Synthesis of Novel β-Cyclodextrin and Calixarene Derivatives and Their Use in Gas Sensing on the Basis of Molecular Recognition

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In order to examine the molecular recognition effect of a three-dimensional hydrophobic cavity, seven β-cyclodextrin derivatives (**1**–**7**) bearing hydrophobic substituents on the primary side, and three structurally related calixarene derivatives (**8**–**10**) were synthesized and used as coating materials for a piezoelectric chemical sensor to detect some aliphatic amines in the gaseous state. The results obtained indicate that these synthetic receptors show considerable sensitivity and selectivity toward the analytes. It is interesting that the cyclodextrins and calixarenes show distinctly different sensitivity profiles for monoamino analytes, which were interpreted from the viewpoint of host-guest chemistry, that is, the response mechanism is mainly based on the molecular recognition behavior of the host compounds. It is also revealed that hydrogen bonding can be the major driving force in the coating-analyte interaction, and that there exists interstitial binding for the ethylenediamine-cyclodextrin interaction. The present study demonstrates that β-cyclodextrin and calixarene derivatives would serve as sensitive coating materials for piezoelectric chemical sensors.

Introduction

The molecular recognition behavior of synthetic receptors has been used extensively in various fields of science and technology. One of the most successful applications is in analytical chemistry. The piezoelectric chemical sensor is a widely employed analytical technique, including practical applications such as environmental monitoring and gas supervision in factories, due to its small volume, simple instrumentation, and high sensitivity.[1−3] As the property of the coating itself can determine the efficiency of the sensor, it is a long-term task in the field of piezoelectric chemical sensors to design and synthesize coating materials with high selectivity, sensitivity, and stability. Supramolecular, polymeric, and biomimetic coatings for chemical sensors have been studied and compared.[4−6] Supramolecular compounds possess inherent advantages for use as coating materials, because their molecular recognition ability and selectivity may be readily adjusted by chemical modification and tailoring. Various macrocyclic receptors, such as crown ethers,[7] cryptands,[8,9] cavitands,[10,11] cyclodextrins[12−15] and calixarenes,[16,17] have therefore been used as coatings for piezoelectric quartz crystal sensors.

Among synthetic macrocycles, cyclodextrins and calixarenes are endowed with fascinating hydrophobic cavities, which enable the encapsulation of diverse small organic molecules by forming inclusion complexes. This kind of interaction possesses the character of both chemisorption and physisorption,[18] which allows cyclodextrins or calixarenes to be used as coatings to resolve the contradiction between the selectivity and the reversibility of the signal response. As is well known, however, the binding forces for the inclusion complexation of cyclodextrin and calixarene are different in nature, even though both of them bear hydrophobic cavities. To be able to design highly effective macrocycle-based coating materials, it is therefore essential to investigate the sensor behavior of some structurally related cyclodextrin derivatives or calixarene derivatives.

Recently,[19−25] we have studied the molecular recognition behavior of cyclodextrins in aqueous solution with various guests, for example aliphatic alcohols, amino acids, and naphthalene derivatives, by using spectrometry and microcalorimetry. The binding mode and inclusion complexation mechanisms were carefully evaluated from the results obtained. More recently,[26] we have investigated and compared the inclusion complexation behavior of water-soluble calixarenes and native cyclodextrins with acridine red in aqueous buffer. The results obtained indicate that calixarenes and cyclodextrins affect the fluorescence of acridine red in a contrasting manner, which means that the inclusion complexation modes are distinctly different. In the present study, therefore, we prepared seven β-cyclodextrin derivatives (**1**−**7**, Scheme 1) and three calixarene derivatives (**8**−**10**) in order to detect a series of aliphatic amines in the gaseous state. The frequency response was obviously correlated with the structures of the analytes and the substituents in the coatings. The sensitivity and selectivity of sensors are discussed from the viewpoint of molecular recognition, in-

