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Stoichiomorphic Halogen-Bonded Cocrystals. A Case Study of 1,4-Diiodotetrafluorobenzene and 3-Nitropyridine

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Abstract

The concept of variable stoichiometry cocrystallization is explored in halogen-bonded systems. Three novel cocrystals of 1,4-diiodotetrafluorobenzene and 3-nitropyridine with molar ratios of 1:1, 2:1, and 1:2, respectively, are prepared by slow evaporation methods. Single-crystal X-ray diffraction analysis reveals key differences between each of the nominally similar cocrystals. For instance, the 1:1 cocrystal crystallizes in the $P2_1/n$ space group and features a single chemically and crystallographically unique halogen bond between iodine and the pyridyl nitrogen. The 2:1 cocrystal crystallizes in the $P\bar{1}$ space group and features a halogen bond between iodine and one of the nitro oxygens in addition to an iodine-nitrogen halogen bond. The 1:2 cocrystal crystallizes with a large unit cell ($V = 9896 \text{ \AA}^3$) in the Cc space group and features 10 crystallographically distinct iodine-nitrogen halogen bonds. Powder X-ray diffraction experiments carried out on the 1:1 and 2:1 cocrystals confirm that gentle grinding does not alter the crystal forms. $^1\text{H} \rightarrow ^{13}\text{C}$ and $^{19}\text{F} \rightarrow ^{13}\text{C}$ cross-polarization magic angle spinning (CP/MAS) NMR experiments performed on powdered samples of the 1:1 and 2:1 cocrystals are used as spectral editing tools to select for either the halogen bond acceptor or donor, respectively. Carbon-13 chemical shifts in the cocrystals are shown to change only very subtly relative to pure solid 1,4-diiodotetrafluorobenzene, but the shift of the carbon directly bonded to iodine nevertheless increases, consistent with halogen bond formation (e.g., a shift of +1.6 ppm for the 2:1 cocrystal). This work contributes new examples to the field of variable stoichiometry cocrystal engineering with halogen bonds.

Keywords

solid-state NMR, X-ray diffraction, halogen bond, cocrystal, polymorphism, stoichiometry, stoichiomorphism

Introduction

Molecular and ionic solids can adopt a range of forms depending on how they are prepared.^{1,2} Such forms include pure crystalline or amorphous phases, hydrates, or solvates. In bicomponent or multicomponent molecular systems, it is often possible to form cocrystals as well as hydrates or solvates of cocrystals. Cocrystals are defined as solids that are crystalline materials composed of two or more molecules in the crystal lattice.^{1,2} Other definitions make reference to a definite stoichiometric ratio of the constituent molecules. Cocrystal engineering is a topic of broad interest with many applications.² Polymorphism refers to the ability of a molecule to crystallize in more than one crystal lattice – i.e., the ability of the same pure chemical components to have different crystal structures. The importance of all of these variations (amorphous vs crystalline, hydrates and solvates vs anhydrous forms, and polymorphism) is by now well known, with particular interest from the pharmaceutical industry due to the differences in physicochemical properties of different forms, and the associated intellectual property concerns.³

Another related distinction which can be explored in cocrystalline phases is that of stoichiometric variability.⁴ Variable stoichiometry cocrystals, or stoichiomorphs, are solid crystalline phases composed of two or more molecular components prepared in different molar or stoichiometric ratios.⁵ Control of the molecular stoichiometry thus offers a further tool to generate distinct crystalline phases composed of the same molecular building blocks.^{6,7,8,9,10,11} It is of interest to explore the stoichiometric landscape for many reasons, including the ability to modulate physicochemical properties (e.g., dissolution rate in the case of cocrystals of active pharmaceutical ingredients) and to improve our fundamental understanding of the role stoichiometry plays in relation to the concepts of polymorphism and solvate formation. For example, stoichiometry has been shown to play a key role in determining the luminescence properties of organic cocrystals.¹²

