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Supporting information for article:

Do Carboximide–Carboxylic Acid Combinations Form Co-crystals? Role of Hydroxyl Substitution on the Formation of Co-crystals and Eutectics

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Section S1: Experimental details

Materials: Commercially available compounds (Sigma-Aldrich, Bengaluru, India) were used without further purification. Solvents were of analytical or chromatographic grade and purchased from local suppliers.

Methods
Grinding: Compounds in molar ratios combined on the 100 mg scale were subjected to both neat and liquid-assisted grinding (with 1-2 mL acetonitrile) for 15 min using a mortar-pestle. The ground materials were analyzed by PXRD and melting point to ascertain the formation of the cocrystal or eutectic.

Evaporative Crystallization: Ground mixtures of different combinations were kept for crystallization at ambient conditions in different solvents viz. methanol, ethanol, propanol, acetone, Tetrahydrofuran (THF), 1,4-dioxane (14D), acetonitrile, ethyl acetate, DMF, DMSO etc. Majority of the cocrystal-forming combinations gave single crystals of cocrystals and eutectic-forming combinations separated into parent compounds upon crystallization.

1:1 SM–4HBA: Ground mixture of SM (10 mg, 0.1 mmol) and 4HBA (14 mg, 0.1 mmol) was dissolved in 5 mL methanol and left for slow evaporation at room temperature. Colorless block crystals were obtained after a few days upon solvent evaporation.

1:1 SM–24DHBA polymorphs: Ground mixture of SM (10 mg, 0.1 mmol) and 24DHBA (15.5 mg, 0.1 mmol) was dissolved in different solvents and left for slow evaporation at room temperature. Polymorph I crystallized as colorless needles from nitromethane and polymorph II as colorless block crystals from 14D after a few days upon solvent evaporation.

1:2 SM–34HBA: Ground mixture of SM (10 mg, 0.1 mmol) and 34DHBA (15.5 mg, 0.1 mmol) was dissolved in 5 mL acetonitrile and left for slow evaporation at room temperature. Colorless plate crystals were obtained after a few days upon solvent evaporation.

1:3:3 SM–35DHBA–H₂O: Ground mixture of SM (10 mg, 0.1 mmol) and 35DHBA (15.5 mg, 0.1 mmol) was dissolved in 5 mL methanol and left for slow evaporation at room temperature. Colorless block crystals were obtained after a few days upon solvent evaporation.
2:1 SM–345THBA polymorphs: Ground mixture of SM (10 mg, 0.1 mmol) and 345THBA (17 mg, 0.1 mmol) was dissolved in different solvents viz. methanol, ethanol, propanol, acetone, Tetrahydrofuran (THF), 1,4-dioxane (14D), acetonitrile, ethyl acetate, DMF, DMSO and left for slow evaporation at room temperature. Polymorph I crystallized as colorless needles from methanol, ethanol, acetone and THF and polymorph II as colorless needles from DMF and DMSO upon solvent evaporation.

1:1 MM–4HBA: Ground mixture of MM (10 mg, 0.1 mmol) and 4HBA (14 mg, 0.1 mmol) was dissolved in 5 mL THF and left for slow evaporation at room temperature. Colorless block crystals were obtained after a few days upon solvent evaporation.

1:1 MM–24DHBA: Ground mixture of MM (10 mg, 0.1 mmol) and 24DHBA (15.5 mg, 0.1 mmol) was dissolved in 5 mL 14D and left for slow evaporation at room temperature. Colorless plate crystals were obtained after a few days upon solvent evaporation.

1:3:3 MM–35DHBA–H2O: Ground mixture of MM (10 mg, 0.1 mmol) and 35DHBA (15.5 mg, 0.1 mmol) was dissolved in 5 mL THF and left for slow evaporation at room temperature. Colorless plate crystals were obtained after a few days upon solvent evaporation.

1:2 GM–4HBA: Ground mixture of GM (11 mg, 0.1 mmol) and 4HBA (14 mg, 0.1 mmol) was dissolved in 5 mL n-propanol and left for slow evaporation at room temperature. Colorless needles crystals were obtained after a few days upon solvent evaporation.

1:1 GM–35DHBA: Ground mixture of GM (11 mg, 0.1 mmol) and 35DHB A (15.5 mg, 0.1 mmol) was dissolved in 5 mL methanol and left for slow evaporation at room temperature. Colorless needles crystals were obtained after a few days upon solvent evaporation.

