

Synthon polymorphism and pseudopolymorphism in co-crystals. The 4,4'-bipyridine – 4-hydroxybenzoic acid structural landscape.

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1. Experimental and Computational Details

The two compounds (4,4'-bipyridine and 4-hydroxybenzoic acid) were taken together in a 1:1 molar ratio and ground with methanol according to the solvent drop grinding method. The powder obtained was dissolved in methanol. Nice plate shaped (Form **1**) and block shaped crystals (Form **2**) of 1:2 4,4'-bipyridine : 4-hydroxybenzoic acid were obtained concomitantly after three days. The same result was also observed when isopropanol was used instead of methanol. A 1:2 ratio of 4,4'-bipyridine and 4-hydroxybenzoic acid was also tried but the result was the same. A 2:1 co-crystal of the two compounds (pseudopolymorph, Form **3**) was obtained concomitantly with Form **2** from DMSO when the compounds were taken in a 1:1 molar ratio. The same 2:1 co-crystal was also obtained from a 2:1 ratio of the starting compounds in methanol. X-Ray Data were collected on a Rigaku Mercury375R/MCCD (XtaLABmini) diffractometer with a graphite monochromator using Mo K α radiation ($\lambda = 0.7 \text{ \AA}^0$), attached with a Rigaku low temperature gas spray cooler. The data were processed with the Rigaku CrystalClear software.¹ Structure solution and refinement were carried out using SHELX97² incorporated in the WinGXsuite.³ All non-hydrogen atoms were refined anisotropically. Aromatic hydrogens were generated using a riding model keeping sof and U_{ij} fixed with U_{iso}= 1.2 U_{eq}(C). Hydroxyl group hydrogens were generated using a riding model on idealised geometry taking the torsion angles from the electron density map and keeping sof and u_{ij} fixed with U_{iso}=1.5 U_{eq}(O). The structure of Form **3** was solved with Sir2008 incorporated in the ilmilione-2.2.0 suite⁴ and refined with SHELXL. DSC was recorded on a Mettler Toledo DSC 823e instrument with a step size of 10 °C/min within a range from 25 to 250 °C. DSC experiments were performed with both the forms (Form **1** and Form **2**) of the co-crystals after separating them manually. The hot stage microscopy (50 °C till melting) was performed on a Wagner & Munz hot stage microscope. The geometry optimization was carried out using the SMART algorithm with rigid groups within Forcite module incorporated in Accelrys Materials Studio. The maximum number of iterations used was equal to 500. Lattice energy calculations were performed using the Dreiding force field. Electrostatic and van der Waals terms were calculated by the Ewald summation method whereas the hydrogen bond terms were calculated with an atom based summation method.

1. (a) CrystalClear 2.0; Rigaku Corporation: Tokyo, Japan. (b) J. W. Pflugrath, *Acta Crystallogr., Sect. D*, 1999, **55**, 1718–1725.
2. G. M. Sheldrick, *Acta Cryst A*, 2008, **A64**, 112-122.
3. L. J. Farrugia, *J. Appl. Cryst.*, 1999, **32**, 837-838.
4. M. C. Burla, R.Caliandro, M. Camalli, B. Carrozzini, G. L. Cascarano, L. De Caro, C. Giacovazzo, G. Polidori, D. Siliqi, R. Spagna, *J. Appl. Cryst.*, 2007, **40**, 609-613.

2. HSM Images

Form 1

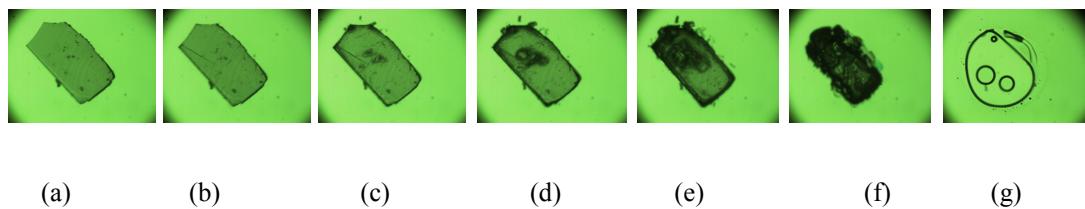


Fig. S1 HSM images of Form 1 at (a) 70 °C, (b) 150 °C, (c) 170 °C, (d) 180 °C, (e) 190 °C, (f) 210 °C, (g) 223.8 °C.

