# *Polymorphism of levofloxacin: structure, properties and phase transformation*

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## Contents of Supporting Information

Support information

**Table S1.** Hydrogen bonds in levofloxacin anhydrate and solvates

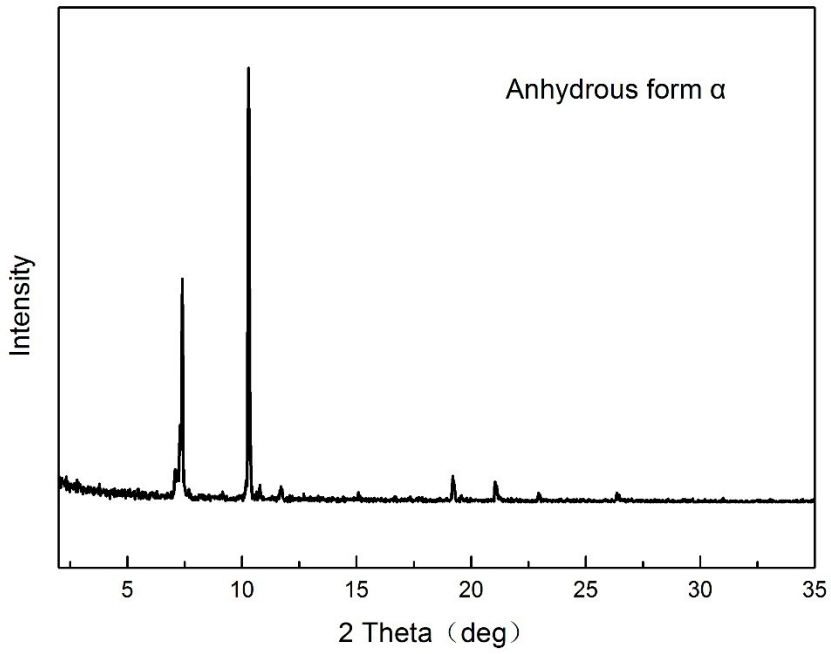
| | D–H···A | d (D–H) (Å) | d (H···A) (Å) | d (D···A) (Å) | θ (DHA) (°) |
|---|---|---|---|---|---|
| Anhydrous | $O_1$–H···$O_3$ | 0.820 | 1.788 | 2.554 | 154.78 |
| | $C_{13}$–H···$O_2$ | 0.960 | 2.535 | 3.427 | 154.61 |
| NprOH:B-C | $C_{11C}$–H···$O_{2B}$ | 1.00 | 2.441 | 3.207 | 132.96 |
| | $C_{13C}$–H···$O_{3B}$ | 0.980 | 2.451 | 3.192 | 132.12 |
| | $C_{11B}$–H···$O_{2C}$ | 1.000 | 2.506 | 3.257 | 131.61 |
| | $C_{1B}$–H···$O_{2C}$ | 0.950 | 2.401 | 3.265 | 151.04 |
| | $C_{17C}$–H···$O_{2B}$ | 0.990 | 2.514 | 3.456 | 159.01 |
| | $C_{1C}$–H···$O_{2B}$ | 0.950 | 2.385 | 3.258 | 152.68 |
| | $C_{12B}$–H···$O_{3C}$ | 0.990 | 2.482 | 3.357 | 147.12 |
| NprOH:A-C | $C_{4A}$–H···$F_{1C}$ | 0.950 | 2.417 | 3.274 | 149.86 |
| | $C_{13A}$–H···$O_{3C}$ | 0.980 | 2.575 | 3.372 | 138.46 |
| | $C_{4C}$–H···$F_{1A}$ | 0.950 | 2.550 | 3.405 | 149.92 |
| | $C_{12C}$–H···$O_{3A}$ | 0.990 | 2.433 | 3.342 | 152.31 |
| | $C_{13A}$–H···$F_{1A}$ | 0.980 | 2.530 | 3.359 | 142.27 |
| NprOH:A-D | $C_{11D}$–H···$O_{2A}$ | 1.000 | 2.295 | 3.106 | 137.45 |
| dimer | $C_{11A}$–H···$O_{2D}$ | 1.000 | 2.500 | 3.252 | 131.66 |
| NprOH:B-D | $C_{12D}$–H···$O_{3B}$ | 0.990 | 2.495 | 3.374 | 147.70 |
| | $C_{17B}$–H···$O_{2D}$ | 0.990 | 2.441 | 3.402 | 163.53 |
| Intramolecula | $O_{1A}$–H···$O_{3A}$ | 0.840 | 1.777 | 2.559 | 154.07 |
| r | $O_{1B}$–H···$O_{3B}$ | 0.840 | 1.731 | 2.507 | 152.56 |
| | $O_{1C}$–H···$O_{3C}$ | 0.840 | 1.756 | 2.531 | 152.51 |
| | $O_{1D}$–H···$O_{3D}$ | 0.840 | 1.768 | 2.526 | 149.12 |
| Glycol | $C_1$–H···$O_2$ | 0.950 | 2.423 | 3.284 | 150.62 |
| 1D | $C_{11}$–H···$O_2$ | 1.000 | 2.444 | 3.200 | 132.01 |

