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Triazolium-promoted highly selective fluorescence “turn-on” detection of fluoride ions

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ABSTRACT

Through copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reactions, new pyrene-appended triazole- and triazolium-based fluorescent probes have been synthesized and their binding capabilities for anion recognition were investigated. The probes showed different fluorescence behavior in response to fluoride (F^-) ions. The probe bearing a triazolium moiety, displayed a high selectivity towards F^- ions *via* C–H···F^- hydrogen bonding interaction and de-protonation that was accompanied by fluorescence “turn-on”. Further, the experimental observations were well supported by ^{1}H NMR spectroscopy and density functional theory (DFT) calculations.

1. Introduction

The ubiquity of anions and their fundamental roles in biological and chemical processes necessitates the development of effective anion recognition systems as a forefront research topic in the field of supramolecular chemistry [1–7]. Of various anions, fluoride (F^-) is one of the most important biological ions and has received considerable interest from scientists because of the indispensable roles of fluoride in the health science. In fact, F^- intake is always regarded as a double-edged sword. Appropriate fluoride intake helps prevent osteoporosis and dental cavities, while excessive intake can lead to dental and skeletal fluorosis and urolithiasis [8–10]. Thus, there is a pressing need for the development of chemosensors that are capable of selectively recognizing F^- ions. Taking advantage of its highly basic nature and strong interactions with H-bond donor groups (*i.e.*, NH group) [11,12], a number of derivatives bearing NH groups have been extensively studied as F^- sensors in which NH–anion hydrogen bonds (NH···F^-) or anion-induced deprotonation of NH bonds ($[F–H–F]^-$) was observed [13–21].

In recent years, the development of Cu(I)-catalyzed azide-alkyne cycloaddition (Click chemistry) reactions (CuAAC) has helped to drive the evolution of new receptor designs. The large dipole moment of 1,2,3-triazole, a featured functional group of CuAAC, makes the C–H bond sufficiently polarized to participate in hydrogen bonding interactions with anions (C–H···A^-) [22–25]. Furthermore, this interaction can be enhanced by converting a triazole ring into a triazolium cation. These polarized C–H bonds have been recently demonstrated as a novel motif for the recognition of several anions [26–30]. However, till date there are only limited reports that utilize C–H bond for the recognition of fluoride ions [31–33].

Herein, we have explored recently established C–H···A^- hydrogen bond interaction to compare recognition abilities and sensing mechanism of triazole and triazolium rings for F^- ions. In this regard, we designed two pyrene-appended fluorescent probes, **1** and **2** (Fig. 1). In both designs, pyrene was chosen as the fluorescent reporter because of its well-defined monomer and excimer emission spectrum. For recognition purposes, probes **1** and **2** were decorated with triazole rings and triazolium rings, respectively. A

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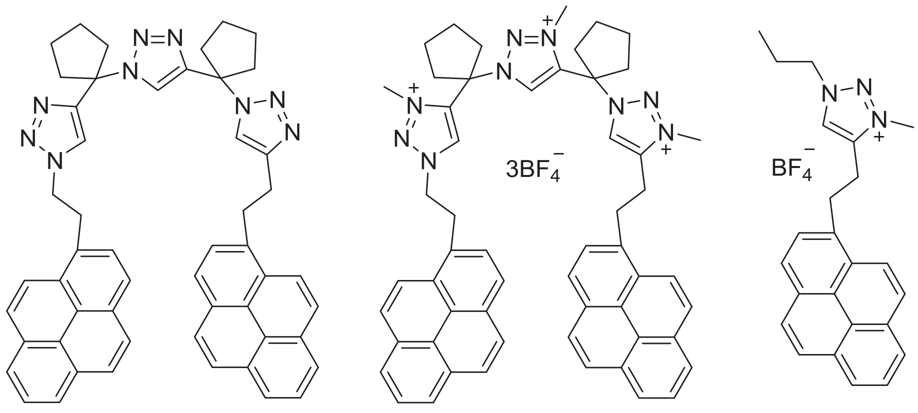

Fig. 1. The structures of probes **1**, **2**, and the reference compound **11**.

cyclopentane moiety was introduced as a bridge between the rings to take advantage of the Thorpe-Ingold effect in providing conformational constraint for the linear system. The experimental results have been further supported by ^1H NMR spectra and density functional theory (DFT) calculations.

2. Materials and methods

2.1. Materials and instrumentation

All fluorescence and UV/Vis absorption data were collected using JP/U-3010 (Hitachi Ltd., Chiyoda, Tokyo, Japan) and FP-6500 (Jasco Inc., Mary's Court Easton, Maryland, USA) spectrophotometers, respectively. NMR was recorded using a Avance 400, Avance 500 (Bruker, Billerica, Massachusetts, USA) and JNM-ECA-600 (Jeol Ltd., Musashino, Akishima, Tokyo) spectrometer (400, 500, or 600 MHz). All reagents and anionic compounds used as tetrabutylammonium salts of Br^-, Cl^-, ClO_4^-, CN^-, F^-, $H_2PO_4^-$, HSO_4^-, I^-, NO_3^-, and OAc^- were purchased from Aldrich (St. Louis, MO, USA). Dimethyl sulfoxide (DMSO) for spectra detection was a technical grade reagent without fluorescent impurity.