Form 2

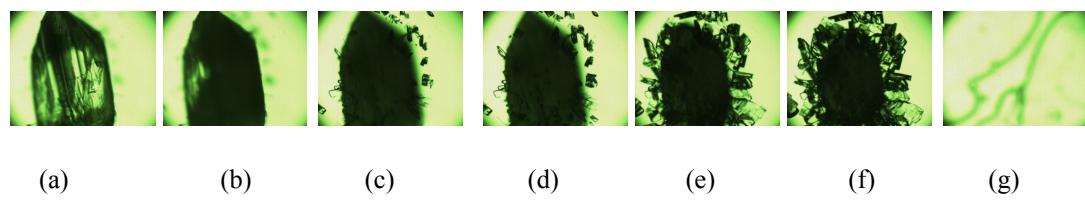
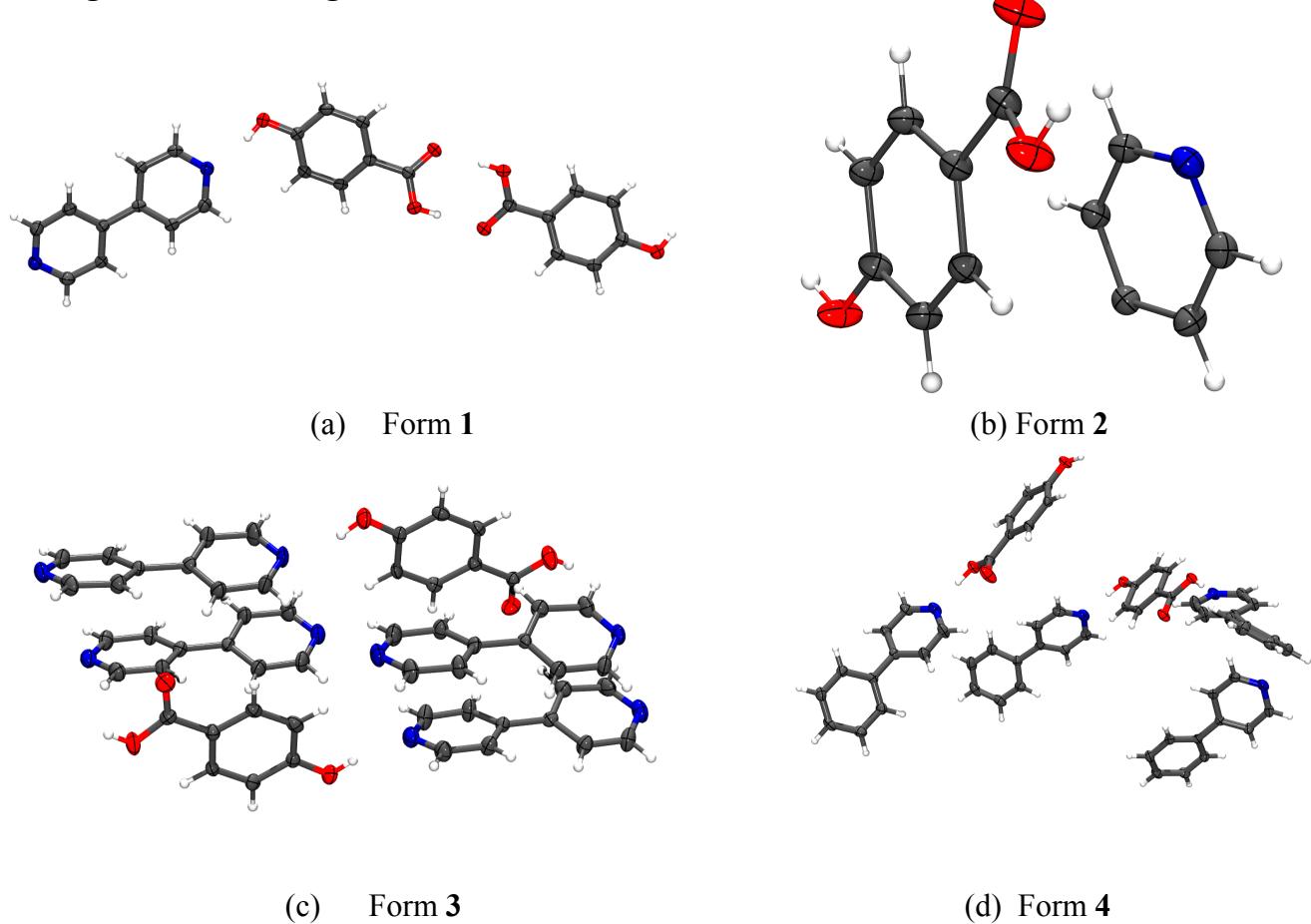


