Volume 1 | Number 1 | Jan 2013 | Pages 1–100

Organic & Biomolecular Chemistry

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Fluorinated liquid crystals: Evaluation of selectively fluorinated facially polarised cyclohexyl motifs for liquid crystal applications

Abstract

This paper explores the synthesis of a series of prototype negative dielectric liquid crystalline (LC) compounds which contain fluorinated cyclohexane motifs. The series are analogues and differ only in that they contain between one to four fluorine atoms. The stereochemistry is such that all of the fluorines/C-F bonds are on one face of the cyclohexane ring. This follows from the recent recognition that cyclohexanes with fluorines orientated in one direction, perpendicular to the ring have a strong molecular dipole, a characteristic that might be an advantage in the design of negative dielectric materials. However it is found that the increased polarity, particularly with two or more oriented C-F bonds, leads to higher melting points and poorer solubility in test matrix formulations, relative to hydrocarbon liquid crystals. This arises due to electrostatic intermolecular interactions between the polarised cyclohexyl and aryl rings. The study highlights that in order to take advantage of these polar cyclohexane motifs for liquid crystal design, appropriate scaffolds are required which are free of aromatic rings and contain peripheral solubilising motifs.

Introduction:

Developments in organic liquid crystals (LCs) technology have been a key element in the

transformational impact of screen displays and personal mobile devices.[1,2] A key challenge is

to prepare molecules which display macromolecular organisation, and which possess an

orientated dipole that can orient rapidly in electric and magnetic fields.[3] Fluorinated

compounds can contribute some of these characteristics if correctly designed.[4,5] The C-F

bond is the most polar in organic chemistry, and the high electronegativity and low

polarizability of fluorine reduces intermolecular interactions and lowers fluxional viscosity

parameters.[6] Thus selectively fluorinated organics such as **1** and **2** have found a role in

modern liquid crystal technology. [1-5] In the case of **1** the fluorine atoms induce a dipole along

the molecular axis; this is known as a +ve dielectric anisotropic liquid crystalline material.[7]

2

An alternative design has the polar substituent perpendicular to the molecular axis such as that found in structure **2**. This is known as a –ve dielectric anisotropic liquid crystalline material, a category of LC that is attracting increasing attention.[8,9]
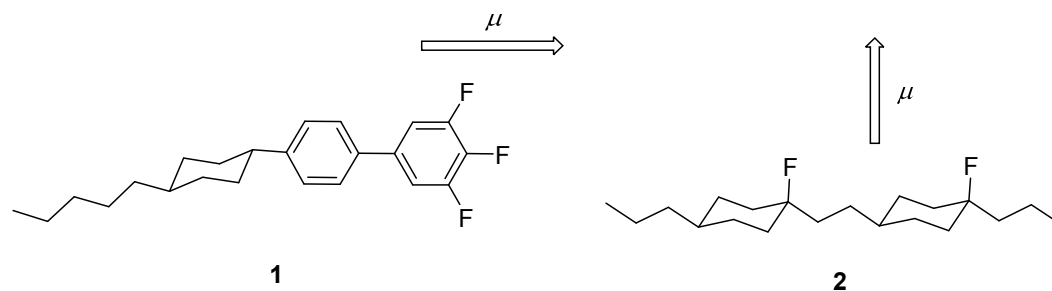

