Supplementary Information

Designing new Iridium(III) arene complexes of naphthoquinone derivatives as anticancer agents: A structure-activity relationship study

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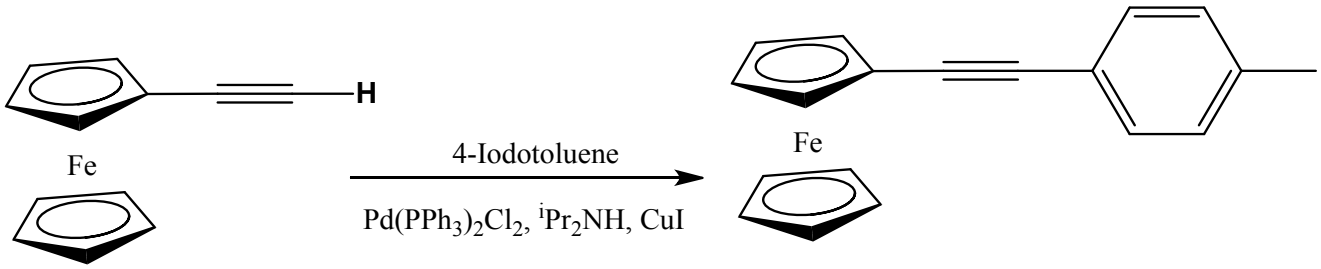
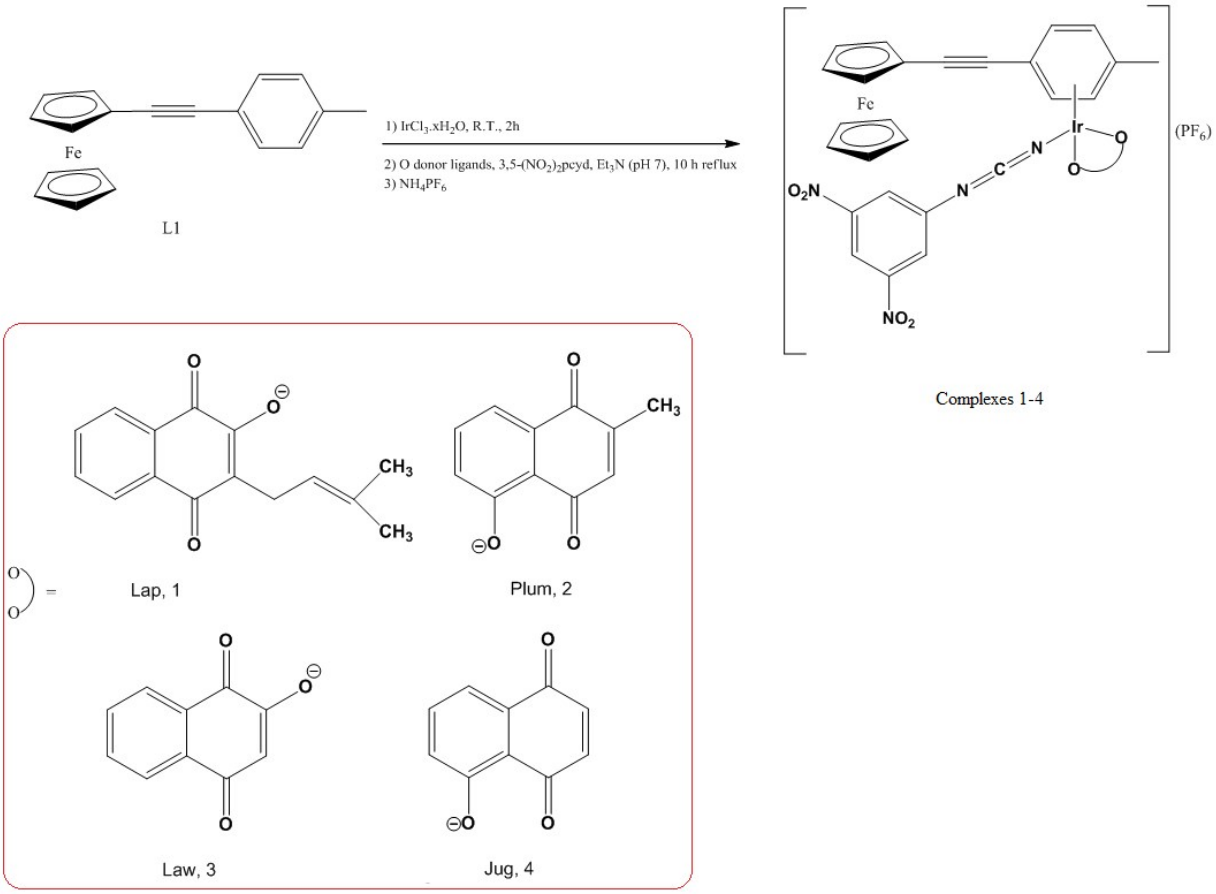


L1

Scheme S1. Synthesis of Ligand L1



Scheme S2. Synthesis of complexes **1**-**4**.

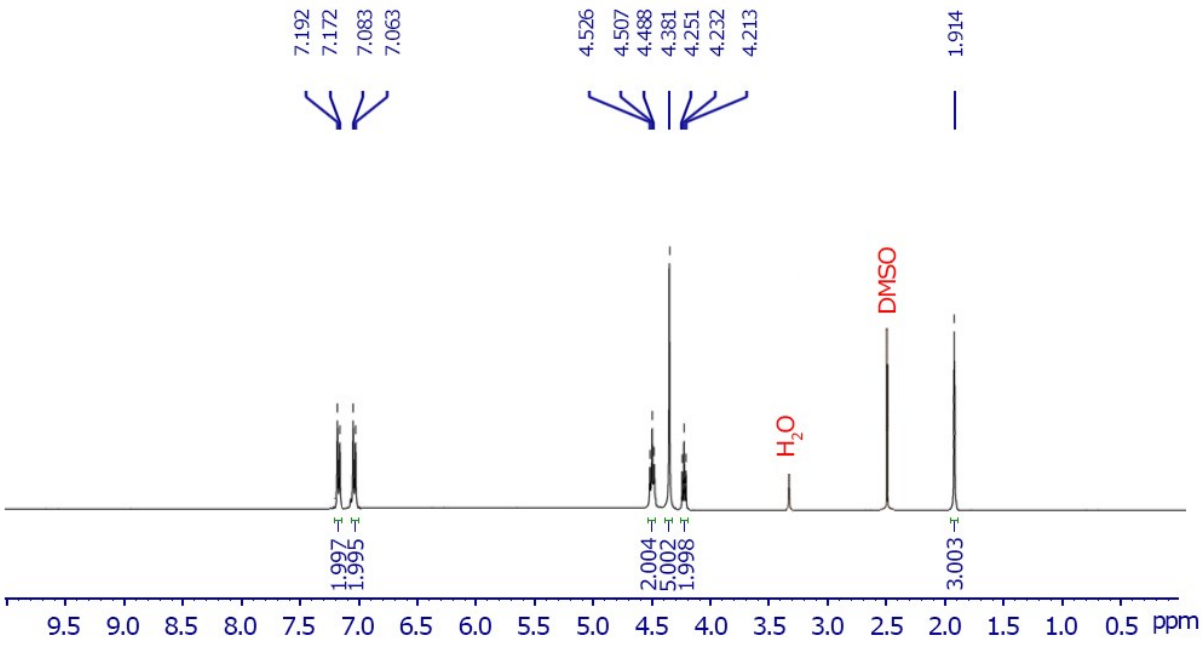


Fig. S1. ^{1}H NMR spectrum of ligand L1.

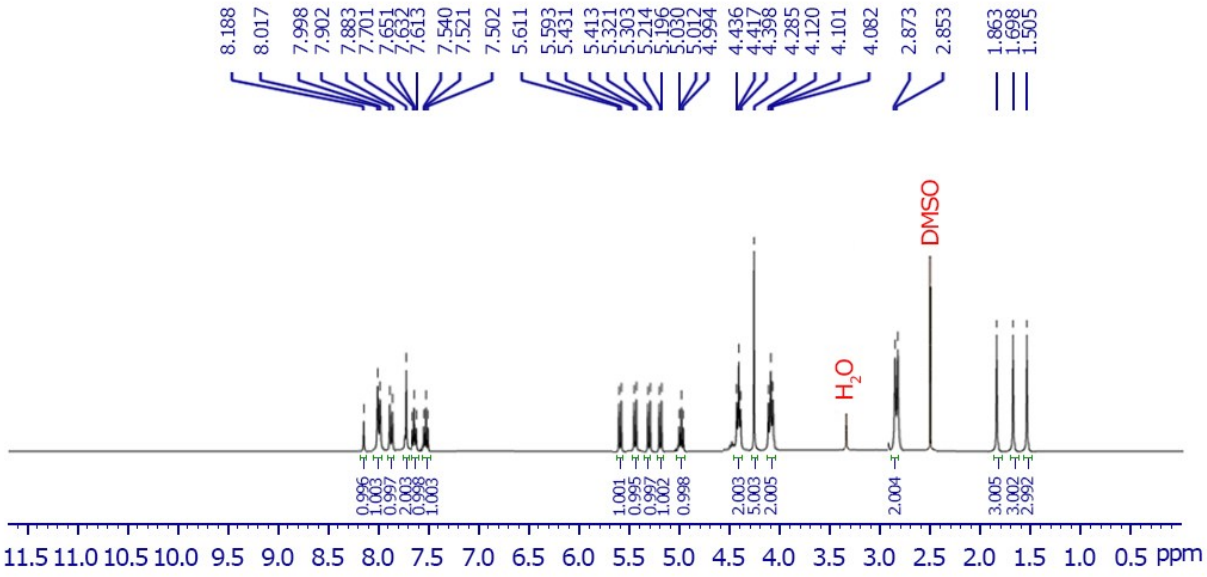


Fig. S2. ^{1}H NMR spectrum of Complex **1**.

