

# Super-Fluorinated Liquid Crystals: Towards the Limits of Polarity

Peer Kirsch,<sup>\*,[a]</sup> Werner Binder,<sup>[b]</sup> Alexander Hahn,<sup>[b]</sup> Kai Jähring,<sup>[b]</sup> Marc Lenges,<sup>[b]</sup> Lars Lietzau,<sup>[b]</sup> David Maillard,<sup>[b]</sup> Volker Meyer,<sup>[b]</sup> Eike Poetsch,<sup>[b]</sup> Andreas Ruhl,<sup>[b]</sup> Gerald Unger,<sup>[b]</sup> and Roland Fröhlich<sup>[c]</sup>

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Highly fluorinated liquid crystals with unprecedented polarity were obtained by introducing a tetrahydropyran moiety into their mesogenic core structure. The new materials exhibit an unusually favourable combination of mesophase properties, excellent solubility and low rotational viscosity,

which renders them highly attractive for application in fast-switching active matrix LCDs.

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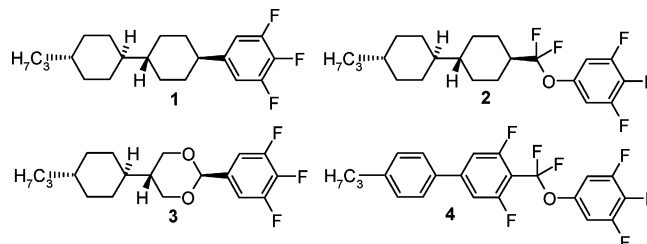
## Introduction

In the recent few years, liquid crystal display (LCD) technology has been firmly established, and it has permeated nearly every aspect of our daily lives. However, the developers of liquid crystalline materials for active matrix (AM) LCD are still facing many technical challenges.<sup>[1,2]</sup>

The most important issue in need of improvement are materials for application in LCD TVs. Here, extreme endurance of the liquid crystal towards long-term thermal or photochemical stress is asked for.<sup>[2]</sup> Another problem area is the design of liquid crystals for displays with very low power consumption, as they are used for mobile devices, such as notebook PCs, mobile phones or PDAs.

On the level of materials design, a major problem is how to combine high dielectric anisotropy ( $\Delta\epsilon$ )<sup>[3,4]</sup> with good mesogenic properties, sufficient solubility and – in particular – high reliability. There are also some limitations in the toolbox of the designer of liquid crystals for AM LCDs: nitrogen heterocycles or nitrile groups that would enhance the molecular dipole moment should not be used, because they either promote photochemical degradation of the LC mixture or cause image sticking in the LCD panel as a result of their strong affinity towards ionic trace impurities.<sup>[5]</sup> Accordingly, all materials currently in use for AM LCD are

so-called super-fluorinated materials (SFM), whose dipole moment is mainly derived from polar carbon–fluorine, and in a few cases from carbon–oxygen, bonds (Scheme 1).



Scheme 1. Examples of highly fluorinated (SFM) liquid crystals currently in use for LCD applications. Compounds 3 and 4 represent the current limits of polarity for commercial materials of AM LCDs.

This leaves three possible strategies for the design of very polar materials, and these methods involve the use of: (1) extremely polar fluorinated terminal groups, such as  $\text{CF}_3$  or  $\text{SF}_5$ ,<sup>[6]</sup> enhanced by laterally fluorinated aromatic ring structures;<sup>[7]</sup> (2) intrinsically polar bridge structures, such as  $\text{CF}_2\text{O}$  bridges<sup>[8]</sup> and (3) polar aliphatic oxygen heterocycles.<sup>[9]</sup> Strategies (1) and (2) alone are usually not sufficient, and the use of 1,3-dioxane building blocks (strategy 3) often causes reliability problems under oxidative or hydrolytic stress. Another problem of polar liquid crystals with extensive aromatic fluorination is their generally quite high melting points, which are limiting the solubility in nematic mixtures.

## Results and Discussion

A structural building block combining the polarity of dioxanes with high chemical stability and a tendency to promote the solubility of its derivatives is the tetrahydropyran

[a] Merck Ltd. Japan, New Technology Office, 4084 Nakatsu, Aikawa-machi, Aiko-gun, Kanagawa 243-0303, Japan  
Fax: +81-46-286-2592

[b] Merck KGaA, Liquid Crystals Division, Frankfurter Str. 250, 64271 Darmstadt, Germany

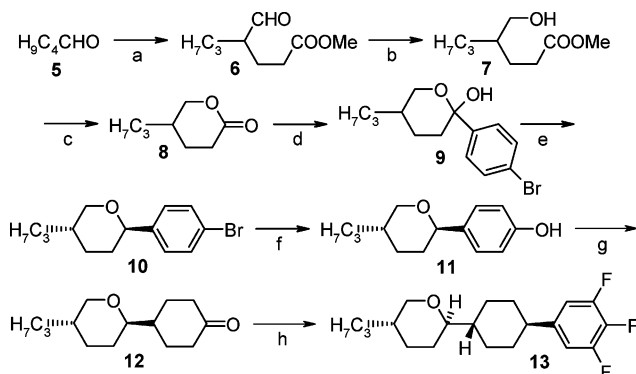
[c] University of Münster, Institute for Organic Chemistry, 48149 Münster, Germany

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(THP) structure. Singular examples of THP-based liquid crystals have been mentioned in the literature for years,<sup>[10]</sup> but several practical obstacles have impeded the systematic exploration of this highly interesting compound class. As the major problem, there is a lack of a generally applicable synthetic procedure. There are several examples for chiral, THP-based liquid crystals where the synthesis starts from natural, chiral pool carbohydrate precursors. The methods reported so far for the preparation of liquid crystals based on racemic THP<sup>[11–14]</sup> often have only a rather limited structural scope.

In order to fully explore the potential of liquid crystals with a THP substructure, we developed two new synthetic approaches: one based on the ring opening of alkyl oxetanes,<sup>[15]</sup> and the other one starting from alkyl  $\delta$ -valerolactones.<sup>[16]</sup>

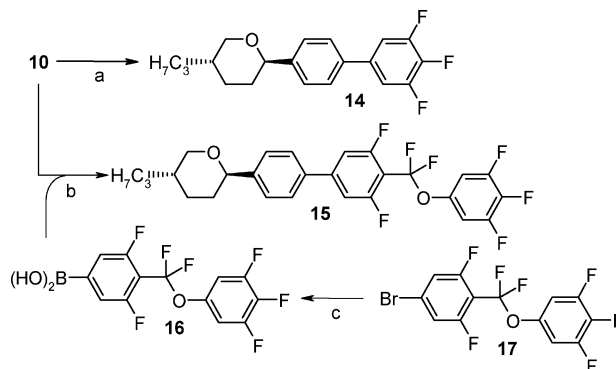
The  $\delta$ -valerolactone synthesis (Scheme 2) gives the best yields for the ethyl, *n*-propyl and *n*-butyl analogues. For longer side chains, an increased tendency towards polymerization decreased the reaction yield as well as the purity of the lactone. Lactone **8** was treated with 4-bromo-1-lithiobenzene, and intermediate **9** was then reduced and isomerized into *trans*-**10**. Bromide **10** can serve as a key intermediate for a variety of liquid crystals that are structurally analogous to commonly used, highly fluorinated materials for AM LCDs. Another central intermediate is ketone **12**, which is readily available in two steps via phenol **11**. For example, addition of Grignard compounds, followed by acid-catalyzed elimination of the tertiary alcohol, hydrogen-



