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S. Jeeva[a]; S. J. Cowling[a]; E. P. Raynes[b]; J. W. Goodby[a]
[a] Department of Chemistry, University of York, York, UK [b] Department of Engineering Science, University of Oxford, Oxford, UK

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INVITED ARTICLE

Chiral liquid crystal dopants derived from optically active drugs

S. Jeeva[a]*, S.J. Cowling[a], E.P. Raynes[b] and J.W. Goodby[a]

[a]*Department of Chemistry, University of York, York YO10 5DD, UK;* [b]*Department of Engineering Science, University of Oxford, Oxford OX1 3PJ, UK*

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In this article we examine the possibility of using chiral pharmaceuticals as reactive substrates in the synthesis of chiral liquid crystals because chiral drugs usually have reproducibly high chemical and optical purities which are important for applications of chiral liquid crystals. Thus we combined racemic and *S*-ibuprofen, racemic and *S*-ketoprofen and *S*-naproxen with a fluoroterphenyl promesogenic material in order to create bent core materials which we predicted would have helical twisting powers depending on the extent of the molecular bending.

Keywords: pharmaceuticals; helical twisting power; chiral nematic materials

1. Introduction

The introduction of molecular asymmetry into liquid crystal systems can have many profound effects, such as the stabilisation of chiral nematic phases (*1–4*), the formation of ferroelectric, ferrielectric and antiferroelectric phases (*5*, *6*), and competition between long-range helical ordering and mesophase structure which leads to large scale frustrations (*7*, *8*). Thus the availability of chiral substrates, templates and dopants for the preparation of chiral mesogens, or the formulation of chiral mixtures, is of considerable interest. One such source of chiral materials/substrates is provided by the pharmaceuticals industry in the form of chiral drugs, which are often obtainable with reproducibly high enantiomeric excesses (*9*). In this article we examine the use of three drugs, ibuprofen (*10*), ketoprofen (*11*), and naproxen (*12*) as substrates in the preparation of liquid crystalline materials, and investigate the physicochemical properties of the materials used as dopants in the creation of chiral nematic phases in conjunction with E7 (*13*) as the achiral host mixture (Merck).

Ibuprofen and ketoprofen are readily available in their racemic and *S*-forms (ee $>$ 99% by chiral GC), and naproxen is available in its *S*-form (ee $>$ 97% by chiral GC), as shown in Figure 1. As they each possess carboxylic acid functionalities they are readily derivatisable *via* esterification. In this study we chose to derivatise the three pharmaceutical materials with 4″-pentyl-3′-fluoro-4-hydroxyterphenyl which, although not liquid crystal in its own right, has often been used as a substrate in the formation of mesomorphic materials. Thus, we prepared both the racemic and *S*-esters in order to compare the properties of the achiral and chiral systems, and to evaluate their liquid crystal properties and determine the helical twisting power of each *S*-enantiomer in the nematic host mixture E7.

2. Experimental

The target materials **5a, 5b, 6a, 6b** and **7** were prepared as shown in the scheme *via* the direct condensation of ibuprofen, **1a** or **1b**, ketoprofen, **2a** or **2b**, and naproxen, **3**, with 4″-pentyl-3′-fluoro-4-hydroxyterphenyl, **4**, in the presence of *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDAC) and dimethylaminopyridine (DMAP) in dichloromethane. Compound **4** was prepared previously *via* Suzuki coupling of benzyloxy 4-bromobenzene with 4′-pentyl 3-fluorobiphenyl-4-boronic acid followed by hydrogenation of the benzyl group using palladium-on-carbon catalyst.

2.1 General methods

Racemic and optically active ibuprofen, **1**, ketoprofen, **2**, naproxen, **3**, EDAC, and DMAP were purchased from Aldrich. General solvents were used as received from commercial suppliers; all of these materials were used without further refinement. Purification of the intermediates and final products was achieved using column chromatography over C60, 230–400 mesh silica gel as the stationary phase (Merck).

