

Supporting Materials

Amberlite IR-120(H) mediated “On water” synthesis of novel anticancer Ruthenium (II)-p-cymene 2-pyridinylbenzothiazole (BTZ), 2-pyridinylbenzoxazole (BOZ) & 2-pyridinylbenzimidazole (BIZ) scaffolds

Sunisha K S[†], Swagata Banerjee[†], Ashaparna Mondal, Priyankar Paira,*

*Department of Chemistry, School of advanced sciences, VIT University, Vellore-632014,
Tamil Nadu, India*

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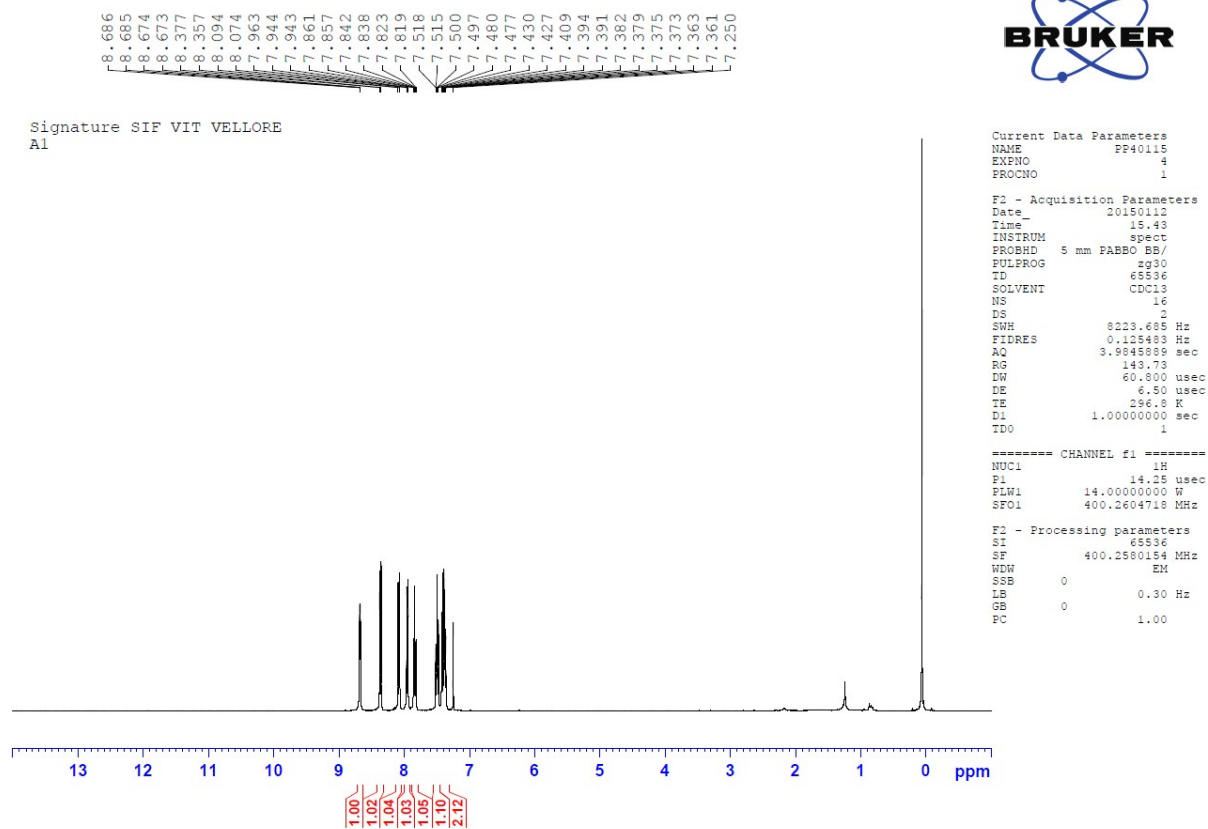
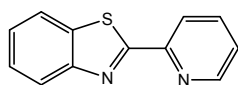
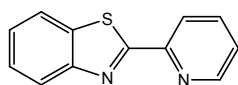
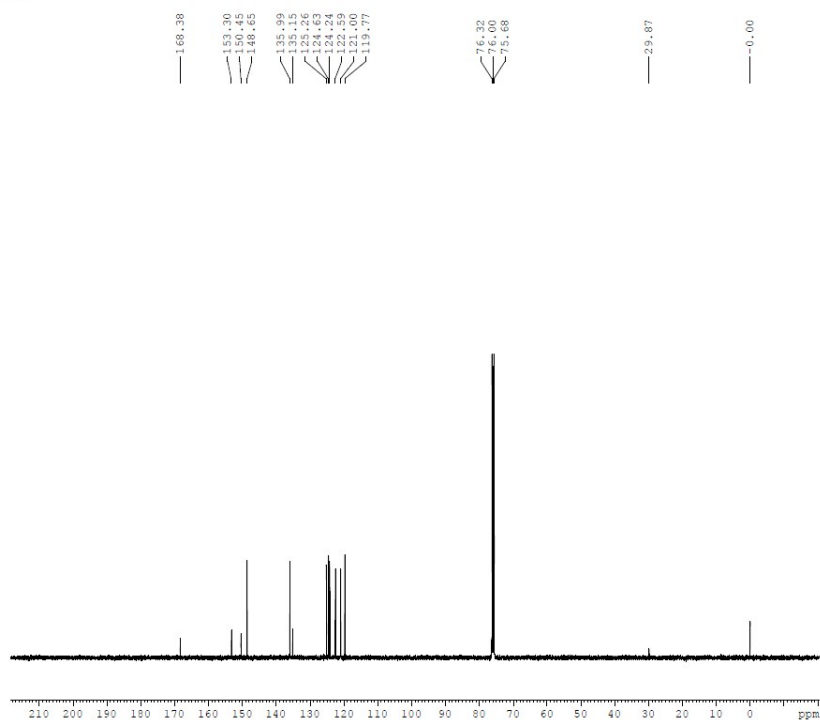


Figure S1-¹H NMR of ligand 3a



Signature SIF VIT VELLORE
A1



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EXPNO 6
PROCNO 1

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Time_ 2.23
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PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 512
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 156.91
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DE 6.50 usec
TE 301.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TDO 1

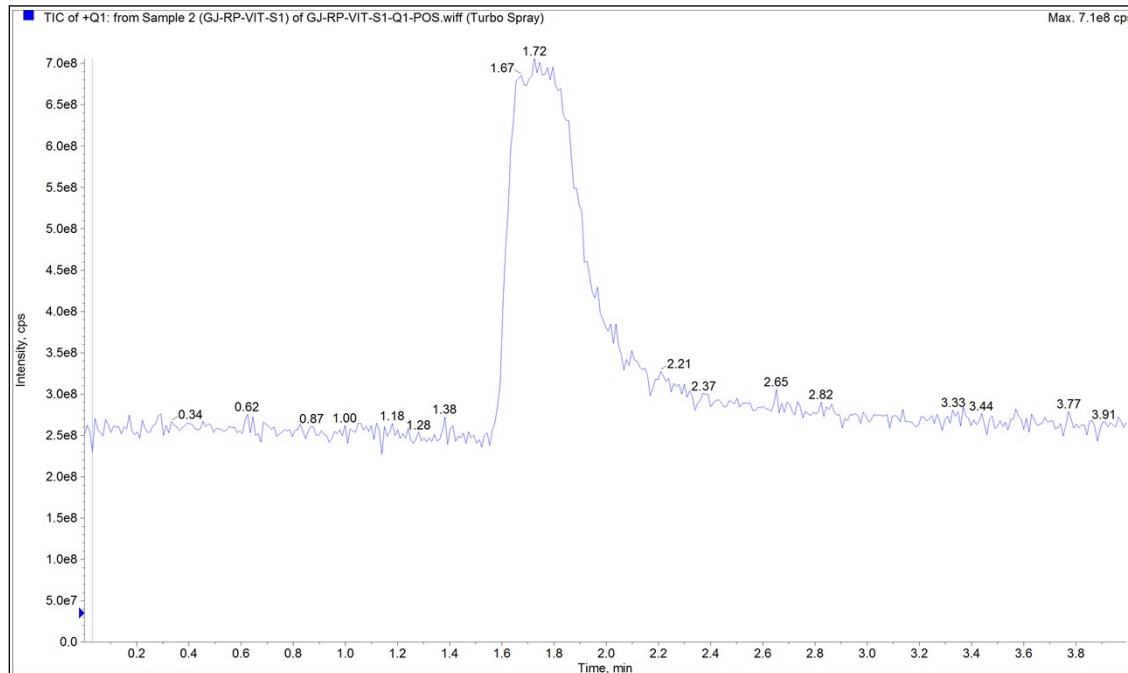
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SFO1 100.6250182 MHz

===== CHANNEL f2 =====
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NUC2 1H
PCPD2 90.00 usec
PLW2 14.00000000 W
PLW12 0.35097000 W
PLW13 0.28428999 W
SFO2 400.2596010 MHz

F2 - Processing parameters
SI 32768
SF 100.6450574 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Figure S2- ^{13}C NMR of ligand **3a**

