Applications of Small Molecule Crystallography

Xiaoping Wang
Neutron Scattering Science Division
Oak Ridge National Laboratory
Applications of Small Molecule Crystallography

Outline

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• Accurate Molecular Structural Determination
  – Impact on Science
• Structure and Bonding
  – Metal-Metal Multiple Bonds
  – From Small Molecule to Superamolecular Assembly
• Case Studies
  – Gas Adsorption Dynamic in a Meal-Organic Framework
  – Electronic Communications Between Dimetal Centers
  – Effects of Crystallization on Molecular Structure
  – Single Crystal to Single Crystal Chemical Reaction
• Future Directions
  – Single Crystal Crystallography in Higher Dimensions
  – Charge Density
  – Spin Density
  – Time Resolved Diffraction
Small Molecule Crystallography

- **Small molecule**
  A neutral or ionic compound of synthetic or biological origin but it is not a polymer, protein or nucleic acid:
  - Inorganic and Organic Compounds
  - Catalysts
  - Natural Products
  - Pharmaceuticals
  - Synthetic Chemicals

- **Small Molecule Crystallography**
  - Use single crystal X-ray/Neutron diffraction methods to determine the three dimensional structure of small molecules at atomic resolution.

**Chemical Crystallography**
- The relationship between molecular structure and chemical, biochemical or biological properties.
Cambridge Structural Database

Stores data for organic molecules & metal-organic compounds

http://www.ccdc.cam.ac.uk/

Basic Research at CCDC
Mean molecular dimensions
Studies of substituent effects
Statistical and numerical data analysis techniques
Structure correlation and reaction pathways
Conformational analysis
Hydrogen bond geometry and directionality
Weak hydrogen bonds
Nonbonded interactions not mediated by hydrogen
Crystal engineering
Crystallographic symmetry and molecular symmetry

The CSD does not store:
Polypeptides and polysaccharides having more than 24 units.
Protein Data Bank http://www.rcsb.org/pdb/
Oligonucleotides. Nucleic Acids Data Bank http://ndbserver.rutgers.edu/
Inorganic structures
Inorganic Crystal Structure Database http://www.fiz-karlsruhe.de/icsd_content.html
Metals and Alloys CRYSTMET® http://www.tothcanada.com/
Accurate Molecular Structural Determination

- **Impact on Science**
  - 12 Nobel Prizes in chemistry and physiology or medicine awarded for work in the field of crystallography from 1956 to 2006.
  - Almost one in four chemistry prizes since 1956 have been for structure work.  


A critical stance is essential to science. Proving other people wrong is a favorite private and public satisfaction—there is nothing some scientists like better. But, excess zeal discounted, doubt serves as a powerful impulse to the advancement of knowledge. We document it here with the discovery of the structure of ferrocene,

Molecular Structure of Ferrocence

Fe(C₅H₅)₂


*The Nobel Prize in Chemistry 1973*

"for their pioneering work, performed independently, on the chemistry of the organometallic, so called sandwich compounds"

*Bis-cyclopentadienyl Iron, a Molecular Sandwich*

Ferrocene: Ironclad History or Rashomon Tale?**

Pierre Laszlo and Roald Hoffmann*


Peter Pauson, private communication, recalls that he had crystals of ferrocene in the fall of 1951. He was trying to decide whether to ask Jack Dunitz, or the senior organic crystallographer of the time, J. Monteath Robertson (real or adopted Scotsmen all). Pauson decided on Robertson. Who, according to Pauson, took the crystals to...Cornell, where he asked Lynn Hoard if someone could look at them. The crystals were assigned to a beginning graduate student, who failed to solve the structure.
What went on in Wilkinson's and Fischer's labs "was science at its best and most exciting," according to chemistry professor F. Albert Cotton of Texas A&M University. …
In his own recollections article in JOMC, Cotton characterizes Wilkinson and Fischer as two "young but mature chemists" who recognized the implications of a serendipitous discovery and pursued it with imagination and experimental skill.
Applications of Small Molecule Crystallography

Structure and Bonding

The Crystal and Molecular Structure of Dipotassium Octachlorodirhenate(III) Dihydrate, \( \text{K}_2[\text{Re}_2\text{Cl}_8] \cdot 2\text{H}_2\text{O} \)

By F. A. Cotton and C. B. Harris

Received September 22, 1964

Why not \( \text{K}[\text{ReCl}_4] \cdot \text{H}_2\text{O} \)?

