Electronic Supplementary Material (ESI) for Metallomics.

Biological activity of manganese(I) tricarbonyl complexes on multidrug-resistant Gram-negative bacteria: From functional studies to *in vivo* activity in *Galleria mellonella*

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Supporting Information

Ligand synthesis

Bis(2-pyridinylmethyl)(2-quinolinylmethyl)amine (bpqa, 3).[1] To a solution of 2-(chloromethyl)quinoline hydrochloride (0.22 g, 1.03 mmol) in deionized water (1 mL) was added a saturated solution of potassium carbonate (152 mg, 1.10 mmol) in water (1 mL). To this suspension, dichloromethane (2 mL) was added to obtain a clear solution. The aqueous phase was discarded and tetrahydrofuran (10 mL), triethylamine (0.2 mL) and bis(2-pyridinylmethyl)amine (200 mg, 1.00 mmol) were added and stirred for 3 d at room temperature. Then, the solvent was removed under vacuum and the brown residue purified by column chromatography on standardized neutral aluminium oxide 90 (Merck, Brockmann grade 1) as the stationary phase and ethyl acetate as the eluent. The product was obtained as a white to yellowish solid material. Yield: 25% (85.0 mg, 0.25 mmol). **IR** (ATR): $\tilde{\nu}$ = 3014 (w), 2978 (w), 2813 (m), 1590 (vs), 1475 (s), 1435 (s), 1121 (m), 824 (s), 762 (vs) cm^{-1}; **^{1}H NMR** (199.93 MHz, $CDCl_3$): δ = 8.52 (d, 2H, ^3J = 4.8 Hz, py-H6) , 8.12 (d, 1H, ^3J = 8.5 Hz, qui-H4), 8.04 (d, 1H, ^3J = 8.5 Hz, qui-H7), 7.82–7.44 (m, 8H, py-H3/5+qui-H3/H8/H9/H10), 7.18–7.08 (m, 2H, py-H4), 4.04 (s, 2H, qui-CH_2), 3.92 (s, 4H, py-CH_2) ppm; **^{13}C NMR** (125.75 MHz, $CDCl_3$): δ = 160.2 (qui-C2), 159.3 (py-C2), 149.1 (py-C6), 147.6 (qui-C6), 136.4 (py-C4), 136.4 (qui-C4), 129.4 (qui-C3), 129.1 (qui-C9), 127.5 (qui-C10), 127.4 (qui-C5), 126.2 (qui-C7), 123.1 (py-C3), 122.0 (py-C5), 121.0 (qui-C8), 60.9 (qui-CH$_2$), 60.3 (py-CH$_2$) ppm; **Elemental analysis** (%) calcd. for $C_{22}H_{20}N_4 \cdot 0.25\ H_2O$: C 76.61, H 5.99, N 16.24, found (%): C 76.17, H 6.38, N 15.69.

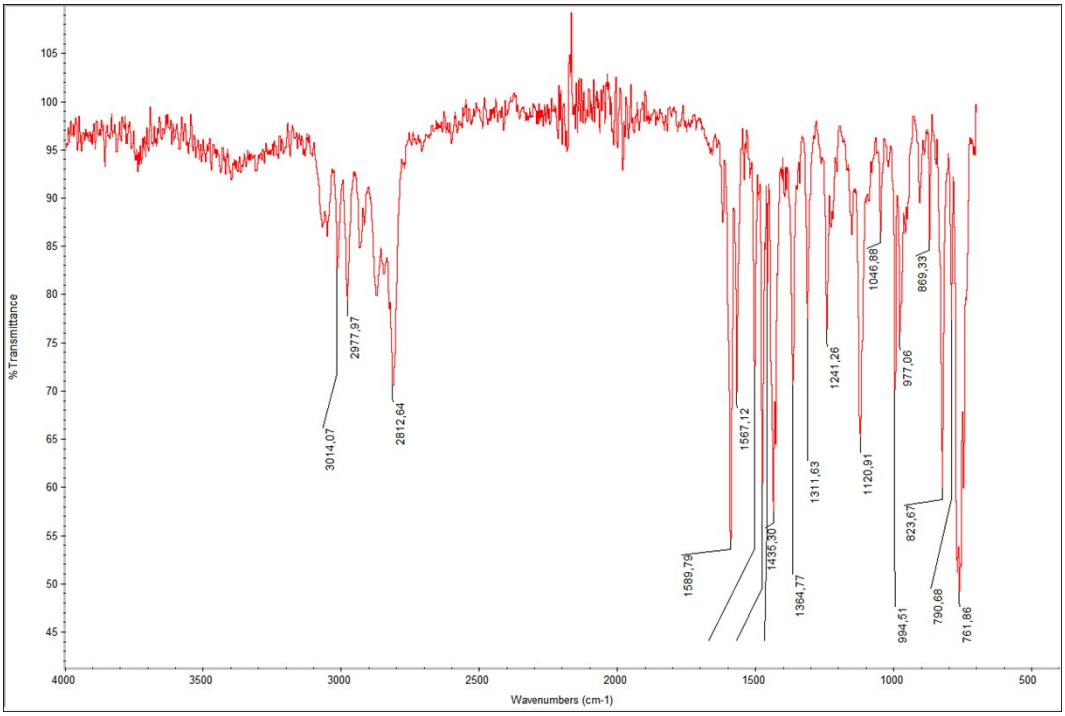

Figure S1. ATR IR spectrum of bpqa (**3**).

