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PAPER

Transfer of chiral information from a chiral solvent to a two-dimensional network†

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Chiral induction in self-assembled monolayers has garnered considerable attention in the recent past, not only due to its importance in chiral resolution and enantioselective heterogeneous catalysis but also because of its relevance to the origin of homochirality in life. Here, we demonstrate the emergence of homochirality in a supramolecular low-density network formed by achiral molecules at the interface of a chiral solvent and an atomically-flat achiral substrate. We focus on the impact of structure and functionality of the adsorbate and the chiral solvent on the chiral induction efficiency in self-assembled physisorbed monolayers, as revealed by scanning tunneling microscopy. Different induction mechanisms are proposed and evaluated, with the assistance of advanced molecular modeling simulations.

Introduction

Chiral surfaces have recently attracted considerable attention as they can be used for chiral separation, enantioselective heterogeneous catalysis and chiroptical materials.^{1,2} Chiral surfaces can be obtained by different approaches. One way is to craft intrinsically chiral surfaces by cutting a crystal along one of its high Miller index directions, giving rise to a crystal plane that lacks mirror symmetry and therefore is chiral.^{3,4} Another approach is to decorate surfaces by the irreversible adsorption of chiral molecules.^{5,6} Similarly, organic building blocks physisorbed on achiral surfaces such as graphite or gold can create nanostructured chiral

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surfaces. In this case, the presence of the surface prohibits the existence of symmetry elements such as inversion centers and mirror planes parallel to the surface. This inherent non-centrosymmetric nature of the surface ensures that not only chiral, but also prochiral molecules can become chiral upon surface confinement. Nevertheless, monolayers formed by prochiral building blocks will always express both mirror image motifs in equal abundances leaving the surface globally achiral. Enantiopure molecules, on the other hand, will form only one chiral motif (the mirror image motif is absent) on the surface, given that the stereogenic centre influences the molecular adsorption and self-assembly process effectively, creating a surface that displays global chirality.^{7–10}

Nonetheless, achiral building blocks can be forced to form globally chiral surfaces. Usually this is done by adding a chiral dopant to the solution of the achiral building block.^{11–17} The chiral dopant or sergeant is incorporated into the monolayer of the achiral building blocks (or soldiers) and transfers in this way its chirality, rendering a chiral surface. A quite similar approach consists of adding a small excess of one enantiomer to the racemate.^{18–22} Here, the majority enantiomer will suppress the formation of the mirror image pattern. Typically, the addition of only a few percent of these sergeants or a small enantiomeric excess is sufficient to obtain global chirality.

Both these approaches were pioneered by Green *et al.* in polymer science and were named “sergeants-and-soldiers” and “majority-rules”, respectively.^{23,24} Over the last couple of years, it was shown that these principles also hold at the liquid/solid interface.

Alternatively, chiral solvents have recently shown great potential to induce homochirality in self-assembled two-dimensional organic networks.^{20,25,26} The self-assembly of a *p*-phenylenevinylene oligomer, for instance, can be biased towards a specific rosette handedness by simply drop-casting it from enantiopure 1-phenyl-1-octanol.²⁷ Also, the high-density network formed by amidophenyl-substituted porphyrin derivatives has been revealed to be sensitive to the presence of chiral hydrogen-bonding solvents.²⁸ Another class of molecules that has been shown to be “sensitive” to the chirality of the solvent, and that will be the subject of this study, are alkoxyated dehydrobenzo[12]annulene (DBA) derivatives (Fig. 1A).^{29–33} The porous networks formed by various DBAs are based on the interdigitation of alkoxy chains of adjacent molecules (Fig. 1). The relative alignment of the four interdigitated alkoxy chains per DBA pair (“+” or “–” type interdigitation) governs the chirality of the resultant honeycomb network. A virtual clockwise (CW) or counterclockwise (CCW) nanowell is obtained by combining six “–” type or “+” type interdigitation patterns, respectively. The labels CW and CCW refer to the sense of rotation of the six alkoxy chains making up the rim of the nanowell, and typically, the chirality of the nanowells is domain-specific.³⁴ Also, “mixed” nanowells (MIX) can be formed by combining both “–” and “+” type interdigitations in various ways. A relatively simple marker for the handedness of the nanowells is the relative shift of the neighboring DBA cores.

