**Supporting Information**

# Cocrystals of nutraceutical *p*-coumaric acid with caffeine and theophylline: polymorphism and solid-state stability explored in detail using their crystal graphs

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**Figure 1.** XRPD of *p*-coumaric acid:caffeine cocrystal, **1**

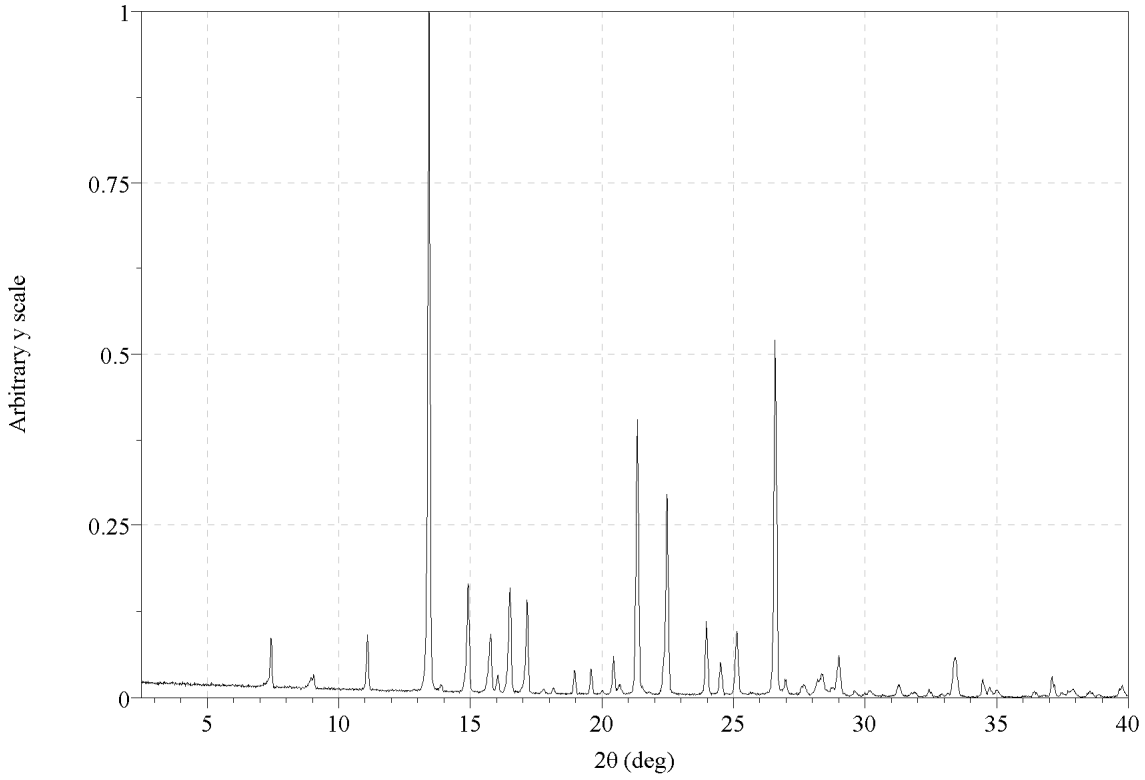

