Electronic Supplementary Material (ESI) for CrystEngComm.

Double Substitution Leads to A Highly Polymorphic System in 5-Methyl-2-*m*-tolylamino-benzoic Acid

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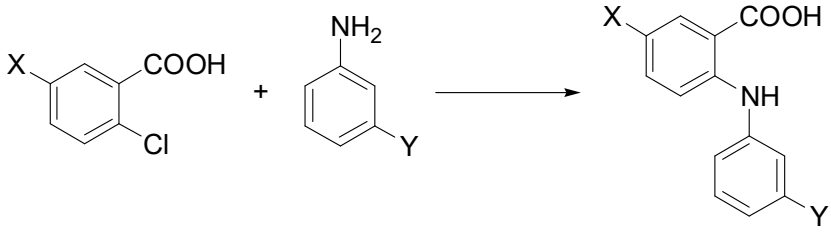
Synthesis

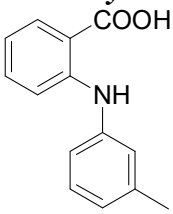


1: X = H, Y = CH_3;
2: X = CH_3; Y = H:
3: X = Y = CH_3.

General procedure for the synthesis:
2-Chloro-5-methyl-benzoic acid (5.8 mmol), aniline (6.5 mmol), K_2CO_3 (11.6 mmol), Cu (2.2 mmol) and Cu_2O (0.6 mmol) were added to a round-bottom flask, and then 3 mL 2-ethoxyethanol was added dropwise. The resulting mixture was refluxed for 24 hours under nitrogen atmosphere at 130°C. After reaction, 30 mL water was added, and the mixture was stirred for several minutes. After removing the unwanted solids by filtration, HCl was used to acidify the solution and the resulting solution was cooled in refrigerator overnight. The crude product was recovered by filtration and purified by column chromatography using eluent (PE/EA/Acetic acid = 200/1/1).

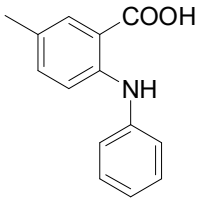
Characterization:

2-m-Tolylamino-benzoic acid (1)



Petroleum ether/ethyl acetate = 15:1 (v / v) was used as eluent for column chromatography. The product was obtained as white solid with a yield of 34.6%. ^{1}H NMR (400MHz, DMSO-d_6) *δppm* 13.08 (s, 1H), 9.61 (s, 1H), 7.98 – 7.84 (m, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.23 (t, *J* = 6.9 Hz, 2H), 7.04 (d, *J* = 6.4 Hz, 2H), 6.88 (d, *J* = 7.4 Hz, 1H), 6.76 (t, *J* = 7.5 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) *δppm* 170.3, 147.4, 140.6, 139.3, 134.5, 132.2, 129.6, 124.2, 122.2, 118.6, 117.6, 114.1, 112.6, 21.3; MS (ESI) [MH^+] *m*/*z* 226.09; mp: 140.3°C.

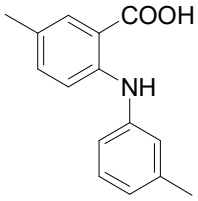
5-Methyl-2-phenylamino-benzoic acid (2)



The product was obtained as yellow solid (0.51 g, yield%: 42.8). ^{1}H NMR (600 MHz, DMSO-d_6) δppm 13.01 (s, 1H), 9.46 (s, 1H), 7.71 (s, 1H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.25 – 7.18 (m, 4H), 7.02 (t, *J* = 7.8 Hz, 1H), 2.22 (s, 3H);^{13}C NMR (150 MHz, DMSO-d_6) δppm 170.2, 143.0, 135.2, 131.9, 129.7, 126.6, 122.7, 120.9, 114.7, 113.1, 20.2; IR (KBr, cm^{-1}) 3440 (s), 3320 (s), 3920 (m),1660 (s), 1590 (s), 1520 (s), 1470 (s), 1430 (s), 1240 (s), 1160 (s), 1080 (s), 899 (s), 816 (s), 789 (s),

752 (s), 696 (s), 675 (s),615 (s), 526 (s); MS (ESI) [MH^+] *m*/*z* 286.14 (+Na, +Cl); mp: 187.4ºC.

