Halogen bonding as a supramolecular dynamics catalyst
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Introduction

- The solid state is far from static. Molecules can exhibit several degrees of freedom in the form of dynamics, having important implications in: rotating catalysts, molecular gyroscopes, CO2 adsorption, molecular machines, and diseased enzymes.
- Halogen bonding has recently gained widespread attention as an attractive non-covalent interaction between the electrophilic region of a halogen, named the \( \sigma \)-hole (see Figure 1), and a Lewis base. Applications include crystal engineering, and supramolecular chemistry, to name a few.

Figure 1. Calculated electrostatic potential map of molecular iodine (I\(_2\)), with the \( \sigma \)-hole indicated in blue. The color legend is shown on the bottom.

- Despite the importance of dynamics in chemistry, little is known on the influence of non-covalent interactions on dynamics.
- Here, we investigate the impact of the halogen bond on the rotating methyl groups of 2,3,5,6-tetramethylpyrazine (TMP, Figure 2) using \( ^2\)H solid-state NMR experiments and spin-lattice (\( T_1 \)) relaxation time measurements. DFT calculations have been performed to support the experimental results.

Figure 2. General halogen bonding motif used in this study, featuring 2,3,5,6-tetramethylpyrazine (TMP). The rotation of the methyl groups on TMP (highlighted in blue) is investigated. R denotes the substituent, either C or I.

Crystal Structures

- Figure 3. Depiction of the X-ray crystal structures and molecular structures of the halogen bonded cocrystals (1-3), hydrogen bonded cocrystals (4, 5), pure starting material (6), hydrochloride salt (7), and hydrobromide salt (8). The arrows denote close contacts between the protons of the methyl groups and nearby atoms.
- The influence of the halogen bond is compared to the hydrogen bond, and nearby Cl\(^-\) / Br\(^-\) anions (HCl / HBr salt).

Experimental Results

- Table 1. Methyl group rotational energy for compounds 1 to 8 (see Figure 3).

<table>
<thead>
<tr>
<th>Sample</th>
<th>Rotational Energy (kJ mol(^{-1}))</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.84 ± 0.14</td>
<td>halogen bonded</td>
</tr>
<tr>
<td>2</td>
<td>3.24 ± 0.13</td>
<td>halogen bonded</td>
</tr>
<tr>
<td>3</td>
<td>3.62 ± 0.13</td>
<td>halogen bonded</td>
</tr>
<tr>
<td>4</td>
<td>4.17 ± 0.09</td>
<td>hydrogen bonded</td>
</tr>
<tr>
<td>5</td>
<td>5.02 ± 0.06</td>
<td>hydrogen bonded</td>
</tr>
<tr>
<td>6</td>
<td>6.31 ± 0.17</td>
<td>pure TMP</td>
</tr>
<tr>
<td>7</td>
<td>6.81 ± 0.16</td>
<td>HCl salt</td>
</tr>
<tr>
<td>8</td>
<td>13.64 ± 0.45</td>
<td>HBr salt</td>
</tr>
</tbody>
</table>

- A significant reduction in the methyl rotational energy in TMP was observed in the halogen bonded cocrystals, surpassing the reduction observed in the hydrogen bonded cocrystal. The halogen bond acts as a dynamics catalyst.
- The mere presence of a nearby halogen (HCl / HBr salts) did not have the same reduction, highlighting the role of the halogen bond.
- DFT calculations attribute the superior catalytic effect of the halogen bond to an electrostatic interaction occurring between the methyl groups and the \( \sigma \)-hole, stabilizing the rotation.

Conclusions

- We report the first instance of the halogen bond acting as a supramolecular dynamics catalyst, surpassing the abilities of the hydrogen bond.
- This effect may provide a strategy for improving molecular machines and correcting diseased enzymes.

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References