http://dx.doi.org/10.5935/0103-5053.20140132

J. Braz. Chem. Soc., Vol. 25, No. 8, 1493-1503, 2014.
Printed in Brazil - ©2014 Sociedade Brasileira de Química
0103 - 5053 $6.00+0.00

Article

Synthesis of New Family of Thiazoline and Thiazole Esters and Investigation of their Thermal Properties

Juliana M. F. M. Schneider, Eric S. Sales, Paolo R. Livotto, Paulo H. Schneider and Aloir A. Merlo*

Instituto de Química, Universidade Federal do Rio Grande do Sul (UFRGS), 90040-060 Porto Alegre-RS, Brazil

Uma nova família de ésteres tiazolínicos e tiazóis foram sintetizados e as propriedades térmicas são apresentadas e discutidas. Os ésteres tiazolínicos foram obtidos pela reação de ciclização de benzonitrilas 4-substituídas com o amino ácido *L*-cisteína seguido da reação de esterificação com álcoois e fenol previamente selecionados. A oxidação dos ésteres tiazolínicos mediado pelo reagente $BrCCl_3$/DBU permitiu a transformação dos respectivos ésteres tiazolínicos em ésteres tiazóis . Os compostos finais dos ésteres tiazolínicos e tiazóis são formados por cadeias alquílicas, (perfluoroalquil)alquílicas e *p*-alcoxifenilas. Alguns cristais líquidos mostraram serem mais relevantes. Um deles apresentou mesofase esmética A (SmA) monotrópica enquanto que outros apresentaram mesofase estável SmA. Como esperado, as cadeias de alcanos semifluorados induziram a formação de mesofase ortogonal via efeito de segregação.

A new family of thiazoline and thiazole esters has been synthesized and their thermal properties are presented and discussed. Thiazoline esters were obtained by cyclization reaction from 4-substituted benzenenitrile and amino acid *L*-cysteine followed by esterification reaction with selected alcohols and phenol. Subsequent oxidation step to transform thiazoline esters into thiazole esters was applied mediated by $BrCCl_3$/DBU. The final thiazoline and thiazole esters are composed by terminal flexible hydrogenated alkyl chain from one side and to the other side by terminal segments of flexible alkyl chains (hydrogenated chain), (perfluoralkyl)alkyl chains (semifluorinated alkane) *p*-alkoxyphenyl chains. Some liquid crystals compounds for thiazoline and thiazole esters showed to be relevant. One of the thiazoline esters display a monotropic smectic A (SmA) mesophase while some thiazole esters show stable SmA mesophase. As expected semifluorinated alkane chain induce the formation of orthogonal mesophase by means of segregation effect.

Keywords: thiazoline and thiazole esters, liquid crystals, semifluorinated alkane and SmA mesophase

Introduction

Liquid crystals (LC) have been long recognized as one of the most extensive and attracting fields of materials research. The first studies, dating from 150 years ago, prompted nowadays researches worldwide increasing scientific interest, focusing on obtaining and monitoring new LC compounds.[1]

The most common application of liquid crystal technology is in liquid crystal displays (LCDs). From the ubiquitous wrist watch and pocket calculator to an advanced computer screen, this type of display has evolved into an important and versatile interface. Since the discovery of interesting electro-optical properties in the middle sixties and the production of the first LCD panel in the beginning of the seventies, many other practical applications of these molecules have been largely studied.

As they show a variety of physical properties, these molecules find application in diverse fields of science, such as display technologies,[2] light emitting diodes[3] and photo/semiconducting materials.[4] Thus, great effort has been made in developing synthetic strategies for acquisition of new and diverse mesomorphic compounds.

Heterocyclic compounds are of great importance in many fields of chemistry. It is very common the observation of interesting biological activity on compounds bearing these

*e-mail: aloir.merlo@ufrgs.br

structures.[5] Insertion of a heterocyclic unit in the skeleton of a mesogenic molecule aggregates many advantages, once one could enhance design possibilities and count up several changes in liquid crystalline properties. Also it is well-known that a minor change in molecular geometry may bring about substantial variations on mesomorphic behavior.[6] Furthermore, the presence of heteroatom alters considerably the polarity and polarisability of the molecule, and the heterocycle core has the ability of impart lateral and/or longitudinal dipoles.[7] In particular 1,3 thiazoles derivatives show bond angles of 153° and 133°, depending on the substitution pattern, and a dipole moment of 1.6 D.[8] In addition, the presence of the electron-rich sulfur atom attains modifications on the ionization potential that could induce smectic mesophases.[9]

Moreover, mesophase morphologies can be further tuned by replacement of a flexible non branched alkyl chain for a perfluorinated segment.[10] The increased rigidity, linearity and low surface energy of the perfluorinated chain compared to the hydrocarbon one, settles particular properties modifications, as the fluorophobic effect, which reduces the miscibility of the fluorinated moieties with other sides of the molecule.[11] Thus, fluoro substituents and perfluorochains have been incorporated to LC compounds leading to a variety of modifications on these substances behaviors, as broad mesomorphic ranges, different mesophase morphologies, lower melting points and transition temperatures as well as stabilization of preexisting mesophases, due to the combination of small size, intense polarity and high strength of the C-F bond.[10]

Such attributes can be successfully comprised in the structure of mesogens and are of major significance in terms of primary structure property relationships, any more than crucial to the development of novel liquid crystal materials.[12] For the thiazole building block showed in Figure 1, the general structure carries always on a flexible alkyl chain from one side of the molecule and a carboxylic group at the other side to be derivatized into aliphatic or aromatic esters and amides. Among the wide range of methodologies for preparation of thiazoline derivatives,[13] the one based on cyclization of nitriles with the natural amino acid *L*-cysteine was elected,[14,15] once it employs readily accessfull and low cost starting materials. Also, this method delivery the target precursor bearing the desirable carboxyl group mentioned above, which enables the possibility to attach a variety of substituents by means of esterification procedures employing different alcohols phenols.

Thiazolines synthesis and their subsequent oxidation to heteroaromatic thiazole rings are an interesting way to prepare building block to be used in many branchs of the synthetic organic chemistry. As demonstrated in this work, a sequential oxidation of the thiazoline to thiazole ring leads to an enhancement of geometrical anisometry of the rigid core contributing for emergence of mesomorphic and photoluminescent properties. Thereby, we wish to report a simple and straightforward methodology for the synthesis of a new class of compounds derived from the thiazoline precursor using the chain elongation strategy as well as to investigate the liquid-crystalline behavior of the final thiazole esters.

