# Electronic Supplementary Information

# Discovery of a Strongly Apoptotic Ruthenium Complex through Combinatorial Coordination Chemistry

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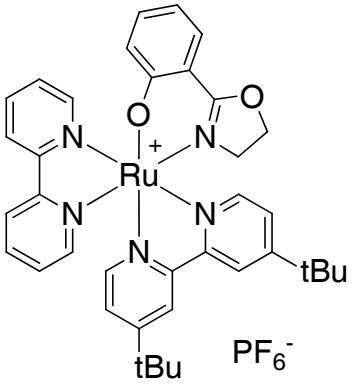
# 1.) Materials and Methods

All preparative-scale reactions were performed in round-bottom flasks or test tubes equipped with rubber septa and a magnetic stirbar under an inert argon or nitrogen atmosphere. Thin layer chromatography was performed with Silicycle (250 μm, indicator F254) or Merck (60 $F_{254}$) plates. Silica gel chromatography was performed with Silia-P Flash Silica gel from Silicycle or Kieselgel 60 M from Macherey-Nagel. Reactions performed in 96-well plates (250 μL well volume, round bottom) were heat-sealed with adhesive aluminum foil and shaken on a KEM-Lab Vortex Mixer from J-KEM Scientific equipped with a nitrogen balloon. Anhydrous DMF, ethylene glycol, and EtOH were obtained from commercial sources and further dried over molecular sieves (4 Å, 8-12 mesh). All other solvents were HPLC grade quality obtained from Fisher or VWR unless otherwise noted. All reagents, including all bidentate ligands and precursor complexes, were either obtained from Acros, Aldrich, Strem, or Alfa Aesar and used without further purification or synthesized from literature procedures providing comparable results.

NMR spectra were recorded on a Bruker Avance (600 MHz), Bruker AM (500 MHz), Bruker DRX (400 MHz) or Bruker DMX (360 mHz) spectrometer. NMR standards used are as follows: ($^1$H NMR) MeOH-$d_4$ – 3.31 ppm, MeCN-$d_3$ – 1.94 ppm. ($^{13}$C NMR) MeOH-$d_4$ – 49.00 ppm, MeCN-$d_3$ – 1.32 ppm. $^1$H NMR data are reported as follows: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad), coupling constant (Hz), and integration. High resolution mass spectra were obtained on a Micromass AutoSpec instrument using either CI or ES ionization or a Thermo Finnigan LTQ FT instrument using ES ionization. Low resolution mass spectra were obtained on an LC platform from Micromass using ESI technique. Infrared spectra

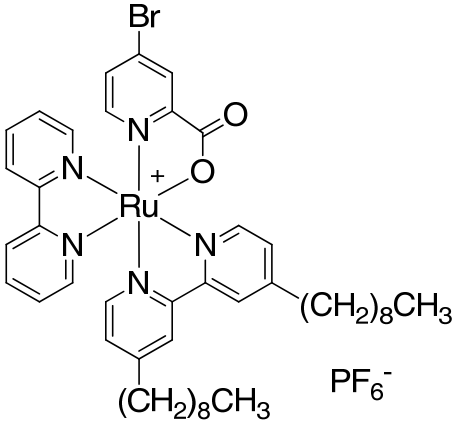
were recorded on a Bruker IFS 88, Perkin Elmer 1600 series FTIR, or Nicolet 510 M FT-IR spectrometer. Photolyses were performed with a medium pressure Hg lamp (150 W or 450 W). LC/MS measurements were performed on an Agilent Technologies 1200 Series HPLC system with an Agilent 6120 Quadrupole MS. HPLC separation was performed on an Agilent 1200 Series HPLC System with UV detection and automated fraction collection. Absorbance and fluorescence measurements were recorded on a Molecular Devices SpectraMax M5 plate reader.

## 2.) Analytical Data for Complexes 3a-i



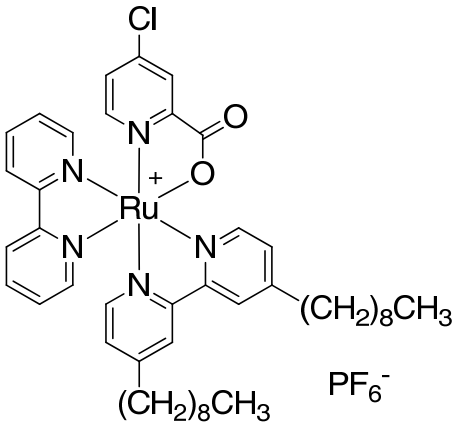

**Compound 3a**. In a test tube, a mixture of precursor complex **2** (5 mg, 0.011 mmol) in DMF (555 μL) was treated with a neutral bidentate ligand, $tBu_2bpy$ (3.3 mg, 0.012 mmol), and heated to 75 ºC (oil bath temperature) with shaking, upon which a deep purple solution developed. After 3 hours, a 20 mM solution of deprotonated 2-(2'-hydroxyphenyl)oxazoline (phox) was prepared in 10:1 EtOH:$H_2O$ by mixing 2-(2'-hydroxyphenyl)oxazoline (Hphox) in EtOH with an appropriate amount of 200 mM aqueous LiOH. This solution (555 μL) was added to the reaction mixture and heated to 80 ºC for another 3 hours. The resulting solution was concentrated *in vacuo* and purified by column chromatography on silica gel using mixtures of MeCN and 100:3:1 MeCN:$H_2O$:$KNO_3$ (sat. aq.) as eluent. The major colored fractions were collected and concentrated to dryness, then redissolved in 8:1 $H_2O$:EtOH and precipitated with

saturated aqueous $NH_4PF_6$. The compound was then centrifuged and washed extensively with water. The purified product was then redissolved in MeCN and tared to provide a 1:1 diastereomeric mixture of $[Ru(bpy)(tBu_2bpy)(phox)]PF_6$ as a purple-brown film (4.8 mg, 60%): IR (thin film) ν ($cm^{-1}$) 3439, 3066, 2963, 2872, 1687, 1653, 1616, 1469, 1445, 1414, 1348, 1238, 1201, 1157, 1129, 1071, 1023, 928, 849, 766, 606. $^1H$ NMR (MeCN-$d_3$) δ (ppm) 8.56-8.58 (m, 2 H), 8.39-8.45 (m, 9 H), 8.30-8.33 (m, 3 H), 8.05 (t, J = 8.1 Hz, 1 H), 7.64-7.80 (m, 7 H), 7.51-7.61 (m, 4 H), 7.44-7.46 (m, 2 H), 7.20-7.26 (m, 4 H), 7.13-7.18 (m, 3 H), 4.36-4.44 (m, 2 H), 4.14-4.24 (m, 2 H), 1.50 (s, 9 H), 1.47 (s, 9 H), 1.38 (s, 14 H), 1.36 (s, 16 H). $^{13}C$ NMR (MeCN-$d_3$) δ (ppm) 159.2, 158.9, 158.8, 136.6, 127.9, 126.9, 125.1, 124.0, 123.8, 123.5, 122.3, 121.1, 74.1, 67.6, 41.4, 36.2, 35.9, 35.9, 35.8, 31.0, 30.8, 30.7, 30.6. HRMS (ESI) calcd for $RuC_{37}H_{40}N_5O_2$ $(M\text{-}PF_6)^+$ 688.2220, found $(M\text{-}PF_6)^+$ 688.2225.



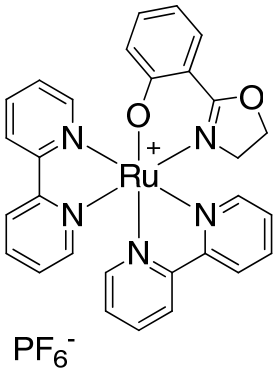

**Compound 3b**. In a test tube, a mixture of precursor complex **2** (5 mg, 0.011 mmol) in DMF (555 μL) was treated with a neutral bidentate ligand, nonyl$_2$bpy (5 mg, 0.012 mmol), and heated to 75 ºC (oil bath temperature) with shaking, upon which a deep purple solution developed. After 3 hours, a 20 mM solution of a monoanionic ligand, lithium 4-bromopicolinate, was prepared in 10:1 EtOH:$H_2O$ by mixing 4-bromopicolinic acid in EtOH with an appropriate amount of 200 mM aqueous LiOH. This solution (555 μL) was added to the reaction mixture and heated to 80 ºC for another 3 hours. The resulting solution was

concentrated *in vacuo* and purified by column chromatography on silica gel using mixtures of MeCN and 100:3:1 MeCN:$H_2O$:$KNO_3$ (sat. aq.) as eluent. The major colored fractions were collected and concentrated to dryness, then redissolved in 8:1 $H_2O$:EtOH and precipitated with saturated aqueous $NH_4PF_6$. The compound was then centrifuged and washed extensively with water. The purified product was then redissolved in MeCN and tared to provide a 1:1 diastereomeric mixture of [Ru(bpy)(nonyl$_2$bpy)(4-bromopicolinate)]$PF_6$ as an orange-red film (6.0 mg, 60%): IR (thin film) ν (cm$^{-1}$) 3067, 2925, 2854, 1687, 1616, 1539, 1469, 1444, 1420, 1347, 1237, 1156, 1070, 954, 767. $^1$H NMR (MeCN-$d_3$) δ (ppm) 8.78 (d, J = 5.4 Hz, 1 H), 8.60 (d, J = 5.6 Hz, 1 H), 8.45-8.49 (m, 2 H), 8.34-8.40 (m, 4 H), 8.27-8.28 (m, 2 H), 8.16-8.17 (m, 2 H), 8.00-8.06 (m, 3 H), 7.81-7.89 (m, 4 H), 7.61-7.65 (m, 2H), 7.48-7.53 (m, 4 H), 7.41-7.42 (d, J = 6.0 Hz, 1 H), 7.31-7.35 (m, 3 H), 7.19-7.25 (m, 3 H), 7.05-7.07 (m, 2 H), 2.82-2.87 (m, 4 H), 2.69-2.75 (m, 4 H), 1.62-1.69 (m, 4 H), 1.73-1.77 (m, 4 H), 1.26-1.41 (m, 48 H), 0.85-0.88 (m, 12 H). $^{13}$C NMR (MeCN-$d_3$) δ (ppm) 171.1, 171.0, 159.6, 159.0, 158.3, 157.9, 157.8, 157.8, 157.4, 155.6, 155.6, 154.2, 153.8, 153.8, 153.1, 152.2, 151.8, 151.7, 151.6, 151.1, 151.0, 150.3, 137.0, 136.9, 136.6, 135.7, 133.4, 131.5, 130.5, 137.7, 127.6, 127.5, 127.5, 127.2, 126.9, 126.9, 126.7, 124.4, 124.3, 124.1, 124.0, 123.9, 123.8, 123.7, 40.8, 35.3, 35.2, 35.1, 35.0, 35.0, 32.0, 32.0, 32.0, 30.5, 30.4, 30.3, 30.3, 29.6, 29.6, 29.6, 29.5, 29.5, 29.5, 29.4, 29.4, 29.4, 29.3, 29.2, 22.8, 22.8, 13.8, 13.8. HRMS (ESI) calcd for $RuC_{44}H_{55}N_5O_2Br$ $(M\text{-}PF_6)^+$ 866.2577, found $(M\text{-}PF_6)^+$ 866.2588.



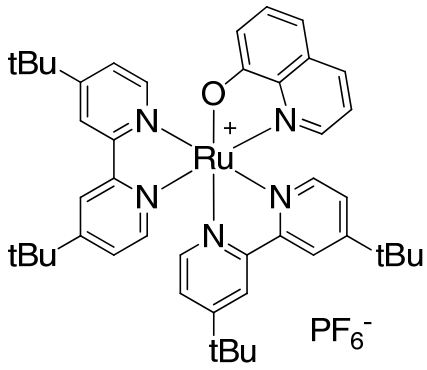

**Compound 3c**. In a test tube, a mixture of precursor complex **2** (5 mg, 0.011 mmol) in DMF (555 μL) was treated with a neutral bidentate ligand, nonyl$_2$bpy (5 mg, 0.012 mmol), and heated to 75 ºC (oil bath temperature) with shaking, upon which a deep purple solution developed. After 3 hours, a 20 mM solution of a monoanionic ligand, lithium 4-chloropicolinate, was prepared in 10:1 EtOH:$H_2O$ by mixing 4-chloropicolinic acid in EtOH with an appropriate amount of 200 mM aqueous LiOH. This solution (555 μL) was added to the reaction mixture and heated to 80 ºC for another 3 hours. The resulting solution was concentrated *in vacuo* and purified by column chromatography on silica gel using mixtures of MeCN and 100:3:1 MeCN:$H_2O$:$KNO_3$ (sat. aq.) as eluent. The major colored fractions were collected and concentrated to dryness, then redissolved in 8:1 $H_2O$:EtOH and precipitated with saturated aqueous $NH_4PF_6$. The compound was then centrifuged and washed extensively with water. The purified product was then redissolved in MeCN and tared to provide a 1:1 diastereomeric mixture of [Ru(bpy)(nonyl$_2$bpy)(4-chloropicolinate)]$PF_6$ as an orange-red film (5.7 mg, 60%): IR (thin film) ν (cm$^{-1}$) 3438, 3070. 2925. 2855, 1686, 1464, 1420, 1339, 1296, 1152, 1024, 818, 766, 482, 427. $^1$H NMR (MeCN-$d_3$) δ (ppm) 8.79 (d, J = 5.2 Hz, 1 H), 8.61 (d, J = 5.8 Hz, 1 H), 8.46-8.48 (m, 2 H), 8.34-8.41 (m, 4 H), 8.28 (d, J = 3.9 Hz, 2 H), 8.00-8.06 (m, 5 H), 7.80-7.87 (m, 4 H), 7.61-7.64 (m, 3 H), 7.48-7.50 (m, 2 H), 7.41-7.44 (m, 3 H), 7.32-7.39 (m, 3 H), 7.20-7.24 (m, 2 H), 7.05-7.07 (m, 2 H), 2.83-2.85 (m, 4 H), 2.70-2.72 (m, 4 H), 1.73-1.76 (t, 4 H), 1.63-1.66 (t, 4 H), 1.26-1.39 (m, 48 H), 0.85 (t, 12 H). $^{13}$C NMR (MeCN-$d_3$) δ

(ppm) 171.8, 171.8, 160.2, 158.9, 158.5, 158.5, 158.4, 156.5, 156.5, 154.8, 154.8, 154.4, 152.8, 152.5, 152.4, 152.3, 152.2, 152.0, 151.6, 151.6, 150.9, 145.5, 137.5, 137.2, 136.3, 129.1, 128.3, 128.2, 128.1, 127.8, 127.5, 127.5, 127.3, 125.0, 124.9, 124.7, 124.6, 124.5, 124.4, 124.4, 41.4, 35.9, 35.8, 35.7, 35.6, 35.6, 32.6, 31.1, 31.0, 30.9, 30.9, 30.2, 30.2, 30.2, 30.1, 30.1, 30.0, 30.0, 30.0, 29.8, 29.8, 23.4, 23.4, 14.4. HRMS (ESI) calcd for $RuC_{44}H_{55}N_5O_2Cl$ $(M\text{-}PF_6)^+$ 822.3082, found $(M\text{-}PF_6)^+$ 822.3096.



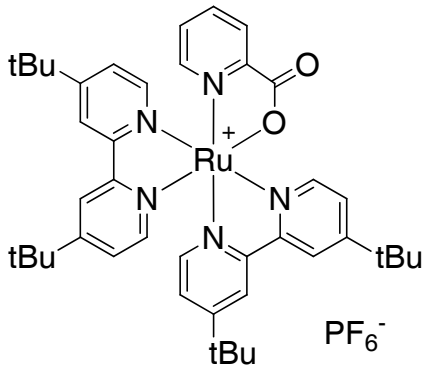

**Compound 3d**. $Ru(bpy)_2Cl_2$ (9.5 mg, 0.02 mmol) in EtOH (1.76 mL) was treated with 1.05 equivalents of a solution of deprotonated 2-(2'-hydroxyphenyl)oxazoline in 10:1 EtOH:$H_2O$ (prepared with one equivalent LiOH) and refluxed for 6 hours. The resulting solution was concentrated *in vacuo* and purified by column chromatography on silica gel using mixtures of MeCN and 100:3:1 MeCN:$H_2O$:$KNO_3$ (sat. aq.) as eluent. The major colored fractions were collected and concentrated to dryness, then redissolved in 8:1 $H_2O$:EtOH and precipitated as with saturated aqueous $NH_4PF_6$. The compound was then centrifuged and washed extensively with water. The purified product was then redissolved in MeCN and tared to provide a purple film (6.8 mg, 57%): IR (thin film) ν ($cm^{-1}$) 3484, 3035, 1617, 1470, 1444, 1419, 1342, 1239, 1071, 1018, 928, 767, 731, 425. $^1$H NMR (MeCN-$d_3$) δ (ppm) 8.78-8.81 (m, J = 6.8 Hz, 2 H), 8.47 (d, J = 8.1 Hz, 1 H), 8.42 (d, J = 8.1 Hz, 1 H), 8.35 (d, J = 8.1 Hz, 2 H), 8.06 (t J = 7.7 Hz, 1 H), 7.95 (t, J = 8.1 Hz, 1 H), 7.75-7.85 (m, 3 H), 7.62 (t, J = 6.4 Hz, 1 H), 7.48-7.56 (m, 3 H), 7.11-7.18 (m, 2 H), 7.02 (t, J = 7.7 Hz, 1 H), 6.34 (d, J = 8.6 Hz, 1 H), 6.26 (br m, 1 H), 4.40-4.47 (m, 1 H), 4.20-4.26 (m, 1 H), 3.54

(br m, 1 H), 2.88 (br m, 1 H). $^{13}$C NMR (MeCN-$d_3$) δ (ppm) 160.6, 159.2, 159.0, 158.7, 154.6, 152.7, 152.4, 151.4, 136.9, 136.7, 136.5, 135.6, 127.7, 127.0, 126.9, 126.5, 124.4, 124.1, 124.0, 123.9, 67.8, 54.7, 41.4. HRMS (ESI) calcd for $RuC_{29}H_{24}N_5O_2$ $(M\text{-}PF_6)^+$ 576.0988, found $(M\text{-}PF_6)^+$ 576.0993.



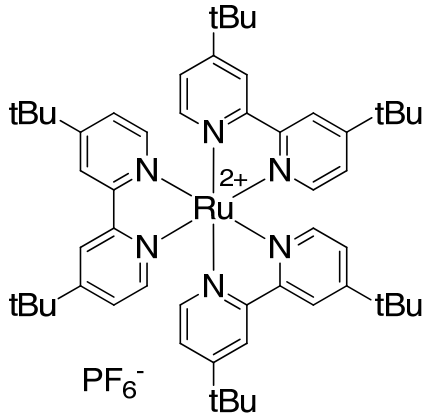

**Compound 3e**. $Ru(tBu_2bpy)_2Cl_2$ (6 mg, 0.008 mmol) in EtOH (800 μL) was treated with 1.1 equivalents of a solution of lithium 8-phenoxyquinoline in 10:1 EtOH:$H_2O$ (prepared from 8-hydroxyquinoline and LiOH, 100 mM) and refluxed for 6 hours. The resulting solution was concentrated *in vacuo* and purified by column chromatography on silica gel using mixtures of MeCN and 100:3:1 MeCN:$H_2O$:$KNO_3$ (sat. aq.) as eluent. The major colored fractions were collected and concentrated to dryness, then redissolved in 8:1 $H_2O$:EtOH and precipitated as with saturated aqueous $NH_4PF_6$. The compound was then centrifuged and washed extensively with water. The purified product was then redissolved in MeCN and tared to provide a purple-red film (4.1 mg, 59%): IR (thin film) ν ($cm^{-1}$) 3435, 2961, 2908, 2873, 1688, 1613, 1566, 1534, 1497, 1481, 1457, 1414, 1369, 1338, 1279, 1202, 1130, 1027, 848, 830, 605. $^1$H NMR (MeOH-$d_4$) δ (ppm) 8.56-8.67 (m, 5 H), 8.06 (d, J = 8.6 Hz, 1 H), 7.82 (dd, J = 2.6, 6.3 Hz, 2 H), 7.61 (d, J = 6.0 Hz, 1 H), 7.58 (dd, J = 2.2, 6.3 Hz, 1 H), 7.47 (dd, J = 1.5, 4.9 Hz, 1 H), 7.41 (dd, J = 2.2, 6.3 Hz, 1 H), 7.32-7.37 (m, 3 H), 7.17 (dd, J = 4.9, 8.6 Hz, 1 H), 6.98 (d, J = 7.8 Hz, 1 H), 6.89 (d, J = 6.9 Hz, 1 H), 1.46 (s, 9 H), 1.45 (s, 9 H), 1.42 (s, 9 H), 1.41 (s, 9 H). $^{13}$C NMR (MeCN-$d_3$) δ (ppm) 161.6, 161.3,

160.7, 158.8, 158.5, 158.4, 151.9, 151.1, 147.5, 136.6, 124.8, 124.5, 124.5, 124.2, 122.6, 121.7, 121.5, 121.4, 47.8, 36.2, 36.1, 36.1, 36.0, 30.7, 30.6, 30.6, 30.5, 9.2. HRMS (ESI) calcd for $RuC_{45}H_{54}N_5O$ $(M\text{-}PF_6)^+$ 782.3366, found $(M\text{-}PF_6)^+$ 782.3375.

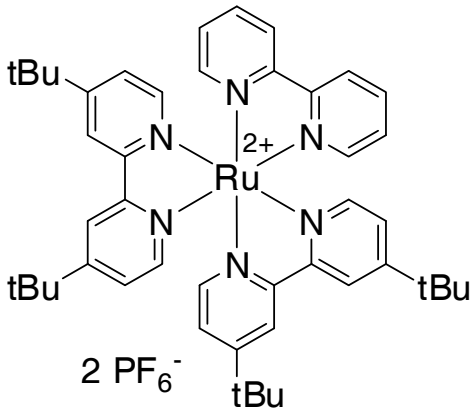



**Compound 3f**. $Ru(tBu_2bpy)_2Cl_2$ (6 mg, 0.008 mmol) in EtOH (800 μL) was treated with 1.1 equivalents of a solution of lithium 2-picolinate in 10:1 EtOH:$H_2O$ (prepared from picolinic acid and LiOH, 100 mM) and refluxed for 6 hours. The resulting solution was concentrated *in vacuo* and purified by column chromatography on silica gel using mixtures of MeCN and 100:3:1 MeCN:$H_2O$:$KNO_3$ (sat. aq.) as eluent. The major colored fractions were collected and concentrated to dryness, then redissolved in 8:1 $H_2O$:EtOH and precipitated as with saturated aqueous $NH_4PF_6$. The compound was then centrifuged and washed extensively with water. The purified product was then redissolved in MeCN and tared to provide an orange film (6.3 mg, 94%): IR (thin film) ν ($cm^{-1}$) 3423, 2961, 1636, 1481, 1413, 1336, 1203, 1140, 1026, 849, 829, 607. $^1$H NMR (MeCN-$d_3$) δ (ppm) 8.69 (d, J = 6.2 Hz, 1 H), 8.48 (dd, J = 2.0, 14.3 Hz, 2 H), 8.41 (dd, J = 1.7, 8.9 Hz, 2 H), 8.05 (d, J = 7.6 Hz, 1 H), 7.87 (td, J = 1.5, 7.6 8.9 Hz, 1 H), 7.82 (d, J = 5.9 Hz, 1 H), 7.72 (d, J = 5.7 Hz, 1 H), 7.67 (dd, J = 2.0, 6.2 Hz, 1 H), 7.45-7.56 (m, 3 H), 7.33-7.41 (m, 1 H), 7.22-7.28 (m, 2 H), 1.47 (s, 9 H), 1.45 (s, 9 H), 1.38 (s, 9 H), 1.37 (s, 9 H). $^{13}$C NMR (MeCN-$d_3$) δ (ppm) 162.2, 161.9, 161.2, 159.9, 158.7, 158.6, 158.1, 154.9, 154.6, 153.6, 152.2, 151.6, 151.4, 151.1, 137.9, 129.2, 128.0, 125.6, 125.3, 124.7, 124.4, 122.1, 121.9, 121.7, 121.6, 41.2, 36.3, 36.2, 36.1, 36.1,

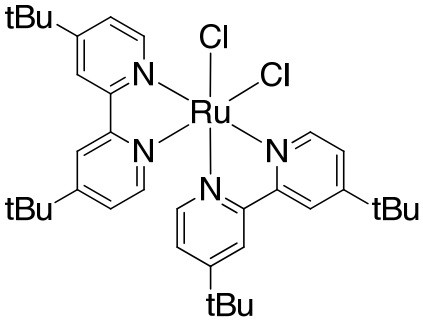
30.7, 30.6, 30.5, 30.5. HRMS (ESI) calcd for $RuC_{42}H_{52}N_5O_2$ $(M\text{-}PF_6)^+$ 760.3159, found $(M\text{-}PF_6)^+$ 760.3163.




**Compound 3g**. $Ru(tBu_2bpy)_2Cl_2$ (6 mg, 0.008 mmol) in EtOH (800 μL) was treated with 1.1 equivalents of a solution of $tBu_2bpy$ in EtOH (100 mM) and refluxed for 6 hours. The resulting solution was concentrated *in vacuo* and purified by column chromatography on silica gel using mixtures of MeCN and 100:3:1 $MeCN:H_2O:KNO_3$ (sat. aq.) as eluent. The major colored fractions were collected and concentrated to dryness, then redissolved in 8:1 $H_2O$:EtOH and precipitated as with saturated aqueous $NH_4PF_6$. The compound was then centrifuged and washed extensively with water. The purified product was then redissolved in MeCN and tared to provide an orange film (7.5 mg, 74%): IR (thin film) ν ($cm^{-1}$) 2961, 2877, 1686, 1615, 1482, 1414, 1367, 1298, 1204, 1142, 1028, 838, 557. $^1$H NMR (MeCN-$d_3$) δ (ppm) 8.46 (d, J = 2.1 Hz, 6 H), 7.55 (d, J = 5.9 Hz, 6 H), 7.39 (dd, J = 1.6, 5.9 Hz, 6 H), 1.41 (s, 54 H). $^{13}$C NMR (MeCN-$d_3$) δ (ppm) 163.4, 157.9, 151.8, 125.6, 122.4, 36.3, 30.5. HRMS (ESI) calcd for $RuC_{54}H_{72}N_6$ $(M\text{-}2PF_6)^{2+}$ 453.3435, found $(M\text{-}2PF_6)^{2+}$ 453.2434.




**Compound 3h**. $Ru(tBu_2bpy)_2Cl_2$ (6 mg, 0.008 mmol) in EtOH (800 μL) was treated with 1.1 equivalents of a solution of 2,2'-bipyridine (bpy) in EtOH (100 mM) and refluxed for 6 hours. The resulting solution was concentrated *in vacuo* and purified by column chromatography on silica gel using mixtures of MeCN and 100:3:1 $MeCN:H_2O:KNO_3$ (sat. aq.) as eluent. The major colored fractions were collected and concentrated to dryness, then redissolved in 8:1 $H_2O$:EtOH and precipitated as with saturated aqueous $NH_4PF_6$. The compound was then centrifuged and washed extensively with water. The purified product was then redissolved in MeCN and tared to provide an orange film (5.4 mg, 59%): IR (thin film) ν ($cm^{-1}$) 2972, 1356, 1028, 839, 557. $^1$H NMR (MeCN-$d_3$) δ (ppm) 8.46-8.50 (m, 6 H), 8.03 (td, J = 1.2, 7.9, 9.3 Hz, 2 H), 7.69 (d, J = 5.3 Hz, 2 H), 7.57 (dd, J = 4.7, 5.9 Hz, 4 H), 7.36-7.41 (m, 6 H), 1.41 (s, 18 H), 1.40 (s, 18 H). $^{13}$C NMR (MeCN-$d_3$) δ (ppm) 163.6, 158.2, 157.8, 152.5, 152.0, 151.8, 138.5, 128.5, 125.6, 125.2, 122.5, 36.4, 30.5. HRMS (ESI) calcd for $RuC_{46}H_{56}N_6$ $(M\text{-}2PF_6)^{2+}$ 397.1799, found $(M\text{-}2PF_6)^{2+}$ 397.1804.

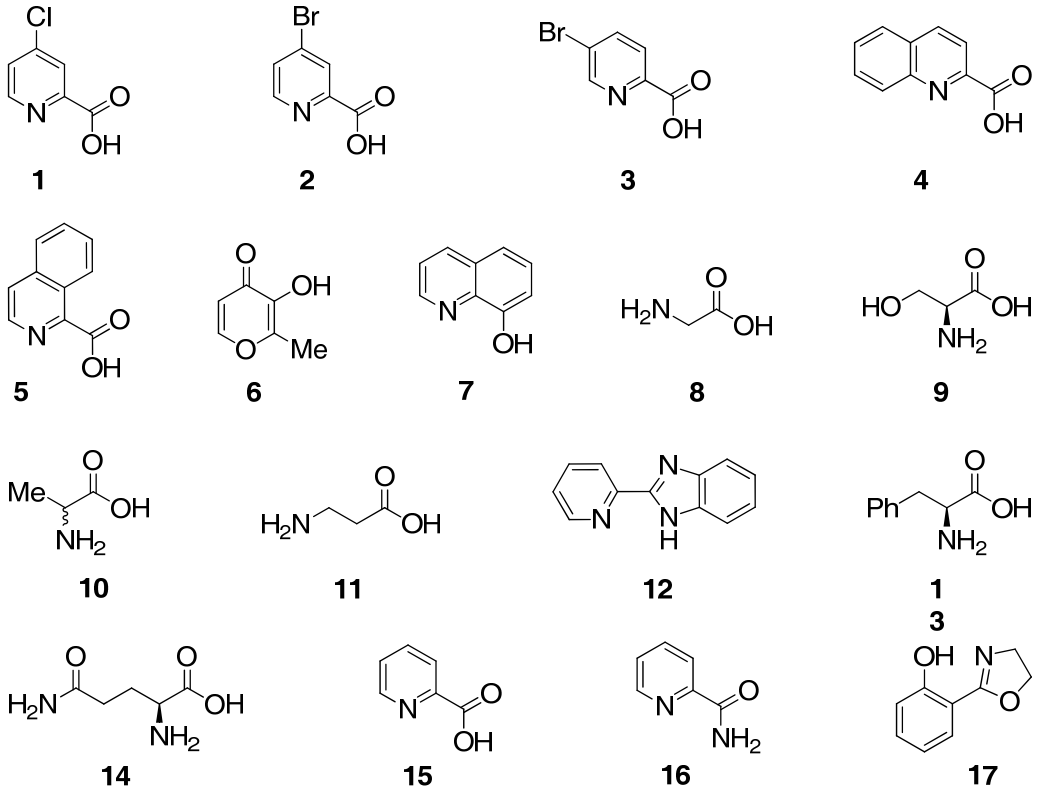



**Compound 3i**. $Ru(tBu_2bpy)(DMSO)_2Cl_2$ (600 mg, 1.01 mmol) and $tBu_2bpy$ (270 mg, 1.01 mmol) were dissolved in dry DMF (100 mL) and heated to reflux. The orange solution became dark purple. After six

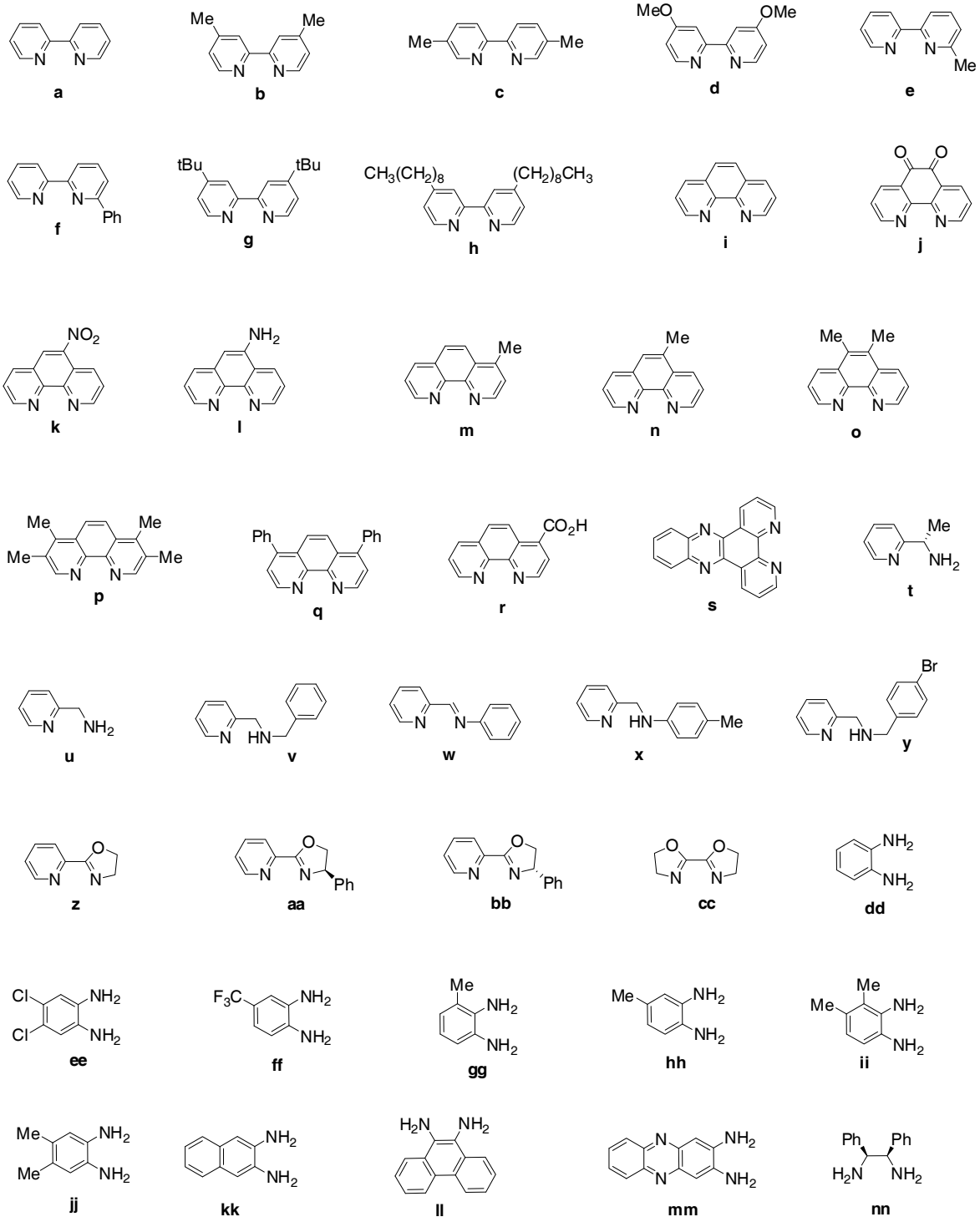
hours, the reaction mixture was cooled to room temperature and concentrated to dryness. The complex was purified on a neutral aluminum oxide plug column (10 cm) with $CH_2Cl_2$, then EtOAc to elute the purple product. The dicationic impurity $[Ru(tBu_2bpy)_3]Cl_2$ stuck to the top of the column. The complex was concentrated to give a purple solid (423 mg, 61%). Analytical data for this compound were consistent with literature values (C. Viala, C. Coudret, *Inorg. Chimica Acta* **2006**, *359*, 984-989).

