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Change of pH indicator's pK_a value *via* molecular imprinting†

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The pK_a value of the indicator is significantly changed up to several orders of magnitude by the imprinting synthesis; this fine-tuning of the reactivity for pH indicators *via* the imprinting synthesis may find novel applications in fabricating pH sensors with tailored pK_a values.

Molecular imprinting[1–9] is a versatile technique to create affinity in solid matrixes toward target chemical species through controlled selection of functional group locations. Imprinting synthesis utilizes either a covalent or a noncovalent interaction between the target molecule and functional ligands in the host matrix. Wulff and his coworker pioneered the former methodology,[1] while Mosbach and his colleague developed the latter technique.[2] Various organic molecules, transition-state analogs, chiral species, and inorganic ions have been successfully imprinted.[1–9] Here, we describe a technique for the successful imprinting of different structural stages of a pH indicator in a hybrid sol–gel matrix. The proton affinity of the indicator is strongly dependent on this imprinting synthesis. Therefore, we can view this imprinting synthesis as a proton-imprinting technique.

The pH indicator used in our current experiment is methyl red. The end result of the proton imprinting technique is the modification of the pK_a value of the indicator in a host matrix. This control over the pK_a value in cross-linked solid matrixes is induced by fine-tuning the combined surrounding polarity, hydrophobicity, and hydrogen bonding interactions for the pH indicator created by the sharply different imprints of the protonated and nonprotonated indicators. Avnir and his coworkers[10] have recently demonstrated a novel technique to fine-tune acidity constants of pH indicators in sol–gel matrixes through the variation of matrix hydrophobicity and polarity properties by co-entrapment of various surfactants. The present work indicates that such shifts of the pK_a values can be generated *via* the imprinting synthesis. The hybrid matrix used in this investigation retains the 'memory' of the different states of a pH indicator (protonated and nonprotonated) by adjusting the surrounding interactions *via* the imprinting synthesis.

We[11] and others[12] have recently demonstrated that the imprinting effect for a target metal ion or an organic molecule can be greatly enhanced by using organic (hydrophobic)–inorganic (hydrophilic) hybrid sol–gel systems. This enhancement is attributed to the tailored hydrophobicity surrounding functional ligands imposed by the imprinting synthesis. In the imprinted materials, hydrophobicity is tailored according to that of the target ions or molecules. No tailoring of the hydrophobicity for the adsorption sites in the nonimprinted materials is expected. In pure inorganic or organic hosts, less tailoring of hydrophobicity is expected for the imprinting synthesis. The imprinted adsorption sites are either hydrophilic or hydrophobic. Very little fine-tuning of the second coordination shell can be made. Accordingly, the induced contrast and the tailored distribution in hydrophobicity of the surrounding environments imparted by the imprint in the hybrid are the key for the enhanced imprinting effect. The hybrid sol–gel host used in this investigation is a bridged silsesquioxane, 1,2-bis(triethoxysilyl-)ethane.[13] Shea, Loy, and their coworkers[13*a*,*c*,*d*] have demonstrated that bridged silsesquioxanes can be used to generate highly porous hybrid materials through sol–gel processing under both acidic and basic conditions. Studies of the dependence of porosity and surface area on the spacing alkyl group indicate that 1,2-bis(triethoxysilyl)ethane is an excellent precursor for making porous hybrid materials with large surface areas and pore volumes.

The pH indicator used in this investigation is methyl red, which was covalently attached to trimethoxysilylpropylamine to form a trimethyoxysilylpropylamide derivative of methyl red (TD-MR) according to the method given by Avnir and coworkers.[10*c*] In a typical preparation of a xerogel doped with TD-MR, a solution containing 0.01 g of TD-MR and 3 ml of bis(trimethoxylsilyl)ethane in 5 ml methanol was sonicated for 5 min. To the above mixture, 3 ml of an aqueous catalyst solution was added with stirring. The catalyst solution was 0.1 M HCl for the preparation of the proton-imprinted xerogel or 0.1 M NaOH for the nonimprinted control. For the acid-catalyzed reaction, the mixture was contained in a covered plastic vial at room temperature overnight. The mixture was then poured into a petri dish (50 mm in diameter, 15 mm high) for the further gelation of the silica matrix and efficient evaporation of the solvent. The gel was aged and shrunk in the petri dish for 2 weeks, resulting in a transparent hard hybrid glass with a thickness of 1 mm. The final xerogel has a bright red color, containing the protonated TD-MR covalently trapped inside the sol–gel matrix. For the base-catalyzed reaction, the mixture was immediately poured into a petri dish after the addition of the 0.1 M NaOH. The mixture was then aged for 2 weeks. The resulting xerogel was light yellow in color. Small-angle X-ray scattering (SAXS) experiments indicated that the base-catalyzed gel is surface fractal while the acid-catalyzed gel has a mass-fractal structure. The surface areas for the imprinted and nonimprinted glasses are 1120 and 555 $m^2 g^{-1}$, respectively. These findings are consistent with the basic structural features of the two gel systems.[14*a*] Both imprinted and nonimprinted samples were washed with deionized water overnight before the titration experiments.

