Insight into amoxicillin sodium heterosolvates and non-solvated form: crystal structures, phase transformation behaviors and desolvation mechanism

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Computational Analysis

The interaction energy (ΔE_C(A-B)) between methanol and amoxicillin sodium of S_{M-M} could be calculated by the following equation[1-3],

$$\Delta E_C(\text{A-B}) = \Delta E(\text{A-BC}) - \Delta E(\text{A-C}) \quad (1)$$

$$\Delta E(\text{A-BC}) = E(\text{ABC}) - E(\text{A}) - E(\text{BC}) \quad (2)$$

$$\Delta E(\text{A-C}) = \Delta E(\text{AC}) - \Delta E(\text{A}) - \Delta E(\text{C}) \quad (3)$$

Therefore,

$$\Delta E_C(\text{A-B}) = E(\text{ABC}) - E(\text{BC}) - E(\text{AC}) + E(\text{C}) \quad (4)$$

The interaction energy (ΔE_A(B-C)) between methanol and methyl acetate of S_{M-M} could be calculated as follows

$$\Delta E_A(\text{B-C}) = E(\text{ABC}) - E(\text{AB}) - E(\text{AC}) + E(\text{A}) \quad (5)$$

where molecule A, B, and C represent amoxicillin sodium, methanol and methyl acetate, respectively.

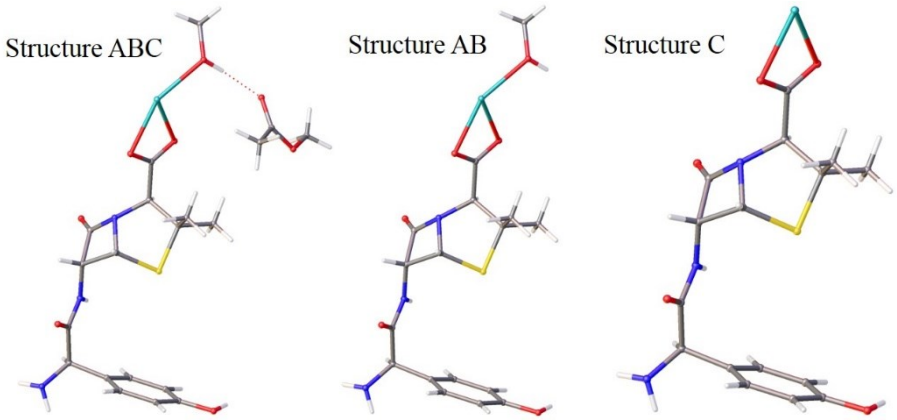

Figure S1. Different structures of S_{M-M} in the computational analysis.

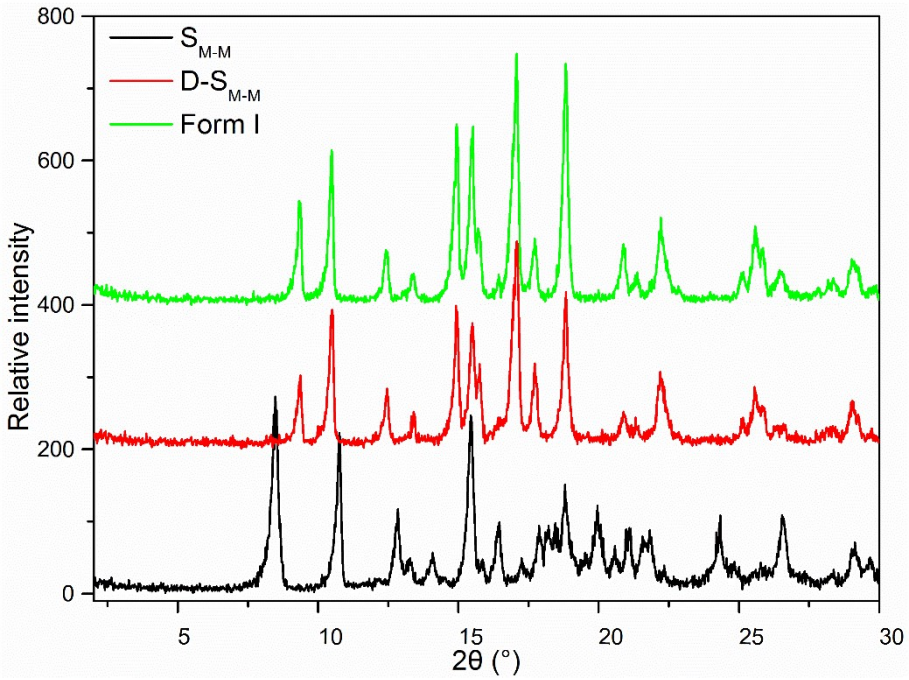

Figure S2. The PXRD patterns of $S_{M\text{-}M}$ before and after drying.

