Electronic Supplementary Material (ESI) for Chemical Communications


# Designing ternary cocrystals with hydrogen bonds and halogen bonds

Srinu Tothadi and Gautam R. Desiraju*

Solid State and Structural Chemistry Unit, Indian Institute of Science, Bangalore 560 012, India.

## Supporting Information

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**Table 1.** List of crystal structures

| | Cocrystals/solvates | |
|---|---|---|
| 1 | 4-Nitrobenzamide: 1,4-diiodobenzene (**1**) | Binary cocrystal |
| 2 | 4-Iodobenzamide: 1,4-dinitrobenzene (**2**) | Binary cocrystal |
| 3 | 4-Nitrobenzamide: oxalic acid: 1,4-diiodobenzene (**3**) | Ternary cocrystal |
| 4 | 4-Nitrobenzamide: fumaric acid: 1,4-diiodobenzene (**4**) | Ternary cocrystal |
| 5 | 4-Nitrobenzamide: oxalic acid: 1-bromo-4-iodobenzene **(5)** | Ternary cocrystal |
| 6 | 4-Nitrobenzamide: 1,4-dioxane (**6**) | Solvate |
| 7 | 4-Nitrobenzamide: adipic acid (**7**) | Binary cocrystal |
| 8 | 4-Nitrobenzamide: benzoic acid (**8**) | Binary cocrystal |
| 9 | 4-Nitrobenzamide: succinic acid (**9**) | Binary cocrystal |
| 10 | 3,5-Dinitrobenzamide: 1,4-diiodobenzene (**10**) | Binary cocrystal |

## Experimental details

### Crystallization.

*4-Nitrobenzamide: oxalic acid: 1,4-diiodobenzene cocrystal* (**3**). 4-Nitrobenzamide, oxalic acid, and 1,4-diiodobenzene were taken in a 2:1:1 molar ratio and ground after adding 2-3 drops of EtOH (solvent drop grinding). The ground sample was dissolved in a minimum amount of MeOH and then filtered. The filtrate was kept for slow evaporation. Yellow coloured good quality crystals, suitable for diffraction, were obtained after five days.

*4-Nitrobenzamide: fumaric acid: 1,4-diiodobenzene cocrystal* (**4**). 4-Nitrobenzamide, fumaric acid and 1,4-diiodobenzene were taken in a 2:1:1 molar ratio and ground after adding 2-3 drops of EtOH. The ground sample was dissolved in a minimum amount of MeOH and filtered. The filtrate was kept for slow evaporation. Yellow coloured, good quality, diamond shape crystals, suitable for diffraction, were obtained after four days.

*4-Nitrobenzamide: fumaric acid: 1-bromo-4-iodobenzene cocrystal* (**5**). 4-Nitrobenzamide, fumaric acid and 1-bromo-4-iodobenzene were taken in a 2:1:1 molar ratio and ground after adding 2-3 drops of EtOH. The ground sample was dissolved in a 1:1 mixture of MeOH/$MeNO_2$ and subsequently filtered. Filtrate was kept for slow evaporation. Yellow coloured, good quality crystals, suitable for diffraction, were obtained after four days.

### Single crystal X-ray crystallography.

Single crystal X-ray data for all binary and ternary cocrystals were collected on a Rigaku Mercury375/M CCD (XtaLAB mini) diffractometer using graphite monochromated Mo−Kα radiation at 150 K. The data were processed with the Rigaku Crystal clear software. Refinement

of coordinates and anisotropic thermal parameters of nonhydrogen atoms were performed with the full-matrix least-squares method. The different treatment of H atoms in any structure depends on the data quality. Most of the hydrogen atoms in $NH_2$ and OH are located from difference Fourier maps. In case where the data were good C–H atoms were located from difference Fourier maps. If there are some problems with the C–H distance then H-atom positions were calculated using the riding model. PLATON was used to prepare material for publication, and Mercury version 3.0 was utilized for molecular representations and packing diagrams. The structure solution and refinement proceeded uneventfully for all compounds except cocrystal **1.** In this case there was some problem in the refinement which led to one or two atoms having unrealistic adp values and some unacceptably large peaks near the iodine atom in the difference Fourier maps. Several attempts were made to resolve these issues, without success. Possibly, these problems arose from poor crystal quality, unresolved chicken-wire problems and the presence of the iodine atom in the molecule. Efforts are ongoing to resolve these issues and structure **1** has been mentioned here because it provides some supporting evidence for the crystal engineering arguments and strategies put forward in this paper.