Figure 1: Selectively fluorinated liquid crystalline materials. Compound **1** is an example of a +ve dielectric anisotropic liquid crystal and **2** a –ve dielectric anisotropic liquid crystal.[1,2]
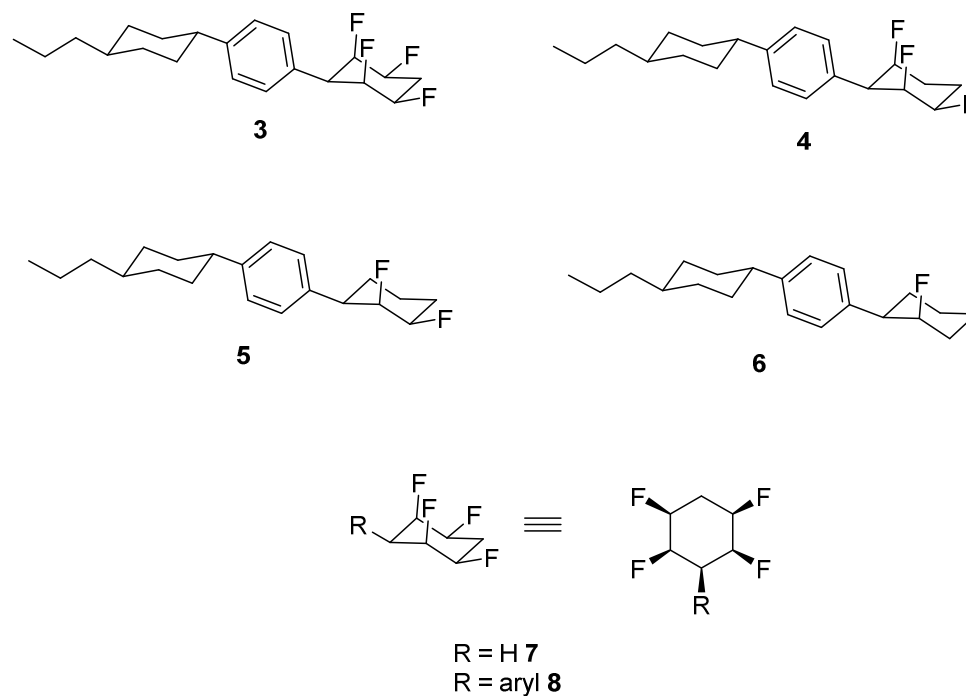

Figure 2: Synthetic targets **3-6** distinguished by having either four, three, two or one C-F bonds on one face of the cyclohexane ring.

2

3

This paper explores compounds **3-6** in the context of preparing prototype –ve dielectric LC properties. In this regard we have recently introduced the all-*cis* 1,2,4,5-tetrafluorocyclohexyl **7** motif and some derivatives such as **8** containing this novel cyclohexane.[10-15] A striking feature of the ring system is that it is facially polarised. There are always two C-F bonds running parallel and 1,3-diaxial to each other, and the other two fluorines are equatorial, but they remain on the same face of the cyclohexyl ring. Thus due to the electronegativity of fluorine, the molecule is polarised perpendicular to the cyclohexane ring. It occurred that if the motif were incorporated into a LC, it would introduce a dipole perpendicular to the molecular axis, attractive in the design of –ve dielectric anisotropic LC's. In this context the tetrafluorocyclohexyl LC **3** became a synthetic target. One feature which has emerged with compounds containing this ring system is that the high polarity of the cyclohexyl ring renders them poorly soluble in non-polar organic solvents. Doped LC's have to function in a cocktail of other hydrophobic hydrocarbon components, therefore co-solubility in the LC matrix is also a necessary design feature, and this was required to be explored. Thus we also set LC-s **4-6** as synthetic targets, as they progressively remove a fluorine from the ring system. Although this will reduce polarity, it was anticipated that it may increase co-solubility. This paper describes the synthesis of LC's **3-6** and reports an initial assessment of the motif as a component in LC design.

Results and discussion.

A synthetic route to LC-**3** is shown in Scheme 1. The route started with a palladium catalysed ([Pd(IPr)(cin)Cl], KOBu-*t*) Suzuki coupling reaction between phenylboronic acid **10** and 1-bromo-4-(trans-4-propylcyclohexyl)benzene **9**,[16] a reaction which was found to proceed well and gave biphenyl **11** in good yield. Birch reduction[17] of **11** followed by epoxidation of the product diene **12**, using an excess of *m*CPBA.[18,19] This furnished *cis*-diepoxide **13** as a single diastereoisomer and with the stereochemistry as shown. This was confirmed by X-ray

crystallography (See SI). Nucleophilic ring-opening of the epoxide rings of **13** with $Et_3N \cdot 3HF$ led to the formation of a 1:1.6 mix of the fluorohydrin regioisomers **14** and **15**, with a bias towards the asymmetric product **15**.[14] This product was taken as a mixture and was converted to the corresponding ditriflates **16** and **17**.[18,20] Without further purification the ditriflate mixture was treated with an excess of $Et_3N \cdot 3HF$, under forcing conditions, to generate tetrafluorocyclohexane **3**.[20,21] This reaction however generated olefin **18** as the major product, a compound which arises *via* an aryl migration after an elimination to give **19**, and then *via* phenonium **20** rearrangement, as previously described for closely related transformations.[10,14]