Fig. 1 shows the spectral variations of the protonated (imprinted) and nonprotonated (nonimprinted) TD-MRs entrapped in the hybrid matrixes under various pH solutions. The corresponding titration curves are given in Fig. 2. The pH values at the reflection points in the two titration curves are proportional to the pK_a values. Because the hybrid matrixes possess high porosities and surface areas, diffusion of the small proton ion inside such matrixes is reasonably fast. In our hybrid matrixes, the equilibria of the proton reactions take less than 15 min. The equilibrium time for each spectrum shown in Fig. 1 is 30 min, which is 2 times the maximum equilibrium time. The pK_a values for TD-MR in the glasses imprinted with and without protons are 7.4 and 2.6, respectively. Accordingly, a very large change of up to 4 orders of magnitude in the proton-

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† Electronic supplementary information (ESI) available: adsorption isotherms, schematic of experimental setup, FTIR spectra of doped sol–gel glasses, SAXS curves, UV–vis spectra of TD-MR and its protonated form, structure of TD-MR, comparison of template environments, SEM images and photograph of imprinted and nonimprinted sol–gel glasses. See http://www.rsc.org/suppdata/cc/b2/b203496d/

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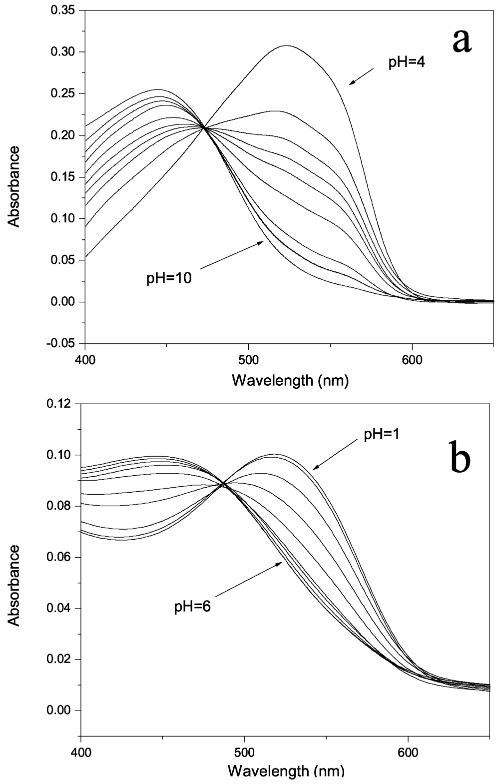

Fig. 1 Variations of optical spectra with pH for (a) proton-imprinted and (b) nonimprinted samples.

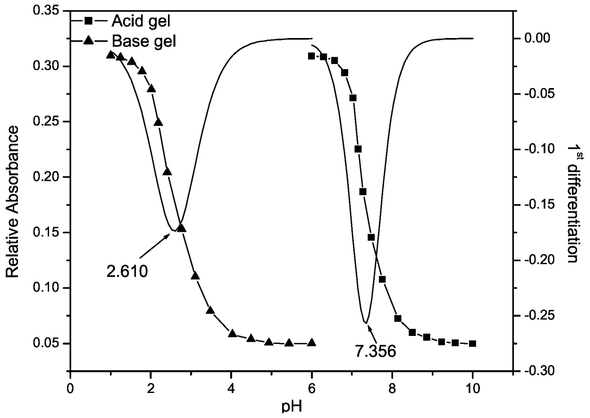

Fig. 2 Titration curves measured by monitoring the absorbance changes at 520 nm for gel glasses prepared by acid and base catalysts.

affinity constant can be induced by the proton-imprinting technique. Such a phenomenon can be rationalized with the very different local environments of TD-MR in the two glasses. In the synthesis of the imprinted glass, the surrounding environment of the indicator was optimized and selected by the protonated indicator, which has a delocalized positive charge and a very hydrophilic structure. Through reaction with the indicator, the charge of the proton is delocalized into a significantly larger structure, thereby changing the hydrophobicity of the indicator. These changes in the structural properties of the indicator can be imprinted. No such optimization of the local environment is expected for the indicator in the control sample. In fact, the local environment of the indicator in the control sample is optimized for the hydrophobic and neutral indicator molecule. Therefore, the affinity of the indicator toward the proton in the former matrix is much greater than that of the latter. The titration experiments were carried out in the pH range of 1 to 10. No damage of the matrix was found during repetitions of titration.

The absorption peak positions of TD-MRs under acidic conditions are 523 and 517 nm for the imprinted and nonimprinted glasses, respectively. Comparing with the position of the absorption peak (520 nm) of TD-MR in the aqueous solution, a slight red shift was observed for the imprinted glass while a blue shift was detected for the nonimprinted glass. The shifts in opposite directions support the assertion that the imprinted and control glasses have different environments for the entrapped indicator.[10]

In conclusion, the change of the indicator's pK_a value by the imprinting synthesis has been demonstrated. This fine-tuning of the reactivity for pH indicators *via* the imprinting synthesis may find application in making pH sensors with tailored pK_a values.[10,14]

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