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Synthesis and Spectroscopic Characterization of Diosmium Carbonyl Clusters with Ferrocenedicarboxylato Ligands

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Synthesis and Spectroscopic Characterization of Diosmium Carbonyl Clusters with Ferrocenedicarboxylato Ligands

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HONORS SCHOLAR

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ABSTRACT

The microwave-assisted reaction of $Os_3(CO)_{12}$ and 1,1'-ferrocenedicarboxylic acid has resulted in the formation of a new diosmium carbonyl sawhorse complex with a chelating 1,1'-ferrocenedicarboxylato ligand, $Os_2(\mu_4$-1,1'-ferrocenedicarboxylato$)(CO)_6$. The optimization of this synthesis was atypical, requiring a decrease in the concentration of reactants used to achieve the optimal yield, 63.3%. Despite the compound readily crystallizing, crystallographic analysis of the compound has not yet been successful due to an abnormal diffraction pattern similar to, but not identical to, crystal twinning. Crystals have been successfully grown of a derivative of this compound, $Os_2(\mu_4$-1,1'-ferrocenedicarboxylato$)(CO)_4[P(p$-tolyl$)_3]_2$, which was synthesized through replacement of axial CO ligands on $Os_2(\mu_4$-1,1'-ferrocenedicarboxylato$)(CO)_6$. The X-ray crystal structure of this latter compound has been determined.

1. Introduction

Cisplatin is used in 50-70% of all cancer cases, but there are serious problems regarding the use of cisplatin in cancer treatments. One major problem is a lack of selectivity. Cisplatin is more toxic to cancer cells than healthy cells, but still affects healthy cells adversely. Another major problem is acquired resistance to cisplatin over time. Cancer mortality is often due to cisplatin-resistant cell lines [1]. Because of these problems, a lot of research in medicinal chemistry involves the search for an effective alternative to cisplatin.

An alternative to cisplatin will need to have a higher selectivity for cancer cells to allow for greater dosage before negative effects begin to arise outside of the tumor. The mechanism of the drug will also need to go through a pathway that will be viable in cisplatin-resistant cell lines as well as non-cisplatin-resistant cell lines. Ideally, the mechanism will also work in such a way as to decrease the likelihood of the development of drug resistance in the cancer cells during the treatment.

One avenue researchers are investigating to improve treatment against cisplatin-resistant cell lines is to find drugs with very different mechanisms of action than cisplatin. Cisplatin creates cross-linkers in the DNA that prevent DNA replication from occurring [2], but there are other mechanisms of action that have shown promise in the lab and in clinical trials. The formation of reactive oxygen species (ROS) in cancer cells can force cancer cells to undergo apoptosis [3]. A series of diruthenium carbonyl sawhorse complexes ($Ru_2(CO)_4(\mu_2\text{-}O_2CCH_3)_2$[5-(4-pyridyl)-10,15,20-triphenyl-21,23H-porphyrin]$_2$, $Ru_2(CO)_4$[μ_2- 5-(4-carboxyphenyl)-10,15,20-triphenyl-21,23H-

porphyrin]$_2$(PPh_3)$_2$, $Ru_2(CO)_4$[μ_2- 5-(4-carboxyphenyl)-10,15,20-triphenyl-21,23H-porphyrin]$_2$(1,3,5-triaza-7-phosphatricyclo[3.3.1.1]decane)$_2$, and $Ru_2(CO)_4$[μ_2- 5-(4-carboxyphenyl)-10,15,20-triphenyl-21,23H-porphyrin]$_2$[5-(4-pyridyl)-10,15,20-triphenyl-21,23H-porphyrin]$_2$) have been shown to be active against certain cancer cell lines through the formation of ROS in cancer cells [4]. Dimetal carbonyl sawhorse complexes (as illustrated in Figure 1) have the formula $M_2(RCO_2)_2(CO)_4L_2$, where M is a metal atom, R is a side chain, and L is a Lewis base. The name "sawhorse complex" comes from the fact that these complexes resemble sawhorses used in construction if they are "set" on their four cis equatorial carbonyl ligands. The complexes are often synthesized where L is a CO ligand, but these complexes readily undergo ligand substitution and can be modified with other Lewis bases, such as phosphine ligands. Sawhorse complexes can also be modified using various R groups. Clusters of dimetal carbonyl sawhorse complexes have been synthesized using di- and tricarboxylato ligands, which serve as bridges between multiple dimetal tetracarbonyl units [4-8].

