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## The role of fluorine substituents in the formation of the ferroelectric nematic phase†

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The synthesis and characterisation of a group of molecules based on the skeletal structures of 4-[(4-nitrophenoxy)carbonyl]phenyl 4-methoxybenzoate and (4-nitrophenyl)-2-methoxy-4-(4-methoxybenzoyl)oxybenzoate is reported. Fluorine substituents are added to these structures and their liquid crystalline behaviour is characterised. All eight compounds reported exhibit the ferroelectric nematic phase,  $N_F$ , and in four of them the antiferroelectric phase labelled  $N_X$  is observed. These include rare examples of enantiotropic  $N_F$  and  $N_X$  phases, and several examples of the direct  $N_F$ -isotropic transition. The addition of a fluorine substituent reduces the nematic–isotropic transition temperature, and this is attributed to the reduction in both shape anisotropy and the ability of the molecules to form antiparallel dimers. The effect of the fluorine substituents on the  $N_F$  and  $N_X$  phases is less regular and interpreted in terms of the changes to the molecular shape and electron distribution. The stability of the  $N_X$  phase follows that of the  $N_F$  phase in the series without a lateral methoxy group. The addition of a lateral methoxy group reduces the stability of the  $N_F$  phase and completely suppresses the  $N_X$  phase.

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## Introduction

Following the experimental discovery of a polar nematic phase in 2017<sup>1,2</sup> and its subsequent assignment in 2020 as the ferroelectric nematic phase,  $N_F$ ,<sup>3</sup> it has rapidly become the hottest topic in liquid crystal science and technology, not least due to its huge application potential. The  $N_F$  phase shows very large polarisation values, strong non-linear optical responses and giant dielectric permittivity values compared to those observed for the conventional nematic,  $N$ , phase.<sup>4–30</sup> We do note, however, that some doubt has been cast on these very large permittivity values by, for example, Erkoreka *et al.*<sup>31</sup> and Clark *et al.*<sup>32</sup> The phase also exhibits other interesting behaviour such as the formation of twisted structures in antiparallel rubbed cells.<sup>33</sup> Critically it is the polar nature of the  $N_F$  phase that gives rise to its fascinating fundamental behaviour and technologically valuable properties. The conventional  $N$  phase presently underpins liquid crystal display technologies<sup>34</sup> and is the least ordered liquid crystal phase. In the  $N$  phase, the molecules show long-range

orientational ordering in the absence of long-range positional ordering. Thus, the rod-like molecules align along a common direction known as the director, which is represented by the unit vector,  $\mathbf{n}$ . The  $N$  phase possesses inversion symmetry such that  $\mathbf{n} = -\mathbf{n}$ , Fig. 1, and hence is non-polar. By comparison, in the  $N_F$  phase, this inversion symmetry is broken such that  $\mathbf{n} \neq -\mathbf{n}$ , Fig. 1, and the phase is polar.

The overwhelming majority of approximately 200 molecules that have been reported to exhibit the  $N_F$  phase can be broadly grouped into one of two molecular templates, RM734 and DIO,

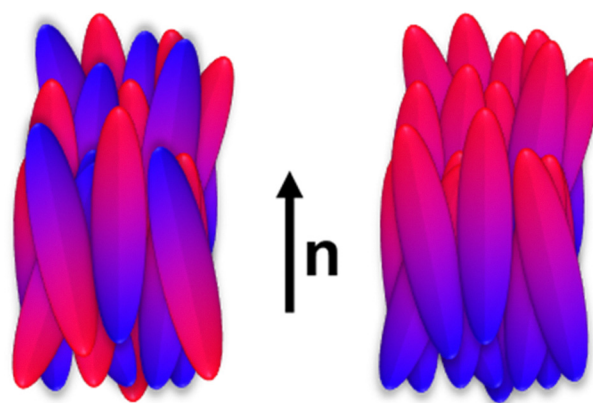


Fig. 1 Schematic representation of the conventional nematic phase (left) and the ferroelectric nematic phase (right).

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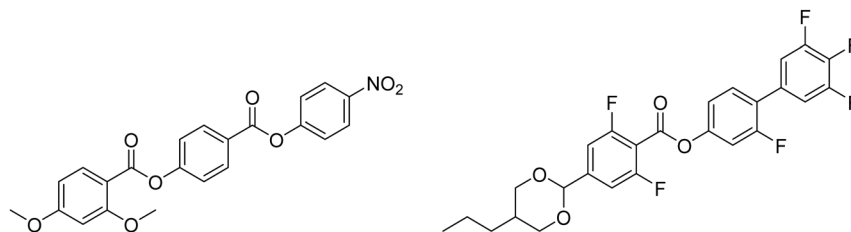


Fig. 2 Molecular structures of RM734 (left panel) and DIO (right panel).

Fig. 2.<sup>6–8,11,13,17,18,20,26,30,35–55</sup> These were the first compounds reported to exhibit the  $N_F$  phase<sup>2,42</sup> and although they appear rather chemically different, both possess a large longitudinal dipole moment and structural elements promoting lateral bulk. It has become apparent that the ester links in these structures play an important role in the formation of the  $N_F$  phase by disrupting the electronic distribution along the molecule such that it may be described as alternating regions of positive and negative charge density as sketched in Fig. 3.<sup>56</sup> This representation of the electron density is similar to the longitudinal charge density waves used by Madhusudana to describe molecules and account for the formation of the  $N_F$  phase.<sup>57</sup> Specifically, the model suggests that the parallel alignment of the molecules is enhanced by minimising the amplitude of the charge density wave at either end of the molecule. Molecular dynamics simulations reported by Mandle also reveal that the molecules are displaced along their long axes to allow the favourable overlap of negative and positive regions in a parallel orientation.<sup>58,59</sup> We recently highlighted the challenge in generating more exotic structures within this structure space through the design of highly polar dimers which, despite appearing to have the features described earlier, did not exhibit the  $N_F$  phase.<sup>60</sup>

We have previously reported on the role played by fluorine substituents in RM734-type compounds in the formation of the

$N_F$  phase, focussing our attention on fluorine substituents on the middle aromatic ring and in the *ortho* position to the terminal nitro group.<sup>8,20,26,36,46,51</sup> Here we extend our study and consider the effects on the  $N_F$  phase of fluorine substituents on the 4-methoxybenzoic acid fragment. This work will look to expand on the fluorinated materials reported by Li *et al.*<sup>6</sup> and this will be undertaken by adding fluorine atoms next to the terminal nitro group and removing the lateral methoxy group in the middle aromatic ring. We recently reported that adding methoxy groups to the middle aromatic ring of RM734-type compounds decreased the value of the  $N_F$  transition temperatures and extinguished the conventional nematic phase. Therefore, we would expect the compounds we are reporting herein, in which the methoxy group is removed from the middle aromatic ring, to show a stabilisation of the  $N_F$  phase. Here we report the synthesis and characterisation of eight compounds structurally related to RM734 each containing fluorine substituents on the 4-methoxybenzoic acid fragment rather than a lateral methoxy group and designed to exhibit the  $N_F$  phase. We refer to these compounds using the code EC*n*F and their structures are shown in Table 1. Of these eight compounds, six are reported here for the first time. The properties of these compounds will allow us to better understand the structural factors that drive the formation of the fascinating  $N_F$  phase which in turn will underpin the rational design of new materials having targeted properties.

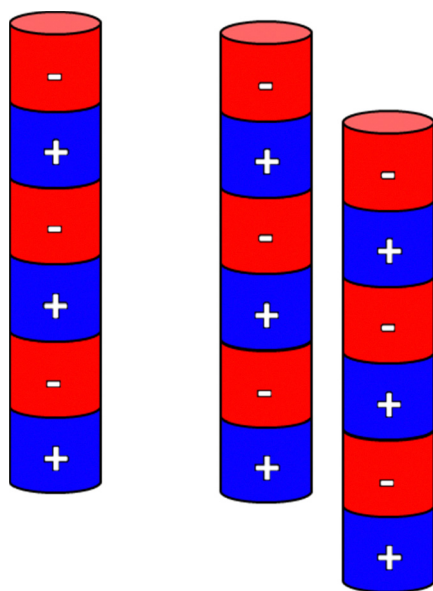


Fig. 3 Sketch of a rod-like molecule with regions of positive and negative charge (left) and the favoured parallel alignment of rods in the  $N_F$  phase (right).

## Experimental

The synthetic route used to prepare EC1F, EC2F, EC5F and EC6F is shown in Scheme 1 and for EC3F, EC4F, EC7F and EC8F in Scheme 2. A detailed description of the preparation of the intermediates and final products, including their structural characterisation, is provided in the ESI.†

### Optical studies

Phase characterisation was performed using polarised light microscopy, using a Zeiss AxioImager A2m equipped with a Linkam THMS600 hot stage. Slides treated for planar alignment were purchased from INSTEC or AWAT with a thickness between 2.9–3.5  $\mu\text{m}$  or 1.8  $\mu\text{m}$ , respectively, and both sets of cells were ITO conducting.

### Differential scanning calorimetry

The phase behaviour of the materials was studied by differential scanning calorimetry performed using a Mettler Toledo DSC1 or DSC3 differential scanning calorimeter equipped with



Table 1 Structures of the target compounds and the codes used to refer to them

| Code | Structure | Code | Structure |
|------|-----------|------|-----------|
| EC1F |           | EC2F |           |
| EC3F |           | EC4F |           |
| EC5F |           | EC6F |           |
| EC7F |           | EC8F |           |

TSO 801RO sample robots and calibrated using indium and zinc standards. Heating and cooling rates were  $10\text{ K min}^{-1}$ , with a 3 min isotherm between either heating or cooling, and all samples were measured under a nitrogen atmosphere. Transition temperatures and associated enthalpy changes were extracted from the heating traces unless otherwise noted. For each sample, two aliquots were measured, and the data listed are the average of the two sets of data.

### Molecular modelling

The geometric parameters of the compounds of interest were obtained using quantum mechanical DFT calculations with Gaussian09 software.<sup>61</sup> Optimisation of the molecular structures was carried out at the B3LYP/6-31G(d) level. Visualisations of electronic surfaces and ball-and-stick models were generated from the optimised geometries using the GaussView 5 software. The electronic surfaces were found using the cubegen utility in GaussView by generating a total density cube using a SCF density matrix and coarse grid, overlaid by an ESP surface map. Visualisations of the space-filling models were produced post-optimisation using the QuteMol package.<sup>62</sup>

### Birefringence measurements

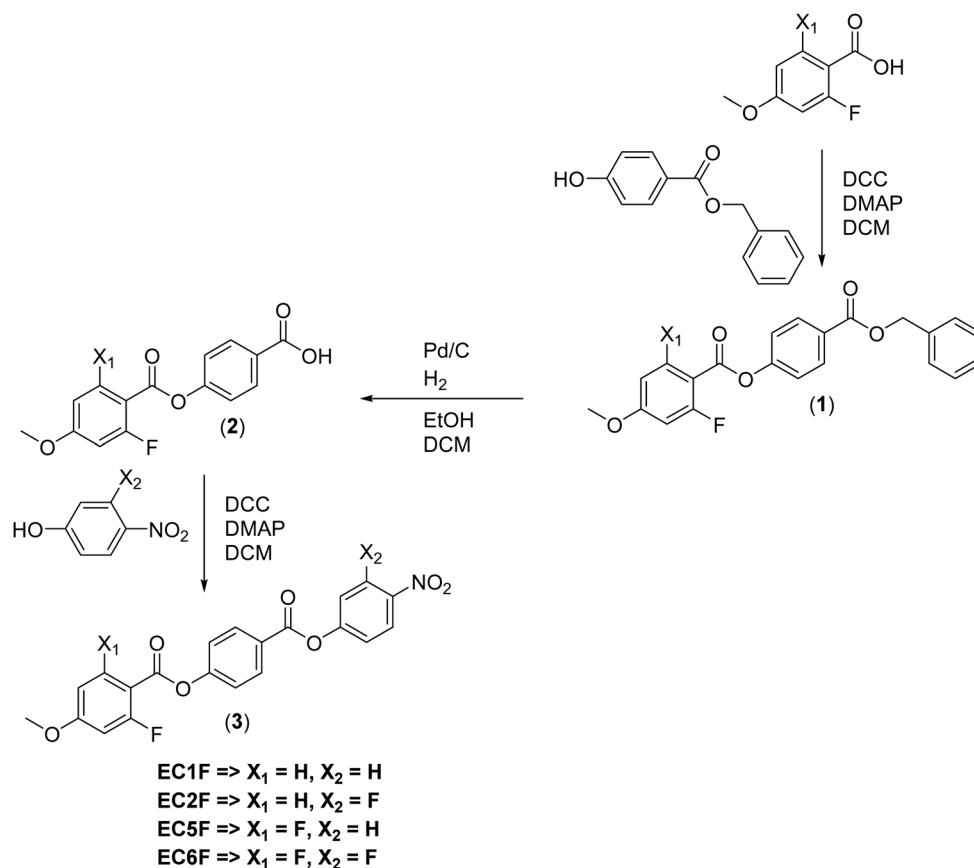
Birefringence was measured with a setup based on a photoelastic modulator (PEM-90, Hinds) working at a modulation frequency  $f = 50\text{ kHz}$ ; as a light source, a halogen lamp (Hamamatsu LC8) was used equipped with narrow bandpass

filter (532 nm). The signal from a photodiode (FLC Electronics PIN-20) was deconvoluted with a lock-in amplifier (EG&G 7265) into  $1f$  and  $2f$  components to yield a retardation induced by the sample. Knowing the sample thickness, the retardation was recalculated into optical birefringence. Samples were prepared in  $3.0\text{ }\mu\text{m}$ -thick cells with planar anchoring. The alignment quality was checked prior to measurement by inspection under the polarised light optical microscope.

### Dielectric spectroscopy

The complex dielectric permittivity,  $\epsilon^*$ , was studied using a Solartron 1260 impedance analyser. Measurements were conducted in the  $10\text{ Hz}$ – $1\text{ MHz}$  frequency ( $f$ ) range, with the probe voltage of  $20\text{ mV}$ , and it was checked by optical observations that such a voltage is below the Fredericks transition threshold. The material was placed in  $9.7\text{ }\mu\text{m}$ -thick glass cells with gold electrodes and no polymer aligning layers. Regardless of the way the dielectric spectroscopy results are interpreted, when a material with a giant permittivity is tested, instead of charging, and thus measuring the capacitor with the LC sample only the surface layers are charged because they have a smaller capacitance even though they are much thinner. Hence cells without polymer aligning layers were used in order to help this somewhat. The lack of a surfactant layer resulted in the random configuration of the director in the liquid crystal phases; microscopic observations of the optical textures suggested a dominant planar orientation without the preferable direction of the long molecular axis.





