ORGANIC LETTERS

2006
Vol. 8, No. 7
1331−1334

Phosphoric Acids as Amplifiers of Molecular Chirality in Liquid Crystalline Media

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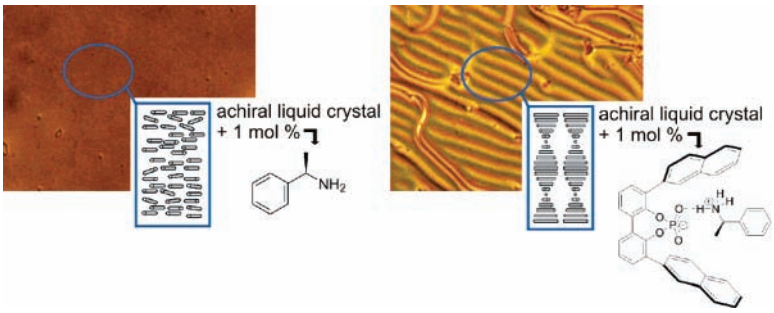
Received January 11, 2006

ABSTRACT



A new system for the double amplification of the molecular chirality of simple chiral amines in achiral liquid crystalline media is described. It involves a conformationally flexible phosphoric acid based receptor that by binding to chiral amines induces chirality in the liquid crystalline matrix. Efficient cholesteric phase formation was shown by several chiral amines that were not able to induce measurable helicity in nematic liquid crystals by themselves.

The amplification of molecular chirality in supramolecular systems is considered a major factor in the origin of homochirality in Nature.[1] Chiral amplification mechanisms have been applied in the detection and analysis of chiral compounds.[2] Recently, we described a new concept for the amplification and detection of molecular chirality in liquid crystalline systems, by a double amplification sequence involving host−guest chemistry.[3] Here, we report a new system for the double amplification of the molecular chirality of simple chiral amines in achiral liquid crystalline media. It involves a conformationally flexible phosphoric acid based receptor that by binding to chiral amines induces chirality in the liquid crystalline matrix (Scheme 1). In doing so it not only provides a new mechanism for cholesteric LC formation but also allows the chirality of the amines to be detected by standard liquid crystal (LC) techniques.

It could also provide a hint at protobiotic amplification mechanisms, as liquid crystallinity and organic phosphate−amine interactions (between DNA or RNA and peptides) are key features of the essential molecules of life.[4,5]

Chiral nematic (or cholesteric) liquid crystals are chiral due to a supramolecular helical organization which results in large optical and circular dichroism (CD) activities.[6] Furthermore, they show macroscopic properties that can be used as a measure of their chiral organization. When the helical organization of an achiral liquid crystalline host is induced by addition of a small chiral molecule (the dopant), the chirality of this dopant is amplified resulting in a large

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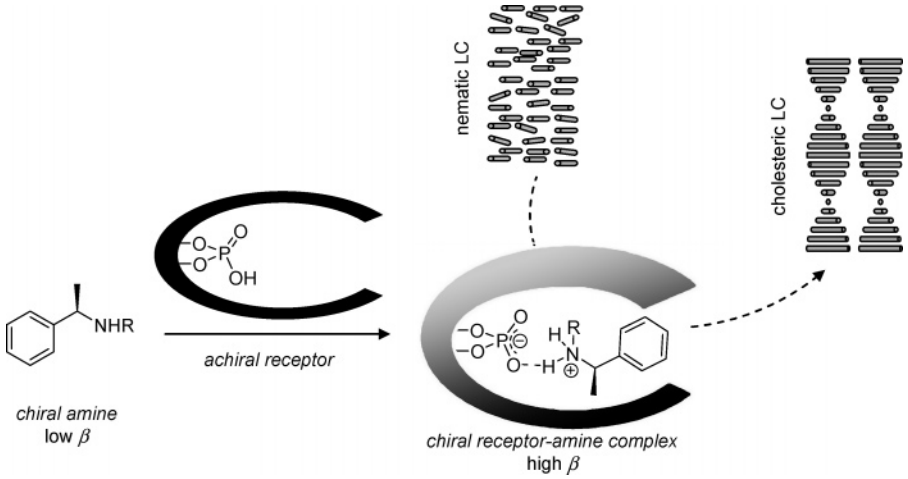
10.1021/ol060076l CCC: $33.50
Published on Web 03/03/2006

