Investigation of the Origin of Selectivity in Cavitand-Based Supramolecular Sensors

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Abstract: The sensing properties of functionalized cavitands have been studied by thin-film coating TMSR chemical sensors and by measuring their responses towards model analytes. We studied the relationship between the sensor performance, in terms of sensitivity and selectivity, and the molecular recognition properties of the cavitands. The Langmuir-like shape of the adsorption isotherm, obtained in the case of short-chain alcohols, demonstrated that selective binding can be achieved by the synergistic interactions of the cavity and the bridging PO_{in} groups. In the absence of these substituents, the peripheral alkyl chains necessary for the formation of highly permeable thin films attenuate the cavity effect because of nonspecific dispersion interactions. This completely overrides the response originating from molecular recognition. The same effect is observed when the PO groups are oriented outward from the cavity. The use of multivariate chemometrics and the study of the correlations between sensors sensitivity and analyte properties provided further evidence of molecular recognition phenomena, whose intensity is enhanced by the permanent free volume created by the rigid cavity surrounding the PO_{in} group.

Keywords: alcohols · cavitands · hydrogen bonding · molecular recognition · sensors

Introduction

In the last few years there has been a huge demand for the monitoring of different chemical environments, such as urban indoor and outdoor atmospheres, food aromas, and others. Chemical sensors are among the most promising devices to be exploited for these applications because they have the great advantage of allowing online measurement suitable to remote control.[1]

The structure of a generic chemical sensor can ideally be divided in two subunits: the sensing material and the transducer. The sensing material interacts with the chemical species present in the environment by changing some of its physicochemical properties, while the transducer transforms these variations into a readable signal, generally an electrical signal.

The sensor performance, in terms of sensitivity, reproducibility, and selectivity, strictly depends on the properties of the sensing materials. For this reason, a great effort has been made to develop sensing materials with improved properties.[2] However, whereas sensitivity, reproducibility, and stability are properties that need to satisified, selectivity needs to be further discussed.

From this point of view, the exploitation of organic compounds as sensing materials is particularly attractive. The progress made in designing synthetic receptors[3] allows sensor selectivity modulation towards different classes of compounds by mastering the weak interactions that occur between the sensing material and the analytes.

Among the large manifold of possibilities, host–guest multiple interactions, such as in crown ethers, cyclodextrins, calixarenes, and cavitands, look extremely appealing. The synthetic chemistry and solution-binding studies of these

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compounds is a well developed discipline; however, when these compounds are exploited in chemical sensors, we have to take into account that complexation with analytes occurs either at the solid–gas or solid–liquid interface where nonspecific interactions such as dispersion forces come into play.

In addition, it is necessary to ensure that the deposition process preserves both the occurrence and the efficiency of the selective interactions, since the thickness, morphology, permeability, and mechanical and chemical stability of the sensing material thin layer can influence both the interaction mechanism and the sensor responses. Frequently, functional groups are introduced into the molecular skeleton of receptor molecules to allow or to improve thin film depositions of sensing materials. All of these features should be addressed in the development of reliable chemical sensors.

Absolute selectivity, that is the ability to detect only a single analyte in any complex mixture, is needed when we must qualitatively and quantitatively detect a target compound, such as a toxin. On the other hand, it is only of limited help when we have to assess the quality of an indoor environment or to judge the edibility of a food sample, in which the complexity of the perceived odor in terms of number of molecular species and relative concentration is mostly unpredictable. For this reason a different concept of selective sensors was introduced in the 1980s.[4] In this new approach, the sensors should not be specific, but rather should respond to many chemical compounds with different affinities for each of them.[5] At the molecular level this approach requires the use of many partially selective receptors. These sensors should be used in an array configuration, which may make it possible to develop artificial olfaction systems capable of mimicking the olfaction systems of mammals.[6]

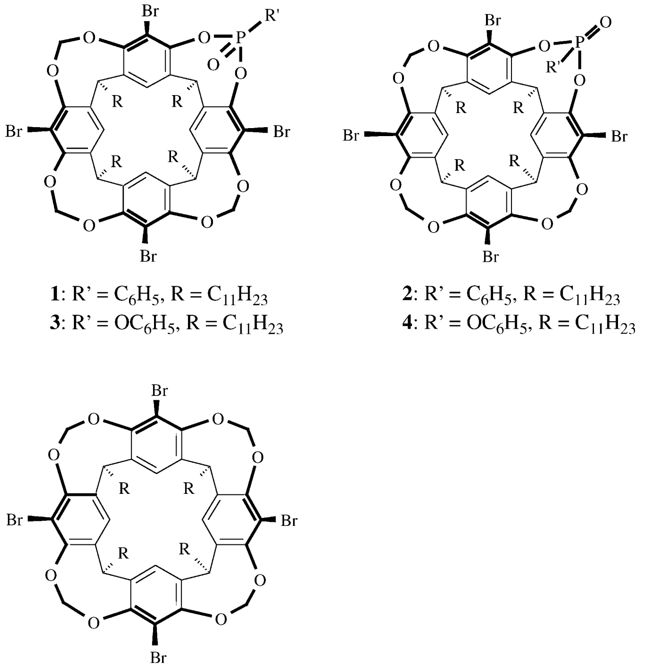
Although absolute selectivity is not strictly essential for many applications, orthogonality in the responses is highly desired. In this way, the sensor responses will not be completely correlated and the maximum of chemical information can be extracted by the sensor array, which can provide recognition and classification of the different measured matrices.[7]