Fig. S2 HSM images of Form 2 at (a) 150 °C, (b) 170 °C, (c) 180 °C, (d) 190 °C, (e) 210 °C, (f) 220 °C, (g) 227 °C

3. Fig. S3 ORTEP Diagrams



4. Comparison between Form 3 and Form 4

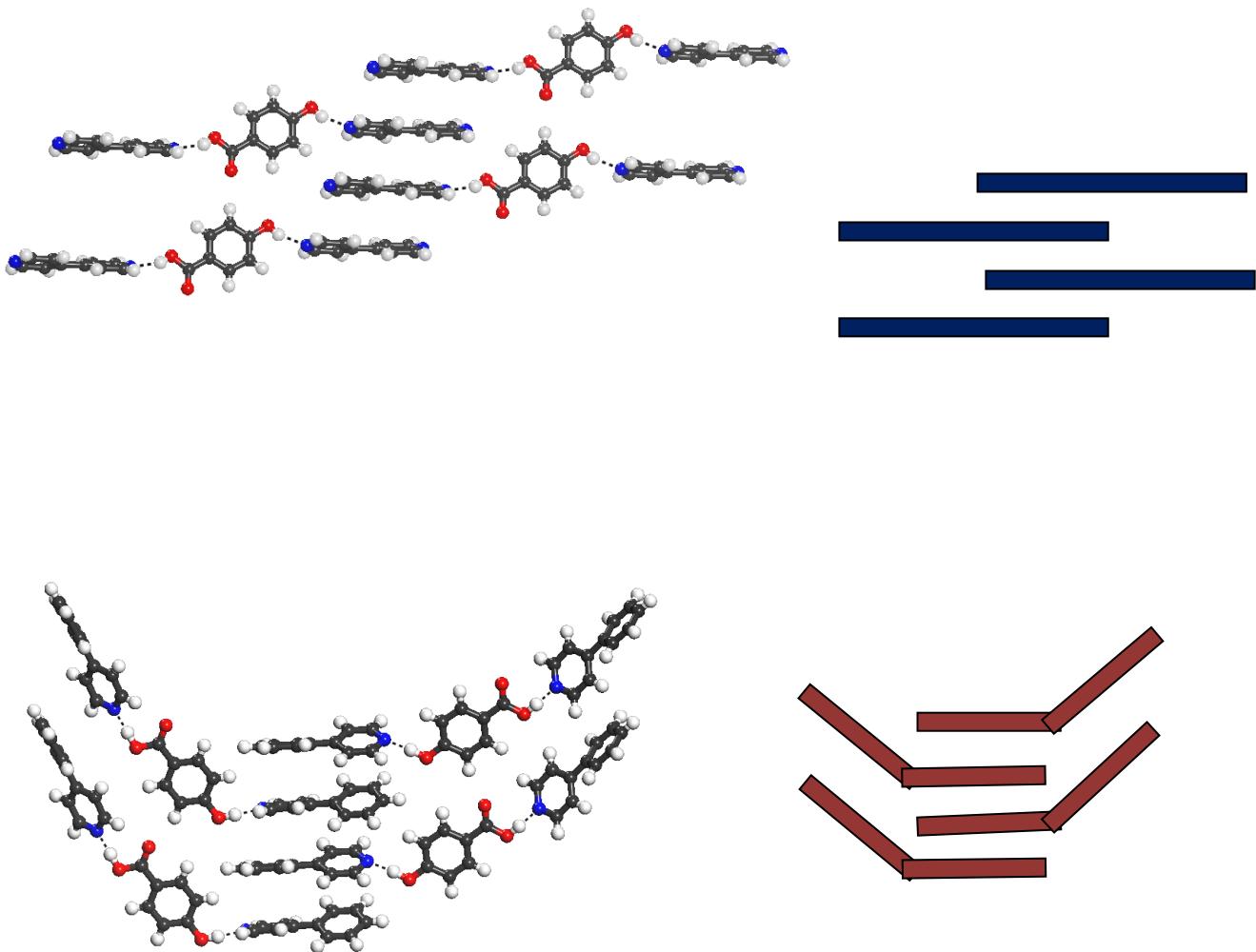


Fig. S4 Structural comparison between Form 3 and Form 4 shows a similarity which motivates us to include Form 4 in the expanded structural landscape.