The structures of the products were analysed using a range of spectral techniques including ^{1}H, ^{13}C and ^{19}F NMR spectrometry (JEOL DELTA ECX 270 MHz spectrometer), where the spectra, unless otherwise stated, were recorded in $CDCl_3$; infra-red spectrometry (Shimadzu IR Prestige-21 FT-IR Spectrophotometer,

*Corresponding author. Email: jwg500@york.ac.uk

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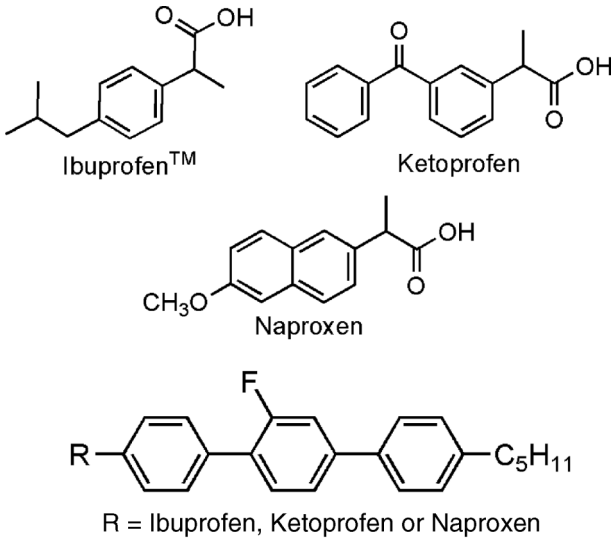


Figure 1. Structures of racemic ibuprofen, ketoprofen, naproxen and the target liquid crystals.

fitted with a Specac Golden Gate ATR crystal adaptor) and mass spectrometry (Bruker Daltronics micrOTOF). Elemental Analysis was achieved using a Carlo Erba 1108 Elemental Analyzer controlled with CE Eager 200 software and weighed using a Mettler MT 5 Microbalance.

Phase identification and determination of transition temperatures were carried out by thermal polarised light microscopy using a Zeiss Axioskop 40 polarising transmitted light microscope equipped with a Mettler FP82HT microfurnace in conjunction with a FP90 Central Processor. Differential scanning calorimetry was used to determine enthalpies of transition and to confirm the phase transition temperatures determined by optical microscopy. Differential scanning thermograms (scan rate 10°C min^{-1}) were obtained using a Mettler DSC822^e operating on the Star^e software. The results obtained were standardised to indium (measured onset 156.68°C, ΔH 28.47 J g^{-1}, lit. value 156.60°C, ΔH 28.45 J g^{-1}) (*14*).

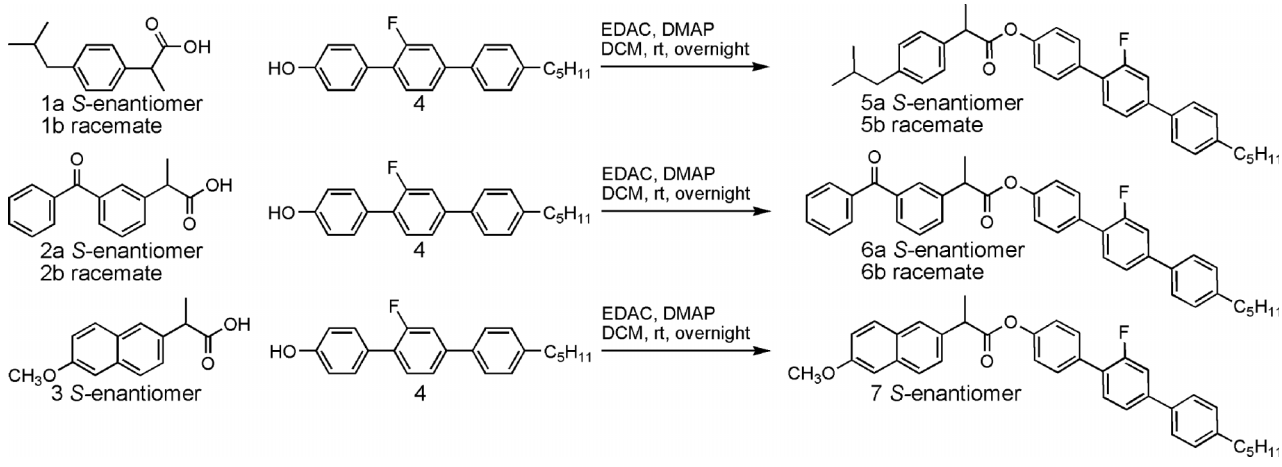
Cano wedges were purchased from EHC with tan(θ) values of 0.0092. The wedge cells were filled with the liquid crystalline material and left to settle overnight in order for the pitch to be determined from the position of the disclination lines.

2.2 Synthetic procedures

2.2.1 Preparation of 2′-fluoro-4″-pentylterphenyl 2-[4-(2-methylpropyl)phenyl]propanoate (**5a, 5b**)

Ibuprofen, **1a** or **1b** (245.5 mg, 1.19 mmol), compound **4** (400.0 mg, 1.19 mmol), EDAC (228.5 mg, 1.19 mmol) and DMAP (14.5 mg, 10 mol%) were dissolved in DCM (50 ml) and stirred overnight at room temperature. The solvent was removed *in vacuo* and the product was purified using column chromatography (eluent: 1:1 hexane and DCM) and recrystallised from ethanol to give the product as a white solid, **5a** or **5b**.

