



Preparation of the ferrocene-substituted 1,3-distal *p*-*tert*-butylcalix[4]arene based QCM sensors array and utilization of its gas-sensing affinities



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ABSTRACT

The article describes the synthesis of the new ferrocene-substituted calix[4]arene derivative **4** as sensitive layer, and suggests that the immobilization of it is on a quartz crystal microbalance gold electrode via the drop-casting method in order to produce the calix[4]arene-based QCM sensor. In addition, sensor response of the calix[4]arene-based QCM sensor was investigated towards carbon dioxide (CO₂) and carbon monoxide (CO). The sensing and selectivity studies show that the ferrocene-substituted calix[4]arene-based QCM sensor is an effective gas sensor toward both carbon dioxide and carbon monoxide.

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Introduction

Carbon dioxide and carbon monoxide are known serious hazard gases for living systems in the atmosphere [1–8]. An increasing concentration of carbon dioxide along with the other greenhouse gases in the atmosphere, is causing the global temperature to increase, and results in its toxic and harmful effects which reaches both people and fauna alike [1–3]. Carbon dioxide is released into the environment by anthropologic movements, fossil fuel combustion, cement production, sewers, grain silos, ship holds, spacecrafts, and submarines [4,5]. Carbon monoxide is also known to be toxic and dangerous for living systems in multiple environments. A dangerous effect is seen in humans, especially, as the bloodstream carries carbon monoxide through the lungs, and causes carbon monoxide to interact with hemoglobin (Hb), which carries the body's oxygen. This interaction creates carboxyhemoglobin (COHb), thereby reducing the oxygen-delivering capacity of the blood leading to the organs and tissues [7,8]. In high concentrations, carbon monoxide causes fatal intoxication in humans [9].

Calixarenes, produced by a condensation reaction of phenol and formaldehyde represent very useful building blocks in supramolecular chemistry [10–13]. Indeed, their easy preparation, unlimited functionalization, and differently-sized cavities of calixarenes make them unique macrocyclic compounds [14–16]. These advantages help calixarenes acquire the promising organic materials for enzyme-mimics, ion carriers, solid-phase support materials, ion selective electrodes, drug-delivery agents, and catalysis applications [17–20]. Chemical modification of them with various functional groups also provides selectivity associating with their complexation properties depending on host-guest, electrostatic, hydrogen bonding, ion-dipole, and dipole–dipole interactions [19–23]. Regarding these properties, calixarenes have also been employed as gas sensors for NO₂, CO₂, and CO, as well as humidity gases [24–26].

In the present study, an amino derivative of calixarene was reacted with ferrocene carboxaldehyde, which exhibits anion recognition effects based on a strong electrostatic interaction, to produce a new ferrocene-conjugated calixarene derivative as an effective sensor for toxic gases. The ferrocene-conjugated calixarene derivative was immobilized for the first time onto a quartz crystal microbalance gold electrode via the drop-casting method in order to investigate its sensor capacity towards carbon monoxide and carbon dioxide gases by using quartz crystal microbalance

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(QCM) techniques, the preferred technique for determining the sorption properties of hosts with respect to the specific gas as a guest.

Experimental

General remarks

TLC analyses were carried out on DC Alufolien Kieselgel 60 F₂₅₄ (Merck). All reactions, unless otherwise noted, were conducted under a nitrogen atmosphere. All starting materials and reagents used were of standard analytical grade from Merck or Aldrich and used without further purification. ¹H NMR was recorded on a Varian 400 MHz spectrometer. FTIR spectra were obtained on a Perkin–Elmer 1605 FTIR spectrometer using KBr pellets and 100/ATR Sampling Accessory. The cyclic voltammetric (CV) studies were carried out according to the literature procedure [27]. Elemental analyses were performed using a Leco CHNS-932 analyzer. Melting points were determined on a Gallenkamp apparatus in a sealed capillary glass tube and are uncorrected. A Shimadzu 160 A UV–vis apparatus was used to analyze absorbance of the ferrocene-conjugated *p*-*tert*-butylcalix[4]arene (**4**) in CH₂Cl₂ solutions.

Syntheses

The syntheses of compounds **1–3** were carried out according to the literature procedures [28–30]. The ferrocene-substituted calix[4]arene (**4**) is herein reported for the first time.