In their recent review, Saikia et al. highlight the fact that while there are a considerable number of reports of new cocrystals on a daily basis, the number of different stoichiomorphs is not high.⁴ In this work, we describe the results of our efforts to explore the stoichiomorphic landscape of a halogen-bonded cocrystal system. Halogen bonds are electrophilic non-covalent interactions between an area of elevated electrostatic potential on a halogen atom and an electron donor moiety.^{13,14,15} 1,4-Diiodotetrafluorobenzene is used as a halogen bond donor and 3-nitropyridine was chosen as a halogen bond acceptor (Figure 1). The former was chosen in part due to its reliable ability to predictably form one-dimensional halogen bonded chains,¹⁴ while the latter was explored as a novel electron donor system potentially capable of interacting at nitrogen and/or oxygen sites, thus increasing the potential for polymorphism and stoichiomorphism. Furthermore, the low melting point of 3-nitropyridine (35-40°C) means that cocrystallization could potentially provide a route to stabilizing this component in a higher-melting solid phase. In addition to employing single-crystal and powder X-ray diffraction methods for characterization of the stoichiomorphs, we also demonstrate the value of $^1\text{H} \rightarrow ^{13}\text{C}$ and $^{19}\text{F} \rightarrow ^{13}\text{C}$ cross-polarization magic angle spinning (CP/MAS) NMR experiments both to confirm cocrystal formation^{16,17,18} in powdered samples and for spectral editing purposes.

Experimental

(i) Sample Preparation

1,4-Diiodotetrafluorobenzene (**1**) and 3-nitropyridine (**2**) were purchased from Sigma-Aldrich. All compounds were used without further purification. In a typical procedure, cocrystal **A** was obtained from the slow evaporation of a solution of the donor **1** (0.1060 g, 0.3 mmol) and 3-nitropyridine (0.1096 g, 0.3 mmol) in ethanol at room temperature (decomp. 80° C).

Cocrystal **C** was obtained from the slow evaporation of a solution of the donor **1** and 3-nitropyridine in dichloromethane (1 mL) at room temperature in a 2:1 molar ratio (decomp. 78-80° C). Cocrystal **D** was obtained from the slow evaporation of the donor **1** and 3-nitropyridine in a 1:1 molar ratio in ethanol (1 mL) at room temperature (decomp. 78-80° C). We presume this to be a decomposition point rather than a true melting point due to the low melting point of one of the components, pure 3-nitropyridine.

(ii) Single-Crystal X-ray Diffraction

Crystallographic data were collected from single crystals mounted on MiTeGen MicroMounts using parabar oil. Data were collected on a Bruker Smart ApexII single crystal diffractometer equipped with a sealed tube Mo K α source ($\lambda = 0.71073$ Å), a graphite monochromator, and an ApexII CCD detector. Samples were held at low temperature using a dry compressed air cooling system. Raw data collection and processing were performed with the Apex3 software package from Bruker.¹⁹ Initial unit cell parameters were determined from 36 data frames from select ω scans. Semi-empirical absorption corrections based on equivalent reflections were applied.²⁰ Systematic absences in the diffraction data-set and unit-cell parameters were consistent with the assigned space group. The initial structural solutions were determined using ShelxT direct methods²¹ and refined with full-matrix least-squares procedures based on F^2 using ShelXL and ShelXle.²² Cocrystal **A** was refined as an inversion twin. Hydrogen atoms were placed geometrically and refined using a riding model. See Table 1 for more information.

(iii) Powder X-ray Diffraction

Crystals were gently ground into fine powders with a mortar and pestle for powder XRD and solid-state nuclear magnetic resonance (SSNMR) experiments. The crystal structure for each

powdered sample was verified by powder X-ray diffraction on a Rigaku Ultima IV instrument with 2θ ranging from 5 to 55° in increments of 0.02° using Cu $K\alpha$ radiation to ensure phase purity. Data were analyzed and plotted using Mercury 2021.1.0 (Build 319587)²³ and Match! 3.12 Build 208 for Windows 32-bit.²⁴

(iv) Solid-State Nuclear Magnetic Resonance Spectroscopy

$^1\text{H} \rightarrow ^{13}\text{C}$ CP/MAS SSNMR experiments with high-power proton two-pulse phase modulated (TPPM) decoupling²⁵ were performed at $B_0 = 9.4$ T on a Bruker Avance III spectrometer, using a Bruker 4 mm HXY MAS probe with spinning frequencies of 10 to 12 kHz. Chemical shifts were referenced to glycine at 176.4 ppm relative to tetramethylsilane (TMS). Typical $\pi/2$ pulse lengths were 3.5 to 4.0 μs . Recycle delays of 15 to 120 s were used. Typical contact times ranged from 3 to 8 ms.

