L-ribose Specific recognition surface constructed by pillar[5]arene-based host–guest interaction

Wenhui Liu, a Weiwei Xu, b Hang-Hang Luan, c Guang Li, b Junan Liu, a Zhiyan Lu, c Fan Zhang, d Haibing Li, b

a The Department of Applied Chemistry, College of Science, Huazhong Agricultural University, Wuhan, P. R. China
b National Key Laboratory of Green Pesticide, College of Chemistry, Central China Normal University, Wuhan 430079, P.R. China, E-mail: lhbing@mail.ccnu.edu.cn
c Department of Forensic Medicine, Zhongnan Hospital of Wuhan University, No. 169 East Lake Road, Wuchang District, Wuhan, 430071, P. R. China. Email: luzhiyan@znhospital.cn
d Hubei Collaborative Innovation Center for Advanced Organic Chemical Materials, Ministry of Education Key Laboratory for the Synthesis and Application of Organic Functional Molecules, College of Chemistry and Chemical Engineering, Hubei University, Wuhan, 430062 P. R China

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Abstract: In living organisms, chiral molecules have specific chiral conformations that produce different physiological effects. Ribose is one of the components of RNA, which mainly plays a role in regulating biological activity. Inspired by the biological recognition of sugars, functional chiral surfaces for recognizing L-ribose through non-covalent interactions were constructed. In the strategy of this study, a functional chiral gold surface based on host-guest interactions were constructed by the assembly of the host molecule single-function alynyl pillar[5]arene(SAP5) and the guest molecule (S)-mandelate-violet (SMV). The surface was shown to sensitively recognize L-ribose and enable disassembly and assembly cycles, thus exemplifying the reusability of the chiral recognition interface.

Keywords: L-ribose; single-function alynyl pillar[5]arene; chirality recognition; host-guest interaction; biomimetic technology
1 Introduction

The term "chirality" was first introduced by Kelvin and formally applied to the literature by Ingold in 1964. Molecules that exhibit mirror-image symmetry in structure but cannot be completely overlapped are called chiral molecules. Two conformations are formed due to differences in the atoms or groups attached. Although these two conformations have the same physical properties, their chemical properties are quite different, including their potency, toxicity and other aspects. In fact, chirality is a fundamental property of living organisms. For example, almost all amino acids in the human body are levorotatory. Drug enantiomers differ in their pharmacological activity and toxicity. For example, R-type thalidomide is a sedative, but its enantiomer can cause fetal malformations. Therefore, the identification and isolation of chiral molecules is an important and meaningful challenge because they are widely used in the pharmaceutical, chemical, agricultural and food industries.