1) TOTAL ION CHROMATOGRAMS (TIC) of ligand **3a**



2) MOLECULAR ION (Q1) FOR 213

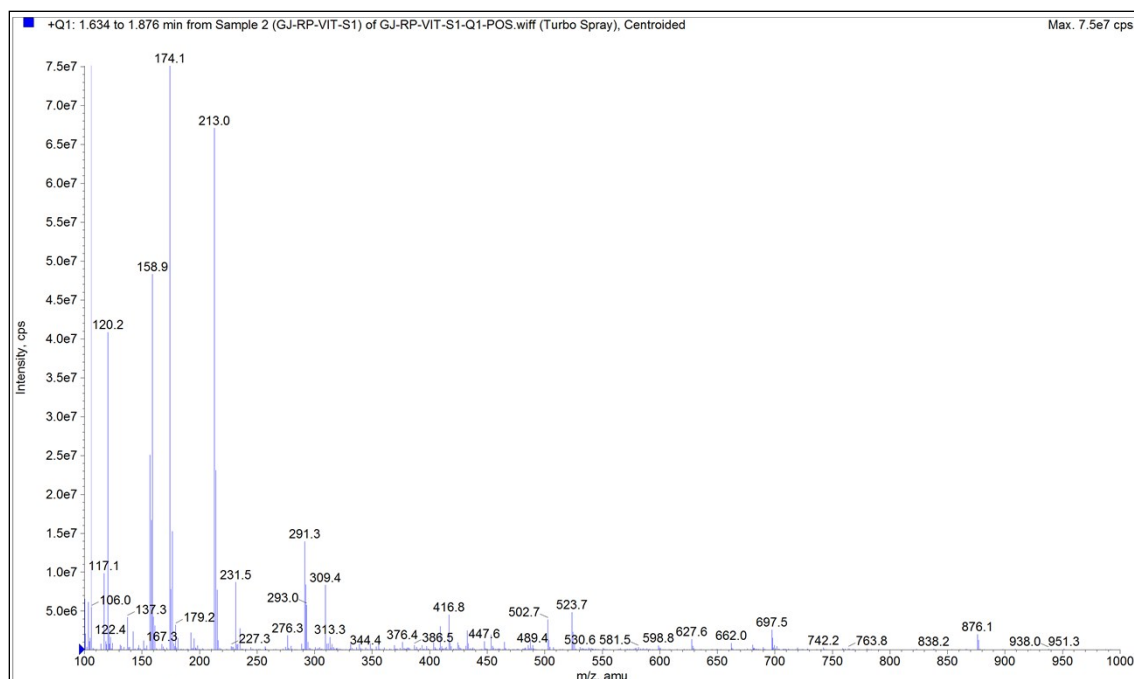


Figure S3- MS data for compound **3a**

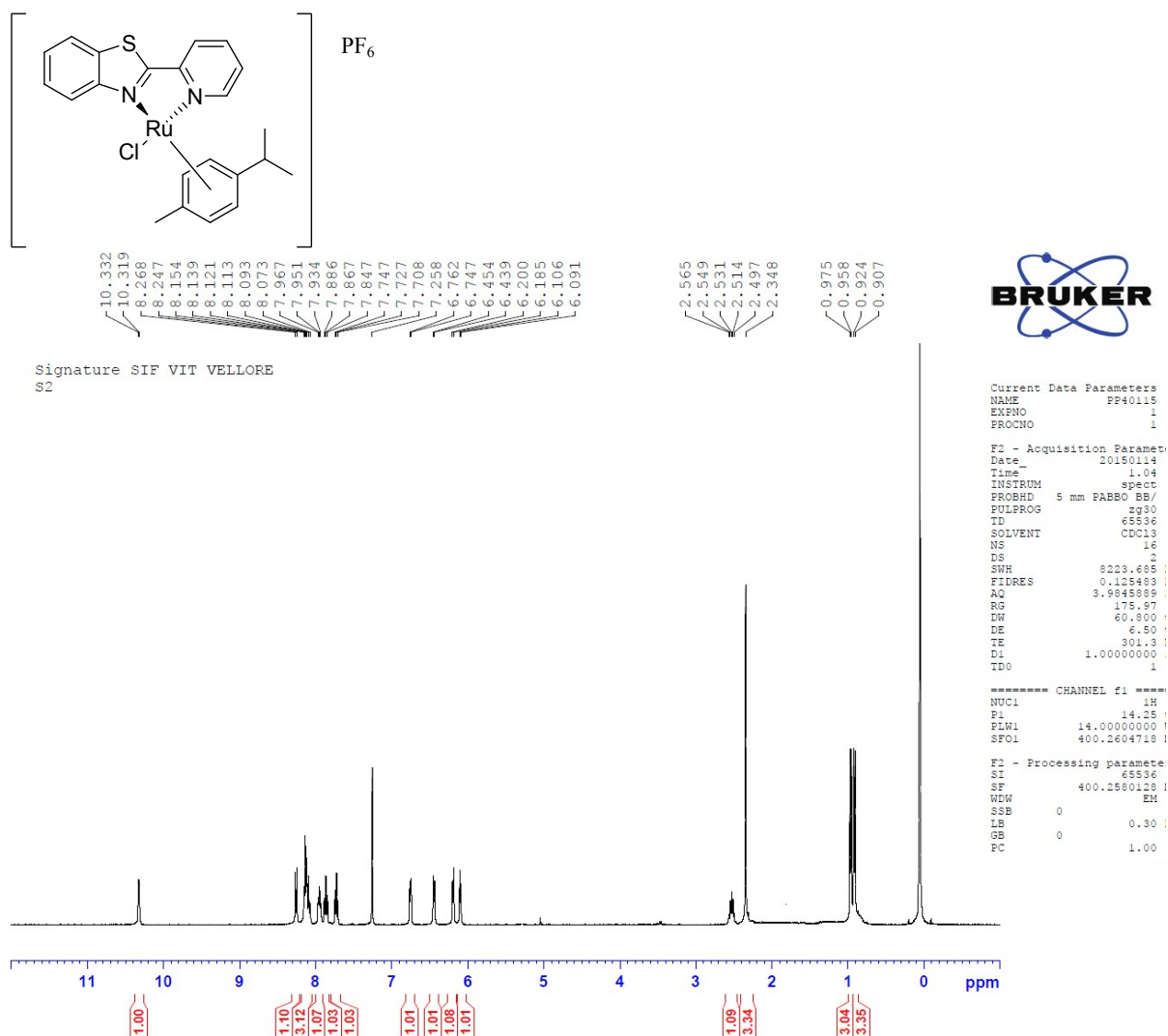


Figure S4- ¹H NMR of complex 4a

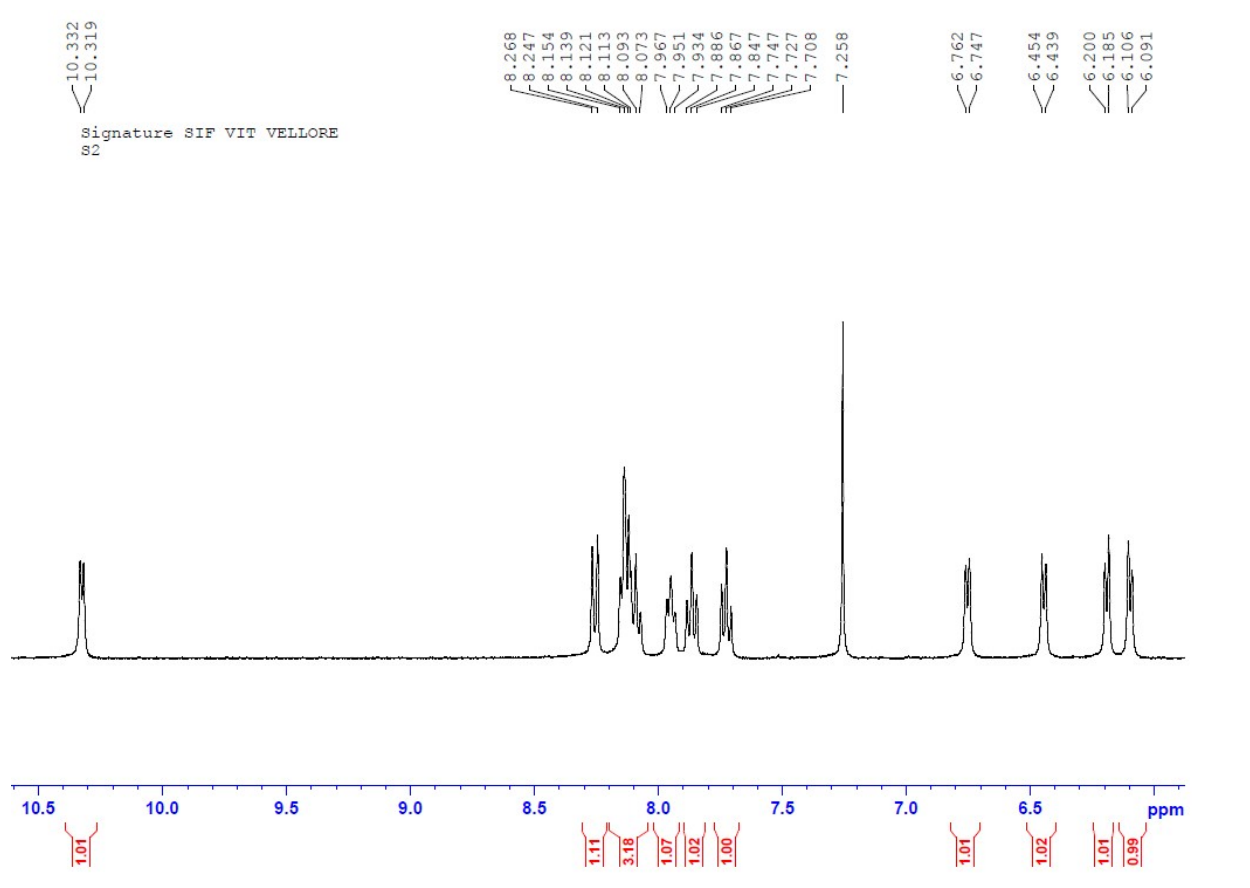


Figure S5- ^1H NMR of complex **4a** (Expansion)

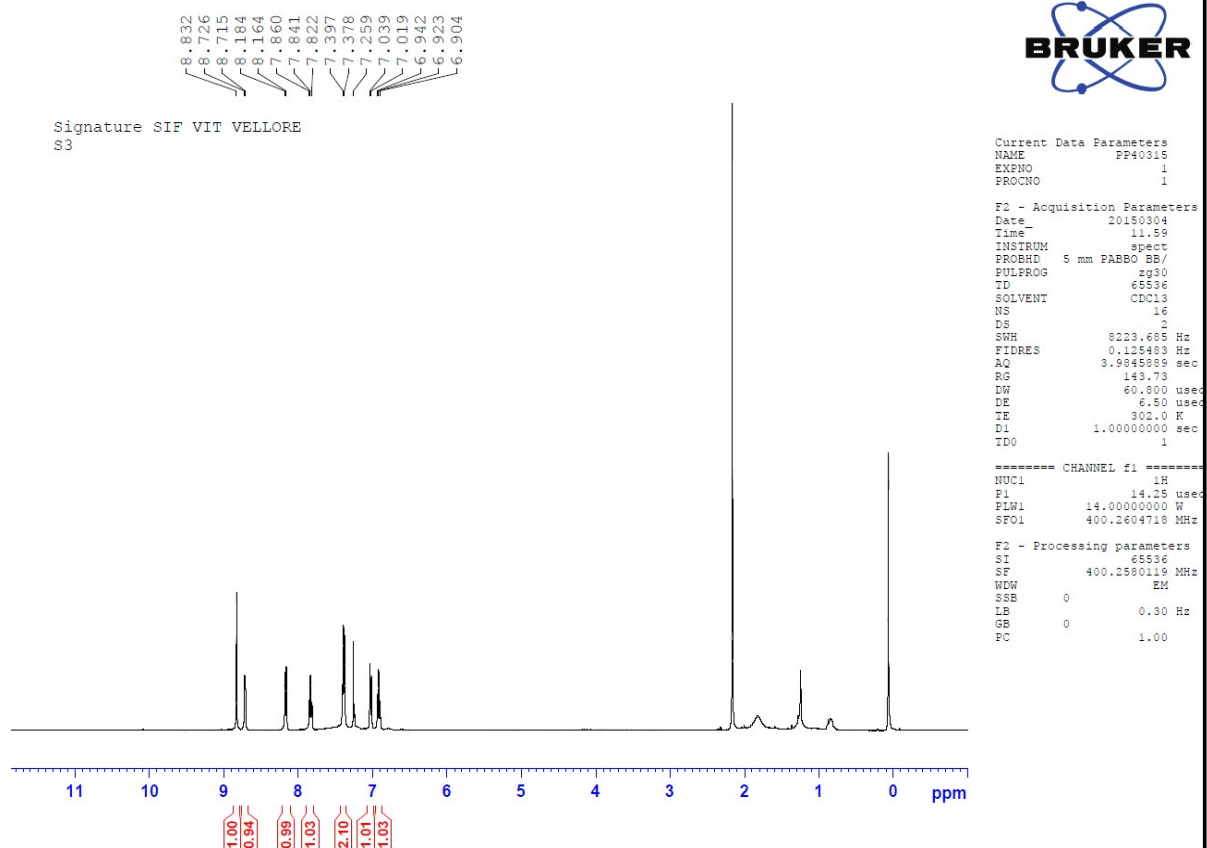
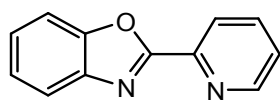
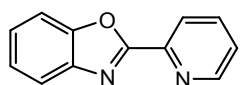
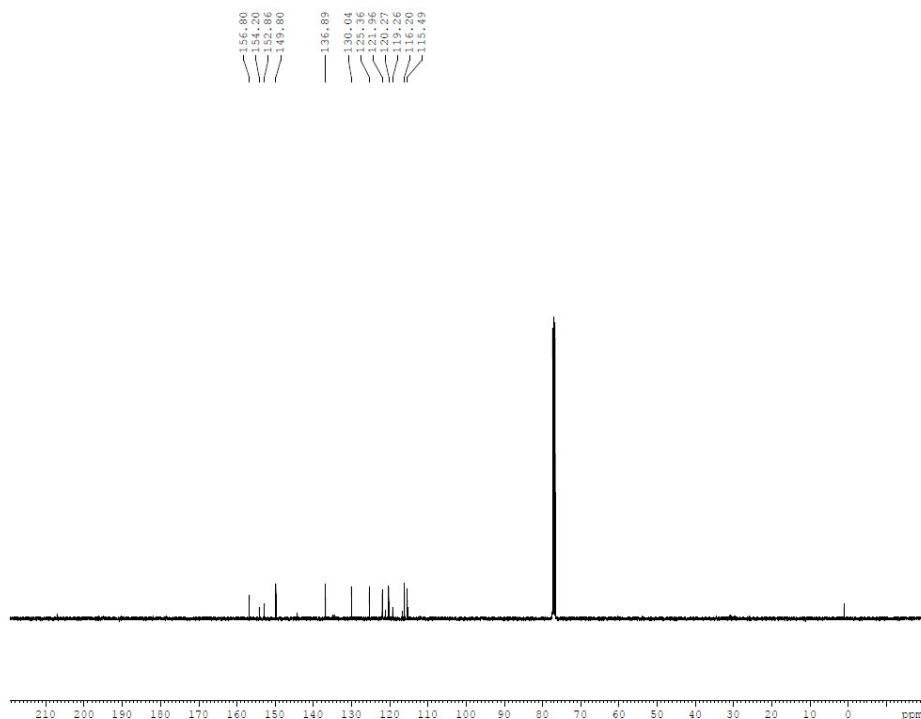


Figure S6- ^1H NMR of ligand **3b**



Signature SIF VIT VELLORE
S3



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Current Data Parameters
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EXPNO     2
PROCNO    1

F2 - Acquisition Parameters
Date_     20150304
Time      13.14
INSTRUM    spect
PROBHD     5 mm PABBO BB/
PULPROG    zgpg30
TD         65536
SOLVENT    CDCl3
NS         512
DS         4
SWH         24038.461 Hz
FIDRES     0.366798 Hz
AQ         1.3631488 sec
RG         156.91
DW         20.800 ns
DE         6.50 ns
TE         302.8 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       13C
P1         9.80 ns
PLW1       58.00000000 W
SFO1       100.6250182 MHz

===== CHANNEL f2 =====
CPDPRG12   waltz16
NUC2       1H
PCPD2      90.00 ns
PLW2       14.00000000 W
PLW12      0.35097000 W
PLW13      0.28428999 W
SFO2       400.2556010 MHz

F2 - Processing parameters
SI         32768
SF         100.6449540 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40
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Figure S7- ^{13}C NMR of ligand **3b**