Scheme 1 Synthetic route used to prepare **EC1F**, **EC2F**, **EC5F** and **EC6F**.

## Second harmonic generation

The SHG activity was tested using a microscopic setup. Solid-state laser EKSPLA NL202 pulses ( $\lambda = 1064$  nm, 9 ns, 10 Hz repetition rate and max. 2 mJ pulse energy) were incident onto a LC sample prepared in 10  $\mu\text{m}$ -thick glass cells with planar anchoring condition. An IR pass filter was placed at the entrance to the sample and a green pass filter at the exit of the sample.

## X-ray diffraction

The X-ray diffraction (XRD) measurements were performed with a Bruker D8 GADDS system (CuK $\alpha$  line, Goebel mirror monochromator, point beam collimator, Vantec2000 area detector). The temperature of the sample was controlled with a precision of  $\pm 0.1$  K. Samples were prepared as droplets on a heated surface.

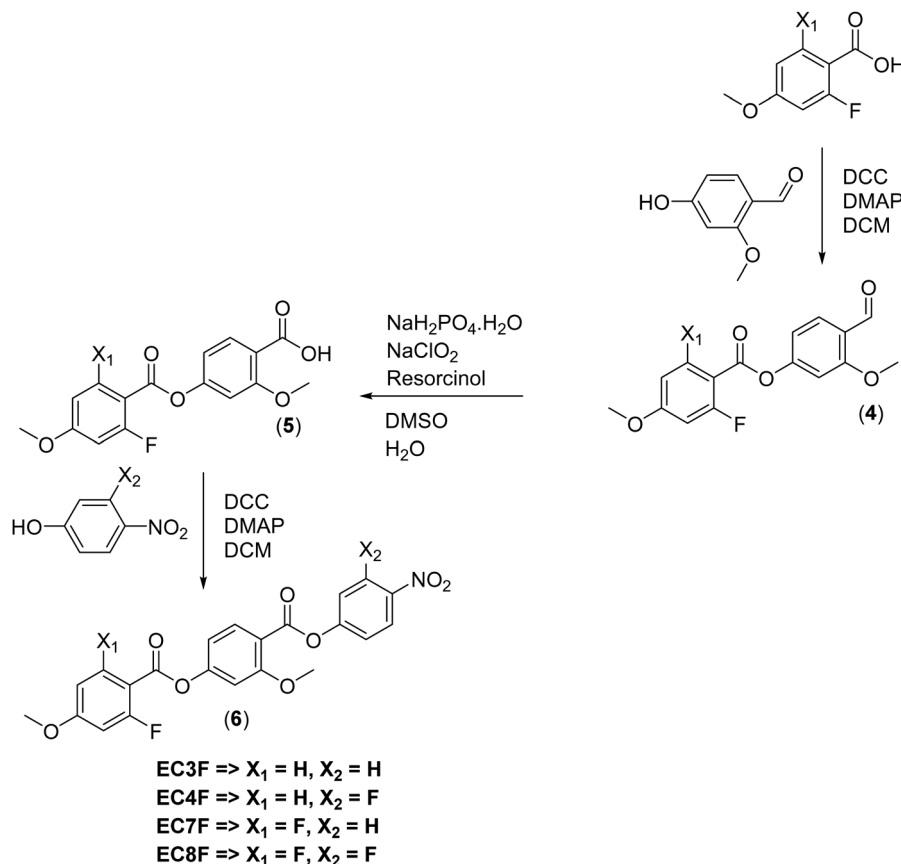
## Results and discussion

The transitional properties of the **EC $n$ F** compounds (Table 1) are listed in Table 2. The transition temperatures of **EC3F** and **EC7F** are in good agreement with those reported previously by Li *et al.*<sup>6</sup> Five of these compounds, specifically **EC1F**, **EC2F**, **EC3F**, **EC5F** and **EC6F**, exhibited the conventional nematic (N) phase and this was assigned on the observation of characteristic textures. Thus, for samples sandwiched between untreated

glass slides a schlieren texture containing two- and four-brush point singularities was observed (Fig. 4(a)) which flashed when subjected to mechanical stress, and for samples in cells treated for planar alignment, a uniform texture was seen (Fig. 4(b)). On cooling the N phase shown by **EC2F**, **EC5F** and **EC6F**, a chevron texture developed indicative of the  $N_x$  phase (Fig. 4(c) and (d)).<sup>8,44,47,51,63</sup> The  $N_x$  phase is also referred to as the  $\text{SmZ}_A$  phase and consists of a regular array of polar domains arranged in an anti-ferroelectric fashion along the direction perpendicular to the director.<sup>44,53,63–65</sup> This question of nomenclature for this phase is yet to be resolved as there is a sharp XRD signal sometimes recorded in this phase, corresponding to the periodic domain structure, which would be considered a feature of a smectic phase. Simultaneously, a diffuse XRD signal is always observed reflecting liquid-like positional correlations for neighbouring molecules, suggesting a more nematic nature to the phase.<sup>47</sup>

On cooling the chevron texture of the  $N_x$  phase seen for **EC2F**, **EC5F** and **EC6F**, a highly birefringent, banded texture (Fig. 4(e)) or a texture showing twisted states (Fig. 4(f)) formed, characteristic of the formation of the  $N_F$  phase.<sup>14,20,30,36,41,51</sup> A similar banded texture was seen on cooling the schlieren texture of the N phase of **EC3F** indicating a  $N_F$ -N transition, and was also observed directly from the isotropic phase for **EC4F**, **EC7F** and **EC8F** implying a  $N_F$ -I transition. The domains apparent in these banded textures (Fig. 4(e)) are areas in which





Scheme 2 Synthetic route used to prepare EC3F, EC4F, EC7F and EC8F.

the director has differing orientations and thus the orientation of the polarisation also differs and appears to be 'banded' due to the differing areas of birefringence within the domains.

**Table 2** Transition temperatures (in °C) and associated entropy changes scaled by the gas constant (values in parentheses) for the ECnF compounds (for structures see Table 1). The transitions are listed on heating (top) and cooling (bottom). The enthalpies of crystallisation on cooling are not listed. The calculated dipole moment,  $\mu$ , is also included

| Name | Phase sequence  | $\mu/\text{D}$ |
|------|---|----------------|
| EC1F | Cr-207 (11.8)-N-278 (0.13)-I<br>I-276 <sup>a</sup> -N-157 <sup>a</sup> -N <sub>X</sub> -144 <sup>a</sup> -N <sub>F</sub> -162 <sup>c</sup> -Cr                                | 10.98          |
| EC2F | Cr-192 (9.85)-N-245 (0.16)-I<br>I-244 (0.18)-N-175 (0.003)-N <sub>X</sub> -166 (0.12)-N <sub>F</sub> -155-Cr  | 12.02          |
| EC3F | Cr-169 (12.4)-N-177 (0.16)-I<br>I-176 (0.21)-N-156 (0.24)-N <sub>F</sub> -141-Cr  | 12.26          |
| EC4F | Cr-172 (15.3)-I<br>I-153 (1.25)-N <sub>F</sub> -112-Cr  | 13.31          |
| EC5F | Cr-186 (9.87)-N-266 <sup>a</sup> -I<br>I-265 <sup>a</sup> -N-177-N <sub>X</sub> -172 (0.09 <sup>b</sup> )-N <sub>F</sub> -134-Cr  | 11.18          |
| EC6F | Cr-181 (8.44)-N <sub>F</sub> -188 (0.17 <sup>b</sup> )-N <sub>X</sub> -191-231 (0.16)-I<br>I-232 (0.16)-N-189-N <sub>X</sub> -187 (0.22 <sup>b</sup> )-N <sub>F</sub> -148-Cr | 12.16          |
| EC7F | Cr-167 (13.6)-I<br>I-159 (1.07)-N <sub>F</sub> -110-Cr  | 12.58          |
| EC8F | Cr-162 (13.0)-I<br>I-149 (1.44)-N <sub>F</sub> -140-Cr  | 13.64          |

<sup>a</sup> Measured using polarised light microscopy. <sup>b</sup> Represents a combined entropy change arising from overlapping peaks in the DSC trace. <sup>c</sup> Crystallisation temperature of sample bulk, mesophases observed in isolated droplets.

The proposed phase assignments are consistent with the values of the associated scaled entropy changes,  $\Delta S/R$ , listed in Table 2. The values of  $\Delta S_{\text{NI}}/R$  range between 0.13 to 0.21, and these are lower than typically measured for a conventional low molar mass nematogen for which  $\Delta S_{\text{NI}}/R \approx 0.3$ . These smaller values presumably reflect the enhanced molecular biaxiality associated with the lateral substituents that reduce the orientational order of the nematic phase and hence, reduce  $\Delta S_{\text{NI}}/R$ .<sup>66</sup> The values of the scaled entropy change associated with the N<sub>F</sub>-I transition,  $\Delta S_{\text{NFI}}/R$ , are several times larger than  $\Delta S_{\text{NI}}/R$  and this additional entropic contribution is associated with the ordering of the dipoles in the N<sub>F</sub> phase.

On cooling the N phase shown by EC1F, crystallisation in the bulk precluded the observation of the characteristic textures for the N<sub>F</sub> and N<sub>X</sub> phases shown in Fig. 4. Instead, the N-N<sub>X</sub> and N<sub>X</sub>-N<sub>F</sub> transitions were observed only for isolated droplets. To assign these phase transitions a phase diagram (Fig. 5) was constructed for binary mixtures of EC1F and the ferroelectric nematogen, 4EC6F (Fig. 6).<sup>47</sup> The compounds were miscible over the entire composition range, and each mixture exhibited N, N<sub>X</sub> and N<sub>F</sub> phases assigned on the observation of characteristic optical textures (Fig. 7). Adding EC1F to 4EC6F sees  $T_{\text{NI}}$ ,  $T_{\text{N}_\text{XN}}$  and  $T_{\text{N}_\text{FN}_\text{X}}$  increase in essentially a linear manner. Extrapolation of the trendlines provides estimates of the virtual transition temperatures for EC1F of  $T_{\text{NI}} = 266$  °C,  $T_{\text{N}_\text{XN}} = 146$  °C and  $T_{\text{N}_\text{FN}_\text{X}} = 137$  °C, with the values for the pure sample





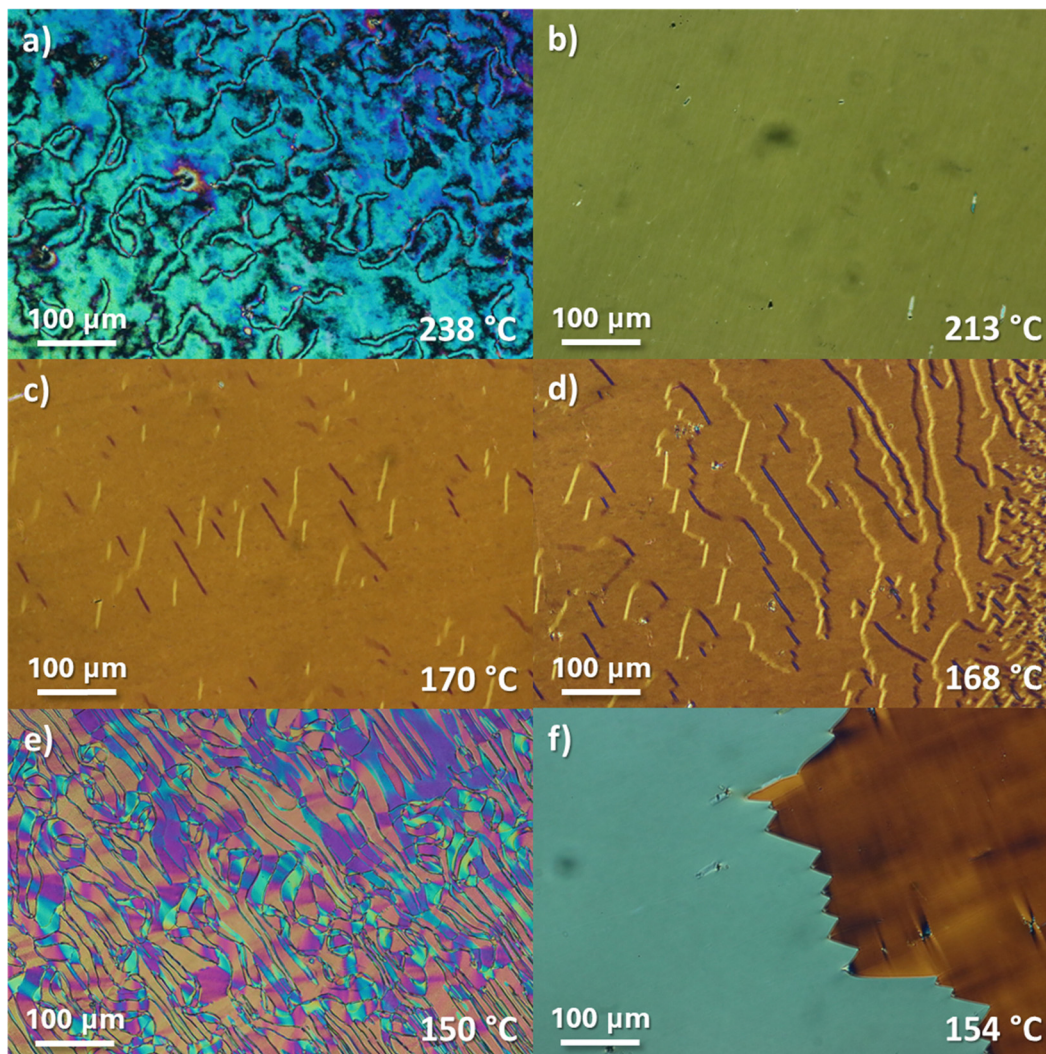


Fig. 4 Optical textures obtained for **EC2F** using polarised optical microscopy: (a) schlieren texture of the nematic phase seen for a sample sandwiched between untreated glass slides; the remaining textures were observed for samples in cells treated for planar anchoring, (b) uniform texture of the nematic phase, (c) and (d) chevron textures of the  $N_X$  phase, (e) banded texture of the ferroelectric nematic phase and (f) texture showing the twisted states of the ferroelectric nematic phase.

of **EC1F** not included. These values are slightly lower than the transition temperatures measured for isolated droplets of **EC1F** using polarised optical microscopy but strongly support the assignments listed in Table 1.