To gain a deeper insight into the course of the reaction, ditriflates **16** and **17** were separated and their individual structures were elucidated by ^{1}H and ^{19}F NMR and by X-ray crystallography (See SI). When **16** was treated under the same conditions only the desired tetrafluorocyclohexane **3** was formed. Conversely, treatment of ditriflate **17** with $Et_3N \cdot 3HF$ furnished trifluorocyclohexene **18**, with only traces of **3** ($\approx$2%) as shown in Scheme 1. Thus each ditriflate isomer contributes a single product isomer. Controlled elimination of the asymmetric ditriflate **17** with DBU efficiently generated difluorocyclohexene **19**.[22] This was a crystalline compound and the structure and stereochemistry was supported by X-ray structure analysis (see SI). Palladium catalysed hydrogenation of **19** gave difluorocyclohexane **21** in almost quantitative yield. Treatment of **20** with $Et_3N.3HF$ under the same conditions furnished the all-*cis* trifluorocyclohexane **4** as a single isomer, this time with an inversion of configuration as shown in Scheme 2. Furthermore, treatment of fluorohydrin mixture **14** and **15** with triflic anhydride (4 equiv) in pyridine afforded symmetric ditriflate **16** and monotriflate **19** in a 4:6 ratio. Separation of the triflates, and then treatment of **19** with $Et_3N \cdot 3HF$, generated the trifluorocyclohexene **18**. This reaction occurs with a retention of configuration and as a single isomer (Scheme 1). These observations are consistent with the presence of the double bond in **19** forcing a half-chair conformation, in

which the aryl and triflate moieties at C-6 and C-5 respectively, are positioned *anti-periplanar* to each other, and this accommodates aryl migration *via* a phenonium ion **20**.[14]
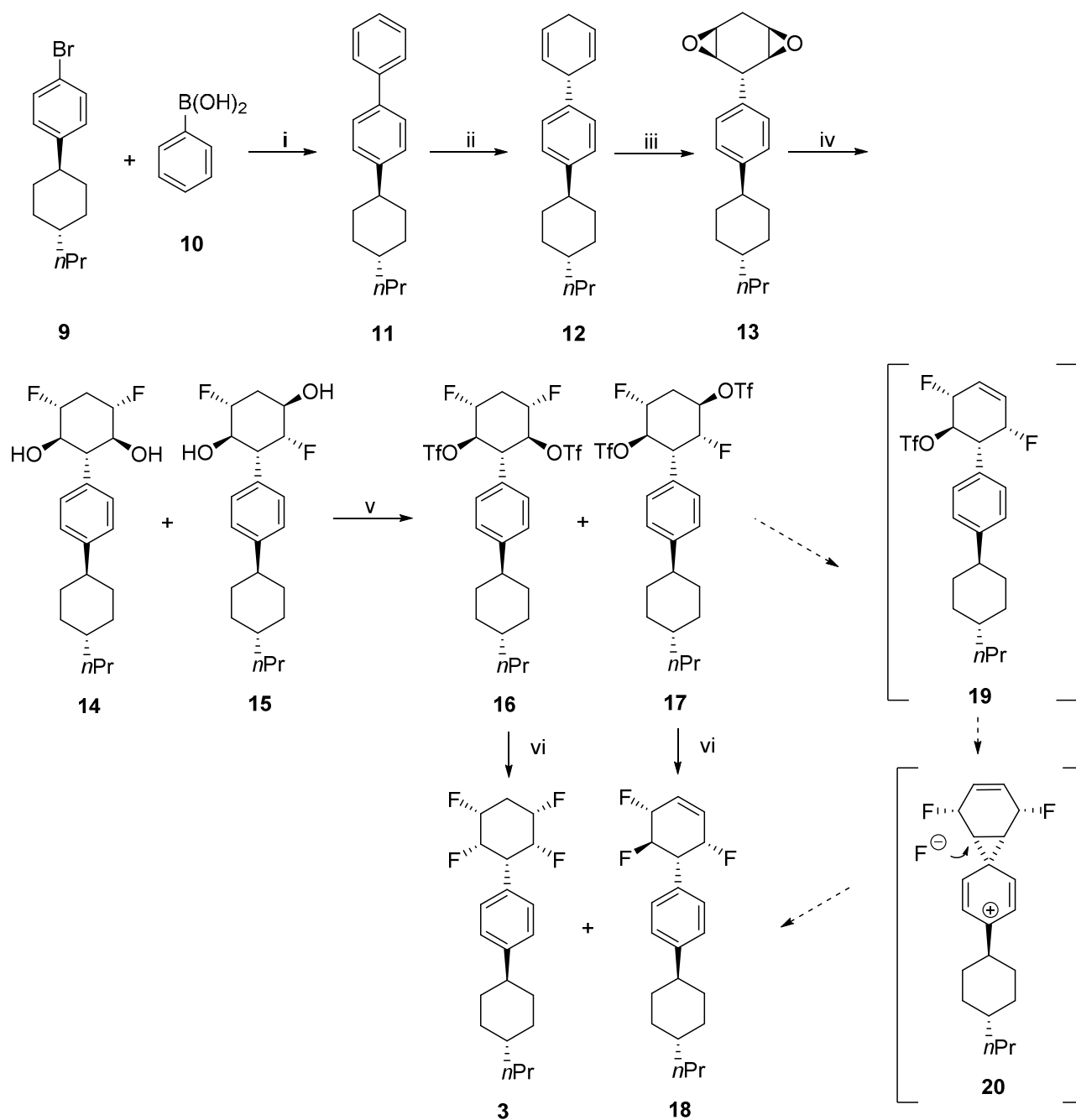

