F_2xx/xxF_2 – Electronic Supplemental Information on 04/07/2016

Short C-H...F interactions involving the 2,5-difluorobenzene group: Understanding the role of fluorine in aggregation and complex C-F/C-H disorder in a 2×6 isomer grid.

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1. Detailed description of synthetic procedures

1.1. F_2 -xx series

To a clean, dry round-bottom flask containing 30 ml of CH_2Cl_2 and a magnetic stirring bar, 0.58 ml (5 mmol) of difluoroaniline was added. The flask was placed on an ice bath. Then, 0.58 ml (5 mmol) of benzoyl chloride was added into the reaction mixture followed by 0.4 ml (5 mmol) of triethylamine. The solution was removed from ice bath and left to stir overnight. The reaction mixture was transferred to 100 ml separating funnel and washed three times with an aqueous 2% w/v solution of KHCO₃. The organic layer was removed and a drying agent, anhydrous MgSO₄ was added. The solution was filtered and the solvent removed on a rotary evaporator. A white crystalline solid was recovered. The solid was removed from the round-bottom flask and placed in a plastic vial.

1.2. $xx-F_2$ series

Condensation reactions were performed with the aniline (0.455 ml, 5 mmol) dissolved in 30 ml of CH_2Cl_2 in a round-bottom flask placed on an ice bath and with subsequent stirring. Then, triethylamine (Et₃N) (0.7 ml, 5 mmol) was added to the flask. Finally, the fluorobenzoyl chlorides (0.6 ml, 5 mmol) were added directly into the solution mixture. Organic washing and work-up was as standard: the organic reaction phase was washed with 20 ml of KHCO₃ (0.1 M) solution *ca*. 3-4 times. Then, anhydrous MgSO₄ was added to the organic solutions for 20 minutes. The flask contents were filtered to remove MgSO₄. The filtrate was evaporated under vacuum and the product recovered.

1.3. Purity assessments and characterisation

The product purity was tested by thin-layer chromatography (TLC) using silica plate and a mixture of chloroform, ethyl acetate and *n*-hexane (2:1:4) as mobile phase. The product was weighed and the % yield was calculated. Finally, characterisation was carried out using a variety of physicochemical and spectroscopic techniques including melting point range analysis, IR (ATR, KBr disc), ¹H-NMR, ¹³C-NMR and ¹⁹F-NMR spectroscopy.

1.4. Experimental techniques (melting points, IR and NMR)

Melting point assessment was performed using a Stuart Scientific SMP40 automated melting point apparatus. IR spectroscopy (KBr discs) was performed on a Thermo Nicolet Avatar 320 FTIR. NMR spectroscopy was performed on a Bruker BioSpin UltraShield NMR spectrometer at 293±1 K, operating at 400 MHz for ¹H, 100.62 MHz for ¹³C and 376.46 MHz for the ¹⁹F resonances. The ¹H spectra were obtained in CDCl₃ and DMSO-*d*₆ and were performed using DMSO-*d*₆ for ¹³C and ¹⁹F. The NMR chemical shifts values (δ) are expressed in ppm and referenced to TMS (Cl₃FC for ¹⁹F NMR) and coupling constants (*J*) are quoted in Hz.

Fig. 1. Schematic diagram (simplified) of the F_2 -xx and xx- F_2 reactions.



Reaction scheme for the synthesis of N-(difluorophenyl)benzamides (F_2 -xx)

 $F \xrightarrow{0}_{F} CI \xrightarrow{H_2N}_{F} \xrightarrow{Et_3N}_{F} \xrightarrow{F} \xrightarrow{V}_{H} \xrightarrow{N}_{H}$

and

Reaction scheme for the synthesis of *N*-(phenyl)difluorobenzamides (**xx-F**₂)

2. ¹H NMR data and spectra

2.1 F2-23

¹H NMR (**CDCl**₃) δ 6.88 (1H, m), 7.06 (1H, m), 7.46 (2H, tt, ³*J*=7.5, ⁴*J*=1.3), 7.54 (1H, tt, ³*J*=7.28, ⁴*J*=1.5), 7.83 (2H, dt, ³*J*=7.0, ⁴*J*=1.5), 8.0 (1H, br s), 8.18 (1H, tt, ³*J*=7.8, ⁴*J*=1.58)



¹H NMR (**DMSO-***d*₆) δ 7.24 (1H, m), 7.33 (1H, m), 7.4 (1H, tt, ³*J*=7.3, ⁴*J*=1.5), 7.55 (2H, tt, ³*J* = 7.5, ⁴*J*=1.5), 7.63 (1H, tt, ³*J*=7.6, ⁴*J*=2), 7.98 (2H, dt, ³*J*=7.1, ⁴*J*=2), 10.35 (1H, br s)





¹H NMR (**DMSO**-*d*₆) δ 7.19 (1H, tq, ³*J*=8.6, ⁴*J*=1.4), 7.44 (1H, m), 7.6 (2H, tt, ³*J*=7.3, ⁴*J*=1.5), 7.67 (2H, tt, ³*J*=7.3, ⁴*J*=1.4), 8.03 (2H, dt, ³*J*=7.1, ⁴*J*=1.4), 10.22 (1H, br s)



2.3 F2-25

¹H NMR (**CDCl**₃) 6.7 (1H, tt, ${}^{3}J$ =8.5, ${}^{4}J$ =3.5), 7.01 (1H, ddd, ${}^{3}J$ =9.9, ${}^{4}J$ =4.8, ${}^{5}J$ =1.4), 7.45 (2H, tt, ${}^{3}J$ =7.3, ${}^{4}J$ =1.5), 7.52 (2H, tt, ${}^{3}J$ =7.3, ${}^{4}J$ =1.7), 7.82 (2H, dt, ${}^{3}J$ =7.8, ${}^{4}J$ =1.7), 8.04 (1H, br s), 8.28 (1H, td, ${}^{3}J$ =8.4, ${}^{4}J$ =3)





¹H NMR (**DMSO-***d*₆) δ 7.18 (1H, m), 7.43 (1H, td, ³*J*=9.5, ⁴*J*=5.2), 7.60 (2H, tt, ³*J*=7.3, ⁴*J*=1.5), 7.68 (2H, tt, ³*J*=7.3, ⁴*J*=1.5), 8.03 (2H, dt, ³*J*=7, ⁴*J*=1.5), 10.30 (1H, br s)

2.4 F2-26

¹H NMR (**CDCl**₃) δ 6.94 (2H, m), 7.17 (1H, m), 7.45 (2H, tt, ³*J*=7.3, ⁴*J*=1.5), 7.33 (1H, br s), 7.44 (2H, tt, ³*J*=7.3, ⁴*J*=1.5), 7.53 (1H, tt, ³*J*=7.3, ⁴*J*=1.7), 7.87 (2H, dt, ³*J*=7.0, ⁴*J*=1.4)



¹H NMR (**DMSO-***d*₆) δ 7.23 (2H, m), 7.42 (1H, m), 7.55 (2H, tt, ³*J*=7.3, ⁴*J*=1.5), 7.64 (1H, tt, ³*J*=7.3, ⁴*J*=1.7), 7.99 (2H, dt, ³*J*=7.0, ⁴*J*=1.3), 10.17 (1H, br s)



