



Development of S_NAr Chemistry on Fluorinated Substrates for Liquid Crystals Applications

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ABSTRACT

Fluorination has been widely utilized in liquid crystals to modify and enhance their range of desirable physical properties. S_NAr reaction on highly fluorinated aromatic substrates appears to be far largely overlooked as an expedient route for the synthesis of fluorine containing liquid crystals. S_NAr reactions on a range of functionalized pentafluorobenzenes are highly *para*-specific and thus ideal for the construction of calamitic (rod-like) molecules. Useful nucleophiles include, not restricted to, alcoholates, thiolates, amines and phenols. A wide range of the requisite monosubstituted highly fluorinated precursors are themselves now commercially available or readily prepared by a number of procedures. In this work, we demonstrate the utility of S_NAr chemistry for the preparation of fluorinated liquid crystals. We report the molecular design, synthesis, and mesogenic properties of symmetric and asymmetric fluorinated *para* terphenyls with a variety of *para* terminal alkoxy and thioalkoxy tails. The fluorinated *para* terphenyl main skeletons were prepared employing practical CuI [or CuI/Phenanthroline]-catalyzed decarboxylative carbon-carbon cross-coupling from their corresponding potassium fluorobenzoate salts and aryl iodides. A convenient synthesis of fluorinated *para* terphenyls liquid crystals bearing ethers and thioethers in rich yields and high purity. These fluorinated terphenyls have been characterized by polarized optical microscopy (POM), differential scanning calorimetry (DSC), X-ray crystallography and by 1H , ^{13}C , and ^{19}F NMR. The mesogenic properties are also examined as a function of the number of fluorine atoms on the *para* terphenyl core.

Introduction

Fluorinated organic materials have received considerable attention in many fields of materials science including liquid crystals, polymers, pesticides and pharmaceuticals [1-3]. Introduction of fluorine substituents in liquid crystals can induce special properties compared to their hydrocarbon analogues such as non-fluorinated *para* terphenyls. These induced properties are a result of the larger size of fluorine atom compared to hydrogen, that causes a considerable steric effects [3]. For example, fluorinated liquid crystals usually display broad range of nematic mesophases with strong dielectric anisotropy, low rotational viscosity, modifications to melting point and low conductivity [3-6]. Exploring these enhanced properties introduces a new generation of commercial liquid crystal materials such as those involved in active matrix liquid crystal displays,

surface stabilized ferroelectric, anti-ferroelectric smectic C displays and twisted nematic liquid crystal displays [3-6].

Perfluoroaromatic materials are known to display high reactivity for cross-coupling reactions [7-9]. Recently, Shang et al. [8] reported the synthesis of highly fluorinated aromatic materials from their corresponding potassium perfluorobenzoates and aryl iodides via CuI-assisted decarboxylative cross-coupling. This synthetic strategy employs inexpensive and less sensitive organometallic reagents, and generates only carbon dioxide as a byproduct. Hence, it can replace the other expensive and sensitive organometallic reagents, such as palladium halide, employed in conventional cross-coupling reactions for the synthesis of fluorinated liquid crystalline materials. There are many publications and considerable research efforts have been made on employing transition metal catalyzed cross-coupling reactions as common approaches in the synthesis of

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fluorinated materials [10-14]. However, they still suffer some disadvantages including low selectivity, side reactions and poor yield. Additionally, a substantial amount of by-products can be formed as a result of those side reactions leading to additional purification costs [15-25]. Herein we describe the design and synthesis of novel liquid crystals comprising a rigid central *para* terphenyl core and flexible side chains. A copper-only decarboxylative cross-coupling starting from the corresponding potassium fluorobenzoate salts and aryl iodides was employed. A convenient synthesis of fluorinated *para* terphenyls bearing ethers and thioethers in rich yields were performed through a regioselective S_NAr reaction between activated fluorinated aromatic compounds and alcoholates and thiolates. This synthetic strategy aim to decrease side reactions, lower production costs and high purity liquid crystalline products. Employing this synthetic strategy, we also identify the number of fluorine atoms in these materials so that they can exhibit atom economy accompanied by a better liquid crystalline performance.

