Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Gallium reactivates first and second generation quinolone antibiotics towards drug-resistant *Klebsiella pneumoniae*

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1. Experimental section

General Considerations

Reagents were purchased from Sigma Aldrich, Merck, Otsuka Pharmaceuticals and Thermo Fisher without the need for further purification. Solvents were purchased from Merck and where required dried using an MBRUAN SPS-800 solvent purification system and stored over 4 Å molecular sieves. All reactions requiring inert conditions were performed under an atmosphere of nitrogen, using over dried glassware and utilising a Schlenk manifold and techniques. ^{1}H and ^{13}C NMR were recorded on a Bruker Ultrashield Plus 600 DRX600 spectrophotometer (600 MHz), chemical shifts were referenced to the appropriate protonated solvent, d_6-DMSO. Infrared Spectra were recorded on an Agilent Technologies Cary 630 FTIR spectrometer, using a range of 4000 – 500 cm^{-1}. Mass spectrometry (ESI) was obtained by Dr. Boujemaa Moubaraki utilising a Micromass Platform QMS spectrometer, with an electrospray source and a cone voltage of 35 eV. Melting point analysis was conducted in open end capillary tubes, on a digital Stuart Scientific melting point apparatus SMP10. Elemental microanalysis was performed on a Perkin Elmer 2400 Series II CHNS/O Elemental Analyser from the School of Chemistry, Monash University.

X-ray crystallography: Crystallographic data was collected on an OXFORD XtaLAB Synergy, Dualflex, HyPix diffractometer equipped with an OXFORD Cryosystems 700 Cryostream and cooled to 173(2) K. Each compound was solved and refined using SHELXL-2014/7 utilising the graphical interface Olex2.[1] Unless otherwise indicated, all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were placed in calculated positions using a riding model with C-H = 0.95 – 0.98 Å and U_{iso}(H) = xU_{iso}(C), x = 1.2 or 1.5 unless otherwise indicated. Complex **1B-3B, 1A** were collected and refined by Dr. Craig Forsyth.

Biological testing

Bacteria preparation and Minimum inhibitory concentration MICs: Fluoroquinolone resistance reference strain *Klebsiella pneumoniae* 1074 was obtained from ATCC. Clinical isolate/multi-drug resistant strains KP-AJ289, KP-MKP103 and KP-RH201207 were obtained from the Alfred Hospital, Melbourne Victoria through collaboration with Professor Chris Greening and Professor Anton Parr. Bacteria from glycerol stocks were streaked onto LB agar and incubated overnight at 37 ˚C and subsequently a single colony was inoculated into 3 mL of RPMI-1640, without phenol red, supplemented with 10% Human serum purchased from Sigma-Alridch without further modification. The inoculum was incubated for 18 to 20 hours at 37 ˚C at 180 rpm to give turbid overnight cultures. Stock solutions were generated by solubilising complexes **1A – 3A** at 5 mM and **1B – 3B** at 10 mM, in biological grade DMSO purchased from Sigma-Aldrich. The stocks were then diluted in 96-well plates, to give a maximum concentration of 100 µM or 50 µM. This was serially diluted by a factor of two with a total of 100 µL/well. Overnight bacterial cultures were diluted to approximately 10^4 colony forming units/mL in RPMI-HS, before addition of 10 µL to each well and incubation at 37 ˚C

for 20 to 22 hours. At time a time point of ~ 20 hrs, 10 µL of resazurin dye was added to each well to give a definitive colour change in regard to growth versus no growth. These were incubated for a further 1 to 2 hours. MIC were defined as the point in which no visual growth was observed. All analyses were done in triplicate.

Cell culture: L929 fibroblasts were cultured and maintained in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% Fetal Bovine Serum (FBS), 1% Pen-Strep and 1% GlutaMAX^{TM} (purchased from Gibco^{TM}) at 37 ˚C in a 5 % CO_2 incubator.

In vitro testing of L929 cells: Resazurin was used for the determination of the percentage viability of L929 fibroblast cells. Working stock solutions were generated by solubilising, complexes 1A-3A at 5mM and 1B-3B at 10 mM in biological grade DMSO. Stock solutions were then sequentially diluted out in the appropriate culture media to give a maximum concentration of 50-100 µM. Volumes of 10^5 L929/mL were seeded and adhered to 96-well plates 24 hours prior to compound addition. 20 hours after compound addition, 15 µL of resazurin in PBS was added to each well, then incubated for a further 4 hours. All cell assays were measured spectroscopically using fluorescence excitation at 560 nm and emission at 590 nm. The compounds were compared to a positive control of no compound and the percent inhibition was calculated. Fluorescence measurements were conducted using a Thermo Scientific Varioskan LUX Multimode Microplate Reader (shaking: 15 s, 300 rpm, high force, single orbital). Experiments were conducted independently in triplicate, with values averaged between the experiments. IC_{50} values were determined using GraphPad Prism 9.

Total iron concentration: 1 mL of RPMI-1640, RPMI-1640 + 10% HS and LB-broth was digested in 1 mL of concentrated nitric acid in triplicate. Each solution was made to a total volume of 5 mL with 2-3% HNO_3. Precipitates were filtered after digestion and prior to analysis through 0.22-micron syringe filters. The samples were analysed using ICP-MS Helium KED mode and the total iron content calculated against a calibration curve of Fe(57).

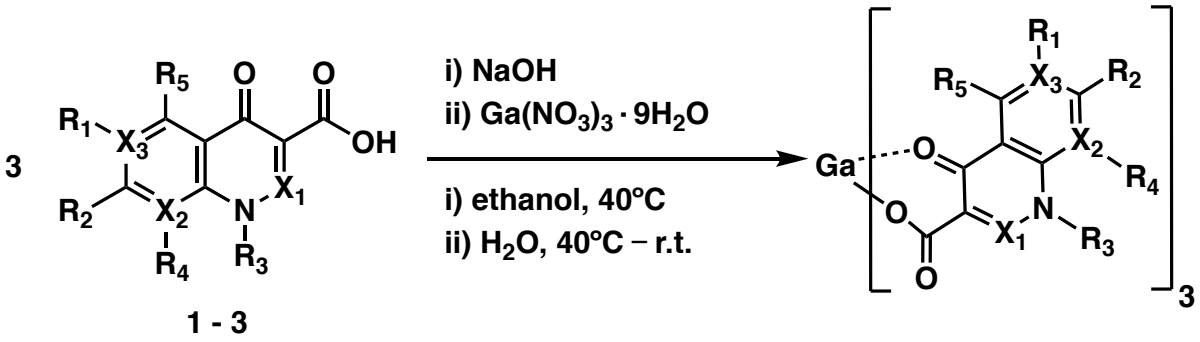
Media protein uptake analysis: 10 µL of compounds **1A** and **1B** were added to 9990 µL of RPMI-HS to a concentration of 200 µM (the highest concentration of compound dissolved into media prior to serial dilution, see **Biological testing**). These solutions were then vortexed vigorously for approximately 60 seconds to allow completed homogenisation of the compound into the media. Studies were taken at initial time and 24 hours incubation at 37 ^{o}C. After the set time, 1000 µL of acetonitrile was added to extract all proteins through precipitation. Samples were then centrifuged to pellet the proteins and the supernatant separated. The pellet was subjected to acid digestion by 70% nitric acid. Both the supernatant and acid digested pellet were then diluted at the appropriate theoretical concentration in 2 – 3 % nitric acid in ultrapure water. Samples were then run on a Perkin Elmer NexIon ICP-OES against a 5-point calibration curve. The gallium content in both the solid phase and aqueous phase was then calculated as a percentage obtain in both to determine the protein binding of the complex in bacterial media. All analyses were done in triplicate.

General procedures:

General procedure 1 (GP1)

Compounds **1A** – **3A** were synthesised via a slightly modified procedure from Mjos, K.D. *et al*., 2016.[2] The synthesis involves two steps. First, the free quinolones **1-3** (3 mmol) were initially converted to their retrospective sodium salts via reaction with NaOH (3 mmol) in hot ethanol

and then isolated as solids and in the synthesis of the homoleptic gallium compounds **1A** – **3A**. The sodium salt of the respective quinolones (1.5 mmol) was dissolved into 25 mL of water (slight heat needed for **3**) to produce a clear solution. This clear solution was then added onto solid gallium nitrate nonahydrate (0.5 mmol) dropwise and the pH was carefully monitored during the addition and maintained below <5 and allowed to stir cooling to room temperature. The product started forming immediately and precipitated as a solid. The final pH was adjusted to 7 via dropwise addition of sodium hydroxide solution (0.1 M) and the reaction mixture left to stir at room temperature overnight. The product was filtered, washed with water (20 mL) and methanol (20 mL) and air dried to affords the homoleptic gallium quinolonate compounds **1A**-**3A**.



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NAD-*H* = 1	X_1 = CH, X_2 = N, X_3 = C, R_2 = CH_3, R_3 = C_2H_5, R_1 = R_4 = R_5 = H	**1A** = 52%
OXO-*H* = 2	X_1 = CH, X_2 = X_3 = C, R_2 = CH_2O_2, R_3 = C_2H_5, R_4 = R_5 = H	**2A** = 81%
NOR-*H* = 3	X_1 = CH, X_2 = X_3 = C, R_1 = F, R_2 = $C_4H_{10}N_2$, R_3 = C_2H_5 , R_4 = R_5 = H	**3A** = 36%

Scheme 1. Schematic diagram to synthesise homoleptic gallium (III) quinolonate complexes **1A**-**3A**.

[Ga(NAD)$_3$], 1A: Compound **1A** was prepared in accordance with **GP1** using the odium salt of nalidixic acid (0.3798 g, 1.5 mmol) and gallium nitrate nonahydrate (0.2090 g, 0.5 mmol). The resulted compound was off-white powder. Yield: 52% (0.1975 g, 0.26 mmol). ^{1}H NMR (400 MHz, 298 K, d_6-DMSO): δ= 9.43 (s), 9.34 (s), 9.26 (s), 9.16 (s) (3 H, a), 8.63-8.61 (d), 8.43-8.31(d) (3 H , b), 7.56-7.54 (d, 3 H, c), 4.74-4.66 (d), 4.65-4.59 (m) (6H, d), 2.71-2.66 (d, 9H, e), 1.45-1.39 (t), 1.33-1.31 (d) (9H, f); FT-IR [cm^{-1}]: 3443(mb) 3026 (m), 2986 (m), 1678 (s), 1633 (s), 1611(s) 1557 (s), 1519 (s), 1494 (s), 1444 (s), 1382 (w), 1349 (m), 1320 (m), 1293 (m), 1259 (s), 1131 (s), 1111 (w), 1090 (m), 992 (w), 898 (m), 809 (s), 778 (s), 707 (w), 666 (m); HRMS (ESI+): m/z ([Ga(NAD)$_3$ + Na]$^+$) for $C_{18}H_{22}FGaN_3O_3Na$ calcd.: 785.1463, found 785.1465; Elemental analysis calcd. (%) for $C_{36}H_{33}GaN_6O_9$.3 H_2O: C 52.90, H 4.81, N 10.28; Found: C 53.04, H 4.42, N 10.24. CCDC: 2264988. Due to the very poor solubility of **1A**, ^{13}C NMR spectrum could not be obtained.

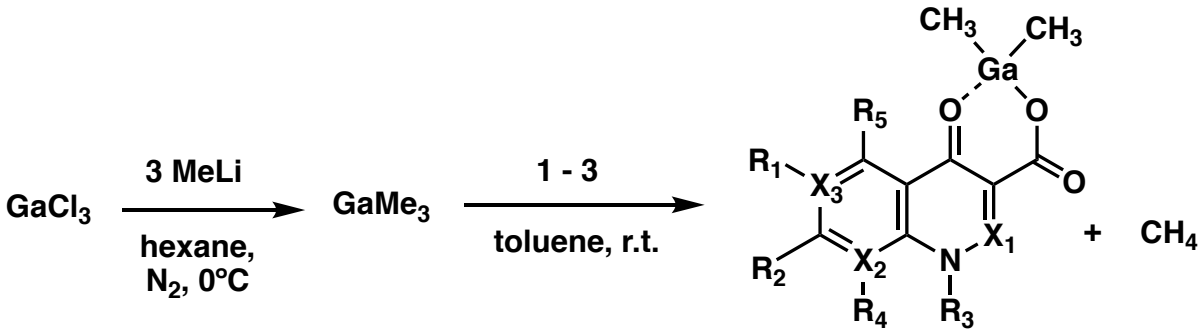
[Ga(OXO)$_3$], 2A: Complex **2A** was prepared in accordance with **GP1** using sodium salt of oxolinic acid (0.4248 g, 1.5 mmol) and gallium nitrate nonahydrate (0.2089 g, 0.5 mmol). The resulted compound was off-white powder. Yield: 81% (0.2695 g, 0.32 mmol). ^{1}H NMR (400 MHz, 298 K, d_6-DMSO): δ= 9.11 (s), 9.03 (s), 9.00 (s), 8.95 (s) (3 H, a), 7.69-7.68 (d), 7.54 (s),

7.37 (s) 7.32-7.31 (d), 7.20 (s) (6 H b,c); 6.27-6.23 (d, 6H, d), 4.63 (q, 6 H, e) 1.43-1.23 (m, 9. H, f); FT-IR [cm^{-1}]: 3402 (mb), 2979 (w), 2005 (w), 1636 (s), 1603 (s), 1566 (m), 1541 (s), 1465(s), 1446 (s), 1384 (m), 1325 (m), 1284 (w), 1255 (s), 1192 (m), 1159 (w), 1127 (w), 1088 (w), 1029 (w), 933 (m), 902 (w), 880 (w), 847 (w), 811(s), 777 (s), 714 (w); HRMS (ESI+): m/z ([$Ga(OXO)_3$ + Na]$^+$) for $C_{39}H_{30}GaN_3O_{15}Na$ calcd.872.0830, found 872.0821; Elemental analysis calcd. (%) for $C_{39}H_{30}GaN_3O_{15}$.4.5 H_2O: C 50.29, H 4.22, N 4.51; Found: C 49.9, H 4.08, N 4.73. Due to the very poor solubility of **2A**, ^{13}C NMR spectrum could not be obtained.

[$Ga(NOR)_3$], 3A: Complex **3A** was prepared in accordance with **GP1** using sodium salt of norfloxacin(0.5120 g, 1.5 mmol) and gallium nitrate nonahydrate (0.2089 g, 0.5 mmol). The resulted compound was pale yellow powder. Yield: 36% (0.1847 g, 0.18 mmol). ^1H NMR (400 MHz, 298 K, d_6-DMSO): δ= 9.19 (s), 9.09 (s), 9.07 (s), 8.9 (s) (3 H C a), 7.94(d), 7.77(d), 7.51 (t) (3 H, b), 7.27 (d), 7.17-7.19 (d) (3 H, c), 4.69-4.49 (m, 6H, d), 3.31-3.32 (m, overlaid with water 24H, e and f), 1.45-1.41 (m), 1.31(t, g); FT-IR [cm^{-1}]: 3391 (mb), 2976(w), 2653 (w), 1639 (s), 1552 (w), 1520 (m), 1474 (s), 1449 (s), 1375 (m), 1321(m), 1315 (s), 1287 (m), 1248 (sb), 1190 (m), 1131 (m), 1037 (m), 971 (w), 934(s), 889 (m), 804 (s), 811 (s), 787 (m), 770 (m), 750 (s), 702(w), 670(w); HRMS (ESI+): m/z ([$Ga(NOR)_3$ + Na]$^+$) for $C_{48}H_{51}F_3GaN_9O_9Na$ calcd.1046.2915, found 1046.2892. Due to the very poor solubility of **3A**, ^{13}C NMR spectrum could not be obtained.

