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Mass Sensors

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7.1 INTRODUCTION

Although the field of supramolecular chemistry or host–guest chemistry[1] is now mature it is only quite recently that applications of hosts in mass sensors have been investigated. This may be due to the fact that in the beginning of this field the focus was mainly on the selective complexation of cations and ammonium salts in water or organic media.[2] Later, neutral molecules were also studied by the groups of Collet,[3] Diederich,[4] Nolte,[5] Rebek,[6] Reinhoudt,[7] Sanders,[8] and others. Even more recent are the studies on the selective recognition of anions.[9] A change in mass is an event that occurs in many detection methods[10] and it is successfully exploited in bulk acoustic waves (BAW), of which the quartz microbalance (QMB) is the well-known representative, and surface acoustic waves (SAW). Potentially the recording of a mass change (or conductivity change) by a frequency change of a BAW or SAW device is very sensitive because, even in the megahertz or higher domain, a shift of a few hertz can be detected very accurately. The basis for the QMB was laid by Sauerbrey[11] and successfully applied by King[12] in 1964 as a hydrocarbon detector with a detection limit of 1 ppm for xylene. The advantage of SAW over BAW is the compatibility with chip technology and the higher sensitivity, due to the fact that they can be operated at higher frequency (see Section 7.2). SAW were first observed by Lord Rayleigh in 1885.[13] Among the first to apply SAW in mass sensors were Wohltjen and co-workers in 1979.[14] The use of polymer matrices as a "selector" in mass sensors relies mainly on trial and error and not so much on a clear molecular concept of recognition. Therefore it does not really belong to the field of supramolecular chemistry, but it is briefly dealt with in this chapter for the sake of completeness.

7.2 THEORY

7.2.1 Bulk Acoustic Waves

The QMB is based on the piezoelectric effect and was first observed by Curie and Curie in 1880.[15] Piezoelectricity occurs in crystals (or other materials) that do not possess a center of symmetry, of which there are 21 classes.[16] The piezoelectric effect arises when pressure on a dielectric material deforms the crystal lattice and causes a separation of the centers of gravity of oppositely charged species, which gives rise to a dipole moment in each molecule. Cady[17] and Voigt[18] performed the early mathematical treatment of this effect.

When an electric sensing circuit is connected via the electrodes to a piezoelectric material a current is observed when deforming the crystal. After releasing the stress a current in the opposite direction occurs. Analogously, an alternating potential will cause the crystal to vibrate. Stable oscillations only occur at the resonant frequency and at that frequency where the crystal presents a low impedance to the exciting voltage. This resonant frequency becomes the determining element of the circuit when it is incorporated into the feedback loop of an oscillating circuit, for its "quality factor" is very high, typically several thousands.

The early attempts used quartz crystals that were cut at specific angles with respect to the principal optical axis. The oscillators employed were cut in the yz plane and the electric field was applied to the x-axis. This method resulted in longitudinal vibrations along the y-axis. As a consequence, the length of the device becomes the frequency-determining factor, limiting the frequency of operation as the lengths required were too small to be practical. An alternative approach using the thickness as the frequency-determining parameter was frustrated by the interference of harmonics and overtones.

A successful attempt was to use the Y-cut crystals, which vibrate in the shear mode.[19] Almost no interfering vibrations occur but a drawback is the large temperature dependence. Lack *et al.*[20] have shown that the temperature dependence and the frequency constant are a function of the angle of rotation. Fortunately, two angles show zero temperature dependence: +35°15′ (AT-cut) and −49°00′ (BT-cut). The AT-cut crystals have found wide application in the mass sensing field. The response, shape, aging, and performance of the crystals is beyond the scope of this chapter, but information and further references can be found in some excellent reviews.[21] Not surprisingly, the QMBs have found wide application in analytical chemistry.[22] For a change in the frequency due to a change in mass Equation (1) can be derived, which is valid for small perturbations.

$$\Delta f = k f_0^2 (\Delta m / A) \tag{1}$$

where Δf is the frequency change (Hz), k is a constant related to material and thickness ($\mathrm{s\,m^2\,kg^{-1}}$), f_0 is the unperturbed resonant frequency (Hz), Δm is the mass change (kg), and A is the active area of the device ($\mathrm{m^2}$).

This equation was derived by Sauerbrey[11] and it applies only to AT-cut crystals which vibrate in the thickness shear mode, with the electric field applied along the y-axis. For quartz the constant k is $-2.3 \times 10^7 \mathrm{s\,m^2\,kg^{-1}}$ and one can predict a mass sensitivity of 10^{-9} g $\mathrm{Hz^{-1}}$ for a 10 MHz crystal. The mathematical treatment of the piezoelectric effect has also been done by Lostisd[23] and Stockbridge[24] with similar results. The QMB can, with limitations, be used for detection in liquids.[25]

7.2.2 Surface Acoustic Waves

The phenomenon of waves occurring at the surface of solids was first described by Lord Rayleigh in 1885[13] and these waves are consequently called Rayleigh waves. The first to apply the Rayleigh waves in a SAW device for the detection of chemical vapors were Wohltjen and co-workers.[14] Two often-used materials for SAW devices are quartz and lithium niobate ($LiNbO_3$) because relatively large, high-quality single crystals can be obtained. SAW devices are becoming more and more popular for a variety of reasons. Intrinsically they are more sensitive than BAW devices because they can be operated at higher frequencies. They are attractive because of their small size (e.g., $0.1\,cm^3$), ruggedness, potentially low cost, electronic output, and compatibility with chip technology.

Figure 1 shows an unstressed surface of a solid and one in which a Rayleigh wave propagates along the surface. The displacement of the particles at the surface consists of two components: a longitudinal (i.e., back and forth, parallel to the surface) and a shear vertical component (i.e., up and down). The vertical displacement amplitude is typically about 1 nm.

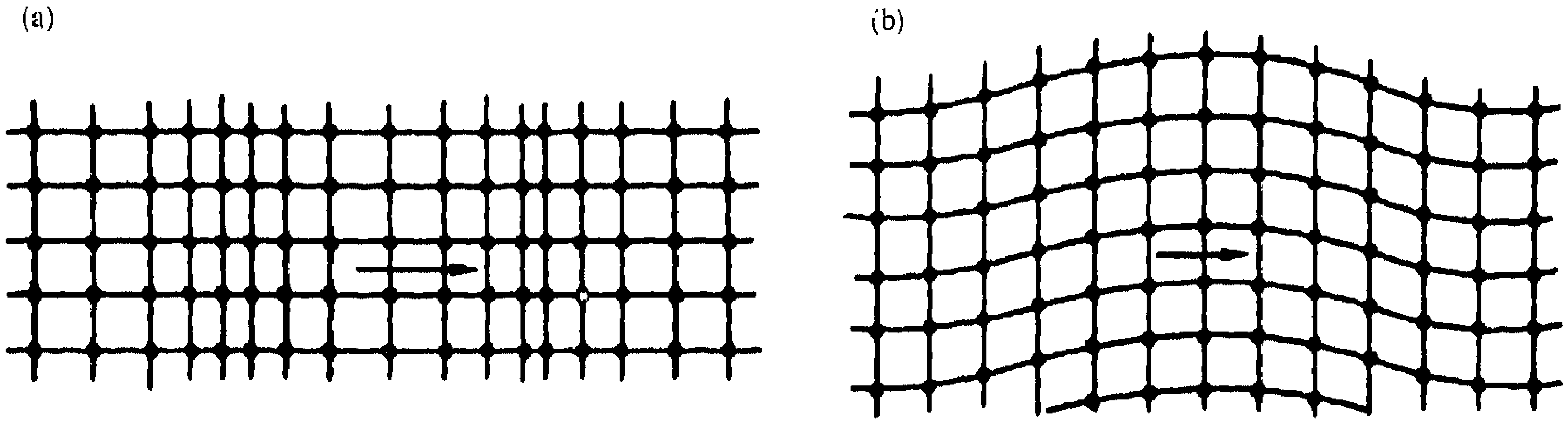


Figure 1 (a) Longitudinal and (b) transverse waves.

As the name implies, these waves have their energy mainly localized in one or two acoustic frequencies in the surface. The localization of the energy in the surface allows a strong interaction with the medium adjacent to this surface. Figure 2 shows a schematic drawing of the SAW delay line with a propagating Rayleigh wave.

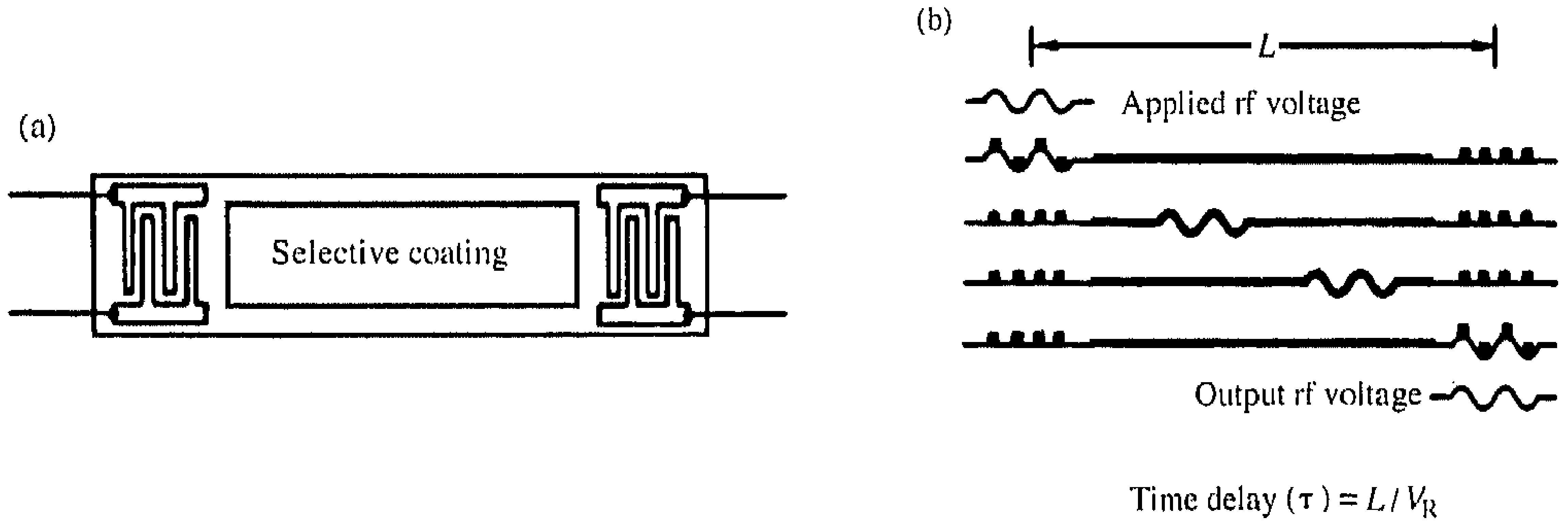


Figure 2 (a) Top view and (b) side view of a SAW delay line propagating a Rayleigh wave. The vertical displacement of the wave is greatly exaggerated for clarity.

