Mechanochemical synthesis of transition metal co-crystals

Siân Thérèse Stables

A thesis submitted as a partial requirement towards the degree of Master of Science

Department of Chemistry

University of Otago, New Zealand

May 2021
Abstract

This thesis describes the synthesis and characterisation of a number of metal halide complexes, and the subsequent mechanochemical synthesis of co-crystals involving these complexes.

Chapter one introduces supramolecular chemistry, with a focus on non-covalent interactions (NCIs) and crystal engineering. It then introduces mechanochemistry, a key synthesis method used throughout this project, as well as powder X-ray diffraction, an analysis technique used extensively in the characterisation of the mechanochemical products.

Chapter two discusses system design, as well as difficulties preventing the use of some typical analysis techniques, before detailing the synthesis of a series of MX$_2$(L)$_2$ complexes with monodentate ligands [M = Cu(II), Co(II), Mn(II); X = Cl, Br; L = nicotinamide (nic), isonicotinamide (iso), nicotinic acid (niacin, nia)]. The mechanochemical synthesis of co-crystals involving these MX$_2$(L)$_2$ complexes and a coformer (1,4-diiodotetrafluorobenzene (1,4-tfib) or terephthalamide) is then described, and evidence of formation analysed using powder X-ray diffraction, IR, and low frequency Raman spectroscopy.

Chapter three describes the system design and subsequent synthesis of a series of MX$_2$(L)$_n$ complexes [M = Co(II), Pd(II); X = Cl, Br; L = 2,9-dimethyl-1,10-phenanthroline (neocuproine, 2,9-mphe$n$), 4,7-dimethyl-1,10-phenanthroline (4,7-mphe$n$), 4,4' -dimethyl-2,2'-bipyridine (4,4-mbpy), 2,2'-bipyridine-4,4'-dicarboxylic acid (4,4-cbpy), 2,2'-bipyridine-6,6'-dicarboxylic acid (6,6-cbpy); $n = 1, 2$]. The crystal structures of some of these complexes are described. The mechanochemical synthesis of co-crystals involving these MX$_2$(L)$_n$ complexes and a coformer (1,4-tfib, terephthalamide) is then described, and evidence of formation analysed using powder X-ray diffraction and IR spectroscopy.
Acknowledgements

I would like to thank Dr Dave McMorran for being the best supervisor I could have wished for. Thank you for your guidance, your time and patience during busy periods, and for your good attitude, even in the face of bad news or negative results.

I would also like the thank Dr Dave Warren, as well as the rest of the outreach team over my time in the chemistry department, for the priceless opportunities that I have had the privilege to receive. It is not an exaggeration to say that being involved in outreach has changed the course of my life, and I cannot express how grateful I am for that.

Thanks to my co-supervisor Professor Lyall Hanton, all the members of the JDC group with whom I have shared a lab over the years, and to all the support staff and technicians without whom the department could not run.

Thank you to Dr Mark Waterland, Sam Brooke and Andre Stowers-Hull at Massey University for performing Raman measurements and calculations.

And, of course, thank you to my friends and family for the unconditional love and support which has kept me going, for which I am so grateful.
# Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>II</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>IV</td>
</tr>
<tr>
<td>ABBREVIATIONS</td>
<td>VIII</td>
</tr>
<tr>
<td>CHAPTER 1</td>
<td>1</td>
</tr>
<tr>
<td>1.1 SUPRAMOLECULAR CHEMISTRY</td>
<td>1</td>
</tr>
<tr>
<td>1.2.1 Hydrogen bonding</td>
<td>3</td>
</tr>
<tr>
<td>1.2.2 Halogen bonding</td>
<td>7</td>
</tr>
<tr>
<td>1.2.3 π bonding</td>
<td>10</td>
</tr>
<tr>
<td>1.2.4 Metal-ligand interactions</td>
<td>13</td>
</tr>
<tr>
<td>1.2 CRYSTAL ENGINEERING</td>
<td>14</td>
</tr>
<tr>
<td>1.2.1 Crystal engineering concepts</td>
<td>14</td>
</tr>
<tr>
<td>1.2.2 Co-crystals</td>
<td>16</td>
</tr>
<tr>
<td>1.2.3 Synthons in Crystal Engineering</td>
<td>19</td>
</tr>
<tr>
<td>1.3 MECHANOCHEMISTRY</td>
<td>21</td>
</tr>
<tr>
<td>1.4 POWDER X-RAY DIFFRACTION</td>
<td>24</td>
</tr>
<tr>
<td>1.5 PROJECT AIM</td>
<td>26</td>
</tr>
<tr>
<td>CHAPTER 2</td>
<td>31</td>
</tr>
<tr>
<td>2.1 INTRODUCTION</td>
<td>31</td>
</tr>
<tr>
<td>2.1.1 System Design</td>
<td>31</td>
</tr>
<tr>
<td>2.1.2 Difficulty with standard analysis techniques</td>
<td>34</td>
</tr>
<tr>
<td>2.1.3 Overview</td>
<td>35</td>
</tr>
<tr>
<td>2.2 RESULTS</td>
<td>37</td>
</tr>
<tr>
<td>2.2.1 pxrd plots</td>
<td>37</td>
</tr>
<tr>
<td>2.2.2 Low frequency Raman plots</td>
<td>59</td>
</tr>
<tr>
<td>2.2.3 Discussion</td>
<td>70</td>
</tr>
<tr>
<td>2.3 EXPERIMENTARY</td>
<td>76</td>
</tr>
<tr>
<td>2.3.1 Synthesis of MX$_2$(nic/iso/nia)$_2$ complexes</td>
<td>76</td>
</tr>
<tr>
<td>2.3.2 Mechanochemical synthesis of MX$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals</td>
<td>82</td>
</tr>
<tr>
<td>2.3.3 Mechanochemical synthesis of MX$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals</td>
<td>88</td>
</tr>
<tr>
<td>CHAPTER 3</td>
<td>95</td>
</tr>
<tr>
<td>3.1 INTRODUCTION</td>
<td>95</td>
</tr>
<tr>
<td>3.1.1 System Design</td>
<td>95</td>
</tr>
<tr>
<td>3.1.2 Difficulty with standard analysis techniques</td>
<td>97</td>
</tr>
<tr>
<td>3.1.3 Overview</td>
<td>98</td>
</tr>
<tr>
<td>Section</td>
<td>Page</td>
</tr>
<tr>
<td>---------</td>
<td>------</td>
</tr>
<tr>
<td>3.2 Results</td>
<td>100</td>
</tr>
<tr>
<td>3.2.1 PXRD plots</td>
<td>100</td>
</tr>
<tr>
<td>3.2.2 X-ray Crystallography</td>
<td>116</td>
</tr>
<tr>
<td>3.2.3 Discussion</td>
<td>122</td>
</tr>
<tr>
<td>3.3 Experimental</td>
<td>125</td>
</tr>
<tr>
<td>3.3.1 Synthesis of MX₂(bpy/phen)ₙ complexes</td>
<td>125</td>
</tr>
<tr>
<td>3.3.2 Mechanochemical synthesis of MX₂(bpy/phen)ₙ/1,4-tfib co-crystals</td>
<td>131</td>
</tr>
<tr>
<td>3.3.3 Mechanochemical synthesis of MX₂(bpy/phen)ₙ/terephthalamide co-crystals</td>
<td>136</td>
</tr>
<tr>
<td>3.4 X-ray Crystallographic Tables</td>
<td>141</td>
</tr>
<tr>
<td>CHAPTER 4</td>
<td>143</td>
</tr>
<tr>
<td>4.1 Conclusions</td>
<td>143</td>
</tr>
<tr>
<td>4.2 Future Work</td>
<td>144</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>145</td>
</tr>
</tbody>
</table>
Abbreviations

1,4-tfib 1,4-diiodo-tetrafluorobenzene

2,9-mphen 2,9-dimethyl-1,10-phenanthroline (neocuproine)

4,4-mbpy 4,4’-dimethyl-2,2’-bipyridine

4,4-cbpy 2,2’-bipyridine-4,4’-dicarboxylic acid

4,7-mphen 4,7-dimethyl-1,10-phenanthroline

6,6-cbpy 2,2’-bipyridine-6,6’-dicarboxylic acid

Anal. Analysis

API Active Pharmaceutical Ingredient

bpy Bipyridine

DMF Dimethylformamide

EtOH Ethanol

H-bonding Hydrogen bonding

HSBM High-speed Ball Milling

HSVM High-speed Vibration Milling

IR Infrared

iso Isonicotinamide

IUPAC International Union of Pure and Applied Chemistry

LAG Liquid Assisted Grinding

MeCN Acetonitrile

MeOH Methanol

NCI Non-covalent Interaction

nia Niacin (nicotinic acid)

nic Nicotinamide

NMR Nuclear Magnetic Resonance

N_{phen} Phenanthroline nitrogen donor atom

N_{py} Pyridine nitrogen donor atom

phen Phenanthroline

pxrd Powder X-ray Diffraction

X-bonding Halogen bonding
Chapter 1

1.1 Supramolecular chemistry

Defined by Jean-Marie Lehn as ‘chemistry beyond the molecule,’ supramolecular chemistry explores the synthesis and properties of multicomponent molecular assemblies formed using non-covalent interactions between component molecules.\textsuperscript{1} Nature has mastered the ability to assemble complex molecular architectures with high replicability, in defined locations and with temporal precision.\textsuperscript{2} Supramolecular chemistry attempts to mimic this amazing ability in synthetic systems and typically relies on the self-assembly of component molecules assembled by reversible interactions, as in biology. Self-assembling systems consist of discrete molecular sub-units that interact to form ordered aggregates.\textsuperscript{3} In nature, an example of this behaviour is exhibited by α-helices and β-sheets, where intermolecular interactions between protein chains inform the overall 3-D structure. In synthetic systems this behaviour is mimicked by ‘foldamers’, where a single molecular chain interacts with a second molecule of itself to form a secondary structure (Figure 1.1).\textsuperscript{4-6} Host-guest systems can be considered to be self-assembling, as can supramolecular coordination systems. In supramolecular systems there can be assembly via covalent bonds, coordination between a metal and an organic ligand with well-defined bond angles, or by non-covalent interactions (NCIs). Systems can form discrete geometric structures or coordination polymers, including metal organic frameworks (MOFs).
Reversible intermolecular interactions allow for constant forming and breaking of molecular units, leading to the eventual formation of the thermodynamically preferred product, as opposed to the kinetic product which is often formed in traditional organic synthesis. Covalent bond formation tends to require significant changes of reaction environment to be reversed, and therefore in a supramolecular chemistry context it is considered irreversible. As covalently linking molecules do not allow for efficient self-assembly, comparatively weak NCIs are preferred. In metal coordinated systems more labile metals are preferable as ligands can more easily dissociate and rearrange. Most non-covalent interactions are relatively weak when compared to a covalent bond, but in a large system the attractive forces of interactions such as π-stacking and hydrogen bonding can cooperatively become quite strong.
1.2.1 Hydrogen bonding

Hydrogen bonding (H-bonding) is one of the most important non-covalent interactions in both biological and synthetic systems, and is responsible for the secondary structure of many complex molecules, including the DNA double helix, proteins, host-guest architectures and other molecular networks. Carboxylic acids and amides are some of the most abundant and easily accessed hydrogen bonding building blocks, making them good candidates for supramolecular architecture assembly.

![Figure 1.2 - Examples of different H-bonding motifs, labelled according to Etter notation](image-url)

Hydrogen bonding is a non-covalent interaction between a positively polarised hydrogen, which is covalently bound to an electronegative atom of an H-bond donor molecule, and a negatively polarised atom of an H-bond acceptor molecule. The negatively polarised atom is often nitrogen or oxygen, as they are the most electronegative elements after fluorine, and are common in many organic fragments. The strongest class of H-bonding involves a charged acceptor molecule, making carboxylic acids ideal for strong interactions, as they can engage in ‘charge assisted H-bonding’ between a protonated and deprotonated acid, e.g. COOH⋯COO⁻. These can have bond strengths of 60-160 kJ mol⁻¹, compared to 20-60 kJ mol⁻¹ for a moderate H-bonding system. H-bonding is a largely electrostatic force, but dispersion forces and orbital interactions also contribute to the strength and nature of the interaction.

![Figure 1.3 - Schematic representation of a) electrostatic interaction, b) charge transfer interactions, c) π-resonance assistance, d) cooperativity, e) Pauli (steric) repulsion, f) dispersion and g) secondary electrostatic interactions](image-url)
### Table 1-1 - Summary of Hydrogen bond properties from X-ray data

<table>
<thead>
<tr>
<th>Strength</th>
<th>Examples</th>
<th>D⋯A / Å</th>
<th>D-H⋯A / °</th>
<th>Energy / kJ mol⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Very Strong</strong></td>
<td>[F-H-F]⁻</td>
<td>2.2-2.5</td>
<td>175-180</td>
<td>60-120</td>
</tr>
<tr>
<td><strong>Strong</strong></td>
<td>O-H⋯O-H</td>
<td>2.6-3.0</td>
<td>145-180</td>
<td>16-60</td>
</tr>
<tr>
<td></td>
<td>O-H⋯N-H</td>
<td>2.6-3.0</td>
<td>140-180</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N-H⋯O=C</td>
<td>2.8-3.0</td>
<td>150-180</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N-H⋯O-H</td>
<td>2.7-3.1</td>
<td>150-180</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N-H⋯N-H</td>
<td>2.8-3.1</td>
<td>135-180</td>
<td></td>
</tr>
<tr>
<td><strong>Weak</strong></td>
<td>C-H⋯O</td>
<td>3.0-4.0</td>
<td>110-180</td>
<td>&lt;12</td>
</tr>
</tbody>
</table>

In traditional solution-based chemistry, donor and acceptor atoms are electronegative i.e. O, N. These classical H-bonds are the only type of H-bonding observed in solution, as the high electronegativity results in strong bonds which are able to overcome the energy barriers of other opposing forces. In the solid state ‘non-classical’ H-bonds can be observed, where the H-bonding motif only includes one electronegative atom i.e. C-H⋯O. These bonds are not observed in solution phase chemistry as they are comparatively very weak, with bond strengths less than 12 kJ mol⁻¹ and so have only become recognised through crystallographic studies.

---

*Figure 1.4 - C-H⋯O hydrogen bonding in p-benzoquinone*
An important feature of H-bonding is the tendency towards linearity. This is caused by the shape of the orbitals involved, which have the highest degree of overlap, and therefore highest strength, when at a 180° bond angle. From an electrostatic point of view this orientation also allows the hydrogen atom to best shield the δ⁻ charges on the donor and acceptor from each other, minimising repulsion. Although this linear alignment is preferred, it is not always accessible within a crystal structure. A crystal structure is determined by the compromises between all of the involved interactions, so it is not uncommon for H-bonds, particularly weaker examples, to be bent. Another impact on the linearity of H-bonds is the formation of bifurcated, or three-centred, H-bonds. These form when an H-bond donor is approached by two H-bond acceptors in an attractive fashion, resulting in two non-linear H-bonds. Bifurcated and occasionally trifurcated H-bonds are more common in organic crystals, as there is typically an excess of acceptors over donors.

Figure 1.5 – Bifurcated H-bonding in N,N’-diphenylurea\textsuperscript{12}
If only simple (two-centred) H-bonds were formed there would be many unsatisfied acceptors, so molecules often prefer to form more complex bonding patterns.\textsuperscript{13} This agrees with Etter's rules\textsuperscript{14} describing the behaviour of H-bonding in crystal environments:

1. All good proton donors and acceptors are used in hydrogen bonding.
2. Six-membered ring intramolecular hydrogen bonds form in preference to intermolecular hydrogen bonds.
3. The best proton donors and acceptors remaining after intramolecular hydrogen-bond formation form intermolecular hydrogen bonds to one another (or to solvent).

The formation of bifurcated H-bonds follows both rule one and rule three, as all donors and acceptors are involved in H-bonding, and bifurcated bonds are often formed intermolecularly.
1.2.2 Halogen bonding

Another supramolecular interaction of increasing interest is halogen bonding. In 2009 the International Union of Pure and Applied Chemistry (IUPAC) began a project\textsuperscript{15} with the aim to “take a comprehensive look at intermolecular interactions involving halogens as electrophilic species and classify them”. A definition was published in 2013 when the project concluded: “A halogen bond occurs when there is evidence of a net attractive interaction between an electrophilic region associated with a halogen atom in a molecular entity and a nucleophilic region in another, or the same, molecular entity.”\textsuperscript{16}

Halogen bonding is a class of electron density donation-based interactions of halogen atoms with nucleophilic regions, such as N, P, O, S, halogen functionalities, and π electron donors.\textsuperscript{17} Halogen-halogen interactions are thought to be caused by anisotropy of electrostatic potentials on the halogen atom surface, which results in electrostatic attraction between electron-rich and electron-poor areas.\textsuperscript{17, 18} This anisotropy is also referred to as a ‘sigma-hole’ interaction.

Halogen bonds are highly tuneable, depending on the interacting partners. They range in energy from 10 kJ mol\textsuperscript{-1} for weak interactions (e.g., N⋯Cl),\textsuperscript{19} up to 150 kJ mol\textsuperscript{-1} (e.g. strong interaction in the I\textsubscript{2}⋯I adduct).\textsuperscript{20} The high strength of many halogen bonds allows the interactions to overcome other weak, non-favourable noncovalent interactions, like π-π stacking.\textsuperscript{21} In the formation of supramolecular systems halogen bonds can cooperate with, or surrender to, H-bonds or other strong NCIs, when of comparable or lesser strength, respectively. As a result, examples of hierarchical assembly have been observed.\textsuperscript{22-24}

Halogen bonds generally have binding strengths of 3-30 kJ mol\textsuperscript{-1}, but in exceptional cases up to 180 kJ mol\textsuperscript{-1}.\textsuperscript{17} Halogen bond strength is very dependent on the surrounding environment, and can be tuned through choice of halogen, as there is a considerable difference in electronegativity and charge density within the halogen series.

Halogen bonds tend to be of a similar length to H-bonds, and are much more directional than H-bonds, with the typical R-X⋯A bond angle (\(\theta_1\)) (where X = halogen and A = halogen bond acceptor) being close to 180\degree.\textsuperscript{25} Sakurai, Sundaralingam, and Jeffrey observed that halogen bond X⋯X contacts tend to fall into two geometric varieties, shown in Figure
1.6 These varieties were categorised as a symmetrical type I contact and a bent type II contact by Desiraju and Parthasarathy (Figure 1.7).

\[ R \cdots X \cdots A \cdots R' \]

\[ \theta_1 \quad \theta_2 \]

\[ \theta_1 = \theta_2 \]

\[ \theta_1 = -180^\circ \]
\[ \theta_2 = -90^\circ \]

Figure 1.6 - Schematic of a halogen bond of the form \( R \cdots X \cdots A \cdots R' \) with angles \( \theta_1 \) and \( \theta_2 \) shown via dotted lines

The predictability of the \( X \cdots A \cdots R' \) angle (\( \theta_2 \)) can be influenced by the \( R' \) group. For example, the location of an sp hybridised nitrile or cyanide lone pair, such as in a cyanometallate, can lead to more predictable angles than equivalent systems containing acceptors with multiple lone pairs (such as halometallates). However, depending on their substituents, nitrile and cyanide groups can also display significant sp\(^2\) character, which promotes a wider range of \( X \cdots N \equiv C \) halogen bond angles. In (3,5-I\(_2\)pyMe)\(_3\)[Co(CN)\(_6\)]\(^{3+}\) (Figure 1.8), which contains perfectly octahedral [Co(CN)\(_6\)]\(^{3+}\) cations, there are three distinct halogen bond angles present (\( X \cdots N \equiv C \) angles (\( \theta_2 \)) = 101°, 104° and 170°), which together result in a two-dimensional network rather than the three-dimensional connectivity predicted by the combination of octahedral nodes with a two-fold symmetric linker.
Both halogen and hydrogen bonding play significant roles in solid-state architectures, both in biology and in synthetic compounds, particularly coordination and organometallic compounds. As both interactions are directional, they often impact the overall shape of compounds, which suggests possible applications in mimicking the binding pockets of enzymes and other biological molecules with interesting and complex reactivities.
1.2.3 π bonding

NCIs involving at least one π system are also common in both biological systems and in supramolecular chemistry. Similar to H-bonding, π-type interactions are seen frequently in protein folding\textsuperscript{43} and ion selectivity.\textsuperscript{44, 45} They also play a significant role in molecular recognition\textsuperscript{46, 47} and self-organisation\textsuperscript{48} processes in some systems. Aromatic rings carry their electron density above and below the ring itself, and the sharing of electrons results in the centre of the ring being electron rich, while the outer hydrogens are electron poor. There are three main types of π-π interactions; stacked, T-shaped, and parallel displaced/offset. π-π systems tend to prefer T-shaped or offset configurations, as these configurations allow for favourable overlap of electron rich and electron poor regions which stabilises the interaction. Figure 1.10 shows the three main types of π-π bonding, as well as polarity reversed π-π bonding, where one ring system has electronegative substituents, resulting in an inverse electron density compared to an unsubstituted ring system. Figure 1.9 shows a representation of stacked π systems in DNA. T-shaped interactions can also occur as C-H⋯π interactions, which are weak but can be numerous in a crystal structure, and therefore have a significant impact on the structure.

