Electronic Supplementary Material (ESI) for ChemComm.

Evaluating structure-property relationship in a new family of mechanically flexible co-crystals

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1. Primary intermolecular interaction in the co-crystals

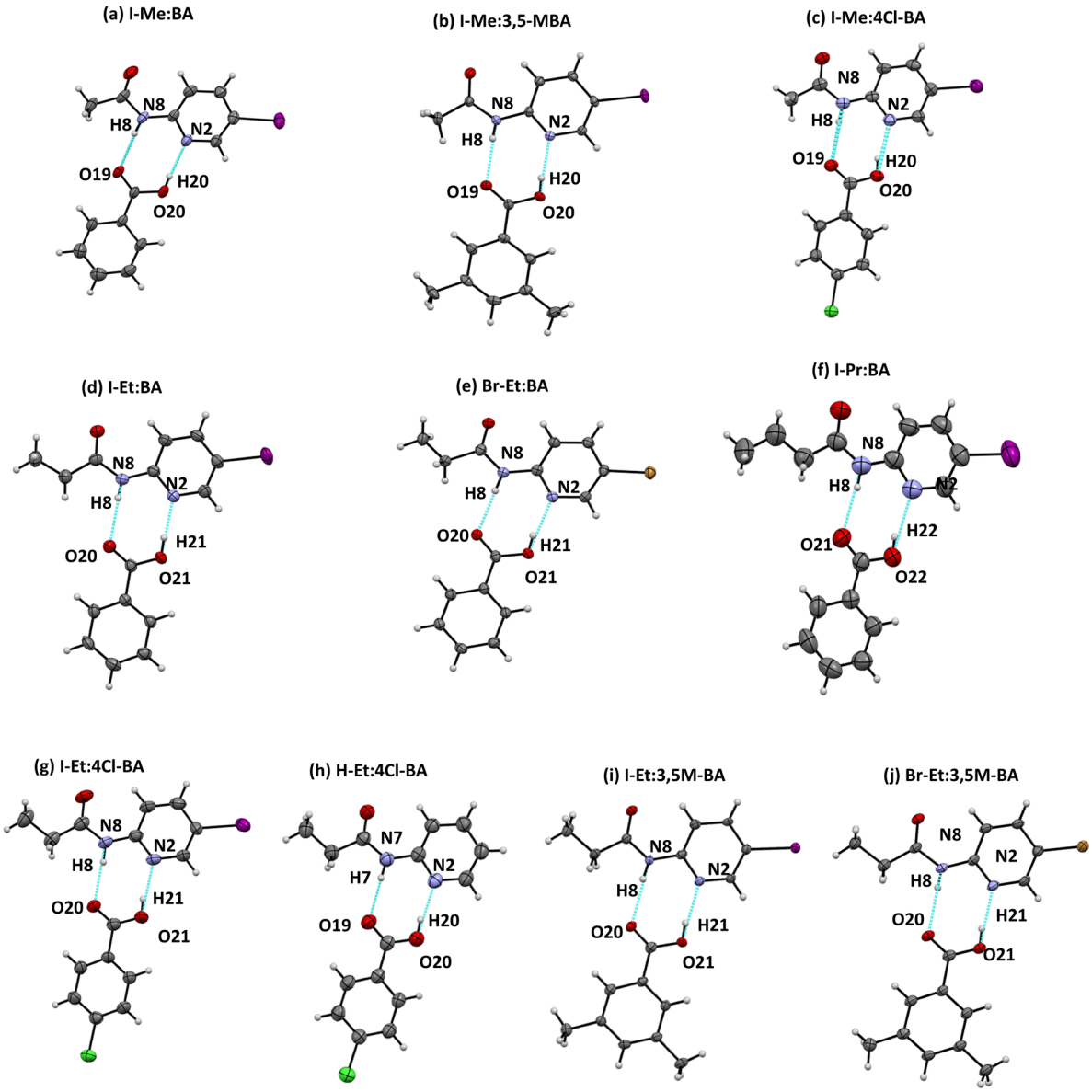

Figure 1. Primary hydrogen-bond interaction interactions in (a) I-Me:BA (b) I-Me:3,5M-BA (c) I-Me:4Cl-BA (d) I-Et:BA (e) Br-Et:BA (f) I-Pr:BA (g) I-Et:4Cl-BA (h) H-Et:4Cl-BA (i) I-Et:3,5-MBA (j) I-Et:3,5-MBA

1.2 Primary hydrogen- and halogen bond interactions in the two plastic co-crystals.

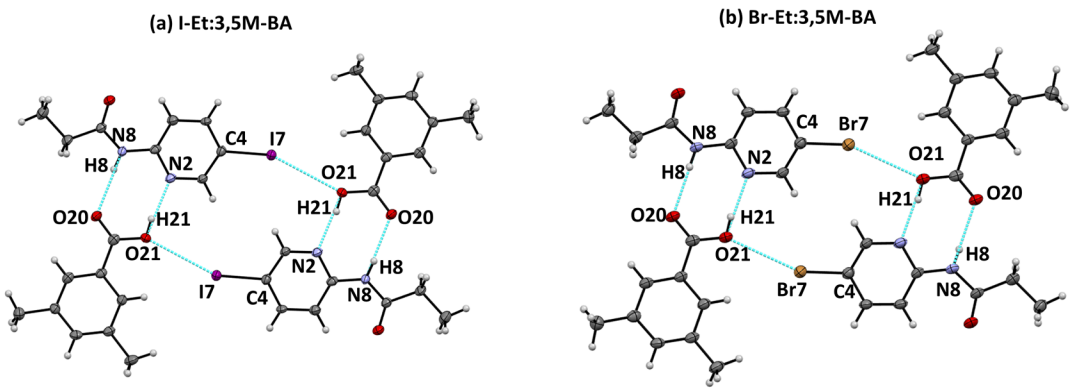

Figure 2. Primary hydrogen- and halogen bond interactions in (a) I-Et:3,5M-BA and (b) Br-Et:3,5M-BA

1.3. Hydrogen- and halogen and bond geometries in these co-crystals

Table 1. The relevant hydrogen- and halogen and bond geometries in these co-crystals

