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A novel anthracene-based receptor: Highly sensitive fluorescent and colorimetric receptor for fluoride

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ABSTRACT

A new highly sensitive colorimetric receptor 1 for fluoride based on anthracene-9,10-dicarbaldehyde bis-p-nitrophenylhydrazone was designed, synthesized and characterized. Experiments showed that the receptor 1 can selectively recognize the fluoride in DMSO and even in 95/5 DMSO/H_2O (v/v) mixtures. The ability of recognition and the bond between receptor 1 and anions were determined using visual inspection, UV–vis and fluorescence analyses. In addition, ^1H NMR experiments were carried out to explore the nature of interaction between receptor 1 and fluoride. Finally, analytical application and detection of fluoride in toothpaste have been studied.

1. Introduction

Since anions play a fundamental role in a wide variety of chemical and biological processes, the development of artificial optical receptor for selective anion recognition has been inspired with significant interest [1–3]. For example, fluoride species play critical roles in a variety of biological processes such as preventing children's dental caries [4] and treating osteoporosis [5,6]. However, fluoride at high concentration in human body leads to fluorosis [7–9], a type of fluoride induced toxicity that generally manifests itself clinically in terms of increasing bone density. Such a diversity in the functions, either beneficial ones or otherwise, makes the fluoride anion recognition considerably attracting. Acetate also plays important roles in organic, environmental, biological processes, etc. In enzymes and antibodies the functions of carboxylate ascribe to their specific biochemical behavior, and make them the critical components for numerous metabolic processes [10]. It is interesting to note that anion binding with the proteins is most often achieved through the neutral amide fragment employing the properties of the amine NH group acting as a hydrogen-bond acceptor [11]. As a result, there is an urge to develop certain sensitive and selective methods that can optically detect anions without resorting to any expensive spectroscopic instrumentation.

Recently, a lot of researches on neutral chromogenic and/or fluorescent anion receptors have been reported, owing to the simplicity and high sensitivity of these receptors suggested [12,13]. In particular, colorimetric-based sensing is especially attractive, as it may allow naked-eye detection of the analyte without resorting to any expensive equipment [14,15]. A number of well-known fluorophores have been reported, such as anthracyl, 8-hydroxyquinoline, and binaphthyl. These groups can be suitably conjugated, with other capturing units, as the signaling units. Especially, anthracyl shows a good performance in fluorescence yield. In addition, nitryl is a desirable group used for colorimetric recognition.

In spite of these accomplishments, there is still a noticeable weakness in the literatures. Generally speaking, the recognition studies were performed in aprotic media (e.g., DMSO, acetonitrile, $CHCl_3$, etc.), to avoid the competition from the protic solvent (e.g., water or alcohols) working as another hydrogen-bonding donor [14]. For all we know, in the real world, these anions often exist in those competitive, protic solvents such as H_2O and CH_3CH_2OH. Thus, it is urgent to develop receptors that are able to bind anions within the competitive media, and to be simultaneously accompanied with the 'naked-eyed' detectable color changes.

In this paper, our research group prepared a new and simple colorimetric anion receptor based on an anthracene derivative, which showed significant color changes upon the presence of anions. This receptor contains the hydrogen-bond-donor group (phenyl hydrazine), fluorophore (anthracyl), and the colorimetric group (nitrophenyl). The experimental results show that receptor 1 is highly selective and effective to recognize F^- in dry DMSO. More importantly, it also presents recognition behavior in DMSO/H_2O (95:5, v/v) solution. The processes of sensing can literally be seen

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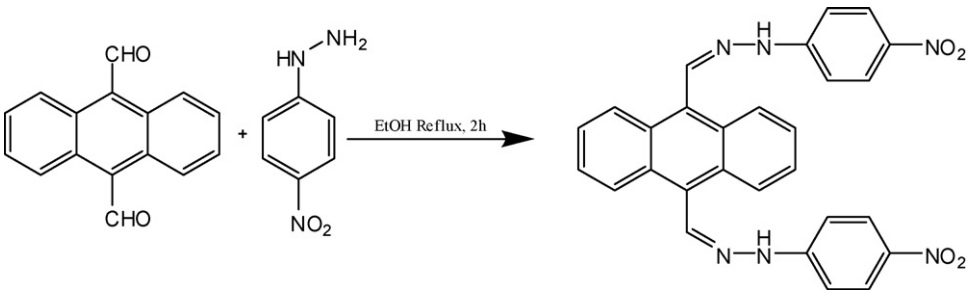


Scheme 1. General synthetic routes to the target receptor 1.

through the 'naked-eye' for the sharp color changes from light red to dark brown.

