Supporting Information

Novel Phosphine Sulphide Gold(I) Complexes: Topoisomerase I Inhibitors and Antiproliferative Agents.

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Table S1. TopI inhibitory activity of compounds **1**-**8** and CPT.[a]

Entry	Cmpd	R^1	R^2	% inhibition		
				15”	**1’**	**3’**
1		CPT		++	++	Θ
2	**1**	-	-	Θ	Θ	Θ
3	**2**	-	-	Θ	Θ	Θ
4	**3a**	2-naphthyl	H	+++	+++	+++
5	**3b**	4-$CF_3C_6H_4$	F	+++	+++	+++
6	**4**	2-naphthyl	H	Θ	Θ	Θ
7	**5**	-	-	Θ	Θ	Θ
8	**6**	-	-	Θ	Θ	Θ
9	**7a**	2-naphthyl	H	+++	+++	+++
10	**7b**	4-$CF_3C_6H_4$	F	+++	+++	+++
11	**8**	2-naphthyl	H	+++	+++	+++

[a] The activity of the compounds to inhibit TopI relaxation was expressed semiquantitatively as follows: Θ, no activity; ++ similar activity to camptothecin; +++ strong activity.

Table S2. Calculated energies and molecular properties computed at B3LYP/6-311G** basis set level of theory for compounds **3**, **4**, **7** and **8**, CPT and auranofin.[a]

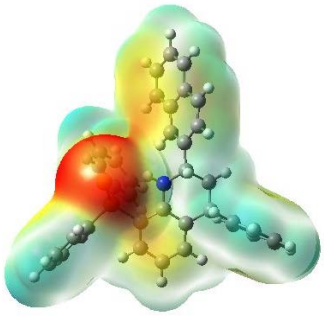
Entry	Cmpd.	ΔG (g) (in a.u.)	ΔG (aq) (in a.u.)	E_{HOMO} (eV)	E_{LUMO} (eV)	Gap (-eV)	η (in a.u.)	μ (in a.u.)	ω (eV)	ΔNmax (in a.u.)	Dipole moment (debye)	Polarizability (in a.u.)
1	**3a**	-2222.26	-2222.28	-0.20443	-0.04402	4.37	0.16041	-0.12422	0.048101	0.77442	4.129	459.406
2	**3b**	-2505.04	-2505.06	-0.21266	-0.04843	4.47	0.16423	-0.13055	0.051885	0.79489	5.067	420.088
3	**4**	-2219.89	-2219.91	-0.20865	-0.07914	3.52	0.12951	-0.14389	0.079939	1.11107	5.632	485.264
4	**7a**	-3085.73	-3085.75	-0.22185	-0.06145	4.36	0.16040	-0.14165	0.062546	0.88310	12.227	570.122
5	**7b**	-3368.51	-3368.53	-0.23032	-0.06665	4.45	0.16367	-0.14848	0.067354	0.90722	12.173	527.748
6	**8**	-3083.37	-3083.39	-0.22258	-0.09552	3.46	0.12706	-0.15905	0.099547	1.25177	14.478	594.428
7	**CPT**	-1182.22	-1182.24	-0.22711	-0.0929	3.65	0.13426	-0.15998	0.095314	1.191569	6.419	265.418
8	**auranofin**	-2334.77	-2334.80	-0.20249	-0.01960	4.98	0.18289	-0.11104	0.033711	0.60717	8.0317	328.53

[a] Abbreviations: ΔG (g): Free energy in gas phase[A]; ΔG (aq): Free energy in aqueous medium[B];Gap: E_{HOMO}-E_{LUMO}; η: Hardnesses[C]; μ:Chemical Potentials[C]; ω:Global Electrophilicities[C] and ΔNmax: Maximun Number of Accepted Electrons[C].

[A] Computed a B3LYP(PCM)/6-311G** +ΔZPVE level; [B] Computed a B3LYP(PCM)/6-311G** +ΔZPVE level using water as solvent; [C]Computed at the B3LYP/6-311G** level of theory according to the approach and equations described previously.[1]

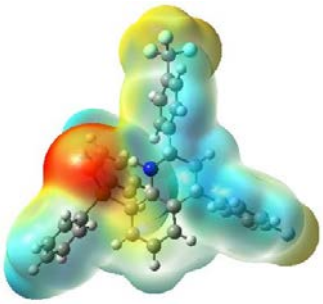
Reference:

[1] B. Lecea, M. Ayerbe, A. Arrieta, F. P. Cossio, V. Branchadell, R. M. Ortuño and A. Baceiredo, *J. Org. Chem.,* 2007, **72**, 357–366.



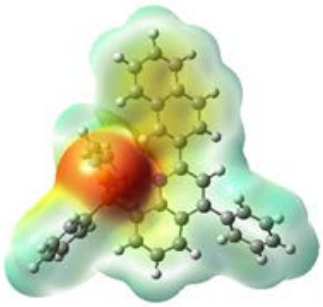
-0.04254 to 0.04254

3a



-0.03872 to 0.03872

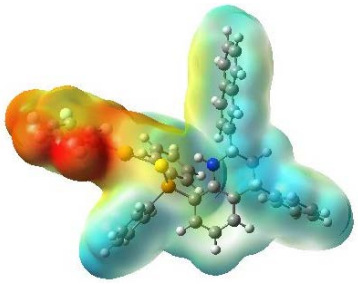
3b



-0.05204 to 0.05204

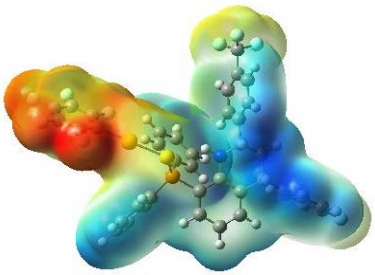
4

Figure S1. MEP surfaces mapped from total electron density for compounds **3** and **4**. Electrostatic potentials are displayed on a 0.002 a.u. isodensity surface. The limits of electrostatic potentials for each molecule are under surfaces. Potential increases in the following order: red (most negative)/orange/yellow/green/blue (most positive).



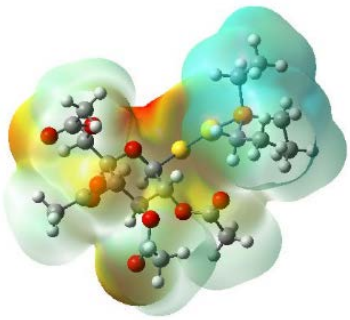
-0.04269 to 0.04269

7a



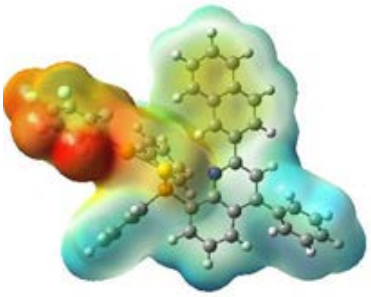
-0.04044 to 0.04044

7b



-0.06330 to 0.06330

Auranofin



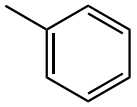
-0.04476 to 0.04476

8

Figure S2. MEP surfaces mapped from total electron density for auranofin and compounds having the Au-perfluorophenyl ligand **7** and **8**. Electrostatic potentials are displayed on a 0.002 a.u. isodensity surface. The limits of electrostatic potentials for each molecule are under surfaces. Potential increases in the following order: red (most negative)/orange/yellow/green/blue (most positive).

