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New Dopa-AIE Compound Used as Fluorescence Sensor Material: Specificity and Quantification for Cu(II)

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As a paramagnetic metal ion, Cu(II) is challenging to be detected by conventional fluorescence sensor because of its unselective paramagnetic quenching effects on common fluorophores. By combining catechol with tetraphenylethene, a typical aggregation-induced emission (AIE) moiety, we have successfully synthesized a new kind of catechol, the dopa-AIE compound. Due to the properties of AIE core, the catechol has the “turn on” mechanism as a fluorescence chemosensor. Specifically, the new catechol has the unique detection selectivity on Cu(II) in solution. The fluorescence intensity has the maximum value when the molar ratio of the catechol to Cu(II) is 1∶1. Before and after this point, the fluorescence intensity shows a linear relationship with the copper ion concentration, increasing or decreasing. Thus, the quantitative calculation for Cu(II) or the dopa-AIE compound could be done according to this response process.

Keywords dopamines, biosensors, copper, fluorescence, redox

Introduction

It is well known that marine mussels can bind strongly to almost any surface in any case by secretory glue proteins. The presence of dopa (3,4-dihydroxy-*L*-phenylalanine) in these proteins is vital to their adhesive properties. Furthermore, the content of dopa in the protein is very important in their adhesive properties too.[1-4] It is generally believed that the dopa adhesion is somehow related to the presence of pyrocatechol, which could bind to metal ions or crosslink themselves under specific conditions. However, the detailed bonding mechanisms of dopa on various substrates are complicated and remain unknown by far.

The molecular structure of dopa is not very complex. However, since it is an amino acid, the interaction between amino and carboxyl group often tends to make the chemical modification inconvenient and not straightforward. Wilker and coworker’s work[5] suggested that the adhesion could be realized by the simple catechol group in poly[(3,4-dimethoxystyrene)-*co*-styrene] polymers. Compared to dopa, the catechol structure they used is simpler and easier to combine with other functional groups. Most importantly, it may still retain major characteristics of dopa. So, sometimes we call some catechols dopa because they have the adhesion property like dopa.

Up to now, there are many reports on dopa and its derivatives. Among them, many researches have been done mainly using dopa as a “middle-tier”, and with the aid of this layer, make further functionalization to fabricate materials with a variety of special features, such as bio-fouling surfaces, antibacterial materials, self-repairing hydrogels, and so on.[6-11] Nevertheless, the preparation of sensor materials using the dopa adhesion properties to directly or indirectly detect/monitor metal ions in literature is seldom reported.

Dopa itself has multiple functional groups: amino, carboxyl and pyrocatechol groups. It can combine with many metal ions such as Fe^{3+}, Co^{2+}, Ni^{2+}, Zn^{2+} and other metal ions[12-14] through complex, coordination or other forms, and can also reduce some metal ions such as Ag^{+} and Au^{3+} to metal nanoparticles.[15,16] Thus, the interaction of dopa with metal ions is of diversity and specificity.

Govindaraju’s group[17] reported an amphiphilic perylene diimide, a bimolecular analog of dopa, as a reversible fluorescence switching probe for the detection of and sensing cationic surfactants of Fe^{3+}/Cu^{2+} in aqueous media, respectively. The as-synthesized compound could serve as a fluorometric probe only for Fe^{3+}/Cu^{2+} by means of fluorescence switch off state due to the formation of metallosupramolecular assemblies. Interestingly, the authors mentioned that the metallo-

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supramolecular assemblies could be disassembled by addition of diethylenetriamine pentaacetic acid. Park *et al.* fabricated dopa-functionalized gold nanoparticles (AuNPs/dopa) that could detect low concentrations of Mn^{2+} in aqueous solution.[18] Probably this is because of the binding forces between dopa and Mn^{2+} ions, which leads to the AuNPs/dopa closer together, decreasing the interparticle distance and aggregating it with a change in color of colloidal solution from red to purplish-blue. And the ratio of absorbance at 700—550 nm was linear against the concentration of Mn^{2+} ions. A fluorosensor, *N*-doped graphene quantum dots, was synthesized by one-step solid-phase method with citric acid as the C source and dopa as the N source.[19] The fluorescence chemosensor is specific for Hg^{2+}, with a detection limit of 8.6 nmol/L. Although the Pb^{2+}, Cd^{2+}, Cu^{2+} and Ni^{2+} ions could interfere with the selectivity for Hg^{2+} detection, this issue could be circumvented by using triethanolamine and hexametaphoshpate as the chelating agents. Therefore, the quantum dots are suitable to detect Hg^{2+} with high sensitivity and selectivity.