| | | | | | |
|---|---|---|---|---|---|
| | $C_4$–H···$F_1$ | 0.950 | 2.495 | 3.387 | 156.20 |
| | $C_{12}$–H···$O_{2S}$ | 0.990 | 2.396 | 3.326 | 156.11 |
| | $O_1$–H···$O_3$ | 0.840 | 1.734 | 2.512 | 153.07 |
| 2D | $C_{12}$–H···$O_3$ | 0.990 | 2.498 | 3.376 | 147.62 |
| | $C_{13}$–H···$O_3$ | 0.980 | 2.583 | 3.294 | 129.45 |
| | $C_{13}$–H···$F_1$ | 0.980 | 2.589 | 3.511 | 156.71 |
| | $C_{17}$–H···$O_2$ | 0.990 | 2.546 | 3.528 | 171.61 |
| | $O_{2S}$–H···$N_3$ | 0.840 | 2.741 | 3.570 | 169.46 |

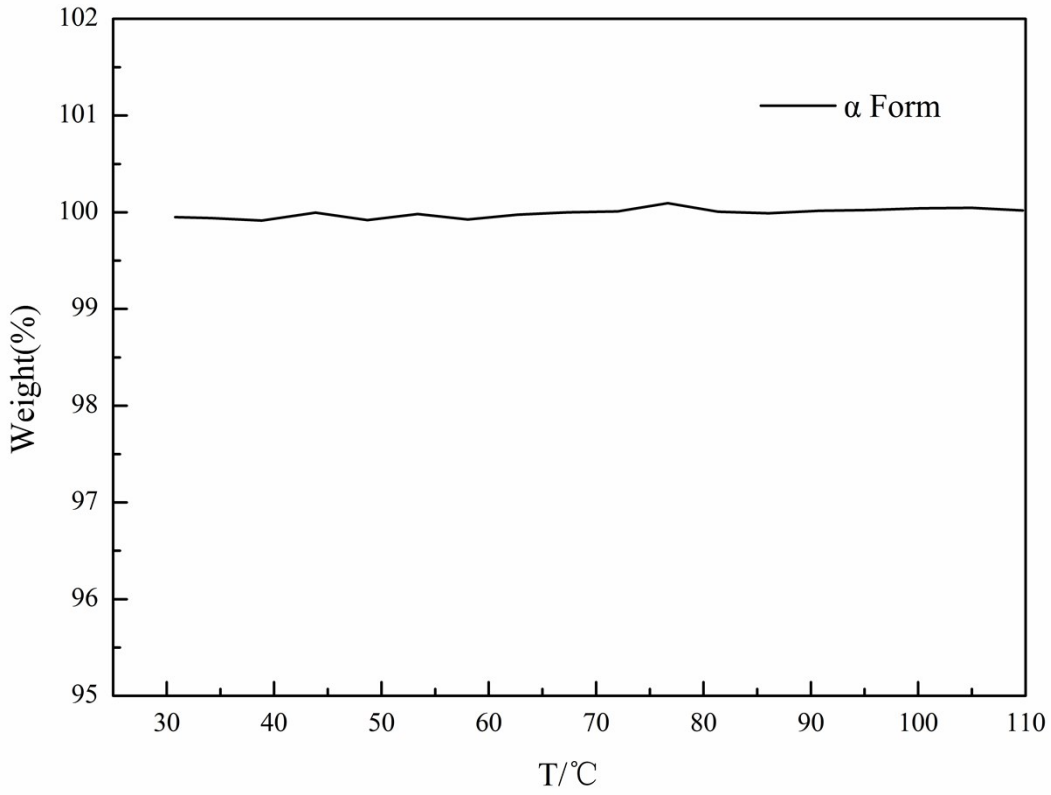
**Table S2**. Crystal forms obtained from the crystallization of levofloxacin hemihydrate in different solvents.

| Solvent | Obtained phase |
|---|---|
| Methanol | Hemihydrate |
| Ethanol | Hemihydrate |
| N-butanol | Hemihydrate |
| Isobutanol | Hemihydrate |
| Tert-butanol | Hemihydrate |
| Ethyl acetate | Hemihydrate |
| Ethyl formate | Hemihydrate |
| N-propanol | N-propanol solvent |
| Isopropanol | Isopropanol solvent |
| Acetonitrile | Form α |
| Acetone | Form α |
| DMSO | Form α |
| DMF | Form α |
| Ethylene glycol | Ethylene glycol solvent |
| Water + acetonitrile | Monohydrate |
| Acetic acid | Acetic acid solvent |

