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In Search of the Ultimate Benzene Sensor: The EtQxBox Solution

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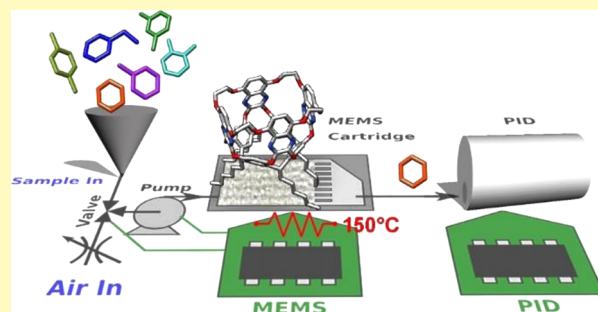
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S Supporting Information

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 cavitant 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 cavitant as fiber coating for BTEX monitoring in air. The cavitant EFs are noticeably higher than those obtained by using the commercial CAR-DVB-PDMS. The LOD and LOQ are calculated in the ng/m³ 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/m³ 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

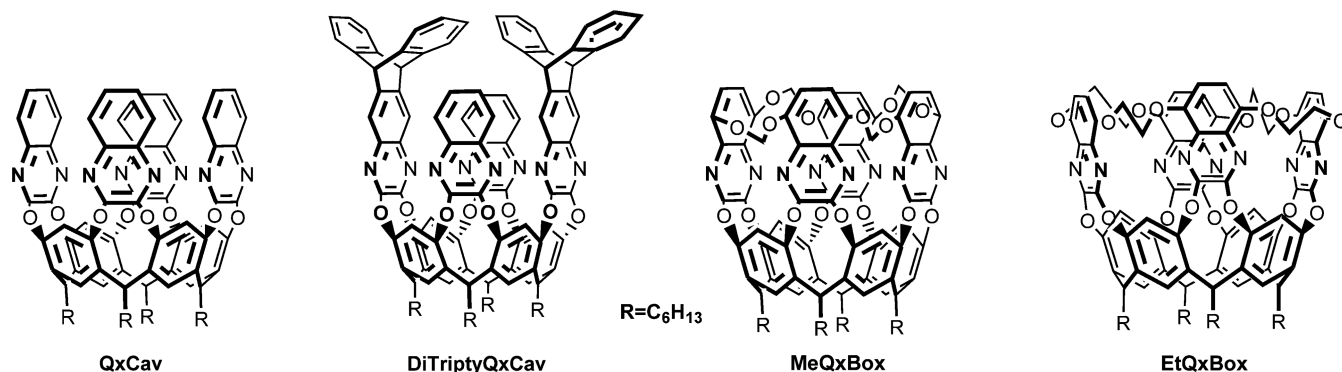
proposed,⁷ the most important being metal oxide sensors (MOS), quartz microbalances (QMB), surface acoustic waveguides (SAW), and polymeric sensors.⁸ These technologies have often reached sufficient sensitivity for the detection of the target gas species, but generally their selectivity is limited and 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. 62

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



63 Recently, some companies launched on the market a hand-
64 held gas detector, a photoionization detector (PID) equipped
65 with a 9.8 eV lamp, with two-mode operation for the rapid
66 detection of benzene and total aromatic compounds (TAC).⁹
67 The default TAC mode screens out all the aliphatic compounds
68 which have an ionization potential higher than 10.0 eV, leaving
69 just the TAC whose ionization potential is below 10.0 eV. If the
70 TAC measurements exceed safety levels, then the benzene can
71 be identified using a prefilter, which contains a strongly
72 oxidizing agent, which reacts with all alkylated VOC aromatics,
73 except benzene. The detection limit is at ppb_v levels and the
74 humidity interference is minimized using a fence electrode.

75 Alternatively, chip measurement systems (CMS) are proposed,
76 which can operate at low ppb_v levels only in the absence of
77 humidity.⁹ None of these detectors, however, meet the
78 stringent environmental limits for benzene detection in air.