Materials and methods

Melting points were obtained by Differential Scanning Calorimetry (TA Instruments 2920). The phase transition temperatures of were studied also by observing textures under a polarizing optical microscope equipped with a hot stage. IR spectra were recorded with a Bruker Vectra-33 IR-Spectrometer with a diamond ATR probe. NMR spectra were recorded using a BRUKER AVANCE 400 spectrometer at 400 MHz; chemical shifts are given in ppm relative to internal standard TMS at 295°K.

Synthetic approaches:

General procedure for the synthesis of a 4-alkoxy-4'-iodobiphenyl from 4-hydroxy-4'-iodobiphenyl:

In a 100 ml round bottom flask equipped with stir bar and N_2 bubbler was placed 4-hydroxy-4'-iodobiphenyl, potassium carbonate DMF, and a 1-iodoalkane. The resulting mixture was stirred at room temperature overnight after which time the TLC indicated all of the biphenol was consumed. The solution was poured into ice water and stirred to give homogeneous slurry. The solid product was isolated by vacuum filtration, washed with water, and air dried on the filter.

General procedure for the synthesis of a 4''-alkoxy-2,3,4,5,6-tetrafluoro-1,1':4',1''-terphenyl from a 4-alkoxy-4'-iodobiphenyl:

In a 200 ml round bottom flask fitted with a stirbar, reflux condenser and an N_2 bubbler was placed a 4-alkoxy-4'-iodobiphenyl, potassium pentafluorobenzoate, and diglyme. The mixture was stirred under a flow of nitrogen and heated in an oil bath. Once the solution had reached 100°C CuI was added and then the mixture was further heated to 140°C. The reaction was followed by TLC using hexane as the eluent. If the reaction ceased before completion the mixture was cooled and more potassium pentafluorobenzoate and CuI were added as needed. The diglyme was removed under vacuum and

the remaining solid was heated up with isooctane and a few grams of both silica gel and Montmorillonite clay. The slurry was boiled and then filtered through fluted filter paper. The solvent was boiled into the filter to remove product and the filtrate was cooled to produce crystals which were collected by vacuum filtration.

General procedure for the synthesis of a 4''-alkoxy-4-alkoxy-2,3,5,6-tetrafluoro-1,1':4',1''-terphenyl from a 4''-alkoxy-2,3,4,5,6-pentafluoro-1,1':4',1''-terphenyl:

In a 100 ml round bottom flask fitted with nitrogen bubbler and stirbar was placed 4''-alkoxy-2,3,4,5,6-pentafluoro-1,1':4',1''-terphenyl and anhydrous solvent. The resulting mixture was heated just until the terphenyl dissolved and the respective alcohol was added. If solid came out of solution, it was heated until dissolution occurred once again. Potassium t-butoxide was added and the reaction was followed by TLC. If the reaction stalled, additional alcohol and base were added. Upon consumption of the starting material (TLC analysis) the solvent was then removed and a recrystallization was performed.

General procedure for the synthesis of a 4''-alkoxy-4-alkylthiol-2,3,5,6-tetrafluoro-1,1':4',1''-terphenyl from a 4''-alkoxy-2,3,4,5,6-tetrafluoro-1,1':4',1''-terphenyl:

In a 100 ml round bottom flask fitted with nitrogen bubbler and stirbar was placed 4''-alkoxy-2,3,4,5,6-tetrafluoro-1,1':4',1''-terphenyl. Anhydrous DMF was added and the mixture was heated until the terphenyl dissolved. The mixture was then cooled and the respective thiol was added and if solid came out of solution, it was heated until dissolution occurred once again. Again, the mixture was removed from heat. Potassium t-butoxide was added and the reaction was followed by TLC. If the reaction halted, additional alcohol and base were added. Upon consumption of the starting material (TLC analysis) the solvent was then removed and recrystallization was performed.