Synthesis of *p*-*tert*-butylcalix[4]arene-diester (**2**)

Yield: 14 g (63.4%); mp: 202–207 °C. FTIR (KBr): 1750 cm⁻¹ (C=O). ¹H NMR (CDCl₃): δ 0.97 (s, 18H, Bu^t), 1.24 (s, 18H, Bu^t), 3.35 (d, 4H, *J* = 12.6 Hz, Ar–CH₂–Ar), 3.85 (s, 6H, –OCH₃), 4.45 (d, 4H, *J* = 12.6 Hz, Ar–CH₂–Ar), 4.78 (s, 4H, –OCH₂CO), 6.85 (s, 4H, ArH), 7.05 (s, 4H, ArH), 7.10 (s, 2H, OH).

Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,27-dihydrazinamidicarbonylmethoxy-26,28-dihydroxy-calix[4]arene (**3**)

Yield: 1.6 g (53.3%); mp: 330–333 °C. FTIR (KBr): 1687 cm⁻¹ (N–C=O). ¹H NMR (400 MHz, CDCl₃): δ 1.02 (s, 18H, Bu^t), 1.26 (s, 18H, Bu^t), 2.15 (d, 4H, *J* = 1.6 Hz, NH₂), 3.42 (d, 4H, *J* = 13.3 Hz, Ar–CH₂–Ar), 4.11 (d, 4H, *J* = 13.2 Hz, Ar–CH₂–Ar), 4.63 (s, 4H, –OCH₂), 6.92 (s, 4H, ArH), 7.10 (s, 4H, ArH), 7.70 (s, 2H, –OH), 9.61 (brs, 2H, NH).

Synthesis of ferrocene-conjugated *p*-*tert*-butylcalix[4]arene (**4**)

To a solution of **3** (0.6 g, 0.756 mmol) in 30 mL THF, a solution of ferrocene carboxyaldehyde (0.3 g, 1.542 mmol) in 150 mL THF was added. The reaction mixture was refluxed for 2 days. The volatile component was evaporated to dryness, and the residue was dissolved in CHCl₃ and washed with water to adjust pH 7.0. The organic layer was then dried over MgSO₄, filtered off and evaporated to dryness. The crude was purified by column chromatography (SiO₂, EtOAc/MeOH, 20/1). Yield: 85%, m.p.: 184–186 °C. FTIR (ATR) cm⁻¹: 1641 (CH=N) and 1674 (C=O). ¹H NMR (400 MHz, CDCl₃): δ 8.20 (s, 2H, HC=N), 7.52 (s, 2H, –NH), 7.13 (s, 4H, ArH), 7.09 (s, 2H, –OH), 6.91 (s, 4H, ArH), 4.75 (s, 4H, OCH₂), 4.66 (brs, 4H, C₅H₄), 4.37 (brs, 4H, C₅H₄), 4.14–4.21 (m, 14H, Ar–CH₂–Ar and C₅H₅), 3.51 (d, 4H, *J* = 13.5 Hz, Ar–CH₂–Ar), 1.27 (brs, 18H, Bu^t), 1.0 (brs, 18H, Bu^t). ¹³C NMR (100 MHz, CDCl₃): δ 169.26 (CO), 153.60, 153.03, 150.43, 139.53, 139.48, 129.46, 129.21, 126.02, 125.25, 76.21, 73.94, 73.80, 68.57, 67.92, 38.98, 37.24, 31.54. Anal. Calcd. for C₇₀H₈₀Fe₂N₄O₆: C, 70.94; H, 6.80; N, 4.73. Found (%): C, 70.74; H, 6.91; N, 4.68.

Preparation of QCM electrodes

In order to prepare QCM electrodes, 4.7 mg of the ferrocene-substituted calixarene **4** or 2.6 mg of *p*-*tert*-butylcalix[4]arene **1**, which was used as a reference molecule, was dissolved in 4 mL of chloroform, respectively. The prepared solutions, each of which were 1 mM, were ultrasonicated for an hour to dissolve the compound thoroughly. Finally, the prepared solutions were kept at room temperature for 48 h. The step after preparation of the solutions was to clean the surface of gold coated QCM electrodes as follows: the QCM electrodes were cleaned in an ultrasonic bath in acetone, ethanol, propanol and distilled water for 15 min, respectively and then dried with high purity nitrogen. After cleaning QCM electrodes, 5 μL of each solution was dropped onto them and they were kept at room temperature to dry. The structures of the calixarene-modified QCM electrodes were determined by FTIR spectrum (see Fig. 1).