2.5 F2-34

¹H NMR (**CDCl**₃) δ 7.07 (1H, t, ³*J*=9), 7.13 (1H, m), 7.44 (2H, tt, ³*J*=7.3, ⁴*J*=1.5), 7.51 (1H, tt, ³*J*=7.3, ⁴*J*=1.7), 7.7 (1H, ddd, ³*J*=9.6, ⁴*J*=2.5, ⁵*J*=2.3), 7.78 (2H, d, ³*J*=1.53), 7.79 (1H, br s)



¹H NMR (**DMSO-***d*₆) δ 7.44 (1H, td, ³*J*=9.5, ⁴*J*=1.5), 7.55 (3H, tt, ³*J*=7.3, ⁴*J*=1.7), 7.62 (1H, tt, ³*J*=7.3, ⁴*J*=1.7), 7.94 (3H, dq, ³*J*=8.5, ⁴*J*=2), 10.47 (1H, br s)



2.6 F2-35

¹H NMR (**CDCl**₃) δ 6.54 (1H, tt, ³*J*=8.9, ⁴*J*=2.3), 7.22 (2H, dd, ³*J*=8.9, ⁴*J*=2.3), 7.44 (2H, tt, ³*J*=7.3, ⁴*J*=1.5), 7.52 (1H, tt, ³*J*=7.3, ⁴*J*=1.5), 7.79 (2H, dt, ³*J*=7.0, ⁴*J*=1.5), 7.83 (1H, d, ⁵*J*=1.1)



¹H NMR (**DMSO-***d*₆) δ 6.98 (1H, tt, ³*J*=9.4, ⁴*J*=2.4), 7.57 (4H, m), 7.63 (1H, tt, ³*J*=7.3, ⁴*J*=1.5), 7.94 (1H, dt, ³*J*=7.0, ⁴*J*=1.5), 10.60 (1H, br s)



2.7 23-F2

¹H NMR (**CDCl**₃) δ 7.12 (1H, tt, ³*J*=7.5, ⁴*J*=1.4), 7.32 (4H, m), 7.59 (2H, d, ³*J*=8.6), 7.84 (1H, m), 8.22 (1H, d, ³*J*=12.5);



¹H NMR (**DMSO-***d*₆) δ 7.13 (1H, t, ³*J*=7.5), 7.36 (1H, br s), 7.48 (1H, br s), 7.70 (3H, m), 10.55 (1H, br s)



2.8 24-F2

¹H NMR (**CDCl**₃) δ 6.88 (1H, m), 6.99 (1H, td, ³*J*=8.2, ⁴*J*=2), 7.11 (1H, tt, ³*J*=7.4, ⁴*J*=1.3), 7.32 (2H, tt, ³*J*= 8.0, ⁴*J*=3.0), 7.58 (2H, dt, ³*J*=7.5, ⁴*J*=1.3), 8.16 (1H, ddd, ³*J*=17.5, ⁴*J*=7.8, ⁵*J*=2.3), 8.28 (1H, d, ³*J*=14.1)





2.9 25-F2

¹H NMR (**CDCl**₃) δ 7.20 (3H, m), 7.41 (2H, tt, ³*J*=8.0, ⁴*J*=2.0), 7.67 (2H, dt, ³*J*=7.5, ⁴*J*=1.3), 7.89 (1H, m), 8.48 (1H, d, ³*J*=14.8)





¹H NMR (**DMSO-***d*₆): δ 7.13 (1H, tt, ³*J*=7.3, ⁴*J*=1.2), 7.37 (2H, tt, ³*J*=7.6, ⁴*J*=1.7), δ 7.44 (2H, m), 7.71 (2H, dt, ³*J*=7.6, ⁴*J*=1.4), δ

2.10 26-F2







2.11 34-F2

¹H NMR (**CDCl**₃) δ 7.12 (1H, tt, ³*J*=7.4, ⁴*J*=1.6), 7.22 (1H, d, ³*J*=8.7), 7.32 (2H, tt, ³*J*=8.0, ⁴*J*=2.0), 7.54 (3H, d, ³*J*=7.5), 7.63 (1H, br s), 7.68 (1H, td, ³*J*=8.8, ⁴*J*=2.5)



¹H NMR (**DMSO-***d*₆) δ 7.12 (1H, tt, ³*J*=7.4, ⁴*J*=1.1), 7.37 (2H, tt, ³*J*=7.9, ⁴*J*=2.0), 7.64 (1H, dd, ³*J*=9, ⁴*J*=2.2), 7.75 (2H, dt, ³*J*=7.6, ⁴*J*=1.5), 7.87 (1H, m), 8.04 (1H, tdd, ³*J*=9.7, ⁴*J*=4.0, ⁵*J*=2.0), 10.33 (1H, br s).



2.12 <u>35-F2</u>

¹H NMR (CDCl₃) δ 6.85, 6.97, 7.09, 7.30, 7.57, 8.12, 8.29 (see below in Figure).

(DMSO-*d*₆) δ 10.37(s, 1H), 7.76(d, *J*=3.60, 2H) 7.69(d, *J*=3.05, 2H) 7.54(t, *J*=8.87, 1H), 7.38(*J*=8.04, 2H), 7.14(t, *J*=7.21H, 1H).



¹⁹C NMR data and spectra (DMSO-d₆)

2.13 F2-23

δ 114.01, 118.88, 122.25, 124.03, 127.83, 128.49, 132.02, 133.62, 148.95, 151.45, 165.40;



2.14 F2-24

 δ 104.36, 111.20, 122.19, 127.74, 128.46, 131.83, 133.62, 154.93, 158.46, 160.87 165.41;



2.15 F2-25

 δ 112.97, 116.75, 127.84, 128.46, 132.03, 133.59, 150.42, 152.80, 156.36, 158.73, 165.53;



2.16 F2-26

δ 111.88, 114.69, 127.82, 128.61, 132.11,133.06, 156.88, 159.37, 165.40;



2.17 F2-34

δ 109.22, 116.49, 117.38, 127.66, 128.44, 131.77, 133.72, 134.37, 136.21, 165.71;



2.18 F2-35

δ 108.98, 109.41, 116.61, 117.45, 127.64, 128.45, 131.86, 134.48, 165.72;



F2_35_CNMR_DMSO



3 ¹⁹F NMR data and spectra (DMSO-d₆)



δ-144.83, -138.52





3.3 F2-25

δ-126.71, -117.89

F2_25_FNMR_DMSO







3.5 F2-34

δ -144.40, -137.37



3.6 F2-35



3.7 23-F2 δ -138.11, -140.69



3.8 24-F2

δ -109.91, -106.28



3.9 25-F2

δ -120.37, -118.08









δ -108.82

IR (ATR)