In the last few years, we have been involved in the study of cavitand sensing properties.[8] These compounds exhibit remarkable properties as sensing materials, which can be finely tuned by synthetic modifications. High selectivity towards short-chain linear alcohols has been obtained by introducing an H-bond acceptor P=O group as a bridging unit at the upper rim of the receptor. Of the two diastereomers obtained, which either have the P=O group oriented inward (PO_{in}) or outward (PO_{out}) with respect to the cavity, only the PO_{in} version is capable of two synergistic interactions with the analytes, namely H-bonding with the PO and CH-π interactions with the cavity.[8d]

Herein, we elucidate the key factors affecting the sensing properties of phosphorus-bridged cavitands, focussing on selective intracavity complexation versus unselective extracavity absorption. These derivatives have been deposited onto thickness shear mode resonator (TSMR) transducers and their performances have been tested with a set of model analytes and interpreted in the frame of the linear sorption energy relationship model (LSER).

Experimental Section

Materials: The molecular structures of the compounds used as sensing materials are reported in Scheme 1. Cavitands **1**–**5** were prepared as previously reported.[8d] Spectroscopic characterization and elemental analyses of all of these compounds are consistent with the proposed structures. ACS grade pentane, benzene, triethylamine, methanol, ethanol, and 2-propanol were used without further purification.



1: R' = C_6H_5, R = $C_{11}H_{23}$
3: R' = OC_6H_5, R = $C_{11}H_{23}$

2: R' = C_6H_5, R = $C_{11}H_{23}$
4: R' = OC_6H_5, R = $C_{11}H_{23}$

5: R = $C_{11}H_{23}$

Scheme 1. Molecular structures of the cavitands employed as sensing materials.

Sensors: TSMRs are AT-cut quartzes (Electroquartz) with a fundamental frequency of 20 MHz; the quartz crystal diameter is 7.0 mm, the gold electrodes diameter is 5.0 mm. Thin films of sensing materials were deposited by spray-coating technique on both sides of TSMR quartz disks from 10^{-3}M $CHCl_3$ solution. TSMRs sensors are mass transducers[9] for which the resonance frequency shift is linearly correlated to mass loading according to the Sauerbrey equation [Eq. (1)].[10]

$$\Delta f = -k_q \delta m \tag{1}$$

The quartz constant was experimentally estimated to be $k_q = 4.8\,\mathrm{Hz\,ng^{-1}}$ with a mass resolution of 0.2 ng, based on a minimum reliable frequency measurement of 1 Hz. TSMRs were connected to an oscillator circuit during the deposition process and the frequency decrease was measured with a frequency counter. A frequency variation of about 60 KHz was obtained for all deposited layers.

Coated TSMRs were housed in a 10-mL stainless steel measurement chamber and were maintained at the constant temperature of 298 K. Each sensor was connected to an electronic oscillator circuit and frequency variations were measured by means of an integrated frequency counter.

Organic vapors of the different analytes were generated by bubbling an N_2 stream into a liquid sample of the compounds. The concentration of the volatile organic compound (VOC) in these saturated vapors was calculated by the Antoine's law.[11] These saturated vapors were diluted with nitrogen and allowed to flow into the sensor chamber by a computer-driven four channel mass-flow controller (MKS). The flow rate was kept at a constant value of 200 mL min^{-1}. The sensors were exposed to the following VOCs: *n*-pentane, methanol, ethanol, isopropanol, benzene, and triethylamine. The maximum analyte concentration was kept at 20% of the saturation pressure in order to avoid condensation effects.

Data analysis: To study the influence of molecular modifications on sensing properties it was useful to consider the whole set of sensors as members of an array and to study their collective properties by using multivariate chemometrics. In particular, the classification of different analytes was investigated in order to study which sensor, and then which molecular configuration, could play a dominant role in the identification of every single analyte. For this purpose, principal component analysis (PCA) was utilized.[12]

PCA offers the advantage of displaying the results in a representation plot in which most of the data variance is preserved and the data distribution and relative importance of each sensor in the array are depicted. All calculations were performed in Matlab.

Results and Discussion

The preparation of the sensing material is the first step of chemical sensor fabrication. One advantage of supramolecular receptors is that they can be rationally designed according to the class of analytes to be detected.

