Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Arene Ruthenium (II) Complexes with Chalcone, Aminoantipyrine and Aminopyrimidine Based Ligands: Synthesis, Structure and Preliminary Evaluation of Anti-leukemia Activity

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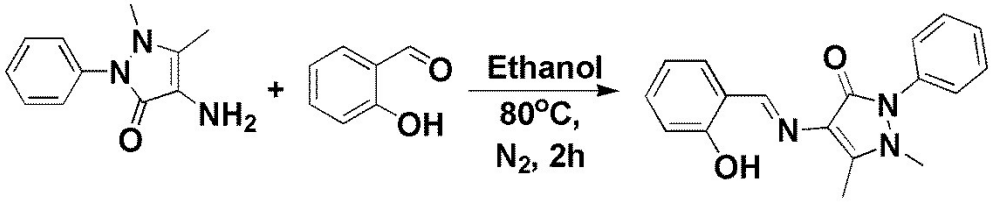
Synthesis of Ligands and Complexes

Synthesis of 4-(2-hydroxybenzylideneamino)-2,3-dimethyl-1-phenyl-1,2-dihydropyrazol-5-one (AAPS):

4-aminoantipyrine (200 mg, 0.98 mmol) and salicylaldehyde (120 mg, 0.98 mmol) were refluxed in ethanol (15 mL) for 2h. Then, the reaction mixture was allowed to cool to room temperature; the resulting precipitate was filtered off and dried under vacuum. The product was obtained as a yellow powder. Yield 0.240 g (79%). NMR (400 MHz, CDCl3) δ 9.80 (s, 1H), 7.57 – 7.41 (m, 3H), 7.41 – 7.33 (m, 4H), 7.33 – 7.26 (m, 1H), 7.06 – 6.95 (m, 1H), 6.93 – 6.85 (m, 1H), 3.28 – 3.04 (m, 3H), 2.53 – 2.25 (m, 3H). IR (KBr): ν = 2910(m), 1653(s), 1593(m), 1491(s), 1413(m), 1267(s), 1138(s), 752(s), 594(m), 549(m).

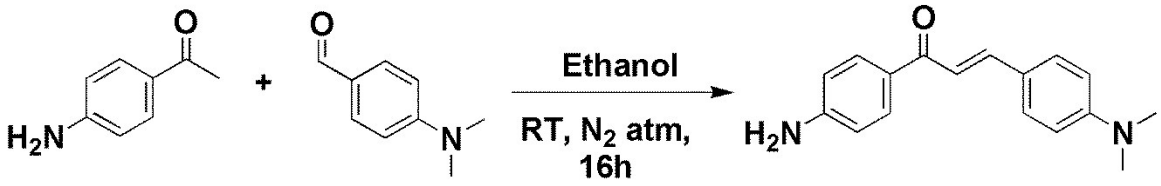
Scheme S1



Synthesis of ADAB: **1-(4-aminophenyl)-3-(4-(dimethylamino)phenyl)prop-2-en-1-one (ADAB):**

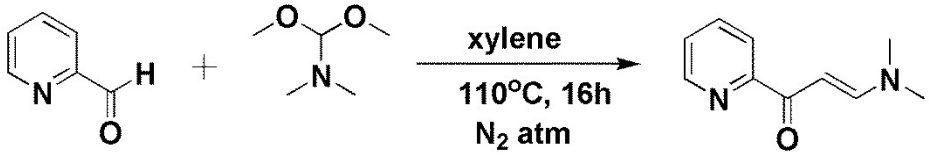
4-aminoacetophenone(1 g, 6.7 mmol) was suspended in ethanol (20 mL), to the suspension 40% of NaOH and 4-dimethylaminobenzaldeyde(0.904 g, 6.7 mmol) were added and stir this reaction mixture at RT for 16h. After completion of the reaction, the reaction mixture was poured into the 100 mL of ice water and P^H is adjusted to 1 by drop wise adding of dil. HCl. The reaction mixture was filtered; the filtrate was neutralized with 5% $NaHCO_3$ and subsequently extracted with CH_2Cl_2. The organic fraction was concentrated in vacuum under reduced pressure. Yield 1.569 g (86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ, 8.10 (dd, *J* = 15.6, 8.5 Hz, 2H), 7.98 – 7.69 (m, 1H), 7.59 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.42 (ddd, *J* = 15.4, 14.6, 6.7 Hz, 2H), 7.20 – 6.89 (m, 2H), 6.75 (dd, *J* = 15.5, 8.8 Hz, 2H), 3.26 – 2.91 (m, 6H), 1.64 (s, 2H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.34 – 161.14 (m), 130.85 (s), 129.58 (s), 121.45 – 121.25 (m), 111.86 (s), 77.35 (s), 77.03 (s), 76.71 (s), 40.17 (s).

Scheme S2



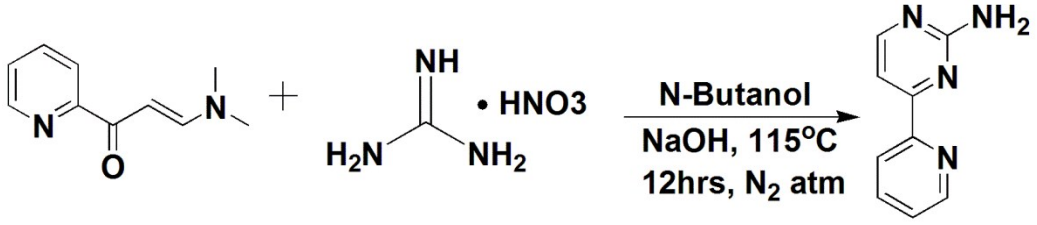
3-(Dimethylamino)-1-(pyridine-2-yl)prop-2-en-1-one. This compound was synthesised based on the literature. The reaction of (2g, 16.5mmol) of 2-acetylpyridine and DMF dimethyl acetal(7.84g) were suspended in 11ml of xylene and stir this reaction mixture for 16h at 110^{o}C. Into the resulting mixture 10 ml of hexane added yellow colour precipitate was formed and allows stirring for 20min at 3^{o}C. Resulting mixture was filtered and dried in vacuum to get a yellow colour powder.

Scheme S3

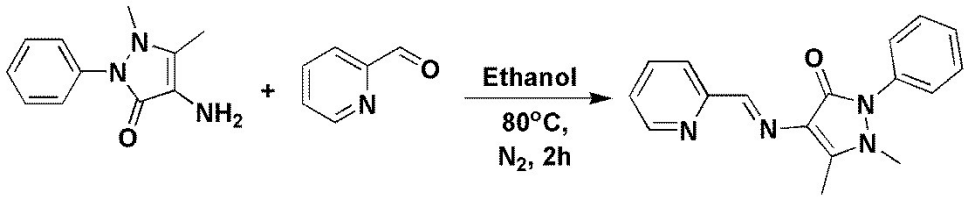


Synthesis of 4-(pyridine-2-yl) pyrimidin-2-amine (P2P). (0.5 g, 2.84 mmol) of (Z)-3-dimethylamino-1-(pyridine-2-yl)prop-2-en-1-one was suspended was suspended in 15ml of n-butanol. To the solution (0.346 g, 2.84 mmol) of guanidine nitrate added and followed by the addition of NaOH(0.114 g, 2.84 mmol) and reflux this mixture at 110^{o}C for 12h. After completion of the reaction the mixture was filtered, the clear yellow solution of filtrate kept for room temperature. After 20 min yellow crystal formed and dried in a vacuum under reduced pressure. Yield (0.296 g, 60%) IR (KBr): 3471, 3142, 1622, 1568, 1463, 1340, 1215, 1095, 993, 783, 650, 524.^{1}H NMR (300 MHz, $CDCl_3$) δ 8.69 (dd, *J* = 11.9, 10.0 Hz, 1H), 8.45 (dd, *J* = 5.1, 2.6 Hz, 1H), 8.40 – 8.20 (m, 1H), 7.85 (ddd, *J* = 17.9, 9.4, 7.3 Hz, 1H), 7.64 (dd, *J* = 5.1, 2.8 Hz, 1H), 7.53 – 7.30 (m, 1H), 5.30 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.49 (s), 163.75 (s), 159.65 (s), 154.75 (s), 149.79 (s), 137.29 (s), 125.41 (s), 121.87 (s), 108.26 (s).

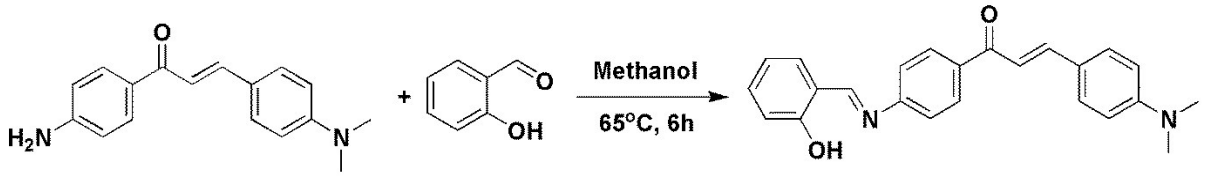
Scheme S4



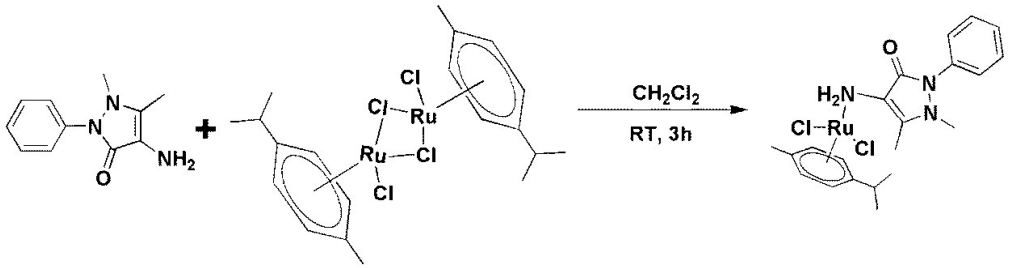
Synthesis of 2,3-dimethyl-1-phenyl-4-(pyridine-2-ylmethyleneamino)-1,2-dihydropyrazol-5-one (AAPPA)
Scheme S5



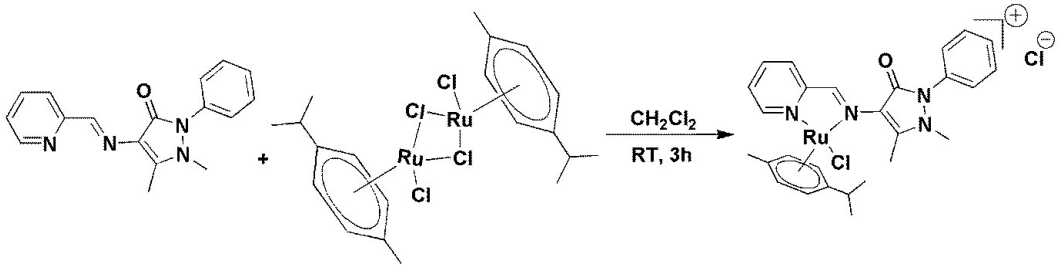
Synthesis of 1-(4-((Z)-2-hydroxybenzylideneamino)phenyl)-3-(4-(dimethylamino) phenyl)prop-2-en-1-one (ADABS)
Scheme S6



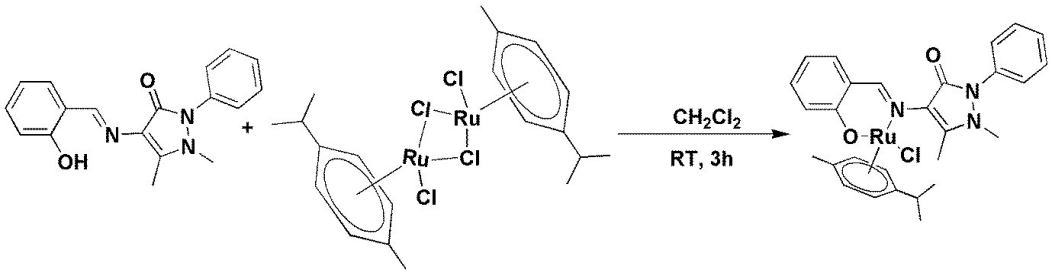
Synthesis of Ru(η^6-*p*-cymene)Cl_2(4-aminoantipyrine) (AAP-Ru)
Scheme S7



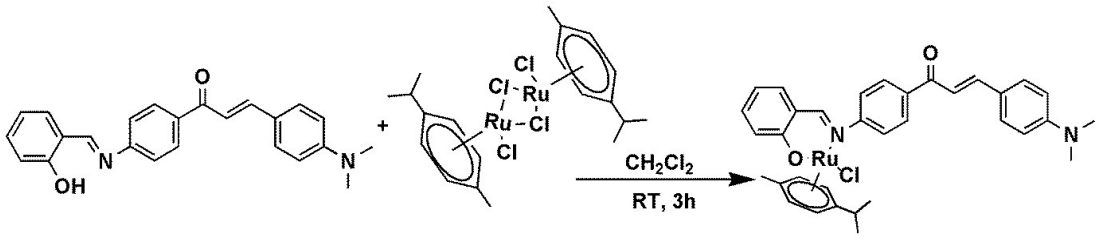
Synthesis of (η^6-*p*-cymene)(2,3-dimethyl-1-phenyl-4-(pyridine-2-ylmethyleneamino)-1,2-dihydropyrazol-5-one)chlororuthenium(II) chloride (AAPPA-Ru)
Scheme S8



