Halo complexes of gold(I) containing glycoconjugate carbene ligands: synthesis, characterization, cytotoxicity and interaction with proteins and DNA model systems

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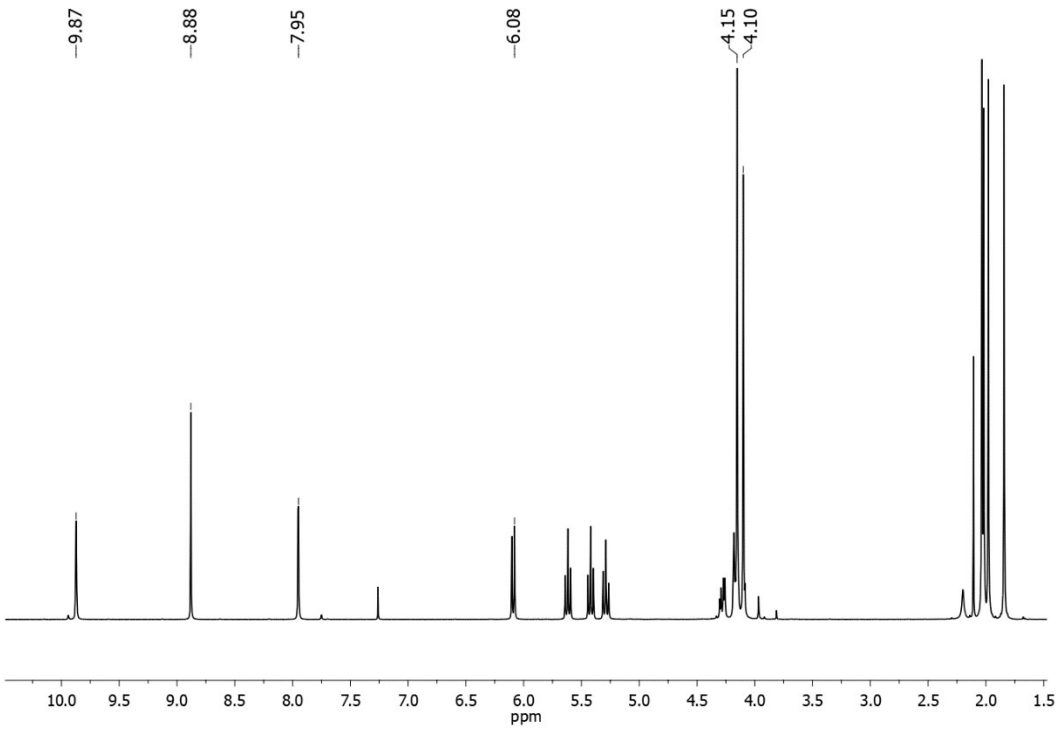


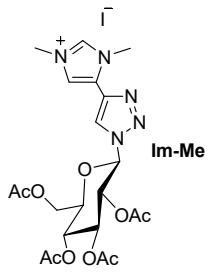
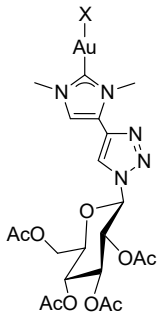


Figure S1. ^{1}H NMR spectrum of **Im-Me** in $CDCl_3$ at 400 MHz.



Au1; X= Cl
Au2; X= Br
Au3; X= I

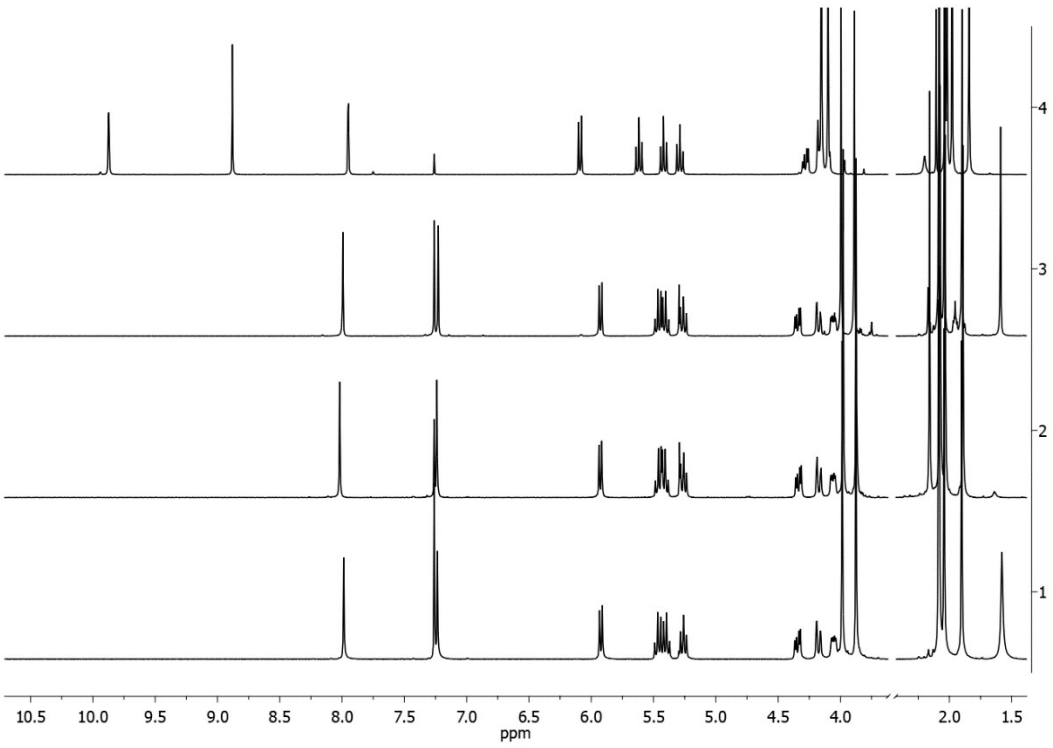


Figure S2. ^{1}H NMR spectra of **Au1** (trace 1), **Au2** (trace 2), **Au3** (trace 3), and **Im-Me** (trace 4) in $CDCl_3$ at 400 MHz.

Table S1 Crystal data and structure refinement details for **Au1**.