Scheme 1. i) [Pd(IPr)(cin)Cl], i-PrOH, KOBu-*t*, rt, overnight, 80%; ii) Li, NH$_3$, THF, -78 ^{o}C to 40 ^{o}C, 4h, 92%; iii) *m*CPBA, DCM, 0 ^{o}C, 5h, 89%; iv) Et$_3$N·3HF, 145 ^{o}C, 20h, 2:3 ratio; v) Tf$_2$O, pyridine, DCM, 0 ^{o}C, 5h, 41% for **16** and 56% for **17**; vi) Et$_3$N·3HF, 100 ^{o}C, 56h.
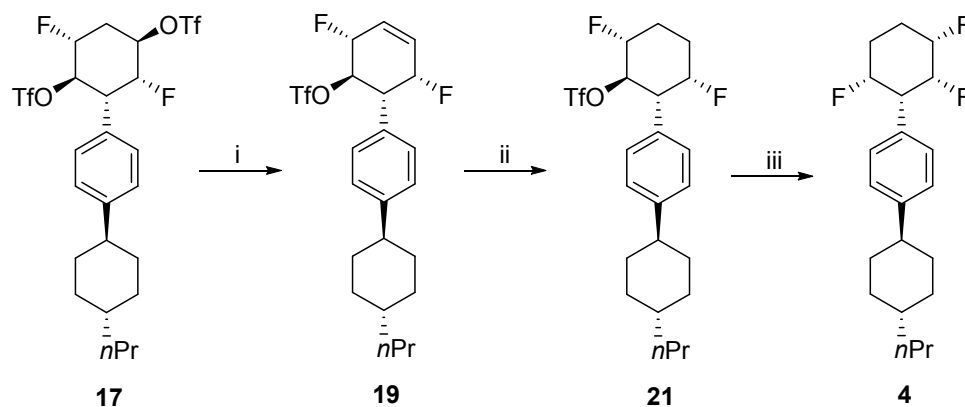
Scheme 2. i) DBU, THF, 0 °C, 5h, 98%; ii) H$_2$, 10% Pd/C, EtOAc, rt, 15h, 100%; iii) Et$_3$N.3HF,100 °C, 56h, 84%.

