Graphical Abstract

Multiple fluorescence color transitions mediated by anion- π interactions and C-F covalent bond formation

Jie Pan^a, Wei Lin^b, Fang Bao^{a,c}, Qinglong Qiao^a, Guixin Zhang^{c,*}, Yao Lu^{a,*},

Zhaochao Xu^{a,*}

^aCAS Key Laboratory of Separation Science for Analytical Chemistry, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, China. E-mail: zcxu@dicp.ac.cn;luyao@dicp.ac.cn.
^bChina Department of Obstetrics and Gynecology, the Affiliated Hospital of Qingdao University, Qingdao, China.
^cGeneral Surgery Department, the First Affiliated Hospital of Dalian Medical University, Dalian, China. E-mail: zgx0109@yeah.net.



The absorption and fluorescence spectra of 15 rhodamine dyes covering the visible to near-infrared regions were tested under exactly the same conditions. Then accurate and comparable data obtained were expected to be used as references for future research and help to understand the structure-fluorescence relationship of rhodamines.

Chinese Chemical Letters

journal homepage: www.elsevier.com

Multiple fluorescence color transitions mediated by anion- π interactions and C-F covalent bond formation

Jie Pan^a, Wei Lin^b, Fang Bao^{a,c}, Qinglong Qiao^a, Guixin Zhang^{c,*}, Yao Lu^{a,*}, Zhaochao Xu^{a,*}

^aCAS Key Laboratory of Separation Science for Analytical Chemistry, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, China. E-mail: zcxu@dicp.ac.cn;luyao@dicp.ac.cn.

^bChina Department of Obstetrics and Gynecology, the Affiliated Hospital of Qingdao University, Qingdao, China.

^cGeneral Surgery Department, the First Affiliated Hospital of Dalian Medical University, Dalian, China. E-mail: zgx0109@yeah.net.

ABSTRACT

Article history: The emission changes of fluorescent dyes under the influence of environmental changes or Received interaction with analytes are the basis for designing ratiometric fluorescent probes and logic Received in revised form gates. However, it is rare that only one external stimulus induces continuous fluorescent color Accepted changes in a fluorescent dye. In this paper, we report a cage-like molecule formed by two Available online benzene rings and three imidazolium salts which produces continuous fluorescence wavelength changes when interacted with fluoride ions. Fluoride ions are first bound to the center of the cage under the action of an interaction, and the $(C-H)^+--F^-$ type ionic hydrogen bonds Keywords: induce the blue-shift of fluorescence. The subsequent formation of C-F covalent bonds with Anion-π fluoride ions makes the fluorophore wavelength continue to blue-shift, and finally obtains Imidazolium continuous multiple fluorescence changes caused by a single external stimulus. According to the C-F bond fluorescence wavelength and intensity, six different fluorescence signal channels can be Miltple color obtained, which can be encoded as six numbers from 0 to 5. We expect that this reaction process Fluorescent probe can find applications in quantitative anion recognition and molecular counters.

The widespread use of fluorescence in bioimaging, biosensing, and luminescent materials has stimulated the development of new fluorescent dyes[1-6] and the study of luminescence mechanisms.[7-11] Among them, changes in the fluorescent color of dyes induced by external stimuli have received special attention, including for the design of ratiometric fluorescent probes for quantitative detection, [12, 13] the development of multicolor materials, and their use as continuous logic gates.[14] Achieving multiple color transitions often requires activation of multiple different stimuli, which limits the range and selectivity of quantitative detection and, in logic gates, the feasibility of future use in molecular computers. Correspondingly, the same stimulus can cause a variety of fluorescent color changes, which is conducive to the quantitative detection of the target, and is also conducive to the precise control of the logic gate. However, relying on one stimulus to produce multiple color changes, especially continuous color changes, has rarely been reported so far.

ARTICLE INFO

Methods to cause changes in the emission wavelength of fluorescent dyes include intramolecular charge transfer caused by changes in environmental polarity,[15-17] control of energy resonance transfer between fluorophores,[18] the effect of intramolecular hydrogen bonds,[19] and the formation or breaking of covalent bonds that alter the conjugation system.[20] Anion- π interaction is a new intermolecular force that has been discovered and confirmed in recent years,[21-23] but it is rarely used in molecular recognition and fluorescent probe design. Anion- π interactions have always been thought to occur only

between aions and electron-deficient aromatics, such as hexafluorobenzene, 1,3,5-trinitrobenzene, and 1,3,5-triazine. This is because an electron-rich aromatics with a negative quadrupole moment would be considered to have a repulsive interaction with anions. And the non-covalent force has been mainly explained as a contribution of electrostatic attraction between the anion and one of the positive ends of the aromatic quadrupole moment. However, in one of our recent work, [24] we demonstrated that anion- π interactions can also exhibit between electron-rich alkylbenzene rings and a fluoride ion. This anomalous effect is most likely due to the polarization of the electron-rich aromatic system due to the repulsion between the anions and the aromatic electrons. In order to clarify the nature of this paradoxical anion- π interaction, here we first studied the interaction process between the anions and aromatics in detail, and found a stepwise binding mode between them.