X-ray diffraction was used to characterise the N,  $N_X$  and  $N_F$  phases and representative diffraction patterns for **EC5F** are shown in Fig. 8. Only diffuse scattering is seen in these patterns arising from the short-range positional ordering of the molecules in all three phases. The periodic structure of the antiferroelectric domains in the  $N_X$  phase should give rise to a sharp reflection at small angles in the X-ray diffraction pattern. This signal has a very low intensity, however, showing that the related electron density modulation is particularly weak, and in practice, a strong synchrotron source is required for it to be observed.<sup>47</sup>

The temperature dependence of the optical birefringence,  $\Delta n$ , for **EC2F** is shown in Fig. 9. A particularly small change in

$\Delta n$  of just  $\approx 0.01$  is seen at the N- $N_X$  transition indicating that the  $N_X$  phase is orientationally very similar to the conventional N phase. This is followed by a larger but still small step-like increase at the  $N_X$ - $N_F$  transition indicative of an increase of the order parameter,  $S$ . These observations are in complete accord with our previous reports of the temperature dependence of the optical birefringence of the  $N_X$  and  $N_F$  phases.<sup>47,51</sup> The polar character of the nematic phases exhibited by **EC2F** was tested by measuring its complex permittivity as a function of temperature and frequency (Fig. 10). On cooling through the nematic phase, a weak dielectric mode begins to develop with a relaxation frequency slightly above  $10^4$  Hz, which shows typical softening due to the increasing polar order, with  $\epsilon'$  increasing to *ca.* 100, while the frequency decreases approaching the N- $N_X$  transition. On entering the  $N_X$  phase, this mode is quenched, most probably due to the antiferroelectric nature of this phase as we have previously reported.<sup>47</sup> The  $N_X$ - $N_F$



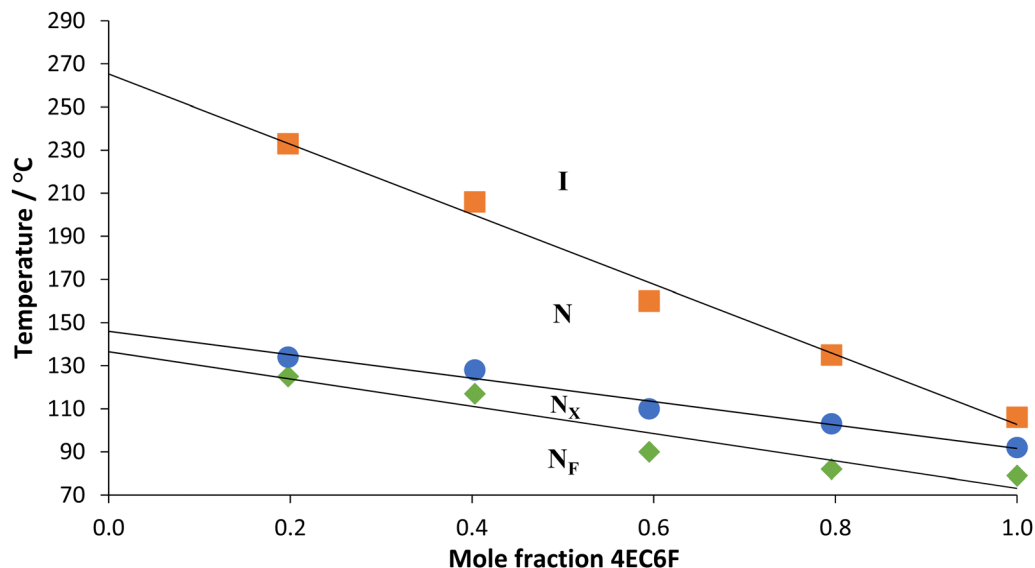


Fig. 5 Phase diagram constructed using binary mixtures of **EC1F** and **4EC6F**.<sup>47</sup> Squares denote  $T_{NI}$ , circles  $T_{NXN}$  and triangles  $T_{NFNX}$ . The trendlines are shown for  $T_{NI}$ ,  $T_{NXN}$  and  $T_{NFNX}$ .

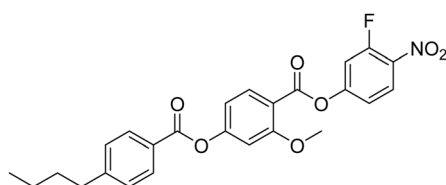


Fig. 6 Molecular structure of **4EC6F**.

transition is marked by the abrupt increase of the measured low-frequency permittivity, by orders of magnitude, which is characteristic of the  $N_F$  phase. While the proper detailed interpretation of the measured permittivity values in the  $N_F$  phase is more complex than previously thought, with many recent articles suggesting a variety of interpretations of what the values should be and why,<sup>12,31,32,67–70</sup> these considerations are beyond the scope of this paper which has a focus on the effect of structural modifications on the phase behaviour. However, the measured temperature dependence of permittivity can be treated as qualitative proof for the determined sequence of polar phases, as it is in excellent agreement with data reported for other ferroelectric nematics.<sup>6–12,14,30</sup> The non-centrosymmetric nature of the  $N_F$  phase in compound **EC2F** has been also confirmed by observation of its SHG activity. Incident IR ( $\lambda = 1064$  nm) radiation resulted in a strong emission of green light (Fig. 10c), proving the ferroelectric ground state of the phase.

We now turn our attention to discuss the transition temperatures listed in Table 2 and how these relate to changes in molecular structure with a particular focus on the role played by fluorine substituents in driving the formation of the  $N_F$  phase. With this in mind, the eight compounds listed in Table 2 may be split into two groups of four depending whether they are based on 4-[(4-nitrophenoxy)carbonyl]phenyl 4-

methoxybenzoate (**11-0-1**)<sup>46</sup> or (4-nitrophenyl)2-methoxy-4-(4-methoxybenzoyloxy)benzoate (**NT3.1**).<sup>20</sup> The structures and transition temperatures of **11-0-1** and **NT3.1** are shown in Fig. 11. **11-0-1** has no lateral substituents and exhibits exclusively conventional N behaviour whereas **NT3.1** possesses a lateral methoxy substituent on the central ring and shows both  $N_F$  and N phases. We note that isolated droplets of the N phase shown by **11-0-1** may be supercooled to 107 °C prior to crystallisation but attempts to measure a virtual  $N_F$ –N transition temperature were not successful.<sup>46</sup> The addition of a fluorine substituent *ortho* to the nitro group in **11-0-1** gives **12-0-1** and this is also exclusively nematic, see Fig. 11.

Fig. 12 maps the changes in the three transition temperatures,  $T_{NI}$ ,  $T_{NXN}$  and  $T_{NFNX}$ , on increasing the number of fluorine substituents from the unsubstituted **11-0-1** to **EC6F** containing three fluorine atoms. **EC6F** is a particularly interesting compound as it exhibits enantiotropic  $N_X$  and  $N_F$  phases. The addition of a fluorine atom always reduces  $T_{NI}$  but the magnitude of this decrease depends on the resulting change in structure. Thus, adding the first fluorine atom to the methoxyphenyl ring reduces  $T_{NI}$  by around 6 K, and the second by about 13 K, irrespective of whether the nitrophenyl ring contains a fluorine atom or not. The addition of the fluorine atom *ortho* to the nitro group reduces  $T_{NI}$  by about 33 K irrespective of the number of fluorine atoms on the methoxyphenyl ring. By contrast, adding fluorine atoms always increases both  $T_{NXN}$  and  $T_{NFNX}$  with the exception of moving from **11-0-1** to **12-0-1** for which  $N_X$  and  $N_F$  phases are not observed. It is clear, however, that  $T_{NFNX}$  and  $T_{NXN}$  must both be higher for **EC1F** than **12-0-1** by at least 44 K and 57 K, respectively, indicating that a fluorine atom *ortho* to the methoxy group is considerably more effective in promoting the  $N_F$  and  $N_X$  phases than if *ortho* to the nitro group. This is also evident in the dramatic increase in  $T_{NFNX}$  and  $T_{NXN}$  passing from **12-0-1** to **EC2F** of at least 66 K and 75 K,





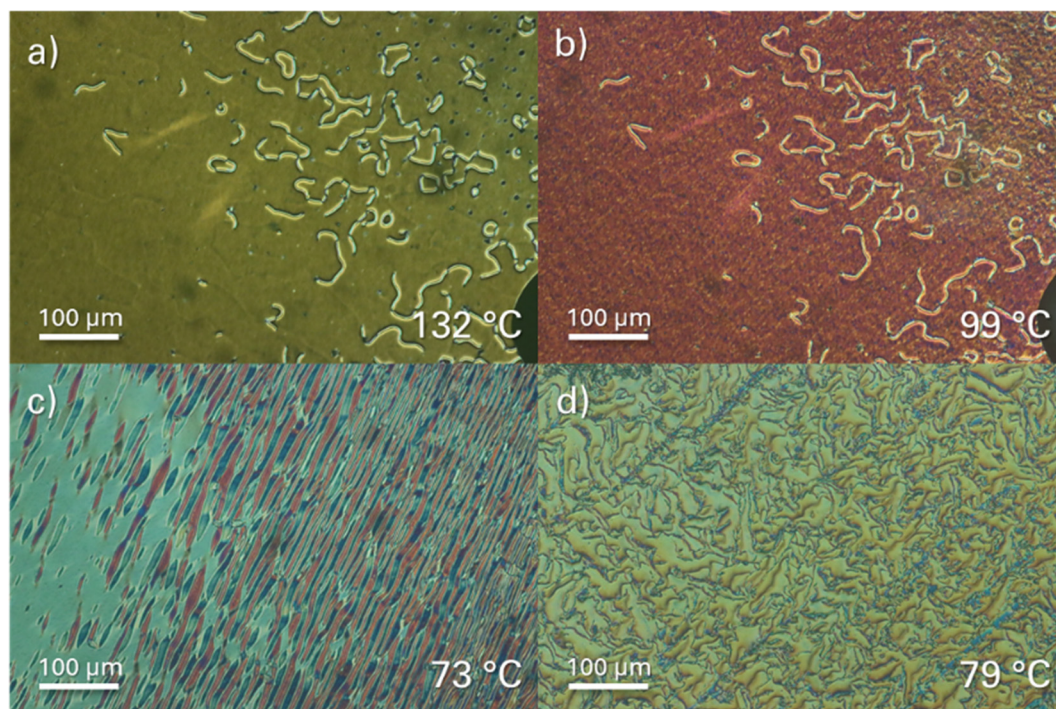


Fig. 7 Optical textures obtained using polarised light microscopy for a binary mixture composed of 40 mol% **EC2F** and 60 mol% **4EC6F** contained in a cell treated for planar alignment in (a) the N, (b) the  $N_X$ , and (c) the  $N_F$  phase. (d) The texture of the  $N_F$  phase obtained for a sample sandwiched between untreated glass slides.

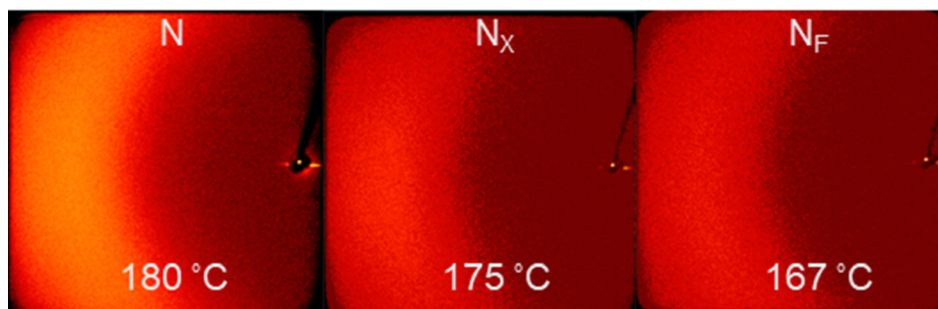


Fig. 8 X-ray diffraction patterns obtained for **EC5F** in (left) the N, (middle)  $N_X$  and (right)  $N_F$  phases.

respectively. After the addition of the first fluorine atom to the methoxyphenyl ring, subsequent fluorine atoms have a much smaller effect, and it appears to make little difference in which order they are added. This culminates in the compound **EC6F** which contains three fluorines within the molecular structure and exhibits both enantiotropic  $N_X$  and  $N_F$  phases.

Fig. 13 shows the changes in  $T_{N_F/N_I}$  and  $T_{N_I}$  on increasing the number of fluorine atoms from the unsubstituted **NT3.1** to **EC8F** containing three fluorine atoms. Again, it is evident that the addition of a fluorine atom always decreases  $T_{N_I}$ . Broadly the trends are the same as described for the **11-0-1**-based materials. The largest decreases in  $T_{N_I}$  are observed on adding a fluorine atom *ortho* to the nitro group. The reduction in  $T_{N_I}$  associated with the addition of the fluorine atoms is sufficiently large for the nematic phase to be extinguished and a direct  $N_F$ -I

transition to be observed for three of the four **NT3.1**-based compounds. The effect of adding a fluorine atom on  $T_{N_F/N_I}$  is smaller than seen for the **11-0-1**-based materials and depending on the structure may be positive or negative, which agrees with our recently published work on other ferroelectric nematic materials.<sup>46</sup>

We have seen that the addition of a fluorine atom to a compound in this collection always leads to a decrease in  $T_{N_I}$  and this effect is most pronounced when the fluorine atom is *ortho* to the nitro group. This reflects, at least in part, the reduction in structural anisotropy arising from the lateral substituent, see Fig. 14, and this is most pronounced for a fluorine atom *ortho* to the nitro group (Fig. 14(d)). This alone, however, cannot account for the observed trends given that these are similar for both sets of materials even though the



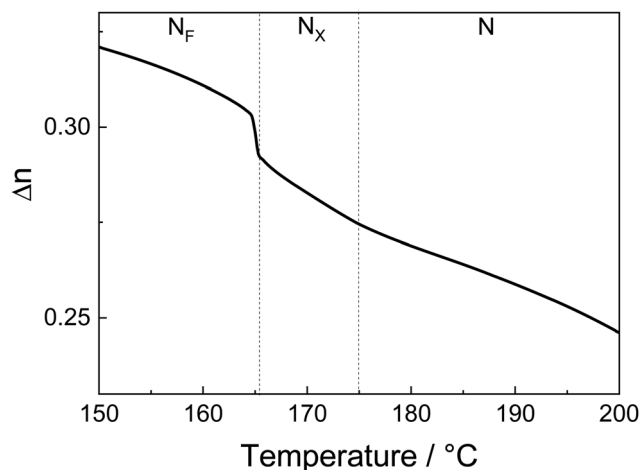


Fig. 9 Temperature dependence of the optical birefringence of **EC2F** measured on cooling with green light ( $\lambda = 532$  nm).

relative change in shape will be smaller for the **NT3.1**-based materials (Fig. 14(c)). This suggests that the fluorine atom *ortho* to the nitro group inhibits the antiparallel association of these molecules and this will also reduce  $T_{NI}$ . This accounts for the smaller reductions in  $T_{NI}$  seen for additions of fluorine atoms to the methoxyphenyl ring as these will have a much smaller effect on the antiparallel association of the molecules. In addition, the effect on shape of the first fluorine atom added to the methoxyphenyl ring is reduced by the molecular structure (Fig. 14(a)). By comparison, the second fluorine atom protrudes from the excluded molecular volume (Fig. 14(b)) and gives rise to a larger reduction in  $T_{NI}$  than seen for the first fluorine atom.