General procedure 2 (GP2)

The synthesis of three heteroleptic organometallic gallium (III) complexes, [$GaMe_2$(NAD)] **1B** [$GaMe_2$(OXO)] **2B**, and [$GaMe_2$(NOR)] **3B** involves two steps. First, $GaMe_3$ (1 mmol) was synthesised *in situ* following the salt metathesis route, where $GaCl_3$ (0.1765 g, 1 mmol) was dissolved into dry hexane (10 mL) and cooled to 0 °C before the dropwise addition of 1.1 mL of methyllithium (MeLi, 3.3 mmol, 3.1 M solution in diethoxymethane). A white solid formed immediately (LiCl, by product) and the soluble $GaMe_3$ was extracted by a filter cannula into another Schlenk. This freshly prepared $GaMe_3$ solution was used to synthesised compounds **1B**-**3B**. The respective quinolone (**1**-**3**) (1 mmol) was added in a Schlenk flask and dried under vacuum for 3 hours before use. Then, 10 mL of toluene was added to suspend the quinolone. $GaMe_3$ (1 mmol) was added by a filter cannula directly into the Schlenk containing the respective quinolones suspended in toluene at room temperature. The reaction mixture was stirred overnight, and the complexes precipitated from the reaction mixture and were isolated by gravity filtration. Synthesised complexes were washed with small amounts of diethyl ether and dried in air to give a yield of approximately 81-84%. All synthesised products were air stable.



NAD-*H* = 1	X_1 = CH, X_2 = N, X_3 = C, R_2 = CH_3, R_3 = C_2H_5, R_1 = R_4 = R_5 = H	**1B** = 84%
OXO-*H* = 2	X_1 = CH, X_2 = X_3 = C, R_2 = CH_2O_2, R_3 = C_2H_5, R_4 = R_5 = H	**2B** = 81%
NOR-*H* = 3	X_1 = CH, X_2 = X_3 = C, R_1 = F, R_2 = $C_4H_{10}N_2$, R_3 = C_2H_5 , R_4 = R_5 = H	**3B** = 82%

Scheme 2. Schematic diagram to synthesise heteroleptic organometallic gallium (III) quinolonate complexes **1B**-**3B**.

[$GaMe_2$(NAD)], 1B: Compound **1B** was prepared in accordance with GP2 using nalidixic acid, **1** (0.230 g, 1 mmol) and *in situ* synthesised $GaMe_3$ (1 mmol). The resulted compound was an off- white powder. Yield: 84% (0.277g, 0.84 mmol). ^{1}H NMR (400 MHz, 298 K, d_6-DMSO): δ= 9.43 (s, 1H, a), 8.73-8.71 (d, 1H, b), 7.78-7.65 (d, 1H, c), 4.77-4.72 (q, 2H, d), 2.74 (s, 3H, e), 1.47 (t, 3H, f), -0.327 (s, 6H, g). ^{13}C NMR (150 MHz, 298 K, d_6-DMSO): δ= 175.3 (C 1), 165.4 (C 2), 163.8 (C 3), 152.0 (C 4), 147.6 (C 5), 135.8 (C 6), 123.3 (C 7), 118.5 (C 8), 112.3 (C 9), 47.3 (C

10), 25.1 (C 11), 15.0 (C 12), -5.6 (C 13); FT-IR [cm^{-1}]: 3049 (w), 2970 (w), 1948 (w), 1639 (s), 1610 (s), 1557 (w), 1497 (s), 1442 (s), 1375 (w), 1347 (m), 1315 (m), 1287 (m), 1257 (s), 1132 (s), 1107 (w), 1037 (w), 961 (w), 896 (m), 804 (s), 749 (s), 689 (w); HRMS (ESI): m/z for $C_{14}H_{18}GaN_2O_3$ calcd.: 331.0573, found 331.0562; Elemental analysis calcd. (%): C 50.80, H 5.18, N 8.46; Found: C 50.89, H 4.92, N 8.44. CCDC: 2264986.

[$GaMe_2$(OXO)], 2B: Compound **2B** was prepared in accordance with GP2 using oxolinic acid, **2** (0.2610 g, 1 mmol) and *in situ* synthesised $GaMe_3$ (1 mmol). The resulted compound was an off-white powder. Yield: 81% (0.2906 g, 0.81mmol). ^{1}H NMR (400 MHz, 298 K, d_6-DMSO): δ= 9.14 (s, 1 H, a); 7.73(s, 1 H, b); 7.69 (s, 1 H, c); 6.32 (s, 2 H, d); 4.64 (d, 2 H, e); 1.41 (t, 3 H, f); -0.360 (s, 6H, g); ^{13}C NMR (150 MHz, 298 K, d_6-DMSO): δ= 175.1 (C 1), 165.4 (C 2), 154.7 (C 3), 149.7 (C 4), 148.3 (C 5), 137.4 (C 6), 122.2 (C 7), 111.6 (C 8), 104.0 (C 9), 102.0 (C 10), 97.3 (C 11), 50.7 (C 12), 15.1 (C 13), -5.5 (C 14); FT-IR [cm^{-1}]: 3058 (w), 2976 (w), 2005 (w), 1857 (w), 1648 (s), 1627 (s), 1570 (m), 1536 (s), 1507(w), 1470 (s), 1410 (w), 1361 (w), 1312 (m), 1266 (w), 1265 (s), 1196 (m), 1158 (w), 1009 (s), 947 (s), 904 (w), 861(s), 808 (s), 779 (s), 664 (w); HRMS (ESI): m/z for $C_{15}H_{17}GaNO_5$ calcd.: 360.0363, found 360.0349; m/z ([$GaMe_2$(OXO) + Na]$^+$) for $C_{15}H_{16}GaNO_5Na$ calcd.: 382.0182, found 382.0166; Elemental analysis calcd. (%): C 50.04, H 4.48, N 3.89; Found: C 49.86, H 4.45, N 3,91. CCDC: 2264991.

[$GaMe_2$(NOR)], 3B: Compound **3B** was prepared in accordance with GP2 using norfloxacin, **3** (0.2610 g, 1 mmol) and *in situ* synthesised $GaMe_3$ (10.319 g, 1 mmol). The resulted compound was pale yellow powder. Yield: 82% (0.341g, 0.81mmol). ^{1}H NMR (400 MHz, 298 K, d_6-DMSO): δ= 9.17 (s, 1 H, a); 7.98(d, 1 H b); 7.20 (d, 1 H, c); 4.70 (q, 2 H, d); 3.26 (dd, 4 H, e), 2.89 (dd, 4 H, f), 1.45 (t, 3 H, g); -0.360 (s, 6H, h); ^{13}CNMR (150 MHz, 298 K, d_6-DMSO): δ= 173.5 (C 1), 164.4 (C 2), 154.6 (C 3), 153.0 (C 4), 151.2(C 5), 146.9 (C 6), 137.8 (C 7), 119.6 (C 8), 111.6 (C 9), 105.4 (C 10), 51.2 (C 11), 50.1 (C 12), 45.8 (*C* 13),14.8 (C 14) -5.4 (C 15); FT-IR [cm^{-1}]: 3049 (w), 2970(w), 2626 (w), 1948 (w), 1639 (s), 1610 (s), 1557 (m), 1497 (s), 1442 (s), 1375 (w), 1347(m), 1315 (s), 1257 (m), 1287 (m), 1257 (s), 1132 (m), 1107 (w), 1037 (w), 989 (w), 961(w), 896 (m), 804 (s), 749 (w), 689 (w); HRMS (ESI): m/z for $C_{18}H_{23}FGaN_3O_3$ calcd.: 418.1058, found 418.1041; m/z ([$GaMe_2$(NOR) + Na]$^+$) for $C_{18}H_{22}FGaN_3O_3Na$ calcd.: 440.0877, found 440.0863; Elemental analysis calcd. (%): C 51.71, H 5.54, N 10.05; Found: C 51.23, H 5.72, N 10.36. CCDC: 2264987.

2. X-ray crystallography

Table S1. Summary of crystallographic data for compounds **1A, [Ga(NAD)$_3$]**, **1B**, **[GaMe$_2$(NAD)]**, **2B**, **[GaMe$_2$(OXO)]** and **3B**, **[GaMe$_2$(NOR)]**.

Identification code	**1A**	**1B**	**2B**	**3B**
Empirical formula	$C_{38}H_{39}GaN_6O_{10}S$	$C_{14}H_{17}GaN_2O_3$	$C_{15}H_{16}GaNO_5$	$C_{19}H_{24}FGaN_2O_3$
Formula weight	841.53	331.01	360.01	417.12
Temperature/K	123.15	123.15	123.15	123.15
Crystal system	triclinic	triclinic	monoclinic	triclinic
Space group	P-1	P-1	C2/c	P-1
a/Å	9.57906(15)	8.0986(6)	18.0209(6)	8.7432(6)
b/Å	12.08921(18)	8.7121(7)	13.5163(6)	9.9407(8)
c/Å	16.5051(2)	10.8649(8)	14.3466(6)	10.8377(7)
α/°	79.9703(12)	77.168(4)	90	94.228(4)
β/°	77.8647(13)	80.358(4)	121.773(2)	100.666(4)
γ/°	86.5916(12)	70.566(4)	90	102.337(4)
Volume/Å^3	1839.56(5)	701.19(9)	2970.8(2)	897.98(11)
Z	2	2	38	2
ρ_{calc}g/cm^3	1.519	1.568	1.610	1.543
μ/mm^{-1}	2.140	1.970	1.875	1.564
F(000)	872.0	340.0	1472.0	432.0
Crystal size/mm^3	0.12 × 0.08 × 0.04	0.26 × 0.21 × 0.15	0.23 × 0.18 × 0.15	0.26 × 0.21 × 0.17
Radiation	Cu Kα (λ = 1.54184)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)
2Θ range for data collection/°	7.428 to 160.88	3.864 to 51.356	4.236 to 55.836	4.874 to 57.392
Index ranges	-12 ≤ h ≤ 12, -14 ≤ k ≤ 15, -20 ≤ l ≤ 20	-9 ≤ h ≤ 9, -10 ≤ k ≤ 10, -12 ≤ l ≤ 13	-21 ≤ h ≤ 23, -17 ≤ k ≤ 17, -18 ≤ l ≤ 11	-11 ≤ h ≤ 11, -13 ≤ k ≤ 13, -14 ≤ l ≤ 14
Reflections collected	38980	6684	40104	36411
Independent reflections	7899 [R_{int} = 0.0534, R_{sigma} = 0.0402]	2632 [R_{int} = 0.0339, R_{sigma} = 0.0436]	3563 [R_{int} = 0.0601, R_{sigma} = 0.0303]	4643 [R_{int} = 0.0535, R_{sigma} = 0.0358]
Data/restraints/parameters	7899/0/513	2632/0/186	3563/0/202	4904/8/215
Goodness-of-fit on F^2	1.075	1.075	1.130	1.130
Final R indexes [I>=2σ (I)]	R_1 = 0.0429, wR_2 = 0.1142	R_1 = 0.0429, wR_2 = 0.1142	R_1 = 0.0396, wR_2 = 0.0812	R_1 = 0.0396, wR_2 = 0.0812
Final R indexes [all data]	R_1 = 0.0477, wR_2 = 0.1178	R_1 = 0.0477, wR_2 = 0.1178	R_1 = 0.0513, wR_2 = 0.0855	R_1 = 0.0513, wR_2 = 0.0855
Largest diff. peak/hole / e Å^{-3}	0.78/-0.89	0.78/-0.89	0.50/-0.69	0.50/-0.69

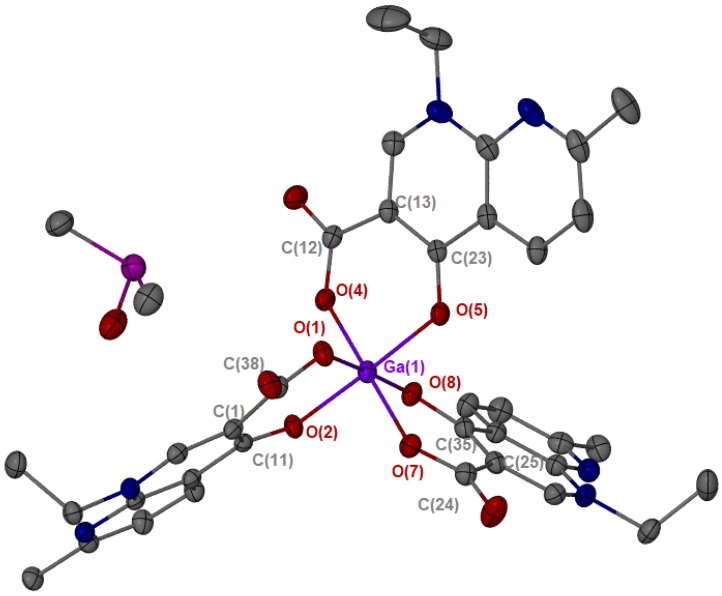


Figure S1. Single crystal x-ray structures of complex **1A, [Ga(NAD)$_3$],** Thermal ellipsoids are at 50% probability and hydrogen atoms have been omitted for clarity. For full data on bond lengths and angles see **Tables S2 – S3**

Table S2. Bond Lengths for **1A**.

Atom	Atom	Length/Å		Atom	Atom	Length/Å
Ga(1)	O(8)	2.0085(15)		C(24)	C(25)	1.508(3)
Ga(1)	O(5)	1.9692(15)		C(2)	C(1)	1.380(3)
Ga(1)	O(4)	1.9405(15)		C(5)	C(10)	1.399(3)
Ga(1)	O(7)	1.9315(16)		C(5)	N(2)	1.351(3)
Ga(1)	O(1)	1.9534(15)		C(29)	N(6)	1.346(3)
Ga(1)	O(2)	1.9563(15)		C(12)	C(13)	1.502(3)
O(8)	C(35)	1.272(3)		C(23)	C(13)	1.421(3)
O(5)	C(23)	1.277(3)		C(23)	C(22)	1.447(3)
O(4)	C(12)	1.284(3)		C(25)	C(26)	1.387(3)
O(7)	C(24)	1.290(3)		C(10)	C(9)	1.407(3)
O(1)	C(38)	1.290(3)		C(17)	N(4)	1.344(3)
O(2)	C(11)	1.275(3)		C(17)	C(22)	1.401(3)
C(38)	O(3)	1.233(3)		N(2)	C(6)	1.334(3)
C(38)	C(1)	1.503(3)		N(6)	C(30)	1.334(3)
O(9)	C(24)	1.222(3)		N(4)	C(18)	1.331(3)
O(6)	C(12)	1.227(3)		C(9)	C(8)	1.371(3)
N(5)	C(29)	1.392(3)		C(21)	C(20)	1.370(3)
N(5)	C(26)	1.339(3)		C(21)	C(22)	1.407(3)
N(5)	C(27)	1.486(3)		C(8)	C(6)	1.411(3)
N(3)	C(14)	1.337(3)		C(6)	C(7)	1.500(3)
N(3)	C(17)	1.387(3)		C(3)	C(4)	1.514(3)
N(3)	C(15)	1.486(3)		C(20)	C(18)	1.411(4)
C(35)	C(34)	1.454(3)		C(33)	C(32)	1.375(3)
C(35)	C(25)	1.408(3)		C(30)	C(32)	1.398(3)
C(14)	C(13)	1.381(3)		C(30)	C(31)	1.504(3)
C(34)	C(29)	1.407(3)		C(18)	C(19)	1.501(3)

C(34)	C(33)	1.402(3)		C(27)	C(28)	1.510(4)
C(11)	C(10)	1.450(3)		C(15)	C(16)	1.523(5)
C(11)	C(1)	1.418(3)		S(1)	O(10)	1.4951(19)
N(1)	C(2)	1.346(3)		S(1)	C(36)	1.780(3)
N(1)	C(5)	1.387(3)		S(1)	C(37)	1.791(3)
N(1)	C(3)	1.486(3)				

Table S3. Bond Angles for **1A**_auto.