Ribose is one of the building blocks of RNA, which is mainly plays the role of regulating biological activity. L-ribose is a rare sugar that is not found in the natural environment, but it is important for existing organisms. However, ribonucleic acid synthesized from D-ribose is highly damaging to normal cells. In addition, many biologically active L-ribose derivatives can be synthesized using L-ribose as the starting material, and these derivatives show great promise in the treatment of hepatitis B virus (HBV), cytomegalovirus (CMV), etc. For patients with diabetes, L-ribose can be freely used in various foods, such as humectant, sweeteners, additives and quality improving reagents. Therefore, it is of great significance to identify and study L-ribose. For instance, Xia et al. modified boric acid on carbon points with fluoror. DiericS. et al. prepared a new gold surface with mercaptolectin multilayer coating, which has specific interaction with D-mannose.
In general, the commonly used analytical techniques for chiral recognition of drug molecules include high performance liquid chromatography, nuclear magnetic resonance, circular dichroism (CD), capillary electrophoresis (CE) and other methods. However, all these methods have the disadvantages of high cost and laborious sample preparation. Therefore, the development of novel chiral recognition interface materials with high sensitivity and low detection limits is a major problem for researchers to address. Supramolecular chemistry is being extensively studied with the aim of developing complex self-assembling systems such as molecular switches, molecular machines, and supramolecular polymers. In the chiral separation process, calixarene, cyclodextrin, cucurbit[n]uril, pillar[n]arenes and crown ether are considered as effective chiral selectors, which make important contributions to the separation of enantiomers. Among them, pillar[n]arenes are a new class of supramolecular hosts that have become one of the hottest topics in supramolecular chemistry since they were first synthesized in 2008. The host-guest chemistry of pillar[n]arenes have been widely explored, due to electron-rich cavities and electrostatic interactions. Pillar[n]arenes are ideal host molecules for the formation of host-guest complexes via C-H-π interactions. Huang group reported first example of the recognition of metal ions by pillar[n]arenes. Single crystal X-ray analysis showed that CF₃COOAg forms a unique binuclear silver structure and permeates into the pillar[5]arenes cavities of these complexes. In addition to the silver-π interaction, multiple C-H-O and C-H-F hydrogen bonds between the counter-ion and the pillar[5]arenes host also contribute to the stabilization and maintenance of the host-guest structure. In a previous research, the chiral ordered mesoporous silica (OMS) nanochannels were prepared by introducing L-alanine- pillar[5]arene into non-chiral OMS. The nanochannel showed excellent selectivity for the isolation of racemic drugs with good reusability and
Currently, most chiral recognition of sugars takes place in solution, with little recognition at the interface. However, the process of recognizing sugars occurs at the cell surface. Therefore, developing a simple, rapid and visual method for the recognition of L-ribose at the surface remains a challenging task. Inspired by the recognition of glycans by chiral receptors on the surface of living cell membranes, as shown in Scheme 1, we modified single-function alkyne pillar[5]arene (SAP5) to the gold interface to construct SAP5 SAMs, and then assembled CVs into SAP5 SAMs to construct functional chiral interfaces (SAP5-CV SAMs). The successful construction of a functional chiral interface was illustrated using contact angle, impedance, XPS and other characterization methods. The functional chiral interface not only proved to be a convenient and effective method for identifying L-ribose, but also allowed the intelligence of the interface by regulation.

Scheme 1. Illustration of the Design of a Biomimetic Chiral Surface for Recognition of L-ribose Based on the Host–Guest Interaction
2 Experimental Section

Materials and Instrumentation. All chemicals were AR grade and purified according to standard procedures. $^1$H NMR data of the compounds were recorded on a Varian Mercury VX400 instrument at ambient temperature (internal standard tetramethylsi-lane). Mass spectra were recorded on an ultrafleXtreme matrix-assisted laser desorption ionization time-of-flight instrument. X-rayphotoelectron spectroscopy (XPS) was carried out using a KRATOSXSAM800 Electron spectrometer (FRR mode). The contact angle (CA) was measured at 25 °C by means of an OCA 20 contact anglesystem (Dataphysics, Germany).

Synthesis of single-function alynyl pillar[5]arene (SAP5). Para-dimethyl ether (0.138g, 1mmol), para-formaldehyde (1.08g, 36mmol) and compound 1 in the Supporting Information (2.172g, 12mmol) were added to 250mL three-necked round-bottomed flask, respectively. Anhydrous 1, 2-dichloroethane (150mL) and boron trifluoride ether...
(2.04g,14.4mmol) were added under nitrogen protection. After the reaction, it was washed with water, dried with anhydrous sodium sulfate, purified by column chromatography with ethyl acetate: petroleum ether =15:1 as eluent. 13mg white solid was obtained with a yield of 10%.

**Preparation of the P5-Modified Gold Substrates.** Alkyne groups can form metal coordination bonds with Au, and the host molecule can be modified to the gold interface through this principle\(^{30}\). The smooth gold sheet was immersed in acetonitrile solution (c=1×10\(^{-3}\)mol/L) dissolved with host molecules of pillar[5]arenes for 12 h to obtain the gold interface (SAP5 SAMs) modified with main molecules of SAP5.

**The assembly of CV guest molecules in SAP5 SAMs.** Based on the principle of assembly of pyridinium salt in CV guest molecules with positive charge energy and pillar[5]arenes with electron-rich cavity\(^ {32} \), the gold interface modified with pillar[5]arenes main molecules was placed in acetonitrile solution (concentration of 1×10\(^{-3}\)mol/L) that dissolved CV guest molecules for 5h to obtain functional chiral interfaces (SAP5-CV SAMs).