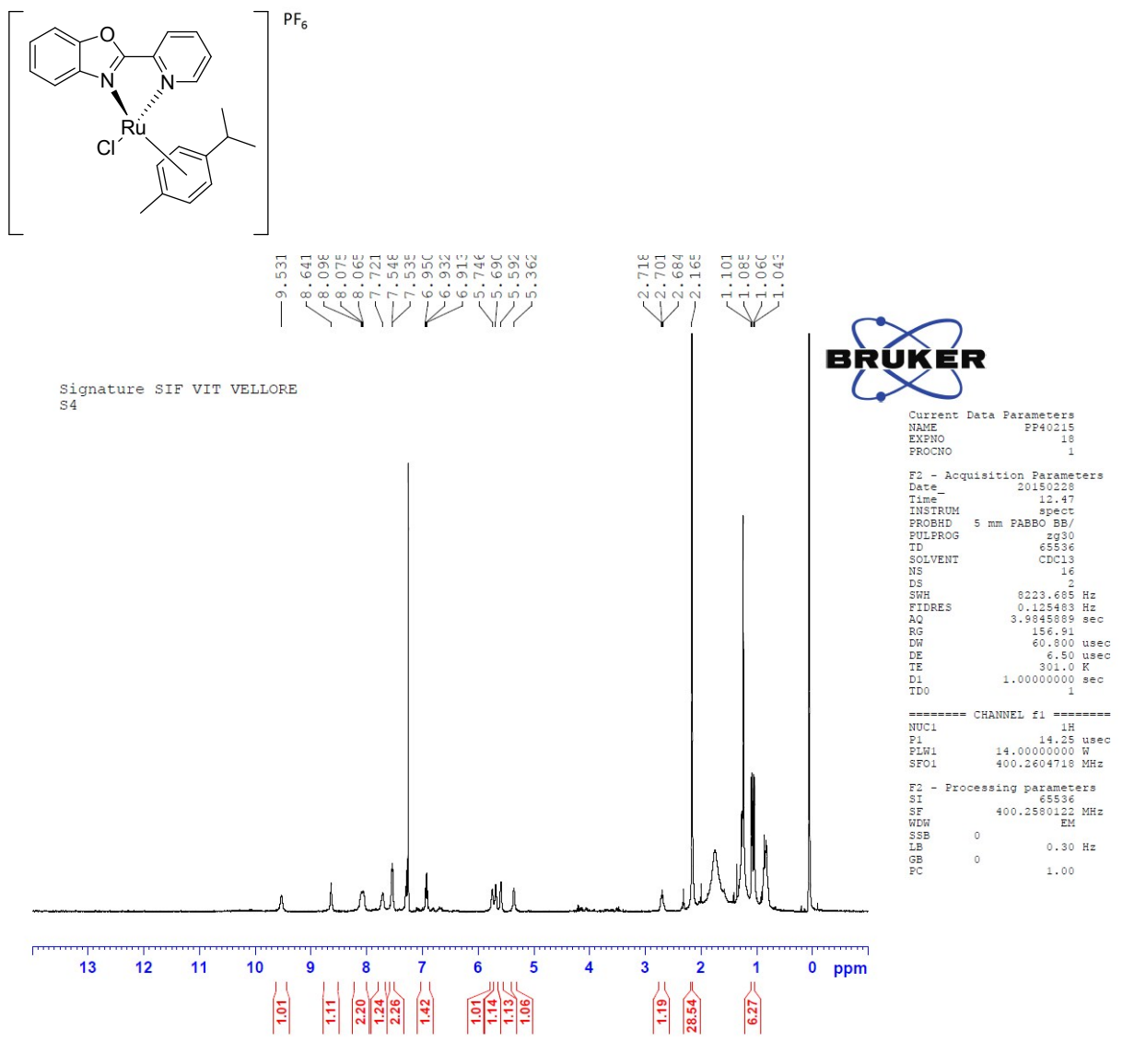


Figure S8- ^1H NMR of complex **4b**

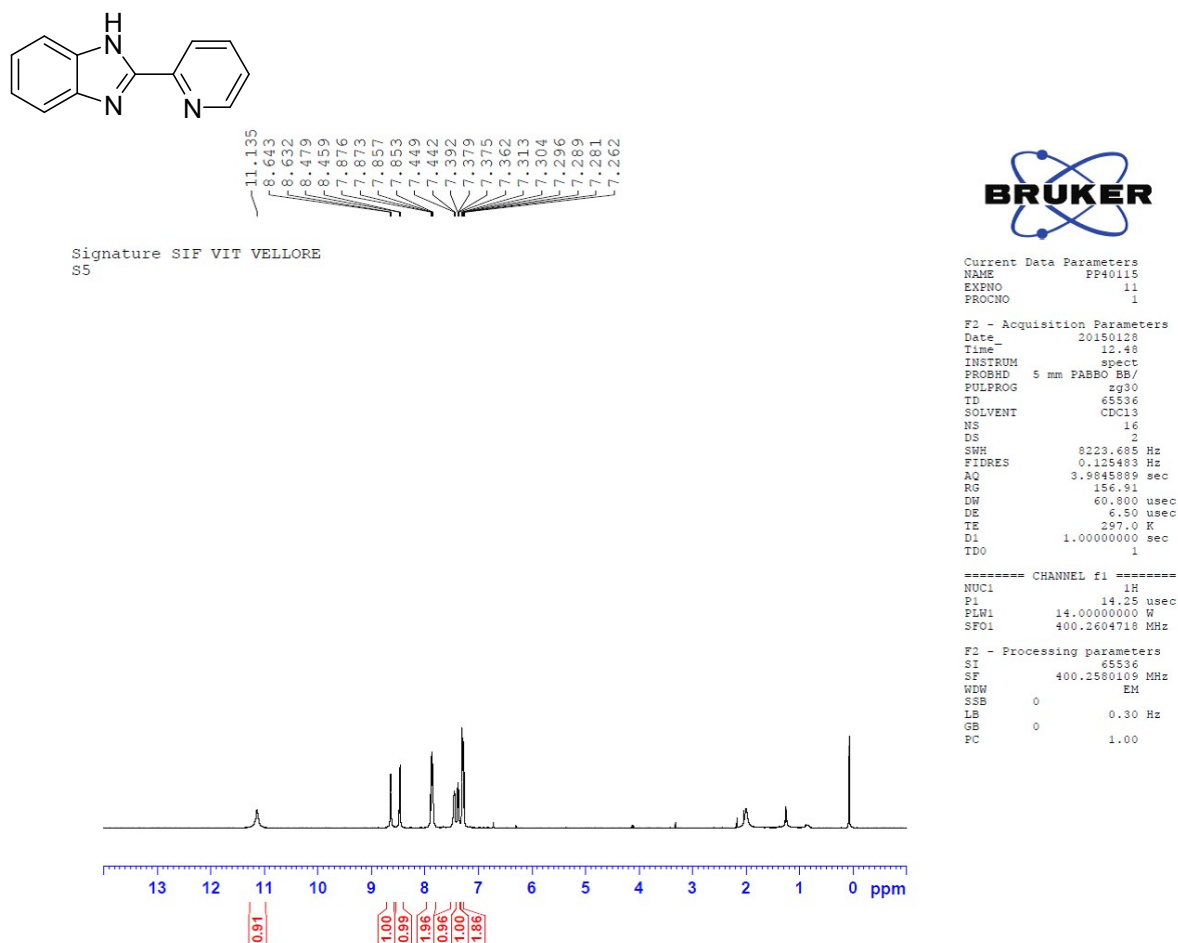
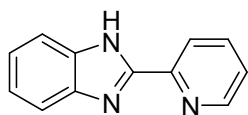
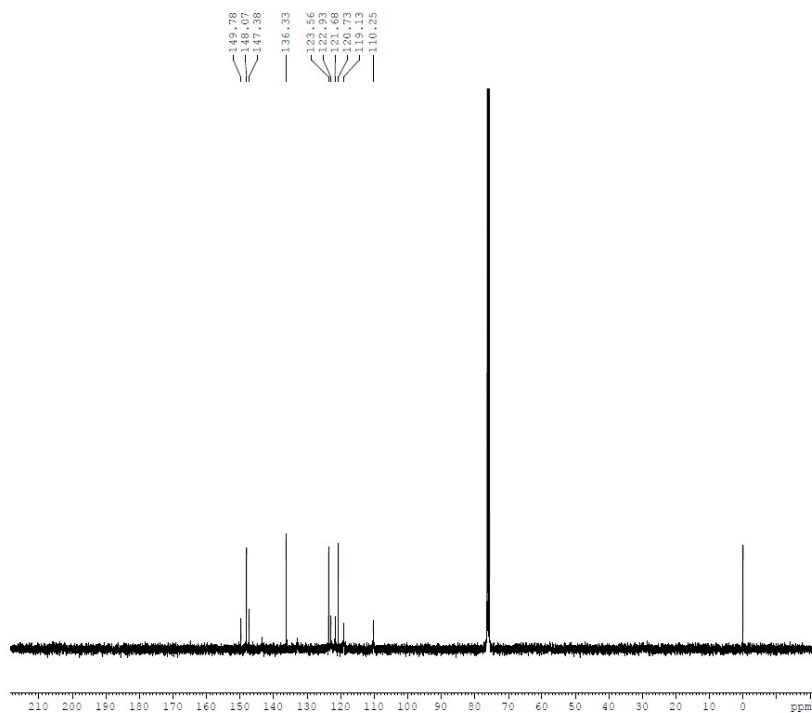


Figure S9- ¹H NMR of ligand 3c



Signature SIF VIT VELLORE
S5



Current Data Parameters
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EXPNO 13
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150130
Time 4.31
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 512
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 156.91
DW 20.800 usec
DE 6.50 usec
TE 302.2 K
D11 2.00000000 sec
D11 0.03000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 13C
P1 9.80 usec
PLW1 58.00000000 W
SFO1 100.6550182 MHz

===== CHANNEL f2 =====
CPDPRG[2] waltz16
NUC2 1H
PCPD2 80.00 usec
PLW2 14.00000000 W
PLW12 0.35097000 W
PLW13 0.28428999 W
SFO2 400.2596010 MHz

F2 - Processing parameters
SI 32768
SF 100.6450560 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Figure S10- ^{13}C NMR of ligand 3c

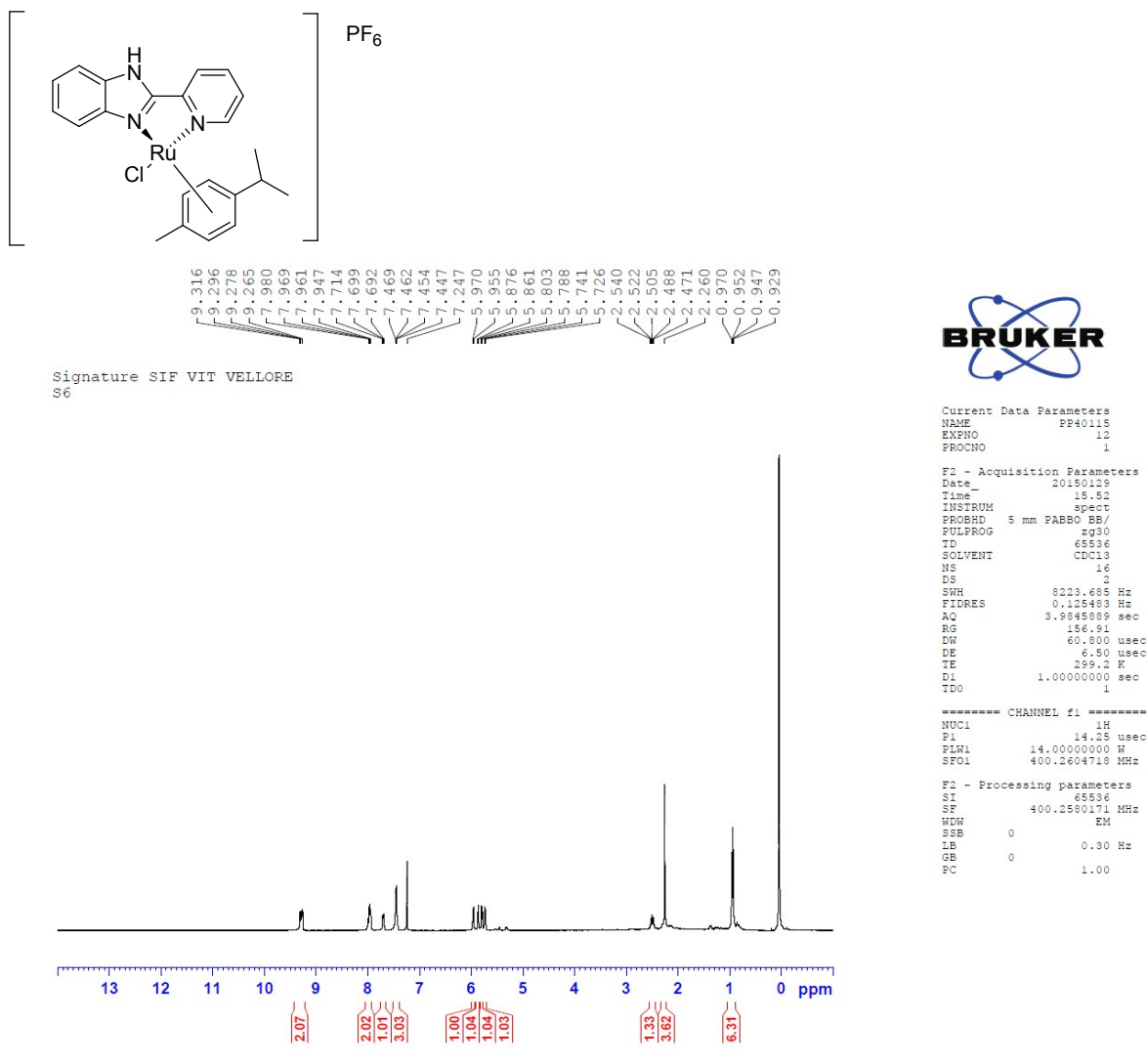


Figure S11- ^1H NMR of complex 4c

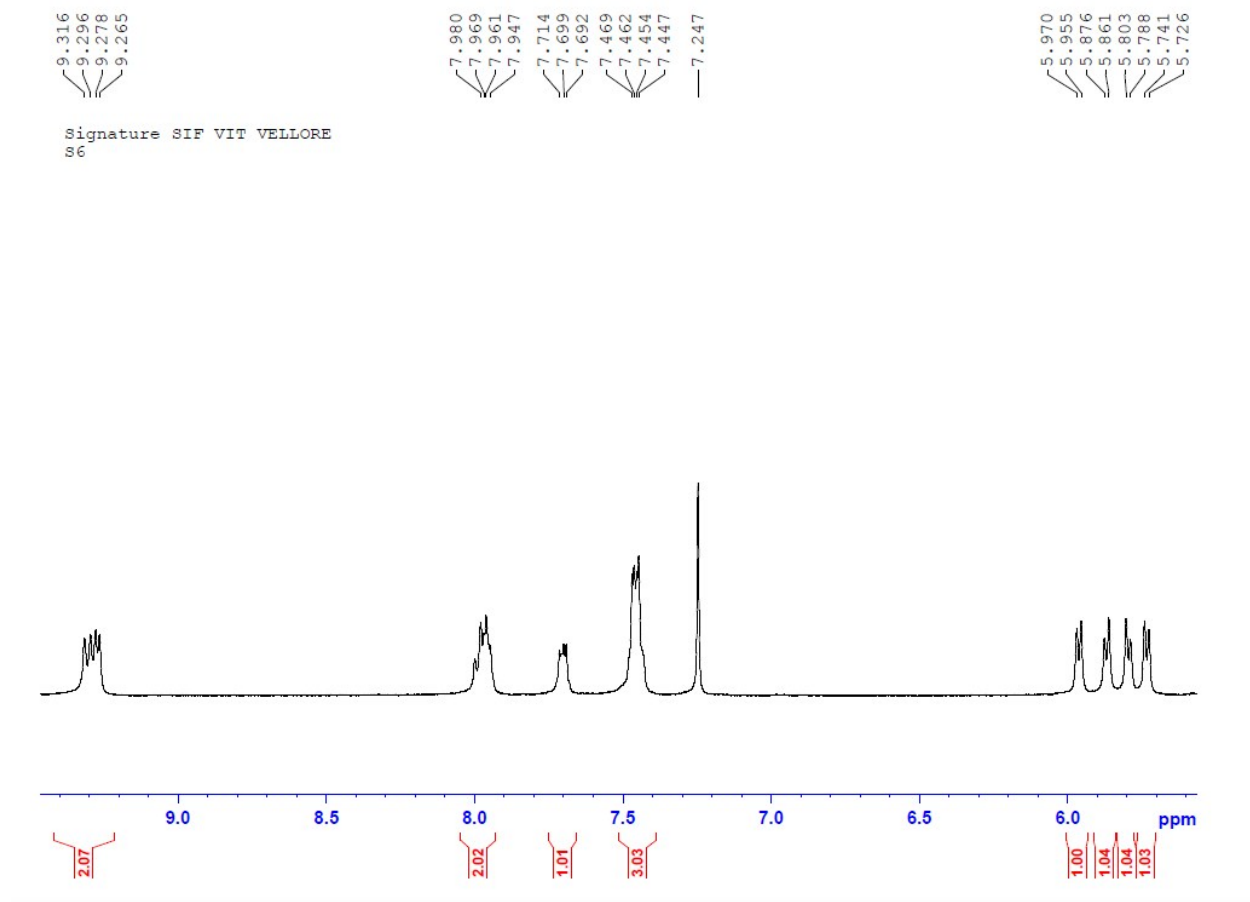


Figure S12- ^1H NMR of complex **4c** (Expansion)