Our previous studies have suggested that a combination of electronic and shape factors drive the formation of the  $N_F$  phase<sup>20,41,46</sup> and even less is presently understood about the  $N_X$  phase.<sup>47,51</sup> For the **11-0-1**-based materials a fluorine atom on the methoxyphenyl ring strongly promotes both  $N_F$  and  $N_X$  phases, whereas a single fluorine atom *ortho* to the nitro group does not. We have already noted that the change in shape

arising from the addition of the first fluorine atom to the methoxyphenyl ring must be small given the associated weak change in  $T_{NI}$ , and hence, the effect on the  $N_F$  and  $N_X$  phases must arise from the change in the electron distribution. The addition of the fluorine atom reduces the electron density associated with the methoxyphenyl ring (Fig. 14(a)). Within the framework of the model proposed by Madhusudana to account for the formation of the  $N_F$  phase<sup>57</sup> described earlier, minimising the amplitude of the charge density wave at either end of the molecule reduces the tendency to adopt anti-parallel structures and the  $N_F$  phase is stabilised. The second fluorine atom further reduces the charge density associated with the methoxyphenyl ring and also enhances the molecular biaxiality (Fig. 14(b)) further promoting the  $N_F$  and  $N_X$  phases. The single fluorine atom *ortho* to the nitro group in **12-0-1** in itself does not promote the formation of the  $N_F$  phase because the molecule does not favourably pack into parallel structures presumably due to its shape. This is despite the fluorine atom reducing the amplitude of the charge density wave at the end of the molecule and is indicative that the position of lateral substituents is a critical consideration in the phase behaviour of these materials. The shape requirement for observing the  $N_F$  phase is satisfied by the addition of fluorine atoms to the methoxyphenyl ring, and the combination of the three fluorine atoms gives rise to the highest values of  $T_{N_F N_X}$  and  $T_{N_X N}$ .

The effects of the fluorine atoms on the  $N_F$  phases shown by the **NT3.1**-based materials are smaller than seen for the **11-0-1**-based compounds and may either increase or decrease the transition temperatures. This cannot be accounted for entirely using Madhusudana's model, which would predict similar behaviour for both sets of compounds.<sup>57</sup> This presumably reflects the weaker change in shape arising from the addition of the fluorine atoms in the case of the **NT3.1**-based compounds and suggests that some optimum molecular shape exists for the observation of the  $N_F$  phase. The presence of both the methoxy and fluorine substituents may exceed this shape constraint and overcome the electronic contributions the fluorine atoms play in the formation of the  $N_F$  such that a decrease in  $T_{N_F/N}$  is observed.

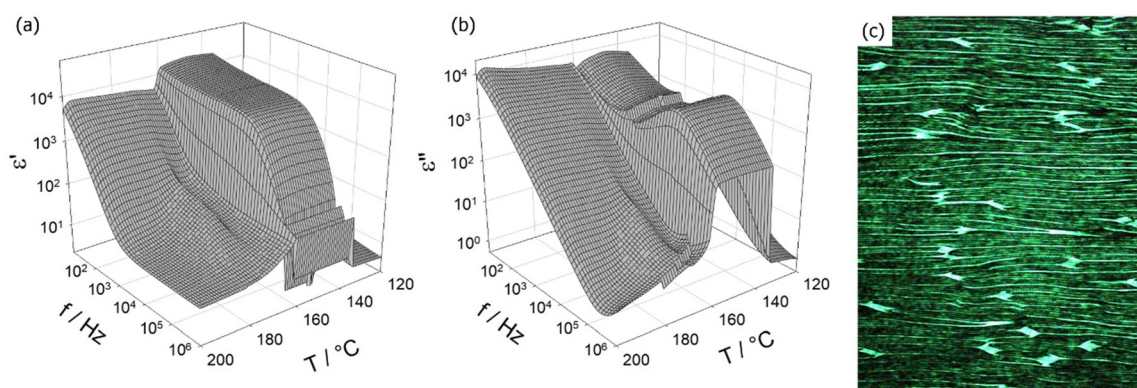


Fig. 10 (a) Real and (b) imaginary parts of the complex dielectric permittivity measured as a function of temperature and frequency for **EC2F**. (c) Image taken with an SHG microscope in the ground state (no applied voltage)  $N_F$  phase (at 155 °C) for a sample prepared in a cell with planar anchoring. Incident IR radiation caused strong emission of double-frequency (green) light.



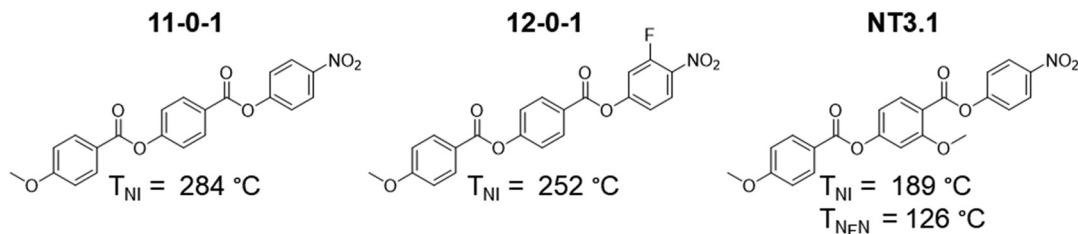


Fig. 11 Structures and transition temperatures of **11-0-1** and **12-0-1**<sup>46</sup> and **NT3.1**.<sup>20</sup>

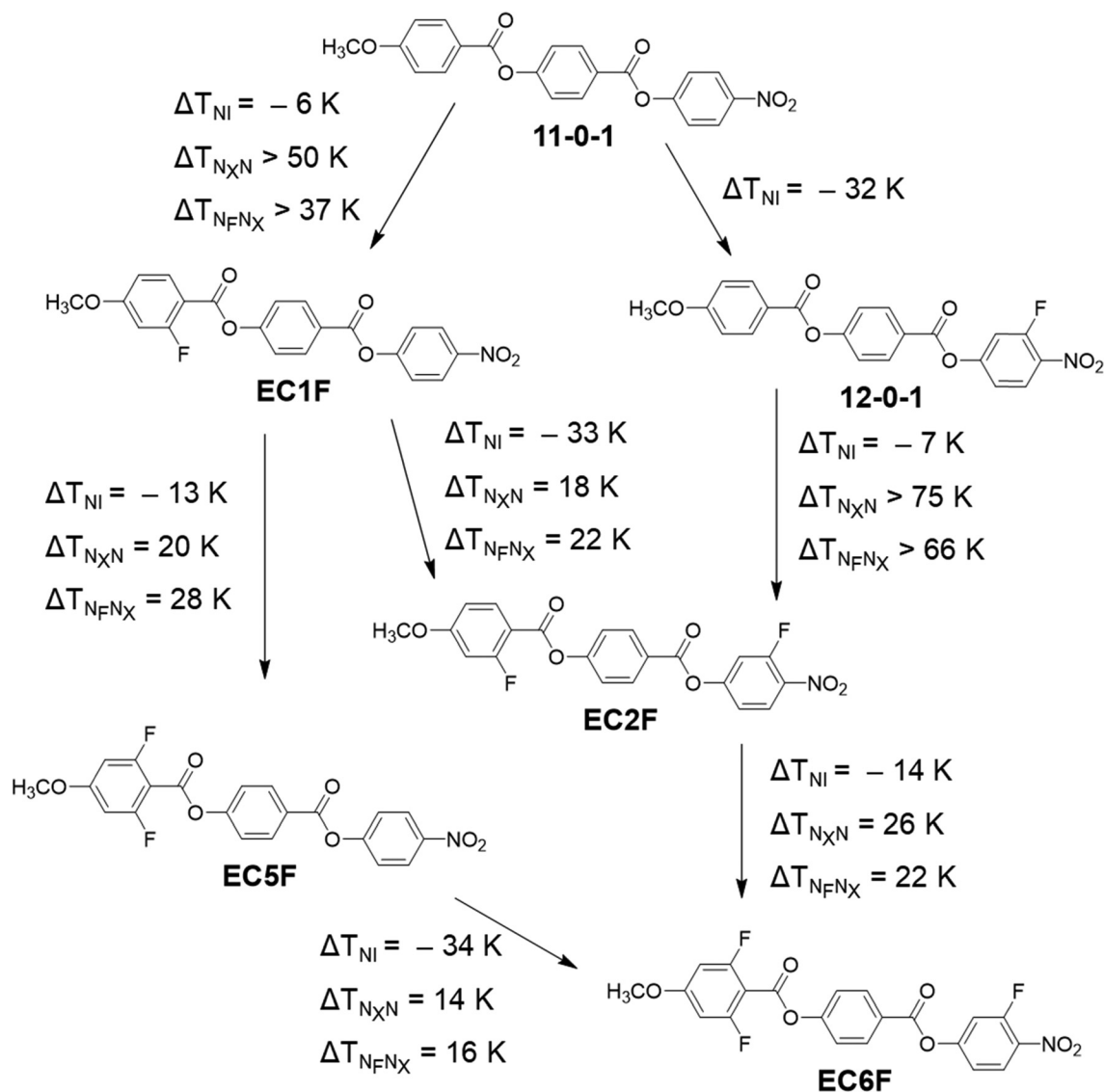


Fig. 12 The differences in transition temperatures between compounds based on **11-0-1**.

Finally, we will consider the role of the methoxy lateral group and compare these two sets of molecules. As would be expected on the basis of shape, the addition of the lateral methoxy group reduces  $T_{NI}$  by around 95 K. The smallest reduction, 82 K, is for the pair of molecules containing the highest number of fluorine substituents, **EC6F** and **EC8F**, and

this reflects the smaller relative change in shape associated with the methoxy group. As we have seen, neither **11-0-1** nor **12-0-1** exhibit the  $N_F$  phase and the addition of the lateral methoxy group to the central phenyl ring has a pronounced effect, increasing  $T_{N_FN}$  by at least 19 K and 42 K, respectively. The situation is more difficult to establish for the remaining pairs of





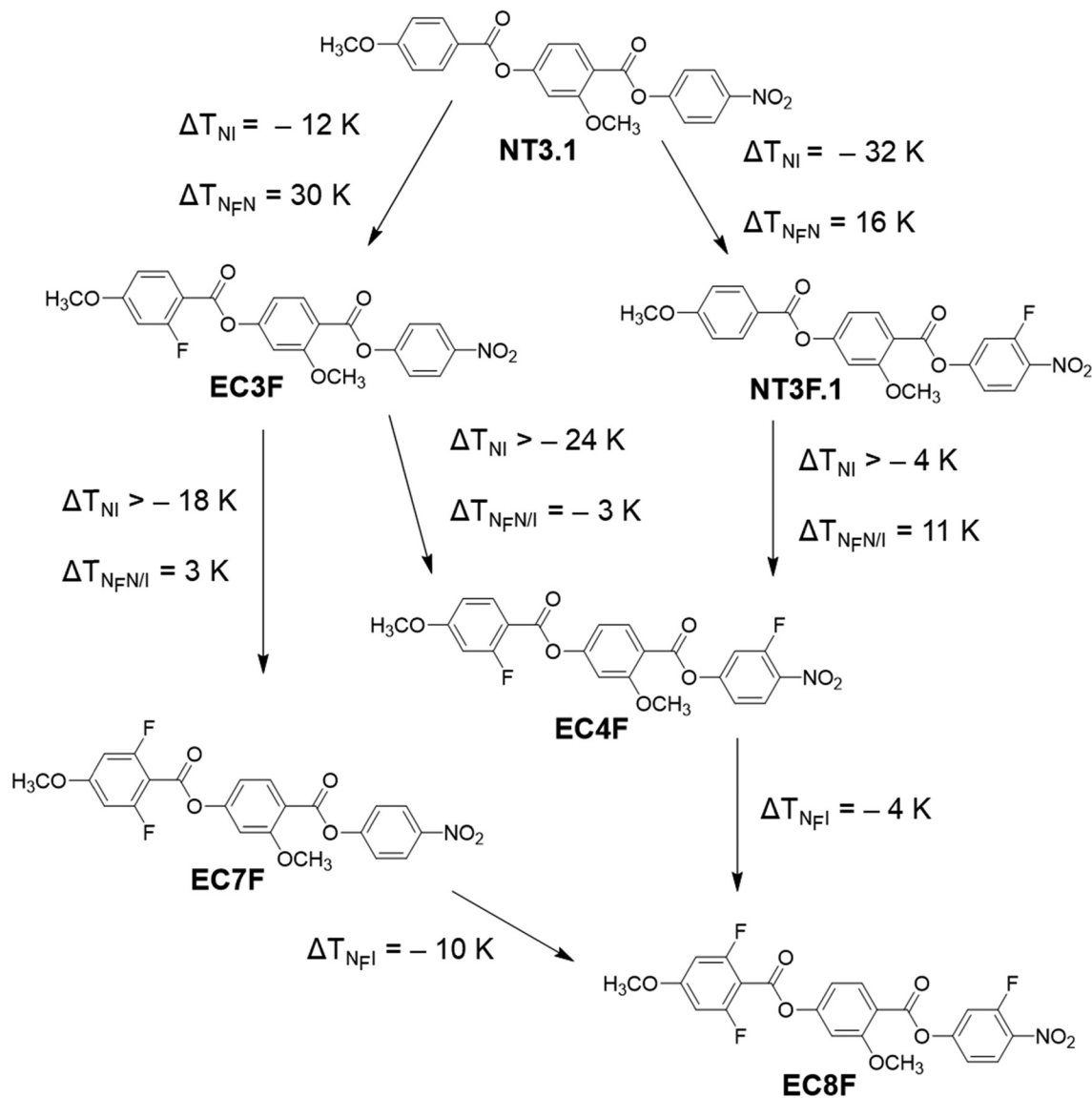


Fig. 13 The differences in transition temperatures between compounds based on **NT3.1**.