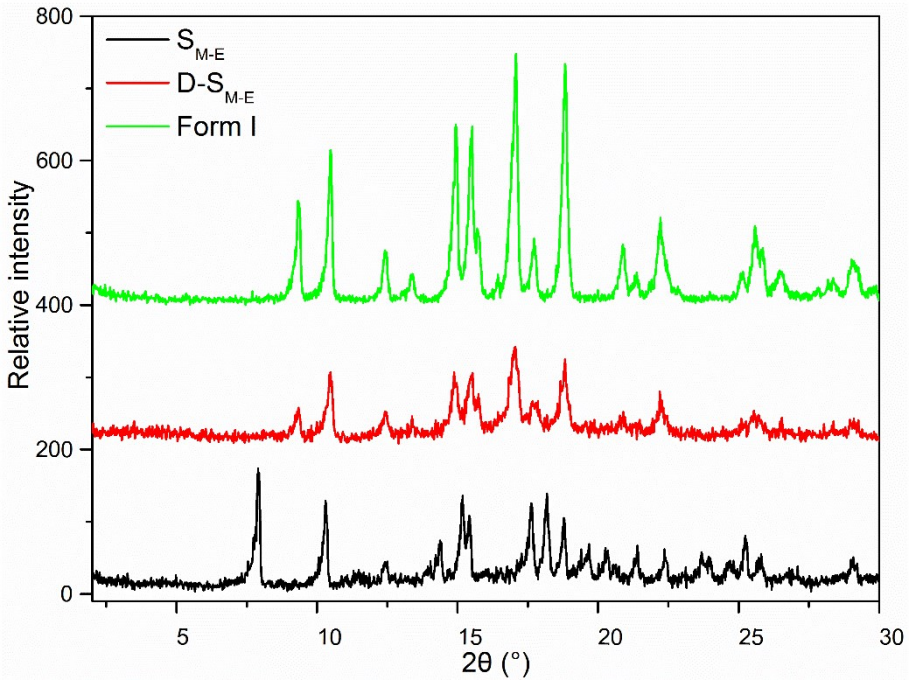

Figure S3. The PXRD patterns of $S_{M\text{-}E}$ before and after drying.

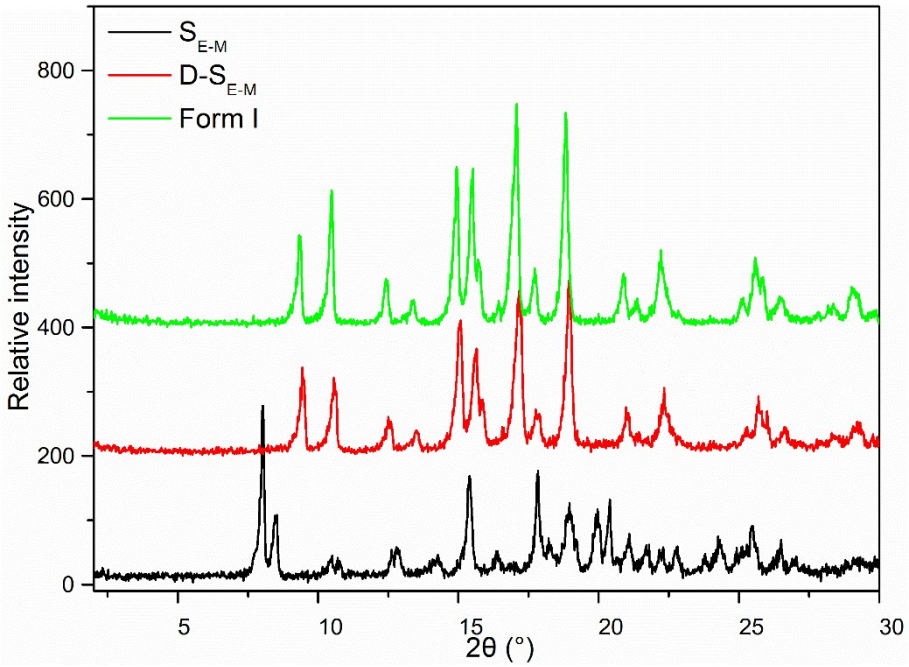

Figure S4. The PXRD patterns of S_{E-M} before and after drying.