The next step is matching the sensing material with the transducer. Usually, this operation consists of a thin film deposition onto the sensitive surface of the transducer. TSMRs are particularly valuable for these studies because they respond to all material – analyte interactions that lead to mass variations, when they are not accompanied by strain – stress deformations of the layer. Furthermore, the relationship between mass variation and the sensor signal being linear, the transducer does not influence the properties of the sensing layers; this allows for a straightforward comparison between different sensing layers. The only precaution necessary in comparing different sensing materials concerns control of the thickness of the deposited film in order to keep the influence on the sensor signal from the limited stiffness of the organic films at a negligible level.

The introduction of long alkyl chains at the lower rim was adopted to increase the permeability of the cavitand layers. For this reason, questions arose about the location of the sorbed vapor, which can be located either in the preorganized cavities at the upper rim or among the alkyl chains at the lower rim. Because the selectivity patterns of several cavitands or other receptors (cyclophanes, cyclodextrins) towards different organic vapors often resemble those of polymeric sensing materials, doubts about the real influence of host – guest interactions have been raised.[13] Related to this issue is the selectivity mechanism, which in many cases can be correlated to dispersion interactions rather than to specific host – guest interactions. Translated into molecular terms this means analyte inclusion within the lower rim alkyl chains or in the lattice voids of the layer instead of complexation within the cavity. Indeed, the mere presence of a preorganized cavity in the receptor does not guarantee selectivity in gas sensing,[14] since on transfer from the gas phase to the condensed phase the analyte experiences a net gain in dispersion interactions, which often override weak host – guest interactions. Geometrically defined and energetically sizable specific interactions between the receptor and the analyte are needed.

We have recently proven that this result can be achieved using a synergistic combination of hydrogen bonding and CH – π interactions.[8d] Comparison of the responses of isomeric PO_{in} and PO_{out} cavitands **1** – **4** towards linear alcohols clearly indicates that the presence of cooperative interactions is the key for achieving selectivity. The selectivity pattern observed for the PO_{in} cavitands **1** and **3** deviates significantly from that of polymers like PIB and PECH, while that of unselective PO_{out} isomers **2** and **4** correlates nicely.

Here we report a detailed analysis of the molecular recognition phenomenon in gas sensing based on the adsorption isotherms of selected cavitands towards different analytes. Figures 1 – 6 depict the responses of five different cavitand-coated sensors to increasing concentrations of the following analytes: methanol, ethanol, isopropanol, benzene, pentane, and triethylamine. Methylene-bridged cavitand **5**, presenting a 4.15 Å deep cavity,[15] has been added to the phosphonate/phosphate cavitand isomers **1** – **4** to assess the influence of CH – π interactions in the absence of hydrogen bonding.

Langmuir-type isotherms are observed only for the PO_{in} isomers **1** and **3** exposed to methanol, ethanol, and isopropanol vapors (Figure 1, Figure 2 and Figure 3), while the other three cavitand coatings show linear responses under the same conditions. The exponential trend at low vapor concentrations is the result of an effective complexation between the analyte and the cavitand receptor. Once the receptor layer becomes saturated, the isotherm flattens assuming a linear course. Moreover, the better H-bond acceptor capability of phosphonates versus phosphates[16] is reflected in the higher responses of **1** versus **3**. The same trend has been observed in a different experimental set up: two sets of sensors were prepared by coating quartzes with different amounts of cavitands **1** – **5** (10 KHz and 20 KHz respectively) and exposed to 1500 ppm

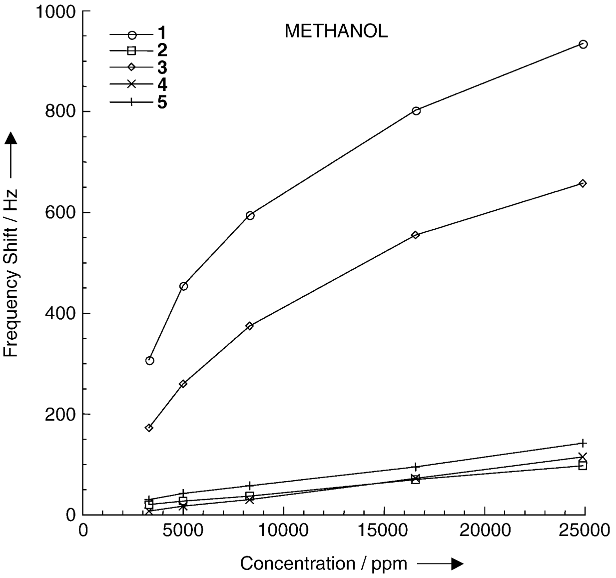


Figure 1. Experimental isotherms for modified TMSR sensors **1** – **5** in the presence of methanol.

