Formation, characterization and computational studies of mono- and dinuclear rhenium(I) chromone compounds

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ABSTRACT

Herein, we report the formation and characterization of a novel dinuclear rhenium(I) compound, fac-(Re(CO)$_3$Br)$_2$(μ-chret) (**1**) [chret = N, N'-bis(2-amino-3-imino)methylenechromone-1,2-ethane] and a mononuclear metal complex, fac-[Re(CO)$_3$(bzch)Br] (**2**) [bzch = 2-benzimidazole-4H-chromen-4-one]. The metal complexes were characterized by ^{1}H NMR-, IR-, UV−Vis, melting point and conductivity measurements. The solid-state structures for **1** and **2** were confirmed via single crystal X-ray analysis. X-ray studies of **2** revealed the transformation of the chb diimine into the bzch chelator (in **2**). The simulated IR spectra for the respective metal complexes provided insight in the interpretation of their corresponding experimental spectra.

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1. Introduction

The considerable attention received by the coordination chemistry of rhenium stems from the ideal properties of its 186- and 188-radionuclides which are well suited for radiotherapy [1–3]. For example, the bone-targeting therapeutic radiopharmaceutical, rhenium-HEDP (HEDP = hydroxyethylidene disphosphonate) has several advantages over the commercially available alternatives in terms of efficacy, safety and the ability to be produced on site, allowing for the rapid treatment of patients with painful bone metastases [4]. Furthermore, the facial tricarbonylrhenium(I) core has shown to serve as an ideal synthon for the formulation of new rhenium radiopharmaceuticals. This is illustrated by the facial tricarbonylrhenium(I) complexes stability under physiological conditions where the small size of the fac-[Re(CO)$_3$]$^+$ core allows binding to various biological entities [5,6]. However, the next generation of potential rhenium radiopharmaceuticals requires chelators which can stabilize the metal centre both in the low and high oxidation states [7]. Furthermore, these multidentate chelators should also cater for the inclusion of biologically active moieties which may aid in the target specific biodistribution of the metallopharmaceuticals [8,9].

In our previous studies, we have reported the isolation of oxo-rhenium(V) and facial tricarbonylrhenium(I) complexes with Schiff bases encompassing uracil, chromone or benz(othiazole/imidazole) moieties [10−12]. These multidentate Schiff base chelators illustrated diverse coordination behaviours leading to mono- or dinuclear rhenium compounds. For example, a unique dinuclear rhenium(I) complex, (μ-bzp)$_2$[Re(CO)$_3$]$_2$ [Hbzp = N-(2-hydroxybenzylidene)-benzimidazole] has a centralized 8-membered chelate ring formed by coordination of the benzimidazole nitrogens to the individual rhenium atoms [11]. Furthermore, different transformations of the chromone mono-imines, 2-(2-thiolphenyliminomethyl)-4H-chromen-4-one (Htch) and H$_3$uch [5-((4-hydroxy-2-methoxy-2H-chromen-3-yl)methyleneamino)-6-amino-1,3-dimethylpyrimidine-2,4(1H, 3H)-dione] were observed upon their coordination reactions with trans-[ReOBr$_3$(PPh$_3$)$_3$] to afford [ReO(Hns)] {H$_2$ns = bis-[(2-phenylthiolate)iminomethyl]-methyl-1-(2-hydroxyphenyl)prop-2-en-1-one} and [ReO(OCH$_3$)(PPh$_3$)(Huch)] [12].