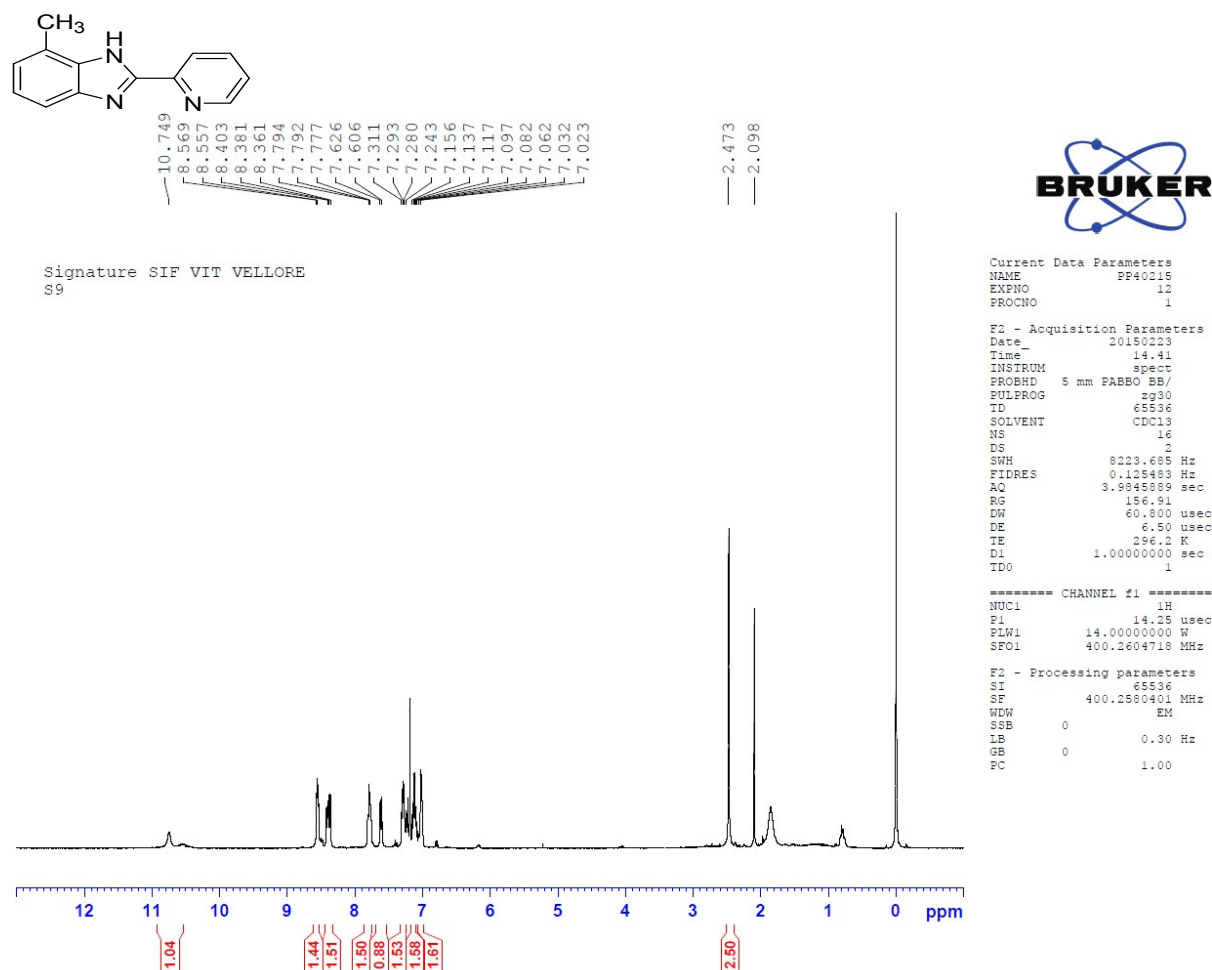
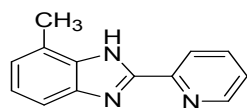
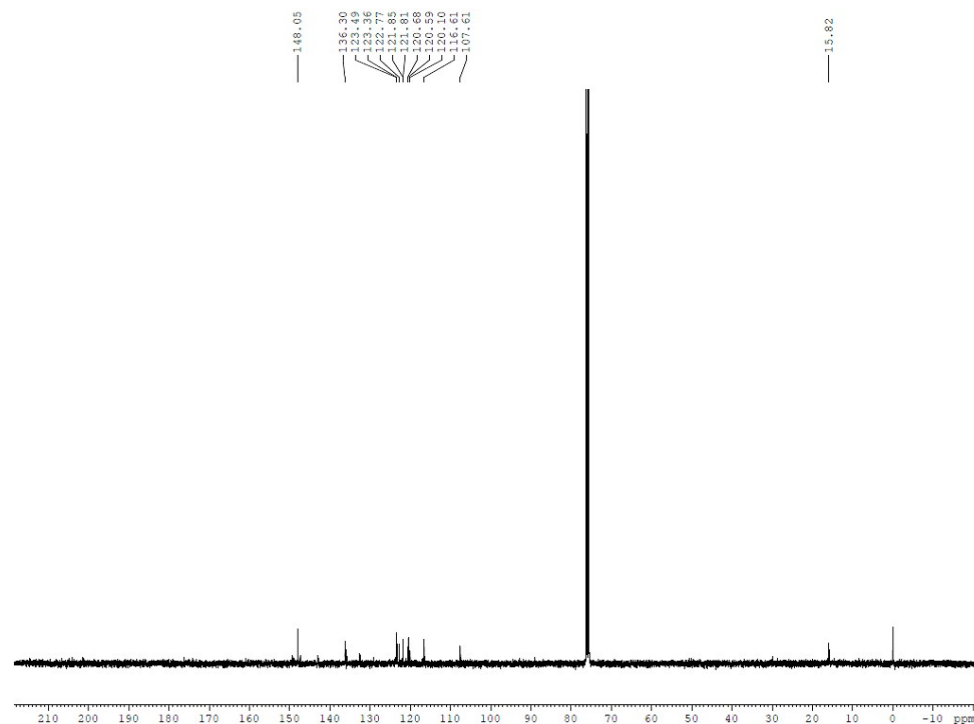


Figure S13- ¹H NMR of ligand **3d**



Signature SIF VIT VELLORE
S9



Current Data Parameters
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EXPNO 13
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150223
Time_ 15.11
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 512
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631498 sec
RG 143.73
DW 20.800 usec
DE 6.50 usec
TE 297.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 13C
P1 9.80 usec
PLW1 58.00000000 W
SFO1 100.6550182 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PLW2 14.00000000 W
PLW12 0.35097000 W
PLW13 0.28428999 W
SFO2 400.2596010 MHz

F2 - Processing parameters
SI 32768
SF 100.6450596 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Figure S14- ¹³C NMR of ligand 3d

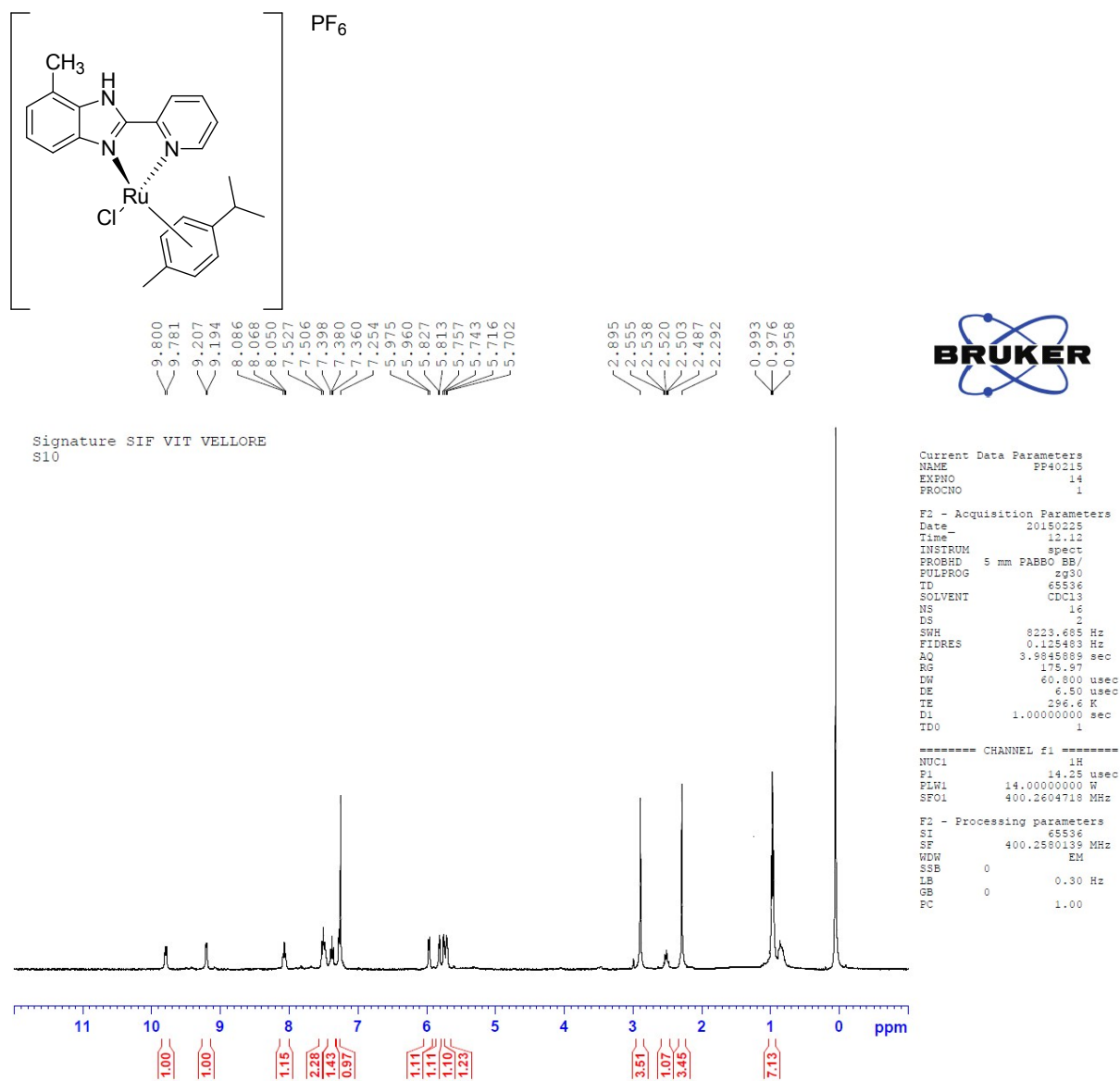


Figure S15- ¹H NMR of complex 4d

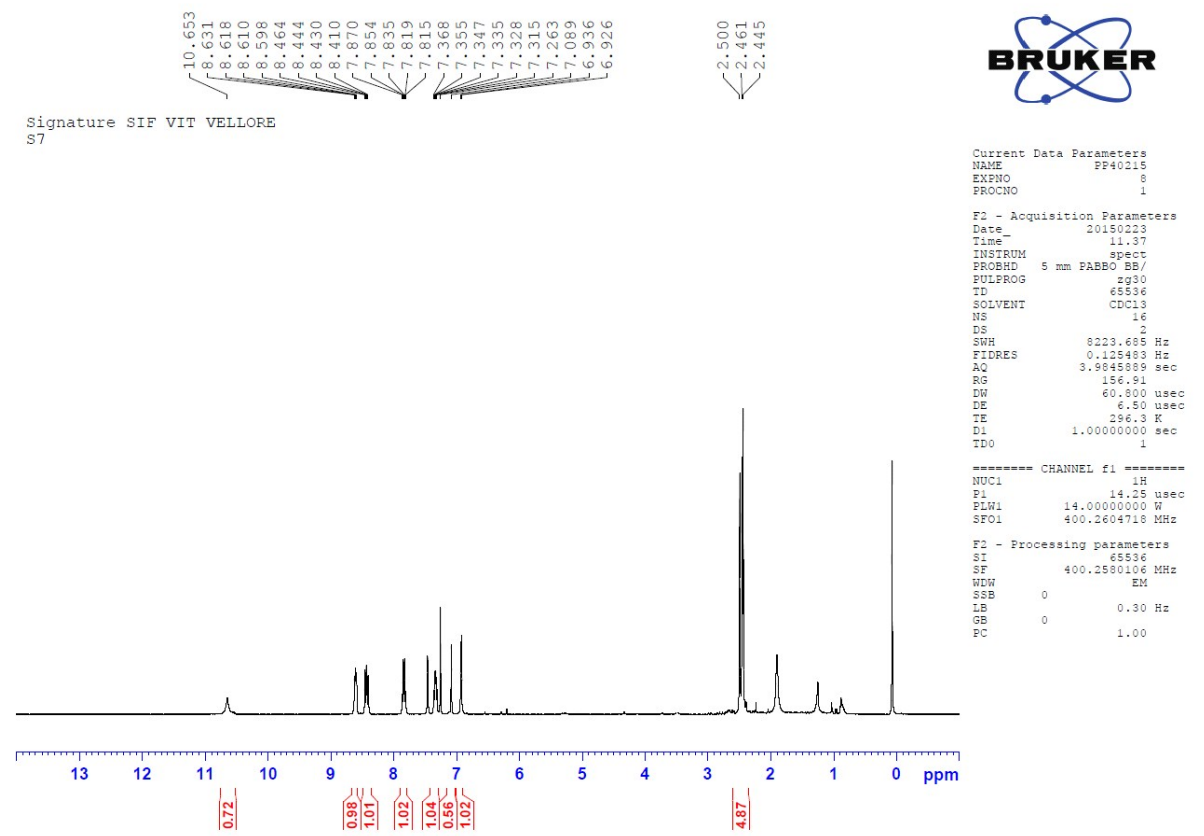
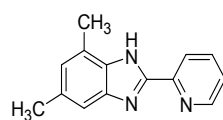
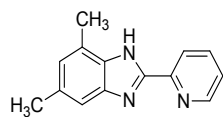
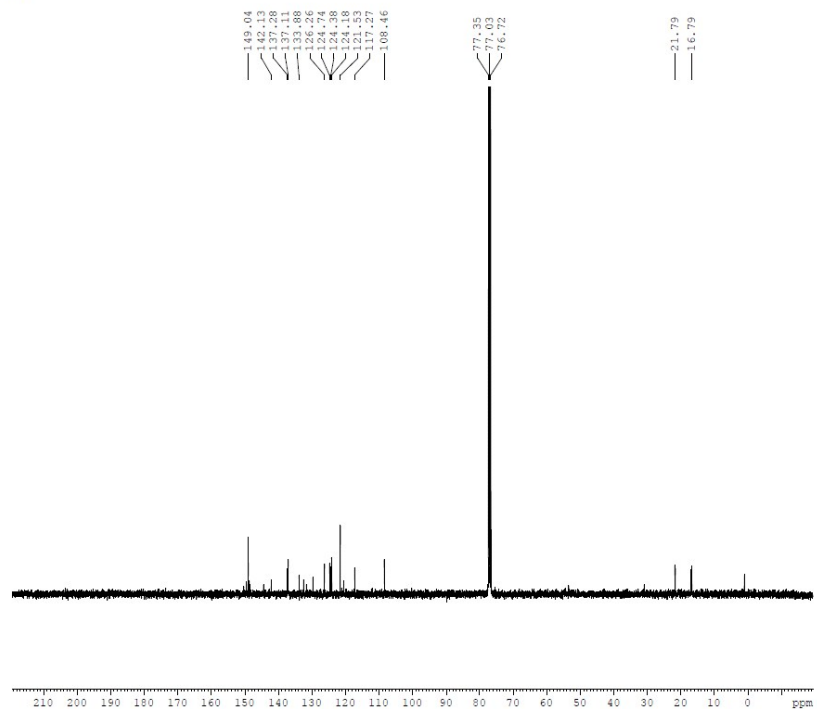


Figure S16- ¹H NMR of ligand 3e



Signature SIF VIT VELLORE
S7



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EXPNO     9
PROCNO    1

F2 - Acquisition Parameters
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Time      12.19
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PROBHD    5 mm PABBO BB/
PULPROG   zgpg30
TD         65536
SOLVENT   CDCl3
NS         512
DS         4
SWH        24038.461 Hz
FIDRES     0.366798 Hz
AQ         1.3631488 sec
RG         63.11
EW         20.800 usec
DE         6.50 usec
TE         297.3 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0        1