\textit{Figure 1.9 – Cartoon representation of pi-stacking between DNA molecules, with \textit{pi} systems represented as square planes\textsuperscript{49}}
Cation-π interactions are an attractive NCI between a cation and the electron rich centre of an aromatic ring system. This behaviour is also seen with the π electrons of simple double bonds, for example ethylene. The interaction is the result of both solvation effects and electrostatic attraction. Cation-π interactions have a wide range of binding energies, with some being as strong as 160 kJ mol⁻¹, while others are less than 4 kJ mol⁻¹. Work by Dougherty and co-workers shows that smaller cations are able to bind more effectively in the gas phase due to shorter contact distances and higher charge densities.

Anion-π interactions are attractive interactions between an anion and a π-system, however, unlike cation-π systems, the π-system must be electron deficient. Intuition would assume that there would be negative repulsion between an electron dense anion and an electron dense π-system, however the electronic properties of a π-system can be altered significantly by constituent groups, allowing for a polarity reversed system. These interactions have been known for over 30 years, but only recently began to attract
attention due to supramolecular systems that allow the study of anion-π interaction in solution.\textsuperscript{54}
1.2.4 Metal-ligand interactions

Metal-ligand complexes are formed through coordinate covalent bonds. In a typical covalent bond, each of the two atoms involved contribute one electron to form the bond. Coordinate covalent bonds differ in that both bonding electrons are contributed by one of the atoms. In the case of metal-ligand complexes the electrons are contributed by the ligand’s donor atom. The bond energies of metal-ligand bonds (60-210 kJ mol\(^{-1}\)) tend to be intermediate between organic covalent bonds (250-500 kJ mol\(^{-1}\)) and most weaker NCIs (3-60 kJ mol\(^{-1}\)).\(^{57}\)

Labile metals such as palladium and silver are often used in supramolecular systems, as they form bonds with energies comparable to strong H-bonds, for example Ag(I)-N\(_{py}\) bonds tend to have a strength of ~50 kJ mol\(^{-1}\), which is weaker than most metal-ligand bonds.\(^{58}\) This is important for supramolecular systems as the weaker bonds can come apart and reform, undergoing self-correction. This allows access to the thermodynamic product instead of the kinetic product.

Transition metals are frequently used in supramolecular chemistry as throughout the group there is a wide range of predictable preferred oxidation states and ligand configurations. While some d-block metals have one preferred configuration, other more labile metals can have several different states with little preference. Having multiple accepted configurations with small energy differences allows ligands to rearrange and form products that are more thermodynamically stable than the starting material or any kinetic intermediates.
1.2 Crystal engineering

1.2.1 Crystal engineering concepts

Crystal engineering as a field has existed for over sixty years, but only began to gain popularity in the 1990s.\textsuperscript{59, 60} Crystal engineering can be considered to be supramolecular synthesis in the solid state, and therefore the non-covalent interactions between molecules make up a much greater component of the overall interactions between molecules than is found in solution, as there are no solvent effects and the molecules are by necessity closely packed. The orientation and interactions between the molecules, as determined by symmetry and long-range order, have been found to influence the physical properties of the crystalline substance, such as solubility, density, mechanical and thermal behaviour, and optical and magnetic properties.\textsuperscript{61}

In crystal engineering the various molecular components involved in the creation of crystals are known as tectons. Tectons can be linked by many different NCIs, the motifs of which are referred to as synthons, following the organic notation originally proposed by E. J. Corey in 1967.\textsuperscript{62} The synthons link together molecular ‘nodes’ to form network structures.\textsuperscript{17}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{synthon}
\caption{Graphical depiction of 4-iodonitrobenzene, where synthons are represented as diamonds and tectons as squares\textsuperscript{17}}
\end{figure}

Crystal engineering utilises the concept of synthon hierarchy, wherein certain synthons are considered more reliable, or more likely to form in a given mixture of molecules. $R^2_2(8)$ COOH homodimers, as shown in Figure 1.12, are considered to be quite reliable, but there are many systems where a different orientation may be preferred.
Acid-amide dimers are frequently occurring and often form instead of the equivalent acid-acid or amide-amide homodimers.\textsuperscript{64} Despite this, in a mixed system involving a strong acid, an amide, and a pyridine functional group, the acid often prefers to interact with the pyridine nitrogen.\textsuperscript{65}

The introduction of metal atoms further complicates synthon hierarchy, as metals can engage in types of interactions not accessible with purely organic molecules, such as metal-metal interactions. Many inorganic complexes involve a charged metal, which can enhance the strength of hydrogen bonding to halogen atoms, but also have associated anions which can introduce competing non-covalent interactions. The different electronic, geometric and photophysical properties of inorganic systems can result in changes in synthon hierarchy compared to purely organic systems.\textsuperscript{8,18}
1.2.2 Co-crystals

The synthesis of co-crystals (i.e. multicomponent molecular crystals) has become a focal point in crystal engineering.\textsuperscript{66} Co-crystal history began with the work of Wöhler in the 1850s on quinhydrone, a 1:1 co-crystal of quinone and hydroquinone,\textsuperscript{67, 68} but the modern understanding of the term `co-crystal' only developed in the last 30 years. The increase in interest owes a great deal to Desiraju’s book on crystal engineering,\textsuperscript{60} as well as Etter’s ground-breaking work on co-crystals.\textsuperscript{14, 69, 70} The exploration of co-crystals can inform our understanding of supramolecular interactions and molecular recognition, nucleation and crystal growth patterns, as well as informing our ability to create solid forms of chemicals by altering their properties with different co-crystal components (co-formers).

One of the defining characteristics of co-crystals is that the co-former molecules are connected only by non-covalent interactions (NCIs), such as hydrogen bonding, halogen bonding or π interactions. Of these interactions hydrogen bonding is the most highly utilised, due to being very well known, predictable, synthetically accessible, and often quite strong. For example, in 4,4’-biphenol bis(4-cyanopyridine) the co-crystal is connected via H-bonding as shown in Figure 1.13.\textsuperscript{71} The structure shows that H-bonding to the N$_{py}$ is preferred over the cyano group, as an example of synthon hierarchy.

![Figure 1.13 - H-bonding in 4,4’-biphenol bis(4-cyanopyridine).](image)

One of the uses of co-crystal formation is the ability to change and tune the chemical, physical and electronic properties of the component molecules. These properties can be tuned by introducing a second molecule or complex to create a co-crystal. Because of these tuneable properties, co-crystals have been used in devices and drug development,
as well as in altering the unfavourable properties of commonly used chemicals, such as reducing the hygroscopicity of urea.\textsuperscript{72} This is of particular interest to pharmaceutical manufacturers, as many drugs on their own have poor aqueous solubility, and therefore cannot easily be administered orally, which is the least invasive form of drug delivery.\textsuperscript{73, 74} There are many other methods devised to improve the aqueous solubility of such drugs, including decreasing particle size to increase surface area,\textsuperscript{75} creating salts with improved dissolution profiles,\textsuperscript{76} solubilisation in co-solvents\textsuperscript{77} and micellar solutions,\textsuperscript{78} encapsulation or complexation with cyclodextrins,\textsuperscript{79} and the use of lipidic systems for delivery of lipophilic drugs.\textsuperscript{80} Although many of these methods are effective, they rely heavily on the physiochemical properties of the specific molecules involved, and are not easily generalised.\textsuperscript{73, 74} Co-crystallisation can also be of use in improving the tableting of drugs that are otherwise brittle, which require large amounts of additional binding agents. For example, the stable polymorph of acetaminophen (commonly known as paracetamol) adopts a herringbone packing pattern and requires large amounts of corn starch to enable tableting, as the material alone is too brittle. A 1:1 co-crystal with theophylline\textsuperscript{81} or its hydrochloride salt,\textsuperscript{82} however, forms a layered structure, and is much easier to tablet.\textsuperscript{74}

![Figure 1.14 - 1:1 co-crystal of acetaminophen/theophylline\textsuperscript{83}](image-url)
The first co-crystal drug to be approved by the FDA was Entresto in 2015. Entresto is a co-crystal of sacubitril (a neprilysin inhibitor) and valsartan (an angiotensin II receptor antagonist) and is used to treat acute heart failure. Many other drugs already on the market are widely considered to be co-crystals, but do not meet the definition decided upon by the FDA, including caffeine citrate and escitalopram oxalate with oxalic acid. The FDA definition requires a patent application to provide evidence that the co-crystal drug meets the following requirements: that both the active pharmaceutical ingredient (API) and co-former are present in the unit cell; that if both API and co-former contain ionisable groups, they must interact non-ionically; and that the API and co-former undergo substantial dissociation before reaching the site of pharmacological activity.

As the formation of co-crystals requires crystallisation, the co-crystal formation tends to be enthalpically favoured in order for co-crystals to form preferentially over crystals of the constituent molecules. In order for the enthalpically favoured product to be formed the intermolecular interactions need to be easily reversible, allowing the molecules to self-assemble.
1.2.3 Synthons in Crystal Engineering

In 1995, Gautam Desiraju proposed the idea of the *supramolecular synthon*, modelled off Corey’s synthon in organic synthesis. Desiraju’s idea is based on defining a molecular crystal structure as a network of nodes (molecules) and node connections (interactions). A supramolecular synthon makes up the node connection by forming a recognisable and repeated non-covalent interaction pattern linking the molecular nodes in the crystal. An example is an interaction between two carboxylic acids, where two H-bonds result in the formation of a ring structure. This type of H-bonding ring is rather common, and has the notation $R^x_y(Z)$, where $x$ and $y$ are the number of H-bond acceptors and donors, respectively, and $Z$ is the total number of atoms in the ring.

![Figure 1.15 – Three examples of simple synthons. A) a hydrogen bonded $R_2^2(8)$ heterosynthon, B) a hydrogen bonded $R_2^2(8)$ $R_2^2(8)$ heterosynthon, C) a halogen bonded $R^2_1(4)$ synthon](image)

Crystal engineering utilises the concept of synthon hierarchy, wherein certain synthons are considered more reliable, or more likely to form in a given mixture of molecules. The reliability of a synthon is based on the likelihood of the synthon forming in a system that includes the relevant functionalities. Unlike the percentage yield in organic synthesis, synthon reliability cannot simply be measured. Instead the reliability is estimated by analysing trends in the crystallographic databases for frequently occurring patterns that correlate to repeated synthon formation. Inorganic systems involve metals, which can engage in types of interactions not accessible with purely organic molecules, such as metal-metal interactions. Many inorganic complexes involve a charged metal, which can enhance the strength of H-bonding to halogen atoms, but also have associated anions which can introduce competing non-covalent interactions. The different electronic,
geometric and photophysical properties of inorganic systems can result in changes in synthon hierarchy compared to purely organic systems.\textsuperscript{8}

Previous work in the McMorran group illustrates the impact that the metal atom can have in an inorganic crystal structure. Figure 1.16 shows two similar pyridyl-pyrazol ligands complexed with PdCl\textsubscript{2} and PtCl\textsubscript{2} centres, respectively.\textsuperscript{90} When bound to a Pd(II) the ligands organise into an R\textsuperscript{2}(8) COOH homodimer, but when the metal is Pt(II) the ligands instead prefer the bifurcated MCl–HOOC and CH–O synthons, proving that the presence and properties of a metal atom can have a significant effect on the synthon formation within a structure.

Figure 1.16 – a) Crystal structure of PdCl\textsubscript{2}(5-(3-(2-Pyridyl)pyrazol-1-ylmethyl)benzene 1,3-dicarboxylic acid)\textsuperscript{90}, b) Crystal structure of PtCl\textsubscript{2}(3-(3-(2-pyridyl)pyrazol-1-ylmethyl)benzoic acid), where carboxylic acid homodimer formation is disrupted by Cl⋯H interactions\textsuperscript{90}
1.3 Mechanochemistry

One of the major hurdles in forming and characterising co-crystals is finding a solvent system. In order to grow X-ray quality crystals, a system must be found in which the final co-crystal must be less soluble than all component molecules. If the co-crystal product is not sufficiently insoluble the co-former molecules will crystallise separately. There is some level of predictability in solubility, but for the most part solvent systems are discovered through trial and error. These solubility issues are problematic, as they drastically reduce the efficacy of co-crystal synthesis. It is also an issue for the significant number of pharmaceutical co-crystals, which need to be free of any potentially harmful solvent molecules when manufactured.

Mechanochemistry is characterised by the application of mechanical energy to facilitate a chemical transformation. The IUPAC Compendium of Chemical Technology denotes mechanochemical reactions as those that are induced by the direct absorption of mechanical energy, which may come from grinding or milling processes. Mechanochemical activation is of interest in regards to ‘green’ chemistry, as no solvents are required during the reaction process. As volatile solvents are the most common waste product from synthetic chemistry, performing reactions without solvent reduces the waste output at laboratory and industrial scale.

There are two main types of automated ball mills used for mechanochemistry, planetary ball mills and mixer (shaker) ball mills (Figure 1.17). The former operates by spinning the reaction chamber, providing friction against the walls due to centrifugal forces as well as impact with the balls or walls when lifting off and colliding with the opposite wall. Mixer mills work by shaking the chamber back and forth horizontally, resulting the reactants and balls impacting with the walls of the chamber. This method is generally called high-speed vibration milling (HSVM) or high-speed ball milling (HSBM).
The chemical selectivity of some reactions can be changed by the addition of small quantities of solvent to the grinding chamber. This method is known as liquid assisted grinding (LAG), and has been explored in more detail in the past decade.\textsuperscript{92-95} When a small amount of organic solvent is added to the grinding chamber, reactions can be accelerated and facilitated. The amount of solvent added is referred to as the $\eta$ value; where $\eta$ is the volume of solvent (in $\mu$L) divided by the sample weight (in mg),\textsuperscript{92} and is often determined by trial and error, although some systematic studies have been repeated.\textsuperscript{92, 94, 95} Solvent volatility is an important factor, as a low vapour pressure solvent can be problematic to remove after grinding, while a high vapour pressure solvent can prove problematic during sample preparation, and may be lost during the mechanochemical process.\textsuperscript{96} Some preferred solvents include alcohols, ethyl acetate, acetonitrile, and nitromethane.\textsuperscript{96}

Mechanochemical activation of reactions has been observed to produce different results than heat or irradiation, an example being the decomposition of silver halides upon grinding, while they melt under high temperatures.\textsuperscript{97, 98} Another example comes from the work of Boldyrew et al, who investigated the decomposition of alkali bromides. The study found that the mechanochemical treatment of MBrO$_3$ (with M = Na, K, Rb, and Cs) proceeded along a different reaction path than when thermally induced. The two methods also resulted in different end products.\textsuperscript{96, 99}

Performing reactions without solvent can also have an effect of the rate of reactions, as there are no solvation phenomena. Reactants are present in very high concentrations during solvent-free reactions, which can have an effect on product selectivity in comparison to the same reaction taking place under standard conditions.\textsuperscript{100}
Mechanochemistry has predominantly been explored for use in organic synthesis, with reported synthesis of thioureas,\textsuperscript{101} dithiocarbamates,\textsuperscript{102} as well as a large number of multistep heterocycles.\textsuperscript{103-106} The lack of solvent also opens up pathways to reaction schemes and products that would otherwise be out of reach. Although there is significant exploration of mechanochemistry as an organic synthesis method, it is much less commonly reported with inorganic compounds.

Mechanochemical synthesis of pharmaceuticals is of great interest as a method to improve the yield and reproducibility of pharmaceutical co-crystal synthesis, as well as lowering the number of undesirable chemicals used in synthesis that must then be removed during purification.\textsuperscript{89, 107} As mechanochemically synthesised co-crystals are held together by NCIs, solvent free methods of structural characterisation must be used, for example solid state NMR, infrared and Raman spectroscopy, as well as thermal analysis. The ideal method of structural characterisation of crystalline products is single crystal X-ray diffraction, however the microcrystalline powders produced by mechanochemical grinding are too small for conventional single crystal analysis. Recent developments of advanced and accessible methods of structural determination from laboratory X-ray powder diffraction data have provided a solution to this problem.\textsuperscript{108-111}
1.4 Powder X-ray Diffraction

The most commonly used type of crystallographic structural determination is single crystal X-ray diffraction, which has a high success/efficacy rate. Many materials, however, are not well suited to this technique, as it requires the sample to be a single crystal with high purity.\textsuperscript{109} This is impossible for some material types, such as alloys, catalysts, microporous materials, energy related materials, as well as samples prepared in the solid state that cannot be dissolved and recrystallised.\textsuperscript{112}

Powder X-ray diffraction (pxrd) is an alternative, technique that allows the use of microcrystalline or polycrystalline samples. The technique is less informative than single crystal X-ray diffraction, as the diffraction patterns of each microcrystal in the sample overlap each other. Reflections in single crystal X-ray diffraction tend to be well defined and can be measured individually, while in pxrd the reflections overlap, often displaying bands of reflection instead of distinct spots.\textsuperscript{113} This results in a significant loss of information and makes accurate structural determination much more difficult,\textsuperscript{112} however advances since the turn of the century have made structural determination from pxrd much more accessible, in both data collection and algorithmic processes.

Even in cases where structural determination is not achievable via pxrd, such as when the data quality is insufficient, the pxrd pattern can still be used for comparison, as with other data collection methods like IR or mass spectrometry. For example, if the pxrd patterns of reactants and products are compared it can be determined if the product has formed, as this will result in new peaks not present in the reactant patterns. The pxrd pattern can also be compared to a simulated pattern if the single crystal X-ray derived structure is known.\textsuperscript{114}
In most cases the presence of a metal atom in the structure makes refinement easier, as metal atoms are dominant X-ray scatterers. Particularly dominant scattering can be a hinderance, however, as it can disguise the pattern caused by other atoms in the structure.
1.5 Project Aim

The aim of this project is to synthesise metal-containing tectons with both H-bonding and X-bonding functionalities in order to explore the competitive binding interactions. The main points of interest were whether the systems would engage in H-bonding or X-bonding behaviours, and if there was any evidence of a clear synthon hierarchy.

