

CAVITANDS: MOLECULES WITH ENHANCED SELECTIVITY FOR CHEM/BIO DETECTION

Devanand K. Shenoy
Center for Bio/Molecular Science and Engineering
Naval Research Laboratory
4555 Overlook Ave. SW
Washington, DC 20375

ABSTRACT

The selective response of supramolecular structures, cavitands, is demonstrated using a sensitive optical transduction scheme, surface plasmon resonance (SPR). The methylene bridged cavitands (MeCav) with shallow cavities do not complex aromatic vapors, the pyrazine bridged cavitands (PzCav) show intermediate selectivity whereas the quinoxaline bridged cavitands (QxCav) with the deepest cavities show the best selectivity for aromatic vapors. A comparison with polymer sensing layers, PECH and PIB, shows cavitands are more selective although the polymer layers were more than twice the thickness of spin coated cavitand layers. Cavitands are therefore promising materials for the selective detection of CW agents.

INTRODUCTION

Chemical threats pose a serious challenge to the security of our nation and to our forces abroad. A significant issue in the development of effective and efficient chemical detectors is the need to reduce false alarms. This will reduce the inconvenient need for the warfighter to don protective clothing unless there is a real threat present. False alarms are caused by insufficient selectivity and sensitivity of the current chemical detectors, which in turn, is partly due to the limited selectivity of the sensing layers¹⁻⁶. For example, if the interaction between the sensing layer and the analyte is not sufficiently specific, there is a finite probability that a false alarm is generated. This becomes highly critical when the differences between the real analyte and an interferent are minimal. Unlike with biological threats, where high specificity antibody receptors are available, there is still a lack of sufficient selectivity with chemical sensing layers. It has therefore become necessary to use higher order strategies, such as the use of pre-concentrators, to enhance the selectivity of sensing layers or post detection methods, such as the use of pattern recognition algorithms. There is therefore a need to develop novel sensing layers comprised of new molecules that can enhance selectivity of detection for specific target analytes⁷⁻¹⁵. This does not guarantee that higher order strategies can be eliminated but at least ensures that the burden on techniques such as pattern recognition is minimized.

Recently, supramolecular structures called cavitands have shown the potential to fill the need for enhancing selectivity of detection towards specific analytes. These molecules have the potential to be selective, because of their unique biomimetic structures, which present cavities to the target analytes so as to form stable guest host complexes¹⁴⁻¹⁵. A combination of the size of the cavities, their shape and synergistic interactions allows for high selectivity to be built into these molecular structures. It is also important to transduce these selective interactions using a highly sensitive technique. We show that, using the surface plasmon resonance (SPR) technique, refractive index changes induced by analyte-cavitand interactions provide selective signals for sensitive chemical detection.

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EXPERIMENTAL SECTION

Cavitands were provided by Prof. Enrico Dalcanale at the University of Parma, Italy and have been extensively characterized in the solution and solid phases by techniques such as NMR and X-ray crystallography by his group⁹⁻¹¹. Three cavitands named MeCav (for methylene bridged), PzCav (pyrazine bridged) and QxCav (quinoxaline bridged) shown in Figure 1, were chosen to demonstrate the feasibility of obtaining selectivity towards aromatic vapors. The presence of alkyl tails (eleven carbons) allowed common solvents to be used for forming solutions used in spin coating the cavitands on surface plasmon resonance substrates. The cavitands were spin coated from a 0.38 mM chloroform solution at 4000 rpm for 60 s at room temperature. A variety of analyte vapors belonging to different chemical classes were studied. QxCav with the deepest cavity was designed to form efficient guest host complexes with aromatic vapors (Prof. Dalcanale's group has independently demonstrated the selectivity of these compounds using the quartz crystal microbalance (QCM) technique) whereas the cavitands with shallow cavities were not expected to be selective towards such guest molecules.