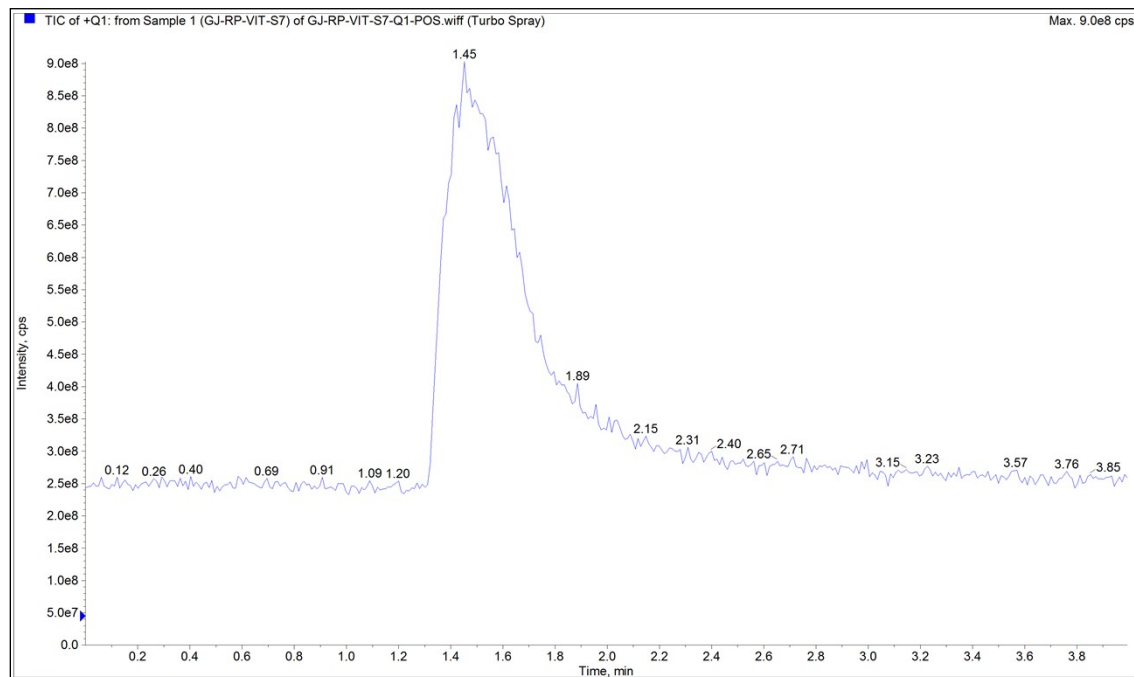
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NUC1       13C
P1         9.80 usec
PLW1       58.00000000 W
SFO1       100.6250182 MHz

===== CHANNEL f2 =====
CPDPRG2    waltz16
NUC2       1H
PCPD2      90.00 usec
PLW2       14.00000000 W
PLW12      0.35097000 W
PLW13      0.28428999 W
SFO2       400.2596010 MHz

F2 - Processing parameters
SI         32768
SF         100.6449540 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40
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Figure S17- ¹³C NMR of ligand 3e

TOTAL ION CHROMATOGRAMS (TIC)



1) MOLECULAR ION (Q1) FOR 224

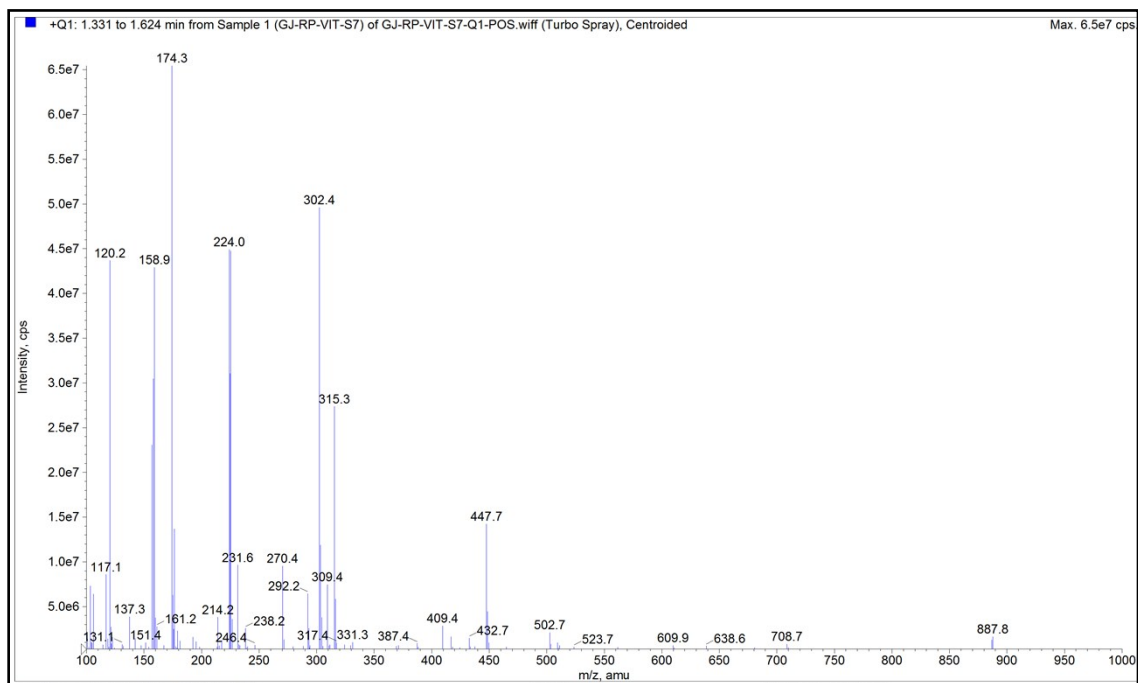


Figure S18- MS data for compound **3e**

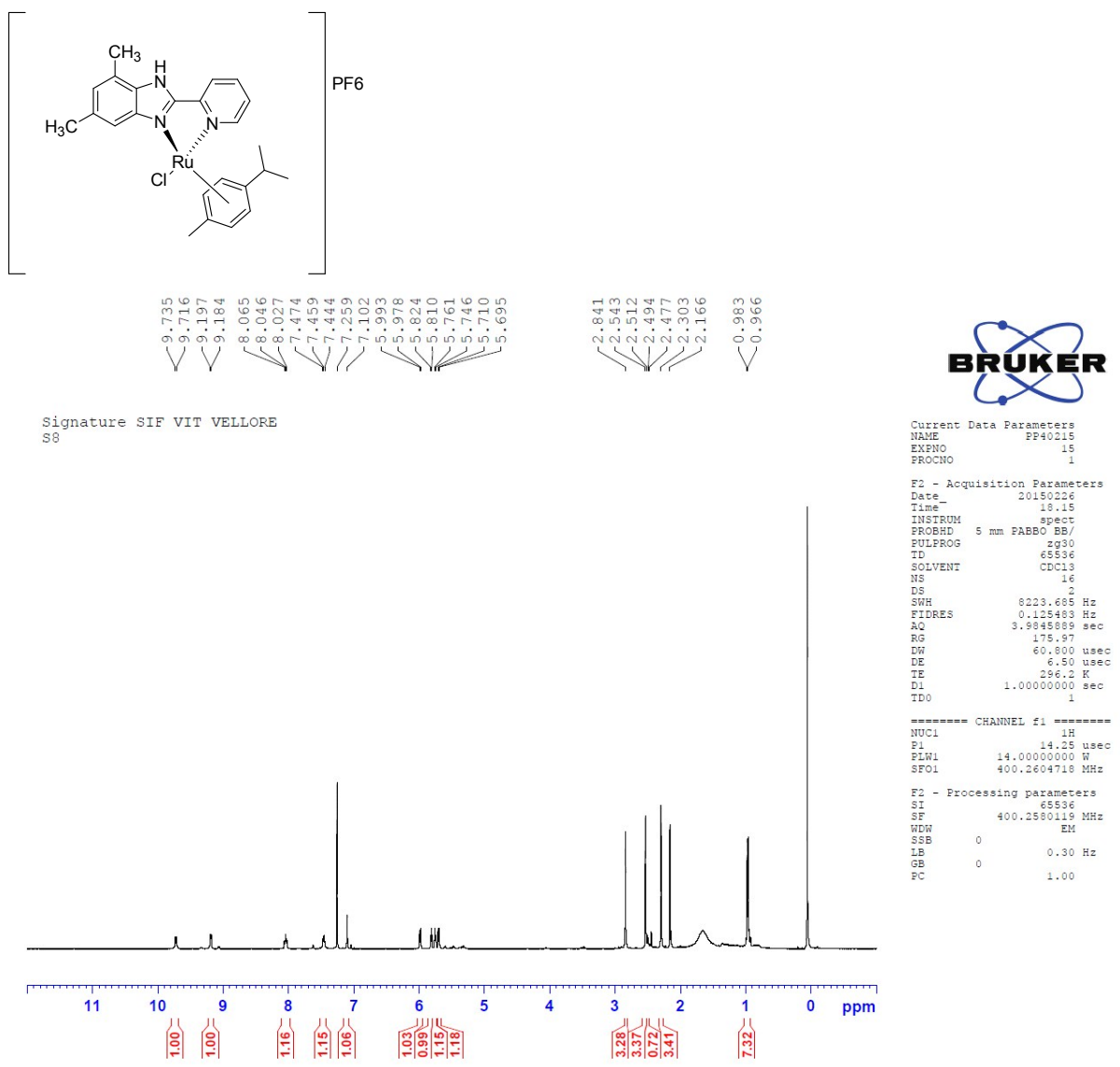
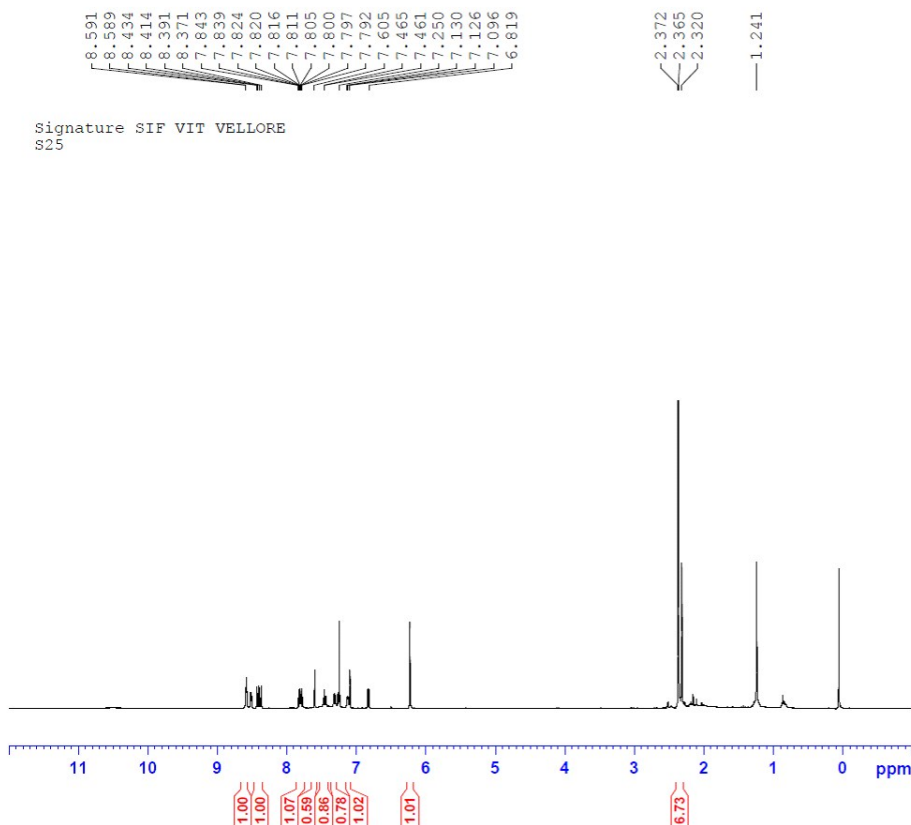
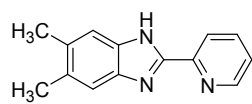


Figure S19- ¹H NMR of complex 4e



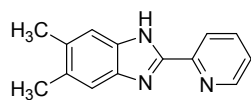
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EXPNO 22
PROCNO 1

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PULPROG zg30
TD 65536
SOLVENT CDC13
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 156.91
DW 60.800 usec
DE 6.50 usec
TE 300.3 K
D1 1.00000000 sec
TD0 1

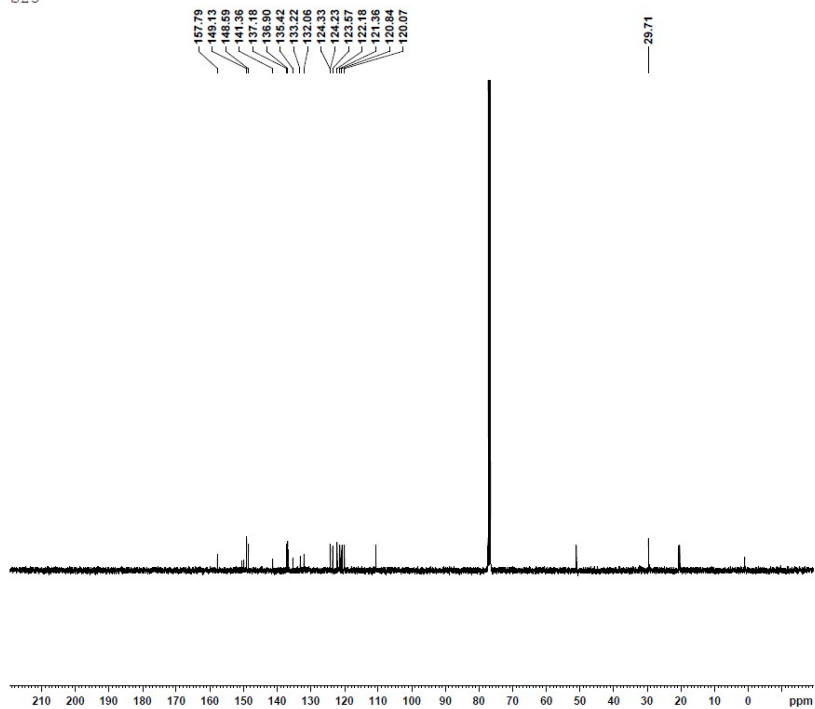
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P1 14.25 usec
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SFO1 400.2604718 MHz

F2 - Processing parameters
SI 65536
SF 400.2580155 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Figure S20- ^1H NMR of ligand **3f**



Signature SIF VIT VELLORE
S25



Current Data Parameters
NAME PF40415
EXPNO 21
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150416
Time 23.24
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 512
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 199.6
DW 20.800 usec
DE 6.50 usec
TE 300.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

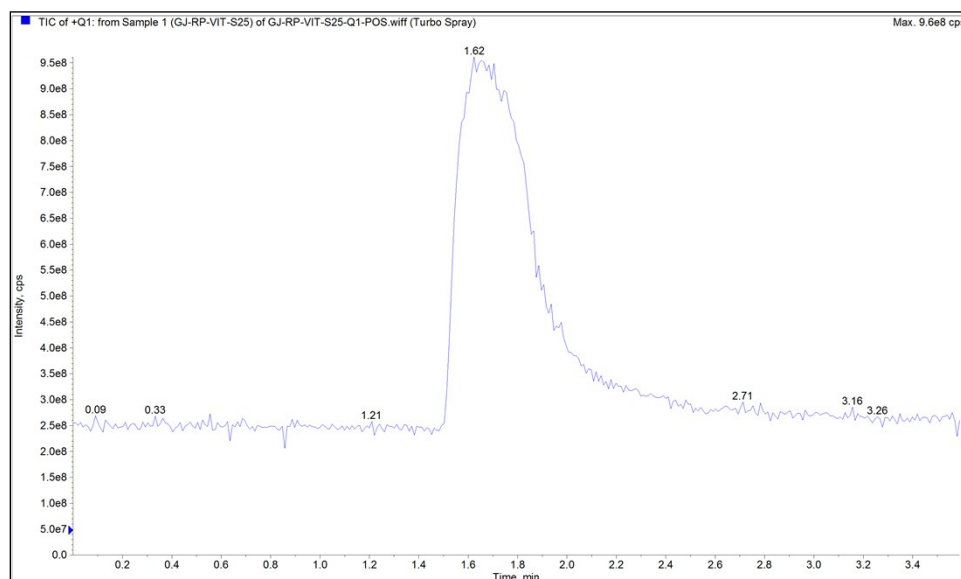
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P1 9.80 usec
PLW1 58.00000000 W
SFO1 100.6550182 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PLW2 14.00000000 W
PLW12 0.35097000 W
PLW13 0.28428999 W
SFO2 400.2596010 MHz