Scheme 2. Synthesis of tetrahydropyran derivatives by the  $\delta$ -valerolactone route. Reagents and conditions: (a) 1. methyl acrylate,  $\text{Et}_2\text{NSiMe}_3$ ,  $\text{CH}_3\text{CN}$ , reflux, 18 h; 2.  $\text{HOAc}$ ,  $\text{H}_2\text{O}$ , reflux, 18 h (68%, crude product used for subsequent step); (b)  $\text{NaBH}_4$ , 2-propanol, room temp., 18 h (87%); (c) 1. cat. *p*-TsOH, toluene, reflux with azeotropic water removal; 2. distillation (61%); (d) 1,4-dibromobenzene, *n*BuLi,  $\text{Et}_2\text{O}$ ,  $-50$  (2 h) to  $-10$  °C (crude product used for subsequent reaction); (e) 1.  $\text{BF}_3\cdot\text{OEt}_2$ ,  $\text{Me}_3\text{SiH}$ ,  $\text{CH}_2\text{Cl}_2$ ,  $-70$  (2 h) to  $-10$  °C (44%); 2.  $\text{AlCl}_3$  (0.2 equiv.),  $\text{CH}_2\text{Cl}_2$ ,  $-20$  °C, 30 min (95%); (f) 1. *n*BuLi, THF,  $-70$  °C (2 h), then  $\text{B(OMe)}_3$ ,  $-70$  (2 h) to  $-10$  °C, 2 N HCl (75%, crystallized from *n*-hexane); 2. 30%  $\text{H}_2\text{O}_2$ ,  $\text{H}_2\text{O}$ ,  $\text{HOAc}$ , THF, room temp., 6 h (89%); (g)  $\text{H}_2$ , 5% Pd-C, xylene, 5 bar,  $120$  °C (75%); (h) 1. 1-bromo-3,4,5-trifluorobenzene, 2-PrMgCl, THF, room temp., 1 h, then **12**, room temp., 1 h; 2.  $\text{MeSO}_2\text{Cl}$ ,  $\text{NEt}_3$ ,  $\text{CH}_2\text{Cl}_2$ ,  $0$  °C to room temp., 18 h (45%); 3.  $\text{H}_2$ , 5% Pd-C, THF, 1 bar, room temp. (60%).

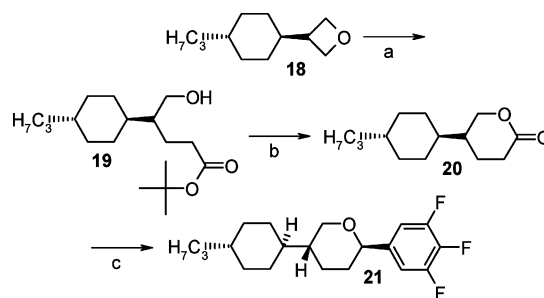
ation and fractionated crystallization of the *trans,trans* isomer gives liquid crystal **13**, which is a structural analogue of **1**.

Bromide **10** is a versatile intermediate for the synthesis of THP derivatives. Suzuki coupling with suitable boronic acids<sup>[17]</sup> furnishes liquid crystals **14** and **15** (Scheme 3).



Scheme 3. Use of bromide **10** as a versatile intermediate for the synthesis of liquid crystals **14** and **15**. Reagents and conditions: (a) 3,4,5-trifluorobenzene boronic acid,  $\text{N}_2\text{H}_4\cdot\text{H}_2\text{O}$ ,  $\text{Na}_3\text{BO}_3\cdot 8\text{H}_2\text{O}$ , cat.  $\text{PdCl}_2(\text{PPh}_3)_2$ ,  $\text{H}_2\text{O}$ , THF, reflux, 90 min (71%); (b) **16**,  $\text{N}_2\text{H}_4\cdot\text{H}_2\text{O}$ ,  $\text{Na}_3\text{BO}_3\cdot 8\text{H}_2\text{O}$ , cat.  $\text{PdCl}_2(\text{PPh}_3)_2$ ,  $\text{H}_2\text{O}$ , THF, reflux, 18 h (61%); (c) 1. *i*PrMgCl, THF,  $-5$  °C, 1 h; 2.  $\text{B(OMe)}_3$ , THF,  $-5$  °C, 1 h; 3. 16% HCl,  $-5$  °C, 30 min (95%).

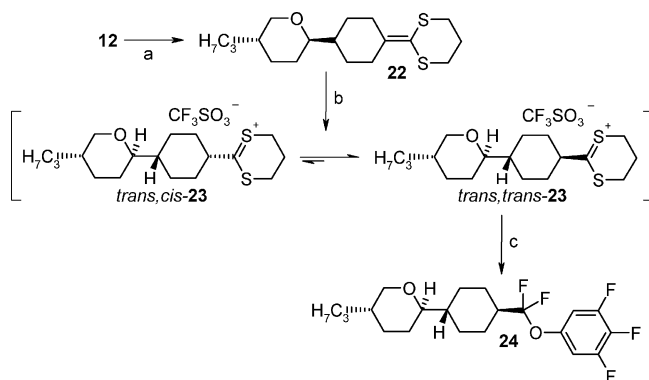
The synthesis of another THP analogue of **1** (Scheme 4) started with oxetane **18**,<sup>[15]</sup> which was treated with an ester enolate<sup>[13]</sup> to give lactone **20**. Addition of 3,4,5-trifluoro-1-lithiobenzene and subsequent reduction of the resulting hemiketal furnished liquid crystal **21**.



Scheme 4. Synthesis of lactone **20** as a precursor of tetrahydropyran-based liquid crystal **21**. Reagents and conditions: (a) *t*BuOAc, LDA, THF,  $-78$  °C, 25 min, then **18**,  $\text{BF}_3\cdot\text{OEt}_2$ ,  $-78$  °C (1 h), then room temp. (27%); (b)  $\text{CF}_3\text{COOH}$ ,  $\text{CH}_2\text{Cl}_2$ , room temp., 18 h (81%); (c) 1.  $\text{LiPhF}_3$ ,  $\text{Et}_2\text{O}$ ,  $-70$  °C (2 h), then room temp. (85% crude); 2.  $\text{BF}_3\cdot\text{OEt}_2$ ,  $\text{Me}_3\text{SiH}$ ,  $\text{CH}_2\text{Cl}_2$ ,  $-70$  (2 h) to  $-10$  °C (54%).

Peterson olefination of versatile intermediate **12** with 2-trimethylsilyl-1,3-dithiane<sup>[18]</sup> furnished ketene dithioketal **22**, which was subsequently converted into difluoroether **24** by a one-step protonation–equilibration–fluorodesulfuration procedure (Scheme 5).<sup>[8]</sup>

The preparation of difluoroether liquid crystal **29** with the THP unit as the middle ring was basically done in analogy to the synthesis of **24**, but required some small but essential modifications (Scheme 6). Enolketene dithioketal **25** was prepared by a Horner–Emmons reaction of lactone **21** with activated phosphonic ester **26**.<sup>[19]</sup> Differently from the



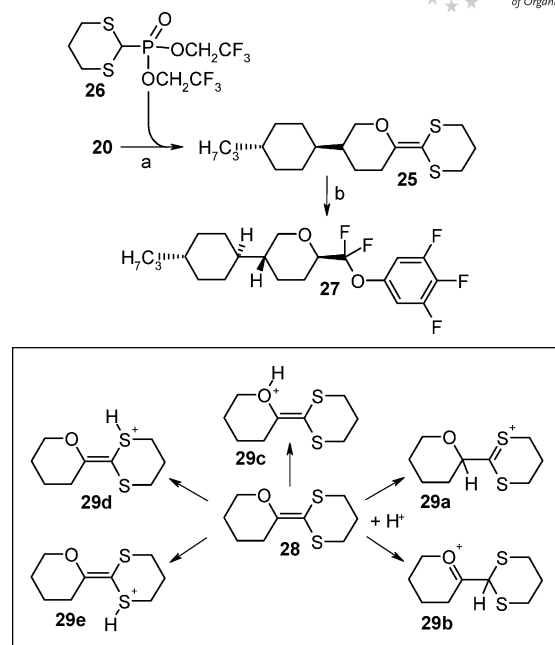
Scheme 5. Synthesis of difluorooxymethylene-linked liquid crystal **24** by the one-pot conversion of ketene dithioketal **22**. Reagents and conditions: (a) 2-Me<sub>3</sub>Si-1,3-dithiane, *n*BuLi, THF, −70 °C to room temp., 18 h (82%); (b) CF<sub>3</sub>SO<sub>3</sub>H, CH<sub>2</sub>Cl<sub>2</sub>, −20 °C to room temp. (30 min) to −70 °C; (c) 1. F<sub>3</sub>PhOH, NEt<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, −70 °C, 30 min; 2. NEt<sub>3</sub>·3HF, −70 °C; 3. DBH, CH<sub>2</sub>Cl<sub>2</sub>, −70 °C (1 h) to room temp. (19%).

usual procedure,<sup>[8]</sup> the protonation–alkoxydifluorodesulfuration had to be carried out at very low temperatures (between −90 and −100 °C) and the reagents had to be added as fast as temperature control allowed. Otherwise, not even trace amounts of any defined product or byproduct were isolated. Only by applying these modifications could difluoroether **27** be obtained in a very modest yield of 0.9%.

