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Chromogenic Signaling of Hydrogen Carbonate Anion with Pyrylium-Containing Polymers

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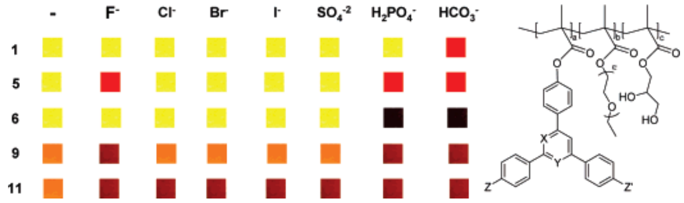
ABSTRACT



Polymeric films containing pyrylium derivatives showing a selective color modulation from yellow to red in the presence of the poorly coordinating hydrogen carbonate anion in water at neutral pH have been developed.

The development of new molecular optical sensors for anions has been grown in interest during the last 10 years.[1] These systems are based on the use of light as a most versatile and valuable output signal, and a number of chromogenic and fluorogenic sensors for anions have been recently developed.[2] However, in spite of this large amount of work, there are still particular problems that deserve further investigations mostly related to the design of chemosensors for target anions in aqueous media and the development of sensitive and selective probes for poorly coordinating anions.

One of these anions is hydrogen carbonate. Hydrogen carbonate is a physiologically important anion that plays vital roles in maintaining the pH of biological fluids and in the signal transduction in intracellular events.[3] However, there are very few examples of receptors for the spectroscopic recognition of this anion. A recent example described by Fabbrizzi et al. was based on a displacement assay with an ensemble formed between a dicopper(II) cage and coumarin 343.[4] The addition of HCO_3^- to the sensing ensemble (in water buffered at pH 7.0) induces the release of the dye with the subsequent restoration of coumarin 343 fluorescence. Parker et al. synthesized europium complexes of heptadentate ligands based on cyclen that resulted in variations in the emission intensity of the europium center upon hydrogen carbonate binding in pure water.[5] In a more complete work, the same research group synthesized several macrocyclic europium complexes incorporating an acridone chromophore that allows ratiometric sensing of hydrogen carbonate at physiological pH.[6] In another approach, Resch-Genger et al. prepared fluorescent sensors based on iminoylthiourea/1,2,4-

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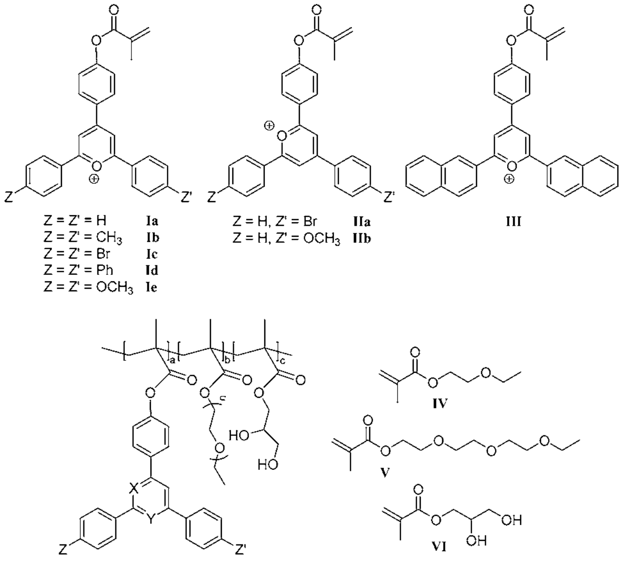
thiadiazole units that showed emission enhancements upon coordination, through hydrogen bonding interactions, with hydrogen carbonate in methanol.[7] Very recently, Suzuki et al. synthesized a receptor consisting of a γ-cyclodextrin connected through a triamine linker with a pyrene residue.[8] In aqueous solutions, two receptors form an association dimer in which two pyrene subunits are in parallel conformation inside the cyclodextrin cavity. Upon binding of HCO_3^- anion with the dimer, the two pyrene units suffer a conformational change that is reflected in the shift of the excimer fluorescence band from 475 to 425 nm.

