Instruments TGA-2050 apparatus (nitrogen flow 60 ml min^{-1}, 2 °C min^{-1}).
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Colorimetric Isomer Probes

Towards the Development of Colorimetric Probes to Discriminate between Isomeric Dicarboxylates**

Felix Sancenón, Ramón Martínez-Máñez, Miguel Angel Miranda, Maria-Jesus Seguí, and Juán Soto*

The development of new chemosensors based on supramolecular concepts is a field of current interest.[1] A significant amount of work has been devoted to obtain specific chemosensors that are able to change, upon complexation with the target guests, one or several macroscopic properties in response to the molecular coordination event. Changes in fluorescence[2] and in absorbance[3] are the output signals used in the development of optical chemosensors. Although a number of chromogenic receptors for the sensing of metal ions have been developed,[4] very few chromogenic receptors for anions have been described in the literature that are based on recognition approaches.[5] Most of the receptors have been developed for the colorimetric sensing of inorganic anions,[6] whereas very few have been designed for recognition of organic anions,[7] particularly in aqueous environments. Thus, the development of chromogenic reagents for such species remains a challenge. In this context, and as an advancement of this field, we wish now to report a chromogenic system for the colorimetric discrimination between certain organic isomers (*cis*/*trans* and *ortho*/*meta*/*para* dicarboxylates). Differentiation of isomers is, in general, a difficult task because of their rather similar chemical and physical properties. To the best of our knowledge, the examples we show here are the first supramolecular-based colorimetric probes for the detection of isomeric anions.

Most of the known colorimetric anion chemosensors are based on host molecules containing anion coordination sites coupled to chromogenic signaling units. In those receptors, coordination of the anion usually modifies the charge-transfer band of the chromogenic group resulting in "naked-eye" anion detection. A different approach involves the use of anion-induced reactions that can be either reversible or irreversible.[8] We have recently reported the use of one such anion-induced reversible reaction for the selective detection of ATP in water/organic solvent mixtures.[9] The system was based on the cyclization of yellow 1,3,5-triarylpent-2-en-1,5-diones to the magenta pyrylium cation. A family of 1,3,5-triarylpent-2-en-1,5-diones were synthesized by electrophilic aromatic substitution of the corresponding aniline derivative with 2,6-diphenylpyrylium perchlorate in DMF at 150 °C. Subsequent column chromatography on aluminum oxide afforded the receptors L^1–L^8 in approximately 35 % yield. The UV/Vis spectra of L^1–L^8 are very similar, with a band centered at around 370–380 nm, which is indicative of their brightly yellow color. The structures of the compounds L^1–L^8 are shown in Scheme 1.

Figure 1 shows a photograph of buffered dioxane/water (70:30 v/v) solutions of L^8 at approximately pH 6 (0.01 M HEPES buffer, HEPES = 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid) containing an equimolar amount of certain carboxylate (acetate, benzoate) and dicarboxylate anions (terephthalate, $^-OOC–(CH_2)_n–COO^-$, $n = 0$ to 7, oxalate, malonate, succinate, glutarate, adipate, pimelate, suberate). The solution remains yellow upon addition of all the above mentioned species, except for the oxalate and malonate ions, whereby the solutions turn red-magenta. This remarkable color change is, as stated above, a result of the anion-induced selective cyclization of L^8 to give the colored 2,4,6-triphenylpyrylium cation (absorption maximum at approximately 550 nm). Figure 1 also shows the color variation observed upon addition of maleate or fumarate dicarboxylate ions to buffered solutions of L^5 (0.01 M HEPES buffer, approximately pH 6). The solution is yellow in the presence

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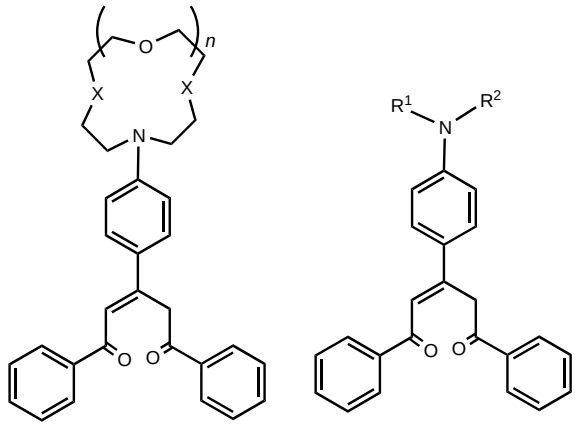

