

# Calixarene-coated piezoelectric quartz crystal sensor for the detection of organic amine in liquids

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Five calixarene compounds were applied as piezoelectric quartz crystal (PQC) sensory coatings for the selective detection of organic amines in liquids. The complexation based on the host–guest interaction between the calixarene coating and the analyte makes the coated PQC sensors sensitive to organic amines and results in quasi-irreversible frequency changes. The relative selectivity of the analytes is explained by the cavity inclusion of analyte molecule, complete or partial, or by steric hindrance interaction. A PQC sensor coated with a calixarene with an acetate ester group exhibits a nearly linear response for analytes in the concentration range 0–200 ppm.

## Introduction

The piezoelectric quartz crystal (PQC) has attracted increasing interest and several applications have been reported since it was introduced by King<sup>1</sup> in 1964 because of its small volume, simple instrumentation and high sensitivity. The variation of frequency (Hz) can be calculated using Sauerbrey's equation:<sup>2</sup>  $\Delta f = -2.3 \times 10^6 f_0^2 (M/A)$  where  $f_0$  is the basic frequency of the piezoelectric crystal (MHz),  $A$  is the coated surface area of the sensitive portion of the crystal (cm<sup>2</sup>) and  $M$  is the change in mass on the surface of the crystal. The theoretical detection limit of an oscillating quartz crystal is reported to be as low as 10<sup>−12</sup> g (if  $f_0 = 10$  MHz) for coating materials according to Sauerbrey's equation.<sup>3,4</sup>

PQCs with appropriate coating materials can interact effectively with specific analytes. To improve the sensitivity and selectivity of PQC sensors, in recent years macrocyclics, *e.g.*, crown ethers, cryptands, cavitants, cyclodextrins and calixarenes, have been used as coatings for gas detection.<sup>5–14</sup>

Simple dispersion forces and dipole–dipole interactions lead to sensor signals with poor selectivity but good reversibility. Hydrogen bonding (biochemistry) and steric interactions (key–lock principle) between the sensor coating and the analyte result in an increased signal intensity but it is quasi-irreversible.

The application of PQC sensors to liquids has provided new analytical possibilities for the chemical industry, environmental science, biotechnology and medicine, but the use of a PQC sensor in liquids is much more difficult than in gases. PQCs are damped significantly through contact with a liquid solution. The frequency shift of the PQC depends on the changes in properties such as density, viscosity, conductivity, permittivity and temperature of the solutions between the sensitive coating and analytes.<sup>15,16</sup> It is possible to obtain good stability of the oscillating frequency in water with specially developed electronics and to measure frequency shifts of coated PQC sensors totally immersed in water by the addition of small amounts of different analytes.

The applications of coated PQCs, for the selective detection of analytes in solution, have been reviewed.<sup>17</sup> However, there are still only limited examples of chemically coated PQCs that strongly respond to and discriminate among organic guests in the liquid phase.<sup>18–21</sup> More recently, calixarenes have demonstrated a remarkable complexing ability not only for metal ions, but also for organic species.<sup>22,23</sup> Because of their high selectivity, calixarenes can potentially be applied as sensor materials for organic species, but few papers have reported

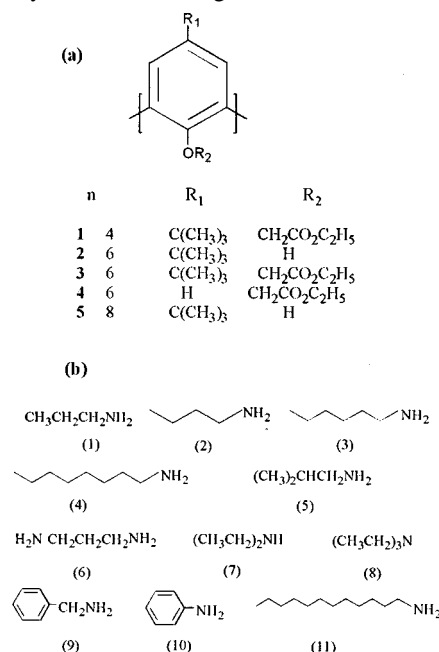
calixarene-coated PQC sensors that respond to organic molecules in liquids.<sup>20,21</sup>

In this study, we developed calixarene-coated PQC sensors for the determination of organic amines in aqueous solution. Organic amines are easily dissolved in water and also oxidized to nitrite compounds that are harmful pollutants in the environment. Many pharmaceutically important substances also contain an amino moiety, and success with such a sensor design for the monitoring and detection of organic amines in solution may have prospects for many analytical applications and great significance in environmental protection.