**Figure S1**




(a)




(b)

**Figure S1.** (a) PXRD pattern and (b) TG of the anhydrous α form.

**Figure S2**

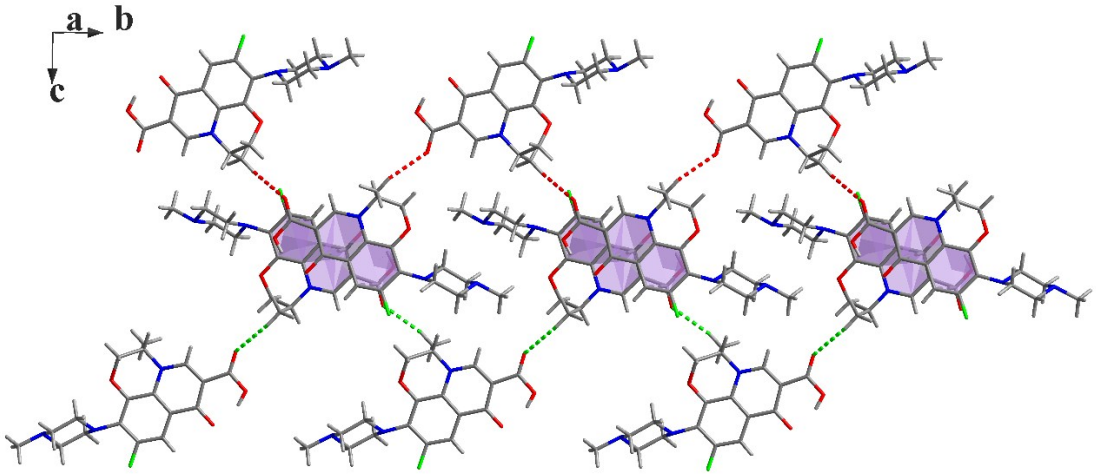



**Figure S2.** The crystal packing of Form α

**Figure S3**

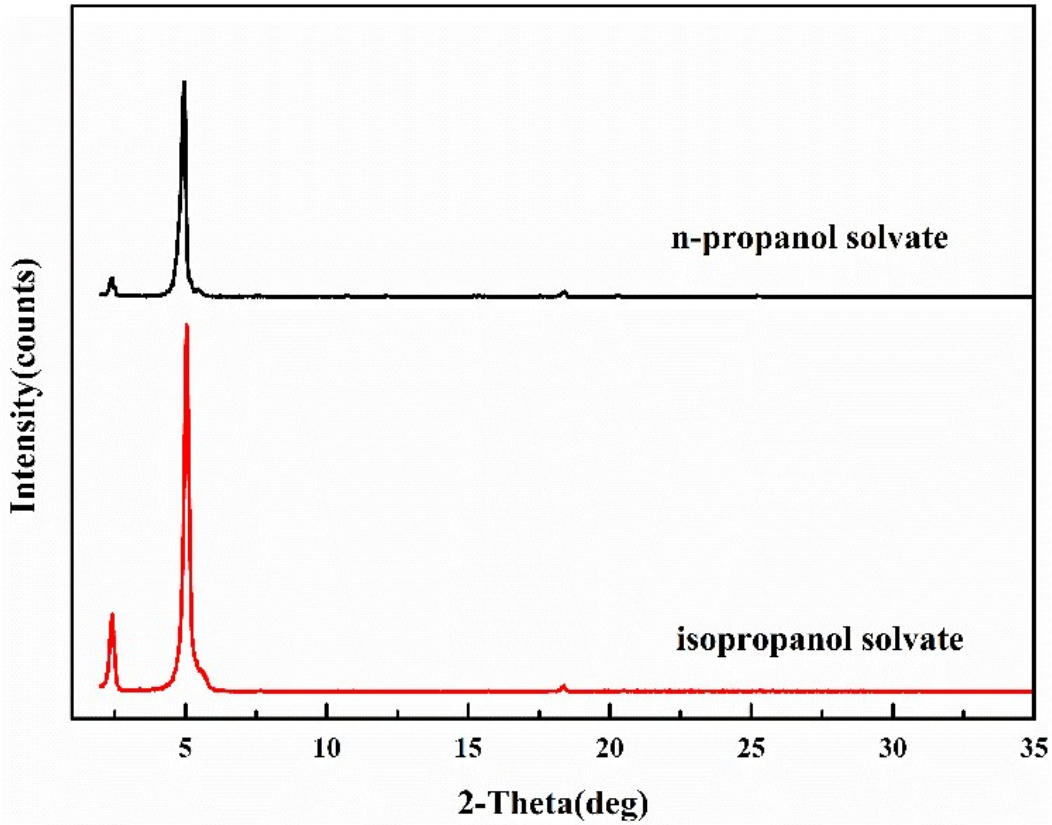