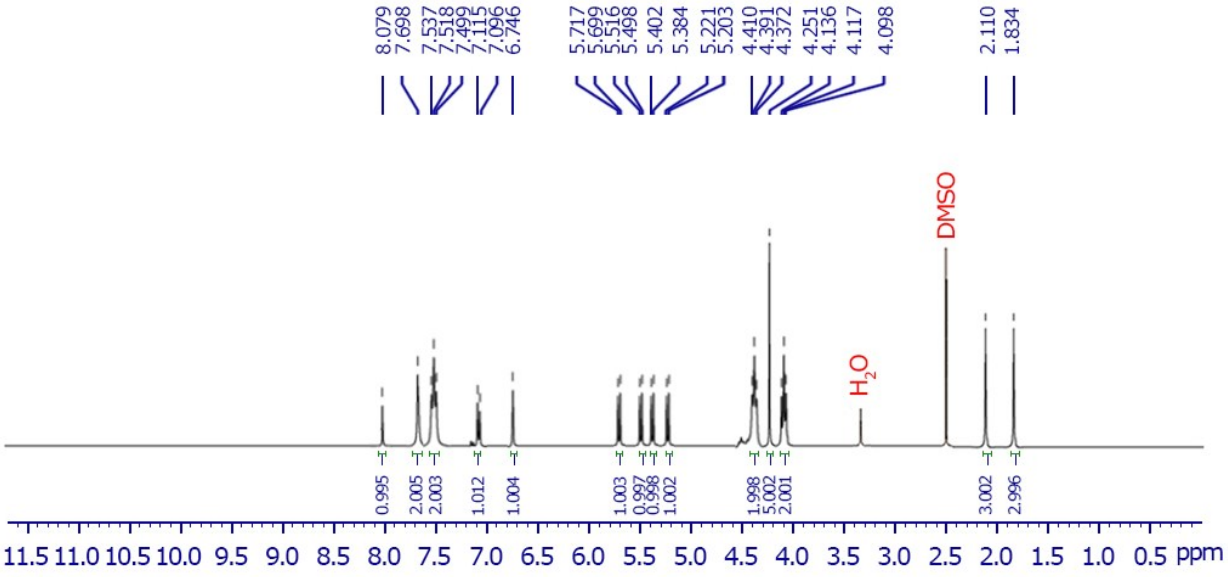


Fig. S3. ^{1}H NMR spectrum of Complex **2**.

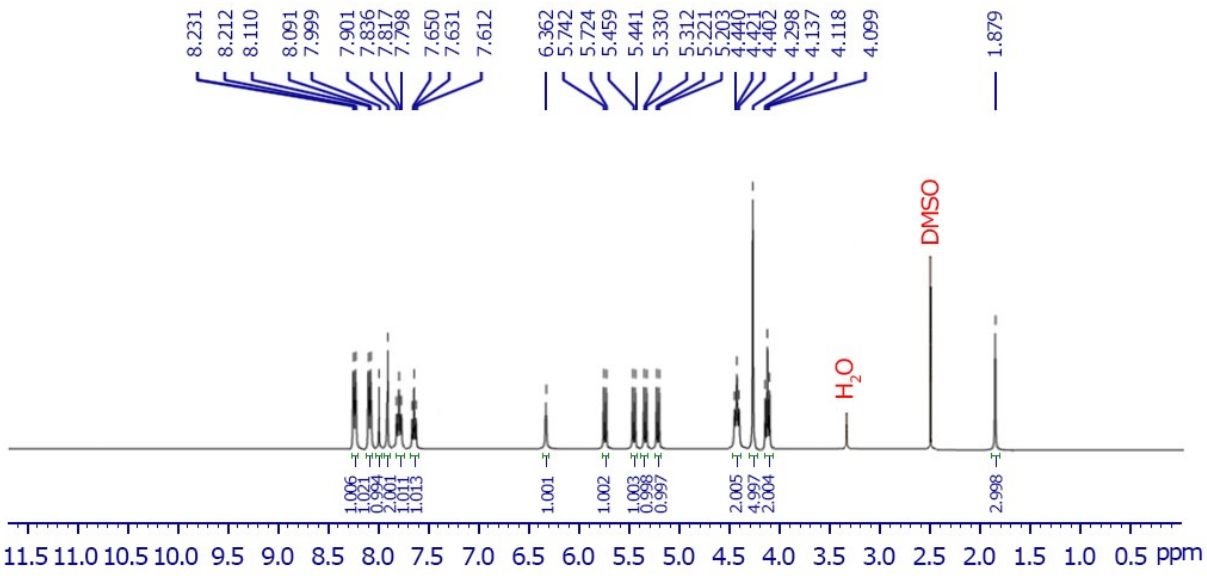


Fig. S4. ^{1}H NMR spectrum of Complex **3**.

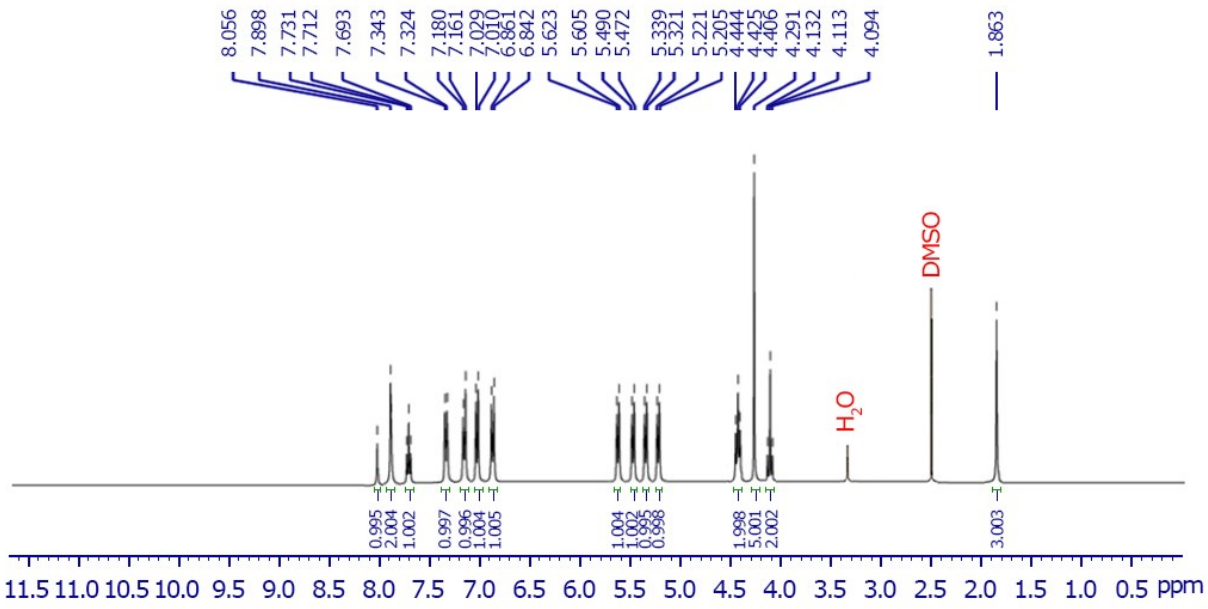


Fig. S5. ^{1}H NMR spectrum of Complex **4**.