General structure of target thiazole esters is presented in Figure 1. Primitive core is formed by aromatic and thiazole ring connected by a single bond. Variable connection means the chemical communication between additional group on the right side and the primitive core intermediated by carboxyl group presented in the target esters. Thiazolines **6a**-**k** and thiazoles **7a**-**k** are composed of a flexible hydrogenated alkyl chain on the left side of Figure 1, except for those from 4-bromophenyl nitrile. On the right side of Figure 1, terminal segments connected by carboxyl group are composed of flexible alkyl chains (hydrogenated chain), (perfluoralkyl) alkyl chains (semifluorinated alkane)[16] and *p*-alkoxyphenyl chains. Figure 1 shows the general structure of the new thiazole esters synthesized in this work.

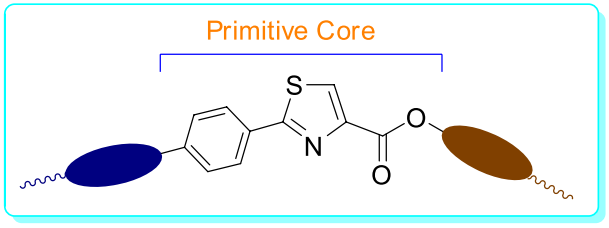


Figure 1. General structure for the target thiazoles.

Results and Discussion

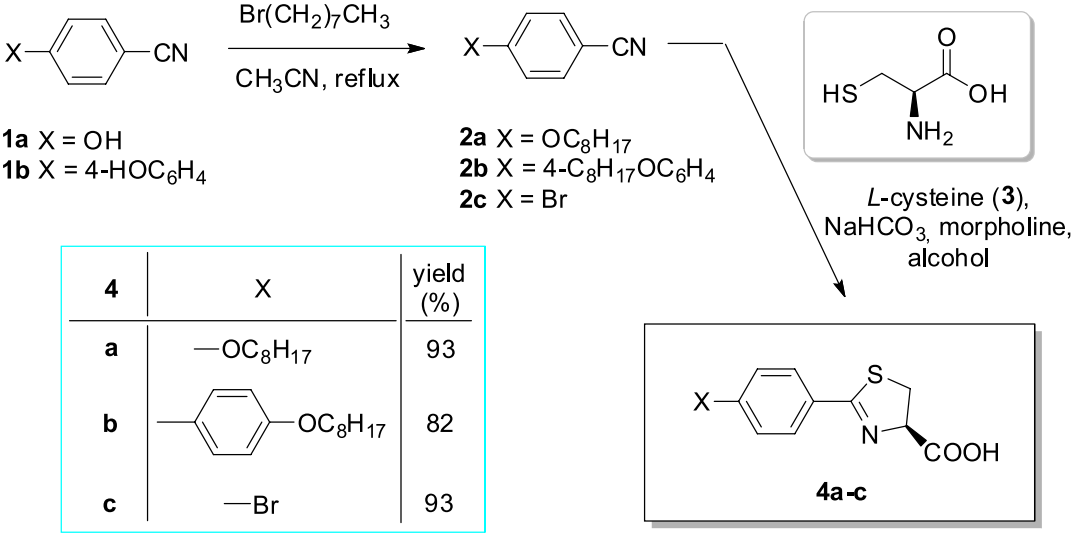
Synthesis

The synthesis of key intermediate thiazoline carboxylic acids **4a**-**c** is outlined in Scheme 1. The strategy applied here begins with the commercially available nitriles **1a** and **1b**, which were submitted to the alkylation reaction with 1-bromoctane under basic conditions, affording the alkylated nitriles **2a** and **2b** in almost quantitatively yields. From this point, in Scheme 1, 4-bromobenzonitrile (**2c**) was added to our plan of the synthesis of **4a**-**c**. Next step nitriles **2a-c** were submitted to cyclization reaction with amino acid *L*-cysteine (**3**) to generate the key intermediates thiazoline derivatives **4a**-**c**. In general, the most common procedure for this reaction involves a system of water/alcohol under buffer control by several days.[17] In our hands

the experimental condition describe above to yield the corresponding thiazoline carboxylic acids **4a-c** gave very low yields of the described thiazoline derivatives. In order to achieve better results, we changed the initial protocol reaction to one that has been used by Loughlin *et al.*.[18] Under the new experimental conditions, we prepared the intermediate **4a-c** in a good yield. Thus, exposing nitriles **2a-c** to *L*-cysteine mediate by sodium bicarbonate, morpholine and reflux in an alcoholic solvent (ethanol or isopropanol), the cyclizated products **4a-c** were afforded in excellent overall yields. This is an interesting and an alternative way to prepare thiazolines in a simple and almost inexpensive methodology.

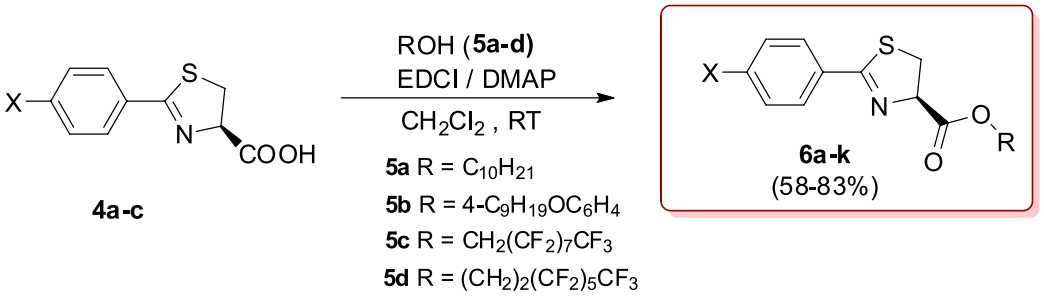
After accomplished successfully the synthesis of **4a-c**, the esters formation was initiated to complete our synthetic plan. Esterification reactions with activation of acids by carbodiimides are probably the most versatile procedures for preparation of ester compounds.[19] The chemical linkage between **4a-c** and **5a-d** to obtain the final thiazoline esters **6a-k** was firstly attempted using the dicyclohexylcarbodiimide/4-*N*,*N*-dimethylaminopyridine (DCC/DMAP) protocol.[20] However, due to the troublesome to remove the by-product urea, we changed DCC to 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDCI) to promote the ester ligation. Thus, thiazoline esters **6a-k** were synthesized as outlined in Scheme 2, by activation of acids **4a-c** with EDCI followed by the reaction with several alcohols **5a-d** in dichloromethane and DMAP as a catalyst. Table 1 summarizes the results for the thiazoline esters **6a-k**. It is noteworthy to mention that EDCI/DMAP couple worked successfully for a variety of chosen alcohols, such as alkyl and (perfluoralkyl)alkyl and phenols, delivering the intermediates compounds **6a-k** to be transformed into LC in good yields by oxidation process.