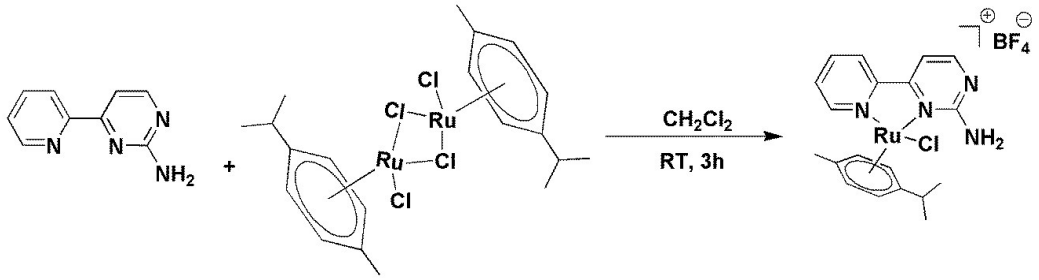
Synthesis of (η^6-*p*-cymene)(4-(2-hydroxybenzylideneamino)-2,3-dimethyl-1-phenyl-1,2-dihydropyrazol-5-one)chlororuthenium(II) (AAPS-Ru)
Scheme S9



Synthesis of (η^6-*p*-cymene)(1-(4-((Z)-2-hydroxybenzylideneamino)phenyl)-3-(4-(dimethylamino) phenyl)prop-2-en-1-one)chlororuthenium(II) (ADABS-Ru)
Scheme S10



Synthesis of (η^6-*p*-cymene)(4-(pyridine-2-yl)pyrimidin-2-amine)chlororuthenium(II) tetrafluoroborate (P2P-Ru) c
Scheme S11



NMR Spectra

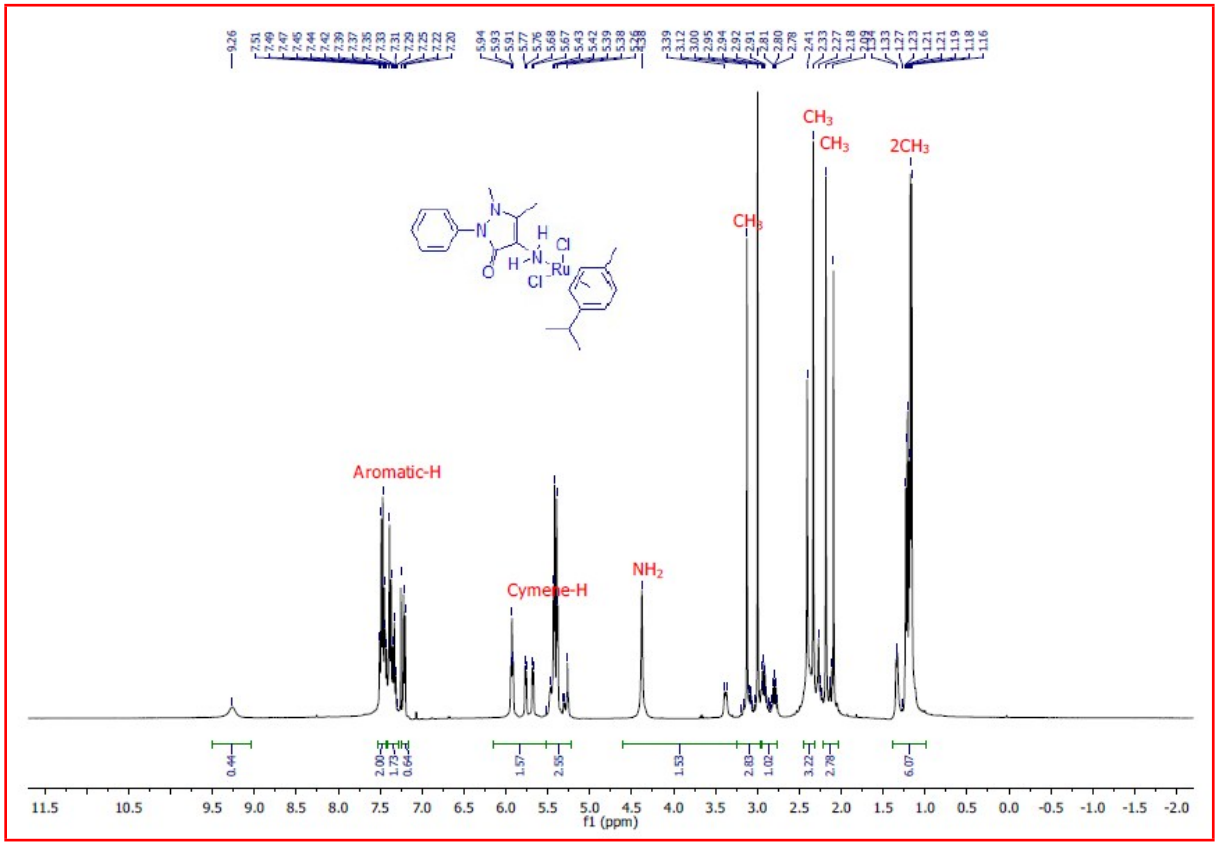


Fig. S1 ^{1}H NMR spectra for AAP-Ru.