L^1, X = O, n = 1
L^2, X = O, n = 2
L^3, X = O, n = 3
L^4, X = S, n = 2

L^5, $R^1 = R^2 = CH_3$
L^6, $R^1 = CH_2CH_2OH$, $R^2 = (CH_2CH_2O)_2CH_2CH_2OH$
L^7, $R^1 = CH_2CH_2OH$, $R^2 = (CH_2CH_2O)_3CH_2CH_2OH$
L^8, $R^1 = CH_2CH_2OH$, $R^2 = (CH_2CH_2O)_4CH_2CH_2OH$

Scheme 1. Schematic representation of L^1–L^8.

of the *trans* isomer, but changes color to magenta in the presence of the *cis* isomer. As far as we know, this is the first reported example of *cis*/*trans* discrimination using colorimetric reagents. In fact, there are very few reports in the literature dealing with the use of synthetically constructed receptors for the colorimetric sensing of carboxylic acids. One such study, by Hamilton and co-workers, was carried out in dichloromethane[10] and, more recently, two reports by Anslyn and coworkers have described chromogenic competition assays for the colorimetric determination of citrate and tartrate species in aqueous organic solvents.[11]

In addition to the use of L^8 and L^5 as receptors (Figure 1), similar results are obtained when using the remaining compounds outlined in Scheme 1, which strongly suggests that the interaction of the anions with the receptors involves a fragment that is common to all of them. This points to the pent-2-en-1,5-dione group, rather than the aza-oxa- or aza-thia-oxa-polyazaalkane fragments, acting as the anion binding site. Thus, although diones can not bind to carboxylates, the corresponding enol tautomers can form hydrogen bonds with the anions (see the upper part of Scheme 2). From all the dicarboxylates studied, only oxalate, malonate, and maleate ions gave color variation. The special feature that these three anions have in common is the presence of carboxylate groups in close proximity. In this context, the potential ability of these guests to bind the hydroxyl group of the receptor by using both carboxylate groups would result in the formation of stronger hydrogen bonds and, therefore, in an enhancement of the nucleophilic character of the hydroxylic oxygen atom. One might refer to this action as "tweezers-like" behavior, in the sense that only diacids shaped like "tweezers" are able to act as chelating ligands towards the OH group, whereas other diacids or monoacids do not. Hence, the recognition process conforms to the supramolecular concept that guests (in our case anions) do not only have charge or size, but also a certain shape (in this case, proximity between carboxylate groups).[12] Scheme 2 describes the steps in the shape-induced recognition process; the tweezers-like carboxylate groups serve to disrupt the hydrogen atom from the hydroxy oxygen atom, which induces nucleophilic attack at the C1 carbon, with subsequent cyclization occuring to give the magenta pyrylium cation.

Figure 1. a) Color changes induced on L^8 (5×10^{-5} mol dm^{-3}) at pH 6 (buffered with 0.01 M HEPES) in dioxane/water (70:30 v/v) in the presence of (from left to right): no anion, oxalate, malonate, succinate, glutarate, adipate, pimelate, suberate, terephthalate, acetate, and benzoate anions. b) Color changes induced on L^5 under the same conditions, in the presence of (from left to right) maleate and fumarate anions.

Further studies also appear to support the mechanism outlined in Scheme 2. Thus, if that mechanism is correct, then the anions should be acting as catalysts for the cyclization. This has been confirmed, and we have found rate constants for the process anion + $L^5 \rightarrow L^5$(cy) + anion of 149.3, 62.6, and 148.7 M^{-1} s^{-1} for oxalate, malonate, and maleate ions, respectively. Furthermore, when kinetic studies were carried out in D_2O/dioxane mixtures, the rate constants were found to be 3–4 times smaller than when water/dioxane was used as solvent. Such an isotope effect suggests that the rate-determining step of the cyclization reaction involves cleavage of the O–H (O–D) bond.

