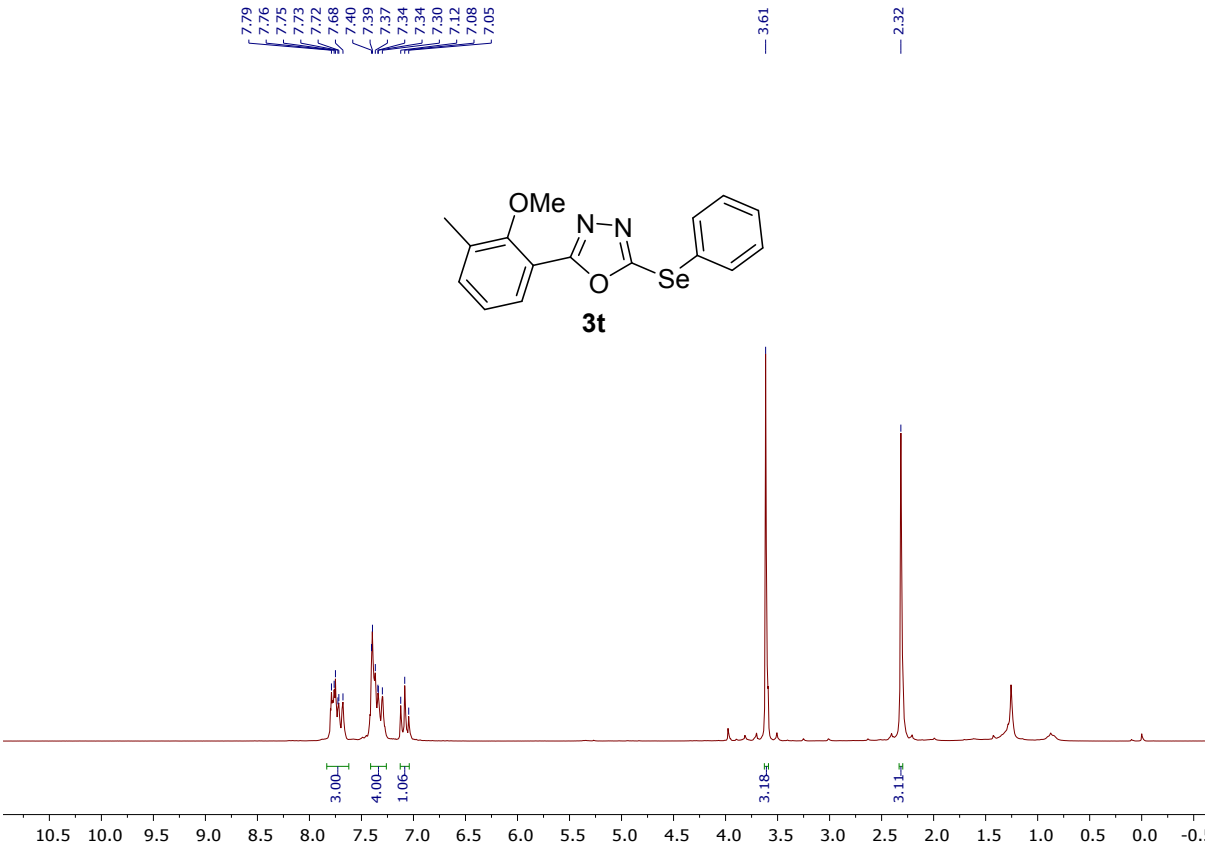
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3r**



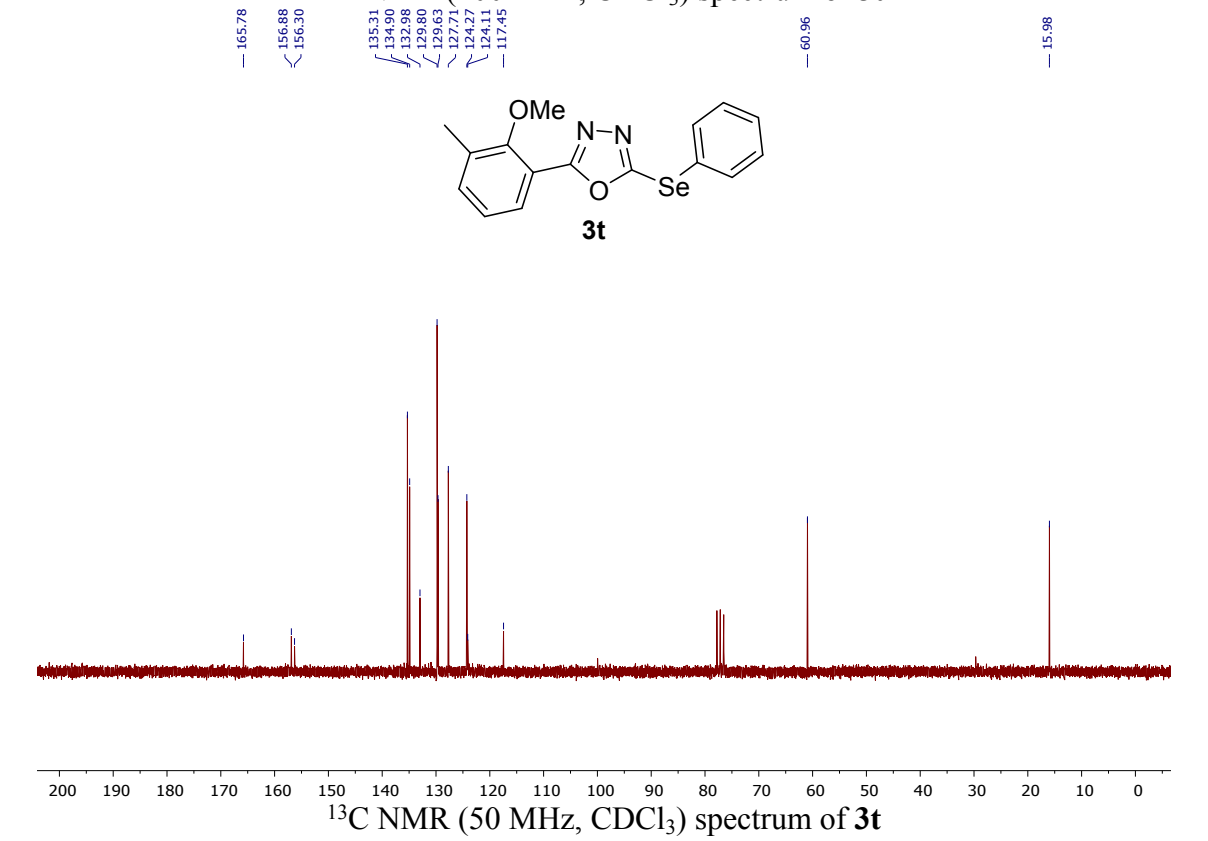
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3s**