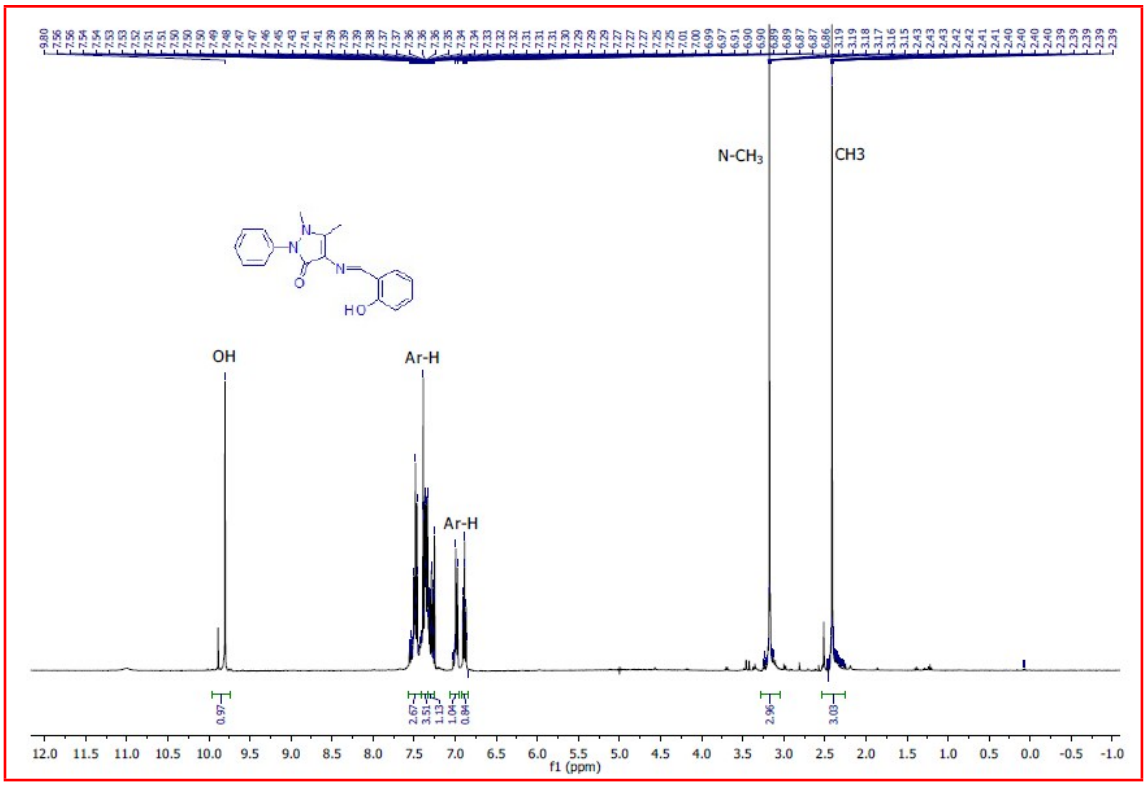


Fig. S2 ^{1}H NMR spectra for AAPS

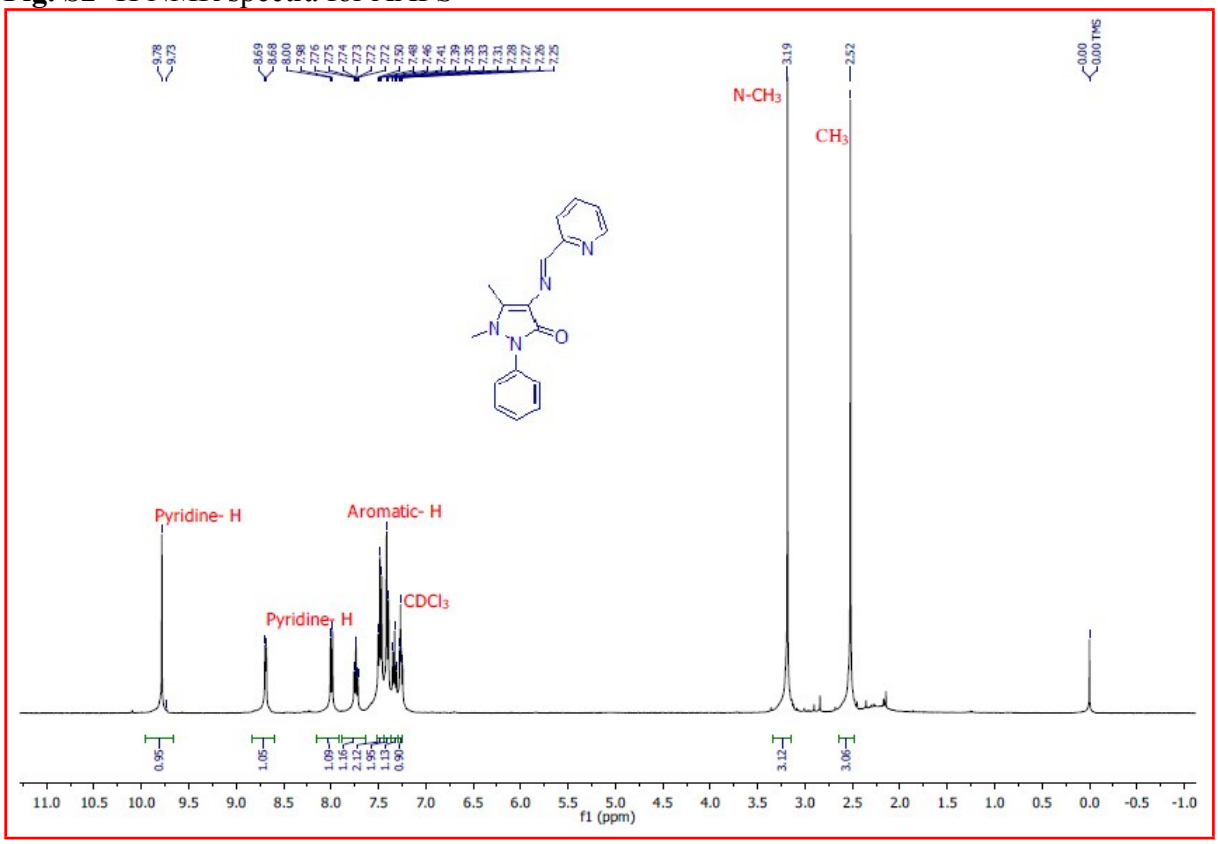


Fig. S3 ^{1}H NMR spectra for AAPPA

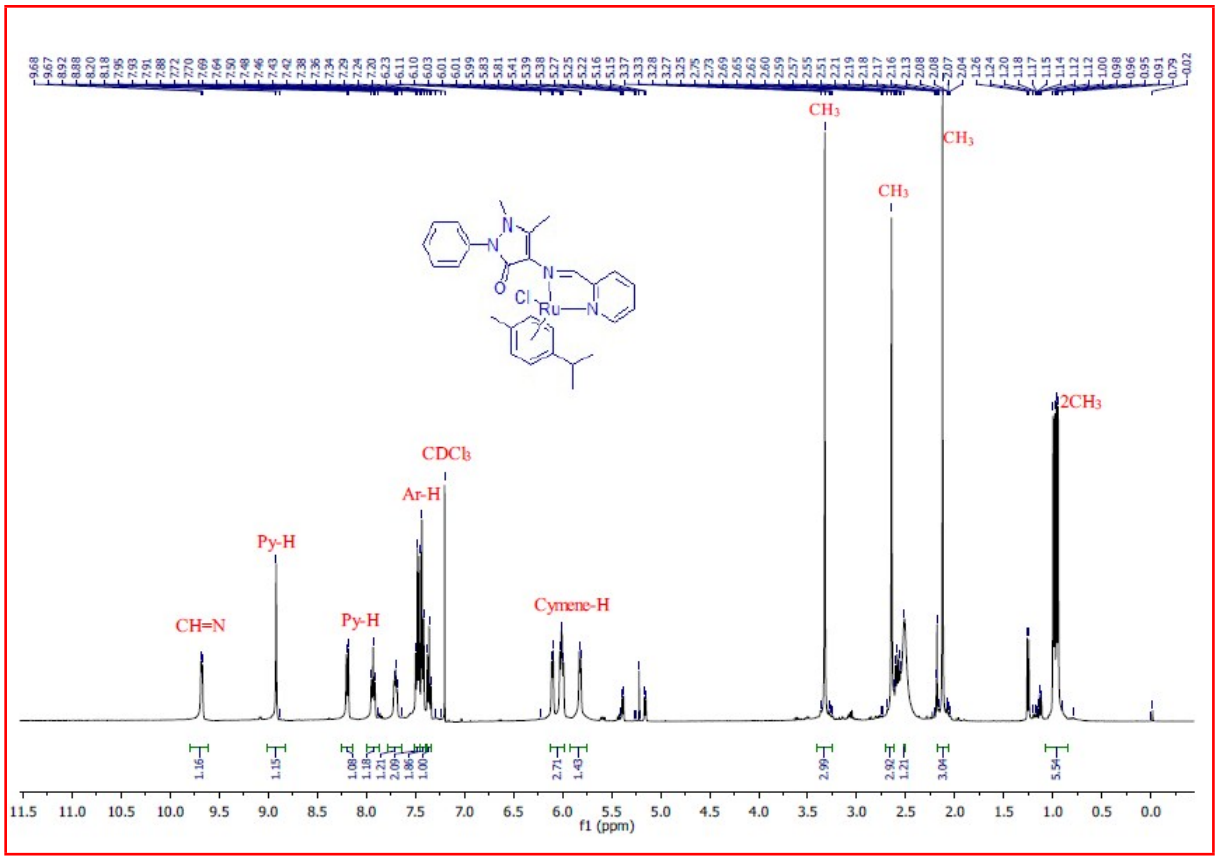


Fig. S4 ^{1}H NMR spectra for AAPPA-Ru.

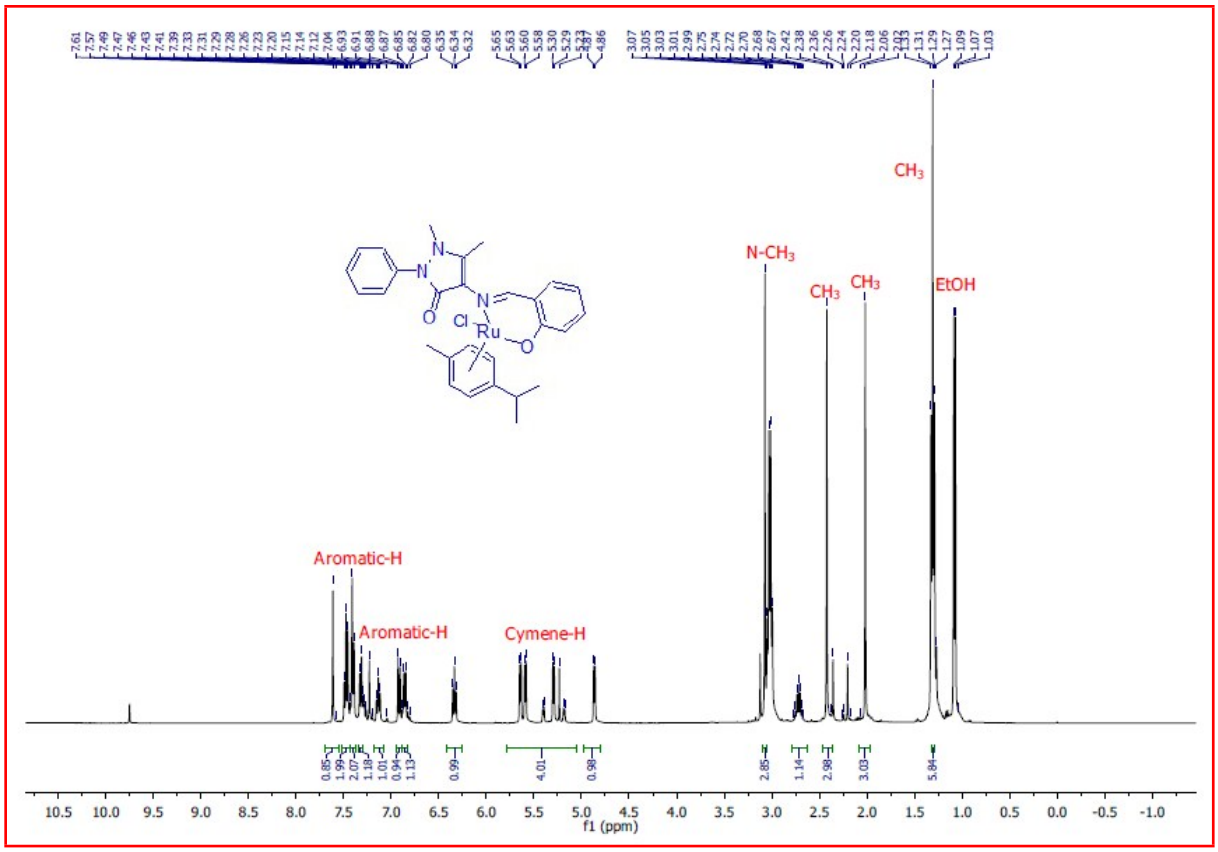


Fig. S5 ^{1}H NMR spectra for AAPS-Ru.

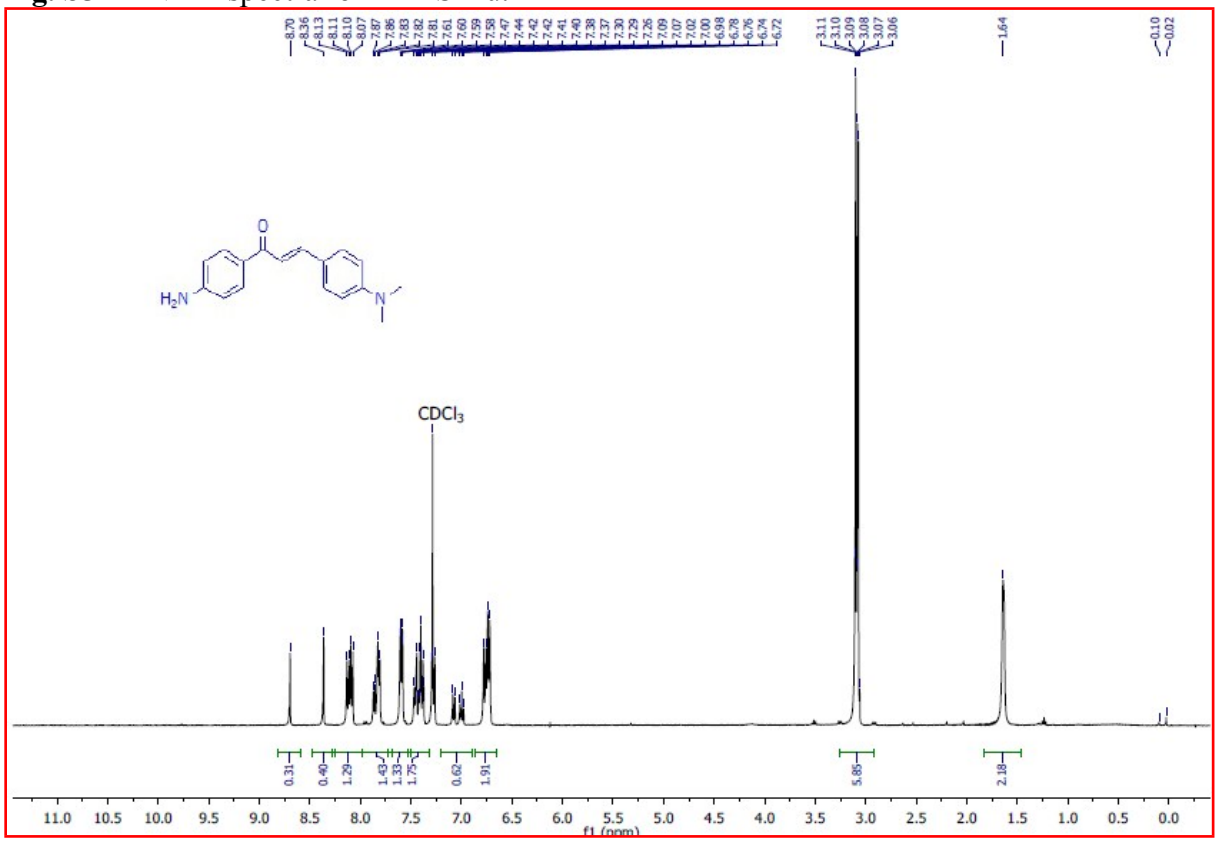


Fig. S6 ^{1}H NMR spectra for ADAB

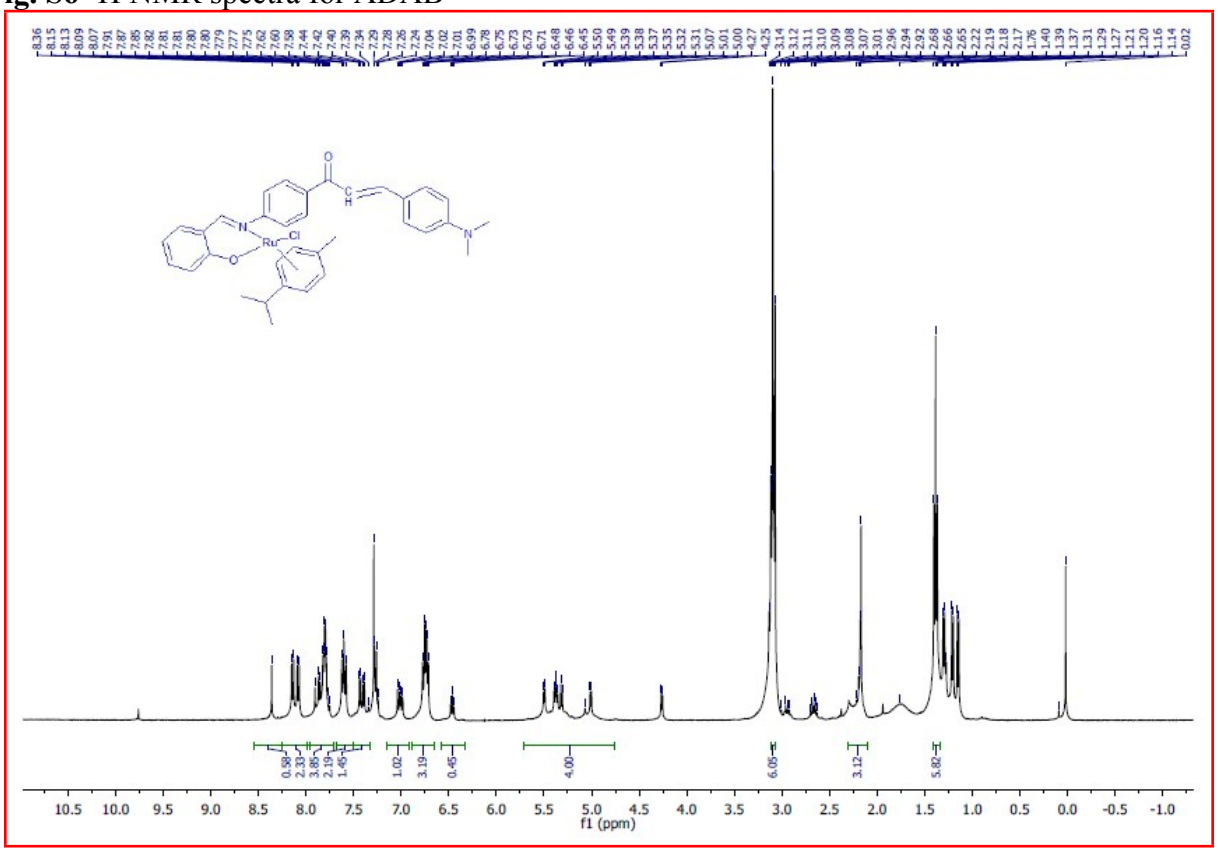


Fig. S7 ^{1}H NMR spectra for ADABS-Ru.