2. Experimental

2.1. Materials

All reagents for synthesis obtained commercially were used without further purification. In the titration experiments, all the anions were added in the form of tetrabutylammonium (TBA) salts, which were purchased from Sigma–Aldrich Chemical, stored in a vacuum desiccator containing self-indicating silica and dried fully before using. DMSO was dried with CaH_2 and then distilled in reduced pressure.

2.2. Apparatus

^{1}H NMR spectra were obtained on a Varian UNITY Plus-400 MHZ Spectrometer. ESI-MS performed with a MARINER apparatus. C, H, N elemental analyses were made on an elementar vario EL. UV–vis spectra were recorded on a Shimadzu UV-2450 Spectrophotometer (Shimadzu 2.1 Apparatus Corp., Kyoto, Japan) with a quartz cuvette (path length = 1 cm) at 298.2 ± 0.1 K. Fluorescent spectra were recorded on a FP-750 fluorescence spectrometer at 298.2 ± 0.1 K and the width of the slits used is 10 nm.

2.3. General method

A 2.0×10^{-3} M solution of the receptor 1 in DMSO was prepared and stored in the dry atmosphere. A 2.0×10^{-5} M solution of the receptor 1 in DMSO/H_2O (95:5, v/v) was also prepared. Solutions of 1.0×10^{-2} and 1.0×10^{-1} M tetrabutylammonium salt of the respective anion were prepared in dried and distilled DMSO and were stored under a dry atmosphere.

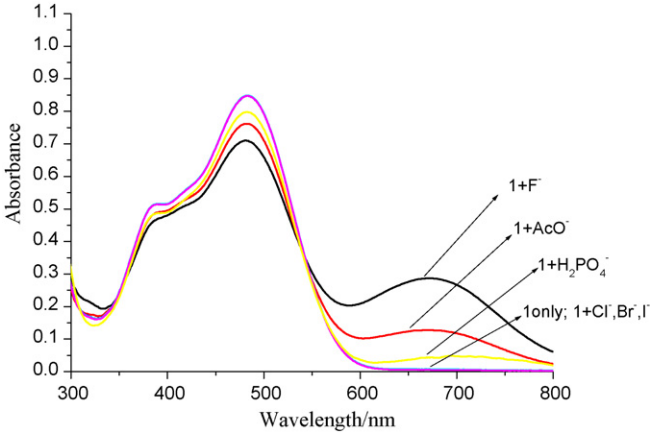


Fig. 1. UV–vis spectrum of 1 (2×10^{-5} M) in DMSO and changes after the addition of 5 times of F^-, AcO^-, $H_2PO_4^-$, Cl^-, Br^-, and I^-.

^{1}H NMR titration experiments were carried out in the DMSO-d_6 solution (TMS as an internal standard). Certain amount of the receptor 1 solution in the DMSO-d_6 was prepared with a concentration of 0.01 M. ^{1}H NMR of the host–guest system was recorded by adding increasing amount of fluoride anion (1.0 M in DMSO-d_6) into the receptor 1 solution.

2.4. Synthesis of anthracene-9,10-dicarbaldehyde bis-p-nitrophenylhydrazone

The receptor 1 was synthesized in two steps (see Scheme 1) starting from anthracene-9,10-dicarbaldehyde that was prepared