Code	D-H/I···A	D/I···A (A)	D-H···A (deg)
I-Me:BA	N8-H8···O19	2.889(6)	173.(6)
	O20-H20···N2	2.664(6)	167.(8)
I-Me:3,5M-BA	N8-H8···O19	2.879(4)	161(5)
	O20-H20···N2	2.683(4)	174(7)
I-Me:4Cl-BA	N8-H8···O19	2.956(7)	169.66(3)
	O20-H20···N2	2.642(6)	167.10(4)
I-Et:BA	N8-H8···O20	2.913(4)	176.(4)
	O21-H21···N2	2.678(4)	174.(5)
Br-Et:BA	N8-H8···O20	2.924(4)	177.32(12)
	O21-H21···N2	2.681	169.3(13)
I-Pr:BA	N8-H8···O21	2.886(6)	173.(7)
	O22-H22···N2	2.715(6)	162.(8)
I-Et:4Cl-BA	N8-H8···O20	2.894(10)	173.(9
	O21-H21···N2	2.643(10)	166.(13)
H-Et:4Cl-BA	N7-H7···O19	2.8619(3)	178(5)
	O20-H20···N2	2.638(7)	173(8)
I-Et:3,5M-BA	N8-H8···O19	2.898 (4)	161.32(9)
	O20-H20···N2	2.687(4)	171.1(7)
	C4-I7···O21	3.324	156.51(10)
Br-Et:3,5M-BA	N8-H8···O20	2.887(2)	163.84(18)
	O21-H21···N2	2.672(4)	170.76(2)
	C4-Br7···O21	3.228(2)	157.08(11)

2. Secondary intermolecular interactions in the co-crystals

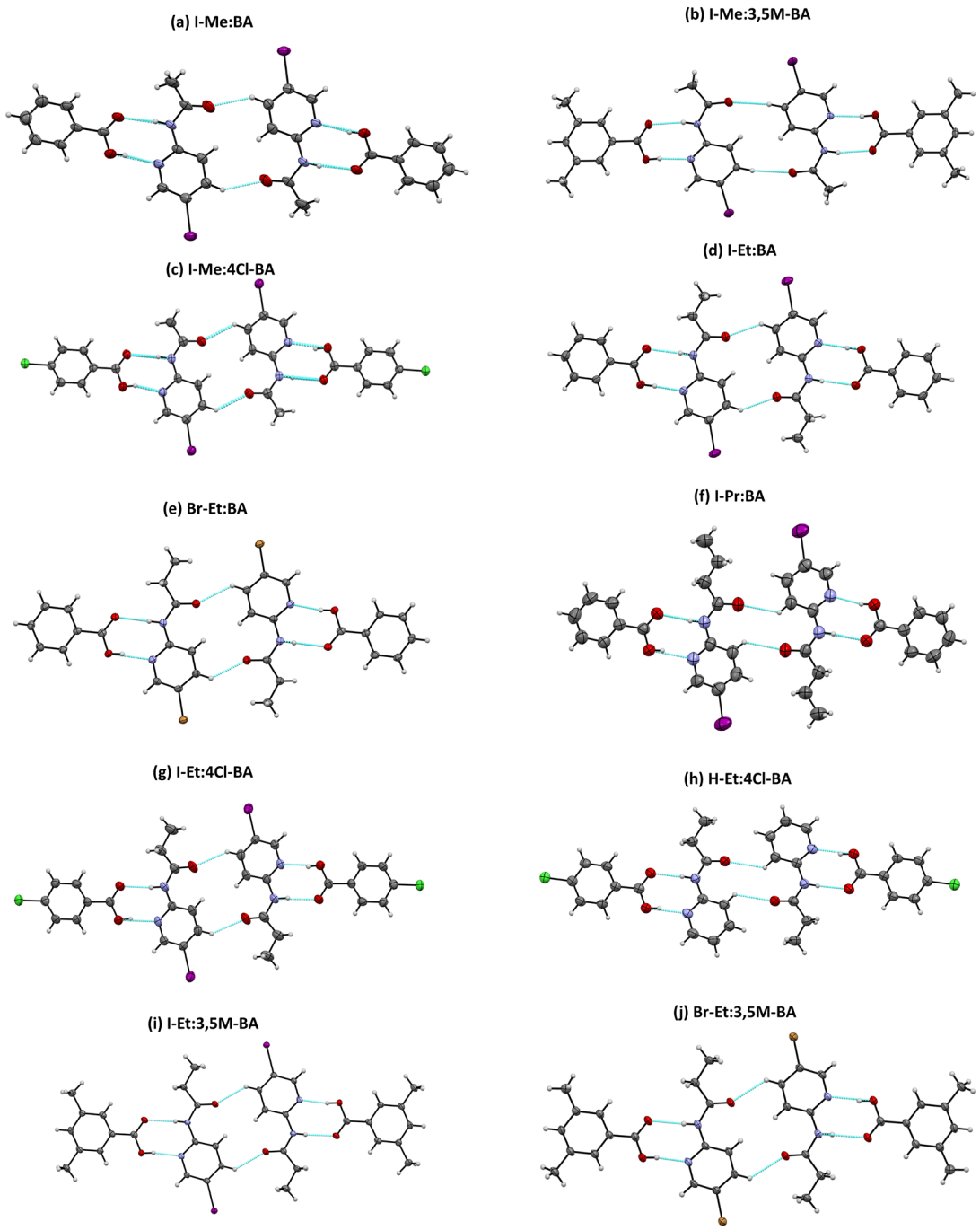

Figure 3. Tetramers in the crystal structures of (a) I-Me:BA (b) I-Me:3,5-MBA (c) I-Me:4Cl-BA (d) I-Et:BA (e) Br-Et:BA (f) I-Pr:BA (g) I-Et:4Cl-BA (h) H-Et:4Cl-BA (i) I-Et:3,5-MBA (j) Br-Et:3,5-MBA

