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In Search of the Ultimate Benzene Sensor: The EtQxBox Solution

Jakub Trzciński,[†,#] Roberta Pinalli,[†] Nicolò Riboni,[†] Alessandro Pedrini,[†] Federica Bianchi,[†,‡] Stefano Zampolli,[§] Ivan Elmi,[§] Chiara Massera,[†] Franco Ugozzoli,[∥] and Enrico Dalcanale*[,†]

[†]Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma and INSTM UdR Parma, Parco Area delle Scienze 17/A, 43124 Parma, Italy

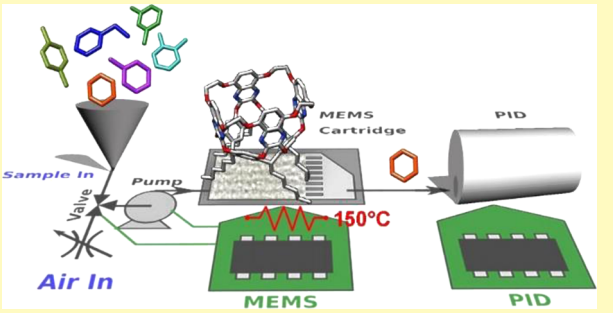
[‡]Centro Interdipartimentale per l'Energia e l'Ambiente, Università di Parma, Parco Area delle Scienze, Podere Campagna, 43124 Parma, Italy

[§]CNR-IMM Bologna, Via P. Gobetti 101, 40129 Bologna, Italy

[∥]Dipartimento di Ingegneria e Architettura, Università di Parma, Parco area delle Scienze 181/A, 43124 Parma, Italy

S *Supporting Information*

ABSTRACT: In this work we report a comprehensive study leading to the fabrication of a prototype sensor for environmental benzene monitoring. The required high selectivity and ppb-level sensitivity are obtained by coupling a silicon-integrated concentration unit containing the specifically designed **EtQxBox** cavitand to a miniaturized PID detector. In the resulting stand-alone sensor, the **EtQxBox** receptor acts at the same time as highly sensitive preconcentrator for BTEX and GC-like separation phase, allowing for the selective desorption of benzene over TEX. The binding energies of the complexes between EtQxBox and BTX are calculated through molecular mechanics calculations. The examination of the corresponding crystal structures confirms the trend determined by computational studies, with the number of C−H···N and CH···π interactions increasing from 6 to 9 along the series from benzene to *o*-xylene. The analytical performances of **EtQxBox** are experimentally tested via SPME, using the cavitand as fiber coating for BTEX monitoring in air. The cavitand EFs are noticeably higher than those obtained by using the commercial CAR-DVB-PDMS. The LOD and LOQ are calculated in the ng/m^3 range, outperforming the commercial available systems in BTEX adsorption. The desired selective desorption of benzene is achieved by applying a smart temperature program on the **EtQxBox** mesh, which starts releasing benzene at lower temperatures than TEX, as predicted by the calculated binding energies. The sensor performances are experimentally validated and ppb$_v$ level sensitivity toward the carcinogenic target aromatic benzene was demonstrated, as required for environmental benzene exposure monitoring in industrial applications and outdoor environment.



KEYWORDS: *benzene sensor, cavitands, preconcentrators, MEMS device, SPME fiber*

Selective monitoring of aromatic volatile organic compounds (VOC) in air, namely, BTEX (benzene, toluene, ethylbenzene and xylenes), is both socially relevant and technologically challenging. Highly selective carcinogenic benzene detection is particularly difficult, due to the concurrent requirements of high selectivity, caused by the presence of overwhelming amounts of other aromatic and aliphatic VOC, and extreme sensitivity (5 μg/m^3 is the present EU limit value for average exposure).[1]

BTEX are generally monitored by passive samplers and successive off-line analyses, resulting in data on averaged exposure levels.[2] Present real-time benzene monitoring systems for in-field environmental applications are bulky and expensive, being automatic high-end systems derived from laboratory instrumentation.[3,4] Recently, miniaturized versions of these systems have been proposed, but they are still limited in terms of response time and high power consumption.[5,6] Simple, low-cost systems based on solid-state gas sensors were recently proposed,[7] the most important being metal oxide sensors (MOS), quartz microbalances (QMB), surface acoustic waveguides (SAW), and polymeric sensors.[8] These technologies have often reached sufficient sensitivity for the detection of the target gas species, but generally their selectivity is limited and not sufficient for reliable quantification or early warning systems. Moreover, these are not viable solutions for distributed sensing, i.e., for stand-alone sensors for urban or industrial monitoring and personal warning systems. Multisite monitoring of benzene needs small, low consumption devices without maintenance service (i.e., carrier gas replacements for GC), amenable to be installed across urban and industrial settings.

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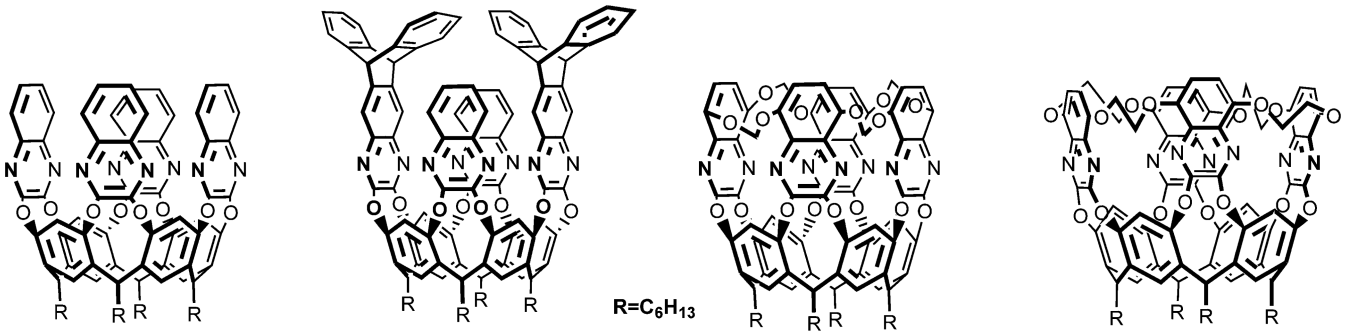
Chart 1. Molecular Structure of the Compounds Used in This Study