79 The exploitation of molecular receptors as sensing materials
80 is particularly attractive to address the selectivity issue. The
81 progress made in designing synthetic receptors enables the
82 modulation of the sensor selectivity toward different classes of
83 compounds by mastering the weak interactions occurring
84 between the sensing material and the analytes.^{10,11}
85 So far, most of the work has focused on receptors for the
86 complexation of aromatic compounds in solution.^{12–15} Solid
87 state recognition of aromatic vapors, with particular emphasis
88 on C8 aromatics, has been achieved using porous materials
89 such as zeolites,¹⁶ MOFs,^{17–19} CD-MOF,^{20,21} clathrates,²² and
90 molecular organic cages.^{23,24} These systems are shape-selective
91 thanks to the presence of well-defined, shape-persistent portals
92 in the solid state. As a remarkable example, complete
93 discrimination between structural isomers mesitylene and 4-
94 ethyltoluene has been achieved.²³ However, shape recognition
95 between airborne benzene and toluene turned out to be elusive
96 so far, thus jeopardizing environmental monitoring via
97 supramolecular sensing.

98 In 2007 we reported an innovative approach to sub-ppb_v
99 level benzene detection in air. A miniaturized system was
100 proposed, composed of a selective supramolecular concen-
101 tration unit, a Si-micromachined GC column and a Si-
102 integrated MOS sensor.²⁵ The issue of achieving at the same
103 time molecular level selectivity and low-ppb_v sensitivity for
104 benzene has been solved by disconnecting the recognition
105 element from the detection unit. The recognition event is
106 assigned to a quinoxaline cavitand receptor (QxCav, Chart 1),
107 capable of selectively trapping aromatic vapors at the gas–solid
108 interface.²⁶ The selective concentration component is inter-
109 faced to the Si-integrated GC column, necessary for the
110 separation of the different aromatic compounds released by the

trapping unit, which are then individually channeled to the
111 MOS detector.²⁷ This system has been successfully tested in
112 the field. Despite its good performance, this device is rather
113 complex and not suited for low-cost distributed sensing,
114 because of the need of GC separation of benzene from TEX.
115 To overcome this problem, we designed and tested two novel
116 quinoxaline cavitands, following two different approaches to
117 maximize benzene selectivity: (i) cavity roofing and (ii) cavity
118 mouth reduction. In both cases the performances of the
119 cavitands were tested using solid-phase micro extraction
120 (SPME) as analytical sampling technique. In the first attempt,
121 the introduction of two triptycene units at the upper rim
122 (DiTriptyQxCav, Chart 1) enhanced the confinement of
123 BTEX within the cavity with respect to the parent QxCav.²⁸ In
124 the second case, the introduction of four methylenedioxy bridges
125 between the quinoxaline wings (MeQxBox, Chart 1) provides
126 both cavity rigidification and reduction of the cavity opening.
127 The result was an exceptional increase in BTEX uptake
128 compared to commercial fiber coatings, accompanied by a
129 partial bias toward benzene.²⁹ However, none of the two
130 approaches was effective in benzene preferential retention over
131 TEX.
132

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

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

RESULTS AND DISCUSSION

154
155 **Design and Synthesis of the Cavitand Receptor.** Our
156 goal was the design of a macrocyclic host capable to complex

157 aromatic VOC with high efficiency and, at the same time, to
 158 bind preferentially TEX over benzene. The starting point was
 159 the understanding of the mechanism of guest uptake/release by
 160 QxCav at the solid–gas interface. In solution, using a related
 161 cavitand, Rebek showed that guest release requires a conforma-
 162 tional opening of the lateral walls, to avoid the prohibitive cost
 163 of complete cavity desolvation.³⁰ The fluttering angle of the
 164 quinoxaline walls in solution has been experimentally evaluated
 165 by Diederich and co-workers using FRET:³¹ the average value
 166 of 16° is in line with the 0–29° range determined by Sum-
 167 Frequency Vibrational Spectroscopy measurements on a
 168 QxCav monolayer.³² This last measurement, coupled with
 169 theoretical calculations, indicates that the QxCav cavity is
 170 “breathing” in the solid state. It is reasonable to assume that the
 171 breathing is amplified increasing the temperature.