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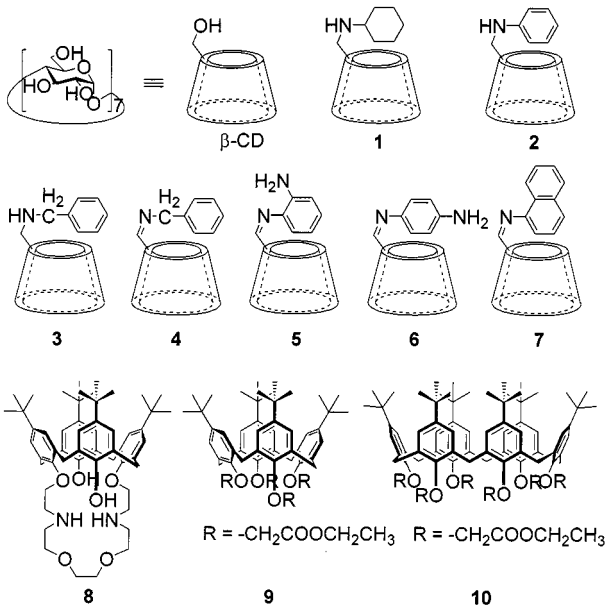


Scheme 1

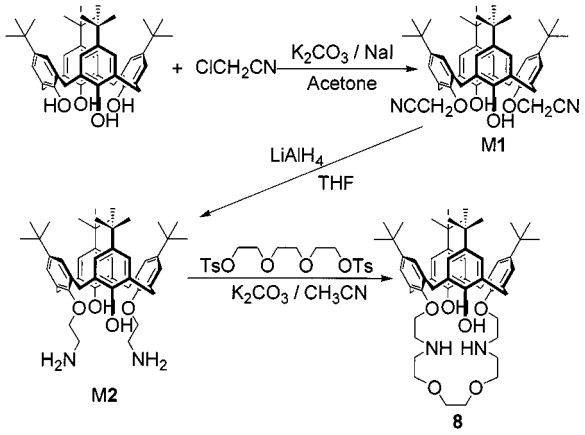
cluding the size/shape-fit concept, geometrical complementarity, and the cooperation of several weak forces. The results obtained not only serve to provide further understanding of the mechanism of the selective binding of guests by hosts, but also provide useful information for the design of highly effective coating materials.

Results and Discussion

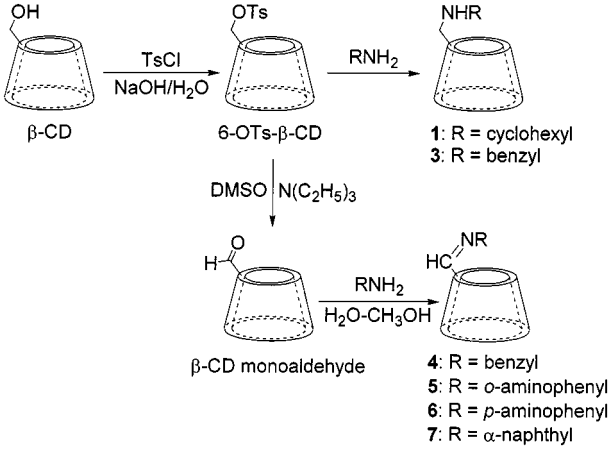
Synthesis

As shown in Scheme 2, the β-cyclodextrin derivatives **1** and **3** were synthesized in satisfactory yields from mono[6-*O*-(*p*-toluenesulfonyl)]-β-cyclodextrin and the corresponding amines directly, while compounds **4**−**7** were prepared in moderate yields by the nucleophilic addition reaction of 6-β-cyclodextrin monoaldehyde and the corresponding aromatic amines. Although acetic acid was used as catalyst in the later reaction, the reaction progress was found to be very slow and a longer reaction period was required. The Schiff base compounds **4**−**7** exhibit distinctly different solubility in water, and hence were purified by gel filtration chromatography and recrystallization as appropriate.

In the synthesis of calix[4]crown **8**, *p-tert*-butylcalix[4]arene was converted into the diacetonitrile derivative M**1** by reaction with chloroacetonitrile in acetone.[27] The intermediate M**1** was then reduced to the amino derivative M**2** in the presence of lithium aluminum hydride,[28] as shown in Scheme 3. Subsequently, the aminocalix[4]arene M**2** was reacted with triethylene glycol di(*p*-toluenesulfonate) under basic conditions to give the target compound **8** in a low yield. It is clear that the high reactivity of the primary amine is responsible for the product.