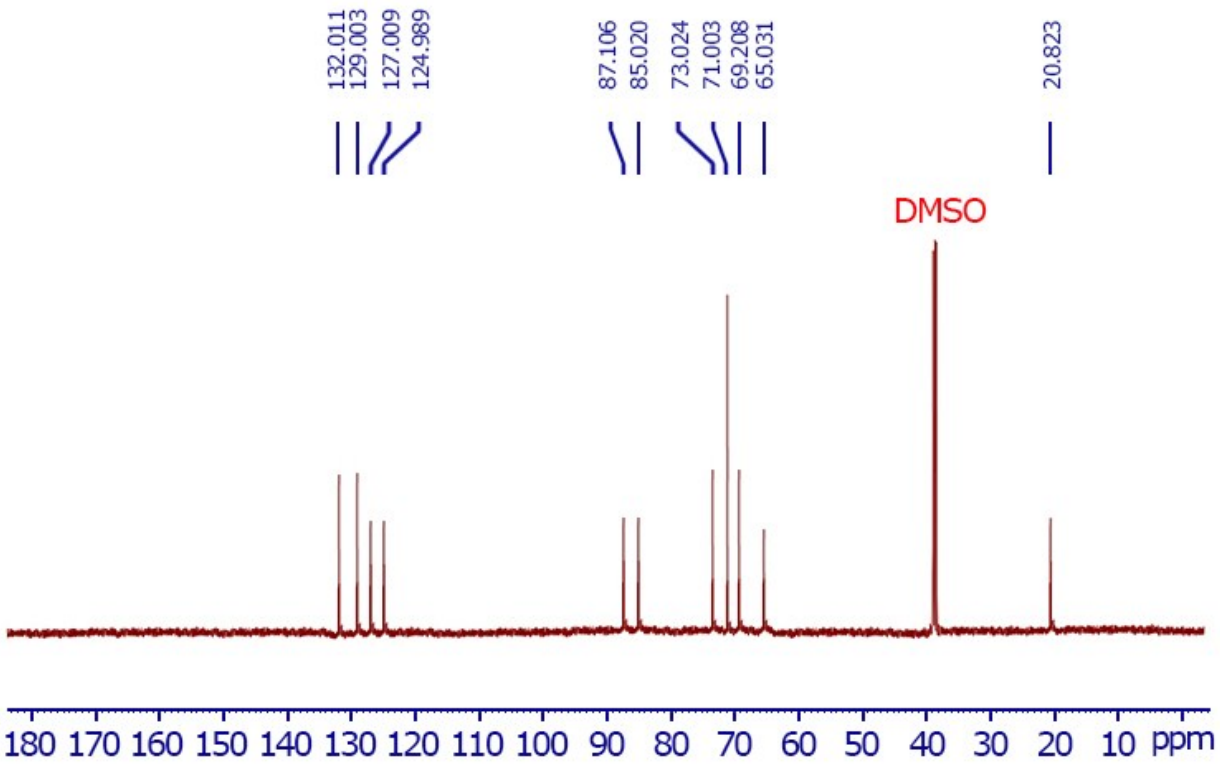


Fig. S6. ^{13}C NMR spectrum of ligand L1.

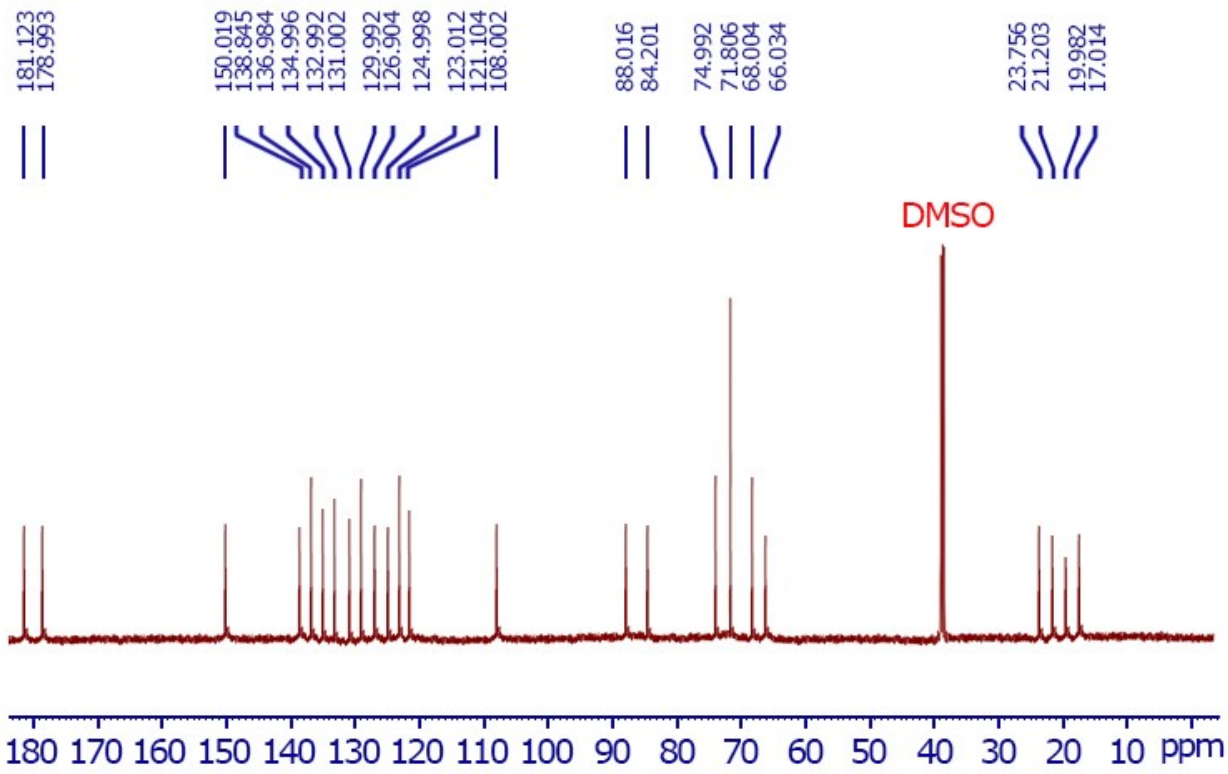


Fig. S7. ^{13}C NMR spectrum of complex **1**.

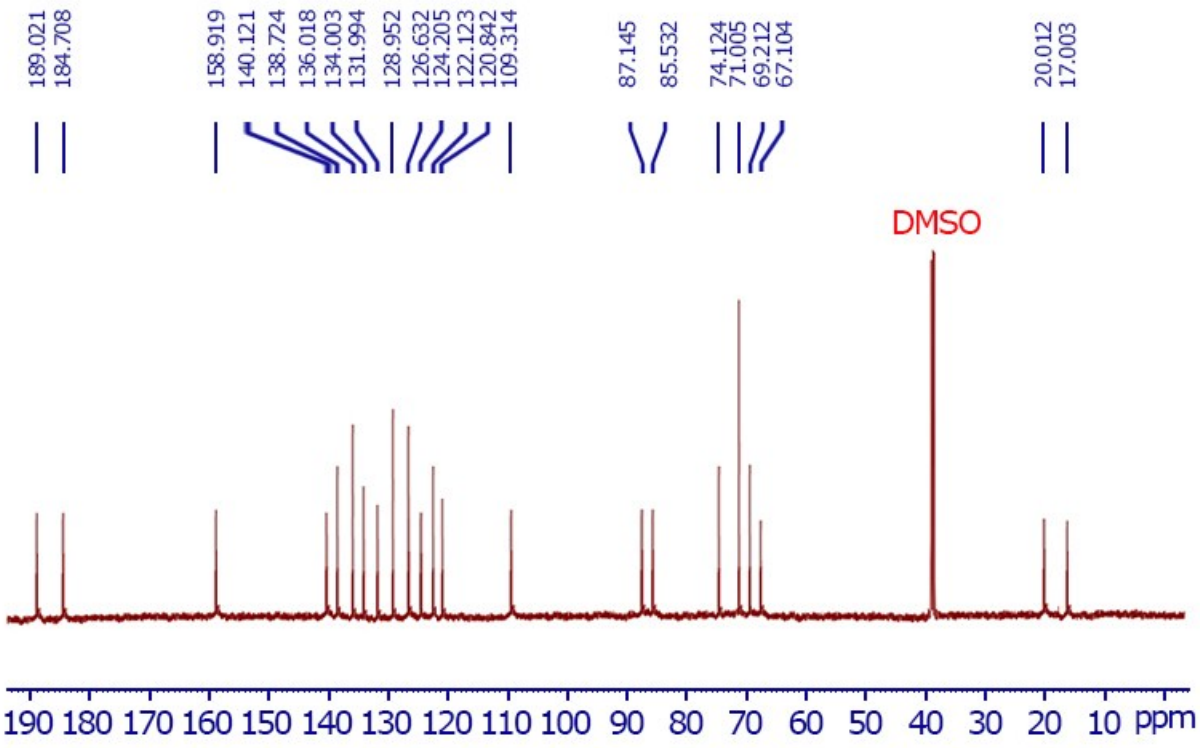


Fig. S8. ^{13}C NMR spectrum of complex **2**.

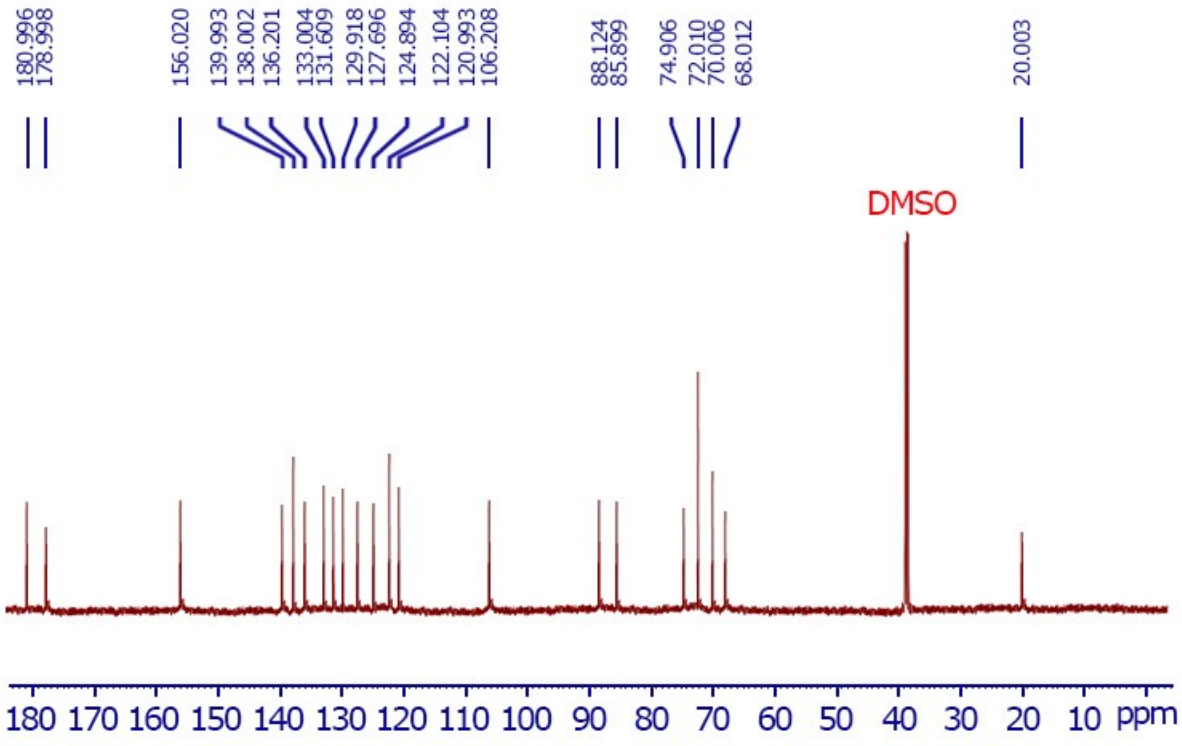


Fig. S9. ^{13}C NMR spectrum of complex **3**.