Additionally, molecular modeling calculations to study the interaction of the enol tautomer of L^5 with different anions[13] have shown that when a carboxylate is placed near the hydroxyl group of the enol tautomer, a hydrogen bond is formed. However, the strength of the hydrogen bond depends on the nature of the anions. The calculations show that the oxalate, malonate, and maleate anions tend to

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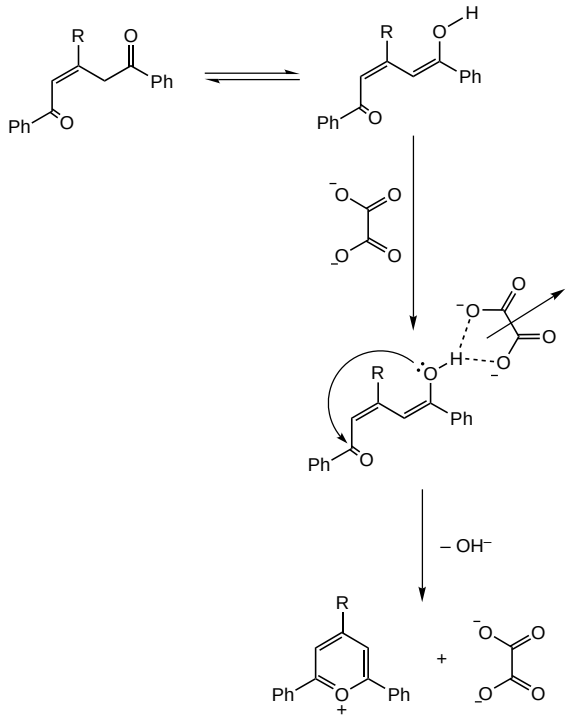

Scheme 2. Proposed mechanism of cyclization by nucleophilic attack of the oxygen atom to the C1 carbon. The Scheme also shows the proposed formation of hydrogen bonds between the dianion and the hydroxy group.

form strong hydrogen bonds, significantly enhancing the electron density of the oxygen atom of the hydroxyl group. This is shown in Figure 2, where the charge on the enolic oxygen atom (from PM3 calculations) of the L^5 receptor bound to the corresponding anion is plotted against the

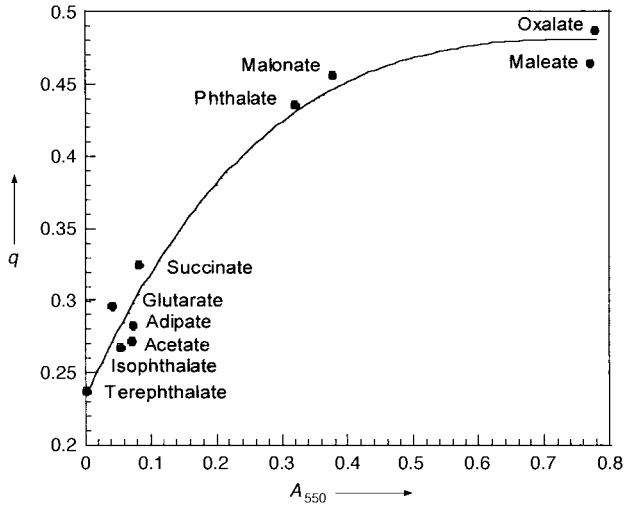

Figure 2. Plot of the charge (q) on the oxygen atom of the hydroxyl group in the enol tautomer of L^5 after forming hydrogen bonds with certain anions, as a function of the absorbance of the 550 nm band. The charge q is calculated from PM3 calculations of the interaction of L^5 and the corresponding anion. All the anions studied form hydrogen bonds with the hydroxyl group.

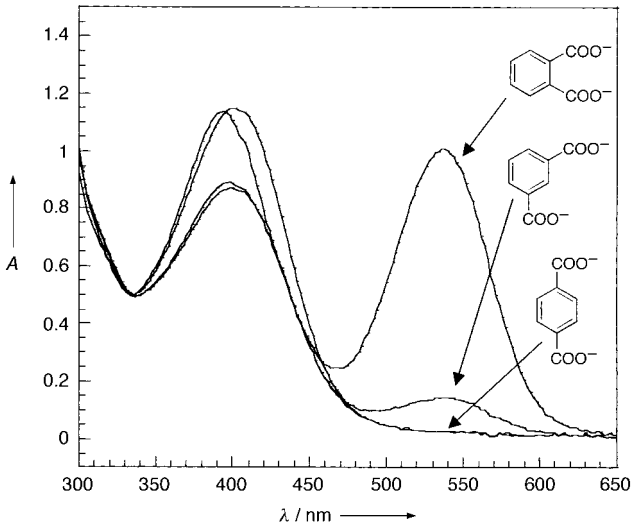

Figure 3. Visible spectra of L^5 (5×10^{-5} mol dm^{-3}) at pH 6 (buffered with 0.01 M HEPES) in dioxane/water (70:30 v/v) in the presence of phthalate, isophthalate, and terephthalate anions.