Scheme 3



Scheme 2

Frequency Signal of the Piezoelectric Chemical Sensor

Figure 1 shows the frequency response of the sensor coated by compound **2** to aliphatic amines. As can be seen from the figure, the frequency of the piezoelectric sensor was significantly changed upon addition of amine guests, indicating that an interaction exists between the coating and

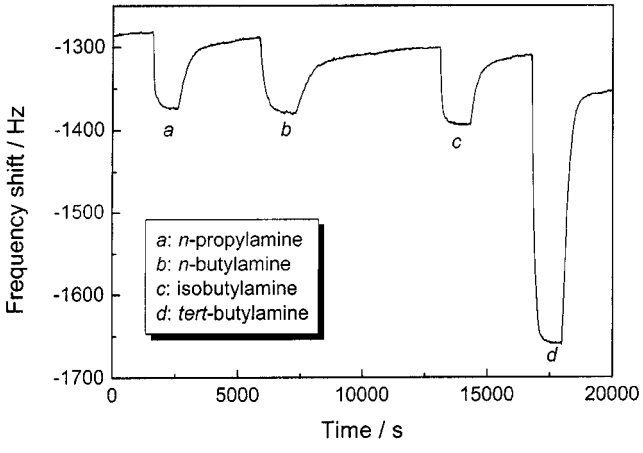


Figure 1. Frequency response of the sensor coated by compound **2** for aliphatic amines

Table 1. Frequency responses of the piezoelectric quart crystal sensors coated with β-cyclodextrin derivatives **1**−**7** and calixarene derivatives **8**−**10** to aliphatic amines in gaseous state at 28 °C

Guest	−Δ*F*/Hz									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
n-Propylamine	20	91	75	150	149	87	85	100	75	200
n-Butylamine	29	91	102	153	146	123	132	190	437	750
iso-Butylamine	25	92	109	198	185	149	131	70	115	210
tert-Butylamine	262	349	503	890	889	807	797	230	100	110
Diethylamine	7	35	61	72	71	91	77	−	65	300
Triethylamine	−	−	−	−	−	−	−	0	37	60
Ethylenediamine	9767	2099	4228	12288	6952	6224	6329	520	237	500
1,3-Propanediamine	2286	1101	2262	7175	6045	3549	3407	−	−	−

the analyte. As illustrated in Equation (1), there is a quantitative relationship between the frequency changes of the quartz crystal and the deposited mass.[29]

$$\Delta F = -2.3 \times 10^6 F^2 (\Delta Ms)/A \quad (1)$$

where ΔF denotes the change in frequency due to the coating (in Hz), F is the fundamental frequency (MHz) of the AT-cut piezoelectric quartz crystal, ΔMs represents the mass of the deposited coating (g), and A refers to the area coated (cm^2). Using the above equation, we calculated the amount of the absorbed guest to conclude guest:host stoichiometry. The results show that most of the guest:host stoichiometries are less than 1:1, whereas in the case of ethylenediamine and 1,3-propanediamine, a guest:host stoichiometry of up to 60:1 could be obtained.

The data of the frequency responses for compounds **1**−**10** are listed in Table 1. For the purpose of visualization, the frequency-change profiles for hosts **1**−**10** with different analytes are also shown in Figure 2.

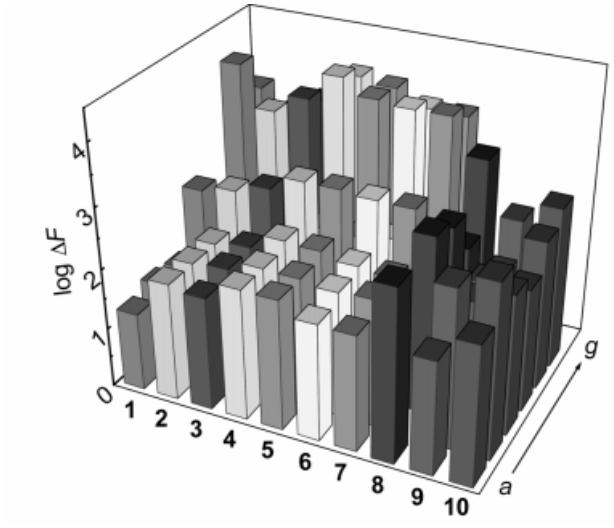


Figure 2. The logarithm frequency responses of the sensor coated by compounds **1**−**10** plotted as a function of aliphatic amines. *a*: diethylamine, *b*: *n*-propylamine, *c*: *n*-butylamine, *d*: *iso*-butylamine, *e*: *tert*-butylamine, *f*: ethylenediamine, *g*: 1,3-propanediamine