2.2. UV/Vis and fluorescence spectroscopic methods

Stock solutions of tetrabutylammonium salts were prepared in DMSO. All spectra were recorded in 6 μM of DMSO solution. Excitation was carried out at 344 nm with all excitation and emission slit widths at 3 nm.

2.3. Theoretical studies

The structures of probes were optimized by density functional theory (DFT) and time-dependent DFT (TDDFT) calculations with M06-2X functional and 6-31G* basis sets using a suite of Gaussian 09 programs [34]. The optimized geometries of all the species were confirmed to be local minima from the all-positive frequencies. The Cartesian coordinates for the optimized probes were summarized.

2.4. Synthetic methods

Compounds **1**, **2**, **4**, **6**–**9**, and **11** were newly synthesized in this study by modifying the procedure (Scheme 1 and S5).

2.4.1. Compound *4*

To a solution of $TMSN_3$ (8.90 mL, 22.5 mmol), p-$TsOH \cdot H_2O$ (4.28 g, 22.5 mmol) and $BF_3 \cdot Et_2O$ (11.1 mL, 45.0 mmol) in CH_2Cl_2 (100 mL), alcohol **3** (6.00 g, 22.5 mmol) in CH_2Cl_2 (20 mL) was slowly added at −78 °C and the mixture was stirred for 30 min at −78 °C. The mixture was allowed to warm up to rt and was stirred for an additional 1.5 h. The reaction mixture was diluted with water and neutralized with $NaHCO_3$. The mixture was extracted with EtOAc and washed with a solution of saturated $NaHCO_3$. The organic layer was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (only hexane) to give **4** (5.65 g, 86%) as a colorless oil. IR (neat, cm^{-1}) υ_{max} 2943, 2891, 2865, 2165, 2100, 674. ^1H NMR ($CDCl_3$, 500 MHz) δ 2.01–1.89 (m, 4H), 1.77–1.74 (m, 4H), 1.07 (s, 3H), 1.06 (s, 18H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 106.1, 86.1, 66.3, 40.5 (2C), 23.3 (2C), 18.5 (6C), 11.0 (3C). HRMS (FAB) calcd. for $C_{16}H_{30}N_3Si$ $[M-H]^+$ 292.2209, found 292.2216.

2.4.2. Compound *6*

A solution of azide **4** (417 mg, 1.43 mmol), acetylene **5** (400 mg, 1.57 mmol), $CuSO_4$ (11.4 mg, 0.08 mmol), sodium ascorbate (28.3 mg, 0.14 mmol) and TBTA (41.7 mg, 0.08 mmol) in t-BuOH/H_2O (29 mL, 1:1) was stirred at 35 °C for 10 h. After the solvents were removed *in vacuo*, the resulting residue was purified by silica-gel column chromatography (hexane/EtOAc, 5:1) to afford **6** (780 mg, quant.) as a light yellow oil. IR (neat, cm^{-1}) υ_{max} 3043, 2943, 2865, 2170, 1461, 1214, 748. ^1H NMR ($CDCl_3$, 500 MHz) δ 8.24 (d, J = 9.5 Hz, 1H), 8.14 (d, J = 7.6 Hz, 2H), 8.06 (d, J = 7.7 Hz, 1H), 8.06 (d, J = 9.3 Hz, 1H), 8.00 (s, 2H), 8.06 (t, J = 7.6 Hz, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.40 (s, 1H), 3.73 (t, J = 7.9 Hz, 2H), 3.29 (t, J = 7.8 Hz, 2H), 2.54–2.52 (m, 2H), 2.28–2.23 (m, 2H), 1.90–1.89 (m, 4H) 0.96 (s, 21H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 146.3, 135.3, 131.3, 130.8, 130.0, 128.7, 127.4, 127.3, 127.2, 126.7, 125.8, 125.0, 124.90, 124.85, 124.7 (2C), 123.1, 120.8, 107.3, 87.1, 65.8, 42.0 (2C), 33.2, 27.6, 23.6 (2C), 18.4 (6C), 10.9 (3C). HRMS (FAB) calcd. for $C_{36}H_{44}N_3Si$ $[M-H]^+$ 546.3305, found 546.3300.

2.4.3. Compound *7*

To a solution of triazole monomer **6** (505 mg, 0.93 mmol) in THF (10 mL) was added acetic acid (115 μL), followed by tetrabutylammonium fluoride (876 mg, 2.78 mmol). The reaction mixture was stirred at rt for 2 h. After the starting materials were consumed, a solution of saturated NH_4Cl was added. The resulting mixture was then extracted with EtOAc, the combined organic layers were dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane/EtOAc, 2:1) to afford acetylene **7** (322 mg, 90%) as a light brown solid. m.p.