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**First sulphur-bridged organometallic compound of rhenium(I) linking
deprotonation and coordination mode of 2-mercaptopyridine-3-carboxylic acid
derivative: Synthesis, X-ray crystallography characterisation, and DFT calculations**

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Abstract

Organometallic complexes of transition metals constitute promising architectural frameworks for the design of pharmaceutical products and catalytic systems that can achieve tailored reactivity and functionality. Herein, we report the synthesis of a novel dinuclear Re(I) complex, *fac*-[Re(CO)₃(μ-mpc)]₂·Et₃NH (**1**), which has been obtained in high yields through a one-pot reaction between Re(CO)₅Cl and 2-mercaptopyridine-3-carboxylic acid (H₂mpc) in toluene followed by the addition of two drops of triethylamine. The coordination behaviour of H₂mpc is linked with its deprotonation, leading to the coordinated (λ¹-oxo)(2-sulfidopyridin-3-yl)methanolate (mpc²⁻) derivative acting as a bidentate monoanionic N∩S⁻ thioxalato chelate, bridging two rhenium(I) ions. The bridging chelates, mpc²⁻ in the metallacycle units of compound **1** shows a Re₂S₂ ring, and uncoordinated pendant acetate groups that are in turn stabilised by the cationic Et₃NH⁺, as confirmed by X-ray crystallography analysis. The solid state of compound **1** has also been supported by elemental analysis for sulphur, oxygen, carbon, nitrogen and hydrogen. Non-intermolecular hydrogen bonding and hydrogen bonding interactions (C-H...O-C, C-H...S, and N-H...O-C) were found to promote the stability of the molecule in its solid state. Density functional theory calculations were performed to gain further insights into the electronic structure, bonding characteristics, and reactivity of H₂mpc and its rhenium(I) complex. Computational analyses, including non-covalent interactions (NCI), molecular electrostatic potential (MEP), frontier molecular orbitals (FMO), conceptual density functional theory (CDFT), electron localisation function (ELF), and Hirshfeld surface analysis (HSA), rationalised experimental findings and provided detailed information on charge delocalisation, donor-acceptor interactions, and the stabilising role of the triethylammonium counter ion.

Keywords: Organometallic, X-ray diffraction, crystal structure, rhenium(I), sulphur-bridged metallacycle

1. Introduction

The coordination behaviour of transition metals with various organic ligands has emerged as an effective approach for the development of multifunctional materials with diverse applications [1,2]. Within this framework, the metal-organic chelate interactions have demonstrated significant potential contribution in responding to the increasing global demand of medicinal products tailored for theranostic applications in the treatment of cancer and other diseases [2,3]. Among the group of transition metal ions, rhenium and technetium have gained particular interest, attributed to their radiation emission and particulate decay profiles [4,5]. Furthermore, the isostructural relationship and similar chemical behaviour of complexes of $^{186/188}\text{Re}$, and those of $^{99\text{m}}\text{Tc}$ allow them to manifest a wide spectrum in the radio-imaging field [6]. The coordination behaviour and β -emission properties of $^{186/188}\text{Re}$ isotopes have been a focus in chemistry for the synthesis of their metal complexes that may be good drug candidates for the treatment of various diseases [7-9]. Various studies have reported the synthesis of diverse organometallic complexes [10,11], as well as their biological applications as the latter compounds have exhibited a broad-spectrum of pharmaceutical activities, including *in vivo* and *in vitro* antibacterial activities [11-14], potential therapeutic activities against ovarian cancer [15-18], and treatment of hypoxia [19]. Additionally, many other isolated organometallic compounds tested against Chagas disease, fungal infections, malaria, and other microbial infections were found to be biologically active [20-22]. Furthermore, other synthesised rhenium(I) organometallic complexes with heterocyclic and macromolecular ligands have shown significant potential for pharmacological applications [1,4,23,24] and biochemical activities [25-28]. Moreover, heterocyclic compounds have been used to design their derivatives with potentially coordinating sites [29-32], and their molecular architecture has facilitated diverse metal-organic binding interactions [33-35]. Recent studies have further explored the structural and electronic relationships between rhenium(I) centres and coordinating ligands in organometallic systems [36-39]. Besides their well-documented biological [40,41], and therapeutic applications [42-48], rhenium(I)-tricarbonyl complexes showed a wide array of other uses, including photocatalysis [10,11,20,49], applications in material science [50], and utilisation in supramolecular assemblies [51]. Among various rhenium(I) cores, the *fac*- $[\text{Re}(\text{CO})_3]^+$ moiety serves as an excellent scaffold for organometallic compounds formation [52], and may be facilitated by ligand modification and structural variation, alongside exhibiting significant quantum yields [53-56]. In this perspective, we explored other recent studies

characterising dimeric complexes containing a Re_2S_2 core involving various heterocyclic ligands, especially those closely related to our study [57]. The crystal X-ray analysis of compound **1** in this study has been readily discussed by comparing its crystal structure with other similar dirhenium complexes. The previously reported organometallic compounds bearing heterocyclic thiols with the *fac*- $[\text{Re}(\text{CO})_3]^+$ core, as well as other rhenium(I) cores, revealed that the ligands preferentially coordinated as bidentate ligands (NS^-), affording dinuclear *fac*- $[\text{Re}_2(\text{CO})_6(\text{NS})_2]$ complexes with a Re_2S_2 core [58,59]. Some examples of these complexes include $\text{Re}_2(\text{CO})_6(\mu\text{-thpymS})_2$ obtained from the reaction of tetrahydropyrimidine-2-thiol (thpymSH) with $\text{Re}_2(\text{CO})_8(\text{NCMe})_2$ [58], as well as *fac*- $[\text{Re}(\text{CO})_3(\text{Spy})]_2$ (HSpy = 2-mercaptopyridine) that was isolated from the reaction of 2-mercaptopyridine with the precursors *fac*-(NEt_4) $_2$ $[\text{Re}(\text{CO})_3\text{Br}_3]$ or $[\text{Re}(\text{CO})_5\text{Br}]$ [59]. The reaction of $[\text{Re}_2(\text{CO})_{10}]$ with pyridine-2-thione (pySH) also led to a dinuclear cluster, $[\text{Re}_2(\text{pyS})_2(\text{CO})_6]$, with the Re_2S_2 core [60]. Similarly, the reaction of $\text{Re}(\text{CO})_5\text{Cl}$ with 8-thiohydroxyquinoline hydrochloride ($\text{HSX}\cdot\text{HCl}$) afforded the dimeric $\text{Re}_2(\text{CO})_6(\text{SX})_2$ complex [61]. The overall common observation from the aforementioned reported complexes to our study is the presence of the Re_2S_2 core and the bridging mode of the coordinated N,S^- ligand, which leads to three fused four-membered rings. The unique behaviour in complex **1** in our study is a rare example of dirhenium carbonyl complexes containing a thiolato ligand coordinated in a k^1 -fashion, leaving an uncoordinated anionic acetate group ($-\text{COO}^-$), as confirmed by the crystallographic data. This allowed us to demonstrate the novelty and unique structural features of compound **1** in the present study, which is governed by the used 2-mercaptopyridine-3-carboxylic acid (H_2mpc) ligand (**Figure 1**). Notably, H_2mpc has gained considerable attention across multiple disciplines, including chemistry, biology, biochemistry, and medicine, primarily due to its remarkable biological and therapeutic applications [62].

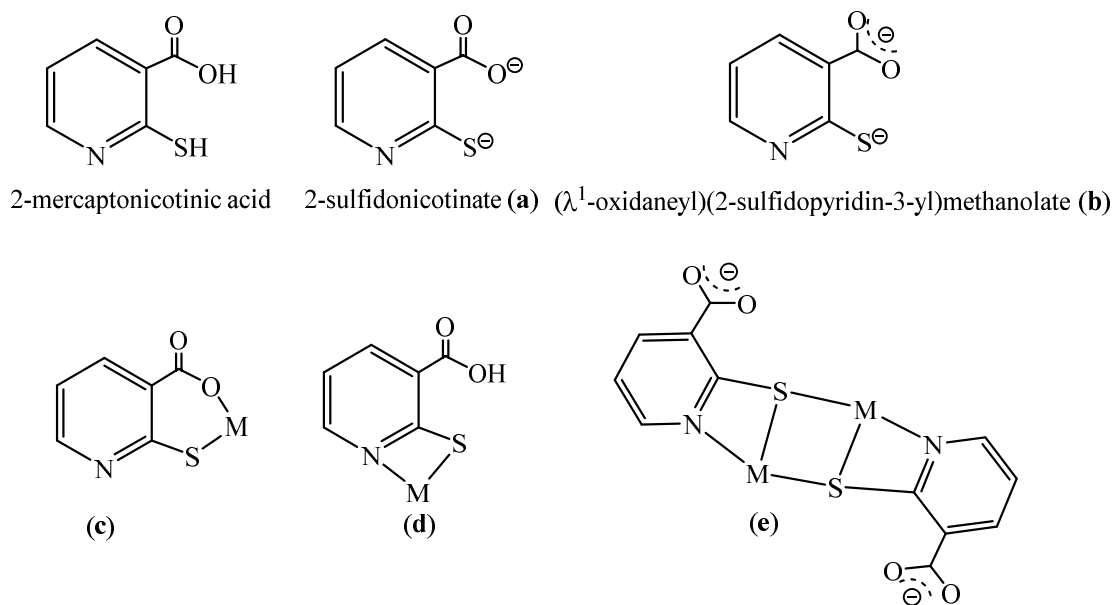


Figure 1: Structures of 2-mercaptopyridine-3-carboxylic acid (H₂mpc) (2-mercaptonicotinic acid), its derivatives (a, b), and their various coordination modes (c, d, e).

The detailed binding behaviour of the H₂mpc derivative, (λ¹-oxidaneyl)(2-sulfidopyridin-3-yl)methanolate (mpc²⁻), around the *fac*-[Re(CO)₃]⁺ core as a bidentate monoanionic N∩S⁻ thioxalato chelate (b) is shown in **Figure 1**. This compound constitutes the first reported example demonstrating the chelation behaviour dominated by an atypical electronic structure in the ligand's pendant acetate group. The negative charge is delocalised between the two oxygen atoms, forming a resonance-stabilised system that is further stabilised through electrostatic interaction with the Et₃NH⁺ counter ion. This case has never been reported for rhenium and is a rare occurring coordination phenomenon in chemistry.

2. Experimental

2.1 Materials and instrumentation

All procedures were performed under a nitrogen atmosphere employing standard Schlenk methods. The [Re(CO)₅Cl] precursor, H₂mpc ligand, triethylamine and all other chemicals were purchased from Sigma-Aldrich Chemicals. Rhenium(I) pentacarbonyl chloride and all other chemicals were used without any further purification, and all used solvents were dried according to the literature. The elemental analyses for carbon, hydrogen, sulphur, and nitrogen were carried

out on a Vario EL (Elementar Analysen system GmbH) instrument. The single crystal X-ray diffraction studies of compound, *fac*-[Re(CO)₃(μ-mpc)]₂·2Et₃NH (**1**) were studied at 200 K using a Bruker Kappa Apex II diffractometer with graphite monochromated Mo Kα radiation ($\lambda = 0.70173 \text{ \AA}$). The data collection was performed using APEX-II, whereas cell refinement and data reduction were carried out using SAINT [63]. To solve the crystal structure, the direct method equipped with SHELXS-2014 was used [64], and the crystal structure was finally refined by least-squares procedures using SHELXL-2014 [64], and with SHELXLE [65] as a graphical interface. All the data have been corrected for absorption effects using the numerical method implemented in SADABS [63]. The crystallographic data and the detailed data of the crystal refinement information are shown in Table 1. The important selected bond parameters (distances and angles) are tabulated in Table 2 (Supplementary Data). The refinement of all non-hydrogen atoms was performed anisotropically. In addition, carbon-bound H atoms were placed in calculated positions, and the C-H bond lengths were included in the refinement in a riding model approximation with $U_{\text{iso}}(\text{H})$ set to $1.2U_{\text{eq}}(\text{C})$. On the other hand, all hydrogen atoms were allowed to undergo the rotation motion on a fixed rotation angle along the C-C bond to best fit the experimental electron density map (HFIX 137 in SHELXL) [68], with $U_{\text{iso}}(\text{H})$ set to $1.5U_{\text{eq}}(\text{C})$. The molecular structure and crystal packing diagrams were drawn with PLATON graphical software [66]. The CCDC 2237762 number, containing the supplementary crystallographic information and all data for *fac*-[Re(CO)₃(μ-mpc)]₂·2Et₃NH (**1**), can be accessed free of charge from the Cambridge Crystallographic Data Centre via <https://www.ccdc.cam.ac.uk/structures/>.

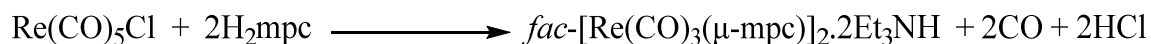
2.2 Synthesis of *fac*-[Re(CO)₃(μ-mpc)]₂·2Et₃NH (**1**)

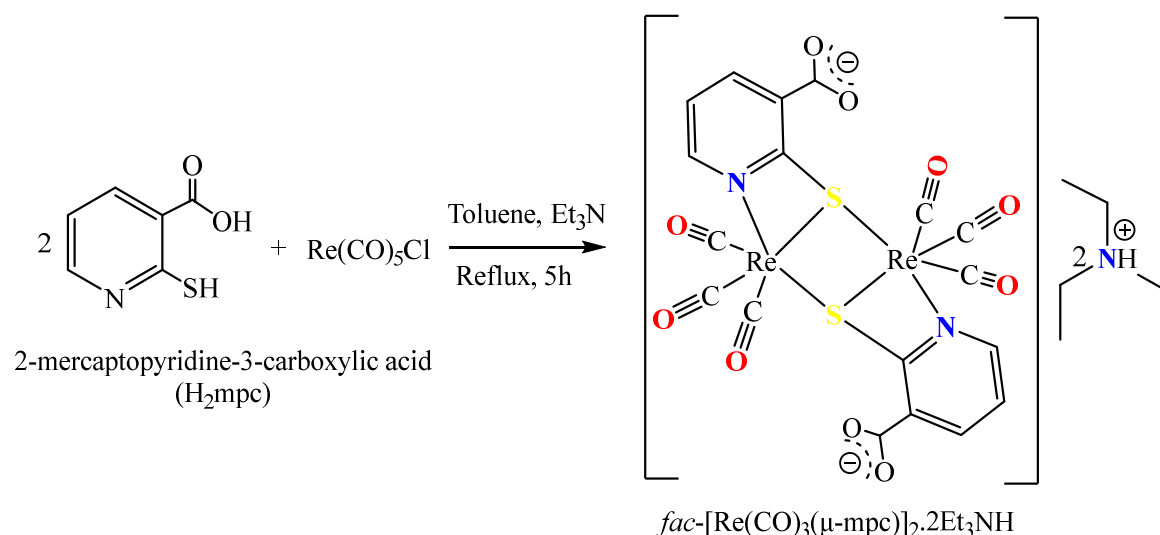
To the mixture of [Re(CO)₅Cl] (150 mg, 416 μmol) and 2-mercaptopyridine-3-carboxylic acid (H₂mpc) (129 mg, 832 μmol) in 20 cm³ of toluene, 3 drops of Et₃N were added. The mixture was heated under reflux for 5 hours in an inert medium with nitrogen, and when heating was stopped, the solution was allowed to cool down to room temperature and filtered. After six days, orange crystals suitable for X-ray crystallography analysis were steadily grown at room temperature upon a slow evaporation of the mother liquor. The obtained crystals were then washed with diethyl ether and dried under vacuum. Yield = 73%, m.p. = 316 °C. Anal. Calcd. (%) for C₁₈H₆N₂O₁₀Re₂S₂·2(C₆H₁₆N): C, 30.31; H, 2.54; N, 4.42; O, 16.82; S, 6.72. Found: C, 30.02; H, 2.41; N, 4.37; O, 16.75; S, 6.63. Conductivity (10⁻³ M, DMF): 9 Ω⁻¹cm²mol⁻¹.