General procedure for the synthesis of a 2,2'',3,3'',4,4'',5,5'',6,6''-decafluoro-1,1':4',1''-terphenyl:

In a 200 ml round bottom flask fitted with a stirbar, reflux condenser, and an N_2 bubbler was placed 1,4-diiodobenzene, potassium pentafluorobenzoate, and diglyme. The mixture was stirred under a flow of nitrogen and heated in an oil bath. Once the solution had reached 100°C CuI was added and then the mixture was further heated to 140°C. The reaction was followed by TLC using hexane as the eluent. It is important to note that there are three spots in total on the TLC, the reactant, the monosubstituted intermediate, and the disubstituted product. If the reaction ceased before completion the mixture was cooled and more potassium pentafluorobenzoate and CuI were added as needed. The diglyme was removed under vacuum and the remaining solid was heated with *iso*-octane and a few grams of both silica gel and Montmorillonite clay. The

slurry was boiled and then filtered through fluted filter paper. The solvent was boiled into the filter to remove product and the filtrate was cooled to produce crystals. The resulting product was then recrystallized from *iso*-octane to afford the final product as white crystals.

General procedure for the synthesis of a 4,4''-dialkoxy-2,2'',3,3'',5,5'',6,6''-octafluoro-1,1':4',1''-terphenyl from 2,2'',3,3'',4,4'',5,5'',6,6''-decafluoro-1,1':4',1''-terphenyl:

In a 100 ml round bottom flask fitted with nitrogen bubbler and stirbar was placed 2,2'',3,3'',4,4'',5,5'',6,6''-decafluoro-1,1':4',1''-terphenyl and anhydrous DMF. The resulting mixture was heated just until the terphenyl dissolved and the respective alcohol was added. If a solid came out of solution, it was heated until dissolution occurred once again. Next two equivalents of potassium *t*-butoxide were added and the reaction was followed by TLC. It is important to note that three spots are to be expected from the TLC: reactant, monosubstituted intermediate, and the disubstituted product. If the reaction stalls, additional alcohol and base were added. Upon completion of the reaction the solvent was then removed and a recrystallization was performed.

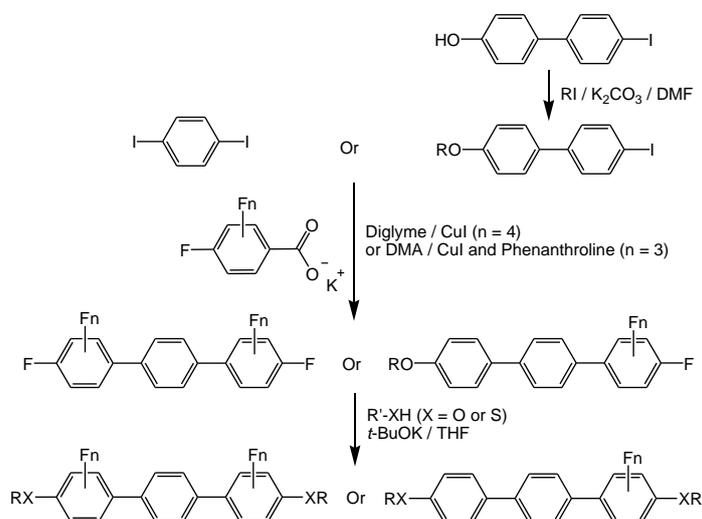
General procedure for the synthesis of a 4''-hexyloxy-2,3,4,5 -tetrafluoro-1,1':4',1''-terphenyl: In a 100 ml round bottom flask under nitrogen environment and magnetic stir bar was placed 4-hexyloxy-4'-iodobiphenyl, potassium 2,3,4,5-tetrafluorobenzoate (2 equiv.), CuI, phenanthroline (20%), and DMA. The mixture was then heated in an oil bath until it reached 160°C and was then maintained at that temperature and allowed to sit for 24 hours with a reflux condenser attached. After the 24 hour heating period the mixture was removed from the oil bath and TLC was performed to verify a complete reaction by separation of the product and the starting material. Then the mixture was placed under vacuum evaporation to remove the DMA. The solid left at the bottom of the round bottom flask was then re-crystallized using boiling *iso*-octane and

filtered through fluted filter paper. After being filtered the filtrate was given time to cool and precipitate. The solid precipitate was then removed from the *iso*-octane through vacuum filtration.