The electrodes are micromachined from a thin, metal film (100–200 nm thick) and will generate a Rayleigh surface wave in the piezoelectric substrate when a radio-frequency voltage is applied. The spacing between the electrodes determines the wavelength, and thus the operating frequency, of the Rayleigh wave. More details on the design and electrical characteristics can be found in some articles and reviews and references cited therein.[26] Quartz and $LiNbO_3$ are popular materials for SAW devices because of low cost, good piezoelectrical properties, low temperature coefficient of delay, and low acoustic losses. Although other materials are available, certain crystalline orientations are frequently chosen to optimize either the piezoelectric coupling efficiency or the temperature behavior of the substrate in SAW applications. The ST-cut of quartz can propagate a Rayleigh wave with a zero temperature coefficient of delay at room temperature. However, the YX-cut has a more efficient piezoelectric coupling but it has a nonzero temperature coefficient. The actual SAW device needed depends strongly on the particular application in mind. Experience has shown that the measurement of SAW velocity perturbations using the delay line oscillator offers vastly superior precision compared to measurement of SAW amplitude perturbations. Therefore, SAW velocity perturbations only will be dealt with here. Information on SAW amplitude perturbations can be found in Ref. 26a.

Auld[27] has derived Equation (2) from a perturbation analysis of a SAW device coated with a nonconducting, isotropic overlay thin film. This equation describes the relative change of the Rayleigh wave frequency for thin films. This means that the film thickness must be smaller than 1% of the wavelength. Equation (2) is an extension of the Sauerbrey equation (Equation (1)).

$$\Delta f = \{(k_1 + k_2)f_0{}^2 h\rho\} - \left\{ k_2 f_0{}^2 h \left[\frac{4\mu}{V_r} \left(\frac{\lambda + \mu}{\lambda + 2\mu} \right) \right] \right\} \tag{2}$$

Here f_0 is the unperturbed resonant frequency (Hz), h is the film thickness (m), V_r is the Rayleigh wave velocity (m s^{-1}), ρ is the film mass density (kg m^{-3}), λ is the Lamé constant of the film (N m^{-2}), μ is the shear modulus of the film (N m^{-2}), and k_1 and k_2 are device constants (m^2 s kg^{-1}).

In Table 1 some typical values of the constants k_1 and k_2 are given. The first part of Equation (2) is independent of the shear modulus of the thin film and for many (soft) polymeric materials the second part of Equation (2) can be neglected. The resulting equation is essentially Equation (1). Thus, a mass change of the thin film is directly translated into a frequency change, which can be easily and accurately detected. The theory predicts a frequency change of −129.6 kHz for a 1 μm (h = 10^{-6} m) thick polymeric film with a density of 1000 kg m^{-3} on a YX-cut quartz SAW device, having $k_1 = -9.33 \times 10^{-8}$ m^2 s kg^{-1} and $k_2 = -4.16 \times 10^{-8}$ m^2 s kg^{-1} and operated at 31 MHz. Rayleigh waves are inadequate for sensing in liquids, because this type of wave shows severe losses when brought into contact with a liquid. SAW devices are not only applied for mass sensing but can also be used to study the viscoelastic properties of polymeric films[27] as is obvious from Equation (2). Like BAW devices, SAW devices have also been applied in analytical chemistry.[28]

Table 1 Material constants for selected SAW substrates.

Substrate	*Raleigh wave velocity*, V_R (m s ^{1})	k_1 (m^2 s kg ^{1})	k_2 (m^2 s kg ^{1})
Y cut X propagating quartz	3159.3	-9.33×10^{8}	-4.16×10^{8}
Y cut Z propagating $LiNbO_3$	3487.7	-3.78×10^{8}	-1.73×10^{8}
Z cut X or Y propagating CdS	1702.2	-8.33×10^{8}	-2.67×10^{8}
Z cut X or Y propagating ZnO	2639.4	-5.47×10^{8}	-2.06×10^{8}
Z cut X propagating silicon	4921.2	-9.53×10^{8}	-6.33×10^{8}

Source: Auld.[29]

7.2.3 Other Types of Waves

As stated above the Rayleigh wave is not suitable for application in liquid media due to the fact that it has a component perpendicular to the surface. This results in severe losses when brought into contact with a liquid. However, there are SAW that do not have this drawback: Lamb waves, Love waves, and Stonely waves. Lamb waves are also called flexural plate waves. In an elastic plate, with stress-free surfaces, parallel to the direction of propagation, an infinite number of two-dimensional plate wave modes, including Lamb waves,[30] can be excited. They can be generated in plates with a thickness smaller than one wavelength. Two types of plate waves are important: the symmetrical plate wave, whereby the longitudinal components are equal and the shear waves have opposite signs, and the asymmetrical plate wave, where on both sides of the meridian plane the longitudinal components change sign, whereas the shear components do not (Figure 3).

Lamb waves of the A_0 mode (lowest order asymmetrical mode) are very suitable for measuring in liquids, provided that the Lamb wave velocity, a design parameter, is lower than the velocity of the longitudinal wave in the adjacent liquid. Zellers *et al.*[26e] have shown that the Lamb-wave device can be at least an order of magnitude more sensitive than the SAW device for operation at the same acoustic wavelength. Wenzel *et al.*[31] have performed an analytical comparison of the

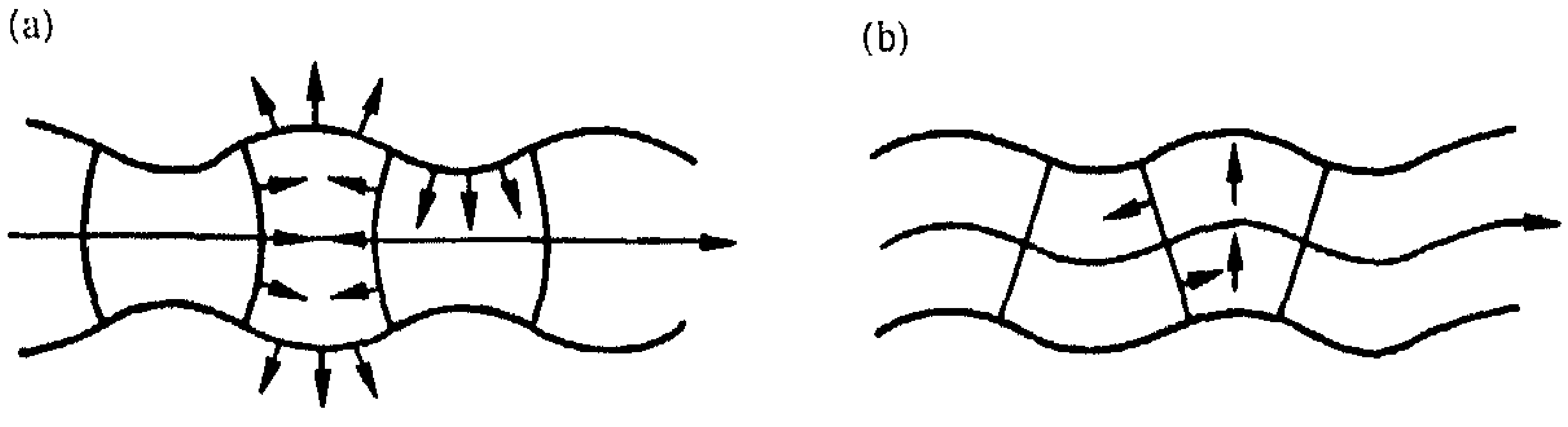


Figure 3 Lamb waves; (a) symmetric and (b) antisymmetric.

sensitivities of BAW, SAW, and Lamb-wave mass sensors. They found sensitivities of $2/\rho\lambda$, $\sim 1/\rho\lambda$, and $1/2\rho\delta$, respectively. Here ρ is the density of the sensor substrate material, λ is the wavelength, and δ is the plate thickness of the flexural-mode sensor.

Another potentially useful wave for measuring in liquid is the Love wave.[32] It is an acoustic-wave mode, where the shear horizontal wave motion is in the plane (interface) of solid and liquid. This Love wave is so interesting because the shear motion is not transferred into the liquid and consequently the acoustic energy transfer is minimal and in the case of ideal (i.e., nonviscous) fluids zero.

Nearly all acoustic-wave modes of interest can be converted, generated, and received by means of an interdigital transducer (IDT). The type of wave generated by an IDT depends on the position, the shape, the construction and the imposed boundary conditions of the sensing element.

