Supplementary information for:

Bilirubin and its Crystal Forms

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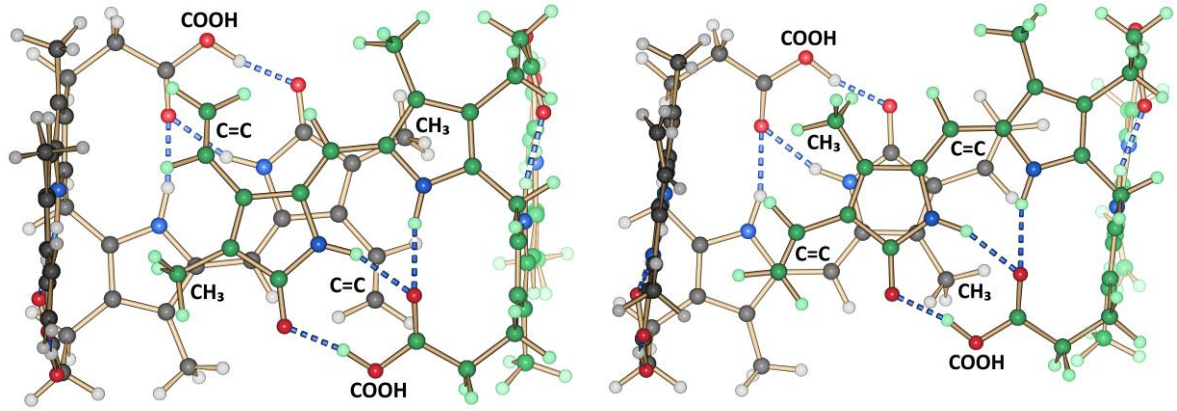

(a) In Forms **I**, **II** and **III**. (b) In Form **II** only

Fig. S1. The two orientations in the most stable molecule…molecule interaction (region 1 in Figure 7) in the three forms of bilirubin. The orientation shown in (a) is common to all three forms, with the distance between centres of mass of the interacting molecules ranging from around 7.60 to 7.94 Å, and the interaction energy ranging from -86 to -102 kJ/mol. In this orientation, the vinyl groups (C=C) of both molecules overlap the carboxylic acid (COOH) of the neighbouring molecule. The orientation shown in (b) is only found in Form **II**, where the methyl groups of both molecules overlap the carboxylic acid (COOH) of the neighbouring molecule. The distance between centres of mass of the interacting molecules ranges from around 8.3 to 8.4 Å, and the interaction energy ranges from -69 to -79 kJ/mol. Both orientations are between molecules that are related by a crystallographic centre of symmetry.

Table S1. The most significant molecule...molecule energies, which are more stable than 20 kJ/mol, calculated with *CLP-PIXEL* are presented for Form **I**, **II**, and **III**. Additionally, the symmetry between the interacting molecules and the breakdown of the energies contributing to the interaction are listed. For detailed explanations of these numbers, see references A. Gavezzotti, *J. Phys. Chem. B*., 2003, **107**, 2344– 2353 and J. Bernstein, J. D. Dunitz and A. Gavezzotti, *Crystal Growth & Design*, 2008, **8**, 2011–2018.

Symmetry (molecule pair)	*PIXEL* (Total) (kJ/mol)	*PIXEL* (Coulombic)	*PIXEL* (Polarization)	*PIXEL* (Dispersion)	*PIXEL* (Repulsion)	Distance (Å)
Form **I**						
-x, 1-y, 2-z	-102.6	-31.1	-12.7	-144.3	85.5	7.8
1-x, 1-y, 1-z	-100.4	-36.2	-17.9	-153	106.7	7.6
+x, -1+y, +z	-69.0	-21.5	-10	-101.1	63.6	9.2
+x, 1+y, +z	-69.0	-21.5	-10	-101.1	63.6	9.2
+x, +y, +z	-65.7	-23	-9.8	-88.3	55.4	8.1
1-x, -y, 1-z	-29.1	-7.9	-2.8	-39.2	20.8	11.6
-x,2-y, 2-z	-28.3	-9.4	-3.5	-35	19.5	11.3
-x, 1-y, 1-z	-25.9	-11.8	-4.9	-23.2	14.1	11.1
Form **II** (orientation 1a; see Figure 7 and S1a)						
1-x, 1-y, -z	-102.1	-32.7	-13.1	-149.8	93.4	7.8
1-x, 1-y, 1-z	-79.4	-10	-7.1	-109.6	47.2	8.3
+x, 1+y, +z	-68.6	-24.6	-12.6	-113.3	81.9	8.9
+x, -1+y, +z	-68.6	-24.6	-12.6	-113.3	81.9	8.9
+x, +y, +z	-62.9	-24.2	-11.3	-95.1	67.7	8.0
2-x, 1-y, 1-z	-41.8	-22.4	-11.1	-54.1	45.7	9.3
1-x, -y, 1-z	-29.2	-5.1	-1.8	-37.8	15.6	11.1
1-x, 2-y, -z	-28.3	-13.4	-6.4	-38.2	29.7	11.1
-x, 1-y, -z	-23.9	-9.6	-3.9	-21.7	11.3	11.1
Form **II** (orientation 1b; see Figure 7 and S1b)						
1-x, 1-y, -z	-98.4	-32.6	-12.9	-146.1	93.3	7.8
+x, 1+y, +z	-69.8	-22.6	-10.5	-107.5	70.8	8.9
+x, -1+y, +z	-69.8	-22.6	-10.5	-107.5	70.8	8.9
1-x, 1-y, 1-z	-69.2	-23.3	-11	-127	92	8.4
+x, +y, +z	-62.2	-24.3	-11.3	-94.4	67.8	8.1
2-x, 1-y, 1-z	-50.1	-30.8	-12.4	-57.6	50.8	9.0
1-x, 2-y, -z	-28.8	-13.1	-6.2	-38.4	28.9	11.1
1-x, -y, 1-z	-27.2	-15.7	-8.1	-41.4	38	11.1
-x, 1-y, -z	-23.9	-9.6	-4	-21.7	11.3	11.1
Form **III** (G. Le Bas, A. Allegret, Y. Mauguen, C. De Rango and M. Bailly, *Acta Crystallogr. B.*, 1980, **36**, 3007–3011.)						
2-x, 1-y, 1-z	-86.6	-28.9	-15	-139.5	96.7	7.9
1-x, 1-y, -z	-74.3	-24.5	-12.9	-107.4	70.6	9.3
1-x, 1-y, 1-z	-60.9	-13.6	-11.5	-86.1	50.2	8.0
2-x, 1-y, -z	-28.0	-9.5	-3.7	-34.1	19.4	11.7
+x, -1+y, +z	-14.3	-1.8	-2	-16.2	5.7	12.0
+x, 1+y, +z	-14.3	-1.8	-2	-16.2	5.7	12.0