## 3.) Bidentate Ligands for Library Synthesis

**Monoanionic ligands (deprotonated with LiOH during library synthesis)**:



## **Neutral ligands**:



# 4.) Cytotoxicity Data for Library Members

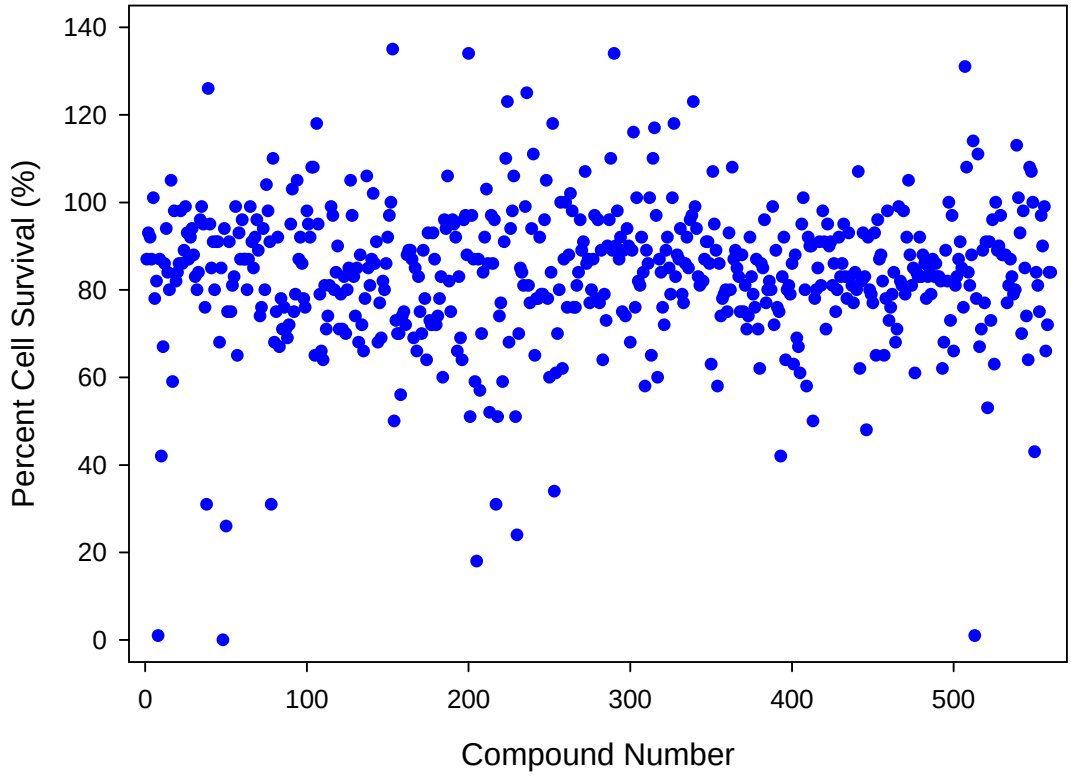
**Cytotoxicities of library members in HeLa cells at approx. 30 μM concentration (% cell survival)**

| Neutral ligand \ Monoanionic Ligand | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **a** | 87 | 85 | 87 | 83 | 78 | 76 | 76 | 96 | 78 | 93 | 89 | 96 | 65 | 76 | 62 | 66 | 75 |
| **b** | 93 | 91 | 135 | 70 | 72 | 78 | 34 | 100 | 82 | 86 | 89 | 107 | 83 | 79 | 86 | 100 | 74 |
| **c** | 92 | 80 | 102 | 77 | 86 | 81 | 65 | 79 | 77 | 96 | 94 | 92 | 83 | 81 | 85 | 93 | 79 |
| **d** | 87 | 91 | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **e** | 101 | 91 | 83 | 88 | 106 | 68 | 51 | 84 | 72 | 79 | 88 | 91 | 71 | 81 | 88 | 77 | 97 |
| **f** | 78 | 68 | 80 | 79 | 80 | 52 | 31 | 59 | 58 | 65 | 60 | 61 | 58 | 50 | 84 | 63 | 53 |
| **g** | 82 | 85 | 65 | 66 | 74 | 51 | 18 | 84 | 74 | 89 | 82 | 42 | 80 | 63 | 88 | 71 | 1 |
| **h** | 1 | 0 | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **i** | 87 | 94 | 79 | 86 | 95 | 75 | 66 | 96 | 73 | 89 | 87 | 86 | 80 | 72 | 98 | 84 | 85 |
| **j** | 42 | 26 | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **k** | 67 | 75 | 75 | 71 | 72 | 72 | 74 | 96 | 86 | 87 | 77 | 88 | 74 | 76 | 71 | 81 | 100 |
| **l** | 86 | 91 | 69 | 75 | 64 | 88 | 76 | 89 | 79 | 80 | 85 | 87 | 78 | 79 | 68 | 72 | 97 |
| **m** | 94 | 75 | 50 | 56 | 88 | 60 | 61 | 62 | 87 | 63 | 58 | 62 | 48 | 77 | 83 | 43 | 64 |
| **n** | 84 | 81 | 86 | 69 | 92 | 77 | 78 | 79 | 86 | 97 | 83 | 83 | 78 | 77 | 79 | 70 | 80 |
| **o** | 80 | 83 | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **p** | 105 | 99 | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **q** | 59 | 65 | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **r** | 98 | 93 | 74 | 72 | 85 | 94 | 24 | 81 | 89 | 101 | 87 | 81 | 95 | 86 | 86 | 81 | 88 |
| **s** | 82 | 87 | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **t** | 84 | 96 | 84 | 71 | 85 | 97 | 51 | 91 | 89 | 110 | 87 | 95 | 92 | 78 | 83 | 100 | 91 |
| **u** | 86 | 87 | 118 | 64 | 81 | 97 | 87 | 92 | 94 | 116 | 81 | 83 | 81 | 88 | 81 | 89 | 78 |
| **v** | 98 | 87 | 105 | 78 | 92 | 96 | 83 | 97 | 90 | 134 | 92 | 85 | 82 | 89 | 79 | 81 | 76 |
| **w** | 86 | 80 | 92 | 76 | 95 | 93 | 78 | 94 | 87 | 97 | 89 | 75 | 92 | 87 | 99 | 83 | 73 |
| **x** | 89 | 87 | 85 | 70 | 93 | 102 | 81 | 91 | 80 | 108 | 83 | 88 | 98 | 84 | 89 | 84 | 90 |
| **y** | 99 | 99 | 73 | 74 | 89 | 84 | 70 | 87 | 91 | 107 | 86 | 82 | 92 | 93 | 83 | 84 | 108 |
| **z** | 93 | 91 | 91 | 82 | 97 | 94 | 78 | 96 | 92 | 123 | 81 | 86 | 93 | 84 | 87 | 98 | 113 |
| **aa** | 87 | 85 | 85 | 66 | 81 | 98 | 70 | 99 | 92 | 118 | 94 | 98 | 90 | 75 | 78 | 87 | 88 |
| **bb** | 92 | 92 | 90 | 83 | 105 | 86 | 74 | 110 | 86 | 117 | 84 | 101 | 90 | 80 | 92 | 89 | 73 |
| **cc** | 94 | 96 | 95 | 81 | 99 | 87 | 57 | 103 | 90 | 76 | 92 | 92 | 79 | 69 | 85 | 77 | 111 |
| **dd** | 88 | 89 | 87 | 76 | 108 | 95 | 69 | 88 | 96 | 90 | 75 | 96 | 80 | 76 | 92 | 88 | 131 |
| **ee** | 83 | 74 | 67 | 71 | 103 | 87 | 83 | 106 | 77 | 78 | 64 | 81 | 83 | 71 | 82 | 87 | 97 |
| **ff** | 80 | 76 | 66 | 89 | 73 | 98 | 84 | 107 | 75 | 87 | 75 | 82 | 73 | 68 | 82 | 84 | 99 |
| **gg** | 84 | 94 | 70 | 75 | 89 | 118 | 80 | 100 | 91 | 95 | 74 | 93 | 80 | 65 | 82 | 81 | 107 |
| **hh** | 96 | 80 | 68 | 80 | 100 | 111 | 92 | 105 | 85 | 99 | 82 | 95 | 83 | 80 | 83 | 85 | 101 |
| **ii** | 99 | 104 | 68 | 78 | 87 | 106 | 85 | 125 | 85 | 83 | 79 | 91 | 91 | 80 | 83 | 83 | 88 |
| **jj** | 95 | 98 | 71 | 70 | 97 | 96 | 77 | 123 | 101 | 97 | 76 | 80 | 90 | 85 | 83 | 90 | 96 |

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **kk** | 76 | 91 | 79 | 71 | 97 | 59 | 70 | 86 | 68 | 101 | 84 | 64 | 86 | 67 | 61 | 91 | 67 |
| | **ll** | 31 | 31 | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| | **mm** | 126 | 110 | 92 | 98 | 108 | 92 | 64 | 134 | 110 | 98 | 89 | 77 | 99 | 75 | 105 | 114 | 108 |
| | **nn** | 95 | 68 | 78 | 69 | 75 | 72 | 60 | 82 | 80 | 96 | 79 | 71 | 79 | 62 | 81 | 91 | 66 |

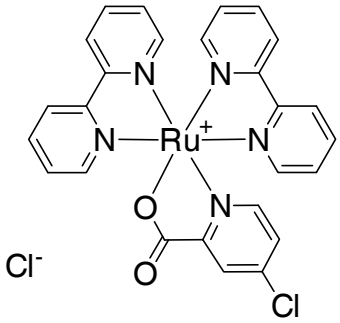
X = Compounds not synthesized due to solubility problems with complexes bearing the indicated ligands.

Visual distribution of cytotoxicity data for the ruthenium complex library (560 data points):

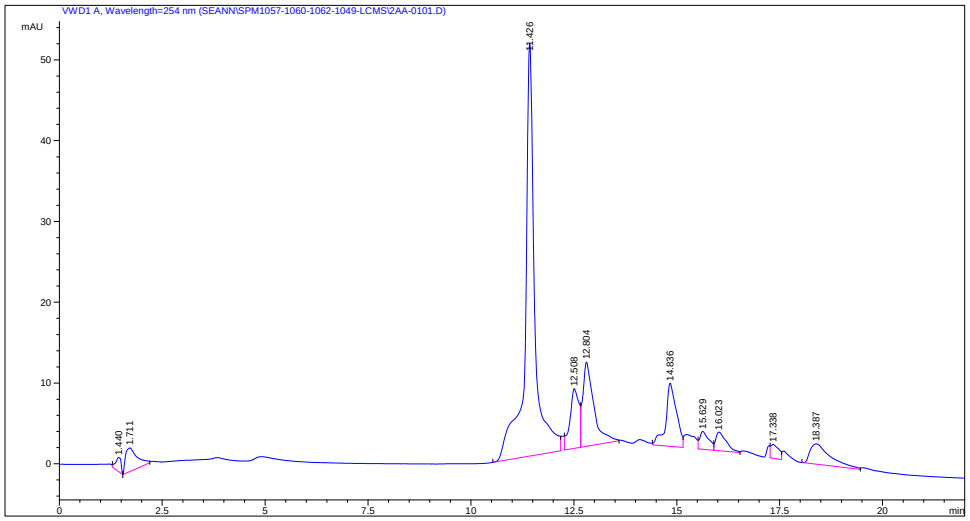


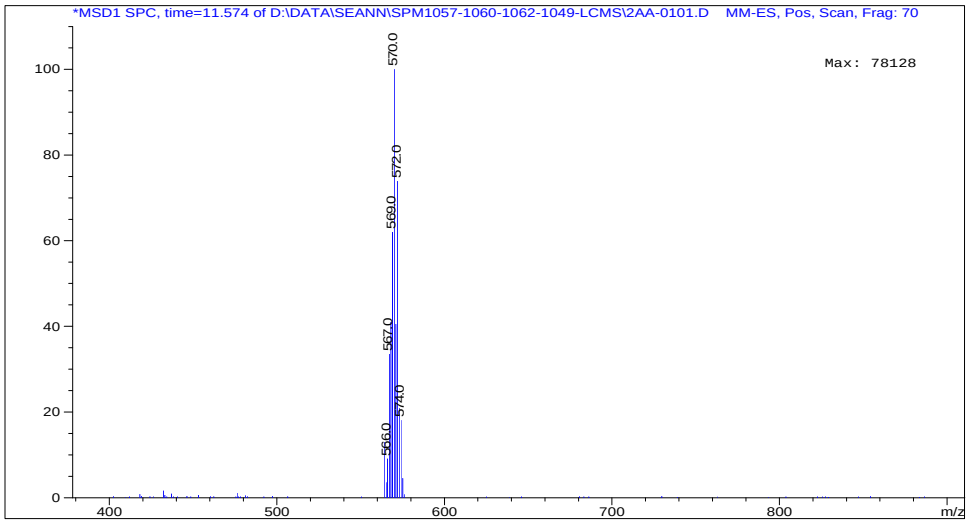
# 5.) Validation of Library Quality

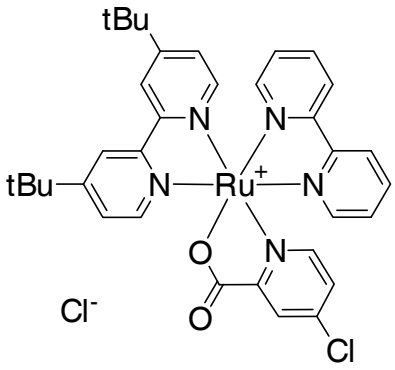
An aliquot of 65 randomly chosen complexes of the 560-membered library (11.6% of library) in DMF:ethylene glycol (10 mM) were diluted to 100 μM in MeCN and injected on an Agilent 1200 Series HPLC system with an Agilent 6120 Quadrupole MS. An analytical Nucleodur C8 Gravity column (Macherey-Nagel) was equilibrated to 5% MeCN/95% $H_2O$ with 0.5% formic acid at 0.3 mL/min. A 5 μL solution of the compound was injected and the MeCN was increased to 95% over 20 minutes. The main peak in the UV chromatogram (254 nm) was then analyzed for its ionized fragments (ESI-POS, 400-900 m/z). The structures of 65 randomly chosen library members are shown below along with their UV-chromatograms and a corresponding mass spectrum of the major peak:



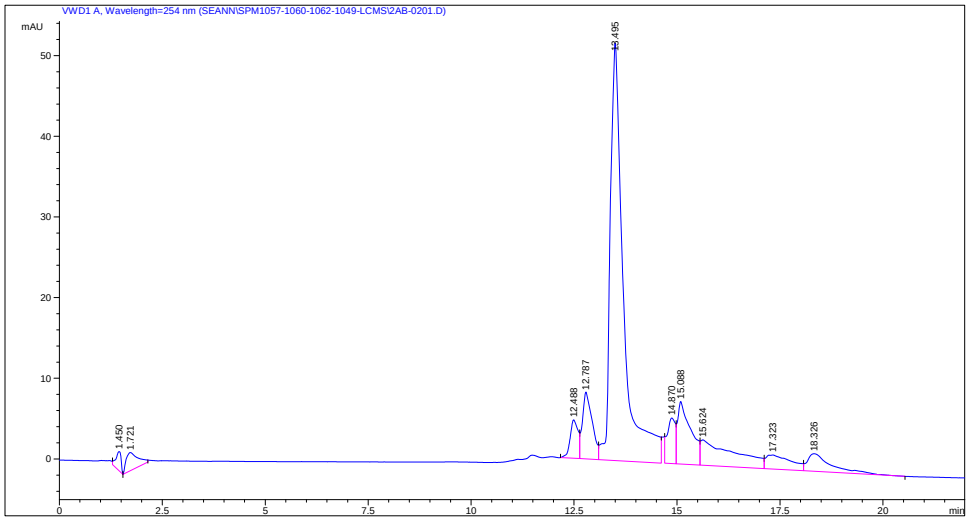

$[M\text{-}Cl]^{+} = 570.0$

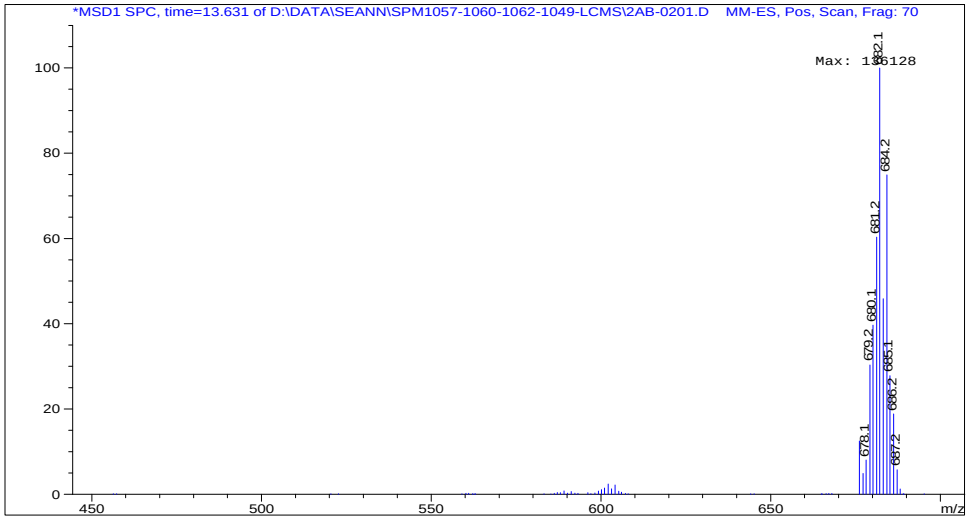


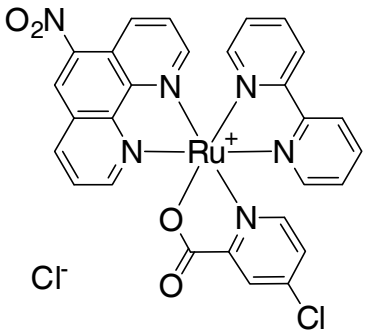





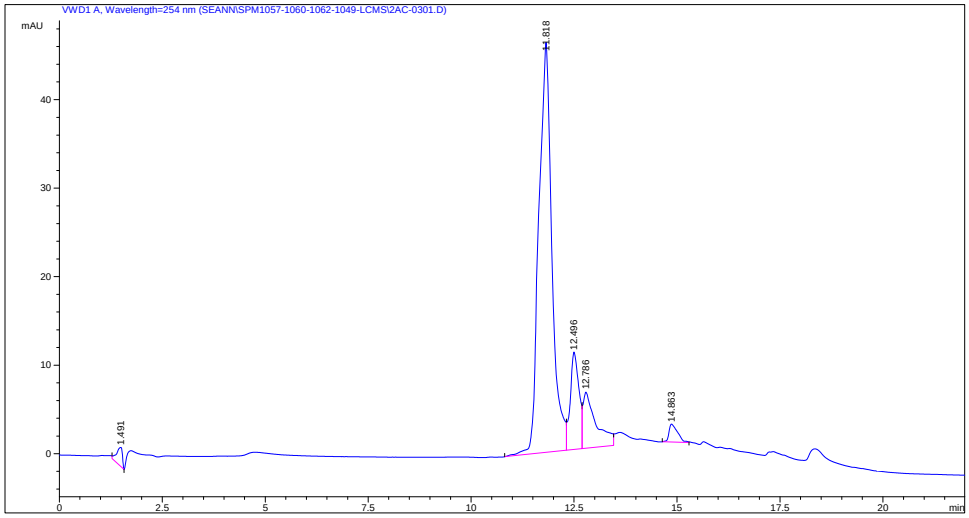

$[M\text{-}Cl]^{+} = 682.2$

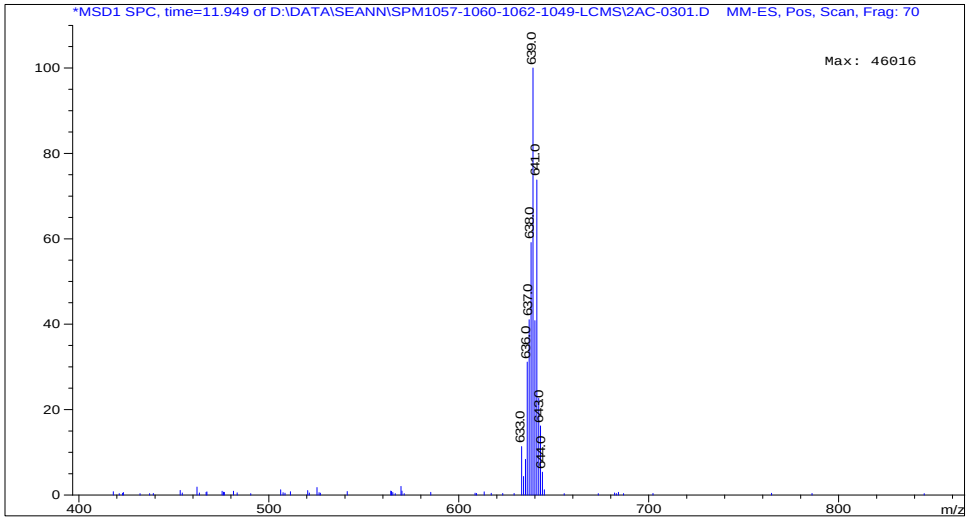


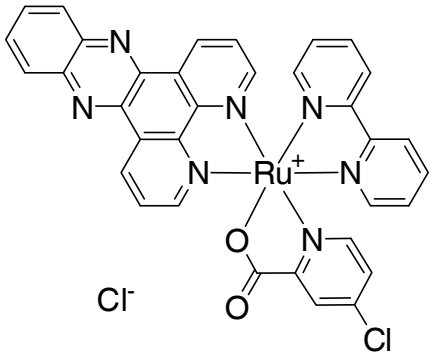





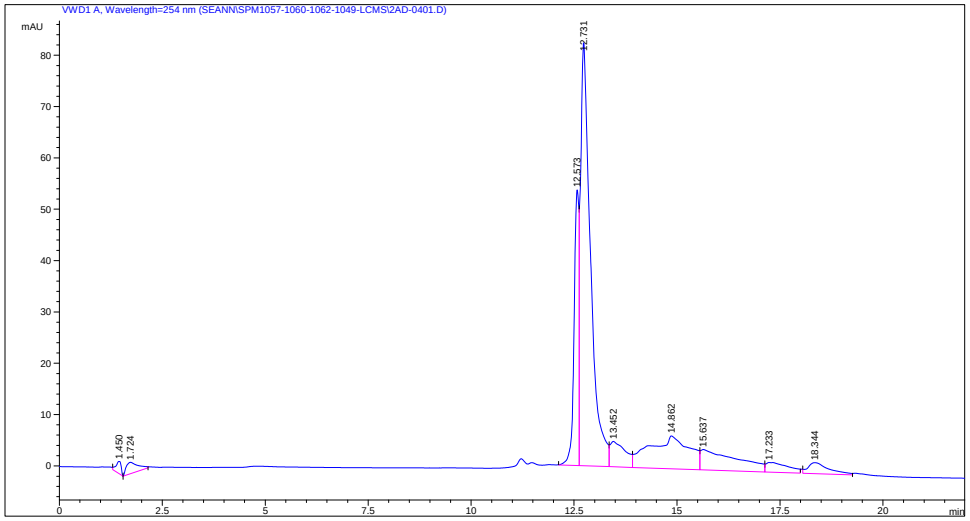

$[M\text{-}Cl]^+ = 639.0$

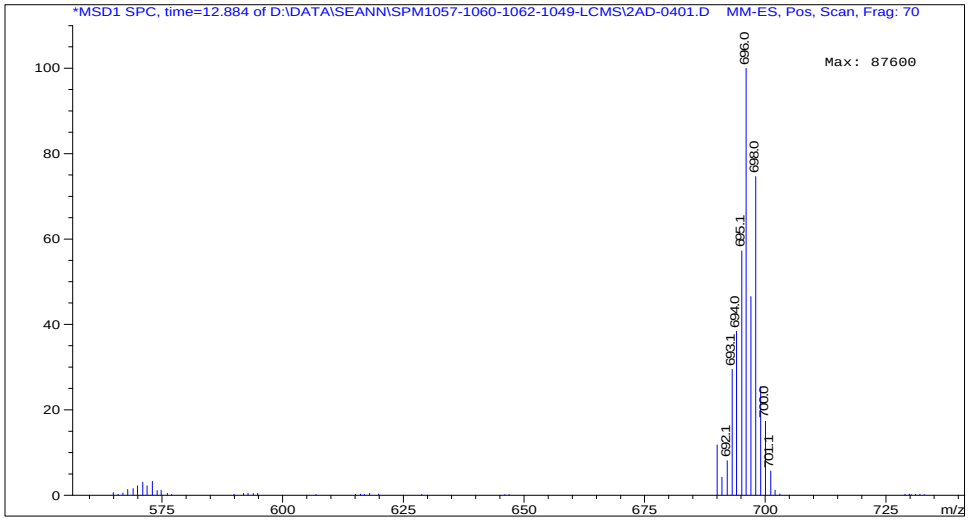


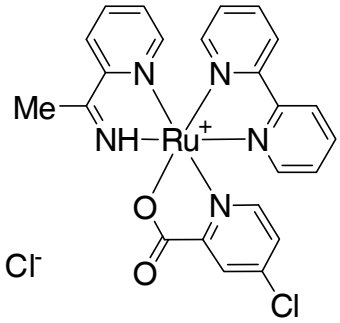





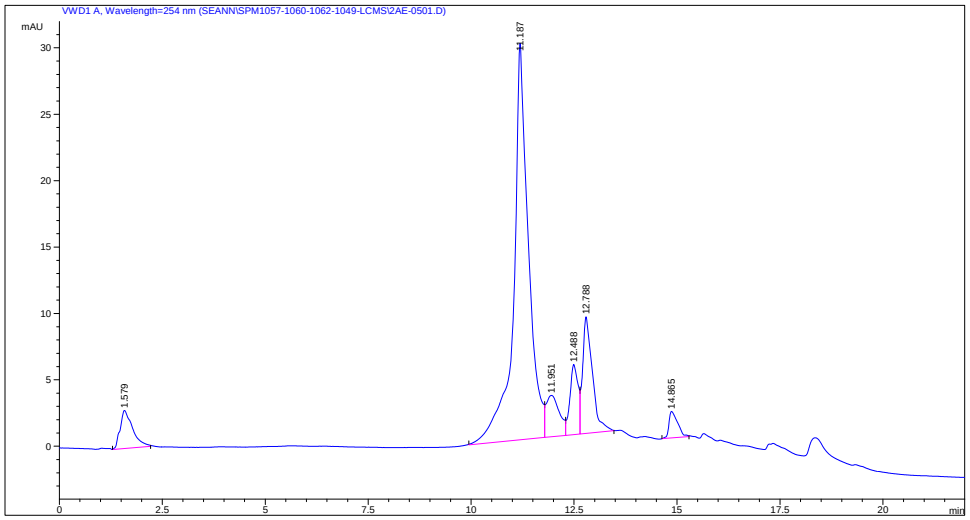

$[M\text{-}Cl]^{+} = 696.1$

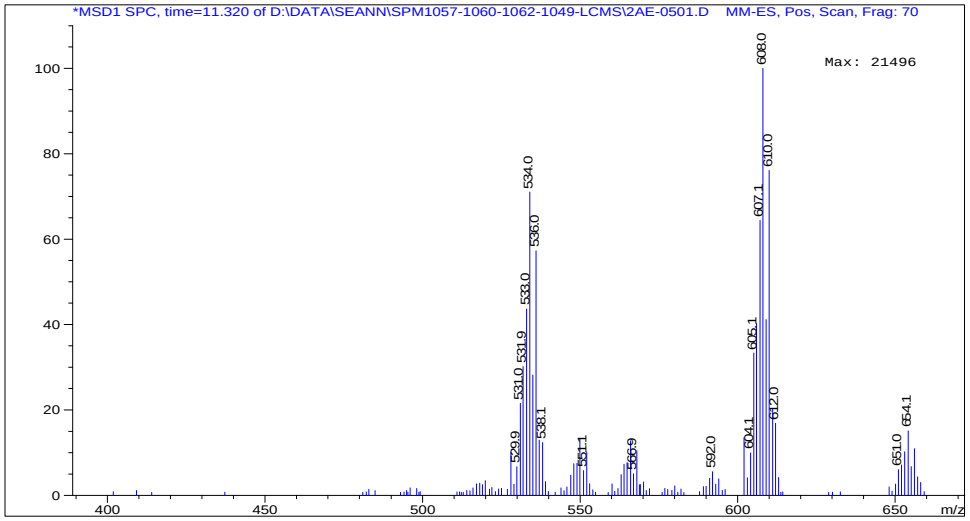


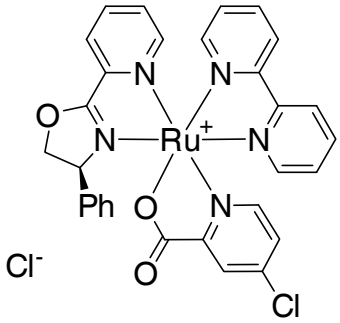





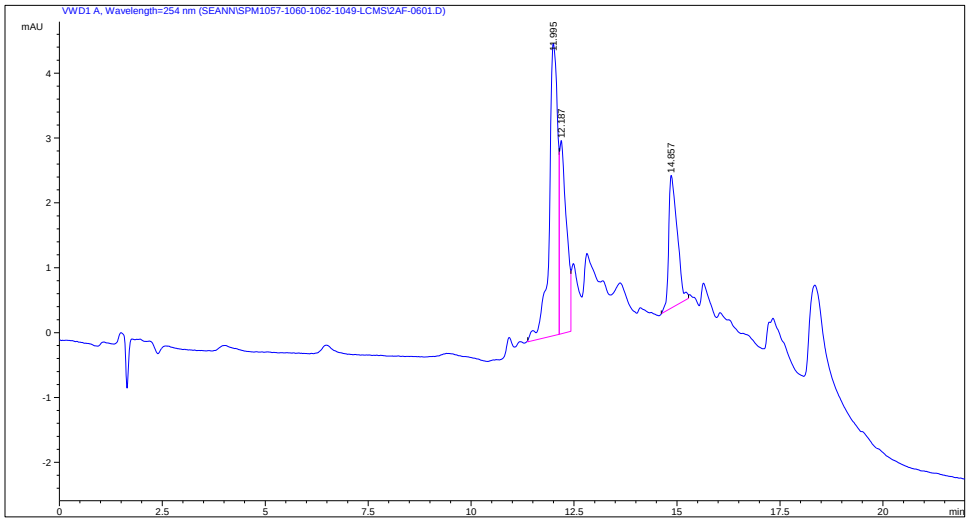

$[M\text{-}Cl]^{+} = 534.0$

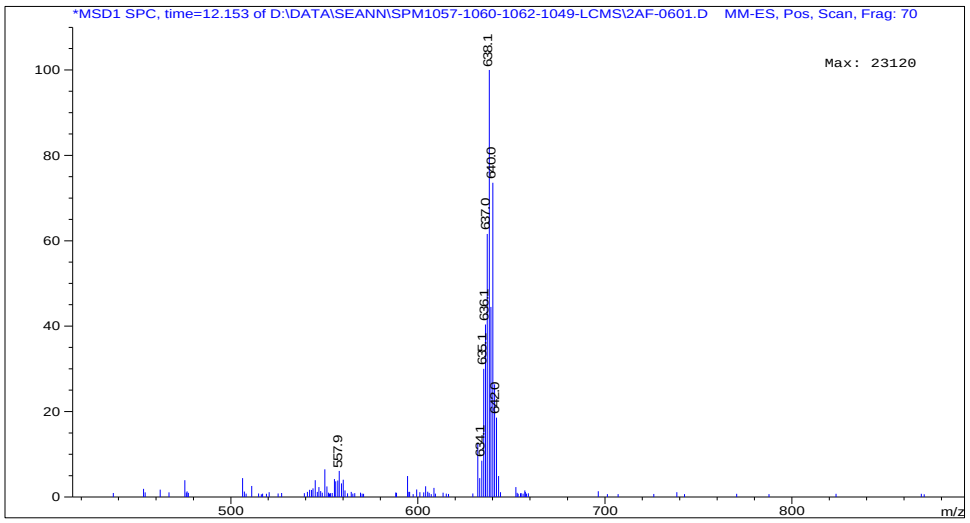


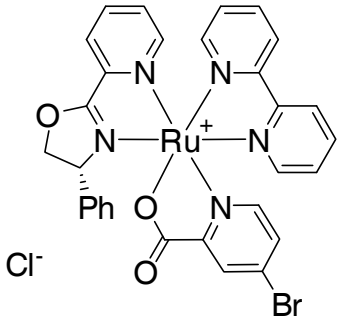





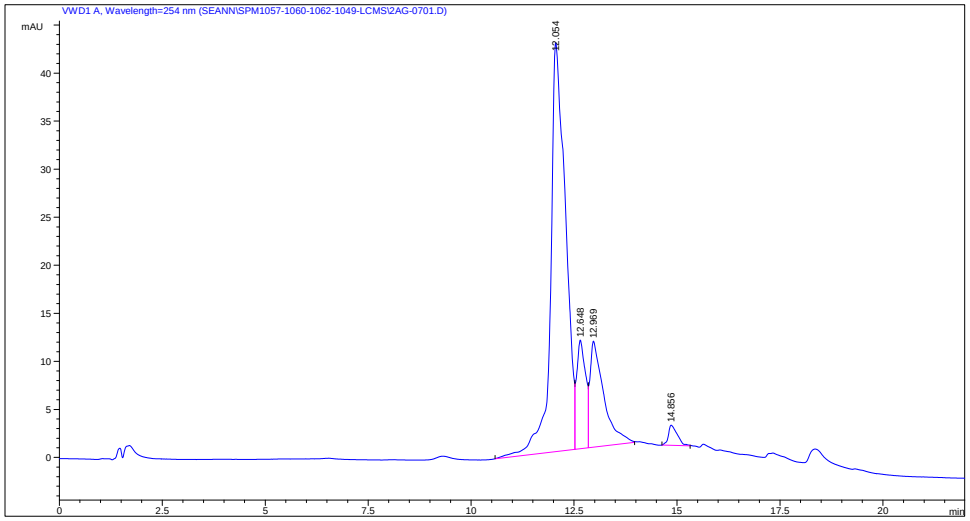

$[M\text{-}Cl]^+ = 638.1$

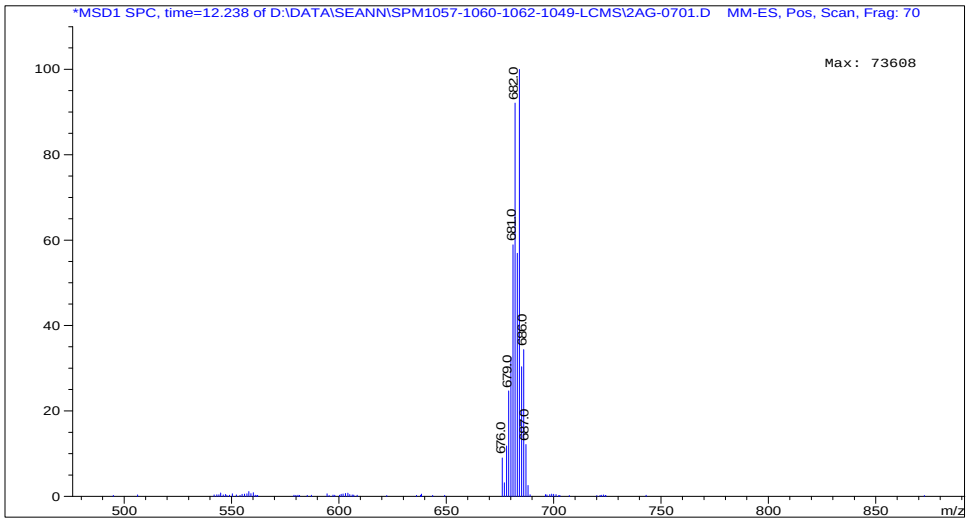


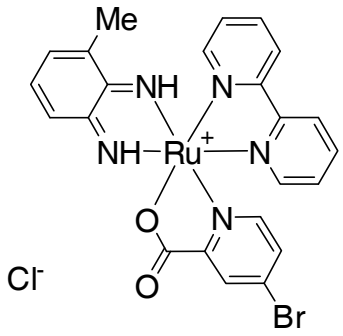





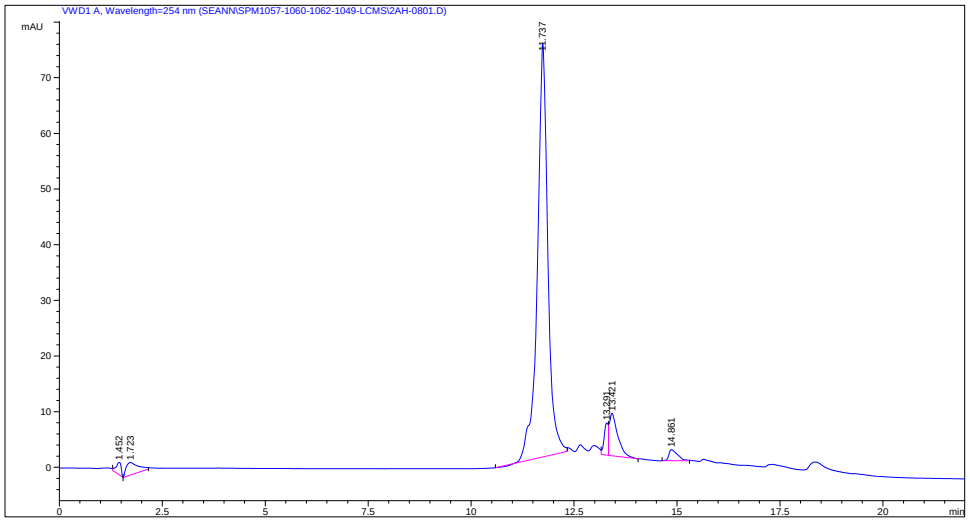

$[M\text{-}Cl]^+ = 682.0$

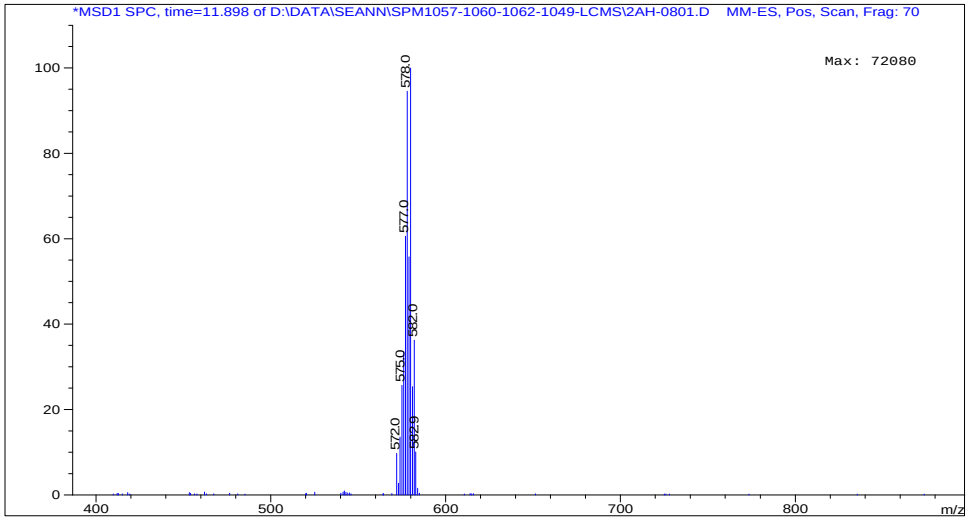


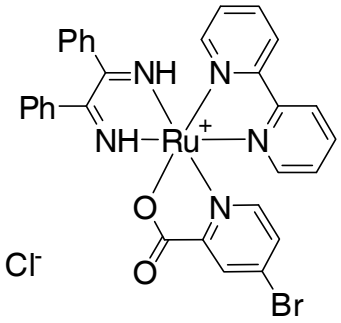





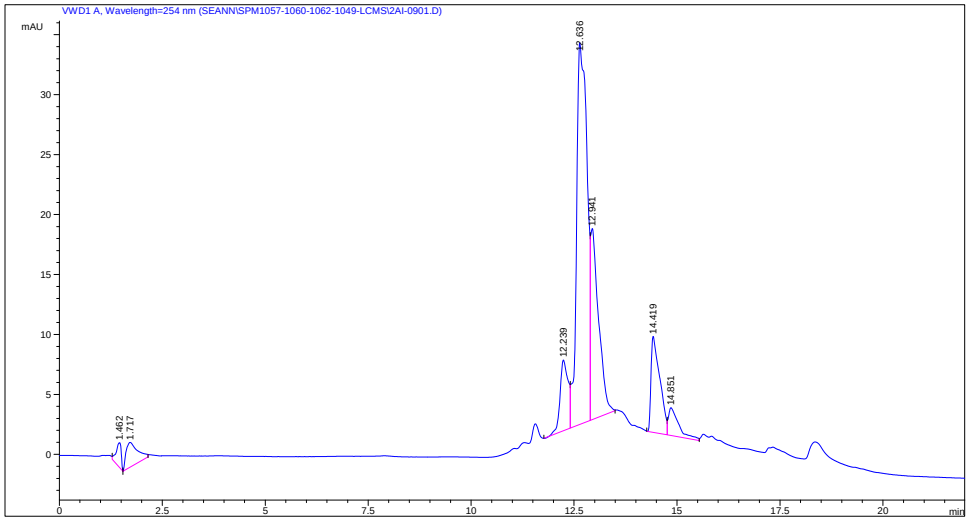

$[M\text{-}Cl]^{+} = 578.0$

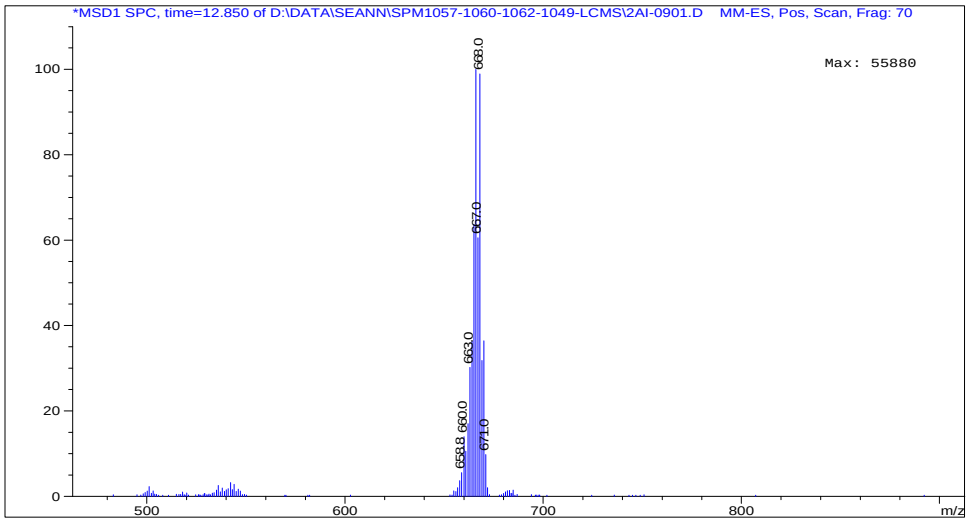


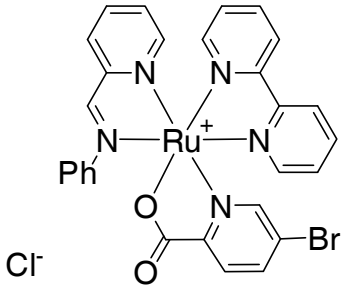





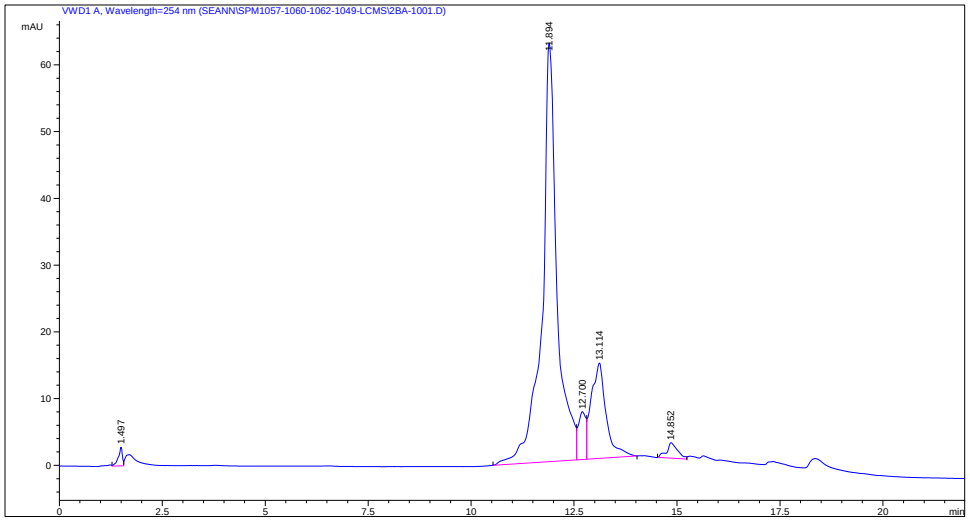

$[M\text{-}Cl]^{+} = 666.0$

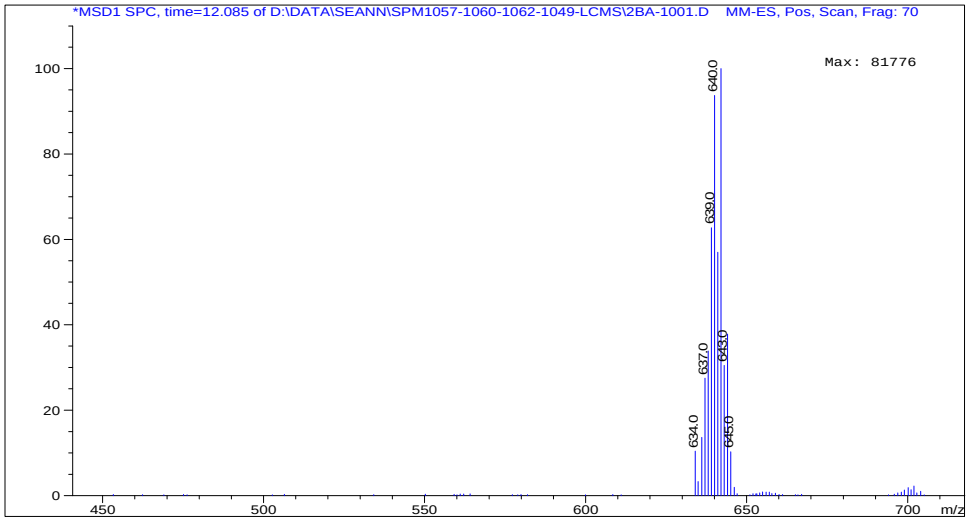


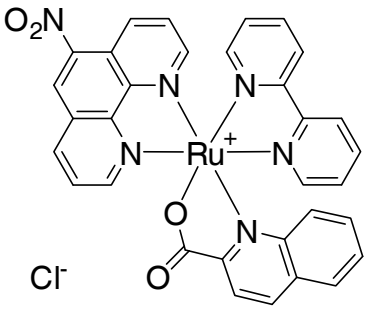





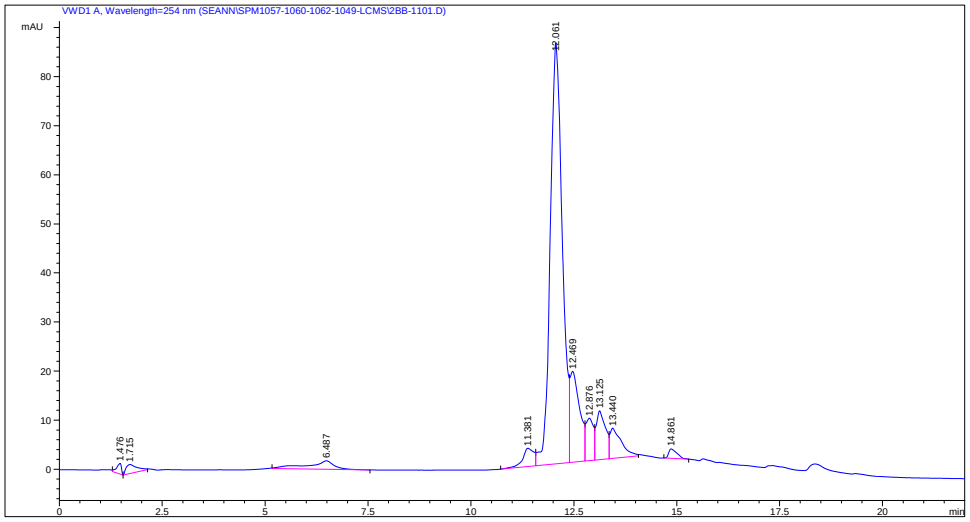

$[M\text{-}Cl]^{+} = 640.0$

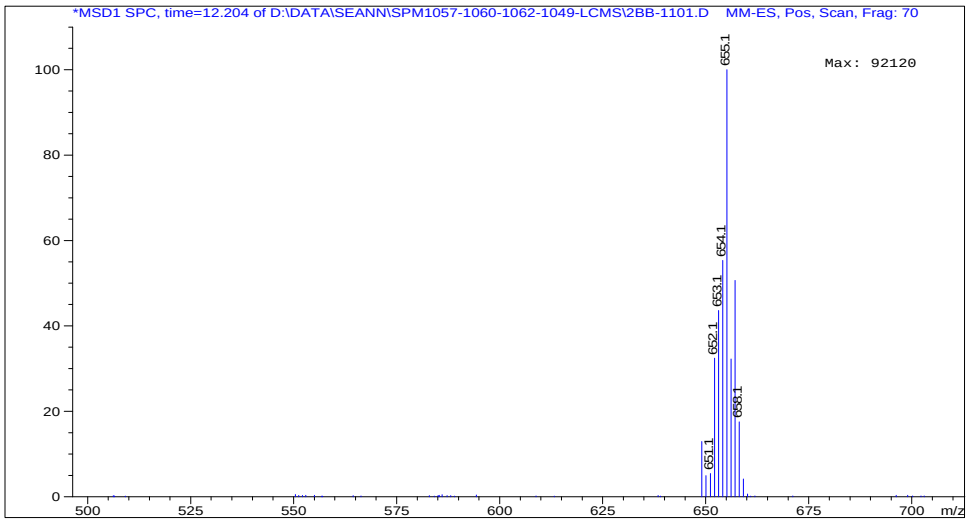


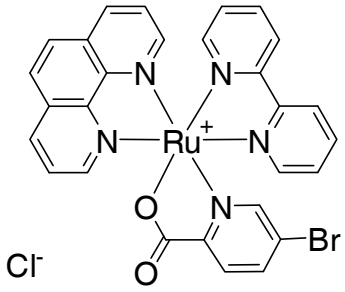





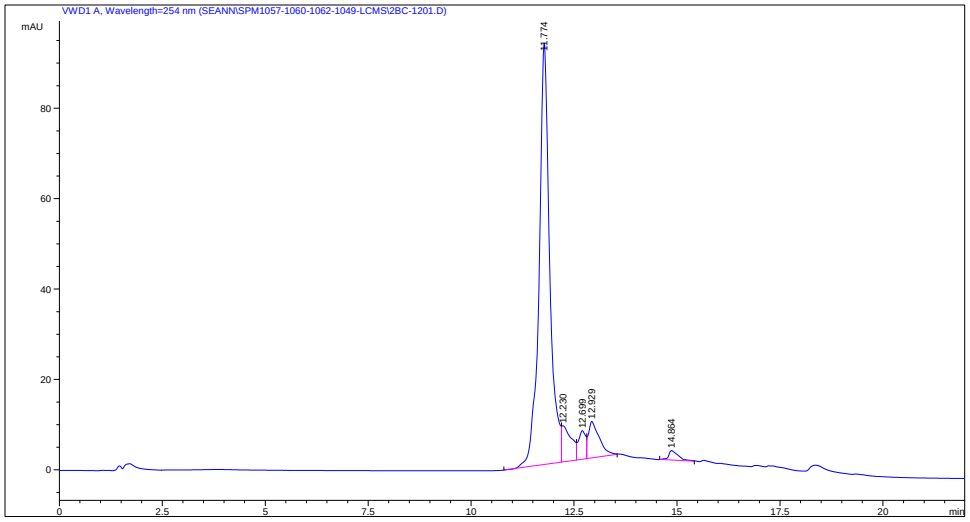

$[M\text{-}Cl]^+ = 655.1$