## Experimental

### Reagents

The structures of the sensing materials and analytes used in the present study are shown in Fig. 1. The calixarene compounds



**Fig. 1** Structures of (a) the sensory materials and (b) the organic amine guests examined in the present study; (1) propylamine; (2) butylamine; (3) hexylamine; (4) octylamine; (5) isobutylamine; (6) 1,3-aminopropane; (7) diethylamine; (8) triethylamine; (9) benzylamine; (10) aniline; (11) dodecylamine.

**1–5** were prepared by methods reported in the literature.<sup>24–27</sup> The analytes propylamine (98%), butylamine (99%), hexylamine (98%), octylamine (98%), dodecylamine (98%), isobutylamine (98.5%), 1,3-diaminopropane (99%), diethylamine (99.5%), triethylamine (99%), benzylamine (99%), and aniline (98.5%) and pure solvents dichloromethane and ethanol were all of analytical-reagent or chemically pure grade (Shanghai Chemical Reagent Co., Shanghai, China).

## Instrumentation

The apparatus consisted of an AT-cut piezoelectric quartz crystal with a fundamental frequency of 9 MHz, 12.0 mm in diameter and with gold- or silver-plated electrodes of 6.0 mm diameter on both sides (No. 707 Factory, Beijing, China). The oscillator circuit powered crystal was designed in this laboratory. The frequency change was monitored by an N3165-type frequency counter attached to a microcomputer system. The data acquisition system was also designed in this laboratory.<sup>28</sup>

## Crystal coating and measurement method

The coating solutions were prepared by dissolving 20 mg of the calixarene in 5 ml of dichloromethane or chloroform. The concentrations of the resulting solutions were about 4 mg ml<sup>-1</sup>. Both sides of the crystals were coated with the calixarene solution *via* the dropping method with a microsyringe. An aliquot of 3.0–5.0 µl of calixarene was dropped on to each side of the quartz crystals. A thin membrane was obtained after solvent evaporation and dried with a hot air blower for approximately 30 s. Fig. 2 depicts the experimental set-up of the PQC sensor detection system with the assembled computer interface. Both sides of the PQC sensors connected with the oscillator system were immersed in water–ethanol solution (95 + 5 v/v). The temperature of the measuring chamber was controlled at 25 ± 0.5 °C using a thermostated water jacket. The frequency of the vibrating crystal was measured with an N3165-type frequency counter connected to a microcomputer system. About 0.2–10.0 µl of analyte was injected into the measuring chamber with approximately 16 ml of measuring medium at a constant stirring rate. The frequency data were recorded every 13 s. The frequency responses of the bare crystal and coated crystal were stable to within ±2 Hz over periods of 6 h in air. The additional sample volume leading to the frequency shift was <5 Hz on injecting <20 µl of sample into the measuring chamber, so the influence on the frequency change of the additional sample volume can be neglected. When the PQC sensors were immersed in a stirred solution, the frequency response was stable within ±10 Hz over 5–6 h.

The static method was adopted to study the adsorption of organic amines on the coated crystals. The waste liquid from the measuring chamber was pumped by a syringe. In order to ensure

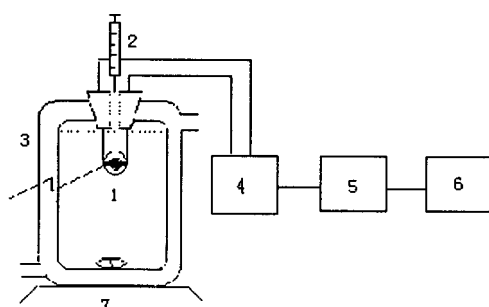
the reproducibility of the tests, the position of the PQC sensor in the measuring chamber was kept fixed. With exposure of the PQC sensor to a constant amine concentration (100 ppm), we measured the frequency change seven times. The relative standard deviation of the seven replicate measurements was <5%. Each sample was detected in triplicate and plotted as the average of three measurements with the sensor.

