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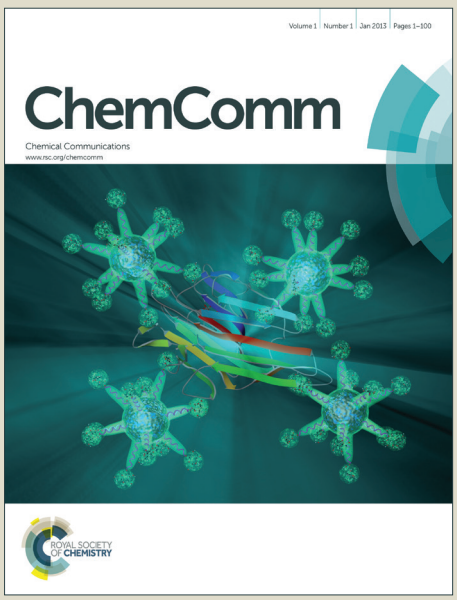

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COMMUNICATION

Enantioselective Extraction Mediated by a Chiral Cavitand-Salen Covalently Assembled on a Porous Silicon Surface†

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A chiral hybrid organic-inorganic material based on porous silicon surface functionalized with a chiral cavitand was designed and synthesized. The affinity of this device in water toward a bromine-marked alkyl-ammonium salt has been evaluated using XPS detection. UV and CD measurements highlighted the enantioselective extraction from a racemic mixture in water of the *S*-enantiomer of the selected guest (e.e. ≥ 80%).

Chirality is a property of matter that plays a key role in several branches of science, from optics to medicine.[1] Many biological processes involve chiral molecules in order to achieve highly specific and selective interactions. The separation of chiral isomers is an appealing burgeoning field that captures the interest of many researchers.[2] Different methods are employed to resolve a racemic mixture in solution, including crystallization,[3] chromatography,[4] and magnetic stirring.[5] Usually, those techniques exploit the enantioselective recognition using chiral metal-ligand complexes,[6] chiral polymers,[7] micelles,[8] gels[9] and enzymes.[10]

An interesting approach for harnessing the full potential of molecular receptors consists of their arrangement in monolayers hosted on an inorganic surface.[11] Moreover the use of heterogeneous solid device for enantioselective recognition would allow reutilize of the solid device, thus increasing the enantiomeric separation in eco-friendly conditions. To date, although some examples of enantiomeric recognition assisted by chiral surfaces have been reported in the literature,[12] to our knowledge, no examples of chiral host molecules anchored on a solid support able to enantiodiscriminate have been hitherto described.

Cavitand receptors have been recently bonded to flat Si (100) to perform molecular recognition tasks at the silicon−liquid[13] and at the silicon−air[14] interfaces. Among these systems, porous silicon (PSi) is a material with unique properties, including, besides the mentioned high surface area, convenient surface chemistry and easy integration in silicon-based devices.[15]

Recently, we reported on the synthesis of diastereomeric triquinoxaline cavitands, containing a salen chiral framework, and their uranyl complexes which were proved to achieve excellent selective molecular recognition of chiral ammonium ion pairs.[16] In particular, we verified the extraction properties of these salen cavitands in a biphasic system (chloroform/water) towards the chiral guest *N*,*N*,*N*-trimethyl-α-methylbenzyl ammonium iodide.[16a] The anchoring of these supramolecular hosts, whose synthesis is expensive and time-consuming, onto a surface is highly desirable since it allows the multiple use of the solid device and reduces the purification steps of the hosts. Taking into account these considerations, we designed and synthesized a chiral hybrid organic-inorganic material (**PSi-SalCav**, Figure 1)[17] based on porous silicon surface functionalized with the chiral **SalCav**, and studied the enantioselection property in water of this device towards (*R*/*S*)-*N*,*N*,*N*-trimethyl-α-methyl-*p*-bromo-benzylammonium iodide (**Br-MBA**) by X-ray photoelectron spectroscopy (XPS) and Circular Dichroism measurements (CD).