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

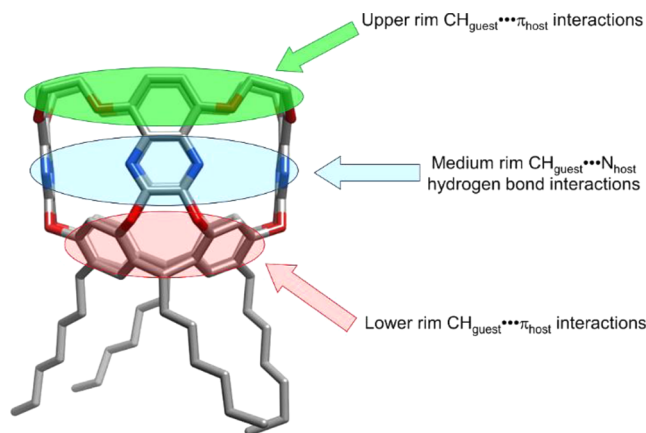


Figure 1. Chemical structure of the EtQxBx host cavitand with lower, medium, and upper rim interaction sites, highlighted in different colors.

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

191 It is thus to be expected that the host–guest binding energy
 192 increases as the number of the attractive interactions increases,
 193 with xylenes, ethylbenzene, and toluene bound more strongly
 194 than benzene. To prove this hypothesis, host–guest
 195 interactions in the solid state were analyzed studying the
 196 crystal structures of three BTX complexes with EtQxBx; the
 197 relative strength of the same complexes was obtained in the gas
 198 phase by molecular modeling calculations. Partial rigidification

of the lateral walls in cavitands has been already reported by
 Diederich³³ and Rebek,³⁴ while Bruce Gibb¹⁵ 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
 ethylenedioxy units connecting the quinoxaline rings laterally.
 EtQxBx 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 AlCl₃ 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 EtQxBx cavitand in 44% overall yield (Scheme S1,
 SI). EtQxBx 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 EtQxBx 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 $\Delta E = -71.62$ (kJ/mol). The binding energy increases (ΔE becomes more negative: -76.26 kJ/mol) in the toluene@EtQxBx 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 EtQxBx. 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 $\Delta E = -79.98$ (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 EtQxBx 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@EtQxBx, the asymmetric unit comprises two cavitands differing one from the other for the orientation of the alkyl legs. In both the hosts,