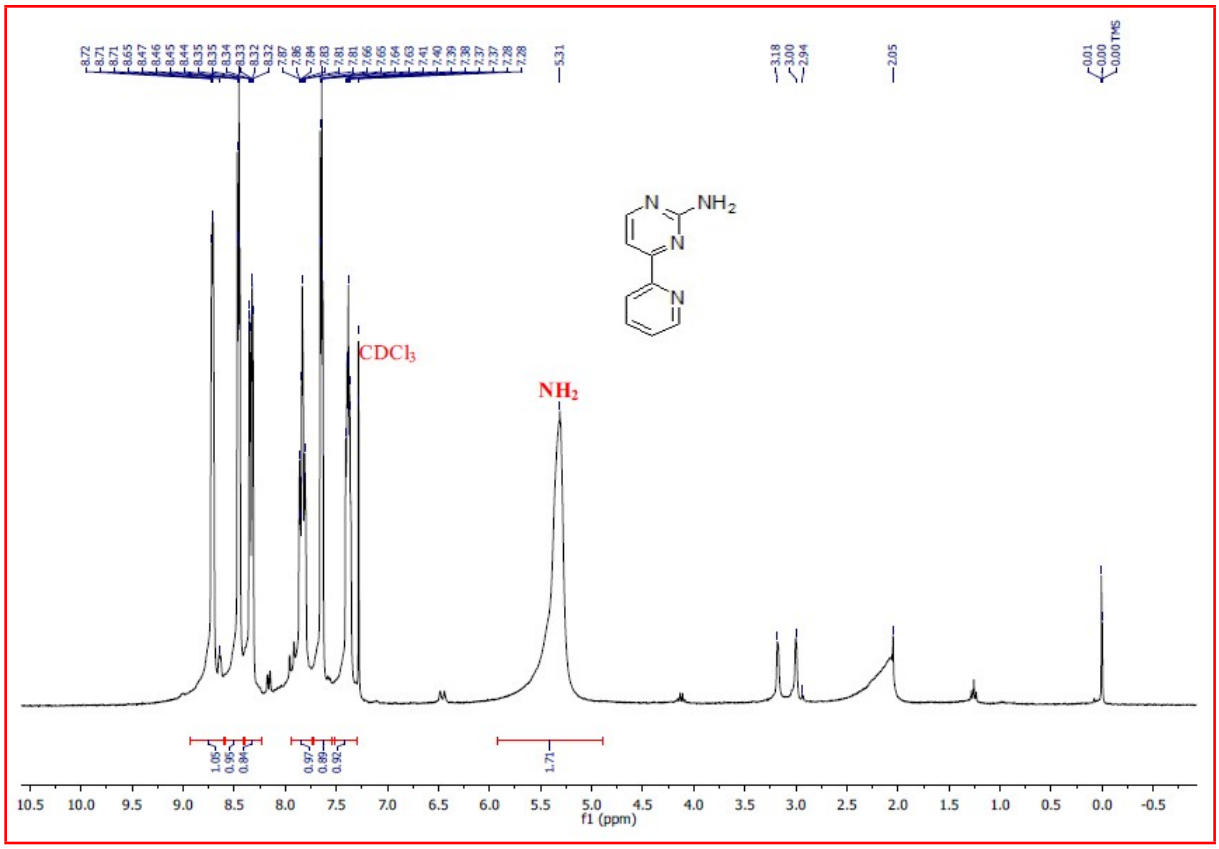


Fig. S8 ^{1}H NMR spectra for P2P

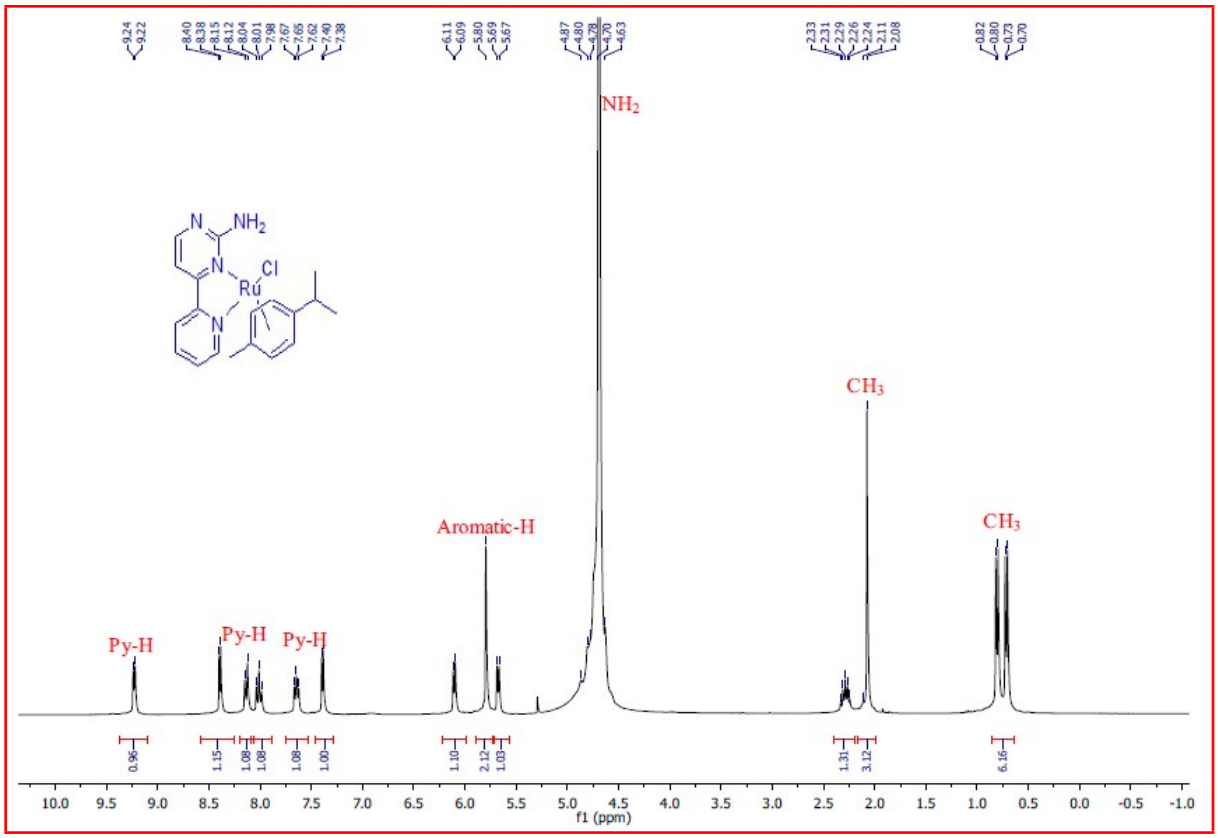


Fig. S9 ^{1}H NMR spectra for P2P-Ru.

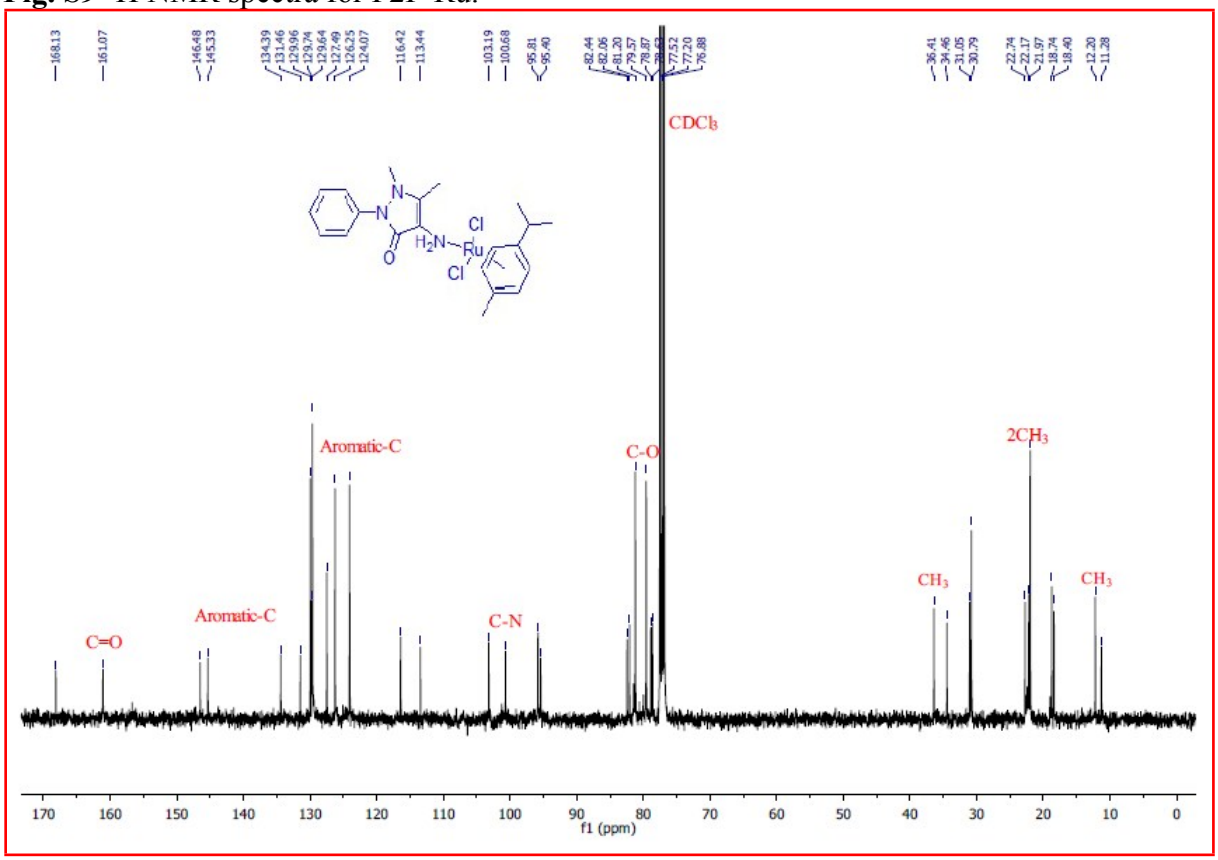


Fig. S10 ^{13}C NMR spectra for AAP-Ru.

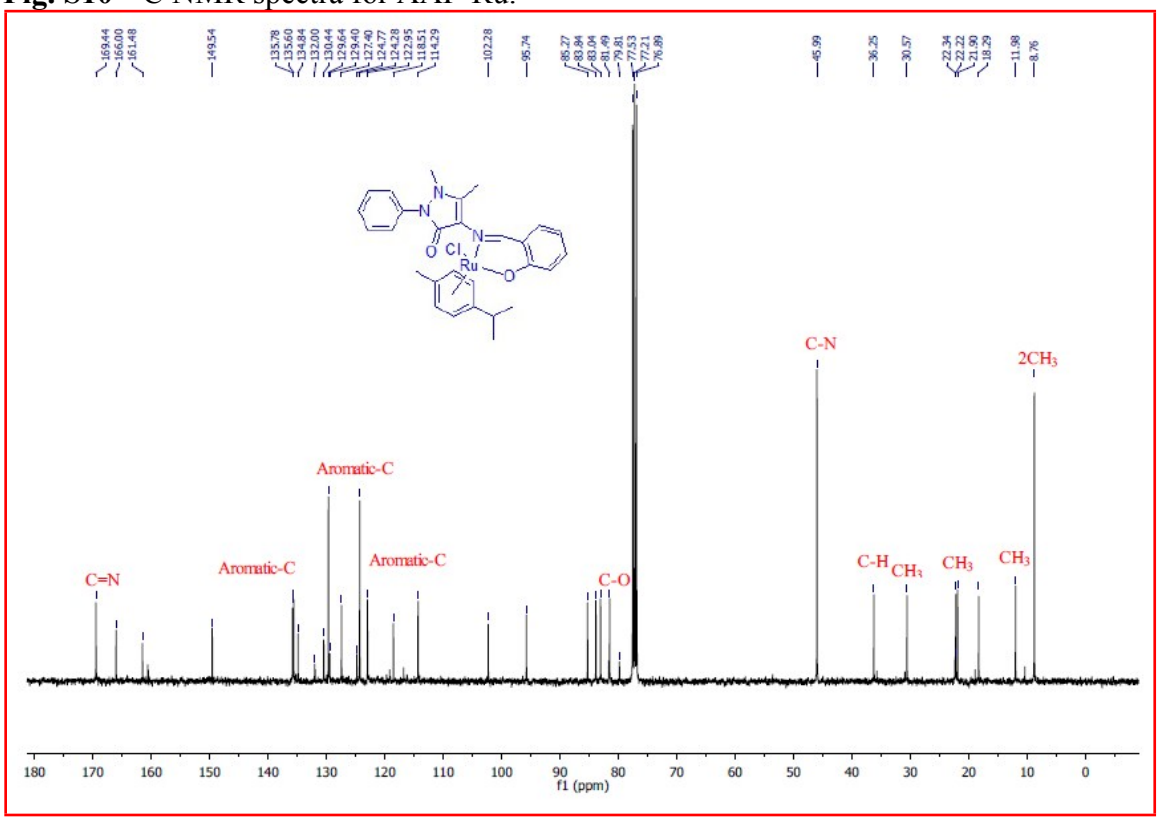


Fig. S11 ^{13}C NMR spectra for AAPS-Ru.