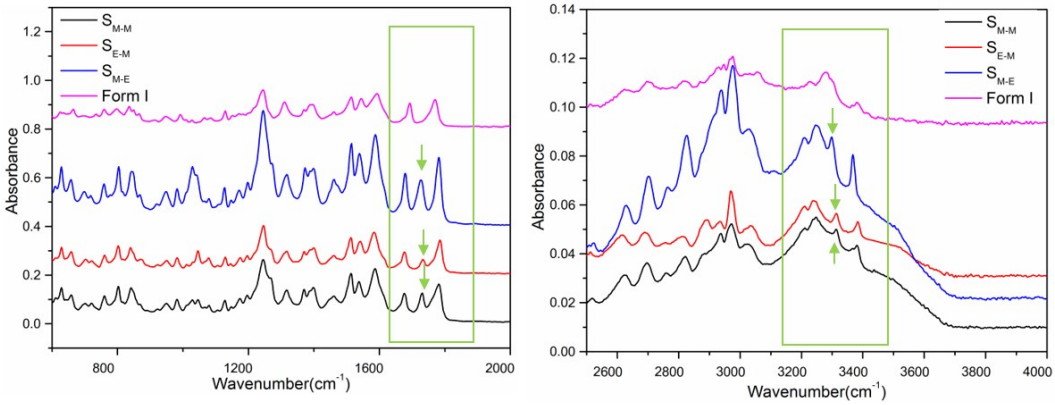

Figure S5. The FTIR spectra of Amoxicillin sodium form I and three heterosolvates.