In spite of these encouraging examples, there are not, as far as we know, chromogenic signaling receptors for carbonate in water. To fill up this gap, we report herein the development of a probe for the colorimetric detection of HCO_3^- in neutral aqueous solution by using polymeric materials containing pyrylium derivatives. Polymeric films can be easily prepared and are ideal candidates for the development of sensory materials for in situ sensing and rapid “naked eye” screening applications. In fact, the combination of certain chromogenic probes and suitable polymeric matrices is an emerging frontier in the development of robust and selective sensory materials for target anions.[9] Polymers not only are excellent supports but also allow fine alterations of their hydrophilic/hydrophobic character that finally result in a tuning of the sensing ability.

Scheme 1. Structure of the Polymeric Films and the Monomers **I**, **II**, **III**, **IV**, **V**, and **VI** Used in Their Synthesis



The sensing principle for the colorimetric signaling of carbonate takes advantage of the electrophilic character of the pyrylium ring (vide infra) due to the presence of a positively charged oxygen atom in its structure.[10] In fact there are recent reported examples using pyrylium derivatives as chromogenic probes,[11] and we have recently reported pyrylium-containing polymers for the colorimetric detection of cyanide in water.[9i] Here, in order to incorporate the pyrylium derivative into a polymeric matrix, several methacrylate esters bearing pyrylium rings were synthesized (**I**–**III**, see Scheme 1). Then, a series of methacrylic copolymer films containing the pyrylium probes were prepared by radical copolymerization of the monomer **IV**, 2-ethoxyethyl methacrylate, **V**, 2-(2-(2-ethoxyethoxy)ethoxy)ethyl methacrylate, **VI**, 2,3-dihydroxypropyl methacrylate, small quantities of ethylene glycol dimethacrylate as cross-linking agent, and 2,2′-azobis(isobutyronitrile) (AIBN) as radical thermal initiator. Eleven different polymer films were prepared by changing three parameters in order to optimize the chemical properties of the synthesized films: (i) the concentration of pyrylium derivatives **I**–**III** (see Scheme 1 and Table 1), (ii) the hydrophobic monomer (**IV** or **V**), and (iii) the ratio of hydrophilic (**VI**) to hydrophobic (**IV** and **V**) monomers.

Table 1. Composition of the Polymeric Films Prepared

films	monomer (2%)[a]	IV[a]	V[a]	VI[a]
1	**Ia**	50	–	50
2	**Ib**	50	–	50
3	**Ib**	–	50	50
4	**Ic**	–	50	50
5	**Ia**	–	50	50
6	**IIa**	–	50	50
7	**IIb**	–	50	50
8	**Id**	–	50	50
9	**Ie**	50	–	50
10	**Ie**	–	50	50
11	**III**	–	50	50

[a] Molar composition ratio of the monomers used for the preparation of the films.

Related to the content of the probe, the best results were obtained with films containing 2% of the corresponding monomer. Films containing less than 2% of pyrylium derivative were pale yellow or colorless, and the color changes upon interaction with the target anions were difficult to observe. Also, the molar ratio between the hydrophobic **IV**, the partially hydrophobic **V**, and the hydrophilic