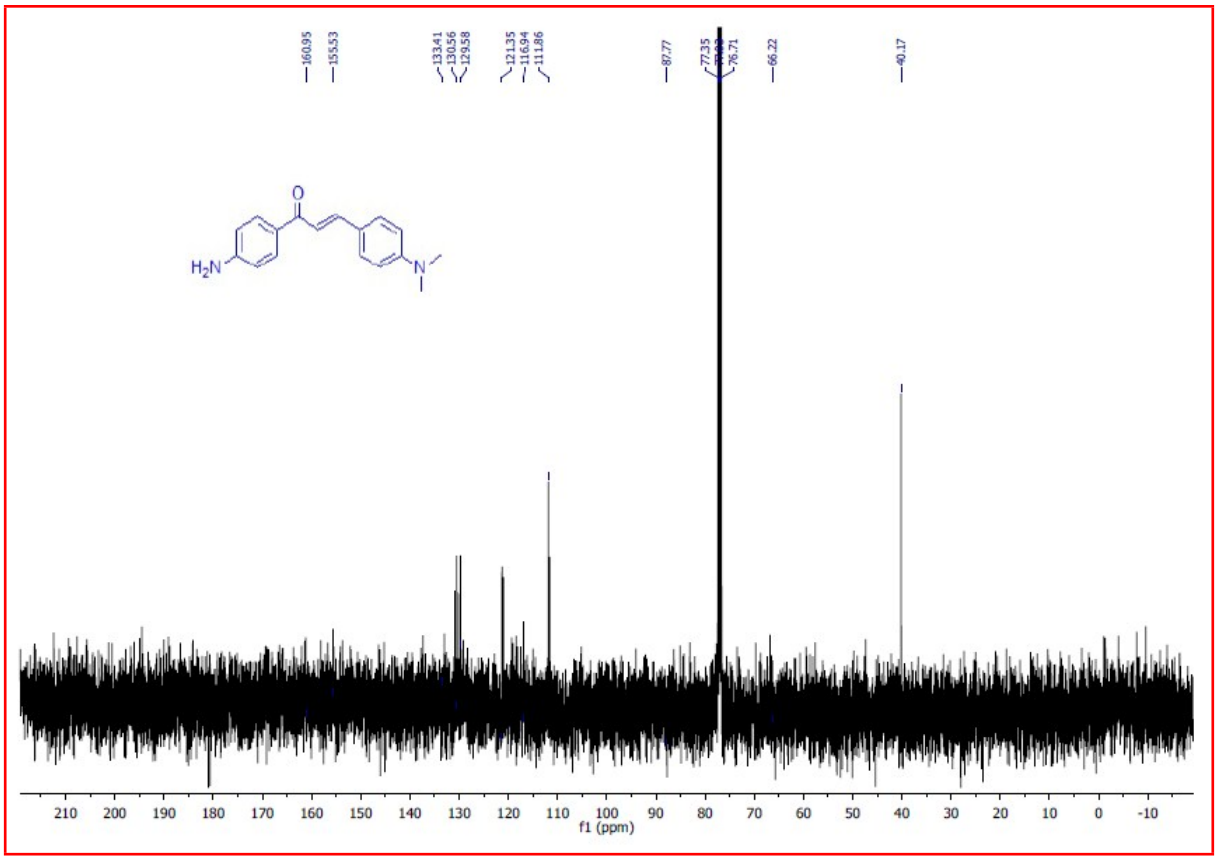


Fig. S12 ^{13}C NMR spectra for ADAB

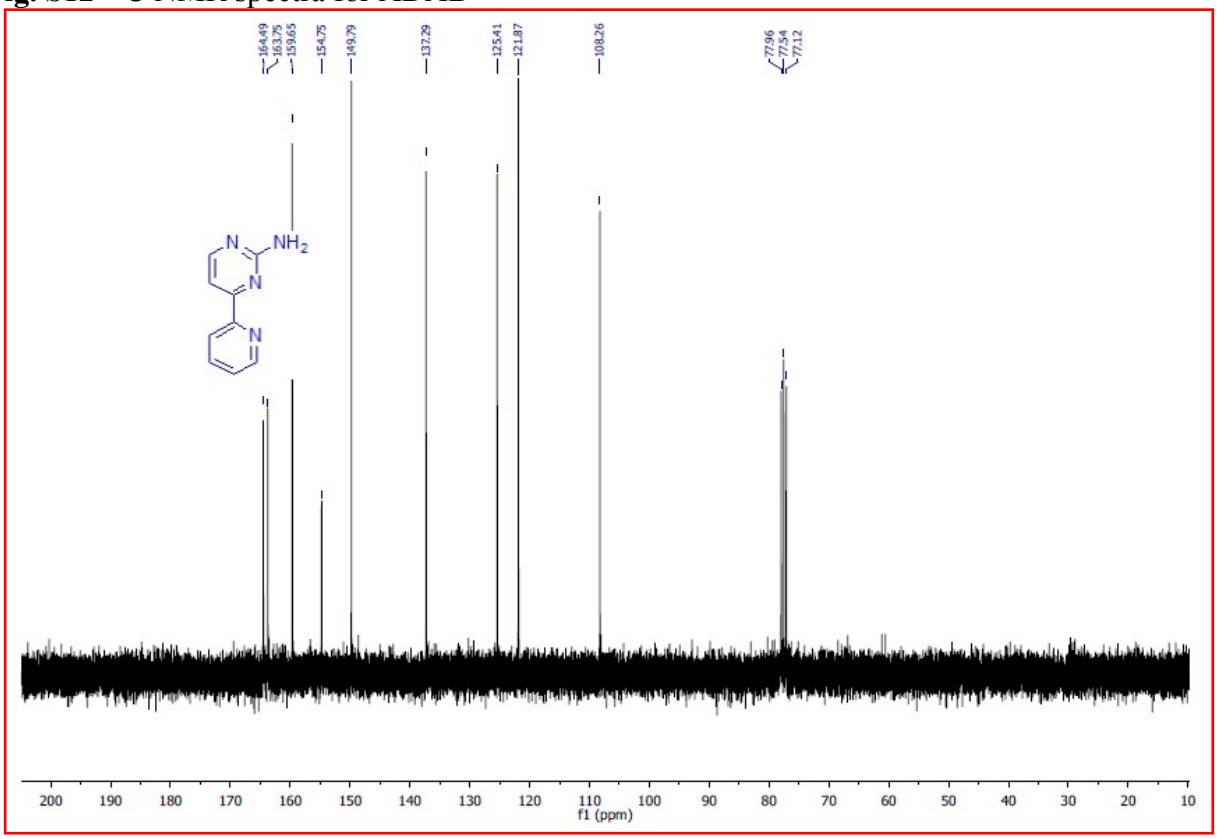


Fig. S13 ^{13}C NMR spectra for P2P

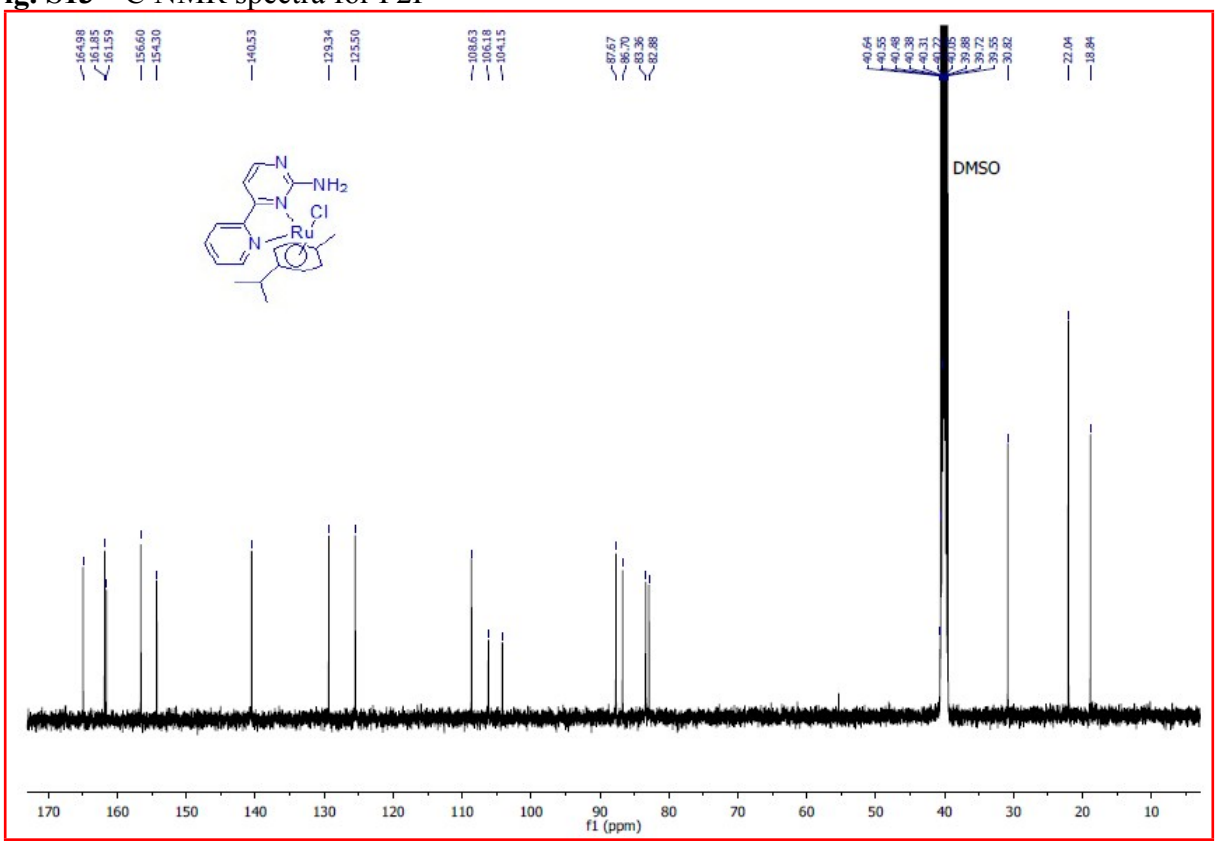


Fig. S14 ^{13}C NMR spectra for P2P-Ru.

IR Spectra

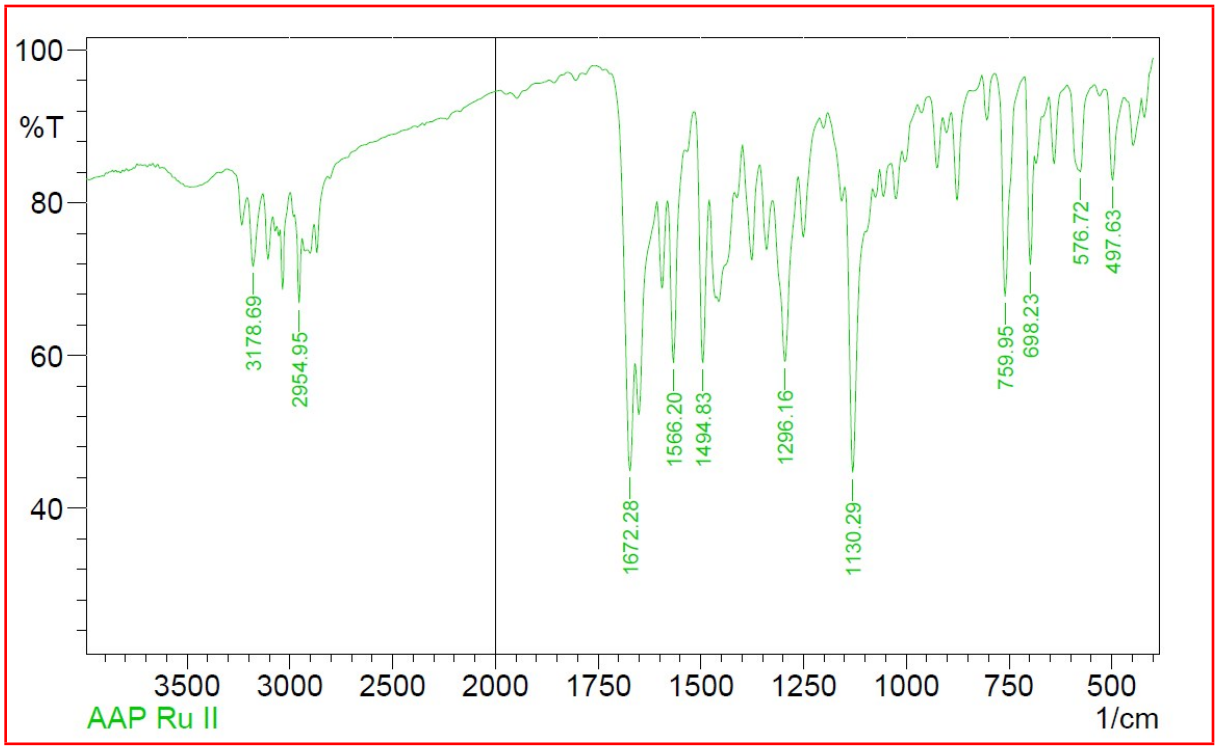


Fig. S15 FT-IR Spectrum for AAP-Ru.

