Making Sense of the Different Modes of Supramolecular Association Occurring in Molecular Crystals

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Research Centre for Crystalline Materials

Sunway Group
1974: tin-mining
Plantation/Property and Construction, Health, Leisure, Education, Travel and Hospitality

Fortuna Eruditis Favet ("Fortune favours the prepared mind")

Crystals?

Why do crystals form?
How do crystals form?

Crystal Engineering
Determine how Molecules pack
Design specific architectures
Optimise for applications
Intermolecular Interactions

Well known, understood and utilised...

Hydrogen-bonding (HB)

\[ \delta^+ \cdot \delta^- \]

\[ \text{D-H} \cdot \cdot \cdot \text{A} \]

Alloxan

Neutron diffraction: 45 K

2-fold symmetry

\( P4_22_2 \)

Bifurcated: N-O = 3.15 & 3.22 Å

\( \text{cf. } \Sigma_{vdW} = 3.07 \AA \)

Alloxan

Phase change < 35 K: \( P2_12_12_1 \)

No symmetry

N-O = 3.11 & 2.99 Å

\( \text{cf. } \Sigma_{vdW} = 3.07 \AA \)
**Alloxan**

Neutron diffraction: 45 K

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The importance of global molecular packing
...most organic molecules feature hydrogen atoms at the periphery and so that C–H⋅⋅⋅X interactions are inevitable.

Cambridge Structural Database

Prevalence of Space Group Adoption

CSD: 865,342 entries

<table>
<thead>
<tr>
<th>Space Group</th>
<th>Entries</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>P2_1/c</td>
<td>279041</td>
<td>34.5</td>
</tr>
<tr>
<td>P1</td>
<td>198014</td>
<td>24.7</td>
</tr>
<tr>
<td>C2/c</td>
<td>67434</td>
<td>8.4</td>
</tr>
<tr>
<td>P2_1_2_1</td>
<td>58438</td>
<td>7.2</td>
</tr>
<tr>
<td>P2_1</td>
<td>41791</td>
<td>5.2</td>
</tr>
<tr>
<td>Pbca</td>
<td>26951</td>
<td>3.3</td>
</tr>
</tbody>
</table>

Six close-packing SG's account for >83% of structures

“Egg Causality Dilemma”
"Hydrogen Bonding and Co-crystal Technology"

Designer crystal: intermolecular interactions, network structures and supramolecular synthons

Gustave R. Desiraju
School of Chemistry, University of Hyderabad, Hyderabad 500 046, India

Speculations relating to the prediction of the second structures of crystals of a given organic molecule from some partially resolved (and often) stereoisomeric analogs seem to indicate that information on the prediction of second (higher) order structures may be used to focus efforts in such hypothesis testing.

Co-crystals: Non-covalent derivatisation

[Diagram of molecular structure]

33%

(C=O)OH…N(py)

Reliable

98% formation in the absence of competition

"Caveat"

Systematic analysis of the probabilities of formation of biomolecular hydrogen-bonded ring motifs in organic crystal structures

Frank H. Allen*,† M. D. Samuel Sheldrick*, Paul R. Batts†, Gregory P. Almehdi* and Binod Paudel

* Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, UK CB3 1FS.
† University of Cambridge, Pembroke College, Cambridge, CB2 3BS

Received in Cambridge, UK 15th September 1998, Accepted 5th November 1998

A methodology has been developed for the prediction of hydrogen-bonded ring motifs formed between the organic molecules within crystal packs knowledge of the (hyper)local arrangement of the motif. The methodology has been applied to predict the organic crystallographic ring motifs in the Cambridge Crystallographic Database (CCDC) by using the known structural models of 1203 organic molecules. The probabilities of occurrence of the motif are predicted by the methodology and the results are listed in Table 1. The probabilities provide insight into the formation of hydrogen bonds in organic molecules.
450 structures with RCO$_2$H and DMF
200 have hydrogen bonding between RCO$_2$H and DMF
40% probability

**Intermolecular Interactions**

Well known...

Hydrogen-bonding (HB)
Halogen-bonding (HB)

Odd Hassel (1897 – 1981)

**Halogen-bonding**

Halogen-bond acceptor
Nucleophilic

Electrophilic

Anisotropic

R

X

δ$^+$

δ$^-$
**Intermolecular Interactions**

Well known...

Hydrogen-bonding (HB)

Halogen-bonding (HB)

\[
\delta^+ \Delta \text{H} \quad \delta^+ \Delta \text{X}
\]

(HB): Similar in energy = 5 - 15 kcal/mol

**ChemComm**

COMMUNICATION

Halogen bonding effects on the outcome of reactions at metal centres

Lucio Carbone, Dick Benet, Michael A. A. Anderson, Antonio Fantozzi, Anthony Frassetto, Peter J. O. A. van Leeuwen, and Andrea Vidal-Araujo

**Molecular packing**

Well known...