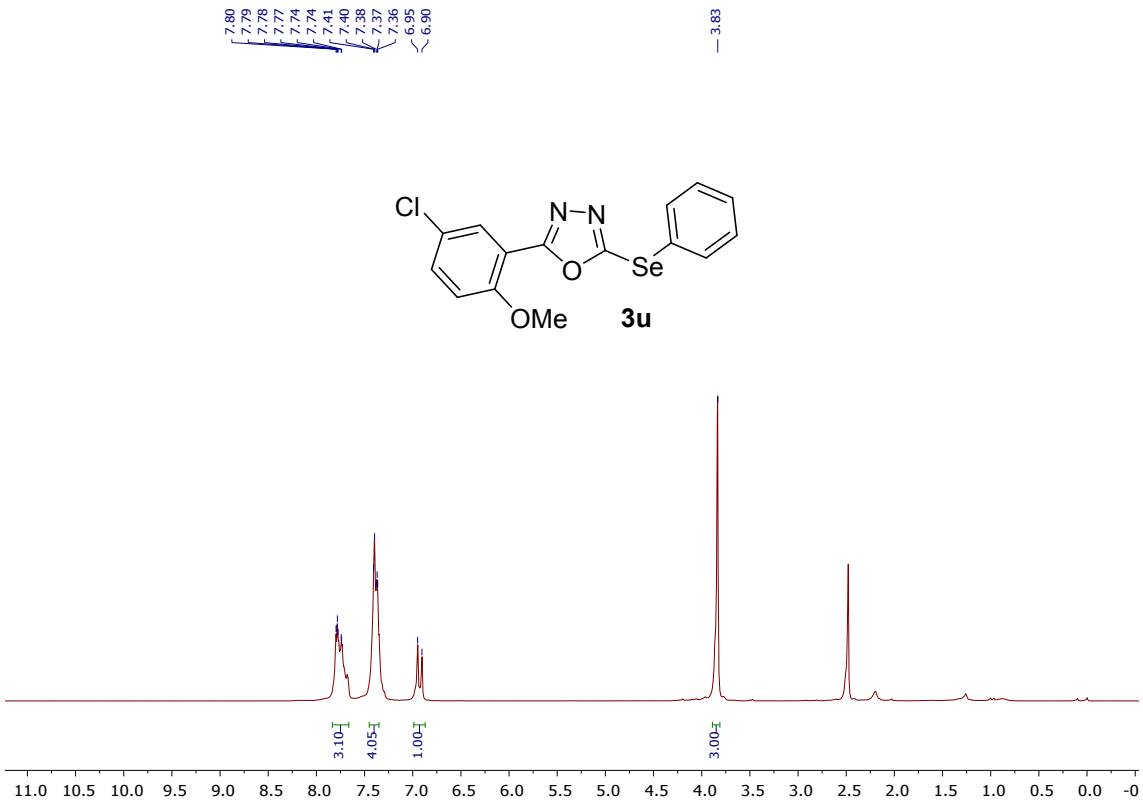
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3s**



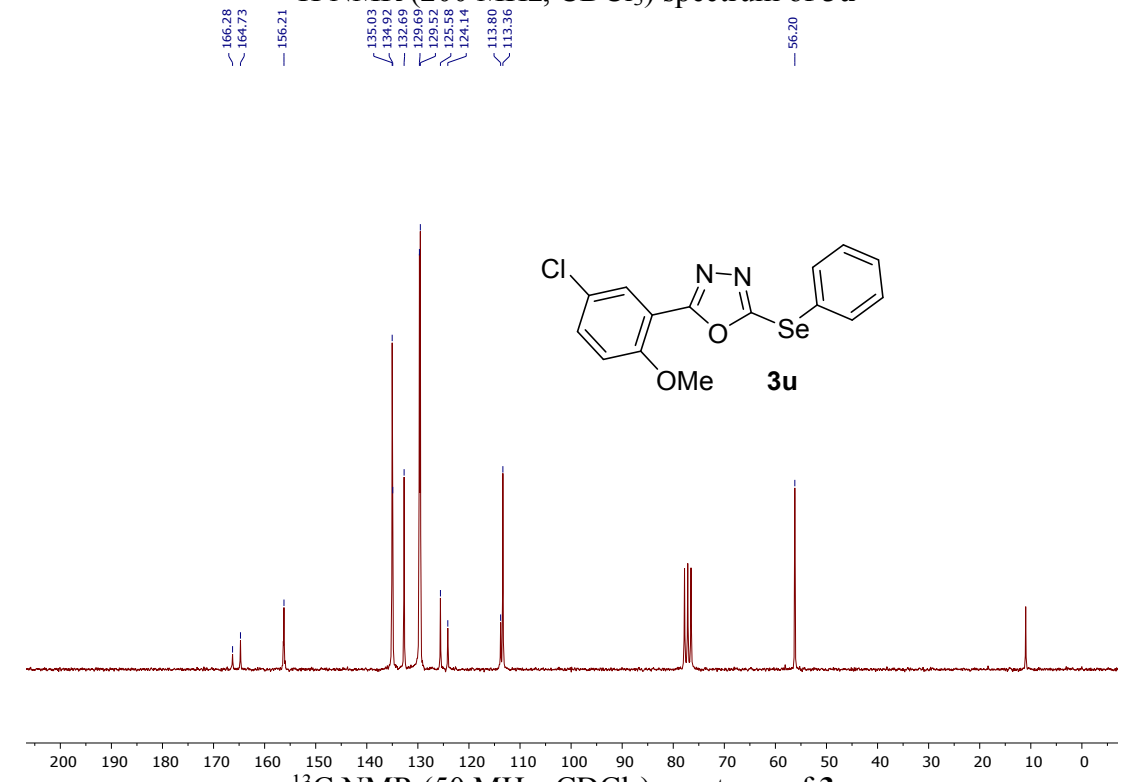
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3t**