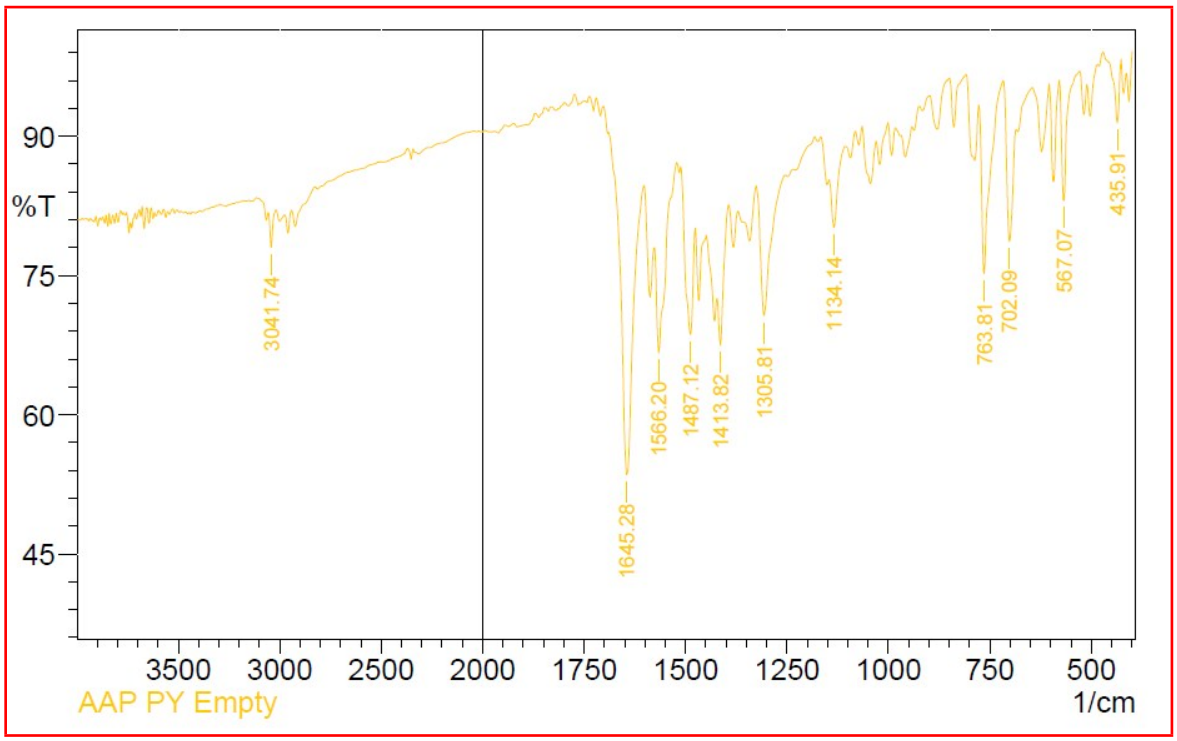


Fig. S16 FT-IR Spectrum for AAPPA

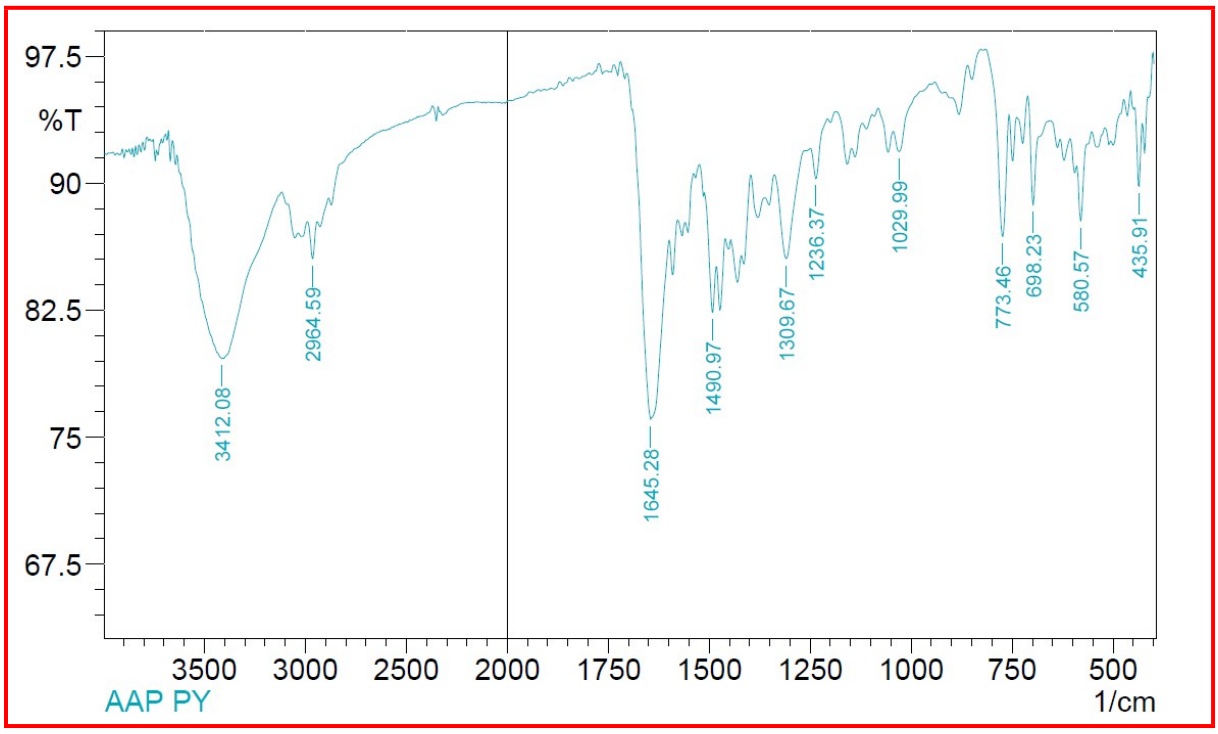


Fig. S17 FT-IR Spectrum for AAPPA-Ru.

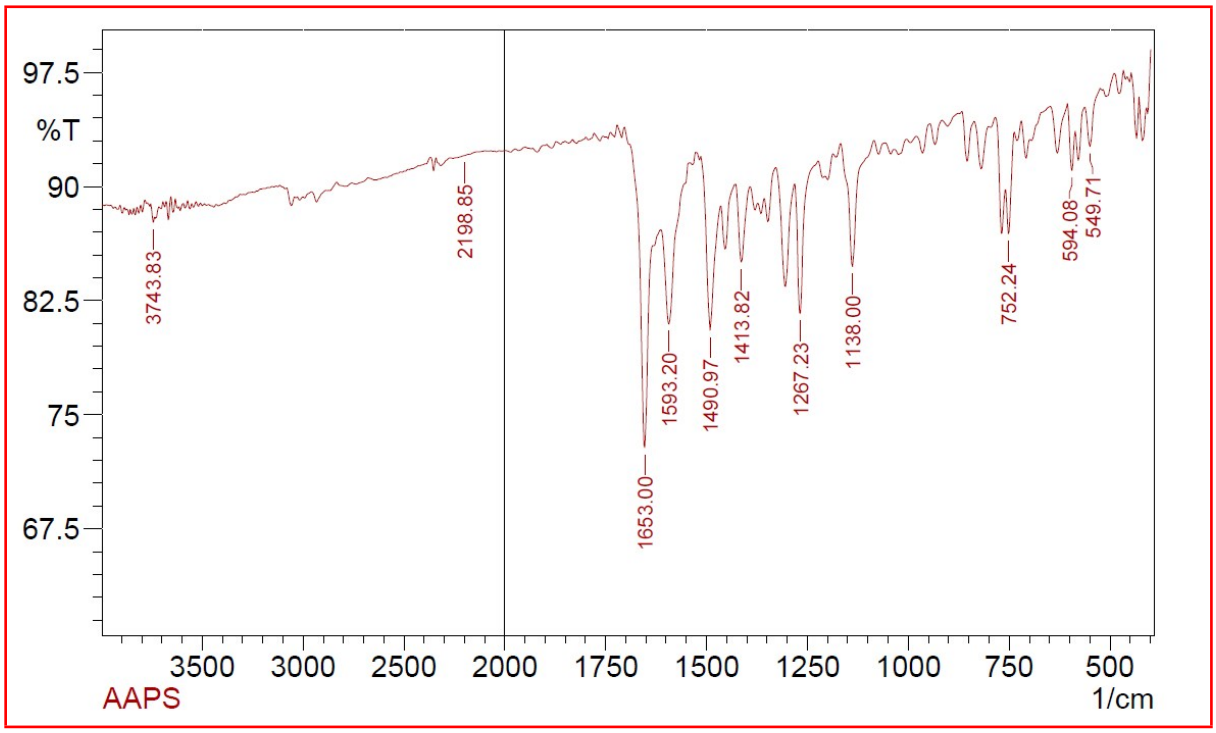


Fig. S18 FT-IR Spectrum for AAPS

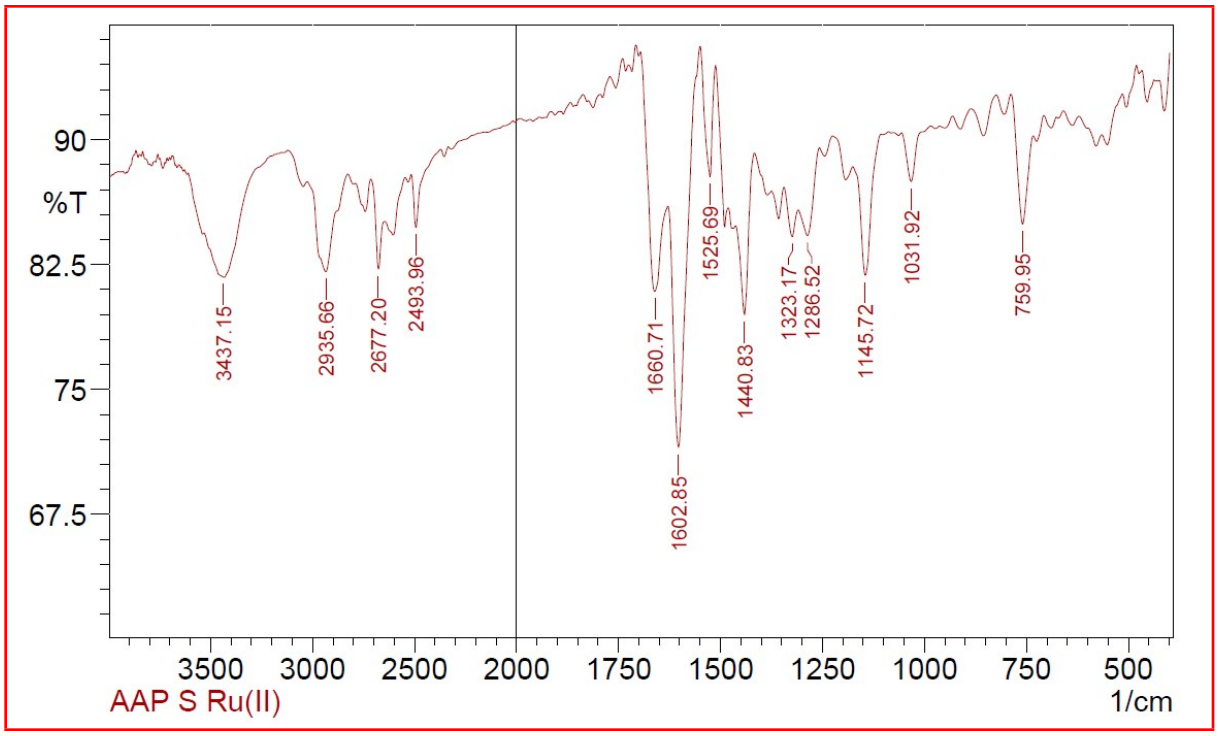


Fig. S19 FT-IR Spectrum for AAPS-Ru.