Sensitivity and Selectivity

Due to the possession of three-dimensional hydrophobic cavities, both cyclodextrin[30] and calixarene[31] may encapsulate neutral and charged organic molecules to form host-guest or supramolecular complexes in solution. The inclusion complexation is driven by various weak forces such as van der Waals, hydrophobic, hydrogen bonding, ion-dipole, and dipole-dipole interactions. However, the microenvironments of these two categories of hosts are constitutionally different owing to their topologies and compositions. As can be seen from Table 1 and Figure 2, the piezoelectric chemical sensor coated by compounds **1**−**10** shows considerable sensitivity and selectivity to the aliphatic amines, depending on the coating itself and the analyte's size and shape. Hence, below will we discuss the sensitivity and the selectivity of the piezoelectric chemical sensor with the two different coatings separately.

Cyclodextrin as Coating

In some previous reports,[19−25] we have demonstrated that in solution cyclodextrins and their derivatives can recognize the size and shape, as well as the chirality of the guest molecule. The complex stability constants and relative selectivity for the inclusion complexation of the guest molecules with cyclodextrin hosts are influenced by several factors, including the relative size of the cyclodextrin's cavity to the guest molecule, the induced dipole of the functional side arm attached to the edge of the cyclodextrin cavity, spatial conformation, and microenviromental hydrophobicity. It would therefore be interesting to investigate the relationship between the frequency response and the analyte's size and shape in the piezoelectric experiment in the gaseous-solid state.

As can be seen from Table 1 and Figure 2, the frequency response of the piezoelectric chemical sensor coated by compounds **1**−**7** is sensitive not only to the type, but also to the size and shape of the analyte molecule, showing good molecular selectivity. The sensor coated by compound **4** shows the strongest frequency response up to 12288 Hz for ethylenediamine. The sensor coated by compound **1**, however, affords the highest molecular selectivity of 1395 for ethylenediamine/diethylamine. These results clearly indicate

that piezoelectric sensors coated by β-cyclodextrin derivatives possess significant sensitivity and molecular selectivity for analytes, at least for the aliphatic amines used.

The data listed in Table 1 also show that the frequency responses to aliphatic amines were strengthened with the increase of hydrophobic chain length in the analytes, i.e. *n*-propylamine < *n*-butylamine. This result seems reasonable, since in aqueous solution the inclusion complexation stability of β-cyclodextrin derivatives with straight chain aliphatic guests increases almost linearly with increasing number of methylenes in the guest molecule.[32] Considering the calculated guest:host stoichiometries (less than 1:1), the above results suggest that these two analytes were encapsulated into the cyclodextrin cavity, and that van der Waals forces play a crucial role in the gaseous-solid interaction.

Furthermore, we note from Table 1 that the frequency response of the sensor is also sensitive to the shape of the guest molecule, i.e. *tert*-butylamine > *iso*-butylamine > *n*-butylamine. These results may be attributable to the dominant role of van der Waals forces. Geometrically, the branched guest molecule may be accommodated into the hydrophobic cavity of the cyclodextrin derivative and have the most contact surface area, thus enhancing the van der Waals interaction between host and guest. This enhancement counteracts the reduction in hydrogen bonding caused by the fact that the amino group in the guest is now not able to access the hydroxyl group in the rim of cyclodextrin. Therefore, it can be deduced that the size/shape fit between host and guest is the contributor to the formation of the inclusion complex, and is apparently the most important factor that determines the selectivity of the sensor.