Recently, some companies launched on the market a hand-held gas detector, a photoionization detector (PID) equipped with a 9.8 eV lamp, with two-mode operation for the rapid detection of benzene and total aromatic compounds (TAC).[9] The default TAC mode screens out all the aliphatic compounds which have an ionization potential higher than 10.0 eV, leaving just the TAC whose ionization potential is below 10.0 eV. If the TAC measurements exceed safety levels, then the benzene can be identified using a prefilter, which contains a strongly oxidizing agent, which reacts with all alkylated VOC aromatics, except benzene. The detection limit is at ppb_v levels and the humidity interference is minimized using a fence electrode. Alternatively, chip measurement systems (CMS) are proposed, which can operate at low ppb_v levels only in the absence of humidity.[9] None of these detectors, however, meet the stringent environmental limits for benzene detection in air.

The exploitation of molecular receptors as sensing materials is particularly attractive to address the selectivity issue. The progress made in designing synthetic receptors enables the modulation of the sensor selectivity toward different classes of compounds by mastering the weak interactions occurring between the sensing material and the analytes.[10,11]

So far, most of the work has focused on receptors for the complexation of aromatic compounds in solution.[12−15] Solid state recognition of aromatic vapors, with particular emphasis on C8 aromatics, has been achieved using porous materials such as zeolites,[16] MOFs,[17−19] CD-MOF,[20,21] clathrates,[22] and molecular organic cages.[23,24] These systems are shape-selective thanks to the presence of well-defined, shape-persistent portals in the solid state. As a remarkable example, complete discrimination between structural isomers mesitylene and 4-ethyltoluene has been achieved.[23] However, shape recognition between airborne benzene and toluene turned out to be elusive so far, thus jeopardizing environmental monitoring via supramolecular sensing.

In 2007 we reported an innovative approach to sub-ppb_v level benzene detection in air. A miniaturized system was proposed, composed of a selective supramolecular concentration unit, a Si-micromachined GC column and a Si-integrated MOS sensor.[25] The issue of achieving at the same time molecular level selectivity and low-ppb_v sensitivity for benzene has been solved by disconnecting the recognition element from the detection unit. The recognition event is assigned to a quinoxaline cavitand receptor (**QxCav**, Chart 1), capable of selectively trapping aromatic vapors at the gas−solid interface.[26] The selective concentration component is interfaced to the Si-integrated GC column, necessary for the separation of the different aromatic compounds released by the trapping unit, which are then individually channeled to the MOS detector.[27] This system has been successfully tested in the field. Despite its good performance, this device is rather complex and not suited for low-cost distributed sensing, because of the need of GC separation of benzene from TEX. To overcome this problem, we designed and tested two novel quinoxaline cavitands, following two different approaches to maximize benzene selectivity: (i) cavity roofing and (ii) cavity mouth reduction. In both cases the performances of the cavitands were tested using solid-phase micro extraction (SPME) as analytical sampling technique. In the first attempt, the introduction of two triptycene units at the upper rim (**DiTriptyQxCav**, Chart 1) enhanced the confinement of BTEX within the cavity with respect to the parent **QxCav**.[28] In the second case, the introduction of four methylendioxy bridges between the quinoxaline wings (**MeQxBox**, Chart 1) provides both cavity rigidification and reduction of the cavity opening. The result was an exceptional increase in BTEX uptake compared to commercial fiber coatings, accompanied by a partial bias toward benzene.[29] However, none of the two approaches was effective in benzene preferential retention over TEX.

These results prompted us to look at the issue from a different perspective, reversing the selectivity scale in favor of TEX complexation over benzene inclusion. However, this bias must be obtained by strengthening the interactions of TEX with the cavitand and not by reducing benzene binding, in order to maintain the required preconcentrator sensitivity.

Herein, we report a comprehensive study leading to the fabrication of a stand-alone prototype sensor for environmental benzene monitoring. The proposed goal has been achieved using a specifically designed cavitand, called **EtQxBox** (Chart 1), which acts at the same time as selective preconcentrator and GC-like separation device. The type and number of the interactions of the **EtQxBox** cavity with the aromatic guests has been determined in the solid state, while the relative strengths of the corresponding complexes were calculated via molecular mechanics calculations. The analytical performances of **EtQxBox** were then evaluated via SPME and compared with those of the other cavitands depicted in Chart 1.[29a] Finally, a miniaturized benzene monitoring sensor equipped with a MEMS cartridge packed with **EtQxBox** was fabricated and validated for benzene detection in air.

RESULTS AND DISCUSSION

Design and Synthesis of the Cavitand Receptor. Our goal was the design of a macrocyclic host capable to complex

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aromatic VOC with high efficiency and, at the same time, to bind preferentially TEX over benzene. The starting point was the understanding of the mechanism of guest uptake/release by **QxCav** at the solid−gas interface. In solution, using a related cavitand, Rebek showed that guest release requires a conformational opening of the lateral walls, to avoid the prohibitive cost of complete cavity desolvation.[30] The fluttering angle of the quinoxaline walls in solution has been experimentally evaluated by Diederich and co-workers using FRET:[31] the average value of 16° is in line with the 0−29° range determined by Sum-Frequency Vibrational Spectroscopy measurements on a **QxCav** monolayer.[32] This last measurement, coupled with theoretical calculations, indicates that the **QxCav** cavity is "breathing" in the solid state. It is reasonable to assume that the breathing is amplified increasing the temperature.