5-Methyl-2-m-tolylamino-benzoic acid (3)



The product was obtained as light yellow solid (415 mg, yield%: 29.3).
^{1}H NMR (500 MHz, DMSO-d_6) δppm 9.36 (s, 1H), 7.65 (s, 1H), 7.14 (dt, *J* = 16.7, 7.7 Hz, 3H), 6.94 (d, *J* = 6.1 Hz, 2H), 6.78 (d, *J* = 7.4 Hz, 1H), 2.22 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (125MHz, DMSO-d_6) δppm 170.2, 145.0, 141.2, 139.1, 135.3, 131.9, 129.5, 126.5, 123.6, 121.5, 117.9, 114.8, 113.0, 21.3, 20.2; IR (KBr, cm^{-1}) 3343 (s), 2916 (m), 1659 (s), 1589 (s), 1576 (s), 1517 (s), 1441 (s), 1318 (s), 1269 (s), 1242 (s), 1156 (s), 1086 (s), 913 (s), 830 (s), 787 (s), 763 (s), 691.8 (s), 676 (s), 560 (s), 500 (s); MS (ESI) [MH^+] *m*/*z* 242.29; mp: 173.5ºC.
Note: the melting points were measured with DSC, and the onset temperature is recorded.

Crystal Growth

Example: 250 mg of **1** was suspended in 5 mL methanol. The mixture was stirred overnight and the remaining solid was removed by pipette filtration. A vial containing the clear solution was covered with perforated parafilm. Slow evaporation led to single crystals in about a week.

Table S1. Solvents used for crystal growth and crystal forms obtained

Solvent	**1**	**2**	**3**
Acetone	I+II	I	I
Chloroform	I	I	IV
Ethyl acetate	I	I	I
Methanol	II	I	II
Dichloromethane	I+II	I	I
Ethanol	I	I	I
Acetonitrile	I	I	III
Ether	I	I	I
iso-Propanol	I	I	III
Dimethyl sulfoxide	I	I	II
Tetrahydrofuran	I	I	I
Acetic acid	I	I	I
N,N-Dimethylformamide	I+II	I	II
Benzene	II	I	III
Toluene	II	I	I
Pyridine	I+II	I	II

IR

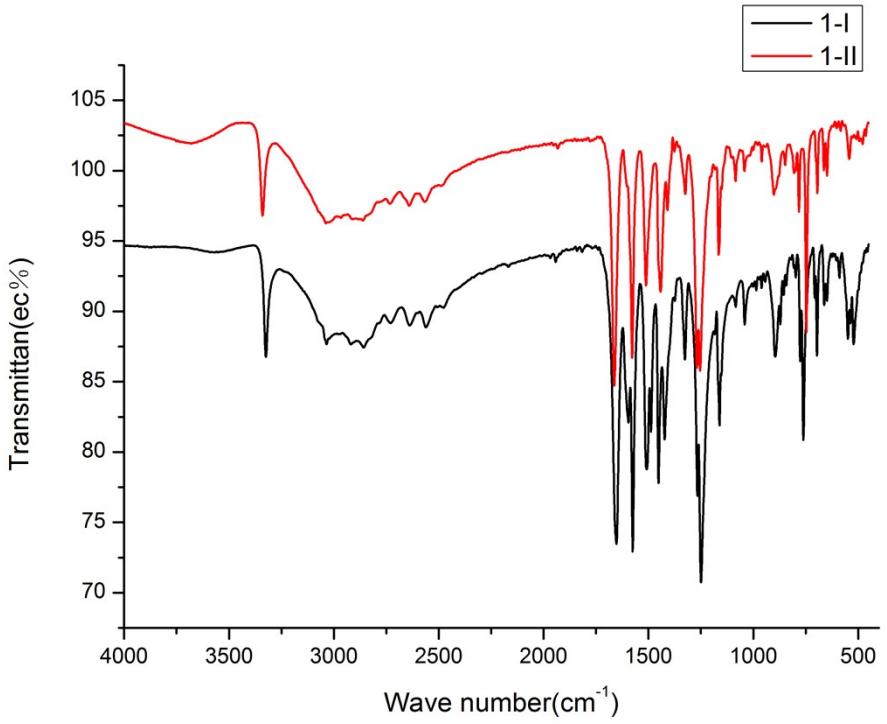


Figure S1. IR spectra of the two forms of **compound 1**.