Analyses for ***5a***: Yield 380 mg (59.0%). MS (ESI) for $C_{37}H_{42}F_1O_2$ 540.3229 M^+; I.R. (cm^{-1}) 1755.2 (C=O); ^{1}H NMR (δ, $CDCl_3$, 270 MHz); 7.60–7.21 (m, 11H; Ar-H), 7.17 (d, 2H; Ar-H), 7.07 (d, 2H; Ar-H), 3.95 (quartet, 1H; Alkyl-H), 2.65 (t, 2H; **CH_2**-Ar), 2.49 (d, 2H; Ar-**CH_2**-CH), 1.87 (m, 1H; Alkyl H), 1.64 (m, 5H; Alkyl H), 1.34 (m, 4H; Alkyl H), 0.90 (t, 9H; 3 × **CH_3**); ^{13}C NMR (δ, $CDCl_3$, 270 MHz) 173.9 (C=O), 159.5 (Ar-F), 150.3 (Ar-O), 142.8 (Ar-C), 140.4 (Ar-C), 137.1 (Ar-C), 130.8 (Ar-C), 130.8 (Ar-C), 129.8 (Ar-C), 129.8 (Ar-C), 129.5 (Ar-H), 128.9 (Ar-H), 127.2 (Ar-H), 126.7 (2 × Ar-H), 121.4 (2 × Ar-H), 114.5 (Ar-H), 114.1 (Ar-H), 45.2 (Ar-**CH_2**-CH), 45.0, (O=C-**CH**-Ar), 35.5 (**CH_2**), 31.5 (**CH_2**), 31.1 (**CH_2**), 30.1 (CH_2-**CH**-CH_3), 22.5 (**CH_2**), 22.3 (2 × CH-**CH_3**), 18.5 (Ar-CH-**CH_3**), 14.0 (CH_2-**CH_3**); ^{19}F NMR (δ, $CDCl_3$, 270 MHz) 117.84;



Scheme 1.

EA for $C_{37}H_{42}FO$ (Analytical calcd.) C; 82.72, H; 7.52. (Found) C; 82.63, H; 7.70; DSC: K 89.3 (SmB* 47.6 SmA* 54.8) Iso Liq °C.

*Analyses for **5b**:* Yield 330 mg (51.3%). MS (ESI) for $C_{37}H_{42}F_1O_2$ 540.3301 M^+; I.R. (cm^{-1}) 1755.2 (C=O). ^{1}H NMR (δ, $CDCl_3$, 270 MHz); 7.60–7.21 (m, 11H; Ar-H), 7.17 (d, 2H; Ar-H), 7.07 (d, 2H; Ar-H), 3.95 (quartet, 1H; Alkyl-H), 2.65 (t, 2H; **CH_2**-Ar), 2.49 (d, 2H; Ar-**CH_2**-CH), 1.87 (m, 1H; Alkyl H), 1.64 (m, 5H; Alkyl H), 1.34 (m, 4H; Alkyl H), 0.90 (t, 9H; 3 × **CH_3**); ^{13}C NMR (δ, $CDCl_3$, 75 MHz); 173.9 (C=O), 159.5 (Ar-F), 150.3 (Ar-O), 142.8 (Ar-C), 140.4 (Ar-C), 137.1 (Ar-C), 130.8 (Ar-C), 130.8 (Ar-C), 129.8 (Ar-C), 129.8 (Ar-C), 129.5 (Ar-H), 128.9 (Ar-H), 127.2 (Ar-H), 126.7 (2 × Ar-H), 121.4 (2 × Ar-H), 114.5 (Ar-H), 114.1 (Ar-H), 45.2 (Ar-**CH_2**-CH), 45.0, (O=C-**CH**-Ar), 35.5 (**CH_2**), 31.5 (**CH_2**), 31.1 (**CH_2**), 30.1 (CH_2-**CH**-CH_3), 22.5 (**CH_2**), 22.3 (2 × CH-**CH_3**), 18.5 (Ar-CH-**CH_3**), 14.0 (CH_2-**CH_3**). ^{19}F NMR (δ, $CDCl_3$, 270 MHz) 117.83; EA for $C_{37}H_{42}FO$ (Analytical calcd.) C; 82.72, H; 7.52. (Found) C; 82.92, H; 8.02; DSC: K 94.7 (SmB 47.0 SmA 54.9) Iso Liq °C.