Since solvation is absent in the solid state, our reasoning was that limiting the breathing of the cavity would boost the guest uptake by filling the empty cavity and thermally stabilize the resulting complex. To this purpose we designed an **EtQxBox** cavitand, in which the three different, well-separated rims of electron-rich surfaces are preorganized for weak intermolecular attractive interactions with the aromatic guests (Figure 1).

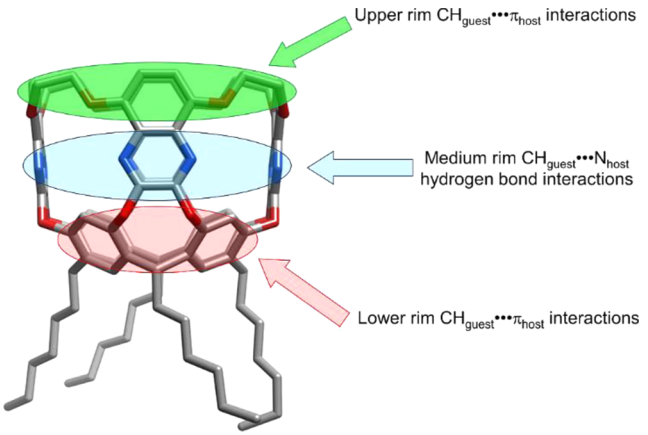

Figure 1. Chemical structure of the **EtQxBox** host cavitand with lower, medium, and upper rim interaction sites, highlighted in different colors.

The rationale of this design can be summarized as follows: (a) at the lower rim, the four aromatic surfaces of the resorcinarene skeleton can interact with two "bottom" C−H groups of benzene, toluene or xylenes via C−H···π interactions; (b) at the medium rim, the nitrogen atoms of the quinoxaline rings can act as hydrogen bond acceptors toward the two "equatorial" C−H groups of benzene, toluene, or xylenes; (c) at this point, the role of the aromatic surfaces at the upper rim of the cavitand becomes crucial for selectivity. In fact, these surfaces, too far to interact with benzene, become available for attractive intermolecular C−H···π interactions with one or two methyl groups in the case of toluene and xylenes, respectively.

It is thus to be expected that the host−guest binding energy increases as the number of the attractive interactions increases, with xylenes, ethylbenzene, and toluene bound more strongly than benzene. To prove this hypothesis, host−guest interactions in the solid state were analyzed studying the crystal structures of three BTX complexes with **EtQxBox**; the relative strength of the same complexes was obtained in the gas phase by molecular modeling calculations. Partial rigidification of the lateral walls in cavitands has been already reported by Diederich[33] and Rebek,[34] while Bruce Gibb[15] reported the preparation of larger, fully blocked deep-cavity cavitands. In our design, the connecting units at the upper rim should not alter cavity shape and depth, to avoid variations in the cavity affinity for aromatic hydrocarbons. Therefore, we opted for introducing ethylendioxy units connecting the quinoxaline rings laterally. **EtQxBox** was obtained following a three-step procedure. First, the hexyl-footed resorcinarene was 4-fold bridged with 2,3-dichoro-5,8-dimethoxy quinoxaline under microwave irradiation, leading to octamethoxy **QxCav 1** (Scheme S1, SI). Then, the eight methyl groups on the quinoxaline flaps were removed using $AlCl_3$ in dry toluene to afford the corresponding octahydroxy **QxCav 2**.[29b] Finally the two-by-two bridging of the four hydroxyl pairs with ethylene di(*p*-toluenesulfonate) afforded **EtQxBox** cavitand in 44% overall yield (Scheme S1, SI). **EtQxBox** in solution adopts a rigid vase conformation, as testified by the 5.79 ppm resonance of the diagnostic resorcinarene bridging methyne (Figure S1, SI).

Gas-Phase Molecular Simulation for EtQxBox Complexes. We carried out molecular mechanics calculations using the MMFF94 Merck molecular force field,[35] which has excellent parametrization of van der Waals and electrostatic intermolecular interactions (comparable with those obtainable with HF/6-31G* calculations).

The calculated geometries and binding energies of the three complexes are shown in Figure 2, together with the weak attractive intermolecular host−guest interactions represented by green lines. The nature of the intermolecular interactions and their calculated geometrical parameters are summarized in Tables S3−S5. The calculations predict that complexation of benzene occurs via two C−H···π interactions (entries 1,2) and two bifurcated C−H···N hydrogen bonds (entries 3−6).

No other host−guest attractive interactions are possible in the case of benzene and the calculated binding energy is ΔE= −71.62 (kJ/mol). The binding energy increases (ΔE becomes more negative: −76.26 kJ/mol) in the **toluene@EtQxBox** complex due to the increased number of the host−guest interactions: eight over six, due to the formation of two additional C−H···π interactions (entries 7,8) involving the methyl group of toluene and the aromatic surfaces at the *upper rim* of **EtQxBox**. The calculations also predict that *o*-xylene is the preferred guest due to the formation of the additional host−guest C−H···π interaction (entry 9) involving the second methyl group present in *o*-xylene. This increases the binding to ΔE = −79.98 (kJ/mol) demonstrating the crucial role of the conformationally blocked aromatic surfaces at the upper rim of the host to achieve the expected scale of selectivity among the three guests.