Fig. S20 FT-IR Spectrum for ADABS

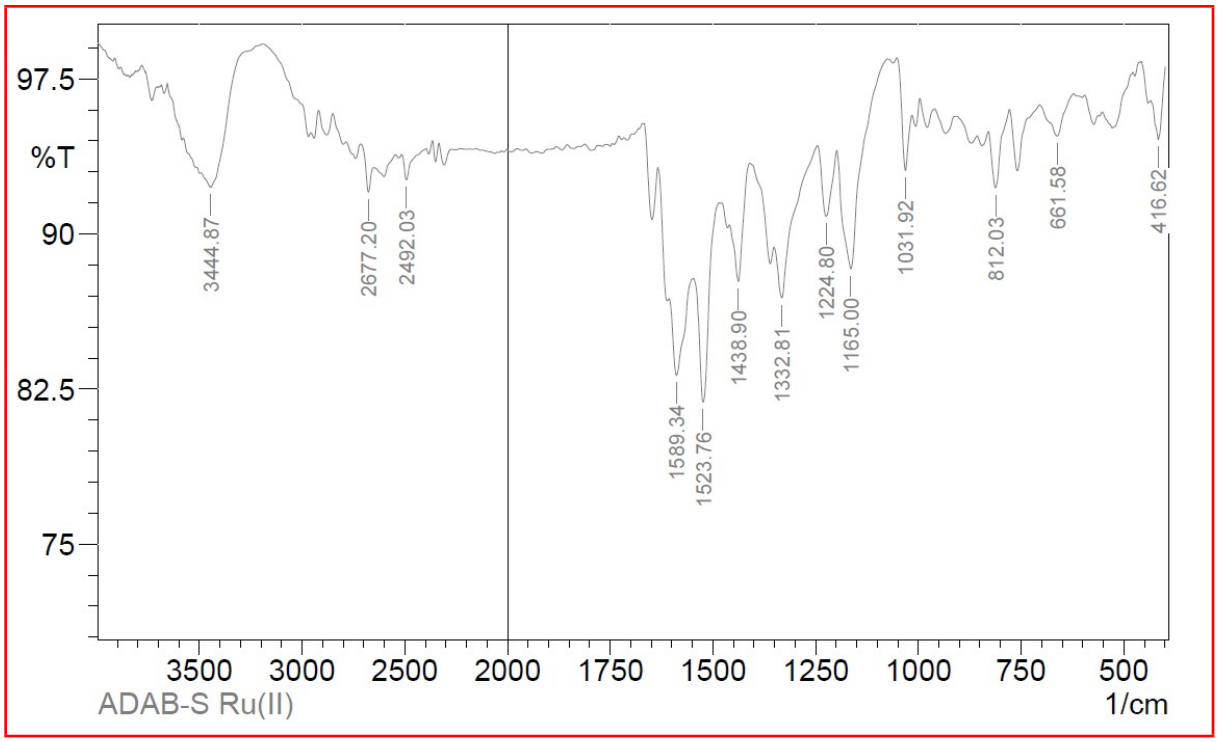


Fig. S21 FT-IR Spectrum for ADABS-Ru.

Fig. S22 FT-IR Spectrum for P2P

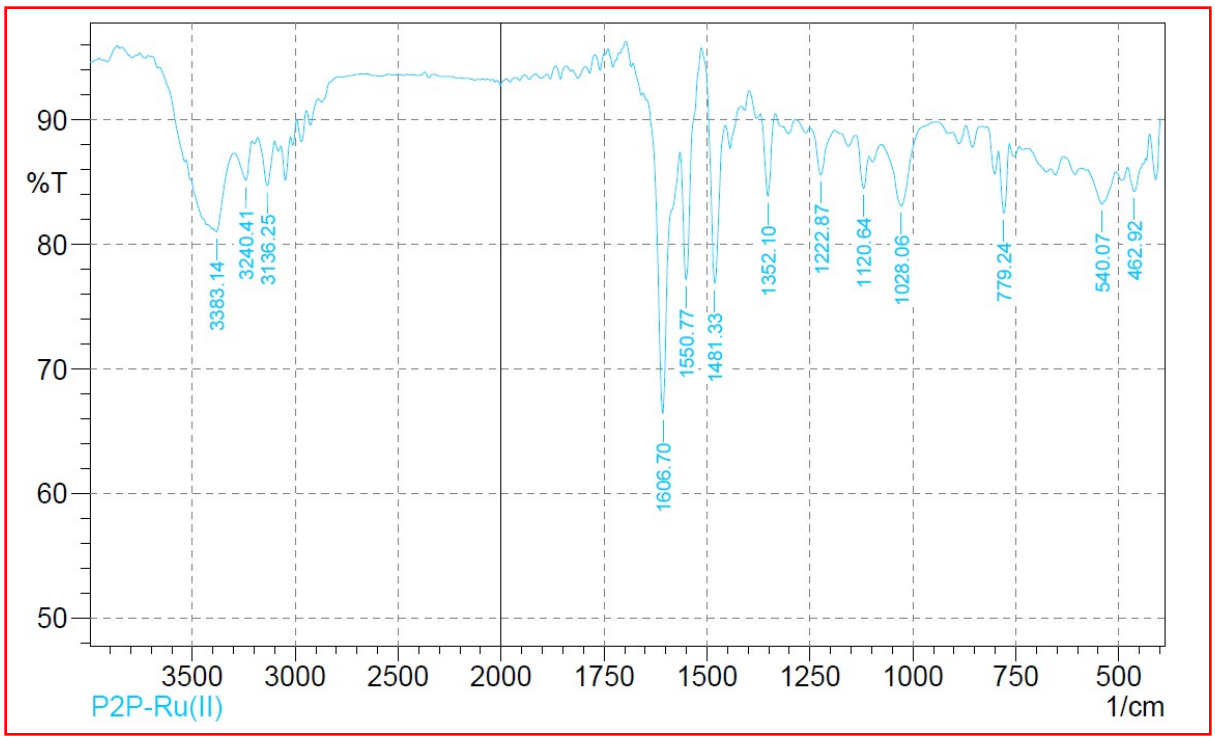


Fig. S23 FT-IR Spectrum for P2P-Ru.

Mass Spectra

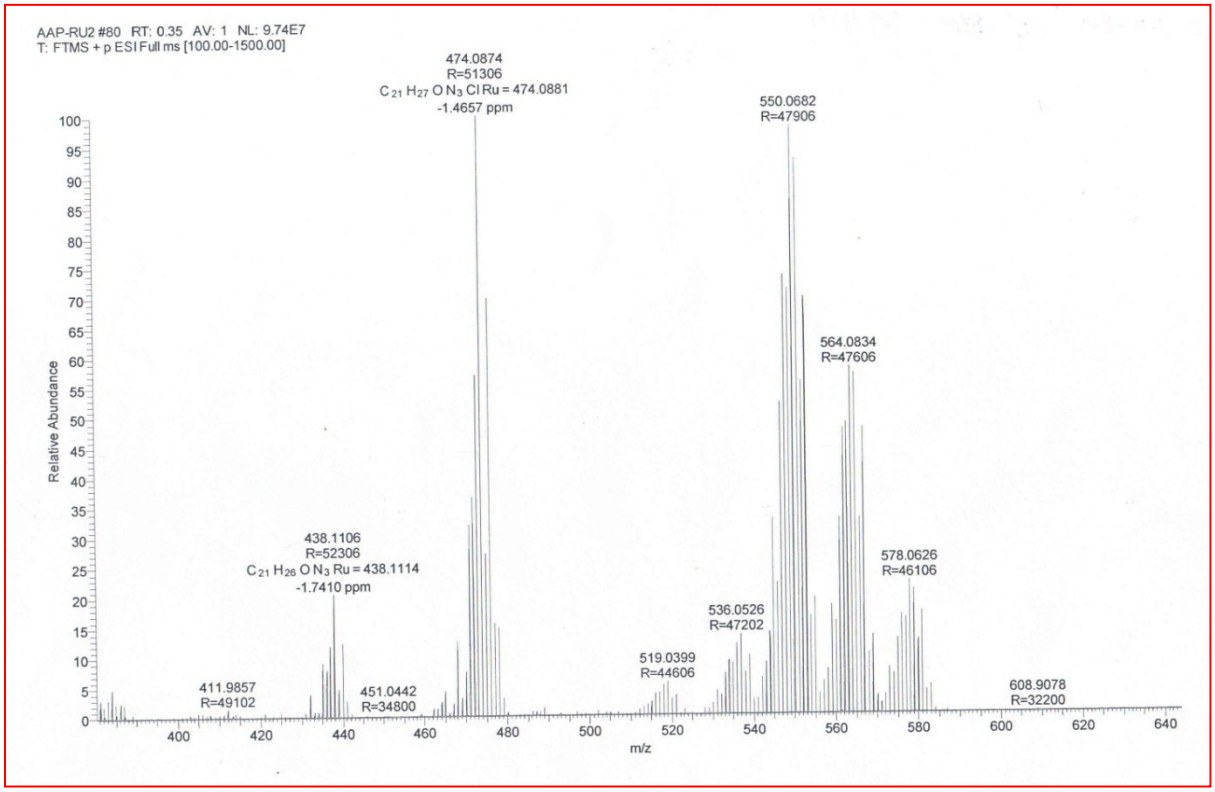


Fig. S24 ESI-MS spectrum for AAP-Ru.

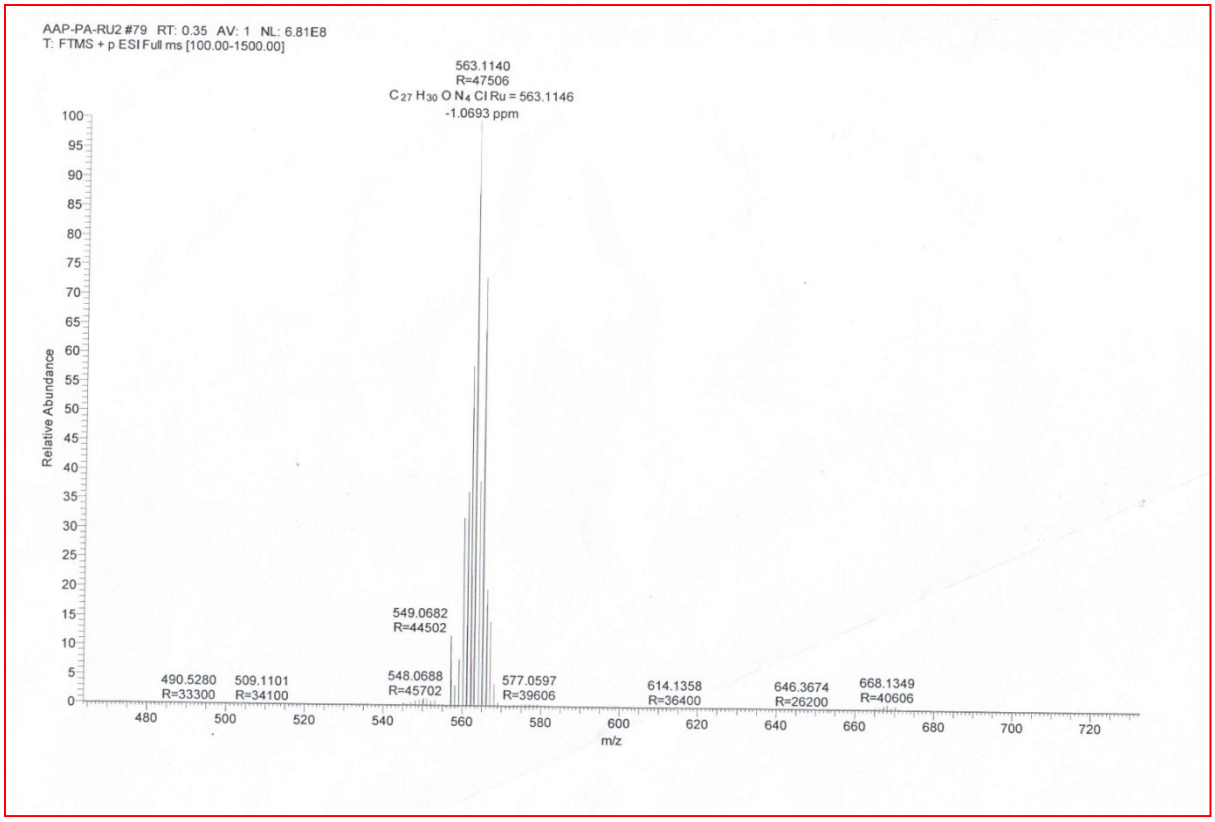


Fig. 25 ESI-MS spectrum of AAPPA-Ru.