2.2.2 *Preparation of 2′-fluoro-4″-pentylterphenyl 2-(3-benzoylphenyl)propanoic acid (**6a, 6b**)*

The synthetic procedure used was identical for the preparation of compound **5a**. The following quantities were used: ketoprofen, **2a** or **2b** (254.0 mg, 1.00 mmol), compound **4** (334.0 mg, 1.00 mmol), EDAC (191.0 mg, 1.00 mmol) and DMAP (12.2 mg, 10 mol%) and DCM (50 ml).

*Analyses for **6a**:* Yield 342 mg (60%). MS (ESI) for $C_{39}H_{35}F_1O_3$ 571.2638 M^+; I.R. (cm^{-1}) 1751.3 (2 × C=O). ^{1}H NMR (δ, $CDCl_3$, 270 MHz); 7.90–7.34 (m, 16H; Ar-H), 7.23 (d, 2H; Ar-H), 7.08 (d, 2H; Ar-H), 4.05 (quartet, 1H; Alkyl-H), 2.63 (t, 2H; **CH_2**-Ar), 1.66 (d, 3H; **CH_3**-CH), 1.66–1.58 (m, 2H; Ar-CH_2-**CH_2**), 1.40–1.30 (m, 4H; Alkyl-H), 0.89 (t, 3H; CH_3); ^{13}C NMR (δ, $CDCl_3$, 75 MHz) 196.4 (C=O), 172.5 (C=O), 161.2 (Ar-F), 150.2 (Ar-O), 142.9 (Ar-C), 140.2 (Ar-C), 138.1 (Ar-C), 137.4 (Ar-C), 136.7 (Ar-C), 133.3 (Ar-C), 132.6 (Ar-C), 131.5 (Ar-C), 130.7 (2 × Ar-H), 130.1 (2 × Ar-H), 129.9 (2 × Ar-H), 129.2 (Ar-H), 128.9 (2 × Ar-H), 128.8 (Ar-H), 128.3 (2 × Ar-H), 126.7 (2 × Ar-H), 122.8 (Ar-H), 121.3 (2xAr-H), 114.4 (Ar-H), 45.5 (O=C-**CH**-Ar), 35.6 (**CH_2**), 31.5 (**CH_2**), 31.1 (**CH_2**), 22.5 (**CH_2**), 18.5 (Ar-CH-**CH_3**), 14.0 (CH_2-**CH_3**); ^{19}F NMR (δ, $CDCl_3$, 270 MHz) 117.83; EA for $C_{39}H_{35}F_1O_3$ (Analytical calcd.) C; 82.08, H; 6.18. (Found) C; 81.67, H; 6.07; DSC: K 67.6 (SmB* 32.4 SmA* 40.9) Iso Liq °C.

*Analyses for **6b***: Yield 280.0 mg (49%). MS (ESI) for $C_{39}H_{35}F_1O_3$ 571.2652 M^+; I.R. (cm^{-1}) 1749.5 (2 × C=O); ^{1}H NMR (δ, $CDCl_3$, 270 MHz); 7.88–7.33 (m, 16H; Ar-H), 7.24 (d, 2H; Ar-H), 7.08 (d, 2H; Ar-H), 4.05 (quartet, 1H; Alkyl-H), 2.63 (t, 2H; **CH_2**-Ar), 1.66 (d, 3H; **CH_3**-CH), 1.66–1.58 (m, 2H; Ar-CH_2-**CH_2**), 1.40–1.30 (m, 4H; Alkyl-H), 0.90 (t, 3H; CH_3); ^{13}C NMR (δ, $CDCl_3$, 75 MHz) 184.2 (C=O), 170.0 (C=O), 159.5 (Ar-F), 150.3 (Ar-O), 142.5 (2 × Ar-C), 140.0 (2 × Ar-C), 137.3 (Ar-C), 131.8 (2 × Ar-C), 130.8 (Ar-C), 129.8 (3 × Ar-H), 129.0 (Ar-H), 128.9 (Ar-H), 128.8 (Ar-H), 128.0 (6 × Ar-H), 127.1 (2 × Ar-H), 124.2 (Ar-H), 121.5 (2 × Ar-H), 118.3 (Ar-H), 45.8 (O=C-**CH**-Ar), 35.6 (**CH_2**), 31.8 (**CH_2**), 31.1 (**CH_2**), 22.5 (**CH_2**), 18.4 (Ar-CH-**CH_3**), 13.8 (CH_2-**CH_3**).; ^{19}F NMR (δ, $CDCl_3$, 270 MHz) 117.84; EA for $C_{39}H_{35}F_1O_3$ (Analytical calcd.) C; 82.08, H; 6.18. (Found) C; 81.98, H; 6.41; DSC: K 65.5 (SmB 32.1 SmA 40.6) Iso Liq °C.