Solid-State Inclusion. In order to experimentally verify the in silico simulations, we studied the inclusion ability of **EtQxBox** toward BTEX by different crystallization experiments, dissolving the cavitand in DMSO and adding benzene, toluene, and *o*-xylene, respectively. In all cases, single crystals suitable for X-ray diffraction analysis were obtained by slow evaporation. The examination of the three crystal structures evidence that all the aromatic compounds are positioned within the host cavity, and that the resulting intermolecular interactions follow the trend observed in the computational studies, with the number of interactions increasing along the series from benzene to *o*-xylene. In the molecular structure of **benzene@EtQxBox**, the asymmetric unit comprises two cavitands differing one from the other for the orientation of the alkyl legs. In both the hosts,

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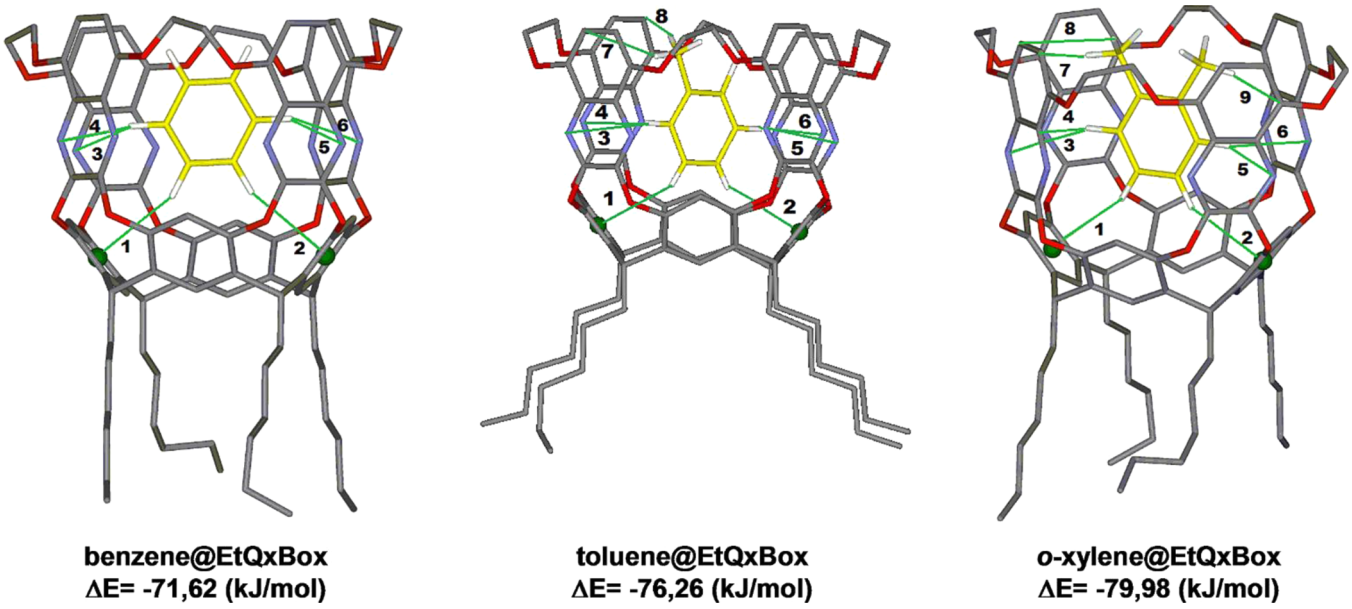

Figure 2. Stick views of the three complexes. Colors: C, gray (C atoms of the guest; yellow); O, red; N, cyan; H, white. Only the guest hydrogen atoms have been shown for clarity. Intermolecular host−guest interactions are represented as green lines.