**CSD Analysis criteria**

CSD structural data analysis was carried out with version 5.34 (November 2012, including two updates). The analysis was confined to purely organic compounds. The geometrical parameters and constraints were given using ConQuest 1.15. Unique intermolecular interactions were considered with longer and shorter I···$O_2$N non-bonded interactions, $D_1$ and $D_2$. For reference, $3.0 < D_1 < 6.5$ Å and $2.9 < D_2 < 4.7$ Å.

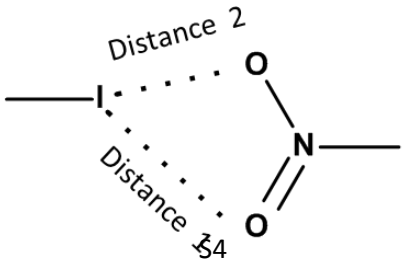

**Table 2.** A list of "unsuccessful" experiments

| No | Compound | Solvent used for crystallization | Space group | Result | R-factor (%) |
|---|---|---|---|---|---|
| 1 | 4-nitrobenzamide: malonic acid: 1-bromo-4-iodobenzene | MeOH | | 4-nitrobenzamide (form I) (reported) | |
| 2 | 4-nitrobenzamide: pimelic acid: 1,4-diiodobenzene | $MeNO_2$ | $P\bar{1}$ | 4-nitrobenzamide: 1,4-diiodobenzene **(1)** | 8.3 |
| 3 | 4-iodobenzamide: oxalic acid: 1,4-dinitrobenzene | $MeNO_2$ | $C2/m$ | 4-iodobenzamide: 1,4-dinitrobenzene **(2)** | 1.6 |
| 4 | 4-nitrobenzamide: fumaric acid: 1,4-diiodobenzene | 1,4-dioxane | $P\bar{1}$ | 4-nitrobenzamide: 1,4-dioxane (**6**) | 3.8 |
| 5 | 4-nitrobenzamide: fumaric acid: 1,4-diiodotetrafluorobenzene | MeOH | | 4-nitrobenzamide (form II) (reported) | |
| 6 | 4-nitrobenzamide: glutaric acid: 1,4-diiodotetrafluorobenzene | MeOH | | 4-nitrobenzamide (form II) (reported) | |
| 7 | 4-nitrobenzamide: adipic acid: 1,4-diiodobenzene | $MeNO_2$ (batch I) | $P2_1/c$ | 4-nitrobenzamide: adipic acid **(7)** | 3.4 |
| 8 | 4-nitrobenzamide: adipic acid: 1,4-diiodobenzene | $MeNO_2$ (batch II) | | 1,4-diiodobenzene (reported) | |
| 9 | 4-nitrobenzamide: azelaic acid: 1,4-diiodobenzene | MeOH | | azelaic acid (reported) | |
| 10 | 4-nitrobenzamide: sebacic acid: 1,4-diiodobenzene | MeCN | | 4-nitrobenzamide (form I) (reported) | |
| 11 | 4-nitrobenzamide: sebacic acid: 1,4-diiodobenzene | MeCN | | new cell but data quality is poor | |
| 12 | 4-nitrobenzamide: sebacic acid: 1-bromo-4-iodobenzene | MeOH | | 1-bromo-4-iodobenzene (reported) | |
| 13 | 4-nitrobenzamide: benzoic acid: 1,4-diiodobenzene | MeOH | $P2_1/c$ | 4-nitrobenzamide: benzoic acid **(8)** | 5.8 |
| 14 | 4-nitrobenzamide: 1-adamantanecarboxylic acid: 1,4-diiodobenzene | MeOH | | 4-nitrobenzamide (form I) (reported) | |