7.3 SURFACE SPECIFIC MASS SENSORS

7.3.1 Immunoassays

For the detection of species in (complicated) biological systems, sensors based on antibodies offer good possibilities because antibodies with a high selectivity can be raised against specific species. The general approach followed is the immobilization of the antibody on the surface of the piezoelectric sensor.

The determination of the pathogenic microbe *Candida albicans* has been achieved by QMB coated with the anti-*Candida* antibody.[33] The frequency shift of the piezoelectric was 10^6–5×10^8 cells cm^{-3}. The sensor showed no response to *Saccharomyces cerevisiae*. Muramatsu *et al.*[33b,34] also used protein A for the detection of human IgG, an antigen, in the concentration range of 10^{-6}–10^{-2} mg mL^{-1}. The protein A was immobilized on the surface of the crystal electrodes with (γ-aminopropyl)triethoxysilane. AT-cut crystals, operated at 9 MHz, were used. The antibody goat antihuman IgG has been used for the detection of IgG. Thompson *et al.*[35] immobilized this antibody onto thin films of polyacrylamide gel and directly onto the QMB (AT-cut, operated at 2.5 MHz and 5.0 MHz). The antibody was bound to the gel by the glutaraldehyde method. Direct attachment of the antibody was achieved by oxidation of the surface-bound glycidoxypropyltrimethoxysilane to the aldehyde, followed by Schiff base formation with the antibody and reduction with $NaBH_4$. It was concluded that the frequency shifts are not necessarily related to the classical microgravimetric signal. It was also noted that the stability of the sensor is doubtful. Roederer and Bastiaans[36] immobilized the goat antihuman IgG on QMB (ST-cut, operated at 10.3 MHz) with a trimethoxyorganosilane as the coupling agent. With a signal-to-noise ratio of 3 Hz as the criterion for the limit of detection they were able to detect 13 μg of the antigen IgG. In principle, the bound IgG can be removed, which leads to a reusable sensor, but the immobilized antibody gradually breaks away from the surface. It was concluded that the greatest limitation of this biosensor is the poor sensitivity and limits of detection primarily due to nonspecific adsorption. The detection limit should be at least three orders of magnitude higher for clinical use. A second limitation common to all immunoassay methods is the requirement of a high molecular weight of the analyte. The human albumin has been detected in the range of 10^{-4}–10^{-1} mg mL^{-1} using the antihuman albumin antibody.[37] The antibody was reacted with protein A that was coated on the piezoelectric crystal. Crystals were regenerated by saturation with albumin and subsequent binding of a new anti-albumin antibody layer. This procedure could be repeated up to five times with the same crystal. Although it is claimed that the sensor is reusable, this is not exactly what is meant by reusable. One simple washing procedure, for example, the removal of the albumin, to regenerate the sensor but not a complete procedure to make a new active layer is within the meaning of reusable. A flow cell with a piezoelectric crystal coated with antihuman albumin has been described[38] for the detection of human albumin in the range of 10^{-4}–10^{-1} mg mL^{-1}. The frequency change of the crystal could be correlated to the adsorption of antihuman and human albumin via radioisotope labeling.

Guilbault and co-workers[39] have used the antibody against parathion *O*,*O*-dimethyl-*O*-(*p*-nitrophenyl)phosphorothioate as the selector on the piezoelectric quartz crystal for the detection of parathion in the gas phase. Parathion could be detected at ppb levels. Compounds related to parathion showed some interference. Besides QMBs, the use of a plate mode sensor is also described based on a Z-cut X-propagating $LiNbO_3$ piezoelectric plate, in which various types of acoustic waves could be excited and received with an interdigital transducer.[40] The capability of this sensor has been demonstrated using the human immunoglobin antibody–antigen model. It is claimed to be applicable for the sensing of viruses such as AIDS (HIV), herpes simplex, and hepatitis.

Ringsdorf and co-workers[41] used the Langmuir–Blodgett (LB) technique to achieve a multilayer system with a top layer of antifluorescyl-antibody fragments (Fab fragments). The Fab fragments were bound to a streptavidin matrix that was bound to biotin lipids embedded in L-α-dipalmitoylphosphatidylethanolamine. The streptavidin matrix was chosen because it forms optically anisotropic two-dimensional crystals on the air–water interface. The maximum frequency change due to the binding of a monolayer of streptavidin was correctly predicted by Equation (1) (see Section 7.2.1). The binding of Fab fragments was observed by a frequency change of 55 Hz. No fluorescence studies were reported.

7.3.2 Enzymes

The use of enzymes as selectors is in principle also a very sensitive approach but they have an advantage over antibodies in that amplification of the signal occurs. The amplification is caused by the accumulation of product from the enzymatic reaction on the piezoelectric crystal.[42] Ebersole and Ward[43] have shown this principle elegantly with the detection of 5-bromo-4-chloro-3-indoxyl phosphate (BCIP) using adenosine 5^1-phosphosulfate (APS) reductase. The APS reductase was immobilized by binding to anti-APS reductase antibodies that were connected to the QMB surface. After the enzymatic conversion of BCIP the resulting 3-hydroxyindole is oxidized to a blue dimer that precipitates on the QMB surface. In this manner, a detection limit of ~5 ng mL^{-1} (10^{-14} M) of APS reductase can be detected. The enzyme formaldehyde dehydrogenase has been placed on a QMB together with the cofactors reduced glutathione and nicotinamide adenine dinucleotide.[44] Formaldehyde dehydrogenase catalyzes the oxidation of formaldehyde to formic acid, in the presence of the appropriate cofactors. The acquired sensivity was in the range of 1–10 ppm formaldehyde, with little or no interference of other aldehydes and alcohols. Immobilized hexokinase has been applied for the detection of glucose in the range of 0.1–20 mM.[45]

7.4 ABSORPTION IN POLYMER MATRICES

The use of polymer matrices to introduce selectivity of QMBs has been exploited since 1964.[12] It relies mainly on trial and error with some sort of like-will-to-like philosophy. King[12] was the first to show that xylenes could be detected at the ppm level by using a suitable polymer matrix. Submicrometer films of various types of asphalt have been exploited on QMBs to study the reaction with oxygen (hardening of the asphalt).[46] Carbowax 1000 has been applied to the detection of explosives.[47] Mononitrotoluenes could be detected in the ppb–ppm range without serious interferences. The response time was only 10 s and a complete reversibility of the response was obtained in less than 50 s. The detector can also be used to indicate the presence of trinitrotoluene. Tomita and Guilbault[48] have developed coated AT-cut 9 MHz QMBs for the detection of organophosphorus pesticides, like diisopropylmethylphosphonate, malathion, and parathion, at the ppm level. Some interferences come from SO_2, H_2S, NH_3, CO, benzene, toluene, chloroform, and ethanol. The detection of 10 ppb of SO_2 and 10 ppm of H_2S in air have been accomplished by using triethanolamine as the coating on a SAW device.[49] The determination of organic acids in dilute hydrocarbon solution using poly(etheneimine) as the coating on a 10 MHz AT-cut QMB has been shown by Charlesworth.[50] The detection limit was estimated to be approximately 25 ppm of phenol in *n*-heptane. As an alternative to eye-irritant tests QMBs coated with dimethyldioctadecylammonium poly(styrene-4-sulfonate) or dipalmitoylphosphatidylethanolamine have been investigated for the detection of 13 kinds of surfactant molecules in a lipid matrix.[51] A good correlation between the partition of the surfactant between the lipid matrix and the QMB and the eye-irritant value (the Draize score), obtained from animal experiments, was observed.

A good selectivity between chemically similar compounds or detection of one species in complicated mixtures is not easily achieved by coating the acoustic devices, but significant improvements can be made by combining several sensors in a neural network (pattern recognition).[52] This approach has been successfully applied to the detection of mixtures of chemical vapors with 4–12 combined SAW devices.[53] Göpel and co-workers[54] have investigated a large number of polymer matrices by means of QMB, capacitance, and calorimetric measurements on exposure to (halogenated) hydrocarbons and alcohols. Their main conclusion has been that the combination of various detection techniques may be useful for subsequent pattern recognition to identify the composition of gas mixtures. In 1994,[55] an interesting approach was published in which simultaneous measurements of the mass and resistance changes of a poly(pyrrole) thin film on exposure to organic vapors were performed. The effect of the homologous series of methanol to butanol was measured and the results indicate that the ratio of change in resistance over change in mass might be useful to distinguish the different components. However, this latter observation has already been pointed out by Slater and Watt.[56] They have also used poly(pyrrole) on a piezoelectric quartz crystal and exposed the sensor to gases like methanol, ammonia, dichloromethane, acetone, hydrocarbons, and H_2S. The interaction of methanol with a poly(pyrrole) film as function of the dopant anion has been investigated by mass and optical spectroscopy, and work function measurements.[57] The chemical nature of the dopant anion has a strong influence on the reversible absorption of the methanol vapor.