The tilt of the line joining the centers of neighboring DBA cores with respect to the rim of the honeycomb can be used to easily identify the type of interdigitation and the handedness of individual nanowells, as well of the domains they form (Fig. 1B and C). In the absence of any chiral influence, achiral DBA molecules (DBA-OC*n*) enantioseparate on highly oriented pyrolytic graphite (HOPG) into equal amounts of mirror image chiral domains, so CW and CCW.^{11,35}

Fig. 1 (A) Molecular structure of an alkoxyated dehydrobenzo[12]annulene ($R = C_nH_{2n+1}$). (B) The interdigitation of the alkoxy chains can lead to the formation of a “–” or “+” type interdigitation depending on the relative alignment of the adjacent DBAs. (C) The combination of six interdigitation types leads to the formation of a hexagonal nanowell. If all “–” types are combined a CW pore is formed, all “+” types lead to a CCW pore and combinations of both lead to “mixed” pores. (D) Top: HR-STM images of the self-assembled networks of DBA-OC10 at the left (S)-2-octanol/HOPG and right (R)-2-octanol/HOPG interface ($I_{\text{set}} = 280$ pA, $V_{\text{bias}} = 230$ mV). Red dashed lines indicate the graphite reference axis. θ is the angle between the graphite reference axis and one of the unit cell vectors. Bottom: Molecular models for the self-assembled networks of DBA-OC10 in left (S)-2-octanol and right (R)-2-octanol. The unit cell parameters are identical in both solvents and they are: $a = 4.0 \pm 0.1$ nm, $b = 4.1 \pm 0.1$ nm, $\gamma = 61.0 \pm 1.0^\circ$. Adapted with permission from the American Chemical Society.

So, how is the self-assembly process of this system affected by the presence of chiral solvent? Previously, we showed that the self-assembly of DBAs with alkoxy chains containing an even number of carbon atoms (DBA-OC_{even} with $n = 6, 8, 10, 12, 14, 16$) at the interface between HOPG and (S)-2-octanol gives rise to the preferential formation of CCW domains on the graphite surface, while deposition from (R)-2-octanol leads to preferential formation of CW domains (Fig. 1D).²⁶ Furthermore, a DBA alkoxy chain length-dependent induction was observed in these chiral solvents: derivatives with short alkoxy chains (e.g. DBA-OC₆) only form domains of one particular chirality (and thus yield homochiral surfaces), while for the derivatives with longer alkoxy chains (e.g. DBA-OC₁₄, DBA-OC₁₆) the surface is not fully homochiral, or in other words, the chiral induction by the solvent seems less efficient.

In order to gain insight into the solvent-based chiral induction mechanism or mechanisms at play, we have carried out additional sets of experiments, and have engaged in extensive molecular modeling simulations. This manuscript is structured as follows. In the first part, we describe the results of a new series of scanning tunneling microscopy (STM) studies, and evaluate to what extent the new experimental results in combination with our previous data support or refute a number of induction mechanisms we propose. In the second part, we engage in advanced molecular modeling simulations to shine light on the most possible induction mechanism(s). Among the several mechanisms that we evaluate, those

that involve on-surface transient complexation of the chiral solvent and the DBA molecules at the moment of nucleation turn out to be the most likely ones.

Results and discussion

The impact of DBA alkyl chain length and odd–even effects

To start with, the self-assembly behavior of DBA was further investigated by looking at three other DBA derivatives. For DBA-OC4, the shortest probed derivative, again CCW domains are obtained upon deposition from (*S*)-2-octanol, while the drop-casting from (*R*)-2-decanol led to only CW domains on the surface. The two other derivatives that were tested have an odd number of carbons in the alkoxy side chains (DBA-OC_{*n*odd}). Surprisingly, both DBA-OC11 and DBA-OC13 turned out to express equal amounts of CW and CCW pores on the surface and these derivatives are thus not in any way influenced by the presence of the chiral solvent. In addition, DBA-C10, the alkylated derivative of DBA-OC10, also displays chiral induction when self-assembled at the interface between HOPG and (*S*)-2-octanol.

In another set of experiments, we looked at the impact of the solvent. The effect of a series of enantiopure 2-alcohols, ranging from 2-hexanol up to 2-dodecanol, on the self-assembly of DBA-OC10 was probed (Fig. 2). The analysis of the STM data reveals that all the probed solvents do not yield a uniform result. Instead again an odd–even effect becomes apparent, in which the chiral solvents with an even chain length (*e.g.* 2-decanol) tend to form 90–95% induced domains and those with an odd chain length (*e.g.* 2-nonanol) only form about 70% induced domains (Fig. 2, Table 1). However, it should be noted that there are some exceptions. In the case of enantiopure (*S*)-2-dodecanol, only about 70% of the surface is covered with induced CCW domains. Note that (*S*)-2-dodecanol has a melting point close to room temperature and as a consequence the solution is

Fig. 2 An overview of the ratio (%) of induced nanowells for DBA-OC10 in a series of enantiopure 2-alcohol solvents. A clear odd–even solvent chain length effect is revealed. (*S*)-Stereogenic centers induce CCW nanowells (■), (*R*)-stereogenic centers induce CW nanowells (■). The error bars reflect the variation in the ratio (%) of induced nanowells in three sessions (about 10 images per session).