| | | | | | |
|---|---|---|---|---|---|
| 15 | 4-nitrobenzamide:<br>sebacic acid:<br>1-bromo-4-iodobenzene | MeOH<br>(batch I) | | 1-bromo-4-iodobenzene<br>(reported) | |
| 16 | 4-nitrobenzamide:<br>sebacic acid:<br>1-bromo-4-iodobenzene | MeOH<br>(batch II) | | 4-nitrobenzamide<br>(form II) (reported) | |
| 17 | 4-nitrobenzamide:<br>oxalic acid:<br>1,4-dibromo tetrafluorobenzene | MeOH<br>(batch I) | | $(\text{oxalic acid})_2:(H_2O)_3$<br>(reported) | |
| 18 | 4-nitrobenzamide:<br>oxalic acid:<br>1,4-dibromotetrafluorobenzene | MeOH<br>(batch II) | | 4-nitrobenzamide<br>(form II) (reported) | |
| 19 | 4-nitrobenzamide:<br>succinic acid:<br>1-bromo-4-iodobenzene | $MeNO_2$ | *C*2/*c* | 4-nitrobenzamide:<br>succinic acid **(9)** | 3.3 |
| 20 | 3,5-dinitrobenzamide:<br>fumaric acid:<br>1,4-diiodobenzene: | MeOH | $P\bar{1}$ | 3,5-dinitrobenzamide:<br>1,4-diiodobenzene **(10)** | 5.3 |
| 21 | 4-nitrobenzamide:<br>1,4-diiodobenzene | MeOH | | 4-nitrobenzamide<br>(form I) (reported) | |
| 22 | 4-nitrobenzamide:<br>pimelic acid:1,4-diiodobenzene | 1,4-dioxane | | 1,4-diiodobenzene<br>(reported) | |
| 23 | 4-nitrobenzamide:<br>fumaric acid:<br>1,4-diiodotetrafluorobenzene | THF | | 4-nitrobenzamide<br>(form II) (reported) | |
| 24 | 4-nitrobenzamide:<br>1,4-diiodotetrafluorobenzene | MeOH<br>(batch I) | | 4-nitrobenzamide<br>(form II) (reported) | |
| 25 | 4-nitrobenzamide:<br>1,4-diiodotetrafluorobenzene | MeOH<br>(batch II) | | 4-nitrobenzamide<br>(form I) (reported) | |
| 26 | 4-nitrobenzamide:<br>1-bromo-4-iodobenzene | MeOH | | 1-bromo-4-iodobenzene<br>(reported) | |
| 27 | 4-nitrobenzamide:<br>1,4-bromobenzene | MeOH | | 1,4-bromobenzene<br>(reported) | |
| 28 | 4-nitrobenzamide:<br>1-bromo-4-iodobenzene | THF | | 4-nitrobenzamide<br>(form II) (reported) | |
| 29 | 4-idobenzamide:<br>oxalic acid | MeOH | | different cell but data<br>quality is poor | |

**Table 3:** Crystallographic data and structure refinement parameters for compounds in this study not mentioned in the main paper[1]