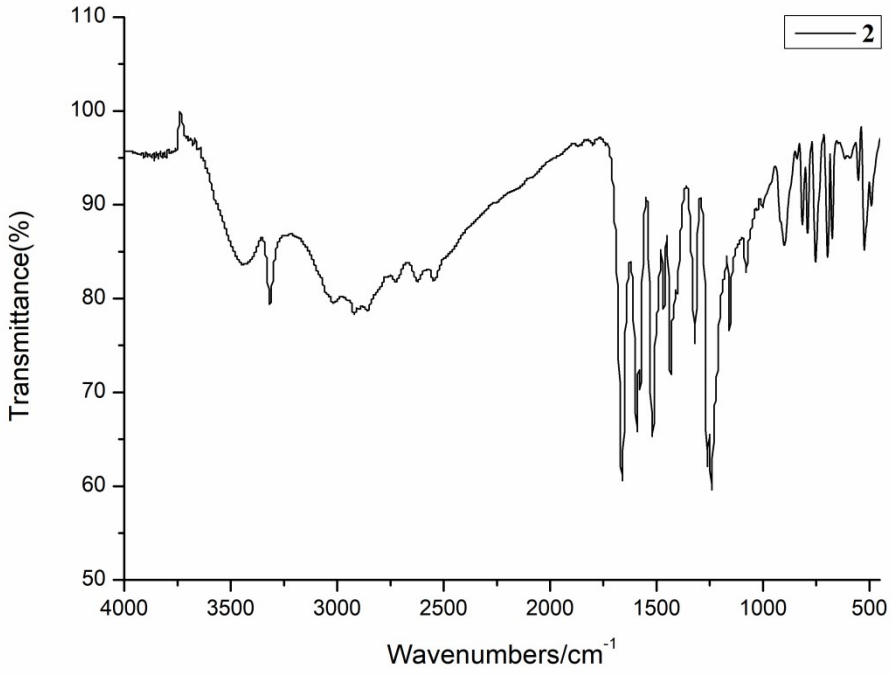


Figure S2. IR spectrum of **compound 2**.

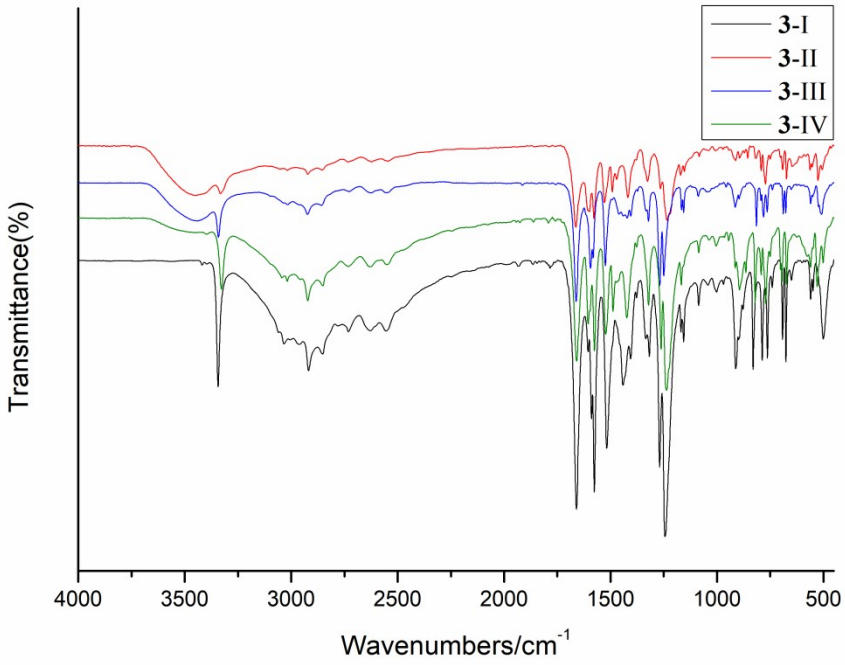


Figure S3. IR spectra of the four forms of **compound 3**.

