Supporting Information

Finding the Perfect Match: Halogen versus Hydrogen Bonding

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Materials and methods

All reactions were performed under argon or nitrogen unless otherwise stated. Chemicals were obtained from Aldrich and used as received. The synthesis and characterization of compounds **1** (X = F, Br, I) and **2** (X = F and I) were reported.[1] Reaction flasks were washed with deionized (DI) water, followed by acetone, and then dried in an oven at 130 °C overnight prior to use. The ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded at 400.19 and 100.6 MHz, respectively, on a Bruker AMX 400 NMR spectrometer. The ^{19}F{^{1}H} NMR spectra were recorded at 356.1 MHz on a Bruker AMX 400 NMR spectrometer. All chemical shifts (δ) are reported in ppm and coupling constants (J) are in Hz. The ^{1}H and ^{13}C{^{1}H} chemical shifts are reported relative to tetramethylsilane (TMS) or to chloroform (δ 7.24 in ^{1}H and δ 77.0 in ^{13}C{^{1}H} NMR). ^{19}F{^{1}H} NMR chemical shifts are relative to hexafluorobenzene in $CDCl_3$ at δ = -163.0 ppm (external reference). Assignments in the ^{13}C{^{1}H} NMR were aided by ^{13}C-DEPT-135 NMR measurements. All measurements were carried out at 298 K. Mass spectrometry was carried out using a Micromass Platform LCZ 4000 instrument.

Preparation of 4′-chloro-2′,3′,5′,6′-tetrafluorostilbazole (**1Cl**). A mixture of 4-chloro-2,3,5,6-tetrafluorobenzaldehyde (2.43 g, 11.5 mmol) and γ-picoline (1.1 mL, 12 mmol) in 10 mL acetic anhydride was stirred at room temperature for 60 h under argon. The mixture became dark and a precipitate formed during this time period. Subsequently, the mixture was poured into cold water at 0°C and was basified to pH = 8-9 by addition of a 15% aqueous solution of Na_2CO_3. The crude product was extracted with

dichloromethane (3 × 50 mL), the combined fractions were dried (Na_2SO_4) and filtered. The solution was treated with decolorizing charcoal overnight. Filtration over celite and evaporation of the solvent yielded yellow oil that crystallized upon addition of hexane. This afforded 1.1 g (32%) of light-green crystals suitable for X-ray analysis. Compound **1Cl** partly undergoes a reaction when subjected to column chromatography on silica gel. Signals of undetermined products were observed by $^{19}F\{^1H\}$ NMR after chromatography. ^1H NMR ($CDCl_3$): δ 8.65 (br dd, $^3J_{HH}$ = 5.9 Hz, $^4J_{HH}$ = 1.3 Hz, 2H, Pyr*H*), 7.41 (d, $^3J_{HH}$ = 5.9 Hz, $^4J_{HH}$ = 1.2 Hz, 2H, Pyr*H*), 7.33 (dd, AB, $^3J_{HH}$ = 17.3 Hz, 2H, CH=CH). $^{13}C\{^1H\}$ NMR (C_6D_6): δ 150.2 (s, *C*-Pyr), 145.8 (m, C_q, C-F), 145.3 (m, C_q, C-F), 143.8 (m, C_q, C-F), 143.3 (m, C_q, C-F), 142.8 (s, C_q, *C*-Pyr), 135.4 (t, $^3J_{FC}$ = 8.3 Hz, CH=CH), 120.8 (s, *C*-Pyr), 116.7 (s, HC=CH), 114.9 (t, C_q, $^2J_{FC}$ = 13.0 Hz, *C*-Cl), 111.3 (m, C_q, *C*-Ar_f). $^{19}F\{^1H\}$ NMR ($CDCl_3$): δ -141.45 (m, 4F). HRMS (FD-TOF): *m/z*: calcd. for $C_{13}H_6ClF_4N$ 287.0125; found 287.0131. *N*-oxide derivatives, **2Cl** and **2Br**, were prepared according a modified published procedure.[1c]

