Supporting Information

Polymorphisms of Aromatic Sulfonamides with Fluorine Groups

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Masahide Tominaga Kentaro Yamaguchi and Isao Azumaya

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^{1}H NMR and ^{13}C NMR spectrum data

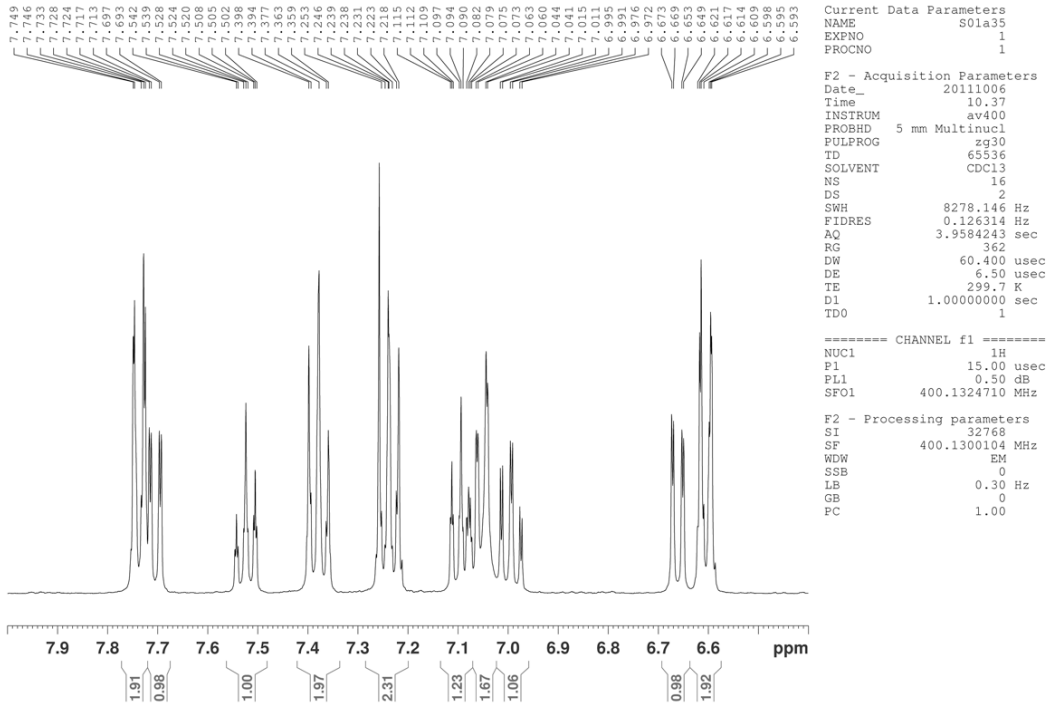


Figure S1. ^{1}H NMR of **1**.

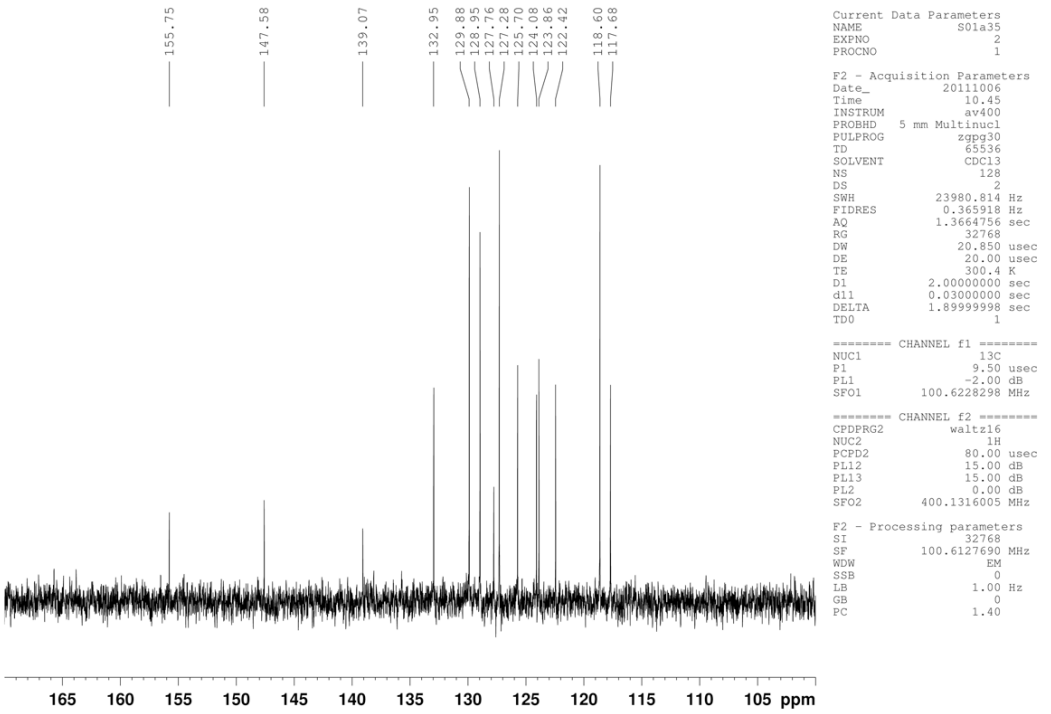


Figure S2. ^{13}C NMR of **1**.

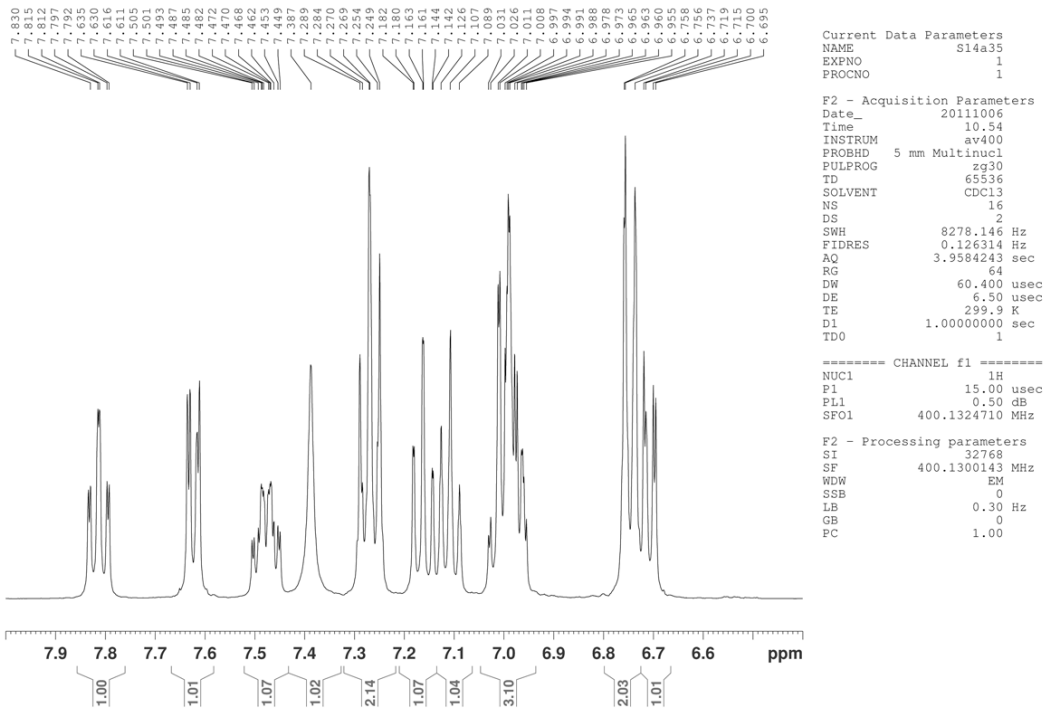


Figure S3. ^{1}H NMR of **2**.

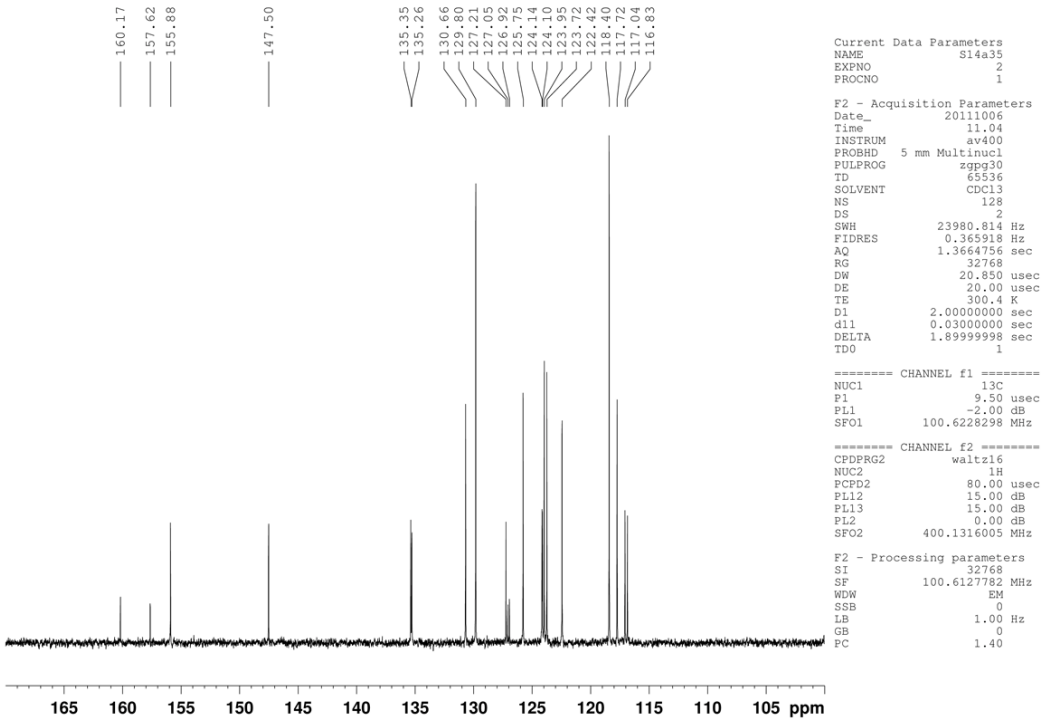


Figure S4. ^{13}C NMR of **2**.