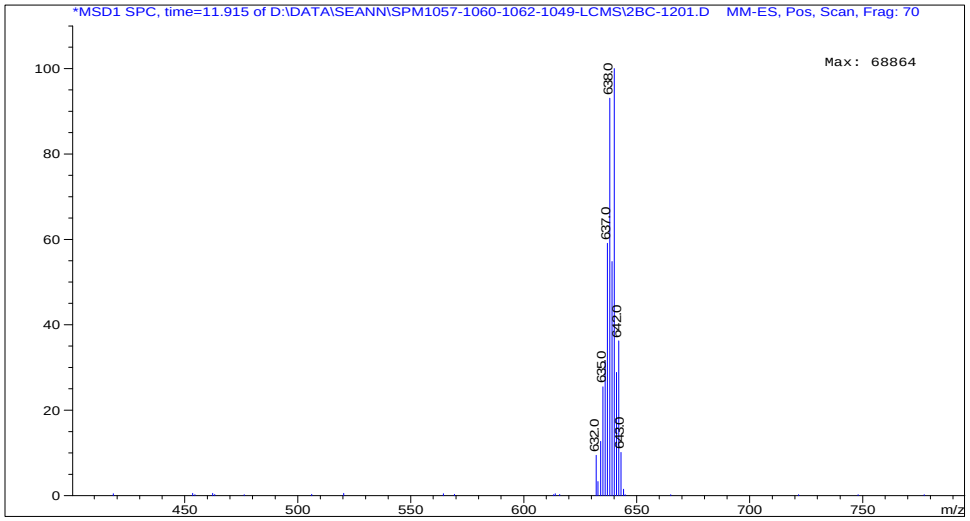


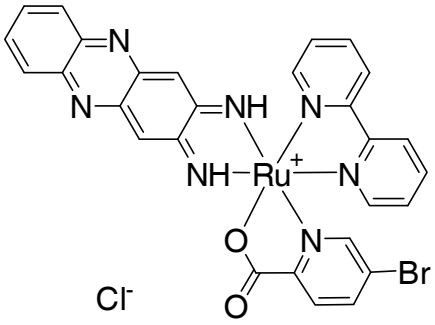





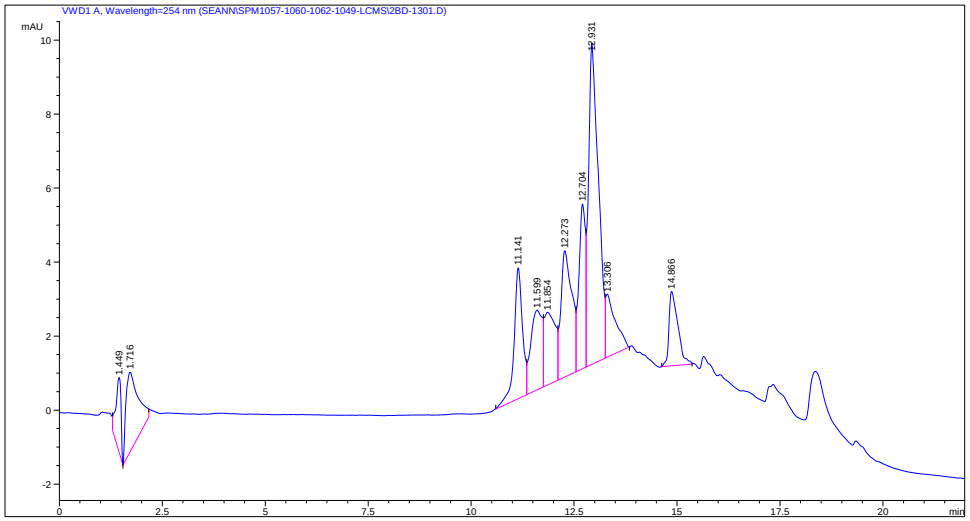

$[M\text{-}Cl]^{+} = 638.0$

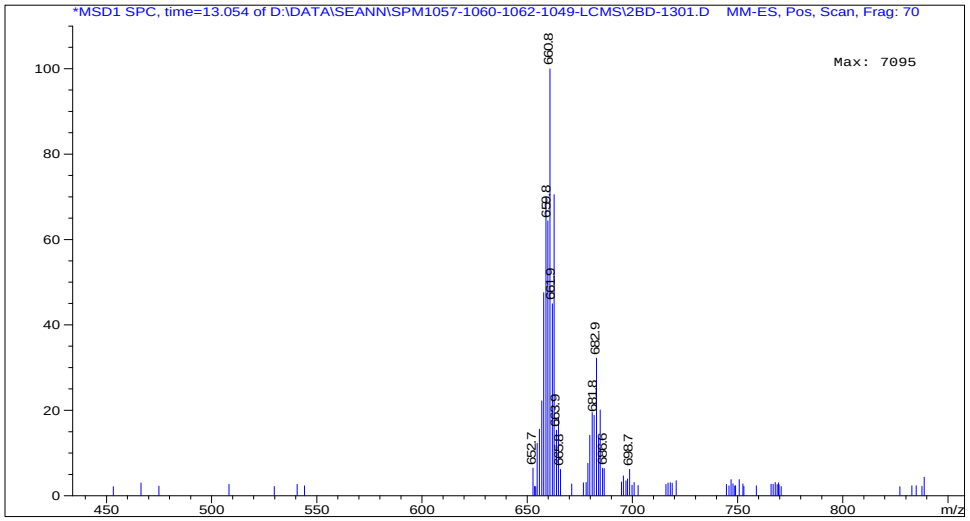


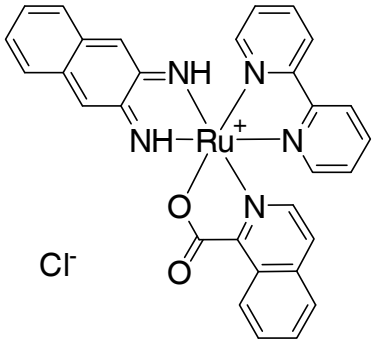





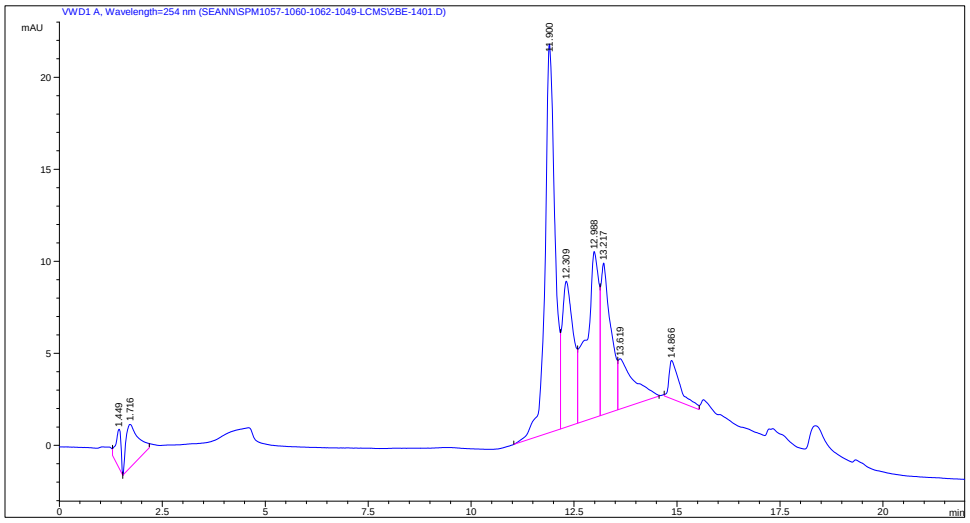

$[M\text{-}Cl]^{+} = 666.0$

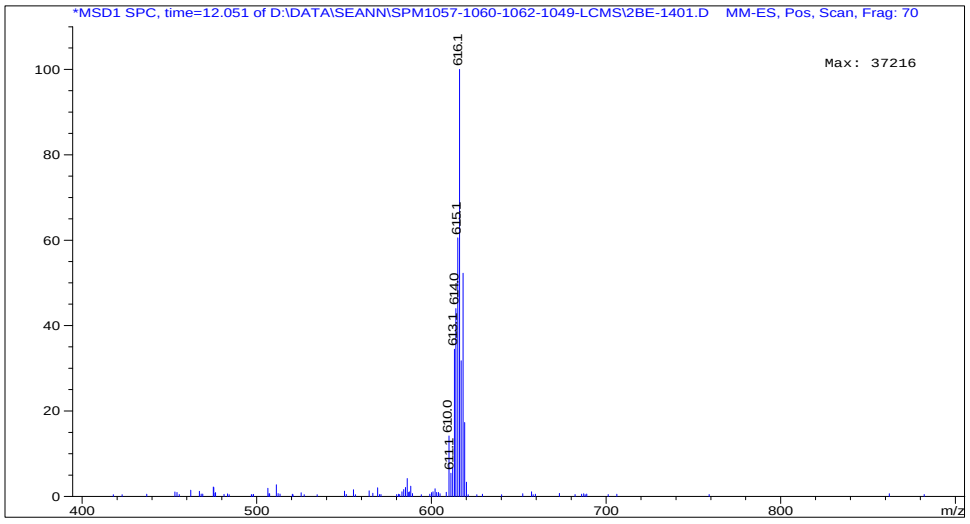


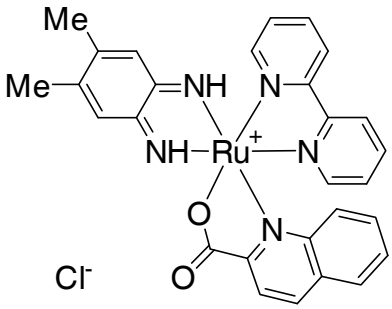





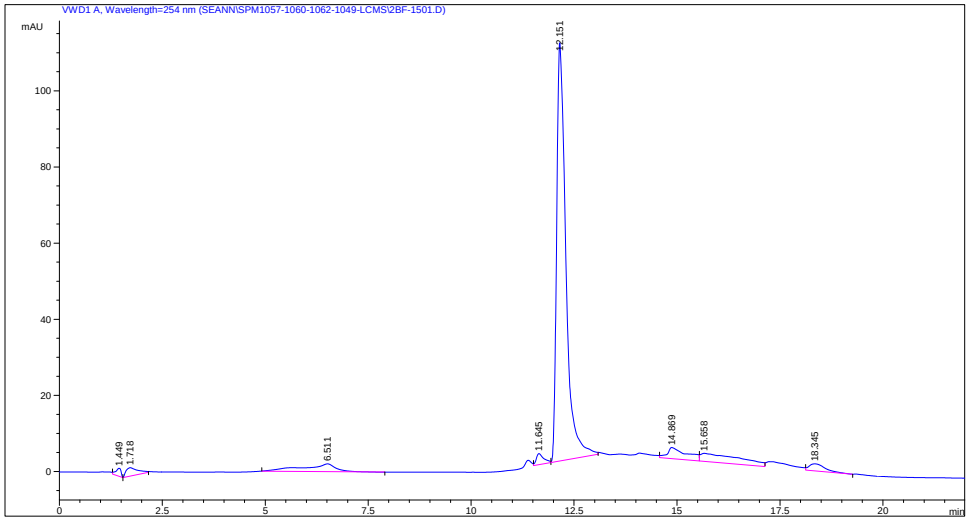

$[M\text{-}Cl]^{+} = 586.08$

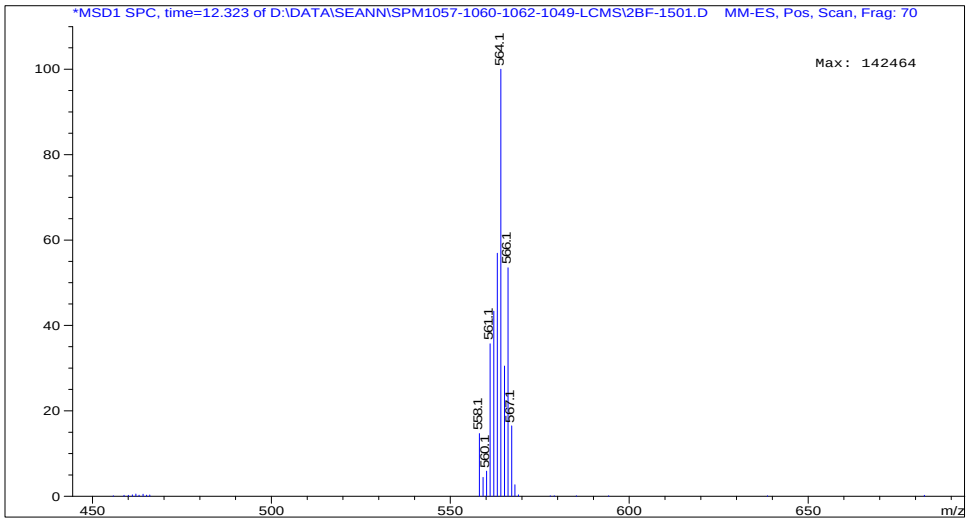


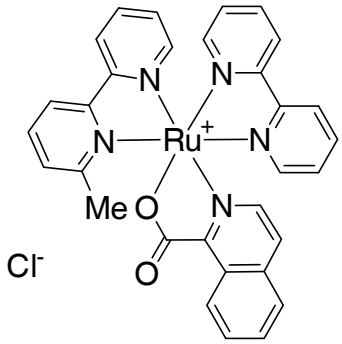





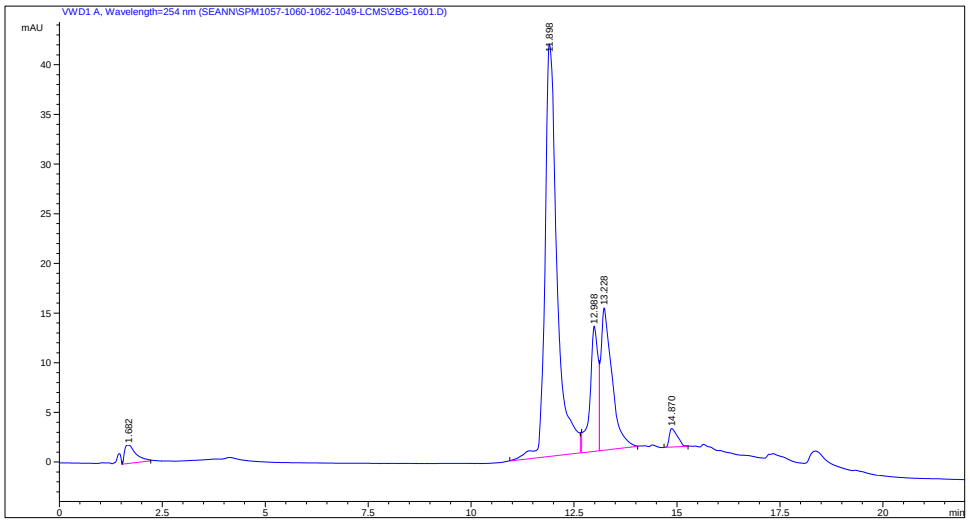

$[M\text{-}Cl]^+ = 564.1$

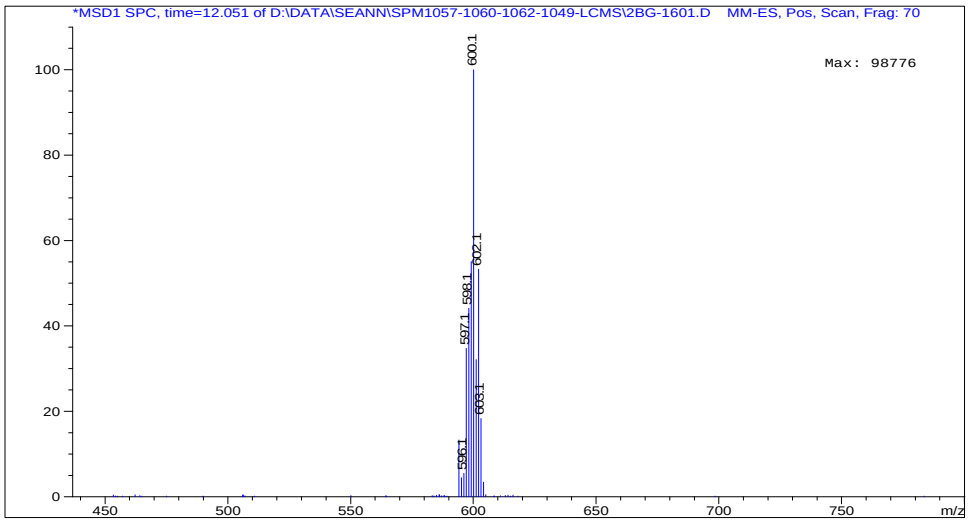


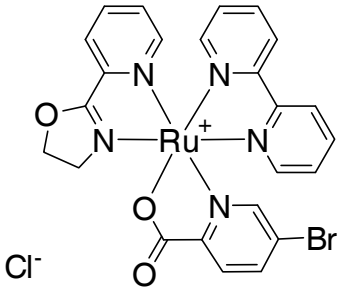





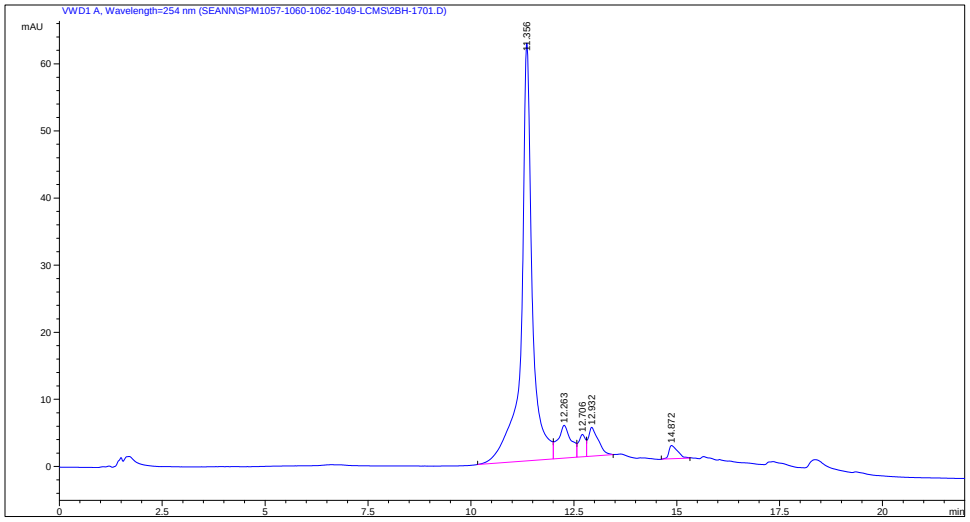

$[M\text{-}Cl]^{+} = 600.1$

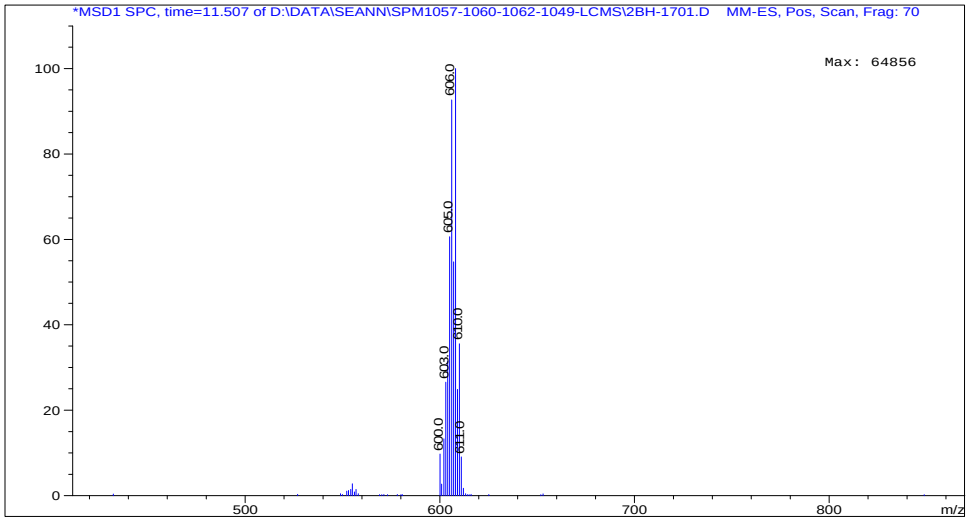


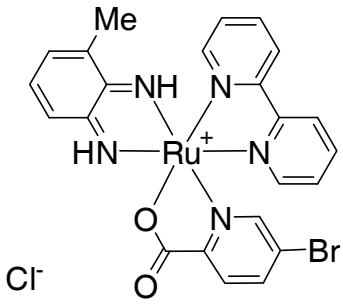





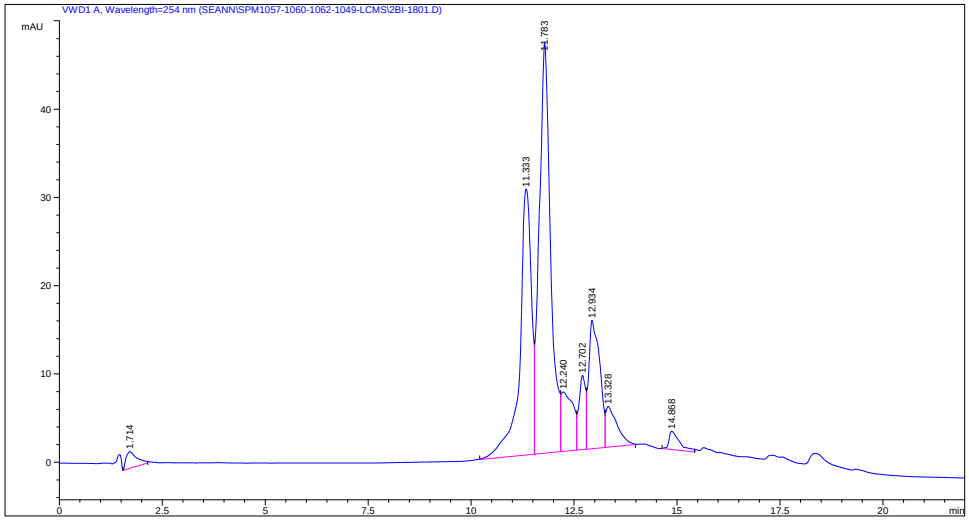

$[M\text{-}Cl]^{+} = 606.0$

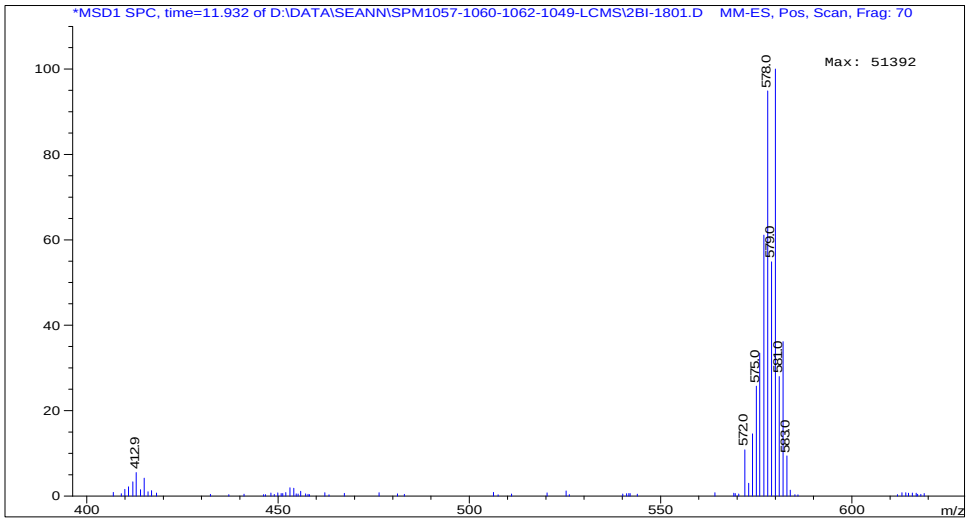


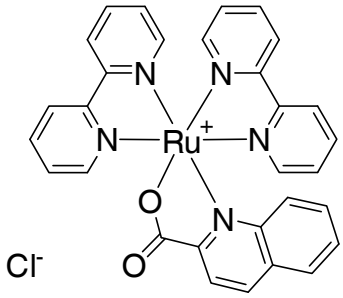





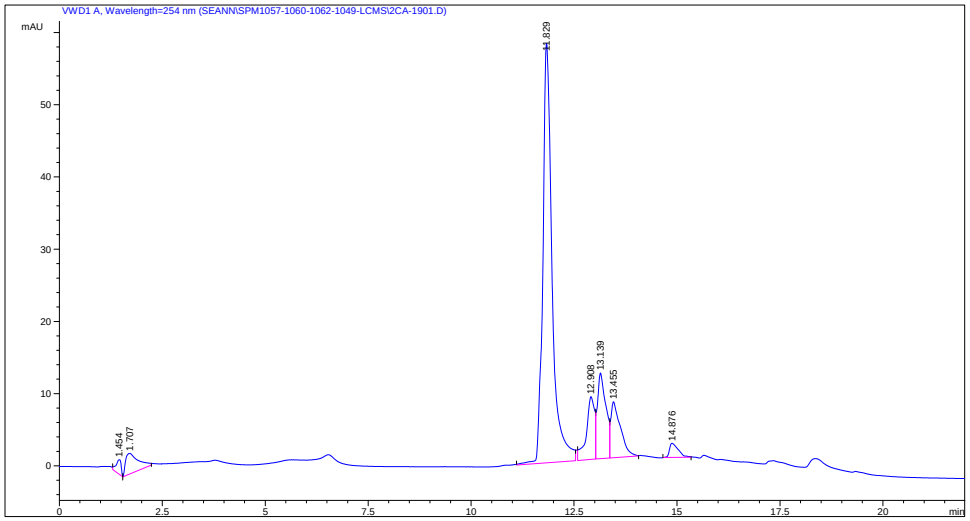

$[M\text{-}Cl]^+ = 578.0$

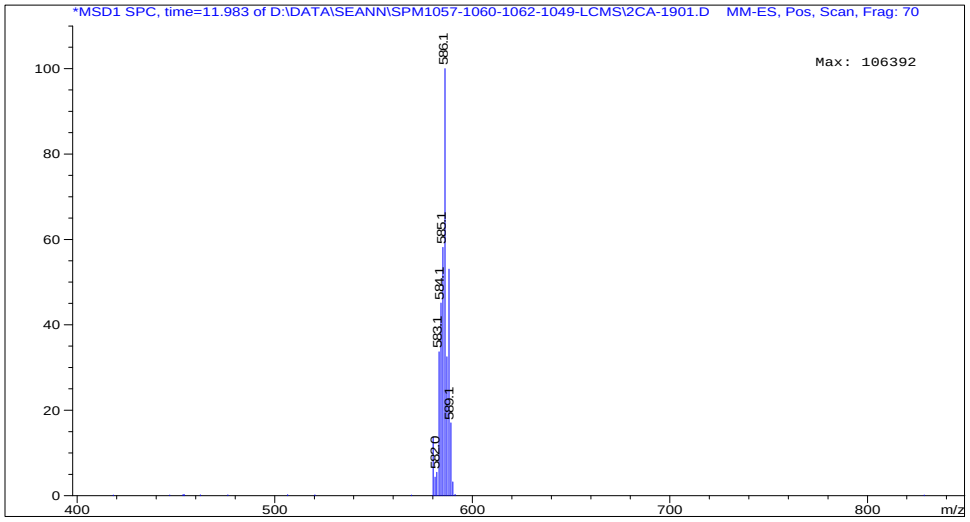


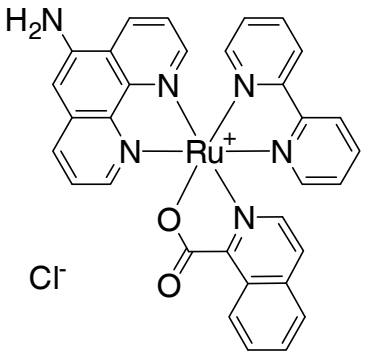





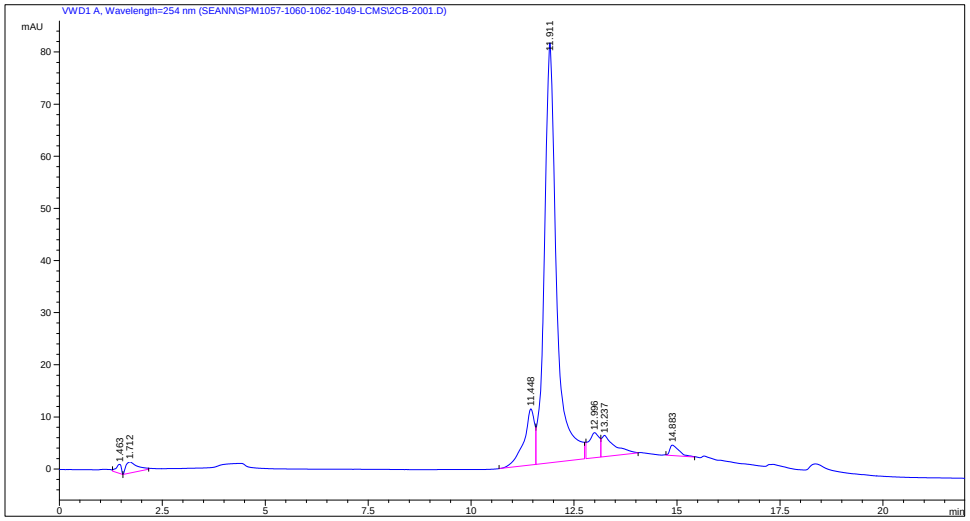

$[M\text{-}Cl]^{+} = 586.1$

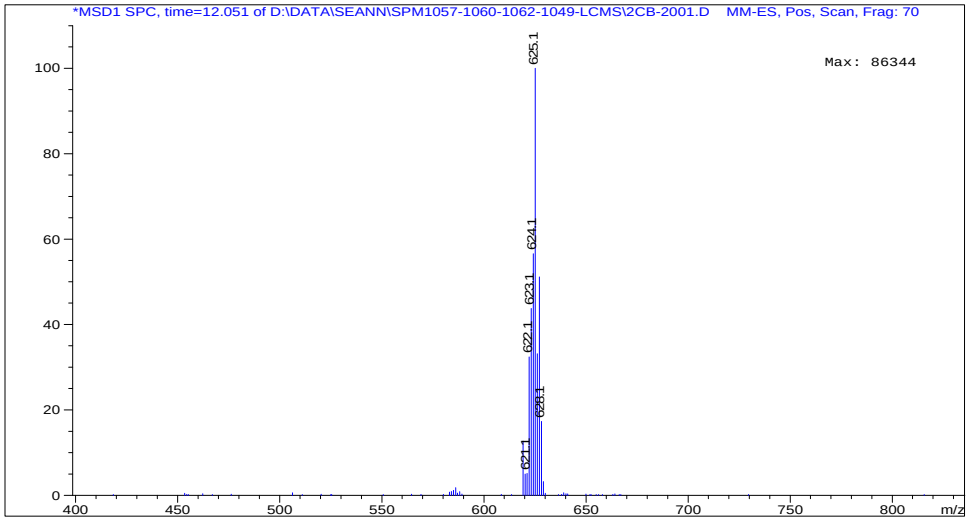


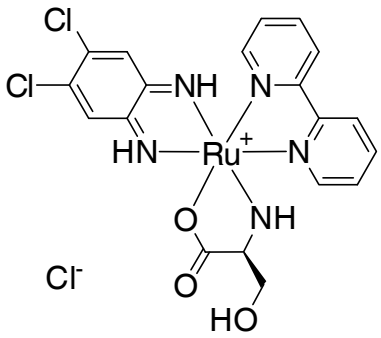





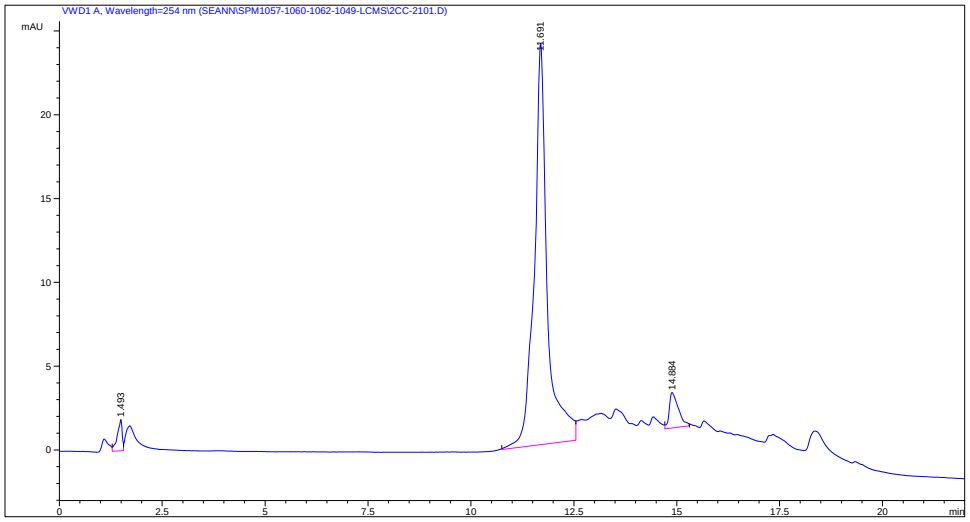

$[M\text{-}Cl]^{+} = 625.1$

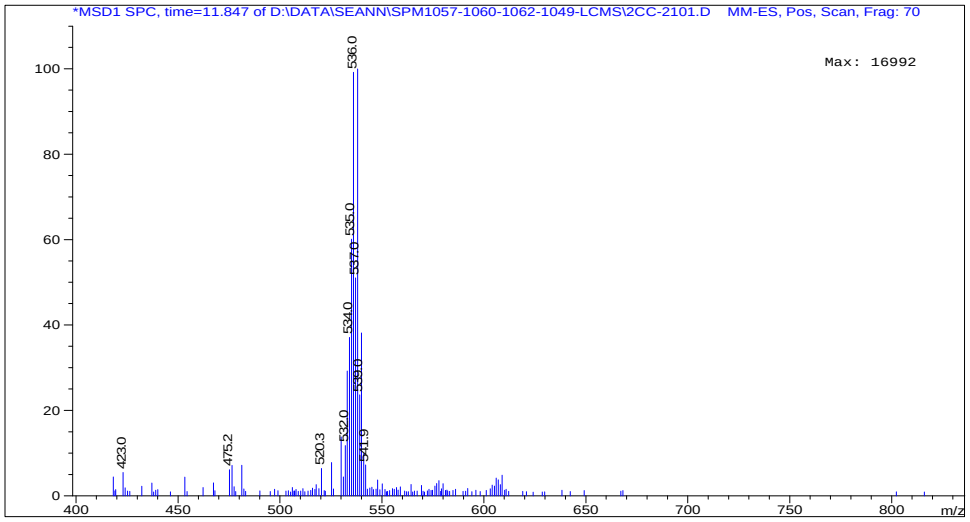


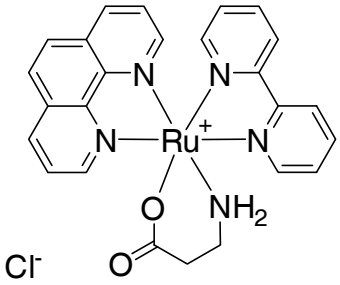





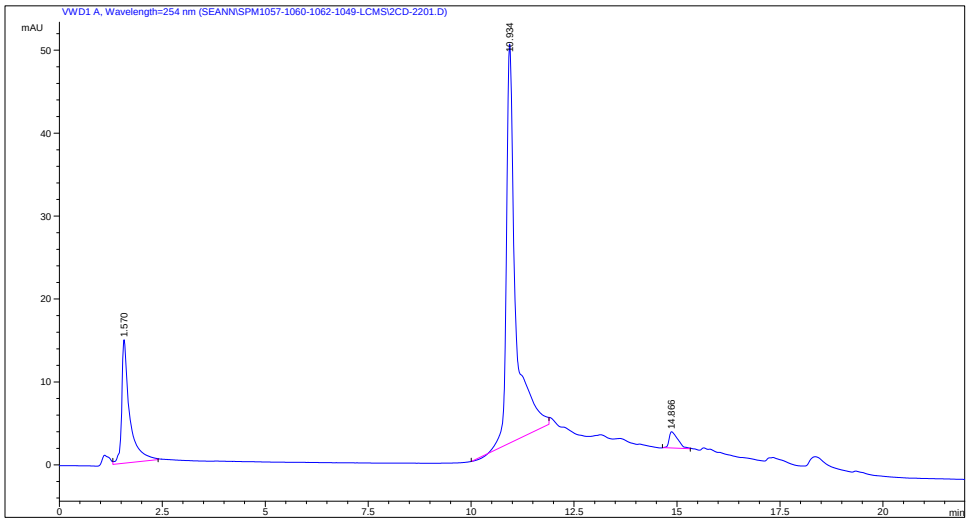

$[M\text{-}Cl]^{+} = 535.0$

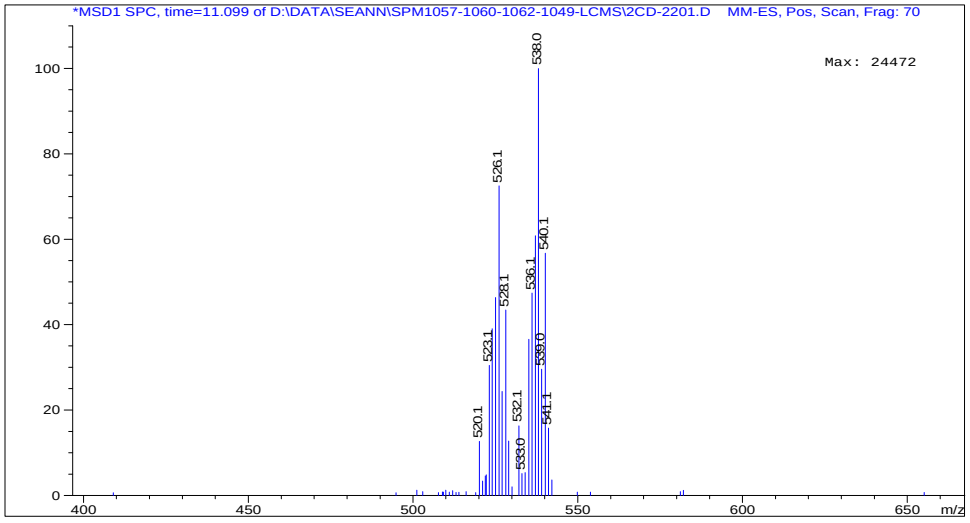


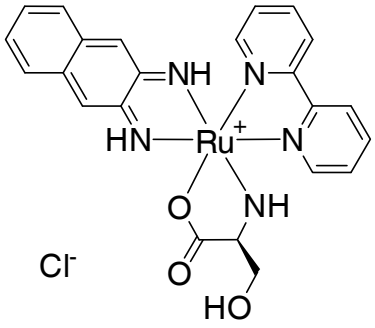