3. Establishing structure-property correlations using crystal packing features

3.1 Packing features of N-(5-iodopyridin-2-yl)acetamide:3,5-dimethyl benzoic acid (I-Me:3,5M-BA)

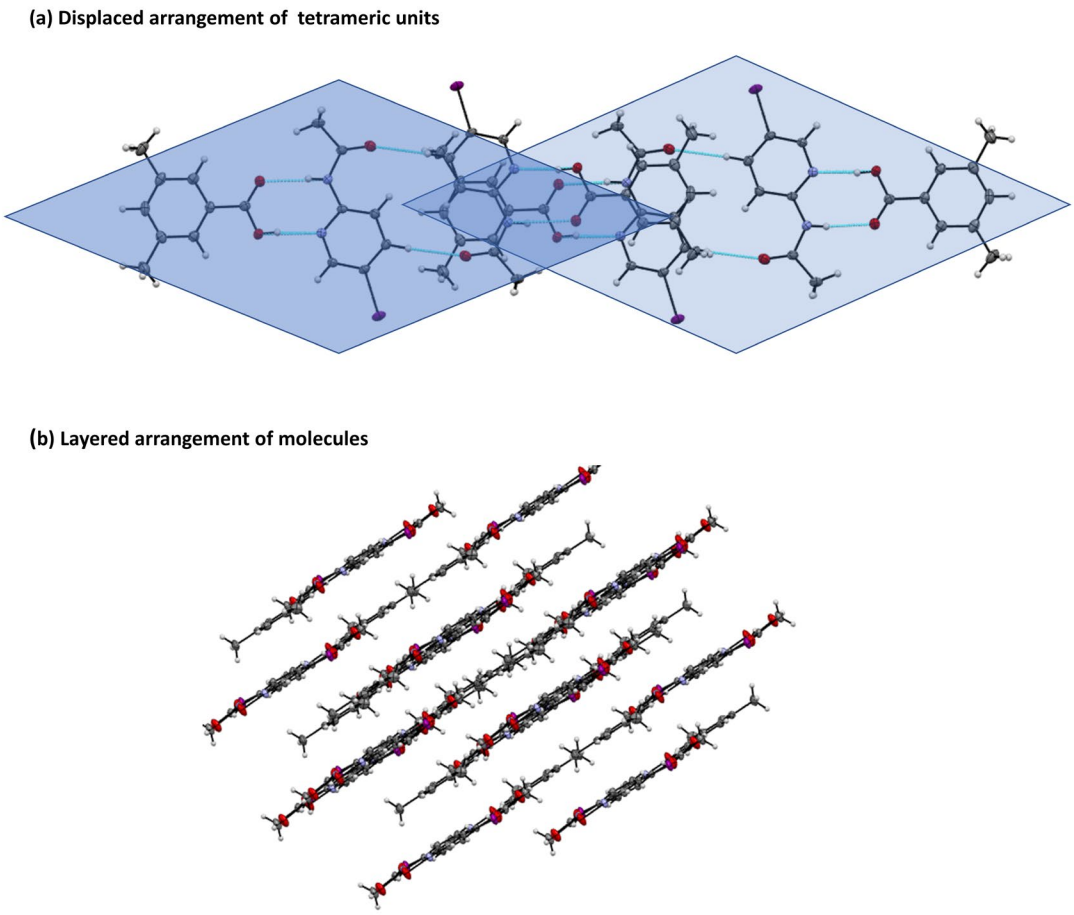

Figure 4. Packing features of I-Me:3,5M-BA (a) Displaced arrangement of tetrameric units (b) layered arrangement of molecules.

3.2 N-(5-iodopyridin-2-yl)acetamide:4-chloro benzoic acid (I-Me:4Cl-BA)

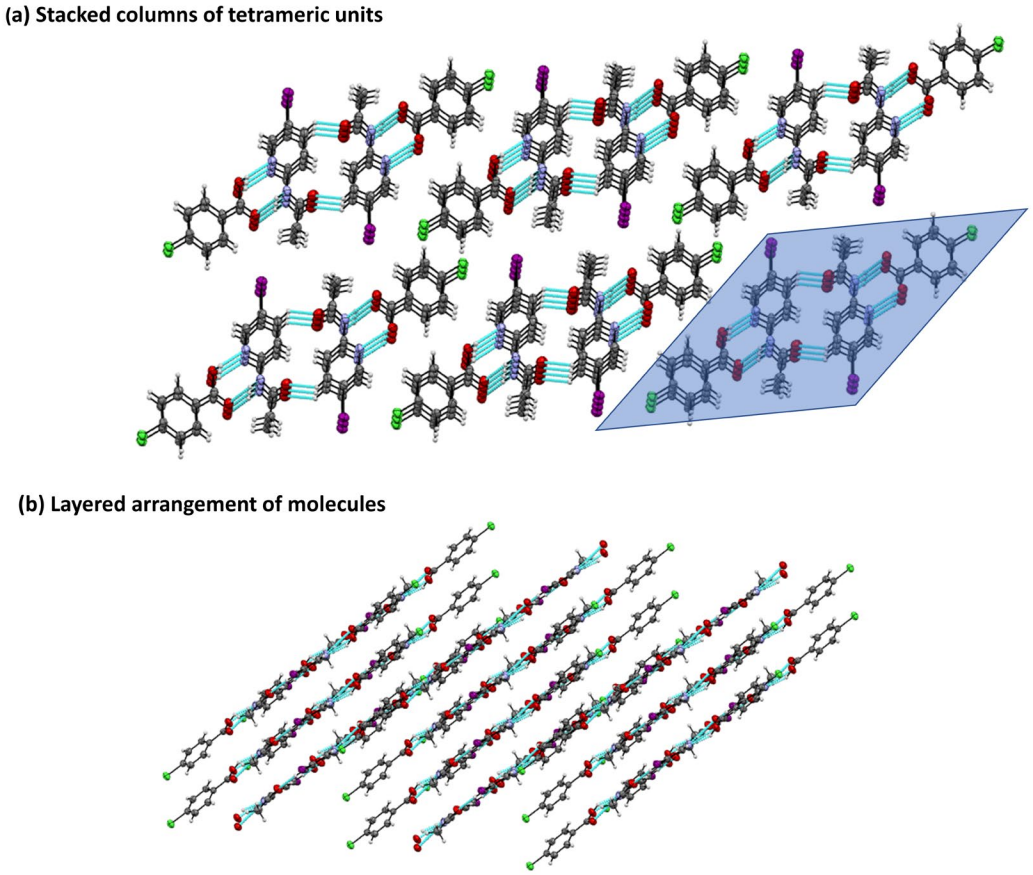

Figure 5 Packing features of I-Me:4Cl-BA (a) Stacked column of tetrameric units (b) layered arrangement of molecules