Scheme 1. Double Amplification of Molecular Chirality by Phosphate-ammonium Interactions Which Effect a Conformational Change in the Receptor that Is Subsequently Expressed in a Transition from a Nematic to a Cholesteric LC Phase



change in the optical and structural properties. The chirality of a cholesteric LC is indicated by the sign and magnitude of the cholesteric pitch. The pitch (p, the length of one turn of the cholesteric helix) is dependent on: (1) the concentration (c) of the chiral dopant, (2) the enantiomeric excess (ee) of the dopant, and (3) the helical twisting power (β) of the dopant, via the relation $p = (c \cdot \beta \cdot \text{ee})^{-1}$. The helical twisting power is an intrinsic property of any chiral dopant in a given LC host, which indicates how efficient this molecule is at inducing the chiral organization of the LC molecules. However, for a molecule to have a significant helical twisting power, some structural resemblance to the mesogenic host is required, although conformational properties of the molecule are also extremely important.[7] For this reason, simple, small chiral organic molecules usually have very low helical twisting powers.[8] To facilitate the induction of a cholesteric phase we developed a β-enhancing receptor.[3] In the reported amplification mechanism, chiral amino alcohols bind to conformationally flexible biphenol receptors, which resulted in a preference for one axially chiral conformation of the receptor. When this complexation and "transfer of chirality" occur in a liquid crystalline matrix, the induced axial chirality of the receptor affects the LC superstructure, as it induces a change from a nematic to a cholesteric LC. In this biphenol−amino alcohol system, the macroscopic stereochemical properties of the LC phase ultimately result from the molecular chirality of the amino alcohols, as this was the only source of chirality present.

To see if the substrate scope and the chiral amplification could be improved, we introduce here a new receptor with a diaryl phosphoric acid as the primary binding motif.[9] Inspired by the phosphate−ammonium interactions found in protein−nucleic acid complexes[5] and in various synthetic host−guest systems,[10] receptor **1** was designed with a flexible biphenol backbone, a phosphoric acid functionality, and two 2-naphthyl moieties that feature a dynamic helical structure (Figure 1). When mixed with a chiral amine, proton transfer

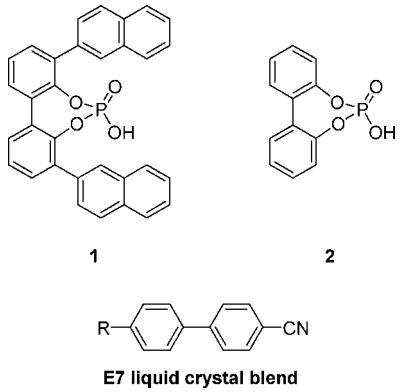


Figure 1. Achiral biphenol-based phosphoric acid receptors **1** and **2** and the structure of liquid crystal blend E7 (R = n-C_5H_{11}, n-C_7H_{15}, n-$C_8H_{17}O$, 4′-n-$C_5H_{11}C_6H_4$.

and subsequent hydrogen bonding combined with electrostatic interactions could then facilitate complexation. The interaction of phosphate groups with neutral or cationic guests has been described in the literature and applied in the recognition of sugars,[10a,11] in NMR-based enantiomeric excess determination of chiral amines,[12] for chiral resolving agents,[13] and for induction of chirality in helical polymers.[14]