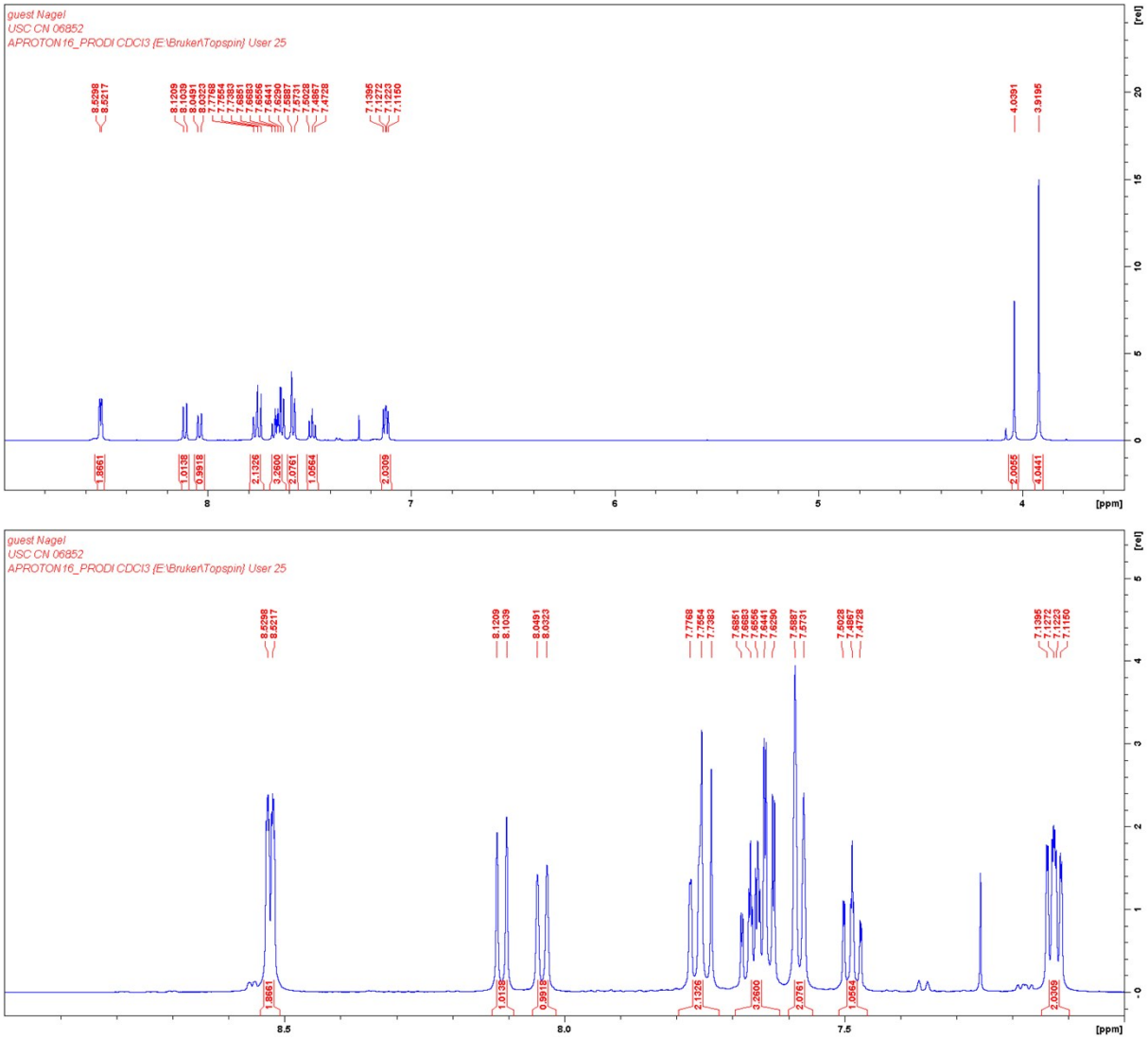

Figure S2. 200 MHz ^{1}H NMR spectrum of bpqa (**3**) in $CDCl_3$.

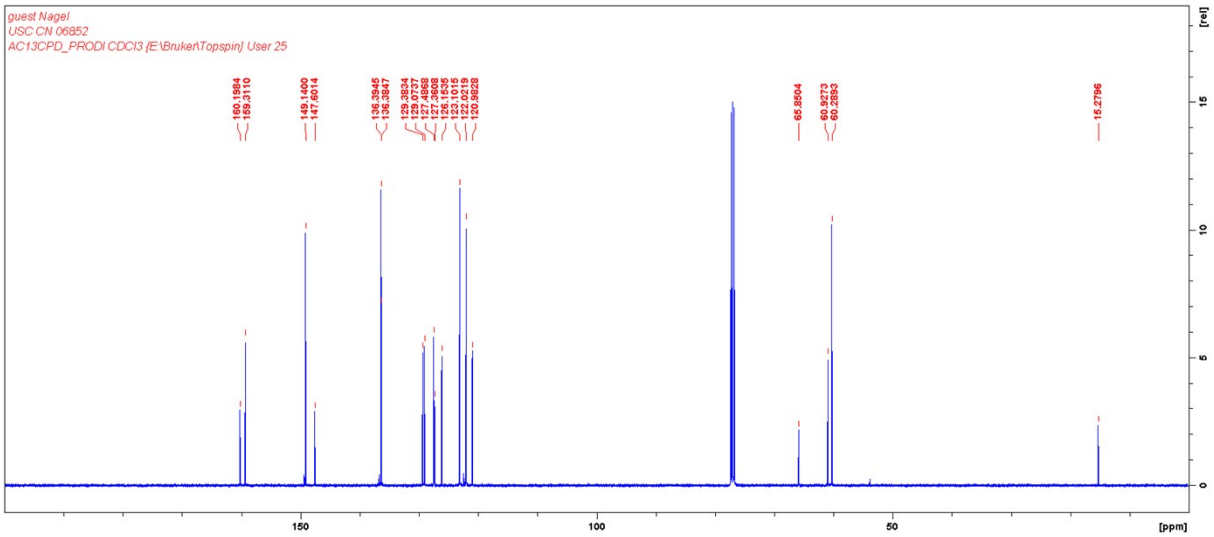

Figure S3. 125 MHz ^{13}C NMR spectrum of bpqa (**3**) in $CDCl_3$.

Bis(2-quinolinylmethyl)(2-pyridinylmethyl)amine (bqpa, 4).[1] 2-(Chloromethyl)quinoline hydrochloride (2.00 g, 9.34 mmol) was dissolved in deionized water (5 mL) and cooled in an ice bath. After addition of 5.3 M sodium hydroxide (5 mL), the reaction mixture was stirred for 5 min. Then, a solution of (2-pyridinylmethyl)amine (0.50 mL, 0.52 g, 4.81 mmol) in dichloromethane (10 mL) was added and the ice bath removed. Over 4 d of stirring, additional 5.3 M sodium hydroxide (5 mL) was added in small portions. The reaction mixture was then washed with 4.4 M sodium hydroxide (10 mL) and the organic phase separated and dried over magnesium sulphate. After removal of the solvent under vacuum, the brown residue was treated with diethylether (45 mL). This resulted in the precipitation of a white solid, which was collected by filtration and dried under vacuum to obtain the product as a white powder. Yield: 26% (493.0 mg, 1.26 mmol). **IR** (ATR): $\tilde{\nu}$ = 3059 (w), 2816 (w), 1601 (m), 1503 (s), 1426 (s), 1116 (m), 994 (m), 825 (s), 756 (s) cm^{-1}; **^{1}H NMR** (500.13 MHz, $CDCl_3$): δ = 8.56 (d, 1H, ^3J = 4.8 Hz, py-H6), 8.14 (d, 2H, ^3J = 8.5 Hz, qui-H4), 8.08 (d, 2H, ^3J = 8.3 Hz, qui-H7), 7.80 (d, 2H, ^3J = 8.2 Hz, qui-H10), 7.77 (d, 2H, ^3J = 8.5 Hz, qui-H3), 7.68–7.66 (m, 3H, pyH4+qui-H9), 7.61 (d, 1H, ^3J = 7.9 Hz, py-H3), 7.50 (ddd, 2H, ^3J = 8.1 Hz, ^4J = 6.9 Hz, ^5J = 1.2 Hz, qui-H8), 7.15 (ddd, 1H, ^3J = 7.4 Hz, ^4J = 4.9 Hz, ^5J = 1.3 Hz, py-H4), 4.11 (s, 4H, qui-CH_2), 3.99 (s, 2H, py-CH_2) ppm; **^{13}C NMR** (125.75 MHz, $CDCl_3$): δ = 160.1 (qui-C2), 159.2 (py-C2), 149.2 (py-C6), 147.6 (qui-C6), 136.4 (py-C4+qui-C4), 129.4 (qui-C9), 129.1 (qui-C10), 127.5 (qui-C7), 127.4 (qui-C5), 126.2 (qui-C8), 123.3 (py-C3), 122.1 (py-C5), 121.1 (qui-C3), 61.1 (qui-*C*H_2), 60.5 (py-*C*H_2) ppm; **Elemental analysis** (%) calcd. for $C_{26}H_{22}N_4$: C 79.97, H 5.68, N 14.35, found (%): C 79.69, H 5.84, N 14.34.