Table 1 Chirality expression of various DBA derivatives in chiral solvents

Compound	Solvent	CCW	CW	Mix	C (mol dm ⁻³)	# pores	# domains
DBA-OC4	(S)-2-Octanol	99%	1%	0%	8.4×10^{-6}	4364	33
	(R)-2-Decanol	0%	99%	1%	8.4×10^{-6}	2691	23
DBA-OC6	(S)-2-Octanol	98%	0%	2%	4.2×10^{-6}	4045	36
	(R)-2-Octanol	0%	100%	0%	4.2×10^{-6}	4163	41
	(S)-2-Nonanol	65%	33%	4%	4.2×10^{-6}	6447	43
	(R)-2-Decanol	0%	99%	1%	2.2×10^{-6}	4007	33
	(S)-2-Dodecanol	76%	16%	8%	8.0×10^{-5}	4748	28
	(S)-2-Octanol	87%	10%	3%	2.1×10^{-6}	2205	34
	(R)-2-Octanol	1%	99%	0%	2.1×10^{-6}	2644	37
	(R)-2-Decanol	3%	97%	0%	2.1×10^{-6}	3292	37
DBA-OC10	(S)-2-Hexanol	79%	18%	2%	1.4×10^{-6}	1897	74
	(S)-2-Heptanol	74%	25%	1%	2.1×10^{-6}	2447	64
	(S)-2-Octanol	94%	6%	0%	2.1×10^{-6}	2081	32
	(R)-2-Octanol	9%	90%	1%	2.1×10^{-6}	2596	33
	(rac)-2-Octanol	51%	49%	0%	2.1×10^{-6}	4439	58
	(S)-2-Nonanol	69%	27%	5%	2.1×10^{-6}	2614	39
	(R)-2-Decanol	5%	90%	5%	2.1×10^{-6}	3169	34
	(S)-2-Dodecanol	73%	18%	10%	8.0×10^{-5}	2081	29
DBA-C10	(S)-2-Octanol	69%	20%	11%	2.1×10^{-6}	2580	34
	(R)-2-Octanol	16%	77%	8%	2.1×10^{-6}	2259	47
DBA-OC11	(S)-2-Octanol	22%	48%	31%	2.1×10^{-6}	2669	34
	(R)-2-Octanol	27%	54%	18%	2.1×10^{-6}	2010	29
	(S)-2-Nonanol	21%	11%	68%	2.1×10^{-6}	3394	39
	(S)-2-Octanol	90%	7%	3%	2.1×10^{-6}	2194	38
DBA-OC12	(R)-2-Octanol	16%	82%	3%	2.1×10^{-6}	1832	34
	(S)-2-Octanol	42%	44%	14%	2.7×10^{-6}	1800	34
DBA-OC13	(R)-2-Octanol	44%	33%	23%	2.7×10^{-6}	1678	34
	(S)-2-Octanol	79%	17%	3%	2.1×10^{-6}	1432	37
DBA-OC14	(R)-2-Octanol	20%	76%	4%	2.1×10^{-6}	1124	32
	(R)-2-Decanol	8%	84%	7%	2.1×10^{-6}	1486	34
DBA-OC16	(S)-2-Octanol	74%	20%	6%	1.4×10^{-6}	1306	31
	(R)-2-Octanol	17%	74%	9%	1.4×10^{-6}	1098	38

quite viscous, which may hinder the system to reach equilibrium. Also, for commercial (S)-2-hexanol the chiral induction is lower than the anticipated value of 90% (79%). In this particular case, the deviation is believed to be caused by the presence of impurities (see Fig. S2†). The induction results for all combinations of DBAs and chiral solvents are summarized in Table 1.

Chiral induction in relation to the different stages of the self-assembled monolayer formation

Before we interpret these results, let's first consider the stage at which the chiral induction takes place. First of all, time-dependent STM experiments do not reveal any significant evolution of the handedness of the supramolecular network with time, indicating that the chiral induction takes place at the level of 2D nucleation, or in the very early stages of monolayer development. Thus, one can readily rule out the formation of racemic domains as a preceding step to the evolution of enantiopure domains.

The different modes of chiral induction

A first important question is where the induction takes place. Is the induction the result of (1) a phenomenon that takes place in the bulk solution, (2) a consequence of a specific interaction of solvent near the surface with adsorbed DBA molecules, the solvent molecules not being adsorbed on the surface, or (3) does the chiral induction require the chiral solvent molecules to be (co)adsorbed on the surface?