**Figure S3.** PXRD patterns of n-propanol solvate and isopropanol solvate

**Figure S4**

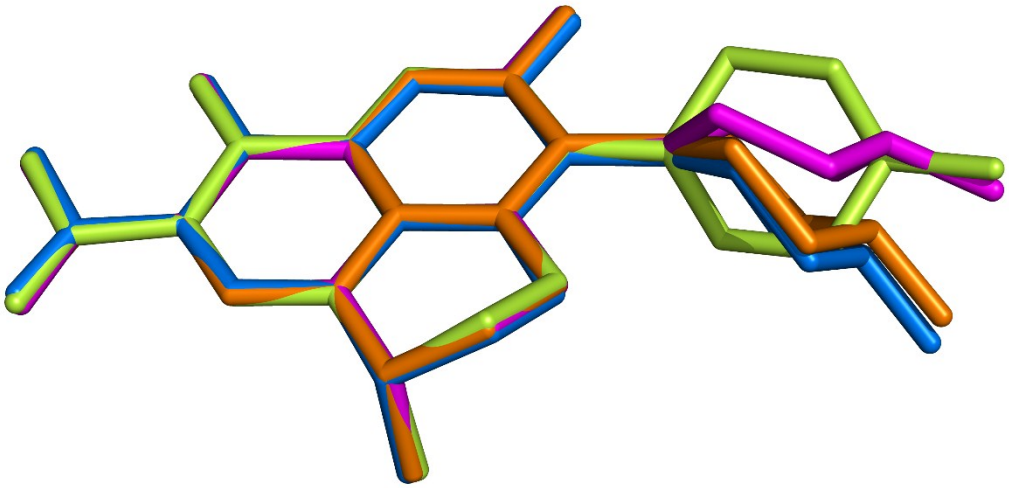


**Figure S4.** Conformational overlay of four levofloxacin molecules in n-propanol solvate: A(magenta), B(orange), C(marine), D(limon).

