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COMMUNICATION

Towards enantioselective adsorption in surface-confined nanoporous systems

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The adsorption of chiral molecules in surface-confined chiral porous networks shows pronounced selectivity, as a result of complementary host-guest interactions.

Mirror image chiral molecules are called enantiomers. The most popular techniques to separate enantiomers are crystallisation and chromatography.¹⁻⁴ In both cases the separation is based on the formation of diastereomeric complexes with the chiral agent or stationary ligand. Due to the different physical properties of diastereomers, resolution of the complexes is straightforward. Diastereomeric segregation on solid surfaces is also possible and few studies report such phenomena with nanoscale resolution using scanning tunneling microscopy (STM).⁵⁻⁷ The resolving agent selectively crystallizes with one of the enantiomers on the surface, leaving the mirror-enantiomer behind in the solution phase.

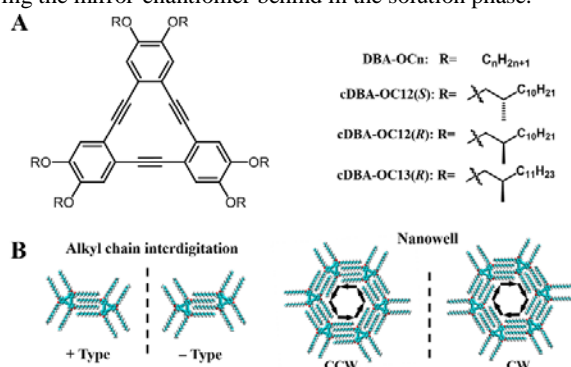


Fig. 1 (A) Chemical structures of achiral and chiral DBAs. (B) Molecular models for the counterclockwise (CCW) and clockwise (CW) nanowells, based on the interdigitation of alkyl chains (+/- type) and the rotation of the vectors pointing from the DBA core to the end of the alkyl chain at the rim of a nanowell.

2D porous networks show great potential in chiral recognition processes.^{8,9} The regular spaced nanowells provide a confined environment together with great accessibility of the pores. Therefore, host-guest interactions can easily be studied. Currently, these systems only show selective interactions towards guest adsorption based on size and/or shape complementarity,¹⁰⁻¹⁶ and chemical environment.¹⁷ Here we show a certain control in the occupation of the 2D porous network based on the chiral complementarity between the guest and the host.

The molecular system we investigated is based on dehydrobenzo[12]annulene (DBA) derivatives (**Fig. 1A**). The self-assembly of this system at the liquid/solid interfaces has been investigated extensively.¹⁴⁻²¹ These alkylated molecules may self-assemble into a nanoporous network at the interface between a liquid and highly oriented pyrolytic graphite (HOPG). Under appropriate solute concentration conditions, highly ordered networks are formed, leaving a regular pattern of hexagonal nanowells.¹⁹ The diameter of these nanowells depends on the length of the alkyl chains of the DBA molecules. Note that the nanowells are chiral, as a result of the alkyl chain interdigitation pattern. Depending on the orientation of the alkyl chains at the pore periphery, we label the nanowells as clockwise (CW) or counterclockwise (CCW), as illustrated in **Fig. 1B**. Achiral DBA molecules form domains with nanowells of opposite handedness, each domain being composed of supramolecular nanowells of the same handedness. In contrast, in the case of chiral DBA (cDBA) enantiomer, only supramolecular nanowells of one particular handedness, not the opposite, are formed. Specifically, R-type enantiomers and S-type enantiomers form CCW and CW porous patterns on surface, respectively.¹⁸ Recently, we showed that mixing of achiral and chiral DBA molecules may lead to the exclusive formation of nanowells of one given handedness.¹⁸ This phenomenon where a few percent of chiral molecules dictates the chirality of the supramolecular complexes, is called the sergeants-and-soldiers principle,²² which has been well established for supramolecular systems in solution.^{23,24}