## Results and discussion

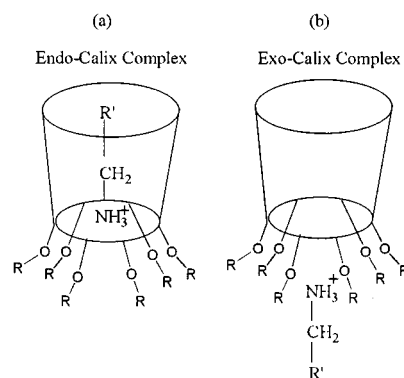
Calixarenes, cyclic oligomers of phenol–formaldehyde condensates, have emerged as attractive molecules for host–guest chemistry, this class of host compounds having a well-defined cavity, which is composed of aromatic rings linked by methylene units at the *meta* position. The outstanding capacity of the calixarenes as receptors is mainly based on their variable chemical modification potential and their conformational pliability, which allows a kind of induced fit to the shape of a suitable guest molecule. Recently, the remarkable selective complexation and transport of alkali metal ions and organic guests by calixarene derivatives, especially those derivatized with acetate ester units on the lower rim, have been reported.<sup>22,23</sup> The well-defined structure of the calix[*n*]arenes' (*n* = 4, 6, 8) cavity could be exploited for inclusion of organic guests. Especially the cavity of calix[6]arene is sufficiently large to accommodate organic guests, whereas that of calix[4]arene is too small. As depicted schematically in Fig. 3, there are two possible geometries for the complexation between the calixarene host and a primary amine guest. The *endo*-calix complex involves tripodal hydrogen bonding with inclusion of the non-polar moiety of the guest in the calixarene cavity and the *exo*-calix complex involves tripodal hydrogen bonding from the opposite side without inclusion in the cavity. Many studies have shown that calixarenes form *endo*-calix complexes with organic amines. The calixarenes bind with a protonated amine only through its NH<sub>3</sub><sup>+</sup> group without any interaction with the non-polar moiety.<sup>29–31</sup>

## Comparison of response behaviour of calixarene-coated PQC sensors to different organic amines

The response curves for calixarene **2**- and **3**-coated PQC sensor detection systems for 100 ppm of 10 organic amines at 25 °C in the measuring chamber are shown in Fig. 4. The response characteristics of PQC sensors coated with calixarenes **1** and **4** to 100 ppm of organic amines were the same as that of calixarene **3**. Calixarenes **2** and **5** gave similar responses. The frequency response curves of PQC sensors with calixarenes **1**, **4** and **5** are omitted. It can be seen that in 5% ethanol solution, the



**Fig. 2** Experimental set-up for the calixarene-coated PQC sensor. 1 = Piezoelectric quartz crystal sensor; 2 = microsyringe; 3 = thermostat; 4 = oscillator; 5 = frequency counter; 6 = computer; 7 = electromagnetic stirrer.



**Fig. 3** Schematic representations of the complexation geometries of the host–guest complexes: (a) *endo*-calix arene and (b) *exo*-calix arene complexes.

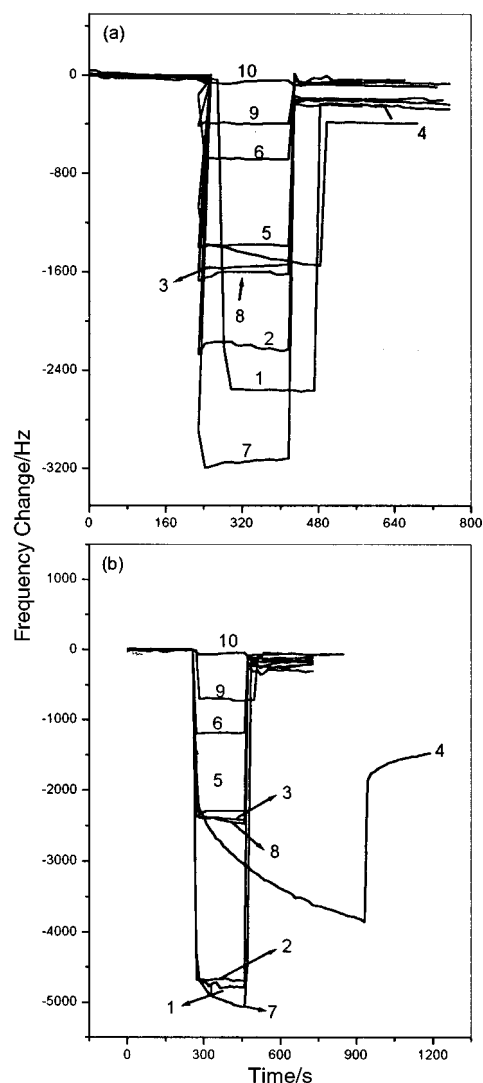
complexation interactions between the calixarene and organic amine guests are stronger and therefore they give relatively high frequency shifts and result in a quasi-irreversible behaviour resulting from hydrogen bonding under the measuring conditions. The relative selectivity of amines to calixarene compounds **1–5** decreases in the order diethylamine > propylamine > butylamine > hexylamine  $\approx$  triethylamine > isobutylamine > 1,3-aminopropane > benzylamine > aniline. The only exception is octylamine. According to its shape, it should give a lower response than butylamine and hexylamine, but its frequency shift is higher than that of these amines. It was observed that the response of octylamine reached stability after 5 min with coatings of calixarenes **1**, **3** and **4**, which have lipophilic acetate ester units on the lower rim, but required more than 10 min to stabilize with coatings of calixarenes **2** and **5**, which have a hydroxyl group. This is attributed to the extra lipophilic acetate ester-stabilized interaction between the host and guest molecules. We also tested dodecylamine with a longer alkyl group and found that its frequency shift is much higher than that of the other amines and its response stabilized after 4 h with all five calixarene coatings. The higher frequency shift of dodecylamine might arise from the ability of its long hydrocarbon chain to form a coil and fill the cavity.<sup>32</sup> It is concluded that a long alkyl group is another important factor controlling the response of organic amines. Comparison of the analyte structures with the selectivities shows that the discrimination of