As a continuation of our research studies on rhenium, herein we consider the coordination behaviours of multidentate diimines encompassing chromone moieties. This secondary metabolite, chromone and its derivatives are known to induce cytotoxic effects in breast cancer cell lines [13,14]. Hence, we report the coordination reactions of [Re(CO)$_5$Br] with the diimines: N, N'-bis(2-amino-3-imino)methylenechromone-1,2-ethane (chret) and N,N'-bis((3-chromone)methylene)benzene-1,2-diamine (chb) to afford a

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novel dinuclear rhenium(I) compound, *fac*-(Re(CO)$_3$Br)$_2$(μ-chret) (**1**) and a mononuclear compound *fac*-[Re(CO)$_3$(bzch)Br] (**2**) [bzch = 2-benzimidazole-4*H*-chromen-4-one].

chret

chb

bzch
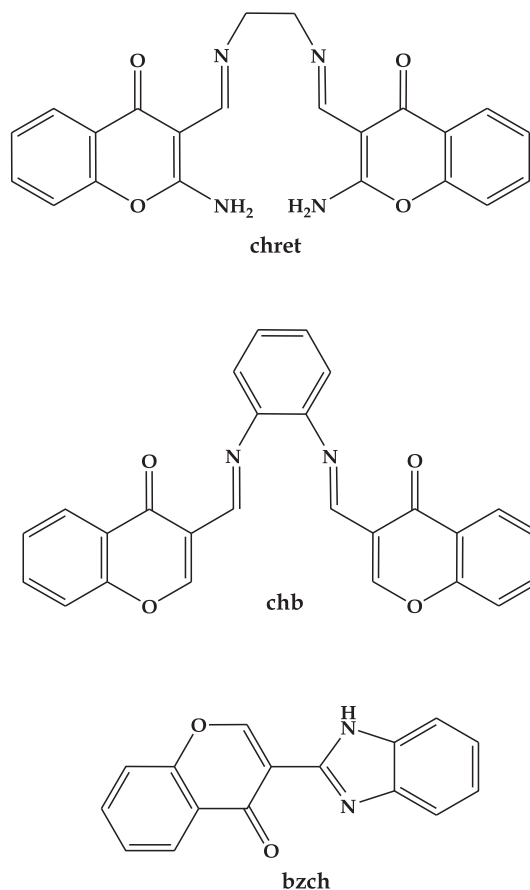
2. Experimental

2.1. Materials and methods

The reagents: bromopentacarbonylrhenium(I), ethylenediamine, 1,2-diaminobenzene, 2-amino-3-formylchromone and 3-formylchromone were obtained from Sigma Aldrich and used as received. All solvents and common salts were obtained from Merck SA. Reagent grade toluene was dried over sodium wire; solvents were used without further purification. The synthetic procedure and characterization data for the free-ligand chret can be found in the online supporting information document, see Figs. S1, S2 and S5. The diimine, chb was obtained from the condensation reaction of 1,2-diaminobenzene with a two-fold molar quantity of 3-formylchromone [15].

The infrared spectra were recorded on a Perkin-Elmer 100 spectrometer in the 4000–450 cm^{-1} range. The ^{1}H NMR spectra were obtained using a Bruker Avance 400 MHz spectrometer. All NMR spectra were recorded in deuterated dimethylsulphoxide. UV–Vis spectra were recorded using a Perkin Elmer Lambda 25. The extinction coefficients (ε) are given in dm^3 mol^{-1} cm^{-1}. Melting points were determined using a Stuart SMP3 melting point apparatus. The conductivity measurements were determined at 295 K on a Radiometer R21M127CDM 230 conductivity and pH meter.

2.2. fac-(Re(CO)$_3$Br)$_2$(μ-chret) (**1**)

A 1:1 M reaction mixture of [Re(CO)$_5$Br] (0.050 g, 0.123 mmol) and chret (0.049 g, 0.123 mmol) in 15 cm^3 of anhydrous toluene was heated at reflux under nitrogen for 4 h. The resultant reaction mixture was cooled to room temperature and filtered. An orange precipitate was dried under vacuum. Pale orange X-ray quality crystalline parallelograms were obtained from layering the precipitate with a 1:1 (*v*:*v*) THF/hexane over a period of five days. M.P = 215–220 °C; yield = 87%; Conductivity (DMSO, 10^{-3} M) 16.93 Ω cm^2 mol^{-1}; IR (ν_{max}/cm^{-1}): ν(N–H) 2920, 2850 (m); ν(C≡O) 2015, 1871 (vs); ν(C=O) 1655 (s); ν(C=N) 1615, 1613 (s); ν(O–C–O) 1464 cm^{-1} (s). ^{1}H NMR (295 K/ppm): 10.91 (br, s, 4H, 2 × *NH$_2$*), 8.95–8.65 (m, 6H, *H10, H12, H16, H19, H24, H26*), 8.12–7.11 (m, 4H, *H9, H11, H23, H25*), 4.69–4.39 (m, 4H, *H17, H17′, H18, H18′*). UV–Vis (DMSO, λ_{max}(ε, M^{-1} cm^{-1})): 269 nm (24159); 296 nm (sh, 20140); 405 nm (sh, 2464).

