Supporting Information

The heterogeneous nucleation of pimelic acid under the effect of template: experimental research and molecular simulation

Peng Yang,[ab] Ian Rosbottom,[b] Zhonghua Li,[a] Vivek Verma,[b] Songgu Wu,[a] Junbo Gong*[a] and Jerry Y. Y. Heng*[b]

[a] School of Chemical Engineering and Technology, Tianjin University, Tianjin 300072, China

[b] Department of Chemical Engineering, Imperial College London, London SW7 2AZ, UK

E-mail: junbo_gong@tju.edu.cn (J. Gong); jerry.heng@imperial .ac.uk (J. Y. Y. Heng).

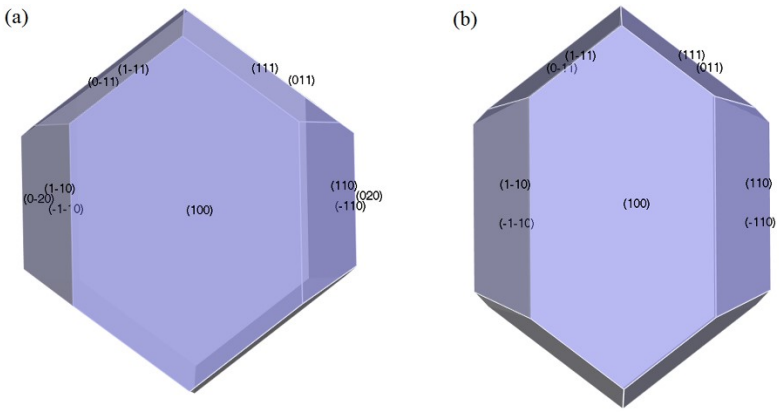

Fig. S1 The predicted morphology of malonamide by AE model (a) and BFDH model (b).

Table S1. The crystal habit parameters of malonamide predicted by AE model.

(*h k l*)	Multiplicity	d_{hkl} /Å	E_{att}(Total) / kcal mol^{-1}	E_{att}(vdW) / kcal mol^{-1}	E_{att}(Electrostatic) / kcal mol^{-1}	Area /%
(1 0 0)	2	12.38	-49.06	-24.56	-24.50	43.08
(1 1 0)	4	7.57	-91.23	-41.67	-49.56	19.01
(0 1 1)	4	5.75	-102.98	-49.79	-53.19	24.87
(1 1 1)	4	5.60	-107.40	-52.18	-55.22	11.94

[a] E_{att} refers to the released energy by adding a growth slice to a growing crystal surface.

Table S2. The crystal habit parameters of pimelic acid predicted by BFDH model.

Polymorph	Crystal face/(*h k l*)	Multiplicity	Area /%
Form I	(2 0 0)	2	43.02
	(1 1 0)	4	15.86
	(2 0 -2)	2	13.14
	(1 1 -1)	4	14.45
Form II	(0 1 1)	4	53.24
	(0 0 2)	2	17.84
	(1 0 -4)	2	14.68
	(1 0 -2)	2	7.78

A point of view for analyzing the selective nucleation of pimelic acid

The adsorption energies between template molecules and main crystal faces of Form I/II were calculated and shown in Table S3 and Fig.S2. In Fig. S2, the adsorption energies between single template molecule and the most dominant crystal faces of Form I/II are -21.84 and -28.04 kcal mol^{-1}, respectively, which means that the adsorption of template molecule on the (0 1 1) face of Form II is significantly stronger than the adsorption on the (2 0 0) face of Form I, so the template is more likely to induce the nucleation of Form II. When the number of template molecules increases from 1 to 10, the total adsorption energies between 10 template molecules and crystal faces increase accordingly.

Table S3. The adsorption energies between template molecules and crystal faces of pimelic acid.