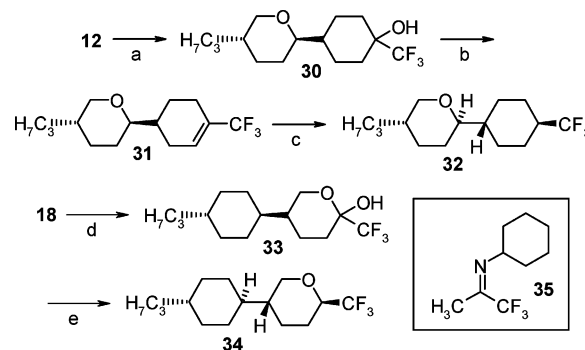
At first, our prime suspect for these complications was that the protonation of the double bond in intermediate **26** might occur at the wrong position. However, computational analysis [MP2/6-311+G(2d,p)//B3LYP/6-31G(d)+ZPE level of theory]<sup>[20]</sup> of the relative energies of the different possible protonation products ruled out this scenario. It might be speculated that during the fluorodesulfuration sequence a competing rearrangement of the THP oxygen atom to one of the transient electrophilic centres occurs.

Compounds **32** and **34** were selected as candidates for polar liquid crystals with very low birefringence ( $\Delta n$ ) – a target that is not easily achievable with purely carbocyclic ring structures. Ketone **12** was treated with the Ruppert–Prakash reagent, Me<sub>3</sub>SiCF<sub>3</sub><sup>[21]</sup> under fluoride catalysis (Scheme 7). Resulting trifluoromethyl carbinol **30** was first eliminated to olefin **31**, which was subsequently hydrogenated to a mixture of the *cis* and *trans* isomers of **32**. Desired isomer *trans,trans*-**32** was isolated by repeated crystallization from *n*-heptane. Isomeric compound **34** was prepared according to our recently developed method.<sup>[15]</sup>

Finally, we wanted to explore the limits of polarity (i.e.,  $\Delta\epsilon$ ) that can be achieved by using the tetrahydropyran structure. As already mentioned, liquid crystals whose strong polarity is derived from extensive aromatic fluorination tend to have very high melting points.<sup>[1]</sup> The corresponding poor solubility in liquid-crystal mixtures limits the size of the mesogenic core structure of practically useful liquid crystals to a maximum of four ring elements. The introduction of the polar and at the same time solubility-enhancing THP ring is supposed to increase this limit to at least five rings, which can infer strong polarity by “heavy”

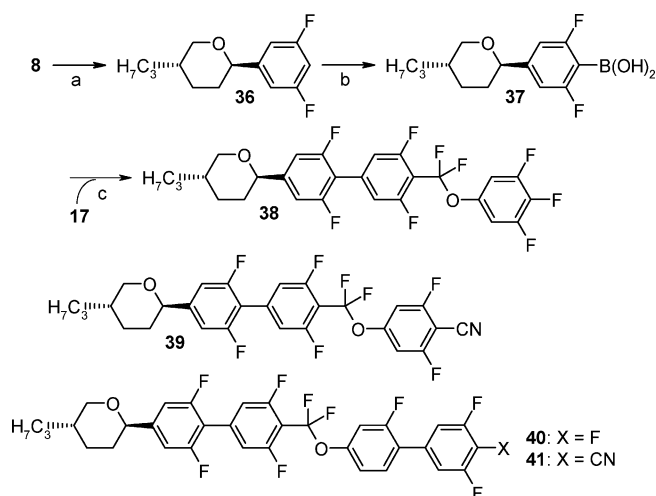


Scheme 6. Conversion of lactone **20** into ketene dithioketal **25** and subsequent one-pot fluorodesulfuration into **27**. Box: The formation of the “right” intermediate protonation product **29a** is energetically preferred by 9.8 kcal mol<sup>−1</sup> [MP2/6-311+G(2d,p)//B3LYP/6-31G(d)+ZPE level of theory] relative to the alternative double-bond protonation product **29b**.<sup>[20]</sup> The relative energies of the other possible O- and S-protonation products **29c–e** are even higher. Reagents and conditions: (a) 1. **26**, *t*BuOK, THF, −10 °C, 1 h; 2. **20**, THF, −10 °C to room temp., 18 h (60%); (b) 1. CF<sub>3</sub>SO<sub>3</sub>H, CH<sub>2</sub>Cl<sub>2</sub>, −25 °C to room temp. (10 min) to −90 °C; 2. F<sub>3</sub>PhOH, NEt<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, −90 °C, 30 min; 3. NEt<sub>3</sub>·3HF, −70 °C; 4. Br<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>, −90 °C (1 h) to room temp. (0.9%).



Scheme 7. Synthesis of the polar, low birefringent liquid trifluoromethyl derivatives **32** and **34**. Reagents and conditions: (a) 1. Me<sub>3</sub>SiCF<sub>3</sub>, Bu<sub>4</sub>NF, THF, 0 °C to room temp.; 2. KF, MeOH, reflux, 3 h (100%, crude product); (b) SOCl<sub>2</sub>, pyridine, room temp., 3 d (73%); (c) H<sub>2</sub>, 5% Pd–C, THF, 1 bar, r.t. (6%); (d) 2,2,6,6-tetramethylpiperidine, *n*BuLi, THF, −78 °C, 20 min, then **35**, −78 °C, 15 min, then **18** (15 min), BF<sub>3</sub>·OEt<sub>2</sub>, −78 °C (2.5 h), then room temp., 13 h (24%); (e) BF<sub>3</sub>·OEt<sub>2</sub>, Me<sub>3</sub>SiH, CH<sub>2</sub>Cl<sub>2</sub>, −50 to 40 °C, 4 h (55%).

lateral fluorination in combination with a polar terminal group and polar bridge structures, such as the difluoroether link. The synthesis of some extremely polar but well-soluble four- and five-ring liquid crystals is depicted in Scheme 8.