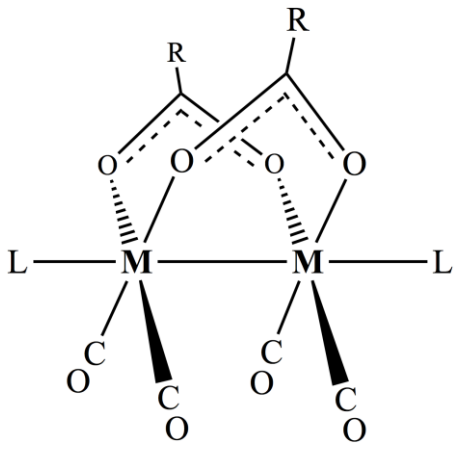

Figure 1. Illustration of a generic dimetal carbonyl sawhorse complex with formula $M_2(RCO_2)_2(CO)_4L_2$.

Another avenue for improving cancer drug selectivity is to attach iron-containing moieties to potential drugs to allow for the species to enter cells through the transferrin pathway. Since iron is a necessary nutrient for dividing cells, transferrin is up-regulated in cancer cells. As a result, drugs that enter through this pathway are somewhat more selective for cancer cells. It is also less likely that cancer cell lines will be able to develop drug resistance towards these drugs since the transferrin pathway is necessary for cell division [9]. One such technique that has been utilized is to replace an aromatic ring in a drug with a ferrocenyl group [10,11].

The purpose of this current project is to combine these two strategies into one drug: selectivity for cancer cells via a ferrocenyl moiety and the potential to form ROS in cancer cells to force them to undergo apoptosis. Previous work in this lab has demonstrated the ability to make stable diosmium carbonyl sawhorse complexes by reacting $Os_3(CO)_{12}$ with mono- and dicarboxylic acids in a microwave reactor [5-7]. This project involved the reaction of $Os_3(CO)_{12}$ with 1,1'-ferrocenedicarboxylic acid in order to make a diosmium carbonyl sawhorse complex with a ferrocenedicarboxylato ligand. The hope is that this complex will be able to enter cells via the transferrin pathway (due to the iron-containing ferrocenedicarboxylato ligand), and then produce ROS in the cells to force them to undergo apoptosis.

2. Results and Discussion

2.1 Optimization of Yield

The first reaction that produced a known yield of $Os_2(\mu_4$-1,1'-ferrocenedicarboxylato$)(CO)_6$ (**1**), illustrated in Figure 2, involved the reaction of 70.2

mg of $Os_3(CO)_{12}$ with a 1.5 molar ratio of 1,1'-ferrocenedicarboxylic acid in 7 mL of 1,2-dichlorobenzene at 192°C for 7.5 minutes (Method A), which resulted in a 29.7% yield of **1** . The ratio of 1 $Os_3(CO)_{12}$ to 1.5 1,1'-ferrocenedicarboxylic acid was chosen because this is the stoichiometric ratio in the balanced reaction to produce diosmium carbonyl sawhorse complexes with dicarboxylato ligands. While this was not the lowest yield observed for a diosmium sawhorse complex with a chelating dicarboxylato ligand, it was important to find a way to increase this yield. Even if this compound has medicinal properties, the low yield combined with the high price of the starting materials will effectively end any future of this compound as a drug. Overall, 19 additional reactions were conducted in efforts to optimize the yield. For brevity's sake, only five of these reactions are discussed in this thesis. The five syntheses discussed are model reactions which summarize the overall efforts to optimize the synthesis of **1**. The five methods are shown in tabular format on Table 1.

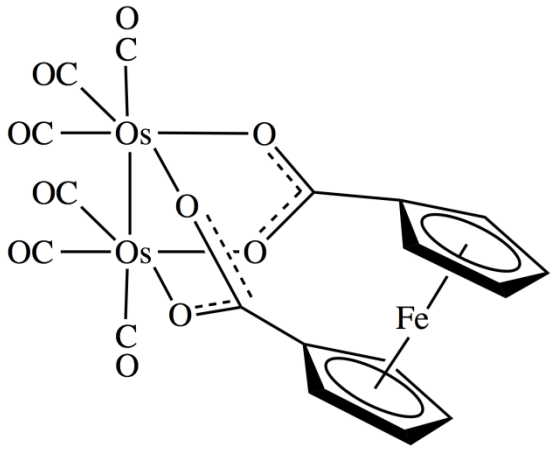

Figure 2. Illustration of the structure of **1**.