Single crystal X-ray diffraction: X-ray reflections on suitable single crystals were collected on an Oxford Xcalibur (Mova) diffractometer equipped with an EOS CCD detector and a microfocus sealed tube using Mo Kα radiation (λ = 0.71073 Å). Data collection and reduction was performed using CrysAlisPro (version 1.171.36.32)S1 and OLEX2 (version 1.2)S2 was used to solve and refine the crystal structures. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms on O and N were located from difference electron density maps (except in 1:3:3
SM–35DHBA–H₂O and 1:3:3 MM–35DHBA–H₂O where hydrogens were vaguely resolved) and all C–H atoms were fixed geometrically using HFIX command. The WinGX package was used for final refinement and production of CIFs and crystallographic tables.

**Powder X-ray Diffraction:** PXRD were recorded on PANalytical X'Pert diffractometer using Cu-Kα X-radiation (λ = 1.54056 Å) at 40 kV and 30 mA. X'Pert HighScore Plus (version 1.0d) was used to collect and plot the diffraction patterns. Diffraction patterns were collected over 2θ range of 5–40° using a step size of 0.06° 2θ and time per step of 1 sec.

**Thermal analysis:** Different compositions of eutectic-forming combinations were analyzed for their solidus-liquidus temperatures on a Labindia visual melting range apparatus (MR 13300710) equipped with a camera and a LCD monitor.

**Packing Diagrams:** X-Seed was used to prepare packing diagrams.
### Section S2:

#### Table S1: Crystallographic parameters of succinimide cocrystals.

| Cocystal                  | 1:1 SM–4HBA | 1:1 SM–24DHBA-II | 1:2 SM–34DHBA | 1:3:3 SM–35DHBA–H₂O | 2:1 SM–345THBA-I | 2:1 SM–345THBA-II |
|---------------------------|-------------|------------------|---------------|---------------------|------------------|------------------|
| **Formula**               | C₁₁H₁₁N₁O₅ | C₁₁H₁₁N₁O₆     | C₁₈H₁₇N₁O₁₀  | C₂₅H₂₃N₁O₁₇       | C₁₅H₁₆N₂O₉     | C₁₅H₁₆N₂O₉      |
| **Formula weight**        | 237.21      | 253.21          | 407.33        | 609.44              | 368.30          | 368.30           |
| **CCDC number**           | 1027541     | 1027542         | 1027543       | 1027544             | 1027545         | 1027546          |
| **Temperature (K)**       | 100(2)      | 100(2)          | 100(2)        | 100(2)              | 130(2)          | 110(2)           |
| **R(int)**                | 0.0341      | 0.0266          | 0.0395        | 0.0302              | 0.0496          | 0.0704           |
| **Crystal system**        | triclinic   | triclinic       | monoclinic   | triclinic           | triclinic       | Orthorhombic     |
| **Space group**           | P₁          | P₁              | P₂₁/c        | P₁                  | P₁              | P₂₁₂₁2₁         |
| **a (Å)**                 | 6.5133(3)   | 6.7358(8)       | 6.7323(2)    | 9.3161(5)           | 7.0213(3)      | 4.9225(4)       |
| **b (Å)**                 | 8.1853(5)   | 6.9119(8)       | 12.1142(5)   | 11.2092(3)          | 8.8214(4)      | 11.7839(10)     |
| **c (Å)**                 | 11.4965(6)  | 12.3937(9)      | 21.2077(8)   | 13.7362(7)          | 25.1416(2)     | 13.8540(16)     |
| **α (°)**                 | 103.458(5)  | 74.468(9)       | 90           | 102.926(3)          | 90              | 97.248(8)       |
| **β (°)**                 | 93.925(4)   | 85.298(8)       | 97.146(3)    | 104.398(4)          | 90              | 96.773(8)       |
| **γ (°)**                 | 113.018(5)  | 73.280(10)      | 90           | 96.571(3)           | 90              | 90.663(6)       |
| **Volume (Å³)**           | 539.85(6)   | 532.43(10)      | 1716.19(11)  | 1332.01(11)         | 1557.22(12)    | 791.35(13)      |
| **Z**                     | 4           | 4                | 12           | 14                  | 12              | 6                |
| **Density (g cm⁻³)**      | 1.46        | 1.58             | 1.58         | 1.52                | 1.57            | 1.55             |
| **μ (mm⁻¹)**              | 0.117       | 0.131            | 0.131        | 0.131               | 0.132           | 0.130            |
| **F (000)**               | 248         | 264              | 848          | 632                 | 768             | 384              |
| **h max, min**            | -8,9        | -8,8             | -8,8         | -10,11              | -8,8            | -6,6             |
| **k max, min**            | -11,11      | -8,6             | -14,13       | -8,13               | -10,10          | -14,14           |
| **l max, min**            | -16,15      | -14,13           | -25,26       | -16,14              | -29,29          | -17,17           |
| **No. of measured reflections** | 13046   | 4016            | 10777        | 9808                | 8817            | 11875            |
| **No. of unique reflections** | 1903    | 1861            | 3365         | 5225                | 2707            | 2784             |
| **No. of reflections used** | 1793     | 1690            | 2818         | 4753                | 2504            | 2267             |
| **No. of parameters**     | 166         | 179             | 290          | 428                 | 259             | 287              |
| **R_all, R_obs**          | 0.032,0.031 | 0.058,0.054     | 0.056,0.044  | 0.081,0.076         | 0.045,0.039    | 0.117,0.100     |
| **wR²_all, wR²_obs**      | 0.084,0.082 | 0.147,0.145     | 0.096,0.091  | 0.191,0.189         | 0.096,0.091    | 0.237,0.231     |
| **Δρ_min, max (e Å³)**   | -0.256,0.200 | -0.370,0.545   | -0.220,0.265 | -0.328,0.738        | -0.179,0.153   | -0.429,0.451    |
| **GOOF**                  | 1.056       | 1.256           | 1.076        | 1.203               | 1.043           | 1.103            |
Table S2 Crystallographic parameters of maleimide cocrystals.