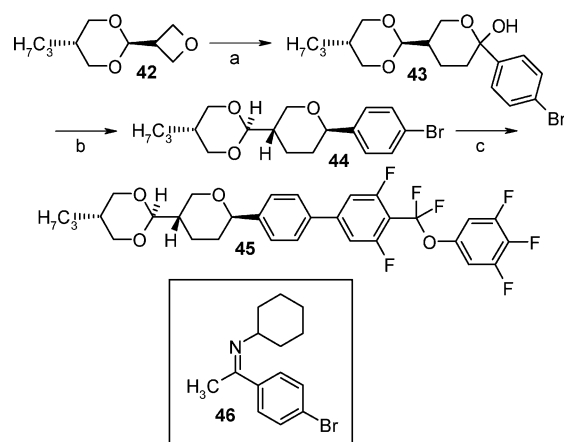


Scheme 8. Synthesis of extremely polar THP-based liquid crystal **38**. Reagents and conditions: (a) 1. 1-bromo-3,5-difluorobenzene, *n*BuLi, Et<sub>2</sub>O, −70 (2 h) to −10 °C; 2. BF<sub>3</sub>·OEt<sub>2</sub>, Me<sub>3</sub>SiH, CH<sub>2</sub>Cl<sub>2</sub>, −70 (2 h) to −10 °C (69%); (b) 1. *n*BuLi, THF, −70 °C, 1 h; 2. B(OMe)<sub>3</sub>, −65 (30 min) to −10 °C; 3. 2 N HCl, room temp. (67%); (c) 17, N<sub>2</sub>H<sub>4</sub>·H<sub>2</sub>O, Na<sub>3</sub>BO<sub>3</sub>·8H<sub>2</sub>O, cat. PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, H<sub>2</sub>O, THF, reflux, 18 h (55%). Compounds **39–41** were prepared by a similar method by using suitable building blocks analogous to **17**.<sup>[17]</sup>

Apart from lateral fluorination, another strategy to induce strong polarity in liquid crystals is the use of 1,3-dioxane building blocks as a part of the mesogenic core structure. The use of multiple dioxane units has been explored previously,<sup>[9]</sup> but this was found to cause poor solubility and a very strong tendency to induce smectic phases. Because the effect of a solubility-enhancing THP unit on the electrooptical properties of liquid crystals is rather similar to that of dioxane, the usefulness of this structural element as a part of extremely polar five-ring liquid crystals was explored. Compound **45** was available through the Lewis acid catalyzed ring opening of oxetane **42** with the lithium iminoenolate of **46**.<sup>[15]</sup> The subsequent reaction steps were analogous to previously described syntheses (Scheme 9).

All THP-based liquid crystals (Table 1) share several common characteristics,<sup>[22]</sup> which renders them highly attractive for practical application in fast switching AM LCDs: they combine strong dielectric anisotropy ( $\Delta\epsilon$ )<sup>[3,4]</sup> with extremely good solubility and a small rotational viscosity ( $\gamma_1$ ), particularly when seen in relation to the high clearing temperatures. Therefore, they can be used as components of liquid-crystal mixtures, even in very high concentrations without the risk of crystallization or formation of smectic phases on long-term storage at low temperatures.

Relative to a cyclohexane moiety, the THP ring increases the  $\Delta\epsilon$  of the liquid crystal by 2–5 units (**1**→**13**, **21**; **2**→**24**, **27**), depending on the location of the THP unit within the mesogenic core structure. The effect is less pronounced than that for the 1,3-dioxane structure, but as a result of the excellent solubility-enhancing effect of the THP moiety, even five-ring materials such as **40**, **41** and **48** show sufficient solubility to be of practical use. Additional aromatic rings can serve as a scaffold for extensive lateral fluorination re-



Scheme 9. Synthesis of extremely polar material **45** containing a sequence of oxygen heterocyclic ring structures. Reagents and conditions: (a) 2,2,6,6-tetramethylpiperidine, *n*BuLi, THF, −78 °C, 30 min, then **46**, −78 °C, 20 min, then **42** (15 min), BF<sub>3</sub>·OEt<sub>2</sub>, −78 °C (1 h), then room temp., 13 h (20%); (b) BF<sub>3</sub>·OEt<sub>2</sub>, Me<sub>3</sub>SiH, CH<sub>2</sub>Cl<sub>2</sub>, −50 to −10 °C, 3 h (69%); (c) **16**, N<sub>2</sub>H<sub>4</sub>·H<sub>2</sub>O, Na<sub>3</sub>BO<sub>3</sub>·8H<sub>2</sub>O, cat. PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, H<sub>2</sub>O, THF, reflux, 18 h (60%).

Table 1. The physical properties of the new pyran-based liquid crystals in comparison to some conventional carbocyclic or 1,3-dioxane-based materials (**1–4**).<sup>[22]</sup>

| No.       | Phase sequence <sup>[a]</sup>      | $\Delta\epsilon_{\text{virt}}$ | $\Delta n_{\text{virt}}$ | $T_{\text{NI,virt}}$ | $\gamma_{1,\text{virt}}$ |
|-----------|------------------------------------|--------------------------------|--------------------------|----------------------|--------------------------|
| <b>1</b>  | C 66 N 94.1 I                      | 9.7                            | 0.0750                   | 74.3                 | 160                      |
| <b>2</b>  | C 44 N 105.3 I                     | 10.5                           | 0.0668                   | 91.5                 | 145                      |
| <b>3</b>  | C 74 N (51.2) I                    | 17.0                           | 0.0680                   | 63.2                 | 201                      |
| <b>4</b>  | C 48 I                             | 25.2                           | 0.1579                   | −20.6                | 96                       |
| <b>13</b> | C 74 I                             | 15.0                           | 0.0744                   | 32.4                 | 136                      |
| <b>14</b> | C 41 I                             | 15.6                           | 0.1363                   | 44.4                 | 178                      |
| <b>15</b> | C 75 N 118.0 I                     | 26.0                           | 0.1401                   | 111.3                | 300                      |
| <b>21</b> | C 57 N (52.2) I                    | 12.7                           | 0.0778                   | 63.6                 | —                        |
| <b>24</b> | C 35 N 66.3 I                      | 14.0                           | 0.0654                   | 58.1                 | 158                      |
| <b>27</b> | C 58 N (39.8) I                    | 12.4                           | 0.0751                   | 41.5                 | —                        |
| <b>32</b> | C? 7 S <sub>B</sub> 15 I           | 10.5                           | 0.0483                   | −77.8                | 76                       |
| <b>34</b> | C 59 I                             | 8.8                            | 0.0606                   | −57.6                | —                        |
| <b>38</b> | C 83 N (83.0) I                    | 35.6                           | 0.1316                   | 56.4                 | 457                      |
| <b>39</b> | C 74 S <sub>C</sub> (67) N 144.8 I | 66.6                           | 0.1568                   | 87.7                 | 1016                     |
| <b>40</b> | C 98 N 193.0 I                     | 37.1                           | 0.1544                   | 134.7                | 1225                     |
| <b>41</b> | T <sub>g</sub> −14 C 96 N 240.6 I  | 70.3                           | 0.1827                   | 167.3                | —                        |
| <b>45</b> | C 127 S <sub>A</sub> 212 N 251.1 I | 35.6                           | 0.1353                   | 212.4                | —                        |

[a] The phase transition temperatures are cited in °C, the rotational viscosities  $\gamma_1$  in mPas; C = crystalline, S = smectic, N = nematic, I = isotropic.

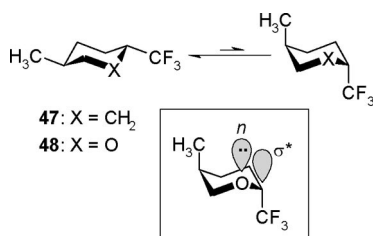
sulting in highly fluorinated liquid crystals with unprecedented polarity: for SFM material **40**, a  $\Delta\epsilon$  value of 37.1 is achieved. By using a terminal cyano group, the value of  $\Delta\epsilon$  is further increased to 70.3 for compound **41**. Also, the combination of THP with polar dioxane rings (**45**) gives satisfactory solubility and a very high clearing point and dielectric anisotropy as well. For conventional, commercially used liquid crystals without a THP moiety, insufficient solubility limits the number of rings within the mesogenic core structure to a maximum of four.

Amongst the various strategies for increasing the molecular dipole moment, the use of THP building blocks offers a particular advantage for liquid crystals with very low bire-

fringence ( $\Delta n$ ). Because lateral fluorination intrinsically relies on the presence of a polarizable aromatic ring, it always produces a concomitant increase in  $\Delta n$ . The THP unit, in contrast, allows the design of polar materials without (**32**, **33**) or with a minimum (**13**, **21**, **26**, **27**) of polarizable double bonds.

Comparison of the isomer pairs **13/21**, **24/27** and **32/34** shows that the position of the THP ring within the mesogenic core structure has a significant influence on the electrooptic, as well as the mesogenic, properties of the liquid crystal. In all three cases, the isomer with the THP moiety closest to the polar terminal group has the lowest dielectric anisotropy.