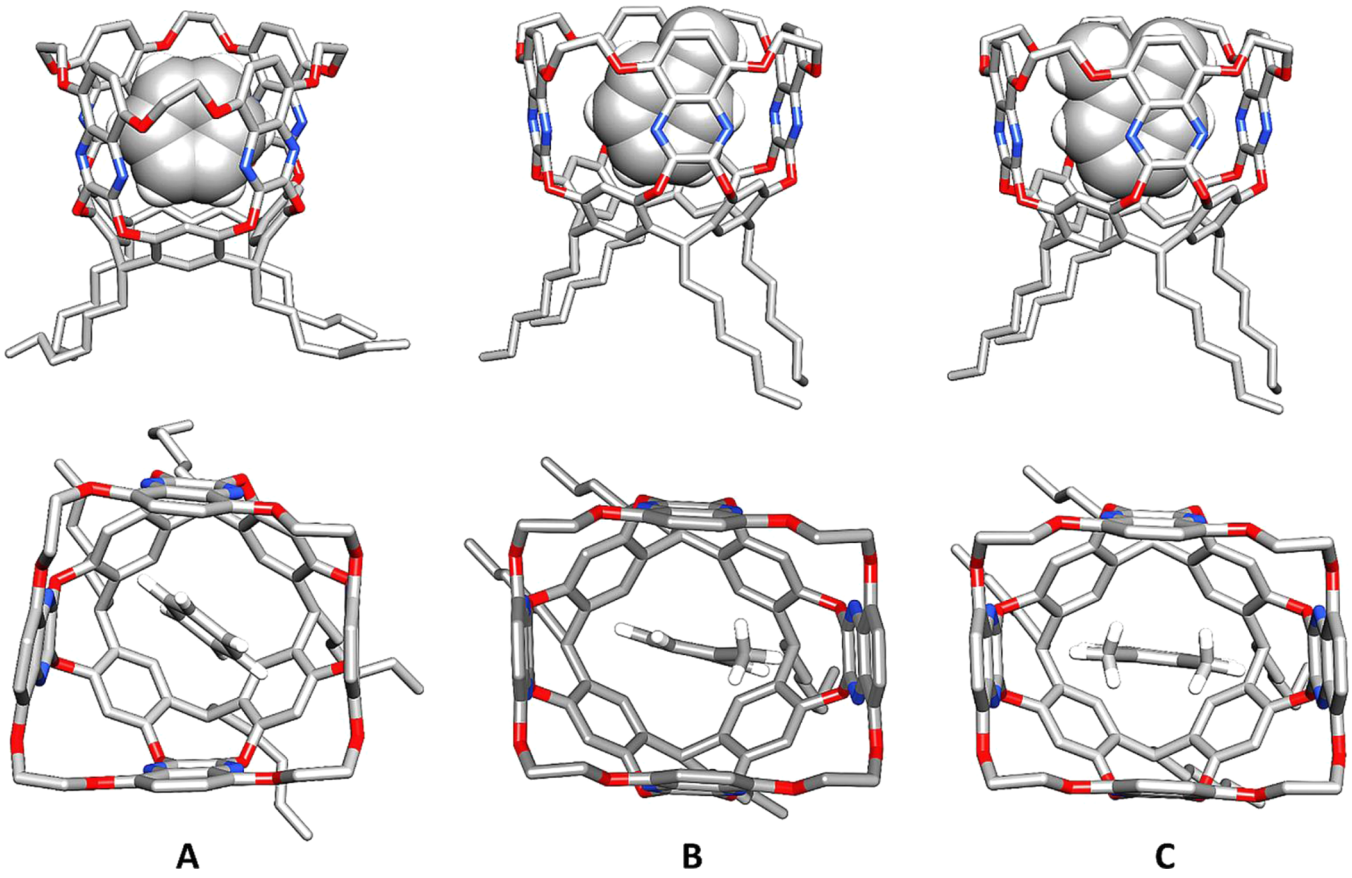

Figure 3. Side and top view of the molecular structures of **benzene@EtQxBox** (A), **toluene@EtQxBox** (B), and ***o*-xylene@EtQxBox** (C). Only the hydrogen atoms of the guest are shown. Benzene and DMSO solvent molecules have been omitted for clarity.

benzene is included deeply within the cavity (see Figure 3A, only one of the two independent cavitands is shown), forming six weak noncovalent interactions (for the geometrical parameters see Table S3): two C−H···π interactions with the lower aromatic bowl of the cavitand, and two bifurcated C−H··· N interactions with the nitrogen atoms of two adjacent quinoxaline moieties, as shown in Figure 2. Indeed, the number and types of interactions in the calculated and in the solid state structure of the complex are the same, even if the benzene guest has a slightly different inclination in the two cases (see Figure S5). The self-assembly of the complexes in the crystal lattice is assisted by several benzene and DMSO solvent molecules

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which fill the voids available. Also in the molecular structure of **toluene@EtQxBox** (Figure 3B), two C−H···π interactions with the lower rim of the cavitand and two bifurcated C−H···N interactions with the two nitrogen atoms of the same quinoxaline ring have been observed. However, the global orientation of the guest differs from that of benzene, being parallel to two quinoxaline walls of the cavitand, to maximize the interactions with the cavity. This orientation allows the methyl group, which is disordered over two equivalent positions, to form C−H···π interactions with the conformationally blocked aromatic rings at the upper rim of the cavitand, again in good agreement with the calculated data. The geometrical parameters for the two disordered C−H···π interactions are reported in Table S4 (see SI). *o*-Xylene behaves essentially like toluene, yielding the complex ***o*-xylene@EtQxBox**, which is perfectly comparable in geometry and host−guest interactions to the toluene analogue (Figure 3C). In this case no disorder occurs, and the two *ortho* methyl groups are both involved in equivalent CH···π interactions (see parameters in Table S5, SI). This additional interaction accounts for the increased complexation binding energy calculated in the gas phase for the ***o*-xylene@EtQxBox** complex.

Solid-Phase Microextraction Analysis (SPME). In order to test the capabilities of the cavitand toward BTEX trapping, an **EtQxBox** SPME coating was developed and characterized. Preliminary investigations by thermogravimetric analyses were performed on **EtQxBox** in air to determine its decomposition temperature and its long-term thermal stability under the required desorption temperatures. **EtQxBox** is stable in air up to 400 °C (Figure S8, SI) and it shows an excellent thermal stability at 250 °C for over 15 h (Figure S9, SI). The introduction of the four ethylendioxy bridging groups does not reduce the thermal stability of the receptor with respect to the parent **QxCav**.[36] The thermal stability of the coating was also evaluated by conditioning the SPME fibers in the GC injector port at 250 °C for 2 min: no significant bleeding was observed, thus confirming the high thermal resistance of the material.

Scanning electron microscopy of the coated SPME fiber showed a homogeneous and uniform distribution of the cavitand all along the fiber with a coating thickness of 40 ± 6 μm (Figure S10, SI). The effectiveness of **EtQxBox** fiber in BTEX sampling was tested by SPME-GC-MS. The analysis of an air mixture containing an amount of aliphatic hydrocarbons (from C6 to C9) 2 orders of magnitude higher than BTEX (38−56 $\mu g/m^3$ vs 385−473 ng/m^3 range), proved that the aromatic analytes are strongly retained into the **EtQxBox** cavity and can be exhaustively desorbed at temperatures higher than 250 °C (Figure S11, SI). These findings are in agreement with the X-ray data, confirming the complexation of the analytes into the cavity. By contrast aliphatic hydrocarbons are completely removed at 50 °C, being only physisorbed in the solid (Figure S11, SI). Repeatability of data, in terms of both intra- and intermediate precision, was assessed by performing 5 replicated measurements along 2 weeks obtaining relative standard deviations (RSD) always lower than 9%.