Results and discussion

Synthesis and characterization

The starting materials 4-hydroxy-4'-iodobiphenyl and 1,4-diiodobenzene are commercially available. 4-Hydroxy-4'-iodobiphenyl was treated with K₂CO₃ and 1-iodoalkane in DMF at room temperature to afford the corresponding 4-alkoxy-4'-iodobiphenyl derivatives in high yields ranging from 91-96% [26,27]. The synthetic route is shown in **Scheme 1**. The fluorinated *para* terphenyls were prepared in high yields starting from the corresponding potassium fluorobenzoate salts and a variety of aryl iodides in solution of diglyme via Cu(I)-catalyzed decarboxylative cross-coupling. As referred by Shang et al. [8] that diglyme can coordinate to potassium cation allowing a better complexation between CuI and perfluorobenzoate anion. The reaction is highly efficient with excellent yields [8]. The scope of the decarboxylative reactions with respect to di-, tri-, and tetrafluorobenzoates (all bearing fluorine atom at the *para* position) are also presented. An obvious lower reactivity of the phenyl rings with fewer fluorine atoms was observed toward decarboxylative carbon-carbon cross-coupling. Although diglyme is an optimum solvent for the decarboxylation of pentafluorobenzoate salt, no yield was detected for fluorobenzoates with fewer fluorine atoms. However, it was found that CuI/Phenanthroline-catalyzed decarboxylative cross-coupling together with dry dimethyl acetamide (DMA) as a solvent introduces better results for tetrafluorobenzoates potassium salts [8]. On the other hand, under these reaction conditions no results were detected with the di-, and trifluorobenzoate potassium salts with a single fluorine atom at the *para* position. In marked contrast, no yield was detected employing CuI as a catalyst, without added phenanthroline, to a solution of tetrafluorobenzoates and aryl iodides.



Scheme 1: Synthesis of fluorinated *para* terphenyls comprising a rigid aromatic core and flexible (thio)alkoxy side chains; X = O or S; R and R' are aliphatic chains; n = 1 - 4

The S_NAr reaction of activated highly fluorinated aromatic compounds and alcoholates and thiolates is evaluated under mild conditions. Highly fluorinated aromatic materials are chemically robust and commercially accessible. In addition, they are known to show high reactivity toward S_NAr reaction under non-forcing conditions [25]. In our attempt to add (thio)alkoxy substituents to the terminal aromatic ring(s), we employ the use of the S_NAr reaction on the highly fluorinated rings to add (thio)alkoxy tail (see Table 1). S_NAr reactions on a range of functionalized fluoroaromatic rings are highly *para* specific and thus ideal for the construction of calamitic (rod-like) molecules. The fluorinated *para* terphenyls produced were then subjected to S_NAr reaction with a variety of alcoholates and thiolates in anhydrous THF as a solvent and *t*-BuOK as a base. As a result of the high nucleophilicity of sulfide anions, the C-S formation from S_NAr reactions demonstrates a higher reactivity than C-O ones. The activation of the *para* fluorine atom as good leaving atom in the S_NAr reaction course comes from the presence of multiple activating fluorine atoms at the *ortho* and *meta* positions of the aromatic ring. Hence, a highly regioselective S_NAr reaction can be achieved at only the *para* position by replacing the activated fluorine atom at the *para* position of the fluorinated aromatic rings to afford fluoroaromatics bearing *para*-alkoxy and -thioalkoxy substituents through nucleophilic aromatic substitution.

Liquid crystalline properties

Most of the systems described here contain highly fluorinated rings and some additional molecular structures with fewer fluorine atoms are also investigated. Being one of the smallest atoms on the periodic table, it was theorized that hydrogen can be sub-