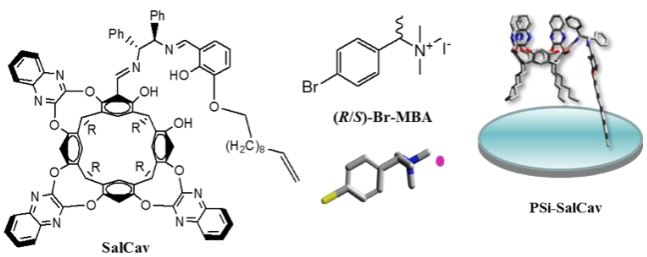

Figure 1. Molecular structures of the chiral cavitand-salen receptor (**SalCav**) and the selected guest (*R*/*S*)-*N*,*N*,*N*-trimethyl-α-methyl-*p*-bromo-benzylammonium iodide (***R*/*S*-Br-MBA**), and schematic representation of **SalCav** grafted on PSi surface (**PSi-SalCav**).

The cavitand monolayer was prepared from a solution of **SalCav** bearing an undecylenic foot, via thermic hydrosilylation of the double bonds on H-terminated PSi, prepared by metal-assisted chemical etching.†[17] The affinity of **PSi-SalCav** surface towards alkyl-ammonium salts has been evaluated using the bromine-marked guest (±)*N*,*N*,*N*-trimethyl-α-methyl-*p*-bromobenzylammonium iodide (**Br-MBA**), to allow easy XPS detection.

Complexation was accomplished through the immersion of **PSi-SalCav** into a racemic ***R*/*S*-Br-MBA** solution in water. The complexation of the **Br-MBA** guest on **PSi-SalCav** has been assessed by XPS measurements.