The enrichment capabilities toward BTEX were also evaluated in terms of enrichment factors (EFs).[37] EFs were calculated as the ratio of the concentration of the analyte in the fiber after the extraction to that of the analyte in the gas standard mixture. As shown in Figure 4, the cavitand EFs were noticeably higher than those obtained by using the commercial CAR-DVB-PDMS 2 cm−50/30 μm fiber. In particular, the EFs

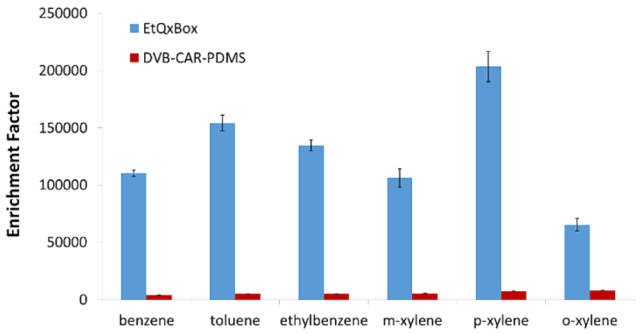

Figure 4. Enhancement factors per coating thickness of the **EtQxBox** fiber for BTEX extraction. HS-SPME conditions: extraction time 15 min, 25 °C (3 replicates).

were up to 30 times higher than those obtained using the commercial fiber. These findings suggested the use of **EtQxBox** for the development of portable devices in which the cavitand is used as trapping material for the online and in situ environmental monitoring of BTEX. Limits of detection (LOD, Table 1) and limits of quantitation (LOQ, Table S8, SI) in the low ng/m^3 range proved the capabilities of the **EtQxBox** as adsorbent for the determination of BTEX in air at trace levels. Finally, the calculated LODs were compared with those achieved both by commercially devices used for air quality monitoring and by supramolecular receptors already developed by our research group, i.e., tetraquinoxaline cavitands functionalized at the upper rim with four methylendioxy bridges (**MeQxBox**)[29] and two triptycene moieties (**DiTriptyQxCav**),[28] respectively (Table 1).

As reported in Table 1, both conformationally blocked quinoxaline-based cavitand receptors showed better performance in terms of sensitivity compared to systems commonly used for air monitoring like Radiello. The same behavior was observed toward both high-end apparatus based on optical fibers and commercial SPME fibers like DVB-CAR-PDMS. Additional advantages rely on both the use of shorter extraction times, thus speeding up BTEX monitoring, and the enhanced selectivity toward aromatic hydrocarbons as already demonstrated by our previous studies.[28,29b]

The comparison of the SPME extraction performances of **MeQxBox** and **EtQxBox** allows one to single out the effect of the length of the bridging units among the quinoxaline walls. The shorter methylendioxy units reduce the cavity mouth entrance leading to the lowest LOD for benzene at the expense of BTEX desorption selectivity. Therefore, the size of the cavity mouth in the QxBox series is pivotal to modulate the thermal release of the various aromatic guests.

Sensor Manufacturing and Benzene Detection. A simple device for benzene monitoring based on **EtQxBox** for BTEX preconcentration and selective benzene desorption into a miniaturized photoionization detector (Mini-PID PPB by IonScience) was designed and tested under laboratory conditions. Compared to the mini-GC device developed by us in 2009,[27] the use of **EtQxBox** instead of **QxCav** allows for combining the preconcentration and the GC separation capabilities into a single MEMS chip packed with 10 mg of a proper mesh of **EtQxBox** cavitand.

In fact, the selectivity between benzene and the other aromatics is achieved by applying a smart temperature program on the EtQxBox mesh, which starts releasing benzene at lower temperatures than toluene and xylene, as predicted by the

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Table 1. Comparison between the LOD Values (ng/m^3) of the Supramolecular Receptors and the Commercially Available Devices

	EtQxBOX	MeQxBOX	DiTriptyQxCav	QxCav	DVB-CAR-PDMS	RADIELLO	optical fiber[38]
extraction time	(15 min)[a]	(15 min)[a]	(15 min)[a]	(15 min)[a]	(15 min)[a]	(24 h)[a]	(25 min)[a]
benzene	0.7	0.4	1.7	5.2	17.1	290	1.6
toluene	0.4	0.6	3.1	7.2	2.1	90	1.5
ethylbenzene	0.4	0.5	1.3	5.7	4.8	40	1.2
m-xylene	0.8	1.2	2.0	10.0	6.1	70	1.3
p-xylene	0.3	0.6	1.3	9.0	6.1	80	1.7
o-xylene	0.5	1.0	2.2	12.5	14.3	10	2.0

[a]Extraction time used in each study.