**Figure 2.** XRPD of *p*-coumaric acid:caffeine cocrystal, **2**

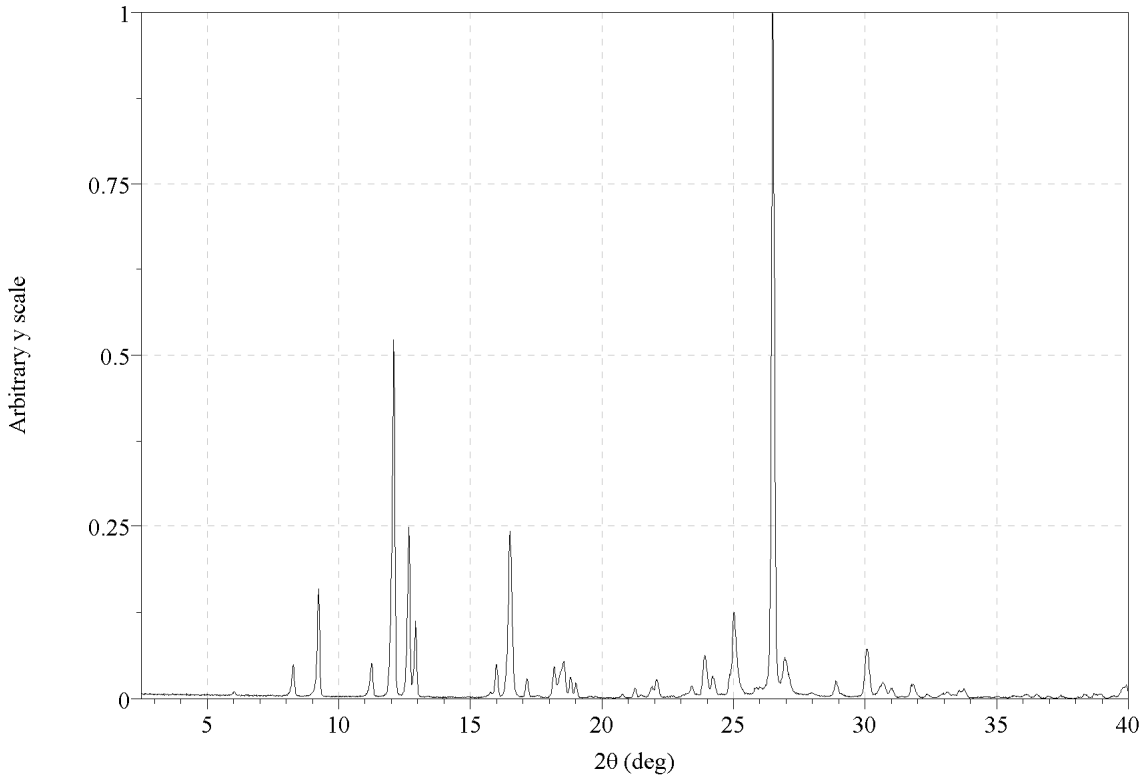

**Figure 3.** XRPD of *p*-coumaric acid:theophylline cocrystal, **3** (Form I)

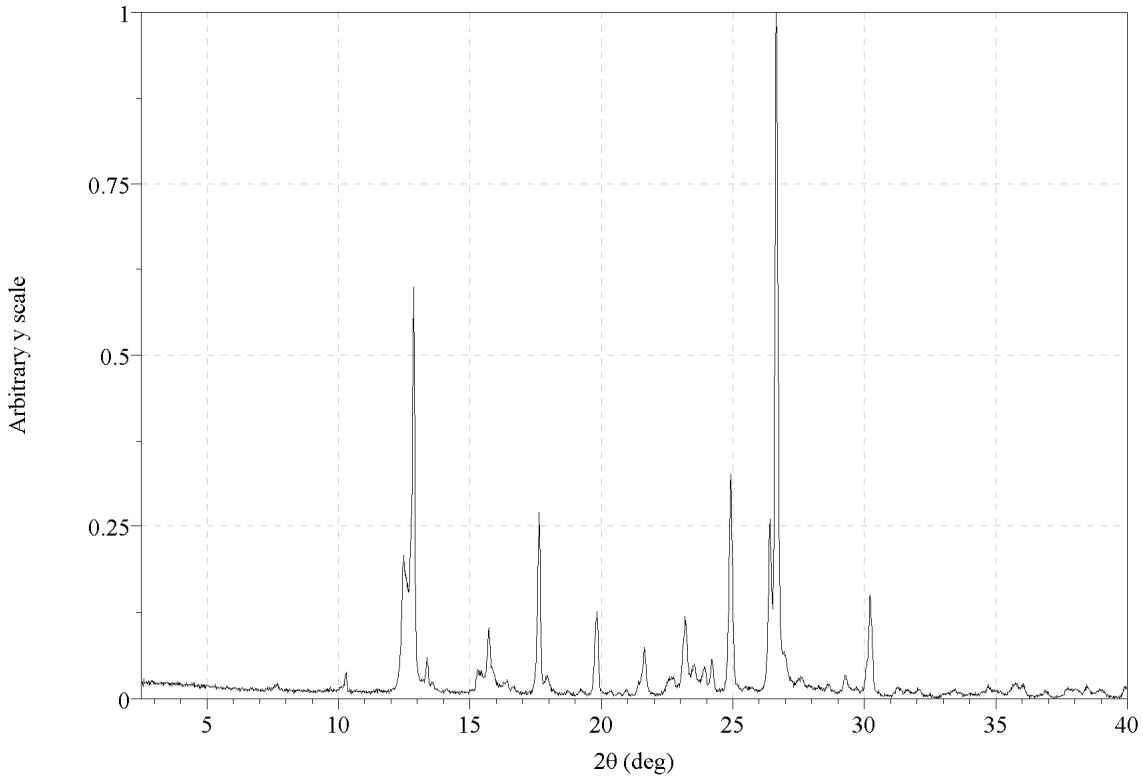

**Figure 4.** XRPD of *p*-coumaric acid:theophylline cocrystal, **4** (Form II)

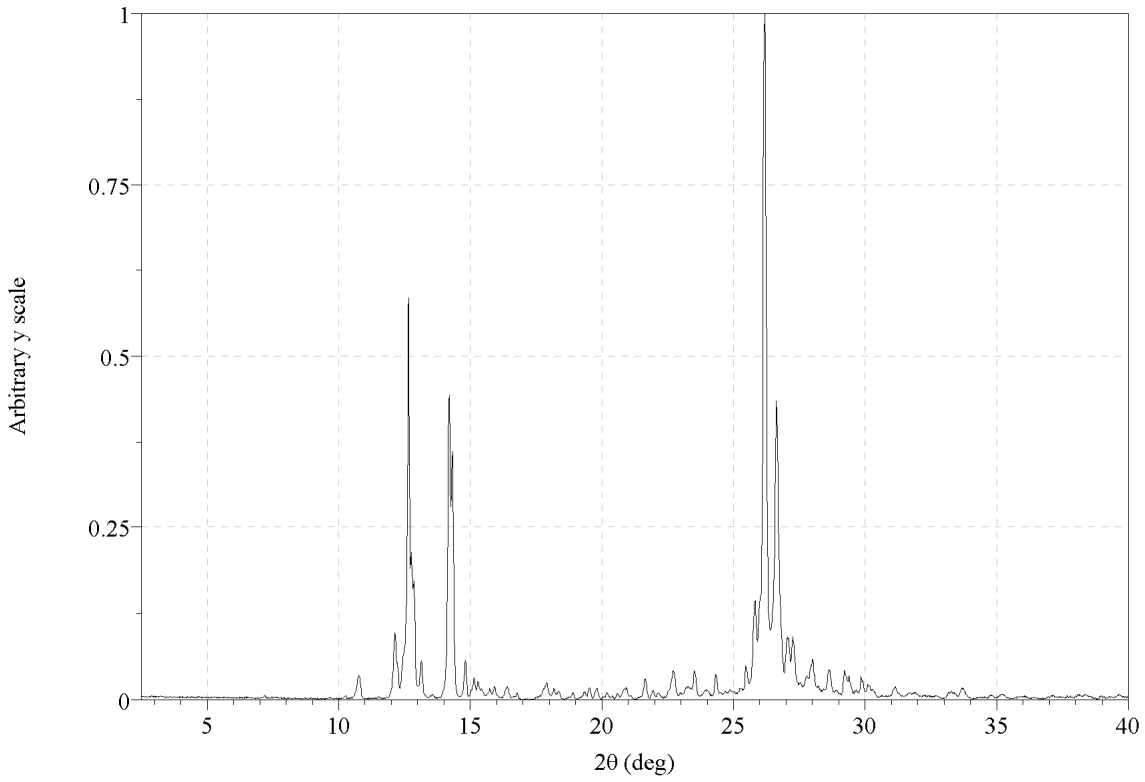