NMR spectra of the gold(I) complexes [Au(C_6F_5)($SPPh_2R$)]

R =



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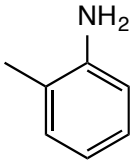

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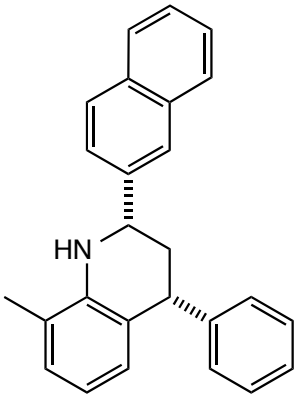
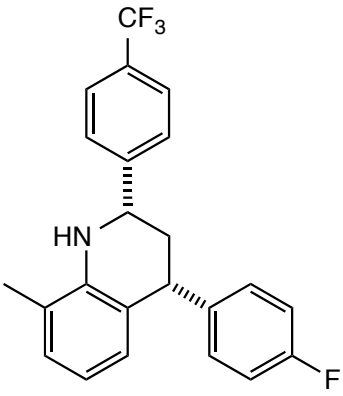
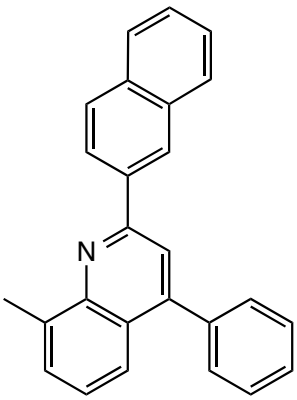