Adsorption and desorption of the ferrocene-substituted calix[4]arene **4** and *p*-*tert*-butylcalix[4]arene **1** were investigated under exposure of CO and CO₂ gas. Gas sensing properties of each derivative was investigated by using the Quartz Crystal Microbalance (QCM) technique. A 2-channel gas-flow system controlled via PC was set. Gas sensor responses of each calixarene film were measured by the frequency shift response with a flow gas system according to the Sauerbrey relation. The schematic of the measurement system is depicted in Fig. 2. A time-resolved electrochemical QCM (EQCM) with the model of CHI400A Series from CH Instruments (Austin, USA) was used to measure the change in the resonance frequency of quartz crystals between gold electrodes during adsorption and desorption. The range of oscillation frequencies of QCM is between 7.995 MHz and 7.950 MHz. AT-cut quartz crystals with a fundamental frequency of 7.995 MHz were obtained from International Crystal Manufacturing Co. (ICM). The density (ρ) of the crystal is 2.684 g/cm³, and the shear modulus (μ) of quartz is 2.947 × 10¹¹ g/cm s². Around oscillation frequency of 7.995 MHz, a net change of 1 Hz corresponds to 1.34 ng of gas molecules adsorbed or desorbed onto the crystal surface of an area of 0.196 cm². Gas flow into test cell were supplied by two mass flow meters (MKS,179A Mass-Flo[®]) and RS232 controlled gas flow control unit (MKS).

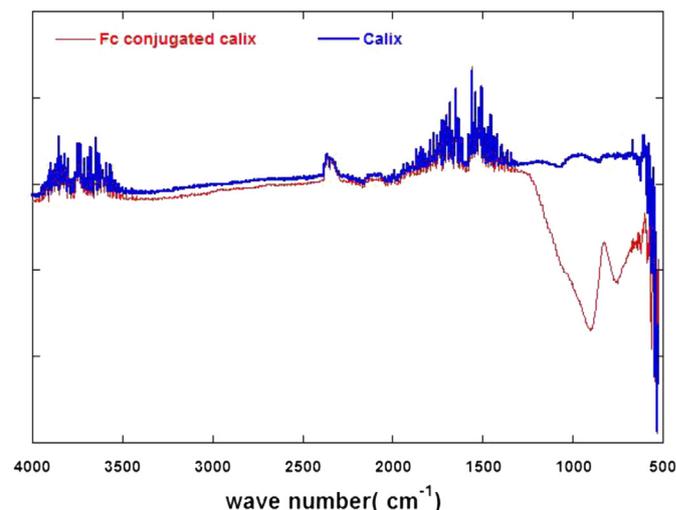


Fig. 1. FTIR spectra of the calixarene-modified QCM electrodes.

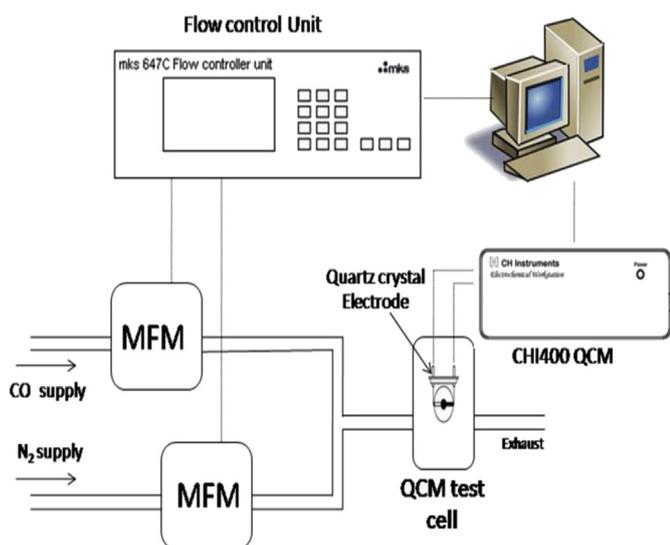


Fig. 2. An experimental QCM setup of calixarene derivatives under different gases.