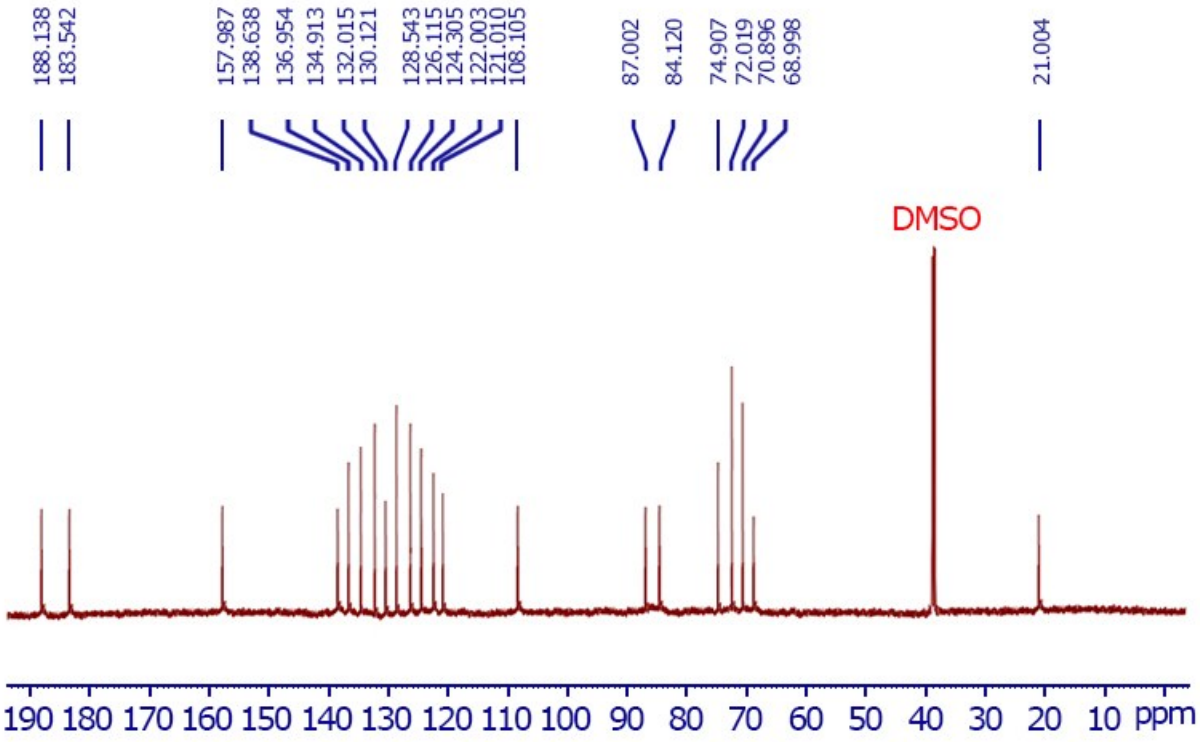


Fig. S10. ^{13}C NMR spectrum of complex **4**.

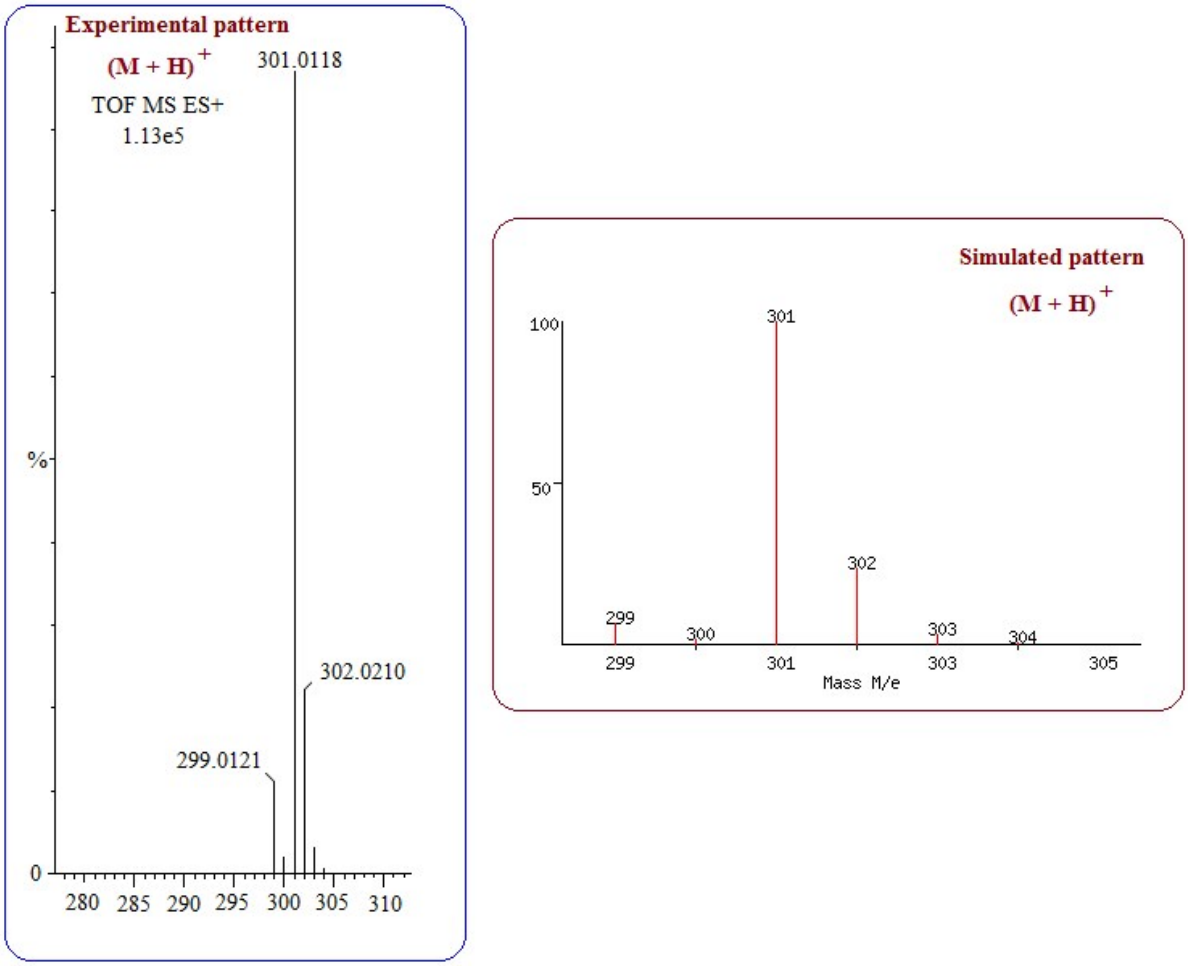


Fig. S11. TOF MS spectrum of ligand L1.

