Supporting information for article:

Probing the structural pathway of conformational polymorph nucleation: by comparing a series of α,ω-alkanedicarboxylic acids

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The solubility measurement methods and results are shown in Table S1. Table S2 and S3 showed the crystallographic data of form I and form II of 6 diacids used in this work, respectively. Table S4 and S5 showed Experimental details of new structures of DA13 and DA15. PES scan of DA5 and DA11 about the rotatable bond $\tau_2$ from -180° to 180° with $\tau_1$ fixed at different values in solvents was presented in Fig. S1. The molecular structures of additives used in this study were shown as Fig. S2.

CCDC 1941171–1941172 (for the structures of form II of DA13 and DA15) contain the supplementary crystallographic data for this paper.

S1. Solubility Measurements

A gravimetric method was employed to determine the solubility of the stable form I of diacids in some mono-solvents (showed in Table S1) at 298.15 K. In this process, excess solid diacids and corresponding single, were added to 50 mL flasks so that to obtain the suspensions. Then the suspensions were shaken by a thermostatic bath shaker (CHY1015, Shanghai Sunny Hengping Scientific Instrument Co. Ltd., China) at a certain temperature under uncertainty of 0.1 K. And this process would last for 12 h which had been proved to be long enough to achieve solid-liquid equilibrium in preliminary experiment. After turning off the bath shaker, 5 mL of the supernatant liquor was filtered by the pre-cooled/heated syringes filters (0.22 µm) and moved into pre-weighted glass dishes as quickly as possible. Immediately, the total weight was determined. After that, the dishes were dried in a vacuum oven (DZ-2BC, Tianjin Taisite Instrument Co. Ltd., China) at $T=343.15$ K and their mass was periodically measured until the data remained constant, which meant that the solvent had been completely evaporated. In all above experiments, the masses were determined by an electronic balance (AB204-N, Mettler-Toledo, Switzerland) with an accuracy of ± 0.0001 g. The experiment was repeated three times for error reduction, and the result was from the average value.

The solubility of metastable form II of diacids was determined by dynamic method using the laser monitoring observation technique. At a given temperature, a fixed mass of solvent was added in the vessel with stirring. To avoid the solvent losses due to evaporation, a condenser was connected to the vessel. After the temperature of vessel was stable, a fixed amount of form II was added in the vessel. When the solid in the vessel disappeared completely, and the intensity of the transmitted laser through the solution reached the maximal value, the maximal value of the intensity was recorded as $I_{\text{max}}$. Then a small amount of form II which was accurately weighed was put into the vessel, after which the intensity of the transmitted laser decreased immediately. However, if the solution is unsaturated, the new added solid will dissolve gradually, and the maximum intensity of transmitted laser will be
reached at the end. The same procedure was repeated until the solution reached the saturation point. Then the total mass of form II added to the vessel was recorded and the solubility can be calculated. The interval of every addition was 60 min. For each measuring point, the same experiment was carried out three times.

The mole fraction solubility of diacids ($x_1$) was calculated by using Eq. (S1):

$$x_1 = \frac{m_1/M_1}{m_1/M_1 + m_2/M_2}$$

(S1)

Where $m_1$ represents the mass of solute diacids, $m_2$ mean the masses of solvents. $M_1$ and $M_2$ are the corresponding molecule mass of them.

The solubility of DA5, DA7, DA9, DA11, DA13 and DA15 (form I) and those of DA7, DA9, DA11, DA13 and DA15 (form II) in 4 mono-solvents was shown in Table S1.

| Solvent         | diacid | Molar solubility(form I) | Molar solubility(form II) |
|-----------------|--------|--------------------------|----------------------------|
| ethyl acetate   | DA5    | 0.123\(^a\)              | -                          |
|                 | DA7    | 0.0517\(^a\)             | 0.0541                     |
|                 | DA9    | 0.0161\(^a\)             | 0.0168                     |
|                 | DA11   | 0.00456                  | 0.00466                    |
|                 | DA13   | 0.00149\(^b\)            | 0.00152                    |
|                 | DA15   | 0.00105                  | 0.00108                    |
| 1,4-dioxane     | DA5    | 0.304                    | -                          |
|                 | DA7    | 0.138                    | 0.155                      |
|                 | DA9    | 0.0823                   | 0.0902                     |
|                 | DA11   | 0.0234                   | 0.0263                     |
|                 | DA13   | 0.0151                   | 0.0165                     |
|                 | DA15   | 0.00680                  | 0.00762                    |
| ethanol         | DA5    | 0.176\(^a\)              | -                          |
|                 | DA7    | 0.104\(^a\)              | 0.120                      |
|                 | DA9    | 0.0707\(^a\)             | 0.0775                     |
|                 | DA11   | 0.0273                   | 0.0321                     |
acetic acid\textsuperscript{a} DA5 0.221\textsuperscript{a} - \\
DA7 0.0964\textsuperscript{a} 0.105 \\
DA9 0.0524\textsuperscript{a} 0.0583 \\
DA11 0.0257 0.0285 \\
DA13 0.00418\textsuperscript{b} 0.00448 \\
DA15 0.00134 0.00150 \\
\textsuperscript{a} Reference(Zhang et al., 2014) is the source of data. \\
\textsuperscript{b} Reference(Tang et al., 2015) is the source of data.