2Cl: ^1H NMR ($CDCl_3$): δ 8.32 (br, 2H, PyrNO*H*), 7.53 (2H, PyrNO*H*), 7.40 (dd, AB, $^3J_{HH}$ = 94.8 Hz, 2H, C*H*=C*H*). $^{13}C\{^1H\}$ NMR ($CDCl_3$): 146.18 (m, C_q, C-F), 145.51 (m, C_q, C-F), 143.67 (m, C_q, C-F), 143.21 (m, C_q, C-F), 136.24 (s, C_q, *C*-PyrNO), 132.12 (CH=CH), 139.65 (s, *C*-PyrNO), 123.64 (s, *C*-PyrNO), 118.02 (s, HC=CH), 114.23 (t, C_q, $^2J_{FC}$ = 13.0 Hz, *C*-Cl), 112.57 (m, C_q, *C*-Ar_f). $^{19}F\{^1H\}$ NMR ($CDCl_3$): δ -141.8 (br, 4F). HRMS (FD-TOF): *m/z*: calcd. for $C_{13}H_6ClF_4NO$: 303.0074; found 303.0081. Crystallization from diethyl-ether at 4°C afforded **2Cl** as yellowish crystals suitable for single-crystal X-ray structure determination.

2Br: ^1H NMR ($CDCl_3$): δ 8.54 (s, br, 2H, NO*H*), 7.68 (s, br, 2H, NO*H*), 7.51 (dd, AB, $^3J_{HH}$ = 69.7 Hz, 2H, CH=CH). $^{13}C\{^1H\}$ NMR ($CDCl_3$): 146.10, 144.65, 139.71, 131.58, 131.42, 125.68, 123.88, 120.33, 114.53. $^{19}F\{^1H\}$ NMR ($CDCl_3$): δ -133.65 (dd, 2F), -140.82 (dd, 2F). HRMS (FD-TOF): *m/z*: calcd. for $C_{13}H_6BrF_4NO$: 369.9467; found 369.9464. Crystallization from diethyl ether produced **2Br** as light yellow crystals, suitable for single-crystal X-ray structure determination.

Crystallization of compounds 1F, 2F and 2I:

1F: Colorless crystals of compound **1F** were obtained upon slow evaporation of a chloroform solution at room temperature.

2F: Compound **2F** was crystallized from diethyl ether at 4 °C.

2I: Recrystallization from ethyl acetate/diisopropyl ether afforded compound **2I** as colorless needles suitable for single-crystal X-ray structure determination.

X-ray Crystallography.

1F *Crystal data***:** $C_{13}H_6F_5N$, colorless, 0.5 × 0.2 × 0.1 mm^3, triclinic, space group P-1, a = 5.766(1) Å, b = 9.081(2) Å, c = 10.927(2) Å, α = 70.74(3)º, β = 85.15(3)°, γ = 81.57(3)º from 20 degrees of data, T = 120(2) K, V = 533.9(2) $Å^3$, Z = 2, F_w = 271.19, D_c = 1.687 $Mg{\cdot}m^{-3}$, μ = 0.161 mm^{-1}. *Data collection and processing*: Nonius KappaCCD diffractometer, MoKα (λ = 0.71073 Å), graphite monochromator, 28897 reflections collected, 4886 independent reflections (R_{int} = 0.058). -7≤h≤7, -11≤k≤11, -14≤l≤14, frame scan width = 1.0°, scan speed 1.0° per 85 sec, typical peak mosaicity 0.682°. The data were processed with Denzo-Scalepack. *Solution and refinement*: Structure solved by direct method with SHELXT-2013.[2] Full matrix least-squares refinement based on F^2 with SHELXL-2013.[2] 196 parameters with 0 restraints, final R_1 = 0.0446 (based on F^2) for data with I>2σ (I) and R_1 = 0.0636 on 2436 reflections. Goodness of fit on F^2 = 1.024, largest electron density peak = 0.408 $e{\cdot}Å^{-3}$, deepest hole = -0.253 $e{\cdot}Å^{-3}$. CCDC 1062744