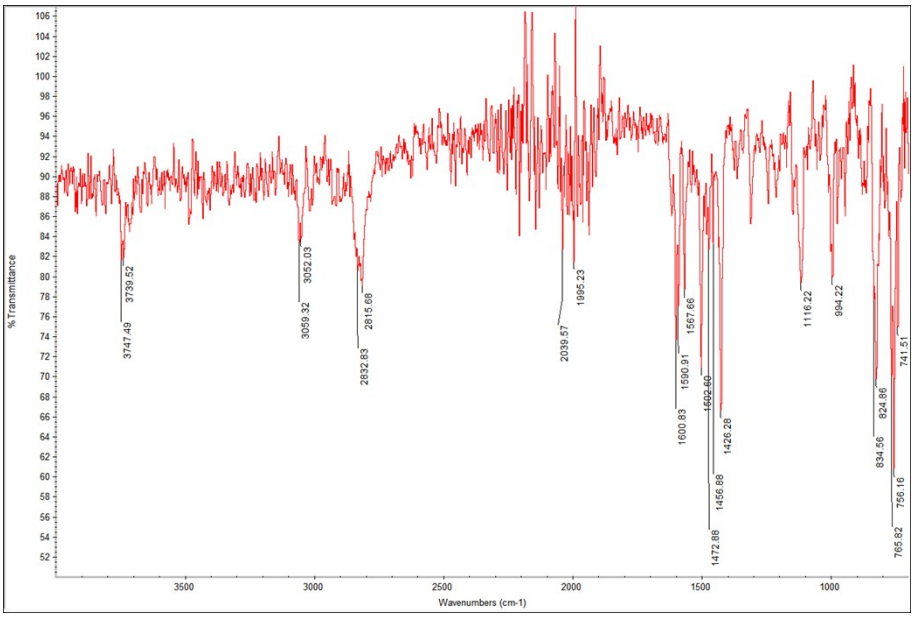

Figure S4. ATR IR spectrum of bqpa (**4**).

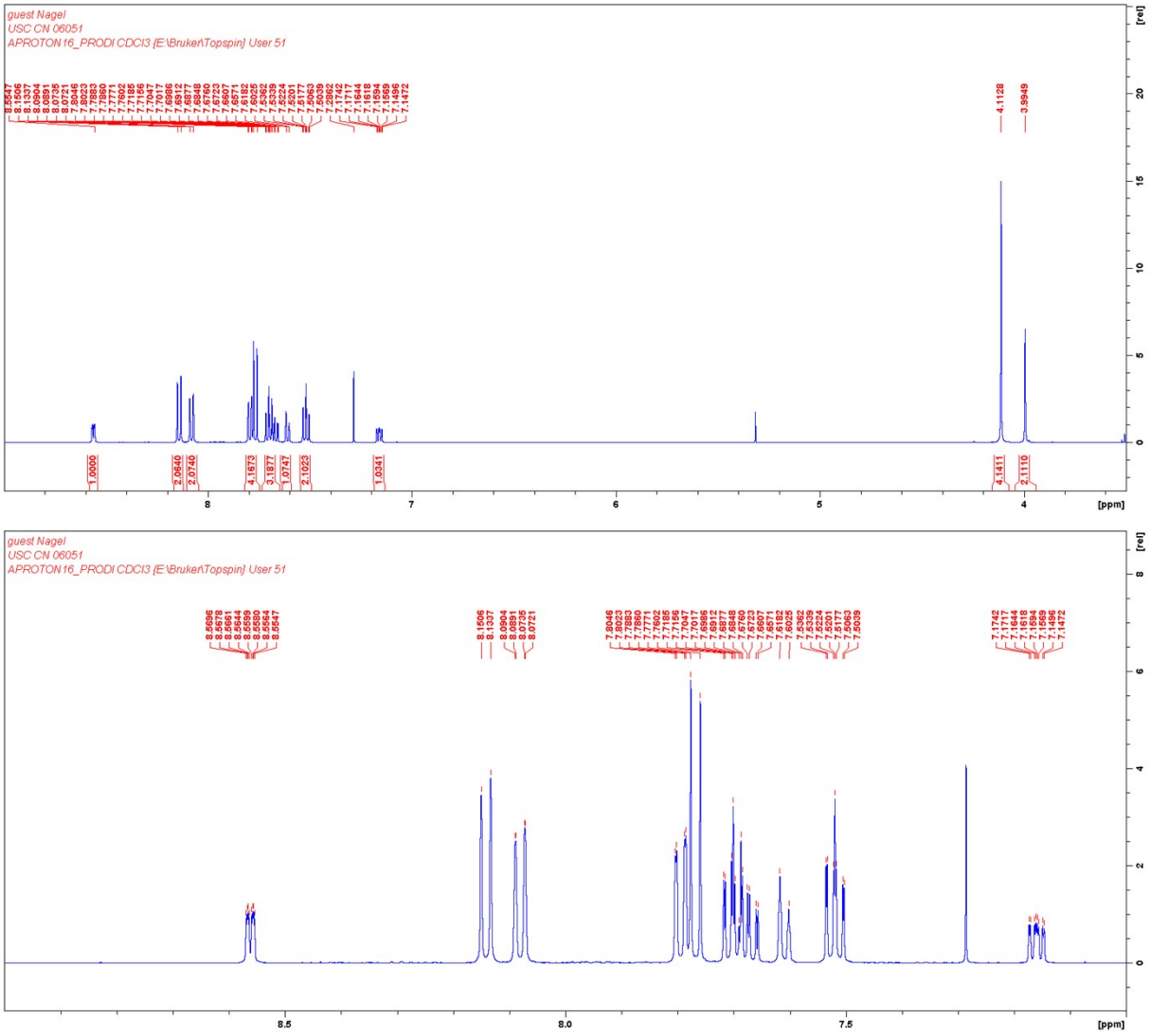

Figure S5. 500 MHz ^{1}H NMR spectrum of bqpa (**4**) in $CDCl_3$.

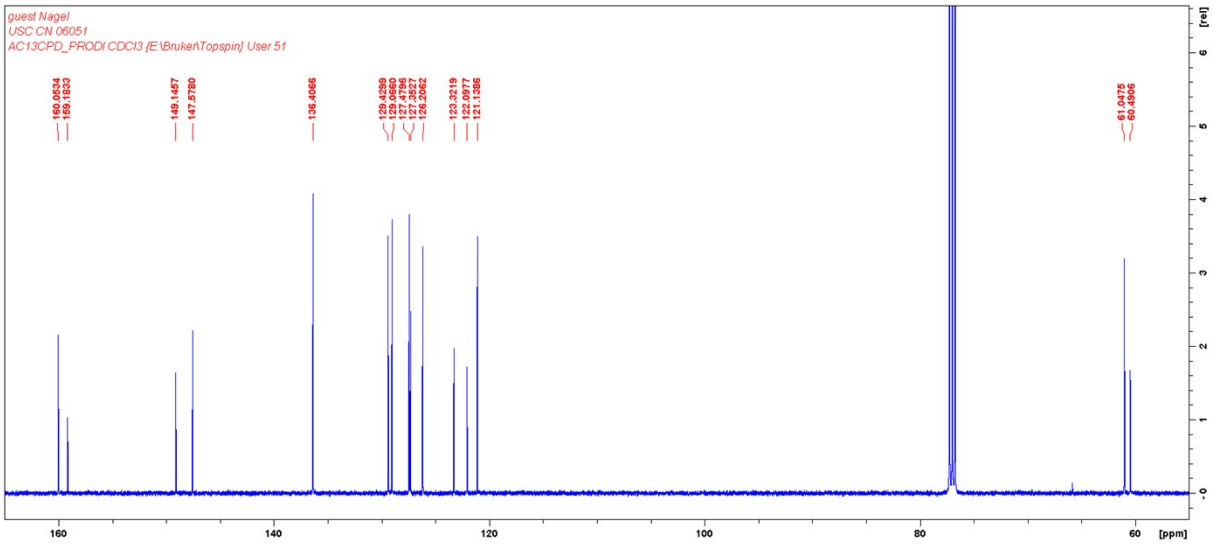

Figure S6. 125 MHz ^{13}C NMR spectrum of bqpa (**4**) in $CDCl_3$.