compounds because differing phase transitions are being compared. It is clear, however, that for three of the pairs, **EC2F**/**EC4F**, **EC5F**/**EC7F** and **EC6F** (which has an enantiotropic  $N_F$ -I transition)/**EC8F**, the stability of the  $N_F$  phase is reduced on the

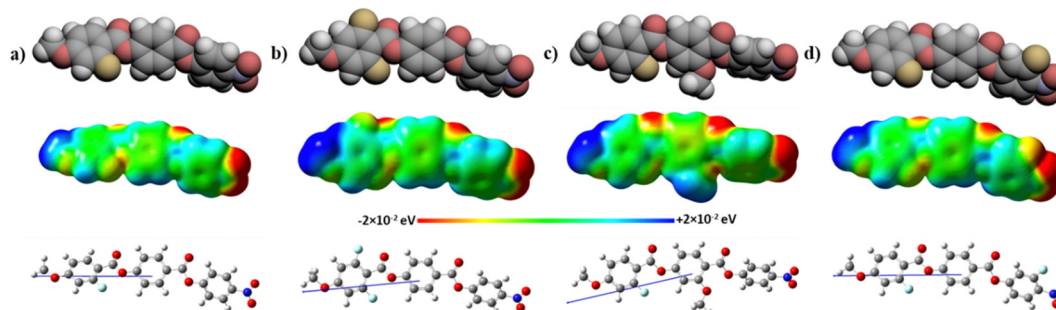


Fig. 14 The space-filling models (top), electrostatic potential surfaces (middle) and ball-and-stick models (bottom) of (a) **EC1F**, (b) **EC5F**, (c) **EC3F** and (d) **EC2F** calculated at the B3LYP/6-31(d) level of theory. The arrow indicates the direction of the calculated dipole moment, with the head representing the positive charge moving to the base which is negative.





addition of the methoxy group and for the fourth, **EC1F/EC3F**, there appears little change. Certainly, the addition of the methoxy group will increase the amplitude of the charge density wave in the centre of the molecule and this will promote the formation of the  $N_F$  phase and hence the observed increase in transition temperatures for the **11-0-1/NT3.1** and **12-0-1/NT3F.1** pairs of molecules. Presumably for the remaining pairs, shape considerations must account for the reduced tendency to exhibit the  $N_F$  phase for the methoxy-substituted materials. It is interesting to note that the methoxy substituent in the middle aromatic ring has suppressed the formation of the  $N_X$  phase and the physical significance of this requires further investigation.

## Conclusions

We report two sets of new ferroelectric nematogens to investigate the role played by fluorine substituents on the formation of the  $N_F$  phase. The addition of fluorine substituents reduces  $T_{NI}$ . The magnitude of this decrease depends on the position of the fluorine atom, and this is interpreted in terms of its effect on molecular shape and the tendency of the molecules to form antiparallel dimers. The effect of fluorine substituents on the stability of the  $N_F$  phase is more strongly dependent on the molecular structure and  $T_{N_F/N_I}$  may increase or decrease. This is interpreted in terms of a competition between changes to molecular shape and electron distribution. It appears that there is some optimum shape for the formation of the  $N_F$  phase and if the addition of lateral substituents enhances the biaxiality beyond this, then the tendency to exhibit the  $N_F$  phase is reduced. The contributions of the electronic effects are well accounted for in terms of the model proposed by Madhusudana.<sup>57</sup> It is interesting to note that the stability of the  $N_X$  phase with respect to changes in the molecular structure appears similar to that of the  $N_F$  phase for the **11-0-1**-based materials and these materials provide a rare opportunity to study this. By contrast, the addition of a lateral methoxy group extinguishes the  $N_X$  phase. The physical significance of this observation is far from clear. In terms of the molecular engineering of materials, fluorine substituents clearly have an important role to play in the design of ferroelectric nematogens and here we report a rare example of a single compound exhibiting both enantiotropic  $N_F$  and  $N_X$  phases.

## Data availability

The data supporting this article have been included as part of the ESI.†

## Conflicts of interest

There are no conflicts to declare.

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# The role of fluorine substituents on the formation of the ferroelectric nematic phase

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## **Experimental Procedures**

### **Synthesis**

#### **Reagents**

All reagents and solvents that were available commercially were purchased from Sigma Aldrich, Fisher Scientific or Fluorochem and were used without further purification unless otherwise stated.

#### **Thin Layer Chromatography**

Reactions were monitored using thin layer chromatography, and the appropriate solvent system, using aluminium-backed plates with a coating of Merck Kieselgel 60 F254 silica which were purchased from Merck KGaA. The spots on the plate were visualised by UV light (254 nm) or by oxidation using either a potassium permanganate stain or iodine dip.

#### **Column Chromatography**

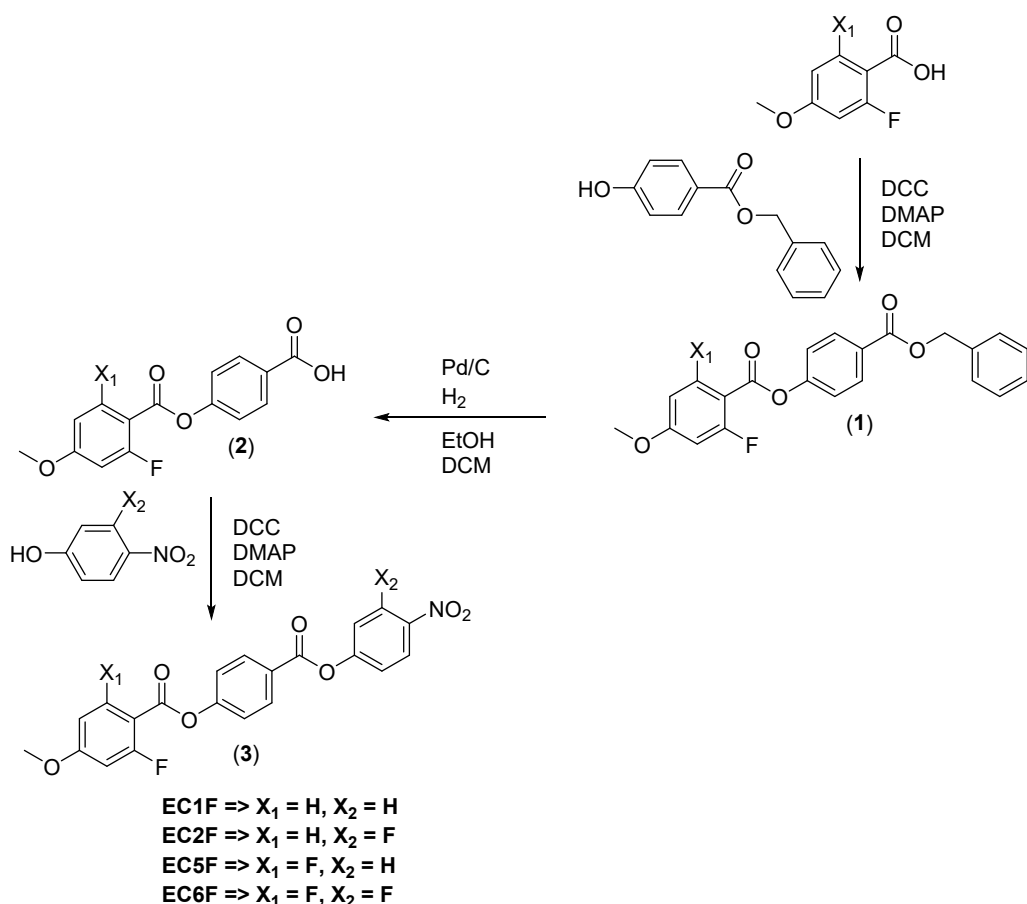
For normal phase column chromatography, the separations were carried out using silica gel grade 60 Å, 40-63 µm particle size, purchased from Fluorochem and using an appropriate solvent system.

#### **Structure Characterisation**

All final products and intermediates that were synthesised were characterised using  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR and infrared spectroscopies. The NMR spectra were recorded on a 400 MHz Bruker Avance III HD NMR spectrometer. The infrared spectra were recorded on a Perkin Elmer Spectrum Two FTIR spectrometer with an ATR diamond cell.

#### **Purity Analysis**

In order to determine the purity of the final products, high-resolution mass spectrometry was carried out using a Waters XEVO G2 QToF mass spectrometer by Dr. Jayne McCaskill at the University of Aberdeen.



Scheme 1. Synthesis of EC1F, EC2F, EC5F and EC6F.

### Compound 1

To a pre-dried flask flushed with argon, 2-fluoro-4-methoxybenzoic acid (1 eq) or 2,6-difluoro-4-methoxybenzoic acid (1 eq), benzyl 4-hydroxybenzoate (1.1 eq) and 4-dimethylaminopyridine (0.13 eq) were added. The solids were solubilised with dichloromethane (80 mL) and stirred for 10 min before *N,N'*-dicyclohexylcarbodiimide (1.3 eq) was added to the flask and the reaction was allowed to proceed overnight. The quantities of the reagents used in each reaction are listed in **Table S1**. The extent of the reaction was monitored by TLC using an appropriate solvent system (RF values quoted in the product data). The precipitate which formed was removed by vacuum filtration and the filtrate collected. The collected solvent was evaporated under vacuum to leave a solid which was recrystallised from hot ethanol (100 mL).

**Table S1.** Quantities of reagents used in the syntheses of **Compound 1**

| Product | 2-Fluoro-4-methoxybenzoic acid/*2,6-Difluoro-4-methoxybenzoic acid | Benzyl 4-hydroxybenzoate | 4-Dimethylaminopyridine            | <i>N,N'</i> -Dicyclohexylcarbodiimide |
|---------|--|--------------------------|------------------------------------|---------------------------------------|
| 1.1     | 3.00 g, 0.0176 mol   | 5.23 g, 0.0194 mol       | 0.280 g, 2.29×10 <sup>-3</sup> mol | 4.72 g, 0.0229 mol                    |
| 1.2     | *3.00 g, 0.0159 mol  | 3.99 g, 0.0175 mol       | 0.253 g, 2.07×10 <sup>-3</sup>     | 4.27 g, 0.0207 mol                    |

|  |  |  |     |  |
|--|--|--|-----|--|
|  |  |  | mol |  |
|--|--|--|-----|--|

### 1.1 4-[(Benzyloxy)carbonyl]phenyl 2-fluoro-4-methoxybenzoate

White solid. Yield: 4.23 g, 63.2 %. RF: 0.60 (40 % ethyl acetate: 60 % 40:60 petroleum ether). M.P = 78 °C

$\nu_{max}/\text{cm}^{-1}$ : 2848, 1731, 1714, 1682, 1620, 1604, 1578, 1508, 1426, 1345, 1288, 1262, 1197, 1163, 1134, 1111, 1077, 1059, 1025, 956, 924, 882, 843, 779, 763, 754, 681, 653, 624, 541, 502, 460, 430, 415, 406

$\delta_{\text{H}}/\text{ppm}$  (400 MHz,  $\text{CDCl}_3$ ): 8.15 (2 H, d, J 8.6 Hz, Ar-H), 8.05 (1 H, dd, J 8.7 Hz, 8.6 Hz, Ar-H), 7.41 (5 H, m, Ar-H), 7.30 (2 H, d, J 8.6 Hz, Ar-H), 6.80 (1 H, dd, J 8.7 Hz, 2.5 Hz, Ar-H), 6.71 (1 H, dd, J 12.7 Hz, 2.5 Hz, Ar-H), 5.38 (2 H, s, O-CH<sub>2</sub>-Ar), 3.89 (3 H, s, O-CH<sub>3</sub>)

$\delta_{\text{F}}/\text{ppm}$  (376 MHz,  $\text{CDCl}_3$ ): -104.21 (1 F, s, Ar-F)

$\delta_{\text{C}}/\text{ppm}$  (100 MHz,  $\text{CDCl}_3$ ): 165.70, 165.46 (d, J 11.7 Hz), 164.06 (d, J 262.0 Hz), 161.89 (d, J 4.6 Hz), 154.50, 135.97, 133.92 (d, J 2.2 Hz), 131.31, 128.63, 128.30, 128.20, 127.69, 121.86, 110.55 (d, J 2.9 Hz), 109.72 (d, J 9.4 Hz), 102.56 (d, J 25.6 Hz), 66.83, 55.95

### 1.2 4-[(Benzyloxy)carbonyl]phenyl 2,6-difluoro-4-methoxybenzoate

Yellow solid. Yield: 4.91 g, 77.5 %. RF: 0.62 (40 % ethyl acetate: 60 % 40:60 petroleum ether). M.P = 68 °C

$\nu_{max}/\text{cm}^{-1}$ : 1727, 1715, 1625, 1601, 1575, 1507, 1496, 1466, 1455, 1438, 1415, 1379, 1355, 1311, 1277, 1249, 1198, 1164, 1146, 1116, 1099, 1071, 1047, 1034, 1017, 976, 890, 836, 797, 773, 760, 728, 693, 655, 619, 600, 555, 536, 516, 499, 458, 405

$\delta_{\text{H}}/\text{ppm}$  (400 MHz,  $\text{CDCl}_3$ ): 8.15 (2 H, d, J 8.7 Hz, Ar-H), 7.41 (5 H, m, Ar-H), 7.32 (2 H, d, J 8.7 Hz, Ar-H), 6.55 (2 H, d, J 10.3 Hz, Ar-H), 5.38 (2 H, s, O-CH<sub>2</sub>-Ar), 3.87 (3 H, s, O-CH<sub>3</sub>)

$\delta_{\text{F}}/\text{ppm}$  (376 MHz,  $\text{CDCl}_3$ ): -106.08 (2 F, s, Ar-F)

$\delta_{\text{C}}/\text{ppm}$  (100 MHz,  $\text{CDCl}_3$ ): 165.64, 164.26 (t, 14.4 Hz), 161.65 (dd, J 258.2 Hz, 8.3 Hz), 159.30 (t, J 2.9 Hz), 154.16, 135.94, 131.34, 128.63, 128.31, 128.20, 127.93, 121.76, 101.97 (t, J 15.9 Hz), 98.90 (dd, J 26.3 Hz, 3.1 Hz), 66.86, 56.18

## Compound 2

To a pre-dried flask flushed with argon, **Compound 1** (1 eq) was dissolved in a mixture of dichloromethane and ethanol and stirred. The mixture was sparged with argon and 5 % Pd/C catalyst was added. The argon atmosphere was evacuated under vacuum and replaced by hydrogen gas. The quantities of the reagents used in each reaction are listed in **Table S2**. The reaction was allowed to proceed for 4 h at room temperature, with the extent of the reaction monitored by TLC using an appropriate solvent system (RF values quoted in the product data). After the reaction was completed, the hydrogen gas was evacuated under vacuum and the flask purged using argon. The mixture was filtered through Celite using copious amounts of dichloromethane, and the collected solvent was evaporated under vacuum to leave a white solid which was carried forwards without any further purification.