Atom	Atom	Atom	Angle/°		Atom	Atom	Atom	Angle/°
O(5)	Ga(1)	O(8)	92.15(6)		N(6)	C(29)	N(5)	116.43(19)
O(4)	Ga(1)	O(8)	87.16(6)		N(6)	C(29)	C(34)	124.7(2)
O(4)	Ga(1)	O(5)	90.83(6)		O(4)	C(12)	C(13)	118.27(18)
O(4)	Ga(1)	O(1)	94.41(7)		O(6)	C(12)	O(4)	122.8(2)
O(4)	Ga(1)	O(2)	86.75(7)		O(6)	C(12)	C(13)	119.0(2)
O(7)	Ga(1)	O(8)	89.95(6)		O(5)	C(23)	C(13)	125.57(19)
O(7)	Ga(1)	O(5)	90.03(7)		O(5)	C(23)	C(22)	118.31(19)
O(7)	Ga(1)	O(4)	177.01(6)		C(13)	C(23)	C(22)	116.12(19)
O(7)	Ga(1)	O(1)	88.46(7)		C(35)	C(25)	C(24)	124.89(19)
O(7)	Ga(1)	O(2)	92.36(7)		C(26)	C(25)	C(35)	119.6(2)
O(1)	Ga(1)	O(8)	177.93(7)		C(26)	C(25)	C(24)	115.25(19)
O(1)	Ga(1)	O(5)	89.17(6)		C(5)	C(10)	C(11)	121.23(18)
O(1)	Ga(1)	O(2)	91.52(6)		C(5)	C(10)	C(9)	117.32(19)
O(2)	Ga(1)	O(8)	87.23(6)		C(9)	C(10)	C(11)	121.41(19)
O(2)	Ga(1)	O(5)	177.53(7)		N(3)	C(17)	C(22)	119.15(19)
C(35)	O(8)	Ga(1)	124.42(14)		N(4)	C(17)	N(3)	116.4(2)
C(23)	O(5)	Ga(1)	124.97(13)		N(4)	C(17)	C(22)	124.5(2)
C(12)	O(4)	Ga(1)	131.34(13)		N(5)	C(26)	C(25)	124.4(2)
C(24)	O(7)	Ga(1)	130.44(15)		C(11)	C(1)	C(38)	124.2(2)
C(38)	O(1)	Ga(1)	129.11(14)		C(2)	C(1)	C(38)	116.88(18)
C(11)	O(2)	Ga(1)	126.00(13)		C(2)	C(1)	C(11)	118.91(19)
O(1)	C(38)	C(1)	117.85(18)		C(14)	C(13)	C(12)	116.04(19)
O(3)	C(38)	O(1)	122.80(19)		C(14)	C(13)	C(23)	119.13(19)
O(3)	C(38)	C(1)	119.3(2)		C(23)	C(13)	C(12)	124.8(2)
C(29)	N(5)	C(27)	120.77(19)		C(6)	N(2)	C(5)	117.14(19)
C(26)	N(5)	C(29)	119.44(19)		C(30)	N(6)	C(29)	117.07(19)
C(26)	N(5)	C(27)	119.76(19)		C(18)	N(4)	C(17)	117.1(2)
C(14)	N(3)	C(17)	119.7(2)		C(8)	C(9)	C(10)	119.3(2)
C(14)	N(3)	C(15)	118.6(2)		C(20)	C(21)	C(22)	119.4(2)
C(17)	N(3)	C(15)	121.60(19)		C(9)	C(8)	C(6)	118.98(19)
O(8)	C(35)	C(34)	118.29(19)		N(2)	C(6)	C(8)	123.13(19)
O(8)	C(35)	C(25)	125.9(2)		N(2)	C(6)	C(7)	117.51(19)
C(25)	C(35)	C(34)	115.83(19)		C(8)	C(6)	C(7)	119.36(19)
N(3)	C(14)	C(13)	124.4(2)		N(1)	C(3)	C(4)	112.13(18)
C(29)	C(34)	C(35)	121.62(19)		C(21)	C(20)	C(18)	118.9(2)
C(33)	C(34)	C(35)	122.0(2)		C(17)	C(22)	C(23)	121.4(2)
C(33)	C(34)	C(29)	116.4(2)		C(17)	C(22)	C(21)	116.9(2)
O(2)	C(11)	C(10)	117.07(18)		C(21)	C(22)	C(23)	121.6(2)
O(2)	C(11)	C(1)	126.46(19)		C(32)	C(33)	C(34)	119.4(2)
C(1)	C(11)	C(10)	116.47(19)		N(6)	C(30)	C(32)	122.8(2)
C(2)	N(1)	C(5)	119.34(18)		N(6)	C(30)	C(31)	116.0(2)

C(2)	N(1)	C(3)	119.48(17)		C(32)	C(30)	C(31)	121.1(2)
C(5)	N(1)	C(3)	121.17(17)		C(33)	C(32)	C(30)	119.5(2)
O(7)	C(24)	C(25)	117.75(19)		N(4)	C(18)	C(20)	123.2(2)
O(9)	C(24)	O(7)	123.7(2)		N(4)	C(18)	C(19)	116.1(3)
O(9)	C(24)	C(25)	118.5(2)		C(20)	C(18)	C(19)	120.8(2)
N(1)	C(2)	C(1)	124.50(19)		N(5)	C(27)	C(28)	112.1(2)
N(1)	C(5)	C(10)	119.40(18)		N(3)	C(15)	C(16)	110.4(2)
N(2)	C(5)	N(1)	116.50(18)		O(10)	S(1)	C(36)	107.36(13)
N(2)	C(5)	C(10)	124.10(19)		O(10)	S(1)	C(37)	106.62(12)
N(5)	C(29)	C(34)	118.91(19)		C(36)	S(1)	C(37)	96.43(14)

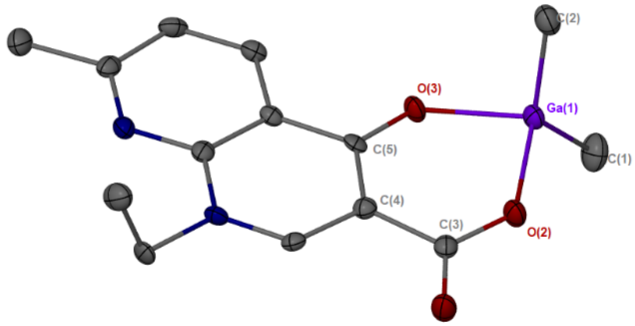


Figure S2. Solid-state structure of complex **1B**, **[GaMe$_2$(NAD)]**. Thermal ellipsoids shown at 50% probability. Hydrogen atoms have been omitted for clarity. For full data on bond lengths and angles see **Tables S4 – S5**

Table S4. Bond Lengths for **1B**.

Atom	**Atom**	**Length/Å**		**Atom**	**Atom**	**Length/Å**
Ga(1)	O(3)	1.984(4)		N(1)	C(8)	1.327(7)
Ga(1)	O(2)	1.920(4)		C(3)	C(4)	1.501(7)
Ga(1)	C(2)	1.942(6)		C(5)	C(6)	1.443(7)
Ga(1)	C(1)	1.942(6)		C(5)	C(4)	1.425(7)
O(3)	C(5)	1.275(6)		C(6)	C(9)	1.400(7)
O(1)	C(3)	1.221(6)		C(6)	C(00C)	1.411(7)
O(2)	C(3)	1.295(6)		C(4)	C(10)	1.380(7)
N(2)	C(9)	1.385(7)		C(00C)	C(7)	1.363(8)
N(2)	C(10)	1.329(7)		C(8)	C(7)	1.403(8)
N(2)	C(13)	1.486(6)		C(8)	C(11)	1.492(7)
N(1)	C(9)	1.337(7)		C(13)	C(14)	1.511(8)

Table S5. Bond Angles for **1B**.								
Atom	**Atom**	**Atom**	**Angle/°**		**Atom**	**Atom**	**Atom**	**Angle/°**
O(2)	Ga(1)	O(3)	92.96(15)		C(4)	C(5)	C(6)	116.9(4)
O(2)	Ga(1)	C(2)	108.5(2)		C(9)	C(6)	C(5)	121.2(5)
O(2)	Ga(1)	C(1)	108.3(2)		C(9)	C(6)	C(00C)	116.4(5)
C(2)	Ga(1)	O(3)	102.4(2)		C(00C)	C(6)	C(5)	122.4(5)
C(1)	Ga(1)	O(3)	106.7(2)		C(5)	C(4)	C(3)	126.2(5)
C(1)	Ga(1)	C(2)	131.0(3)		C(10)	C(4)	C(3)	116.0(5)
C(5)	O(3)	Ga(1)	123.9(3)		C(10)	C(4)	C(5)	117.7(5)
C(3)	O(2)	Ga(1)	130.5(3)		N(2)	C(9)	C(6)	119.1(5)
C(9)	N(2)	C(13)	119.9(4)		N(1)	C(9)	N(2)	116.4(5)
C(10)	N(2)	C(9)	119.6(4)		N(1)	C(9)	C(6)	124.5(5)
C(10)	N(2)	C(13)	120.5(4)		C(7)	C(00C)	C(6)	118.9(5)
C(8)	N(1)	C(9)	118.1(5)		N(2)	C(10)	C(4)	125.4(5)
O(1)	C(3)	O(2)	123.0(5)		N(1)	C(8)	C(7)	121.7(5)
O(1)	C(3)	C(4)	118.7(5)		N(1)	C(8)	C(11)	116.4(5)
O(2)	C(3)	C(4)	118.4(5)		C(7)	C(8)	C(11)	121.9(5)
O(3)	C(5)	C(6)	118.1(4)		C(00C)	C(7)	C(8)	120.4(5)
O(3)	C(5)	C(4)	125.0(5)		N(2)	C(13)	C(14)	110.4(4)

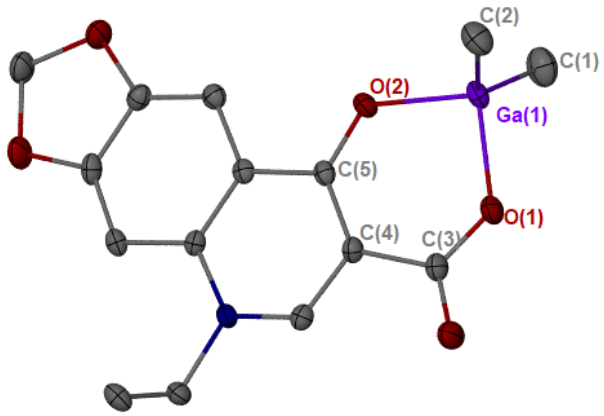


Figure S3. Single crystal x-ray structures of complex **2B, [$GaMe_2$(OXO)].** Thermal ellipsoids are at 50% probability and hydrogen atoms have been omitted for clarity. For full data on bond lengths and angles see **Tables S6 – S7**

Table S6. Bond Lengths for **2B**.						
Atom	**Atom**	**Length/Å**		**Atom**	**Atom**	**Length/Å**
Ga(1)	O(2)	1.9423(15)		N(1)	C(12)	1.390(3)
Ga(1)	O(1)	1.9120(17)		C(7)	C(6)	1.412(3)
Ga(1)	C(1)	1.953(2)		C(7)	C(8)	1.354(3)
Ga(1)	C(2)	1.951(2)		C(6)	C(5)	1.445(3)
O(2)	C(5)	1.290(3)		C(6)	C(12)	1.411(3)
O(1)	C(3)	1.294(3)		C(13)	C(14)	1.511(3)

O(5)	C(10)	1.365(3)		C(8)	C(10)	1.398(3)
O(5)	C(9)	1.427(3)		C(10)	C(11)	1.357(3)
O(4)	C(8)	1.367(3)		C(5)	C(4)	1.414(3)
O(4)	C(9)	1.430(3)		C(11)	C(12)	1.417(3)
O(3)	C(3)	1.224(3)		C(15)	C(4)	1.375(3)
N(1)	C(13)	1.482(3)		C(3)	C(4)	1.502(3)
N(1)	C(15)	1.335(3)				

Table S7. Bond Angles for **2B**.

Atom	**Atom**	**Atom**	**Angle/°**		**Atom**	**Atom**	**Atom**	**Angle/°**
O(2)	Ga(1)	C(1)	105.57(10)		C(7)	C(8)	C(10)	121.6(2)
O(2)	Ga(1)	C(2)	108.36(9)		O(5)	C(10)	C(8)	109.3(2)
O(1)	Ga(1)	O(2)	94.61(7)		C(11)	C(10)	O(5)	127.1(2)
O(1)	Ga(1)	C(1)	107.17(10)		C(11)	C(10)	C(8)	123.6(2)
O(1)	Ga(1)	C(2)	108.18(10)		O(2)	C(5)	C(6)	117.57(19)
C(2)	Ga(1)	C(1)	127.90(11)		O(2)	C(5)	C(4)	125.29(19)
C(5)	O(2)	Ga(1)	124.71(14)		C(4)	C(5)	C(6)	117.14(19)
C(3)	O(1)	Ga(1)	128.88(15)		C(10)	C(11)	C(12)	115.8(2)
C(10)	O(5)	C(9)	106.52(18)		N(1)	C(15)	C(4)	124.5(2)
C(8)	O(4)	C(9)	105.97(18)		O(1)	C(3)	C(4)	118.6(2)
C(15)	N(1)	C(13)	118.42(19)		O(3)	C(3)	O(1)	122.6(2)
C(15)	N(1)	C(12)	120.11(19)		O(3)	C(3)	C(4)	118.8(2)
C(12)	N(1)	C(13)	121.47(17)		N(1)	C(12)	C(6)	118.63(19)
C(8)	C(7)	C(6)	117.6(2)		N(1)	C(12)	C(11)	120.01(19)
C(7)	C(6)	C(5)	118.98(19)		C(6)	C(12)	C(11)	121.3(2)
C(12)	C(6)	C(7)	120.18(19)		C(5)	C(4)	C(3)	126.0(2)
C(12)	C(6)	C(5)	120.8(2)		C(15)	C(4)	C(5)	118.78(19)
N(1)	C(13)	C(14)	111.80(18)		C(15)	C(4)	C(3)	115.1(2)
O(4)	C(8)	C(10)	109.93(19)		O(5)	C(9)	O(4)	108.22(18)
C(7)	C(8)	O(4)	128.5(2)					

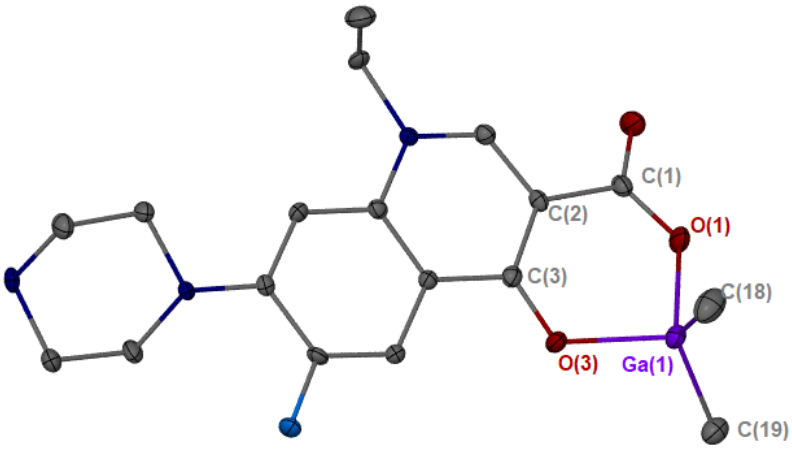


Figure S4. Single crystal x-ray structures of complex **3B, [GaMe$_2$(NOR)].** Thermal ellipsoids are at 50% probability and hydrogen atoms have been omitted for clarity. For full data on bond lengths and angles see **Tables S8 – S9**

Table S8. Bond Lengths for **3B**.