**Figure 5.** DSC and TGA overlay of **1**

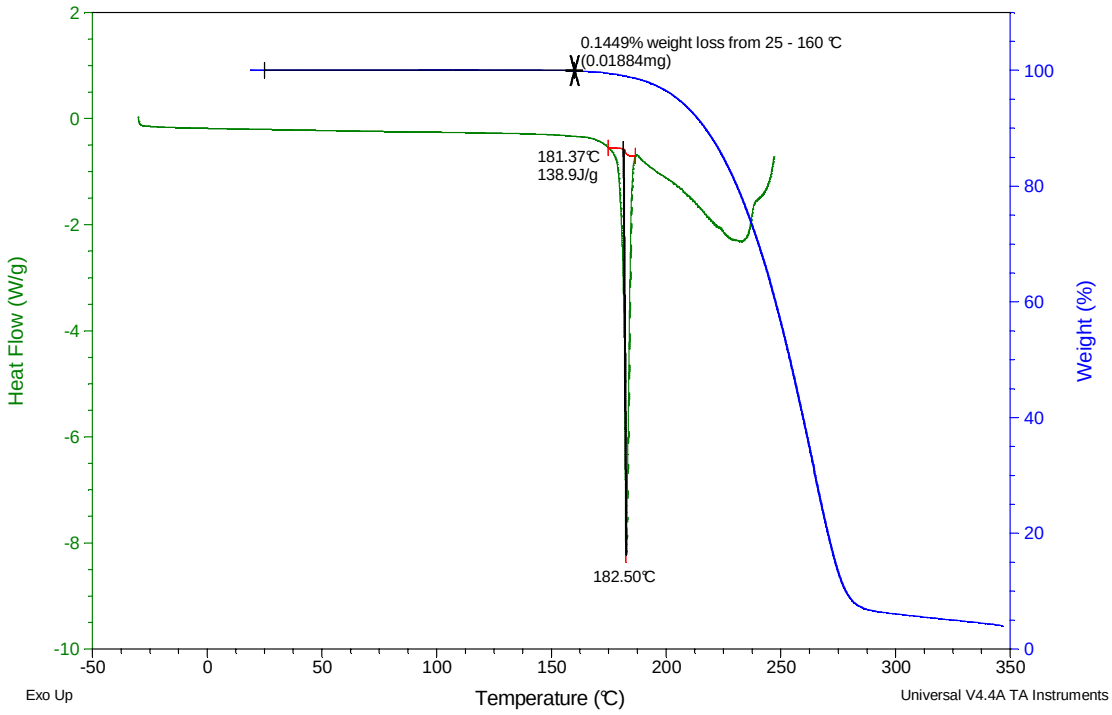

**Figure 6.** DSC and TGA overlay of **2**

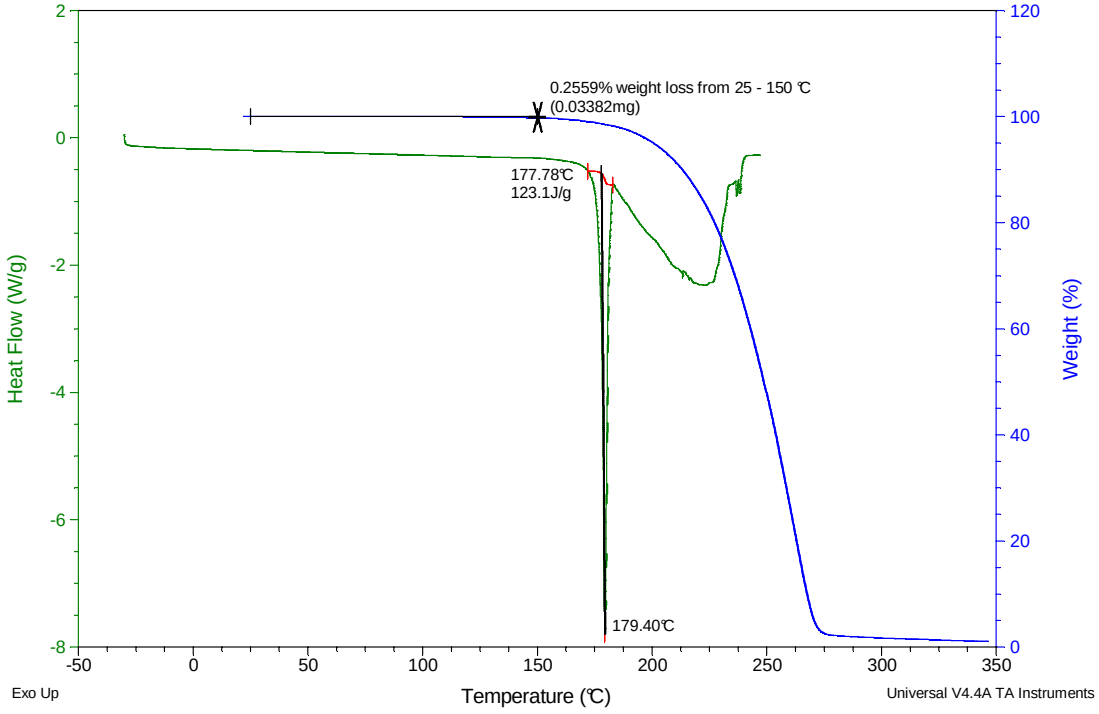

**Figure 7.** DSC and TGA overlay of **3** (Form I)

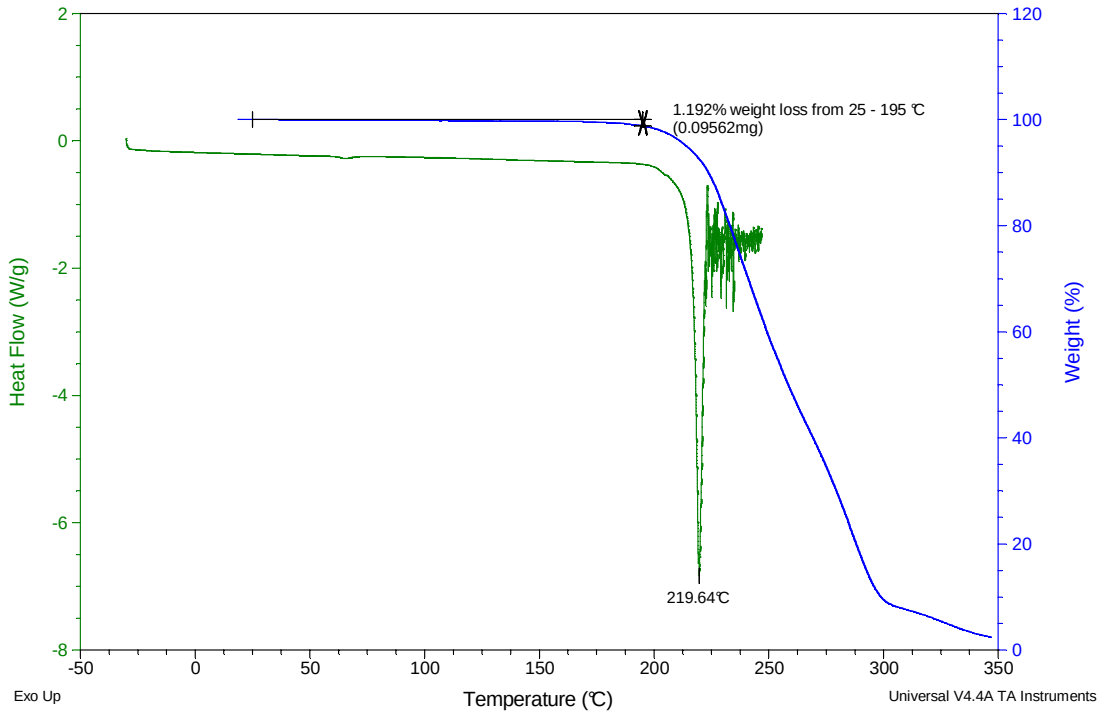

