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A selective colorimetric chemodosimeter for the naked eye detection of benzoate anion

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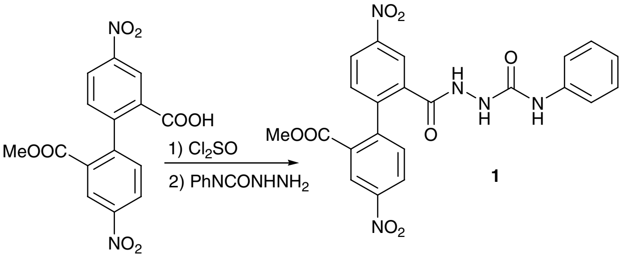
Abstract—A new semicarbazide biphenyl derivative is able to act as a selective chemodosimeter for benzoate.

Anion recognition and sensing is an area of interest that has undergone significant development in the last few years. The most widespread strategy to prepare colorimetric anion sensors is the binding site-signalling unit approach in which an appropriate photoactive group is attached to a specific anion receptor.[1] However, the use of chemodosimeters for anion sensing has received less attention[2] even though this approach has been shown to be very useful in the preparation of selective sensors for some cations mainly Hg(II).[3]

The chemodosimeter strategy is based on the use of a selective reaction (generally irreversible) that is induced by the target species and gives rise to some observable signal. If we take into account the idea that the simpler the detection system, the better the sensor, then compounds that are able to give rise to naked-eye detectable signals are of great interest.

As a further advancement in the field of colorimetric chemodosimeters, we report herein the preparation of ligand **1** which is useful for the selective recognition of benzoate versus other aromatic carboxylates. The design of the ligand was based on two points: (a) amidoureas or amidothioureas have demonstrated to be useful in carboxylate complexation[4] and (b) the experience of our research group in the use of 4,4′-dinitrobiphenyl as a signalling unit in colorimetric anion sensors.[5]

Ligand **1** was easily prepared as shown in Scheme 1. The monomethylester of 4,4′-dinitro-2,2′-diphenic acid[6] was transformed into its acyl chloride by reaction with thionyl chloride. The subsequent treatment with 4-phenylsemicarbazide gave rise to compound **1**.[†]



Scheme 1. Synthesis of ligand **1**.

Sensing experiments with benzoate and several 4-substituted benzoates (4-nitro-, 4-methoxy, 4-amino-, 4-methyl-, 2-hydroxy-; all of them as their tetrabutylammonium salts) were carried out in both acetone and DMSO. Two types of response were observed in these experiments. Thus, the less basic anions (4-nitro- and

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[†] ^{1}H NMR (300 MHz, CD_3COCD_3) δ 9.67 (1H, bb, NH), 8.75 (1H, d, $J = 2.3$ Hz, Ar-H), 8.65 (1H, d, $J = 2.3$ Hz, Ar-H), 8.47 (1H, dd, $J_1 = 2.3$ Hz, $J_2 = 8.3$ Hz, Ar-H), 8.43 (1H, dd, $J_1 = 2.3$ Hz $J_2 = 8.3$ Hz, Ar-H), 8.29 (1H, bb, *NH*), 7.67 (1H, d, $J = 8.3$ Hz, Ar-H), 7.66 (1H, d, $J = 8.3$ Hz, Ar-H), 7.63 (1H, bb, *NH*), 7.45 ($2H_a$, d, $J = 8.7$ Hz, Ar-H), 7.23 ($2H_b$, t, $J = 7.5$ Hz, Ar-H), 6.97 ($1H_c$, t, $J = 7.5$ Hz, Ar-H), 3.73 (3H, s, –COOCH_3). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 166.12, 165.21, 155.72, 153.41, 147.86, 147.53, 147.13, 146.83, 140.24, 134.89, 132.76, 131.65, 131.58, 129.00, 126.39, 125.14, 124.89, 123.08, 122.09, 118.74, 52.59. IR ν_{max} (KBr) 3565, 3356, 1716, 1634, 1605, 1524, 1348 cm^{-1}. HRMS (FAB^+): $(M+1)^+$ found 480.1132. $C_{22}H_{18}N_5O_8$ calculated 480.1155. Mp: 222–223 °C.