The 2,5-disubstituted thiazole core in the final compounds **7a-k** was accomplished as described in Scheme 3. Several methods were evaluated to perform this transformation, such as reactions with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ),[21] NiO_2[22] and MnO_2.[23] First attempts employing this later strategy resulted in poor yields of target final products, as well as a complex mixture of by-products detected by thin layer chromatography (TLC) analysis of crude reaction extract. In order to improve the obtention of these target mesogens, the

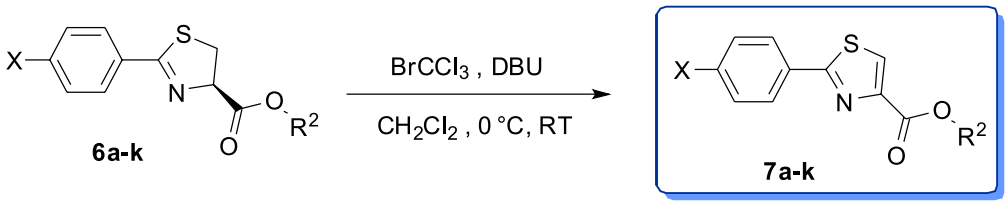


4	X	yield (%)
a	—OC_8H_{17}	93
b	—OC_8H_{17}	82
c	—Br	93

Scheme 1. Preparation of thazoline precursors **4a-c**.



Scheme 2. Obtention of thiazoline esters **6a-k**.



Scheme 3. Oxidation of thiazoline esters **6a-k** to the final mesogens **7a-k** intermediate by $BrCCl_3$/DBU.

oxidative dehydrogenation step was most conveniently performed using a mixture of bromotrichloromethane and 1,8-diazabicyclo[5.4.0]undec-7-ene ($BrCCl_3$/DBU).[24] In comparison to the ones mentioned above, this synthetic protocol is advantageous for its milder conditions and tolerating to a large variety of functional groups. Therefore, the bromination takes place first in **6a**-**k** and then, the dehidrobromination in presence of DBU in dry DCM furnished the final products **7a-k** in good to excellent yields (Table 2).[25]

Liquid crystal properties

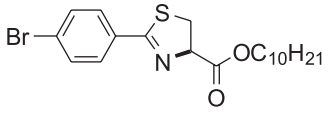
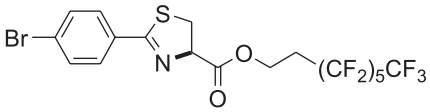
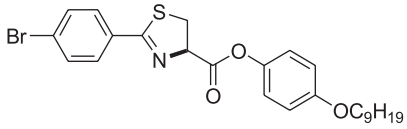
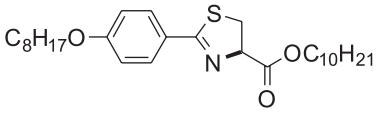
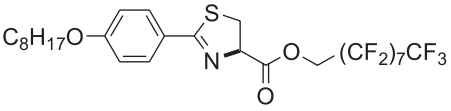
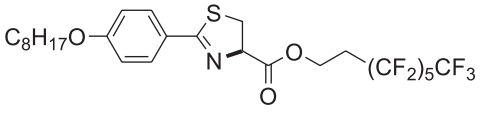
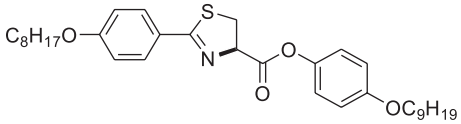
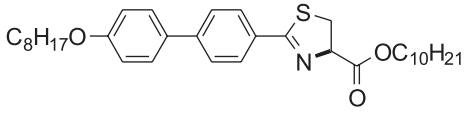
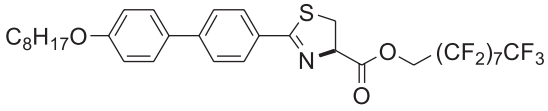
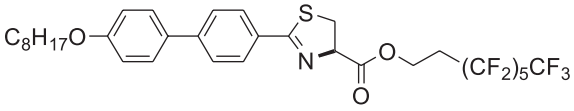
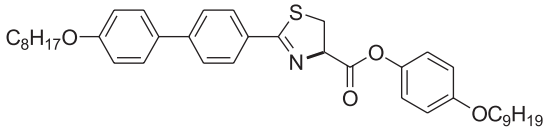
Transition temperatures of thiazoline and thiazol esters are tabulated in Table 1 and 2, respectively. Table 1 and 2 display the transition temperatures of eleven thiazoline and thiazol esters synthesized in this work. The primitive core (rigid core) contains at least a phenyl group connected to heterocyclic moiety. Esters here are composed of flexible alkyl chains (hydrogenated chain), (perfluoralkyl)alkyl chains (semifluorinated alkane)[16] and *p*-alkoxyphenyl chains. Thiazolines esters are not LC as we can see in Table 1, except for **6i**, which displayed smectic A mesophase (SmA) upon cooling. They are mostly crystalline solid with melting point (mp) in the range between 40 °C to 140 °C, and only **6a** is liquid at room temperature. Melting point was dependent on how flexible is the aliphatic chain ester. For example, **6a** is a liquid, while **6b** and **6c** are solids with mp being bigger than **6c**, which is, of course, more anisotropic but not liquid crystal. This tendency in the mp extends to the others thiazolines in Table 1. As it moves from more flexible alkyl chain to (perfluoralkyl)alkyl chains the stiffness becomes higher. Also, for **6c**, **6g** and **6k**, the phenyl group contributes to the stiffness of the compounds. So in this sense, mp tends to be higher as the molecular rigid core becomes more anisotropic. Additionally, **6d**, **6e** and **6f** are good examples to compare the stiffness effect caused by fluorine atom at alkyl chain. The higher mp is seen in the more rigid thiazoline **6e**. Additional phenyl group has a higher contribution to molecular stiffness as expected; comparing **6d** and **6g**, **6d** and **6h** and **6g** with **6k**.[26] This is irrespective on the relative position of the phenyl group into the rigid rod core. The behavior was observed even in the longest and more anisotropic **6k** it was not able to show some evidence of liquid-crystalline behavior.