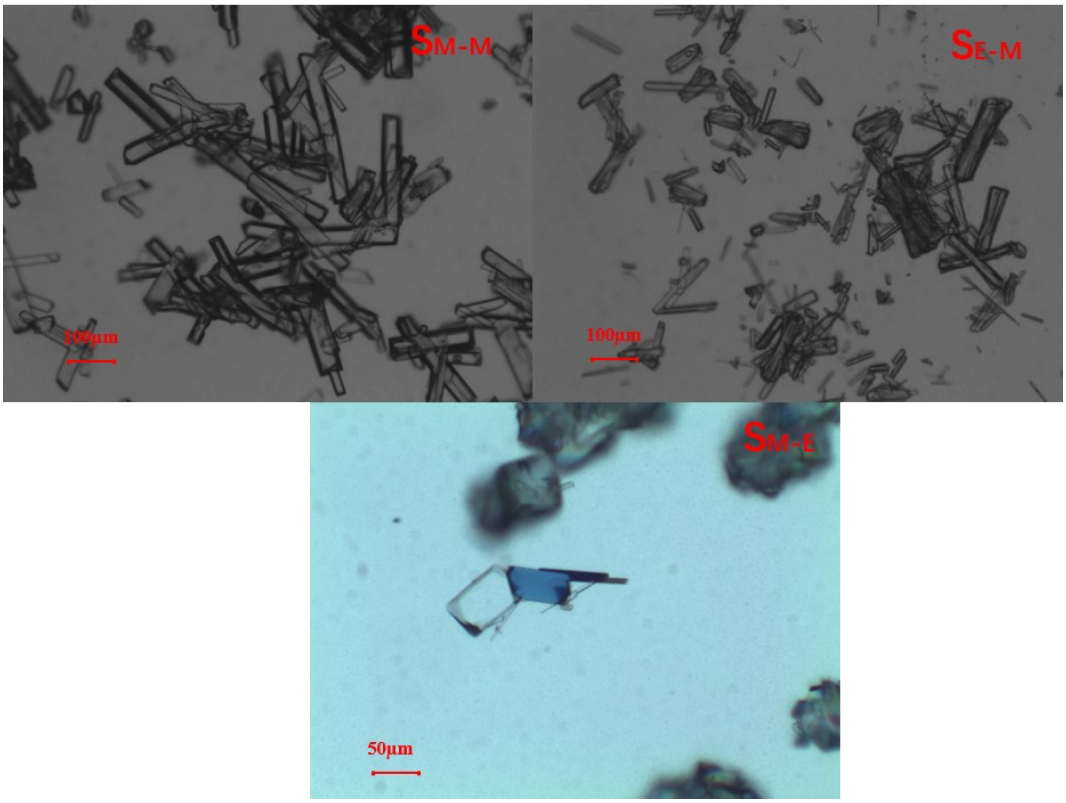

Figure S6. Polarizing microscopy images of three heterosolvates.

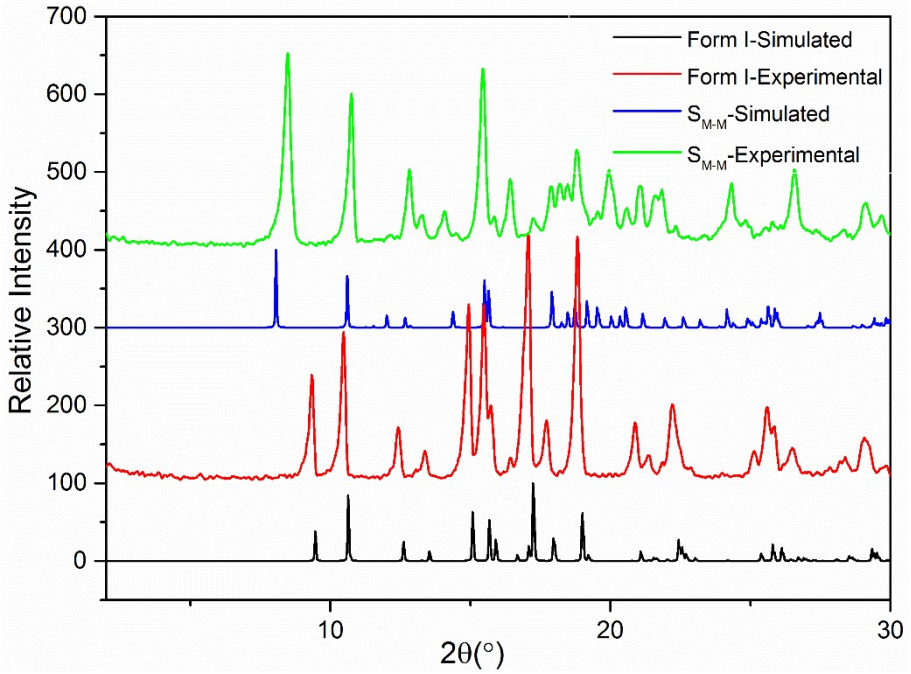

Figure S7. Experimental and simulated PXRD patterns of form I and $S_{M\text{-}M}$.

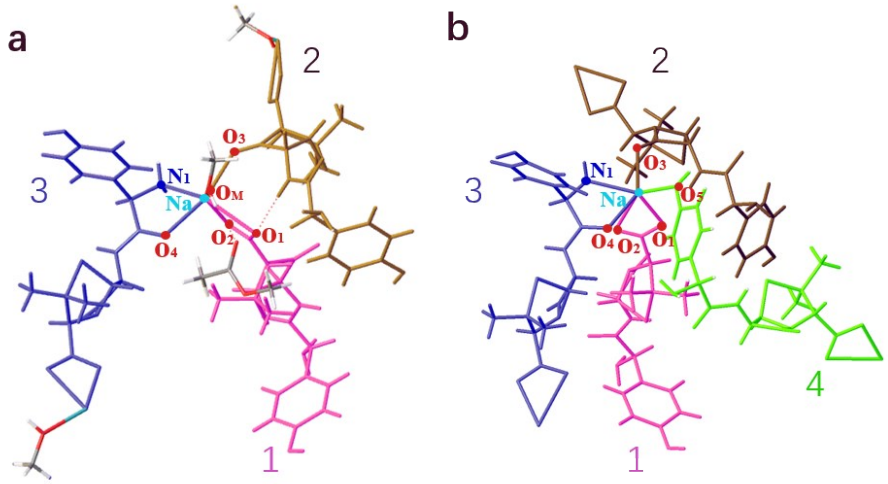

Figure S8. Coordinate bonds in crystal structure (a. $S_{M\text{-}M}$, b. Form I).