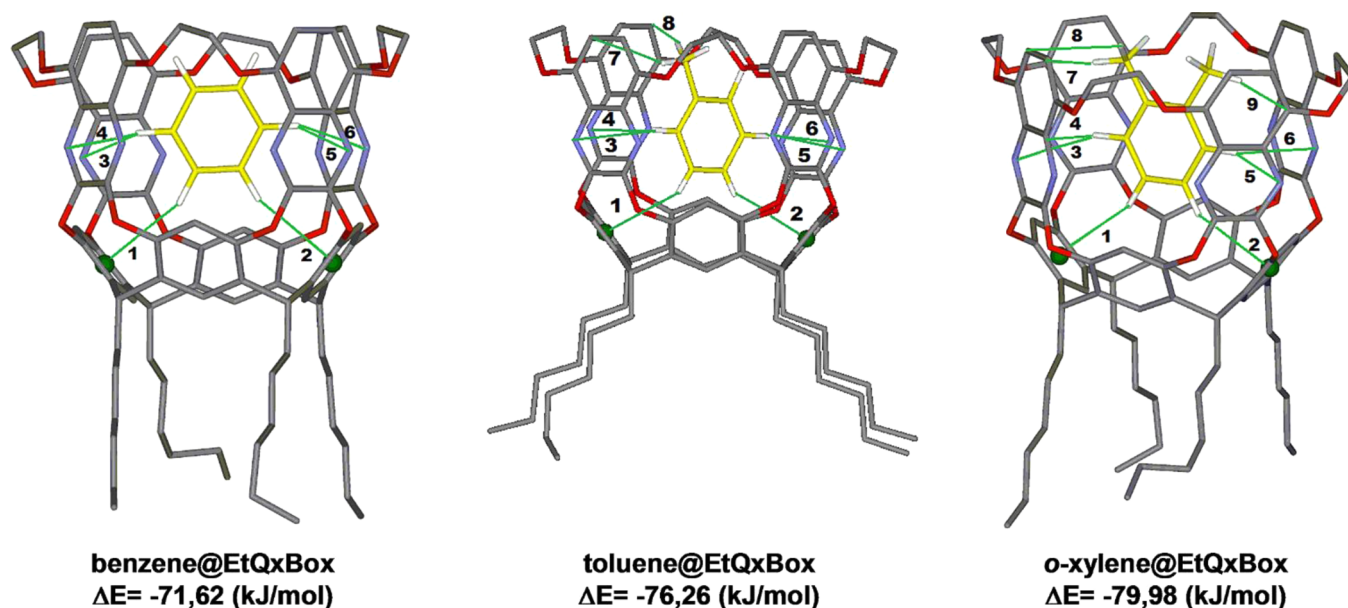


Figure 2. Stick views of the three complexes. Colors: C, gray (C atoms of the guest; yellow); O, red; N, cyan; H, white. Only the guest hydrogen atoms have been shown for clarity. Intermolecular host–guest interactions are represented as green lines.

