

The Power of Nonconventional Phenyl C—H···N Hydrogen Bonds: Supportive Crystal-Packing Force and Dominant Supramolecular Engineering Force

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Supporting Information

ABSTRACT: The role of phenyl C–H···N interactions in crystal engineering is explored with a variety of fluorinated phenyl-containing compounds. In particular, we show that this interaction can guide the formation of one-dimensional phenyl C–H···N hydrogen-bonded ribbons with, for example, 4-(2,3,5,6-tetrafluorophenylethynyl)pyridine. The interaction is shown to also control the formation of self-complementary homodimers with 3-(2,3,4,5-tetrafluorophenylethynyl)-pyridine. We also demonstrate that the phenyl C–H···N hydrogen bond interaction is capable of enticing co-



crystallization of molecules such as 2,3,5,6,2',3',5',6'-octafluorobiphenyl and 4,4'-dipyridyl. Finally, we describe the use of an intramolecular scaffold to evaluate the effect of electron-withdrawing substituents on the strength of a phenyl C-H…N hydrogen bond.

■ INTRODUCTION

The importance of the supportive role of weak interactions between organic molecules has long been recognized in crystal engineering.¹ One of these weaker interactions is the nonconventional C-H...N hydrogen bond. We have been particularly interested in exploring and maximizing these weak interactions with select molecules that contain phenyl and pyridyl rings due to the rigid and well-defined geometric environment in these moieties. Our first investigation using this methodology involved sp¹ C-H···N hydrogen bonding where we were able to demonstrate that the interaction was strong enough to promote co-crystallization of a series of diynes with a series of dipyridines.^{2,3} It should be noted that the strength of the C-H...N hydrogen bond is predicted to decrease with changing hybridization of the C atom in the order $sp^1 > sp^2 >$ sp^{3,4} A recent search of the Cambridge structural database⁵ reveals more than 2000 reports of close phenyl C-H···N interactions of which there are 338 reports with a H…N distance 0.3 Å less than the sum of the van der Waals radii of nitrogen (1.55 Å) and hydrogen (1.20 Å).⁶ Most of these reports correspond to coincidental observation of short C-H··· N interactions in structures in which other intermolecular forces or coordination bonds are the dominant intermolecular interactions. Clear examples of the more dominant role of sp^2 C-H...N in crystallization include the co-crystallization of pyridine and 3,5-dinitrobenzonitrile⁷ and crystallization of 4-(2-(2,4,6-trinitrophenyl)vinyl)pyridine,⁸ which both feature a fairly strong phenyl C-H···N pyridine hydrogen bond. The cocrystallization of tricyanobenzene with hexamethylbenzene is also a classic example which features multiple phenyl C–H…N nitrile interactions.⁹ Significantly, the structure of the hindered compound 2-(2,4,6-trifluorophenyl)pyridine, which was determined to provide proof of structure related to a synthetic methodology paper, also exhibites a relatively strong sp² C–H…N hydrogen bond with N…H and N…C bond distances of 2.389 and 3.305 Å with a C–H…N angle of 161.98°.¹⁰

Thus, it is fair to say that, while the sp² C–H…N interaction is common and although it plays a well-recognized role in crystal packing, it has seldom been exploited as one of the major intermolecular interactions in crystal engineering. These few examples do, however, suggest that the phenyl C–H…N interaction can be a major control element in supramolecular chemistry and crystal engineering. Furthermore, we were prompted to explore this interaction following the unexpected observation of a C–H…N hydrogen bonding interaction which seemed to trump a C–Br…N halogen bonding interaction in a separate study.¹¹

In this study, we explore the sp² C–H···N hydrogen bond between phenyl hydrogen atoms and pyridines. We reasoned that the most acidic phenyl hydrogens would provide the strongest phenyl C–H···N hydrogen bonding and, therefore, provide the best opportunity for this interaction to be the major

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and controlling intermolecular interaction in crystallization and co-crystallization. Furthermore, it is well-documented that the acidity of a phenyl proton is drastically increased on fluorination of the benzene ring. For example, the pK_a of a proton on benzene is estimated at about 43, while the pK_a of the hydrogen in pentafluorobenzene is reduced to 24.¹² Indeed, a theoretical investigation by Radom et al. indicated that fluoro substitution would increase the strength of the sp² C–H…N hydrogen bond between ethylene and ammonia from 1.7 kJ/ mol to 8.1–8.6 kJ/mol for the interaction between $\alpha_{,\beta}$ -difluoroethylene and ammonia.¹³ This rationale, and acidity data, was supported by electrostatic potential calculations performed with Spartan.¹⁴ The electrostatic potential of benzene and pentafluorobenzene is shown in Figure 1, where the enhanced polarity/acidity of the pentafluorophenyl hydrogen is striking.