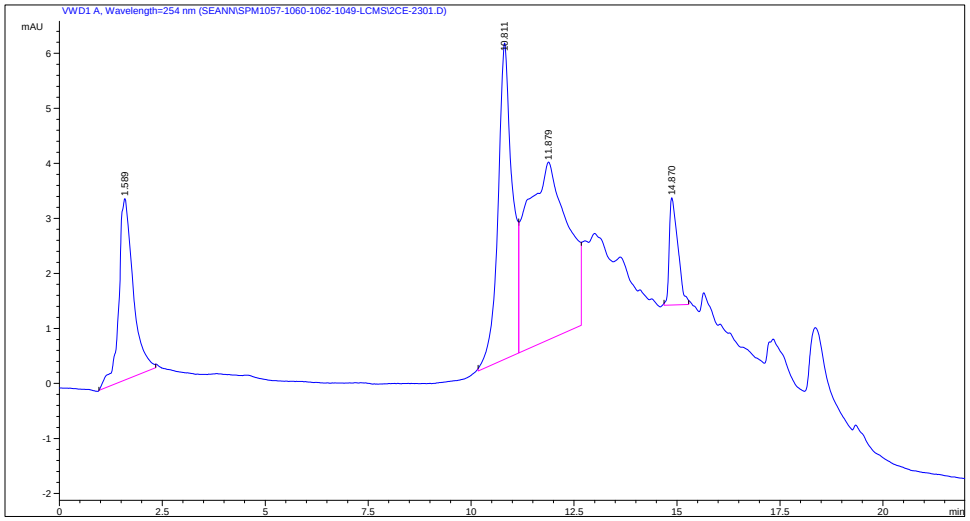

$[M\text{-}Cl]^{+} = 526.1$

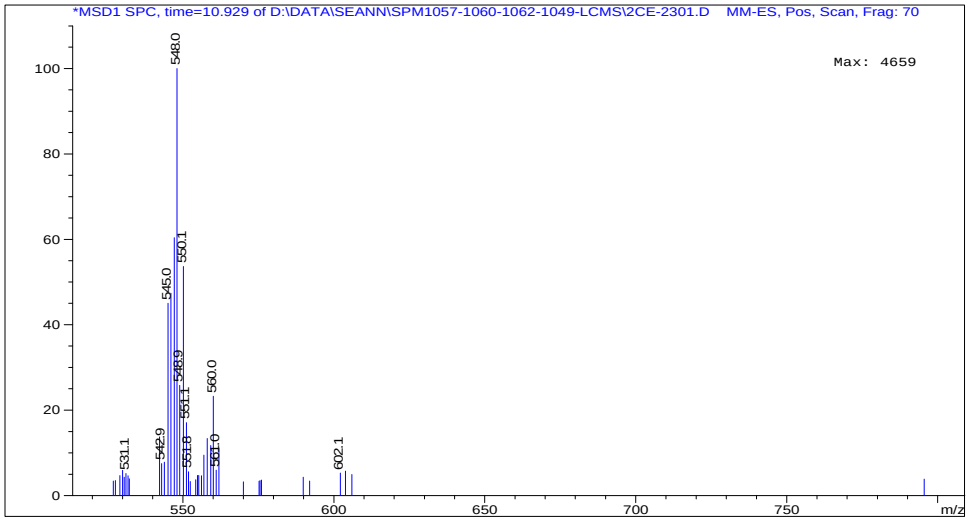


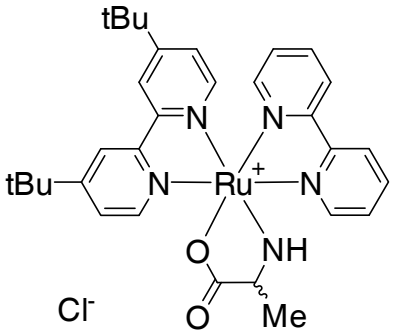





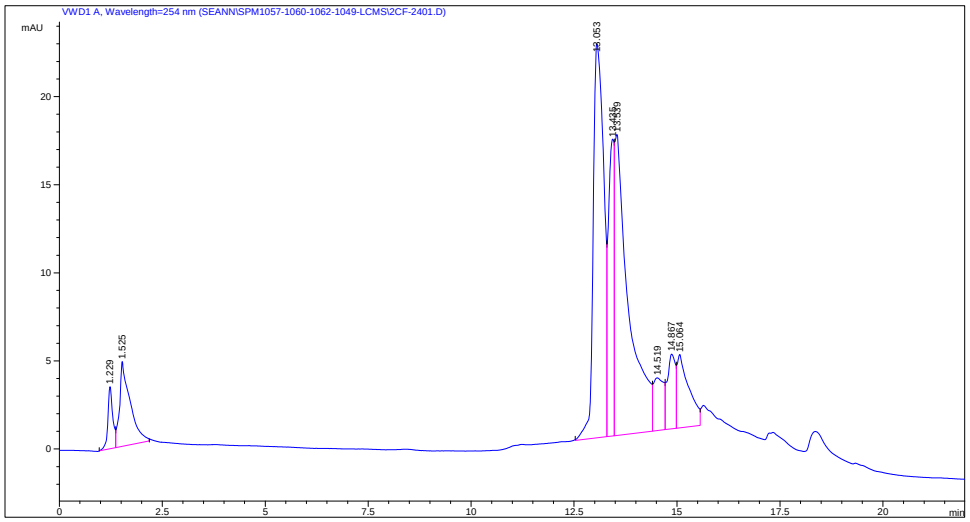

$[M\text{-}Cl]^{+} = 517.1$

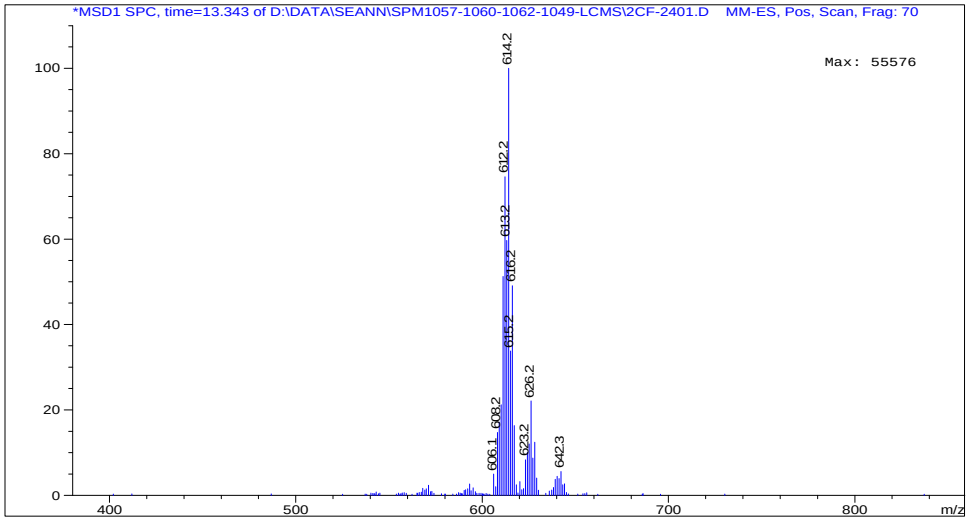


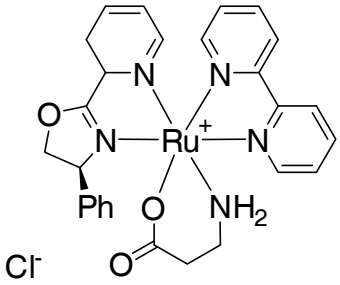





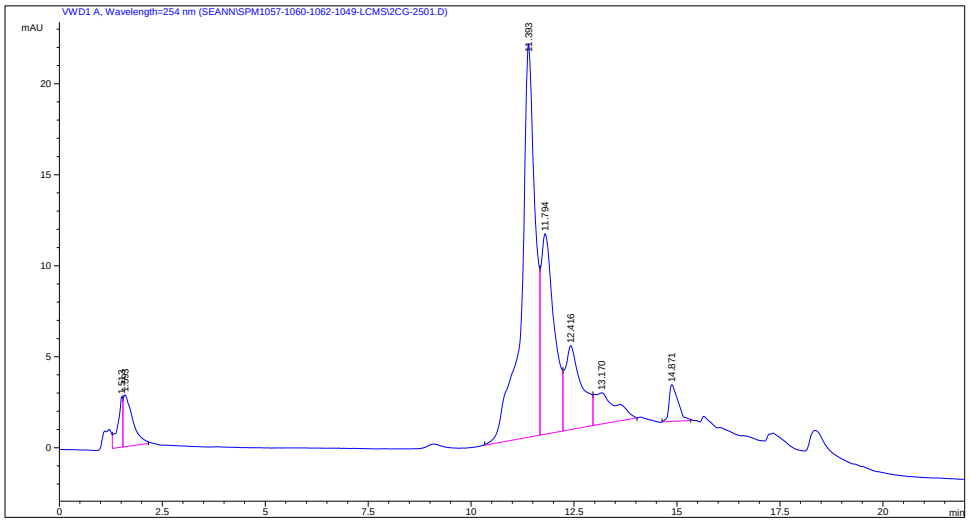

$[M\text{-}Cl]^+ = 613.2$

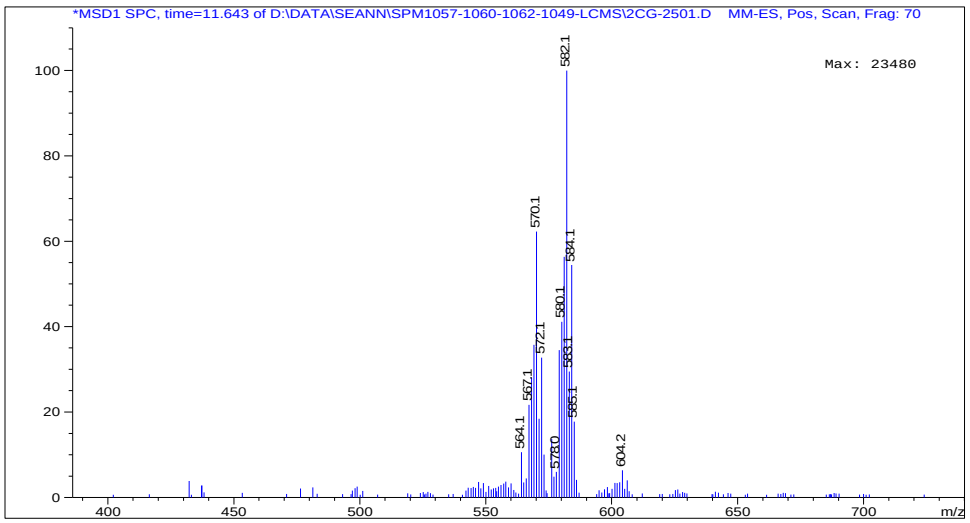


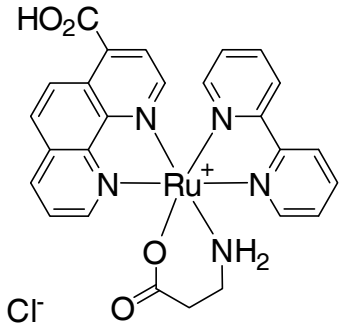





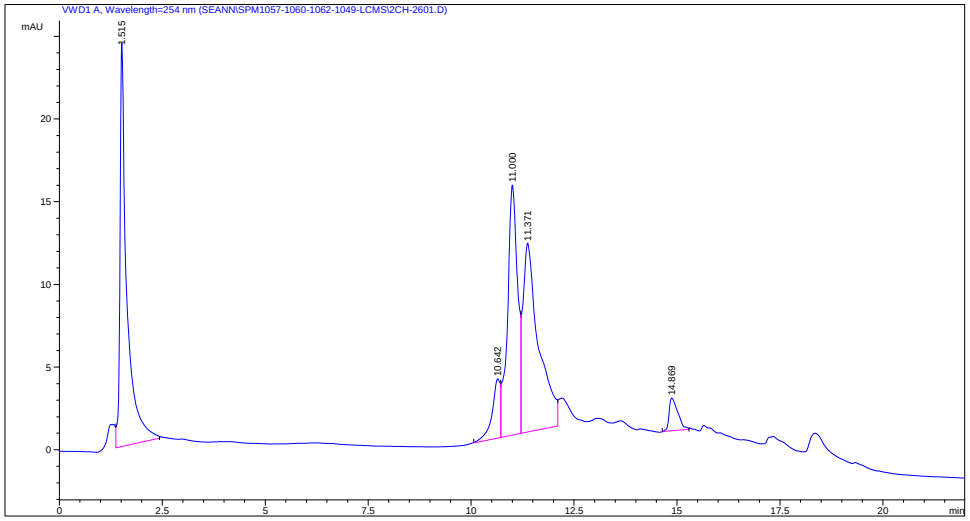

$[M\text{-}Cl]^{+} = 572.1$

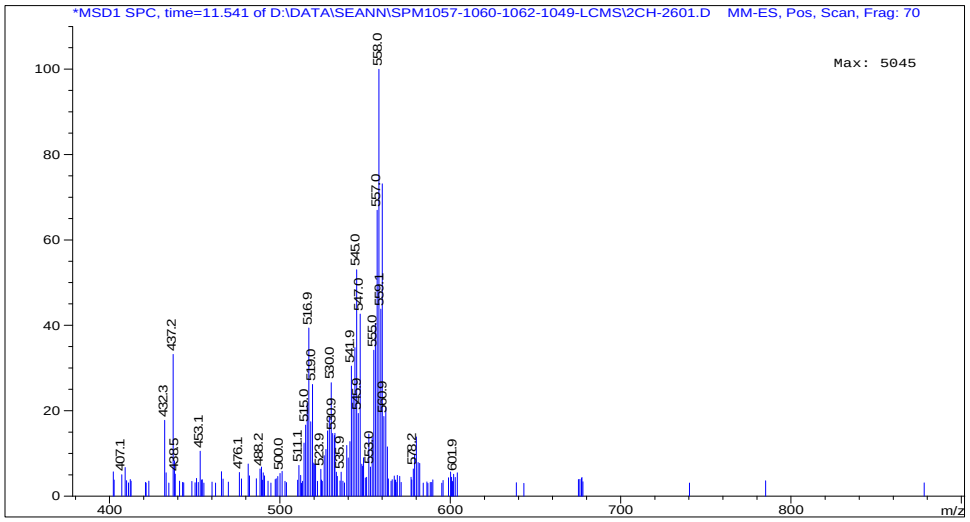


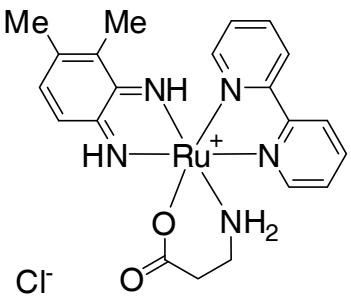





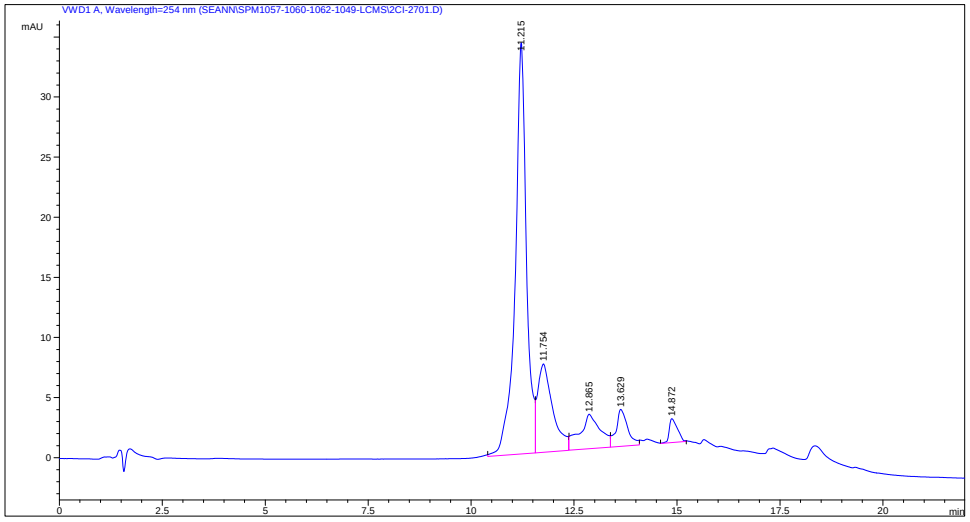

$[M\text{-}Cl]^{+} = 570.1$

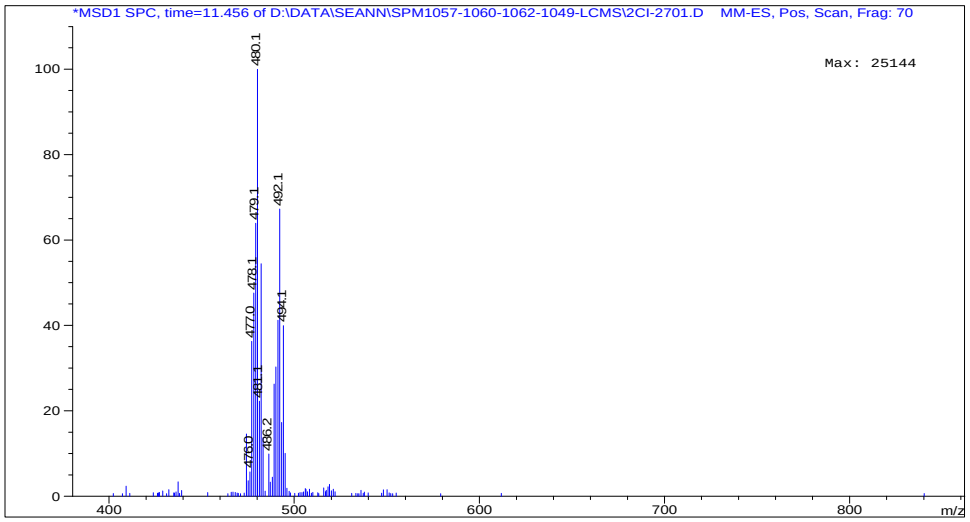


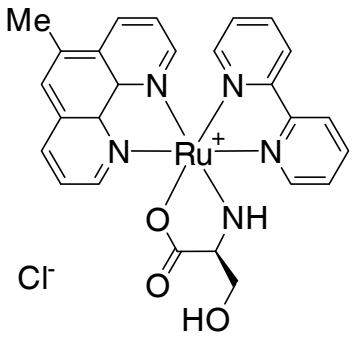





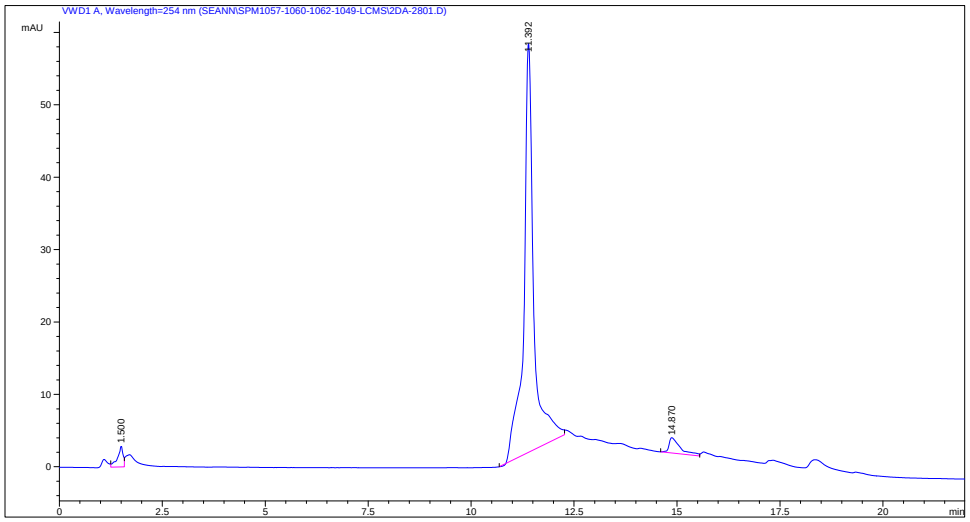

$[M\text{-}Cl]^+ = 480.1$

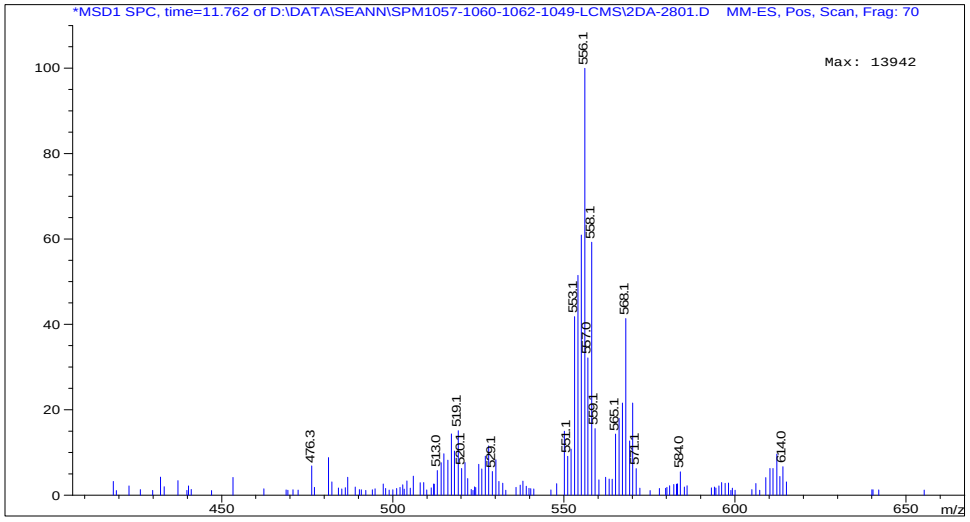


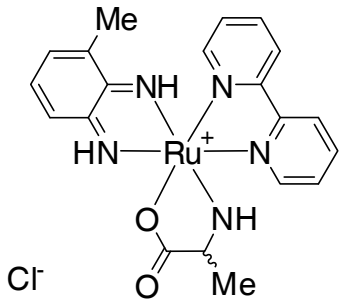





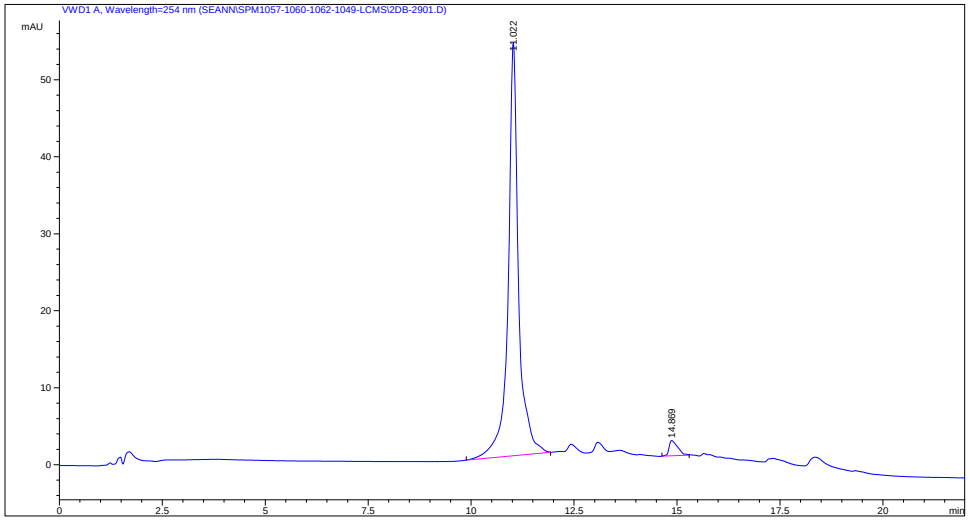

$[M\text{-}Cl]^+ = 557.1$

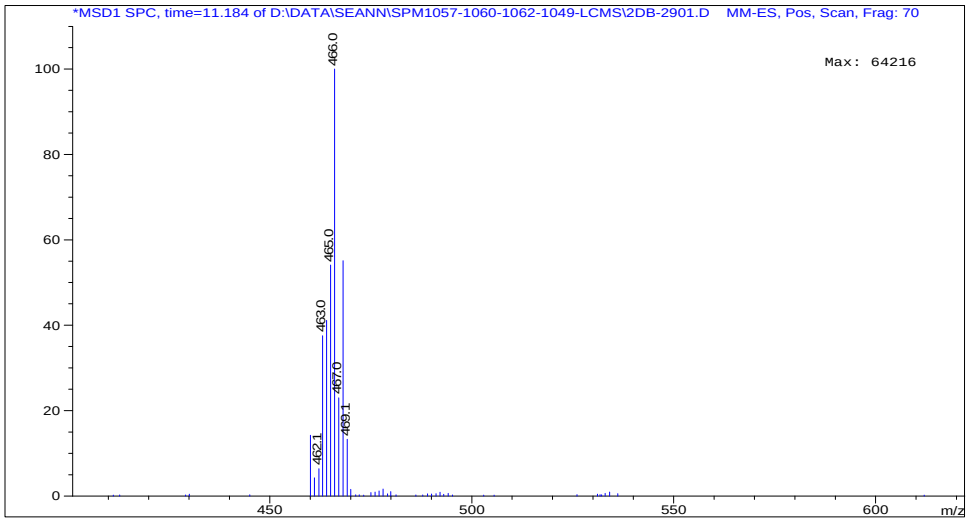


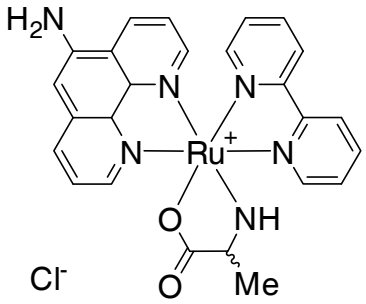





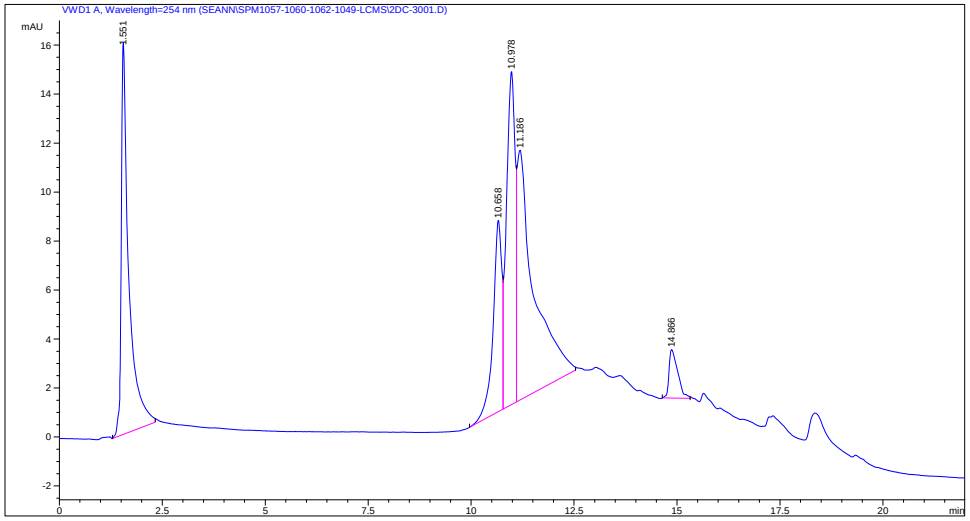

$[M\text{-}Cl]^{+} = 465.1$

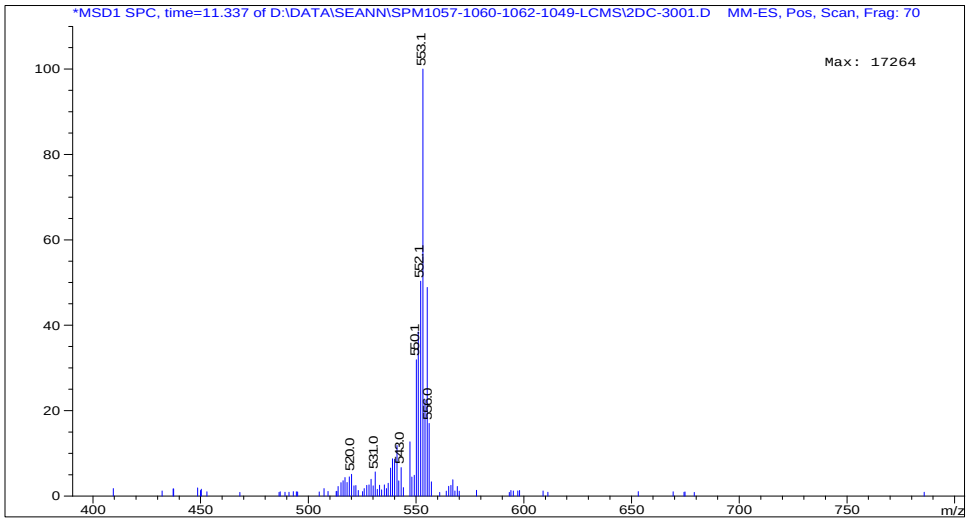


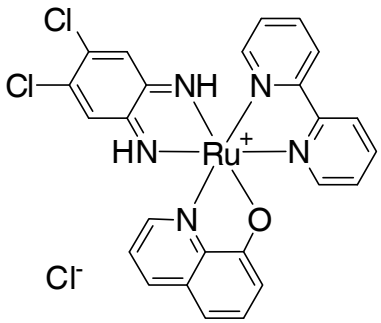





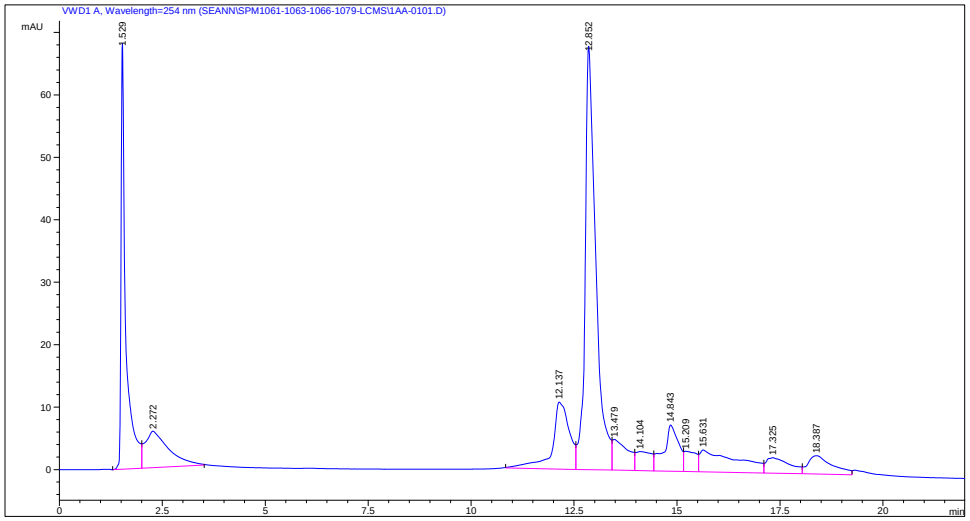

$[M\text{-}Cl]^{+} = 542.1$

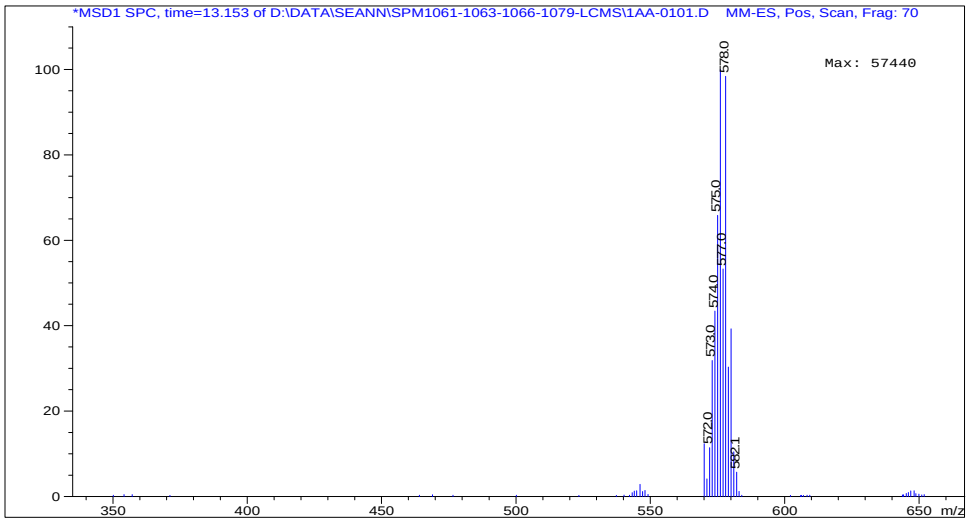


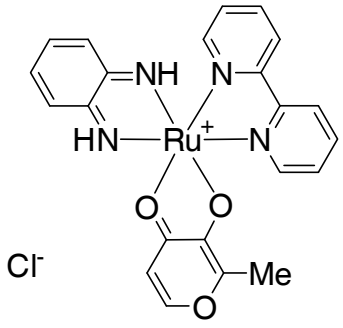





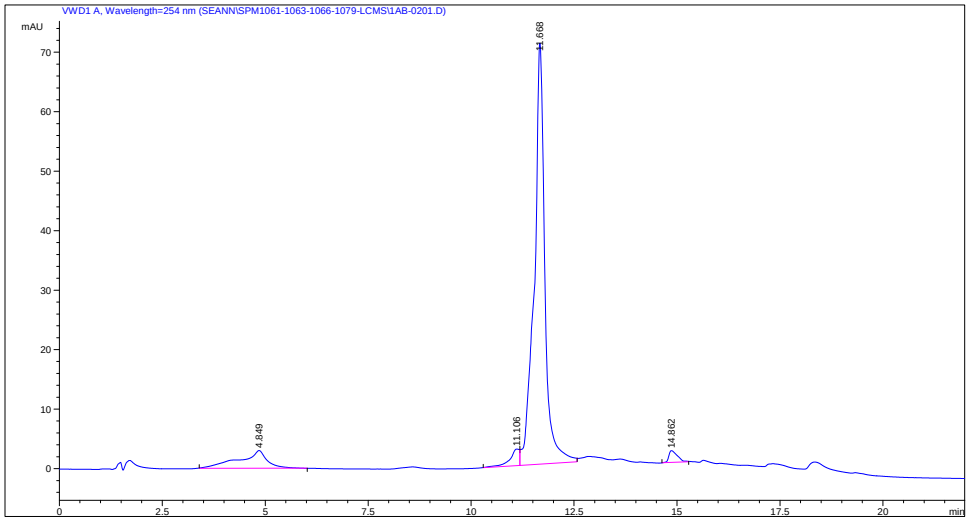

$[M\text{-}Cl]^{+} = 576.0$

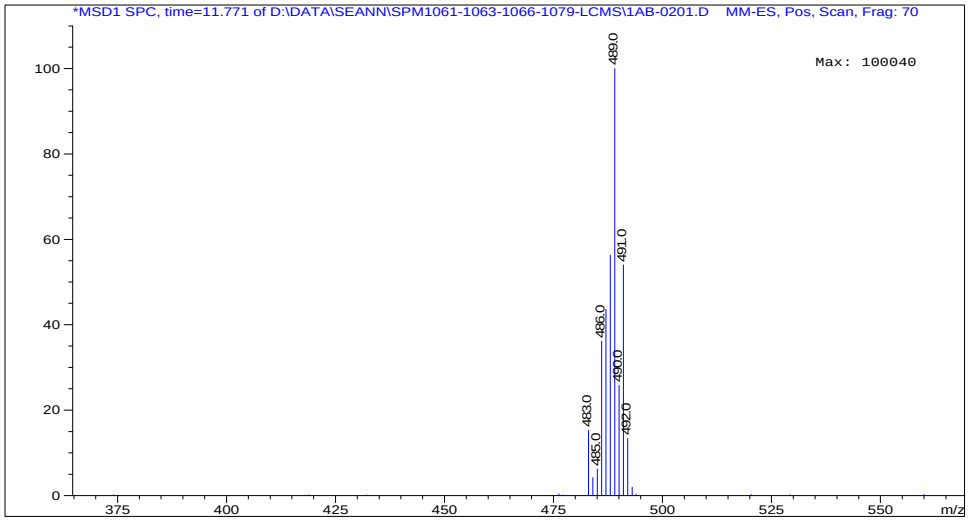


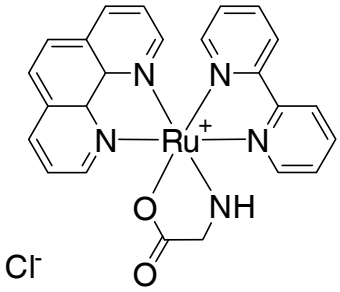





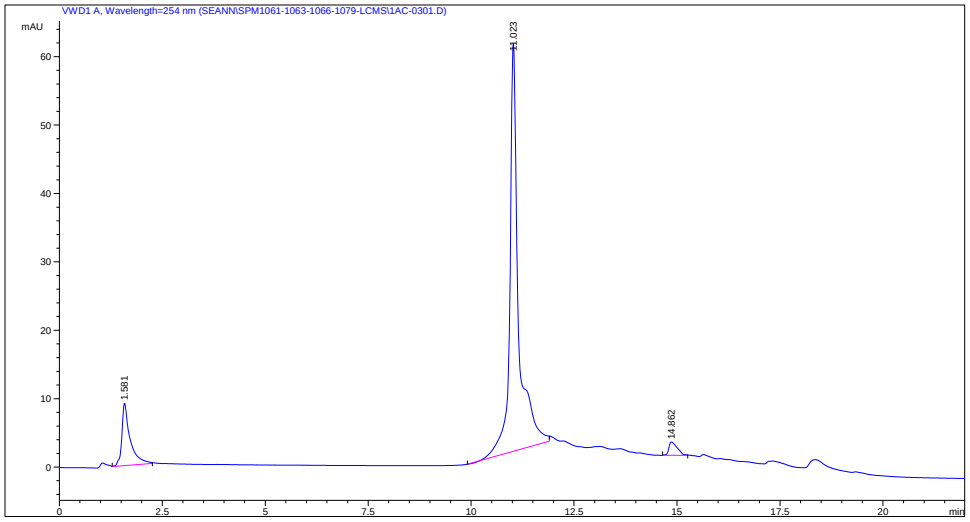

$[M\text{-}Cl]^{+} = 489.1$

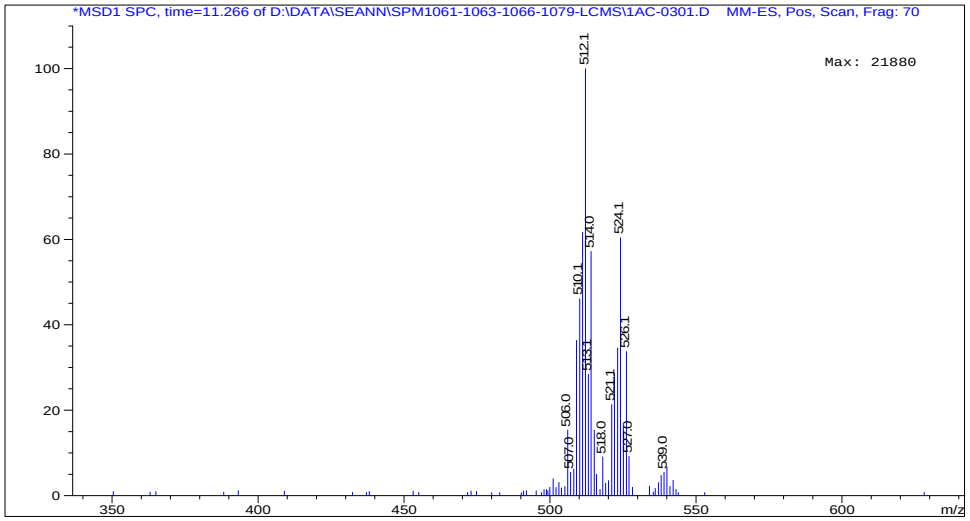