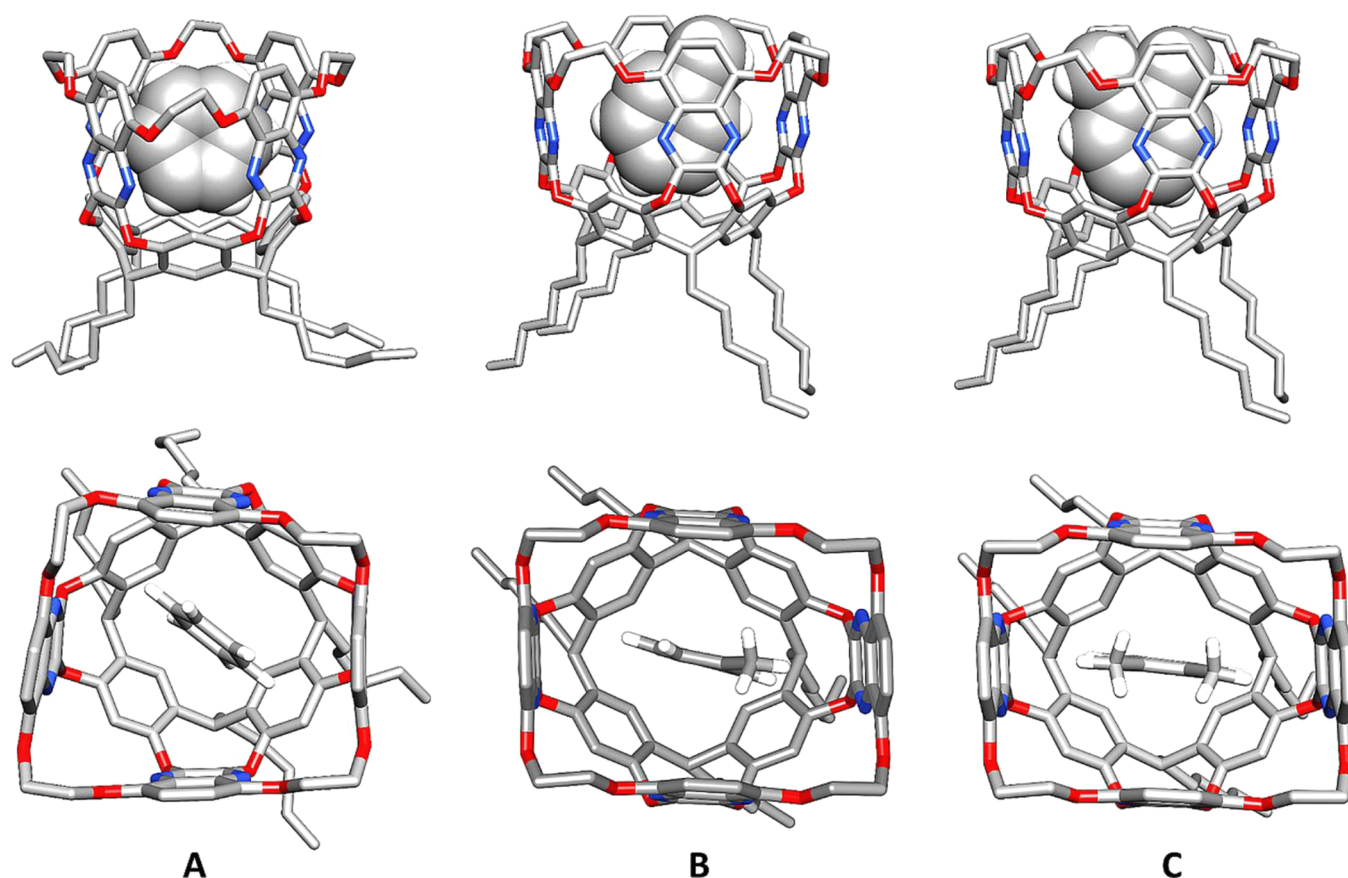


Figure 3. Side and top view of the molecular structures of **benzene@EtQxBox** (A), **toluene@EtQxBox** (B), and **o-xylene@EtQxBox** (C). Only the hydrogen atoms of the guest are shown. Benzene and DMSO solvent molecules have been omitted for clarity.

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

274 which fill the voids available. Also in the molecular structure of
 275 **toluene@EtQxBox** (Figure 3B), two C–H $\cdots\pi$ interactions
 276 with the lower rim of the cavitand and two bifurcated C–H \cdots N
 277 interactions with the two nitrogen atoms of the same
 278 quinoxaline ring have been observed. However, the global
 279 orientation of the guest differs from that of benzene, being
 280 parallel to two quinoxaline walls of the cavitand, to maximize
 281 the interactions with the cavity. This orientation allows the
 282 methyl group, which is disordered over two equivalent
 283 positions, to form C–H $\cdots\pi$ interactions with the conforma-
 284 tionally blocked aromatic rings at the upper rim of the cavitand,
 285 again in good agreement with the calculated data. The
 286 geometrical parameters for the two disordered C–H $\cdots\pi$
 287 interactions are reported in Table S4 (see SI). *o*-Xylene
 288 behaves essentially like toluene, yielding the complex *o*-
 289 **xylene@EtQxBox**, which is perfectly comparable in geometry
 290 and host–guest interactions to the toluene analogue (Figure
 291 3C). In this case no disorder occurs, and the two *ortho* methyl
 292 groups are both involved in equivalent CH $\cdots\pi$ interactions (see
 293 parameters in Table S5, SI). This additional interaction
 294 accounts for the increased complexation binding energy
 295 calculated in the gas phase for the *o*-xylene@EtQxBox
 296 complex.

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

312 Scanning electron microscopy of the coated SPME fiber
 313 showed a homogeneous and uniform distribution of the
 314 cavitand all along the fiber with a coating thickness of 40 ± 6
 315 μm (Figure S10, SI). The effectiveness of **EtQxBox** fiber in
 316 BTEX sampling was tested by SPME-GC-MS. The analysis of
 317 an air mixture containing an amount of aliphatic hydrocarbons
 318 (from C6 to C9) 2 orders of magnitude higher than BTEX
 319 ($38\text{--}56 \mu\text{g}/\text{m}^3$ vs $385\text{--}473 \text{ ng}/\text{m}^3$ range), proved that the
 320 aromatic analytes are strongly retained into the **EtQxBox** cavity
 321 and can be exhaustively desorbed at temperatures higher than
 322 250 °C (Figure S11, SI). These findings are in agreement with
 323 the X-ray data, confirming the complexation of the analytes into
 324 the cavity. By contrast aliphatic hydrocarbons are completely
 325 removed at 50 °C, being only physisorbed in the solid (Figure
 326 S11, SI). Repeatability of data, in terms of both intra- and
 327 intermediate precision, was assessed by performing 5 replicated
 328 measurements along 2 weeks obtaining relative standard
 329 deviations (RSD) always lower than 9%.