**3 Results and discussion**

**Construction of functional chiral interface.** Inspired by the recognition of glycans by chiral receptors on the surface of living cell membranes, SAP5 SAMs were constructed by SAP5 at the gold interface, and then functional chiral interfaces (SAP5-CV SAMs) were constructed by assembling CVs into SAP5 SAMs. All compounds were characterized by \(^{1}H\) NMR spectroscopy, \(^{13}C\) NMR spectroscopy and mass spectrometry, and the details are given in the Supporting Information.

The contact angle measures the angle between water and a solid surface at room temperature, and it is a measure of the degree of wetting. As shown in Figure 1a, the contact Angle of the bare gold sheet is 95.4±2°. After modification of SAP5SAMs on the
upper SAP5 the contact Angle becomes hydrophobic with an angle of 151±2°. After the assembly of CVs and SAP5 SAMs, the interface changed from hydrophobic to hydrophilic with a contact angle of 66.9±2°. By the change of hydrophilic and hydrophobic contact angles, we can tentatively consider that a functional chiral interface was successfully constructed. Aside from the contact angle characterization of the constructed functional chiral interfaces, electrochemical characterization was also performed. Cyclic voltammetry was utilized to test their electrochemical impedance. The impedance changes are shown in Figure 1b and Figure S13. The impedance of the bare electrode is 200 Ω, which increases to 2300 Ω when the host molecule of the SAP5 is modified. When the gold electrode modified SAP5 are assembled with CVs, the impedance drops significantly to 130 Ω. A functional chiral interface can be successfully established by impedance changes. To further characterize the functional chiral interface, an XPS examination of the interface was performed, as shown in Figure 1c and Figure S14. As shown in Figure S14, C and O peaks appeared in the XPS maps of the gold interface modified with the SAP5, indicating the successful construction of the interface of SAP5 SAMs. In Figure 1c, an F peak appears in the XPS map of the gold interface assembled by CV and SAP5 SAMs. The above characterization indicated that the functional chiral interface was successfully constructed by assembly.
Figure 1. (a) Contact angle changes at functional chiral interfaces; (b) Impedance changes at functional chiral interfaces; (c) XPS diagram of the CV functionalized chiral interface.

Selective recognition of L/D ribose at the modulated functionalized chiral interface. A functional chiral interface was successfully built by contact angle, impedance and XPS characterization. Subsequently, the selective recognition of L/D-ribose was characterized at the functional chiral interface. As shown in Figure 2a and Figure S15, the contact angle between the functional chiral interface and D-ribose was 58.4 ± 2°. When interacting with L-ribose, the contact angle was 41.7 ± 2°. Comparing the above contact angle values, it is found that L-ribose is more hydrophilic. The probable factor is the functional chiral interface interacting with L-ribose. To further investigate the selective recognition of D/L-ribose at the constructed chiral functional interface, electrochemical experiments were performed. As shown in Figure 2b, the impedance of SAP5-CV SAMs is 200 Ω. When the working electrode interacts with D-ribose, the impedance is 600 Ω.
and when it interacts with L-ribose, the impedance becomes 2200 Ω. Comparing the impedance values of the two electrodes, we found that the impedance of the SAP5-CV SAMs gold electrode interacting with L-ribose is much larger than that of the electrode interacting with D-ribose. The possible reason is that the working electrode interacts with L-ribose. According to the above experiments, the constructed functional chiral interface can recognize L-ribose.

To further explore the recognition performance of this functional chiral interface for L-ribose. In Figure S17, the impedance increased to 500 Ω when the concentration of L-ribose was $1 \times 10^{-7}$ mol/L. When the concentration of L-ribose became $1 \times 10^{-6}$ mol/L, the impedance became 700 Ω. As the concentration of L-ribose continued to increase, the impedance also increased accordingly. When the concentration of L-ribose was $1 \times 10^{-4}$ mol/L, the impedance increased significantly. Figure 2c shows the contact angle as a function of L-ribose concentration. As the L-ribose concentration increases, the contact competition becomes smaller and the interface becomes more hydrophilic. When the L-ribose concentration is $1 \times 10^{-4}$ mol/L, there is a clear hydrophilic change in the contact angle. By impedance and contact angle detection, we found that the constructed functional interface has good detection effect on L-ribose in the range of $1 \times 10^{-7}$ mol/L-$1 \times 10^{-2}$ mol/L.
Figure 2. (a) Contact angle diagram for selective recognition of D/L ribose at the functionalized chiral interface; (b) Impedance diagram of selective recognition of D/L-ribose at the functionalized chiral interface; (c) The limit contact angle diagram of L-ribose (1×10⁻⁷ mol/L-1×10⁻² mol/L) at the functionalized chiral interface.

