Supramolecular Sensors

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Highly Selective Chemical Vapor Sensing by Molecular Recognition: Specific Detection of C_1–C_4 Alcohols with a Fluorescent Phosphonate Cavitand**

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In the last few years there has been a huge demand to monitor different chemical species in the vapor phase, such as environmental pollutants, hazardous chemicals, food aromas, explosives, and volatiles in breath for disease diagnosis.[1] Chemical vapor sensors are among the most promising devices to be exploited for these applications, because they have the great advantage of allowing an online measure suitable for remote control.[2] In this context, the need to develop sensors specific for different classes of analytes is well-recognized and confirmed by the considerable research efforts spent for the preparation of more and more efficient devices.[3] The crucial parameter to define the success of a given sensor is therefore selectivity,[4] and for this reason the strategy to prepare the sensing material following the principle of supramolecular chemistry has quickly gained increasing importance.[5] However, the realization of selective chemical vapor sensors requires particular attention since they operate at the gas–solid interface. Any given analyte, upon moving from the vapor to the solid phase, experiences a dramatic increase in non-specific dispersion interactions, which tend to override any specific complexation event responsible for the selective responses.[6] As a result, the sensor selectivity drops and false positive responses soar. A possible solution to this general problem relies on transduction modes activated exclusively by the molecular recognition event.

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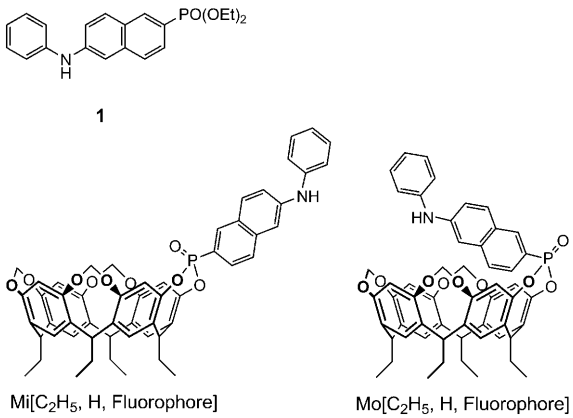
Following this approach, we present herein a new solid-state fluorescent sensor based on phosphonate cavitand Mi[C_2H_5, H, fluorophore][7] (Scheme 1) for detecting short-chain alcohols in the gas phase. Phosphonate cavitands are



Scheme 1. Structure of fluorescent model compound **1** and the fluorescent phosphonate cavitands Mi and Mo.

molecular receptors that present one or more P^V moieties as bridging units.[7] In previous studies, we have shown that there are two key factors affecting the sensing performances of mono-,[8] di-,[9] and tetraphosphonate[10] cavitands toward alcohols: 1) the simultaneous presence of hydrogen bonding with one of the P=O groups and CH–π interactions with the π-basic cavity, which require an inward orientation of the P=O bridges; and 2) a cavity that provides a permanent free volume for the analyte around the inward P=O groups, which is pivotal for effective hydrogen bonding.[5d,10] Increasing the number of inward-facing P=O groups enhances the sensor responses through the entropic stabilization of host–guest complexes, but does not change the observed selectivity trend.

At first, a systematic study was undertaken to assess the complexation properties of phosphonate cavitands towards alcohols in the solid state. The compact tetraphosphonate cavitand Tiiii[H, CH_3, CH_3] was chosen as host for its tendency to crystallize. Crystallization trials of this cavitand were performed by the vapor diffusion method with sitting drops in Linbro multiwell plates containing trifluoroethanol (TFE) as solvent. The addition of a short-chain alcohol in the reservoir solution, through vapor diffusion in the drop, allowed the easy and fast growth of monoclinic crystals of