3. Results and discussions

3.1 Structural characterisation

Initially, the synthesis procedure was carried out in toluene and an excess of ligand to isolate the title compound *fac*-[Re(CO)₃(μ-mpc)]₂·2Et₃NH (**1**). This dimeric complex was obtained from the reaction of H₂mpc and Re(CO)₅Cl in the presence of triethylamine. The coordination process was accompanied by a Lewis base dissociation/association reaction of two CO ligands and an elimination reaction of HCl. Good quality orange crystals of compound **1**, suitable for X-ray analysis, were obtained *via* partial evaporation of toluene solvent, leading to a good yield of around 73%. A commonly known challenge for acidic ligands is the basic nature of the carboxylate functional group, which causes them to be weak coordinating chelates around metal centres. To address this limited coordination ability arising from the acidic functional group, we employed triethylamine (Et₃N) as a strong deprotonating and coordinating base to remove the acidic proton. This strategy facilitated the coordination behaviour of the ligand, thereby enhancing the overall ligand binding affinity. Surprisingly, the obtained crystal structure confirmed that the H₂mpc ligand exhibited double deprotonation, losing the protons from the thiol and acidic groups, respectively, and one of them transferred its proton to the triethylamine, which in turn became a conjugate acid of the resulting anionic pendant group with a delocalised negative charge between the two oxygen atoms. This phenomenon allowed the ligand to coordinate as a monoanionic chelate *via* *N,S*-donor atoms around the rhenium(I) metal centre. The complex is soluble in many organic solvents and melts at 316 °C. The proposed reaction for the synthesis of compound **1** is given in **Scheme 1**.





Scheme 1: Synthetic route of complex *fac*-[Re(CO)₃(μ-mpc)]₂·2Et₃NH.

The ORTEP [67] drawing of the *fac*-[Re(CO)₃(μ-mpc)]₂·2Et₃NH molecule showing atom numbering is presented in **Figure 2**. The detailed molecular structure study showed the impact of various ligand substituents on the coordination mode of the parent compound. The octahedral coordination sphere around the central atom is created by three carbonyl ligands in a *facial* configuration, as well as the deprotonated derivative of the mother ligand H₂mpc, which coordinated as a monoanionic N/S[−] thioxalato chelate, mpc^{2−}. The crystal structure of compound **1** can be simplified as a symmetrical M₂L₂ dimer, formulated as *fac*-[Re(CO)₃(μ-mpc)]₂·2Et₃NH, whereby the *fac*-[Re(CO)₃]⁺ moieties are bridged *via* two Re-S bridging bonds forming a Re₂S₂ ring. Interestingly, it has been noted that compound **1** displays the anionic pendant group resulting from the deprotonation of the acidic functional group of the ligand, which in turn is stabilised as an acetate group with a delocalised negative charge between the two oxygen atoms. In addition, the cationic tertiary amine, Et₃NH⁺, is present in the crystal structure of the title compound, thus confirming the transfer of a proton to the trimethylamine (**Scheme 1**). The coordination mode of various substituents around the rhenium metal centres in the crystal of compound **1** is significantly dominated by the replacement of the monodentate chloride ligand with anionic thiol sulphur of the coordinated chelate to maintain the number of valence electrons (NVE) count at 18e. The nitrogen in the pyridine ring coordinated as a neutral donor atom. The synthetic route also accessed the suitable starting materials through triple-ligand exchange by substituting three carbonyl groups. In its molecular structure, each rhenium is coordinated to the charged thiolate sulphur as Re(1)-S(2)

and Re(1ⁱ)-S(2ⁱ), forming a rhombus core (Re₂S₂). The neutral pyridinic nitrogen atom N(1) around Re(1), as well as N(1ⁱ) around Re(1ⁱ) of the mpc-chelates, in addition to the three carbonyl ligands, determines the geometry of the molecule.

The atoms O(11), O(12), O(13), and O(14) of the pendant acetate groups are not involved in any bond formation with rhenium(I) metal centres; rather, these atoms are involved in other molecular interactions. For the molecule to stabilise in its overall electroneutrality entity, the uncoordinated acetate ion was stabilised by the counter-ion (Et₃NH⁺) (**Figure 2**), as also shown in synthetic **Scheme 1**. Each single [Re(CO)₃]⁺ moiety lies in a facial arrangement, and this is supported by the non-linear *trans* bond angles S(2)-Re(1)-C(3) [164.2(3)°], N(1)-Re(1)-C(4) [168.5(5)°], and S(2_a)-Re(1)-C(2) [173.6(4)°], which strongly deviate from linearity. The Re₂S₂ ring is not coplanar with a Re(1)-S(2)-Re(1_a) bond angle of 92.52(8)°, which led to the formation of bond angles Re(1)-S(2)-Re(1ⁱ) and Re(1)-S(2_i)-Re(1ⁱ) in the plane. In addition, the selected torsion angles S(2_a)-Re(1)-S(2)-Re(1_a) [22.72(7)], N(1)-Re(1)-S(2)-C(12) [3.4(4)], N(1)-Re(1)-S(2)-Re(1_a) [112.1(2)], and C(2)-Re(1)-S(2)-C(12) [98.5(5)] in the planes are described by the connectivity of atoms in a molecule, and the later dihedral angles confirm undoubtedly the conformation and geometry of compound **1**.

The octahedral geometry of the molecule is also described by the bite angles of 64.9(2)° and 86.4(2)° for N(1)-Re(1)-S(2) and S(2_a)-Re(1)-N(1), respectively. The angle N(1)-Re(1)-S(2) highly deviates from orthogonality, whereas the angle S(2_a)-Re(1)-N(1) slightly deviates from orthogonality. The Re(1)-C(3) [1.928(11) Å] bond length *trans* to S(2) is longer than the bond distance Re(1)-C(4) [1.902(11) Å] which is *trans* to pyridinic nitrogen, whereas the Re(1)-C(2) [1.891(2) Å] bond distance *trans* to S(2ⁱ) is shorter than the Re-CO bond *trans* to N(1). This may be due to various coordination modes of the sulphur atom, which can coordinate to metal centres in its neutral thiol form or as a deprotonated thiolate donor. All the Re-C bond distances in the molecule are in the range of 1.900(2)-1.928(2) Å, aligning well with those reported for similar rhenium(I) complexes [68]. The two Re-S bond distances are not equal [Re(1)-S(2) = 2.529(3), Re(1)-S(2_a) = 2.545(2) Å], supporting the difference in the coordination behaviour of sulphur around the metal centre as reported in the previous studies [69-71]. The Re-N(1) bond distance of 2.164(7) Å is also in the range for Re(I)-N_{pyridine} bond distance [70,72].

Focusing on the moiety of mpc^{2-} , a consideration in the formation of bonds within the backbone of the ligand, the bond parameters describe the information on the effect of its coordination behaviours. In the anionic bidentate mpc^{2-} chelate the bond lengths C(1)-O(11) [1.245(12) Å] and C(1)-C(12) [1.234(13) Å], as well as the angle O(11)-C(1)-O(12) [126.6(10)°] are dominated by the double characters due to the negative charge that is delocalised between the two oxygen atoms. On the other hand, the S(2)-C(12) [1.772(9) Å] is single, confirming that sulphur coordinated as an anionic thiol species (S^-), while both the N(1)-C(12) [1.344(13) Å] and N(1)-C(13) [1.332(13) Å] bonds are double. The two coordinated 2-sulfidonicotinate (mpc^{2-}) groups are oriented in a *cis* conformation along the Re_2S_2 core, and the pendant acetate groups on the two pyridyl groups are oriented in opposite directions. The bridging sulphur atoms are also arranged in different directions, leading to a twisting in the Re_2S_2 ring. Compound **1** exhibited various C-H $\cdots\pi$ interactions to stabilise the structure (**Figure 3**). These interactions were observed between CH_{21} groups of the uncoordinated cationic tertiary amine Et_3NH^+ and sulphur (S2) and oxygen O(12) of the coordinated (λ^1 -oxidaneyl)(2-sulfidopyridin-3-yl)methanolate (mpc^{2-}) groups with distances of 3.760(12) and 3.153(15) Å for C(21)H(21A) $\cdots$ S2 and C(21)H(21B) $\cdots$ O(12), respectively. The CH_{22} and CH_{23} groups of Et_3NH^+ also showed interactions with oxygen O(12) and displayed C(22)H22B $\cdots$ O12 [3.537(16) Å] and C(23)H23A $\cdots$ O12 [3.326(15) Å]. The co-planarity of the uncoordinated Et_3NH^+ with the acetate pendant group in backbone of the ligand is probably due to the two hydrogen bonds (N-H $\cdots$ O) formed between the N(2) of Et_3NH^+ and the oxygen atoms O(11) and O(12) of the acetate group of the coordinating (λ^1 -oxidaneyl)(2-sulfidopyridin-3-yl)methanolate (mpc^{2-}) chelate leading to N(2)H(2) $\cdots$ O(11) [2.678(12) Å] and N(2)H(2) $\cdots$ O(12) [3.169(13)] Å (Figure 3 and Table 3 in supplementary data).

Other previous studies have also tried to use the H_2mpc ligand during the synthesis of some complexes of different metals, including Ca, Mg, Ba, Sr, and Pb [62]. In these investigations, hydrazine and water were employed as co-ligands during the synthetic procedures, leading to the formation of monomeric metal complexes, such as $[\text{Ca}(\text{N}_2\text{H}_4)_2(\text{Hmpc})(\text{H}_2\text{O})_2]$, $[\text{Sr}(\text{N}_2\text{H}_4)(\text{Hmpc})(\text{H}_2\text{O})_3]$, $[\text{Ba}(\text{N}_2\text{H}_4)_2(\text{Hmpc})\text{H}_2\text{O}]$, $[\text{Pb}(\text{N}_2\text{H}_4)_5(\text{Hmpc})_2]$, and $[\text{Mg}(\text{N}_2\text{H}_4)_4(\text{Hmpc})]\cdot 4\text{H}_2\text{O}$. The overall observation shows that in all these complexes, the Hmpc^- ligands are coordinated to the metal centres in monodentate fashion [62]. Additionally, a new series of Pt(II), Pd(II), Re(III), Mo(VI), Pt(II), and Mo(V) compounds with 2-mercaptonicotinic acid (HnicSH) chelate were previously synthesised and the compounds

[Pt(bipy)(HnicS)₂] $\cdot$ CH₃OH, [Pt(PPh₃)(HnicS)₂] $\cdot$ NEt₃ $\cdot$ H₂O, [MoO₂(CH₃NicS)₂], [Pd(PPh₃)(HnicS)₂] $\cdot$ 0.5CH₃OH, [Pt(HnicS)₂], [Pd(HnicS)₂] $\cdot$ CH₃OH, [ReI₂(PPh₃)₂(HnicS)], [Mo₂O₃(CH₃nicS)₄] $\cdot$ DMF, and [Re(PPh₃)(OCH₃)(HnicS)₂] were isolated [72]. It has been noted that the crystal structure of [Re(PPh₃)(OCH₃)(HnicS)₂] contains two HnicS[−] ligands bonding monodentately *via* sulphur atoms, whereas [ReI₂(PPh₃)₂(HnicS)] bears one HnicS[−] coordinating as a bidentate chelate *via* nitrogen and sulphur donor atoms [72].

Table 1: Crystallographic data and structure refinement data for *fac*-[Re(CO)₃(μ -mpc)]₂ $\cdot$ 2Et₃NH.