The $^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS SSNMR experiments with high-power ^{19}F swept-frequency²⁶ TPPM decoupling were performed at $B_0 = 11.7$ T on a Bruker Avance spectrometer, using a Bruker 4 mm HXY MAS probe with various spinning speeds. The spectra were referenced to powdered polytetrafluoroethylene at 111.3 ppm relative to TMS. The $\pi/2$ pulse length was 3.5 μs . Recycle delays of 60 to 180 s were used. The contact time was 5 ms.

Results and Discussion

Three novel stoichiometric cocrystals of 1,4-diiodotetrafluorobenzene (**1**) and 3-nitropyridine (**2**) were prepared via slow evaporation methods and characterized by single-crystal X-ray diffraction (SCXRD; Table 1).

Cocrystal **A**, obtained via slow evaporation from ethanol, has a stoichiometry of two molecules of 3-nitropyridine to one molecule of 1,4-diiodotetrafluorobenzene. SCXRD shows that this stoichiomorph packs in the monoclinic Cc space group with a large unit cell of 9896.3(14) Å³. As summarized in Table 2, there are ten crystallographically distinct C-I...N halogen bonds between 1,4-diiodotetrafluorobenzene and 3-nitropyridine molecules which play a key role in the overall crystallographic structure. Each iodine atom of the halogen bond donor interacts with a ring pyridyl atom (Figure 2). Interestingly, none of the atoms of the nitro group engage in halogen bonding. The halogen bonds in cocrystal **A** range in distance from 2.865 to 2.990 Å and the C-I...N angles range from 169.6 to 174.9°. These distances represent a range of reduced distance parameters, R_{XB} , ranging from 0.81 to 0.85. The value of R_{XB} is calculated as the ratio of the halogen bond distance to the sum of the van der Waals radii²⁷ of the interacting atoms: $R_{XB} = \frac{d_{I...N}}{\sum d_{vdW}}$. Although halogen bonds apparently play the dominant role in determining the crystal structure of **A**, additional weak non-covalent interactions are also noted between pyridyl ring hydrogen atoms and nearby fluorine atoms of **1** (~2.5 Å), as well as between pyridyl ring hydrogen atoms and one of the nitro oxygen atoms (~2.5 to 2.6 Å). Despite repeated attempts, it was not possible to produce sufficient quantities of cocrystal **A** in powdered form for either PXRD or solid-state NMR characterization.

Cocrystal **D**, also obtained via slow evaporation from ethanol, has a stoichiometry of one molecule of 3-nitropyridine to one molecule of 1,4-diiodotetrafluorobenzene. SCXRD shows that this stoichiomorph packs in the monoclinic $P2_1/n$ space group. There is a single crystallographically distinct C-I...N halogen bond between 1,4-diiodotetrafluorobenzene and 3-nitropyridine characterized by a distance of 2.896 Å ($R_{XB} = 0.82$) and an angle of 175.6° (Table 2; Figure 3). Neither of the nitro oxygen atoms forms a halogen bond to iodine. Instead, some short

intermolecular oxygen-hydrogen contacts are noted (~ 2.6 Å). Cocrystal **D** was reproducibly prepared in quantities sufficient for characterization by PXRD. As seen in Figure 4, the polymorph which was characterized via SCXRD is also obtained in powder form; manual grinding with a mortar and pestle for PXRD experiments did not alter the polymorphic form.