7.5 LANGMUIR–BLODGETT FILMS AND SELF-ASSEMBLED (MONO)LAYERS

7.5.1 Langmuir–Blodgett Films

The LB[58] technique to deposit a reasonably structured layer on a solid substrate is well known. An often-used representative is cadmium stearate because it forms stable LB films. The *in situ* weighing on a 9 MHz AT-cut quartz crystal has been reported[59] and the gradual evaporation of water through the thin film was observed when exposed to air. LB-coated acoustic sensors for the detection of NO_2 at the ppb level in dry air have been reported[60] by applying pyridinium tetracyanoquinomethane on both QMB and SAW devices. The number of LB layers showed a linear relation with the change in frequency of the QMB and the change in frequency was correctly predicted by Equation (1). This strongly indicates that the subsequent layers are ordered and densely packed. Although the sensitivity for NO_2 is high, no possible interfering vapors were studied. Holcroft and Roberts[61] also reported a selectivity to 40 ppb NO_2 in dry air using LB films in which a phthalocyanine derivative was incorporated. Almost negligible interference of NH_3 was observed. A hybrid gas sensor using both fluorescence changes and frequency changes of a quartz oscillator coated with a LB film of a squarylium dye has been reported for the detection of NO_2, NH_3, and trichloroethene.[62] On exposure to NO_2, the fluorescence was quenched in addition to a decrease of the oscillation frequency. A smaller quenching of the fluorescence on exposure to NH_3 and no quenching of the fluorescence on exposure to trichloroethene, both accompanied by the expected decrease of the oscillation frequency, was observed. This study clearly shows that with hybrid sensing devices an improved selectivity or better classification can be obtained. Detection of acetic acid[61] was achieved by coating SAW devices with several layers of ω-tricosenoic acid and mixed with dodosylamine. The latter systems showed a decreased response on exposure to acetic acid. Katritzky and co-workers[63] reported an extensive investigation on the use of various pyridine derivatives on SAW devices for the detection of dimethyl methylphosphonate (DMMP), chloroethyl ethyl sulfide (CEES), and water vapor. In general only a small change of the frequency was observed on exposure to water. The most sensitive LB films for DMMP and CEES comprise pyridinium betaines and pyridine *N*-oxides. Poly(vinyltetradecanal) has been deposited by the LB technique on various SAW devices and the response to toluene, 1,2-dichloroethane, isooctane, 2-butanone, 1-butanol, 2-propanol, and nitromethane has been measured.[64] The frequency change due to the stimulant was correctly predicted by theory. The response to the organic vapors decreased from toluene to nitromethane in the given order. The interaction of proteins with LB films of phospholipid monolayers at the water–lipid interface has been studied by applying a QMB at the air–lipid interface.[65] At low surface pressure ($10\,\mathrm{mN\,m^{-1}}$) the adsorption of protein was manifested by both a change in the oscillating frequency and surface pressure. At a surface pressure of 40 mN m^{-1} a frequency change was observed upon adsorption of protein, but virtually no change in the surface pressure occurred.

7.5.2 Self-assembled (Mono)layers

In the mid-1990s, the self-assembly of thiols and related derivatives[66] on gold is attracting a lot of interest for it is a simple way of preparing well-defined and stable monolayers. Ricco, Crooks, and co-workers[67] used *n*-alkylthiols on gold, deposited on a SAW device, for the detection of organophosphates. The monolayer formation could be monitored by the SAW device and it was found that longer alkyl chains result in slower kinetics. Detection of organophosphates has been accomplished via interaction with Cu^{2+} that was coordinated to terminal carboxylate moieties in the self-assembled monolayers (see Section 7.8). The interaction of vapor phase *n*-alkylamines with self-assembled monolayers having carboxylic or sulfonic acid terminal groups has been studied by SAW devices, FTIR, and ellipsometry.[68] The results indicate that proton transfer from the surface acidic group to the amino moiety is controlled by the proton affinity and the degree of structural order in the self-assembled monolayer. The resulting bilayers are stable after proton transfer for many hours. Li and Swanson[69] used C_{60}, bound covalently to the SAW device, for the detection of organic vapors. The C_{60} was not only bound to the substrate but also to itself via spacers, leading to a three-dimensional network. A high molecular weight polymer with C_{60} moieties was prepared, which spontaneously forms a thin layer with the silicon oxide of the substrate via reaction of $Si(OMe)_3$ groups. The resulting SAW devices were most sensitive to decahydronaphthalene, perchloroethene, and toluene, which is consistent with the fact that these compounds are good solvents for C_{60}.

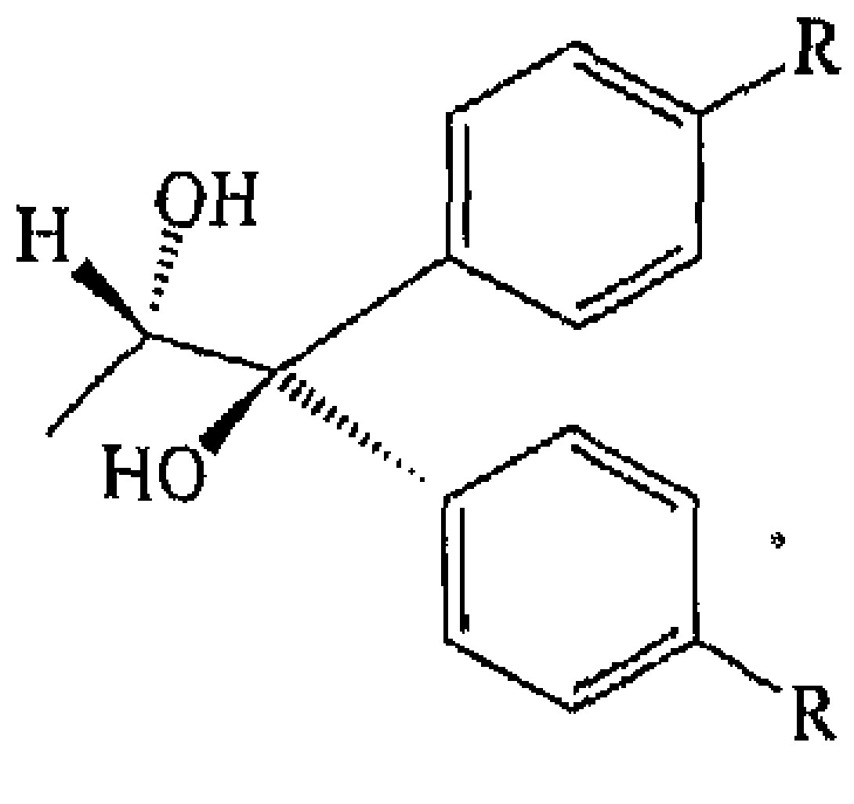
7.5.3 Miscellaneous

Kurth and Bein studied the reaction of 3-aminopropyltriethoxysilane (APS) with the surface of a QMB.[70] The change in the frequency could be related to the formation of a hardly ordered monolayer when the surface was reacted with APS from the vapor phase. It was further demonstrated that nearly all amino groups were accessible for reaction with chlorodimethylsilane. A complete reaction of terminal functional groups is normally not found for well-ordered monolayers, like self-assembled and LB monolayers. APS has also been used for the detection of nitrobenzene derivatives.[71] The strategy used is based on the formation of hydrogen bonds between the amino and nitro group. Thompson and co-workers[71] coated a SAW device with aminopropyltriethoxysilane, resulting in a monolayer with terminal amino groups. The interaction with nitrobenzene derivatives was investigated and they found a reasonable selectivity of the nitrobenzenes over acetone, toluene, and benzene. Interfering substances are 3-fluorotoluene, anisole, and 2-fluorotoluene. Their theoretical calculations (AM1) were in reasonable agreement with the observed selectivities and indicate that the differences in hydrogen bond strength and dipole moment are the important factors.

Polymeric bilayer-forming amphiphiles have been applied[72] on an AT-cut QMB and the interaction of hydrophobic alcohols and cholesterol has been studied in aqueous solution. It was observed that the largest frequency change was obtained by intercalation of primary alcohols and cholesterol. Branched and sterically hindered alcohols can hardly penetrate into the bilayer matrices. Bitter substances, like strychnine, quinine, papaverine, and octaacetylsucrose, can also be measured with such a bilayer-coated mass balance.[73] The intercalation of dye molecules into a DNA–lipid complex, coated on an AT-cut QMB, was reported in 1993.[74] Mierzwinski and Witkiewicz[75] have used liquid crystals of "classical" compounds as coatings on QMBs for the detection of gases like benzene, toluene, chlorobenzene, and so on. Detection limits down to μg L^{-1} have been obtained. They found a decrease in sensitivity and selectivity with increasing temperature, which was explained by a decrease in the ordered structure of the liquid crystal. A principal problem in the use of liquid crystals as coating materials for QMBs is the effect of the acoustic wave on their structure. The structure is at least partly lost due to the acoustic wave.

7.6 CLATHRATES

Not surprisingly, clathrates,[76] crystal lattice inclusion compounds, have been used on gravimetric detection devices for they can be tuned by a systematic structural variation. The diols (**1**) have been applied on QMBs and the interaction with 1-butanol, acetone, methanol, 2-propanol, and dioxane has been studied.[77] For compound (**1a**) it could be demonstrated that with dioxane a 2:1 inclusion ratio ((**1a**):dioxane) occurred, which is exactly the observed ratio in a cocrystallized sample. Although cyclohexane is similar in shape, little or no interference was observed. Compound (**1b**) is very selective for 1-butanol over acetone, methanol, and 2-propanol. Triphenylsilanol has been used as a coating and it has been shown that ethanol is favored over methanol as the intercalating species by a factor of 35.[78] Urea is one of the prototypes of clathrate-forming compounds. When exposed to long aliphatic hydrocarbon urea does not crystallize in a tetragonal form, but an open channel structure results in which the *n*-alkanes bind. After removal of the guest, by heating or vacuum, the tetragonal form is restored. However, a 40 nm thick layer of urea on a 10 MHz QMB showed only very small responses when exposed to *n*-heptane.[78] This is due to the fact that the sensor layer incorporated only a few percent of *n*-heptane in contrast to the ratio in cocrystallized systems.



(**1**)
(a) R = H
(b) R = Bu^t

Not only do many organic molecules form clathrates but many inorganic compounds also do. Yan and Bein[80] used organoclays on QMBs since their intercalating properties can be controlled to a large extent by the choice of layer charge density and structure and chain length of the alkylammonium ions. In this sense they are complementary to zeolites. By a proper choice of the countercations a good selectivity of benzene over cyclohexane could be achieved. Even more remarkable is the large selectivity of benzene over toluene, which is normally not easily achieved. This was explained by the tight fit of benzene in the host material. Interference of water is in general very large.