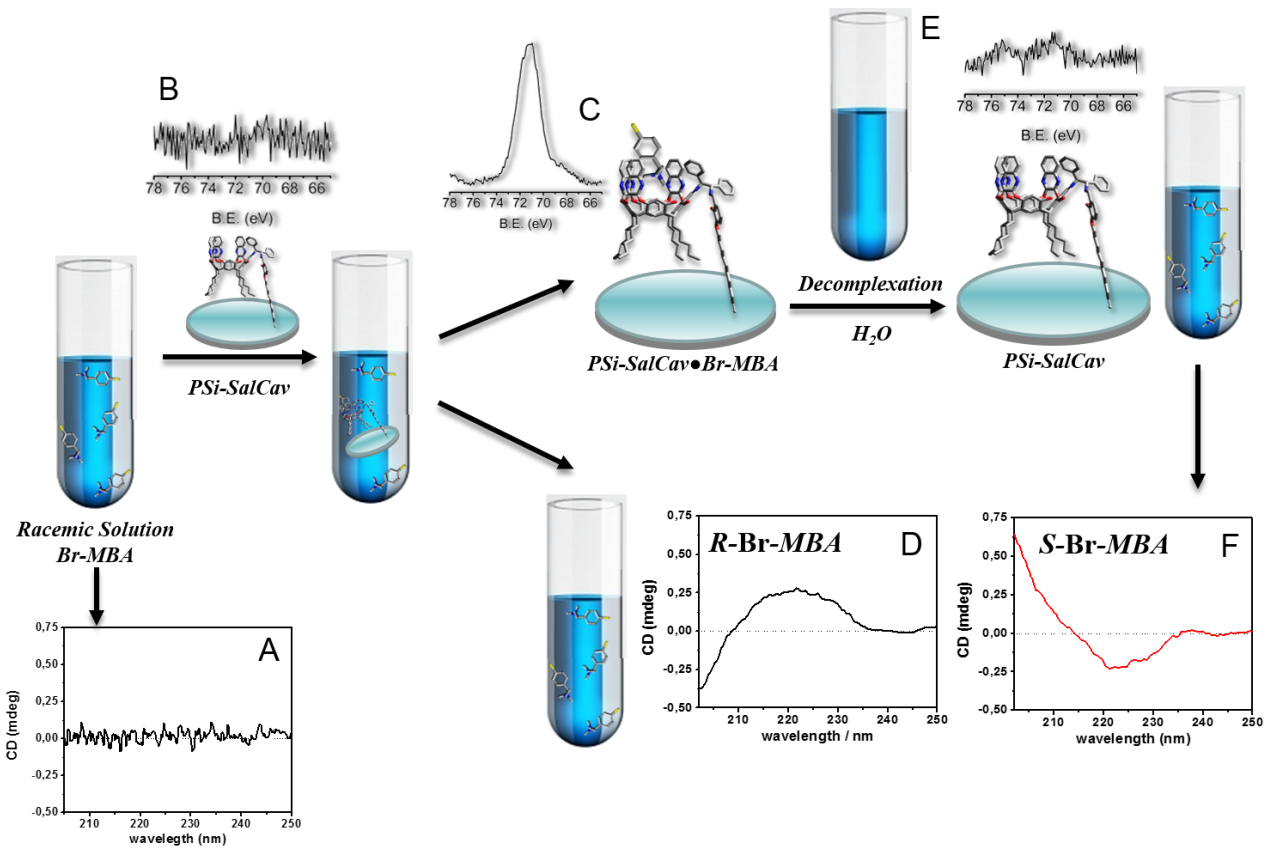

Figure 2. XPS and CD experiments of **PSi-SalCav** surface: A) CD spectrum of the racemic mixture ***R/S*-Br-MBA** in water, B) XPS region of Br of **PSi-SalCav**; C) XPS region of Br of **PSi-SalCav** complexed with **Br-MBA** (**PSi-SalCav•Br-MBA**); D) CD spectrum of the resulting mixture of ***R/S*-Br-MBA** after the immersion of **PSi-SalCav**; E) XPS region of Br of **PSi-SalCav** after decomplexation with water; F) CD spectrum of the resulting water solution used for the decomplexation of **PSi-SalCav•Br-MBA**.

In Figure 2 B the XPS of the Br 3d spectral region of **PSi-SalCav** before complexation shows no signal for any Br. After dipping the **PSi-SalCav** into **Br-MBA** solution, the presence of the Br 3d bands in the XPS spectrum of **PSi-SalCav** confirms the complexation ability of the cavitand-functionalized surface (**PSi-SalCav•Br-MBA**, Figure 2, C). Note that complete decomplexation of **Br-MBA** was obtained by a simple immersion of **PSi-SalCav•Br-MBA** in water for 15 min, as shown by the disappearance of the Br 3d signal (Figure 2, E). These experiments give rise to the reversible recognition of **Br-MBA** on the **PSi-SalCav** surface, due to the inclusion of the guest inside the cavities of the cavitands. Furthermore to rule out the possibility that the recognition on PSi surface occurs even without **SalCav** functionalization, control experiments were performed. Unfunctionalized PSi surfaces were immersed for 2 h into a solution of **Br-MBA.** The XPS of the Br 3d spectral region of the treated Psi surface did not show any evidence of the guest, thus indicating that interaction does not occur without **SalCav** functionalization.[†]

To evaluate the enantioselectivity properties of the functionalized surface and to estimate the enantiomeric excess towards **Br-MBA**, CD measurements were carried out. The device was dipped in a racemic solution of **Br-MBA** (1 mM, Figure 2, A). After the removal of the functionalized surface, a CD spectrum of the resulting **Br-MBA** solution, diluted to 30 μM, was performed.[18] As shown in Figure 2 D, a small positive CD signal at 223 nm is observed, indicating an excess of ***R*-Br-MBA** enantiomer in the resulting solution. Thus, this data suggests that **PSi-SalCav** preferentially recognize the *S*-enantiomer of **Br-MBA**.

Considering that enantiomer molecules show mirror image CD spectra, the selective extraction of the *S*-enantiomer of **Br-MBA** by the chiral surface has to be confirmed by performing the CD spectrum of the extracted guest. As expected, the immersion of the **PSi-SalCav•Br-MBA** in water for 15 min leaded to a desorbed solution, whose CD spectrum is the mirror image of the ***R*-Br-MBA**, establishing the selective extraction of the *S*-enantiomer (Figure 3).