Previous work in the McMorrán group has explored metal-containing systems with pendent COOH groups which have shown interesting H-bonding behaviour, for example 4-(3-(2-pyridyl)pyrazol-1-ylmethyl)benzoic acid (L1).\textsuperscript{116} This ligand, shown in Figure 1.19, forms a helical structure in which the COOH group H-bonds with the N\textsubscript{py} of the adjacent ligand. When complexed with silver to form [Ag(L1)\textsubscript{2}]OTf•1.5H\textsubscript{2}O (Figure 1.20), the molecules form interrupted dimers, where two H\textsubscript{2}O molecules bridge between the COOH groups of adjacent ligands, forming an R\textsuperscript{4}(12) H-bonding motif. This motif, along with the distorted tetrahedral orientation at the silver centre causes the complex to form a meso-helical structure.

![Image of L1 performing COOH⋯N\textsubscript{py} H-bonding, forming an overall helical structure\textsuperscript{116}](image-url)
Figure 1.20 – [Ag(L1)2]OTf·1.5H2O with interrupted COOH dimers

Other work in the group used the similar ligand 4-(3-(2-pyridyl)pyrazol-1-ylmethyl)benzamide (L2) to form the zinc complex ZnL2Cl2, which was co-crystallised with 1,4-diiodo-tetrafluorobenzene (1,4-tfib). This co-crystal, shown in Figure 1.21, contains dimers of ZnL2Cl2 molecules linked by $R^2_2(8)$ amide homodimers. These dimers are arranged in layers, with $\pi$-stacking interactions between the pyridyl-pyrazole aromatic systems. The zinc bound chloride atoms are H-bonding to an aromatic hydrogen on an adjacent dimer, as well as X-bonding to one of the iodine atoms on 1,4-tfib. The 1,4-tfib atoms are X-bonding to each other through Cl⋯Cl interactions in a layer perpendicular to the layers of ZnL2Cl2. There is also Cl⋯H bonding between 1,4-tfib and aromatic hydrogens on L2, which further bridges the disparate dimers.
Zinc halide complexes of nicotinamide (nic) were also synthesised. These complexes were used in the attempted mechanochemical synthesis of co-crystals with 1,4-tfib and were analysed using pxrd and low frequency Raman spectroscopy.

The comparative Raman spectroscopy plot of the ZnI$_2$(nic)$_2$ complex, 1,4-tfib, and the supposed ZnI$_2$(nic)$_2$/1,4-tfib co-crystal (Figure 1.22a) shows significant difference throughout the 50-1800 cm$^{-1}$ range, particularly in the sub-800 cm$^{-1}$ region, where there are numerous new or shifted peaks in the spectrum of the ZnI$_2$(nic)$_2$/1,4-tfib co-crystal.

Comparative pxrd was also reported for the preparation of ZnI$_2$(nic)$_2$/1,4-tfib (Figure 1.23), where there are new peaks very clearly apparent, notably at around 6°, 8-10°, 12°, and 14°.

In this project similar methods will be employed to prepare and characterise metal halide-based complexes. The metals used will be Cu(II), Co(II), Mn(II) and Pd(II), which will be complexed with both monodentate and bidentate ligands.
Figure 1.22 - a) Comparative Raman plot of $\text{ZnI}_2(\text{nic})_2$, 1,4-tfib, and $\text{ZnI}_2(\text{nic})_2$/1,4-tfib co-crystal. b) Structure of $\text{ZnI}_2(\text{nic})_2$

Figure 1.23 - Comparative X-ray powder patterns of $\text{ZnI}_2(\text{nic})_2$, 1,4-tfib, and $\text{ZnI}_2(\text{nic})_2$/1,4-tfib co-crystal
Chapter 2

2.1 Introduction
2.1.1 System Design

Three pyridine-based compounds, nicotinamide (nic), isonicotinamide (iso) and nicotinic acid (nia), were chosen as ligands. The ligands are structurally similar, with nic and iso having an amide group in the three or four position, respectively, while nia has a carboxylic acid in the three position. Pyridine-based compounds are known to bind readily to metal atoms through the N$_{py}$. The addition of functional groups allow the ligands to influence the supramolecular architecture of a system through NCIs such as H-bonding, as well as π-stacking from the pyridine ring itself.$^{58, 118-120}$

![Figure 2.1 – Nicotinamide (left), isonicotinamide (centre) and nicotinic acid (right)](image)

The ligands are small, simple, and readily available from chemical suppliers. The simplicity and lack of steric bulk are important as the behaviour of interest in this project is H-bonding and X-bonding. Bulky ligands could interfere in complex formation or efficient packing, and more functional groups could engage in other types of NCIs, as well as further complicating the steric interactions around the metal centre.

As the ligands are commonly available, several synthetic methods for these metal halide complexes have been reported.$^{121-124}$

Cu(II), Co(II), and Mn(II) are all period four d-block metals, and as such have similar atomic radii. As d-block metals they are all able to form complexes with multiple possible coordination numbers and geometries. In the MX$_2$(L)$_2$ complexes described in this chapter it is expected that all will assume a tetrahedral geometry, as that is the most stable configuration for a four coordinate d-block metal, and Cu(II), Co(II), and Mn(II) do not show a preference for square planar complexes, unlike Pd(II) and Pt(II).
The molecules 1,4-diiodotetrafluorobenzene (1,4-tfib) and terephthalamide were chosen as co-formers. 1,4-tfib has a benzene backbone, with iodine in the one and four positions, and fluorine in the two, three, five, and six positions. This substitution results in a high potential for X-bonding, as the fluorine atoms are extremely electron withdrawing, making the iodine atoms slightly electron deficient. This increases the ‘sigma hole’, making it more likely for the metal-bound halides to engage in X-bonding with the co-former instead of H-bonding with another complex molecules. The iodine atoms in the one and four positions should result in linear interactions between molecules if it acts as a bridge, and makes it more likely for both atoms to engage in interactions as there will be less steric hinderance than if they were in the one and three positions, which would promote a bent geometry. There is also potential for H-bonding to either the functional groups or aromatic protons on the ligands, as either primary interactions or secondary to X-bonding.

![Figure 2.2 – 1,4-tfib (left) and terephthalamide (right)](image)

Terephthalamide also has a benzene base, this time with two amide groups in the one and four positions. Similar to 1,4-tfib this functional group positioning promotes linear interactions, which reduces the issue of steric hinderance. The amide groups can engage in H-bonding with either the amide/carboxylic acid groups on the ligands, forming an $R^2_2(8)$ dimer, or with the metal-bound halide groups.

Both co-formers have potential to engage in either H-bonding or X-bonding with the MX$_2$(L)$_2$ complexes, or possibly a combination of both, making them ideal for investigating the synthon hierarchy in these systems. Some of the possible bonding motifs are shown in Figure 2.3.
Figure 2.3 – Two potential interaction motifs between CoCl₂(nic)₂ and a) 1,4-tfib or b) terephthalamide. Each co-former has the potential to interact with the metal-bound halides or H-bond with either functional group or aromatic hydrogens.
2.1.2 Difficulty with standard analysis techniques

The three metals chosen, Cu(II), Co(II), and Mn(II) are all paramagnetic, and as such typical $^1\text{H}/^1\text{C}$ NMR is of little use. Paramagnetic materials can be analysed by NMR, but the peaks are broadened to the point that most splitting is hidden, and the chemical shifts can be extreme, for example the $^1\text{H}$ NMR spectrum of a series of paramagnetic 3$d$ metallocenes ranged from -253 to +320 ppm, with the $^{13}\text{C}$ NMR ranging from -510 to +1514 ppm. High spin d$^7$ or d$^6$ systems experience rapid electron relaxation, which can result in relatively well resolved peaks despite the paramagnetism. Examples in the literature reported DFT calculations to model the systems and predict the chemical shift window, which is required so that the detection window can be set accurately. These predictions were also required during peak assignment.

The MX$_2$(L)$_2$ complexes also had very low solubility in most common lab solvents, which made preparing a sample for potential NMR studies problematic. This also posed a problem for sample preparation for liquid chromatograph mass spectrometry (LCMS), as this method also requires a dissolved sample. The low solubility of the metal complexes also made growing crystals difficult.

Because of these solubility issues, elemental analysis was heavily relied upon. As all of the MX$_2$(L)$_2$ complexes in this chapter have been reported previously in the literature, the results were compared with these examples.

The low solubility is what inspired the use of mechanochemistry, as the typical method of co-crystallisation from solution was not accessible.
2.1.3 Overview

MX₂(L)₂ complexes (M = Cu(II), Co(II), Mn(II); X = Cl, Br; L = nic, iso, nia) were synthesised following reported methods. Solutions of MX₂ and L were combined in a 1:2 molar ratio. Initially the solvent used was MeOH and the reaction was done at reflux,¹²²,¹²⁹,¹³⁰ however the MnX₂ and some CoX₂ complexes had low solubility, which resulted in impure product. The solvent was changed to EtOH,¹²¹,¹²³ with heating only to dissolve. The complexes all precipitated out of solution, and were filtered in vacuo, washed with the reaction solvent and dried over vacuum.

This method was successful for all but MnBr₂(nia)₂, which formed only a small quantity of precipitate that was determined to be uncomplexed nia. The reaction was repeated twice with the same result, so this complex and subsequent attempts at co-crystals were not pursued.

Each MX₂(L)₂ complex was combined mechanochemically with both 1,4-tfib and terephthalamide. Each experiment consisted of mixing the MX₂(L)₂ complex and co-former in a 1:1 molar ratio with a total mass in the range of 20-50 mg. All mechanochemical experiments were performed in a Retsch MM200 mixer mill. The samples were placed inside a stainless steel chamber with a 10 mL volume, along with a 5 mm stainless steel ball bearing. The grinding time and frequency was one minute at 10 Hz, then four minutes at 20 Hz. This short reaction time was chosen as it allowed a large library of compounds to be synthesised quickly as a proof of concept.

The potential co-crystal products of the mechanochemical synthesis were characterised by pxrd and IR, with the 1,4-tfib series also being analysed by low frequency Raman spectroscopy. Pxrd and IR spectra of the MX₂(L)₂ complexes, 1,4-tfib, and terephthalamide were also taken for comparison.

Milled powder samples were mounted in paratone-N oil on a nylon loop. Powder diffraction data were collected on an Agilent Technologies Supernova system at room temperature (approx. 24 °C) at the University of Otago using Mo-Kα (λ = 0.71073) radiation. Data was baselined and normalised using CrysAlisPro software.¹³¹ The data was then plotted and stacked in Microsoft Excel. Data was originally collected using a copper radiation source, but it broke halfway through the project, and therefore the data was recollected using a molybdenum source.
Raman measurements and calculations were performed by Dr Mark Waterland, Sam Brooke and Andre Stowers-Hull at Massey University.

Raman spectra were recorded under ambient conditions with a custom-built Raman microscope. 785 nm excitation (Warsash Scientific) was filtered through a Bragg Bandpass Filter (OptiGrate) and focused onto a solid sample of the compound pressed onto a microscope slide via a microscope objective (40x magnification, NA = 0.65). The laser power at the sample was approx. 10 mW. Back-scattered Raman and Rayleigh scattered light was collected by the same objective and the Rayleigh component was rejected by a series of three Bragg Notch Filters (Optigrate) and focused onto the entrance slit of a Teledyne (Princeton) Instruments LS785 spectrograph with a PIXIS400b CCD. Spectral data were acquired using LightField 6.1 software. No background removal was applied during data collection. The detector exposure time was 1 second and between 30 – 120 exposures were captured and stored separately prior to data analysis. Individual frames were background corrected and averaged, using Jupyter Notebooks (v. 6.0.1 with Python 3.7.4).

Vibrational frequencies, normal modes and Raman intensities were calculated on the optimised equilibrium geometry using the Gaussian09 package. The M062X functional was implemented with a 6-31G(d) basis set. G09 log files were parsed using cclib. Calculated spectra were generated from the output parsed by cclib using Jupyter Notebooks (v. 6.0.1 with Python 3.7.4).

Microanalyses were conducted at the Campbell Microanalytical Laboratory at the University of Otago.
2.2 Results

2.2.1 pxrd plots
Milled powder samples were mounted in paratone-N oil on a nylon loop. Powder diffraction data were collected on an Agilent Technologies Supernova system at room temperature (approx. 24 °C) at the University of Otago using Mo-Kα (λ = 0.71073) radiation.

**CuCl$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals**

![Figure 2.4 - Comparative X-ray powder patterns of CuCl$_2$(nic)$_2$, 1,4-tfib, and CuCl$_2$(nic)$_2$/1,4-tfib co-crystal](image)
Figure 2.5 - Comparative X-ray powder patterns of CuCl$_2$(iso)$_2$, 1,4-tfib, and CuCl$_2$(iso)$_2$/1,4-tfib co-crystal

Figure 2.6 - Comparative X-ray powder patterns of CuCl$_2$(nia)$_2$, 1,4-tfib, and CuCl$_2$(nia)$_2$/1,4-tfib co-crystal
CuBr$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

Figure 2.7 - Comparative X-ray powder patterns of CuBr$_2$(nic)$_2$, 1,4-tfib, and CuBr$_2$(nic)$_2$/1,4-tfib co-crystal

Figure 2.8 - Comparative X-ray powder patterns of CuBr$_2$(iso)$_2$, 1,4-tfib, and CuBr$_2$(iso)$_2$/1,4-tfib co-crystal
Figure 2.9 - Comparative X-ray powder patterns of CuBr$_2$(nia)$_3$, 1,4-tfib, and CuBr$_2$(nia)$_2$/1,4-tfib co-crystal
CoCl$_2$(nic/iso/niia)$_2$/1,4-tfib co-crystals

Figure 2.10 - Comparative X-ray powder patterns of CoCl$_2$(nic)$_2$, 1,4-tfib, and CoCl$_2$(nic)$_2$/1,4-tfib co-crystal

Figure 2.11 - Comparative X-ray powder patterns of CoCl$_2$(iso)$_2$, 1,4-tfib, and CoCl$_2$(iso)$_2$/1,4-tfib co-crystal
Figure 2.12 - Comparative X-ray powder patterns of $\text{CoCl}_2(\text{nia})_2$, 1,4-tfib, and $\text{CoCl}_2(\text{nia})_2/1,4$-tfib co-crystal
CoBr\(_2\)(nic/iso/ria)\(_2\)/1,4-tfib co-crystals

Figure 2.13 - Comparative X-ray powder patterns of CoBr\(_2\)(nic)\(_2\), 1,4-tfib, and CoBr\(_2\)(nic)\(_2\)/1,4-tfib co-crystal

Figure 2.14 - Comparative X-ray powder patterns of CoBr\(_2\)(iso)\(_2\), 1,4-tfib, and CoBr\(_2\)(iso)\(_2\)/1,4-tfib co-crystal
Figure 2.15 - Comparative X-ray powder patterns of CoBr$_2$(nia)$_2$, 1,4-tfib, and CoBr$_2$(nia)$_2$/1,4-tfib co-crystal
MnCl$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

Figure 2.16 - Comparative X-ray powder patterns of MnCl$_2$(nic)$_2$, 1,4-tfib, and MnCl$_2$(nic)$_2$/1,4-tfib co-crystal

Figure 2.17 - Comparative X-ray powder patterns of MnCl$_2$(iso)$_2$, 1,4-tfib, and MnCl$_2$(iso)$_2$/1,4-tfib co-crystal
Figure 2.18 - Comparative X-ray powder patterns of MnCl$_2$(nia)$_2$, 1,4-tfib, and MnCl$_2$(nia)$_2$/1,4-tfib co-crystal
MnBr$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

Figure 2.19 - Comparative X-ray powder patterns of MnBr$_2$(nic)$_2$, 1,4-tfib, and MnBr$_2$(nic)$_2$/1,4-tfib co-crystal

Figure 2.20 - Comparative X-ray powder patterns of MnBr$_2$(iso)$_2$, 1,4-tfib, and MnBr$_2$(iso)$_2$/1,4-tfib co-crystal
Figure 2.21 - Comparative X-ray powder patterns of CuCl$_2$(nic)$_2$, terephthalamide, and CuCl$_2$(nic)$_2$/terephthalamide co-crystal

Figure 2.22 - Comparative X-ray powder patterns of CuCl$_2$(iso)$_2$, terephthalamide, and CuCl$_2$(iso)$_2$/terephthalamide co-crystal
Figure 2.23 - Comparative X-ray powder patterns of CuCl$_2$(nia)$_2$, terephthalamide, and CuCl$_2$(nia)$_2$/terephthalamide co-crystal
CuBr$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals

Figure 2.24 - Comparative X-ray powder patterns of CuBr$_2$(nic)$_2$, terephthalamide, and CuCl$_2$(nic)$_2$/terephthalamide co-crystal

Figure 2.25 - Comparative X-ray powder patterns of CuBr$_2$(iso)$_2$, terephthalamide, and CuCl$_2$(iso)$_2$/terephthalamide co-crystal
Figure 2.26 - Comparative X-ray powder patterns of CuBr$_2$(nia)$_2$, terephthalamide, and CuCl$_2$(nia)$_2$/terephthalamide co-crystal
CoCl$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals

Figure 2.27 - Comparative X-ray powder patterns of CoCl$_2$(nic)$_2$, terephthalamide, and CoCl$_2$(nic)$_2$/terephthalamide co-crystal

Figure 2.28 - Comparative X-ray powder patterns of CoCl$_2$(iso)$_2$, terephthalamide, and CoCl$_2$(iso)$_2$/terephthalamide co-crystal
Figure 2.29 - Comparative X-ray powder patterns of CoCl$_2$(nia)$_2$, terephthalamide, and CoCl$_2$(nia)$_2$/terephthalamide co-crystal
CoBr$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals

Figure 2.30 - Comparative X-ray powder patterns of CoBr$_2$(nic)$_2$, terephthalamide, and CoBr$_2$(nic)$_2$/terephthalamide co-crystal

Figure 2.31 - Comparative X-ray powder patterns of CoBr$_2$(iso)$_2$, terephthalamide, and CoBr$_2$(iso)$_2$/terephthalamide co-crystal
Figure 2.32 – Comparative X-ray powder patterns of CoBr$_2$(nia)$_2$, terephthalamide, and CoBr$_2$(nia)$_2$/terephthalamide co-crystal
MnCl$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals

Figure 2.33 - Comparative X-ray powder patterns of MnCl$_2$(nic)$_2$, terephthalamide, and MnCl$_2$(nic)$_2$/terephthalamide co-crystal

Figure 2.34 - Comparative X-ray powder patterns of MnCl$_2$(iso)$_2$, terephthalamide, and MnCl$_2$(iso)$_2$/terephthalamide co-crystal
Figure 2.35 - Comparative X-ray powder patterns of MnCl$_2$(nia)$_3$ terephthalamide, and MnCl$_2$(nia)$_2$/terephthalamide co-crystal.
MnBr$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals

![Graph showing X-ray powder patterns of MnBr$_2$(nic)$_2$, terephthalamide, and MnBr$_2$(nic)$_2$/terephthalamide co-crystal](image1)

Figure 2.36 - Comparative X-ray powder patterns of MnBr$_2$(nic)$_2$, terephthalamide, and MnBr$_2$(nic)$_2$/terephthalamide co-crystal

![Graph showing X-ray powder patterns of MnBr$_2$(iso)$_2$, terephthalamide and MnBr$_2$(iso)$_2$/terephthalamide co-crystal](image2)

Figure 2.37 - Comparative X-ray powder patterns of MnBr$_2$(iso)$_2$, terephthalamide and MnBr$_2$(iso)$_2$/terephthalamide co-crystal
2.2.2 Low frequency Raman plots

$\text{CuCl}_2(\text{nic/iso/nia})_2/1,4$-tfib co-crystals

![Figure 2.38 - Comparative Raman plot of CuCl$_2$(nic)$_2$, 1,4-tfib, and CuCl$_2$(nic)$_2$/1,4-tfib co-crystal](image)