3.13 F2-23

IR (ATR): **3253** (m), 3133 (w), 3077 (w), 3040 (w), 2921 (w), 1758 (m), 1725 (w), **1657** (s), 1621 (m), 1601 (m), 1581 (m), 1523 (m), 1498 (s), 1464 (s), 1447 (m), 1312 (m), 1302 (m), 1284 (m), 1272 (m), 1247 (m), 1221 (m)



3.14 F2-24 IR (ATR): **3293** (m), 3070 (w), **1649** (s), 1611 (m), 1601 (m), 1580 (m), 1526 (s), 1503 (s), 1489 (s), 1457 (m), 1448 (m), 1429 (s), 1329 (m), 1292 (m), 1257 (s) 1205 (s)







3.16 F2-26

IR (ATR): **3258** (m), 3067 (w), **1670** (m), **1659** (s), 1623 (m), 1601 (m), 1582 (m), 1520 (s), 1502 (s), 1490 (m), 1461 (s), 1309 (s), 1286 (m), 1271 (m), 1242 (s)







3.18 F2-35

IR (ATR): **3323** (m), 3128 (w), 3093 (w), **1656** (s), 1626 (m), 1606 (s), 1580 (m), 1534 (s), 1494 (m), 1477 (m), 1452 (m), 1433 (s), 1407 (m), 1308 (m), 1275 (m), 1213 (w)



3.19 23-F2 Infra-red spectral details (a summary of the xx-F₂ spectra in cm⁻¹)

IR (KBr disc): 3340 (m), 2925 (w), 1655 (s), 1599 (m), 1538 (s), 1479 (s), 1444 (m), 1325 (w), 1272 (w).

3.20 24-F2

IR (KBr disc): 3385 (w), 2925(w), 2360 (w), 1663 (m), 1560 (m), 1542 (m), 1496 (m), 1444 (m), 1325 (w), 1272 (w).

3.21 25-F2

IR (KBr disc): 3378 (m), 2924 (w), 1657 (s), 1600 (m), 1589 (m), 1541 (s), 1490 (s), 1446 (s), 1420 (w), 1322 (m), 1268 (m).

3.22 26-F2

IR (KBr disc): 3314 (m), 2925 (m), 1649 (m), 1595 (m), 1535 (m), 1444 (m), 1314 (m), 1243 (w).

3.23 34-F2

IR (KBr disc): 3361 (w), 2924 (w), 1656 (s), 1597 (m), 1533 (m), 1514 (s), 1444 (s), 1328 (m), 1290 (m).

3.24 35-F2

IR (KBr disk): 3334 (w), 2908 (m), 1655 (s), 1598 (s), 1528 (s), 1489 (s), 1438 (s), 1329 (s), 1114 (s).

5. Molecular and Crystal structure data.

The primary intermolecular feature for the six F_2 -xx and six xx- F_2 structures (xx = 2,3-; 2,4-; 2,5-; 2,6-; 3,4- and 3,5difluoro substituted, either on the acyl C₆CO labelled as xx- F_2 or amino benzene HNC₆ aromatic rings as F_2 -xx) is the N-H...O=C intermolecular interaction (in the absence of any other strong donor or acceptor atom/group). This contrasts with our NxxF¹⁴ and Fxx¹⁶ isomer grids (x = *para-*, *meta-*, or *ortho*-substituted) where aggregation can be either *via* intermolecular N-H...O=C or intermolecular/intramolecular N-H...N interactions or even both. Of the twelve F_2 -xx/xx- F_2 structures, nine crystallize without disorder as the F_2 -23, F_2 -26, F_2 -34, F_2 -35 and 23- F_2 , 24- F_2 , 26- F_2 , 34- F_2 structures whereas F_2 -24, 25- F_2 and 35- F_2 have extensive disorder and often with associated twinning. The series was analysed for comparisons with related di-fluorinated pyridine aromatics published by us in 2008 and 2009.^{24,25}

4.1 The F_2 -xx series of F_2 -23, F_2 -24, F_2 -25, F_2 -26, F_2 -34 and F_2 -35

The six \mathbf{F}_2 -xx compounds crystallise from halogenated solvents and aggregate *via* typical amide...amide interactions as N-H...O=C *C*(4) chains but with different secondary interactions and often involving the F atoms and aromatic rings. The six \mathbf{F}_2 -xx compounds were re-crystallised from CH₂Cl₂ or CHCl₃. Data were collected at 294(1) K to greater than 99% completion to a 26° minimum on θ for most of the structures. Only \mathbf{F}_2 -24 is disordered.

A CSD search shows that the six $F_2C_6H_3$ -NHC=O moieties are relatively rare from a structural viewpoint when compared to molecules incorporating the monofluorobenzene and pentafluorobenzene groups.^{1,2} This is not unusual as the di-fluorobenzene group is relatively rarely utilised and has not been studied in structural chemistry to any great extent (apart from the 2,6-difluorophenyl group). The current group of six *N*-(difluorophenyl)benzamides will augment our knowledge and by being able to make comparisons between a group of twelve isomers and the related monofluorophenyl substituted $C_{13}H_9N_1O_1F_2$ isomers of CIYXAK(01), JAVWIN(01), and QITTIX, QITTOD, QITTUJ, QITVAR reported by Chopra and Row (in 2008).¹⁰ See the F_2 -24 structure below for close comparisons between it and JAYWIN01 in *P*₂₁ (also F_2 -25). Recently in 2016, Mondal and Chopra have reported additional fluorinated benzamides (while this full paper was being prepared for submission) and are compared in the manuscript text.²³ All three disordered crystal structures are discussed in detail below (supplementing the main paper text).

4.1.1 F₂**-24** *crystal and molecular structure* - *Complete molecular disorder*:

 F_{2} -24 is a completely disordered structure (full molecular disorder but without twinning in the crystal structure) that merits discussion because of the nature of the disorder and how the disorder was analysed. F_{2} -24 crystallises in space group *Pn* (No. 7) with *Z* = 1 and withdata obtained from a colourless needle-like crystal. The structure solves without difficulty in *Pn* (but not in *P2/n*) to *R* = 6.5% with no refined disorder sites/components but with a relatively high residual electron density maxima/minima of +0.38/-0.19 e. Å⁻³. The presence of the top 5/6 sites in the difference electron density maps indicates both F atom and amide group disorder.¹² Treatment of the F_{2} -24 disorder and refinement of the 6 minor sites with partial occupancy and isotropic displacement parameters drops the *R*-factor from 6.5%→3.7% with residual electron density maxima/minima of +0.13/-0.11 e. Å⁻³. Final refinement gives an *R*-factor of 3.5% with components having anisotropic displacement parameters, but 'tight' restraints and final residual electron density of +0.09/-0.10 e. Å⁻³. The type of disorder in benzamides is well-known as reported by Guru-Row.¹²

The disorder process is such that F_{2} -24 is fully rotated with the major orientation present with a site occupancy factor of 0.88 and a minor component [site occupancy factor of 0.12] related by rotation about a non-crystallographic two-fold axis which lies in the [010] direction. The disorder results in two minor occupancy F atom sites present at sites close to the H14 (C14) and H16 (C16) hydrogen atoms. A secondary disorder process is also noted such that the *ortho*-F22 atom adopts another conformation after a 180° rotation about the N1-C21 bond with a minor occupancy F atom site as F26B (close to H26). This type of disorder is not uncommon in 2,4-difluorobenzene derivatives. Therefore, three minor F atom sites (as F14B, F16B, F26B) in tandem with the minor sites for the amide O=C-N group constitute a three component disordering process BUT with no detectable minor sites near C12-H12 (no rotation about C1-C11). The disorder process means that the F22 and F24 site occupancies must differ as the site occupancy for F24 = site occupancy factor F22+F26B. However, the F14B and F16B occupancies are identical and refine to, then fixed at 0.12.