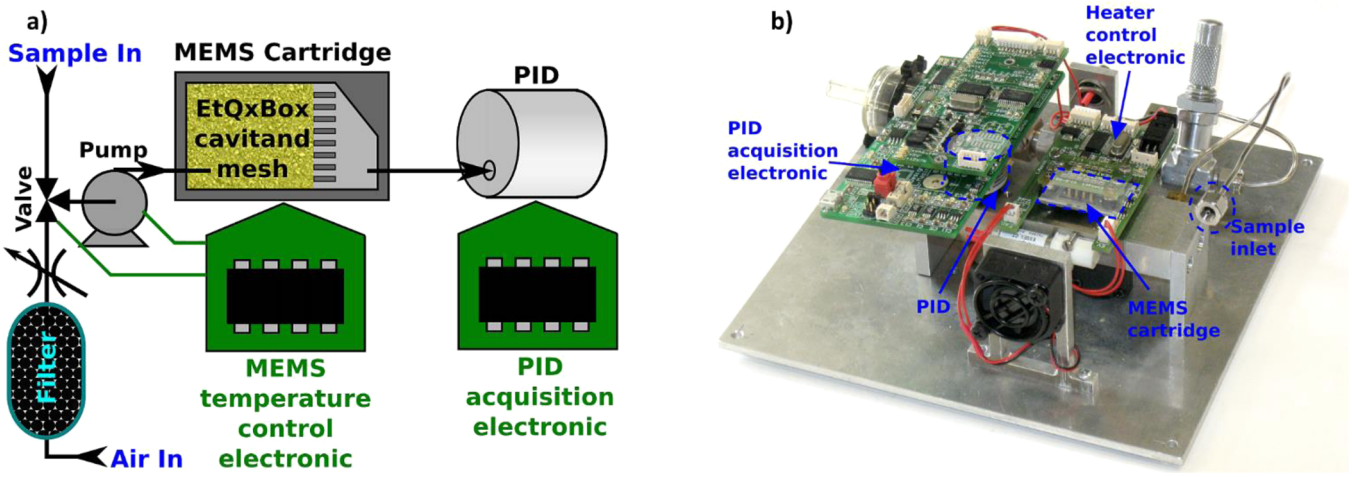

Figure 5. Schematic representation of the benzene monitoring device (a) and photograph of the prototype (b) with an inset showing the MEMS chip packed with **EtQxBox**.

calculated binding energies ΔE. Under these conditions, the use of a temperature desorption ramp replaces the GC minicolumn.

The fabrication process for the packed MEMS preconcentrators was reported previously.[27] Figure 5a shows a schematic representation of the device, while Figure 5b shows a photograph of the prototype used for this work. The interconnections between the single components are made through a stainless steel block with suitable machining, which mounts a pump (KNF Neuberger model NMP09B), a bistable 3-way microvalve (by The Lee Company), the PID, and the MEMS chip.

The sampling step consists of pumping the sample at a flow of up to 120 mL/min into the MEMS chip. The duration and flow rate of the sampling step can be adapted to specific applications, and different configurations were tested. In particular, with long sample times (50 min) at higher flow rates (120 mL/min) ppb$_v$-level sensitivity to benzene was demonstrated. For the injection/separation step, the 3-way valve is switched and an activated carbon filter is used to provide clean air into the MEMS, which is heated at a rate of >50 °C/s to release the sampled aromatics. The flow during the separation phase can be regulated by means of a needle-valve, and several flow-rates were tested. The best results in terms of selectivity to benzene over toluene were found with a 30 mL/min flow. Figure 6 shows some typical signals acquired by the PID detector during the desorption temperature ramp. In these plots, the MEMS cartridge filled with **EtQxBox** was kept at room temperature using the pump to sample the test mixture from the sample inlet at 120 mL/min up to t = 5 min, when the valve was switched to the filter line with a reduced flow of 30 mL/min.

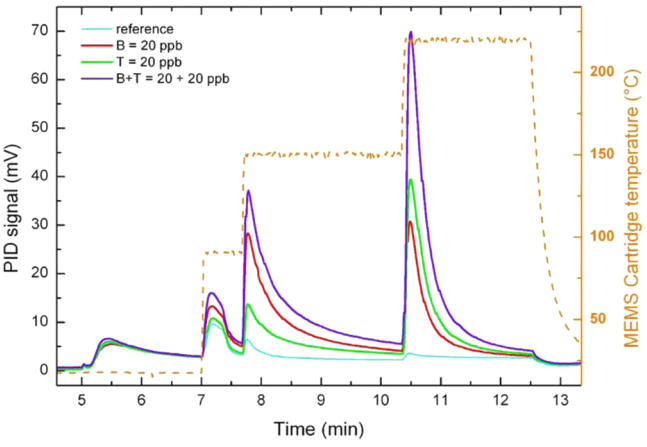

Figure 6. Typical responses of the PID detector to a temperature ramp for benzene (B, red), toluene (T, green), and a mixture of benzene and toluene (B+T, purple), compared to a "reference" sample of only air (cyan).

Starting at t = 7 min, the temperature was increased to 90 °C for 40 s to release any nonspecifically adsorbed species. The next temperature step at 150 °C is applied to release preferentially benzene. As can be seen from the plots, the "reference" injection (only air, cyan line) results in a very small signal, while the injection of 20 ppb$_v$ of benzene yields a relevant peak (red line), which is only slightly smaller than the peak of 20 ppb$_v$ benzene + 20 ppb$_v$ toluene (purple line).

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This first result demonstrates how only a very small amount of toluene is released at 150 °C (see green line, 20 ppb_v of toluene only). This first temperature step is the most significant for benzene quantification, since toluene interferes only slightly during the 150 °C step. During the next temperature step at 220 °C, more toluene (green) than benzene (red) is released. It is evident that the separation between benzene and toluene is not complete, due to the very short cartridge used for this work. Nevertheless, by calibrating the system and using a simple linear combination of the responses at the two temperatures (150 and 220 °C), the small signal generated by toluene at the 150 °C step can be easily subtracted (see SI for more details), and a very good prediction of the benzene concentration in mixtures with much higher toluene concentrations can be achieved, as shown in Figure 7. The data reported in Figure 7