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Figure 1. From left to right: 0.021 M solution of 1 in DMSO, 0.021 M solution of 1 in DMSO + 5 equiv of TBA benzoate, 0.021 M solution of 1 in DMSO + 5 equiv of TBA 4-nitrobenzoate, 0.021 M solution of 1 in DMSO + 5 equiv of TBA 4-methoxybenzoate. The picture was taken 7 days after the preparation of the sample.

o-hydroxybenzoate) only gave rise to a slight change in the solution colour. By contrast, the solution colour immediately changed from pale yellow to dark red with all the other anions. When the solutions were either kept at room temperature for 1 week, or were heated at 60 °C for 12 h, the benzoate solution changed colour from red to dark green (Fig. 1).

The green colour observed in the benzoate solution is the result of a chemical reaction induced in the basic medium. This reaction is irreversible and produces a time-dependent dosimetric response that is controlled by the reaction kinetics.

In order to gain an insight into both the reaction involved and the behaviour exhibited by the different anions, several additional experiments were carried out. First of all, studies were carried out by registering the ^{1}H NMR spectra of DMSO-d_6 solutions of the ligand in the presence of 5 equiv of the different carboxylates. Figure 2 shows the aromatic zone of the ligand in the free form and in the presence of 4-nitro- and 4-methoxybenzoate. As shown, a clearly different behaviour was observed with these two anions. Whereas the nitro derivative only shows a shift of signals, the presence in the solution of 4-methoxybenzoate gives rise to very broad signals. A similar behaviour to that shown by 4-methoxybenzoate was not only observed with 4-amino-, 4-methylbenzoate, but also with the parent compound benzoate when the spectrum was registered immediately after sample preparation.

^{1}H NMR titration experiments carried out with 4-nitrobenzoate allows us to affirm that this anion forms a complex with 2:1 stoichiometry (Fig. 3) and with a complexation constant $\log\beta = 2.10 \pm 0.03$.[7]

Apparently, the 2:1 complex involves both the nitro and the carboxylate groups present in the anion. A structural proposal for this complex is shown in Figure 4 with the carboxylate group forming a Y-type[8] complex with the urea NH of one of the ligand molecules and the nitro group interacting with one NH of the second ligand molecule.[9]

The loss of resolution in the NMR spectra of the solutions containing ligand **1** and an excess of 4-methoxy-, 4-methyl- or 4- aminobenzoate preclude the use of this technique to carry out titration experiments to determine complex stoichiometry and complexation constants. On the other hand, the UV–vis spectra of these solutions show a new band in the 450 nm region that is responsible for the red colour (Fig. 5). This colour seems to be due to the deprotonated ligand that is generated by the carboxylate.