For the pairs **24/27** and **32/34**, the tendency to form thermodynamically stable mesophases is also diminished for these isomers. One possible reason for the pronounced differences in the physical properties of the isomers may be a stereoelectronic effect, analogous to the anomeric effect,<sup>[23]</sup> which is well known in carbohydrate chemistry. In compounds **27** and **34**, a strongly electron-withdrawing group is directly connected to the 2-position of the THP ring. Energetically favourable interaction of the axial oxygen lone electron pair with the axial  $\sigma^*$  orbital of the C–C bond connecting the electronegative  $\text{CF}_3$  or  $\text{CF}_2\text{OR}$  group to the THP ring stabilizes the bis(axial) conformation of the 2,5-substituents relative to the situation in the corresponding cyclohexane system. In contrast, the bis(equatorial) conformation is a prerequisite for the elongated, rod-like shape of nematic liquid crystals. This means, an increased equilibrium population of the bis(axial) conformer will result in a reduced clearing point, as well as a general decrease in the anisotropic properties, of the nematic mesophase (Scheme 10).



Scheme 10. The influence of the anomeric effect on the conformational equilibrium of liquid crystalline tetrahydropyran derivatives: In cyclohexane-based system **47**, the bis(equatorial) conformer is energetically preferred by  $4.5 \text{ kcal mol}^{-1}$  and for THP system **48** only by  $2.7 \text{ kcal mol}^{-1}$  [MP2/6-311+G(2d,p)//B3LYP/6-31G(d)+ZPE level of theory].<sup>[20]</sup>

The THP-based liquid crystals discussed so far are all racemic mixtures. Because there are various applications for chiral liquid crystals,<sup>[24]</sup> we also wanted to explore the properties of a pure enantiomer of at least one of the new liquid crystals. In order to measure the helical twisting power (HTP) of the enantiomers, a sample of *rac*-**49** (the pentyl homologue of **24**) was separated by preparative HPLC on a chiral phase. The crystal structure of one of the enantiomers was determined by anomalous X-ray diffraction,<sup>[25]</sup> which allowed the correlation of the chiroptical properties

with the absolute configuration (Figure 1). The absolute HTP of the THP enantiomers of **49** is  $0.8 \mu\text{m}^{-1}$  (Table 2),<sup>[22]</sup> which is very low relative to commonly used chiral dopants for liquid-crystal mixtures with an HTP of  $10 \mu\text{m}^{-1}$  or more.<sup>[24]</sup>

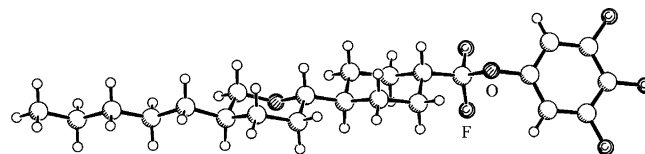


Figure 1. The absolute configuration of L-**49** as determined by X-ray crystallography.<sup>[25]</sup>

Table 2. Comparison of the physical properties of racemic and enantiopure liquid crystal **49**.<sup>[22]</sup>

| No.                    | Phase sequence <sup>[a]</sup> | $\Delta H_{\text{CN}}$ | $\Delta H_{\text{NI}}$ | $[\alpha]_{\text{D}}^{20}$ | HTP  |
|------------------------|-------------------------------|------------------------|------------------------|----------------------------|------|
| <i>rac</i> - <b>49</b> | C 39 N 75.3 I                 | 5900                   | 100                    | –                          | –    |
| D- <b>49</b>           | C 41 N* 73.3 I                | 7400                   | 100                    | +4.5                       | +0.8 |
| L- <b>49</b>           | C 42 N* 74.3 I                | 7400                   | 100                    | –4.9                       | –0.8 |

[a] The phase-transition temperatures are cited in  $^{\circ}\text{C}$ , the melting enthalpies ( $\Delta H_{\text{CN}}$ ) and the enthalpy of nematic-isotropic transition ( $\Delta H_{\text{NI}}$ ) in  $\text{cal mol}^{-1}$ , the optical rotations in  $^{\circ}$  and the helical twisting power (HTP) in  $\mu\text{m}^{-1}$ ; C = crystalline, N = nematic, N\* = chiral nematic (cholesteric), I = isotropic.

Comparison of the melting enthalpies of the pure enantiomers of **49** and racemate *rac*-**49** (Table 2) points out the possible reason for the generally excellent solubility of THP-derived liquid crystals in nematic host mixtures: the racemate has a significantly lower melting enthalpy although the phase-transition temperatures are very similar.

## Summary and Outlook

The incorporation of a tetrahydropyran (THP) moiety into the mesogenic core structure of liquid crystals allows the design of new materials with an unprecedented combination of extremely high dielectric anisotropy ( $\Delta\epsilon$ ), high clearing point, low rotational viscosity ( $\gamma_1$ ) and excellent solubility in nematic liquid crystal mixtures. This unique property profile is of particular interest for so-called super-fluorinated materials (SFM) for use in AM LCDs, but it may also open the way to totally new display applications requiring materials with extreme electrooptical or mesogenic properties.

## Experimental Section

**General:** All reactions were performed in carefully dried solvents and under a dry nitrogen atmosphere. Intermediates **6–8**, **19** and **20** tend to polymerize even on short-term storage and should be used immediately.

**6:** A solution of pentanal (117 mL, 1.10 mol), methyl acrylate (100 mL, 1.10 mol; stabilized with hydroquinone monomethyl ether) and  $\text{Et}_2\text{NSiMe}_3$  (214 mL, 1.10 mol) in acetonitrile (1.3 L) was heated at reflux under a nitrogen atmosphere for 3 d. The mix-

ture was concentrated at 10 mbar. The residue (227 g) was treated with 96% acetic acid (250 mL) and water (500 mL), and the solution was heated at reflux for 18 h. After cooling down to room temperature, water (2.5 L) was added, and the mixture was extracted with methyl *tert*-butyl ether (MTBE; 4×). The combined organic phase was washed with water, saturated aqueous NaHCO<sub>3</sub> and water, dried with Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to yield crude **6** (133 g) as a yellowish oil, which was used for the next step without further purification.

**7:** NaBH<sub>4</sub> (90 g, 2.37 mol) was dissolved in 2-propanol (3.6 L) and water (360 mL). Then, crude **6** (1000 g, 5.8 mol) was added dropwise under cooling at 15 °C, and the mixture was stirred for 18 h at room temperature. After the addition of MTBE (1500 mL), the solution was acidified with 15% HCl (1000 mL) under ice cooling. The major part of the volatiles was removed in vacuo, the residue was diluted with MTBE (1000 mL), and the aqueous phase was separated. The organic phase was washed with brine (2 × 500 mL) and dried with Na<sub>2</sub>SO<sub>4</sub>. The volatiles were removed in vacuo to yield crude **7** (878 g) as a yellowish oil, which was used for the next step without further purification.

**8:** A solution of crude **7** (68 g, 390 mmol) and *p*-toluenesulfonic acid (10 g, 53 mmol) in toluene (150 mL) was heated at reflux under azeotropic water removal for 2 h. When the boiling point of toluene (109 °C) was reached, another 100 mL of toluene was added, and the solution was heated at reflux for an additional 1 h. After cooling, the mixture was washed with water, saturated aqueous NaHCO<sub>3</sub> and water, dried with Na<sub>2</sub>SO<sub>4</sub> and filtered, and the solvent was removed in vacuo. The residue (53.1 g) was distilled (b.p. 89–92 °C/0.05 mbar) to furnish **8** (29.8 g, 44%) as a colourless oil (purity 82% by GC). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, 303 K): δ = 4.36–4.30 (m, 1 H), 3.99–3.92 (m, 1 H), 2.61–2.43 (m, 1 H), 2.37–2.26 (m, 1 H), 2.06–1.86 (m, 2 H), 1.69–1.22 (m, 5 H), 0.93 (t, *J* = 7.0 Hz, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, 303 K): δ = 204.1, 73.4, 33.5, 32.3, 28.8, 25.3, 19.7, 13.8 ppm. MS (EI, 70 eV): *m/z* (%) = 142 (36) [M]<sup>+</sup>, 110 (23), 84 (100), 74 (16), 70 (40), 60 (20), 55 (81).