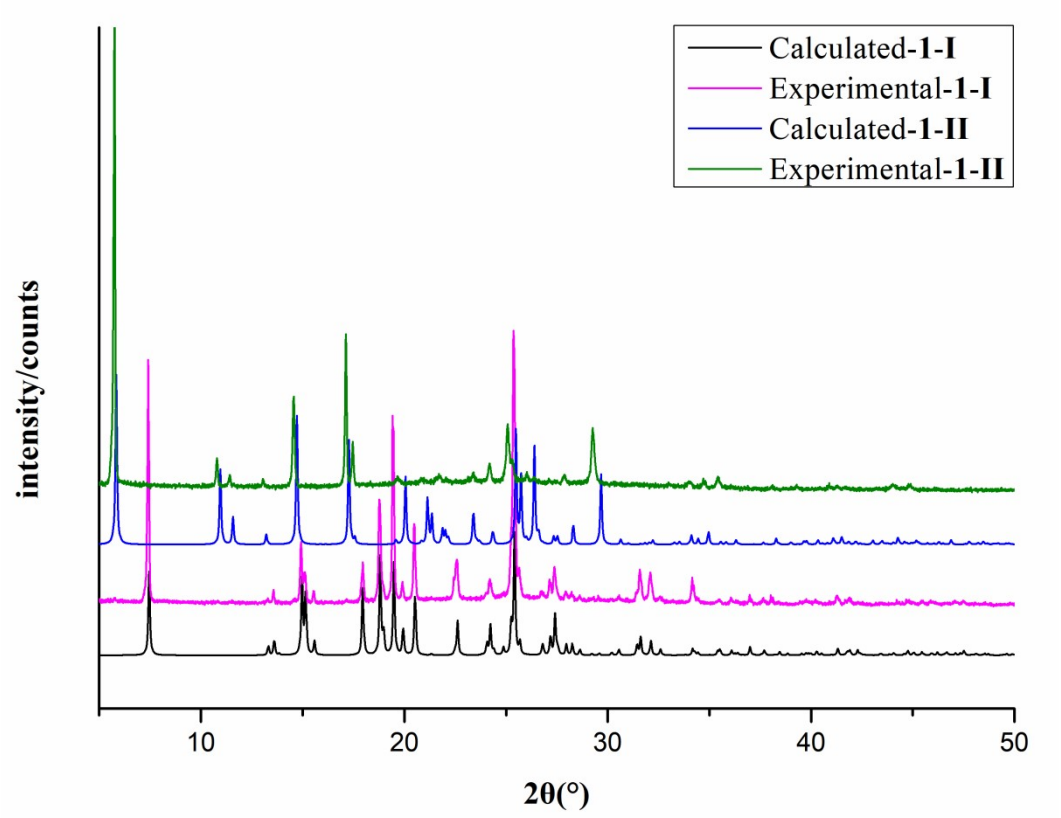


Figure S4. Experimental and calculated PXRD patterns of the two forms of compound **1**