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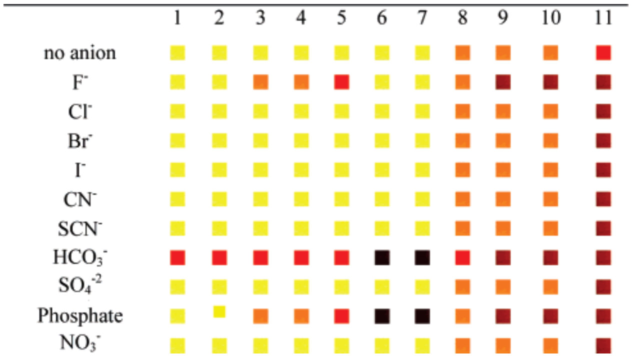
monomer (**VI**) fixes the physical properties of the resulting films. In this respect, polymers with a high content of monomer 2,3-dihydroxypropyl methacrylate (**VI**) resulted in highly hydrophilic polymers but were very rigid, brittle, and difficult to handle, whereas polymers with high contents in 2-ethoxyethylmethacrylate (**IV**) and 2-(2-(2-ethoxyethoxy)-ethoxy)ethylmethacrylate (**V**) were hydrophobic, the polymer with monomer **IV** being much more hydrophobic than the one containing monomer **V**. The diffusion rate of the anion into the polymeric matrix was reduced with the increasing hydrophobicity. The best polymeric films for sensing purposes were obtained by fixing the molar ratio between hydrophilic and hydrophobic monomers at 50:50. With these facts in mind, we prepared the 11 polymeric films. Most of them are yellow (absorbance maxima centered at 425 nm for **1**−**7** films) and fluorescent (emission band centered at 480 nm), except those prepared with pyrylium derivatives containing electron donor methoxy groups that are orange and naphthyl moieties which are red.

The signaling ability of the polymeric materials was tested in the presence of the anions F^-, Cl^-, Br^-, I^-, CN^-, SCN^-, HCO_3^-, SO_4^{-2}, phosphate, and NO_3^- in aqueous solutions buffered at pH 7.5 (HEPES 0.1 mol dm^{-3}). The chromogenic response obtained is showed in Table 2. In general, the films showed a color change in the presence of basic anions. Thus, polymers **8**, **9**, **10**, and **11** showed a color modulation from orange to deep red ($\lambda = 527$ nm) in the presence of HCO_3^-, F^-, and phosphate. However, the soaking of the films into aqueous solutions of other anions (Cl^-, Br^-, I^-, CN^-, SCN^-, SO_4^{-2}, and NO_3^-) did not induce any significant color change. Polymers **3**−**7** show a certain and unselective response for the same anions. The interaction of **3**, **4**, and **5** with HCO_3^-, F^-, and phosphate results in the evolution of a new band at $\lambda = 527$ nm responsible for the color modulation from yellow to orange-red, whereas for **6** and **7**, the band was observed at $\lambda = 561$ nm, with an overall color transformation from yellow to dark brown with HCO_3^- and phosphate.

Table 2. Chromogenic Response[a] of the Films upon Soaking in Aqueous Solutions Buffered at pH 7.5 (HEPES 0.1 mol dm^{-3}) of Several Anions



	1	2	3	4	5	6	7	8	9	10	11
no anion	🟨	🟨	🟨	🟨	🟨	🟨	🟨	🟧	🟧	🟧	🟥
F^-	🟨	🟨	🟧	🟧	🟥	🟨	🟨	🟧	🟫	🟫	🟫
Cl^-	🟨	🟨	🟨	🟨	🟨	🟨	🟨	🟧	🟧	🟧	🟫
Br^-	🟨	🟨	🟨	🟨	🟨	🟨	🟨	🟧	🟧	🟧	🟫
I^-	🟨	🟨	🟨	🟨	🟨	🟨	🟨	🟧	🟧	🟧	🟫
CN^-	🟨	🟨	🟨	🟨	🟨	🟨	🟨	🟧	🟧	🟧	🟫
SCN^-	🟨	🟨	🟨	🟨	🟨	🟨	🟨	🟧	🟧	🟧	🟫
HCO_3^-	🟥	🟥	🟥	🟥	🟥	⬛	⬛	🟥	🟫	🟫	🟫
SO_4^{-2}	🟨	🟨	🟨	🟨	🟨	🟨	🟨	🟧	🟧	🟧	🟫
Phosphate	🟨	🟨	🟧	🟧	🟥	⬛	⬛	🟧	🟫	🟫	🟫
NO_3^-	🟨	🟨	🟨	🟨	🟨	🟨	🟨	🟧	🟧	🟧	🟫

[a] Colors are taken from photographs of the polymers in the presence of the corresponding anion.

The sensing ability of films **1**−**11** was also studied in the presence of other anions such as acetate, hydrogen sulfite, hydrogen sulfide, and nitrite, but no colorimetric response was observed.