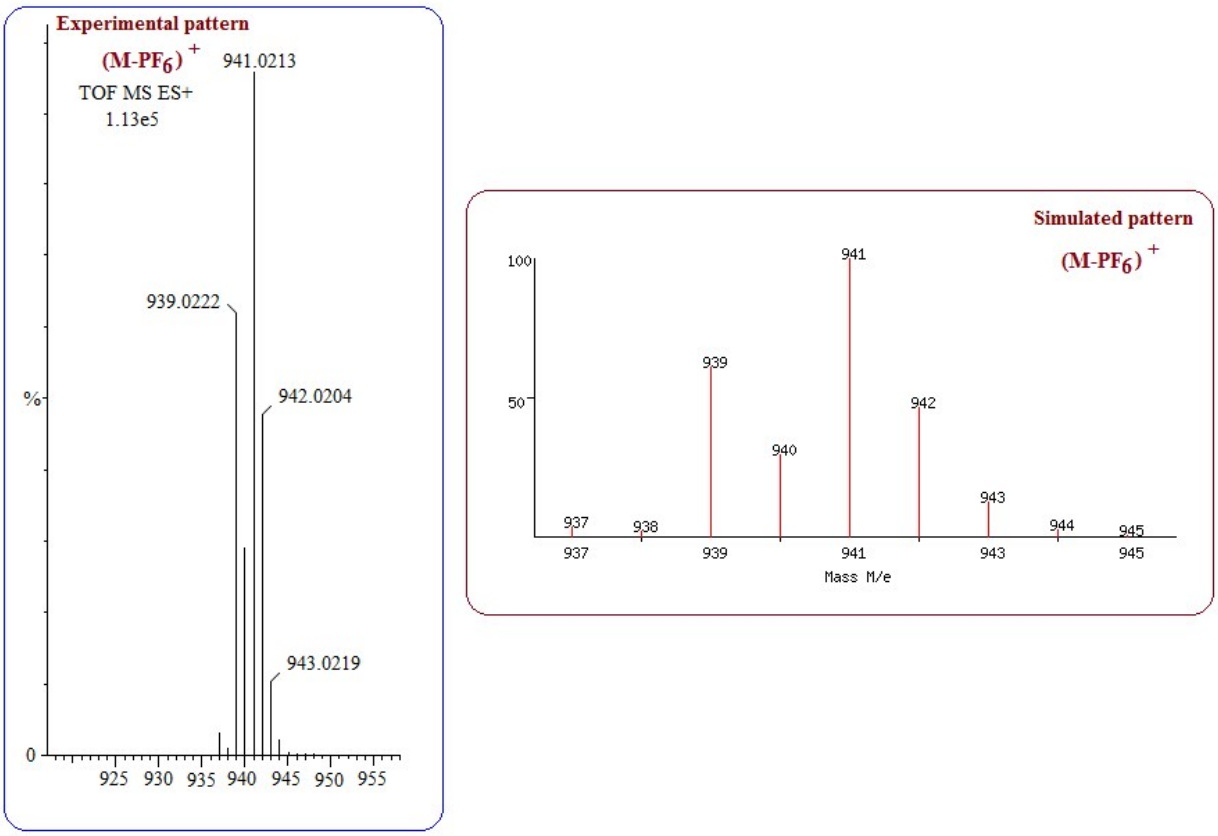


Fig. S12. TOF MS spectrum of complex **1**.

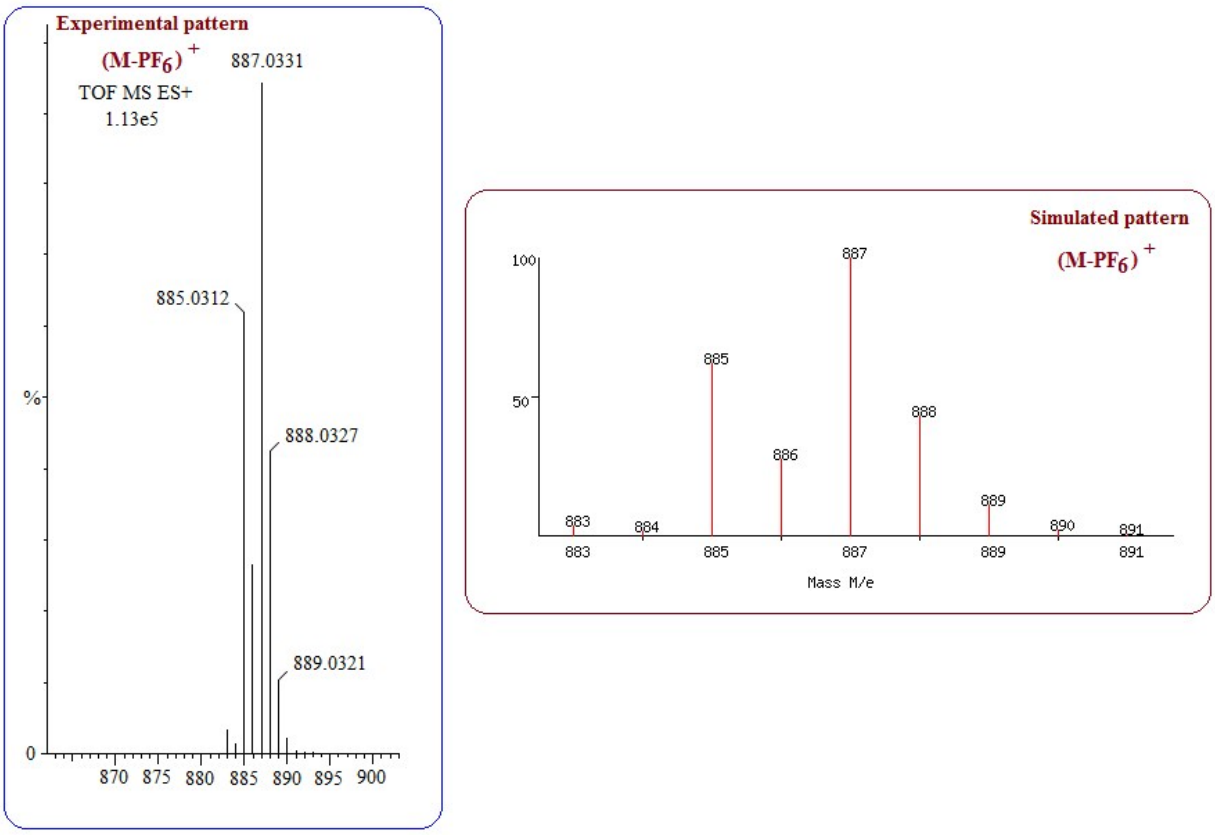


Fig. S13. TOF MS spectrum of complex **2**.

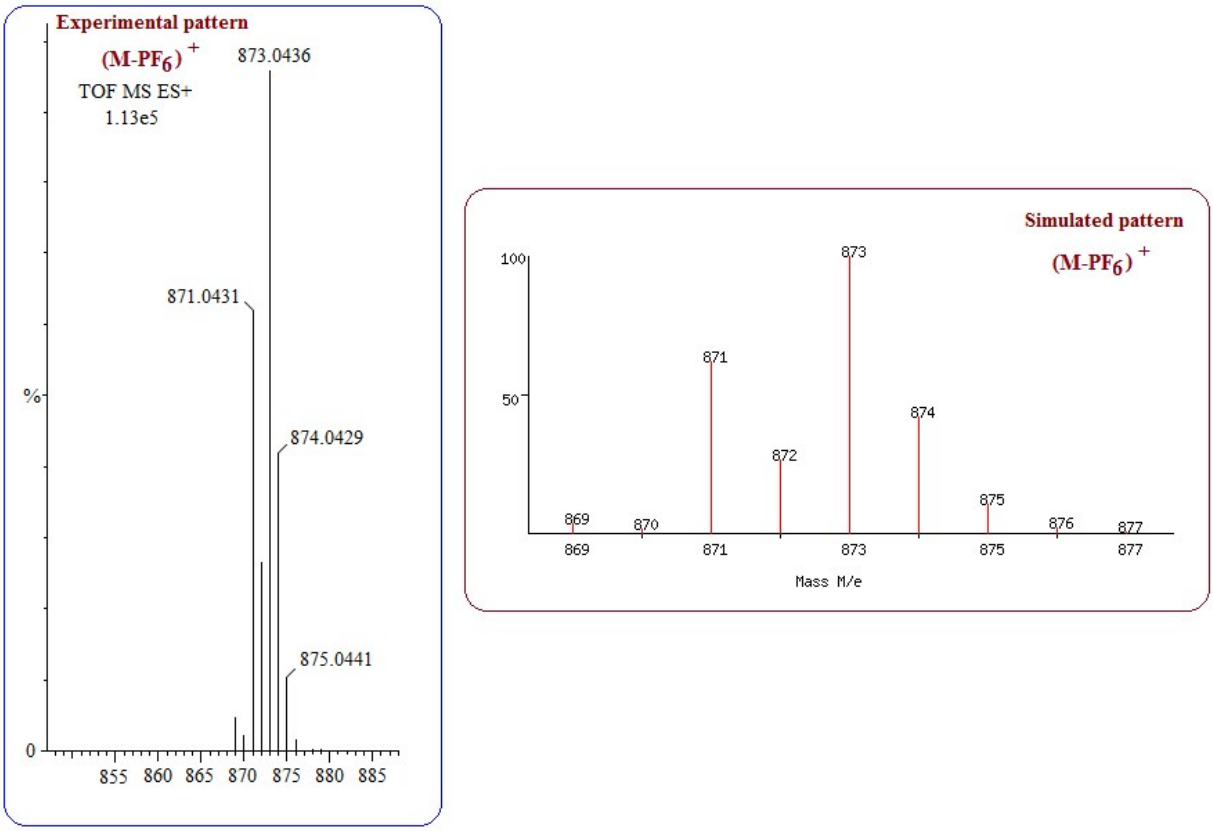


Fig. S14. TOF MS spectrum of complex **3**.