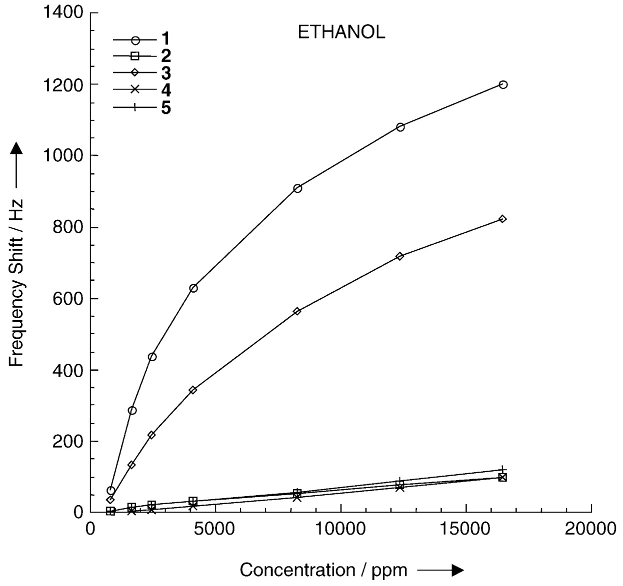


Figure 2. Experimental isotherms for modified TMSR sensors **1**–**5** in the presence of ethanol.

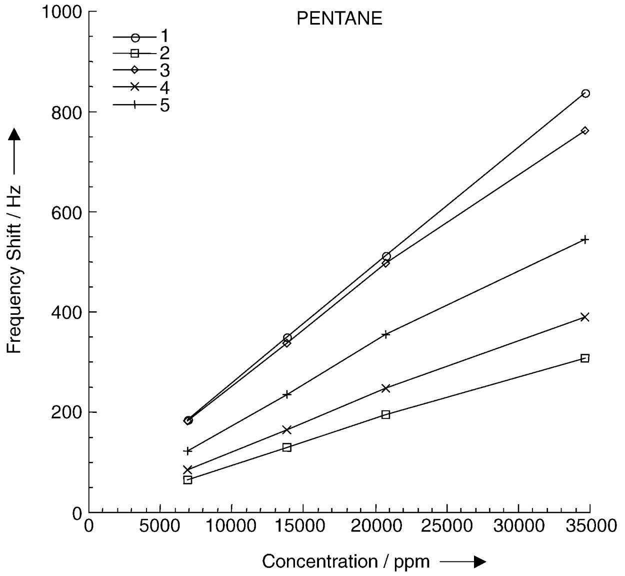


Figure 4. Experimental isotherms for modified TMSR sensors **1**–**5** in the presence of pentane.

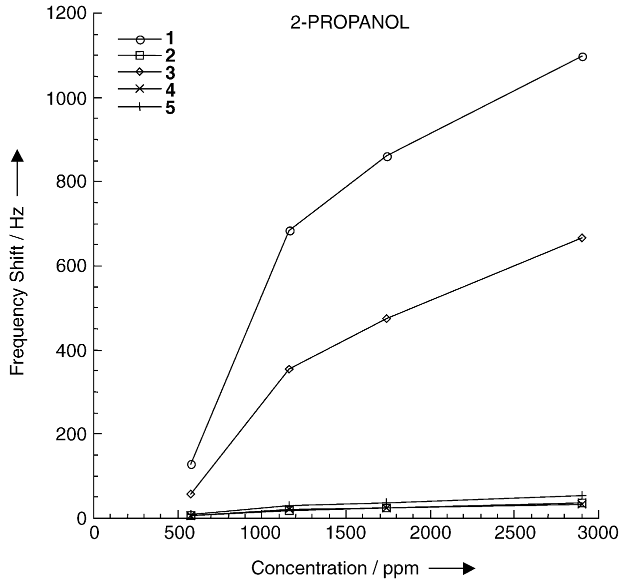


Figure 3. Experimental isotherms for modified TMSR sensors **1**–**5** in the presence of 2-propanol.

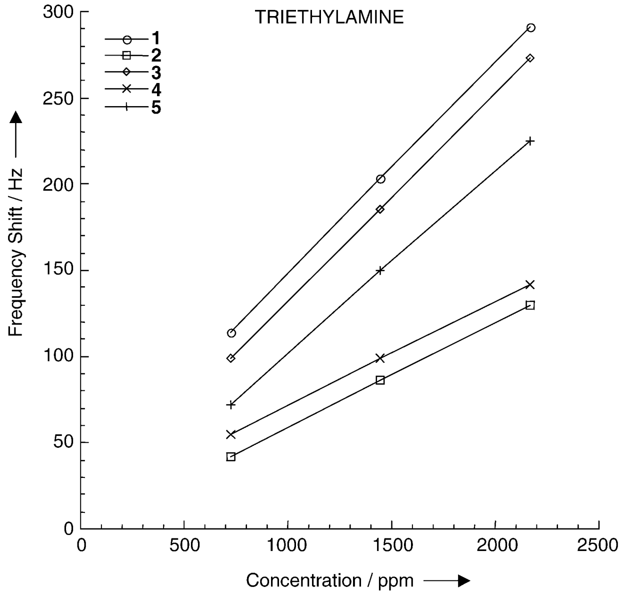


Figure 5. Experimental isotherms for modified TMSR sensors **1**–**5** in the presence of triethylamine.

of ethanol. The selective layers of **1** and **3** increased their responses four times upon doubling the coating, while the unselective layers of **2**, **4**, and **5** just doubled them.