2.2.3 *Preparation of 2′-fluoro-4″-pentylterphenyl 2-(6-methoxynaphthalen-2-yl)propanoic acid (7)*

The synthetic procedure used was identical for the preparation of compound **5a**. The following quantities were used: naproxen, **7** (230.2 mg, 1.00 mmol), compound **4** (334.0 mg, 1.00 mmol), EDAC (191.0 mg, 1.00 mmol) and DMAP (12.2 mg, 10 mol%) and DCM (50 ml).

Analyses for 7: Yield 270.0 mg (49%). MS (ESI) for $C_{37}H_{35}F_1O_3$ 546.5389 M^+; I.R. (cm^{-1}) 1756.2 (C=O). ^{1}H NMR (δ, $CDCl_3$, 270 MHz); 7.80–7.70 (m, 3H; Ar-H), 7.56–7.05 (m, 14H, Ar-H), 4.14 (quartet, 1H; Alkyl-H), 3.94 (s, 3H; OCH_3), 2.65 (t, 2H; **CH_2**-Ar), 1.79 (d, 3H, **CH_3**-CH), 1.79–1.69 (m, 2H; Ar-CH_2-**CH_2**), 1.40–1.34 (m, 4H; Alkyl H), 0.92 (t, 3H; **CH_3**); ^{13}C NMR (δ, $CDCl_3$, 270 MHz); 172.8 (C=O), 158.5 (Ar-F), 150.3 (Ar-O), 146.0 (Ar-O), 142.4 (Ar-C), 140.8 (Ar-C), 136.8 (Ar-C), 134.2 (Ar-C), 134.0 (Ar-C), 130.6 (Ar-C), 129.5 (Ar-H, Ar-C), 129.0 (Ar-C), 128.8 (2 × Ar-H), 128.4 (Ar-H), 128.0 (3 × Ar-H), 127.1 (2 × Ar-H), 126.9 (2 × Ar-H), 122.0 (Ar-H), 121.6 (2 × Ar-H), 118.5 (2 × Ar-H), 105.3 (Ar-H), 54.6 (OCH_3), 45.0 (O=C-**CH**-Ar), 34.8 (Ar-**CH_2**), 30.8 (**CH_2**), 30.4 (**CH_2**), 22.5 (**CH_2**-CH_3), 18.5 (Ar-CH-**CH_3**), 14.0 (CH_2-**CH_3**). ^{19}F NMR (δ, $CDCl_3$, 270 MHz) 117.81; EA for $C_{37}H_{35}F_1O_3$ (Analytical calcd.) C; 81.29, H; 6.45. (Found) C; 81.07, H; 6.90; DSC: K 145.2 Iso Liq °C.

3. Results and discussion

3.1 Phase identification and transition temperatures

The transition temperatures were determined by thermal polarised microscopy (POM) and differential scanning calorimetry (DSC). Table 1 shows the melting points found by DSC, and the phase transition temperatures, which were found to be monotropic, by POM for both the ibuprofen and ketoprofen

Table 1. Transition temperatures (°C) and melting points of compounds **5a**, **5b**, **6a**, **6b** and **7** where ( ) denotes a monotropic phase transition. The enthalpy values [ΔH] for the phase transitions are given in J g^{-1}.

Compound	Crystal		SmB*/B		SmA*/A		Iso Liquid
5a	•	89.3 [38.74]	•	47.6 [0.79]	•	54.8) [4.82]	•
5b	•	94.7 [86.23]	•	47.0 [2.81]	•	54.9) [10.78]	•
6a	•	67.6 [55.51]	•	32.4 [2.08]	•	40.9) [6.71]	•
6b	•	89.8 [65.53]	•	32.1 [1.93]	•	40.6) [6.60]	•
7	•	145.2 [90.23]	–	–	–	–	•

materials, **5** and **6**. The naproxen material, **7**, did not exhibit mesomorphic behaviour. It can be seen from the table that the melting points for the racemates (**5b** and **6b)** are consistently higher than the melting points for the *S*-enantiomers, whereas the mesophase transitions were essentially unchanged.