A briefly comment is addressed to **6i**, which displays a monotropic SmA mesophase. The monotropic nature of the mesophase to **6i** means that mesophase appeared only upon cooling, it is thermally unstable with an unpredictable and short mesophase temperature range. The mesophase range is too narrow with $\Delta T = 2$ °C. Why **6i**, among all compounds listed in Table 1, displays a LC behavior? The answer of this question may be associated to perfluoroalkyl chain effect, close to the thiazoline ring. The molecular segregation is the driving force for the formation of liquid-crystalline phase of **6i**. Incompatibility of totally flexible alkyl chain, rigid anisometric core and less flexible semifluorinated alkane chain are responsible for the formation of positional ordered liquid-crystalline phases[27] as observed for **6i** and the thiazole series in Table 2. We have to say more about the mesomorphic properties (see thiazole discussion) but the linearity deviation and non-coplanarity of the thiazoline ring (broken anisometry) is the main force of the absence of the mesophase in this series.[28]

Figure 2 displays a typical growth of SmA *bâtonnets* (bright) from the isotropic phase (black) upon cooling at 161 °C of thiazoline **6i**. Bright and black colors in Figure 2 are observed due to crossed polarizers, using optical microscopy and the molecular orientation of the samples sandwiched between the glass plates. Upon cooling coalescing, *bâtonnets* will form full focal conic SmA fan texture. Sometimes, black areas from isotropic state remain black due to the perpendicular orientation of the molecules. Black areas of the sample have a homeotropic alignment. In this case, the long molecular axis is perpendicular to the glass plates. When the growth of *bâtonnets* is completed, the fan focal-conic is observed. The color is a consequence of the orientation of the director which basically lies in the plane of the substrate and the structured layers are curved across the fans.[29]

Table 2 displays the thermal data of thiazoles **7a**-**k** that were obtained by oxidation process from thiazolines **6a**-**k**. As expected, some thiazoles in Table 2 display liquid-crystalline behavior as evidenced by the texture observed using polarized optical microscopy (POM). The phase transition temperatures (in °C) were obtained by POM and

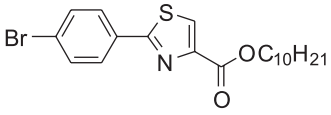
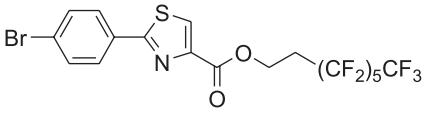
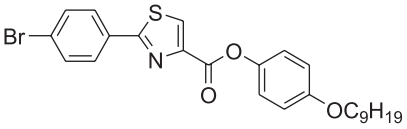
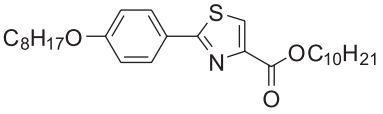
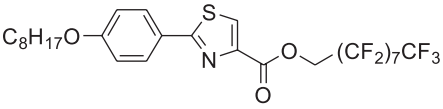
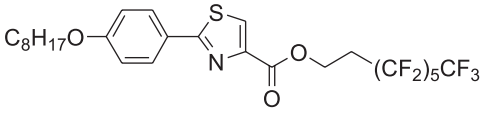
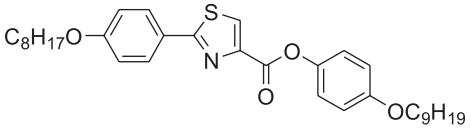
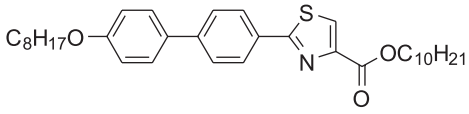
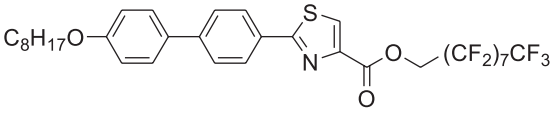
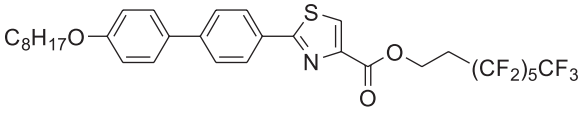
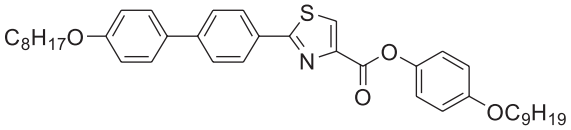
Table 1. Transition temperature (°C) for thiazoline esteres **6a-k**[a]

entry	Chemical structure	Yield / %	Heating/cooling
6a		71	Oil (liquid)
6b		70	Cr 56 I I 30 Cr
6c		62	Cr 107 I I 91 Cr
6d		78	Cr 43 I [b]
6e		60	Cr 97 I I 87 Cr
6f		58	Cr 62 I I 43 Cr
6g		83	Cr 104 I I 86 Cr
6h		56	Cr 108 I I 95 Cr
6i		76	Cr 168 I I 163 SmA 161 Cr
6j		72	Cr 139 I I 131 Cr
6k		80	Cr 153 I I 145 Cr

[a]Data were acquired by POM analysis; [b]no recrystalization was observed; Cr = crystal phase; SmA = smectic A mesophase.

by differential scanning calorimetry (DSC) experiments. To the first four thiazoles **7a-d**, no liquid-crystalline behavior was observed. Even for **7c**, a more anisotropic one, a transition crystal to isotropic state at 128 °C was obtained. The relative compound **6c** (Table 1), the melting point is $\Delta T = 21$ °C below **7c**, showing that in the crystal state, the packing of molecules of thiazoles is better than thiazolines molecules.[30] The increase in the melting point is also observed in **7a-d** in comparison to the **6a-d**. The tendency noted to these compounds is also seen in the others

Table 2. Transition temperature (°C) for thiazoles ester **7a-k**[a]

entry	Chemical structure	Yield / %	Heating/cooling
7a		82	Cr 65 I / I 49 Cr
7b		66	Cr 109 I / I 81 Cr
7c		51	Cr 128 I / I 114 Cr
7d		74	Cr 62 I / I 46 Cr
7e		74	Cr 119 SmA 129 I I 126 SmA 117 Cr
7f		76	Cr 78 SmA 85 I / I 80 SmA 65 Cr
7g		50	Cr 108 I / I 95 Cr
7h		70	Cr 119 I I 115 SmX 109 Cr
7i		73	Cr 175 SmA 205 I I 197 SmA 163 Cr
7j		75	Cr 142 Cr_1 152 SmA 191 I I 181 SmA 154 Cr_1 128 Cr
7k		58	Cr 143 I / I 135 Cr

[a]Data were acquired by POM analysis; Cr = crystal phase; SmA = smectic A mesophase; SmX = mesophase with texture not related with the model pattern; probably is a SmA mesophase.

compounds in Table 2. However, compounds **7e**, **7f**, **7h**, **7i** and **7J** have also an additional mesophase intercalated between the crystal and isotropic phase. The LC thiazoles above display a structured orthogonally layer which was characterized as smectic A mesophase according to the texture analysis of POM. This smectic fluid A mesophase

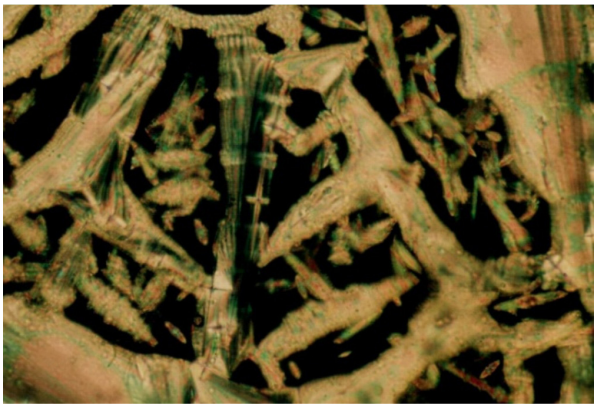


Figure 2. Growth of SmA *bâtonnets* (bright) of fan focal-conic texture of SmA mesophase upon cooling at 161 °C of thiazoline **6i**.