F2 - Processing parameters
SI 32768
SF 100.6449540 MHz
WDW EM
SBB 0
LB 1.00 Hz
GB 0
PC 1.40

Figure S21- ^{13}C NMR of ligand **3f**

TOTAL ION CHROMATOGRAMS (TIC)



1) MOLECULAR ION (Q1)

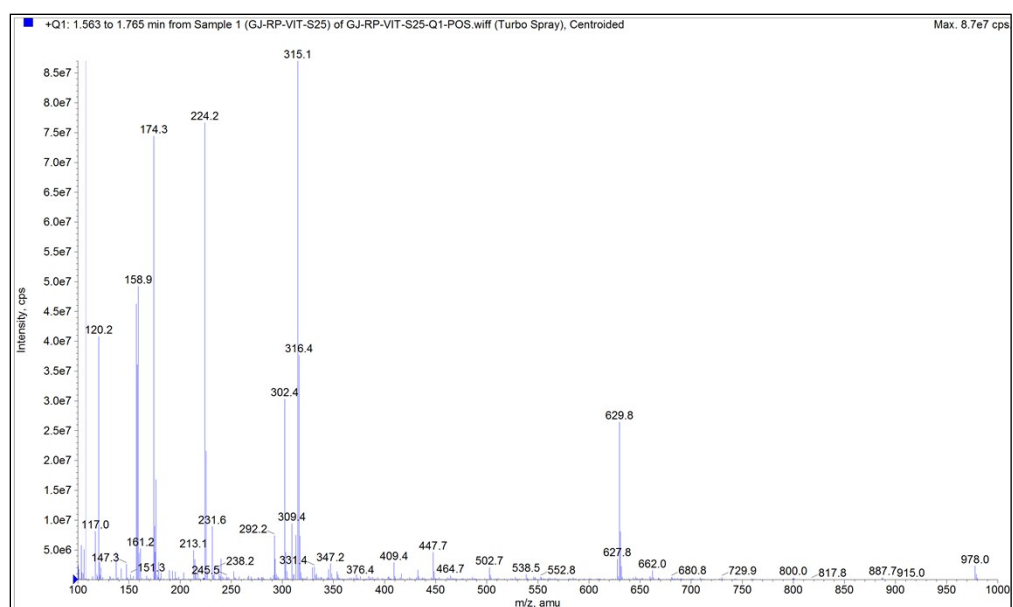


Figure S22- MS data for compound **3f**

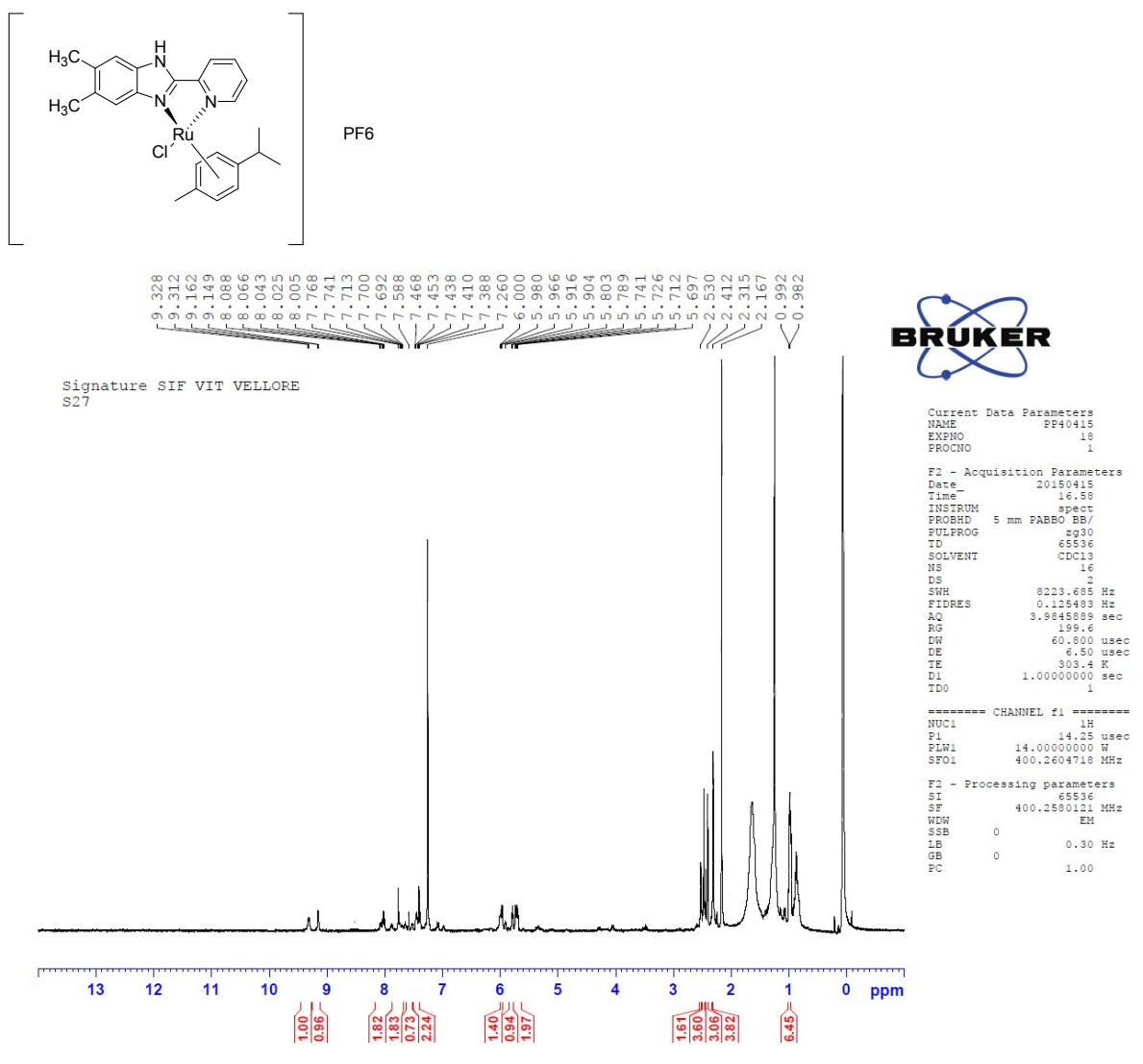


Figure S23- ¹H NMR of complex 4f

TOTAL ION CHROMATOGRAMS (TIC)

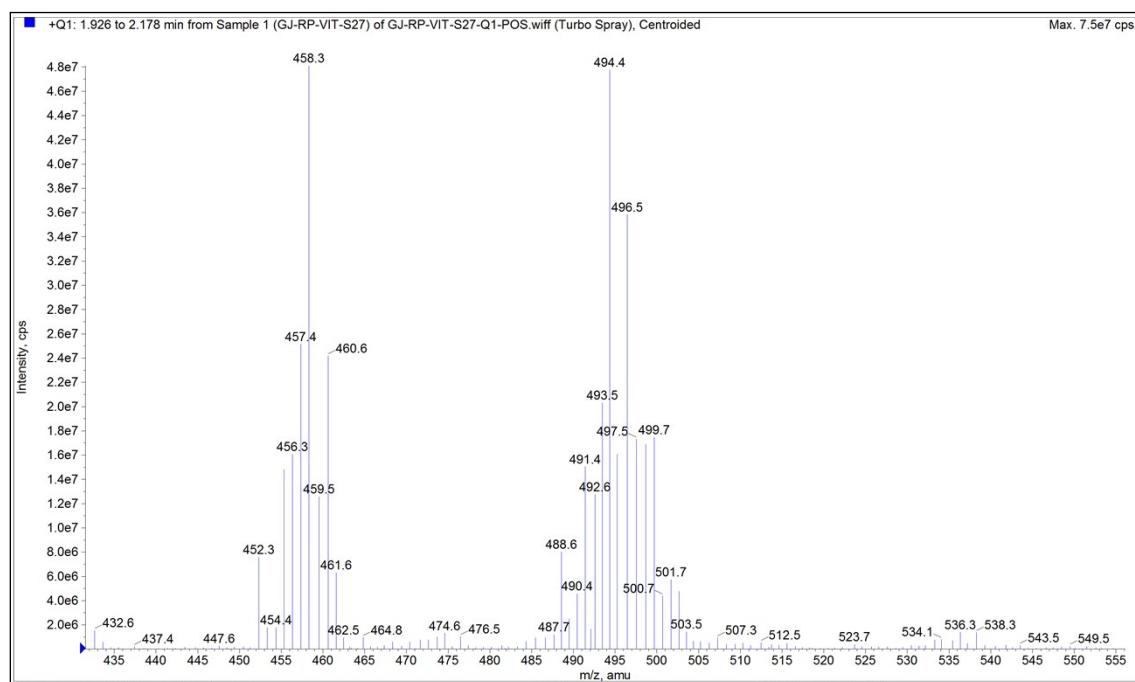
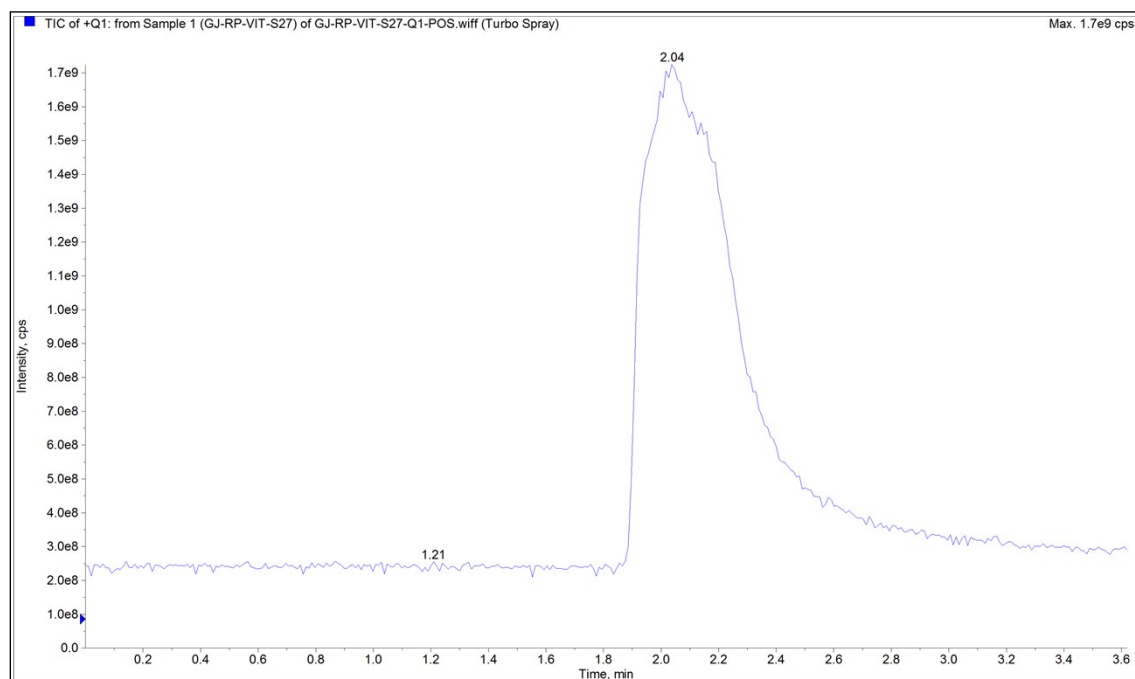