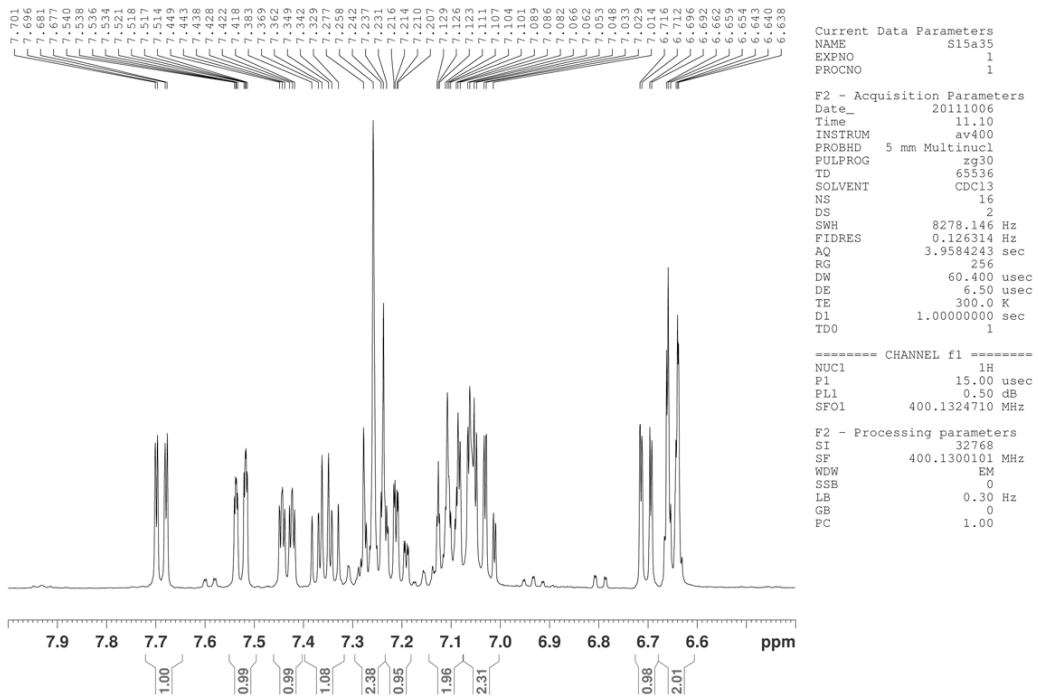


Figure S5. ^{1}H NMR of **3**.

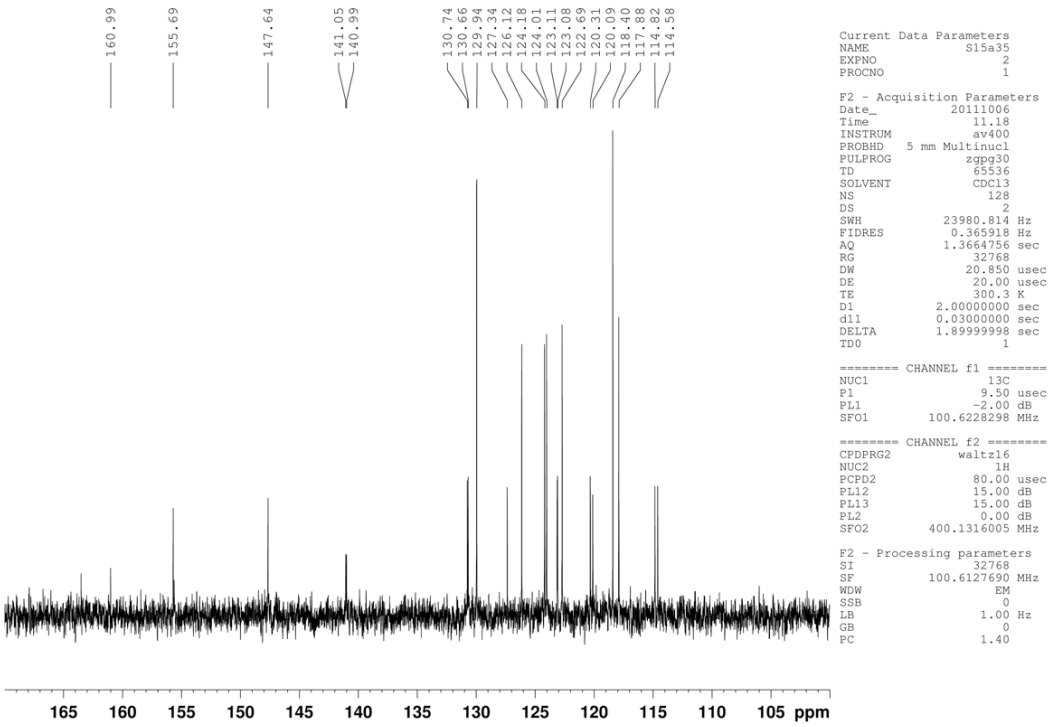


Figure S6. ^{13}C NMR of **3**.

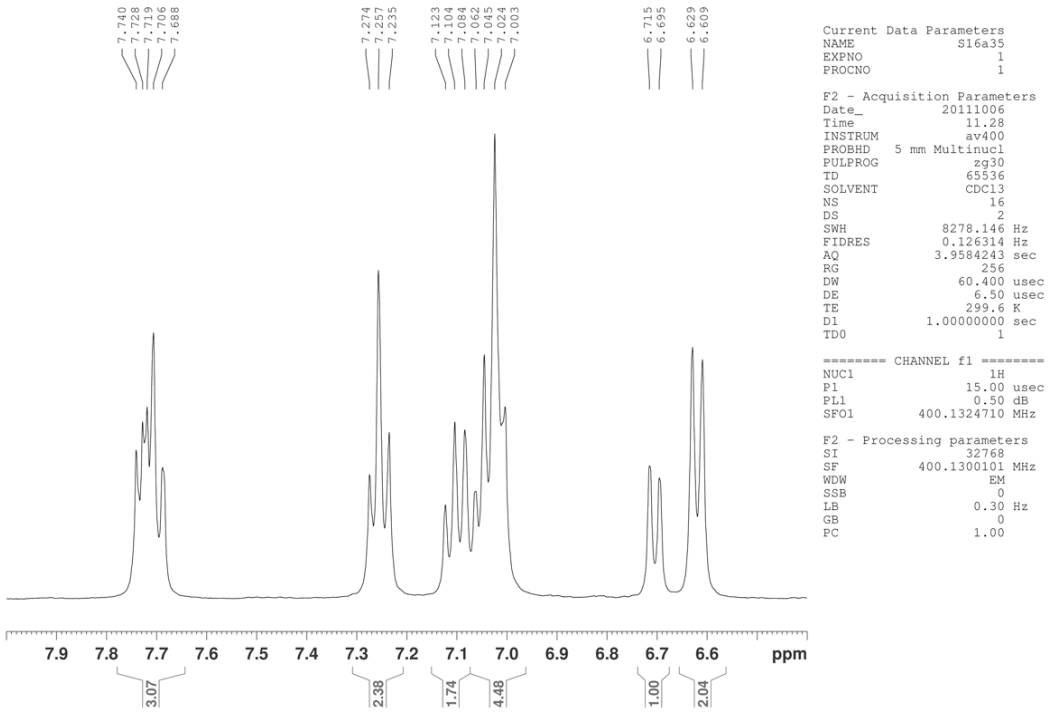


Figure S7. ^{1}H NMR of **4**.

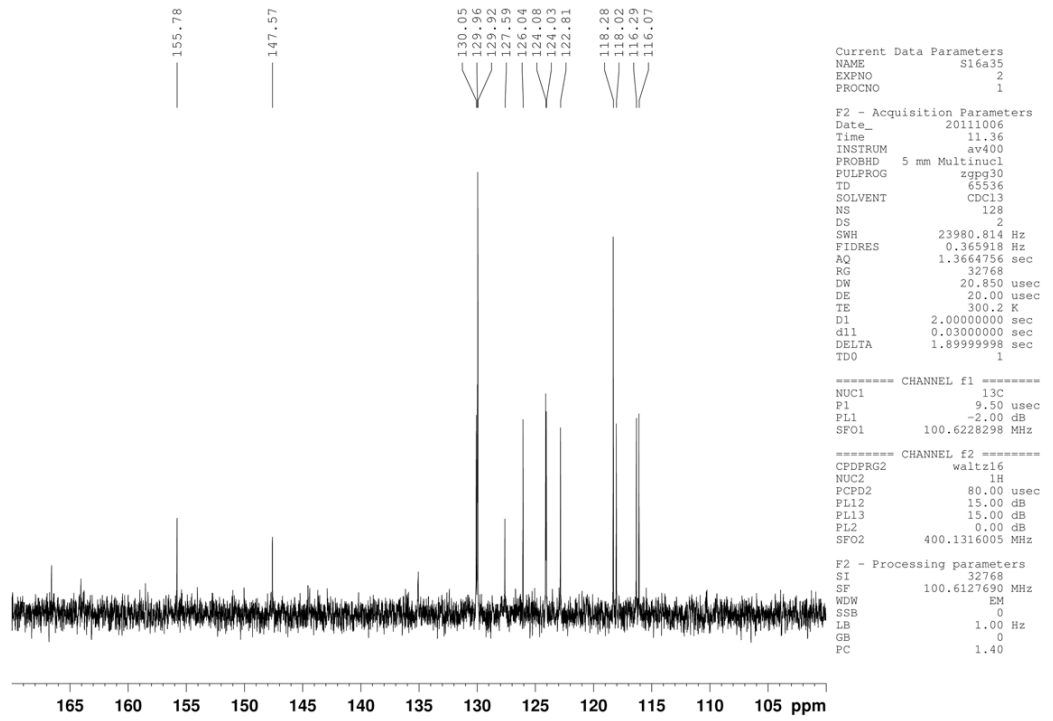


Figure S8. ^{13}C NMR of **4**.

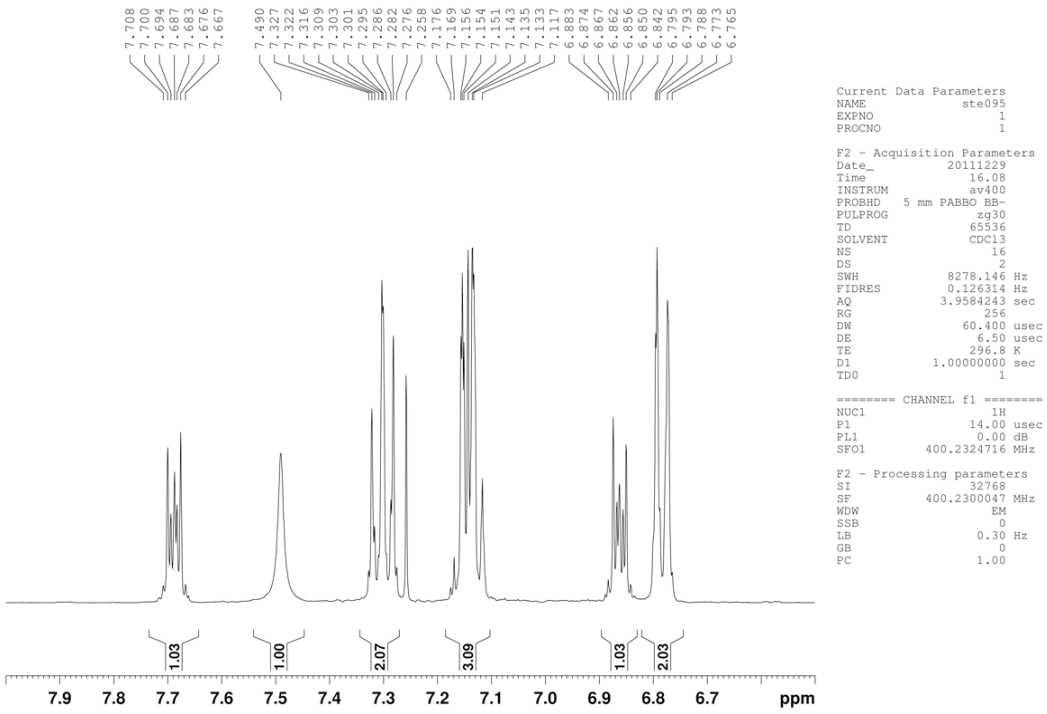


Figure S9. ^{1}H NMR of **5**.