In the cases of pentane, triethylamine, and benzene, all sensors responded in a linear fashion, differentiating their sensitivity in the order: **1** > **3** > **5** > **2**,**4** (Figure 4, Figure 5 and Figure 6). This trend can be rationalized by comparing the exposed surfaces of the receptors, assuming that no specific interactions are operating in the cases of **1**–**5** with these three analytes. Occlusion of the cavity by the aryl substituents on the PO group in the cases of **2** and **4** drastically reduces the available surface for unspecific dispersion interactions with the analytes. Cavitand **5** lies in an intermediate situation presenting a wide concave surface. Cavitands **1** and **3** offer the largest surface available having a concave cavity with one appended substituent.

The overall trend can be rationalized assuming a dual mode interaction:[17] the energetically more favorable cavity binding dominates at low analyte concentration, whereas nonspecific extracavity absorption is preponderant at high analyte concentration. As a consequence, when the exponential trend is absent (Figures 4–6), the molecular recognition events are either absent or negligible.

To further confirm this hypothesis, we investigated the sensitivity of the five cavitands. For some sensors, a nonlinear behavior between sensor response and concentration is expected, in particular, for those cavitands functionalized to improve hydrogen-bonding interactions. For these sensors the

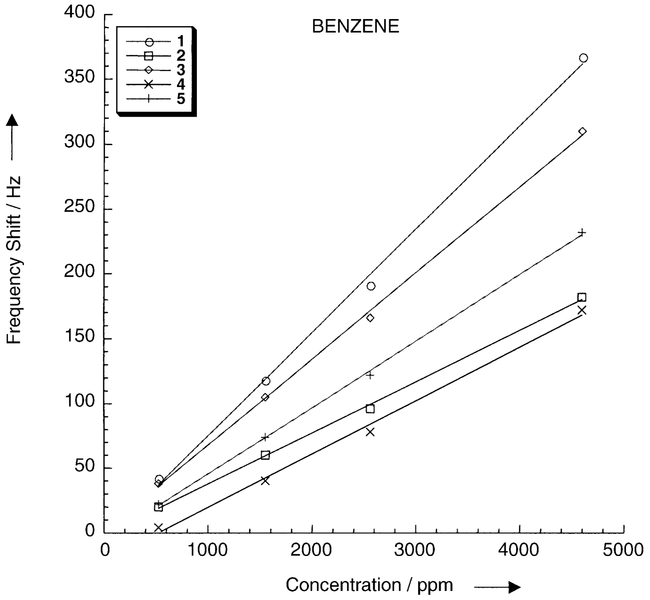


Figure 6. Experimental isotherms for modified TMSR sensors **1**–**5** in the presence of benzene.

sensitivity, defined as $S = \frac{\Delta f}{\Delta c}$, is a function of the concentration with its maximum value at low concentrations. This behavior is easily explained considering that, the number of interaction sites being limited, the isotherm is expected to be steeper at low concentrations and to have a lower slope at higher concentrations when most of the interaction sites are occupied. These behaviors have been recorded several times, in cases where an absorbing layer also has specific interaction sites.[18, 19] To take account of this fact and also to consider the sensor sensitivity at its best, the sensitivity of these sensors was calculated at low concentrations where its value is higher. The results obtained are reported in Table 1.

Table 1. Sensitivities[a] of cavitands **1**–**5** toward different analytes.

Analyte	Cavitand 1 S_1 [Hz ppm^{-1}]	Cavitand 2 S_2 [Hz ppm^{-1}]	Cavitand 3 S_3 [Hz ppm^{-1}]	Cavitand 4 S_4 [Hz ppm^{-1}]	Cavitand 5 S_5 [Hz ppm^{-1}]
methanol	0.088	0.004	0.053	0.005	0.005
ethanol	0.226	0.006	0.112	0.006	0.007
2-propanol	0.955	0.012	0.509	0.011	0.017
pentane	0.023	0.008	0.022	0.011	0.015
triethylamine	0.122	0.060	0.120	0.060	0.106
benzene	0.079	0.039	0.066	0.041	0.051

[a] These values are extrapolated from the fitting of the isotherms.

In the case of nonspecific interactions, the sensitivity is constant over the entire concentration range because the adsorption mechanism is regulated by Henry's law. This is confirmed for cavitands **2** and **4**. The same behavior is present for cavitands **1** and **3** in the case of benzene, pentane, and triethylamine, showing that molecular recognition is not present. On the other hand, cavitands **1** and **3** show higher sensitivities for alcohols at low concentrations and a significant decrease at higher concentrations. This result confirms the presence of specific interactions at lower concentrations, where the adsorption interactions are dominated by the synergistic cavity hydrogen-bonding sensing mechanism, while at higher concentrations the vast majority of the molecular recognition sites are occupied and only dispersion interactions are active for analyte binding.