1Cl *Crystal data***:** $C_{13}H_6ClF_4N$, green prisms, 0.5 × 0.3 × 0.3 mm^3, monoclinic, space group $P2_1/c$, a = 9.199(2) Å, b = 10.765(2) Å, c=11.907(2) Å, β = 108.31(3)°, T = 120(2) K, V = 1119.5(4) $Å^3$, Z = 4, Fw = 287.64, D_c = 1.707 $Mg{\cdot}m^{-3}$, μ = 0.378 mm^{-1}. *Data collection and processing*: Nonius KappaCCD diffractometer, MoKα (λ = 0.71073 Å), 17248 reflections collected, 2809 independent reflections (R_{int} = 0.050). -12≤h≤12, 14≤k≤13, -15≤l≤15, frame scan width = 1.0°, scan speed 1.0° per 60 sec, typical peak mosaicity 0.509°. The data were processed with Denzo-Scalepack. *Solution and refinement*: Structure solved by SHELXT-2013,[2] Full matrix least-squares refinement based on F^2 with SHELXL-2013.[2] 196 parameters with 0 restraints, final R_1 = 0.0367

(based on F^2) for data with I>2σ (I) and R_1 = 0.0488 on 2654 reflections. Goodness of fit on F^2 = 1.007, largest electron density peak = 0.384 e·Å^{-3}, deepest hole = -0.317 e·Å^{-3}. CCDC 1062743

2F $2C_{13}H_6F_5NO + H_2O$, colorless chunk, 0.39 × 0.23 × 0.16 mm^3, tetragonal, space group $P4_32_12$, a = b = 6.3949(2) Å, c = 57.5399(18) Å, from 25 degrees of data, T = 100(2) K, V = 2353.08(13) Å^3, Z = 4, Fw = 529.39, D_c = 1.672 Mg·m^{-3}, μ = 0.163 mm^{-1}. *Data collection and processing*: Bruker Apex-II diffractometer, MoKα (λ = 0.71073 Å), graphite monochromator, -8≤h≤7, -6≤k≤8, -69≤l≤72, frame scan width = 0.5°, scan speed 1.0° per 90 sec, typical peak mosaicity 0.55°, 13648 reflections collected, 2683 independent reflections (R_{int} = 0.0264). The data were processed SAINT. *Solution and refinement*: Structure solved by Bruker AutoSolve and refined with full matrix least-squares refinement based on F^2 with SHELXL-2013.[2] 188 parameters with 0 restraints, final R_1 = 0.0430 (based on F^2) for data with I>2σ (I) and R_1 = 0.0477 on 2683 reflections. Goodness of fit on F^2 = 1.135, largest electron density peak = 0.643 e·Å^{-3} and hole = -0.376 e·Å^{-3}. CCDC 1062739

2Cl *Crystal data***:** $C_{13}H_6ClF_4NO$, colorless plates, 0.18 × 0.18 × 0.04 mm^3, monoclinic, space group $P2_1/c$, a = 10.0782(3) Å, b = 12.6478(4) Å, c=9.6673(3) Å, α = 90º, β = 108.784(1)°, γ = 90º, from 18 degrees of data, T = 120(2) K, V = 1166.63(6) Å^3, Z = 4, F_w = 303.64, D_c = 1.729 Mg·m^{-3}, μ = 0.374 mm^{-1}. *Data collection and processing*: Bruker KappaApex CCD diffractometer, MoKα (λ = 0.71073 Å), graphite monochromator, MiraCol optics, -12≤h≤14, -18≤k≤17, -13≤l≤13, frame scan width = 0.5°, scan speed 1.0° per 60 sec, typical peak mosaicity 0.79°, 2θ_{max} = 61.22, 13260 reflections collected, 3545 independent reflections (R_{int} = 0.023). The data were processed with Bruker Apex-II. *Solution and refinement*: Structure solved by Bruker AutoSolve and refined with Full matrix least-squares refinement based on F^2 with SHELXL-2013.[2] 205 parameters with 0 restraints, final R_1 = 0.0325 (based on F^2) for data with I>2σ (I) and R_1 = 0.0424 on 3544 reflections. Goodness of fit on F^2 = 1.032, largest electron density peak = 0.452 e·Å^{-3} and hole = -0.229 e·Å^{-3}. CCDC 1062741