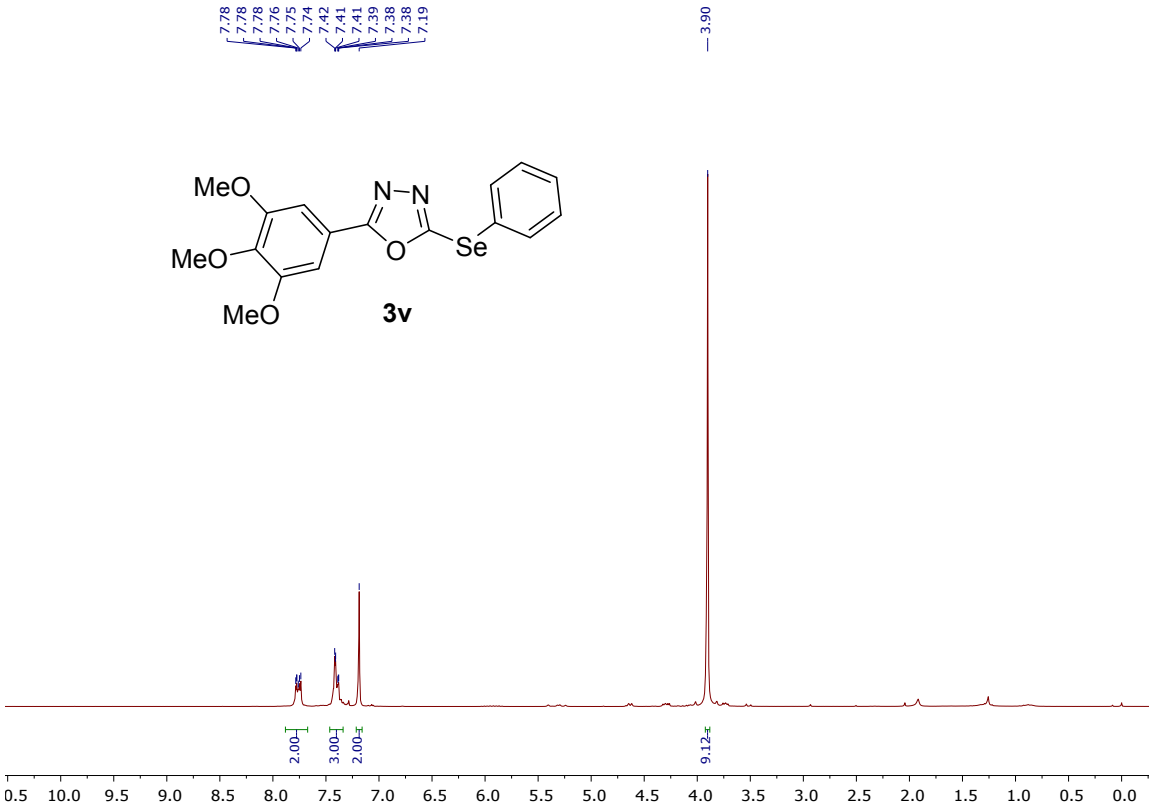
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3t**



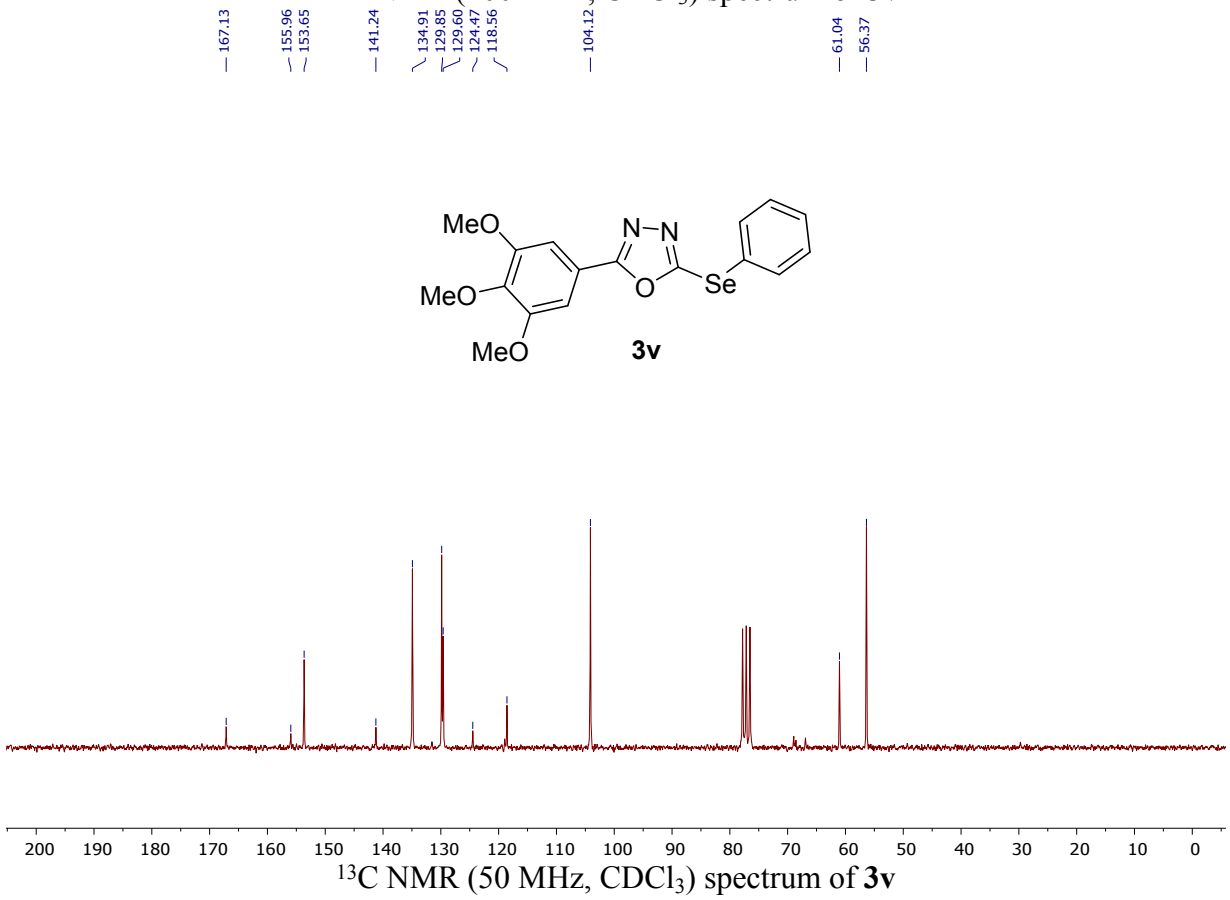
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3u**