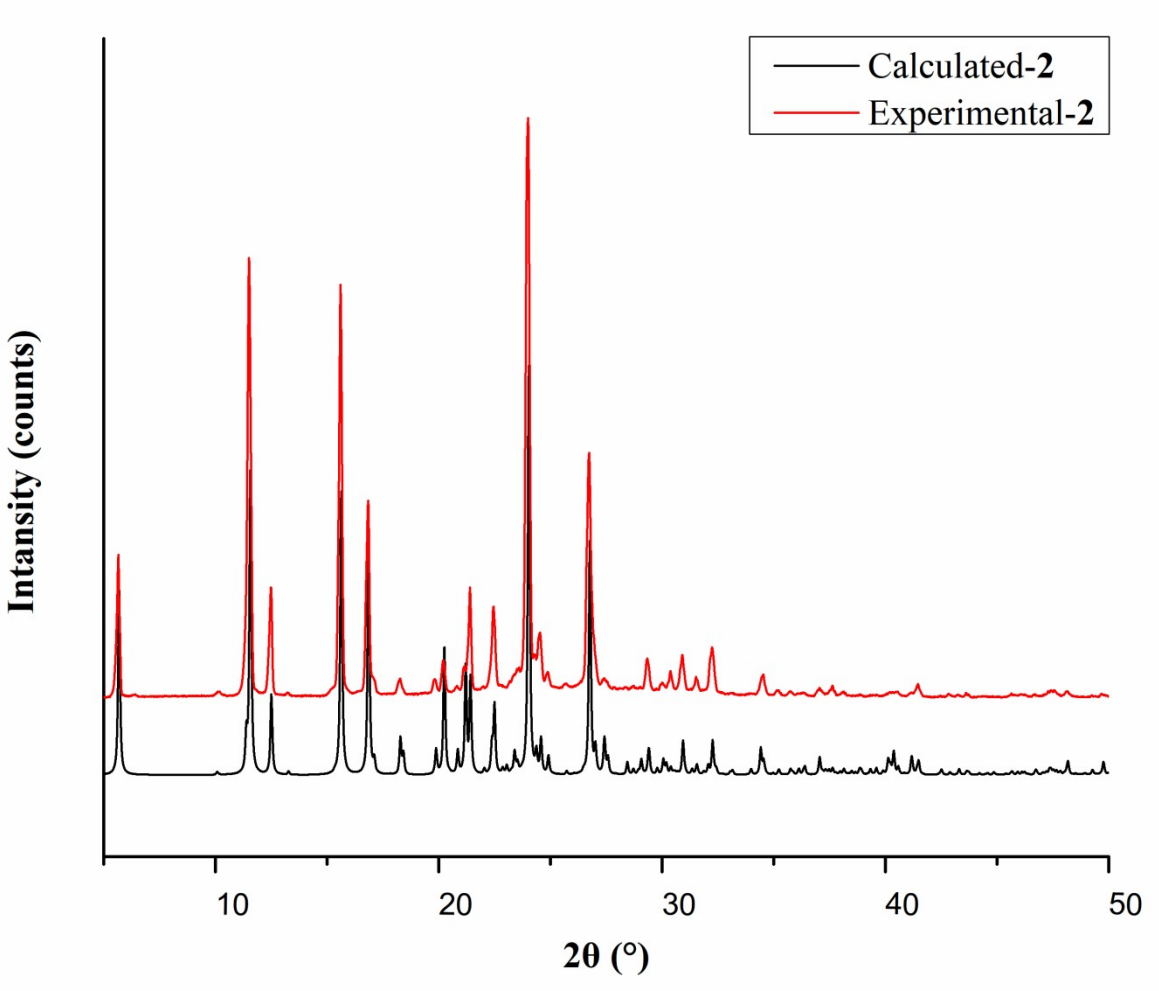


Figure S5. Experimental and calculated PXRD patterns of **2**

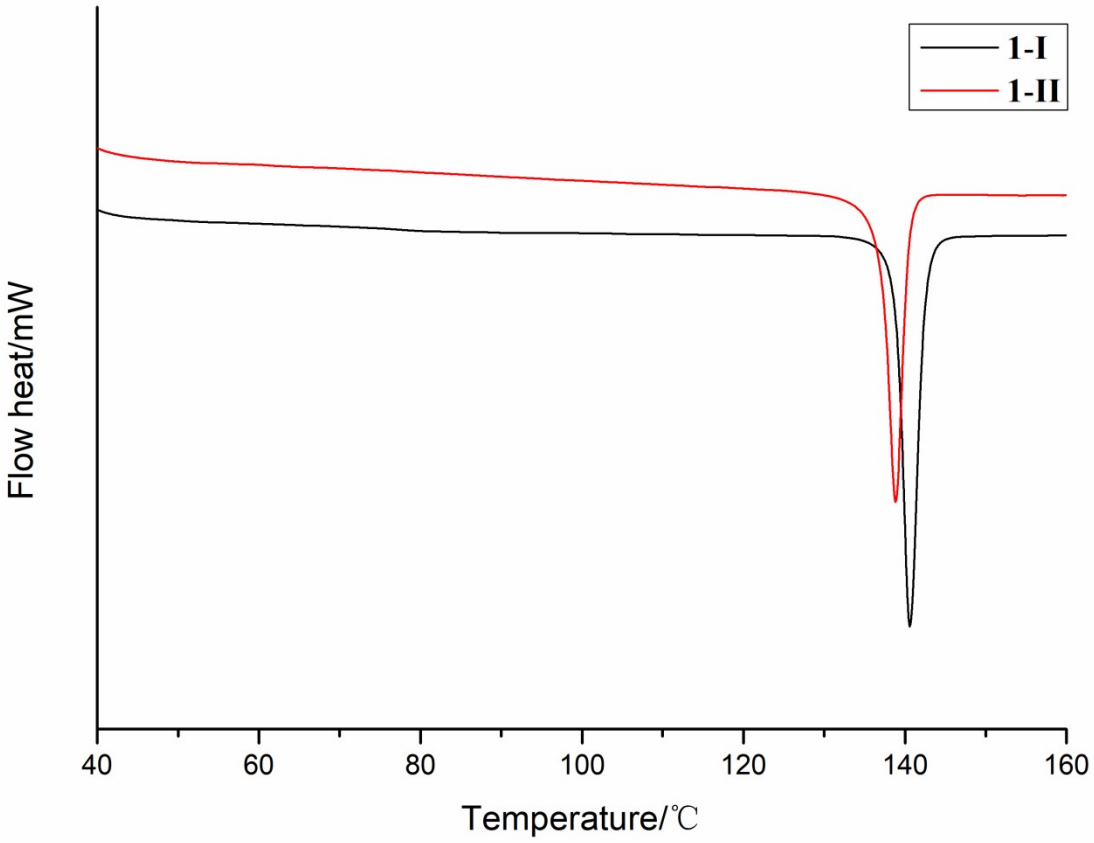


Figure S6. DSC thermograms of the polymorphs of **1**

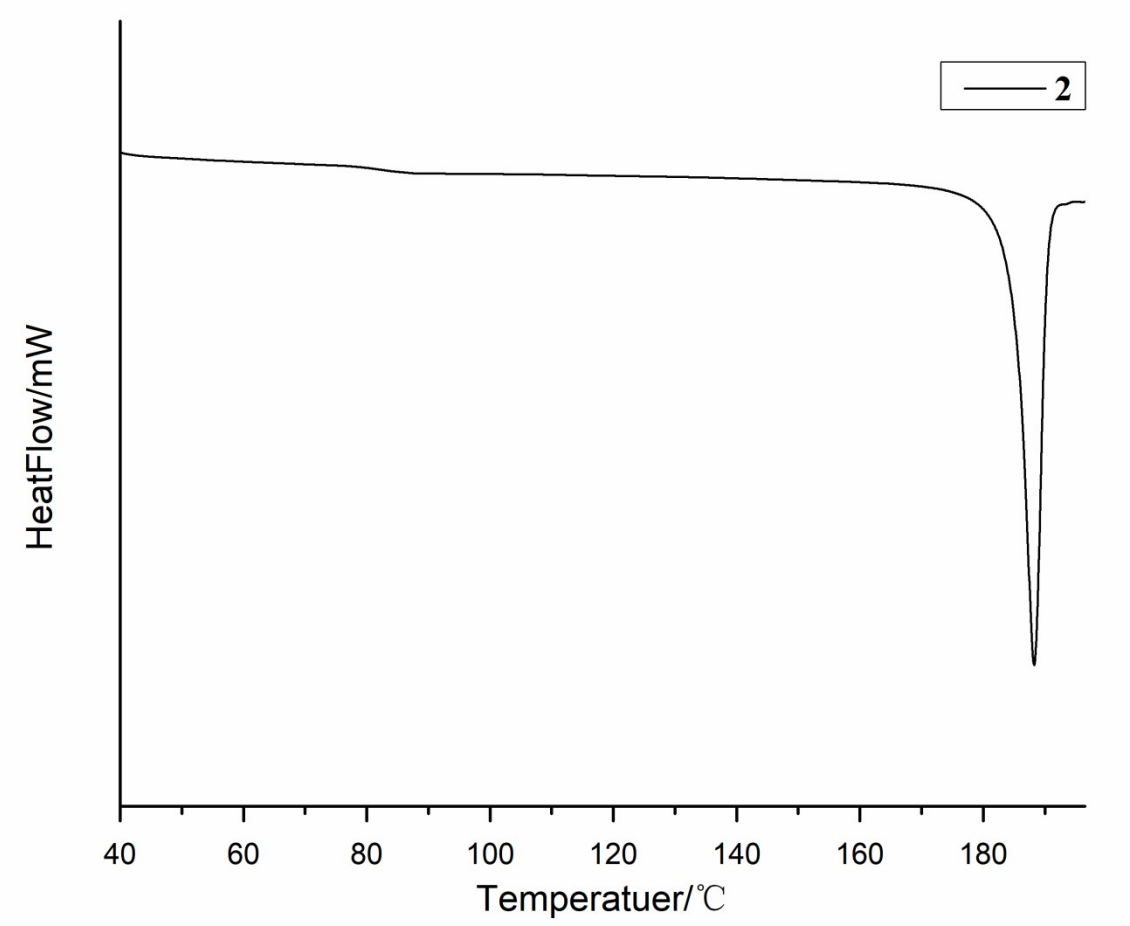


Figure S7. DSC thermogram of **2**

3-III and **3-IV** crystals were ground and then heated at 130℃, 158℃ and kept for 5 minutes, respectively, and then cooling to room temperature. The PXRD of the samples after thermal treatment were performed at ambient temperature.