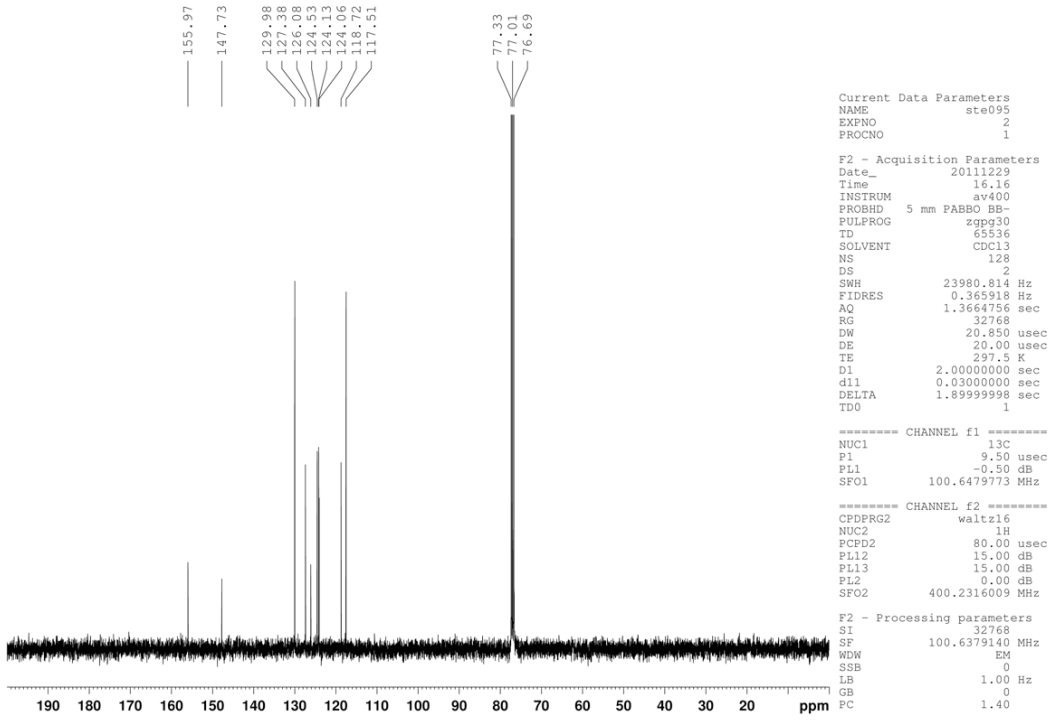


Figure S10. ^{13}C NMR of **5**.

X-ray Crystallographic Analysis.

Crystal data for 1. $C_{18}H_{15}NO_3S$; M = 325.37 g mol^{-1}, colorless prism measuring 0.50 × 0.20 × 0.20 mm, monoclinic, $P2_1/n$, a = 9.376(3), b = 12.139(4), c = 13.585(4) Å, β = 90.636(5) °, V = 1546.1(8) Å^3, Z = 4, D_c = 1.398 Mg m^{-3}, T = 150 K, μ(MoKα) = 0.224 mm^{-1}, $2\theta_{max}$ = 55.22°, 9087 reflections, 3501 unique reflections (R_{int} = 0.0289) which were used in all calculations. R_1 = 0.0369, wR_2 = 0.0880 (all data) R_1 = 0.0326, wR_2 = 0.0850 ($I > 2\sigma(I)$) for 212 parameters. CCDC reference number 860537.

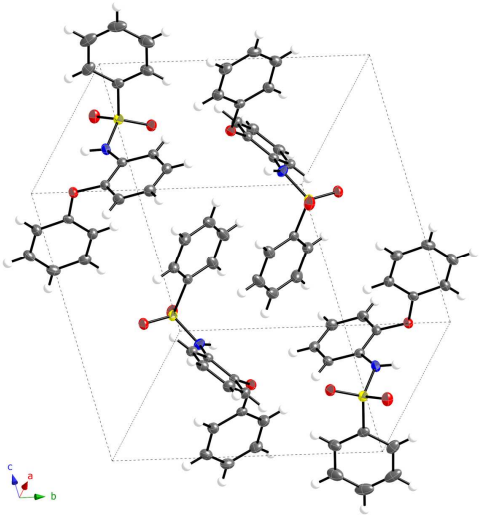


Figure S11. Thermal ellipsoid model of unit cell in a crystal of **1**.

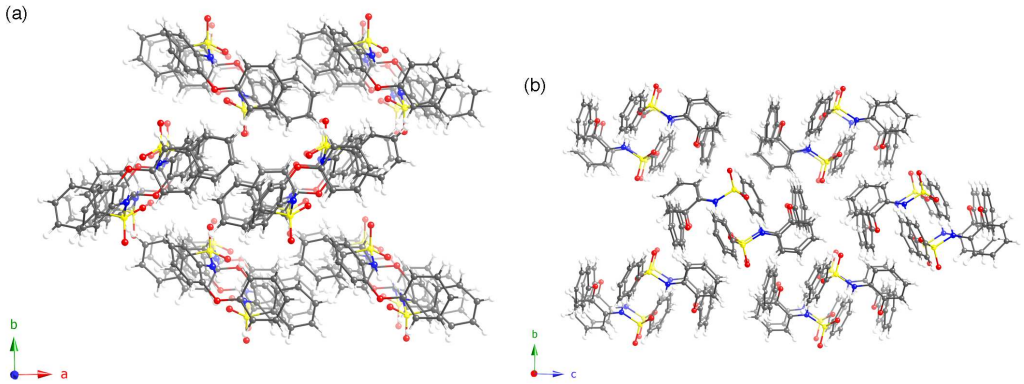


Figure S12. Ball and stick model of packing structure in a crystal of **1**, (a) view along the *ab* plane and (b) view along the *bc* plane.

Crystal data for 2a. $C_{18}H_{14}FNO_3S$; M = 343.36 g mol^{-1}, colorless prism measuring 0.40 × 0.35 × 0.30 mm, monoclinic, $P2_1/n$, a = 9.446(2), b = 12.131(2), c = 13.454(3) Å, β = 90.798(2) °, V = 1541.4(5) Å^3, Z = 4, D_c = 1.480 Mg m^{-3}, T = 120 K, μ(MoKα) = 0.238 mm^{-1}, $2\theta_{max}$ = 54.72°, 7404 reflections, 3136 unique reflections (R_{int} = 0.0017) which were used in all calculations. R_1 = 0.0396, wR_2 = 0.0903 (all data) R_1 = 0.0340, wR_2 = 0.0859 ($I > 2\sigma(I)$) for 217 parameters. CCDC reference number 860538.

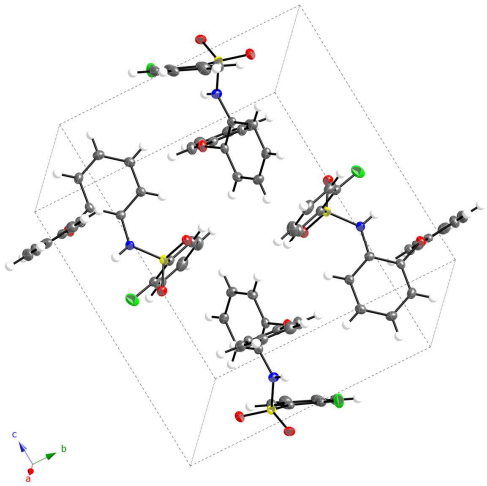


Figure S13. Thermal ellipsoid model of unit cell in a crystal of **2a**.

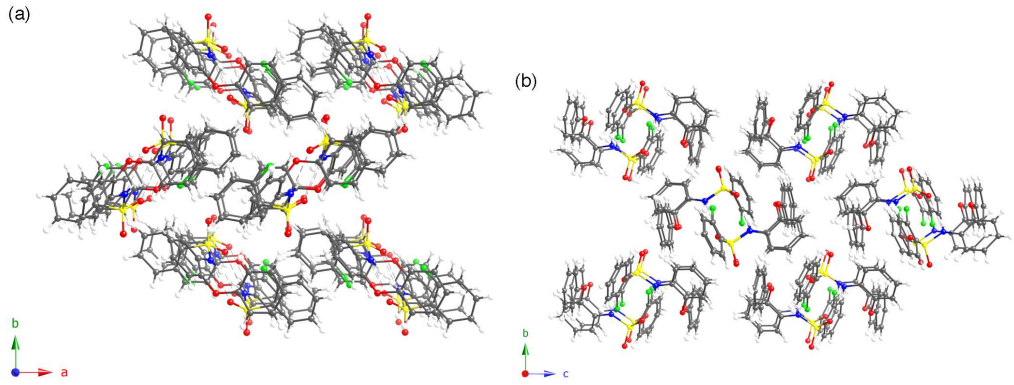


Figure S14. Ball and stick model of packing structure in a crystal of **2a**, (a) view along the *ab* plane and (b) view along the *ac* plane.

Crystal data for 2b. $C_{18}H_{14}FNO_3S$; $M = 343.36$ g mol^{-1}, colorless prism measuring 0.30 × 0.20 × 0.20 mm, triclinic, *P*-1, $a = 8.196(3)$, $b = 9.587(3)$, $c = 11.428(4)$ Å, $\alpha = 101.227(3)$, $\beta = 90.798(2)$, $\gamma = 103.611(4)$ °, $V = 790.4(4)$ Å^3, $Z = 2$, $D_c = 1.443$ Mg m^{-3}, $T = 120$ K, μ(MoKα) = 0.232 mm^{-1}, $2\theta_{max} = 54.48°$, 3915 reflections, 3000 unique reflections ($R_{int} = 0.0111$) which were used in all calculations. $R_1 = 0.0402$, $wR_2 = 0.0915$ (all data) $R_1 = 0.0351$, $wR_2 = 0.0880$ ($I > 2\sigma(I)$) for 217 parameters. CCDC reference number 860539.

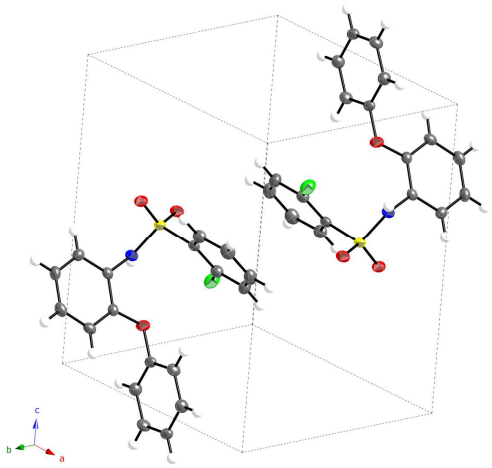


Figure S15. Thermal ellipsoid model of unit cell (left) and packing structure (right) in a crystal of **2b**.