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

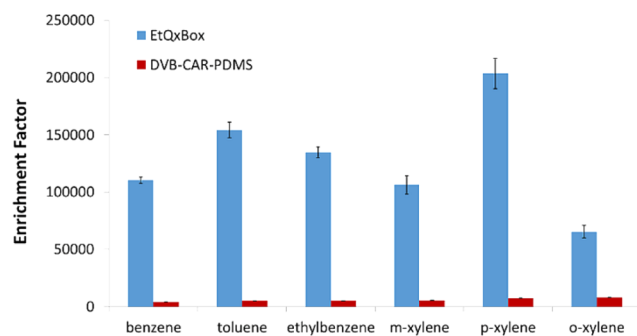


Figure 4. Enhancement factors per coating thickness of the **EtQxBox** fiber for BTEX extraction. HS-SPME conditions: extraction time 15 min, 25 °C (3 replicates).

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 methylenedioxy
 bridges (**MeQxBox**)²⁹ and two triptycene moieties (**DiTripty-**
QxCav),²⁸ respectively (Table 1).

As reported in Table 1, both conformationally blocked
 quinoxaline-based cavitand receptors showed better perform-
 ance 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 demon-
 strated 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 methylenedioxy 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 383

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
<i>m</i> -xylene	0.8	1.2	2.0	10.0	6.1	70	1.3
<i>p</i> -xylene	0.3	0.6	1.3	9.0	6.1	80	1.7
<i>o</i> -xylene	0.5	1.0	2.2	12.5	14.3	10	2.0

^aExtraction time used in each study.

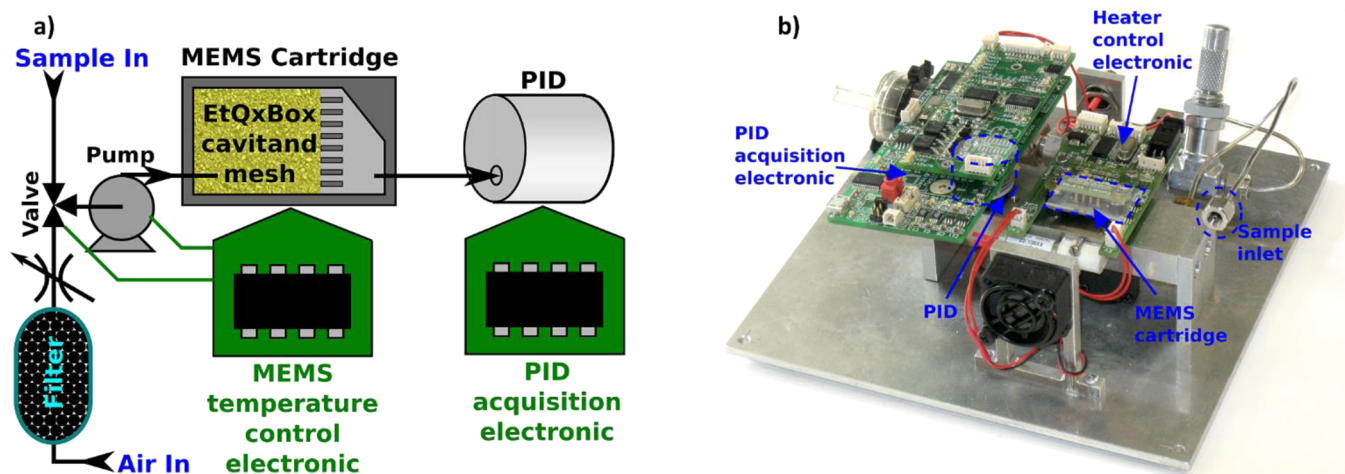


Figure 5. Schematic representation of the benzene monitoring device (a) and photograph of the prototype (b) with an inset showing the MEMS chip packed with EtQxBox.