**Figure S5**

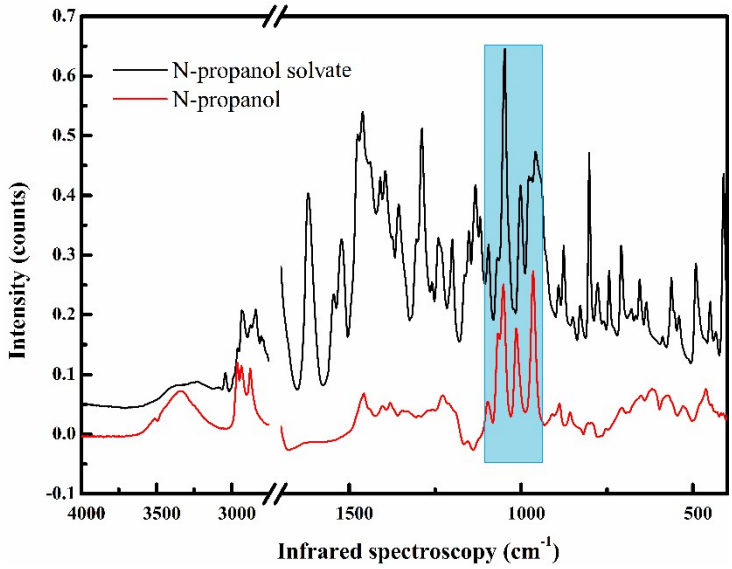
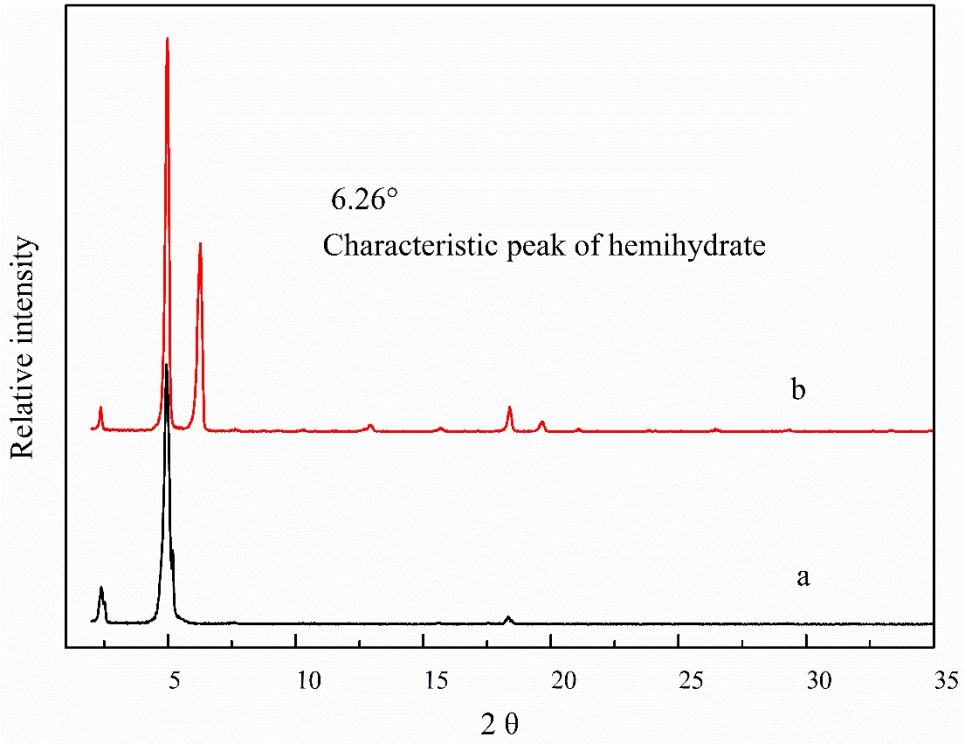
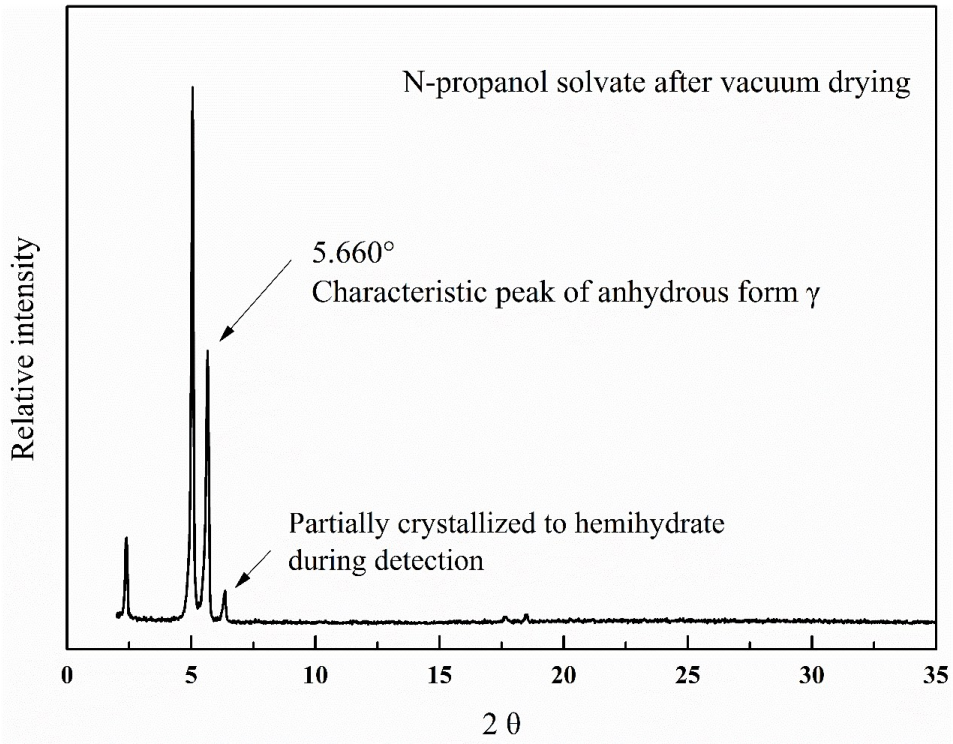



**Figure S5.** Compared Fourier-transform infrared spectroscopy patterns of n-propanol solvate (black) with pure solvent n-propanol (red).

