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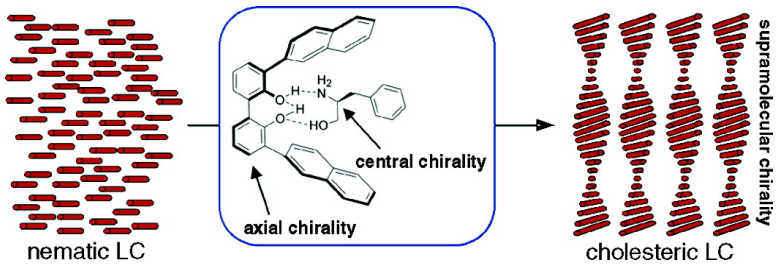

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Macroscopic Expression of the Chirality of Amino Alcohols by a Double Amplification Mechanism in Liquid Crystalline Media

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Amplification of chirality is of tremendous importance from both a fundamental and a practical point of view. It is considered an essential factor in the origin of homochirality in nature, triggered from an initially small chiral bias.[1] Amplification of chirality has been applied in several practical methods for detection and analysis of chiral compounds.[2] Among these, there are a few methods involving doped liquid crystalline (LC) systems.[3] Here, we report the transfer of chirality from a single stereogenic center to a supramolecular system, by a double chiral amplification sequence. This (prototype) system not only makes it possible to assess the chirality of simple amino alcohols from the macroscopic chiral properties of the LC phase but also shows an intriguing transfer of central chirality via axial chirality to supramolecular chirality.

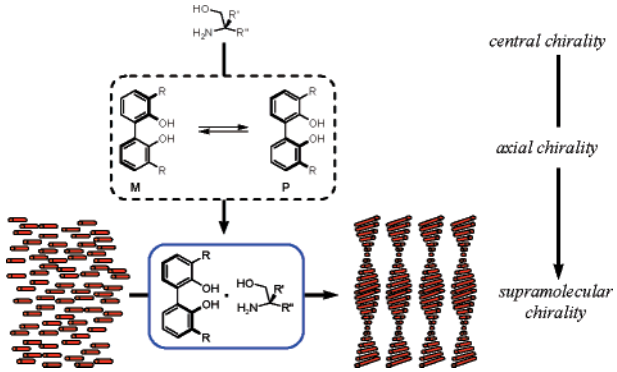
In recent years, beautiful examples of amplification of chirality in enantioselective autocatalysis,[4] supramolecular assemblies,[5] and polymeric systems[2,6] have been reported. Liquid crystalline materials are also known to act as amplifiers of chirality,[7] as they can lead to chiral mesophases upon doping with a small amount of a suitable chiral dopant. Cholesteric (or chiral nematic) liquid crystals are characterized by large supramolecular chiral organization, and as a result these materials display very large optical and CD activities.[8] In addition they show macroscopic properties that can be used as a measure of their chiral organization and, therefore, indirectly as a measure of the chirality of the dopant.[3,8a]

The chirality of a cholesteric LC is indicated by the sign and magnitude of the cholesteric pitch.[8a,9] The pitch (p, the length of one turn of the cholesteric helix) is dependent on: (1) the concentration (c) of the dopant, (2) the helical twisting power (β) of the dopant, and (3) the enantiomeric excess (ee) of the dopant.