A. Chiral induction in the bulk (1). The “bulk solution process” (1) can be ruled out. This would require some interactions in solution between chiral solvent and DBA molecules, prior to molecular self-assembly on surfaces, beyond the formation of some transient solvent–DBA complexes in solution. UV-absorption, ^1H NMR and circular dichroism measurements do not reveal any sign of such pre-organization in solution.²⁶ While we don't rule out specific solvent–molecule interactions in the bulk, these do not lead to chiral supramolecular seeds in solution that would retain their structure upon adsorption on the surface.

B. Chiral induction orthogonal to the surface (2). Having ruled out the “bulk solution process”, we consider the formation of a (transient) complex between one or more adsorbed or adsorbing DBA molecules and one or more chiral solvent molecules that are located in the supernatant solution just above the surface, but are not adsorbed on the surface (2). Irrespective of the mode of interaction, in a process where solvent molecules act from above the surface rather than on the surface, structural variations such as length should have a limited effect on the induction of chirality. However, the experimentally observed odd–even solvent and alkyl chain length behavior (Table 1, Fig. 2) cannot be reconciled with such a mechanism where solvent molecules act from the liquid phase on the adsorbed DBA molecules. While the experimental observations don't rule out such a mode of interaction, its importance, relative to other induction processes, should be moderate.

C. Chiral induction on and parallel to the surface (3). This brings us to the hypothesis where adsorbed solvent molecules are crucial in the chiral induction process. The outcomes of the experiments described in the next section hint indeed to the importance of (co)adsorbed solvent molecules in direct contact with the substrate. In this set of experiments, the chiral solvent is diluted with an achiral solvent, and competitive solvent adsorption is probed. DBA-OC10 was deposited from a mixture of 1-octanol and (*S*)-2-octanol at various volume ratios. A clear linear dependency can be observed between the chirality of the DBA network and the v/v% of the solvents (Fig. 3A). This seems to imply that the transfer efficiency of chiral information is rather poor; alternatively, this linear behavior might demonstrate the equal adsorption affinity of both solvents as 1-octanol and (*S*)-2-octanol, which seems quite reasonable since they have similar alkyl chain lengths and will thus compete for the same adsorption sites on graphite. To put the latter interpretation to the test, the experiment was repeated with achiral and chiral solvents of different chain length, as several studies have indicated that upon self-assembly of bi-component systems, the molecule with the longest chain length is preferentially adsorbed.^{36–40} Hence DBA-OC10 was deposited from a mixture of 1-hexanol and (*R*)-2-decanol at various v/v ratios: 50/50, 75/25 and 90/10. The analysis of the STM data now clearly shows a non-linear

Fig. 3 Chirality expression of monolayers formed by DBA-OC10 in mixtures of an achiral and a chiral solvent, showing the population of the CW ($\blacktriangle$), CCW ($\blacksquare$) and MIX ($\bullet$) nanowells.

dependency between the v/v% and the induced CW nanowells (Fig. 3B). This indicates that in the previous case the linear dependency indeed reflected the similar adsorption affinity of both solvents. In this case, only about 50 v/v% of the enantiopure solvent is needed in order to gain the same monolayer chirality as for the pure enantiopure solvent. In addition, a control experiment was performed with 1-decanol and (*S*)-2-hexanol. From Fig. 3C, a negative non-linear dependency can be observed, although obscured by the presence of MIX pores. But the equal amounts of CW and CCW honeycombs present for 75/25 v/v% of 1-decanol/(*S*)-2-hexanol clearly illustrate the diminished chiral induction. The fact that the longer solvent always has the upper hand is a strong indication for the involvement of solvent adsorption as part of the mechanism for the transfer of chiral information to the two-dimensional network. All data are also presented in Table S1.†

This insight doesn't provide us with the mechanism yet, as several induction mechanisms can still be considered where (co)adsorbed solvent molecules are involved. We will now consider a few of them and evaluate their relative importance.

C1. Induction via a chiral self-assembled solvent layer. Indeed, there are quite some examples of self-assembled systems that are adsorbed on top of a static solvent buffer layer. Typically these layers are formed on top of a self-assembled layer of pentacontane or other long alkanes.^{41,42} But also shorter hydrogen-bonding solvents like 1-decanol can act as a buffer layer.⁴³ One characteristic that all these solvents have in common is their ability to form well-ordered long-range domains which can be visualized by STM. However, the enantiopure 2-alcohols in this study show no ordered monolayer formation at room temperature and, even so, the stereogenic centre would probably create steric restraints for the formation of the DBA overlayer as either the hydroxyl or the methyl group (whichever is not adsorbed on the surface) must point in that direction. So, we regard this mechanism, based upon the formation of chiral self-assembled solvent layers on top of which the DBA molecules self-assemble, as unlikely.