2Br *Crystal data***:** $C_{13}H_6BrF_4NO + 0.5H_2O$, colorless prism, 0.22 × 0.20 × 0.14 mm^3, monoclinic, space group C2/c, a = 25.4609(1) Å, b = 7.0954(3) Å, c=15.6162(8) Å, α = 90º, β = 117.609(3)°, γ = 90º from 18 degrees of data, T = 100(2) K, V = 2499.91(2) $Å^3$, Z = 8, F_w = 357.11, D_c = 1.898 $Mg \cdot m^{-3}$, μ = 3.337 mm^{-1}. *Data collection and processing*: Bruker KappaApex-II diffractometer, MoKα (λ = 0.71073 Å), graphite monochromator, MiraCol optics, -39≤h≤20, -10≤k≤10, -21≤l≤24, frame scan width = 0.5°, scan speed 1.0° per 20 sec, typical peak mosaicity 0.69°, 33058 reflections collected, 4773 independent reflections (R_{int} = 0.034). The data were processed with Bruker Apex-II. *Solution and refinement*: Structure solved by Bruker AutoSolve and refined with full matrix least-squares refinement based on F^2 with SHELXL-2013.[2] 189 parameters with 0 restraints, final R_1 = 0.0241 (based on F^2) for data with I>2σ (I) and R_1 = 0.0296 on 5773 reflections. Goodness of fit on F^2 = 1.043, largest electron density peak = 1.446 $e \cdot Å^{-3}$ and largest electron density hole -0.264 $e \cdot Å^{-3}$. CCDC 1062742

2I *Crystal data***:** $2C_{13}H_6F_4INO + 3H_2O$, colorless needles, 0.56 × 0.15 × 0.12 mm^3, monoclinic, space group $P2_1/n$, a = 16.6858(6) Å, b = 4.7557(2) Å, c=17.1322(6) Å, β = 90.634(2)° from 30 degrees of data, T = 120(2) K, V = 1359.40(9) $Å^3$, Z = 2, F_w = 844.22, D_c = 2.062 $Mg \cdot m^{-3}$, μ = 2.410 mm^{-1}. *Data collection and processing*: BrukerApex II KappaCCD diffractometer, MoKα (λ = 0.71073 Å), graphite monochromator, -25≤h≤21, -7≤k≤6, -26≤l≤25, frame scan width = 0.5°, scan speed 1.0° per 40 sec, typical peak mosaicity 0.68°, 15556 reflections collected, 6997 independent reflections (R_{int} = 0.0307. The data were processed with Apex-II. *Solution and refinement*: Structure solved by Bruker AutoSolve and refined with Full matrix least-squares refinement based on F^2 with SHELXL-2013.[2] 209 parameters with 5 restraints, final R_1 = 0.0231 (based on F^2) for data with I>2σ (I) and R_1 = 0.0296 on 5142 reflections. Goodness of fit on F^2 = 1.040, largest electron density peak = 1.612 $e \cdot Å^{-3}$ and hole = -0.658 $e \cdot Å^{-3}$. CCDC 1062740

Table S1. Selected intermolecular interaction geometries for **1F-I** and **2F-I**.

Compound	Interaction type	Distance (Å)	Angles (deg)	R[a]
1F	C(18)–H(18)···N(17)	2.49(2)	150.3(15)	0.906
	C(19)–H(19)···F(2)	2.52(2)		
	C(16)–H(16)···F(8)	2.66(2)		
	π–π	3.262		
1Cl	C(1)–Cl(1)···N(1)	2.967(2)	177.39(6)	0.890
	F(3)···F(2)	2.859(2)		0.970
	C(7)–H···F(2)	2.65(2)		
	π–π	3.508		
1Br[1a]	C–Br···N	2.841	177.76	0.831
	F···F	2.832		
	π–π	3.357		
1I[1b]	C–I···N	2.713	177.75	0.768
	C–H···F	2.537		
	π–π	3.60		
2F	C(12)–H(12)···O(1)	2.264(3)	133.0(3)	0.832
	F(1)···F(2)	2.812(2)		
	C(10)–H(10)···F(4)	2.588(3)		
	π–π	3.047		
2Cl	C(12)–H(12)···O(1)	2.34 (2)	163.1(14)	0.860
	C(10)–H(10)···O(1)	2.49(2)	138.2(12)	0.915
	C(8)–H(8)···F(4)	2.44(2)		
	F(1)···F(4)	2.761(1)		
	F(3)···F(4)	2.878(1)		
	π–π	3.318		
2Br	C(1)–Br(1)···O(1)	2.801(1)	162.98(4)	0.826
	C(11)–H(11)···O(1)	2.571(4)	156.8(1)	0.940
	C(7)–H(7)···F(2)	2.623(1)		
	C(10)–H(10)···F(2)	2.542(1)		
	C(12)–H(12)···F(1)	2.435(2)		
	F(2)···F(4)	2.927(1)		
	π–π	3.356		
2I	C(1)–I(1)···O(1)	2.785(1)	174.44(5)	0.790
	C(11)–H(11)···F(1)	2.561(2)		
	F(4)···F(4)	2.769(2)		
	π–π	3.489		