From the few reported sensor materials based on dopa (catechol), such dopa-detectors are of highly exceptional selectivity and sensitivity, which is just the thing for preparation of sensor material. Judging from the detection mechanism, changes in fluorescence intensity of the dopa-sensors are usually based on the "turn off" mechanism. From the visual effect, however, the "turn on" mechanism is of higher sensitivity, and better than the "turn off" mechanism, since "turn off" mechanism usually requires relatively high concentration at the time of initial inspection.

To develop dopa based sensor materials with "turn on" mechanism, we firstly combined catechol with tetraphenylethene, a typical aggregation-induced emission (AIE) moiety, and successfully synthesized a new dopa-AIE compound. Generally speaking, the aggregation of chromophore would cause quenching light emission.[20,21] However, in 2001, Tang's group found an opposite phenomenon that is the "aggregation-induced emission".[22] Therefore, the as-synthesized dopa-AIE compound should be of "turn on" mechanism when used as a fluorescence chemosensor, which is different from the previously reported "turn off" sensor materials based on dopa (catechol). Specifically, the dopa-AIE compound we designed here has the unique detection selectivity on Cu^{2+} in solution. As it is well known that low concentration copper is an important substance for almost all kinds of life.[23] High level free Cu^{2+}, however, is known to elicit toxicity to cells and may cause liver or kidney damage while long-term exposure.[24] Some serious neurodegenerative diseases were found to be closely related to the copper metabolism disorders, such as Alzheimer's, Parkinson's, Menkes, and so on.[25,26] So, both on-site/real-time detection and quantification of Cu^{2+} ions are very important.[27-29] The bad news is that, as a paramagnetic metal ion, Cu^{2+} is challenging to detect with conventional fluorescence sensors because of its unselective paramagnetic quenching effects on common fluorophores. Therefore, the new kind of catechol we designed and synthesized here should be of great value in practical application because it has unique detection selectivity and quantification on Cu^{2+}.

Experimental

Synthesis of bis(3,4-dimethoxyphenyl)methanone (1)

Anhydrous dichloromethane (25 mL) was put into a 100 mL round flask. After the solvent was bubbled with argon for 20 min, veratrole (1.1 mL, 8.5 mmol) and 3,4-dimethoxybenzoyl chloride (2.0 g, 10 mmol) were added. Then, aluminum chloride anhydrous (1.8 g, 13.44 mmol) was carefully added in multiple portions slowly. After the mixture was bubbled with argon for another 5 min, the reaction solution was then heated at reflux in an oil bath for 2 h. After cooled down to room temperature, the mixture was poured into acid ice water (1 mol/L HCl, 20 mL) and stirred for 10 min. The organic phase was extracted by dichloromethane, washed by water 3 times, and then dried by anhydrous sodium sulfate. After removing dichloromethane, the final product as white powder was obtained by recrystallization in ethanol with the yield of 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50—7.40 (m, 4H), 6.95 (d, J=6.94 Hz, 2H), 4.01 (s, 6H), 3.99 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 56.30, 114.97, 123.44, 133.70, 149.65, 152.82. MS (*m*/*z*) calcd for **1**: 302.3218, found 302.2017.

Synthesis of 4-(1-(3,4-dimethoxyphenyl)-2,2-diphenylvinyl)-1,2-dimethoxybenzene (2)

Diphenylmethane (2.0 g) was dissolved in 15 mL of THF. Then, *n*-butyl lithium (4.54 mL, 2.5 mol/L in hexane) was slowly added to the solution at 0 ℃ in argon atmosphere. After 40 min, compound **1** (3.424 g) was added to the mixture in solid and the resulting mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with saturated aqueous ammonium chloride solution followed by a standard aqueous workup, affording the crude alcohol in nearly quantitative yield. Subsequently, the crude alcohol was dissolved in toluene and refluxed in the presence of a catalytic amount of *p*-toluenesulfonic acid with an azeotropic removal of water using a Dean-Stark trap to get the product. The final product was purified by crystallization from a mixture of dichloromethane and methanol with the yield of 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.19—7.06 (m, 10H), 6.70—6.58 (m, 6H), 3.87 (s, 6H), 3.53 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 56.26, 115.97, 123.44, 126.24, 133.70, 135.94, 146.30. MS (*m*/*z*) calcd for **1**: 452.5409, found 452.1753.