Intensity data were collected by the equi-inclination Weissenberg method with Cu K\(\alpha\) radiation ...

Intensities were estimated visually using an intensity wedge prepared by timed exposures of one reflection from the same crystal.

Metal-Metal Multiple Bonds

Metal–Metal Bonding in $[\text{Re}_2\text{X}_3]^{2-}$ Ions and Other Metal Atom Clusters

By F. A. Cotton

Received September 22, 1964

The metal–metal bonding in the $[\text{Re}_2\text{X}_3]^{2-}$ ions is treated by a simple MO method similar to that previously used for other metal atom cluster compounds. A quadruple bond between the rhenium atoms is proposed and it is shown that this accounts for the eclipsed rotameric configuration. The assignment of the absorption spectrum of $[\text{Re}_2\text{Cl}_4]^{2-}$ species is discussed. Finally, the consistency of observed bond lengths with the calculated bond orders for all of the known halo metal atom cluster compounds is demonstrated.


$[\text{Re}_2\text{Cl}_8]^{2-}$

$\sigma^2 \pi^4 \delta^2$
C–H–Metal Interactions in a Tantalum-Neopentylidene Complex

Agostic Interaction

H1–Ta  2.119(4) Å

[Ta(CHCMe₃)(PMe₃)Cl₃]₂

Activation of C-H bond is critical to olefin metathesis.

Molybdenum-alkylidene Complexes

Development of the metathesis method in organic synthesis

Grubbs Catalyst for Olefin Metathesis

1st generation Grubbs
Commercially available

RuCl₂(=CH-p-C₆H₄Cl)(PCy₃)₂


Robert H. Grubbs, Richard R. Schrock and Yves Chauvin
Nobel Prize in Chemistry 2005
Structure of a Terminal Pt(IV)-Oxo Complex

Key intermediates in the photocatalytic oxidation of water to produce molecular oxygen.

Preparation and DFT structure of complex 2.

Room temperature Intramolecular oxo transfer product.

A Ta-Ta Bond without Bridging Ligands?

Preparation of the First Ditantalum(III) Complex Containing a Ta-Ta Bond without Bridging Ligands

Luďmila Scoles, Kamalesh B. P. Ruppa, and Sandro Gambarotta*


Crystal data.
monoclinic \( C2/c \),
\[ a = 48.833(1) \text{ Å} \]
\[ b = 10.960(1) \text{ Å} \]
\[ c = 22.317(1) \text{ Å} \]
\[ \alpha = 95.99(1)° \]

\( \text{Ta–N} \) 2.05(1) to 2.28(1) Å
\( \text{C–C} \) 0.86 to 1.70 Å

\( [(\text{Cy}_2\text{N})_2\text{ClTa}]_2 \)
A Wonderful Bond that Wasn’t There

A Wonderful Bond That Wasn’t There: Reformulation of a Compound “Containing a Ta-Ta Bond without Bridging Ligands” as $[(\text{Cy}_2\text{N})_2\text{ClTa}(\mu-\text{H})]_2$

F. Albert Cotton,*† Lee M. Daniels,† Carlos A. Murillo,*†‡ and Xiaoping Wang†


Crystal data.
monoclinic C2/c,
\[a = 42.234(5) \text{ Å}\]
\[b = 10.804(1) \text{ Å}\]
\[c = 22.765(2) \text{ Å}\]
\[\alpha = 94.702(8)^\circ\]

$[(\text{Cy}_2\text{N})_2\text{ClTa}(\mu-\text{H})]_2$
β-H Abstraction Between Amide Ligands

\[
2\text{Ta(NMe}_2\text{)}_5 + 2\text{H}_2\text{SiR'}\text{Ph} \rightarrow (\text{Me}_2\text{N})_3\text{Ta(H)}\text{I} \text{Ta(NMe}_2\text{)}_3 + 2 \text{HSiR'}\text{Ph} \text{NMe}_2 + \text{HNMe}_2
\]

R' = Me, Ph

Neutron Structure
IPNS SCD
Now at LANSCE

A Side-on Bonded H₂ Ligand - Cubas H₂ Bond

Structure of the first molecular hydrogen complex, W(CO)₃(P-i-Pr)₂(η²-H₂).
Combined refinement of neutron and X-ray data.