The three F atom minor sites are easily treated in refinement. Both C_6 aromatic rings have slightly larger displacement parameters and these twelve C atoms (refined with 100% occupancy) have U_{iso} from 0.0531(12) to 0.0803(14) Å² which is reasonable for a294 K dataset. There is no electron density of consequence remaining in the final refinement cycles and the two C_6 aromatic rings have a good fit despite the disorder but being slightly offset and both C_6 rings were refined with 100% site occupancy. The three atom O=C-N amide group gave problems as the minor sites refine to 12% (occupancy) and are positioned at reasonable positions/locations close to the major conformation (0.88). However, realistically, there should be at least 6 minor sites for the two minor OCN orientations and some of these overlap with the three 'modelled' sites as well as the major orientation. It is not really practical to rigidly restrain the amide groups of the two minor conformations and in fact both C1B and N1B should contain minor sites of N and C which are superimposed, respectively. In the final refinement cycles only six minor atom sites, 3 F and the three atom alternate O=C-N were used to produce a structure where a disorder model is understood. The principal intermolecular hydrogen bonding interaction is the N-H...O=C hydrogen bond as C(4) chains along the (010) direction. Of further note is that there is only one other significant intermolecular interaction in the crystal structure involving C25-H25...F2^{*iv*} with iv = x-1, 1+y, z (with the symmetry code from **Table S4.2**, pages 59-60). There are F...F contacts involving low site occupancy F atoms and some C-H...F contacts involving the minor F atom sites at F16B and F26B (2.17, 2.47 Å as measured from refinement) but as these are low occupancy (12%) the structure can more than cope with these apparent steric contacts. Given that the sites are rather poorly determined it is probable that the actual distances are slightly longer. For a structure with short C-H...F interactions, see the **EMIBOS** structure which has a plethora of C-H...F interactions.¹ In **F**₂-24, the N1-H1 distance is constrained to be 0.86 Å and was assigned 100% occupancy for convenience.

CSD code EMIBOS: A.G. Dikundwar, Ch. Venkateswarlu, R.O. Piltz, S. Chandrasekaran and T.N. Guru Row, CrystEngComm, 2011, 13, 1531.

4.2 The xx-F₂ series of 23-F₂, 24-F₂, 25-F₂, 26-F₂, 34-F₂ and 35-F₂

The six $xx-F_2$ compounds crystallise (from *n*-hexane) and aggregate principally *via* the typical amide...amide interaction as N-H...O=C *via* C(4) chains but with different secondary interactions and often involving the F atoms. Data were collected at 294(1) K to greater than 99% completion and a 26° minimum on θ and for structures F_2 -26 and F_2 -34 to higher angles and with a 28° minimum.

4.2.1 25-F₂ crystal and molecular structure: *Refinement of a twinned structure*:

25-F₂ crystallizes in space group Pc (No. 7) with a dataset from a spear-like crystal shard having redundancy of 3.3, average $F^2 = 11.5$ and R_{int} value = 0.064 [original 10-017 dataset]. There is considerable disorder in the **25-F₂** crystal structure (Z'=2). The crystal structure was originally refined with $\beta = 90^{\circ}$ in an orthorhombic system setting and based on the indicated unit cell solution. The structure gives a poor quality solution in space group $Pca2_1$ and refines to R = 9% with no electron density > 0.3e.Å⁻³ remaining in the difference maps. A solution obtained in $P2_1$ refines to 8% (with a twin parameter incorporated, but before a disorder model is used) but with several atoms having non-positive definite anisotropic displacement parameters in FMLS refinement. The mean $|E^2-1| = 0.689_{rest}$ and a majority (>65%) of the most disagreeable reflections have $F_0 > F_c$.

A second crystal was examined [original 10-020 dataset] and this showed that the crystal system was probably monoclinic with the β angle close to 90° and twinned by *pseudomerohedry*. The systematic absences indicated $P_{2_1/c}$ but strategies to obtain a solution did not yield a plausible structure. Examination in $P_{2/c}$ and P_c yielded a solution in space group P_c but not in $P_{2/c}$. The 10-017 refinement with appropriate twin law of (100, 0-10, 00-1) demonstrates the P_c solution with the *R*-factor dropping to 7.1% (with all atoms anisotropic but with one molecule having non-H atoms with larger displacement parameters). Examination of the [10-020] dataset provided the following:

The refinement steps and treatment of the disorder/twinning problem in 25-F₂ [10-020 example]:

- a) All non-H atoms isotropic for molecules A and B gives R = 20% in space group Pc.
- b) With all H atoms in and the F/O/N atoms anisotropic, R = 16%.
- c) All non-H atoms anisotropic, R = 15%.
- d) A disorder model with 7 non-H atoms included gives R = 14%.
- e) A full disorder model with 90:10 for molecules A/C and 75:25 for molecules B/D gives R = 12%.
- f) Modified disorder for molecule A = 100% and molecules B/D at 50:50% occupancy gives R = 11%.
- e) Application of TWIN law $(1 \ 0 \ 0, \ 0 \ -1)$ and BASF = 0.5 gives R = 5%.
- g) All H atoms in for the alternative D component and with DFIX off gives R = 4.5%.
- *h*) Use of EXTI = 0.025 gives a final *R*-factor = 4.3% (SHELXL97 refinement).

The refinement provides a solution with one molecule A (not disordered) and one molecule as two components B/D with site occupancy factors 0.60:0.40. This was treated such that the 2,5-difluorobenzamide or $2,5-C_6H_3F_2CONH$ group is rotated by 180° about the C21_B-N21_{B/D} axis (to relate orientations B \leftrightarrow D) with site occupancy factors of 0.60:0.40 [the refinement gives 0.60(1):0.40(1)]. A subsequent test refinement using 50:50 B/D site occupancy raises the *R* factor from 0.045 to 0.048 in SHELXL97 and with a substantial increase in the WGHT card value. Of further note is that the [10-020] crystal structure proceeds with molecules B/D refining to 50:50 occupancy. Therefore, we surmise it is possible that over the entire crystal sample there is a variable twinning per sample.