Figure 1. Electrostatic potential map of benzene and pentafluorobenzene (right) drawn with the same range of -225 to 225 kJ/mol. Blue indicates positive charge.

EXPERIMENTAL SECTION

Chemicals. The dipyridyl ligand, 1,2-bis(4'-pyridyl)ethyne, was available from an earlier study.² 4,4'-Dipyridine, 1,2-bis(4'-pyridyl)ethene, and 2,3,5,6,2',3',5',6'-octafluorobiphenyl were purchased and used as received.

Synthesis. 3-Ethynylpyridine and 4-ethynylpyridine were prepared by Sonogashira coupling of the corresponding bromopyridine with trimethylsilylacetylene, followed by deprotection using potassium hydroxide in methanol.¹⁵

Synthesis of 4-(2,3,5,6-tetrafluorophenylethynyl)pyridine, 1. 4-Ethynylpyridine, (0.098 g, 0.95 mmol), 1-bromo-2,3,5,6-tetrafluorobenzene (0.226 g, 1 mmol), $PdCl_2(PPh_3)_2$ (11 mg), CuI (2 mg), and triethylamine (1 mL) and THF (0.5 mL) were reacted under an argon atmosphere at 50 °C for 24 h. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed with water (4 × 50 mL). The organic layer was separated, dried over anhydrous Na₂SO₄, and filtered, and the solvent was evaporated. The crude product was purified using flash chromatography with a 2:1 mixture of hexane and ethyl acetate as eluant. The product was isolated as an off white solid (0.12 g, 51%) which was recrystallized from absolute ethanol.

¹H NMR: (400 MHz, CDCl₃) δ 7.13 (tt, *J* = 7.2, 9.8 Hz, 1H), 7.44 (d, *J* = 5.6 Hz, 2H), 8.67 (br d, *J* = 5 Hz, 2H). ¹³C NMR: 78.4 (m), 98.4 (m), 107.4 (t, *J*=22.8 Hz), 125.6 129.7, 130.37 (dd, *J* = 11.8, 62.4 Hz), 145.9 (dddd, *J* = 3.7, 10.3, 13.3, 248.9 Hz), 146.9 (tdd, *J* = 3.0, 14.6, 254.4 Hz), 150.1. ¹⁹F NMR: -135.9 (m, 2F), -138.4 (quintet, *J* = 10 Hz, 2F).

Synthesis of 4-(2,3,4,5-tetrafluorophenylethynyl)pyridine, 2. 4-Ethynylpyridine (0.10 g, 1.0 mmol), 1-bromo-2,3,4,5-tetrafluorobenzene (0.22 g, 1.0 mmol), $PdCl_2(PPh_3)_2$ (13 mg), and CuI (2 mg) were reacted under an argon atmosphere in triethylamine (2 mL) at 50 °C for 12 h. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed with water (4 × 50 mL). The organic layer was separated, dried over anhydrous Na_2SO_4 , and filtered, and the solvent was evaporated. The crude product was purified using flash chromatography with a 2:1 mixture of hexane and ethyl acetate as eluant. The product was isolated as a colorless solid (0.080 g, 24%) which was recrystallized from absolute ethanol.

¹H NMR: (400 MHz, CDCl₃) δ 8.66 (br d, $J \sim 5$ Hz, 2H), 7.44 (d, J = 5.6 Hz, 2H), 7.17 (dddd, J = 2.4, 5.6, 9.6, 16.0 Hz, 1H). ¹³C NMR: 83.65 (m), 93.26 (m), 107.4 (m), 114.4 (dd, J = 3.7, 21.6 Hz), 125.5, 129.8, 141.0 (dddd, J = 4.4, 12.5, 17.0, 254.1 Hz), 141.5 (dddd, J = 3.0, 12.5,15.3, 257.8 Hz, 146.9 (tdd, J = 3.0, 10.4, 248.2 Hz), 148.4 (dddd, J = 2, 3.5, 11.1, 256.3 Hz), 149.9. ¹⁹F NMR: -134.2 (dm, J = 20.7 Hz 1F), -138.5 (m, 1F), -151.7 (ddt, J = 4.5, 8.0, 20.5 Hz, 1F), -154.3 (tt, J = 2.5, 20.5 Hz, 1H).