Results and discussion

Selectively synthesis of calixarene containing organoiron derivative as a sensor

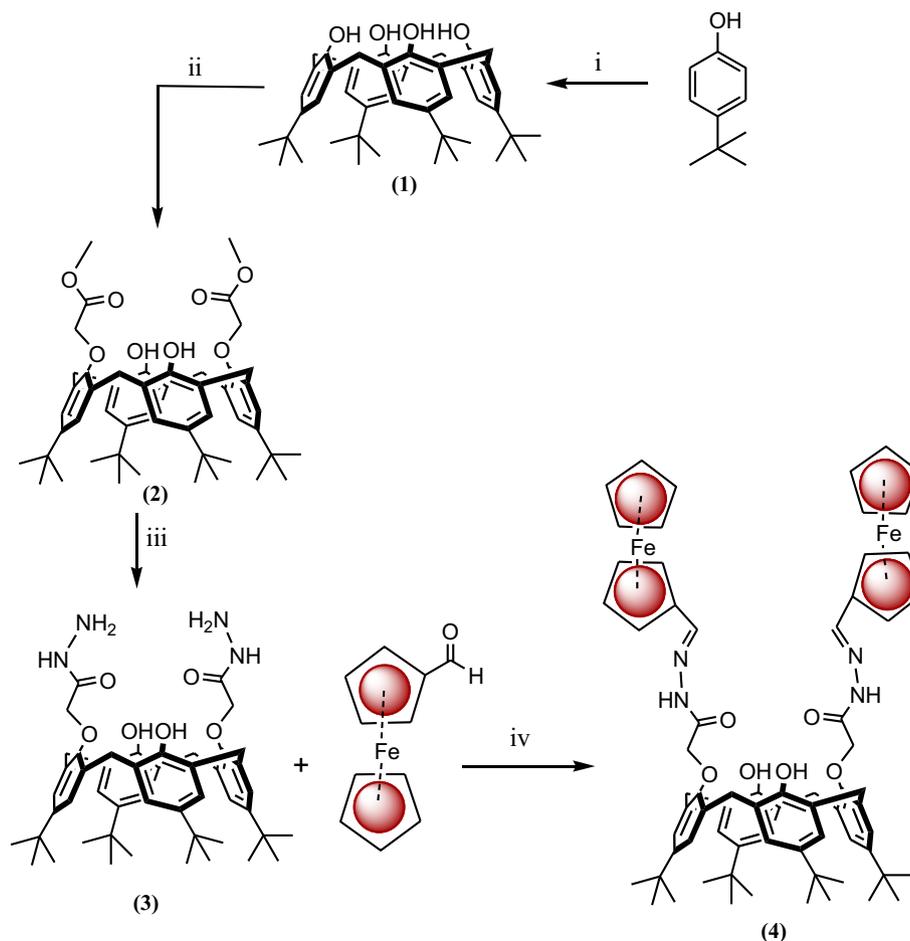
The main goal of this work was the synthesis of a new calixarene, containing organoiron derivative **4**, and the exploration of its

binding properties toward carbon monoxide and carbon dioxide gases as a new effective sensor. For this purpose, *p*-*tert*-butylcalix[4]arene **1**, and its diester derivative **2**, were synthesized according to the literature procedures [28,29]. The functionalization of the diester derivative **2** at the lower rim was conducted with hydrazine to produce 5,11,17,23-tetra-*tert*-butyl-25,27-dihydrazinamidecarbonylmethoxy-26,28-dihydroxy-calix[4]arene (**3**) according to the literature [30]. Next, **3** was treated with ferrocene carboxaldehyde to produce a target calixarene-organoiron derivative **4** (Scheme 1). All calixarene derivatives were characterized by using FTIR, ¹H NMR and elemental analysis techniques.

The FTIR spectra of the ferrocene-substituted calixarene **4** confirms its structure by appearing additional peak at 1641 cm⁻¹ wherein belongs the vibration stretch of CH=N bond. Moreover, ¹H NMR spectrum also confirms the formation of the ferrocene-substituted calixarene **4** by the appearance of the characteristic peak of imine protons (HC=N) at 8.20 ppm.

The UV–vis spectra for **4** in CH₂Cl₂ solvent at 200–600 nm are depicted in Fig. 3. The ferrocene-substituted calixarene **4** exhibits a strong absorption at 290 nm, corresponding to the π→π* transitions, and a weak band at 460 nm due to the d–d transition for the iron of ferrocene [27].

The cyclic voltammetric (CV) study was used to investigate the electrochemical properties of the ferrocene-substituted calixarene **4** (see Fig. 4). From the CV, it is clearly seen that the ferrocene-substituted calixarene **4** exhibit one reversible oxidation wave Fc–Fc⁺ at E_{1/2} = 0.53 V. The oxidation states given in Fig. indicate that calixarene has an electronic communication with the ferrocene units.