is characterized by positional order of molecules' centers of mass in one dimension in addition to the long range orientational order of the director phase *n* which is associated parallel to the long molecular axis. Locally, the SmA mesophase can be regarded as a two dimensional liquids due to the molecules' centers of mass are arranged in layers and their projection onto the smectic layer plane are isotropically distributed with no positional correlation being observed within or across the layer planes.[29]

Figure 3 displays (left) the growth of SmA *bâtonnets* (bright) of fan focal-conic texture of SmA mesophase upon cooling at 176 °C of thiazole **7j**; typical fan-shaped texture of a SmA phase upon cooling at 187 °C of thiazole **7i** (right). Lighter and darker regions seen in Figure 3 (right), in the fans, are due to the molecular layers of sample and cross polarizers that are used in POM study.

As expected, LC properties of thiazoles are affected mainly by the flatness and coplanarity of the heterocyclic ring. Strong π-stacking in the lattice is observed in crystal phase with 3.73 Å the distance between two adjacent thiazole rings.[30] Of course, to be a classical rod-shape liquid crystal the molecular shape of the structures has to be more elongated as possible to compensate bent-shape of thiazole ring.[8,31] The mesophase nature is also dependent on the terminal group connected to the rigid and anisometric core. In the current study, SmA mesophase was found particularly due to the presence of two aliphatic chains with distinct chemical nature. We can see from Table 2 the predominance of orthogonal SmA mesophase for all LC compounds listed. The significance of semifluorinated alkyl chain is clearly seen when we compare compounds **7a**, **7d** and **7h**. They have flexible hydrogenated alkyl chain in both sides of arylthiazol esters except for **7a**. For the longer aryl moiety **7h**, which at first would favor the appearance of stable mesophase, it is possible to observe only a monotropic SmA mesophase. Usually, molecules with longer molecular length, tend to be more elongated and consequently more anisotropic due to length-to-breadth ratio of two molecular axes. Also, it is well-known for biphenyl and others systems that, the increase of carbon atoms in the flexible alkyl chain favors the formation of smectic mesophases, usually SmA and SmC.[32] The result founded in **7h** definitively emphasizes the function of perfluoroalkyl chain plays on the mesomorphic properties in this study. For aryl esters **7c**, **7g** and **7k**, and even for **7k**, which has a more anisometric core, no mesophase was observed. Again, the result observed to **7c**, **7g** and **7k** is suggesting the importance of perfluoroalkyl chain on the mesomorphic behavior. Obviously it is possible to assume that the absence of mesophase to these compounds in terms of an equilibrium of *Z*- and *E*-rotamers, that are observed in esters when they entry to the mesophase, similarly to the behavior of liquid crystal dimers where the mesophases are governed by the populations of linear and bent molecules.[33] Attempt to correlate carbonyl group frequency ($\nu_{C=O}$ cm^{-1}) in the IR spectrum of **6c/7c**, **6g/7g** and **6k/7k** in the solid state (KBr pellets) with the composition of the rotamers *E* and *Z* of esters has failed. The band of carbonyl group associated to those compounds in solid state looks like strong and

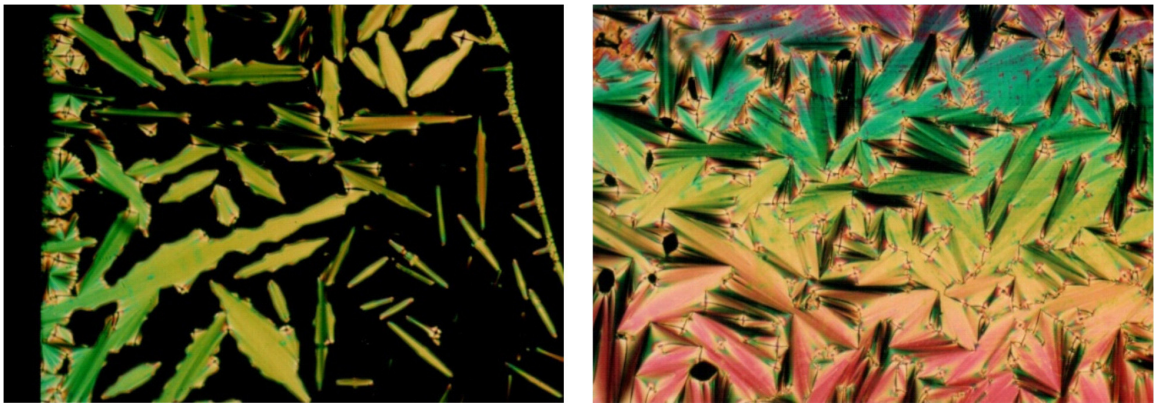


Figure 3. Growth of SmA *bâtonnets* (bright) of fan focal-conic texture of SmA mesophase upon cooling at 176 °C of thiazole **7J** (left); typical fan-shaped texture of a SmA phase upon cooling at 187 °C of thiazole **7i** (right).

sharp. Thus, it is impossible to assume that the non liquid-crystalline behavior of **7c**, **7g**, **7k** is due to the composition of the rotamers in the equilibrium between the more anisotropic *Z*-rotamer and the less anisotropic *E*-rotamer. Now we are turning our attention to the four LC: **7e**, **7f**, **7i** and **7j**. All LC compounds listed in Table 2 have one semifluorinated alkyl chain connected to the carboxyl group of thiazole ring and a flexible hydrogenated alkyl chain on the opposite side. They are LC with SmA mesophase as expected considering that the individual molecules possess specific groups which repel or attract each other strongly. This effect begins among a few molecules at molecular level on cooling and very fast amplifies to large scale, where the nanoscale segregation is the driven force. The aggregation is promoting by these groups favoring the smectic ordering. Terminal groups such as siloxanes, fluorinated, halogenated and even diol favor the smectic ordering.[34] The mesophase range for **7i** and **7j** is bigger than **7e** and **7f** as a consequence of the more anisometric biphenyl group in **7i** and **7j**. For example, **7i** displays a mesophase range of 30 °C, while for **7e** is 10 °C. Transition temperatures associated to the Cr → SmA and SmA → I phase transition reveals the effect of proximity of perfluoroalkyl chain to carboxyl group.