7a



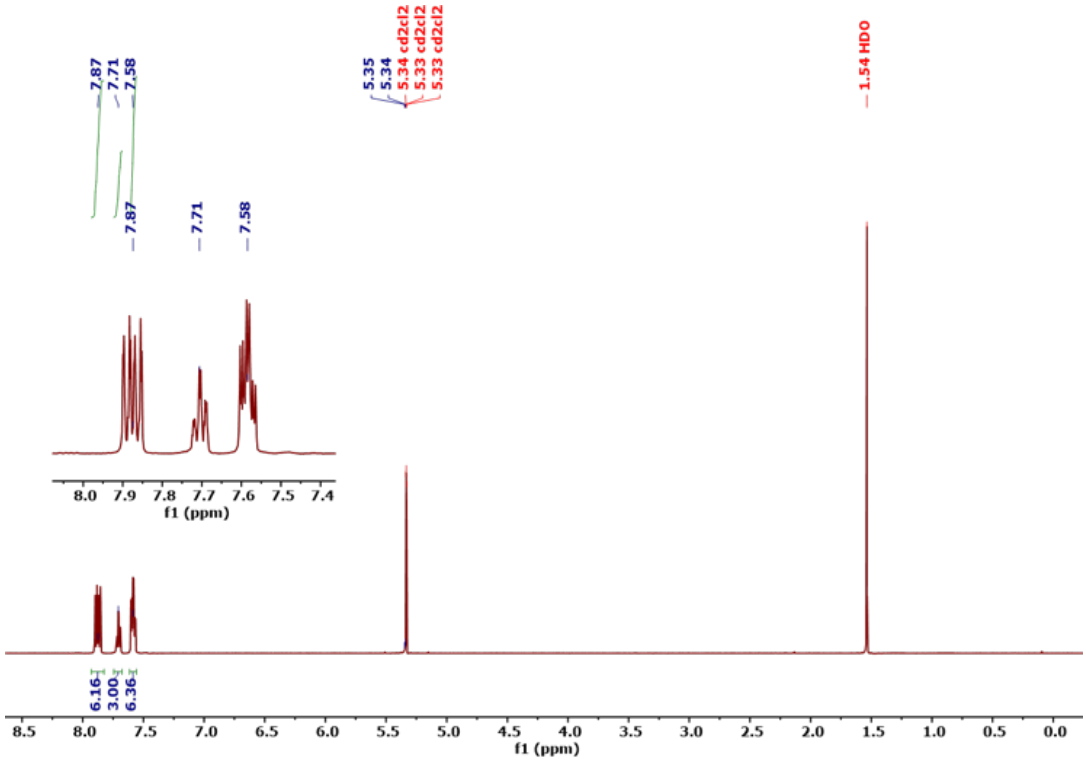
7b



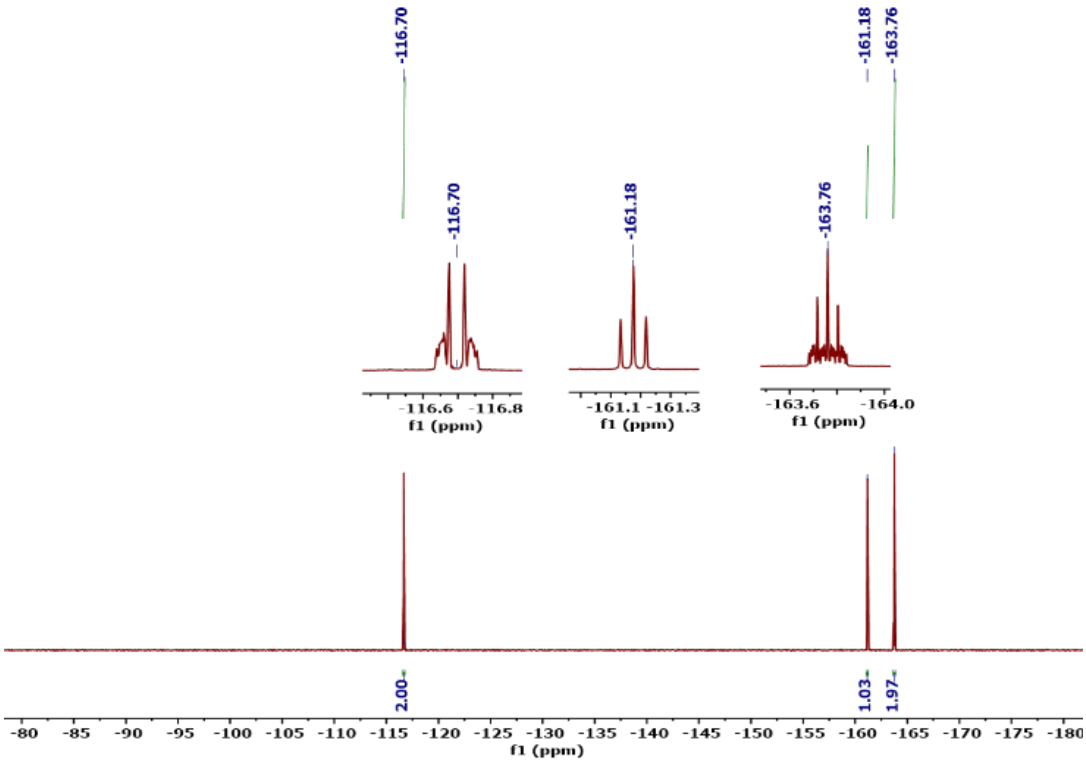
8

Complex 5

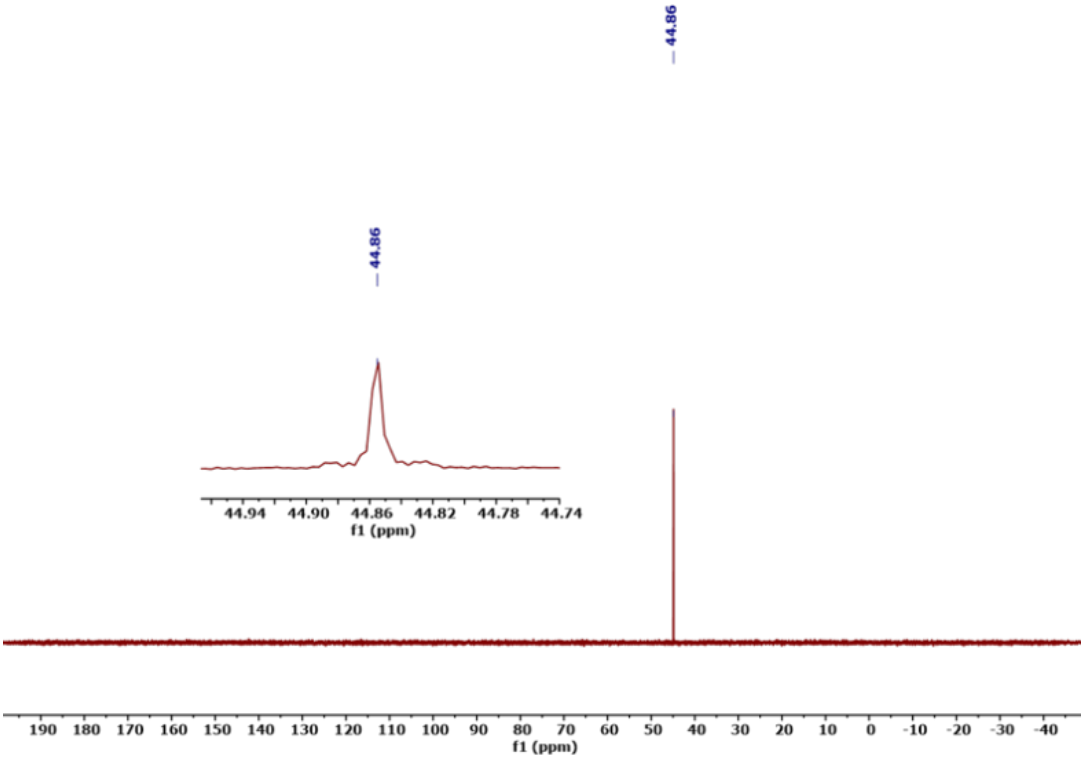
^{1}H NMR (499.70 MHz, CD_2Cl_2, 298 K)



^{19}F NMR (470.17 MHz, CD_2Cl_2, 298 K)

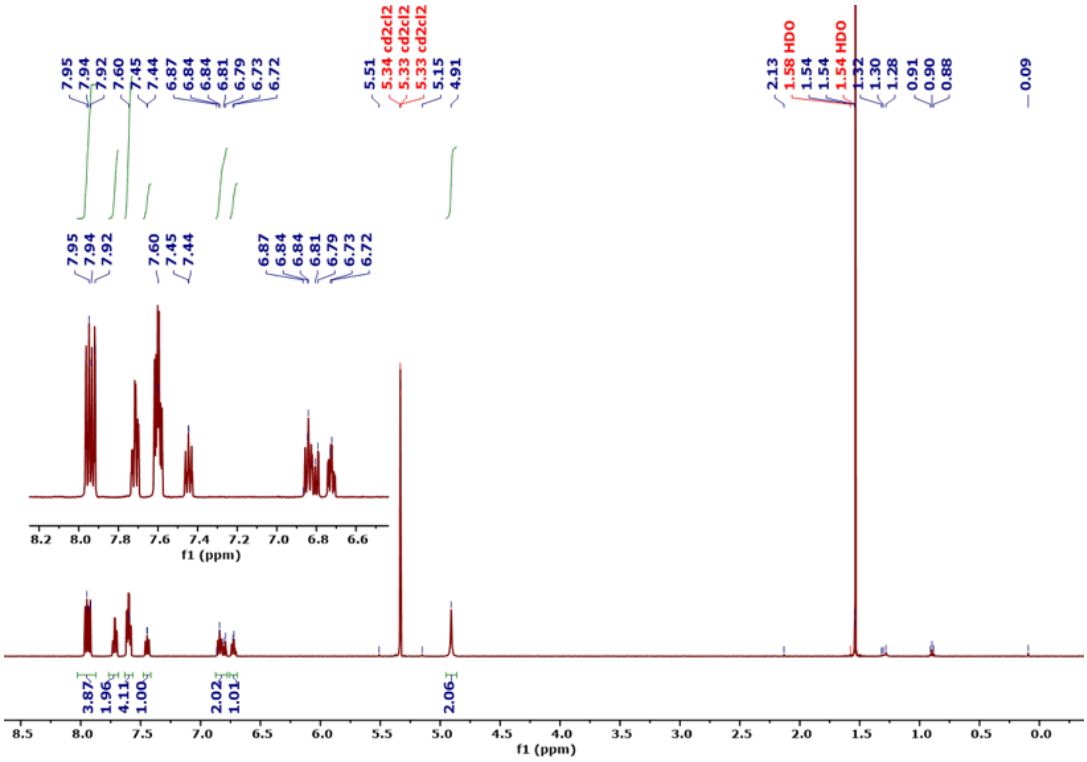


$^{31}P\{^{1}H\}$ NMR (202.31 MHz, CD_2Cl_2, 298 K)