| Cocrystal          | 1:1 MM–4HBA          | 1:1 MM–24DHBA         | 1:3:3 MM–35DHBA–H₂O  |
|--------------------|----------------------|-----------------------|-----------------------|
| Formula            | C₁₁H₉N₁O₅            | C₁₁H₉N₁O₆             | C₂₅H₁₀N₁O₁₇           |
| Formula weight     | 235.19               | 251.19                | 605.41                |
| CCDC number        | 1027547              | 1027548               | 1027549               |
| Temperature (K)    | 100(2)               | 100(2)                | 100(2)                |
| R(int)             | 0.0246               | 0.0409                | 0.082                 |
| Crystal system     | monoclinic           | monoclinic            | triclinic             |
| Space group        | P2₁/n                | P2₁/a                 | P1                    |
| a (Å)              | 10.8426(8)           | 12.5506(4)            | 9.3796(10)            |
| b (Å)              | 6.5202(4)            | 6.6807(2)             | 10.3981(12)           |
| c (Å)              | 16.1326(13)          | 26.1586(8)            | 15.6415(16)           |
| α (°)              | 90                   | 90                    | 80.620(9)             |
| β (°)              | 106.391(8)           | 98.815(3)             | 72.913(9)             |
| γ (°)              | 90                   | 90                    | 66.089(10)            |
| Volume (Å³)        | 1094.16(14)          | 2167.41(9)            | 1331.35(3)            |
| Z                  | 8                    | 16                    | 14                    |
| Density (g cm⁻³)   | 1.43                 | 1.54                  | 1.51                  |
| μ (mm⁻¹)           | 0.115                | 0.128                 | 0.131                 |
| F (000)            | 488                  | 1040                  | 624                   |
| hmin, max          | -13,14               | -15,15                | -11,11                |
| kmin, max          | -8,8                 | -8,8                  | 12,12                 |
| lmin, max          | -22,21               | -32,32                | -19,18                |
| No. of measured reflections | 5081               | 21462                 | 12476                 |
| No. of unique reflections | 2375               | 2137                  | 12476                 |
| No. of reflections used | 1679               | 2002                  | 4751                  |
| No. of parameters  | 166                  | 179                   | 396                   |
| R_all, R_obs       | 0.070, 0.048         | 0.057, 0.053          | 0.212, 0.110          |
| wR²_all, wR²_obs   | 0.118,0.107          | 0.136, 0.133          | 0.321, 0.285          |
| Δρ_min,max (e Å⁻³) | -0.170,0.152         | -0.246,0.669          | -0.490,0.854          |
| GOOF               | 1.030                | 1.164                 | 0.914                 |
Table S3: Crystallographic parameters of glutarimide cocrystals.