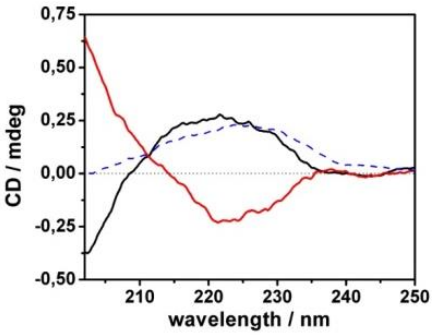

Figure 3. CD spectra of: resulting solution of **Br-MBA** 30 μM after the immersion of **PSi-SalCav** (black curve), desorbed solution (red curve) and 3 μM solution of ***R*-Br-MBA** (dashed blue curve).

To quantify the enantiomeric excess CD and UV data were combined. The CD spectrum of the solution of **Br-MBA** salt, after the immersion of **PSi-SalCav**, showed an excess of 3.28 μM of the ***R*-Br-MBA** enantiomer.† UV data of this solution indicated a concentration decrease of 4.1 μM (from 30 μM to 25.9 μM, Figure 4, B), suggesting that 8.2 x 10^{-2} μmol of ***R*/*S*-Br-MBA** were extracted from the initial racemic solution.[19] Bearing in mind that 3.28 μM is the concentration of the pure *S* extracted enantiomer (i. e. 6.56 x 10^{-2} μmol, calculated from CD data, Figure 4, D, green area), the remaining 0.82 μM consists in an equimolar mixture of *S* and *R* enantiomers (1.64 x 10^{-2} μmol, Figure 4, D, blue area), thus obtaining an enantiomeric excess ≥ 80%.[20] Notable, the concentration value of the solution obtained by dipping the device into 2 mL of water is ~ 4.1 μM (Figure 4, E), in good agreement with the total amount of ***R*/*S*-Br-MBA** extracted by **PSi-SalCav** (Figure 4, D), thus confirming the whole decomplexation as previously reported by XPS experiments.

Hence, the complexation/decomplexation reversibility of the **PSi-SalCav** surface with a racemic mixture of **Br-MBA** guest was tested. Interestingly, upon three successive experiments in which the **PSi-SalCav** surface was first rinsed in different freshly prepared racemic solutions of **Br-MBA** for two hours, and then immerged in water for 15 min, the recorded CD spectra revealed a positive curve centered at 223 nm, indicating the enantiomeric excess of ***R*-Br-MBA**,† demonstrating the robustness and the reusability of this functionalized surface.

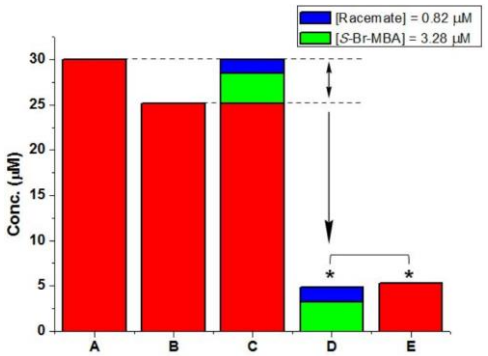

Figure 4. Concentration of: A) racemate (**Br-MBA** salt racemic solution 30 μM); B) resulting solution of racemate after immersion for 2 h of **PSiSalCav**; C) and D) concentrations of pure *S* enantiomer (green) and racemic mixture of ***R*-** and ***S*-Br-MBA** (blue) extracted by the surface from the initial racemic mixture; E) concentration of desorbed solution after the immersion of the device in 2 mL of water.