In this paper, we reported that the cage-like molecule **H-1** composed of two benzene rings and three imidazolium salts can produce continuous fluorescence color changes during the interaction with fluoride ions (Figure 1). Fluoride ion was first bound to the center of the cage under the action of anion- π interaction, and the (C–H)⁺---F⁻ type ionic hydrogen bonds induced the blue-shift of fluorescence. The subsequent formation of C-F covalent bonds with fluoride ions made the fluorophore wavelength continue to blue-shift, and finally obtained continuous multiple fluorescence changes. According to the fluorescence wavelength and intensity, six different fluorescence

signal channels can be obtained, which can be encoded as six numbers from 0 to 5.



Figure 1. The interaction between compound **H-1** and fluoride ions. Based on the anion- π interaction and the formation of C-F covalent bonds, compounds **HF-1**, **CF-1**, **CF-2**, **CF-3** were successively formed, and the fluorescence maximum emission wavelength was converted from 480 nm to 400 nm and 37 5nm successively.

Compound H-1 was synthesized according to the reported method.[24] In compound H-1, the benzene rings at both ends compressed the (C-H)⁺ of the three naphthimidazolium salts in the middle of the cage and toward the inside of the cage in a symmetrical fashion. Due to the electron-withdrawing ability of the imidazolium salt and the delocalization in the imidazole, H-1 can emit cyanine fluorescence with a maximum emission wavelength of 480 nm. With the addition of the first equivalent of fluoride ion, the strong electrostatic attraction and interaction between the fluoride ion and one of the imidazolium salts gradually pulled the fluoride ion closer to the cage and had a strong interaction with aother imidazolium salt. At the same time, the three ethyl substituents on the benzene ring played a decisive role in the polarization of the benzene ring under the action of fluoride ions, so that the initial repulsive force between the benzene ring and the fluoride ion changed with the polarization of the benzene ring to attraction force, and finally fluoride ions entered the cavity, forming a supramolecular structure such as **HF-1**, including the anion- π interaction with the upper and lower benzene rings and the electrostatic interaction with three imidazolium salts. Due to the interaction between fluoride ion and imidazolium salt, the positive charge delocalization of imidazolium salt was deteriorated, and the fluorescence wavelength of naphthimidazolium salt was also blue-shifted to 400 nm. The steric position of the naphthimidazole group had a certain rigidity, and more importantly, the positive charge was more localized on the carbon atom between two nitrogens. As more fluoride ions were added, a nucleophilic addition reaction between the fluoride ions and the activated carbon atoms in the imidazolium salt occured. The newly generated chromophore no longer had the structure of imidazolium salt, but emited fluorescence similar to naphthalenediamine, and its maximum emission was at 375 nm. With the continuous addition of fluoride ions, the three imidazolium salts continued to generate C-F bonds, so that compounds **CF-1**, **CF-2** and **CF-3** were generated successively, and these three compounds contained one to three C-F bonds, respectively. The fluorescence spectra also produced corresponding changes, that was, the fluorescence emission at 400 nm gradually decreased, while the fluorescence emission at 375 nm appeared and gradually became stronger.



Figure 2. Fluorescence spectra of 10 μ M **H-1** in the presence of different concentrations of F⁻ (a: 0 to 1 equiv; b: 1 to 4 equiv; c: 4 to 30 equiv) in CH3CN.

Compounds HF-1, CF-1, CF-2 and CF-3 were verified by NMR respectively (Figure 3), and we were lucky to get the crystal structure of compound CF-2. The NMR analysis of the anion- π interaction in HF-1 was reported previously. It can be seen from the ¹H-NMR spectra that the symmetry of the cage-like molecule was broken as the C-F bond was formed. Based on the ¹H-NMR spectra of CF-1 and CF-2, the fluoride ion was no longer between the upper and lower benzene rings,

but was located outside the cage. Naphthalene molecules containing C-F and naphthalene molecules that attract fluoride ions by electrostatic hydrogen bonds had significantly different chemical shifts (Figure 3a-b). The crystal of **CF-2** can better illustrate this mode of action (Figure 3c-d). The two C-F-containing naphthalene molecules were twisted in a



Figure 3. ¹H-NMR spectra of H-1, HF-1, CF-1, CF-2, CF-3 in CD₃CN at room temperature and crystal structure of CF-2.

coplanar structure, and the two F atoms are facing the outside. The upper and lower benzene rings were in a parallel and overlapping configuration. It should be specially pointed out that even after the C-F bond was generated, the C-H in the three imidazole rings were still oriented towards the center of the cage and had high symmetry (Figure 3c). And one equivalent of free fluoride ion in the crystal appeared to form the F-F interaction with one C-F, and the bond length was 2.342 Å (Figure 3d).