| | **6** | **7** | **8** | **9** | **10** |
|---|---|---|---|---|---|
| | 4NBZ: DIOXANE | 4NBZ:AA | 4NBZ:BA | 4NBZ:SA | 35DNBZ: 14DIBZ |
| *Formula* | $(C_7H_6N_2O_3)\cdot 0.5(C_4H_8O_2)$ | $(C7H_6N_2O_3)\cdot 0.5(C_6H_{10}O_4)$ | $(C_7H_6N_2O_3)\cdot (C_7H_6O_2)\cdot$ | $(C_7H_6N_2O\cdot 0.5(C_4H_6O_4)$ | $2(C_7H_5N_3O_5)\cdot (C_6H4I_2)$ |
| *Formula weight* | 210.19 | 239.21 | 288.26 | 225.18 | 752.17 |
| *Crystal System* | Triclinic | Monoclinic | Monoclinic | Monoclinic | Triclinic |
| *Space group* | $P\bar{1}$ | $P2_1/c$ | $P2_1/c$ | $C2_1/c$ | $P\bar{1}$ |
| *a (Å)* | 6.9143(9) | 6.3620(9) | 7.3472(12) | 31.134(8) | 9.5268(13) |
| *b (Å)* | 7.4292(10) | 13.8657(19) | 19.841(3) | 5.1606(13) | 9.6155(13) |
| *c (Å)* | 10.0061(13) | 13.6664(17) | 9.2185(15) | 12.670(3) | 13.8866(19) |
| *α (°)* | 94.403(7) | 90 | 90 | 90 | 81.082(6) |
| *β (°)* | 95.082(7) | 116.646(7) | 106.837(7) | 107.206(7) | 70.278(5) |
| *γ (°)* | 111.305(8) | 90 | 90 | 90 | 88.850(6) |
| *V (Å$^3$)* | 473.68(11) | 1077.5(3) | 1286.2(4) | 1944.6(8) | 1182.3(3) |
| *Z* | 2 | 4 | 4 | 8 | 2 |
| *$\rho_{calc}$ (gcm$^{-3}$)* | 1.474 | 1.475 | 1.489 | 1.538 | 2.113 |
| *F(000)* | 220.0 | 500.0 | 600.0 | 936.0 | 724.0 |
| *μ(mm$^{-1}$)* | 0.118 | 0.120 | 0.115 | 0.128 | 2.730 |
| *Temp(K)* | 150 | 150 | 150 | 150 | 150 |
| *Total ref.* | 4747 | 10650 | 8432 | 9260 | 8053 |
| *Unique ref.* | 2149 | 2464 | 2927 | 2235 | 5321 |
| *Observed ref. (I > 2σ(I))* | 1971 | 2191 | 1929 | 2020 | 4435 |
| *R* | 0.0387 | 0.0342 | 0.0583 | 0.0336 | 0.0528 |
| *wR2* | 0.1100 | 0.0889 | 0.1438 | 0.0891 | 0.1502 |
| *S* | 1.025 | 1.066 | 0.997 | 1.074 | 1.111 |
| *CCDC No.* | 940333 | 940329 | 940330 | 940331 | 940332 |

[1]4NBZ, 4-nitrobenzamide; DIOXANE, 1,4-dioxane; AA, adipic acid; BA, benzoic acid; SA, succinic acid; 35DNBZ, 3,5-dinitrobenzamide; 14DIBZ, 1,4-diiodobenzene;

**List of byproducts in the ternary/binary cocrystallization experiments**

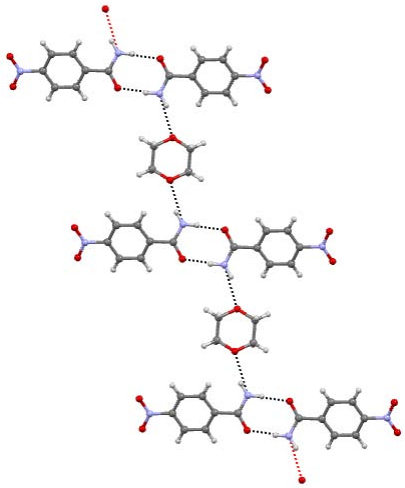

**Figure S1**. 4-Nitrobenzamide: 1,4-dioxane solvate (**6**). Two successive amide···amide dimers are connected by 1,4-dioxane molecule. See (a) V. S. S. Kumar, S. S. Kuduva and G. R. Desiraju, *J. Chem. Soc*., *Perkin Trans. 2*, 1999, 1069–1073. (b) S. Tothadi and G. R. Desiraju, *Acta Cryst.* 2012. **E68**, o2661.