3.3 N-(5-bromopyridin-2-yl)propionamide:benzoic acid (Br-Et:BA)

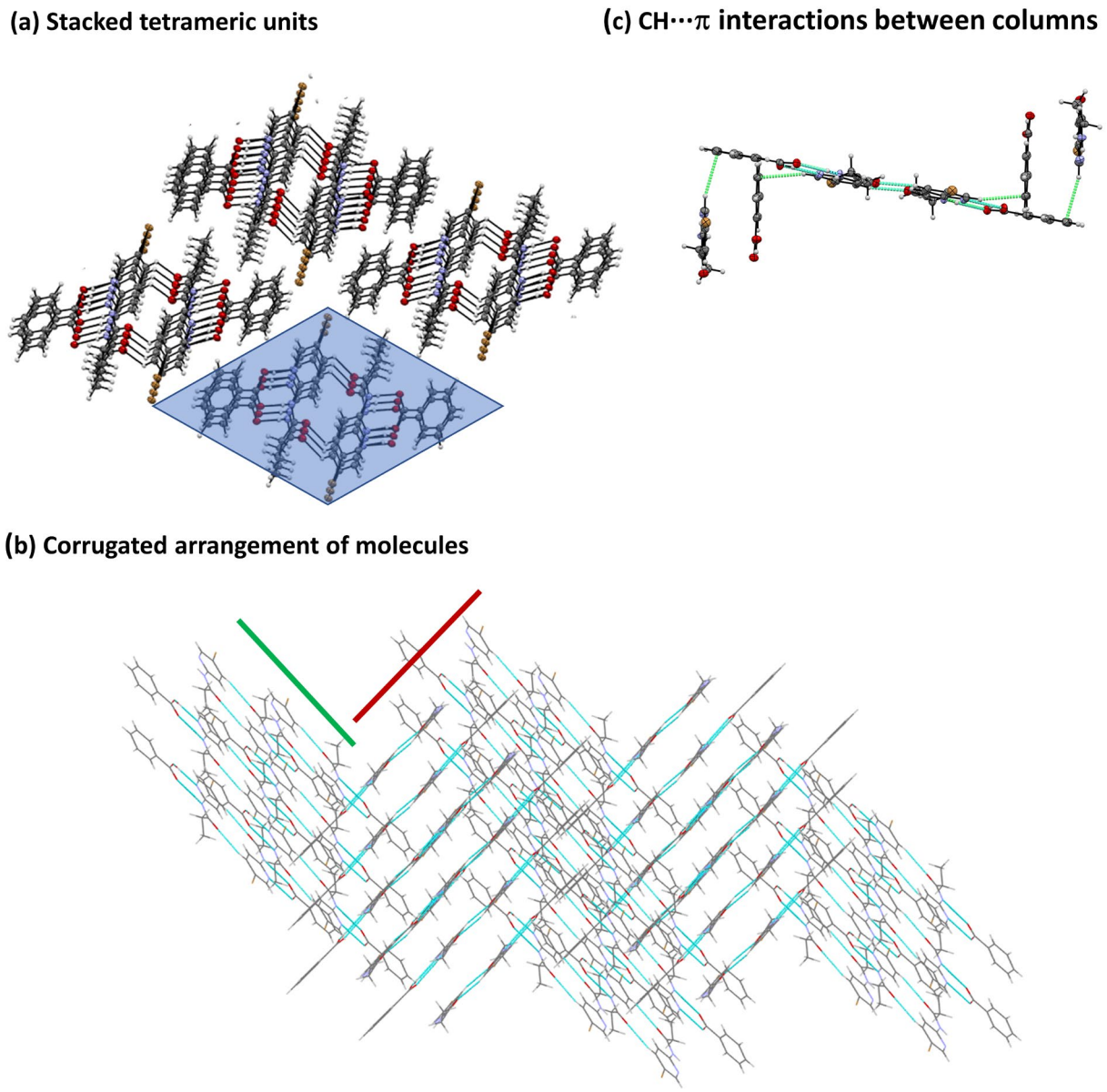

Figure 6. Packing features of Br-Et:BA (a) Stacked tetrameric units (b) Corrugated arrangement of molecules (c) CH···π interactions between columns

3.4 N-(5-iodopyridin-2-yl)butyramide:benzoic acid (I-Pr:BA)

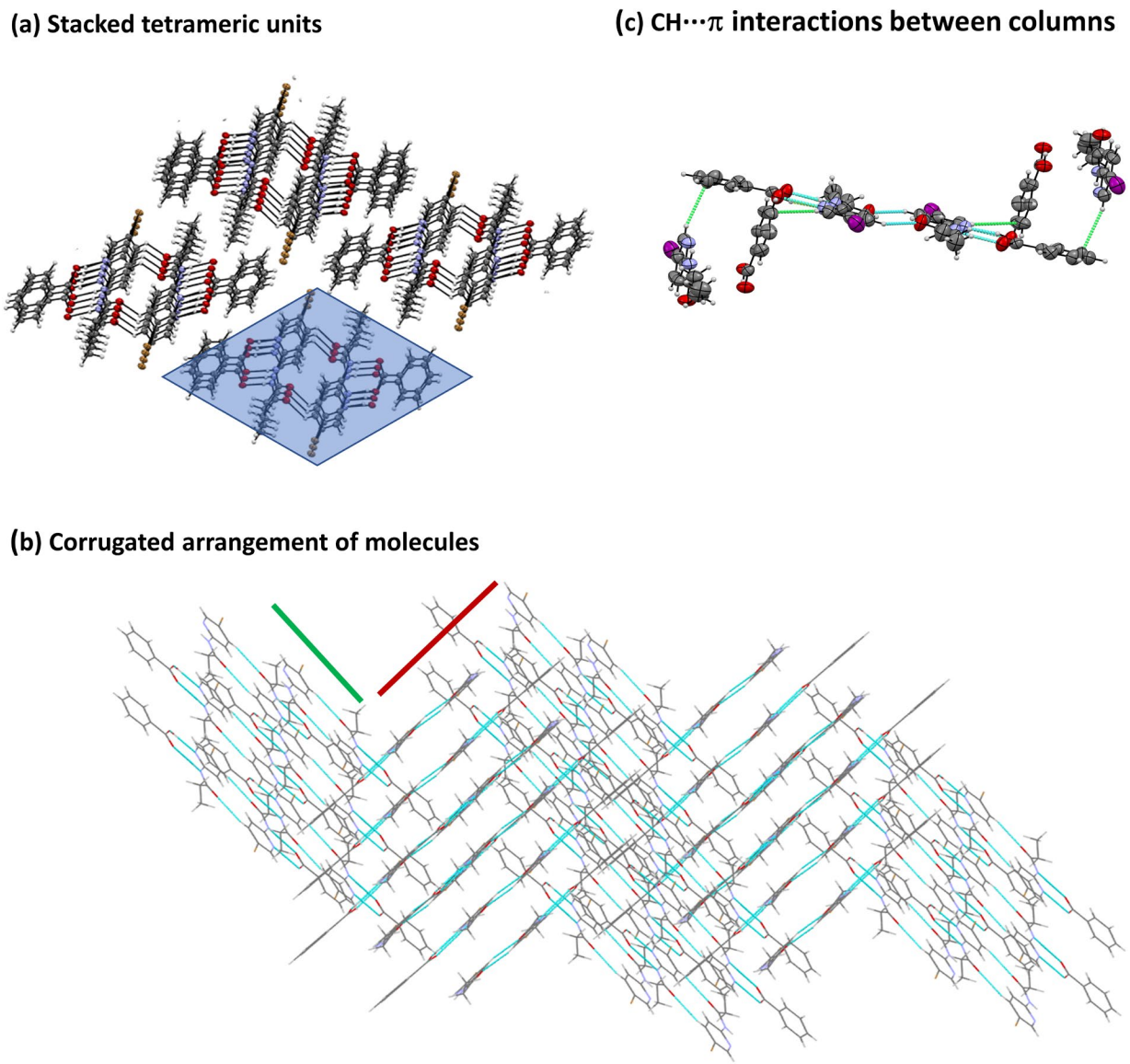

Figure 7. Packing features of I-Pr:BA (a) Stacked tetrameric units (b) Corrugated arrangement of molecules (c) CH···π interactions between columns