The best results in terms of selectivity, sensitivity, and mechanical strength of all the sensory films tested were obtained with **1** and **2**. These two polymeric materials were yellow and, upon soaking in buffered aqueous solutions (pH 7.5, HEPES 0.1 mol dm^{-3}) containing HCO_3^-, became red. Figure 1 shows the change in the UV−visible spectra of polymer **1** upon addition of increasing quantities of HCO_3^-. The band centered at 425 nm of the pyrylium derivative disappears, upon gradual addition of HCO_3^- anion, with a concomitant appearance of a novel broad absorption centered at 527 nm. Additionally, Figure 2 shows the absorbance of the band centered at 527 nm versus the concentration of certain anions for polymeric material **1**. As could be observed, only addition of HCO_3^- induced significant increases of the 527 nm band. From the titration curves, a

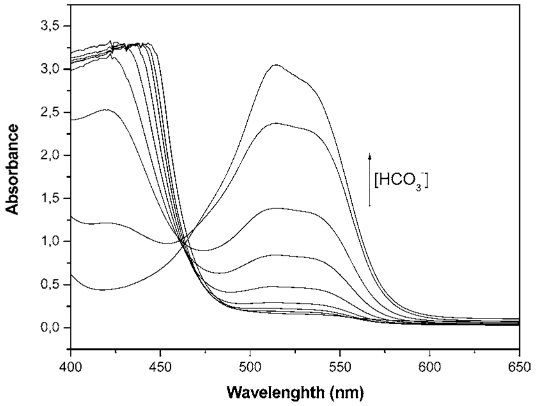


Figure 1. UV−visible spectra of polymer **1** upon exposure to increasing quantities of HCO_3^- anion (from 1.0×10^{-5} to 1.0×10^{-1} mol dm^{-3}) in water at pH 7.5.

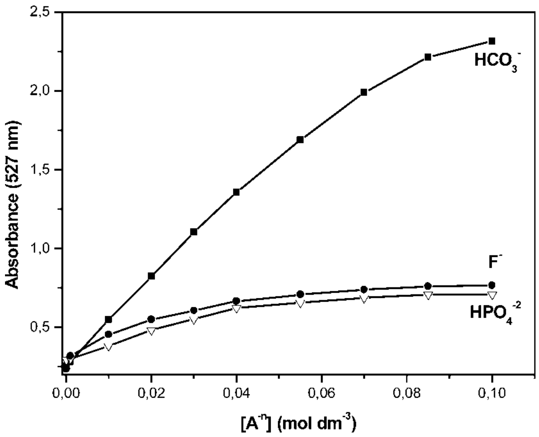


Figure 2. Titration profiles of polymeric film **1** with HCO_3^-, F^-, and HPO_4^{-2} anions in water at pH 7.5.

detection limit for HCO_3^- of 1.0 ppm for polymers **1** and **2** was measured.

By a careful observation of the selectivity trend presented by the films and their composition (molar ratio between monomers **IV**, **V**, and **VI**), the best selectivity toward hydrogen carbonate (films **1** and **2**) was prepared with the monomer **IV**, whereas the remaining polymeric films were synthesized using monomer **V**. The only difference between these two monomers is the presence of two additional oxygen atoms in **V**. These two oxygen atoms impart a less hydrophobic character to monomer **V** when compared with that of **IV**.

In order to clarify the color change mechanism, it is important to remark that the color changes in the presence of fluoride, phosphate, and hydrogen carbonate are observed only in the polymeric matrix; that is, there is no color changes upon addition of these anions to aqueous or acetonitrile solutions of the pyrylium monomer **I**, **II**, or **III**. Another clue for the elucidation of the mechanism arises from the fact that the band developed upon anion addition is the same for a certain polymer, and also, the same band is developed upon addition of hydroxide anion. The electrophilic character of the pyrylium ring has been known for a long time, and the reaction with a hydroxide nucleophile results in the formation of the colored hydroxyenone derivative that we believe accounts for the color changes observed.[12]