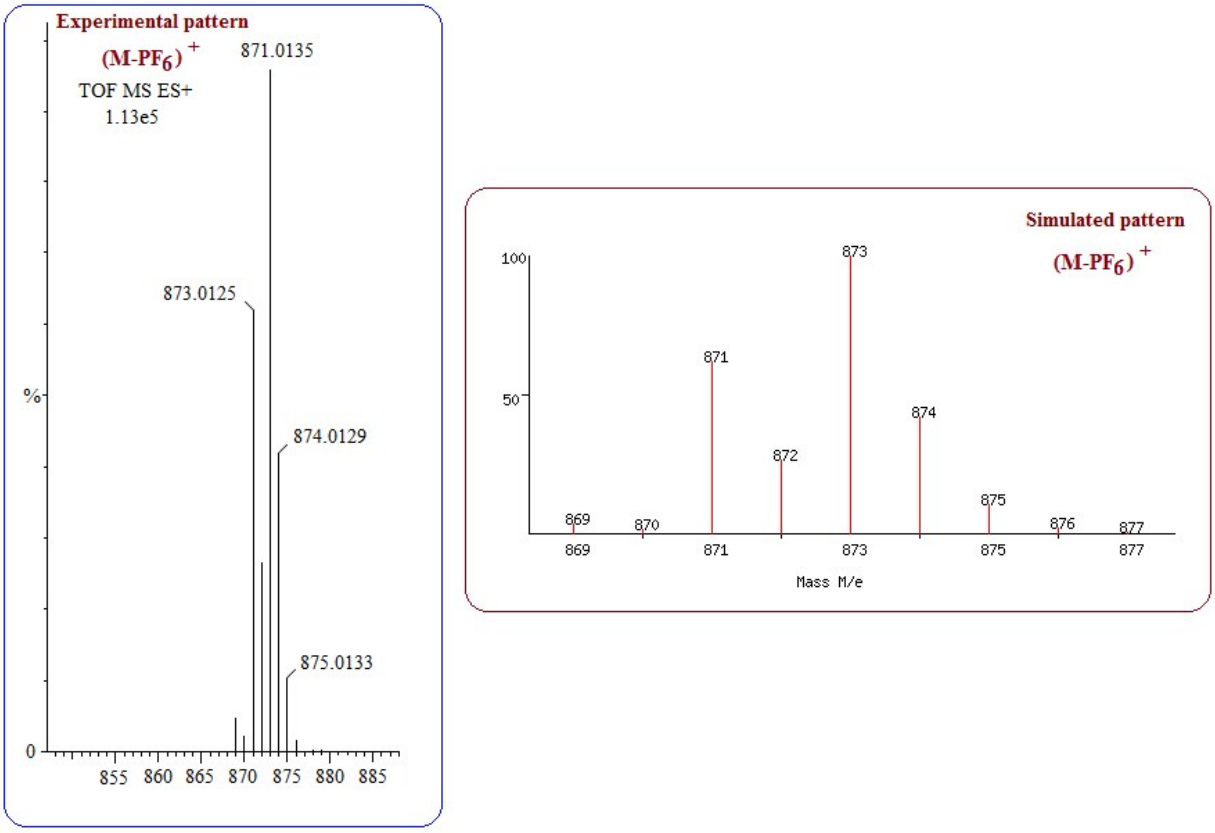


Fig. S15. TOF MS spectrum of complex **4**.

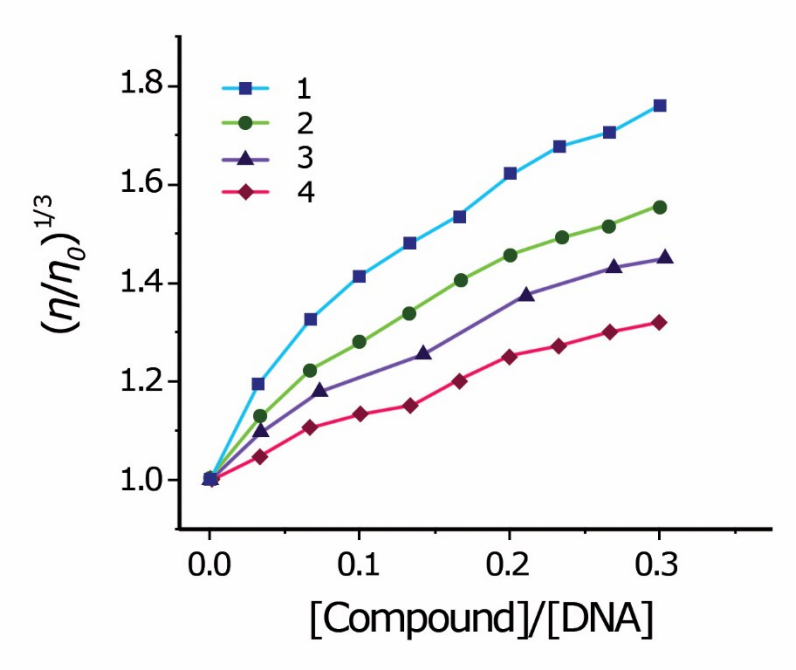


Fig. S16. Effect of increasing amounts of complexes **1-4** on the relative viscosity of CT DNA at 37.0 ± 0.1 ºC. [DNA] = 5 μM and [complexes] = 0-5 μM. (inset: plot of [DNA]/(ε_a - ε_b) vs. [DNA]).

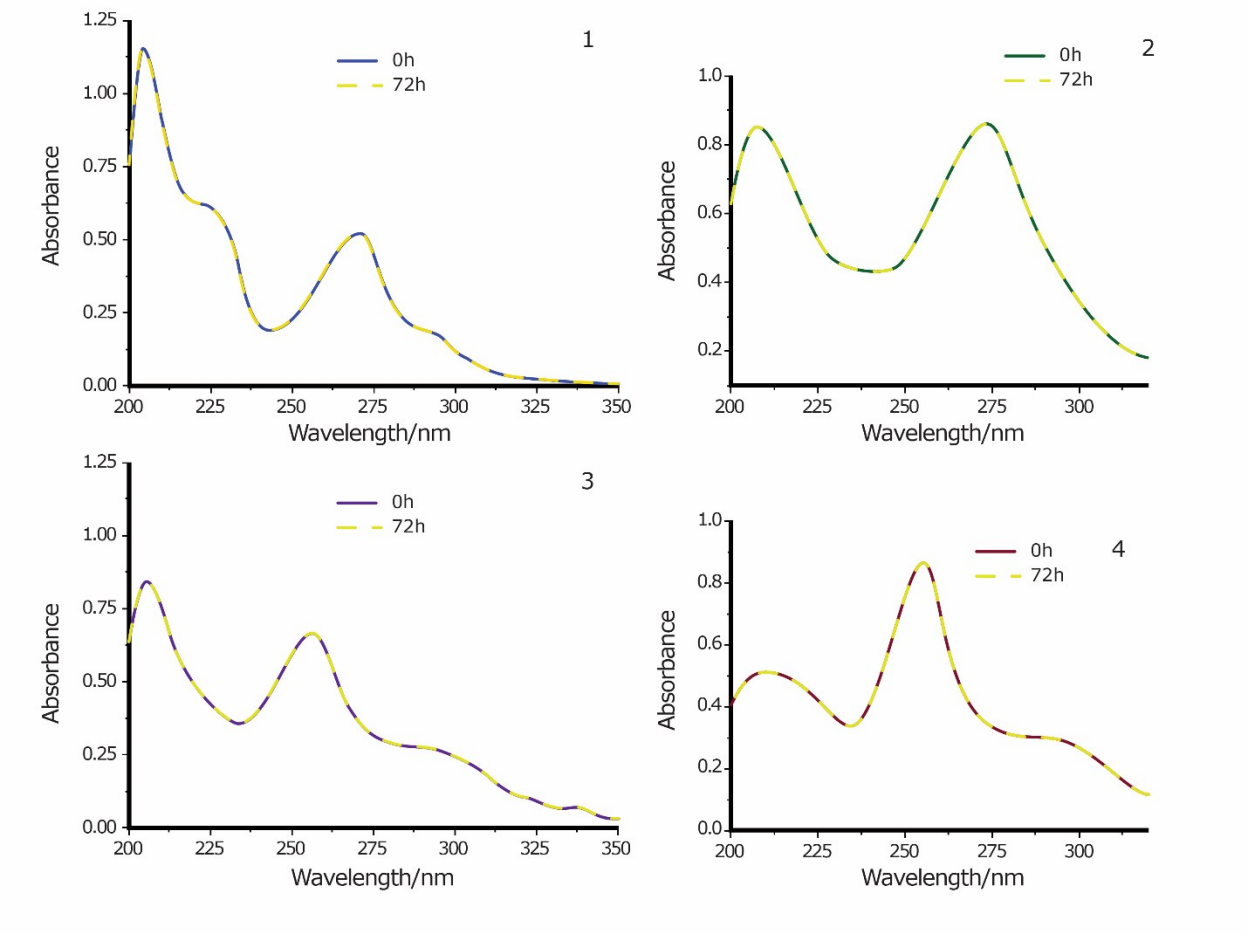


Fig. S17. UV–vis absorption spectra of complex **1-4** in Tris buffer at pH 7.2 and 37 ºC (physiological conditions) and at different time intervals (0h and 72h).