Tris(2-quinolinylmethyl)amine (tqa, 5).[1] To a solution of 2-(chloromethyl)-quinoline (2.00 g, 9.34 mmol) and 25% aqueous ammonium hydroxide (7.2 mL, 3.4 mmol) in tetrahydrofuran (12 mL), solid sodium hydroxide (360 mg, 9 mmol) was added to adjust the solution to pH 9. Then, the reaction mixture was stirred at room temperature for 12 d. The white precipitate which had formed during that time was filtered off and washed with ice-cold tetrahydrofuran (10 mL). Then, the white solid was resuspended in dichloromethane (20 mL), water (20 mL) added and the resulting mixture stirred for 2 d at room temperature. After removal of the organic solvent under reduced pressure, the resulting white solid was dried under vacuum for 4 d. Yield: 14% (195 mg, 0.44 mmol). **IR** (ATR): $\tilde{\nu}$ = 2840 (w), 1601 (s), 1503 (s), 1427 (s), 1311 (w), 1120 (m), 826 (vs), 767 (vs), 737 (s) cm^{-1}; **^{1}H NMR** (500.13 MHz, $CDCl_3$): δ = 8.12 (d, 3H, ^3J = 8.5 Hz, qui-H4), 8.06 (d, 3H, ^3J = 8.5 Hz, qui-H8), 7.77 (dd, 3H, ^3J = 8.2 Hz, ^4J = 1.1 Hz, qui-H7), 7.74 (d, 3H, ^3J = 8.5 Hz, qui-H5), 7.68 (ddd, 3H, ^3J = 8.1 Hz, ^3J = 6.9 Hz, ^4J = 1.4 Hz, qui-H6), 7.50 (ddd, 3H, ^3J = 8.1 Hz, ^3J = 6.9 Hz, ^4J = 1.1 Hz, qui-H3), 4.13 (s, 6H, CH_2), ppm; **^{13}C NMR** (125.75 MHz, $CDCl_3$): δ = 160.2 (qui-C2), 147.8 (qui-C8a), 136.5 (qui-C4), 129.5 (qui-C7), 129.3 (qui-C8), 127.6 (qui-C5), 127.5 (qui-C4a), 126.3 (qui-C6), 121.3 (qui-C3), 61.3 (*C*H_2) ppm; **MS** (ESI$^+$, CH_3OH): *m*/*z* = 441.2072 $[M\text{-}H]^+$; **Elemental analysis** (%) calcd. for $C_{30}H_{24}N_4 \cdot 2\ H_2O$: C 75.61, H 5.92, N 11.76, found (%): C 75.57, H 5.46, N 11.44.

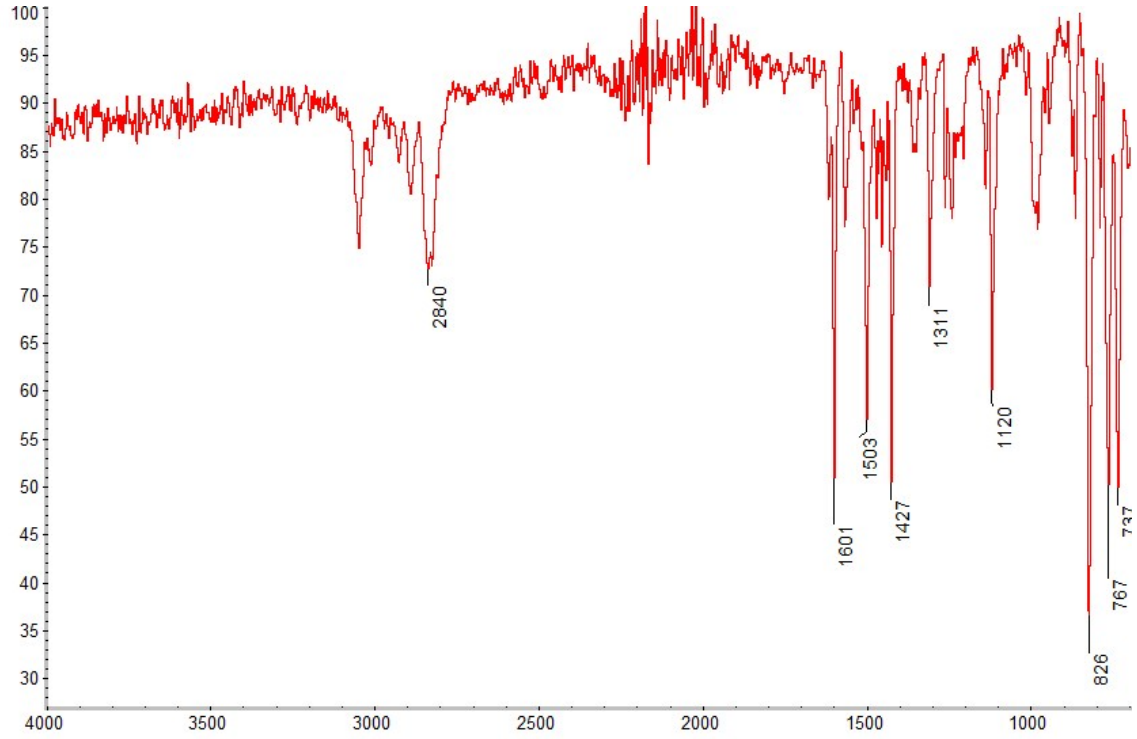

Figure S7. ATR IR spectrum of tqa (**5**).

