Tetrahedron 70 (2014) 4626-4630

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

The influence of vicinal *threo*-difluorination on electro-optic and mesogenic properties of propyleneoxy-linked nematic liquid crystals

Nawaf Al-Maharik^a, Peer Kirsch^{b,*}, Alexandra M.Z. Slawin^a, David O'Hagan^{a,*}

^a EaStCHEM School of Chemistry, University of St. Andrews, St. Andrews, Fife KY16 9ST, UK ^b Merck KGaA, Liquid Crystals R&D Chemistry, Frankfurter Str. 250, D-64293 Darmstadt, Germany

ARTICLE INFO

Article history: Received 10 February 2014 Received in revised form 28 April 2014 Accepted 12 May 2014 Available online 17 May 2014

ABSTRACT

A protocol for the preparation of a series of liquid crystals is presented, where the structures carry a central propyleneoxy motif carrying two vicinal *threo*-C–F bonds. The negative dielectric anisotropy $(-\Delta\varepsilon)$ of the resultant liquid crystals has been explored. The stereoelectronic relationship between the vicinal C–F bonds was anticipated to orientate the fluorine atoms *gauche* to each other when the propylene chain is extended. This is shown to be the case. This orientation of the C–F bonds generates a net dipole perpendicular to the molecular axis, a prerequisite for the design of dielectrically negative liquid crystals. However the molecules adopt a conformation where one C–F bond reinforces the net molecular dipole, and the other has a counter effect, thus the introduction of the motif has an almost neutral effect on dielectric anisotropy $(\Delta\varepsilon_{virt})$ of these candidate liquid crystals. However, introduction of the difluoro motif raises the melting points of the liquid crystals and increases their conformational rigidity.

© 2014 Elsevier Ltd. All rights reserved.

1. Introduction

Novel liquid crystals (LCs) are in high demand presently as a consequence of the exponential growth in global personal device ownership, such as smart phones.^{1,2} As the specifications for display screens for such devices are increasingly being improved, new component materials are required to follow or even anticipate the on-going technological developments in order to keep pace with product diversification and consumer demand.^{3,4} Organofluorine compounds constitute an important subclass of the materials used in display screen development.⁵ This is because the C-F bond is polarised and contributes a large dipole moment, however, the fluorine atom itself is not polarisable, and displays only weak intermolecular interactions. This latter property often confers low viscosity on organofluorine compounds and thus they orientate rapidly under the influence of changing electric fields. Another effect of fluorination is its positive impact on mesogenic properties, such as wide nematic phase ranges and high clearing temperatures.⁵ Also the strength of the C–F bond adds durability and thus reliability over the product lifetime. In this context, dielectrically negative LC materials have become attractive in the design of molecular components in particular for LCD-TV and PC monitors.^{6–10} Such compounds have a molecular dipole moment, which is orientated perpendicular to the molecular axis. This can be contrasted with dielectrically positive compounds, which have the molecular dipole orientated along the molecular axis.¹¹

It became an objective to prepare a series of dielectrically negative LC candidates carrying a vicinal difluoro motif on an aliphatic linker.¹² Given that the central alkyl chain will preferentially adopt an *anti*-zig-zag conformation, then a *threo* (rather than *erythro*) arrangement of C-F bonds is required to place the two vicinal C-F bonds gauche to each other. Additional stability for this arrangement is expected as it is well known that vicinal C-F bonds have a conformational preference, which predisposes them to align gauche to each other. This comes from the stereoelectronic gauche effect, which recognises that C-H bonds adopt preferred anti orientations to C-F bonds, such that the electron density of the C-H bond can hyperconjugate into the σ^*_{C-F} antibonding orbital.^{13,14} The stabilising effect is relatively weak contributing up to 1.0 kcal mol^{-1} for a *gauche* over *anti* preference in 1,2difluoroethane, but it should enhance or 'rigidify' the inherent zig-zag conformation of the alkyl linker. It is expected that the gauche orientation of the C-F bonds will raise the overall molecular dipole perpendicular to the long molecular axis of the liquid crystal. We report in this study the synthesis of the six LC candidates **1–6**, five of which have a vicinal threo-difluoro motif. Their LC characteristics are then compared relative to each other (Fig. 1).