3.5 N-(5-iodopyridin-2-yl)propionamide:4-chloro benzoic acid, I-Et:4Cl-BA

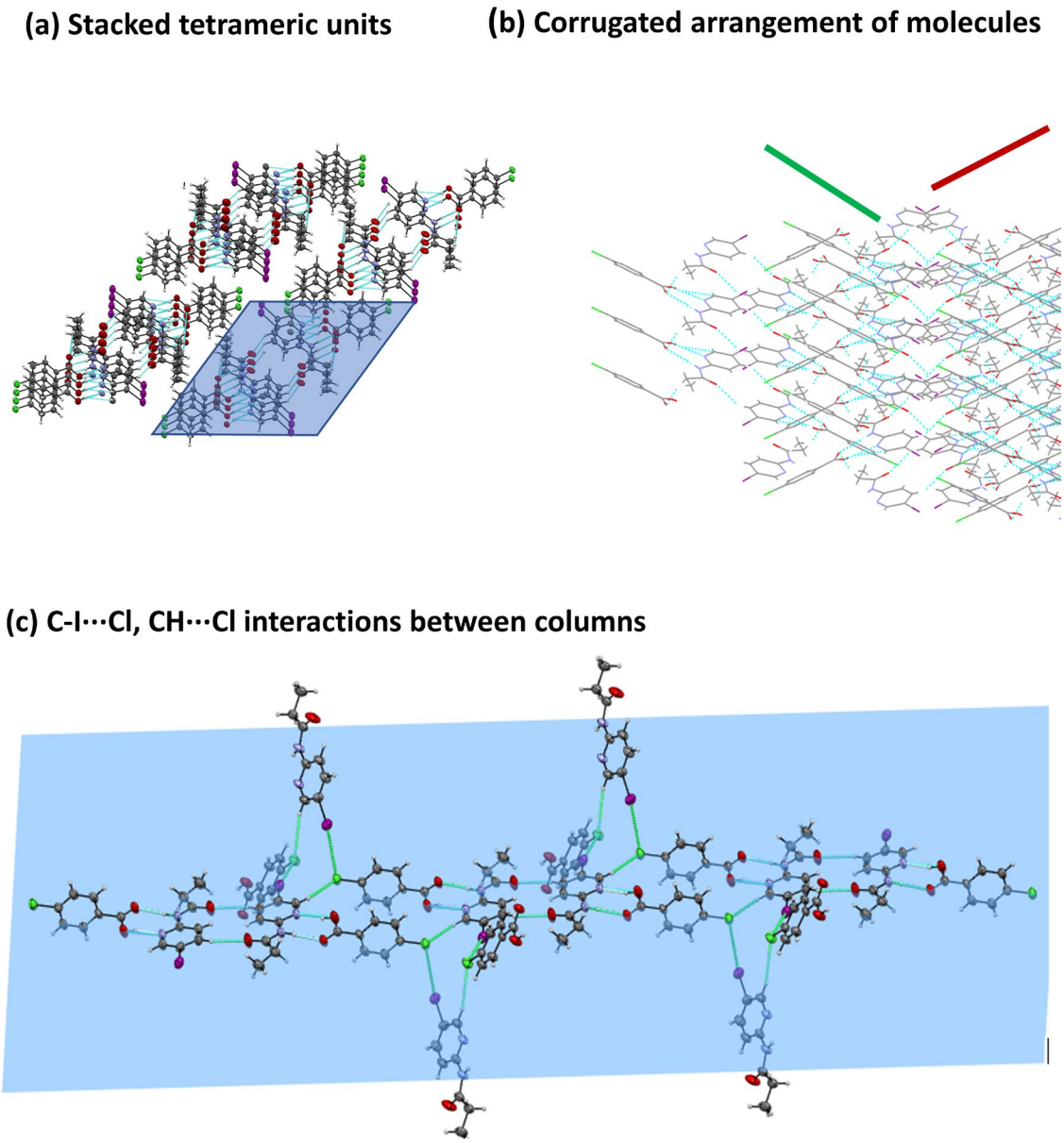

Figure 8. Packing features of I-Et:4Cl-BA (a) Stacked tetramers (b) Corrugated arrangement of molecules (c) C-I···Cl, C-H···Cl interactions between columns