In conclusion, a promising chiral hybrid organic-inorganic device, based on a chiral cavitand-salen covalently assembled on a porous silicon surface, having enantioselection properties in water solution, exploiting non-covalent interaction, was disclosed. This chiral surface paves the way for the developing of synthetic heterogeneous enantioselective catalysts. Furthermore, the facile handling of the chiral surface and its successive reutilize, appoint this device as an ideal material for the enantioselective recognition of chiral guests.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Synthesis of guest, Porous Silicon preparations, procedure for the extraction, XPS and CD data using an unfunctionalized PSi surface, CD calibration, UV spectra of Br-MBA solution after extraction and reversibility experiments. See DOI: 10.1039/b000000x/

1 G. H. Wagniere, On Chirality and the Universal Asymmetry (Wiley-VCH, Zurich, Weinheim, 2007.
2 (a) G. A. Hembury, V. V. Borovkov, Y. Inoue, *Chem. Rev.* 2008, **108**, 1; (b) Yan Liu, Weimin Xuan, Yong Cui, *Adv. Mater.* 2010, **22**, 4112.
3 C. Viedma, P. Cintas, *Chem. Commun.* 2011, **47**, 12786.
4 B. Schuur,B. J. V. Verkuijl, A. J. Minnaard,J. G. de Vries,H. J. Heeres, B. L. Feringa, *Org. Biomol. Chem.* 2011, **9**, 36.
5 A. D'Urso, R. Randazzo, L. Lo Faro, R. Purrello, *Angew. Chem. Int. Ed.* 2010, **49**, 108.
6 (a) G. Bianchini, A. Cavarzan, A. Scarso and G. Strukul, *Green Chem.* 2009, **11**, 1517; (b) C. Jahier, M. Coustou, M. Cantuel, N. D. McClenaghan, T. Buffeteau, D. Cavagnat, M. Carraro, S. Nlate, *Eur. J. Inorg. Chem.* 2011, 727.
7 (a) E. Yashima, K. Maeda, Y. Okamoto, *Nature* 1999, **399**, 449; (b) V. Berl, I. Huc, R. G. Khoury, M. J. Krische, J.-M. Lehn, *Nature* 2000, **407**, 720; (c) T. Miyabe, H. Iida, M. Banno, T. Yamaguchi, E. Yashima, *Macromolecules* 2011, **44**, 8687; (d) F. Song, G. Wei, X. Jiang, F. Li, C. Zhu, Y. Cheng, *Chem. Commun.* 2013, **49**, 5772.
8 C. Bombelli, C. Bernardini, G. Elemento, G. Mancini, A. Sorrenti, C. Villan, *J. Am. Chem. Soc.* 2008, **130**, 2732.
9 (a) X. Chen, Z. Huang, S.-Y. Chen, K. Li, X.-Q. Yu, L. Pu, *J. Am. Chem. Soc.* 2010, **132**, 7297; (b) T. Tu, W. Fang, X. Bao, X. Li, K. H. Dötz, *Angew. Chem. Int. Ed.* 2011, **50**, 6601; (c) H. Jintoku, M. Takafuji, R. Odac, H. Ihara, *Chem. Commun.* 2012, **48**, 4881; (d) Q. Jin, L. Zhang, X. Zhu, P. Duan, M. Liu, *Chem.–Eur. J.* 2012, **18**, 4916.
10 A. Ghanem, M. N. Aboul-Enein, A. El-Azzouny, M. F. El-Behairy, E. Al-Humaidi, A. A. Alaidan, K. Amin, M. N. Al-Ahdal, *Chirality* 2008, **20**, 871.
11 (a) G. G. Condorelli, A. Motta, M. Favazza, I. L. Fragalà, M. Busi, E. Menozzi, E. Dalcanale, L. Cristofolini, *Langmuir* 2006, **22**, 11126; (b) Y. L. Bunimovich, Y. S. Shin, W.-S. Yeo, M. Amori, G. Kwong, J. R. Heath, *J. Am. Chem. Soc.* 2006, **128**, 16323; (c) A. Motta, C. Tudisco, G. G. Condorelli, *Sci. Adv. Mater.* 2011, **3**, 362.
12 (a) M. O. Lorenzo, C. J. Baddeley, C. Muryn, R. Raval, *Nature* 2000, **404**, 376; (b) V. Humblot, S. Haq,C. Muryn, W. A. Hofer, R. Raval, *J. Am. Chem. Soc.* 2002, **124**, 503; (c) A. Kuhnle,T. R. Linderoth, B. Hammer, F. Besenbacher, *Nature* 2002, **415**, 891; (d) R. Ouyang, J. Lei, H. Ju, Y. Xue, *Adv. Funct. Mater.* 2007, **17**, 3223; (e) Y. Fu, L. Wang, Q. Chen, J. Zhou, *Sensor Actuat B-Chem* 2011, **155**, 140; (f) Q. Han, Q. Chen, Y. Wang, J. Zhou, Y. Fu, *Electroanalysis* 2012, **24**, 332; (g) Y. Yun, A. J. Gellman, *Angew. Chem. Int. Ed.* 2013, **52**, 3394; (h) R. Kaminker, X. de Hatten, M. Lahav, F. Lupo, A. Gulino, G. Evmenenko, P. Dutta, C. Browne, J. R. Nitschke, M. E. van der Boom, *J. Am. Chem. Soc.* 20012 **135**, 17052.
13 (a) E. Biavardi, M. Favazza, A. Motta, I. L. Fragalà, C. Massera, L. Prodi, M. Montalti, M. Melegari, G. G. Condorelli, E. Dalcanale, *J. Am. Chem. Soc.* 2009, **131**, 7447; (b) F. Lupo, C. Capici, G. Gattuso, A. Notti, M. F. Parisi, A. Pappalardo, S. Pappalardo, A. Gulino, *Chem. Mater.* 2010, **22**, 2829; (c) D. A. Cristaldi, I. Fragalà, A. Pappalardo, R. M. Toscano, F. P. Ballistreri, G. A. Tomaselli, A. Gulino, *J. Mater. Chem.*, 2012, **22**, 675; (d) E. Biavardi, C. Tudisco,