Synthesis of 4-(1-(3,4-dihydroxyphenyl)-2,2-diphenylvinyl)benzene-1,2-diol (3)

To a 50 mL round flask were added compound **2** (1 mmol, 453 mg) and 5 mL of anhydrous dichloromethane. Argon atmosphere was established and maintained. The mixture was cooled in liquid nitrogen/ethyl acetate bath (about −80 ℃) and boron tribromide (0.42 mL, 4.4 mmol) was added through a septum with use of a syringe. Then, the cold bath was removed and the mixture was stirred for 30 min, poured into ice water, stirred for another 30 min, saturated with salt, and extracted with dichloromethane. The extract was dried by anhydrous magnesium sulfate and concentrated. The yield of the final product was 95%. ^{1}H NMR (400 MHz, DMSO) δ: 7.19—7.00 (m, 6H), 6.98—6.84 (m, 4H), 6.52—6.28 (m, 4H), 6.26—6.13 (m, 2H); ^{13}C NMR (100 MHz, DMSO) δ: 116.38, 118.64, 123.80, 126.50, 128.38, 132.26, 136.39, 145.26. MS (m/z): calcd for **3**: 396.4346, found 396.1356.

Results and Discussion

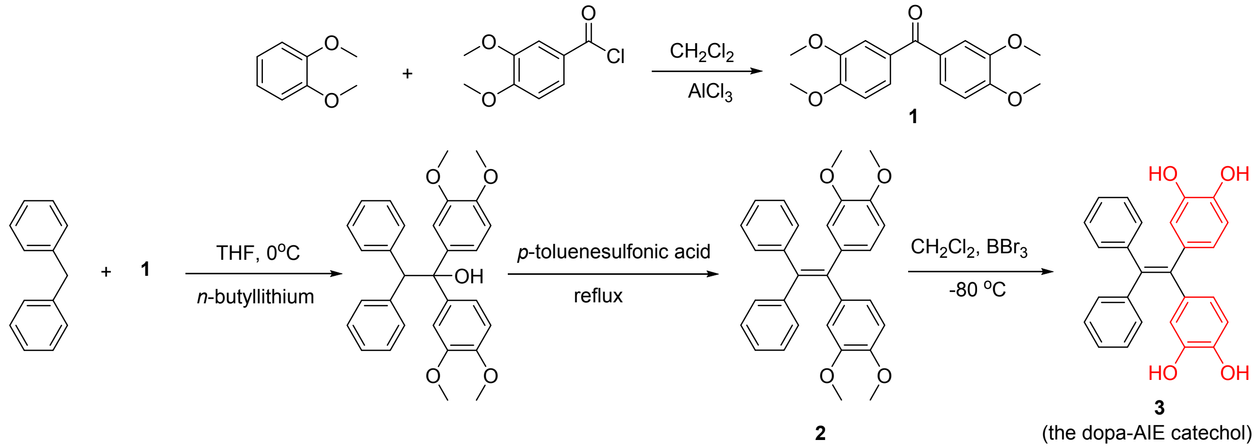
The synthetic routes of the catechol are shown in Scheme 1. Compound **1** was synthesized according to the literature[30] and verified by ^{1}H NMR, ^{13}C NMR and MS. Tetraarylethylene, the compound **2**, was synthesized by a modified two-step reaction method reported before.[31] By using a standard boron tribromide cleavage method, the designed dopa-AIE catechol, compound **3**, was obtained by ether cleavage from compound **2**.

Traditionally, most fluorescence compounds have the properties of the so-called "aggregation-caused quenching (ACQ)" of light emission in the aggregated state because of the severe intermolecular interaction.[20,21] The aggregation-induced emission (AIE) molecules, on the other hand, are usually non-emissive in dilute solutions, but they show strong light emission in their aggregated state.[32,33,34] The molecular structure we synthesized in this article can be divided into two motifs: tetraphenylethene (the AIE core) and pyrocatechols (the dopa motif). Through investigation of the compound's florescent curves in THF/water mixture solution, we found that the new compound has a typical AIE property (Figure 1). By introduction of catechols into tetraphenylethene, the compound still shows good AIE property.