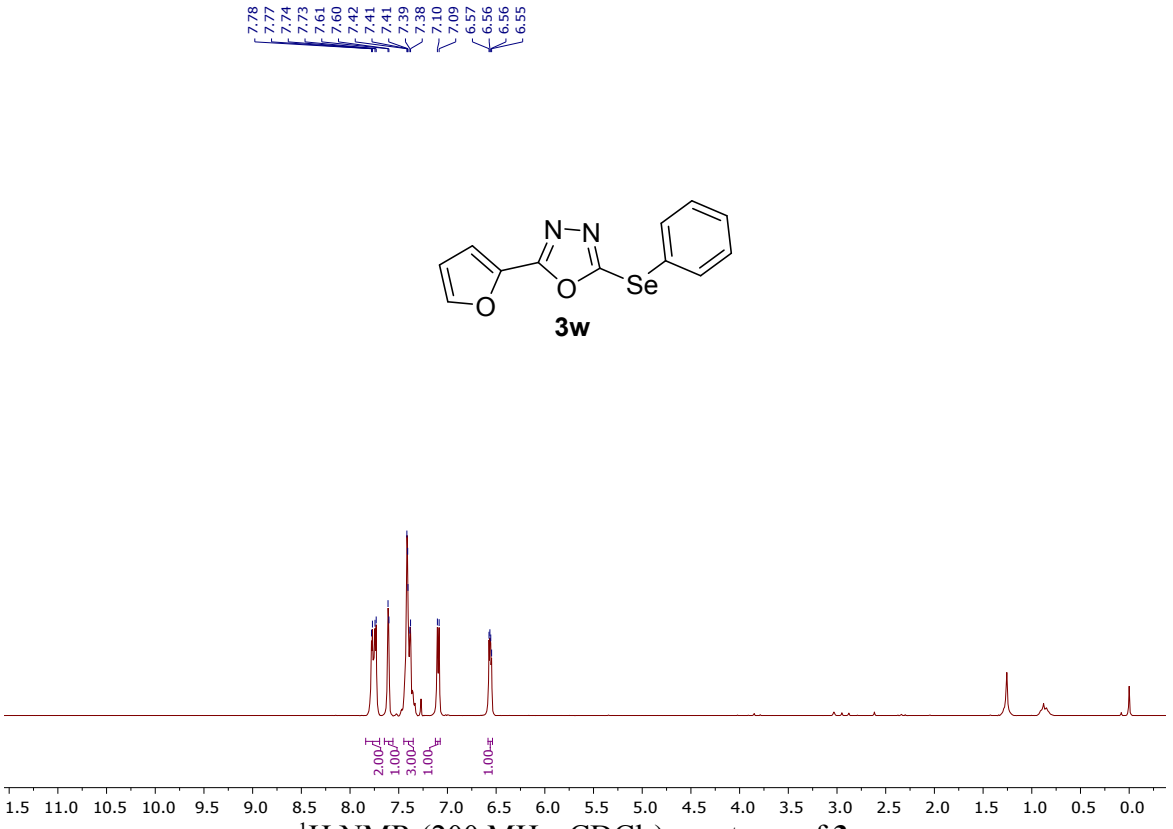
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3u**



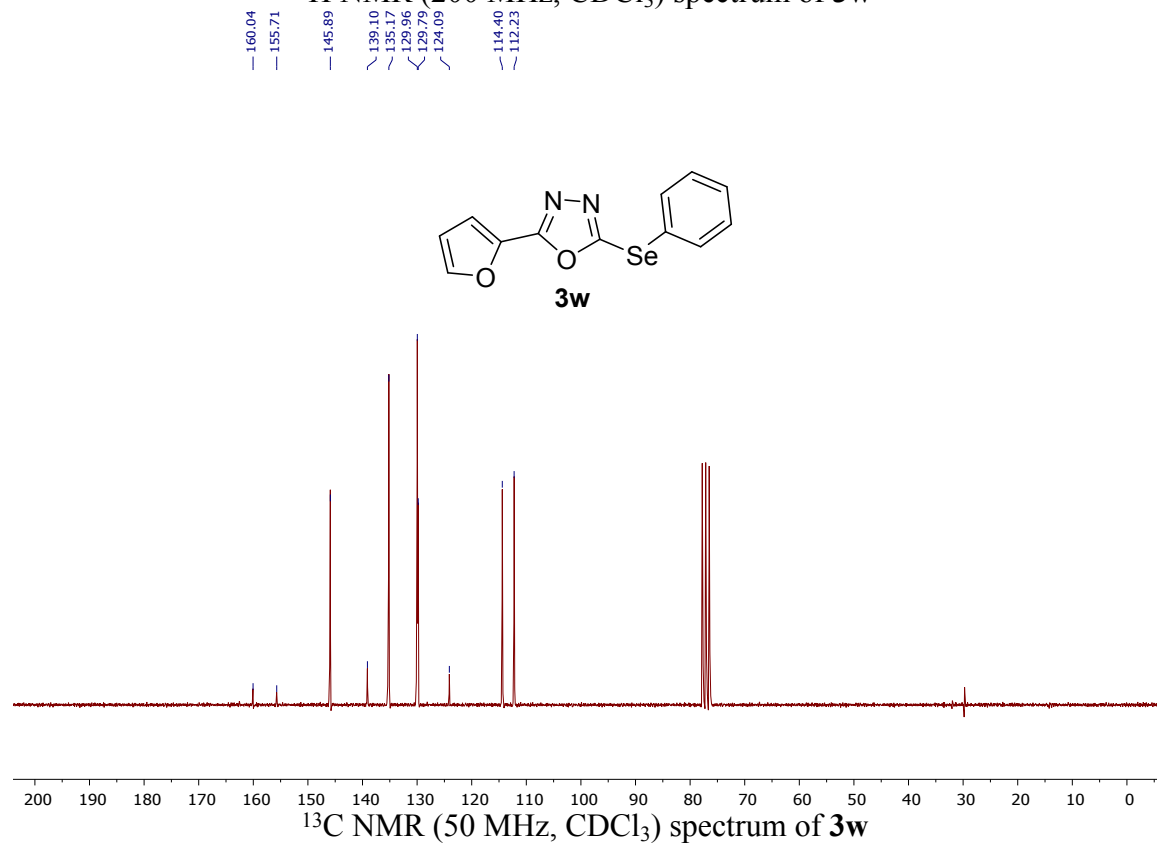
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3v**