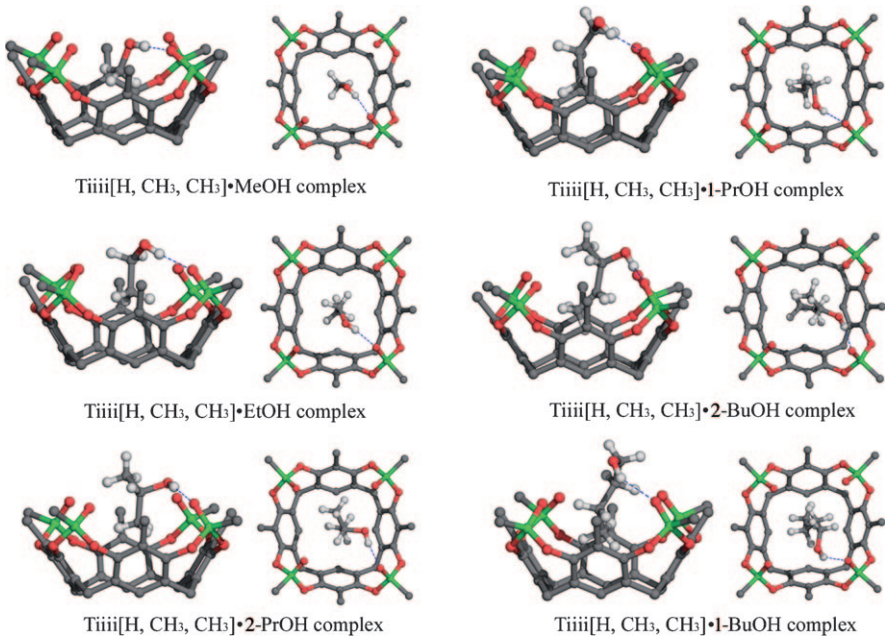


Figure 1. Top and side views of the crystal structures of the six Tiiii[H, CH_3, CH_3]·alcohol complexes.

the corresponding host–guest complex. A whole series of isomorphic crystal structures of the TFE disolvate of C_1–C_4 alcohol–cavitand complexes were obtained (Figure 1). All six host–guest complexes present the same interaction pattern: an H-bond between the alcoholic OH group and one of the P=O units, and CH–π contacts between the π-rich cavity and one methyl group of the alkyl chain. The relevant geometric parameters describing the host–guest interaction are reported in Table 1. In the case of 1-butanol, the contemporary onset of

Table 1: Geometric parameters describing the host–guest interaction in C_1–C_4 alcohol–cavitand complexes.[a]

Alcohol	H-bond [Å]	O_{alc} oop [Å]	$CH_{3\,alc}$ oop [Å]
MeOH	2.704 (4)	0.039 (3)	−1.264 (4)
EtOH	2.765 (9)	1.150 (3)	−1.028 (4)
2-PrOH	2.816 (9)	0.926 (3)	−0.964 (4)
1-PrOH	2.730 (3)	1.409 (3)	−1.341 (4)
2-BuOH	2.75 (1)	1.357 (8)	−1.43 (1)
1-BuOH	2.85 (1)	1.926 (7)	−1.521 (7)

[a] Hydrogen-bond distances ($O_{alcohol}$···O=P) and distances of the hydroxy and methyl groups from the mean plane of oxygen atoms of P=O groups (out-of-plane, oop) are given. Atoms inside the cavity have a negative sign for the oop distances.

both interactions with the cavitand requires the deep insertion of the methyl group of the guest into the cavity and the weakening of the H-bond. The presence of a single additional methylene unit is sufficient to completely suppress the crystallization process of the complex, as observed in the case of 1-pentanol (Supporting Information, Figure S8).

The solid-state study clearly indicates that the two interactions responsible for the high selectivity of phosphonate cavitands towards alcohols occur simultaneously only in the C_1–C_4 alcohol series. Taken alone, none of them is sufficient to bind alcohols in the solid state. This result can be extended to the case of mono and diphosphonate cavitands, as their interaction mode with alcohols in the solid state is the same.[5d]

The next step was the selection of a transduction mechanism activated exclusively by this specific complexation mode to suppress the contribution of dispersion interactions to the overall response registered by QCM (quartz crystal microbalance) transducers.[6b] It is well known that, among the different sensors, those based on luminescence present many advantages, such as high sensitivity, low cost, ease of operation, and versatility.[3,11,12] The introduction of a fluorescent moiety on the receptor was necessary because the absorbance and fluorescence of the phosphonate cavitand family is too far in the UV region to be used for practical applications.[13] We chose to introduce at the phosphonate site a fluorophore, similar to the commercial 2-anilinonaphthalene-6-sulfonic acid (2,6-ANS), because of the charge-transfer character of its excited state. The rationale of this design was based on the belief that the formation of the hydrogen bond between the P=O and the alcohol OH group could decrease the electronic density on the phosphorus atom to a such an extent to modify the energy of excited state of the fluorophore. As in the excited state of 2,6-ANS a charge transfer from the aniline to the naphthalene moiety occurs, and for this reason the formation of the hydrogen bond was expected to make the charge transfer easier, leading to a red-shift of the emission band. This design was also conceived to offer a high specificity, as only the formation of a hydrogen bond could cause such a spectral shift. A single P=O unit was introduced on the cavitand to funnel the H-bond perturbation on a single site, to maximize the desired red-shift.[14] Monophosphonate cavitands offer the additional advantage of being water insensitive, as at least two P=O units are necessary to bind water efficiently.[10,15]

The target cavitand Mi[C_2H_5, H, fluorophore], from now onward referred to as Mi (Scheme 1), which presents at the upper rim the inward oriented P=O and three methylene bridges, was synthesized by introducing the fluorescent phosphonate moiety on a trimethylene-bridged resorcinarene[16] (see the Supporting Information for details of the preparation). The out isomer, Mo, obtained as a byproduct in the last step, was used as control system to exclude unspecific responses, and to demonstrate the need of the inward orientation of the P=O unit to synergistically activate both H-bonding and CH–π interactions.