The different magnitudes of the sensitivities of cavitands **1** and **3** towards the three alcohols is a direct effect of the mass transduction performed by the TSMR, where the frequency shift (Δf) is directly proportional to the number of absorbed molecules multiplied by their molecular mass. The sensitivities of **1** and **3** to alcohols is then linearly proportional to the molecular mass of the alcohol as shown in Figure 7.

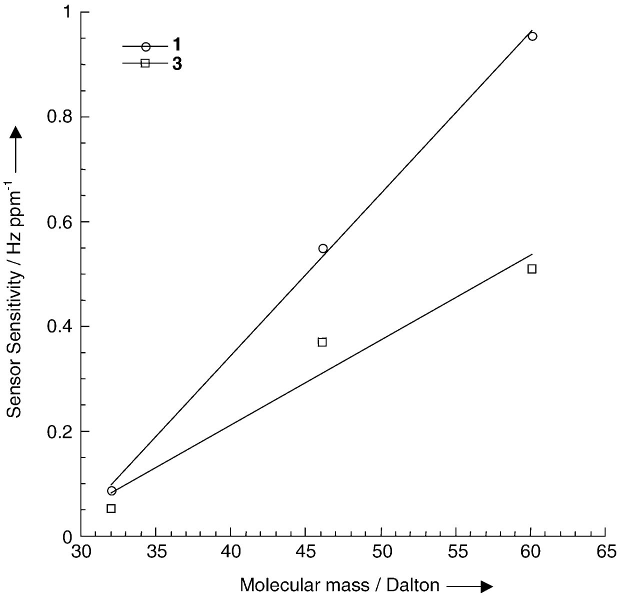


Figure 7. Dependence of sensor sensitivity S on analyte molecular weight for cavitands **1** and **3**.

A quantitative expression of the importance of these synergic cavity hydrogen-bonding interactions for the sensing behavior can be obtained by evaluating the increase in sensitivity expressed as the sensitivity ratio between PO_{in}/PO_{out} functionalized cavitands. In Table 2 we report the results obtained. Again, we observe a negligible difference of sensitivity for benzene, pentane, and triethyl-

Table 2. Selected sensitivity ratios.

Analyte	S_1/S_2	S_3/S_4	S_5/S_2
methanol	22.0	10.6	1.2
ethanol	37.7	18.7	1.2
2-propanol	79.6	46.3	1.4
pentane	2.9	2.0	1.9
triethylamine	2.0	2.0	1.8
benzene	2.0	1.6	1.3

amine, where the molecular recognition phenomenon is not present, while a significant increase is observed in the case of alcohols, up to 80 times for isopropanol in the case of S_1 versus S_2. The comparison between S_5 and S_2 indicates a limited effect on selectivity of the preorganized cavity alone.

We further investigated the influence of peripheral alkyl groups and molecular recognition phenomena on the sensing properties of the corresponding sensors by exposing the five coated TSMRs to variable concentrations of the same analytes and analyzing the results by data analysis techniques.

A deeper insight about the relationship between sensor response and interaction mechanism can be gained by considering the way in which each volatile compound is expected to interact when in contact with a solid phase. In our case the material is deposited as amorphous solid, as shown by optical microscopy experiments.[20] These interactions can be modeled using the linear sorption energy relationship model (LSER).[21]

According to this method and under the hypothesis of weak solubility interactions, the logarithm of the partition coefficient of a sorbent layer with respect to a certain volatile species is the linear combination of five terms expressing the intensity of five basic interaction mechanisms. They are in the order: polarizability, dipolarity, H-bond acidity and basicity, and the solubility terms related to dispersion interactions.

The relation can be expressed as Equation (2), in which K_p is the layer partition coefficient and $R_2, \pi_2^H, \alpha_2^H, \beta_2^H$, and $\log L^{16}$ are the solute parameters of the volatile compounds and *r*, *s*, *a*, *b*, and *l* are coefficients relative to the absorbing material.

$$\log K_p = c + r \cdot R_2 + s \cdot \pi_2^H + a \cdot \alpha_2^H + b \cdot \beta_2^H + l \cdot \log L^{16} \qquad (2)$$

The values of the five parameters for the six volatile compounds we considered are listed in Table 3.[21] All these compounds have a strong solubility interaction, nonetheless

Table 3. LSER analyte vapor solvation parameters.