stituted by fluorine in some terphenyls known to show mesogenic properties without too much steric interference. Additionally, fluorine has a high electronegativity; this causes the C-F bond to have a dipole moment much higher than that of a C-H bond [3]. The liquid crystalline properties are investigated by polarizing optical microscopy (POM) and differential scanning calorimetry (DSC). Changing the number of fluorine atoms on the aromatic core, in addition to the variation of the peripheral (thio)alkoxy substituents are the main factors in changing the mesogenic properties. The symmetric fluorinated *para* terphenyls displayed only traditional melting-decomposition behavior and no liquid crystalline properties were detected. On the other hand, the asymmetric fluorinated *para* terphenyls display interesting mesogenic properties. Hence, we mainly focus on the rod-like asymmetric fluorinated molecular systems with a (thio)alkoxy terminal groups. The mesogenic properties are also examined as a function of the alkoxy aliphatic chains on the *para* terphenyl core. It was found that only the (thio)alkoxy chains on fluorinated phenyl ring affects the polarizability and packing making the molecule more likely to display liquid crystal phases. Figure 1 shows the DSC thermogram (2nd cycle) of compound 7. On heating, compound 7 shows crystal phases below 125.4 °C, a mesophase between 125.4 °C and 143.1 °C, and an isotropic liquid phase above 143.1 °C. On the subsequent cooling scan, the reverse phase transitions are observed. compound 7 shows the first isotropic smectic phase transition, between 124.1 °C and 141.8 °C, then a transition to the new crystalline phase (crystal 3) at 124.1 °C, followed by another two transition crystalline phases (crystal 2 and 1) at 103.4 °C and 50.7 °C, respectively.

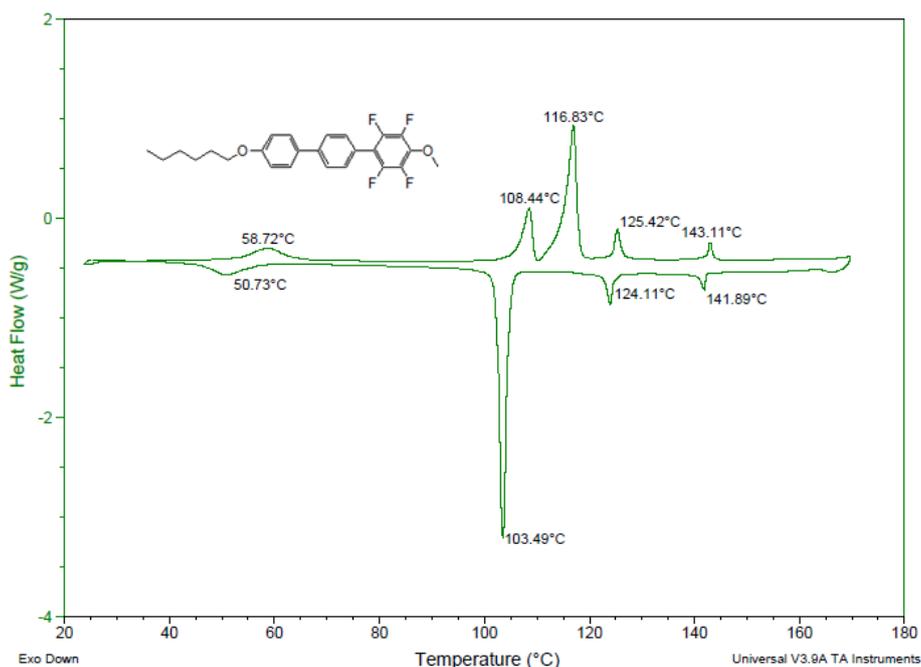


Fig. 1: DSC thermogram (2nd cycle) of compound 7 displaying phase transition temperatures

Table (1): Symmetric and asymmetric highly fluorinated *para* terphenyls with their respective (thio)alkoxy chain lengths, corresponding yields from S_NAr reaction, and phase properties