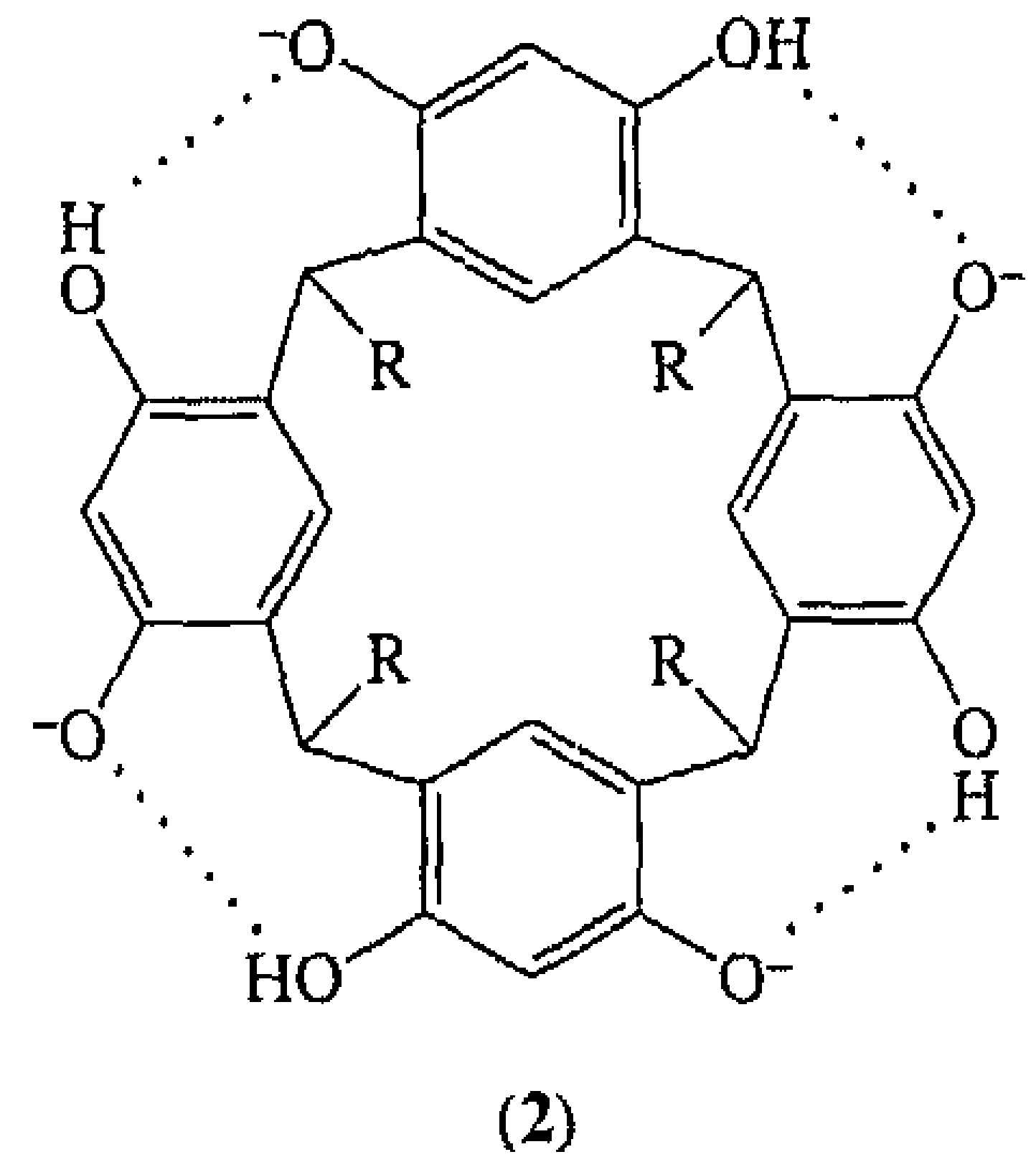
7.7 INCLUSION

7.7.1 Zeolites

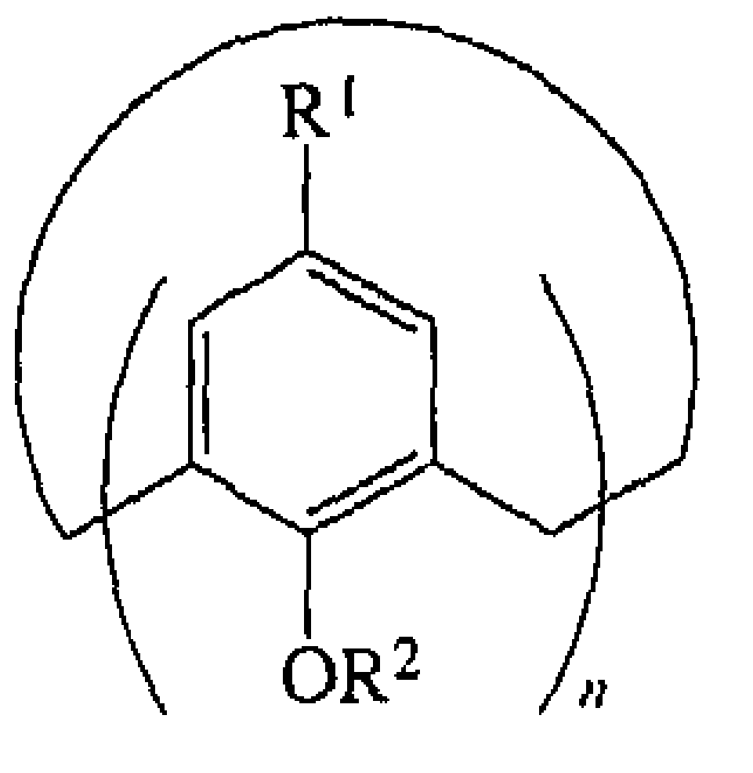
Bein and co-workers[81] have used thin layers of zeolites on mass balances for the detection of low molecular weight organic species. The zeolites are covalently bound to the active area of the oscillating device. When ZSM-5 was used and exposed to methanol and propanol a response of 500–800 ng cm^{-2} was obtained, whereas isooctane gave a minimal response (< 5 ng cm^{-2}). This can be understood when the kinetic diameters of the guest species are compared to the pore size. The latter compound has the largest kinetic diameter and therefore, it cannot easily penetrate the zeolite. Using the rather hydrophobic zeolite "silicalite" as coating on a QMB a selective ethanol detection could be achieved.[81b] Vapor pressures down to approximately 50 ppm of ethanol could be detected. Little interference of water and virtually no interference of isooctane was observed. Methanol is expected to be a major interfering species. With zeolite 3A the selectivity is water $\gg$ *n*-hexane and isooctane. The latter molecule is too large to enter the pores. With zeolite Y, which has even larger pores, sensitivity towards isooctane can be achieved. A 100 times higher uptake is possible with zeolite Y compared to silicalite and a 50 times higher uptake compared to zeolite 3A is possible. Similar observations were made for *n*-hexane. The results also suggest that higher molecular size-based selectivity and larger uptake (leading to higher sensitivity) can be achieved at the lowest vapor pressures, a feature of obvious importance for sensor applications.

7.7.2 Calixarenes

As obvious organic host molecules, calixarenes[82] and related compounds such as resorcinarenes (Högberg compounds) have been tested as materials to introduce selectivity and sensitivity onto QMBs. Göpel and co-workers[83] used the tetraphenolate (**2**) on a QMB and studied the interaction with CO_2, CO, NO_2, $Cl_2C{=}CHCl$, $Cl_2C{=}CCl_2$, and C_8H_{18}. The 10 MHz quartz crystal showed only marginal changes of frequency. A larger sensitivity could be obtained using the calixarenes (**3a–d**) on a 10 MHz QMB.[54] The mass changes on exposure to $Cl_2C{=}CCl_2$ increase in the order (**3d**) > (**3c**) > (**3b**) > (**3a**). With (**3b**) as coating a 2 ppm $Cl_2C{=}CCl_2$ content in air resulted in a frequency charge of about 15 Hz. The change of mass corresponds to one molecule of $Cl_2C{=}CCl_2$ per 60–120 molecules of (**3b**)! It was further observed that increasing sensitivity increased with increasing thickness of the coating and unfortunately also aging effects occur, which are not explained. Dickert and co-workers[84] also applied calixarenes (**3a**) and (**3e–l**) on QMBs. Reasonable to large sensitivity for $Cl_2C{=}CCl_2$ was found with the calixarenes (**3a**), (**3f**), (**3i**), (**3j**), and (**3l**). Calixarene (**3j**) gave a frequency change of > 400 Hz on exposure to 0.5% $Cl_2C{=}CCl_2$. Although the unmodified calixarenes (**3g**) and (**3j**) gave large responses, an undesired water cross-sensitivity resulted. The silylated calixarene (**3l**) did not show any significant water cross-sensitivity and gave a frequency change of > 4000 Hz on exposure to 100 ppm $Cl_2C{=}CCl_2$.