Slight changes to the reaction time and temperature were made which only resulted in a slight increase in yield. The reaction of 70.2 mg of $Os_3(CO)_{12}$ with a 1.5

molar ratio of 1,1'-ferrocenedicarboxylic acid in 8 mL of 1,2-dichlorobenzene at 180°C for 12 minutes resulted in a 32.7% yield of **1** (Method B). This only seemingly insignificant increase in yield suggested that more drastic changes were needed if the yield could be increased.

Table 1. Summary of reaction conditions and yields for the synthesis of **1**, Methods A-E.

Reaction	Ratio ($Os_3(CO)_{12}$:acid)	Conc. of acid	Time	Temp.	Yield
Method A	1:1.5	4.54 mg/mL	7.5 min.	192°C	29.7%
Method B	1:1.5	4.03 mg/mL	12 min.	180°C	32.7%
Method C	1:4	10.5 mg/mL	10 min.	180°C	12.8%
Method D	1:0.5	1.7 mg/mL	12 min.	189°C	43.3%
Method E	1:1.6	1.78 mg/mL	15 min.	190°C	63.3%

The previous reactions relied on essentially stoichiometric amounts of 1,1'-ferrocenedicarboxylic acid, and so it was thought that an excess of 1,1'-ferrocenedicarboxylic acid would increase the yield. However, increases in the molar ratio of 1,1'-ferrocenedicarboxylic acid actually resulted in significantly lower yields. For instance, the reaction of 69.7 mg of $Os_3(CO)_{12}$ with a 4 molar ratio of 1,1'-ferrocenedicarboxylic acid in 8 mL of 1,2-dichlorobenzene at 180°C for 10 minutes resulted in a 12.8% yield of **1** (Method C). This result was in stark contrast to previous projects where an increase in the molar ratio of ligand resulted in a higher yield of the resulting complex [6].

It was then suspected that 1,1'-ferrocenedicarboxylic acid undergoes a side reaction that competes with the synthesis of **1**. This would potentially explain the lower yields of **1** in the presence of a higher molar ratio of 1,1'-ferrocenedicarboxylic acid and the appearance of dark brown insoluble residue that appears in reactions between

$Os_3(CO)_{12}$ and 1,1'-ferrocenedicarboxylic acid, but not in reactions between $Os_3(CO)_{12}$ and other dicarboxylic acids. In response to this hypothesis, a synthesis was attempted with excess $Os_3(CO)_{12}$. The reaction of 69.5 mg of $Os_3(CO)_{12}$ and a 0.5 molar ratio of 1,1'-ferrocenedicarboxylic acid in 7 mL of 1,2-dichlorobenzene and 2 drops of acetonitrile at 189°C for 12 minutes resulted in a 43.3% yield of **1** (Method D). However, this reaction involved using an excess of $Os_3(CO)_{12}$. While some of that could be recovered and purified again for further use again, this method was less than ideal.

It was noted that Method D differed from the other methods in another notable manner. All of the other reactions had a roughly similar concentration of 1,1'-ferrocenedicarboxylic acid, while Method D employed a much smaller concentration. Method A used a 4.54 mg/mL concentration of 1,1'-ferrocenedicarboxylic acid. Method B used a 4.03 mg/mL concentration of 1,1'-ferrocenedicarboxylic acid. Method C used a 10.5 mg/mL concentration of 1,1'-ferrocenedicarboxylic acid. Method D used a 1.7 mg/mL concentration of 1,1'-ferrocenedicarboxylic acid. Still under the assumption that a competing side reaction of 1,1'-ferrocenedicarboxylic acid was taking place, a synthesis was proposed that involved a lower concentration of 1,1'-ferrocenedicarboxylic acid, while once again using an approximately stoichiometric ratio of $Os_3(CO)_{12}$. The reaction of 44.3 mg of $Os_3(CO)_{12}$ and a 1.6 molar ratio of 1,1'-ferrocenedicarboxylic acid in 12 mL of 1,2-dichlorobenzene at 195°C for 15 minutes resulted in a 63.3% yield of **1** (Method E). This method involved a 1.78 mg/mL concentration of 1,1'-ferrocendicarboxylic acid. This is actually the highest yield of any known diosmium carboxylate sawhorse complex with dicarboxylato ligands. While more work still needs

to be done to confirm that the lower reagent concentration was the primary reason for the increase in yield of **1**, the overall goal of increasing the yield was accomplished.