As can be seen from Table 1, the frequency response of sensors to the guests possessing two functional groups, i.e. ethylenediamine and 1,3-propanediamine, is much higher than with the other amine guests. As we have pointed out previously, the guest:host stoichiometries for these two analytes are up to 60:1. The inclusion complexation mechanism therefore does not work with guests having two functional groups. Because the sensing experiments are run at low enough guest vapor pressures (approx. 10% or less of saturation), there should no analyte condensation on the sensor. Therefore, it seems that the amino groups in these guest molecules may form many intermolecular hydrogen bonds with the hydroxyl on both sides of cyclodextrin, and interstitial binding also probably exists.[33] Interestingly, it should be noted that the frequency responses for ethylenediamine are somewhat larger than those for 1,3-propanediamine. This observation further verifies that physisorption or hydrogen-bonding interactions dominate the frequency response to ethylenediamine and 1,3-propanediamine.

The hydrophobic sidearm attached to the β-cyclodextrin can significantly alter not only the sensitivity, but also the selectivity of the piezoelectric sensor. As can be seen from Table 1, compound **1** generally gives the lowest frequency response for amino analytes among the seven cyclodextrin hosts, although the selectivity for ethylenediamine/diethylamine is much higher than the other analogs. The nonplanar substituent should influence the host-guest interaction in a different way to the aromatic substituents. It is interesting to compare the frequency responses of compounds **2** and **3**, because there is only an additional methylene group in the substituent of compound **3**. From Table 1, it can be seen that the frequency responses of compound **3** for most analytes are larger than those of compound **2**, which indicates that the flexibility of the sidearm apparently affects the host-guest interaction. Structurally, the sidearm of compound **3** is more favorable for forming a self-inclusion complex, and therefore its effective cavity is more suitable for the small size analytes than compound **2**. It may be noted that compounds **4**−**7** generally afford higher frequency responses for analytes than compounds **1**−**3**. Although we have no direct evidence to explain this phenomenon, it seems that the imide (C=N) group contributes to the interaction with the guest molecules. In addition, the spatial arrangement of the functional group on the aromatic moiety also influences the selectivity of the piezoelectric sensor. As can be seen from Table 1, the sensor coated by compound **5** is more sensitive to aliphatic amines than that coated by compound **6**, except for diethylamine. This phenomenon reveals that the microstructural change of the host molecule apparently governs the selectivity of the sensor.

Calixarene as Coating

It has been demonstrated that calixarene derivatives may form an *endo* or an *exo* complex upon interaction with a primary amine guest.[34−36] In an *endo* complex, the amine guest enters the calixarene's cavity from the upper rim and the amino group forms hydrogen bonds with the oxygen atoms at the lower rim, while the apolar moiety is included into the hydrophobic cavity. In an *exo* complex, the amino group forms hydrogen bonds with the oxygen atoms at the lower rim and the apolar moiety stays outside of the cavity. Most studies have revealed that an amine guest forms a complex with a calixarene in the *endo* mode.

From Table 1 and Figure 2, we can see that the piezoelectric quartz sensor coated by calixarene derivatives affords much higher frequency responses to *n*-butylamine than *n*-propylamine, which can be ascribed to the fact that the size of *n*-butylamine matches the cavity of the calixarene. The frequency response to the three isomers of butylamine, however, is in the order of *n*-butylamine > *iso*-butylamine > *tert*-butylamine. Obviously, the bulky *tert*-butylamine could not form a stable *endo* complex with the calixarene derivatives due to steric hindrance. It could also be noted that the frequency response to triethylamine is lower than to diethylamine, as a result of steric hindrance, and the coating host **8** even shows no frequency response to triethylamine.

Just as cyclodextrins, the piezoelectric chemical sensor coated by calixarenes shows a higher frequency response to ethylenediamine than the other analytes. This phenomenon could also be attributable to the stronger hydrogen-bonding interaction between host and guest, and an associated complex may form accordingly. As we can see, the frequency response of coating **8** is generally higher than coatings **9**

and **10** upon binding amino guests. It seems that the four oxygen and two nitrogen atoms in the crown moiety of **8** are favorable for forming hydrogen bonds with primary amines. Consequently, the absorption effect of coating **8** is greater than coatings **9** and **10**. Interestingly, we may note from Table 1 that cyclodextrin derivatives afford a much higher frequency shift to ethylenediamine than calixarene derivatives. Apparently, the numerous hydroxyl groups in the former provide many more hydrogen-bonding sites.