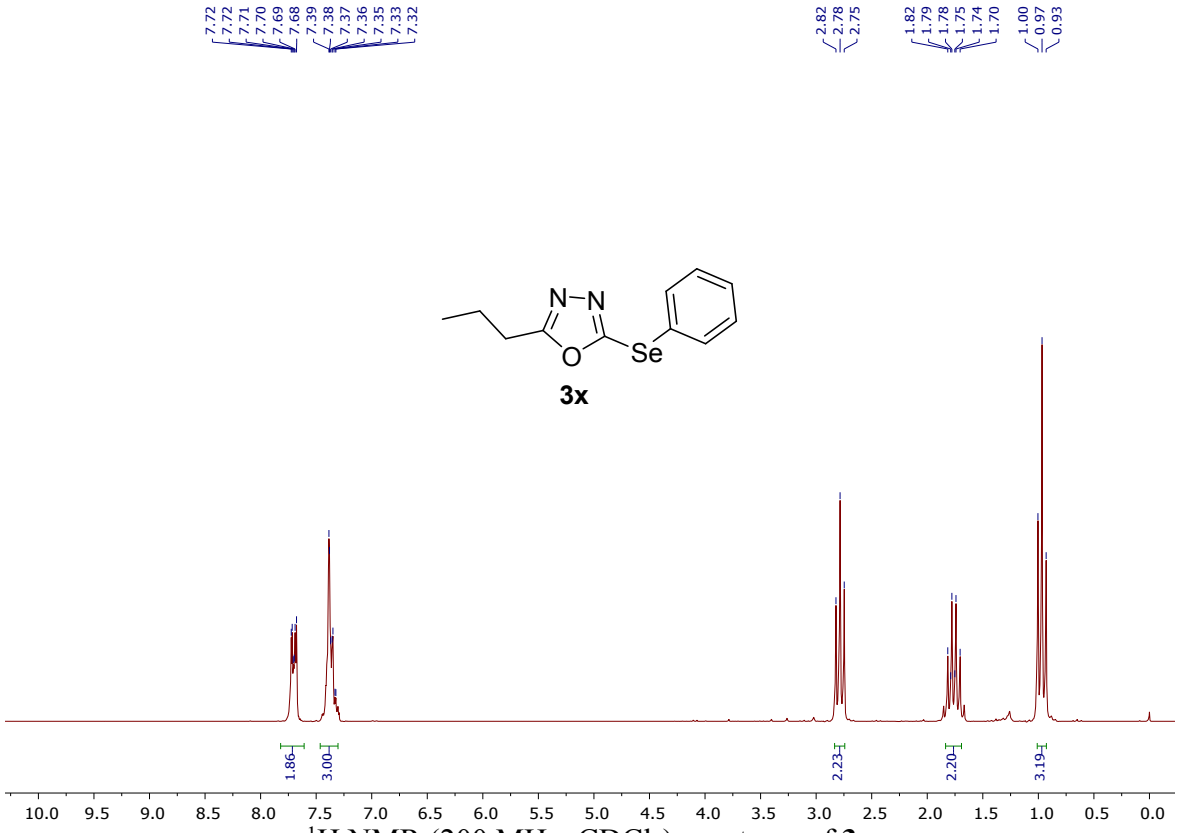
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3v**



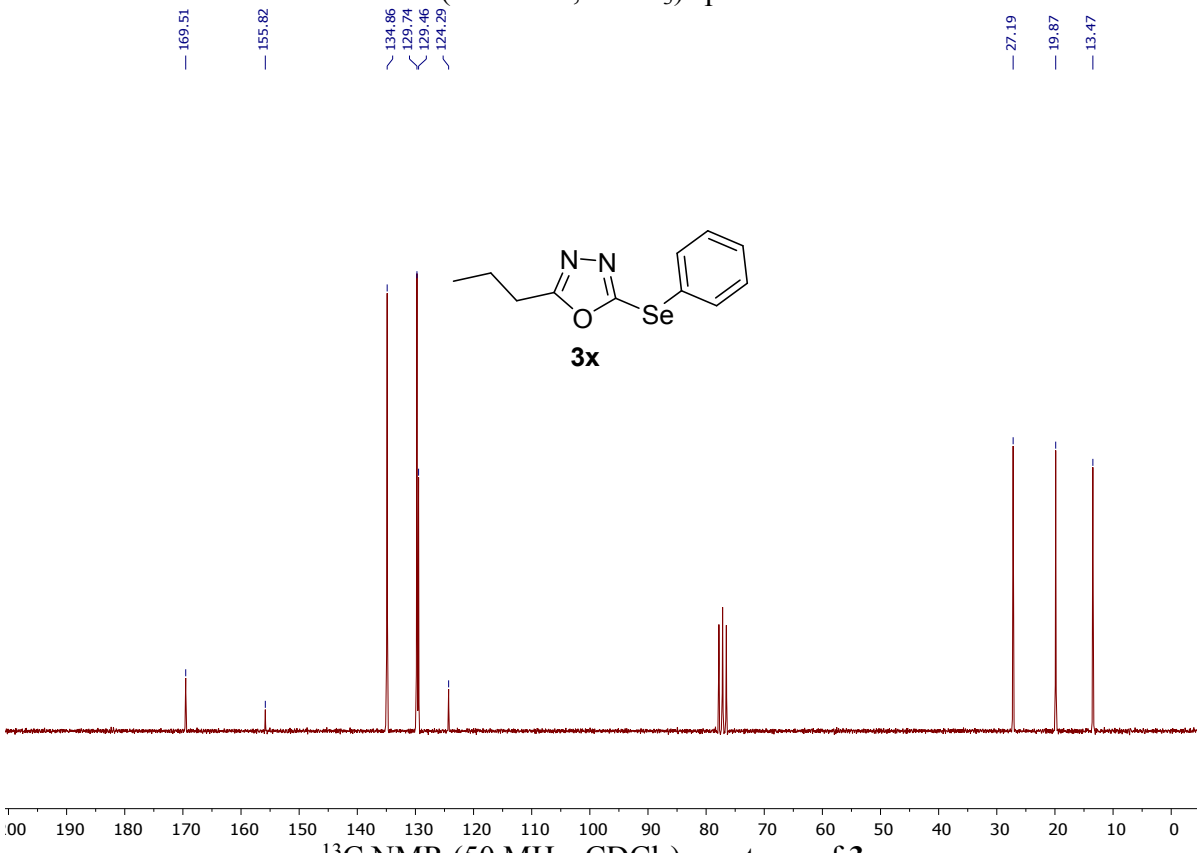
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3w**