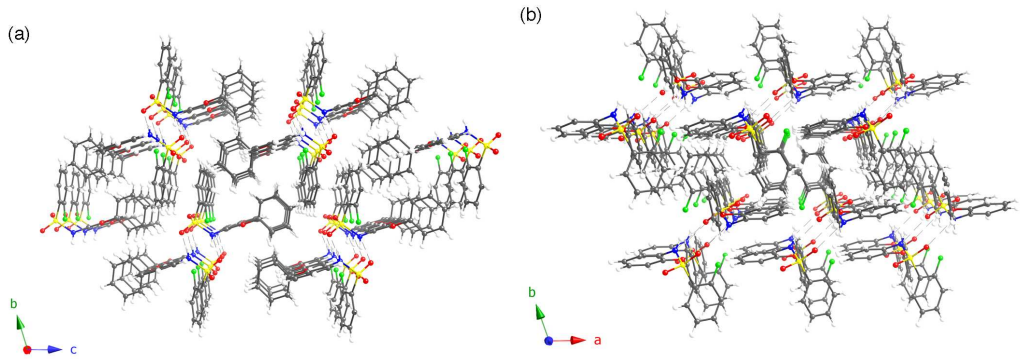


Figure S16. Ball and stick model of packing structure in a crystal of **2b**, (a) view along the *bc* plane and (b) view along the *ac* plane.

Crystal data for 3a. $C_{18}H_{14}FNO_3S$; M = 343.36 g mol^{-1}, colorless prism measuring 0.30 × 0.20 × 0.20 mm, monoclinic, $P2_1/n$, a = 9.489(2), b = 12.364(3), c = 13.425(3) Å, β = 91.139(2) °, V = 1574.8(5) Å^3, Z = 4, D_c = 1.448 Mg m^{-3}, T = 150 K, μ(MoKα) = 0.233 mm^{-1}, $2\theta_{max}$ = 54.46°, 7457 reflections, 3126 unique reflections (R_{int} = 0.0188) which were used in all calculations. R_1 = 0.0395, wR_2 = 0.0875 (all data) R_1 = 0.0332, wR_2 = 0.0835 ($I > 2\sigma(I)$) for 217 parameters. CCDC reference number 860540.

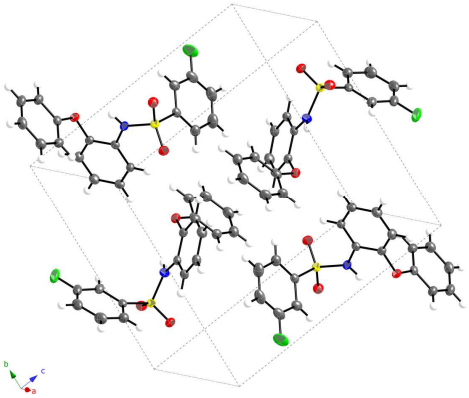


Figure S17. Thermal ellipsoid model of unit cell in a crystal of **3a**.

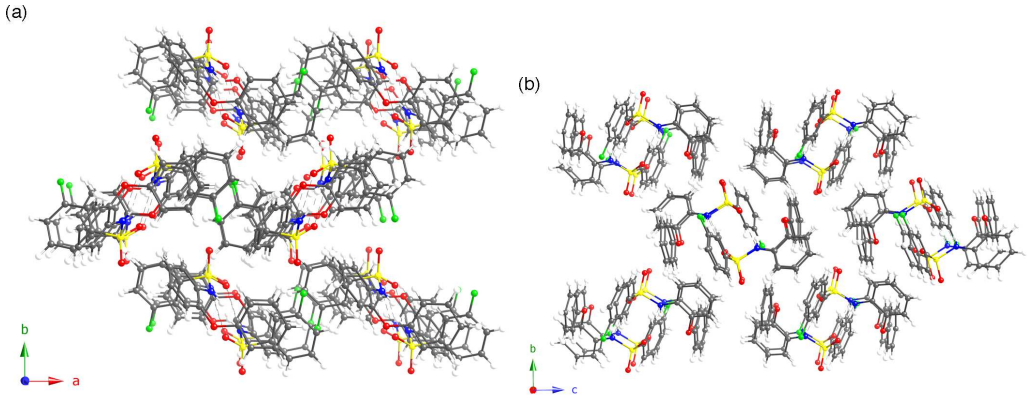


Figure S18. Ball and stick model of packing structure in a crystal of **3a**, (a) view along the *ab* plane and (b) view along the *bc* plane.

Crystal data for 3b. $C_{18}H_{14}FNO_3S$; $M = 343.36$ g mol^{-1}, colorless prism measuring 0.30 × 0.30 × 0.25 mm, monoclinic, $P2_1/n$, $a = 8.664(8)$, $b = 12.364(3)$, $c = 13.425(3)$ Å, $\beta = 91.139(2)$ °, $V = 1574.8(5)$ Å^3, $Z = 4$, $D_c = 1.377$ Mg m^{-3}, $T = 296$ K, μ(MoKα) = 0.221 mm^{-1}, $2\theta_{max} = 54.42°$, 7697 reflections, 3353 unique reflections ($R_{int} = 0.0365$) which were used in all calculations. $R_1 = 0.0997$, $wR_2 = 0.2273$ (all data) $R_1 = 0.0603$, $wR_2 = 0.1812$ ($I > 2\sigma(I)$) for 272 parameters. CCDC reference number 860541.

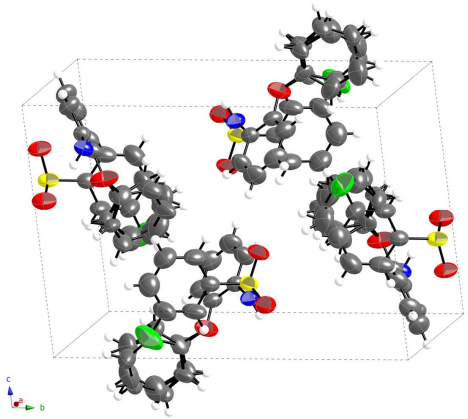


Figure S19. Thermal ellipsoid model of unit cell in a crystal of **3b**.

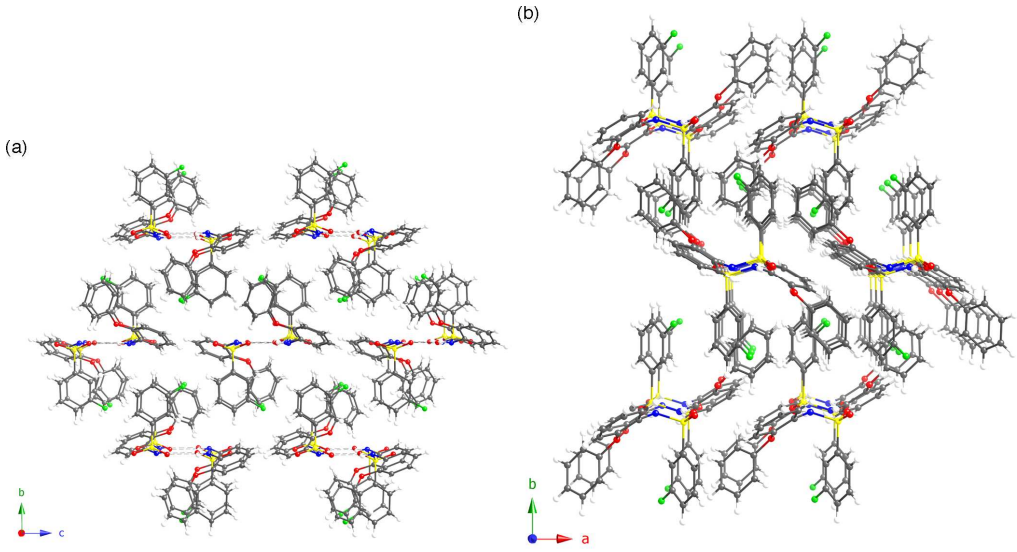


Figure S20. Ball and stick model of packing structure in a crystal of **3b**, (a) view along the *bc* plane and (b) view along the *ab* plane.

Crystal data for 4a. $C_{18}H_{14}FNO_3S$; M = 343.36 g mol^{-1}, colorless prism measuring 0.40 × 0.20 × 0.20 mm, triclinic, *P*-1, a = 8.250(3), b = 9.528(3), c = 11.468(4) Å, α = 102.597(4), β = 107.235(4), γ = 104.579(3) °, V = 790.3(4) Å^3, Z = 2, D_c = 1.443 Mg m^{-3}, T = 120 K, μ(MoKα) = 0.232 mm^{-1}, $2\theta_{max}$ = 54.38°, 3852 reflections, 2959 unique reflections (R_{int} = 0.0209) which were used in all calculations. R_1 = 0.0837, wR_2 = 0.1433 (all data) R_1 = 0.0542, wR_2 = 0.1275 ($I > 2\sigma(I)$) for 217 parameters. CCDC reference number 860542.

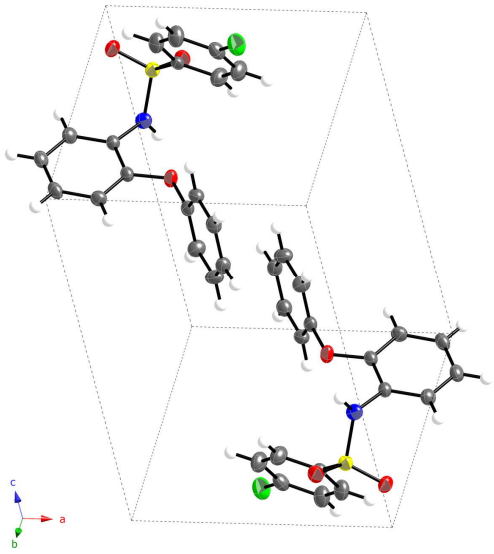


Figure S21. Thermal ellipsoid model of unit cell in a crystal of **4a**.

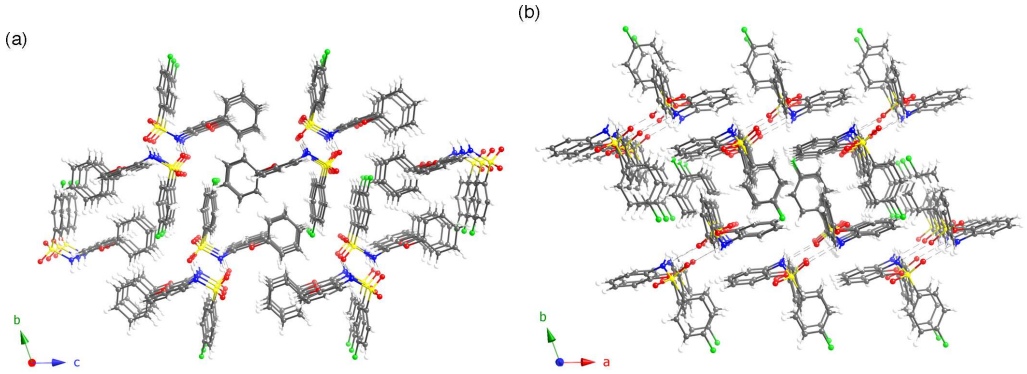


Figure S22. Ball and stick model of packing structure in a crystal of **4a**, (a) view along the *bc* plane and (b) view along the *ab* plane.

Crystal data for 4b. $C_{18}H_{14}FNO_3S$; $M = 343.36$ g mol^{-1}, colorless needle measuring 0.20 × 0.10 × 0.05 mm, monoclinic, $P2_1/c$, a = 9.667(2), b = 5.535(1), c = 28.746(6) Å, β = 97.790(2) °, V = 1524.1(6) Å^3, $Z = 4$, $D_c = 1.496$ Mg m^{-3}, $T = 120$ K, μ(MoKα) = 0.240 mm^{-1}, $2\theta_{max} = 54.70°$, 7119 reflections, 3085 unique reflections ($R_{int} = 0.0311$) which were used in all calculations. $R_1 = 0.0600$, $wR_2 = 0.1052$ (all data) $R_1 = 0.0408$, $wR_2 = 0.0969$ ($I > 2\sigma(I)$) for 217 parameters. CCDC reference number 860543.

