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SUPPLEMENTARY INFORMATION

Quasi-Enantiomeric Single-Nucleoside and *Quasi*-Racemic Two-Nucleosides Hydrochloride Salts and Ruthenium Complexes of Cytidine and 2',3'-Dideoxycytidine Analogs Unveiling the Negligible Structure-Driving Role of the 2',3'-Moieties

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Table S1 - Crystal data and refinement statistics for the multicomponent molecular forms [zalcitabine hydrochloride (**2**) and lamivudine zalcitabine hydrochloride (**3**)] and ruthenium(II) complexes {*trans*-[Ru(PPh_3)$_2$(3TC)(bipy)]ClO_4 (**4**) and *trans*-[Ru(PPh_3)$_2$(CYD)(bipy)]ClO_4 (**5**)} prepared in this study.

		2		**3**		**4**	**5**
structural formula		$(C_9H_{14}N_3O_3)Cl$		$(C_9H_{14}N_3O_3)(C_8H_{12}N_3O_3S)2Cl$		$[RuC_{54}H_{49}N_5O_2P_2S].ClO_4.H_2O.(CH_3)_2CO$	$2[RuC_{55}H_{50}N_5O_5P_2].(ClO_4)_2.1½H_2O.½CH_3OH.(CH_3CH_2)_2O$
fw (g/mol)		247.68		513.40		1185.59	2364.08
cryst dimensions (mm^3)		0.60 x 0.12 x 0.06		0.13 x 0.11 x 0.09		0.18 x 0.08 x 0.07	0.31 x 0.11 x 0.05
cryst syst		monoclinic		triclinic		orthorhombic	monoclinic
space group		$P2_1$		$P1$		$P2_12_12_1$	$P2_1$
Z / Z'		2 / 1		2 / 2		4/4	2/4
T (K)		298(2)	150(2)	298(2)	150(2)	293(2)	293(2)
unit cell dimensions	a (Å)	5.5482(2)	5.467 (2)	6.706(3)	6.692(1)	9.800(5)	10.432(1)
	b (Å)	12.0260(5)	11.978 (3)	9.155(8)	8.886(1)	16.008(5)	20.600(3)
	c (Å)	8.5725(3)	8.540(2)	10.512(7)	10.412(1)	34.268(5)	27.012(5)
	α (°)	90	90	105.81(2)	105.22(1)	90	90
	β (°)	104.639(2)	105.327(2)	98.48(1)	99.04(1)	90	98.20(5)
	γ (°)	90	90	108.40(2)	107.50(1)	90	90
V ($Å^3$)		553.41(4)	539.3(3)	569.6(7)	550.7(1)	5376(3)	5745.5(1)
calculated density (Mg/m^3)		1.486	1.525	1.497	1.548	1.465	1.367
				Refinement (only on low temp. data)			
absorption coefficient μ (mm^{-1})		0.342	0.351		0.438	0.502	0.437
Transmission factors for absorption correction (Gaussian)		T_{min} = 0.882 T_{max} = 0.981	T_{min} = 0.860 T_{max} = 0.980		T_{min} = 0.959 T_{max} = 0.985	T_{min} = 0.937 T_{max} = 0.971	T_{min} = 0.906 T_{max} = 0.972
θ range for data collection (°)		3.97 – 24.85	3.05 – 25.37		3.30-25.11	3.02 to 25.25	3.02 to 26.38
index ranges	h	-6 to 6	-6 to 6		-7 to 7	-11 to 11	-13 to 13
	k	-13 to 13	-15 to 15		-10 to 10	-19 to 18	-25 to 25
	l	-9 to 9	-10 to 10		-11 to 11	-41 to 33	-33 to 33
data collected		4896	11644		7307	24783	44046
unique reflections		1653	2237		3091	9650	22785
symmetry factor (R_{int})		0.0655	0.0759		0.0517	0.0884	0.0380
completeness to θ_{max} (%)		97.1	97.6		99.5	99.2	99.5
F (000)		260	260		268	2448	2444
parameters refined		157	157		232	686	1414
goodness-of-fit on F^2		1.074	1.068		1.099	0.999	1.004
final R factors for $I > 2\sigma(I)$		R_1 = 0.0407 wR_2 = 0.1048	R_1 = 0.0403 wR_2 = 0.1035		R_1 = 0.0656 wR_2 = 0.1453	R1 = 0.0657 wR2 = 0.1443	R1 = 0.0470 wR2 = 0.1081

R factors for all data		*R1* = 0.0440 *wR2* = 0.1083	*R1* = 0.0413 *wR2* = 0.1053	*R1* = 0.0792 *wR2* = 0.1558	R1 = 0.0963 wR2 = 0.1560	R1 = 0.0768 wR2 = 0.1184
largest diff. peak / hole (e/Å^3)		0.380/-0.160	0.246/-0.338	0.391/-0.369	2.476 and -0.533	1.026 and -0.418
absolute structure	Flack parameter	0.05(9)	-0.02(7)	0.03(16)	0.05(4)	0.09(2)
	Friedel pairs	779	1054	1408	4256	10747
CCDC deposit number		788023	788024	787748	976187	976188

Table S2 - Selected Torsion Angles (deg.) for the conformationally variable structure moieties of lamivudine and zalcitabine and descriptors for planarity between cytosine and chloride (r.m.s. deviation and chloride deviation in Å) in the single-drug hydrochloride salts (**1**[12] and **2**) and in the two-drugs one (**3**) determined by single-crystal X-ray diffraction data at 150 K.