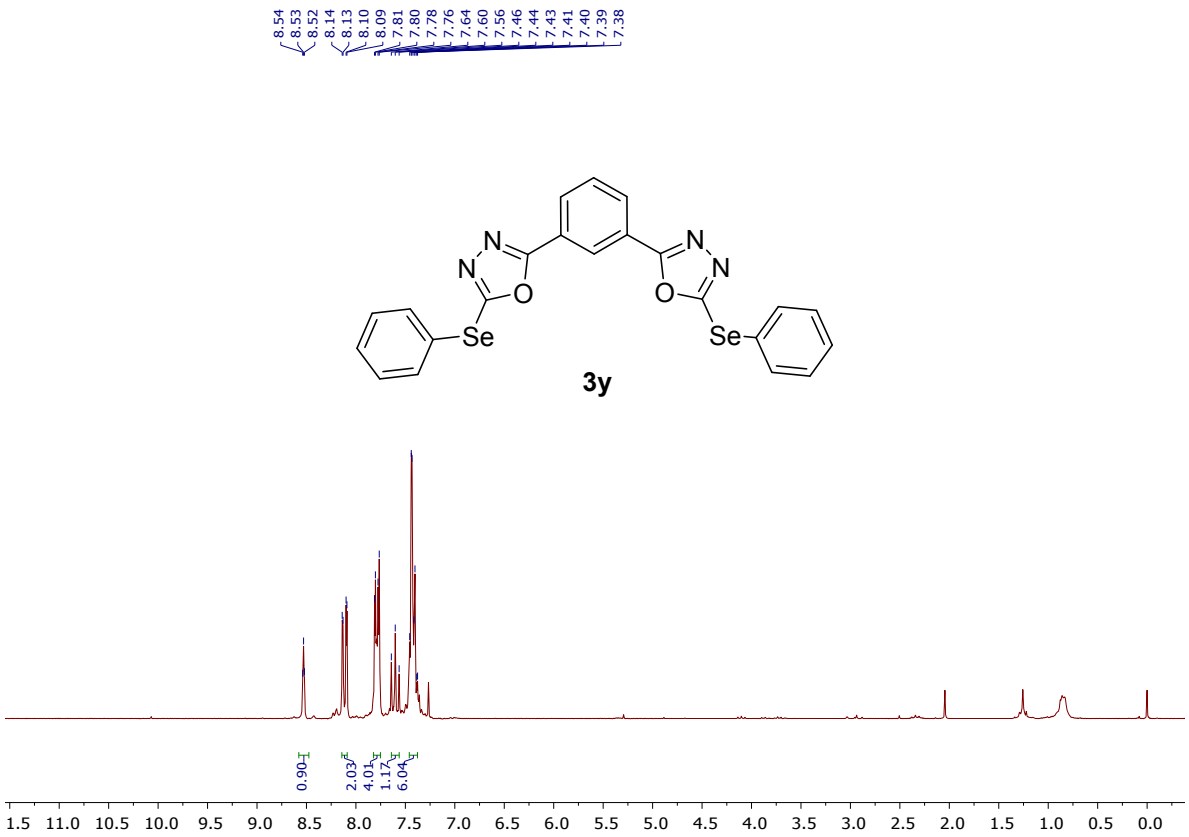
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3w**



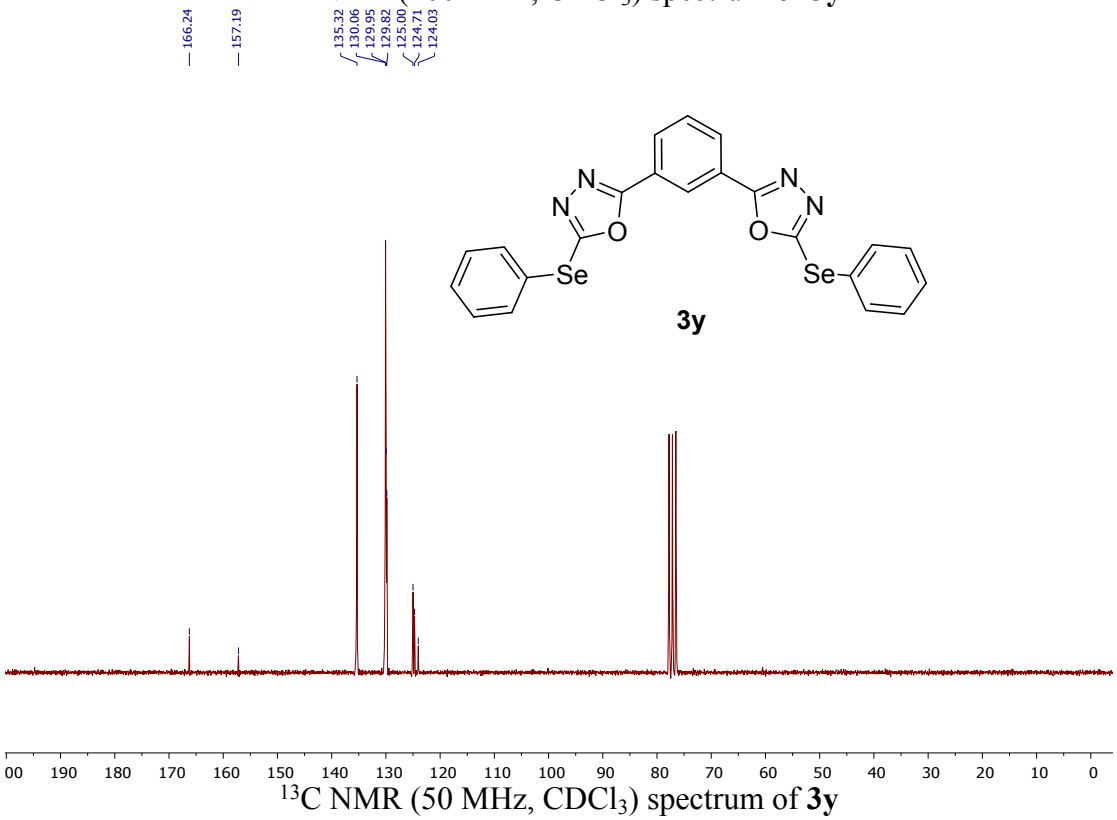
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3x**



