Highly Efficient Chirality Inducers Based on Steroid-Derived 2,6,9-Trioxabicyclo[3.3.1]nonanes

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Introduction

Conversion of an achiral nematic mesophase into a chiral nematic mesophase can be achieved by the addition of a small amount of a chiral compound, and the degree of chirality induction is measured by a molecular property termed the helical twisting power β_M.[1] The relationship between the structure of a chirality inducer and the magnitude β_M has been the subject of several investigations.[1−8] Inter alia, it has been found that the presence of two quasi-planes oriented at an angle to one another leads to high twisting powers.[2,9] Recently, we studied the chirality-inducing properties of diesters **1** of (5*RS*,8*RS*)-
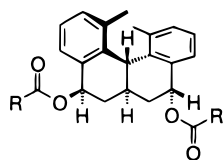

1a: R = Me   **1d**: R = *p*-C$_6$H$_4$(CH$_2$)$_6$CH$_3$

1b: R = (CH$_2$)$_2$CH$_3$ **1e**: R = *p*-C$_6$H$_4$(*p*-C$_6$H$_4$)(CH$_2$)$_6$CH$_3$

1c: R = (CH$_2$)$_{10}$CH$_3$

trans-5,6,6a,7,8,12b-hexahydrobenzo[*c*]phenanthrene-5,8-diol.[10] It was determined that the magnitude of the helical twisting power was strongly dependent on the nature of the acyl substituents with long, rodlike substituents containing aromatic residues being associated with larger β_M values.

In this paper, we report on the exceptional chirality-inducing properties of another class of compounds possessing angularly disposed quasi-planes, dimeric steroid-derived 2,6,9-trioxabicyclo[3.3.1]nonanes **2** and **3**.[11] The

results of investigations into the relationship between the structures of **2** and **3** and the magnitude of the helical twisting power[1] β_M are described.
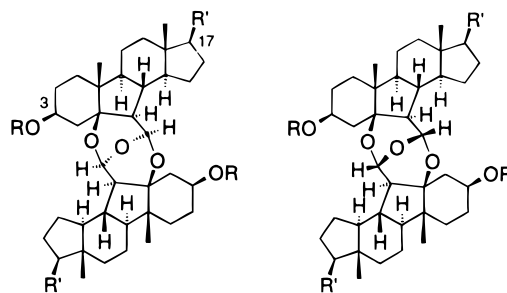
concave   planar

2a: R = H; R′ = C$_8$H$_{17}$ **3a**: R = H; R′ = C$_8$H$_{17}$

2b: R = Me; R′ = C$_8$H$_{17}$ **3b**: R = Me; R′ = C$_8$H$_{17}$

2c: R = Bz; R′ = C$_8$H$_{17}$ **3c**: R = Bz; R′ = C$_8$H$_{17}$

2d: R = Bz; R′ = OBz

Results and Discussion

The steroid dimers were available as two diastereomeric series: the "concave" series **2** and the "planar" series **3**. The angles between the large quasi-planes of compounds **2c** (R = Bz, R′ = C$_8$H$_{17}$) and **3c** (R = Bz, R′ = C$_8$H$_{17}$) are approximately 65° and 165°, respectively, as indicated from the energy-minimized structures of the isomers (Figure 1).

The helical twisting powers β_M of dimers **2a−d** and **3a−c** in the nematic phases 4-*n*-butyl-*N*-(4′-methoxy-benzylidene)aniline (MBBA) **4** and 4′-*n*-heptyl-4-biphenylcarbonitrile (7BCN) **5** were determined by the droplet method.[12] The sign of β_M (positive or negative) is of no significance to this work, and hence, only *absolute* values of β_M were determined (Table 1).

All of the dimers investigated were found to have high twisting powers with three compounds **2c**, **2d**, and **3c** exhibiting *exceptionally high twisting powers* in both MBBA **4** and 7BCN **5** with magnitudes being 1 or 2 orders of magnitude larger than those ordinarily encountered.[1]

All of the dimers **2** and **3** possess significantly larger quasi-planes than those of the helical diesters **1**, and this may be the reason for their exceptionally high twisting power (Table 1). Indeed, the twisting powers of **2c** and **3c** in MBBA **4** and **2c**, **2d**, and **3c** in 7BCN **5** exceed the magnitudes of twisting power found by Heppke and co-workers[9] who reported "unusual high helical twisting powers" for mesogenic chiral esters (e.g. **6**) dissolved in the nematic liquid crystal RO-TN 404 (Hoffmann−La Roche). When expressed in the same units[9] it transpires that the most efficient chirality inducer **6** reported by Heppke is only 57%[14] as effective as the concave dimer **2c** (Table 1, entry 3).