As for the 23-/24- F_2 structures, the N1_{A/B/D}-H1_{A/B/D}...F12_{A/B/D} intramolecular interaction is also present in 25- F_2 . The primary intermolecular hydrogen bonding comprises the N-H...O=C chains in both A and B/D molecules along the *a*-axis or (100) direction. For the B/D chain the ordering is 60% in one direction and 40% in the opposite direction. Chains are linked by **strong short directional** C-H...F intermolecular interactions as C16A...F12A and C16A-H16A...F12A [parallel with the (102) plane] as similar though slightly longer than F_2 -25. For the A molecules the combination of N-H...O=C chains and C-H...F interactions is to link the chains into a stacked column *ca*. 12.4 Å wide

or half the unit cell *b* dimension. The aggregation process is similar for the disordered B/D molecules but the two A and B/D columns are weakly linked by long C-H...F interactions involving $F15_{A/B/D}$ along the *b*-axis direction. The structural twinning/disorder almost certainly stems for the crystallization of alternating columns whereby the second stack can adopt two distinct energetically favourable orientations (B/D) and within the same volume element for one molecule without deformation of the crystal structure. The effect of rotational disorder gives the *appearance* of a tetra-F substituted 2,3,5,6-aromatic ring. Refinement was finalised using SHELXL14/7.

4.2.2 35-F₂ *crystal and molecular structure - A second polymorph*

35-F₂ crystallizes in space group Pn (No. 7) and needed considerable crystal structure analysis. Initial cell reduction trials indicated the possibility of an orthorhombic setting with the software opting for this. However, a trial unit cell of 5.12, 44.27, 9.47 Å, 90.00, 90.01, <u>90.35</u>° (Z=2) demonstrates an angle deviating considerably from 90°..! Further investigation of other possible settings yielded a plausible monoclinic reduced cell of 5.11, 9.46, 22.23 Å, 90, 96.28, 90° and two space groups, *P2/n* and *Pn* (No. 7). The systematic absences and $|E^2-1|$ values indicated the possibility of space group *P2/n* (but with no plausible solution), a result was obtained in space group *Pn*.

The monoclinic dataset has redundancy of 1.8, an average $F^2 = 11$ and R_{int} value of 0.023 (*Pn* data originally merged in refinement). The structure solves in *Pn* (*Z*=2) but with complete molecular disorder for both molecules A and B. The final refinement gave sites that refined to and subsequently were fixed with site occupancy factors of 0.78:0.22 (for A/C) and 0.85:0.15 (for B/D) components; unusually no twinning was observed. The minor components (C, D) were treated with common isotropic displacement parameters for the C₆ rings, aromatic rings as rigid hexagons and with the minor F/N/O atom sites having restrained anisotropic displacement parameters.

The final *R*-factors are 0.036 (0.093 all) with no shift/esd's > 0.001 and with no non-positive definite displacement parameters. Apart from the fixed site occupancy factors there were no constraints/restraints imposed on the major sites A and C. The disorder mechanism and disposition towards disorder may stem from molecular symmetry with the angle between the aromatic rings in the major sites of molecules of A and B with their respective amide residues being nearly 30°: the aromatic rings are almost co-planar and within 3°. The combined effect of the $3,5-C_6H_3F_2$ ring being symmetrical combined with the geometric orientation of the aromatic rings with respect to the amides facilitates two orientations of the molecule A (as A and a minor component C). The amide residue is such that the O=C-NH is rotated so that there is an approximate fit with HN-C=O.

For comparisons with **35-F**₂ are the related molecular and crystal structures of **QITSIW/QITSIW01** [3-Fluoro-*N*-phenylbenzamide]¹⁰ and **CIYXAK/CIYXAK01** [3-Fluoro-*N*-(3-fluorophenyl)benzamide]³⁵ which differ by one less F on the same ring (former) and a H/F and a F/H swop (latter) as reported by Chopra and Row.^{10,35} In **QITSIW/QITSIW01**¹⁰ the molecular disorder manifests by complete rotation of the molecule (by a 2-fold molecular rotation/180°) so that one phenyl ring is rotated onto the second and *vice-versa*; the entire molecule is disordered but with a reasonable atomic fit that is only seen in the F atoms and amide group. In **CIYXAK/CIYXAK01**³⁵ which exists as polymorphs in *P2*₁ and *C2/c* there is complete molecular disorder involving two complete molecular flips though with different site occupancies. The reason for the disorder remains unclear but derives from the inherent molecular symmetry, reasonable fit on molecular flipping and the interchangeability of the H/F atoms.

Note in addition (4th February 2016):

In the compilation of this full paper for submission we became aware of the recent 2016 January publication by Mondal and Chopra (*CrystEngComm*, 2016, 48-53).²³ In the Mondal and Chopra (M&C) paper, eight (at 150 K) of the twelve crystal structures are very briefly mentioned that we have reported on and analysed at 294 K. Therefore, in our analysis, only important features and substantial differences are commented on. Of further interest, the fifteen M&C crystal structures exhibit no disorder and all crystal structures have $Z^2=1$.²³ We note that **P0034** and **P3400** pair are isomorphous in P-1 (No.2) and that the **P2324** and **P2423** are *essentially* isomorphous in $P2_1/n$ (*ca.* 100 K).²³

CCDC (M&C, 2016) crystal structure data:

https://summary.ccdc.cam.ac.uk/structure-summary?pid=ccdc:1407974-1407988&eissn=1466-8033&year=2016&pages=48-53&volume=18&id=doi:10.1039/c5ce01721a&sid=RSC

The **35-F**₂ disordered structure in *Pn* (294 K) (details above) or the ordered **P0035** in *P-1* (150 K) structures (using the M&C terminology) crystallise in two different space groups and can be regarded as polymorphs. The crystal structures are substantially different and the crystals were grown from different solvents. The melting point range is 137.8-139.7°C (for **35-F**₂) in space group *Pn* (No. 7) and is 140.9°C (for **P0034**)²³ in P-1 (No. 2).

While there is overlap in terms of the compounds studied though at different temperatures, there is great potential to engage in a thorough and systematic study of this and related series of benzamide/benzanilide compounds and structures in series of isomer and related (congener) grids.¹²⁻¹⁶, ²³⁻²⁵

Table S4.1. Experimental details

For all twelve crystal structures: $C_{13}H_9F_2NO$, $M_r = 233.21$. Experiments were carried out at 294 K with Mo $K\alpha$ radiation using an Oxford Diffraction Xcalibur, Sapphire3, Gemini Ultra diffractometer.