2.2 Crystallization Attempts

To confirm the structure of **1**, X-ray crystallographic analysis was desired. However, problems arose which have so far prevented publishable X-ray crystallographic data from being obtained. Normally, problems with X-ray crystallographic analysis result from the inability to produce quality crystals of the compound. However, **1** is interesting in that it readily crystallizes. Crystals have once even formed in a ring above the solvent in the microwave reaction vessel as the vessel was cooled after a reaction. The problem does not arise with the ability to obtain crystals or the quality of the crystals themselves. (One crystallographer who worked on crystals of **1** described them as "beautiful.") The problem seems to be with something in the crystal lattice itself. The most recent attempt to obtain X-ray crystallographic data resulted in a mostly solved structure, which molecular modeling clearly displayed as one diosmium carbonyl sawhorse complex with a chelating 1,1'-ferrocenedicarboxylato ligand. However, there were still numerous areas of high electron density which could not be reconciled with the known structure. This phenomenon can often occur with twinned crystals, but the crystallographers assisting in this analysis did not recognize this phenomenon as simple twinning. Whether this phenomenon is an exceedingly rare form of twinning or something else entirely remains to be seen.

In other diosmium carbonyl sawhorse complexes, replacing the axial CO ligands with P(*p*-tolyl)$_3$ ligands has resulted in increased stability of the complexes. In most

diosmium carbonyl sawhorse complexes, the axial CO ligands are labile; they tend to dissociate from the complex and leave as carbon monoxide gas, which results in decomposition of the complex [5]. Replacing these axial CO ligands with phosphine ligands such as P(*p*-tolyl)$_3$ that are much less labile prevents this decomposition from occurring. An added benefit to replacing these axial CO ligands with P(*p*-tolyl)$_3$ is crystals of the diosmium carbonyl complexes with axial P(*p*-tolyl)$_3$ seem to crystallize more readily than the diosmium carbonyl complexes with axial CO ligands [5]. While crystals of **1** were of good quality, the strange properties discussed previously prevented publishable data from being collected, so an attempt was made to synthesize a derivative of **1** with P(*p*-tolyl)$_3$ axial ligands. Crystals of the resulting compound, $Os_2(\mu_4$-1,1'-ferrocenedicarboxylato)$(CO)_4[P(p\text{-tolyl})_3]_2$ (**2**), gave quality data that confirmed the structure of **2** (illustrated in Figure 3), and as a result, the structure of **1**.

The complex sits on a two-fold axis that goes through the center of the Os-Os bond and the center of the Fe atom. There is some conformational strain associated with the carboxylate carbon atoms of the 1,1'-ferrocenedicarboxylato ligand. Due to pi bonding these carbon atoms would prefer to be coplanar with the cyclopentadiene rings that form two parallel planes sandwiching the Fe atom. However, the carboxylate carbon atoms are forced to be 0.23 Å out of those parallel planes in order to allow the ligand to bridge the diosmium core. As observed with other substituted diosmium carbonyl species, the P-Os-Os-P moiety does not make a perfectly linear axis. Instead, the P atoms bend slightly upward towards the dicarboxylato ligand, making a P-Os-Os bond angle of 168.15°, rather than 180°. There is also a slight torsional twist associated with the equatorial CO ligands. These ligands are not fully eclipsed across the dimetal unit since

the C1A-Os1A-Os1-C2 torsion angle is 2.57°. The Os-Os bond distance is 2.763 Å, which is similar in length to other diosmium carbonyl sawhorse complexes with substituted axial ligands [5,6]. Refinement details and structural parameters are summarized in Table 2.