[a] R = distance/sum of van der Waals radii for H, 1.20 Å; O, 1.52 Å; N, 1.55 Å; F, 1.47 Å; Cl, 1.75 Å; Br, 1.87 Å; I, 1.98 Å. The relative shortening of the C–X···N bond when going from X = Cl to Br and then I, compared with the sum of vdW radii, was found to be ~11%, 17%, and 23%, respectively. These observations are in agreement with the relative XB donor strength of X (I>Br>Cl), resulting in weaker XB interactions in **1Cl**.[3]

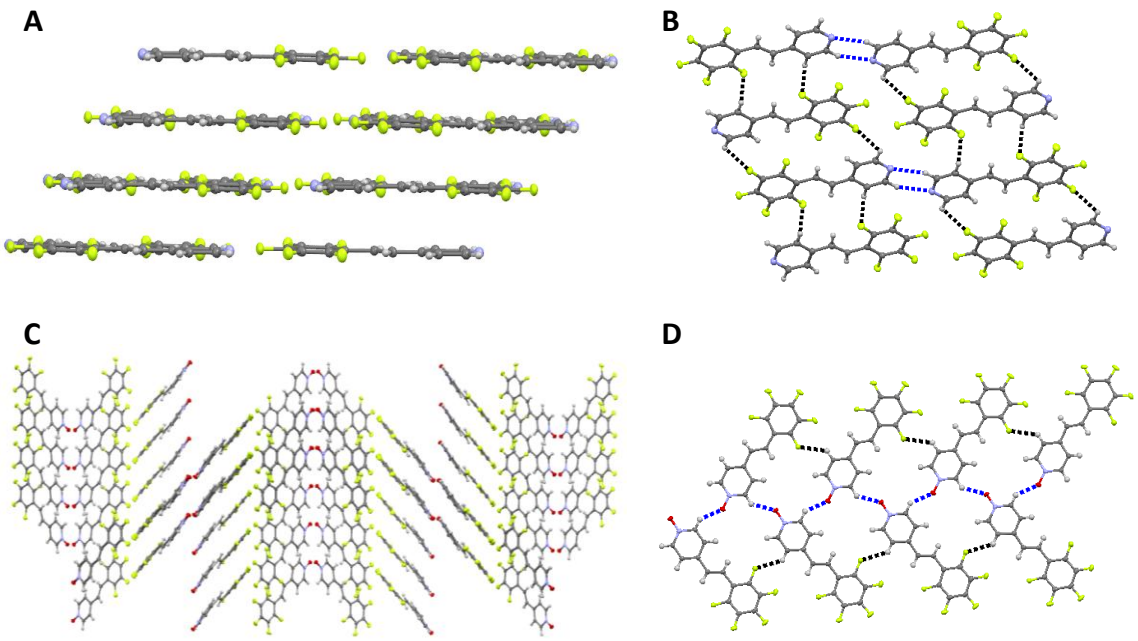

Figure S1. Molecular packing of compounds (A,B) **1F** and (C,D) **2F**. The dashed lines in B and D indicate short contacts (blue dashed line: hydrogen bonding; black dashed line: other). Atomic color scheme: carbon, gray; nitrogen, blue; fluorine, yellow; oxygen, red. Water molecules in C and D are omitted for clarity (see Figure S5).