Tetrahedron

^{*} Corresponding authors. Tel.: +44 1334 467176; fax: +44 1334 463808 (D.O'H.); e-mail addresses: peer.kirsch@merckgroup.com (P. Kirsch), do1@st-andrews.ac.uk (D. O'Hagan).



Fig. 1. Target liquid crystalline (LC) candidates with 2–6 containing the difluoro threo-vicinal motif.

2. Results and discussion

The target LCs **1–6** have a common general structure. They all possess a propyl-cyclohexyl motif linked through the propyl chain to a phenol ether. For structures **2–6**, the difluorovicinal motif was introduced by conversion of an epoxide ring in intermediates **13a–e** by sequential stereospecific conversion of the original epoxide C–O bonds to C–F bonds.^{15,16} Thus epoxides **13a–e** were key intermediates. They were prepared by the Horner–Wordsworth–Emmons reaction of cyclohexylaldehyde **7** and phosphonate **8**.¹⁷ The resultant (*E*)- α , β -unsaturated ester **9** formed as a 1:4 mixture of isomers due to the configuration of substituents across the cyclohexyl ring. This isomeric ratio could be improved by epimerisation to a 1:9 ratio after treatment of **9** with base (KOH/ EtOH)¹⁸ (Scheme 1).

Reduction to allylic alcohol 10 was straightforward, and then epoxidation with *m*-CPBA generated epoxy alcohol **11**, which was isolated as a single diastereoisomer after chromatography. Epoxy alcohol 11 served as a common intermediate to the vicinal difluorinated LC targets 2-6. At this stage it was treated with a series of different phenols, 12a-e under conditions described previously⁶ to generate ethers **13a–e**. The epoxide functionality of 13a-e was then taken through to the corresponding vicinal difluoro motifs in a three step protocol.^{7,9} This involved epoxide ring opening with Et₃N·3HF, to give a mixture of fluorohydrin regio-isomers, namely 14a-e and 15a-e. These reactions did not show any particular selectivity and the regio-isomers were generally formed in 1:1 ratios. Regio-isomers 14a-d were purified by chromatography whereas regio-isomer 14e was inseparable from **15e.** and in that case both isomers were treated together to generate a mixture of **16e** and **17e**. Compounds **14a–d** were obtained after two rounds of chromatography and were converted to their corresponding triflates 16a-d. The triflates were then treated, without further purification, with Et₃N · 3HF (65 °C) to generate the desired vicinal difluoro products 1-5. This protocol displayed complete stereointegrity, and only the threo-vicinal difluoro isomers were formed. On the other hand, when trifates 17a, 17c and 17e generated from regio-isomers 15a, 15c and 15e were subjected to identical fluorination conditions, these substrates gave complex rearrangement product mixtures. The products were not characterised, but the presence of significant levels of fluoromethyl groups was obvious in the ¹⁹F NMR spectra of the product mixtures.

Samples of each of the difluoro ethers **1–5** derived from **16a–d**, were further purified by preparative HPLC, such that analytically pure samples (\sim 400 mg) were available for LC property analyses.

The non-fluorinated analogue **6** was also prepared. This was required such that it could be assessed as a comparative compound,

particularly relative to analogue **3**, to determine the influence of the fluorine atoms on the LC properties. The synthesis route to **6** is illustrated in Scheme 2. In this case allylic alcohol **10** was hydrogenated to generate alcohol **18**, and the alcohol was then subjected to etherification with phenol **12c**, to generate **6**. An analytically pure sample was also prepared by semi-preparative HPLC for LC property analysis.

The properties of the prepared compounds **1–6** were assessed for their LC characteristics, and the data is summarised in Table 1.

The liquid crystals **1–6** do not show any mesophases. This is also reflected in the low virtual clearing temperatures, which are all below -10 °C. However, the melting points of the difluoropropyleneoxy-linked materials **1–5** are all significantly higher (>53 °C) than for the non-fluorinated propyl-ether linked compound **6** (33 °C). This is an indication of fluorine-induced intermolecular electrostatic interactions, stabilising the crystal lattice.