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Phosphoric acid receptor **1** is highly insoluble in various organic solvents, including LC blend E7. However, mixing **1** with enantiomerically pure (*R*)-α-phenylethylamine **3** (amine/receptor = 1.5:1; 0.038 μmol receptor/mg E7) (Figure 2) produced a soluble complex, which when dissolved in

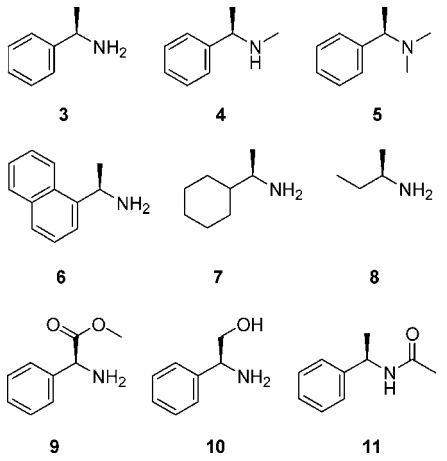

Figure 2. Structures of chiral amines **3**−**11**.

E7 led to polygonal and Grandjean−Cano LC textures, indicating a cholesteric phase (Figure 3a,b).[15] The pitch of this cholesteric phase was 10 μm, which is shorter than all previously reported values.[3] When **3** was mixed with E7 at a similar concentration, in the absence of **1**, no chiral induction was observed (Figure 3c).[16] The interaction of **3** with **1** should lead to protonation of **3**, so it could be possible that it is merely the protonated form of **3** inducing the cholesteric phase. However, this was ruled out by mixing E7 with the **3**·HCl or the complex of **3** with phosphoric acid **2** lacking the 3,3′-naphthyl moieties. **3**·HCl was insoluble in E7 (Figure 3d), whereas **3**·**2** led to a highly disturbed LC phase (Figure 3e). Neither showed any sign of cholesteric induction.

To assess the chiral induction and substrate scope of receptor **1**, mixtures with several chiral amines were dissolved in E7 (amine/**1** = 1.5:1; 0.038 μmol **1**/mg E7), and the cholesteric pitch was measured using the Grandjean−Cano technique (Table 1). Amines **3** and **4** induce the shortest pitches, indicating the largest chiral induction (entries 1 and 3). When the enantiomer of **3** was applied, a cholesteric phase with opposite helical sign was obtained, again showing that the cholesteric induction is associated with the chirality and absolute configuration of the amines (entry 2).[9] Similar but less efficient cholesteric induction was obtained with amine **6** and amino ester **9** (entries 5 and 8).

In striking contrast to the primary and secondary amines **3** and **4**, complexation of dimethylated amine **5** to **1** did not induce a measurable cholesteric pitch. This suggests that the additional methyl group creates steric congestion in the binding pocket, or a different mode of binding as the protonated form of **5** has only one hydrogen available for hydrogen bonding, instead of two or three in the other cases. Both effects could lead to a change in complex conformation with an associated lower helical twisting power. Finally, it was shown that chiral amide **11** also induces a cholesteric phase when mixed with **1** in E7. Although the obtained pitch is comparable to that obtained with either **3** or **4**, the binding to **1** is believed to proceed via a different motif as **11** does not contain a basic enough nitrogen. All these experiments were conducted at a receptor/amine ratio of 1:1.5 to ensure complete dissolution of **1** and to avoid disturbance of the LC matrix by large quantities of free amine. As this ratio has an influence on the concentration of chiral complex in the LC phase, **1** and **3** were mixed in different ratios, varying from 1:1 to 1:5 prior to doping in E7. However, this did not lead to significant variation in the cholesteric pitch, suggesting a large binding constant for the **1**·**3** complex in the LC matrix.[9]

Table 1. Pitch of E7 Doped with **1**·Amine

entry	amine	pitch (μm)
1	(*R*)-**3**	+10
2	(*S*)-**3**	−10
3	(*R*)-**4**	11
4	(*R*)-**5**	*a*
5	(*R*)-**6**	45
6	(*R*)-**7**	*a*
7	(*R*)-**8**	*a*
8	(*S*)-**9**	32
9	(*S*)-**10**	*a*
10	(*R*)-**11**	16

[a] No Grandjean−Cano lines were observed.