Structure moiety	Torsion	**1**	**2**	**3**	
				zalcitabine	lamivudine
N1—C1' bridge between cytosine and the five-membered rings	C2—N1—C1'—O1'	161.9(2)	-162.5(2)	-165.3(8)	158.6(8)
	C6—N1—C1'—O1'	-22.1(3)	17.9(3)	22(1)	-27(1)
	C2—N1—C1'—C2'	-78.1(3)	79.7(2)	77(1)	-83(1)
	C6—N1—C1'—C2'	97.9(3)	-99.8(2)	-96(1)	91(1)
Five-membered ring	O1'—C1'—C2'—C3'(S3')	35.4(4)	-25.8(2)	-28.8(9)	33.5(8)
	C1'—C2'—C3'(S3')—C4'	-41.4(3)	35.8(2)	37.3(9)	-41.9(7)
	C2'—C3'(S3')—C4'—O1'	38.7(3)	-34.1(2)	-35.7(9)	40.2(7)
	C3'(S3')—C4'—O1'—C1'	-24.8(4)	19.1(2)	19(1)	-27.5(9)
	C4'—O1'—C1'—C2'	-6.6(5)	4.6(2)	7(1)	-4(1)
5'-CH_2OH branch	O1'—C4'—C5'—O5'	-175.8(2)	172.5(2)	60(1)	-142(2)[a]/ -75(2)[b]
	C3'(S3')—C4'—C5'—O5'	65.1(3)	-69.2(3)	-174.8(8)	71(1)[a] / 165(2)[b]
cytosine least-square (l.s.) plane	N1—C2—O2—N3—C4—N4—C5—C6 r.m.s.d.	0.0310	0.0172	0.0720	0.0721
chloride-cytosine coplanarity	Cl[c] deviation from the cytosine l.s. plane	0.092(1)	0.079(1)	0.144(2)	0.059(3)
	Cl[d] deviation from the cytosine l.s. plane	1.434(1)	1.673(1)	0.052(2)	0.172(3)

[a] The fractions of the C5' and O5' atoms are in the major 60% occupancy sites. [b] The fractions of the C5' and O5' atoms are in the minor 40% occupancy sites. [c] Chloride counterion held together through two hydrogen bonds in which protonated cytosine ring of the drugs is a donor through its imine and amine moieties. [d] Chloride counterion involved in just one hydrogen bonding in which amine moiety is donor through its hydrogen opposite to imine moiety.

Table S3 - Intermolecular hydrogen bonding geometry of the multicomponent molecular forms prepared in this study at low temperature (150 K).

D—H●●●R	D—H (Å)	H●●●R (Å)	D●●●R (Å)	D—H●●●R (°)
2				
$N_3^{(+)}$—H_3●●●$Cl_1^{(-)}$	0.90(3)	2.19(3)	3.047(2)	159(3)
N_4—H_{4Nx}●●●$Cl_1^{(-)}$	1.05(3)	2.38(3)	3.343(2)	152(3)
N_4—H_{4Ny}●●●$Cl_1^{(-)}$ [a]	0.89(3)	2.44(3)	3.259(2)	152(3)
$O_{5'}$—$H_{5'O}$●●●O_2 [b]	0.82(3)	1.94(3)	2.734(3)	163(3)
3				
$N_{3L}^{(+)}$—H_{3L}●●●$Cl_1^{(-)}$	0.86	2.22	3.057(9)	164
N_{4L}—H_{4NxL}●●●$Cl_1^{(-)}$	0.86	2.63	3.379(9)	146
N_{4L}—H_{4NyL}●●●$Cl_1^{(-)}$ [c]	0.86	2.58	3.385(9)	157
$N_{3Z}^{(+)}$—H_{3Z}●●●$Cl_2^{(-)}$	0.86	2.28	3.118(9)	164
N_{4Z}—H_{4NxZ}●●●$Cl_2^{(-)}$	0.86	2.65	3.393(9)	146
N_{4Z}—H_{4NyZ}●●●$Cl_2^{(-)}$ [d]	0.86	2.57	3.382(9)	159
$O_{5'L}$—$H_{5'OL}$●●●$O_{5'Z}$ [e]	0.82	2.09	2.77(1)	140
$O_{5'L'}$—$H_{5'OL'}$●●●$Cl_2^{(-)}$	0.82	2.34	3.11(1)	158
$O_{5'Z}$—$H_{5'OZ}$●●●Cl1$^{(-)}$	0.82	2.46	3.114(7)	134

Symmetry operators: [a] - 1 - x; 0,5 + y; 1 - z; [b] - x; 0,5 + y; - z; [c] 1 + x; y; z; [d] - 1 + x; y; z; [e] 1 + x; 1 + y; - 1 + z.

Table S4 - Selected bond and angle lengths (Å, °) for $[Ru(PPh_3)_2(3TC)(bipy)]ClO_4$ and $[Ru(PPh_3)_2(CYD)(bipy)]ClO_4$ around the metal center and the main bond lengths of the cytosine ring and five-membered ring.

Fragment	**4**	**5**	
		Molecule A	*Molecule B*
Metal center			
d Ru1—N3	2.165(5)	2.122(6)	2.128(5)
d Ru1—N4	2.150(6)	2.146(5)	2.129(4)
d Ru1—N2	2.071(6)	2.060(5)	2.071(5)
d Ru1—N5	2.039(6)	2.044(5)	2.055(5)
d Ru1—P1	2.387(2)	2.389(2)	2.384(2)
d Ru1—P2	2.396(2)	2.403(2)	2.401(2)
< N3—Ru1—N4	61.3(2)	61.5(2)	61.18(19)
<N2—Ru1—N5	77.2(2)	78.3(2)	77.0(2)
< P1—Ru1—P2	179.43(7)	176.13(6)	176.46(6)
<N2—Ru1—N3	172.0(2)	171.7(2)	173.7(2)
<N2—Ru1—N4	110.7(2)	110.3(2)	112.5(2)
<N3—Ru1—N5	110.8(2)	109.9(2)	109.2(2)
< P1—Ru1—N3	88.4(2)	88.69(16)	88.90(15)
<P1—Ru1—N4	87.5(1)	89.67(16)	87.67(16)
< P2—Ru1—N3	91.8(2)	87.54(16)	87.78(15)
<P2—Ru1—N4	92.1(2)	87.77(16)	89.66(16)
Cytosine ring			
d C2—O2	1.238(8)	1.285(8)	1.198(8)
d C4—N4	1.324(9)	1.302(8)	1.305(7)
d C4—N3	1.360(9)	1.378(8)	1.370(8)
d C2—N3	1.346(9)	1.334(8)	1.360(8)
d C2—N1	1.427(9)	1.393(9)	1.410(8)
d N1—C6	1.378(10)	1.358(10)	1.391(9)
d C5—C6	1.335(11)	1.276(10)	1.377(9)
d C5—C4	1.444(10)	1.437(8)	1.429(8)
Five-membered ring			
d N1—C1’	1.463(9)	1.524(8)	1.444(8)
d C1’—O1’	1.430(9)	1.418(8)	1.382(7)
d C1’—C2’	1.483(11)	1.479(9)	1.483(10)
d O1’—C4’	1.442(9)	1.422(9)	1.459(7)
d C4’—S3’(C3’)	1.840(8)	1.514(12)	1.510(11)
d C2’— S3’(C3’)	1.817(8)	1.529(9)	1.516(13)