**Figure 8.** DSC and TGA overlay of **4** (Form II)

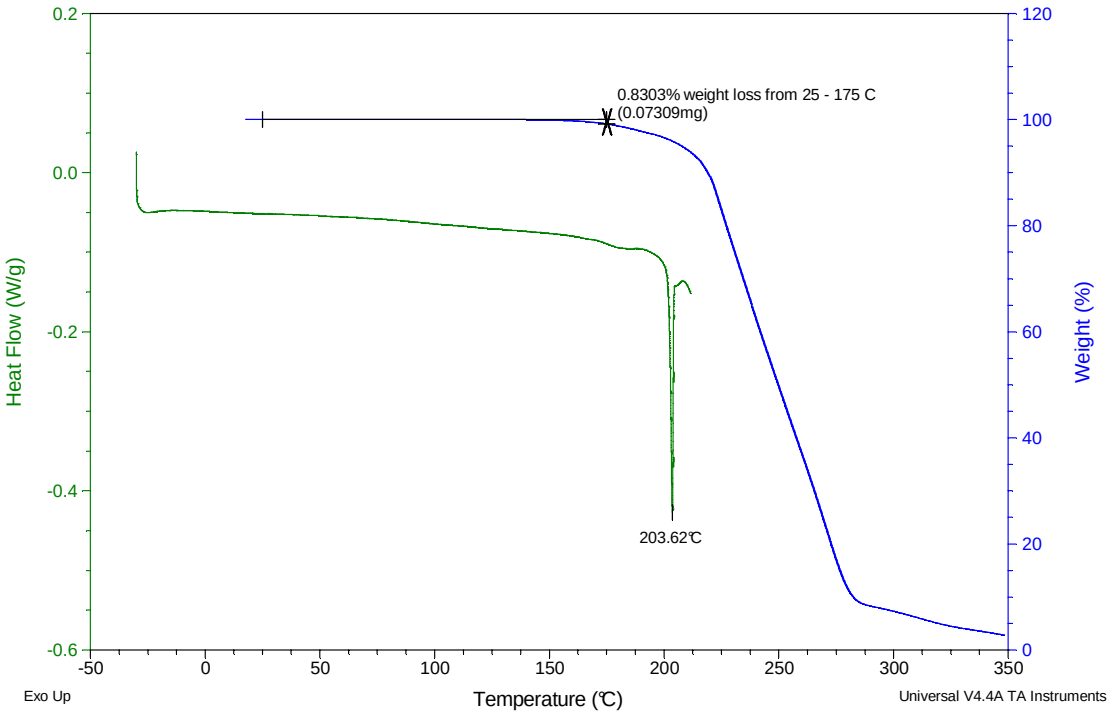

**Figure 9**. Example of inter-layer molecular interaction. This is the strongest interaction, found in Form II, with a strength of −10.529 kcal/mol. The molecule in the top layer is represented by a stick model, whereas the bottom molecule is represented by a CPK model. Partial atomic charges, as produced by the COMPASS force field are shown for the top molecule. The charges for the bottom molecule are related by inversion symmetry therefore having the same charges. The atoms at minimal distance generate atomic Coulomb energies for the pairs with the following atomic charges (each pair occurring twice): −0.500 ··· +0.485, +0.532··· −0.239, −0.334···0.064. The total Coulomb interaction energy is −1.533 kcal/mol, whereas the Van der Waals energy is −8.996 kcal/mol. This interaction clearly does not exhibit any π···π stacking contribution. This shows that the inter-layer interactions are still mostly due to dispersion forces.