$$\text{pitch } (p) = (c\,\beta\,\text{ee})^{-1}$$

The helical twisting power is an intrinsic property of any chiral dopant which indicates how efficient this molecule is in inducing a chiral orientation in the LC material. However, for a molecule to have a significant helical twisting power, some structural resemblance to the mesogenic host is required.[10] For instance the helical twisting powers of amines could be enhanced by covalent attachment of a moiety resembling the LC structure.[11] Yet, for rapid chiral analysis purposes,[12] this is a rather time-consuming process, which led us to consider "β-enhancing functionalization" by noncovalent interactions, with the ultimate goal of developing a simple mixing procedure for LC based chiral analysis. Biphenol based receptors were chosen due to their ability to form noncovalent complexes with amines by hydrogen bonding.[13] Furthermore, it was anticipated that mixing of a chiral amine and a conformationally flexible biphenol would result in diastereoselective binding, which would enhance the helical twisting power of the former. Normally, these biphenols exist in two chiral conformations (P and M helices), which rapidly interconvert in solution at room temperature (Scheme 1). Diastereoselective binding of a chiral amine could result in an excess of one of the axially chiral conformers. Based on this principle we envisioned that it would be possible to transfer the chirality of an amine to an LC phase by complexation to an achiral biphenol derivative in a doped LC system (Scheme 1), taking advantage of the often relatively high helical twisting powers of chiral biphenyls.[14]

Scheme 1. Double Amplification of Chirality



As initial attempts using 2,2′-biphenol, the simplest biphenol available, with several amino alcohols proved unsuccessful, biphenol derivatives **1** and **2** were synthesized (Figure 1).[15] By introduction of aryl substituents flanking the biphenol binding area, enhanced interactions with the amino alcohols and more efficient chiral induction in the mesophase were expected.[16] Biphenols **1** and **2** were mixed separately with (*R*)-**3** and (*S*)-**3**, and doped in liquid crystal blend E7 (amino alcohol/biphenol = 1.5:1; 0.038 μmol biphenol/mg E7).[17] This afforded cholesteric mesophases, which, when aligned on a rubbed polyimide surface and placed under a plane-convex lens, displayed clear Grandjean−Cano lines (Figure 2). At higher doping concentrations (>0.076 μmol biphenol/mg E7) only wormlike cholesteric textures were observed. When (*S*)-**3** was doped in E7 at similar, or twice as high, concentrations, but without biphenols **1** or **2** present, no Grandjean−Cano lines or wormlike textures were ever observed. At higher dopant concentrations (*S*)-**3** started to crystallize out. From the observed Grandjean−Cano lines the cholesteric pitch was determined, for the complexes described above, as well as for similar complexes of **1** and **2** with (*S*)-**4** (Table 1).[18] It was found that the combination **2•3** gave the shortest pitch, meaning the largest chiral induction.[19]

NOESY measurements on **1•3** showed that the aliphatic part of the amino alcohol is situated deep in the cleft between the two naphthalene moieties (Figure 1). This was confirmed by upfield shifts of all aliphatic and some aromatic protons upon complexation, indicating that they are in the shielding zone of the naphthalenes. Although the exact structure of these complexes remains unknown so far, IR experiments in benzonitrile suggest that all OH-groups in this system participate in hydrogen bonding.[15] This could also explain why (*S*)-α-phenylethylamine and (*S*)-phenylalanine

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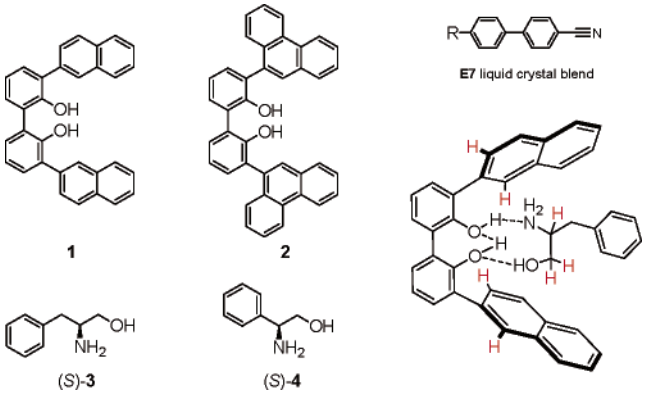

Figure 1. Structures of 3,3′-disubstituted biphenols **1** and **2**, amino alcohols **3** and **4**, and E7 liquid crystal blend where R = *n*-C_5H_{11}, *n*-C_7H_{15}, *n*-$C_8H_{17}O$, 4′-*n*-C_5H_{11}−C_6H_4; and a proposed mode of binding for **1•3**. The protons with the strongest intermolecular NOEs are designated in red.