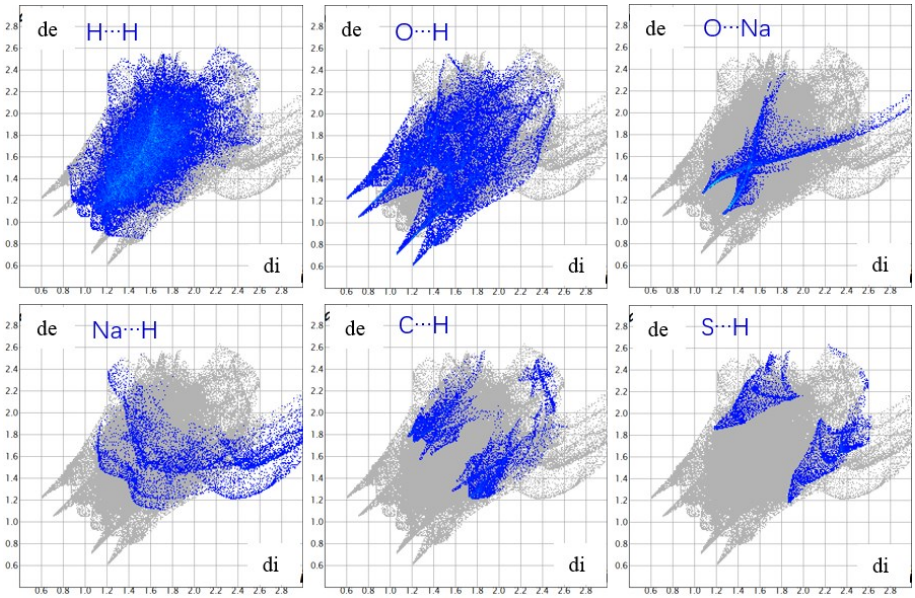

Figure S9. Detailed distribution of different interactions in form I.