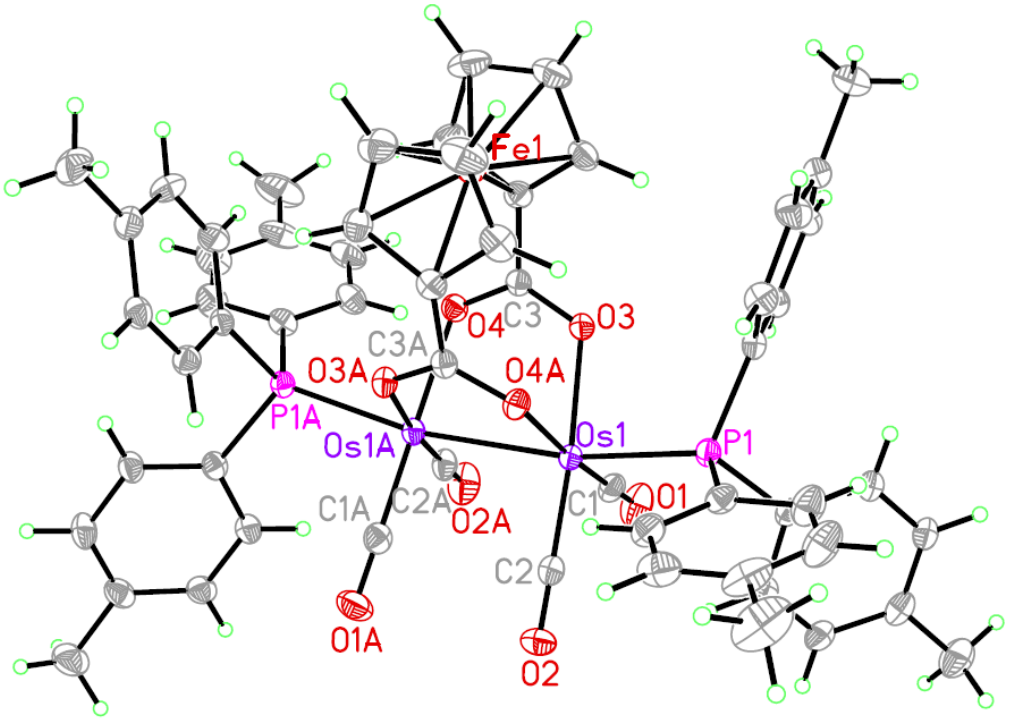

Figure 3. Thermal ellipsoid plot of **2** with the heteroatoms and carbonyl C atoms labeled.

In 8 of the 20 reactions conducted between $Os_3(CO)_{12}$ and 1,1'ferrocenedicarboxylic acid, another band on the TLC plate was collected with an IR spectrum very similar to that of **1**. Other than the similar IR spectrum, this compound (**1b**) appears to behave differently than **1**. Crystals of **1** are grown extraordinarily easily, but all attempts at crystallization of **1b** have failed thus far. This phenomenon of bands with similar IR spectra has also been observed in numerous other reactions between

$Os_3(CO)_{12}$ and other dicarboxylic acids, but never in reactions between $Os_3(CO)_{12}$ and monocarboxylic acids [5-7]. A possible explanation is that there is more than one binding mode available for a given dicarboxylato ligand. In other words, a given reaction might synthesize a dinuclear species, $Os_2[\mu_4\text{-}OOC(R)COO](CO)_6$, as well as a tetranuclear species, $[Os_2(CO)_6]_2[\mu_4\text{-}OOC(R)COO]_2$. This hypothesis would explain why two bands on a TLC plate, which are clearly separated, have similar (sometimes identical) IR spectra, why these two bands appear to have different properties, and why this phenomenon is only observed in diosmium carbonyl sawhorse complexes with dicarboxylato ligands. However, this hypothesis has a serious challenge in that in two separate reactions between $Os_3(CO)_{12}$ and two different dicarboxylic acids, crystals have been grown of both bands, and both crystals had the same X-ray crystal structure [12]. One explanation for this result could be that it is possible for a dicarboxylato ligand to have more than one binding mode, but these complexes also have the ability to interconvert in solution. Currently, more data needs to be obtained before any conclusions can be made regarding these complexes.

While the evidence might lean towards multiple binding modes, conclusive proof is needed. However, conclusive proof is difficult to obtain given the similarity that would naturally exist between two complexes which are both composed of Os_2 carbonyl sawhorse units and dicarboxylato ligands. One stark difference that would exist is in molecular weight. As a result, samples of **1** and **1b** were sent to a collaborator at Baylor University who has a mass spectrometer capable of obtaining MS data for high molecular weight compounds. If the molecular weight of **1b** is a multiple of the molecular weight of

1, this would be conclusive proof that **1b** is of the form $[Os_2(CO)_6]_n[\mu_4$-1,1'-ferrocenedicarboxylato$]_n$ (where n = 2, 3, 4...).