![Figure 2.39 - Comparative Raman plot of CuCl$_2$(iso)$_2$, 1,4-tfib, and CuCl$_2$(iso)$_2$/1,4-tfib co-crystal](image)
Figure 2.40 – Comparative Raman plot of CuCl\(_2\)(nia)\(_2\), 1,4-tfib, and CuCl\(_2\)(nia)\(_2\)/1,4-tfib co-crystal.
CuBr$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

**Figure 2.41** – Comparative Raman plot of CuBr$_2$(nic)$_2$, 1,4-tfib, and CuBr$_2$(nic)$_2$/1,4-tfib co-crystal

**Figure 2.42** – Comparative Raman plot of CuBr$_2$(iso)$_2$, 1,4-tfib, and CuBr$_2$(iso)$_2$/1,4-tfib co-crystal
Figure 2.43 – Comparative Raman plot of \( \text{CuBr}_2(\text{nia})_2 \), \( 1,4\text{-tfib} \), and \( \text{CuBr}_2(\text{nia})_2/1,4\text{-tfib} \) co-crystal
CoCl$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

![Raman spectra comparison](image1)

*Figure 2.44 – Comparative Raman plot of CoCl$_2$(nic)$_2$, 1,4-tfib, and CoCl$_2$(nic)$_2$/1,4-tfib co-crystal*

![Raman spectra comparison](image2)

*Figure 2.45 – Comparative Raman plot of CoCl$_2$(iso)$_2$, 1,4-tfib, and CoCl$_2$(iso)$_2$/1,4-tfib co-crystal*
Figure 2.46 – Comparative Raman plot of $\text{CoCl}_2(\text{nia})_2$, 1,4-tfib, and $\text{CoCl}_2(\text{nia})_2/1,4$-tfib co-crystal
CoBr$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

Figure 2.47 – Comparative Raman plot of CoBr$_2$(nic)$_2$, 1,4-tfib, and CoBr$_2$(nic)$_2$/1,4-tfib co-crystal

Figure 2.48 – Comparative Raman plot of CoBr$_2$(iso)$_2$, 1,4-tfib, and CoBr$_2$(iso)$_2$/1,4-tfib co-crystal
Figure 2.49 - Comparative Raman plot of $\text{CoBr}_2(\text{nia})_2$, 1,4-tfib, and $\text{CoBr}_2(\text{nia})_2$/1,4-tfib co-crystal
MnCl$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

Figure 2.50 - Comparative Raman plot of MnCl$_2$(nic)$_2$, 1,4-tfib, and MnCl$_2$(nic)$_2$/1,4-tfib co-crystal

Figure 2.51 - Comparative Raman plot of MnCl$_2$(iso)$_2$, 1,4-tfib, and MnCl$_2$(iso)$_2$/1,4-tfib co-crystal
Figure 2.52 - Comparative Raman plot of MnCl$_2$(nia)$_2$, 1:4-tfib, and MnCl$_2$(nia)$_2$/1:4-tfib co-crystal
MnBr$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

Figure 2.53 - Comparative Raman plot of MnBr$_2$(nic)$_2$, 1,4-tfib, and MnBr$_2$(nic)$_2$/1,4-tfib co-crystal

Figure 2.54 - Comparative Raman plot of MnBr$_2$(iso)$_2$, 1,4-tfib, and MnBr$_2$(iso)$_2$/1,4-tfib co-crystal
2.2.3 Discussion

Each supposed co-crystal was analysed using pxrd and IR, which could then be compared to the pxrd patterns and IR spectra of the respective reactants. The patterns were overlaid and analysed for new peaks or shifts in the co-crystal pattern.

The overlaid pxrd plots (Figure 2.4 to Figure 2.37) show that for most of the attempted co-crystals there is no significant difference between the patterns. Many of the supposed co-crystal patterns are almost identical to the MX₂(L)₂ complex pattern or contain peaks from both the complex and the co-former, but with no novel peaks or shifting of any extant peaks. This is indicative that these samples have formed physical mixtures, with no intermolecular interactions occurring between complex and co-former.

Of the 34 attempted co-crystal syntheses, six show promising signs of new compounds being formed: CoCl₂(nia)₂/1,4-tfib (Figure 2.12), CoBr₂(iso)₂/1,4-tfib (Figure 2.14), MnBr₂(nic)₂/1,4-tfib (Figure 2.19), CuBr₂(nic)₂/terephthalamide (Figure 2.24), CuBr₂(iso)₂/terephthalamide (Figure 2.25), and CoCl₂(nia)₂/terephthalamide (Figure 2.29). Some of the new or shifted peaks of interest are shown in Table 2-1 below. While these changes imply that interactions are occurring, they do not contain any information on how the interactions occur.

<table>
<thead>
<tr>
<th>Co-crystal</th>
<th>Selected new peaks (2θ °)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CoCl₂(nia)₂/1,4-tfib</td>
<td>8.5, 9.2, 13.0</td>
</tr>
<tr>
<td>CoBr₂(iso)₂/1,4-tfib</td>
<td>9.2, 11.5, 12.9, 14.1, 22.7</td>
</tr>
<tr>
<td>MnBr₂(nic)₂/1,4-tfib</td>
<td>10.0, 12.1, 14.4, 17.1, 18.2</td>
</tr>
<tr>
<td>CuBr₂(nic)₂/terephthalamide</td>
<td>11.4, 14.0, 14.8, 15.7, 17.5, 19.1, 19.8, 20.9, 24.4</td>
</tr>
<tr>
<td>CuBr₂(iso)₂/terephthalamide</td>
<td>8.8, 16.7, 19.1, 22.9, 24.1</td>
</tr>
<tr>
<td>CoCl₂(nia)₂/terephthalamide</td>
<td>7.7, 9.2, 11.5, 12.9, 14.1, 22.8</td>
</tr>
</tbody>
</table>

The series of co-crystals including 1,4-tfib were also analysed using low frequency Raman spectroscopy. The resulting plots were processed and displayed as stack plots for easy differentiation (Figure 2.38 - Figure 2.54). The Raman results are consistent with the pxrd analysis, with the majority of compounds displaying a pattern where every peak aligns
with either the original MX$_2$(L)$_2$ complex or with 1,4-tfib. The samples which display differences are consistent with the pxrd: CoCl$_2$(nia)$_2$/1,4-tfib (Figure 2.46), CoBr$_2$(iso)$_2$/1,4-tfib (Figure 2.48), and MnBr$_2$(nic)$_2$/1,4-tfib (Figure 2.53).

In all three cases there are clear differences throughout the whole displayed range (5-1800 cm$^{-1}$), indicating that there are new intermolecular NCIs occurring in the co-crystal product. In a physical mixture the molecules do not engage in any intermolecular interactions, and therefore would not result in any new bands in the Raman spectra.

The CoBr$_2$(L)$_2$ series of metal complexes were modelled in the Gaussian9 package, from which simulated spectra were produced. From these the Co-Br stretching and bending modes were predicted.

<table>
<thead>
<tr>
<th>Complex</th>
<th>Co-Br asymmetric stretching mode (cm$^{-1}$)</th>
<th>Co-Br symmetric bending mode (cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CoBr$_2$(nic)$_2$</td>
<td>341</td>
<td>234</td>
</tr>
<tr>
<td>CoBr$_2$(iso)$_2$</td>
<td>334</td>
<td>234</td>
</tr>
</tbody>
</table>

The region of each spectrum with the most significant change in band position is the sub-800 cm$^{-1}$ region, which contains the region predicted to contain the Co-Br modes in the calculated spectra. In particular, each of the three spectra show new or shifted peaks just under 250 cm$^{-1}$ and at about 300 cm$^{-1}$ in the co-crystal spectra compared to the complex spectra. This implies that the co-crystals may be interacting through X-bonding with the metal-bound halides on the MX$_2$(L)$_2$ complex. The distinctive modes of the ligands appear over a large range at higher wavenumbers, where difference is also seen, implying that the ligands are also experiencing some form of NCI with 1,4-tfib. These bands are in similar positions as bands previously observed when metal-bound halogens engage in X-bonding. Raman data reported by Contreras and Gnecco$^{133}$ includes Hg-X vibrations in the range of 209-274 cm$^{-1}$, while Nguyen et al$^{134}$ reported C-I stretching modes in the region of 197-248 cm$^{-1}$ in a series of X-bonded co-crystals. Lisac et al$^{135}$ reported changes in the sub-500 cm$^{-1}$ region when forming X-bonded co-crystals with a number of metal centres.
IR spectroscopy was also performed, with spectra of relevant co-crystals displayed in Figure 2.55 through Figure 2.60. In these spectra there are clear differences in positions of bands related to functional groups that can undergo H-bonding, for example in the 2900-3100 cm\(^{-1}\) region where amide and carboxylic acid bands appear. There are also significant differences in the sub-1700 region, likely caused by H-bonding involving the aromatic hydrogens.

![Figure 2.55 – Stacked IR plot of CoCl\(_2\)(nia)\(_2\), 1,4-tfib, and CoCl\(_2\)(nia)\(_2\)/1,4-tfib co-crystal](image1)

![Figure 2.56 – Stacked IR plot of CoBr\(_2\)(iso)\(_2\), 1,4-tfib, and CoBr\(_2\)(iso)\(_2\)/1,4-tfib co-crystal](image2)
Figure 2.57 – Stacked IR plot of MnBr$_2$(nic)$_2$, 1,4-tfib, and MnBr$_2$(nic)$_2$/1,4-tfib co-crystal

Figure 2.58 – Stacked IR plot of CuBr$_2$(nic)$_2$, terephthalamide, and CuCl$_2$(nic)$_2$/terephthalamide co-crystal

Figure 2.59 – Stacked IR plot of CuBr$_2$(iso)$_2$, terephthalamide, and CuCl$_2$(iso)$_2$/terephthalamide co-crystal
Figure 2.60 – Stacked IR plot of \( \text{CoCl}_2(\text{nia})_2 \), terephthalamide, and \( \text{CoCl}_2(\text{nia})_2/\text{terephthalamide} \) co-crystal

The pxrd, Raman and IR spectra of \( \text{CoCl}_2(\text{nia})_2/1,4\text{-tfib} \), \( \text{CoBr}_2(\text{iso})_2/1,4\text{-tfib} \), \( \text{MnBr}_2(\text{nic})_2/1,4\text{-tfib} \), \( \text{CuBr}_2(\text{nic})_2/\text{terephthalamide} \), \( \text{CuBr}_2(\text{iso})_2/\text{terephthalamide} \), and \( \text{CoCl}_2(\text{nia})_2/\text{terephthalamide} \) all show significant differences when compared to the spectra of their respective metal complex and co-former. This is evidence that the mechanochemical synthesis of these co-crystals may have been successful. When comparing the pxrd patterns of the metal complex to the respective co-crystal it is apparent that the majority of the peaks associated with the complex have either shifted or disappeared, which implies that the conversion of reactants to products is near 100%.

The Raman spectra of the 1,4-tfib-containing co-crystals shows evidence that the metal-bound halides are involved in some form of NCI with 1,4-tfib that is not occurring in the metal complex alone. As the 1,4-tfib co-former does not have any hydrogen atoms to engage in H-bonding, this implies that the co-crystal is engaging in X-bonding, likely through the iodine atoms of 1,4-tfib, as their sigma hole is increased by the very electron-withdrawing fluorides present in the two, three, five, and six positions.

There are also significant differences in regions of the Raman and IR spectra that correspond to groups found on the ligands, which implies that H-bonding is also taking place. As these changes are seen between the metal complex and co-crystal it is likely that these H-bonding interactions are also involving the co-former.

It is possible that conducting the mechanochemical experiments over a longer period of time could result in co-crystal formation in some of the systems that did not show signs
of reaction. Many mechanochemical reactions default to 30+ minutes of grinding at 20-30 Hz, although this is not necessarily required for reactions or co-crystals to form. A recent study exploring mechanochemical synthesis of co-crystals composed of 9-anthracene carboxylic acid and either 1,2-bis(4-pyridyl)ethylene or 1,2-bis(4-pyridyl)ethane found that when using LAG pure co-crystal was formed within five minutes, with no change observed when the reaction time was increased to 30 minutes.\(^{136}\)
2.3 Experimental

2.3.1 Synthesis of MX$_2$(nic/iso/nia)$_2$ complexes

Synthesis of CuCl$_2$(nic/iso/nia)$_2$ complexes

Reactions were done following literature methods.$^{121}$

Synthesis of CuCl$_2$(nic)$_2$

CuCl$_2$ (51.9 mg, 0.371 mmol) was dissolved in MeOH (10 mL) and added to a solution of nicotinamide (46.6 mg, 0.371 mmol) in MeOH (10 mL). The mixture was stirred at reflux for 30 minutes. The resulting light blue precipitate was filtered by vacuum filtration and washed with MeOH. (52.2 mg, 36%) Anal. Calcd. For C$_{12}$H$_{12}$Cl$_2$CuN$_4$O$_2$: C, 38.06; H, 3.19; N, 12.51. Found: C, 36.79; H, 3.60; N, 12.51. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3412, 3174, 1702, 1610, 1554, 1419, 1390, 1232, 848, 762, 644, 485.

Synthesis of CuCl$_2$(iso)$_2$

CuCl$_2$ (50.6 mg, 0.371 mmol) was dissolved in MeOH (10 mL) and added to a solution of isonicotinamide (47.3 mg, 0.371 mmol) in MeOH (10 mL). The mixture was stirred at reflux for 30 minutes. The resulting light blue precipitate was filtered by vacuum filtration and washed with MeOH. (63.1 mg, 44%) Anal. Calcd. For C$_{12}$H$_{12}$Cl$_2$CuN$_4$O$_2$: C, 38.06; H, 3.19; N, 12.51. Found: C, 37.00; H, 3.40; N, 13.12. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3412, 3174, 1702, 1610, 1554, 1419, 1390, 1232, 848, 762, 644, 485.

Synthesis of CuCl$_2$(nia)$_2$

CuCl$_2$ (171.12 mg, 1.00 mmol) was dissolved in MeOH (10 mL) and added to a solution of nicotinic acid (243.3 mg, 2.00 mmol) in MeOH (10 mL). The mixture was stirred at reflux for 30 minutes. The resulting light blue precipitate was filtered by vacuum filtration and washed with MeOH. (439.2 mg, 49%) Anal. Calcd. For C$_{12}$H$_{10}$Cl$_2$CuN$_2$O$_4$: C, 37.86; H, 2.65; N, 7.36. Found: C, 30.68; H, 2.20; N, 5.77. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3413, 3176, 1702, 1610, 1554, 1419, 1389, 1232, 848, 762, 644, 483.
Synthesis of CuBr$_2$(nic/iso/nia)$_2$ complexes

Reactions were done following literature methods.$^{121}$

Synthesis of CuBr$_2$(nic)$_2$

CuBr$_2$ (50.4 mg, 0.223 mmol) was dissolved in MeOH (10 mL) and added to a solution of nicotinamide (55.8 mg, 0.447 mmol) in MeOH (10 mL). The mixture was stirred at reflux for 30 minutes. The resulting green precipitate was filtered by vacuum filtration and washed with MeOH. (85.3 mg, 81%) Anal. Calcd. For C$_{12}$H$_{10}$Br$_2$CuN$_2$O$_4$: C, 30.82; H, 2.59; N, 11.98. Found: C, 30.78; H, 2.62; N, 10.66. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3413, 3321, 3269, 3214, 3189, 1653, 1619, 1601, 1390, 1200, 795, 623, 539.

Synthesis of CuBr$_2$(iso)$_2$

CuBr$_2$ (53.9 mg, 0.223 mmol) was dissolved in MeOH (10 mL) and added to a solution of isonicotinamide (56.2 mg, 0.447 mmol) in MeOH (10 mL). The mixture was stirred at reflux for 30 minutes. The resulting green precipitate was filtered by vacuum filtration and washed with MeOH. (95.5 mg, 85%) Anal. Calcd. For C$_{12}$H$_{10}$Br$_2$CuN$_2$O$_4$: C, 30.82; H, 2.59; N, 11.98. Found: C, 30.81; H, 2.62; N, 10.82. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3421, 3308, 3175, 3106, 3082, 1698, 1610, 1553, 1418, 1388, 1223, 1064, 760, 642, 476.

Synthesis of CuBr$_2$(nia)$_2$

CuBr$_2$ (53.5 mg, 0.223 mmol) was dissolved in MeOH (10 mL) and added to a solution of nicotinic acid (55.0 mg, 0.447 mmol) in MeOH (10 mL). The mixture was stirred at reflux for 30 minutes. The resulting green precipitate was filtered by vacuum filtration and washed with MeOH. (70.7 mg, 78%) Anal. Calcd. For C$_{12}$H$_{10}$Br$_2$CuN$_2$O$_4$: C, 30.69; H, 2.15; N, 5.97. Found: C, 30.68; H, 2.20; N, 5.77. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3082, 2669, 2554, 1696, 1602, 1415, 1298, 1194, 748, 682, 452.
Synthesis of CoCl$_2$(nic/iso/nia)$_2$ complexes

Reactions were done following literature methods.$^{124}$

Synthesis of CoCl$_2$(nic)$_2$

CoCl$_2$ (101.1 mg, 0.420 mmol) was dissolved in MeOH (5 mL) and added to a solution of nicotinamide (101.1 mg, 0.840 mmol) in hot MeOH (8 mL). The mixture was stirred at room temperature for two hours. The resulting light purple precipitate was filtered by vacuum filtration and washed with MeOH. (124.9 mg, 79%) Anal. Calcd. For C$_{12}$H$_{12}$Cl$_2$CoN$_4$O$_2$: C, 38.53; H, 3.23; N, 14.98. Found: C, 37.75; H, 3.53; N, 14.45. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3400, 3305, 3265, 3191, 3078, 1657, 1612, 1392, 1197, 1145, 1094, 1048, 823, 795, 762, 691, 576, 528.

Synthesis of CoCl$_2$(iso)$_2$

CoCl$_2$ (49.8 mg, 0.2101 mmol) was dissolved in MeOH (5 mL) and added to a solution of isonicatinamide (49.6 mg, 0.4202 mmol) in hot MeOH (10 mL). The mixture was stirred at room temperature for two hours. The resulting light purple precipitate was filtered by vacuum filtration and washed with MeOH. (25.5 mg, 33%) Anal. Calcd. For C$_{12}$H$_{12}$Cl$_2$CoN$_4$O$_2$: C, 38.53; H, 3.23; N, 14.98. Found: C, 38.12; H, 3.33; N, 14.21. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3400, 3164, 1707, 1611, 1553, 1415, 1378, 1121, 845, 757, 642, 543, 493.

Synthesis of CoCl$_2$(nia)$_2$

CoCl$_2$ (99.7 mg, 0.420 mmol) was dissolved in MeOH (5 mL) and added to a solution of nicotinic acid (103.2 mg, 0.840 mmol) in hot MeOH (8 mL). The mixture was stirred at room temperature for two hours. The resulting light purple precipitate was filtered by vacuum filtration and washed with MeOH. (78.1 mg, 50%) Anal. Calcd. For C$_{12}$H$_{10}$Cl$_2$CoN$_2$O$_4$: C, 38.33; H, 2.68; N, 7.45. Found: C, 38.35; H, 2.94; N, 5.46. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3076, 2672, 2560, 1698, 1605, 1416, 1294, 914, 744, 683.
Synthesis of CoBr$_2$(nic/iso/nia)$_2$ complexes

Reactions were done following literature methods.$^{121, 123}$

Synthesis of CoBr$_2$(nic)$_2$

CoBr$_2$ (0.324 g, 1.0 mmol) was dissolved in hot EtOH (10 mL) and added to a solution of nicotinamide (0.248 g, 2.00 mmol) in hot EtOH (5 mL). The mixture was stirred at room temperature for two hours. The resulting magenta precipitate was filtered by vacuum filtration and washed with EtOH. (0.423 g, 92%) Anal. Calcd. For C$_{12}$H$_{12}$Br$_2$CoN$_4$O$_2$: C, 31.13; H, 2.61; N, 12.10. Found: C, 31.12; H, 3.60; N, 11.12. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3413, 3304, 3263, 3188, 1653, 1618, 1600, 1576, 1197, 1048, 794, 690, 624, 557, 524.