The synthesis of **5** and **6** started with the preparation of alkene **23** by sequential Miyaura borylation[23] followed by a Miyaura-Suzuki[24-26] coupling as indicated in Scheme 3. Palladium (Pd$_2$(dba)$_3$/XPhos) catalysed borylation of **9** with bis(pinocolate)diborane gave pinacolboronate **22** in good yield. Suzuki coupling of **22** with cyclohex-2-enyl acetate in MeOH proceeded in the presence Pd(dba)$_2$ and KF to afford alkene **23**, which in turn was treated with an excess of *m*CBPA at 0 °C to give epoxide **24** in 82% yield.[18,21] The epoxide was subjected to ring opening/fluorination with Et$_3$N.3HF at 140 °C giving a 4:5 mixture of the fluorohydrins **25** and **26** respectively. Treatment with Tf$_2$O in pyridine generated 3-fluoro-3-*O*-triflatecyclohexane **27** and monofluorocyclohexene **28** and which could be separated by chromatography. Displacement of the triflate moiety of **27** with fluoride was achieved using Et$_3$N·3HF to give *cis*-difluorocyclohexane **5**. The monofluorocyclohexane **6** was the prepared by hydrogenation of fluorocyclohexene **28** in good yield and high purity.
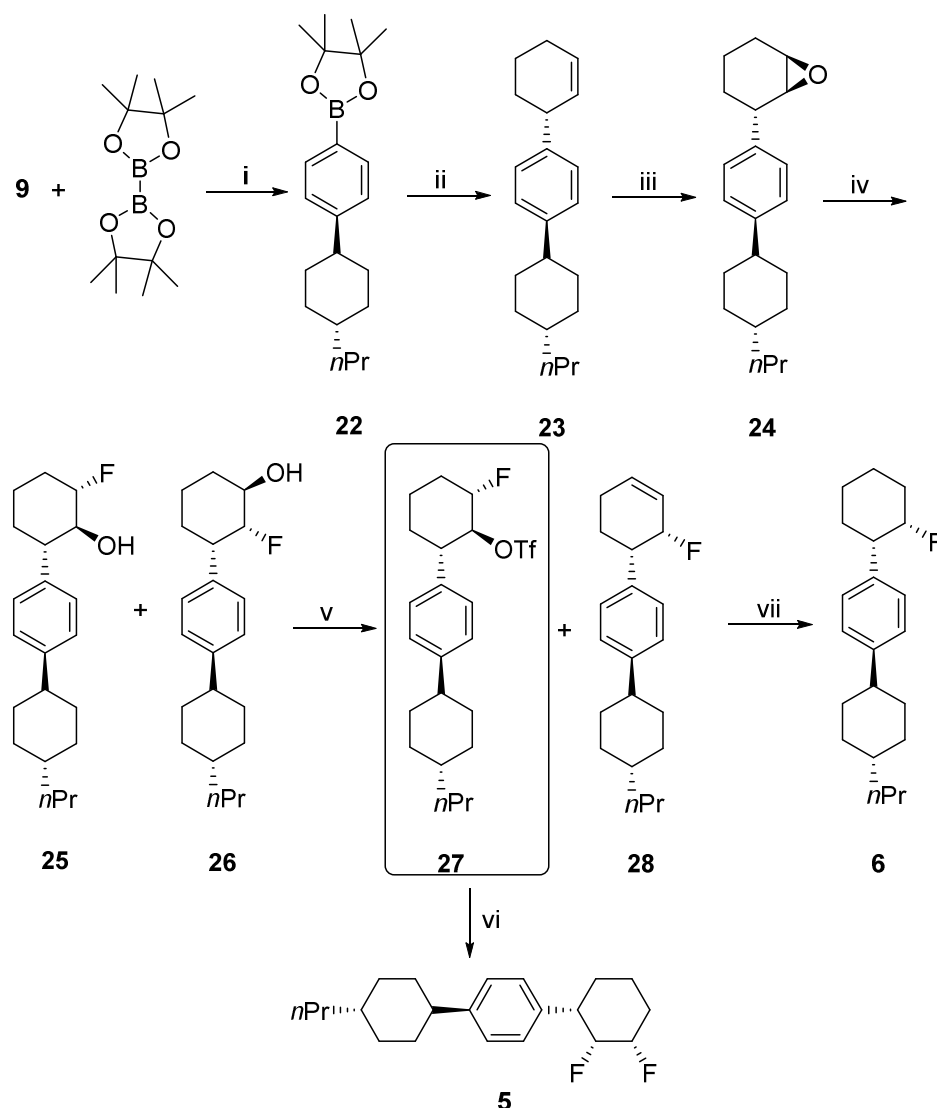
Scheme 3. i) Pd$_2$(dpa)$_3$, XPhos, KOAc, 1,4-dioxane, 90 $^\circ$C, 5h, 89%; ii) Pd(dba)$_2$, KF, cyclohex-2-enyl acetate, MeOH, reflux, 20h, 58%; iii) mCPBA, DCM, 0 $^\circ$C, 5h, 83%; iv) Et$_3$N·3HF, 145 $^\circ$C, 20h, 1:0.8 ratio, 98%; v) Tf$_2$O, pyridine, 0 $^\circ$C, 5h; vi) Et$_3$N·3HF, 100 $^\circ$C, 56h, 88%; vii) H$_2$, 10% Pd/C, EtOAc, 99%.