Table S2  Crystallographic data of form I of 6 diacids.

|           | DA5-1\textsuperscript{a} | DA7-1\textsuperscript{b} | DA9-1\textsuperscript{b} | DA11-1\textsuperscript{c} |
|-----------|---------------------------|---------------------------|---------------------------|---------------------------|
| Formula   | C\textsubscript{5}H\textsubscript{8}O\textsubscript{4} | C\textsubscript{7}H\textsubscript{12}O\textsubscript{4} | C\textsubscript{9}H\textsubscript{16}O\textsubscript{4} | C\textsubscript{11}H\textsubscript{20}O\textsubscript{4} |
| Crystal system | monoclinic | monoclinic | monoclinic | monoclinic |
| Space group | C2/c | C2/c | C2/c | C2/c |
| T(K)      | 150(2) | 130 | 130 | 133(2) |
| a(Å)      | 12.964(18) | 17.7028(9) | 22.6366(1) | 26.597(7) |
| b(Å)      | 4.758(7) | 4.7270(2) | 4.7143(1) | 4.7030(11) |
| c(Å)      | 9.747(14) | 9.6713(4) | 9.6162(3) | 9.604(3) |
| β(°)      | 98.12(2) | 106.580(1) | 110.809(2) | 107.899(4) |
| Cell volume(Å\textsuperscript{3}) | 595.2(15) | 775.656 | 959.261 | 1143.2(5) |
| Density(g/cm\textsuperscript{3}) | 1.474 | 1.372 | 1.303 | 1.257 |
| Z         | 4 | 4 | 4 | 4 |
| R\textsubscript{int} & 0.0389 | - | - | 0.0344 |
| R\textsubscript{1}(I>2σ(I)) & 0.0376 | 0.0507 | 0.0454 | 0.0309 |
| CCDC      | 1061299 | 1233866 | 1104213 | 1841530 |

\textsuperscript{a} Reference(Mishra et al., 2015) is the source of data. \\
\textsuperscript{b} Reference(Thalladi et al., 2000) is the source of data. \\
\textsuperscript{c} Reference(Shi et al., 2018) is the source of data.
Table S3  Crystallographic data of form II of 6 diacids.

|                | DA5-II<sup>a</sup> | DA7-II<sup>b</sup> | DA9-II<sup>c</sup> | DA11-II<sup>c</sup> | DA13-II | DA15-II |
|----------------|--------------------|--------------------|--------------------|--------------------|---------|---------|
| Formula        | C₅H₈O₄            | C₇H₁₂O₄           | C₉H₁₆O₄           | C₁₁H₂₀O₄          | C₁₃H₂₄O₄| C₁₅H₂₈O₄|
| Crystal system | monoclinic         |                    |                    |                    |         |         |
| Space group    | C₂/c               | P₂₁/c              | P₂₁/c              | P₂₁/c              | P₂₁/n   | P₂₁/c   |
| T(K)           | 348                | 204                | 120                | 133                | 133     | 128     |
| a(Å)           | 25.593             | 5.5593             | 5.5124             | 5.5078             | 5.5195  | 5.4671  |
| b(Å)           | 5.0024             | 9.5787             | 9.4609             | 9.4058             | 9.4058  | 9.2806  |
| c(Å)           | 10.1667            | 15.1193            | 18.8726            | 22.554             | 26.283  | 29.8270 |
| β(°)           | 92.740             | 90.972             | 95.932             | 94.018             | 90.84   | 94.449  |
| Cell volume(Å³) | 1300.1             | 805                | 978.978            | 1165.6             | 1364.3  | 1508.80 |
| Density(g/cm³) | 1.355              | 1.313              | 1.277              | 1.232              | 1.189   | 1.199   |
| Z              | 8                  | 4                  | 4                  | 4                  | 4       | 4       |
| R<sub>int</sub>| 0.0719             | 0.0502             | 0.0774             | 0.0421             | 0.0811  | 0.0691  |
| R₁(I>2sigma(I))| -                  | 0.0386             | 0.0689             | 0.0326             | 0.0575  | 0.0483  |
| CCDC           | 891106             | 929796             | 929807             | 1841531            | 1941171 | 1941172 |

<sup>a</sup> Reference (Espeau et al., 2013) is the source of data.

<sup>b</sup> Reference (Bhattacharya et al., 2013) is the source of data.

<sup>c</sup> Reference (Shi et al., 2018) is the source of data.