Atom	Atom	Length/Å		Atom	Atom	Length/Å
Ga(1)	O(1)	1.9078(14)		N(3)	C(16)	1.451(3)
Ga(1)	O(3)	1.9374(14)		C(1)	C(2)	1.506(3)
Ga(1)	C(18)	1.951(2)		C(2)	C(3)	1.408(3)
Ga(1)	C(19)	1.950(2)		C(2)	C(10)	1.380(3)
F(1)	C(6)	1.350(2)		C(3)	C(4)	1.440(3)
O(1)	C(1)	1.292(2)		C(4)	C(5)	1.408(3)
O(2)	C(1)	1.218(2)		C(4)	C(9)	1.402(2)
O(3)	C(3)	1.283(2)		C(5)	C(6)	1.351(3)
N(1)	C(9)	1.389(2)		C(6)	C(7)	1.419(3)
N(1)	C(10)	1.328(2)		C(7)	C(8)	1.382(3)
N(1)	C(12)	1.479(2)		C(8)	C(9)	1.395(3)
N(2)	C(7)	1.391(2)		C(12)	C(13)	1.509(3)
N(2)	C(14)	1.481(2)		C(14)	C(15)	1.510(3)
N(2)	C(17)	1.463(2)		C(16)	C(17)	1.512(3)
N(3)	C(15)	1.450(3)				

Table S9. Bond Angles for **3B**.								
Atom	**Atom**	**Atom**	**Angle/°**		**Atom**	**Atom**	**Atom**	**Angle/°**
O(1)	Ga(1)	O(3)	93.56(6)		O(3)	C(3)	C(4)	118.13(17)
O(1)	Ga(1)	C(18)	107.86(9)		C(2)	C(3)	C(4)	116.53(16)
O(1)	Ga(1)	C(19)	109.04(8)		C(5)	C(4)	C(3)	120.39(16)
O(3)	Ga(1)	C(18)	107.71(9)		C(9)	C(4)	C(3)	121.50(17)
O(3)	Ga(1)	C(19)	106.62(8)		C(9)	C(4)	C(5)	118.04(17)
C(19)	Ga(1)	C(18)	126.92(9)		C(6)	C(5)	C(4)	120.18(17)
C(1)	O(1)	Ga(1)	128.30(13)		F(1)	C(6)	C(5)	118.22(16)
C(3)	O(3)	Ga(1)	121.53(13)		F(1)	C(6)	C(7)	118.58(16)
C(9)	N(1)	C(12)	120.91(15)		C(5)	C(6)	C(7)	123.13(17)
C(10)	N(1)	C(9)	120.14(16)		N(2)	C(7)	C(6)	120.50(16)
C(10)	N(1)	C(12)	118.93(16)		C(8)	C(7)	N(2)	123.11(17)
C(7)	N(2)	C(14)	113.87(15)		C(8)	C(7)	C(6)	116.37(17)
C(7)	N(2)	C(17)	116.07(15)		C(7)	C(8)	C(9)	121.66(17)
C(17)	N(2)	C(14)	111.93(15)		N(1)	C(9)	C(4)	118.31(17)
C(15)	N(3)	C(16)	108.52(16)		N(1)	C(9)	C(8)	121.10(16)
O(1)	C(1)	C(2)	118.36(17)		C(8)	C(9)	C(4)	120.58(17)
O(2)	C(1)	O(1)	122.72(18)		N(1)	C(10)	C(2)	124.29(17)
O(2)	C(1)	C(2)	118.92(17)		N(1)	C(12)	C(13)	111.49(16)
C(3)	C(2)	C(1)	124.92(17)		N(2)	C(14)	C(15)	110.82(16)
C(10)	C(2)	C(1)	116.04(16)		N(3)	C(15)	C(14)	109.04(16)
C(10)	C(2)	C(3)	119.01(17)		N(3)	C(16)	C(17)	108.70(16)
O(3)	C(3)	C(2)	125.34(17)		N(2)	C(17)	C(16)	110.57(16)

3. Biological data

Table S10. Minimum inhibitory concentration (MIC) of complexes **1A** – **3A**, **1B** – **3B** and quinolones, **1** – **3** in RPMI + 10% HS towards quinolone resistance *K. Pneumoniae.* All analyses were performed in triplicate.

Compound	*KP RH201207*	*KP MKP103*	*KP AJ289*	*KP 1074*
NAD*H* (**1**)	> 100	> 100	> 100	> 100
OXO*H* (**2**)	> 100	> 100	> 100	> 100
NOR*H* (**3**)	> 100	> 100	> 100	> 100
$[Ga(NAD)_3]$ (**1A**)	0.781	0.195	0.781	0.781
$[Ga(OXO)_3]$ (**2A**)	0.391	0.195	0.195	0.391
$[Ga(NOR)_3]$ (**3A**)	0.781	0.195	0.391	0.391
$[GaMe_2(NAD)]$ (**1B**)	**0.391**	**0.195**	**0.391**	**0.024**
$[GaMe_2(OXO)]$ (**2B**)	**0.098**	**0.024**	**0.049**	**0.098**
$[GaMe_2(NOR)]$ (**3B**)	**0.098**	**0.024**	**0.049**	**0.049**

Table S11. Minimum inhibitory concentration (MIC) of complexes **1A** – **3A**, **1B** – **3B** and quinolones, **1** – **3** in LB-broth towards quinolone resistance *K. Pneumoniae.* All analyses were performed in triplicate.

Compound	*KP RH201207*	*KP MKP103*	*KP AJ289*	*KP 1074*
NAD*H* (**1**)	> 100	> 100	> 100	> 100
OXO*H* (**2**)	> 100	> 100	> 100	> 100
NOR*H* (**3**)	> 100	> 100	> 100	> 100
$[Ga(NAD)_3]$ (**1A**)	> 50	> 50	> 50	> 50
$[Ga(OXO)_3]$ (**2A**)	> 50	> 50	> 50	> 50
$[Ga(NOR)_3]$ (**3A**)	> 50	> 50	> 50	> 50
$[GaMe_2(NAD)]$ (**1B**)	> 100	> 100	> 100	> 100
$[GaMe_2(OXO)]$ (**2B**)	> 100	> 100	> 100	> 100
$[GaMe_2(NOR)]$ (**3B**)	> 100	> 100	> 100	> 100

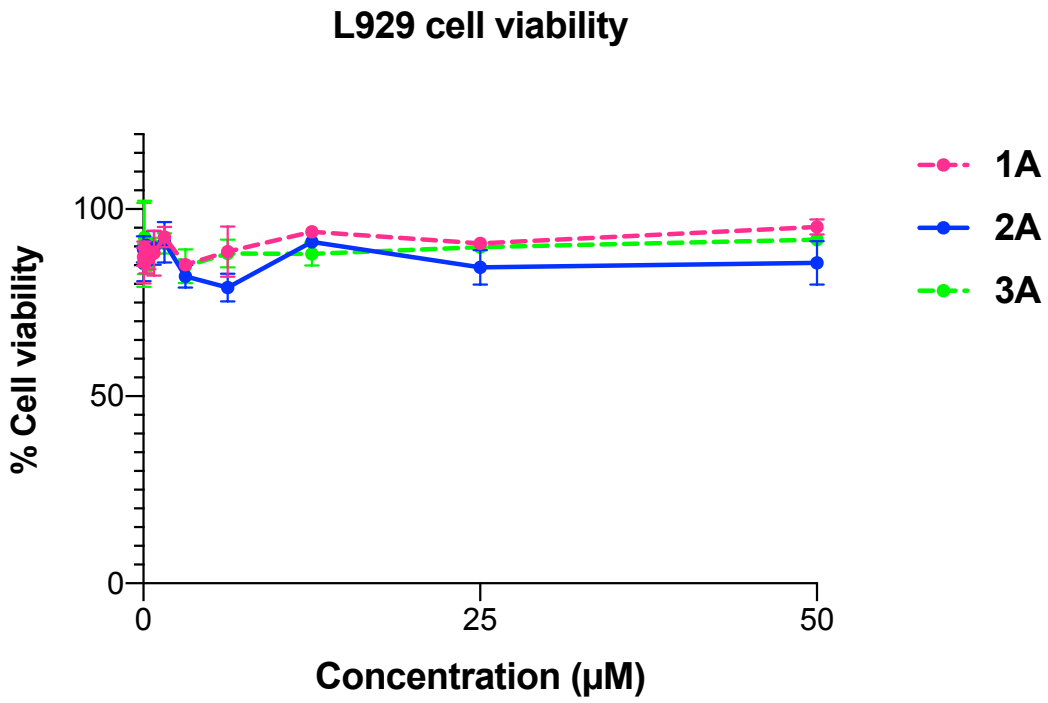


Figure S5. Percentage cell viability after treatment with complexes **1A– 3A** against L292 fibroblast cells. Dose response curves were generated over a range of concentrations (24nm – 50 µM) in the appropriate culture media from 5 mM DMSO stock solutions. All readings were compared spectroscopically to non-treated control and the percent growth inhibition calculated. All analyses were completed in triplicate.

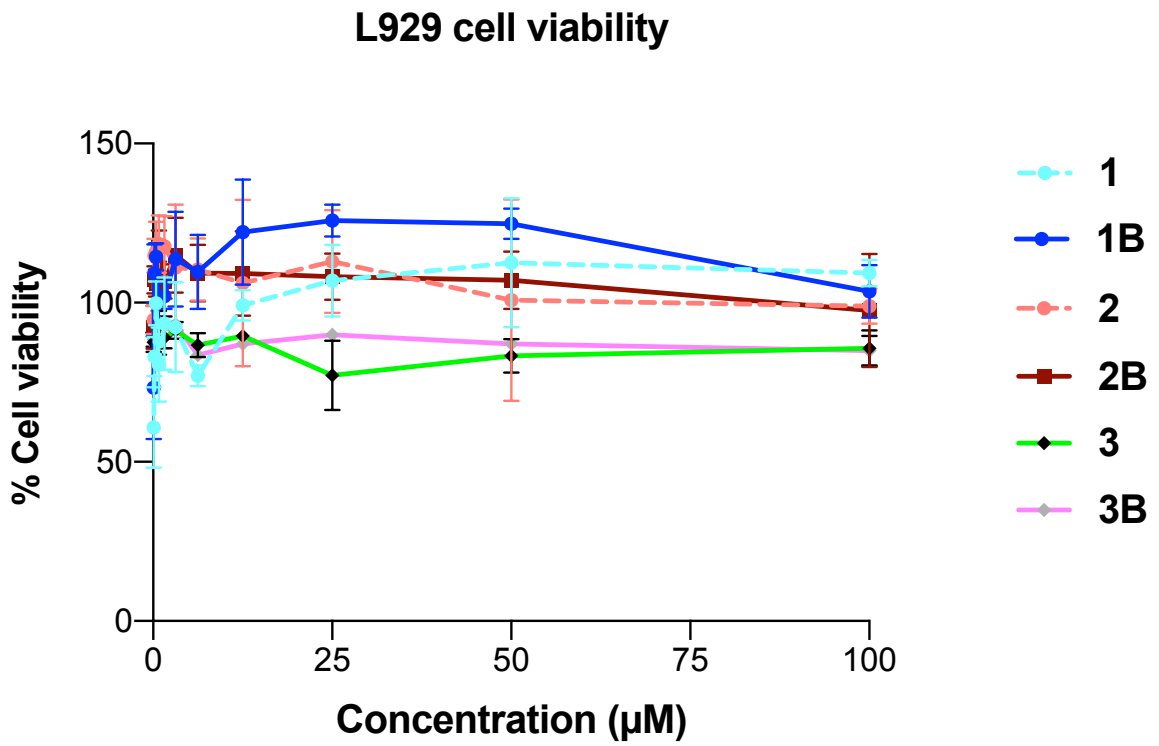


Figure S6. Comparison of percentage cell viability after treatment with complexes **1B – 3B** and free acids **1 - 3**, against L292 fibroblast cells. Dose response curves were generated over a range of concentrations (48nm – 100 µM) in the appropriate culture media from 10 mM DMSO stock solutions. All readings were compared spectroscopically to non-treated control and the percent growth inhibition calculated. All analyses were completed in triplicate.

L929 Cell viability assay

The method is same as the discussed in page number S4 under section *cell culture* and *In vitro testing of L929 cells.* The only change has been made is 10% human serum used instead of 10% Fetal Bovine Serum (FBS) as suggested by the reviewer. The results showed that the compounds are non-toxic against L929 cells with the highest tested concentration which is up to 100 µM.

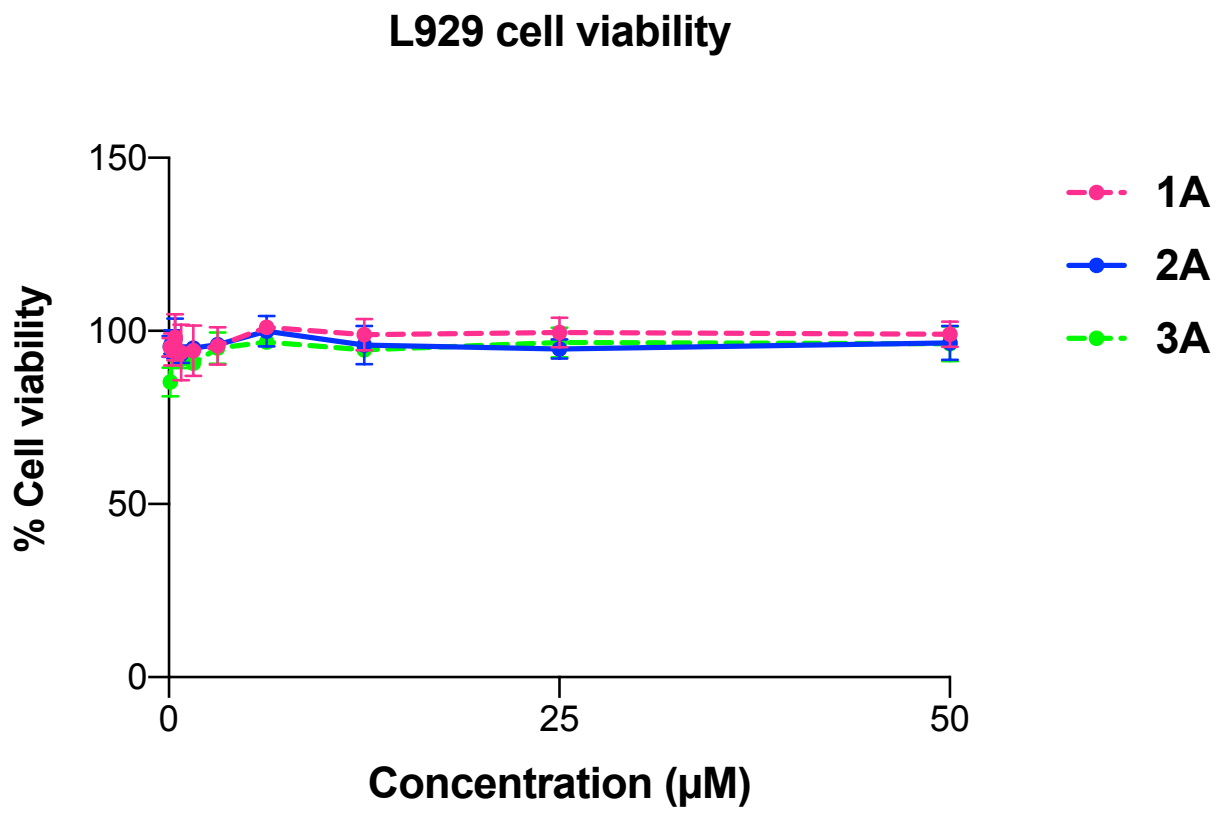


Figure S7. Percentage cell viability after treatment with complexes **1A– 3A** against L292 fibroblast cells. Dose response curves were generated over a range of concentrations (97 nm – 50 µM) in the appropriate culture media from 5 mM DMSO stock solutions. All readings were compared spectroscopically to non-treated control and the percent growth inhibition calculated. All analyses were completed in triplicate.