**Figure S6**



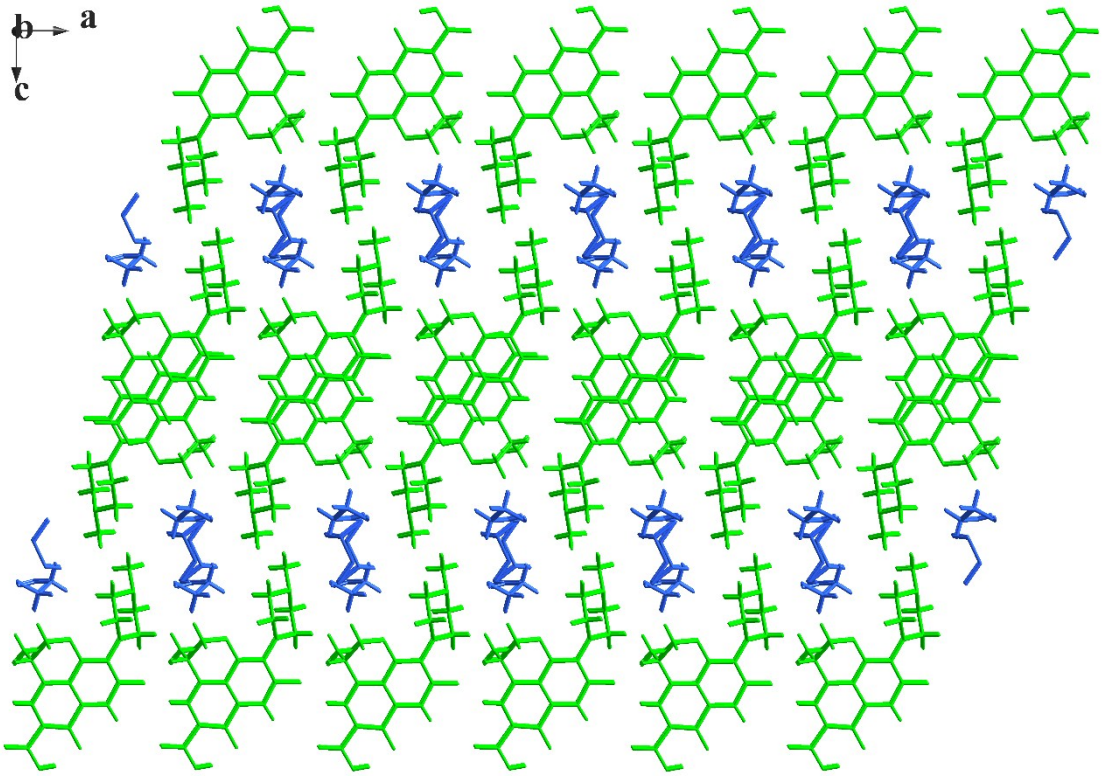

(a)



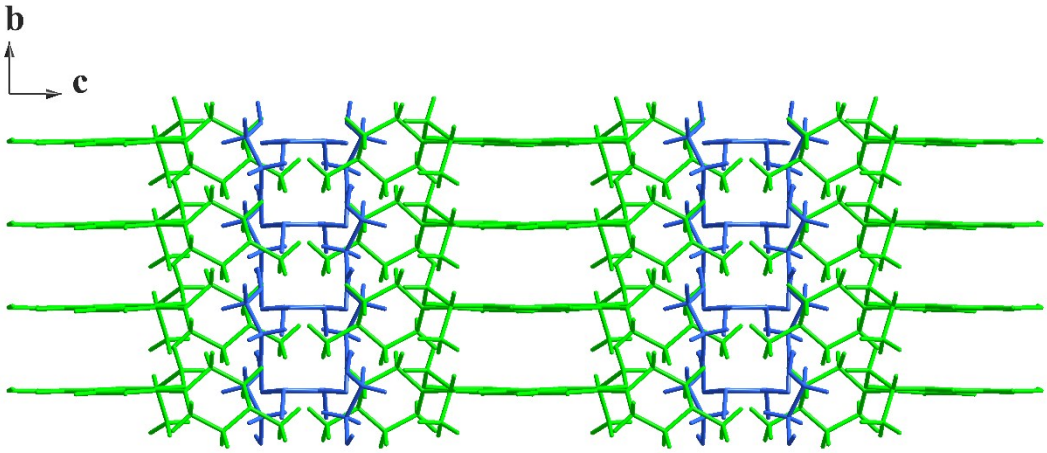

(b)

**Figure S6.** Compared PXRD patterns of n-propanol solvate after several days at air environment (a) and vacuum(b).

**Figure S7**




(a)




(b)