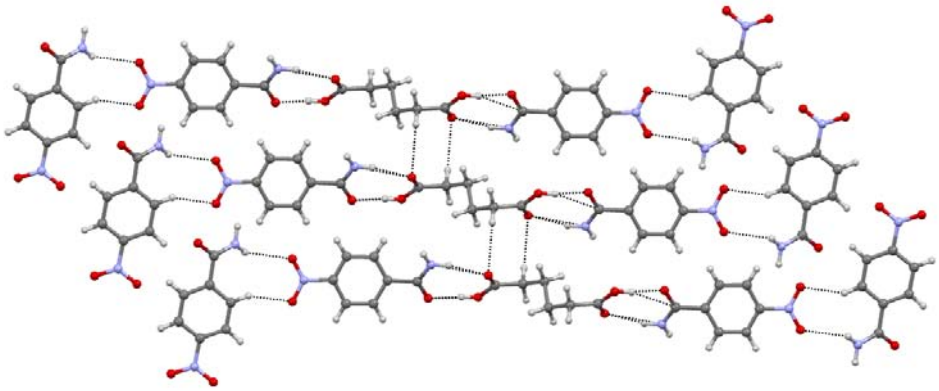

**Figure S2**. 4-Nitrobenzamide: adipic acid cocrystal (**7**). Molecules are packed with the acid···amide heterosynthon. Notice that the O atom of the $NO_2$ group is involved in crystal packing *via* N–H···O and C–H···O two point synthons.

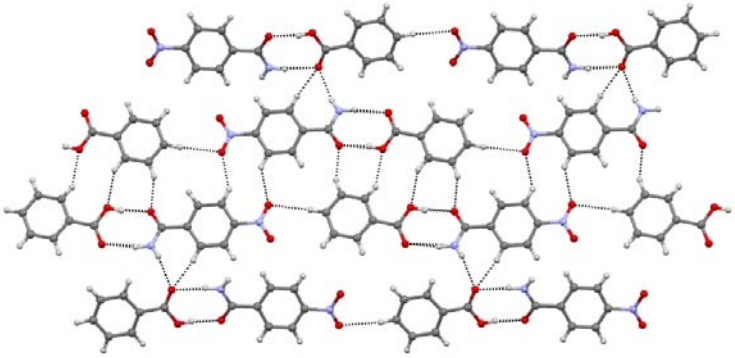

**Figure S3**. 4-Nitrobenzamide: benzoic acid cocrystal (**8**). Molecules are packed with acid···amide heterosynthon and N–H···O and C–H···O interactions.

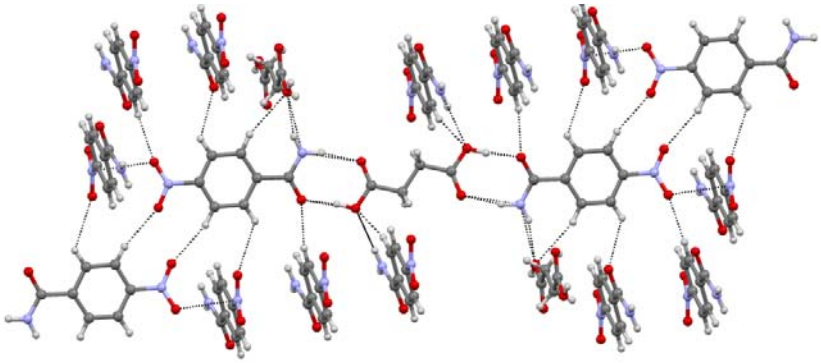

**Figure S5**. 4-Nitrobenzamide: succnic acid cocrystal (**9)** forms acid···amide dimer. Molecules are further packed with N–H···O and C–H···O interactions.

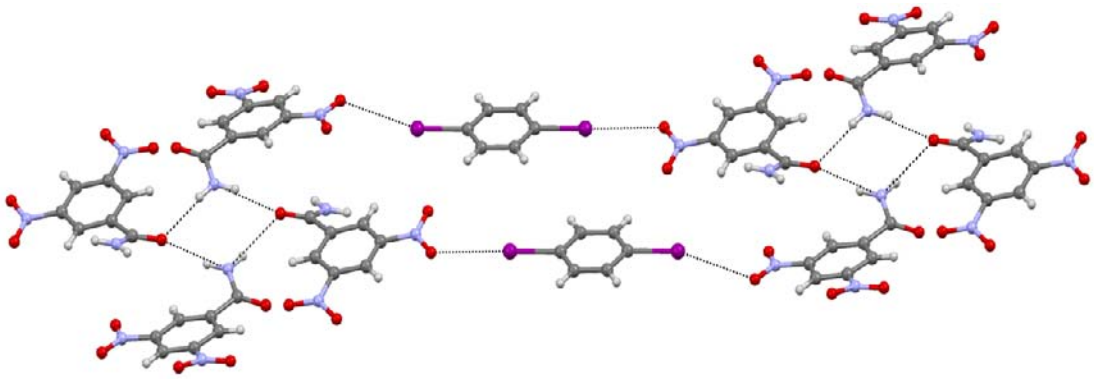

**Figure S6**. 3,5-Dinitrobenzamide: 1,4-diiodobenzene cocrystal (**10)**. Iodine forms unsymmetrical (**Q**) contacts with $NO_2$. Notice that the amide functional group forms tetramers (not amide···amide dimers)