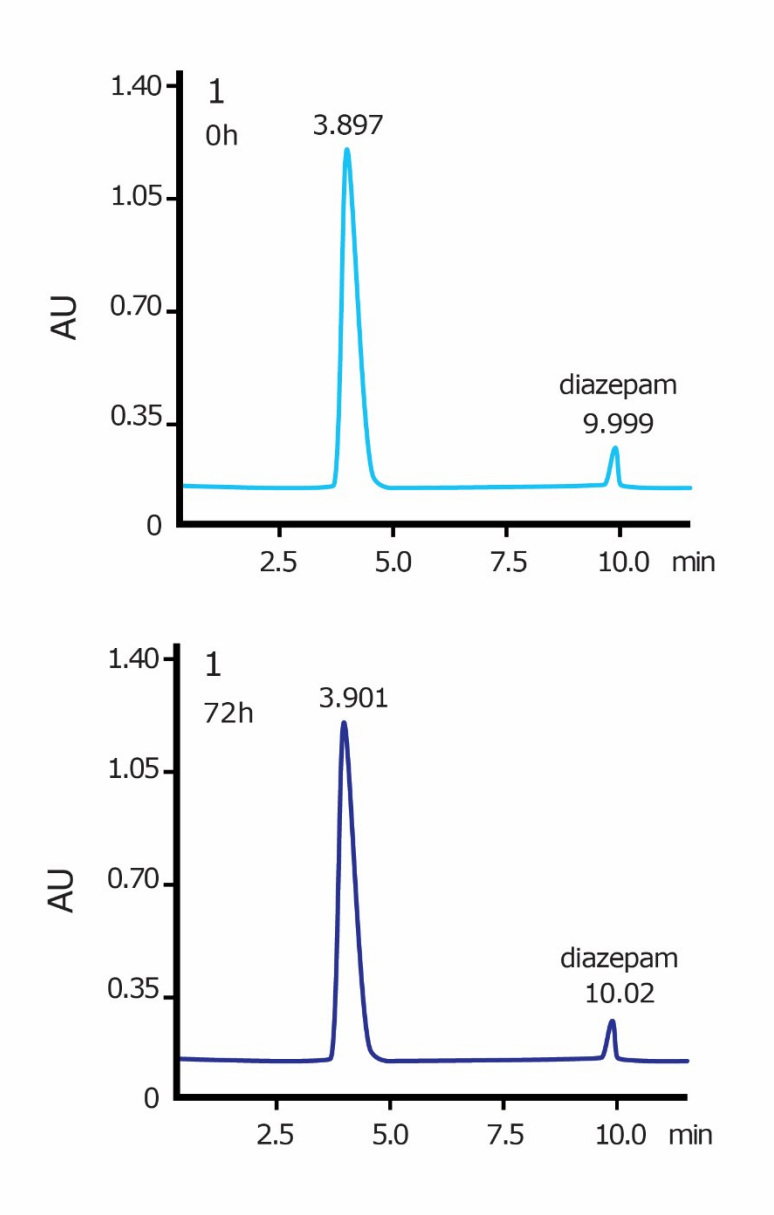


Fig. S18. LC-UV traces of plasma incubated with complex **1** (20 μM, 37 ˚C) at t = 0 and 72 h. (Diazepam was used as internal standard).

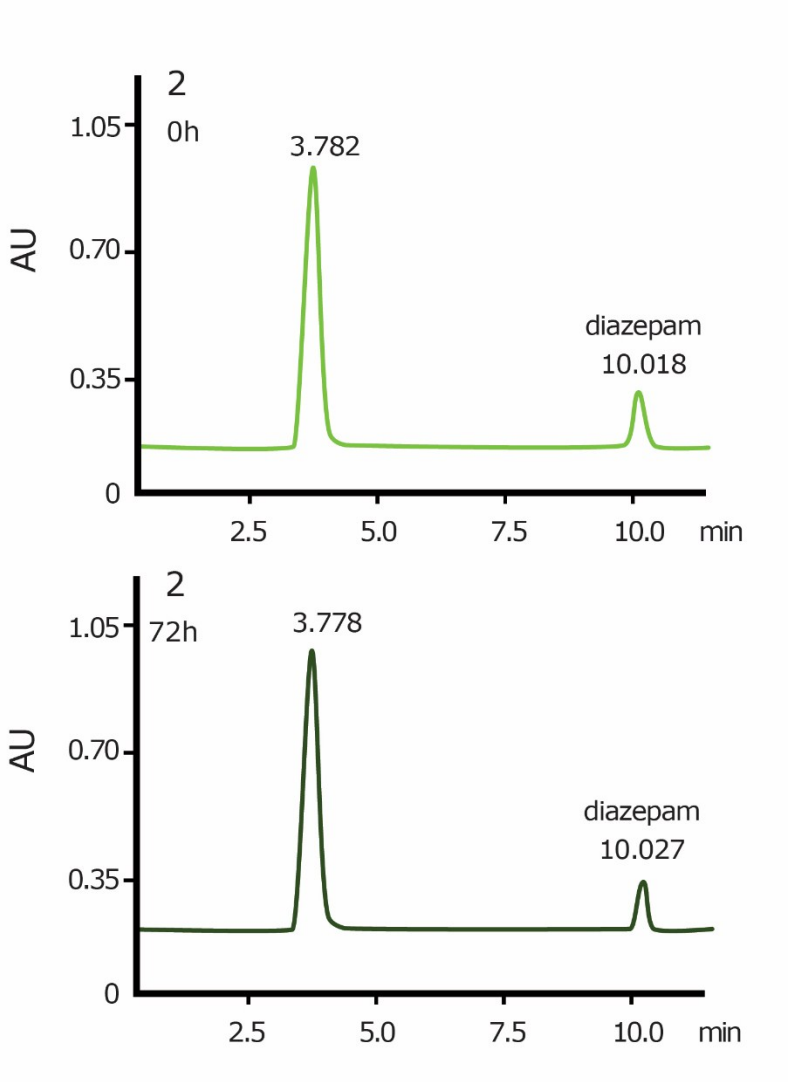


Fig. S19. LC-UV traces of plasma incubated with complex **2** (20 μM, 37 ˚C) at t = 0 and 72 h. (Diazepam was used as internal standard).

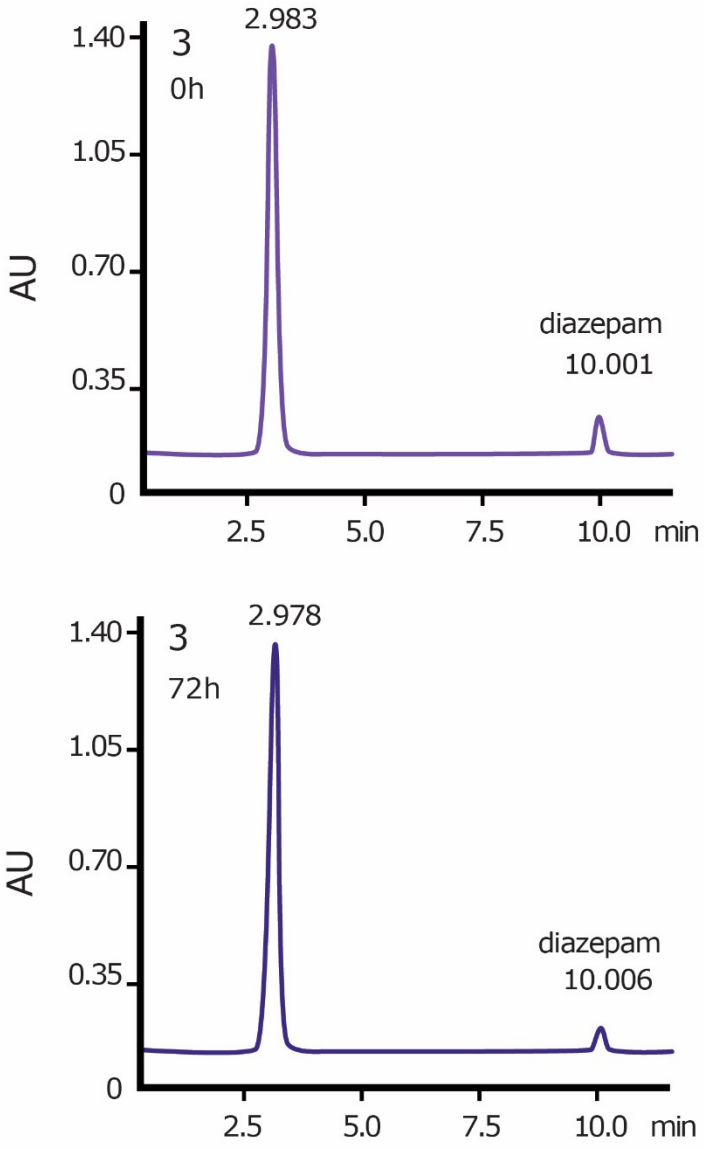


Fig. S20. LC-UV traces of plasma incubated with complex **3** (20 μM, 37 ˚C) at t = 0 and 72 h. (Diazepam was used as internal standard).