**Research on recognition cycle performance of functional chiral interface.** The previous experiments have shown that the constructed functional chiral interface has a highly selective recognition of L-ribose with a good detection limit. However, as a constructed functional chiral interface, it is more meaningful to highlight the controllability and intelligence of the interface. To this end, as shown in Figure 3b, we investigated the cycling of the interface and found that it can be repeated five times with good cyclability. To further explore the assembly and disassembly of the host and guest, we performed ¹H NMR, Gaussian simulations and colorimetric experiments. Above Figure S18 is the ¹H NMR of L-ribose recognition of aromatic hydrocarbons and CV assembly in SAP5, and below is the ¹H NMR of CV falling off the cavity of SAP5 after adding 10 times equivalent
zinc powder. From the assembly and disassembly spectra, it was found that the peak of CV pyridine ring between 8.0 ppm and 9.5 ppm shifted to the high field when zinc powder was added as a reducing agent. The possible reason is that the zinc powder loses electrons and oxidizes to zinc ions and the pyridine ring of CV gains electrons and changes from electron deficient to electron rich. As the electron cloud density increases, the shielding effect is enhanced and the chemical potential moves to higher domains. The energy of the CV and the assembly of the SAP5 are important because the electron-poor pyridine ring can bind to the SAP5 in the electron-rich cavity by electrostatic interactions. When Zinc powder is added, the pyridine ring was changed from electron-poor to electron-rich, and the original electrostatic effect disappeared, leading to the disintegration of the CV from the SAP5 cavity. It can also be evidenced from the Gaussian simulation calculations in Figure 2c that there is a pyridine ring in the SAP5 cavity of the CV before reduction. After reduction, the pyridine ring gains electrons and the pyridine ring leaves the SAP5 cavity. Meanwhile, the color of the solution changed during assembly and disassembly. By $^1$HNMR, Gaussian simulation and colorimetric analysis, it was founded that the redox properties of SAP5 and CV can be utilized for assembly and disassembly.

The assembly and disassembly processes of CV and SAP5 could be obtained by Gaussian simulation and $^1$HNMR, but the dynamic processes of assembly and disassembly could not be attained. To further explore the dynamic processes of assembly and disassembly, we used the open-circuit voltage measurement method in electrochemistry to obtain the dynamic processes of assembly and disassembly of CV and SAP5 by measuring the voltage change on the electrode surface according to the property that CV itself has a positive charge. As shown in Figure S22, part A is the dynamic assembly diagram of CV and SAP5. The assembly of CV and SAP5 on the
The electrode surface is completed when the voltage on the electrode surface drops rapidly at 500s and there is no significant change in voltage after 500s. The possible reason for the voltage drop on the electrode surface during the assembly process is that the chiral CVs are positively charged. When it is assembled with SAP5 modified on the electrode surface, the electrode surface turns from uncharged to positively charged, which increases the ability of the electrode surface to trap electrons in solution, so the voltage drops rapidly. In Figure S22b, the voltage on the electrode surface no longer increases after 4400 s. The cause is that the CV on the electrode surface falls off from SAP5, the electrode surface changes from positively charged to neutral, the ability of the electrode to capture electrons decreases, and the voltage increases. The above data demonstrated that we successfully obtained the dynamic process of the assembly and disassembly of CV and SAP5.

Figure 3. (a) Disassembly and assembly diagram of the functional chiral interface; (b) Contact
angle cycles for functional chiral interface recognition of L-ribose; (c) 8mM host-guest complex and 10equiv of Zn power addition and cycling experiment on wettability switching behavior of host-guest complexation surfaces with L-ribose and water.

