Electronic Supplementary Material (ESI) for RSC Advances.
This journal is © The Royal Society of Chemistry 2014

SUPPORTING INFORMATION:

Mechanistic Insight into the Selective Crystallization of the Metastable Polymorph of Tolbutamide in Ethanol-water Solution

Jinli Zhang, Yujia Wu, Anyuan Liu, Wei Li, You Han*

School of Chemical Engineering & Technology, Tianjin University, Tianjin 300072, People's Republic of China

* To whom correspondence should be addressed.

Dr. You Han

Associate Professor

School of Chemical Engineering and Technology,

Tianjin University

92 Weijin Road, Tianjin 300072, china

Tel: +86-22-27401476

Fax: +86-22-27403389

E-mail: yhan@tju.edu.cn

Website: http://cpi.tju.edu.cn/

Table S1. Crystallographic Data of TB Polymorphs

Crystal Data	Form I[L]	Form II	Form III	Form IV	Form V
Chemical formula	C12H18N2O3S	C12H18N2O3S	C12H18N2O3S	C12H18N2O3S	C12H18N2O3S
Formula weight	270.34	270.34	270.34	270.34	270.34
Space group	Pna21	Pc	P21/n	P21/c	Pbcn
Temperature (K)	153	153	153	298	298
a/ Å	19.626(9)	9.087(8)	11.735(2)	10.091	15.851(6)
b/ Å	7.803(4)	17.228(3)	9.042(8)	15.646	9.288(4)
c/ Å	9.058(4)	17.951(4)	13.732(3)	9.261	19.691(8)
α（°）	90	90	90	90	90
β（°）	90	95.01(3)	103.57(3)	100.49	90
γ（°）	90	90	90	90	90
Z	4	8	4	4	8
V/ Å^3	1387.3(11)	2799.8(10)	1416.4(5)	1438.9	2899.2(19)
d_{calc}/g cm^{-3}	1.294	1.283	1.268	1.248	1.239

The crystallographic data of TB polymorphs were obtained from the work of Tan[1] and Nangia[2].