	F ₂ -23	23-F ₂	F ₂ -24	24-F ₂			
	(from CH ₂ Cl ₂)	(from <i>n</i> -hexane)	(from CH ₂ Cl ₂)	(from <i>n</i> -hexane)			
Crystal data							
Crystal system,	Monoclinic,	Monoclinic,	Monoclinic,	Monoclinic,			
space group	Рс	Pc	Pn	$P2_{1}/n$			
<i>a</i> , <i>b</i> , <i>c</i> (Å)	4.9955 (1),	5.2115 (2),	5.5268 (3),	5.4250 (2),			
	17.1031 (4),	6.4193 (3),	4.9905 (2),	7.7256 (3),			
	13.0176 (3)	16.1911 (7)	19.7058 (11)	25.4216 (8)			
α, β, γ (°)	90, 100.380(2), 90	90, 97.894(4), 90	90, 90.665(5), 90	90, 92.708(3), 90			
$V(Å^3)$	1094.00(4)	536.53(4)	543.48(5)	1064.26(7)			
Ζ	4	2	2	4			
μ (mm ⁻¹)	0.11	0.12	0.11	0.12			
Crystal size (mm)	$0.63 \times 0.17 \times 0.05$	$0.36 \times 0.23 \times 0.13$	$0.50 \times 0.07 \times 0.04$	$0.19 \times 0.11 \times 0.06$			
Data collection							
Absorption correction	Analytical (ABSFAC, Clark & Reid, 1998)	Multi-scan (ABSPACK)	Analytical (ABSFAC, Clark & Reid, 1998)	Analytical (ABSFAC, Clark & Reid, 1998)			
T_{\min}, T_{\max}	0.878, 0.974	0.73, 1.00	0.971, 0.996	0.984, 0.993			
No. of measured, independent & observed $[I > 2\sigma(I)]$ reflections	9209, 3670, 2456	3561, 1810, 1466	6736, 2370, 1051	7313, 2297, 1038			
R _{int}	0.024	0.022	0.053	0.061			
$(\sin \theta / \lambda)_{max} (\text{\AA}^{-1})$	0.654	0.646	0.652	0.640			
Refinement							
$R[F^2 > 2\sigma(F^2)],$ wR(F ²), S	0.044, 0.099, 0.99	0.039, 0.106, 1.03	0.035, 0.051, 0.77	0.048, 0.094, 0.84			
No. of reflections	3670	1810	2370	2297			
No. of parameters	315	158	209	159			
No. of restraints	2	2	53	0			
H-atom treatment	H atoms treated by independent and constrained refinement						
$\Delta \rangle_{\text{max}}, \Delta \rangle_{\text{min}} (e \text{ Å}^{-3})$	0.25, -0.12	0.15, -0.12	0.08, -0.09	0.30, -0.22			
Absolute structure, (parameter)	Flack x from 642 quotients, 0.2(4)	Flack x from 445 quotients, 0.4(7)	Flack x from 394 quotients, 0.9(7)	_			

Four structures with the 2,3- and 2,4-difluorobenzene substitution patterns:

Γ	1	1	I	
	F ₂ -25	25-F ₂	F ₂ -26	26-F ₂
	(from CHCl ₃)	(from <i>n</i> -hexane)	(from CHCl ₃)	(from <i>n</i> -hexane)
Crystal data				
Crystal system,	Orthorhombic,	Monoclinic,	Monoclinic,	Orthorhombic,
space group	$Pca2_1$	Рс	$P2_{1}/n$	$Pna2_1$
<i>a</i> , <i>b</i> , <i>c</i> (Å)	24.4897 (16),	5.1850 (8),	11.0951 (3),	10.1031 (18),
	5.0316 (3),	24.767 (4),	12.1037 (3),	21.838 (3),
	8.6187 (6)	8.3089 (19)	16.9753 (3)	4.8875 (6)
α, β, γ (°)	90, 90, 90	90, 90.206(17), 90	90, 94.195(2), 90	90, 90, 90
$V(Å^3)$	1062.02(12)	1067.0(3)	2273.54(9)	1078.3(3)
Ζ	4	4	8	4
μ (mm ⁻¹)	0.12	0.12	0.11	0.12
Crystal size (mm)	$0.37 \times 0.19 \times 0.12$	$0.30 \times 0.20 \times 0.10$	$0.56 \times 0.33 \times 0.28$	$0.53 \times 0.09 \times 0.05$
Data collection				
Absorption correction	Analytical (ABSFAC, Clark & Reid, 1998)	Multi-scan (ABSPACK)	Analytical (ABSFAC, Clark & Reid, 1998)	Multi-scan (ABSPACK)
T_{\min}, T_{\max}	0.963, 0.987	0.89, 1.00	0.954, 0.974	0.919, 1.00
No. of measured, independent & observed $[I > 2\sigma(I)]$ reflections	5645, 2078, 1819	7448, 3629, 1816	21895, 6011, 3551	7275, 1980, 1187
R _{int}	0.045	0.069	0.025	0.044
$(\sin \theta / \lambda)_{max} (\text{\AA}^{-1})$	0.638	0.643	0.694	0.649
Refinement	•			•
$R[F^2 > 2\sigma(F^2)], wR(F^2), S$	0.059, 0.168, 1.07	0.046, 0.098, 0.82	0.063, 0.173, 1.03	0.034, 0.067, 0.85
No. of reflections	2078	3629	6011	1980
No. of parameters	158	384	315	158
No. of restraints	1	140	0	1
H-atom treatment	H atoms treated by independent and constrained refinement	H-atom parameters constrained	H atoms treated by independent and constrained refinement	H atoms treated by independent and constrained refinement
$\Delta \rangle_{\rm max}, \Delta \rangle_{\rm min} ({\rm e} ~ {\rm \AA}^{-3})$	0.24, -0.24	0.16, -0.18	0.22, -0.27	0.11, -0.11
Absolute structure, (parameter)	Flack x from 635 quotients, 1.7(10)	Flack x from 487 quotients, -2.8(10)	_	Flack x from 298 quotients, -0.8(8)

Four structures with the 2,5- and 2,6-difluorobenzene substitution patterns:

	F ₂ -34	34-F ₂	F ₂ -35	35-F ₂		
	(from CHCl ₃)	(from <i>n</i> -hexane)	(from CHCl ₃)	(from <i>n</i> -hexane)		
Crystal data						
Crystal system,	Triclinic,	Triclinic,	Monoclinic,	Monoclinic,		
space group	<i>P</i> ⁻ 1	<i>P</i> ⁻ 1	$P2_{1}/n$	Pn		
<i>a</i> , <i>b</i> , <i>c</i> (Å)	5.4841 (3),	5.4519 (2),	10.3601 (2),	5.1095 (1),		
	7.8068 (6),	7.7415 (5),	5.1575 (1),	9.4583 (4),		
	12.6875 (5)	12.9335 (7)	20.2429 (4)	22.2306 (8)		
α, β, γ (°)	106.756(5),	106.965(5),	90, 103.012(2), 90	90, 96.284(3), 90		
	98.878(4),	100.535(4),				
	90.151(5)	90.213(4)				
$V(Å^3)$	513.26(5)	512.37(5)	1053.85(4)	1067.89(6)		
Ζ	2	2	4	4		
μ (mm ⁻¹)	0.12	0.12	0.12	0.12		
Crystal size (mm)	$0.38 \times 0.25 \times 0.22$	$0.35 \times 0.21 \times 0.06$	$0.60 \times 0.23 \times 0.17$	$0.61 \times 0.06 \times 0.05$		
Data collection						
Absorption correction	Analytical	Analytical	Analytical	Analytical		
	(ABSFAC, Clark	(ABSFAC, Clark	(ABSFAC, Clark	(ABSFAC, Clark		
	& Reid, 1998)	& Reid, 1998)	& Reid, 1998)	& Reid, 1998)		
T_{\min}, T_{\max}	0.963, 0.980	0.986, 0.997	0.952, 0.982	0.963, 0.995		
No. of measured,	4632, 2666, 2320	7552, 2183, 1781	6778, 2266, 1996	6521, 3400, 1894		
independent & observed $U > 2\sigma(D)$ reflections						
D	0.010	0.017	0.015	0.032		
Λ_{int}	0.010	0.017	0.015	0.032		
$(\sin \theta/\lambda)_{\max} (A^{-1})$	0.693	0.641	0.639	0.637		
Refinement	,	1	1	1		
$R[F^2 > 2\sigma(F^2)], wR(F^2), S$	0.041, 0.117, 1.04	0.033, 0.098, 1.06	0.034, 0.090, 1.04	0.036, 0.093, 0.86		
No. of reflections	2666	2183	2266	3400		
No. of parameters	158	159	159	411		
No. of restraints	0	0	0	70		
H-atom treatment	H atoms treated by	H atoms treated by	H atoms treated by	H-atom parameters		
	independent and	independent and	independent and	constrained		
	constrained	constrained	constrained			
$\Lambda \rightarrow \Lambda \rightarrow (e Å^{-3})$	0.31 -0.18	0.24 -0.16	0.22 -0.15	0 11 -0 13		
Δ/\max , $\Delta/\min(e^{2x})$	0.01, 0.10	0.21, 0.10	0.22, 0.12	Γ_{122} = from 401		
(parameter)	_	_	_	quotients, $2.2(10)$		