The identification of the two isomers was achieved by ^1H and ^{31}P NMR spectroscopy. The ^1H NMR spectrum shows an upfield shift of the resonances belonging to the naphtalenic

moiety oriented inside the cavity in Mo, which is the result of the shielding effect exerted by the aromatic rings of the resorcinarene skeleton. For the same reason, the ^{31}P NMR spectrum of Mo also presents a significant upfield shift compared to Mi, as already reported by Dutasta et al.[17]

The fluorescent model compound **1**, synthesized in two steps starting from aniline and 6-bromo-2-naphthol (see the Supporting Information), was used as a model system to demonstrate the importance of the cavity surrounding the P=O unit in the recognition event.

PVC thin films containing 0.2 % w/w of cavitands Mi, Mo, and model compound **1** were deposited on glass substrates by spin coating. Dioctyl sebacate was added to these matrixes as plasticizer before deposition to enhance the layer permeability. To measure the surface fluorescence of a solid substrate subject to a continuous gas flow, we designed a cell with some special features (Supporting Information, Figure S2,S3). The orientation of the cell was optimized to minimize the reflection of the excitation light and to maximize the fluorescence signal. An attenuator filter was used to diminish the number of incoming photon to decrease problems related to photochemical stability, thus allowing long measurements in continuous flow. The single-wavelength emission was monitored at 460 nm, where the highest intensity excursion is observed upon complexation.

Upon excitation at 350 nm, the Mi film showed an intense broad and unstructured band emission with a maximum at 414 nm. Upon exposure to different alcohols, the maximum of this band was red-shifted by 5 nm, with a more pronounced difference in the tail of the spectrum (Supporting Information, Figure S4). Although relatively small, this difference was sufficient to monitor the concentration of the alcohols in the gas phase. Figure 2 shows the profile of the fluorescence intensity of a PVC film containing Mi exposed to a flux of pure N_2 alternated with a flux of ethanol in N_2 with an increasing concentration from 40 ppm to 630 ppm. The changes in fluorescence intensity were fast and fully reversible. Under the same conditions, films of Mo and of **1** showed negligible changes in the emission maximum. The relative fluorescence intensity changes of the Mi film exposed to different alcohols at various concentrations in N_2 are shown in Figure 3. The intensity changes were comparable for the whole C_1–C_4 alcohol series with the exception of 1-butanol (Figure 3), which caused lower responses. This result implies that its H-bond with the P=O of Mi is less effective, as inferred by the crystal structure of Tiiii[H, CH_3, CH_3]·n-butanol.

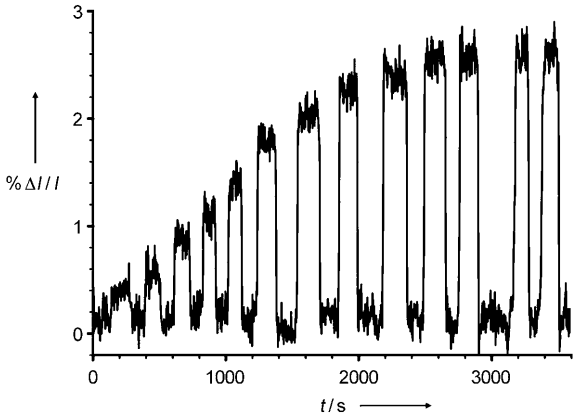


Figure 2. Fluorescence intensity (λ_{exc} = 350 nm, λ_{exc} = 460 nm) of a PVC film containing the receptor Mi subject to a pure N_2 flux alternated with a ethanol flux in N_2 with increasing concentration (from 40 to 630 ppm; see also Figure 3).

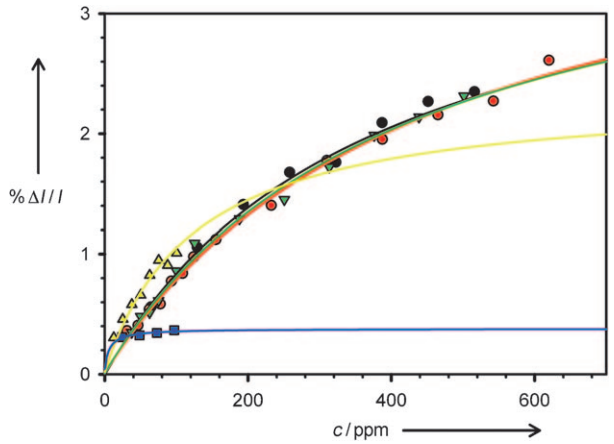


Figure 3. Relative fluorescence intensity changes (λ_{exc} = 350 nm, λ_{exc} = 460 nm) of a PVC film containing the receptor Mi exposed to different alcohols in N_2: black trace: methanol; red: ethanol; green: 1-propanol; yellow: 2-butanol; blue: 1-butanol.