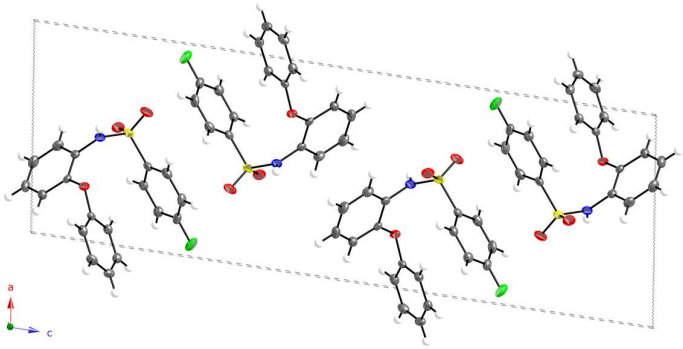


Figure S23. Thermal ellipsoid model of unit cell in a crystal of **4b**.

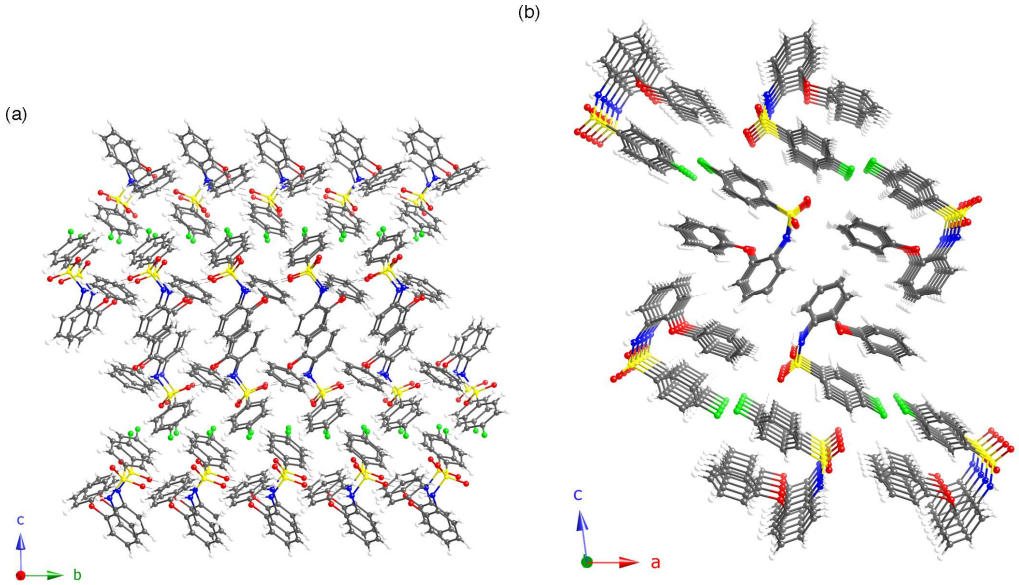


Figure S24. Ball and stick model of packing structure in a crystal of **4b**, (a) view along the *bc* plane and (b) view along the *ac* plane.

Crystal data for 5a. $C_{18}H_{10}F_5NO_3S$; M = 415.33 g mol^{-1}, colorless needle measuring 0.30 × 0.20 × 0.10 mm, monoclinic, $P2_1/n$, a = 8.865(3), b = 19.508(6), c = 9.849(3) Å, β = 98.662(3) °, V = 1683.9(8) Å^3, Z = 4, D_c = 1.638 Mg m^{-3}, T = 120 K, μ(MoKα) = 0.266 mm^{-1}, $2\theta_{max}$ = 54.64°, 7994 reflections, 3388 unique reflections (R_{int} = 0.0158) which were used in all calculations. R_1 = 0.0364, wR_2 = 0.0850 (all data) R_1 = 0.0323, wR_2 = 0.0829 ($I > 2\sigma(I)$) for 257 parameters. CCDC reference number 860544.

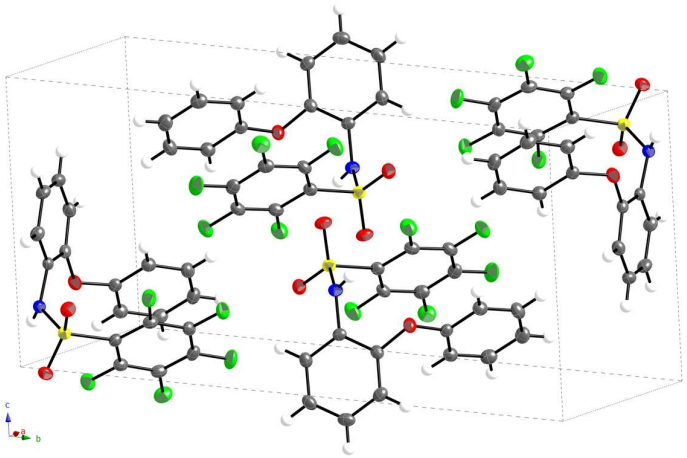


Figure S25. Thermal ellipsoid model of unit cell in a crystal of **5a**.

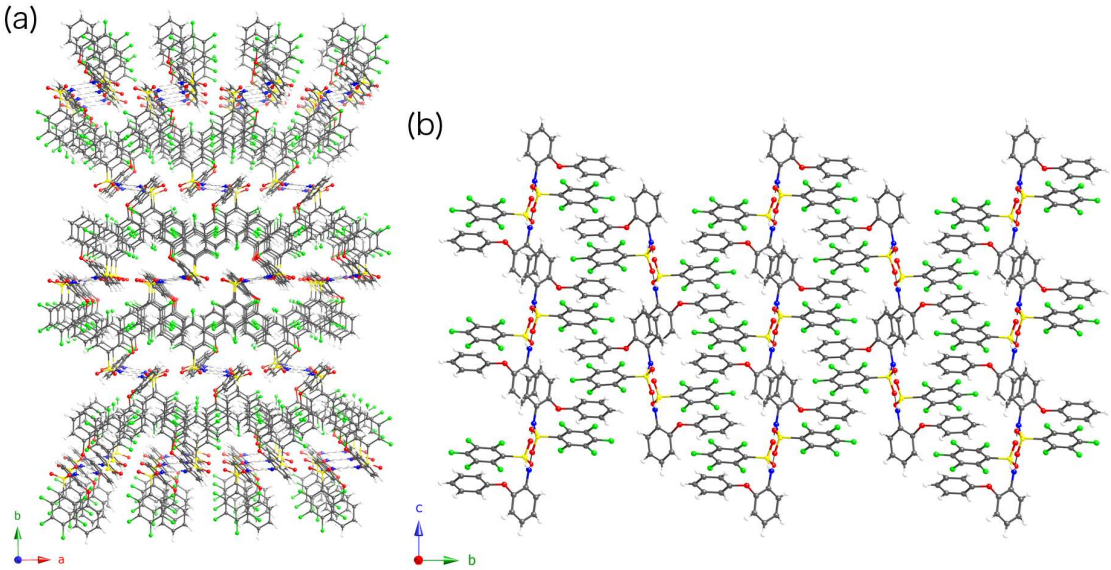


Figure S26. Ball and stick model of packing structure in a crystal of **5a**, (a) view along the *ab* plane and (b) view along the *bc* plane.

Crystal data for 5b. $C_{18}H_{10}F_5NO_3S$; M = 415.33 g mol^{-1}, colorless needle measuring 0.50 × 0.40 × 0.05 mm, monoclinic, $P2_1$, a = 7.887(3), b = 5.8359(19), c = 17.557(6) Å, β = 93.745(4) °, V = 806.4(5) Å^3, Z = 2, D_c = 1.710 Mg m^{-3}, T = 100 K, μ(MoKα) = 0.278 mm^{-1}, $2\theta_{max}$ = 53.84°, 3903 reflections, 2638 unique reflections (R_{int} = 0.0159) which were used in all calculations. R_1 = 0.0384, wR_2 = 0.0782 (all data) R_1 = 0.0330, wR_2 = 0.0756 ($I > 2\sigma(I)$) for 257 parameters. CCDC reference number 860545.

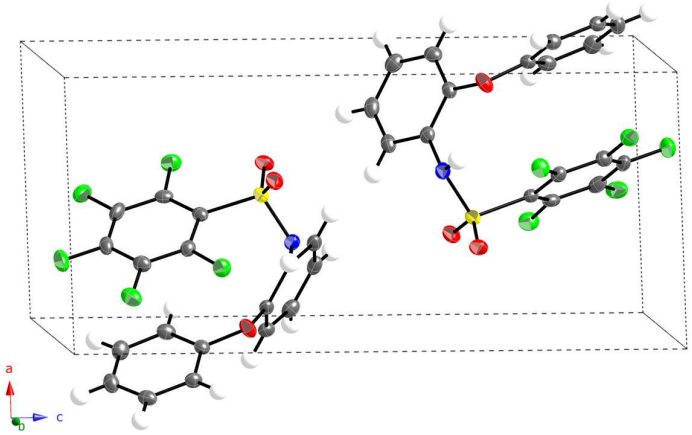


Figure S27. Thermal ellipsoid model of unit cell in a crystal of **5b**.

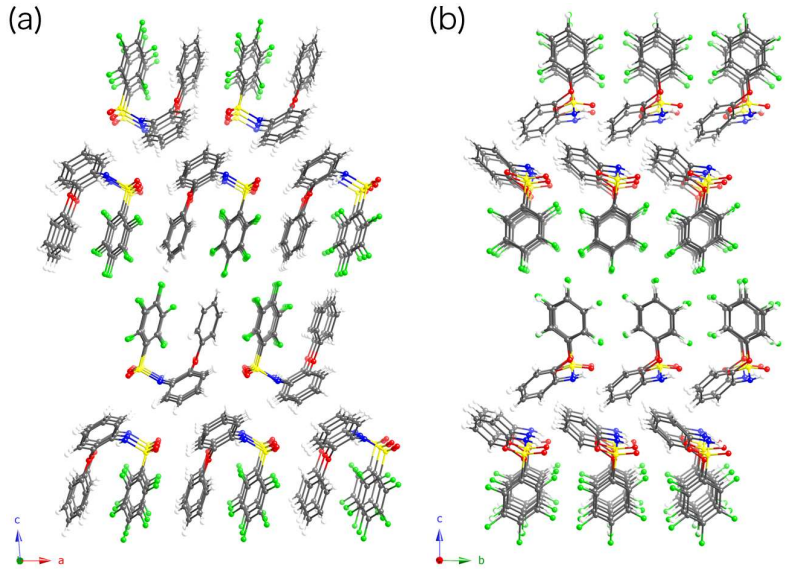


Figure S28. Ball and stick model of packing structure in a crystal of **5b**, (a) view along the *ac* plane and (b) view along the *bc* plane.