Analyte	R	π	α	β	$\log L^{16}$
methanol	0.278	0.44	0.43	0.47	0.97
ethanol	0.246	0.42	0.37	0.48	1.485
2-propanol	0.236	0.42	0.37	0.48	2.031
pentane	0.000	0.00	0.00	0.00	2.162
triethylamine	0.101	0.15	0.00	0.79	3.04
benzene	0.610	0.52	0.00	0.14	2.786

Figures 1–6 highlight different sensitivities depending on the molecular configuration of the cavitands. This suggests that the differences between the other four interaction terms are essential in studying their interaction with cavitands. It is worth noting that pentane interacts only through solubility and benzene has a very small hydrogen-bonding term, while H-bonding is strongly present for alcohols.

For a TSMR sensor, the partition coefficient turned out to be proportional to the overall sensitivity of the sensor.[22] Consequently, to study the qualitative dependence of sensor response on the features of the volatile compounds, the partition coefficient can easily be replaced by the sensor sensitivity. Table 4 reports the linear correlation coefficients between the logarithm of the sensor sensitivity and each LSER parameter.

Table 4. LSER regression coefficients for cavitands **1**–**5**.

LSER coefficients	**1**	**2**	**3**	**4**	**5**
r	0.17	0.23	0.14	0.19	0.10
s	0.53	−0.10	0.44	−0.18	−0.24
a	0.60	−0.73	0.44	−0.80	−0.79
b	0.55	0.23	0.59	0.15	0.19
l	−0.11	0.95	0.07	0.96	0.97

The responses of cavitands **2**, **4**, and **5** are strongly correlated with the dispersion interaction term. In Figure 8 the sensitivities of these cavitands towards all analytes are plotted versus the solvation parameter $\log L^{16}$, which measures the importance of dispersion interactions. The almost linear relationship demonstrates that the sensing mechanism in these sensors is driven by dispersion interactions. This result confirms the assumption that nonspecific interactions are operating in the sensing mechanism of such receptors. On the other hand, in the cases of cavitands **1** and **3**, the functionalization increases the dependence of sensor sensitivity on hydrogen-bonding and polarization parameters, again confirming that these interactions dominate in the sensing mechanism of these compounds, and the selectivity towards alcohols is a consequence. Furthermore, the functionalization effect is so strong as to completely hide the dependence on the dispersion interaction, whose correlation coefficients become negligible.

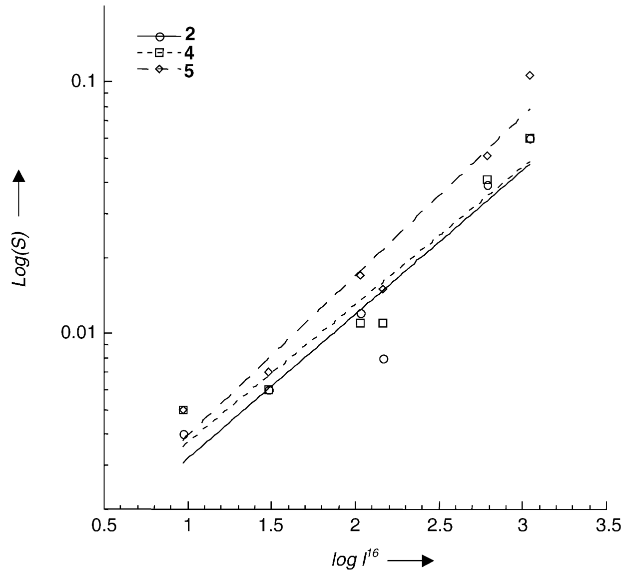


Figure 8. Plots of sensor sensitivity S of cavitands **2**, **4**, and **5** (on logarithmic scale) versus $\log L^{16}$ of the six analytes.

At this point it is worth considering why the hydrogen-bonding ability of PO_{out} in **2** and **4** is totally ineffective in alcohol detection. A possible explanation could be related to the different environment experienced by the PO_{in} and PO_{out} groups. For the PO_{in} isomers **1** and **3** the presence of a rigid, preorganized cavity embracing the PO group eliminates the need for generating a void in the lattice for the incoming analyte. On the other hand, the PO group in **2** and **4** is on the exterior surface of the receptor, in close contact to other molecules. The analyte must carve out a space to hydrogen-bond with the PO_{out}, which is energetically demanding. Therefore, we propose that the role played by the cavity is twofold: it complexes the analyte through $CH-\pi$ interactions, and it generates a permanent "free volume" in the PO_{in} neighbor, which facilitates hydrogen bonding.[23]

For the sake of completeness and to gain a different insight into the differences in sensor behavior resulting from the structural modifications of the cavitands, the sensor data have been treated from a multivariate point of view. In this way, the cooperative effects of the different materials are studied and the characteristics of each sensor are easily compared with those of the other sensors. The most simple and useful approach to this is to consider the principal component analysis (PCA) of the matrix formed by all the measurements. Such a matrix has a number of columns equal to the number of sensors and a number of rows equal to the number of measurements.