**Powder X-ray diffraction (PXRD).** X-ray powder diffraction data (PXRD), for all ternary cocrystals were collected on a Philips X'pert Pro X-ray powder diffractometer equipped with X'cellerator detector. The scan range was $2\theta = 5$ to 40°.

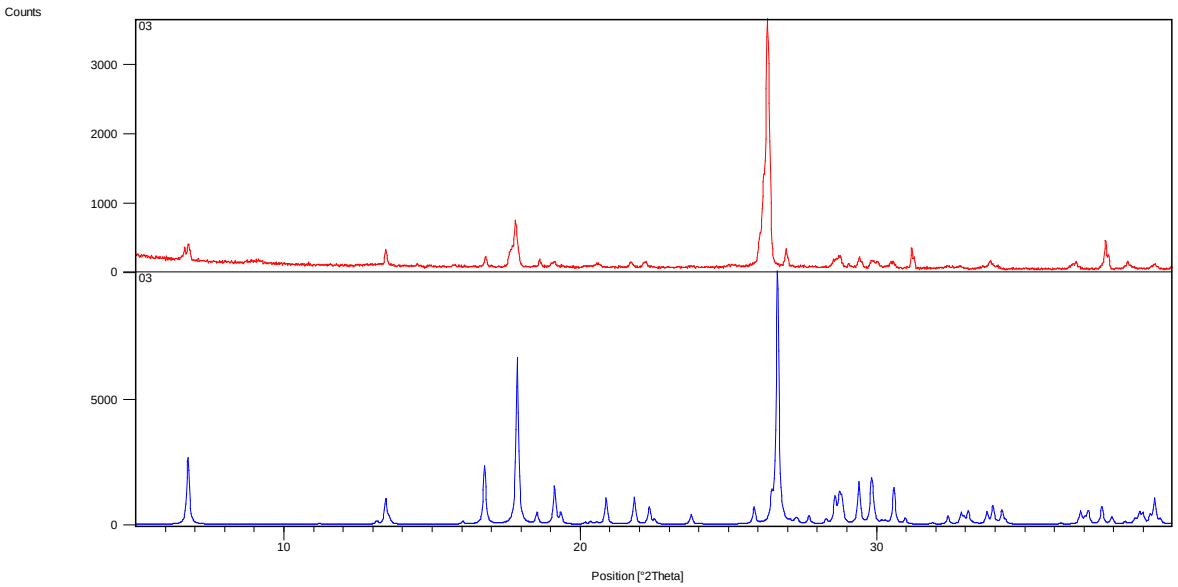


**Figure S7.** PXRD pattern of 2:1:1 Ternary cocrystal of 4-nitrobenzamide: oxalic acid: 1,4-diiodobenzene, **3**. Experimental powder pattern (red) simulated powder pattern (blue)