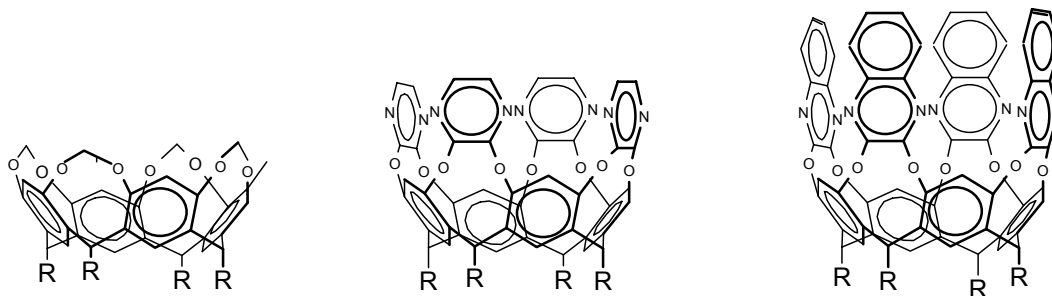


FIGURE 1. The three cavitands MeCav (methylene bridged), PzCav (pyrazine bridged), and QxCav (quinoxaline bridged) shown respectively from left to right differ both in the depth of the cavities as well as the specific interactions presented by the cavities

A surface plasmon resonance (SPR) experimental set up (see Figure 2), based on the Kretschmann configuration¹⁶⁻¹⁷ was used to make all the measurements. The glass prism, made of standard BK7 glass, (90 degrees, 17 mm high, 22 mm by 32 mm at the base, refractive index $n = 1.5$, Howard Jonson Optical Laboratories), was index matched to the gold coated cover glass which was used as the sample substrate ($n=1.51$) using an index matching liquid from Cargille Inc. The thickness of the gold film was nominally 50 nm and had an underlying chromium adhesion layer of about 2 nm thickness. A 635 nm diode laser (from Lasermax, Inc.) was used as the light source. A Glan Thompson linear polarizer was placed in the path of the light beam to ensure that only p-polarized light was incident on the glass prism (surface plasmons are excited by p-polarized radiation). The reflected light was monitored using a photodiode (818 Series, Newport Corporation) calibrated for the chosen wavelength. Variable angles were selected by means of a stepper motor controlled goniometer with an angular resolution of 0.01 degrees. The experimental data acquisition system was computer controlled, with a typical angular scan (from 40° to 80°) taking about 8 minutes.

Recently, we have also set up a new SPR system based on wavelength interrogation¹⁸ with real time detection capabilities. Preliminary results indicate that the results obtained using wavelength interrogation are qualitatively similar to that obtained using angular interrogation. Differences can arise due to a combination of wavelength, angle and sensitivities in various components of the set up such as polarization purity, photodetector quantum efficiencies and

properties of the dielectric layer coated on the SPR substrates. Quantitative comparisons are currently in progress.

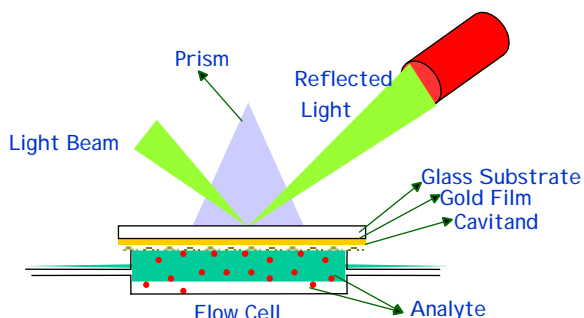


FIGURE 2. A schematic of the surface plasmon resonance (SPR) experimental arrangement is shown. The SPR set up used angular interrogation and had a resolution of the order of 0.01 degrees.

The sample chamber/flow cell was constructed from a block of teflon to expose organic vapors of precisely known concentration to cavitands coated on the SPR substrate. An inlet and outlet was provided for the analyte vapors and a rectangular aperture allowed the cavitand coated glass slide and prism to be placed over it. An O-ring was used to provide a good seal between the prism/slide and Teflon chamber.