Synthesis of 3-(2,3,4,5-tetrafluorophenylethynyl)pyridine, 3. 3-Ethynylpyridine (0.27 g, 2.6 mmol), 1-bromo-2,3,4,5-tetrafluorobenzene (0.60 g, 2.6 mmol), $PdCl_2(PPh_3)_2$ (49 mg), CuI (6.5 mg), and triethylamine (15 mL) were reacted under an argon atmosphere at 50 °C. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed with water (4 × 50 mL). The organic layer was separated, dried over anhydrous Na₂SO₄, filtered, and the solvent was evaporated. The crude product was purified using flash chromatography with a 2:1 mixture of hexane and ethyl acetate as eluant, and the product was isolated as an off-white solid (0.504 g, 76%) which was recrystallized from absolute ethanol.

¹H NMR: (400 MHz, CDCl₃) δ 7.16 (m, 1H), 7.32 (ddd, J = 1, 5, 8 Hz, 1H), 7.83 (td, J = 2.0, 8.0 Hz, 1H), 8.61 (dd, J = 1.6, 4.8 Hz, 1H), 8.78 (br d, J = 1.2 Hz, 1H). ¹³C NMR: 82.6 (m), 92.8 (m), 107.6 (m), 114.2 (dd, J = 3.5, 20.6 Hz), 119.0, 128.4 (d, J = 12.5 Hz), 132.0 (d, J = 9.6 Hz), 141.0 and 141.2 (overlapping dm, each J = 250 Hz), 146.2 (dddd, J = 2.5, 3.7, 10.3, 248.2 Hz), 148.24 (dddd, J = 2.5, 3.7, 9.6, 250 Hz), 149.5, 152.2. ¹⁹F NMR: -134.8 (dddd, J = 5.4, 6.7, 11.5, 21.8 Hz, 1F), -138.9 (dddd, J = 2.8, 10.3, 12.9, 23.3, 1F), -152.6 (ddt, J = 4.6, 8.0, 20.1, 1F), -154.7 (tt, J = 2.9, 20.1, 1F).

Synthesis of 9. A one-pot modification of the procedure reported by Bunz et al. was used.¹⁶ Thus, 2-ethynylpyridine, (1.03 g, 10 mmol), 4,5-diiodoveratrole (4.84 g, 12.4 mmol), PdCl₂(PPh₃)₂ (101 mg), and CuI (26 mg) were reacted in triethylamine (15 mL) under an argon atmosphere at 40 °C until TLC indicated that all the 2-ethynylpyridine was consumed. 3 mL of trimethylsilyl acetylene was then added, and the reaction was heated for 3 days when another 1.5 mL of trimethylsilylacetylene was added. After 7 days total reaction time, the reaction was worked up and the crude product was purified using flash chromatography and increasingly polar mixtures of hexane and ethyl acetate as eluant. 4,5-Bis(2-trimethylsilylethynyl)veratrole (1.69 g, 41%) was first eluted, followed by the trimethylsilyl-protected 9 (1.27 g, 38%). Finally, the dipyridyl product (0.39 g, 9%) was eluted. The trimethylsilyl-protected 9 was deprotected using KOH in ethanol to give 9 as a brown oil in quantitative yield.

Synthesis of 7. Compound 9, (0.20 g, 0.76 mmol), 1-bromo-2,3,4,5-tetrafluorobenzene (0.24 g, 1.04 mmol), PdCl₂(PPh₃)₂ (22 mg), and CuI (4 mg) were reacted under an argon atmosphere in triethylamine (15 mL) at 50 °C for 24 h. The crude product was purified using flash chromatography with a 1:1 mixture of hexane and ethyl acetate as eluant. The product 7 was isolated as an off-white solid (0.090 g, 29%) which was recrystallized from absolute ethanol. ¹H NMR: (400 MHz, CDCl₃) δ 8.65 (md, J = 5 Hz, 1H), 7.70 (dt, J = 2, 8 Hz, 1H), 7.54 (d, J = 8 Hz, 1H), 7.51 (m, 1H), 7.26 (ddd, J = 1, 5, 8 Hz, 1H), 7.13 (s, 1H), 7.03 (s, 1H), 3.94 (s, 3H), 3.93 (s, 3H). ¹³C NMR: 150.1, 149.9, 149.7, 148 (md, J = 250 Hz), 146.9 (md, J = 250 Hz), 143.3, 140.9, 140.8 (md, J = 250 Hz), 136.3, 127.0, 122.9, 118.5, 118.0, 114.9 (dd, J = 3, 21 Hz), 114.5, 113.9, 108.6 (m), 95.2 (dd, J = 2, 4 Hz), 91.9, 87.6, 83.0 (m), 56.15. ¹⁹F NMR: -135.5 (m, 1F), -139.4 (m, 1F), -153.9 (ddt, J = 4, 8, 20 Hz, 1F), -155.4 (tt, J = 3, 20 Hz, 1F).