Computer programs: *CrysAlis PRO*, Agilent Technologies, Version 1.171.34.49 (release 20-01-2011 CrysAlis171 .NET) (compiled Jan 20 2011, 15:58:25), *SHELXS14*/7 (Sheldrick, 2014), *SHELXS14*/6 (Sheldrick, 2014), *SHELXL97* and *SHELXL14*/7 (Sheldrick, 2008) & SORTX (McArdle, 1995), *PLATON* 2015 version (Spek, 2009).

D—H···A	<i>D</i> —H (Å)	$H \cdots A(Å)$	$D \cdots A$ (Å)	D—H···A (°)		
F ₂ -23						
N1A—H1A····O1A ⁱ	0.81 (5)	2.15 (5)	2.914 (4)	158 (4)		
N1B—H1B····O1B ⁱ	0.79 (5)	2.18 (5)	2.920 (4)	157 (4)		
C14B—H14B…F22B ^{<i>ii</i>}	0.93	2.52	3.160 (5)	126		
23-F ₂		·		·		
N1—H1···O1 ^{i}	1.00 (4)	2.13 (4)	3.071 (3)	157 (3)		
N1—H1…F12	1.00 (4)	2.27 (4)	2.823 (4)	114 (3)		
С22—Н22…О1	0.93	2.40	2.875 (4)	112		
F ₂ -24		·		·		
N1—H1…O1 ⁱⁱⁱ	0.86	2.14	2.948 (5)	157		
С26—Н26…О1	0.93	2.40	2.854 (5)	110		
C25—H25···F22 ^{<i>iv</i>}	0.93	2.47	3.393 (5)	175		
24-F ₂						
N1—H1…O1 ^v	0.79 (2)	2.58 (2)	3.281 (3)	148 (2)		
N1—H1…F12	0.79 (2)	2.16 (2)	2.740 (2)	131 (2)		
С22—Н22…О1	0.93	2.33	2.873 (3)	117		
F ₂ -25						
N1—H1···O1 ⁱⁱⁱ	0.93 (6)	2.17 (6)	3.010 (4)	151 (6)		
С26—Н26…О1	0.93	2.41	2.893 (5)	112		
C26—H26···F22 ^{vi}	0.93	2.28	3.153 (5)	156		
25-F ₂						
N1A—H1A…O1A ⁱ	0.86	2.40	3.170 (9)	149		
N1A—H1A…F12A	0.86	2.14	2.729 (8)	125		
N1B—H1B…F12B	0.86	2.24	2.785 (19)	121		
N1D—H1D…F12D	0.86	2.37	2.83 (4)	114		
F ₂ -26						
N1A—H1A…O1B	0.89 (2)	2.00 (2)	2.864 (2)	164.2 (19)		
N1B—H1B····O1A ^{vii}	0.84 (2)	2.12 (2)	2.870 (2)	148 (2)		
C24B—H24B⋯F22A ^{viii}	0.93	2.49	3.361 (4)	157		
C25B—H25B····F26A ^{ix}	0.93	2.57	3.382 (4)	147		
26-F ₂						
N1—H1···O1 x	0.93 (3)	1.99 (3)	2.878 (2)	160 (2)		
N1—H1…F16	0.93 (3)	2.44 (2)	2.818 (3)	104.6 (18)		
C15—H15···F12 xi	0.93	2.47	3.279 (3)	145		
C15—H15…O1 ^{xi}	0.93	2.68	3.500 (3)	148		

 Table S4.2. Selected hydrogen-bond parameters for the twelve isomers

F_2xx/xxF_2 –	- Electronic	Supplemental	Information	on 04/07/2016
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0.93	2.52	2.960 (4)	109			
0.843 (16)	2.483 (17)	3.2582 (14)	153.3 (14)			
0.93	2.56	3.2489 (15)	131.3			
0.93	2.42	2.8939 (15)	111.9			
0.824 (17)	2.493 (17)	3.2594 (15)	155.3 (15)			
0.93	2.42	2.9182 (16)	114			
0.843 (16)	2.225 (16)	3.0069 (13)	154.5 (14)			
0.93	2.36	2.8598 (15)	113			
35-F ₂						
0.86	2.21	3.015 (6)	157			
0.86	2.18	2.992 (6)	157			
0.86	2.20	2.95 (3)	146			
0.86	2.25	3.10 (4)	171			
	0.93 0.843 (16) 0.93 0.93 0.93 0.93 0.824 (17) 0.93 0.843 (16) 0.93 0.843 (16) 0.93 0.86 0.86 0.86	0.93 2.52 0.843 (16) 2.483 (17) 0.93 2.56 0.93 2.42 0.824 (17) 2.493 (17) 0.93 2.42 0.843 (16) 2.225 (16) 0.93 2.36 0.86 2.21 0.86 2.20 0.86 2.25	0.93 2.52 $2.960 (4)$ $0.843 (16)$ $2.483 (17)$ $3.2582 (14)$ 0.93 2.56 $3.2489 (15)$ 0.93 2.42 $2.8939 (15)$ $0.824 (17)$ $2.493 (17)$ $3.2594 (15)$ 0.93 2.42 $2.9182 (16)$ $0.843 (16)$ $2.225 (16)$ $3.0069 (13)$ 0.93 2.36 $2.8598 (15)$ 0.86 2.18 $2.992 (6)$ 0.86 2.20 $2.95 (3)$ 0.86 2.25 $3.10 (4)$			

Symmetry code(s):

(i) x+1, y, z; (ii) x+1, -y, z+1/2; (iii) x, y-1, z; (iv) x-1, y+1, z; (v) x-1, y, z; (vi) -x+1/2, y+1, z-1/2; (vii) x-1/2, -y+1/2, z-1/2; (viii) -x+1/2, y-1/2, -z+1/2; (ix) -x+1, -y, -z; (x) x, y, z+1; (xi) x-1/2, -y+1/2, z+1.