experimental absorbance of the band at 550 nm after a reaction time of 30 min (this absorbance indicates the extent to which the magenta pyrylium cation is obtained). In fact, a very good correlation is found. It is interesting that carboxylates showing the above-described tweezers-like shape tend to induce a significant increase in negative-charge density at the oxygen atom of the hydroxyl group.

Colorimetric recognition of the tweezers-like dicarboxylates appears to be of general application (Figure 3), as the yellow L^1–L^8 receptors also change color to magenta in the presence of phthalate anions, whereas they remain yellow in the presence of isophthalate or terephthalate anions (dioxane/water (70:30 v/v) solutions, 0.01M HEPES buffer, approximately pH 6).

In summary, the use of relatively simple receptors combined with a specific anion shape allows remarkable colorimetric recognition of certain organic guests in water/dioxane mixtures. The recognition process, which is based on the cyclization of 1,3,5-triarylpent-2-en-1,5-diones, has proved to be very sensitive to the presence of tweezers-like carboxylates. Thus, for the first time, shape-induced cyclization allows for the design of probes for the selective colorimetric recognition of certain organic isomers. For instance, receptors L^1–L^8 are suitable chromogenic reagents for selective discrimination between *cis*/*trans* dicarboxylates and *ortho*/*meta*/*para* dicarboxylates in water/organic solvent mixtures at nearly neutral pH values. We believe that the interaction of target molecules with suitable chemical reactions, associated with a color change, can play a significant role in the development of a new generation of colorimetric sensors or reagents for the detection of target organic guests.

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Porphyrin-Containing [3]Rotaxanes

Synthesis of Porphyrin-Containing [3]Rotaxanes by Olefin Metathesis**

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Rotaxanes are fascinating examples of interlocked molecules. Their synthesis is now well-established, and a large variety of interesting rotaxane-based architectures have been reported.[1,2] Our interest in rotaxanes partly arises from the reports by others on the synthesis of these molecules and their application in molecular devices, but predominantly by the impressive way nature makes use of catalytically efficient (pseudo)rotaxane structures in processes such as DNA replication and degradation.[3] In these structures the enzyme (for example, DNA polymerase III)[3] completely encircles the DNA strand and performs numerous rounds of catalysis (for example, template polymerization or hydrolysis) on the macromolecular substrate before dissociating from it. These so-called processive enzymes are therefore very efficient. Inspired by this concept, we have initiated a research project to construct synthetic analogues of these processive enzymes. For this purpose we have designed porphyrin host **1** (see Scheme 1), which can form very stable 1:1 host–guest complexes with viologen derivatives ($K_{ass} > 10^6\,M^{-1}$),[4] and have synthesized simple porphyrin-containing [2]rotaxanes.[5] It was also shown that the manganese derivative of **1** is a very active epoxidation catalyst.[6] A polymeric rotaxane with double bonds in the polymeric thread and host **1** as the circular component is needed to be able to construct a processive mimic. The latter molecule can then slide over the thread and epoxidize the double bonds (Figure 1). Herein we report the synthesis of such a rotaxane molecule by using olefin metathesis protocols.

Grubbs and co-workers have developed an elegant and efficient route to synthesize end-functionalized polybutadienes. They showed that an acyclic olefin can act as a chain transfer agent (CTA) in the ring opening metathesis polymerization (ROMP) of 1,5-cyclooctadiene (COD), using ruthenium carbenes **2** and **3** (Scheme 1) as initiators.[7] The CTA is incorporated at both ends of the polymer, with the average number of end groups per polymer chain (F_n) being close to 2. We decided to apply this protocol to synthesize the desired

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