Figure S24- MS data for compound 4f

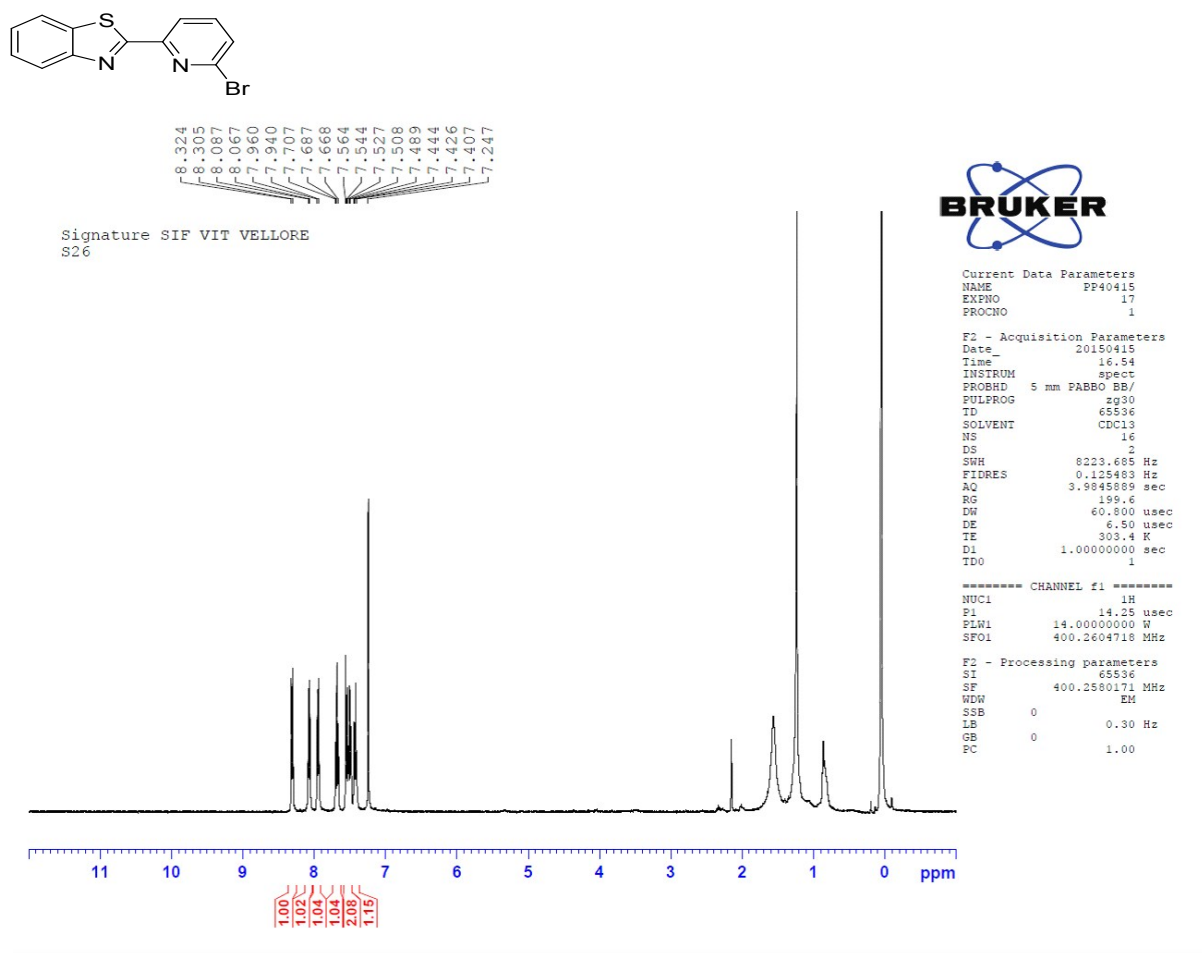
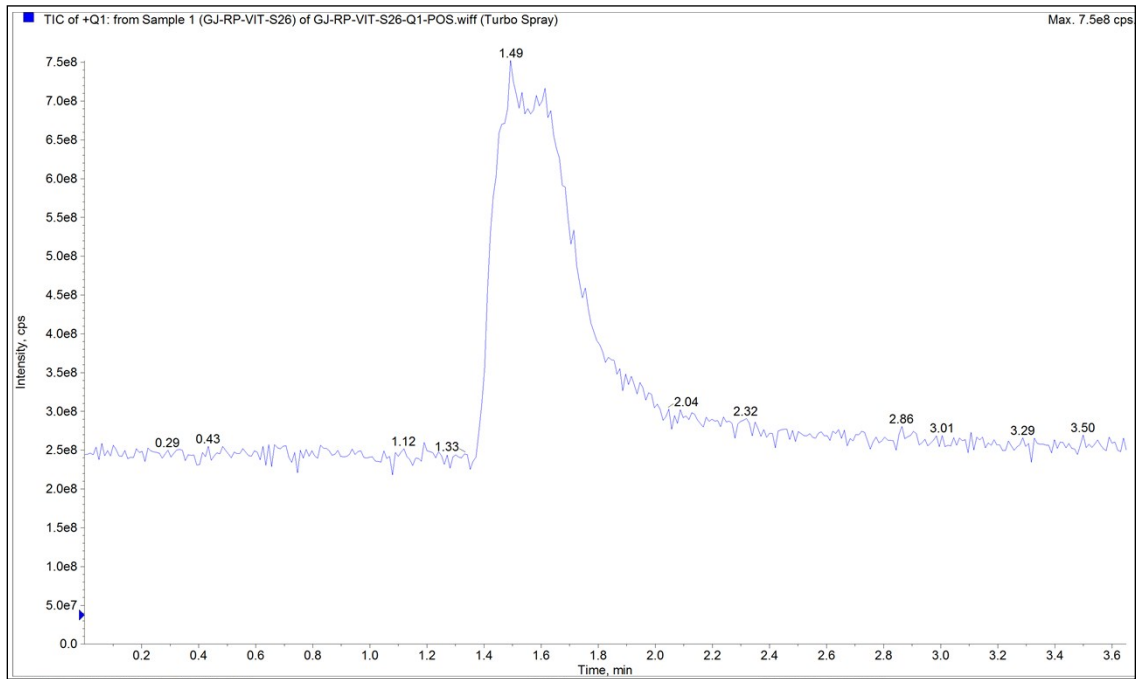
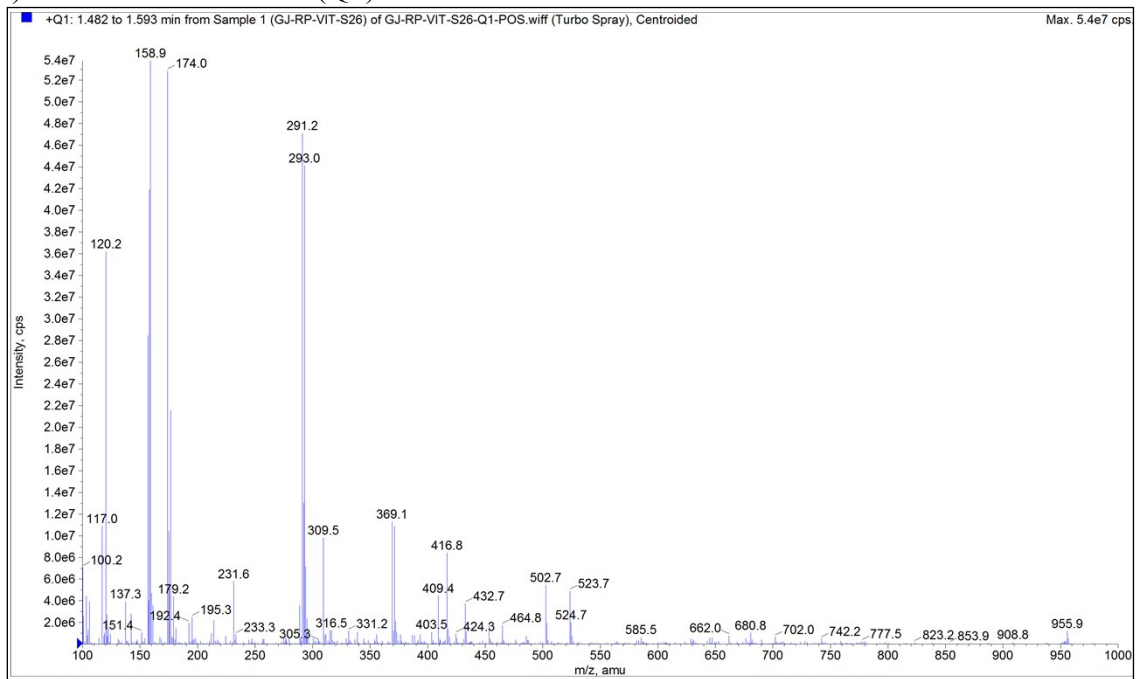


Figure S25- ^1H NMR of ligand **3g**

TOTAL ION CHROMATOGRAMS (TIC)



1) MOLECULAR ION (Q1)



2) ZOOM IN VIEW

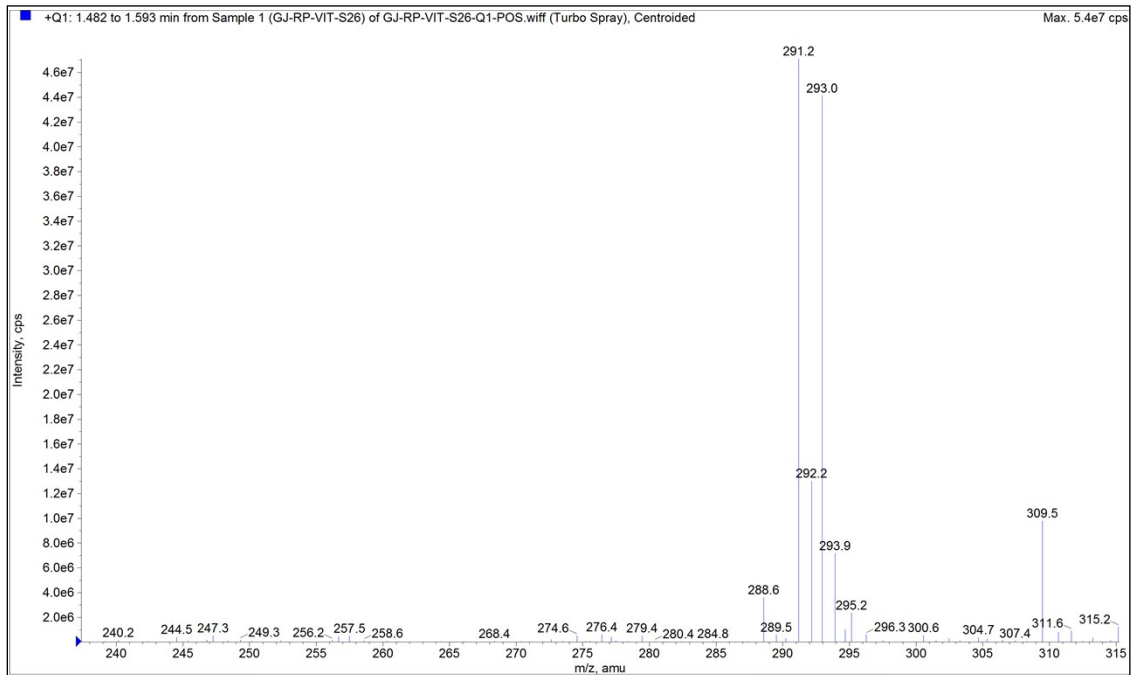
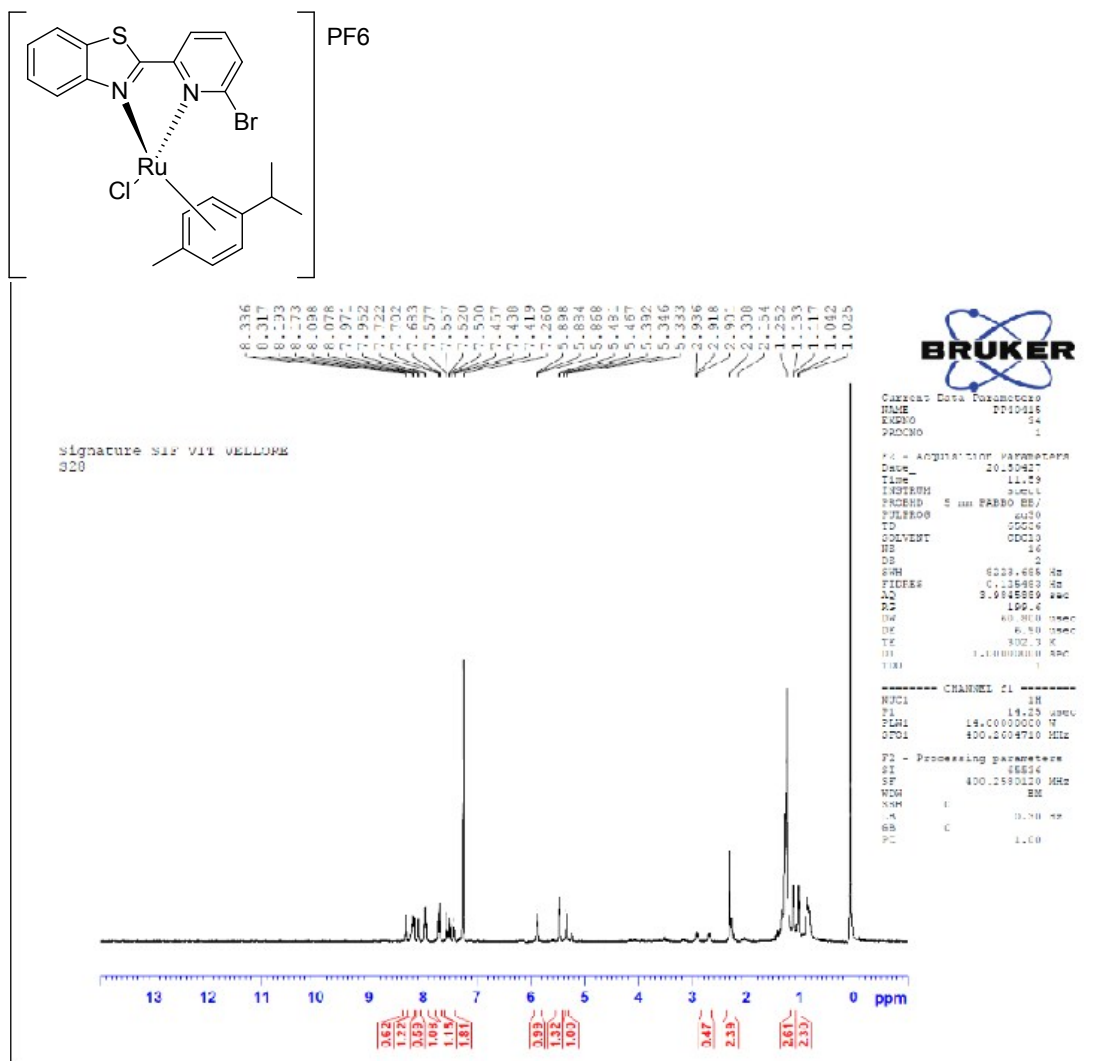