Parameters	Compound 1	
Chemical formula	C ₁₈ H ₆ N ₂ O ₁₀ Re ₂ S ₂ $\cdot$ 2(C ₆ H ₁₆)	
Empirical formula	C ₃₀ H ₃₈ N ₂ O ₁₀ S ₂ Re ₂	
Formula weight	1051.18	
Temperature (K)	200 K	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions (Å, °)	a=22.3139(15)	$\alpha = 90$
	b=10.3895(7)	$\beta = 105.687(4)$
	c=16.3486(12)	$\gamma = 90$
Crystal size/mm ³	0.07 x 0.20 x 0.41	
Volume (Å ³)	3648.9(4)	
Z	4	
Density (calc.) (g/m ³)	1.913	
Absorption coefficient (mm ^{−1})	0.056	
<i>F</i> (000)	2032	
Radiation	Mo K α ($\lambda = 0.71073$)	
θ range for data collection (deg)	2.2 to 28.4	
Index ranges <i>h,k,l</i> max	−29 $\leq h \leq$ 25, −13 $\leq k \leq$ 13, −20 $\leq l \leq$ 21	
Reflections Measured	3181	
Reflections collected	15333	
Independent reflections	4529	

Data/parameters	4529/220
Goodness-of-fit on F^2	1.03
Final R indexes [$I > 2 \sigma(I)$]	$R_1 = 0.0550$, $wR_2 = 0.1556$
Largest diff. peak and hole ($e/\text{\AA}^3$)	6.50/-2.41

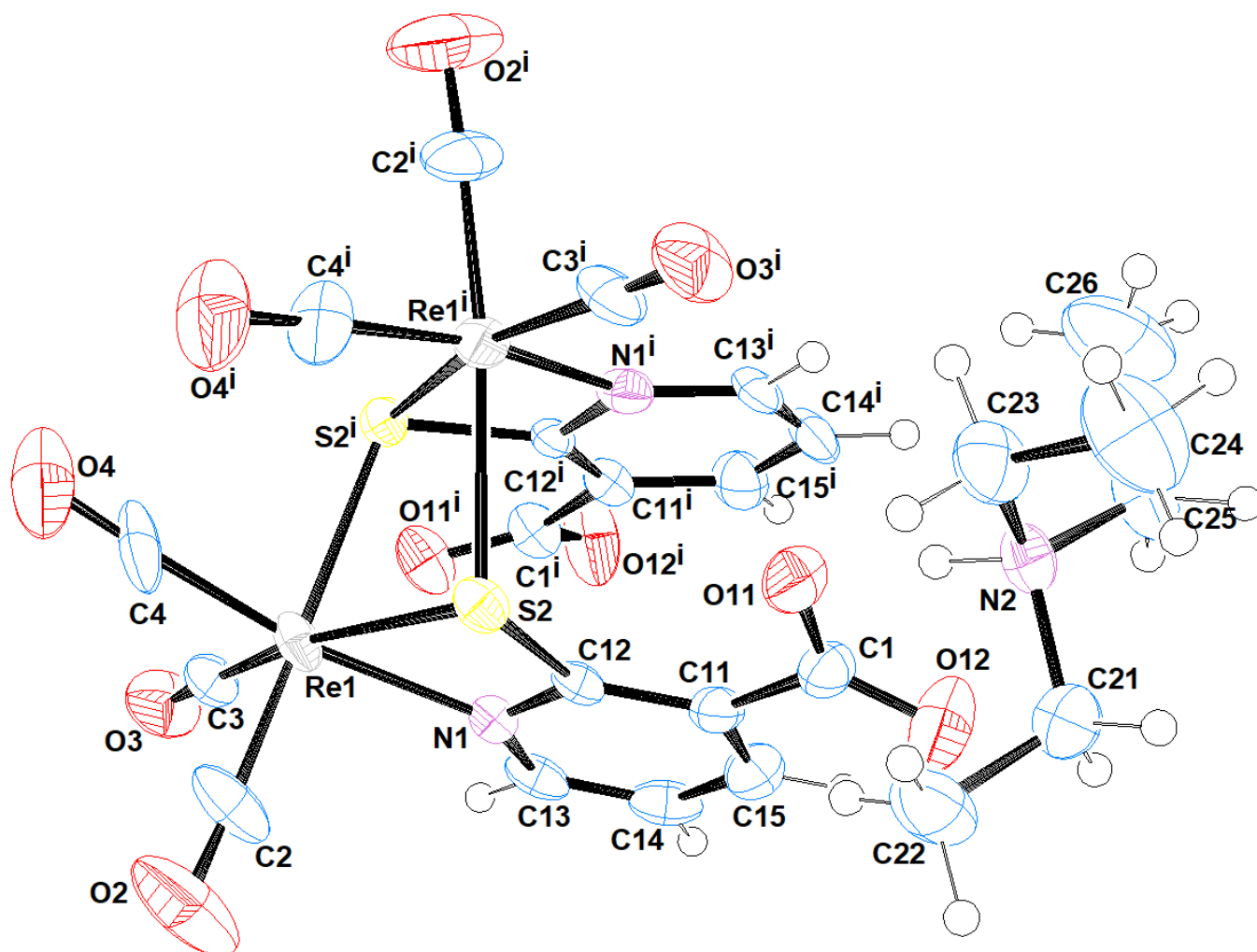


Figure 2: ORTEP diagram of compound **1** with thermal ellipsoids shown at the 50% probability level and hydrogen atoms as spheres of arbitrary size. The atom labelling in the crystal structure of **1** is displayed. Colour codes: Carbon = blue, Hydrogen = white, Nitrogen = purple, Oxygen = red, Sulphur = yellow, Rhenium = grey.

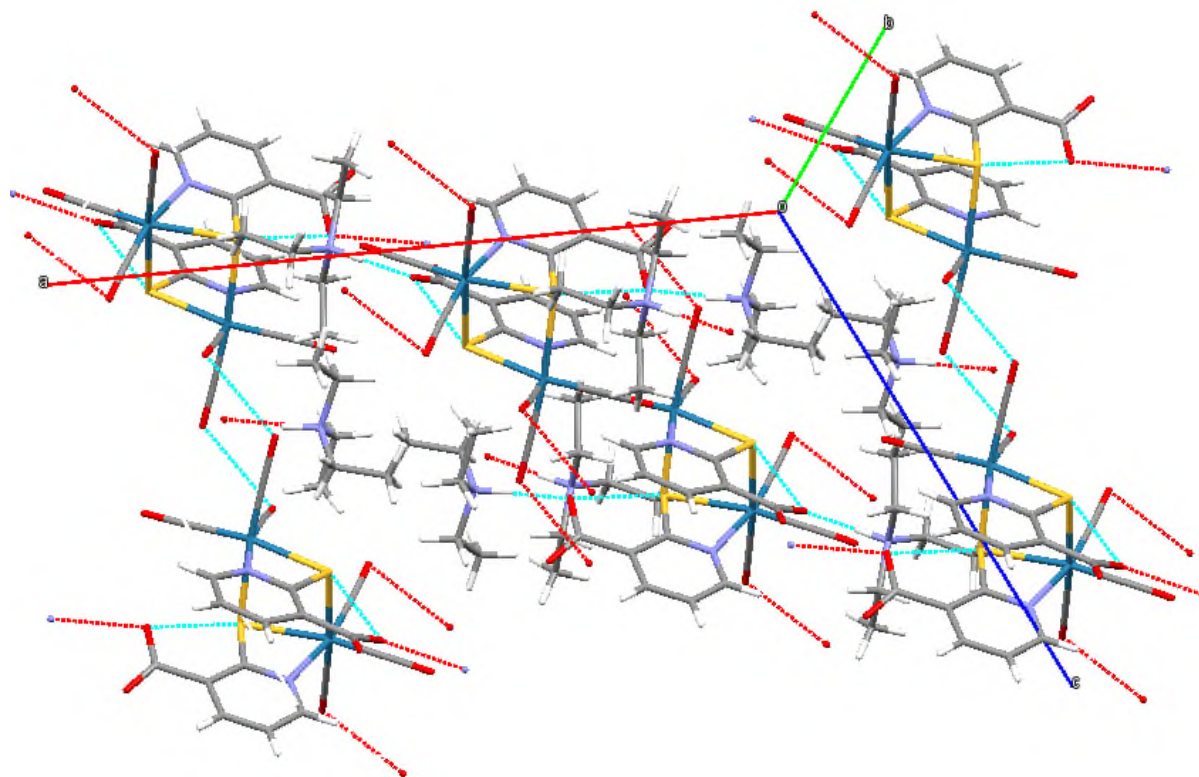
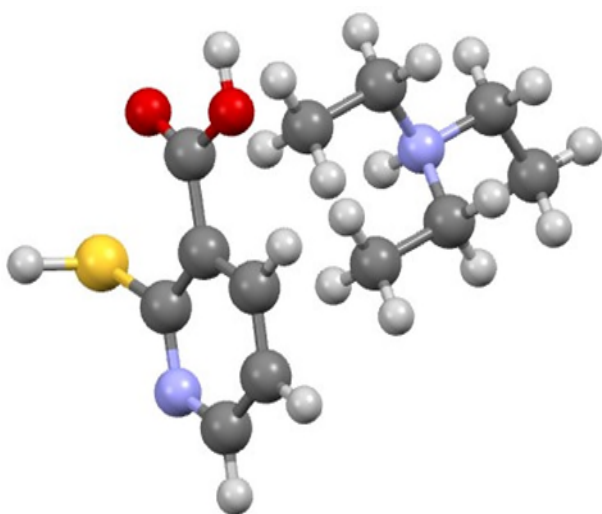


Figure 3: Packing diagram and perspective view in the unit cell of compound **1** displaying hydrogen-bond and other weak molecular interactions.

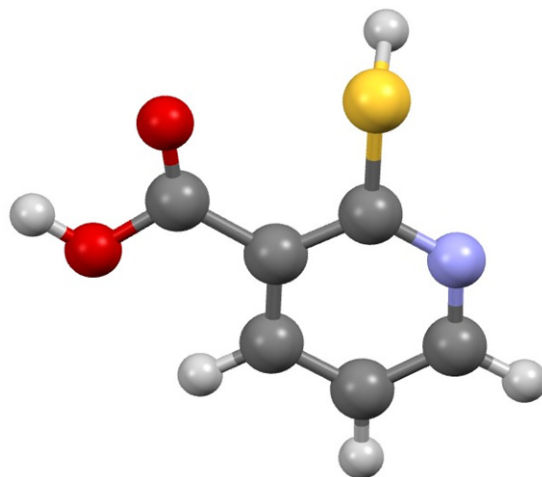
3.2 DFT calculations

DFT calculations were performed on the ligand (without triethylamine counter ions) and the ligand with triethylamine counter ions at the 6-31g(d,p) level of theory [76], as well as their respective complexes at the Def2TZVP level of theory [77] using the polarisable continuum model (PCM) in toluene [78]. This was accomplished through Gaussian 09 rev software [79]. Upon completing optimisation, minimum conformation energies and frequency calculations were reached to produce the structures in Figure 4. To test the reliability of the selected model for optimisation, selected experimental bond lengths were compared to theoretical ones (Table 4). After optimisation, fchk files were then generated as input to execute quantum theory of atoms in molecules (QTAIM) analysis using multiwfn [80] and visual molecular dynamics (VMD) [81] software using conceptual density functional theory (CDFT) calculations. This revealed non-covalent interactions (NCI), molecular electrostatic potentials (MEP), frontier molecular orbitals (FMO), and electron localisation function (ELF) analyses. The NCI index detects weak electron density and electron

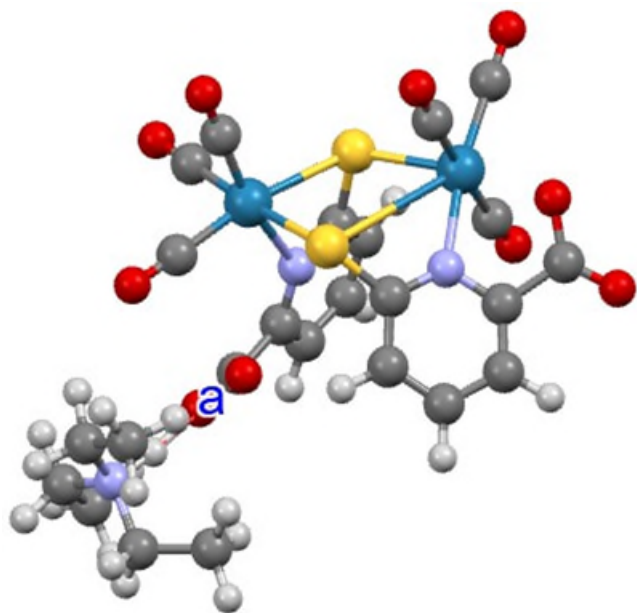
density gradients below the QTAIM analysis identification threshold [82], while MEP and CDFT chemical descriptors rely on variations in electron densities to probe reactive sites in certain regions of molecules [83,84]. ELF, on the other hand, can analyse the localisation and delocalisation of electrons in a certain region of the molecule through a determinant derived from the electron kinetic energy density [85]. A comprehensive description of the molecular properties is revealed by these analyses, which explains the reactivity, geometry of formation of compounds and serves as input data for describing biological properties. Furthermore, these analyses can also serve as a predictive tool for the reactivities and properties of compounds [86-88]. Lastly, Hirshfeld Surface Analysis (HSA) and two-dimensional fingerprint plots were done on the rhenium complex at the B3LYP/DGDZVP level of theory.



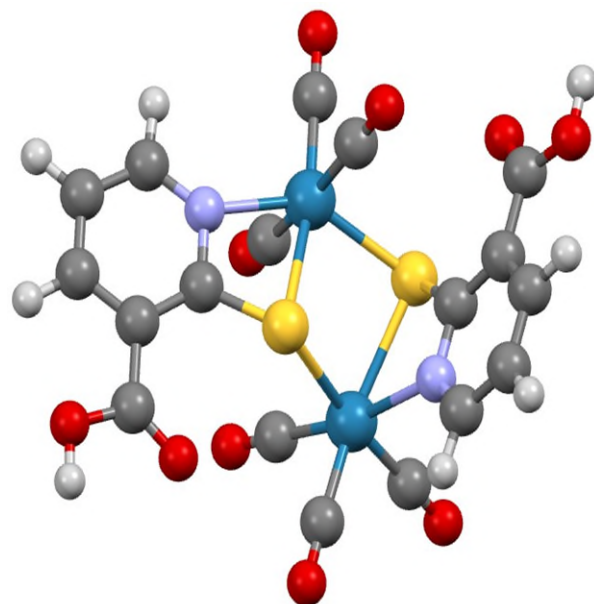
H₂mpc with Et₃NH



H₂mpc only



Re-mpc complex with Et₃NH



Re-Hmpc complex

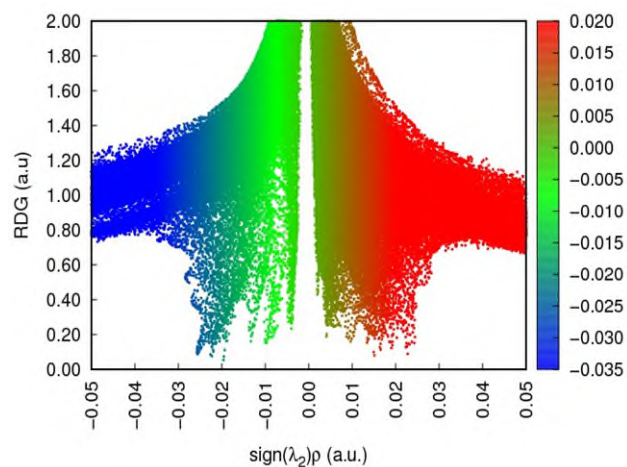
Figure 4: Optimised structures of ligands and complexes generated from Mercury software.

Table 4: Comparison between experimental bond lengths and electronic bond lengths in *fac*-[Re(CO)₃(μ-mpc)]₂·2Et₃NH.