It is interesting to compare the X-ray structures and crystal packing of compounds **3-6**. The tetrafluorocyclohexane **3** packs as a dimer in the unit cell, with molecules orientated in opposing directions. Conspicuously the electropositive hydrogen face of the cyclohexane ring interacts with the electronegative aryl ring of another molecule of **3** in F-C-H…π-interactions. This has been noted for related phenyltetrafluorocyclohexane motifs[27, 28] and is a preferred stacking mode, dictated by compensating electrostatics. For the trifluorocyclohexane crystal structure **4**, the molecules are arranged orientated in the same

direction. Again packing is dominated by intermolecular F-C-H…π-interactions between the cyclohexane and the aryl ringsof adjacenet molecules.
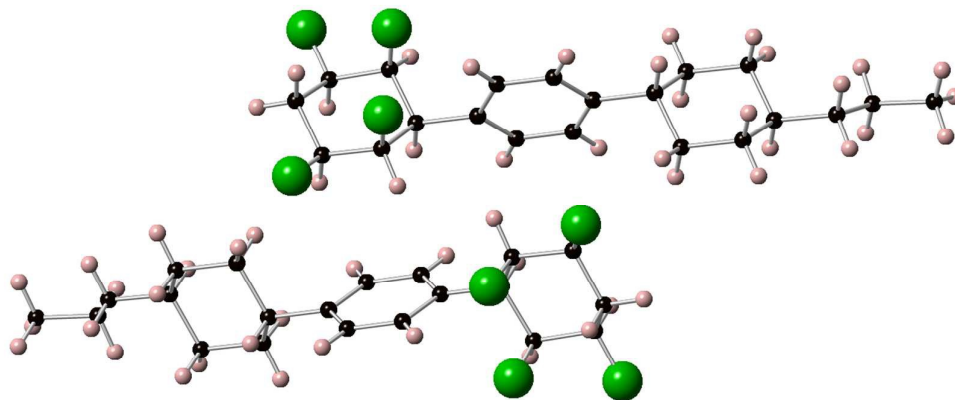

Figure 1 X-ray structure of **3** showing reciprocal F-C-H…π-interactions between the cyclohexane and aryl rings of each molecule within a dimer arrangement.
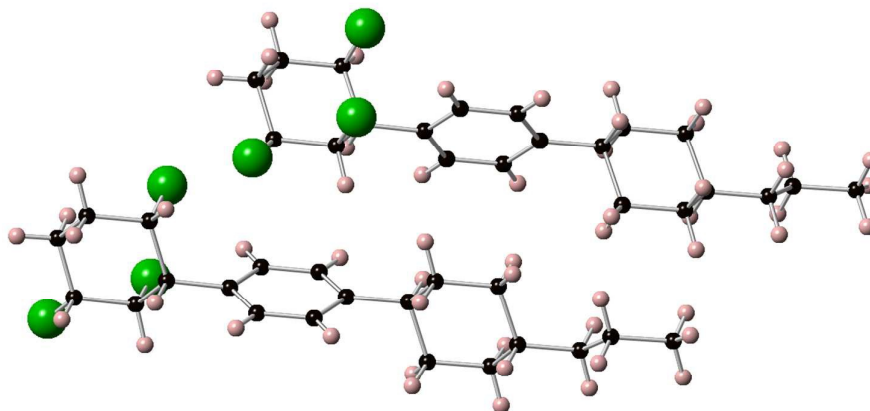

Figure 2 X-ray structure of **4** showing F-C-H…π-interactions between adjacent molecules.