F. Maffei, A. Motta, C. Massera, G. G. Condorelli, E. Dalcanale, *Proc. Natl. Acad. Sci.USA* 2012, **109**, 2263.

14 (a) K. D. Schierbaum, T. Weiss, E. U. Thoden van Veizen, J. F. J. Engbersen, D. N. Reinhoudt, W. Göpel, *Science* 1994, **265**, 1413; (b) G. G. Condorelli, A. Motta, M. Favazza, E. Gurrieri, P. Betti, E. Dalcanale, *Chem. Commun.* 2010, **46**, 288; (c) C. Tudisco, P. Betti, A. Motta, R. Pinalli, L. Bombaci, E. Dalcanale, G. G. Condorelli, *Langmuir* 2012, **28**, 1782.

15 B. Chen, S. Xiang, G. Qian, *Acc. Chem. Res.* 2010, **43**, 1115.

16 (a) M. E. Amato, F. P. Ballistreri, S. D'Agata, A. Pappalardo, G. A. Tomaselli, R. M. Toscano, G. Trusso Sfrazzetto, *Eur. J. Org. Chem.* 2011, 5674; (b) M. E. Amato, F. P. Ballistreri, A. Pappalardo, G. A. Tomaselli, R. M. Toscano, G. Trusso Sfrazzetto, *J. Org. Chem.* 2012, **77**, 7684.

17 C. Tudisco, G. Trusso Sfrazzetto, A. Pappalardo, A. Motta, G. A. Tomaselli, I. L. Fragalà, F. P. Ballistreri, G. G. Condorelli, *Eur. J. Inorg. Chem.* 2011, 2124.

18 Due to the high extinction coefficient of **Br-MBA** (33253 $cm^{-1}M^{-1}$), in order to record the CD spectra, the initial racemic solution was diluted from 1 mM to 30 μM (Figure 4, A).

19 Considering a total volume of 2 mL of the solution, the decreasing of 4.1 μM corresponded to 8.2 x 10^{-2} μmol of ***R*/S-Br-MBA**.

20 Enantiomeric excess: ee = ([*S*]-[*R*])/([*S*]+[*R*]), where [*S*] = (3.28 + 0.41) μM and [*R*] = 0.41 μM.