**9:** A solution of 1,4-dibromobenzene (48.3 g, 205 mmol) in diethyl ether (350 mL) was cooled to –50 °C and then treated dropwise under temperature control with *n*-butyllithium (15% solution in hexane; 130 mL, 207 mmol). After stirring at –50 °C for 1 h, a solution of **8** (29.5 g, 170 mmol) in diethyl ether (50 mL) was added dropwise. The mixture was stirred for 30 min at the same temperature and then warmed up to 0 °C. After careful addition of water (100 mL), the aqueous phase was separated and extracted with MTBE (2×). The combined organic phase was dried with Na<sub>2</sub>SO<sub>4</sub>, and the solvent was evaporated to dryness. Crude product **9** (51.1 g) was used for the next step without further purification. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, 303 K): δ = 7.41 (m, 4 H, ar-*H*), 5.33 (m, 1 H), 4.32 (m, 1 H), 3.72 (t, *J* = 10.2 Hz, 1 H), 2.24–2.16 (m, 1 H), 2.02–1.92 (m, 1 H), 1.86–0.85 (m, 10 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, 303 K): δ = 150.7, 131.2, 126.0, 121.5, 97.7, 69.5, 39.7, 39.6, 37.4, 33.3, 30.5, 30.0, 25.4, 20.0, 14.4 ppm. MS (EI, 70 eV): *m/z* (%) = 213 (11), 198/200 (57), 183/185 (95), 164 (100), 157 (18), 155 (18), 152 (18), 132 (13), 121/123 (20), 109 (23), 107 (13), 104 (11), 95 (22), 93 (10), 83 (17), 79 (16), 69 (30), 67 (35), 55 (46).

**10:** A solution of adduct **9** (51.1 g, 171 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (400 mL) was treated dropwise at –75 °C first with triethylsilane (47.0 g, 404 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and then with BF<sub>3</sub>·OEt<sub>2</sub> (51 mL, 406 mmol). The mixture was stirred for 3 h at the same temperature and then warmed up to –10 °C. The reaction was quenched and neutralized by careful addition of saturated aqueous NaHCO<sub>3</sub>. The organic phase was separated, and the aqueous phase was extracted

with CH<sub>2</sub>Cl<sub>2</sub> (2×). The combined organic layer was washed with brine and dried with Na<sub>2</sub>SO<sub>4</sub>, and the solvent was evaporated to dryness. The crude product was dissolved in *n*-heptane/toluene (1:1) and filtered through a short silica-gel column. Recrystallization from *n*-pentane at –20 °C afforded **10** (30.6 g, 61%) as colourless crystals (96% purity by HPLC). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, 303 K): δ = 7.44 (d, *J* = 8.5 Hz, 2 H, ar-*H*), 7.21 (d, *J* = 8.5 Hz, 2 H, ar-*H*), 4.21 (dd, *J* = 11.3 Hz, *J* = 2.3 Hz, 1 H), 4.06 (dquart., *J* = 11.1 Hz, *J* = 2.0 Hz, 1 H), 3.18 (t, *J* = 7.4 Hz, 1 H), 2.00–1.87 (m, 1 H), 1.83–1.79 (m, 1 H), 1.75–1.08 (m, 7 H), 0.91 (t, *J* = 7.3 Hz, 3 H, CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, 303 K): δ = 142.7, 131.7, 128.0, 121.4, 79.7, 74.5, 35.7, 35.1, 34.5, 31.2, 20.2, 14.7 ppm.

**10a:** A solution of **10** (90.5 g, 320 mmol) in THF (600 mL) was cooled to –70 °C and treated dropwise with *n*-butyllithium (15% solution in hexane; 210 mL, 334 mmol). After stirring for 2 h at the same temperature, trimethyl borate (38.0 mL, 341 mmol) was added slowly. After stirring for another 2 h, the solution was warmed up to –10 °C. HCl (2 N) was added in order to adjust the pH to ca. 2, and the mixture was extracted with MTBE. The combined organic phase was washed with water, dried with Na<sub>2</sub>SO<sub>4</sub> and filtered, and the solvent was evaporated to dryness to furnish crude boronic acid intermediate **10a** (85 g), which was used for the next step without further purification.

**11:** A mixture of crude **10a** (79.4 g, 320 mmol), THF (1.2 L), water (150 mL) and acetic acid (150 mL) was treated at room temperature (temperature control by water cooling) with 30% H<sub>2</sub>O<sub>2</sub> (65 mL, 630 mmol) and stirred for 6 h. After addition of water (500 mL) and toluene (500 mL), the organic phase was separated and washed with water and brine. The aqueous phase was extracted with toluene (300 mL). The combined organic phase was stirred with aqueous FeCl<sub>2</sub> (5% w/v) until the mixture was peroxide free. The organic phase was separated, washed with water (2×) and brine (1×). Then, the combined aqueous phase was extracted with toluene (3 × 100 mL). The combined organic phase was dried with Na<sub>2</sub>SO<sub>4</sub> and filtered, and the solvent was evaporated in vacuo. The crude product (80 g) was purified first by chromatography (silica gel; toluene/ethyl acetate, 4:1), then by crystallization from *n*-heptane at room temperature to yield **11** (52.9 g, 74%) as colourless crystals (99.1% purity by GC). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, 303 K): δ = 7.20 (d, *J* = 8.8 Hz, 2 H, ar-*H*), 6.73 (d, *J* = 8.5 Hz, 2 H, ar-*H*), 5.06 (br. s, 1 H, OH), 4.20 (dd, *J* = 11.1 Hz, *J* = 2.3 Hz, 1 H), 4.06 (dquart., *J* = 11.2 Hz, *J* = 2.1 Hz, 1 H), 3.20 (t, *J* = 11.1 Hz, 1 H), 2.03–1.92 (m, 1 H), 1.87–1.79 (m, 1 H), 1.75–1.54 (m, 2 H), 1.37–1.07 (m, 5 H), 0.91 (t, *J* = 7.3 Hz, 3 H, CH<sub>3</sub>) ppm. MS (EI, 70 eV): *m/z* (%) = 220 (96) [M]<sup>+</sup>, 203 (18), 159 (25), 133 (16), 121 (100), 107 (48), 94 (42), 77 (15), 69 (21), 65 (17), 55 (33).

**12:** A solution of **11** (70.0 g, 318 mmol) in xylene (isomer mixture; 460 mL) was hydrogenated in the presence of wet 5% Pd–C (water content 54%; 4.55 g) and Na<sub>2</sub>CO<sub>3</sub> (340 mg, 3.2 mmol) under H<sub>2</sub> (5 bar) at 120 °C for 8 h. The mixture was filtered through Celite, and the solvent was evaporated to dryness. The residue was dissolved in *n*-heptane (500 mL) and stirred together with pyridine–SO<sub>3</sub> complex (10 g) for 2 h at 40 °C in order to remove phenol and alcohol byproducts. After filtration through Celite, the solution was washed with water, dried with Na<sub>2</sub>SO<sub>4</sub> and filtered, and the solvent was evaporated to dryness to furnish **12** (47 g, 84%) as a colourless oil (95% purity by GC). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, 303 K): δ = 3.97–3.90 (m, 1 H), 3.10–2.95 (m, 2 H), 2.45–2.19 (m, 5 H), 2.08–0.99 (m, 13 H), 0.89 (t, *J* = 7.2 Hz, 3 H) ppm. MS (EI, 70 eV): *m/z* (%) = 224 (35) [M]<sup>+</sup>, 220 (14), 127 (100), 121 (16), 109 (77), 97 (11), 83 (34), 69 (25), 67 (38), 55 (55).