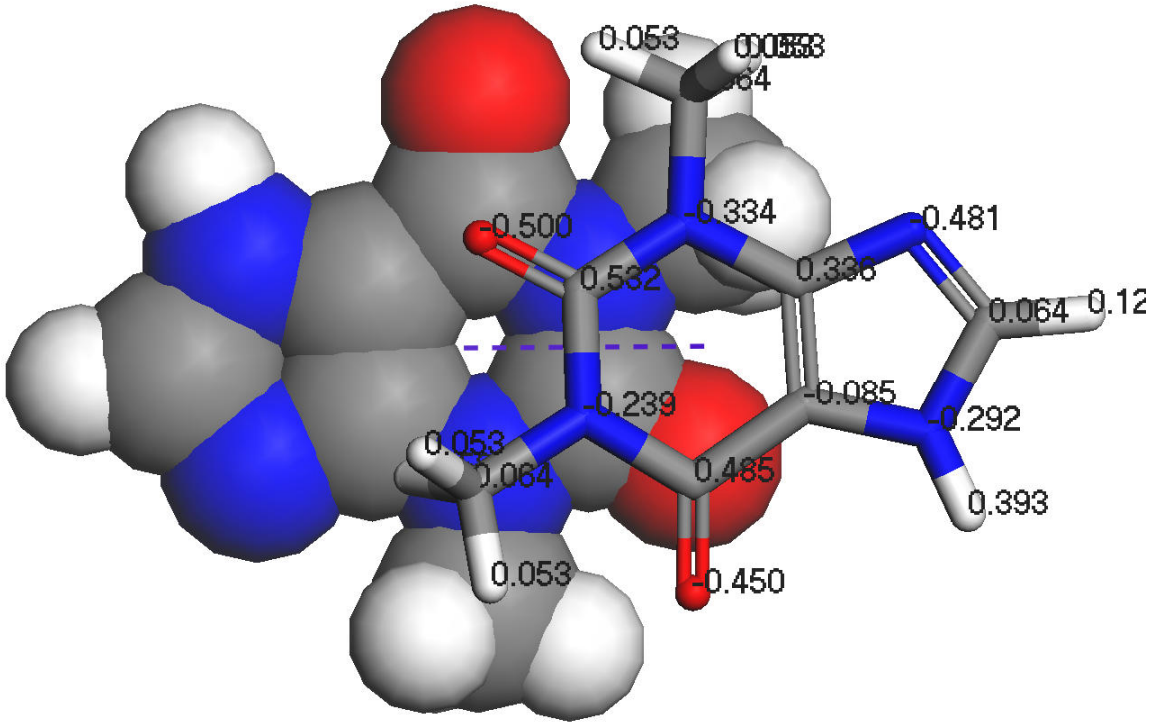

**Table 1**. Crystal graph for Form I at the default bond cutoff of −0.596 kcal/mol.

**key**

| Number | Molecule | Reference Coordinate[1] |
|---|---|---|
| 1 | C7 H8 N4 O2 | (0.0221497, 0.574097, 0.729905) |
| 2 | C7 H8 N4 O2 | (0.589332, 0.0899427, 0.867573) |
| 3 | C7 H8 N4 O2 | (0.410668, 0.9100573, 0.13243) |
| 4 | C7 H8 N4 O2 | (0.9778503, 0.425903, 0.270095) |
| 5 | C9 H8 O3 | (0.499478, 0.420611, 0.293522) |
| 6 | C9 H8 O3 | (0.164907, 0.941541, 0.398635) |
| 7 | C9 H8 O3 | (0.500522, 0.579389, 0.706478) |
| 8 | C9 H8 O3 | (0.835093, 0.0584591, 0.601365) |

**interactions**

| Molecule 1 | Molecule 2 | Translation[2] | Multiplicity[3] | Length (Å)[4] | Energy (kcal/mol) |
|---|---|---|---|---|---|
| 1 | 5 | [-1 0 0] | 2 | 8.75699 | -13.0476 |
| 2 | 6 | [0 -1 0] | 2 | 8.75689 | -12.7897 |
| 2 | 3 | [0 -1 1] | 1 | 4.23979 | -10.5289 |
| 1 | 7 | [-1 0 0] | 2 | 4.05232 | -9.37448 |
| 1 | 5 | [0 0 1] | 2 | 9.00814 | -8.54775 |
| 2 | 6 | [1 -1 1] | 2 | 8.97188 | -8.45311 |
| 2 | 8 | [0 0 0] | 2 | 4.34486 | -7.63309 |
| 1 | 7 | [0 0 0] | 2 | 3.67814 | -7.27969 |
| 6 | 8 | [0 1 0] | 1 | 6.74735 | -4.95618 |
| 6 | 1 | [0 0 0] | 2 | 6.18964 | -4.43241 |
| 5 | 7 | [0 0 0] | 1 | 7.08201 | -4.18584 |
| 2 | 7 | [0 0 0] | 2 | 6.65223 | -4.13371 |
| 6 | 4 | [-1 1 0] | 2 | 6.62399 | -4.10297 |
| 2 | 8 | [-1 0 0] | 2 | 7.40349 | -4.09185 |
| 5 | 7 | [0 0 -1] | 1 | 8.34279 | -3.81668 |
| 2 | 1 | [0 0 0] | 2 | 7.59937 | -3.50016 |
| 2 | 3 | [1 -1 1] | 1 | 7.55594 | -3.24017 |

[1] The reference coordinate represents the position of the molecule in the unit cell, in fractional coordinates, by its center of mass.
[2] The translation to a neighbouring unit cell in which molecule 2 is located.
[3] Space group symmetry applies to the interactions. Multiplicity is the number of occurrences of the interaction in the unit cell.
[4] Length is the distance between reference points.