Transition temperatures depend on how close to the carboxyl group is the perfluoralkyl chain. Comparing **7i** with **7j** and **7e** with **7f** it is possible to note that **7i** and **7e** display higher transition temperature from crystal to mesophase and mesophase to isotropic phase. Only **7j** displays a second transition Cr → CrX and it has the biggest mesophase range ($\Delta T = 39$ °C) for SmA mesophase to isotropic state. According to Höpken *et al*.,[35] the thermal behavior of (perfluoroalkyl) alkane can be explained in terms of conformational aspect of hydrogenated and perfluorated chains. Alkyl chain tends to be more amorphous in the mesomorphic state while perfluorinated alkyl chain tends to be more organized, which of course affect the transition temperatures. In the solid state both chains self-organize in crystalline way. Of course, alkyl chain may assume predominantly an extend all-*trans* conformation while perfluoralkyl chain tends to be kink due to the gauche effect.[36] When the solid enters to the mesophase, the hydrocarbon portion must have liquid-like conformational freedom, while perfluoralkyl chains behave as a hard molecular segment owing its polar nature. Due to stiffness, fluorinated segments are packed regularly in the solid state, which favors the high melting point and even the high clearing point. In another way, when the sample on cooling enters into the mesophase state, the conformational disordering of the hydrocarbon segments upon the transition from isotropic state to the smectic mesophase is bigger than the perfluoralkyl segments. The molecular aggregation is faster to the perfluoralkyl chains favoring the attraction between rigid segments. Soft segments in the mesophase are still mobile and conformationally disordered. And finally, when the sample starts to crystallize again, hard molecular segments are packed more efficiently than the soft molecular. It is important to mention that in the mesophase more mobility is expected to more amorphous segments. Thus, the contribution of one and two methylene carbon atoms is causing the behavior observed to that thiazoles LC ester **7e**, **7f**, **7i** and **7j**.

Conclusion

We have synthesized a new family of thiazoline and thiazole esters **6a**-**k** and **7a**-**k**. The final thiazoline and thiazole esters are composed by terminal flexible hydrogenated alkyl chain from one side and to the other side by terminal segments of flexible alkyl chains (hydrogenated chain), (perfluoralkyl)alkyl chains (semifluorinated alkane) *p*-alkoxyphenyl chains. **6i** was the only compound belonging to the family of thiazoline esters to display monotropic SmA mesophase. Thiazole esters family presented enantiotropic SmA mesophase for **7e**, **7f**, **7h**, **7i** and **7j**. The combination of better conjugation of thiazole ring and polar effect of semifluorinated alkane chain induces the formation of structured layer mesophase by means of segregation effect.

Experimental

General methods

All starting materials were purchased from commercial suppliers (Sigma Aldrich Chemical Co., Acros Organics and ABCR Chemicals) and used without further purification. All reactions were carried out under a nitrogen atmosphere in oven-dried glassware with magnetic stirring. Solvents were dried, purified and degassed under classical methods. Solvents used in extraction and purification were distilled prior to use. TLC was performed using silica gel 60 F254 aluminum sheets and the visualization of the spots has been done under UV light (254 nm) or stained with iodine vapor. Products were purified by flash chromatography on silica gel 60 M, 230-400 mesh. Melting and mesophase transition temperatures and textures of the samples points were measured using an Olympus BX43 microscope equipped with a Mettler Toledo FP82HT Hot Stage FP90. ^{1}H (^{13}C) NMR spectra were recorded at 300 (75) MHz on a Varian Inova and 400 (100) MHz Bruker spectrometer using $CDCl_3$ as solvent. The ^{1}H and ^{13}C chemical shifts were reported in parts *per* million (δ) referenced to residual solvent signals at $\delta_{H/C}$ 7.26/77.00 ($CDCl_3$) relative to tetramethylsilane (TMS) as internal standard. Coupling

constants *J* [Hz] were directly taken from the spectra and are not averaged. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). Low-resolution mass spectra were obtained with a Shimadzu GC-MS-QP5050 mass spectrometer interfaced with a Shimadzu GC-17A gas chromatograph equipped with a DB-17 MS capillary column. HRMS spectra were obtained from a Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer equipped with an Infinity™ cell, a 7.0 Tesla superconducting magnet, an RF-only hexapole ion guide and an external electrospray ion source (off axis spray) and with ESI(+)-MS and tandem ESI(+)-MS/MS using a hybrid high-resolution and high accuracy MicroTOF-Q II mass spectrometer (Bruker Daltonics), or on a Micromass Q-TOFmicro instrument.

General procedure for the synthesis of thiazolines **4a-c**

A solution of *L*-cysteine hidrochloride (60 mmol; 10.8 g), $NaHCO_3$ (60 mmol; 5.3g), the appropriate nitrile (20 mmol) in 85 mL of ethanol was refluxed for 30 min. After, the pH was adjusted to 8.0 by adding a few drops of morpholine, and the reflux was continued for additional 12 h. The ethanol was removed, the residue dissolved in distilled water and acidified to pH 1.5 by adding concentrated HCl. The product was extracted with CH_2Cl_2 (3 × 50 mL), the organic layers where combined, dried over $MgSO_4$ and the solvent removed under vacuum. The products were obtained with satisfactory purity and were used in the next step without further purification.

Representative data for (*R*)-2-[4-(octyloxy)phenyl]-4,5-dihydrothiazole-4-carboxylic acid (**4b**)

Beige solid; mp 103.5 °C; yield: 88%; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.84 (t, 3H, *J* 6.4, CH_3), 1.38-1.24 (m, 10H, $(CH_2)_2$), 1.72-1.65 (m, 2H, CH_2), 3.63-3.60 (m, 2H, CH_2S), 3.99 (t, 2H, *J* 6.5, OCH_2), 5.23 (t, 1H, *J* 8.3, CHN), 6.99 (d, 2H, *J* 8.9, Ar-H), 7.71 (d, 2H, *J* 8.9, Ar-H); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 171.96, 167.45, 161.38, 129.91, 124.82, 114.48, 78.25, 67.77, 34.94, 31.25, 28.74, 28.67, 28.57, 25.47, 22.09, 13.93.

General procedure for esterification of thiazolines **6a-k**

To a stirred solution of the corresponding thiazoline **4a-c** (2.0 mmol) in dry CH_2Cl_2 (8 mL) under N_2 atmosphere at room temperature, were added subsequently the corresponding alcohol (2.0 mmol) EDCI (2.0 mmol) and catalytic amount of DMAP. After 16 h, the organic phase was transferred to an extraction funnel, washed with saturated $NaHCO_3$ (2 × 10 mL), water (2 × 10 mL) and the organic layer was dried with Na_2SO_4. The solvent was evaporated and the remaining product was purified by chromatography (hexanes/AcOEt = 80:20).