Table 2. Crystallographic data and structural refinement data for complex **2**.

Compound	Cluster **2**
Molecular formula	$C_{58}H_{50}FeO_8Os_2P_2 \cdot 2CH_2Cl_2$
Formula weight	1543.02
Temperature	220(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	C2/c
a (Å)	18.9626(7)
b (Å)	15.9663(7)
c (Å)	21.1632(8)
α (°)	90
β (°)	110.752(2)
γ (°)	90
Volume ($Å^3$)	5991.7(4)
Z	4
Density (calculated)	1.711 Mg/m^3
Absorption coefficient	4.754 mm^{-1}
F(000)	3016
Crystal size (mm)	0.17 x 0.11 x 0.08
Theta range	1.72-27.10°
Reflections collected	62868
Unique reflections/R_{int}	5683/0.0350
Data/restraints/parameters	5683/0/352
Goodness-of-fit on F^2	1.025
Final R indices [I > 2sigma(I)]	R1 = 0.0272
	wR2 = 0.0885
R indices (all data)	R1 = 0.0372
	wR2 = 0.1001
Residual extrema ($e \cdot Å^{-3}$)	2.192 and -0.881

3. Experimental

3.1 Materials and Methods

Syntheses involving microwave heating were performed in a Discover-SP microwave reactor (2455 MHz, CEM Corp., Matthews, NC). Reagents and a small magnetic stir bar were placed in a 35-mL glass CEM vessel that was sealed with a PTFE-lined cap before insertion into the reactor. The highest stir rate was used for all of the microwave reactions. Due to the toxicity of CO and metal carbonyl compounds, all manipulations were carried out in a highly efficient fume hood. For reactions under pressure, special precautions were taken to lower the fume hood sash until a few minutes following the release of pressure by the reactor. $Os_3(CO)_{12}$ was prepared from OsO_4 as previously reported [13]. Tri-*p*-tolylphosphine was purchased from Strem, 1,1'-ferrocenedicarboxylic acid was purchased from Chem-Impex International, Inc., and 1,2-dichlorobenzene was purchased from Sigma-Aldrich. All other solvents were purchased from Pharmco-Aaper. All reagents were used as received. Preparative thin-layer chromatography (TLC) was carried out on Analtech silica gel 60 (0.50 mm) plates. Sawhorse complexes were identified through characteristic absorptions in the CO region of infrared spectra [5-7]. Infrared spectra were acquired using a Nicolet Avatar FT-IR spectrometer with a CaF_2 solution cell.

*3.2 Synthesis of $Os_2(\mu_4$-1,1'-ferrocenedicarboxylato)$(CO)_6$ (**1**), Method A*

A mixture of $Os_3(CO)_{12}$ (70.2 mg, 0.0774 mmol), 1,1'-ferrocenedicarboxylic acid (31.8 mg, 0.116 mmol), and 1,2-dichlorobenzene (7.0 mL) was irradiated and stirred in the microwave reactor at 192°C for 7.5 min. The pressure in the vessel reached 21 psi. A reddish-brown solution with black flakes was formed. The solvent was removed and the residue was redissolved in CH_2Cl_2. TLC using an eluent of 1.25:1 hexanes/CH_2Cl_2 resulted in two major bands. Band 1 (R_f = 0.57) consisted of 28.3 mg (29.7% yield) of **1**.

IR (ν_{CO}, $CHCl_3$): 2099 w; 2085 s; 2067 s; 2036 w,sh; 2017 vs; 1994 vs; 1962 w,sh; 1939 w cm^{-1}. Band 2 (R_f = 0.36) consisted of an unknown compound. IR (ν_{CO}, $CHCl_3$): 2099 w; 2085 w; 2066 s; 2014 m,sh; 1997 vs cm^{-1}.

*3.3 Synthesis of **1**, Method B*

A mixture of $Os_3(CO)_{12}$ (70.2 mg, 0.0775 mmol), 1,1'-ferrocenedicarboxylic acid (32.2 mg, 0.118 mmol), 1,2-dichlorobenzene (8.0 mL) was irradiated and stirred in the microwave reactor at 180°C for 12 min. The pressure in the vessel reached 17 psi. A reddish-brown solution was formed. The solvent was removed and the residue was redissolved in CH_2Cl_2. TLC using an eluent of 1.22:1 hexanes/CH_2Cl_2 resulted in four bands. Band 1 (yellow, R_f = 0.89) consisted of an unknown compound. Band 2 (yellow, R_f = 0.79) consisted of an unknown compound. Band 3 (orange, R_f = 0.58) consisted of 31.2 mg (32.7% yield) of **1**. IR (ν_{CO}, $CHCl_3$): 2100 m; 2067 vs; 2015 s; 1998 vs cm^{-1}. Band 4 (yellow, R_f = 0.45) consisted of 5.9 mg of an unknown compound.