CCDC deposit N.	2151285
Empirical formula	C_{21} H_{27} N_5 O_9 Au Cl , C7 H8
Formula weight	818.02
Temperature	173(2)K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, P 2_1 2_1 2_1
Unit cell dimensions	a = 6.5360(13)Å α = 90°
	b = 18.648(5)Å, β = 90°
	c = 26.673(8)Å, γ = 90°
Volume	3251.0(15)Å^3
Z, Calculated density	4, 1.671 Mg/m^3
Absorption coefficient	4.665mm^{-1}
F(000)	1624
Crystal size	0.500 x 0.200 x 0.05mm
Theta range for data collection	2.665 to 27.524°
Reflections collected / unique	17910 / 7233 [R(int) = 0.0503]
Data / restraints / parameters	7233 / 86 / 446
Goodness-of-fit on F2	0.983
Final R indices [I>2sigma(I)]	*R1* = 0.0391, *wR2* = 0.0679
R indices (all data)	*R1* = 0.0758, *wR2* = 0.0781
Absolute structural parameter	0.030(11)
Largest diff. peak and hole	0.718 and -0.570e·Å^{-3}

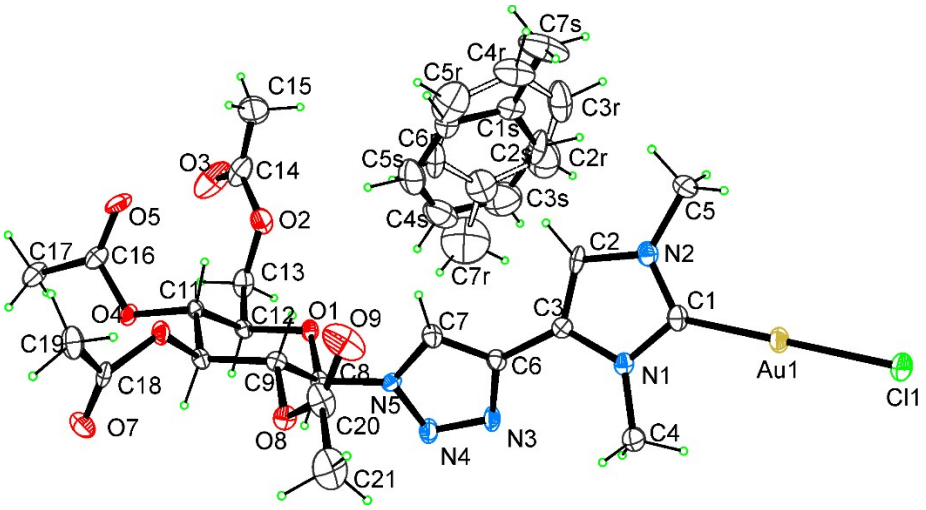


Figure S3. Ortep view of **Au1** molecular structure with thermal ellipsoids drawn at 30% probability level. The minor part of disordered toluene solvent molecule is shown with open bonds.

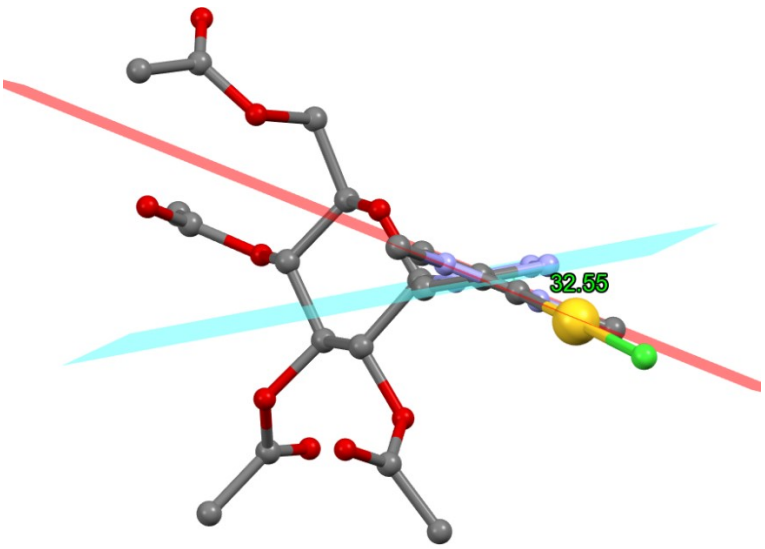


Figure S4. View of the molecule in the direction of the bond C3-C6. The angle between the mean planes of imidazole (red) and triazole (cyan) rings is shown. H atoms are not drawn for clarity.

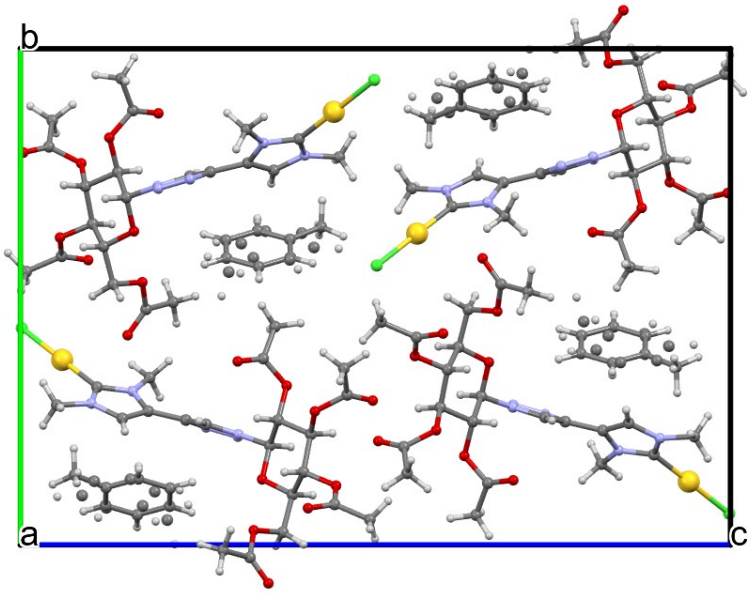


Figure S5. Crystal packing of **Au1** viewed along the **a** axis direction.

Table S2. Selected bond lengths [A] and angles [deg] for **Au1**.