The liquid crystal phases were identified from their defect textures using transmitted polarised light microscopy. Both materials exhibited homeotropic and focal-conic textures and were therefore found to exhibit orthogonal smectic phases, A and B (*15*). The focal-conic defect texture formed first on cooling from the isotropic liquid for the racemate, **5b**, is shown in Figure 2(a). Subsequent cooling, Figure 2(b), showed the focal-conic defects becoming crossed with lines, called transition bars, parallel to the planes of the ellipses in the conical sections, indicating phase segregation and the formation of a B phase. Further cooling induced healing of the transitions bars and the formation of the focal-conic texture of the B phase, see Figure 2(c). Comparison of Figure 2(a) with 2(c) shows that 2(c) has far fewer parabolic defects associated with the focal-conic defects than does 2(a). Reheating to the higher temperature smectic phase resulted in the focal-conic defects becoming patterned by parabolic defects, indicating a volume change at the phase transition. Although it can never be certain without X-ray diffraction studies on the mesophases, microscopy clearly indicates that compound **3** exhibits a smectic A to hexatic B phase transition (*16*) rather than a smectic A to crystal B phase change (*17*). For a crystal B phase to be present, one would have expected to observe long-range out-of-plane correlations in such focal-conic defects.

Moreover, the low value of the enthalpy of transition for the smectic A to smectic B transition partially confirms that the B phase is hexatic in nature. If the B phase were crystallinic a larger value of the heat of transition would have been expected because of the inclusion of the lattice energy.

Although the results reported here were for the racemate **5b**, almost identical results were obtained for the *S*-enantiomer, **5a** and the ketoprofen materials, **6a** and **6b**. This fact also indicates that the mesophases found were orthogonal variants, with the long axes of the molecules being perpendicular to the layer planes.

3.2 Molecular simulations

The microscopy studies show that both the ibuprofen and ketoprofen materials exhibit orthogonal smectic monotropic mesophases. The reason why the liquid crystal phases are so strongly monotropic is borne out via molecular simulations (see Figure 3). The figure shows all three of the chiral compounds and reveals that their molecular structures are relatively rigid and overall they have a bent shape with a typical bend angle of 115–120°. Compound **5a** has a more of a hockey-stick shape that the other two compounds, and that of the ibuprofen motif is branched and also relatively inflexible in comparison to the pentyl chain of the terphenyl moiety. Modelling also shows a minimum energy position where the fluoro-substituent of the terphenyl has the ability to couple with the carbonyl of the ester linking unit. This allows the methyl group of the chiral centre to protrude, which will lower melting points and mesophase transition temperatures in comparison to systems possessing four aromatic rings. Compound **6a** is the most flexible of the compounds where the flexibility centres about the carbonyl linkage in the ketoprofen unit. Compound **6a**, despite being more V-shaped than compound **5a**, adopts a similar conformation and hence exhibits a similar phase sequence. However, one would expect a V-shaped compound to exhibit higher mesophase stability than the hockey-stick shaped compound, but the reduction in the mesophase stability can be attributed to the polarity of the carbonyl unit of the ketoprofen moiety. Compound **7** is of similar conformation to the other compounds