(**2**)

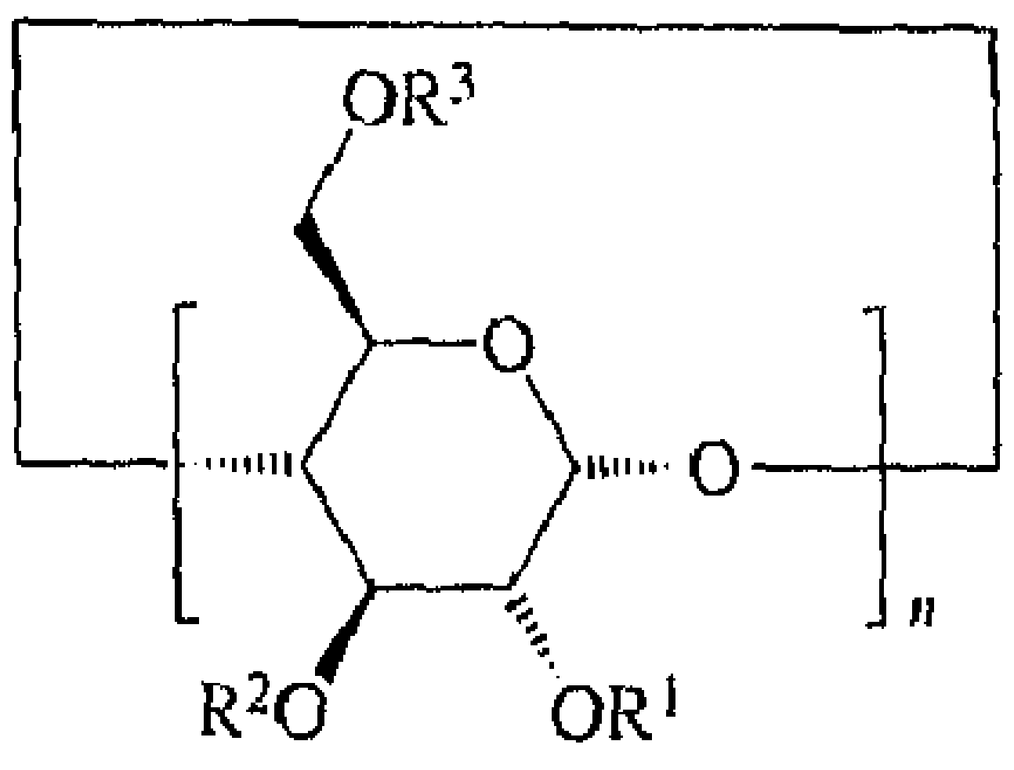


(**3**)

(a) $R^1 = Bu^t, R^2 = H, n = 4$
(b) $R^1 = Pr^i, R^2 = H, n = 4$
(c) $R^1 = Bu^t, R^2 = CH_2CO_2Et, n = 4$
(d) $R^1 = Bu^t, R^2 = H, n = 8$
(e) $R^1 = Bu^t, R^2 = Me, n = 4$
(f) $R^1 = Bu^t, R^2 = TMS, n = 4$
(g) $R^1 = Bu^t, R^2 = H, n = 6$
(h) $R^1 = Bu^t, R^2 = Me, n = 6$
(i) $R^1 = Bu^t, R^2 = TMS, n = 6$
(j) $R^1 = Bu^t, R^2 = H, n = 8$
(k) $R^1 = Bu^t, R^2 = Me, n = 8$
(l) $R^1 = Bu^t, R^2 = TMS, n = 8$

7.7.3 Cyclodextrins

The cyclodextrins α, β, and γ are well known for their interaction with small organic molecules.[85] Stoddart and co-workers[86] used (chemically modified) α- and β-cyclodextrins (**4a–e**) on a 9 MHz AT-cut QMB and studied the interaction with benzene, methane, propane, butane, pentane, ethyne, ammonia, nitrobenzene, and toluene. All sensing materials introduced selectivity for benzene with toluene as the most serious interfering gas. The QMB coated with (**4b**) gave a frequency change of 528 Hz on exposure to 396 mg dm^{-3} of benzene vapor. The interference of toluene for this sensor is < 20% with equal amounts of benzene and toluene in the gas phase. A stability of more than 20 d is reported. Göpel *et al.*[83] applied the parent α- and β-cyclodextrins on a 10 MHz AT-cut QMB and studied the interaction with CO_2, CO, NO_2, $Cl_2C{=}CHCl$, $Cl_2C{=}CCl_2$, and C_8H_{18}. Only the QMB coated with α-cyclodextrins gave appreciable responses on exposure to $Cl_2C{=}CHCl$, $Cl_2C{=}CCl_2$, and C_8H_{18}. The β-cyclodextrin-coated QMB seems quite sensitive to NO_2 ($\delta f = 5$ Hz at 1 ppm). Little can be said on the selectivity for no measurements on mixtures were reported. Dickert and Bauer[87] studied (modified) α- and β-cyclodextrins on QMBs and SAWs. They showed that the unmodified β-cyclodextrin is very sensitive towards water vapor (Δf > 1500 Hz at 20 °C and 85% relative humidity). This water sensitivity can be almost completely suppressed on methylation of all the hydroxy groups. The use of methylated α-cyclodextrin on a QMB did not result in a sensitivity for $Cl_2C{=}CCl_2$, but with methylated β-cyclodextrin a frequency change of approximately 400 Hz was observed on exposure to 0.35% $Cl_2C{=}CCl_2$ (20 °C and 50% relative humidity). With a 430 MHz SAW device similar results were obtained. β-Cyclodextrin, modified with a lipophilic chain, embedded in a lipophilic monolayer, which was covalently bound to the quartz surface, has been used for the detection of $Cl_2C{=}CCl_2$.[79] A reversible mass sensor with a sensitivity of 100 Hz per 70 ppm $Cl_2C{=}CCl_2$ in air was obtained using a 433 MHz SAW device.

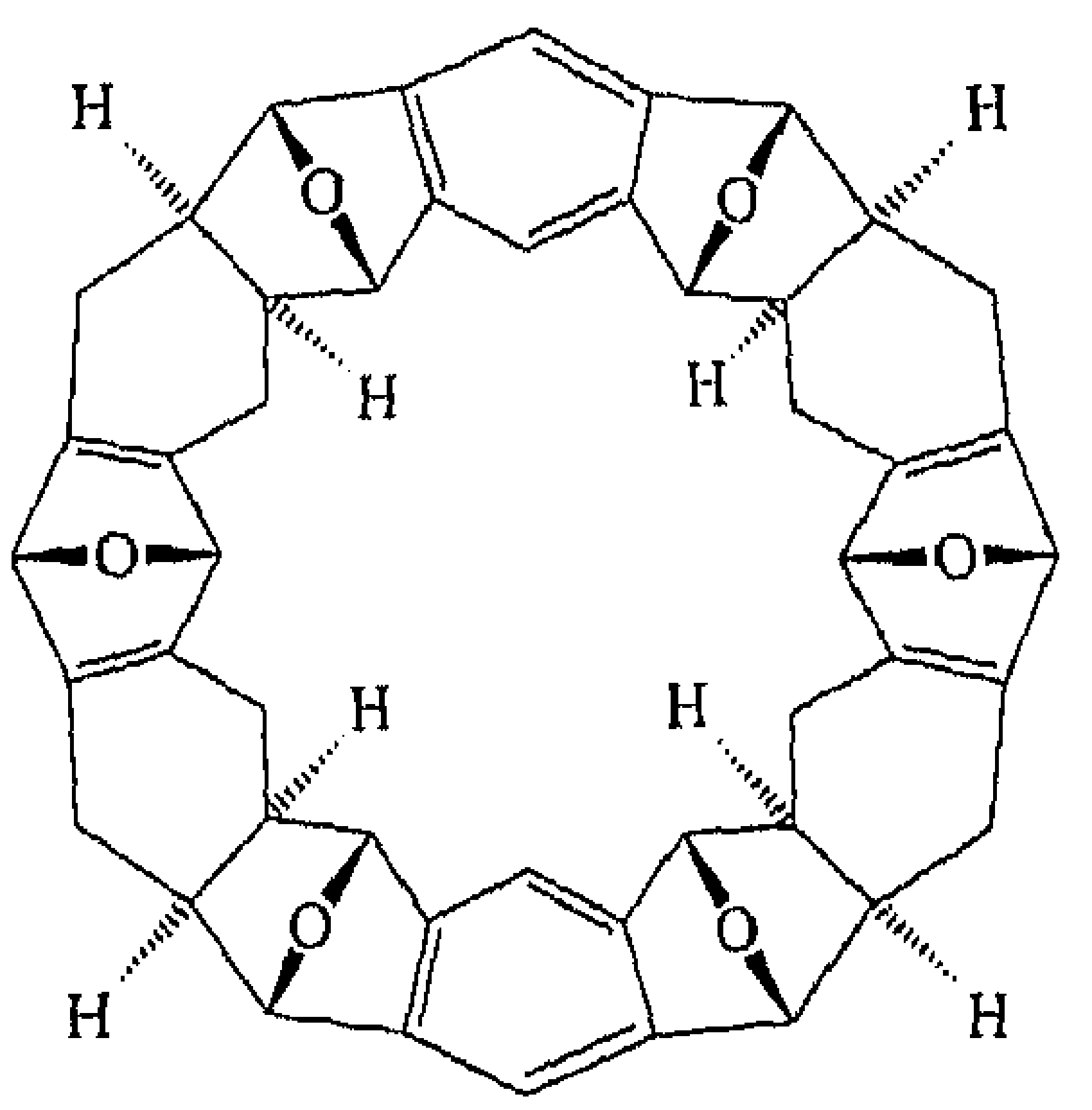


(4)

