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Short communication

Cholestane-based liquid crystals containing a difluorooxymethylene bridge

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Abstract

A new class of steroid-based liquid crystals was synthesized and characterized with regard to their mesogenic and chiroptical properties. The β-selective formation of the cholestanyl difluoromethyl ether bridge was achieved by an oxidative fluorodesulfuration procedure.

Keywords: Chiral nematic; Cholestane; Fluorodesulfuration, oxidative; Helical twisting power; Liquid crystals; Steroids

1. Introduction

Reinitzer's discovery in 1888 [1] that cholesteryl benzoate (**1**) forms at elevated temperatures an up to then unknown state of matter – a liquid crystalline mesophase – triggered a development culminating in the last few years in the ubiquitous presence of liquid crystal displays (LCD) in our daily lives [2,3]. The mesophase formed by cholesteryl benzoate was later classified as ''chiral nematic'' or simply ''cholesteric'' (Scheme 1) [4].

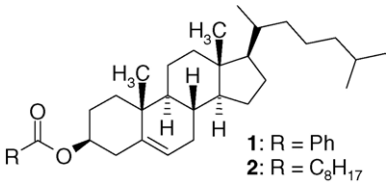
Cholesterol esters, such as the nonanoate **2**, are still widely used as additives for modern liquid crystal mixtures in order to induce chirality in an otherwise achiral nematic host, rendering the whole mixture cholesteric [5]. The ability to induce chirality in a nematic phase is quantified as the helical twisting power (HTP) [6].

From a practical point of view, cholesterol esters sometimes cause problems. This is mostly due to the intrinsic lability of the ester bond which can either hydrolyse or eliminate the carboxylic acid component. If not carefully controlled, this may result in unpredictable changes of the pitch of the cholesteric phase during the mixture and LCD panel production process. Therefore, there is a need for chiral dopants which are easily accessible, chemically more robust and fully compatible with any type of active matrix LCD technology [2]. Additional favourable features may be improved solubility and the ease of adaptation of the electrooptical properties of the chiral dopant to different types of nematic liquid crystal preparations.

2. Results and discussion

From our previous work [7] we knew that liquid crystals containing a difluorooxymethylene bridge in their mesogenic core structure do not only fulfil LCD manufacturers' stability criteria. In addition – compared to their directly or ester linked analogues – they usually show a dramatically improved solubility in combination with a significant extention of their nematic phase range.

For the design of our new class of chiral dopants, the cholesteryl moiety containing one double bond was replaced by a cholestanyl group, in order to avoid complications during the synthesis of the difluorooxymethylene bridge [7]. Starting from



Scheme 1. Cholesteryl benzoate (**1**), the prototype of ''cholesteric'', i.e., chiral nematic, liquid crystals. Other cholesterol esters, such as cholesteryl nonanoate (**2**), are currently used as chiral dopants for liquid crystal compositions.