In conclusion, we reported a cage-like molecule formed by two benzene rings and three imidazolium salts which produces continuous fluorescence wavelength changes when interacted with fluoride ions. Fluorescence has an extremely sensitive response performance to environmental changes. In this system, fluoride ions from 1 to 4 equivalents produced distinct fluorescence changes, which can be used for quantitative detection of fluoride ions. At the same time, this quantitative relationship corresponds to different fluorescent signals. We use naphthimidazolium salt, imidazolium salt-F complex, and C-F compound as the signal units. With the interaction between fluoride ion and H-1, the number of these three signal units will alternately change. If this quantization relationship is encoded as a signal channel, the six numbers 0-5 can be represented. Combined with microfluidics, we are conducting molecular-based counting, addition and subtraction research.

Acknowledgments

We are grateful for the financial support from the National Natural Science Foundation of China (22078314, 21878286,

21908216) and Dalian Institute of Chemical Physics (DICPI201938, DICPZZBS201805).

References

- [1] C. Wang, W. Chi, Q. Qiao, et al., Chem. Soc. Rev. 50 (2021) 12656-12678.
- [2] X. Liu, Q. Qiao, W. Tian, et al., J. Am. Chem. Soc. 138 (2016) 6960-6963.
- [3] W. Zhou, X. Fang, Q. Qiao, et al., Chin. Chem. Lett. 32 (2021) 943-946.
- [4] Z. Xu, Coord. Chem. Rev. 444 (2021) 214036.
- [5] W. Liu, L. Miao, X. Li, Z. Xu, Coord. Chem. Rev. 429 (2021) 213646.
- [6] W. Liu, J. Chen, Z. Xu, Coord. Chem. Rev. 429 (2021) 213638.
- [7] C. Wang, Q. Qiao, W. Chi, et al., Angew. Chem., Int. Ed. 59 (2020) 10160-10172.
- [8] J. Chen, C. Wang, W. Liu, et al., Angew. Chem., Int. Ed. 60 (2021) 25104-25113.
- [9] Q. Qi, S. Jiang, Q. Qiao, et al., Chin. Chem. Lett. 31 (2020) 2985-2987.
- [10] W. Chi, Q. Qiao, C. Wang, et al., Angew. Chem., Int. Ed. 59 (2020) 20215-20223.
- [11] W. Chi, J. Chen, W. Liu, et al., J. Am. Chem. Soc. 142 (2020) 6777-6785.
- [12] W. Liu, R. Li, F. Deng, et al., ACS Appl. Bio Mater. 4 (2021) 2104-2112.
- [13] X. Fang, W. Liu, X. Wu, et al., Results Chem. 3 (2021) 100092.
- [14] S. Kou, H.N. Lee, D. van Noort, et al., Angew. Chem., Int. Ed. 47 (2008) 872-876.
- [15] F. Deng, Z. Xu, Chin. Chem. Lett. 30 (2019) 1667-1681.
- [16] S. Long, W. Chi, L. Miao, et al., Chin. Chem. Lett. 30 (2019) 601-604.
- [17] S. Long, L. Miao, R. Li, et al., ACS Sens. 4 (2019) 281-285.
- [18] X. Li, J. Zheng, W. Liu, et al., Chin. Chem. Lett. 31 (2020) 2937-2940.
- [19] Q. Qi, W. Chi, Y. Li, et al., Chem. Sci. 10 (2019) 4914-4922.
- [20] F. Deng, Q. Qiao, J. Li, et al., J. Phys. Chem. B 124 (2020) 7467-7474.
 - [21] B.L. Schottel, H.T. Chifotides, K.R. Dunbar, Chem. Soc. Rev. 37 (2008) 68-83.
 - [22] D.X. Wang, M.X. Wang, J. Am. Chem. Soc. 135 (2013) 892-897.
 - [23] I.A. Rather, S.A. Wagay, R. Ali, Coord. Chem. Rev. 415 (2020) 213327.
 - [24] Z. Xu, N.J. Singh, S.K. Kim, et al., Chem. Eur. J. 17 (2011) 1163-1170.