Synthesis of CoBr$_2$(iso)$_2$

CoBr$_2$ (0.325 g, 1.0 mmol) was dissolved in hot EtOH (10 mL) and added to a solution of isonicotinamide (0.250 g, 2.00 mmol) in hot EtOH (5 mL). The mixture was stirred at room temperature for two hours. The resulting magenta precipitate was filtered by vacuum filtration and washed with EtOH. (0.380 g, 83%) Anal. Calcd. For C$_{12}$H$_{12}$Br$_2$CoN$_4$O$_2$: C, 31.13; H, 2.61; N, 12.10. Found: C, 30.75; H, 2.77; N, 9.63. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3418, 3167, 1700, 1609, 1553, 1414, 1380, 1016, 840, 757, 638, 483.

Synthesis of CoBr$_2$(nia)$_2$

CoBr$_2$ (0.322 g, 1.0 mmol) was dissolved in MeOH (5 mL) and added to a solution of nicotinic acid (0.243 g, 2.0 mmol) in hot MeOH (8 mL). The mixture was stirred at room temperature for two hours. The resulting magenta precipitate was filtered by vacuum filtration and washed with MeOH. (0.322 g, 70%) Anal. Calcd. For C$_{12}$H$_{10}$Br$_2$CoN$_2$O$_4$: C, 31.00; H, 2.17; N, 6.02. Found: C, 30.90; H, 2.37; N, 4.82. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3079, 1693, 1600, 1414, 1300, 1196, 915, 746, 684, 549.
Synthesis of MnCl$_2$(nic/iso/nia)$_2$ complexes

Reactions were done following literature methods.$^{121, 123}$

Synthesis of MnCl$_2$(nic)$_2$

MnCl$_2$ (0.197 g, 1.0 mmol) was dissolved in hot EtOH (10 mL) and added to a solution of nicotinamide (0.243 g, 2.00 mmol) in hot EtOH (5 mL). The mixture was stirred at room temperature for two hours. The resulting pale pink precipitate was filtered by vacuum filtration and washed with EtOH. (0.338 g, 92%) Anal. Calcd. For C$_{12}$H$_{12}$Cl$_2$MnN$_4$O$_2$: C, 38.74; H, 3.27; N, 15.26. Found: C, 39.00; H, 3.00; N, 15.26. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3421, 3295, 2360, 1700, 1599, 1371, 960, 690, 649, 517.

Synthesis of MnCl$_2$(iso)$_2$

MnCl$_2$ (0.197 g, 1.0 mmol) was dissolved in hot EtOH (10 mL) and added to a solution of isonicotinamide (0.245 g, 2.00 mmol) in hot EtOH (5 mL). The mixture was stirred at room temperature for two hours. The resulting pale pink precipitate was filtered by vacuum filtration and washed with EtOH. (0.457 g, 124% (wet)) Anal. Calcd. For C$_{12}$H$_{12}$Cl$_2$MnN$_4$O$_2$: C, 38.74; H, 3.27; N, 15.26. Found: C, 39.00; H, 3.27; N, 15.14. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3410, 3170, 1702, 1610, 1554, 1414, 1385, 1121, 1014, 848, 765, 503, 407.

Synthesis of MnCl$_2$(nia)$_2$

MnCl$_2$ (0.198 g, 1.0 mmol) was dissolved in hot EtOH (10 mL) and added to a solution of nicotinic acid (0.248 g, 2.00 mmol) in hot EtOH (5 mL). The mixture was stirred at room temperature for two hours. The resulting pale pink precipitate was filtered by vacuum filtration and washed with EtOH. (0.357 g, 96%) Anal. Calcd. For C$_{12}$H$_{10}$Cl$_2$MnN$_2$O$_4$: C, 38.74; H, 2.71; N, 7.53. Found: C, 38.28; H, 2.78; N, 6.07. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3079, 2673, 2570, 1683, 1600, 1304, 1198, 1045, 924, 746, 688, 640, 548.
Synthesis of \( \text{MnBr}_2(\text{nic/iso/nia})_2 \) complexes

Reactions were done following literature methods.\textsuperscript{121, 123}

**Synthesis of \( \text{MnBr}_2(\text{nic})_2 \)**

\( \text{MnBr}_2 \) (0.287 g, 1.0 mmol) was dissolved in hot \( \text{EtOH} \) (10 mL) and added to a solution of nicotinamide (0.244 g, 2.00 mmol) in hot \( \text{EtOH} \) (5 mL). The mixture was stirred at room temperature for two hours. The resulting pale pink precipitate was filtered by vacuum filtration and washed with \( \text{EtOH} \). (0.356 g, 77\%) Anal. Calcd. For \( \text{C}_{12}\text{H}_{12}\text{Cl}_2\text{MnN}_4\text{O}_2 \): C, 38.74; H, 3.27; N, 15.26. Found: C, 31.49; H, 2.59; N, 11.09. Selected IR \( \nu_{\text{max}}/\text{cm}^{-1} \): 3411, 3304, 3186, 3071, 1656, 1619, 1599, 1441, 1392, 1200, 1045, 793, 646, 514.

**Synthesis of \( \text{MnBr}_2(\text{iso})_2 \)**

\( \text{MnBr}_2 \) (0.214 g, 1.0 mmol) was dissolved in hot \( \text{EtOH} \) (10 mL) and added to a solution of isonicotinamide (0.244 g, 2.00 mmol) in hot \( \text{EtOH} \) (5 mL). The mixture was stirred at room temperature for two hours. The resulting pale pink precipitate was filtered by vacuum filtration and washed with \( \text{EtOH} \). (0.437 g, 127\% (wet)) Anal. Calcd. For \( \text{C}_{12}\text{H}_{12}\text{Br}_2\text{MnN}_4\text{O}_2 \): C, 31.40; H, 2.64; N, 12.21. Found: C, 31.49; H, 2.59; N, 11.09. Selected IR \( \nu_{\text{max}}/\text{cm}^{-1} \): 3417, 3167, 1699, 1609, 1553, 1414, 1380, 1013, 845, 759, 636, 491.

**Attempted synthesis of \( \text{MnBr}_2(\text{nia})_2 \)**

\( \text{MnBr}_2 \) (0.290 g, 1.0 mmol) was dissolved in hot \( \text{EtOH} \) (10 mL) and added to a solution of nicotinic acid (0.243 g, 2.00 mmol) in hot \( \text{EtOH} \) (5 mL). The mixture was stirred at room temperature for two hours. The resulting white precipitate was filtered by vacuum filtration and washed with \( \text{EtOH} \). (0.078 g, 17\%) Elemental analysis of the product confirmed that the complex had not formed, and the small amount of solid formed was nicotinic acid. The reaction was repeated twice, with both attempts yielding similar results.

81
2.3.2 Mechanochemical synthesis of MX$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

Synthesis of CuCl$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

CuCl$_2$(nic)$_2$ (10 mg, 0.026 mmol) and 1,4-tfib (21.2 mg, 0.052 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3399, 3153, 1702, 1603, 1460, 1375, 940, 757.

Synthesis of CuCl$_2$(iso)$_2$/1,4-tfib

CuCl$_2$(iso)$_2$ (10 mg, 0.026 mmol) and 1,4-tfib (21.2 mg, 0.052 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3413, 3176, 1703, 1610, 1555, 1459, 1419, 1391, 940, 757, 644, 486.

Synthesis of CuCl$_2$(nia)$_2$/1,4-tfib

CuCl$_2$(nia)$_2$ (10 mg, 0.026 mmol) and 1,4-tfib (21.2 mg, 0.052 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3077, 2826, 2673, 2560, 1698, 1605, 1459, 1416, 1293, 939, 746, 684, 546.
Synthesis of CuBr$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

Synthesis of CuBr$_2$(nic)$_2$/1,4-tfib

CuBr$_2$(nic)$_2$ (10 mg, 0.021 mmol) and 1,4-tfib (17.18 mg, 0.042 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3418, 3326, 3271, 3214, 3190, 2322, 1655, 1620, 1460, 1389, 1200, 940, 757, 691.

Synthesis of CuBr$_2$(iso)$_2$/1,4-tfib

CuBr$_2$(iso)$_2$ (10 mg, 0.021 mmol) and 1,4-tfib (17.18 mg, 0.042 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3420, 3174, 2320, 1697, 1609, 1553, 1460, 1418, 1387, 940, 757, 476.

Synthesis of CuBr$_2$(nia)$_2$/1,4-tfib

CuBr$_2$(nia)$_2$ (10 mg, 0.026 mmol) and 1,4-tfib (21.1 mg, 0.052 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3083, 2670, 2553, 2325, 1697, 1603, 1459, 1418, 1298, 939, 757, 683.
Synthesis of CoCl$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

Synthesis of CoCl$_2$(nic)$_2$/1,4-tfib

CoCl$_2$(nic)$_2$ (10 mg, 0.026 mmol) and 1,4-tfib (21.4 mg, 0.053 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3401, 3302, 3265, 3191, 3079, 1660, 1622, 1458, 1393, 939, 757, 690, 562.

Synthesis of CoCl$_2$(iso)$_2$/1,4-tfib

CoCl$_2$(iso)$_2$ (10 mg, 0.026 mmol) and 1,4-tfib (21.4 mg, 0.053 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3083, 1688, 1601, 1460, 1418, 1305, 940, 757, 746, 687, 553.

Synthesis of CoCl$_2$(nia)$_2$/1,4-tfib

CoCl$_2$(nia)$_2$ (10 mg, 0.026 mmol) and 1,4-tfib (21.4 mg, 0.053 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3076, 2672, 2560, 1698, 1605, 1450, 1416, 1331, 1294, 965, 914, 828, 744, 683.
Synthesis of $\text{CoBr}_2 (\text{nic/iso/nia})_2 / 1,4$-tfib co-crystals

**Synthesis of $\text{CoBr}_2 (\text{nic})_2 / 1,4$-tfib**

$\text{CoBr}_2 (\text{nic})_2$ (10 mg, 0.026 mmol) and 1,4-tfib (21.4 mg, 0.053 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. Selected IR $\nu_{\text{max}}/\text{cm}^{-1}$: 3413, 3308, 3263, 3189, 1656, 1619, 1601, 1459, 1392, 1198, 1049, 939, 759, 690, 561.

**Synthesis of $\text{CoBr}_2 (\text{iso})_2 / 1,4$-tfib**

$\text{CoBr}_2 (\text{iso})_2$ (10 mg, 0.026 mmol) and 1,4-tfib (21.4 mg, 0.053 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. Selected IR $\nu_{\text{max}}/\text{cm}^{-1}$: 3083, 1685, 1601, 1305, 1196, 924, 746, 685, 552.

**Synthesis of $\text{CoBr}_2 (\text{nia})_2 / 1,4$-tfib**

$\text{CoBr}_2 (\text{nia})_2$ (10 mg, 0.021 mmol) and 1,4-tfib (17.2 mg, 0.043 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. Selected IR $\nu_{\text{max}}/\text{cm}^{-1}$: 3414, 3316, 3191, 1663, 1601, 1459, 1425, 1302, 1197, 1048, 939, 759, 686.
Synthesis of MnCl$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

Synthesis of MnCl$_2$(nic)$_2$/1,4-tfib

MnCl$_2$(nic)$_2$ (15 mg, 0.028 mmol) and 1,4-tfib (11.4 mg, 0.056 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3421, 3200, 1700, 1599, 1372, 1051, 742, 690, 649, 516, 421.

Synthesis of MnCl$_2$(iso)$_2$/1,4-tfib

MnCl$_2$(iso)$_2$ (15 mg, 0.028 mmol) and 1,4-tfib (11.4 mg, 0.056 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3410, 3168, 1701, 1610, 1554, 1461, 1414, 1385, 1013, 941, 848, 760, 636, 503, 407.

Synthesis of MnCl$_2$(nia)$_2$/1,4-tfib

MnCl$_2$(nia)$_2$ (10 mg, 0.026 mmol) and 1,4-tfib (21.6 mg, 0.053 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3079, 2882, 2676, 2562, 1689, 1600, 1460, 1417, 1305, 1199, 940, 746, 688.
Synthesis of MnBr$_2$(nic/iso/nia)$_2$/1,4-tfib co-crystals

Synthesis of MnBr$_2$(nic)$_2$/1,4-tfib

MnBr$_2$(nic)$_2$ (15 mg, 0.028 mmol) and 1,4-tfib (11.4 mg, 0.056 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3417, 3309, 3170, 1700, 1610, 1460, 1414, 1382, 1214, 941, 759, 636, 494.

Synthesis of MnBr$_2$(iso)$_2$/1,4-tfib

MnBr$_2$(iso)$_2$ (15 mg, 0.028 mmol) and 1,4-tfib (11.4 mg, 0.056 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3418, 3308, 3169, 1701, 1610, 1460, 1414, 1381, 940, 845, 759, 637, 494.
2.3.3 Mechanochemical synthesis of MX$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals

Synthesis of CuCl$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals

Synthesis of CuCl$_2$(nic)$_2$/terephthalamide

CuCl$_2$(nic)$_2$ (10 mg, 0.026 mmol) and terephthalamide (8.66 mg, 0.052 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu$ /cm$^{-1}$: 3397, 3361, 3154, 1705, 1657, 1604, 1409, 1376, 1128, 865, 803, 734, 685, 646, 527.

Synthesis of CuCl$_2$(iso)$_2$/terephthalamide

CuCl$_2$(iso)$_2$ (10 mg, 0.026 mmol) and terephthalamide (8.66 mg, 0.052 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu$ /cm$^{-1}$: 3362, 3164, 1705, 1660, 1616, 1411, 1388, 1129, 800, 735, 643, 512.

Synthesis of CuCl$_2$(nia)$_2$/terephthalamide

CuCl$_2$(nia)$_2$ (10 mg, 0.026 mmol) and terephthalamide (8.62 mg, 0.052 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu$ /cm$^{-1}$: 3360, 3158, 3078, 2818, 2672, 2567, 1704, 1657, 1607, 1409, 1296, 1127, 800, 733, 684, 626, 526.
Synthesis of CuBr$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals

Synthesis of CuBr$_2$(nic)$_2$/terephthalamide

CuBr$_2$(nic)$_2$ (10 mg, 0.021 mmol) and terephthalamide (7.02 mg, 0.042 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu$$_{max}$/cm$^{-1}$: 3422, 3360, 3158, 1702, 1657, 1614, 1386, 1128, 862, 800, 732, 640, 478.

Synthesis of CuBr$_2$(iso)$_2$/terephthalamide

CuBr$_2$(iso)$_2$ (10 mg, 0.021 mmol) and terephthalamide (7.02 mg, 0.042 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu$$_{max}$/cm$^{-1}$: 3358, 3158, 1654, 1617, 1406, 1386, 1128, 794, 732, 691, 622, 525.

Synthesis of CuBr$_2$(nia)$_2$/terephthalamide

CuBr$_2$(nia)$_2$ (10 mg, 0.021 mmol) and terephthalamide (6.98 mg, 0.042 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu$$_{max}$/cm$^{-1}$: 3264 (broad), 3055 (broad), 2363, 1715, 1652, 1594, 1418, 1381, 840, 775, 714, 595, 438.
Synthesis of CoCl$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals

Synthesis of CoCl$_2$(nic)$_2$/terephthalamide

CoBr$_2$(nic)$_2$ (10 mg, 0.026 mmol) and terephthalamide (8.77 mg, 0.053 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $v_{\text{max}}$/cm$^{-1}$: 3401, 3302, 3265, 3191, 1660, 1622, 1458, 1393, 1197, 939, 757, 690, 562.

Synthesis of CoCl$_2$(iso)$_2$/terephthalamide

CoBr$_2$(iso)$_2$ (10 mg, 0.026 mmol) and terephthalamide (8.77 mg, 0.053 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $v_{\text{max}}$/cm$^{-1}$: 3402, 3160, 1707, 1611, 1554, 1459, 940, 641, 544.

Synthesis of CoCl$_2$(nia)$_2$/terephthalamide

CoBr$_2$(nia)$_2$ (10 mg, 0.026 mmol) and terephthalamide (8.73 mg, 0.053 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $v_{\text{max}}$/cm$^{-1}$: 3360, 3157, 3077, 2671, 2566, 1704, 1656, 1606, 1408, 1387, 1331, 1295, 1126, 800, 732, 683, 625, 525.
Synthesis of CoBr$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals

Synthesis of CoBr$_2$(nic)$_2$/tere

CoBr$_2$(iso)$_2$ (10 mg, 0.021 mmol) and terephthalamide (7.09 mg, 0.043 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. Selected IR $\nu_{\max}$/cm$^{-1}$: 3359, 3159, 1655, 1616, 1407, 1386, 1128, 865, 795, 647, 623, 563, 524.

Synthesis of CoBr$_2$(iso)$_2$/terephthalamide

CoBr$_2$(iso)$_2$ (10 mg, 0.021 mmol) and terephthalamide (7.09 mg, 0.043 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. Selected IR $\nu_{\max}$/cm$^{-1}$: 3420, 3360, 3162, 704, 1657, 1612, 1409, 1385, 1128, 802, 733, 638.

Synthesis of CoBr$_2$(nia)$_2$/terephthalamide

CoBr$_2$(nia)$_2$ (10 mg, 0.021 mmol) and terephthalamide (7.09 mg, 0.043 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. Selected IR $\nu_{\max}$/cm$^{-1}$: 3360, 3160, 1657, 1601, 1409, 1300, 1160, 1128, 802, 734, 688, 622, 526.
Synthesis of MnCl$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals

Synthesis of MnCl$_2$(nic)$_2$/terephthalamide

MnCl$_2$(nic)$_2$ (10 mg, 0.027 mmol) and terephthalamide (8.89 mg, 0.054 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3421, 3361, 3162, 1704, 1657, 1618, 1600, 1409, 1373, 1128, 865, 737, 632, 518, 420.

Synthesis of MnCl$_2$(iso)$_2$/terephthalamide

MnCl$_2$(iso)$_2$ (10 mg, 0.027 mmol) and terephthalamide (8.89 mg, 0.054 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3360, 3160, 1706, 1657, 1613, 1409, 1385, 1128, 1014, 802, 733, 636, 505.

Synthesis of MnCl$_2$(nia)$_2$/terephthalamide

MnCl$_2$(nia)$_2$ (10 mg, 0.027 mmol) and terephthalamide (8.82 mg, 0.053 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3361, 3160, 3079, 1657, 1617, 1600, 1409, 1387, 1302, 803, 734, 688, 637, 527.
Synthesis of MnBr$_2$(nic/iso/nia)$_2$/terephthalamide co-crystals

Synthesis of MnBr$_2$(nic)$_2$/terephthalamide

MnBr$_2$(nic)$_2$ (10 mg, 0.021 mmol) and terephthalamide (7.15 mg, 0.043 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3360, 3321, 3161, 1656, 1617, 1387, 1128, 793, 734, 694, 647, 624, 525.