The $^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS and $^1\text{H} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectra of a powdered sample of cocrystal **D** are presented in Figure 5 (b,c). The $^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectrum of pure 1,4-diiodotetrafluorobenzene is also presented in Figure 5(a) for comparison purposes. As seen in Figure 5(b), the $^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS experiment cleanly selects for those carbon atoms which are on the diiodotetrafluorobenzene ring, and suppresses those which are on the 3-nitropyridine molecule. This is attributed to the mechanism of polarization transfer from ^{19}F to ^{13}C , namely via the through-space dipolar interaction which is apparently too weak in this case to polarize ^{13}C spins on the spatially distant 3-nitropyridine molecule. This has been used previously as a spectral editing tool in various halogen-bonded cocrystals and is again shown to be useful in the present case.¹⁶ In addition to the dominant aromatic C-F resonances at ~ 147 ppm, a weaker and broader peak at ~ 77 ppm is attributed to the carbons directly bonded to iodine (see Table 3). This substantial frequency shift is due to relativistic heavy-atom effects on light-atom shielding (HALA) effects^{28,29,30,31} of the heavy ^{127}I nuclide on ^{13}C , and has been noted previously in several halogen-bonded systems.^{16,18,32,33} A close inspection of the C-I peak for pure 1,4-diiodotetrafluorobenzene and that for cocrystal **D** reveals only a very small change in peak position, from 76.8 ± 1.4 ppm to 77.2 ± 1.5 ppm. The shift to higher ^{13}C frequencies upon formation of a halogen bond to iodine is consistent with several previous reports.^{16,33} It should be noted that a previous multifield study of the ^{13}C resonance in 1,4-diiodotetrafluorobenzene enabled a proper measurement of the actual isotropic chemical shift rather than simply the peak position;

these may not necessarily coincide (and are likely to have different errors) due to residual dipolar coupling to ^{127}I , which is a spin-5/2 nucleus with 100% natural abundance. Thus, while the errors assigned to these peak positions are large in order to reflect the fact that the peak positions are not necessarily the exact chemical shift values, a small shift of the peak maximum from 76.8 to 77.2 ppm is clearly observed presently. The $^1\text{H} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectra of cocrystal **D** (Figure 5(c)) also show that this method is a useful spectral editing tool in cocrystals, selecting only for the 3-nitropyridine molecules. The fact that this spectrum was obtained at room temperature with MAS is further proof of cocrystal formation, as the acquisition of $^1\text{H} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectra of pure 3-nitropyridine would require cooling due to a melting point for the latter of 35 to 40°C. ^{13}C NMR line widths of approximately 125 to 180 Hz are also consistent with the formation of a solid cocrystal incorporating 3-nitropyridine; line widths for melted pure 3-nitropyridine are an order of magnitude less (see Supporting Information).

Cocrystal **C** was obtained via slow evaporation from dichloromethane and has a stoichiometry of two 1,4-diiodotetrafluorobenzene molecules to one molecule of 3-nitropyridine. SCXRD shows that this system packs in the triclinic $P\bar{1}$ space group. There is a single crystallographically distinct C-I $\cdots$ N halogen bond between 1,4-diiodotetrafluorobenzene and 3-nitropyridine characterized by a distance of 2.940 Å ($R_{\text{XB}} = 0.83$) and an angle of 175.4° (Table 2; Figure 6).

In addition, this stoichiometric cocrystal is the only one of the three studied in this work to feature a halogen bond between iodine and one of the oxygen atoms of the nitro group (Table 2; Figure 6). The two distinct halogen bonds result in the formation of chains of molecules. The C-I $\cdots$ O halogen bond is characterized by a distance of 3.036 Å ($R_{\text{XB}} = 0.867$) and an angle of 177.5°. Cocrystal **C** was prepared in powdered form as well, and PXRD shows a good agreement between

the diffractogram predicted from the SCXRD structure and that obtained experimentally, despite poor signal-to-noise (Figure 7). These data confirm that the polymorphic form of the crystal was retained upon light grinding with a mortar and pestle.

The $^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS and $^1\text{H} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectra of a powdered sample of cocrystal **C** are presented in Figure 8 (b,c). The $^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectrum of pure 1,4-diiodotetrafluorobenzene is also presented in Figure 8(a). As is evident in Figure 8(b), the $^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS experiment cleanly selects for those carbon atoms which are on the diiodotetrafluorobenzene ring, whereas the $^1\text{H} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectrum selects for those which are on the 3-nitropyridine molecule; this was also seen for cocrystal **D** (vide supra). In comparison to the case of cocrystal **D**, slightly larger ^{13}C NMR frequency shifts are seen Figure 8 upon formation of cocrystal **C**, relative to pure 1,4-diiodotetrafluorobenzene. The ^{13}C peaks for carbons directly bonded to fluorine show a decrease in average chemical shift of approximately 0.7 ppm upon cocrystallization whereas those bonded to iodine show an increase of approximately 1.6 ppm (Table 3). This seems to be opposite the general trend that a shorter halogen bond results in a larger increase in the C-I chemical shift;^{16,33} however, the differences both in halogen bond length and ^{13}C chemical shifts when comparing cocrystals **C** and **D** are small.