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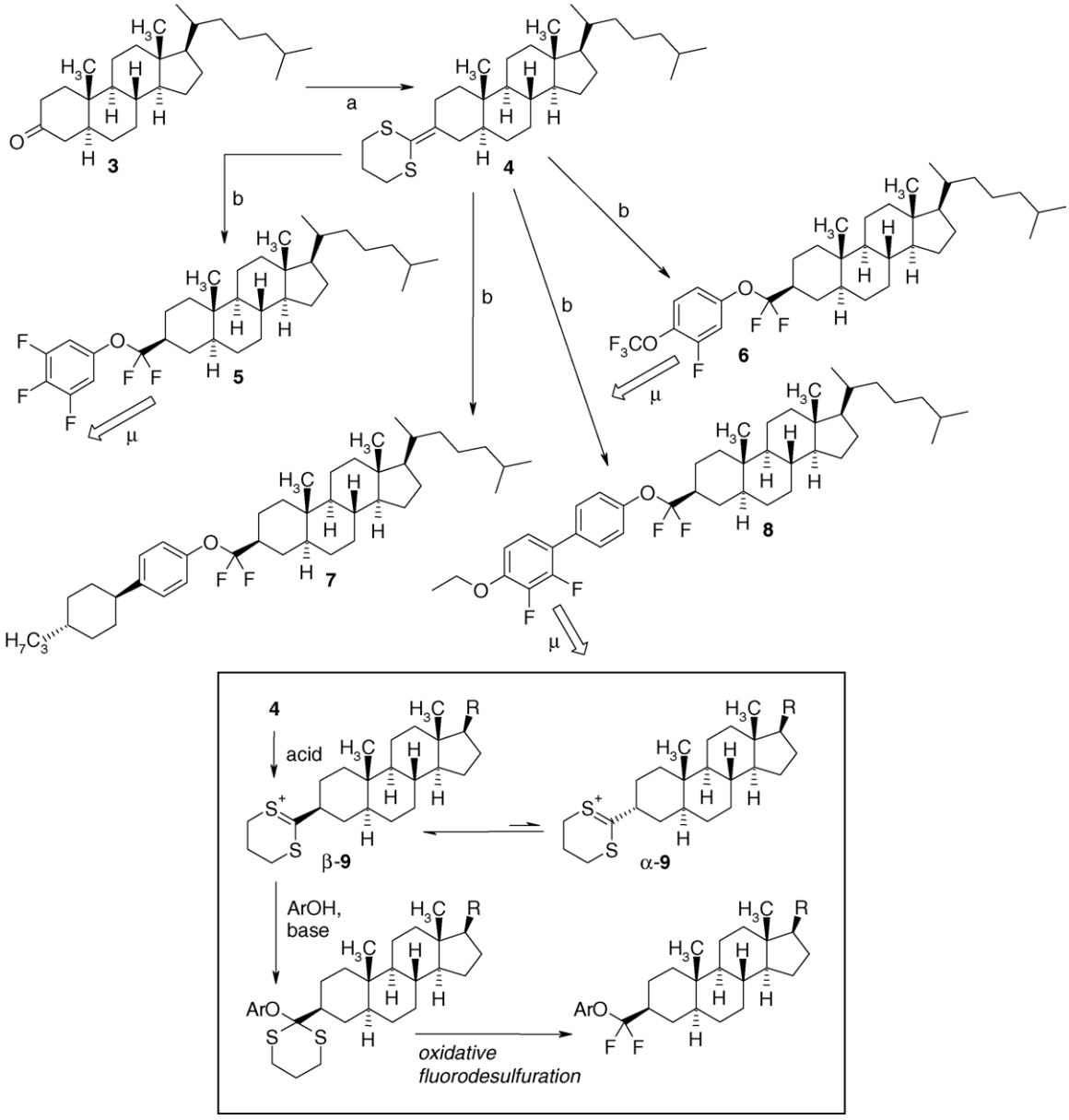
cholestanone (**3**), the ketenedithioketal **4** [8] was synthesized as the central steroid building block. By a simple four-step one-pot procedure, the different phenol components could now be attached via a protonation–equilibration–addition–fluorodesulfuration reaction sequence, furnishing the liquid crystals **5**–**8** in good yields. The exclusive formation of the desired β-cholestanyl isomers was achieved by allowing the primarily formed cholestanyl dithianylium salt α/β-isomer mixture (**9**) to equilibrate to the thermodynamically preferred β-dithianylium salt at room temperature for a few minutes (Scheme 2) [7].

All new compounds were fully characterized by mass spectrometry, ^{1}H, ^{13}C and ^{19}F NMR spectroscopy, and optical rotation. Their purity was verified to be >98.5% by HPLC. As expected, the liquid crystals **5**–**8** showed relatively low melting points (especially if their high molecular weight is taken into account) and good solubility in combination with broad nematic phases. The compounds **7** and **8**, derived from a two-ring phenol component, had smectic A phases in addition.