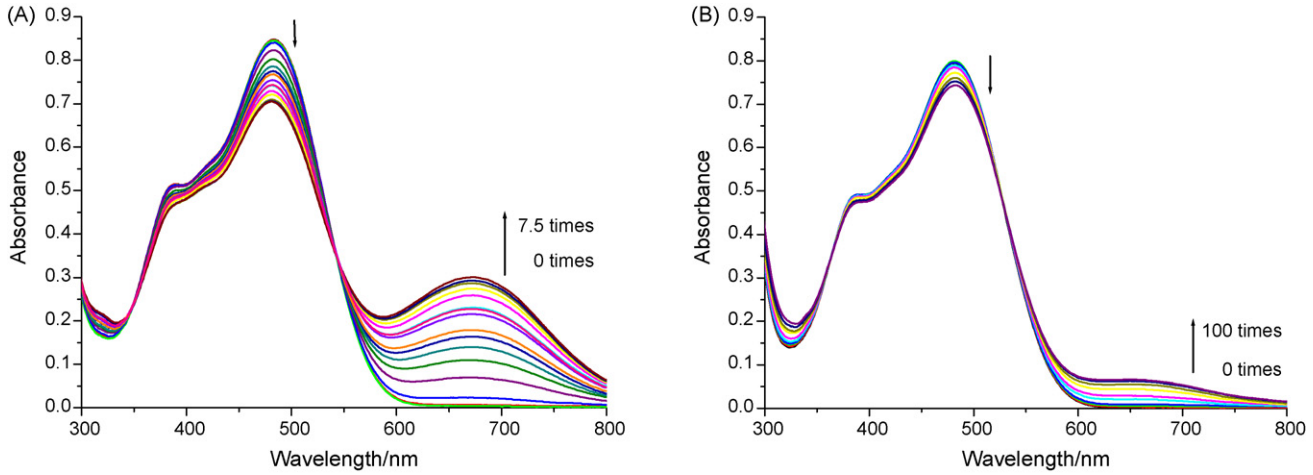


Fig. 2. Evolution of the UV–vis spectrum of receptor 1 (2.0×10^{-5} M) during the titration with F^- (A) in DMSO and (B) in DMSO/H_2O (95:5, v/v).

by the literature [16,17]. A mixture of 0.234 g (1 mmol) anthracene-9,10-dicarbaldehyde, 0.306 g *p*-nitrophenylhydrazine (2 mmol) and three drops of acetic acid were dissolved in 60 ml CH_3CH_2OH and then the resulting solution was heated and refluxed 2 h. The mixture solution was cooled at room temperature after reaction. The formed precipitate was filtered off, and then 0.383 g red solid was obtained after recrystallization from CH_3CN. This procedure yields 0.383 g (76%). ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.22 (d, 4H, Anthracene-H), 7.70 (d, 4H, Anthracene-H), 8.22 (d, 4H, Ar–H), 8.71 (d, 4H, Ar–H), 9.24 (s, 2H, C–H), 11.70 (s, 2H, N–H) (see Fig. S1). ESI-MS (*m*/*z*): calcd. for $C_{28}H_{20}N_6O_4$ $[M]^+$: 503.15, found: 503.11 (see Fig. S2). Elemental analysis calcd. for $C_{28}H_{20}N_6O_4$: C, 66.66; H, 4.00; N, 16.66. Found: C, 66.57; H, 4.05; N, 16.61.

3. Results and discussion

3.1. UV–vis anion titration studies

In order to study binding selectivity of the receptor 1, UV–vis titrations were carried out in DMSO at a concentration of 2.0×10^{-5} M by adding tetrabutylammonium salts of anions. Obviously spectral changes were observed after adding F^- to the solution (see Fig. 1). Moreover the color of solution of 1 was changed from light red to dark brown. However no detectable color responses were observed when adding AcO^-, $H_2PO_4^-$, Cl^-, Br^- and I^- ions, even in a large amount (up to 100 times) to the solution. These results suggest that receptor 1 can distinguish F^- from many other anions.

Then UV–vis titrations were carried out in DMSO at a concentration of 2.0×10^{-5} M for 1 by adding the tetrabutylammonium salt of F^- to study the anion-binding properties (see Fig. 2). The presence of fluoride resulted in the intensity of the absorbance band at 482 nm decreasing gradually and that at 672 nm increasing gradually, accompanied by the formation of an isosbestic point at 540 nm and the significant color changes from light red to dark brown, which indicates the intramolecular charge-transfer (ICT) between the anion binding with the –NH moiety and the electron-deficient $-NO_2$ moiety [18]. Especially, the changes in the UV–vis spectra are attributed to the interactions between the –NH sites of the hydrazone subunits and the fluoride ions via H-bond. Additionally, as the intensity of the polarization is increased by the $-NO_2$ substituent, the electron density of the hydrazone is transferred to the nitro moiety resulting in the possibility of realizing visual inspection. The presence of acetate ion has induced similar changes in UV–vis spectrum, but much greater amount of acetate ion than fluoride was required to achieve the reaction equilibrium (see Fig. S3). It is also proved that receptor 1 has good selectivity for recognizing fluoride.