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

386 The fabrication process for the packed MEMS preconcentrators
387 was reported previously.²⁷ Figure 5a shows a schematic
388 representation of the device, while Figure 5b shows a
389 photograph of the prototype used for this work. The
390 interconnections between the single components are made
391 through a stainless steel block with suitable machining, which
392 mounts a pump (KNF Neuberger model NMP09B), a bistable
393 3-way microvalve (by The Lee Company), the PID, and the
394 MEMS chip.

395 The sampling step consists of pumping the sample at a flow
396 of up to 120 mL/min into the MEMS chip. The duration and
397 flow rate of the sampling step can be adapted to specific
398 applications, and different configurations were tested. In
399 particular, with long sample times (50 min) at higher flow
400 rates (120 mL/min) ppb_v-level sensitivity to benzene was
401 demonstrated. For the injection/separation step, the 3-way
402 valve is switched and an activated carbon filter is used to
403 provide clean air into the MEMS, which is heated at a rate of
404 >50 °C/s to release the sampled aromatics. The flow during the
405 separation phase can be regulated by means of a needle-valve,
406 and several flow-rates were tested. The best results in terms of
407 selectivity to benzene over toluene were found with a 30 mL/
408 min flow. Figure 6 shows some typical signals acquired by the
409 PID detector during the desorption temperature ramp. In these
410 plots, the MEMS cartridge filled with EtQxBox was kept at
411 room temperature using the pump to sample the test mixture
412 from the sample inlet at 120 mL/min up to $t = 5$ min, when the

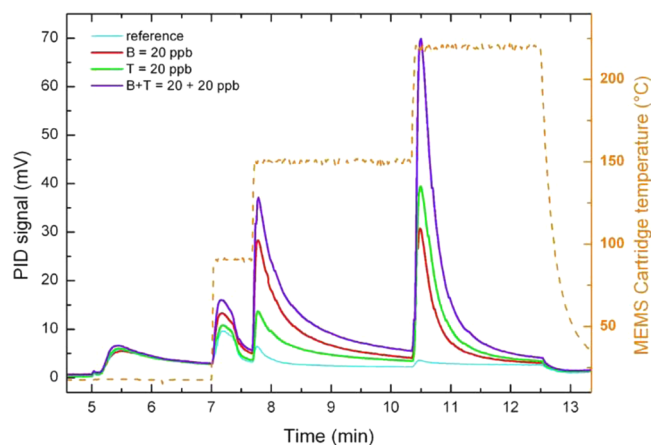


Figure 6. Typical responses of the PID detector to a temperature ramp for benzene (B, red), toluene (T, green), and a mixture of benzene and toluene (B+T, purple), compared to a “reference” sample of only air (cyan).

413 valve was switched to the filter line with a reduced flow of 30
414 mL/min.

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

423 This first result demonstrates how only a very small amount
 424 of toluene is released at 150 °C (see green line, 20 ppb_v of
 425 toluene only). This first temperature step is the most significant
 426 for benzene quantification, since toluene interferes only slightly
 427 during the 150 °C step. During the next temperature step at
 428 220 °C, more toluene (green) than benzene (red) is released. It
 429 is evident that the separation between benzene and toluene is
 430 not complete, due to the very short cartridge used for this work.
 431 Nevertheless, by calibrating the system and using a simple
 432 linear combination of the responses at the two temperatures
 433 (150 and 220 °C), the small signal generated by toluene at the
 434 150 °C step can be easily subtracted (see SI for more details),
 435 and a very good prediction of the benzene concentration in
 436 mixtures with much higher toluene concentrations can be
 437 achieved, as shown in Figure 7. The data reported in Figure 7