The dielectric anisotropies ($\Delta\varepsilon$) of the materials are determined by the nature of the phenol component used for their syntheses. Compounds **5** and **6** have strong dipole moments parallel to their long molecular axes, resulting in positive dielectric anisotropies. The only weakly polar compound **7** is dielectrically neutral, whereas the liquid crystal **8** with its dipole moment perpendicular to the long molecular axis has a negative dielectric anisotropy. The birefringences



Scheme 2. Syntheses of the cholestanone-derived liquid crystals **5**–**8**, and the orientation of their molecular dipole moments (μ) relative to the long molecular axes: (a) 2-trimethylsilyl-1,3-dithiane, *n*-BuLi, THF; −70 °C → RT (79%). (b) 1—CF_3SO_3H, CH_2Cl_2, −15 °C (5 min) → RT (30 min) → −70 °C; 2—X-PhOH (**5**: 3,4,5-trifluorophenol, **6**: 3-fluoro-4-trifluoromethoxyphenol, **7**: 4-(*trans*-4-propylcyclohexyl)phenol and **8**: 4-ethoxy-2,3-difluoro-4′-hydroxybiphenyl), NEt_3, CH_2Cl_2, −70 °C; 3—$NEt_3{\cdot}3HF$, −70 °C, 4—1,3-dibromo-5,5-dimethyl hydanthoin (DBH), CH_2Cl_2, −70 °C → −20 °C (**5**: 66%, **6**: 70%, **7**: 50% and **8**: 67%). The dithianylium salt intermediates α-**9** and β-**9** (*box*) are controlling the stereochemistry. A detailed analysis of the mechanism of the four-step one-pot procedure (b) is provided in ref. [7].

(Δn), particularly of the compounds **5–7** containing only one aromatic moiety, are exceptionally low. This is presumably due to the combination of low polarizability with a relatively large lateral extent of the cycloaliphatic steroid skeleton.

Quite surprisingly, the nematic phases of all the supposedly ''cholesteric'' liquid crystals **5–8** did not show any cholesteric texture under the polarization microscope. Also, in solution in achiral nematic host mixtures (ZLI-4792 and MLC-6260) [9] they showed no propensity to induce a cholesteric phase detectable under the polarization microscope.

3. Conclusion

Oxidative fluorodesulfuration was used as a simple and convenient method to obtain aromatic β-cholestanyl difluoromethyl ethers with complete stereoselectivity. This new class of chemically very robust liquid crystalline compounds was characterized with regard to their mesogenic and chiroptical properties. Even though the practical value of the synthetic procedure was demonstrated so far only for the preparation of liquid crystals, the method is expected to be a useful addition also to the toolbox of bioorganic and medicinal chemistry.

4. Experimental

*Representative synthetic procedure for **5***: A solution of **4** [8] (12.9 g, 24.6 mmol) in CH_2Cl_2 (110 mL) was treated at −15 °C dropwise with triflic acid (2.20 mL, 24.6 mmol). The mixture was allowed to warm up, stirred for 30 min at room temperature and then cooled down to −70 °C. First, a mixture of 3,4,5-trifluorophenol (5.5 g, 36.8 mmol), NEt_3 (6.1 mL, 44.2 mmol) and CH_2Cl_2 (40 mL) was added dropwise, followed after 5 min by $NEt_3{\cdot}3HF$ (19.9 mL, 123 mmol) and 1,3-dibromo-5,5-dimethyl hydanthoin (35.1 g, 123 mmol; in small portions) after additional 5 min. The orange-coloured mixture was stirred for 1 h at −70 °C, then allowed to warm up to −20 °C and poured into ice-cold 1N NaOH (500 mL). The organic layer was separated, washed with saturated aqueous $NaHCO_3$ and water, dried over Na_2SO_4, filtered and evaporated to dryness. The crude product was chromatographed (silica gel; *n*-heptane/CH_2Cl_2 2:1) and crystallized from *i*-propanol at 5 °C. Yield: 9.3 g (66%) of **5** as a colourless solid with a purity of 98.6% (HPLC). For mesophases and optical rotation see Table 1; ^{1}H NMR (500 MHz, $CDCl_3$, 303 K): δ = 6.84 (t, J = 8.1 Hz, 2H, ar-*H*), 2.09–0.87 (m, 41H), 0.81 (s, 3H, CH_3), 0.66 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 303 K): δ = 106.9 (d, J = 23 Hz, ar-*C*), 56.6, 56.4, 54.4, 45.7, 43.8 (t, J = 25 Hz, *C*HCF$_2$O), 42.6, 40.1, 39.6, 37.4, 36.2, 35.8, 35.6, 32.0, 28.8, 28.2, 28.0, 27.7, 24.2, 23.9, 22.8, 22.6, 21.0, 18.7, 12.2, 12.1; ^{19}F NMR (235 Hz, $CDCl_3$, 300 K): δ = −79.16 (d, J = 8.6 Hz, 2F, CF$_2$O), −133.69 (dd, J = 20.9 and 8.1 Hz, 2F, ar-3,5-*F*), −165.13 (tt, J = 20.9 and 5.9 Hz, 1F, ar-4-*F*); MS (EI, 70 eV): *m*/*z* (%) = 568 [M^+] (57), 553 (20), 428 (13), 413 (100), 399 (19), 345 (27), 305 (7), 135 (6), 123 (24), 109 (21), 95 (28), 81 (25).