**Figure S7.** Spatial arrangement of ethylene glycol solvate:

**Figure S8**

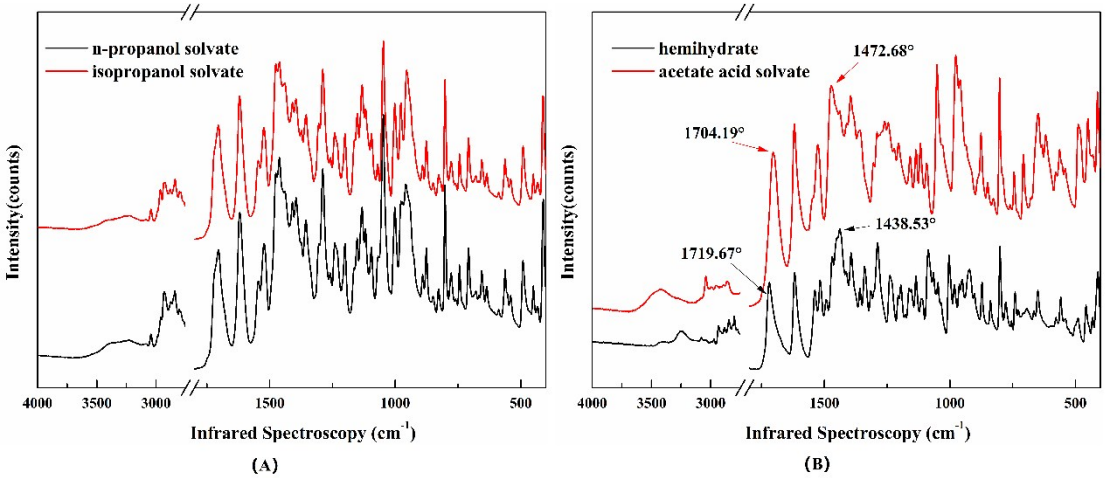



**Figure S8.** Compared Fourier-transform infrared spectroscopy patterns of n-propanol solvate with isopropanol solvate (A) and acetic acid solvate with hemihydrate (B).

**Figure S9**

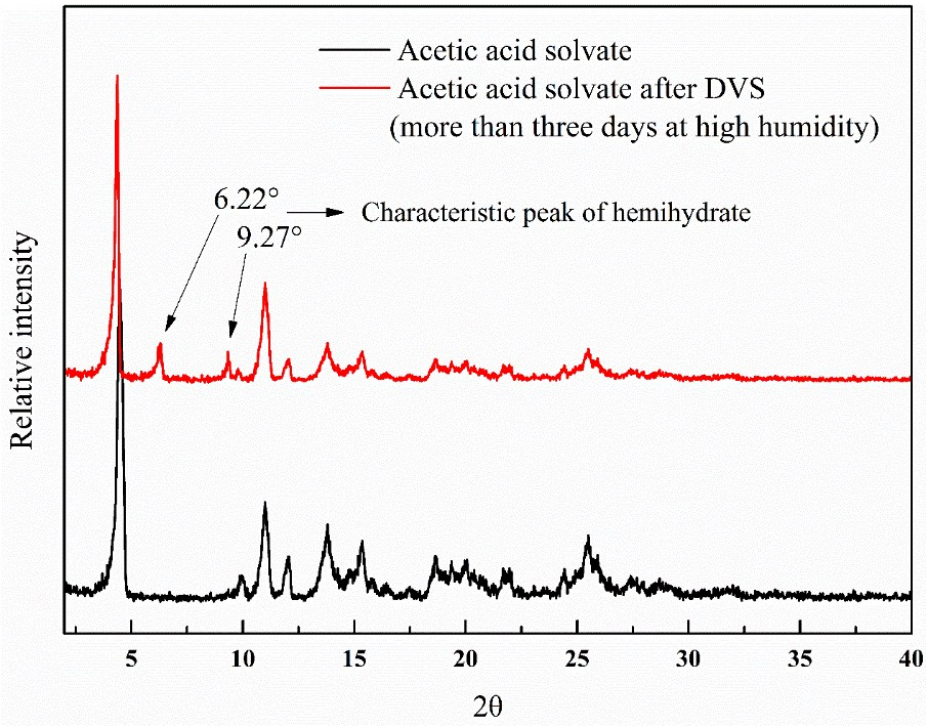



**Figure S9.** Compared PXRD patterns of acetic acid solvate after DVS experiment (more than three days at high humidity)