C2. Induction via a dynamic interfacial solvent (mono)layer. Rather than adsorbing on top of those solvent molecules, DBA molecules may nucleate on the HOPG surface, thereby repelling solvent molecules from the surface. As those flexible solvent molecules get expelled, they contribute in entropy gain. But how would such a process lead to chiral induction? The DBA orientation with respect to HOPG symmetry lattices is different for odd and even DBAs and for *R*- and *S*-alcohols (see the ESI†), which means that the number of *S*-alcohol molecules replaced by CCW and CW nuclei would be different—hence chirality induction (for the details of the orientational aspects, we refer to the ESI†). Note that this mechanism does not require specific intermolecular interactions.

C3. Induction via co-adsorbed solvent with the DBA molecules on the surface. The formed DBA-solvent complex at the moment of nucleation or in the very early stages of monolayer development could potentially be stabilized by hydrogen bonds and van der Waals interactions between the adsorbed DBA and the adsorbed solvent molecules. In addition, solvent-substrate interactions could further enhance the stability of this DBA-solvent complex. Again, we can differentiate between a number of different cases.

C3.1. Stabilization of the nanowells. In the first case, solvent molecules could become co-adsorbed in the nanowells and stabilize nanoporous structures of a given handedness. Previous studies on DBAs in other solvents have revealed that

solvent molecules can co-adsorb on the surface, in the nanopores. One DBA-OC16 pore for instance can host up to nineteen 1,2,4-trichlorobenzene molecules,³² and also tetradecane molecules have been found to co-adsorb inside the DBA network.³⁹ One could expect to find the alcohol solvent molecules along the rim of the hexagonal pores to maximize the van der Waals contacts, supplemented by the ability to form hydrogen bonds with the DBA oxygen atoms. However, from the high resolution (HR) STM images obtained on the DBA derivatives in the two enantiomeric 2-octanol solvents, no 2-octanol molecules could be found inside the CW or CCW rotated nanowells of the low-density honeycomb phase. Even 2-dodecanol, which should be less dynamic when co-adsorbed in the pores, was not observed. So co-adsorbed solvent molecules could never be clearly visualized inside CW or CCW nanowells. While this observation does not rule out that the mechanism described above is active, it suggests that the solvent molecules must be mobile, which somehow could weaken if not their stabilizing effect, most likely their induction effect.

C3.2. Formation of on-surface DBA-solvent complex and integration in the monolayer. The second possible mechanism to consider is the chirality induction through the nucleation of a stable DBA-alcohol complex. Such a complex would act as a chiral “sergeant” defining the alkyl chain interdigitation of the other DBAs in the growing domain. An example of solvent-containing defects in DBA domains is shown in Fig. 4. Here, trapping solvent molecules between the alkoxy chains of DBA is reminiscent of the related co-assemblies of *n*-tetradecane and DBA-OC16,

Fig. 4 (A) STM image of DBA-OC10 in 1-octanol/(S)-2-octanol (99 : 1) revealing the existence of defects involving co-adsorbed solvent molecules. The tunneling parameters are $I_{\text{set}} = 750$ pA; $V_{\text{bias}} = -200$ mV. (B) Model of the observed defect. In the model, 2-octanol molecules are adsorbed with an arbitrary orientation of the hydroxyl groups. There is no experimental evidence to justify the orientation. Moreover, in solvent mixtures with 1-octanol, most likely also 1-octanol is adsorbed, maybe even predominantly.

reported earlier.⁴⁴ There is, however, no evidence that: (1) such defects indeed form during domain nucleation and not at later stages (growth or ripening), and (2) that their formation is sufficiently enantioselective to promote chirality induction. Furthermore, alcohol inclusion was not observed if the difference between the carbon chain length in the alcohols and DBAs was larger than two methylene groups. Therefore, even if valid, such a chirality induction pathway cannot account for the majority of the DBA-alcohol combinations studied in this work.

C3.3. Transiently formed DBA-solvent complexes at the stage of nucleation. As a third case, we envision that surface-confined solvent-DBA complexes can transiently be formed as part of the nucleation process, promoting one form of interdigitation (“+” or “−”), while penalizing the other form of interdigitation. Upon formation of the nanowell, the co-complexed solvent molecules are released in the supernatant solution. This mechanism will be discussed in more detail in the modeling section.