Hydrogen bonding

Halogen bonding

"Emerging"

Secondary bonding

M-M interactions

M-H interactions

Interactions involving chelate rings

**α-hole**

Halogen bonding

Chalcogen bonding

Pnicogen bonding

Tetrel bonding

Aerogen bonding

Clark, T.; Hennemann, M.; Murray, J. S.; Politzer, P.


...favorable noncovalent interaction between a covalently bonded atom of Group 18 (known as noble gases or aerogens) and a negative site, for example, a lone pair of a Lewis base or an anion.
Repackaging:

Tetrel, pnictogen and chalcogen bonds

Electrophilic sites from Groups 14, 15 & 16, resp.
Steric Effects and Secondary Bonding

\[ \text{Steric Effects and Secondary Bonding} \]

\[ "\text{Hg(S}_2\text{CN})_2\text{R}_2" \]

Sum of the van der Waals radii for Hg and S = 3.35 Å

increasing size of R
Systematic analysis of $R_3Sn(O_2CR')$

$R$ solution $^{117}Sn$ solid-state

Cy -8.5 23.7
Me 24.7 148.1

$Me_3Sn(O_2CR'')$

Tetrel Bonding: Energy

$T = C, Si, Ge & Sn$

$n = 0$ 0.9 kcal/mol
$n = 1^*$ 6 – 9 kcal/mol
$SnF_4$ 25.5 kcal/mol

Gold Chemistry

Competition between

i) Au-Au and hydrogen-bonding

Comparable in energy to HB

Polymorphs of (dppm)(AuCl)$_2$


Intermolecular Au-$\pi$-arene interactions

PLATON output:

<table>
<thead>
<tr>
<th>Deprotonated (D)</th>
<th>Hydrogen Bonding (HB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(D)</td>
<td>(HB)</td>
</tr>
<tr>
<td>Au…Au</td>
<td>Au…Au</td>
</tr>
<tr>
<td>Au…π(arene)</td>
<td>Au…π(arene)</td>
</tr>
</tbody>
</table>

Intermolecular Au…π(arene) interactions

0-D

1-D

PLATON output:

The sum of the van de Waals radii = 1.66 + 1.85 = 3.51 Å

Intermolecular Au…π(arene) interactions

0-D

1-D

Gold Chemistry

Competition between
i) Au…Au and hydrogen bonding
ii) Au…Au and Au…π(arene)

(HB)$^2$: Similar in energy = 5 - 15 kcal/mol

Intermolecular M(lp)…π(arene) interactions

"Menšutkin complexes"
**Intermolecular M(lp) π(arene) interactions**

![Chemistry: Fundamentals, Frontiers and Applications (2008) Chp. 3](image1)

**Chem. Commun. 47 (2011) 7608.**

**Biology?**

![Energy?](image2)

**ChemComm**

**COMMUNICATION**

On the nature of the stabilisation of the E-π pnicogen bond in the SbCl₃-π-toluene complex

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Energy (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SbCl₃ + C₆H₅</td>
<td>7.7</td>
</tr>
<tr>
<td>SbCl₃ + C₆H₅Me</td>
<td>9.6</td>
</tr>
<tr>
<td>SbCl₃ + C₆Me₅</td>
<td>15.5</td>
</tr>
</tbody>
</table>

**π-Systems in Supramolecular Chemistry**

**Classic π-systems/interactions**

face-to-face  edge-to-face

**π-Systems in Supramolecular Chemistry**

**TM Chelate π-systems/interactions**

Snezana Zarić  face-to-face  edge-to-face

\( \pi(\text{chelate}) \cdots \pi(\text{chelate}) \text{ interactions} \)


\[ \pi(\text{chelate}) \cdots \pi(\text{arene}) \approx 6 \text{ kcal/mol} \]

\[ \pi(\text{chelate}) \cdots \pi(\text{chelate}) \approx 9 \text{ kcal/mol} \]

**Main group arene-\(H\)–\(\pi\)(chelate) interactions**

\[ \text{C–H} \cdots \pi(\text{chelate}) \approx 15 \text{ kcal/mol} \]

**C–H–\(\pi\)(chelate) interactions:**

\[ \text{Pd–S} \]

\[ 16 \text{ kcal/mol} \]

\[ \text{C–H} \cdots \pi(\text{chelate}) \]

\[ 15 \text{ kcal/mol} \]
Family of Intermolecular Interactions

- H·B: 6-15 kcal/mol
- Hal·B: 6-15 kcal/mol up to 12 kcal/mol
- M·M: 6-15 kcal/mol
- M·π: up to 12 kcal/mol
- M(lp)·π: up to 15 kcal/mol
- C·H·π(chel): up to 15 kcal/mol
- π(chel)·π: up to 9 kcal/mol

"Where are we..."

More to supramolecular life than (HB)²
"Emerging" interactions are competitive
Global molecular packing

www.asca2019.org