C(1)-N(2)	1.347(10)
C(1)-N(1)	1.360(10)
C(1)-Au(1)	1.970(8)
C(2)-C(3)	1.338(11)
C(2)-N(2)	1.383(9)
C(3)-N(1)	1.395(9)
C(3)-C(6)	1.456(11)
C(4)-N(1)	1.445(9)
C(5)-N(2)	1.466(9)
C(6)-C(7)	1.347(11)
C(6)-N(3)	1.359(9)
C(7)-N(5)	1.347(9)
C(8)-O(1)	1.418(8)
C(8)-N(5)	1.446(9)
C(1)-Au(1)-Cl(1)	179.6(3)
N(1)-C(1)-Au(1)	127.9(6)
N(2)-C(1)-Au(1)	126.8(6)

N(2)-C(1)-N(1)	105.2(7)
C(7)-C(6)-N(3)	108.7(7)
C(7)-C(6)-C(3)	127.6(8)
N(3)-C(6)-C(3)	123.6(7)
C(1)-N(1)-C(3)	110.3(7)
C(1)-N(1)-C(4)	122.8(7)
C(3)-N(1)-C(4)	126.8(7)
C(1)-N(2)-C(2)	110.5(7)
C(1)-N(2)-C(5)	124.9(7)
C(2)-N(2)-C(5)	124.7(7)

Table S3. Selected torsion angles [deg] for **Au1.**

C(2)-C(3)-C(6)-C(7)	-28.9(14)
N(1)-C(3)-C(6)-C(7)	148.4(8)
C(2)-C(3)-C(6)-N(3)	147.2(9)
N(1)-C(3)-C(6)-N(3)	-35.5(12)

Table S4. Hydrogen bonds for **Au1** [Å and deg.]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(4)-H(4A)...O(3)#1	0.98	2.55	3.358(12)	139.5
C(11)-H(11)...N(4)#2	1.00	2.63	3.519(10)	148.3
C(12)-H(12)...O(5)#3	1.00	2.42	3.116(10)	126.3
C(17)-H(17C)...Cl(1)#4	0.98	2.80	3.734(9)	158.9
C(19)-H(19A)...O(4)#5	0.98	2.57	3.274(10)	128.9

Symmetry transformations used to generate equivalent atoms:

#1 -x,y-1/2,-z+3/2 #2 x+1,y,z #3 x-1,y,z

#4 -x,y+1/2,-z+3/2 #5 x+1/2,-y+3/2,-z+2

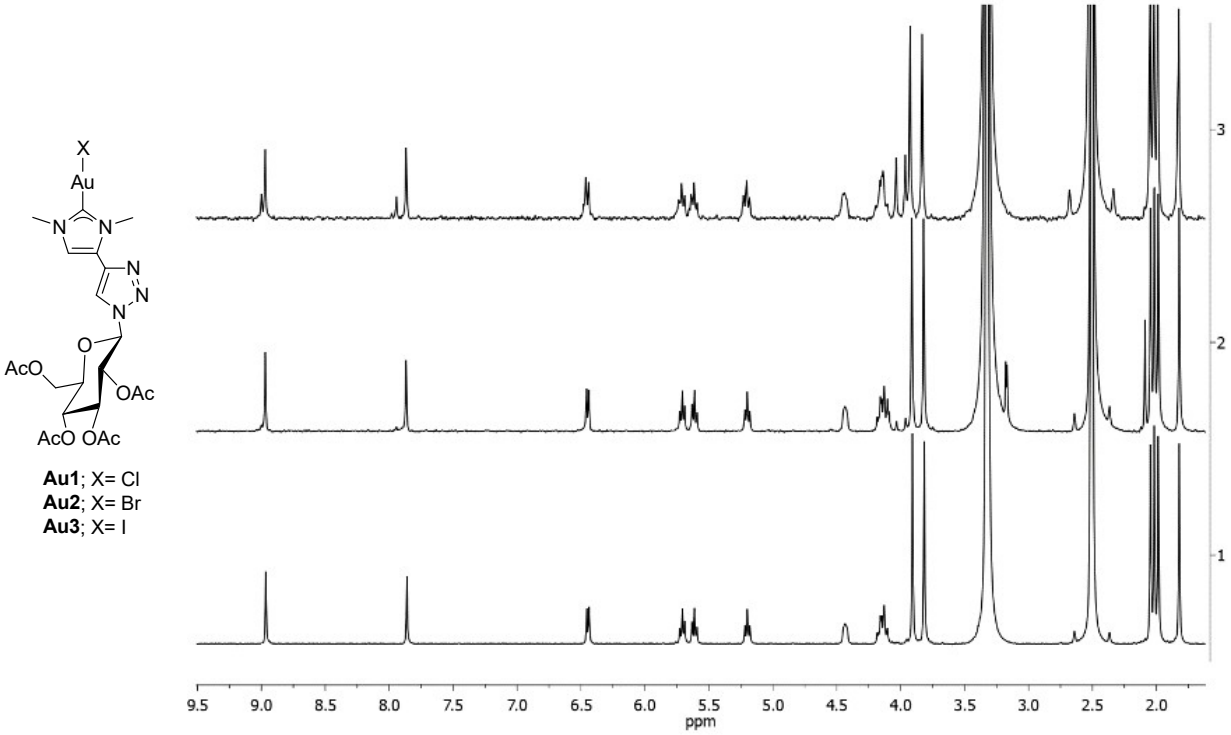


Figure S6. ^{1}H NMR spectra of **Au1** (trace 1), **Au2** (trace 2) and **Au3** (trace 3) in DMSO-d_6