Table S5 - Selected Torsion Angles (deg.) for the conformationally variable structure moieties of lamivudine and cytidine into ruthenium complexes.

Structure moiety	Torsion	**4**	**5**	
			cytidine A	cytidine B
N1—C1' bridge between cytosine and the five-membered rings	C2—N1—C1'—O1'	120.9(7)	-150.1(6)	-159.1(6)
	C6—N1—C1'—O1'	-54.9(9)	29.6(10)	5.5(10)
	C2—N1—C1'—C2'	-120.1(8)	93.3(8)	79.9(9)
	C6—N1—C1'—C2'	64.1(10)	-87.0(10)	-115.6(8)
Five-membered ring	O1'—C1'—C2'—C3'(S3')	-43.5(8)	38.3(8)	-28.6(9)
	C1'—C2'—C3'(S3')—C4'	-25.8(6)	-22.4(10)	38.3(9)
	C2'—C3'(S3')—C4'—O1'	-3.6(6)	-0.1(12)	-34.7(9)
	C3'(S3')—C4'—O1'—C1'	-21.4(8)	23.3(12)	19.1(9)
	C4'—O1'—C1'—C2'	43.2(9)	-38.2(9)	6.0(8)
5'-CH_2OH branch	O1'—C4'—C5'—O5'	-66.7(9)	-62.5(17)	-64.6(13)
	C3'(S3')—C4'—C5'—O5'	-53.7(9)	58.5(16)	54.9(15)

Table S6 – Main intermolecular hydrogen bonding geometry of the metal complexes.

D—H•••R	D—H (Å)	H•••R (Å)	D•••R (Å)	D—H•••R (°)
4				
N_4—H_4•••O_{1s} [a]	0.86	2.73	3.533(11)	155
O_{1w}—H_{1w}•••O_5' [b]	0.85	2.02	2.844(10)	162
O_{1w}—H_{2w}•••O_2	0.85	2.21	2.919(9)	141
5				
N_4—H_4•••O_{2s}	0.86	2.43	3.236(11)	157
N_{4A}—H_{4A}•••O_{7s} [c]	0.86	2.53	3.332(10)	156
O_{1w}—H_{12w}•••O_5" [d]	0.85	2.27	3.114(16)	175
O_{3wa}—H_{23a}•••O_2' [e]	0.85	2.13	2.90(2)	149

Symmetry operators: [a] x,+y-1,+z; [b] 1+x,y,z; [c] -1+x,y,z; [d] -x, -½+y,1-z; [e] -x, ½+y,-z.

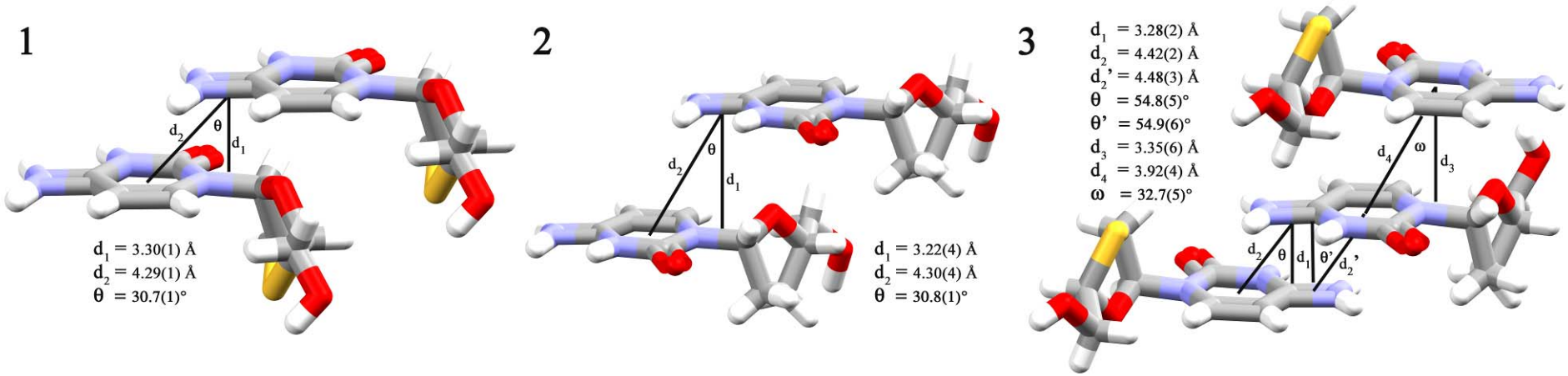

Figure S1- Complete geometry of the π-π base-stacking interactions in the hydrochloride salts **1**-**3** determined by single-crystal X-ray diffraction data at 150 K. The distance d_1 was calculated between the cytosine least-square (l.s.) planes (see Table S2 for plane definition and r.m.s. deviation). The distance d_2, as well as d_2', was calculated between two centroids, namely, that between C4 and N4 and that among the N1—C2—N3—C4—C5—C6 atoms. The distance d_3 was calculated between the cytosine least-square (l.s.) planes of lamivudine and zalcitabine (see Table S2 for planes definition and r.m.s. deviation), while d_4 is the distance between the centroids among the N1—C2—N3—C4—C5—C6 atoms.