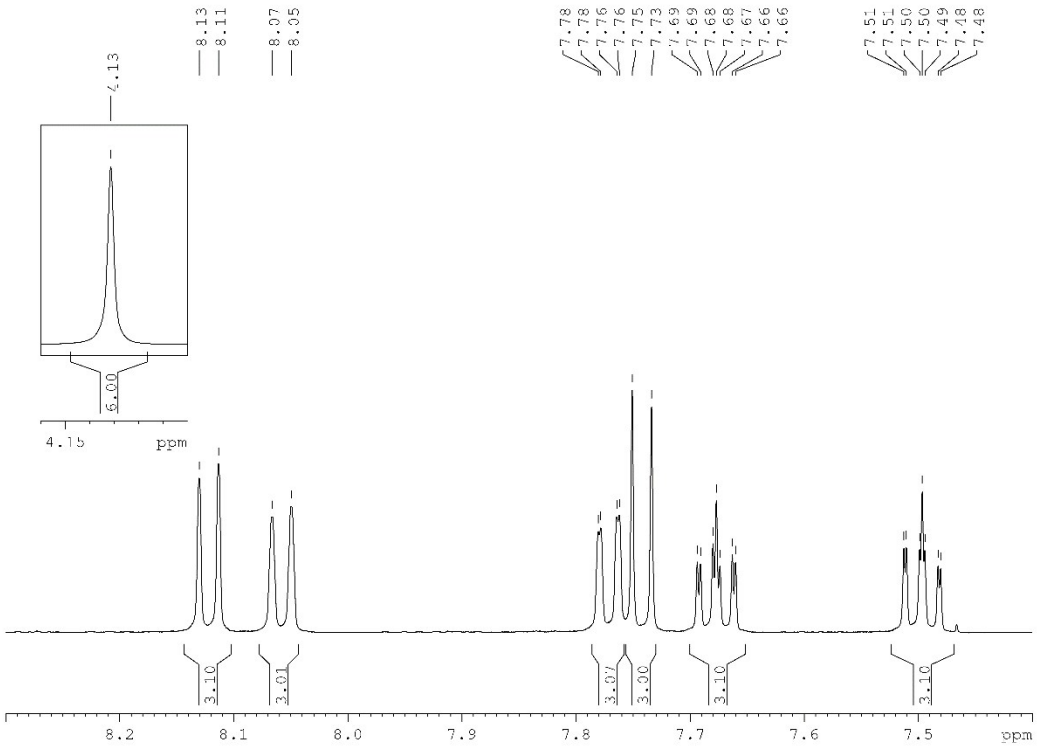

Figure S8. 500 MHz ^{1}H NMR spectrum of tqa (**5**) in $CDCl_3$.

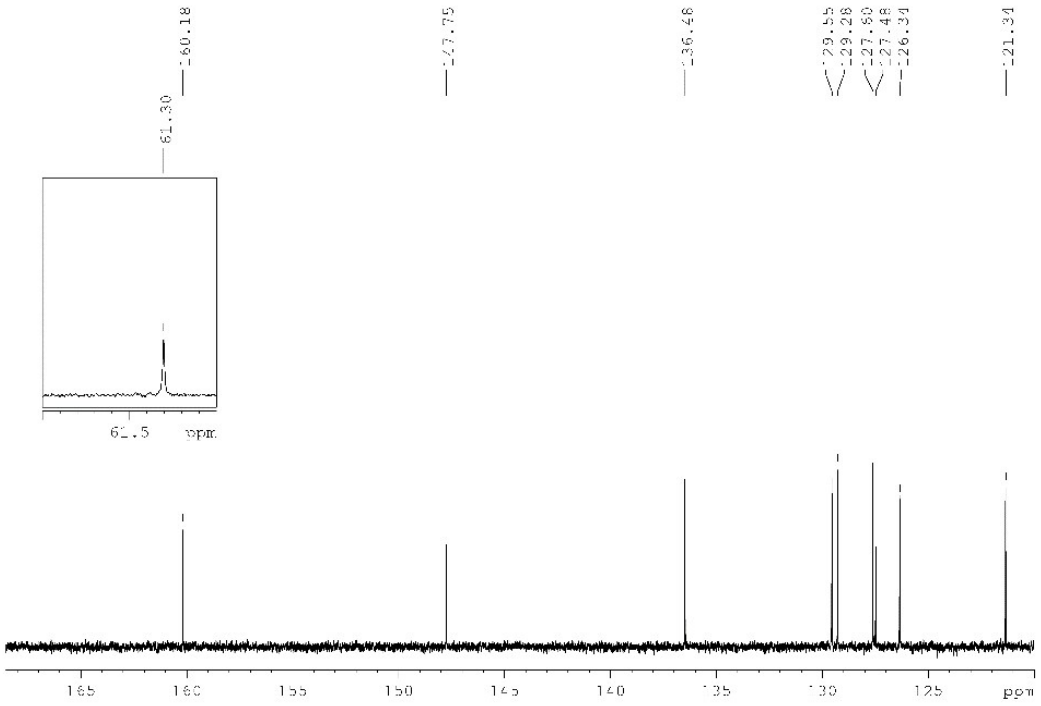

Figure S9. 125 MHz ^{13}C NMR spectrum of tqa (**5**) in $CDCl_3$.

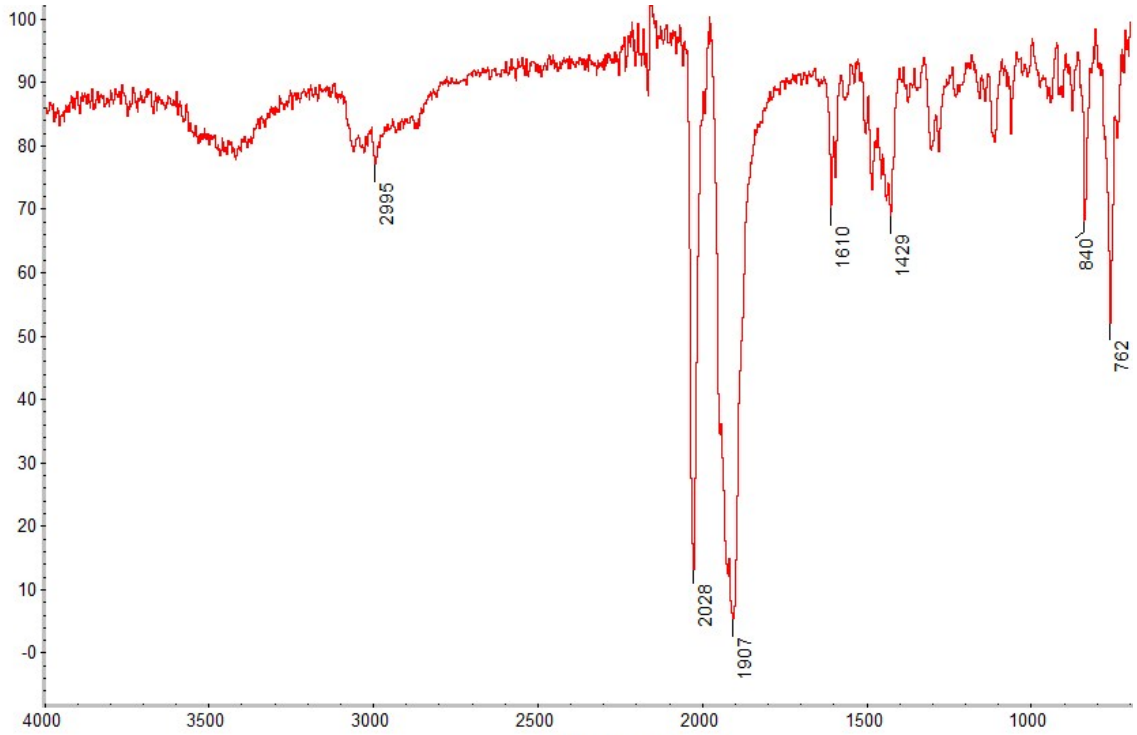

Figure S10. ATR IR spectrum of [Mn(bpqa-κ^3*N*)(CO)$_3$]Br (**7**).