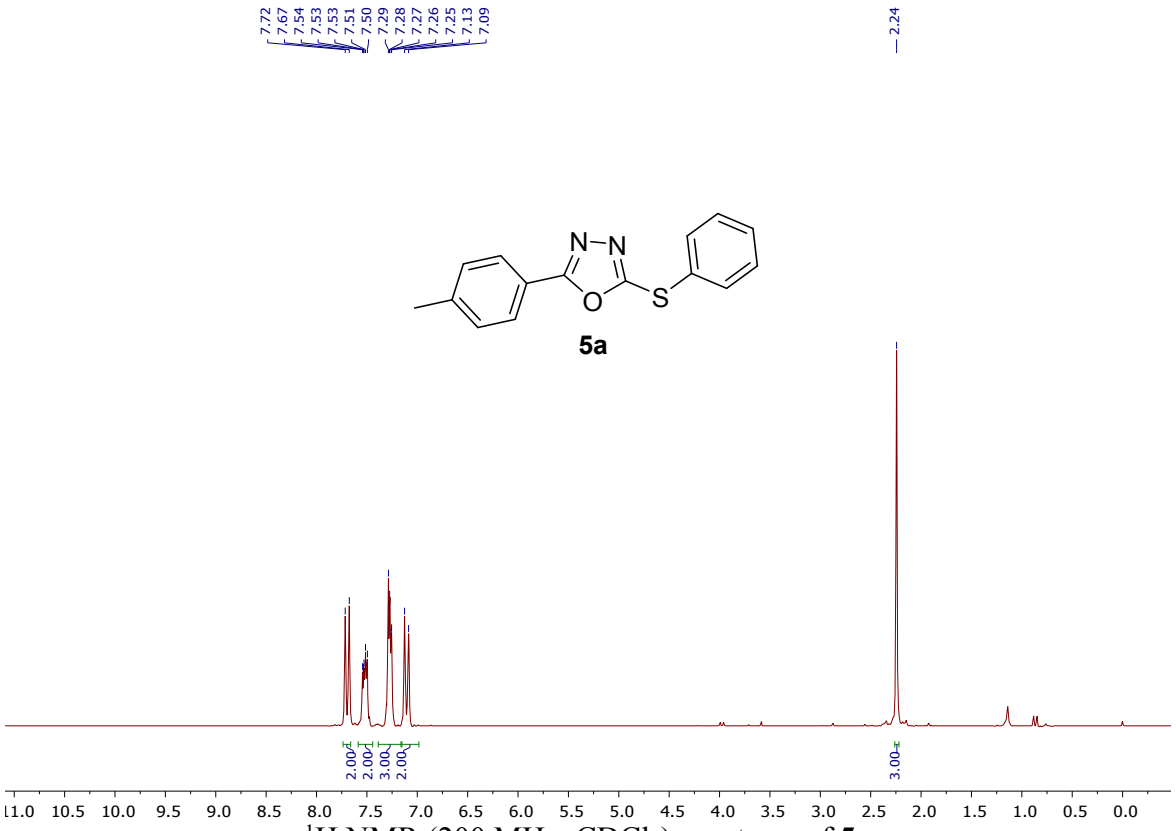
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3x**



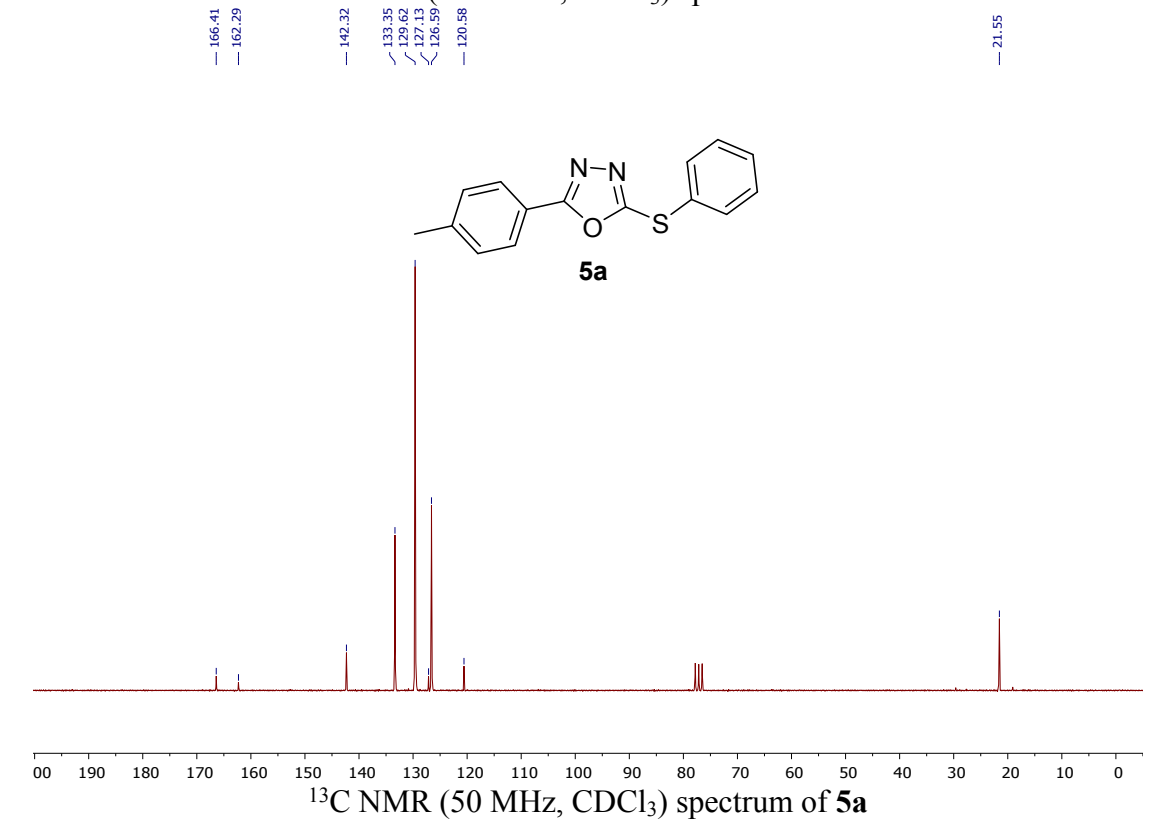
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **3y**