**Table S2.** Quantities of reagents used in the syntheses of **Compound 2**

| Product | Compound 1.1/1.2*   | 5 % Palladium on Carbon            | Dichloromethane | Ethanol |
|---------|---------------------|------------------------------------|-----------------|---------|
| 2.1     | 4.00 g, 0.0105 mol  | 0.223 g, $2.10 \times 10^{-3}$ mol | 70 mL           | 70 mL   |
| 2.2     | *4.70 g, 0.0118 mol | 0.251 g, $2.36 \times 10^{-3}$ mol | 80 mL           | 80 mL   |

**2.1 4-(2-Fluoro-4-methoxybenzoyloxy)benzoic acid**

Yield: 0.878 g, 28.8 %. RF: 0.057 (40 % ethyl acetate: 60 % 40:60 petroleum ether).

T<sub>CrN</sub> 220 °C T<sub>NI</sub> 225 °C

$\nu_{max}/\text{cm}^{-1}$ : 1732, 1713, 1615, 1602, 1579, 1508, 1454, 1440, 1431, 1414, 1377, 1311, 1296, 1277, 1252, 1199, 1164, 1131, 1114, 1050, 1017, 954, 936, 888, 849, 819, 795, 756, 729, 693, 680, 611, 632, 619, 600, 554, 541, 517, 500, 457, 440, 410

$\delta_{\text{H}}/\text{ppm}$  (400 MHz, DMSO- $d_6$ ): 13.05 (1 H, br, (C=O)-OH), 8.04 (3 H, m, Ar-H), 7.38 (2 H, d, J 8.7 Hz, Ar-H), 7.05 (1 H, dd, J 13.2 Hz, 2.4 Hz, Ar-H), 6.97 (1 H, dd, J 8.9 Hz, 2.4 Hz, Ar-H), 3.89 (3 H, s, O-CH<sub>3</sub>)

$\delta_{\text{F}}/\text{ppm}$  (376 MHz, DMSO- $d_6$ ): -105.54 (1 F, s, Ar-F)

$\delta_{\text{C}}/\text{ppm}$  (100 MHz, DMSO- $d_6$ ): 167.22, 165.78 (d, J 12.0 Hz), 163.73 (d, J 259.4 Hz), 161.71 (d, J 4.5 Hz), 154.07, 134.19 (d, J 2.1 Hz), 131.32, 129.62, 122.57, 111.69 (d, J 2.8 Hz), 109.39 (d, J 9.3 Hz), 103.21 (d, J 25.6 Hz), 56.77

**2.2 4-(2,6-Difluoro-4-methoxybenzoyloxy)benzoic acid**

Yield: 1.23 g, 33.8 %. RF: 0.057 (40 % ethyl acetate: 60 % 40:60 petroleum ether).

T<sub>CrN</sub> 228 °C T<sub>NI</sub> 241 °C

$\nu_{max}/\text{cm}^{-1}$ : 2849, 1721, 1684, 1630, 1603, 1578, 1507, 1449, 1424, 1363, 1313, 1288, 1263, 1200, 1152, 1127, 1108, 1084, 1049, 1033, 1015, 961, 920, 884, 838, 779, 760, 683, 650, 629, 581, 559, 554, 526, 502, 449, 413

$\delta_{\text{H}}/\text{ppm}$  (400 MHz, DMSO- $d_6$ ): 13.12 (1 H, br, (C=O)-OH), 8.04 (2 H, d, J 8.7 Hz, Ar-H), 7.39 (2 H, d, J 8.7 Hz, Ar-H), 6.97 (2 H, d, J 11.1 Hz, Ar-H), 3.89 (3 H, s, O-CH<sub>3</sub>)

$\delta_{\text{F}}/\text{ppm}$  (376 MHz, DMSO- $d_6$ ): -106.98 (2 F, s, Ar-F)

$\delta_{\text{C}}/\text{ppm}$  (100 MHz, DMSO- $d_6$ ): 167.05, 164.92 (t, J 15.1 Hz), 162.60 (dd, J 255.5 Hz, 8.7 Hz), 159.30 (t, J 2.8 Hz), 153.77, 131.52, 129.42, 122.46, 101.27 (t, J 16.0 Hz), 99.98 (dd, J 26.2 Hz, 2.9 Hz), 57.21

**Compound 3**

To a pre-dried flask flushed with argon, **Compound 2** (1 eq), 4-nitrophenol (1.2 eq) or 3-fluoro-4-nitrophenol (1.2 eq), and *N,N'*-dicyclohexylcarbodiimide (1.5 eq) were added to the flask. The solids were solubilised with a mixture of dichloromethane (30 mL) and tetrahydrofuran (15 mL) and stirred for 30 min before 4-dimethylaminopyridine (0.15 eq) was added. The quantities of the reagents used in each reaction are listed in **Table S3**. The temperature of the reaction mixture was increased to room temperature and the reaction was allowed to proceed overnight. The white precipitate which formed was removed by vacuum filtration and the filtrate collected. The solvent was removed under vacuum and the crude product was purified using a silica gel column with an appropriate solvent system (RF

values quoted in product data). The eluent fractions of interest were evaporated under vacuum to leave a white solid which was recrystallised from hot ethanol (80 mL).

**Table S3.** Quantities of reagents used in the syntheses of **Compound 3**

| Product | Compound 2.1/2.2*                  | 4-Nitrophenol/*3-Fluoro-4-nitrophenol | <i>N,N'</i> -Dicyclohexylcarbodiimide | 4-Dimethylaminopyridine            |
|---------|------------------------------------|---------------------------------------|---------------------------------------|------------------------------------|
| 3.1     | 0.300 g, $1.03 \times 10^{-3}$ mol | 0.172 g, $1.24 \times 10^{-3}$ mol    | 0.297 g, $1.55 \times 10^{-3}$ mol    | 0.019 g, $1.55 \times 10^{-4}$ mol |
| 3.2     | 0.300 g, $1.03 \times 10^{-3}$ mol | *0.195 g, $1.24 \times 10^{-3}$ mol   | 0.297 g, $1.55 \times 10^{-3}$ mol    | 0.019 g, $1.55 \times 10^{-4}$ mol |
| 3.3     | *0.300 g, $9.73 \times 10^{-4}$    | 0.163 g, $1.17 \times 10^{-3}$ mol    | 0.280 g, $1.46 \times 10^{-3}$ mol    | 0.018 g, $1.46 \times 10^{-4}$ mol |
| 3.4     | *0.300 g, $9.73 \times 10^{-4}$    | *0.184 g, $1.17 \times 10^{-3}$ mol   | 0.280 g, $1.46 \times 10^{-3}$ mol    | 0.018 g, $1.46 \times 10^{-4}$ mol |

### 3.1 4-[(4-Nitrophenoxy)carbonyl]phenyl 2-fluoro-4-methoxybenzoate

Yield: 0.107 g, 25.3 %. RF: 0.272 (100 % dichloromethane).

$T_{CrN}$  207 °C  $T_{N_F N_X}$  (144 °C)  $T_{N_X N}$  (157 °C)  $T_{Ni}$  278 °C

$\nu_{max}/cm^{-1}$ : 1737, 1720, 1625, 1605, 1588, 1578, 1517, 1506, 1484, 1474, 1442, 1432, 1414, 1339, 1268, 1235, 1194, 1165, 1110, 1061, 1017, 964, 954, 892, 862, 836, 819, 754, 726, 693, 681, 663, 641, 628, 543, 505, 486, 479, 457, 422, 414

$\delta_H/ppm$  (400 MHz, DMSO- $d_6$ ): 8.37 (2 H, d, 9.2 Hz, Ar-H), 8.26 (2 H, d, 8.8 Hz, Ar-H), 8.09 (1 H, dd, J 8.8 Hz, 8.7 Hz, Ar-H), 7.66 (2 H, d, 9.2 Hz, Ar-H), 7.55 (2 H, d, 8.8 Hz, Ar-H), 7.07 (1 H, dd, J 13.2 Hz, 2.4 Hz, Ar-H), 6.99 (1 H, dd, J 8.8 Hz, 2.4 Hz, Ar-H), 3.90 (3 H, s, O-CH<sub>3</sub>)

$\delta_F/ppm$  (376 MHz, DMSO- $d_6$ ): -105.44 (1 F, s, Ar-F)

$\delta_C/ppm$  (100 MHz, DMSO- $d_6$ ): 165.90 (d, J 12.1 Hz), 163.81 (d, J 259.4 Hz), 163.72, 161.56 (d, J 4.2 Hz), 155.95, 155.40, 145.69, 134.27 (d, J 1.7 Hz), 132.27, 126.51, 125.80, 123.86, 123.27, 111.74 (d, J 2.7 Hz), 109.24 (d, J 9.1 Hz), 103.24 (d, J 25.5 Hz), 56.81

MS = [M+H]<sup>+</sup>: Calculated for C<sub>21</sub>H<sub>15</sub>NO<sub>7</sub>F: 412.0833. Found: 412.0848. Difference: 3.6 ppm

### 3.2 4-[(3-Fluoro-4-nitrophenoxy)carbonyl]phenyl 2-fluoro-4-methoxybenzoate

Yield: 0.120 g, 27.1 %. RF: 0.324 (100 % dichloromethane).

$T_{CrN}$  192 °C  $T_{N_F N_X}$  (166 °C)  $T_{N_X N}$  (175 °C)  $T_{Ni}$  245 °C

$\nu_{max}/cm^{-1}$ : 1746, 1716, 1615, 1601, 1574, 1548, 1507, 1482, 1443, 1426, 1413, 1341, 1324, 1284, 1267, 1240, 1196, 1164, 1137, 1110, 1093, 1056, 1013, 964, 953, 891, 846, 808, 751, 687, 664, 640, 616, 605, 594, 543, 504, 473, 457, 406

$\delta_{\text{H}}$ /ppm (400 MHz,  $\text{CDCl}_3$ ): 8.26 (2 H, d, 8.7 Hz, Ar-H), 8.20 (1 H, dd, J 8.9 Hz, 8.6 Hz, Ar-H), 8.06 (1 H, dd, 8.7 Hz, 8.6 Hz, Ar-H), 7.42 (2 H, d, 8.7 Hz, Ar-H), 7.30 (1 H, dd, 11.2 Hz, 2.4 Hz, Ar-H), 7.23 (1 H, ddd, J 8.9 Hz, 2.4 Hz, 1.33 Hz, Ar-H), 6.82 (1 H, dd, J 8.9 Hz, 2.4 Hz, Ar-H), 6.73 (1 H, dd, 12.7 Hz, 2.4 Hz, Ar-H), 3.91 (3 H, s, O- $\text{CH}_3$ )

$\delta_{\text{F}}$ /ppm (376 MHz,  $\text{CDCl}_3$ ): -104.01 (1 F, s, Ar-F), -113.05 (1 F, s, Ar-F)

$\delta_{\text{C}}$ /ppm (100 MHz,  $\text{CDCl}_3$ ): 165.66 (d, J 11.7 Hz), 164.13 (d, J 262.2 Hz), 163.03, 161.72 (d, J 4.6 Hz), 156.22 (d, J 267.0 Hz), 155.75, 155.64, 134.89 (d, J 7.1 Hz), 133.96 (d, J 2.1 Hz), 132.06, 127.25 (d, J 2.1 Hz), 125.55, 122.43, 118.09 (d, J 4.0 Hz), 112.41 (d, J 23.9 Hz), 110.66 (d, J 2.9 Hz), 109.44 (d, J 9.3 Hz), 102.61 (d, J 25.7 Hz), 55.99

MS =  $[\text{M}+\text{Na}]^+$ : Calculated for  $\text{C}_{21}\text{H}_{13}\text{NO}_7\text{F}_2\text{Na}$ : 452.0558. Found: 452.0543. Difference: 3.3 ppm

### **3.3 4-[(4-Nitrophenoxy)carbonyl]phenyl 2,6-difluoro-4-methoxybenzoate**

Yield: 0.079 g, 18.9 %. RF: 0.270 (100 % dichloromethane).

$T_{\text{CrN}}$  186 °C  $T_{\text{N}_\text{F}\text{N}_\text{X}}$  (172 °C)  $T_{\text{N}_\text{X}\text{N}}$  (177 °C)  $T_{\text{Ni}}$  265 °C

$\nu_{\text{max}}/\text{cm}^{-1}$ : 1734, 1637, 1615, 1604, 1592, 1577, 1523, 1506, 1491, 1447, 1414, 1350, 1318, 1259, 1207, 1157, 1108, 1084, 1062, 1045, 1029, 1013, 956, 880, 864, 843, 771, 751, 743, 702, 685, 665, 652, 625, 592, 557, 523, 504, 480, 448, 430, 407

$\delta_{\text{H}}$ /ppm (400 MHz,  $\text{CDCl}_3$ ): 8.34 (2 H, d, 9.2 Hz, Ar-H), 8.28 (2 H, d, 8.8 Hz, Ar-H), 7.43 (4 H, m, Ar-H), 6.58 (2 H, d, J 10.3 Hz, Ar-H), 3.89 (3 H, s, O- $\text{CH}_3$ )

$\delta_{\text{F}}$ /ppm (376 MHz,  $\text{CDCl}_3$ ): -105.64 (2 F, s, Ar-F)

$\delta_{\text{C}}$ /ppm (100 MHz,  $\text{CDCl}_3$ ): 164.45 (t, J 14.6 Hz), 163.45, 163.02 (dd, J 258.4 Hz, 8.4 Hz), 159.18 (t, J 2.8 Hz), 155.61, 155.08, 145.49, 132.03, 126.24, 125.32, 122.64, 122.26, 101.73 (t, J 15.7 Hz), 98.97 (dd, J 26.3 Hz, 3.0 Hz), 56.22

MS =  $[\text{M}+\text{H}]^+$ : Calculated for  $\text{C}_{21}\text{H}_{14}\text{NO}_7\text{F}_2$ : 430.0738. Found: 430.0732. Difference: 1.4 ppm

### **3.4 4-[(3-Fluoro-4-nitrophenoxy)carbonyl]phenyl 2,6-difluoro-4-methoxybenzoate**

Yield: 0.092 g, 21.1 %. RF: 0.297 (100 % dichloromethane).