3.6 N-(5-pyridin-2-yl)propionamide:4-chloro benzoic acid (H-Et:4Cl-BA)

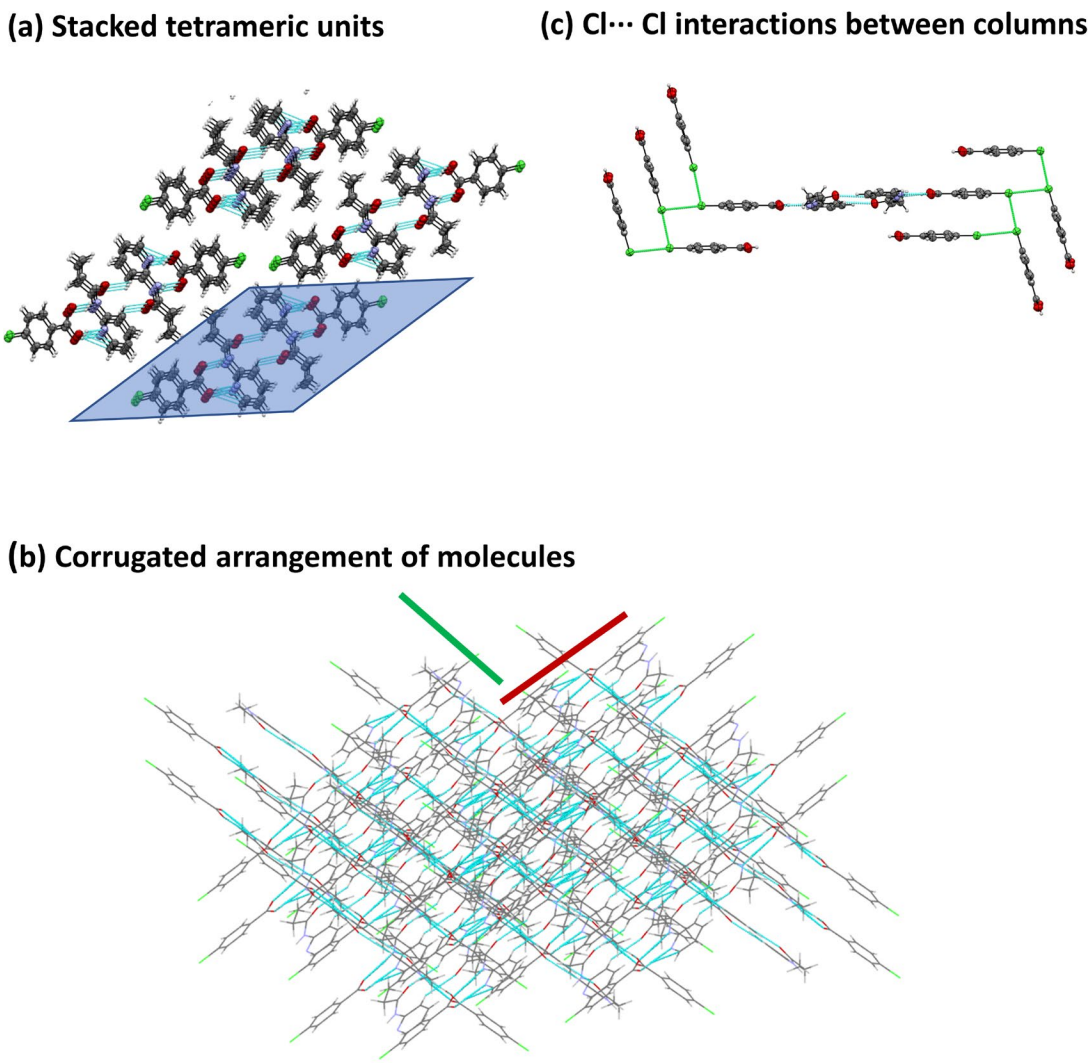

Figure 9. Packing features of H-Et:4Cl-BA (a) Stacked tetrameric units (b) Corrugated arrangement of molecules (c) Cl···Cl interactions between columns.

3.7 N-(5-bromopyridin-2-yl)propionamide: 3,5-dimethyl benzoic acid (Br-Et:3,5-MBA)

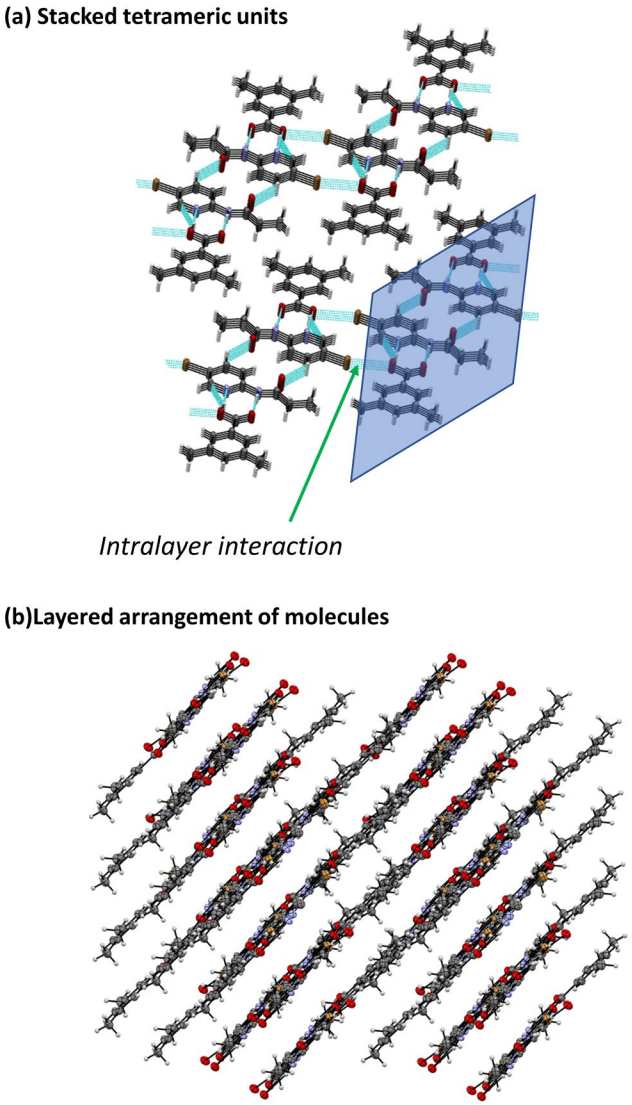

Figure 10. Packing features of Br-Et:3,5M-BA (a) Stacked column of tetrameric units interlinked by halogen bonding (b) layered arrangement of molecules

4. X-ray crystallography results

Table 2. X-ray crystallography results

Code	I-Me:BA	I-Me:3,5M-BA	I-Me:4Cl-BA	I-Et:BA	Br-Et:BA
CCDC. Deposit no.	2092007	2092009	2092010	2092012	2103264
Formula moiety	$(C_7H_7IN_2O)$ $(C_7H_6O_2)$	$(C_7H_7IN_2O)$ $(C_9H_{10}O_2)$	$(C_7H_7IN_2O)$ $(C_7H_5ClO_2)$	$(C_8H_9IN_2O)$ $(C_7H_6O_2)$	$(C_8H_9BrN_2O)$ $(C_7H_6O_2)$
Empirical formula	$C_{14}H_{13}IN_2O_3$	$C_{16}H_{17}IN_2O_3$	$C_{14}H_{12}ClIN_2O_3$	$C_{15}H_{15}IN_2O_3$	$C_{15}H_{15}BrN_2O_3$
Molecular weight	384.16	412.21	418.61	398.19	351.20
Color, Habit	Colorless, Parallelepiped	Colorless, Block	Colorless, Needle	Colorless, Rectangular	Colorless, Needle
Crystal system	Triclinic	Triclinic	Triclinic	Monoclinic	Monoclinic
Space group, *Z*	P -1, 2	P -1, 2	P -1, 2	P 1 21/n 1, 4	P 1 21/n 1, 4
a, Å	4.1768(8)	7.4358(2)	4.35000(10)	14.2075(8)	14.0457(6)
b, Å	11.513(2)	10.5039(2)	11.5717(2)	4.9292(3)	4.9964(3)
c, Å	15.476(3)	11.7955(3)	15.4381(3)	22.1266(12)	21.3687(7)
α, º	78.42(3)	69.3730(10)	78.041(2)	90	90
β, º	86.37(3)	82.684(2)	88.920(2)	90.025(2)	90.928(3)
γ, º	86.54(3)	73.631(2)	87.755(2)	90	90
Volume, Å^3	726.7(3)	826.87(4)	759.61(3)	1549.56(15)	1499.41(12)
Density, g/cm^3	1.756	1.656	1.830	1.707	1.556
T, ºK	200.(2)	199.99	200(2)	200.(2)	200.00(10)
Crystal size, min x mid x max	0.064 x 0.165 x 0.413	0.065 x 0.08 x 0.11	0.016 x 0.032 x 0.236	0.065 x 0.105 x 0.200	0.021 x 0.038 x 0.108
X-ray wavelength, Å	1.54178	1.54178	1.54184	1.54178	1.54184
μ, mm^{-1}	17.400	15.337	18.289	16.344	3.846
Trans min / max	0.05 / 0.40	0.5234/ 0.7533	0.45933 / 1.00000	0.14 / 0.42	0.55829 / 1.00000
ϑ_{min}, º	2.92	4.006	2.926	3.70	3.738
ϑ_{max}, º	70.27	70.173	76.860	68.40	77.353
Reflections					
collected	11978	11691	15874	10580	12344
independent	2543	2904	3214	2742	3137
observed	2443	2697	3028	2488	2338
R_{int}	0.0567	0.0630	0.0426	0.0488	0.0524
Threshold expression	> 2σ(*I*)	> 2σ(*I*)	> 2σ(*I*)	> 2σ(*I*)	> 2σ(*I*)
No. parameters	190	211	192	199	192
No. restraints	2	2	0	0	0
R_1 (observed)	0.0479	0.0387	0.0228	0.0402	0.0441
wR_2 (all)	0.1257	0.0911	0.0615	0.1075	0.1300
Goodness of fit (all)	1.059	1.050	1.102	1.053	1.022
ρ_{max}, ρ_{min}, e Å^{-3}	1.616, -1.123	1.266, -1.016	0.426, -0.425	0.796, -1.147	0.604, -0.535
Completeness to 2ϑ limit	0.924	0.924	0.994	0.969	0.985