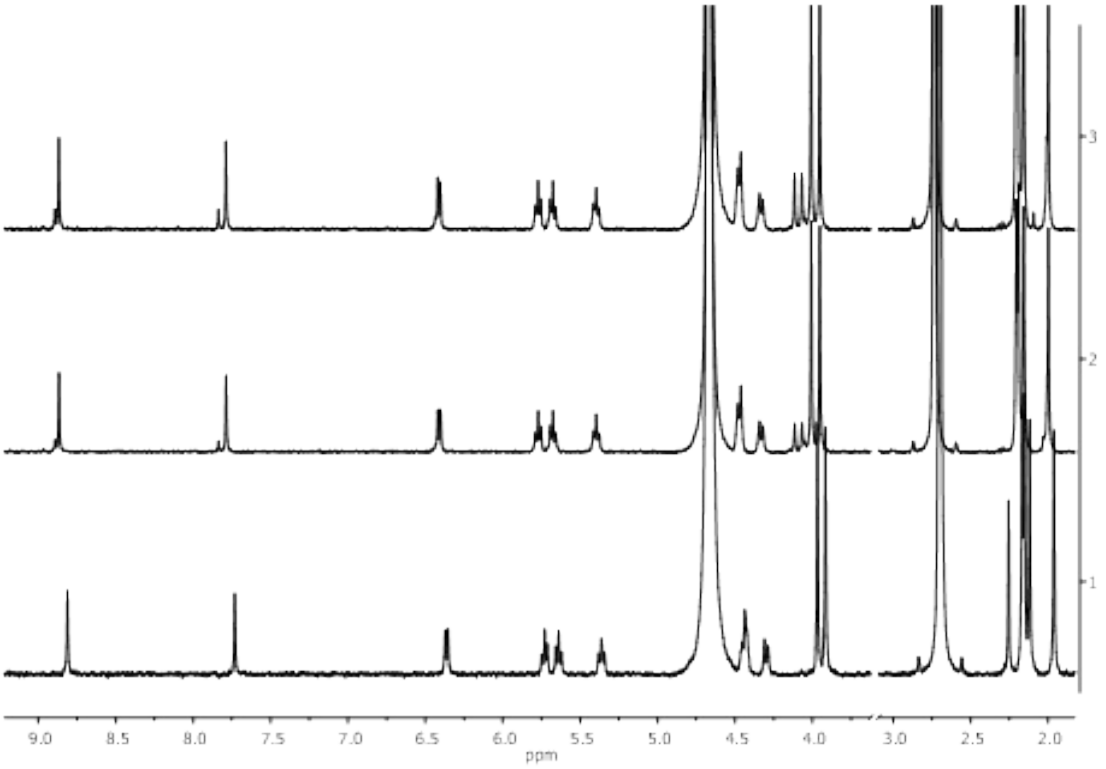


Figure S7. ^{1}H NMR spectra of **Au2** in 50%-50% D_2O-DMSO-d_6 following the dissolution (trace 1), after 4 h (trace 2), and after 24 h (trace 3).

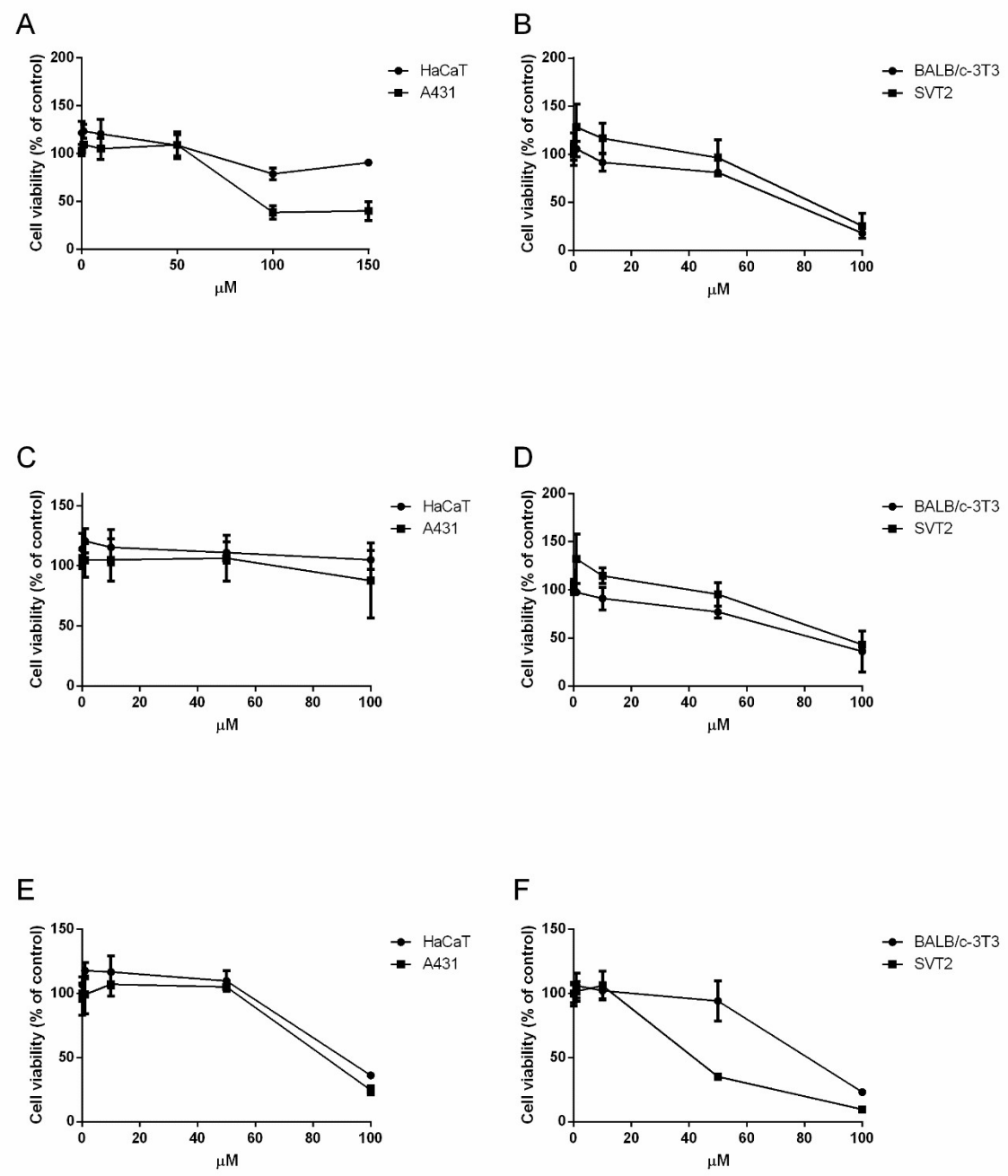


Figure S8. Effect of Au1-Au3 complexes on cell viability. Dose-response curve of cells incubated for 48 h with increasing concentration of Au1-Au3. **A**, **C** and **E**, HaCaT and A431 cells; **B**, **D** and **F,** BALB/c-3T3 and SVT2 cells. **A**: HaCaT and A431 cells were incubated with increasing amount of Au1 (0.1-150 μM); **B:** BALB/c-3T3 and SVT2 cells were incubated with increasing amount of Au1 (0.1-100 μM); **C**, **D:** cells were incubated with increasing amount of Au2 (0.1-100 μM); **E**, **F:** cells were incubated with increasing amount of Au3 (0.1-100 μM). Cell viability was assessed by the MTT assay and reported as a function of concentration. Data shown are means ± S.D. of three independent experiments.