Discussion

Which of these “solvent-on-a-surface” induction models is most likely? The problem is that the time-resolution of STM is not fast enough to evaluate the existence of transient solvent-DBA complexes on the surface. Therefore the argumentation is rather qualitative or semi-quantitative at best. The fact that we can’t image self-assembled monolayers of the solvent itself lowers the probability that self-assembled DBA monolayers are formed on top of a solvent monolayer (C1). The lack of any experimental evidence for structured solvent adsorption in nanowells disfavors also that pathway (C3.1). And if solvent co-adsorption is observed, it happens rather rarely, and doesn’t give rise to the anticipated honeycomb lattice (C3.2). However, a solvent monolayer can be dynamic in nature and may still act at the moment of nucleation, not for DBA molecules adsorbing on top of the solvent layer, but for DBA molecules adsorbing in such a solvent layer, potentially making a transient DBA-solvent complex (C3.3.) – *i.e.*, a process that would be enthalpically-driven, or by replacing solvent molecules and expelling those to the supernatant solution in an enantiospecific way (C2) – *i.e.*, a process that would be entropically-driven. It is also possible that more than one mechanism is at play. While it is quite reasonable to assume that hydrogen bonding interactions involving the hydroxy group of the solvent and the oxygen atoms of the DBA alkoxy chains are at play, the simple fact that a DBA molecule with alkyl groups instead of alkoxy groups also undergoes chiral induction, though less efficiently, hints to the fact that several mechanisms act simultaneously or in a compound-specific fashion.

All these experiments were performed at room temperature. However, annealing to 60 °C leads, for many DBA derivatives, to quite different results. The high density phase, with no nanopores present, is favored for DBA-OC10, DBA-OC11 and DBA-OC14 (Fig. S5†). Only in the case of DBA-OC10, a honeycomb lattice is still observed. The same chiral induction, though, is observed for DBA-OC10, regardless of the chiral 2-alcohol used, and upon annealing, chiral induction is more efficient, *i.e.* more domains of a given handedness are observed compared to the corresponding layers at room temperature. So, the outcome of the monolayer formation at room temperature is, for a number of systems,

probably not the thermodynamically most stable phase. However, the fact that the type of chiral induction (CW or CCW) remains upon annealing supports the fact that our discussion on the induction mechanism at room temperature is still valid.

Molecular modeling simulations

In order to gain insight into the chiral induction mechanisms involving interactions between DBA molecules and solvent molecules at the substrate surface, we have performed force-field-based simulations on model systems related to processes C3.1 (stabilization of the nanowells) and C3.3 (formation of a DBA–solvent complex at the nanopore nucleation stage).

All molecular modeling simulations have been conducted with the Biovia Materials Studio 7 molecular modeling package using the DREIDING force field. The choice of the force field was motivated by the fact that DREIDING comprises a specific H-bonding interaction term, which is essential for this study. The atomic charges were calculated for the DBA and solvent isolated molecules by using the Gasteiger method as implemented in Materials Studio. The graphite surface was modeled by using two flat, infinite (periodic), stacked graphene layers, which are kept rigid. No charges are assigned to the graphite carbon atoms; hence, the surface–molecule interactions are only van der Waals interactions. All molecular dynamics (MD) simulations were conducted in the NVT ensemble at a temperature of 250 K, kept constant by using the Andersen thermostat with a collision rate of 1. The time step used for the MD runs is 1 fs.

To test mechanism C3.1, we have modeled how (*S*)-2-octanol adsorbs in the nanopores of DBA-OC12. Those simulations examined the arrangement of the solvent molecules in the pore in contact with a solvent supernatant layer. In the data analysis, particular attention was paid to the orientation of the solvent molecules with respect to the pore rims and H-bonding interactions with the DBA molecules. Despite very extensive simulations involving a large number of different initial conditions, we have not found any indication for the stabilization of one type of nanopore (CW or CCW) by one solvent enantiomer. Concerning mechanism C3.3, most likely a (transient) complex can be formed between the oxygen atoms of the adsorbed DBA alkoxy chains and the hydroxyl group of the enantiopure solvent *via* stereospecific hydrogen-bonding.

In order to examine the relevance of the formation of such a complex to the DBA interdigitation process and the subsequent pore nucleation, we have simplified the system used in the simulations by making the following assumptions, based on the experimental findings:

- We assume that the DBA molecules interdigitate at the solvent/surface interface and do not aggregate in the liquid phase.
- We assume that the chiral induction occurs at the nucleation stage of the monolayer formation, where the presence of chiral solvent molecules will favor only one type of DBA interdigitation, *i.e.* + or –, leading to the formation of only one type of monolayer.