| Asymmetric fluorinated terphenyl bearing alkoxy tails | | |  |
|--|----------------------|------------|--|
| Comp. # | R, R' | Yield % | Phase Change Data (°C) |
| 7 | hexyl, methyl | 74 (n = 4) | Iso 143.1 N 125.4 H 116.8 SmA 108.3 Cr |
| 8 | hexyl, ethyl | 90 (n = 4) | Iso 149.9 N 123.7 SmA 116.3 Cr |
| 9 | hexyl, hexyl | 50 (n = 4) | Iso 138.0 N 118.9 SmA 113.5 Cr |
| 10 | dodecyl, methyl | 74 (n = 4) | Iso 123.8 SmA 116.4 SmC 112.7 H 103.8 Cr |
| 11 | dodecyl, ethyl | 84 (n = 4) | Iso 130.8 SmA 123.6 Cr 88.4 Cr |
| 12 | dodecyl, hexyl | 96 (n = 4) | Iso 124.5 SmA 102.5 SmC 79.8 SmX |
| 13 | hexyl, isopropyl | 82 (n = 4) | Iso 111.0 SmA 87.94 Cr |
| 14 | hexyl, 2-methylbutyl | 84 (n = 4) | Iso 124.3 SmA 101.2 Cr |
| 16 | propyl, hexyl | 47 (n = 4) | Iso 142.6 SmA 97.1 Cr |
| 17 | propyl, ethyl | 63 (n = 4) | Iso 119.3 SmA 106.5 N 91.8 Cr |
| 28 | hexyl, hexyl (n = 3) | 37 (n = 4) | Iso 128.6 SmA 119.2 Cr |
| Asymmetric fluorinated terphenyl bearing alkoxy/thioalkoxy tails | | |  |
| Comp. # | R, R' | Yield % | Phase Change Data (°C) |
| 18 | hexyl, hexyl | 39 (n = 4) | Iso 120.6 SmA 110.7 SmX |
| 19 | propyl, hexyl | 80 (n = 4) | Iso 129.1 SmA 112.4 Cr |
| 20 | dodecyl, hexyl | 70 (n = 4) | Iso 123.7 SmA 112.7 SmC 96.6 SmX |
| 29 | hexyl, hexyl (n = 3) | 24 (n = 3) | Iso 128.3 SmA 111.5 Cr |
| Symmetrical fluorinated terphenyl bearing alkoxy tails | | |  |
| Comp. # | R | Yield % | Phase Change Data (°C) |
| 22 | ethyl | 98.3 | Cr 203.3 iso |
| 23 | propyl | 61.6 | Cr 192.4 iso |
| 24 | hexyl | 55.1 | Cr 138.1 iso |
| 25 | dodecyl | 61.2 | Cr 117.3 iso |
| Symmetric fluorinated terphenyl bearing thioalkoxy tails | | |  |
| Comp. # | R | Yield % | Phase Change Data (°C) |
| 26 | hexyl | 56 | Cr 133.1 iso |

The polarized optical microscopy (POM) was employed to study the texture of the mesophases observed for compound **7** at different temperatures. POM photographs display the textures of the mesophases for compound **7** are shown in **Figure 2**. A phase transition is observed upon heating from Crystal phase at 99.8°C to Smectic A (b) phase at 110.3°C followed by Homotropic (c) at 111.0°C. Another Smectic A (d, e, and f) phase transition is observed upon heating at 124.7°C. Also phase transition is observed upon cooling from Nematic (g and h) phase at 142.7°C to Homotropic (i) at 142.0°C. The textures of mesophases observed for compounds **12** and **18** at different temperatures are shown in **Figure 3**. For compound **12**, a phase transition is observed upon cooling from isotropic at 126.4°C to Smectic A (a) phase at 124.5°C followed by Smectic C (b) phase at 102.5°C.

Another higher order Smectic X (c) phase transition is observed upon cooling at 79.8°C. For compound **18**, a phase transition is observed upon cooling from isotropic at 127.2°C to Smectic A (d) phase at 120.6°C followed by a higher order Smectic X (e) phase transition at 110.7°C.

As seen in **Table 1**: The majority of the asymmetric products with a single perfluorinated phenyl ring exhibit liquid crystal properties. There are number of liquid crystal phases that are presented. The majority of compounds display Smectic A and Nematic phases, as well as some combination of the two. Compound **18** is the sulfur analogue of compound **9**. Although thiols are much more reactive than alcohols, making for quicker and cleaner reactions, the size of the sulfur atom is larger than oxygen; this affects the packing making the molecule less likely to display liquid crystal phases.