Representative data for (*R*)-3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 4,5-dihydro-2-[4-(octyloxy)phenyl] thiazole-4-carboxylate (**6f**)

Yield 58%; white solid; mp 62 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.80 (d, 2H, *J* 8.8 Hz, Ar-H), 6.89 (d, 2H, *J* 8.9 Hz, Ar-H), 5.26 (t, 1H, *J* 8.9 Hz, NCH), 4.57-4.47 (m, 2H, SCH_2), 3.98 (t, 2H, *J* 6.6 Hz, OCH_2), 3.72-3.53 (m, 2H, OCH_2), 2.68-2.45 (m, 2H, OCH_2CF_2), 1.85-1.71 (m, 2H, CH_2), 1.55-1.16 (m, 10H, $(CH_2)_5$), 0.88 (t, 3H, *J* 6.8 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.72, 170.59, 162.09, 130.35, 124.99, 120.00-107.00 (6C), 114.23, 77.93, 68.14, 57.36, 35.20, 31.84, 30.38 (t, CF_2, *J* 21.7 Hz), 29.51, 29.50, 29.32, 29.27, 29.07, 25.93, 22.62, 13.99.

General procedure for the synthesis of tiazoles **7a-k**

The thiazoline ester (1 mmol) (**6a-k**) and dry CH_2Cl_2 (5 mL) were added to a round bottomed flask under N_2 atmosphere. The system was cooled to 0 °C, and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (2 mmol) was added and the reaction mixture was stirred for 20 min. Bromotrichloromethane ($BrCCl_3$) (2 mmol) was then added and stirred for additional 16 h at room temperature. The reaction was quenched with saturated NH_4Cl and the organic layer washed with water (2 × 10 mL), saturated NaCl (2 × 10 mL) and dried over Na_2SO_4. The solvent was finally evaporated and the remaining product was purified by chromatography ($CHCl_3$).

Representative data for 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-(4-bromophenyl)thiazole-4-carboxylate (**7b**)

Yield 66%; IR (KBr) ν/cm^{-1} 2919, 2850, 2364, 1745, 1509, 1454, 1344, 1245, 1211, 1072, 1014, 827, 634; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.11 (s, 1H, CHS), 7.81 (d, 2H, *J* 8.4 Hz, Ar-H), 7.52 (d, 2H, *J* 8.4 Hz, Ar-H), 4.62 (t, 2H, *J* 6.5 Hz, OCH_2), 2.80-2.34 (m, CF_2CH_2, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.86, 160.62, 147.14, 132.23, 131.48, 128.33, 128.04, 125.28, 122-106 (6C), 57.24, 30.55 (t, *J* 21.7 Hz). HRMS (ESI) *m/z*, calcd for $C_{18}H_{10}BrF_{13}NO_2S$ [M+H$^+$]: 629.9408; found: 629.9404.

Supplementary Information

Supplementary data (experimental description, ^{1}H NMR and ^{13}C NMR spectrum) are available free of charge at http://jbcs.sbq.org.br as PDF file.

Acknowledgments

The authors gratefully acknowledge the INCT-Catálise, Edital 01/12-PPG-Química-UFRGS and Fapergs-Edital PqG 2012. The authors are also grateful to Sidnei Moura e Silva [Universidade de Caxias do Sul (UCS)] for the HRMS analysis. Eric S. Sales thanks to PIBIC-UFRGS for fellowship.