As for the structure of this compound, from another angle, we can say that tetraphenylethene is attached to two pyrocatechols. It is well known that many catechol compounds have excellent coating performance like dopa.[7] So we tested the film-forming property of this new kind of catechol. The synthesized compound (10 mg) was dissolved into a mixture solution of 1 mL of dimethyl sulfoxide and 9 mL of tris(hydroxymethyl) aminomethane hydrochloride buffer with Mg^{2+}inside. Then the cleaned glass substrate was put in and the solution was kept shaking for 24h for film-coating on a shaking table. The color of the glass substrate changed from colorless to pink/red, and the modified glass substrates could glow under ultraviolet light. These indicated that these glass substrates were coated successfully by this compound (Figure 2). Another interesting phenomenon is that when the compound's suspension (in water) was put aside overnight, on the glass wall there would leave a uniform fluorescent coating (Figure 3). The formed coating is very stable. We have tried to use water, ethanol, acetone, dichloromethane and tetrahydrofuran to clean the bottles, even aided by ultrasound; however, the fluorescence coating has no apparent change. As a comparison, under the same conditions, we investigated the film-coating property of compound **2**. There is no fluorescence coating inside the bottle at all after clean by water. Therefore, we speculate that the two pyrocatechols are very vital for the film-forming property, just like dopa. In other words, catechol groups may keep its film-coating property when they are connected to some other organic compounds. Because of this, we could design and synthesize new functional catechol-compounds with good film-coating property.

Nevertheless, the compound we synthesized here with both AIE and filming forming property is not beyond our expectation. Much to our surprise is that the compound has a unique fluorescence detection response to Cu^{2+} in THF/water solution (under similar conditions, we have investigated many other ions such as Ca^{2+}, Mg^{2+}, Zn^{2+}, Co^{2+}, Ni^{2+}, Hg^{2+}, Mn^{2+}, $Fe^{2+}$and Fe^{3+}).

Scheme 1 Synthetic routes for the dopa-AIE catechol



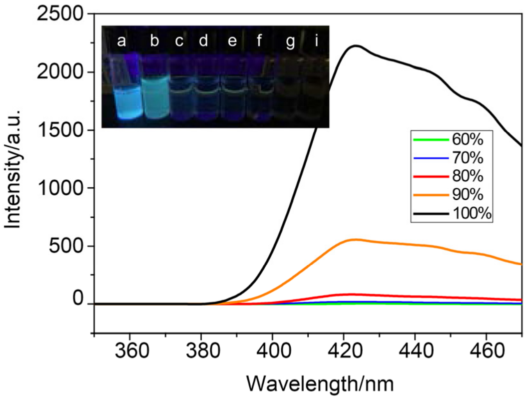
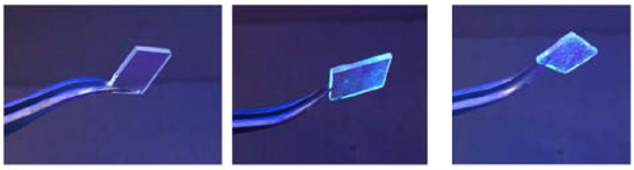
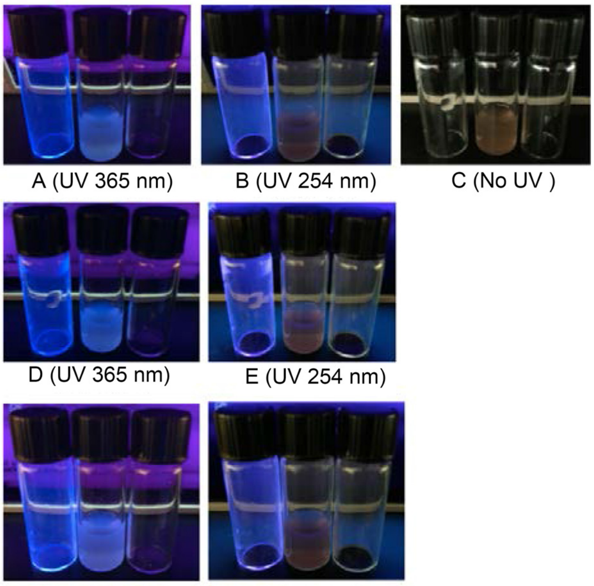


Figure 1 PL spectra of the catechol (**3**) in THF/water mixtures with different water fractions. By increasing the water fractions in the mixture, the intensity of the fluorescence is increased. The inset picture is the catechol solution (or suspension) under 365 nm UV irradiation in different THF/water mixture from 30% to 100% content of water (from e to a). The curves of i to e are similar to curve e.