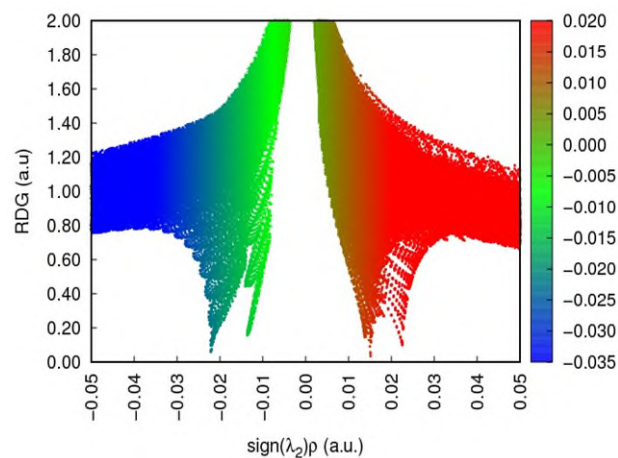
Experimental bond lengths (Å)		Electronic bond lengths (Å)	
Re(1)-S(2)	2.529(3)	Re(1)-S(2)	2.540
Re(1)-S(2_a)	2.545(2)	Re(1)-S(2_a)	2.70
Re(1)-C(2)	1.878(11)	Re(1)-C(2)	1.890
Re(1)-C(3)	1.928(11)	Re(1)-C(3)	1.907
Re(1)-C(5)	1.902(11)	Re(1)-C(5)	1.903
Re(1)-N(1)	2.164(7)	Re(1)-N(1)	2.291

3.2.1 Non-covalent interactions (NCI)

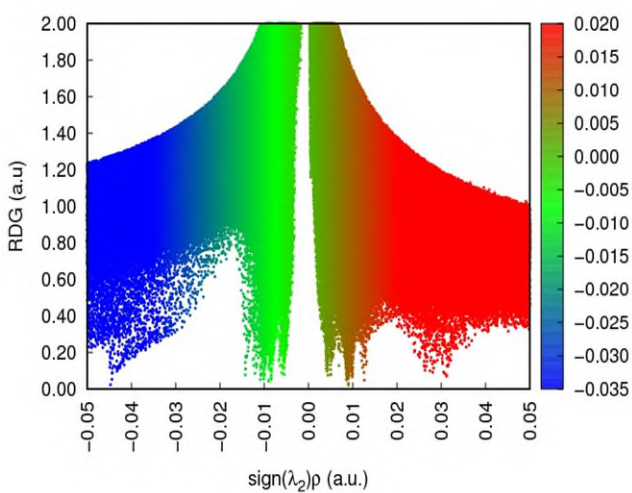
Contributions to NCI analysis of macromolecular stabilisation, the efficiency and specificity of enzymic reactions, and compound identification drive significant aspects of biological systems. This can be accomplished by factors such as properties of interacting groups or atoms, their separation distances, and the surrounding entity that leads to the formation and stability of each compound [89,90]. Additionally, multicomponent structures that form a key part in crystal engineering can also be constructed by NCI analysis [91], allowing both quantitative and qualitative information that probes the location of these interactions, resulting in the most stable geometries being adopted by compounds. For analysing the loci in space to obtain data where the reduced density gradient (RDG) approaches zero, well-defined troughs are formed, and a parameter “ s ” is required (Figure 5). Small gradients, along with the density values (ρ), cause this and produce isosurfaces (Figure 6). Weak interactions occur when both “ s ” and ρ have low values. Green colours represent van der Waals attractive forces, steric repulsions are indicated by red colours, and hydrogen bonding is blue, with more intense colours denoting stronger interactions. The strength of the interaction is measured by ρ , where a trough with the highest value denotes the strongest interaction and all forces involved are encompassed by the eigenvalue λ_2 [80]. As $S \cdots O$ NCI is common in the ligands and complexes except for the triethylamine-free Re-Hmpc (Figure 7), quantitative data were obtained along this interacting path (Table 5). Hydrogen bonds, van der Waals attractive forces, and steric repulsion are observed in two-dimensional scattermaps and are supported by three-dimensional isosurfaces. Stronger interactions are observed in the ligands than in the complexes. Electrons are also locally more depleted and less localised than in the complexes.



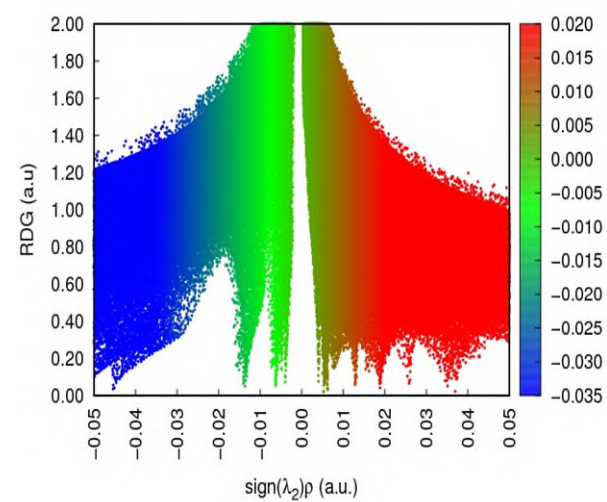
H₂mpc with Et₃NH



H₂mpc only



Re-mpc complex with Et₃NH



Re-Hmpc complex (no Et₃NH)

Figure 5: Two-dimensional scattermaps of non-covalent interactions for the ligands and complexes.

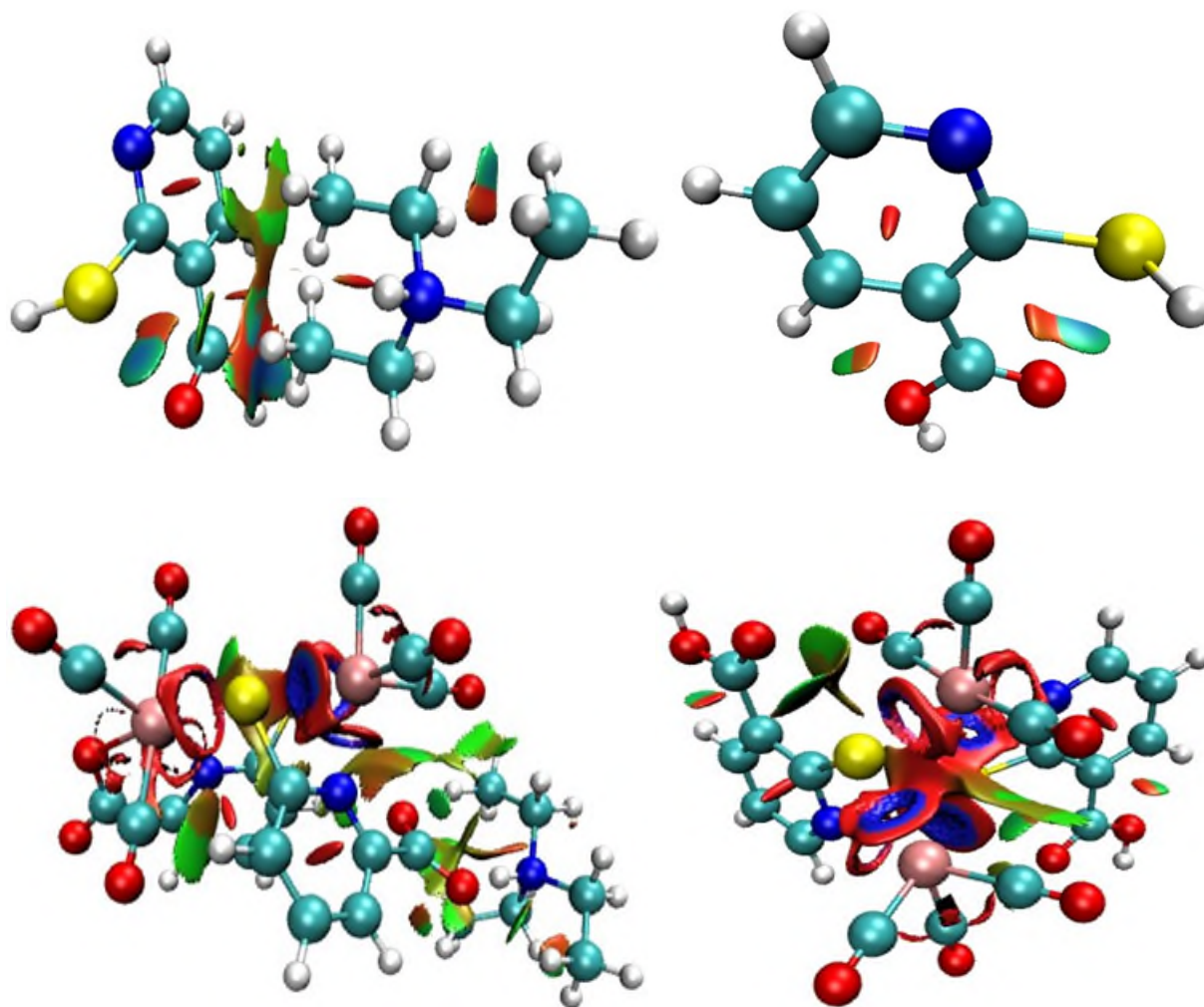
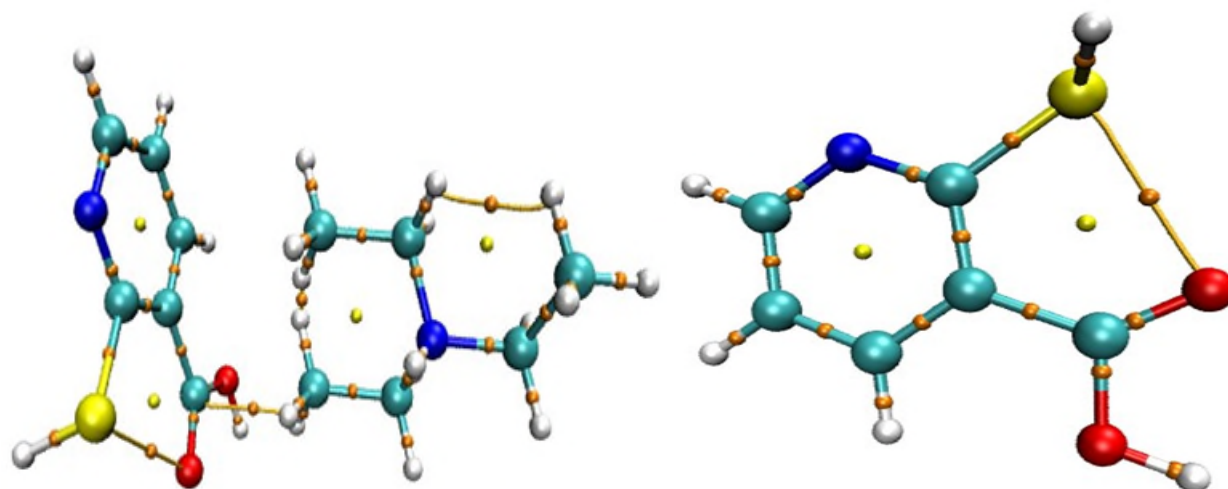


Figure 6: Three-dimensional isosurfaces for non-covalent interactions in ligands and complexes.



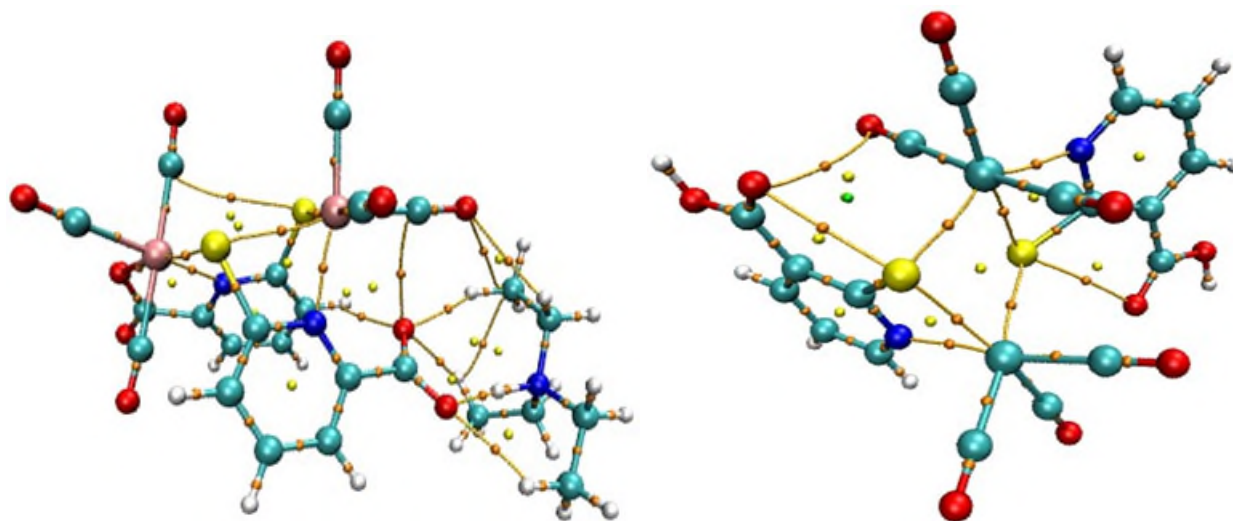


Figure 7: Interacting paths for non-covalent interactions in the ligands and complexes.

Table 5: Non-covalent interaction data between O and S within the ligands and complexes.

Compound	$-\lambda(\rho)$	$E(r)$	$\nabla^2\rho(r)$	ELF	RDG (1×10^{-15})	ALIE
H₂mpc with Et₃NH	0.02239	0.003481	0.07441	0.07247	0.3075	0.4050
H₂mpc only	0.02211	0.006581	0.07502	0.07093	0.2992	0.4642
Re-mpc complex with Et₃NH	-	-	-	-	-	-
Re-Hmpc complex (no Et₃NH)	0.01408	0.001795	0.05489	0.03774	0.2797	0.4993
	0.01367	0.001795	0.05266	0.03747	1.9180	0.4944

3.2.2 Molecular electrostatic potentials (MEP)

To measure the differences in electronegativities on atoms in molecules, a chemical descriptor called the molecular electrostatic potential (MEP) can be used. When doing so, an electron density

map is generated with different colours in the region of the compound that indicates where either an electrophilic or a nucleophilic attack can occur (Figure 8). Across these regions, the electron concentrations reduce in the order blue>green>yellow>orange>red, which indicates that a blue colour has a high probability for a nucleophilic attack, while a red colour reveals a strong possibility where an electrophilic attack can occur. This means that MEP can probe the reactivity of a compound and is primarily responsible for long-range interactions [83]. As the donor atoms N and S are the atoms of interest (Figure 9, Supplementary data), quantitative values of MEP data across these atoms were generated and depicted in Table 6; Supplementary data. The larger MEP values of 383.7 and 365.7 in H₂mpc with Et₃NH around N8 and S33 respectively, compared to MEP values of 329.9 and 255.8 around N8 and S10 respectively in H₂mpc only indicate that the counter ion induces larger electronegativities across these donor atoms. Thus, it appears that through hydrogen bonding, the counter ion injects more electrons into the donor atoms of the ligand. Upon coordination, the electronegativities across the donor atoms reduce substantially except on S9 in the Re-mpc complex with Et₃NH which shows a MEP value of 274.8 (see Figure 9 and Table 6; Supplementary data). It appears that hydrogen bonding still plays a role in injecting more electrons into the donor atoms. A correlation between the average local ionisation energy (ALIE), and MEP is also observed, with more ALIE being required to remove an electron from sulfur donor atom (S) if it has a lower electron density. This agrees with previous findings [92]. However, a large discrepancy was observed when comparing S10 to S23 in the triethylamine-free Re-Hmpc complex.