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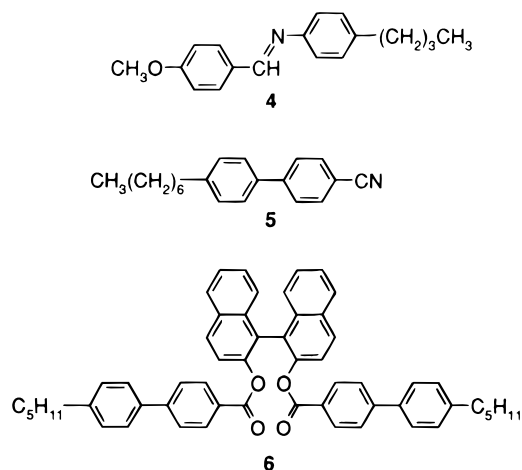(8) Park, J. J., Ph.D. Thesis, University of Sydney, 1998.

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(13) SYBYL in SPARTAN version 5.0; Wavefunction Inc. 18401 Von Karman, Suite 370, Irvine, CA 92715.

4

5

6

While this comparison may not be strictly accurate because Heppke used a different nematic mesophase, it appears that, prima facie, the concave dimer **2c** is the *most effective chirality inducer so far discovered.* This was found in two nematogens and it has been observed in these laboratories[8] that dramatic changes in the helical twisting power do not occur between nematic phases of this type. Therefore, comparison with Heppke's results is justified.

The results summarized in Table 1 show the effect of substitution at 3β of the steroidal units in the dimers **2** and **3**.

While the diols **2a** (Table 1, entry 1) and **3a** (Table 1, entry 5) had high twisting powers in both nematic phases, higher still twisting powers were observed for the dimethyl ether derivatives **2b** (Table 1, entry 2) and **3b** (Table 1, entry 6). This increase may be due to the increase in the size of the groups at the 3β-positions of the steroidal units as the presence of the significantly larger benzoyloxy groups at the 3β-positions brought about a further and exceptional increase in the twisting power (Table 1, entries 3 and 7). This effect was particularly marked in the nematic phase 7BCN **5**.

These results suggest that the rigidly oriented quasi-planes of the steroidal units of each diastereomer may act to anchor the substituents at the 3β-positions at a particular orientation to each other. The interaction between the solute and nematogen molecules would then take place as an interaction between the relatively fixed groups at the 3β-positions of the steroid dimer and the nematogen. Thus, the larger these groups are, the greater the interaction between the chirality inducer and the nematogen. This model offers a plausible explanation for the increase in the twisting power observed for the dimethyl ether derivative **2b** over the diol **2a**. However, there may also be an effect due to hydrogen bonding interactions between the hydroxyl groups of either **2a** and **3a** and the nematogen. These hydrogen bonding interactions may lower the effect of the size of the 3β-substituents. In the case of concave dimer **2c**, the significantly larger benzoyloxy groups at the 3β-positions may take part in favorable $\pi-\pi$ stacking interactions[8,15,16] with the aromatic rings of the nematic phase, further amplifying
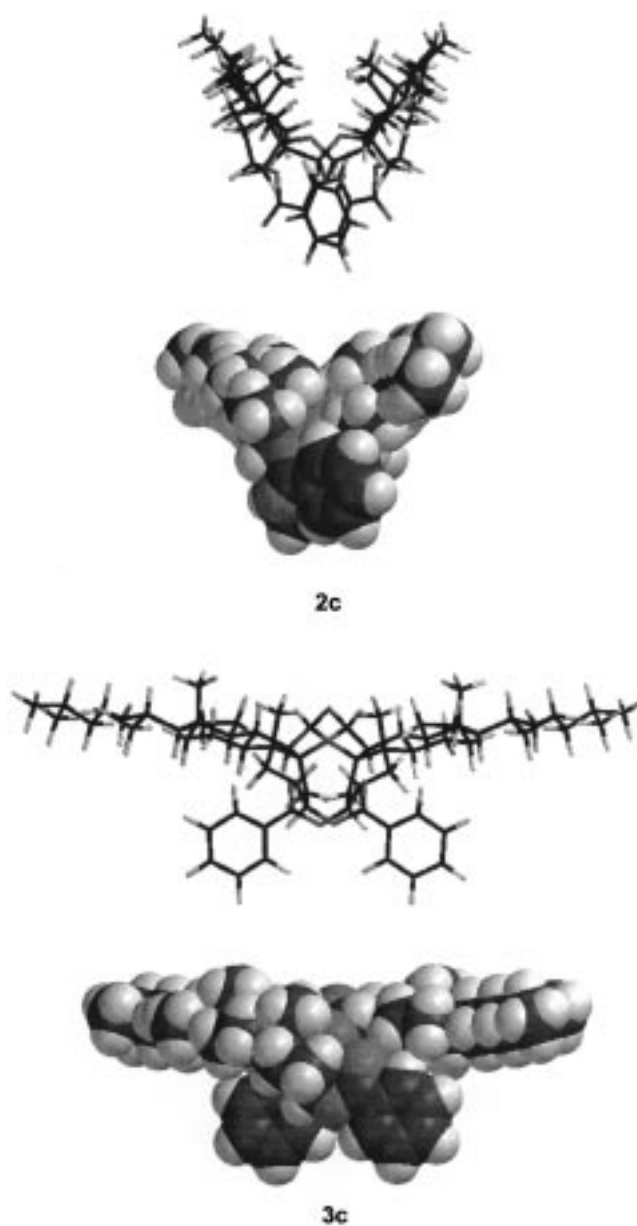

2c

3c

Figure 1. Side-on views of energy-minimized structures[13] of 2,6,9-trioxabicyclo[3.3.1]nonanes **2c** (concave) and **3c** (planar).