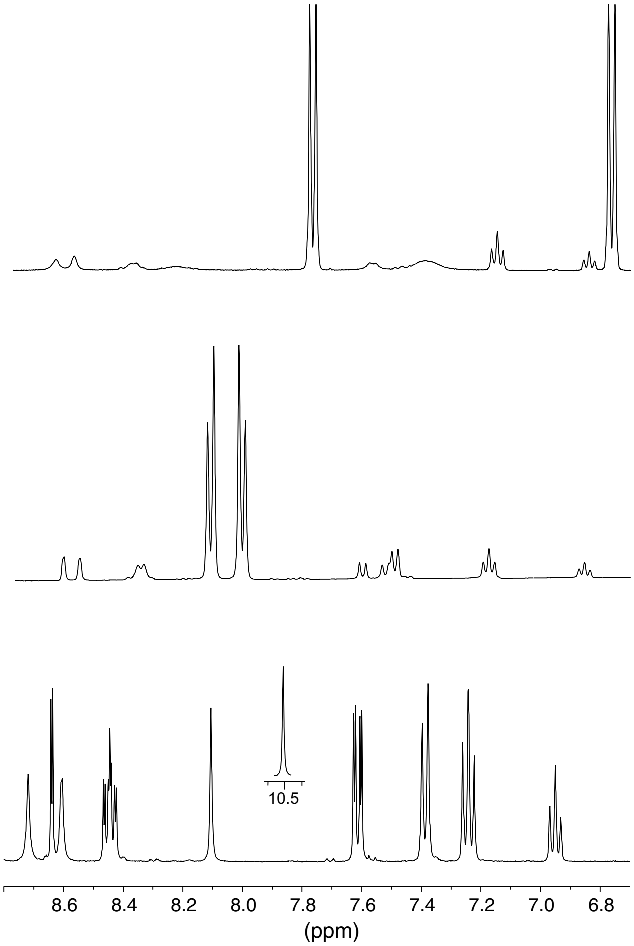

Figure 2. From bottom to top: ^{1}H NMR spectrum in DMSO of free ligand, free ligand + 5 equiv of TBA 4-nitrobenzoate, free ligand + 5 equiv of TBA 4-methoxybenzoate.

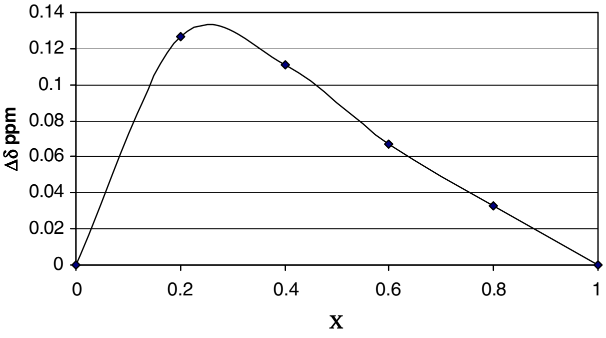

Figure 3. Job plot for the complexation of ligand **1** with TBA 4-nitrobenzoate in DMSO.

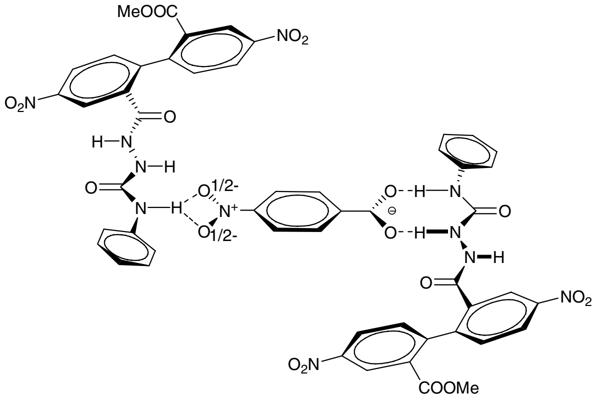

Figure 4. 2:1 complex formed between ligand **1** and TBA 4-nitrobenzoate.

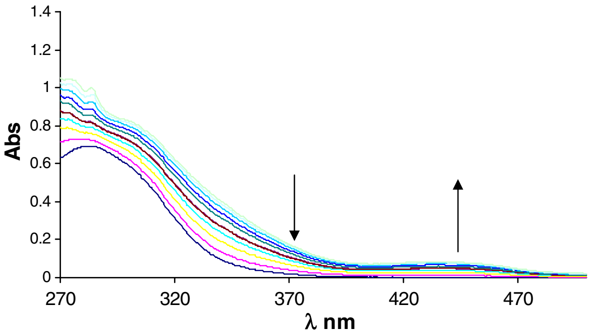

Figure 5. UV spectra of ligand **1** in DMSO in the presence of increasing amounts of TBA 4-methoxybenzoate.