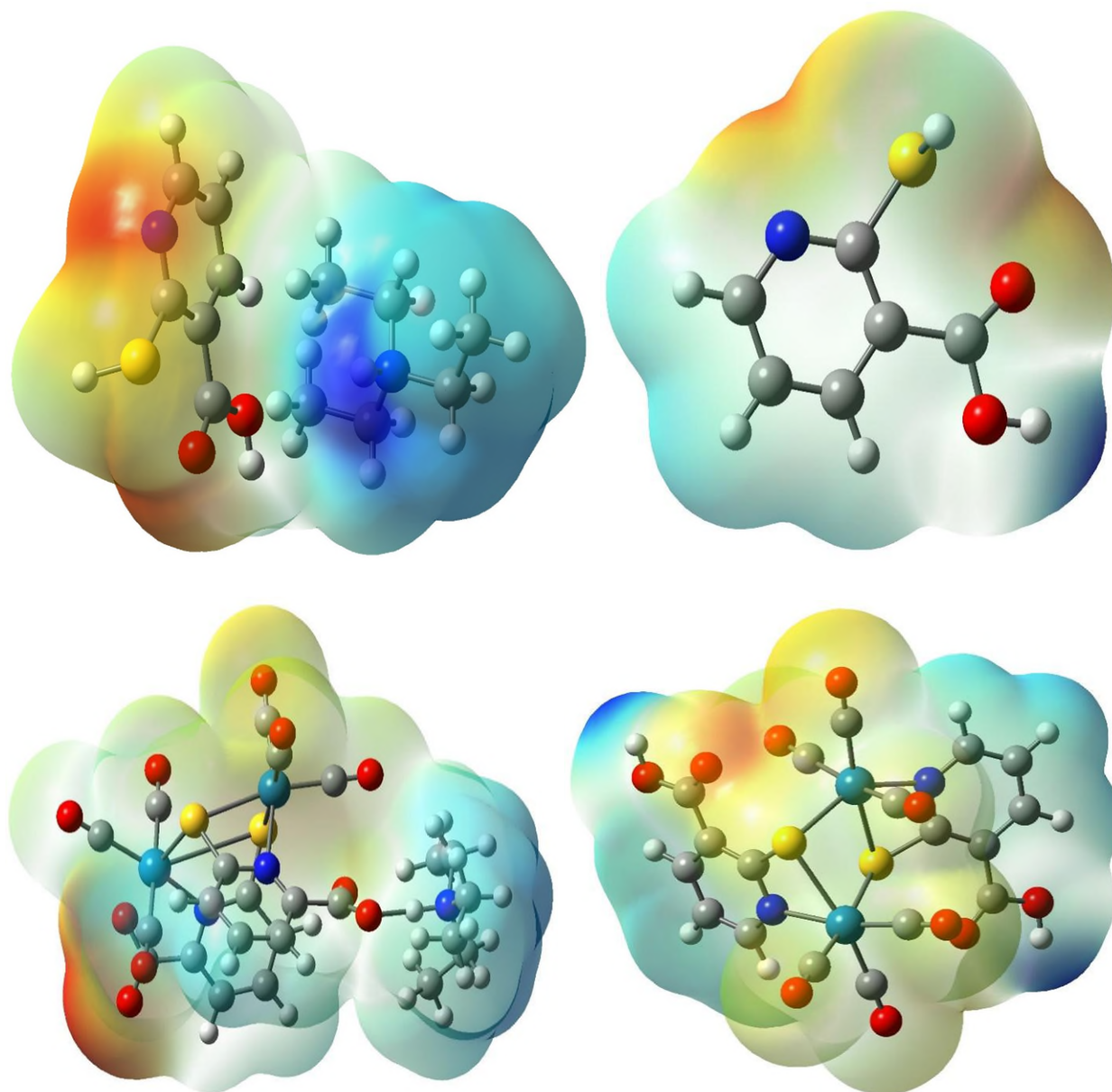


Figure 8: Electron density map for the molecular electrostatic potential that reveals reactive sites in the ligands (H_2mpc with Et_3NH and H_2mpc only) and complexes (Re-mpc complex with Et_3NH and Re-Hmpc complex).

3.2.3 Frontier Molecular Orbital (FMO) analysis

Another chemical descriptor that measures reactive sites is Frontier Molecular Orbitals (FMO). This chemical descriptor uses parameters like chemical potentials (μ), ionisation potentials (IP), global softness (δ), nucleophilicity indices (N), electron affinities (EA), electrophilicity indices (ω),

electronegativity (χ), and global hardness (η) on compounds (**Equations 1–8**). Calculating these parameters require Koopman's theorem [93].

$$EA = -E_{LUMO} \quad (1)$$

$$IP = -E_{HOMO} \quad (2)$$

Calculating χ is accomplished by using the Mulliken theory [94]

$$\chi = \frac{IP - EA}{2} \quad (3)$$

while η and δ are given by

$$\eta = \frac{IP + EA}{2} \quad (4)$$

$$\delta = \frac{1}{\eta} \quad (5)$$

Utilising the Parr and Pearson relation [95], the chemical potential (μ) can be obtained

$$\mu = -\frac{IP - EA}{2} \quad (6)$$

From Parr and Young's theory [96], the electrophilicity index (ω) can measure the electron-accepting tendency of a species

$$\omega = \frac{\mu^2}{2\eta} \quad (7)$$

The index (ΔN_{max}) defines the maximum amount of electronic charge and is given by the relation

$$\Delta N_{max} = \frac{-\mu}{\eta} \quad (8)$$

Measuring the resistance of an atom to charge transfer (CT) [97, 98] is normally achieved by the descriptor η , while δ measures the ability of a group of atoms or an atom to receive electrons, measuring the reactivity of a compound [99], and the stabilisation energy is predicted by saturating electrons using ω to predict biological activities [95,100-102]. A change in energy occurs between a nucleophile and a suitable electrophile, which results in ω [100, 103-105]. Measuring the electrophilic and nucleophilic characters of compounds can be performed by the nucleophilicity index (N) [99]. An electron that occupies the lowest unoccupied molecular orbital (LUMO) sheds energy, and is measured by EA of the electron-accepting power of an accepting molecule [97]. A

covalent bond can be formed through the ability of a compound to draw electrons towards itself, and is revealed by a description of χ [106]. *IP* energy can dislodge an electron from its highest occupied molecular orbital (HOMO), and measures the electron-donating power of a donor molecule [107]. Although there is a general belief that an electron that occupies the HOMO energy level will be automatically excited to the LUMO energy level [108], a study by Bulat *et al.* debunked this by discovering that an electron's position in atomic space and the contour of a molecule also play a role in electron excitations [109]. Nevertheless, HOMO-LUMO energy gaps still play a significant role in describing the reactivities of many organic molecules [110]. While H₂mpc with Et₃NH and Re-mpc complex with Et₃NH split into alpha and beta orbitals, which usually occurs when orbitals become more spread out, a significantly large energy gap is observed in H₂mpc (Table 7). For the alpha orbitals in H₂mpc, electrons appear to be delocalised away from COO⁻ upon excitation (Figure 10). When it splits into beta orbitals, then they are delocalised towards the counter ion. In the absence of the counter ion, electrons are delocalised across the whole compound. Upon complexation to form the Re-mpc complex with Et₃NH, electrons are delocalised across the whole aromatic ring in both alpha and beta orbitals. A similar phenomenon was observed in the triethylamine-free Re-Hmpc complex, where electrons are being delocalised away from the sulphur atoms and rhenium core. The energy gap increases upon complexation in the alpha orbitals but not in the beta orbitals. The energy gap also decreases upon complexation in the triethylamine-free compound. Observing Table 7, it is clear that the counter ion makes it easier to ionise the ligand but not the complex. This counter ion also makes the compound less resistant to CT, and upon complexation, it becomes even less resistant. Although the counter ion enhances the reactivity of the compound, it becomes less reactive upon complexation. The absence of the counter ion enhances the biological activities in the ligands but not in the complexes. The latter does however, display much greater biological activities than the former. As expected, the nucleophilicity of the compound increases in the presence of the counter ion.

Table 7: Frontier molecular orbital data for ligands and complexes.

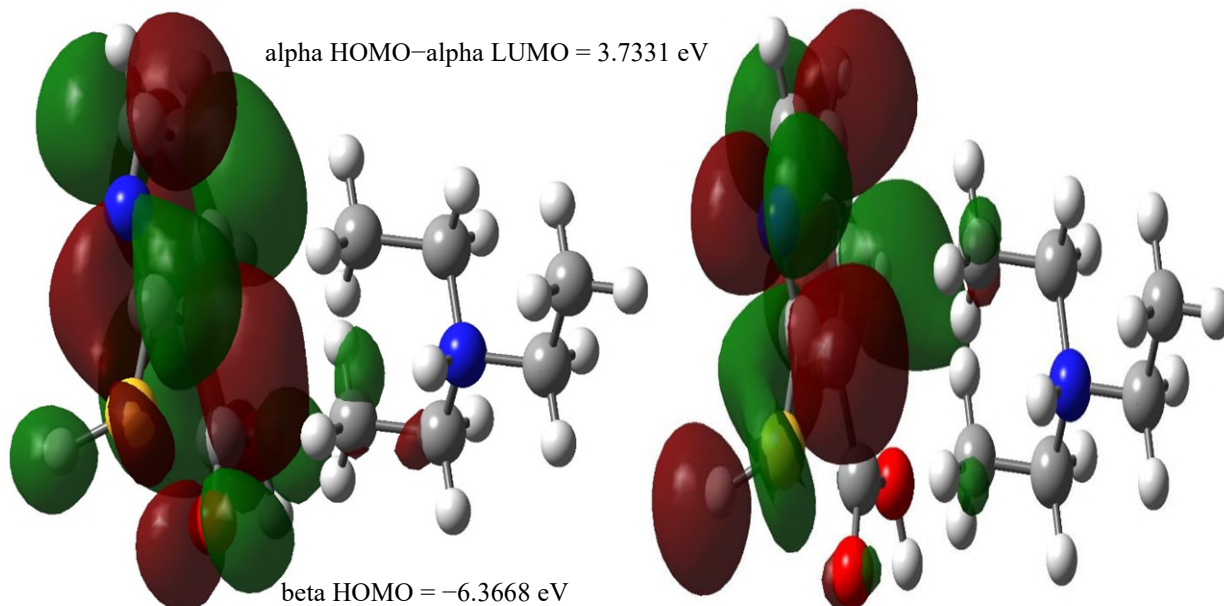
Compound	H ₂ mpc with Et ₃ NH	H ₂ mpc only	Re-mpc complex with Et ₃ NH	Triethylamine- free Re-Hmpc complex
HOMO (eV)	*-2.5084 † -6.3668	-7.7675	*-6.9546 † -6.9501	-6.9269
LUMO (eV)	*1.2247 † 1.1188	-0.91160	*-1.2720 † -2.8060	-1.4881
Energy gap (eV)	*3.7331 † 7.4856	6.8559	*5.6827 † 4.1442	5.4388
<i>IP</i> (eV)	2.8527	8.2364	7.2913	6.9023
<i>EA</i> (eV)	-1.6356	-0.0891	2.8805	1.3759
χ (eV)	0.6086	4.0736	5.0859	4.1391
η (eV)	4.4883	8.3255	4.4107	5.5263
δ (1×10^{-2})	2.2280	1.2010	1.2267	1.1810
Ω	0.0413	0.9966	2.9322	1.5500
<i>N</i> (eV)	7.9719	3.1394	3.6154	3.5259
μ (eV)	-0.6086	-4.0736	-5.0859	-4.1391