Compound **1** is distinct in that it does not carry a polar terminal group, therefore, the dielectric anisotropy of **1** is mainly caused by the electronegative threo-difluoro motif in the linker. This moderate negative dielectric anisotropy ($\Delta \varepsilon_{virt}$) indicates that the overall molecular dipole moment is oriented in a perpendicular manner relative to the long molecular axis, as is well known for other liquid crystals with a vicinal-difluoroalkylene subunit.⁴ In the case of compounds 2 and 5, the polar fluorine substituents on the aromatic head groups twist the overall dipole moment more in line with the long molecular axis, rendering liquid crystal 2 dielectrically nearly neutral in spite of the presence of seven electronegative heteroatoms. This indicates that the angle between the overall dipole moment vector and the director of the nematic phase-approximated by the long molecular axis—is around 53°, where $\Delta \varepsilon$ becomes zero, independent from the molecular dipole moment.⁵ In contrast, compounds 3, 4 and 6 with a 2,3-difluorophenyl head group show strong negative dielectric anisotropy. In general 1alkoxy-2,3-difluorobenzenes prefer an anti arrangement of the aryl-alkoxy bond by about 10:1 over the syn conformation, which is reflected nicely in the crystal structure of **4**.⁶ A comparison between 3 and 6 allows some conclusions to be drawn on the preferred conformation; the virtual clearing point of 3 is 18.1 K higher than that of the analogue 6 with the non-fluorinated linker. This can be seen as evidence for the conformational rigidification of the linker group by threo-difluorination.

Unexpectedly, the comparison of the dielectric anisotropies of **3** ($\Delta \varepsilon_{virt}$ =-5.69) and **6** ($\Delta \varepsilon_{virt}$ =-5.77) are very similar. A closer look at the crystal structure of **3** suggests a rationale assuming this is a highly populated conformer in the LC phase; the all-*gauche* conformation around the fluorine and oxygen atoms in the linear





Scheme 2. Preparation of reference liquid crystal 6 without an aliphatic vicinal threo-difluoro motif.

linker chain shows a uniform handedness $(g^+g^+g^+ \text{ or } g^-g^-g^-)$. In the 2,3-difluorophenylene unit, the ether oxygen and the 3-fluorine substituent are pointing their local dipole moments roughly in the same direction, whereas the 4-fluorine of the linker is pointing in the opposite direction. This results in a partial cancellation of the overall dipole moment and a reduction of the overall dielectric anisotropy. In summary, this means that the difluoropropyleneoxy

chain is moderately effective in rigidifying the liquid crystal's mesogenic core structure, but it is counter-productive for increasing the negative dielectric anisotropy. Geometrically it is impossible to combine in such a 3,4-difluoropropyl ether, an all*gauche* conformation—a $g^+g^-g^+$ or $g^-g^+g^-$, the conformation necessary to avoid the dipole cancellation of the electronegative heteroatoms with the required linear zig-zag conformation of the

Table 1	
The phase transition temperatures are given in	۱°C

No.	Phase transitions (Mp in $^\circ$ C)	T _{NI,virt}	$\Delta \varepsilon_{\rm virt}$	$\Delta n_{\rm virt}$
1	C 53 I	-32.1	-4.71	_
2	C 54 I	-71.0	-0.43	_
3	C 63 I	-33.7	-5.69	0.0855
4	C 73 I	-10.1	-7.35	0.090
5	C 69 I	_	—	_
6	C 33 I	-51.8	-5.77	0.0898

C=crystalline, Mp=melting point, I=isotropic. The virtual parameters $T_{\rm NI,virt}$ and $\Delta n_{\rm virt}$ were determined by linear extrapolation from a 10% w/w solution in the commercially available Merck mixture ZLI-4792 ($T_{\rm NI}$ =92.8 °C, $\Delta \epsilon$ =5.3, Δn =0.0964). The extrapolated values are corrected empirically for differences in the order parameter. $\Delta \epsilon_{\rm virt}$ was extrapolated from ZLI-2857 ($T_{\rm NI}$ =82.3 °C, $\Delta \epsilon$ =-1.4, Δn =0.0776). The phase transition onset temperatures (Mps) were determined by differential scanning calorimetry (DSC). The heating/cooling rate was 10 K/min.

linker group, thus there are limitations to this motif in maximising the molecular dipole moment. The highest dielectric anisotropy is found with **4** ($\Delta \varepsilon_{virt}$ =-7.35), which is clearly a consequence of the additional oxygen atom of the *para*-substituted ethoxy ether, pointing its dipole to reinforce that of the C–F bonds of the difluoroaryl moiety (see X-ray of **4**, Fig. 2).