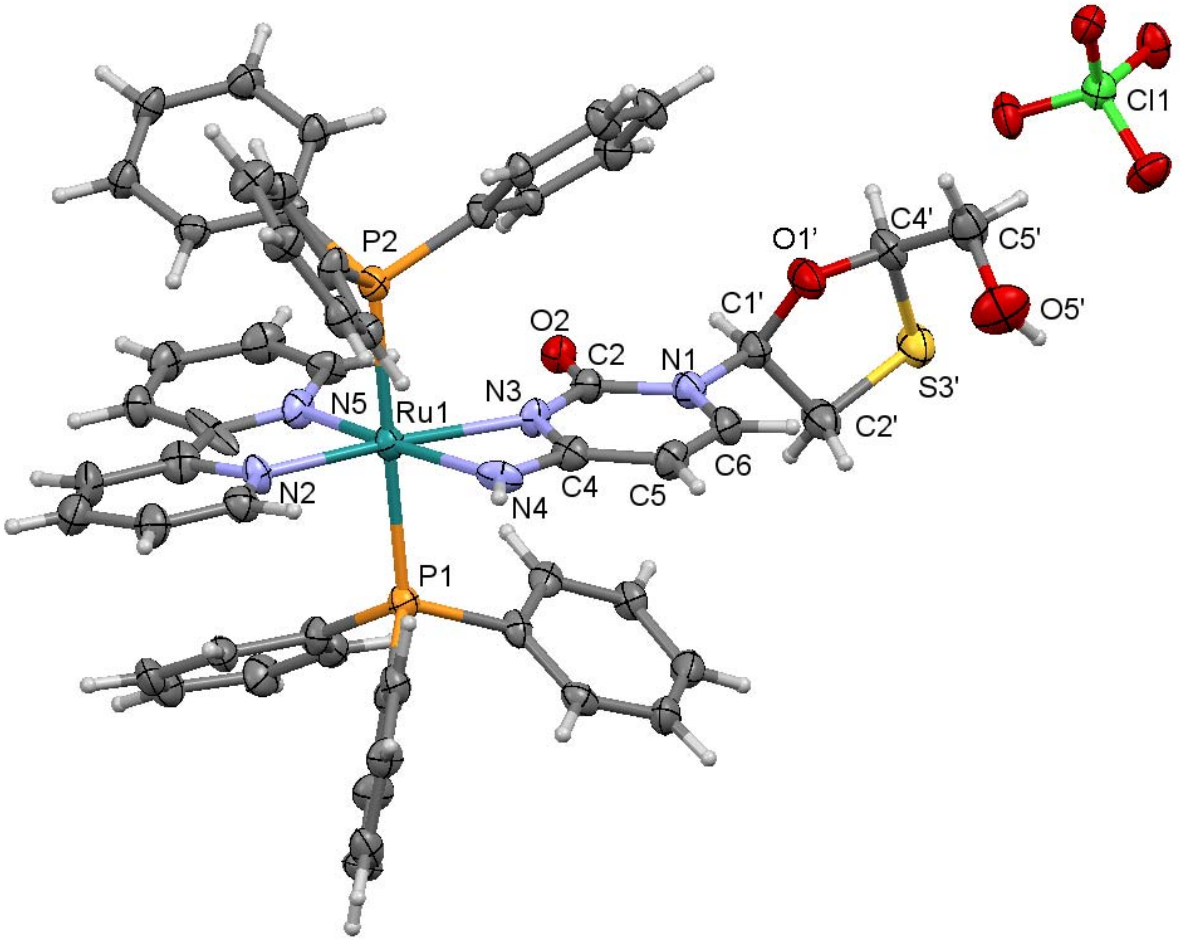

Figure S2- 30% Probability ellipsoids drawing for non-hydrogen atoms of *trans*-$[Ru(PPh_3)_2(3TC)(bipy)]ClO_4$.