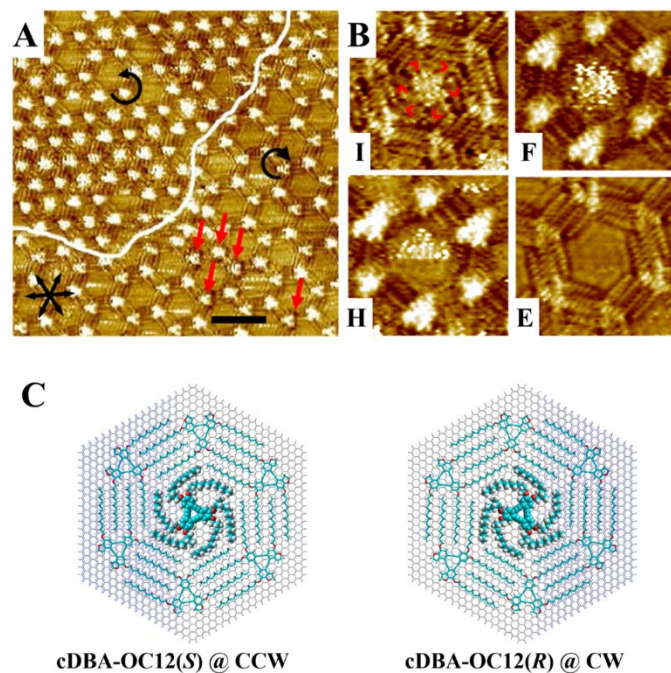


Fig. 2 (A) STM image of a premixed solution containing 30 mol% cDBA-OC12(S) and 70 mol% DBA-OC12. $I_{set} = 200$ pA and $V_{bias} = -250$ mV. The white line marks the boundary between a CCW domain (upper left) and a CW domain (lower right). The black arrows indicate the major symmetry axes of the HOPG surface underneath. The scale bar measures 5 nm. The red arrows indicate cDBA-OC12(S) sergent molecules. (B) Examples of four different types of pores: incorporated (I), fuzzy (F), half-fuzzy (H) and empty (E). Alkyl chains of the guest molecule are marked with red arrows. (C) Modelling of completely confined ('incorporated') cDBA-OC12(S/R) guest molecules in CCW and CW DBA-OC12 nanowells, respectively. For clarity, only the guest molecules are displayed in ball-type.

During the course of sergeants-and-soldiers experiments, we identified another interesting phenomenon, which we label as auto-enantioselective adsorption, the topic of this communication. As expected, a premixed solution of 30 mol% cDBA-OC12(S) and 70 mol% DBA-OC12 at a total concentration of 2.5×10^{-6} M self-assembles at the interface between 1-phenyloctane and HOPG, which results in a porous adlayer with amplified clockwise (CW) hexagons ($95 \pm 3\%$ CW hexagons, **Table S1**). **Fig. 2A** shows an STM image of the co-adsorption of chiral and achiral molecules as part of the porous CW network. The co-adsorption of these chiral molecules directs the overall chirality of the network. We identify the chiral molecules as those having a dark rim around the bright central triangular core.¹⁸

While most of the pores in the network are "empty", i.e. they don't show a particularly pronounced contrast, some pores differ in contrast, i.e. they appear (in part) brighter than the rest. This suggests that such pores are filled by molecular species that differ from the ones without particular contrast. The latter ones are most probably filled by solvent molecules in a transient way, i.e. the solvent molecules are dynamic and can't be captured at the time scale of the STM imaging.

Remarkably, there is a clear difference in occupation of the pores of CW and CCW domains: the domains in which the porous network

consists only out of achiral molecules, i.e. the CCW domains, shows a higher degree of occupied pores. The mirror image situation is observed for monolayers formed from mixtures of cDBA-OC12(R) and achiral DBA-OC12 (**Fig. S1**, **Table 1**), confirming that this phenomenon is a genuine one. No such kind of preference of nanowell occupation is observed for pure samples of DBA-OC12 (**Fig. S2**, **Table S2**).