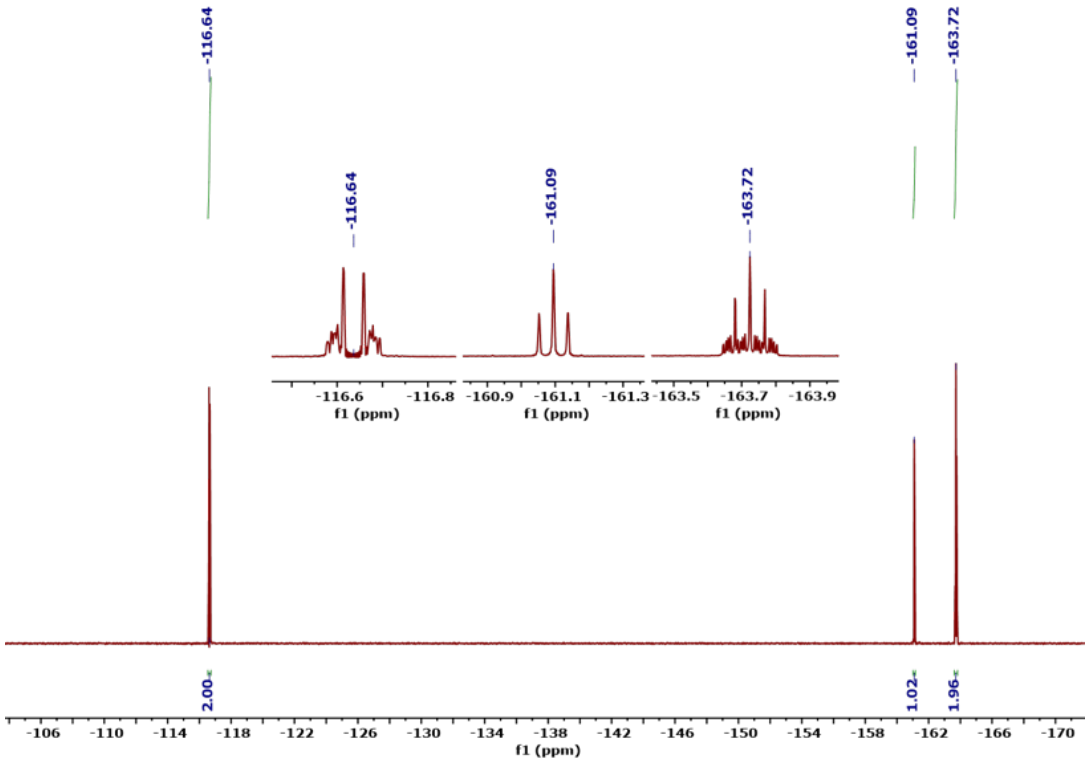


Complex 6

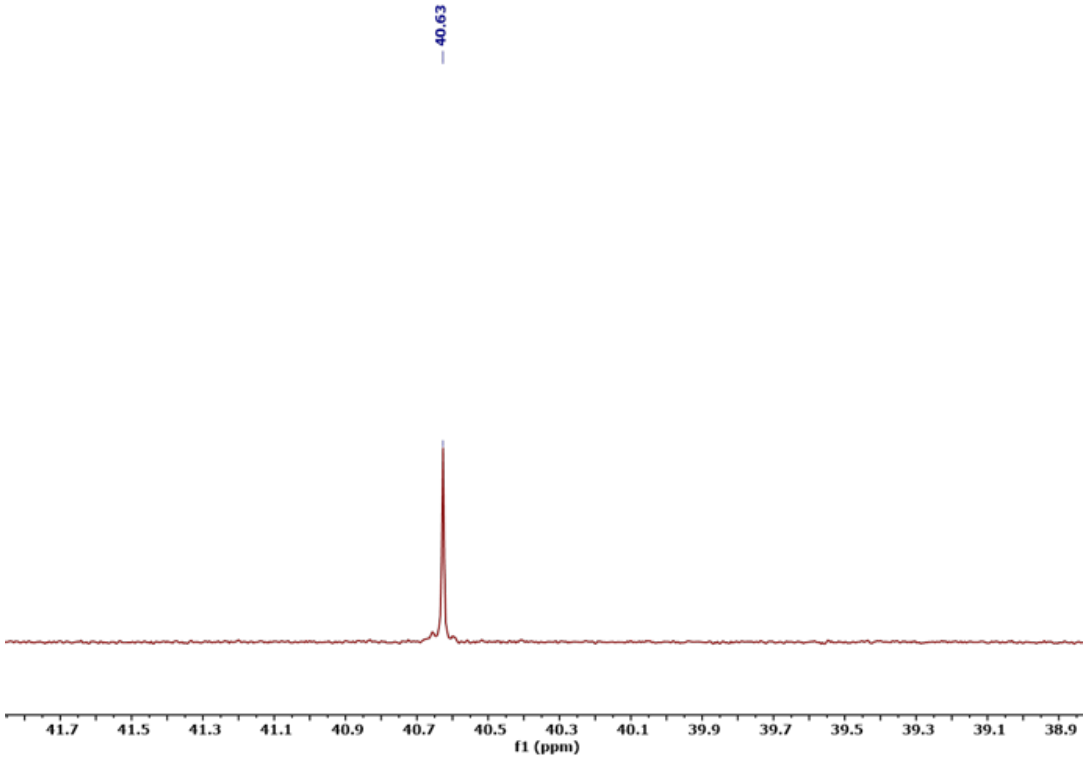
^{1}H NMR (499.70 MHz, CD_2Cl_2, 298 K)



^{19}F NMR (470.17 MHz, CD_2Cl_2, 298 K)

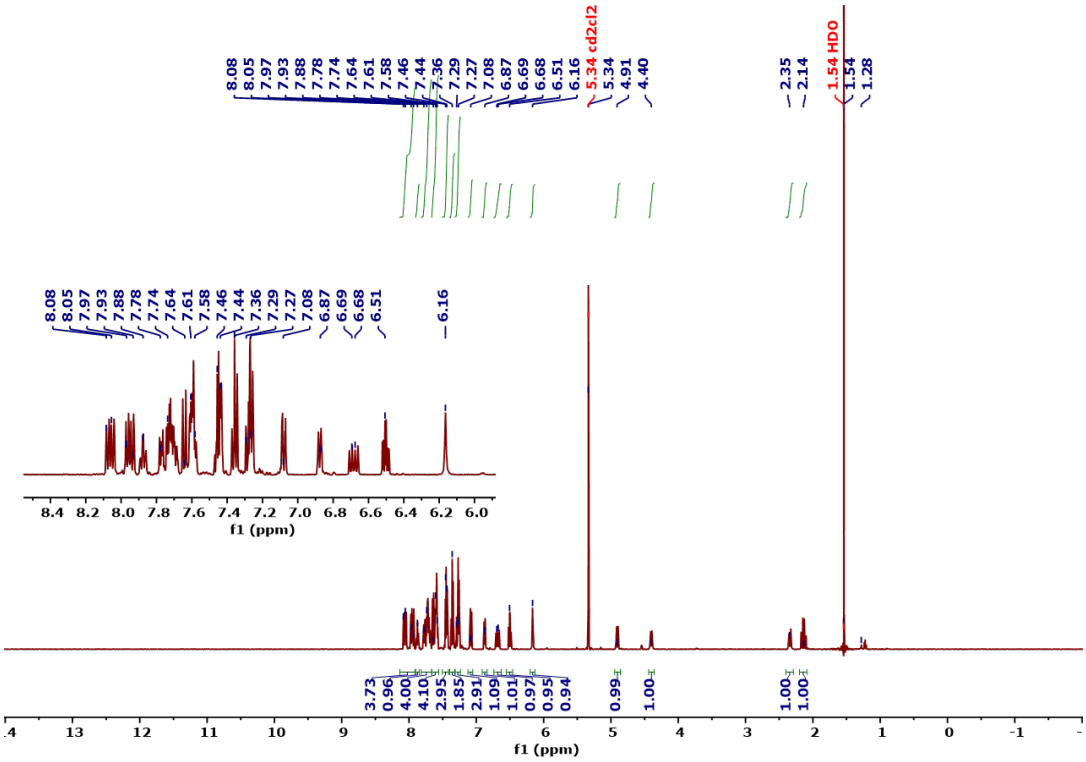


$^{31}P\{^{1}H\}$ NMR (202.31 MHz, CD_2Cl_2, 298 K)