In the case of the difluoro compound **5**, the molecules form dimer arrangements again with the hydrogen face of the cyclohexane contacting the aryl ring of its partner through F-C-H…π-interactions. For the monofluoro system **6** however there are no F-C-H…π-interactions suggesting that the ordering of the cyclohexane and aryl groups in this manner is reduced as the number of fluorines is removed, presumably due to fewer possible F-C-H…π-

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interactions. This is consistent too with the progressive lowering of the melting point in going from the tetra fluoro **3** to the mono fluoro **6** systems (see Table 1).
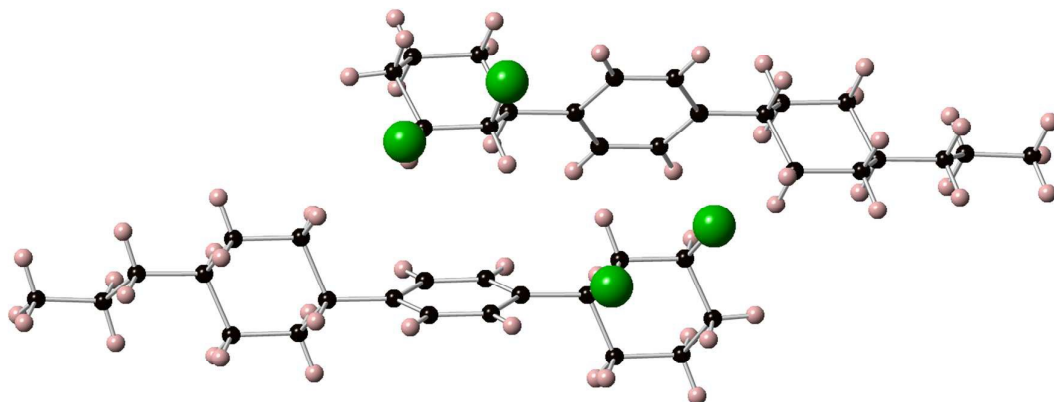
Figure 3 X-ray structure of **5** showing reciprocal interactions between the cyclohexane and aryl rings of each molecule within a dimer arrangement.
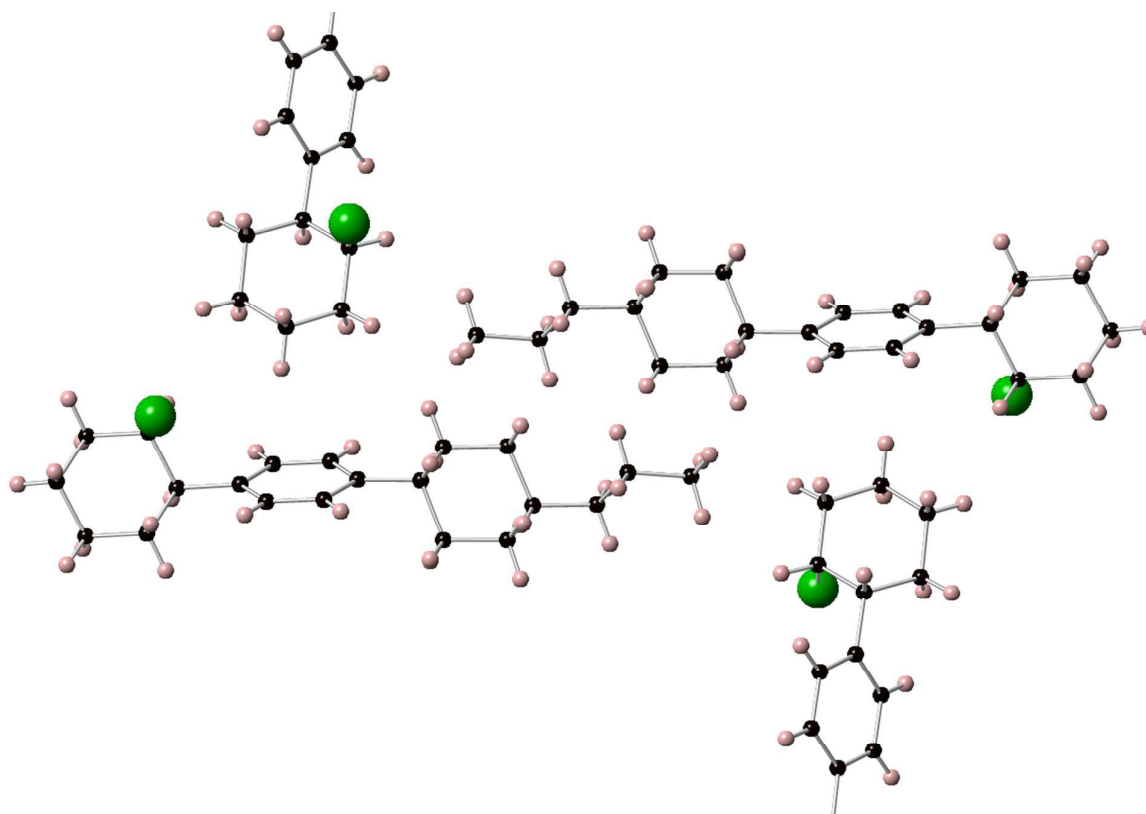
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Figure 4 X-Ray structure of monofluoro cyclohexane **6** without any obvious F-C-H…π-interactions, and packing is stabilised by hydrophobic interactions.