Figure S26- MS data for compound **3g**



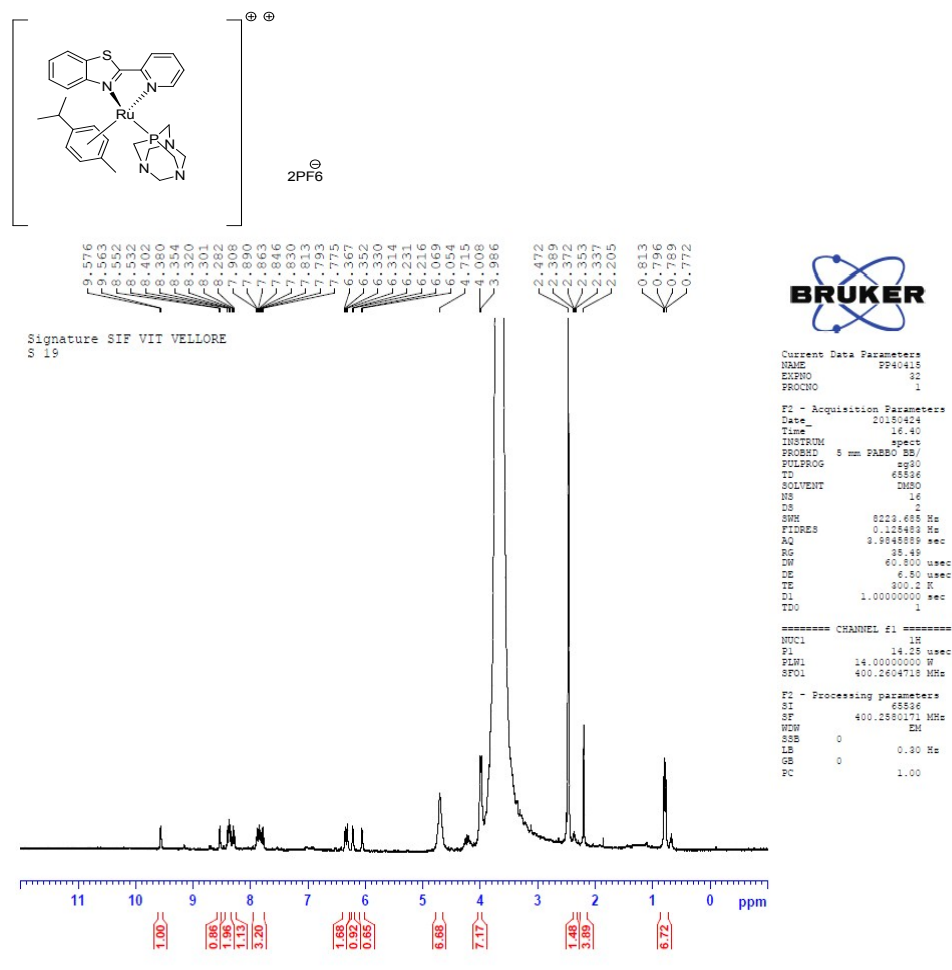


Figure S28- ¹H NMR of complex 5a

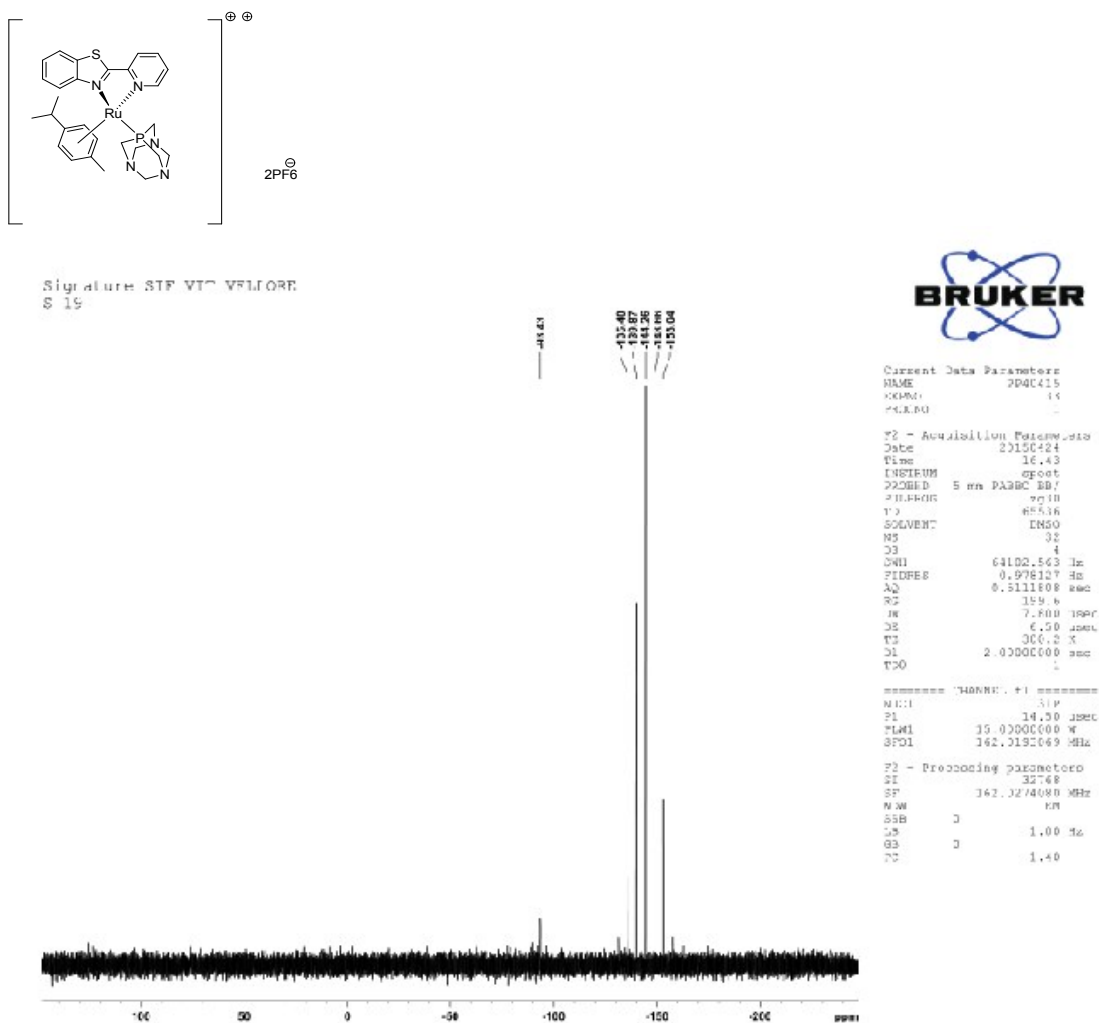


Figure S29- ^{31}P NMR of complex $[(\eta^6\text{-}p\text{-cymene})\text{RuPTA}\{2\text{-(pyridin-2-yl)benzo[d]thiazole}\}]\cdot 2\text{PF}_6$ (**5a**)

TOTAL ION CHROMATOGRAMS (TIC)

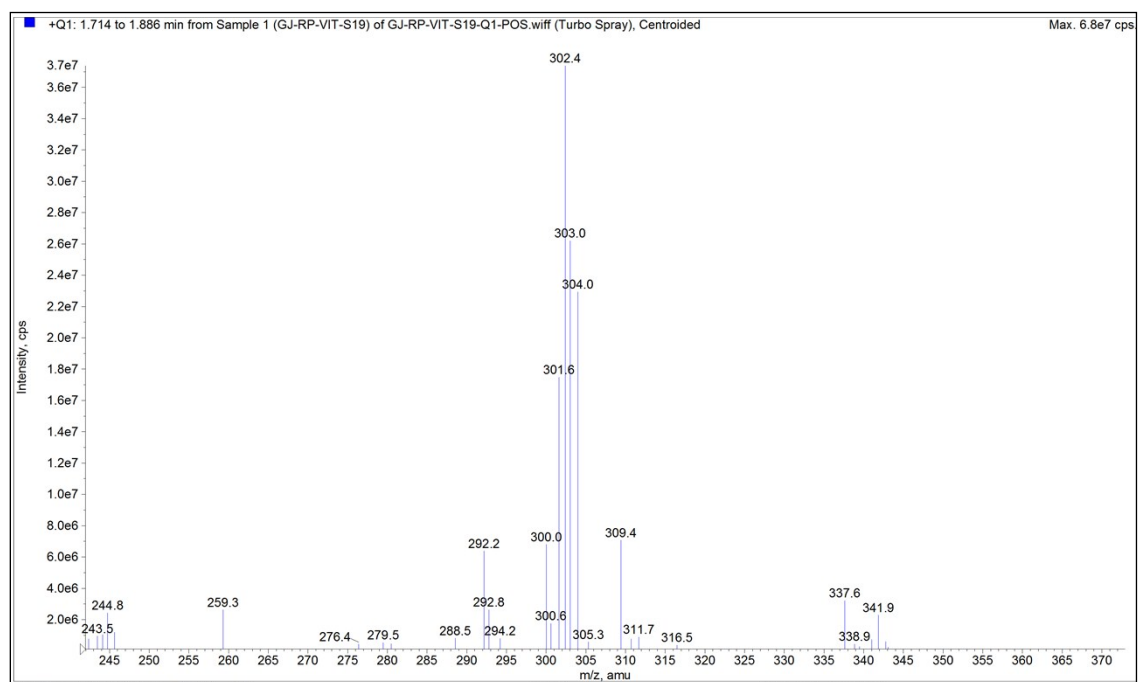
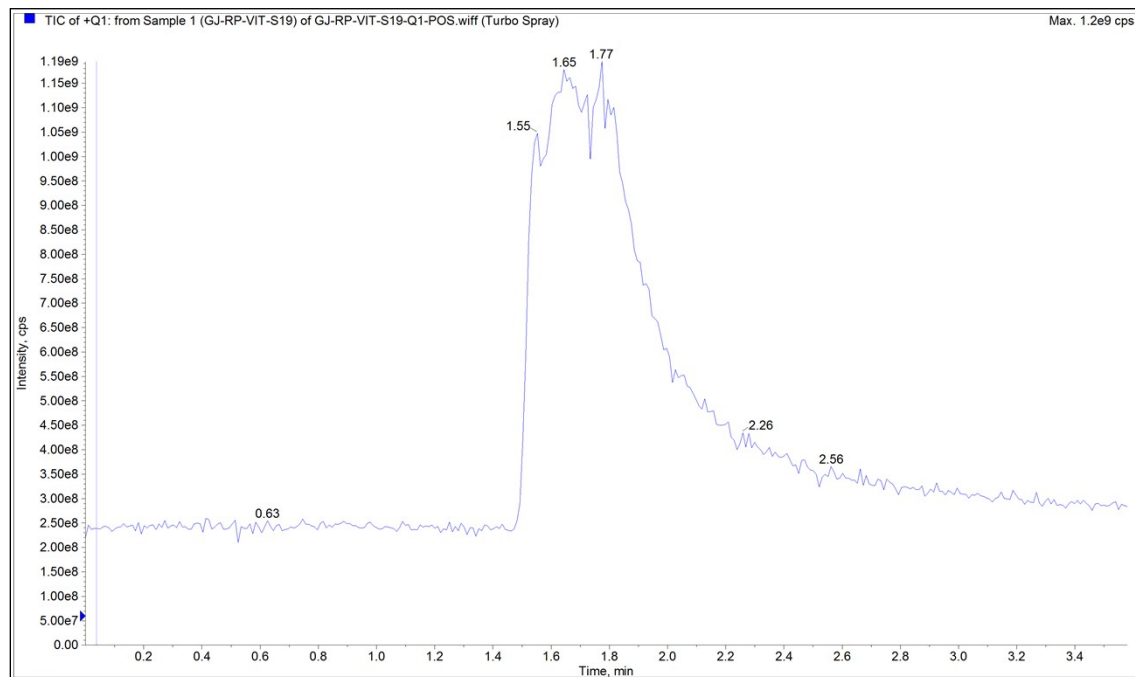


Figure S30- MS data for compound 5a

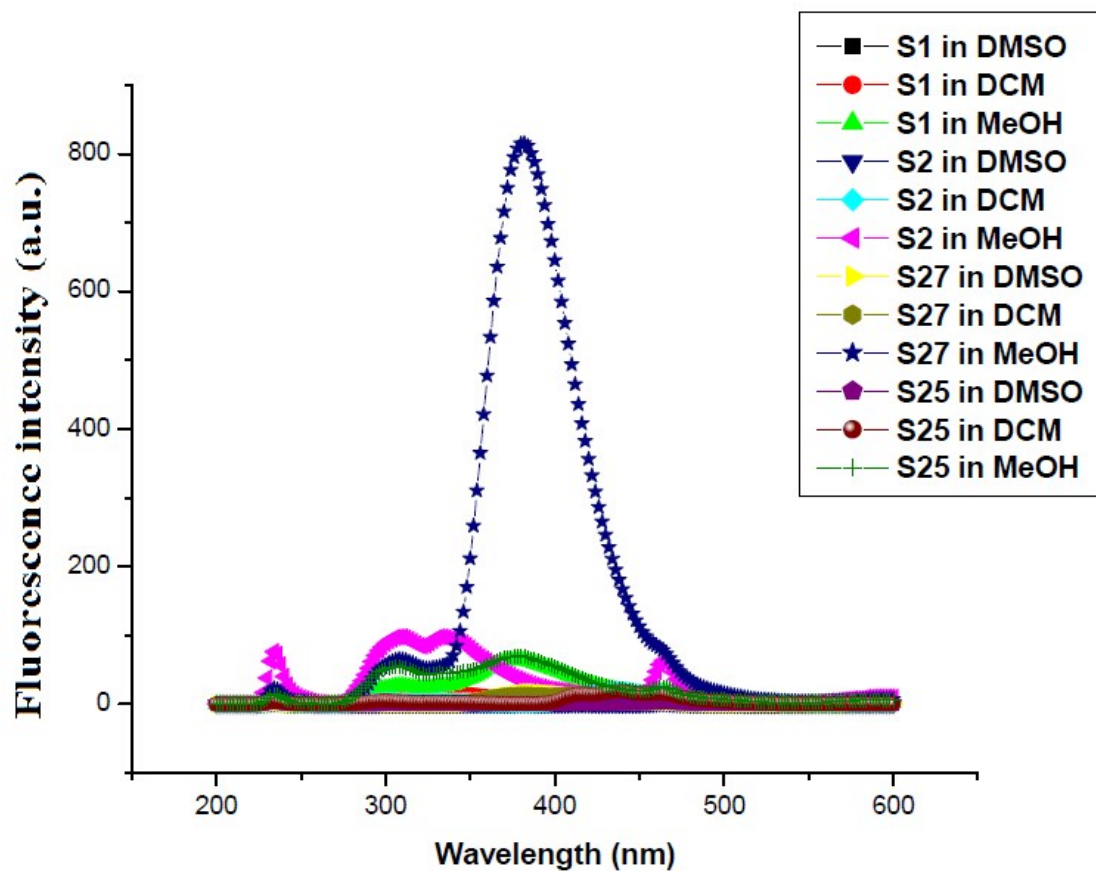


Figure S31- Fluorescence spectra of compound 3a (S1), 4a (S2), 3g (S25), 4g (S27)

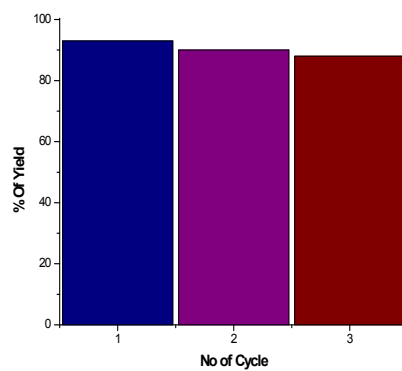


Figure S32 Reusability of Amberlite IR-120 resin for the synthesis of complex 4a

***In vitro* cytotoxic activities (MTT assay):** *In vitro* cytotoxicity was determined using the standard MTT assay.^[1] The MTT proliferation assay is based on the reduction of the yellow MTT tetrazolium salt (3-[4,5-dimethylthiazol-2-yl]-2,5diphenyltetrazolium bromide) by mitochondrial dehydrogenases to form a blue MTT formazan in viable cells. Test compounds (**4a-g**, **5a**) were practiced prior to the experiment by dissolving in 0.1% DMSO and then serial dilution with medium. Four different types of cancer cell lines i.e. MCF-7 (breast cancer cell line) and human Epitheloid Cervix Carcinoma (HeLa), A2780 and one normal fibroblast MRC-5 were used in the assay. Approximately 4×10^3 cells per well for A2780 and 1×10^4 cells per well for either MCF-7 and MRC-5 were cultured in 100 μ L of a growth medium in 96-well plates and incubated at 37 °C under a 5% CO₂ atmosphere. The cells were then treated with different concentrations of the drugs (1-100 μ M) in the volume of 100 μ M /well. Cisplatin has been used as a standard positive control drug. Cells in the control wells accepted the same volume of medium containing 0.1% DMSO. After 24 h, the medium was discarded and cell cultures were incubated with 100 μ L MTT reagent (1 mg/ml) for 5 h at 37° C. Then the suspension was placed on microvibrator for 10 min and subsequently the absorbance was recorded by the ELISA reader at $\lambda = 620$ nm. The experiment was also performed in triplicate. The data were expressed as the growth inhibition percentage calculated according to the equation: % growth inhibition = $100 - [(AD \times 100)/AB]$, where AD is the measured absorbance in wells containing samples and AB is the absorbance measured for blank wells (cells with a medium and a vehicle). Human cancer cell lines, MCF-7 and HeLa cells were cultured in MEM medium supplemented with 10% FBS, 1% glutamine and 50 mM/ml gentamicin sulphate in a CO₂ incubator in a humidified atmosphere of 5% CO₂ and 95% air. The growth media RPMI 1640 with 10% fetal bovine serum (FBS) and 2 mM Lglutamine in a 95% air, 5% CO₂ atmosphere for A2780 cells, minimum essential medium eagle (EMEM) with 10% FBS in 95% air, 5% CO₂ atmosphere for MRC-5 has been used.

References

- 1 (a) T. Mossman, *J. Immunol. Methods*, 1983, **65**, 55-63.; (b) S. Saeed, N. Rashid, P. G. Jones, M. Ali and R. Hussain, *Eur. J. Med. Chem.*, 2010, **45**, 1323-1331.