An iterative MD/quench scheme has been devised in order to locate preferential interaction sites between a DBA and a chiral solvent molecule. For this scheme, an initial 100 ps MD run is performed, and a structure for the system is extracted from the trajectory every 500 step. Those structures are then optimized

and the lowest-energy optimized structure is used as a starting point for a new 100 ps-long MD run. The cycle is iterated until the energy of the optimized structures does not decrease further.

A second iterative scheme has been devised to obtain the energy profile for the interdigitation process between two DBA molecules, in the presence of chiral solvent molecules. This scheme consisted of an initial alignment between two DBA molecules, each one carrying a single chiral solvent molecule in its preferential adsorption site, which was previously obtained from the MD/quench scheme. Each DBA molecule is considered as a rigid object and the DBA-solvent complex is considered to be a group. At each iteration of the process, one group is moved towards the other by 1 Å, and the geometry of the system is optimized and then used as input for the next iteration.

DBA-OC6-2-alcohol complexation: 1-octanol, (*S*)-2-octanol, (*R*)-2-octanol

First we test our assumption that molecules of 1-octanol, (*S*)-2-octanol and (*R*)-2-octanol have preferred interaction sites with the DBA molecules. For this, we consider a single DBA-OC6 molecule adsorbed on graphite, and we observe how a solvent molecule, also adsorbed on the surface, interacts with the DBA core in two different places, called docking site A, DSA, and docking site B, DSB (Fig. 5).

In DSA, the solvent molecule can form hydrogen bonds with the oxygen atoms in the alkoxy groups, while in DSB an OH- π interaction can take place between the hydrogen of the hydroxyl group and the triple bond of the alkyne group of the annulene ring. When in DSA, the polar head of the solvent molecule strongly tends to interact *via* hydrogen bonding with the two oxygen atoms, labeled interaction site 1, IS1, and interaction site 2, IS2, of the DBA molecule. The space in DSA is large enough to allow for some conformational freedom of the solvent molecules. In particular, the alkyl part of the solvent molecule can align with one alkyl chain of the DBA molecule, either the one containing IS1 or the one containing IS2 (see Fig. 5C and D). Because of the presence of the stereogenic center in the solvent molecule, those two situations, which are called IS1 and IS2 below, are not equivalent.

To better assess the consequences of the IS1 *vs.* IS2 interaction, we modeled three systems, where a single molecule of 1-octanol, (*S*)-2-octanol or (*R*)-2-octanol is placed in the DSA site of a DBA-OC6 molecule, which is adsorbed on the graphite surface (Table 2). The MD/quench iterative scheme is used to find the most stable geometry for those systems when the solvent molecule is made to interact either with IS1 or IS2.

In the system with 1-octanol, the solvent molecule does not show a preferential interaction with one particular site in DSA, as the energies of the systems in the two situations differ only by about 0.7 kcal mol⁻¹, *i.e.*, about the thermal energy k_bT available at room temperature.

In contrast, when a chiral solvent molecule is considered, there is a clear indication of a preferential interaction site within DSA: (*S*)-2-octanol prefers to interact with IS1, while (*R*)-2-octanol prefers to interact with IS2. In both cases, the energy difference between the molecule interacting with the preferred site with respect to the other one is in the order of 3 kcal mol⁻¹, *i.e.*, 5 times k_bT . The difference in stability stems from the configuration around the polar head of the molecule.

Fig. 5 (A) The molecule used in this work as a model for DBA-OC6 with indication of the different possible docking and interaction sites. (B) (*S*)-2-Octanol interacting in DSB, (C) (*S*)-2-octanol interacting in DSA with IS1 and (D) (*R*)-2-octanol interacting in DSA with IS2.

Table 2 Energies for the most stable structures obtained from the MD/quench iterative scheme for three different solvents in the DSA site of a DBA-OC6 molecule

Solvent	E_{IS1} (kcal mol ⁻¹)	E_{IS2} (kcal mol ⁻¹)	$\Delta E_{IS1/IS2}$ (kcal mol ⁻¹)
(<i>S</i>)-2-Octanol	-14.4	-11.4	-3.00
(<i>R</i>)-2-Octanol	-11.2	-14.1	2.90
1-Octanol	-10.4	-9.7	-0.70

Because the solvent molecule aligns with one of the alkoxy groups in the DSA cavity, the symmetry of DSA is broken and one kind of interdigitation may be hindered by the presence of the solvent molecule. In particular, when the solvent molecules interact with IS1, “+” interdigitation can be favored, while “-” interdigitation can be favored when the solvent molecules are interacting with IS2 (Fig. 6). This could be the reason explaining why a chiral solvent can promote chiral induction in the assembly of DBA molecules.