As represented as such when referenced with data in the main paper text.

Supplementary diagrams





Supershort interaction in F_2 -25 (using C-H bond lengths from SHELXL14)^{31a} and a Fingerprint plot using Crystal Explorer^{31e} of the H...F supershort contact of 2.28 Å (highlighted in colour beside the H...O interaction of 2.17(6) Å, in grey).



Cyclic rings of N-H/C-H...F interactions in 24m,²⁵ $25m^{25}$ and $23p^{24}$; 1-D chains in JAVWIN01.³⁷ H...F distances are in the range 2.40 to 2.50 Å (not normalised values). For 24m and 23p the N-H...O=C interaction (centre) is depicted for comparison.



a) **F**₂-23 molecule 1; *b*) 24-**F**₂ F...N contact; *c*) **F**₂-26 molecule 1; *d*) 34-**F**₂ F...F contact.

Fingerprint plots^{31e} highlighting the short, strong N-H...O=C hydrogen bonding interaction that dominates in the *a*) F_2 -23 and *c*) F_2 -26 structures and comparing with the impact of *b*) F...N and *d*) F...F contacts in 24- F_2 and 34- F_2 , respectively on their structures.



Examples of very short intramolecular and intermolecular C-H...F interactions.¹

5. Ab initio calculation results

5.1. Potential energy surface (PES) scans of the six F2-xx conformers (rotamers), optimised in gas phase



For the **F2-23**, **F2-24** and **F2-25** isomers, conformational analysis of **F**-ring gives the same PES profile with one global maximum located at -175° ($TS_{F23}^{III} = 43.19 \text{ kJ.mol}^{-1}$, $TS_{F24}^{III} = 44.76 \text{ kJ.mol}^{-1}$ and $TS_{F25}^{III} = 45.59 \text{ kJ.mol}^{-1}$). The three isomers have a plateau at -110° ($TS_{F23}^{I'} = 22.18 \text{ kJ.mol}^{-1}$, $TS_{F24}^{I'} = 22.18 \text{ kJ.mol}^{-1}$ and $TS_{F25}^{I'} = 24.32 \text{ kJ.mol}^{-1}$) and local maximum at 95° ($TS_{F23}^{I} = 22.39 \text{ kJ.mol}^{-1}$). While the **F2-24** and **F2-25** local maxima are present at 100° ($TS_{F24}^{I} = 19.85 \text{ kJ.mol}^{-1}$) and $TS_{F25}^{I} = 24.54 \text{ kJ.mol}^{-1}$), a local

minimum for **F23** and **F24** rings is present at 125° ($LM_{F23}^{I} = 18.78 \text{ kJ.mol}^{-1}$, $LM_{F24}^{I} = 17.96 \text{ kJ.mol}^{-1}$) and for **F25** ring local minimum is present at 130° ($LM_{F25}^{I} = 20.82 \text{ kJ.mol}^{-1}$). Finally, they have one global minimum at 0°.

In **F2-26** isomer conformational analysis of the **F26** ring gives a specific PES profile with two global minima at 0° and \pm 180° in addition to two global maxima at -120° and 65° (TS_{F26}^{II} = 21.85 kJ.mol⁻¹) and two local maxima at -40° and 145° (TS_{F26}^{I'}, TS_{F26}^I = 6.10 kJ.mol⁻¹), moreover, two local minima are present at -65° and 120° (LM_{F26}^{I'} = 3.70 kJ.mol⁻¹).

The conformational analyses of **F34** and **F35** rings provide similar PES profile with two global maxima at -95° and 90° for the **F2-34** isomer ($TS_{F34}^{I} = 15.76 \pm 0.03 \text{ kJ.mol}^{-1}$) and for **F2-35** isomer the global maxima are present at -95° and 85° ($TS_{F35}^{I} = 19.05 \pm 0.02 \text{ kJ.mol}^{-1}$). The symmetric **F35** shows two global minima at 0° and ±180°, while the asymmetric **F34** has one global minimum at 0° and one local minimum at ±180°.

The rotation of the phenyl ring (**B**-ring) gives a similar PES profile for all **F2-xx** isomers excluding the **F2-26** isomer with two global maxima at -65° ($TS_B^{II} = 13.4\pm0.55$ kJ.mol⁻¹), and at around 120° ($TS_B^{II} = 13.3$ kJ.mol⁻¹). The PES diagrams also show two local maxima at around -150° and 30° ($TS_B^{I} = 1.33-2.01$ kJ.mol⁻¹) and four global minima at -130°, 0°, around 55° and at ±180°. The **B**-ring of the **F2-26** isomer shows two global maxima at -65° and 110° ($TS_B^{I} = 14.70$ kJ.mol⁻¹), two plateaux at -140° and 40° ($TS_B^{I} = 3.8$ kJ.mol⁻¹) and two global minima at 0° and ±180°.



5.2. Potential energy surface (PES) scans of the six xx-F2 conformers (rotamers), optimised in gas phase

For the **23-F2**, **24-F2** and **25-F2** isomers, the conformational analysis of their **F**-rings gives the same PES profile with one global maximum located at around $\pm 180^{\circ}$ (30.53 kJ.mol⁻¹), two local maxima at around $\pm 100^{\circ}$ (18.78 kJ.mol⁻¹), two local minima for **23-F2** and **24-F2** are present at $\pm 130^{\circ}$ (LM_{F23}^I = 16.06 kJ.mol⁻¹, LM_{F24}^I = 18.14 kJ.mol⁻¹) and for **25-F2** the two local minima are present at around $\pm 120^{\circ}$ (LM_{F25}^I = 17.78 kJ.mol⁻¹). Finally, they have one global minimum at 0°.

The conformational analysis of the **F**-ring of **26-F2** isomer gives a different PES profile with four global minima at 0°, 105°, -70° and \pm 180° in addition to the two global maxima at -125° and 55° (TS_{F26}^{II} = 7.80 kJ.mol⁻¹) and two local maxima at -35° and 145° (0.67 kJ.mol⁻¹).

The conformational analysis of the **F**-rings in **34-F2** and **35-F2** isomers gives similar PES profiles with two global maxima at around - 60° and 120° for the **34-F2** isomer ($TS_{F34}^{I} = 12.93 \text{ kJ.mol}^{-1}$; $TS_{F35}^{I} = 11.50 \text{ kJ.mol}^{-1}$). In **35-F2** isomer there are four global minima at 0°, -130°, 55° and ±180°. However, in **35-F2** isomer there are only two global minima at 0° and 55°, but two local minima at -130° and ±180°.

The rotation of the phenyl ring (**B**-ring) gives the same PES profile for all **xx-F2** isomers with two global maxima at around $\pm 90^{\circ}$ (TS_B^{II'} = 14.5 kJ.mol⁻¹) and two global minima at 0° and $\pm 180^{\circ}$.