5. Insertion of 4, 4'-bipyridine in 4-hydroxybenzoic acid native structure to give Form 2

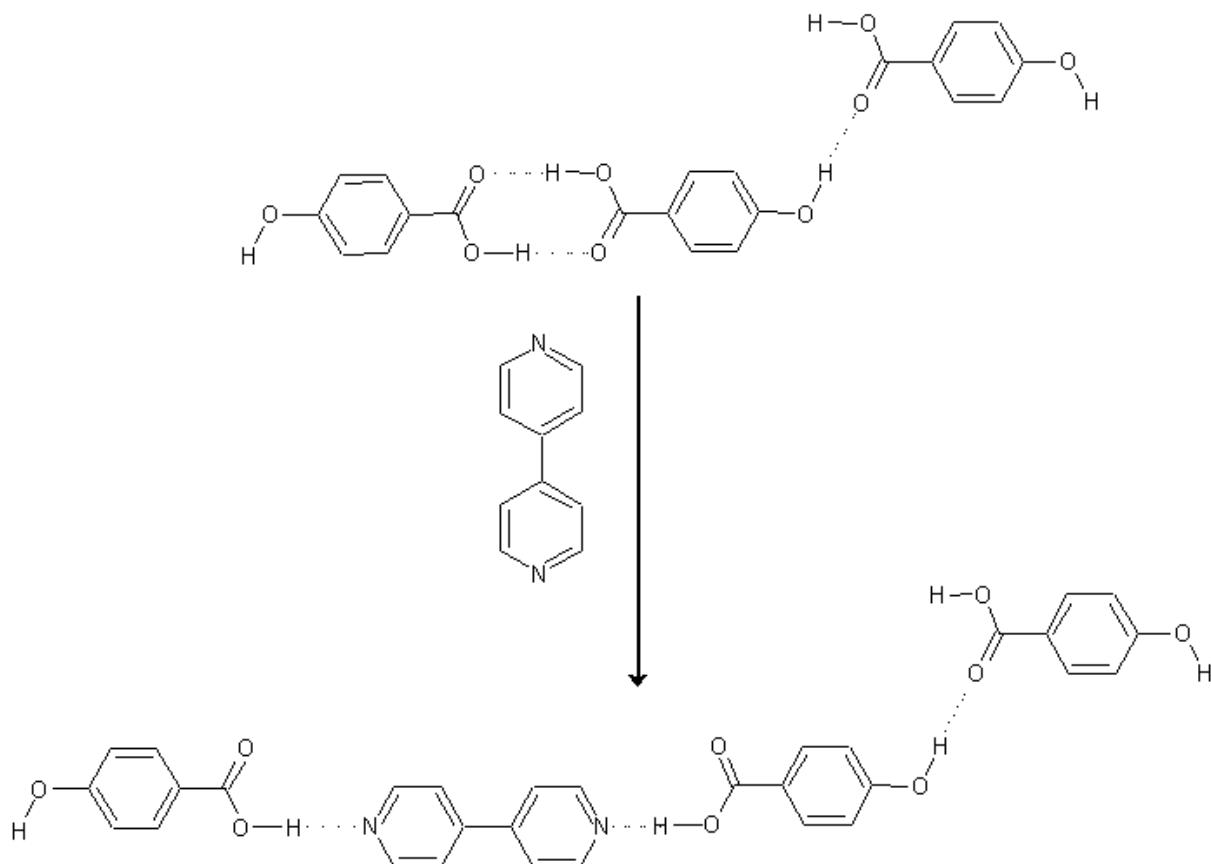


Fig. S5 Form 2 can be explained by an insertion of 4, 4'-bipyridine molecules into one of the native structures of 4-hydroxybenzoic acid.

6. Packing Diagram of Form 2

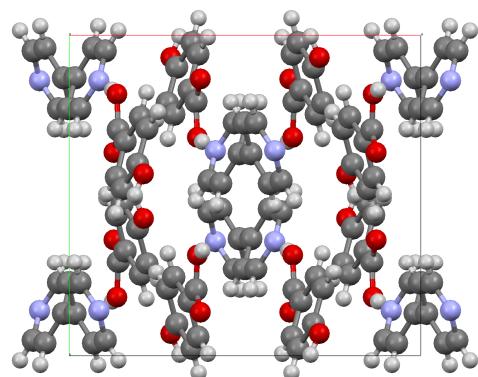


Fig. S6 Packing diagram of Form 2 as viewed down the c-axis.