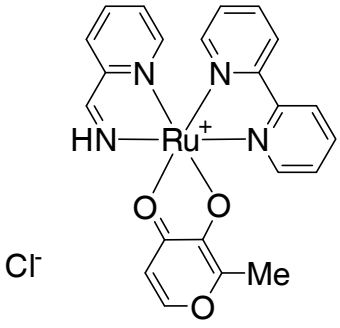





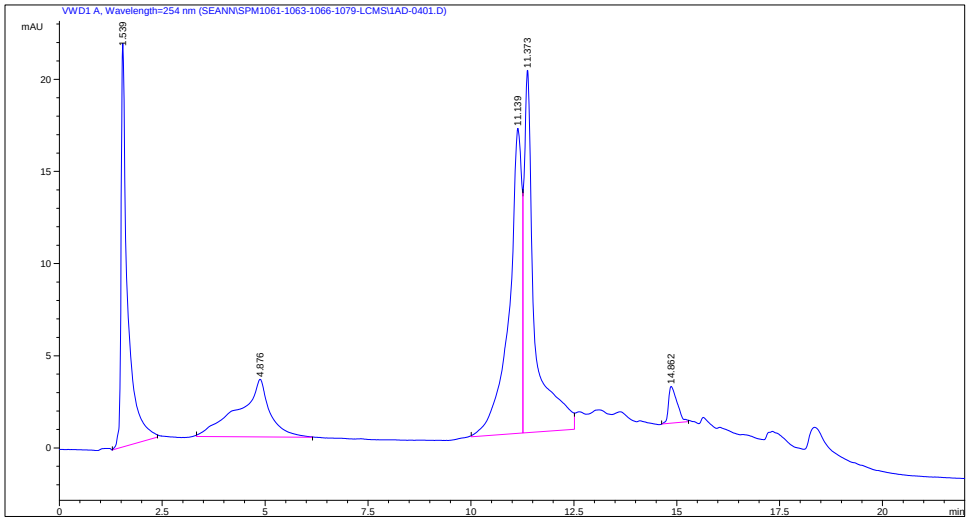

$[M\text{-}Cl]^{+} = 513.1$

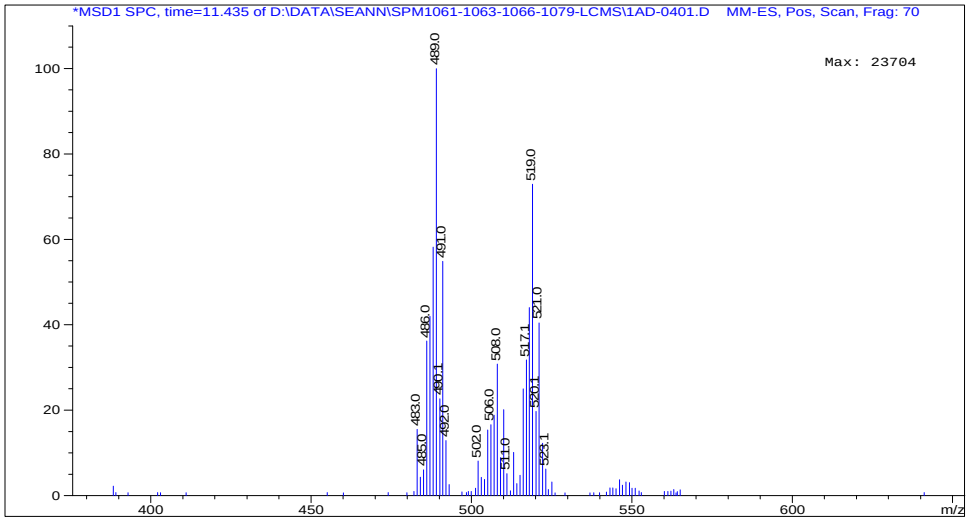


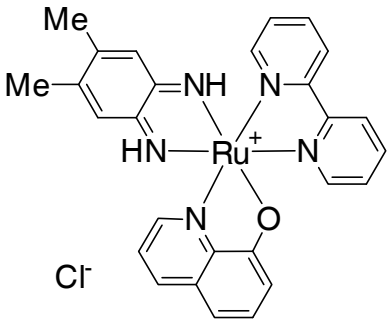





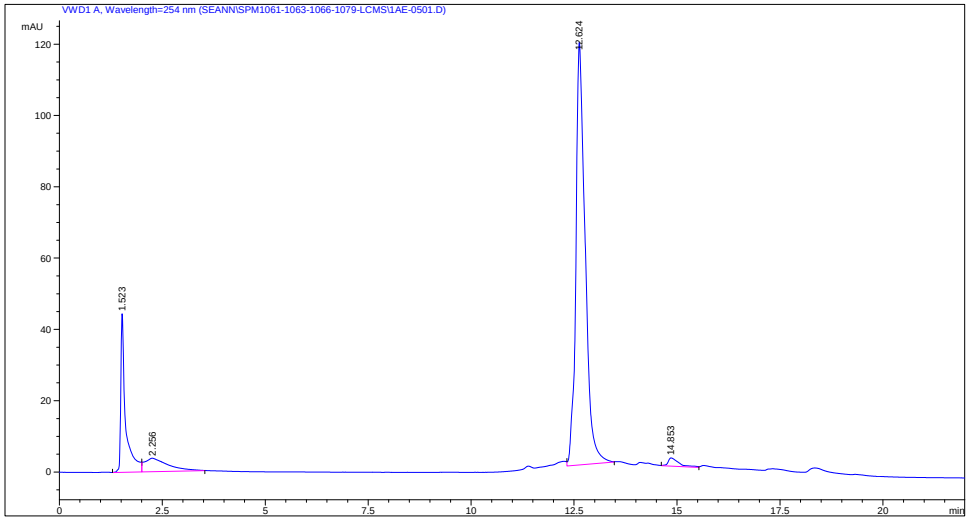

$[M\text{-}Cl]^{+} = 489.1$

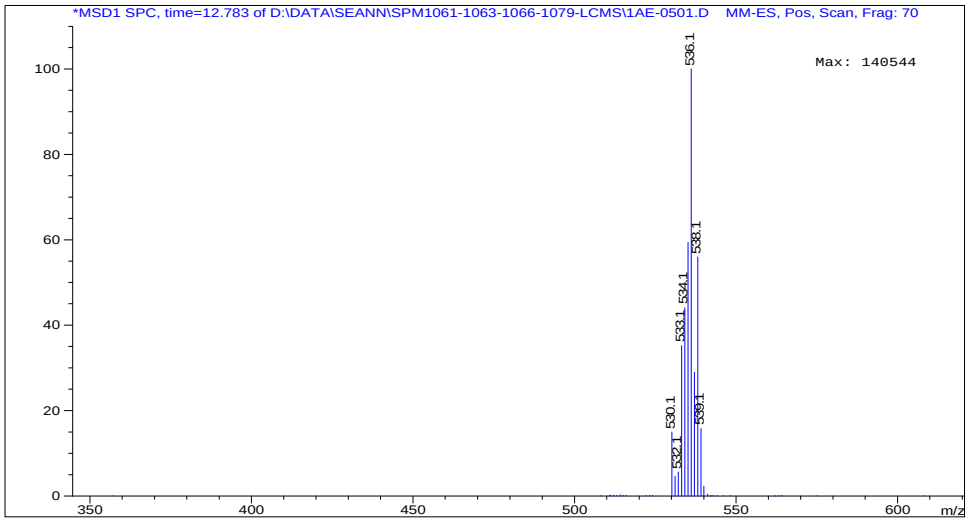


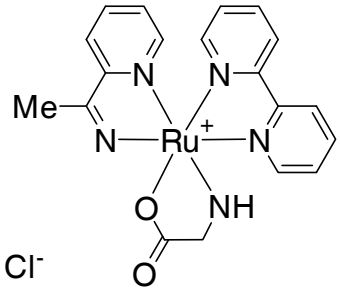





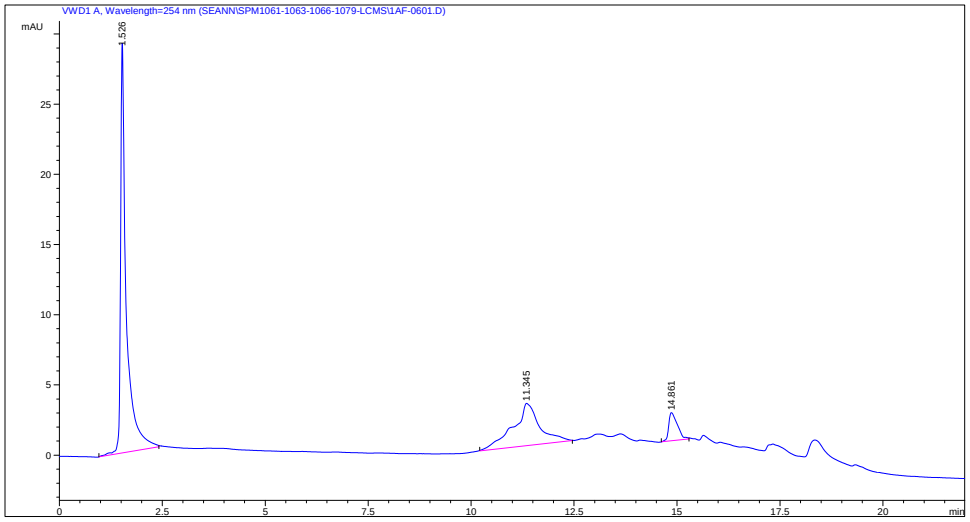

$[M\text{-}Cl]^+ = 536.1$

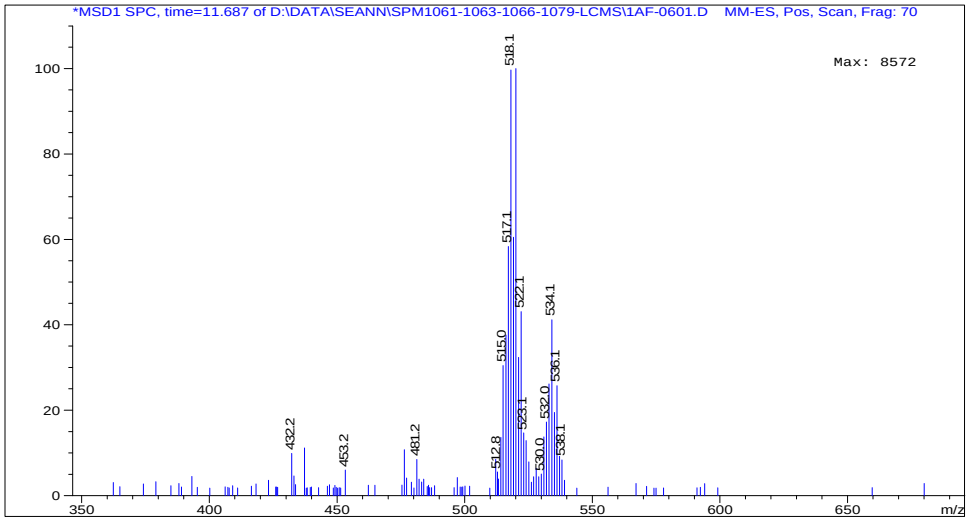


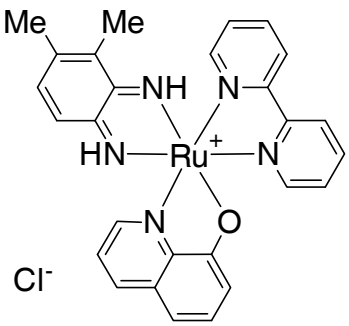





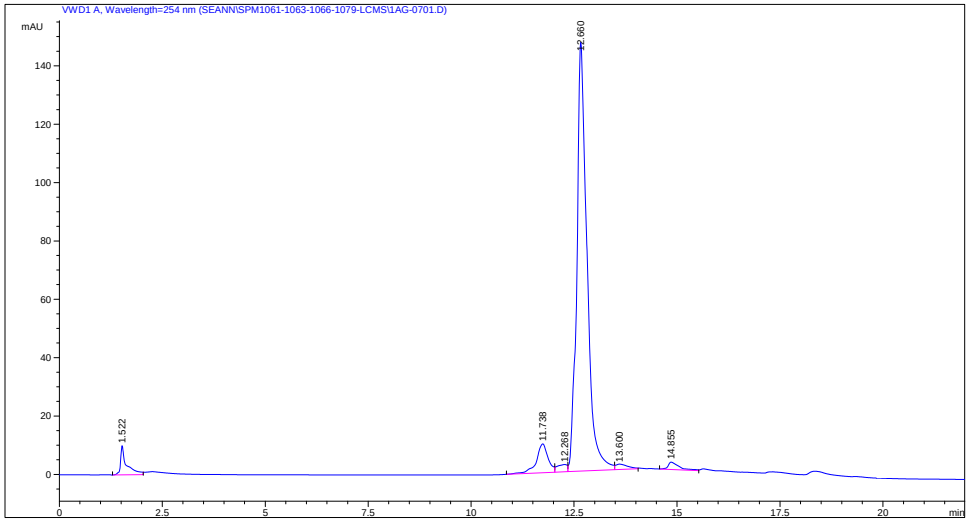

$[M\text{-}Cl]^{+} = 450.1$

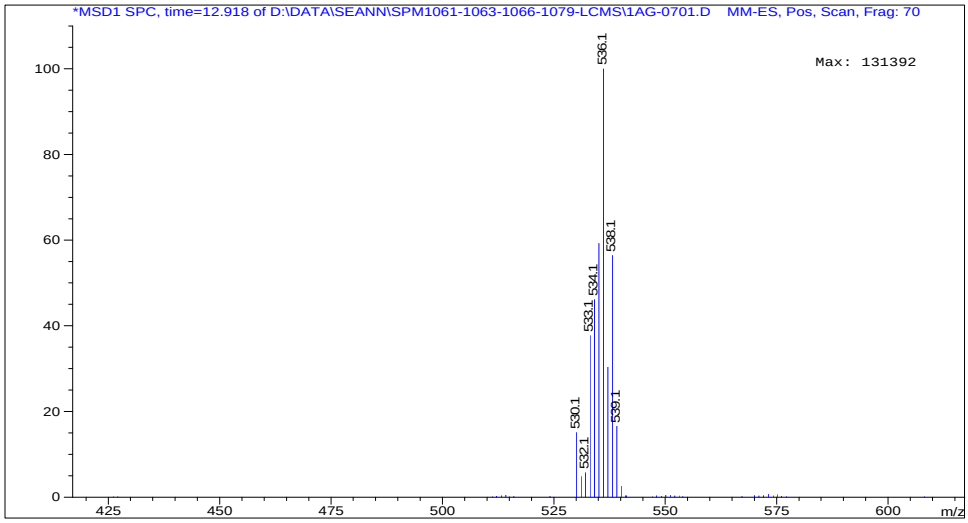


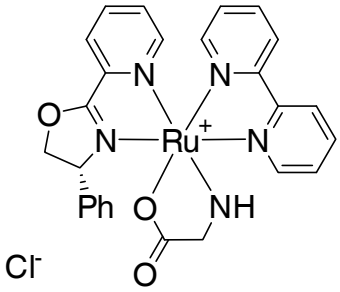





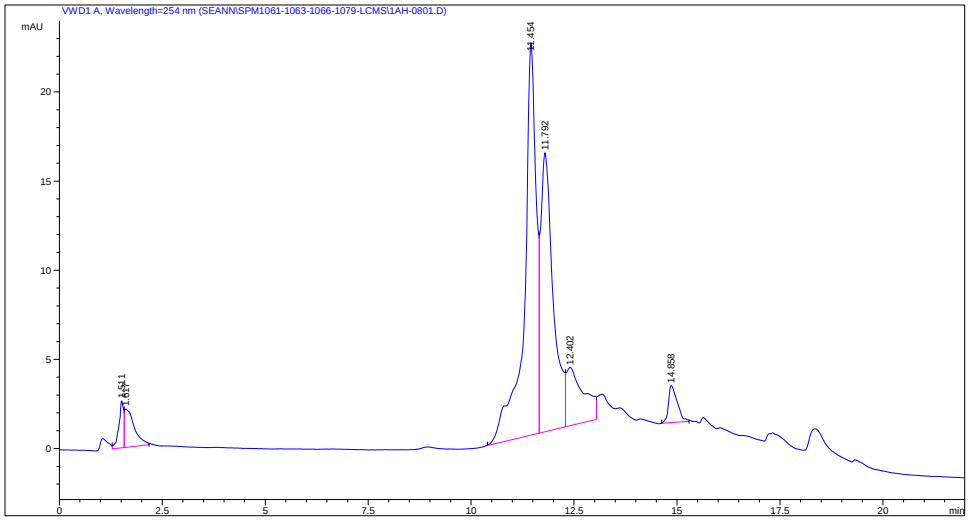

$[M\text{-}Cl]^+ = 536.1$

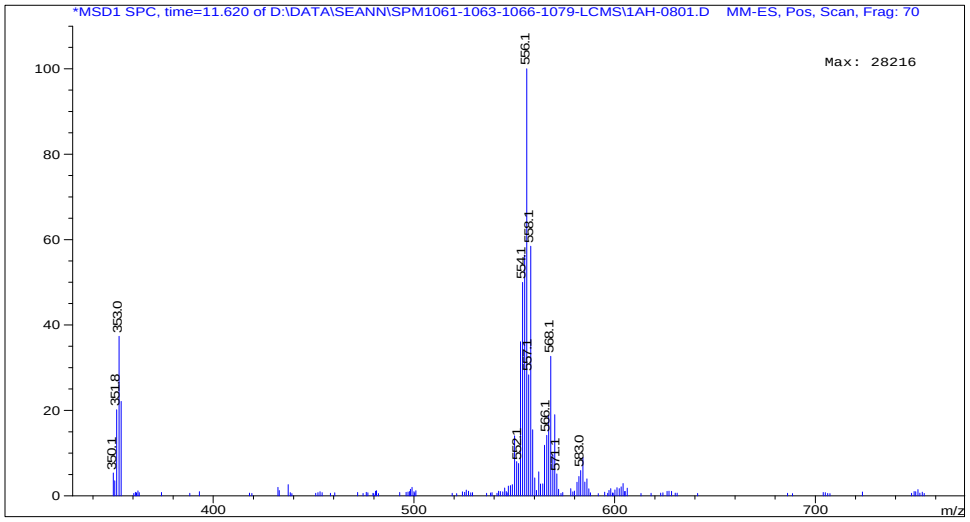


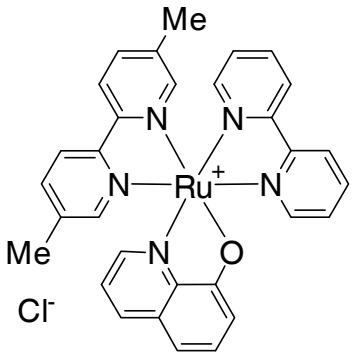





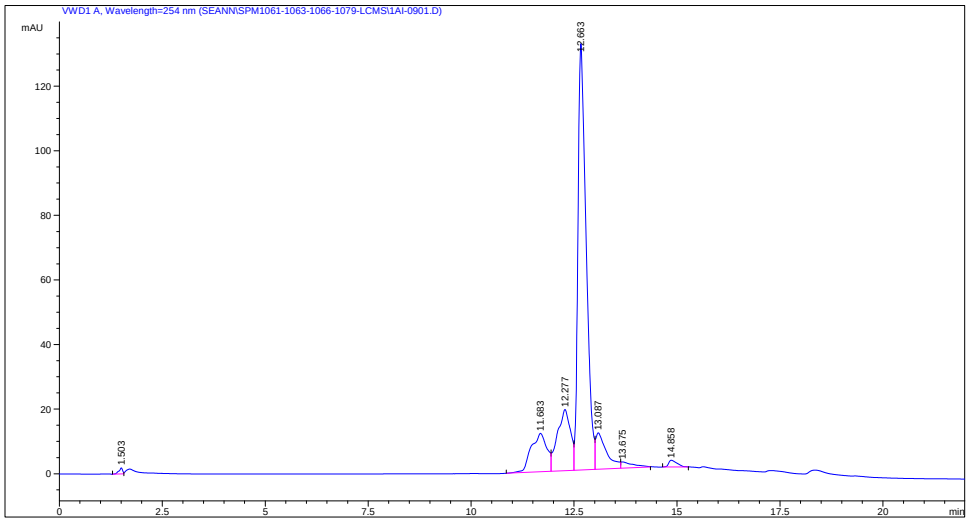

$[M\text{-}Cl]^+ = 555.1$

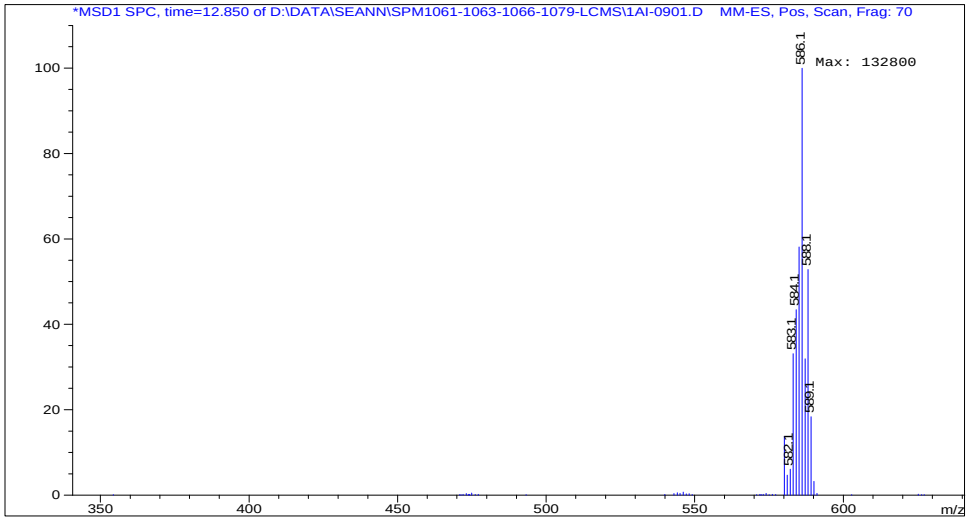


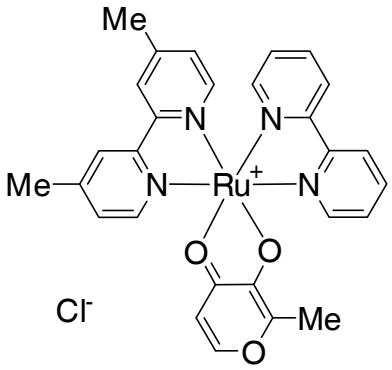





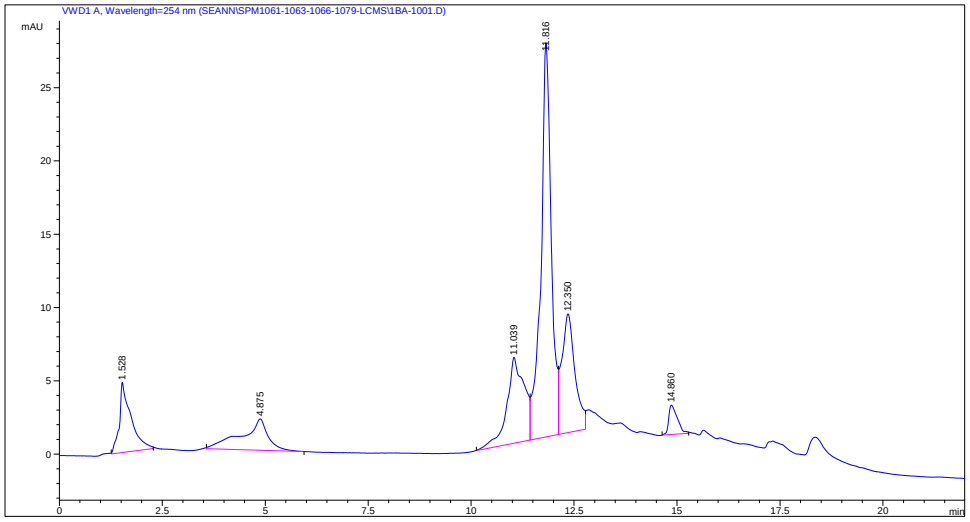

$[M\text{-}Cl]^{+} = 586.1$

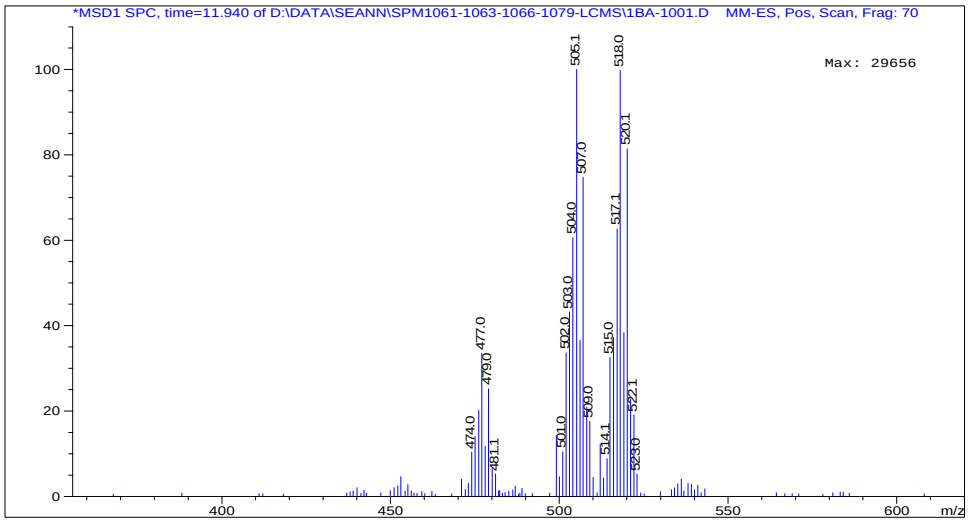


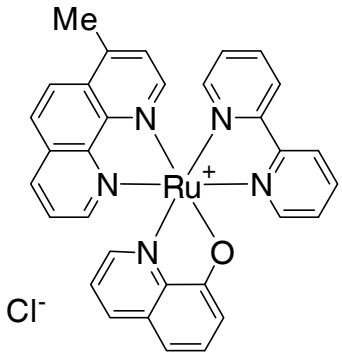





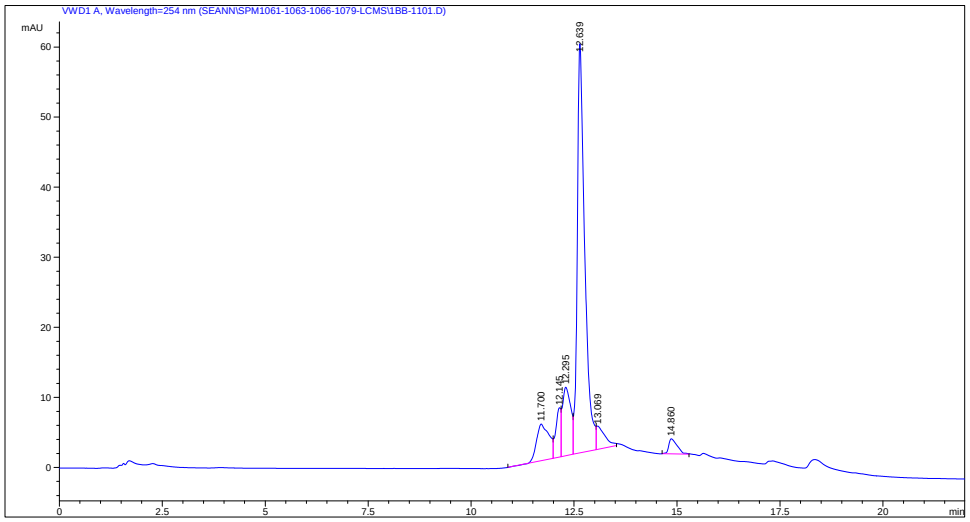

$[M\text{-}Cl]^{+} = 567.1$

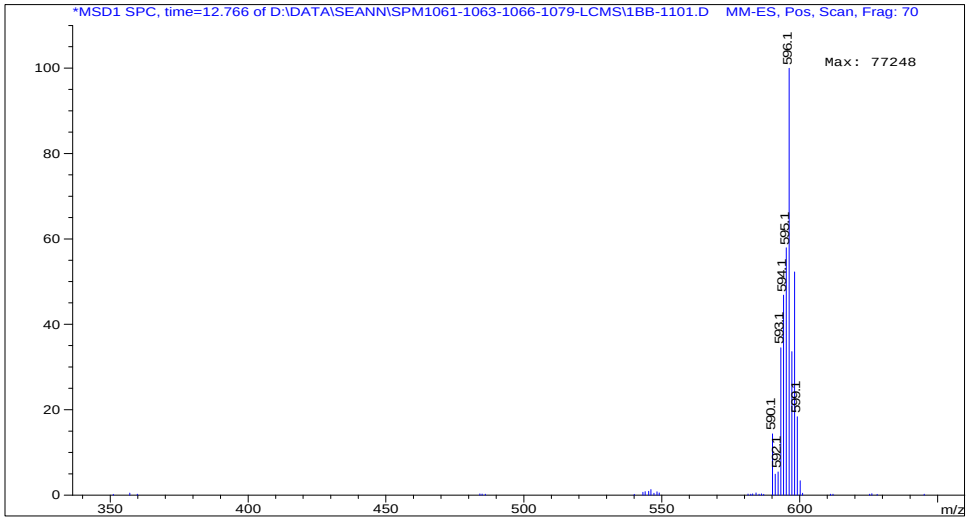


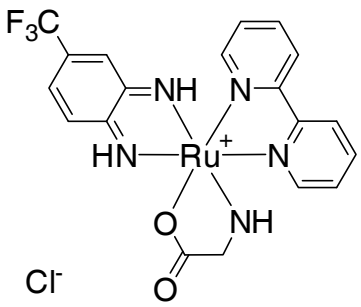





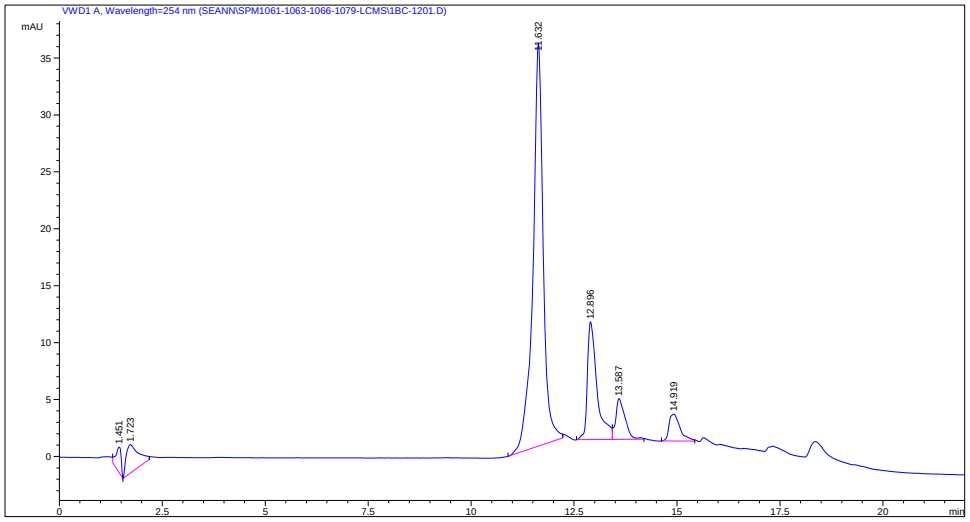

$[M\text{-}Cl]^{+} = 596.1$

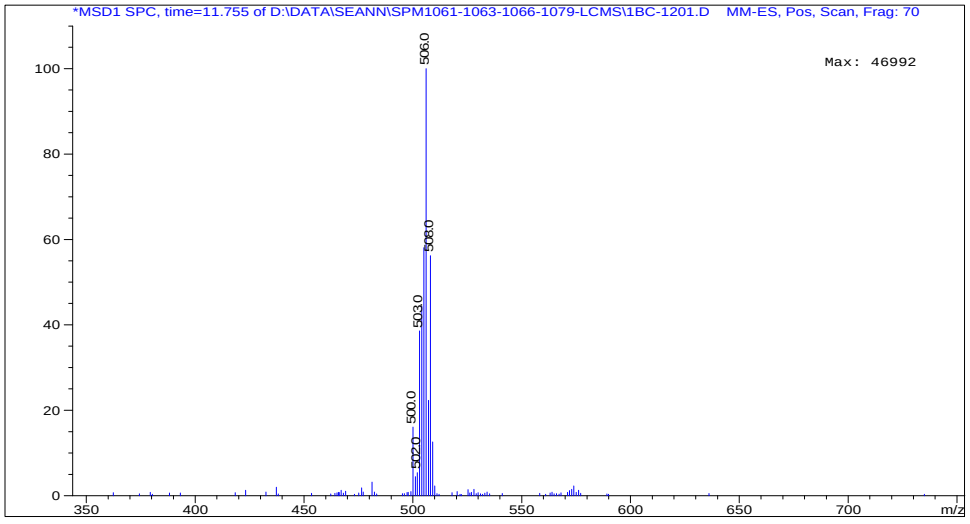


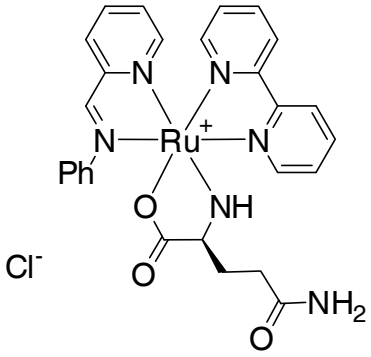





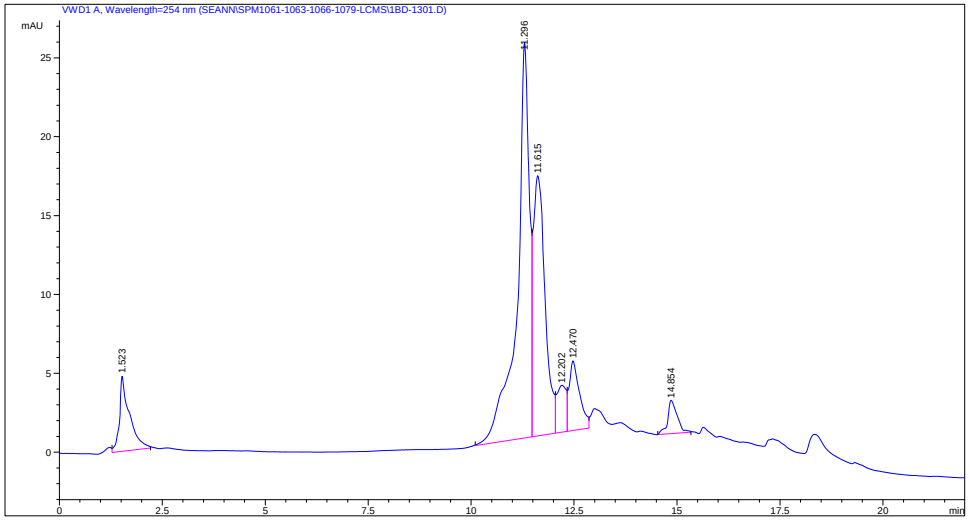

$[M\text{-}Cl]^{+} = 505.0$

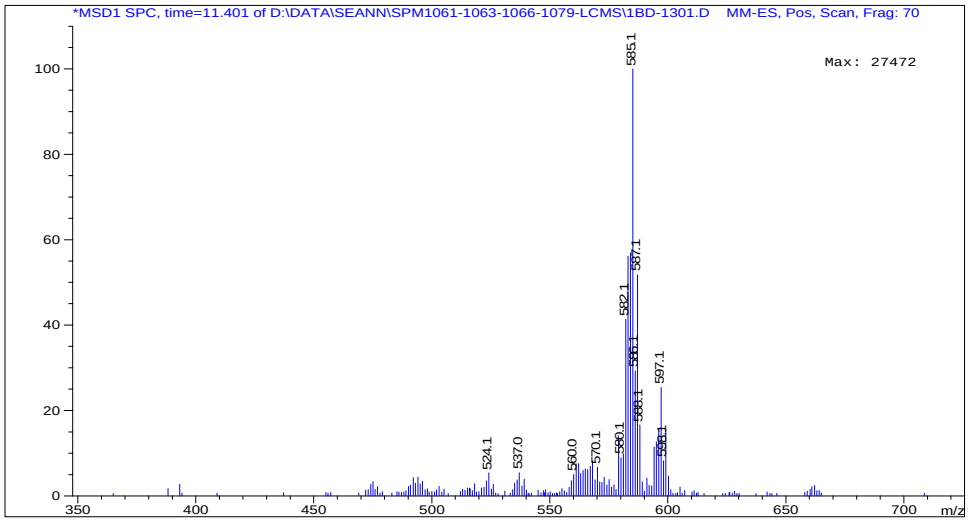


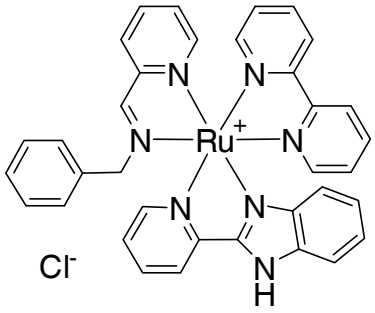





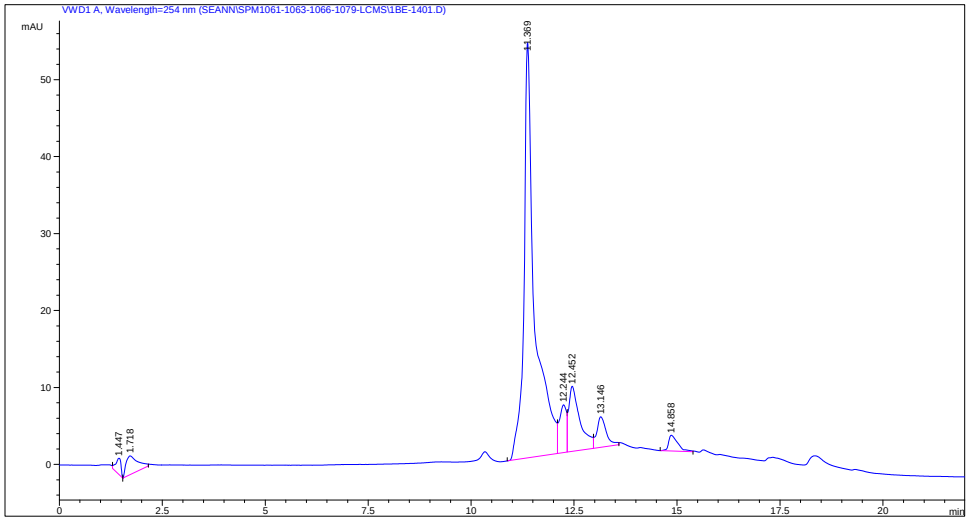