Table S4  Experimental details of DA13

| Crystal data |
|--------------|
| Chemical formula | C₁₃H₂₄O₄  |
| M<sub>r</sub>   | 244.32     |
| Crystal system, space group | Monoclinic, P₂₁/n |
| Temperature (K) | 113        |
| a, b, c (Å)     | 5.5195 (11), 9.4058 (19), 26.283 (5) |
β (°) 90.84 (3)

$V$ (Å$^3$) 1364.3 (5)

$Z$ 4

Radiation type Mo $K\alpha$

$\mu$ (mm$^{-1}$) 0.09

Crystal size (mm) 0.20 × 0.18 × 0.15

Data collection

Diffractometer Rigaku Saturn 70 CCD

Absorption correction Multi-scan

$T_{\text{min}}, T_{\text{max}}$ 0.764, 1

No. of measured, independent and observed [I > 2σ(I)] reflections 12368, 3215, 2511

$R_{\text{int}}$ 0.053

(sin $\theta$/λ)$_{\text{max}}$ (Å$^{-1}$) 0.658

Refinement

$R[F^2 > 2\sigma(F^2)], wR(F^2), S$ 0.057, 0.235, 1.03

No. of reflections 3215

No. of parameters 156

H-atom treatment H-atom parameters constrained

$\Delta\rho_{\text{max}}, \Delta\rho_{\text{min}}$ (e Å$^{-3}$) 0.47, −0.50

Computer programs: CrystalClear (Rigaku Inc., 2008), ShelXT (Sheldrick, 2015), SHELXL (Sheldrick, 2015), Olex2 (Dolomanov et al., 2009)

Table S5 Experimental details of DA15

Crystal data

Chemical formula C$_{15}$H$_{28}$O$_4$
Crystal system, space group: Monoclinic, $P2_1/c$

Temperature (K): 128

$a, b, c$ (Å): 5.4671 (3), 9.2806 (5), 29.8270 (14)

$\beta$ (°): 94.449 (4)

$V$ (Å$^3$): 1508.80 (14)

$Z$: 4

Radiation type: Mo $K\alpha$

$\mu$ (mm$^{-1}$): 0.09

Crystal size (mm): 0.34 × 0.26 × 0.16

Data collection

Diffractometer: Rigaku Saturn 70

Absorption correction: CrystAlis PRO 1.171.39.46 (Rigaku Oxford Diffraction, 2018) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.

$T_{\text{min}}, T_{\text{max}}$: 0.787, 1.000

No. of measured, independent and observed [$I > 2\sigma(I)$] reflections: 14484, 3599, 2690

$R_{\text{int}}$: 0.052

$(\sin \theta/\lambda)_{\text{max}}$ (Å$^{-1}$): 0.658

Refinement

$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, $S$: 0.048, 0.130, 1.04

No. of reflections: 3599

No. of parameters: 180
H-atom treatment  

\[ \Delta \rho_{\text{max}}, \Delta \rho_{\text{min}} \text{ (e Å}^{-3} \text{)} \quad 0.27, -0.20 \]

Computer programs: CrystalClear (Rigaku, 2008), CrysAlis PRO 1.171.39.46 (Rigaku OD, 2018), ShelXT (Sheldrick, 2015), SHELXL (Sheldrick, 2015), Olex2 (Dolomanov et al., 2009).

Figure S1  PXRD patterns of DA5 for experiments in Table 1.
**Figure S2** PXRD patterns of DA7 for experiments in Table 1.
Figure S3  PXRD patterns of DA9 for experiments in Table 1.

Figure S4  PXRD patterns of DA11 for experiments in Table 1.
Figure S5 PXRD patterns of DA13 for experiments in Table 1.

Figure S6 PXRD patterns of DA15 for experiments in Table 1.
Figure S7  PES scan of DA5 and DA11 about the rotatable bond τ2 from -180° to 180° with τ1 fixed at different values in solvents. (a) DA5 in ethanol; (b) DA11 in ethanol; (c) DA5 in 1,4-dioxane; (d) DA11 in 1,4-dioxane.

Figure S8  The molecular structures of additives.
**Figure S9**  PXRD patterns of DA5 for additive experiments in Table 3(AA as additives)

**Figure S10**  PXRD patterns of DA5 for additive experiments in Table 3(BA as additives)
Figure S11  PXRD patterns of DA7 for additive experiments in Table 3 (AA as additives)

Figure S12  PXRD patterns of DA7 for additive experiments in Table 3 (BA as additives)
**Figure S13**  PXRD patterns of DA9 for additive experiments in Table 3 (AA as additives)

**Figure S14**  PXRD patterns of DA9 for additive experiments in Table 3 (BA as additives)
**Figure S15**  PXRD patterns of DA11 for additive experiments in Table 3(AA as additives)

**Figure S16**  PXRD patterns of DA11 for additive experiments in Table 3(BA as additives)
Figure S17 Solution IR spectra of additives in DA5 solution at initial 1.75 M in dioxane over a concentration range. (b) adipic acid; (d) benzoic acid.