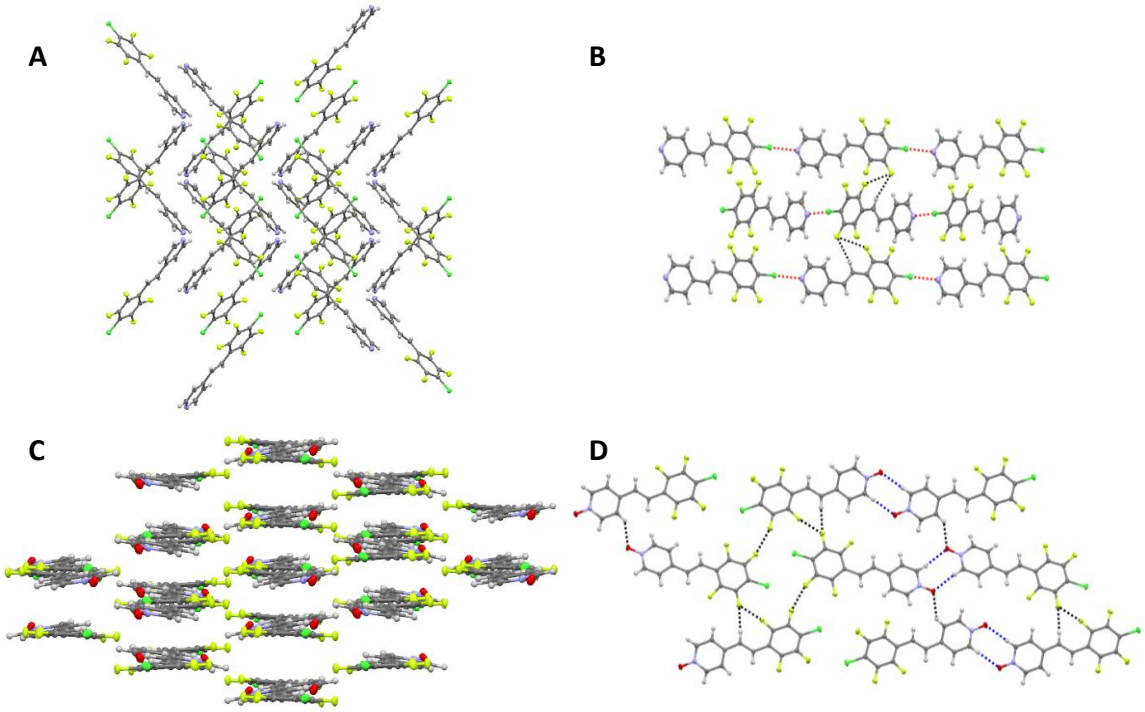

Figure S2. Molecular packing of compounds (A,B) **1Cl** and (C,D) **2Cl**. The Cl atom in **2Cl** is not involved in any short contacts as demonstrated in C and D. The dashed lines in B and D indicate short contacts (red dashed line: halogen bonding; blue dashed line: hydrogen bonding; black dashed line: other). Atomic color scheme: carbon, gray; nitrogen, blue; fluorine, yellow; oxygen, red; green, chlorine.