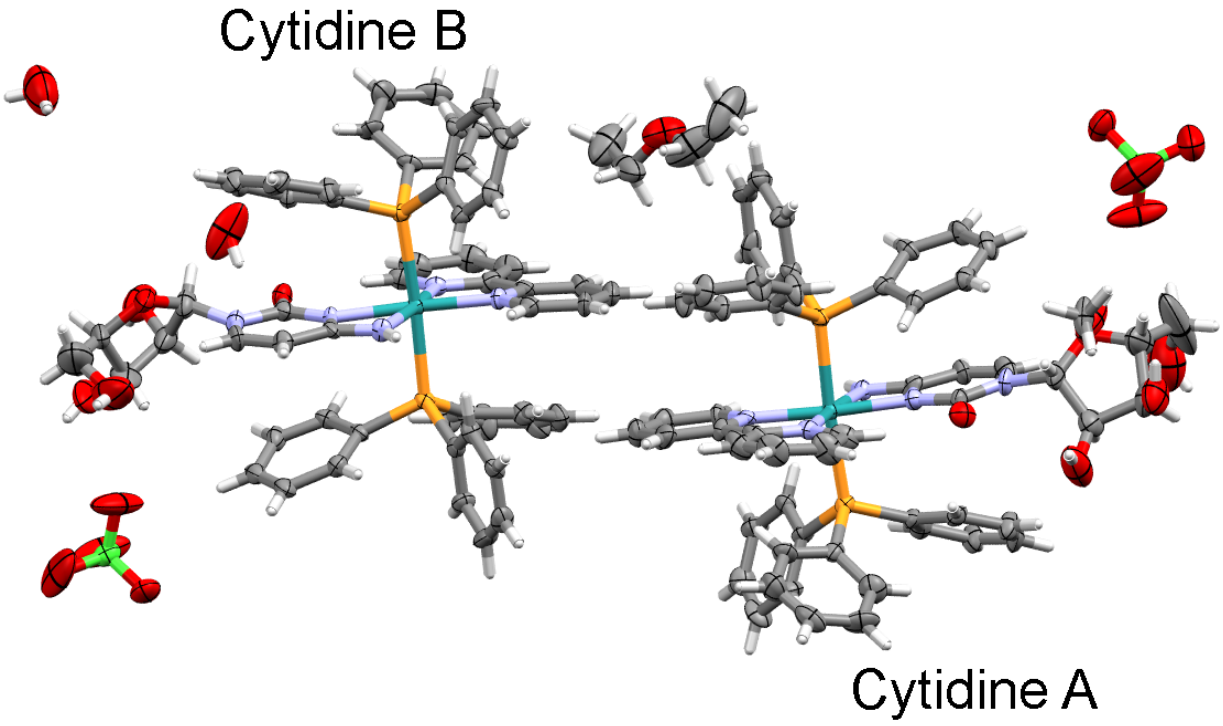

Figure S3 - 30% Probability ellipsoids drawing for non-hydrogen atoms of *trans*-$[Ru(PPh_3)_2(CYD)(bipy)]ClO_4$.

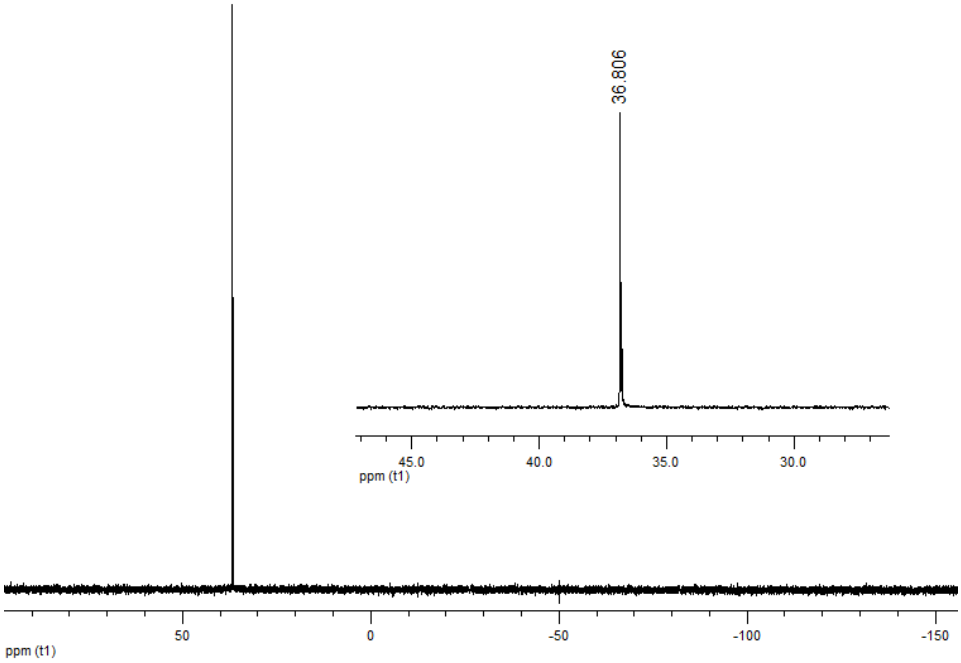

Figure S4 - ^{31}P NMR spectrum for *trans*-$[Ru(PPh_3)_2(3TC)(bipy)]ClO_4$, in $CDCl_3$.

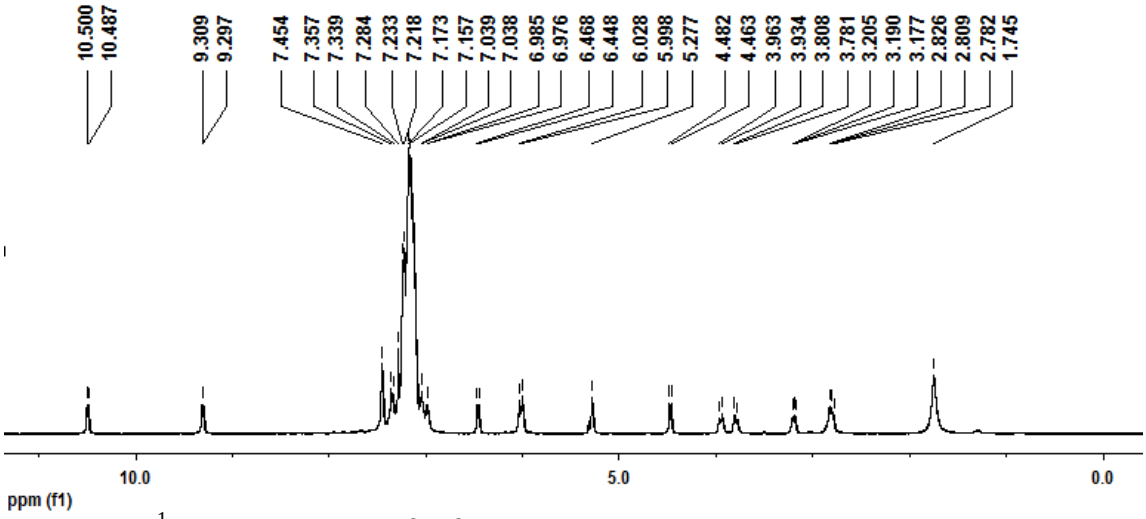

Figure S5 - ^{1}H NMR spectrum for for *trans*-$[Ru(PPh_3)_2(3TC)(bipy)]ClO_4$, in $CDCl_3$.