| | | | | | |
|---|---|---|---|---|---|
| 1 | 4 | [-1 0 0] | 1 | 7.70752 | -2.92737 |
| 6 | 4 | [-1 0 0] | 2 | 8.33562 | -2.18623 |
| 2 | 7 | [0 -1 0] | 2 | 8.33297 | -2.13929 |
| 6 | 8 | [-1 1 0] | 1 | 4.34183 | -2.09630 |
| 6 | 7 | [0 0 0] | 2 | 6.31560 | -1.93940 |
| 2 | 5 | [0 0 1] | 2 | 8.79523 | -1.69596 |
| 2 | 5 | [0 0 0] | 2 | 8.52143 | -1.57281 |
| 5 | 7 | [1 0 0] | 1 | 11.0010 | -1.47991 |
| 6 | 5 | [0 1 0] | 2 | 7.22027 | -1.44556 |
| 2 | 1 | [1 0 0] | 2 | 7.61871 | -1.25770 |
| 1 | 4 | [-1 0 1] | 1 | 7.66426 | -1.18557 |
| 2 | 4 | [0 0 1] | 2 | 9.43033 | -0.988586 |
| 6 | 5 | [-1 1 0] | 2 | 7.93649 | -0.861979 |
| 6 | 1 | [1 0 0] | 2 | 8.87328 | -0.853893 |
| 2 | 1 | [1 -1 0] | 2 | 8.41860 | -0.840349 |
| 2 | 1 | [0 -1 0] | 2 | 9.64668 | -0.786347 |
| 1 | 5 | [0 0 0] | 2 | 7.88932 | -0.747859 |
| 2 | 4 | [0 0 0] | 2 | 9.20499 | -0.711493 |
| 6 | 5 | [0 0 0] | 2 | 8.08576 | -0.694136 |
| 6 | 6 | [-1 0 0] | 2 | 7.70166 | -0.662726 |
| 6 | 8 | [-1 1 -1] | 1 | 11.9018 | -0.648548 |
| 2 | 4 | [0 -1 1] | 2 | 9.93399 | -0.637214 |
| 1 | 1 | [-1 0 0] | 2 | 7.70166 | -0.615454 |
| 2 | 2 | [-1 0 0] | 2 | 7.70166 | -0.613198 |

**Table 2**. Crystal graph for Form II at the default bond cutoff of −0.596 kcal/mol.

**key**

| Number | Molecule | Reference Coordinate |
|---|---|---|
| 1 | C7 H8 N4 O2 | (0.195864, 0.665954, 0.907673) |
| 2 | C7 H8 N4 O2 | (0.695864, 0.834046, 0.407673) |
| 3 | C7 H8 N4 O2 | (0.804136, 0.334046, 0.09233) |
| 4 | C7 H8 N4 O2 | (0.304136, 0.165954, 0.59233) |
| 5 | C9 H8 O3 | (0.246106, 0.424849, 0.216406) |
| 6 | C9 H8 O3 | (0.253894, 0.924849, 0.283594) |
| 7 | C9 H8 O3 | (0.753894, 0.575151, 0.783594) |
| 8 | C9 H8 O3 | (0.746106, 0.075151, 0.716406) |

**interactions**

| Molecule 1 | Molecule 2 | Translation | Multiplicity | Length (Å) | Energy (kcal/mol) |
|---|---|---|---|---|---|
| 1 | 5 | [0 0 0] | 4 | 8.77147 | -13.1050 |
| 1 | 6 | [0 0 0] | 4 | 8.74081 | -7.11590 |
| 1 | 7 | [-1 0 0] | 4 | 3.82655 | -7.04750 |
| 1 | 7 | [0 0 0] | 4 | 4.82726 | -6.51352 |
| 5 | 7 | [0 0 0] | 2 | 6.68224 | -6.12720 |
| 5 | 7 | [-1 0 0] | 2 | 7.64219 | -4.23363 |
| 1 | 2 | [-1 0 0] | 4 | 6.60999 | -4.13485 |
| 1 | 5 | [0 0 1] | 4 | 6.83216 | -2.75957 |
| 1 | 1 | [0 0 -1] | 4 | 8.70347 | -2.21550 |
| 5 | 7 | [-1 0 -1] | 2 | 5.97089 | -2.15436 |
| 1 | 7 | [-1 0 -1] | 4 | 9.89452 | -2.07529 |
| 1 | 6 | [0 0 1] | 4 | 7.49143 | -2.03350 |
| 1 | 7 | [0 0 1] | 4 | 8.12411 | -1.75621 |
| 1 | 2 | [-1 0 1] | 4 | 7.51421 | -1.70961 |
| 5 | 5 | [0 0 -1] | 4 | 8.70347 | -1.01598 |
| 1 | 3 | [0 0 1] | 2 | 9.61863 | -0.785475 |
| 5 | 7 | [0 0 -1] | 2 | 6.88794 | -0.707682 |
| 1 | 1 | [-1 0 0] | 4 | 6.87812 | -0.677421 |