$T_{\text{CrN}_\text{F}}$  181 °C  $T_{\text{N}_\text{F}\text{N}_\text{X}}$  188 °C  $T_{\text{N}_\text{X}\text{N}}$  191 °C  $T_{\text{Ni}}$  231 °C

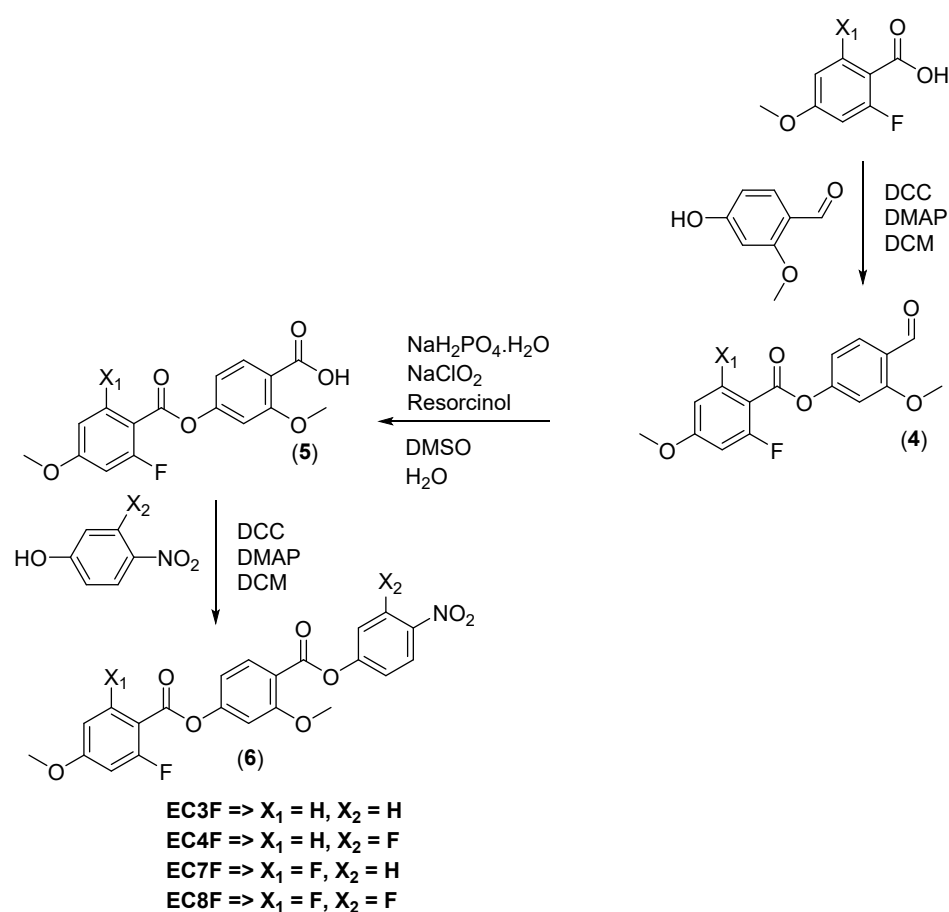
$\nu_{\text{max}}/\text{cm}^{-1}$ : 1741, 1637, 1601, 1578, 1531, 1504, 1484, 1446, 1415, 1347, 1317, 1250, 1207, 1158, 1145, 1093, 1078, 1044, 1027, 1015, 967, 954, 878, 836, 808, 770, 750, 702, 683, 655, 649, 622, 605, 587, 555, 522, 502, 476, 458, 413, 402

$\delta_{\text{H}}$ /ppm (400 MHz,  $\text{CDCl}_3$ ): 8.26 (2 H, d, 8.8 Hz, Ar-H), 8.20 (1 H, dd, J 8.8 Hz, 8.6 Hz, Ar-H), 7.44 (2 H, d, 8.8 Hz, Ar-H), 7.30 (1 H, dd, 11.2 Hz, 2.4 Hz, Ar-H), 7.23 (1 H, ddd, J 8.8 Hz, 2.4 Hz, 1.33 Hz, Ar-H), 6.57 (2 H, d, 10.37 Hz, Ar-H), 3.89 (3 H, s, O- $\text{CH}_3$ )

$\delta_{\text{F}}$ /ppm (376 MHz,  $\text{CDCl}_3$ ): -105.86 (2 F, s, Ar-F), -113.03 (1 F, s, Ar-F)

$\delta_{\text{C}}$ /ppm (100 MHz,  $\text{CDCl}_3$ ): 164.55 (t, J 14.6 Hz), 163.03 (dd, J 258.3 Hz, 8.2 Hz), 162.98, 159.13 (t, J 3.0 Hz), 156.22 (d, J 267.0 Hz), 155.67 (d, J 10.5 Hz), 155.26, 134.91 (d, J 7.2 Hz), 132.10, 127.26 (d, J 2.0 Hz), 125.80, 122.35, 118.09 (d, J 4.0 Hz), 112.41 (d, J 23.8 Hz), 101.67 (t, J 16.0 Hz), 98.98 (dd, J 26.2 Hz, 3.0 Hz), 56.23

MS = [M+H]<sup>+</sup>: Calculated for C<sub>21</sub>H<sub>13</sub>NO<sub>7</sub>F<sub>3</sub>: 448.0644. Found: 448.0626. Difference: 1.8 ppm



Scheme 2. Synthesis of EC3F, EC4F, EC7F and EC8F.

### Compound 4

To a pre-dried flask flushed with argon, 2-fluoro-4-methoxybenzoic acid (1 eq) or 2,6-difluoro-4-methoxybenzoic acid, (1 eq), 4-hydroxy-2-methoxybenzaldehyde (1.1 eq) and 4-dimethylaminopyridine (0.13 eq) were added. The solids were solubilised with dichloromethane (100 mL) and tetrahydrofuran (50 mL) while being stirred for 10 min before *N,N'*-dicyclohexylcarbodiimide (1.3 eq) was added to the flask and the reaction was allowed to proceed overnight. The quantities of the reagents used in each reaction are listed in **Table S4**. The extent of the reaction was monitored by TLC using an appropriate solvent system (RF values quoted in the product data). The precipitate which formed was removed by vacuum filtration and the filtrate collected. The collected solvent was evaporated under vacuum to leave a solid which was recrystallised from hot ethanol (200 mL).

**Table S4.** Quantities of reagents used in the syntheses of **Compound 4**

| Product | 2-Fluoro-4-methoxybenzoic acid/*2,6-Difluoro-4-methoxybenzoic acid | 4-Hydroxy-2-methoxybenzaldehyde | 4-Dimethylaminopyridine | <i>N,N'</i> -Dicyclohexylcarbodiimide |
|---------|--|---------------------------------|-------------------------|---------------------------------------|
|         |  |                                 |                         |                                       |



|     |                     |                    |                                    |                    |
|-----|---------------------|--------------------|------------------------------------|--------------------|
| 4.1 | 3.00 g, 0.0176 mol  | 2.95 g, 0.0194 mol | 0.280 g, $2.29 \times 10^{-3}$ mol | 4.72 g, 0.0229 mol |
| 4.2 | *3.00 g, 0.0159 mol | 2.66 g, 0.0175 mol | 0.253 g, $2.07 \times 10^{-3}$ mol | 4.27 g, 0.0207 mol |

#### 4.1 4-Formyl-3-methoxyphenyl 2-fluoro-4-methoxybenzoate

Yield: 2.88 g, 53.8 %. RF: 0.400 (40 % ethyl acetate: 60 % 40:60 petroleum ether). M.P = 185 °C

$\nu_{\max}/\text{cm}^{-1}$ : 1737, 1675, 1620, 1605, 1589, 1574, 1503, 1470, 1457, 1445, 1436, 1416, 1396, 1309, 1245, 1239, 1194, 1171, 1154, 1141, 1100, 1051, 1024, 950, 883, 867, 829, 816, 795, 758, 738, 685, 664, 612, 584, 555, 524, 484, 463, 442, 431, 419, 410

$\delta_{\text{H}}/\text{ppm}$  (400 MHz,  $\text{CDCl}_3$ ): 10.42 (1 H, s, (C=O)-H), 8.05 (1 H, dd, J 8.7 Hz, 8.6 Hz, Ar-H), 7.90 (1 H, d, J 9.0 Hz, Ar-H), 6.91 (2 H, m, Ar-H), 6.80 (1 H, dd, J 9.0 Hz, 2.5 Hz, Ar-H), 6.71 (1 H, dd, J 12.7 Hz, 2.5 Hz, Ar-H), 3.94 (3 H, s, O-CH<sub>3</sub>), 3.90 (3 H, s, O-CH<sub>3</sub>)

$\delta_{\text{F}}/\text{ppm}$  (376 MHz,  $\text{CDCl}_3$ ): -104.14 (1 F, s, Ar-F)

$\delta_{\text{C}}/\text{ppm}$  (100 MHz,  $\text{CDCl}_3$ ): 188.67, 165.59 (d, J 11.6 Hz), 164.10 (d, J 262.1 Hz), 162.82, 161.69 (d, J 4.6 Hz), 156.80, 133.93 (d, J 2.2 Hz), 129.89, 122.68, 114.33, 110.62 (d, J 3.0 Hz), 109.53 (d, J 9.3 Hz), 105.79, 102.59 (d, J 25.8 Hz), 55.97, 55.94

#### 4.2 4-Formyl-3-methoxyphenyl 2,6-difluoro-4-methoxybenzoate

Yield: 3.31 g, 64.6 %. RF: 0.514 (40 % ethyl acetate: 60 % 40:60 petroleum ether). M.P = 176 °C

$\nu_{\max}/\text{cm}^{-1}$ : 1747, 1732, 1672, 1633, 1604, 1575, 1491, 1469, 1446, 1416, 1399, 1358, 1252, 1213, 1194, 1152, 1103, 1084, 1046, 1025, 958, 941, 873, 828, 817, 799, 775, 737, 665, 650, 620, 590, 527, 487, 457, 414

$\delta_{\text{H}}/\text{ppm}$  (400 MHz,  $\text{CDCl}_3$ ): 10.42 (1 H, s, (C=O)-H), 7.90 (1 H, d, J 9.0 Hz, Ar-H), 6.92 (2 H, m, Ar-H), 6.56 (1 H, d, J 10.4 Hz, Ar-H), 3.94 (3 H, s, O-CH<sub>3</sub>), 3.87 (3 H, s, O-CH<sub>3</sub>)

$\delta_{\text{F}}/\text{ppm}$  (376 MHz,  $\text{CDCl}_3$ ): -105.93 (2 F, s, Ar-F)

$\delta_{\text{C}}/\text{ppm}$  (100 MHz,  $\text{CDCl}_3$ ): 188.65, 164.41 (t, J 14.6 Hz), 162.99 (dd, J 258.3 Hz, 8.3 Hz), 162.82, 159.09 (t, J 3.0 Hz), 156.40, 129.92, 122.84, 114.22, 105.68, 101.75 (t, J 15.7 Hz), 98.95 (dd, J 26.4 Hz, 3.1 Hz), 56.21, 55.98

#### Compound 5

To a pre-dried flask flushed with argon, **Compound 4** (1 eq) and resorcinol (1.5 eq) were solubilised in tetrahydrofuran (80 mL) and *N,N'*-dimethylformamide (60 mL). Sodium chlorite (4 eq) and sodium hydrogen phosphate monohydrate (3.5 eq) were solubilised in water (60 mL) before being slowly added to into the reaction flask and the resultant mixture was stirred at room temperature overnight. The quantities of the reagents used in each reaction are listed in **Table S5**. The extent of the reaction was monitored by TLC using an appropriate solvent system (RF values quoted in the product data). The reaction mixture was diluted with water (300 mL) and the pH of the mixture was adjusted to 1 using 32% hydrochloric acid (25 mL). A white solid precipitated after acidification which was collected by vacuum filtration and recrystallised from hot ethanol (200 mL).

**Table S5.** Quantities of reagents used in the syntheses of the **Compound 5**

| Product | Compound 4.1/4.2*                  | Sodium Chlorite    | Sodium Hydrogen Phosphate Monohydrate | Resorcinol         |
|---------|------------------------------------|--------------------|---------------------------------------|--------------------|
| 5.1     | 2.60 g, $8.55 \times 10^{-3}$ mol  | 3.09 g, 0.0342 mol | 4.13 g, 0.0299 mol                    | 1.41 g, 0.0128 mol |
| 5.2     | *3.00 g, $9.31 \times 10^{-3}$ mol | 3.36 g, 0.0372 mol | 4.50 g, 0.0326 mol                    | 1.54 g, 0.0140 mol |

**5.1 4-((2-Fluoro-4-methoxybenzoyl)oxy)-2-methoxybenzoic acid**

Yield: 1.75 g, 63.9 %. RF: 0.086 (40 % ethyl acetate: 60 % 40:60 petroleum ether). M.P = 205 °C

$\nu_{\max}/\text{cm}^{-1}$ : 2980, 1741, 1719, 1698, 1624, 1607, 1576, 1515, 1463, 1435, 1402, 1308, 1253, 1188, 1163, 1148, 1131, 1102, 1050, 1021, 953, 869, 838, 812, 795, 771, 758, 739, 684, 658, 632, 615, 596, 555, 524, 464, 440, 410

$\delta_{\text{H}}/\text{ppm}$  (400 MHz, DMSO- $d_6$ ): 12.66 (1 H, br, (C=O)-OH), 8.05 (1 H, dd, J 8.9 Hz, 8.7 Hz, Ar-H), 7.74 (1 H, d, J 8.4 Hz, Ar-H), 6.99 (4 H, m, Ar-H), 3.89 (3 H, s, O-CH<sub>3</sub>), 3.82 (3 H, s, O-CH<sub>3</sub>)

$\delta_{\text{F}}/\text{ppm}$  (376 MHz, DMSO- $d_6$ ): -105.51 (1 F, s, Ar-F)

$\delta_{\text{C}}/\text{ppm}$  (100 MHz, DMSO- $d_6$ ): 167.04, 165.76 (d, J 12.0 Hz), 163.73 (d, J 259.5 Hz), 161.65 (d, J 4.5 Hz), 159.89, 154.47, 134.21 (d, J 2.1 Hz), 132.32, 119.19, 114.08, 111.66 (d, J 2.6 Hz), 109.41 (d, J 9.3 Hz), 107.30, 103.18 (d, J 25.5 Hz), 56.77, 56.59