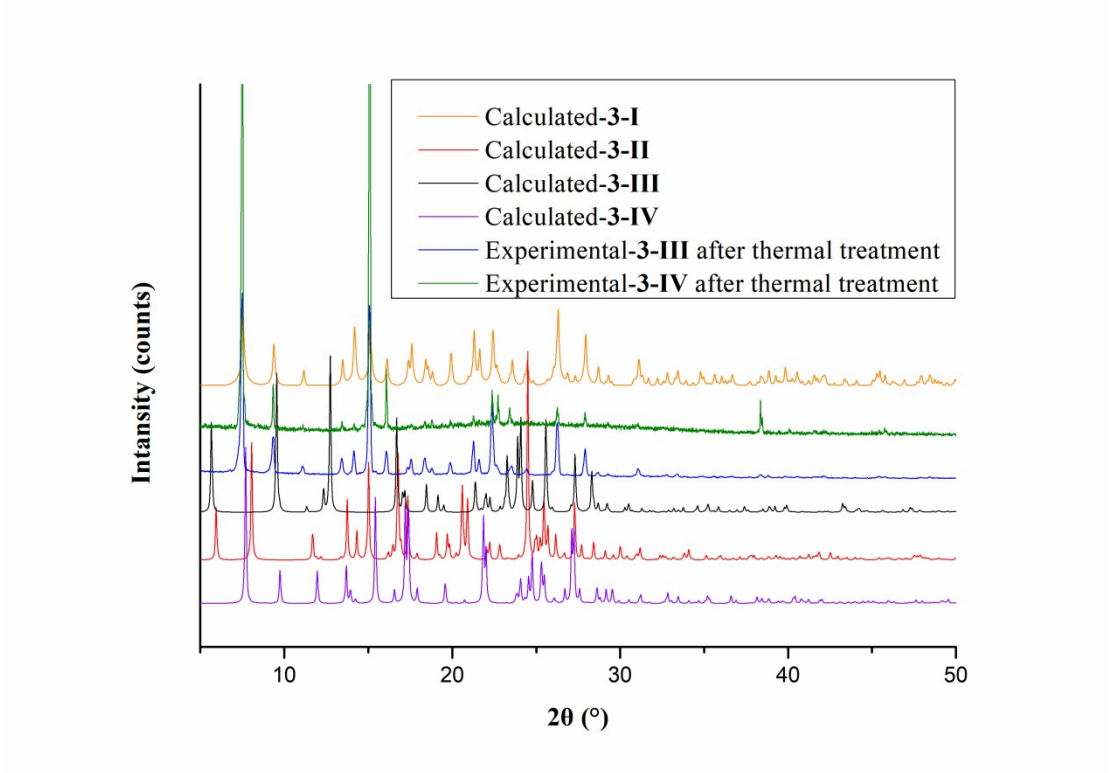


Figure S8. Calculated PXRD of the four polymorphs of **3** and experimental patterns of **3-III, 3-IV** after thermal treatment