$[M\text{-}Cl]^{+} = 584.1$

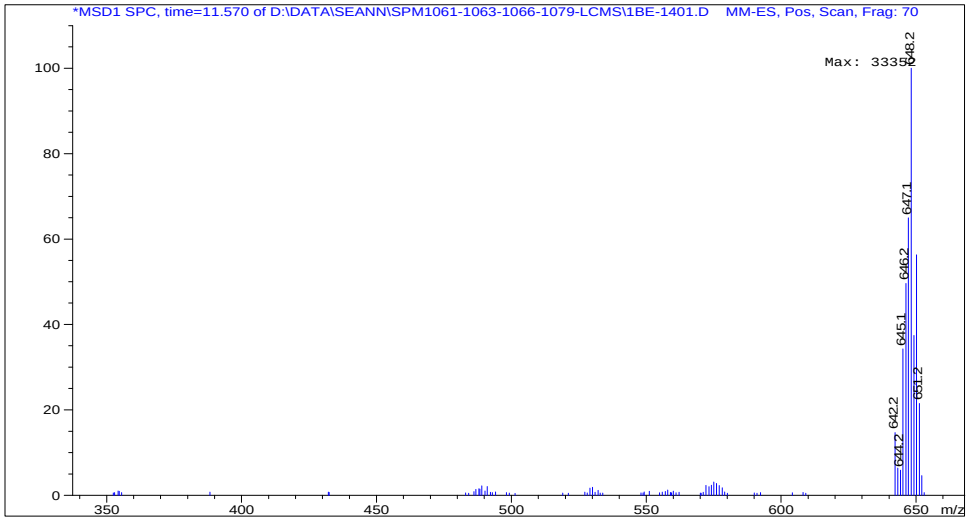


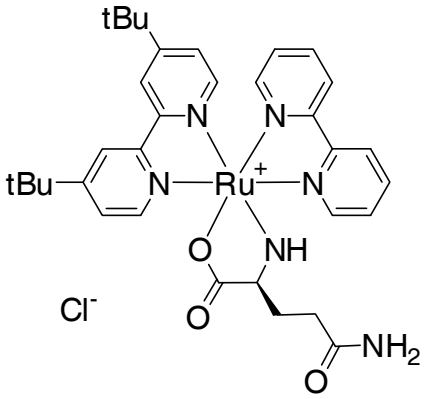





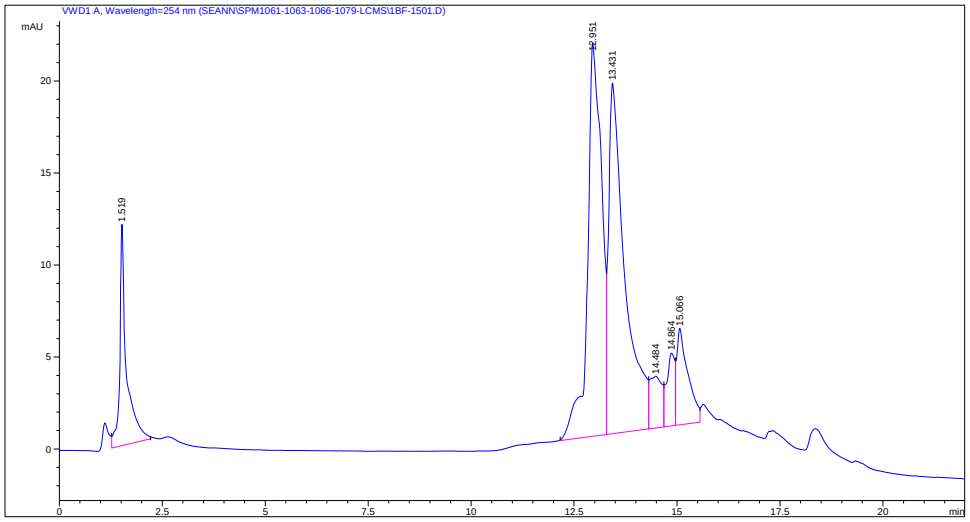

$[M\text{-}Cl]^{+} = 549.2$

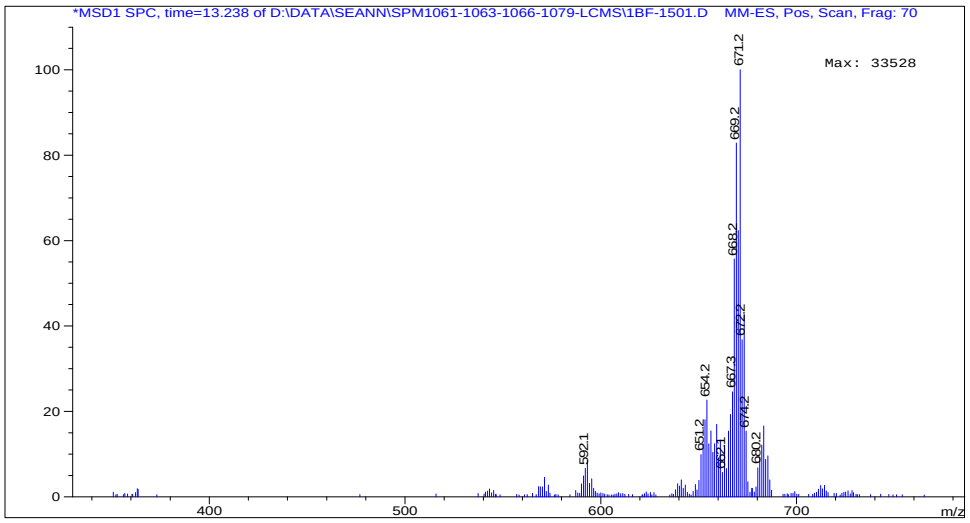


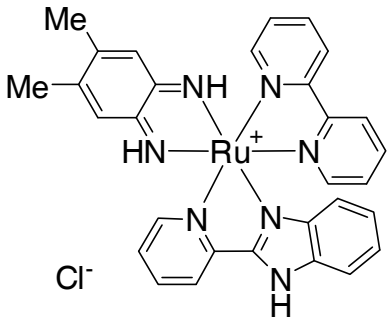





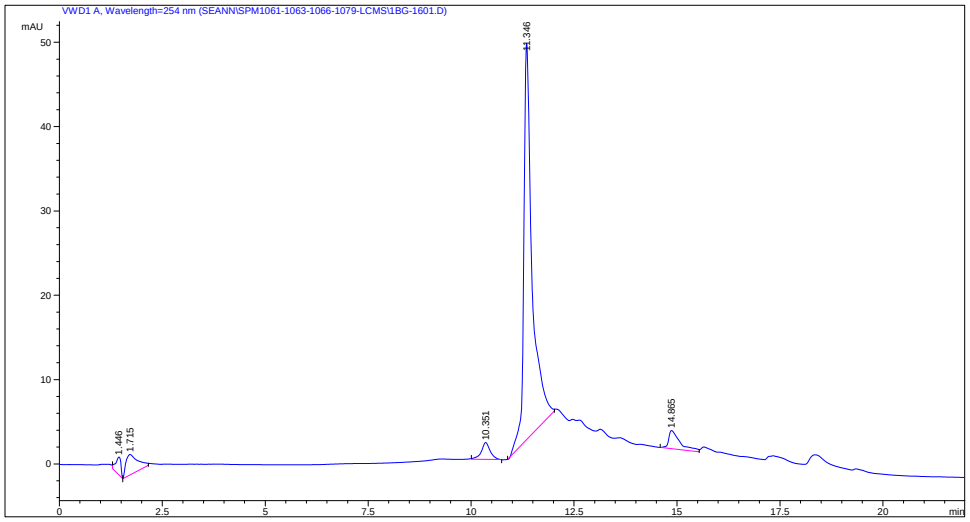

$[M\text{-}Cl]^{+} = 670.2$

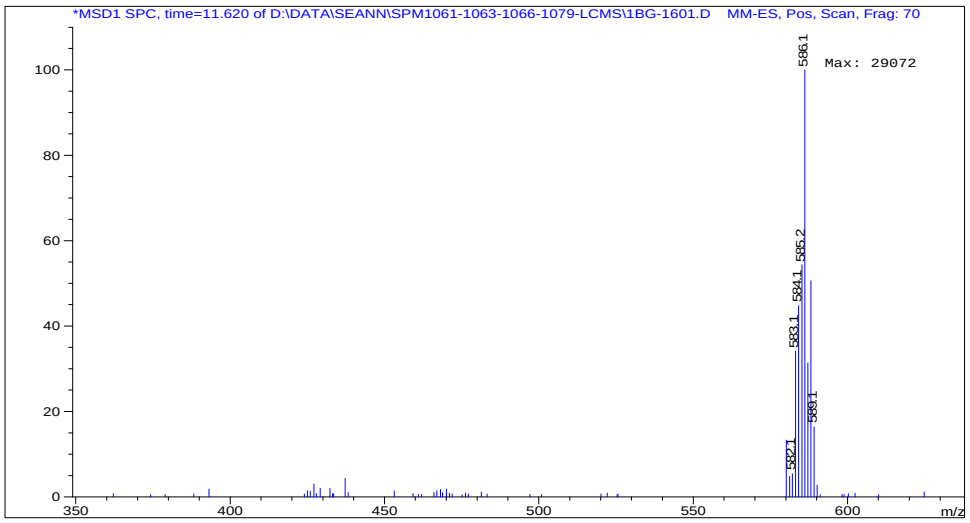


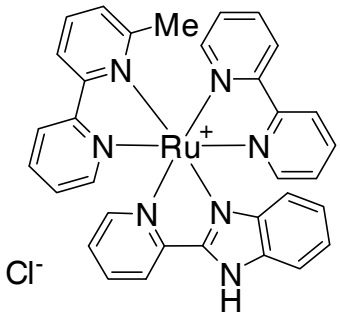





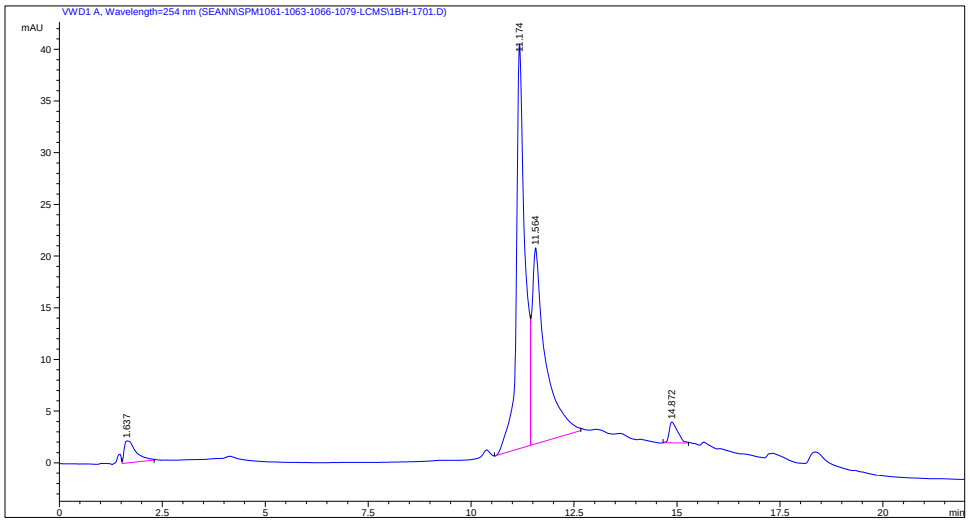

$[M\text{-}Cl]^+ = 587.1$

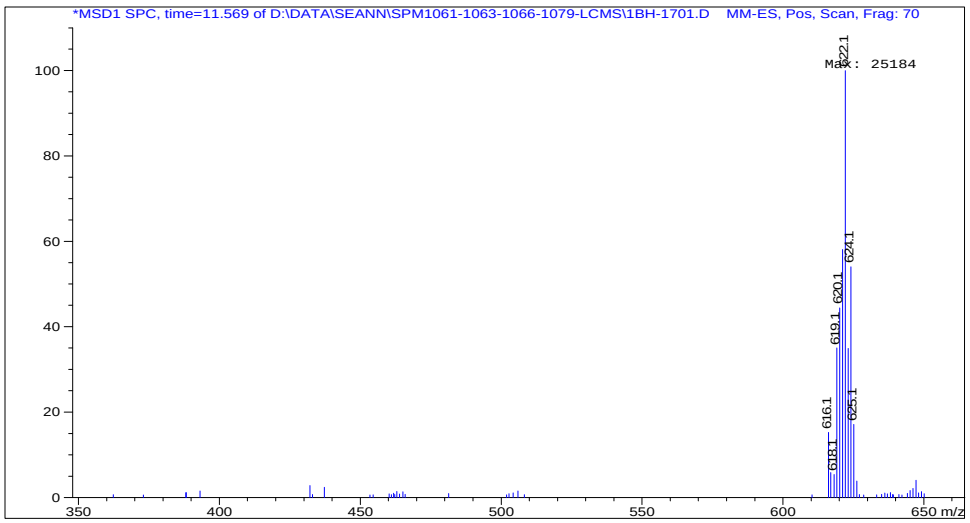


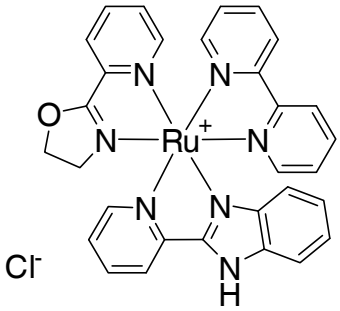





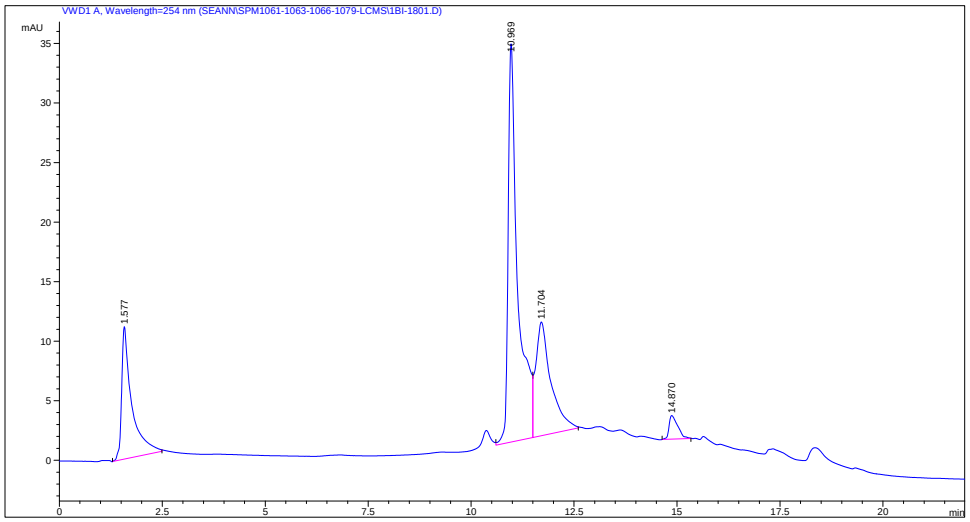

$[M\text{-}Cl]^{+} = 623.1$

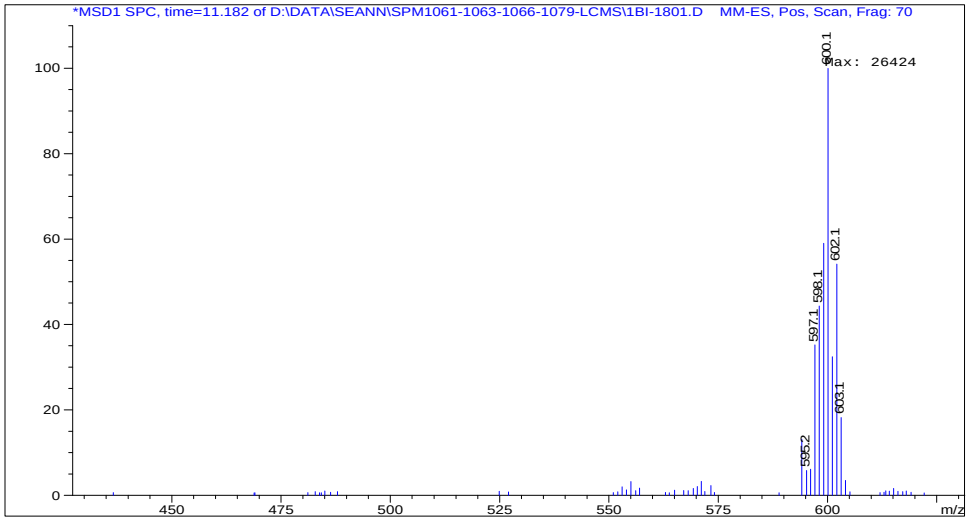


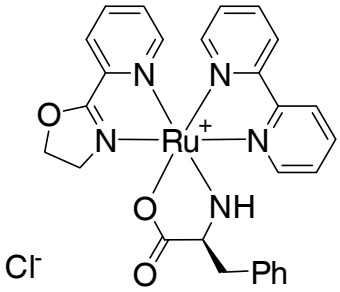





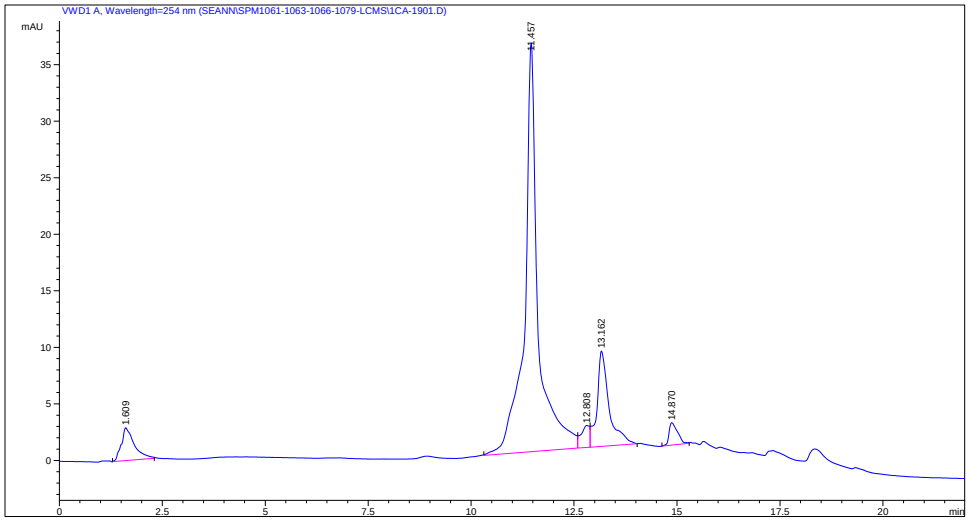

$[M\text{-}Cl]^{+} = 601.1$

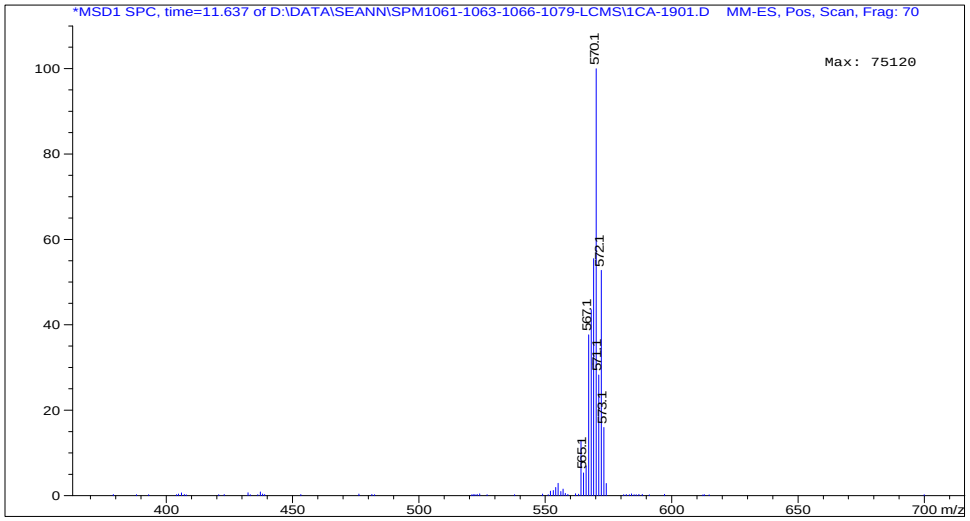


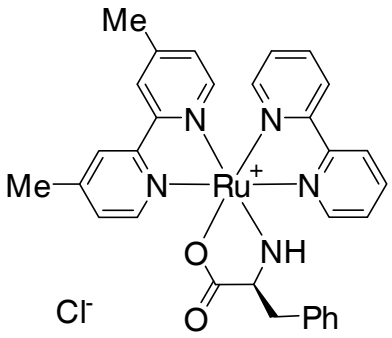





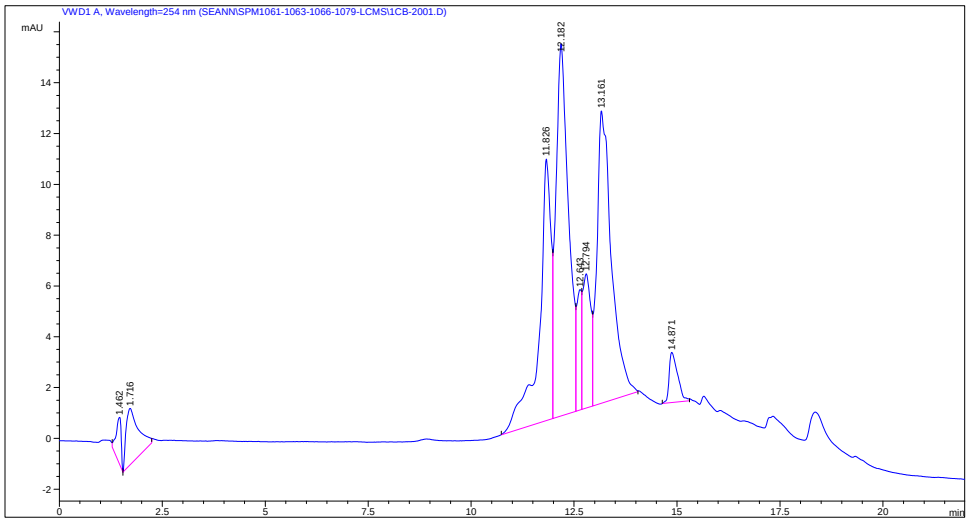

$[M\text{-}Cl]^{+} = 569.1$

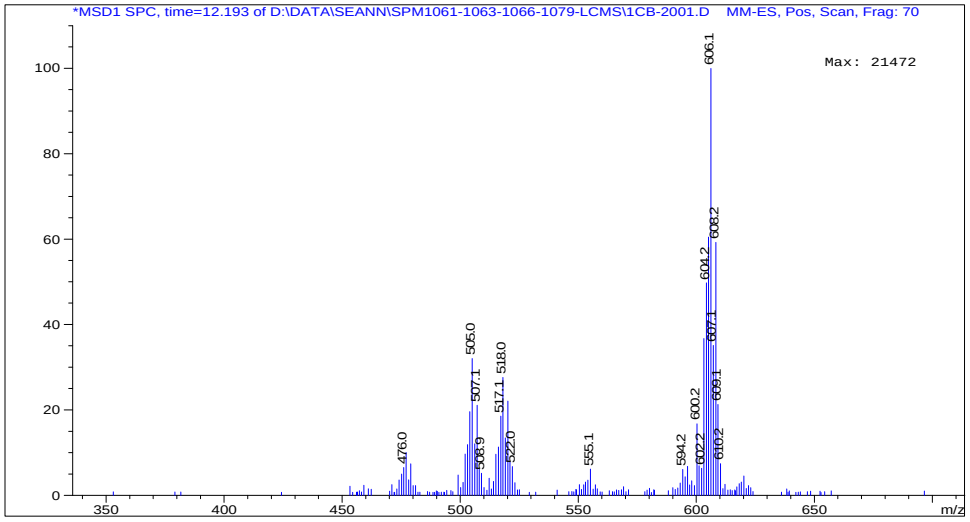


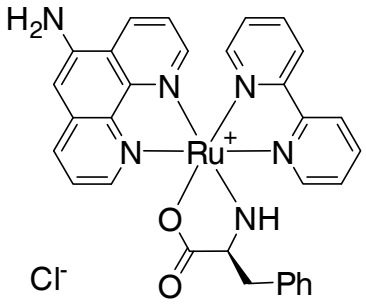





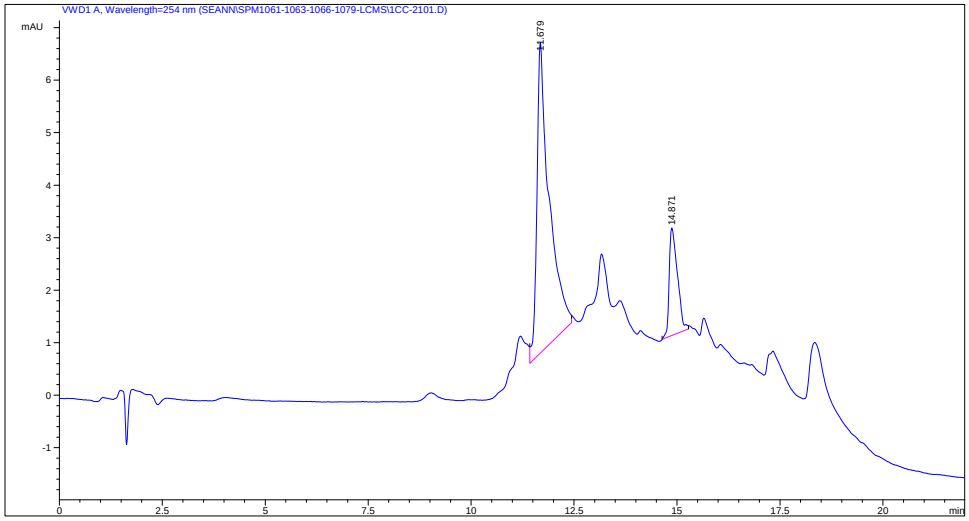

$[M\text{-}Cl]^+ = 605.1$

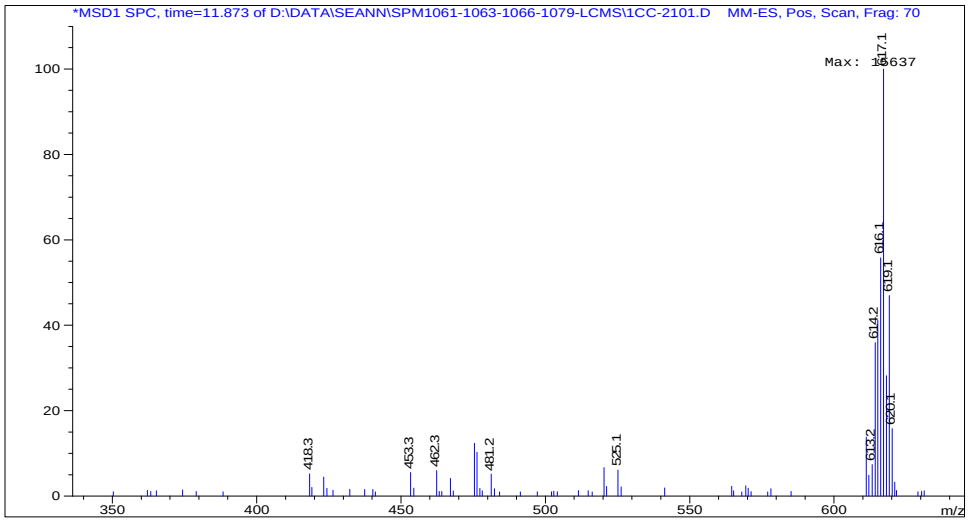


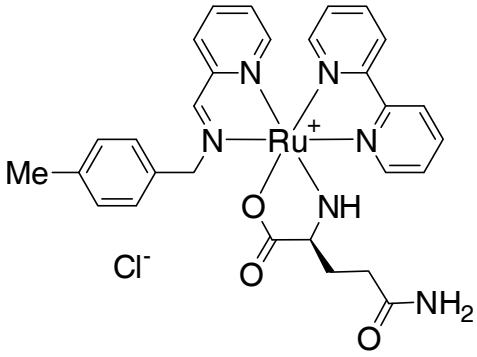





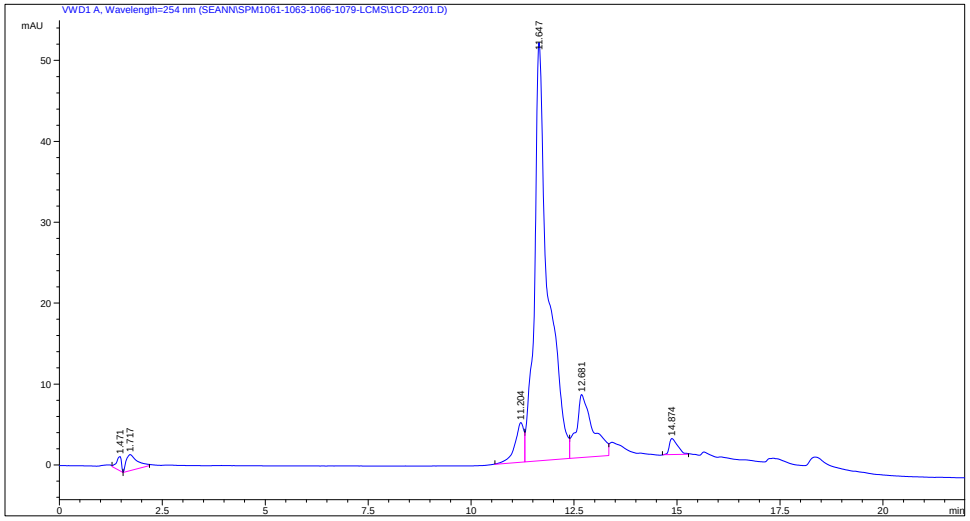

$[M\text{-}Cl]^{+} = 616.1$

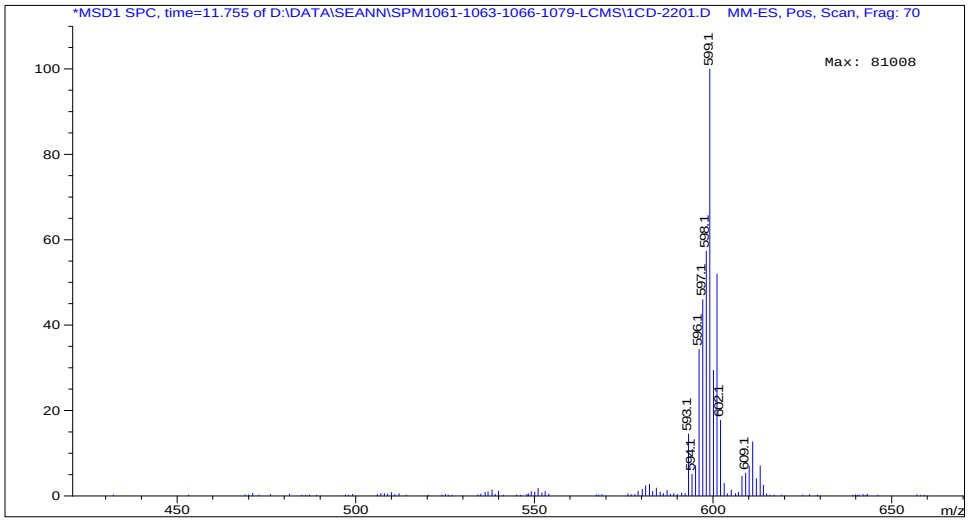


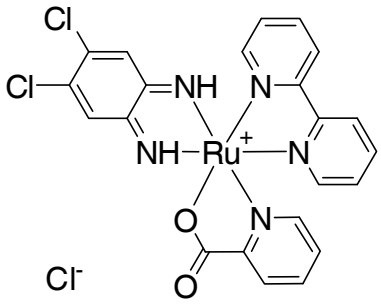





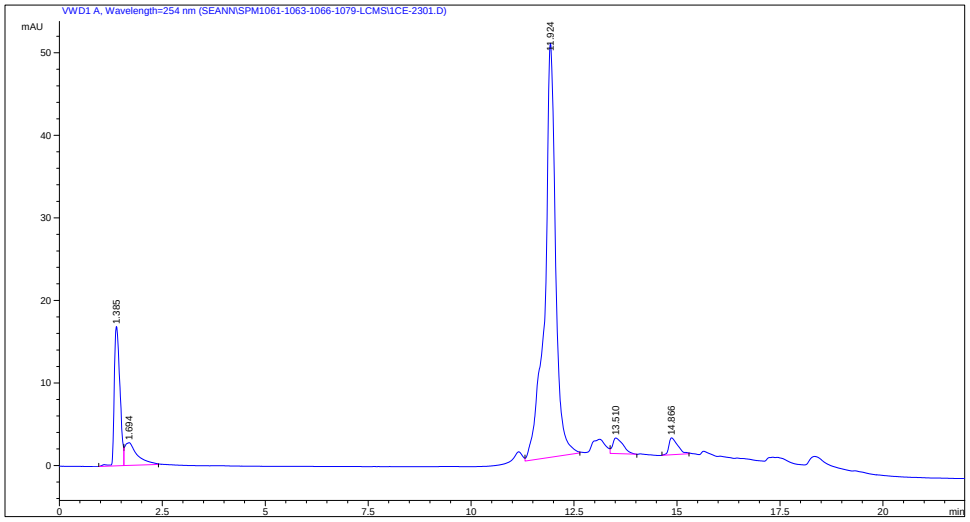

$[M\text{-}Cl]^{+} = 612.1$

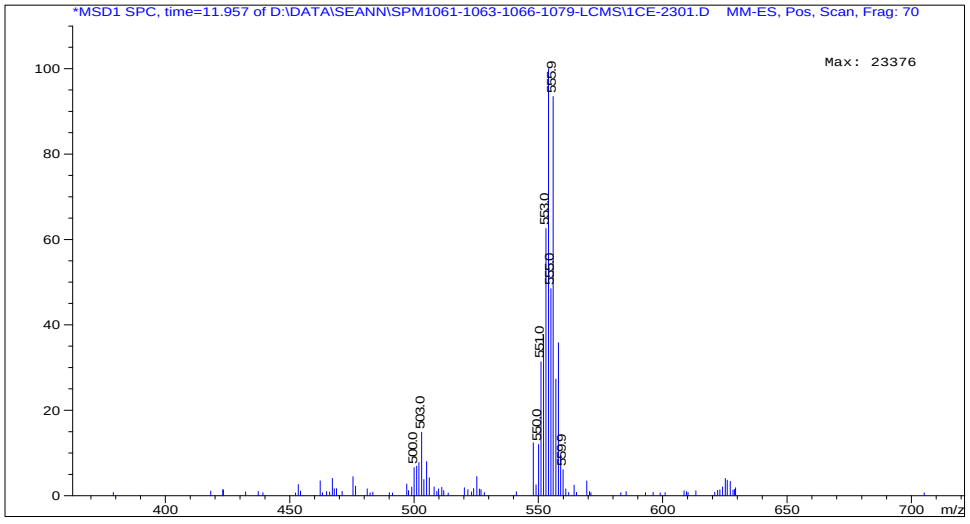


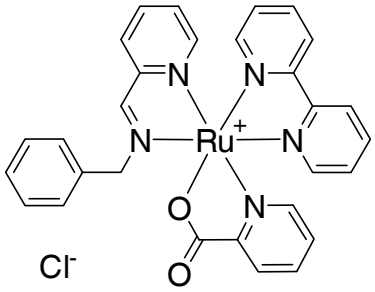





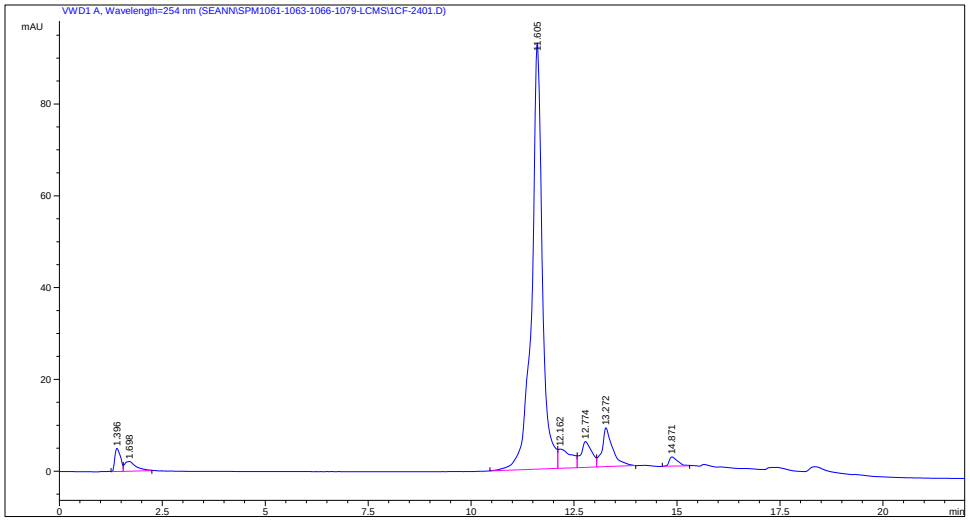

$[M\text{-}Cl]^{+} = 554.0$

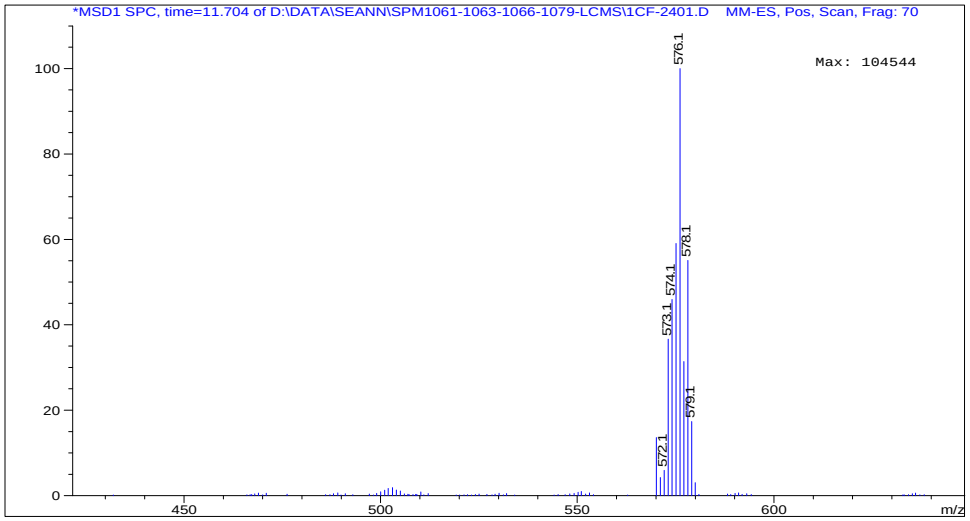