Crystal data for 5c. $C_{18}H_{10}F_5NO_3S{\cdot}C_4H_8O$; M = 487.43 g mol^{-1}, colorless needle measuring 0.50 × 0.30 × 0.20 mm, monoclinic, $P2_1/n$, a = 9.363(3), b = 24.015(8), c = 9.747(3) Å, β = 101.286(4) °, V = 2149.2(13) Å^3, Z = 4, D_c = 1.506 Mg m^{-3}, T = 120 K, μ(MoKα) = 0.224 mm^{-1}, $2\theta_{max}$ = 40.28°, 5364 reflections, 2001 unique reflections (R_{int} = 0.0165) which were used in all calculations. R_1 = 0.0846, wR_2 = 0.1900 (all data) R_1 = 0.0795, wR_2 = 0.1864 ($I > 2\sigma(I)$) for 299 parameters. CCDC reference number 860546.

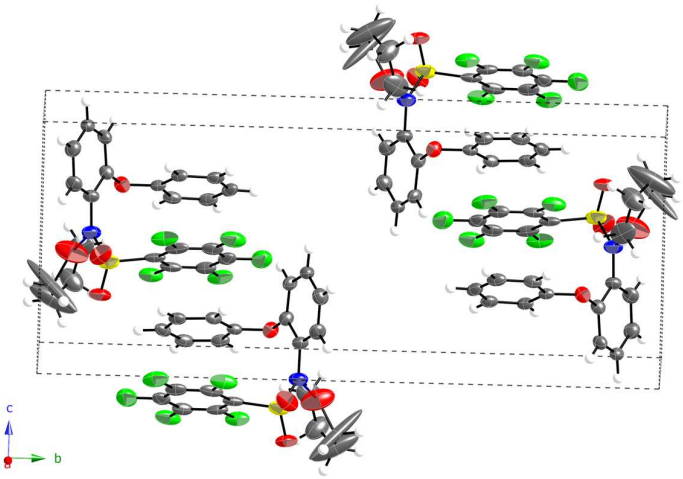


Figure S29. Thermal ellipsoid model of unit cell in a crystal of **5c**.

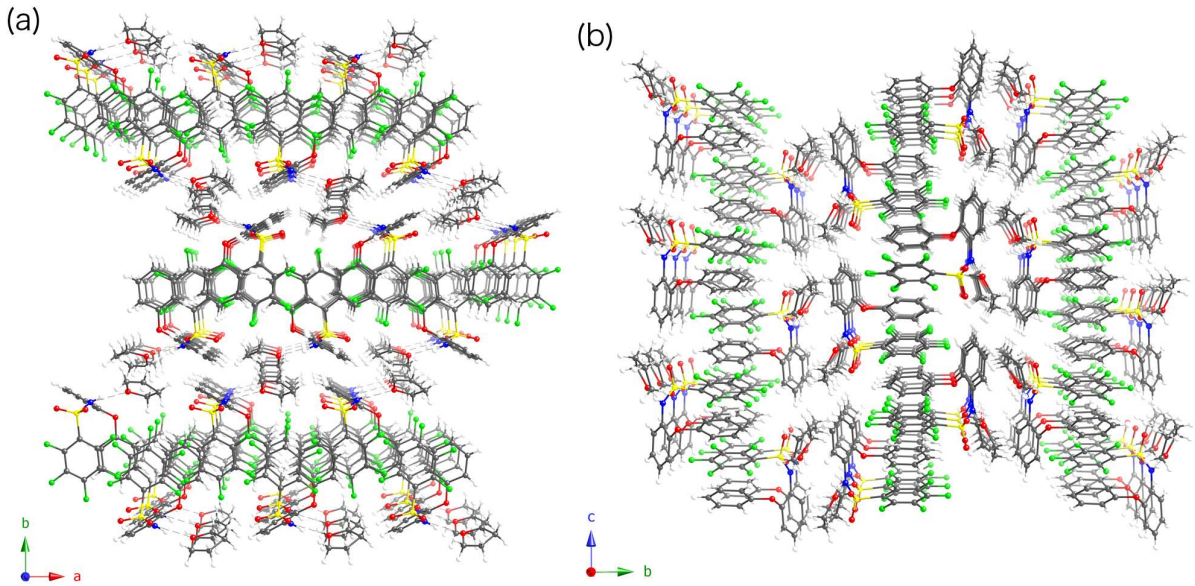


Figure S30. Ball and stick model of packing structure in a crystal of **5c**, (a) view along the *ab* plane and (b) view along the *bc* plane.

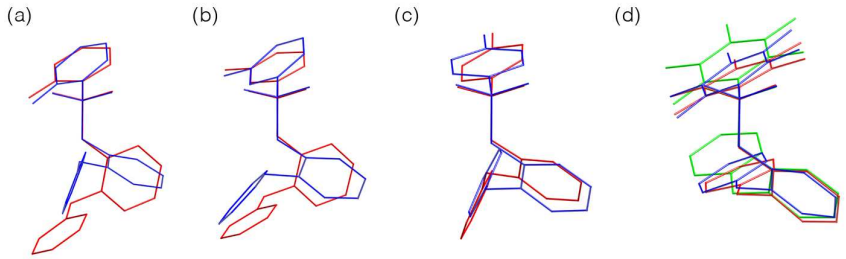


Figure 31. Overlay of polymorphs in the sulfonamides: (a) **2**, (b) **3**, (c) **4** and (d) **5**. **2a**, **3a**, **4a** and **5a** are shown as red, **2b**, **3b**, **4b** and **5b** is shown as blue and **5c** is shown as green, respectively. Hydrogen atoms are omitted for clarity.

Table S1. Distances (*d*) and angles (∠) of intermolecular hydrogen bonds in the crystals **1**, **2**, **3**, **4** and **5**.

Crystal	D···H_A[a, b]	*d*(D···H) Å	*d*(H···A) Å	*d*(D···A) Å	∠(DHA) deg
1	N1–H1···O2 #1	0.86	2.10	2.933(2)	163.2
2a	N1–H1···O1 #2	0.88	2.16	2.932(2)	146.0
2b	N1–H1···O2 #3	0.88	2.26	3.047(2)	148.8
	N1–H1···F1 #3	0.88	2.44	3.091(2)	131.4
	C11–H11···F1 #4	0.95	2.57	3.216(2)	116.9
3a	N1–H1···O1 #5	0.88	2.29	2.958(2)	132.4
3b	N1–H1···O2 #6	0.77	2.24	3.009(5)	170.0
	C2–H2···F1 #7	0.93	2.54	3.236(6)	151.9
4a	N1–H1···O1 #8	0.81	2.20	2.989(3)	165.0
4b	N1–H1···O2 #9	0.88	2.58	3.383(3)	151.4
	C5–H5···F1 #10	0.95	2.65	3.409(3)	154
5a	N1–H1···O1 #11	0.86	2.20	3.016(2)	160.9
	C10–H10···O1 #12	0.95	2.56	3.416(2)	150
5b	C9–H9···O1 #13	0.95	2.44	3.134(3)	130
5c	N1–H1···O4 #14	0.88	1.90	2.765(10)	166
	C18–H18···F2 #15	0.95	2.43	3.269(8)	147
	C22–H22···O1 #13	0.99	2.59	3.38(2)	136

[a] Symmetry transformation used to generate equivalent atoms:

#1 −x, −y+1, −z+1; #2 −x, −y+1, −z+2; #3 −x, −y+1, −z; #4 −x+1, y, z; #5 −x, −y+2, −z+1; #6 −x+1, −y, −z; #7 x−1/2, −y+1/2, z+1/2; #8 −x+1, −y+1, −z; #9 x, y+1, z; #10 −x+2, y−1/2, −z+1/2; #11 −x, −y, −z; #12 x, y, z+1; #13 x−1, y, z; #14 x+1, y, z; #15 x+1/2, −y+1/2, z+1/2.

[b] The positions of hydrogen atoms were calculated based on geometrical adequacy.

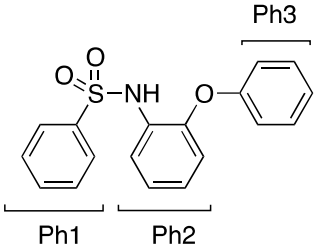
Table S2. Aromatic–aromatic interactions in the crystals **1**, **2**, **3**, **4** and **5**.

Crystal	interaction[a, b]	distance Å[c]	angle deg
1	Ph1–Ph1 #1	3.768(2)	0.00
	Ph1–Ph3 #2	3.979(2)	16.08(7)
	Ph2–Ph1 #3	4.909(2)	72.53(7)
2a	Ph1–Ph1 #4	3.805(1)	0.00
	Ph1–Ph3 #5	4.012(1)	16.71(8)
	Ph2–Ph1 #6	4.828(2)	73.31(8)
2b	Ph1–Ph1 #7	3.670(2)	0.00
	Ph2–Ph3 #8	4.851(2)	89.0(1)
	Ph3–Ph2 #9	4.928(2)	89.0(1)
3a	Ph1–Ph1 #8	3.943(1)	0.00
	Ph1–Ph3 #10	3.919(1)	14.98(8)
	Ph2–Ph1 #6	4.928(2)	74.06(8)
3b	Ph1–Ph3 #11	4.176(5)	23.0(6)
	Ph1–Ph3 #12	4.345(5)	22.6(6)
4a	Ph1–Ph1 #13	3.897(2)	0.00
	Ph2–Ph3 #14	5.035(3)	88.2(2)
	Ph2–Ph3 #15	4.857(2)	88.2(2)
4b	Ph2–Ph3 #16	5.181(2)	89.8(1)
	Ph3–Ph1 #17	4.649(2)	57.5(1)
	Ph3–Ph2 #18	4.989(2)	89.8(1)
5a	Ph1–Ph3 #19	3.749(2)	3.09(2)
5b	Ph1–Ph3 #11	4.026(2)	3.86(2)
5c	Ph1–Ph3 #19	3.701(4)	4.24(3)

[a] Symmetry transformation used to generate equivalent atoms:

#1 –x+1, –y+1, –z+1; #2 –x, –y+1, –z+1; #3 x–1/2, –y+1/2, z–1/2; #4 –x+1, –y+1, –z+2; #5 –x, –y+1, –z+2; #6 x–1/2, –y+3/2, z–1/2; #7 –x, –y+2, –z; #8 –x+1, –y+2, –z+1; #9 –x+1, y, z; #10 –x, –y+2, –z+1; #11 x+1, y, z; #12 x+1/2, –y+1/2, z+1/2; #13 –x+1, –y+2, –z; #14 –x+2, –y+1, –z+1; #15 –x+2, –y+2, –z+1; #16 x, y–1, z; #17 x, y+1, z; #18 –x+2, –y+1, –z+1; #19 x+1/2, –y+1/2, z–1/2.

[b] Refer to under figure for phenyl group number.



[c] The distances were measured from the centre of the ring to the centre of the ring.