Scheme 1. Synthesis of the ferrocene-substituted calix[4]arene **4**. Reaction conditions: i) HCHO, NaOH; ii) methylbromoacetate, K₂CO₃, acetonitrile; iii) hydrazine, toluene/methanol; iv) THF.

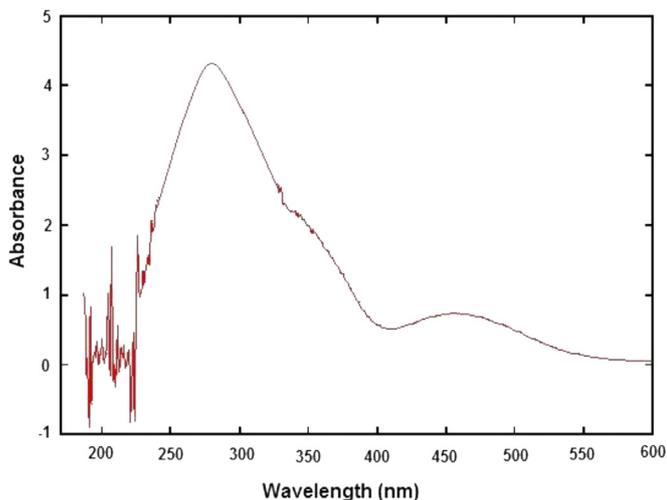


Fig. 3. UV-vis spectrum of the ferrocene-substituted calix[4]arene **4** (1.0×10^{-5} M in CH_2Cl_2).

Sensing studies

The removal of carbon monoxide (CO) and carbon dioxide gases (CO_2) from the atmosphere has gained high levels of attention because of the toxic and serious hazardous effects of the gases on the living systems. For this purpose, we were interested in synthesizing a new *p*-*tert*-butylcalix[4]arene derivative at lower rim, substituted with the ferrocene units as a host having well-binding lobes for carbon monoxide and carbon dioxide gases. In order to estimate sensing capacity of the ferrocene-substituted calixarene **4**, it was immobilized onto a quartz crystal microbalance gold electrode via the drop-casting method [26]. Additionally, to determine the impact of the organoiron units (ferrocene) of product **4** in the sensing studies, *p*-*tert*-butylcalix[4]arene **1** was also immobilized onto a quartz crystal microbalance gold electrode.

The sensing results indicated that the frequency responses of *p*-*tert*-butylcalix[4]arene **1** immobilized QCM and the ferrocene-substituted calixarene **4** immobilized QCM electrodes during the sorption process under CO and CO_2 gases (Figs. 5 and 6). Figs. 5 and 6 show that all calixarene-immobilized QCM electrodes have different responses towards carbon monoxide and carbon dioxide. The reason why the QCM electrode-immobilized with *p*-*tert*-

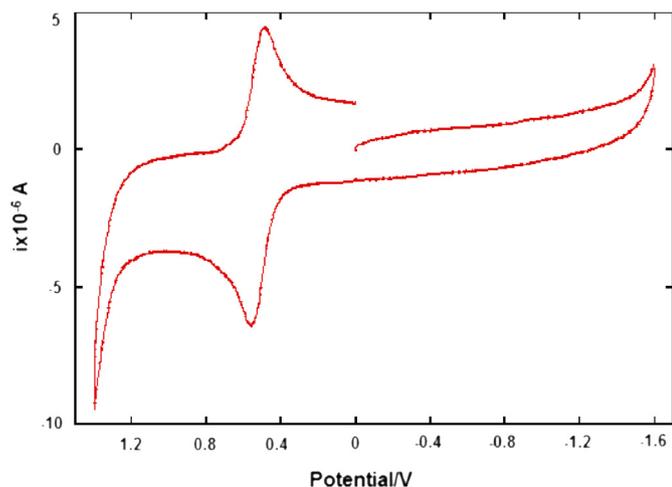


Fig. 4. Cyclic voltammogram of the ferrocene-substituted calix[4]arene **4** (1.0×10^{-4} M solution in CH_2Cl_2 , and 0.1 M Bu_4NPF_6) estimated at a scan speed of 100 mV/s.