The histograms of Figure 4 are even more revealing of the agreement between solid-state structures and sensor responses. The Mo film showed negligible responses to all C_1–C_4 alcohols, as expected owing to the disconnection of the two interaction modes. The drop in fluorescence intensity experienced by the Mi film exposed to 500 ppm of 1-butanol

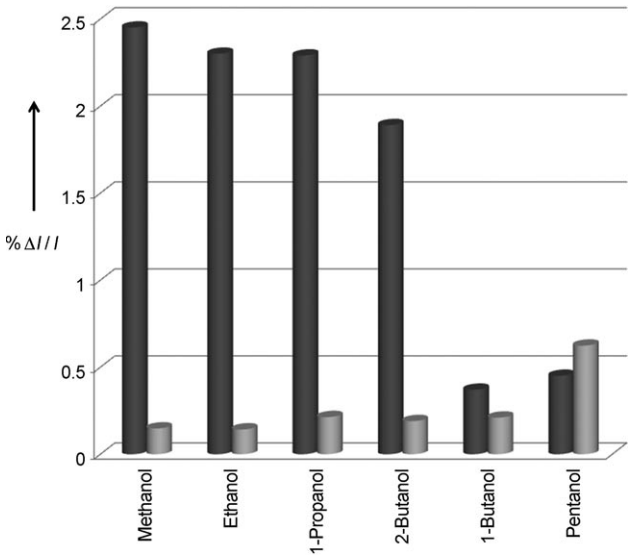


Figure 4. Relative fluorescence intensity changes (λ_{exc} = 350 nm, λ_{exc} = 460 nm) of PVC films containing the receptor Mi (dark gray) or Mo (light gray) exposed to different alcohols in N_2: methanol, ethanol, 1-propanol, 2-butanol, 1-butanol, 1-pentanol (500 ppm each).

and 1-pentanol is indicative of their limited complexation in the layer. The inversion of response between Mi and Mo films, observed in the case of 1-pentanol, supports the nonspecific origin of this fluorescence change, which can be attributed to extra-cavity H-bonding. The high sensor selectivity was demonstrated by comparing the responses of the Mi and Mo films to high concentrations of ethanol, acetone, and hydrocarbons: very low responses were obtained for both films in the case of acetone, n-pentane, and n-heptane, and for the Mo film in the case of ethanol (Supporting Information, Figure S5,S6). Competition experiments between ethanol and water showed that the low responses of the Mi layer to water are totally suppressed in the presence of ethanol vapors (Supporting Information, Figure S7).

In conclusion, this work demonstrates that it is possible to achieve high selectivity in chemical vapor sensing by harnessing the binding specificity of a cavitand receptor. The key requirement for transferring the molecular recognition properties from the solid-state to the gas–solid interface is the selection of the transduction mechanism, which must be turned on exclusively by the desired complexation mode with the analyte. In our case, the H-bonding of the alcohol to the P=O induces a detectable red-shift of the fluorescence emission of the 2,6-ANS fluorophore directly linked to the phosphonate acceptor. The source of selectivity can be dissected into three components. First, the ubiquitous nonspecific layer adsorption, being luminescence-silent, does not contribute to the overall response, as it did in QCM devices.[6b] Second, in the layer the intracavity H-bonding in Mi is highly favored over the extra-cavity form in Mo or **1**, owing to the cavity free-volume effect. Third, the synergy between CH–π interactions and H-bonding in Mi leads to a strong bias toward C_1–C_4 alcohol detection. The molecular level resolution of this last contribution is outstanding, as it allows the discrimination of alcohols on the basis of a single methylene unit difference. In this way, the responses owing to nonspecific interactions of the analytes and competitive binding by interferents have been almost completely removed. Although it is still necessary to improve the characteristics of the fluorescence moiety to increase sensitivity and the signal-to-noise ratio, we think that Mi is an important step forward to the design of more efficient chemical vapor sensors.

As most organic and polymer-based sensors detect analytes mainly on the basis of polarity,[6a] the approach described herein is a viable solution to the general problem of discriminating analytes by chemical class, rather than by polarity, in vapor sensing. This approach can be extended to many different classes of organic receptors, thus opening the way for the rational design of sensor materials as function of the analytes to be detected.

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