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Computational study on fluoride recognition by an urea-activated phthalimide chemosensor

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Dedicated to Professor Miguel Ángel Miranda on the occasion of his 60th birthday

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ABSTRACT

The mechanism of the fluoride anion recognition by an urea–phthalimide chemosensor has been studied in detail by means of CASPT2//CASSCF calculations. Computational data are in well-agreement with changes in the photophysical properties previously reported experimentally in the presence or absence of fluoride anion. In both cases, fast relaxation from the S_2 potential energy surface leads to S_1 population. Deactivation of the excited state is in agreement with the experimental change in fluorescence observed when the anion is present. Mechanistic information obtained allows to provide an explanation of the experimental data and to suggest some modifications to improve the synthetic applicability of this type of chemosensors.

1. Introduction

Design and development of new anion receptors in chemistry constitute a highly active area of research.[1] As a general trend, hydrogen bonding and/or electrostatic interactions are involved in the anion receptor coordination. Fluorescent sensors appear to be the most suitable and attractive tools for anion recognition because of a high sensitivity at low analyte concentration.[2] Thus, photoinduced electron transfer (PET),[3] excimer/exciplex formation,[4] intramolecular charge transfer (ICT),[5] and excited state proton transfer[6] are some of the signaling mechanism reported.

The role of the urea moiety as an appropriate receptor for anions is well-established; Wilcox[7] and Hamilton[8] showed for the first time the interaction of urea-derivatives with phosphonates, sulfates and carboxylates forming stable 1:1 complexes. Accordingly, recognition and detection of other anions, such as fluoride have attracted considerable interest because of its established role in dental care,[9] treatment of osteoporosis[10] and its association with chemical weapons (nerve gases, such as sarin, soman, and GF chemical warfare agents) or terrorism (sarin gas was released in the Tokyo subway attack killing 12 people and injuring 5500 in May, 1995).[11] Examples of fluorescent sensors with urea-containing receptor that detect selectively fluoride anion have been reported[12] and explored by theoretical techniques.[13,20] In this context, chemosensors based on amido–phthalimide derivatives or different urea based receptors have been subjected to density functional level of theory (DFT) calculations.

In a previous study, a new receptor–fluorophore system based on a chiral urea–phthalimide was synthetized and found to be a selective sensor for fluoride anion.[14] Thus, the appearance of a new absorption band at longer wavelengths together with no changes in the singlet lifetime of the phthalimide chromophore in the presence of fluoride confirmed fluorescence static quenching as signaling mechanism. Formation of a charge transfer complex in the ground state through hydrogen bonding interaction rather than urea deprotonation in the recognition process was supported by DFT calculations. A weak bond-elongation of the urea protons after complex formation with fluoride was observed and a possible hydrogen abstraction was ruled out.

With this background, it appeared relevant to perform a detailed theoretical exploration of the interaction between a urea-activated phthalimide chemosensor and fluoride, in order to gain a better understanding of the recognition mechanism previously proposed[14] and to examine the acidity of the urea protons either in

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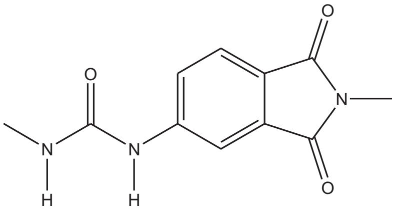
ground state or singlet excited state in the absence and presence of fluoride. Therefore, a computational analysis based on CASSPT2//CASSCF strategy[15] was carried out using the phthalimide derivative **1** (Fig. 1) as model compound with a structure close to that of the previous experimental study.[14]



1

Fig. 1. Urea-activated phthalimide chemosensor, **1**, as model compound.