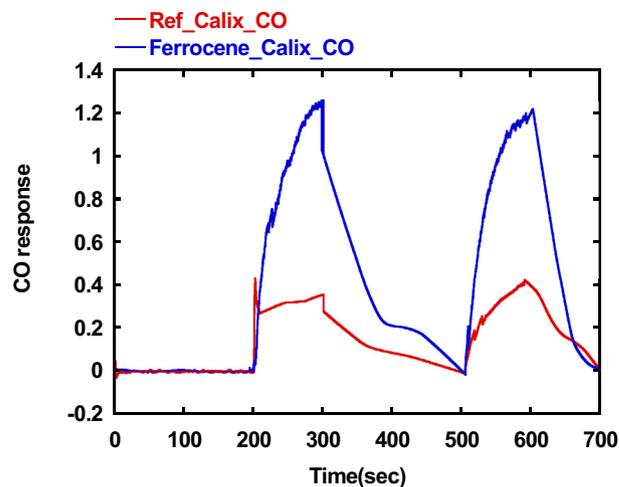


Fig. 5. QCM frequency shifts of the QCM electrode modified with ferrocene-substituted calix[4]arene **4** (Ferrocene_Calix_CO) and the QCM electrode coated with *p*-*tert*-butylcalix[4]arene **1** (Ref_Calix_CO) for adsorption and desorption cycles under carbon monoxide gas (CO).

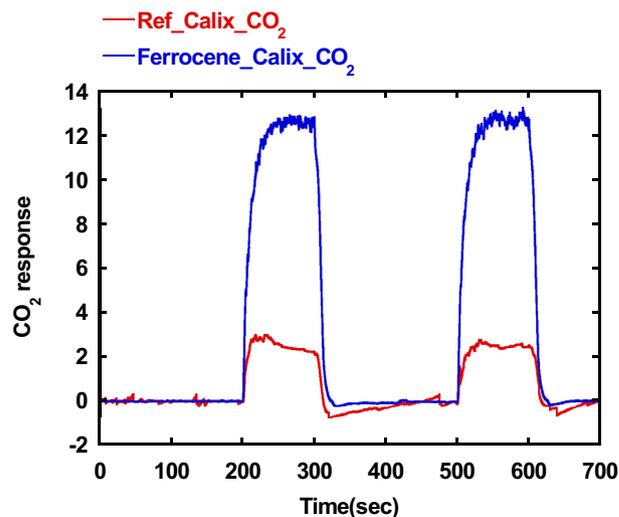


Fig. 6. QCM frequency shifts of the QCM electrode coated with ferrocene-substituted calix[4]arene **4** (Ferrocene_Calix_CO₂) and the QCM electrode coated with *p*-*tert*-butylcalix[4]arene **1** (Ref_Calix_CO₂) for adsorption and desorption cycles under carbon dioxide gas (CO_2).

butylcalix[4]arene **1** has a sensing capacity for CO and CO_2 gases might be that calixarenes have a rigid structure and also have strong complexation abilities such as host-guest, ion-dipole, dipole-dipole, and hydrogen bonding interactions. However, the fact that the QCM electrode-immobilized with the ferrocene-substituted calixarene **4** exhibited more sensing affinity than the QCM electrode-immobilized with *p*-*tert*-butylcalix[4]arene **1** for both gases would be assessed. This result was not surprising, because the organoiron units (ferrocene) of calixarene **4** provide additional complexation properties, such as cooperative affinities and strong anion binding capabilities, to calixarene derivatives.

Conclusion

A new the ferrocene-substituted calix[4]arene **4** was synthesized and then immobilized onto the surface of a quartz crystal microbalance gold electrode by using the drop-casting method to fabricate an organoiron-substituted calixarene-based QCM

electrode for the sensing of carbon monoxide and carbon dioxide gases. *p*-*tert*-Butylcalix[4]arene was also immobilized onto the QCM electrode, and its sensing capacity toward CO and CO₂ gases was investigated in order to compare and estimate the importance of the calixarene contained within the ferrocene units. The results indicated that both calixarene-immobilized QCM electrodes depend on strong complexation properties of the calixarene framework, such as host-guest, ion-dipole, dipole–dipole, and hydrogen bonding interactions, which were effective receptors for the adsorption of CO and CO₂ gases. However, the QCM electrode coated with ferrocene-substituted calix[4]arene **4** exhibited higher sensing affinity than the QCM electrode coated with *p*-*tert*-butylcalix[4]arene because it acquired more complexation properties, such as strongly anion binding and cooperative abilities, which came with the organoiron units of calixarene derivative. Hence, offering more complexation abilities of the QCM electrode coated with ferrocene-substituted calix[4]arene **4** would open new options for gas-sensing applications.

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