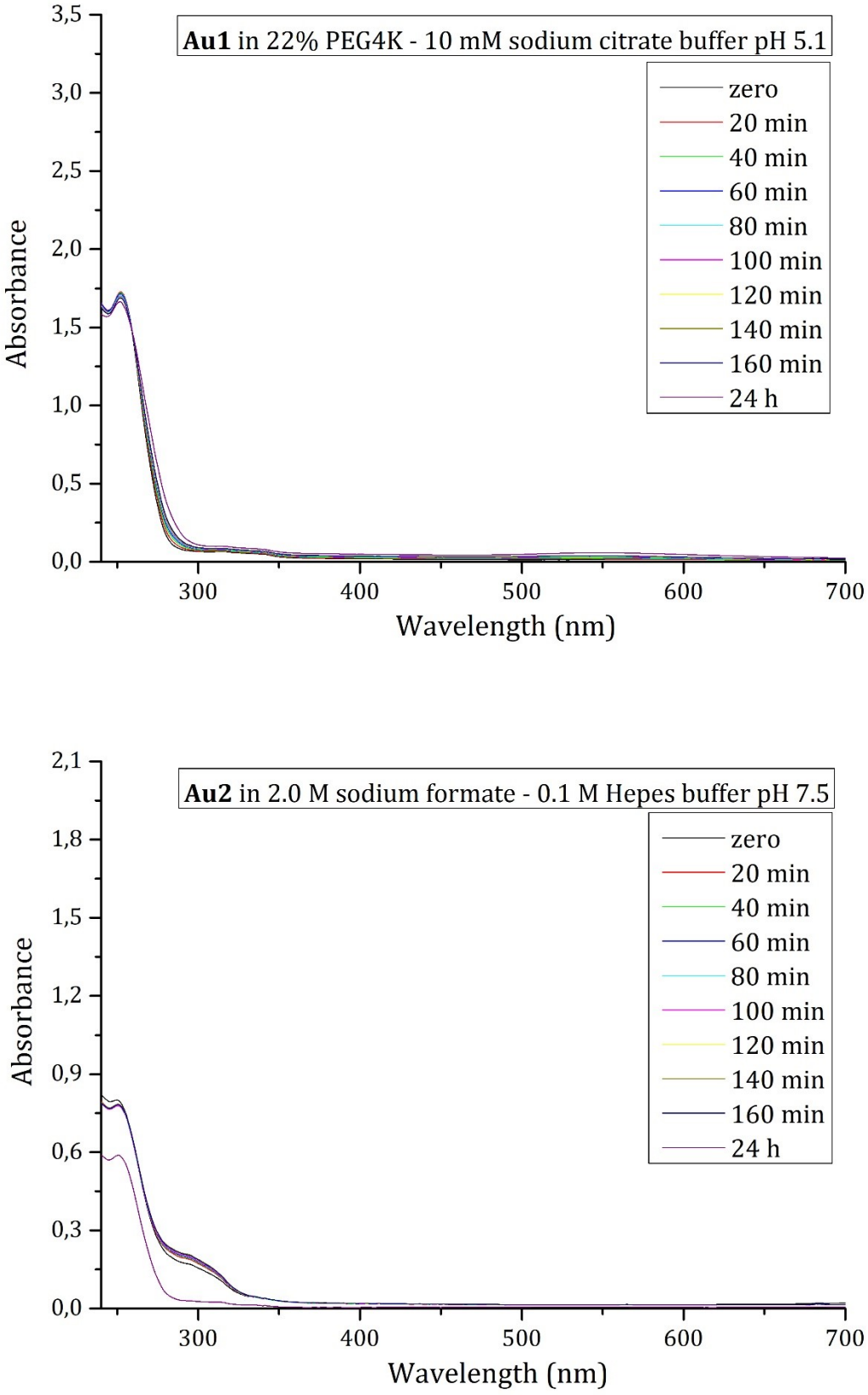


Figure S9. UV-vis spectra of (A) **Au1** in 22% PEG4K and 10 mM sodium citrate buffer pH 5.1 as function of time and (B) **Au2** in 2.0 M sodium formate and 10 mM Hepes buffer pH 7.5 as function of time. Compound concentration: 100 μM.

Table S5. Data collection and refinement statistics for gold-proteins adducts.

	HEWL crystals exposed to Au2	RNase A crystals exposed to Au1
Data collection statistics		
Space group	P 4_3 2_1 2	C2
a (Å)	77.00	100.72
b (Å)	77.00	32.72
c (Å)	37.27	72.71
α/β/γ (°)	90.000/90.000/90.000	90.000/90.261/90.000
Resolution range (Å)	34.43-1.10 (1.11-1.10)	50.36-1.42 (1.45-1.42)
Observations	806262 (5116)	276569 (13784)
Unique reflections	44982 (1372)	43181 (2063)
Completeness (%)	95.6 (58.8)	96.1 (94.2)
Redundancy	17.9 (3.7)	6.4 (6.7)
†R_{merge} (%)	0.060 (0.551)	0.073 (0.599)
Average I/σ(I)	28.4 (2.4)	12.9 (3.6)
$CC_{1/2}$	0.999 (0.635)	0.998 (0.807)
Anom. completeness (%)	94.7 (51.6)	96.4 (95.0)
Anom. Multiplicity	9.5 (2.1)	3.3 (3.4)
Refinement statistics		
Resolution range (Å)	34.43-1.10	50.36-1.42
N. of reflections	42171	41335
N. of reflections (test set)	2238	2132
R-factor/R-free (%)	0.132/0.170	0.189/0.219
N. of atoms	1370	2259
Average B-factors (Å^2)		
All atoms	16.62	23.39
Au atoms	23.53/48.66/54.16	51.03/65.77
Au occupancy	0.20/0.20/0.20	0.30/0.30
R.m.s. deviations		
Bond lengths (Å)	0.037	0.013
Bond angles (°)	2.71	1.79
Ramachandran statistics (Coot analysis) N. of residues in Preferred/Allowed/Disallowed regions	85 (98.84%)/1 (1.16%)/0 (0.0%)	201 (94.81%)/7 (3.30%)/4 (1.89%)

†Rmerge= $\Sigma h \Sigma i \, |I(h,i)-\langle I(h)\rangle| / \Sigma h \Sigma i \, I(h,i)$, where I(h,i) is the intensity of the i^{th} measurement of reflection h and $\langle I(h)\rangle$ is the mean value of the intensity of reflection h.