Code	I-Pr:BA	I-Et:4Cl-BA	H- Et:4Cl-BA	I- Et:3,5M-BA	Br-Et:3,5M-BA
CCDC. Deposit no.	2092013	2092014	2092015	2092016	2092017
Formula moiety	$(C_9H_{11}IN_2O)$ $(C_7H_6O_2)$	$(C_8H_9IN_2O)$ $(C_7H_5ClO_2)$	$(C_8H_{10}N_2O)$ $(C_7H_5ClO_2)$	$(C_8H_9IN_2O)$ $(C_9H_{10}O_2)$	$(C_8H_9BrN_2O)$ $(C_9H_{10}O_2)$
Empirical formula	$(C_{16}H_{17}IN_2O_3)$	$(C_{15}H_{14}ClIN_2O_3)$	$C_{15}H_{15}N_2O_3Cl$	$(C_{17}H_{19}IN_2O)$	$(C_{17}H_{19}BrN_2O)$
Molecular weight	412.21	432.63	306.74	426.24	379.25
Color, Habit	Colorless, Rectangular	Colorless, Rectangular	Colorless, Needle	Colorless, Block	Colorless, Needle
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic	Triclinic
Space group, *Z*	P 1 21/n 1, 4	C 1 2/c 1, 8	P 1 21/n 1, 4	*P*$\bar{1}$, 2	*P*$\bar{1}$, 2
a, Å	15.6069(6)	34.113(3)	15.3651(2)	4.5288(2)	4.7003(3)
b, Å	4.7766(2)	4.0412(3)	4.47304(5)	12.8682(4)	12.7927(5)
c, Å	22.7736(8)	28.573(2)	21.7942(3)	15.2840(4)	14.1635(6)
α, º	90	90	90	97.439(2)	97.664(3)
β, º	92.088(3)	124.614(3)	106.2128(14)	94.401(3)	93.157(5)
γ, º	90	90	90	93.065(3)	91.561(4)
Volume, Å^3	1696.60(11)	3241.8(4)	1438.32(3)	878.80(5)	842.24(7)
Density, g/cm^3	1.614	1.773	1.417	1.611	1.495
T, ºK	296.(2)	200.(2)	200.00(10)	200.00(10)	100.01(10)
Crystal size, min x mid x max	0.040 x 0.065 x 0.110	0.042 x 0.065 x 0.130	0.02 x 0.062 x 0.344	0.059 x 0.089 x 0.155	0.078 x 0.126 x 0.83
X-ray wavelength, Å	1.54178	1.54178	1.54178	1.54184	1.54184
μ, mm^{-1}	14.949	17.165	2.463	14.451	3.467
Trans min / max	0.29/ 0.59	0.21/0.53	0.67801/1.00000	0.66677/ 1.00000	0.72908/ 1.00000
ϑ_{min}, º	3.49	3.15	3.146	2.926	3.154
ϑ_{max}, º	70.46	68.21	77.583	77.029	77.194
Reflections					
collected	13110	12254	13927	24138	9084
independent	3111	2888	3062	3664	3358
observed	2171	2636	2862	3224	3072
R_{int}	0.0525	0.0500	0.0223	0.0500	0.0650
Threshold expression	> 2σ(*I*)	> 2σ(*I*)	> 2σ(*I*)	> 2σ(*I*)	> 2σ(*I*)
No. parameters	208	208	192	213	212
No. restraints	2	2	0	0	0
R_1 (observed)	0.0497	0.0668	0.0346	0.1082	0.0560
wR_2 (all)	0.1550	0.1737	0.1024	0.1082	0.1568
Goodness of fit (all)	1.109	1.170	1.085	1.076	1.106
ρ_{max}, ρ_{min}, e Å^{-3}	0.730, -0.908	1.943, -0.876	0.224, -0.259	0.954, -1.052	1.135, -1.134
Completeness to 2ϑ limit	0.961	0.976	0.996	0.982	0.945

5. Synthesis of target molecules.

- Synthesis of N-(5-iodopyridin-2-yl)acetamide (I-Me)

2-Amino-5-iodopyridine (2.20 g, 10.0 mmol) was dissolved in 50 mL of pyridine and cooled in an ice bath. Acetyl chloride (1.06 mL, 14.8 mmol) was added dropwise maintaining the temperature between 0-5 ºC. After the addition was complete the contents were stirred at room temperature until no further starting material (2-amino-5-iodopyridine) was detected by TLC. Upon completion, chilled water (100 mL) was added and stirred for 15 minutes. The reaction contents were extracted with dichloromethane and the organic layer was washed with saturated sodium bicarbonate solution, brine, water and dried with anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to isolate the pure product. Yield 88 %, m.p 154 – 156°C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.60 (s, 1H), 8.51 (s, 1H), 8.10 (s, 1H), 7.96 (s, 1H), 2.08 (s, 3H).