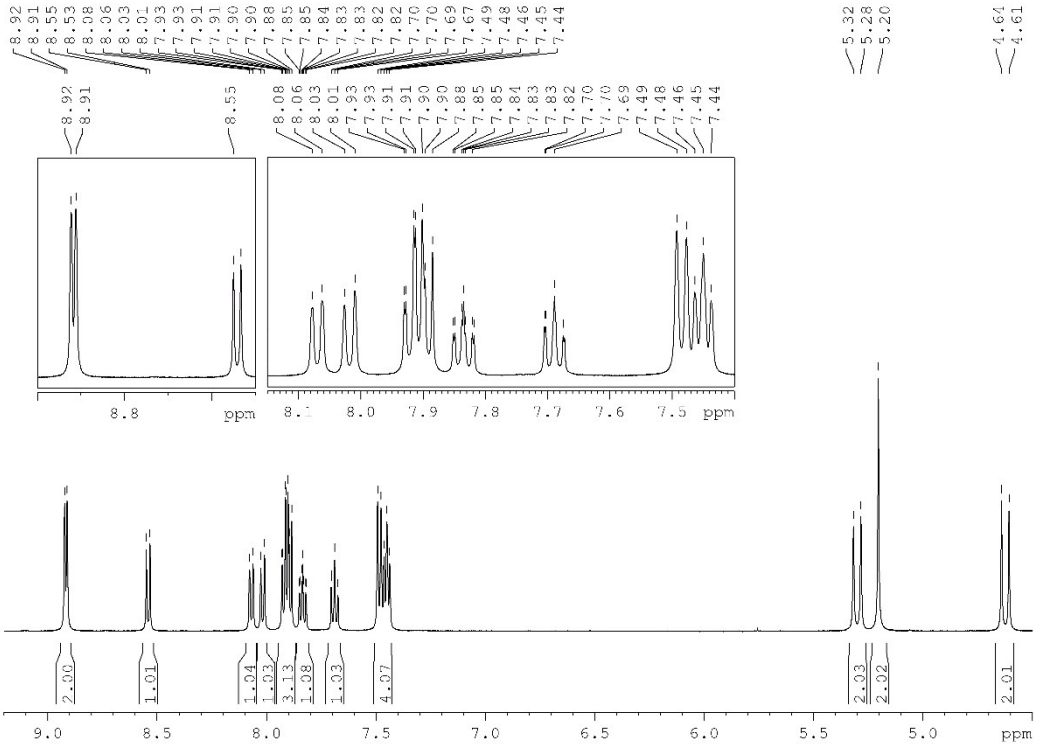

Figure S11. 500 MHz ^{1}H NMR spectrum of [Mn(bpqa-κ^3*N*)(CO)$_3$]Br (**7**) in DMSO-d_6.

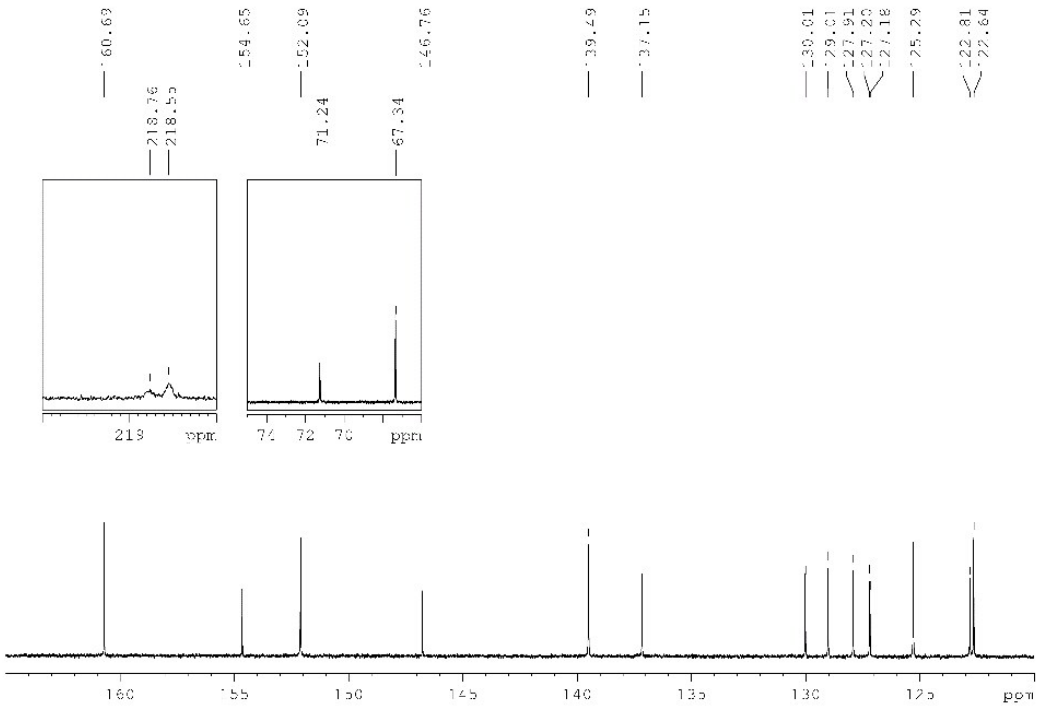

Figure S12. 125 MHz ^{13}C NMR spectrum of [Mn(bpqa-κ^3*N*)(CO)$_3$]Br (**7**) in DMSO-d_6.

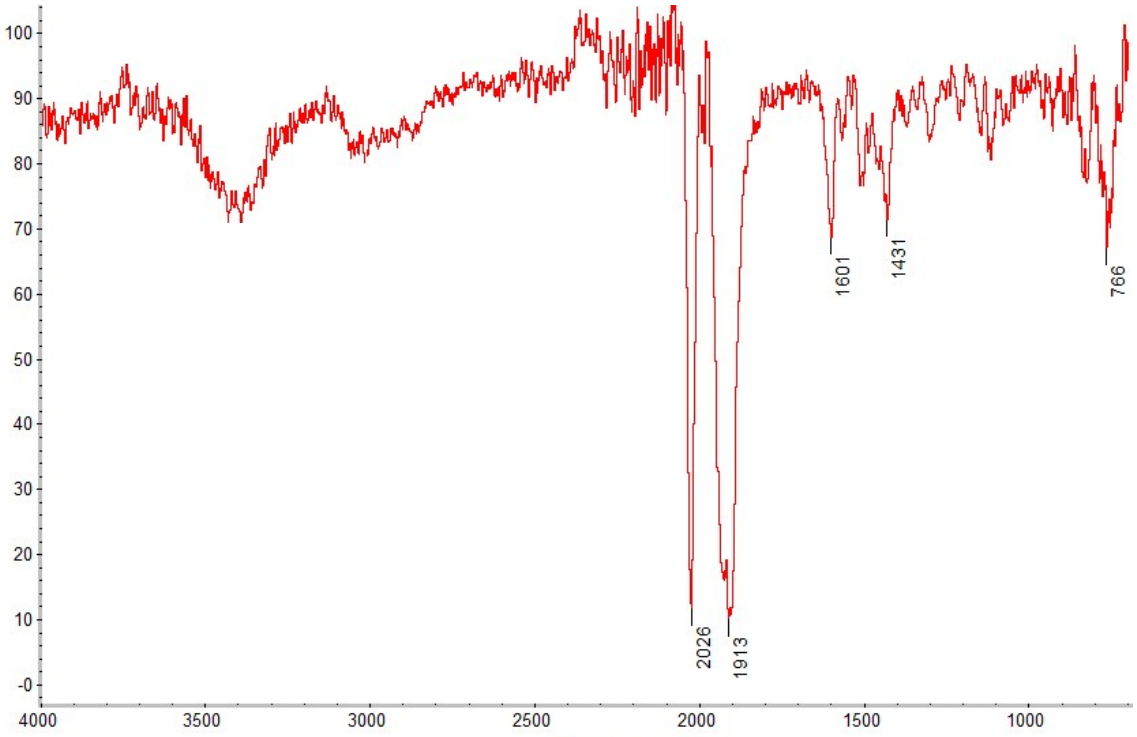

Figure S13. ATR IR spectrum of [Mn(bqpa-κ^3*N*)(CO)$_3$]Br (**8**).