The large number of crystallographically distinct C-I $\cdots$ N halogen bonds (twelve) in the three stoichiometric cocrystals studied here provides an interesting opportunity to assess the relationship between halogen bond distance and angle maintaining the same nominal chemical composition. However, even under these controlled conditions, no strong correlation was observed (Figure 9).

Conclusions

Three novel stoichiometric cocrystals of 1,4-diiodotetrafluorobenzene and 3-nitropyridine with molar ratios of 1:1, 2:1, and 1:2, respectively, have been prepared by slow evaporation methods and characterized by single-crystal X-ray diffraction, powder-X-ray diffraction, and $^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS and $^1\text{H} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectroscopy. These three stoichiomorphs each pack in a different space group and they all feature halogen bonds between iodine and the pyridyl ring nitrogen. In only one case is a halogen bond between iodine and an oxygen atom on the nitro group observed. Ten crystallographically distinct halogen bonds are observed in the 1:2 cocrystal. Thus, significant crystallographic differences are seen for a set of three chemically identical (with varying stoichiometry) systems. ^{13}C solid-state NMR spectroscopy showed small frequency shifts in particular of the C-I peak of 1,4-diiodotetrafluorobenzene upon halogen bond formation, and cross-polarization from ^{19}F to ^{13}C vs ^1H to ^{13}C provided clean spectral editing, with the former experiment generating a subspectrum of the fluorinated halogen bond donor and the latter generating a subspectrum of the halogen bond acceptor. Cocrystallization of the low-melting 3-nitropyridine provided a route to maintain this component in the solid state over a larger temperature range. Overall, this work contributes to the systematic exploration of the polymorphic and stoichiometric cocrystal landscape of halogen-bonded systems.

Supporting Information Available

Crystallographic information files have been uploaded to the CCDC with accession numbers 2101747, 2101748, and 2101750. Figure showing the ^{13}C NMR spectrum of pure 3-nitropyridine.

Competing interests

The authors declare there are no competing interests.

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Table 1. Selected X-ray Crystallographic Data for the Stoichiometric Cocrystals Studied Herein

	Cocrystal A	Cocrystal C	Cocrystal D
empirical formula	C ₁₆ H ₈ F ₄ I ₂ N ₄ O ₄	C ₁₁ H ₄ F ₄ I ₂ N ₂ O ₂	C ₁₆ H ₈ F ₄ I ₂ N ₄ O ₄
formula weight (g · mol ⁻¹)	650.06	525.96	650.06
crystal system	monoclinic	triclinic	monoclinic
space group	<i>C c</i>	<i>P 1̄</i>	<i>P 2₁/n</i>
<i>a</i> (Å)	6.1328(5)	7.5779(9)	10.889(5)
<i>b</i> (Å)	54.226(4)	7.8895(10)	5.277(2)
<i>c</i> (Å)	29.852(2)	13.6245(17)	16.830(8)
α (deg)	90	76.189(3)	90
β (deg)	94.548(5)	80.848(3)	94.294(5)
γ (deg)	90	63.945(3)	90
<i>V</i> (Å ³)	9896.3(14)	709.24(15)	964.3(8)
<i>Z</i>	20	2	2
<i>T</i> (K)	200(2)	203(2)	203(2)
ρ_{calcd} (g · cm ⁻³)	2.182	2.463	2.239
μ (mm ⁻¹)	3.246	4.483	3.332
$2\theta_{\text{max}}$ (deg)	50.000	61.426	52.788
total/unique reflections	52387/17392	17297/4391	11712/1969
Reflections [<i>I</i> ₀ ≥ 2σ(<i>I</i> ₀)]	12518	3594	1603
<i>R</i> ₁ , <i>wR</i> ₂ [<i>I</i> ₀ ≥ 2σ(<i>I</i> ₀)]	0.0642, 0.1339	0.0243, 0.0502	0.0430, 0.1034
goodness of fit	1.025	1.031	1.064
CCDC Number	2101747	2101748	2101750