**Figure S10**

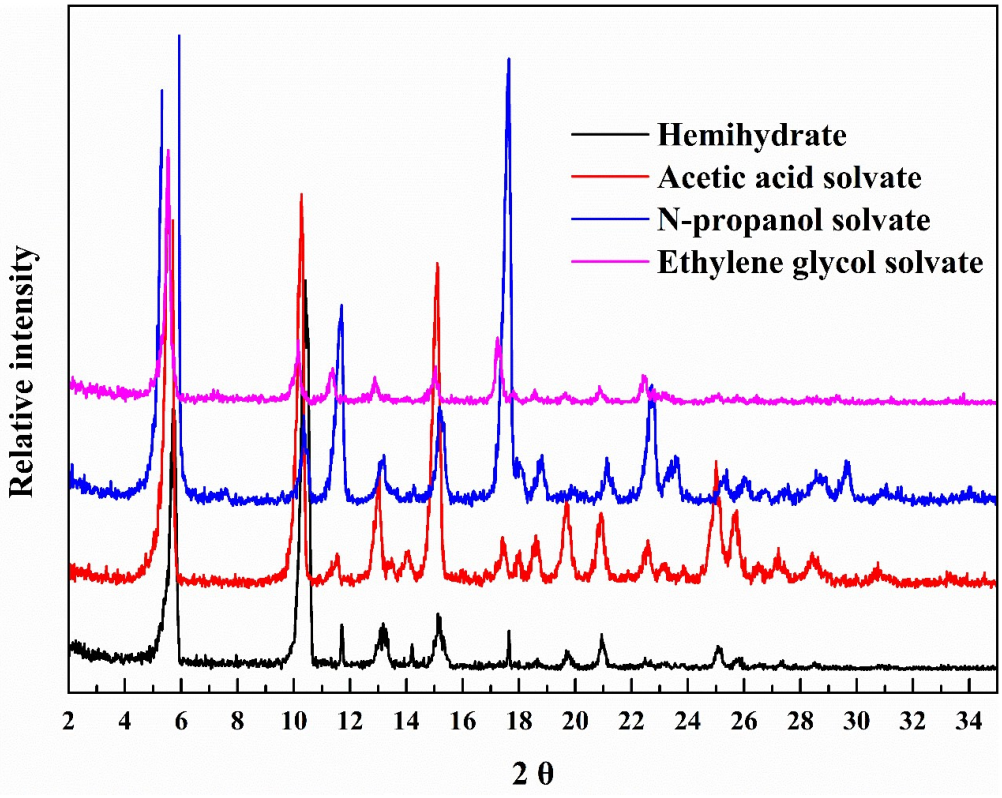



**Figure S10.** Compared PXRD patterns of the newly obtained solvates after desolvation process. (In order to facilitate careful comparison, extremely high characteristic peaks of n-propanol solvate have been eliminated)

**Figure S11: γ-β-α**

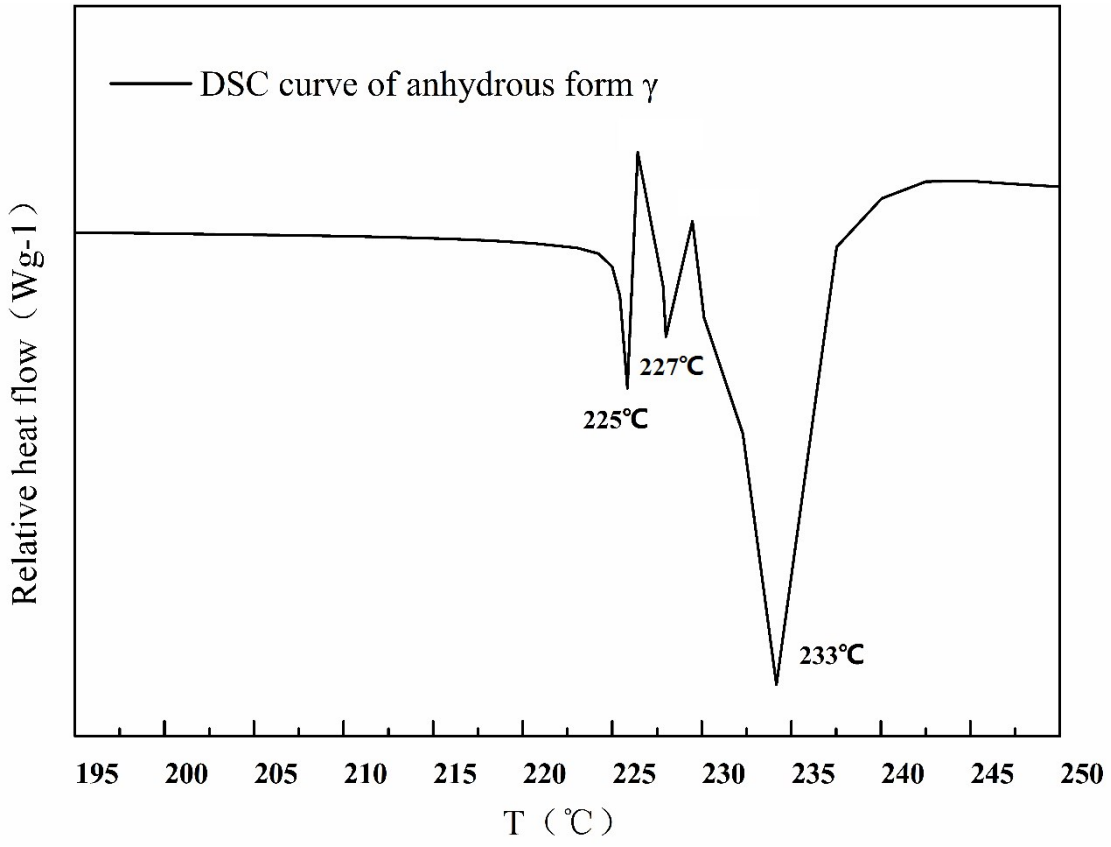



**Figure S11.** DSC curve of anhydrous form γ before melting: anhydrous form γ→anhydrous form β→anhydrous form α.