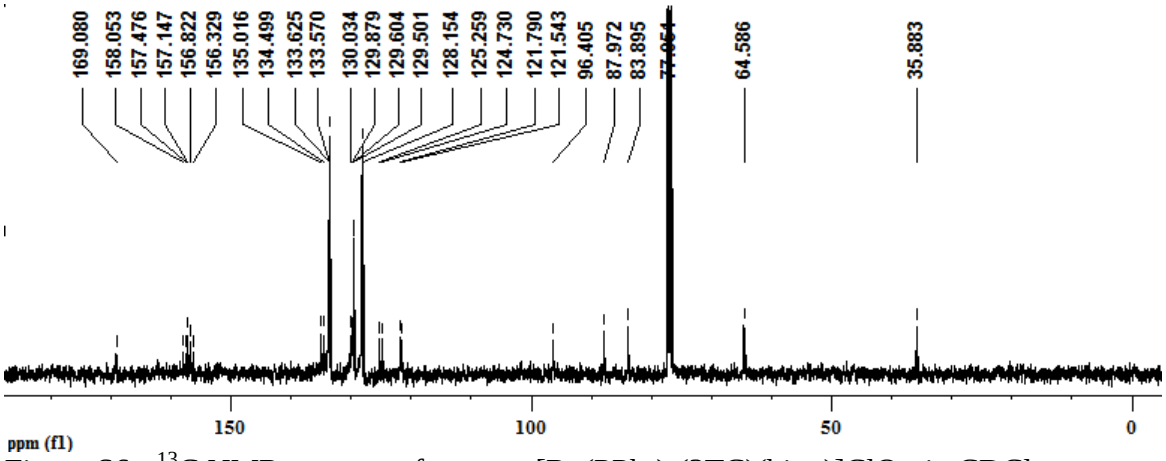

Figure S6 - ^{13}C NMR spectrum for *trans*-[$Ru(PPh_3)_2(3TC)(bipy)$]ClO_4, in $CDCl_3$.

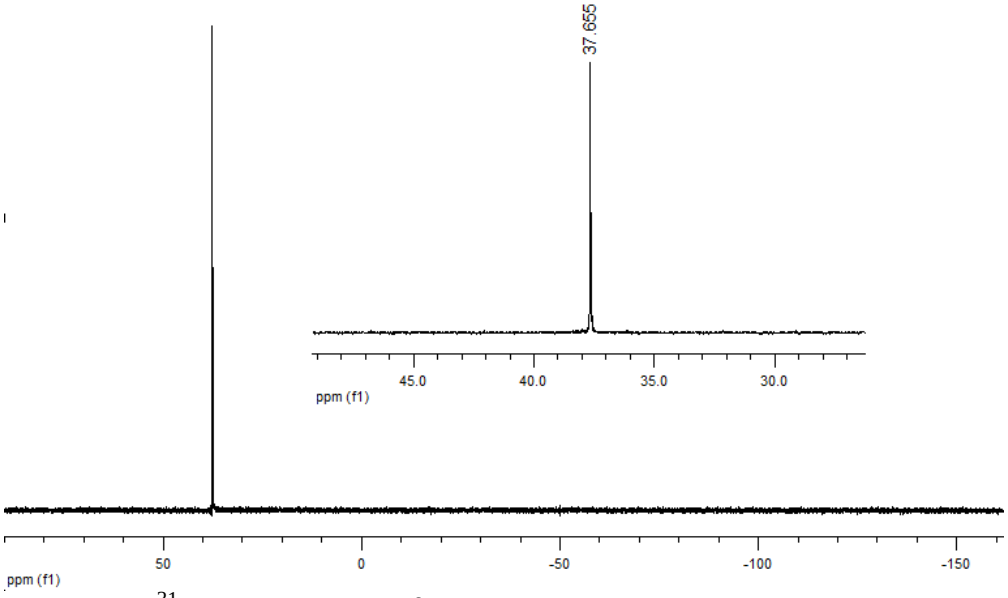

Figure S7 - ^{31}P NMR spectrum for *trans*-[$Ru(PPh_3)_2(CYD)(bipy)$]ClO_4, in $CDCl_3$.

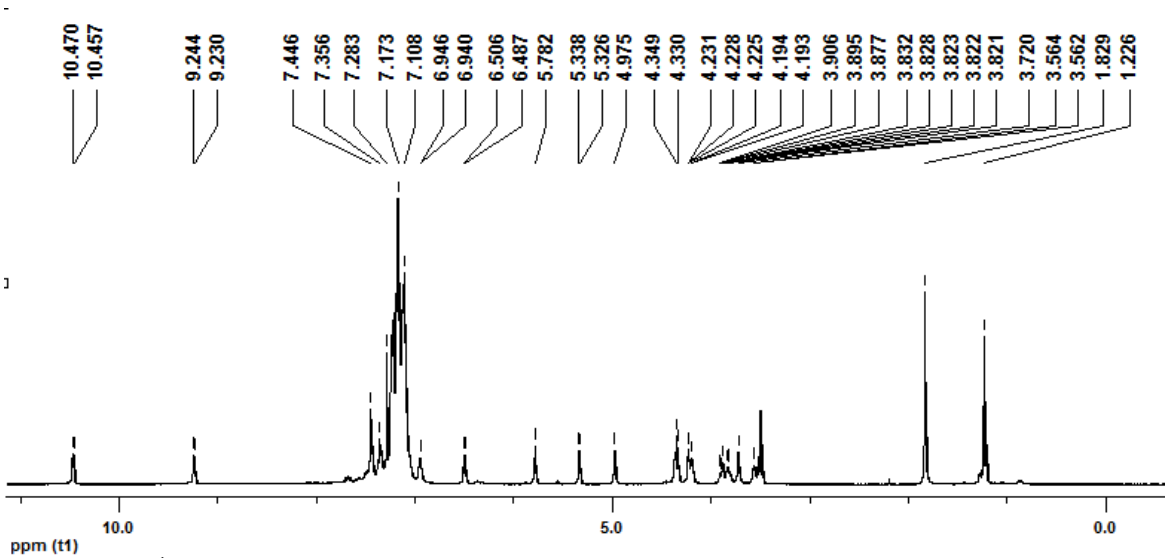

Figure S8 - ^{1}H NMR spectrum for *trans*-[$Ru(PPh_3)_2(CYD)(bipy)$]ClO_4, in $CDCl_3$.