Differential Scanning Calorimetry (DSC) chart

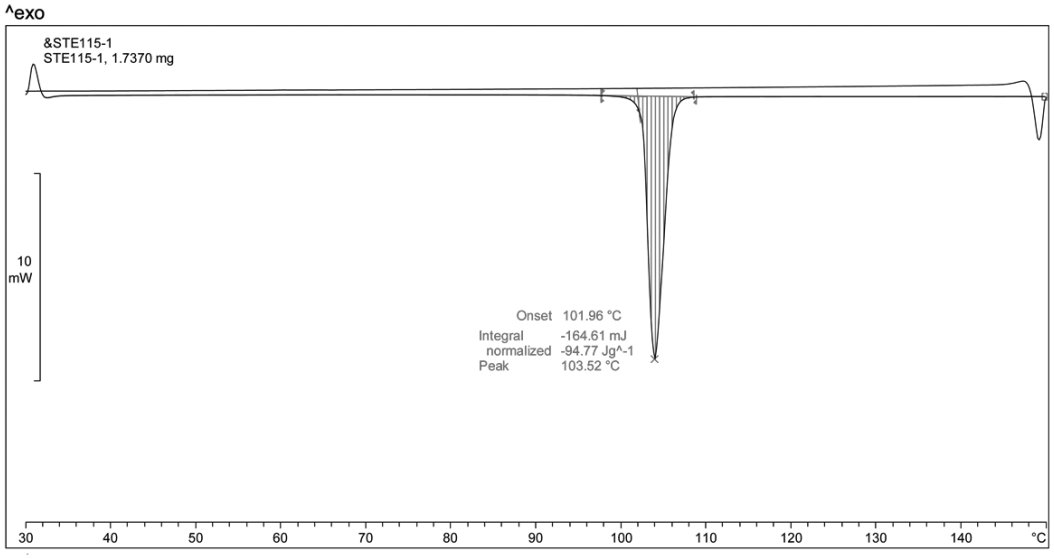


Figure S32. DSC chart of the crystal **1**.

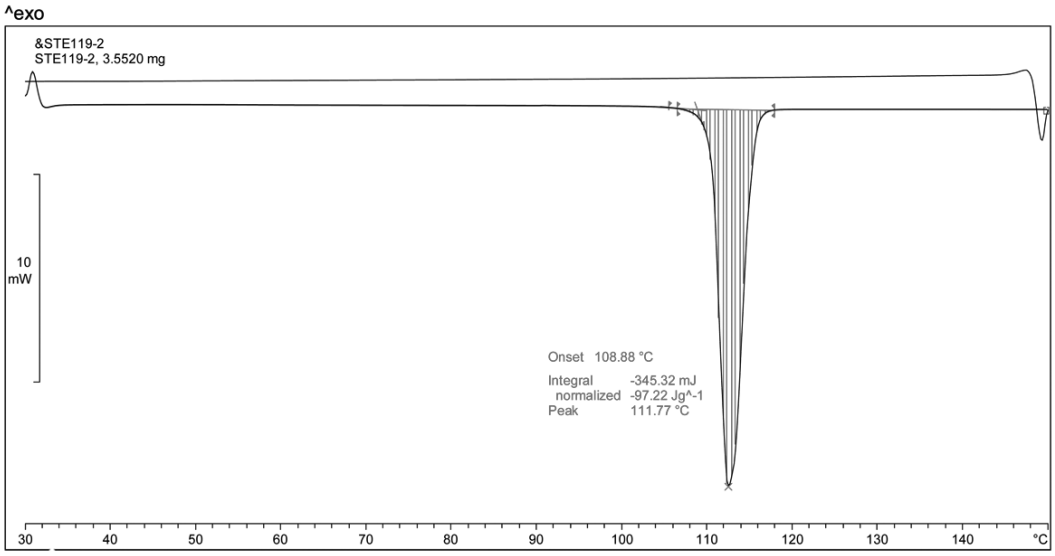


Figure S33. DSC chart of the crystal **2a**.

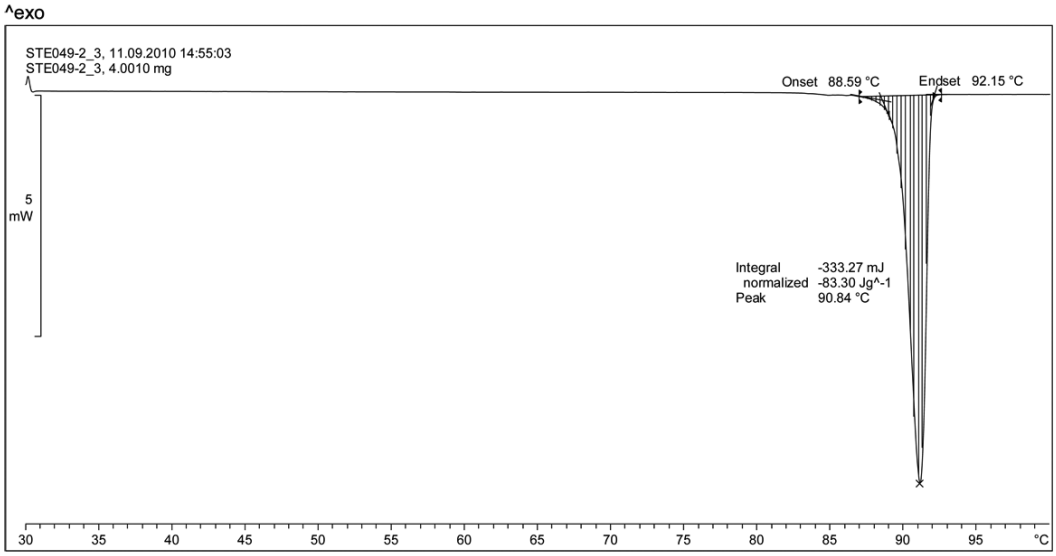


Figure S34. DSC chart of the crystal **2b**.

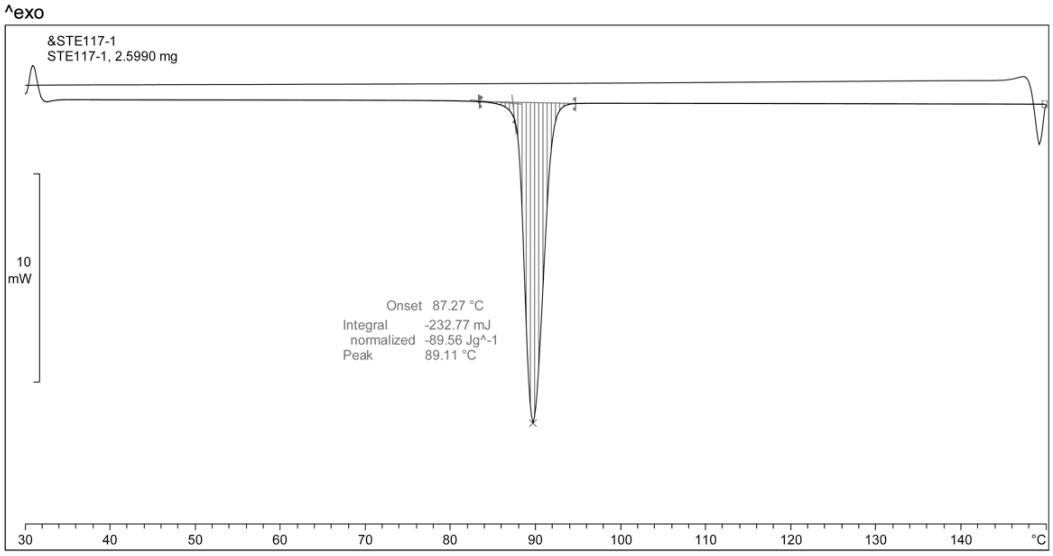


Figure S35. DSC chart of the crystal **3a**.

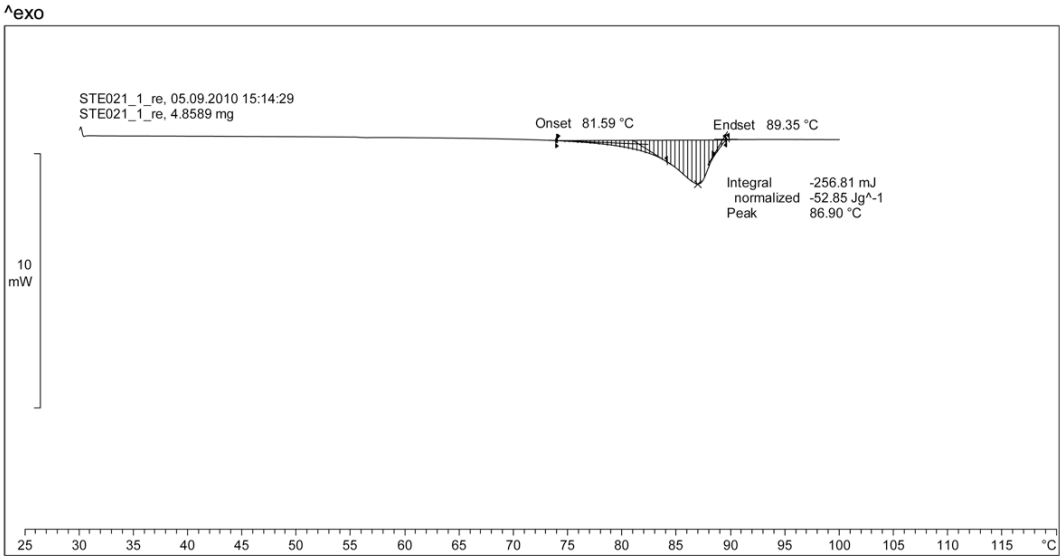


Figure S36. DSC chart of the crystal **3b**.

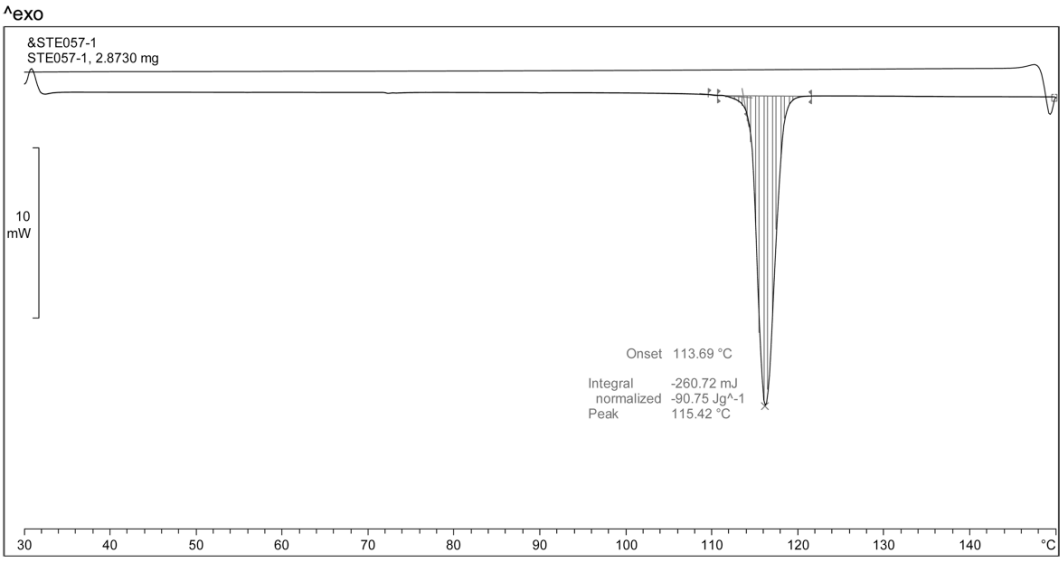


Figure S37. DSC chart of the crystal **4a**.