This suggestion agrees with the disappearance of the NH signal around 10.5 ppm. The deprotonation reaction only requires an equivalent of anion, as also observed by Gale with related receptors.[4b]

Nevertheless the most interesting results were observed when TBA benzoate was added. In the presence of an excess of this carboxylate (2 equiv), the solution colour containing the ligand (in acetone or DMSO) changes immediately from yellow to dark red in a similar way as that shown by 4-methoxy-, 4-methyl- and 4-amino-benzoate. However, ligand **1** is able to act as a chemodosimeter only with this anion (Fig. 6). The mechanism seems to be a double (Lossen and Hofmann)[10] rearrangement reaction that gives rise to compound **2** (see Chart 1).[‡]

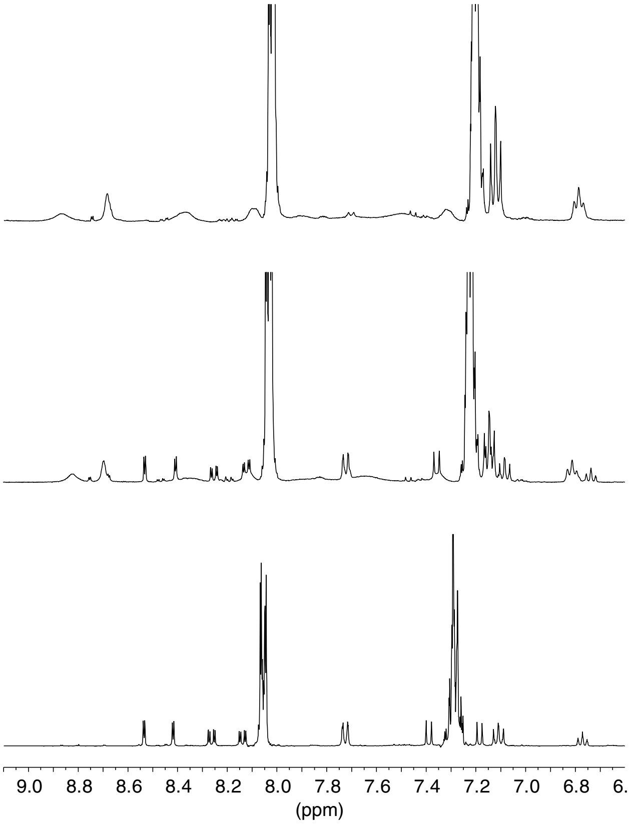

Figure 6. From top to bottom: ^{1}H NMR spectrum in $(CD_3)_2CO$ of a freshly prepared mixture of free ligand **1** + 5 equiv of TBA benzoate, sample after 48 h, sample after 3 months.

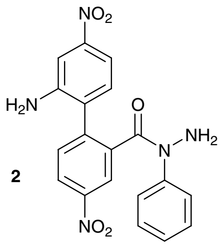

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Chart 1.

The green colour developed in the solution ($\lambda = 658$ nm) is due to the simultaneous presence of the nitro and amino groups in the structure and in the appropriate positions to allow for an electronic delocalization between both aromatic rings. Similar behaviour has been proposed with related sensors which are able to act as anion sensors.[11] This suggestion agrees with the negative colorimetric results observed when benzoylphenylsemicarbazide was used in control experiments. Finally, experiments carried out to know the influence of concentration on sensing properties showed that at least 2 equiv of the TBA benzoate with a concentration of the ligand around 0.021 M were necessary for the naked eye detection of the green colour. By contrast, the detection limit was around 7 mM when UV was used to detect the anion.

Anions such as 4-methoxy- 4-methyl- and 4-aminobenzoate did not develop the green colour even though the corresponding solution was heated at 90 °C for 2 days. The corresponding ^{1}H NMR spectra showed that the reaction in the presence of these ligands only took

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[‡] Compound **2** only presents a carbonyl group that is not that corresponding to the ester due to the absence of a signal corresponding to the methoxy group in both ^{1}H and ^{13}C NMR spectra. The IR spectrum suggests an amide type carbonyl because of the bands at 1713 and 1680 cm^{-1} (amide I and amide II bands). In addition, the $FAB^{+}MS$ spectrum shows a peak at *m*/*e* 393. Additionally, the UV–vis spectrum shows a new band at 658 nm, which is responsible for the green colour shown by this compound (Supplementary data).

place in a small proportion (see Supplementary data). Additional experiments carried out to determine the reaction mechanism and to also understand the role played by the anion (and therefore the influence that the substituents on the aromatic anion have on the reaction) are being developed.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.07.019.

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