6: For mesophases and optical rotation see Table 1; ^{1}H NMR (500 MHz, $CDCl_3$, 303 K): δ = 7.27–7.25 (m, 1H, ar-*H*; overlapped by $CHCl_3$ signal at 7.26 ppm), 7.06 (dd, J = 10.7 and 2.8 Hz, 1H, ar-*H*), 6.97 (d, J = 9.2 Hz, 1H, ar-*H*), 2.15–0.87 (m, 41H), 0.82 (s, 3H, CH_3), 0.66 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 303 K): δ = 154.8 (d, $^1J_{CF}$ = 254 Hz, ar-*C*F), 150.0 (d, $^3J_{CF}$ = 10 Hz, ar-*C*), 124.3 (ar-*C*H), 117.9 (ar-*C*H), 111.6 (d, $^2J_{CF}$ = 21.6 Hz, ar-*C*H), 56.9, 56.7, 54.8, 46.1, 44.2 (t, $^2J_{CF}$ = 26 Hz, *C*HCF$_2$O), 43.0, 40.4, 39.9, 37.8, 36.6, 36.2, 35.9, 32.4, 29.2, 28.6, 28.4, 28.1, 24.6, 24.3, 23.2, 23.0, 21.5, 19.1, 12.6, 12.5; ^{19}F NMR (235 Hz, $CDCl_3$, 300 K): δ = −59.45 (s, 3F, ar-4-OC*F*$_3$), −79.00 (d, J = 8.7 Hz, 2F, CF$_2$O), −126.06 (mc, 1F, ar-3-*F*); MS (EI, 70 eV): *m*/*z* (%) = 616 [M^+] (60), 601 (20), 476 (12), 461 (100), 447 (20), 123 (23), 121 (15), 109 (22), 95 (30), 81 (27), 79 (12).

7: For mesophases and optical rotation see Table 1; ^{1}H NMR (500 MHz, $CDCl_3$, 303 K): δ = 7.14 (d, J = 8.6 Hz, 2H, ar-*H*), 7.06 (d, J = 8.6 Hz, 2H, ar-*H*), 2.46–2.41 (mc, 1H), 2.00–1.95 (mc, 1H), 2.13–2.04 (mc, 1H), 2.00–0.85 (m, 55H), 0.82 (s, 3H, CH_3), 0.66 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 303 K): δ = 148.9 (ar-*C*), 145.1 (ar-*C*), 127.8 (ar-*C*H), 121.9 (ar-*C*H), 57.0, 56.8, 54.8, 46.2, 44.4 (t, $^2J_{CF}$ = 27 Hz, *C*HCF$_2$O), 43.0, 40.5, 40.1, 40.0, 37.9, 37.4, 36.6, 36.2, 36.0, 34.8, 34.0, 32.5, 29.3, 28.7, 28.4, 28.3, 24.6, 24.3, 23.2, 23.0, 21.6, 21.5, 20.4, 19.1, 14.8, 12.6, 12.5; ^{19}F NMR (235 Hz, $CDCl_3$, 300 K): δ = −78.29 (d, J = 8.4 Hz, 2F, CF$_2$O); MS (EI, 70 eV): *m*/*z* (%) = 638 [M^+] (100), 623 (16), 498 (12), 483 (38), 415 (12), 218 (23), 133 (21), 125 (19), 123 (14), 121 (11), 109 (13), 107 (24), 95 (19), 83 (19), 81 (19).