Synthesis of 8. Compound 9 (0.25 g, 0.95 mmol), 1-bromo-2,3,4-trifluorobenzene (0.31 g, 1.2 mmol), $PdCl_2(PPh_3)_2$ (33 mg), and CuI (7 mg) were reacted under an argon atmosphere in triethylamine (15 mL) at 50 °C for 24 h. The crude product was purified using flash chromatography with a 1:1 mixture of hexane and ethyl acetate as eluant. The product 8 was isolated as an off-white solid (0.37 g, 96%) which was recrystallized from absolute ethanol. ¹H NMR: (400 MHz, CDCl₃) δ 8.63 (d, J = 4.8 Hz, 1H), 7.68 (dt, J = 2.0, 8.0 Hz, 1H), 7.54

Table 1. Crystallographic	c Data for Compou	inds 1, 2, 3, 7, 8 an	nd Co-crystals 4, 5,	and 6				
	1	2	б	4	S	6	7	80
formula	$C_{13}H_5F_4H$	$C_{13}H_5F_4H$	$C_{13}H_5F_4H$	$C_{22}H_{10}F_8N_2$	$C_{24}H_{10}F_8N_2$	$C_{24}H_{12}F_8N_2$	$\mathrm{C}_{23}\mathrm{H}_{13}\mathrm{F}_4\mathrm{NO}_2$	$\mathrm{C}_{23}\mathrm{H}_{14}\mathrm{F}_{3}\mathrm{NO}_{2}$
formula weight	251.18	251.18	251.18	454.32	478.34	480.36	411.34	393.35
dim. (mm^3)	$0.30 \times 0.15 \times 0.03$	$0.30 \times 0.20 \times 0.15$	$0.40 \times 0.30 \times 0.20$	$0.20 \times 0.18 \times 0.10$	$0.40 \times 0.10 \times 0.05$	$0.43 \times 0.43 \times 0.34$	$0.40 \times 0.20 \times 0.20$	$0.40 \times 0.37 \times 0.17$
crystal system	triclinic	monoclinic	triclinic	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic
space group	$P\overline{1}$	$P2_1/c$	$P\overline{1}$	C2/c	C2/c	Cc	$P2_1/c$	$P2_1/c$
a (Å)	5.9634(16)	5.970(2)	5.9023(11)	13.8283(19)	13.527(3)	13.5900(6)	9.9813(4)	9.9218(9)
<i>b</i> (Å)	8.768(2)	21.499(8)	9.8718(19)	20.692(4)	23.296(7)	23.0149(10)	22.0356(8)	22.347(2)
c (Â)	11.076(3)	8.325(3)	10.399(2)	7.4577(10)	7.5729(18)	7.4980(3)	8.7097(3)	8.7060(8)
α (deg)	99.846(3)	90	63.113(3)	06	90	06	06	06
β (deg)	105.527(3)	101.819(5)	74.909(3)	121.774(2)	123.553(3)	122.641(1)	108.094(1)	108.1450(10)
γ (deg)	101.235(4)	90	77.066(3)	06	60	06	06	90
Z	2	4	2	4	4	4	4	4
$V(\hat{A}^3)$	531.8(2)	1045.9(6)	517.8(2)	1814.1(5)	1988.8(9)	1974.79(15)	1820.91(12)	1834.3(3)
$ ho_{ m calcd} ({ m g/cm^3})$	1.569	1.595	1.611	1.663	1.598	1.616	1.500	1.424
T (K)	66	100	100	100	100	66	66	100
$\mu \ (\mathrm{mm}^{-1})$	0.142	0.145	0.146	0.157	0.148	0.149	0.124	0.112
reflns.	2384	10290	6464	11239	10839	13223	23507	19766
unique refins.	1601	2322	2316	1993	2219	4534	4011	4029
$R_{ m int}$	0.0281	0.0497	0.0156	0.0420	0.0491	0.0207	0.0221	0.0531
goodness of fit	1.019	1.039	1.071	1.058	1.126	1.028	1.035	1.074
R1/wR2	0.041/0.102	0.050/0.125	0.034/0.095	0.048/0.132	0.058/0.182	0.029/0.074	0.032/0.085	0.067/0.181
R1/wR2 (all data)	0.071/0.119	0.081/0.145	0.040/0.099	0.068/0.144	0.083/0.198	0.032/0.076	0.037/0.089	0.086/0.197
largest diff. peak/hole/e $ m \AA^{-3}$	0.3/-0.24	0.32/-0.26	0.36/-0.24	0.26/-0.36	0.41/-0.33	0.33/-0.19	0.28/-0.21	1.28/-0.38