From Table 1 and Figure 2, it can be seen that coating **10** is more sensitive to the analytes than coating **9**. Structurally, host **10** possesses a calix[6]arene moiety, whereas host **9** bears a calix[4]arene backbone. Therefore, the larger cavity of calix[6]arene is more favorable for accommodating organic molecules than calix[4]arene. In order to promote the frequency response of the calix[4]arene coating, extra hydrogen-bonding sites should be introduced, as in the case of host **8**.

Conclusion

In conclusion, the piezoelectric chemical sensors with β-cyclodextrin derivatives **1**−**7** and calixarene derivatives **8**−**10** as coatings show considerable sensitivity and selectivity toward aliphatic amines. The response mechanism is mainly based on the molecular recognition behavior of the host compounds, and several factors cooperate to influence the frequency response. Among them, van der Waals interactions are the major driving force on complexation with the guest molecules, while hydrogen-bonding interaction and physisorption are also responsible for the frequency shifts. Furthermore, induced-fit, geometric compensation, and the topology of the functional substituent play crucial roles in this association procedure. Piezoelectric chemical sensors with high sensitivity and selectivity towards specific analytes may be obtained by using a suitable macrocycle with a hydrophobic cavity as a coating. It can be anticipated that the molecular recognition phenomenon will have an extensive application in piezoelectric chemical sensors.

Experimental Section

General: Elemental analyses were performed on a Perkin−Elmer 240 instrument. ^{1}H NMR spectra were recorded in D_2O, [D_6]DMSO or $CDCl_3$ on a Bruker ACP-20 spectrometer at 200 MHz. UV/Vis spectra were measured on a Shimadzu UV-2401/PC instrument. Mass spectra were obtained with a JEOC JMS-DX-303 instrument. The apparatus used in the gas sensing experiment consisted of an AT-cut piezoelectric quartz crystal with a fundamental frequency of 9.31 MHz, 6.0 mm in diameter, and with gold or silver-plated electrodes of 3.0 mm diameter on both sides. The oscillator circuit powered crystal and data acquisition system were designed according to the method of Xing et al.[37] The frequency change was monitored by an N3165-type frequency counter attached to a microcomputer system.

Materials: All guest amines were of commercially available analytical-grade reagent or chemically pure grade and used without further purification. β-Cyclodextrin of reagent grade was recrystallized twice from water and dried in vacuo at 90 °C for 12 h prior to use. Coating host **2**[19] and coating hosts **8** and **9**[38,39] were synthesized according to the procedures described previously, and were characterized by using combustion analyses, ^{1}H NMR, UV/Vis spectra and FAB-MS.

Mono(6-cyclohexylamino-6-deoxy)-β-cyclodextrin (1): Mono[6-*O*-(*p*-toluenesulfonyl)]-β-cyclodextrin (6-OTs-β-CD) was prepared by the reaction of β-cyclodextrin and *p*-toluenesulfonyl chloride in alkaline aqueous solution.[40] Compound **1** was synthesized by the reaction of 6-OTs-β-CD (2 g) with cyclohexylamine (30 mL) at 70 °C and stirring the mixture for three days under N_2. The reaction solvents were then evaporated to dryness in vacuo. The residue was dissolved in a small amount of hot water and then poured into acetone (300 mL) to give a gray precipitate, which was collected by filtration. After drying, the crude product was recrystallized twice from water, and dried in vacuo to give a white pure sample (yield 57%). FAB-MS: *m*/*z* = 1217 [M + H^+ − $6H_2O$]. ^{1}H NMR ([D_6]DMSO, TMS): δ = 1.0−1.8 (m, 11 H), 3.4−3.8 (m), 4.4−4.6 (s), 4.82 (m, 7 H), 5.66 (m, 14 H). FT-IR (KBr): $\tilde{\nu}$ = 3295 cm^{-1}, 2928, 2851, 1650, 1451, 1414, 1368, 1336, 1299, 1241, 1205, 1154, 1097, 1032, 943, 858. $C_{48}H_{81}NO_{34}\cdot 6H_2O$ (1324): calcd. C 43.54, H 7.08, N 1.06; found C 43.56, H 7.54, N 1.01.[41,42]