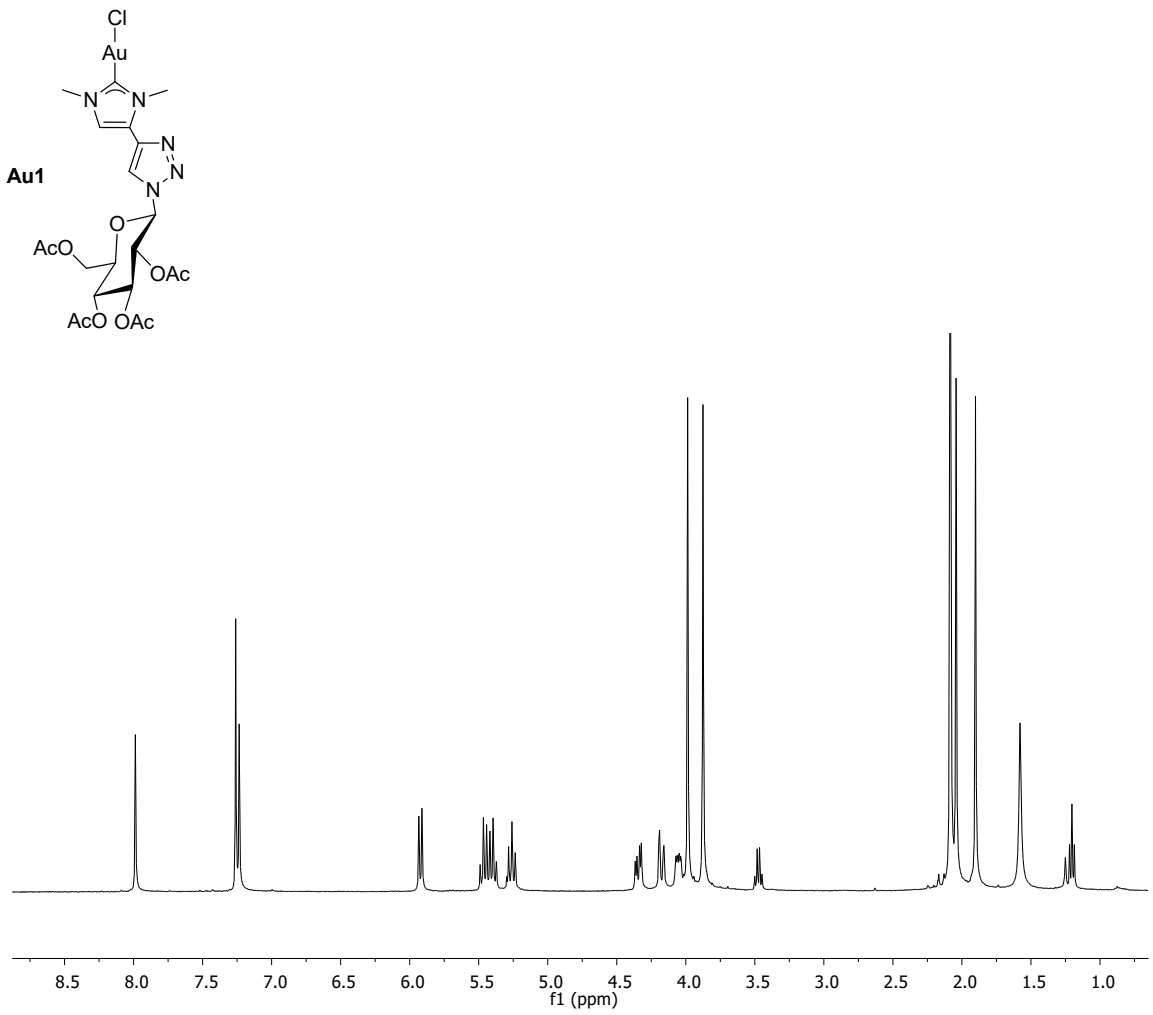


Figure S10. ^{1}H NMR spectrum of **Au1** in $CDCl_3$ at 400 MHz.

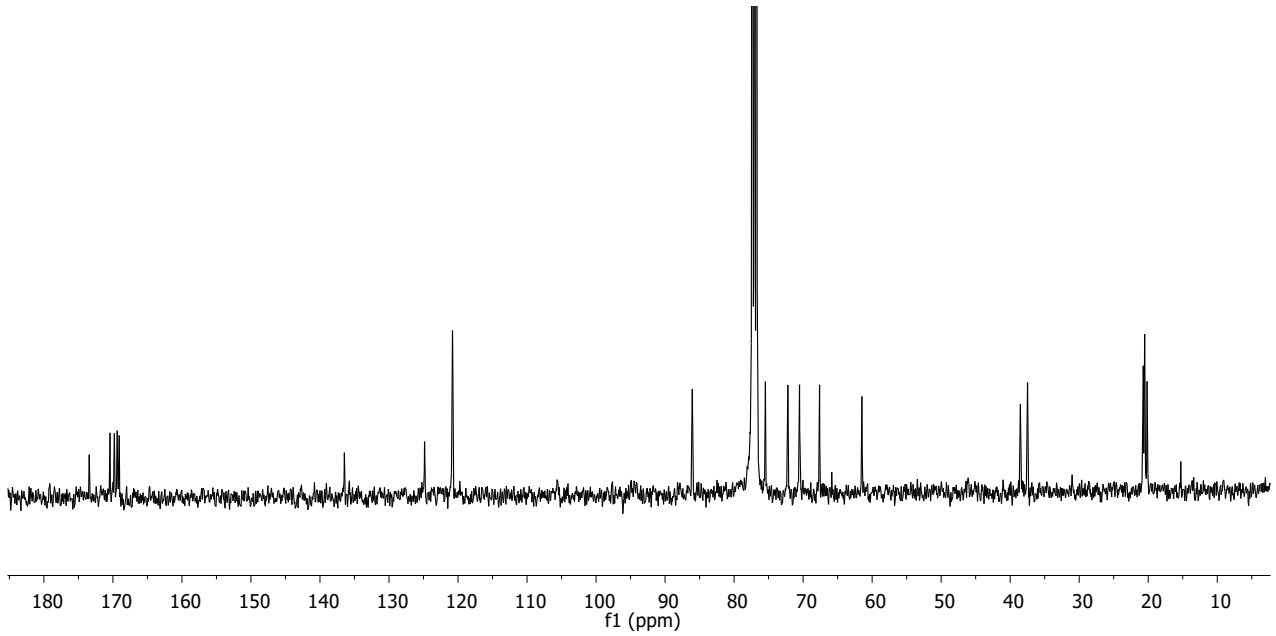


Figure S11. ^{13}C NMR spectrum of **Au1** in $CDCl_3$ at 100 MHz.