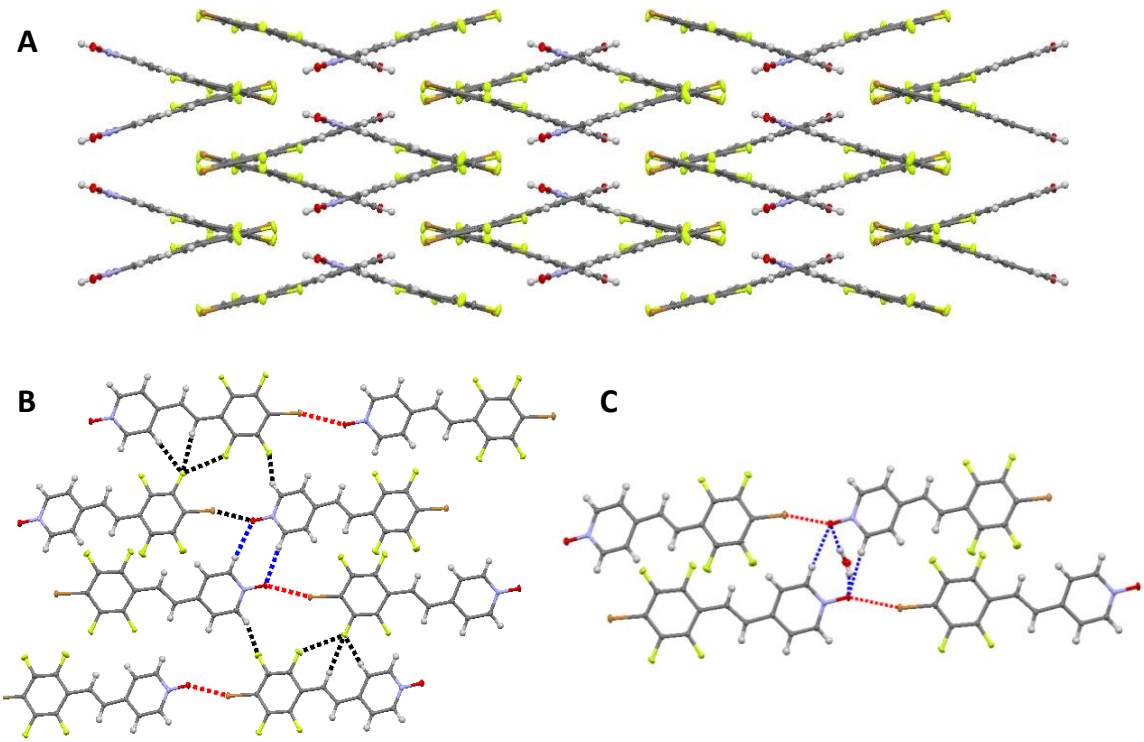

Figure S3. Molecular packing of compound **2Br** (A,B) omitting and (C) displaying the water molecules incorporated in the structure. The water molecules trapped in the solid framework of **2Br** do not interfere with the primary C–Br···O$^-$ or C–H···O$^-$ interactions. The dashed lines in B and C indicate short contacts (red dashed line: halogen bonding; blue dashed line: hydrogen bonding; black dashed line: other). Atomic color scheme: carbon, gray; nitrogen, blue; fluorine, yellow; oxygen, red; green; brown, bromine.