Active Site in [NiFe]Hydrogenase Enzymes

Coordination sphere of the S-bridged bimetallic catalytic center.

Model of the Active Site in Hydrogenase -
Dinuclear Ni(μ-H)Ru Complex

Crystal Structure of Chiral Molecules

- **Chiral Linker**
  
  Prepared from hydroquinone and ethyl (S)-lactate

\[
\text{EtO}_2\text{Me triflate} + \text{HO-}[\text{1,4-phenylenebis(oxy)}]_{\text{bis}}(2\text{R})\text{-propanoic acid} \rightarrow \text{K}_2\text{CO}_3 /\text{MeCN}
\]

Anion of 2,2'-[1,4-phenylenebis(oxy)]bis[(2R)-propanoic acid]
Chiral Loops

A double Mobius Strip


Ants on a Mobius strip
by M.C. Escher
Supramolecular Self-Assembly of a Carceplex

Complexes with permanently imprisoned guests


\[
4[cis-Rh_2(DAniF)_2(CH_3CN_{eq})_4(CH_3CN_{ax})_2](BF_4)_2 + 2(NEt_4)_4(calix[4]arene(CO_2)_4)
\]

\[
\{NEt_4\subset[cis-Rh_2(DAniF)_2L]_4(calix[4]arene(CO_2)_4)_2\}BF_4 + 7NEt_4BF_4
\]
Hydrogen Absorption Sites in MOF-5

MOF-5


Zeolitic Imidazolate Framework, ZIF

Cubic
\[ a = 71.9797(4) \, \text{Å} \]
\[ V = 372,932(4) \, \text{Å}^3 \]

ZIF-100

Hybrid Organic-Inorganic Molecular Shuttle

**Functionalized Fluorous MOF**

**Higher Binding Energy**
- H-bonding between H₂ and F atoms

**Control at Molecular Level**
- Gate function

3,5-bis(trifluoromethyl)-1,2,4-triazolate, Tz

\[
\text{Ag}^+ 
\]

\[
\{\text{Ag}_2[\text{Ag}_4\text{Tz}_6]\}_n
\]

Synthesis

Perfluorinated Channels in FMOF-1

[Evacuated Structure]  

\[
\begin{array}{c}
a / \text{Å} \quad 14.0733(5) \\
c / \text{Å} \quad 37.675(3)
\end{array}
\]
### Gas Adsorption Dynamic Processes in FMOF-1

<table>
<thead>
<tr>
<th>Temperature</th>
<th>295 K</th>
<th>119 K</th>
<th>90 K</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_{\text{void}} / V_{\text{cell}}$</td>
<td>43.6%</td>
<td>37.8%</td>
<td>47.3%</td>
</tr>
<tr>
<td>$V_{\text{void(small cage)}} / V_{\text{cell}}$</td>
<td>1.1%</td>
<td>0%</td>
<td>4.1%</td>
</tr>
<tr>
<td>Surface Area $\text{m}^2/\text{cm}^3$</td>
<td>901.1</td>
<td>838.3</td>
<td>1005.0</td>
</tr>
</tbody>
</table>

Filling of the small cavities with $N_2$ initiates the *Negative Thermal Expansion* processes.

Electronic Communication Between Dimetal Units

\[ \text{E}_{1/2} (\text{I}) \quad \text{Mo}_2 \xrightarrow{\text{- e}} \text{Mo}_2 \quad \text{Mo}_2 \xrightarrow{\text{+ e}} \text{Mo}_2 \quad \text{E}_{1/2} (\text{II}) \]

Localized

\[ \text{E}_{1/2} (\text{II}) - \text{E}_{1/2} (\text{I}) : \text{small} \]

Delocalized

\[ \text{E}_{1/2} (\text{II}) - \text{E}_{1/2} (\text{I}) : \text{large} \]


Conformational Effects of Oxamidate Linkers

\[
\begin{array}{c|c|c}
\text{Conformation} & \Delta E_{1/2} & K_C \\
\hline
\alpha & 191 \text{ mV} & 1.7 \times 10^3 \\
\beta & 540 \text{ mV} & 1.3 \times 10^9 \\
\end{array}
\]

[Mo_2(DAniF)_3]_2(AniNC(O)C(O)NAni)
Understanding the Donor-Acceptor Properties

In the α form:
Metal-metal interaction cannot be established by $\delta$ (metal)$-\pi^*$ (Linker) orbital interaction. Intramolecular electron transfer is blocked.