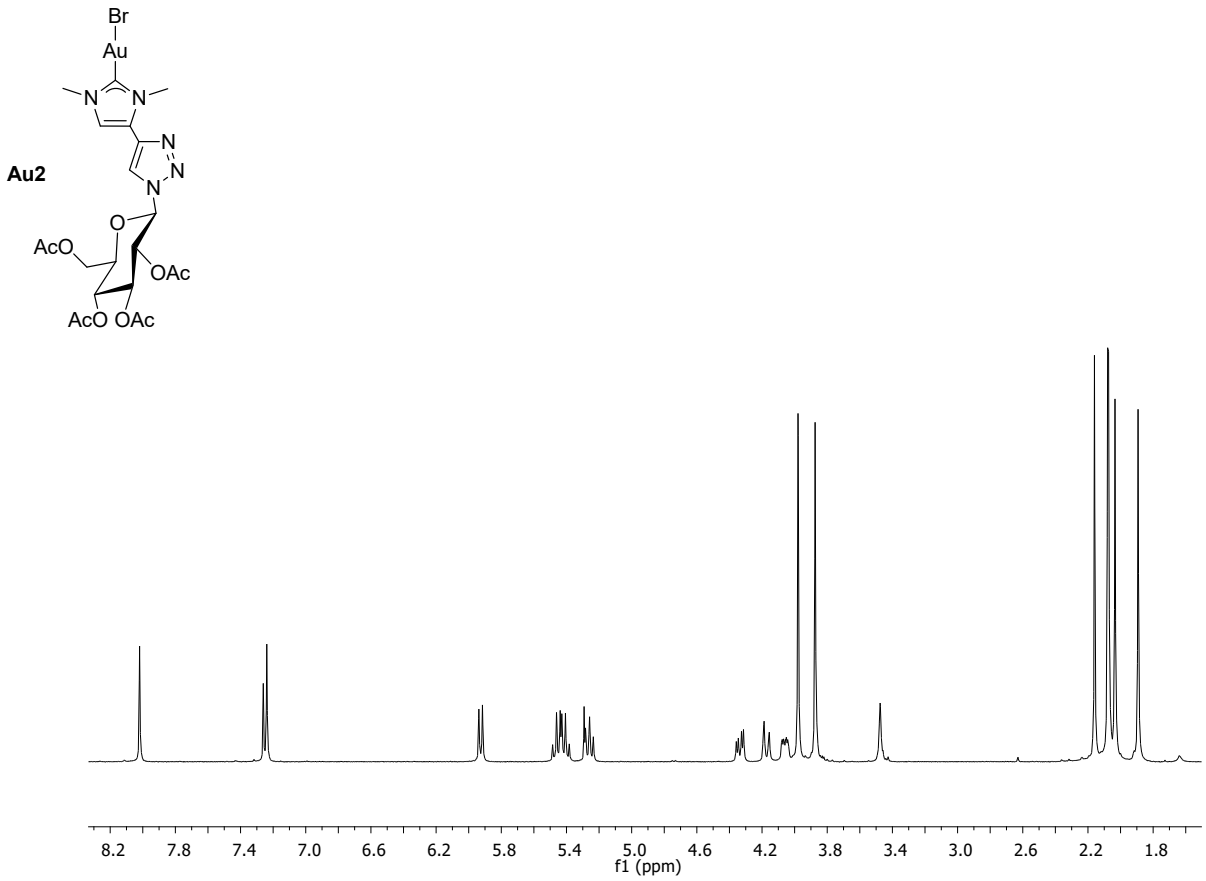


Figure S12. ^{1}H NMR spectrum of **Au2** in $CDCl_3$ at 400 MHz.

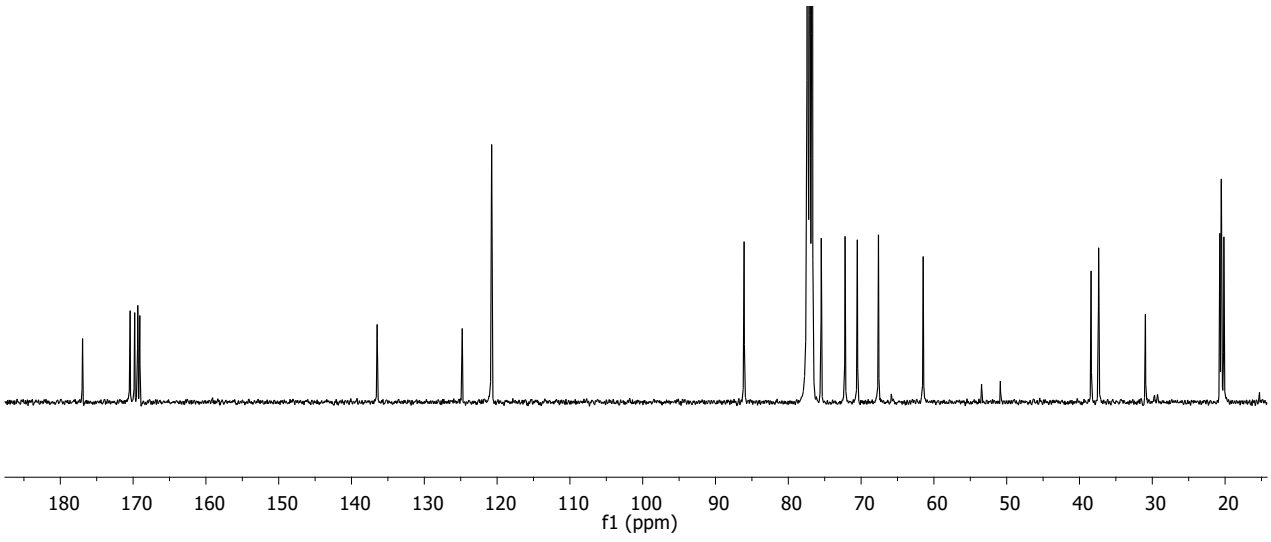


Figure S13. ^{13}C NMR spectrum of **Au2** in $CDCl_3$ at 100 MHz.