It is well-known that upon adding the protic solvents such as water or methanol will competitively form hydrogen-bonding with the binding site of receptor for anions. In view of the high selectivity of receptor 1 in the dry DMSO, we also design the experiments in DMSO–water (95:5, v/v) and DMSO–water (90:10, v/v) solution, respectively, to further investigate their performance. Fortunately, similar phenomenon was actually observed in DMSO–water (95:5, v/v), so the receptor 1 may still have recognition capability for F^- (see Fig. 2).

3.2. Fluorescent anion titration studies

To have a better understanding of the binding mode, the fluorescence titration experiments were carried out (see Fig. 3). There was a strong emission band centered at 623 nm, when excited at $\lambda = 540$ nm. The fluorescence emission of 1 was quenched effectively upon addition of 8 times F^-. The photoinduced electron transfer (PET) mechanism was exploited to explain fluorescence quenching. As we all know, the fluorescence of the anionic PET chemoreceptor generally was 'switched off' rather than 'switched on' upon the sensing started, that was very different from most PET receptors for cations [19]. So upon interaction with anions, the quenching of the fluorescence of receptor 1 was increased, and in other words, the electron transfer from the electron rich amide group, bound by the anion, to the electron-deficient $-NO_2$ moiety became more feasible. And after more F^- anions were added to the system, it appeared that the deprotonated species were more electron rich compared with the hydrated F^- anion, and activated the PET process more efficiently, resulting in even greater quenching [20]. There were similar changes in the fluorescence emission of 1 induced by the addition of AcO^- (see Fig. S4), but addition of excess times $H_2PO_4^-$, Cl^-, Br^- and I^- ions had only slight effect on fluorescence intensity.

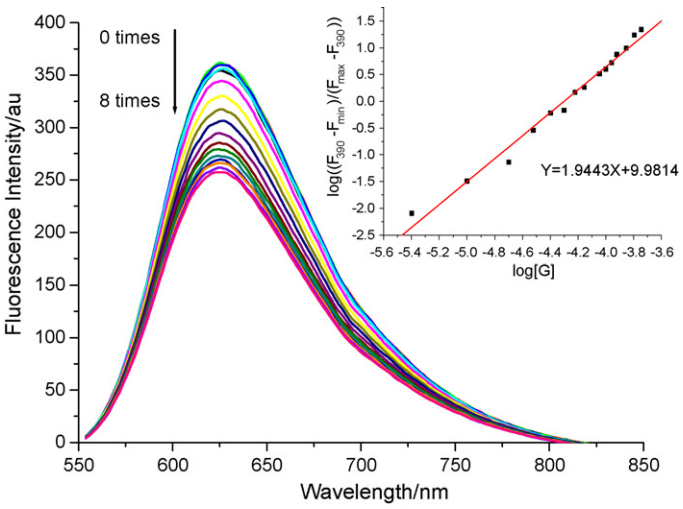


Fig. 3. Fluorescence spectra of 1 in DMSO in the presence of increasing concentration of F^-. $\lambda_{ex} = 540$ nm. $[1] = 2.0 \times 10^{-5}$ M. *Inset*: The fluorescence response fits to a Hill equation of 1.9443.

3.3. Determination of the binding constant and stoichiometry

The total fluorescence signal intensity *F* can be expressed by the following equation [21]:

$$F = \frac{[G]^n F_{max} + 10^{-B} F_{min}}{10^{-B} + [G]^n} \quad (1)$$

In the spectrofluorometry of this work, F_{min}, F_{max} and *F* are the emission intensities of the solution at wavelength 623 nm in the absence of guest, presence of the saturated guest, and after addition of a given amount of guest to certain concentration, respectively. [G] is the concentration of guest, *n* is the number of G bound per receptor 1. The sigmoidal curve was obtained and the total binding constant $\log \beta$ was deduced.

The equation can be linearised in the form of Hill plot and the Hill coefficient (*n*) can be obtained from equation [22–25] (see Fig. 3):

$$\log \frac{F - F_{min}}{F_{max} - F} = n \log[G] + B \quad (2)$$

As shown in Fig. 5, the binding constant of receptor 1 to F^- ($\log \beta$ or *B*) is 9.9814, and the Hill coefficient (*n*) is 1.9443 indicating receptor 1 binds the fluoride anion guest with a ratio of 1:2 which is consistent with the Job's plot (see Figs. S5 and S6). Job's plot was obtained according to the method reported by Connors [26]. Job's plot of receptor 1 and F^- in DMSO show the maximum at a molar fraction of 0.33, which indicates that the receptor 1 binds F^- guest

Table 1
Affinity constants of receptor 1 with anions in DMSO and DMSO/H_2O (95:5, v/v) at 298.2 ± 0.1 K.