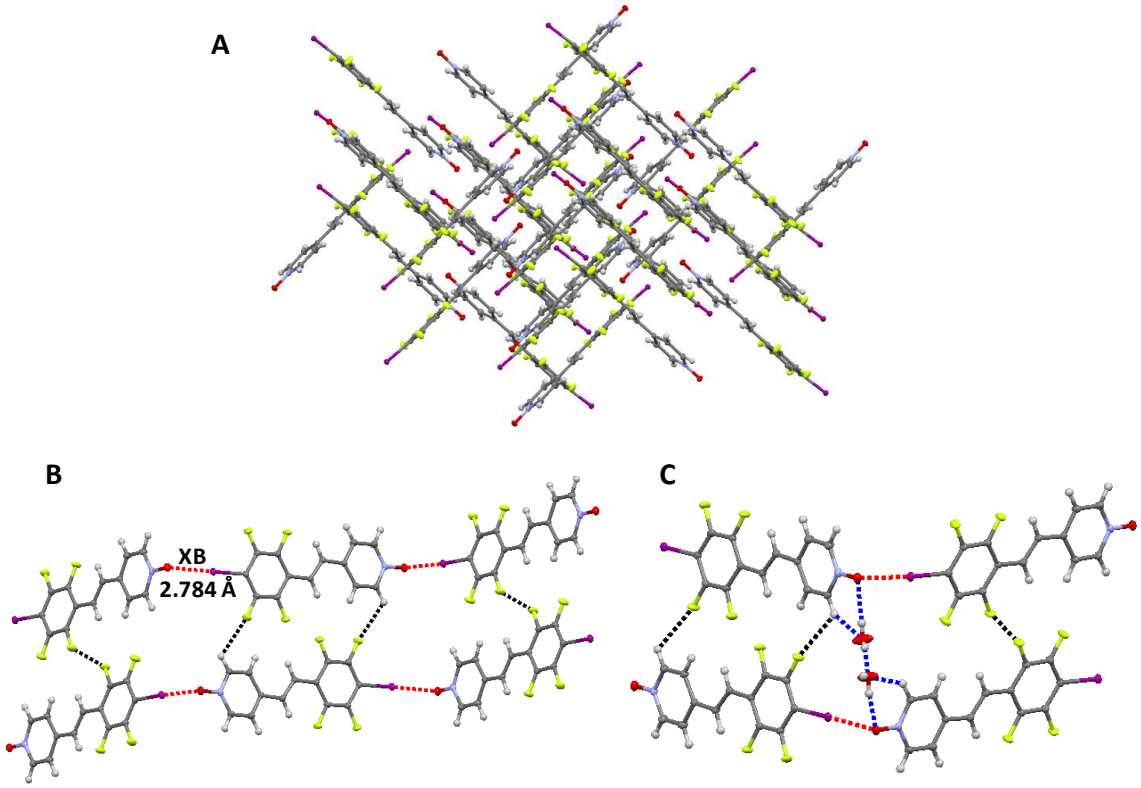

Figure S4. Molecular packing of compound **2I** (A,B) omitting and (C) displaying the water molecules incorporated in the structure. Two adjacent pyridine-*N*-oxide moieties are bridged by two water molecules incorporated in the crystal structure, via a network of hydrogen bonds. Apparently, this does not interfere with the formation of the XB-based network. The dashed lines in B and C indicate short contacts (red dashed line: halogen bonding; blue dashed line: hydrogen bonding; black dashed line: other). Atomic color scheme: carbon, gray; nitrogen, blue; fluorine, yellow; oxygen, red; green, purple, iodine.

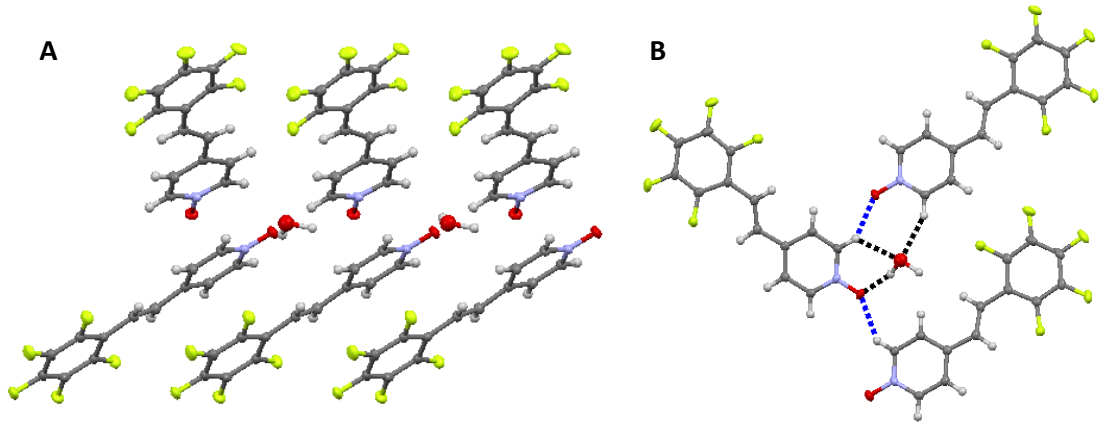

Figure S5. (A, B) Molecular packing of compound **2F** displaying the water molecules incorporated in the structure. The dashed lines in B indicate short contacts (blue dashed line: hydrogen bonding; black dashed line: other). Atomic color scheme: carbon, gray; nitrogen, blue; fluorine, yellow; oxygen, red; green.

References

(1) a) Lucassen, A. C. B.; Vartanian, M.; Leitus, G.; van der Boom, M. E. *Cryst. Growth Des.* **2005**, *5*, 1671; b) Aakeröy, C. B.; Schultheiss, N.; Desper, J.; Moore, C. *CrystEngComm* **2007**, *9*, 421; c) Shirman, T.; Arad, T.; van der Boom, M. E. *Angew. Chem. Int. Ed.* **2010**, *49*, 926; d) Shirman, T.; Kaminker, R.; Freeman, D.; van der Boom, M. E. *ACS Nano* **2011**, *5*, 6553.

(2) Sheldrick, G. *Acta. Crystallogr. C* **2015**, *71*, 3.

(3) Clark, T.; Hennemann, M.; Murray, J.; Politzer, P. *J. Mol. Model.* **2007**, *13*, 291.