| Cocrystal   | 1:2 GM–4HBA | 1:1 GM–35DHBA |
|-------------|-------------|---------------|
| Formula     | C$_{10}$H$_{19}$N$_{1}$O$_{8}$ | C$_{12}$H$_{13}$N$_{1}$O$_{6}$ |
| Formula weight | 389.35 | 267.23 |
| CCDC number | 1027550 | 1027551 |
| Temperature (K) | 100(2) | 100(2) |
| R(int)       | 0.0585 | 0.0314 |
| Crystal system | orthorhombic | triclinic |
| Space group  | Pca$_{2_1}$ | P $\bar{T}$ |
| $a$ (Å)      | 40.6920(30) | 6.6761(3) |
| $b$ (Å)      | 5.4524(3)   | 9.1128 (4) |
| $c$ (Å)      | 16.3546(9)  | 10.9447(4) |
| $\alpha$ ($^\circ$) | 90 | 93.397(3) |
| $\beta$ ($^\circ$) | 90 | 107.694(3) |
| $\gamma$ ($^\circ$) | 90 | 108.173(4) |
| Volume (Å$^3$) | 3628.58(4) | 593.92(13) |
| $Z$          | 24         | 4            |
| Density (g cm$^{-3}$) | 1.43 | 1.49 |
| $\mu$ (mm$^{-1}$) | 0.112 | 0.121 |
| F (000)      | 1632 | 280 |
| $h_{\text{min, max}}$ | -40,50 | -8,8 |
| $k_{\text{min, max}}$ | -6,6 | -11,11 |
| $l_{\text{min, max}}$ | -15,20 | -13,13 |
| No. of measured reflections | 15134 | 11839 |
| No. of unique reflections | 5638 | 2329 |
| No. of reflections used | 4868 | 2156 |
| No. of parameters | 594 | 212 |
| $R_{\text{all}}, R_{\text{obs}}$ | 0.057, 0.048 | 0.033, 0.031 |
| $wR_{2,\text{all}}, wR_{2,\text{obs}}$ | 0.108,0.102 | 0.088, 0.087 |
| $\Delta\rho_{\text{min, max}}$ (e Å$^{-3}$) | -0.218,0.220 | -0.214,0.258 |
| GOOF         | 1.027     | 1.058        |
Section S3: PXRD pattern comparison of cocrystals with that of their respective parent materials.

Figure S1 PXRD of 1:1 maleimide–3,4-dihydroxybenzoic acid ground material (blue) exhibits distinct diffraction peaks compared to the parent materials, maleimide (magenta) and 3,4-dihydroxybenzoic acid (red), and also their polymorphs and solvates found in the CSD.\textsuperscript{S7} (a) 2 theta range in 5-40°. (b) New peaks about 13.4° and 19.2° for the combination indicate the formation of cocrystal.
Figure S2 PXRD of 1:1 maleimide–3,4,5-trihydroxybenzoic acid ground material (blue) exhibits distinct diffraction peaks compared to the parent materials, maleimide (magenta) and 3,4,5-trihydroxybenzoic acid (red), and also their polymorphs and solvates found in the CSD. (a) 2θ range in 5-40°. (b) New/distinct peaks about 16.8°, 20.6 and 27.5° for the combination indicate the formation of cocrystal.
Figure S3 PXRD of 1:1 glutarimide–2,4-dihydroxybenzoic acid ground material (blue) exhibits distinct diffraction peaks compared to the parent materials, glutarimide (magenta) and 2,4-dihydroxybenzoic acid (red), and also their polymorphs and solvates found in the CSD.
Figure S4 PXRD of 1:1 glutarimide–3, 4-dihydroxybenzoic acid melt-crystallized material (blue) exhibits distinct diffraction peaks compared to the parent materials, glutarimide (magenta) and 3,4-dihydroxybenzoic acid (red), and also their polymorphs and solvates found in the CSD. (a) Shows full 2theta range, (b and c) shows enlarged PXRD in the range of 6-16° and 20-26°. The new peaks appear at 6.8°, 8.4°, 13.4°, 21.25°, 26.2°, 27.3°, 34.6° and 40.4°. 
Figure S5 PXRD of 1:1 glutarimide–3,4,5-trihydroxybenzoic acid ground material (blue) exhibits distinct diffraction peaks compared to the parent materials, glutarimide (magenta) and 3,4,5-trihydroxybenzoic acid (red), and also their polymorphs and solvates found in the CSD.
Section S4: PXRD pattern comparison of eutectics with that of their respective parent materials.

Figure S6 Comparison of PXRD patterns of (a) succinimide (magenta), benzoic acid (red) and their 1:1 ground material (blue) shows that the combination does not exhibit any new or distinct peaks characteristic of a cocrystal. Melting point analysis established the combination as a eutectic system. Similar observations can be seen for (b) succinimide–2-hydroxybenzoic acid and (c) succinimide–3-hydroxybenzoic acid systems.
Figure S7 Comparison of PXRD patterns of (a) maleimide (magenta), benzoic acid (red) and their 1:1 ground material (blue) shows that the combination does not exhibit any new or distinct peaks characteristic of a cocrystal. Melting point analysis established the combination as a eutectic system. Similar observations can be seen for (b) maleimide–2-hydroxybenzoic acid and (c) maleimide–3-hydroxybenzoic acid systems.
Figure S8 Comparison of PXRD patterns of (a) glutarimide (magenta), benzoic acid (red) and their 1:1 ground material (blue) shows that the combination does not exhibit any new or distinct peaks characteristic of a cocrystal. Melting point analysis established the combination as a eutectic system. Similar observations can be seen for (b) glutarimide–2-hydroxybenzoic acid and (c) glutarimide–3-hydroxybenzoic acid systems.
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S7. Cambridge Structural Database, ver. 5.35, ConQuest 1.16, www.ccdc.cam.ac.uk.