Anions (M^{-1})	F^-	AcO^-	$H_2PO_4^-$	Cl^-	Br^-	I^-
$\lg K_{ass}$ [a]	9.98 ± 0.15	6.51 ± 0.03	ND[b]	ND	ND	ND
$\lg K_{ass}$ [c]	9.62 ± 0.10	6.90 ± 0.11	ND	ND	ND	ND
$\lg K_{ass}$ [d]	3.40 ± 0.13	3.00 ± 0.12	ND	ND	ND	ND

[a] The affinity constants determined by fluorescence in dry DMSO.
[b] ND = cannot determined.
[c] The affinity constants determined by UV–vis in dry DMSO.
[d] The affinity constants determined by UV–vis in DMSO/H_2O (95:5, v/v) solution.

at a 1:2 ratio.

The results drawn from the data of fluorescence spectrum are qualitatively matched with those from the UV–vis spectral titrations. The constants of the receptor 1 binding to other anions were also calculated (see Table 1).

According to the results from UV–vis titrations and fluorescent titrations, the proposed mode for the host–guest bonding in solution was depicted in Scheme 2. In the structure, anions such as F^- are located on two sides of receptor 1 via N–H···anion hydrogen bonds.

As clearly shown in Table 1, the order of binding affinity of 1 with anions (in DMSO or DMSO–water) is $F^- > AcO^- \gg H_2PO_4^- \sim Cl^- \sim Br^- \sim I^-$. The main reasons for preferring F^- can be ascribed to the basicity of the guest molecule and the shape complementarity between the receptor and the anionic guests [27], and the same is true in DMSO/H_2O (95:5, v/v) solution (see Table 1).

3.4. ^1H NMR titrations

To further elucidate the nature of the intermolecular interactions between anions and receptor 1, ^1H NMR spectral changes upon addition of F^- in their tetrabutylammonium salt forms to the DMSO-d_6 solution of receptor 1 (1.0×10^{-2} M) were investigated. Obviously, the proton signal at 11.70 ppm which was assigned to the –NH group can be observed in the absence of the F^- (see Fig. 4). Upon addition of 0.08 times of F^-, the signals of the –NH moiety broadened and those of phenyl rings and anthryl rings exhibited an upfield shift slightly. The results of the ^1H NMR titrations show that a hydrogen-bond complex is formed at this stage. As increasing the addition of F^-, the signals from binding sites of the receptor 1 downshifted and eventually disappeared, which displayed the complete deprotonation of the receptor 1.

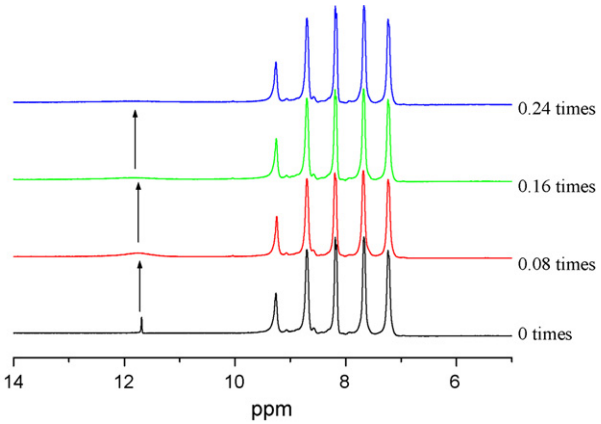
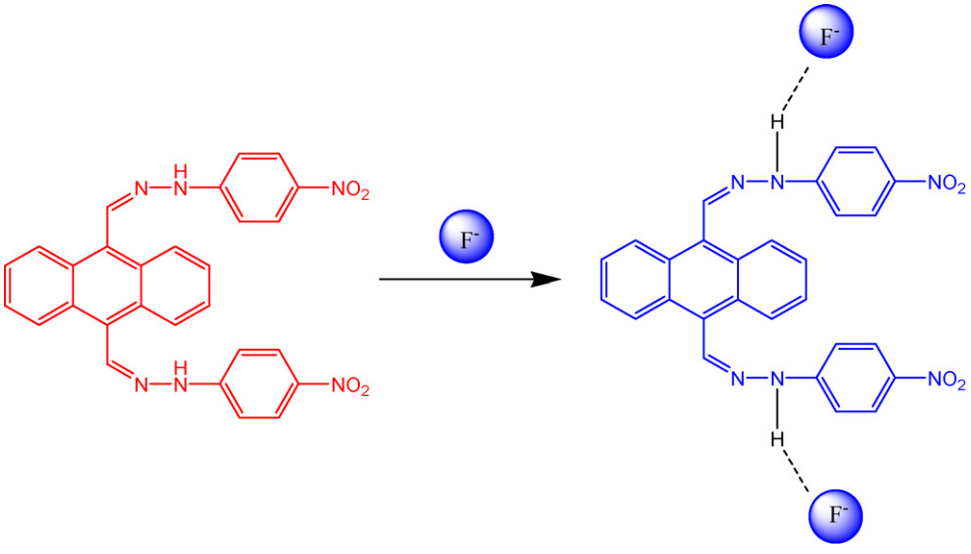