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(d, J = 7.7 Hz, 1 H), 7.38 (m, 1H), 7.38 (m, 1H), 7.23 (ddd, J = 1, 4.8, 7.6 Hz, 1H), 7.12 (s, 1H), 7.02 (s, 1H), 6.95 (m, 1H), 3.93 (s, 3H), 3.91 (s, 3H). ¹³C NMR: 151.7 (ddd, J = 255, 10, 4 Hz), 151.4 (ddd, 253, 10, 4 Hz), 150.1, 149.6 (d, J = 3 Hz), 143.5, 140.2 (td, J = 15.4, 252 Hz), 136.2, 127.3 (dd, J = 7, 3 Hz), 127.1 (d, J = 2 Hz), 122.8, 118.3, 118.1, 114.7, 114.0, 112.3 (dd, J = 4, 18 Hz), 110.0 (dd, J = 4, 13 Hz), 94.1 (dd, J = 2, 4 Hz), 91.7, 87.8, 83.7 (dd, J = 2, 4 Hz), 56.12, 56.10. ¹⁹F NMR: -130.4 (td, J = 7.5, 20.7 Hz, 1F), -132 (m, 1F), -159.7 (ddt, J = 2.3, 7, 20.7 Hz).

Preparation of Co-crystals. Solutions of each pair of the dipyridines (0.1 mmol) with an equivalent amount of 4H,4'H-octafluorobiphenyl were prepared in dichloromethane (3 mL) in screw cap vials. Slow evaporation yielded a homogeneous mass of crystals in each case: 4 (4,4'-dipyridine; 4H,4H'-octafluorobiphenyl); 5 (1,2-bis(4'-pyridyl)ethyne; 4H,4H'-octafluorobiphenyl); 6 (*trans*-1,2-bis(4'-pyridyl)ethene; 4H,4H'-octafluorobiphenyl).

X-ray Structure Determination. For each compound or cocrystal, a single crystal was mounted on a Kryoloop using viscous hydrocarbon oil. Data were collected using a Bruker Apex1 CCD diffractometer equipped with Mo K α radiation with $\lambda = 0.71073$ Å. Data collection at low temperature was facilitated by use of a Kryoflex system with an accuracy of ±1 K. Initial data processing was carried out using the Apex II software suite.¹⁷ Structures were solved by direct methods using SHELXS-2013 and refined against F^2 using SHELXL-2013.¹⁸ In all structures, hydrogen atoms were located in the difference maps but were placed in idealized positions and refined with a riding model. The program X-Seed was used as a graphical interface.¹⁹ The crystallographic data are collected in Table 1.

RESULTS AND DISCUSSION

Molecular Design, Synthesis, and Evaluation of Tetrafluorophenylethynylpyridines. The design of the



Figure 2. Tetrafluorophenylethynylpyridines prepared to evaluate the role of phenyl C–H…N interactions in supramolecular chemistry.

molecules in this study was modeled on two of our earlier studies, the co-crystallization of pyridines and alkynes² and the formation of self-complementary halogen-bonded dimers.¹¹ Thus, we prepared compound 1 (Figure 2) expecting that this would favor the formation of linear ribbons of hydrogen-bonded molecules because the direction of the activated C-H

bond is opposite to that of the pyridine nitrogen. The formation of linear one-dimensional hydrogen-bonded ribbons has often been used to showcase weak intermolecular interactions with molecules that contain the appropriate donor and acceptor sites.^{2,20} Compound 2, on the other hand, was chosen to determine how robust the C–H…N interaction is since the hydrogen bond donor and hydrogen bond acceptor do not have the favorable hydrogen bonding angles that compound 1 has. In contrast, compound 3 was designed with the expectation that it would form self-complementary C–H…N hydrogen-bonded dimers due to the relative placement of the pyridine N and the activated C–H bond.

Each of the compounds 1, 2, and 3 was prepared in modest yield by Sonogashira coupling of the appropriate ethynylpyridine with the corresponding iodo- or bromotetrafluorobenzene, as detailed in the Experimental Section. This series of compounds was recrystallized from warm ethanol. X-ray analysis of each of the clear colorless crystals revealed that the compounds were all essentially planar in the solid state with the torsional angle less than 2° in all three structures. The bond distances and angles in each of the three compounds are unexceptional.