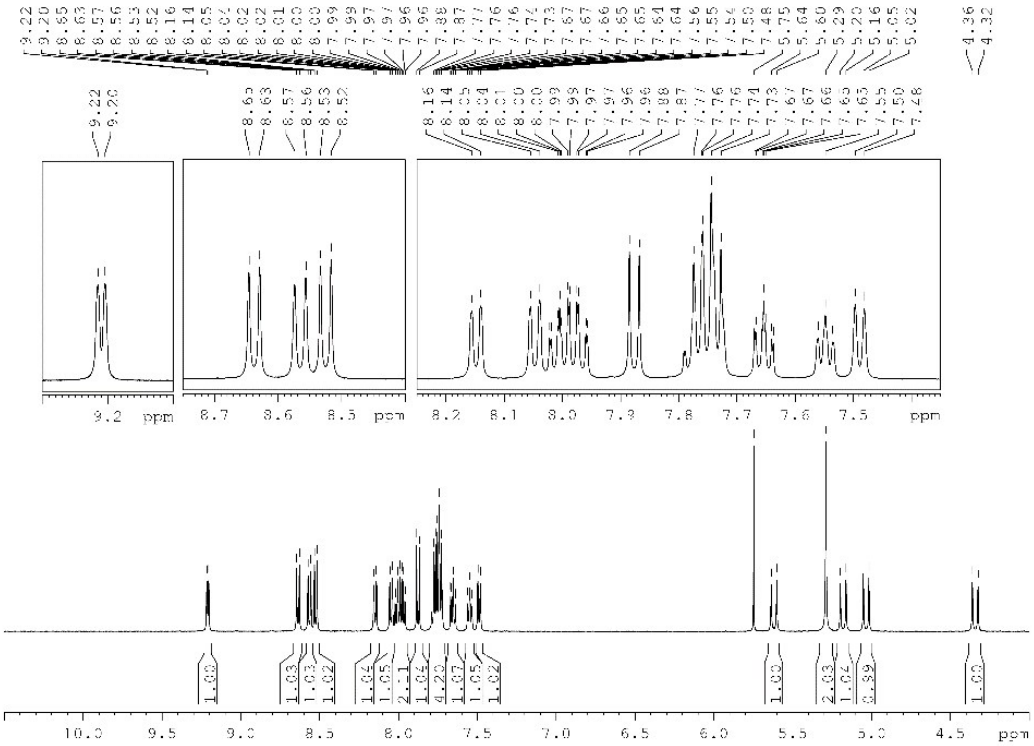

Figure S14. 500 MHz ^{1}H NMR spectrum of [Mn(bqpa-κ^3*N*)(CO)$_3$]Br (**8**) in DMSO-d_6.

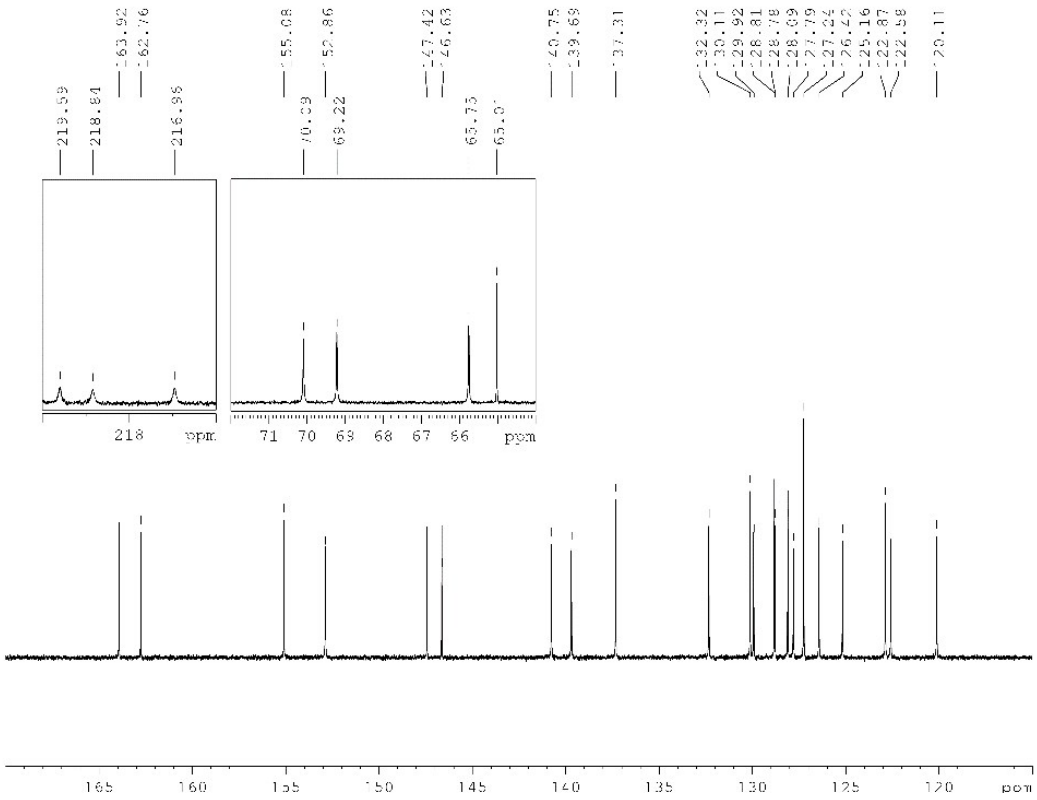

Figure S15. 125 MHz ^{13}C NMR spectrum of [Mn(bqpa-κ^3*N*)(CO)$_3$]Br (**8**) in DMSO-d_6.