two vicinal fluorines of the hydrocarbon would orientate to increase the molecular dipole and as a consequence increase the –ve dielectric anisotropy of the various analogues. A direct comparison of the properties of compounds **3** and **6**, which differ only in the influence of the vicinal *threo*-difluorines, indicated that these fluorines had a neutral impact on the $-\Delta\varepsilon$ dielectric anisotropy. Essentially one C–F bond has a reinforcing effect and the second orientated to counter the overall molecular dipole. This was apparent from X-ray structures. It is found, however, that melting points increase when the vicinal difluoro linker is introduced, indicative of increased electrostatic interaction between molecules, and thus a rigidifying effect of this motif. This information will be used to refine the design of more effective –ve dielectric anisotropic liquid crystalline candidates.

Experimental details are provided in Supplementary data.

Acknowledgements

D.O'H. thanks the European Research Council for an Advanced Investigator Grant and the Royal Society for a Wolfson Merit Award. P.K. thanks Andreas Ruhl and David Till of Merck, Darmstadt, for technical assistance.



Fig. 2. X-ray-derived structures of three (**3**, **6** and **4**) of the prepared liquid crystals. For structures **3** (CCDC 997680) and **4** (CCDC 997681), the 4-fluoro substituent of the propyleneoxy linker group is pointing into a direction opposite to the other carbon–heteroatom bonds, resulting in a partial cancellation of the local dipole moments and concomitant reduction of the overall molecular dipole moment. Structure **6** (CCDC 997682) is a reference compound indicating, by comparison that the *threo*-difluoro linker does not change the overall conformation of these liquid crystals.

3. Conclusion

In conclusion we have demonstrated a relatively efficient synthesis protocol to prepare samples of nematic liquid crystals, carrying a vicinal *threo*-difluoro motif. The idea was to explore if the

Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2014.05.027.

References and notes

- Chen, Y.; Peng, F.; Yamaguchi, T.; Song, X.; Wu, S.-T. *Crystals* 2013, 3, 483–503.
 Chen, Y.; Luo, Z.; Peng, F.; Wu, S.-T. *J. Display Technol.* 2013, 9, 74–77.
 Tariq, M.; Hameed, S.; Bechtold, I. H.; Bortoluzzi, A. J.; Melo, A. A. *J. Mater. Chem.*

- Jahle, M., Halleed, S., Bechlord, F.H., Berondzer, A.J., Hiele, A.P.J., Huele, A.P. 2013, 52, 8880-8896.

- S. Kiasen, M.; Bremer, M.; Tarumi, K. *Jpn. J. Appl. Phys.* 2000, *39*, L1180–L1182.
 Kirsch, P.; Heckmeier, M.; Tarumi, K. *Liq. Cryst.* 1999, *26*, 449–452.
 Kirsch, P.; Bremer, M.; Taugerbeck, A.; Wallmichrath, T. *Angew. Chem., Int. Ed.* **2001**, 40, 1480–1484.
- 10. Kirsch, P.; Bremer, M.; Huber, F.; Lannert, H.; Ruhl, A.; Lieb, M.; Wallmichrath, T. J. Am. Chem. Soc. 2001, 123, 5414-5417.
- 11. Steinsträsser, R. Angew. Chem., Int. Ed. Engl. 1972, 11, 633–634.
- 12. Nicoletti, M.; Bremer, M.; Kirsch, P.; O'Hagan, D. Chem. Commun. 2007, 5075-5077.
- 13. Hunter, L. Beilstein J. Org. Chem. 2010, 6, 38.
- 14. Wiberg, K. B.; Murcko, M. A.; Laidig, K. E.; MacDougall, P. J. J. Phys. Chem. 1990, 94, 6956-6959.
- 15. O'Hagan, D.; Rzepa, H. S.; Schüler, M.; Slawin, A. M. Z. Beilstein. J. Org. Chem. **2006**, *2*, 19.
- 16. Hamatani, T.; Matsubara, S.; Matsuda, H.; Schlosser, M. Tetrahedron 1988, 44, 2875–2881.
- Wadsworth, W. S.; Emmons, W. D. J. Am. Chem. Soc. 1961, 83, 1733–1738.
 Hunter, L.; Kirsch, P.; Slawin, A. M. Z.; O'Hagan, D. Angew. Chem., Int. Ed. 2009, 48, 5457-5460.