In the β form:
Strong metal-metal interaction is provoked by $\delta$ (metal)$-\pi^*$ (Linker) orbital interaction. The $\delta$ electrons are delocalized over the two dimetal units through the linker.
Chemical Oxidation of 
$\beta\text{-}[\text{Mo}_2(\text{DAniF})_3]_2(\text{N}_2\text{N}'\text{-di-}p\text{-anisyloxamidate})$

$\Delta E_{1/2} = 523 \text{ mV}$
$K_C = 6.9 \times 10^8$

<table>
<thead>
<tr>
<th>State</th>
<th>Mo—Mo bonds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutral</td>
<td>2.0944(4) Å</td>
</tr>
<tr>
<td>Singly oxidized</td>
<td>2.111(1), 2.114(1) Å</td>
</tr>
<tr>
<td>Doubly oxidized</td>
<td>2.1446(8), 2.1418(8) Å</td>
</tr>
</tbody>
</table>

Applications of Small Molecule Crystallography

Single Crystal to Single Crystal Chemical Reaction

From $[\text{Mo}_2\text{(DAniF)}_3]_2(\text{OD})_2$ to $[\text{Mo}_2\text{(DAniF)}_3]_2(\text{O})_2$

Oxidation Reaction in a Single Crystal

Time Dependence of Mo–Mo and Mo–O Distances

Distance (Å)

Time (h)

Mo-O Distances

Mo-Mo Distance
Applications of Small Molecule Crystallography

Unit Cell Transformation

\[ P1, Z=2 \]
\[ a = 14.8324(18) \text{ Å} \]
\[ b = 17.394(2) \text{ Å} \]
\[ c = 17.804(2) \text{ Å} \]
\[ \alpha = 87.946(2)^\circ \]
\[ \beta = 88.125(2)^\circ \]
\[ \gamma = 86.966(2)^\circ \]
\[ V = 4582(1) \text{ Å}^3 \]

\[ P\bar{1}, Z=2 \]
\[ a = 14.661(3) \text{ Å} \]
\[ b = 17.247(3) \text{ Å} \]
\[ c = 17.539(3) \text{ Å} \]
\[ \alpha = 91.456(3)^\circ \]
\[ \beta = 91.093(3)^\circ \]
\[ \gamma = 95.927(3)^\circ \]
\[ V = 4408(2) \text{ Å}^3 \]

t=00 h

\[ (-1, 0, 0, 1, 0, 0, 0, -1) \]

\[ P\bar{1}, Z=2 \]
\[ a = 14.8324(18) \text{ Å} \]
\[ b = 17.394(2) \text{ Å} \]
\[ c = 17.804(2) \text{ Å} \]
\[ \alpha = 92.054(2)^\circ \]
\[ \beta = 88.125(2)^\circ \]
\[ \gamma = 93.034(2)^\circ \]
\[ V = 4582(1) \text{ Å}^3 \]

t=312 h
Effects of Crystallization on Molecular Structure

Can crystal structure determine molecular structure? For $\text{Co}_3(\text{dpa})_4\text{Cl}_2$, yes

F. Albert Cotton, Carlos A. Murillo and Xiaoping Wang

(s-$\text{Co}_3(\text{dpa})_4\text{Cl}_2$·$\text{CH}_2\text{Cl}_2$)

Cl(1) — Co(1) — Co(2) — Co(1A) — Cl(1A)
2.4881(8) 2.3369(4) 2.3369(4) 2.4881(8) Å

(μ-$\text{Co}_3(\text{dpa})_4\text{Cl}_2$·2$\text{CH}_2\text{Cl}_2$)

Cl(1) — Co(1) — Co(2) — Co(3) — Cl(2)
2.434(2) 2.299(1) 2.471(1) 2.363(2) Å

Magnetic Property of $u$-Co$_3$(dpa)$_4$Cl$_2$·2CH$_2$Cl$_2$

$\chi = \frac{1}{3}(2\chi_\perp + \chi_\parallel)$

Spin Crossover $S = 1/2$ To $S = 3/2$

Going Beyond Three Dimensional Space

\[ q = 0.125a^* + 0b^* + 0c^* \]