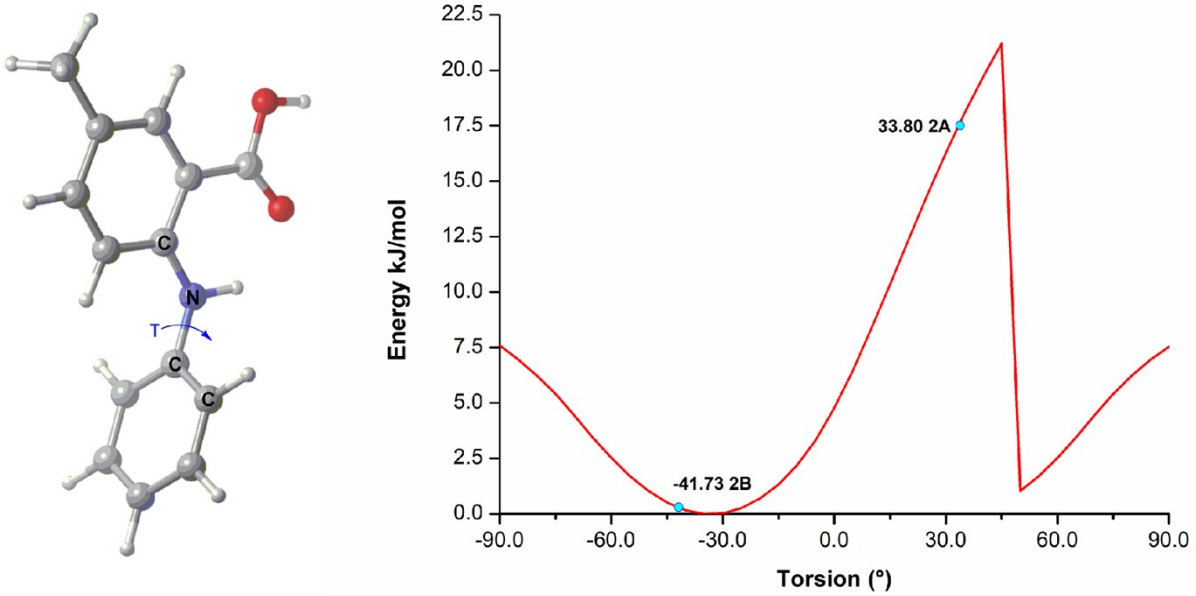


Figure S9. Ball and stick model of **2** and conformational scan of single molecule.

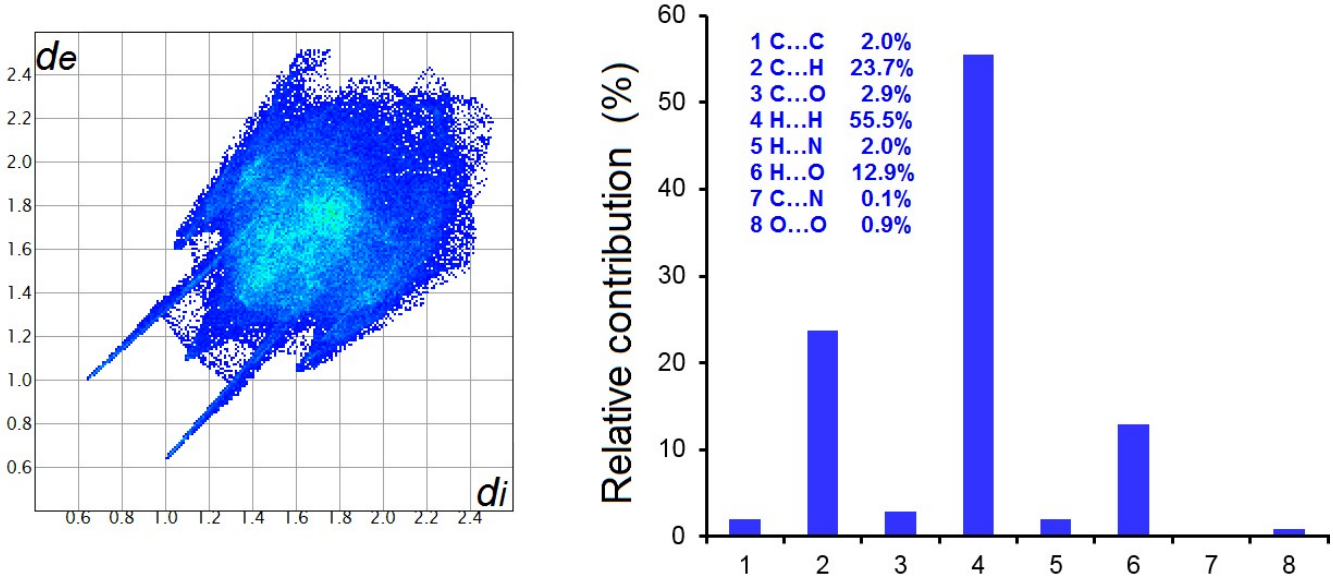


Figure S10. 2D fingerprint plots of Hirshfeld surface and relative contributions to the Hirshfeld surface by various intermolecular contacts in the crystal of **2**.