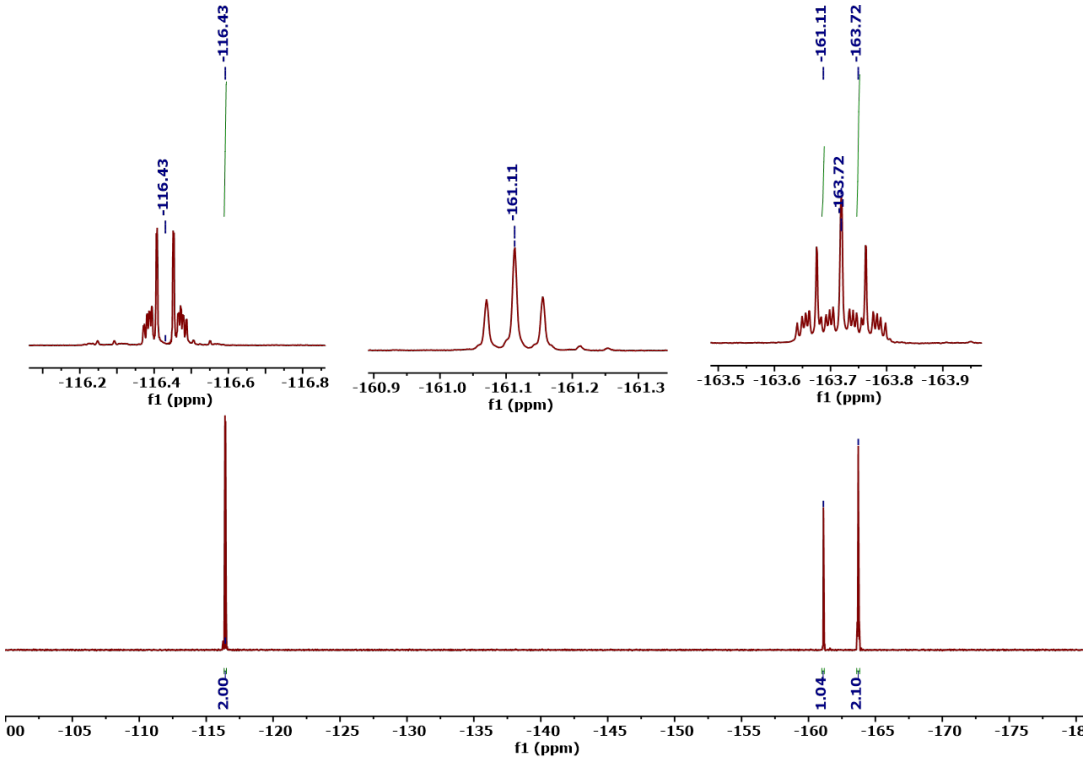


Complex 7a

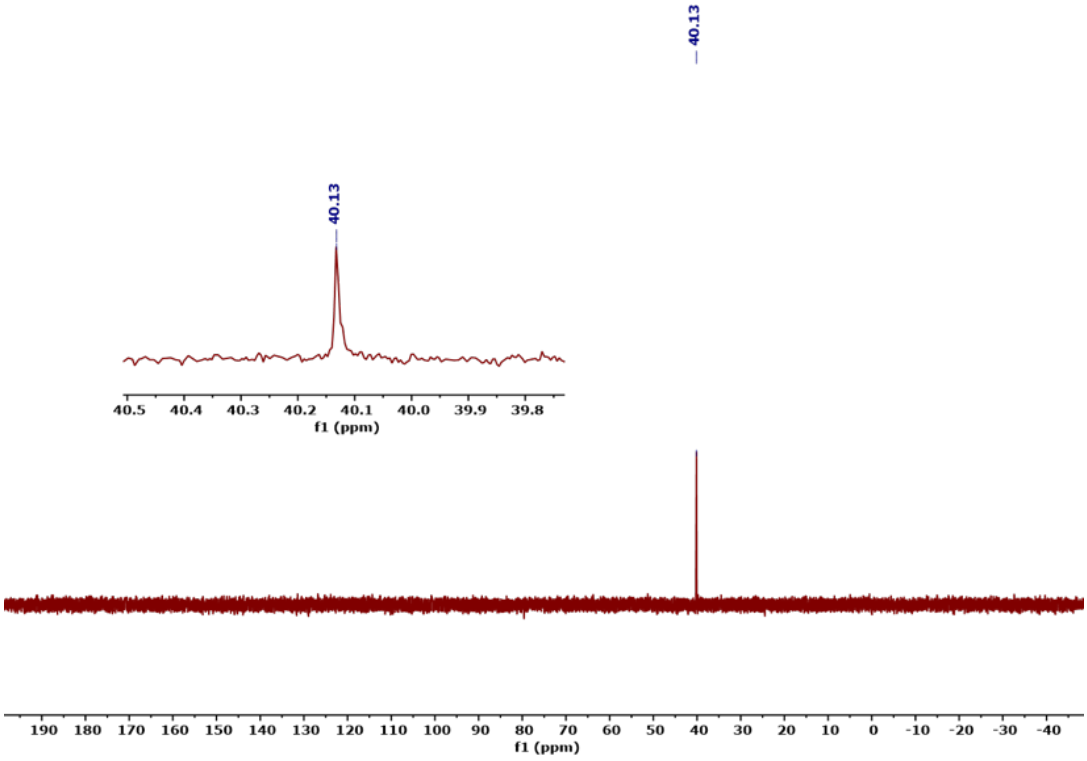
^{1}H NMR (499.70 MHz, CD_2Cl_2, 298 K)



^{19}F NMR (470.17 MHz, CD_2Cl_2, 298 K)