**22:** A solution of 2-trimethylsilyl-1,3-dithiane (43.0 g, 223 mmol) in THF (800 mL) was treated dropwise at  $-70^{\circ}\text{C}$  with *n*-butyllithium (15% solution in hexane; 142 mL, 226 mmol) and warmed up to  $0^{\circ}\text{C}$  over 4 h. Then, the mixture was cooled again to  $-70^{\circ}\text{C}$ , and a solution of **12** (47.3 g, 200 mmol) in THF (200 mL) was added slowly. After removing the cooling bath, the viscous, yellow mixture was stirred for 18 h at room temperature. Saturated aqueous  $\text{NaHCO}_3$  (1 L) and MTBE (500 mL) were added, and the organic phase was separated. The aqueous phase was extracted with MTBE ( $2 \times 250$  mL). The combined organic phase was washed with water ( $2 \times 350$  mL) and dried with  $\text{Na}_2\text{SO}_4$ , and the solvent was evaporated to dryness. The crude residue (74.4 g) was recrystallized from *n*-heptane (350 mL) to furnish **22** (53.4 g, 82%) as colourless crystals (99.9% purity by GC).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 303 K):  $\delta$  = 3.95–3.88 (m, 1 H), 3.20–3.08 (m, 2 H), 3.01–2.82 (m, 6 H), 2.17–2.07 (m, 2 H), 2.04–1.97 (m, 1 H), 1.90–1.70 (m, 4 H), 1.67–1.00 (m, 11 H), 0.88 (t,  $J$  = 7.2 Hz, 3 H) ppm. MS (EI, 70 eV):  $m/z$  (%) = 326 (92)  $[\text{M}]^+$ , 218 (17), 197 (20), 179 (67), 171 (100), 119 (23), 91 (14), 81 (11), 67 (12), 55 (27).

**24:** To a solution of **22** (26.7 g, 82 mmol) in  $\text{CH}_2\text{Cl}_2$  (600 mL) was dropwise added trifluoromethanesulfonic acid (7.5 mL, 85 mmol) at  $-20^{\circ}\text{C}$ . The cooling bath was removed, and the mixture was stirred for 30 min at room temperature. Then, the mixture was cooled down to  $-70^{\circ}\text{C}$ , and a solution of 3,4,5-trifluorophenol (18.0 g, 122 mmol) and triethylamine (20 mL, 144 mmol) in  $\text{CH}_2\text{Cl}_2$  (100 mL) was added. After stirring for 1 h at  $-70^{\circ}\text{C}$ ,  $\text{NEt}_3 \cdot 3\text{HF}$  (66 mL, 409 mmol) was added. After 5 min, a suspension of DBH (1,3-dibromo-5,5-dimethylhydanthoin; 117 g, 409 mmol) in  $\text{CH}_2\text{Cl}_2$  (300 mL) was added portionwise over a time period of 30 min. After stirring for an additional 60 min, the mixture was warmed up to  $0^{\circ}\text{C}$  and then poured into ice-cold 2 N aqueous NaOH (2 L); the pH of the resulting mixture was ca. 9. The organic layer was separated, washed with water, dried with  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo. The residue was dissolved in *n*-heptane/toluene (3:2) and filtered through a short silica-gel column. The crude product was then further purified by chromatography (silica gel; *n*-heptane/toluene, 7:3) and two crystallizations (*n*-heptane;  $-20^{\circ}\text{C}$ ) to furnish **24** (6.2 g, 19%; 99.9% purity by GC). For mesophases see Table 1.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 303 K):  $\delta$  = 6.86–6.81 (m, 2 H), 3.96–3.90 (m, 1 H), 3.02–2.92 (m, 2 H), 2.09–1.85 (m, 6 H), 1.65–1.47 (m, 2 H), 1.43–1.25 (m, 6 H), 1.15–0.99 (m, 5 H), 0.88 (t,  $J$  = 7.3 Hz, 3 H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ , 303 K):  $\delta$  = 107.0, 106.7, 81.8, 74.0, 43.5 (t,  $J$  = 25.8 Hz), 42.4, 35.8, 34.8, 30.6, 28.7, 27.6, 27.4, 25.2, 19.8, 14.3 ppm.  $^{19}\text{F}$  NMR (235 Hz,  $\text{CDCl}_3$ , 300 K):  $\delta$  =  $-165.2$  (mc, 1 F, ar-4-*F*),  $-133.7$  (mc, 2 F, ar-3,5-*F*),  $-79.3$  (d,  $J$  = 8.0 Hz, 2 F,  $\text{CF}_2\text{O}$ ) ppm. MS (EI, 70 eV):  $m/z$  (%) = 148 (9), 127 (100), 109 (56), 83 (19), 67 (22), 55 (29).

**19:** To a cooled ( $-78^{\circ}\text{C}$ ) solution of *tert*-butyl acetate (18.1 mL, 134 mmol) in THF (130 mL) was slowly added lithium diisopropylamide (2 M solution in heptane/THF/ethyl benzene; 66.5 mL, 133 mmol). After stirring for 25 min, a solution of **18**<sup>[1]</sup> (8.0 g, 44 mmol) in THF (130 mL) was added dropwise, followed by  $\text{BF}_3 \cdot \text{OEt}_2$  (16.6 mL, 132 mmol). The mixture was stirred for 1 h at  $-78^{\circ}\text{C}$  and then warmed up to room temperature. After stirring for 15 h, the reaction was finally quenched by addition of aqueous  $\text{NH}_4\text{Cl}$  (100 mL). The phases were separated, and the aqueous layer was extracted with MTBE. The combined organic extract was washed with brine, dried with  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo. The crude product was chromatographed (silica gel; *n*-heptane/ethyl acetate, 6:1) to afford **19** (3.5 g, 27%) as a colourless oil, which was used for the subsequent step without further purification.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 303 K):  $\delta$  = 4.75–4.69 (m, 1 H),

4.49–4.44 (m, 1 H), 3.60–3.56 (m, 1 H), 2.28 (t,  $J$  = 7.0 Hz, 2 H), 1.78–1.58 (m, 7 H), 1.45 (s, 9 H), 1.35–0.84 (m, 13 H) ppm. MS (EI, 70 eV):  $m/z$  (%) = 152 (100), 123 (71), 109 (81), 95 (31), 81 (77), 67 (81), 55 (45).

**20:** A solution of **19** (24.1 g, 80.7 mmol) in  $\text{CH}_2\text{Cl}_2$  (300 mL) was treated dropwise at  $0^{\circ}\text{C}$  with trifluoroacetic acid (30 mL, 389 mmol). The mixture was subsequently stirred at room temperature for 18 h and then poured into water (500 mL). The phases were separated, and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic phase was washed with saturated aqueous  $\text{NaHCO}_3$ , dried with  $\text{Na}_2\text{SO}_4$  and filtered, and the solvent was evaporated to dryness. The residue was purified by chromatography (silica gel; *n*-heptane/ethyl acetate, 4:1) to furnish lactone **20** (14.8 g, 81%) as a colourless oil (98.7% purity by GC).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 303 K):  $\delta$  = 4.40–4.33 (m, 1 H), 4.08 (dd,  $J$  = 10.1 Hz,  $J$  = 9.9 Hz, 1 H), 2.67–2.39 (m, 2 H), 2.01–1.90 (m, 1 H), 1.80–1.55 (m, 6 H), 1.35–0.93 (m, 10 H), 0.87 (t,  $J$  = 7.1 Hz, 3 H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ , 303 K):  $\delta$  = 172.2, 72.5, 39.9, 39.7, 38.7, 37.6, 33.4, 30.6, 30.4, 29.7, 23.3, 20.3, 14.7 ppm. MS (EI, 70 eV):  $m/z$  (%) = 224 (33)  $[\text{M}]^+$ , 193 (17), 176 (20), 151 (19), 140 (100), 127 (12), 122 (43), 109 (32), 100 (49), 95 (31), 81 (70), 69 (80), 55 (85).