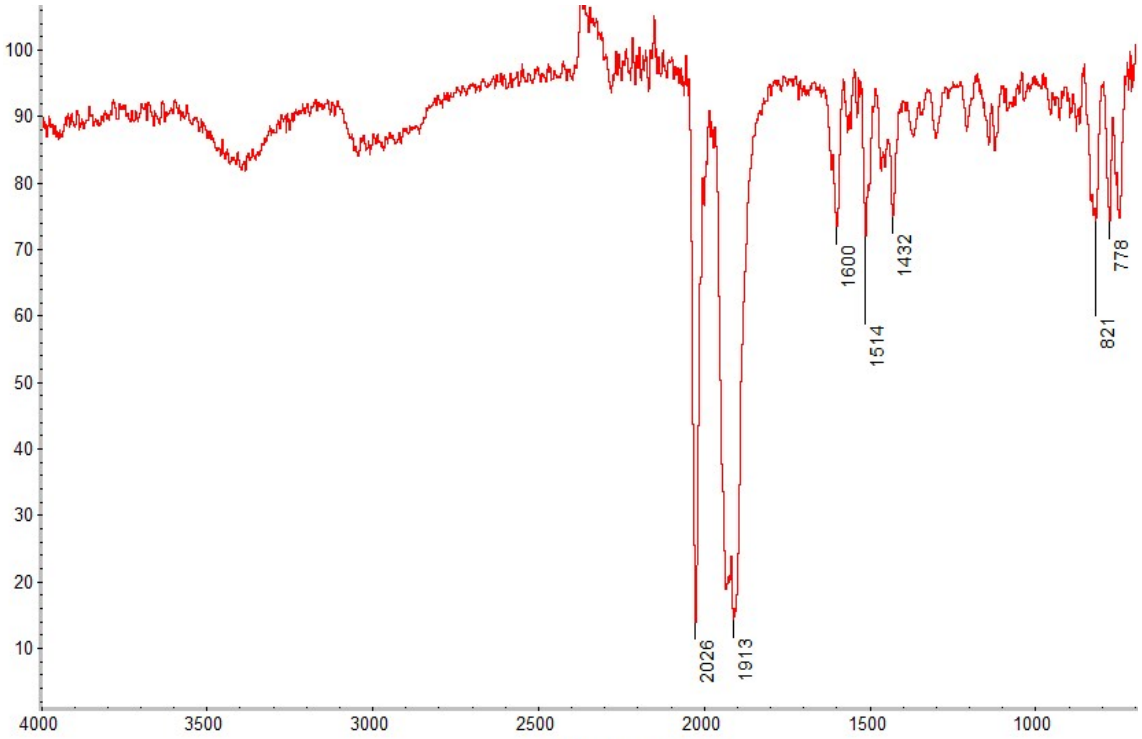

Figure S16. ATR IR spectrum of [Mn(CO)$_3$(tqa-κ^3*N*)]Br (**9**).

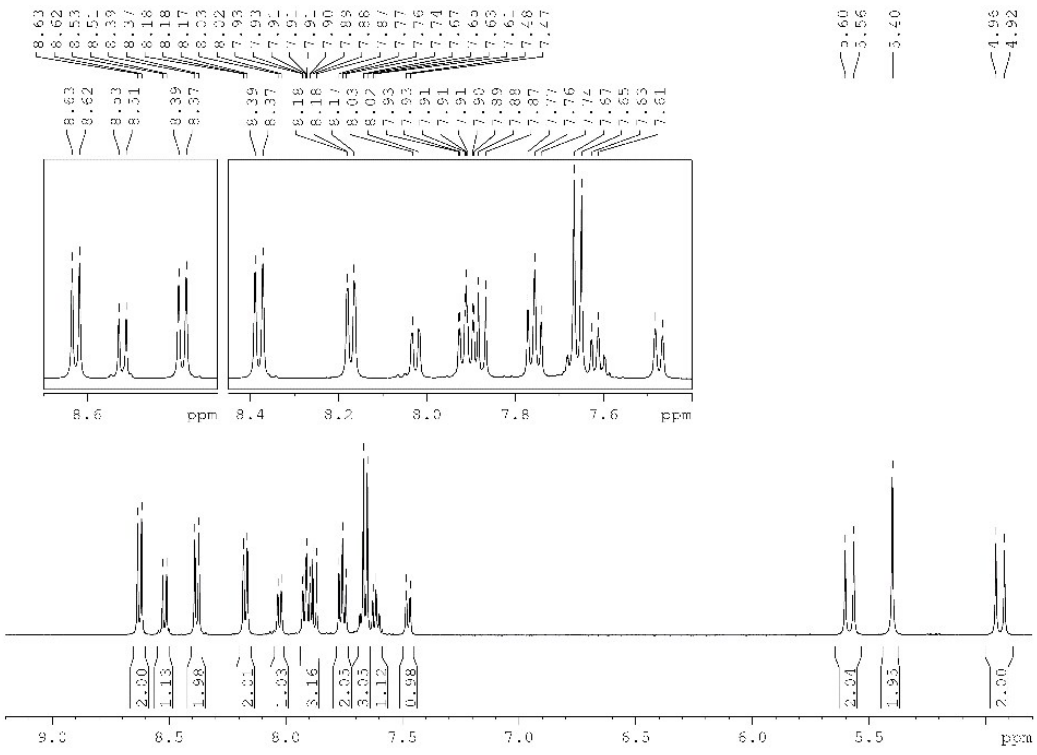

Figure S17. 500 MHz ^{1}H NMR spectrum of [Mn(CO)$_3$(tqa-κ^3*N*)]Br (**9**) in DMSO-d_6.

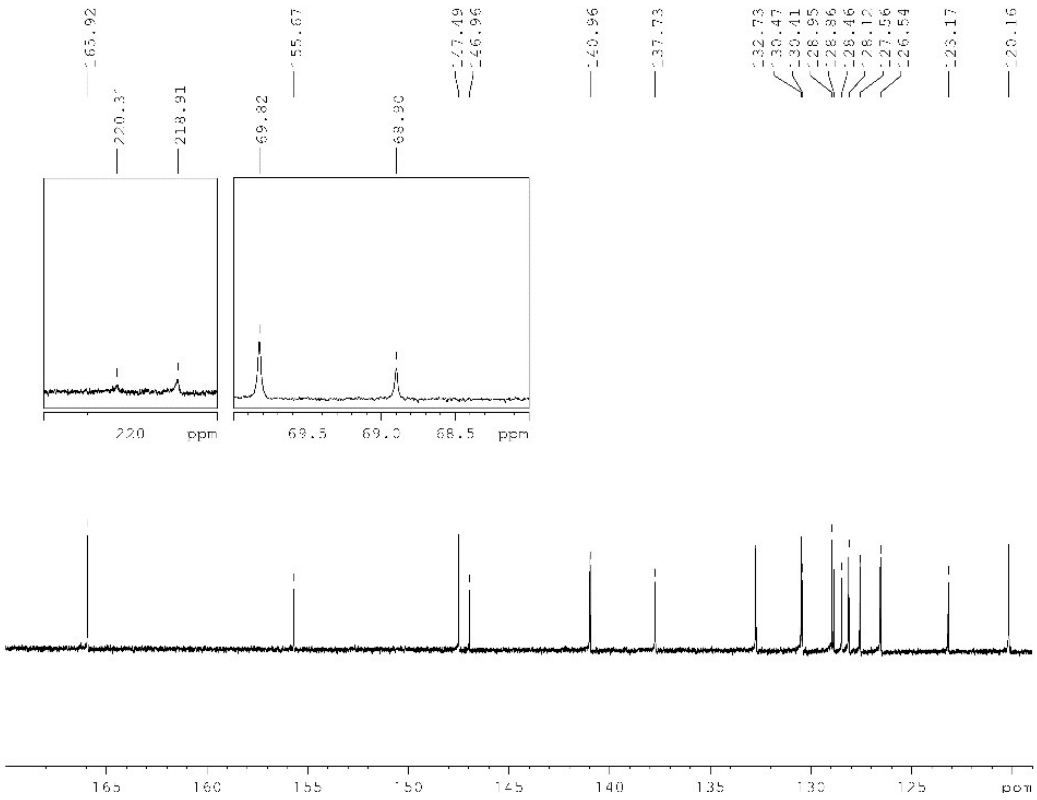

Figure S18. 125 MHz ^{13}C NMR spectrum of [Mn(CO)$_3$(tqa-κ^3*N*)]Br (**9**) in DMSO-d_6.

References

[1] N. Wei, N. N. Murthy, Q. Chen, J. Zubieta, K. D. Karlin, *Inorg. Chem.* **1994**, *33*, 1953-1965.