*3.4 Synthesis of **1**, Method C*

A mixture of $Os_3(CO)_{12}$ (69.7 mg, 0.0770 mmol), 1,1'-ferrocenedicarboxylic acid (84.3 mg, 0.308 mmol), and 1,2-dichlorobenzene (8.0 mL) was irradiated and stirred in the microwave reactor at 180°C for 10 min. The pressure in the vessel reached 20 psi. A dark brown solution was formed. The solvent was removed and the residue was redissolved in CH_2Cl_2. TLC using an eluent of 1.22:1 hexanes/CH_2Cl_2 resulted in three bands. Band 1 (UV, R_f = 0.90) consisted of mostly $Os_4H_4(CO)_{12}$ [14]. IR (ν_{CO}, $CHCl_3$): 2085 m; 2067 vs; 2034 m,sh; 2020 s; 1998 m,sh; 1942 m,sh cm^{-1}. Band 2 (orange, R_f = 0.56) consisted of 12.1 mg (12.8%) of **1**. IR (ν_{CO}, $CHCl_3$): 2100 m; 2067 vs; 2015 s; 1998

vs cm^{-1}. Band 3 (yellow, R_f = 0.39) consisted of a product (**1b**) with an IR spectrum similar to **1** and other diosmium sawhorse complexes [5-7]. IR (ν_{CO}, $CHCl_3$): 2099 w; 2065 s; 2035 m,sh; 2014 s,sh; 1997 vs; 1967 m,sh; 1943 m,sh cm^{-1}.

*3.5 Synthesis of **1**, Method D*

A mixture of $Os_3(CO)_{12}$ (69.5 mg, 0.0766 mmol), 1,1'-ferrocenedicarboxylic acid (11.9 mg, 0.0434 mmol), 1,2-dichlorobenzene (7.0 mL), and 2 drops of acetonitrile was irradiated and stirred in the microwave reactor at 189°C for 12 min. There was no buildup of pressure in the vessel during the reaction. A reddish-brown solution was formed. The solvent was removed and the residue was redissolved in CH_2Cl_2. TLC using an eluent of 1:1 hexanes/CH_2Cl_2 resulted in six bands. Band 1 (purple, R_f = 0.89) consisted of mostly $Os_3(\mu\text{-}H)_2(CO)_{10}$. IR ($\nu_{CO}$, $CHCl_3$): 2074 s; 2067 m,sh; 2061 m,sh; 2024 vs; 2010, m,sh; 1986 w,sh cm^{-1}. Band 2 (yellow, R_f = 0.86) consisted of mostly unreacted $Os_3(CO)_{12}$. IR (ν_{CO}, $CHCl_3$): 2085 w,sh; 2068 vs; 2034 m; 2023 m,sh; 2016 m,sh; 1999 w,sh cm^{-1}. Band 3 (dark yellow, R_f = 0.82) consisted of an unknown compound. IR (ν_{CO}, $CHCl_3$): 2081 m,sh; 2067 vs; 2034 m; 2017 m; 2000 w,sh cm^{-1}. Band 4 (yellow, R_f = 0.60) consisted of 1.4 mg of an unknown compound. IR (ν_{CO}, $CHCl_3$): 2104 w; 2075 vs; 2039 s; 2011 m; 1999 m,sh; 1991 m,sh cm^{-1}. Band 5 (orange, 0.53) consisted of 15.4 mg (43.3%) of **1**. IR (ν_{CO}, $CHCl_3$): 2100 w; 2067 vs; 2015 m; 1998 vs cm^{-1}. Band 6 (pale yellow, R_f = 0.31) consisted of 3.2 mg of an unknown compound. IR (ν_{CO}, $CHCl_3$): 2111 vw; 2011 vw; 2085 w,sh; 2069 s; 2060 m,sh; 2021 vs; 1999 m,sh cm^{-1}.