2. Computational details

Compound **1** was chosen as model since the complete structure of the previously reported sensor[14] was found to be too large for CASSPT2//CASSCF calculations and the urea-linked stereogenic part is not relevant for the fluoride-association, which is investigated herein. Hence, compound **1** should reproduce all of the photophysical and photochemical properties at a much lower computational cost. The geometries of the critical points as well as all the reaction paths were computed using fully unconstrained ab initio quantum chemical computations in the framework of a CASPT2//CASSCF strategy.[15] This required the reaction coordinate to be computed at the complete active space self-consistent field (CASSCF) level of theory and the corresponding energy profile to be re evaluated at the multi-configurational second-order Møller–Plesset perturbation theory level. Conical intersections were located at the CASSCF level using the method developed by Bearpark et al.[16] This method also provided the components of the branching space. The Gaussian 03[17] program package was used for CASSCF computations. The energy of the CASSCF geometries was recalculated using the CASPT2 method implemented in MOLCAS-6.4,[18] taking into account the effect of electron dynamic correlation. All CASPT2 results were obtained with state average with equal weights for each state. Both CASSCF and CASPT2 calculations were done using the standard 6-31G* basis set. The effect of the basis set was explored by using the ANO-RCC basis set in single point calculations. For most calculations, the active space was formed by 12 electrons in 11 orbitals: π and π^* orbitals of the aromatic ring and both conjugated ketones were included as part of the chromophore and the n orbital of phthalimide nitrogen atom. To explore the relevance of the oxygen n orbitals, single point calculations with an increased active space of (16, 13) including the carbonyl groups oxygen n orbitals in the phthalimide moiety and the π system were performed.

Minimum energy paths (MEPs) were computed at the CASSCF level using the methodology present in MOLCAS-6.4. MEPs representing steepest descendent minimum energy reaction paths were built through a series of geometry optimizations, each requiring the minimization of the potential energy on a hyperspherical cross section of the potential energy surface centered on a given reference geometry and characterized by a predefined radius. The paths were computed using a value of 0.1 amu for the steps. Starting from the Franck–Condon (FC) structure, the path was followed to a conical intersection point. Once the first lower energy optimized structure was converged, this was taken as the new hypersphere center, and the procedure was iterated until energy surface reached the bottom.

Bulk solvent effects on the stability of model compound were included using the polarizable continuum model (PCM)[19] as implemented in GAUSSIAN03. The molecule was considered as included in a cavity surrounded by an infinite medium with the dielectric constant corresponding to the specific solvent. The standard value of 36.64 for acetonitrile was used in these calculations using DFT methods (B3LYP, 6-31G*).

3. Results and discussion

Experimentally, the formation of a charge transfer complex in the ground state through hydrogen bonding interaction rather than urea deprotonation was proposed as signaling mechanism.[14] A further exploration of this issue, especially the effect of the solvent on the stability of this hydrogen interaction, was performed before studying the excited state behavior of **1**. Thus, three different situations to evaluate this interaction in gas phase and bulk acetonitrile were computed (Fig. 2). In gas phase, the preferred situation was found to be **B** where fluoride anion abstracted a hydrogen atom from the sensor. In **C**, with the anion far away from **1**, the energy was more than 20 kcal/mol higher, whereas situation **A** collapsed directly to **B** and thus showed a higher energy value at the B3LYP 6-31G* level of theory. By contrast, when solvent effect was considered by PCM calculations, **A** became clearly the ideal situation, being in agreement with our previous experimental and theoretical results[14] and confirming the existence of a charge transfer complex in the ground state between the F^- ion and **1**. Furthermore, the preference for situation **A** in acetonitrile could be relevant for the practical competence of **1** to act as a sensor through several cycles as stated below. Similar results have been previously reported for simplified urea receptors from DFT calculations.[20]

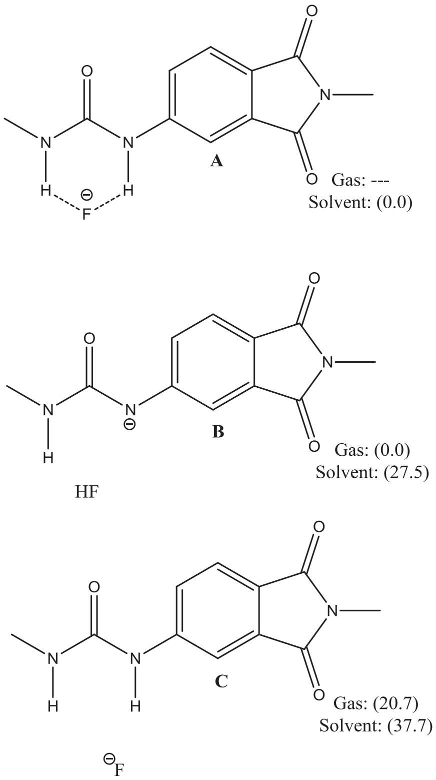


Fig. 2. Model sensor **1** and fluoride anion interactions in gas phase and acetonitrile. Energy differences in kcal/mol relative to the most stable structure.

Having established the most stable situation for the complex $[\mathbf{1}\text{-F}]^-$, an exhaustive exploration of the potential energy surface (PES) for the photochemical aspects of the sensing process was carried out.