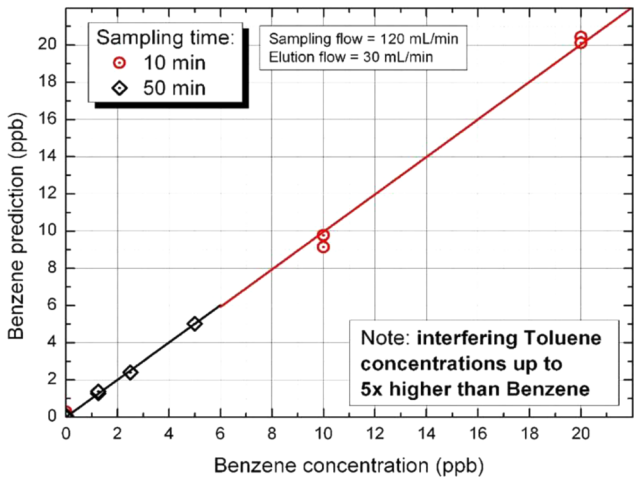

Figure 7. Benzene concentrations calculated using the equations (eqs 1a and 1b in SI) on a set of measurements performed with the prototype shown in Figure 5b. These values were calculated on samples where interfering toluene concentrations were up to 5 times higher than the benzene concentration.

refers to a campaign of 36 measurements where benzene concentrations between 1.25 and 20 ppb_v were injected together with interfering toluene concentrations which were up to 5 times higher than the benzene concentrations, to prove the good prediction capability of the proposed sensor device.

The selectivity of benzene toward toluene, as shown in Figure 6, is expected to be improved in future works by using a longer MEMS cartridge filled with the **EtQxBox**, to increase the separation effect. Nevertheless, the current implementation has already demonstrated the capability of selectively quantifying benzene with a detection range spanning from 1.25 to 20 ppb_v. The superior benzene complexation capabilities of **EtQxBox** versus the previously reported **QxCav** can be disclosed from the plots of Figure 8, where the effect of the temperature during the sampling step is compared for the two cavitands. For both plots, the sensitivity is normalized to the value of 20 °C, resulting in arbitrary units on the *y*-axis. At temperatures slightly higher than 20 °C, **QxCav** rapidly decreases the complexation efficiency in adsorption, while **EtQxBox** has the same preconcentration capabilities up to temperatures close to 60 °C, while around 100 °C the beginning desorption regime is evident. This widens the working temperature regime available for the corresponding device a lot. These findings demonstrate that the presence of a conformationally blocked cavity is able to

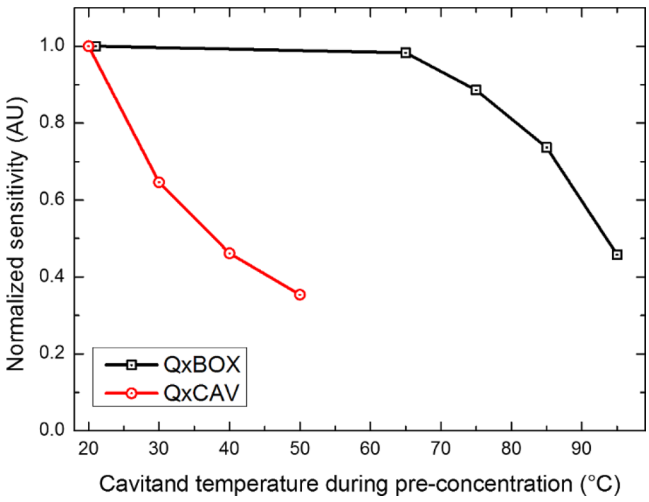

Figure 8. Normalized sensitivity toward benzene at increasing temperatures compared for **QxCav** (red line) and **EtQxBox** (black line). The higher binding energy of **EtQxBox** results in the capability of preconcentrating benzene efficiently up to over 60 °C.

strengthen the host–guest interactions, thus increasing the selectivity of the proposed device.

CONCLUSIONS

This work describes a new sensor for ppb level detection of benzene in air, in which high selectivity and extremely high sensitivity are obtained by coupling a MEMS-integrated supramolecular concentration unit to a miniaturized PID detector. By mastering molecular recognition at the gas–solid interface we have been able to produce a stand-alone sensor, in which the cavitand receptor **EtQxBox** acts at the same time as selective preconcentrator and GC-like separation device. **EtQxBox** is capable of selectively trapping BTEX at the ng/m^3 level within its conformationally rigid cavity delimited by four quinoxaline walls linked via ethylenedioxy bridges. The conformational rigidity of the cavitand maximizes the binding of TEX with respect to benzene by increasing the number of synergistic CH···π interactions in the latters. With respect to previous cavitands used for the selective benzene detection and quantification, **EtQxBox** features an enhanced overall BTEX trapping efficiency, while the different binding energies for the single aromatics are responsible of the GC-like separation. These characteristics allows for the fabrication of a simplified detection system, in which a single MEMS device provides high efficiency preconcentration and BTEX separation capabilities. It is noteworthy that the ppb_v-level sensitivity was demonstrated with a simple, stand-alone, and unsupervised sensing device, autonomously sampling and analyzing the test samples. In perspective, **EtQxBox** is the preconcentrator of choice to build a highly efficient stand-alone sensor for personal benzene exposure monitoring in industrial settings.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acssensors.7b00110.

Experimental procedures and characterization (Scheme S1, Figure S1); supporting crystallographic data (Tables S1–S2–S6–S7, Figures S2–S7); MMFF94 Merck

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molecular force field calculations (Tables S3−S4−S5); TGA analyses (Figures S8−S9); fiber characterization (Figure S10). SPME analysis (Figure S11); GC/MS analysis (Table S8); system calibration and prediction of benzene concentration (eqs 1a-b and 2a-b) (PDF)

AUTHOR INFORMATION

Corresponding Author

*E-mail: enrico.dalcanale@unipr.it.

ORCID

Roberta Pinalli: 0000-0002-0000-8980

Alessandro Pedrini: 0000-0003-3949-7563

Federica Bianchi: 0000-0001-7880-5624

Enrico Dalcanale: 0000-0001-6964-788X

Present Address

#Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1, 35131 Padova.

Author Contributions

All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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