Aperiodic Crystals

\[
\text{H}_2\text{N}\rightleftharpoons\text{C} \rightleftharpoons \text{NH}_2 \quad \text{C}_{19}\text{D}_{40}
\]

urea-\(d_4\) \hspace{1cm} \text{nonadecane-}d_{40}

Symmetry Breaking in Superspace

A molecular solid can change from one structure to another in a way that can only be described properly using four-dimensional space.

\[ G_{hkln} = h\mathbf{a}^* + kb^* + l\mathbf{c}_{\text{host}}^* + m\mathbf{c}_{\text{guest}}^* \]

Applications of Small Molecule Crystallography

**Charge Density Analysis**

- **X-Ray Intensity**
- **Theory**

**Geometry**

**Bonding?**

**Electron Density**

*Deformation density*

*Topological analysis*

[Charge Density]

**Chemical Bonding**

**Molecular Property**

**Intermolecular Interaction**

Research Facilities - Synchrotron Sources

ChemMatCARS (15-ID) at APS, Argonne National Laboratory

Very high-energy synchrotron radiation ~6 to 32 KeV
  ➢ Extinction-free diffraction

Use of much smaller crystals
Beam size 80 to 500 μm
  ➢ Minimize extinction and absorption

Low temperature Liquid Helium cryostat T = 15-70 K
  ➢ Reduced ADPs
Research Facilities – Neutron Sources

Light atom positions
Magenetic structure
Magnetic spin density w/ polarized neutrons

TOPAZ at SNS

Pulsed Neutron
Neutron time of flight
Laue technique
3-D Reciprocal space mapping (x, y, λ)
Cooperative Features in a Bioactive Molecule

Static deformation-density map for salicylic acid.

Bond-paths (BCP) along the hydrogen bonds

Laplacian distribution of the O–H···O hydrogen bonds.

Spin-Density Distribution in \( \text{K}_2\text{FeCl}_5 \cdot \text{H}_2\text{O} \)

Polarized Neutron Diffraction

\( \text{D23 at ILL} \)

High Spin Fe(III)

Color Projection of the spin-density fit in the plane containing the Fe–O–H–Cl–Fe pathway from the multipole expansion approach.

Time Resolved Diffraction

Reversible Molecular excitation
Irreversible (Photo)-initiated chemical reaction

Supramolecular Time-resolved diffraction

Ground State Excited State

Contraction of the Cu–Cu distance in the $[\text{Cu(NH}_3\text{)}_2]^2+$ ion (from 3.02 to 2.72 Å)

Pulsed laser-excitation (532 nm) at 17 K
A triplet excited state lifetime of 4.2 ms
Pause repeat frequency at 12 kHz.

$[\text{Cu(NH}_3\text{)}_2][\text{THPE}]_2\cdot3.25\text{H}_2\text{O}$

Science at TOPAZ

Single Molecule Magnets:
Supramolecular Dimers of Mn4 \([\text{[Mn}_4\text{Pr}_2\cdot\text{MeCN (NA}_{3}\text{)]}]\): Example of exchange-biased Quantum Tunnelling of Magnetization

\[ Yb_{14}\text{MnSb}_{11} \]
Ferromagnet regarded as a rare example of an underscreened Kondo lattice. \((T_C = 53 \text{ K})\)
Tetragonal with space group \(I4_1/acd\)
1 Mn atom
4 inequivalent Sb atoms
2 Sb (2) involved in Mn-Sb tetrahedra

\[ \rightarrow \text{maximum entropy magnetization density reconstruction reveals the presence of a magnetic moment on the Sb site with opposite sign with respect to the Mn moment} \]

Garlea, et al. ACNS 2005, Phensant Run, IL.

Diffuse Scattering:
Structure modulations in Benzil exhibit diffuse scattering patterns

Welberry et al., J. Appl. Cryst., 2003

Terminal hydrogen or water on the Pt in the Late-Transition Metal-Oxo Complex, \(O=\text{Pt(H}_2\text{O})L\rightarrow L = [\text{PW}_9\text{O}_{34}]^{9-}\)
Interesting catalyst

-> Large unit cell [29x32x38]
-> High H content
-> Disordered lattice water

Welberry et al., J. Appl. Cryst., 2003

OAK RIDGE NATIONAL LABORATORY
Single crystal diffractometer, TOPAZ