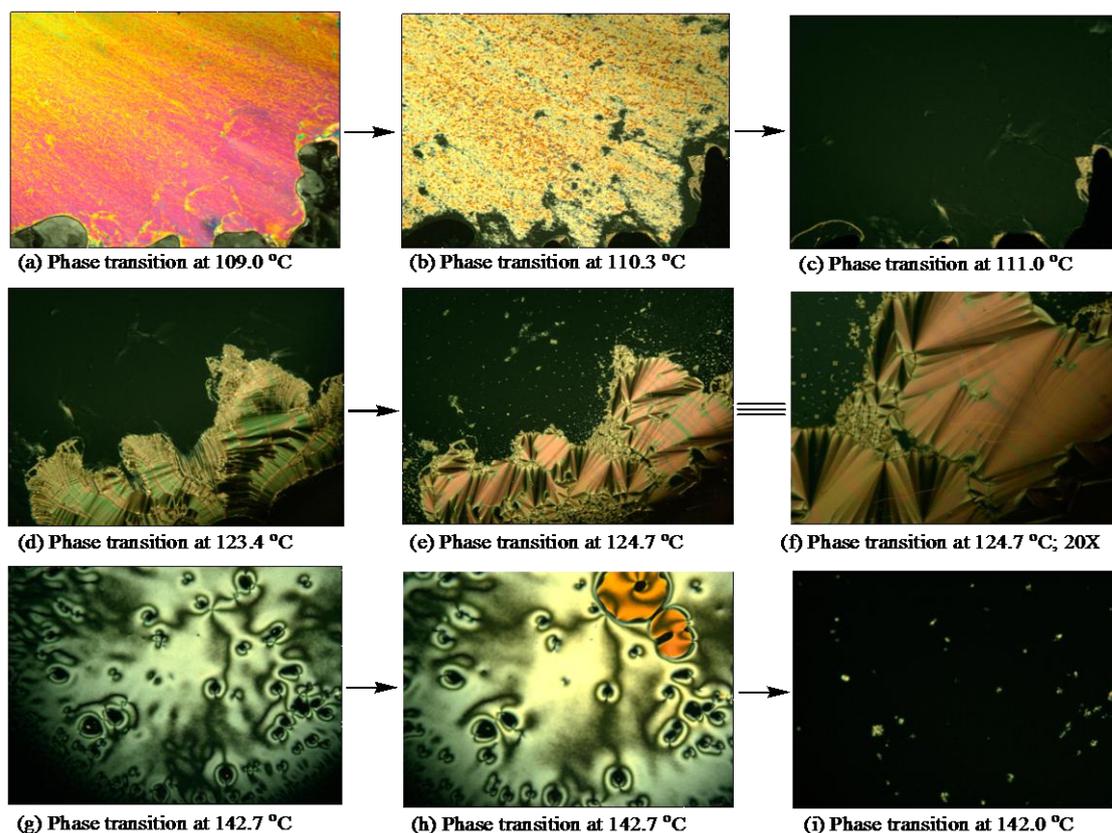


Fig. 2: POM photographs display textures of mesophases for compound 7.

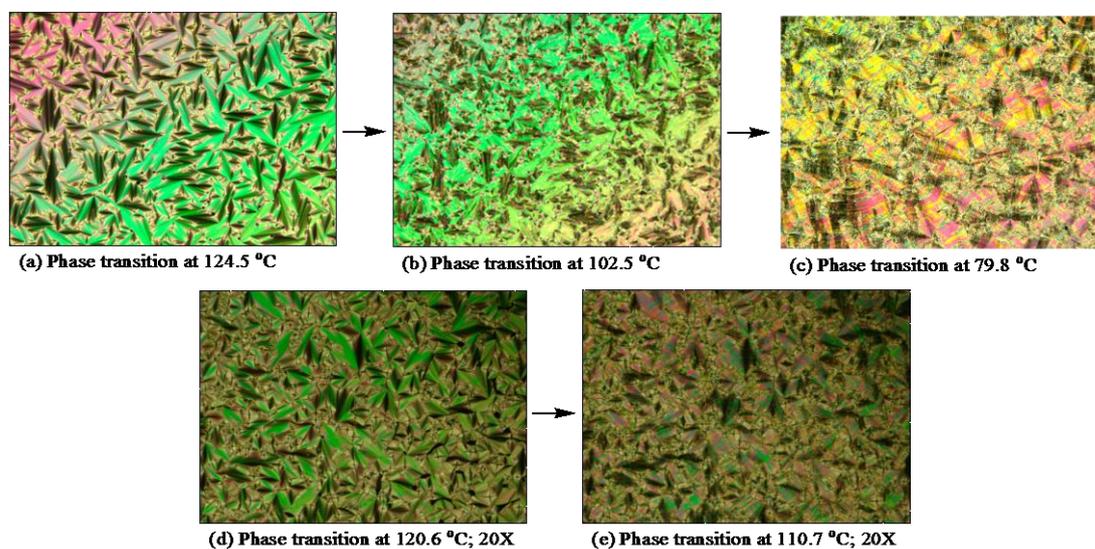


Fig. 3: POM photographs display textures of mesophases for compounds 12 (top) and 18 (bottom).