Unmodified Modified (UV 365 nm) Modified (UV 365 nm)

Figure 2 The glass substrates were coated by the catechol in buffer. After thoroughly cleaning by pure water, the modified glass substrates cast a blue-green glow under UV light.



A (UV 365 nm) B (UV 254 nm) C (No UV)

D (UV 365 nm) E (UV 254 nm)

F (UV 365 nm) G (UV 254 nm)

Figure 3 The catechol could form a uniform coating on glass bottle. In each photo, there are three bottles, the right one was a new empty bottle, and the left one was filled with the compound's suspension overnight at the beginning. As a comparison, some of the suspensions were transferred from the left to the middle one. (A, B, C) The left bottle was washed by water assisted with ultrasound; (D, E) After ultrasonic washing by using ethanol and acetone for 5 min respectively; (F, G) After ultrasonic washing by using THF for 10 min.

Due to the amphiphilic structure, the catechol has poor solubility in pure water. The fluorescence detection experiments were carried out in the mixture of THF/water (6∶4, *V*∶*V*). In a cuvette containing 2.5 mL of the catechol solution (0.5 mg/mL), 5 μL of $CuCl_2$ solution (20 mg/mL) were added successively. The fluorescence spectra were recorded immediately after each addition and well mixing (Figures 4a and 4b). At the beginning, the total amount of catechol in the cuvette is 3.153 μmol and the amount of Cu^{2+} in each 5 μL solution is 0.744 μmol. The molar ratio of pyrocatechol in the catechol to Cu^{2+} is just 2∶1 after successive addition of $CuCl_2$ solution 4.2 times (5 μL for each addition). The changes can be clearly seen from its fluorescence spectra. The fluorescence intensity increases along with the copper ions addition. The fluorescence intensity reaches the maximum value at the fifth addition of $CuCl_2$ (Figure 4a). In the meantime, the ratio of pyrocatechol (two such groups in one catechol molecular) in the compound to Cu^{2+} is approximately 2∶1 (the ratio just for 2∶1 when adding 4.2 times of $CuCl_2$). Since then, the fluorescence intensity decreases with further addition of $CuCl_2$ (Figure 4b). Therefore, we speculate that the catechol and Cu^{2+} interact in some way with the molar ratio of one to one since there are two pyrocatechols in this one catechol compound. Fluorescence intensity increased and decreased linearly with copper ion concentration (Figure 4c). To make full use of this advantage, in theory, we can figure out the exact concentration of copper by measuring two or three different concentration of catechol solution, and vice versa. In addition, by graphing the wavelength at maximum fluorescence intensity against the addition number of copper ions, we found that there is a blue shift, from 412 nm to 402 nm, existing in these fluorescence spectra along with the addition of copper ions (Figure 4d). It indicates that the energy level structure of the catechol (or the formed complex with copper) may have been changed because of the copper ions. Besides, in the compound's solution, about 2 or 3 h after the addition of copper ions, the color of the solution would change from colorless to brown, and then formed dark precipitation overnight. We separated the precipitation and found that the structure had not changed as verified by ^{1}H NMR and mass spectrometer, with the same peaks as the original compound. We speculate that when copper ions were added to the catechol solution, they would form an unstable network structure, rather than a stable complex.