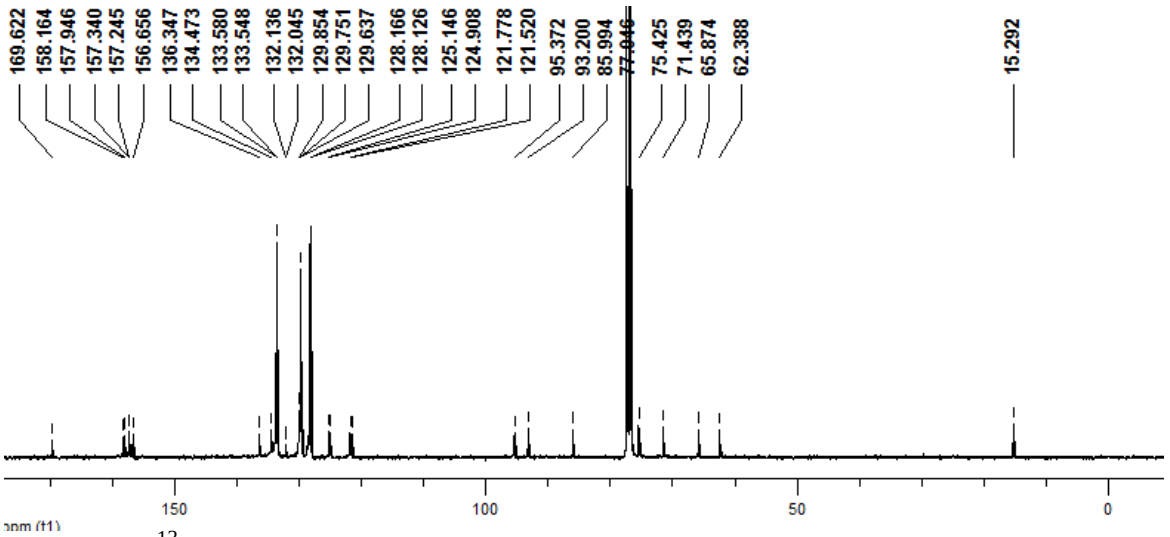

Figure S9 - ^{13}C NMR spectrum for *trans*-[$Ru(PPh_3)_2(CYD)(bipy)$]ClO_4, in $CDCl_3$.

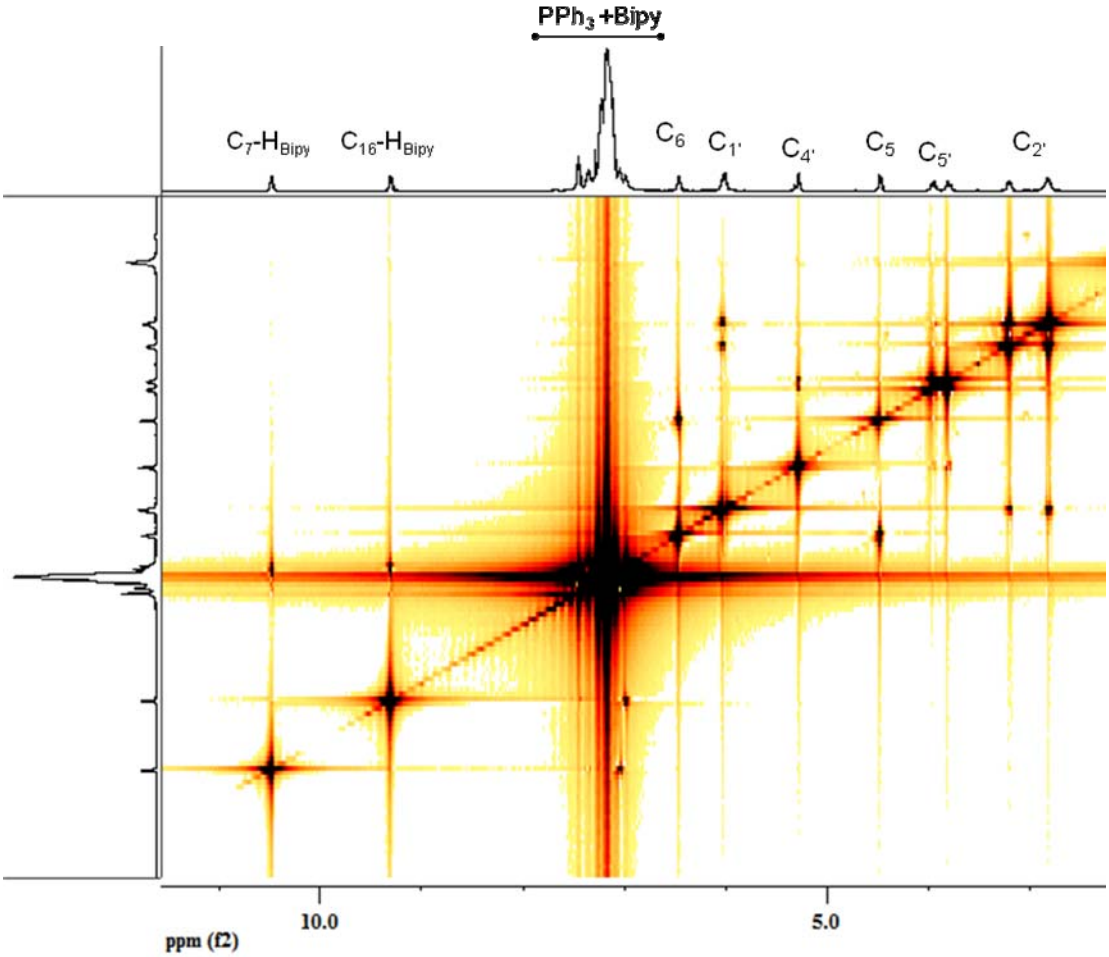

Figure S10 - 2D [^1H,^1H]-COSY spectrum for *trans*-[$Ru(PPh_3)_2(3TC)(bipy)$]ClO_4, in $CDCl_3$.