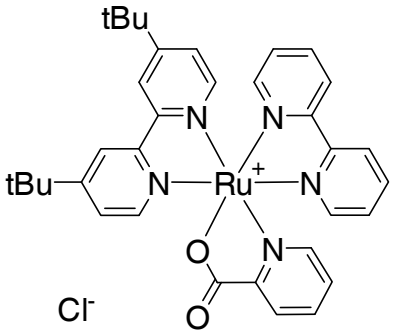





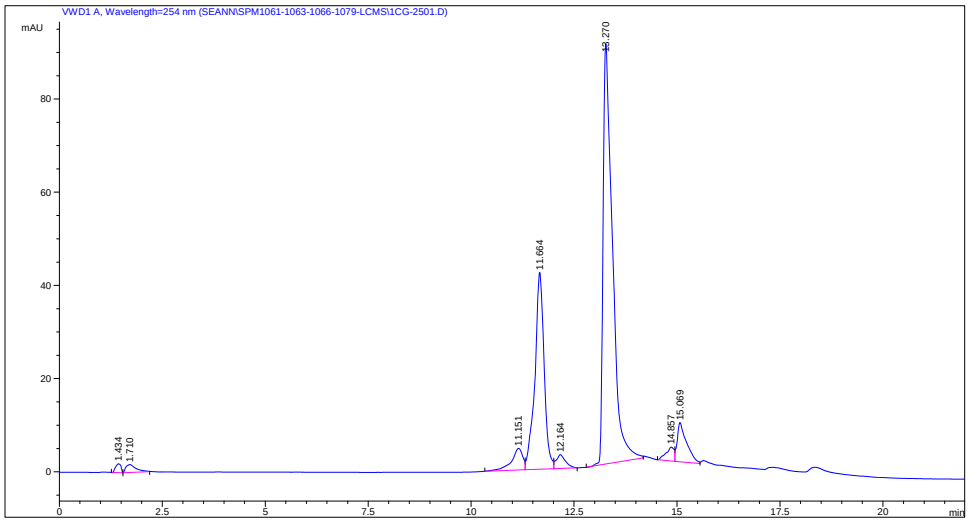

$[M\text{-}Cl]^{+} = 576.1$

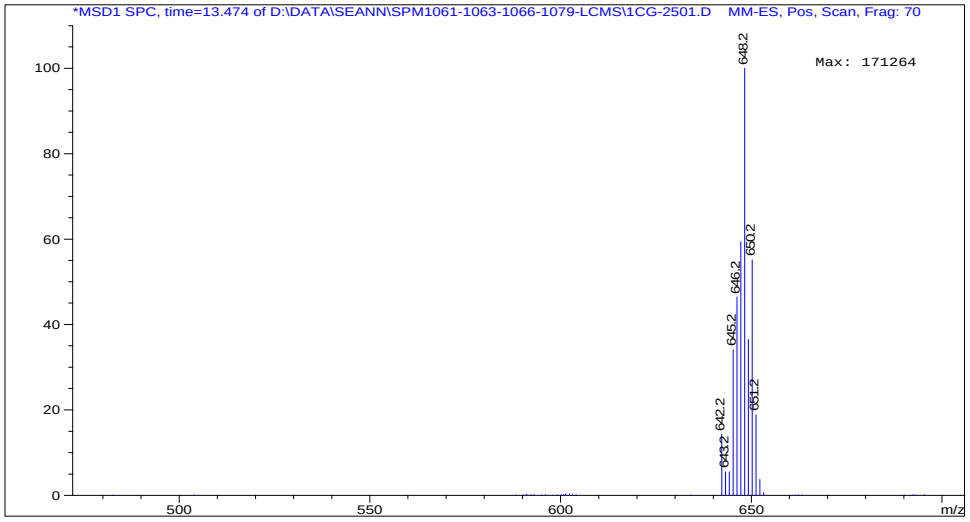


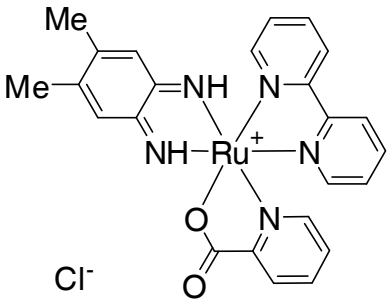





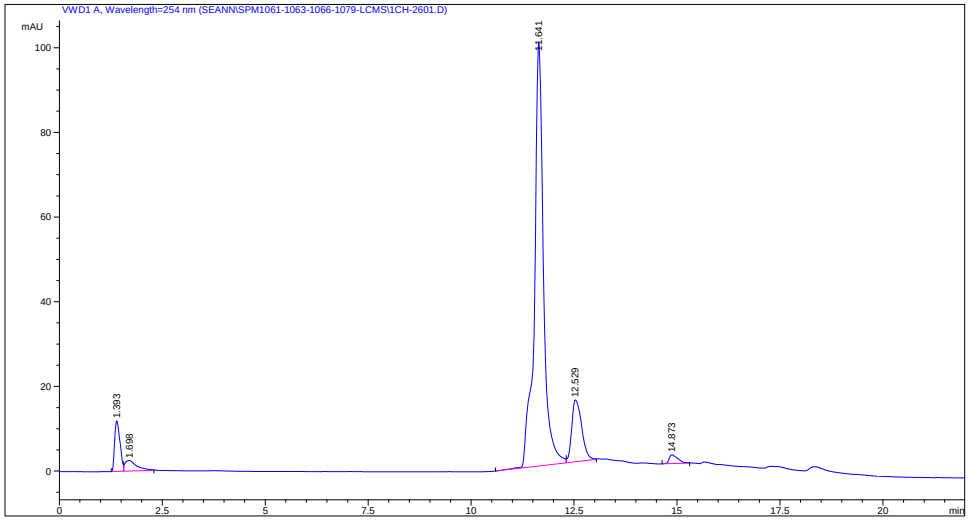

$[M\text{-}Cl]^+ = 648.2$

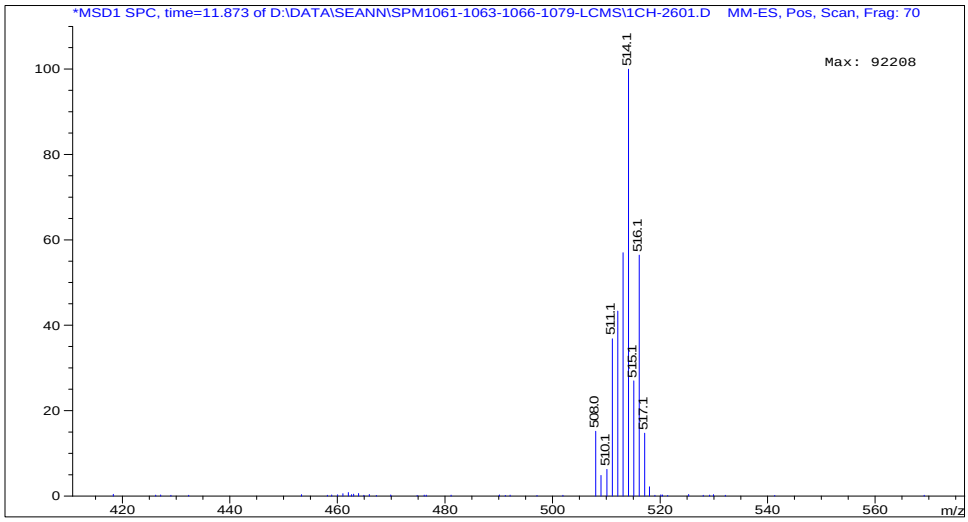


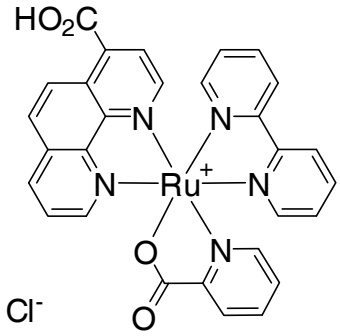





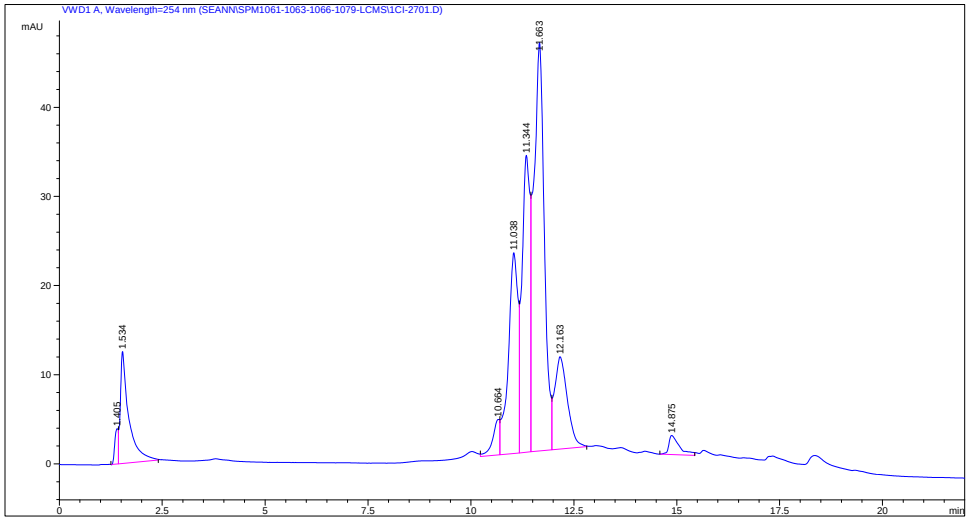

$[M\text{-}Cl]^{+} = 514.1$

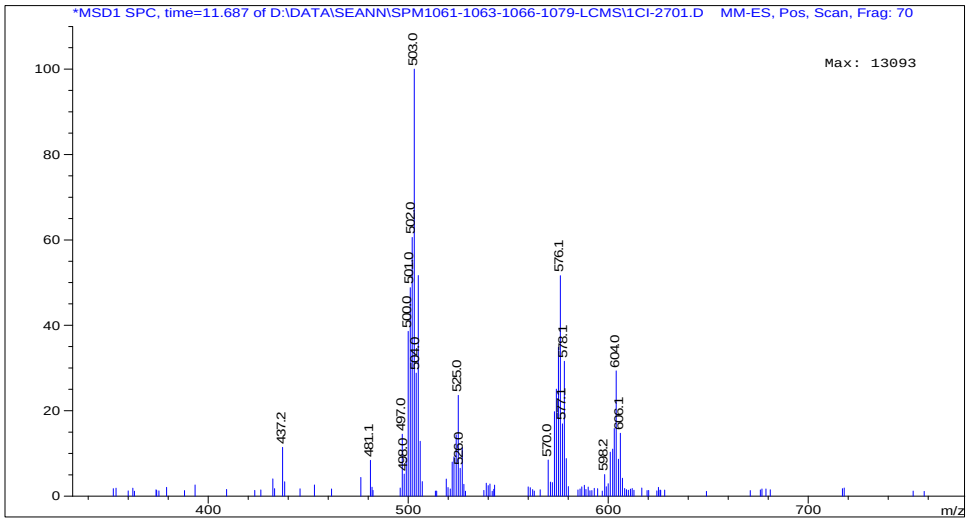


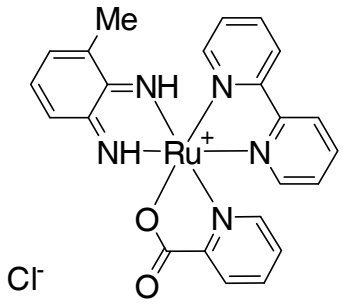





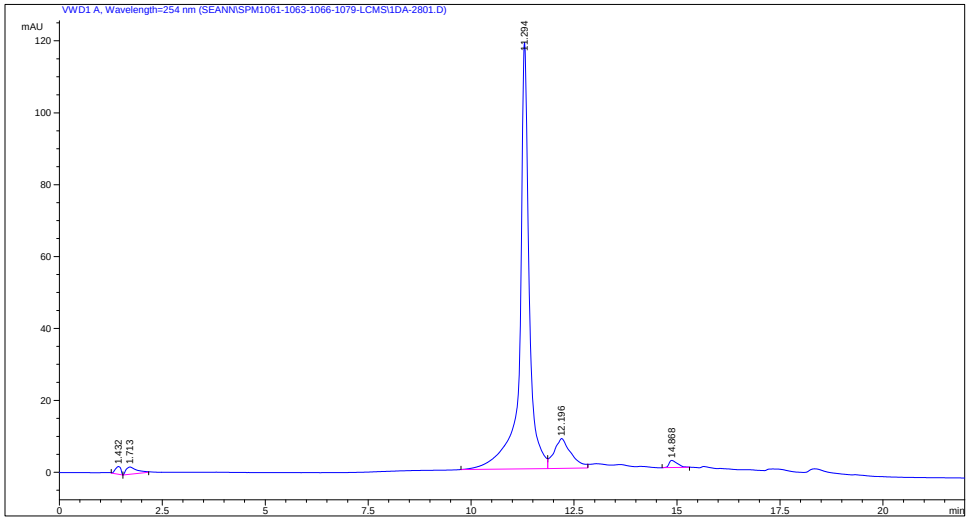

$[M\text{-}Cl]^+ = 604.1$

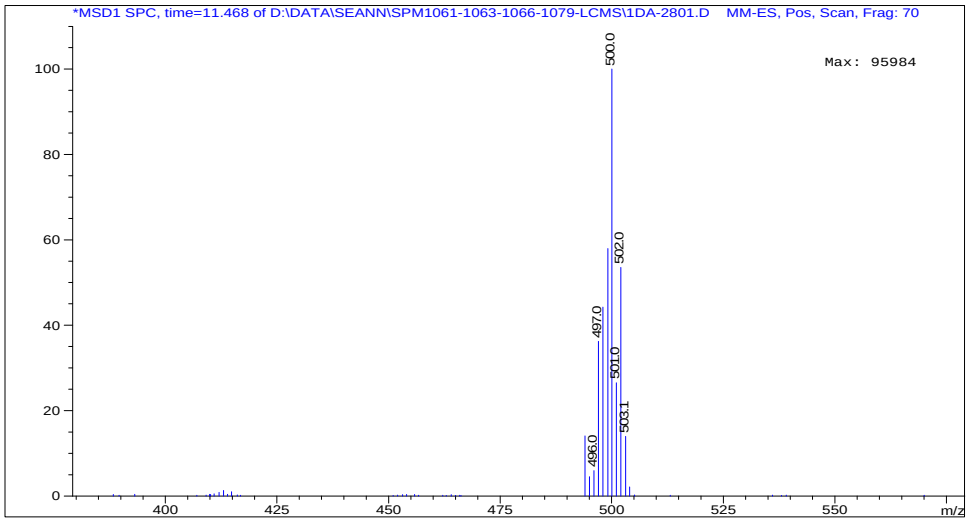


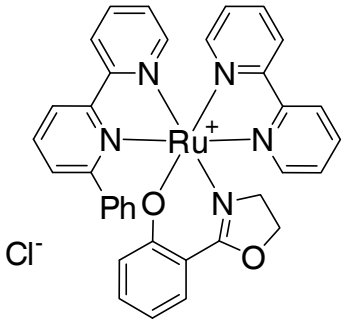





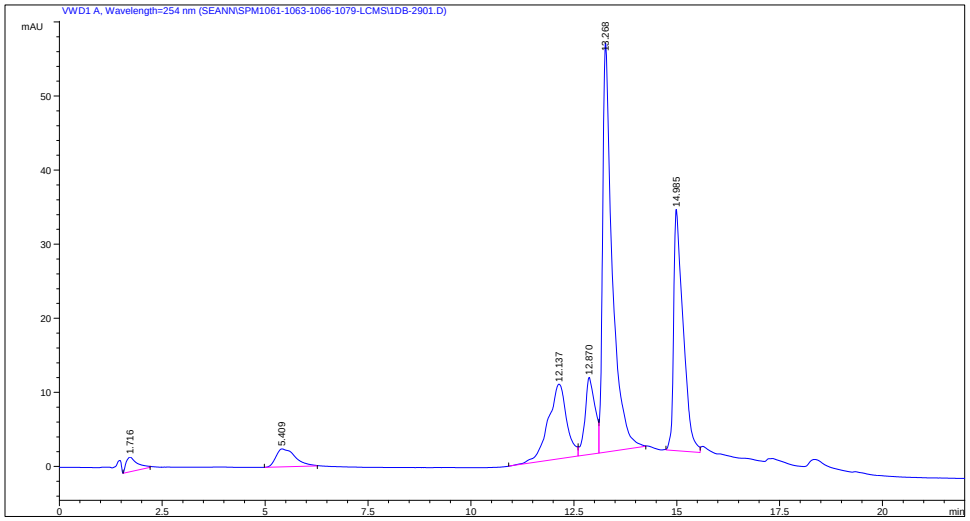

$[M\text{-}Cl]^+ = 500.1$

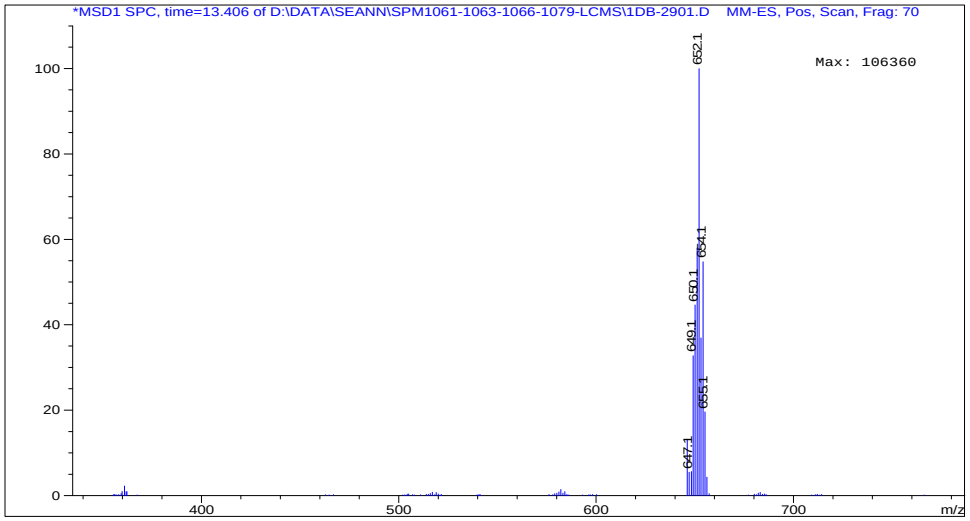


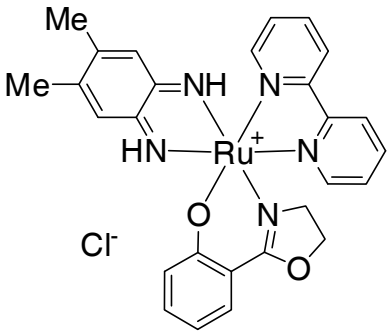





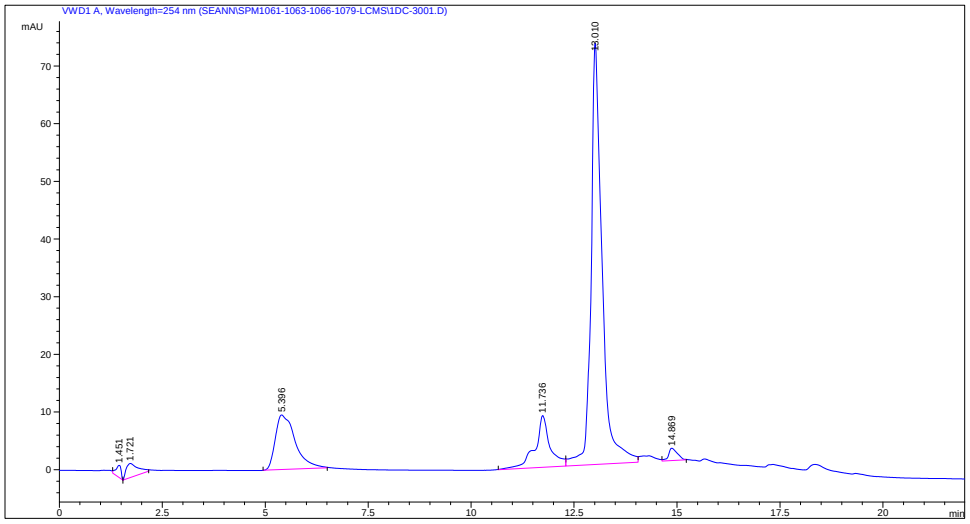

$[M\text{-}Cl]^+ = 652.1$

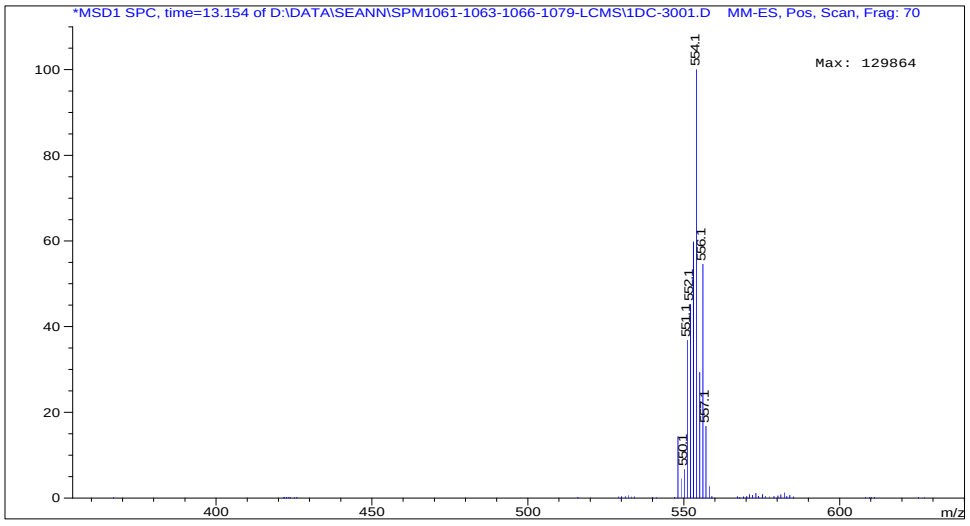


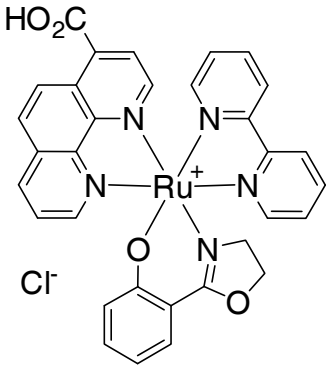





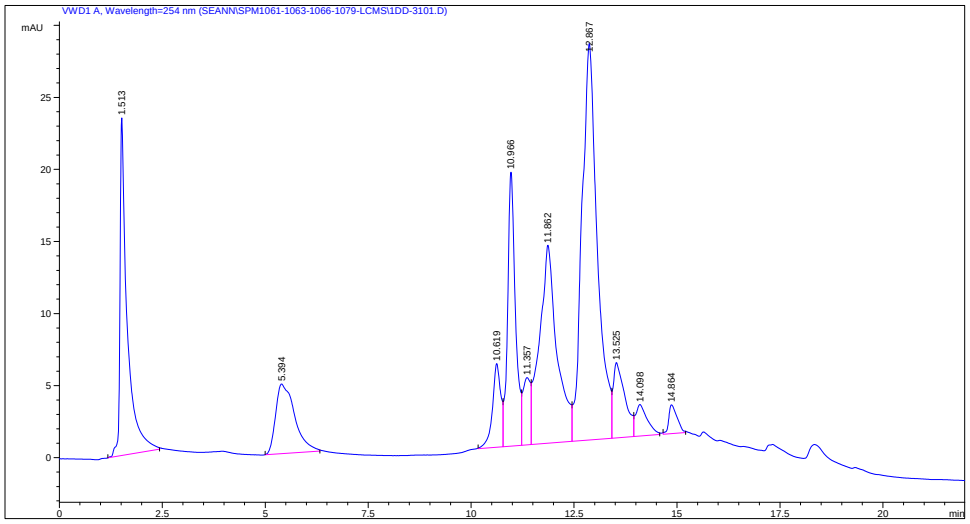

$[M\text{-}Cl]^+ = 554.1$

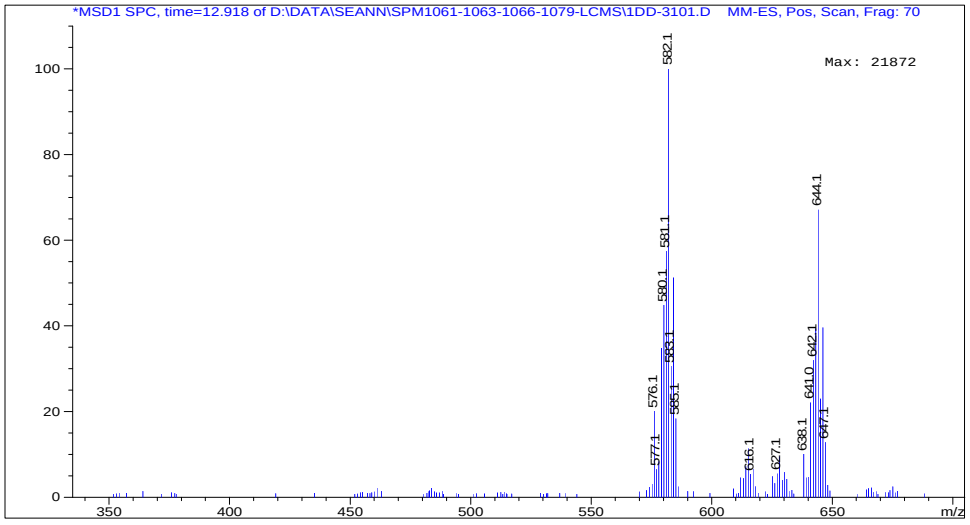


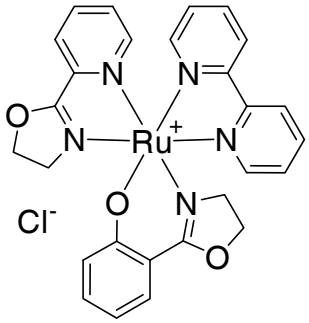





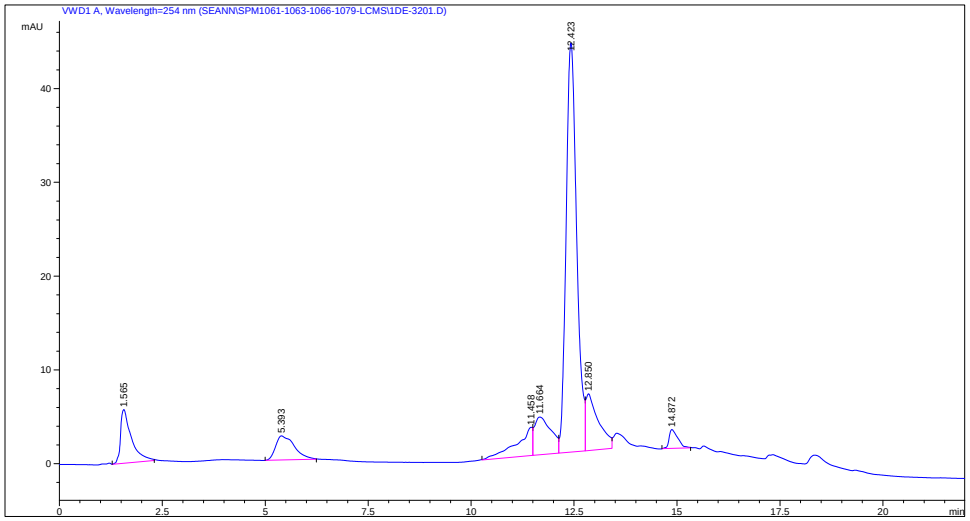

$[M\text{-}Cl]^{+} = 644.1$

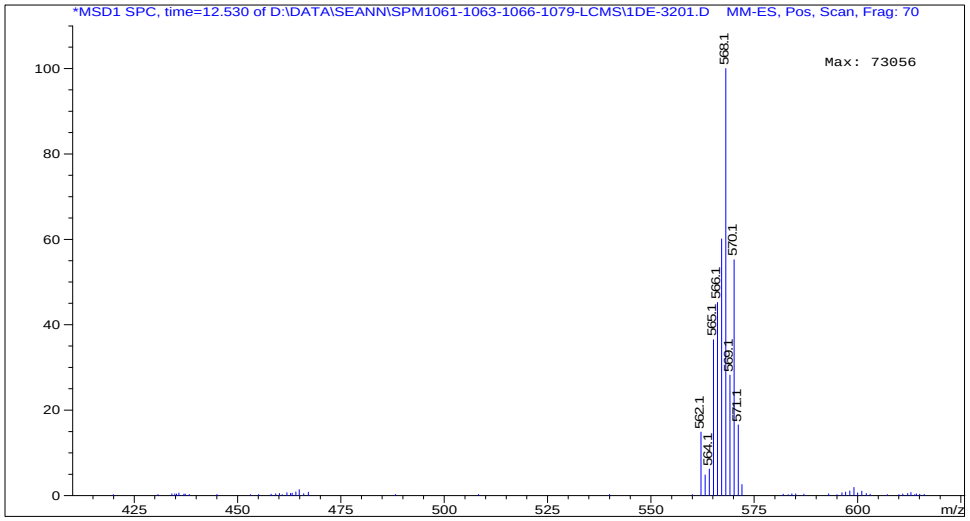


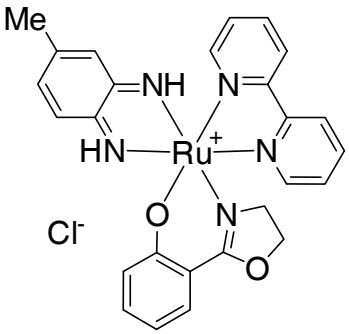





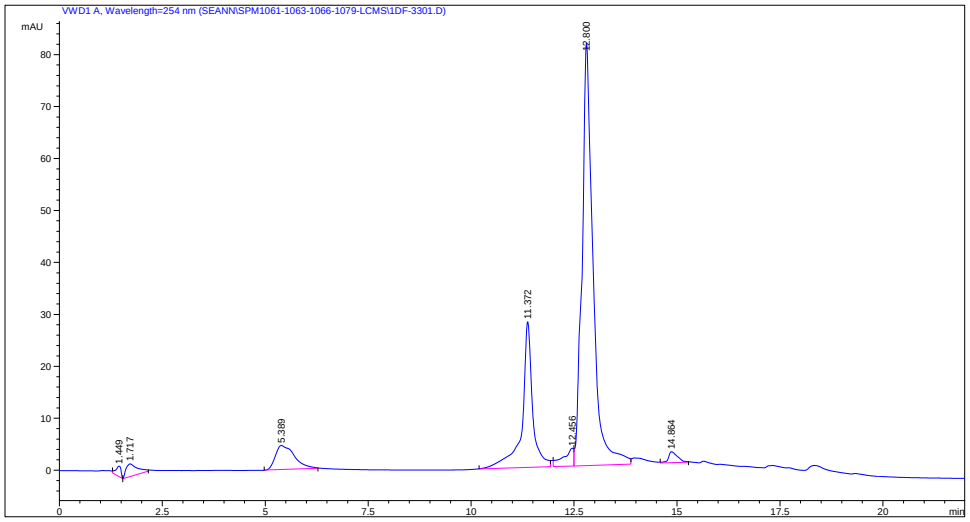

$[M\text{-}Cl]^{+} = 568.1$

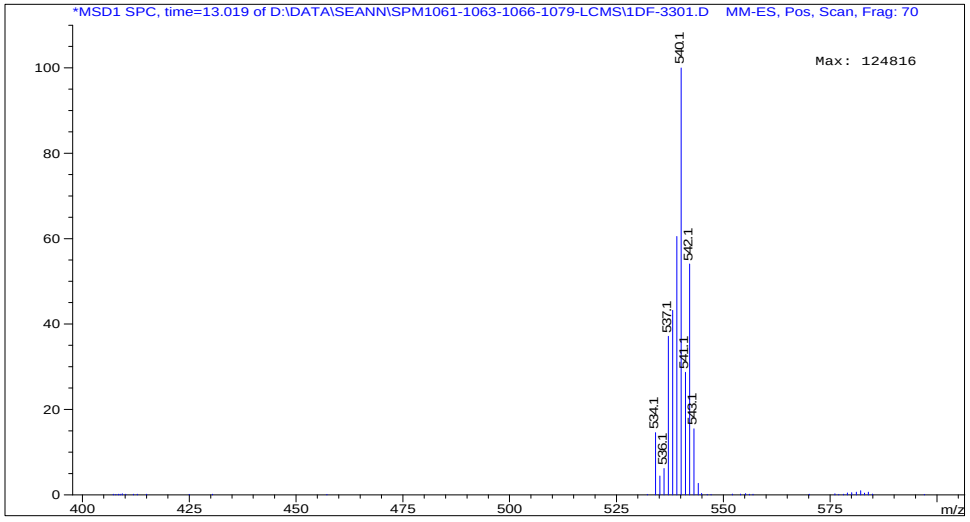


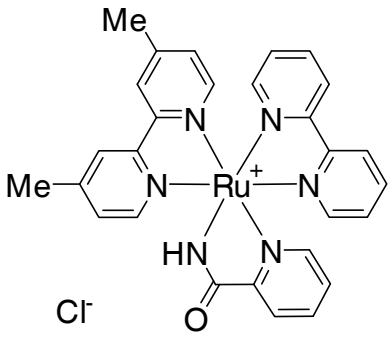





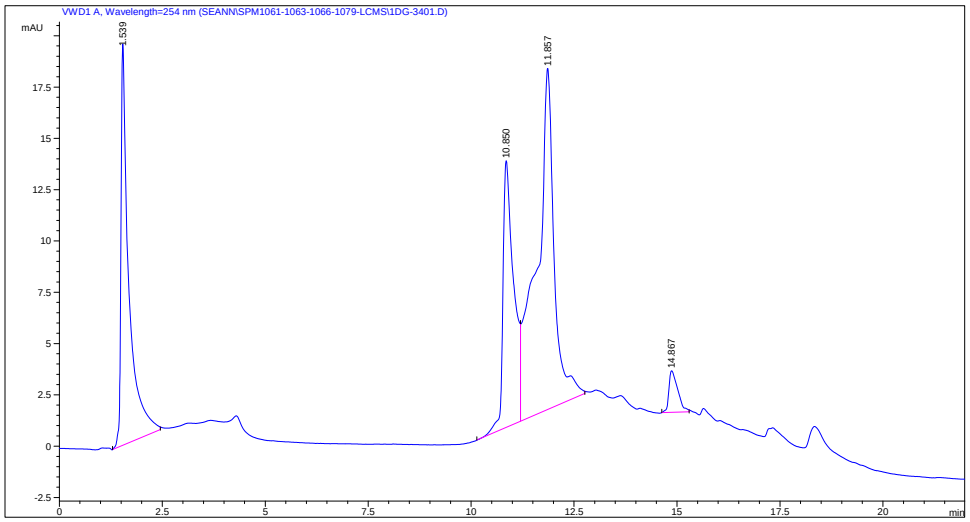

$[M\text{-}Cl]^+ = 540.1$

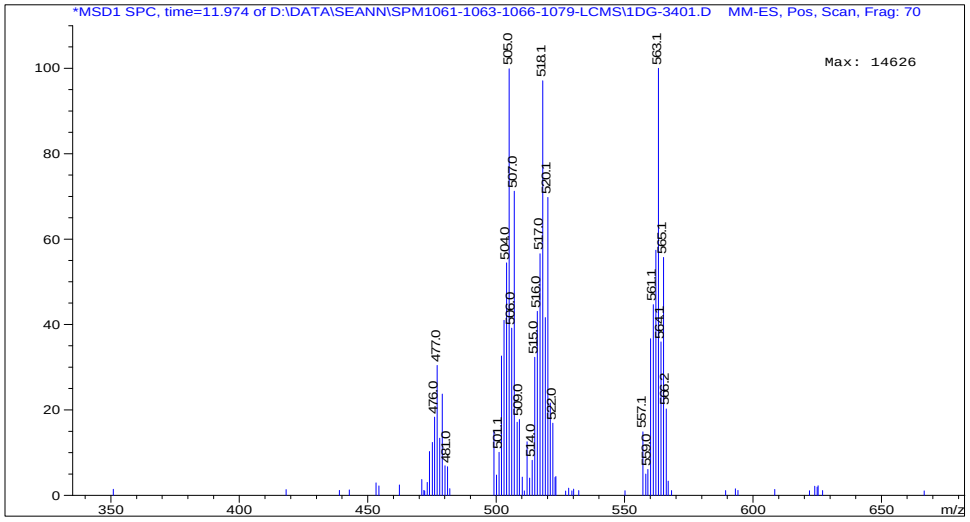


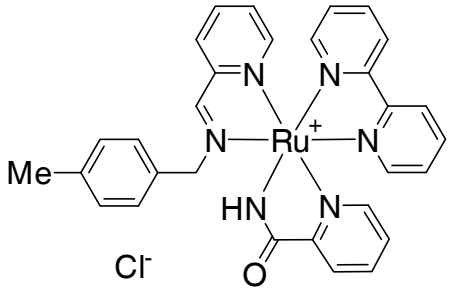






$[M\text{-}Cl]^+ = 563.1$






$[M\text{-}Cl]^{+} = 589.1$