To investigate the oxidation states of copper after addition to the catechol solution, we measured its XPS spectrum (Figure 5). The result indicates that some of the Cu^{2+} ions are reduced into Cu^{+}. The peak around 955.8 eV is obviously asymmetric, indicating that there

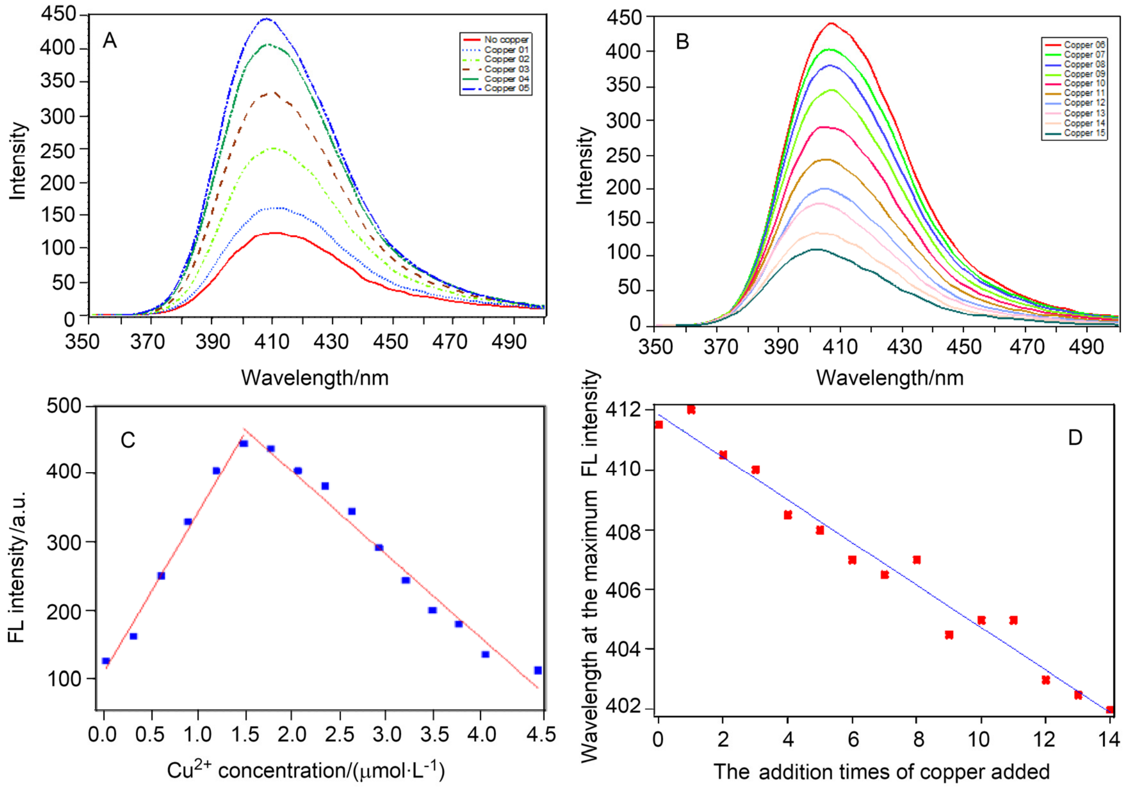


Figure 4 The fluorescence intensity of the compound in THF/water (6∶4 *V*/*V*) was changed by addition of $CuCl_2$ solution. In the cuvette there are 2.5 mL of the catechol with the concentration at 0.5 mg/mL, and 5 μL of $CuCl_2$ solution (20 mg/mL) were added successively to the cuvette. So, the molar ratio of pyrocatechol in the catechol to Cu^{2+} is 2∶1 after successive addition of $CuCl_2$ solution 4.2 times. (A) The fluorescence intensity changes with the first 5 times addition of $CuCl_2$; (B) The fluorescence intensity changes with the following next 10 times addition of $CuCl_2$; (C) The maximum value of the fluorescence intensity changes along with the concentration of Cu^{2+}. (D) The wavelength at the maximum value of the fluorescence intensity changes along with the addition times of copper.

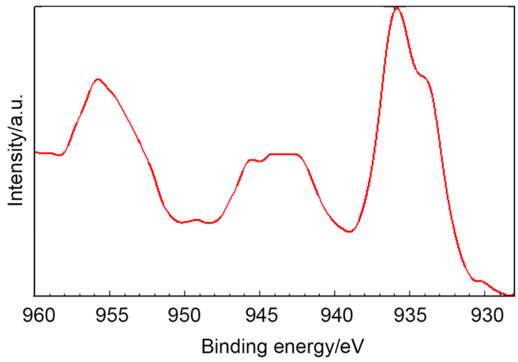


Figure 5 The Cu 2p scan spectrum of the mixture of the catechol and $CuCl_2$. The powdered sample was prepared as follows: The catechol was dissolved in THF, and an equal amount of $CuCl_2$ was added; subsequently, the solvent was evaporated after the mixture was stirred for 30 min.