* alpha; † beta

alpha HOMO = -2.5084 eV

alpha LUMO = 1.2247 eV

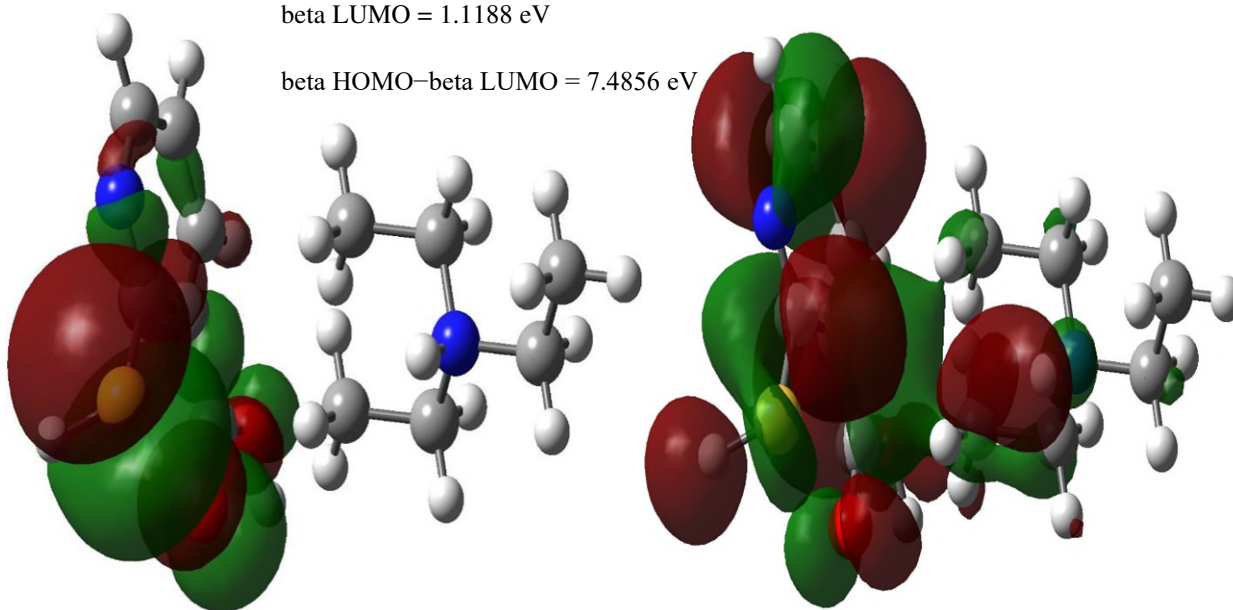
alpha HOMO-alpha LUMO = 3.7331 eV



beta HOMO = -6.3668 eV

beta LUMO = 1.1188 eV

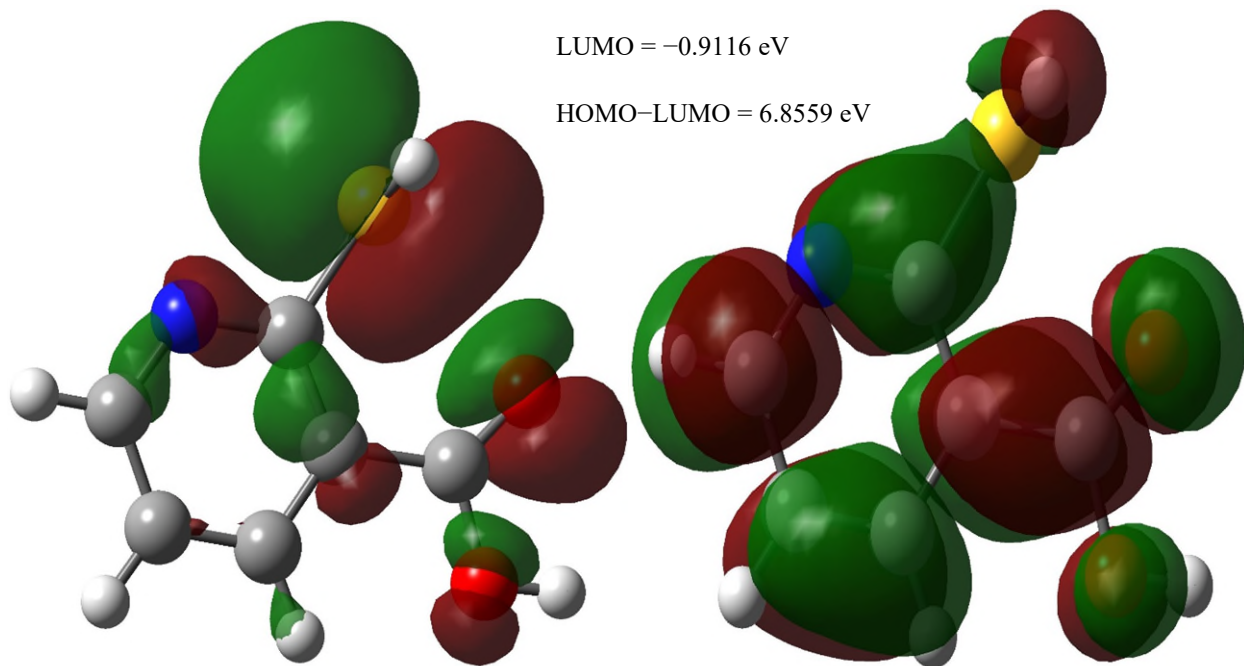
beta HOMO-beta LUMO = 7.4856 eV



HOMO = -7.7675 eV

LUMO = -0.9116 eV

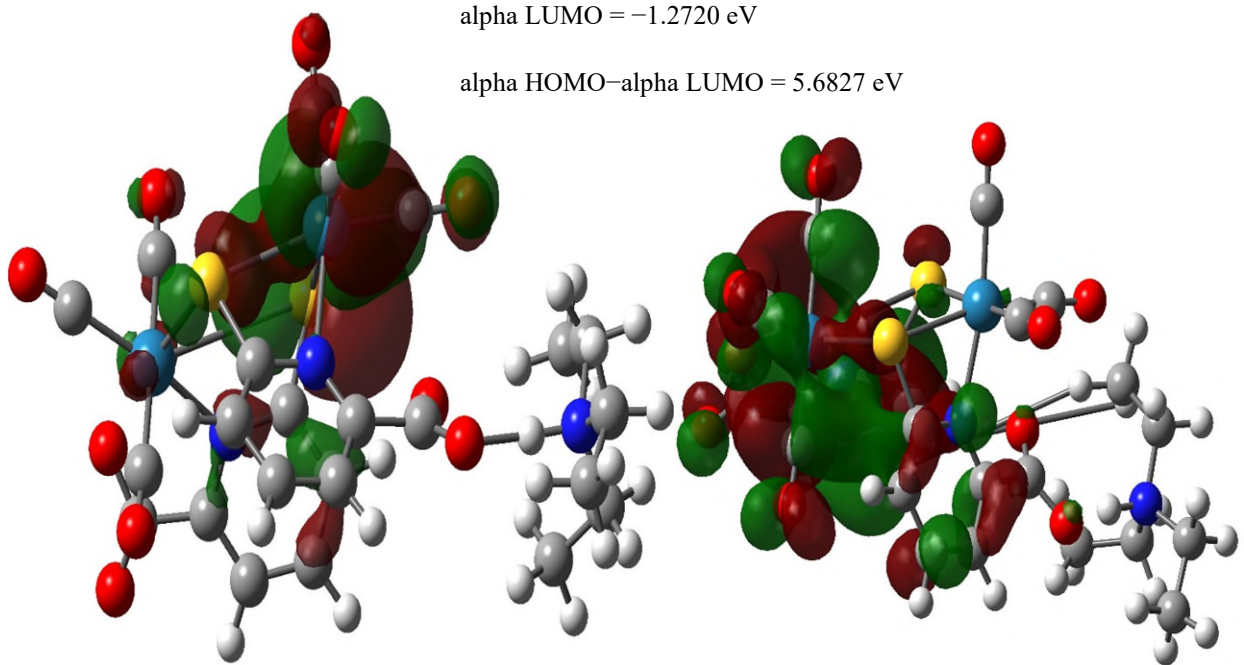
HOMO-LUMO = 6.8559 eV



alpha HOMO = -6.9546 eV

alpha LUMO = -1.2720 eV

alpha HOMO-alpha LUMO = 5.6827 eV



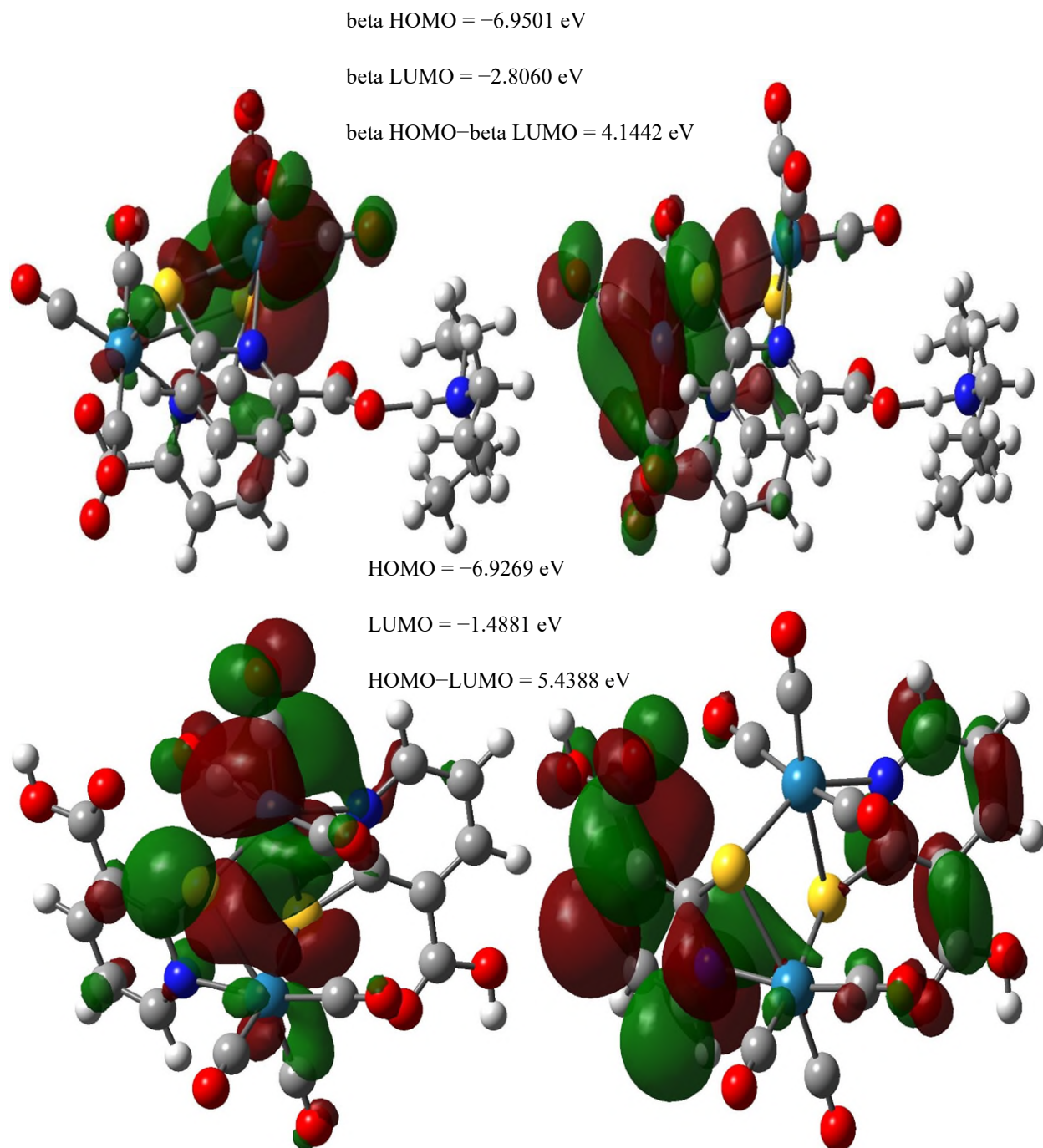


Figure 10: Highest occupied molecular orbitals and lowest unoccupied molecular orbitals for ligands and complexes.

3.2.4 Conceptual density functional theory (CDFT)

Conceptual density functional theory (CDFT) is an alternative chemical descriptor to MEP that also probes reactive sites on compounds. Unlike MEP, this descriptor can also reveal active sites

for radical attacks. Since these attacks denote active sites that absorb and inactivate reactive oxygen species (ROS), they can pinpoint atomic locations for structure-activity relationships between compounds and receptors for antioxidant studies [111-115]. The evaluation of the reactivity and selectivity of specific atomic sites on a compound is performed by CDFT, using a descriptor called the Fukui function f that is defined by **Equation 9** [116].

$$f(\vec{r}) = \frac{\partial \rho}{\partial N} v(\vec{r}) = \left(\frac{\delta \mu}{\delta v \vec{r}} \right) N \quad (9)$$

Equation 10 is used to indicate a nucleophilic attack on an active site on the compound

$$f^+(\vec{r}) = q_r(N+1) - q_r(N) \quad (10)$$

For an electrophilic attack, **Equation 11** is usually used

$$f^-(\vec{r}) = q_r(N) - q_r(N-1) \quad (11)$$

and when a radical attack occurs, then **Equation 12** is selected

$$f^0(\vec{r}) = q_r(N+1) - q_r(N-1) \quad (12)$$

where q_r represents the Hirshfeld charges on the active sites of each compound [110]. Additionally, $f^0(\vec{r})$ is regarded as a dual descriptor that can reveal regions for a possibility of either an electrophilic attack or a nucleophilic attack, with positive values indicating electrophilic attacks and negative values indicating nucleophilic attacks. Thus, f^0 measures the electron densities across these atomic sites on the molecule [117]. As expected, a high probability of an electrophilic attack is observed on the donor atoms of H₂mpc with Et₃NH (Table 8 in supplementary data). A high probability of an electrophilic attack is also observed on S10 (0.2531) of triethylamine-free H₂mpc. Unlike the MEP analysis in the Re-mpc complex with Et₃NH, the electron density on S39 (0.0743) does not decrease upon coordination. This usually occurs due to quasi-degeneracy between HOMO and HOMO-1 orbitals [118]. Then there appears to be a higher probability of a radical attack on the sulphur atom in the presence of the counter ion in the ligand compared to the nitrogen atom. In the absence of the counter ion, the probability of radical attack on the sulphur atom increases fourfold. However, it decreases significantly upon complexation. The electron densities across the other donor atoms, however, decrease upon coordination.

3.2.5 Electron localisation function (ELF)

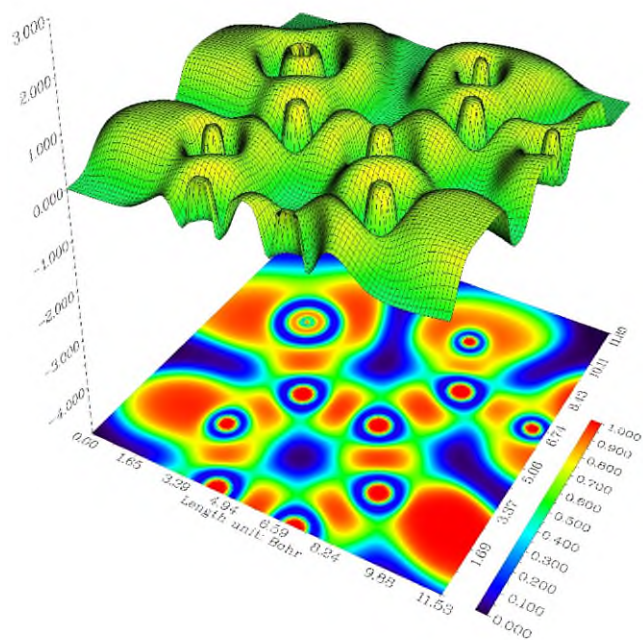
When employing a reference electron with the same spin as its corresponding Fermi hole in a similar vicinity, it can locate the probability of probing an electron pair, allowing a comprehensive description of the spatial location of these electron pairs. This enables a revelation where a smaller probability induces larger localisation of the reference electron, allowing information about spatial electron localisation from its kinetic energy density to be extracted. This can be performed with Becke and Edgecombe's dimensionless scalar electron localisation function (ELF) using **Equation 13**.

$$H = \frac{1}{1 + \left(\frac{D_{\sigma}}{D_{\sigma,0}}\right)^2} \quad (13)$$

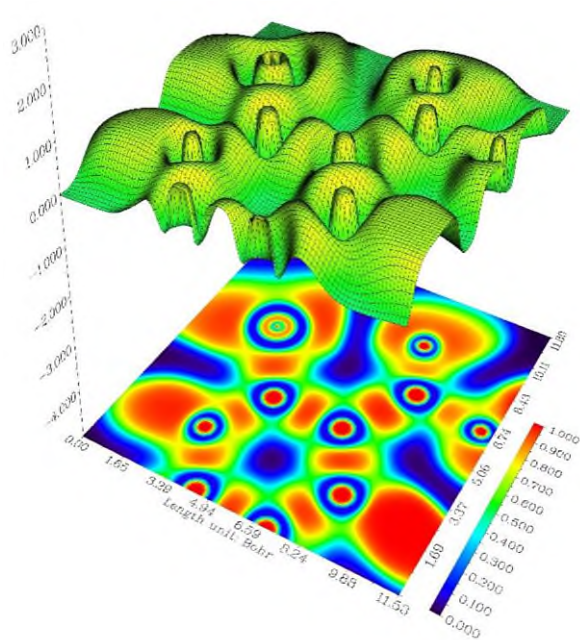
where

$$D_{\sigma,0}(r) = \left(\frac{3}{5}6\pi^2\right)^{2/3}[\rho_{\sigma}(r)]^{5/3} \quad (14)$$