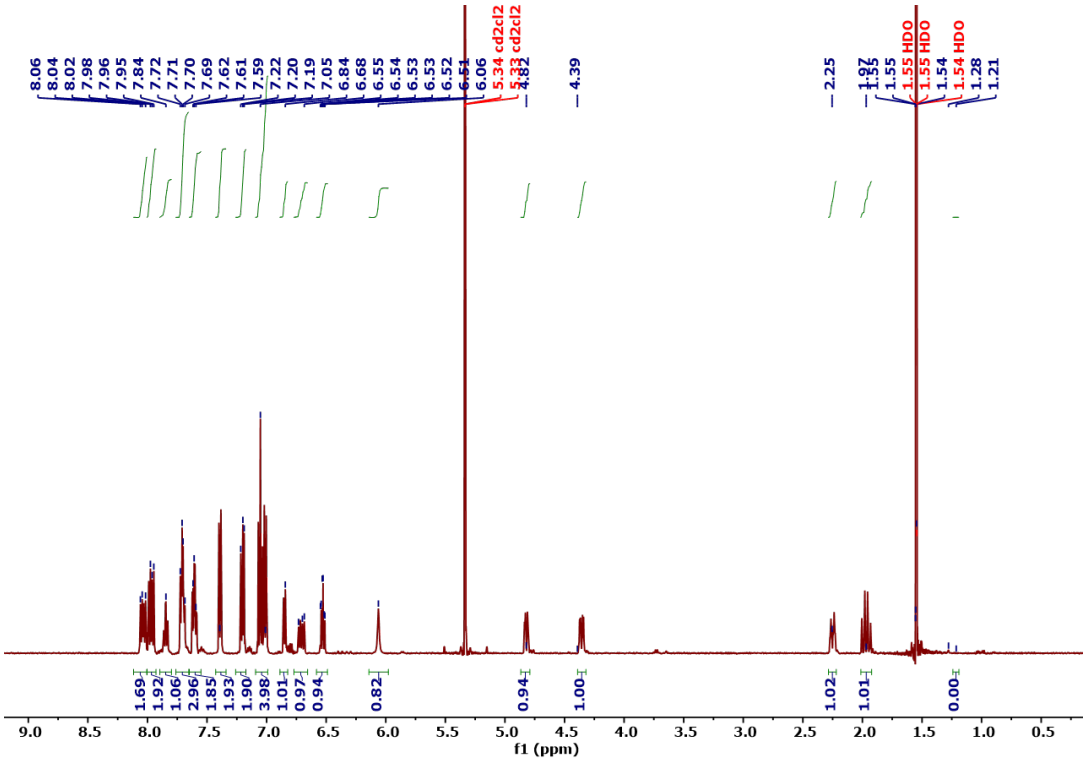


$^{31}P\{^{1}H\}$ NMR (202.31 MHz, CD_2Cl_2, 298 K)



Complex 7b

^{1}H NMR (499.70 MHz, CD_2Cl_2, 298 K)



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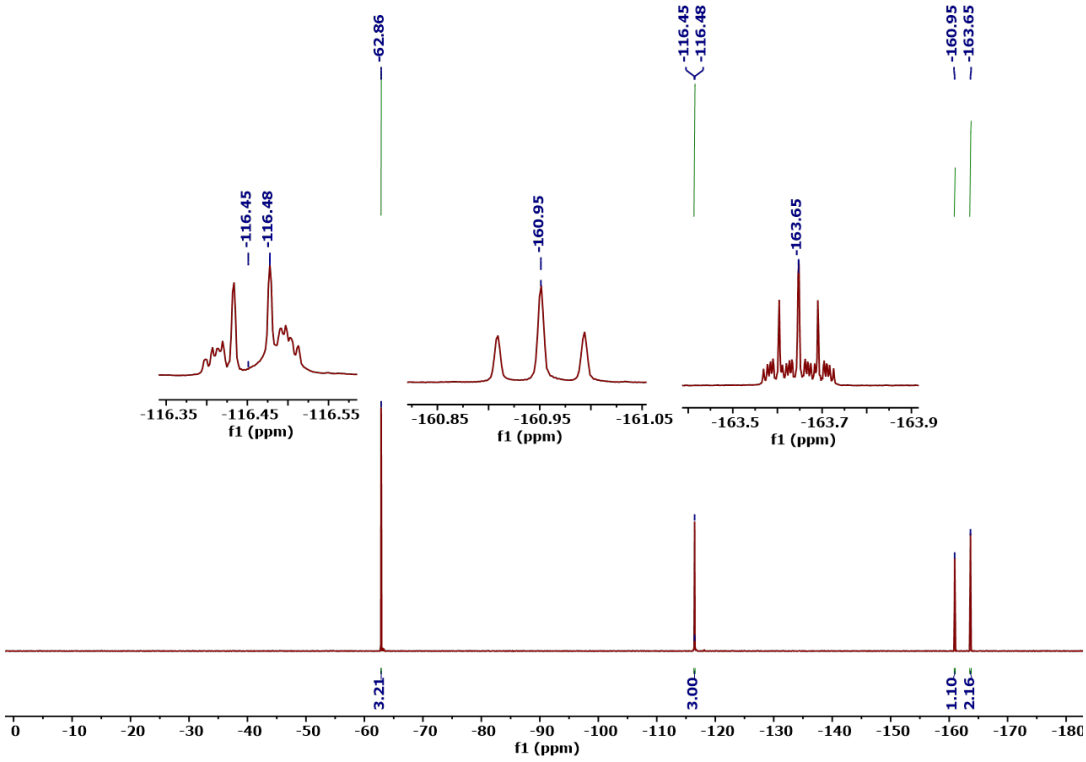
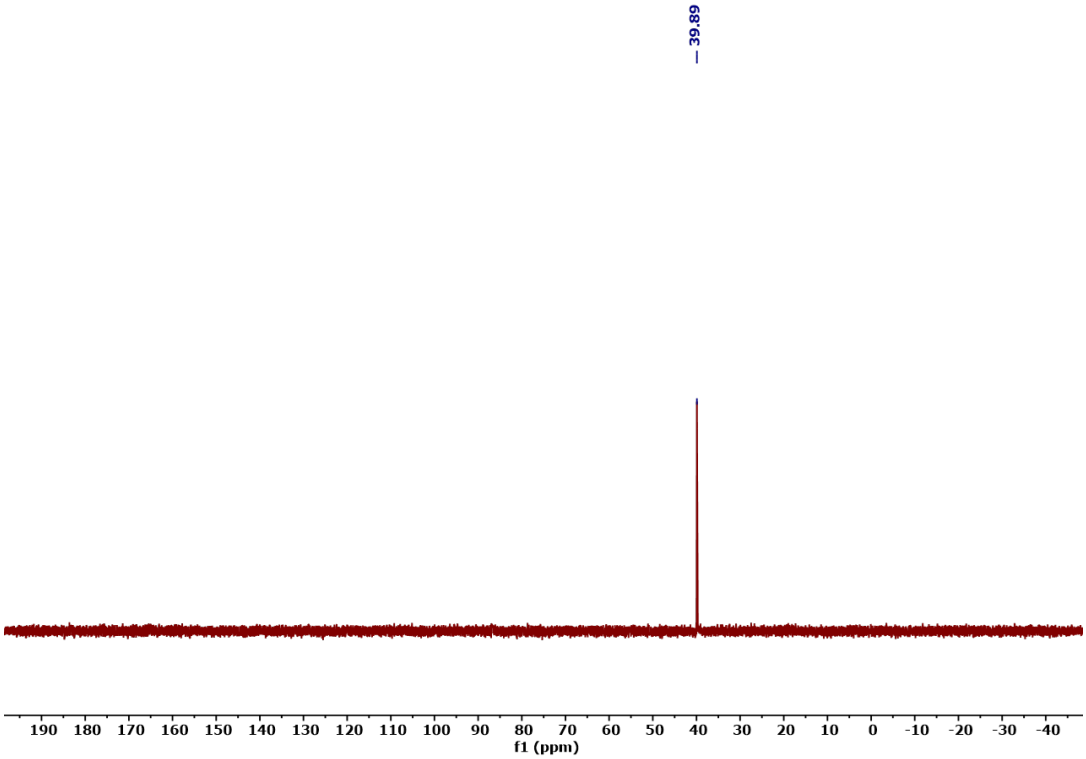


$^{31}P\{^{1}H\}$ NMR (202.31 MHz, CD_2Cl_2, 298 K)