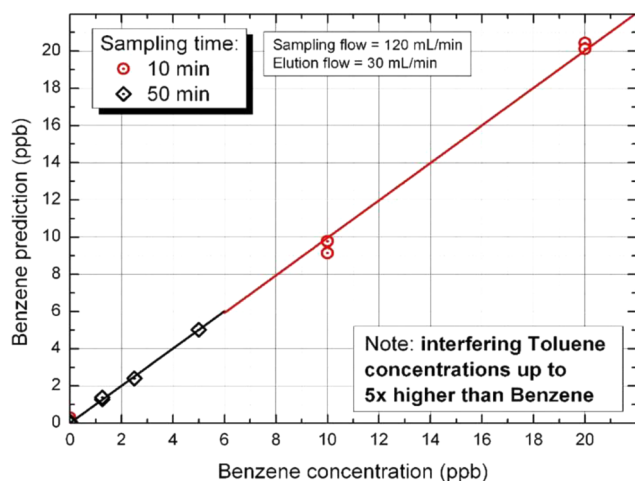


Figure 7. Benzene concentrations calculated using the equations (eqs 1a and 1b in SI) on a set of measurements performed with the prototype shown in Figure 5b. These values were calculated on samples where interfering toluene concentrations were up to 5 times higher than the benzene concentration.

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

443 The selectivity of benzene toward toluene, as shown in
 444 Figure 6, is expected to be improved in future works by using a
 445 longer MEMS cartridge filled with the EtQxBox, to increase the
 446 separation effect. Nevertheless, the current implementation has
 447 already demonstrated the capability of selectively quantifying
 448 benzene with a detection range spanning from 1.25 to 20 ppb_v.
 449 The superior benzene complexation capabilities of EtQxBox
 450 versus the previously reported QxCav can be disclosed from
 451 the plots of Figure 8, where the effect of the temperature during
 452 the sampling step is compared for the two cavitands. For both
 453 plots, the sensitivity is normalized to the value of 20 °C,
 454 resulting in arbitrary units on the y-axis. At temperatures
 455 slightly higher than 20 °C, QxCav rapidly decreases the
 456 complexation efficiency in adsorption, while EtQxBox has the
 457 same preconcentration capabilities up to temperatures close to
 458 60 °C, while around 100 °C the beginning desorption regime is
 459 evident. This widens the working temperature regime available
 460 for the corresponding device a lot. These findings demonstrate
 461 that the presence of a conformationally blocked cavity is able to

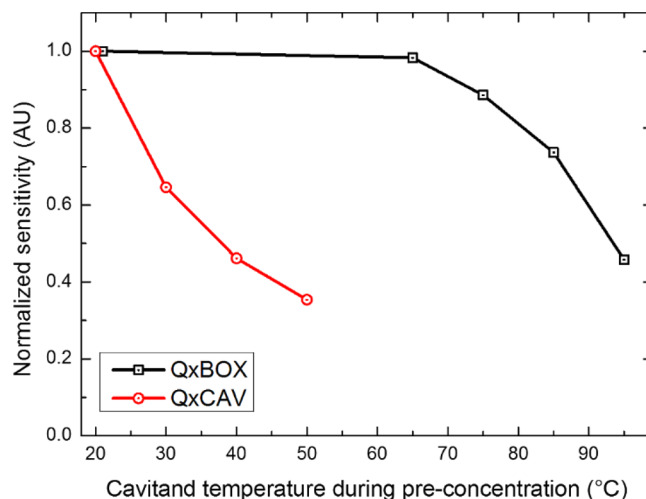


Figure 8. Normalized sensitivity toward benzene at increasing temperatures compared for QxCav (red line) and EtQxBox (black line). The higher binding energy of EtQxBox results in the capability of preconcentrating benzene efficiently up to over 60 °C.

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 cavitant 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/m³ level within its conformationally rigid cavity delimited by four quinoxaline walls linked via ethylenedioxy bridges. The conformational rigidity of the cavitant maximizes the binding of TEX with respect to benzene by increasing the number of synergistic CH $\cdots\pi$ interactions in the latter. 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

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

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519 Notes

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