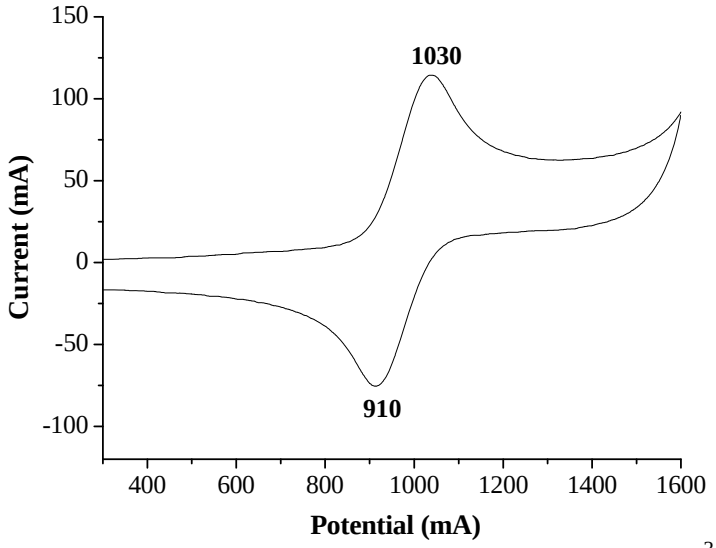

Figure S11 - Cyclic voltammetry for $[Ru(PPh_3)_2(3TC)(bipy)]ClO_4$, 1.0×10^{-3} $molL^{-1}$ in CH_2Cl_2 with 0.1 $molL^{-1}$ of NBu_4ClO_4, scan rate 100 mVs^{-1}, measured at a platinum electrode.

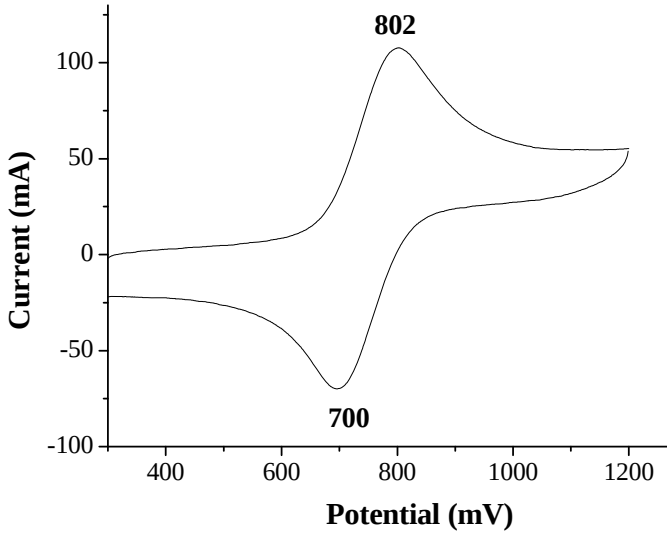

Figure S12 - Cyclic voltammetry for $[Ru(PPh_3)_2(CYD)(bipy)]ClO_4$, 1.0×10^{-3} $molL^{-1}$ in CH_2Cl_2 with 0.1 $molL^{-1}$ of NBu_4ClO_4, scan rate 100 mVs^{-1}, measured at a platinum electrode.

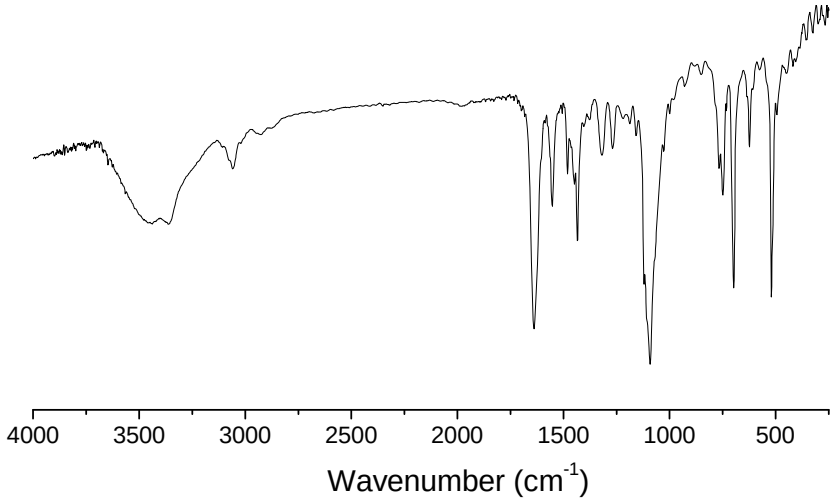

Figure S13 - Infrared spectrum for $[Ru(PPh_3)_2(3TC)(bipy)]ClO_4$, in KBr pallets.

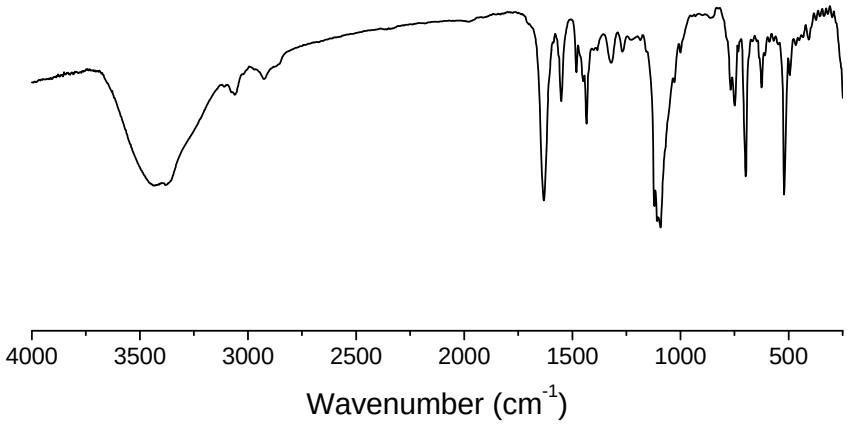

Figure S14 - Infrared spectrum for $[Ru(PPh_3)_2(CYD)(bipy)]ClO_4$, in KBr pallets.