As we hoped, the molecules of compound 1 formed linear C-H…N hydrogen-bonded ribbons in the solid state, as shown in Figure 3. The N1-H11 and C11-N1 distances are 2.299 and 3.244(2) Å, respectively, and the C11-H11-N1 and C3(para to N)-N1-H11 angles are 172.59° and 175.15°, respectively. Adjacent strands of the head-to-tail hydrogenbonded ribbons have alternating directionality with the tetrafluorophenyl ring adjacent to the pyridine ring providing supporting and stabilizing C-H…F interactions. The hydrogen fluorine distance is 2.593 Å for both F3-H2 and F4-H1, slightly less than the sum of the van der Waals radii of hydrogen and fluorine, which is 2.67 Å. 6 The C–H–F angles are 128.54 $^\circ$ and 161.46° for C2-H2-F3 and C1-H1-F4, respectively. These distances and angles compare favorably to those reported for a series of polyfluorobenzenes reported by Thallandi et al. in 1998.²¹ This supporting but weak C-H…F interaction is consistently observed in this study. Indeed, this is the major interaction between adjacent C-H-N hydrogenbonded ribbons and helps stabilize the formation of twodimensional sheets, as shown in Figure 3. The two-dimensional sheets are π -stacked with π -stacked layers slightly offset with



Figure 3. View of three adjacent C-H···N hydrogen-bonded ribbons of compound 1, 4-[(2,3,5,6-tetrafluorophenyl)ethynyl]pyridine, forming a twodimensional sheet. Select molecules shown as space-filling models to highlight the weak cohesive C-H···F interactions.



Figure 4. View of adjacent C-H···N hydrogen-bonded ribbons formed from compound 2, 4-[(2,3,4,5-tetrafluorophenyl)ethynyl]pyridine, forming an essentially planar two-dimensional sheet. Select molecules shown as space-filling models to highlight the weak cohesive C-H…F interactions.



Figure 5. View of a series of adjacent phenyl C-H···N hydrogen-bonded self-complementary dimers formed on crystallization of compound 3, 3-[(2,3,4,5-tetrafluorophenyl)ethynyl]pyridine.



Figure 6. View of a portion of the one-dimensional C-H···N hydrogen-bonded ribbons in the co-crystals formed between 4H,4H'octafluorobiphenyl and 4,4'-bipyridine, 4, in (A); 4H,4H'-octafluorobiphenyl and 1,2-bis(4'-pyridyl)ethyne, 5, in (B); and 4H,4H'octafluorobiphenyl and 1,2-bis(4'-pyridyl)ethene, 6, in (C).

alternating head-to-tail arrangement of molecules within the stack. The interplanar distance is approximately 3.4 Å.

Compound 2 was prepared to evaluate the effect of positional mismatch on the role of the C-H…N interaction

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Figure 7. Crystal packing of the hydrogen-bonded ribbons of co-crystals formed between 4H,4H'-octafluorobiphenyl and 4,4'-bipyridine, complex **4**, in (**A**); 4H,4H'-octafluorobiphenyl and 1,2-bis(4'-pyridyl)ethyne, complex **5**, in (**B**); and 4H,4H'-octafluorobiphenyl and 1,2-bis(4'-pyridyl)ethene, complex **6**, in (**C**) as viewed along the *b*-axis.



Figure 8. Crystal packing of the hydrogen-bonded ribbons of cocrystals formed between 4H,4H'-octafluorobiphenyl and 4,4'-bipyridine, 4, with the C-H···F interactions shown as dashed lines.

on its crystallization and crystal structure. Despite the mismatch, the structure reveals the formation of zigzag phenyl C–H…N hydrogen-bonded ribbons of **2** shown in Figure 4. Not surprisingly, the N1–H13 and C13–N1 distances are slightly longer than the related distances in the structure of compound **1** at 2.472 and 3.364(3) Å, respectively, while the C13–H13–N1 and C3–N1–H13 angles of 156.41° and 164.68°, respectively, reflect the imperfect alignment of the hydrogen bond donor and acceptor.

The packing of adjacent phenyl C–H…N hydrogen-bonded zigzag ribbons of **2** shown in Figure 4 again highlights multiple supporting and stabilizing C–H…F and F…F interactions with F–H distances ranging between 2.493 and 2.628 Å and F…F distances between 2.890(2) and 3.384(2) Å. The two-dimensional layers also π -stack with interplanar distances slightly less than 3.4 Å.

In contrast to these two structures, X-ray analysis of the clear colorless crystals of compound 3 revealed the formation of an essentially planar self-complementary dimer, as shown in Figure 5. The short N1–H13 and C13–N1 distances of 2.375 and 3.320(2) Å, respectively, and the C13–H13–N1 and C4–N1–H13 angles of 173.47° and 164.95°, respectively, are indicative

of a good geometric match between the donor and acceptor sites in this molecule.