8: For mesophases and optical rotation see Table 1; ^{1}H NMR (500 MHz, $CDCl_3$, 303 K): δ = 7.45 (d, J = 8.1 Hz, 2H, ar-*H*), 7.22 (d, J = 8.1 Hz, 2H, ar-*H*), 7.06 (dt, J = 8.4 Hz, J = 2.0 Hz, 1H, ar-*H*), 6.78 (t, J = 8.0 Hz, 1H, ar-*H*), 4.15 (quart, J = 9.7 Hz, 2H, OCH_2), 2.17–1.09 (mc, 1H), 1.99–1.97 (mc, 1H), 1.87–1.98 (m, 3H), 1.70–1.67 (mc, 1H), 1.64–0.87 (m, 38H), 0.83 (s, 3H, CH_3), 0.66 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 303 K): δ = 150.6 (ar-*C*), 149.2 (dd, $^1J_{CF}$ = 249 Hz, $^2J_{CF}$ = 11 Hz, ar-*C*F), 148.1 (ar-*C*), 142.2 (dd, $^1J_{CF}$ = 247 Hz, $^2J_{CF}$ = 15 Hz, ar-*C*F), 132.2 (ar-*C*), 130.0 (ar-*C*H), 126.3 (ar-*C*), 123.9 (ar-*C*H), 122.1 (ar-*C*H), 109.9 (ar-*C*H), 65.8 (OCH_2), 57.0, 56.8, 54.8, 46.1, 44.4 (t, $^2J_{CF}$ = 26 Hz, *C*HCF$_2$O), 43.0, 40.5, 40.0, 37.8, 36.6, 36.2, 35.9, 32.5, 29.3, 28.7, 28.4, 28.3, 24.6, 24.3, 23.2, 23.0, 21.5, 19.1, 15.2, 12.6, 12.5; ^{19}F NMR (235 Hz, $CDCl_3$, 300 K): δ = −78.35 (d, J = 8.6 Hz, 2F, CF$_2$O), −142.12 (ddd, J = 19.3 Hz, J = 8.0 Hz, J = 1.1 Hz, 1F, ar-*F*), −159.07 (ddd, J = 22.1 Hz, J = 7.6 Hz, J = 2.7 Hz, 1F, ar-*F*);

Table 1
The physical properties of the steroid-based liquid crystals **1**, **2** and **5–8**

No.	Phase sequence	$\Delta\varepsilon_{virt}$	Δn_{virt}	HTP	$[\alpha]_D^{20}$
1	C 145 N* 179 I	–	–	–	–
2	C 81 $S_?$ 78 N* 92 I	–	–	−4.4	–
5	C 102 N 149.0 I	7.3	0.026	<0.05	+20.2
6	C 94 N 175.1 I	7.2	0.034	<0.05	+19.2
7	C 112 S_A 206 N >300 I	0.3	0.026	<0.05	+18.7
8	C 105 S_A 211 N 312.8	−3.0	0.077	<0.05	+18.0

The phase transition temperatures are given in °C, the helical twisting powers (HTP) in μm^{-1}, and the optical rotations $[\alpha]_D^{20}$ in degrees [9] (C: crystalline, S_A: smectic A, $S_?$: unidentified smectic phase, N: nematic, N*: chiral nematic and I: isotropic).

MS (EI, 70 eV): m/z (%) = 670 [M^+] (100), 530 (9), 515 (8), 250 (13), 222 (10), 123 (5), 109 (5), 95 (9).

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[9] The helical twisting powers (HTP) were measured at 20 °C in the Merck liquid crystal mixtures ZLI-1132 (T_{NI} = 71.0 °C, $\Delta\varepsilon$ = 12.8, Δn = 0.140) (for **2**) or MLC-6260 (T_{NI} = 103.5 °C, $\Delta\varepsilon$ = 4.0, Δn = 0.088) (for **5**–**8**) and are given in μm^{-1}. The "virtual" dielectric ($\Delta\varepsilon$) and optical anisotropies (Δn) were extrapolated from a 10% (w/w) solution of the analyte in ZLI-4792 (T_{NI} = 92.6 °C, $\Delta\varepsilon$ = 5.3, Δn = 0.097). The optical rotations $[\alpha]_D^{20}$ were determined from a 0.01 g mL^{-1} solution in CH_2Cl_2. The phase transition temperatures were measured by differential scanning calorimetry (DSC), the identity of the mesophases was assigned by optical polarization microscopy