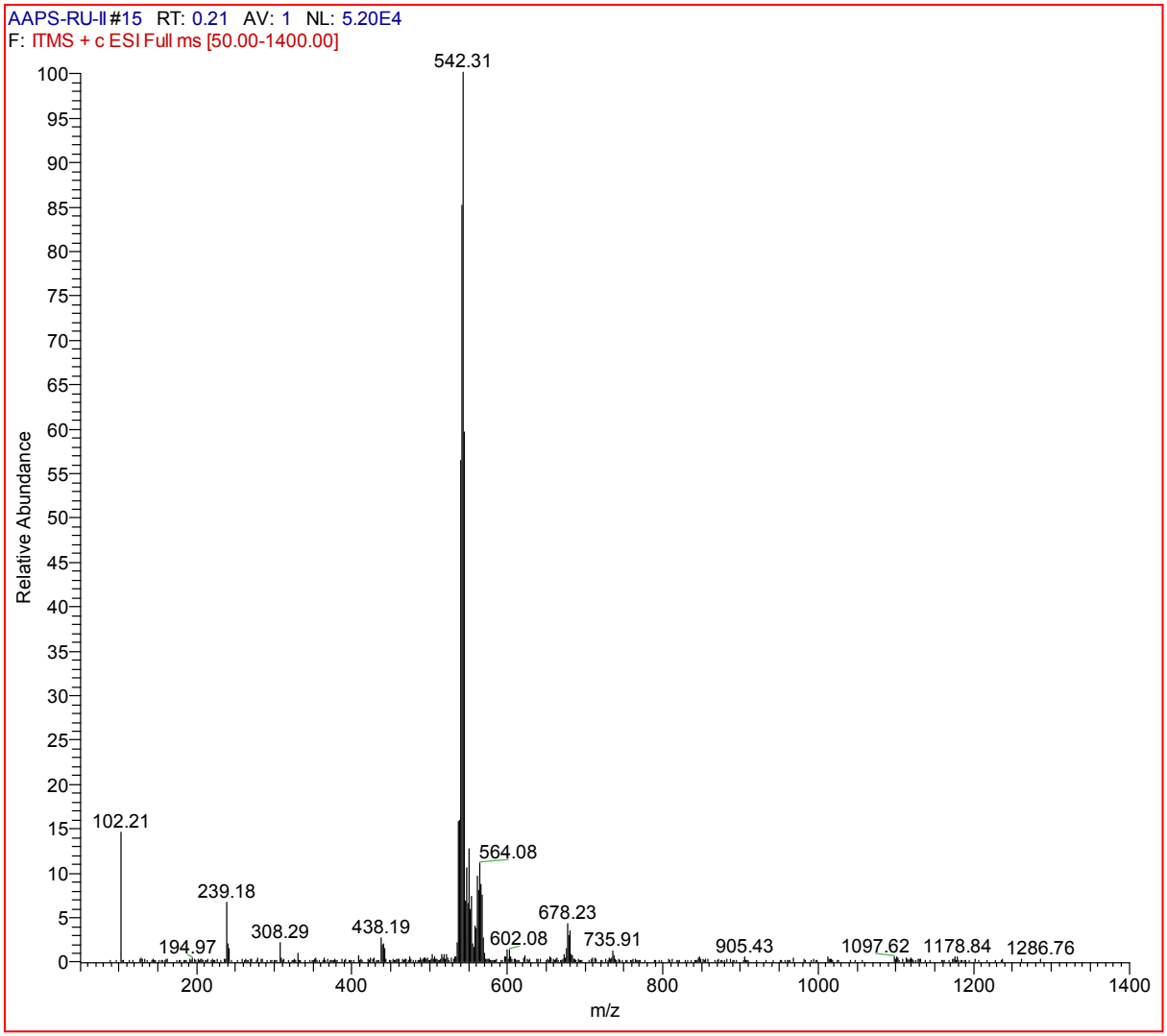


Fig. S26 ESI-MS spectrum for AAPS-Ru.

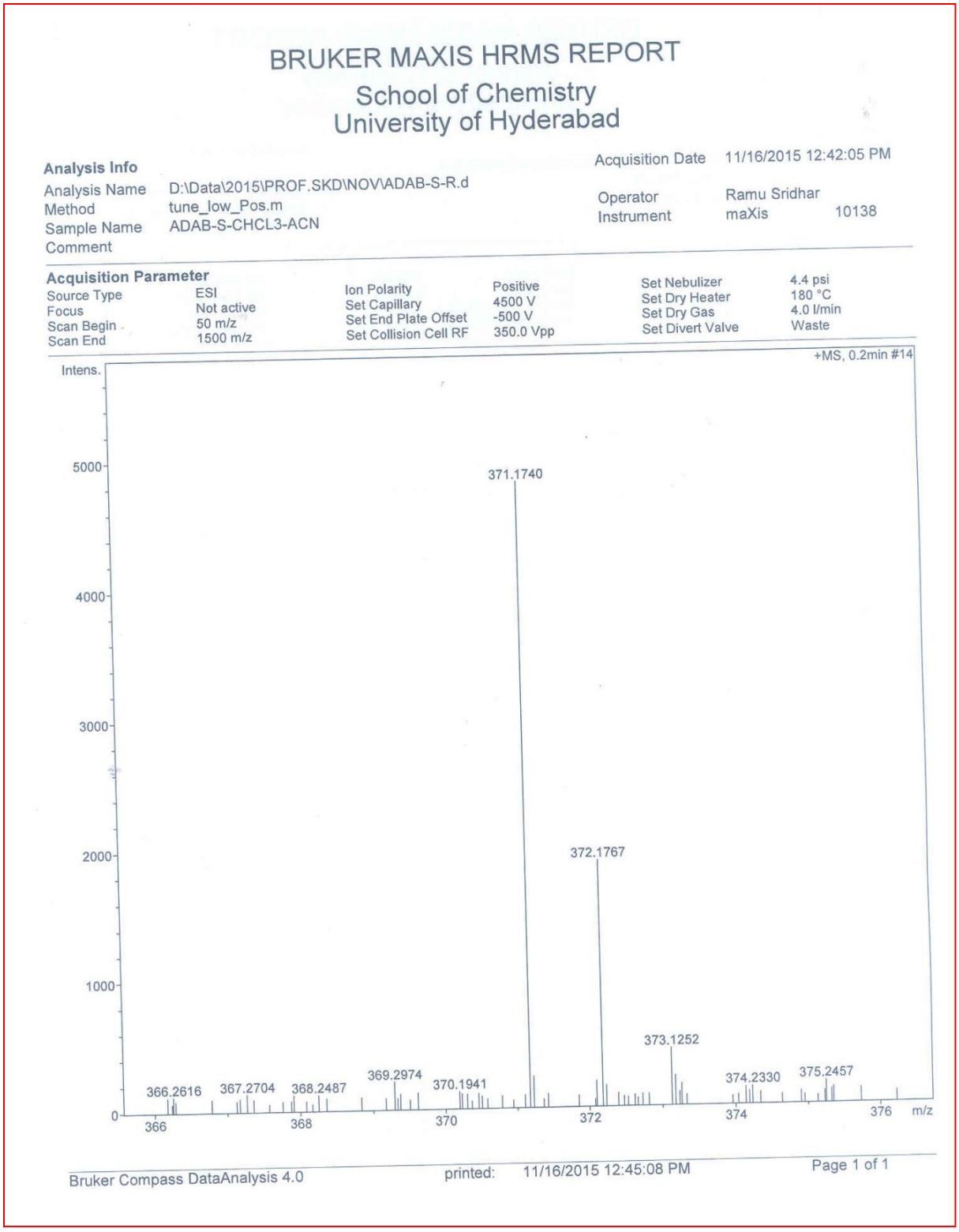


Fig. S27 ESI-MS spectrum for ADABS

Single Crystal X-ray Data

Single Crystal X-ray Structure Determination

A single crystal of AAP-Ru, ADABS-Ru and P2P-Ru was coated with paratone-N oil and the diffraction data were measured at 100 K with synchrotron radiation (l = 0.60999 Å) on an ADSC Quantum-210 detector at 2D SMC with a silicon (111) double crystal monochromator (DCM) at the Pohang Accelerator Laboratory, Korea. The ADSC Q210 ADX program[4] was used for data collection (the detector distance is 63 mm, omega scan; Do = 31, the exposure time is 2 s per frame) and HKL3000sm (Ver. 703r)[5] was used for cell refinement, reduction and absorption correction. The crystal structure of AAP-Ru, ADABS-Ru(II) and P2P-Ru(II) was solved by the direct method using the SHELX-XT (2014/4) program and refined by full-matrix least square calculations using the SHELX-XL (2014/7) program package.[6] All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were assigned an isotropic displacement coefficient of Uiso(H) = 1.2 or 1.5Ueq, and their coordinates were allowed to ride on their respective atoms. Selected bond distances and angles are tabulated in Table S1, S2 and S3.

Table S1. Selected Bond lengths [Å] and angles [°] for Complex **AAP-Ru**

Ru(1)-C(18)	2.161(2)	Ru(1)-C(17)	2.162(2)
Ru(1)-N(1)	2.1723(18)	Ru(1)-C(14)	2.182(2)
Ru(1)-C(16)	2.199(2)	Ru(1)-Cl(2)	2.4047(7)
Ru(1)-Cl(1)	2.4143(7)	O(1)-C(1)	1.227(3)
C(16)-C(17)	1.410(3)	C(16)-C(19)	1.513(3)
C(18)-Ru(1)-C(17)	38.68(8)	C(18)-Ru(1)-N(1)	96.64(8)
C(17)-Ru(1)-N(1)	93.87(7)	C(18)-Ru(1)-C(14)	68.40(9)
C(17)-Ru(1)-C(14)	81.39(8)	N(1)-Ru(1)-C(14)	161.31(8)
N(1)-Ru(1)-C(15)	154.97(7)	C(14)-Ru(1)-C(15)	37.32(8)
C(13)-Ru(1)-C(16)	81.67(8)	C(18)-Ru(1)-Cl(2)	159.01(6)
C(17)-Ru(1)-Cl(2)	120.35(6)	N(1)-Ru(1)-Cl(2)	81.77(5)
C(14)-Ru(1)-Cl(2)	116.27(6)	C(15)-Ru(1)-Cl(2)	91.97(6)
C(18)-Ru(1)-Cl(1)	113.36(6)	C(17)-Ru(1)-Cl(1)	151.53(6)
C(15)-Ru(1)-Cl(1)	121.13(6)	C(13)-Ru(1)-Cl(1)	88.81(6)
C(16)-Ru(1)-Cl(1)	159.37(6)	Cl(2)-Ru(1)-Cl(1)	87.32(3)
C(14)-C(13)-C(12)	120.1(2)	C(18)-C(13)-Ru(1)	69.80(12)
C(14)-C(13)-Ru(1)	70.40(12)	C(12)-C(13)-Ru(1)	129.19(15)
C(14)-C(15)-Ru(1)	71.18(12)	C(16)-C(15)-Ru(1)	71.38(11)
C(15)-C(16)-Ru(1)	70.37(11)	C(19)-C(16)-Ru(1)	132.73(15)

Table S2. Selected bond lengths [Å] and angles [°] for complex **ADABS-Ru**

Ru(1)-O(1)	2.0668(12)	Ru(1)-N(1)	2.0801(14)
Ru(1)-C(4)	2.1767(15)	Ru(1)-C(5)	2.1773(16)
Ru(1)-C(7)	2.1777(16)	Ru(1)-C(3)	2.1847(16)
Ru(1)-C(2)	2.1998(17)	Ru(1)-C(6)	2.2006(16)
Ru(1)-Cl(1)	2.4409(6)	O(1)-C(11)	1.3017(18)
O(2)-C(24)	1.228(2)	N(1)-C(17)	1.291(2)
N(1)-C(18)	1.436(2)	C(1)-C(2)	1.503(2)
O(1)-Ru(1)-N(1)	88.37(6)	O(1)-Ru(1)-C(4)	116.20(6)
N(1)-Ru(1)-C(4)	93.78(6)	O(1)-Ru(1)-C(5)	88.73(6)
N(1)-Ru(1)-C(5)	120.38(6)	C(4)-Ru(1)-C(5)	37.88(6)
O(1)-Ru(1)-C(7)	116.26(6)	N(1)-Ru(1)-C(7)	154.66(6)
C(4)-Ru(1)-C(7)	81.03(7)	C(5)-Ru(1)-C(7)	69.02(7)
O(1)-Ru(1)-C(3)	154.50(6)	N(1)-Ru(1)-C(3)	92.87(6)
C(4)-Ru(1)-C(3)	38.30(6)	N(1)-Ru(1)-C(2)	116.63(6)
N(1)-Ru(1)-C(6)	158.79(6)	C(3)-Ru(1)-C(6)	79.92(7)
O(1)-Ru(1)-Cl(1)	84.86(4)	N(1)-Ru(1)-Cl(1)	86.91(5)
C(4)-Ru(1)-Cl(1)	158.93(5)	C(5)-Ru(1)-Cl(1)	151.80(4)
C(7)-Ru(1)-Cl(1)	89.35(5)	C(3)-Ru(1)-Cl(1)	120.64(5)
C(6)-Ru(1)-Cl(1)	113.97(5)	C(11)-O(1)-Ru(1)	128.72(10)

Table S3. Selected bond lengths [Å] and angles [°] for Compound **P2P-Ru**

Ru(1)-N(1)	2.082(2)	Ru(1)-N(2)	2.112(2)
Ru(1)-C(4)	2.185(2)	Ru(1)-C(3)	2.199(2)
Ru(1)-C(7)	2.204(2)	Ru(1)-C(5)	2.208(2)
Ru(1)-C(2)	2.211(2)	Ru(1)-C(6)	2.213(2)
Ru(1)-Cl(1)	2.4040(8)	C(2)-C(3)	1.401(3)
C(2)-C(7)	1.437(3)	N(1)-Ru(1)-N(2)	76.33(8)
N(1)-Ru(1)-C(4)	92.43(9)	N(2)-Ru(1)-C(4)	115.75(8)
N(2)-Ru(1)-C(3)	152.80(8)	N(1)-Ru(1)-C(7)	158.03(8)
N(2)-Ru(1)-C(7)	125.54(8)	C(4)-Ru(1)-C(7)	80.13(9)
C(3)-Ru(1)-C(5)	67.93(9)	N(1)-Ru(1)-C(6)	154.62(8)
N(2)-Ru(1)-C(6)	98.46(8)	N(1)-Ru(1)-Cl(1)	87.60(6)
C(4)-Ru(1)-Cl(1)	156.41(7)	C(7)-Ru(1)-Cl(1)	91.13(7)
C(3)-C(2)-C(7)	118.1(2)	C(3)-C(2)-Ru(1)	71.00(13)

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