Preliminary study on the mechanism of recognition and regulation of functional chiral interface by L-ribose. The interaction between host-guest complex and L-ribose was confirmed by $^1$H NMR spectroscopic analysis. As shown in Figure 4b, the $H_1$ and $H_2$ resonances of the protons on the pyridine ring underwent upfield shifts of 0.05 ppm, the $H_3$ resonances of the protons on the methyl underwent upfield shifts of 0.03 ppm. And the $H_4$ resonances of the protons on alynyl of SAP5 shifted downfield by 0.03 ppm. The chemical shifts indicated that pyridine of CV interacted with SAP5. Gaussian simulation showed that the pyridine ring of CV was binded by the electron-rich cavity of SAP5. And the interactions might be C-H…π and π-stacking. For the Gauss simulation, one pyridine ring of CV entered the cavity of SAP5, and their hydrogen sizes were from 2.4Å to 3.3Å. In addition to studying the interaction between host and guest, we also investigated the complexation constant and complexation ratio of host and guest by UV titration. As shown in FigureS19-21, absorption was enhanced at 270nm. UV titration of SAP5 ($10^{-5}$ M, CH$_3$CN) was performed by adding SMV ($10^{-5}$M, CH$_3$CN), and the association constant ($K_a$) for SMAV was calculated to be $2.95\times10^4$ M$^{-1}$ using the Benesi-Hildebrand equation with a 1:1 ratio.

To further explore the recognition of L-ribose after the assembly of CV and SAP5, we found that the assembly of CV and SAP5 could achieve the recognition of L-ribose using $^1$HNMR and Gaussian simulation calculations. As shown in Figure 4c, L-ribose recognition $^1$HNMR is assembled according to the CV and SAP5, $H_1$ of L-ribose moves 0.04ppm to the lower field, $H_2$ moves 0.03ppm to the lower field. Figure 4a showed the Gaussian simulation calculation. The recognition energy of L-ribose after the assembly of
CV and SAP5 is $-1.17 \times 10^7$ kJ / mol. By $^1$HNMR and Gauss simulation, the CV can selectively recognize L-ribose when assembled with SAP5.

Figure 4. (a) Gaussian simulation of the assembly of host and guest molecules of SAP5 and Gaussian simulation diagram of L-ribose recognition by CV and SAP5 assembly; (b) Assembly of $^1$HNMR between SAP5 and CV; (c) $^1$H NMR diagram of L-ribose recognition by SAP5 and CV assembly.

4 Conclusion

Inspired by the recognition of glycans by chiral receptors on the surface of living cell membranes, we constructed SAP5 SAMs by modifying monofunctional SAP5 onto gold interfaces, and then constructed functional chiral interfaces by loading CVs onto SAP5 SAMs. The successful construction of the functional chiral interface was illustrated using contact angle, impedance, and XPS characterization methods. Next, we constructed a functional chiral interface that recognizes L/ D-ribose. Based on the impedance and contact angle, this chiral functional interface can selectively recognize L-ribose. To further
explore the performance of this functional interface, we prepared L-ribose solutions with
concentrations ranging from $1 \times 10^{-7}$ M$^{-1}$ to $1 \times 10^{-2}$ M$^{-1}$, and found that the interface had
good recognition effect in this range by impedance and contact angle detection. Due to
the construction of a chiral functional interface and the tunability and intelligence of the
interface, we realized the assembly and disassembly of host and guest molecules by
using the redox property of CV, thus achieving the organic combination of interface
recognition and intelligence.

Meanwhile, to further explore the mechanism of the functional interface, we obtained
the model of this recognition system and the action sites of assembly and recognition by
$^1$HNMR characterization. Through the simulation of Gaussian calculation, we can
represent this recognition model more vividly and objectively. We also obtained the
quantitative data of the host-guest assembly by UV titration and other methods. In
conclusion, we successfully constructed a functional chiral interface to achieve selective
recognition of L-ribose, and achieved the intelligence of the interface by regulation.

Author Information

Corresponding Author

*E-mail: lhbing@mail.ccnu.edu.cn

*Phone: +86-13871150664;

ORCID

Haibing Li*: 0000-0002-6374-4694

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