- Synthesis of N-(5-iodopyridin-2-yl)propionamide (I-Et)

2-Amino-5-iodopyridine (2.20 g, 10.0 mmol) was dissolved in 50 mL of pyridine and cooled in an ice bath. Propionyl chloride (1.09 mL, 15.4 mmol) was added dropwise maintaining the temperature between 0-5 ºC. After the addition was complete the contents were stirred at room temperature until no further starting material (2-amino-5-iodopyridine) was detected by TLC. Upon completion, chilled water (100 mL) was added and stirred for 15 minutes. The reaction contents were extracted with dichloromethane and the organic layer was washed with saturated sodium bicarbonate solution, brine, water and dried with anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to isolate the pure product. Yield 90 %, m.p 139 – 141°C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.53 (s, 1H), 8.50 (s, 1H), 8.09 (s, 1H), 7.98 (s, 1H), 2.37 (s, 2H), 1.05 (s, 3H).

- Synthesis of N-(5-bromopyridin-2-yl)propionamide (Br-Et)

2-Amino-5-bromopyridine (1.73 g, 10.0 mmol) was dissolved in 50 mL of pyridine and cooled in an ice bath. Propionyl chloride (1.09 mL, 15.4 mmol) was added dropwise maintaining the temperature between 0-5 ºC. After the addition was complete the contents were stirred at room temperature until no further starting material (2-amino-5-bromopyridine) was detected by TLC. Upon completion, chilled water (100 mL) was added and stirred for 15 minutes. The reaction contents were extracted with dichloromethane and the organic layer was washed with saturated sodium bicarbonate solution, brine, water and dried with anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to isolate the pure product. Yield 85 %, m.p 136 – 138 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.58 (s, 1H), 8.40 (s, 1H), 8.08 (s, 1H), 7.97 (s, 1H), 2.37 (s, 2H), 1.07 (s, 3H).

- Synthesis of N-(5-pyridin-2-yl)propionamide (H-Et)

2-Aminopyridine (0.94 g, 10.0 mmol) was dissolved in 50 mL of pyridine and cooled in an ice bath. Propionyl chloride (1.09 mL, 15.4 mmol) was added dropwise maintaining the temperature between 0-5 ºC. After the addition was complete the contents were stirred at room temperature until no further starting material (2-amino-5-pyridine) was detected by TLC. Upon completion, chilled water (100 mL) was

added and stirred for 15 minutes. The reaction contents were extracted with dichloromethane and the organic layer was washed with saturated sodium bicarbonate solution, brine, water and dried with anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to isolate the pure product. Yield 75%, ^{1}H NMR (400 MHz, DMSO-d6) δ 10.39 (s, 1H), 8.29 (s, 1H), 8.09 (s, 1H), 7.76 (s, 1H), 7.07 (s, 1H), 2.37 (s, 2H), 1.05 (s, 3H).

- Synthesis of N-(5-iodopyridin-2-yl)butyramide (I-Pr)

2-Amino-5-iodopyridine (2.20 g, 10.0 mmol) was dissolved in 50 mL of pyridine and cooled in an ice bath. Butyryl chloride (1.54 mL, 14.8 mmol) was added dropwise maintaining the temperature between 0-5 ºC. After the addition was complete the contents were stirred at room temperature until no further starting material (2-amino-5-iodopyridine) was detected by TLC. Upon completion, chilled water (100 mL) was added and stirred for 15 minutes. The reaction contents were extracted with dichloromethane and the organic layer was washed with saturated sodium bicarbonate solution, brine, water and dried with anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to isolate the pure product. Yield 86, %, m.p 136 – 138°C ^{1}H NMR (400 MHz, DMSO-d6) δ 10.55 (s, 1H), 8.50 (s, 1H), 8.09 (s, 1H), 7.96 (s, 1H), 2.35 (s, 2H), 1.55 (s, 2H), 0.87 (s, 3H).

6. Synthesis of co-crystals

All 10 co-crystals were synthesized by slow evaporation of 0.034 mmol the target (I-acetyl/I-propyl/Br-propyl/H-propyl/ I-butyl) and 0.034 mmol of co-former (Benzoic acid, BA/ 4-Chloro benzoic acId, 4Cl-BA/ 3,5-Dimethyl benzoic acid, 3,5-MBA) combined in a 1:1 molar ratio in a solution of Ethyl acetate. The melting points of the co-crystals determined by differential scanning calorimetry (DSC) are given (Table 3) .

Table 3. Melting points of the co-crystals

Composition	Code	m.p
N-(5-iodopyridin-2-yl)acetamide:benzoic acid	I-Me:BA	122 – 124 ℃
N-(5-iodopyridin-2-yl)acetamide:3,5-dimethyl benzoic acid	I-Me:3,5M-BA	151 – 153 ℃
N-(5-chloropyridin-2-yl)acetamide: benzoic acid	I-Me:4Cl-BA	145 – 147 ℃
N-(5-iodopyridin-2-yl)propionamide:benzoic acid	I-Et:BA	123 – 125 ℃
N-(5-bromopyridin-2-yl)propionamide:benzoic acid	Br-Et:BA	120 – 122 ℃
N-(5-iodopyridin-2-yl)butyramide:benzoic acid	I-Pr:BA	99 – 101 ℃
N-(5-iodopyridin-2-yl)propionamide:4-chloro benzoic acid	I-Et:4Cl-BA	133 – 135 ℃
N-(5-pyridin-2-yl)propionamide:4-chloro benzoic acid	H-Et:4Cl-BA	96 – 98 ℃
N-(5-iodopyridin-2-yl)propionamide: 3,5-dimethyl benzoic acid	I-Et:3,5-MBA	144 – 146 ℃
N-(5-bromopyridin-2-yl)propionamide: 3,5-dimethyl benzoic acid	Br-Et:3,5-MBA	131 – 133 ℃

7. Images of crystals demonstrating flexibility

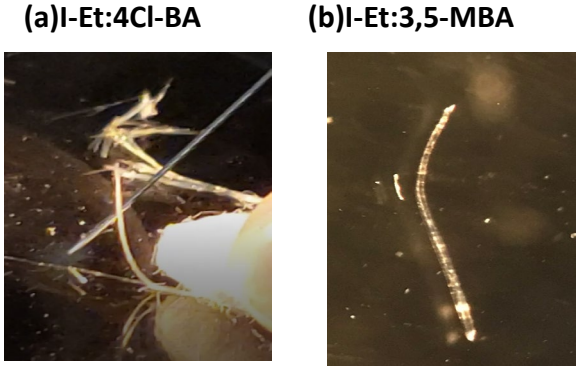

Figure 11. Bent co-crystals (a) I-Et:4Cl-BA - elastic and (b) I-Et:3,5-MBA - plastic