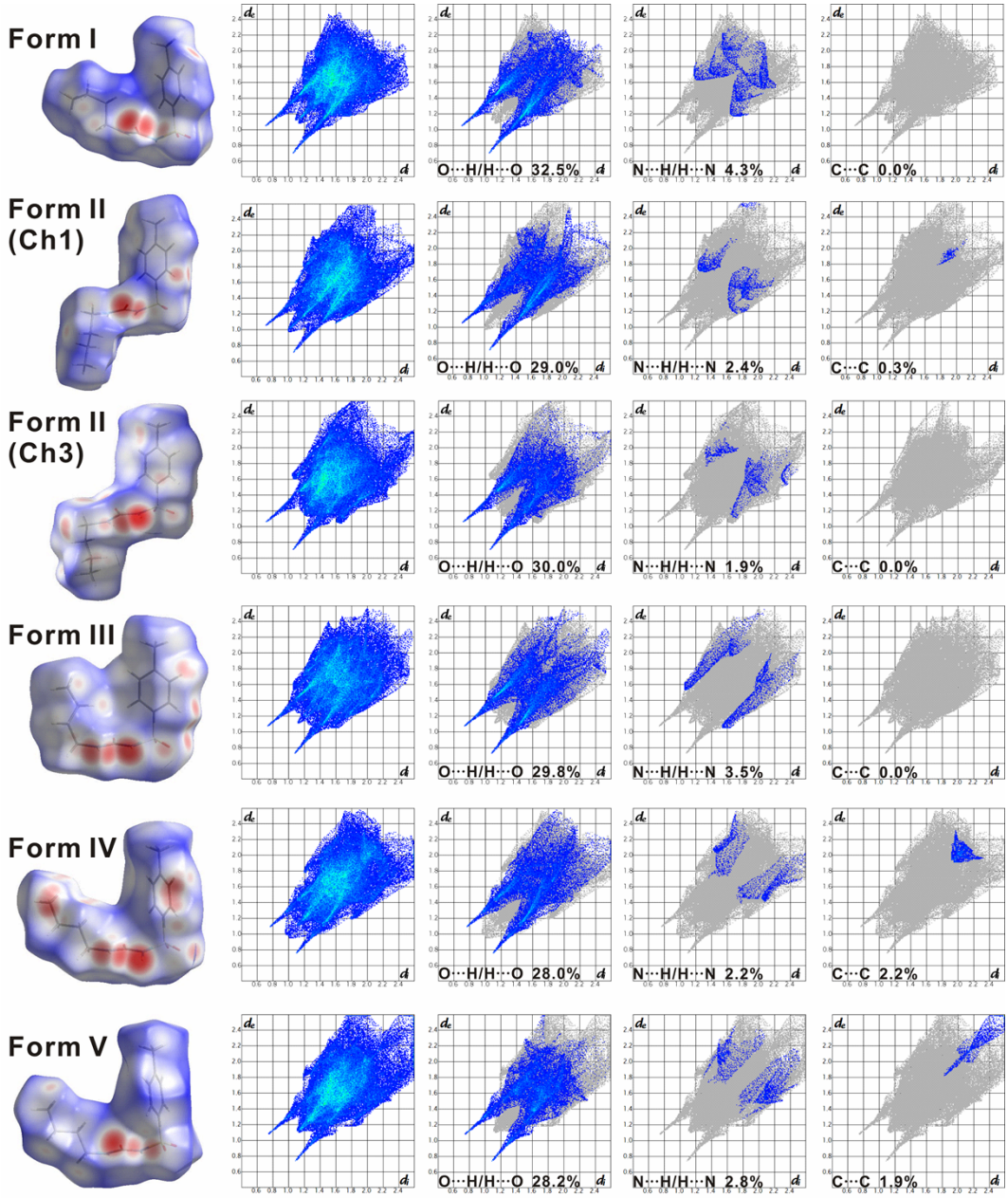

Figure S1. Hirshfeld surfaces mapped with d_{norm} and 2D fingerprint plots of TB polymorphs: Full (left) and resolved into O···H/H···O , N···H/H···N and C···C (right) contacts showing the percentages of contacts contributed to the total Hirshfeld surface area of molecules (Ch2 and Ch4 in Form II are not shown due to similarity of Ch1 and Ch2, Ch3 and Ch4).

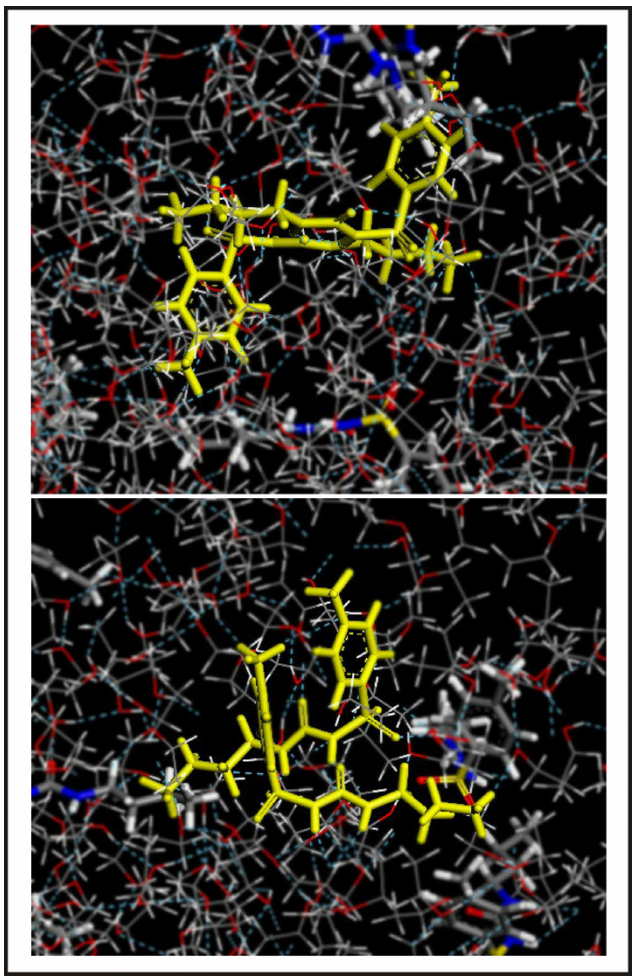

Figure S2. Snapshots of the MD trajectory showing the A-type (top) and B-type (bottom) dimers of TB molecules, respectively.