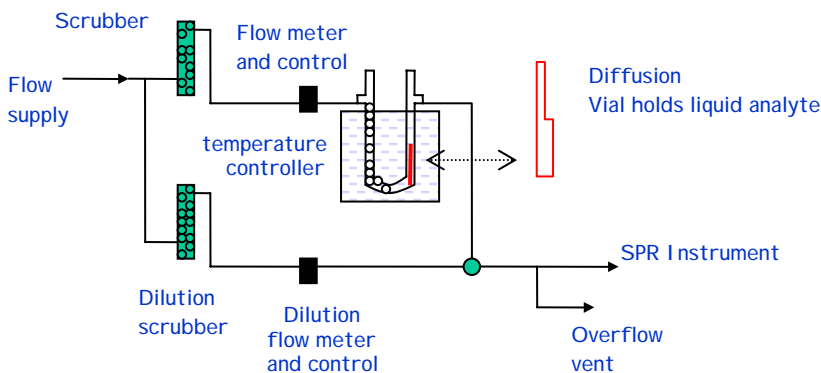


FIGURE 3. A schematic of the vapor generation system is shown. The system was calibrated against a gas chromatograph to ensure accuracy of vapor concentration.

To generate organic vapors of variable concentrations in the 0 to 1000 ppm range, a diffusion vial from VICI Metronics was used (D-5.0 mm capillary). This was filled with analyte liquid using 5 ml syringe needles (VICI Metronics) and placed in a U-tube containing glass beads on one side of the tube and vial on the other. The U-tube in turn was placed in a temperature controlled water bath from PolySciences Inc with a nominal control of about 0.1 degrees. A stream of nitrogen carrier gas served to dilute the analyte vapors. The flow of both the carrier gas and the analyte vapor were precisely controlled (accuracy of 1-2%) using mass flow controllers (DFC26, AALBORG INC.) and mixed in the appropriate proportions before being introduced

into the flow cell for exposure to the cavitands. A software program controlled the flow of the carrier gas as well as the organic vapors. The actual concentrations of analytes were calculated from the vapor pressures using Antoine's law. To ensure measurements be done under equilibrium conditions, the SPR angular scan was initiated about five minutes after analyte exposure to the sensing surface.

RESULTS AND DISCUSSION

Figure 4 shows surface plasmon angle shifts due to the spin coated cavitands on the SPR substrate. The curve with the smallest plasmon angle minimum is that obtained with the bare gold substrate while successively higher shifts were obtained due to MeCav, PzCav, and QxCav coated substrates respectively. Referring to Figure 1, it is seen that the presence of polarizable groups on the molecules causes a larger shift of the plasmon angle (the order of the plasmon angle shifts is $QxCav > PzCav > MeCav$). This is to be expected since refractive index changes arise from the presence of polarizable electrons and the plasmon angle is sensitive to such changes. These shifts were then used as baseline shifts for comparing the shifts obtained due to the interaction of the cavitands with the analyte vapors.

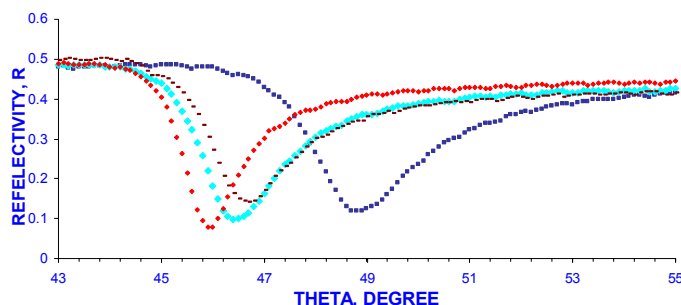


FIGURE 4. Surface Plasmon angle data showing the plasmon angle minima. The plasmon angle minima starting from left to right are for a) bare gold b) MeCav coated substrate c) PzCav coated substrate and d) for QxCav coated substrate. Note the sizeable shift due to the polarizable groups present on the cavitand walls.

The plasmon angle shifts obtained due to the interaction of various analytes (ethyl acetate, dichloromethane, acetonitrile, toluene, and benzene) with the three different cavitands are shown in Figure 5. For comparison of the selectivity of the cavitands with other sensing layers, we carried out similar experiments with polymer coated layers. Specifically, we compared the signals obtained with two polymer layers, polyepichlorhydrin (PECH) and polyisobutylene (PIB) which have been demonstrated, in the past, to show selective response towards aromatic vapors²⁻³. It is seen from the figure that for comparable concentrations of the vapors (100 ppm), the polymer sensing layers do not generate a signal sufficient to be observed. This is despite the fact that the polymer layers were about twice as thick as the cavitand layers since we used identical spin coating conditions in both cases. This clearly demonstrates the higher selectivity of the cavitands. It is also seen that not all cavitands are selective towards aromatic vapors. MeCav, with the shallow cavity, shows hardly any response towards the aromatic vapors while PzCav with a slightly deeper cavity shows a signal well above the baseline. However, QxCav with the deepest cavity shows the largest response towards the aromatic vapors, benzene and toluene. Clearly, the enhancement in selectivity due to the size and shape of the cavities plays an important role in enhancing the signal due to the cavitand-analyte interactions. Figure 5 shows a pattern of response to several analytes and multiple sensing layers. Such patterns can be used with pattern recognition algorithms to identify known and possibly unknown analytes. A detailed