In contrast, the smaller available space in DSB for the solvent molecule forces it to stay in the middle of the site and to align to both the alkoxy groups of the DBA

Fig. 6 Favorable (A) versus unfavorable (B) interdigitation for DBA-OC6 in the presence of a chiral solvent molecule in DSA.

molecule (Fig. 5B). So interaction at DSB is not expected to play a role in favoring “+” or “–” interdigitation.

The impact of the length of the alkoxy chains

It is experimentally known that at room temperature for a chiral solvent such as (*S*) or (*R*)-2-octanol, the chiral induction on DBA-OC6 self-assembly is 100%, while for DBA-OC12 self-assembly, the degree of chiral induction is lowered to about 80%. The results from the simulations to determine the preferential interaction site for (*S*)-2-octanol and (*R*)-2-octanol interacting with DBA-OC12 show that the solvent selectivity of the interaction site drops from 3 kcal mol^{−1} in the case of DBA-OC6 to 2 kcal mol^{−1}, *i.e.*, to about 3 k_bT , for DBA-OC12. This is consistent with the experimental data. In both cases, (*S*)-2-octanol prefers to interact with IS1. The modeling of the influence on the chiral induction of the even or odd number of carbon atoms in the alkoxy chain is presented in the ESI (S6).†

The impact of the length of the chiral solvent molecule

Another aspect to consider, when trying to determine how much the selectivity of the solvent molecule to interact with IS1 or IS2 can hinder a particular type of interdigitation, is the length of the solvent molecule with respect to the length of the interdigitating alkoxy groups. As shown in Fig. 5, the length of the –OC6 alkoxy groups is comparable with that of a (*S*)-2-octanol molecule interacting with IS1.

This suggests that (*S*)-2-octanol favors “+” interdigitation whereas (*R*)-2-octanol, which preferentially interacts with IS2, favors “–” interdigitation, due to steric hindrance. When a (*S*)-2-octanol molecule is interacting with a DBA-OC12 molecule in IS1, the length of the alkoxy group will be double that of the alcohol. This suggests that, while “+” interdigitation is still favored, DBA molecules could begin to interdigitate, before being hindered by the presence of the solvent molecule (see Fig. 7, left panel). This hypothesis, together with the reduced selectivity for a specific interaction site, could explain why the chiral

Fig. 7 (A) Model used to compute the interdigitation profile for DBA-OC12 in the presence of (*S*)-2-octanol (“-” interdigitation is shown). DBA1 is the molecule at the top of the image. (B) Interdigitation profiles for DBA-OC12 in the presence of (*S*)-2-octanol.

induction observed for the DBA-OC12 monolayers is less marked than for the DBA-OC6 monolayers. To test this hypothesis, we computed an interdigitation profile between two interdigitating DBA-OC12 molecules, as explained in the methodology section. Fig. 7 shows the model built to compute the interdigitation profile, forcing molecule DBA2 (at the bottom of the image) to move towards molecule DBA1 (on the top of the image) from a distance $r = 19$ Å (no interdigitation) down to $r = 8$ Å (maximum amount of interdigitation tested).

As expected, at the beginning of the interdigitation, there is no selectivity between the “+” and “-” interdigitation: the two energy profiles are superimposed. But from a certain degree of interdigitation ($r = 15$ Å), when the incoming alkoxy group starts to feel the presence of the solvent molecule, the “+” interdigitation becomes increasingly more favorable, with respect to the “-” counterpart: by up to 18 kcal mol⁻¹ for the maximum amount of interdigitation tested ($r = 8$ Å).

It is important to note that at the end of the interdigitation process, the solvent molecule is expelled from the DSA site, suggesting that the strength of the interaction of the solvent molecule with the DBA is not sufficient to permanently keep the DBA-solvent complex together. This, in fact, would prevent DBA molecules from fully interdigitating to build the observed monolayers.

Conclusions

In conclusion, we have shown that chiral solvents can induce homochirality in surface-confined low-density networks. Moreover, odd-even chain length behavior was observed for both the chiral solvent and the DBA building block. An attempt to unravel the mechanism behind the chiral induction has led to the proposition of various mechanisms that could be responsible for the transfer of chiral information from a chiral solvent to a two-dimensional network. Albeit not fully conclusive, out of all the proposed mechanisms two are very compelling. These two mechanisms rely on the fact that solvent-substrate interactions are key. This means that the solvent molecules could form a DBA-solvent precursor

complex that biases a specific handedness of the porous network, or that the solvent molecules could form a (metastable) layer from which solvent molecules have to be released upon DBA adsorption. Advanced modeling protocols provided valuable information on the DBA–solvent precursor induction mechanism. While chiral induction can be explained on the basis of thermodynamic considerations, kinetic aspects are also at play and have an impact on the extent of chiral induction at a given temperature.

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