organic amine guests is in the order of the steric shapes of their non-polar moieties and the basicity of the amine. Small amine molecules, having a higher frequency change, are relatively easily included in the calixarene cavity. The lower response of benzylamine and aniline is due to the bulkiness of their non-polar moieties, which cannot be incorporated in the cavity (Fig. 3). Aniline gives nearly no response.

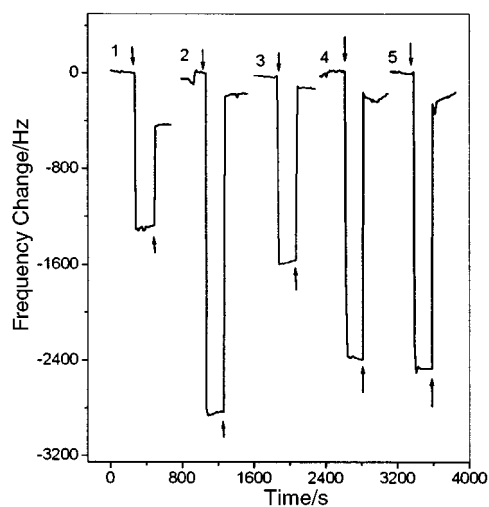
### Comparison of response behaviour of different calixarene coatings to 100 ppm hexylamine

Fig. 5 depicts the response behaviour of five calixarene-coated PQC sensors to 100 ppm hexylamine. It can be seen that the magnitude of the response of the coatings to hexylamine decreases in the order **2** > **5** > **4** > **3** > **1**. The Corey–Pauling–Koltun (CPK) molecular models of calixarenes indicate that the approximate hydroxyl end cavity diameter ranges of ligands are *p*-tert-butylcalix[4]arene 0.68–0.92, *p*-tert-butylcalix[6]arene 2.1–2.8 and *p*-tert-butylcalix[8]arene 4.0–4.5 Å. Although the cavity diameter decreases in the order calix[8]arene > calix[6]arene > calix[4]arene, the organic amine response decreases in the sequence calix[6]arene > calix[8]arene > calix[4]arene. It is probable that the close correspondence between the relative magnitudes of the organic amine (ionic diameter of ammonium ion = 2.96 Å) and the calixarene cavity diameters is an important factor in determining the complexation interactions between the calixarene and the amine guests.