are at least two different valences of copper ions in the mixture. Thus, the peak at 933.8 eV could be attributed to Cu^{+} and the peak at 935.8 eV could be attributed to Cu^{2+}. Probably this change may have some relationship with the blue shift in Figure 4d. It is well known that many compounds with catechol structures can form complexes by complexation with metal ions. For the as-synthesized compound, due to its special detection of Cu^{2+}, we believe that the compound not only forms complexes with the copper ion, more importantly, a certain degree of redox reactions may also occur between copper and the catechol. Usually, redox reactions occur depending on the potentials of the two matches. Too much difference between them will lead to irreversible oxidation and/or reduction; while for too small difference, there may not be a redox reaction. The calculated HOMO-LUMO gap of the catechol is −0.139 eV. It might be due to the suitable change from Cu^{2+} to Cu^{+} (+0.159 eV) for the catechol to cause the fluorescence intensity change. And this redox process may be occurring inside the complex without destroying the catechol structure. Maybe this is the reason that we cannot tell the structural difference of the catechol with/without copper by ^{1}H NMR and MS.

Conclusions

In summary, a new kind of catechol, dopa-AIE compound, has been synthesized and investigated. From the structural point of view, the as-synthesized compound simultaneously has two functional group units, AIE moiety as the core and dopa as the side group. Both of them can reflect their own characteristics independently. That is, it not only has the similar characteristics of AIE compounds, but also has similar adhesion properties to dopa. Most importantly, the combination of AIE core and dopa results in some new features for the new catechol, showing the synergistic effect. The new catechol has a unique fluorescence detection response to Cu(II) in solution, and the response is quantitative. The fluorescence intensity has the maximum value when the molar ratio of the catechol to copper is 1∶1. Before and after this point, the fluorescence intensity has a linear relationship with the copper ion concentration. This result can help us design and fabricate Cu(II) sensor, particularly for Cu(II) bio-sensor because of the paramagnetism of Cu(II).