Each measure can be thought as an element of a vector space whose dimension is the number of sensors. In such a space, PCA defines a representation subspace of reduced dimensionality in which most of the data variance is preserved. The linear projections of the measures in the representation space are called scores, and the coordinates of the original axis (the sensors) are the loadings. In most of the cases, as will be explained later, the representation space is a plane, making the graphical representation of high-dimension data possible.

Figure 9 shows, in the same plot, the scores and the loadings in the plane identified by the first two principal components of the sensor dataset. More than 99% of the total data variance is explained in this plot. Measurements of different compounds are arranged along paths that follow concentration. The first evidence in this plot is represented by the different directions of the three alcohols with respect to the rest of the compounds. This demonstrates that the interactions of triethylamine, pentane, and benzene with this sensor array are substantially similar, while for alcohols another kind of interaction takes place.

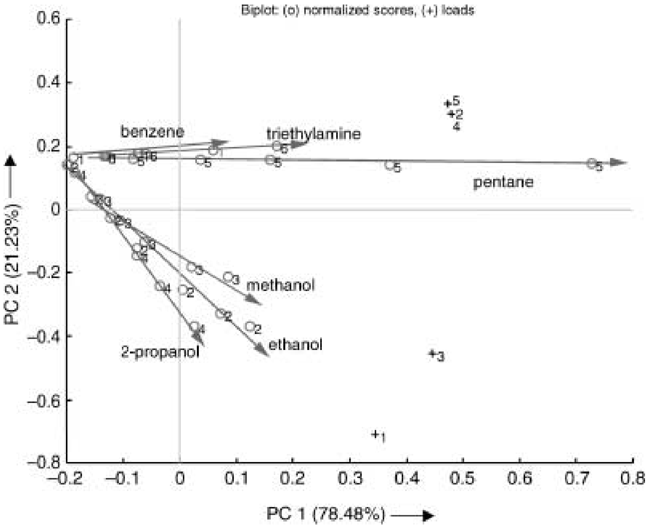


Figure 9. Biplot representation of scores and loadings of the PCA of all the collected sensor responses. Scores are labeled with circles and the number identifies the volatile compound. Multiple points for each compound are related to different concentrations and the arrows indicate the direction of increasing concentration. Loadings are labeled with crosses and referred to the cavitand numbering as in the text.

The position of the sensors is also of great interest. Cavitands **1** and **3** lie in the same direction of the alcohol, in accordance with their peculiar selectivity towards this species, while cavitands **2**, **4**, and **5** behave similarly and are thus superimposed on the plot.

Multivariate analysis indicates that this array can selectively identify the alcohols with respect to other compounds. This identification overcomes the concentration problem, since these sensors, although oriented towards one molecular class, still preserve a residual sensitivity towards many other species. This behavior makes the response of any one such sensors ambiguous, because the same sensor signal can correspond either to an alcohol at low concentration or to any other species at higher concentration. The use of the array of functionalized and nonfunctionalized cavitands allows the selective identification of alcohol, regardless of analyte concentration, since alcohols and other species evolve, with concentration, along well-defined directions.

Conclusion

Herein, we investigated the properties of chemical sensors based on the mass transduction of solid-state films of cavitands. The basic resorcinarene framework is generally functionalized by the introduction of alkyl chains at the lower rim, to give a sensing material with acceptable sensitivity and response time. On the other hand, the presence of these alkyl chains results in an increase of dispersion interactions that override the selectivity interactions attributed to the aromatic cavity, leading to unselective sensors.

The introduction of phosphate or phosphonate substituents at the upper rim of the resorcinarene skeleton, with the PO groups oriented towards the cavity, allows synergistic H-bonding/π-cavity interactions, which give rise to an effective molecular recognition of alcohols. The molecular recognition effect for these molecules becomes so important as to make negligible, in the low concentration regime, the dependence of the amount of absorbed molecules on the dispersion interactions, as demonstrated by adsorption isotherm shape and sensitivity analysis.

On the other hand, the presence of the same PO group, but in an outward direction with respect to the cavity, does not qualitatively change the interactions between volatile compounds and absorbing film, which are completely dominated by the dispersion interaction term. This last finding implies a hitherto unrevealed role of the cavity in providing the free volume pivotal for effective hydrogen bonding.

The application of such sensors in an array configuration, with the consequent multivariate analysis of sensor response through the PCA, gave rise to evidence that an array composed of both PO_{in}- and PO_{out}-functionalized cavitands can lead to the selective identification, at any concentration, of alcohols from other substances.

Overall, our results are relevant because they highlight possible solutions to the general problem of minimizing the undesired dispersion interactions among analytes and sensing materials. Two major alternatives can be envisioned: 1) boosting specific responses by favoring the access of analytes to the receptor sites, which requires the presence of permanent free volume around each interaction site in the solid state, using receptors with enclosed cavities permeable only to the desired analytes; and 2) eliminating the need for peripheral alkyl chains by resorting to nanoporous materials equipped with appropriate receptor sites.[24] Both approaches are currently being pursued in our laboratories.

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