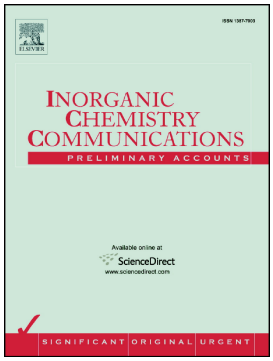

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Rhenium(I) complexes with aliphatic Schiff bases appended to bio-active moieties

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Novel *facial* tricarbonylrhenium(I) complexes, *fac*-[Re(urca)$_2$(CO)$_3$Cl] (1) and *fac*-[Re(bzta)(CO)$_3$Cl] (2) were isolated from the coordination reactions of 5-((5-hydroxypentylimino)methyl)uracil (urca) and 2-((5-hydroxypentylimino)methyl)benzothiazole (bzta) with [Re(CO)$_5$Cl], respectively. Spectral characterization of metal complexes 1 and 2 were supported by their X-ray crystal structures. DNA interactions were assessed *via* UV-Vis calf-thymus (CT)-DNA binding titrations and gel electrophoresis. Redox properties of the metal complexes were probed using voltammetry.

Keywords: Rhenium, benzothiazole, uracil, spectral characterization, crystal structure, DNA interaction.

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The design of novel target-specific therapeutic rhenium radiopharmaceuticals is reliant on the fundamental coordination chemistry of rhenium [**1**, **2**]. More specifically, the biodistribution of a radiopharmaceutical is conditional on its stability, charge, molecular weight, geometry as well as the nature of co-ligands occupying the coordination sphere. Current design strategies entail appending bio-active components within ligand scaffolds which are aimed at improving the biodistribution patterns of potential metallopharmaceuticals [**3**-**5**].

In this research study, we designed two Schiff bases encompassing uracil and benzothiazole moieties as they are pharmacores of known anticancer compounds. For example, 5-fluorouracil and uracil mustard are well established chemotherapeutic drugs while rhenium complexes with 2-(4′-aminophenyl)benzothiazole and its 6-methyl derivative have shown to be potential candidates for the targeted radiotherapy of breast cancer [**6**-**8**]. Furthermore, the hydrophobic alkyl chains and the respective bio-active components of our formulated Schiff bases could induce the formation of micelles [**9**, **10**]. This feature could potentially allow rhenium complexes with this class of ligands to mimic the biodistribution patterns of ^{188}Re-labelled liposomes and other liposomal drugs [**11**].

Compounds **1** and **2** were isolated from the 1:2 (in the case of **1**) or 1:1 (in the case of **2**) stoichiometric reactions between the individual Schiff base ligands and [Re(CO)$_5$Cl] [**12**, **13**]. Two molecules of **2** occupy their triclinic unit cell and form hydrogen-bonded dimers [Cl···HX-O1X/ ClX···H-O1 = 2.26(3) Å] with neighbouring molecules. The rhenium atom is at the centre of a distorted octahedron induced by the constrained bite angle of 74.30(5)^o [N1-Re-N2] which deviates significantly from the ideal octahedral value of 90°, see **Fig. 1**. Consequently, the Cl-Re-C14 [177.17(5)°], N1-Re-C16 [175.11(6)°] and N2-Re-C15 [169.99(6)°] angles are non-linear.

The effects of cyclometallation is also evident from the C5-N1-C6 [118.01(1)°] bond angle being narrower than the expected 120° bond angle for a bridging *sp*^{2} hybridized nitrogen atom. However, the bond distances for the Re-N$_{imino}$ [2.182(1) Å] and Re-N$_{benzothiazole}$ [2.194(1) Å] of **2** are similar to other *facial* tricarbonylrhenium(I) complexes with bidentate nitrogen-donor chelating ligands [**14**-**16**]. For example, *fac*-[Re(CO)$_3$(dcbpy)Cl] {dcpby = 4, 4′-dicyano-2,2′-bipyridyl}, *fac*-[Re(CO)$_3$(bcpbpy)Cl] {bcpbpy = 4, 4′-*bis*-(4-cyanophenyl)-2,2′-bipyridyl}, *fac*-[Re(CO)$_3$ (bz$_2$en)Cl] {bz$_2$en = *N*, *N*′-*bis*-(benzophenone)-1,2-diiminoethane} and *fac*-[Re(CO)$_3$(2-m'bzen)Cl] {2-m'bzen = *N*, *N*′-*bis*-(2-methylbenzaldehyde)-1,2-diiminoethane} with a range of Re-N$_{imino}$ bond lengths from 2.15(1) Å to 2.217(3) Å. In addition, the benzothiazole moiety lies out of the C15C16N1N2 least squares mean plane by 8.06°. The remaining coordination sphere bonds of **2** [Re-Cl = 2.4903(5) Å, Re-C14 = 1.922(2) Å, Re-C15 = 1.924(1) Å and Re-C16 = 1.916(2)] are within the Re-Cl [Re-Cl: 2.452(3) – 2.513(5) Å] and

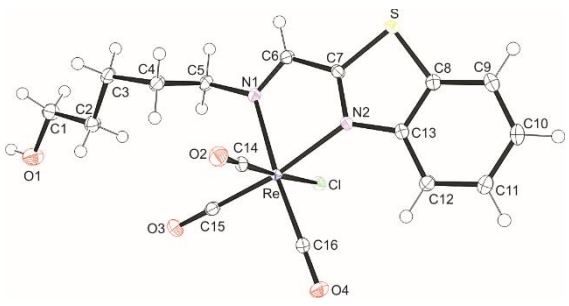

Fig. 1: *An ORTEP view of* **2** *showing 50 % probability displacement ellipsoids and the atom labelling.*