Synthesis of MnBr$_2$(iso)$_2$/terephthalamide

MnBr$_2$(iso)$_2$ (10 mg, 0.021 mmol) and terephthalamide (7.15 mg, 0.043 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3418, 3361, 3161, 1703, 1657, 1613, 1409, 1384, 1128, 1014, 800, 733, 636, 493, 415.
Chapter 3

3.1 Introduction
3.1.1 System Design

Five pyridine-based ligands were chosen, with two being phenanthroline-based and three being bipyridine-based. Pyridine-based ligands were again chosen because of the \( N_{py} \) readily binding to metals. All five ligands are bidentate, and so will occupy two binding sites in the coordination sphere.

![Figure 3.1](image_url)

There are two phenanthroline based ligands: neocuproine (\textbf{2,9-mphen}) and 4,7-dimethyl-1,10-phenanthroline (\textbf{4,7-mphen}). The other three ligands are bipyridine based: 4,4′-dimethyl-2,2′-bipyridine (\textbf{4,4-mbpy}), 2,2′-bipyridine-4,4′-dicarboxylic acid (\textbf{4,4-cbpy}), and 2,2′-bipyridine-6,6′-dicarboxylic acid (\textbf{6,6-cbpy}).

Bidentate ligands were chosen to contrast the monodentate ligands used previously. An \( MX_2(L)_2 \) complex with monodentate ligands will most likely form either a tetrahedral or
square planar geometry, while the same metal-ligand ratio with bidentate ligands will result in octahedral geometry. It is also possible for only one ligand to attach, resulting in a distorted tetrahedra, or for the halides to be displaced, forming a (ML\(_2\))\(^2+\)X\(_2\) complex. These ligands are also larger than the monodentate ligands used, and therefore have more steric bulk, which can influence the geometry and bonding of the complex and subsequent co-crystals.

Two metals were chosen for investigation in this section: cobalt and palladium. These metals were chosen as they have several key differences. Pd(II) is known for having a very strong preference for being 4-coordinate in a square planar configuration, while Co(II) is much more flexible with its coordination sphere. Pd(II) is also diamagnetic and therefore NMR active, unlike Cu(II), Co(II), or Mn(II). Palladium tends to be very labile, which allows ligands to coordinate and dissociate much easier than for most other metals. This often means that reactions can be performed quite quickly and at room temperature.

Because Pd(II) has a strong preference for being square planar, it is likely that only one ligand will bind, especially in the case of 2,9-mphen and 6,6-cbpy, which have functional groups extending in the direction of the binding site. This is likely to introduce too much steric strain to allow two ligands in a square planar configuration without considerable unfavourable distortion of the ligands.
3.1.2 Difficulty with standard analysis techniques

As with the previous library of compounds $^1\text{H}$ NMR was inaccessible for all Co(II) complexes due to solubility issues, as well as Co(II) being paramagnetic. In contrast Pd(II) is diamagnetic, allowing for $^1\text{H}$ NMR spectra to be measured, although solubility was still an issue, with DMF-$\delta$7 being the only NMR solvent in which any complexes would dissolve. Even so, PdCl$_2$(6,6-cbpy) was insufficiently soluble for a spectrum to be recorded. All other PdCl$_2$(L) complexes had clean $^1\text{H}$ NMR spectra with clear shifts proving that complexation had occurred and that no excess ligand remained in the sample.

The low solubility of the complexes proved a challenge in producing high quality single crystals for X-ray diffraction. As the complexes had poor solubility crystals had to be attained from diffusing solutions of the precursor metal halide and ligand.
3.1.3 Overview

MX\(_2\)(L)\(_n\) complexes (M = Co(II), Pd(II); L = 2,9-mphen, 4,7-mphen, 4,4-mbpy, 4,4-cbpy, 6,6-cbpy; n = 1, 2) were synthesised following literature procedures. CoX\(_2\)(L)\(_n\) complexes were synthesised by mixing solutions of metal halide and ligand in a 1:2 molar ratio in EtOH at reflux for at least six hours. The resulting precipitates were then filtered and dried over vacuum and analysed using elemental analysis and IR spectroscopy. A 1:2 ratio was used as there was potential for two ligands to bind a single metal in a tetrahedral configuration.

The PdCl\(_2\)(L) complexes were produced in a similar manner, with MeCN as the solvent, and at room temperature. If the reactions were performed in MeOH the PdCl\(_2\)(MeCN)\(_2\) rapidly dissociated resulting in the formation of metallic palladium.

Each of the MX\(_2\)(L)\(_n\) complexes were combined mechanochemically with both 1,4-tfib and terephthalamide. Each experiment consisted of mixing the MX\(_2\)(L)\(_n\) complex and co-former in a 1:1 molar ratio with a total mass in the range of 20-50 mg. All mechanochemical experiments were performed in a Retsch MM200 mixer mill. The samples were placed inside a stainless steel chamber with a 10 mL volume, along with a 10 mm stainless steel ball bearing. The grinding time and frequency was one minute at 10 Hz, then four minutes at 20 Hz. This short reaction time was chosen as it allowed a large library of compounds to be synthesised quickly as a proof of concept.

The potential co-crystal products of the mechanochemical synthesis were characterised by pxrd and IR, with spectra of the MX\(_2\)(L)\(_n\), 1,4-tfib, and terephthalamide also being taken for comparison.

Milled powder samples were mounted in paratone-N oil on a nylon loop. Powder diffraction data were collected on an Agilent Technologies Supernova system at room temperature (approx. 24°C) at the University of Otago using Mo-K\(\alpha\) (\(\lambda = 0.71073\)) radiation. Data was baselined and normalised using CrysAlisPro software. The data was then plotted and stacked in Microsoft Excel.

Single crystals were mounted in paratone-N oil on a nylon loop. X-ray diffraction data were collected on an Agilent Technologies Supernova system at 100 K at the University of Otago using Mo-K\(\alpha\) (\(\lambda = 0.71073\)) radiation, and data were treated using CrysAlisPro.
The structures were solved using SHELXT\textsuperscript{137} and weighted full-matrix refinement on F2 was carried out using SHELXL-97,\textsuperscript{137} both running within the OLEX2-v1.2.9 package.\textsuperscript{138} All non-hydrogen atoms were refined anisotropically. Hydrogen atoms attached to carbons were placed in calculated positions and refined using a riding model.

Microanalyses were conducted at the Campbell Microanalytical Laboratory at the University of Otago.
3.2 Results

3.2.1 pxrd plots

CoCl$_2$(bpy/phen)$_n$/1,4-tfib co-crystals

![pxrd plots](image)

*Figure 3.2* Comparitive X-ray powder patterns of CoCl$_2$(2,9-mphen), 1,4-tfib, and CoCl$_2$(2,9-mphen)/1,4-tfib co-crystal
Figure 3.3 - Comparative X-ray powder patterns of CoCl$_2$(4,7-mphen)$_2$, 1,4-tfib, and CoCl$_2$(4,7-mphen)/1,4-tfib co-crystal

Figure 3.4 - Comparative X-ray powder patterns of CoCl$_2$(4,4-mbpy)$_2$, 1,4-tfib, and CoCl$_2$(4,4-mbpy)$_2$/1,4-tfib co-crystal
Figure 3.5 - Comparative X-ray powder patterns of $\text{CoCl}_2(4,4\text{-cbpy})_2$, $1,4\text{-tfib}$, and $\text{CoCl}_2(4,4\text{-cbpy})_2/1,4\text{-tfib}$ co-crystal

Figure 3.6 - Comparative X-ray powder patterns of $\text{CoCl}_2(6,6\text{-cbpy})_2$, $1,4\text{-tfib}$, and $\text{CoCl}_2(6,6\text{-cbpy})_2/1,4\text{-tfib}$ co-crystal
CoBr$_2$(bpy/phen)$_n$/1,4-tfib co-crystals

Figure 3.7 - Comparative X-ray powder patterns of CoBr$_2$(2,9-mphen), 1,4-tfib, and CoBr$_2$(2,9-mphen)/1,4-tfib co-crystal

Figure 3.8 - Comparative X-ray powder patterns of CoBr$_2$(4,7-mphen), 1,4-tfib, and CoBr$_2$(4,7-mphen)/1,4-tfib co-crystal
Figure 3.9 - Comparative X-ray powder patterns of $\text{CoBr}_2(4,4\text{-mbpy})_2\text{I,4-tfib}$, and $\text{CoBr}_2(4,4\text{-mbpy})_2/1,4\text{-tfib}$ co-crystal

Figure 3.10 - Comparative X-ray powder patterns of $\text{CoBr}_2(6,6\text{-cbpy})_2\text{I,4-tfib}$, and $\text{CoBr}_2(6,6\text{-cbpy})_2/1,4\text{-tfib}$ co-crystal
PdCl$_2$(bpy/phen)/1,4-tfib co-crystals

**Figure 3.11** - Comparative X-ray powder patterns of PdCl$_2$(2,9-mphen), 1,4-tfib, and PdCl$_2$(2,9-mphen)/1,4-tfib co-crystal

**Figure 3.12** - Comparative X-ray powder patterns of PdCl$_2$(4,7-mphen), 1,4-tfib, and PdCl$_2$(4,7-mphen)/1,4-tfib co-crystal
Figure 3.13 - Comparative X-ray powder patterns of $\text{PdCl}_2(4,4\text{-mbpy})$, 1,4-tfib, and $\text{PdCl}_2(4,4\text{-mbpy})$/1,4-tfib co-crystal

Figure 3.14 - Comparative X-ray powder patterns of $\text{PdCl}_2(4,4\text{-cbpy})$, 1,4-tfib, and $\text{PdCl}_2(4,4\text{-cbpy})$/1,4-tfib co-crystal
Figure 3.15 - Comparative X-ray powder patterns of \( \text{PdCl}_2(6,6\text{-cbpy}) \), 1,4-tfib, and \( \text{PdCl}_2(6,6\text{-cbpy})/1,4\text{-tfib} \) co-crystal
CoCl$_2$(bpy/phen)$_n$/terephthalamide co-crystals

Figure 3.16 - Comparative X-ray powder patterns of CoCl$_2$(2,9-mphen), terephthalamide, and CoCl$_2$(2,9-mphen)/terephthalamide co-crystal

Figure 3.17 - Comparative X-ray powder patterns of CoCl$_2$(4,7-mphen), terephthalamide, and CoCl$_2$(4,7-mphen)/terephthalamide co-crystal
Figure 3.18 - Comparative X-ray powder patterns of $\text{CoCl}_2(4,4\text{-mbpy})_2$, terephthalamide, and $\text{CoCl}_2(4,4\text{-mbpy})_2$/terephthalamide co-crystal

Figure 3.19 - Comparative X-ray powder patterns of $\text{CoCl}_2(4,4\text{-cbpy})_2$, terephthalamide, and $\text{CoCl}_2(4,4\text{-cbpy})_2$/terephthalamide co-crystal
Figure 3.20 - Comparative X-ray powder patterns of \( \text{CoCl}_2(6,6\text{-cbpy}) \), terephthalamide, and \( \text{CoCl}_2(6,6\text{-cbpy})/\text{terephthalamide} \) co-crystal
CoBr$_2$(bpy/phen)$_n$/terephthalamide co-crystals

Figure 3.21 - Comparative X-ray powder patterns of CoBr$_2$(2,9-mphen), terephthalamide, and CoBr$_2$(2,9-mphen)/terephthalamide co-crystal

Figure 3.22 - Comparative X-ray powder patterns of CoBr$_2$(4,7-mphen), terephthalamide, and CoBr$_2$(4,7-mphen)/terephthalamide co-crystal
Figure 3.23 - Comparative X-ray powder patterns of \( \text{CoBr}_2(4,4\text{-mbpy})_2 \), terephthalamide, and \( \text{CoBr}_2(4,4\text{-mbpy})_2/\text{terephthalamide} \) co-crystal

Figure 3.24 - Comparative X-ray powder patterns of \( \text{CoBr}_2(6,6\text{-cbpy}) \), terephthalamide, and \( \text{CoBr}_2(6,6\text{-cbpy})/\text{terephthalamide} \) co-crystal
PdCl$_2$(bpy/phen)/terephthalamide co-crystals

Figure 3.25 - Comparative X-ray powder patterns of PdCl$_2$(2,9-mphen), terephthalamide, and PdCl$_2$(2,9-mphen)/terephthalamide co-crystal

Figure 3.26 - Comparative X-ray powder patterns of PdCl$_2$(4,7-mphen), terephthalamide, and PdCl$_2$(4,7-mphen)/terephthalamide co-crystal
Figure 3.27 - Comparative X-ray powder patterns of $\text{PdCl}_2(4,4\text{-mbpy})$, terephthalamide, and $\text{PdCl}_2(4,4\text{-mbpy})$/terephthalamide co-crystal

Figure 3.28 - Comparative X-ray powder patterns of $\text{PdCl}_2(4,4\text{-cbpy})$, terephthalamide, and $\text{PdCl}_2(4,4\text{-cbpy})$/terephthalamide co-crystal
Figure 3.29 - Comparative X-ray powder patterns of $\text{PdCl}_2(6,6\text{-cbpy})$, terephthalamide, and $\text{PdCl}_2(6,6\text{-cbpy})$/terephthalamide co-crystal
3.2.2 X-ray Crystallography

Diffraction quality single crystals of \( \text{CoCl}_2(2,9\text{-mphen}) \) were grown by recrystallising from a small quantity of DMF which was allowed to evaporate slowly. This resulted in large blue crystals of two morphologies, needles and cubes. Both morphologies resulted in the same structure. A crystal with cubic morphology was used for the following structural interpretation. The structure involves complex molecules interacting through Cl⋯H H-bonds between a metal bound chloride and an aromatic hydrogen. These interactions form a chain of molecules, which interacts with other molecular chains through offset π-stacking. The distance between π systems was measured from a centroid to the nearest carbon atom of the other π system as 3.715 Å, which is within the typical range for π-stacking interactions. The structure also confirmed that only one \( 2,9\text{-mphen} \) ligand had attached to the cobalt centre, corroborating the elemental analysis. This is likely because of the methyl groups in the two and nine position which caused too much steric interference when a second ligand approached. The complex crystallised in the \( \text{Pnma} \) space group.

![Figure 3.30 – Crystal structure of CoCl₂(2,9-mphen), showing Cl⋯H bonding between molecules](image)

Because \( 2,9\text{-mphen} \) is a planar molecule the complex is forced to form a distorted tetrahedral geometry around the cobalt centre. The bond angle between the two \( \text{N}_{\text{phen}} \) sites on the ligand is 82.79(11)°, which forces all the other bond angles to be between
112.31(4)° and 116.99(3)° instead of the ideal 109.5° of a perfect tetrahedra. The $\tau_4$ value is 0.916,\textsuperscript{140} indicating an almost perfect tetrahedral coordination geometry.

The length of the Cl⋯H bond 2.943 Å, with all Cl⋯H bonds being symmetry repeated. This is less than the sum of the Van der Waals radii of chlorine and hydrogen, which is 2.95 Å.\textsuperscript{141}

![Crystal structure of CoCl$_2$(2,9-mphen)](image)

Figure 3.31 - Crystal structure of CoCl$_2$(2,9-mphen). The structure consists of chains of offset molecules interacting through Cl⋯H bonding which interact with other chains through π-stacking.

Structures that appear isomorphous have been reported twice before,\textsuperscript{142,143} collected at 298 K and 173 K, while this structure was collected at 100 K. However, in these literature examples the molecules are associating only through π-π stacking interactions, and no Cl⋯H bonding is observed. The Cl⋯H distance in the literature structure is 2.993 Å, as opposed to 2.943 Å in this structure. The Cl⋯C distances are 3.737 Å and 3.686 Å, respectively.

An isomorph of CoCl$_2$(2,9-mphen) was crystallised through layer diffusion, where solutions of metal salt, co-former, and ligand were layered to allow slow mixing. The CoCl$_2$ and 1,4-tfib were dissolved in EtOH, and the 2,9-mphen ligand was dissolved in MeCN and layered on top, with a small layer of EtOH separating the solutions. The 1,4-tfib co-former did not co-crystallise through this method. The crystals grown using this method were flat rectangles, while the DMF evaporation method gave both needles and cubes. In this polymorph one molecule of MeCN per complex molecule is included in the
lattice. This polymorph crystallised in the $P2_1/n$ space group and shows different packing behaviour. The $\tau_4$ value is 0.864, indicating that the geometry at the cobalt centre is more distorted from tetrahedral than in the other polymorph.

The CoCl$_2$(2,9-mphen) complex molecules assemble into dimers with each molecule rotated 180° to the next, allowing the chlorides on each molecule to H-bond to an aromatic hydrogen on the adjacent molecule, as shown in Figure 3.32a. The Cl⋯H bond length within the dimers is 2.931 Å.

These dimers form π-stacked 2D chains. These stacks of dimers form in a herringbone orientation to each other, as shown in Figure 3.32b. The Cl⋯H bond length between dimer stacks is 2.940 Å.

Diffraction quality single crystals of CoBr$_2$(2,9-mphen) were grown through layer diffusion, where solutions of metal salt and ligand were layered to allow slow mixing. This method was used as the CoBr$_2$(2,9-mphen) was less DMF soluble than the CoCl$_2$(2,9-mphen), and as such the slow evaporation method was not accessible.

Over the course of several weeks the solutions were allowed to mix, forming dark green crystals of two morphologies, thin needles and large plates. Solving the structures of both

Figure 3.32 – Structure of CoCl$_2$(2,9-mphen)/MeCN. a) shows the formation of dimers through Cl⋯H H-bonding, b) shows the herringbone packing motif (MeCN solvent molecules omitted for clarity)
morphologies showed that, similar to CoCl$_2$(2,9-mphen), only one ligand has bound to the cobalt, resulting in a distorted tetrahedral geometry, with bond angle between N$_{py}$ being 82.45(13)$^\circ$. The other bond angles range between 109.02(9)$^\circ$ and 119.44(9)$^\circ$ as a result of this distortion. The $\tau_4$ value is 0.917, indicating tetrahedral coordination geometry.

The CoBr$_2$(2,9-mphen) complex is isostructural with the CoCl$_2$(2,9-mphen)/MeCN polymorph but does not include any solvent molecules (Figure 3.33). The complex also crystallised in the $P 2_1/n$ space group. The Br⋯H bond lengths are longer than the respective Cl⋯H bond lengths due to the increased atomic radii. The Cl⋯H bond length within a dimer is 2.931 Å, and between chains is 2.940 Å. The respective bond lengths in the CoBr$_2$(2,9-mphen) complex are 2.998 Å and 2.942 Å.