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The dimers form two-dimensional sheets within which adjacent dimers have alternating directionality in one dimension, which maximizes the interactions between the tetrafluorophenyl ring and the pyridine ring, thereby maximizing the supporting and stabilizing C–H…F interactions. The hydrogen fluorine distances range from 2.554 to 2.780 Å for F2–H3, F1–H4, F4–H2, F3–H3, and F3–H3 with carbon–fluorine distances between 3.255(2) and 3.724(2) Å. In addition, there are several close F…F contacts with distances of 2.906(2), 2.721(2), and 2.968(2) Å. The two-dimensional sheets π -stack, and the dimers are slip-stacked with interplanar distances around 3.3 Å.

Co-crystallization of Bipyridines and Octafluoro**biphenyl.** Following the observation of relatively strong C-H…N interactions in the crystalline compounds 1-3, we thought it reasonable that this interaction could entice the cocrystallization of separate molecules. In fact, we believe that weak interaction driven co-crystallization is a more powerful indication of the potential of these interactions. We decided to take advantage of the relatively rigid and directional nature of octafluorobiphenyl and 4,4'bipyridyl, 1,2-bis(4'-pyridyl)ethene and 1,2-bis(4'-pyridyl)ethyne in order to maximize the potential for co-crystallization. Separate equimolar solutions containing octafluorobiphenyl and each of the bipyridyls were dissolved in dichloromethane and allowed to crystallize over the period of a week. Clear colorless homogeneous co-crystals were formed from each of the three mixtures labeled 4, 5, and 6, respectively. X-ray analysis revealed that one-dimensional C-H…N hydrogen-bonded ribbons were formed with strong C-H…N hydrogen bonds as the major cohesive force in each of the three co-crystals. Portions of each of these C-H...N hydrogen-bonded ribbons are shown in Figure 6.

Relatively short hydrogen bond distances are observed in all three structures. Thus, in the complex **4** (4,4'bipyridine and



Figure 9. Design of original *trans*-coordinating ligand for transition metals (A) and as adapted to probe intramolecular C-H. N hydrogen bonding (B) and their synthesis from common precursor 9.



Figure 10. View of compounds 7 (A) and 8 (B) showing the intramolecular $C-H\cdots N$ hydrogen bond with thermal ellipsoids drawn at the 50% level and the asymmetric units labeled.

Table 2.	С–Н…N Н	ydrogen Bo	ond Lengths ar	nd Angles
complex	$d_{\rm N-H}$ (Å)	$d_{\rm N-C}({\rm \AA})$	∠NHC (deg)	∠C ^p NH (deg)
1	2.299	3.244(2)	172.59	175.15
2	2.472	3.364(3)	156.41	164.68
3	2.375	3.320(2)	173.47	164.95
4	2.300	3.250(3)	180	180
	2.283	3.233(3)	180	180
5	2.294	3.244(4)	180	180
	2.304	3.254(4)	180	180
6	2.288	3.232(3)	172.11	176.94
	2.289	3.235(3)	173.73	177.18
7	2.393	3.339(2)	173.59	161.10
8	2.559	3.505(4)	174.10	163.49

octafluorobiphenyl), the N1-H14, N2-H7 and the N1-C14, N2-C7 distances are 2.300, 2.283 and 3.250(3), 3.233(3) Å, respectively. In complex 5, between 1,2-bis(4-pyridyl)ethyne and octafluorobiphenyl, the N1-H1, N2-H8 and the N1-C1, N2-C8 distances are 2.294, 2.304 and 3.244(4), 3.254(4) Å, respectively, and in complex 6, between 1,2-bis(pyridyl)ethyne and octafluorobiphenyl, the N1-H13, N2-H22 and the N1-C13, N2-C22 distances are 2.289, 2.288 and 3.235(3), 3.232(3) Å, respectively. In the structures 4 and 5, the atoms involved in the hydrogen bonding lie on an axis of symmetry, and therefore, all the angles about the C-H...N hydrogen bonds are 180°, while in complex 6, the angle C13-H13-N1 is almost linear at 173.73°. The aromatic rings of each component in each of the co-crystals are not coplanar. Thus, the torsional angle between the bipyridyl rings in co-crystal 4 is about 45° and the angle between the two tetrafluorophenyl rings is about $57^\circ\!.$ Similar torsional angles of 51° and 60° are observed in the complex 5 and angles of about 50° and 59° for complex 6 for the bipyridyl and biphenyl rings, respectively. This similarity is clear when the crystal packing is shown viewed along the *b*-axis, as shown in Figure 7.