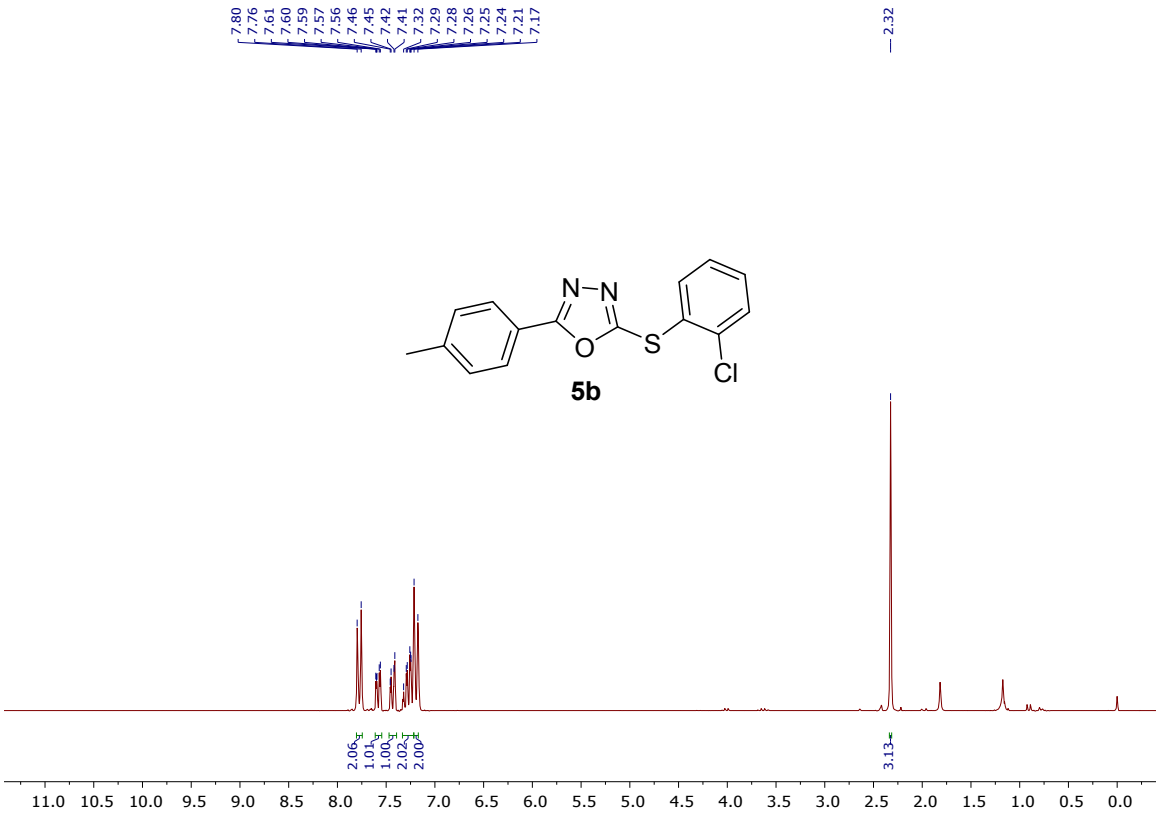
^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **3y**



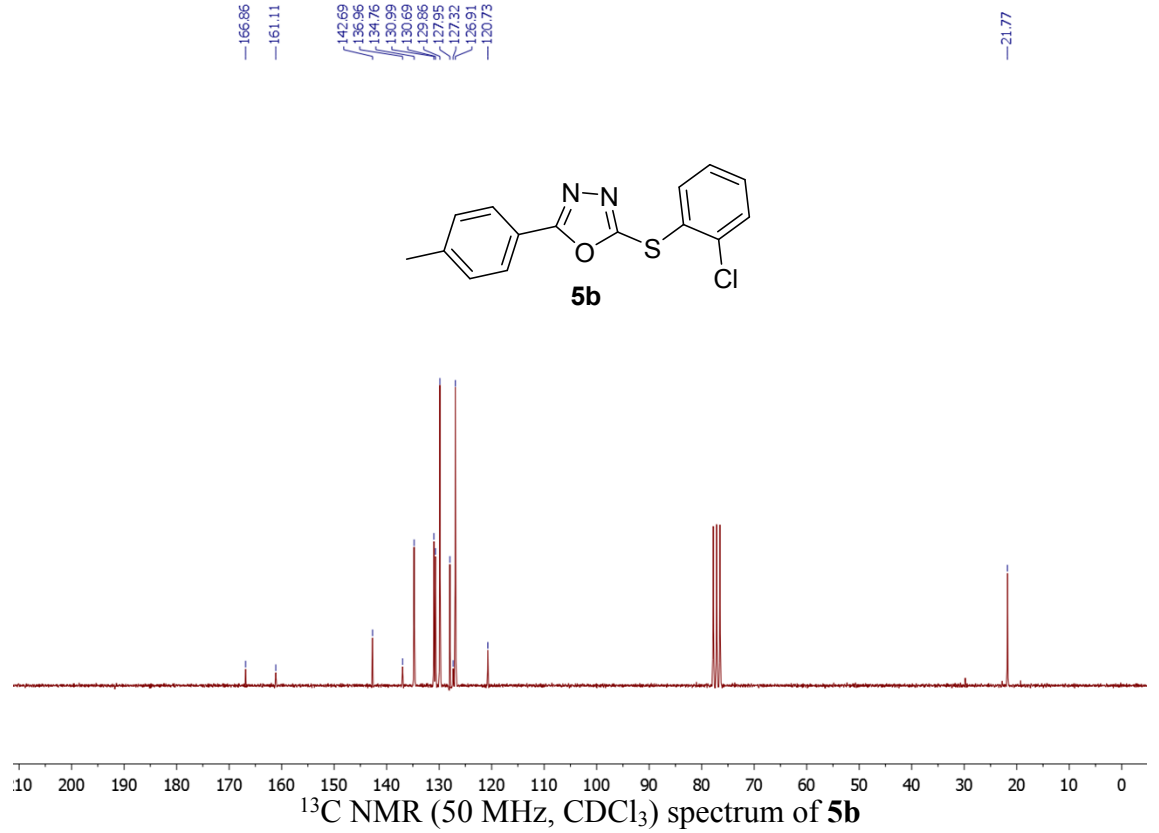
^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **5a**



^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **5a**



^{1}H NMR (200 MHz, $CDCl_3$) spectrum of **5b**



^{13}C NMR (50 MHz, $CDCl_3$) spectrum of **5b**