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References

[1] Waite, J. H.; Tanzer, M. L. *Science* **1981**, *212*, 1038.
[2] Papov, V. V.; Diamond, T. V.; Biemann, K.; Waite, J. H. *J. Biol. Chem.* **1995**, *270*, 20183.
[3] Waite, J. H.; Qin, X. X. *Biochemistry* **2001**, *40*, 2887.
[4] Lee, H.; Lee, B. P.; Messersmith, P. B. *Nature* **2007**, *448*, 338.
[5] Westwood, G.; Horton, T. N.; Wilker, J. J. *Macromolecules* **2007**, *40*, 3960.
[6] Wu, F. X.; Jun, L. L.; Messersmith, P. B. *Biomacromolecules* **2006**, *7*, 2443.
[7] Sileika, T. S.; Barrett, D. G.; Zhang, R.; Lau, K. H. A.; Messersmith, P. B. *Angew. Chem.* **2013**, *125*, 10966.
[8] Ham, H. O.; Park, S. H.; Kurutz, J. W.; Szleifer, I. G.; Messersmith, P. B. *J. Am. Chem. Soc.* **2013**, *135*, 13015.
[9] Black, K. C.; Sileika, T. S.; Yi, J.; Zhang, R.; Rivera, J. G.; Messersmith, P. B. *Small* **2014**, *10*, 169.
[10] Sedo, J.; Saiz-Poseu, J.; Busque, F.; Ruiz-Molina, D. *Adv. Mater.* **2013**, *25*, 65.
[11] Faure, E.; Falentin-Daudre, C.; Jerome, C.; Lyskawa, J.; Fournier, D.; Woisel, P.; Detrembleur, C. *Prog. Polym. Sci.* **2013**, *38*, 236.
[12] Barrett, D. G.; Fullenkamp, D. E.; Lihong, H.; Andersen, N. H.; Lee, K. Y. C.; Messersmith, P. B. *Adv. Funct. Mater.* **2013**, *23*, 1111.
[13] Andersen, N. H.; Jaishankar, A.; Harrington, M. J.; Fullenkamp, D. E.; DiMarco, G.; Lihong, H.; McKinley, G. H.; Messersmith, P. B.; Lee, K. Y. C. *J. Mater. Chem. B* **2014**, *2*, 2467.
[14] Fullenkamp, D. E.; Barrett, D. G.; Miller, D. R.; Kurutz, J. W.; Messersmith, P. B. *RSC Adv.* **2014**, *4*, 25127.
[15] Lee, H.; Dellatore, S. M.; Miller, W. M.; Messersmith, P. B. *Science* **2007**, *318*, 426.
[16] Li, G.; Chen, L. C.; Chen, M. M.; Gao, B.; Xiong, X. L. *Chem. J. Chin. Univ.* **2013**, *34*, 2493.
[17] Dwivedi, A. K.; Pandeeswar, M.; Govindaraju, T. *ACS Appl. Mater. Interfaces* **2014**, *6*, 21369.
[18] Narayanan, K. B.; Park, H. H. *Spectrochim. Acta*, *Part A* **2014**, *131*, 132.
[19] Shi, B. F.; Zhang, L. L.; Lan, C. Q.; Zhao, J. J.; Su, Y. B.; Zhao, S. L. *Talanta* **2015**, *142*, 131.
[20] Saragi, T. P. I.; Spehr, T.; Siebert, A.; Fuhrmann, L. T.; Salbeck, J. *Chem. Rev.* **2007**, *107*, 1011.
[21] Grimsdale, A. C.; Chan, K. L.; Martin, R. E.; Jokisz, P. G.; Holmes, A. B. *Chem. Rev.* **2009**, *109*, 897.
[22] Luo, J. D.; Xie, Z. L.; Lam, J. W. Y.; Cheng, L.; Tang, B. Z.; Chen, H. Y.; Qiu, C. F.; Kwok, H. S.; Zhan, X. W.; Liu, Y. Q.; Zhu, D. B. *Chem. Commun.* **2001**, 174.
[23] Viguier, R. F. H.; Hulme, A. N. A. *J. Am. Chem. Soc.* **2006**, *128*, 11370.
[24] Georgopoulos, P. G.; Roy, A.; Yonone-Lioy, M. J.; Opiekun, R. E.; Lioy, P. J. *J. Toxicol. Environ. Health B* **2001**, *4*, 341.
[25] Geng, J.; Li, M.; Wu, L.; Ren, J. S.; Qu, X. G. *J. Med. Chem.* **2012**, *55*, 9146.
[26] Barnham, K. J.; Masters, C. L.; Bush, A. I. *Nat. Rev. Drug Discovery* **2004**, *3*, 205.
[27] Viquier, R. F.; Hulme, A. N. *J. Am. Chem. Soc.* **2006**, *128*, 11370.
[28] Zhou, H.; Ye, Q.; Wu, X. Y.; Song, J.; Cho, C. M.; Zong, Y.; Tang, B. Z.; Hor, T. S. A.; Yeow, E. K. L.; Xu, J. W. *J. Mater. Chem. C* **2015**, *3*, 11874.
[29] Zhang, S.; Yan, J. M.; Qin, A. J.; Sun, J. Z.; Tang, B. Z. *Chinese Chem. Lett.* **2013**, *24*, 668.
[30] Silvestri, M. A.; Naqarajan, M.; De Clercq, E.; Pannecouque, C.; Cushman, M. *J. Med. Chem.* **2004**, *47*, 3149.
[31] Banerjee, M.; Emond, S. J.; Lindeman, S. V.; Rathore, R. *J. Org. Chem.* **2007**, *72*, 8054.
[32] Chi, Z. G.; Zhang, X. Q.; Xu, B. J.; Zhou, X.; Ma, C. P.; Zhang, Y.; Liu, S. W.; Xu, J. R. *Chem. Soc. Rev.* **2012**, *41*, 3878.
[33] Zhang, G. F.; Chen, T.; Chen, Z. Q.; Aldred, M. P.; Meng, X. G.; Zhu, M. Q. *Chin. J. Chem.* **2015**, *33*, 939.
[34] Zhang, Y. H.; Kong, L. W.; Shi, J. B.; Tong, B.; Zhi, J. G.; Feng, X.; Dong, Y. P. *Chin. J. Chem.* **2015**, *33*, 701.

(Lu, Y.)