Mono(6-benzylamino-6-deoxy)-β-cyclodextrin (3): Compound **3** was prepared in 37% yield from 6-OTs-β-CD and benzylamine according to the procedure described above. FAB-MS: *m*/*z* = 1224 [M^+ − $7H_2O$]. UV/Vis (H_2O): λ_{max} (log ε) = 258 nm (2.44). ^{1}H NMR ([D_6]DMSO, TMS): δ = 3.1−4.0 (m), 4.7−4.9 (m, 7 H), 7.3 (m, 5 H). FT-IR (KBr): $\tilde{\nu}$ 3367 cm^{-1}, 2905, 1736.3, 1693.1, 1626, 1598.8, 1545.9, 1499.5, 1403.6, 1342.5, 1258.5, 1149.3, 1073.1, 1023.8, 942.8, 851. $C_{49}H_{77}NO_{34}\cdot 7H_2O$ (1350): calcd. C 43.59, H 6.79, N 1.04; found C 43.35, H 6.72, N 1.09.[42]

Mono(6-benzylimino-6-deoxy)-β-cyclodextrin (4): 6-OTs-β-CD was converted into 6-β-cyclodextrin monoaldehyde by oxidizing with DMSO at 80 °C.[43] Benzylamine (30 mL) and monoaldehydic β-cyclodextrin (1 g) were dissolved in 30 mL mixed solvent of water and methanol (v/v: 1:2), and several drops of acetic acid were added to catalyze the reaction. The reaction mixture was stirred at room temperature under N_2 for five days, and the solvent was then evaporated under reduced pressure. The residue was dissolved in a small amount of water, and the resulting solution was poured into acetone with vigorous stirring to produce a brown precipitate, which was collected by filtration. The crude product was purified by column chromatography on Sephadex G-25 with water as eluent to give a pure sample (yield 31%). FAB-MS: *m*/*z* = 1221 [M − H^+ − $6H_2O$]. UV/Vis (H_2O): λ_{max} (log ε) = 233 nm (3.57), 289.5 (3.74). ^{1}H NMR (D_2O, TMS): δ = 3.2−4.0 (m), 5.29 (m, 7 H), 7.0−7.7 (m, 6 H). FT-IR (KBr): $\tilde{\nu}$ = 3326 cm^{-1}, 2927, 1652, 1453, 1410, 1364, 1332, 1298, 1241, 1203, 1154, 1078, 1033, 945, 858. $C_{49}H_{75}NO_{34}\cdot 6H_2O$ (1330): calcd. C 44.24, H 6.59, N 1.05; found C 44.16, H 6.24, N 1.04.[42]

Mono[6-(*o*-aminophenyl)imino-6-deoxy]-β-cyclodextrin (5): Compound **5** was synthesized by the reaction of monoaldehydic β-cyclodextrin and *o*-phenylenediamine according to the procedure described above, in 31% yield. FAB-MS: *m*/*z* = 1221 [M − $2H^+$ − $5H_2O$], 1244 [M + Na^+ − H − $5H_2O$]. UV/Vis (H_2O): λ_{max} (log ε) = 280 nm (3.85), 273 (3.86), 243 (3.87). ^{1}H NMR (D_2O, TMS): δ = 3.0−4.0 (m, 42 H), 5.27 (m, 7 H), 6.7−7.6 (m, 5 H). FT-IR (KBr): $\tilde{\nu}$ = 3300 cm^{-1}, 2931, 1649, 1636, 1455, 1415, 1366, 1334,

1152, 1078, 1030, 936, 852. $C_{48}H_{74}N_2O_{34}\cdot 5H_2O$ (1313): calcd. C 43.90, H 6.45, N 2.13; found C 43.96, H 6.35, N 2.04.

Mono[6-(*p*-aminophenyl)imino-6-deoxy]-β-cyclodextrin (6): Compound **6** was synthesized by the reaction of monoaldehydic β-cyclodextrin and *p*-phenylenediamine according to the procedure described above, in 29% yield. FAB-MS: m/z = 1221 [M − $2H^+$ − $2H_2O$]. UV/Vis (H_2O): λ_{max} (log ε) = 320 nm (3.72), 247 (3.99). ^{1}H NMR (D_2O, TMS): δ = 3.0−4.0 (m, 42 H), 5.32 (m, 7 H), 6.4−7.6 (m, 5 H). FT-IR (KBr): $\tilde{\nu}$ = 3337 cm^{-1}, 2930, 1644, 1628, 1515, 1457, 1419, 1362, 1339, 1155, 1079, 1029, 944, 859. $C_{48}H_{74}N_2O_{34}\cdot 2H_2O$ (1259): calcd. C 45.79, H 6.24, N 2.23; found C 45.73, H 5.98, N 2.15.