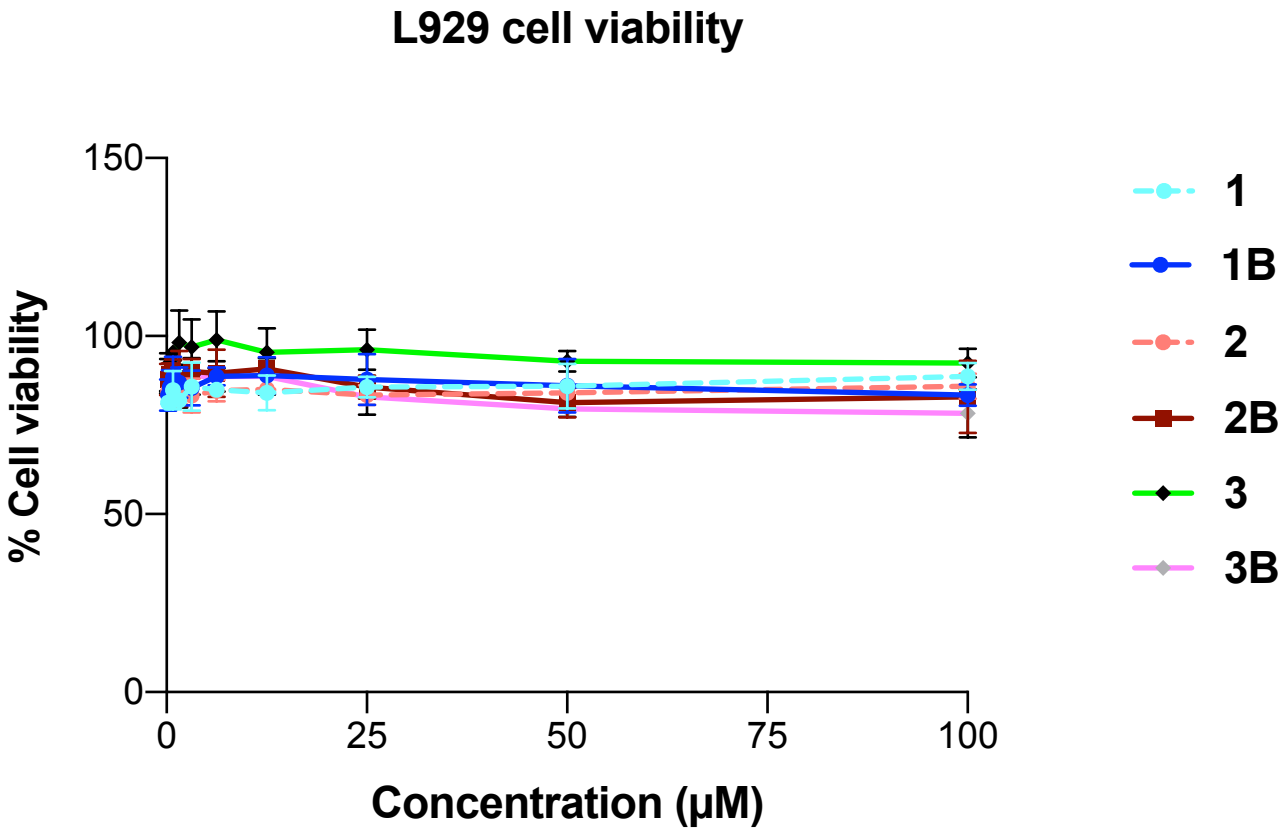


Figure S8. Comparison of percentage cell viability after treatment with complexes **1B – 3B** and free acids **1 - 3**, against L292 fibroblast cells. Dose response curves were generated over a range of concentrations (193 nm – 100 μM) in the appropriate culture media from 10 mM DMSO stock solutions. All readings were compared spectroscopically to non-treated control and the percent growth inhibition calculated. All analyses were completed in triplicate.

1. **Other analytical data**

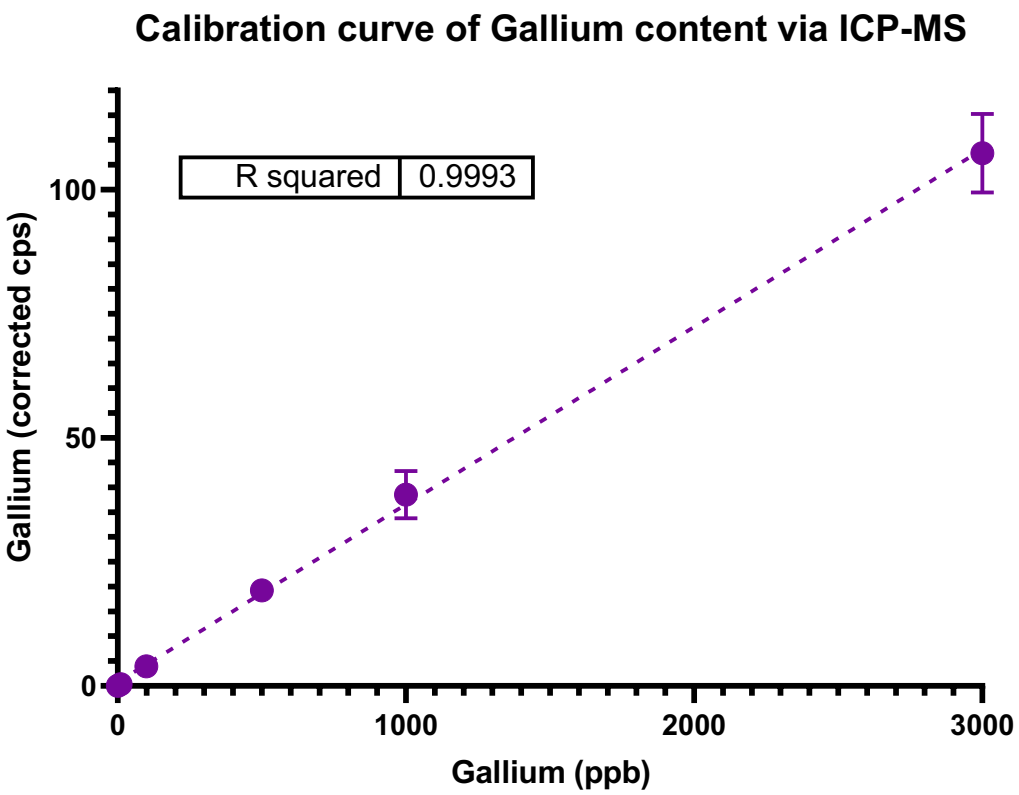


Figure S9. Calibration curve of gallium concentration in ppb measured via ICP-MS. All analyses were completed in triplicate.

2. Characterisation

Compound 1A:

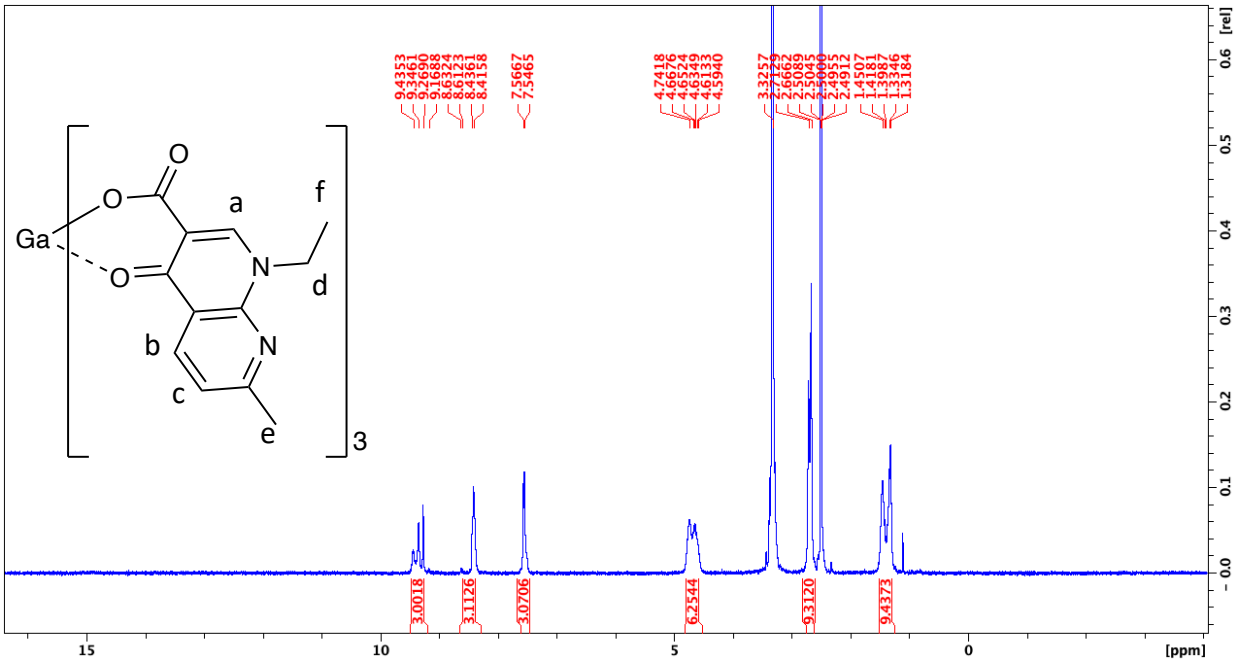


Figure S10: ^{1}H NMR (400 MHz, 298 K) of complex **1A** in d_6-DMSO

Compound 2A:

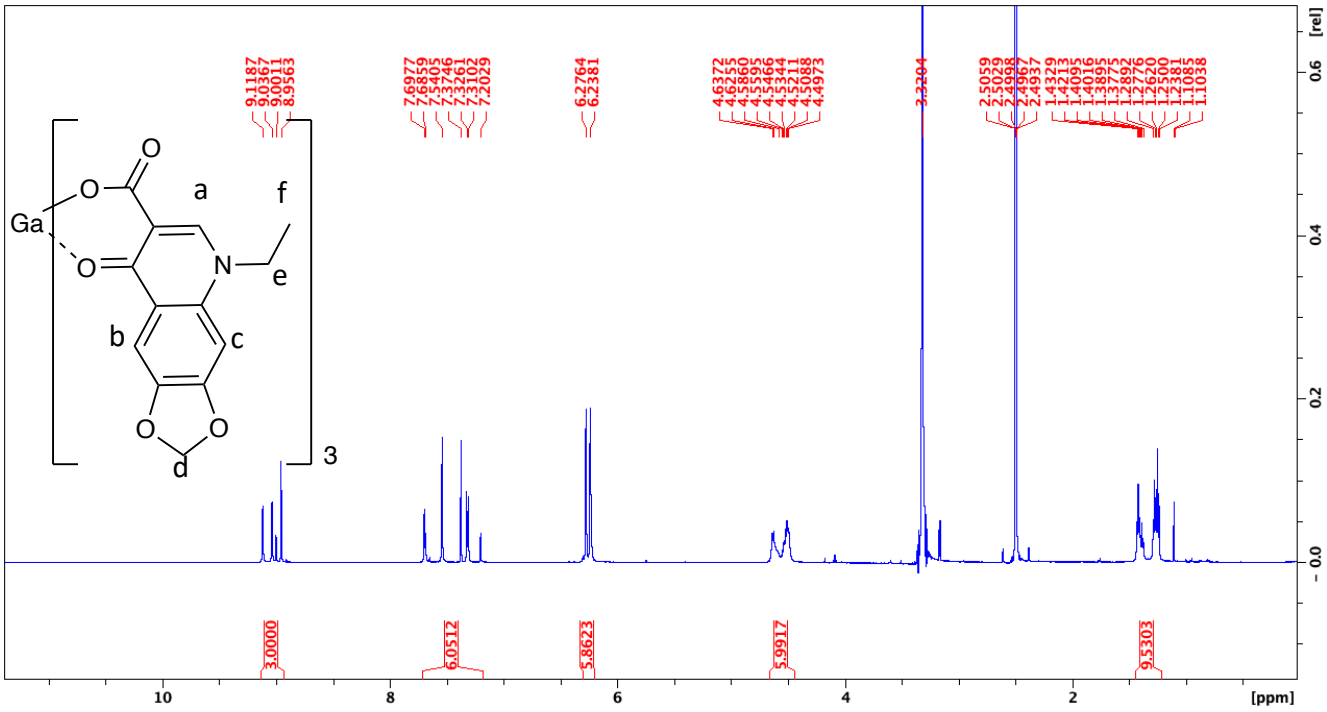


Figure S11: ^{1}H NMR (400 MHz, 298 K) of complex **2A** in d_6-DMSO

Compound 3A:

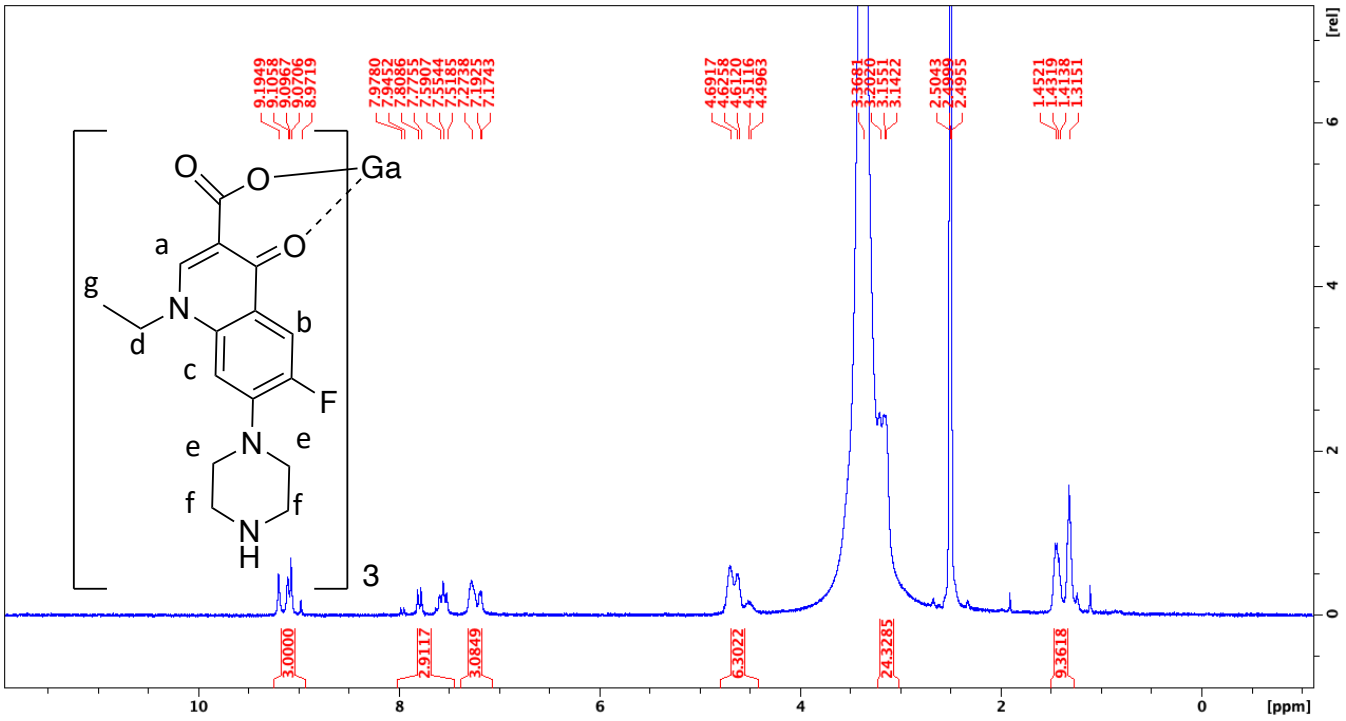


Figure S12: ^{1}H NMR (400 MHz, 298 K) of complex **3A** in d_6-DMSO

Compound 1B:

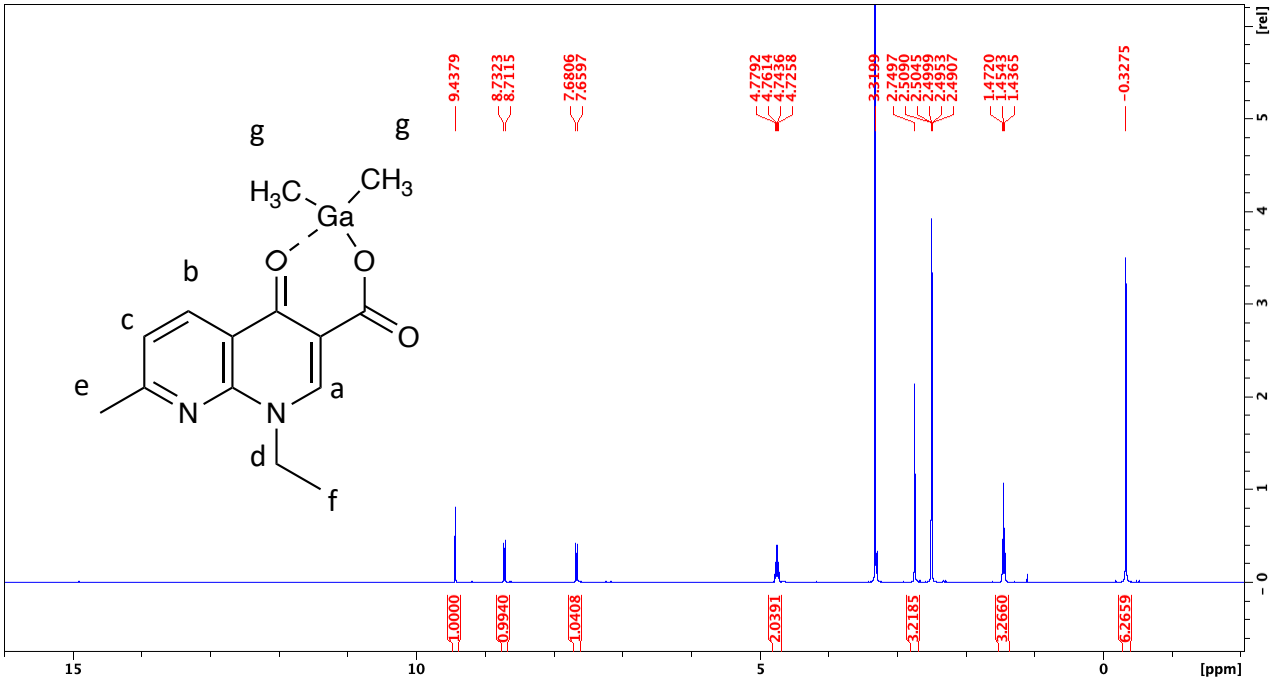


Figure S13: ^{1}H NMR (400 MHz, 298 K) of complex **1B** in d_6-DMSO

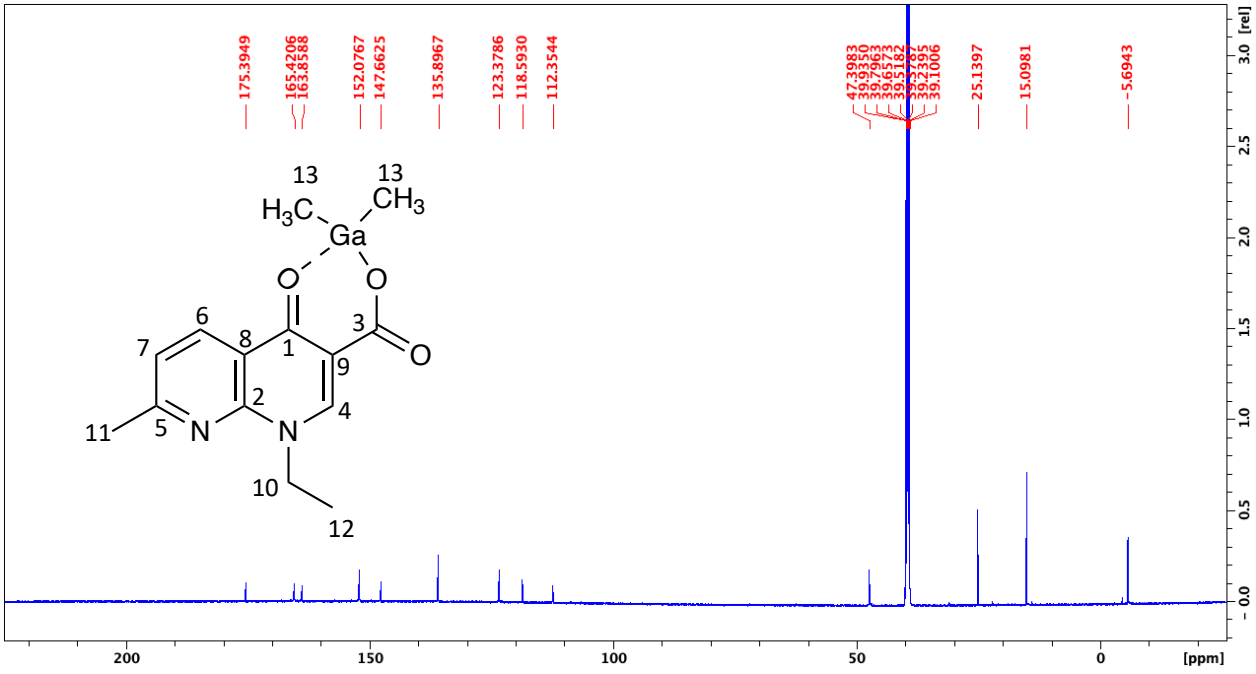


Figure S14: ^{13}C NMR (150 MHz, 298 K) of complex **1B** in d_6-DMSO

Compound 2B:

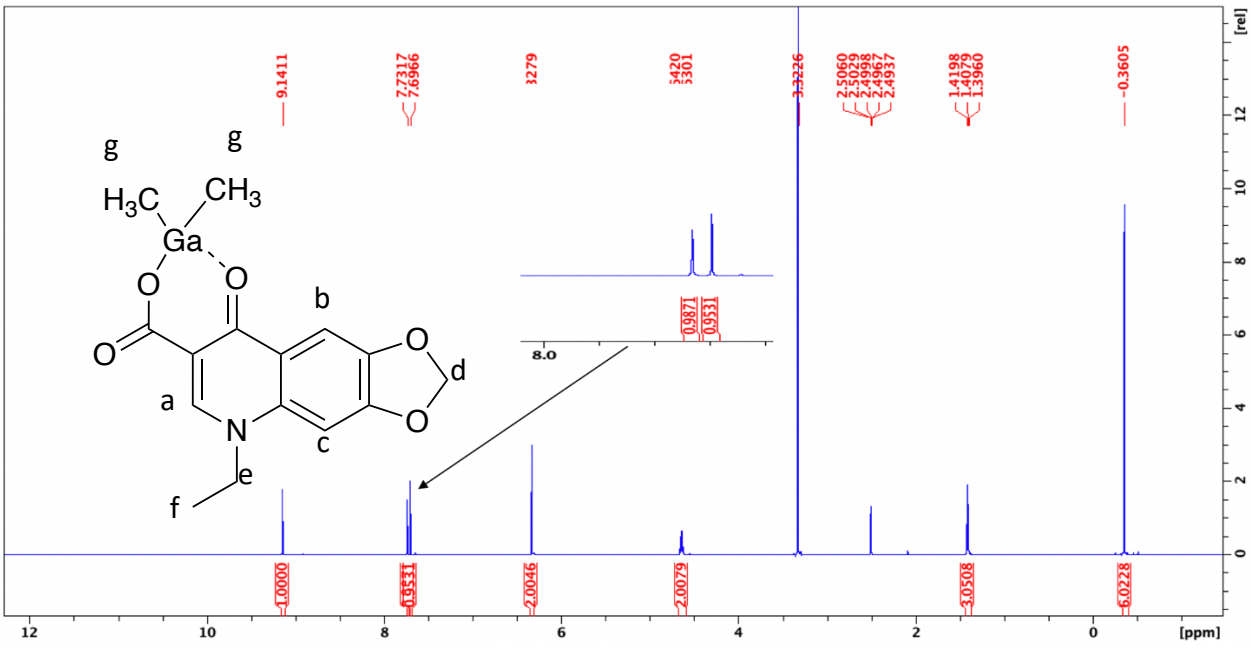


Figure S15: ^{1}H NMR (400 MHz, 298 K) of complex **2B** in d_6-DMSO

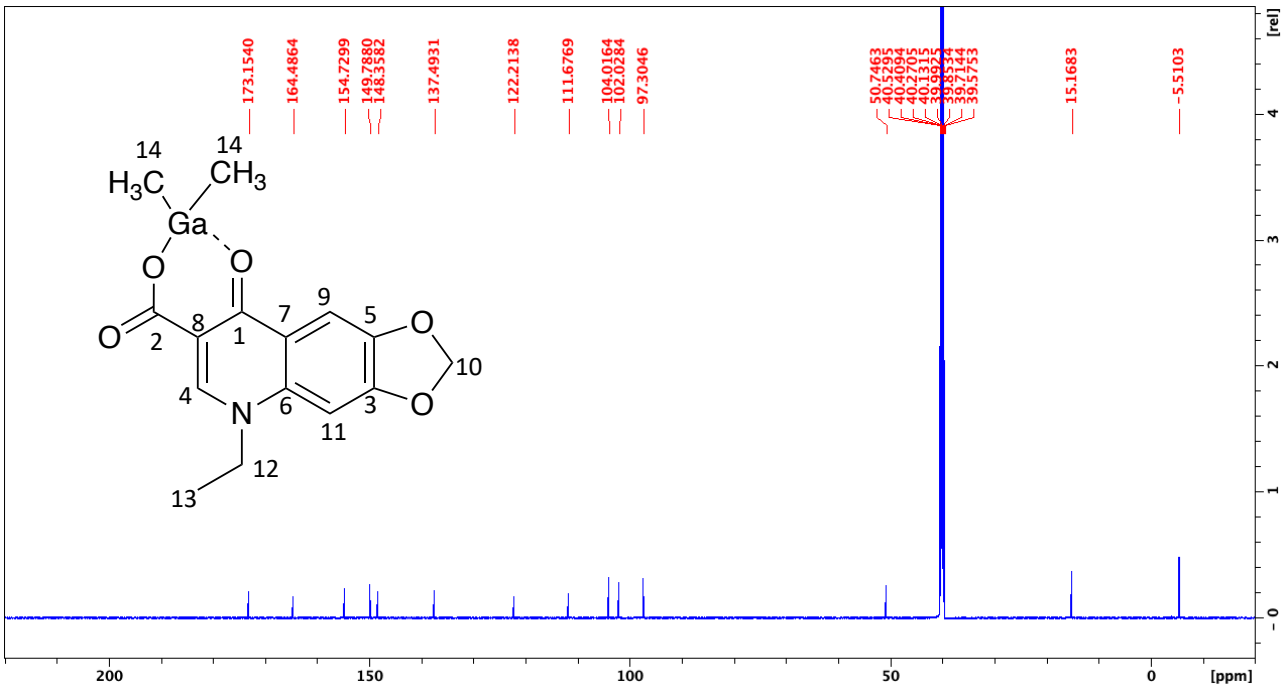


Figure S16: ^{13}C NMR (150 MHz, 298 K) of complex **2B** in d_6-DMSO.

Compound 3B:

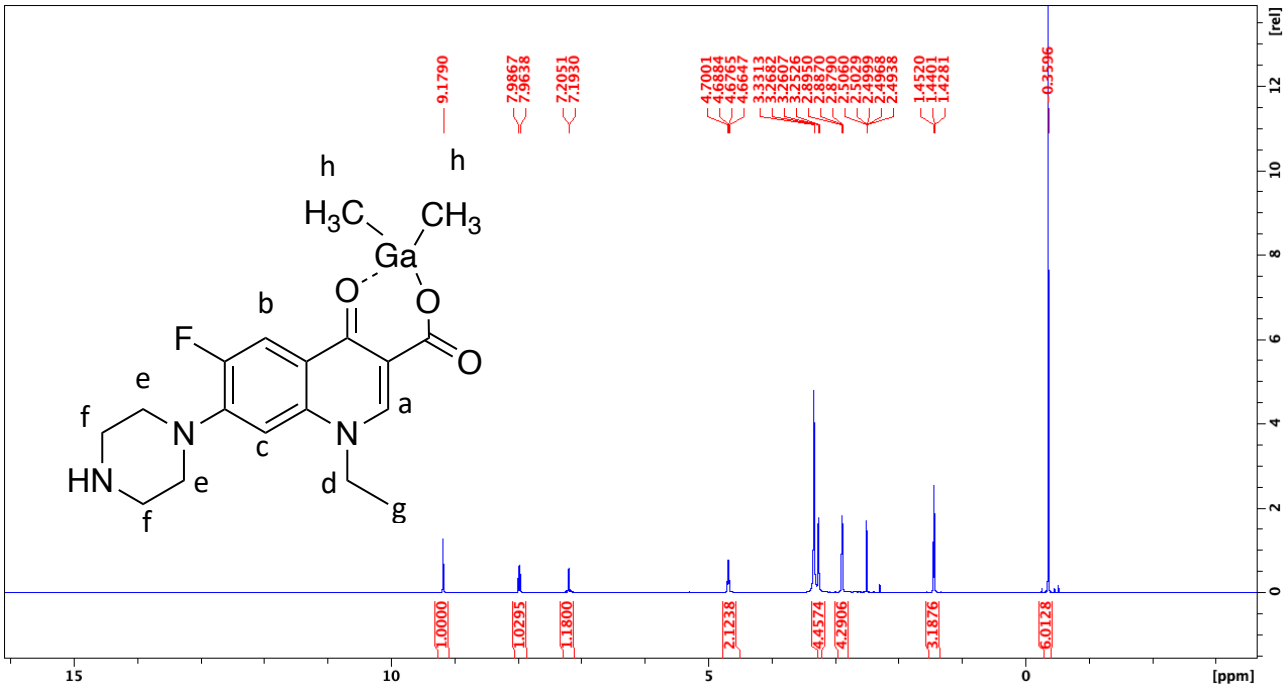


Figure S17: ^{1}H NMR (400 MHz, 298 K) of complex **3B** in d_6-DMSO

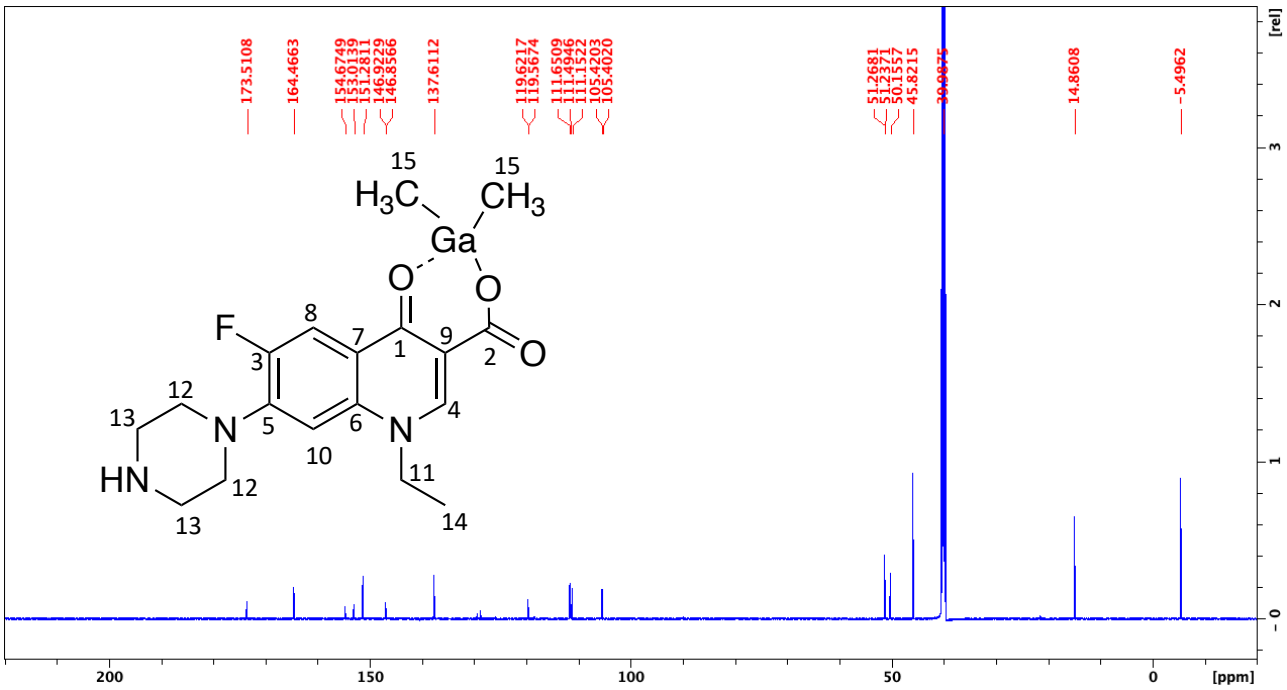
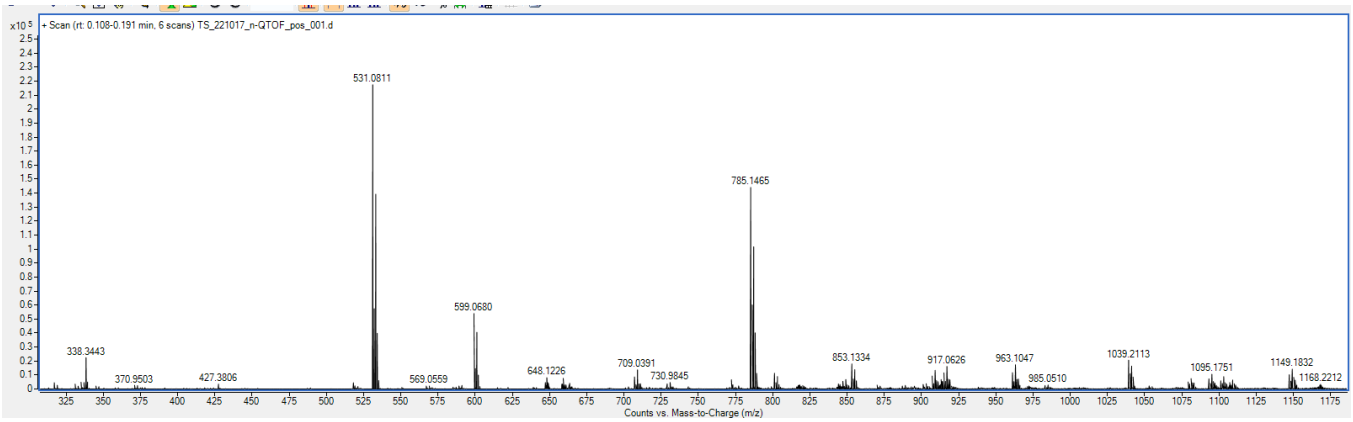
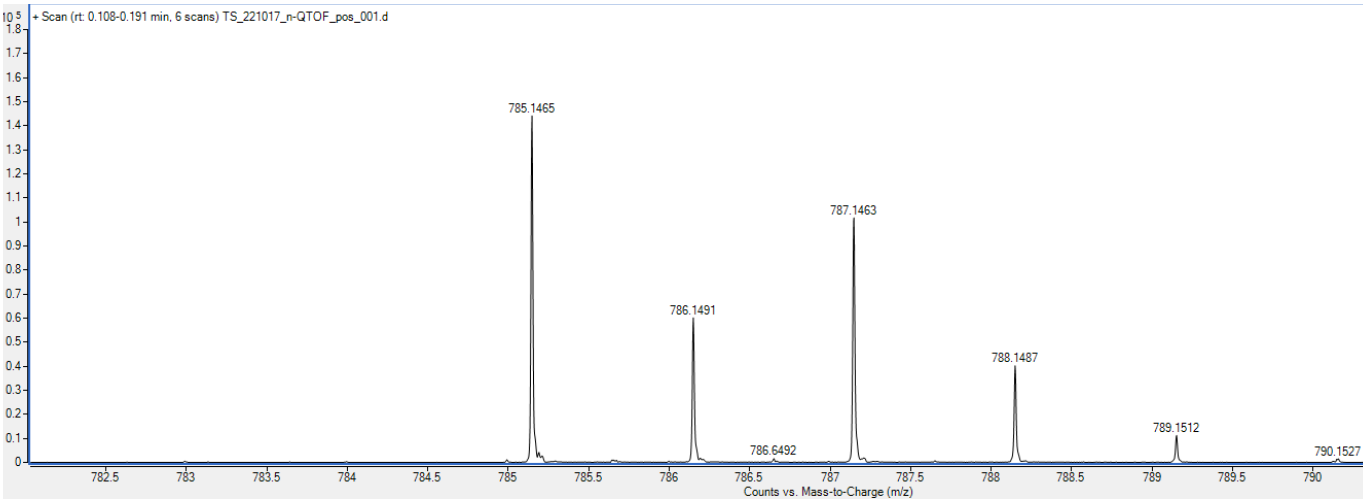


Figure S18: ^{13}C NMR (150 MHz, 298 K) of complex **3B** in d_6-DMSO

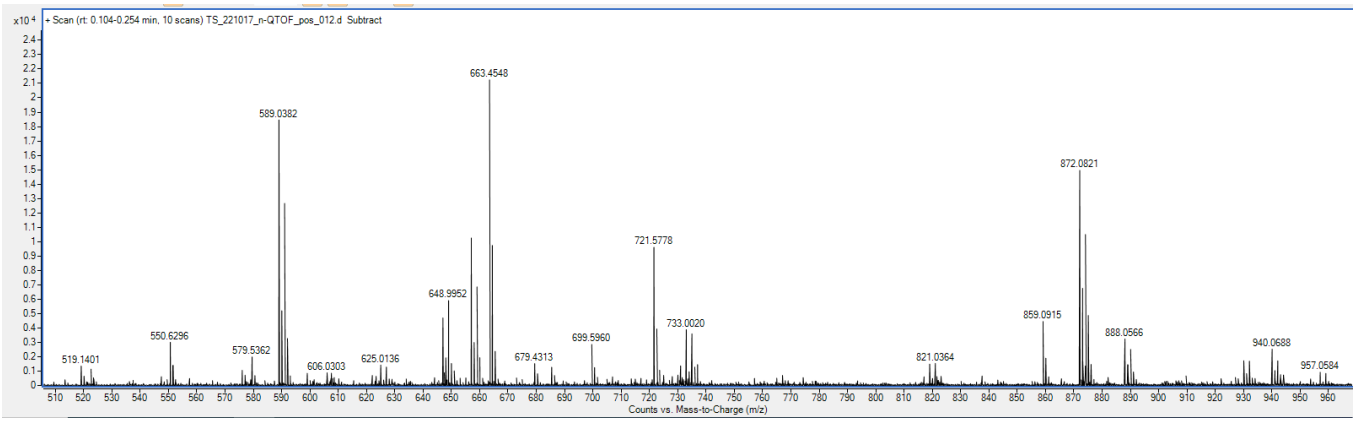
HR-MS data

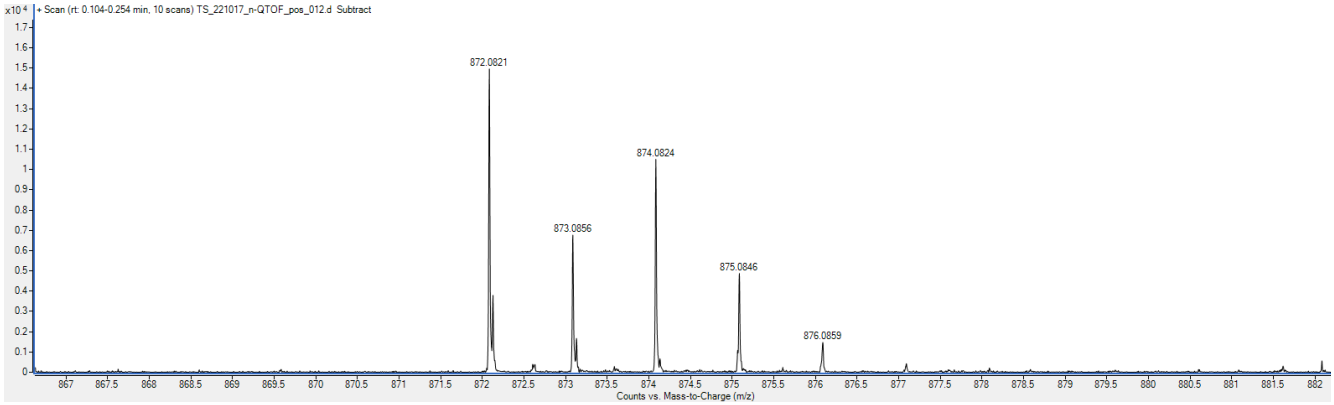
1A HR-MS:



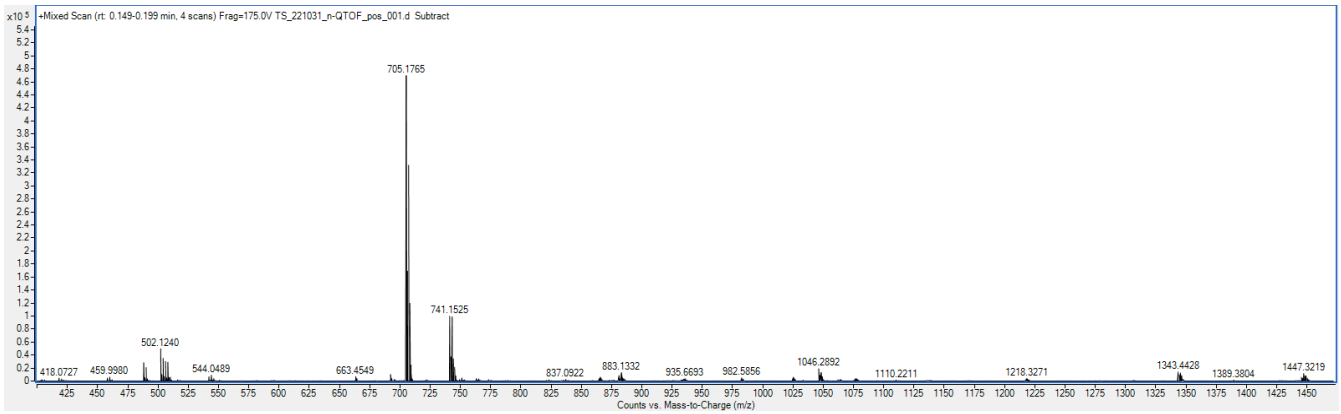


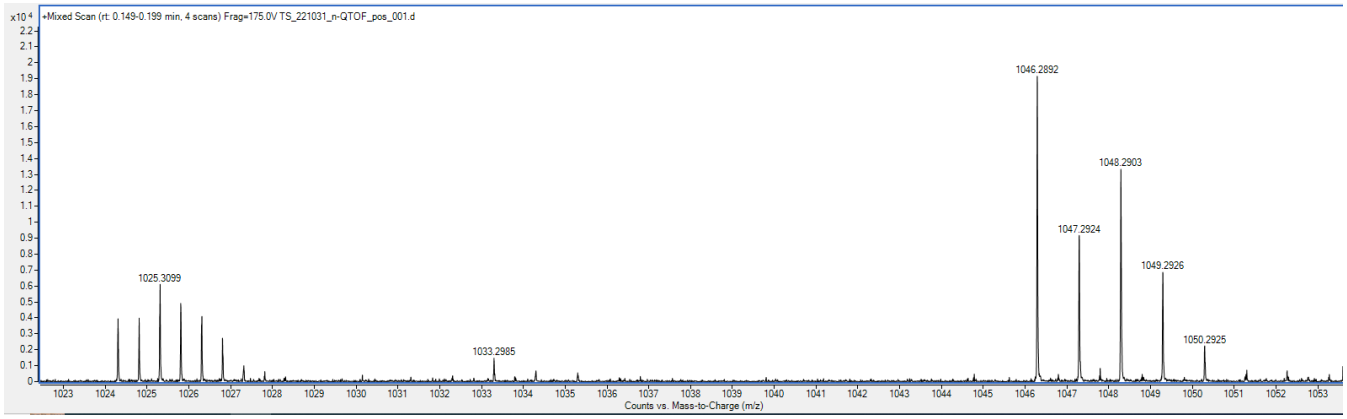
2A HR-MS:



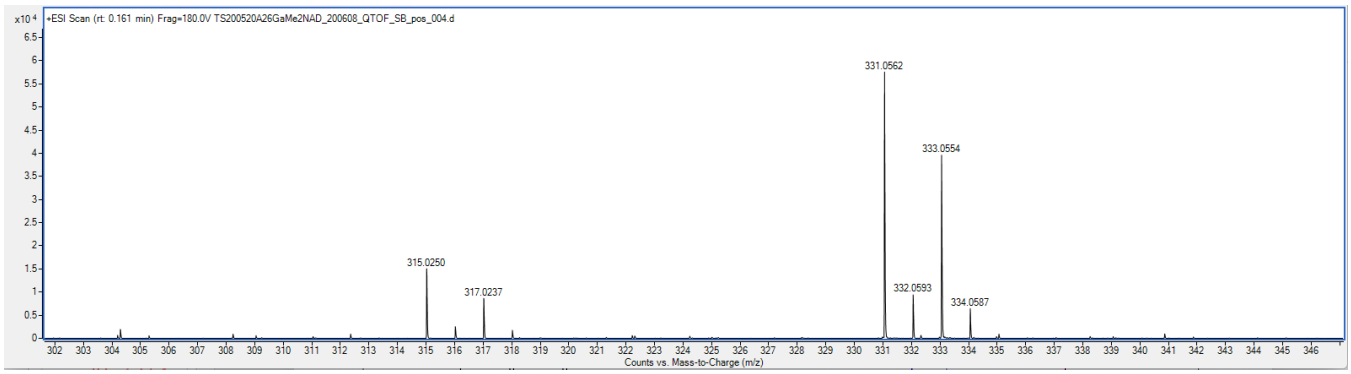

+ Scan (rt: 0.104-0.254 min, 10 scans) TS_221017_n-QTOF_pos_012.d Subtract
872.0821
874.0824
873.0856
875.0846
876.0859
Counts vs. Mass-to-Charge (m/z)

3A HR-MS:

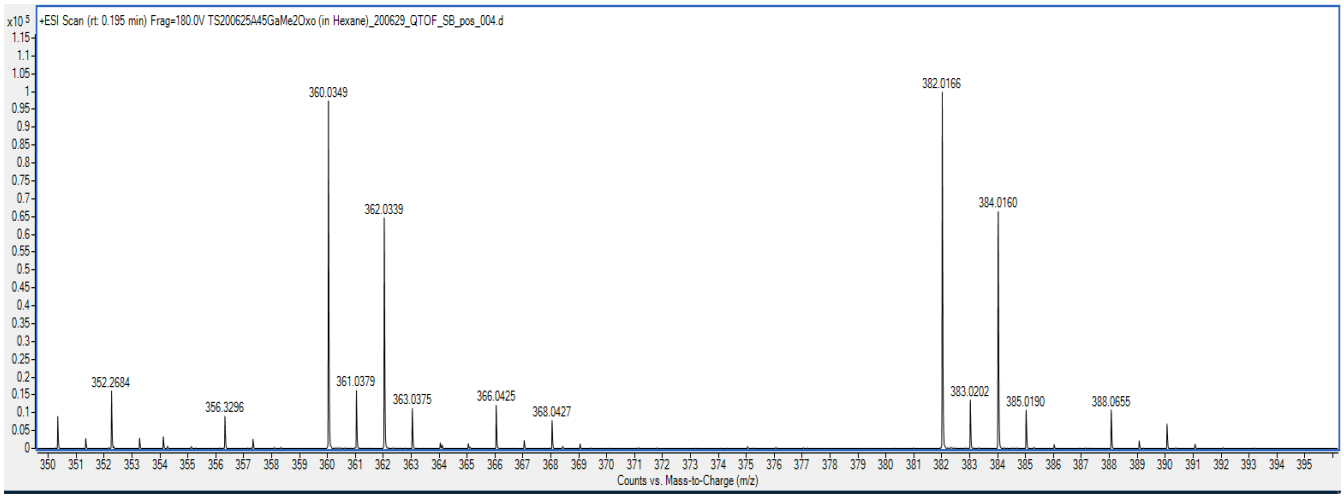

+Mixed Scan (rt: 0.149-0.199 min, 4 scans) Frag=175.0V TS_221031_n-QTOF_pos_001.d Subtract
705.1765
741.1525
502.1240
418.0727
459.9980
544.0489
663.4549
837.0922
883.1332
935.6693
982.5856
1046.2892
1110.2211
1218.3271
1343.4428
1389.3804
1447.3219
Counts vs. Mass-to-Charge (m/z)