Compounds **3-6** were assessed as for their LC properties. Unlike reference compounds **1** and **2** none of these compounds displayed any mesogenic phase changes (See Table 1) most probably due to the absence of a second alkyl chain on the cyclohexane ring. The polar fluorine motifs and the absence of a solubilising alkyl group also rendered them largely insoluble in the test host mixture, and they all have melting points (crystalline (C) to isotropic (I); C→I) above that for **1** and **2**. Only compound **6** was sufficiently soluble to be assessed for LC properties, and it did display a –ve dielectric anisotropy of -1.9, consistent with prediction.

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No.	Mesophases/mp	$\Delta\,\varepsilon_{virt}$
1	C 25 N 54.8 I	
2	C 68 S_B 120 I	
3	C 214 I	
4	C 175 I	
5	C 128 I	
6	C 94 I	-1.19[29]

Table 1 mesogenic/melting point data for compounds **1-6**. (C= crystalline, N = nematic, S_B, semectic B, I isotropic). $\Delta\varepsilon_{virt}$ is the virtual dielectric anisotropy, experimentally determined for **6** only. Phase transition temperatures are noted in °C.

In conclusion, we report the synthesis of a series of fluorinated cyclohexanes **3-6** as prototype negative dielectric anisotropic liquid crystals. The structures contain one to four fluorine atoms which have all their fluorines on one face of the cyclohexane ring. Aliphatic compounds with fluorines orientated perpendicular to the cyclohexane ring are polar, particularly if there are two diaxial fluorines. X-ray structural studies indicate significant F-C-H…π- intermolecular interactions in the solid state consistent with this polarity. It is shown that a regression from four to one fluorine decreases the melting point of these compounds. Only the monofluoro compound **6** was sufficiently soluble in the nematic liquid crystal host and showed LC properties. It displayed the anticipated –ve dielectric anisotropic tendency. It follows that if fluorinated cyclohexanes with more than one fluorine are to be introduced into an LC material, to capitalise on their high polarity, then the design scaffold should be devoid of aromatic rings and should accommodate peripheral solubilising groups to lower the melting points and counter the poor solubility created by the polar motif.

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29.   For **6** , $\Delta\varepsilon_{virt}$ was extrapolated from ZLI-2857 (T_{NI} = 82.3°C, $\Delta\varepsilon$ = -1.4, Δn = 0.0776). For the pure substances the mesophases were identified by optical microscopy, and the phase transition temperatures by differential scanning calorimetry (DSC).

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Graphical Abstract

Fluorinated liquid crystals: Evaluation of selectively fluorinated facially polarised cyclohexyl motifs for liquid crystal applications

Nawaf Al-Maharik, Peer Kirsch*, Alexandra M. Z. Slawin, David B. Cordes and David O'Hagan*

A series of prototype negative dielectric liquid crystalline (LC) compounds which contain the facially polarised all *cis*-fluorinatedcyclohexane motifs is explored