![Figure 3.33](image)

*Figure 3.33 – a) Partial structure of CoBr$_2$(2,9-mphen) showing dimer formation, b) Structure of CoBr$_2$(2,9-mphen) showing herringbone relationship between dimer stacks*
This structure of CoBr$_2$(2,9-mphen) has been reported before,\textsuperscript{143-145} although the reported structures contain solvent molecules in the packing pattern. A solvent-free polymorph has also been reported, where the complex molecules crystallise in the \( P2_1/c \) space group.\textsuperscript{143, 146, 147}

The same solution diffusion method as described for CoCl$_2$(2,9-mphen) was used in an attempt to form the PdCl$_2$(2,9-mphen)/1,4-tfib co-crystal. Diffraction quality crystals grew over the course of 4 days. As with the CoX$_2$(2,9-mphen) crystals, 1,4-tfib did not co-crystallise. Unlike those examples, the palladium formed a complex with two ligand molecules, as well as retaining a chloride, forming a five-coordinate complex, which is unusual for palladium. One of the Pd-N$_\text{phen}$ bonds is longer than the others, being 2.576(9) Å, while the other Pd-N$_\text{phen}$ bonds average to 2.057(9) Å. Also unusual is the presence of a [PdCl$_3$(MeCN)]$^-$ complex in the crystal lattice. There is only one example in the literature of such a complex.\textsuperscript{148} The [PdCl(2,9-mphen)$_2$]$^+$ cation has a \( \tau_5 \) value of 0.20,\textsuperscript{149} showing that while distorted, the shape is closer to square pyramidal that trigonal bipyramidal.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3.34.png}
\caption{Structure of [PdCl(2,9-mphen)$_2$]$^+$/[PdCl$_3$(MeCN)]$^-$ showing \( \pi \)-stacking and H-bonding}
\end{figure}

The molecules arrange with adjacent [PdCl(2,9-mphen)$_2$]$^+$ cations \( \pi \)-stacking through a 2,9-mphen \( \pi \)-system, while the chloride on one molecule forms a bifurcated H-bond to two aromatic protons on the other molecule. The bifurcated bond lengths are 2.864 Å and 2.864 Å. This bonding pattern occurs with both ligand molecules, resulting in a twisted chain of molecules (Figure 3.36). The [PdCl$_3$(MeCN)]$^-$ anions arrange slightly offset along
the b* axis, with Cl⋯H bonding alternating between linear bonds between adjacent [PdCl₃(MeCN)]⁻ anions and forming a large R₄⁺(14) ring involving two [PdCl₃(MeCN)]⁻ anions and two [PdCl(2,9-mphen)₂]⁺ cations, as shown in Figure 3.35. The bond lengths of the symmetry-related pairs of Cl⋯H bonds in this ring are 2.856 Å and 2.751 Å.

![Figure 3.35 - Structure of [PdCl(2,9-mphen)₂]/[PdCl₃(MeCN)] showing alternating H-bonding pattern of [PdCl₃(MeCN)]⁻](image1)

![Figure 3.36 - Structure of PdCl(2,9-mphen)₂/PdCl₃(MeCN) showing π-stacked chains](image2)

All structures collected make extensive use of X⋯H bonding interactions, but none show any signs of X-bonding in their crystal lattice.
3.2.3 Discussion

Each supposed co-crystal was analysed using pxrd and IR, which could then be compared to the pxrd patterns and IR spectra of the respective reactants. The patterns were overlaid and analysed for new peaks or shifts in the co-crystal pattern. These patterns are displayed in Figure 3.2 through Figure 3.29.

From this set there were five compounds that showed promising differences in their pxrd patterns: CoCl2(2,9-mphen)/1,4-tfib (Figure 3.2), CoCl2(4,4-mbpy)2/1,4-tfib (Figure 3.4), CoBr2(2,9-mphen)/1,4-tfib (Figure 3.7), PdCl2(2,9-mphen)/1,4-tfib (Figure 3.11), and PdCl2(4,4-mbpy)/1,4-tfib (Figure 3.13).

Table 3.1 – Selected pxrd points of difference

<table>
<thead>
<tr>
<th>Co-crystal</th>
<th>Selected new peaks (2θ°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CoCl2(2,9-mphen)/1,4-tfib</td>
<td>7.7, 8.3, 9.2</td>
</tr>
<tr>
<td>CoCl2(4,4-mbpy)2/1,4-tfib</td>
<td>8.2, 10.9, 19.4</td>
</tr>
<tr>
<td>CoBr2(2,9-mphen)/1,4-tfib</td>
<td>9.0, 11.1, 13.5, 16.0, 17.2, 19.4</td>
</tr>
<tr>
<td>PdCl2(2,9-mphen)/1,4-tfib</td>
<td>6.4, 10.0, 11.1, 13.0, 16.4</td>
</tr>
<tr>
<td>PdCl2(4,4-mbpy)/1,4-tfib</td>
<td>6.8, 8.1, 9.0, 11.9, 13.0, 16.5, 20.3</td>
</tr>
</tbody>
</table>

All of the complexes that formed co-crystals involve ligands with methyl groups, which indicates that the carboxylic acid-containing ligands may be in some way resistant to interacting with 1,4-tfib. This could potentially be because the R2_2(8) COOH homodimer is a more reliable synthon than any that 1,4-tfib or the metal-bound halide can contribute. If this is the case the preferred crystal structure could involve packing that prevents 1,4-tfib from interacting with the metal-bound halogens, as X-bonding should also contribute to a difference in the pxrd pattern. However, as crystal structures of the carboxylic acid-containing complexes were not attained, no definitive reasoning can be made. Although the pxrd indicates that some form of NCI is occurring, it does not provide any way to differentiate whether the complex is performing H-bonding or X-bonding.

IR spectroscopy was also performed, with spectra of relevant co-crystals displayed in Figure 3.37 through Figure 3.41. In these spectra there are clear differences in positions of bands related to functional groups that can undergo H-bonding, mostly in the sub-1700 cm⁻¹ region that corresponds to interactions involving the aromatic regions of the ligands.
Both pxrd and IR measurements of CoCl$_2$(2,9-mphen)/1,4-tfib, CoCl$_2$(4,4-mbpy)$_2$/1,4-tfib, CoBr$_2$(2,9-mphen)/1,4-tfib, PdCl$_2$(2,9-mphen)/1,4-tfib, and PdCl$_2$(4,4-mbpy)/1,4-tfib show evidence of new intermolecular NCIs occurring in the spectra of the co-crystal when compared to the respective metal complex and 1,4-tfib. This is evidence that the mechanochemical synthesis may have been successful in these systems. Although the pxrd pattern itself does not indicate what kind of interactions are occurring, the IR is suggestive of H-bonding involving both the ligand’s functional groups and potentially hydrogens in the aromatic systems. When comparing the pxrd patterns of the metal complex to the respective co-crystal it is apparent that the majority of the peaks associated with the complex have either shifted or disappeared, which implies that the conversion of reactants to products is near 100%.

![Stacked IR plot of CoCl$_2$(2,9-mphen), 1,4-tfib, and CoCl$_2$(2,9-mphen)/1,4-tfib co-crystal](image1)

*Figure 3.37 – Stacked IR plot of CoCl$_2$(2,9-mphen), 1,4-tfib, and CoCl$_2$(2,9-mphen)/1,4-tfib co-crystal*

![Stacked IR plot of CoCl$_2$(4,4-mbpy)$_2$, 1,4-tfib, and CoCl$_2$(4,4-mbpy)$_2$/1,4-tfib co-crystal](image2)

*Figure 3.38 – Stacked IR plot of CoCl$_2$(4,4-mbpy)$_2$, 1,4-tfib, and CoCl$_2$(4,4-mbpy)$_2$/1,4-tfib co-crystal*
Figure 3.39 – Stacked IR plot of CoBr$_2$(2,9-mphen), 1,4-tfib, and CoBr$_2$(2,9-mphen)/1,4-tfib co-crystal

Figure 3.40 – Stacked IR plot of PdCl$_2$(2,9-mphen), 1,4-tfib, and PdCl$_2$(2,9-mphen)/1,4-tfib co-crystal

Figure 3.41 – Stacked IR plots of PdCl$_2$(4,7-mphen), 1,4-tfib, and PdCl$_2$(4,7-mphen)/1,4-tfib co-crystal
3.3 Experimental
3.3.1 Synthesis of MX\(_2\)(bpy/phen)\(_n\) complexes

Reactions were done following literature methods.\(^{129, 142, 144-147}\)

Synthesis of CoCl\(_2\)(bpy/phen)\(_n\) complexes

Synthesis of CoCl\(_2\)(2,9-mphen)

CoCl\(_2\)\(\cdot\)6H\(_2\)O (0.5104 g, 1.45 mmol) and 2,9-mphen (0.603 g, 2.89 mmol) were dissolved in EtOH (20 mL) and stirred at reflux for six hours. The resulting bright blue precipitate was filtered in vacuo. (0.712 g, 65%) Anal. Calcd. For C\(_{14}\)H\(_{12}\)Cl\(_2\)CoN\(_2\): C, 49.74; H, 3.58; N, 8.29. Found: C, 49.98; H, 4.25; N, 7.85. Selected IR \(\nu_{\text{max}}/\text{cm}^{-1}\): 1590, 1568, 1498, 857.

Synthesis of CoCl\(_2\)(4,7-mphen)

4,7-mphen (0.609 g, 2.89 mmol) was dissolved in EtOH (15 mL) and added to a solution of CoCl\(_2\)\(\cdot\)6H\(_2\)O (0.501 g, 1.45 mmol) in EtOH (5 mL). The reaction mixture was heated at reflux overnight. The resulting dark green precipitate was filtered by vacuum filtration. (0.580 g, 58%) Anal. Calcd. For C\(_{14}\)H\(_{12}\)Cl\(_2\)CoN\(_2\): C, 49.74; H, 3.58; N, 8.29. Found: C, 44.45; H, 3.64; N, 7.56. Selected IR \(\nu_{\text{max}}/\text{cm}^{-1}\): 3609, 3551, 1620, 1575, 1521, 1403, 826, 728.

Synthesis of CoCl\(_2\)(4,4- mbpy)\(_2\)

CoCl\(_2\)\(\cdot\)6H\(_2\)O (0.510 g, 3.85 mmol) and 4,4- mbpy (1.059 g, 5.78 mmol) were dissolved in EtOH (20 mL) and stirred at reflux for six hours. The solvent was then removed and ethyl acetate (10 mL) was added and sonicated. The resulting light brown precipitate was filtered by vacuum filtration. (1.253 g, 65%) Anal. Calcd. For C\(_{24}\)H\(_{24}\)Cl\(_2\)CoN\(_4\)O\(_8\): C, 57.85; H, 4.85; N, 11.24. Found: C, 53.94; H, 5.42; N, 9.90. Selected IR \(\nu_{\text{max}}/\text{cm}^{-1}\): 3358, 3027, 1614, 1245, 1037, 829, 518, 419.

Synthesis of CoCl\(_2\)(4,4-cbpy)\(_2\)

4,4-cbpy (0.699 g, 2.89 mmol) was added 1:1 EtOH/DMF (10 mL) and heated to reflux. CoCl\(_2\)\(\cdot\)6H\(_2\)O (0.500 g, 1.49 mmol) was dissolved in EtOH (10 mL) and added to the bipyridine suspension and refluxed overnight. The resulting red-purple precipitate was filtered by vacuum filtration. (1.09 g, 86%) Anal. Calcd. For C\(_{24}\)H\(_{16}\)Cl\(_2\)CoN\(_4\)O\(_8\): C, 46.63; H,
2.61; N, 9.06. Found: C, 45.87; H, 5.42; N, 9.61. Selected IR ν_{max}/cm^{-1}: 3066, 1751, 1620, 1592, 1549, 1420, 1380, 1365, 1227, 680, 666.

Synthesis of CoCl$_2$(6,6-cbpy)

6,6-cbpy (0.710 g, 2.89 mmol) and CoCl$_2$·6H$_2$O (0.501 g, 1.45 mmol) were dissolved in EtOH (20 mL) and stirred at reflux overnight. The resulting purple precipitate was filtered by vacuum filtration. (0.563 g, 44%) Anal. Calcd. For C$_{12}$H$_8$Cl$_2$CoN$_2$O$_4$: C, 38.53; H, 2.16; N, 7.49. Found: C, 38.54; H, 2.85; N, 7.62. Selected IR ν_{max}/cm^{-1}: 3263, 3067, 1714, 1651, 1593, 1418, 1381, 774, 714.
Synthesis of CoBr$_2$(bpy/phen)$_n$ complexes

Reactions were done following literature methods.$^{129, 142, 144-147}$

**Synthesis of CoBr$_2$(2,9-mphen)**

CoBr$_2$·6H$_2$O (0.5104 g, 1.45 mmol) and 2,9-mphen (0.603 g, 2.89 mmol) were dissolved in EtOH (20 mL) and stirred at reflux for six hours. The resulting teal precipitate was filtered by vacuum filtration. (0.712 g, 65%) Anal. Calcd. For C$_{14}$H$_{12}$Br$_2$CoN$_2$: C, 39.38; H, 2.83; N, 6.56. Found: C, 39.36; H, 2.60; N, 6.46. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 1589, 1566, 1499, 1441, 1426, 1375, 1361, 1149, 859, 782, 726.

**Synthesis of CoBr$_2$(4,7-mphen)$_2$**

4,7-mphen (0.609 g, 2.89 mmol) was dissolved in EtOH (15 mL) and added to a solution of CoBr$_2$·6H$_2$O (0.501 g, 1.45 mmol) in EtOH (5 mL). The reaction mixture was heated at reflux overnight. The resulting red brown precipitate was filtered by vacuum filtration. (0.580 g, 58%) Anal. Calcd. For C$_{28}$H$_{24}$Br$_2$CoN$_4$: C, 52.94; H, 3.56; N, 8.82. Found: C, 51.03; H, 3.56; N, 8.19. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 1621, 1574, 1519, 1422, 1233, 1175, 857, 724.

**Synthesis of CoBr$_2$(4,4-mbpy)$_2$**

CoBr$_2$·6H$_2$O (0.510 g, 3.85 mmol) and 4,4-mbpy (1.059 g, 5.78 mmol) were dissolved in EtOH (20 mL) and stirred at reflux for six hours. The solvent was then removed and ethyl acetate (10 mL) was added and sonicated. The resulting brown precipitate was filtered by vacuum filtration. (1.253 g, 65%) Anal. Calcd. For C$_{24}$H$_{24}$Br$_2$CoN$_4$: C, 49.09; H, 4.12; N, 9.54. Found: C, 45.51; H, 4.73; N, 8.10. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3385, 3022, 1615, 1418, 1222, 827.

**Attempted synthesis of CoBr$_2$(4,4-cbpy)**

4,4-cbpy (0.699 g, 2.89 mmol) was added 2:1 EtOH/DMF (15 mL) and heated to reflux. CoBr$_2$·6H$_2$O (0.500 g, 1.49 mmol) was dissolved in EtOH (10 mL) and added to the bipyridine suspension and refluxed overnight. The resulting white precipitate was filtered by vacuum filtration. (1.09 g, 86%) Anal. Calcd. For C$_{24}$H$_{16}$Br$_2$CoN$_4$O$_8$: C, 40.76; H, 2.28; N, 7.92. Found: C, 57.35; H, 2.29; N, 11.02. Analysis suggests that the precipitate is uncomplexed ligand. The reaction was repeated twice with the same result.
Synthesis of CoBr$_2$(6,6-cbpy)$_2$

6,6-cbpy (0.710 g, 2.89 mmol) and CoBr$_2$·6H$_2$O (0.501 g, 1.45 mmol) were dissolved in EtOH (20 mL) and stirred at reflux overnight. The resulting pink precipitate was filtered by vacuum filtration. (0.563 g, 44%) Anal. Calcd. For C$_{24}$H$_{16}$Br$_2$CoN$_4$O$_8$: C, 40.76; H, 2.28; N, 7.92. Found: C, 41.99; H, 2.72; N, 7.45. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3298, 3055, 1694, 1650, 1582, 1419, 1263, 1157, 1079, 832, 761, 713, 593.
Synthesis of PdCl$_2$(bpy/phen) complexes

Reactions were done following literature methods.$^{129, 142, 144-147}$

**Synthesis of PdCl$_2$(2,9-mphen)**

2,9-mphen (0.161 g, 0.7709 mmol) was dissolved in MeCN (10 mL) and added to a solution of PdCl$_2$(MeCN)$_2$ (0.161 g, 0.358 mmol) in MeCN (10 mL). The reaction mixture was stirred at room temperature for 4 hours, then the resulting brown solid was filtered by vacuum filtration. (0.114 g, 83%) Anal. Calcd. For C$_{14}$H$_{12}$Cl$_2$N$_2$Pd: C, 43.61; H, 3.14; N, 7.27. Found: C, 42.77; H, 2.85; N, 9.12. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3060, 2969, 2038, 1614, 1478, 1418, 1379, 1220, 1030, 924, 830, 566, 517, 420. $^1$H NMR (400 MHz, DMF-$d_7$) $\delta$ 8.90 (d, $J$ = 8.3 Hz, 2H), 8.32 (s, 2H), 8.03 (d, $J$ = 8.2 Hz, 2H), 2.94 (s, 6H).

**Synthesis of PdCl$_2$(4,7-mphen)**

4,7-mphen (0.634 g, 3.06 mmol) was dissolved in MeCN (10 mL) and added to a solution of PdCl$_2$(MeCN)$_2$ (0.510 g, 1.530 mmol) in MeCN (10 mL). The reaction mixture was stirred at room temperature for 4 hours, then the resulting light brown solid was filtered by vacuum filtration. (0.631 g, 123%(wet)) Anal. Calcd. For C$_{14}$H$_{12}$Cl$_2$N$_2$Pd: C, 43.61; H, 3.14; N, 7.27. Found: C, 41.38; H, 3.14; N, 7.13. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3568, 3124, 1622, 1578, 1517, 1418, 1375, 1225, 1169, 1028, 844, 711. $^1$H NMR (400 MHz, DMF-$d_7$) $\delta$ 9.35 (d, $J$ = 5.5 Hz, 2H), 8.45 (s, 2H), 8.06 (d, $J$ = 5.7 Hz, 2H), 3.01 (s, 6H).

**Synthesis of PdCl$_2$(4,4-mbpy)**

4,4-mbpy (0.0732 g, 0.358 mmol) was added to a solution of PdCl$_2$(MeCN)$_2$ (0.0980 g, 0.358 mmol) in MeCN (15 mL). The reaction mixture was stirred at room temperature for 4 hours, then the resulting yellow solid was filtered by vacuum filtration. (0.104 g, 75%) Anal. Calcd. For C$_{12}$H$_{12}$Cl$_2$N$_2$Pd: C, 39.86; H, 3.35; N, 7.75. Found: C, 37.33; H, 3.35; N, 7.60. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3060, 2969, 2910, 1614, 1478, 1418, 1220, 1030, 830, 566, 517, 420. $^1$H NMR (400 MHz, DMF-$d_7$) $\delta$ 8.57 (d, $J$ = 4.9 Hz, 2H), 8.30 (s, 2H), 7.30 (d, $J$ = 4.9 Hz, 2H), 2.45 (s, 6H).

**Synthesis of PdCl$_2$(4,4-cbpy)**

4,4-cbpy (0.0493 g, 0.193 mmol) was added to a solution of PdCl$_2$(MeCN)$_2$ (0.0496 g, 0.193 mmol) in MeOH (10 mL). The reaction mixture was stirred at room temperature
for 4 hours, then the resulting yellow solid was filtered by vacuum filtration. (0.0718 g, 88%) Anal. Calcd. For C\textsubscript{12}H\textsubscript{8}Cl\textsubscript{2}N\textsubscript{2}O\textsubscript{4}Pd: C, 34.19; H, 1.91; N, 6.65. Found: C, 33.83; H, 2.33; N, 6.17. Selected IR $\nu_{\text{max}}$/cm\textsuperscript{-1}: 3629, 3391, 3193, 3114, 3077, 2470, 2470, 1865, 1727, 1693, 1558, 1408, 1374, 1270, 1237, 1207, 1069, 810, 760, 661. $^1$H NMR (400 MHz, DMF-$d_7$) $\delta$ 9.52 (d, $J = 5.2$ Hz, 2H), 9.15 (s, 2H), 8.37 (d, $J = 5.7$ Hz, 2H).