The structure of the complexes of receptor **1** with amines **3** and **4** was studied by ^{1}H NMR and CD spectroscopy. The complex stoichiometry of **1**·**3** in $CDCl_3$ was determined by ^{1}H NMR titration, which revealed a 1:1 complexation.[9] ^{1}H NMR and 2D NOESY measurements in $CDCl_3$ confirm that amines **3** and **4** are situated deep in the cleft between the naphthalenes flanking the binding site.[9] CD measurements of **1**·**3** and **1**·**4** in $CHCl_3$ showed small but significant induced CD signals of **1** at 295 and 305 nm, indicating the transfer of chirality from the amines to the receptor. Although ^{1}H NMR measurements show binding of **5** to **1**, CD spectroscopy of the complex did not show induced CD in receptor **1** by chiral amine **5**, which could reflect its lack in ability to induce a cholesteric phase.[9]

In conclusion, we have demonstrated that it is possible to amplify the chirality of chiral amines by host−guest interactions in a liquid crystalline environment. Binding of the amine to a conformationally flexible phosphoric acid based receptor results in a chirality transfer to the receptor, leading to a chiral conformation. When this conformational change takes place in the LC matrix it causes a transition from the nematic to the cholesteric phase. Without the assistance of

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(16) Only addition of extremely large amounts of **3** (1:1 mol/mol compared to E7) led to a chiral phase, judging from the polygonal line texture observed under the microscope.

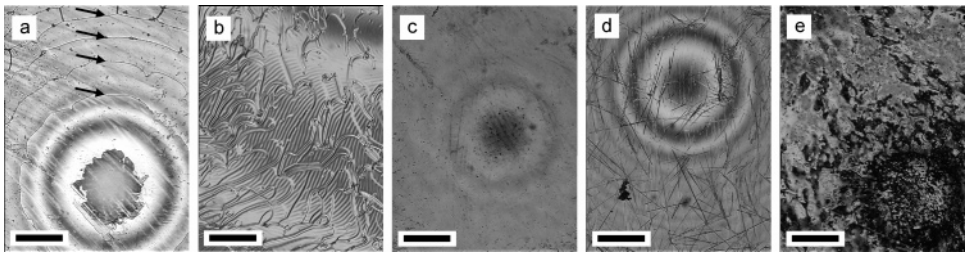

Figure 3. Optical micrographs of doped E7: (a) E7 doped with **1**·(*R*)-**3**; the arrows point at the Grandjean−Cano lines, caused by the helical organization in the LC; (b) the same sample without the plane-convex lens[9] showing a polygonal cholesteric texture (c) E7 doped with (*R*)-**3**; (d) E7 doped with (*R*)-**3**·HCl; (e) E7 doped with **2**·(*R*)-**3**. In (a), (c), (d), and (e), an out-of-focus circular artifact is visible that is caused by the presence of the plane-convex lens lying on the LC film. Bar represents 300 μm.

the receptor, formation of a chiral LC phase cannot be detected. With this approach, it was possible to generate cholesteric phases employing several amines that are not capable of inducing detectable helicity in cholesteric phases by themselves. This could ultimately lead to LC-based materials for the detection of small chiral organic molecules. Moreover, preliminary results show that it is also possible to amplify the chirality of amides, which could have implications for the detection of peptides and their role in chiral amplification phenomena.

Acknowledgment. This work was supported by the Chemical Sciences Division of the Dutch Organization for Scientific Research (NWO-CW).

Supporting Information Available: Experimental procedures and spectral data of **1**, NMR data of **1**·**3**, **2**·**3**, and **1**·**4**, and CD of **1**·**3**, **1**·**4**, and **1**·**5**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL060076L