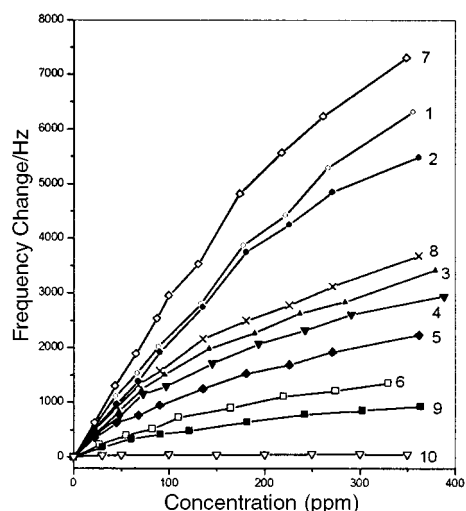
It can be seen that the response of three calix[6]arene hosts to hexylamine decreases in the order of calix[6]arene **2** > calix[6]arene **4** > calix[6]arene **3**. The frequency shift of a calixarene with a hydroxyl group is higher than that of a calixarene with an acetate ester group. The calixarenes with the extra lipophilic acetate ester group favour the formation of an *endo* complex over an *exo* complex (Fig. 3) between the host and guest molecules. The ammonium group of the guest is anchored in the pseudo-cavity of the host both by the tripodal hydrogen bonding interaction  $N^+ \cdots H \cdots O=C$  (host) and by the ion–dipole interaction  $N^+ \cdots O=C$  (host), similarly to many alkylammonium crown ether complex systems.<sup>33</sup> The calix[6]arene **3** having a bulky *tert*-butyl group on the aromatic ring of the host would deter the organic amine guest from interacting with its endopolarization site and gave the lowest response. The hosts with a hydroxyl group gave stronger frequency responses. This is because calixarenes interact fairly strongly with organic amines in polar solvents and form *endo*-calix complexes which are thought to involve proton transfer from the calixarene to the



**Fig. 4** Responses of PQC coated with (a) calix[6]arene **2** and (b) calix[6]arene **3** to 10 organic amines. 1, propylamine; 2, butylamine; 3, hexylamine; 4, octylamine; 5, isobutylamine; 6, 1,3-aminopropane; 7, diethylamine; 8, triethylamine; 9, benzylamine; 10, aniline.



**Fig. 5** Effect of calixarene coating on frequency shifts of PQC sensors to 100 ppm hexylamine. Traces 1–5: coating calixarenes **1–5** respectively. ↓, inject into amine; ↑, transfer into blank measuring medium.



**Fig. 6** Response characteristics of PQC sensor with calixarene **3** for organic amines at 25 °C in water-ethanol solution. Analytes: 1, propylamine; 2, butylamine; 3, hexylamine; 4, octylamine; 5, isobutylamine; 6, 1,3-aminopropane; 7, diethylamine; 8, triethylamine; 9, benzylamine; 10, aniline.

amine to produce a calixarene anion and an ammonium cation, followed by ion pairing.<sup>32</sup> It is expected that the host-guest match will be manifested by a complementary relationship in terms of the size and the lipophilic effect between the organic amine and the calixarene. The host-guest electronic complementarity, steric complementarity and host preorganization determine the response behaviour of PQC sensors.

Fig. 6 is the calibration graph obtained for calixarene **4** as the sensitive layer with 10 organic amine guests in water-ethanol solution. It can be seen that the frequency changes increased gradually with increasing amine concentration and gave a nearly linear response in the range 0–200 ppm. The frequency change is no longer proportional to amine concentrations at higher concentration. In this work, the limit of detection (LOD) for each amine in Fig. 6 was calculated by extrapolating the response curves to a frequency shift of 60 Hz, three times the baseline noise (20 Hz). The LODs of propylamine, butylamine, hexylamine, octylamine, isobutylamine, 1,3-aminopropane, diethylamine, triethylamine and benzylamine are 2.84, 2.95, 4.29, 5.15, 7.47, 9.43, 2.31, 3.82 and 17.6 ppm, respectively. Aniline gave no frequency change.

## Conclusion

In this study, we investigated five calixarene-coated PQC sensors for the detection of organic amines in liquids. The relative sensitivity of amines is based on host-guest complexation between the organic amine and the calixarene. The response slopes of amines are linear at low concentrations. Stronger responses were observed for small amine molecules which are easy included in the calixarene cavity. The response of the amines with a bulky group (benzylamine, aniline) is weak, since the bulky group hinders the amine from being included in the cavity. The calixarenes with a hydroxyl group on the lower rim, forming stronger complexes in ion pairing with organic amines, gave larger frequency shifts than those having an acetate ester group on the lower rim. The experimental

results show that the organic amines interact with the calixarenes to form only *endo*-calix complexes. The calixarene-coated PQC sensors provide the shape discrimination of analytes via the inclusion of organic amine molecules completely or partially or by hindrance.

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