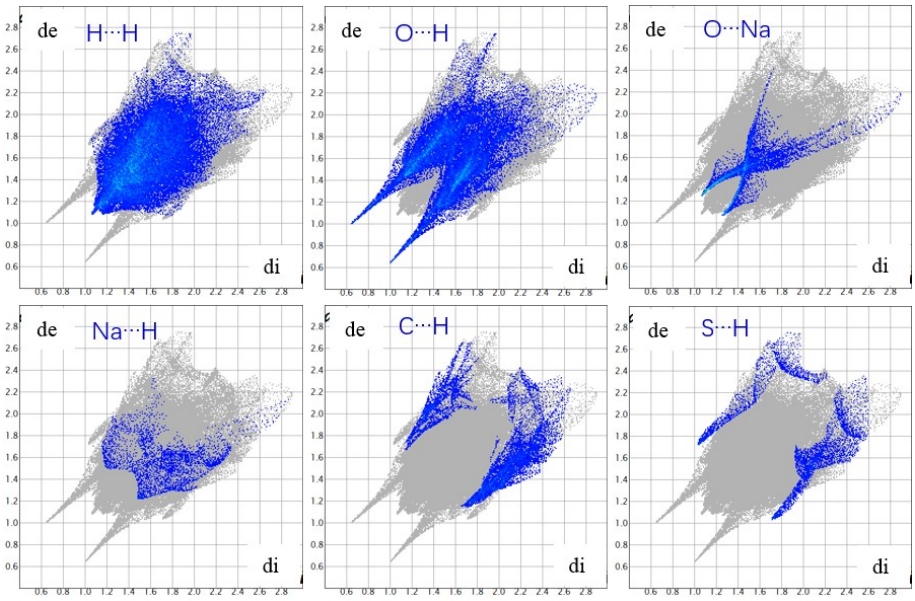

Figure S10. Detailed distribution of different interactions in $S_{M\text{-}M.}$

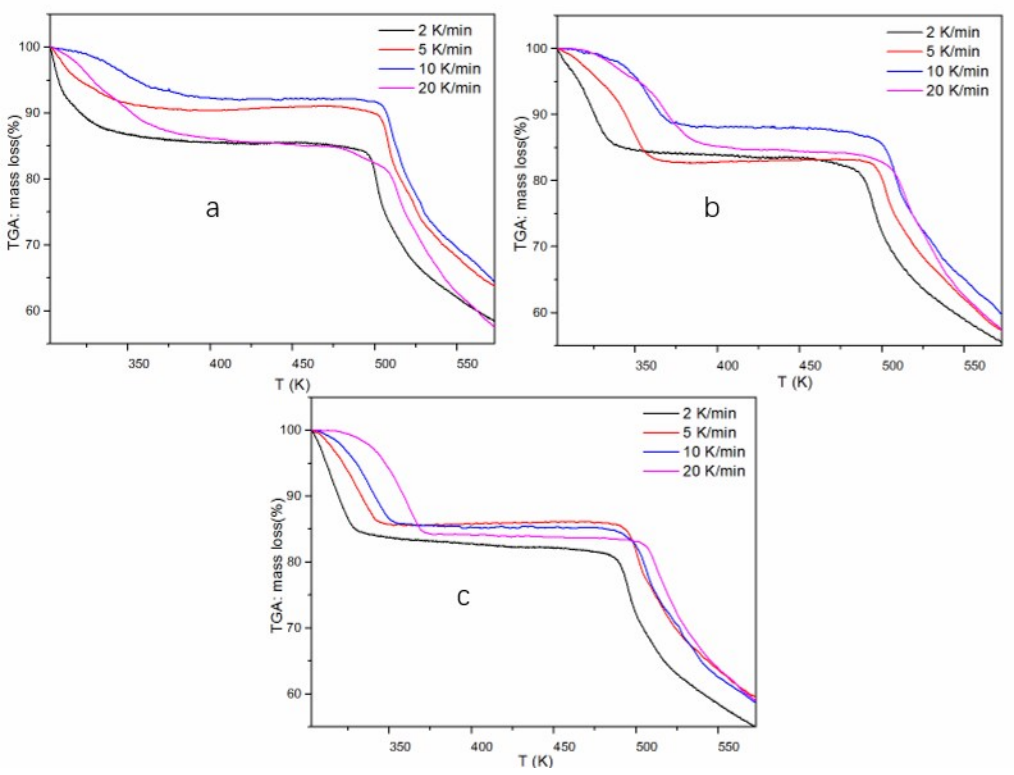

Figure S11. TGA curves of three solvates using different heating rates: (a) $S_{M\text{-}M}$ (b) $S_{E\text{-}M}$ (c) $S_{M\text{-}E}$