Table 1 shows the different phase properties of the symmetric products. Unfortunately none of the symmetric products examined have displayed liquid crystalline properties. The rigid terphenyl core of the mesomorphic asymmetric compounds under study reveals unsaturated residues that are rich in π -electrons. These fluoroaromatic rings are particularly attractive to extend the π -electron conjugation through the rod-like molecules in addition to increase the polarizability along the main molecular *para* terphenyl core. This higher

polarizability of the rigid terphenyl core in asymmetric compounds improves the molecular packing compared to the lower polarizability of the rigid terphenyl core in symmetric compounds. This was investigated through the use of X-ray crystallography of compounds 17 and 22 (see Figures 4 and 5). Both of face-to-face and head-to-tail packings are observed in the crystal structure of asymmetric compounds. On the other hand, only face-to-face packing is observed in the crystal structure of symmetric compounds.

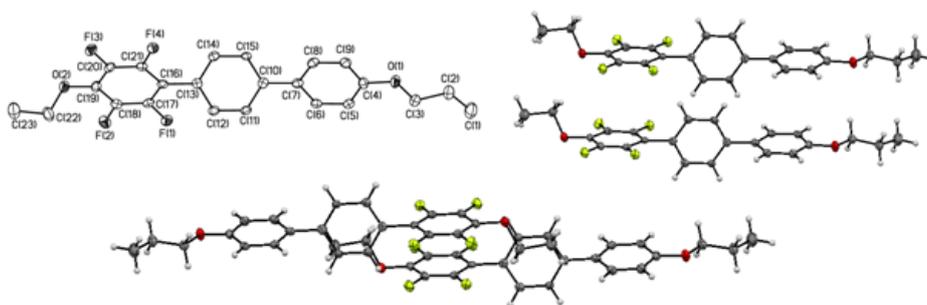


Fig. 4: X-ray crystallography of compound **17**; (top-left) Crystal structure (ORTEP view) of **17**; (top-right) Face-to-face intermolecular packing; (bottom) Head-to-tail intermolecular packing.

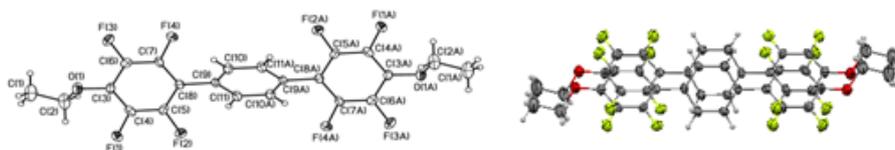


Fig. 5: X-ray crystallography of compound **22**; (left) Crystal structure (ORTEP view) of **22**; (right) Face-to-face intermolecular packing only observed.

Conclusions

Novel symmetric and asymmetric terphenyls with fluorinated aromatic rings bearing different (thio)alkoxy tails are presented in terms of synthesis and mesogenic properties. A majority of the asymmetric analogues were found to exhibit at least one liquid crystal phase over a wide temperature range. The fluorinated *para* terphenyl main skeletons were prepared by an improved practical CuI (or CuI/Phenanthroline)-catalyzed decarboxylative cross-coupling from their corresponding potassium fluorobenzoate salts and aryl iodides. A convenient synthesis of fluorinated *para* terphenyls bearing ethers and thioethers in high yields were performed by S_NAr chemistry. Majority of the asymmetric products with a single highly fluorinated phenyl ring exhibit liquid crystal properties displaying smectic A and Nematic phases, as well as some combination of the two. Thiols are more reactive than alcohols, making for quicker and cleaner reactions; the size of the sulfur atom is larger than oxygen. This affects the packing making the molecule less likely to display liquid crystal phases.

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