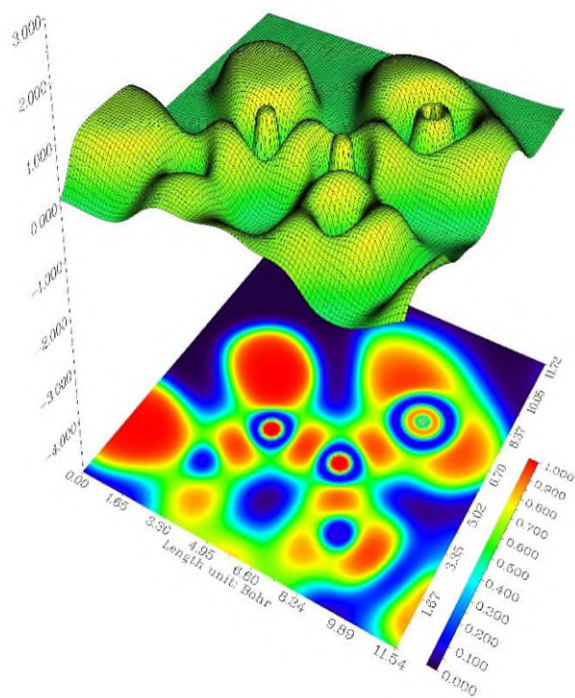
A description of the kinetic energy density of a homogeneous electron gas with spin density locally equal to $\rho_{\sigma}(r)$ can be obtained using **Equation 14**, with ELF being constrained in the region $0 \leq \eta \leq 1$. An electron is completely localised at $\eta = 1$ and displays a homogenous electron gas-like pair probability (electron delocalisation) if $\eta = \frac{1}{2}$. Obtaining a value of near zero is an indication of the border between electron pairs [85]. When rationalising molecular and atomic shell structures using ELF, a topological interpretation of molecular space is revealed, providing support for identifying regions such as chemical bonds, lone pairs, and core regions [119, 120]. Although the presence of the triethylamine counter ion has no influence on both C-C-S and C-N-S planes, it does appear to have some kind of influence along these planes upon complexation (Figure 11). Along the C-C-S plane, electrons appear to become more delocalised upon complexation in the presence of the triethylamine counter ion. In the absence of this counter ion along the same plane, they appear to be more localised although they were observed to be less localised than in the ligands. A similar scenario is observed along the C-N-S plane. These might be due to hydrogen bonding.



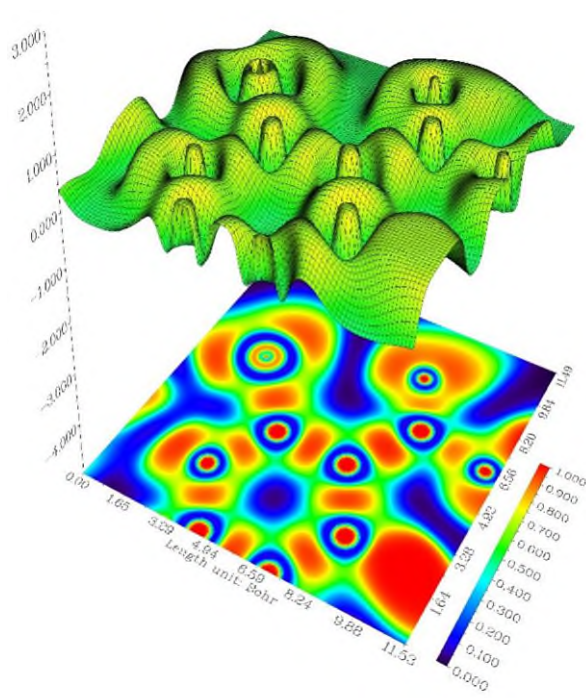
(a)



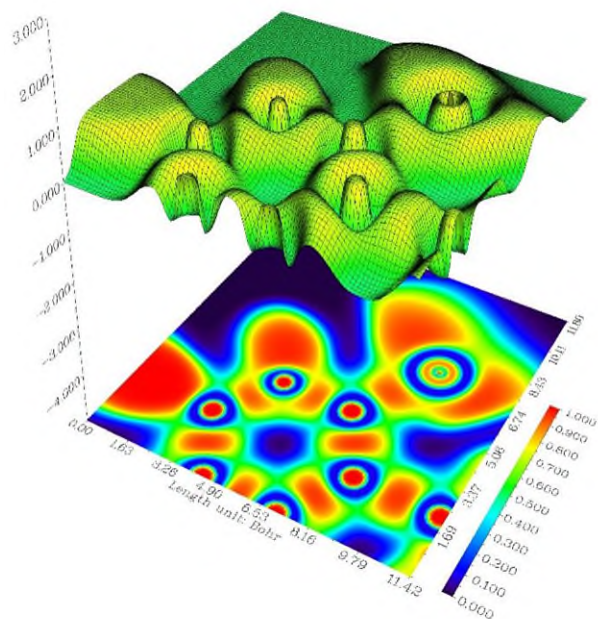
(b)



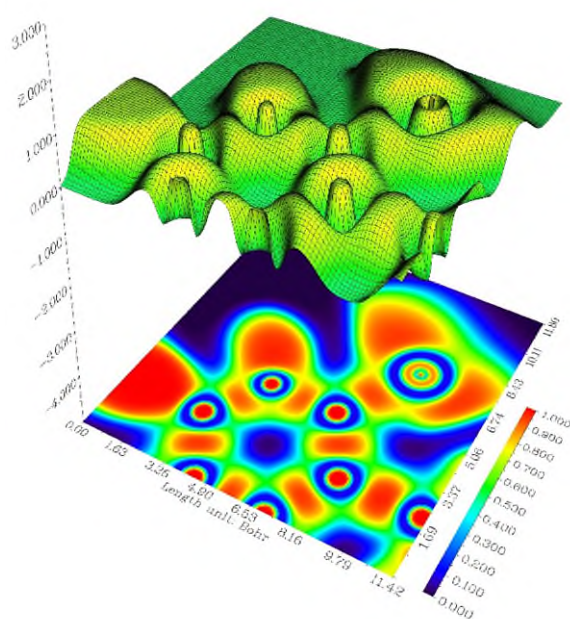
(c)



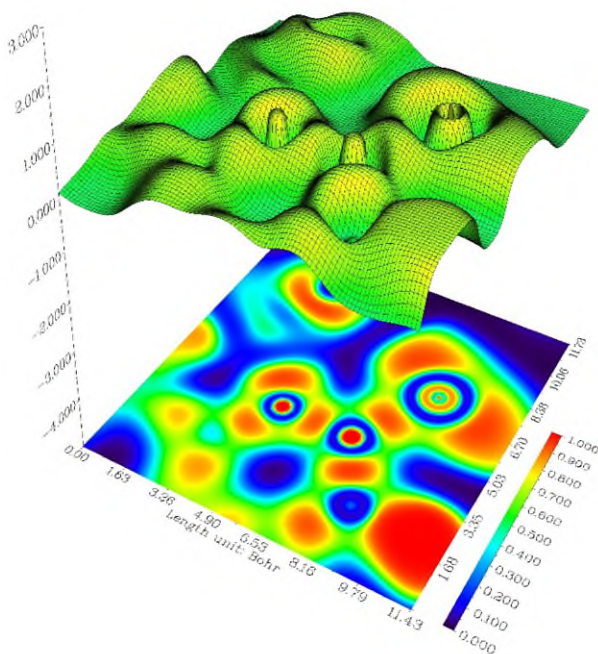
(d)



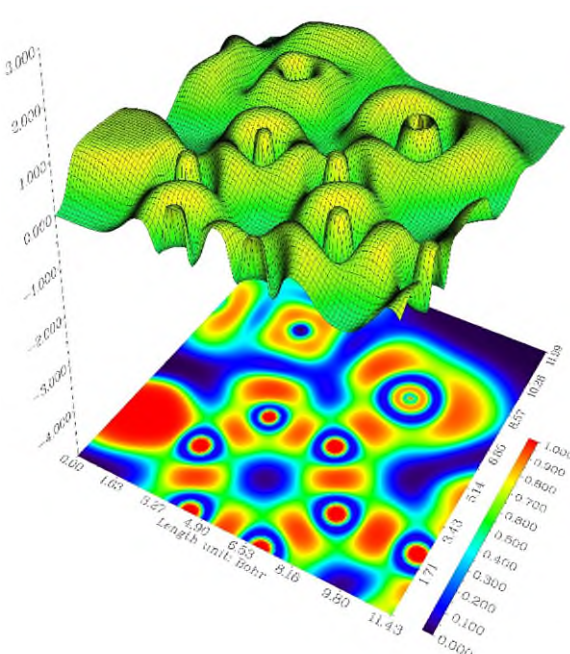
(e)



(f)



(g)



(h)

Figure 11: Electron localisation function along the C-C-S plane for (a) **H₂mpc with Et₃NH**, (b) **triethylamine-free H₂mpc**, (c) **Re-mpc complex with Et₃NH**, (d) **triethylamine-free Re-Hmpc**

complex, and along the C-N-S plane for (e) **H2mpc with Et3NH**, (f) **triethylamine-free H2mpc**, (g) **Re-mpc complex with Et3NH**, and (h) **triethylamine-free Re-Hmpc complex**.

3.2.6 Hirshfeld Surface Analysis (HSA)

Hirshfeld surface (HS) is a visual representation of an electron density jacket that wraps a molecule, revealing intermolecular interactions between neighbouring molecules within the molecular cluster. These interactions display areas of electron accumulation or depletion, playing a significant role in hydrogen bonding and van der Waals interactions, which are crucial for obtaining knowledge in pharmaceuticals and material science. A colour scale from red (0-0.701 a.u.) to blue (1.798 a.u.) was used to produce high-resolution images of this analysis (Figure 12). An electron cloud is generated by Equation 15 for visualising interacting sites between neighbouring molecules from the surface to the adjacent atom exterior (d_e plots) or interior (d_i plots) inside the crystalline environment at a normalised contact distance (d_{norm}). This produces coloured isosurfaces with strong interactions being revealed by red spots, van der Waals interactions being indicated by white areas, and blue isosurfaces indicative of no interactions.

$$d_{norm} = \frac{d_i - r_i^{vdw}}{r_i^{vdw}} + \frac{d_e - r_e^{vdw}}{r_e^{vdw}} \quad (15)$$

In addition to these calculations, two-dimensional fingerprint plots in the range 0.6-2.6 Å are also generated, providing a quantitative measure for percentage atomic contributions between interacting atoms in the molecular cluster (Figure 13). A significant aspect of these contributions is the number of atomic interactions that exceed 1%. Most of these cases involve hydrogen due to hydrogen bonding. This is further supported by the significant interaction between O and H that exceed 30%, followed by H...H interactions. Thus, hydrogen bonding is quite significant in these interactions. The C...H interaction is also an indication of van der Waals interactions that are present in this compound, while an O...O interaction is also observed, which could be due to steric repulsions [121].