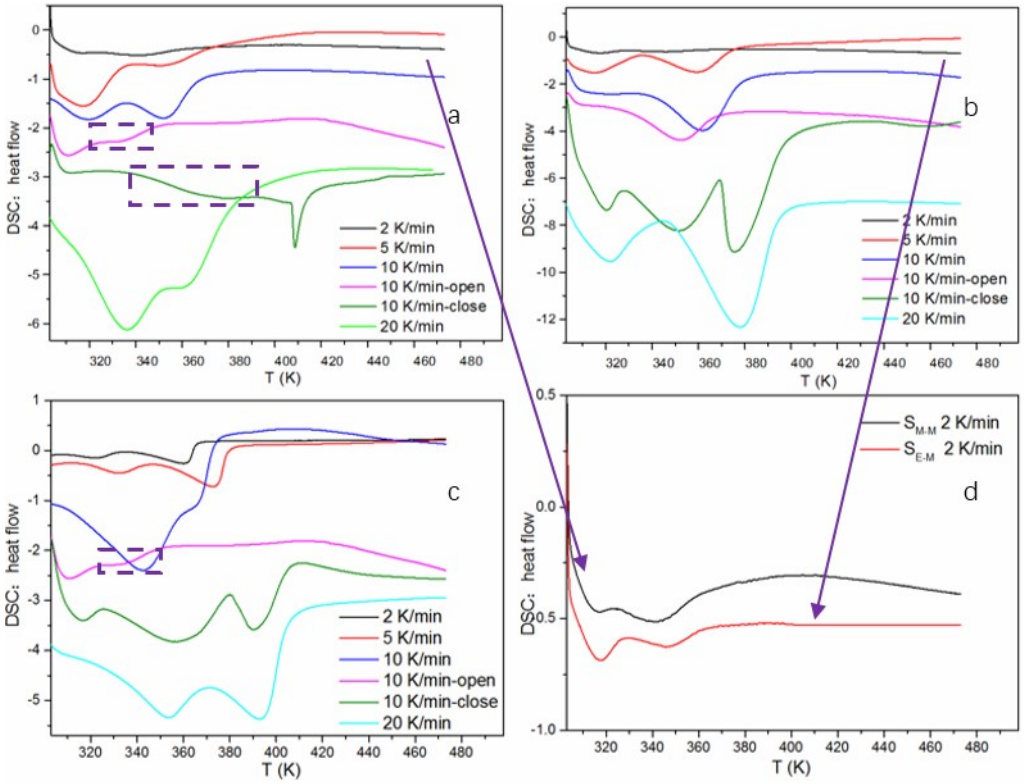

Figure S12. DSC curves of these three solvates using different heating rates: (a) $S_{M\text{-}M}$ (b) $S_{E\text{-}M}$ (c) $S_{M\text{-}E}$ (d) $S_{M\text{-}M}$ and $S_{E\text{-}M}$ with 2 K/min (wide endothermic peaks are marked with dotted line)

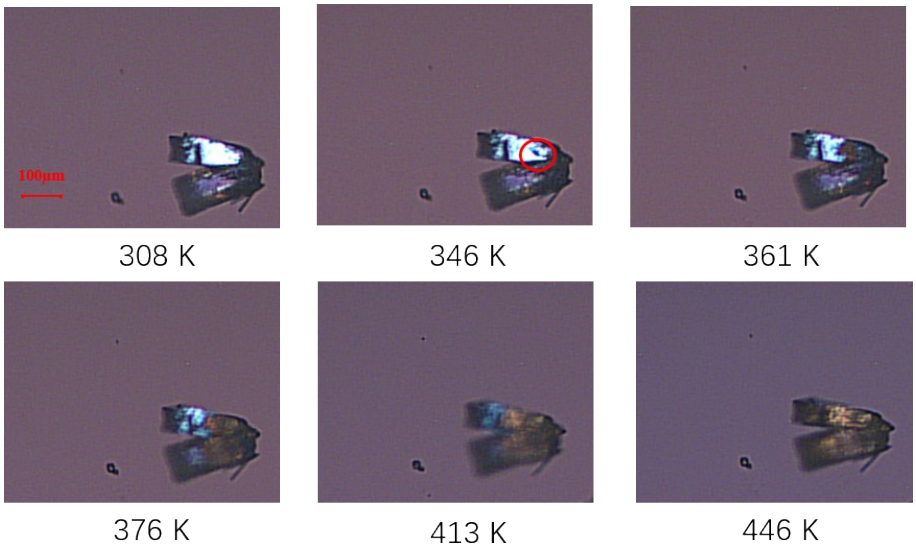

Figure S13. HSM images of $S_{E\text{-}M}$ during the heating process.

Figure S14. HSM images of S_{M-E} during the heating process.

Table S1 Relevant hydrogen bond data of form I and S_{M-M}

	D-H···A	d(D-H), Å	d(H···A), Å	d(D-A), Å	∠(DHA), °
Form I	O_5-H···O_2	0.942	1.817	2.565	133.580
	C_{15A}-H···O_4	0.93	1.992	2.875	157.818
S_{M-M}	O_{MT}-H···O_{MAC}	0.848	2.337	2.863	174.366
	N_2-H···O_1	0.880	2.063	2.941	175.080
	O_5-H···O_2	0.840	1.808	2.610	159.150

Table S2 The relevant data in the calculation of the packing coefficient C_k

	V_{mol}	V_{cell}	C_k
Form I	337.84	1852.9	0.7293
Structure 2	372.71	2388.6	0.6322
S_{M-M}	442.05	2388.6	0.7403

Notes and references

1. D. J. J.J. McKinnon, M.A. Spackman, , *Chem Commun (Camb)*, 2007 3814-3816.

2. R. Li, Q. Li, J. Cheng, Z. Liu and W. Li, *Chemphyschem*, 2011, **12**, 2289-2295.

3. J. Rezac, Y. Huang, P. Hobza and G. J. Beran, *J Chem Theory Comput*, 2015, **11**, 3065-3079.