**25:** A solution of **26**<sup>[2]</sup> (16.4 g, 45.0 mmol) in THF (100 mL) was cooled to  $-10^{\circ}\text{C}$ , and then a solution of potassium *tert*-butoxide (5.0 g, 44.6 mmol) in THF (50 mL) was added dropwise. After stirring for 1 h, a solution of **20** (9.9 g, 44.1 mmol) in THF (50 mL) was added dropwise at  $-10^{\circ}\text{C}$ . The mixture was stirred for 18 h at room temperature, and it was then diluted with MTBE (300 mL) and water (500 mL). The aqueous phase was separated and extracted with MTBE ( $2 \times$ ). The combined organic phase was washed with brine, dried with  $\text{Na}_2\text{SO}_4$  and filtered, and the solvent was evaporated to dryness. The crude product was purified by chromatography (silica gel; 1-chlorobutane) and subsequent crystallization (*n*-heptane) to furnish **25** (8.7 g, 60%) as colourless crystals (96.8% purity by GC).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 303 K):  $\delta$  = 4.69–4.93 (m, 0.5 H), 4.54 (s, 0.5 H), 4.24–4.16 (m, 1 H), 3.74–3.54 (m, 1.5 H), 3.26–3.16 (m, 0.5 H), 2.96–2.75 (m, 3 H), 2.62–2.53 (m, 0.5 H), 2.30–0.84 (m, 22.5 H) ppm. MS (EI, 70 eV):  $m/z$  (%) = 326 (100)  $[\text{M}]^+$ , 161 (80), 119 (25), 69 (8), 55 (19).

**27:** To a solution of **25** (7.9 g, 24.2 mmol) in  $\text{CH}_2\text{Cl}_2$  (150 mL) was dropwise added trifluoromethanesulfonic acid (2.2 mL, 25 mmol) in  $\text{CH}_2\text{Cl}_2$  (15 mL) at  $-30^{\circ}\text{C}$ . The cooling bath was removed, and the mixture was stirred for 10 min at room temperature. Then, the mixture was cooled down to  $-90^{\circ}\text{C}$ , and a solution of 3,4,5-trifluorophenol (6.5 g, 43.9 mmol) and triethylamine (6.5 mL, 46.9 mmol) in  $\text{CH}_2\text{Cl}_2$  (50 mL) was added. After stirring for 30 min at  $-90^{\circ}\text{C}$ ,  $\text{NEt}_3 \cdot 3\text{HF}$  (19.5 mL, 121 mmol) was added. Then, a solution of  $\text{Br}_2$  (6.2 mL, 121 mmol) in  $\text{CH}_2\text{Cl}_2$  (35 mL) was added dropwise under strict temperature control (never exceeding  $-85^{\circ}\text{C}$ !). After stirring for 60 min at  $-80^{\circ}\text{C}$ , the mixture was warmed up to room temperature and then poured into ice-cold aqueous NaOH (0.1 N, 400 mL); the pH of the resulting mixture was ca. 9. The aqueous layer was separated and extracted with  $\text{CH}_2\text{Cl}_2$  ( $2 \times$ ). The combined organic phase was washed with water ( $2 \times$ ), dried with  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo. The residue was dissolved in *n*-heptane/MTBE (4:1) and filtered through a short silica-gel column. The crude product (0.5 g) was then further purified by crystallization from *n*-heptane and subsequent preparative HPLC (RP-18 Super 250–4; acetonitrile) to furnish **27** (85 mg, 0.9%) as colourless crystals (99.8% purity by GC). For mesophases, see Table 1.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 303 K):  $\delta$  = 6.93–6.83 (m, 2 H), 4.20–4.15 (m, 1 H), 3.68–3.64 (m, 1 H), 3.26–3.19 (m, 1 H),

2.04–2.00 (m, 1 H), 1.93–1.86 (m, 1 H), 1.77–1.10 (m, 12 H), 1.05–0.82 (m, 8 H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ , 303 K):  $\delta$  = 107.3, 107.0, 72.4, 40.6, 39.9, 39.7, 37.4, 33.2, 30.2, 29.9, 26.2, 24.8, 20.0, 14.4 ppm.  $^{19}\text{F}$  NMR (235 Hz,  $\text{CDCl}_3$ , 300 K):  $\delta$  = –164.3 (mc, 1 F, ar-4-F), –133.3 (mc, 2 F, ar-3,5-F), –83.5 (mc, 2 F,  $\text{CF}_2\text{O}$ ) ppm. MS (EI, 70 eV):  $m/z$  (%) = 406 (13)  $[\text{M}]^+$ , 258 (17), 208 (100), 191 (42), 135 (13), 123 (15), 109 (31), 95 (24), 86 (13), 83 (46), 69 (72), 55 (76).

*rac*-49 was prepared in analogy to 24.

**Enantiomer Separation of D-49 and L-49:** *rac*-49 (1.35 g) was dissolved in a mixture of acetonitrile (13.5 mL) and methanol (81.0 mL) and separated in nine portions over two columns in series (Hibar  $25 \times 5$  cm Chiralpak AD 20  $\mu\text{m}$ ) with methanol as the eluent. Fraction 1 (600 mg) had an *ee* of 98.6% and fraction 2 (580 mg) of 97.1%. Both fractions were crystallized from ethanol to afford *ee* values of 100% (Fraction 1, D-49) and 99% (Fraction 2, L-49).

**Supporting Information** (see footnote on the first page of this article): Selected crystal data of L-49; computational analysis of 28 and its protonation products; calculated proton affinities and relative energies of possible protonation products 29a–e.

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in the commercially available Merck mixture ZLI-4792 ( $T_{NI} = 92.8\text{ }^{\circ}\text{C}$ ,  $\Delta\epsilon = 5.3$ ,  $\Delta n = 0.0964$ ). The extrapolated values are corrected empirically for differences in the order parameter, which are induced by the analyte. For the pure substances, the phase-transition temperatures were measured by differential scanning calorimetry (DSC), and the phase type was assigned by optical polarization microscopy. The helical twisting powers (HTP) were measured at  $20\text{ }^{\circ}\text{C}$  in the Merck liquid crystal mixture MLC-6260 ( $T_{NI} = 103.5\text{ }^{\circ}\text{C}$ ,  $\Delta\epsilon = 4.0$ ,  $\Delta n = 0.088$ ) and are given in  $\mu\text{m}^{-1}$ . The optical rotations  $[\alpha]_D^{20}$  were determined from a  $0.01\text{ g mL}^{-1}$  solution in  $\text{CH}_2\text{Cl}_2$ .

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$4.888(2)\text{ \AA}$ ,  $b = 46.787(5)\text{ \AA}$ ,  $c = 9.591(1)\text{ \AA}$ ,  $\beta = 96.89(1)^{\circ}$ ,  $V = 2177.6(9)\text{ \AA}^3$ ,  $\rho_{\text{calcd.}} = 1.325\text{ g cm}^{-3}$ ,  $\mu = 0.953\text{ mm}^{-1}$ , empirical absorption correction ( $0.555 \leq T \leq 0.797$ ),  $Z = 4$ , monoclinic, space group  $P2_1$  (No. 4),  $\lambda = 1.54178\text{ \AA}$ ,  $T = 223\text{ K}$ ,  $\omega$  scans, 4975 reflections collected ( $+h, +k, \pm l$ ),  $[(\sin\theta)/\lambda] = 0.62\text{ \AA}^{-1}$ , 4455 independent ( $R_{\text{int}} = 0.026$ ) and 3273 observed reflections [ $I \geq 2\sigma(I)$ ], 544 refined parameters,  $R = 0.050$ ,  $wR_2 = 0.167$ , Flack parameter 0.0(2), max. residual electron density  $0.29\text{ }(-0.29)\text{ e \AA}^{-3}$ , hydrogen atoms calculated and refined as riding atoms. A second crystal structure as well as more detailed information on the measurement technique is provided in the Supporting Information of this paper. CCDC-667613 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

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