This brings us to the issue of identification of the trapped species. STM imaging is not very helpful in this. However, one important element is the difference in guest occupation based on the chirality of the nanowells. In addition, opposite preferences for occupation in the solutions containing cDBA-OC12(S) and cDBA-OC12(R) leave no other option than that in case of the absence of chiral impurities, the chiral DBA molecules themselves occupy the nanowells.

Closer inspection of the occupied pores reveals some differences in STM appearance (**Fig. 2B**). We identify three different occupation levels: incorporated (I), fuzzy (F) and half-fuzzy (H). Guest molecules appearing as a bright round blob surrounded with some kind of fine structure inside the pore are defined as incorporated, which is barely observed in the monolayers formed by pure DBAs (**Fig. S2**). This bright rounded blob is assigned to the conjugated DBA-core having some degree of mobility inside the pore. The fine structure surrounding the bright blob can be attributed to the presence of the cDBA alkyl chains with windmill-like conformation. Pores that are defined as fuzzy appear as diffuse bright clouds that cover the complete hexagonal void. This appearance may be related to a higher degree of mobility. Finally "half-filled" pores are defined as half-fuzzy. In line with the previous reasoning, these guests are highly mobile. In addition also empty pores (E), with a more homogeneous dark contrast appearance inside the void, are defined. For sure, this type of classification leaves some room for interpretation. The proposed assignment is to a certain extent arbitrary, however, evaluation of the total occupation level of the nanowells is more robust. Nevertheless, there is a relation between the classification and the mobility of the guest molecules. Fuzzy and half-fuzzy guests move easily between consecutive images. All the pores that appear fuzzy and half-fuzzy (blue circles in **Fig. S3**) are observed as empty in the consecutive STM images. This is valid for guests adsorbed in CW and CCW pores. In contrast 8 out of 19 incorporated guests (highlighted by the green circles in **Fig. S3**) remained incorporated in the same host-pore between consecutive STM images. This lesser degree of dynamics is a clear sign of a better interaction between the host and guest.

We have performed complementary modelling of these host-guest complexes with molecular mechanics force field, recently demonstrated²⁵ to properly describe intricate relationship between various supramolecular interactions in DBA assemblies. Using developed protocol we have modelled 'incorporated', i.e. fully confined (**Fig. 2B**) DBAs with windmill-like conformation, and got the optimized structures of cDBA-OC12(S/R) in CCW and CW nanowells (**Fig. 2C**), respectively, which is well consistent with the experimental observations. And we also found that indeed, for similar molecular conformations, CW/CCW pores are more favourable, by 6 kcal/mol, for cDBA-OC12(S)/cDBA-OC12(R) guests, respectively (**Fig. S4**, **S5**). The major contribution to this energy difference comes from fewer van der Waals contacts between the methylene units when the chirality of the host does not match the direction of the windmill-like conformation of the guest, which in turn, is totally defined by the methyl groups at the stereogenic centers of cDBAs. Thus, it appears that chiral recognition in these systems happens via the alkyl chain interactions.

Table 1 Statistics of the guest adsorption in the adlayers of premixed solutions of cDBA-OC12(S/R) and DBA-OC12 and sequential deposition of DBA-OC12 and cDBA-OC12(S/R). The total number of pores analysed (complete dataset) per void handedness for a specific solution mixture is also specified. non-C6 refers to irregular hexagonal nanowells.