Table 1. Helical Twisting Powers (β_M) of 2,6,9-Trioxabicyclo[3.3.1]nonanes 2 and 3 in MBBA 4 and 7BCN 5

		β_M (μm^{-1} mol^{-1})	
entry	compound	MBBA **4**	7BCN **5**
1	**2a:** R = H; R′ = C_8H_{17}	76.8	51.7
2	**2b:** R = Me; R′ = C_8H_{17}	136	79.4
3	**2c:** R = Bz; R′ = C_8H_{17}	369	334
4	**2d:** R = Bz; R′ = OBz	250	276
5	**3a:** R = H; R′ = C_8H_{17}	162	134
6	**3b:** R = Me; R′ = C_8H_{17}	220	120
7	**3c:** R = Bz; R′ = C_8H_{17}	324	319

the effect of having larger groups at the 3β-positions and thus leading to the exceptionally high twisting powers observed for both diastereomers.

In addition to the effect of the substituents at the 3β-positions on the twisting power in both series, the

(14) Heppke and co-workers[9] reported the twisting power of compound **6** in RO TN 404 as 53200 m^2 mol^{-1} at 20 °C. Recalculation of the β_M value of **2c** in the present work to units compatible with the value of Heppke and co-workers[9] yields the twisting power of **2c** in 7BCN **5** to be 92600 m^2 mol^{-1} at 22 °C.

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importance of the relative configuration of the diastereomers is apparent: it appears that the angle at which the large quasi-planes are oriented (Figure 1) is important for the ordering of the host nematogen by the chirality inducer. The fact that reasonably high and markedly different β_M values are obtained for R = H and R = Me in both series suggests that the quasi-planes themselves are interacting in an ordered manner with the nematic phase. This is consistent with the finding that the helical diesters **1**, which have almost no contribution to the helical twisting power by the quasi-planes, exhibit low β_M values of $7-12$ μm^{-1} mol^{-1} when the substituents are either small or devoid of an aromatic residue (**1a**−**c**).[10] Generally, in the absence of benzoyloxy substituents, higher twisting powers were observed for compounds having the relative configuration of the planar dimer **3** (Table 1, entries 5, 6, and 7).

Introduction of a 3β-benzoyloxy group provides a second interaction, $\pi-\pi$ stacking, which either competes with the interaction of the steroid quasi-planes or is additive to it. In each diastereomer, the orientation of the benzoyloxy groups must be quite different, owing to the different angles at which the quasi-planes are oriented in each diastereomer. It is apparent from the larger increase in β_M from R = Me to R = Bz that the orientation is particularly favorable in the concave dimer (Table 1, entries 2 and 3).

The dibenzoate derivative **2c** and the tetrabenzoate derivative **2d** differ in substitution at the 17β-positions of the steroidal units (Table 1, entries 3 and 4). In this case, the tetrabenzoate derivative **2d** has two sets of benzoyloxy groups that could participate in $\pi-\pi$ interactions. However, this compound exhibits a lower β_M than that of **2c**. This suggests that both $\pi-\pi$ interactions are acting in a competitive manner thereby lowering the overall effect of having aromatic substituents. Interestingly, the magnitudes of the twisting power were similar in both liquid crystals, and further, the trends were found to be the same.

In summary, it appears that the presence of large quasi-planar fragments is crucial for overall high twisting powers and that the orientation of the quasi-planes with respect to each other is important. The presence of benzoyloxy groups at the 3β-positions of the steroidal units is also an important factor in achieving the exceptionally large twisting powers found for compounds **2c**, **2d**, and **3c** in both liquid crystals MBBA **4** and 7BCN **5**. It is likely that the relatively large size of the benzoyloxy group, the specific manner in which it is oriented by the quasi-planes, and favorable $\pi-\pi$ stacking interactions have a combined or synergistic effect on the helical twisting power.

Experimental Section

Compounds **2a**−**c** and **3a**−**c** were prepared as previously described.[11] Details of the preparation of compound **2d** will be reported elsewhere.[17] 4-*n*-Butyl-*N*-(4′-methoxybenzylidene)-aniline (MBBA) **4** was prepared by the method described by Flannery Jr. and Haas.[18] 4′-Heptyl-4-biphenylcarbonitrile (7BCN) **5** was purchased from Aldrich Chemical Co.

The magnitudes of the pitch of induced helices were determined on an Olympus BHSP polarizing microscope. Optical patterns were illuminated with plain white light and appeared as radial disclinations or concentric circles and as such gave no clear indication of "handedness" of the induced helices. The graticule was calibrated with a 1 mm scale with 10 μm divisions at ×40 magnification. The temperature of the stage was maintained at 22 ± 0.2 °C by a Linken MS100 controller and warm stage. The errors in the magnitude of the helical twisting power β_M are estimated[8] to range typically from 1% to 6% based on the standard deviation of β_M.

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