Complex 8

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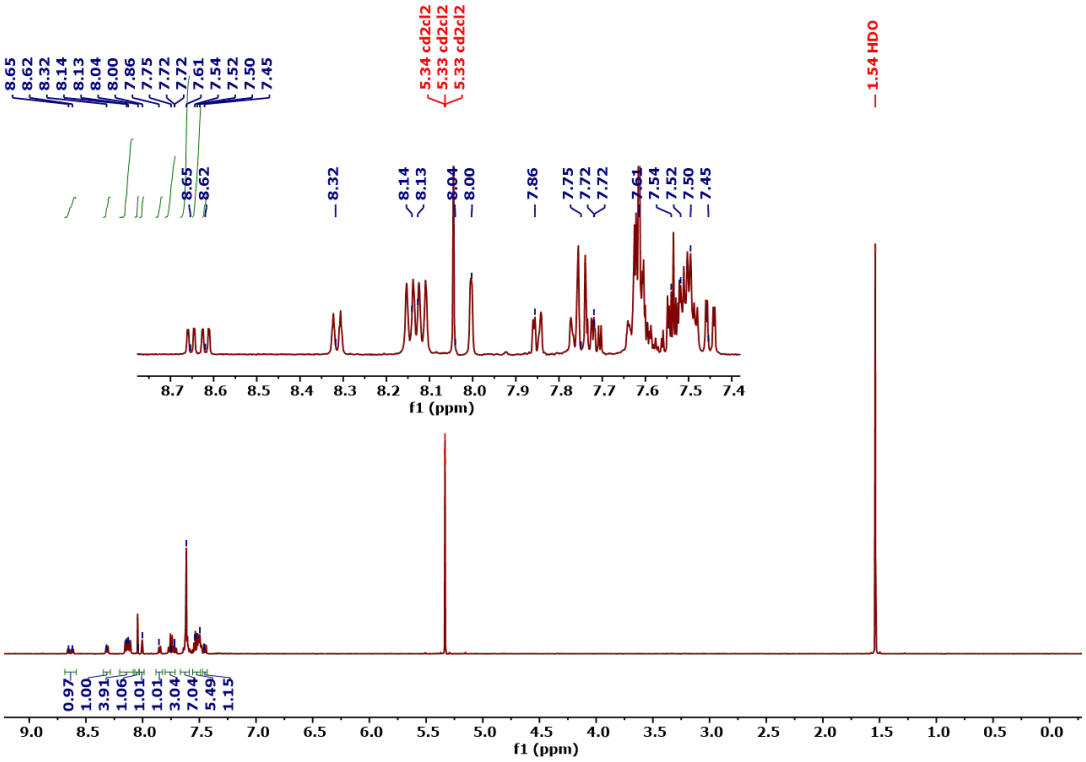

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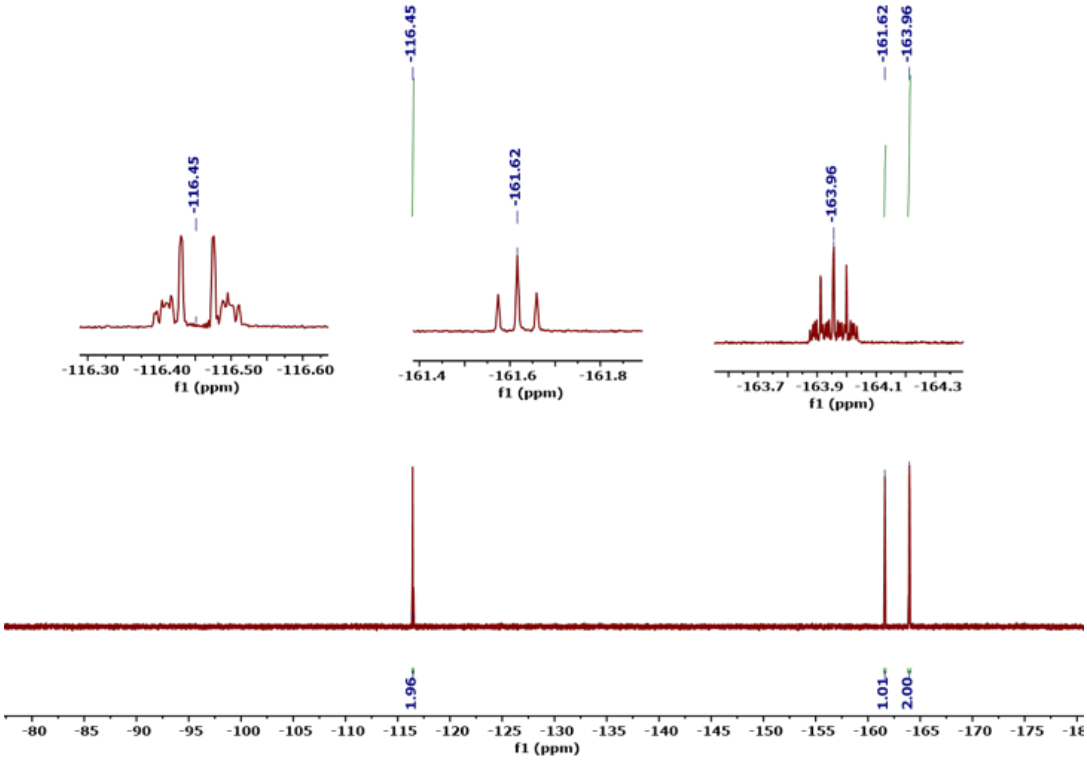

$^{31}P\{^{1}H\}$ NMR (202.31 MHz, CD_2Cl_2, 298 K)

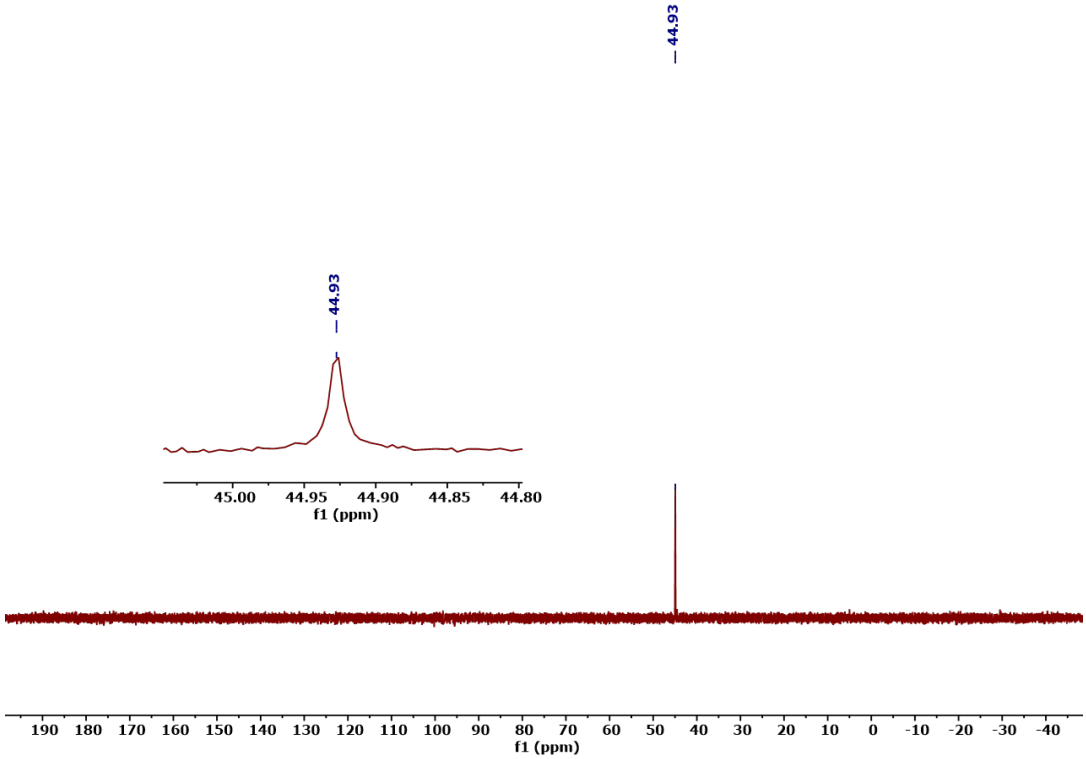

Table S1. Crystal data and structure refinements for complexes **5**, **6** and **8**.