2.3. fac-[Re(CO)$_3$(bzch)Br] (**2**)

The equimolar coordination reaction between [Re(CO)$_5$Br] (0.050 g, 0.123 mmol) and chb (0.052 g, 0.123 mmol) was conducted in 15 cm^3 of anhydrous toluene heated at reflux under nitrogen for 4 h. The resultant reaction mixture was cooled to room temperature and an orange precipitate was filtered and dried under vacuum. Pale orange cubic crystals suitable for X-ray analysis were obtained from dissolving the precipitate in tetrahydrofuran and layering with hexane. M.P = 210–211 °C; yield = 93%; Conductivity (DMSO, 10^{-3} M): 23.72 Ω cm^2 mol^{-1}; IR (ν_{max}/cm^{-1}): ν(N–H) 2915 (w), ν(C≡O) 2015, 1871 (vs); ν(C=O) 1628, 1607 (s); ν(C=N) 1567 (s); ν(O–C–O) 1461 (s). ^{1}H NMR (295 K/ppm): 9.69 (s, 1H, *H1*); 9.39 (s, 1H, *NH*); 8.27–7.22 (m, 8H, *H3, H4, H5, H6, H12, H13, H14, H15*). UV–Vis (DMSO, λ_{max}(ε, M^{-1} cm^{-1})): 275 nm (sh, 26107); 282 nm (27295); 309 nm (sh, 22025); 394 nm (6614); 418 nm (sh, 4394).

2.4. X-ray diffraction

The X-ray data for C$_{28}$H$_{18}$Br$_2$N$_4$O$_{10}$Re$_2$.3(C$_4$H$_8$O) and C$_{19}$H$_{10}$BrN$_2$O$_5$Re.C$_7$H$_8$ were recorded on a Bruker Apex Duo equipped with an Oxford Instruments Cryojet operating at 100(2) K and an Incoatec microsource operating at 30 W power. Crystal and structure refinement data are given in Table 1. Selected bond lengths and angles are given in Tables 2 and 3. In both cases the data were collected with Mo Kα (λ = 0.71073 Å) radiation at a crystal-to-detector distance of 50 mm. The following conditions were used for data collection: omega and phi scans with exposures taken at 30 W X-ray power and 0.50° frame widths using APEX2 [16]. The data were reduced with the program SAINT [16] using outlier rejection, scan speed scaling, as well as standard Lorentz and polarization correction factors. A SADABS semi-empirical multi-scan absorption correction [17] was applied to the data. Direct methods, SHELX-2014 [18] and WinGX [19] were used to solve both structures. All non-hydrogen atoms were located in the difference density map and refined anisotropically with SHELX-2014 [20]. All hydrogen atoms were included as idealised contributors in the least squares process. Their positions were calculated using a standard riding model with C-H$_{aromatic}$ distances of 0.93 Å and U$_{iso}$ = 1.2 U$_{eq}$, C-H$_{methylene}$ distances of 0.99 Å and U$_{iso}$ = 1.2 U$_{eq}$ and C–H$_{methyl}$ distances of 0.98 Å and U$_{iso}$ = 1.5 U$_{eq}$. The amine hydrogen atoms were located in the difference density map and allowed to refine isotropically.

2.5. Computational details

Molecular simulations were conducted with GAUSSIAN 09W