Polymorph	Crystal face /(*h k l*)	Area /%	E_{ad}(with 1 template molecule) /(kcal mol^{-1})	E_{ad}(average energy for 10 template molecules) /(kcal mol^{-1})
Form I	(2 0 0)	43.02	-21.84	-22.12
	(1 1 0)	15.86	-21.31	-19.17
	(2 0 -2)	13.14	-24.31	-17.82
	(1 1 -1)	14.45	-28.59	-22.65
Form II	(0 1 1)	53.24	-28.04	-23.86
	(0 0 2)	17.84	-20.93	-20.49
	(1 0 -4)	14.68	-25.40	-19.03
	(1 0 -2)	7.78	-28.19	-19.17

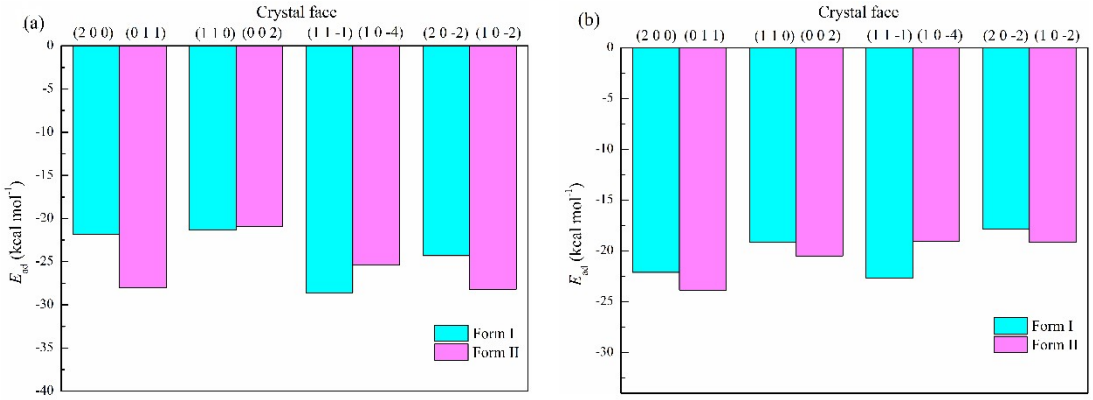

Fig. S2 Adsorption energies between template molecules and crystal faces of API: (a) single template molecule; (b) the average energy for 10 template molecules.

Furthermore, the average energy for 10 template molecules in Fig. S2b indicates that the template molecules adsorb more strongly to the (0 1 1) face of Form II with an adsorption energy that is -23.86 kcal mol^{-1} higher than that of the (2 0 0) face of Form I (-22.12 kcal mol^{-1}). As a result, the adsorption energies between the template molecules and dominant crystal faces may further explain the induction effect of the template on the nucleation of Form II. In addition, the picture of 10 molecules adsorbed on the crystal surface is shown in Fig.S3.

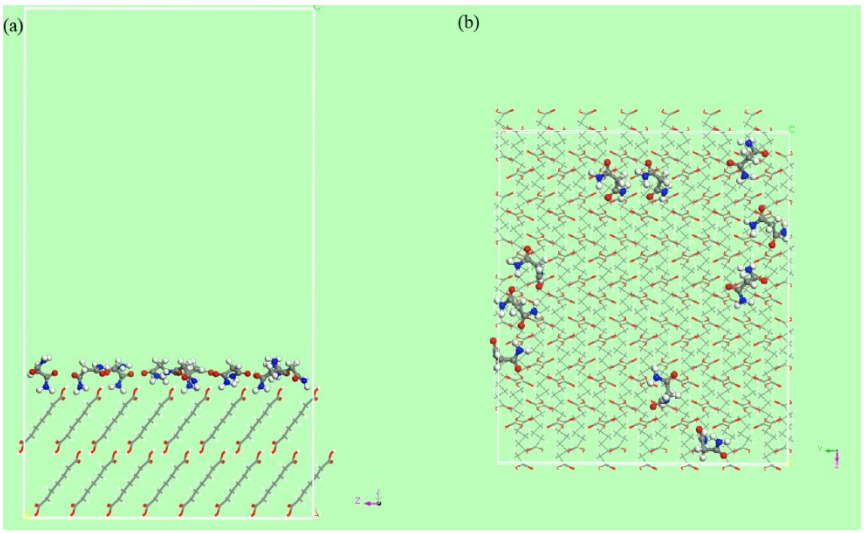

Fig. S3 The picture of 10 molecules adsorbed on the crystal surface:(a) main view, (b) top view.