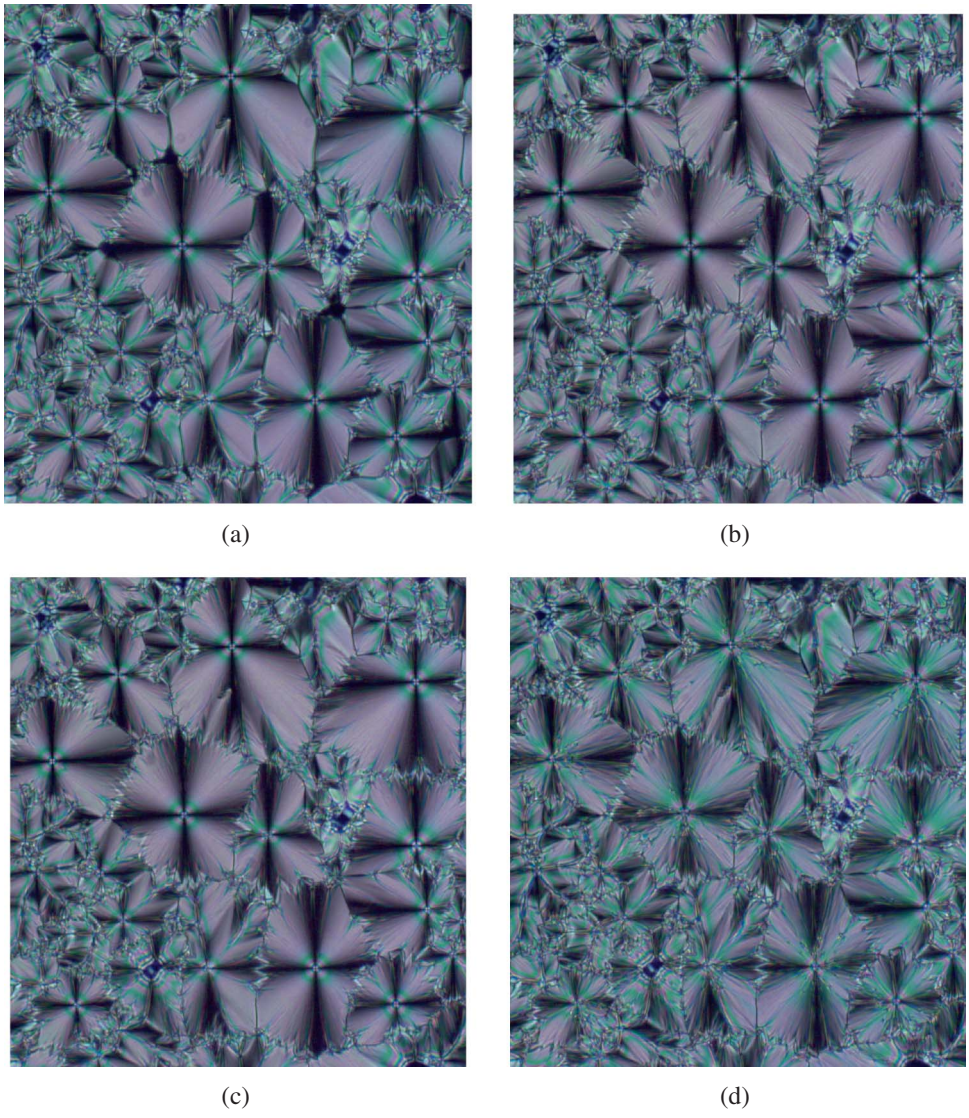
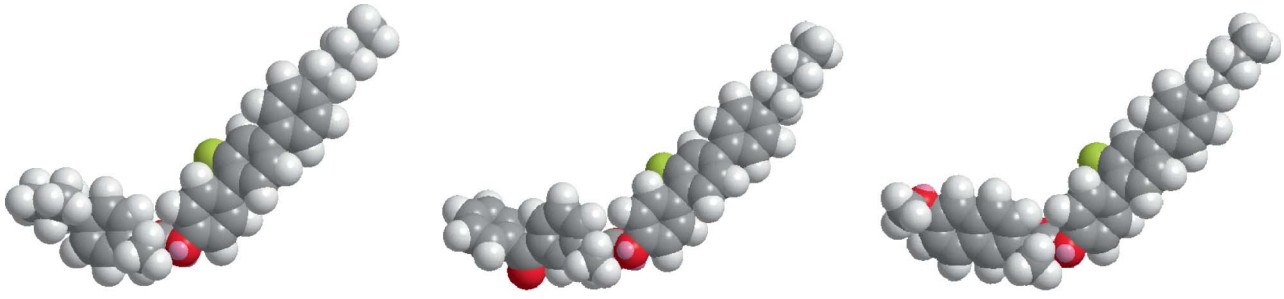


Figure 2. The focal-conic defect textures of compound **5b**; (a) the smectic A phase, (b) the transition between the hexatic B and smectic A phase showing faint transition bars, (c) the focal-conic texture of the smectic B phase showing few parabolic defects, (d) the texture of the smectic A phase formed on reheating showing a large number of parabolic defects (all × 100).

and is of similar shape to **6a**, but it does not exhibit any mesophase behaviour. The high melting behaviour of this compound coupled with the inflexibility of the naphthalene unit of the naproxen prevents the observation of monotropic phases that would be expected based on the behaviour of the other compounds examined.