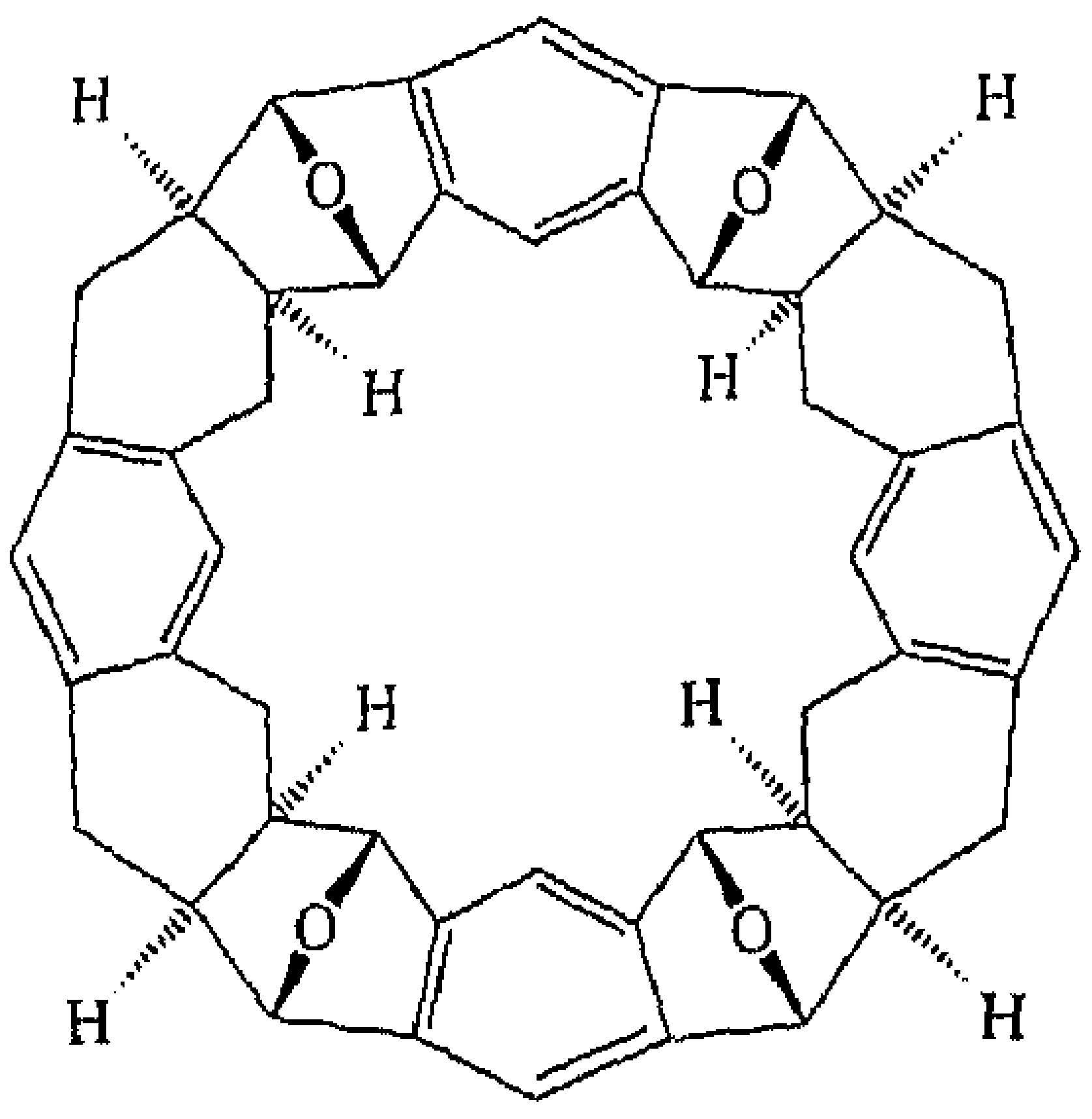
(a) $R^1=R^2=R^3=H$, $n=6$
(b) $R^1=R^3=TBDMS$, $R^2=H$, $n=6$
(c) $R^1=R^3=allyl$, $R^2=H$, $n=6$
(d) $R^1=R^3=Me$, $R^2=H$, $n=7$
(e) $R^1=R^3=Me$, $R^2=Bz$, $n=7$

7.7.4 Miscellaneous

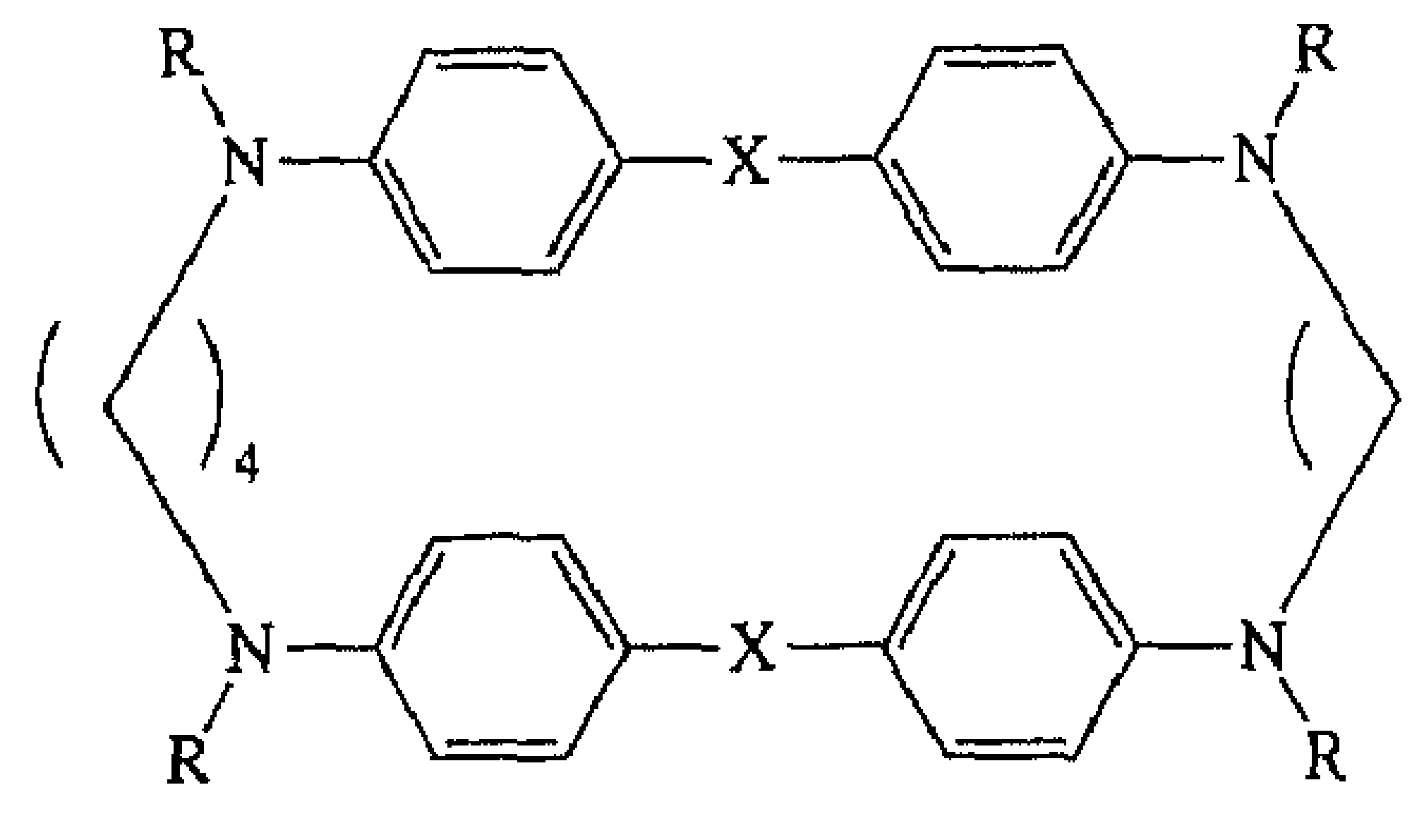
The collar belt molecule (**5**) of Stoddart has been used on an AT-cut QMB and the sensitivity towards substituted benzenes and ammonia has been studied.[88] The use of (**5**) resulted in a selectivity of nitrobenzene over benzene, toluene, chlorobenzene, bromobenzene with serious interference of 2- and 3-nitrotoluene and ammonia. The lifetime of the sensor was at least nine weeks, although a decrease of the sensitivity occurred. Application of compound (**6**) did not lead to any selectivity. Dickert and co-workers used the tetraazamacrocycles (**7**).[78,89] Application of (**7a**) on a 10 MHz AT-cut QMB gave a sensor suitable for the detection of chlorinated hydrocarbons. The observed sensitivity was largest for 1,1,2,2-tetrachloroethane (50 Hz per 0.1%), followed by tetrachloroethene (16 Hz per 0.1%). Interference of CCl_4, $CHCl_3$, CH_2Cl_2, and benzene was most serious (4–7 Hz per 0.1%), compared to other studied gases (methanol, ethanol, acetone, and cyclohexane). For indicative purposes the interaction energies between host and guest were calculated by molecular mechanics calculations and plotted vs. the sensor effect. A quite reasonable linear correlation was obtained, with benzene as the exception. With compound (**7b**) as selector a large sensitivity for toluene and $Cl_2C{=}CCl_2$ was obtained (Δf = 45 Hz for 0.5% vapor in air). Other cyclophanes have been used[88] for the detection of, among others, $Cl_2C{=}CCl_2$. A good sensitivity and no water interference has been obtained. A linear correlation between sensor effect and interaction energy was also obtained here. With a 433 MHz SAW device 10 ppm of $Cl_2C{=}CCl_2$ in air could be easily detected. Göpel *et al.*[83] showed that the use of the hexalactam (**8**) gave sensors with sensitivity towards $Cl_2C{=}CHCl$, $Cl_2C{=}CCl_2$, and C_8H_{18}.