**5.2 4-((2,6-Difluoro-4-methoxybenzoyl)oxy)-2-methoxybenzoic acid**

Yield: 2.11 g, 67.0 %. RF: 0.023 (30 % ethyl acetate: 70 % 40:60 petroleum ether). M.P = 198 °C

$\nu_{\max}/\text{cm}^{-1}$ : 2978, 1750, 1698, 1671, 1637, 1607, 1580, 1496, 1476, 1460, 1436, 1402, 1359, 1306, 1254, 1202, 1185, 1149, 1135, 1103, 1079, 1048, 1033, 1022, 949, 915, 877, 841, 817, 794, 774, 740, 688, 658, 620, 597, 587, 565, 525, 422, 413

$\delta_{\text{H}}/\text{ppm}$  (400 MHz, DMSO- $d_6$ ): 12.70 (1 H, br, (C=O)-H), 7.75 (1 H, d, J 8.4 Hz, Ar-H), 7.06 (1 H, d, J 2.0 Hz, Ar-H), 6.97 (2 H, d, J 11.5 Hz, Ar-H), 6.90 (1 H, dd, J 8.4 Hz, 2.0 Hz, Ar-H), 3.89 (3 H, s, O-CH<sub>3</sub>), 3.83 (3 H, s, O-CH<sub>3</sub>)

$\delta_{\text{F}}/\text{ppm}$  (376 MHz, DMSO- $d_6$ ): -106.69 (2 F, s, Ar-F)

$\delta_{\text{C}}/\text{ppm}$  (100 MHz, DMSO- $d_6$ ): 166.98, 164.91 (t, J 15.1 Hz), 162.65 (dd, J 255.7 Hz, 8.6 Hz), 159.93, 159.24 (t, J 3.0 Hz), 153.98, 132.44, 119.51, 113.83, 107.03, 101.27 (t, J 15.8 Hz), 99.97 (dd, J 26.3, 2.9 Hz), 57.21, 56.62

**Compound 6**

To a pre-dried flask flushed with argon, **Compound 5** (1 eq), 4-nitrophenol (1.2 eq) or 3-fluoro-4-nitrophenol (1.2 eq), and *N,N'*-dicyclohexylcarbodiimide (1.5 eq) were added to the flask. The solids were solubilised with dichloromethane (30 mL) and stirred for 30 min before 4-dimethylaminopyridine (0.15 eq) was added. The quantities of the reagents used in each reaction are listed in **Table S6**. The temperature of the reaction mixture was increased to room temperature and the reaction was

allowed to proceed overnight. The white precipitate which formed was removed by vacuum filtration and the filtrate collected. The solvent was removed under vacuum and the crude product was purified using a silica gel column with an appropriate solvent system (RF values quoted in product data). The eluent fractions of interest were evaporated under vacuum to leave a white solid which was recrystallised from hot ethanol (80 mL).

**Table S6.** Quantities of reagents used in the syntheses of the **Compound 6**

| Product | Compound 5.1/5.2*                  | 4-Nitrophenol/*3-Fluoro-4-nitrophenol | <i>N,N'</i> -Dicyclohexylcarbodiimide | 4-Dimethylaminopyridine            |
|---------|------------------------------------|---------------------------------------|---------------------------------------|------------------------------------|
| 6.1     | 0.300 g, $9.37 \times 10^{-4}$ mol | 0.156 g, $1.12 \times 10^{-3}$ mol    | 0.270 g, $1.41 \times 10^{-3}$ mol    | 0.017 g, $1.41 \times 10^{-4}$ mol |
| 6.2     | 0.300 g, $9.37 \times 10^{-4}$ mol | *0.176 g, $1.12 \times 10^{-3}$ mol   | 0.270 g, $1.41 \times 10^{-3}$ mol    | 0.017 g, $1.41 \times 10^{-4}$ mol |
| 6.3     | *0.300 g, $8.87 \times 10^{-4}$    | 0.147 g, $1.33 \times 10^{-3}$ mol    | 0.255 g, $1.33 \times 10^{-3}$ mol    | 0.016 g, $1.33 \times 10^{-4}$ mol |
| 6.4     | *0.300 g, $8.87 \times 10^{-4}$    | *0.167 g, $1.33 \times 10^{-3}$ mol   | 0.255 g, $1.33 \times 10^{-3}$ mol    | 0.016 g, $1.33 \times 10^{-4}$ mol |

### 6.1 3-Methoxy-4-((4-nitrophenoxy)carbonyl)phenyl 2-fluoro-4-methoxybenzoate

Yield: 0.062 g, 15.0 %. RF: 0.485 (1 % ethyl acetate: 99 % dichloromethane).

$T_{CrN}$  169 °C  $T_{NfN}$  (156 °C)  $T_{Ni}$  177 °C

$\nu_{max}/cm^{-1}$ : 1720, 1710, 1628, 1607, 1584, 1577, 1519, 1491, 1478, 1454, 1445, 1433, 1414, 1344, 1316, 1286, 1272, 1237, 1208, 1184, 1162, 1112, 1058, 1023, 951, 879, 862, 837, 810, 762, 744, 683, 670, 651, 635, 622, 612, 587, 530, 500, 461, 418, 411

$\delta_H/ppm$  (400 MHz, DMSO- $d_6$ ): 8.35 (2 H, d, J 9.2 Hz, Ar-H), 8.08 (2 H, m, Ar-H), 7.59 (2 H, d, J 9.2 Hz, Ar-H), 7.26 (1 H, d, J 2.1 Hz, Ar-H), 7.06 (2 H, m, Ar-H), 6.99 (1 H, dd, J 8.9 Hz, 2.5 Hz, Ar-H), 3.90 (3 H, s, O-CH<sub>3</sub>), 3.89 (3 H, s, O-CH<sub>3</sub>)

$\delta_F/ppm$  (376 MHz, DMSO- $d_6$ ): -105.40 (1 F, s, Ar-F)

$\delta_C/ppm$  (100 MHz, DMSO- $d_6$ ): 165.87 (d, J 11.8 Hz), 163.80 (d, J 259.4 Hz), 162.67, 161.47 (d, J 4.5 Hz), 161.25, 156.11, 155.98, 145.54, 134.28 (d, J 1.8 Hz), 133.66, 125.77, 123.87, 115.62, 114.59, 111.71 (d, J 2.3 Hz), 109.28 (d, J 9.2 Hz), 107.80, 103.22 (d, J 25.6 Hz), 56.98, 56.80

MS = [M+Na]<sup>+</sup>: Calculated for C<sub>22</sub>H<sub>16</sub>NO<sub>8</sub>FNa: 464.0758. Found: 464.0781. Difference: 5.0 ppm

### 6.2 3-Methoxy-4-((3-fluoro-4-nitrophenoxy)carbonyl)phenyl 2-fluoro-4-methoxybenzoate

Yield: 0.083 g, 19.3 %. RF: 0.455 (1 % ethyl acetate: 99 % dichloromethane).

$T_{CrI}$  172 °C  $T_{NfI}$  (153 °C)

$\nu_{max}/\text{cm}^{-1}$ : 1748, 1718, 1627, 1604, 1585, 1523, 1497, 1474, 1449, 1430, 1406, 1343, 1264, 1221, 1197, 1187, 1159, 1125, 1113, 1088, 1072, 1013, 970, 954, 877, 845, 833, 810, 763, 755, 743, 678, 659, 628, 610, 573, 558, 535, 458, 403

$\delta_{\text{H}}/\text{ppm}$  (400 MHz,  $\text{CDCl}_3$ ): 8.18 (1 H, dd, J 8.9 Hz, 8.7 Hz, Ar-H), 8.09 (2 H, m, Ar-H), 7.28 (1 H, dd, J 11.4 Hz, 2.4 Hz, Ar-H), 7.21 (1 H, ddd, J 8.9 Hz, 2.5 Hz, 1.3 Hz, Ar-H), 6.97 (2 H, m, Ar-H), 6.82 (1 H, dd, J 8.9 Hz, 2.5 Hz, Ar-H), 6.73 (1 H, dd, J 12.7 Hz, 2.4 Hz, Ar-H), 3.97 (3 H, s, O- $\text{CH}_3$ ), 3.91 (3 H, s, O- $\text{CH}_3$ )

$\delta_{\text{F}}/\text{ppm}$  (376 MHz,  $\text{CDCl}_3$ ): -104.03 (1 F, s, Ar-F), -113.37 (1 F, s, Ar-F)

$\delta_{\text{C}}/\text{ppm}$  (100 MHz,  $\text{CDCl}_3$ ): 165.68 (d, J 11.8 Hz), 164.14 (d, J 262.1 Hz), 161.85, 161.79, 161.66 (d, J 4.6 Hz), 156.40, 156.22 (d, J 266.5 Hz), 155.92 (d, J 10.5 Hz), 134.67 (d, J 7.0 Hz), 133.96 (d, J 2.2 Hz), 133.77, 127.11 (d, J 2.1 Hz), 118.20 (d, J 3.9 Hz), 114.60, 113.89, 112.45 (d, J 23.7 Hz), 110.68 (d, J 2.8 Hz), 109.43 (d, J 9.3 Hz), 106.48, 102.61 (d, J 25.6 Hz), 56.38, 56.00

MS =  $[\text{M}+\text{Na}]^+$ : Calculated for  $\text{C}_{22}\text{H}_{15}\text{NO}_8\text{F}_2\text{Na}$ : 482.0663. Found: 482.0670. Difference: 1.5 ppm

### **6.3 3-Methoxy-4-((4-nitrophenoxy)carbonyl)phenyl 2,6-difluoro-4-methoxybenzoate**

Yield: 0.073 g, 17.9 %. RF: 0.368 (1 % ethyl acetate: 99 % dichloromethane).

$T_{\text{CrI}}$  167 °C  $T_{\text{NfI}}$  (159 °C)

$\nu_{max}/\text{cm}^{-1}$ : 1737, 1637, 1611, 1580, 1517, 1490, 1447, 1408, 1346, 1321, 1256, 1204, 1186, 1152, 1134, 1086, 1048, 1023, 958, 878, 864, 844, 758, 744, 685, 671, 653, 642, 610, 594, 544, 533, 520, 499, 418, 402

$\delta_{\text{H}}/\text{ppm}$  (400 MHz,  $\text{DMSO}-d_6$ ): 8.35 (2 H, d, J 9.0 Hz, Ar-H), 8.10 (1 H, d, J 8.6 Hz, Ar-H), 7.60 (1 H, d, J 9.0 Hz, Ar-H), 7.22 (1 H, d, J 2.1 Hz, Ar-H), 7.05 (1 H, dd, J 8.6 Hz, 2.1 Hz, Ar-H), 7.00 (2 H, m, Ar-H), 3.91 (3 H, s, O- $\text{CH}_3$ ), 3.90 (3 H, s, O- $\text{CH}_3$ )

$\delta_{\text{F}}/\text{ppm}$  (376 MHz,  $\text{DMSO}-d_6$ ): -106.40 (2 F, s, Ar-F),

$\delta_{\text{C}}/\text{ppm}$  (100 MHz,  $\text{DMSO}-d_6$ ): 165.05 (t, J 15.0 Hz), 162.76 (dd, J 256.0 Hz, 8.5 Hz), 162.63, 161.28, 159.07 (t, J 3.2 Hz), 155.95, 155.59, 145.56, 133.79, 125.78, 123.87, 115.92, 114.34, 107.54, 101.17 (t, J 15.8 Hz), 100.03 (dd, J 26.4 Hz, 2.7 Hz), 57.25, 57.01

MS =  $[\text{M}+\text{H}]^+$ : Calculated for  $\text{C}_{22}\text{H}_{16}\text{NO}_8\text{F}_2$ : 460.0844. Found: 460.0858. Difference: 3.0 ppm

### **6.4 3-Methoxy-4-((3-fluoro-4-nitrophenoxy)carbonyl)phenyl 2,6-difluoro-4-methoxybenzoate**

Yield: 0.130 g, 30.7 %. RF: 0.417 (1 % ethyl acetate: 99 % dichloromethane).

$T_{\text{CrI}}$  162 °C  $T_{\text{NfI}}$  (149 °C)

$\nu_{max}/\text{cm}^{-1}$ : 1744, 1717, 1638, 1609, 1578, 1532, 1493, 1474, 1456, 1448, 1413, 1348, 1314, 1286, 1251, 1230, 1202, 1146, 1112, 1098, 1083, 1058, 1043, 1025, 968, 954, 877, 839, 811, 772, 760, 745, 679, 644, 625, 605, 586, 577, 515, 456, 421, 411

$\delta_{\text{H}}/\text{ppm}$  (400 MHz,  $\text{DMSO}-d_6$ ): 8.30 (1 H, dd, J 8.9 Hz, 8.8 Hz, Ar-H), 8.11 (1 H, d, J 8.6 Hz, Ar-H), 7.73 (1 H, dd, J 12.0 Hz, 2.4 Hz, Ar-H), 7.43 (1 H, ddd, J 8.9 Hz, 2.4 Hz, 1.2 Hz, Ar-H), 7.22 (1 H, d, J 2.1 Hz, Ar-H), 7.05 (1 H, dd, J 8.6 Hz, 2.1 Hz, Ar-H), 7.00 (1 H, d, 11.2 Hz, Ar-H), 3.91 (3 H, s, O- $\text{CH}_3$ ), 3.90 (3 H, s, O- $\text{CH}_3$ )

$\delta_{\text{F}}/\text{ppm}$  (376 MHz,  $\text{DMSO}-d_6$ ): -106.37 (2 F, s, Ar-F), -115.41 (1 F, s, Ar-F)

$\delta_c$ /ppm (100 MHz, DMSO- $d_6$ ): 165.06 (t, J 15.3 Hz), 163.21 (dd, J 255.9 Hz, 8.4 Hz), 162.10, 161.48, 159.05 (t, J 3.1 Hz), 156.06 (d, J 11.1 Hz), 155.77, 155.73 (d, J 262.8 Hz), 135.08 (d, J 7.3 Hz), 133.98, 127.97 (d, J 1.8 Hz), 119.73 (d, J 3.8 Hz), 115.45, 114.36, 113.29 (d, J 23.7 Hz), 107.57, 101.07 (t, J 15.7 Hz), 100.03 (dd, J 26.1 Hz, 2.7 Hz), 57.25, 57.02

MS =  $[M+Na]^+$ : Calculated for  $C_{22}H_{14}NO_8F_3Na$ : 500.0569. Found: 500.0571. Difference: 0.4 ppm