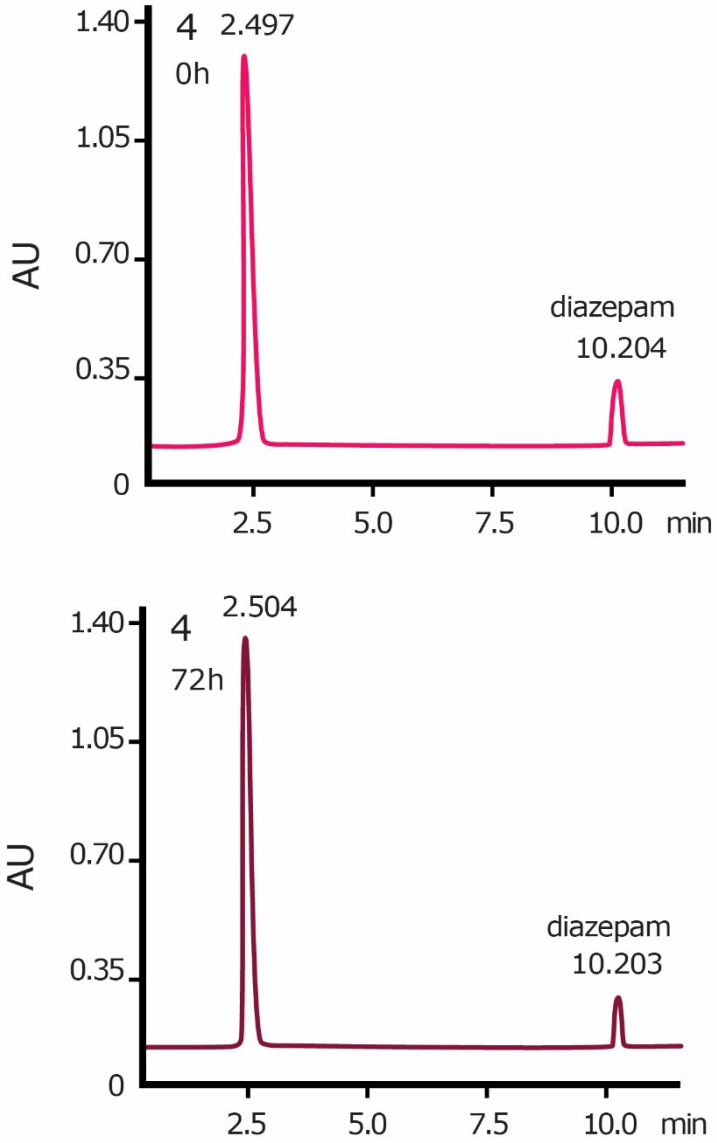
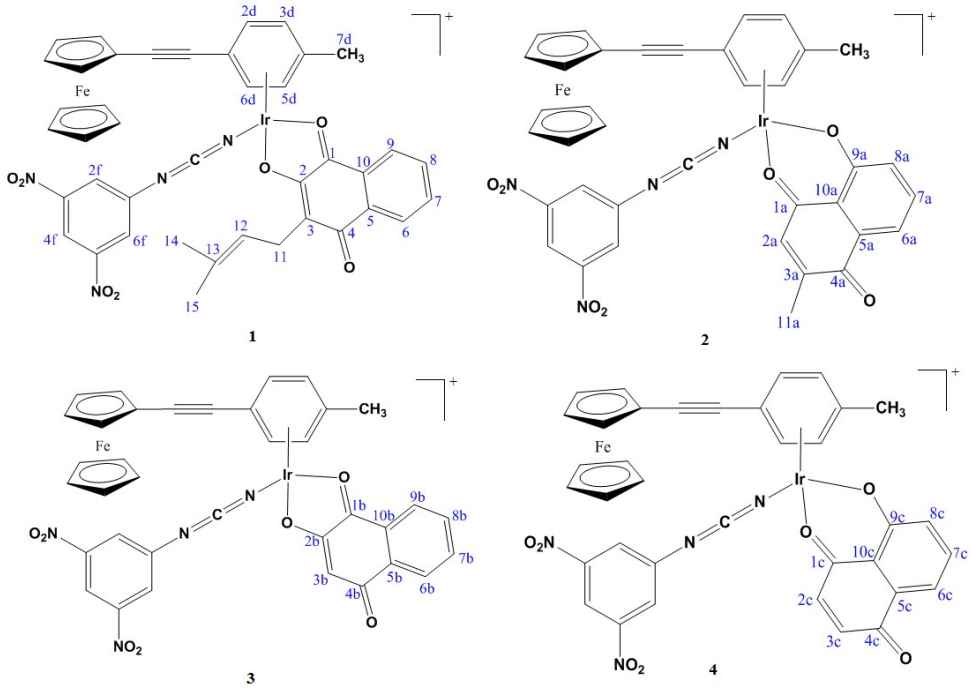


Fig. S21. LC-UV traces of plasma incubated with complex **4** (20 μM, 37 ˚C) at t = 0 and 72 h. (Diazepam was used as internal standard).

Table S1. Selected ^{1}H NMR data of the free ligands and complexes **1-4** (DMSO-d_6, δ: ppm**).**



Protons	Ligands	**1**	**2**	**3**	**4**
H-OH (Lap)	11.09 (s, 1H)	-	-	-	-
H-6	8.09 (d, 1H, ^{3}J 7.6)	8.00 (d, 1H, ^{3}J 7.6)	-	-	-
H-9	7.97 (d, 1H, ^{3}J 7.6)	7.89 (d, 1H, ^{3}J 7.6)	-	-	-
H-7	7.82 (t, 1H, ^{3}J 7.6)	7.63 (t, 1H, ^{3}J 7.6)	-	-	-
H-8	7.61 (t, 1H, ^{3}J 7.6)	7.52 (t, 1H, ^{3}J 7.6)	-	-	-
H-12	5.17 (t, 1H, ^{3}J 7.2)	5.01 (t, 1H, ^{3}J 7.2)	-	-	-
H-11	3.08 (d, 2H, ^{3}J 7.2)	2.86 (d, 2H, ^{3}J 8.0)	-	-	-
H-14 or H-15	1.79 (s, 3H)	1.69 (s, 3H)	-	-	-
H-14 or H-15	1.63 (s, 3H)	1.50 (s, 3H)	-	-	-
H-(OH) (Plum)	11.38 (s, 1H)	-	-	-	-
H-7a ,8a	7.62 (t, 2H, ^{3}J 7.6)	-	7.51 (t, 2H, ^{3}J 7.6)	-	-
H-6a	7.30 (d, 1H, ^{3}J 7.6)	-	7.10 (d, 1H, ^{3}J 7.6)	-	-
H-2a	6.90 (s, 1H)	-	6.74 (s, 1H)	-	-
H-11a	2.21 (s, 3H)	-	2.11 (s, 3H)	-	-
H-(OH) (Law)	11.51 (s, 1H)	-	-	-	-
H-3b	6.25 (s, 1H)	-	-	6.36 (s, 1H)	-

H-6b or 9b	8.00 (d, 1H, ^3J 7.6)	-	-	8.22(d, 1H, ^3J 7.6)	-
H-6b or 9b	7.91 (d, 1H, ^3J 7.6)	-	-	8.10 (d, 1H, ^3J 7.6)	-
H-7b or 8b	7.81 (t, 1H, ^3J 7.6)	-	-	7.63 (t, 1H, ^3J 7.6)	-
H-7b or 8b	7.89 (t, 1H, ^3J 7.6)	-	-	7.81 (t, 1H, ^3J 7.6)	-
H-(OH) (Jug)	11.58 (s, 1H)	-	-	-	-
H-7c	7.81 (t, 1H, ^3J 7.6)	-	-	-	7.71 (t, 1H, ^3J 7.6)
H-6c or 8c	7.39 (d, 1H, ^3J 7.6)	-	-	-	7.33 (d, 1H, ^3J 7.6)
H-6c or 8c	7.25 (d, 1H, ^3J 7.6)	-	-	-	7.17 (d, 1H, ^3J 7.6)
H-2c or 3c	7.13 (d, 1H, ^3J 7.6)	-	-	-	7.01 (d, 1H, ^3J 7.6)
H-2c or 3c	7.00 (d, 1H, ^3J 7.6)	-	-	-	6.85 (d, 1H, ^3J 7.6)
H-Cp	4.38 (s, 5H)	4.28 (s, 5H)	4.25 (s, 5H)	4.29 (s, 5H)	4.29 (s, 5H)
H-Cp	4.23 (t, 2H, ^3J 7.6)	4.10 (t, 2H, ^3J 7.6)	4.11 (t, 2H, ^3J 7.6)	4.11 (t, 2H, ^3J 7.6)	4.11 (t, 2H, ^3J 7.6)
H-Cp	4.50 (t, 2H, ^3J 7.6)	4.41 (t, 2H, ^3J 7.6)	4.39 (t, 2H, ^3J 7.6)	4.42 (t, 2H, ^3J 7.6)	4.42 (t, 2H, ^3J 7.6)
H-Ph (L1)	7.18 (d, 2H, ^3J 8.0)	5.60 (d, 1H, ^3J 7.2)	5.69 (d, 1H, ^3J 7.2)	5.73 (d, 1H, ^3J 7.2)	5.61 (d, 1H, ^3J 7.2)
H-Ph (L1)	7.07 (d, 2H, ^3J 8.0)	5.42 (d, 1H, ^3J 7.2)	5.49 (d, 1H, ^3J 7.2)	5.44 (d, 1H, ^3J 7.2)	5.48 (d, 1H, ^3J 7.2)
H-Ph (L1)	-	5.31 (d, 1H, ^3J 7.2)	5.39 (d, 1H, ^3J 7.2)	5.32 (d, 1H, ^3J 7.2)	5.33 (d, 1H, ^3J 7.2)
H-Ph (L1)	-	5.20 (d, 1H, ^3J 7.2)	5.21 (d, 1H, ^3J 7.2)	5.21 (d, 1H, ^3J 7.2)	5.21 (d, 1H, ^3J 7.2)
H- 7d	1.91 (s, 3H)	1.86 (s, 3H)	1.83 (s, 3H)	1.88 (s, 3H)	1.86 (s, 3H)
H-2f,6f *	7.75 (s, 2H)	7.70 (s, 2H)	7.69 (s, 2H)	7.90 (s, 2H)	7.89 (s, 2H)
H-4f *	8.29 (s, 1H)	8.18 (s, 1H)	8.07 (s, 1H)	7.99 (s, 1H)	8.05 (s, 1H)
H-NH *	8.48 (S, 1H)	-	-	-	-

* L. Tabrizi, H. Chiniforoshan, *Dalton Trans.* 2016, **45**, 18333-18345.

Table S2. Ratio of peak areas of complex/diazepam

	1	**2**	**3**	**4**
t = 0 h	9.85	7.82	8.97	8.11
t = 72 h	9.91	7.79	8.92	8.06