	Premixed solutions						Sequential deposition					
	30 mol% cDBA-OC12(S)			30 mol% cDBA-OC12(R)			30 mol% cDBA-OC12(S)			30 mol% cDBA-OC12(R)		
	CCW (%)	non-C6 (%)	CW (%)	CCW (%)	non-C6 (%)	CW (%)	CCW (%)	non-C6 (%)	CW (%)	CCW (%)	non-C6 (%)	CW (%)
Total pores	145	2	1616	4291	6	775	960	10	1397	1758	5	1713
Incorporated	60 ± 4	0 ± 0	0 ± 0	0 ± 0	0 ± 0	18 ± 9	65 ± 1	0 ± 0	6 ± 2	1 ± 1	0 ± 0	38 ± 4
Fuzzy	3 ± 1	0 ± 0	7 ± 2	9 ± 3	0 ± 0	7 ± 2	12 ± 1	10 ± /	5 ± 1	6 ± 4	0 ± 0	2 ± 4
Half fuzzy	3 ± 3	0 ± 0	8 ± 4	8 ± 2	0 ± 0	12 ± 3	5 ± 1	0 ± 0	7 ± 1	4 ± 2	0 ± 0	4 ± 1
Empty	34 ± 1	100 ± /	85 ± 7	83 ± 3	100 ± /	63 ± 11	18 ± 4	90 ± /	82 ± 2	88 ± 6	100 ± /	55 ± 3

The degree of occupation of the different pores for the premixed solutions, containing 30 mol% cDBA and a total concentration of 2.5×10^{-6} M, was quantified according to the former listing. The results are summarised in **Table 1**. The details of the analysis and the calculation of the error bars are specified in supporting information. The results of the cDBA-OC12(S) mixture shows indeed some higher level of interaction with the CCW pores (only $34 \pm 1\%$ CCW pores are empty versus $85 \pm 7\%$ CW empty pores) and the cDBA-OC12(R) mixture has better interaction with the CW pores (only $63 \pm 11\%$ CW pores are empty versus $83 \pm 3\%$ CCW empty pores). There is an unexpected difference in guest occupancy in these two experiments which we can't explain. We reason that kinetic factors might be at play. Most importantly, the trend is robust: cDBA-OC12(S) prefers CCW pores while cDBA-OC12(R) prefers to adsorb in CW pores. This is also confirmed by the control experiments described below.

To examine if the ratio between CW and CCW pores on the surface has any influence on the interaction with the guest molecules, the deposition method was varied. In particular, we aimed at creating an equal surface coverage of CW and CCW pores. To equalize the number of CW and CCW nanowells on the surface, firstly 12 μ L achiral DBA-OC12 (2.5×10^{-6} M) is deposited (which yields equal amount of CW and CCW pores). After 30 min 6 μ L of cDBA-OC12(S/R) (2.5×10^{-6} M) is added. We call this procedure sequential deposition. Upon ideal mixing and in absence of competitive adsorption, this preparation method should yield a solution mixture with 33 mol% of cDBA and can as such be compared directly with the previous results. The data are also summarized in **Table 1**. In case of cDBA-OC12(S), $18 \pm 4\%$ CCW pores are empty versus $82 \pm 2\%$ CW pores. If cDBA-OC12(R) is deposited in addition to DBA-OC12, $55 \pm 3\%$ CW pores are empty versus $88 \pm 6\%$ CCW empty pores. Upon comparing the results from the premixed solutions with those from the sequentially deposited solutions, one can conclude that there is indeed a more favourable interaction with CCW pores in case the solution mixture contains cDBA-OC12(S) and with CW pores in case of cDBA-OC12(R). It should be noted that the occupancy in non-C6 nanowells, so those that are formed by a combination of + and - alkyl chain interdigitation patterns, is pretty low in all cases.

We conclude that the deposition method (pre-mixing vs. sequential deposition) does not change the qualitative outcome of the experiments. Moreover, studies with different ratios of chiral and achiral molecules, having an impact on the ratio of CCW and CW domains, show the same qualitative trend: the occupation of nanowells that have less favoured handedness induced by a chiral DBA is always larger (**Fig. S6** and **Table S4**). We tested if there is any significant evolution of guest occupancy in time (dynamics). No significant time effects were observed (**Table S3**).