References

1. Bruce, D. W.; Heyns, K.; Vill, V.; *Liq. Cryst.* **1997**, *23*, 813.
2. Klein, S.; *Liq. Cryst. Rev*. **2013**, *1,* 52.
3. Vlachos, P.; Mansoor, B.; Aldred, M. P.; O'Neill, M.; Kelly, S. M.; *Chem. Commun*. **2005**, 2921; Cristiano, R.; Ely, F.; Gallardo, H.; *Liq. Cryst*. **2005**, *32*, 15; Wang, R.; Liu, D.; Ren, H.; Zhang, T.; Yin, H.; Liu, G.; Li, J.; *Adv. Mater*. **2011**, *23*, 2823.
4. Chen, W.; Chen, Y.; Li, F.; Chen, L.; Yuan, K.; Yao, K.; Wang, P.; *Sol. Energy Mater. Sol. Cells* **2012**, *96*, 266; Yazaki, S.; Funahashi, M.; Kagimoto, J.; Ohno, H.; Kato, T.; *J. Am. Chem. Soc*. **2010**, *132*, 7702; Zhang, X.; Hudson, S. D.; DeLongchamp, D. M.; Gundlach, D. J.; Heeney, M.; McCulloch, I.; *Adv. Funct. Mater*. **2010**, *20*, 4098; Zhao, X.; Zhan, X.; *Chem. Soc. Rev*. **2011**, *40*, 3728.
5. Hughes, R. A.; Thompson, S. P.; Alcaraz, L.; Moody, C. J.; *J. Am. Chem. Soc.* **2005**, *127*, 15644; Glover, C.; Merritt, E. A.; Bagley, M. C.; *Tetrahedron Lett*. **2007**, *48*, 7027.
6. Niori, T.; Sekine, T.; Watanabe, J.; Furukawa, T.; Takezoe, H.; *J. Mater. Chem*. **1996**, *6*, 1231; Reddy, R. A.; Tschierske, C.; *J. Mater. Chem*. **2006**, *16*, 907; Rampon, D. S.; Rodembusch, F. S.; Schneider, J. M. F. M.; Bechtold, I. H.; Gonçalves, P. F. B.; Merlo, A. A.; Schneider, P. H.; *J. Mater. Chem.* **2010**, *20*, 715; Vasconcelos, U. B.; Merlo, A. A.; *Synthesis* **2006**, 1141.
7. Lai, C. K.; Chen, C.-J.; Wu, Y.-C.; Sheu, H.-S.; Lee, G.-H.; *Tetrahedron* **2011**, *67*, 114; Ritter, O. M. S.; Giacomelli, F. C.; Passo, J. A.; da Silveira, N. P.; Merlo, A. A.; *Polym. Bull.* **2006**, *56*, 549.
8. Seed, A. J.; *Chem. Soc. Rev.* **2007**, *36*, 2046.
9. Ha, S.-T.; Koh, T.-M.; Lee, S.-L.; Yeap, G.-Y.; Lin, H.-C.; Ong, S.-T.; *Liq. Cryst*. **2010**, *37*, 547.
10. Hird, M.; *Chem. Soc. Rev*. **2007**, *36*, 2070.
11. Meijer, E. W.; van Houtem, M. H. C. J.; Benaskar, F.; Fitié, C. F. C.; Martin-Rapún, R.; *Org. Biomol. Chem*. **2012**, *10*, 5898; Krafft, M. P.; Riess, J. G.; *Chem. Rev***. 2009**, *109*, 1714.
12. Kirsch, P.; Binder, W.; Hahn, A.; Jährling, K.; Lenges, M.; Lietzau, L.; Maillard, D.; Meyer, V.; Poetsch, E.; Ruhl, A.; Unger, G.; Fröhlich, R.; *Eur. J. Org. Chem.* **2008**, 3479-3487.
13. Gaumont, A.-C.; Gulea, M.; Levillain, J.; *Chem. Rev*. **2009**, *109*, 1371.
14. Bergereon, R. J.; Wiegand, J.; McManis, J. S.; Bharti, N.; Singh, S.; *J. Med. Chem*. **2008**, *51*, 5993.
15. Loughlin, W. A.; Knevitt, S. A.; Hosking, R. E.; Marshall, R. L.; *Aust. J. Chem*. **2000**, *53*, 457.
16. Höpken, J.; Möller, M.; *Macromolecules* **1992**, *25*, 2482.
17. Lu, Y.; Li, C.-M.; Wang, Z.; Ross, C. R.; Chen, J.; Dalton, J. T.; Li, W.; Miller, D. D.; *J. Med. Chem*. **2009**, *52,* 1701; Bergeron, R. J.; Wiegand, J.; Dionis, J. B.; Egii-Karmakka, M.; Frei, J.; Huxley-Tencer, A.; Peter, H. H.; *J. Med. Chem*. **1999**, *34*, 2072.
18. Loughlin, W. A.; Knevitt, S. A.; Hosking, R. E.; Marshall, R. L.; *Aust. J. Chem*. **2000**, *53*, 457.
19. Mikolajczyk, M.; Kielbasinski, P.; *Tetrahedron* **1981**, *37*, 233; Montalbetti, C. A. G. N.; Falque, V.; *Tetrahedron* **2005**, *61*, 10827.
20. Neises, B.; Steglich, W.; *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 569; Tavares, A.; Livotto, P. R.; Gonçalves, P. F. B.; Merlo, A. A.; *J. Braz. Chem. Soc.* **2009**, *20*, 1742.
21. Bose, D. S.; Idrees, M.; *Tetrahedron Lett*. **2007**, *48*, 669.
22. Evans, D. L.; Minster, D. K.; Jordis, U.; Hecht, S. M.; Mazuu, A. L.; Meyers, A. I.; *J. Org. Chem*. **1979**, *44*, 497; Bock, M.; Dehn, R.; Kirschning, A.; *Angew. Chem., Int. Ed*. **2008**, *47*, 91.
23. Yu, Y. B.; Chen, H.-L.; Wang, L.-Y.; Chen, X.-Z.; Fu, B.; *Molecules* **2009**, 4858.
24. Phillips, A. J.; Uto, Y.; Wipf, P.; Reno, M. J.; Williams, D. R.; *Org. Lett.* **2000**, *2*, 1165; Wagner, B.; Schumann, D.; Linne, U.; Koert, U.; Marahiel, M. A.; *J. Am. Chem. Soc*. **2006**, *128*, 10513; Vilela, G. D.; da Rosa, R. R.; Schneider, P. H.; Bechtold, I. H.; Eccher, J.; Merlo, A. A.; *Tetrahedron Lett.* **2011**, *52*, 6569.
25. Williams, D. R.; Lowder, P. D.; Gu, Y.-G.; Brooks, D. A.; *Tetrahedron Lett*. **1997**, *38*, 331; Williams, D. R.; Patnaik, S.; Clark, M. P.; *J. Org. Chem*. **2001**, *66*, 8463.
26. Collings, P. J.; Hird, M.; *Introduction to Liquid Crystals. Chemistry and Physics*, Taylor & Francis: London, 1997.
27. Tschierske, C.; *J. Mater. Chem*. **1998**, *8*, 1485.
28. Liu, Y.; Zhao, B.; Li, Y.; Zheng, L.; Liu, J.; *Synthesis* **2011**, 3133.
29. Dierking, I.; *Texture of Liquid Crystals,* WILEY-VCH Verlag GmbH & Co. KGaA: Weinheim, 2003.
30. Di Credico, B.; Reginato, G.; Gonsalvi, L.; Peruzzini, M.; Rossin, A.; *Tetrahedron* **2011**, *67*, 267.
31. Seed, A. J.; Toyne, K. J.; Goodby, J. W.; *J. Mater. Chem.* **1995**, *5*, 653; Matharu, A. S.; Karadakov, P. B.; Cowling, S. J.; Hegde, G.; Komitov, L.; *Liq. Cryst.* **2011**, *38*, 207.
32. Tariq, M.; Hameed, S.; Bechtold, I. V.; Bortoluzzid, A. J.; Merlo, A. A.; *J. Mater. Chem. C* **2013**, *1*, 5583.
33. Imrie, C. T.; Luckhurst, G. R. In *Handbook of Liquid Crystals*; Demus, D.; Goodby, J. W.; Gray, G. W.; Spiess, H. W.; Vill, V., eds.; Wiley-VCH: Weinheim, 1998; Imrie, C. T.; Henderson, P. A.; *Chem. Soc. Rev.* **2007**, *36*, 2096.
34. Lagerwall, J. P. F.; Giesselmann, F.; *ChemPhysChem* **2006**, *7,* 20; Kapernaum, N.; Giesselmann, F.; *Phys. Rev. E*

2008, *78,* 062701; Roberts, J.; Kapernaum, N.; Song, Q.; Nonnemacher, D.; Ayub, K.; Giesselmann, F.; Lemieux, R. P.; *J. Am. Chem. Soc.* **2010**, *132*, 364; Roberts, J. C.; Kapernaum, N.; Giesselmann, F.; Lemieux, R. P.; *J. Am. Chem. Soc.* **2008**, *130*, 13842; Chattham, N.; Zhu, C.; Cheng, X.; Limtrakul, J.; Tschierske, C.; Maclennan, J. E.; Clark, N. A.; *Soft Matter*, **2011**, 7, 9978; Hentrich, F.; Tschierske, C.; Siegmar-Diele, S.; Saue, C.; *J. Mater. Chem*. **1994**, *4*, 1547.

35. Höpken, J.; Pugh, C.; Richtering, W.; Möller, M.; *Makromol. Chem*. **1988**, *189*, 911.
36. Peer, K.; *Modern Fluoroorganic Chemistry*, WILEY-VCH Verlag GmbH & Co. KGaA: Weinheim, 2004; Lemal, D. M.; *J. Org. Chem.* **2004**, *69*, 1; Zimmer, L. E.; Sparr, C.; Gilmour, R.; *Angew. Chem., Int. Ed*. **2011**, *50*, 11860; Terashima, Y.; Sakurai, T.; Bando, Y.; Seki, S.; Maeda, H.; *Chem. Mater*. **2013**, *25*, 2656; Haldar, S.; Sinha, D.; Mandala, P. K.; Goubitz, K.; Peschar, R.; *Liq. Cryst.* **2013**, *40*, 689; Kenwright, A. M.; Sandford, G.; Tadeusiak, A. J.; Yufit, D. S.; Howard, J. A. K.; Kilickiran, P.; Nelles, G.; *Tetrahedron* **2010**, *66*, 9819.

Submitted on: March 27, 2014
Published online: June 6, 2014