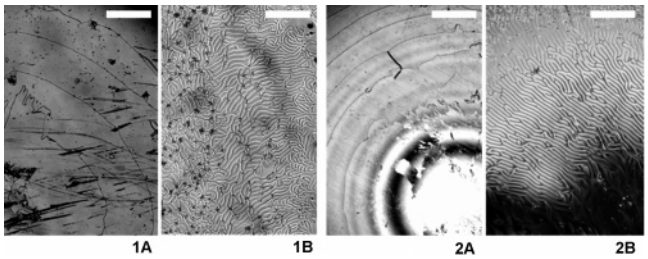

Figure 2. (1) Textures observed for **1**•(*S*)-**3** in E7: Grandjean-Cano lines (1A) and wormlike cholesteric structures (1B). (2) Textures observed for **2**•(*S*)-**3** in E7: Grandjean−Cano lines (2A) and wormlike cholesteric structures (2B). Bar represents 300 μm.

Table 1. Pitch of E7 Doped with Biphenol•Amino Alcohol

	pitch (μm)		
amino alcohol	no biphenol	**1**[a]	**2**[a]
(*S*)-**3**	*b*	+21	+12
(*R*)-**3**	*b*	−21	−12
(*S*)-**4**	*b*	35	16

[a] All measured at the same reduced temperature.[15] [b] No Grandjean−Cano lines were observed.

methylester, both lacking a hydroxyl moiety, give, respectively, infinite and relatively large pitches (p = 66 μm for **2**•(*S*)-phenylalanine methylester). The complex stoichiometry of **1•3** in $CDCl_3$ was established at 1:1 by Job's plot analysis, and CD measurements showed small but significant induced CD signals of biphenol **1** with absorptions at 281 and 318 nm upon complexation to **3** in $CHCl_3$ solution, reflecting the diastereomeric excess in **1•3**.[15,20]

The results presented here show that it is possible to amplify the chirality of simple amino alcohols, by transfer of their central chirality to a dynamically axially chiral biphenol and subsequent expression as supramolecular chirality by effecting a change from a nematic to a cholesteric LC. Without the complexation to the biphenol, no cholesteric phase is found with these chiral dopants. Aligned cholesteric LCs are known to reflect light of a wavelength related to their pitch.[11,21] Although at this point the induced cholesteric pitch is too large, it is anticipated that, upon increasing the chiral induction, application of this new principle in an LC based color test for ee determination by simple complexation is feasible.[22]

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Supporting Information Available: Experimental procedures and spectral data for the synthesis of all new compounds, CD, IR, and NMR data of **1•3** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) The pitch is generally determined by the Grandjean−Cano technique, a method which requires an aligned LC sample to be placed between a plane-convex lens and a flat surface. The pitch can then be obtained from the distances between the distinct lines seen through a polarizing microscope. See: Heppke, G.; Oestreicher, F. *Mol. Cryst. Liq. Cryst.* **1977**, *41*, 245−249.
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(17) At higher amino alcohol to biphenol ratios, partial phase separation was observed. At lower ratios, highly disturbed phases were obtained, of which the pitch was found to be impossible to measure, although wormlike textures were still observed, indicating a cholesteric phase.
(18) Interestingly, using this new principle it is also possible to amplify the chirality of a molecule with a measurable helical twisting power. **1** · *N*,*N*-dimethylphenylalaninol in E7 has a pitch of 11 μm, whereas the uncomplexed amino alcohol, at the same concentration, gives rise to a pitch of 28 μm.
(19) The presence of an arene moiety in the amino alcohol appears to be essential, as complexes of aliphatic amino alcohols valinol and t-leucinol in E7 had pitches that were too large to measure; IR studies did not indicate participation of nitrile groups (as present in E7).
(20) While this work was in progress, a paper describing the diastereoselective binding of chiral amines to biphenols appeared: Takagi, H.; Mizutani, T.; Horiguchi, T.; Kitagawa, S.; Ogoshi, H. *Org. Biomol. Chem.* **2005**, *3*, 2091−2094.
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