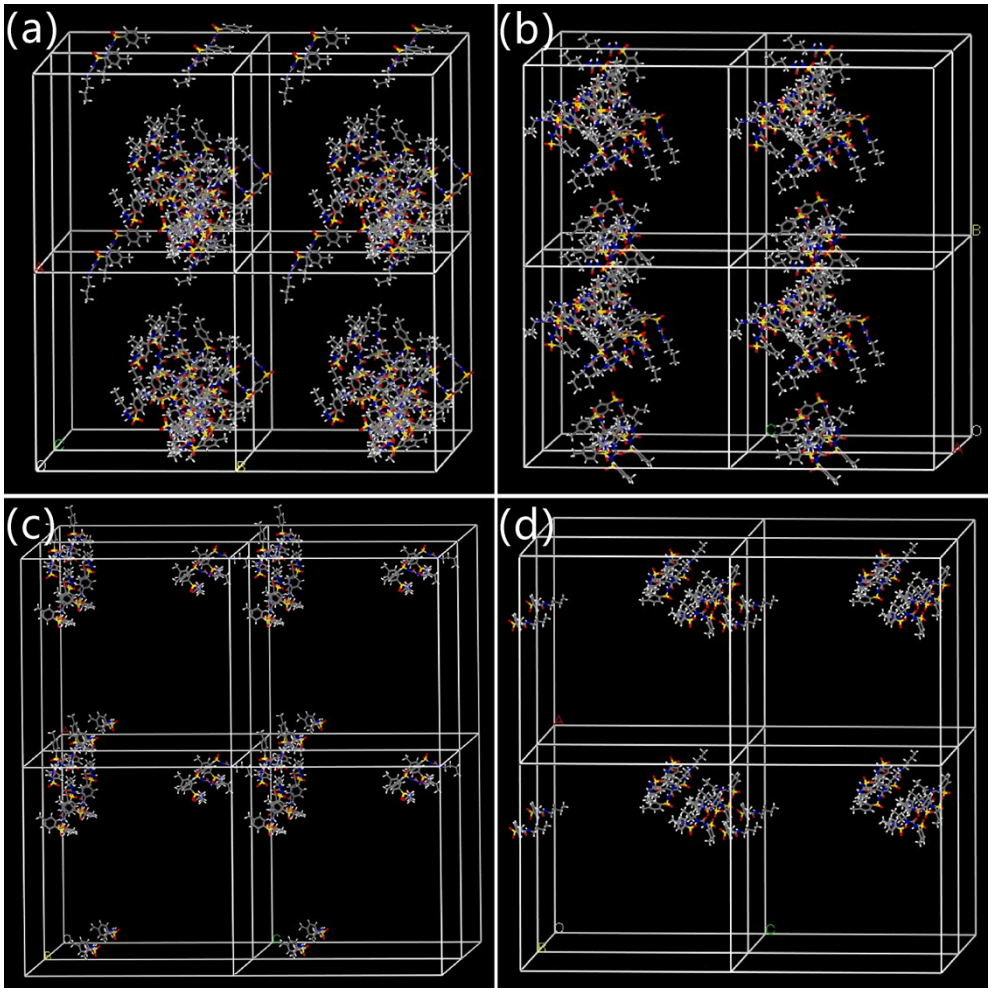

Figure S3. Snapshots of the TB clusters for (a) S_e=3.5 system (b) S_e=2.7 system (c) $S_{e\text{-}w}$=3.5 system (d) $S_{e\text{-}w}$=2.7 system at the end of the simulation (ethanol and water molecules are not shown for clarity).

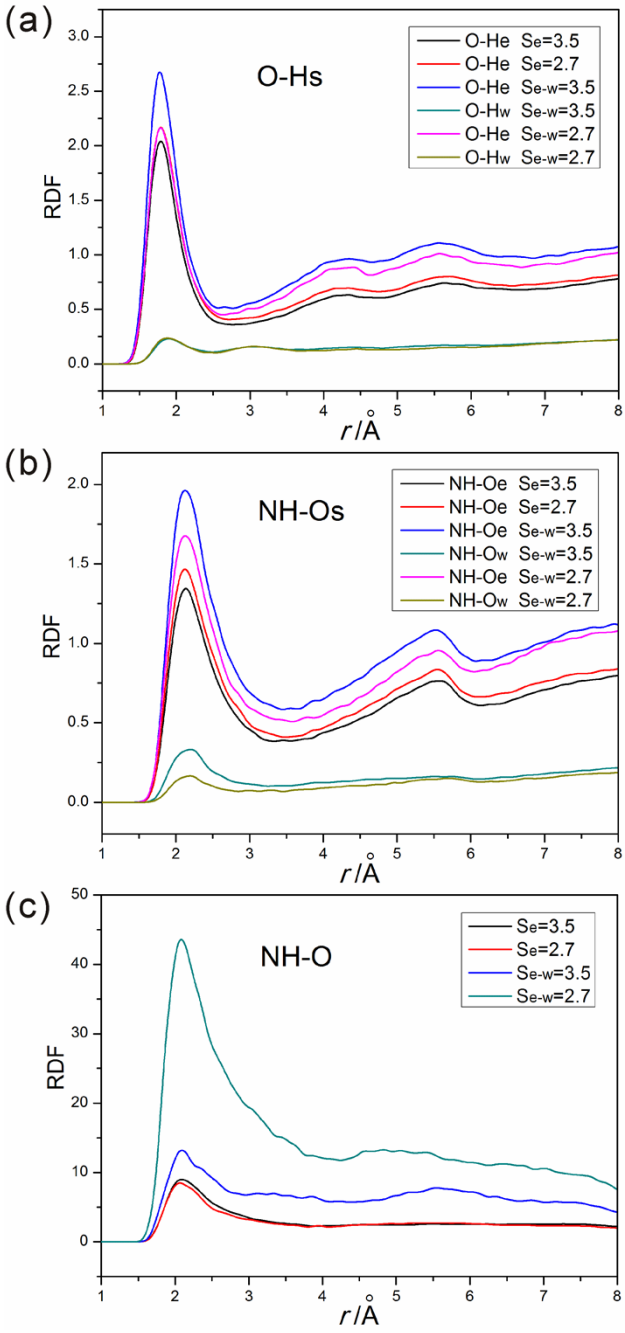

Figure S4. RDFs between (a) O atoms in TB molecules and H atoms in solvent molecules (b) NH atoms in TB molecules and O atoms in solvent molecules (c) intermolecular NH atoms and O atoms in TB molecules under different conditions.

Literature Cited in this supplementary material.

1 S. Thirunahari, S. Aitipamula, P. S. Chow and R. B. H. Tan, *J. Pharm. Sci.*, 2010, **99**, 2975-2990.
2 N. K. Nath and A. Nangia, *CrystEngComm*, 2011, **13**, 47-51.