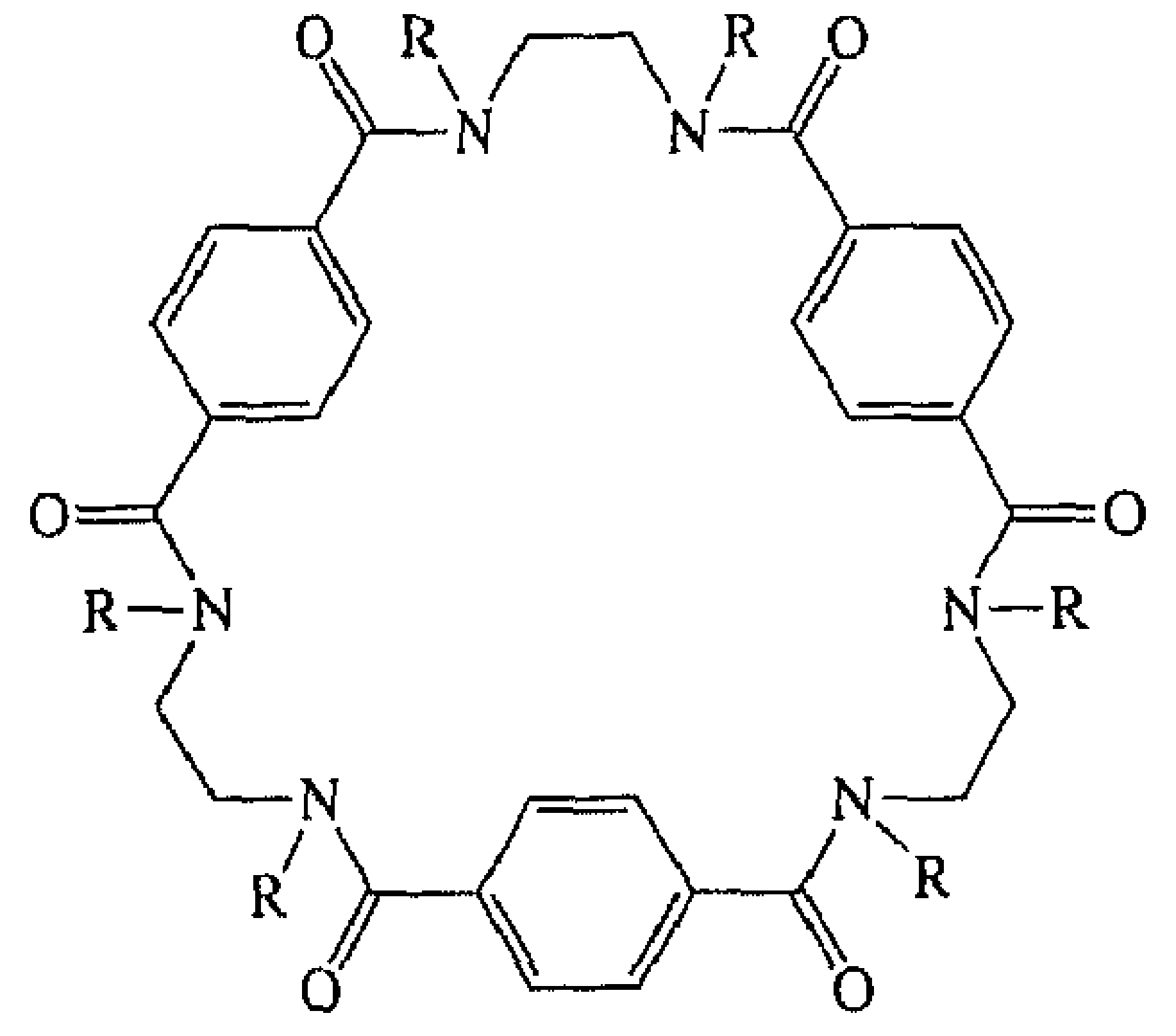
(5)



(6)



(7)
(a) R=Me, X=—
(b) R=*n*-pentyl, X=O



(8)

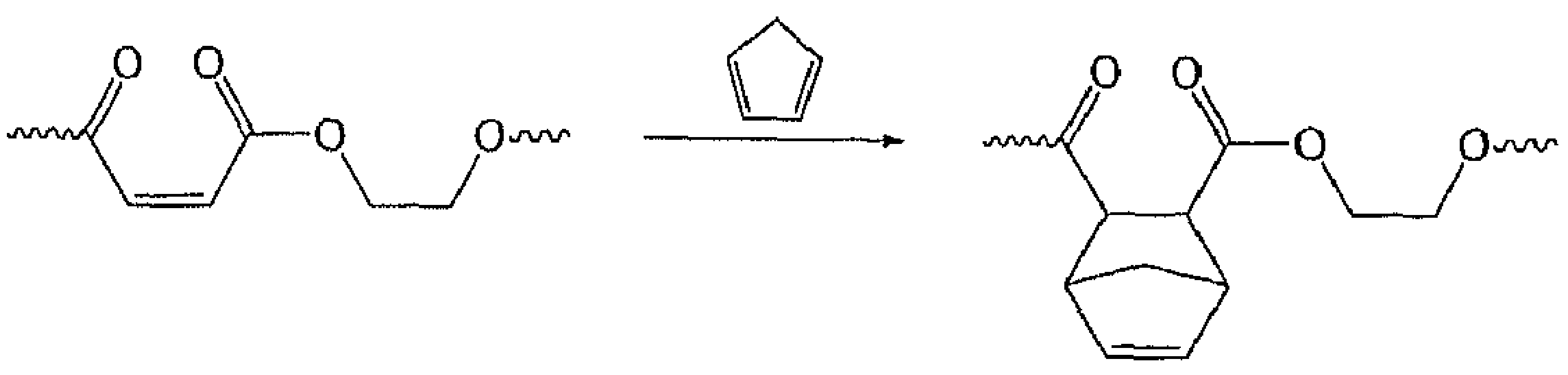
7.8 COORDINATION COMPOUNDS

Kepley *et al.*[90] used Cu^{2+} sites that were coordinated to carboxylate groups of a self-assembled monolayer of *n*-thioundecanoic acid on gold for the detection of diisopropyl methylphosphonate (DIMP). The architecture used resulted in a fast response to changes in the DIMP concentration, which can be explained by the fact that, in the ideal case, only changes at the Cu^{2+} surface have to occur. The detection limit was as low as 100 ppb. Interference of CCl_4, H_2O, C_6H_{12}, and MeOH was observed. It was speculated that the solvent penetrates the monolayer. The Cu^{2+} complexes of TMEDA, ethylenediamine, and diethylenetriamine have been investigated, incorporated in a polymer matrix, for the detection of DIMP.[91] It was observed that by increasing the number of nitrogen atoms coordinated to Cu^{2+} the sensitivity decreased. The largest sensitivity was observed with ethylenediamine (Δf for DIMP per μg coating = 2.6 $\mathrm{Hz}\,\mu\mathrm{g}^{-1}$). Not surprisingly, interference of ammonia, hydrogen sulfide, hydrogen chloride, and organic solvents was observed. Zellers and co-workers[92] have applied platinum(II) complexes, like $PtCl_2$·pyridine·ethene, for the detection of unsaturated compounds such as styrene, butadiene, methyl acrylate, and so on. The principle of detection is the substitution of the original ethene by the other unsaturated compound. In their first report a detection limit of 3 ppm of styrene at 25 °C was calculated, using a SAW device that was operated in the delay-line configuration. The sensitivity at 40 °C increased to 0.6 ppm of styrene. It was noted that in this way a durable sensor could not be obtained due to the fact that eventually all ethene will be replaced by styrene. However, this problem can be overcome by regeneration with butadiene which is an effective competitor of styrene.[92b] A detailed study with structurally related alkenes and α, β-unsaturated esters revealed that the selectivity is dependent on the relative reaction rates.

In general the less hindered isomer gives the highest selectivity.[92c] Using the same strategy a very sensitive butadiene sensor was developed.[92d] With a 30 MHz SAW oscillator 150 ppb of butadiene in air can be detected and a detection limit of 101 ppb was calculated. The detection limit could be improved to 24 ppb by using a 60 MHz oscillator. The relative humidity and also nonalkene organic gases and vapors gave no interference. The sensor could be easily regenerated by exposure to 1-hexene. Honeybourne *et al.*[93] have applied phthalocyanines, porphyrins, and related cyclic tetradentate ligands for the detection of NO_2. Detection limits of 10 ppm NO_2 could be obtained with Cl_2, HCl, NH_3, and H_2S as the most serious interfering gases. Ricco and co-workers[94] used lead phthalocyanine for the detection of NO_2 and were able to detect 10 ppm in a nitrogen atmosphere. Nieuwenhuizen and co-workers[95] have investigated phthalocyanine and its metallated derivative (Mg, Fe, Co, Ni, Cu, and Pb) as coatings on SAW devices. Cobalt phthalocyanine gave the highest selectivity and sensitivity for NO_2 at 150 °C, but copper phthalocyanine is preferred as the response time is important. Ammonia interferes to a small extent.

7.9 MISCELLANEOUS

It seems that so far only one reference can be found in which a chemical reaction was used to detect gaseous species. Snow and Wohltjen[96] used the Diels–Alder reaction of poly(ethene maleate), the coating on the SAW device, and cyclopentadiene vapor (Scheme 1). The nonreversible Diels–Alder reaction resulted in a sensor that was capable of detecting 200 ppm cyclopentadiene in 1 min. Significantly lower detection limits were possible if longer integration periods were allowed. Some interference of acetone, dichloromethane, benzene, methanol, and pentane was observed.



Scheme 1

7.10 CONCLUSIONS

This chapter briefly described the theoretical background of bulk and surface acoustic waves for application in mass sensors. The important parameters and the limitations were discussed. The variety of approaches which can be followed were then shown. The use of antibodies or enzymes is potentially a very sensitive and selective approach, although nonspecific adsorption in biological samples seems hard to avoid. Absorption in polymer matrices is in general not very selective, but combined with neural networks they may develop into good analytical tools.

The impression is that major improvements may be obtained with approaches based on self-assembled and LB films, clathrates, and inclusion and coordination compounds. In principle, they can be optimized for a specific guest by the shape of the host matrix and, of course, the interactions between guest and host matrix. A problem that seems hard to avoid with, for example, inclusion compounds is the additional inclusion between two or more hosts, instead of only in the host. Tightly packed self-assembled (mono)layers may provide the answer to this problem. It is quite clear that an increasing number of articles will appear in which supramolecular chemistry and mass sensing will be fruitfully combined.

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