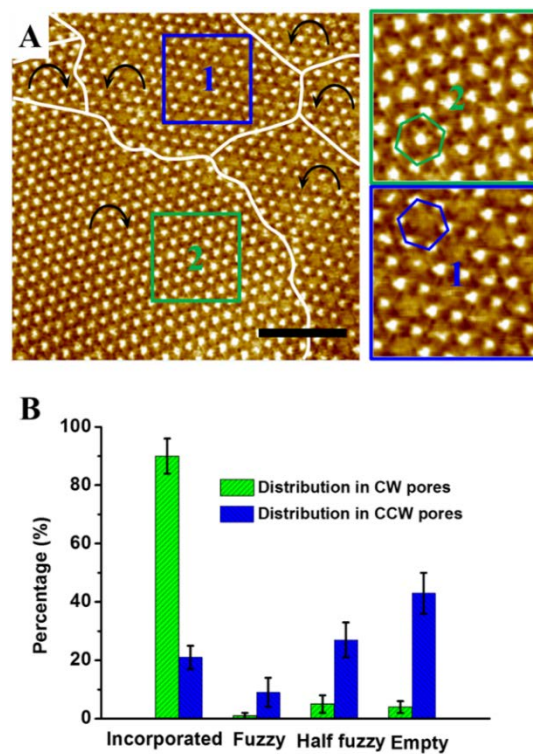


Fig. 3 (A) STM image and (B) statistics of the guest adsorption of the monolayers formed through sequential depositing DBA-OC13 (1×10^{-6} M) and cDBA-OC13(R) (5×10^{-6} M) on surface. $I_{set} = 280$ pA and $V_{bias} = -230$ mV. Scale bar: 20 nm. Close-up images of the selected areas are shown on the right. Green and blue hexagons indicate the CW and CCW pores respectively.

In a further attempt, we performed similar experiments for a DBA derivative with a different alkyl chain length: cDBA-OC13(R) and DBA-OC13, in a different solvent, 1-octanoic acid, to show the generality of this approach. cDBA-OC13(R) molecules form exclusively CCW hexagonal nanowells (**Fig. S7**). cDBA-OC13(R) acts as a sergent molecule too. A premixed solution of 30% cDBA-OC13(R) and 70% DBA-OC13, with a total concentration of 1×10^{-6} M gives rise to CCW dominated porous networks (**Table S1**), akin the sergeants-and-soldiers effect observed for cDBA-OC12(S)/(R) and DBA-OC12.

Porous networks with an equal amount of CW and CCW domains were generated through depositing a droplet of DBA-OC13 solution with a concentration of 1×10^{-6} M (Fig. S7). Upon further adding one droplet of cDBA-OC13(R) solution (5×10^{-6} M) to the preformed DBA-OC13 network, a clear difference in pore occupation was observed: up till 90% of the CW pores are filled, while only around 20% for the CCW pores (Fig. 3A). A domain boundary can be easily identified from the STM image. Moreover, adsorbed cDBA-OC13(R)s are more mobile in CCW than in CW pores, which is reflected by their appearance in the STM images. The selectivity is also supported by the statistics of occupation types (Fig. 3B). It should be noted that the amount of cDBA-OC13(R) in solution phase is five times higher than DBA-OC12, but still a lot of CCW nanowells are empty.

In conclusion, we have demonstrated the first example of enantioselective adsorption in surface-confined nanoporous networks. Enantiopure DBAs have a preference to adsorb in nanowells of a given handedness. These results obtained with different molecules, solvents, and sample preparation conditions suggest that this effect is genuine. The recognition seems to be guided by the optimization of van der Waals interactions of the methylene units between the intrinsically chiral guests and supramolecular porous host networks. Future studies will focus on deepening of our understanding of this interesting phenomena: the determination of the most important structural aspects at molecular and supramolecular levels and the design of new systems capable of efficient chiral recognition.

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Notes and references

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[†] Electronic Supplementary Information (ESI) available: Materials and methods, additional experimental data, details of molecular modelling and synthesis of cDBA-OC12(R). See DOI: 10.1039/c000000x/

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