	5	**6**	**8**
Empirical formula	$C_{24}H_{15}AuF_5PS$	$C_{24}H_{16}AuF_5NPS$	$C_{43}H_{26}AuF_5NPS$
Formula weight	658.36	673.37	911.64
Temperature/K	293	293	293.0
Crystal system	triclinic	monoclinic	triclinic
Space group	P-1	$P2_1/n$	P-1
a/Å	7.3678(4)	12.2818(5)	8.9368(3)
b/Å	9.2749(5)	12.6786(5)	13.7072(6)
c/Å	16.2849(8)	15.1093(6)	15.0808(5)
α/°	83.944(4)	90	79.195(3)
β/°	79.946(4)	104.371(4)	78.797(3)
γ/°	89.716(5)	90	88.661(3)
Volume/Å^3	1089.53(10)	2279.14(16)	1779.88(12)
Z	2	4	2
ρ_{calc}g/cm^3	2.007	1.962	1.701
μ/mm^{-1}	6.973	6.670	4.296
F(000)	628.0	1288.0	892.0
Crystal size/mm^3	0.27 × 0.22 × 0.08	0.41 × 0.11 × 0.09	0.29 × 0.18 × 0.05
Radiation	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)
2θ range for data collection/°	6.902 to 59.388	6.85 to 58.938	6.796 to 59.488
Index ranges	$-8 \le h \le 10$, $-11 \le k \le 12$, $-21 \le l \le 22$	$-16 \le h \le 15$, $-16 \le k \le 13$, $-18 \le l \le 13$	$-12 \le h \le 11$, $-16 \le k \le 17$, $-20 \le l \le 20$
Reflections collected	8331	13272	13693
Independent reflections	5059 [R_{int} = 0.0365, R_{sigma} = 0.0761]	5479 [R_{int} = 0.0366, R_{sigma} = 0.0539]	8294 [R_{int} = 0.0289, R_{sigma} = 0.0659]
Data/restraints/parameters	5059/0/289	5479/0/299	8294/0/469
Goodness-of-fit on F^2	0.994	1.024	1.047
Final R indexes [I>=2σ (I)]	R_1 = 0.0423, wR_2 = 0.0630	R_1 = 0.0409, wR_2 = 0.0714	R_1 = 0.0441, wR_2 = 0.0766
Final R indexes [all data]	R_1 = 0.0671, wR_2 = 0.0742	R_1 = 0.0779, wR_2 = 0.0849	R_1 = 0.0736, wR_2 = 0.0892
Largest diff. peak/hole /e Å^{-3}	0.79/-1.01	0.86/-0.97	0.98/-0.82

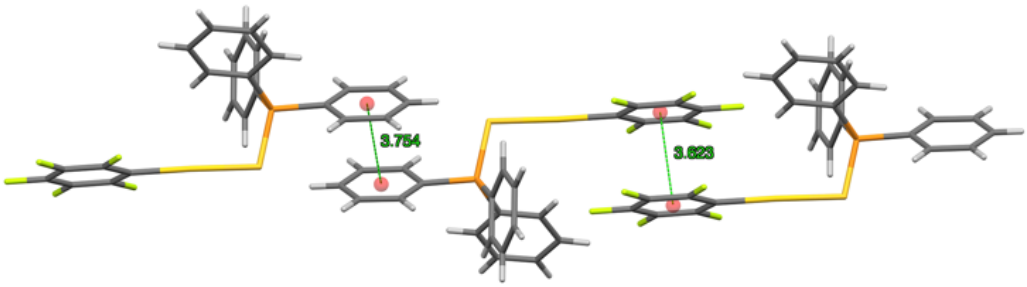

Figure S3. Partial view of crystal packing of **5**. Centroids of C_6F_5 rings are shown as red circles and centroid···centroid distance is 3.754 Å . Color code: C, dark gray; P, orange; Au, S, yellow; F, green and H, gray.

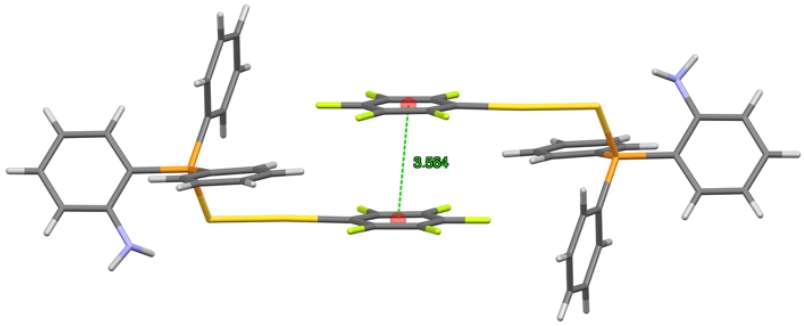

Figure S4. Partial view of crystal packing of **6**. Centroids of C_6F_5 rings are shown as red circles and centroid···centroid distance is 3.554 Å . Color code: C, dark gray; P, orange; Au, S, yellow; F, green; N blue and H, gray.

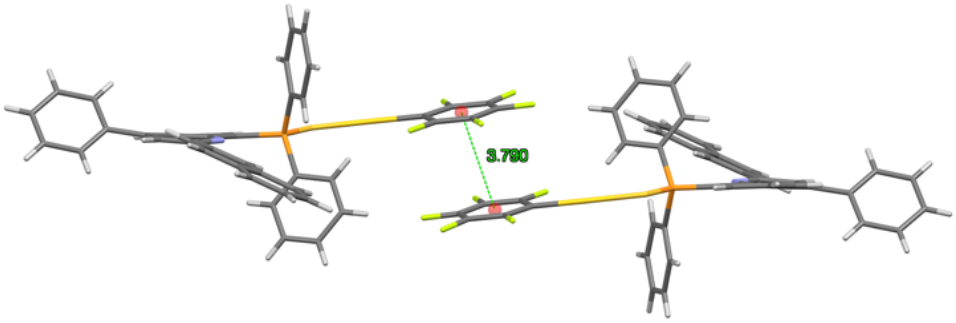

Figure S5. Partial view of crystal packing of **8**. Centroids of C_6F_5 rings are shown as red circles and centroid···centroid distance is 3.790 Å . Color code: C, dark gray; P, orange; Au, S, yellow; F, green and H, gray.