Table 2. Key Geometric Descriptors of Halogen Bonds in the Stoichiomorphs

cocrystal	<i>r</i> _{N...I} / Å	C-I ... N angle
C	2.940; 3.036 ^a	175.4°; 177.5° ^a
D	2.896	175.6°
A (site 1)	2.913	172.0°
A (site 2)	2.925	174.9°
A (site 3)	2.867	169.6°
A (site 4)	2.946	174.1°
A (site 5)	2.936	173.3°
A (site 6)	2.938	174.0°
A (site 7)	2.990	174.8°
A (site 8)	2.914	173.6°
A (site 9)	2.865	172.1°
A (site 10)	2.929	174.3°

^a. O...I halogen bond.

Table 3. Carbon-13 Isotropic Chemical Shifts Measured in the Solid State

	$^1\text{H} \rightarrow ^{13}\text{C}$ CP/MAS	$^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS ^b
<i>p</i> -diiodotetrafluorobenzene ^a	n/a	147.6 ± 0.3 , 76.8 ± 1.4
cocrystal C	125.9 ± 0.2 , 132.6 ± 0.2 , 146.1 ± 0.2 , 153.4 ± 0.2	147.1 ± 0.3 , 78.4 ± 1.5
cocrystal D	125.9 ± 0.2 , 132.5 ± 0.2 , 146.0 ± 0.2 , 153.3 ± 0.2	147.6 ± 0.3 , 77.2 ± 1.5

a. From reference 16 and also reconfirmed in this work.

b. For carbons bonded to iodine, these are peak positions and are thus only the approximate true isotropic chemical shifts due to residual dipolar coupling between ^{13}C and ^{127}I . The peak positions are clearly different for different samples (see e.g., Figure 8); however, large errors are assigned due to uncertainty in the quantitative effects of the residual dipolar coupling on the peak positions. Errors on other chemical shifts for carbons not bonded to iodine reflect the reproducibility of the measurement.

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Figure 1. Molecular structures of halogen bond donor **1** (1,4-diiodotetrafluorobenzene) and halogen bond acceptor **2** (3-nitropyridine).

Figure 2. Unit cell of cocrystalline stoichiomorph **A** as seen along the a axis. Halogen bonds are indicated by dashed red and turquoise lines.

Figure 3. Halogen-bonded molecules of cocrystalline stoichiomorph **D**. The I1-N2 distance is shown.

Figure 4. Experimental (i) and simulated (ii) powder X-ray diffraction patterns for cocrystalline stoichiomorph **D**.

Figure 5. (a) $^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectrum of solid *p*-diiodotetrafluorobenzene ($\nu_r = 10$ kHz); (b) $^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectrum of cocrystal **D** ($\nu_r = 12$ kHz); (c) $^1\text{H} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectrum of cocrystal **D** ($\nu_r = 11$ kHz). A small halogen-bond induced chemical shift of 0.4 ppm is seen for the C-I carbons at ~ 77 ppm. Asterisks denote spinning sidebands.

Figure 6. Halogen-bonded network of cocrystalline stoichiomorph **C**. The I1-N2 distance and I2-O2 distances are shown.

Figure 7. Experimental (i) and simulated (ii) powder X-ray diffraction patterns for cocrystalline stoichiomorph C.

Figure 8. (a) $^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectrum of solid *p*-diiodotetrafluorobenzene ($\nu_r = 10$ kHz); (b) $^{19}\text{F} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectrum of cocrystal C ($\nu_r = 12$ kHz); (c) $^1\text{H} \rightarrow ^{13}\text{C}$ CP/MAS NMR spectrum of cocrystal C ($\nu_r = 11$ kHz). A halogen-bond induced chemical shift of -0.7 ppm is seen for the C-F carbons at 147.6 ppm and of +1.6 ppm is seen for the C-I carbons at ~77 ppm. Asterisks denote spinning sidebands.

Figure 9. Lack of correlation between nitrogen-iodine halogen bond distances and angles in stoichiometric cocrystals **A**, **C**, and **D**.

Graphical Abstract

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