study of the interaction of these cavitands with several chemical vapors over a range of concentrations has been completed and is due to be published shortly⁷⁻⁸.

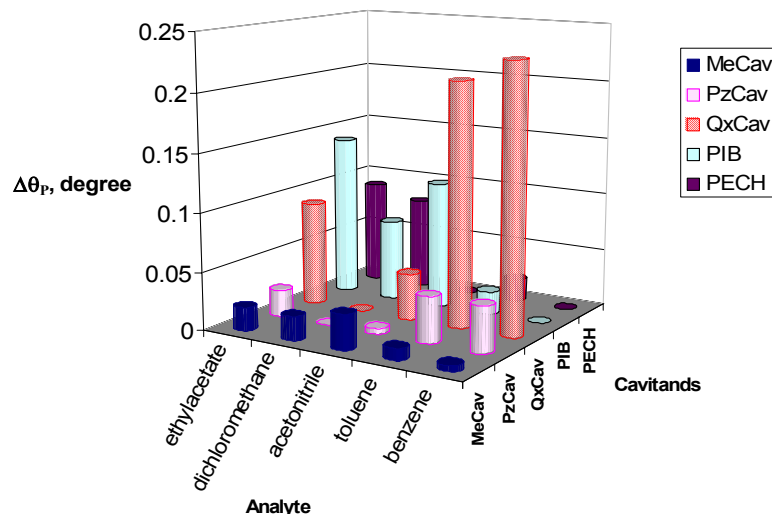


FIGURE 5. A summary of the selectivity pattern observed for different vapors and the three cavitands, MeCav, PzCav, and QxCav are shown. The comparison is for a fixed concentration of 100 ppm for all vapors. Also shown for comparison are the polymer sensing layers, PECH and PIB that are known to complex aromatic vapors. The quinoxaline bridged cavitands are highly selective towards aromatic vapors due to the complementary cavity size and interactions.

It is believed that the selectivity between the cavitands and aromatic vapors arises primarily through the presence of non covalent interactions such as CH- π interactions and dipole dipole interactions. These allow for stable guest host complexes to be formed. However, the guests (analyte molecules) can be removed from the hosts (cavitands). We have demonstrated that by forcing a steady stream of nitrogen gas through the guest host complexes, the analytes may be removed from the cavities. This has been confirmed by comparing the surface plasmon angle before and after removal of analyte. Cavitand sensing layers can hence be used in a sensor format. Preliminary data on the time response of the cavitand-analyte interactions suggest that this takes several seconds. Finally, it is important to point out that cavitands are highly robust, synthetic receptors and therefore afford an opportunity to integrate them into rugged detectors with potential for long shelf lives.

CONCLUSIONS

Cavitands appear to be highly promising as supramolecular structures for the selective complexation of chemical vapors. This selectivity arises due to the size, shape and interaction complementarity between the analyte and cavitands. The methylene bridged cavitands (MeCav) with shallow cavities do not complex aromatic vapors, the pyrazine bridged cavitands (PzCav) show intermediate selectivity whereas the quinoxaline bridged cavitands (QxCav) with the deepest cavities show the best selectivity for aromatic vapors. A comparison with polymer sensing layers, PECH and PIB, shows that cavitands have higher selectivity despite the fact that

the polymer layers were more than twice the thickness of the spin coated cavitated layers. Clearly, this selectivity arises from the unique structures of the cavitateds. Combined with the fact that cavitateds are robust synthetic receptors, they appear to be promising materials for the selective detection of chemical warfare agent vapors. Cavitateds for CW simulant vapors have been synthesized and testing is currently in progress.

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