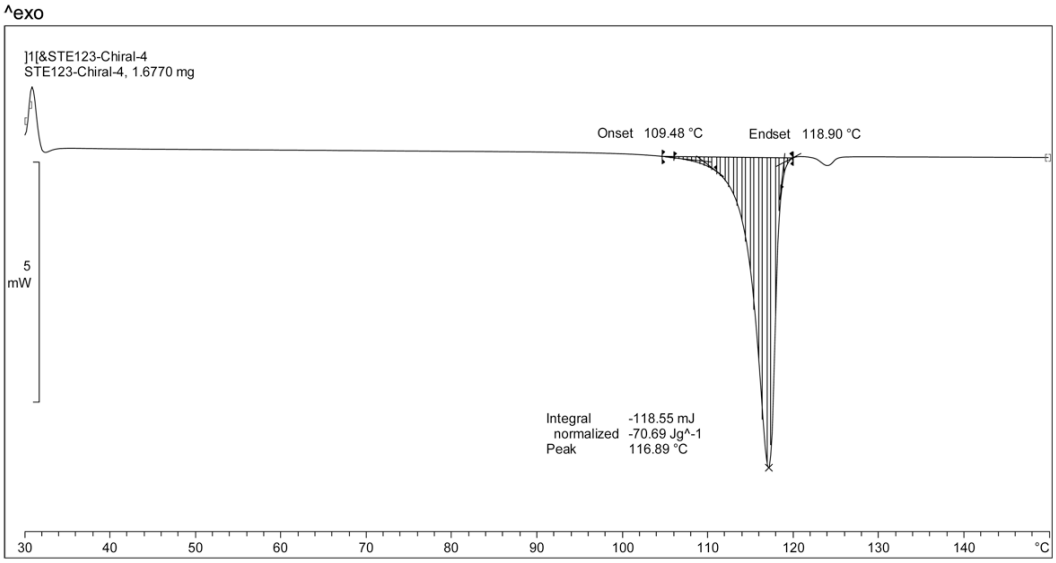


Figure S38. DSC chart of the crystal **5a**.

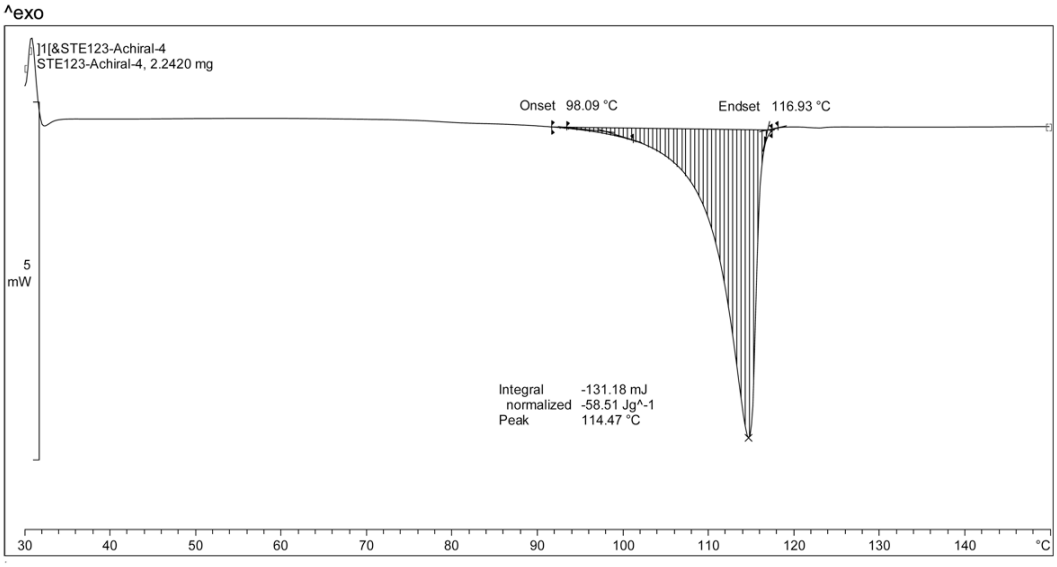


Figure S39. DSC chart of the crystal **5b**.

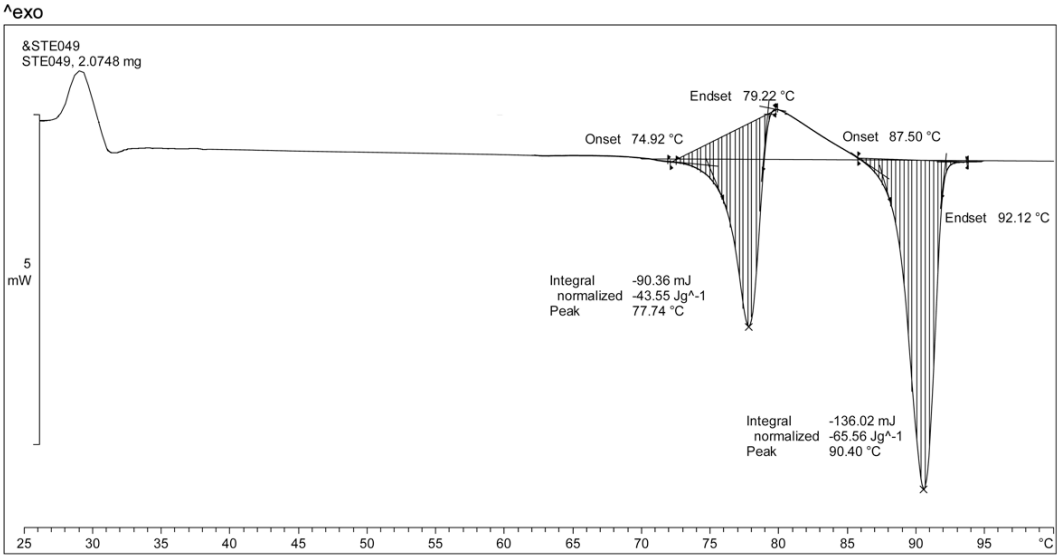


Figure S40. DSC chart of the crystal **5c**.

Thermogravimetry/differential Thermal Analysis (TG/DTA) chart

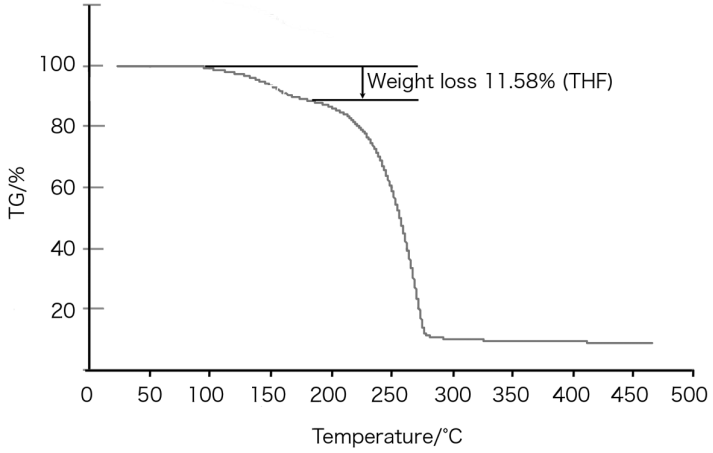


Figure S41. Thermogravimetric carve of the crystal **5c**.

Crystallization Screening

Crystallization. The sulfonamides were dissolved with chloroform, ethyl acetate or tetrahydrofuran as good solvents. Each solution were put into micro tubes which included chloroform, ethyl acetate, toluene, hexane, methanol, acetone, acetonitrile and tetrahydrofuran as poor solvents. Different types of single crystals were obtained by crystallization from 24 combinations of solvents.

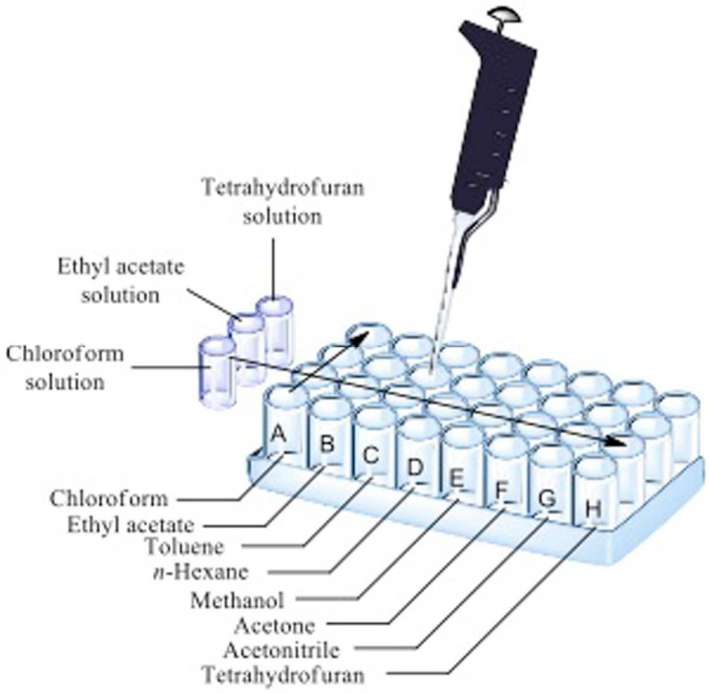


Figure S42. Crystallization Screening.

Table S3. Crystallization conditions and crystal forms of **1**–**5**.

	Good solvent / Poor solvent	Chloroform	Ethyl acetate	Methanol	Acetonitrile	Tetrahydrofuran	Toluene	*n*-Hexane	Cyclohexane
1	Tetrahydrofuran	**1**	**1**	—[b]	—[b]	—[b]	—[b]	**1**	**1**
	Ethyl acetate	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**
	Chloroform	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**[a]
2	Tetrahydrofuran	—[b]	—[b]	**2b**[a]	—[b]	—[b]	—[b]	—[b]	—[b]
	Ethyl acetate	**2a**	**2a**	**2a**	**2a**	**2a**	**2a**	**2a**[a]	**2a**
	Chloroform	**2a**	**2a**	—[b]	**2a**	**2a**	—[b]	**2a**	**2a**
3	Tetrahydrofuran	—[b]	—[b]	—[b]	—[b]	—[b]	—[b]	**3a**[a]	—[b]
	Ethyl acetate	**3a**	**3a**	**3a**	**3a**	**3b**	—[b]	**3a**	**3a**
	Chloroform	**3a**[a]	**3a**	—[b]	—[b]	**3b**	—[b]	**3a**	**3a**
4	Tetrahydrofuran	**4a**	—[b]	**4a**	—[b]	—[b]	—[b]	—[b]	**4b**
	Ethyl acetate	**4a**	**4a**	**4a**	**4a**	**4a**[a]	—[b]	**4a**	**4a**
	Chloroform	**4a**	**4a**	**4a**	**4a**	**4b**[a]	—[b]	**4a**	**4a**
5	Tetrahydrofuran	**5c**	—[b]	—[b]	—[b]	**5c**	**5c**	**5c**[a]	**5c**
	Ethyl acetate	—[b]	—[b]	—[b]	—[b]	—[b]	**5b**[a]	—[b]	—[b]
	Chloroform	**5a**	**5a**	**5a**	**5a**	**5a**	**5a**	**5a**	**5a**[a]

[a] Crystals suitable for crystallographic analysis were provided.
[b] Crystals were not obtained.