Mono[6-(α-naphthyl)imino-6-deoxy]-β-cyclodextrin (7): Compound **7** was synthesized by the reaction of monoaldehydic β-cyclodextrin and α-naphthylamine according to the procedure described above. The pure sample was obtained in 27% yield by recrystallizing from water. FAB-MS: m/z = 1258 [M^+ − $8H_2O$]. UV/Vis (H_2O): λ_{max} (log ε) = 234 nm (4.17), 305.5 (3.60). ^{1}H NMR ([D_6]DMSO, TMS): δ = 3.1−3.8 (m), 4.82 (d, 7 H), 6.5−8.1 (m, 8 H). FT-IR (KBr): $\tilde{\nu}$ 3326 cm^{-1}, 2927, 1704, 1650, 1632, 1579, 1514, 1454, 1406, 1365, 1332, 1298, 1237, 1202, 1153, 1078, 1031, 944, 856. $C_{52}H_{75}NO_{34}\cdot 8H_2O$ (1402): calcd. C 44.54, H 6.54, N 1.00; found C 44.48, H 6.48, N 0.88.

1,3-Calix[4]-dinitra-crown-6 (8): A mixture of 5,11,17,23-tetrakis-(*tert*-butyl)-25,27-di(aminoethylene)calix[4]arene (5.7 g)[28] and potassium carbonate (9.81 g) in 350 mL of acetonitrile was stirred for 0.5 h at room temperature. Subsequently, triethylene glycol di(*p*-toluenesulfonate) (3.25 g) was added and the reaction mixture was stirred under reflux for 7 days. After being cooled to room temperature, the solvent was evaporated to dryness. Then, dichloromethane (350 mL) was added, and 1 N hydrochloric acid was used to adjust the system to high acidity. The organic phase was collected and dried with anhydrous sodium sulfate. The solvent was evaporated and the residue was recrystallized from methanol to give a pure sample in 7.8% yield. FAB-MS: m/z = 849.7 [M − 3HCl + H^+]. ^{1}H NMR ($CDCl_3$, TMS): δ = 0.89 (s, 18 H, *t*Bu), 1.27 (s, 18 H, *t*Bu), 3.38 (t, 8 H, NCH_2), 3.64 (d, 8 H, $ArCH_2Ar$), 4.00−4.34 (12 H, OCH_2), 6.72 (s, 4 H, ArH), 7.06 (s, 4 H, ArH). FT-IR (KBr): $\tilde{\nu}$ 3436 cm^{-1}, 2961, 2906, 2871, 1628, 1484, 1463, 1363, 1300, 1200, 1123, 873. $C_{54}H_{76}N_2O_6\cdot 3HCl$ (958.6): calcd. C 67.66, H 8.31, N 2.92; found C 67.34, H 8.08, N 3.18.

Crystal Coating and Measurement Method: The coating solutions were prepared by dissolving 10 mg of the β-cyclodextrin derivative in 5 mL of hot water, or 25 mg of the calixarene derivative in 5 mL of chloroform. Both sides of the crystals were coated with the host solution via the dropping method with a microsyringe. The investigation on the effect of the coating amount suggested that the frequency changes increase almost linearly in the range of 1−3 μL, although they tend to level out on exceeding 3 μL. Therefore, an aliquot of 3.0 μL of the coating solution was dropped on to each side of the quartz crystals. The sensors were obtained after solvent evaporation. The sensors connected with the oscillator system were put into the measuring chamber (640 mL) and the temperature maintained at 28±0.1 °C using a thermostated water jacket. The initial air in the chamber was cleaned with N_2, then 5.0 μL of analyte was injected into the measuring chamber. The change of frequency was 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 nitrogen. The static method was adopted to study the adsorption of organic amines on the coated crystals. In order to ensure the reproducibility of the tests, the position of the piezoelectric quartz crystal sensor in the measuring chamber was kept fixed. Each sample was measured in triplicate and the relative standard deviation of the measurements was <5%.

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