Considering the kinetics of polymerization, the rate parameter of a monomer gives an idea of its reactivity in bulk or in solution radical polymerization. When two or more monomers of different reactivity (significantly different rate parameters) are copolymerized, blocks can be obtained. Thus, according to the differences in the values of the rate parameter of monomers **IV**, **V**, and **VI** [$(2f)^{1/2}K_p/\langle K_t\rangle^{1/2}$ = 0.18, 0.26, and 0.72 $L^{1/2}$ $mol^{-1/2}$ $s^{-1/2}$, respectively],[13,14] the radical copolymerization of **IV** and **VI** or **V** and **VI** could lead to the formation of short blocks leading to hydrophobic and hydrophilic chain sequences.

Moreover, different polymer random coils could favor the interaction of the lipophilic blocks and also the hydrophilic ones to give interpenetrating vicinal lipophilic and hydrophilic microdomains. Thus, the anions could penetrate into the water swelled film core by diffusion through the water rich hydrophilic microdomains, the sensing occurring in the lipophilic zones by diffusion of certain anions to these less hydrophilic microphases.

Bearing in mind these considerations, a likely mechanism is as follows: (i) in the first step, there is a diffusion of certain anions from water into the water swelled hydrophilic domains; (ii) some anions migrate from the hydrophilic to the lipophilic domains of the film; (iii) it is known that certain anions enhance its basic character in nonaqueous lipophilic solvents; (iv) inside the lipophilic film, there is an acid–base reaction between the anion (A^-) and water molecules, resulting in the protonation of the anion (HA) and the release of OH^-; and (v) finally, the nucleophilic hydroxide anion attacks the C-2 position of the pyrylium probe, leading to the red hydroxyenone derivative. A tentative scheme of the mechanism is depicted in Figure 3.

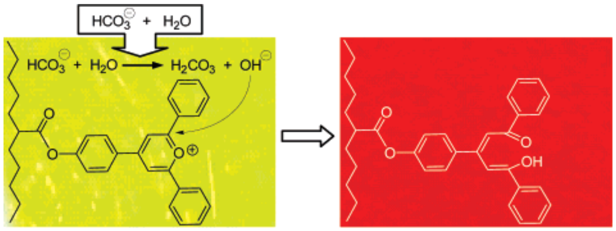


Figure 3. Schematic representation of the proposed mechanism operating in polymer **1** upon addition of HCO_3^-. The background shows the real color of polymer **1** alone and in the presence of HCO_3^- anion.

The reversibility of the reaction between hydroxide anions and pyrylium rings allows the attractive possibility of attaining reusable colorimetric probes. In this respect, red films of polymer **1** after reaction with aqueous solutions of HCO_3^- could be soaked in 0.01 mol dm^{-3} hydrochloric acid in order to recover the original yellow color of the pyrylium-doped film. This cyclic process was repeated at least five times without significant degradation of the colorimetric response of the film.

In summary, we have presented here a family of polymeric sensory materials containing pyrylium cations. The data above show that, by a control of the ratio between the lipophilic (**IV** and **V**) and hydrophilic (**VI**) monomers and the electrophilicity of the different pyrylium rings, it is possible to obtain a tailor-made polymer with a general response to basic anions and particularly a selective chromogenic response to hydrogen carbonate in pure water. These results form the foundation for developing reusable colorimetric easy-to-use in situ naked eye probes for hydrogen carbonate that is applicable in a wide range of different sites and environments.

Acknowledgment. We thank the Ministerio de Ciencia y Tecnología (projects CTQ2006-15456-C04-01 and MAT2005-01355), Junta de Castilla y León (project BU003A05), Generalitat Valenciana (project GV06/101), and Universidad Politécnica de Valencia (project 5711) for support. B.G.-A. thanks the Generalitat Valenciana for a Doctoral Fellowship.

Supporting Information Available: Experimental procedures and characterization data for compounds **Ia**–**Ib**, **IIa**, **IIb**, and **III** are described. Also, the experimental procedure for the sensing experiments is described. This material is available free of charge via the Internet at http://pubs.acs.org.

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