Fig. 4. ^1H NMR titration of a 1.0×10^{-2} M solution of 1 in DMSO-d_6 with [Bu_4N] F.

4. Analytical application

Experimental result is given to show the performance of receptor 1: it has high selectivity for the F^- anion. Color changes were observed obviously, turning from light red to dark brown upon addition of only 1 time of F^- to the solution of 1 (2.0×10^{-4} M). However, no detectable color responses were observed when adding other anions such as AcO^-, $H_2PO_4^-$, Cl^-, Br^- and I^- ions.

When the concentration of receptor 1 is 2×10^{-5} M in DMSO, the linear relationship between the absorption intensity and the added concentration of F^- accords with the calibration equa-



Scheme 2. The proposed 1–F^- binding mode in solution.

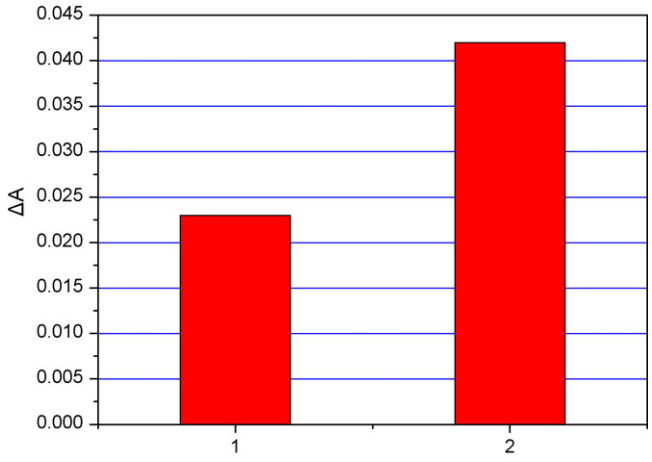


Fig. 5. The proof of concept for fluoride detection in toothpaste. (1) $1 + F^-$; (2) $1 + F^-$ + toothpaste ($\Delta A = A_{host} + A_{guest} - A_{host\ only}$).

tion $y = 1653x - 0.0006$, the related coefficient is 0.9906, the linear dynamic range of the $[F^-]$ is 2.0×10^{-6}–1.2×10^{-4} M, and the limit of $[F^-]$ detection (LOD) is 2×10^{-6} M, so we hope receptor 1 may be applied in detection of biologically important anions such as the fluoride ion. In order to further develop its real-life application, we design the toothpaste experiment according to the literature [28]. We prepared the samples that contained the commercially available toothpaste 10 mg/ml, 2×10^{-3} M of F^- (as tetrabutylammonium salts) and 2×10^{-5} M of receptor 1 in DMSO/H_2O (95:5, v/v). Then we measured and compared the UV–vis absorbance spectra in the absence or presence of toothpaste (see Fig. 5). It was shown that the signal from the F^- contaminated toothpaste solution (2) was stronger than that from the one without toothpaste (1), indicating the concentration of fluoride in solution (2) is higher than in (1). In this way the receptor 1 could be applied in qualitative detection of fluoride in toothpaste.

5. Conclusion

To sum up, we have presented a simple and colorimetric charge-neutral receptor, based on anthracene, which could recognize fluoride among the anions investigated. The whole processes can be observed by the 'naked-eye', for its sharp color changes from light red to dark brown. Moreover, the receptor 1 could detect the fluoride in toothpaste conveniently even at low concentration of F^-, so it is expected to have many applications in the detection of anions in real-life.

Acknowledgement

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.talanta.2010.01.045.

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