**Synthesis of PdCl\textsubscript{2}(6,6-cbpy)**

6,6-cbpy (0.0455 g, 0.193 mmol) was added to a solution of PdCl\textsubscript{2}(MeCN)\textsubscript{2} (0.0516 g, 0.193 mmol) in MeOH (10 mL). The reaction mixture was stirred at room temperature for 4 hours, then the resulting orange solid was filtered by vacuum filtration. (0.0574 g, 71%) Anal. Calcd. For C\textsubscript{12}H\textsubscript{8}Cl\textsubscript{2}N\textsubscript{2}O\textsubscript{4}Pd: C, 34.19; H, 1.91; N, 6.65. Found: C, 35.49; H, 1.86; N, 6.59. Selected IR $\nu_{\text{max}}$/cm\textsuperscript{-1}: 3193, 3061, 2923, 2423, 1742, 1632, 1596, 1404, 1343, 1238, 1182, 1158, 1112, 820, 766, 666. The complex was insufficiently soluble in DMF for $^1$H NMR.
3.3.2 Mechanochemical synthesis of $\text{MX}_2(\text{bpy/phen})_n/1,4$-tfib co-crystals

Synthesis of $\text{CoCl}_2(\text{bpy/phen})_n/1,4$-tfib co-crystals

Synthesis of $\text{CoCl}_2(2,9\text{-mphen})/1,4$-tfib

$\text{CoCl}_2(2,9\text{-mphen})$ (10 mg, 0.029 mmol) and 1,4-tfib (23.77 mg, 0.059 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3358, 3155, 1657, 1615, 1407, 1385, 1128, 865, 799, 731, 623.

Synthesis of $\text{CoCl}_2(4,7\text{-mphen})/1,4$-tfib

$\text{CoCl}_2(4,7\text{-mphen})$ (10 mg, 0.029 mmol) and 1,4-tfib (23.70 mg, 0.059 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3608, 3182, 3112, 2323, 1620, 1576, 1459, 1213, 940, 862, 757.

Synthesis of $\text{CoCl}_2(4,4\text{-mbpy})_2/1,4$-tfib

$\text{CoCl}_2(4,4\text{-mbpy})_2$ (10 mg, 0.020 mmol) and 1,4-tfib (16.12 mg, 0.040 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3357, 3155, 2781, 1656, 1614, 1385, 1127, 732, 615, 524, 416.
Synthesis of CoCl$_2$(4,4-cbpy)$_2$/1,4-tfib

CoCl$_2$(4,4-cbpy)$_2$ (10 mg, 0.016 mmol) and 1,4-tfib (13.00 mg, 0.032 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3065, 2879, 1893, 1721, 1613, 1549, 1460, 1419, 1380, 1284, 1138, 1069, 1012, 940, 758, 666.

Synthesis of CoCl$_2$(6,6-cbpy)/1,4-tfib

CoCl$_2$(6,6-cbpy) (10 mg, 0.027 mmol) and 1,4-tfib (10.70 mg, 0.027 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3263, 3067, 1714, 1651, 1593, 1461, 1440, 1417, 1381, 1084, 940, 758.
Synthesis of CoBr$_2$(bpy/phen)$_n$/1,4-tfib co-crystals

Synthesis of CoBr$_2$(2,9-mphen)/1,4-tfib

CoBr$_2$(2,9-mphen) (10 mg, 0.023 mmol) and 1,4-tfib (9.41 mg, 0.023 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3350, 3186, 1618, 1591, 1457, 1378, 1362, 1151, 938, 857, 783.

Synthesis of CoBr$_2$(4,7-mphen)/1,4-tfib

CoBr$_2$(4,7-mphen) (20 mg, 0.031 mmol) and 1,4-tfib (12.65 mg, 0.031 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3361, 3158, 3035, 1620, 1574, 1519, 1457, 1421, 940, 857, 757, 724.

Synthesis of CoBr$_2$(4,4-mbpy)$_2$/1,4-tfib

CoBr$_2$(4,4-mbpy)$_2$ (10 mg, 0.025 mmol) and 1,4-tfib (9.97 mg, 0.025 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3330, 3054, 1616, 1457, 1247, 1211, 939, 823, 757.

Synthesis of CoBr$_2$(6,6-cbpy)/1,4-tfib

CoBr$_2$(6,6-cbpy) (10 mg, 0.021 mmol) and 1,4-tfib (8.68 mg, 0.021 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3294, 3033, 1694, 1581, 1460, 1419, 1263, 940, 758.
Synthesis of PdCl$_2$(bpy/phen)/1,4-tfib co-crystals

Synthesis of PdCl$_2$(2,9-mphen)/1,4-tfib

PdCl$_2$(2,9-mphen) (10 mg, 0.026 mmol) and 1,4-tfib (10.40 mg, 0.026 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 2326, 1656, 1592, 1459, 939, 855, 758, 547.

Synthesis of PdCl$_2$(4,7-mphen)/1,4-tfib

PdCl$_2$(4,7-mphen) (10 mg, 0.025 mmol) and 1,4-tfib (10.4 mg, 0.025 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 1579, 1519, 1461, 941, 843, 758, 711.

Synthesis of PdCl$_2$(4,4-mbpy)/1,4-tfib

PdCl$_2$(4,4-mbpy) (10 mg, 0.027 mmol) and 1,4-tfib (11.11 mg, 0.027 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 1618, 1461, 1301, 937, 830, 758, 513.

Synthesis of PdCl$_2$(4,4-cbpy)/1,4-tfib

PdCl$_2$(4,4-cbpy) (10 mg, 0.023 mmol) and 1,4-tfib (9.53 mg, 0.023 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3628, 3391, 3192, 2458, 1863, 1728, 1560, 1461, 1207, 940, 758, 661.
Synthesis of PdCl₂(6,6-cbpy)/1,4-tfib

PdCl₂(6,6-cbpy) (10 mg, 0.023 mmol) and 1,4-tfib (9.53 mg, 0.023 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR \( \nu_{\text{max}}/\text{cm}^{-1} \): 3091, 1739, 1634, 1461, 1236, 1182, 941, 758.
3.3.3 Mechanochemical synthesis of MX$_2$(bpy/phen)$_n$/terephthalamide co-crystals

Synthesis of CoCl$_2$(bpy/phen)$_n$/terephthalamide co-crystals

Synthesis of CoCl$_2$(2,9-mphen)/terephthalamide

CoCl$_2$(2,9-mphen) (20 mg, 0.059 mmol) and terephthalamide (19.40 mg, 0.118 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3357, 3154, 1657, 1614, 1510, 1487, 1407, 1386, 1298, 1128, 799, 732, 622.

Synthesis of CoCl$_2$(4,7-mphen)/terephthalamide

CoCl$_2$(4,7-mphen) (20 mg, 0.059 mmol) and terephthalamide (19.40 mg, 0.118 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3360, 3156, 1657, 1617, 1576, 1520, 1407, 1389, 1298, 1235, 1128, 861, 730, 634.

Synthesis of CoCl$_2$(4,4-mbpy)$_2$/terephthalamide

CoCl$_2$(4,4-mbpy)$_2$ (20 mg, 0.040 mmol) and terephthalamide (13.17 mg, 0.080 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3358, 3156, 1658, 1617, 1409, 1385, 1128, 861, 727, 633.
Synthesis of CoCl$_2$(4,4-cbpy)$_2$/terephthalamide

CoCl$_2$(4,4-cbpy)$_2$ (20 mg, 0.032 mmol) and terephthalamide (5.30 mg, 0.064 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3358, 3156, 1658, 1615, 1408, 1384, 1297, 862, 622.

Synthesis of CoCl$_2$(6,6-cbpy)/terephthalamide

CoCl$_2$(6,6-cbpy) (20 mg, 0.053 mmol) and terephthalamide (8.77 mg, 0.053 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. A colour change was observed, with the lilac and white reagents combining to form a pale blue product. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3263, 3067, 1714, 1651, 1593, 1462, 1382, 1277, 941, 774, 714, 595, 522, 437.
Synthesis of CoBr$_2$(bpy/phen)$_n$/terephthalamide co-crystals

Synthesis of CoBr$_2$(2,9-mphen)/terephthalamide

CoBr$_2$(2,9-mphen) (20 mg, 0.049 mmol) and terephthalamide (7.68 mg, 0.049 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3359, 3156, 1656, 1616, 1500, 1407, 1386, 1297, 1150, 858, 727, 680.

Synthesis of CoBr$_2$(4,7-mphen)/terephthalamide

CoBr$_2$(4,7-mphen) (20 mg, 0.031 mmol) and terephthalamide (5.16 mg, 0.031 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3358, 3155, 1658, 1618, 1519, 1421, 1385, 858, 806, 724.

Synthesis of CoBr$_2$(4,4-mbpy)$_2$/terephthalamide

CoBr$_2$(4,4-mbpy)$_2$ (20 mg, 0.049 mmol) and terephthalamide (8.14 mg, 0.049 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3356, 3154, 3067, 1658, 1614, 1407, 1384, 861.

Synthesis of CoBr$_2$(6,6-cbpy)/terephthalamide

CoBr$_2$(6,6-cbpy) (20 mg, 0.043 mmol) and terephthalamide (7.09 mg, 0.043 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3359, 3292, 3156, 1696, 1656, 1618, 1600, 1582, 1410, 1382, 1263, 1158, 761.
Synthesis of PdCl$_2$(bpy/phen)/terephthalamide co-crystals

Synthesis of PdCl$_2$(2,9-mphen)/terephthalamide

PdCl$_2$(2,9-mphen) (20 mg, 0.051 mmol) and terephthalamide (8.51 mg, 0.051 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3356, 3156, 1657, 1388, 1508, 1128, 862, 794, 731, 628.

Synthesis of PdCl$_2$(4,7-mphen)/terephthalamide

PdCl$_2$(4,7-mphen) (20 mg, 0.051 mmol) and terephthalamide (8.51 mg, 0.051 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3357, 3155, 1657, 1387, 1128, 797, 732, 619.

Synthesis of PdCl$_2$(4,4-mbpy)/terephthalamide

PdCl$_2$(4,4-mbpy) (20 mg, 0.055 mmol) and 1,4-tfib (9.08 mg, 0.055 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3357, 3156, 1657, 1613, 1388, 1128, 866, 796, 732, 631, 515, 416.

Synthesis of PdCl$_2$(4,4-cbpy)/terephthalamide

PdCl$_2$(4,4-cbpy) (20 mg, 0.047 mmol) and terephthalamide (7.78 mg, 0.047 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3627, 3359, 3157, 1728, 1657, 1407, 1208, 765, 661.
Synthesis of PdCl$_2$(6,6-cbpy)/terephthalamide

PdCl$_2$(6,6-cbpy) (20 mg, 0.047 mmol) and terephthalamide (7.78 mg, 0.047 mmol) were combined in a 5 mL stainless steel grinding chamber with a 5 mm diameter ball bearing. The mixture was ground with a mixer mill at 10 Hz for one minute, then at 20 Hz for four minutes. No colour change was observed. Selected IR $\nu_{\text{max}}$/cm$^{-1}$: 3359, 3157, 1745, 1654, 1405, 1388, 1237, 1182
### 3.4 X-ray crystallographic tables

<table>
<thead>
<tr>
<th></th>
<th>[PdCl(2,9-mphen)$_2$]/[PdCl$_3$(MeCN)]$^+$</th>
<th>CoBr$_2$(2,9-mphen)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Empirical formula</strong></td>
<td>C$<em>{28}$H$</em>{24}$Cl$<em>4$Pd/C$</em>{2}$H$_{3}$Cl$_3$NPd</td>
<td>C$<em>{14}$H$</em>{12}$Br$_2$CoN$_2$</td>
</tr>
<tr>
<td><strong>Formula weight</strong></td>
<td>812.22</td>
<td>427.01</td>
</tr>
<tr>
<td><strong>Crystal system</strong></td>
<td>monoclinic</td>
<td>monoclinic</td>
</tr>
<tr>
<td><strong>Space group</strong></td>
<td>$P2_1/c$</td>
<td>$P2_1/n$</td>
</tr>
<tr>
<td><strong>a/ Å</strong></td>
<td>12.1869(10)</td>
<td>7.6772(5)</td>
</tr>
<tr>
<td><strong>b/ Å</strong></td>
<td>32.4778(18)</td>
<td>12.1842(9)</td>
</tr>
<tr>
<td><strong>c/ Å</strong></td>
<td>7.8793(5)</td>
<td>17.7248(12)</td>
</tr>
<tr>
<td><strong>α/°</strong></td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td><strong>β/°</strong></td>
<td>91.030(7)</td>
<td>99.910(7)</td>
</tr>
<tr>
<td><strong>γ/°</strong></td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td><strong>V/ Å$^3$</strong></td>
<td>3118.2(4)</td>
<td>1633.2(2)</td>
</tr>
<tr>
<td><strong>Z</strong></td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td><strong>T/K</strong></td>
<td>100.01(10)</td>
<td>100.01(10)</td>
</tr>
<tr>
<td><strong>μ/mm$^{-1}$</strong></td>
<td>1.525</td>
<td>5.931</td>
</tr>
<tr>
<td><strong>Reflections</strong></td>
<td>14972</td>
<td>9156</td>
</tr>
<tr>
<td><strong>Unique reflections</strong></td>
<td>6238 (0.0854)</td>
<td>3463 (0.0702)</td>
</tr>
<tr>
<td>($R_{int}$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>R$_1$ indexes [I&gt;2σ(I)]</strong></td>
<td>0.0821</td>
<td>0.0399</td>
</tr>
<tr>
<td><strong>wR$_2$ [all data]</strong></td>
<td>0.1876</td>
<td>0.0891</td>
</tr>
<tr>
<td></td>
<td>CoCl$_2$(2,9-mphen) (1)</td>
<td>CoCl$_2$(2,9-mphen) (2)</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-------------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td><strong>Empirical formula</strong></td>
<td>C$<em>{14}$H$</em>{12}$Cl$_2$CoN$_2$/$C_2$H$_3$N</td>
<td>C$<em>{14}$H$</em>{12}$Cl$_2$CoN$_2$</td>
</tr>
<tr>
<td><strong>Formula weight</strong></td>
<td>379.15</td>
<td>338.10</td>
</tr>
<tr>
<td><strong>Crystal system</strong></td>
<td>monoclinic</td>
<td>orthorhombic</td>
</tr>
<tr>
<td><strong>Space group</strong></td>
<td>$P2_1/n$</td>
<td>$Pnma$</td>
</tr>
<tr>
<td><strong>a/Å</strong></td>
<td>7.5893(5)</td>
<td>11.160(1)</td>
</tr>
<tr>
<td><strong>b/Å</strong></td>
<td>12.5618(8)</td>
<td>7.3252(5)</td>
</tr>
<tr>
<td><strong>c/Å</strong></td>
<td>17.5605(10)</td>
<td>17.6337(14)</td>
</tr>
<tr>
<td><strong>$\alpha$/°</strong></td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td><strong>$\beta$/°</strong></td>
<td>101.573(6)</td>
<td>90</td>
</tr>
<tr>
<td><strong>$\gamma$/°</strong></td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td><strong>V/Å$^3$</strong></td>
<td>1640.10(18)</td>
<td>1441.5(2)</td>
</tr>
<tr>
<td><strong>Z</strong></td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td><strong>T/K</strong></td>
<td>100.01(10)</td>
<td>100.01(10)</td>
</tr>
<tr>
<td><strong>$\mu$/mm$^{-1}$</strong></td>
<td>1.370</td>
<td>1.547</td>
</tr>
<tr>
<td><strong>Reflections collected</strong></td>
<td>6736</td>
<td>4892</td>
</tr>
<tr>
<td><strong>Unique reflections ($R_{int}$)</strong></td>
<td>3096 (0.0290)</td>
<td>1670 (0.0355)</td>
</tr>
<tr>
<td><strong>$R_1$ indexes [I&gt;=2$\sigma$ (I)]</strong></td>
<td>0.0318</td>
<td>0.0340</td>
</tr>
<tr>
<td><strong>wR$_2$ [all data]</strong></td>
<td>0.0655</td>
<td>0.0982</td>
</tr>
</tbody>
</table>
Chapter 4

4.1 Conclusions

MX\(_2\)(L)\(_2\) complexes (M = Cu(II), Co(II), Mn(II), L = nic, iso, nia) and MX\(_2\)(L)\(_n\) complexes (M = Co(II), Pd(II); L = 2,9-mphen, 4,7-mphen, 4,4-mbpy, 6,6-cbpy; n = 1, 2) were synthesised through conventional methods and characterised via elemental analysis, IR spectroscopy, pxrd and low frequency Raman spectroscopy. Each of the MX\(_2\)(L)\(_2\) complexes were combined mechanochemically with a co-former (1,4-tfib or terephthalamide), and the resultant supposed co-crystal samples were analysed using IR spectroscopy and pxrd. The MX\(_2\)(L)\(_2\)/1,4-tfib series were also analysed using low frequency Raman.

The IR, pxrd and Raman plots were stacked and inspected for new or shifted peaks that suggest the formation of co-crystals. The data set for the first series suggests that six co-crystals were formed, these being: CoCl\(_2\)(nia)\(_2\)/1,4-tfib, CoBr\(_2\)(iso)\(_2\)/1,4-tfib, MnBr\(_2\)(nic)\(_2\)/1,4-tfib, CuBr\(_2\)(nic)/terephthalamide, CuBr\(_2\)(iso)/terephthalamide, and CoCl\(_2\)(nia)/terephthalamide. The data set for the second series suggests that six co-crystals were formed, these being CoCl\(_2\)(2,9-mphen)/1,4-tfib, CoCl\(_2\)(4,4-mbpy)/1,4-tfib, CoBr\(_2\)(2,9-mphen)/1,4-tfib, PdCl\(_2\)(2,9-mphen)/1,4-tfib, and PdCl\(_2\)(4,4-mbpy)/1,4-tfib.

The IR, pxrd, and, where applicable, low frequency Raman results all agree with each other in the cases of co-crystal formation, as well as agreeing when there is no sign of co-crystal formation, which gives credence to the accuracy of this analysis system. Although it is clear which co-crystals formed, it is not obvious why these particular examples were successful when others were not.

Synthesis of X-ray quality single crystals of some of these co-crystals was attempted using liquid diffusion methods, but the metal complexes crystallised alone in all attempts.
4.2 Future work

From this work it seems that the mechanochemical synthesis of such metal containing co-crystals has promise. Some potential future continuations of this work include repeating some of the unsuccessful co-crystal synthesis attempts with a considerably longer grinding time. As this project was largely proof of concept, a short reaction time was chosen to facilitate a larger number of experiments. Most mechanochemical reactions are performed on a 20-30 minute time scale, as opposed to the five minute reaction time used in this work. As in the first series of experiments there does not seem to be a strong preference for a specific metal or ligand in the successful co-crystals, it is possible that simply extending the time scale of the reaction would result in more success.

In the second series the successful co-crystals all include either 2,9-mphen or 4,4-mbpy, with no carboxylic acid containing complexes showing signs of co-crystallisation. There is potential that as 4,4-cbpy and 6,6-cbpy are di-carboxylic acids, polymers could form using R^2_2(8) homodimers. A potential way to avoid this is through the use of ligands with only one carboxylic acid, such as those shown in Figure 4.1, which would only be able to form dimers, and as such might be more amenable to engaging in NCIs with the co-former. However, the synthesis of such ligands would likely be difficult and time consuming.

This work shows that mechanochemical synthesis of co-crystals can be very quick and simple, compared to solvent based cocrystallisation, which is often very time consuming and inefficient.

Figure 4.1 – 2,2’-bipyridine-4-carboxylic acid (left), 2,2’-bipyridine-6-carboxylic acid (right)
References


104. Estevez, V.; Villacampa, M.; Menendez, J. C., Three-component access to pyrroles promoted by the CAN-silver nitrate system under high-speed vibration milling conditions: a generalization of the Hantzsch pyrrole synthesis. Chemical Communications 2013, 49 (6), 591-593.


143. Smolko, L.; Černák, J.; Kuchár, J.; Rajnák, C.; Titiš, J.; Boča, R., Field-Induced Slow Magnetic Relaxation in Mononuclear Tetracoordinate Cobalt(II) Complexes Containing a