+Mixed Scan (rt: 0.149-0.199 min, 4 scans) Frag=175.0V TS_221031_n-QTOF_pos_001.d
1046.2892
1048.2903
1047.2924
1049.2926
1025.3099
1033.2985
1050.2925
Counts vs. Mass-to-Charge (m/z)

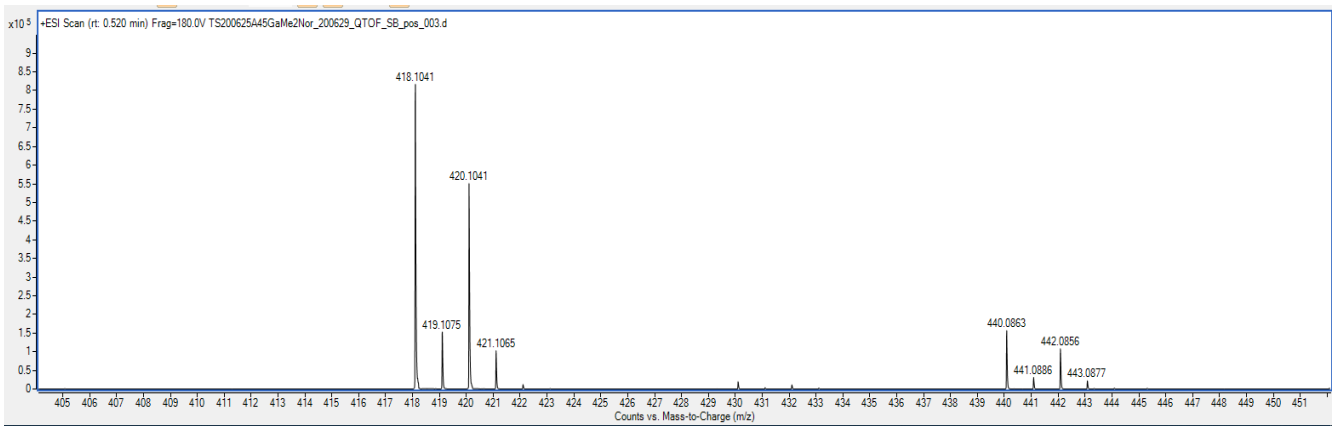
1B HR-MS:



2B HR-MS:



3B HR-MS:



3. Solution state stability

Compound 1A:

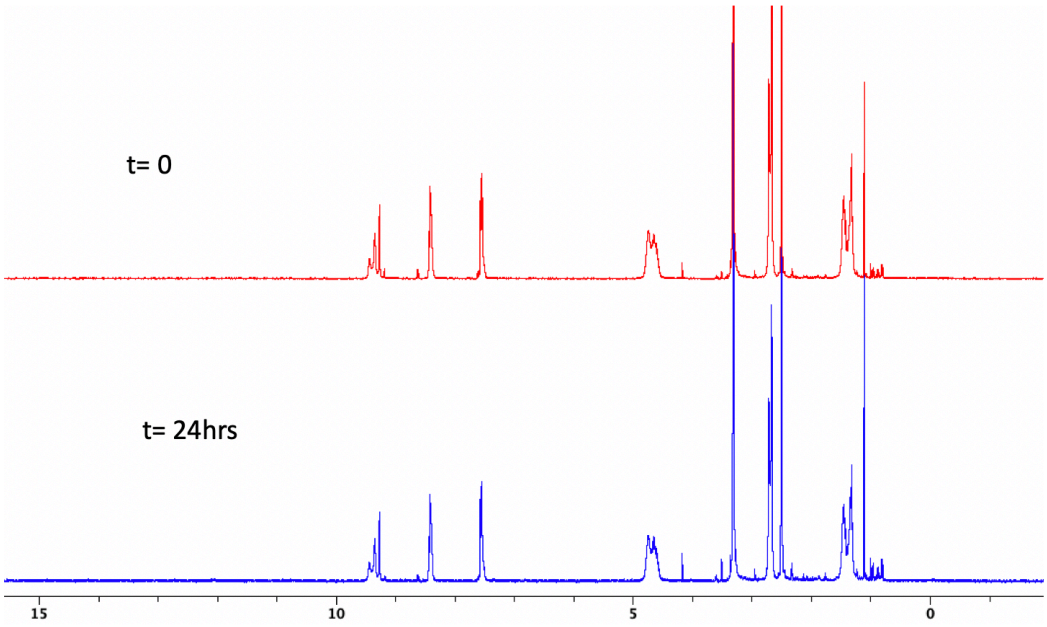


Figure S19: A representative example of ^{1}H NMR (400 MHz, 298 K) of complex **1A** in d_6-DMSO at 0 timepoint (red color) and 24 hrs timepoint (blue color)

Compound 2B:

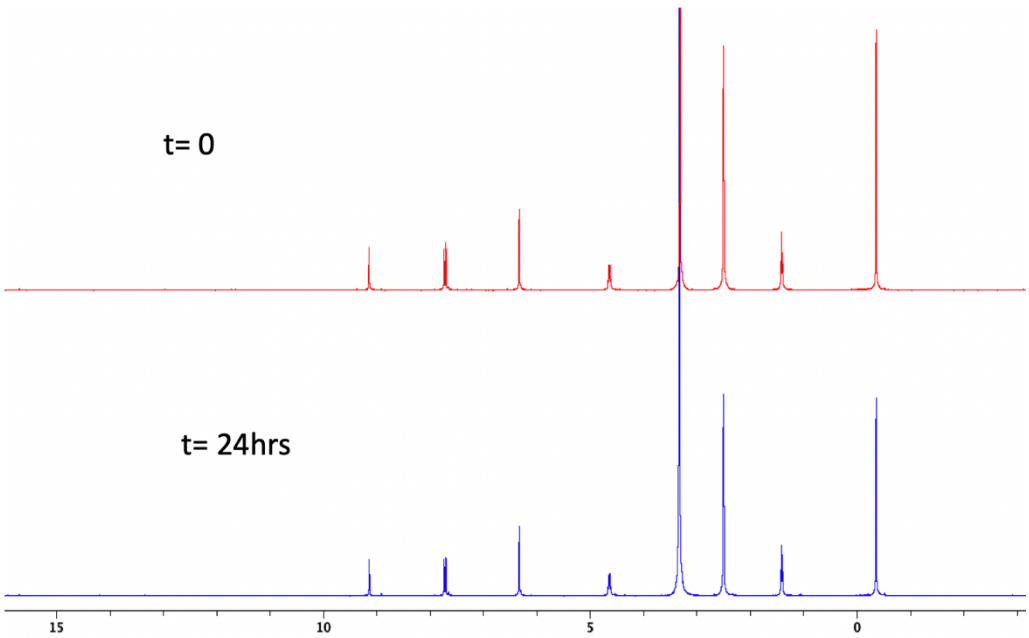


Figure S20: A representative example of ^{1}H NMR (400 MHz, 298 K) of complex **2B** in d_6-DMSO at 0 timepoint (red color) and 24 hrs timepoint (blue color)

Compound 1B:

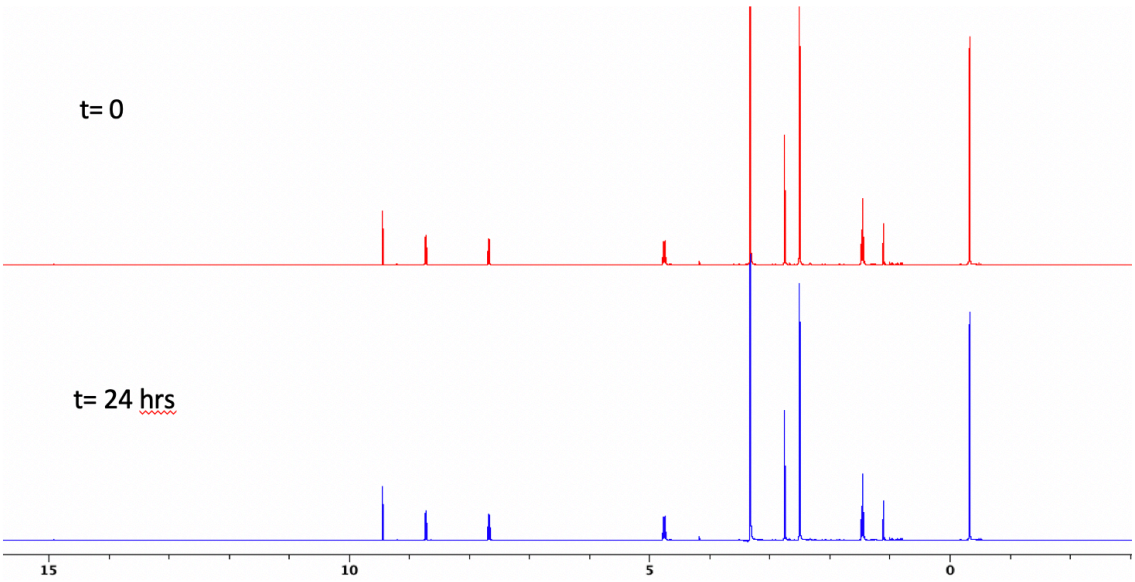


Figure S21: ^{1}H NMR (400 MHz, 298 K) of complex **1B** in d_6-DMSO at 0 timepoint (red color) and 24 hrs timepoint (blue color)

4. ICP-MS analysis

Gallium recovered total ppb 0hrs	1B - pellet	1B - Supp	1A - pellet	1A - supp	Gallium recovered total ppb 24hrs	1A - pellet	1A - Supp	1B - pellet	1B - supp
ppb	5867.1252	22641.8824	7737.4990	1547.4998		17615.1583	7600.3040	8247.4952	919.1654
Ppm	5.8671	22.6419	7.7375	1.5475		17.6152	7.6003	8.2475	0.9192
mg/mL	0.0059	0.0226	0.0077	0.0015		0.0176	0.0076	0.0082	0.0009
TOTAL Ga	0.0143		0.0093		**TOTAL**	0.0126		0.0092	
Total Ga recovered %	102.5%		66.8%		**Total Ga recovered %**	90.71%		65.95%	

Calculation example:

Gallium content in 200 µM of complex **1B** = 22.16%, therefore at 200 µM concentration of the complex **1B** in 1 mL of media at 303.0496 g/mol is 0.066 mg/mL. Therefore, there is 0.066 x (22.16/100) = 0.0139 mg/mL of total potential gallium.
At 0hrs, the total gallium in supernatant and pellet is 0.014mg/mL, therefore 102.5% gallium recovered. Errors associated with pipetting of sample may account for this. At 24 hrs for **1B** the total gallium recovered is 91%.
Complex **1A** had minor issues with precipitation after the protein digestion was completed, samples were filtered using 0.22-micron syringe filters prior to ICP-MS analysis to prevent blockage of the nebulizer. This may account for the ~30% loss of total gallium. All percentages were therefore normalised to the total gallium recovered.

Note: Product specification sheet does not list the total transferrin content however studies into healthy humans have determined that there is approximately 2.0 – 3.0g/L of transferrin in human serum. 1 mg of transferrin will bind approximately 1.4 µg of iron.[3] The iron content in the human serum based on Sigma Aldrich's specification sheet is listed at 35 – 180 ug/dl. Please refer to Sigma Aldrich product code H4522-100ML for further details.

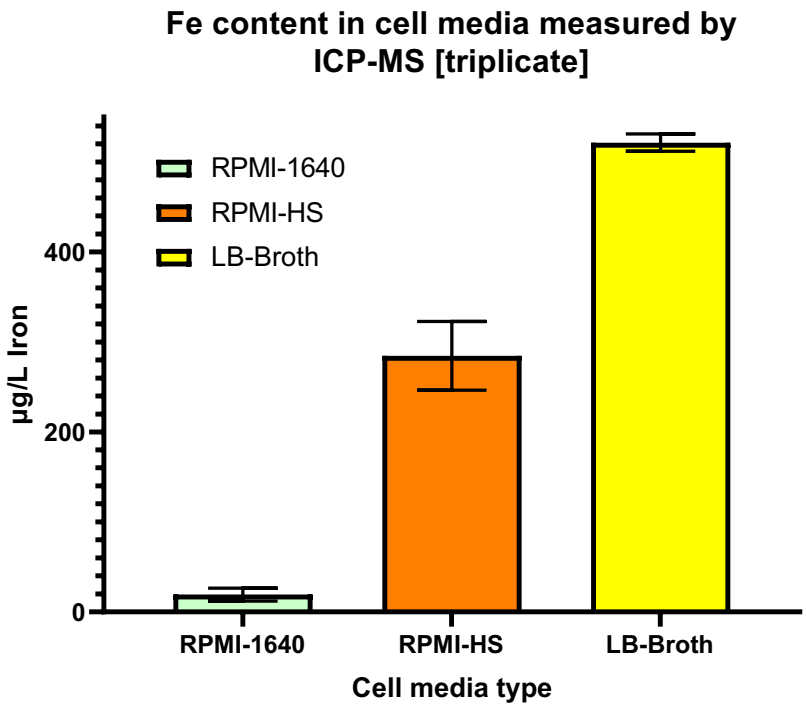


Figure S22. ICP-MS analysis of the total iron content in different cell media.

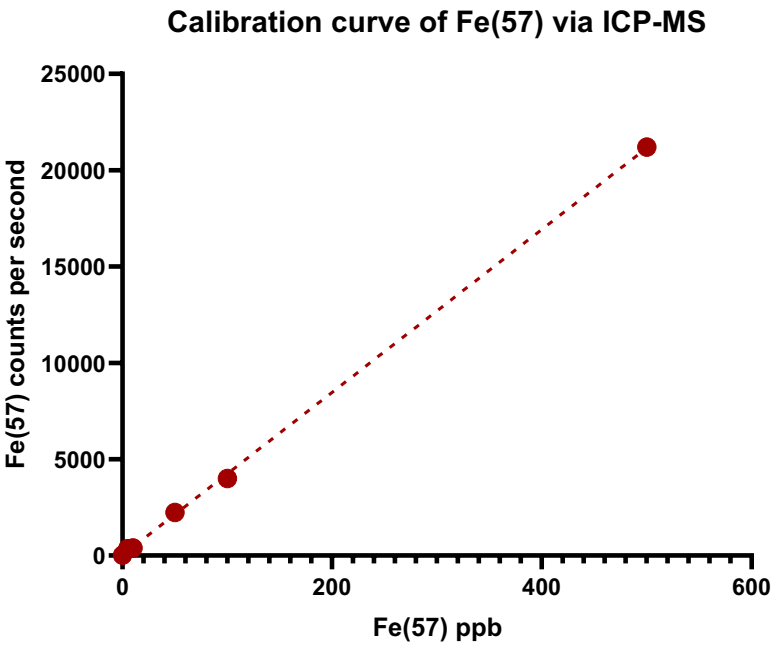


Figure S23. Calibration curve of Fe(57) measure via ICP-MS

Table S12. Total iron content in cell medias analysed via ICP-MS

Media type	Total iron content (µg/L)
RPMI-1640	19.26 ± 7.160
RPMI-1640 + 10% human serum	284.5 ± 38.23
LB-Broth	521.4 ± 9.619

5. References for supporting information

1. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. Howard, H. Puschmann, *J. Appl. Crystallograph.* 2009, **42**, 339-341.
2. K. D. Mjos, J. F. Cawthray, E. Polishchuk, M. J. Abrams and C. Orvig, *Dalton Trans.*, 2016, **45**, 13146-13160.
3. M. Worwood, A. M. May, B. J. Bain, in *Dacie and Lewis Practical Haematology (Twelfth Edition)* (Eds.: B. J. Bain, I. Bates, M. A. Laffan), Elsevier, **2017**, pp. 165-186.