3.3 Determination of helical twisting power

The Cano-wedge method (*18*) was used to determine the helical twisting power (HTP) of compounds **5a**, **6a** and **7** by dissolving them at low concentrations in a nematic liquid crystal host, E7, and measuring the pitch from the distance between the disclination lines at room temperature. Thus, mixtures of 0.25, 1.00, and 4.00% (by wt) of each compound in E7 were prepared and a Cano-wedge for each mixture was filled by capillary action and left overnight to settle. The results obtained *via* optical microscopy are shown in Tables 2–4, and plotted in Figure 4. Figure 4 shows that there is a linear relationship between the pitch and the reciprocal of the concentration for each of the materials in E7. The HTP for each compound was determined, with the HTP for the ibuprofen compound, **5a**, being the lowest at 3.6 μm^{-1}. The pitches observed for the ketoprofen and naproxen materials **6a** and **7** in E7 are much shorter than for the ibuprofen compound and hence their HTP values are also much higher, at 7.6 μm^{-1} and 10.9 μm^{-1}, respectively. These results bear comparison with standard chiral dopants,



a) b) c)

Figure 3. Minimised structures in the gas phase using Chem Draw 3D^{TM} of the *S*-enantiomers of: (a) ibuprofen, **5a**; (b) ketoprofen, **6a**; (c) naproxen, **7**.

Table 2. Measurement of pitch (μm) as a function of concentration (wt%) for compound **5a** in mixtures with E7 at room temperature.

Wt% of **5a** in E7	Distance between disclination lines (μm)	Pitch (μm)
0.25	6000	110
1.03	1500	27
3.94	400	7.5

Table 3. Measurement of pitch (μm) as a function of concentration (wt%) for compound **6a** in mixtures with E7 at room temperature.

Wt% of **6a** in E7	Distance between disclination lines (μm)	Pitch (μm)
0.25	2900	53
0.99	669	12
4.00	170	3.1

Table 4. Measurement of pitch (μm) as a function of concentration (wt%) for compound **7** in mixtures with E7 at room temperature.

Wt% of **7** in E7	Distance between disclination lines (μm)	Pitch (μm)
0.25	2000	37
1.00	502	9
3.97	121	2.2

such as *S*-4′-(2-methylbutyl)-4-cyanobiphenyl (CB15) which has a value of 8.5 μm^{-1} (*19*).

The HTP for each of the materials can be rationalised by comparing their flexibilities and the shape of the drug moiety. The ibuprofen compound has a relatively rigid structure with only one phenyl ring in the drug moiety compared with three for the terphenyl segment, and

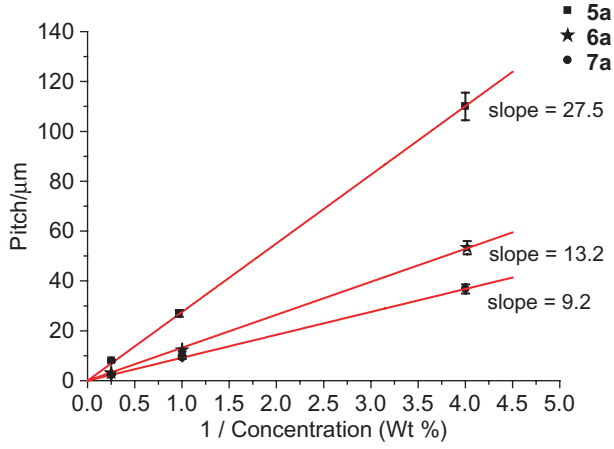


Figure 4. Pitch (μm) as a function of the reciprocal concentration of compounds **5a, 6a** and **7** in mixtures with the liquid crystal host E7.

hence only a small amount of the chirality is transferred to the host liquid crystal. The naproxen compound, **7**, is also rigid but has more of a V-shaped molecular structure, with the naphthalene unit on one side of the molecule being longer and wider than the phenyl ring of the ibuprofen. This added length and width results in a greater transfer of chirality due to the opportunity for increased interactions, and hence the greater HTP value. The ketoprofen material, **6a**, is similar in shape to the naproxen compound but it exhibits a greater flexibility in structure which, when considered with the polarity of the carbonyl unit between the two phenyl rings, may lead to reduced interactions with the host liquid crystal compared with the naproxen compound, and hence may explain why the HTP value is lower.

4. Conclusion

We show that chiral pharmaceuticals are a readily available source of chiral substrates of closely defined and reproducible optical purity for the preparation of,

or use as, dopants for applications in liquid crystals. In particular, we demonstrate the use of ibuprofen, ketoprofen and naproxen as substrates in the synthesis of chiral liquid crystals, which were subsequently used as dopants in E7 to create chiral nematic mixtures. We demonstrate that the length and flexibility of the pharmaceutical moiety in the liquid crystal structure has a big effect on the efficiency of the material to promote chirality transfer into the host liquid crystal system. In addition to their use in nematic systems, such materials may also be used as dopants for ferro- and anti-ferroelectric liquid crystals, thereby removing the associated ambiguities of enantiomeric excess relating to helical pitch length, spontaneous polarisation, and tilt angle.

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