This adoption of a nonplanar geometry by the bipyridyls, which are generally coplanar in similar hydrogen-bonded complexes,² is quite possibly driven by other crystal packing forces due to the fact that the octafluorobiphenyl is nonplanar due to the steric interactions between the orthofluorine groups. In that regard, it is noteworthy that there is a significant contribution from stabilizing C-H…F interactions between adjacent pyridyl and fluorophenyl rings. Figure 8 highlights the C-H…F interactions within the complex 4. In this complex, the H…F distances are 2.700, 2.636, 2.700, and 2.774 Å for interactions F1-H1, F2-H2, F3-H5, and F4-H6, respec-

tively. The corresponding C-F distances are 3.531(3), 3.470(3), 3.553(3), and 3.613(3) Å, respectively.

Intramolecular Activated C–H···N Hydrogen Bonding. We have previously used the 1,2-bis(2-pyridinylethynyl)benzene scaffold (A in Figure 9) to prepare ligands for transition-metal complexation,²² and more recently, we have adapted this framework to investigate intramolecular halogen bonding.²³ It became apparent that this scaffold is in fact perfect to investigate intramolecular C–H···N hydrogen bonding. Accordingly, the ligand was modified to include a polyfluorophenyl ring in place of one of the pyridyl rings shown as **B** in Figure 9. The compounds were prepared using Sonogashira coupling from the common precursor ethynyl compound 9^{16} with 1-bromo-2,3,4,5-tetrafluorobenzene and 1bromo-2,3,4-trifluorobenzene to synthesize 7 and 8, respectively.

To date, two polyfluoro molecules have been synthesized: the tetrafluoroderivative 7 and the trifluoroderivative 8. Both have been crystallized and analyzed by X-ray diffraction. In both cases, the molecule is essentially planar with evidence for a strong intramolecular $C-H\cdots N$ hydrogen bond. The two structures are shown in Figure 10.

As expected, the C-N···H hydrogen bond in the more activated tetrafluorophenyl compound is slightly stronger than that in the less activated trifluorophenyl compound. In compound 7, the N1-H21 and C21-N1 distances are 2.393 and 3.339(2) Å, respectively, whereas in compound 8, the N1-H21 and C21-N1 distances are 2.559 and 3.505(4) Å, respectively. The angles about the hydrogen bond are similar in the two compounds. For compound 7, the angles C21-H21-N1 and C3-N1-H21 are 173.59° and 161.10°, respectively, whereas for compound 8, these angles are 174.10° and 163.49° , respectively. It is clear in both structures that the C-H···N interaction is strong enough to pull the fluorophenyl and pyridine rings closer together. This flexing of the ethynyl linkages is spread over multiple bonds and angles and cannot be evaluated by simply comparing two angles. Nevertheless, the nonbonding angle C13-C8--C2 reflects this flexing with reduced angles of 113.56° in compound 7 and 115.79° in compound 8.

Overview. The phenyl C–H···N hydrogen bond distances and angles are collected in Table 2. The phenyl C–H···N hydrogens bonds reported here are among the shortest reported to date. The hydrogen bonds reported for the tetrafluorphenyl N···H distance in compounds 1,2 and cocrystals 4, 5, and 6 are all less than 2.375 Å, while compound 3, which was designed to have mismatched donor and acceptor atom geometry, has a longer N···H distance of 2.490 Å. As expected based on the reduced acidity of the trifluorophenyl hydrogens, the intramolecular trifluorophenyl C–H···N hydrogen bond in compound 8 was significantly longer (0.166 Å) than the analogous intermolecular C–H···N tetrafluorophenyl hydrogen bond in compound 7.

CONCLUSIONS

We have demonstrated that fluoro-activated phenyl hydrogen atoms can form strong phenyl C–H···N hydrogen bonds and have the ability to be a dominant force in the crystallization of simple molecules in which the activated phenyl hydrogen and the basic nitrogen atom have favorable geometry. Furthermore, the phenyl C–H···N hydrogen bond is strong enough to consistently guide the co-crystallization of different molecules. Finally, we have demonstrated the use of a diphenylpyridyl scaffold as a means to quantify the activation effect of atoms/ groups on the strength of the C–H···N hydrogen bond, and we plan to use this to evaluate the relative strengths of activated phenyl C–H···N interactions. It is also noteworthy that multiple stabilizing weak phenyl C–H···F interactions are observed within each of the reported structures.

Our future studies will further explore this interesting interaction and will probe the incorporation of this phenyl $C-H\cdots N$ interaction along with other well-established, and stronger, crystal engineering forces, into complex co-crystals.

ASSOCIATED CONTENT

S Supporting Information

CIF files of synthesized compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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