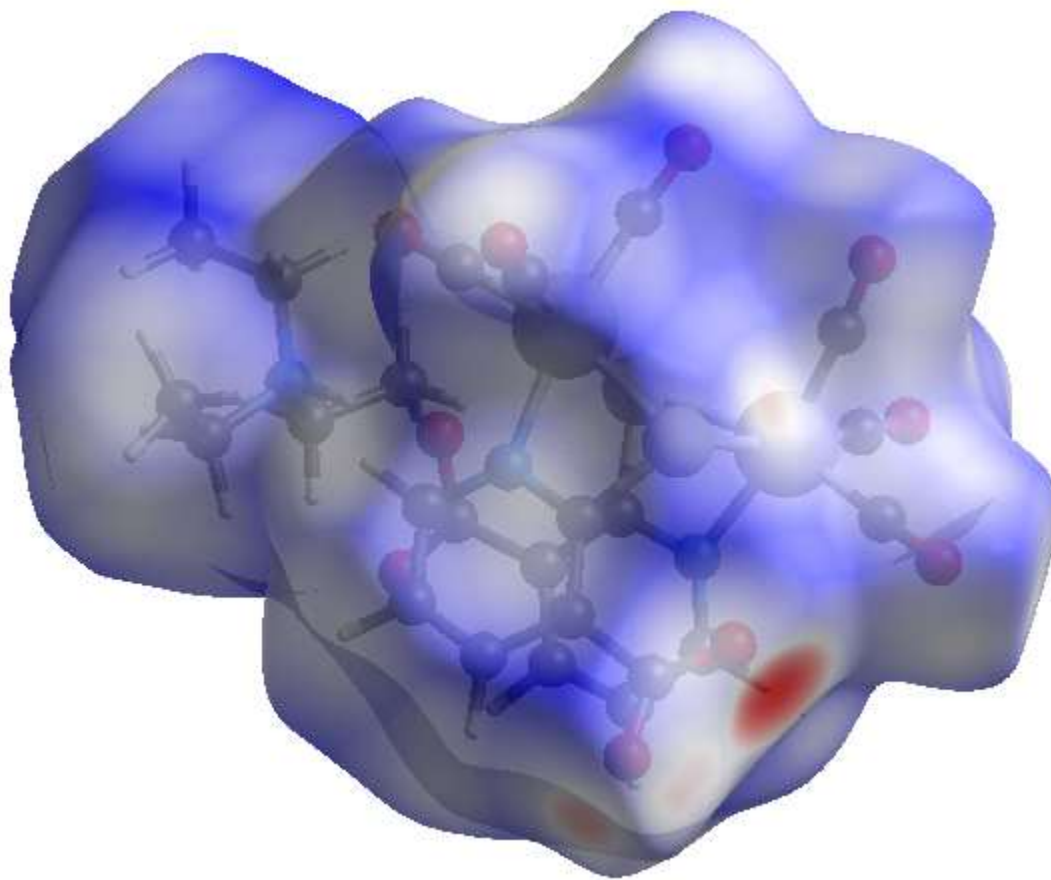
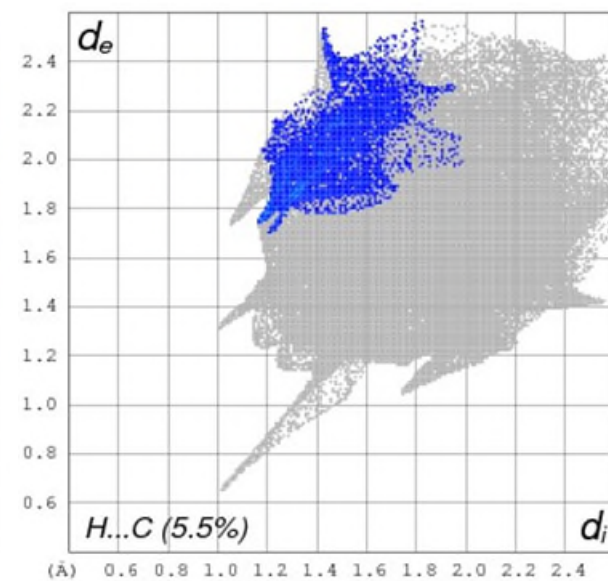
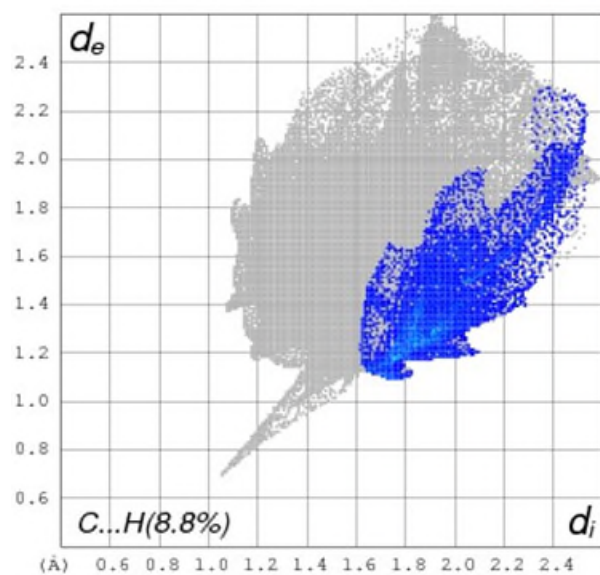
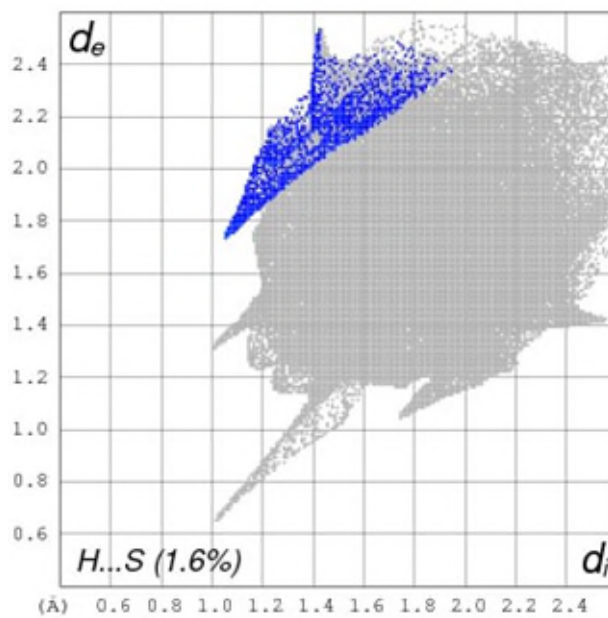
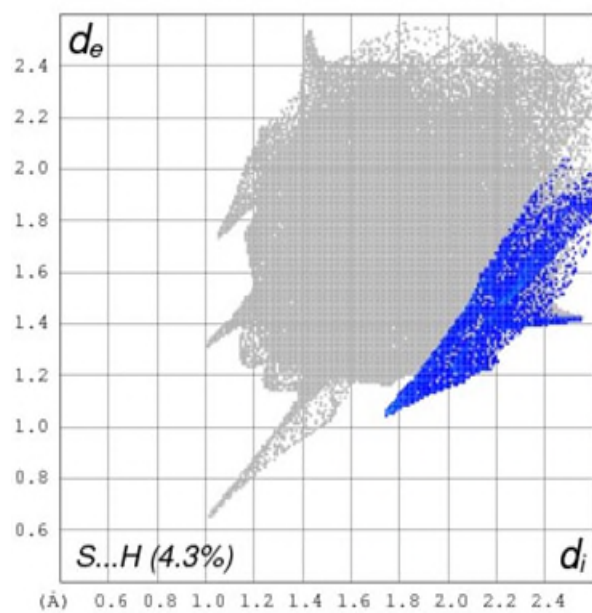
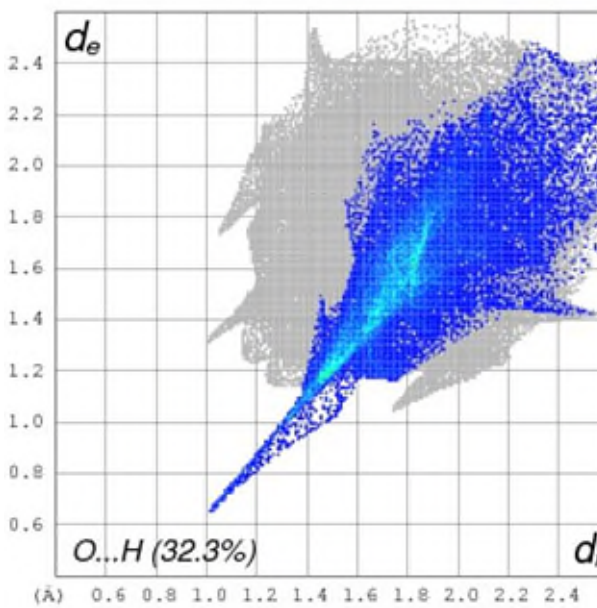
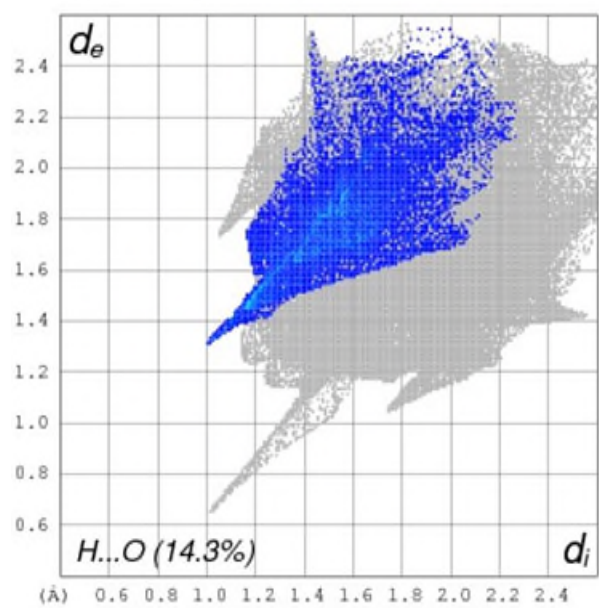
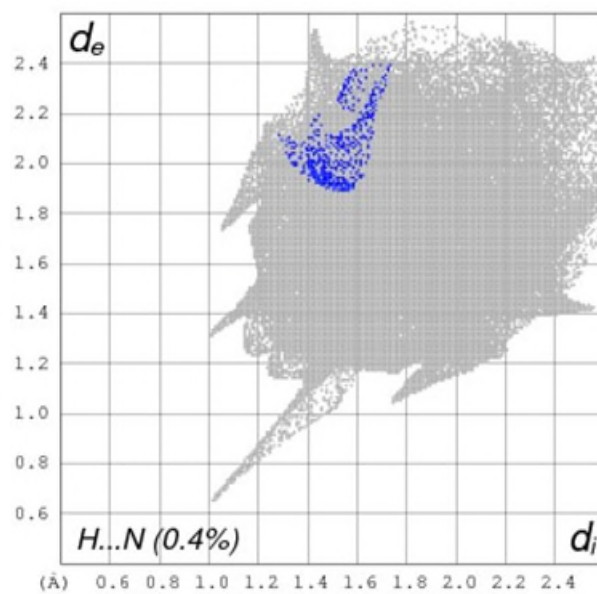
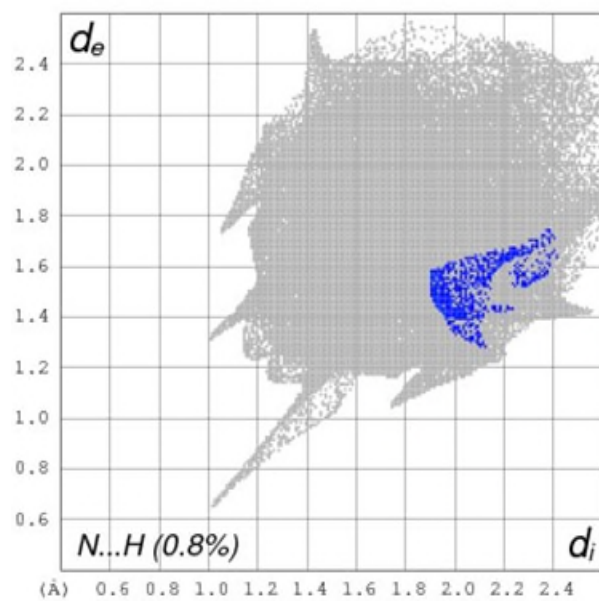


Figure 12: Electron density map of the Hirshfeld surface of $fac-[Re(CO)_3(\mu\text{-mpc})]_2 \cdot 2Et_3NH$, where different colours reveal interactions between neighbouring molecules in the molecular cluster.





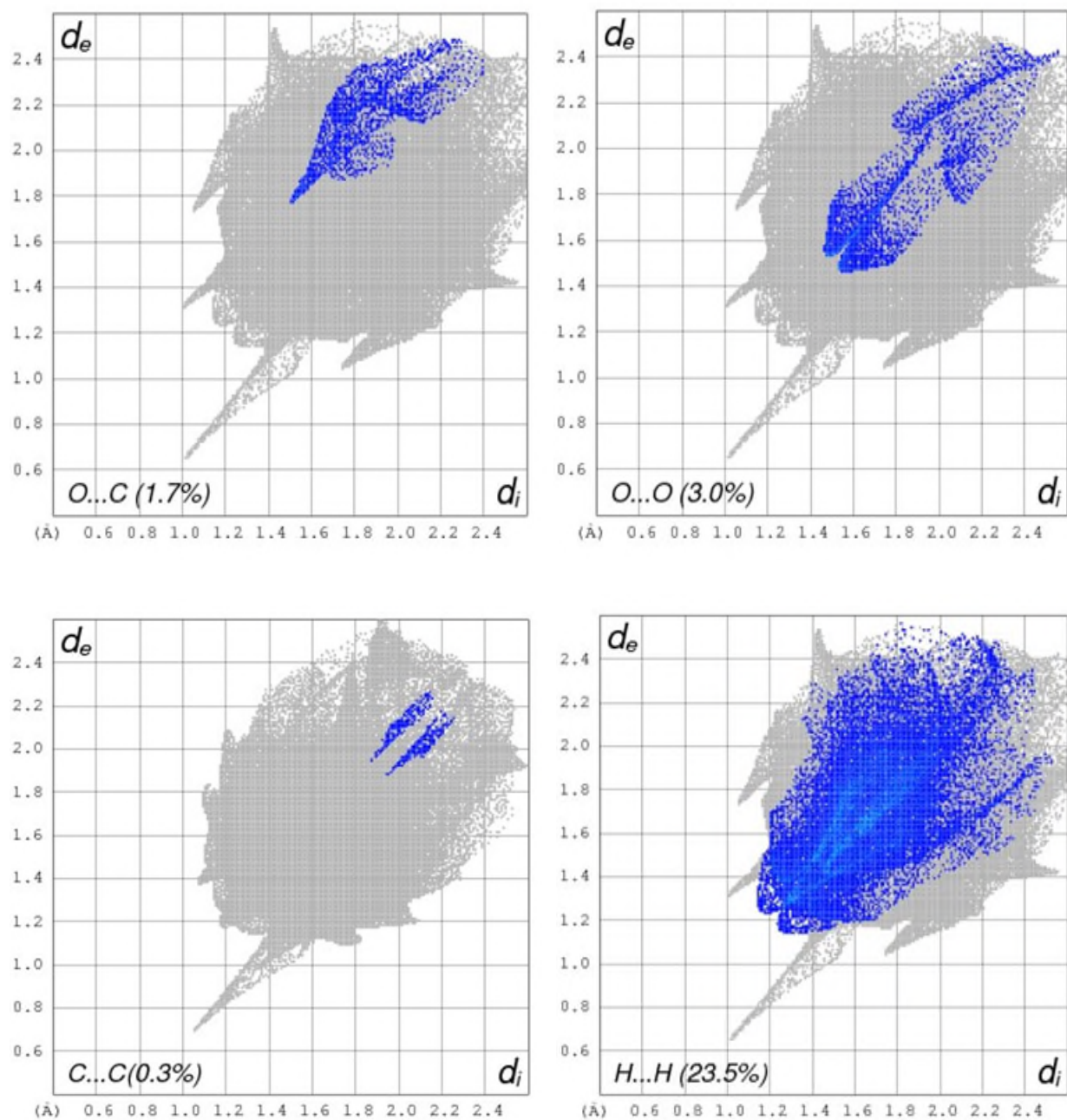


Figure 13: Two-dimensional fingerprint plots with intermolecular atomic interactions between neighbouring molecules in *fac*-[Re(CO)₃(μ-mpc)]₂·2Et₃NH.

4. Conclusions

Early development of organometallic complexes of 2-mercaptopyridine-3-carboxylic acid with various transition metals led to complexes with various coordination modes around the metal centres. In this study, a novel rhenium(I)-tricarbonyl complex, *fac*-[Re(CO)₃(μ-mpc)]₂·2Et₃NH, derived from 2-mercaptopyridine-3-carboxylic acid (H₂mpc), was isolated. The crystal structure of compound **1** confirms the formation of the Re₂S₂ bridge which leading to a simplified general formula, *fac*-[{(CO)₃Re(μ-L)₂Re(CO)₃}]. This metallocyclorhenium(I) complex was formed in high yield and consists of rhenium(I) metal centres bridged *via* two (λ¹-oxidaneyl)(2-sulfidopyridin-3-yl)methanolate (mpc⁻) chelates, where each mpc⁻ acts as a bidentate monoanionic N∩S⁻ thioxalato ligand, as confirmed by X-ray crystallography. The overall observation from the X-ray crystallographic data showed that the coordinated ligand underwent deprotonation, leading to an uncoordinated pendant acetate group with a negative charge delocalised between the two oxygen atoms. The solid state of compound **1** is stabilised by the counter ion, Et₃NH⁺, different hydrogen bonds, as well as weak interactions. DFT calculations revealed that hydrogen bonding between the counter ion and the complex enhanced both its chemical stability and biological activity. Future work will focus on synthesising rhenium complexes with 2-mercaptopyridine-3-carboxylic acid using other rhenium cores, in addition to their full characterisation. The biological studies of the isolated complexes will also be investigated.

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Declaration of competing interest

The authors declare that they do not have any form of competing interests or personal relationships that could have appeared to influence the reported work in this research article. All information and data needed to explore the conclusions in this article are presented in this paper as well as in the supplementary (SI) materials.

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