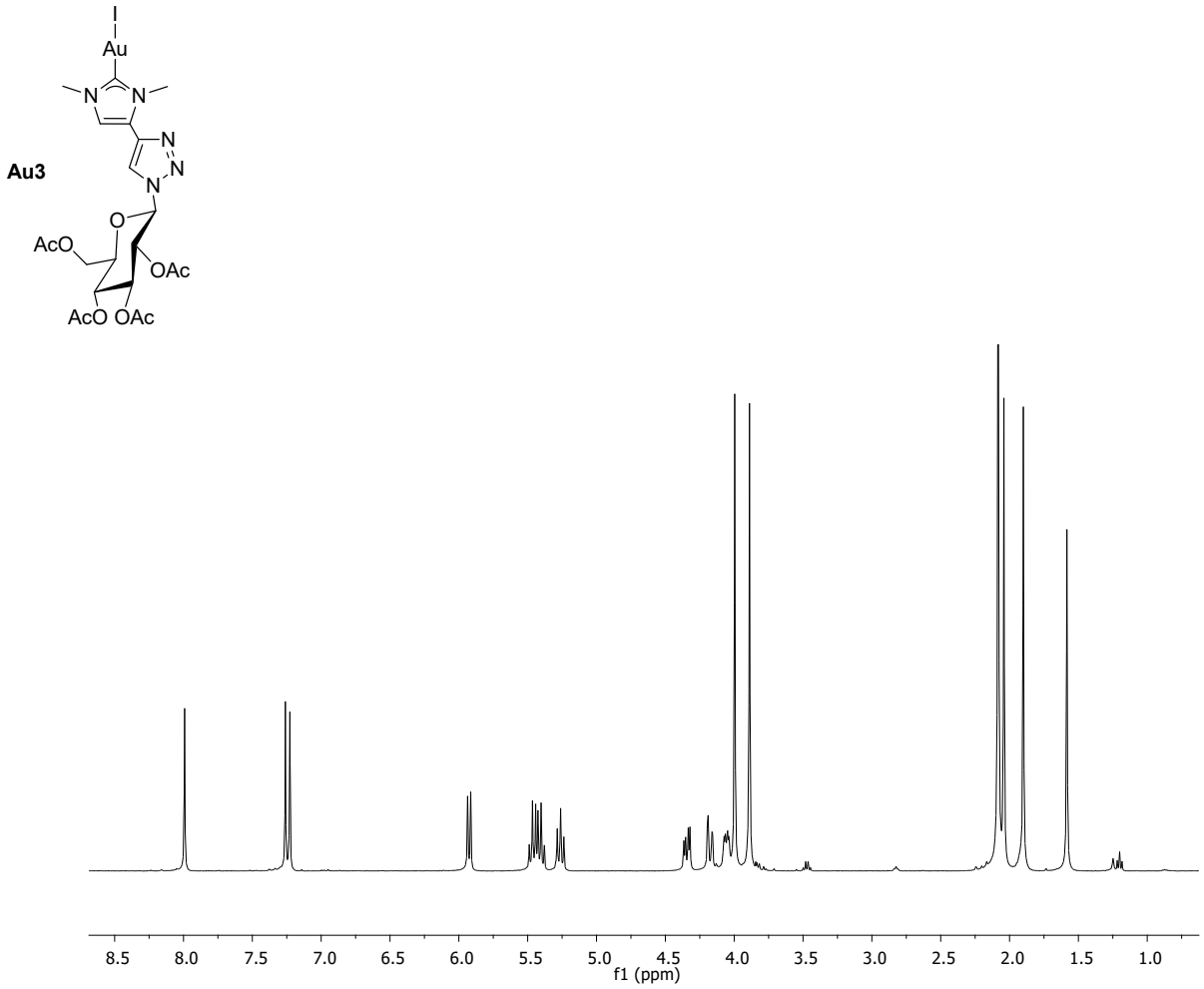


Figure S14. ^{1}H NMR spectrum of **Au3** in $CDCl_3$ at 400 MHz.

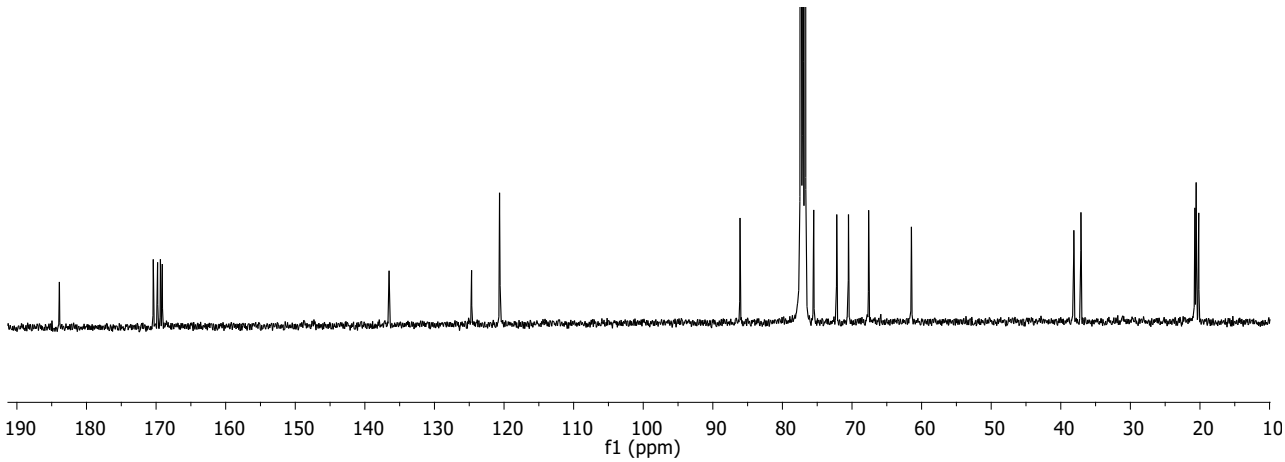


Figure S15. ^{13}C NMR spectrum of **Au3** in $CDCl_3$ at 100 MHz.