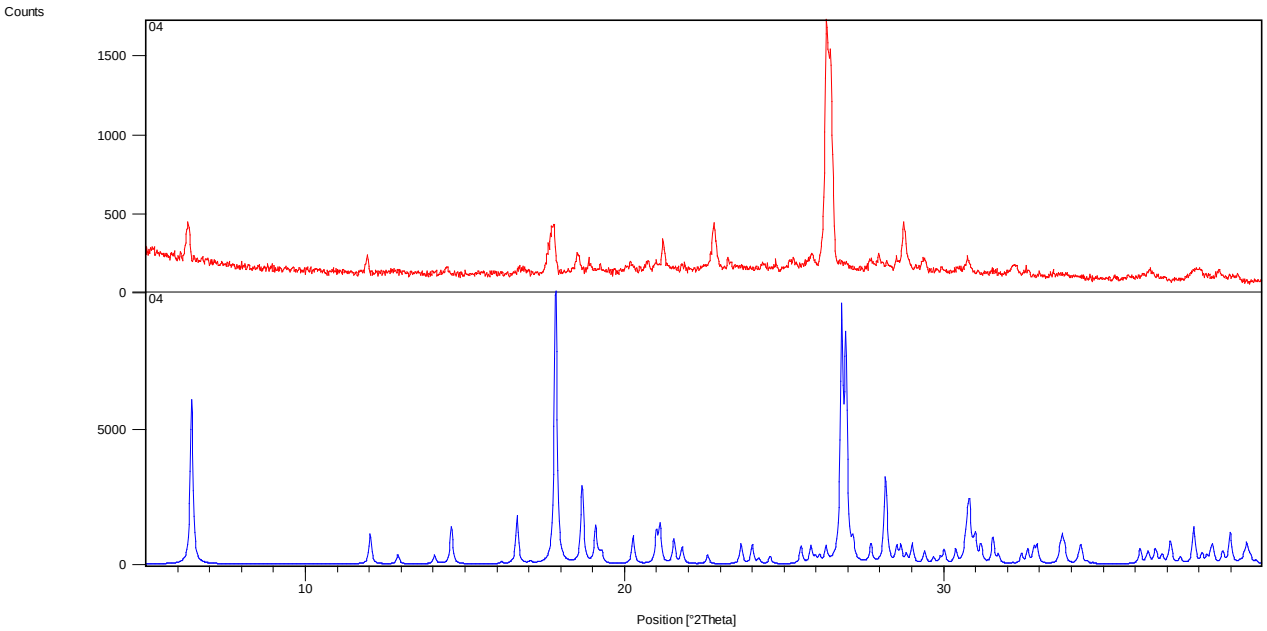


**Figure S8.** PXRD pattern of 2:1:1 Ternary cocrystal of 4-nitrobenzamide: fumaric acid: 1,4-diiodobenzene, **4**. Experimental powder pattern (red) simulated powder pattern (blue)

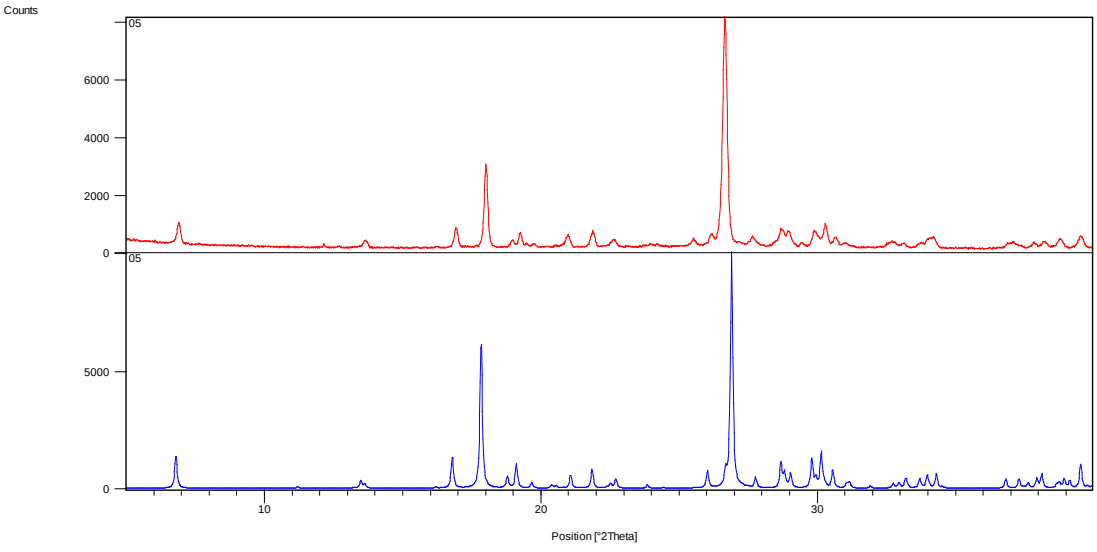


**Figure S9.** PXRD pattern of 2:1:1 Ternary cocrystal of 4-nitrobenzamide: oxalic acid: 1-bromo 4-iodobenzene, **5**. Experimental powder pattern (red) simulated powder pattern (blue)