*3.6 Synthesis of **1**, Method E*

A mixture of $Os_3(CO)_{12}$ (44.3 mg, 0.0489 mmol), 1,1'-ferrocenedicarboxylic acid (21.4 mg, 0.0781 mmol), and 1,2-dichlorobenzene (12.0 mL) was irradiated and stirred in the microwave reactor at 195°C for 15 min. The pressure in the vessel reached 18 psi. A golden brown solution with black flakes was formed. The solvent was removed and the residue was redissolved in CH_2Cl_2. The solution was filtered through filter paper to remove insoluble impurities. TLC using an eluent of 1:1 hexanes/CH_2Cl_2 resulted in one band. Band 1 (orange, R_f = 0.74) consisted of 38.1 mg (63.3% yield) of **1**. IR (ν_{CO}, $CHCl_3$): 2100 m; 2067 s; 2014 s; 1998 vs cm^{-1}.

*3.7 Synthesis of $Os_2(\mu_4$-1,1'-ferrocenedicarboxylato)$(CO)_4[P(p\text{-}tolyl)_3]_2$ (**2**)*

A mixture of $Os_3(CO)_{12}$ (105.0 mg, 0.116 mmol), 1,1'-ferrocenedicarboxylic acid (49.1 mg, 0.179 mmol), and 1,2-dichlorobenzene (8.0 mL) was irradiated and stirred in the microwave reactor at 180°C for 12 min. A dark brown solution was formed. The solvent was removed and the residue was redissolved in a mixture of 30 mL $CHCl_3$ and 2 mL MeCN. Tri-*p*-tolylphosphine, P(*p*-tolyl)$_3$, (27.7 mg) was added and the mixture was heated to reflux for 1.5 hours. The solvent was removed and the residue was redissolved in CH_2Cl_2. TLC using an eluent of 1:1 hexanes/CH_2Cl_2 resulted in three major bands. Band 1 (yellow, R_f = 0.91) consisted of 10.8 mg of an unknown compound. IR (ν_{CO}, $CHCl_3$): 2068 vs; 2028 s cm^{-1}. Band 2 (orange, R_f = 0.70) consisted of 28.9 mg (14.4%) of **2**. IR (ν_{CO}, $CHCl_3$): 2098 w; 2067 m; 2035 w,sh; 2013 vs; 1997 m,sh; 1970 w; 1938 s cm^{-1}. Band 3 (orange, R_f = 0.58) consisted of 15.2 mg of an unknown compound. IR (ν_{CO}, $CHCl_3$): 2099 vw; 2072 vs; 2033 w; 2003 vs; 1977 s; 1925 w cm^{-1}.

3.8 X-ray Crystallography

Single crystals of **2** were obtained by slow evaporation of a CH_2Cl_2/hexanes solution. The crystal structure determination was carried out on a Bruker APEX-TT CCD by Dr. Vladimir Nesterov at UNT.

4. Conclusion

Microwave irradiation of $Os_3(CO)_{12}$ in the presence of 1,1'-ferrocenedicarboxylic acid results in the formation of a diosmium carbonyl sawhorse complex with a chelating 1,1'-ferrocenedicarboxylato ligand, **1**. The optimization of this synthesis relied on decreasing the concentration of reagents during the reaction, possibly due to the existence of a competing side reaction that occurs at higher concentrations of reagents. The resulting yield is the highest for any known diosmium carbonyl sawhorse complex with dicarboxylato ligands. X-ray crystallographic analysis of **1** has not been completely successful, but X-ray crystallographic analysis of **2**, a derivative of **1**, has confirmed the structure.

The synthesis of **1** results in another product, **1b**, which bears a very similar IR spectrum to **1**. A similar phenomenon has occurred in the synthesis of numerous diosmium carbonyl sawhorse complexes with other dicarboxylato ligands. Samples of **1** and **1b** have been sent to Baylor University for mass spectrometry, which could potentially confirm the presence of multiple binding modes of diosmium carbonyl sawhorse complexes with dicarboxylato ligands.

Future work on this project at ACU will involve confirming the presence of a competing side reaction of 1,1'-ferrocenedicarboxylic acid, and testing the effects of lower reagent concentrations in the syntheses of diosmium carbonyl sawhorse complexes

with other dicarboxylato ligands. Other future work on this project will involve testing the toxicity of **1** and **2** on cancer cell lines and investigating if **1** and **2** have higher cellular uptake in cancer cells versus healthy cells.

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